POSITION PAPER

Value for Whom?

Incorporating Patient Perspectives into Value Assessment for Novel Cell and Gene Therapies

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Authored by:

HEALTH ADVANCES

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EVERYLIFE FOUNDATION FOR RARE DISEASES

Frank F. Zhou[1], Katelyn Ward[1], Annie Kennedy[2], Thayer Surette Roberts[3], Julia A. Gaebler[1]

[1]Health Advances, [2]EveryLife Foundation, [3]Partnership to Improve Patient Care

Table of Contents

Executive Summary

Cell and gene therapies (C&GTs) are revolutionary advancements that offer potentially life-altering therapies – and in some cases even cures – for patients with rare and severe diseases. Around the globe, various health technology assessment (HTA) and value assessment organizations are attempting to estimate the health and economic value of new C&GTs to better inform healthcare decision making. These organizations most commonly employ cost-effectiveness analysis (CEA), which seeks to determine whether the costs of a given therapy are justified by its benefits; that is, whether it is a "good buy."

However, CEA often fails to capture or reconcile key issues of importance to the valuation of C&GTs. Because C&GTs utilize unique methods of administration, often treat small patient populations, and often lack long-term data at launch, traditional CEA methods struggle to determine the true value of these therapies. Furthermore, CEA has historically been intended only for a payer audience, while data on the perspectives of other stakeholders, including patients, are often not fully incorporated. Many challenges therefore remain in achieving comprehensive, patient-centered value assessment of C&GTs, including:

- Uncertainties in the available data make it difficult to choose an appropriate duration of effect for clinical benefits.
- Patient heterogeneity and subgroup analyses are often not considered, instead focusing only on the "average" patient.
- CEA relies on Quality-Adjusted Life Year (QALY) gains as a generic measure of health or disease burden, but the QALY cannot capture societal preferences around resource allocation and is widely seen as discriminatory towards patients with disabilities.
- Estimating QALYs gained is also difficult for the rare diseases that many C&GTs treat; the underlying utility scores may not accurately represent the patient experience.
- Commonly cited cost-effectiveness thresholds may be too low for the rare diseases often treated by C&GTs.
- Additional elements of value afforded by C&GTs, such as increased productivity and reduction of caregiver burden, are often omitted in CEA base case analyses.
- Further elements of value important to patients, such as the value of hope and insurance value, are generally not quantified.
- The discount rate used for value assessment may be overly punitive when applied to C&GTs with durable clinical effects.

These shortcomings have the potential to lead to very real consequences for patients in the form of restricted and delayed access to novel therapies. It is therefore essential that value assessors incorporate patient experience data more fully into their analyses. A movement to incorporate this information known as patient-focused drug development (PFDD) has already gained traction in other medical research communities. By joining this effort, value assessors can ensure that their evaluations of C&GTs deliver more accurate and informative evidence for patients and other healthcare decision makers, not just payers.

Introduction

The rapidly expanding cell and gene therapy (C&GT) landscape continues to introduce truly innovative and unprecedented treatments for patients with high unmet needs. C&GTs rely on the transfer of genetic or cellular material into a patient to produce therapeutic effects. In the last three years, new therapies such as Luxturna, Kymriah, Yescarta, and Zolgensma have offered significant clinical benefit to those living with retinal dystrophy, lymphoma, spinal muscular atrophy, and more. Hundreds of additional C&GTs are in the US drug pipeline, including therapies for beta thalassemia, myotubular myopathy, hemophilia A, and multiple myeloma, and the FDA expects to see 10-20 new C&GTs per year by 2025.[1] These novel therapies can offer significant clinical benefit to patients and play an important role in the positive shift towards personalized and precision medicine for patients, but they have also raised questions about how to appropriately measure their comparative clinical effectiveness and finance them for patient access.

To put it simply, the innovative approach of the “one-time” therapeutic delivery with a lasting therapeutic benefit is a tremendous paradigm shift that requires changes to the ecosystem that supports the delivery of such products. This includes the way in which clinical outcomes are measured and evaluated long-term, how C&GTs are reimbursed by payers, and how decisions are made about which treatments should be taken by which patients at which stage of disease.

In an attempt to inform this decision-making, value assessment frameworks are being increasingly applied to the valuation of new C&GTs. Value assessment can take many forms, but its most basic goal is to gather evidence on the benefits and costs of such therapies to help healthcare decision-makers make informed decisions. The most frequently used type of value assessment is cost-effectiveness analysis (CEA) using the Quality-Adjusted Life Year (QALY) as a generic measure of disease burden. This method is used widely by nationally recognized health technology assessment (HTA) bodies outside of the United States to determine which treatments should be financed by national health systems. These bodies include the National Institute for Health and Care Excellence (NICE) in the United Kingdom and the Canadian Agency for Drugs and Technology in Health (CADTH). Though the United States does not have a formal HTA body, the Institute for Clinical and Economic Review (ICER), an independent nonprofit, has garnered attention for conducting CEA assessments since its

inception in 2006. With over 60 completed assessments of new healthcare innovations, ICER has captured the attention of payers, patients, and pharmaceutical companies.

Given that healthcare costs continue to rise globally and innovative new drugs for patients with rare diseases can be expensive, there is an important role for value assessment to determine the best therapies for society to finance and utilize. However, these frameworks have historically only been used to determine value for payers, and not for other stakeholders, such as patients. It is critical to ensure that the methods used when assessing value of healthcare interventions reflect the value to the patient receiving the treatment and not just the payer. Optimally, value assessments should be anchored in evidence and values deemed meaningful to patients and caregivers and could even become an additional resource to aid in patient-provider healthcare decision making.

While most concerns regarding traditional CEA are applicable to a broad range of therapies, certain limitations in CEA are especially amplified for C&GTs. Many of these limitations stem from the inherent uncertainties of CEA, particularly for C&GTs that address disease where there is limited clinical data and significant patient heterogeneity. Traditional elements of CEA, such as the use of QALYs and established cost-effectiveness thresholds, provide unique challenges when applied to C&GTs and suggest alternative methods should be explored. Additionally, societal elements of value, most salient for potential cures that last a patient's lifetime are not quantitively assessed by CEA, thereby devaluing C&GTs.

The primary goal of this paper is to assess the extent to which current CEA-based value assessment frameworks adequately determine "value," particularly in reference to C&GTs. First, we present an overview of CEA, the most common value assessment methodology today. Then, we describe the main challenges of applying traditional CEA methods to the valuation of C&GTs, and how these established methods may currently fail to capture the complete value of these therapies for patients. Last, we discuss how value assessment can and should do more to establish evidence of value to a broader set of critical stakeholders, particularly patients.

Value Assessment Methods

There are various mechanisms to assess the value of a new medical treatment or intervention, but the most frequently used method to date is CEA. In CEA, the incremental cost-effectiveness ratio (ICER) statistic is derived by the difference in cost between two possible interventions, divided by the difference in their effect (***Figure 1***). Depending on the perspective of the analysis, the cost-based numerator either includes only healthcare spending by payers (the healthcare sector perspective), or all costs regardless of who incurs them (the societal perspective). In the US, payers place most emphasis on the therapy price and direct medical costs (e.g., hospital inpatient and outpatient visits, Emergency Department visits), while in the societal perspective, additional costs such as patient transportation costs, workplace losses, caregiver costs, and patient time costs can also be included.

Figure 1: Traditional Cost-Effectiveness Analysis Framework

$$ICER = \frac{Cost_{New} - Cost_{Standard\ of\ Care}}{Effectiveness_{New} - Effectiveness_{Standard\ of\ Care}}$$

The denominator of the ICER statistic represents the difference in the clinical benefit between the two interventions, measured most commonly by the QALY, a generic measure of disease burden, which includes both the quality and the quantity of life lived. Calculating a QALY first involves defining the health states of interest by a utility score that usually ranges from 0 (death) to 1 (perfect health). The QALY score is then calculated by multiplying this utility score by the number of years lived in that health state, with and without the new intervention. Factors that influence the QALY can include the physical, cognitive, and psychological function of patients, their health perceptions, and their social function.[2]

If the final ICER statistic falls below a certain cost per QALY threshold, a therapy is deemed cost-effective and therefore deemed to be of good value at specific pricing thresholds for payers. This threshold can vary widely by geography, organization, and therapy of interest. For example, in the UK, NICE sets a threshold of £30,000/QALY for most therapies, although they will also evaluate drugs for very rare diseases using a sliding scale between £100,000 and £300,000/QALY.[3] In the US, ICER currently sets a threshold for cost-effectiveness somewhere between the range of $50,000 and $200,000 per QALY.[4]

Challenges in Value Assessment for Cell and Gene Therapies

Value assessment and CEA methods have been historically tailored for payers by focusing almost exclusively on whether the additional benefits of a given new therapy, relative to some standard of care or comparator, are justified by its costs. Payers then use these evaluations to help determine funding, coverage, and access policies for therapies. Unfortunately, this approach to value assessment has historically not captured other clinical and non-clinical aspects of value that patients and caregivers ultimately care about. Consequently, some patients have registered that the elements of value captured and quantified in these assessments, and the resulting implications, do not reflect their true preferences. Research societies such as The International Society for Pharmaceutical Outcomes Research (ISPOR) have thus highlighted the need for increased inclusion of patient perspectives in value assessments.[38] Today, there is increasing recognition that the inclusion of patient experience data and patient preferences must be more central to the value assessment framework and process.[5]

This need is particularly salient in the context of C&GT evaluation. Many C&GTs are expected to utilize single or short-term administration, with durable benefits potentially extending over the lifetime. While payers require information to inform short-term coverage determinations, value assessment frameworks and methods must also incorporate longer-term considerations, such as how patients weigh long-term benefits against short-term costs, and unique elements of therapeutic value to patients.[6] Additionally, long-term data on clinical benefit for C&GTs are usually infeasible to collect in a short-term clinical trial, and patient views on this uncertainty are not usually explored in CEA. C&GTs are also frequently indicated for rare or severe diseases, where the utility scores of various health states should be (but are not) derived from extensive patient input.[7] Assessing the value to patients of C&GTs can therefore be difficult, and there is a need to reflect patient perspectives more closely in value assessment of C&GTs.

Due to uncertainties in the long-term effectiveness and clinical durability of C&GTs, accurately assessing their valuation over the long-term, for patients, payers, and society at large continues to cause concern. Patients and people with disabilities have long-standing criticisms about the discriminatory nature of the QALY and its cousin the Disability Adjusted Life Year

(DALY), which have been cornerstones of CEA to date. Current value assessment methods do not fully incorporate all the elements of value that may be of importance to patients, such as reductions in caregiver burden or increases in productivity.[6] Consequently, value assessment results which undervalue a new C&GT may serve to impede patient access or create disincentives for the research and development of newer agents. These challenges will each be explored in more detail below.

Uncertainties Inherent to CEA Are Amplified When Applied to C&GTs

A major challenge in the valuation of C&GTs arises from underlying uncertainties about the treatment duration, which, as noted previously, can lead to undervaluation and restricted access to these innovative therapies. Because many C&GTs target small population sizes and meet significant unmet needs in these patient populations, they have previously been approved in the US with limited long-term efficacy or safety data. Balancing the hope for long-term potential benefit of these medicines against a relatively small amount of clinical data at launch is challenging, and organizations such as ICER have traditionally leaned on more conservative estimates of duration of treatment effect. For example, the ICER value assessment of Luxturna (for a rare inherited retinal disease) assumed a base case scenario with a 10-year benefit followed by diminished efficacy over time thereafter.[8] However, stakeholders including the Center for Value-Based Medicine argued that the treatment effect should have been extended, possibly for the patient's lifetime.[8] Therapies with the potential to be curative hold tremendous value, while assumptions of diminished efficacy over time underestimate this value. As a result, assumptions of diminished efficacy over time may create an access barrier to patients due to decisions by payers based on faulty value assessment assumptions.

Furthermore, value assessment of C&GTs today does not do enough to address patient heterogeneity and instead only considers the "average" patient. This is in part due to practical and ethical constraints that limit the size of clinical trials for C&GTs. Many C&GTs target rare diseases with small patient populations, limiting eligibility for trial participation.[7] Various C&GTs also require highly invasive methods of administration, so that even if a larger placebo-controlled trial could be performed, many patients would undergo potentially risky placebo procedures.[6] There is also the additional risk of trial participants developing harmful immune response to C&GTs, and patients must consider the potential benefits and risks of joining a

trial where the optimal dose has not yet been established and dose escalation may not be a possibility.[9,10] Therefore, C&GT trials will likely remain small, single-arm studies. For example, a recent review of gene therapy studies reported that 47% of trials enrolled fewer than 20 patients.[11] Furthermore, the pivotal trials for Luxturna, Kymriah, and Yescarta each consisted of small sample sizes of between 30-100 patients each.[12–14] As a result, these trials do not capture enough data on patient heterogeneity. In order for the perspectives of varying patient types to become incorporated into value assessment, it is important for HTA bodies and other value assessment organizations to recognize these issues, seek alternative ways of gathering data by patient type, and avoid generalizing their results for the "average" patient. Yet more than four-fifths of cost effectiveness assessments published in 2014 did not report patient subgroup results.[15] In an effort to address this issue, ICER has committed to a broadened discussion of patient heterogeneity and subgroup analysis in its new 2020-2023 value assessment framework, but only "when appropriate,"[4] raising additional questions about how much emphasis will actually be placed on this issue.

Limitations of the QALY Are Compounded in C&GT Valuation

As described above, most governmental HTA bodies and independent, non-governmental organizations such as ICER continue to rely on the QALY as their primary measure of benefit in CEA. While there are many limitations of the QALY that are recognized in traditional CEA, these limitations are compounded when applied to the rare diseases that C&GTs often aim to address. For instance, there may be greater societal willingness to allocate extra resources to C&GTs, which tend to treat rare diseases, severe diseases, and diseases disproportionately affecting children.[16,17] However, standard, generic quality of life instruments like the EQ-5D, which are used in trials to identify preference weights for health states and then combined with time to compute QALYs, are disease-agnostic and measure individual, not societal preferences, and therefore cannot account for these contextual nuances.

QALYs also present serious ethical concerns in measuring health preferences for patients with severe diseases and disabilities. Because patients with severe diseases and disabilities experience lower maximum baseline health than those without disabilities, a treatment that improves their quality of life may result in fewer QALYs gained than a similar treatment for the non-disabled. Yet patients with disabilities may value the treatment just as highly as those who do not have a disability.[18] Thus, the QALY is frequently criticized by disability activists and

patient communities as discriminatory. The National Council on Disability, an independent government agency, has recently raised concerns that its use limits access to lifesaving medicines in various countries.[19] In recognition of this ethical dilemma, the use of the QALY in the US has historically been restricted. Most recently, this has taken the form of the 2010 Affordable Care Act prohibiting Medicare and the Patient Centered Outcomes Research Institute from using QALYs or any other similarly discriminatory measure.[19] Regardless, non-federal entities such as ICER continue to utilize the QALY.

In addition, evaluation of C&GTs using QALYs is particularly troublesome due to the lack of well-defined health state preference weights for the diseases that C&GTs seek to treat. Estimating QALYs requires robust data for health state utility scores, but given the rarity of these conditions, they have yet to be defined and/or lack adequate patient input. For example, patients and clinical experts alike testified that the health state utility weights in ICER's evaluation of Luxturna underestimated the extent of disease burden for the group not receiving the C&GT.[8] As a result, the model underestimated the clinical benefit afforded by the novel therapy and its calculations did not reflect the substantial quality-of-life improvements of patients in the real world. Due in part to this feedback, ICER has indicated that it will attempt to incorporate more patient testimony and real-world evidence in its future reports.[4] To date, however, ICER has not committed to a formal mechanism for this, and it is not clear what sources of patient-derived data ICER is willing to accept.

In response to these and other concerns about the QALY, several HTA bodies such as those in Germany, Italy, Hungary, Columbia, and Thailand have started using or experimenting with alternative, potentially more comprehensive and flexible methods of value assessment, such as multi-criteria decision analysis (MCDA).[20–23] As long as federally recognized HTA bodies and independent value assessment organizations, including NICE, CADTH, and ICER, continue to stand by the QALY, its use in assessing C&GTs will remain problematic.

Cost-Effectiveness Thresholds for Rare Diseases Are Too Low

The cost-effectiveness threshold plays an important role in determining whether a given C&GT is deemed value for money by payers. Historically, ICER has assessed therapies for "ultra-rare diseases" using a cost-effectiveness threshold range of up to $500,000/QALY.[24] However,

ICER recently changed their methods and now intends to perform all analyses using thresholds in the $50,000 to $200,000/QALY range, with no allowances for higher thresholds for rare diseases or special circumstances.[4] This foregoes the global recognition among HTA organizations that rare diseases, which many C&GTs treat, likely warrant higher cost-effectiveness thresholds due to smaller populations from which to recoup research and development costs.[25] For example, Garrison et al. have specifically argued that innovative C&GTs addressing ultra-rare diseases should be held to a higher threshold, perhaps in excess of $300,000/QALY, if one were to consider the broader value afforded by such therapies.[26] ICER's new, lower cost-effectiveness threshold range will likely result in assessments for C&GTs that do not meet the threshold criteria and are then not seen by payers as a "good buy." Private payers who look to data from ICER when determining coverage may then determine the treatment is not medically necessary, choose to introduce access barriers to therapy, or even not cover it altogether.

Inconsistent Reporting of the Societal Perspective

Value assessments of C&GTs have been frequently criticized for reporting only what is of value to payers, namely the near-term costs and benefits that are key to the healthcare system perspective. More often than not, the societal perspective, which more fully accounts for all potential sources of value including caregiver impact and lost productivity, is either not reported, or relegated to a "nice to have" scenario. While the 2nd Panel on Cost Effectiveness in Health (2016) recommends the use of the societal perspective in the reference case alongside the health sector perspective,[27] ICER has historically only considered the health sector scenario, and NICE only considers a societal perspective in circumstances where interventions are funded by the public sector.[28] As such, elements of societal value that are particularly salient to C&GTs have been infrequently or inconsistently assessed in value assessments to date. This can result in undervalued therapies, an ICER statistic that is higher than the threshold, and the recommendation that a therapy is not cost-effective at a given pric*Caregiver Impact*

Because C&GTs frequently target severe, genetic disorders that manifest in childhood, such as spinal muscular atrophy (SMA), the impact on caregivers cannot be overstated. Before the approval of Zolgensma for SMA, in families with a baby or child with SMA, one or more family members would often need to forgo or reduce employment in order to provide care for the child with SMA. In addition, care often required breathing treatments and nutritional support,

assistance throughout the night, specialty clinician visits, physical, respiratory, and other therapy visits multiple days a week, and much more. Now, innovative therapies available to a segment of the SMA patient community allow caregivers the convenience of managing a therapy that commonly requires only one-time administration, greater opportunity to return to work, and a significant reduction to physical, emotional, and psychological stress.

ICER's process for the assessment of Zolgensma did include meaningful SMA patient community representation in the Policy Roundtable, and the ICER Council members did recognize the benefits Zolgensma offered families with respect to reduction of household financial burden, stress, and the benefits offered by a one-time administration of therapy. However, the final valuation did not include an assessment of caregiver burden in either its base case or the modified societal scenario, citing that "the methods for performing economic evaluations including caregiver burden are still under development."[29] Value assessments that omit an analysis of caregiver burden for both the intervention and the comparator may underestimate the true value and impact of C&GTs to patients and their families.

Productivity Gains

Furthermore, C&GTs can lead to significant productivity gains by transforming the lives of patients living with severe, rare diseases. For example, a 2020 analysis by the Alliance for Regenerative Medicine (ARM) and Marwood Group determined that $3B of lost productivity from diseases such as multiple myeloma, sickle cell disease and hemophilia A could be recouped by C&GTs within a ten-year period.[30] Yet ICER has previously only looked at productivity *costs* and not productivity *gains* in its past reports of the chimeric antigen receptor T-cell (CAR-T) therapies Kymriah and Yescarta. This has been criticized as openly biased against C&GTs.[31] Given that methods for evaluating productivity gains are relatively advanced, a critical element of societal value is missing in the frameworks currently utilized by NICE and ICER when assessing C&GTs.

In response to these critiques, ICER stated that its 2020-2023 value assessment framework will promote and conduct a societal perspective base case as equally important as the health sector perspective base case when the societal costs of a drug are relatively large and the impact of treatment on these costs is substantial.[4] This is a step forward, but ICER's persistent focus on societal costs rather than societal gains remains a point of contention. In order to fully

assess the value of C&GTs, integration of complete and consistent evaluations of caregiver impact and productivity gains are fundamental to include in the societal base case.

Additional Considerations of Value Are Ignored

In addition to patient and caregiver burden productivity gains and losses, other elements of value that are key to patients remain unaccounted for in C&GT valuation. For example, recent literature has introduced the "value of hope", where patients are willing to accept riskier or newer therapies such as C&GTs in hope for robust, life-altering outcomes – and potentially even a cure.[32] In the US, ICER has proposed to include a qualitative evaluation of the value of hope in its "single and short-term therapy" (SST)framework, but the practical implementation of this has yet to be seen, and a full quantitative assessment is still pending.

Furthermore, patients often describe significant emotional and quality of life improvements offered by C&GTs, including reduced stress and increased independence.[33] Because the administration of C&GTs is often a short-term rather than chronic process, additional value is derived from decreased out-of-pocket costs, medical visits, productivity losses, and transport times. However, these elements of value are also rarely incorporated into value assessments today.

Another element of value that value assessment organizations such as ICER do not currently incorporate in their assessments is the "insurance value" afforded to healthy patients who are now protected from future disease and financial risk. As posited by Garrison et al, insurance value may be particularly salient for C&GTs that target severe, rare diseases with no prior cure.[26] As such, quantitatively considering this insurance value would likely allow ICER and other organizations to more accurately capture the value of C&GTs to patients with high unmet need.

The Discount Rate Is Not Suitable

The discount rate is yet another variable in CEA that impacts the ICER statistic. The discount rate, when applied to therapy effects, seeks to capture patient preferences for receiving positive outcomes earlier rather than later. Downstream clinical benefits realized at future time-points are thus commonly discounted by a specified annual percentage. At present, ICER sets

this at a rate of 3%,[34] while some HTA bodies in countries such as Portugal and Australia set an even higher discount rate of 5%.[35] However, for C&GTs, where patients may see lasting high value in curative effects that persist many years into the future, these discount rates may be too high and result in devaluation of these therapies. Other organizations, such as NICE and the UK Treasury, are now recommending a lower discount rate of 1.5% for long-term health effects when evaluating therapies with curative potential.[36,37] In comparison to these recommendations, the discount rates used by ICER and some other HTA bodies may be overly punitive for C&GTs and result in higher ICER statistics, ultimately biasing the results against therapies with durable clinical outcomes.

Patient-Centric Value Assessment Methodologies Under Development

In recognition of patient-centered goals, some organizations that conduct CEA have taken steps to improve on existing value assessment frameworks for the evaluation of C&GTs. In November 2019, after a year-long development process with stakeholders that included patient advocacy groups, ICER released its alternative methods for evaluating potentially curative treatments and other SSTs such as C&GTs.[34] As part of this revision, additional elements of patient-centered value (namely the *value of hope* and *option value*) will now be considered qualitatively as part of the overall report. However, they will not be integrated quantitatively into the cost-effectiveness calculations, which is concerning as this is typically the element considered for decision-making purposes. Furthermore, ICER continues to rely on the discriminatory QALY metric for its calculations. As a result, there still remains much to be done in CEA to make it a comprehensive and appropriate method for determining value to the patient and entire healthcare system.

In fact, the integration of patient experience data is already well underway in the clinical trial enterprise and regulatory ecosystem through a growing emphasis on Patient-Focused Drug Development (PFDD). PFDD is a scientific and systematic model to ensure that patients' perspectives and experiences are meaningfully integrated into drug development. This approach is championed by federally sanctioned bodies, like the FDA.[39] There is thus a clear need for an extension of this same science of patient input within the value assessment space.

To that end, there are several methodologies under development with an emphasis on patient-centricity. One such method is Multi-Criteria Decision Analysis (MCDA), which allows value assessments to capture a broad variety of inputs, including patient-reported outcomes, thus giving a more personalized and sensitive analysis.[23,40] The advantage of MCDA over QALY-based CEA is that it can account for a greater variety of factors of interest to decision-makers, and can represent the interests of more stakeholders.

One organization attempting to use MCDA to address this issue is the Innovation Value Initiative (IVI). IVI is developing open source platforms for modeling value and decision-making tools anchored in patient perspectives on value. To date, they have developed fully transparent models for rheumatoid arthritis and epidermal growth factor receptor (EGFR+) non-small cell lung cancer, which serve to advance the science of value assessment and build consensus on best practices.[41] They, along with select others, are innovating to move value assessments away from population-based averages with the goal of understanding the needs of the specific patients impacted by the condition in question.[42]

The Patient-Driven Values in Healthcare Evaluation (PAVE) Center is also spearheading efforts to expand incorporation of the patient perspective in value assessment. The center supports research, partnerships and education programs to measure patient values and preferences for health-related benefits and risks, test different methods for value assessment, and perform patient-driven cost-effectiveness analyses.[43] They have also led a multi-stakeholder collaboration to develop empirically derived patient-informed value elements for use within any existing value assessment framework.[44]

Lastly, the Patient Centered Outcomes Research Institute (PCORI) is undertaking multi-stakeholder collaborations to build out the science of patient-centered outcomes research along with education, and dissemination. This type of input would be very helpful in evaluating very specialized treatments for small populations, like C&GTs. As a result of these various initiatives, we imagine a likely future where value assessment is used to assess the value of C&GTs not just for payers, but also for patients and greater society.

Conclusion

Cell and gene therapies represent a revolutionary new frontier in medicine. For many patients with severe or rare diseases, these therapies offer tremendous promise of life-altering outcomes, improved quality of life, and potential cures. Value assessment can be one of many useful tools for patients, payers, policy makers and other stakeholders when making complex decisions around pricing, access, and therapy selection, and is ultimately a meaningful endeavor. However, in its current incarnation, value assessment has principally served to inform value to payers, not patients or healthcare providers, and it faces many important limitations when applied to cell and gene therapies. To better inform the value of cell and gene therapies to patients, value assessment frameworks must improve on the ability to handle uncertainties in clinical evidence, revisit the use of the Quality-Adjusted Life Year measurement, incorporate additional elements of patient-centered value, and solicit proactively the patient voice at more points in the evaluation process. In the US, the Institute for Clinical and Economic Review has demonstrated some willingness to better address elements of cell and gene therapies that are of value to patients, while other organizations are leading the development of more holistically patient-centric methodologies. We must build on this momentum to ensure that patient communities treated by new therapies are among the intended audiences for value assessment. Only then can value assessment become a more valuable resource for all healthcare stakeholders while also safeguarding access to life-changing therapies for patients and their families.

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