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

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Online version: https://right-to-trial-impact.acceleratedmedicine.org

Table of contents

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

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

> **Please help us improve this impact analysis.** We want to help policymakers and the public understand the enormous potential benefits of universal patient access to clinical trials and a continually learning system for global treatment-effectiveness rankings and outcome labels. Comment below, or highlight any text and log in with Hypothesis to leave a note. Co-authors welcome.

The short version

About 6,650 diseases (95% CI: 5,700 diseases-8,232 diseases) rare diseases still have no effective treatment. The model uses this queue as a proxy for the wider therapeutic frontier. At the current rate, roughly 15 diseases receive their first effective treatment each year. At that pace, exploring the queue takes approximately 443 years (95% CI: 255 years-841 years), and the average therapeutic target waits about 222 years (95% CI: 128 years-420 years).

The problem is not a shortage of possible treatments. Many post-Phase-1 compounds, repurposed drugs, combinations, doses, and disease-specific uses are never tested because nobody can finance conventional Phase 2 and Phase 3 trials.

Universal Right to Try[3] with Evidence changes that financing constraint. Licensed centers provide eligible experimental treatments while patients or payers cover treatment-related care, trial-site services, and permitted study costs. Trial participants follow shared protocols, and other eligible uses contribute separately labeled observational outcomes. Treatments that were not economically viable to investigate become testable. State law does not waive federal authorization or evidence requirements.

If all 50 states adopt the framework and it produces the modeled increase in treatment discovery, the conditional central estimates are:

Result	Conditional central estimate
Treatment-discovery multiplier	5.48x
Average first treatment arrives	181 years earlier
Premature deaths prevented	9.19 billion

Result	Conditional central estimate
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 totals across future generations. They do not mean that billions of currently living people are saved, and they do not assume that passing a law automatically produces the modeled scientific effect.

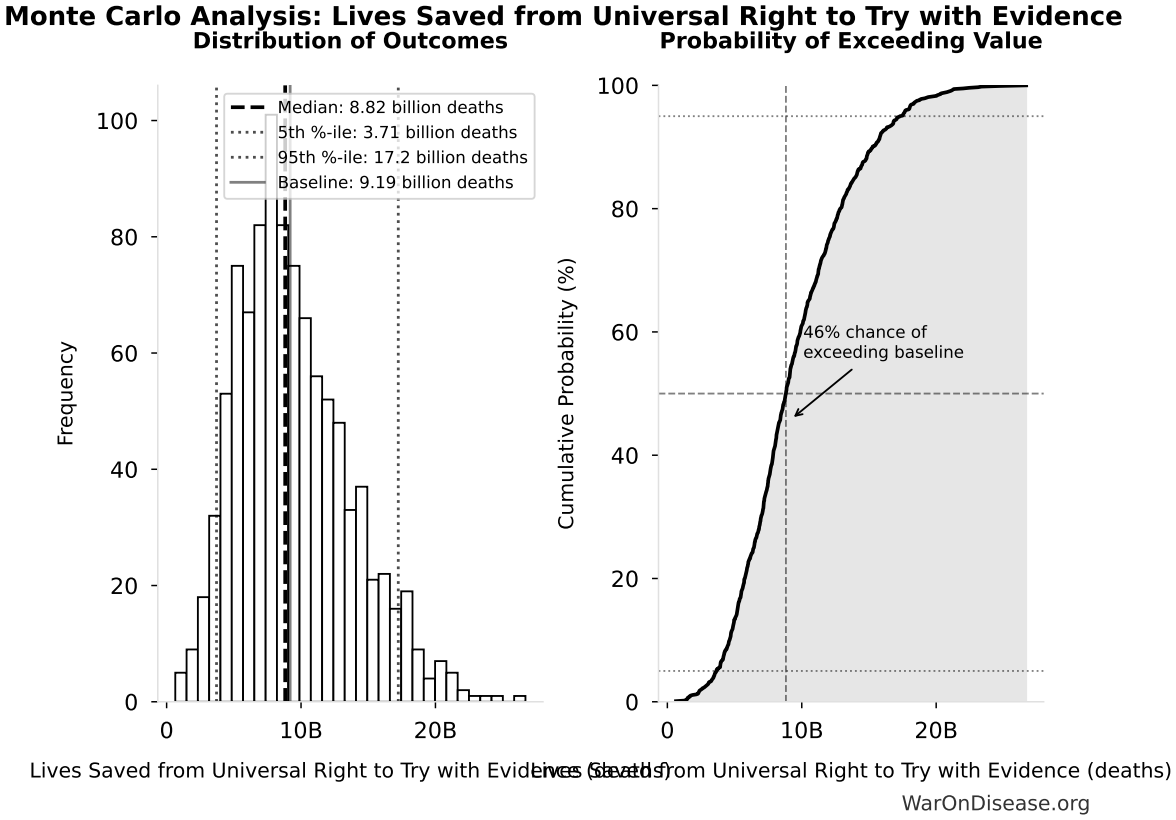


Figure 1: Monte Carlo Distribution: Lives Saved from Universal Right to Try with Evidence (10,000 simulations)

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

Statistic	Value
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.

What the legislation changes

Montana has already created licensed experimental treatment centers. Senate Bill 535 covers treatments that have completed Phase 1 but are not approved for general FDA use. It permits centers to establish payment arrangements, charges a $10,000 license application fee and $5,000 annual renewal fee, and directs 2% of annual net profits toward access for qualifying Montana residents[4].

That creates a lawful state-regulated place to provide experimental treatment. It does not by itself create a clinical trial system. Montana's rules require centers to track treatment, patient outcomes, and serious adverse events, but the rules explicitly state that the centers do not administer clinical trials[5]. Observational outcomes can reveal promising or dangerous signals. Without a credible comparison, they cannot reliably show that a treatment caused the result.

The model bill 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 result is access with evidence. Participating patients receive treatments that sponsors make available and contribute to a common learning system. Every result can improve the next treatment decision.

Why treatments that cannot attract conventional funding matter

A candidate treatment can have completed initial human safety testing and still be commercially impossible to develop. A conventional Phase 3 trial costs about $41,000 (95% CI: $20,000-$120,000) per participant. The existing model estimates that an embedded pragmatic trial can reduce that to approximately $929 (95% CI: $97-$3,000) per participant, a 44.1x (95% CI: 12.8x-210x) reduction.

That does not mean every trial becomes 44.1x (95% CI: 12.8x-210x) cheaper. Complex and high-risk studies will still need specialized sites, procedures, and monitoring. It means routine care can often replace dedicated research visits and duplicate data collection while retaining prespecified outcomes, safety reporting, reliable analysis, and a comparison group.

The candidate pool is much larger than a count of compounds. One compound may be tested for several diseases, doses, combinations, or subtypes. Additional candidates do not multiply disease burden. They increase the chance that the first effective treatment for each condition is found sooner.

One policy-effect input instead of a pretend forecast

Nobody knows how many centers will open, how many patients will enroll, how many shelved treatments will return, or what fraction of well-designed evaluations will find an effective treatment. Modeling each unknown as a separate multiplier would manufacture precision and create opportunities to count the same benefit twice.

The model compresses the entire policy mechanism into one uncertain input: a 5.48-fold treatment-discovery multiplier. It represents:

- patient or payer funding of treatment and evidence generation;
- treatments revived because conventional trials were not economically viable;
- enough candidate-condition pairs and eligible participants to sustain evaluation;
- protocols capable of producing credible efficacy evidence; and
- the share of completed evaluations that find a first effective treatment.

The central value is a calibration assumption, not an observed causal estimate. The automatic Monte Carlo samples uncertainty in this multiplier, launch cost, avoidable disease burden, and their upstream inputs. It does not capture political adoption risk or model-form uncertainty in using the rare-disease queue as a proxy for the wider therapeutic frontier. The physical health totals are undiscounted. Applying a time discount rate would reduce their present value, but adding a preferred discount rate would not change the underlying schedule shift.

The calculation, one step at a time

The arithmetic asks how much sooner the average first treatment arrives if the discovery rate increases:

Step	Question	Conditional central result
1	How long would the remaining treatment queue take at the current discovery rate?	443 years (95% CI: 255 years-841 years)
2	How long does the average therapeutic target wait?	222 years (95% CI: 128 years-420 years)
3	How much earlier does treatment arrive at the modeled discovery rate?	181 years
4	How many global healthy years does that schedule shift restore?	483 billion DALYs
5	What is the campaign and registry-launch cost per restored healthy year?	$0.000134

The full calculation 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:

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

The rare-disease treatment queue is the clearest available count of diseases still awaiting a first effective treatment. The model uses it as a proxy for the pace of exploring the wider therapeutic frontier, then applies the resulting schedule shift to eventually avoidable global disease and aging-related burden. That is the model's strongest assumption. It is stated directly because it drives the scale of the result.

What the headline numbers mean

The 9.19 billion deaths estimate 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 1.65 quadrillion hours estimate 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 that every hour represents maximum conscious pain.

The global estimate assumes discoveries become public knowledge and eventually benefit patients outside the United States. The access right itself remains state law.

The model does not count the uncertain direct health effect on participating patients. Earlier access to an effective treatment could help them immediately. Ineffective or unsafe treatments could harm them. Those effects are real, but they are a separate channel from the treatment-discovery schedule shift and are not included in the headline totals.

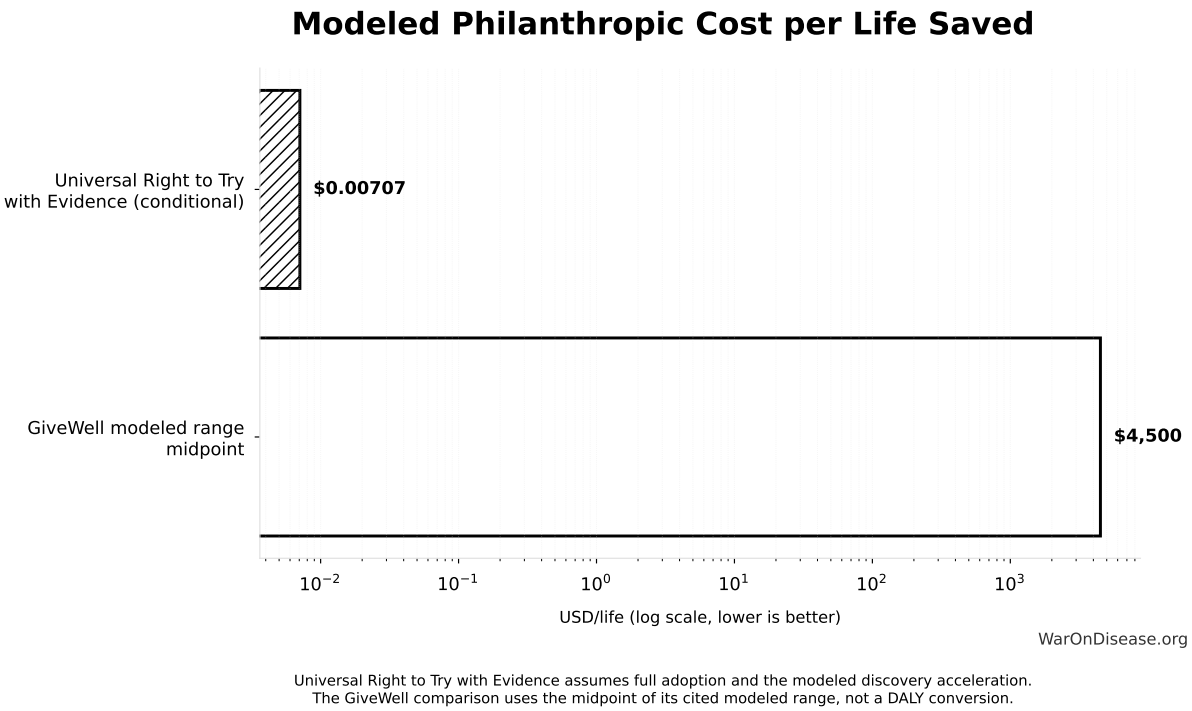
What philanthropy and investment pay for

Philanthropy funds the shared public good

Philanthropy pays for the 50-state campaign, common evidence standards, and the shared registry's first ten years. Participating centers then sustain the registry through license or enrollment assessments. The model does not require a new state appropriation.

The conditional philanthropic cost per DALY divides that public-good investment by the health benefit if all 50 states adopt and the mature system produces the modeled discovery rate. It excludes patient and payer spending on treatment delivery because those payments buy care and evidence generation rather than consuming the philanthropic campaign budget.

At the central estimate, the 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[6]. The comparison is so large because a relatively small campaign and registry are assumed to unlock treatment, sponsor, payer, clinic, and investor spending that philanthropists do not supply.



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

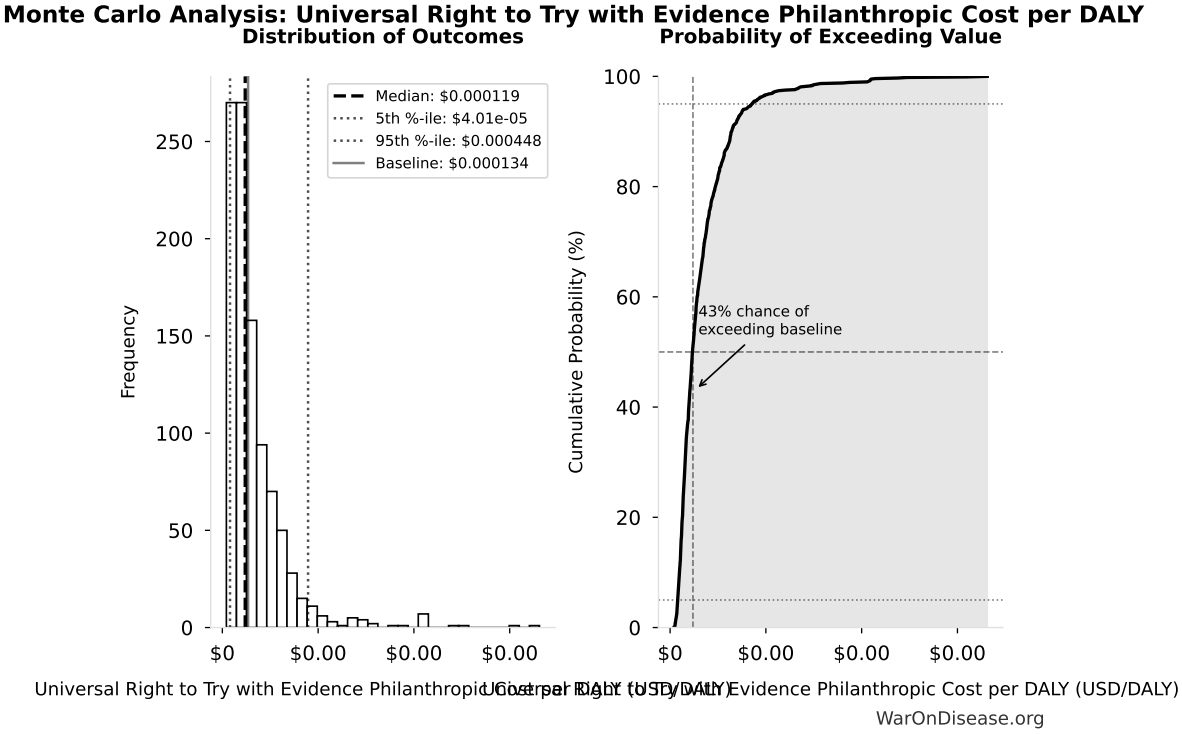


Figure 2: Monte Carlo Distribution: Universal Right to Try with Evidence Philanthropic Cost per DALY (10,000 simulations)

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.

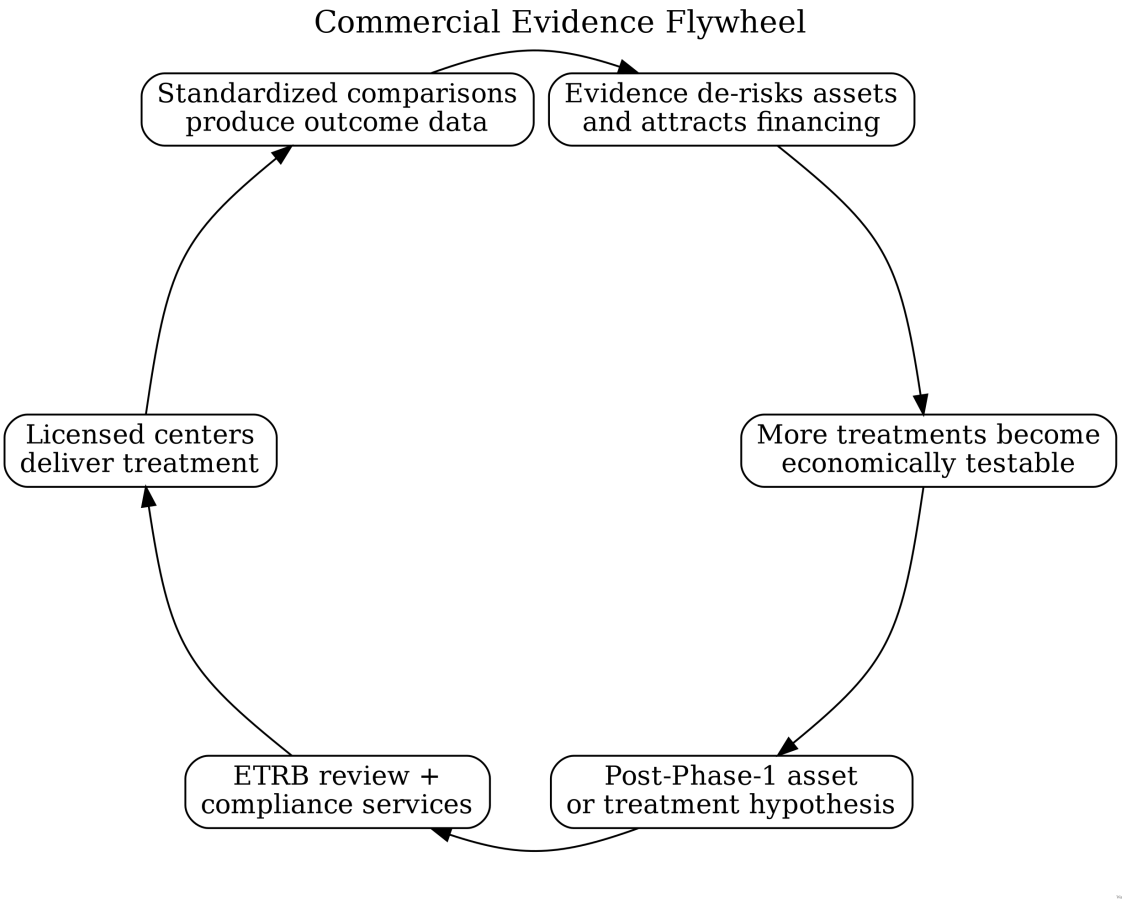
For a grant decision, multiply the conditional benefit by the donor's own probability that the grant produces full adoption, mature implementation, and the modeled scientific effect. Equivalently, divide the conditional cost per life saved by that probability. Keeping that judgment outside the model avoids another arbitrary scenario parameter.

Commercial capital funds the parts that can earn revenue

Review, compliance, clinical administration, manufacturing, monitoring, data infrastructure, and successful treatment assets can all produce revenue. Commercial capital can therefore finance:

- experimental treatment review board services and compliance;
- 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; and
- payer contracts that condition coverage on evidence production.

Donors fund the public-good layer that no company can capture. Investors fund services and assets that can earn revenue. Neither group has to finance the entire system.



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

The federal boundary

State legislation does not approve drugs, waive federal trial authorization, or lower FDA's evidence standard. Federal Right to Try is limited to eligible patients who are unable to participate in a clinical trial involving the drug[7]. A patient enrolled in an interventional pragmatic trial must instead participate under an active investigational new drug application or another applicable FDA-authorized pathway. Patients who cannot join a trial may contribute separately labeled observational outcomes through federal Right to Try or expanded access if eligible.

FDA's standard remains substantial evidence from adequate and well-controlled investigations. FDA guidance allows one rigorous investigation plus confirmatory evidence in some circumstances, while still requiring sufficient safety evidence and a favorable benefit-risk assessment[8]. FDA also supports streamlined randomized trials integrated into routine clinical practice[9]. Project Pragmatica applies this design logic to approved oncology products through simpler eligibility and routine-practice enrollment[10]. These programs show that pragmatic design can reduce collection burden. They do not authorize states to bypass federal law.

Federal charging rules also remain in force. An IND sponsor needs FDA authorization to charge for an investigational drug and generally may recover only direct drug costs. Trial sites may separately recover pharmacy, nursing, equipment, and study-related procedure costs without authorization under that charging rule[11]. The model therefore assumes that patients or payers cover treatment delivery, site services, and permitted study costs. Whether lawful revenue is sufficient to sustain the modeled discovery multiplier remains uncertain.

Medicare already uses the analogous payment principle in Coverage with Evidence Development. Specified services may be covered within an approved study while evidence is collected, then CMS can reconsider coverage using the results[12]. Universal Right to Try with Evidence applies the same basic idea outside Medicare: access now, standardized evidence from every use, and stronger decisions over time. The Continuous Evidence Generation Protocol[13] provides one compatible technical design. The legislation does not need to mandate that specific protocol.

Montana can prove it works

Montana has already completed the politically difficult first step. It created the licensed-center and independent-review framework. Infinita describes a coordinated pathway involving experimental treatment review board review, licensed clinical administration, monitoring, evidence generation, and early commercialization for post-Phase-1 therapies[14].

The next step is a transparent Montana demonstration that adds interoperable enrollment, credible comparisons, pooled outcomes, documented fees, and safety monitoring. If that system produces useful evidence while remaining commercially sustainable, other states have a model they can copy.

The original Right to Try model spread from its first state in 2014 to 41 states by 2018[15]. That history establishes a distribution channel, not a guarantee. The evidence amendment must prove its value in operation.

Any implementing bill should require Enroll, Compare, Pool, and Publish. That turns 50 possible access experiments into one continually learning treatment system.

Methodology, Parameters, and Calculations

Overview

This appendix documents all 23 parameters used in the analysis, organized by type:

- External sources (peer-reviewed): 8
- Calculated values: 11
- Core definitions: 4

Quick Navigation

Calculated Values (11 parameters) • External Data Sources (8 parameters) • Core Definitions (4 parameters)

Calculated Values

Parameters derived from mathematical formulas and economic models.

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)

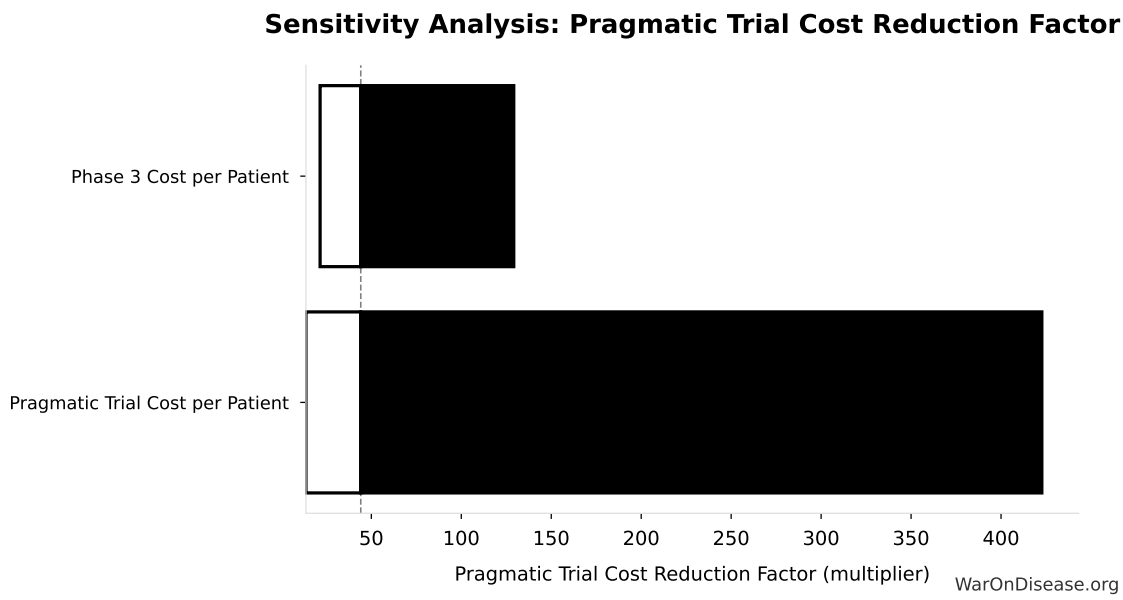
Inputs:

- 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

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.

Monte Carlo Distribution

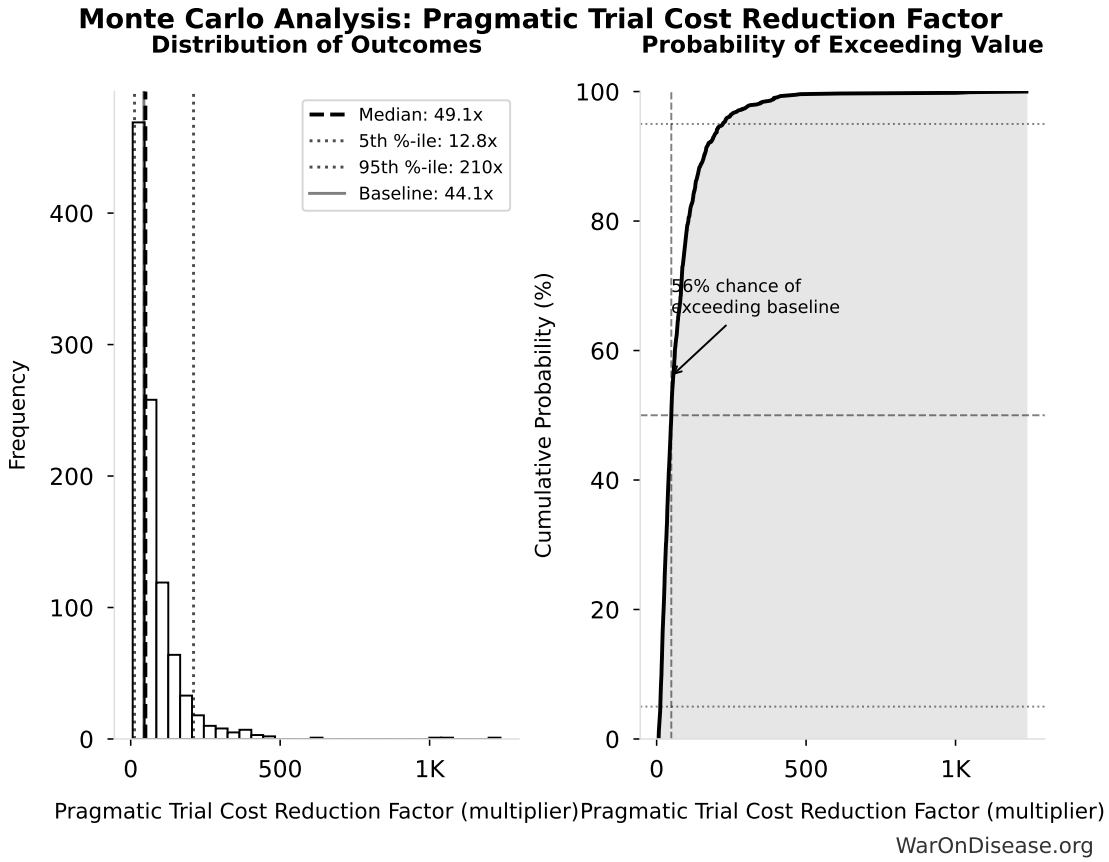


Figure 3: Monte Carlo Distribution: Pragmatic Trial Cost Reduction Factor (10,000 simulations)

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.

Exceedance Probability

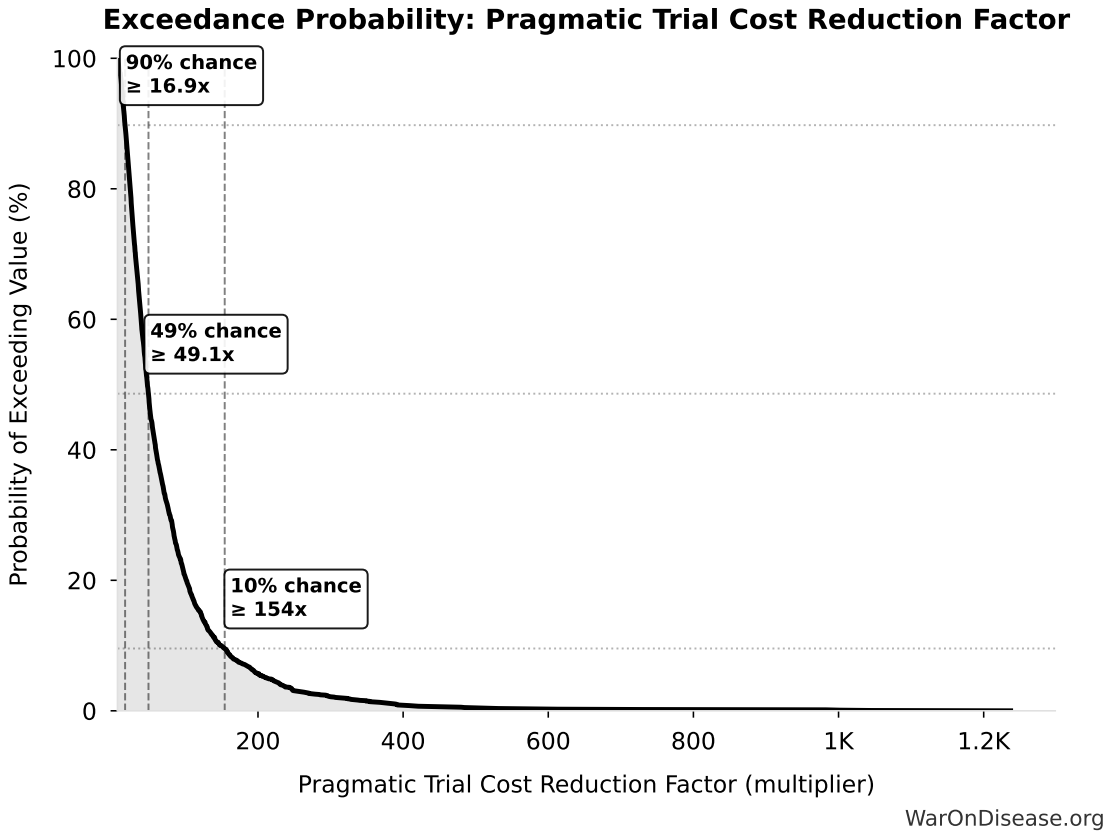


Figure 4: Probability of Exceeding Threshold: Pragmatic Trial Cost Reduction Factor

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.

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.

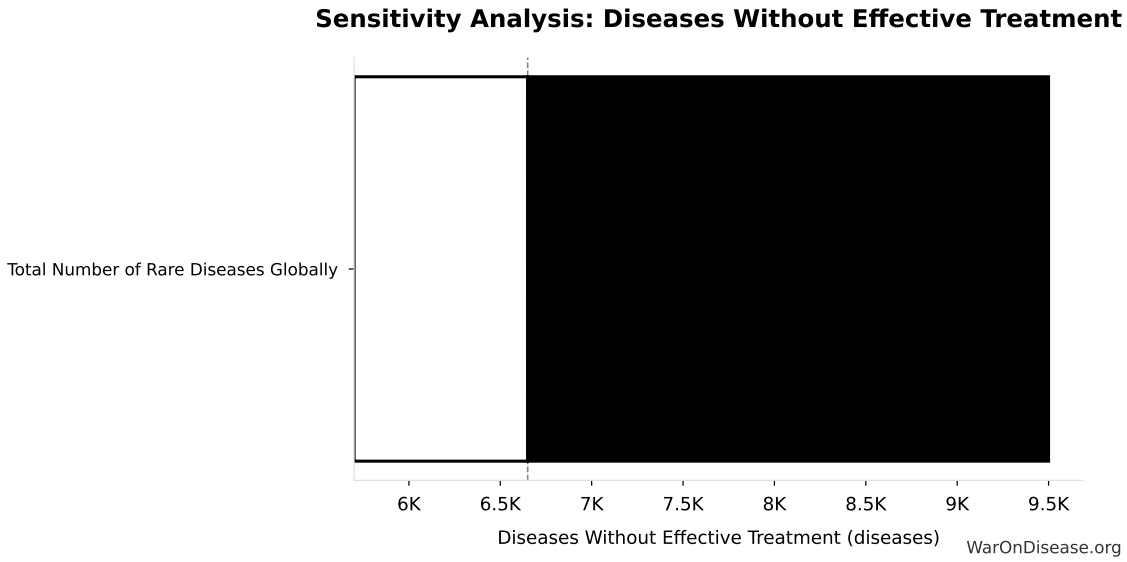
Inputs:

- 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:[16]
~ *Medium confidence*

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.

Monte Carlo Distribution

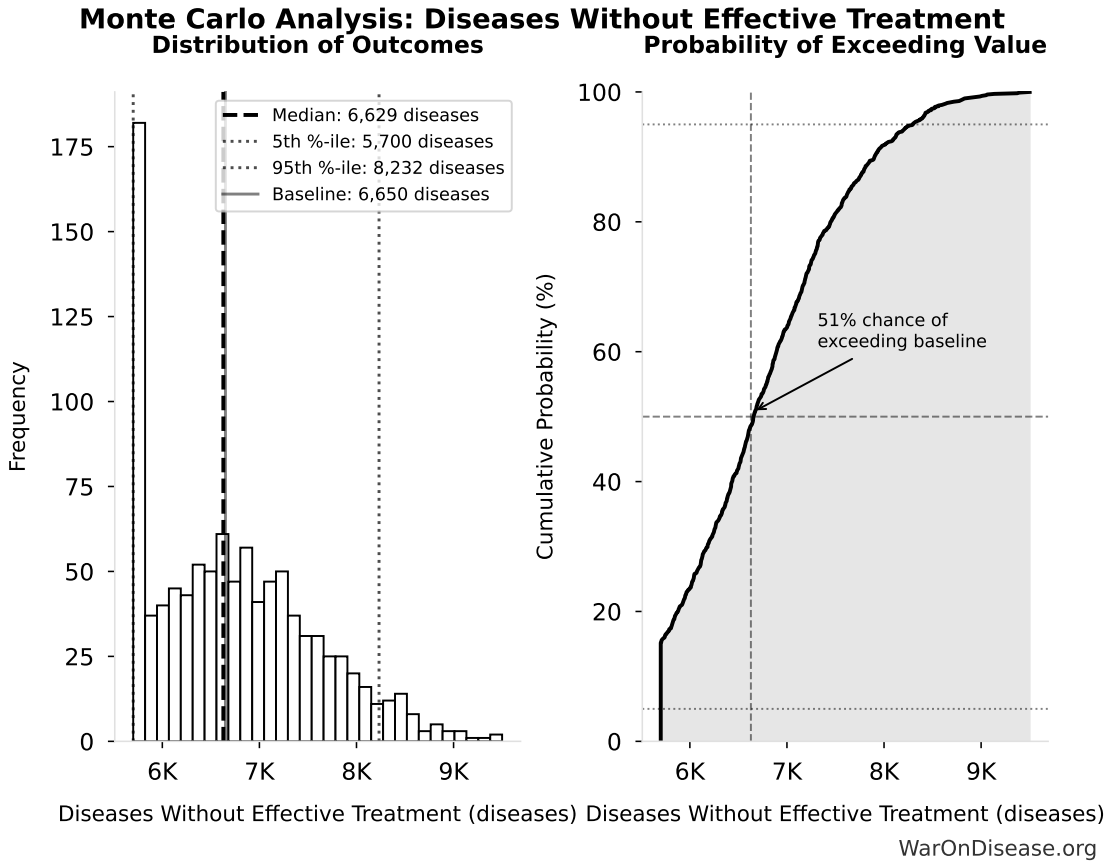


Figure 5: Monte Carlo Distribution: Diseases Without Effective Treatment (10,000 simulations)

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.

Exceedance Probability

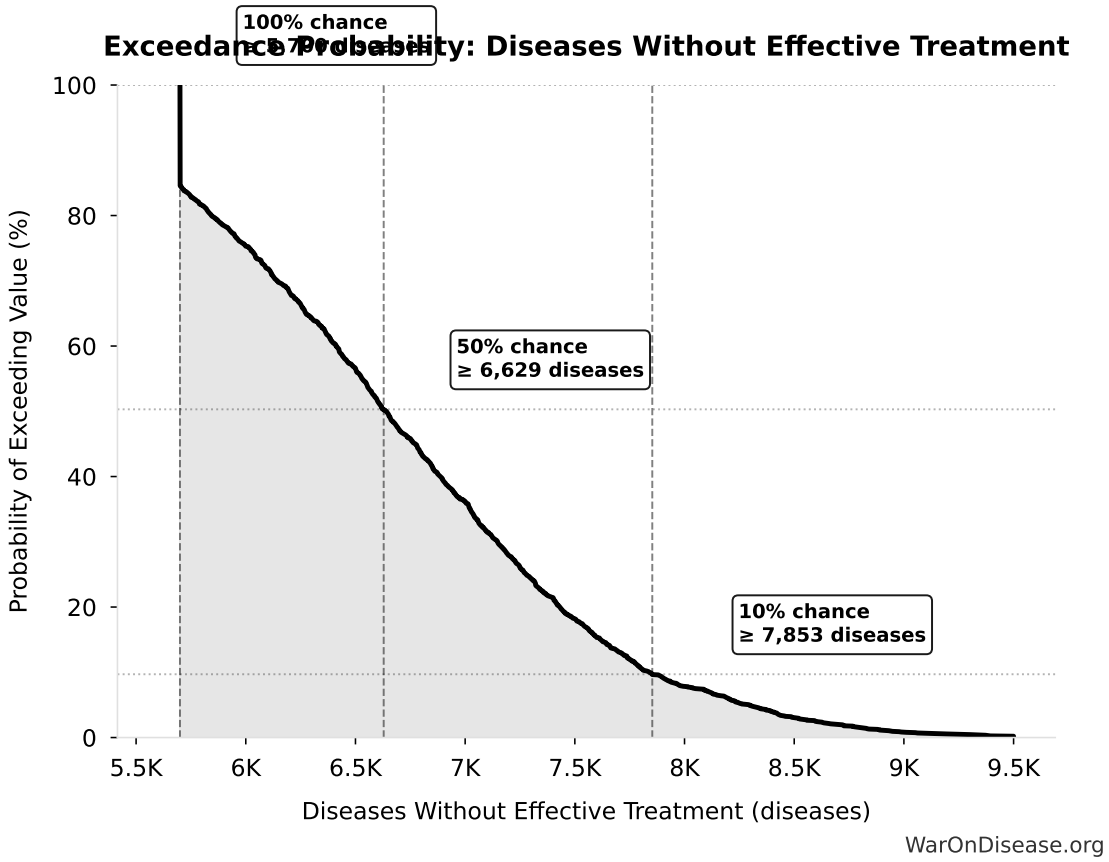


Figure 6: Probability of Exceeding Threshold: Diseases Without Effective Treatment

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.

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:

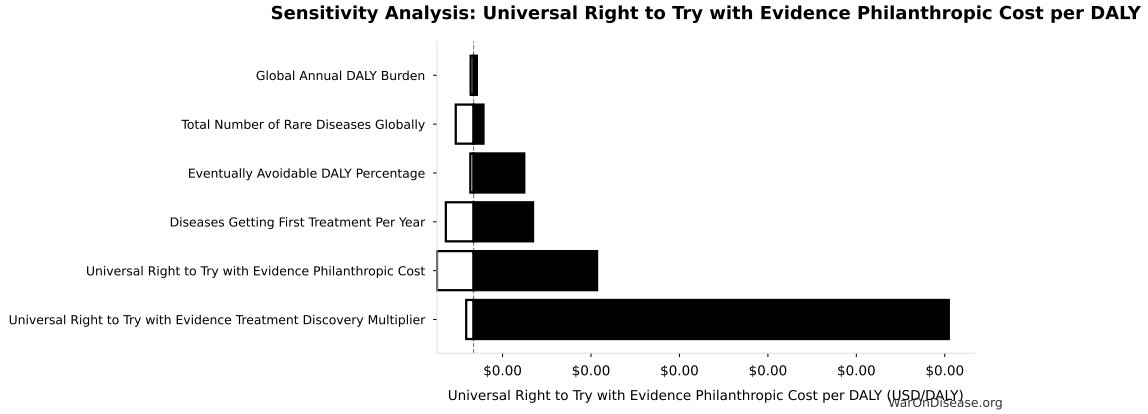
$$
\begin{aligned}
&T_{queue,SQ} \\
&= \frac{N_{untreated}}{Treatments_{new,ann}} \\
&= \frac{6{,}650}{15} \\
&= 443
\end{aligned}
$$

where:

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

? Low confidence

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.

Monte Carlo Distribution

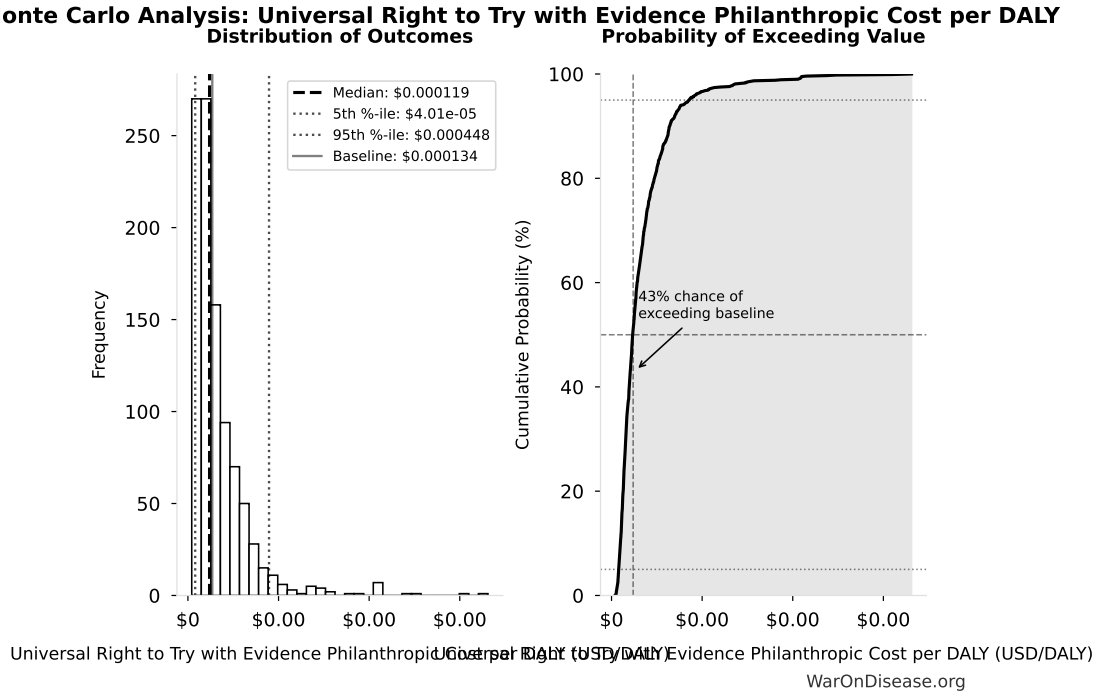


Figure 7: Monte Carlo Distribution: Universal Right to Try with Evidence Philanthropic Cost per DALY (10,000 simulations)

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.

Exceedance Probability

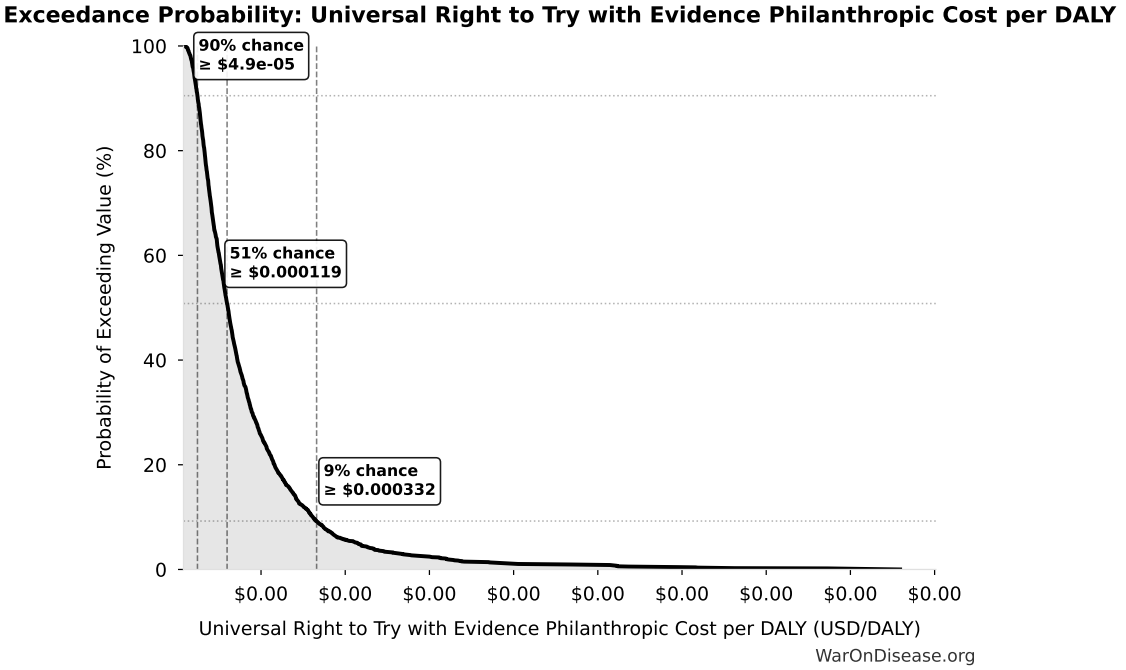


Figure 8: Probability of Exceeding Threshold: Universal Right to Try with Evidence Philanthropic Cost per DALY

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.

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:

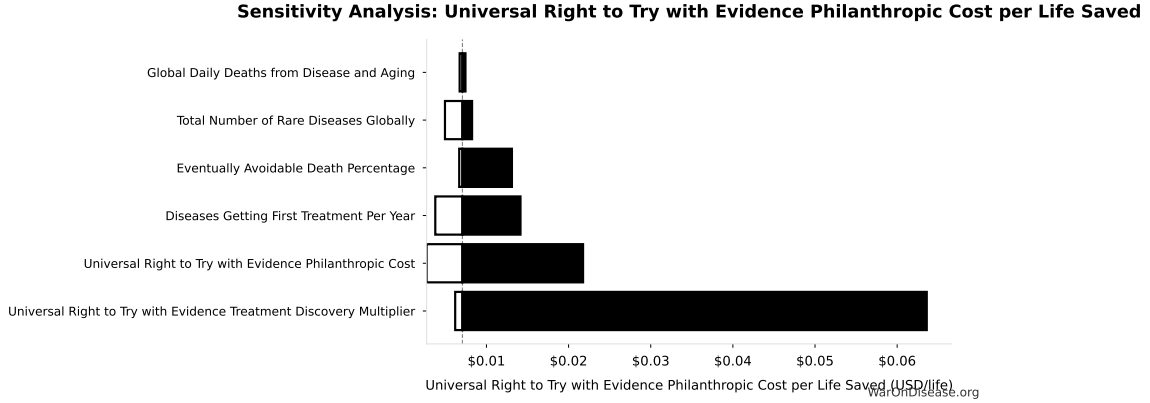
$$
\begin{aligned}
&T_{queue,SQ} \\
&= \frac{N_{untreated}}{Treatments_{new,ann}} \\
&= \frac{6{,}650}{15} \\
&= 443
\end{aligned}
$$

where:

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

? Low confidence

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.

Monte Carlo Distribution

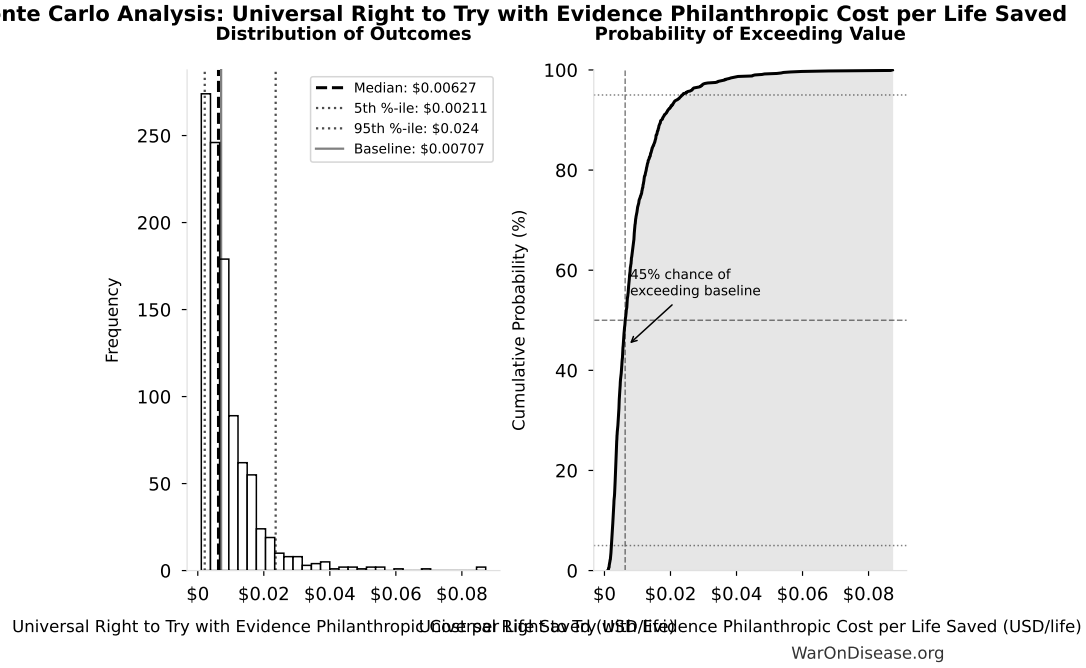


Figure 9: Monte Carlo Distribution: Universal Right to Try with Evidence Philanthropic Cost per Life Saved (10,000 simulations)

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.

Exceedance Probability

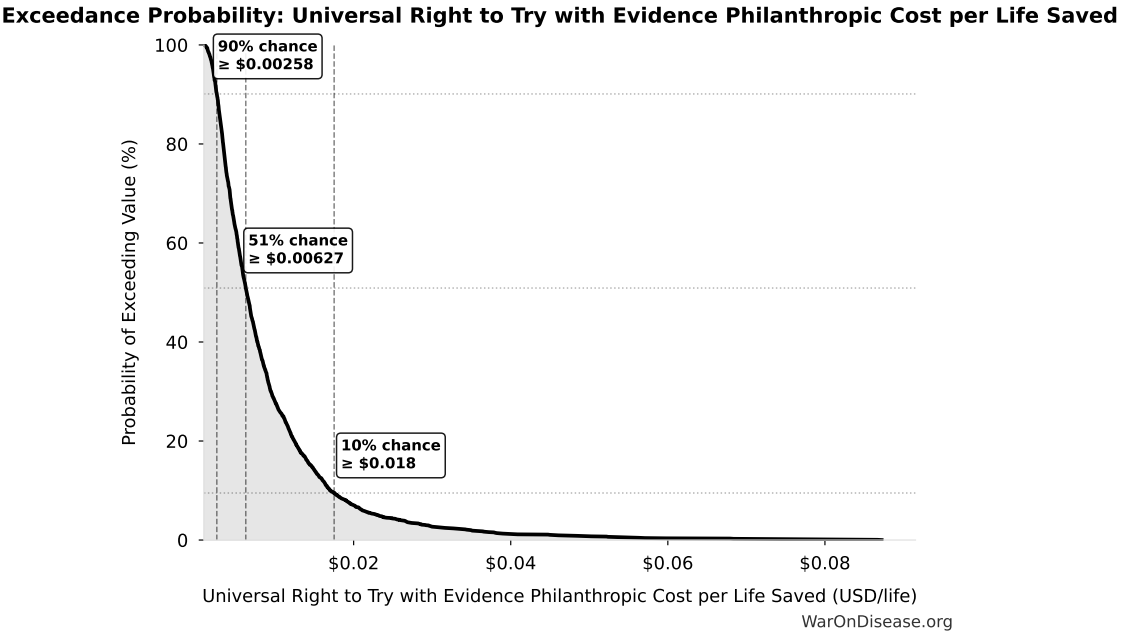


Figure 10: Probability of Exceeding Threshold: Universal Right to Try with Evidence Philanthropic Cost per Life Saved

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.

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

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

where:

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

where:

$$T_{first,SQ}$$
$$= T_{queue,SQ} \times 0.5$$
$$= 443 \times 0.5$$
$$= 222$$

where:

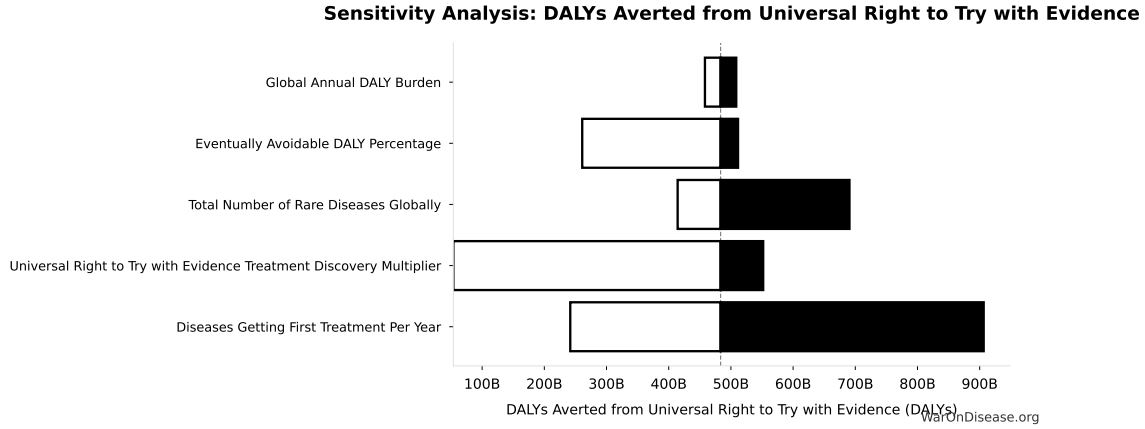
$$T_{queue,SQ}$$
$$= \frac{N_{untreated}}{Treatments_{new,ann}}$$
$$= \frac{6{,}650}{15}$$
$$= 443$$

where:

$$N_{untreated}$$
$$= N_{rare} \times 0.95$$
$$= 7{,}000 \times 0.95$$
$$= 6{,}650$$

? Low confidence

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.

Monte Carlo Distribution

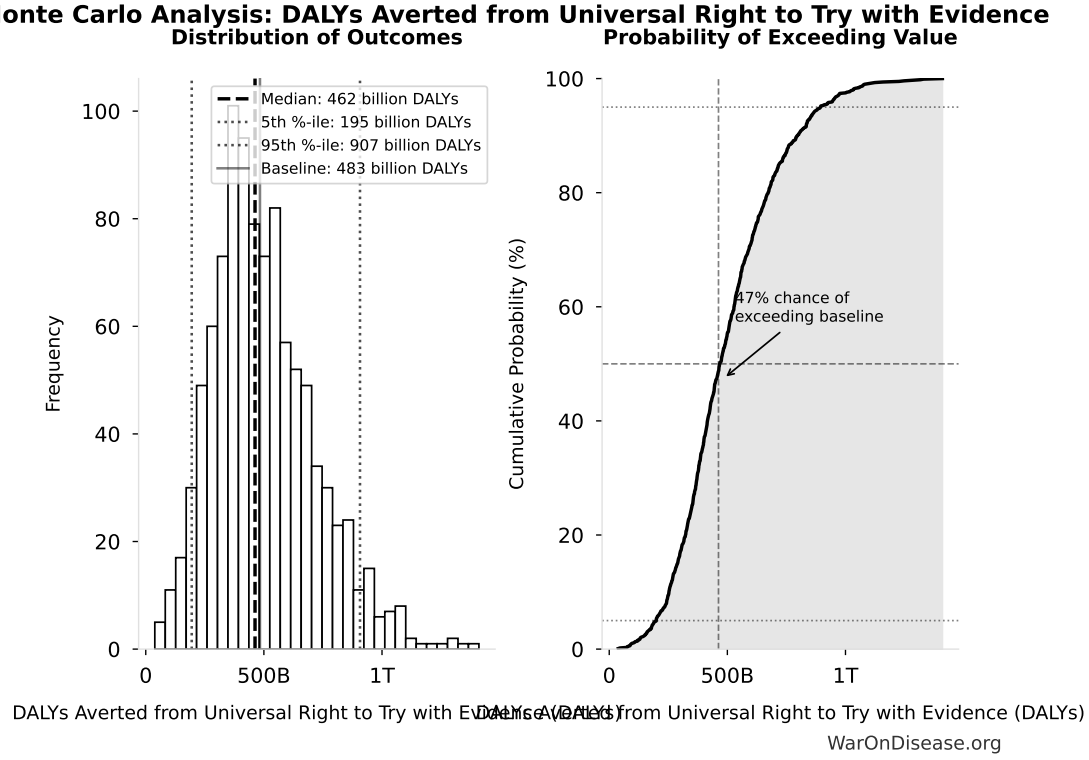


Figure 11: Monte Carlo Distribution: DALYs Averted from Universal Right to Try with Evidence (10,000 simulations)

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.

Exceedance Probability

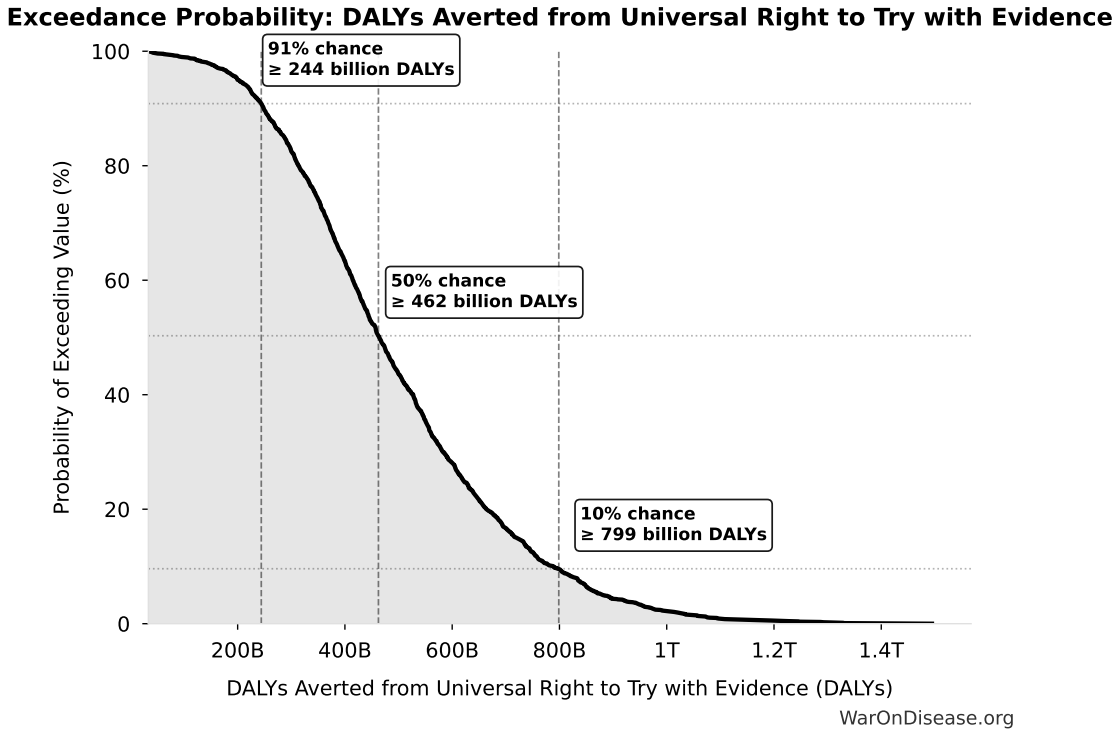


Figure 12: Probability of Exceeding Threshold: DALYs Averted from Universal Right to Try with Evidence

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.

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:

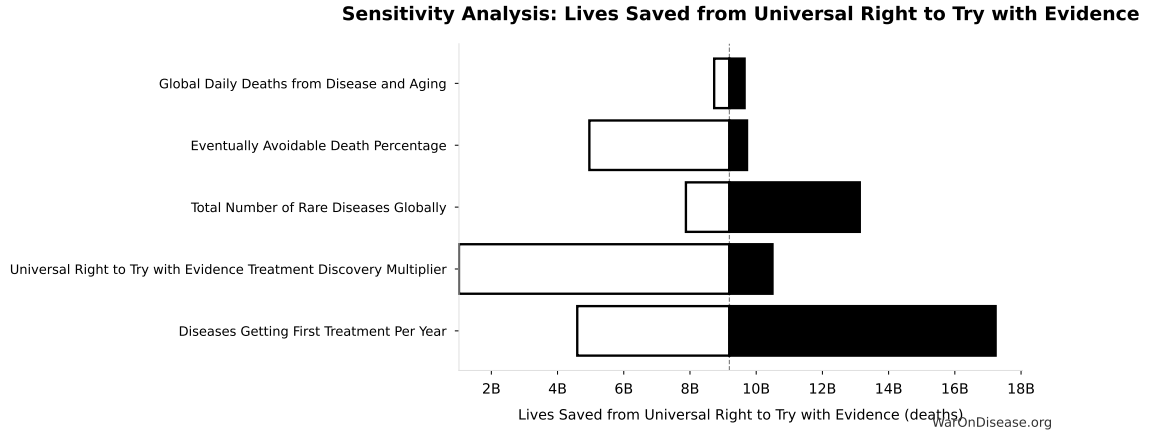
$$
\begin{aligned}
&T_{queue,SQ} \\
&= \frac{N_{untreated}}{Treatments_{new,ann}} \\
&= \frac{6{,}650}{15} \\
&= 443
\end{aligned}
$$

where:

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

? Low confidence

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.

Monte Carlo Distribution

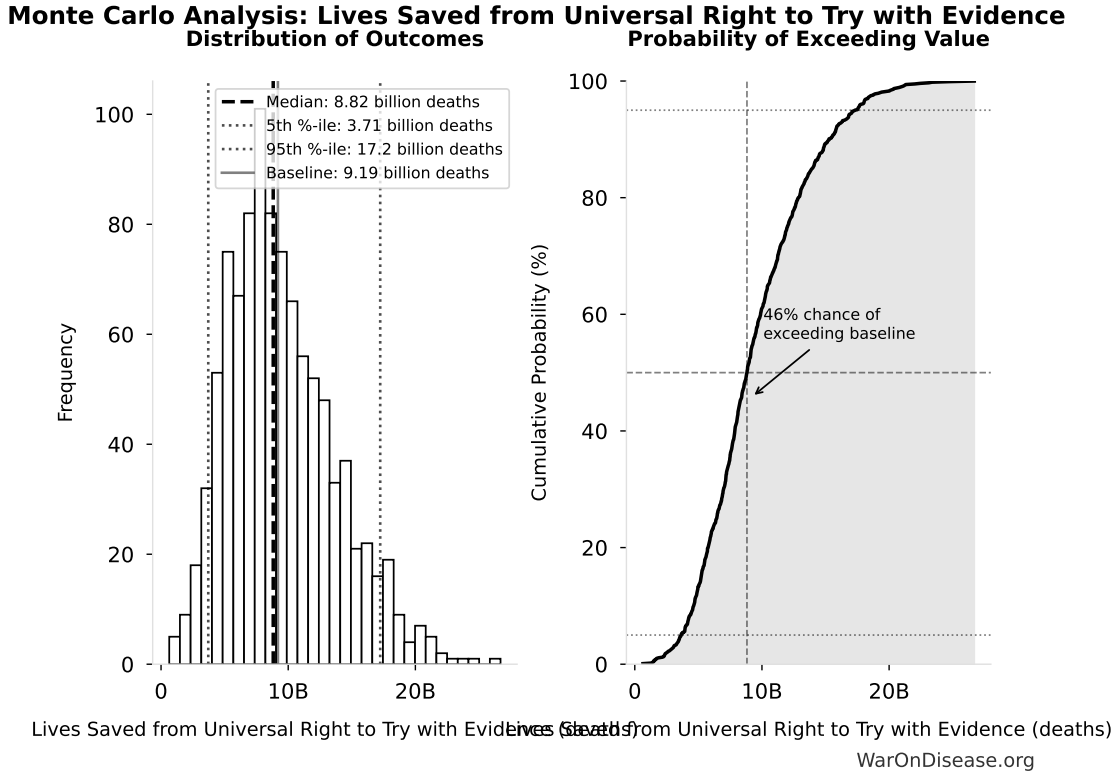


Figure 13: Monte Carlo Distribution: Lives Saved from Universal Right to Try with Evidence (10,000 simulations)

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.

Exceedance Probability

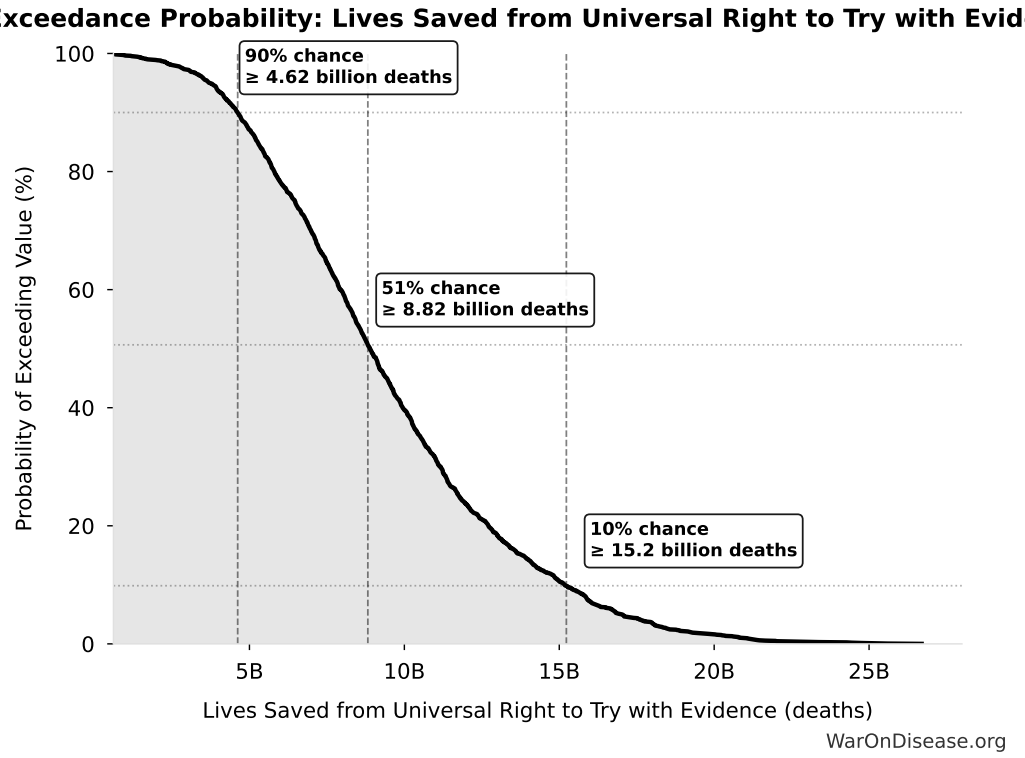


Figure 14: Probability of Exceeding Threshold: Lives Saved from Universal Right to Try with Evidence

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.

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:

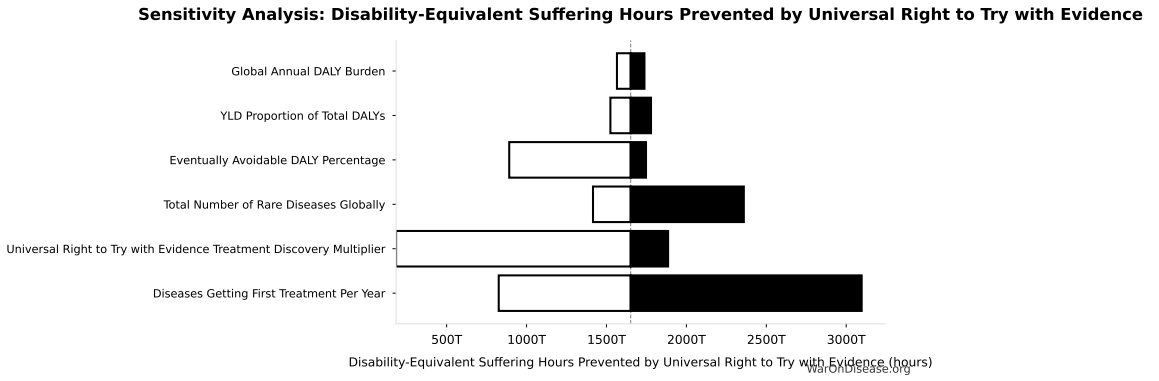
$$
\begin{aligned}
&T_{queue,SQ} \\
&= \frac{N_{untreated}}{Treatments_{new,ann}} \\
&= \frac{6{,}650}{15} \\
&= 443
\end{aligned}
$$

where:

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

? Low confidence

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.

Monte Carlo Distribution

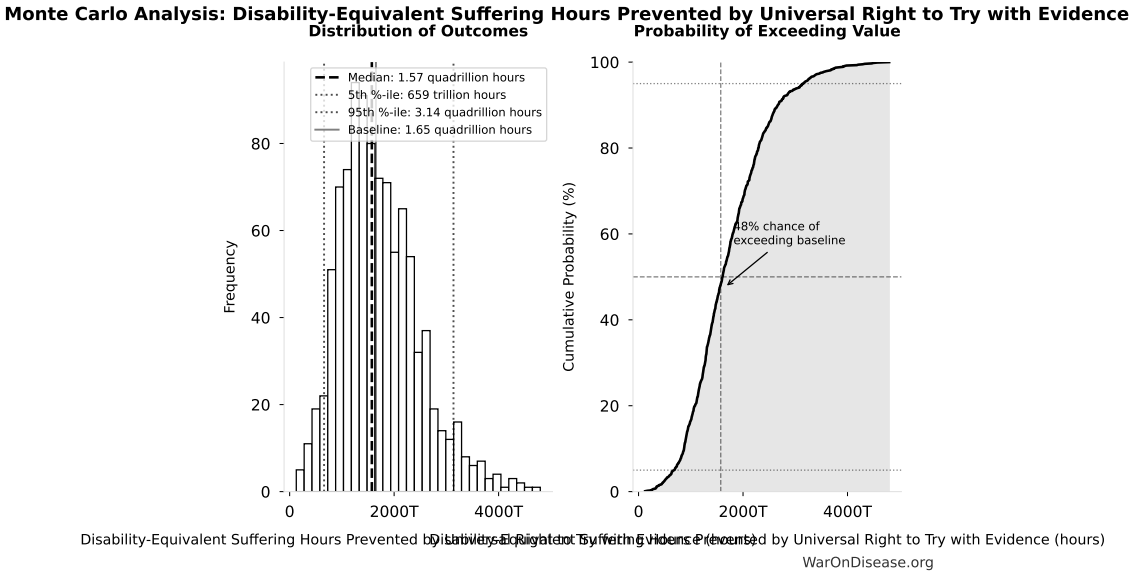


Figure 15: Monte Carlo Distribution: Disability-Equivalent Suffering Hours Prevented by Universal Right to Try with Evidence (10,000 simulations)

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.

Exceedance Probability

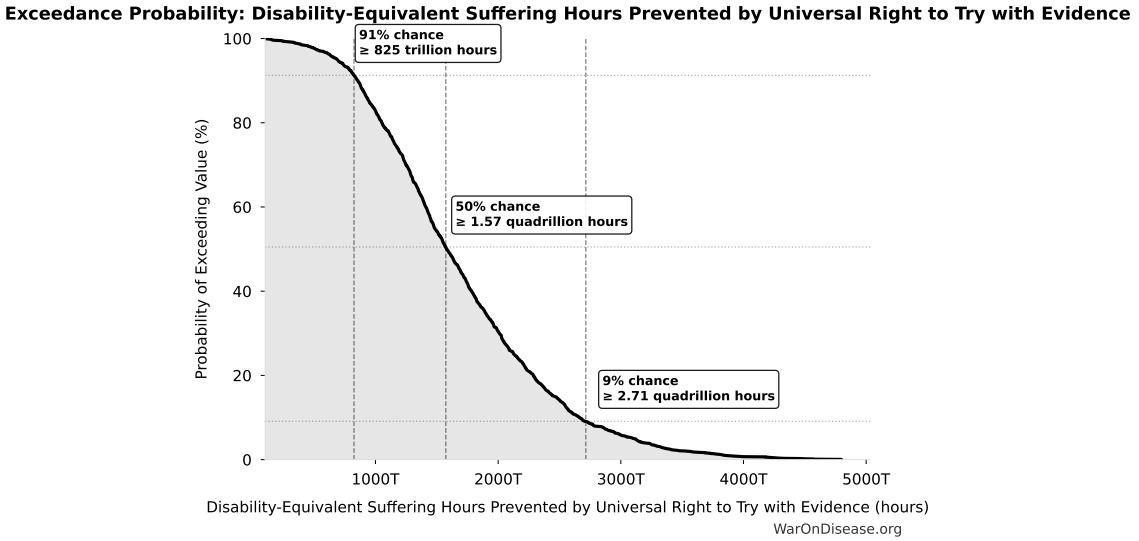


Figure 16: Probability of Exceeding Threshold: Disability-Equivalent Suffering Hours Prevented by Universal Right to Try with Evidence

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.

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:

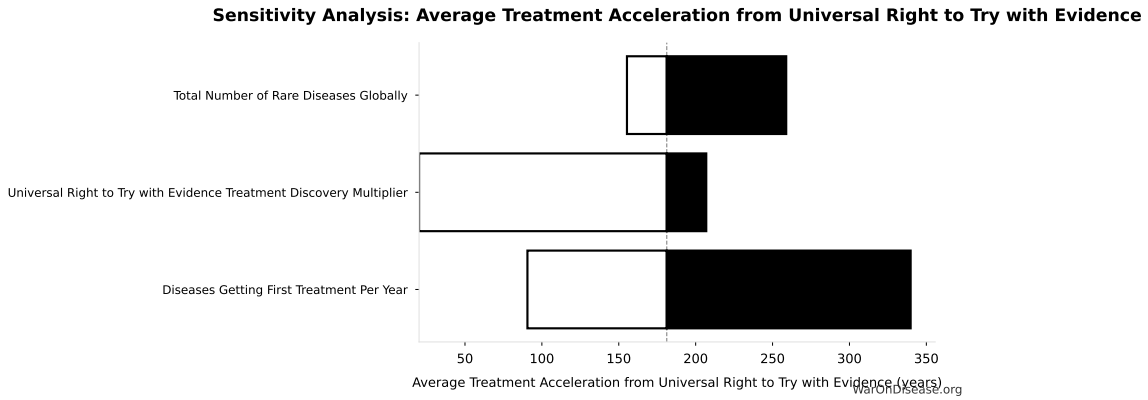
$$
\begin{aligned}
&T_{queue,SQ} \\
&= \frac{N_{untreated}}{Treatments_{new,ann}} \\
&= \frac{6{,}650}{15} \\
&= 443
\end{aligned}
$$

where:

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

? Low confidence

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.

Monte Carlo Distribution

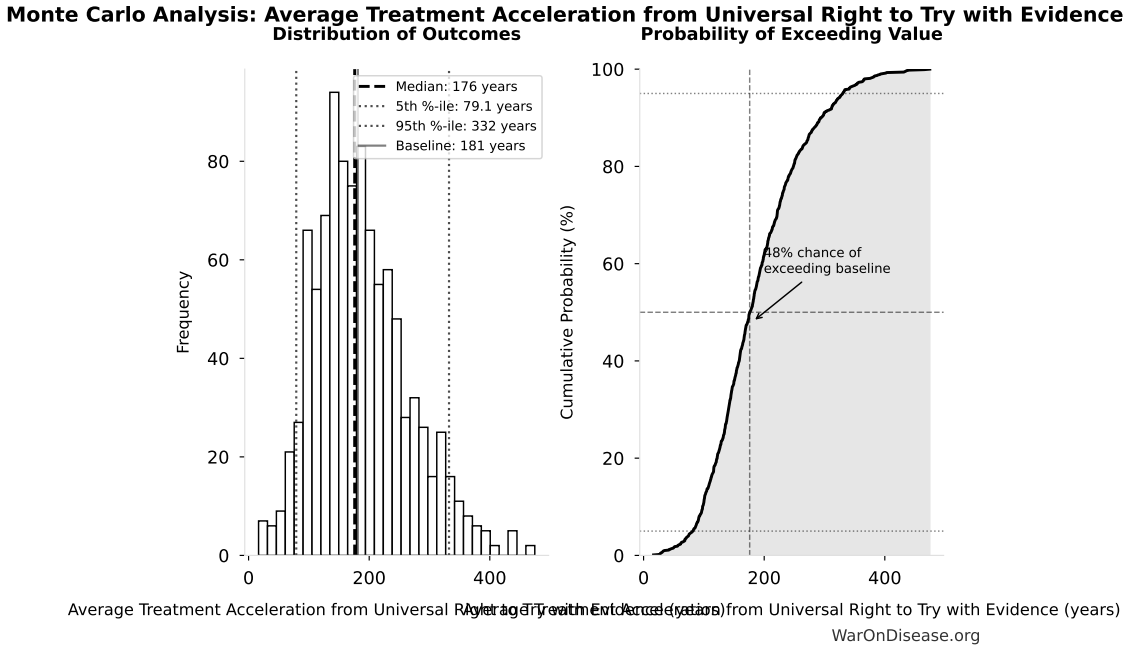


Figure 17: Monte Carlo Distribution: Average Treatment Acceleration from Universal Right to Try with Evidence (10,000 simulations)

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.

Exceedance Probability

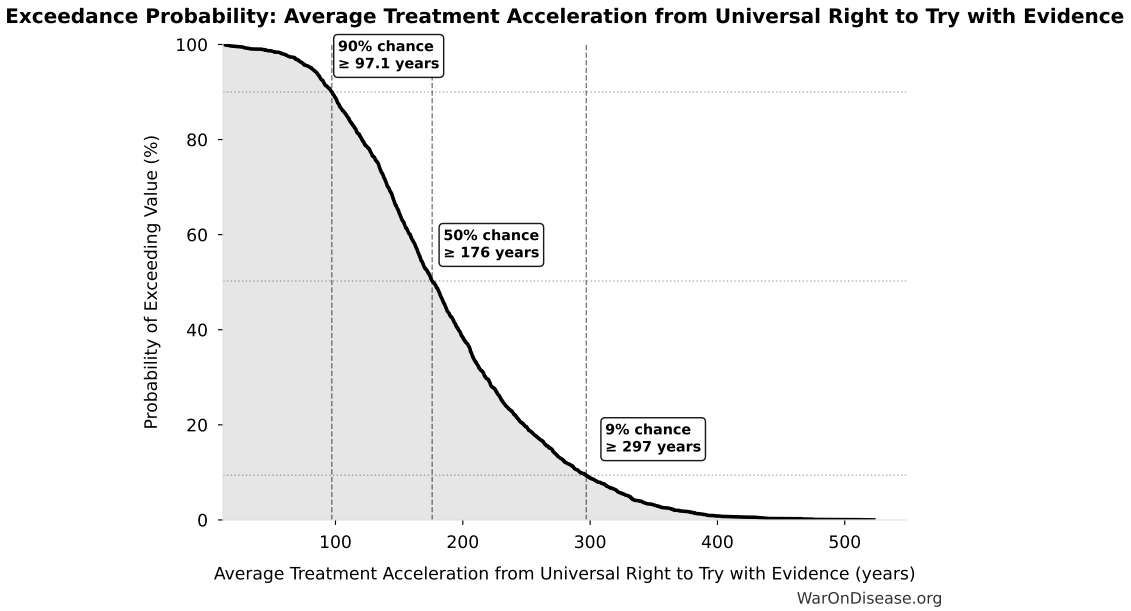


Figure 18: Probability of Exceeding Threshold: Average Treatment Acceleration from Universal Right to Try with Evidence

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.

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:

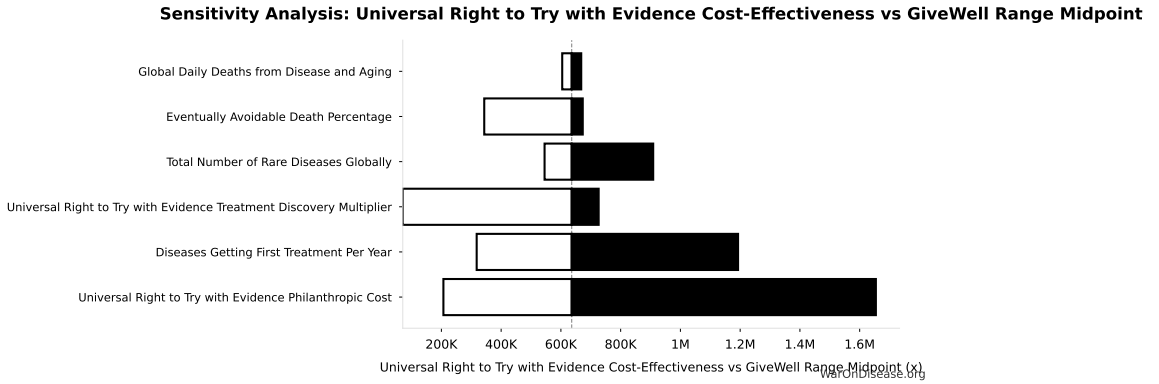
$$
\begin{aligned}
&T_{queue,SQ} \\
&= \frac{N_{untreated}}{Treatments_{new,ann}} \\
&= \frac{6{,}650}{15} \\
&= 443
\end{aligned}
$$

where:

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

? Low confidence

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.

Monte Carlo Distribution

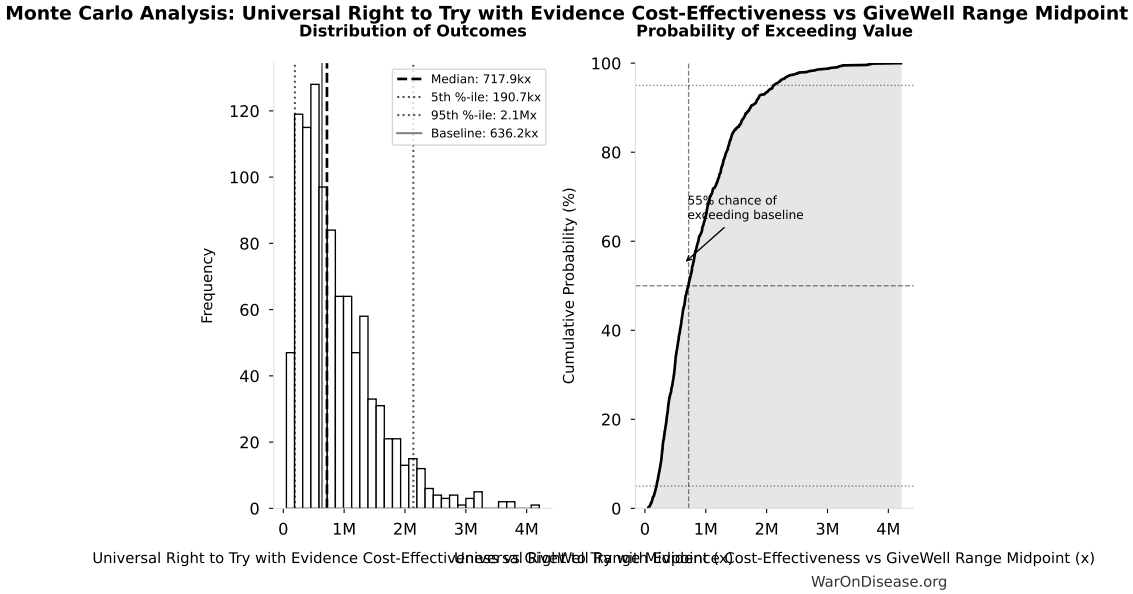


Figure 19: Monte Carlo Distribution: Universal Right to Try with Evidence Cost-Effectiveness vs GiveWell Range Midpoint (10,000 simulations)

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.

Exceedance Probability

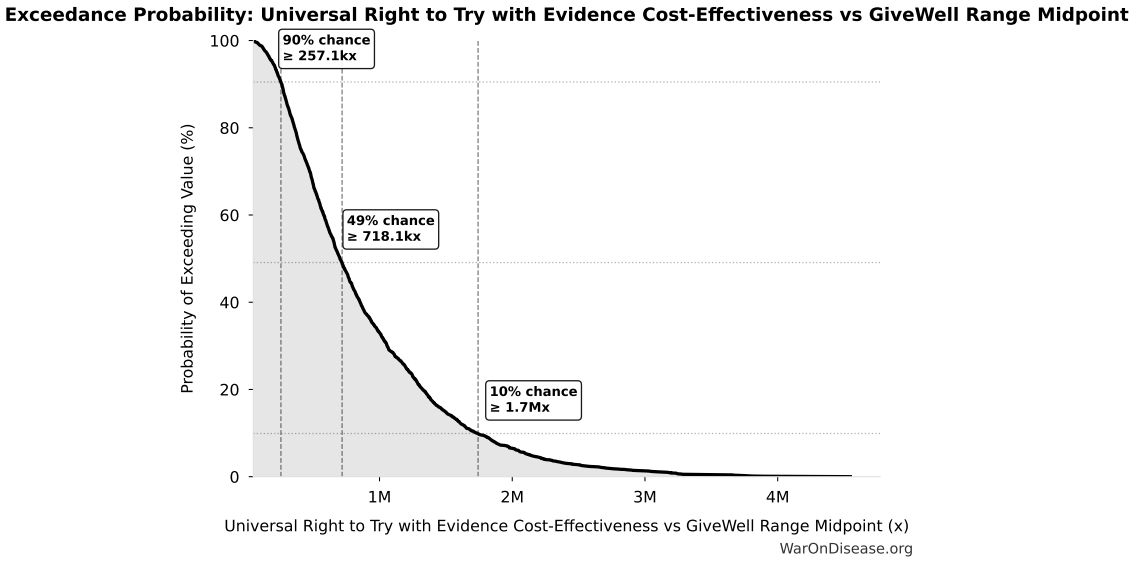


Figure 20: Probability of Exceeding Threshold: Universal Right to Try with Evidence Cost-Effectiveness vs GiveWell Range Midpoint

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.

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:

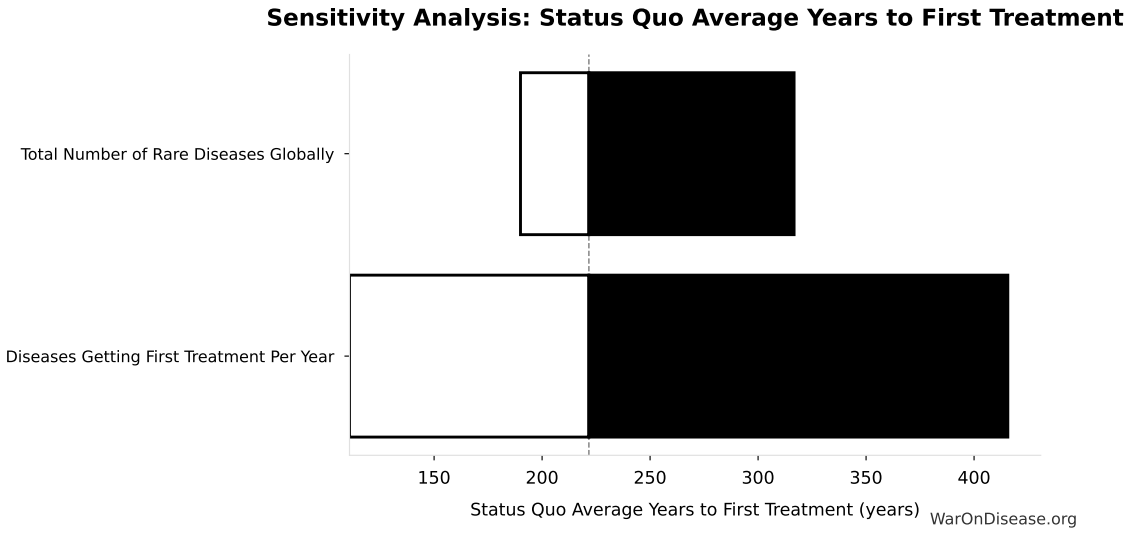
$$
\begin{aligned}
& T_{queue,SQ} \\
&= \frac{N_{untreated}}{Treatments_{new,ann}} \\
&= \frac{6{,}650}{15} \\
&= 443
\end{aligned}
$$

where:

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

Methodology:[17]
? Low confidence

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.

Monte Carlo Distribution

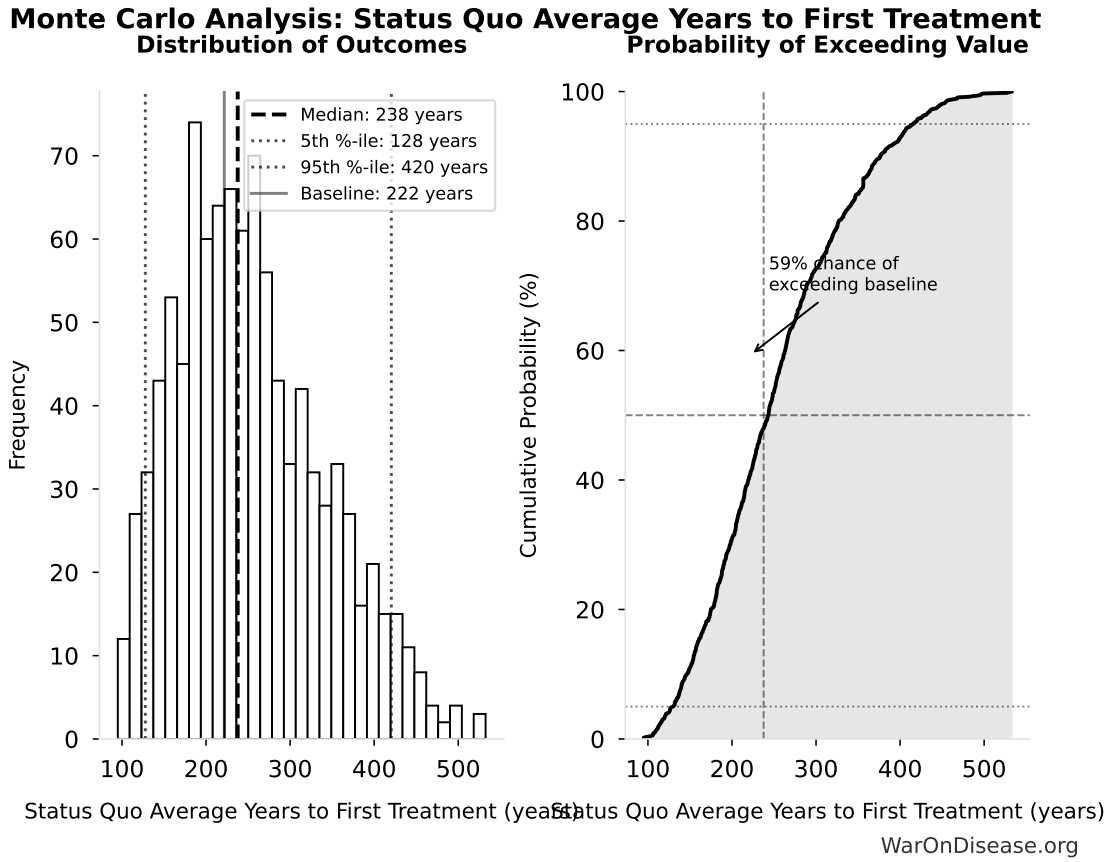


Figure 21: Monte Carlo Distribution: Status Quo Average Years to First Treatment (10,000 simulations)

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.

Exceedance Probability

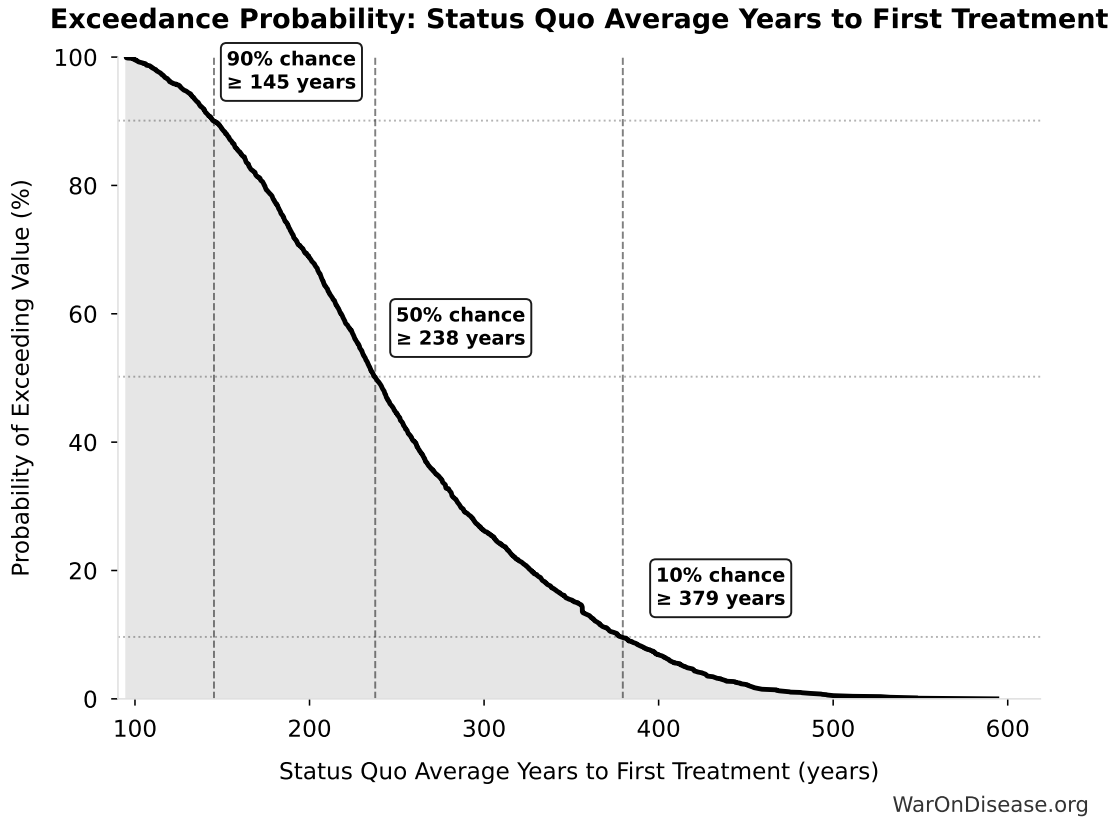


Figure 22: Probability of Exceeding Threshold: Status Quo Average Years to First Treatment

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.

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)

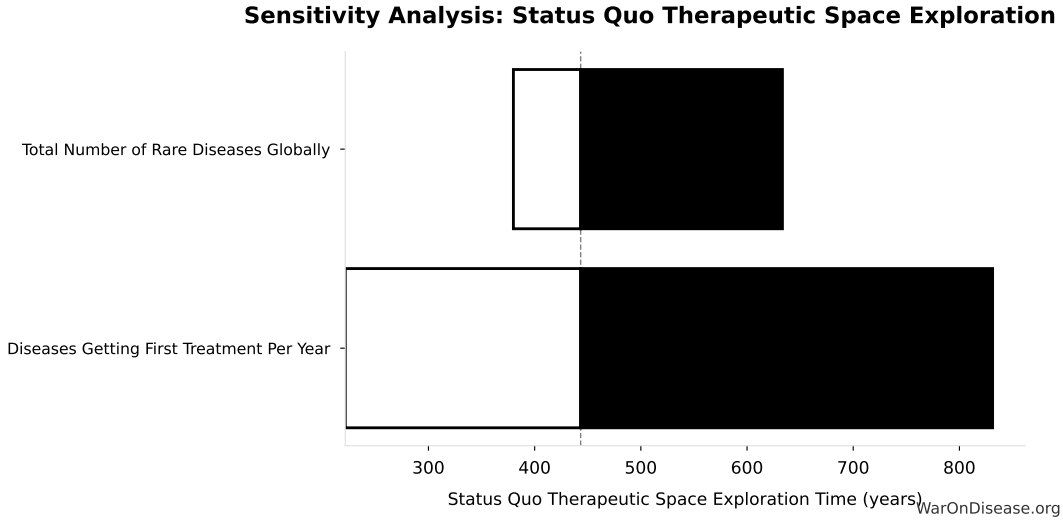
$$\begin{aligned} & T_{queue,SQ} \\ &= \frac{N_{untreated}}{Treatments_{new,ann}} \\ &= \frac{6{,}650}{15} \\ &= 443 \end{aligned}$$

where:

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

Methodology:[17]
? Low confidence

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.

Monte Carlo Distribution

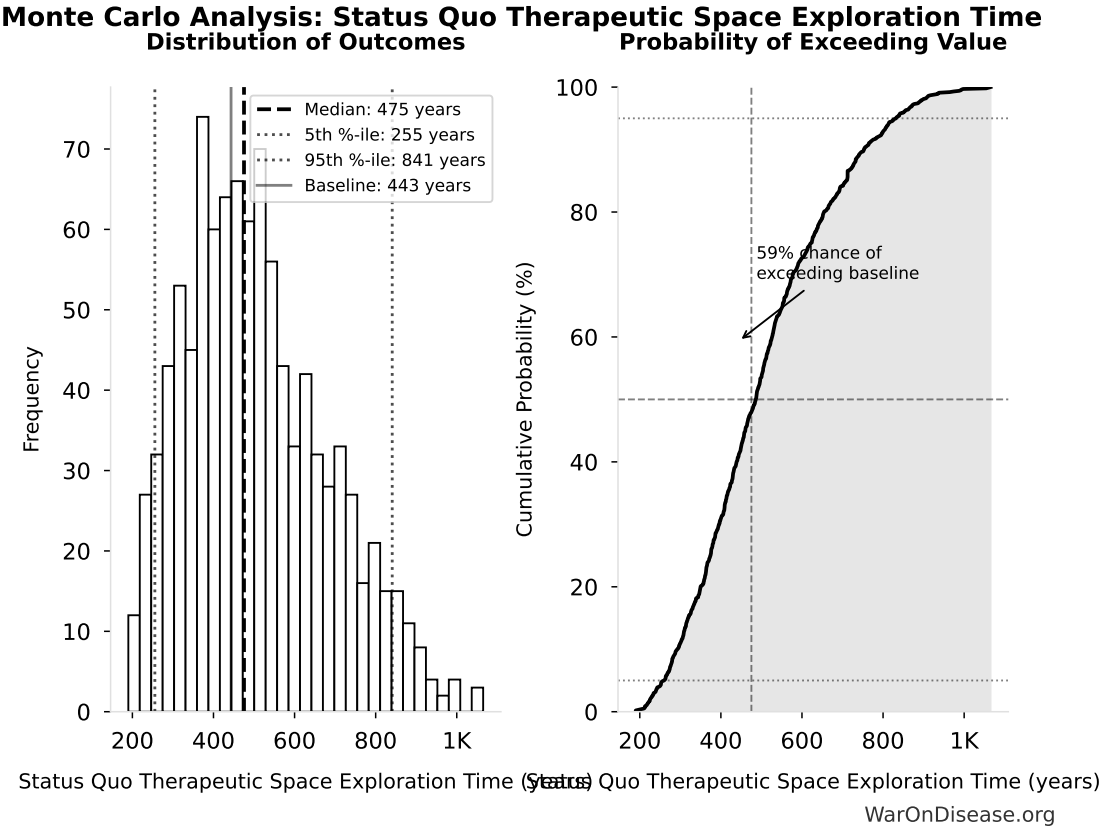


Figure 23: Monte Carlo Distribution: Status Quo Therapeutic Space Exploration Time (10,000 simulations)

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.

Exceedance Probability

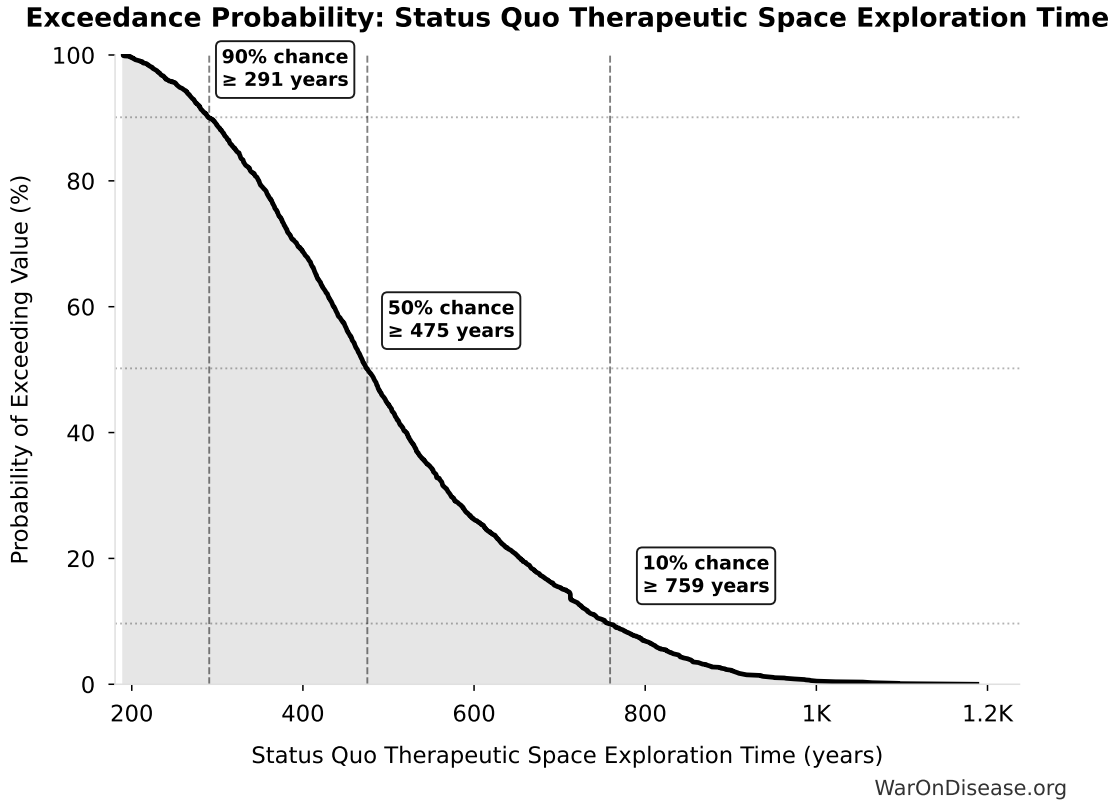


Figure 24: Probability of Exceeding Threshold: Status Quo Therapeutic Space Exploration Time

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.

External Data Sources

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

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]

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).

Input Distribution

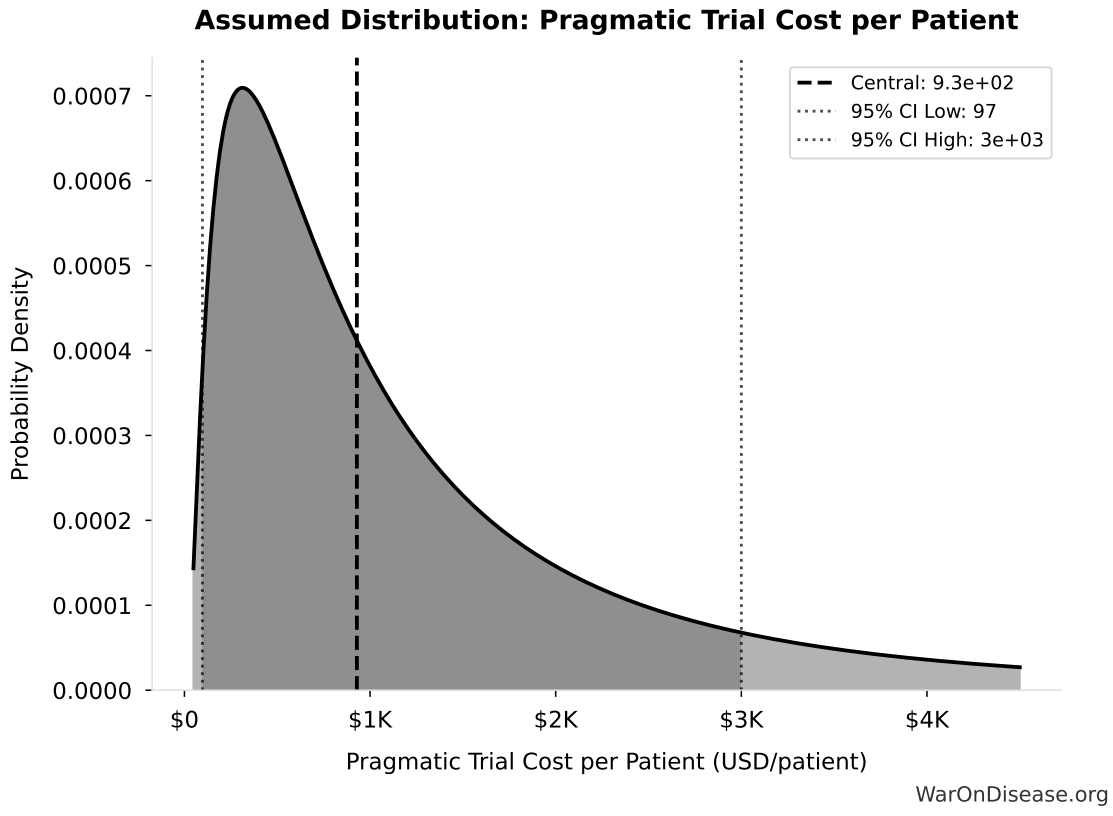


Figure 25: Probability Distribution: Pragmatic Trial Cost per Patient

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

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:[6]

Uncertainty Range

Technical: Distribution: Fixed
High confidence

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:[18]

Uncertainty Range

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

Input Distribution

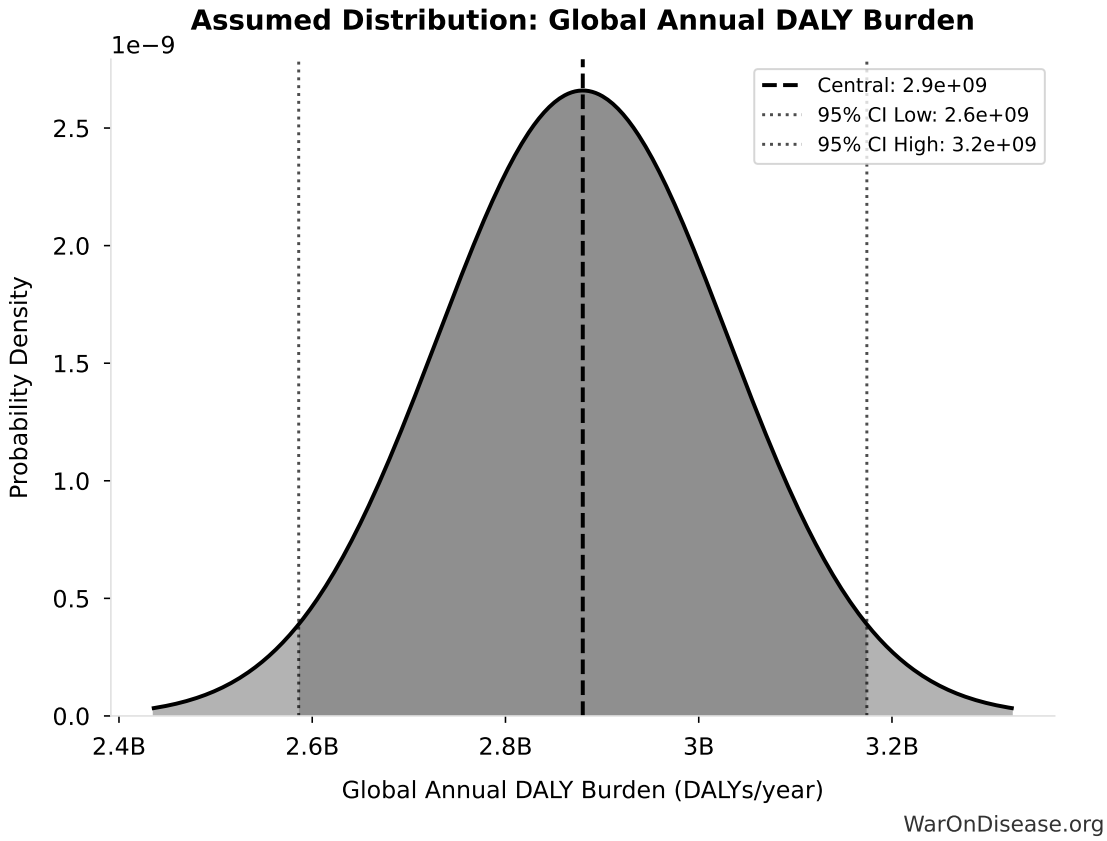


Figure 26: Probability Distribution: Global Annual DALY Burden

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*

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:[19]

Uncertainty Range

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

Input Distribution

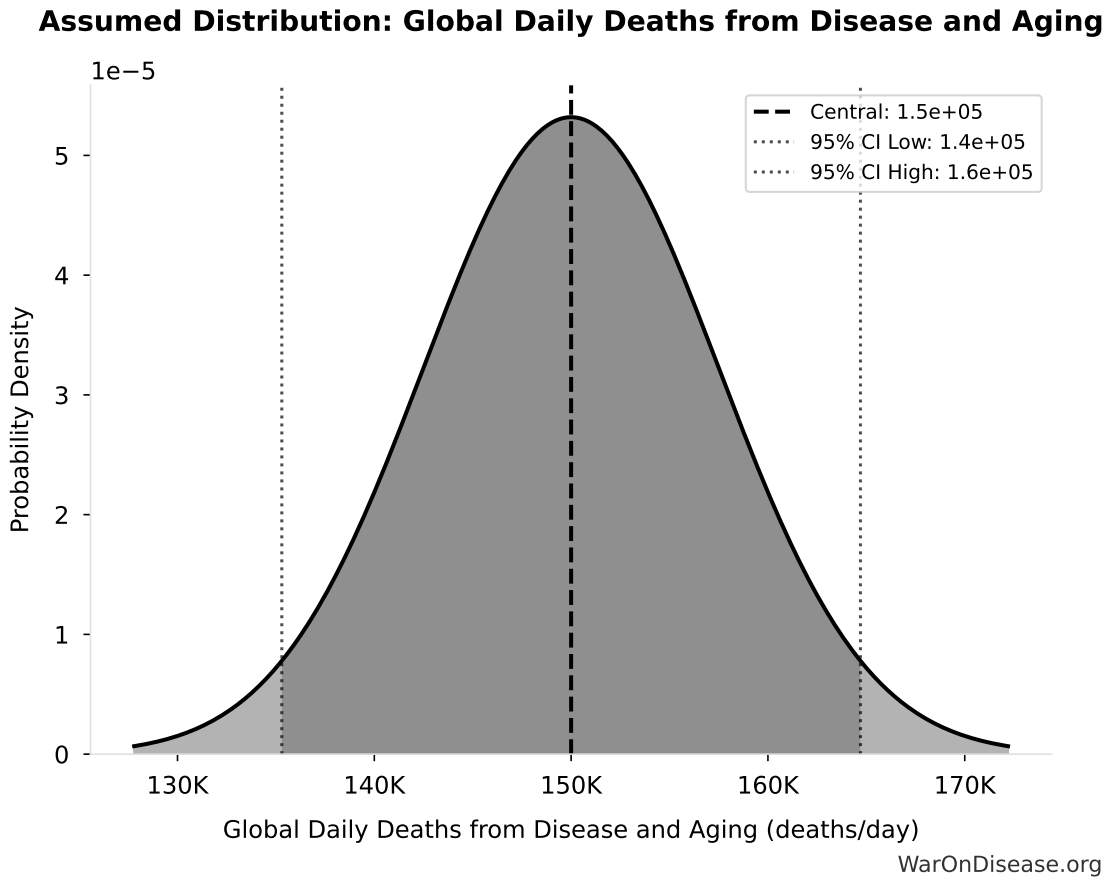


Figure 27: Probability Distribution: Global Daily Deaths from Disease and Aging

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*

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:[18]

Uncertainty Range

Technical: Distribution: Normal (SE: 0.03 proportion)

Input Distribution

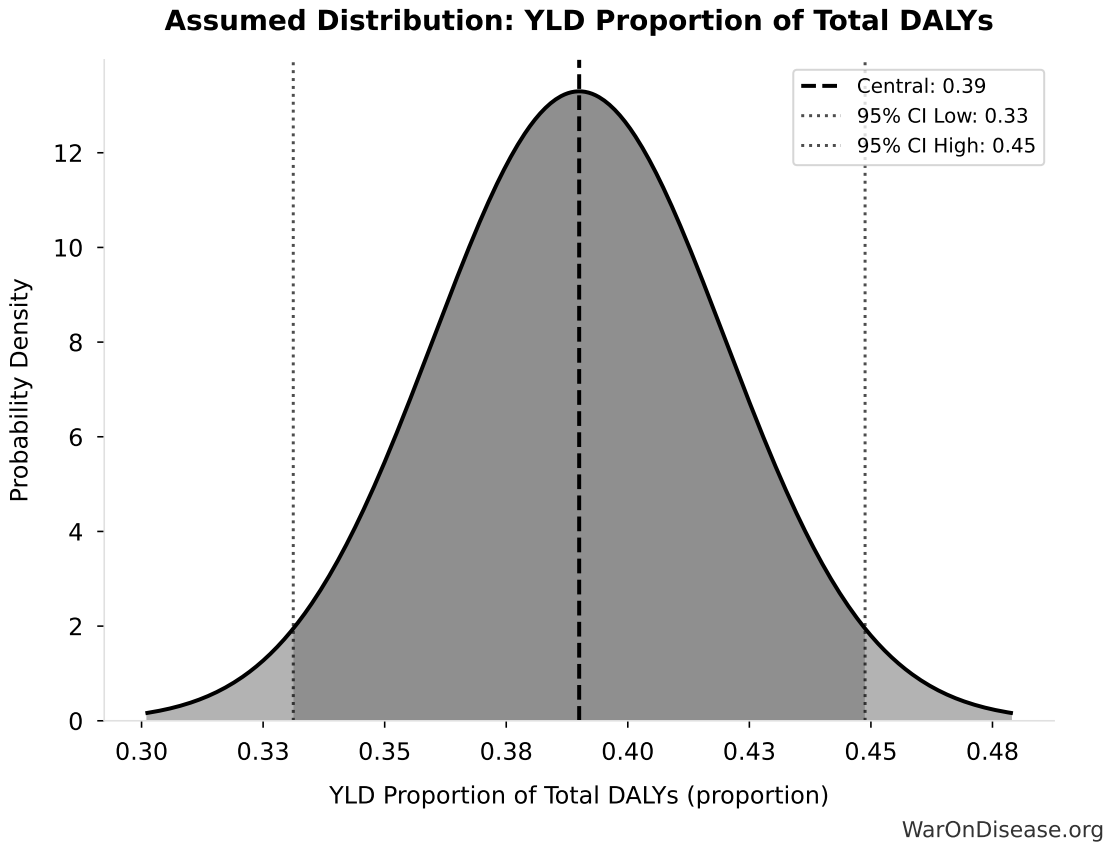


Figure 28: Probability Distribution: YLD Proportion of Total DALYs

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*

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:[20]

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).

Input Distribution

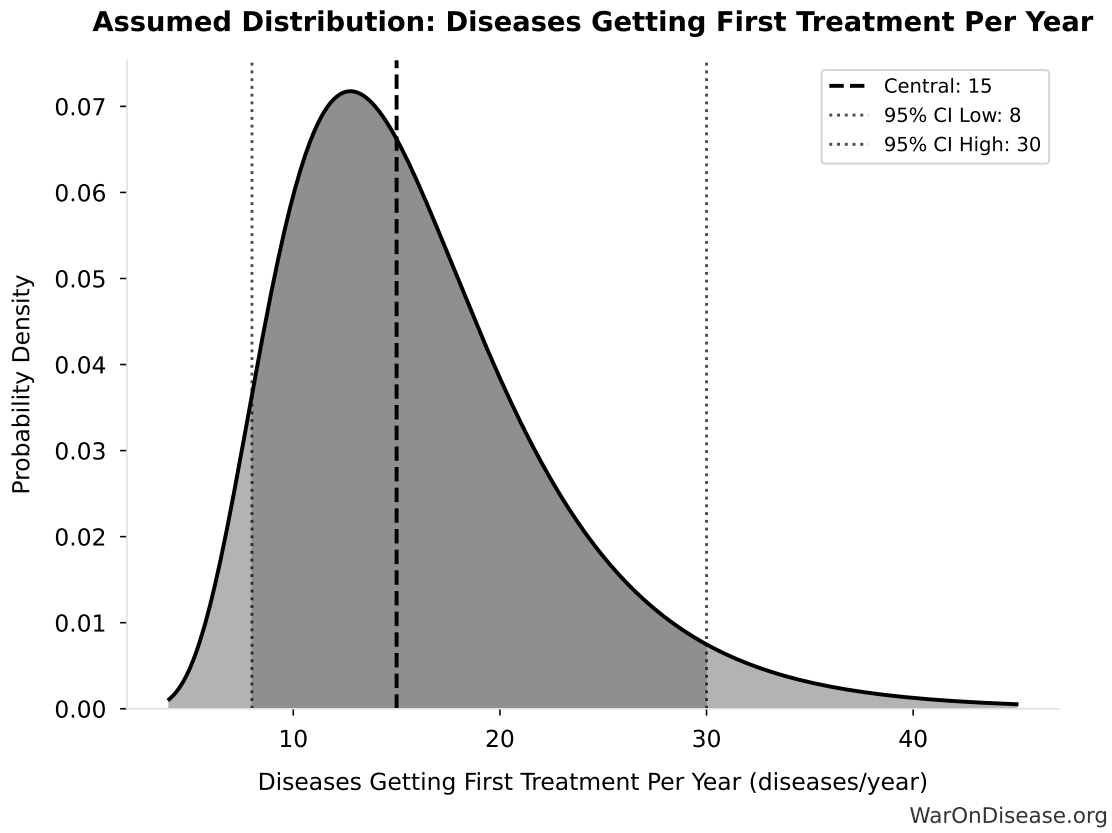


Figure 29: Probability Distribution: Diseases Getting First Treatment Per Year

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

Total Number of Rare Diseases Globally: 7,000 diseases

Details

Total number of rare diseases globally
Source:[21]

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.

Input Distribution

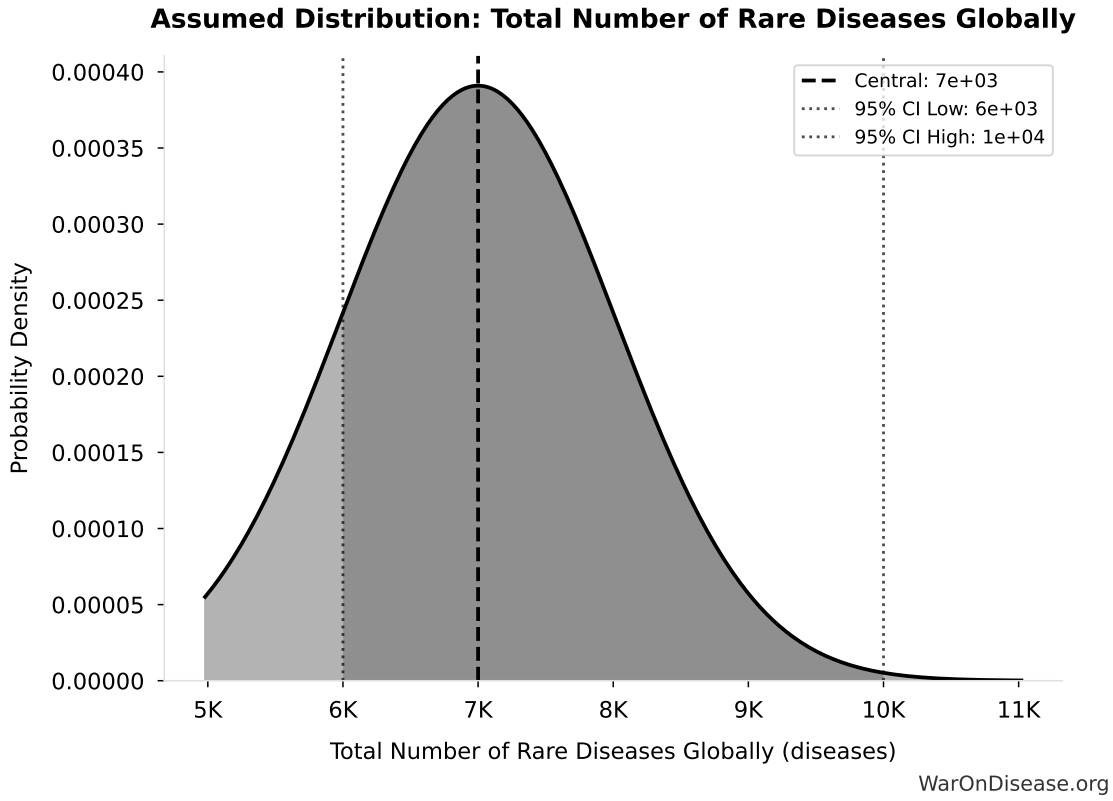


Figure 30: Probability Distribution: Total Number of Rare Diseases Globally

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

Phase 3 Cost per Patient: $41,000

Details

Phase 3 cost per patient (median from FDA study)
Source:[2]

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).

Input Distribution

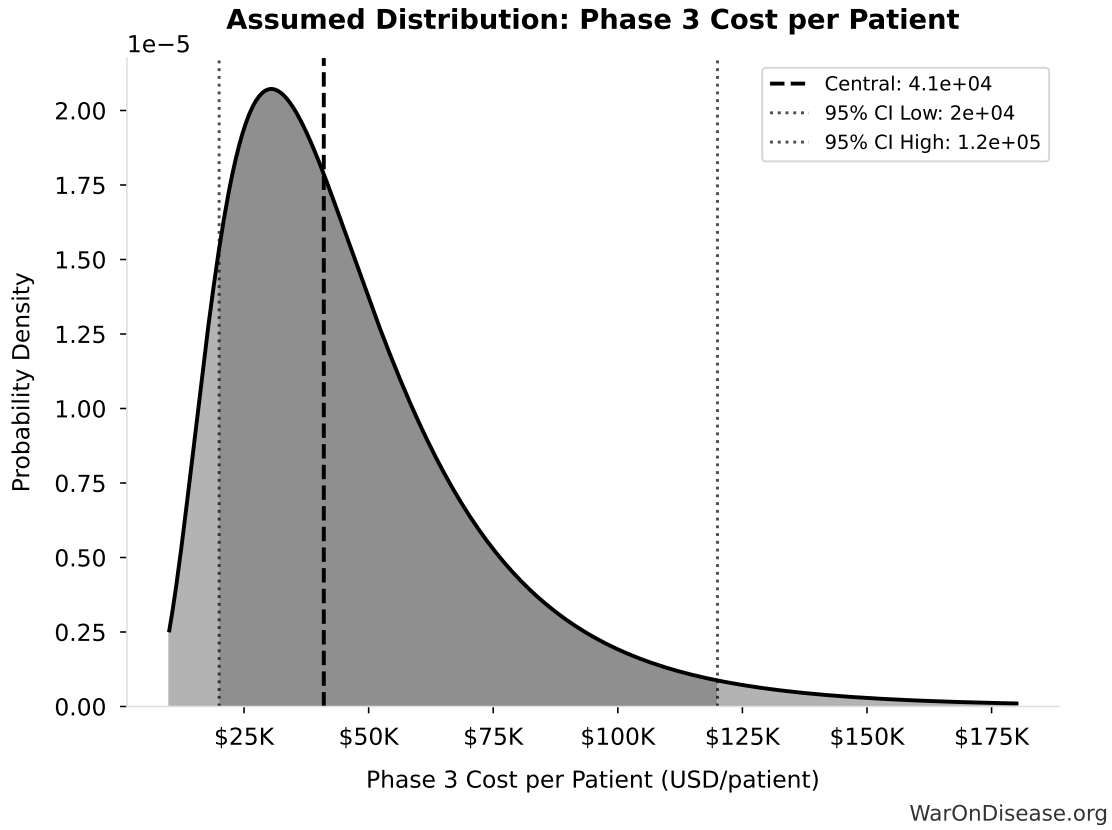


Figure 31: Probability Distribution: Phase 3 Cost per Patient

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

Core Definitions

Fundamental parameters and constants used throughout the analysis.

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.

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.

Input Distribution

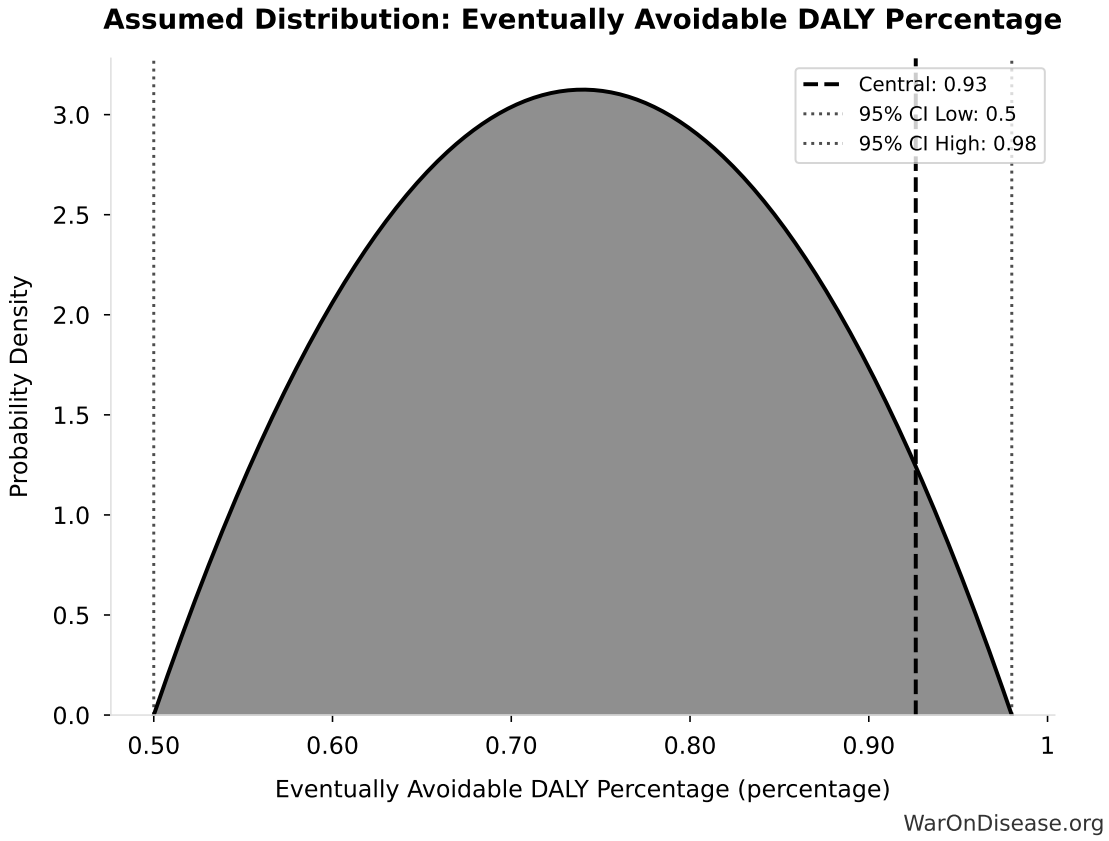


Figure 32: Probability Distribution: Eventually Avoidable DALY Percentage

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

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.

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.

Input Distribution

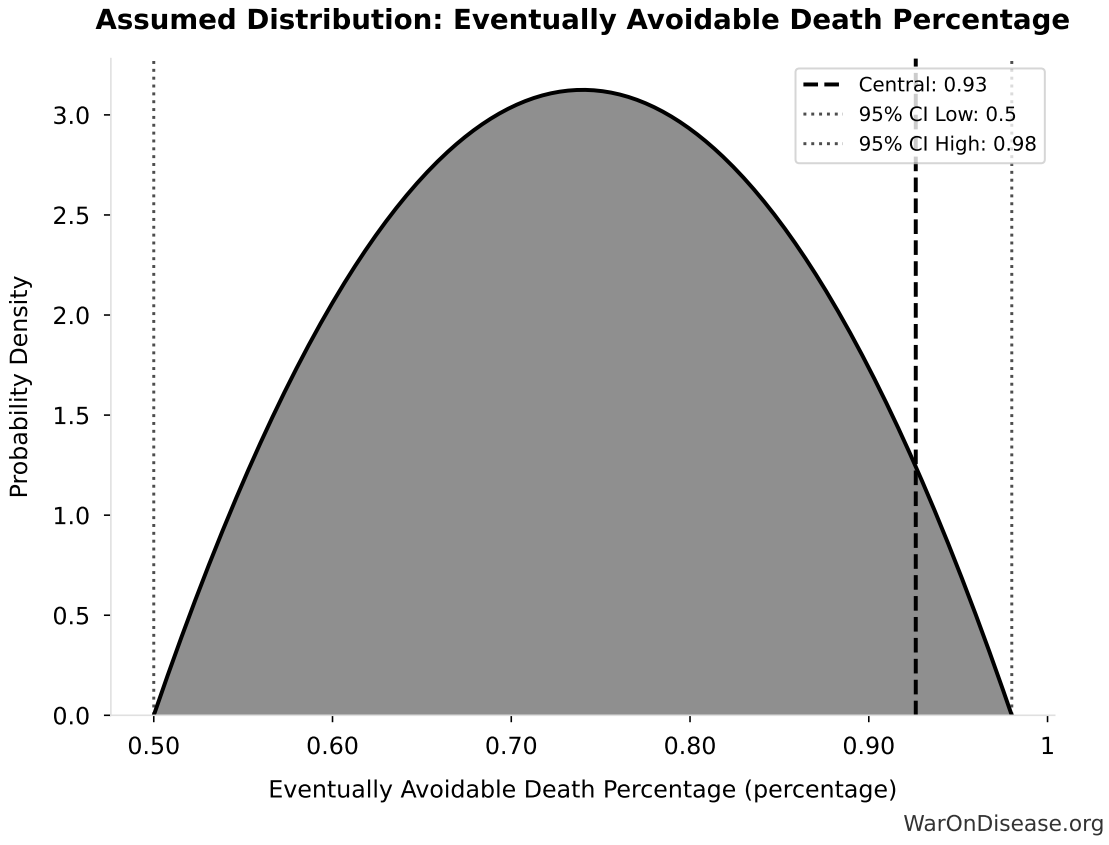


Figure 33: Probability Distribution: Eventually Avoidable Death Percentage

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

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.

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).

Input Distribution

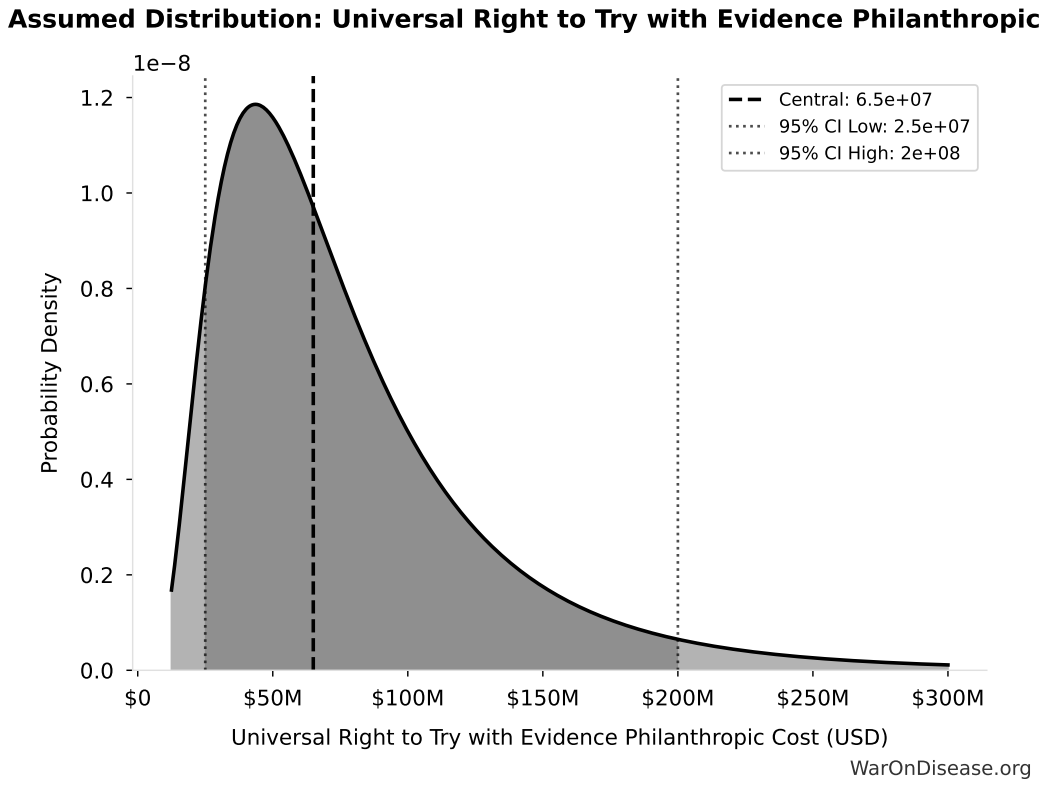


Figure 34: Probability Distribution: Universal Right to Try with Evidence Philanthropic Cost

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

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.

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).

Input Distribution

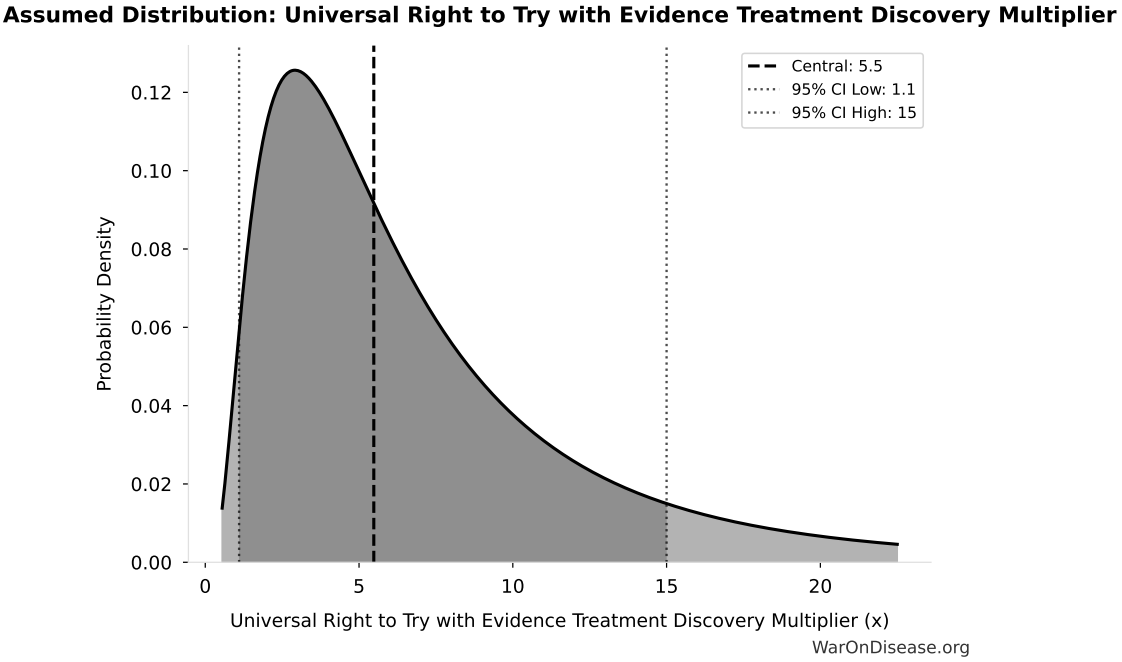


Figure 35: Probability Distribution: Universal Right to Try with Evidence Treatment Discovery Multiplier

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

1. NIH Common Fund. NIH pragmatic trials: Minimal funding despite 30x cost advantage. *NIH Common Fund: HCS Research Collaboratory* https://commonfund.nih.gov/hcscollaboratory (2025)
The NIH Pragmatic Trials Collaboratory funds trials at $500K for planning phase, $1M/year. for implementation-a tiny fraction of NIH's budget. The ADAPTABLE trial cost $14 million for 15,076 patients (= $929/patient) versus $420 million for a similar traditional RCT (30x cheaper), yet pragmatic trials remain severely underfunded. PCORnet infrastructure enables real-world trials embedded in healthcare systems, but receives minimal support compared to basic research funding. Additional sources: https://commonfund.nih.gov/hcscollaboratory | https://pcornet.org/wp-content/uploads/2025/08/ADAPTABLE_Lay_Summary_21JUL2025.pdf | https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5604499/
2. FDA Study via NCBI. Trial costs, FDA study. *FDA Study via NCBI* https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6248200/
Overall, the 138 clinical trials had an estimated median (IQR) cost of $19.0 million ($12.2. million-$33.1 million)... The clinical trials cost a median (IQR) of $41,117 ($31,802-$82,362) per patient. Additional sources: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6248200/
3. Sinn, M. P. *Right to Trial & FDA Upgrade Act*. https://right-to-trial.acceleratedmedicine.org (2025) doi:10.5281/zenodo.19076852
A universal right to try, with evidence. The Act authorizes commercial access after initial human safety testing and makes every covered treatment use teach us something.
4. Montana 69th Legislature. Senate bill no. 535: An act revising laws related to experimental treatments. (2025).
5. Montana Department of Public Health and Human Services. Notice of adoption: MAR notice no. 2026-427.2, new rules 1 through 25 pertaining to experimental treatment centers. (2026).
6. GiveWell. GiveWell cost per life saved for top charities (2024). *GiveWell: Top Charities* https://www.givewell.org/charities/top-charities
General range: $3,000-$5,500 per life saved (GiveWell top charities) Helen Keller International. (Vitamin A): $3,500 average (2022-2024); varies $1,000-$8,500 by country Against Malaria Foundation: $5,500 per life saved New Incentives (vaccination incentives): $4,500 per life saved Malaria Consortium (seasonal malaria chemoprevention): $3,500 per life saved VAS program details: $2 to provide vitamin A supplements to child for one year Note: Figures accurate for 2024. Helen Keller VAS program has wide country variation ($1K-$8.5K) but $3,500 is accurate average. Among most cost-effective interventions globally Additional sources: https://www.givewell.org/charities/top-charities | https://www.givewell.org/charities/helen-keller-international | https://ourworldindata.org/cost-effectiveness
7. U.S. Food and Drug Administration. Right to try.
8. U.S. Food and Drug Administration. Demonstrating substantial evidence of effectiveness for human drug and biological products. (2026).
9. U.S. Food and Drug Administration. Integrating randomized controlled trials for drug and biological products into routine clinical practice: Draft guidance for industry. (2024).
10. U.S. Food and Drug Administration. Project pragmatica. (2025).
11. U.S. Food and Drug Administration. Charging for investigational drugs under an IND: Questions and answers. (2024).
12. Centers for Medicare & Medicaid Services. Medicare coverage with evidence development. (2024).

13. Sinn, M. P. *The Continuous Evidence Generation Protocol: Two-Stage Validation (RWE → Pragmatic Trials)*. https://spec.dfda.earth (2025) doi:10.5281/zenodo.18203375
We present the Predictor Impact Score (PIS), a novel composite metric operationalizing Bradford Hill causality criteria for automated signal detection from aggregated N-of-1 observational studies. Combined with pragmatic trial confirmation (based on evidence from 108+ embedded trials), this two-stage framework would generate validated outcome labels at 44.1x lower cost than traditional Phase III trials. This enables continuous, population-scale pharmacovigilance and precision dosing recommendations.
14. Infinita. Bridging the gap from biotech to clinic. (2026).
15. Goldwater Institute. Alaska becomes 41st state to enact right to try legislation. (2018).
16. Orphanet Journal of Rare Diseases (2024). Rare disease treatment gap. *Orphanet Journal of Rare Diseases (2024)* https://ojrd.biomedcentral.com/articles/10.1186/s13023-024-03398-1 (2024)
Most patients wait 5 to 10 years to get an accurate diagnosis - and only about 5% of rare diseases have an FDA-approved treatment. Over the 40 years of the ODA, 6,340 orphan drug designations were granted, representing drug development for 1,079 rare diseases out of 7,000-10,000 known rare conditions.
17. Composite estimate based on Orphanet. Average time to cure under current system.
Queue-based calculation: 7,000 diseases without effective treatment ÷ 15 diseases getting first treatment per year = 467 years for the average disease to receive a cure under the status quo system. This is consistent with the fact that only 5% of rare diseases have treatments after 40+ years of the Orphan Drug Act. Well-funded diseases may take 30-50 years; underfunded diseases 100-500+ years; and neglected diseases effectively never within human planning horizons.
18. Institute for Health Metrics and Evaluation (IHME). IHME global burden of disease 2021 (2.88B DALYs, 1.13B YLD). *Institute for Health Metrics and Evaluation (IHME)* https://vizhub.healthdata.org/gbd-results/ (2024)
In 2021, global DALYs totaled approximately 2.88 billion, comprising 1.75 billion Years of Life. Lost (YLL) and 1.13 billion Years Lived with Disability (YLD). This represents a 13% increase from 2019 (2.55B DALYs), largely attributable to COVID-19 deaths and aging populations. YLD accounts for approximately 39% of total DALYs, reflecting the substantial burden of non-fatal chronic conditions. Additional sources: https://vizhub.healthdata.org/gbd-results/ | https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(24)00757-8/fulltext | https://www.healthdata.org/research-analysis/about-gbd
19. World Health Organization. WHO global health estimates 2024. *World Health Organization* https://www.who.int/data/gho/data/themes/mortality-and-global-health-estimates (2024)
Comprehensive mortality and morbidity data by cause, age, sex, country, and year Global. mortality: 55-60 million deaths annually Lives saved by modern medicine (vaccines, cardiovascular drugs, oncology): 12M annually (conservative aggregate) Leading causes of death: Cardiovascular disease (17.9M), Cancer (10.3M), Respiratory disease (4.0M) Note: Baseline data for regulatory mortality analysis. Conservative estimate of pharmaceutical impact based on WHO immunization data (4.5M/year from vaccines) + cardiovascular interventions (3.3M/year) + oncology (1.5M/year) + other therapies. Additional sources: https://www.who.int/data/gho/data/themes/mortality-and-global-health-estimates

20. Calculated from Orphanet Journal of Rare Diseases (2024). Diseases getting first effective treatment each year. *Calculated from Orphanet Journal of Rare Diseases (2024)* https://ojrd.biomedcentral.com/articles/10.1186/s13023-024-03398-1 (2024)
Under the current system, approximately 10-15 diseases per year receive their FIRST effective treatment. Calculation: 5% of 7,000 rare diseases (350) have FDA-approved treatment, accumulated over 40 years of the Orphan Drug Act = 9 rare diseases/year. Adding 5-10 non-rare diseases that get first treatments yields 10-20 total. FDA approves 50 drugs/year, but many are for diseases that already have treatments (me-too drugs, second-line therapies). Only 15 represent truly FIRST treatments for previously untreatable conditions.

21. GAO. 95% of diseases have 0 FDA-approved treatments. *GAO* https://www.gao.gov/products/gao-25-106774 (2025)
95% of diseases have no treatment Additional sources: https://www.gao.gov/products/gao-25-106774 | https://globalgenes.org/rare-disease-facts/