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

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

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30 **Abstract**

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

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

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

40 **Setting:** Population-based.

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

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

46 **Results:** Per \$10,000,000 (USD 2019) increase in healthcare expenditures, 1860 (95% UI:
47 1080-2840) individuals were simulated to become uninsured, causing 5 (95% UI: 3-11)
48 deaths, 81 (95% UI: 40-170) and 15 (95% UI: 6-32) QALYs lost from mortality and
49 morbidity, respectively, implying a cost-effectiveness threshold of \$104,000/QALY (95% UI:
50 \$51,000-\$209,000 USD 2019). Given available evidence, there is about 14% probability that
51 the threshold exceeds \$150,000/QALY and about 48% probability it lies below
52 \$100,000/QALY.

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

56 **Conclusion:** Given current evidence, treatments with ICERs above the range \$100,000-
57 \$150,000/QALY are unlikely to be cost-effective in the US.

58 **Primary Funding Source:** None.

59

60 Abstract Word Count: 275/275

61 **Introduction**

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

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

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

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

102 The independent, non-governmental Institute for Clinical and Economic Review
103 (*ICER*) has increased the visibility of cost-effectiveness as a tool for payers to negotiate
104 prices (21,22). In 2018, CVS Caremark announced a pharmacy benefits package where
105 treatments with ICERs above \$100,000/QALY as assessed by *ICER* risk exclusion from its
106 formulary (23). In 2018, the New York State Drug Utilization Review Board used an *ICER*
107 assessment to recommend the state's Medicaid program pursue a manufacturer's rebate for
108 cystic fibrosis treatment lumacaftor/ivacaftor (Orkambi) to bring its ICER below
109 \$150,000/QALY (24). The US Veteran's Administration is also collaborating with *ICER* to

110 support drug coverage and price negotiation using value-based price benchmarks based on a
111 range of cost-effectiveness thresholds from \$100,000-\$150,000/QALY (25).

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

125 In this paper, we assess potential cost-effectiveness thresholds for the US using a
126 health opportunity cost approach. This approach starts with the assumption that we wish to
127 get the most population health for what we already spend on healthcare. The question of
128 whether we spend too much or too little on healthcare overall is set aside temporarily.
129 Holding healthcare spending fixed, covering a new, more costly treatment potentially
130 benefitting one group of patients means spending less on other healthcare received by other
131 patients. Health opportunity cost reflects the health lost among patients for whom healthcare
132 expenditures are reduced to pay for the new treatment. When a new treatment costs more per
133 QALY gained than the healthcare it displaces, then health opportunity costs exceed health

134 benefits, and overall population health (measured in QALYs) declines (36). The point where
135 this occurs defines the threshold.

136 In countries with fixed healthcare budgets and centralized decision-making, health
137 opportunity cost makes a lot of sense. That's why, for example, researchers have based
138 estimates of the UK cost-effectiveness threshold on how much health is lost when less care is
139 provided to the NHS patient population (largely through decreased services, including longer
140 wait times and more restrictive treatment eligibility criteria) to pay for a new treatment (37–
141 40). These estimates suggest that services displaced when paying for new treatments in the
142 UK cost about £5,000-£15,000 to produce one QALY (38), well below the £20,000-
143 £30,000/QALY threshold that NICE uses to judge cost-effectiveness.

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

154 **Methods**

155 The first step in our simulation was to estimate how many individuals would become
156 uninsured due to a premium increase. We simulated a cohort having the same age distribution
157 as the US population covered by direct purchase insurance (46). Using 2019 average ACA
158 Marketplace premiums (47) as a baseline, we then estimated the percentage premium

159 increase necessary for an insurance plan to fully pass along a hypothetical healthcare cost
160 increase to plan members. Using estimates of the percent of plan members becoming
161 uninsured per percent premium increase (known as the premium elasticity of coverage) by
162 age group from a study of ACA Marketplace premium increases (48), we simulated the
163 number who would become uninsured by year of age.

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

181 Using these estimates, we then calculated health opportunity costs as QALYs lost per
182 each additional dollar spent (2019 USD). We note that multiplying additional expenditures by
183 a factor results in a directly proportional effect on QALYs lost. Therefore, the health

184 opportunity cost ratio stays constant for any hypothetical cost increase. For similar reasons,
185 the health opportunity cost ratio does not vary with cohort size. For interpretability, we report
186 QALYs lost attributable to a hypothetical \$10,000,000 expenditure increase in a cohort of
187 100,000 plan members, causing a \$100 (1.6%) per-member per year premium increase. The
188 implied cost-effectiveness threshold is the reciprocal of the health opportunity cost ratio.

189 Because our model inputs come from uncertain estimates, we used a Bayesian
190 approach to see how uncertainty affects the threshold. We repeated the simulation 50,000
191 times, using different sets of model inputs randomly chosen from probability distributions
192 with means and spreads reflecting available evidence about each input's likely value. We
193 estimated the probability that the threshold exceeds a specified value by counting the number
194 of times the simulated threshold exceeded that value and dividing by 50,000. For policy
195 relevance, we assessed the probabilities that the threshold lies above and below the \$100,000-
196 \$150,000/QALY range *ICER* uses for value-based pricing (42). For a detailed description of
197 our simulation, see the Technical Appendix.

198 *Role of the Funding Source*

199 None.

200 *IRB Approval*

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

202 **Results**

203 For each additional \$10,000,000 (USD 2019) in healthcare expenditures, about 1,860
204 (95% UI: 1,080-2,840) individuals with direct purchase private insurance were simulated to
205 become uninsured due to passed-through premium increases, causing 5 additional deaths
206 (95% UI: 3-11), 81 QALYs lost due to mortality (95% UI: 40-170) and 15 QALYs lost due to
207 morbidity (95% UI: 6-32). A new treatment with incremental cost of \$10,000,000 would
208 therefore need to increase QALYs by at least 96 (95% UI: 48-195) to avoid reducing total

209 population health, implying a threshold of $\$10,000,000/96 \text{ QALYs} = \$104,000/\text{QALY}$ (95%
210 UI: $\$51,000$ - $\$209,000$ USD 2019).

211 The threshold exceeded $\$150,000/\text{QALY}$ in 7,006/50,000 simulations, suggesting
212 14% probability that the threshold exceeds $\$150,000/\text{QALY}$ (Figure 1). The threshold was
213 less than $\$100,000/\text{QALY}$ in 23,902/50,000 simulations, suggesting 48% probability that the
214 threshold lies below $\$100,000/\text{QALY}$. Input base case values and one-way sensitivity
215 analysis results are presented in Table 1 (for additional details see Appendix Tables 1 and 2
216 and Appendix Figure 1). Estimated thresholds were most sensitive to the effect of losing
217 insurance on mortality followed by premium elasticity of coverage among 18-34-year-olds,
218 and 35-54-year-olds. Input values indicating a larger effect of becoming uninsured on
219 mortality and morbidity, a larger number of individuals dropping coverage due to premium
220 increases, or a larger proportion of costs passed through to plan members increased the
221 opportunity cost and therefore lowered the threshold.

222 **Discussion**

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

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

241 All three of the thresholds referenced above are grounded in “welfarist economics,”
242 where individuals make choices to maximize their overall well-being, not just their health
243 (59,60). If consumers are rational and well-informed about the true benefits and costs of
244 healthcare relative to other things they could do with their money, and if healthcare is bought
245 and sold in a perfectly competitive market, then willingness to pay per QALY should
246 coincide with the full opportunity cost of healthcare expenditures (61).

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

256 Second, our analysis considered just one possible mechanism of action, or as
257 economists like to say, one margin – the effect of treatment cost increases on direct purchase

258 private insurance premiums and insurance coverage. We did not consider other relevant
259 margins – for example, the possible effects of increasing healthcare costs on patient co-pays
260 or wait times, or on the offering and generosity of employer-sponsored insurance coverage or
261 on public insurance programs such as Medicare and Medicaid. In such cases, the opportunity
262 costs of increasing healthcare expenditures will be borne by someone (e.g., on the health and
263 finances of insured patients, the take-home income of employees, on taxpayers or
264 beneficiaries of other government expenditures). The existence of multiple margins
265 emphasizes that there are many potential opportunity costs in the heterogeneous US health
266 economy, and therefore a range of thresholds may be valid.

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

278 Other studies have estimated US thresholds based on health opportunity costs by
279 extrapolating from other countries. Using estimates for the UK by Claxton et al. (37), Woods
280 et al. estimated a range for the US threshold of \$24,283-\$40,112/QALY (67). Their analysis
281 assumes a consistent relationship between GDP per capita and health opportunity costs across
282 several countries, which given fundamental differences between the US healthcare system

283 and others, may be strained. Ochalek and Lomas estimated the US threshold to be \$60,475-
284 \$97,851 per disability-adjusted life year (DALY) averted based on cross-sectional country-
285 level estimates of disability and life-expectancy as a function of national expenditures on
286 healthcare and other determinants of health, including income, education and sanitation (68).
287 Beyond difficulties in comparison due to the use of DALYs (69), their range may be lower
288 than ours due to the ecological assumption that the relationship of healthcare expenditures to
289 health outcomes across countries applies to within the US.

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

307 substantial uncertainty. Using the Borgschulte and Vogler estimate would increase our
308 estimated threshold to \$115,000/QALY.

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

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

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

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

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

349

350 Protocol: not available

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

352 Data: National Health Measurement Study available at:

353 <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.

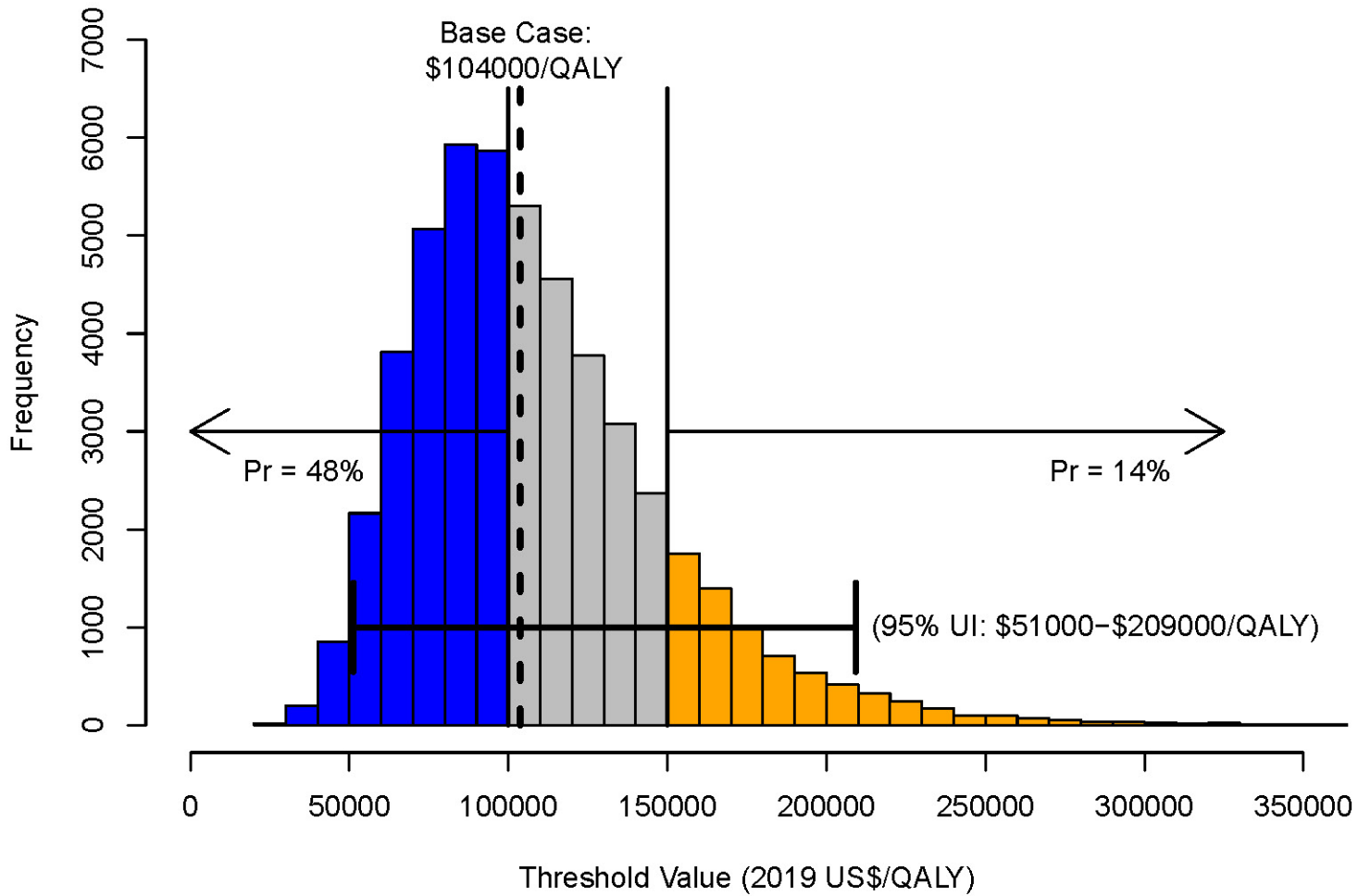


Figure 1. Frequency of calculated threshold values in 50,000 simulations with varying input values. Blue shaded area contains $23,902/50,000 = 48\%$ threshold values less than \$100,000/QALY and orange shaded area contains $7,006/50,000 = 14\%$ threshold values greater than \$150,000/QALY. Horizontal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