Universal Right to Try with Evidence: Potential Impact of Adoption in All 50 States

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Version note. This document is an archival snapshot. Latest interactive version: https://right-to-trial-impact.acceleratedmedicine.org.

Chapter 1

Universal Right to Try with Evidence: Potential Impact of Adoption in All 50 States

1.1 Summary

Universal Right to Try with Evidence[183] would create licensed centers where patients can pay for treatment-related care while eligible participants enroll in standardized, pooled pragmatic trials. Patient and payer revenue can cover treatment delivery, trial-site services, and permitted study costs. Treatments abandoned because nobody can profitably finance conventional Phase 2 and Phase 3 trials become testable.

If all 50 states adopt, the central model estimates:

Result	Conditional central estimate
Treatment-discovery multiplier	5.48x
Average first treatment arrives	181 years earlier
Premature deaths prevented	9.19 billion
Healthy years restored	483 billion DALYs
Disability-equivalent suffering prevented	1.65 quadrillion hours
Campaign plus shared registry cost	$65 million
Philanthropic cost per healthy year restored	$0.000134

These are conditional lifetime schedule-shift totals across future generations. They are not claims that billions of people alive today are saved, or that passage guarantees the modeled effect.

The headline is allowed to be enormous because its conditional parameter uncertainty is visible. The Monte Carlo varies the launch cost, treatment-discovery multiplier, avoidable disease burden, and upstream inputs already in the model. It does not include the chance of political adoption or model-form uncertainty about using the rare-disease queue as a proxy for the global therapeutic frontier.

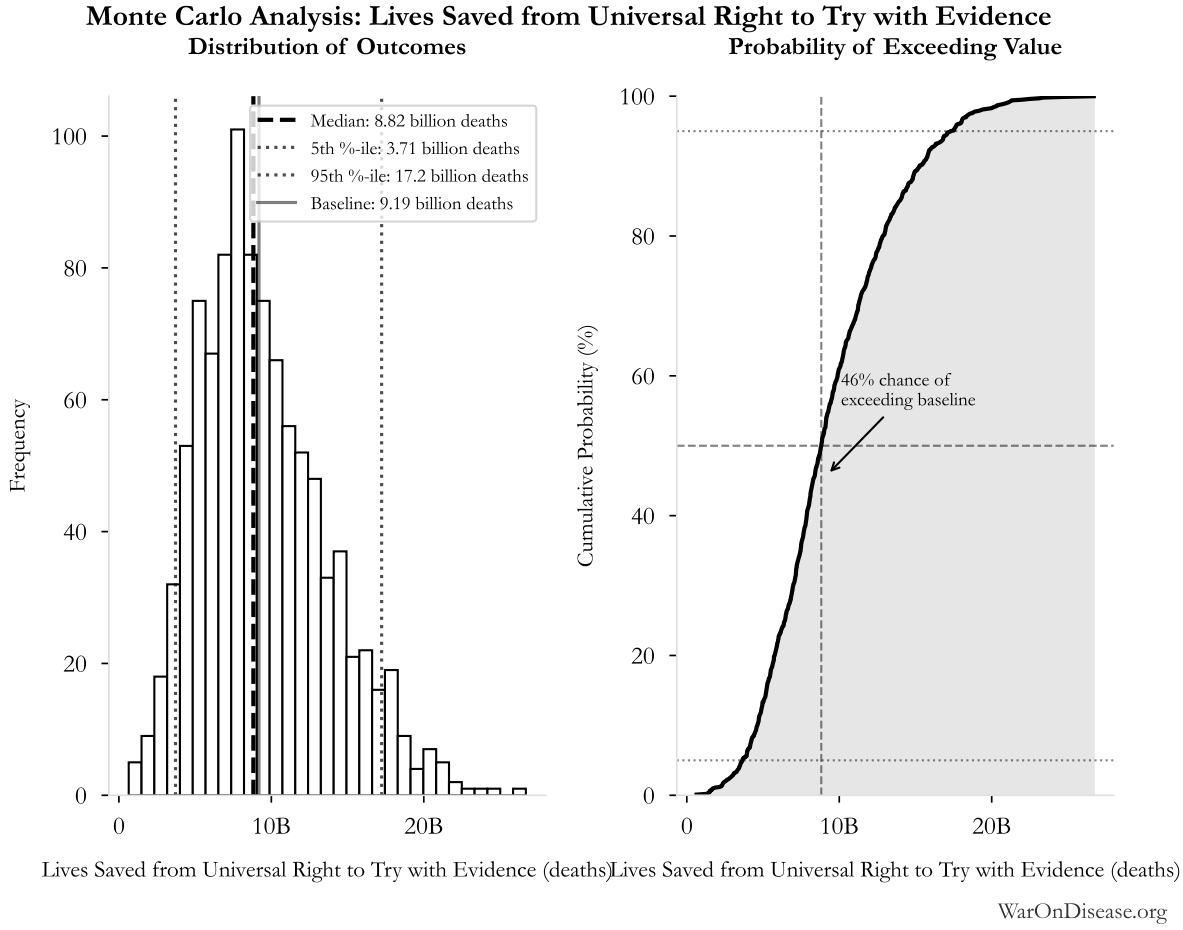


Figure 1.1: Monte Carlo Distribution: Lives Saved from Universal Right to Try with Evidence (10,000 simulations)

Simulation Results Summary: Lives Saved from Universal Right to Try with Evidence

Statistic	Value
Baseline (deterministic)	9.19 billion
Mean (expected value)	9.4 billion
Median (50th percentile)	8.82 billion
Standard Deviation	4.13 billion
90% Range (5th-95th percentile)	[3.71 billion, 17.2 billion]

The histogram shows the distribution of Lives Saved from Universal Right to Try with Evidence across 10,000 Monte Carlo simulations. The CDF (right) shows the probability of the outcome exceeding any given value, which is useful for risk assessment.

1.2 The legislation

Montana has already created licensed experimental treatment centers. Its law covers treatments that have passed Phase 1 but are not approved for general FDA use, permits centers to charge patients, and requires part of center profits to support access[184].

Montana's rules require centers to track treatments and patient outcomes, report serious adverse events, and publish annual aggregate safety and treatment outcomes. The same rules explicitly state that the centers do not administer clinical trials[185]. Outcome tracking is useful. It is not automatically causal evidence.

The model bill therefore adds four requirements:

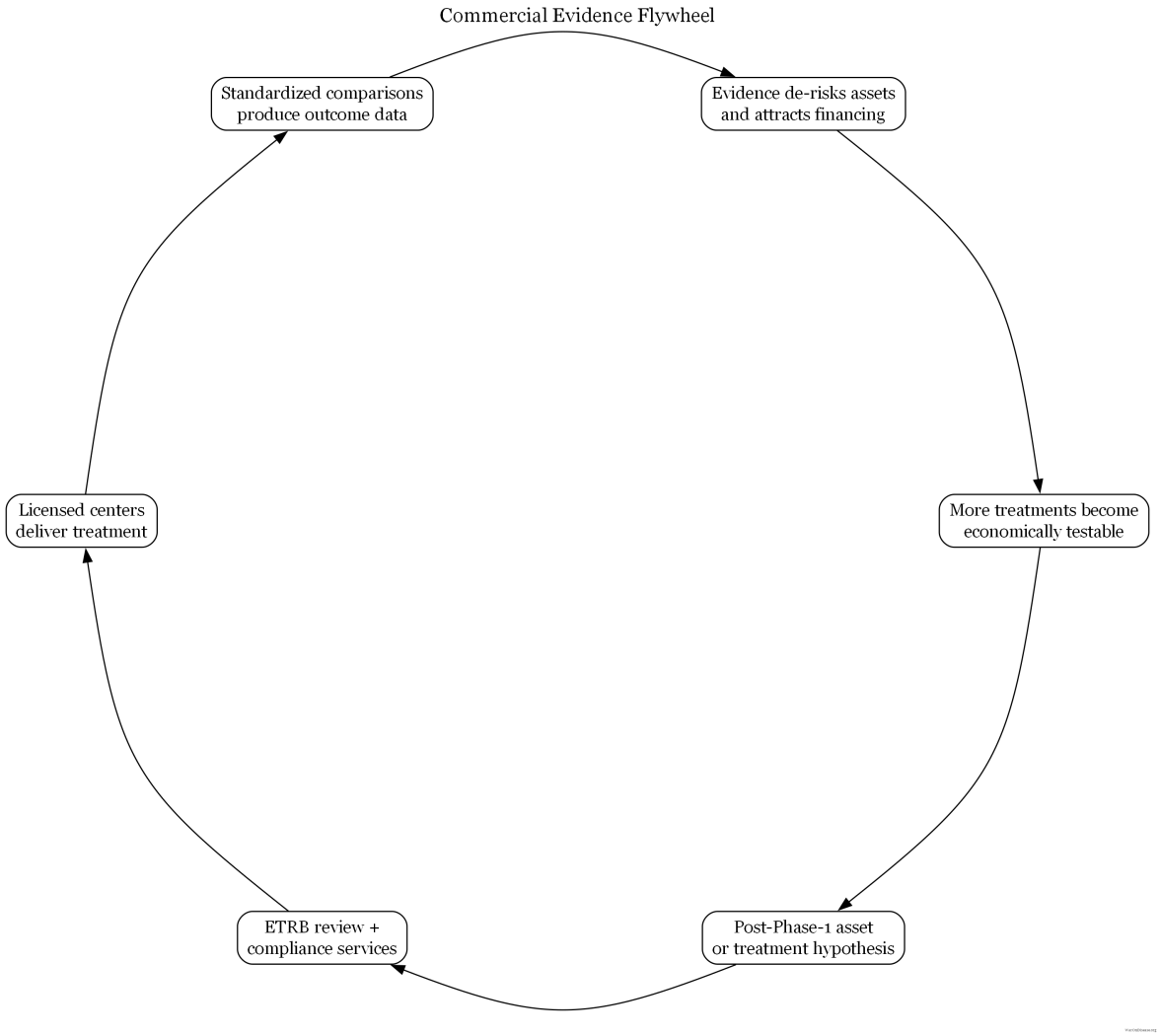
1. **Enroll.** Register a prospective protocol, obtain informed consent, report serious safety events, and place each patient in the applicable federal trial or treatment-access pathway.
2. **Compare.** Prespecify outcomes and use simple randomization or another adequate control when feasible. Without an adequate comparison, label the result a signal, not a validated treatment effect.
3. **Pool.** Send standardized, de-identified baseline and outcome data to a shared registry.
4. **Publish.** Continuously publish results for each treatment-condition pair, including negative and harmful results.

The philanthropic budget pays for the shared registry's first ten years. The model bill requires participating centers to fund continued registry operation through license or enrollment assessments after that launch period. This keeps the lifetime schedule shift from depending on a ten-year data system that then disappears.

1.3 Montana can be the first node

Montana has already done the politically difficult part: it created the licensed-center and independent-review framework. The next move is to make its protocols interoperable, make every eligible treatment generate standardized data and comparable controlled evidence when feasible, and give other states a model they can copy.

Infinita publicly describes a coordinated pathway that includes experimental treatment review board (ETRB) review, licensed clinical administration, monitoring, evidence generation, and early commercialization for post-Phase-1 therapies[186]. That matters because the system is not only a philanthropic expense. Review, compliance, treatment delivery, manufacturing, registry infrastructure, and successful treatment assets can all produce revenue. Revenue can keep evidence generation alive after the original donors go home to fund a building with their name on it.



The flywheel is a map of possible cash flows, not a promise of investor returns. Actual returns depend on treatment demand, lawful charging, reimbursement, liability, protocol quality, and whether the evidence changes clinical or regulatory decisions.

1.4 Same evidence logic, lower collection cost

This does not give a state registry the power to approve drugs or lower the federal evidence standard. It changes where and how effectiveness evidence is produced.

Universal Right to Try with Evidence and federal Right to Try are not the same legal pathway. Federal Right to Try is limited to eligible patients who are unable to participate in a clinical trial involving the drug[187]. A patient enrolled in an interventional pragmatic trial must instead be treated under an active investigational new drug application or another applicable FDA-authorized pathway. Patients who cannot join the trial may still contribute separately labeled observational outcomes through federal Right to Try or expanded access if eligible. The state bill supplies centers, consent, comparison, and shared data rules. It does not waive federal trial authorization or Right to Try

eligibility.

FDA's statutory standard remains substantial evidence from adequate and well-controlled investigations. Its June 2026 draft guidance explains that one rigorous investigation plus confirmatory evidence can sometimes satisfy that standard, while approval still requires sufficient safety evidence and a favorable benefit-risk assessment[188]. FDA also supports streamlined randomized trials integrated into routine clinical practice[189]. Project Pragmatica applies the same design logic to approved oncology products through simpler eligibility, routine-practice enrollment, and reduced data-collection burden while maintaining safety and data integrity[190]. It is an example of pragmatic design, not precedent for bypassing authorization of an unapproved drug.

A pragmatic randomized trial is still a randomized controlled trial. It keeps a comparison group, prespecified outcomes, safety reporting, and reliable analysis. It can reduce dedicated research visits and duplicate data collection when ordinary care can do the job. The existing cost model estimates $41,000 (95% CI: $20,000-$120,000) per participant for a traditional Phase 3 trial versus $929 (95% CI: $97-$3,000) for an embedded pragmatic trial, a 44.1x (95% CI: 12.8x-210x) reduction. That is a per-participant comparison, not a claim that every approval becomes 44.1x (95% CI: 12.8x-210x) cheaper. Complex or high-risk studies will still need specialized sites, procedures, and monitoring.

Federal charging rules remain in force. An IND sponsor needs FDA authorization to charge for the investigational drug and generally may recover only direct drug costs. FDA separately states that trial sites may recover pharmacy, nursing, equipment, and study-related procedure costs without charging authorization under that rule[191]. The model therefore assumes patient or payer revenue covers treatment delivery, site services, and permitted study costs, while center assessments sustain the common registry. It does not assume that states can finance research through unrestricted profits on the investigational drug. Whether lawful revenue is sufficient to sustain the modeled system is part of the uncertain discovery multiplier.

Medicare already uses the analogous payment principle in Coverage with Evidence Development: specified services may be covered only within an approved study while additional evidence is collected, then CMS can reconsider coverage using the resulting evidence[192]. Universal Right to Try with Evidence is access with evidence development, financed primarily by patients and participating centers rather than Medicare. The Continuous Evidence Generation Protocol[193] provides the fuller technical design.

The original Right to Try model spread from its first state in 2014 to 41 states by 2018[194]. That establishes a distribution channel. It does not prove that this broader access-plus-data bill will spread at the same speed.

1.5 Why previously unprofitable treatments matter

Post-Phase-1 compounds, repurposing candidates, combinations, doses, and disease subtypes can each produce multiple treatment hypotheses. The relevant candidate pool is therefore much larger than a count of compounds. No precise inventory exists.

Candidate abundance is not multiplied by global disease burden. Ten successful treatments for one disease cannot avert that disease's burden ten times. Additional candidates matter because they raise the rate at which the first effective treatment is found.

The model compresses the entire causal mechanism into one uncertain input: 5.48x. That input represents all of the following together:

- patient-funded treatment and evidence generation;
- treatments revived because conventional trials were not economically viable;
- enough candidate-condition pairs to keep enrollment capacity occupied;
- protocols capable of producing credible efficacy evidence;
- the share of completed evaluations that find an effective first treatment.

This avoids pretending that patient volume, candidate supply, evaluation size, and success rates are independent benefit multipliers. The automatic Monte Carlo samples the resulting discovery multiplier directly. The 5.48x central value is a calibration assumption, not a measured causal effect.

1.6 Why the model covers global diseases and aging

The goal is to move forward treatments for the entire eventually treatable global burden, including common diseases and aging-related degeneration. The model therefore applies the treatment-schedule shift to global avoidable deaths and DALYs, not only to rare-disease burden.

The status quo treatment queue is built from untreated rare diseases because that is the clearest available count of diseases still awaiting a first effective treatment. Here it serves as a proxy for the pace of exploring the wider therapeutic frontier. That is a strong modeling assumption. It is intentional, not an accidental multiplication of rare-disease benefits by global burden.

1.7 The schedule-shift calculation

At the status quo discovery rate, the average therapeutic target waits 222 years (95% CI: 128 years-420 years) for its first effective treatment. A 5.48x discovery rate moves the average first treatment forward by 181 years.

The global DALY benefit is annual avoidable disease burden multiplied by that schedule shift. Premature deaths use the same schedule shift and global avoidable mortality. Disability-equivalent hours convert the years-lived-with-disability share of DALYs into hours. The full cost-per-DALY chain is:

$$\begin{aligned} & Cost_{RTT,DALY} \\ &= \frac{C_{RTT}}{DALYs_{RTT}} \\ &= \frac{\$65M}{483B} \\ &= \$0.000134 \end{aligned}$$

where:

$$\begin{aligned} & DALYs_{RTT} \\ &= DALYs_{global,ann} \times Pct_{avoid,DALY} \times T_{accel,RTT} \\ &= 2.88B \times 92.6\% \times 181 \\ &= 483B \end{aligned}$$

where:

$$
\begin{aligned}
&T_{accel,RTT} \\
&= T_{first,SQ} \times \left(1 - \frac{1}{k_{RTT}}\right) \\
&= 222 \times \left(1 - \frac{1}{5.48}\right) \\
&= 181
\end{aligned}
$$

where:

$$
\begin{aligned}
&T_{first,SQ} \\
&= T_{queue,SQ} \times 0.5 \\
&= 443 \times 0.5 \\
&= 222
\end{aligned}
$$

where:

$$
\begin{aligned}
&T_{queue,SQ} \\
&= \frac{N_{untreated}}{Treatments_{new,ann}} \\
&= \frac{6{,}650}{15} \\
&= 443
\end{aligned}
$$

where:

$$
\begin{aligned}
&N_{untreated} \\
&= N_{rare} \times 0.95 \\
&= 7{,}000 \times 0.95 \\
&= 6{,}650
\end{aligned}
$$

1.8 Why there is no ramp parameter

This model values a permanent shift in the cure-arrival schedule, not only patient benefits received during the campaign's first decade. A temporary rollout changes the effective start date by a few years. It does not multiply the lifetime benefit by the fraction of mature volume reached in year one.

The discovery multiplier is conditional on full adoption and a mature operating system. If advocacy fails to produce that system, the modeled benefit is not partially rescued by inventing a ramp curve. That political and implementation risk belongs in an external realization-probability adjustment.

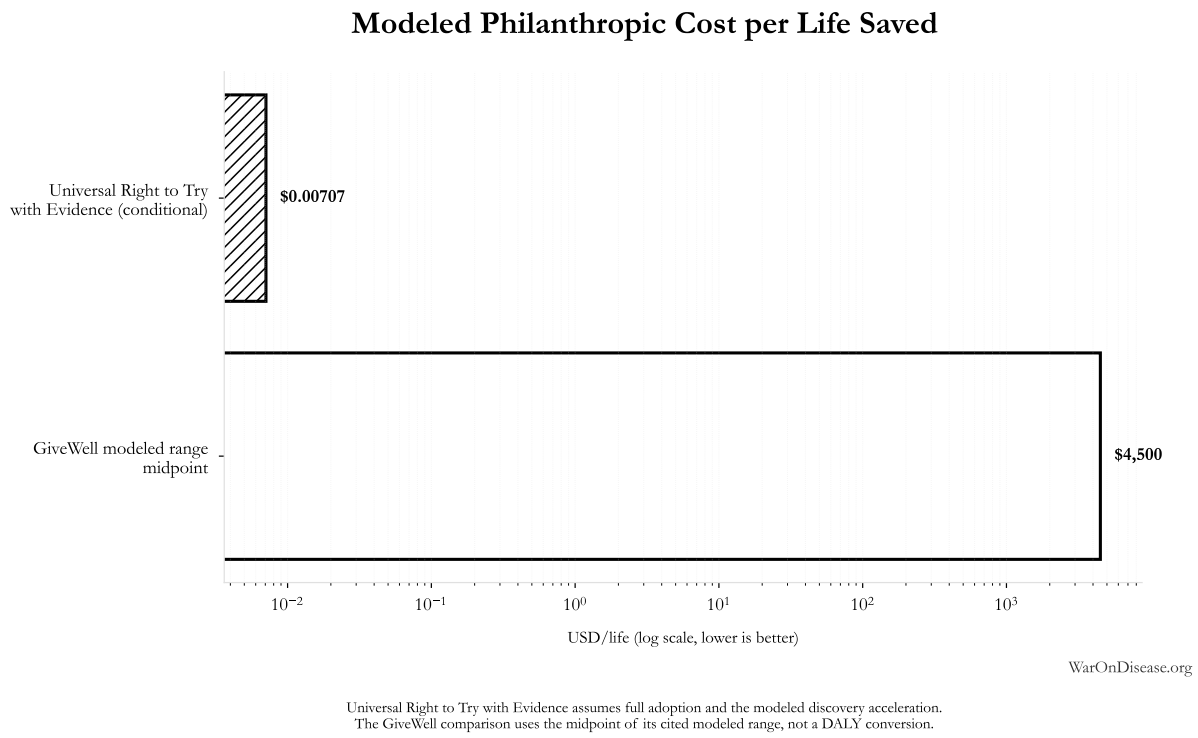
1.9 What the money buys

1.9.1 Philanthropy: an asymmetric bet

Conditional cost per DALY is campaign plus registry-launch cost divided by the health benefit if the 50-state system operates at the modeled discovery rate. It excludes patient or payer spending

on treatment delivery, trial-site services, and permitted study costs because those payments buy care and evidence generation rather than consuming the philanthropic budget.

At the central estimate, Universal Right to Try with Evidence's modeled philanthropic cost per life saved is $0.00707, which is 636.2k times lower than the midpoint of GiveWell's cited modeled range across top charities[9]. This is not because legislation cures people by itself. It is because a relatively small campaign and shared registry are modeled to unlock treatment, sponsor, payer, clinic, and investor spending that philanthropists do not have to supply.



The cost-per-DALY Monte Carlo below shows uncertainty in the conditional estimate itself.

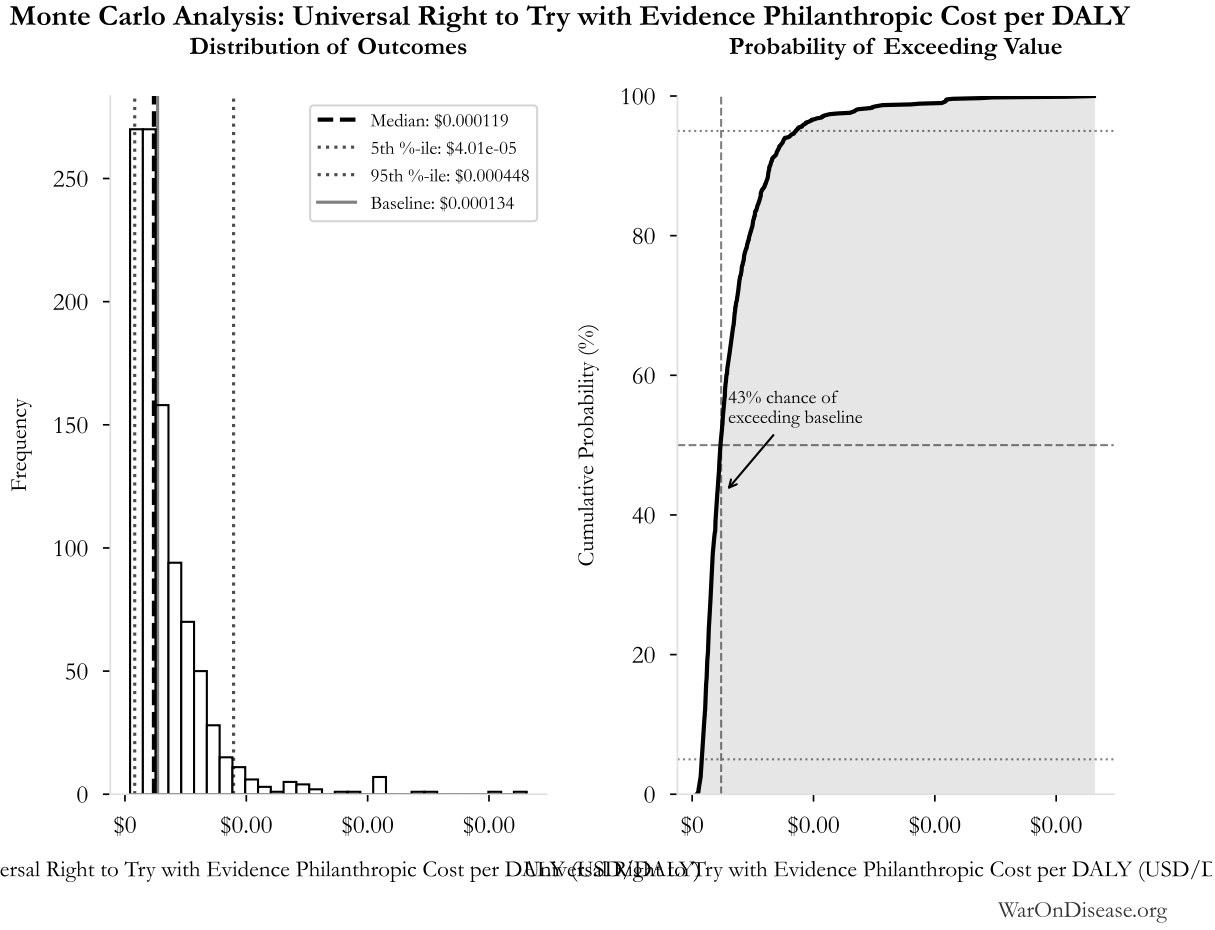


Figure 1.2: Monte Carlo Distribution: Universal Right to Try with Evidence Philanthropic Cost per DALY (10,000 simulations)

Simulation Results Summary: Universal Right to Try with Evidence Philanthropic Cost per DALY

Statistic	Value
Baseline (deterministic)	$0.000134
Mean (expected value)	$0.000171
Median (50th percentile)	$0.000119
Standard Deviation	$0.000192
90% Range (5th-95th percentile)	[$4.01e-05, $0.000448]

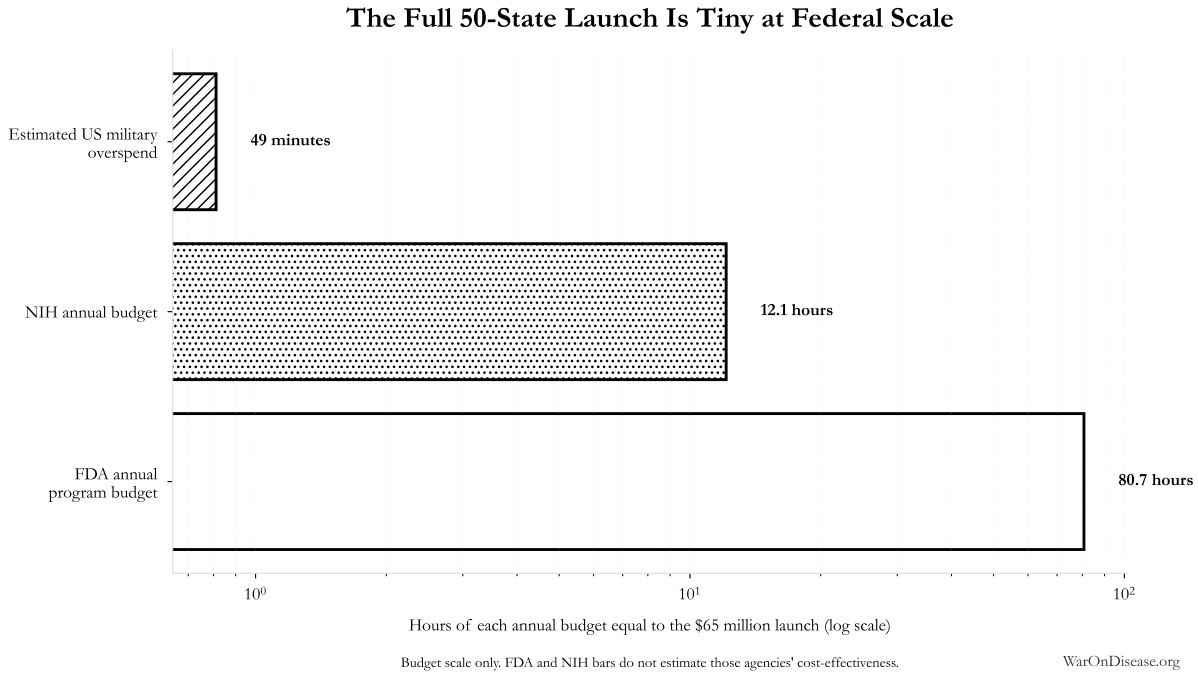
The histogram shows the distribution of Universal Right to Try with Evidence Philanthropic Cost per DALY across 10,000 Monte Carlo simulations. The CDF (right) shows the probability of the outcome exceeding any given value, which is useful for risk assessment.

For a grant decision, multiply conditional lives saved by the donor's own probability that the grant

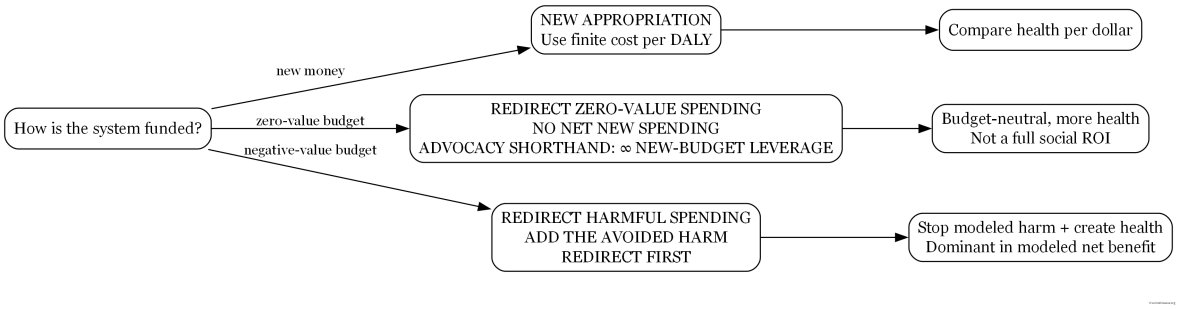
produces full adoption, mature implementation, and the modeled discovery effect. Equivalently, divide conditional cost per life saved by that probability. The probability judgment stays outside the model, so it does not require another scenario parameter.

1.9.2 Government: finite, budget-neutral, or redirect first

The full philanthropic launch is 80.7 hours of the FDA's annual program budget, 12.1 hours of the NIH budget, or 0.811 hours of estimated annual US military overspending[48,108]. This compares budget scale, not the effectiveness of every FDA or NIH dollar.



A normal multiplier works when the government adds spending. Then compare health per dollar. If it redirects existing spending from an activity with zero marginal value without increasing the total budget, there is no net new spending. The advocacy shorthand is **infinite new-budget leverage**, but that is not a conventional social ROI because the real resources still have an opportunity cost. If the displaced activity has negative value, do not divide by a negative denominator. Add the avoided harm to the health benefit and redirect it first.



The cost-benefit analysis of US military hegemony estimates negative marginal returns for spending

above a first-principles baseline for preventing direct attacks on people in the United States, while historical research finds that regime-change wars commonly fail and that most forms of great-power retrenchment do not reliably invite catastrophe[195,196]. On those assumptions, redirecting excess power-projection spending is the chart's **REDIRECT FIRST** case: stop modeled harm, then create modeled health. For the budget request, the decisive fact is that no net new spending is required. Earth only needs one launch.

1.9.3 Impact investors and operators: make evidence pay for itself

Philanthropy pays for the public-good layer that no single company can capture: legislation, common standards, and the shared registry launch. Commercial capital can finance the layers that can earn revenue:

- ETRB review and compliance services;
- licensed treatment and pragmatic-trial sites;
- manufacturing and distribution;
- treatment sponsors and holders of shelved post-Phase-1 assets;
- interoperable registry, analytics, and monitoring infrastructure;
- payer contracts that condition coverage on evidence production.

That separation is the point. Donors do not need to finance every future treatment. Investors do not need to pretend that legislation itself is a security. Each pays for the part whose returns it can actually capture.

1.10 What the numbers mean

The 9.19 billion deaths figure exceeds the current world population because it sums premature deaths prevented across approximately 181 years of future generations. It is a schedule-shift estimate, not a count of currently identifiable people.

The model also excludes the uncertain net direct health effect on participants, including earlier benefits from effective treatments and harms from ineffective or unsafe ones. That is a separate unmodeled channel, not part of the discovery schedule shift.

The 1.65 quadrillion hours figure means disability-weighted equivalent hours. A disability weight of 0.25 sustained for four hours equals one full-disability-equivalent hour. It does not mean the person consciously experienced maximum pain for one hour.

The global result assumes discoveries become public knowledge and eventually benefit patients outside the United States. The access right itself remains state law. State legislation also does not override federal FDA authority. The durable federal version is the Right to Trial and FDA Upgrade Act[183].

1.11 Who can make it happen

Audience	Next move
Infinita and participating Montana ETRBs	Publish an interoperable protocol, document fees and outcomes, and help other states copy the model.
Governors, legislators, and health departments	Sponsor the model bill, license centers and ETRBs, and require Enroll, Compare, Pool, Publish.
Philanthropists and foundations	Fund the 50-state campaign, shared registry, legal work, independent evaluation, and open standards.
Patient and rare-disease organizations	Define cohorts and outcomes, recruit participants, demand the bill, and insist that all results are published.
Biotech developers and owners of shelved assets	Submit eligible candidates, finance lawful treatment and evidence generation, and share standardized outcomes.
ETRBs, clinics, clinicians, CROs, manufacturers, and data firms	Adopt common protocols, price services transparently, pool data, monitor safety, and publish negative results.
Impact and longevity investors	Finance review, clinics, manufacturing, data systems, and sponsor companies with explicit impact reporting.
Insurers, self-insured employers, Medicaid, and CMS	Pilot reimbursement conditional on registration, comparison, safety reporting, and pooled outcomes.
FDA and federal policymakers	Clarify authorization and charging pathways, accept interoperable evidence when it meets federal standards, and remove needless duplication.

The coalition is larger than donors and legislators because the system has to survive after the bill-signing photograph. Patients supply demand. Developers supply treatments. ETRBs and clinics supply lawful operations. Payers and investors supply recurring capital. The shared protocol turns all of that activity into evidence instead of expensive folklore.

1.12 What could make the estimate wrong

The arithmetic is short. The causal claim is not.

The result is too high if self-selected treatment purchases fail to produce credible causal evidence, if treatment demand fragments across too many candidate-condition pairs, if discoveries do not diffuse globally, if the rare-disease queue is a poor proxy for the wider therapeutic frontier, or if the eventually avoidable share of global disease and aging is much smaller than modeled.

The result is too low if patient-funded research supports more than the modeled treatment-discovery rate, if rare-disease effects require much smaller samples, or if the system creates valuable treatments for poorly treated common diseases that the untreated-disease queue does not fully represent.

The primary empirical test is therefore simple: after adoption, measure credible first-treatment discoveries per year. Every other headline follows from that rate. The scientific multiplier does not include a separate atom for "thousands of valid trials occur but none produce useful discoveries." The model instead tests the productivity of the operating system directly and keeps failure to build that system in the advocacy probability adjustment.

Chapter 2

Methodology, Parameters, and Calculations

2.1 Overview

This appendix documents all 37 parameters used in the analysis, organized by type:

- External sources (peer-reviewed): 11
- Calculated values: 16
- Core definitions: 10

2.1.1 Quick Navigation

Calculated Values (16 parameters) • External Data Sources (11 parameters) • Core Definitions (10 parameters)

2.2 Calculated Values

Parameters derived from mathematical formulas and economic models.

2.2.1 Pragmatic Trial Cost Reduction Factor: 44.1x

Details

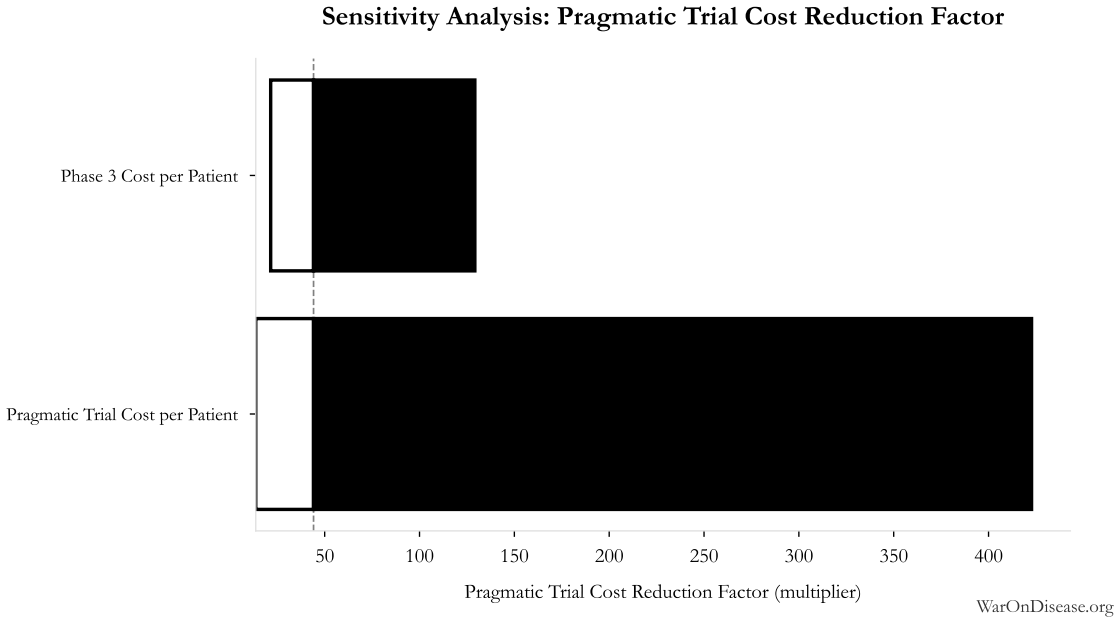
Cost reduction factor projected for embedded pragmatic trials (traditional Phase 3 cost / pragmatic trial cost per patient)
Inputs:

- Phase 3 Cost per Patient : $41,000 (95% CI: $20,000 - $120,000)
- Pragmatic Trial Cost per Patient : $929 (95% CI: $97 - $3,000)

$$
\begin{aligned}
k_{reduce} &= \frac{Cost_{P3,pt}}{Cost_{pragmatic,pt}} \\
&= \frac{\$41K}{\$929} \\
&= 44.1
\end{aligned}
$$

High confidence

2.2.1.1 Sensitivity Analysis



Sensitivity Indices for Pragmatic Trial Cost Reduction Factor
Regression-based sensitivity showing which inputs explain the most variance in the output.

Input Parameter	Sensitivity Coefficient	Interpretation
Phase 3 Cost per Patient (USD/patient)	0.5310	Strong driver
Pragmatic Trial Cost per Patient (USD/patient)	-0.4880	Moderate driver

Interpretation: Standardized coefficients show the change in output (in SD units) per 1 SD change in input. Values near ±1 indicate strong influence; values exceeding ±1 may occur with correlated inputs.

2.2.1.2 Monte Carlo Distribution

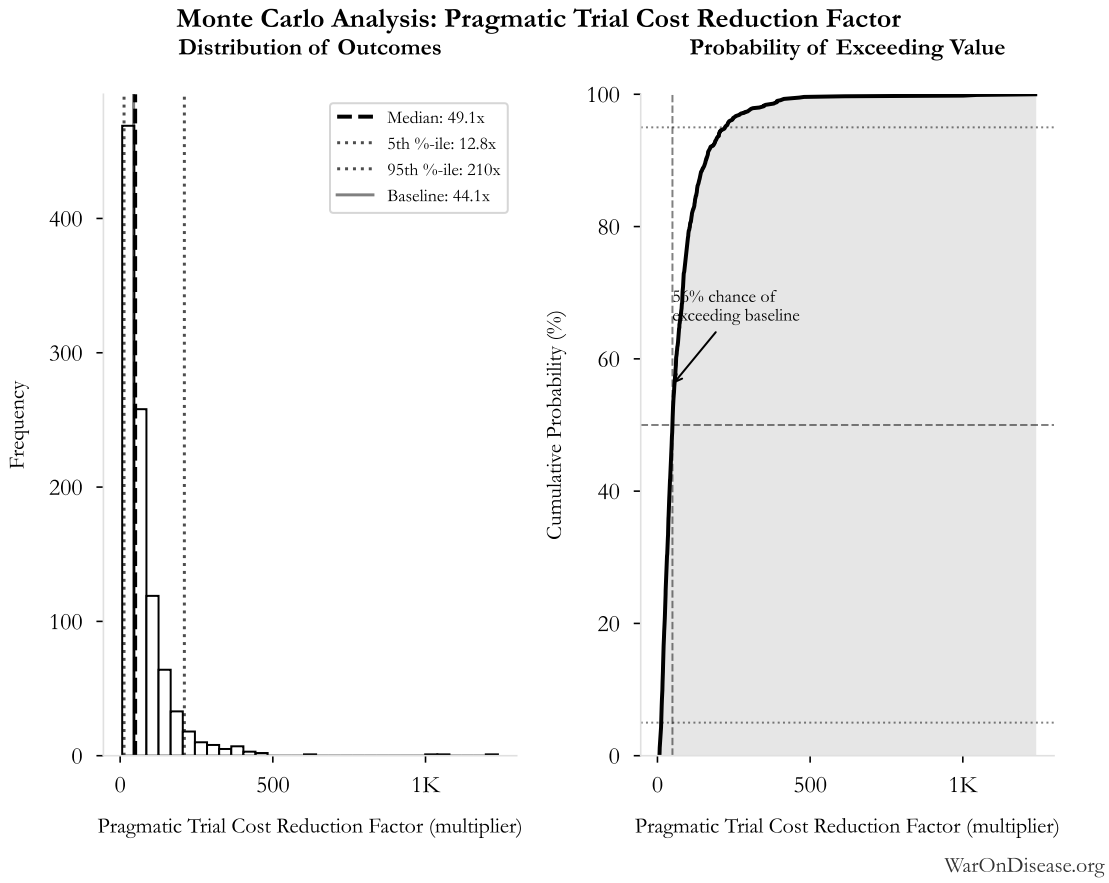


Figure 2.1: Monte Carlo Distribution: Pragmatic Trial Cost Reduction Factor (10,000 simulations)

Simulation Results Summary: Pragmatic Trial Cost Reduction Factor

Statistic	Value
Baseline (deterministic)	44.1x
Mean (expected value)	73x
Median (50th percentile)	49.1x
Standard Deviation	78.5x
90% Range (5th-95th percentile)	[12.8x, 210x]

The histogram shows the distribution of Pragmatic Trial Cost Reduction Factor across 10,000 Monte Carlo simulations. The CDF (right) shows the probability of the outcome exceeding any given value, which is useful for risk assessment.

2.2.1.3 Exceedance Probability

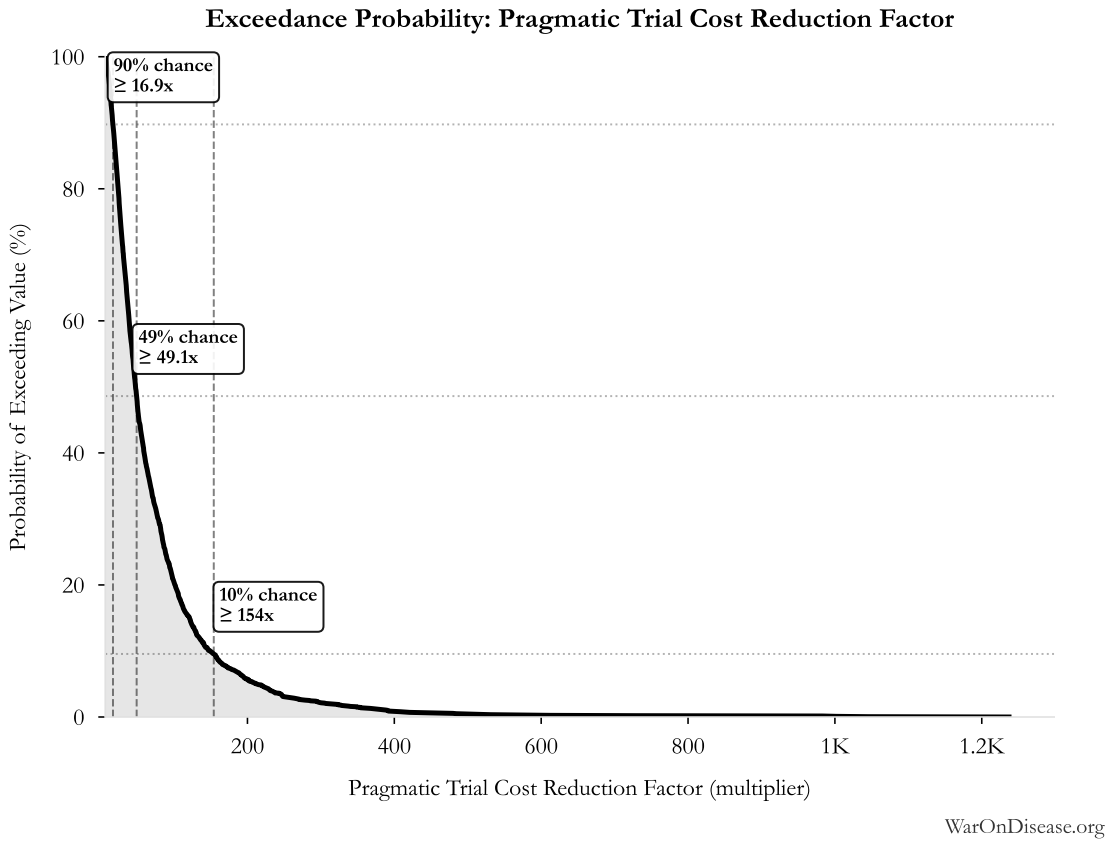


Figure 2.2: Probability of Exceeding Threshold: Pragmatic Trial Cost Reduction Factor

This exceedance probability chart shows the likelihood that Pragmatic Trial Cost Reduction Factor will exceed any given threshold. Higher curves indicate more favorable outcomes with greater certainty.

2.2.2 Diseases Without Effective Treatment: 6,650 diseases

Details

Number of diseases without effective treatment. 95% of 7,000 rare diseases lack FDA-approved treatment (per Orphanet 2024). This represents the therapeutic search space that remains unexplored.

Inputs:

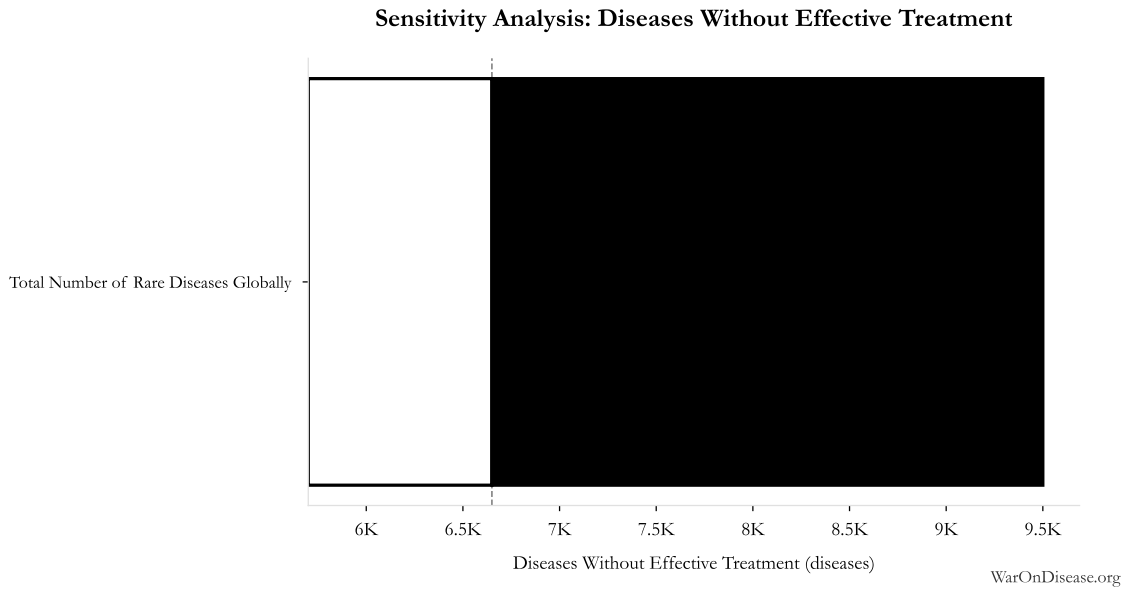
- Total Number of Rare Diseases Globally : 7,000 diseases (95% CI: 6,000 diseases - 10,000 diseases)

$$\begin{aligned} & N_{untreated} \\ &= N_{rare} \times 0.95 \\ &= 7{,}000 \times 0.95 \\ &= 6{,}650 \end{aligned}$$

Methodology:[197]

~ *Medium confidence*

2.2.2.1 Sensitivity Analysis



Sensitivity Indices for Diseases Without Effective Treatment

Regression-based sensitivity showing which inputs explain the most variance in the output.

Input Parameter	Sensitivity Coefficient	Interpretation
Total Number of Rare Diseases Globally (diseases)	1.0000	Strong driver

Interpretation: Standardized coefficients show the change in output (in SD units) per 1 SD change in input. Values near ±1 indicate strong influence; values exceeding ±1 may occur with correlated inputs.

2.2.2.2 Monte Carlo Distribution

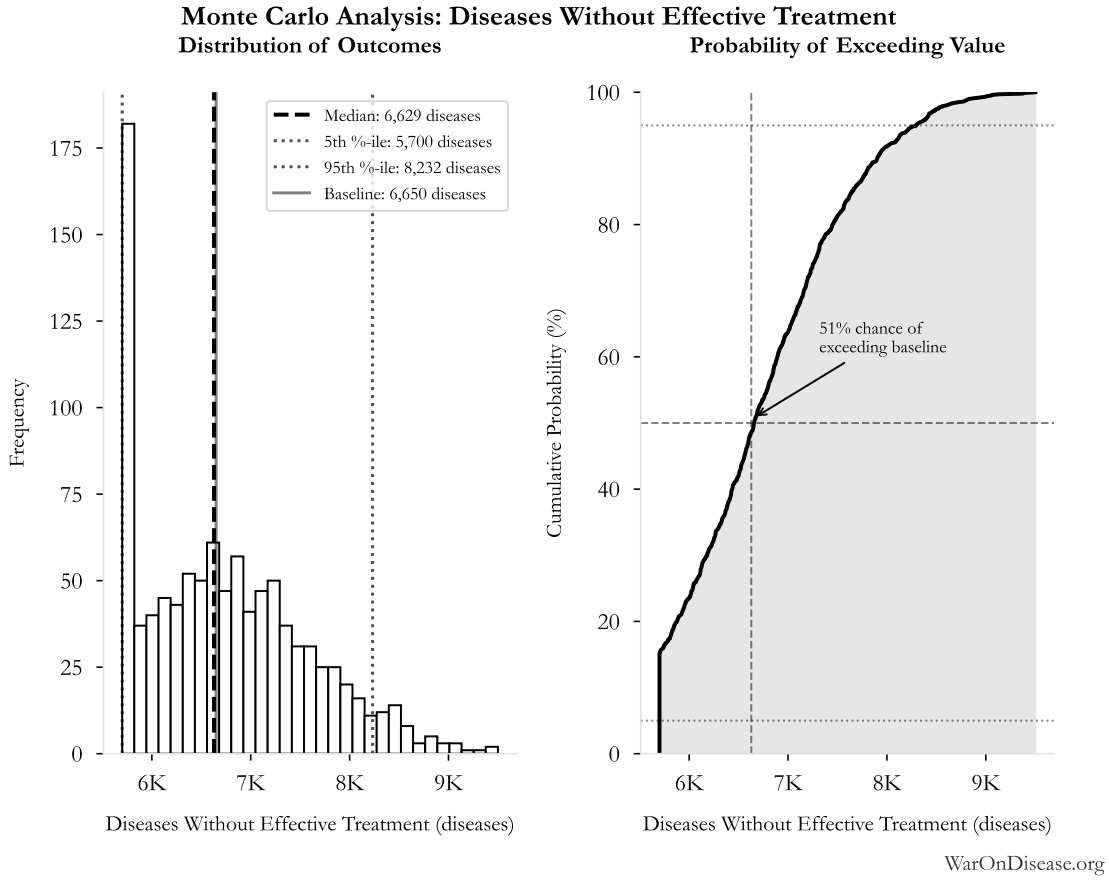


Figure 2.3: Monte Carlo Distribution: Diseases Without Effective Treatment (10,000 simulations)

Simulation Results Summary: Diseases Without Effective Treatment

Statistic	Value
Baseline (deterministic)	6,650
Mean (expected value)	6,718
Median (50th percentile)	6,629
Standard Deviation	827
90% Range (5th-95th percentile)	[5,700, 8,232]

The histogram shows the distribution of Diseases Without Effective Treatment across 10,000 Monte Carlo simulations. The CDF (right) shows the probability of the outcome exceeding any given value, which is useful for risk assessment.

2.2.2.3 Exceedance Probability

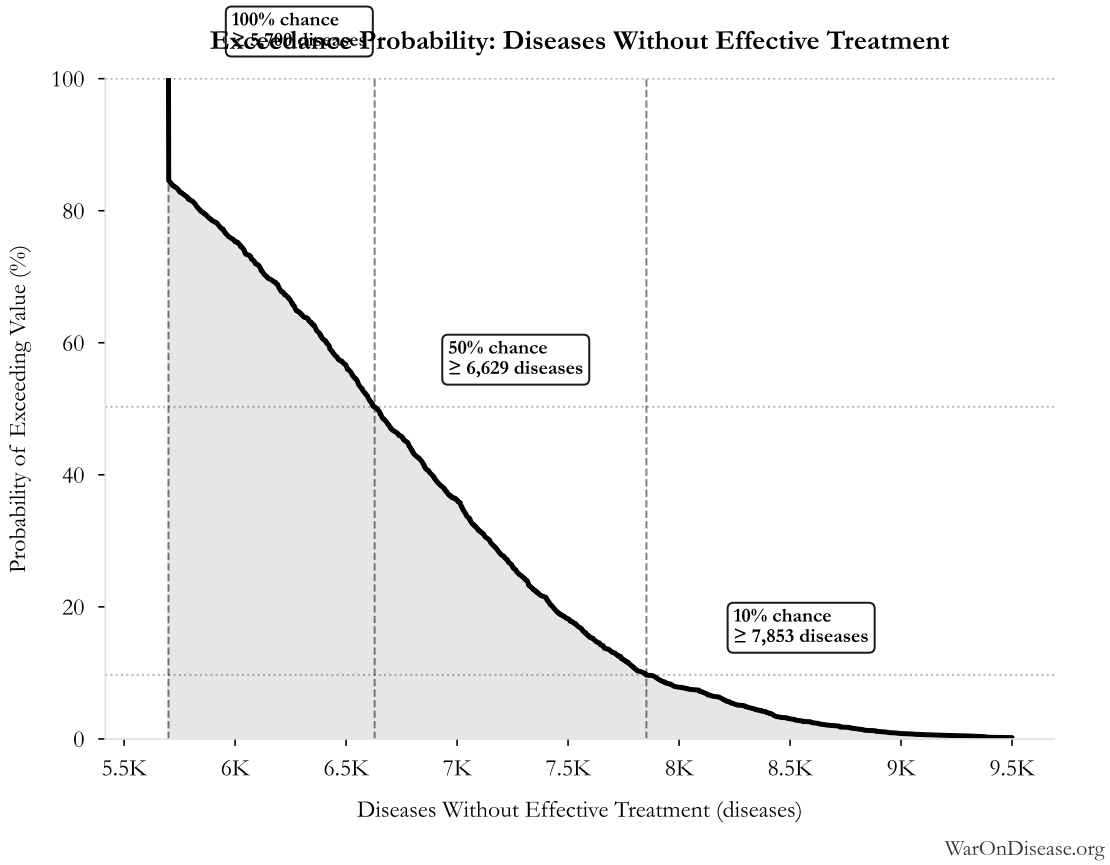


Figure 2.4: Probability of Exceeding Threshold: Diseases Without Effective Treatment

This exceedance probability chart shows the likelihood that Diseases Without Effective Treatment will exceed any given threshold. Higher curves indicate more favorable outcomes with greater certainty.

2.2.3 Universal Right to Try with Evidence Cost in FDA Budget Hours: 80.7 hours

Details

Hours of the FDA annual program budget equal to the full central philanthropic launch cost for adopting Universal Right to Try with Evidence in all 50 states. This is a scale comparison, not a claim about FDA cost-effectiveness.

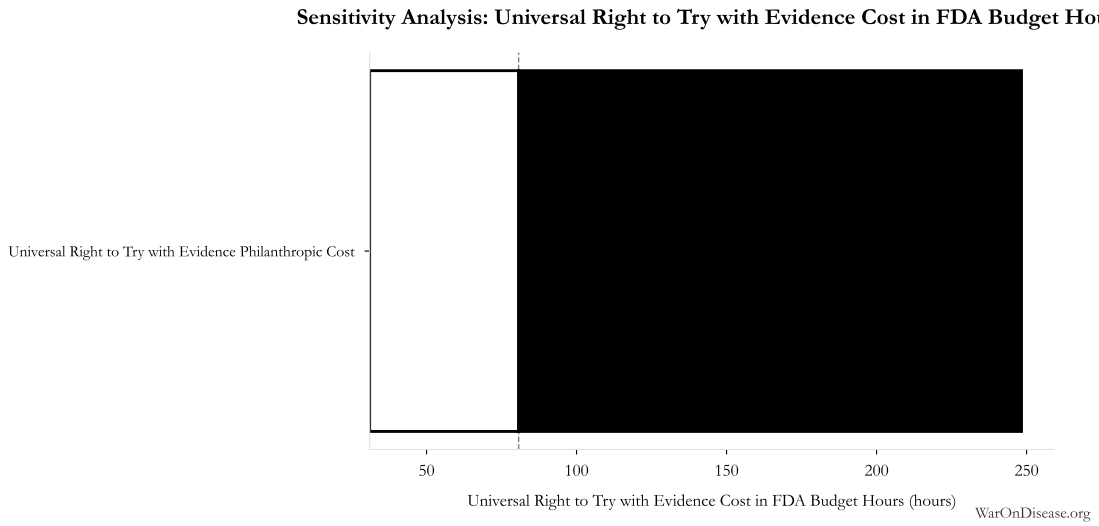
Inputs:

- Universal Right to Try with Evidence Philanthropic Cost: $65 million (95% CI: $25 million - $200 million)
- FDA Annual Program Budget : $7.06 billion

$$Hours_{RTT,FDA} = \frac{C_{RTT}}{Budget_{FDA}} \times 8,760$$

? Low confidence

2.2.3.1 Sensitivity Analysis



Sensitivity Indices for Universal Right to Try with Evidence Cost in FDA Budget Hours

Regression-based sensitivity showing which inputs explain the most variance in the output.

Input Parameter	Sensitivity Coefficient	Interpretation
Universal Right to Try with Evidence Philanthropic Cost (USD)	1.0000	Strong driver

Interpretation: Standardized coefficients show the change in output (in SD units) per 1 SD change in input. Values near ±1 indicate strong influence; values exceeding ±1 may occur with correlated inputs.

2.2.3.2 Monte Carlo Distribution

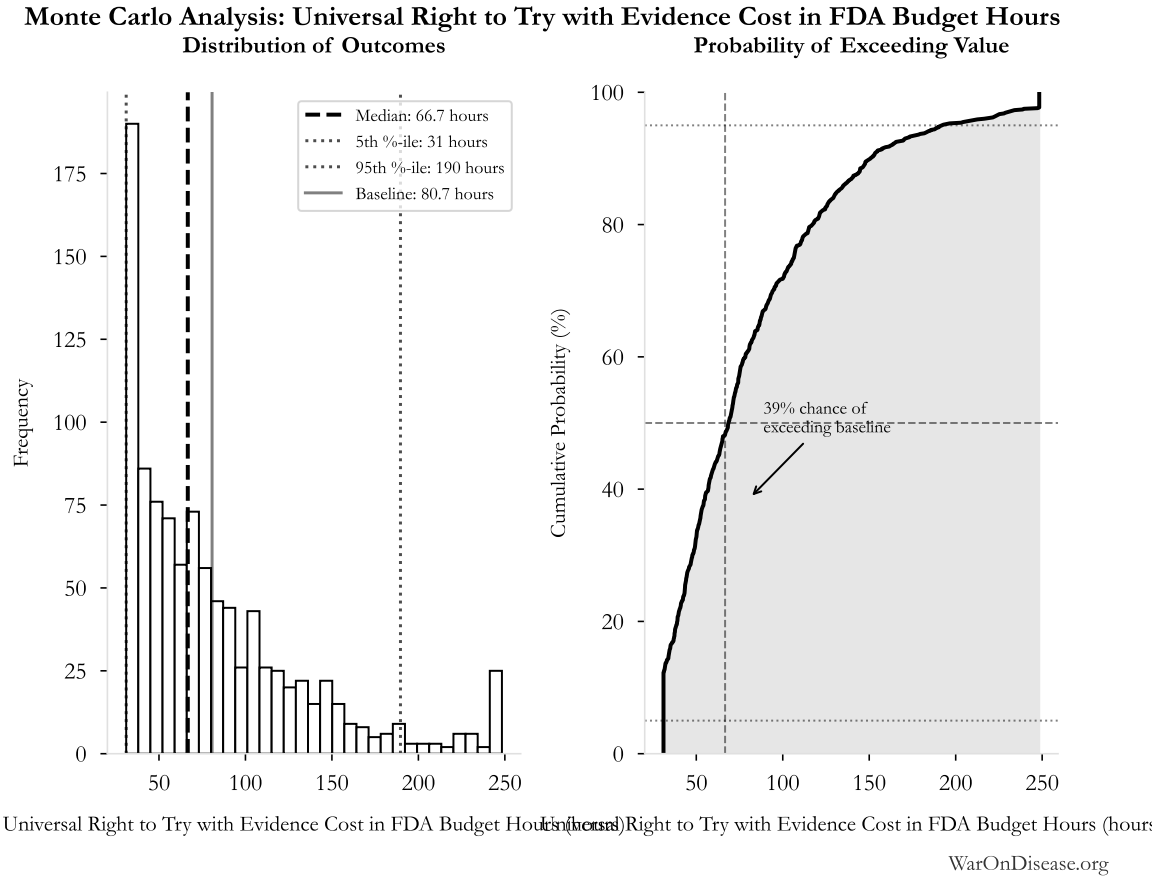


Figure 2.5: Monte Carlo Distribution: Universal Right to Try with Evidence Cost in FDA Budget Hours (10,000 simulations)

Simulation Results Summary: Universal Right to Try with Evidence Cost in FDA Budget Hours

Statistic	Value
Baseline (deterministic)	80.7
Mean (expected value)	81.2
Median (50th percentile)	66.7
Standard Deviation	50
90% Range (5th-95th percentile)	[31, 190]

The histogram shows the distribution of Universal Right to Try with Evidence Cost in FDA Budget Hours across 10,000 Monte Carlo simulations. The CDF (right) shows the probability of the outcome exceeding any given value, which is useful for risk assessment.

2.2.3.3 Exceedance Probability

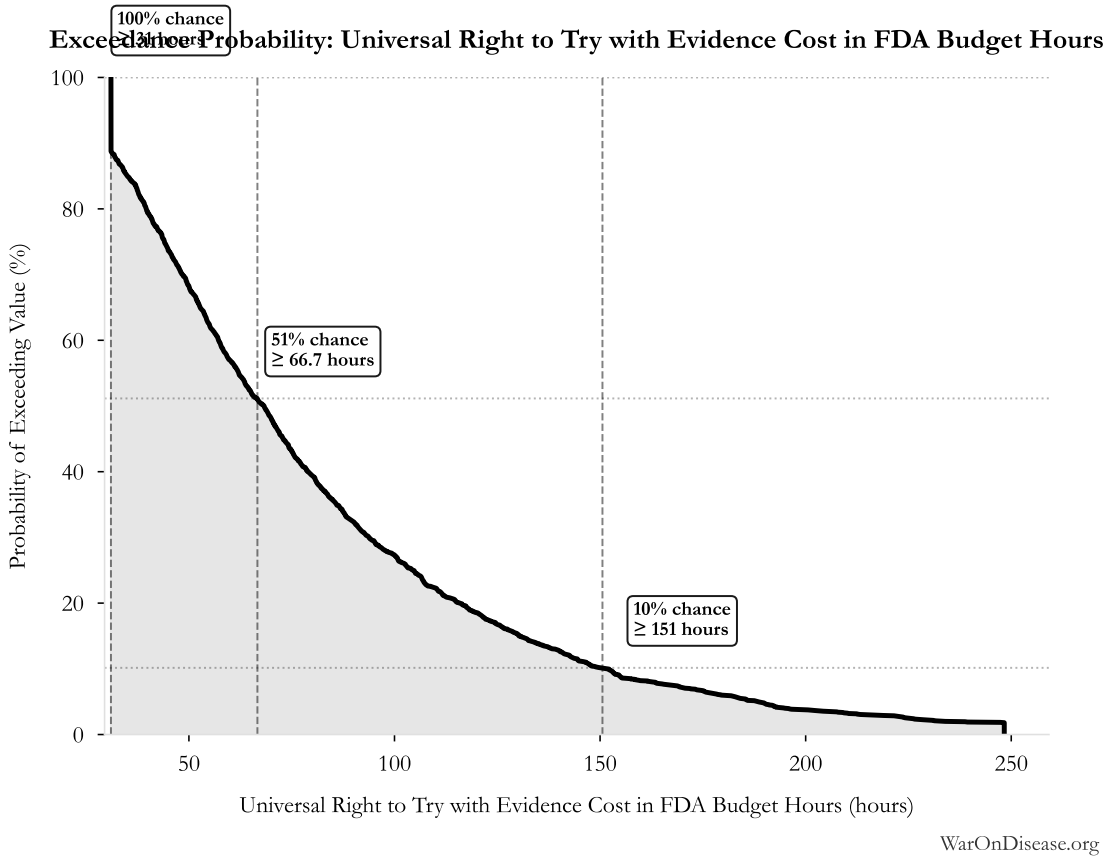


Figure 2.6: Probability of Exceeding Threshold: Universal Right to Try with Evidence Cost in FDA Budget Hours

This exceedance probability chart shows the likelihood that Universal Right to Try with Evidence Cost in FDA Budget Hours will exceed any given threshold. Higher curves indicate more favorable outcomes with greater certainty.

2.2.4 Universal Right to Try with Evidence Cost in NIH Budget Hours: 12.1 hours

Details

Hours of the NIH annual budget equal to the full central philanthropic launch cost for adopting Universal Right to Try with Evidence in all 50 states. This is a scale comparison, not a claim about NIH cost-effectiveness.

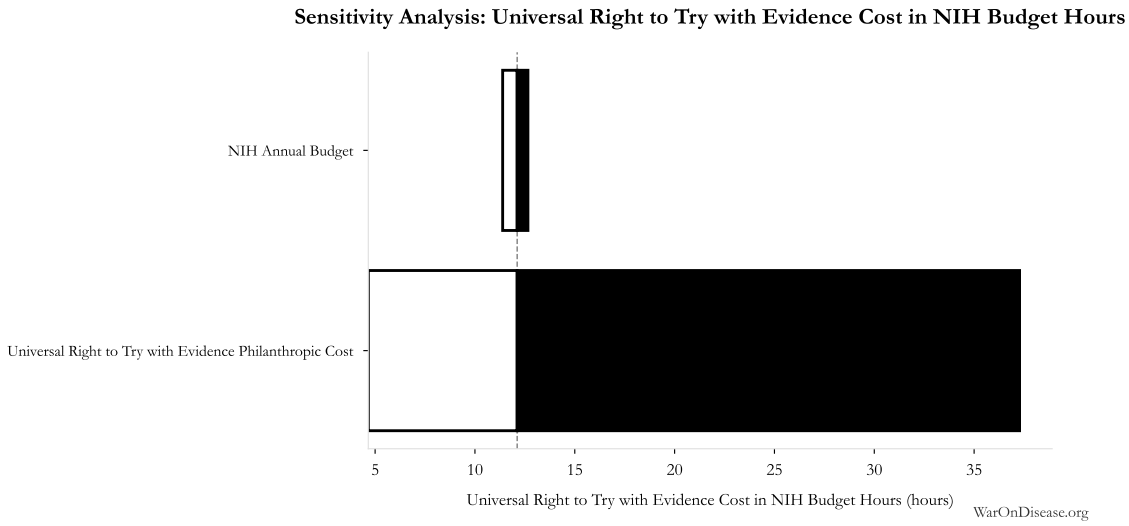
Inputs:

- Universal Right to Try with Evidence Philanthropic Cost: $65 million (95% CI: $25 million - $200 million)
- NIH Annual Budget : $47 billion (95% CI: $45 billion - $50 billion)

$$Hours_{RTT,NIH} = \frac{C_{RTT}}{Budget_{NIH}} \times 8,760$$

? Low confidence

2.2.4.1 Sensitivity Analysis



Sensitivity Indices for Universal Right to Try with Evidence Cost in NIH Budget Hours

Regression-based sensitivity showing which inputs explain the most variance in the output.

Input Parameter	Sensitivity Coefficient	Interpretation
Universal Right to Try with Evidence Philanthropic Cost (USD)	1.0000	Strong driver

Interpretation: Standardized coefficients show the change in output (in SD units) per 1 SD change in input. Values near ±1 indicate strong influence; values exceeding ±1 may occur with correlated inputs.

2.2.4.2 Monte Carlo Distribution

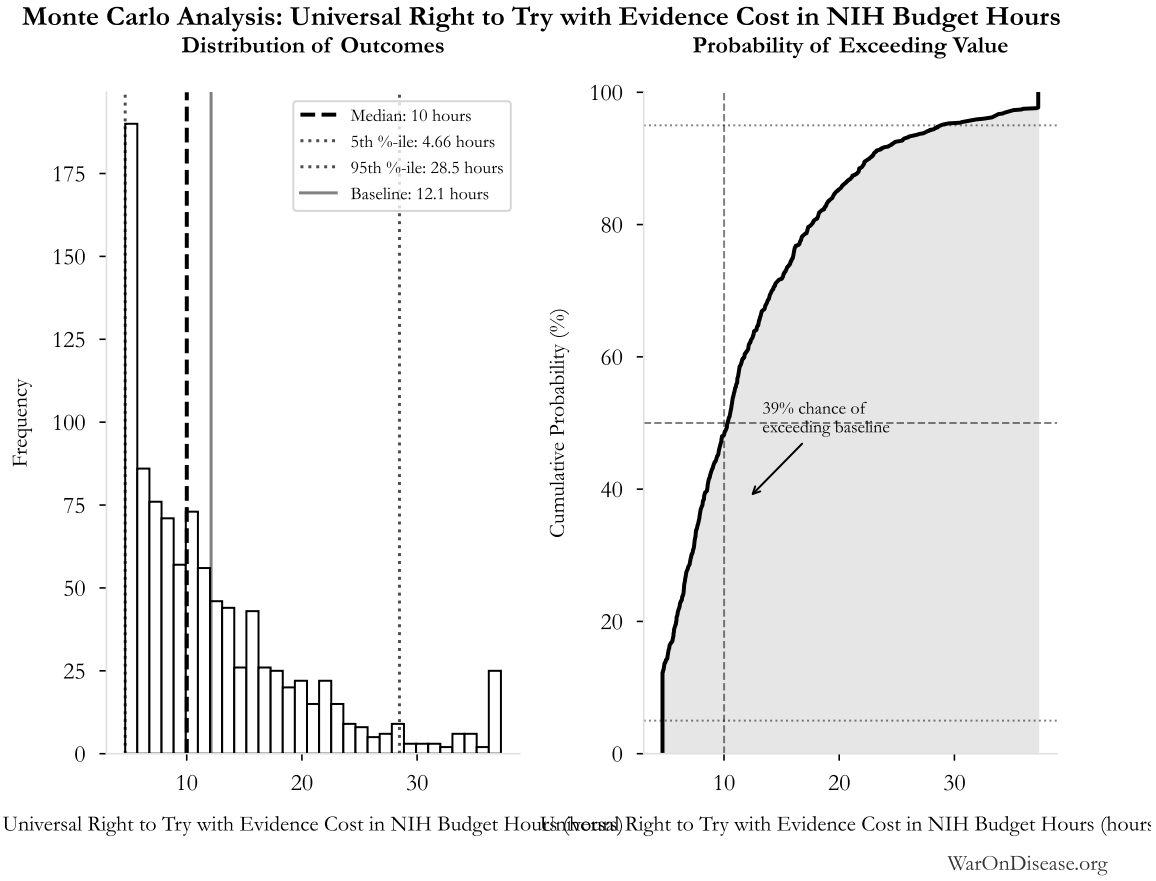


Figure 2.7: Monte Carlo Distribution: Universal Right to Try with Evidence Cost in NIH Budget Hours (10,000 simulations)

Simulation Results Summary: Universal Right to Try with Evidence Cost in NIH Budget Hours

Statistic	Value
Baseline (deterministic)	12.1
Mean (expected value)	12.2
Median (50th percentile)	10
Standard Deviation	7.5
90% Range (5th-95th percentile)	[4.66, 28.5]

The histogram shows the distribution of Universal Right to Try with Evidence Cost in NIH Budget Hours across 10,000 Monte Carlo simulations. The CDF (right) shows the probability of the outcome exceeding any given value, which is useful for risk assessment.

2.2.4.3 Exceedance Probability

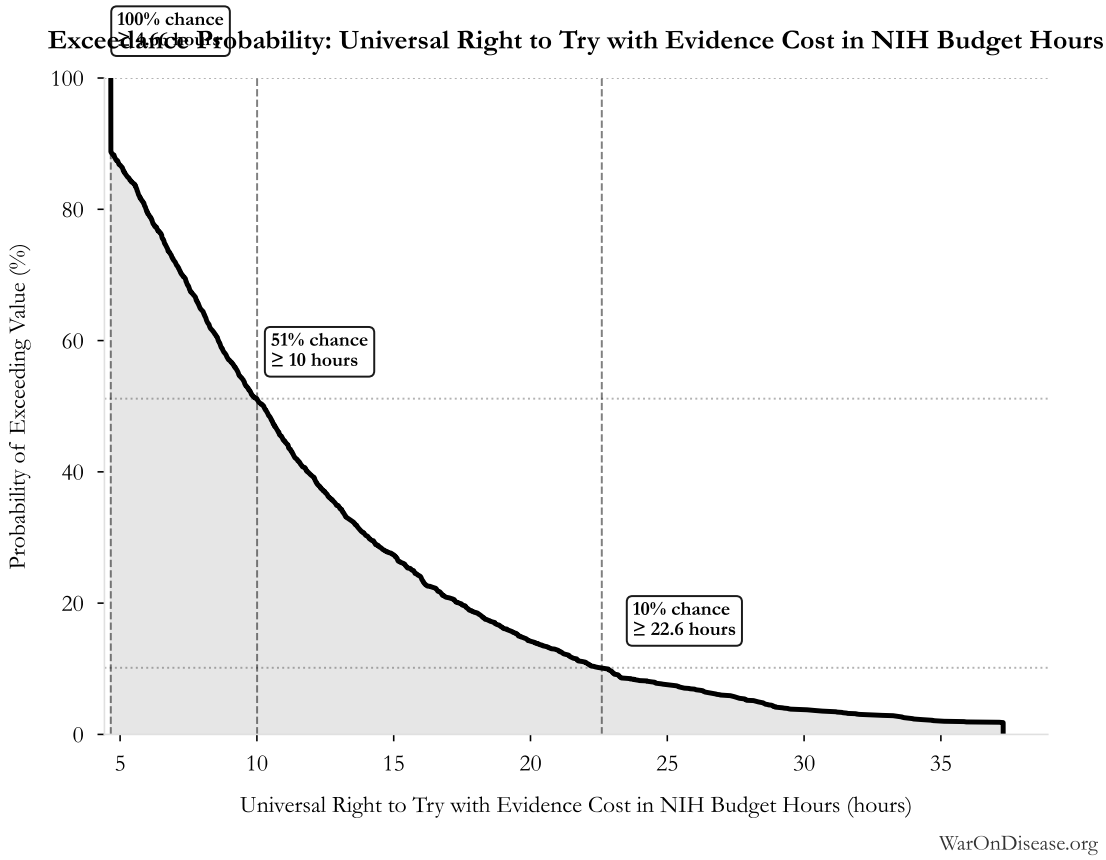


Figure 2.8: Probability of Exceeding Threshold: Universal Right to Try with Evidence Cost in NIH Budget Hours

This exceedance probability chart shows the likelihood that Universal Right to Try with Evidence Cost in NIH Budget Hours will exceed any given threshold. Higher curves indicate more favorable outcomes with greater certainty.

2.2.5 Universal Right to Try with Evidence Philanthropic Cost per DALY: $0.000134

Details

Conditional philanthropic cost per DALY if all 50 states adopt, a mature pooled pragmatic-trial system operates under applicable federal authorization, and the modeled treatment-discovery acceleration occurs. The numerator includes the 50-state campaign and ten-year registry launch costs, excludes patient or payer spending on treatment delivery, trial-site services, and permitted study costs, and assumes center assessments fund the registry thereafter. The denominator counts the global treatment schedule shift once.

Inputs:

- Universal Right to Try with Evidence Philanthropic Cost: $65 million (95% CI: $25 million - $200 million)
- DALYs Averted from Universal Right to Try with Evidence : 483 billion DALYs

$$
\begin{aligned}
&Cost_{RTT,DALY} \\
&= \frac{C_{RTT}}{DALYs_{RTT}} \\
&= \frac{\$65M}{483B} \\
&= \$0.000134
\end{aligned}
$$

where:

$$
\begin{aligned}
&DALYs_{RTT} \\
&= DALYs_{global,ann} \times Pct_{avoid,DALY} \times T_{accel,RTT} \\
&= 2.88B \times 92.6\% \times 181 \\
&= 483B
\end{aligned}
$$

where:

$$
\begin{aligned}
&T_{accel,RTT} \\
&= T_{first,SQ} \times \left(1 - \frac{1}{k_{RTT}}\right) \\
&= 222 \times \left(1 - \frac{1}{5.48}\right) \\
&= 181
\end{aligned}
$$

where:

$$
\begin{aligned}
&T_{first,SQ} \\
&= T_{queue,SQ} \times 0.5 \\
&= 443 \times 0.5 \\
&= 222
\end{aligned}
$$

where:

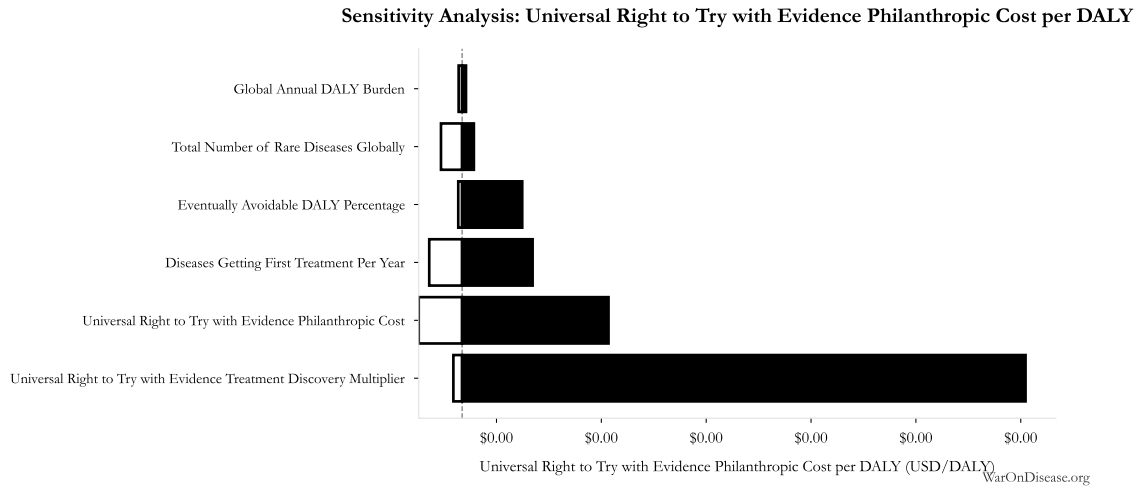
$$
\begin{aligned}
&T_{queue,SQ} \\
&= \frac{N_{untreated}}{Treatments_{new,ann}} \\
&= \frac{6{,}650}{15} \\
&= 443
\end{aligned}
$$

where:

$$
\begin{aligned}
&N_{untreated} \\
&= N_{rare} \times 0.95 \\
&= 7{,}000 \times 0.95 \\
&= 6{,}650
\end{aligned}
$$

? Low confidence

2.2.5.1 Sensitivity Analysis



Sensitivity Indices for Universal Right to Try with Evidence Philanthropic Cost per DALY
Regression-based sensitivity showing which inputs explain the most variance in the output.

Input Parameter	Sensitivity Coefficient	Interpretation
Universal Right to Try with Evidence Philanthropic Cost (USD)	0.5604	Strong driver
DALYs Averted from Universal Right to Try with Evidence (DALYs)	-0.4511	Moderate driver

Interpretation: Standardized coefficients show the change in output (in SD units) per 1 SD change in input. Values near ±1 indicate strong influence; values exceeding ±1 may occur with correlated inputs.

2.2.5.2 Monte Carlo Distribution

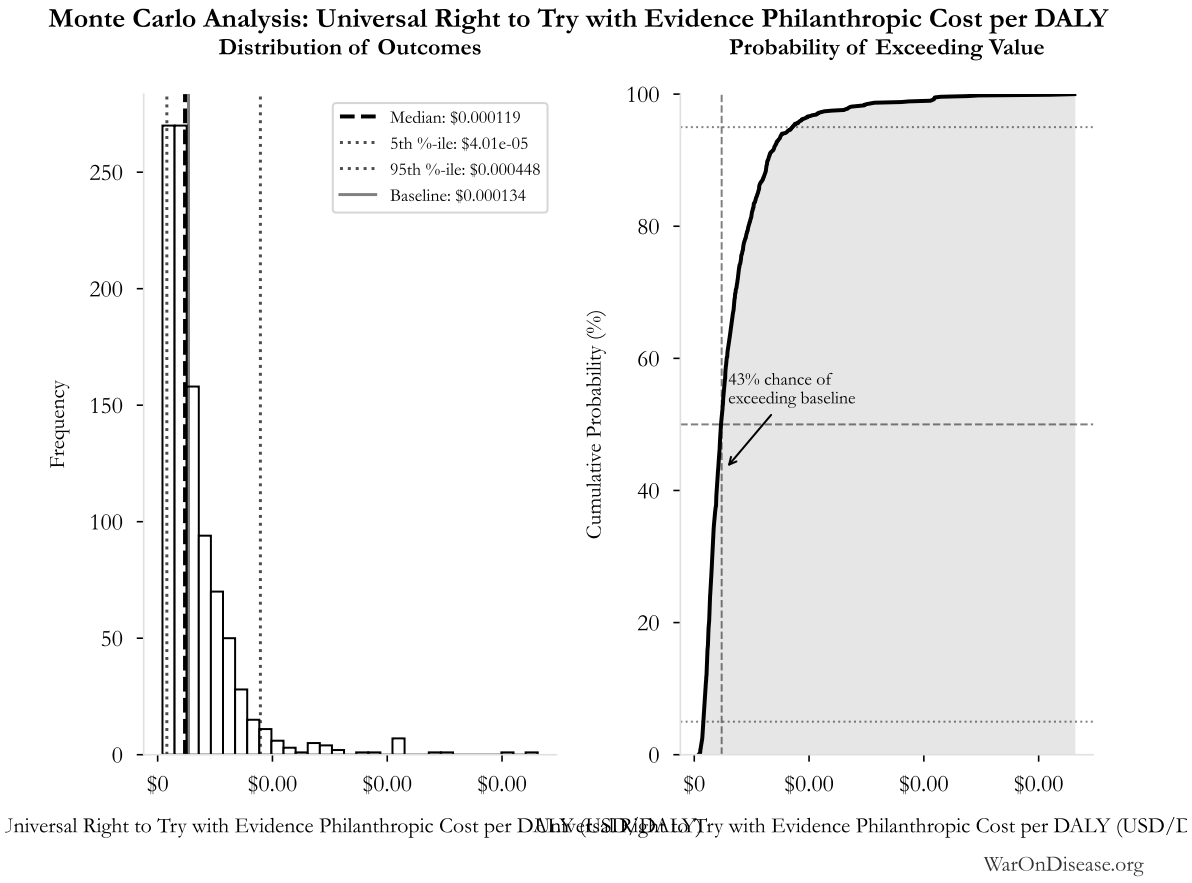


Figure 2.9: Monte Carlo Distribution: Universal Right to Try with Evidence Philanthropic Cost per DALY (10,000 simulations)

Simulation Results Summary: Universal Right to Try with Evidence Philanthropic Cost per DALY

Statistic	Value
Baseline (deterministic)	$0.000134
Mean (expected value)	$0.000171
Median (50th percentile)	$0.000119
Standard Deviation	$0.000192
90% Range (5th-95th percentile)	[$4.01e-05, $0.000448]

The histogram shows the distribution of Universal Right to Try with Evidence Philanthropic Cost per DALY across 10,000 Monte Carlo simulations. The CDF (right) shows the probability of the outcome exceeding any given value, which is useful for risk assessment.

2.2.5.3 Exceedance Probability

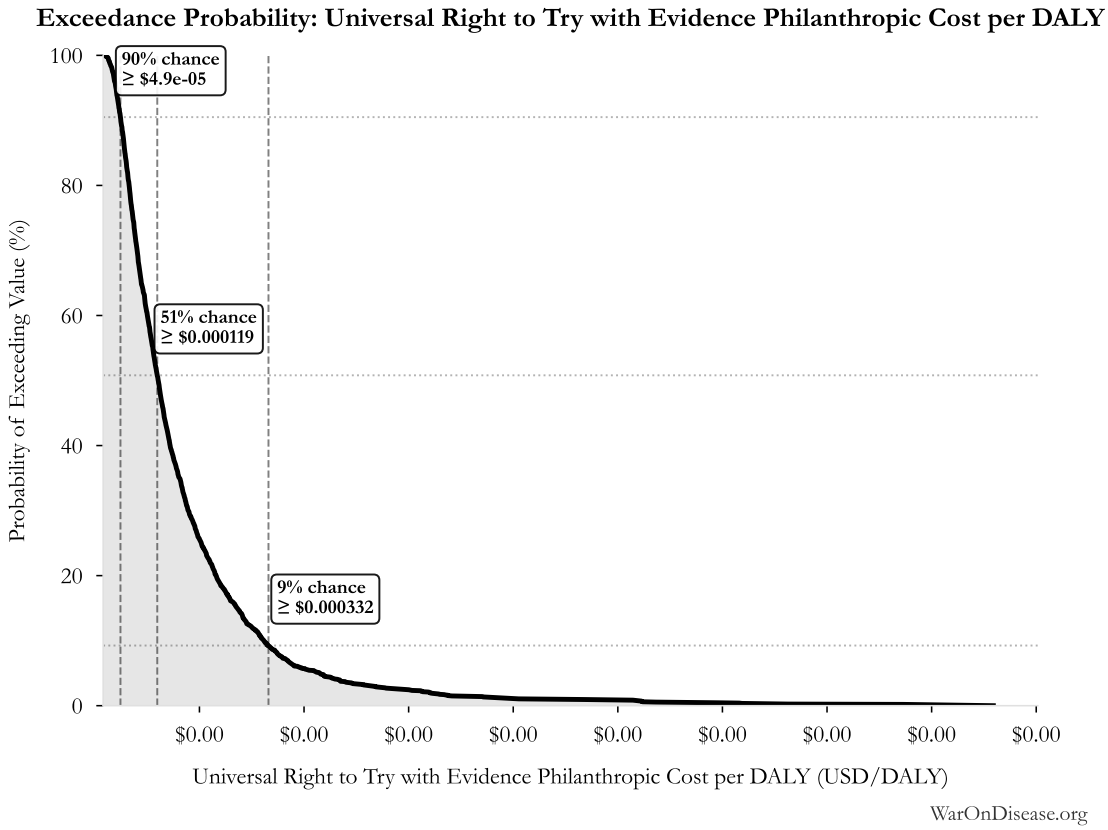


Figure 2.10: Probability of Exceeding Threshold: Universal Right to Try with Evidence Philanthropic Cost per DALY

This exceedance probability chart shows the likelihood that Universal Right to Try with Evidence Philanthropic Cost per DALY will exceed any given threshold. Higher curves indicate more favorable outcomes with greater certainty.

2.2.6 Universal Right to Try with Evidence Philanthropic Cost per Life Saved: $0.00707

Details

Conditional philanthropic cost per modeled premature death prevented if all 50 states adopt, a mature pooled pragmatic-trial system operates, and the modeled treatment-discovery acceleration occurs. This uses the same campaign and registry numerator as the cost-per-DALY estimate.

Inputs:

- Universal Right to Try with Evidence Philanthropic Cost: $65 million (95% CI: $25 million - $200 million)
- Lives Saved from Universal Right to Try with Evidence : 9.19 billion deaths

$$
\begin{aligned}
&Cost_{RTT,life} \\
&= \frac{C_{RTT}}{Lives_{RTT}} \\
&= \frac{\$65M}{9.19B} \\
&= \$0.00707
\end{aligned}
$$

where:

$$
\begin{aligned}
&Lives_{RTT} \\
&= Deaths_{disease,daily} \times Pct_{avoid,death} \times T_{accel,RTT} \times 365 \\
&= 150{,}000 \times 92.6\% \times 181 \times 365 \\
&= 9.19B
\end{aligned}
$$

where:

$$
\begin{aligned}
&T_{accel,RTT} \\
&= T_{first,SQ} \times \left(1 - \frac{1}{k_{RTT}}\right) \\
&= 222 \times \left(1 - \frac{1}{5.48}\right) \\
&= 181
\end{aligned}
$$

where:

$$
\begin{aligned}
&T_{first,SQ} \\
&= T_{queue,SQ} \times 0.5 \\
&= 443 \times 0.5 \\
&= 222
\end{aligned}
$$

where:

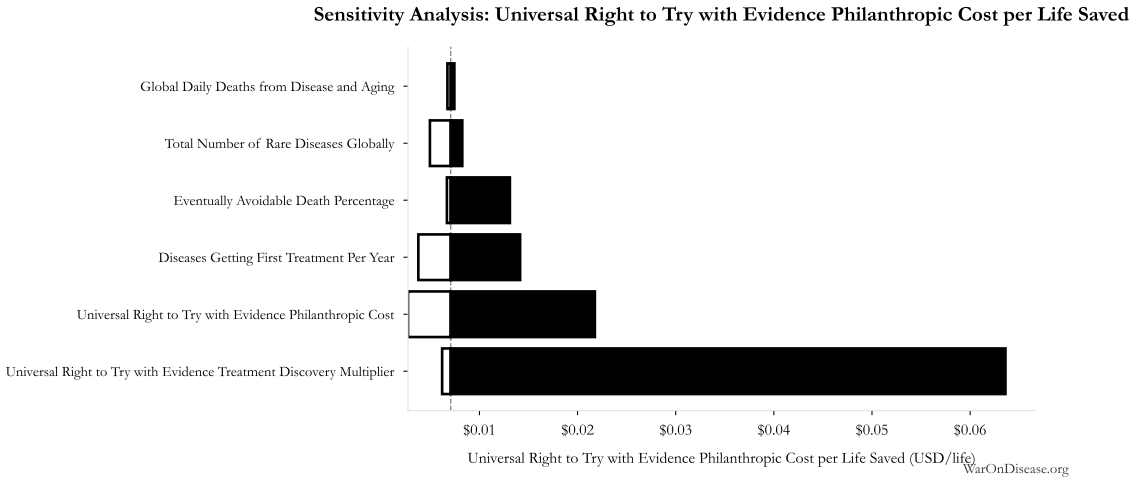
$$
\begin{aligned}
&T_{queue,SQ} \\
&= \frac{N_{untreated}}{Treatments_{new,ann}} \\
&= \frac{6{,}650}{15} \\
&= 443
\end{aligned}
$$

where:

$$
\begin{aligned}
& N_{untreated} \\
&= N_{rare} \times 0.95 \\
&= 7{,}000 \times 0.95 \\
&= 6{,}650
\end{aligned}
$$

? Low confidence

2.2.6.1 Sensitivity Analysis



Sensitivity Indices for Universal Right to Try with Evidence Philanthropic Cost per Life Saved
Regression-based sensitivity showing which inputs explain the most variance in the output.

Input Parameter	Sensitivity Coefficient	Interpretation
Universal Right to Try with Evidence Philanthropic Cost (USD)	0.5418	Strong driver
Lives Saved from Universal Right to Try with Evidence (deaths)	-0.4450	Moderate driver

Interpretation: Standardized coefficients show the change in output (in SD units) per 1 SD change in input. Values near ±1 indicate strong influence; values exceeding ±1 may occur with correlated inputs.

2.2.6.2 Monte Carlo Distribution

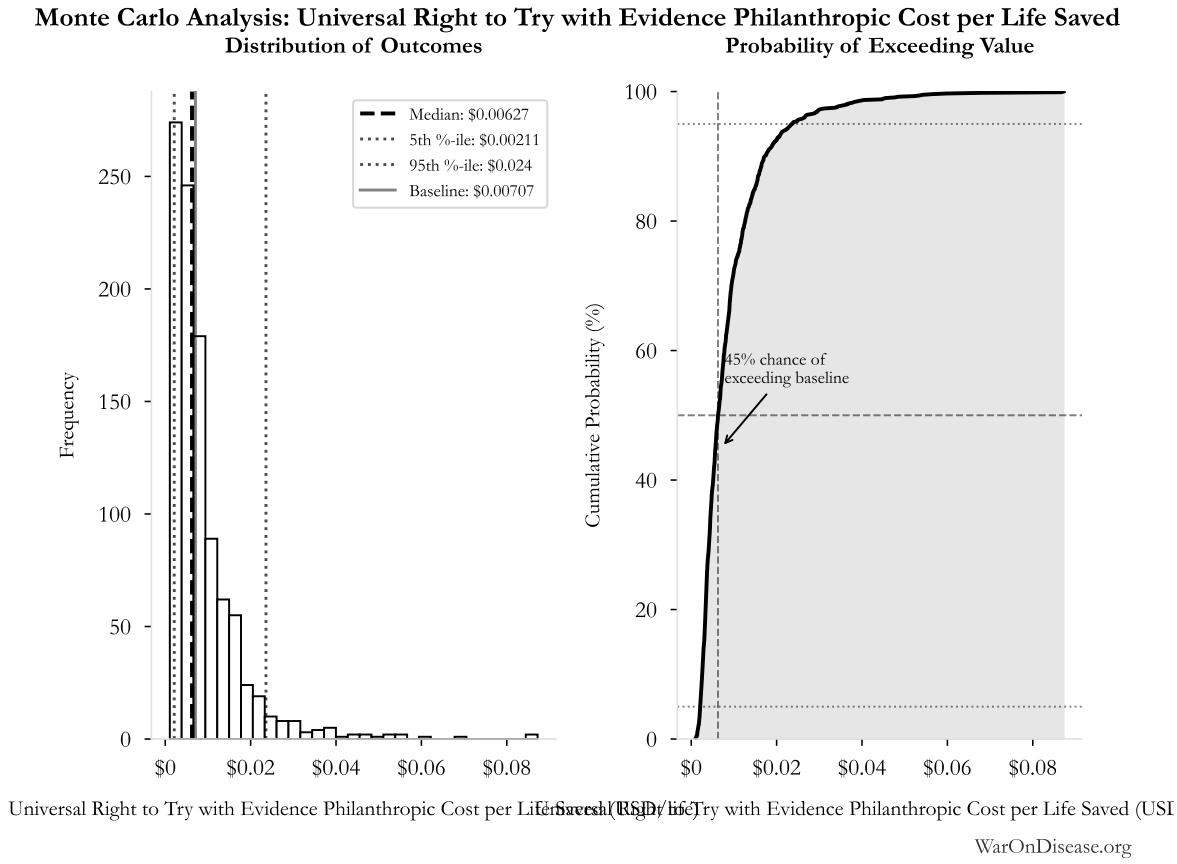


Figure 2.11: Monte Carlo Distribution: Universal Right to Try with Evidence Philanthropic Cost per Life Saved (10,000 simulations)

Simulation Results Summary: Universal Right to Try with Evidence Philanthropic Cost per Life Saved

Statistic	Value
Baseline (deterministic)	$0.00707
Mean (expected value)	$0.00907
Median (50th percentile)	$0.00627
Standard Deviation	$0.01
90% Range (5th-95th percentile)	[$0.00211, $0.024]

The histogram shows the distribution of Universal Right to Try with Evidence Philanthropic Cost per Life Saved across 10,000 Monte Carlo simulations. The CDF (right) shows the probability of the outcome exceeding any given value, which is useful for risk assessment.

2.2.6.3 Exceedance Probability

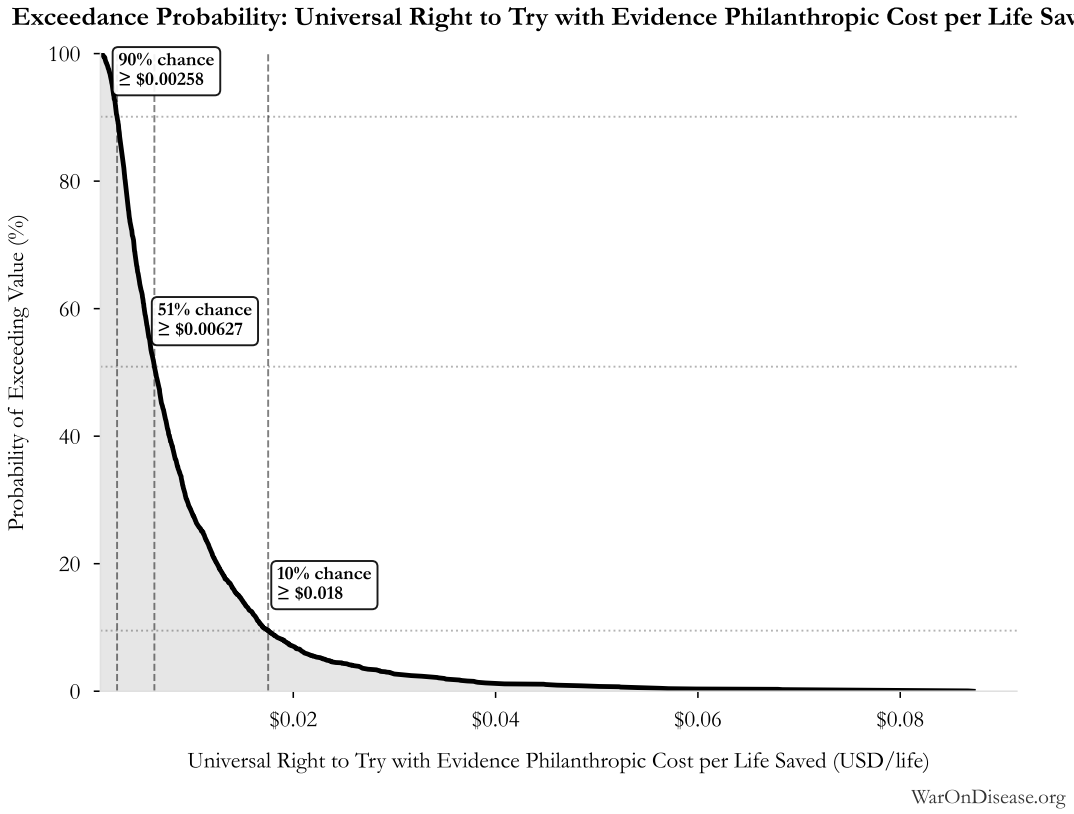


Figure 2.12: Probability of Exceeding Threshold: Universal Right to Try with Evidence Philanthropic Cost per Life Saved

This exceedance probability chart shows the likelihood that Universal Right to Try with Evidence Philanthropic Cost per Life Saved will exceed any given threshold. Higher curves indicate more favorable outcomes with greater certainty.

2.2.7 DALYs Averted from Universal Right to Try with Evidence: 483 billion DALYs

Details

Conditional lifetime DALYs averted by shifting the global treatment-discovery schedule forward. By design, this applies the therapeutic-discovery timeline proxy to the eventually avoidable burden of all global diseases and aging-related degeneration. It is a schedule-shift calculation across future generations, not an observed epidemiological forecast.

Inputs:

- Global Annual DALY Burden : 2.88 billion DALYs/year (SE: ±150 million DALYs/year)
- Eventually Avoidable DALY Percentage: 92.6% (95% CI: 50% - 98%)
- Average Treatment Acceleration from Universal Right to Try with Evidence : 181 years

$$
\begin{aligned}
&DALYs_{RTT} \\
&= DALYs_{global,ann} \times Pct_{avoid,DALY} \times T_{accel,RTT} \\
&= 2.88B \times 92.6\% \times 181 \\
&= 483B
\end{aligned}
$$

where:

$$
\begin{aligned}
&T_{accel,RTT} \\
&= T_{first,SQ} \times \left(1 - \frac{1}{k_{RTT}}\right) \\
&= 222 \times \left(1 - \frac{1}{5.48}\right) \\
&= 181
\end{aligned}
$$

where:

$$
\begin{aligned}
&T_{first,SQ} \\
&= T_{queue,SQ} \times 0.5 \\
&= 443 \times 0.5 \\
&= 222
\end{aligned}
$$

where:

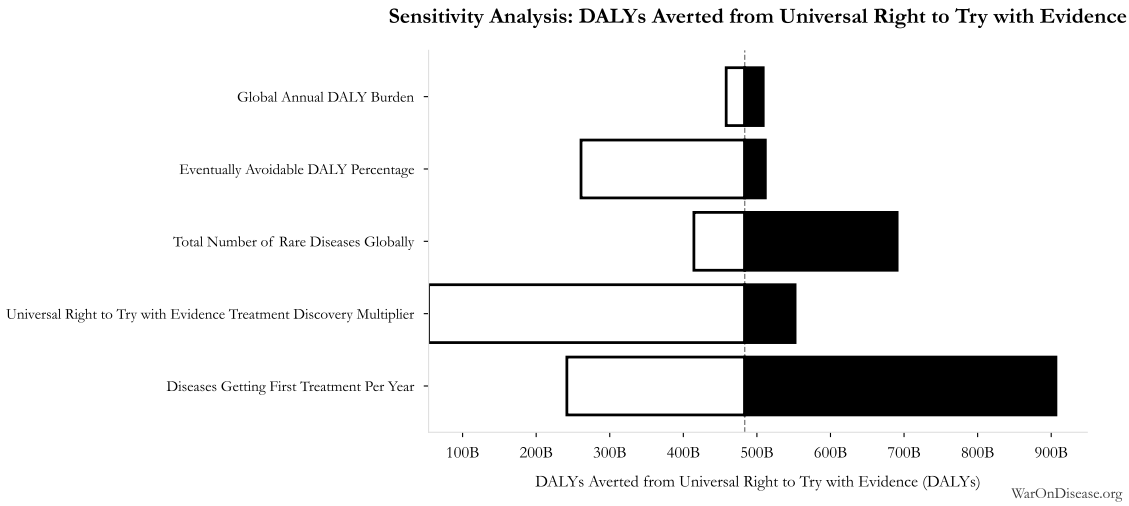
$$
\begin{aligned}
&T_{queue,SQ} \\
&= \frac{N_{untreated}}{Treatments_{new,ann}} \\
&= \frac{6{,}650}{15} \\
&= 443
\end{aligned}
$$

where:

$$
\begin{aligned}
&N_{untreated} \\
&= N_{rare} \times 0.95 \\
&= 7{,}000 \times 0.95 \\
&= 6{,}650
\end{aligned}
$$

? Low confidence

2.2.7.1 Sensitivity Analysis



Sensitivity Indices for DALYs Averted from Universal Right to Try with Evidence
Regression-based sensitivity showing which inputs explain the most variance in the output.

Input Parameter	Sensitivity Coefficient	Interpretation
Average Treatment Acceleration from Universal Right to Try with Evidence (years)	0.9488	Strong driver
Eventually Avoidable DALY Percentage (percentage)	0.2682	Weak driver
Global Annual DALY Burden (DALYs/year)	0.1167	Weak driver

Interpretation: Standardized coefficients show the change in output (in SD units) per 1 SD change in input. Values near ±1 indicate strong influence; values exceeding ±1 may occur with correlated inputs.

2.2.7.2 Monte Carlo Distribution

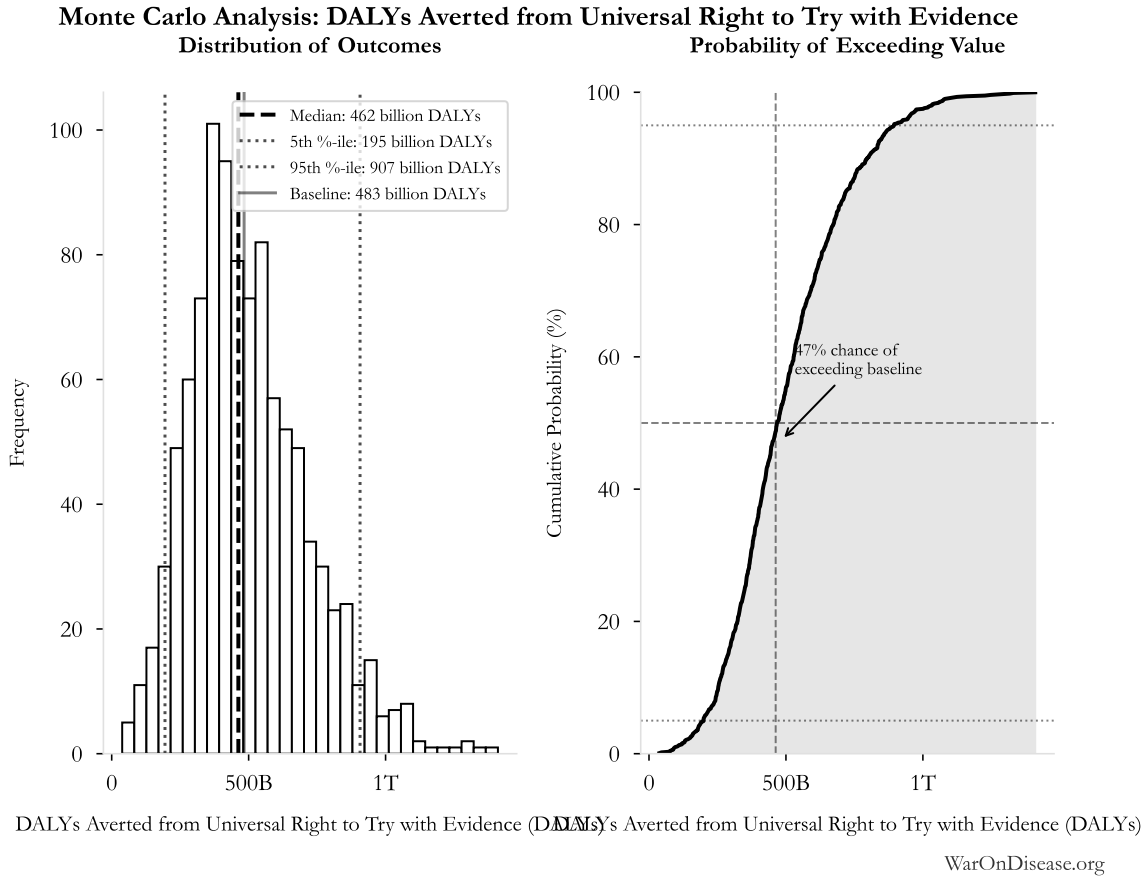


Figure 2.13: Monte Carlo Distribution: DALYs Averted from Universal Right to Try with Evidence (10,000 simulations)

Simulation Results Summary: DALYs Averted from Universal Right to Try with Evidence

Statistic	Value
Baseline (deterministic)	483 billion
Mean (expected value)	495 billion
Median (50th percentile)	462 billion
Standard Deviation	217 billion
90% Range (5th-95th percentile)	[195 billion, 907 billion]

The histogram shows the distribution of DALYs Averted from Universal Right to Try with Evidence across 10,000 Monte Carlo simulations. The CDF (right) shows the probability of the outcome exceeding any given value, which is useful for risk assessment.

2.2.7.3 Exceedance Probability

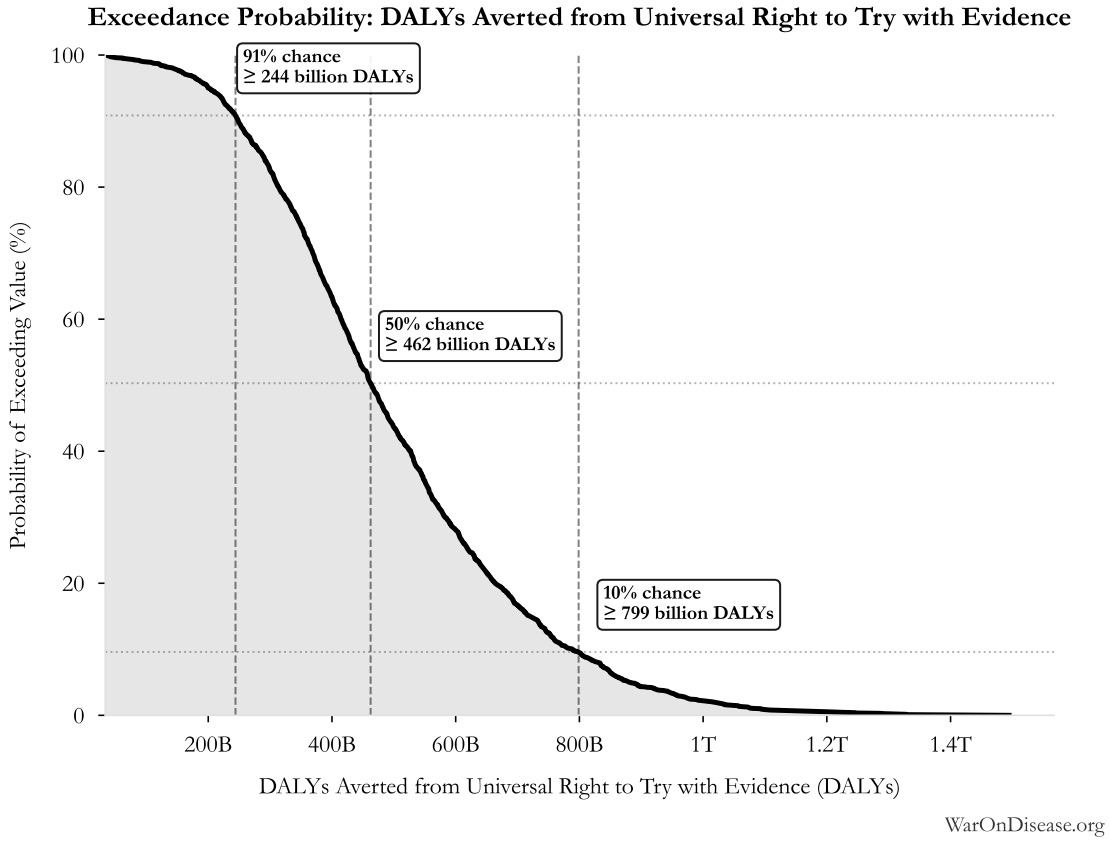


Figure 2.14: Probability of Exceeding Threshold: DALYs Averted from Universal Right to Try with Evidence

This exceedance probability chart shows the likelihood that DALYs Averted from Universal Right to Try with Evidence will exceed any given threshold. Higher curves indicate more favorable outcomes with greater certainty.

2.2.8 Lives Saved from Universal Right to Try with Evidence: 9.19 billion deaths

Details

Conditional cumulative premature deaths from global diseases and aging prevented across future generations by shifting the treatment-discovery schedule forward. The total can exceed the current population because it sums deaths prevented over the full acceleration period.
Inputs:

- Global Daily Deaths from Disease and Aging : 150 thousand deaths/day (SE: ±7,500 deaths/day)
- Eventually Avoidable Death Percentage: 92.6% (95% CI: 50% - 98%)
- Average Treatment Acceleration from Universal Right to Try with Evidence : 181 years

$$
\begin{aligned}
&Lives_{RTT} \\
&= Deaths_{disease,daily} \times Pct_{avoid,death} \times T_{accel,RTT} \times 365 \\
&= 150{,}000 \times 92.6\% \times 181 \times 365 \\
&= 9.19B
\end{aligned}
$$

where:

$$
\begin{aligned}
&T_{accel,RTT} \\
&= T_{first,SQ} \times \left(1 - \frac{1}{k_{RTT}}\right) \\
&= 222 \times \left(1 - \frac{1}{5.48}\right) \\
&= 181
\end{aligned}
$$

where:

$$
\begin{aligned}
&T_{first,SQ} \\
&= T_{queue,SQ} \times 0.5 \\
&= 443 \times 0.5 \\
&= 222
\end{aligned}
$$

where:

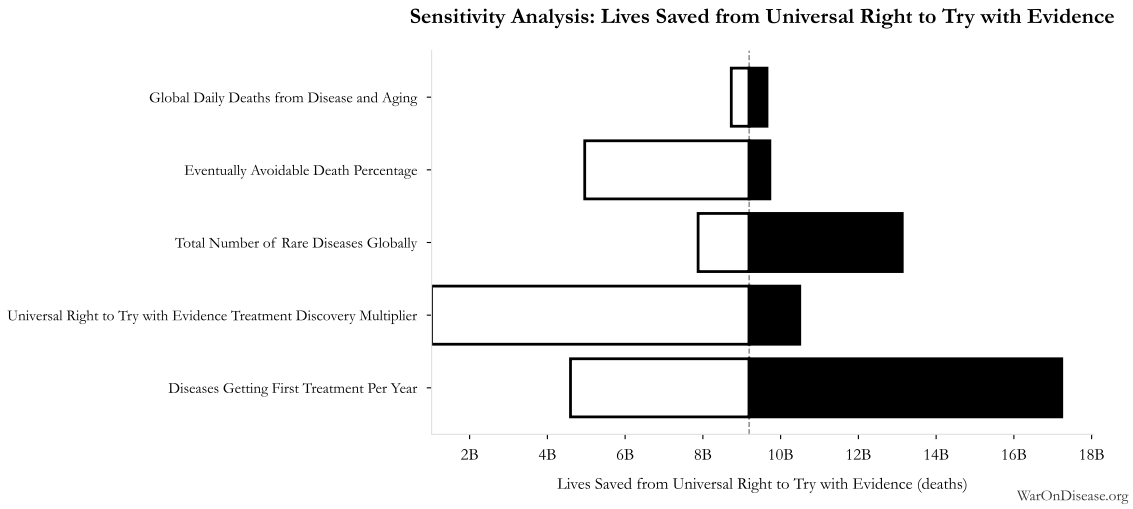
$$
\begin{aligned}
&T_{queue,SQ} \\
&= \frac{N_{untreated}}{Treatments_{new,ann}} \\
&= \frac{6{,}650}{15} \\
&= 443
\end{aligned}
$$

where:

$$
\begin{aligned}
&N_{untreated} \\
&= N_{rare} \times 0.95 \\
&= 7{,}000 \times 0.95 \\
&= 6{,}650
\end{aligned}
$$

? Low confidence

2.2.8.1 Sensitivity Analysis



Sensitivity Indices for Lives Saved from Universal Right to Try with Evidence
Regression-based sensitivity showing which inputs explain the most variance in the output.

Input Parameter	Sensitivity Coefficient	Interpretation
Average Treatment Acceleration from Universal Right to Try with Evidence (years)	0.9436	Strong driver
Eventually Avoidable Death Percentage (percentage)	0.2710	Weak driver
Global Daily Deaths from Disease and Aging (deaths/day)	0.1115	Weak driver

Interpretation: Standardized coefficients show the change in output (in SD units) per 1 SD change in input. Values near ±1 indicate strong influence; values exceeding ±1 may occur with correlated inputs.

2.2.8.2 Monte Carlo Distribution

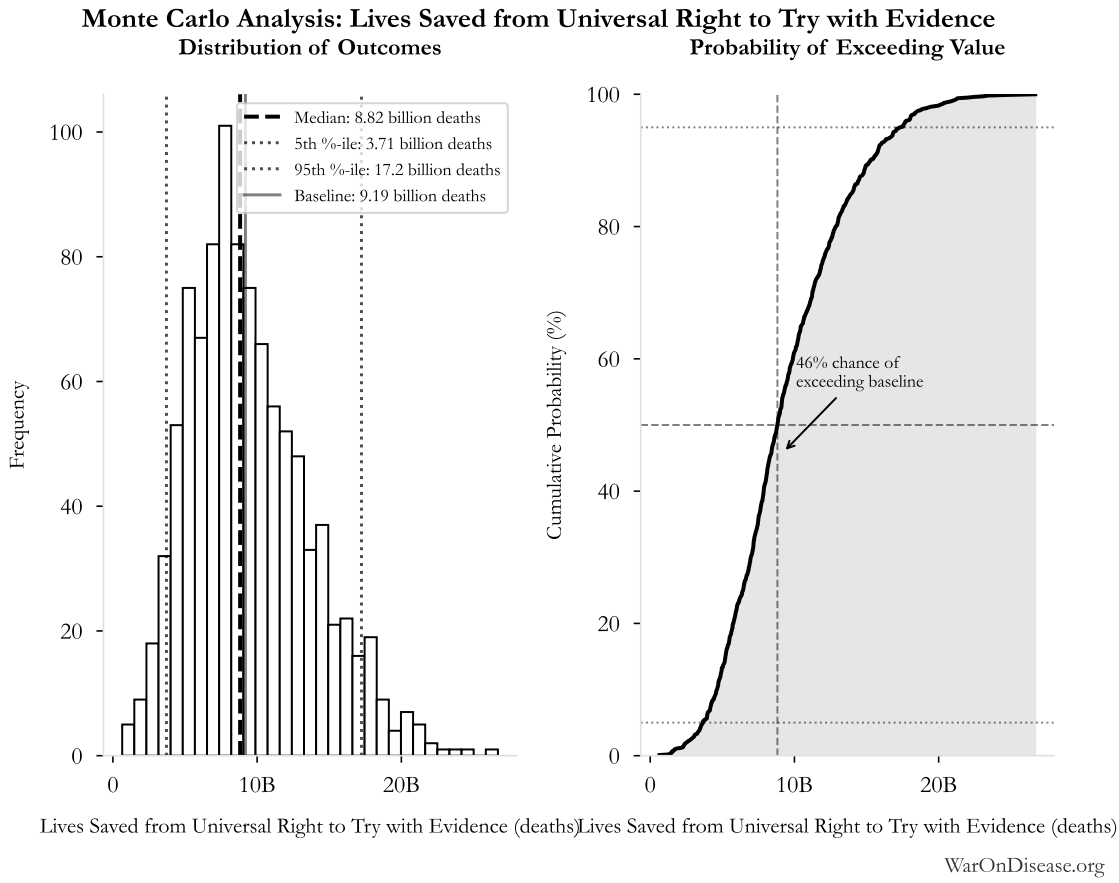


Figure 2.15: Monte Carlo Distribution: Lives Saved from Universal Right to Try with Evidence (10,000 simulations)

Simulation Results Summary: Lives Saved from Universal Right to Try with Evidence

Statistic	Value
Baseline (deterministic)	9.19 billion
Mean (expected value)	9.4 billion
Median (50th percentile)	8.82 billion
Standard Deviation	4.13 billion
90% Range (5th-95th percentile)	[3.71 billion, 17.2 billion]

The histogram shows the distribution of Lives Saved from Universal Right to Try with Evidence across 10,000 Monte Carlo simulations. The CDF (right) shows the probability of the outcome exceeding any given value, which is useful for risk assessment.

2.2.8.3 Exceedance Probability

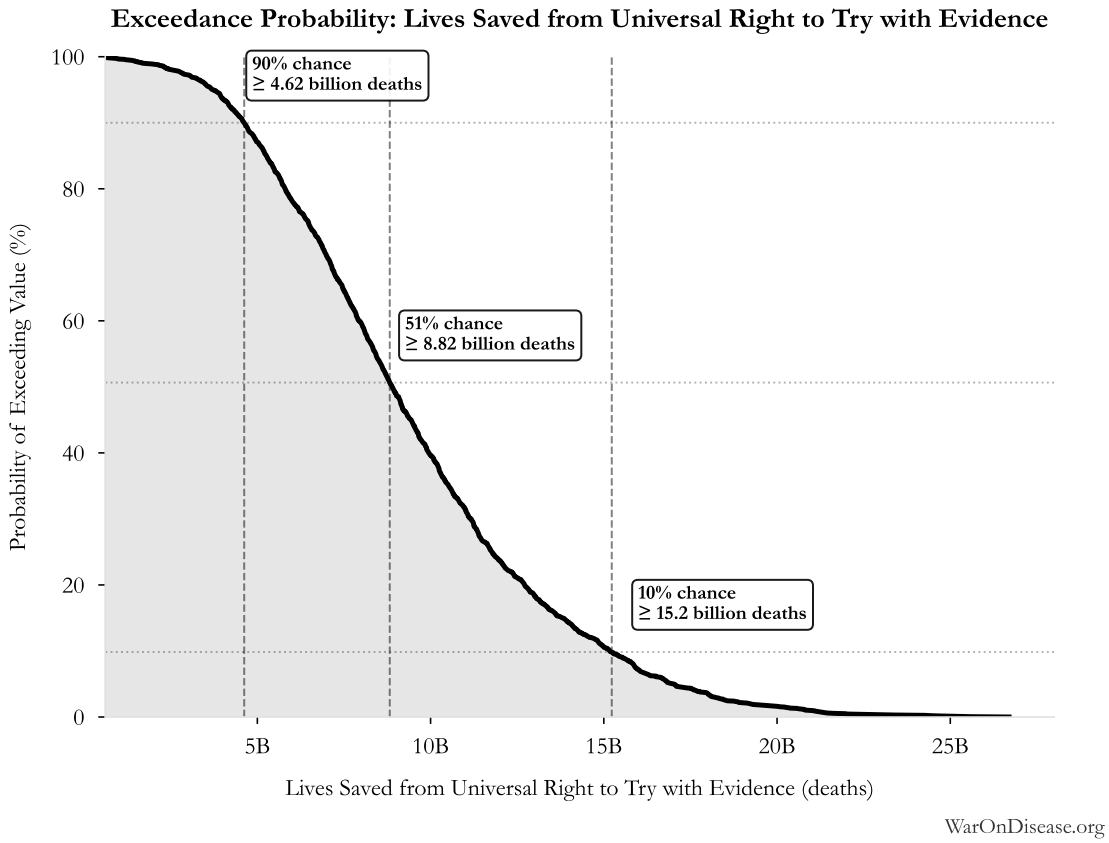


Figure 2.16: Probability of Exceeding Threshold: Lives Saved from Universal Right to Try with Evidence

This exceedance probability chart shows the likelihood that Lives Saved from Universal Right to Try with Evidence will exceed any given threshold. Higher curves indicate more favorable outcomes with greater certainty.

2.2.9 Disability-Equivalent Suffering Hours Prevented by Universal Right to Try with Evidence: 1.65 quadrillion hours

Details

Conditional disability-equivalent hours prevented by the treatment schedule shift. Converts the years-lived-with-disability share of DALYs into hours; it does not claim every hour is an hour of conscious pain.

Inputs:

- DALYs Averted from Universal Right to Try with Evidence : 483 billion DALYs
- YLD Proportion of Total DALYs : 0.39 proportion (SE: ±0.03 proportion)

$$
\begin{aligned}
&Hours_{suffer,RTT} \\
&= DALYs_{RTT} \times Pct_{YLD} \times 8760 \\
&= 483B \times 0.39 \times 8760 \\
&= 1650T
\end{aligned}
$$

where:

$$
\begin{aligned}
&DALYs_{RTT} \\
&= DALYs_{global,ann} \times Pct_{avoid,DALY} \times T_{accel,RTT} \\
&= 2.88B \times 92.6\% \times 181 \\
&= 483B
\end{aligned}
$$

where:

$$
\begin{aligned}
&T_{accel,RTT} \\
&= T_{first,SQ} \times \left(1 - \frac{1}{k_{RTT}}\right) \\
&= 222 \times \left(1 - \frac{1}{5.48}\right) \\
&= 181
\end{aligned}
$$

where:

$$
\begin{aligned}
&T_{first,SQ} \\
&= T_{queue,SQ} \times 0.5 \\
&= 443 \times 0.5 \\
&= 222
\end{aligned}
$$

where:

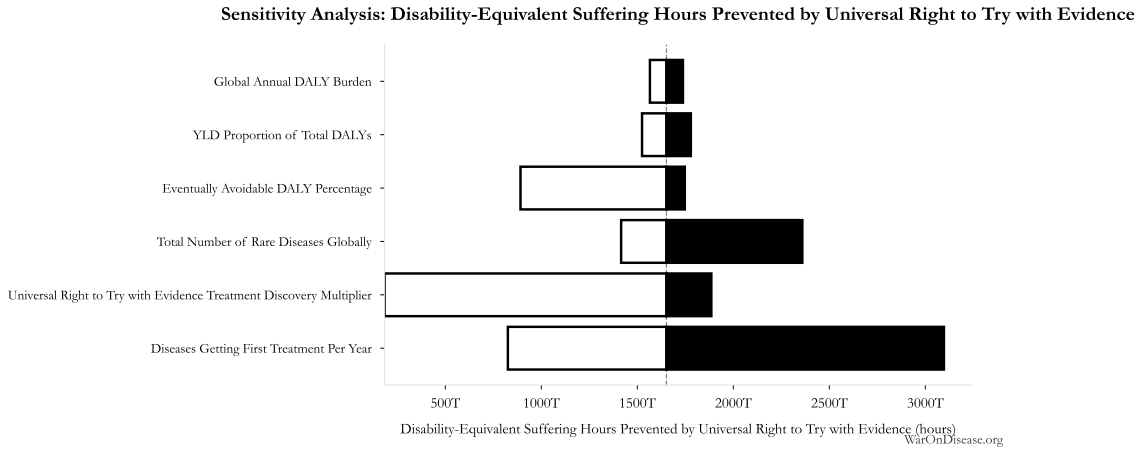
$$
\begin{aligned}
&T_{queue,SQ} \\
&= \frac{N_{untreated}}{Treatments_{new,ann}} \\
&= \frac{6{,}650}{15} \\
&= 443
\end{aligned}
$$

where:

$$\begin{aligned} & N_{untreated} \\ &= N_{rare} \times 0.95 \\ &= 7{,}000 \times 0.95 \\ &= 6{,}650 \end{aligned}$$

? Low confidence

2.2.9.1 Sensitivity Analysis



Sensitivity Indices for Disability-Equivalent Suffering Hours Prevented by Universal Right to Try with Evidence
Regression-based sensitivity showing which inputs explain the most variance in the output.

Input Parameter	Sensitivity Coefficient	Interpretation
DALYs Averted from Universal Right to Try with Evidence (DALYs)	0.9822	Strong driver
YLD Proportion of Total DALYs (proportion)	0.1721	Weak driver

Interpretation: Standardized coefficients show the change in output (in SD units) per 1 SD change in input. Values near ±1 indicate strong influence; values exceeding ±1 may occur with correlated inputs.

2.2.9.2 Monte Carlo Distribution

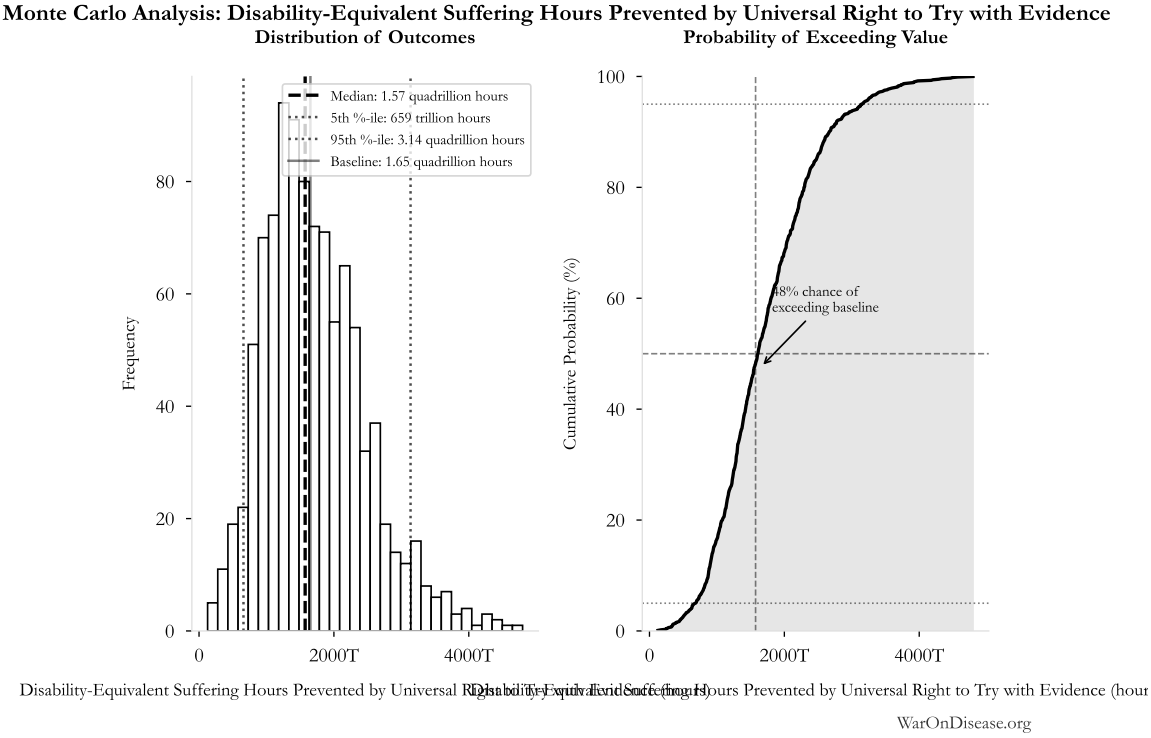


Figure 2.17: Monte Carlo Distribution: Disability-Equivalent Suffering Hours Prevented by Universal Right to Try with Evidence (10,000 simulations)

Simulation Results Summary: Disability-Equivalent Suffering Hours Prevented by Universal Right to Try with Evidence

Statistic	Value
Baseline (deterministic)	1.65 quadrillion
Mean (expected value)	1.69 quadrillion
Median (50th percentile)	1.57 quadrillion
Standard Deviation	756 trillion
90% Range (5th-95th percentile)	[659 trillion, 3.14 quadrillion]

The histogram shows the distribution of Disability-Equivalent Suffering Hours Prevented by Universal Right to Try with Evidence across 10,000 Monte Carlo simulations. The CDF (right) shows the probability of the outcome exceeding any given value, which is useful for risk assessment.

2.2.9.3 Exceedance Probability

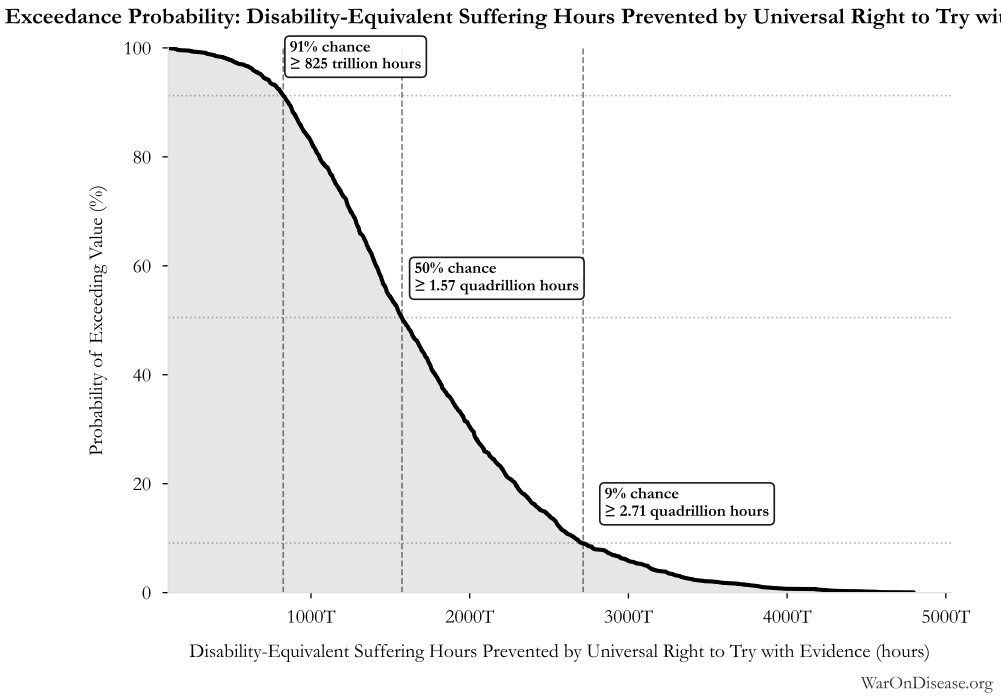


Figure 2.18: Probability of Exceeding Threshold: Disability-Equivalent Suffering Hours Prevented by Universal Right to Try with Evidence

This exceedance probability chart shows the likelihood that Disability-Equivalent Suffering Hours Prevented by Universal Right to Try with Evidence will exceed any given threshold. Higher curves indicate more favorable outcomes with greater certainty.

2.2.10 Average Treatment Acceleration from Universal Right to Try with Evidence: 181 years

Details

Average years earlier the first effective treatment arrives across the global therapeutic frontier after all 50 states adopt Universal Right to Try with Evidence. Uses the same schedule-shift structure as the 1% Treaty impact model: the status quo discovery timeline multiplied by one minus the inverse treatment-discovery multiplier.
Inputs:

- Status Quo Average Years to First Treatment : 222 years
- Universal Right to Try with Evidence Treatment Discovery Multiplier: 5.48x (95% CI: 1.1x - 15x)

$$
\begin{aligned}
&T_{accel,RTT} \\
&= T_{first,SQ} \times \left(1 - \frac{1}{k_{RTT}}\right) \\
&= 222 \times \left(1 - \frac{1}{5.48}\right) \\
&= 181
\end{aligned}
$$

where:

$$
\begin{aligned}
&T_{first,SQ} \\
&= T_{queue,SQ} \times 0.5 \\
&= 443 \times 0.5 \\
&= 222
\end{aligned}
$$

where:

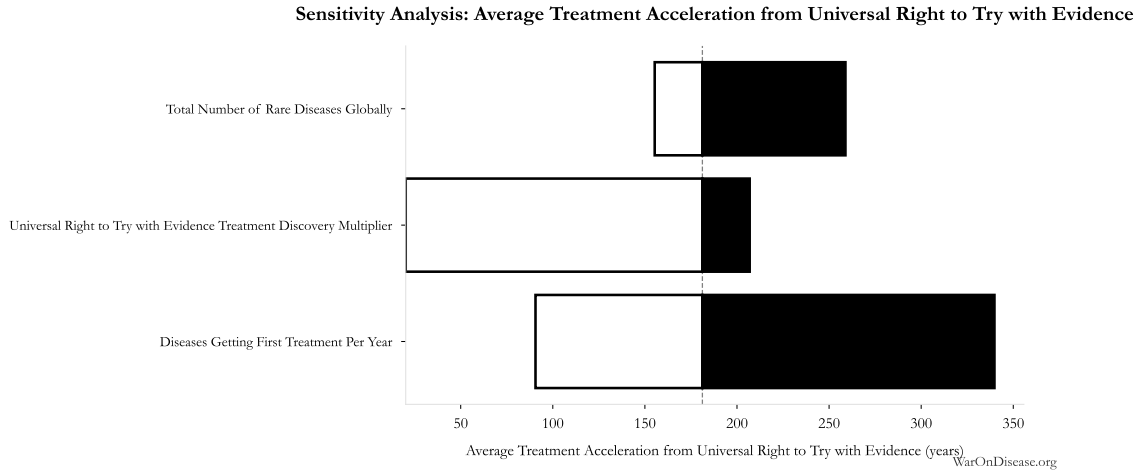
$$
\begin{aligned}
&T_{queue,SQ} \\
&= \frac{N_{untreated}}{Treatments_{new,ann}} \\
&= \frac{6{,}650}{15} \\
&= 443
\end{aligned}
$$

where:

$$
\begin{aligned}
&N_{untreated} \\
&= N_{rare} \times 0.95 \\
&= 7{,}000 \times 0.95 \\
&= 6{,}650
\end{aligned}
$$

? Low confidence

2.2.10.1 Sensitivity Analysis



Sensitivity Indices for Average Treatment Acceleration from Universal Right to Try with Evidence

Regression-based sensitivity showing which inputs explain the most variance in the output.

Input Parameter	Sensitivity Coefficient	Interpretation
Status Quo Average Years to First Treatment (years)	0.8444	Strong driver
Universal Right to Try with Evidence Treatment Discovery Multiplier (x)	0.3959	Moderate driver

Interpretation: Standardized coefficients show the change in output (in SD units) per 1 SD change in input. Values near ±1 indicate strong influence; values exceeding ±1 may occur with correlated inputs.

2.2.10.2 Monte Carlo Distribution

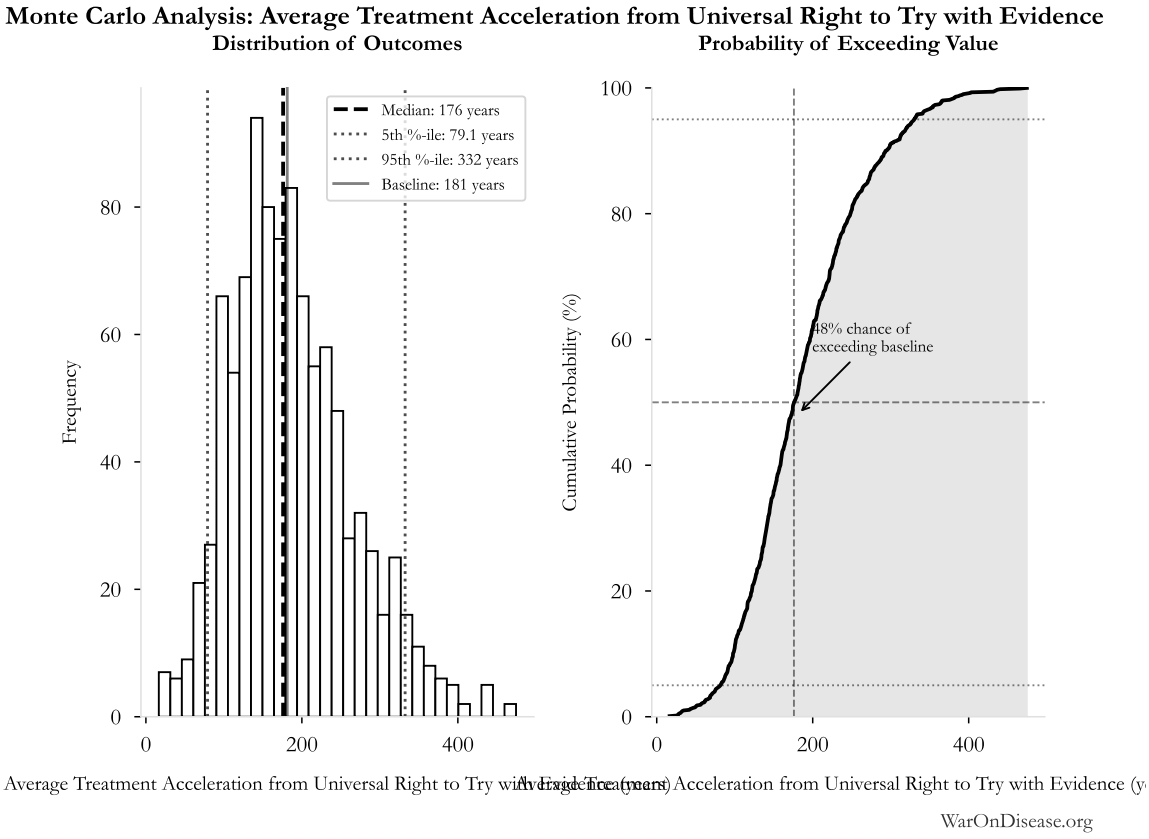


Figure 2.19: Monte Carlo Distribution: Average Treatment Acceleration from Universal Right to Try with Evidence (10,000 simulations)

Simulation Results Summary: Average Treatment Acceleration from Universal Right to Try with Evidence

Statistic	Value
Baseline (deterministic)	181
Mean (expected value)	187
Median (50th percentile)	176
Standard Deviation	77.8
90% Range (5th-95th percentile)	[79.1, 332]

The histogram shows the distribution of Average Treatment Acceleration from Universal Right to Try with Evidence across 10,000 Monte Carlo simulations. The CDF (right) shows the probability of the outcome exceeding any given value, which is useful for risk assessment.

2.2.10.3 Exceedance Probability

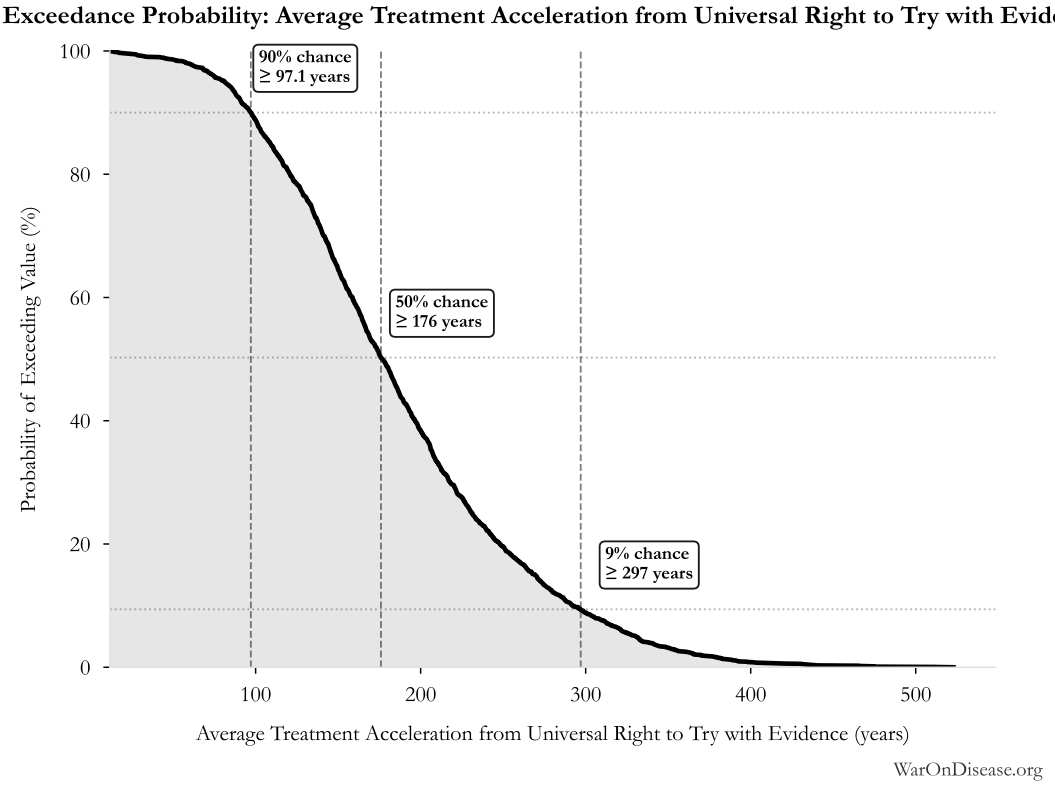


Figure 2.20: Probability of Exceeding Threshold: Average Treatment Acceleration from Universal Right to Try with Evidence

This exceedance probability chart shows the likelihood that Average Treatment Acceleration from Universal Right to Try with Evidence will exceed any given threshold. Higher curves indicate more favorable outcomes with greater certainty.

2.2.11 Universal Right to Try with Evidence Cost in US Military Overspend Hours: 0.811 hours

Details

Hours of estimated annual US military spending above the first-principles baseline for preventing direct attacks on people in the United States equal to the full central philanthropic launch cost for adopting Universal Right to Try with Evidence in all 50 states.

Inputs:

- Universal Right to Try with Evidence Philanthropic Cost: $65 million (95% CI: $25 million - $200 million)
- Military Overspend : $702 billion

$$Hours_{RTT,mil} = \frac{C_{RTT}}{W_{military}} \times 8,760$$

where:

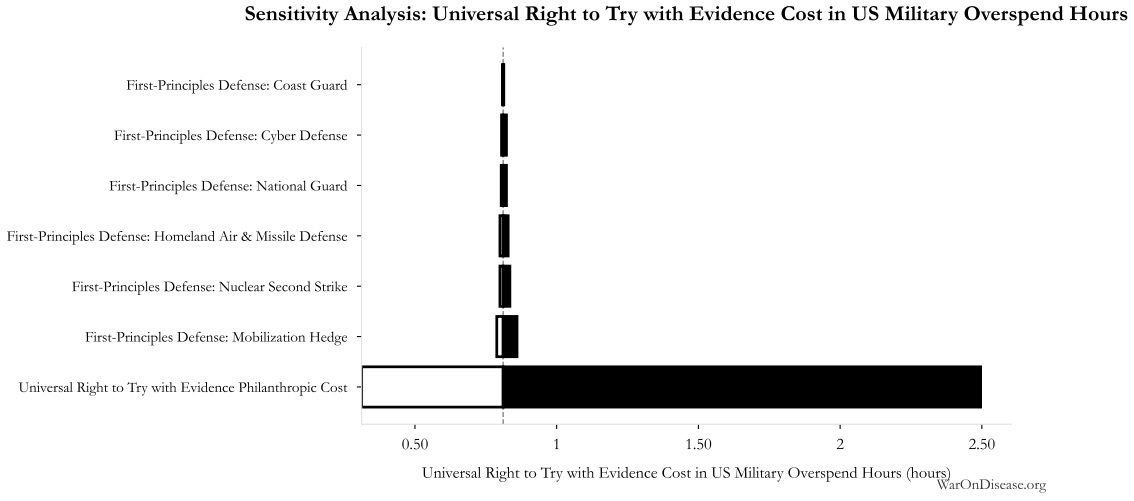
$$\begin{aligned} & W_{military} \\ & = Spending_{US,2024} - D_{optimal} \\ & = \$886B - \$184B \\ & = \$702B \end{aligned}$$

where:

$$\begin{aligned} & D_{optimal} \\ & = D_{nuclear} + D_{air} + D_{cg} + D_{guard} + D_{cyber} \\ & + D_{hedge} \\ & = \$30B + \$35B + \$14B + \$30B + \$15B + \$60B \\ & = \$184B \end{aligned}$$

? Low confidence

2.2.11.1 Sensitivity Analysis



Sensitivity Indices for Universal Right to Try with Evidence Cost in US Military Overspend Hours

Regression-based sensitivity showing which inputs explain the most variance in the output.

Input Parameter	Sensitivity Coefficient	Interpretation
Universal Right to Try with Evidence Philanthropic Cost (USD)	0.9985	Strong driver
Military Overspend (USD)	-0.0402	Minimal effect

Interpretation: Standardized coefficients show the change in output (in SD units) per 1 SD change in input. Values near ±1 indicate strong influence; values exceeding ±1 may occur with correlated inputs.

2.2.11.2 Monte Carlo Distribution

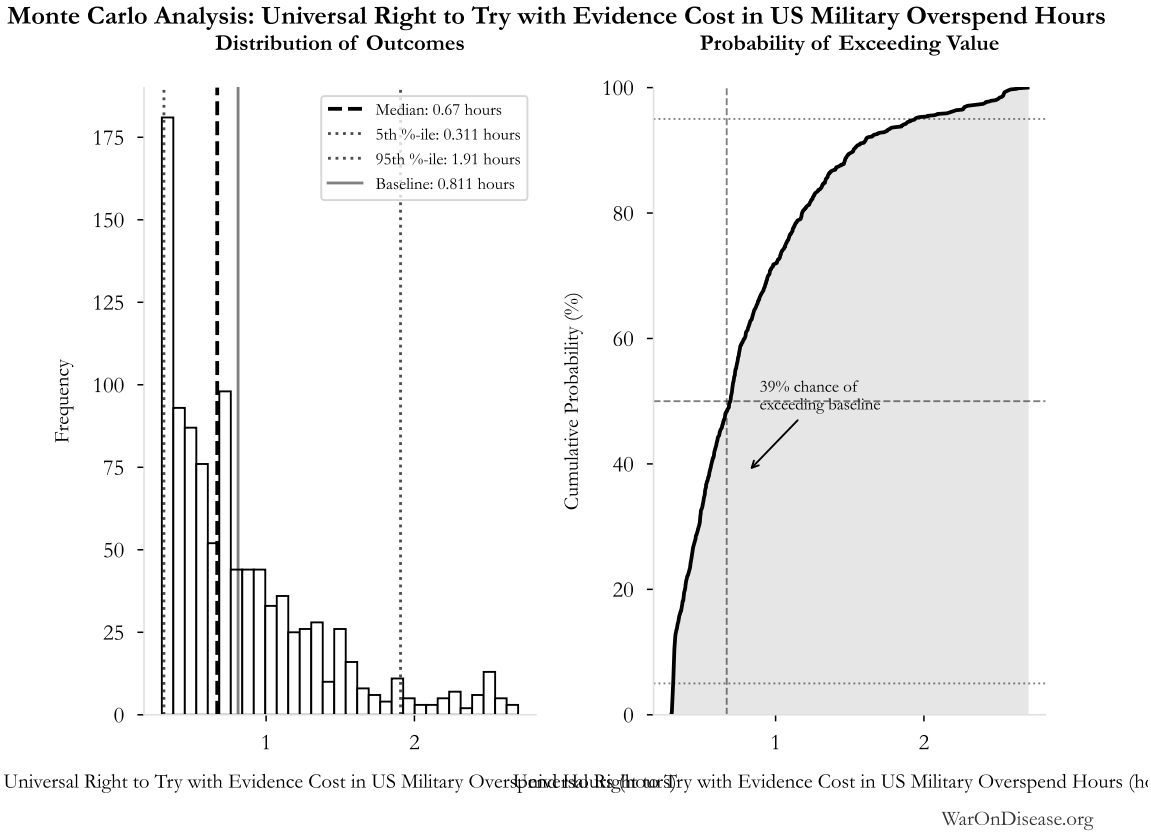


Figure 2.21: Monte Carlo Distribution: Universal Right to Try with Evidence Cost in US Military Overspend Hours (10,000 simulations)

Simulation Results Summary: Universal Right to Try with Evidence Cost in US Military Overspend Hours

Statistic	Value
Baseline (deterministic)	0.811
Mean (expected value)	0.818
Median (50th percentile)	0.67
Standard Deviation	0.504
90% Range (5th-95th percentile)	[0.311, 1.91]

The histogram shows the distribution of Universal Right to Try with Evidence Cost in US Military Overspend Hours across 10,000 Monte Carlo simulations. The CDF (right) shows the probability of the outcome exceeding any given value, which is useful for risk assessment.

2.2.11.3 Exceedance Probability

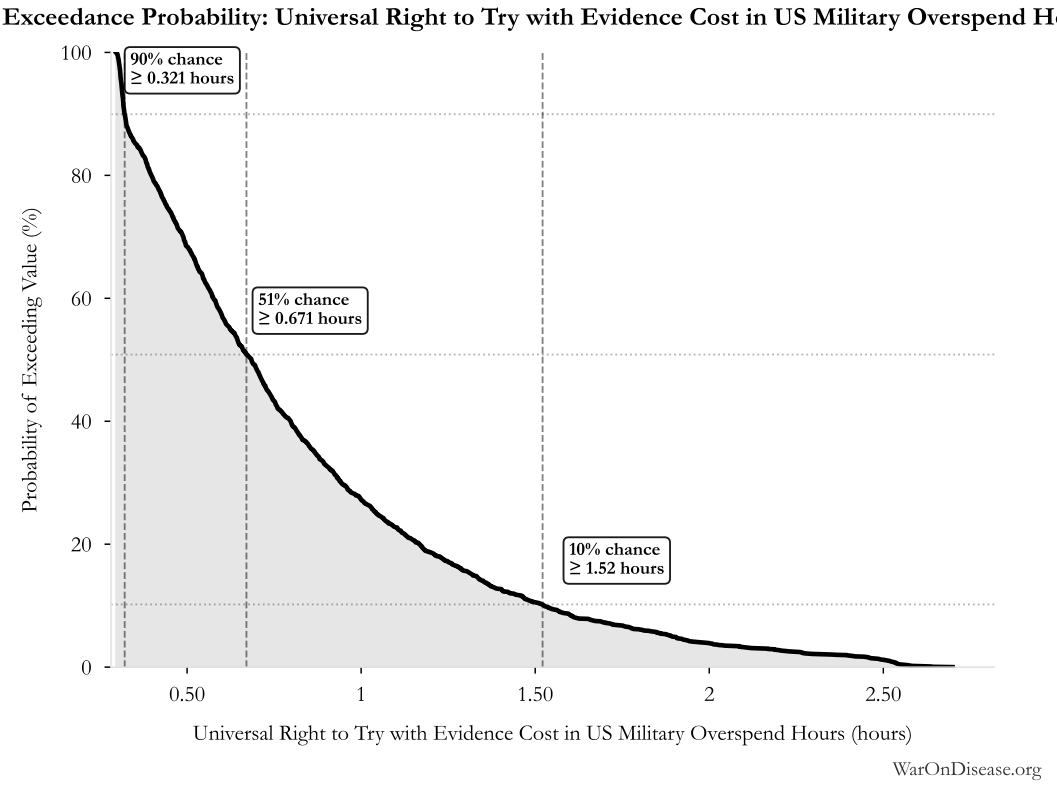


Figure 2.22: Probability of Exceeding Threshold: Universal Right to Try with Evidence Cost in US Military Overspend Hours

This exceedance probability chart shows the likelihood that Universal Right to Try with Evidence Cost in US Military Overspend Hours will exceed any given threshold. Higher curves indicate more favorable outcomes with greater certainty.

2.2.12 Universal Right to Try with Evidence Cost-Effectiveness vs GiveWell Range Midpoint: 636.2kx

Details

Conditional philanthropic cost-effectiveness of adopting Universal Right to Try with Evidence in all 50 states relative to the midpoint of GiveWell's cited modeled cost-per-life-saved range. The cost scopes differ: the Right to Try numerator excludes patient and payer spending on treatment delivery, trial-site services, and permitted study costs, while the GiveWell figure includes full program costs. This comparison is valid only if full adoption and mature implementation produce the modeled treatment schedule shift.

Inputs:

- GiveWell Midpoint of Modeled Cost per Life Saved Range : $4,500
- Universal Right to Try with Evidence Philanthropic Cost per Life Saved : $0.00707

$$
\begin{aligned}
&k_{RTT,GiveWell} \\
&= \frac{Cost_{GW,avg}}{Cost_{RTT,life}} \\
&= \frac{\$4.5K}{\$0.00707} \\
&= 636{,}000
\end{aligned}
$$

where:

$$
\begin{aligned}
&Cost_{RTT,life} \\
&= \frac{C_{RTT}}{Lives_{RTT}} \\
&= \frac{\$65M}{9.19B} \\
&= \$0.00707
\end{aligned}
$$

where:

$$
\begin{aligned}
&Lives_{RTT} \\
&= Deaths_{disease,daily} \times Pct_{avoid,death} \times T_{accel,RTT} \times 365 \\
&= 150{,}000 \times 92.6\% \times 181 \times 365 \\
&= 9.19B
\end{aligned}
$$

where:

$$
\begin{aligned}
&T_{accel,RTT} \\
&= T_{first,SQ} \times \left(1 - \frac{1}{k_{RTT}}\right) \\
&= 222 \times \left(1 - \frac{1}{5.48}\right) \\
&= 181
\end{aligned}
$$

where:

$$
\begin{aligned}
&T_{first,SQ} \\
&= T_{queue,SQ} \times 0.5 \\
&= 443 \times 0.5 \\
&= 222
\end{aligned}
$$

where:

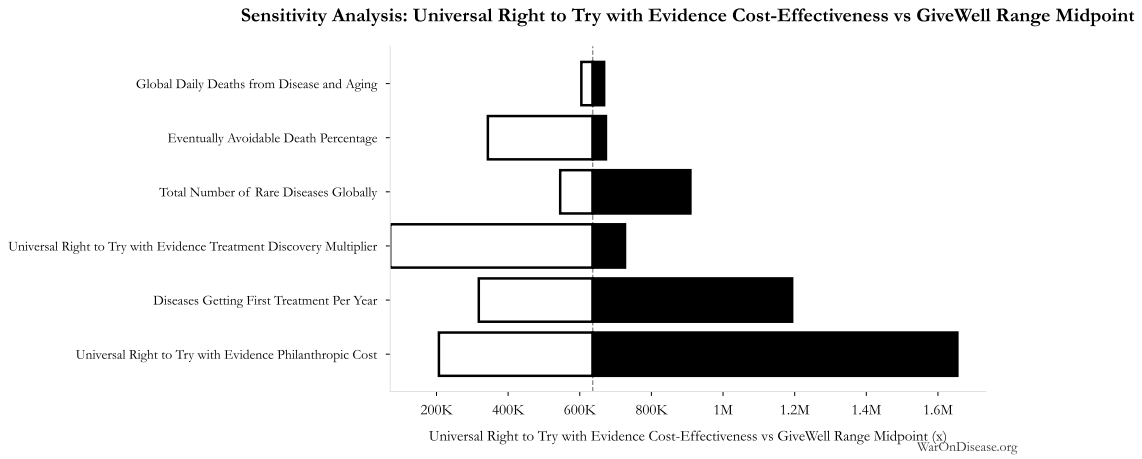
$$
\begin{aligned}
&T_{queue,SQ} \\
&= \frac{N_{untreated}}{Treatments_{new,ann}} \\
&= \frac{6{,}650}{15} \\
&= 443
\end{aligned}
$$

where:

$$
\begin{aligned}
&N_{untreated} \\
&= N_{rare} \times 0.95 \\
&= 7{,}000 \times 0.95 \\
&= 6{,}650
\end{aligned}
$$

? Low confidence

2.2.12.1 Sensitivity Analysis



Sensitivity Indices for Universal Right to Try with Evidence Cost-Effectiveness vs GiveWell Range Midpoint
Regression-based sensitivity showing which inputs explain the most variance in the output.

Input Parameter	Sensitivity Coefficient	Interpretation
Universal Right to Try with Evidence Philanthropic Cost per Life Saved (USD/life)	-0.5292	Strong driver

Interpretation: Standardized coefficients show the change in output (in SD units) per 1 SD change in input. Values near ±1 indicate strong influence; values exceeding ±1 may occur with correlated inputs.

2.2.12.2 Monte Carlo Distribution

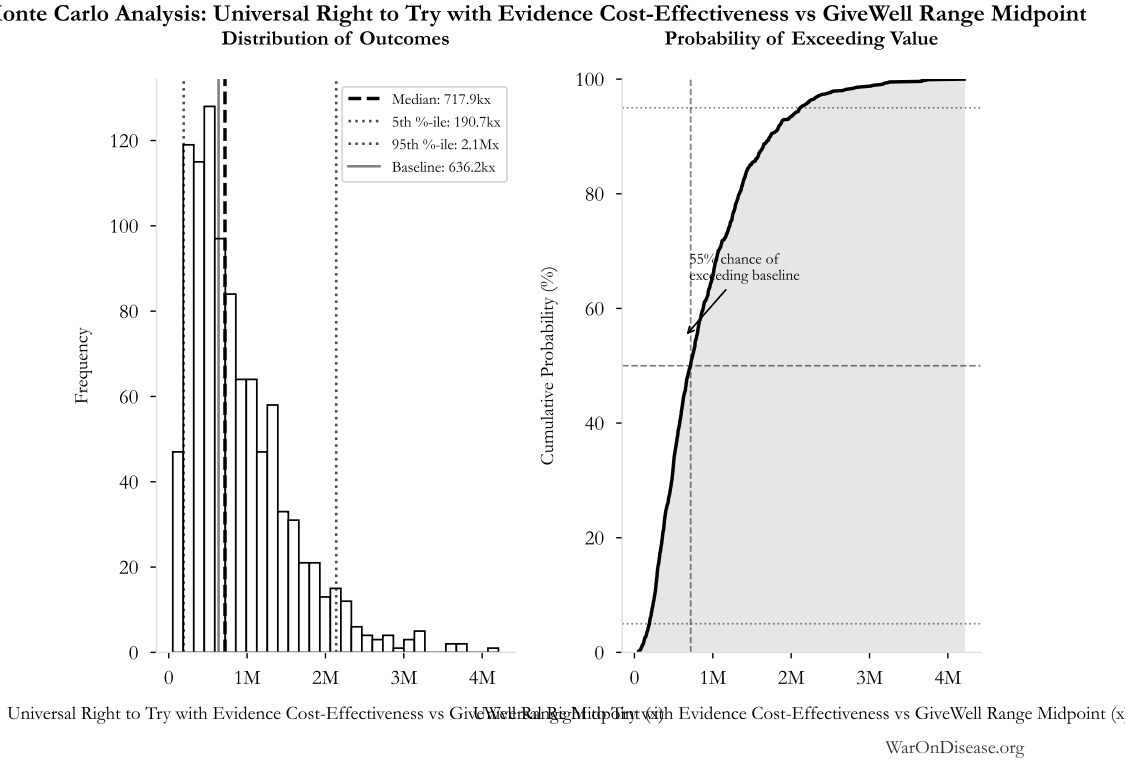


Figure 2.23: Monte Carlo Distribution: Universal Right to Try with Evidence Cost-Effectiveness vs GiveWell Range Midpoint (10,000 simulations)

Simulation Results Summary: Universal Right to Try with Evidence Cost-Effectiveness vs GiveWell Range Midpoint

Statistic	Value
Baseline (deterministic)	636.2kx
Mean (expected value)	881.6kx
Median (50th percentile)	717.9kx
Standard Deviation	629.4kx
90% Range (5th-95th percentile)	[190.7kx, 2.1Mx]

The histogram shows the distribution of Universal Right to Try with Evidence Cost-Effectiveness vs GiveWell Range Midpoint across 10,000 Monte Carlo simulations. The CDF (right) shows the probability of the outcome exceeding any given value, which is useful for risk assessment.

2.2.12.3 Exceedance Probability

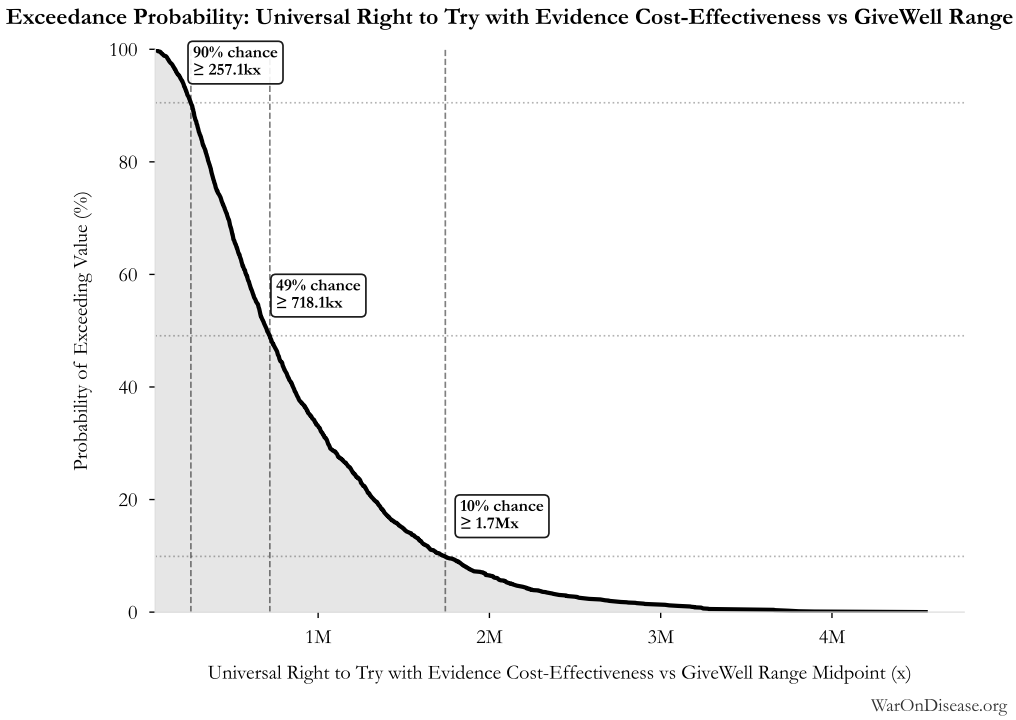


Figure 2.24: Probability of Exceeding Threshold: Universal Right to Try with Evidence Cost-Effectiveness vs GiveWell Range Midpoint

This exceedance probability chart shows the likelihood that Universal Right to Try with Evidence Cost-Effectiveness vs GiveWell Range Midpoint will exceed any given threshold. Higher curves indicate more favorable outcomes with greater certainty.

2.2.13 Status Quo Average Years to First Treatment: 222 years

Details

Average years until first treatment discovered for a typical disease under current system. At current discovery rates, the average disease waits half the total exploration time (~443/2 = ~222 years).

Inputs:

- Status Quo Therapeutic Space Exploration Time : 443 years

$$
\begin{aligned}
&T_{first,SQ} \\
&= T_{queue,SQ} \times 0.5 \\
&= 443 \times 0.5 \\
&= 222
\end{aligned}
$$

where:

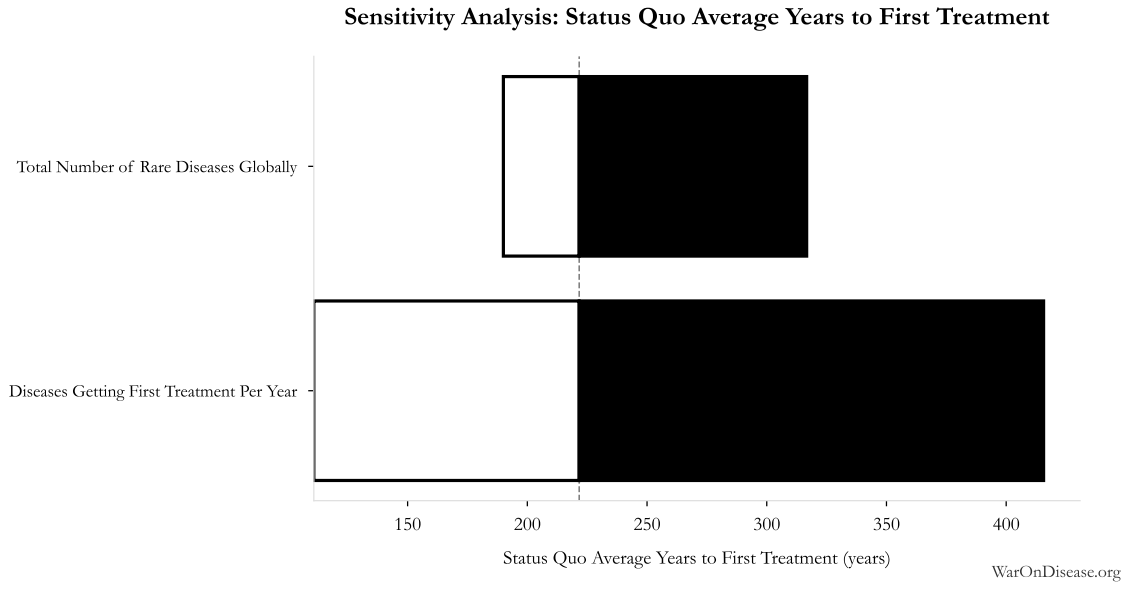
$$
\begin{aligned}
&T_{queue,SQ} \\
&= \frac{N_{untreated}}{Treatments_{new,ann}} \\
&= \frac{6{,}650}{15} \\
&= 443
\end{aligned}
$$

where:

$$
\begin{aligned}
&N_{untreated} \\
&= N_{rare} \times 0.95 \\
&= 7{,}000 \times 0.95 \\
&= 6{,}650
\end{aligned}
$$

Methodology:[198]
? Low confidence

2.2.13.1 Sensitivity Analysis



Sensitivity Indices for Status Quo Average Years to First Treatment
Regression-based sensitivity showing which inputs explain the most variance in the output.

Input Parameter	Sensitivity Coefficient	Interpretation
Status Quo Therapeutic Space Exploration Time (years)	1.0000	Strong driver

Interpretation: Standardized coefficients show the change in output (in SD units) per 1 SD change in input. Values near ±1 indicate strong influence; values exceeding ±1 may occur with correlated inputs.

2.2.13.2 Monte Carlo Distribution

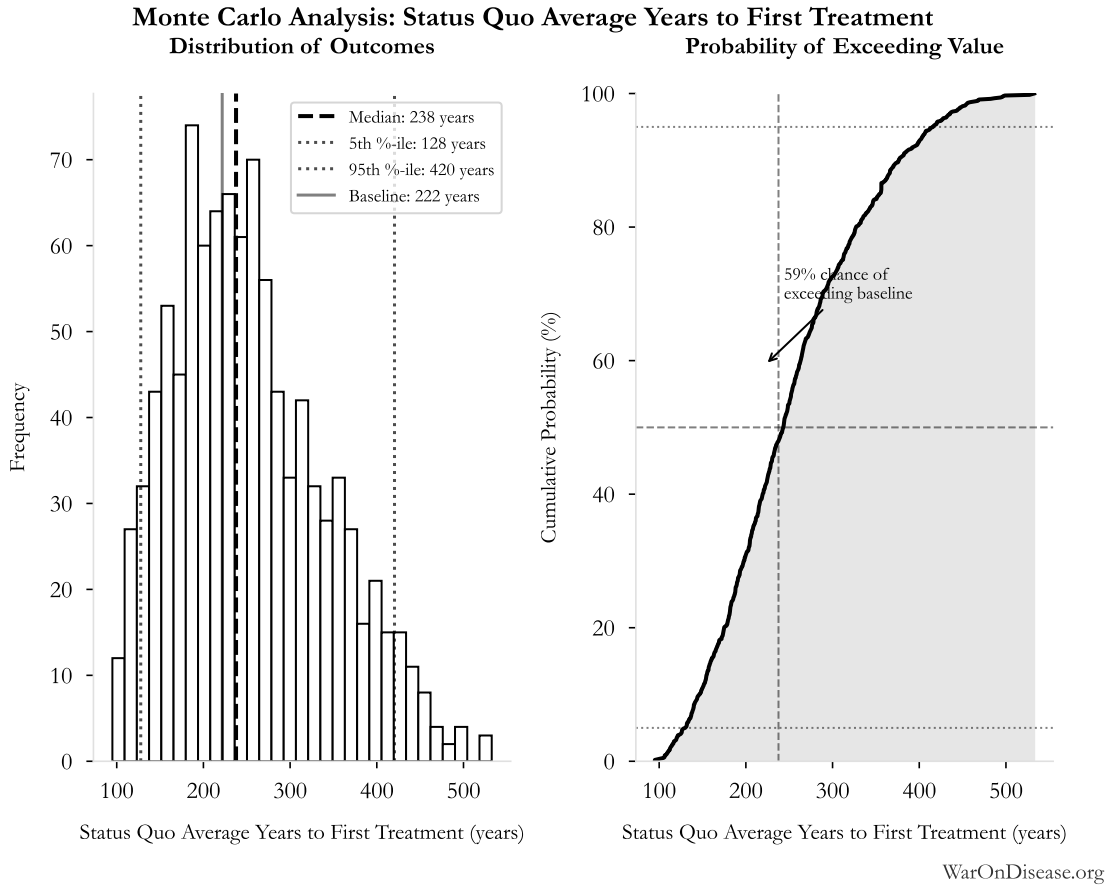


Figure 2.25: Monte Carlo Distribution: Status Quo Average Years to First Treatment (10,000 simulations)

Simulation Results Summary: Status Quo Average Years to First Treatment

Statistic	Value
Baseline (deterministic)	222
Mean (expected value)	251
Median (50th percentile)	238
Standard Deviation	88.8
90% Range (5th-95th percentile)	[128, 420]

The histogram shows the distribution of Status Quo Average Years to First Treatment across 10,000 Monte Carlo simulations. The CDF (right) shows the probability of the outcome exceeding any given value, which is useful for risk assessment.

2.2.13.3 Exceedance Probability

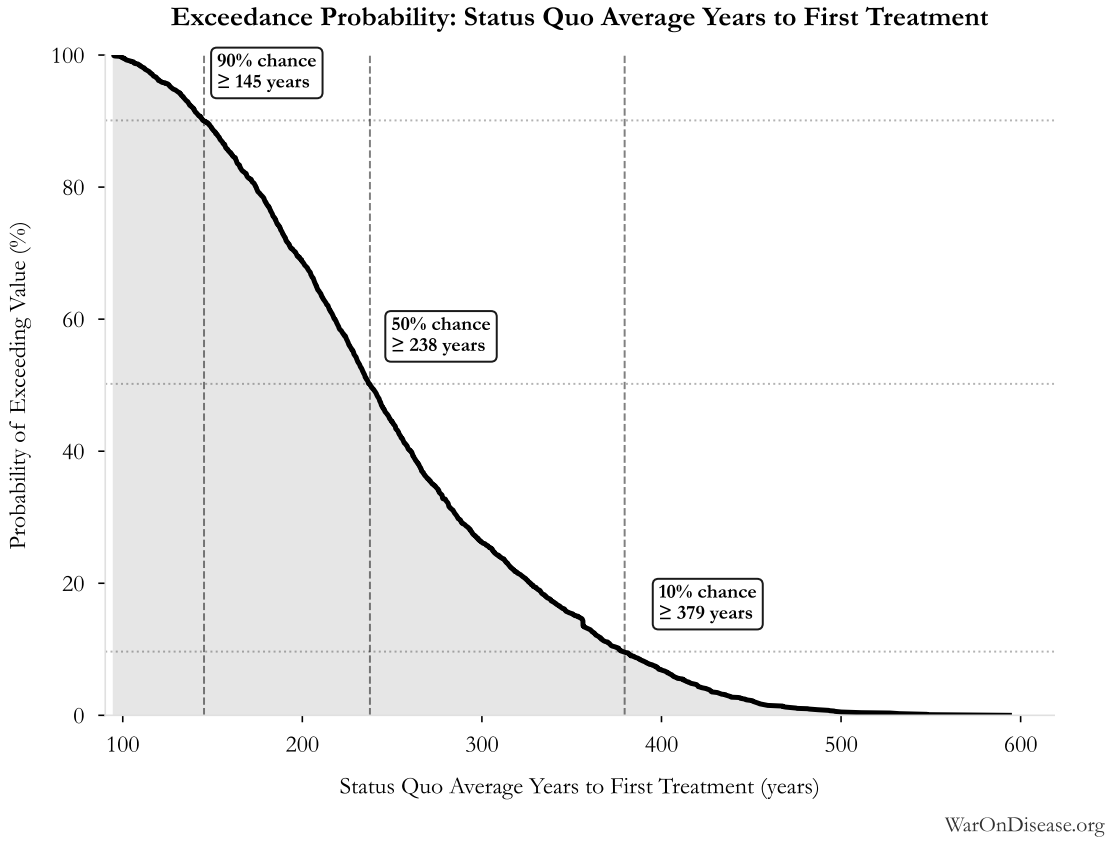


Figure 2.26: Probability of Exceeding Threshold: Status Quo Average Years to First Treatment

This exceedance probability chart shows the likelihood that Status Quo Average Years to First Treatment will exceed any given threshold. Higher curves indicate more favorable outcomes with greater certainty.

2.2.14 Status Quo Therapeutic Space Exploration Time: 443 years

Details

Years to explore the entire therapeutic search space under current system. At current discovery rate of ~15 diseases/year getting first treatments, finding treatments for all ~6,650 untreated diseases would take ~443 years.

Inputs:

- Diseases Without Effective Treatment : 6,650 diseases
- Diseases Getting First Treatment Per Year : 15 diseases/year (95% CI: 8 diseases/year - 30 diseases/year)

$$
\begin{aligned}
&T_{queue,SQ} \\
&= \frac{N_{untreated}}{Treatments_{new,ann}} \\
&= \frac{6{,}650}{15} \\
&= 443
\end{aligned}
$$

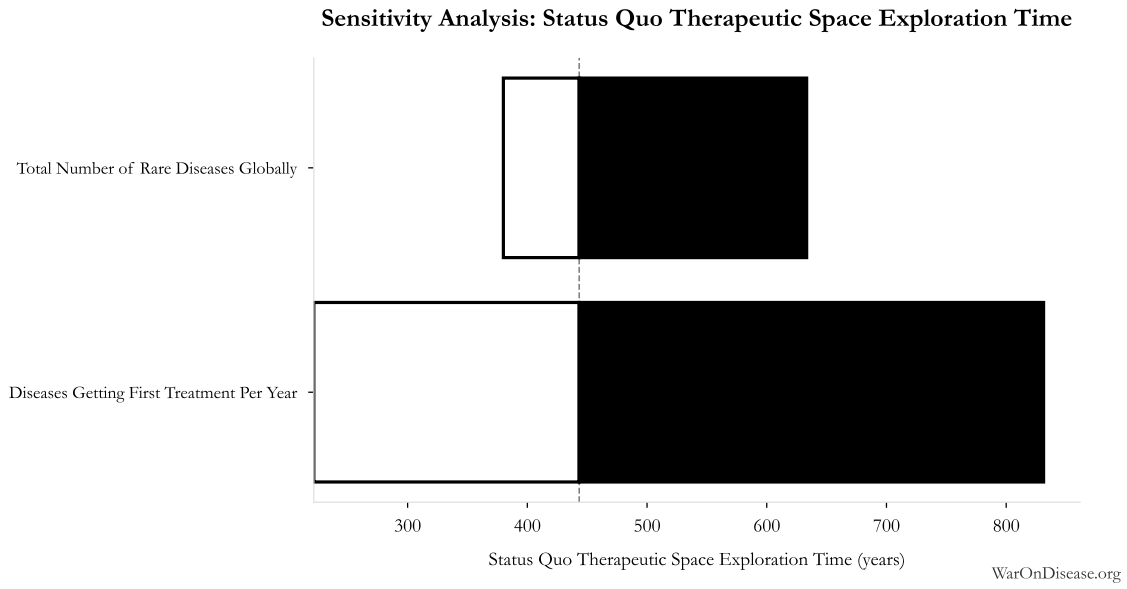
where:

$$
\begin{aligned}
&N_{untreated} \\
&= N_{rare} \times 0.95 \\
&= 7{,}000 \times 0.95 \\
&= 6{,}650
\end{aligned}
$$

Methodology:[198]

? Low confidence

2.2.14.1 Sensitivity Analysis



Sensitivity Indices for Status Quo Therapeutic Space Exploration Time
Regression-based sensitivity showing which inputs explain the most variance in the output.

Input Parameter	Sensitivity Coefficient	Interpretation
Diseases Getting First Treatment Per Year (diseases/year)	-0.8696	Strong driver
Diseases Without Effective Treatment (diseases)	0.3427	Moderate driver

Interpretation: Standardized coefficients show the change in output (in SD units) per 1 SD change in input. Values near ±1 indicate strong influence; values exceeding ±1 may occur with correlated inputs.

2.2.14.2 Monte Carlo Distribution

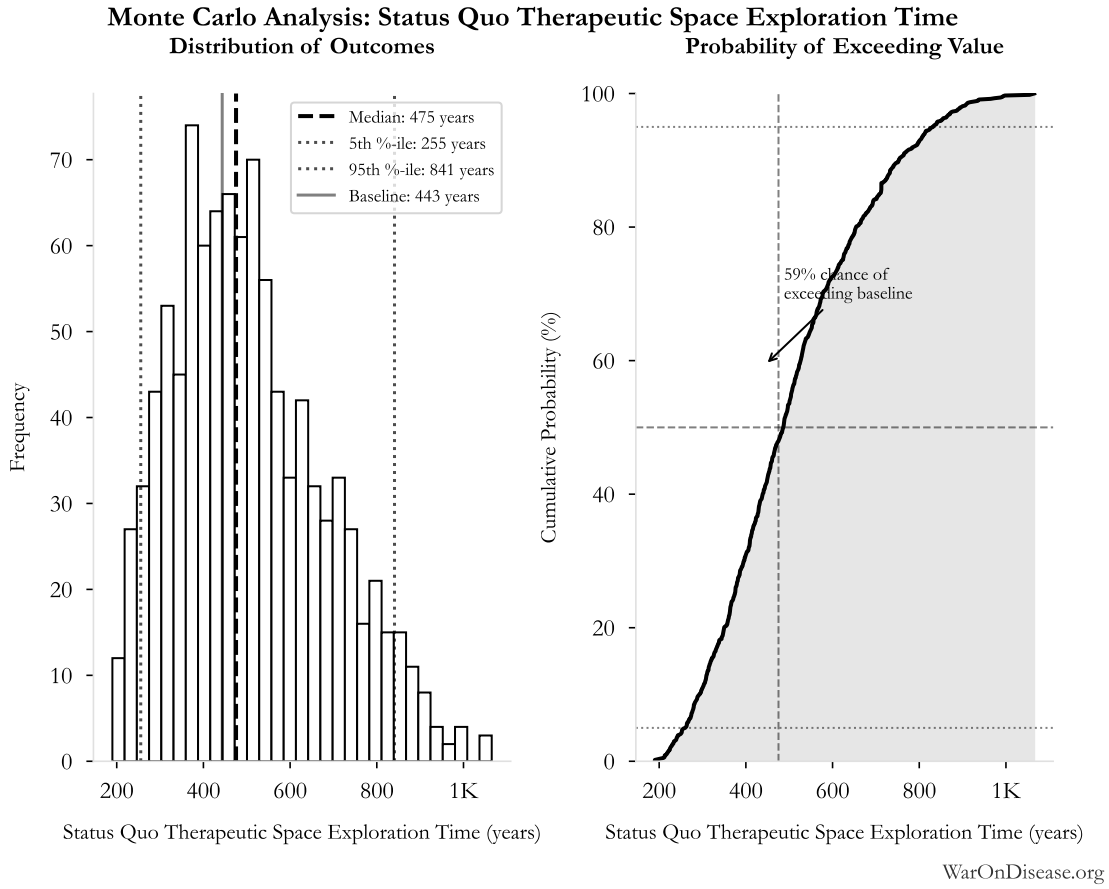


Figure 2.27: Monte Carlo Distribution: Status Quo Therapeutic Space Exploration Time (10,000 simulations)

Simulation Results Summary: Status Quo Therapeutic Space Exploration Time

Statistic	Value
Baseline (deterministic)	443
Mean (expected value)	502
Median (50th percentile)	475
Standard Deviation	178
90% Range (5th-95th percentile)	[255, 841]

The histogram shows the distribution of Status Quo Therapeutic Space Exploration Time across 10,000 Monte Carlo simulations. The CDF (right) shows the probability of the outcome exceeding any given value, which is useful for risk assessment.

2.2.14.3 Exceedance Probability

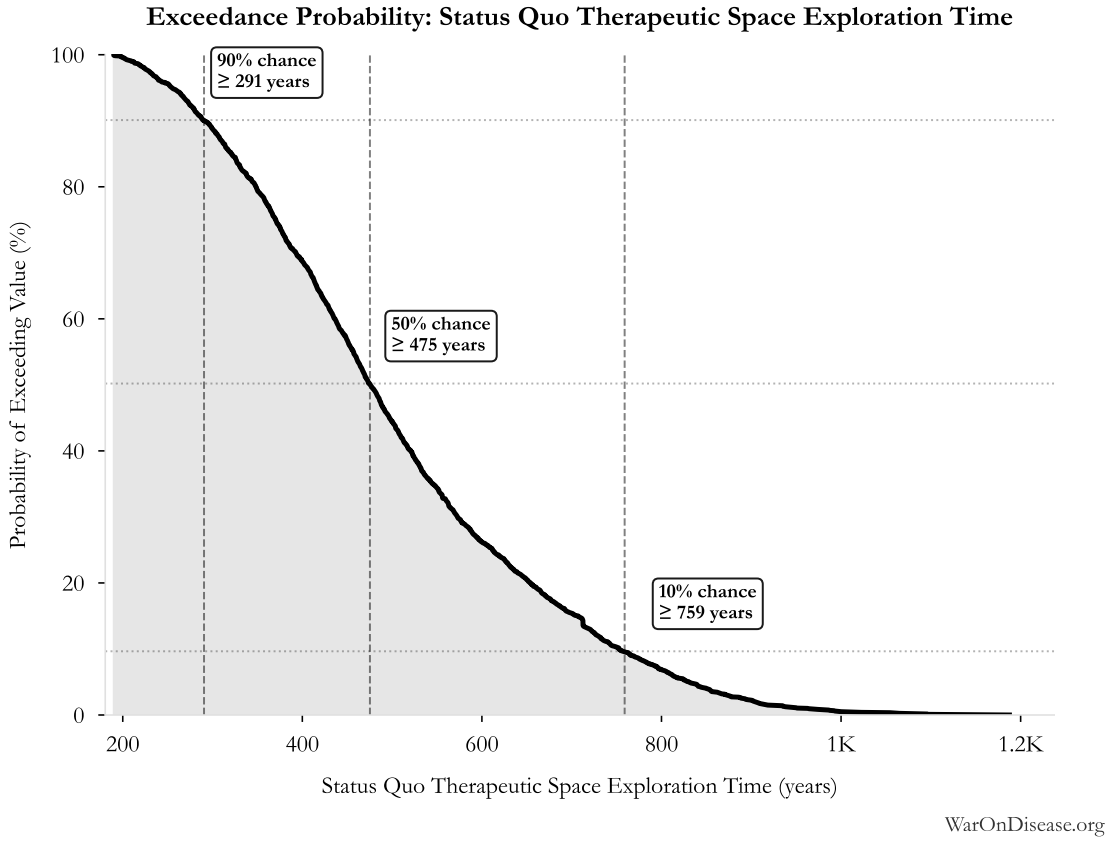


Figure 2.28: Probability of Exceeding Threshold: Status Quo Therapeutic Space Exploration Time

This exceedance probability chart shows the likelihood that Status Quo Therapeutic Space Exploration Time will exceed any given threshold. Higher curves indicate more favorable outcomes with greater certainty.

2.2.15 First-Principles Optimal US Defense Budget: $184 billion

Details

First-principles optimal US homeland-defense budget: the bottom-up sum of what defending the United States actually requires at efficient prices. Nuclear second strike $30B + homeland air/missile defense $35B + Coast Guard $14B + National Guard $30B + cyber defense $15B + mobilization hedge $60B = ~$184B. Honest range ~$130-260B. Compare: current ~$886B. Restraint-school proposals (Posen, Cato) and peer benchmarks land higher (~$450-675B) because they cost reduced hegemony and allied/peer deterrence, not homeland defense.

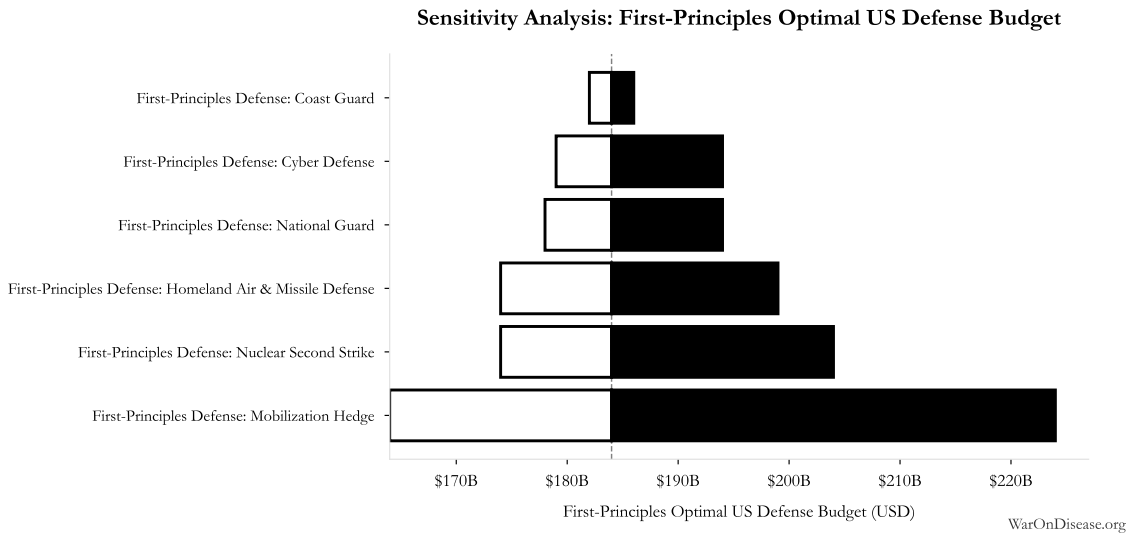
Inputs:

- First-Principles Defense: Nuclear Second Strike: $30 billion (95% CI: $20 billion - $50 billion)
- First-Principles Defense: Homeland Air & Missile Defense: $35 billion (95% CI: $25 billion - $50 billion)
- First-Principles Defense: Coast Guard: $14 billion (95% CI: $12 billion - $16 billion)
- First-Principles Defense: National Guard: $30 billion (95% CI: $24 billion - $40 billion)
- First-Principles Defense: Cyber Defense: $15 billion (95% CI: $10 billion - $25 billion)
- First-Principles Defense: Mobilization Hedge: $60 billion (95% CI: $40 billion - $100 billion)

$$
\begin{aligned}
&D_{optimal} \\
&= D_{nuclear} + D_{air} + D_{cg} + D_{guard} + D_{cyber} \\
&\quad + D_{hedge} \\
&= \$30B + \$35B + \$14B + \$30B + \$15B + \$60B \\
&= \$184B
\end{aligned}
$$

~ *Medium confidence*

2.2.15.1 Sensitivity Analysis



Sensitivity Indices for First-Principles Optimal US Defense Budget
Regression-based sensitivity showing which inputs explain the most variance in the output.

Input Parameter	Sensitivity Coefficient	Interpretation
First-Principles Defense: Mobilization Hedge (USD)	0.7817	Strong driver
First-Principles Defense: Nuclear Second Strike (USD)	0.4131	Moderate driver
First-Principles Defense: Homeland Air & Missile Defense (USD)	0.3684	Moderate driver
First-Principles Defense: National Guard (USD)	0.2171	Weak driver
First-Principles Defense: Cyber Defense (USD)	0.2081	Weak driver
First-Principles Defense: Coast Guard (USD)	0.0717	Minimal effect

Interpretation: Standardized coefficients show the change in output (in SD units) per 1 SD change in input. Values near ±1 indicate strong influence; values exceeding ±1 may occur with correlated inputs.

2.2.15.2 Monte Carlo Distribution

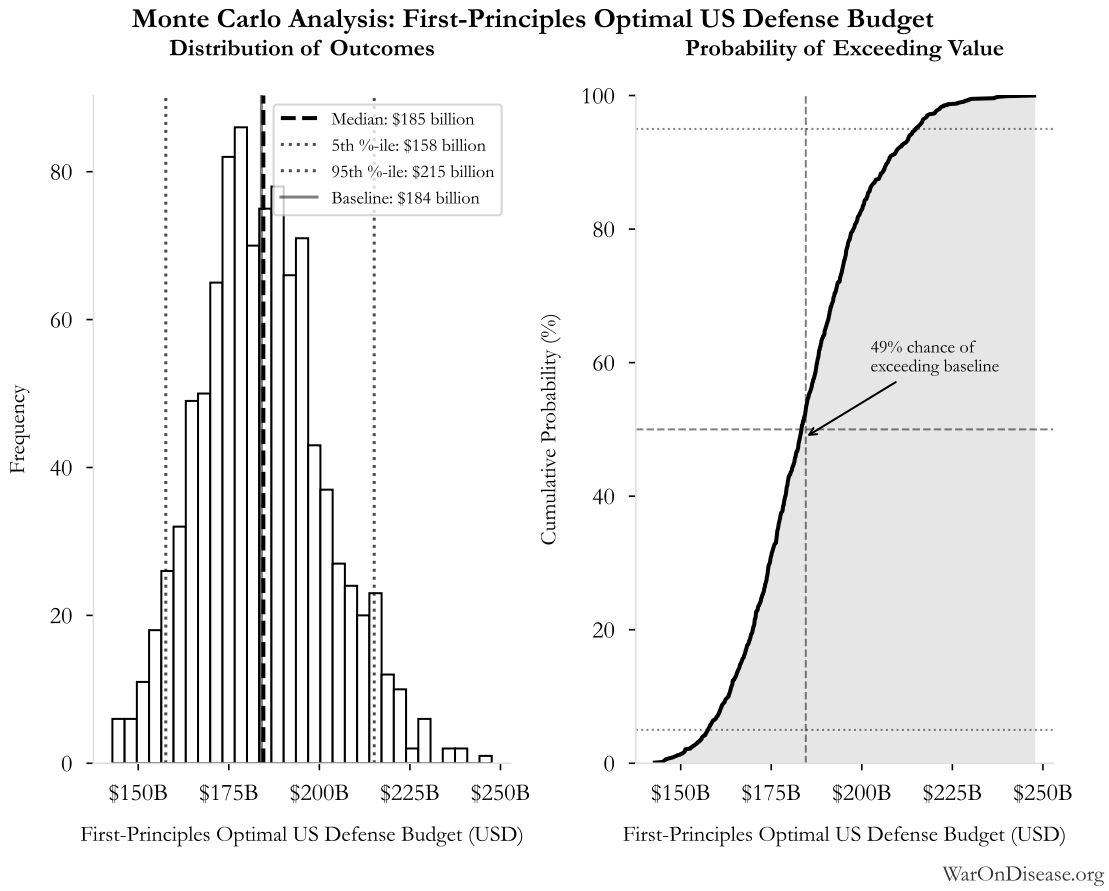


Figure 2.29: Monte Carlo Distribution: First-Principles Optimal US Defense Budget (10,000 simulations)

Simulation Results Summary: First-Principles Optimal US Defense Budget

Statistic	Value
Baseline (deterministic)	$184 billion
Mean (expected value)	$185 billion
Median (50th percentile)	$185 billion
Standard Deviation	$17.4 billion
90% Range (5th-95th percentile)	[$158 billion, $215 billion]

The histogram shows the distribution of First-Principles Optimal US Defense Budget across 10,000 Monte Carlo simulations. The CDF (right) shows the probability of the outcome exceeding any given value, which is useful for risk assessment.

2.2.15.3 Exceedance Probability

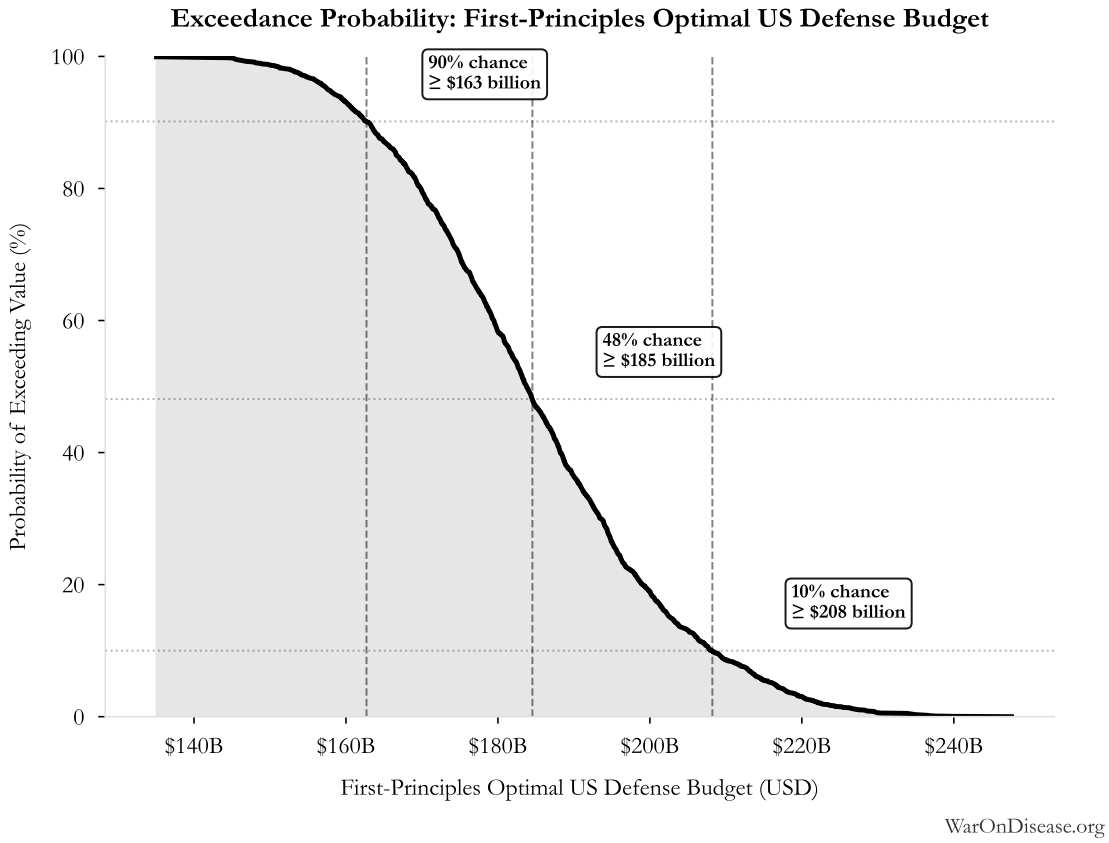


Figure 2.30: Probability of Exceeding Threshold: First-Principles Optimal US Defense Budget

This exceedance probability chart shows the likelihood that First-Principles Optimal US Defense Budget will exceed any given threshold. Higher curves indicate more favorable outcomes with greater certainty.

2.2.16 Military Overspend: $702 billion

Details

US military spending above the first-principles homeland-defense optimum. Current US military spending (~$886B) supports global power projection (~750 overseas bases). A bottom-up, threat-by-threat homeland-defense budget is ~$184B (nuclear second strike $30B, homeland air/missile defense $35B, Coast Guard $14B, National Guard $30B, cyber defense $15B, mobilization hedge $60B). Delta = $886B - $184B = ~$702B 'Hegemony Tax'. [CATEGORY 1: Direct Spending]

Inputs:

- US Military Spending in 2024 : $886 billion
- First-Principles Optimal US Defense Budget : $184 billion

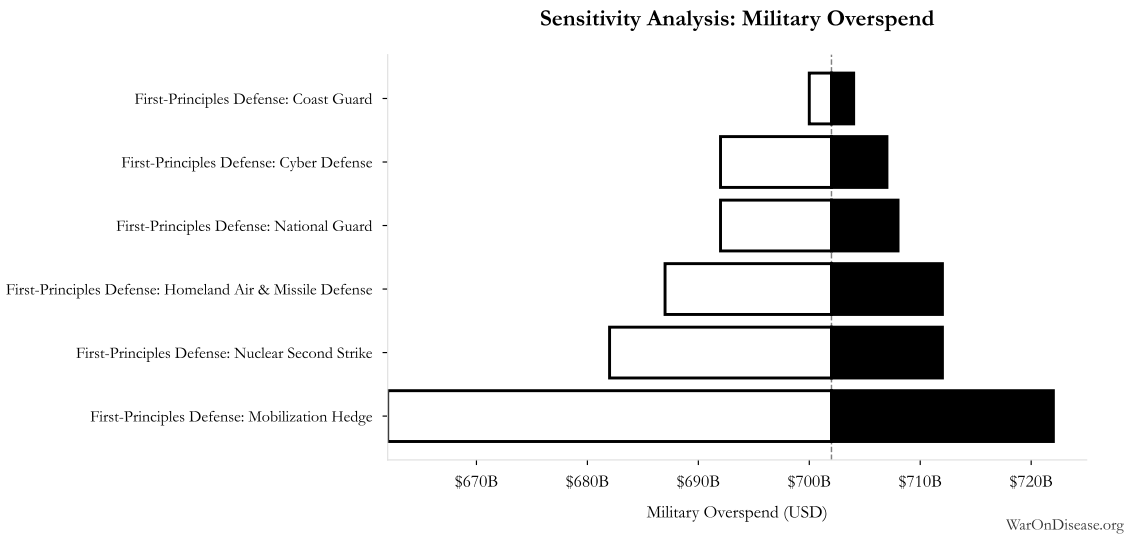
$$
\begin{aligned}
& W_{military} \\
&= Spending_{US,2024} - D_{optimal} \\
&= \$886B - \$184B \\
&= \$702B
\end{aligned}
$$

where:

$$
\begin{aligned}
& D_{optimal} \\
&= D_{nuclear} + D_{air} + D_{cg} + D_{guard} + D_{cyber} \\
&\quad + D_{hedge} \\
&= \$30B + \$35B + \$14B + \$30B + \$15B + \$60B \\
&= \$184B
\end{aligned}
$$

~ *Medium confidence*

2.2.16.1 Sensitivity Analysis



Sensitivity Indices for Military Overspend

Regression-based sensitivity showing which inputs explain the most variance in the output.

Input Parameter	Sensitivity Coefficient	Interpretation
First-Principles Optimal US Defense Budget (USD)	-1.0000	Strong driver

Interpretation: Standardized coefficients show the change in output (in SD units) per 1 SD change in input. Values near ±1 indicate strong influence; values exceeding ±1 may occur with correlated inputs.

2.2.16.2 Monte Carlo Distribution

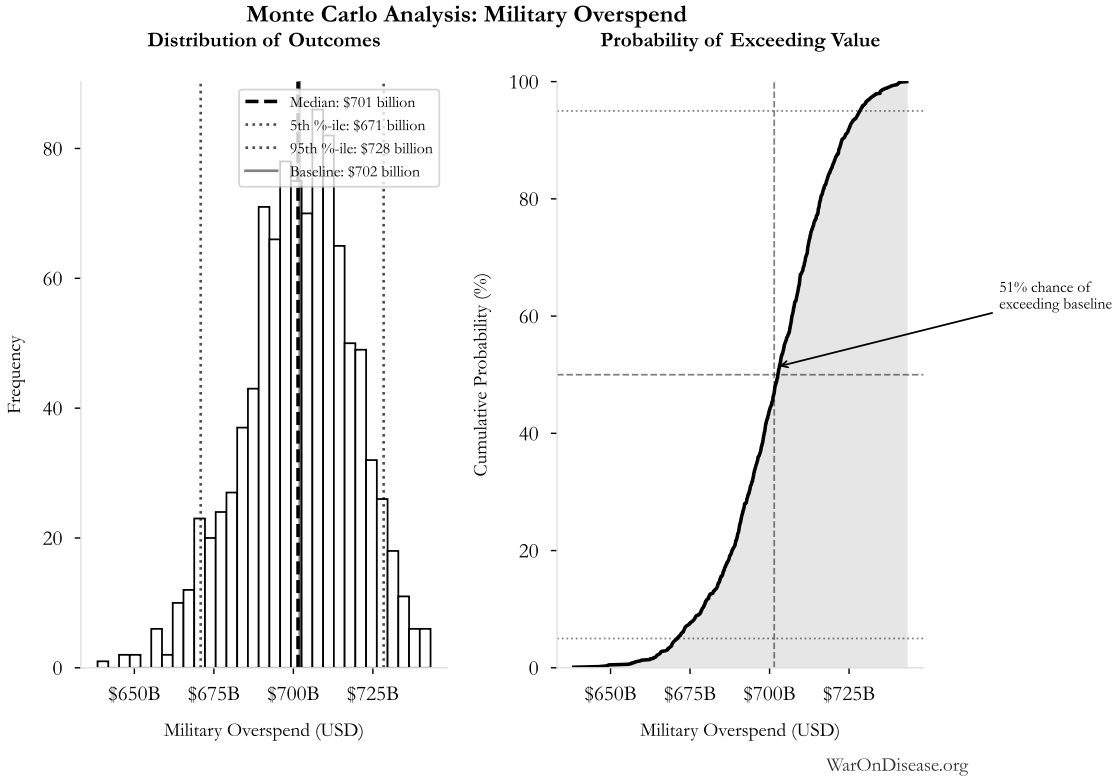


Figure 2.31: Monte Carlo Distribution: Military Overspend (10,000 simulations)

Simulation Results Summary: Military Overspend

Statistic	Value
Baseline (deterministic)	$702 billion
Mean (expected value)	$701 billion
Median (50th percentile)	$701 billion
Standard Deviation	$17.4 billion
90% Range (5th-95th percentile)	[$671 billion, $728 billion]

The histogram shows the distribution of Military Overspend across 10,000 Monte Carlo simulations. The CDF (right) shows the probability of the outcome exceeding any given value, which is useful for risk assessment.

2.2.16.3 Exceedance Probability

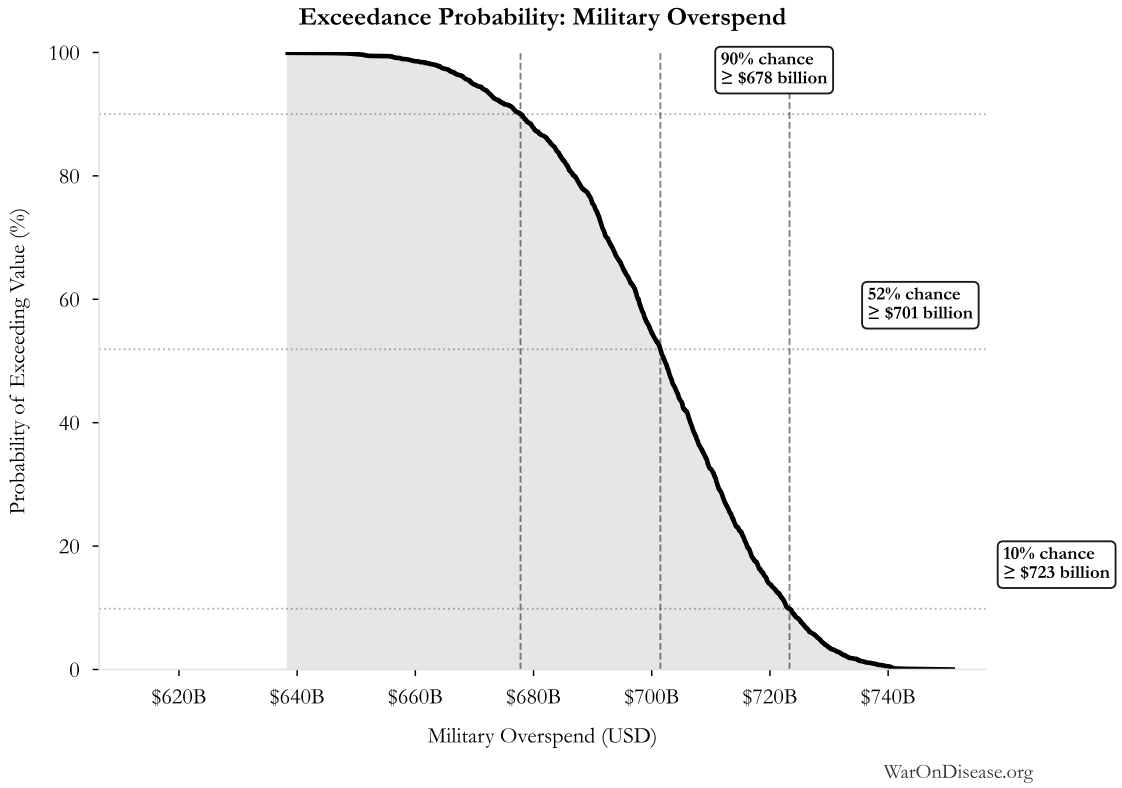


Figure 2.32: Probability of Exceeding Threshold: Military Overspend

This exceedance probability chart shows the likelihood that Military Overspend will exceed any given threshold. Higher curves indicate more favorable outcomes with greater certainty.

2.3 External Data Sources

Parameters sourced from peer-reviewed publications, institutional databases, and authoritative reports.

2.3.1 Pragmatic Trial Cost per Patient: $929

Details

Embedded pragmatic trial cost per patient. Uses ADAPTABLE trial ($929) as DELIBERATELY CONSERVATIVE central estimate. Ramsberg & Platt (2018) reviewed 108 embedded pragmatic trials; 64 with cost data had median of only $97/patient - this estimate may overstate costs by 10x. Confidence interval spans meta-analysis median to complex chronic disease trials. **Source**:[1]

2.3.1.1 Uncertainty Range

Technical: 95% CI: [$97, $3,000] • Distribution: Lognormal
What this means: This estimate is highly uncertain. The true value likely falls between $97 and $3,000 (±156%). This represents a very wide range that our Monte Carlo simulations account for when calculating overall uncertainty in the results.
The lognormal distribution means values can't go negative and have a longer tail toward higher values (common for costs and populations).

2.3.1.2 Input Distribution

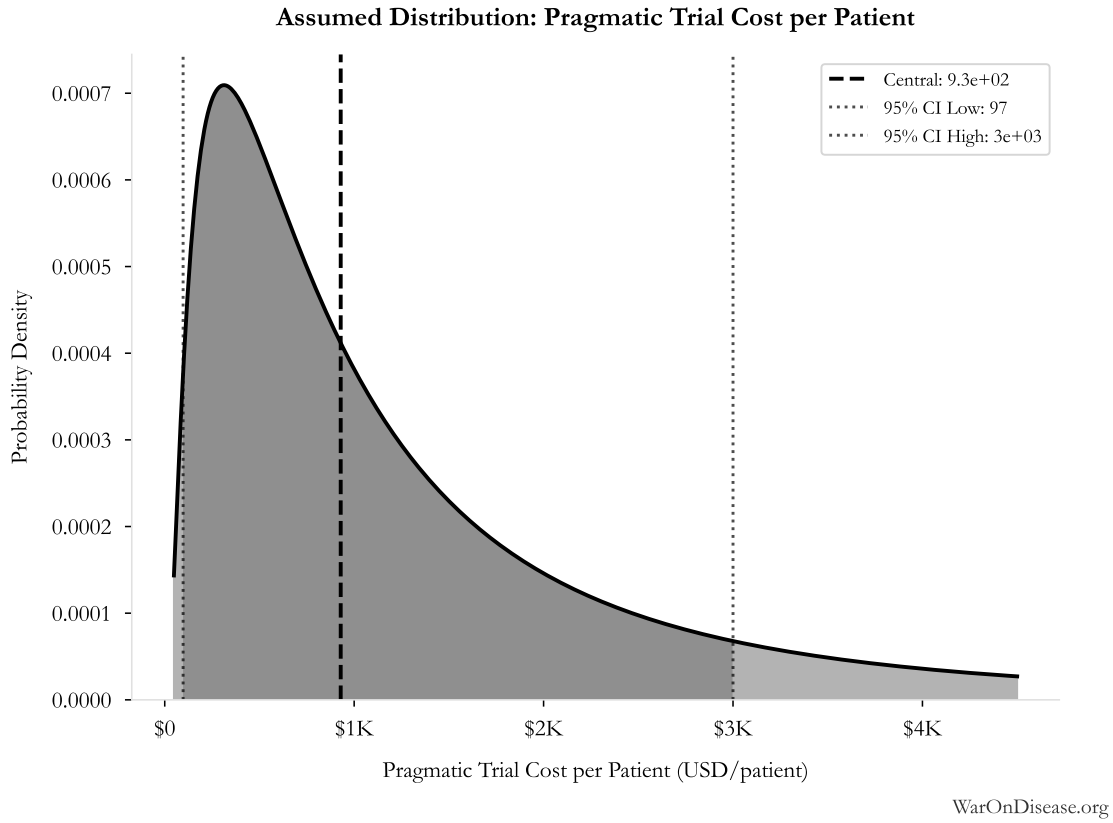


Figure 2.33: Probability Distribution: Pragmatic Trial Cost per Patient

This chart shows the assumed probability distribution for this parameter. The shaded region represents the 95% confidence interval where we expect the true value to fall.
~ Medium confidence

2.3.2 FDA Annual Program Budget: $7.06 billion

Details

FDA total program level in the FY 2026 operating plan. This is used only for a budget-scale comparison, not as an estimate of FDA cost-effectiveness.
Source:[48]

2.3.2.1 Uncertainty Range

Technical: Distribution: Fixed
High confidence

2.3.3 GiveWell Midpoint of Modeled Cost per Life Saved Range: $4,500

Details

Midpoint of GiveWell's cited $3,500 to $5,500 modeled cost-per-life-saved range across top charities
Source:[9]

2.3.3.1 Uncertainty Range

Technical: Distribution: Fixed
High confidence

2.3.4 Global Annual DALY Burden: 2.88 billion DALYs/year

Details

Global annual DALY burden from all diseases and injuries (WHO/IHME Global Burden of Disease 2021). Includes both YLL (years of life lost) and YLD (years lived with disability) from all causes.
Source:[57]

2.3.4.1 Uncertainty Range

Technical: Distribution: Normal (SE: 150 million DALYs/year)

2.3.4.2 Input Distribution

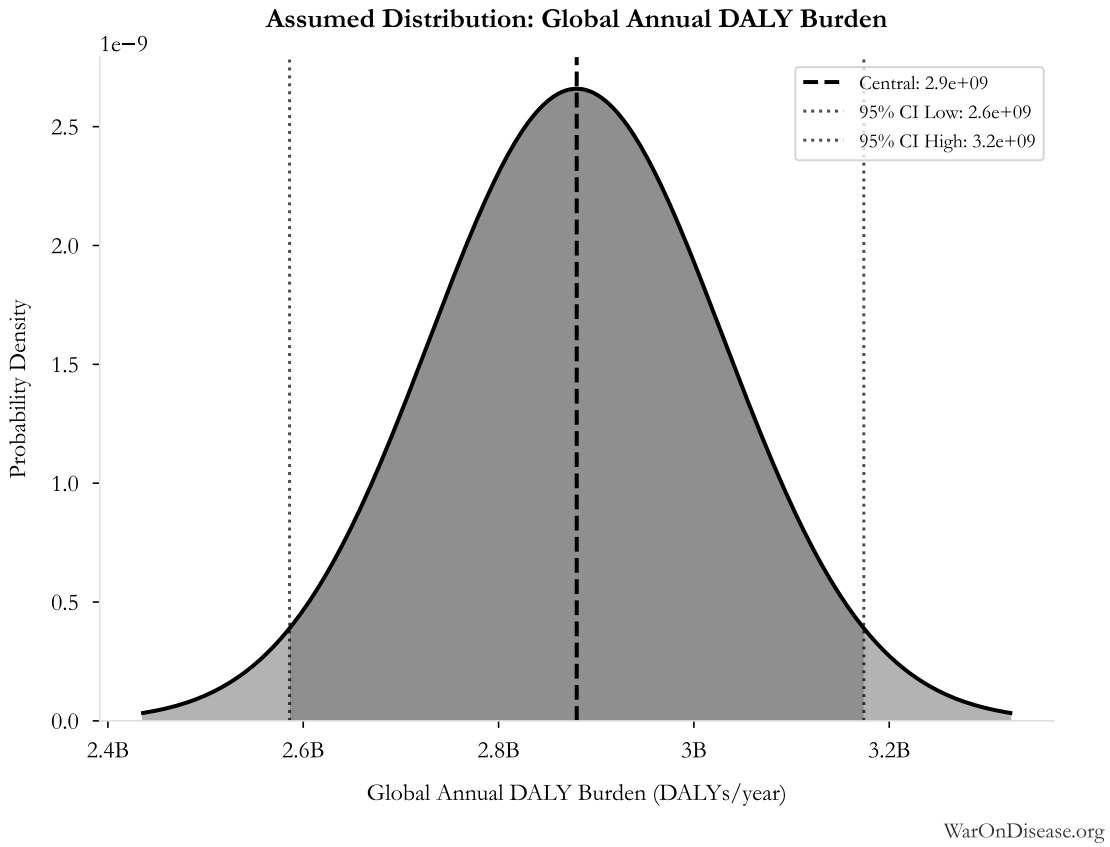


Figure 2.34: Probability Distribution: Global Annual DALY Burden

This chart shows the assumed probability distribution for this parameter. The shaded region represents the 95% confidence interval where we expect the true value to fall.
High confidence • *Peer-reviewed*

2.3.5 Global Daily Deaths from Disease and Aging: 150 thousand deaths/day

Details

Total global deaths per day from all disease and aging (WHO Global Burden of Disease 2024)
Source:[8]

2.3.5.1 Uncertainty Range

Technical: Distribution: Normal (SE: 7,500 deaths/day)

2.3.5.2 Input Distribution

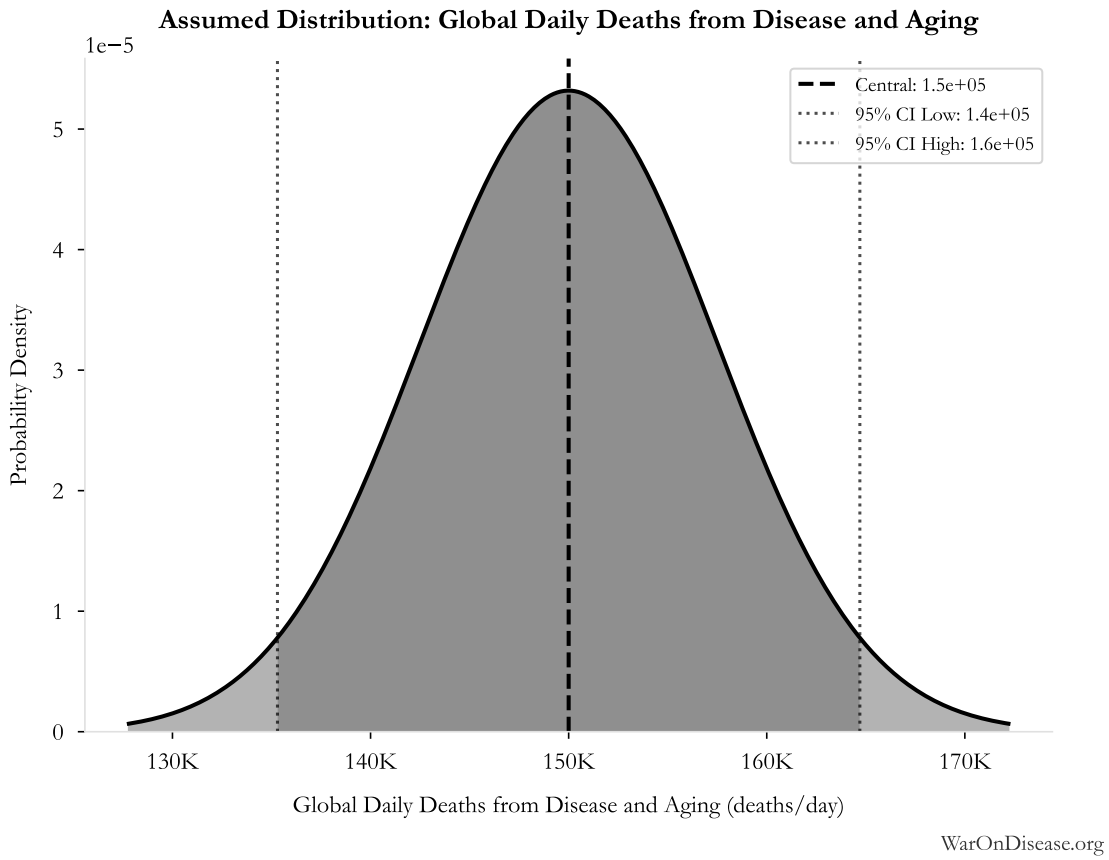


Figure 2.35: Probability Distribution: Global Daily Deaths from Disease and Aging

This chart shows the assumed probability distribution for this parameter. The shaded region represents the 95% confidence interval where we expect the true value to fall.
High confidence • *Peer-reviewed*

2.3.6 YLD Proportion of Total DALYs: 0.39 proportion

Details

Proportion of global DALYs that are YLD (years lived with disability) vs YLL (years of life lost). From GBD 2021: 1.13B YLD out of 2.88B total DALYs = 39%.
Source:[57]

2.3.6.1 Uncertainty Range

Technical: Distribution: Normal (SE: 0.03 proportion)

2.3.6.2 Input Distribution

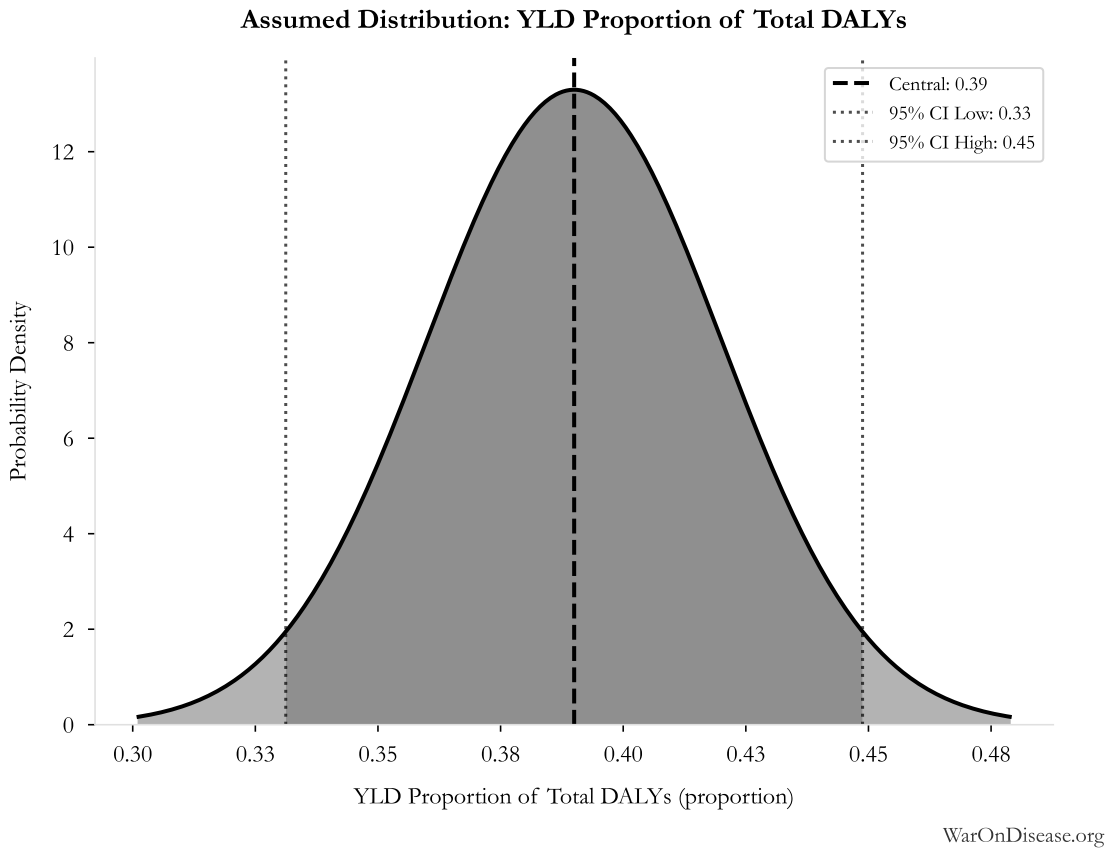


Figure 2.36: Probability Distribution: YLD Proportion of Total DALYs

This chart shows the assumed probability distribution for this parameter. The shaded region represents the 95% confidence interval where we expect the true value to fall.

High confidence • *Peer-reviewed*

2.3.7 Diseases Getting First Treatment Per Year: 15 diseases/year

Details

Number of diseases that receive their FIRST effective treatment each year under current system. ~9 rare diseases/year (based on 40 years of ODA: 350 with treatment ÷ 40 years), plus ~5-10 common diseases. Note: FDA approves ~50 drugs/year, but most are for diseases that already have treatments.

Source:[107]

2.3.7.1 Uncertainty Range

Technical: 95% CI: [8 diseases/year, 30 diseases/year] • Distribution: Lognormal
What this means: This estimate is highly uncertain. The true value likely falls between 8 diseases/year and 30 diseases/year (±73%). This represents a very wide range that our Monte Carlo simulations account for when calculating overall uncertainty in the results.
The lognormal distribution means values can't go negative and have a longer tail toward higher values (common for costs and populations).

2.3.7.2 Input Distribution

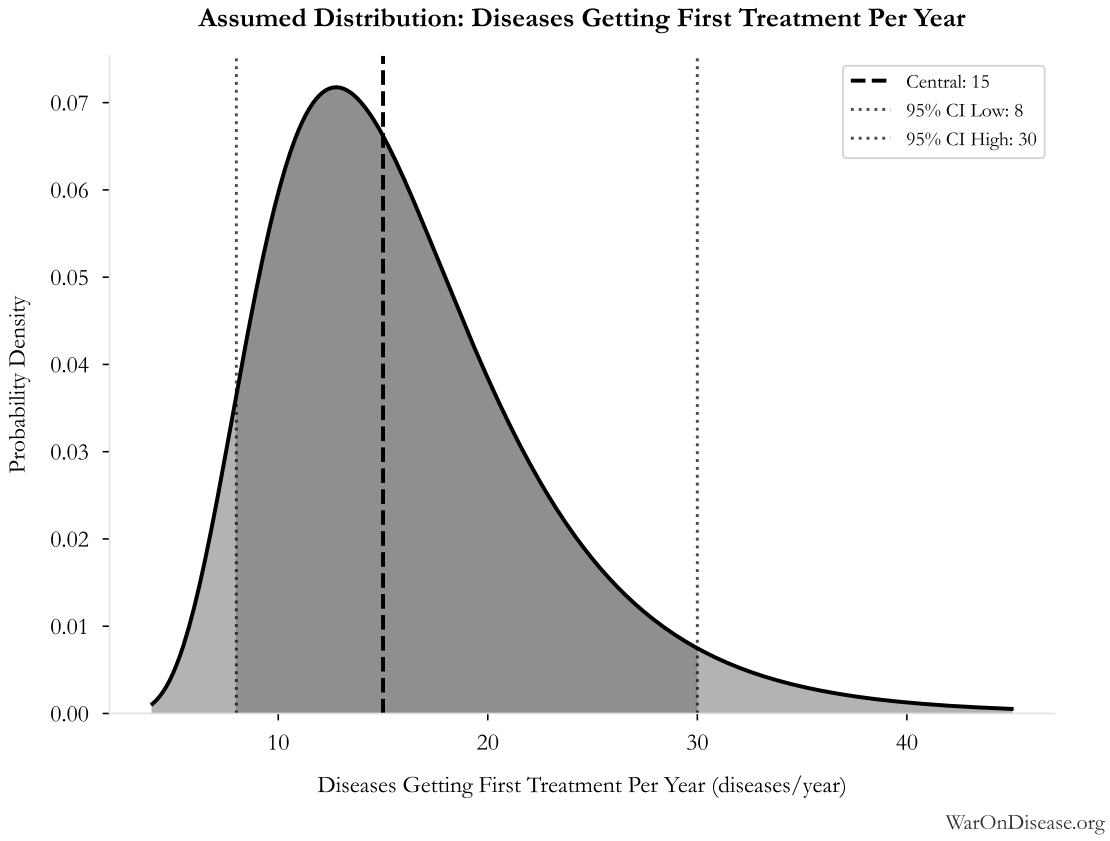


Figure 2.37: Probability Distribution: Diseases Getting First Treatment Per Year

This chart shows the assumed probability distribution for this parameter. The shaded region represents the 95% confidence interval where we expect the true value to fall.
? Low confidence

2.3.8 NIH Annual Budget: $47 billion

Details

NIH annual budget (FY2024/2025)
Source:[108]

2.3.8.1 Uncertainty Range

Technical: 95% CI: [$45 billion, $50 billion]
What this means: We're quite confident in this estimate. The true value likely falls between $45 billion and $50 billion (±5%). This represents a narrow range that our Monte Carlo simulations account for when calculating overall uncertainty in the results.

2.3.8.2 Input Distribution

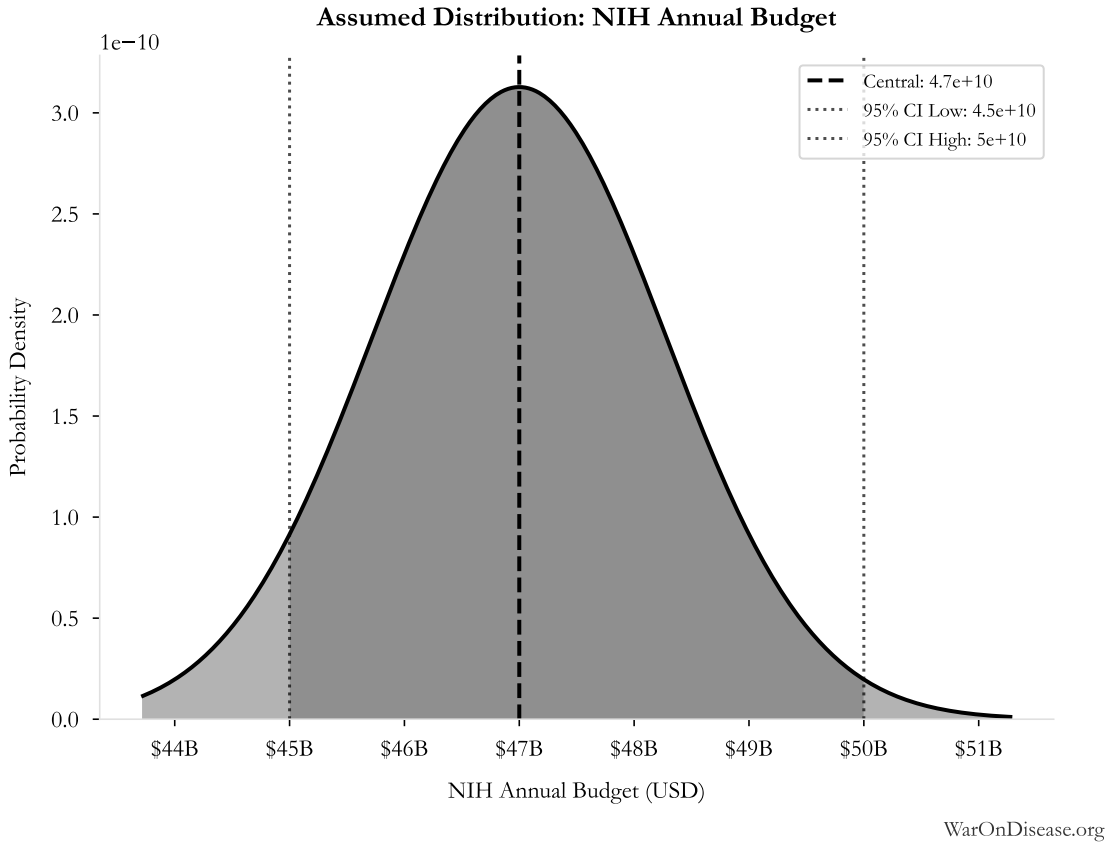


Figure 2.38: Probability Distribution: NIH Annual Budget

This chart shows the assumed probability distribution for this parameter. The shaded region represents the 95% confidence interval where we expect the true value to fall.
High confidence

2.3.9 Total Number of Rare Diseases Globally: 7,000 diseases

Details

Total number of rare diseases globally
Source:[128]

2.3.9.1 Uncertainty Range

Technical: 95% CI: [6,000 diseases, 10,000 diseases] • Distribution: Normal
What this means: There's significant uncertainty here. The true value likely falls between 6,000 diseases and 10,000 diseases (±29%). This represents a wide range that our Monte Carlo simulations account for when calculating overall uncertainty in the results.
The normal distribution means values cluster around the center with equal chances of being higher or lower.

2.3.9.2 Input Distribution

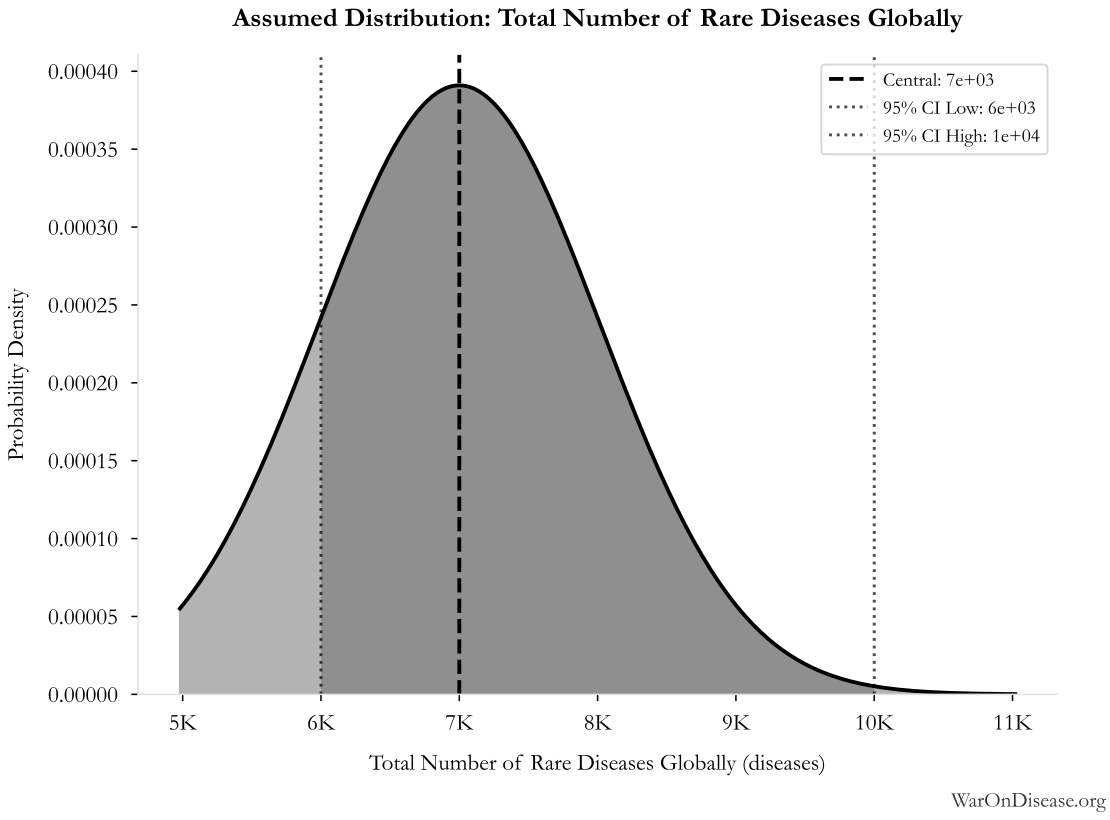


Figure 2.39: Probability Distribution: Total Number of Rare Diseases Globally

This chart shows the assumed probability distribution for this parameter. The shaded region represents the 95% confidence interval where we expect the true value to fall.

High confidence

2.3.10 Phase 3 Cost per Patient: $41,000

Details

Phase 3 cost per patient (median from FDA study)
Source:[148]

2.3.10.1 Uncertainty Range

Technical: 95% CI: [$20,000, $120,000] • Distribution: Lognormal
What this means: This estimate is highly uncertain. The true value likely falls between $20,000 and $120,000 (±122%). This represents a very wide range that our Monte Carlo simulations account for when calculating overall uncertainty in the results.
The lognormal distribution means values can't go negative and have a longer tail toward higher values (common for costs and populations).

2.3.10.2 Input Distribution

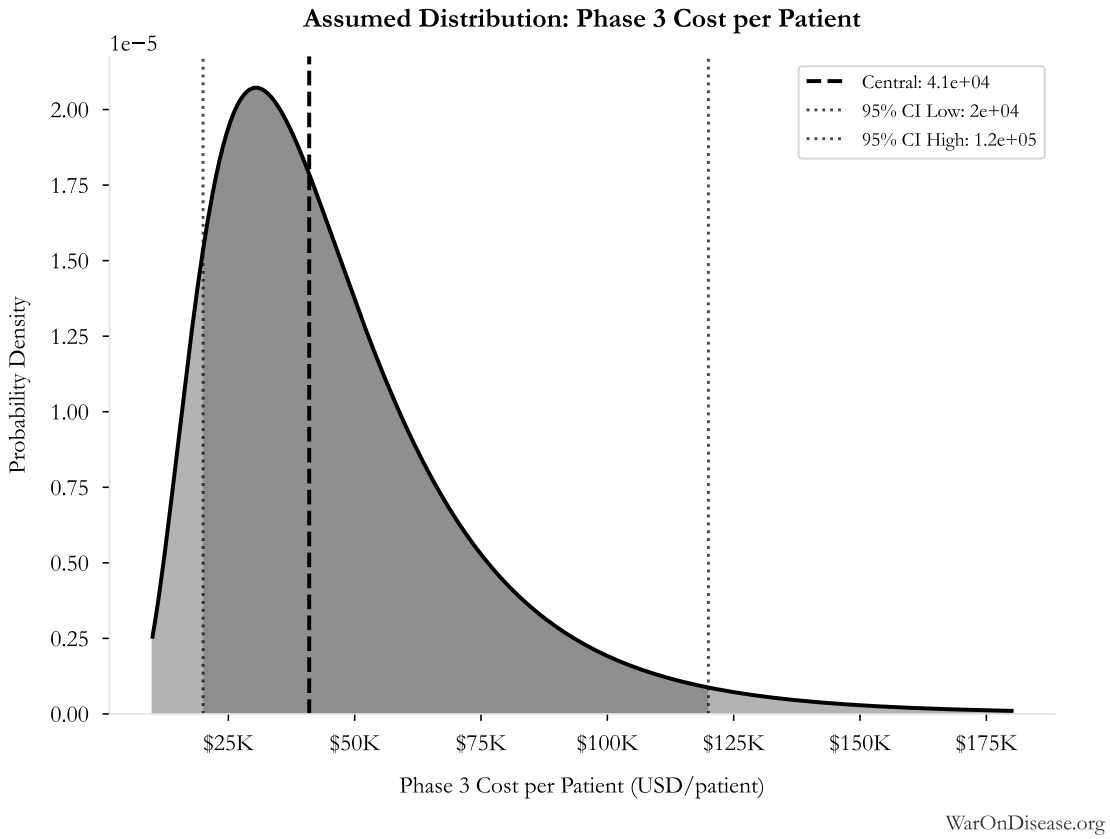


Figure 2.40: Probability Distribution: Phase 3 Cost per Patient

This chart shows the assumed probability distribution for this parameter. The shaded region represents the 95% confidence interval where we expect the true value to fall.
High confidence

2.3.11 US Military Spending in 2024: $886 billion

Details

US military spending in 2024 in constant dollars
Source:[168]

2.3.11.1 Uncertainty Range

Technical: Distribution: Fixed
High confidence

2.4 Core Definitions

Fundamental parameters and constants used throughout the analysis.

2.4.1 Eventually Avoidable DALY Percentage: 92.6%

Details

Percentage of DALYs that are eventually avoidable with sufficient biomedical research. Uses same methodology as EVENTUALLY_AVOIDABLE_DEATH_PCT. Most non-fatal chronic conditions (arthritis, depression, chronic pain) are also addressable through research, so the percentage is similar to deaths.

2.4.1.1 Uncertainty Range

Technical: 95% CI: [50%, 98%] • Distribution: Beta
What this means: There's significant uncertainty here. The true value likely falls between 50% and 98% (±26%). This represents a wide range that our Monte Carlo simulations account for when calculating overall uncertainty in the results.
The beta distribution means values are bounded and can skew toward one end.

2.4.1.2 Input Distribution

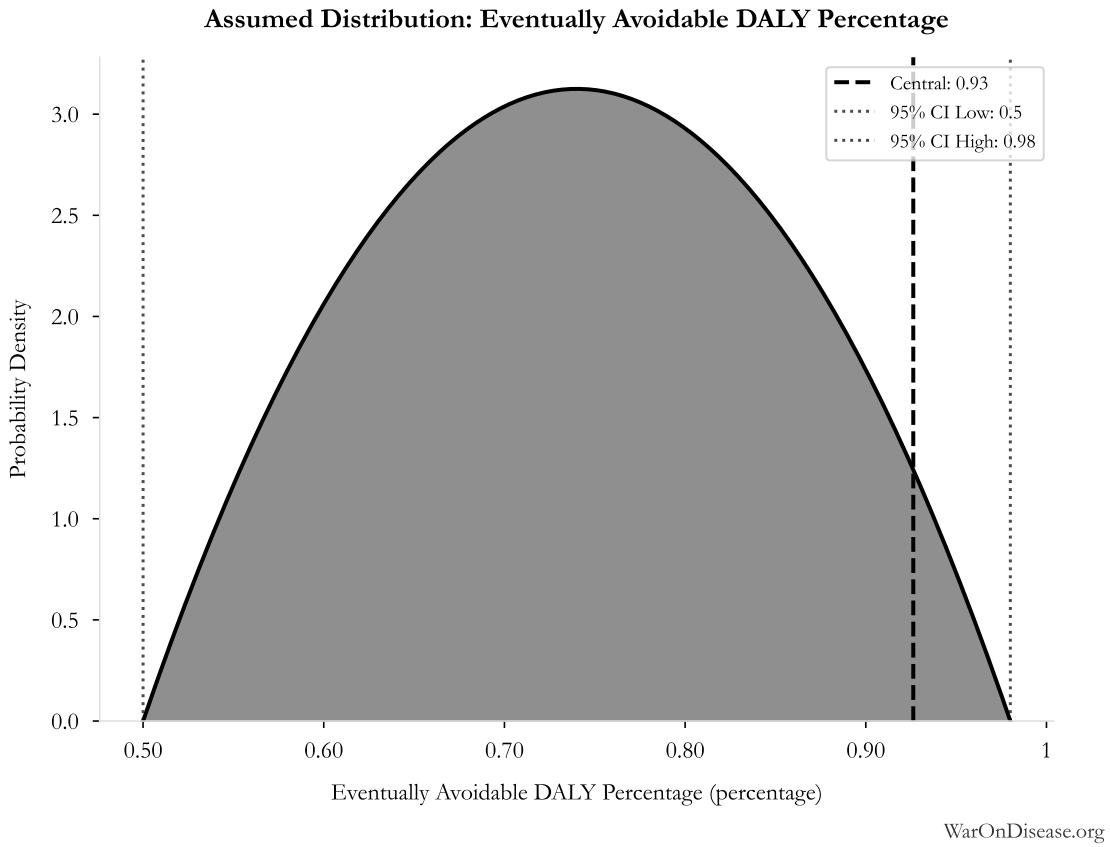


Figure 2.41: Probability Distribution: Eventually Avoidable DALY Percentage

This chart shows the assumed probability distribution for this parameter. The shaded region represents the 95% confidence interval where we expect the true value to fall.
Core definition

2.4.2 Eventually Avoidable Death Percentage: 92.6%

Details

Percentage of deaths that are eventually avoidable with sufficient biomedical research and technological advancement. Central estimate ~92% based on ~7.9% fundamentally unavoidable (primarily accidents). Wide uncertainty reflects debate over: (1) aging as addressable vs. fundamental, (2) asymptotic difficulty of last diseases, (3) multifactorial disease complexity.

2.4.2.1 Uncertainty Range

Technical: 95% CI: [50%, 98%] • Distribution: Beta

What this means: There's significant uncertainty here. The true value likely falls between 50% and 98% (±26%). This represents a wide range that our Monte Carlo simulations account for when calculating overall uncertainty in the results.
The beta distribution means values are bounded and can skew toward one end.

2.4.2.2 Input Distribution

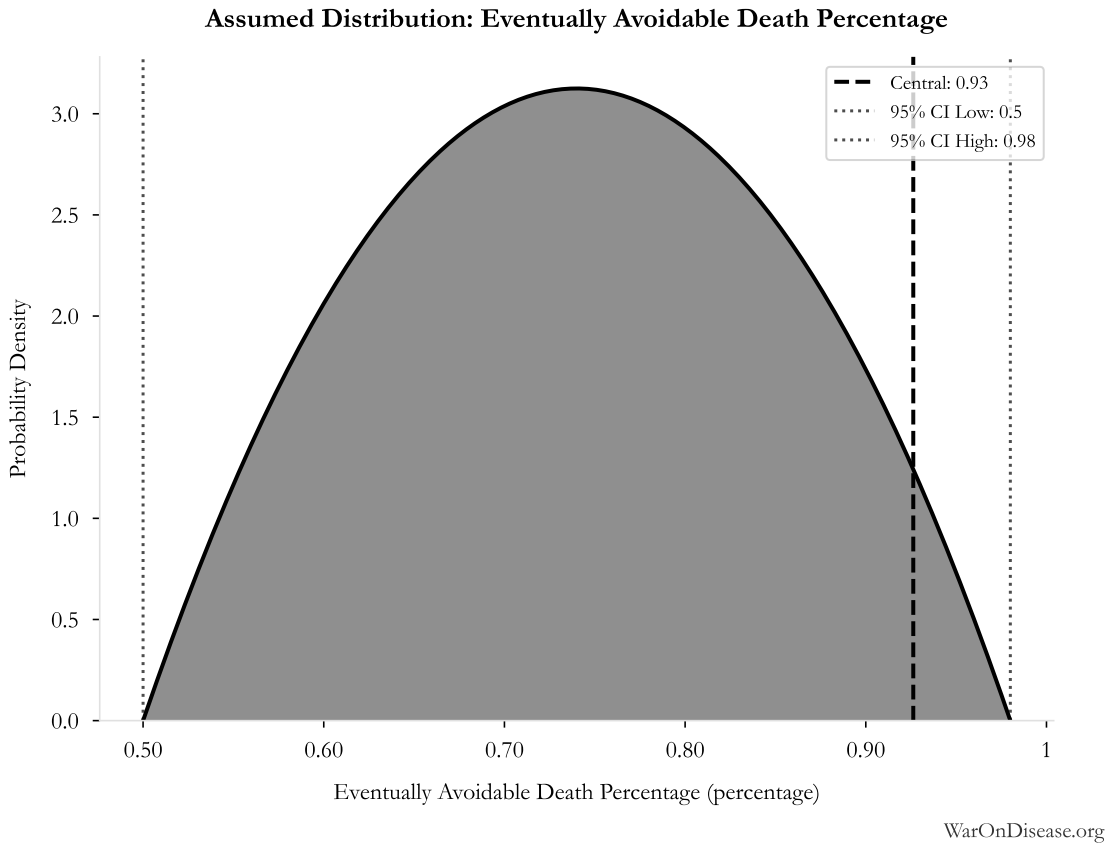


Figure 2.42: Probability Distribution: Eventually Avoidable Death Percentage

This chart shows the assumed probability distribution for this parameter. The shaded region represents the 95% confidence interval where we expect the true value to fall.
Core definition

2.4.3 Universal Right to Try with Evidence Philanthropic Cost: $65 million

Details

Total philanthropic cost of adopting Universal Right to Try with Evidence in all 50 states: a central $15 million campaign estimate covering legislation or amendment in all 50 states plus $50 million for the shared registry's first ten years. The model bill requires participating centers to fund continued registry operation after year ten. This philanthropic numerator excludes patient or payer spending on treatment delivery, trial-site services, and permitted study costs. The wide interval represents campaign and infrastructure cost uncertainty without separate scenario parameters.

2.4.3.1 Uncertainty Range

Technical: 95% CI: [$25 million, $200 million] • Distribution: Lognormal
What this means: This estimate is highly uncertain. The true value likely falls between $25 million and $200 million (±135%). This represents a very wide range that our Monte Carlo simulations account for when calculating overall uncertainty in the results.
The lognormal distribution means values can't go negative and have a longer tail toward higher values (common for costs and populations).

2.4.3.2 Input Distribution

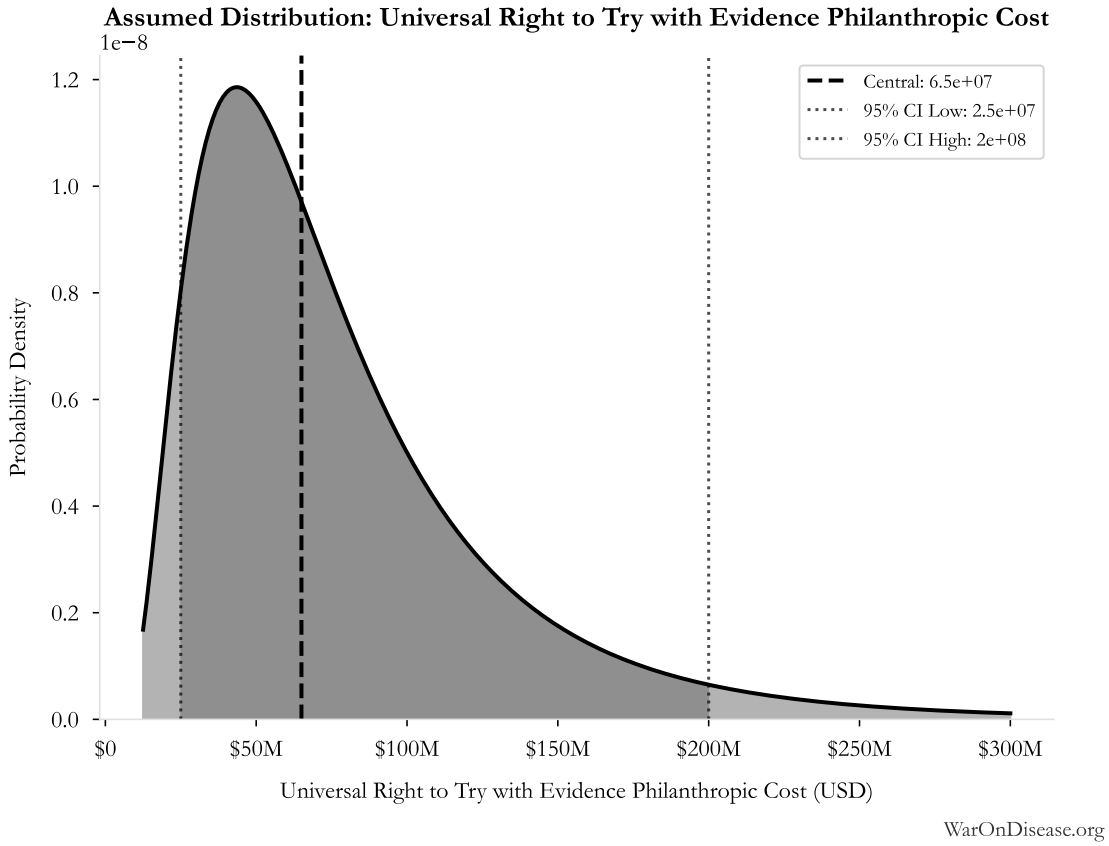


Figure 2.43: Probability Distribution: Universal Right to Try with Evidence Philanthropic Cost

This chart shows the assumed probability distribution for this parameter. The shaded region represents the 95% confidence interval where we expect the true value to fall.
Core definition

2.4.4 Universal Right to Try with Evidence Treatment Discovery Multiplier: 5.48x

Details

Conditional multiplier on the worldwide first-treatment discovery rate after all 50 states adopt and a mature pooled pragmatic-trial system operates under applicable federal authorization. The 5.48x central calibration reproduces the prior model's 82.2 versus 15 first treatments per year; it is an assumption, not an observed effect estimate. This single input incorporates patient or payer funding of treatment delivery, trial-site services, and permitted study costs,

newly viable post-Phase-1 treatment-condition pairs, evaluable protocol quality, candidate supply, and scientific success. Its range describes productivity of an operating system, not the separate probability that advocacy achieves full adoption and implementation.

2.4.4.1 Uncertainty Range

Technical: 95% CI: [1.1x, 15x] • Distribution: Lognormal
What this means: This estimate is highly uncertain. The true value likely falls between 1.1x and 15x (±127%). This represents a very wide range that our Monte Carlo simulations account for when calculating overall uncertainty in the results.
The lognormal distribution means values can't go negative and have a longer tail toward higher values (common for costs and populations).

2.4.4.2 Input Distribution

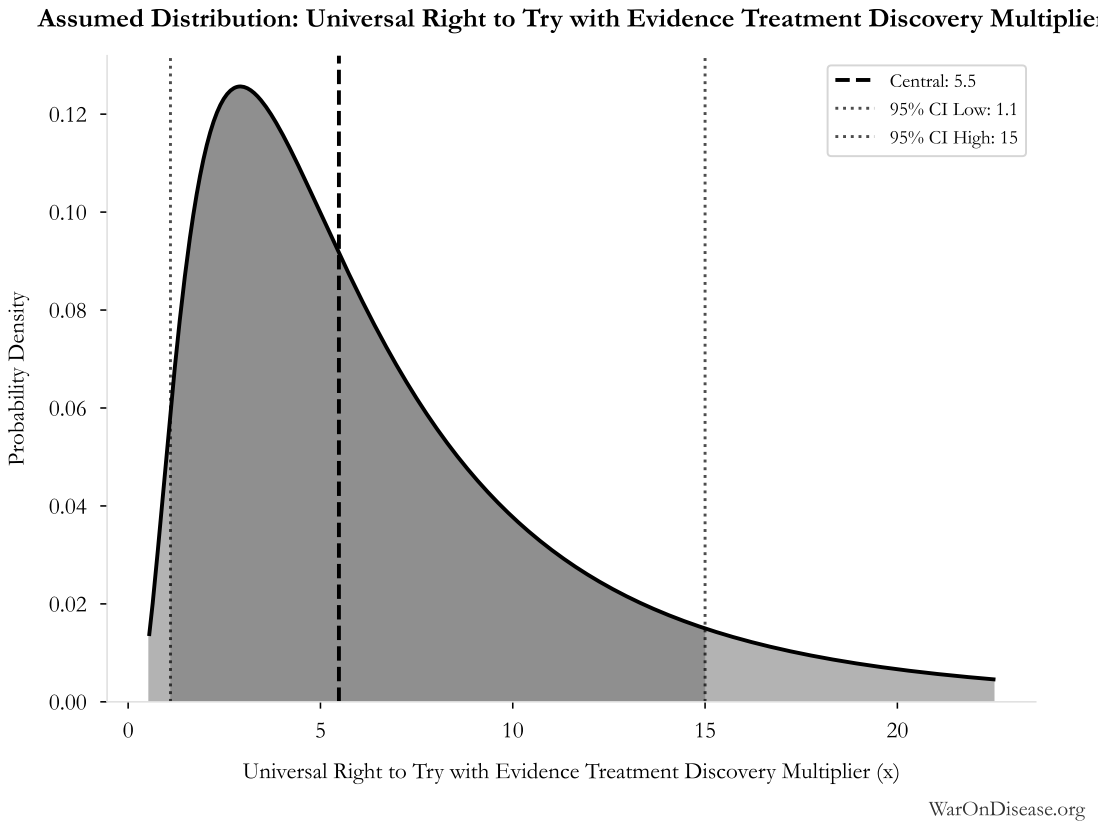


Figure 2.44: Probability Distribution: Universal Right to Try with Evidence Treatment Discovery Multiplier

This chart shows the assumed probability distribution for this parameter. The shaded region represents the 95% confidence interval where we expect the true value to fall.
Core definition

2.4.5 First-Principles Defense: Coast Guard: $14 billion

Details

US Coast Guard (actual budget ~$14B). Maritime homeland security and coastal defense.

2.4.5.1 Uncertainty Range

Technical: 95% CI: [$12 billion, $16 billion] • Distribution: Normal (SE: $1.5 billion)
What this means: This estimate has moderate uncertainty. The true value likely falls between $12 billion and $16 billion (±14%). This represents a reasonable range that our Monte Carlo simulations account for when calculating overall uncertainty in the results.
The normal distribution means values cluster around the center with equal chances of being higher or lower.

2.4.5.2 Input Distribution

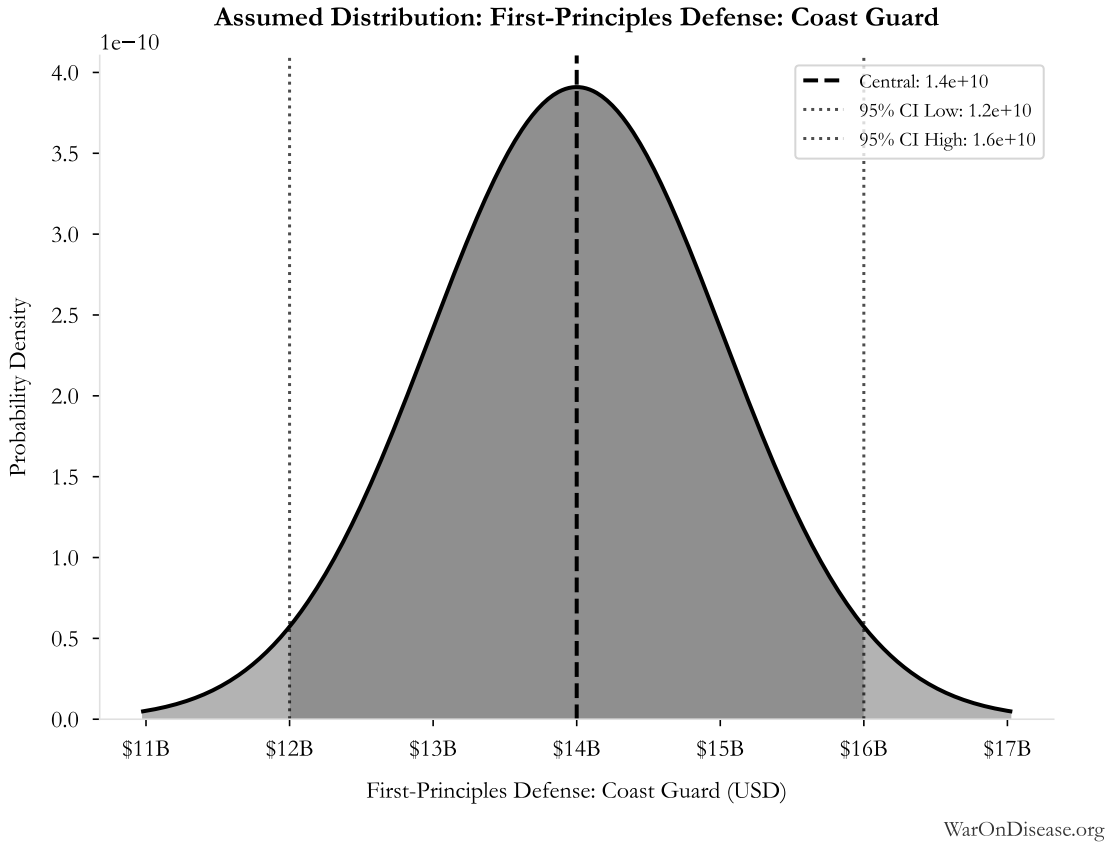


Figure 2.45: Probability Distribution: First-Principles Defense: Coast Guard

This chart shows the assumed probability distribution for this parameter. The shaded region represents the 95% confidence interval where we expect the true value to fall.

Core definition

2.4.6 First-Principles Defense: Cyber Defense: $15 billion

Details

Cyber defense of critical infrastructure: the primary modern attack vector that crosses oceans in milliseconds and is not stopped by geography.

2.4.6.1 Uncertainty Range

Technical: 95% CI: [$10 billion, $25 billion] • Distribution: Normal (SE: $4 billion)
What this means: There's significant uncertainty here. The true value likely falls between $10 billion and $25 billion (±50%). This represents a wide range that our Monte Carlo simulations account for when calculating overall uncertainty in the results.
The normal distribution means values cluster around the center with equal chances of being higher or lower.

2.4.6.2 Input Distribution

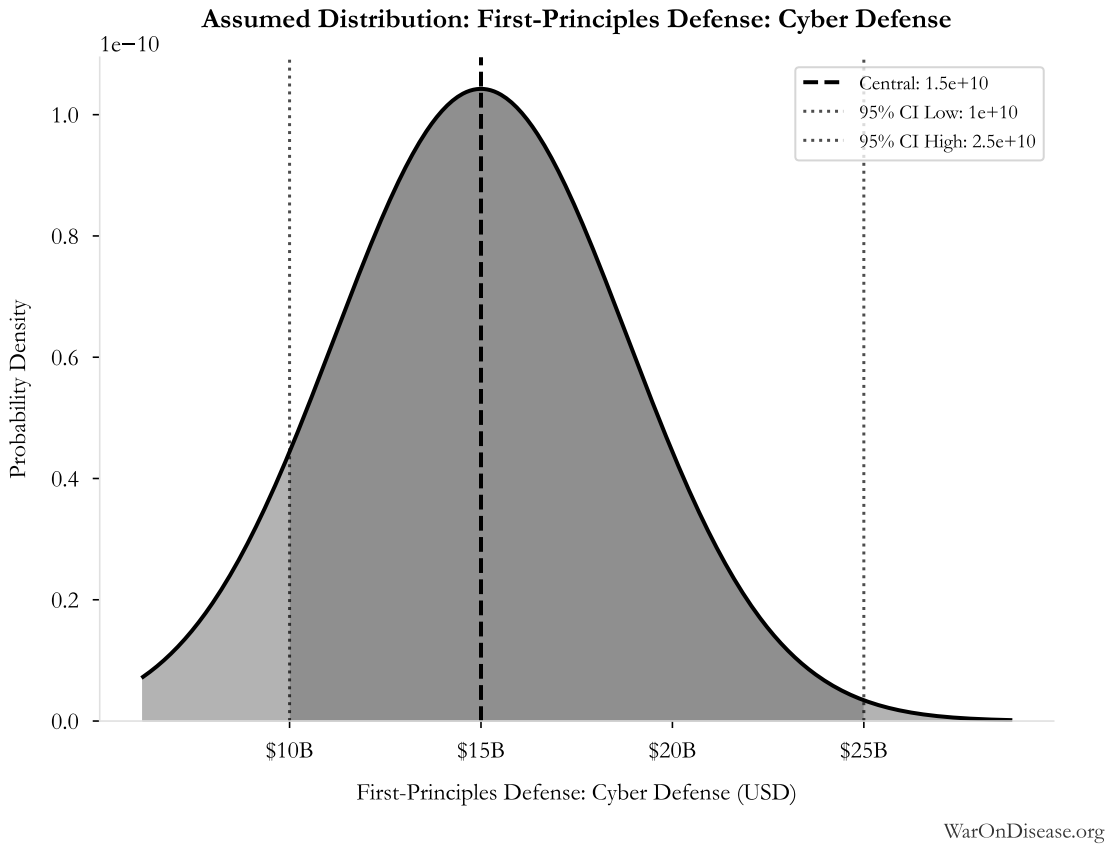


Figure 2.46: Probability Distribution: First-Principles Defense: Cyber Defense

This chart shows the assumed probability distribution for this parameter. The shaded region represents the 95% confidence interval where we expect the true value to fall.
Core definition

2.4.7 First-Principles Defense: Homeland Air & Missile Defense: $35 billion

Details

Continental air and missile defense plus early warning (NORAD, ground-based midcourse defense, interceptor aircraft). Defensive only; no expeditionary or power-projection air power.

2.4.7.1 Uncertainty Range

Technical: 95% CI: [$25 billion, $50 billion] • Distribution: Normal (SE: $7 billion)
What this means: There's significant uncertainty here. The true value likely falls between $25 billion and $50 billion (±36%). This represents a wide range that our Monte Carlo

simulations account for when calculating overall uncertainty in the results.
The normal distribution means values cluster around the center with equal chances of being higher or lower.

2.4.7.2 Input Distribution

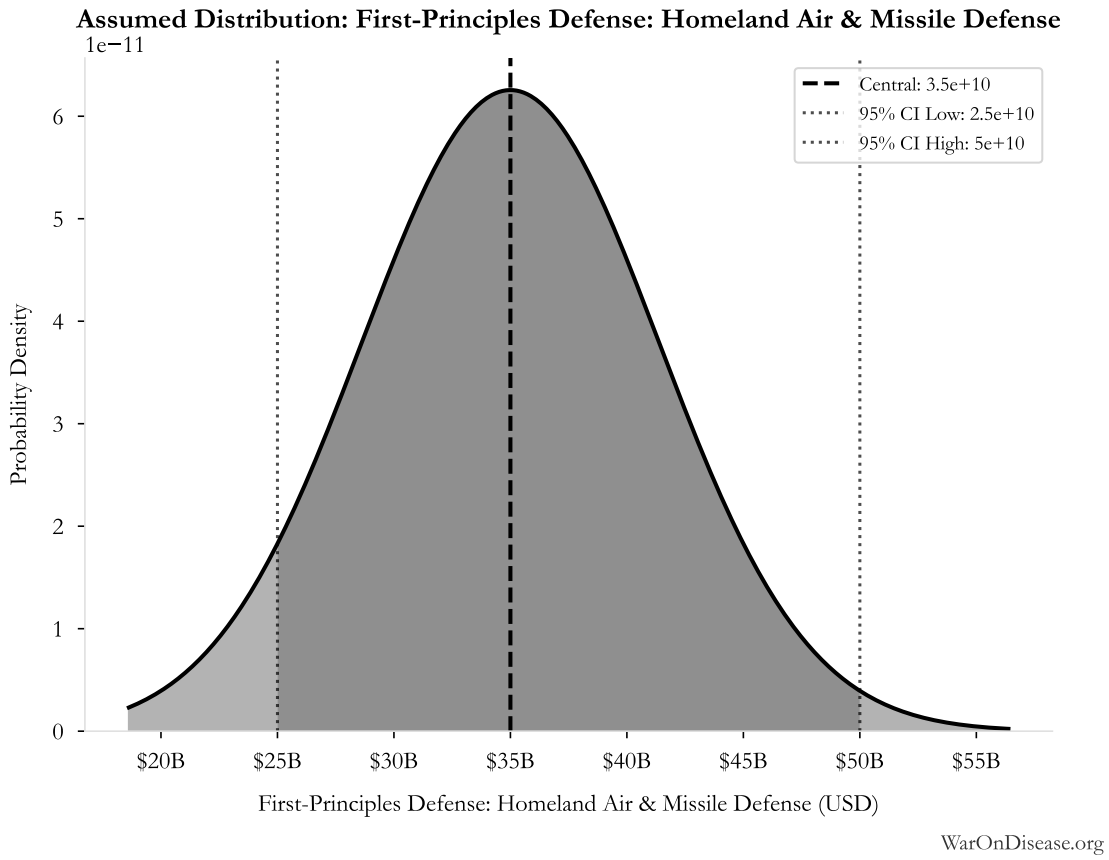


Figure 2.47: Probability Distribution: First-Principles Defense: Homeland Air & Missile Defense

This chart shows the assumed probability distribution for this parameter. The shaded region represents the 95% confidence interval where we expect the true value to fall.
Core definition

2.4.8 First-Principles Defense: Mobilization Hedge: $60 billion

Details

Mobilization hedge: defense R&D, a maintained industrial base, and a professional cadre force. The WWII lesson is to maintain the capacity to scale, not a standing empire: a peer buildup gives years of warning, and the US went from the 17th-ranked army in 1939 to victory in four years. This is the cheapest insurance and the most neglected.

2.4.8.1 Uncertainty Range

Technical: 95% CI: [$40 billion, $100 billion] • Distribution: Normal (SE: $15 billion)
What this means: There's significant uncertainty here. The true value likely falls between $40 billion and $100 billion (±50%). This represents a wide range that our Monte Carlo simulations account for when calculating overall uncertainty in the results.
The normal distribution means values cluster around the center with equal chances of being higher or lower.

2.4.8.2 Input Distribution

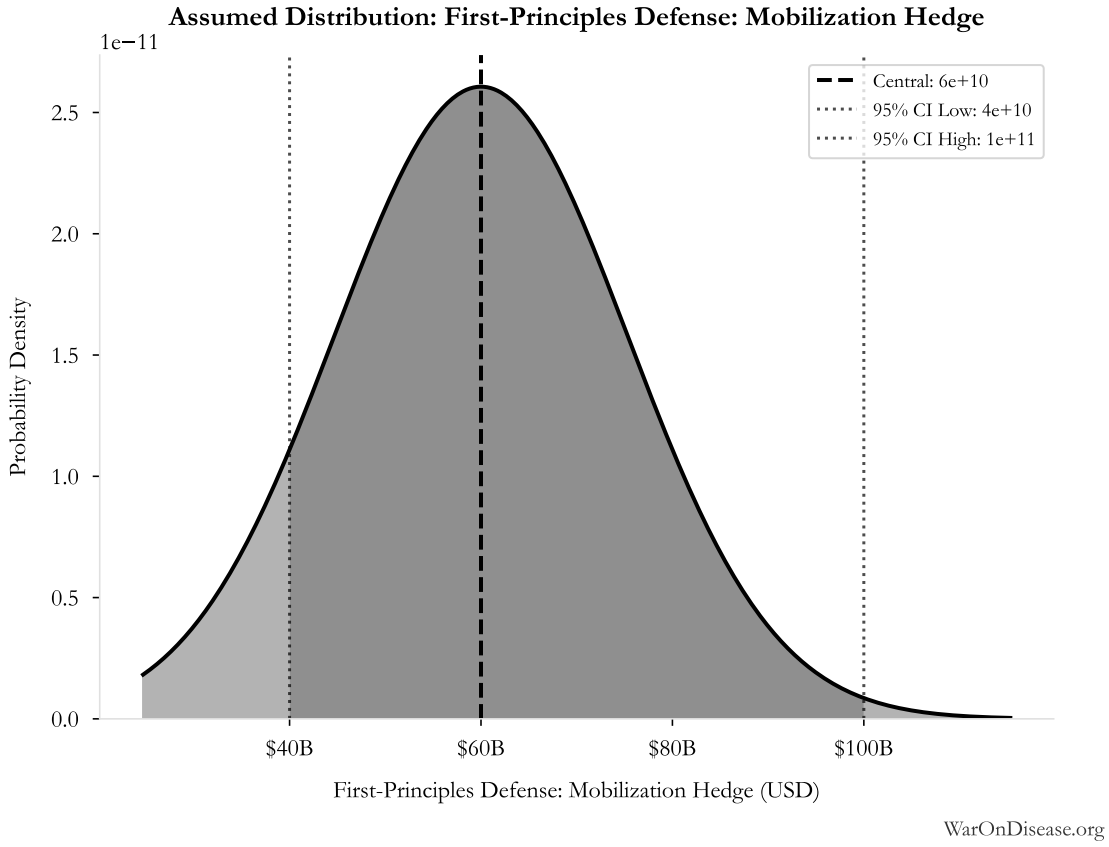


Figure 2.48: Probability Distribution: First-Principles Defense: Mobilization Hedge

This chart shows the assumed probability distribution for this parameter. The shaded region represents the 95% confidence interval where we expect the true value to fall.
Core definition

2.4.9 First-Principles Defense: National Guard: $30 billion

Details

National Guard / territorial land defense: a citizen-soldier reserve (the Switzerland model) for homeland defense and disaster response.

2.4.9.1 Uncertainty Range

Technical: 95% CI: [$24 billion, $40 billion] • Distribution: Normal (SE: $4 billion)
What this means: There's significant uncertainty here. The true value likely falls between $24 billion and $40 billion (±27%). This represents a wide range that our Monte Carlo simulations account for when calculating overall uncertainty in the results.
The normal distribution means values cluster around the center with equal chances of being higher or lower.

2.4.9.2 Input Distribution

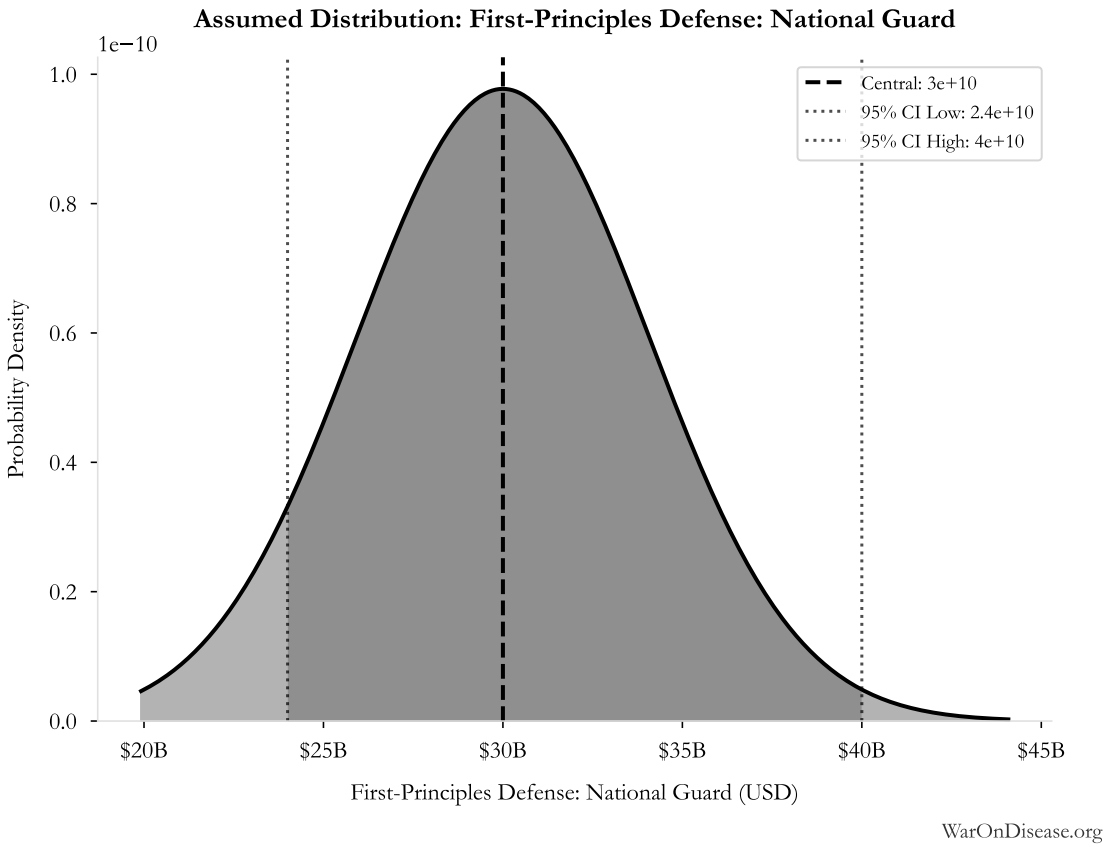


Figure 2.49: Probability Distribution: First-Principles Defense: National Guard

This chart shows the assumed probability distribution for this parameter. The shaded region represents the 95% confidence interval where we expect the true value to fall.
Core definition

2.4.10 First-Principles Defense: Nuclear Second Strike: $30 billion

Details

Survivable nuclear second strike: an SSBN-centric minimum credible deterrent (~100-200 survivable warheads on ballistic-missile submarines). The one threat geography does not neutralize. Drops the first-strike-attractive ICBM silos and the bomber leg. The UK and France each sustain continuous-at-sea deterrents within total defense budgets under $80B.

2.4.10.1 Uncertainty Range

Technical: 95% CI: [$20 billion, $50 billion] • Distribution: Normal (SE: $8 billion)

What this means: There's significant uncertainty here. The true value likely falls between $20 billion and $50 billion (±50%). This represents a wide range that our Monte Carlo simulations account for when calculating overall uncertainty in the results.
The normal distribution means values cluster around the center with equal chances of being higher or lower.

2.4.10.2 Input Distribution

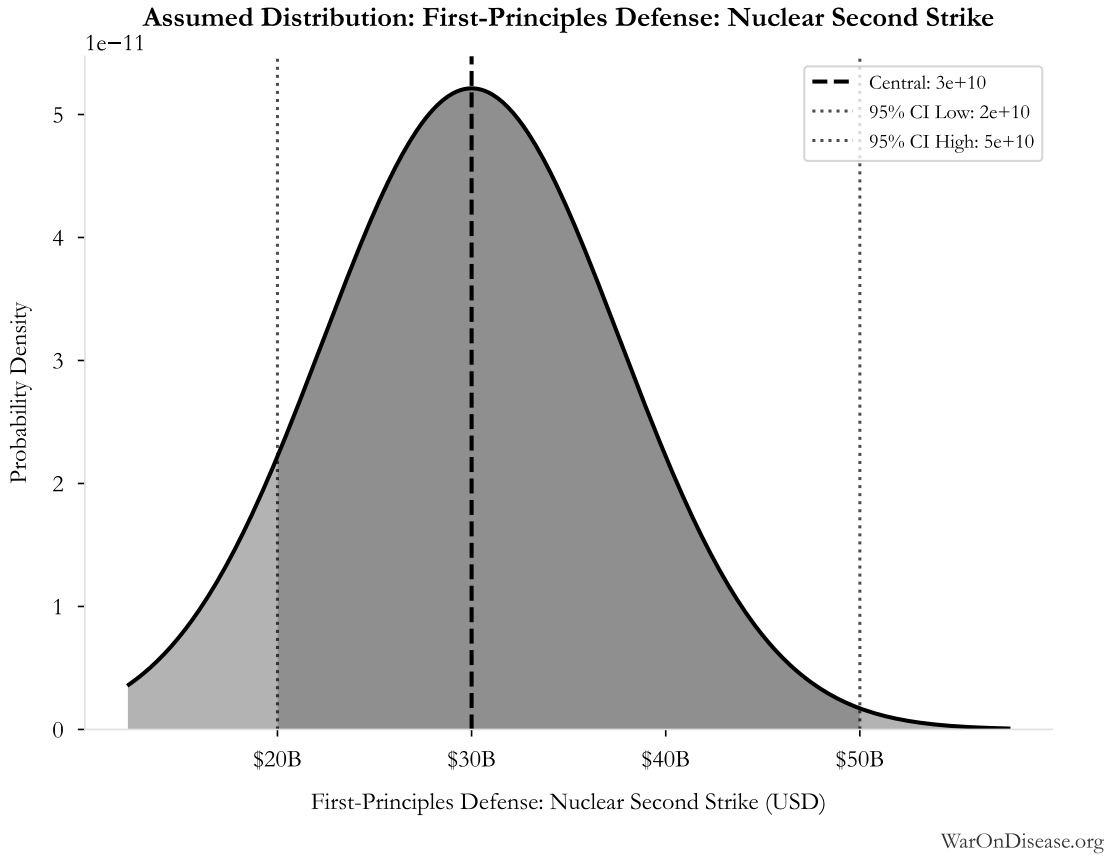


Figure 2.50: Probability Distribution: First-Principles Defense: Nuclear Second Strike

This chart shows the assumed probability distribution for this parameter. The shaded region represents the 95% confidence interval where we expect the true value to fall.
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Berkshire's compounded annual return from 1965 through 2024 was 19.9%, nearly. double the 10.4% recorded by the S&P 500. Berkshire shares skyrocketed 5,502,284% compared to the S&P 500's 39,054% rise during that period. Additional sources: https://www.cnbc.com/2025/05/05/warren-buffetts-return-tally-after-60-years-5502284percent.html | https://www.slickcharts.com/berkshire-hathaway/returns

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2024: 233,597 deaths (30% increase from 179,099 in 2023) Deadliest conflicts: Ukraine. (67,000), Palestine (35,000) Nearly 200,000 acts of violence (25% higher than 2023, double from 5 years ago) One in six people globally live in conflict-affected areas Additional sources: https://acleddata.com/2024/12/12/data-shows-global-conflict-surged-in-2024-the-washington-post/ | https://acleddata.com/media-citation/data-shows-global-conflict-surged-2024-washington-post | https://acleddata.com/conflict-index/index-january-2024/
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The $50,000/QALY threshold is widely used in US health economics literature, originating. from dialysis cost benchmarks in the 1980s. In US cost-utility analyses, 77.5% of authors use either $50,000 or $100,000 per QALY as reference points. Most successful health programs cost $3,000-10,000 per QALY. WHO-CHOICE uses GDP per capita multiples (1× GDP/capita = "very cost-effective", 3× GDP/capita = "cost-effective"), which for the US ($70,000 GDP/capita) translates to $70,000-$210,000/QALY thresholds. Additional sources: https://pmc.ncbi.nlm.nih.gov/articles/PMC5193154/ | https://pmc.ncbi.nlm.nih.gov/articles/PMC9278384/
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