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# Valuing potential cures:

An examination of ICER's approach to assessing high-impact single and short-term therapies

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## Key takeaways

Cell and gene therapies, single-administration medicines with durable, potentially curative effects, hold the promise to revolutionize healthcare, introducing groundbreaking advancements for patients with diseases that were previously thought incurable. Recognizing and rewarding the value of cures is critically important for patients. Failure to do so could endanger meaningful access to these innovative therapies and undermine incentives for the development of future transformational medicines.

However, many conventional methods of health technology assessment (HTA) are rooted in 20th century models and medical science and are thus not well-suited to emerging transformative therapies. Recognizing this challenge, the Institute for Clinical and Economic Review (ICER) took the commendable step of seeking to update its basic cost-effectiveness framework for assessing single and short-term therapies (SSTs). We examined the methodology and application of ICER's SST framework to determine the degree to which it addresses shortcomings in ICER's traditional value assessment framework, and found limitations and concerns in both areas:

### **Methodology: ICER's SST framework lacks scientific rigor and does not reflect important considerations raised by diverse stakeholders**

- ICER's shared savings approach reflects a policy bias that undermines the scientific objectivity and credibility of its framework and could disincentivize the development and use of curative treatments
- ICER's approach does not ensure the use of a societal perspective or meaningfully incorporate patient-centered elements of value
- ICER's methodological approach relies heavily on traditional cost-effectiveness methods and does not account for the unique considerations of SSTs, which may lead to inappropriate value assessments of transformative therapies

### **Application: Inconsistency in ICER's application of its SST framework undermines its credibility**

- ICER disregarded its stated process and updated the SST framework without transparency or public discourse
- Despite lacking a sound scientific rationale, ICER's shared savings scenarios are no longer exploratory, having become the determinants of pricing benchmarks and the focal point of ICER's report-at-a-glance summaries in several reviews
- ICER is progressively conducting more extreme scenario analyses
- ICER's inclusion of the societal perspective and patient-centered value elements in SST reviews is very limited

ICER is not adhering to commitments outlined in its SST framework and is employing untested methodologies that lack empirical evidence or scientific justification; its SST processes lack the transparency and stakeholder engagement that ICER heralds as a bedrock of its methods. Delivering on the promise of SSTs requires rigorous value assessment methods that are fit for purpose. Moreover, SSTs and similar transformative medicines pose particular challenges for traditional cost-effectiveness models and a more fundamental rethinking of value assessment and its application to decision-making is needed.

In pursuing better value assessment and HTA methods, we owe it to patients to take a "first do no harm" approach. Like any HTA, ICER's value assessments are a tool, not a rule, and should not be considered the benchmark for determining value in the United States (U.S.). The needs of patients are best served with comprehensive value assessment using appropriate methodologies. ICER's SST framework methodology and application need to improve and evolve in a transparent and evidence-based manner, guided by multi-stakeholder input.



## Background and methodology

In 2017, the U.S. Food and Drug Administration (FDA) approved the first gene therapy for use in the U.S., paving the way for groundbreaking innovation in treating serious and life-threatening diseases.<sup>1</sup> Today, nearly 500 cell and gene therapies are in development, demonstrating the magnitude of the industry investment in creating transformational treatments.<sup>2</sup>

Given the promising pipeline of new therapies with curative potential, it is critically important that the U.S. health system recognize and reward the full value of these transformational medicines. Doing so is essential for providing meaningful access to cures for today's patients and preserving incentives for future research and development to bring cures to tomorrow's patients.

Innovative curative treatments require equally innovative methods of value assessment that account for the unique considerations associated with these novel therapies. In August 2019, ICER proposed adapted value assessment methods for high-impact SSTs to guide its assessments of emerging SSTs (draft SST framework).<sup>3</sup>

**Single and short-term therapies (SSTs):** Therapies that are delivered through a single intervention or a short-term course (less than one year) of treatment that offer a significant potential for substantial and sustained health benefits extending throughout patients' lifetimes

ICER's draft SST framework was met with a strong response from a wide variety of stakeholders, including academics, patient advocacy organizations, payers, industry, and trade groups.<sup>4</sup> In September 2019, 38 organizations submitted public comments on ICER's draft SST framework, many critiquing the lack of rigor, utility, and patient-centeredness in ICER's proposed approach.

Stakeholder comments provided insightful input for ICER's November 2019 SST "final adaptations" framework (SST framework).<sup>5</sup> However, many stakeholder concerns were not addressed, including the use of arbitrary shared savings price caps, inadequate inclusion of broader value elements and the societal perspective, and the lack of inclusion of alternative discount rate scenarios. In December 2022, ICER quietly posted an update to the SST framework for which there had been no public discourse or visibility (updated SST framework).<sup>6</sup>

To better understand ICER's SST framework and its application in ICER's value assessment reviews, we conducted a thorough evaluation of the SST framework methodology and the completed ICER evidence reviews in which it had been applied as of June 30, 2023: hemophilia A (2020), beta thalassemia (2022), and hemophilia A and B (2022).<sup>7-9</sup> We also reviewed public comments to identify areas of stakeholder concern and conducted a targeted scan of the literature to identify evolving perspectives on ICER's approach and opportunities to improve SST assessment.

## Results

### ICER's SST framework lacks scientific rigor and does not reflect important considerations raised by diverse stakeholders

A thorough examination of ICER's SST framework reveals numerous limitations related to ICER's methodological approach and processes for assessing SSTs.

#### *ICER's shared savings approach reflects a policy bias that undermines the scientific objectivity and credibility of its framework and could disincentivize the development and use of cures*

ICER's SST framework introduced new and untested elements into its methods for assessing transformative medicines that prioritize cost containment and "fair sharing of economic surplus" over objective and rigorous HTA. Specifically, the SST framework included two "hypothetical" scenarios for "sharing" a treatment's cost offsets with "the health system" by excluding a portion of the treatment's cost offsets from the cost-effectiveness analysis (CEA):

**50/50 shared savings scenario:** 50% of cost offsets are awarded to the treatment and 50% are excluded from the CEA

**Cost-offset cap scenario:** Cost offsets awarded to the treatment are capped at \$150,000 per year, and the remainder is excluded from the CEA

Overall, the arbitrary nature of ICER's designated cost-offset cap and shared savings allocations lack methodological rigor and scientific justification. Recognizing the risk associated with ICER conducting methodologically unsupported analyses (even as a tool to stimulate policy conversation), numerous stakeholders raised concerns regarding the application of ICER's shared savings scenarios. Despite this input, ICER formalized its shared savings approach in its final SST framework.

ICER makes multiple assertions to justify the use of its shared savings scenarios, which are not supported by empirical evidence or grounded in real-world experience, and which reflect a departure beyond objective assessment of value and into subjective policy choices.<sup>10</sup>



#### ICER's Claim:

ICER asserts that using traditional CEA to assess SSTs that treat conditions with an expensive standard of care (eg, hemophilia) will reinforce existing price distortions and perpetuate pricing inefficiencies for future therapy generations. ICER seeks to account for these potential pricing distortions by capping cost offsets, such as applying a \$150K per year cap.



#### The Facts:

ICER's scientific reasoning and methodological approach are not supported by empirical evidence. ICER recognizes that the estimate is not reflective of actual disease-related cost offsets and arbitrarily selected the \$150K cap on cost offsets because it aligns with the top of ICER's designated value-based price threshold. In fact, ICER acknowledges the introduction of SSTs may often result in real-world cost offsets that far exceed \$150K per year. In such cases, ICER's application of its cost-offset cap will result in value-based price determinations that are artificially low and do not reflect the full value of the assessed treatments. This presents an interesting paradox: ICER introduced the cost-offset cap to prevent perpetual price distortions fueled by expensive standards of care. But in doing so, it may, in fact, perpetuate the use of inefficient and expensive standards of care because it underestimates the value of transformative therapies.



### ICER's Claim:

ICER cites concerns that the potential magnitude of health gains and cost offsets associated with SSTs would allocate too much of the economic surplus to innovators and result in unaffordable treatments if traditional cost-effectiveness methods are used.



### The Facts:

This concern has not been validated by empirical research. An analysis of consumer and producer surpluses for pharmaceuticals and other healthcare interventions between 1997 and 2017 found that innovators captured only a small portion of the surplus generated by innovative treatments.<sup>11</sup>



### ICER's Claim:

ICER asserts that many SSTs, particularly cell and gene therapies, may never face generic competition equivalent to that of traditional therapies, which will shift the long-term balance of economic surplus toward innovators.



### The Facts:

As the first gene therapy approval in the U.S. was in 2017, the extent of potential generic competition is undetermined and ICER's assertion is not based upon evidence. Further, ICER fails to account for all forms of market competition. Products on patent are still subject to competitive pressure from other market entrants, as was previously demonstrated in the hepatitis C therapeutic space when the entrance of numerous brand competitors stimulated a substantial fall in net prices. Moreover, the significant pipeline of cell and gene therapies across disease areas indicates that SSTs will be subject to robust competition, with researchers estimating approximately 50 to 75 U.S. market approvals by 2030.<sup>12</sup> There is also significant competition within disease areas, as demonstrated by the product pipeline for multiple myeloma which includes over 20 cell and gene therapies currently in phase 1 to phase 3 clinical trial development,<sup>13</sup> as well as the fact that there are numerous approvals for chimeric antigen receptor T-cell (CAR-T) therapies for overlapping indications in the U.S. Additionally, because many of the genetic deficiencies and mutations targeted by emerging cell and gene therapies are a matter of public record, SSTs may, in fact, face more robust in-class competition as demonstrated in a recent example of approved CAR-T therapies facing competition from other emerging CAR-T products.<sup>14</sup>

A thorough examination of ICER's claims reveals the subjective nature of its shared savings approach and underscores the methodological limitations associated with their application. ICER's concerns that SSTs will not be subject to competition or that too much economic surplus will be allocated to innovators are both speculative and irrational, as they are not supported by empirical evidence and disregard core health economics principles. Theoretically, the health system and broader policy environment should reward and encourage innovative treatments that yield substantial cost offsets and displace inefficient standards of care.

However, ICER's shared savings approach may do the opposite, as it applies punitive and arbitrary cost-offset caps on assessed SST interventions that treat conditions with "distorted," high-cost standards of care. A more appropriate approach to value assessment would be to conduct HTAs for existing treatments, broadening assessments beyond just pharmaceutical interventions, to objectively identify sources of low-value care. Prioritizing subjective cost containment over objective value assessment for transformative therapies may result in relative underestimations of value, which holds important implications for the delivery of effective and efficient patient-centered care and for the future research and development of innovative treatments.

These points were echoed by multiple organizations in their public comments, with many recommending that ICER remove its shared savings scenarios from the final SST framework.

**We are concerned that potential impact on innovation is not sufficiently considered, which could have significant implications for patients and the potential for having future 'choice among treatments with a different balance and timing of risks and benefits.'**

**...[W]e believe inclusion of a discussion on fair sharing of economic surplus in ICER value assessment reports is premature and recommend ICER not include the analyses or this section at this time.**

– The National Health Council (2019)

Additionally, numerous stakeholders were concerned about how the implementation of shared savings scenarios may impact future research and development of transformational medicines.

**There are likely to be unintended consequences of dis-incentivizing curative therapies in favor of chronic therapies by encouraging pricing to long-term 'shared savings' at the outset.**

– Alliance for Regenerative Medicine (2019)

Despite strong stakeholder opposition, ICER formalized its shared savings approach in its SST framework.

### *ICER's approach does not ensure the use of a societal perspective or meaningfully incorporate patient-centered elements of value*

When reviewing traditional pharmaceutical interventions, ICER calculates the incremental cost-effectiveness of assessed treatments using the healthcare perspective as the base case and often only provides the societal perspective in a scenario analysis. This approach conflicts with widely cited recommendations from the Second Panel on Cost-Effectiveness in Health and Medicine, which specify that reference case analyses should report CEA results from a societal perspective in addition to a healthcare perspective.<sup>15</sup>

Using the societal perspective to assess the incremental cost-effectiveness of SSTs is even more important given their potential to deliver groundbreaking advancements in patient health outcomes and replace expensive and less effective standards of care. The societal perspective provides a more representative assessment of the value of SSTs, as it captures the overall cost impacts and public benefit generated by transformational medicines by accounting for surplus resources that could be used for other purposes in non-healthcare sectors.<sup>16</sup> Moreover, the societal perspective is superior to the healthcare perspective in capturing outcomes important to the patient community including productivity and quality of life for patients and caregivers, insurance value, and spillover effects.

In alignment with the Second Panel on Cost-Effectiveness, there was broad stakeholder agreement that ICER should use a societal perspective as the base case when assessing SSTs. Despite this agreement, ICER did not commit to using a societal perspective as a base case in its SST framework. However, when a treatment is deemed to be an SST for an ultra-rare disease, ICER committed to applying both its SST framework and its methods adaptations for ultra-rare diseases, which presents a health benefit price benchmark (HBPB) linked to the societal perspective alongside the standard HBPB.<sup>17</sup>

Additionally, stakeholders including the Center for Evaluation of Value and Risk in Health (CEVR), the Professional Society for Health Economics and Outcomes Research (ISPOR), the Muscular Dystrophy Association, the Partnership to Fight Chronic Disease, the National Health Council, as well as several pharmaceutical companies criticized ICER's approach to incorporating broader elements of value. They questioned why certain elements, such as productivity, caregiver burden, insurance value, value of hope, as well as several other factors, were not incorporated quantitatively given a growing body of literature supporting such analyses. Excluding these elements prevents the full potential benefit of curative therapies from being recognized.

**Finally, curative and transformative treatments can have a very significant impact on the family of the patients in terms of productivity and quality of life. Since ICER is very interested in the societal and health system impact of SST, and in keeping with the recommendations of the Second Panel, we encourage further consideration of these broader societal elements of value and their impact to the health system and society.**

**Ignoring several potential 'novel' elements of value related to uncertainty could seriously bias the assessment of some technologies—and particularly in the case of health-catastrophic ultra-orphan conditions.**

– ISPOR (2019)

**Including a societal perspective of value would provide a more holistic understanding of the persons most closely associated with the treatment under review, with important factors such as functional ability, productivity, caregiver support, and quality of life taken fully into account. We recommend including a societal perspective on value as an additional base case for SSTs.**

– Partnership to Fight Chronic Disease (2019)

*ICER's methodological approach relies heavily on traditional cost-effectiveness methods and does not account for the unique considerations of SSTs, which may lead to inappropriate value assessments of transformative therapies*

ICER's SST framework largely aligns with the methodological approach outlined in ICER's traditional value assessment framework, borrowing key components including the discounting assumption and designated cost-effectiveness thresholds. In doing so, ICER limits its ability to account for the unique characteristics and value attributes associated with transformational cell and gene therapies.

For example, ICER's SST framework applies a 3% discounting rate to both health outcomes and costs. However, the unique characteristics of SSTs and the novel benefits associated with these treatments suggest that additional scenario analyses are needed. Notably, ICER's approach is out of step with other HTA organizations including the United Kingdom's National Institute for Health and Care Excellence (NICE), which considers differential discounting of healthcare costs and benefits when a therapy affords substantial health improvements over a long time horizon and the Joint Committee on Vaccination and Immunization, which uses a 3% discounting rate but often conducts sensitivity analyses using discount rates of 1.5% and 0%.<sup>18-20</sup>

Given that SSTs are potentially associated with exceptionally long-term benefits, application of an inaccurate discount rate could result in ICER substantially underestimating a product's value, which could have adverse impacts on access and incentives for innovation. Public comments from CEVR, ISPOR, and the National Bleeding Disorders Foundation (formerly the National Hemophilia Foundation) emphasized concerns about ICER's discounting rate assumptions. However, despite numerous comments encouraging ICER to include sensitivity analyses or otherwise adjust its discounting assumption, ICER made no changes to its final framework.

**We understand and endorse the 3% standard for discount rates. However, given ICER's propensity to consider sensitivity analyses for many other factors, we are not sure it's consistent to rule out sensitivity analysis on the discount rate used for these therapies, especially when over a lifetime it can make quite a difference (eg, a fully healthy 75 years of life expectancy becomes 30.6 years at a 3% discount rate, but is 39.5 years at 2% and 24.6 years at 4%).**

– ISPOR (2019)

**In many situations (eg, life-saving therapies for young children, therapies that significantly halt or slow functional decline) it may be worth exploring how sensitive model results are to changes in the discount rate.**

– CEVR (2019)

Furthermore, numerous organizations also expressed concern about the inappropriateness of ICER's use of a \$150K/quality-adjusted life-year (QALY) threshold, citing that such a low threshold is not representative of typical practice when assessing SSTs. For example, NICE uses much higher cost-effectiveness thresholds for highly specialized technologies that treat ultra-rare conditions than it does for conventional treatments to reflect the high cost of developing treatments for rare disease populations.<sup>21,22</sup>

Additionally, ICER's SST approach makes only minor modifications to its existing value assessment framework and does not promote alternative, non-traditional approaches to value assessment such as multi-criteria decision analysis (MCDA). Numerous stakeholder comments suggested that ICER incorporate methods beyond CEA (like MCDA) to allow for more comprehensive, transparent, and fit-for-purpose assessments of SSTs.

Despite considerable cross-stakeholder alignment on key components of the framework including concerns about the shared savings scenarios, the discounting assumption, and ICER's narrow inclusion of novel value elements, ICER's final framework incorporated minimal revisions in these areas.

### Inconsistency in ICER's application of its SST framework undermines its credibility

We examined three complete ICER reviews of SSTs, including hemophilia A (2020), beta thalassemia (2022), and hemophilia A and B (2022). Our analysis reveals that since the publication of its SST framework in November 2019, ICER has failed to keep many of its commitments and has made numerous adjustments to its methods and processes for evaluating SSTs (**Table 1**). Many of these adjustments have been made without transparency, public discourse, or scientific justification, and they have significant implications for assessment results and public framing.

**Table 1.** ICER's SST framework commitment vs real-world implementation

ICER's SST framework commitment	ICER's real-world implementation
<b>Future SST updates</b> will occur simultaneously with updates to ICER's standard framework	<ul style="list-style-type: none"> <li>The SST framework was updated in isolation without transparency or public discourse</li> <li>The update was posted without a public announcement</li> </ul>
<b>Shared savings scenarios</b> will only be exploratory and will not be used to determine value-based prices	<ul style="list-style-type: none"> <li>Scenarios are used to estimate price benchmarks</li> <li>Scenarios have become the focal point of ICER's report-at-a-glance summaries</li> <li>ICER may be laying the groundwork for more extreme scenarios and price caps in the future</li> </ul>
<b>The societal perspective</b> will be included as a co-base case when assessed SST interventions target ultra-rare diseases	<ul style="list-style-type: none"> <li>In the hemophilia reviews, the societal perspective is relegated to a scenario analysis with incomplete results</li> </ul>
<b>Three additional value domains</b> will be incorporated in reviews under both SST and standards frameworks	<ul style="list-style-type: none"> <li>ICER inconsistently includes these and other value elements in its reviews</li> </ul>

Key: ICER – Institute for Clinical and Economic Review; SST – single and short-term therapy.



## ICER disregarded its stated process and updated the SST framework without transparency or public discourse

On December 21, 2022, the day before the Hemophilia A & B Final Report was published, ICER silently posted an updated SST framework, without its usual press release and public fanfare. The update deviated from ICER's stated process for updating its framework methods, which includes public visibility into the update and the opportunity to provide stakeholder input. The updated SST framework recontextualized the purpose of ICER's shared savings scenarios, created new selection criteria for identifying the most "policy relevant" scenario for calculating the HBPB, and paved the way for ICER to conduct new scenarios in the future.<sup>6</sup> Although ICER included a (single) hyperlink to the new methodology in the Hemophilia A & B Final Report, ICER did not publicly announce changes to its SST framework or seek stakeholder comments.<sup>8</sup>

ICER's updates to the SST framework raise concerns about credibility, transparency, and stakeholder engagement:

- Such updates do not adhere to ICER's stated process for modifying its SST framework. ICER's 2019 SST framework states, "In the future, updates to methods for high-impact SSTs will be performed simultaneously with the updates to the overall value assessment framework." ICER did not meet this commitment and instead silently updated its methods without announcement or public discourse.
- ICER's decision to circumvent its formal processes for updating its methods and processes undermines ICER's claims that its value assessments are transparent and informed by multi-stakeholder engagement.
- Revisions to the SST framework do not cite empirical evidence or provide scientific justification to support changes in shared savings methodology, despite these changes having consequential impact on ICER's assessments of treatment value. ICER's implementation of unsubstantiated methods calls into question the scientific rigor and credibility of its SST analyses.

## Despite lacking a sound scientific rationale, ICER's shared savings scenarios are no longer exploratory, having become the determinants of pricing benchmarks and the focal point of ICER's report-at-a-glance summaries in several reviews

In its original SST framework (November 2019), ICER stated that its shared savings scenarios threshold analyses "will be presented but will not be suggested as normative guides to pricing."<sup>4</sup> Furthermore, in a response to a stakeholder comment on the draft SST framework, ICER went as far as to explicitly state that the shared savings scenarios "will not be considered part of the base case or used to determine value-based prices."<sup>23</sup> However, in practice, ICER has quietly elevated the status of the initially "exploratory" shared savings analyses in multiple reviews, promoting them to the determinants of its HBPB, despite not having any empirical research to support their use.<sup>8,9</sup>

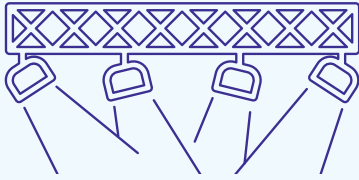
In all reviews, ICER's application of a shared savings scenario resulted in a substantially lower cost-effectiveness threshold price than the base case (**Table 2**). Despite ICER's initial assurance that its shared savings scenarios would be "exploratory," the cost-offset cap scenario was used to calculate ICER's HBPB in the 2022 hemophilia review and the 50/50 shared savings scenario was used in the beta thalassemia review. In both reviews, the shared savings analyses were the sole HBPB results included in the report-at-a-glance summary documents, with the standard base case results completely excluded.

**Table 2.** Price to achieve cost-effectiveness at \$150,000/QALY (healthcare system perspective) implementation

	Hemophilia A ROCTAVIAN (2020)	Hemophilia A ROCTAVIAN (2022)	Hemophilia B HEMGENIX (2022)	Beta thalassemia ZYNTEGLO (2022)
<b>Base case:</b> 100% of cost offsets awarded to treatment	\$7.5M	\$6.72M	\$994M	\$2.4M
<b>50/50 shared savings scenario:</b> 50% of cost offsets awarded to treatment	\$3.2M	\$3.47M	\$5.13M	\$1.6M
<b>Cost-offset cap scenario:</b> Cost offsets awarded to treatment capped at \$150K/year	\$1.6M	\$1.96M	\$2.96M	\$2.4M
<b>Extreme scenario:</b> 0% of cost offsets awarded to treatment	n/a	\$335,000	\$322,000	\$750,000 <sup>24</sup>
<b>ICER's recommended HBPB range</b> from report-at-a-glance	n/a (cost saving)	\$1.96M	\$2.93-\$2.96M	\$1.3-\$1.8M

Key: HBPB – health benefit price benchmark; ICER – Institute for Clinical and Economic Review; M – million; QALY – quality-adjusted life-year.

Emphasizing only the shared savings analyses highlights the more conservative HBPB while concealing the higher value-based price estimates from the base case, resulting in summary documents that lack sufficient context for the users of ICER's assessments. Given that some payers and other healthcare decision-makers may only review the summary documents associated with an ICER assessment, it is important that the shared savings results are appropriately contextualized alongside the base case, with the full range of cost-effective prices included.



## Spotlight on hemophilia

### The paradox of ICER's shared savings scenarios

- ICER applied the cost-offset cap shared savings scenario in its 2022 review of hemophilia A and B treatments, resulting in revised price benchmarks that discard more than 2/3 of the base case price benchmark
- By eliminating the vast majority of real-world cost offsets for hemophilia A and B, which far exceed \$150K/year, ICER's price benchmarks dramatically underestimate the value of the assessed treatments
- Paradoxically, such a dramatic underestimate of treatment value could result in the perpetuation of inefficient and expensive standard of care

### ICER is progressively conducting more extreme scenario analyses

ICER is also using its modified SST framework to justify conducting increasingly extreme scenario analyses in its evidence reports and authored commentaries. For example, in the Hemophilia A & B Final Report, ICER introduced a "no savings" scenario where cost offsets were set to 0. This scenario dramatically decreased the cost-effective threshold price, resulting in a 95% to 97% reduction in the estimated price for the assessed treatments (**Table 2**). Although this scenario was not included in the evidence report for beta thalassemia, ICER authors posited a similar scenario for beta thalassemia in a 2023 Health Affairs Forefront analysis.<sup>24</sup> These shared savings scenarios have limited to no scientific justification and the idea of setting cost offsets to zero is entirely impractical for informing ongoing policy discussions.

### ICER's inclusion of the societal perspective and patient-centered value elements in SST reviews is very limited

In public comments on ICER's SST framework (November 2019), numerous stakeholders emphasized the need for ICER to use the societal perspective when assessing SSTs. In response, ICER committed to including co-base cases from both healthcare and societal perspectives when assessed SST interventions involve ultra-rare diseases.<sup>17</sup> However, in the hemophilia reviews, the societal perspective is relegated to a scenario analysis with incomplete results, even in the appendices. ICER only included the societal perspective as a base case in the beta thalassemia review.

In response to a high volume of public comments on the need to incorporate novel value elements in assessments of SSTs, ICER identified three additional value domains in its SST framework that it would incorporate in reviews of all drugs, not just SSTs:

- A potential advantage for therapies that offer a new treatment choice with a different balance or timing of risks and benefits that may be valued by patients with different risk preferences
- A potential advantage for therapies that, if successful, offer the potential to increase access to future treatment that may be approved over patients' lifetime
- A potential disadvantage for therapies that, if not successful, could reduce or even preclude the potential effectiveness of future treatments

Despite this commitment, ICER inconsistently included these dimensions of value (labeled as "Option of receiving future treatments" and "Balance or timing of risks and benefits" in **Table 3**) in its assessments of SSTs and rarely included other novel value elements.

**Table 3.** Inclusion of qualitative value elements in SST reviews

Value element	Hemophilia A ROCTAVIAN (2020)	Hemophilia A ROCTAVIAN (2022)	Hemophilia B HEMGENIX (2022)	Beta thalassemia ZYNTEGLO (2022)
Caregiver quality of life	✓	✓	✓	✓
Complexity	✓	✓	✓	✓
Mechanism of action	✓	-	-	-
Productivity	✓	-	-	-
Health equities	✓	-	-	✓
Model uncertainty and assumptions	✓	-	-	-
Absolute QALY shortfall	✓	-	-	-
Option of receiving future treatments	✓	-	-	-
Balance or timing of risks and benefits	✓	-	-	✓
Proportional QALY shortfall	✓	-	-	-
Major life goals	-	✓	✓	✓
Acuity of need	-	✓	✓	✓
Lifetime impact	-	✓	✓	✓

Key: QALY – quality-adjusted life-year; SST – single and short-term therapy.

## Discussion

We analyzed stakeholder comments on ICER's draft SST framework (August 2019) and examined ICER's November 2019 SST framework to identify the methodological strengths and limitations of ICER's approach and to assess the extent to which stakeholder comments were incorporated. We also examined ICER's application of its SST framework across three evidence reviews and conducted a targeted scan of the literature to identify opportunities to improve the assessment of SSTs and explore ICER's participation in the public discourse surrounding value assessment for transformational therapies.

Our analysis uncovered multiple limitations to ICER's methodology and process for assessing the value of SSTs. We identified the following recommendations to help advance rigorous, fit-for-purpose methods for assessing SSTs.

**Recommendation: ICER's processes for assessing SSTs should embrace full transparency and meaningful stakeholder engagement.**

ICER is making updates to its SST framework without disclosing changes to the public and allowing for public discourse. Making updates in this way undermines ICER's claims that their assessments are transparent and informed by multi-stakeholder engagement.

**Recommendation: ICER should uphold its stated processes and the commitments outlined in its SST framework.**

Our analysis found that ICER is not adhering to its stated processes or meeting numerous commitments outlined in its SST framework. Examples include not incorporating the societal perspective in assessments of SSTs for ultra-rare diseases, not including additional value domains as outlined in its SST and general value assessment framework, and not framing its shared savings results as exploratory. By failing to meet these commitments, ICER's assessments are less comprehensive and less rigorous.

**Recommendation: ICER should not employ untested methodologies that lack empirical evidence or scientific justification.**

ICER's recent updates to its shared savings approach do not cite empirical evidence. Such actions undermine the scientific rigor of ICER's assessments. Moreover, ICER is demonstrating its willingness to experiment with scenarios that have limited practicality (eg, setting cost offsets to zero) but will not conduct analyses with strong practicality such as sensitivity analyses for discounting rates, which have robust stakeholder support and have been applied by other HTA bodies.

**Recommendation: ICER's SST assessments should be one of many tools stakeholders use to inform decision-making.**

Delivering on the promise of SSTs requires rigorous value assessment methods that are fit for purpose. The field of value assessment in the U.S. is relatively nascent, and we owe it to patients to take a "first do no harm" approach. While ICER has made some strides, significant opportunities exist for ICER to improve its methods and processes of value assessment, particularly in relation to assessments of SSTs. ICER's lack of transparency in updating its SST framework, coupled with limitations to its methodology, reinforces that ICER value assessments should, at most, be only one of many tools used to inform healthcare decision-making.

Acknowledging the limitations of ICER methods and processes is becoming increasingly important as ICER narrows its focus on gene therapies and SSTs.<sup>25-27</sup> Moving forward, it will be crucial for stakeholders to closely monitor ICER's application of its SST framework to track whether they continue to advance untested methodologies or continue to deviate from their own stated processes.

Payers and policymakers are relying on ICER reports to make important coverage decisions, which, in the absence of much-needed caveats and context, may undermine meaningful access for patients. The needs of patients are best served with comprehensive value assessment using appropriate methodologies. ICER's SST framework methodology and application need to improve and evolve in a transparent and evidence-based manner, guided by multi-stakeholder input.



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