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Vanness, David, Lomas, James orcid.org/0000-0002-2478-7018 and Ahn, Hannah (2020) A Health Opportunity Cost Threshold for Cost-Effectiveness Analysis in the United States. Annals of Internal Medicine. ISSN 0003-4819

https://doi.org/10.7326/M20-1392

A Health Opportunity Cost Threshold for Cost-Effectiveness Analysis in the United States

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Running Title: Health Opportunity Cost Threshold for CEA in the US

Financial Support: None.

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Abstract

Background: Cost-effectiveness analysis is an important tool for informing treatment coverage and pricing decisions, yet no consensus exists about what threshold for the incremental cost-effectiveness ratio (ICER) in dollars per quality-adjusted life year gained (QALY) indicates whether treatments are likely to be cost-effective in the United States (US).

Objective: To estimate a US cost-effectiveness threshold based on health opportunity costs.

Design: Simulation of short-term mortality and morbidity attributable to individuals dropping health insurance due to increased healthcare expenditures passed though as premium increases. Model inputs came from demographic data and the literature; 95% uncertainty intervals (UI) were constructed.

Setting: Population-based.

Participants: Simulated cohort of 100,000 individuals from the US population with direct purchase private health insurance.

Measurements: Per $10,000,000 (USD 2019) population treatment cost increase: the number of individuals dropping insurance coverage, the number of additional deaths, and QALYs lost from increased mortality and morbidity.

Results: Per $10,000,000 (USD 2019) increase in healthcare expenditures, 1860 (95% UI: 1080-2840) individuals were simulated to become uninsured, causing 5 (95% UI: 3-11) deaths, 81 (95% UI: 40-170) and 15 (95% UI: 6-32) QALYs lost from mortality and morbidity, respectively, implying a cost-effectiveness threshold of $104,000/QALY (95% UI: $51,000-$209,000 USD 2019). Given available evidence, there is about 14% probability that the threshold exceeds $150,000/QALY and about 48% probability it lies below $100,000/QALY.

Limitations: Estimates were sensitive to inputs, most notably the effects of losing insurance on mortality and of premium increases on becoming uninsured. Health opportunity costs may vary by population. Non-health opportunity costs were excluded.

Conclusion: Given current evidence, treatments with ICERs above the range $100,000-$150,000/QALY are unlikely to be cost-effective in the US.

Primary Funding Source: None.

Abstract Word Count: 275/275

Introduction

As healthcare spending in the United States (US) continues to rise (1), life expectancy gains have failed to keep pace and are showing signs of reversal (2). Seeking partial explanations for both trends, economists point out that the US healthcare system readily adopts and pays for costly new treatments without requiring improvements in health outcomes to justify those costs (3–8). Spending less on treatments offering little or no improvement in outcomes would allow more spending on other treatments potentially offering larger health gains, while not increasing the overall healthcare budget. Of course, we could simply spend more on healthcare overall, but that would leave us with less to spend on other important determinants of health and well-being, like education, housing, the environment or poverty reduction (9). Either way, if we accept improving population health as a central goal of the healthcare system, then we should seek to use healthcare resources more efficiently.

Cost-effectiveness analysis is a tool for assessing whether a new treatment is an efficient use of limited resources (10). The incremental cost-effectiveness ratio (ICER) measures net resources needed to improve health outcomes by one unit when using a new treatment compared to the next-best available treatment for a condition. The resources considered go beyond just treatment prices and include costs (or savings) resulting from treatment effects over time. Although any measurable health outcome (e.g., complete response, tobacco quits, or %HbA1c) can go in the denominator of an ICER, the most common measure is the quality-adjusted life year (QALY), which integrates differences between treatments in both mortality and health-related quality of life (11). Using a broad measure like the QALY provides a common denominator for comparing the efficiency of treatments across the spectrum of healthcare, from cancer treatment to smoking cessation to diabetes management.

Many countries with centralized systems of healthcare provision or payment use cost-effectiveness to guide treatment coverage and pricing (12). In the United Kingdom (UK), for example, the National Institute for Health and Care Excellence (NICE) generally recommends that treatments with ICERs above a £20,000-£30,000/QALY threshold not be covered by the National Health Service (NHS) in England and Wales (13,14). Thresholds used for recommending coverage or negotiating prices vary across countries; sometimes they are explicitly stated, while other times they are inferred from past decisions (15).

Until recently, cost-effectiveness has played more of an informative and less of a formal role in the US. Due to public and political concerns over rationing, Medicare has long avoided using cost-effectiveness in coverage decisions (16). In 2010, lawmakers even inserted language into the Patient Protection and Affordable Care Act (ACA) preventing Medicare from using a cost-per-QALY threshold to determine treatment coverage (17). So, what's changed? With rapid growth in healthcare costs (and in the amount of those costs paid by patients), clinicians are increasingly aware of "financial toxicity" and its effect on the health of their patients (18,19). Calls for national action have included "value-based pricing" based on cost-effectiveness (20).

The independent, non-governmental Institute for Clinical and Economic Review (*ICER*) has increased the visibility of cost-effectiveness as a tool for payers to negotiate prices (21,22). In 2018, CVS Caremark announced a pharmacy benefits package where treatments with ICERs above $100,000/QALY as assessed by *ICER* risk exclusion from its formulary (23). In 2018, the New York State Drug Utilization Review Board used an *ICER* assessment to recommend the state's Medicaid program pursue a manufacturer's rebate for cystic fibrosis treatment lumacaftor/ivacaftor (Orkambi) to bring its ICER below $150,000/QALY (24). The US Veteran's Administration is also collaborating with *ICER* to support drug coverage and price negotiation using value-based price benchmarks based on a range of cost-effectiveness thresholds from $100,000-$150,000/QALY (25).

The Elijah E. Cummings Lower Drug Costs Now Act (H.R. 3), passed in 2019 by the US House of Representatives (26), would cap federally-negotiated drug prices at 120% of an Average International Market price based on six countries, five of which either explicitly (Australia, Canada, UK) or optionally (France and Germany) use cost-effectiveness in coverage and pricing (27–30), with another (Japan) considering formalizing its use (31). The Congressional Budget Office estimated that H.R. 3 would lower Medicare Part D spending by $456 billion from 2020-2029, assuming the federal government will not agree to prices resulting in an ICER exceeding $520,000/QALY (32,33). Although its status is unknown (34), a presidential executive order issued on July 24, 2020 would tie Medicare Part B drug prices to those in “economically comparable” countries, many of which base pricing and coverage on cost-effectiveness. These actions may pressure manufacturers to be more open to cost-effectiveness analysis in the US, preferring prices negotiated under a US threshold to being tied to other countries where thresholds are likely lower (35).

In this paper, we assess potential cost-effectiveness thresholds for the US using a health opportunity cost approach. This approach starts with the assumption that we wish to get the most population health for what we already spend on healthcare. The question of whether we spend too much or too little on healthcare overall is set aside temporarily. Holding healthcare spending fixed, covering a new, more costly treatment potentially benefitting one group of patients means spending less on other healthcare received by other patients. Health opportunity cost reflects the health lost among patients for whom healthcare expenditures are reduced to pay for the new treatment. When a new treatment costs more per QALY gained than the healthcare it displaces, then health opportunity costs exceed health benefits, and overall population health (measured in QALYs) declines (36). The point where this occurs defines the threshold.

In countries with fixed healthcare budgets and centralized decision-making, health opportunity cost makes a lot of sense. That's why, for example, researchers have based estimates of the UK cost-effectiveness threshold on how much health is lost when less care is provided to the NHS patient population (largely through decreased services, including longer wait times and more restrictive treatment eligibility criteria) to pay for a new treatment (37–40). These estimates suggest that services displaced when paying for new treatments in the UK cost about £5,000-£15,000 to produce one QALY (38), well below the £20,000-£30,000/QALY threshold that NICE uses to judge cost-effectiveness.

The Second US Panel on Cost-Effectiveness in Health and Medicine (US Panel) and *ICER* have both called for research on opportunity cost-based cost-effectiveness thresholds for the US (41,42). However, in the US, there is no single defined budget for healthcare, and costs are spread across health insurance risk pools funded by taxes and premiums. Identifying where health opportunity costs fall is more challenging. To overcome this challenge, we relax the assumption that healthcare expenditures are fixed and instead consider what happens when private insurers spend more, but increase premiums to cover costs (41,43–45). We identify health opportunity costs for the US population with direct purchase health insurance based on empirical estimates of the percentage of plan members likely to drop coverage when premiums increase, experiencing increased mortality and morbidity as a result.

Methods

The first step in our simulation was to estimate how many individuals would become uninsured due to a premium increase. We simulated a cohort having the same age distribution as the US population covered by direct purchase insurance (46). Using 2019 average ACA Marketplace premiums (47) as a baseline, we then estimated the percentage premium increase necessary for an insurance plan to fully pass along a hypothetical healthcare cost increase to plan members. Using estimates of the percent of plan members becoming uninsured per percent premium increase (known as the premium elasticity of coverage) by age group from a study of ACA Marketplace premium increases (48), we simulated the number who would become uninsured by year of age.

The second step was to estimate how much mortality and morbidity would likely result among individuals losing insurance coverage in step one. Using an estimate of the number needed to gain health insurance to avert one death over a short time horizon from a study of mortality reductions associated with ACA Medicaid expansion (49), we solved for the implied relative risk of mortality from becoming uninsured, which, when applied to mortality rates by age from US life tables (50) in proportion to the age distribution of those simulated to drop coverage in step one, would yield the expected number of deaths in one year. This allowed us to apportion deaths attributable to becoming uninsured to each year of age, reflecting varying baseline mortality. We estimated QALYs lost due to mortality accounting for remaining life expectancy using US life tables, to which we applied health-related quality of life (SF-6D-12V2) by year of age estimated from the National Health Measurement Study (51). Lost quality-adjusted life expectancy was discounted at 3% per year, following US Panel recommendations (41). Finally, we estimated QALYs lost due to morbidity attributable to becoming uninsured among survivors for one year. Based on a recent evidence synthesis (52), we assumed 10% of morbidity is amenable to healthcare. We further assumed losing insurance had the same proportional effect on amenable morbidity as it had on mortality.

Using these estimates, we then calculated health opportunity costs as QALYs lost per each additional dollar spent (2019 USD). We note that multiplying additional expenditures by a factor results in a directly proportional effect on QALYs lost. Therefore, the health opportunity cost ratio stays constant for any hypothetical cost increase. For similar reasons, the health opportunity cost ratio does not vary with cohort size. For interpretability, we report QALYs lost attributable to a hypothetical $10,000,000 expenditure increase in a cohort of 100,000 plan members, causing a $100 (1.6%) per-member per year premium increase. The implied cost-effectiveness threshold is the reciprocal of the health opportunity cost ratio.

Because our model inputs come from uncertain estimates, we used a Bayesian approach to see how uncertainty affects the threshold. We repeated the simulation 50,000 times, using different sets of model inputs randomly chosen from probability distributions with means and spreads reflecting available evidence about each input's likely value. We estimated the probability that the threshold exceeds a specified value by counting the number of times the simulated threshold exceeded that value and dividing by 50,000. For policy relevance, we assessed the probabilities that the threshold lies above and below the $100,000-$150,000/QALY range *ICER* uses for value-based pricing (42). For a detailed description of our simulation, see the Technical Appendix.

Role of the Funding Source

None.

IRB Approval

Our study was not human subjects research as covered under 45 CFR part 46.

Results

For each additional $10,000,000 (USD 2019) in healthcare expenditures, about 1,860 (95% UI: 1,080-2,840) individuals with direct purchase private insurance were simulated to become uninsured due to passed-through premium increases, causing 5 additional deaths (95% UI: 3-11), 81 QALYs lost due to mortality (95% UI: 40-170) and 15 QALYs lost due to morbidity (95% UI: 6-32). A new treatment with incremental cost of $10,000,000 would therefore need to increase QALYs by at least 96 (95% UI: 48-195) to avoid reducing total population health, implying a threshold of $\$10{,}000{,}000/96\ \text{QALYs} = \$104{,}000/\text{QALY}$ (95% UI: $51,000-$209,000 USD 2019).

The threshold exceeded $150,000/QALY in 7,006/50,000 simulations, suggesting 14% probability that the threshold exceeds $150,000/QALY (Figure 1). The threshold was less than $100,000/QALY in 23,902/50,000 simulations, suggesting 48% probability that the threshold lies below $100,000/QALY. Input base case values and one-way sensitivity analysis results are presented in Table 1 (for additional details see Appendix Tables 1 and 2 and Appendix Figure 1). Estimated thresholds were most sensitive to the effect of losing insurance on mortality followed by premium elasticity of coverage among 18-34-year-olds, and 35-54-year-olds. Input values indicating a larger effect of becoming uninsured on mortality and morbidity, a larger number of individuals dropping coverage due to premium increases, or a larger proportion of costs passed through to plan members increased the opportunity cost and therefore lowered the threshold.

Discussion

Historically, US cost-effectiveness studies have compared ICERs to a variety of thresholds ranging from roughly $50,000-$300,000/QALY (53–56). The lower end of that range has been justified on an apocryphal argument that Medicare revealed its willingness to pay per QALY by creating a special program covering dialysis for end-stage renal disease, a treatment supposedly having an ICER of about $50,000/QALY (53). The upper end of that range is supported by Braithwaite et al., who estimated individual willingness to pay to reduce morbidity and mortality through purchases of private insurance that increase healthcare use (56). Our uncertainty analysis suggests that these bounds are likely inconsistent with a threshold based on health opportunity costs, given available evidence (Figure 1).

Recently, Phelps derived a threshold directly from principles of individual economic choice (57). Assuming individuals with typical aversion to financial risk balance their expenditures on health and other consumption over time to maximize their expected well-being, Phelps found that individuals with incomes of $50,000 (approximately US per-capita disposable personal income of $50,731 in December 2019) (58) should be willing to pay twice that amount ($100,000) to increase quality-adjusted life expectancy by one QALY. This result is close to our own base case estimate of $104,000/QALY despite being based on a very different approach.

All three of the thresholds referenced above are grounded in "welfarist economics," where individuals make choices to maximize their overall well-being, not just their health (59,60). If consumers are rational and well-informed about the true benefits and costs of healthcare relative to other things they could do with their money, and if healthcare is bought and sold in a perfectly competitive market, then willingness to pay per QALY should coincide with the full opportunity cost of healthcare expenditures (61).

Our analysis cannot make such a claim. First, although we rely on empirical estimates of individuals choosing whether or not to continue purchasing health insurance when premiums increase, we do not assume their choices are fully informed or made in perfectly competitive markets. Health economists have long recognized that healthcare is unlike other goods and services because full information about its benefits is never known by all parties in advance (62), and many factors about the US market for healthcare cause prices to differ from actual costs (63,64), A reviewer noted that if consumers underestimate the health risks of becoming uninsured, then observed premium elasticity of coverage may be higher than optimal, and our estimate could serve as a lower bound for the willingness to pay threshold.

Second, our analysis considered just one possible mechanism of action, or as economists like to say, one margin – the effect of treatment cost increases on direct purchase private insurance premiums and insurance coverage. We did not consider other relevant margins – for example, the possible effects of increasing healthcare costs on patient co-pays or wait times, or on the offering and generosity of employer-sponsored insurance coverage or on public insurance programs such as Medicare and Medicaid. In such cases, the opportunity costs of increasing healthcare expenditures will be borne by someone (e.g., on the health and finances of insured patients, the take-home income of employees, on taxpayers or beneficiaries of other government expenditures). The existence of multiple margins emphasizes that there are many potential opportunity costs in the heterogeneous US health economy, and therefore a range of thresholds may be valid.

Third, we do not estimate the full opportunity cost of increased healthcare expenditures (including reduced overall well-being from consuming less goods and services like housing, food or education, from reduced savings, or from the lost value of financial risk protection that having health insurance is meant to confer). Rather, we frame our argument on health opportunity costs alone. While our approach is incomplete from the standpoint of welfarist economics, it is consistent with so-called "extra-welfarism (59,65)." Under that framework, the goal of health policy-makers is to maximize total population health given available healthcare resources, a goal that requires understanding health opportunity costs. We believe this perspective is valid and compelling. By focusing on health opportunity costs, the trade-off between the health of identified patients and the overall population is brought to the surface.(66)

Other studies have estimated US thresholds based on health opportunity costs by extrapolating from other countries. Using estimates for the UK by Claxton et al. (37), Woods et al. estimated a range for the US threshold of $24,283-$40,112/QALY (67). Their analysis assumes a consistent relationship between GDP per capita and health opportunity costs across several countries, which given fundamental differences between the US healthcare system and others, may be strained. Ochalek and Lomas estimated the US threshold to be $60,475-$97,851 per disability-adjusted life year (DALY) averted based on cross-sectional country-level estimates of disability and life-expectancy as a function of national expenditures on healthcare and other determinants of health, including income, education and sanitation (68). Beyond difficulties in comparison due to the use of DALYs (69), their range may be lower than ours due to the ecological assumption that the relationship of healthcare expenditures to health outcomes across countries applies to within the US.

Our approach has other limitations. Although informed by theory and empirical estimates, our model inputs are uncertain. For example, estimates of the premium elasticity of coverage vary substantially (70–72). We used an estimate by Saltzman (48) due to its recency, its focus on the ACA Marketplace, and its estimation of elasticity by age group, which we felt was important given age-related differences in morbidity and mortality. While the weight of evidence demonstrates that extending health insurance coverage reduces morbidity and mortality, estimates of that effect vary widely (73–76). We chose the midpoint of a range of 239-316 individuals needed to gain insurance to avert one death for those newly covered by Medicaid expansions in California and Washington estimated by Sommers (49). Individuals who gained Medicaid coverage may differ from those covered by direct purchase private insurance; however we note that many people cycle between Medicaid, direct purchase insurance and being uninsured (77). Sommers noted that up to 20% of the estimated mortality reduction may have come from increased use of antiretroviral drugs for HIV in the late 1990s and early 2000s. A recent study by Borgschulte and Vogler of post-ACA Medicaid expansions from 2014 to 2017 estimated that 310 individuals would need to gain insurance to avert one death (75), which is within the 239-316 range estimated by Sommers. Our sensitivity analysis range is wider still (Range: 65-701, 95%UI 155.9-435.1), reflecting substantial uncertainty. Using the Borgschulte and Vogler estimate would increase our estimated threshold to $115,000/QALY.

We also note that our analysis assumes health opportunity cost in QALYs lost per dollar spent is a constant ratio, regardless of the magnitude of additional health expenditures considered. Blockbuster treatments for common chronic diseases, or those that offer potential cures for uncommon but life-threatening diseases, may be cost-effective when assessed against a fixed threshold, but not be affordable (78). As such treatments claim a larger share of a healthcare budget, opportunity costs may increase disproportionately – effectively lowering the threshold (79). Price negotiations for treatments with large budget impacts could target the lower end of a range of threshold values to account for affordability (80).

Given overall uncertainty about cost-effectiveness thresholds, it would be prudent to avoid the temptation to set in stone any single threshold as the sole test for determining whether treatments are of individual or social value (81). While there have been attempts to broaden economic evaluation of new treatments beyond costs per QALY gained (82), we must recognize that cost-effectiveness analysis, as currently practiced, largely ignores important ethical considerations, including concerns for equity and the instrumental value of human life regardless of age or underlying health (83).

New treatments are often rightly met with enthusiasm from patient groups and clinicians, but the health consequences that increased treatment costs have on others in the healthcare system more broadly also tend to be ignored. Individuals bearing health opportunity costs through the mechanism we describe are likely to come from poorer population groups lacking political constituency. In a review of health economist Uwe Reinhardt's final work, *Priced Out*, Jeff Goldsmith notes: "those who remain out in the cold [the uninsured] are a diverse bunch, united only by their marginality or invisibility and lacking organized advocacy in Congress (84)."

Although we cannot expect individual clinicians to consider the health of any patients other than their own while at the bedside, the health opportunity costs borne by anonymous members of society remain an ethical and policy imperative (66). Collectively, clinicians have substantial power to shape the debate over affordability of care they provide. Clinicians can and do play a role in making healthcare costs visible to the public and to policymakers. The question of whether and where to draw the line on what makes a treatment cost-effective is becoming a matter of urgent economic and clinical significance. Clinicians who are concerned about the effects of increasing costs on patient and population health, or who are wary of the ethical, economic or health consequences of using cost-effectiveness thresholds should engage in this debate.

Despite the limitations of our analysis, and of cost-effectiveness more broadly, we believe it is reasonable to expect that when an authority, be it a government agency or a private insurance plan, agrees on whether or how much to pay for a treatment, that decision will, "first, do no harm" to population health. Setting cost-effectiveness thresholds too high (or ignoring them altogether) sustains current conditions for a self-reinforcing cycle of escalating healthcare costs and continued disappointing progress on improving population health.

Protocol: not available

Simulation Code: Available on GitHub: https://github.com/djvanness/USthreshold

Data: National Health Measurement Study available at: https://www.disc.wisc.edu/archivereport/downloadForm2.asp

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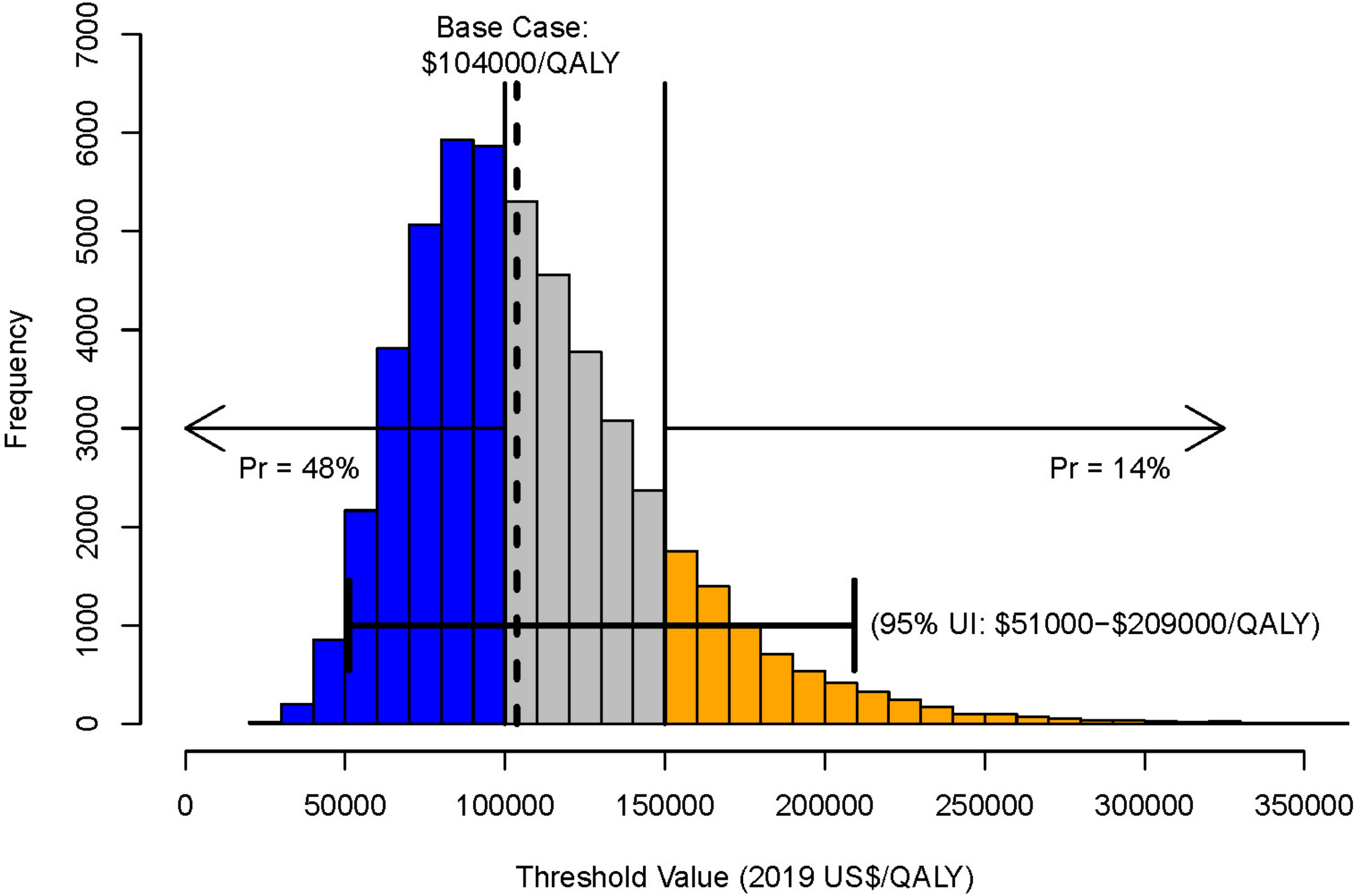
Table 1. Key Input Values and One-Way Sensitivity Analysis Results

Model Input (units)*	Input Base Case Value	Input 95% Uncertainty Interval	Threshold 95% Uncertainty Interval 2019 USD/QALY**	Input Values: Threshold < $100,000/QALY	Input Values: Threshold > $150,000/QALY	Source
Number needed to lose insurance to result in one expected death in one year (persons)	277.5	(155.9 to 435.1)	($61,000 to $157,000)	< 267	> 414	Sommers(49)
Premium elasticity of coverage: age 18-34 (%/%)	-1.5	(-2.38 to -0.62)	($78,000 to $152,000)	< -1.6	> -0.65	Saltzman(48)
Premium elasticity of coverage: age 35-54 (%/%)	-1.05	(-1.78 to -0.43)	($81,000 to $136,000)	< -1.15	> -0.24	Saltzman(48)
Percentage of additional costs passed through as premium increases (%)	100%	(83% to 117%)	($125,000 to $89,000)	> 104%	< 69%	Assumption
Baseline annual direct purchase private insurance premium (2019 USD)	$6,214	($5,147 to $7,369)	($86,000 to $123,000)	< $5,993	> $8,990	Centers for Medicare and Medicaid Services(47)
Percentage of morbidity amenable to healthcare (%)	10%	(5.7% to 15.5%)	($111,000 to $95,000)	> 12.2%	NV	Kaplan and Milstein(52)
Premium elasticity of coverage: age 55-64 (%/%)	-0.7	(-1.23 to -0.28)	($99,000 to $105,000)	< -1.16	NV	Saltzman(48)

*Inputs are ordered from most to least influential on the width of the 95% uncertainty interval for the resulting threshold value.

**The ordering of values in the threshold 95% uncertainty intervals corresponds with the ordering of inputs in the input 95% uncertainty interval.

NV = No value for this input can cause the threshold to exceed $150,000/QALY when all other inputs are fixed at their base case value.



Base Case:
$104000/QALY
Pr = 48%
Pr = 14%
(95% UI: $51000−$209000/QALY)
Frequency
0
1000
2000
3000
4000
5000
6000
7000
0
50000
100000
150000
200000
250000
300000
350000
Threshold Value (2019 US$/QALY)

Figure 1. Frequency of calculated threshold values in 50,000 simulations with varying input values. Blue shaded area contains 23,902/50000 = 48% threshold values less than $100,000/QALY and orange shaded area contains 7,006/50,000 = 14% threshold values greater than $150,000/QALY. Horizontal error bar depicts the 95% uncertainty interval. The vertical dashed line depicts the base case estimate of $104,000/QALY.