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# Defining Elements of Value in Health Care—A Health Economics Approach: An ISPOR Special Task Force Report [3]

*Darius N. Lakdawalla, PhD[1,*], Jalpa A. Doshi, PhD[2], Louis P. Garrison Jr, PhD[3], Charles E. Phelps, PhD, MBA[4], Anirban Basu, PhD[3], Patricia M. Danzon, PhD[5]*

[1]*Schaeffer Center for Health Policy and Economics, University of Southern California, Los Angeles, CA, USA;* [2]*Division of General Internal Medicine, University of Pennsylvania, Philadelphia, PA, USA;* [3]*The Comparative Health Outcomes, Policy, and Economics (CHOICE) Institute, University of Washington, Seattle, WA, USA;* [4]*Economics, Public Health Sciences, Political Science, University of Rochester, Gualala, CA, USA;* [5]*The Wharton School, University of Pennsylvania, Philadelphia, PA, USA*

ABSTRACT

The third section of our Special Task Force report identifies and defines a series of elements that warrant consideration in value assessments of medical technologies. We aim to broaden the view of what constitutes value in health care and to spur new research on incorporating additional elements of value into cost-effectiveness analysis (CEA). Twelve potential elements of value are considered. Four of them—quality-adjusted life-years, net costs, productivity, and adherence-improving factors—are conventionally included or considered in value assessments. Eight others, which would be more novel in economic assessments, are defined and discussed: reduction in uncertainty, fear of contagion, insurance value, severity of disease, value of hope, real option value, equity, and scientific spillovers. Most of these are theoretically well understood and available for inclusion in value assessments. The two exceptions are equity and scientific spillover effects, which require more theoretical development and consensus. A number of regulatory authorities around the globe have shown interest in some of these novel elements. Augmenting CEA to consider these additional elements would result in a more comprehensive CEA in line with the "impact inventory" of the Second Panel on Cost-Effectiveness in Health and Medicine. Possible approaches for valuation and inclusion of these elements include integrating them as part of a net monetary benefit calculation, including elements as attributes in health state descriptions, or using them as criteria in a multicriteria decision analysis. Further research is needed on how best to measure and include them in decision making.

***Keywords:*** cost-effectiveness analysis, economics of medical technology, health technology assessment, value of health care.



## Introduction

The First Panel on Cost-Effectiveness in Health and Medicine [1] had underscored the need for health care sector decision makers to evaluate both health and cost impacts in considering the adoption and use of health care technologies. To date, payers, politicians, and other stakeholders in the United States have often been reluctant to embrace formal approaches for health care resource allocation decisions [2–4]. Nevertheless, cost-effectiveness analysis (CEA) is now gaining prominence given its use by value framework developers such as the Institute for Clinical and Economic Review, the American College of Cardiology with the American Heart Association, as well as the publication of new guidelines from the Second Panel on Cost-Effectiveness in Health and Medicine [5,6].

In this section, we identify and define a series of elements that warrant consideration in value assessments of medical technologies. We aim to broaden the view of what constitutes value in health care and to spur new research on incorporating additional elements of value into CEA or cost-utility analysis (CUA). On the basis of our understanding of current CEA and health technology assessment (HTA) practices, and input from our broader Expert Advisory Board and Stakeholder Advisory Panel, we identified a list of elements, ranging from the conventional to the cutting-edge. These have been discussed in a range of relevant literatures—economic, clinical, ethical, and so forth. In the technical appendix in Supplemental Materials found at https://doi.org/10.1016/j.jval.2018.12.007, we illustrate how to incorporate many of these elements into a logically consistent microeconomic model of health care technology value

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* *Address correspondence to:* Darius N. Lakdawalla, Schaeffer Center for Health Policy and Economics, University of Southern California, 635 Downey Way, Los Angeles, CA 90089.

E-mail: dlakdawa@usc.edu

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assessment. Here, we confine our presentation to an intuitive explanation of these elements.

For ease of exposition, we begin our analysis with the conventional and long-practiced approach to measuring value in health care and then progressively expand toward the "frontier," where we find more novel value elements. Figure 1 presents a value "flower" that summarizes the concepts to be discussed. The elements in green are considered the core elements of value assessments. The elements in light blue are common but inconsistently used in value assessments. The ones in dark blue are more novel, and not typically considered. The blue lines indicate value concepts from the traditional payer or health plan perspective, and the red lines indicate concepts also included from the broader societal perspective. Each of these 12 elements in the figure's value flower—quality-adjusted life-years (QALYs), net costs, productivity, adherence-improving factors, reduction in uncertainty, fear of contagion, insurance value, severity of disease, value of hope, real option value, equity, and scientific spillovers—is discussed in subsequent sections, with an extended description of the concept and references to previous research.

## Costs and QALYs

As discussed in the section by Garrison et al. [7], the underlying concept of value from a health economic perspective is typically measured using CEA. The cost-effectiveness of a medical technology is always calculated relative to alternative choices. For this reason, CEA focuses on *incremental costs* and *incremental benefits*.

As recommended by the Second Panel [6], a wide range of costs or cost savings—present and future—should be considered, so long as they result directly from the interventions of interest. Future cost savings resulting from a treatment today should be subtracted from the direct treatment cost to yield the net incremental cost of treatment. When relevant, future net costs should be appropriately adjusted for uncertainty and discounted from the year of occurrence. The set of costs included should reflect the perspective of the relevant decision maker. If the perspective is that of the payer, then the focus is on costs borne by the payer. If the perspective is of a government, then the effects on tax revenue, prison spending, public assistance spending, and the like might need to be considered.

Benefit is measured from the perspective of the patient (or potential patient) given the health care technology in question. For instance, the benefit of a drug will depend on what the treated patient thinks about it, and not the prescribing physician or even the insurance company paying for it. Nevertheless, valuation of these benefits to patients can be based on a broader societal perspective. Various different health benefits ought to be considered. For instance, a medical technology might influence a patient's life expectancy, mobility, experience of pain, sleep quality, or a nearly limitless set of other health-related factors. Ideally, we would have some way of capturing all these changes in terms of a common unit.

To solve this problem, health economists have developed the concept of QALY, which can in principle be used to measure the health benefit of any technology, regardless of the disease it treats [8]. The QALY is the fraction of a perfectly healthy life-year that remains after accounting for the damaging effects of an illness or condition. For instance, potential patients (or consumers) might feel that 1 year spent with total blindness is equal in value to 6 months spent in perfect health. In principle, any health state—whether blindness, mobility impairment, debilitating pain, and so on—can be equated to some fraction of a perfectly healthy life-year. This fractional value, when compared with 1 year of perfectly healthy life, is also called a health state "utility." This is the reason that CEA using the QALY is often referred to as CUA, which is a very useful form of CEA.

As an example, suppose that patients with lung cancer can expect to live an average of 4 years. Suppose also that they value each year spent with lung cancer as equal to 6 months of life spent in perfect health. Thus, they experience 2 QALYs. Now suppose that a new drug is introduced that extends life expectancy to 4.5 years. Suppose further that it reduces some of the disabilities and comorbidities associated with lung cancer such that patients now value 1 year spent with lung cancer as being

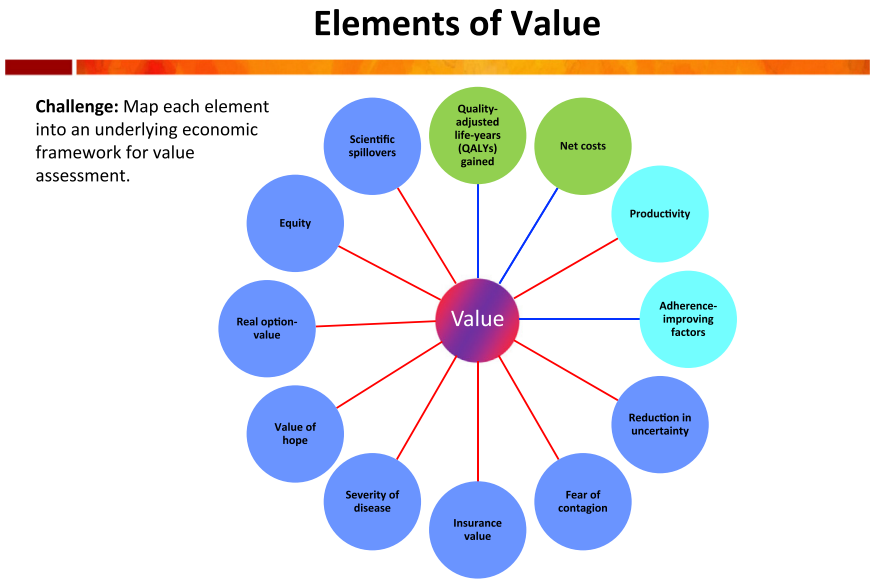


**Fig. 1 – Elements of value. Note. Green circles: core elements of value; light blue circles: common but inconsistently used elements of value; dark blue circles: potential novel elements of value; blue line: value element included in traditional payer or health plan perspective; and red line: value element also included in societal perspective.**

equal to 8 months of life spent in perfect health. When treated with this drug, therefore, patients experience 3 QALYs, and the incremental benefit of the drug is equal to 1 additional QALY.

With the incremental QALY gain in hand, the next challenge lies in obtaining a monetary value that society, payers, consumers, or patients place on each QALY. For example, if each QALY is worth $150,000, the lung cancer drug in our example produces $150,000 worth of incremental benefit. If that drug costs $125,000, we would then conclude that its net value or net monetary benefit (NMB) is $25,000 (i.e., $150,000-$125,000).

The value of a QALY gain can be calculated via "stated preference" or "revealed preference" methods. A stated preference method uses surveys that elicit statements of preferences from consumers. For example, we might survey a group of people to determine whether they would rather live for 6 months in perfect health or for 1 year with lung cancer. Such an approach would imply the QALYs gained from 1 year spent with lung cancer. In addition, we can ask these respondents how much money they would be willing to give up in exchange for an additional month of perfect health or an additional month spent with lung cancer. This is called "contingent valuation." Either of these approaches allows us to assign a dollar value to a QALY change. Such stated preference methods are straightforward to understand, and they can be adapted to almost any treatment or disease area of interest. Survey respondents, however, have weak incentives to get their answers right. Thus, given the intellectually challenging nature of questions such as these, one might wonder about the accuracy of the answers. Indeed, researchers have pointed out various errors that survey respondents make, such as failure to adjust their estimated willingness to pay in response to changes in the magnitude of health harms [9].

The alternative is revealed preference, which uses real-world behavior to infer (or "reveal") the underlying value placed on a QALY. Revealed preference proceeds from the assumption that prices in the marketplace reflect consumer and patient preferences. Thus, if we can determine how the price of treatment changes when it adds one more QALY, in theory we can determine the value of a QALY revealed by the marketplace [10]. This approach, however, relies on several assumptions that might be questioned. First, revealed preference works when market prices are set efficiently by well-informed marketplace participants [11]. This assumption may fail in health care: indeed, CEA using the QALY is often justified by a presumed need to evaluate whether prices are being set correctly. Second, revealed preference methods rely on the completeness of markets. In many cases, we are interested in the value of QALY gains that are not observable. For instance, new therapies might increase QALYs well beyond historically observed levels; thus, it is difficult to infer the value of such QALY gains from data before the launch of these new therapies.

In practice, neither of these approaches is perfect. Recognizing this, analysts draw from a range of different studies and methods, including both stated and revealed preference methods. Well-cited literature reviews, for example, combine studies of both types to come up with plausible ranges for the value of a QALY [12].

QALYs and costs often form the basis of value assessments based on CEA, and as noted earlier, this is labeled CUA. Nevertheless, QALYs capture only a subset of benefits that may be produced by a health care intervention. This framework neglects numerous alternative aspects of benefits that should also be considered. Some of those benefits accrue to the patient, but others could accrue to society at large. We now turn our attention to these other elements of value (see Table 1) in the balance of this section. We first discuss elements that are increasingly, albeit inconsistently, being incorporated into value assessments, and then discuss novel elements or elements that are currently omitted from conventional CEA.

Many of these additional value elements can be reflected in calculations of NMB, which is an alternative way of expressing value and cost effectiveness. NMB equals the monetary value of all benefits considered, less all costs considered. It yields decisions that are equivalent to CEA using the QALY whenever both use the same dollars per QALY value.

## Labor Productivity

QALYs do not capture well the effects of health improvement on productivity in the workplace or outside of it. Many HTAs include effects on workplace productivity as a separate element of value [13]. Consider two services that generate the same gain in incremental health, and imagine that one is delivered to a working-age population and the other to retirees. If the working-age population experiences an increase in time spent working, then that could be included as an element of value.

The measurement issues are challenging. Most utility assessment tools do not capture the productivity effect well. Thus, some researchers have argued that productivity could be added to the value of the base gain in QALYs [14–16]. Separating productivity gains from base QALY gains can be useful when the model's perspective changes. For example, a payer might not be interested in considering the productivity gain, whereas an employer or a government might value such gains as contributing to profits or tax revenues, respectively. Separating the two allows the researcher to include the productivity gain only when relevant to the decision context. NMB calculations can easily incorporate the productivity gain as an additional element of benefit. Alternatively, the productivity benefit can be converted into a QALY and incorporated into the CEA.

This approach, although theoretically justified, also generates equity concerns. It would imply that a service that generates an extra year in perfect health for a working-age person is worth more than a service that generates an extra year in perfect health for a retiree. Similar issues arise related to sex, race, or income if wages or labor force participation differs by those traits.

The Second Panel recommends explicitly measuring and valuing productivity gains and losses due to health care interventions [6]. The panel recognizes that these costs or benefits represent the production value of time that is spent in formal and informal labor markets and in household production. Individuals participate in the formal labor market when their marginal product of labor is at least as large as the wages plus fringe benefits offered. Therefore, at the margin, productive time spent in the formal labor market should be valued using wages plus fringe benefits. Expected productivity is estimated by multiplying the probability of labor force participation, hours spent in the labor force, and total compensation per hour (wages plus fringe benefits). A more nuanced approach would involve measuring absenteeism (an employee's absence from work because of an illness or health condition) and presenteeism (attending work while sick) even though the individual has not formally left the labor market.

There is a growing body of work that has shown that elderly individuals, who do not usually directly participate in formal labor markets, contribute in informal labor markets by volunteering time for various activities (e.g., babysitting, counseling, and mentoring younger people) [17]. In general, people of all ages who are not actively engaged in formal labor force activities often make substantial contributions through household production. This production should also be valued using wages plus fringe benefits, which can be matched to the specific occupational

**Table 1 – Value elements inventory.**

| Elements of value | Type of element | Features of medical technologies in which element is relevant in value assessment | Consideration under health care perspective[§] | Consideration under societal perspective[§] |
|---|---|---|---|---|
| Net costs[*] | Core | All | Yes | Yes |
| QALYs gained[*] | Core | All | Yes | Yes |
| Productivity[†] | Common but inconsistently included | Relevant when treatment has an impact on productivity | No | Yes |
| Adherence-improving factors[†] | Common but inconsistently included | Relevant when features of the treatment itself improve adherence with the treatment | Yes | Yes |
| Value of reduction of uncertainty due to a new diagnostic[‡] | Novel | Relevant when the treatment is accompanied by a companion diagnostic test | Yes | Yes |
| Fear of contagion[‡] | Fear (novel) | Relevant when dealing with treatments for infectious diseases | Yes | Yes |
| Risk of contagion[‡] | Risk (common) | | | |
| Insurance value[‡] | Novel | Relevant when baseline health status is particularly poor | No | Yes |
| Severity of disease[‡] | Novel | Relevant when considering treatments for end-of-life care or high-severity conditions | No | Yes |
| Value of hope[‡] | Novel | Relevant when therapies have uncertain effects that cannot be predicted beforehand by a diagnostic test | No | Yes |
| Real option value[‡] | Novel | Relevant when technology extends the life of patient | No | Yes |
| Equity[‡] | Novel | All | No | Yes |
| Scientific spillovers[‡] | Novel | Relevant when technology identifies a new mechanism of action or mode of delivery | No | Yes |

QALY, quality-adjusted life-year.
[*] Core elements of value.
[†] Common but inconsistently used elements of value.
[‡] Potential novel elements of value.
[§] Health care versus societal perspectives are as defined by the Second Panel on Cost-Effectiveness.

categories that are being produced. The most neutral approach—in terms of distributive justice—would be to value all productive time at a generic mean wage plus fringe benefits in society.

## Adherence-Improving Factors

Health care intervention can also influence patient behaviors that are themselves directly related to health. Some medical technologies offer advantages over existing alternatives such as simpler dosing schedules, alternate routes of administration, or combination treatments. To the extent that these improve patient adherence to treatments and health outcomes, they may impact the estimation of the value of the medical technology in the aggregate [18]. For example, the value to each individual user might increase if each patient adheres better to the therapy. Such adherence-improving factors will influence the value assessment via an impact on both costs and effectiveness associated with the technology. On the effectiveness side, technologies that promote greater adherence may directly increase the technology's health benefit as well as encourage greater uptake in a population. On the cost side, there is a direct and immediate impact of increasing costs of the technology (e.g., increase in drug costs because of an increase in adherence with or refills for the medication) but an indirect and longer term impact of reducing consequent medical resource utilization and costs (via improved health outcomes). The net impact on cost effectiveness will depend on the magnitude of the aforementioned countervailing effects and will vary on the basis of the type of drug, disease condition, and the mechanism for nonadherence to the comparator treatments (e.g., Do patients completely discontinue filling subsequent prescriptions or refill without using them?).

Despite the potential effect of adherence-improving factors in value measurement, the literature suggests that adherence is not included routinely in published CEAs, and when it is included, methodological problems are pervasive [18,19]. Instead, CEAs often assume perfect adherence when determining clinical effectiveness, or they assume that real-world adherence will be similar to adherence in the underlying clinical trial used to assess benefit. Even the latter assumption is not likely to be correct [20]. Sometimes, this is due to the lack of rigorous data on real-world adherence (and effectiveness) especially at product launch when only clinical trial data are available. Various approaches have been proposed in the literature for incorporating adherence-improving effects into CEA of medical technologies [18].

## Value of Reducing Uncertainty due to a New Diagnostic

Another element commonly included in HTAs is the value of diagnostics for a disease. We can illustrate this element by imagining a companion diagnostic test that would differentiate "good responders" and "poor responders." Such a test could obviously be valuable to patients and their clinician advisors. Avoiding an ineffective treatment in poor responders would save treatment

costs (e.g., costs of the medicine) as well as the costs of treatment-related adverse events [21,22]. Furthermore, it could help poor responders to move more quickly to better alternative treatments.

At the same time, some types of diagnostics might predict treatment effectiveness more accurately, for example, companion diagnostics that determine whether a patient's genotype matches a therapy's mechanism of action. In these cases, the arrival of the diagnostic might increase utilization and cost, and also increase value if it encourages use of the drug in high-value cases in which success is more likely. At a population level, more certainty about response would improve adherence and encourage greater uptake, thereby generating greater value.

Such diagnostics are—in technical terminology—economic complements to the accompanying treatment. It is clear that the combination would be more valuable than either alone, and thus there is additional value produced that can be estimated. In addition, there can be some psychological benefit to the patient—the "value of knowing," which can be estimated using stated preference methods. This latter component is independently valuable, even holding fixed the QALY gains associated with a diagnostic. There is an additional challenge in allocating value between the two complements—the test and treatment. This issue has been discussed in the literature, but different health systems have handled this reimbursement split in different ways [23,24].

## Fear of Contagion

When studying infectious diseases, cost-effectiveness analysts typically include the benefits of a medical intervention that extend beyond the treated patients. Infectious disease treatment limits the spread of disease to others, who benefit from it, too. This external benefit represents what economists call an "externality," or a situation in which one person's behavior adds costs to others (a negative externality) or confers benefits on others (a positive externality), but in which these external costs or benefits are not considered in individuals' behavior.

In the case of positive externalities from treating infectious disease, the sum of all benefits to vaccinated (or treated) persons is less than the sum of all societal benefits, including those accruing to nonvaccinated people. The societal perspective on value assessment would account for all these positive external benefits of infectious disease treatments, for example, the costs of quarantine. Payers might also account for these benefits, to the extent they accrue within their covered population.

Although these benefits are typically included in value assessments, the fear associated with the spread of disease is not. A good example is a treatment for a largely dormant, but potentially virulent, disease such as Ebola or even Nipah virus (contracted by consuming infected pork). Reducing the anxiety associated with the risk of future spread may be valuable to the society, even if the expected number of cases prevented is low. In contrast to other factors, fear plagues all consumers who might potentially be exposed to the disease, not just those who are sick or are actually exposed. Thus, the per-capita value of avoiding fear may become quite significant in value assessments. Fear can be quantified using survey methods designed to elicit the individual's willingness to pay to eliminate the possibility of exposure.

## Insurance Value

The fear of contagion represents one of the more novel elements of value rarely, if ever, included in technology assessments. More generally, traditional value assessment tends to ignore the role of risk and uncertainty in mediating the value of health technology. Recent literature has begun to advance this frontier. The conventional approach treats value as the benefit accruing to the sick person, net of the technology's costs. If sick patients paid for technology, this perspective would be complete and appropriate. Health technologies are, however, financed jointly by sick patients making co-payments and "healthy" consumers who pay the premiums or taxes that support health care spending. This distinction matters, because healthy consumers have different perspectives on the value of medical technology.

To a healthy person, illness represents a risk, not a current condition. New medical technology reduces the "physical risk" of getting sick. New treatments make illness less unpleasant and thus improve well-being in the "sick" state. For example, every person is at risk from Alzheimer's disease. If an effective treatment were to become available, we would all have less to fear from it, even though not all of us will develop Alzheimer's disease. Even though some diseases do not pose a risk to everyone, in general, the number of consumers willing to pay for a medical technology exceeds the number who will ever need it. This reflects the "physical risk protection" value created by a new technology [25].

In addition, new medical technologies make financial insurance policies more useful. In real-world markets, consumers cannot buy insurance policies that protect them against getting sick; they can buy only those policies that protect them against spending money on medical care. Thus, greater options for medical care expand the possibilities for insuring against illness. This is sometimes called "financial risk protection" for the healthy.

Together, these two components—physical risk protection and financial risk protection—constitute the "insurance value" of medical technology. Insurance value can be incorporated into calculations of NMB in at least two ways. First, one can measure it using estimates of how much consumers are willing to pay for health insurance, coupled with estimates for the standard value of medical technology to sick patients. The technical appendix in Supplemental Materials provides the specific mathematics behind this result, which is shown in the study by Lakdawalla et al. [25]. Alternatively, researchers may choose to specify an explicit mathematical model of consumer utility maximization, and use it to calculate an estimate of insurance value. In this case, one needs to specify the model of utility itself and have access to the following parameters: 1) the per-period incremental cost of the medical technology in question and 2) the per-period incremental health benefit of the technology. Details are provided in the technical appendix in Supplemental Materials.

Insurance value is likely to be quantitatively meaningful, particularly in the treatment of highly severe diseases. Existing estimates suggest that insurance value accounts for up to 40% to 60% of the conventional value of morbidity improvements [25]. Mortality improvements present more complexity, because the conventional economic model for the value of life implies that people are approximately risk-neutral over changes in their life expectancy.

## Severity of Disease

Other novel elements of value also focus on how the severity of disease might affect the value of treatment [26]. This concept is intimately related to insurance value, which also implies that a given gain in health is more valuable to a consumer with a poorer baseline prognosis [25]. In terms of QALYs, this implies that a gain in quality of life from (say) 0.3 to 0.5 on the scale is worth more than a gain from 0.5 to 0.7 [27,28]. Researchers have also suggested that treatments for individuals near end of life (or proximity to death) may be more valuable, either because the

individuals themselves place higher value on the health gain or because they feel that society should give priority to treating those with severe disease. Some recent literatures link these two concepts by arguing that a consideration in providing treatment should be the "proportional QALY shortfall" that individuals face, namely, the difference between the remaining QALYs they are likely to experience with their current disease, as compared with a healthy person of their age [29].

The literature on whether the general public places a greater weight on a unit of health gain at the end of life has recently been reviewed by Shah [30]. In interpreting this literature, a key question is whether individuals are responding on the basis of views about care for themselves or on what they believe society should do for others. The vast majority of studies focus on the latter issue, although sometimes there are doubts about the basis on which respondents have answered the questions [29]. Nevertheless, one recent study, by Taylor et al. [28], suggests that individuals place a greater weight (for themselves) on improvements in health from more severe health states than on equivalent improvements from less severe states.

The various surveys regarding end-of-life valuation have used a range of methods, including willingness to pay, time trade-off, and discrete choice experiments. Review of the literature mentioned earlier reveals some studies indicating a strong premium for end-of-life care, and others suggesting no premium. Similarly, there are differences in response concerning whether QALYs gained by extending life are valued more or less than an equivalent number of QALYs gained by improving quality of life. It is likely that framing effects and a lack of understanding by respondents in surveys are important reasons for the inconclusive results.

## Value of Hope

Another novel element of value revolves around the risk that a particular treatment may or may not work for a particular patient. Health economists and other analysts have identified situations in which patients might be willing to take gambles that do not focus solely on maximizing expected QALYs (i.e., they become "risk lovers"). This situation has been referred to as patients perceiving the "value of hope" [31]. Recent research pointed out how this concept fits into discussions about how patients perceive the cost of uncertainty and the value of risk reduction [32].

In the traditional analytic approach, analysts consider average benefits and average costs. Nevertheless, patients may also independently care about the uncertainty in benefits and costs, not simply the mean outcomes. Consider two different technologies—both produce the same mean outcome, but one involves much greater uncertainty around that mean. If patients value hope, they may gravitate to the high-variance treatment, in the hope that they will be one of the lucky few to benefit. In contrast, if patients are risk-averse, they may gravitate to the "sure bet" that insulates them against an unlucky outcome. Either way, they are making a definite choice between two goods that should appear identical if we focused only on average costs and benefits.

The basic idea underlying the value of hope is intuitively plausible: many severely ill patients may be willing to trade off some survival (e.g., undertaking a risky procedure) for a chance at a "cure"—even if only for a small probability of that much longer expected survival or cure. Technologies that provide an opportunity for a cure would thus be more valuable to many patients, and a payer, acting as their agent, would be willing to pay more on their behalf. Empirical work relying on discrete choice experiments provides support for this element and demonstrates how to value it [31,33].

Quantitatively, the value of hope is likely to be most important in situations in which a therapy has uncertain effects that cannot be predicted beforehand by a diagnostic test or assessment. One estimate suggests that patients will pay about $35,000 for each 1-year increase in the standard deviation of survival [31]. Other studies have quantified this in survival terms, finding that patients would trade up to one full year of average survival gains in exchange for increases in the variance of survival outcomes [34].

## Real Option Value

Patients also face uncertainty about when and how future advances in medicine will occur. Thus, extending life provides patients with an option to enjoy these uncertain future benefits. This "real option value" is generated when a health technology that extends life creates opportunities for the patient to benefit from other future advances in medicine [35]. Previous economics literature has identified real option value as an additional element of value that may be relevant for specific medical products [36,37]. This element is not generally captured or reflected in the intervention-specific projections of QALYs gained, which account for a combination of expected survival and the health-related utility at any point in time during the remaining lifetime.

Real option value recognizes the impact of other disease-specific effects on mortality. Hypothetically, if a patient had to choose between two diseases offering the same expected QALY gain, they might prefer the one that offers the greater life expectancy: this provides a greater chance to benefit from access to future scientific and clinical advances. By analogy with financial options when payment is made now for the option to buy or sell a stock in the future, investing in (i.e., using) the current life-extending medical technology can be interpreted as buying an option to benefit from advances that are coming through the pipeline. Other things equal, a technology that extends life in an area with a strong scientific hypothesis or rich pipeline is more valuable. Payers, acting as the agent for plan members, may want to encourage those areas by paying more for these technologies.

Research has estimated that option value adds about 10% to the "conventional" NMB of technologies treating chronic myeloid leukemia or about 25% to the conventional NMB in the case of breast cancer [36,37]. These studies demonstrate how to incorporate the option value for mortality risks, by accounting for projected increases in survival using established forecasting models. Because these analyses focus on mortality risks alone, the total option value might be even larger.

## Equity

There exists considerable evidence that people care about equity and more generally about the well-being of others in the context of health care. Some public programs—for example, the US Medicaid program—exist primarily because the public is willing to subsidize health care for lower income Americans. We refer to this motive as "altruism." In addition, people might wish for more equal outcomes across rich and poor groups, or across healthy and sick groups. This is distinct from altruism, and we refer to it as the motive for "equity." Depending on the precise definition of equity, some outcomes that are efficient might reflect outcomes that are inequitable, and vice versa. Furthermore, although there may sometimes be a complicated trade-off between efficiency and equity, analysis of these trade-offs is complicated even further because there are different concepts of equity that themselves can involve trade-offs [38].

Despite the long-standing interest in these subjects, relatively few attempts have been made to incorporate altruism or equity formally into assessments of health care value. In terms of the recently promulgated US value assessment frameworks, none directly defines equity or proposes to include an empirical measure of it. DrugAbacus does, however, consider "rarity" and "unmet need" as potential elements [39]. These relate to the severity of illness, but could sometimes be seen as equity considerations: one might argue that patients unlucky enough to suffer from rare, untreated illness are being treated inequitably, compared with their peers, who happen to suffer from treatable conditions. And the Institute for Clinical and Economic Review is planning to include issues concerned with equity and cost-effectiveness by allowing experts to adjust cost-effectiveness thresholds by "contextual considerations," though there is no explicit quantification of these factors [40].

Given a target equity objective, one can gauge how the projected distribution of costs and benefits across the population performs in meeting the objective. Cookson et al. [41] describe two methodologies for addressing health equity concerns: 1) equity impact analysis and 2) equity trade-off analysis. The former "quantifies the distribution of costs and effects by equity-relevant variables …" and the latter "quantifies trade-offs between improving total health and other equity objectives." "Extended" CEA—an example of the former—has been developed and applied to evaluate a wide range of global health interventions [42] (see also the discussion in the section by Phelps et al [43]). Asaria et al. [44] also cite "distributional" CEA as another type of equity impact analysis, focusing on the impact on the distribution of health opportunity costs among different subgroups. They also describe two types of equity trade-off analyses: 1) equity constraint analysis and 2) equity weighting analysis. The former estimates the efficiency sacrificed to meet an equity objective, and the latter requires the specification of equity weights that can be used to compare how a policy affects both equity and efficiency.

Baltussen et al. [45] comment that these approaches can be seen as a kind of multicriteria decision analysis (also described in the section by Phelps et al [43]). Welfare economics does not imply a particular notion of equity, but as with CEA, distributional impacts can be projected and evaluated given some externally provided equity criteria. For example, Morton [46] proposes a welfare economics approach in which the social planner places less weight on health gains for those who are already healthier. Furthermore, many deliberative HTA bodies, charged with technology adoption decisions or negotiations on access and price, consider equity.

It remains unclear how equity enters the preferences of voters, taxpayers, or consumers. For instance, do consumers focus on equity in overall well-being, or specifically on equity in health? Or do they ignore equity in itself, but instead value increases in health for the poor, independent of the level of inequity? Note that these questions are distinct; for example, consumers may value increases in health, but also value equity in overall well-being. Finally, researchers need to understand better the costs of redistributing wealth and the cost of redistributing health. For example, if consumers have preferences over both equity in well-being and equity in health, the relative costs of redistribution become important. Thus, incorporating equity into HTA remains an important area for future research.

## Scientific Spillovers

Another widely discussed but underdeveloped element of value pertains to the impact of a new technology on future generations of patients. For example, a drug with a new mechanism of action might not in itself be very valuable, but the knowledge that the mechanism works might lead to other more valuable drugs in the future, even to treat very different diseases. The first drug unlocked the value of the later innovations. To account for this element, some value assessment frameworks—either proposed or in use—have some allowance for the "scientific novelty" of a therapy. Currently, it is not so clear how these approaches are operationalized or how this concept is valued. It has been argued that conventional CEA augmented to include additional elements of utility, as we have described it thus far, has overlooked the externality on future innovation, sometimes called scientific spillovers [32,47].

Scientific spillovers occur "when the benefit of scientific advances cannot be entirely appropriated by those making them" [32]. This may be important, because the patent system requires a quid pro quo in that the innovator must share the knowledge about the science of their invention. Others can learn from and build upon it. All this creates a "commons" problem implying potential underinvestment: payers, as agents of the patients, may wish to reward developers with higher prices to encourage knowledge generation [22,24]. As with equity, the empirical implications of scientific spillovers for value remain a fertile area for future research, although the economic literature on innovation has made relevant progress. Early literature makes the case that innovations with little stand-alone value still merit patent protection if they stimulate follow-on innovation [48]. Economists have empirically documented the causal effect of early innovation on future breakthroughs using National Institutes of Health funding as a natural experiment and clinical trial starts as an outcome [49]. And studies have shown that the extent of spillover varies with institutions such as patent rights using the public human genome project as a comparator to the company Celera's patent-protected genome sequencing discoveries [50]. These studies are the exceptions that prove that clean measures of innovation outcomes and compelling empirical identification of causal increases in "original" innovation are often difficult to come by.

## Conclusions

In this section, we have described a series of elements that deserve consideration in value assessments of health care technologies. Our discussion of some of the more novel elements of value broadens the view of what constitutes value in health care over and above QALYs and costs. In fact, a number of regulatory authorities around the globe have shown interest in some of these novel elements discussed here, thus suggesting the need for more systematic research to expand the frame of CEA. For example, in England, the National Institute for Health and Care Excellence allows its technology appraisal committee to assign a higher value to QALYs gained at end of life, defined as having a life expectancy of less than 2 years [51]. In Sweden, although there is no official cost-per-QALY threshold, the Dental and Pharmaceutical Benefits Board (*Tandvårds- och läkemedelsförmånsverket*) makes adjustments in its decisions to take of other criteria, including "need" that is related to disease severity [52]. Finally, other jurisdictions, such as Scotland and Premera (a health plan in the US Pacific Northwest), take account of whether there is a lack of other treatments of proven therapeutic benefit for the condition concerned, or "unmet need" [53,54].

To pursue a careful and systematic program of research in the elements of value, we would recommend the following:

1. Despite its challenges, the QALY remains the most accepted measure for capturing the incremental benefit of a treatment for use in population-level decision making. Nevertheless, some additional elements that may reflect value but are not normally captured in CEA with the QALY should be considered as well, depending on the perspective of the analysis.

2. Productivity gains, net of consumption, should be included for societal-level perspectives in the incremental cost calculations for CEA.
3. Best practice for CEA measurement includes capturing the effects (on both outcomes and costs) of real-world behavior such as adherence to an intervention.
4. Some value elements, such as the value of knowing as part of diagnosis, or the psychic fear of contagion, are generally not captured but should be considered when relevant.
5. Other value elements including value of insurance, severity of disease, value of hope, and real option value have been shown to modify QALY estimates, but are not commonly used in CEA. Further research to evaluate their potential for more standard use is warranted.
6. Two other potential value elements—equity (beyond severity effects discussed earlier) and scientific spillover effects—may have individual as well as societal implications; more research on how to measure and incorporate these elements is also suggested.
7. Augmenting CEA to consider these additional elements would result in a more comprehensive CEA in line with the Second Panel's "Impact Inventory."

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## Supplementary Materials

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