The 1% Treaty: Harnessing Greed to Eradicate Disease

Mike P. Sinn

Institute for Accelerated Medicine

m@warondisease.org | ORCID: 0009-0006-0212-1094

Online version: https://impact.warondisease.org

Abstract

6.65 thousand diseases have 0 FDA-approved treatments. At current trial capacity (15 diseases/year), exploring the therapeutic search space takes ~443 years. Redirect 1% of military spending ($27.2B/year) to pragmatic clinical trials. Trial capacity jumps 12.3x. Search space explored in ~36 years instead of centuries. Average treatment reaches patients 212 years sooner. Timeline shift saves 10.7 billion deaths, valued at $84.8 quadrillion. Cost-effectiveness: $0.0018/DALY, 50.3kx better than bed nets. Even at 1% probability of treaty adoption, risk-adjusted cost-effectiveness remains superior to the best existing global health interventions. Incentive Alignment Bonds address political feasibility by tying legislators' career incentives to a public voting scorecard.

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The 1% Treaty: Harnessing Greed to Eradicate Disease

6.65 thousand diseases (95% CI: 5.70 thousand diseases-8.24 thousand diseases) have 0 FDA-approved treatments. At current trial capacity (15 diseases/year (95% CI: 8 diseases/year-30 diseases/year)), exploring the therapeutic search space takes ~443 years (95% CI: 324 years-712 years).

Redirect 1% of military spending ($27.2B/year) to pragmatic clinical trials. Trial capacity jumps 12.3x (95% CI: 4.19x-61.3x). Search space explored in ~36 years (95% CI: 11.6 years-77.2 years) instead of centuries. Average treatment reaches patients 212 years (95% CI: 135 years-355 years) sooner. Timeline shift saves 10.7 billion deaths (95% CI: 7.39 billion deaths-16.2 billion deaths), valued at $84.8 quadrillion (95% CI: $62.4 quadrillion-$97.3 quadrillion).

Cost-effectiveness: $0.0018 (95% CI: $0.0007-$0.0041)/DALY, 50.3kx (95% CI: 23.7kx-111.7kx) better than bed nets. Even at 1% (95% CI: 0.1%-10%) probability of treaty adoption, risk-adjusted cost-effectiveness remains superior to the best existing global health interventions. Incentive Alignment Bonds address political feasibility by tying legislators' career incentives to a public voting scorecard.

Abstract

The bottleneck: Approximately 6.65 thousand diseases (95% CI: 5.70 thousand diseases-8.24 thousand diseases) lack effective treatments. At current trial capacity (~15 diseases/year (95% CI: 8 diseases/year-30 diseases/year) new treatments/year), systematically testing all 9.50 million combinations plausible drug-disease combinations would take ~443 years (95% CI: 324 years-712 years). Effectively never.

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

The solution: Redirecting 1% of global military spending ($27.2B/year) to pragmatic clinical trials increases capacity 12.3x (95% CI: 4.19x-61.3x) (to ~185 diseases/year (95% CI: 107 diseases/year-490 diseases/year) treatments/year). Pragmatic trials cost $929 (95% CI: $97-$3K)/patient versus $41K

(95% CI: $20K-$120K)/patient for traditional trials, enabling vastly more parallel research. This reduces time to explore all therapeutic possibilities from ~443 years (95% CI: 324 years-712 years) to ~36 years (95% CI: 11.6 years-77.2 years).

The impact: Treatments that would have taken decades to even begin researching under the status quo get discovered and delivered decades earlier. Combined with eliminating the 8.2 years (95% CI: 4.85 years-11.5 years)-year regulatory efficacy delay (via opt-in access to ubiquitous trials after Phase I safety), the average treatment reaches patients 212 years (95% CI: 135 years-355 years) sooner. This timeline shift saves 10.7 billion deaths (95% CI: 7.39 billion deaths-16.2 billion deaths), valued at $84.8 quadrillion (95% CI: $62.4 quadrillion-$97.3 quadrillion).

Cost-effectiveness: $0.0018 (95% CI: $0.0007-$0.0041)/DALY via treaty advocacy (50.3kx (95% CI: 23.7kx-111.7kx) better than bed nets) or $0.841 (95% CI: $0.242-$1.75)/DALY via direct funding. ROI ranges from 637:1 (95% CI: 569:1-790:1) (R&D savings only) to 84.8M:1 (95% CI: 46.6M:1-144M:1) (complete benefits). This qualifies as cost-saving: it reduces costs while improving outcomes.

Robustness: Even at 1% (95% CI: 0.1%-10%) probability of treaty adoption, risk-adjusted cost-effectiveness ($0.177 (95% CI: $0.029-$3.20)/DALY) remains 503x (95% CI: 29.9x-3.0kx) better than bed nets. Monte Carlo simulation (10,000 trials) confirms the intervention remains cost-saving across parameter uncertainty. Incentive Alignment Bonds provide the political mechanism: by tying legislators' electoral support and post-office career prospects to a public voting scorecard, they convert treaty support from political liability to career advantage.

Impact Mechanism: The 212 years (95% CI: 135 years-355 years)-year average timeline shift combines two complementary effects:

Benefit Type	Timeline Shift	Mechanism	Impact
Efficacy Lag Elimination	8.2 years (95% CI: 4.85 years-11.5 years)	Offer conditional access via opt-in pragmatic trials after Phase I safety, with continuous real-world monitoring replacing Phase II/III efficacy delay	All newly discovered treatments reach patients 8.2 years (95% CI: 4.85 years-11.5 years) sooner

Benefit Type	Timeline Shift	Mechanism	Impact
Discovery Acceleration	204 years (95% CI: 123 years-350 years) average	Scale trial capacity 12.3x (95% CI: 4.19x-61.3x) (from 15 diseases/year (95% CI: 8 diseases/year-30 diseases/year) to 185 diseases/year (95% CI: 107 diseases/year-490 diseases/year) diseases/year), enabling parallel exploration of therapeutic space	Treatments that already exist among safe compounds are discovered 204 years (95% CI: 123 years-350 years) earlier
Combined Total	**212 years (95% CI: 135 years-355 years)**	Both effects act simultaneously	**212 years (95% CI: 135 years-355 years)-year average timeline shift** for treatment delivery

Interpreting the 212 years (95% CI: 135 years-355 years)-Year Timeline Figure: This is a **discovery capacity model result**, not "time travel" or a prediction that we will achieve results centuries from now. If we must test 9.50 million combinations drug-disease combinations to find all effective treatments, the current system (15 diseases/year (95% CI: 8 diseases/year-30 diseases/year) treatments/year) would take ~443 years (95% CI: 324 years-712 years) to explore this therapeutic search space. Scaling capacity 12.3x (95% CI: 4.19x-61.3x) reduces exploration time to ~36 years (95% CI: 11.6 years-77.2 years). The "212 years (95% CI: 135 years-355 years)" represents the average time a treatment that *could* be discovered today would have waited under the old system versus the new system. Treatments discovered sooner save lives during the intervening period; this cumulative benefit over the acceleration period yields the headline mortality and economic figures.

How the 12.3x (95% CI: 4.19x-61.3x) capacity increase works: Redirecting $27.2B/year at $929 (95% CI: $97-$3K)/patient (based on ADAPTABLE trial; RECOVERY achieved $500 (95% CI: $400-$2.50K)/patient under exceptional NHS/COVID conditions) enables 23.4 million patients/year (95% CI: 9.44 million patients/year-96.8 million patients/year) annual trial participants vs. current 1.90 million patients/year (95% CI: 1.50 million patients/year-2.30 million patients/year), increasing trial completion rate from 15 diseases/year (95% CI: 8 diseases/year-30 diseases/year) to 185 diseases/year (95% CI: 107 diseases/year-490 diseases/year) diseases/year. This removes the primary bottleneck to medical progress: currently less than 0.06% of willing patients can access trials, and over 9.50 thousand compounds (95% CI: 7.00 thousand compounds-12.0 thousand compounds) proven-safe compounds (FDA-approved drugs + GRAS substances) remain untested

for most conditions they could improve.

Methods: Cost-benefit analysis, NPV calculations, QALY modeling, and ICER analysis using SIPRI military expenditure data, WHO mortality statistics, Harvard meta-analysis of 108 embedded pragmatic trials[132], and published clinical trial cost literature. Conservative estimates exclude research acceleration effects; complete estimates include all quantifiable benefits. All parameters, data sources, and uncertainty ranges documented in Parameters and Calculations.

Implications: This intervention corrects a fundamental capital misallocation: military spending creates depreciating assets (weapons become obsolete), while medical research creates appreciating assets (treatments compound in value). Comparable to smallpox eradication (280:1 ROI), it represents the highest-ROI reallocation available to policymakers.

Important limitations: (1) Economic value estimates are cumulative over the ~212 years (95% CI: 135 years-355 years)-year timeline shift, not annual values. (2) All estimates are conditional on successful treaty implementation. (3) Phase I safety testing remains mandatory. What changes is eliminating post-safety efficacy delays. (4) The "quadrillion dollar" figures represent monetized value of lives saved over centuries of accelerated medical progress, using standard QALY methodology.

Keywords: 1% Treaty, pragmatic clinical trials, regulatory delay, cost-effectiveness analysis, DALY, peace dividend

Key Findings

The proposal: Redirect 1% of global military spending ($27.2B/year) to fund pragmatic clinical trials that allow patient access after Phase I safety verification, rather than waiting 8.2 years (95% CI: 4.85 years-11.5 years) additional years for Phase II/III efficacy confirmation before patient access.

Metric	Value	Context
Efficacy Lag Eliminated	8.2 years (95% CI: 4.85 years-11.5 years)	Conditional access via opt-in pragmatic trials after Phase I safety
Cost-Effectiveness	$0.0018 (95% CI: $0.0007-$0.0041)/DALY	50.3kx (95% CI: 23.7kx-111.7kx) better than bed nets ($89 (95% CI: $78-$100)/DALY)
Cost-Effectiveness (Risk-Adjusted)	$0.177 (95% CI: $0.029-$3.20)/DALY	At 1% (95% CI: 0.1%-10%) success probability, still 503x (95% CI: 29.9x-3.0kx) better than bed nets
Treaty Leverage	475x (95% CI: 329x-462x)	$1B campaign unlocks $475B (95% CI: $211B-$651B) (vs direct funding at $0.841 (95% CI: $0.242-$1.75)/DALY)
ROI (Conservative)	637:1 (95% CI: 569:1-790:1)	R&D savings only (44.1x (95% CI: 39.4x-89.1x) cheaper trials)
ROI (Complete)	84.8M:1 (95% CI: 46.6M:1-144M:1)	Complete health timeline shift benefits (efficacy lag + discovery acceleration)

Metric	Value	Context
Discovery Acceleration	204 years (95% CI: 123 years-350 years) average	From 12.3x (95% CI: 4.19x-61.3x) trial capacity enabling parallel therapeutic space exploration
Total Timeline Shift	212 years (95% CI: 135 years-355 years)	Discovery acceleration (204 years (95% CI: 123 years-350 years) yrs) + efficacy lag (8.2 years (95% CI: 4.85 years-11.5 years) yrs)
Lives Saved (Total)	10.7 billion deaths (95% CI: 7.39 billion deaths-16.2 billion deaths)	One-time benefit over 212 years (95% CI: 135 years-355 years)-year timeline shift
DALYs Averted	565 billion DALYs (95% CI: 361 billion DALYs-877 billion DALYs)	Captures morbidity, not just mortality
Total Economic Value	\$84.8 quadrillion (95% CI: \$62.4 quadrillion-\$97.3 quadrillion)	10.7 billion deaths (95% CI: 7.39 billion deaths-16.2 billion deaths) standard QALY valuation
Research Acceleration	12.3x (95% CI: 4.19x-61.3x)	246 years (95% CI: 83.8 years-1.23 thousand years) research-equivalent years in 20 calendar years
Therapeutic Space Explored	36 years (95% CI: 11.6 years-77.2 years)	Time to test first treatments for ALL diseases (vs. 443 years (95% CI: 324 years-712 years), effectively never)
Investment Required	\$1B	Annual benefits (\$172B (95% CI: \$140B-\$213B)) exceed costs

Bottom line: Cost-saving intervention comparable to smallpox eradication (280:1 ROI).

> **!** How Pragmatic Trials Increase Safety
>
> **Phase I safety testing remains mandatory.** This is the testing that prevented thalidomide in the United States. What changes is eliminating the 8.2 years (95% CI: 4.85 years-11.5 years)-year *efficacy* delay (Phase II/III) after safety is verified.

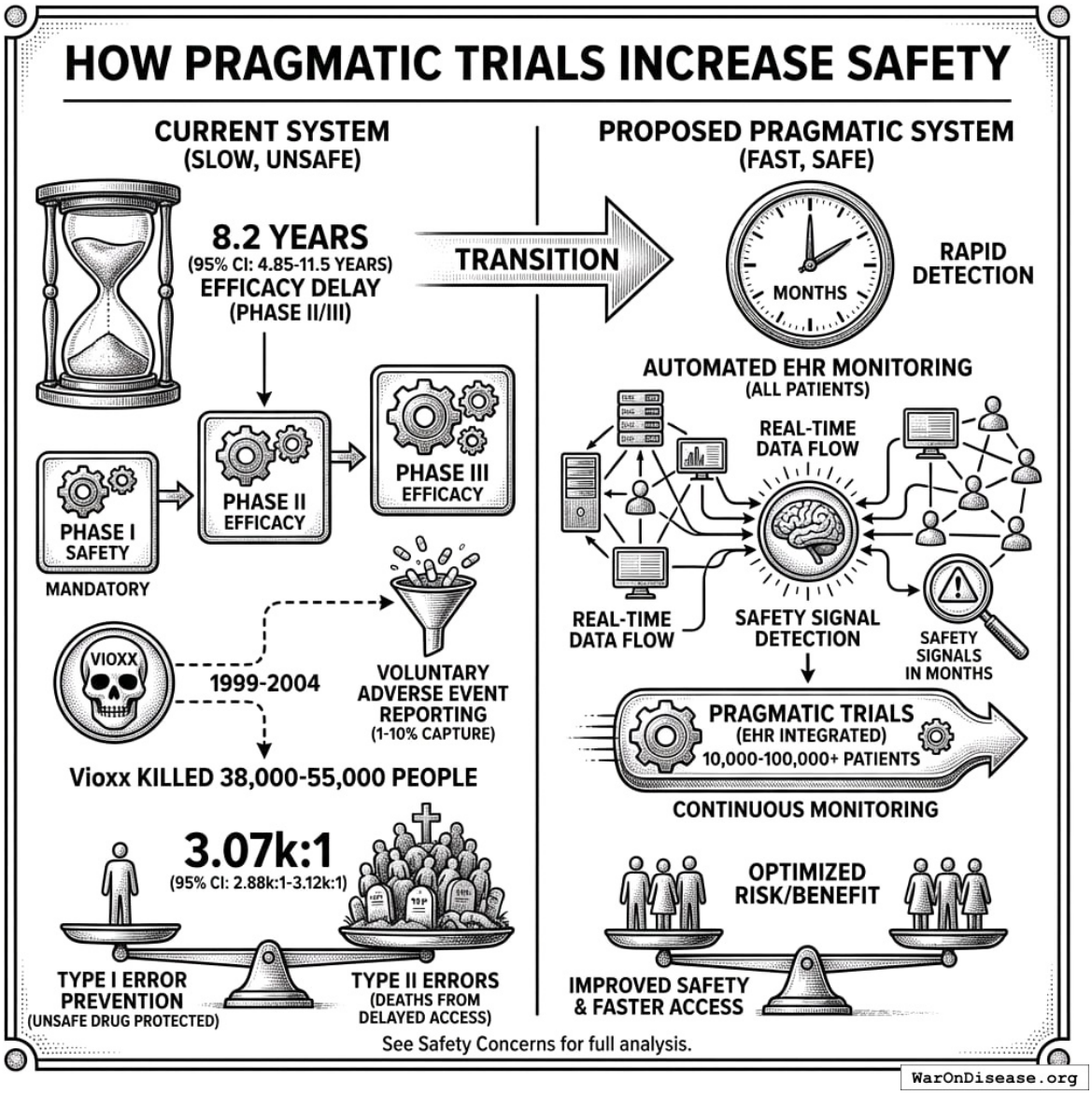


Figure 1: A side-by-side comparison of the current clinical trial system versus pragmatic trials, illustrating the differences in patient scale, monitoring speed, and the disproportionate impact of treatment delays compared to safety risks.

The current system is demonstrably unsafe:

- **Vioxx** killed 38,000-55,000 people over 5 years (1999-2004) under the "safe" current system because voluntary adverse event reporting captures only 1-10% of events
- **Proposed system** uses automated EHR monitoring of all patients, detecting safety signals in months instead of years
- Traditional trials test 100-300 patients; pragmatic trials test 10,000-100,000+ patients with continuous monitoring

For every person protected from an unsafe drug (Type I error prevention), the current system kills 3.07k:1 (95% CI: 2.88k:1-3.12k:1) people by delaying access to beneficial treatments (Type

> II errors). See Safety Concerns for full analysis.

Introduction

Historical Precedents for Grand Challenges

Health economics literature identifies three historical cost-saving interventions:

1. **Smallpox eradication** (1967-1980): 280:1 ROI[89], eliminating a disease that killed 300-500 million people in the 20th century alone
2. **Childhood vaccination programs**: Self-funding interventions generating $15B (95% CI: $8.79B-$23.3B) in annual economic benefits[7]
3. **Water fluoridation**: 23:1 ROI in dental health improvements[129]

These successes share common features: systemic interventions that address root causes rather than symptoms, positive externalities that compound over time, and political consensus achieved through demonstrated value. They also share a critical limitation: they targeted specific diseases or conditions. No historical intervention has systematically accelerated the discovery process itself.

The Medical Research Bottleneck

Current medical research faces fundamental capacity constraints that limit our ability to discover which treatments actually work:

Current System Limitation	Value	Impact
Trial participation rate	0.06% of willing patients	Massive unmet research capacity[11]
Untested safe compounds	9.50 thousand compounds (95% CI: 7.00 thousand compounds-12.0 thousand compounds) proven-safe (FDA-approved drugs + GRAS)	0.342% (95% CI: 0.21%-0.514%) of drug-disease space explored[22]
Traditional trial cost	$41K (95% CI: $20K-$120K)/patient	Makes comprehensive testing economically infeasible[101]

Current System Limitation	Value	Impact
Pragmatic trial cost	$929 (95% CI: $97-$3K)/patient	44.1x (95% CI: 39.4x-89.1x) cost reduction enables systematic exploration (meta-analysis of 108+ trials[132])

Multiple large-scale pragmatic trials and systematic reviews demonstrate that pragmatic trial design maintains scientific rigor while dramatically reducing costs. A Harvard meta-analysis of 108 embedded pragmatic trials found median costs of $97/patient[132]. The Oxford RECOVERY trial achieved $500 (95% CI: $400-$2.50K)/patient (under exceptional NHS/COVID conditions), while the PCORnet ADAPTABLE trial achieved $929 (95% CI: $929-$1.40K)/patient under normal conditions[1]. Our system projections use the conservative ADAPTABLE estimate ($929 (95% CI: $97-$3K)/patient). This 44.1x (95% CI: 39.4x-89.1x) cost reduction transforms the economics of medical research: what was previously too expensive to test becomes systematically explorable.

Contribution to Literature

Key Contributions to Health Economics Literature:

1. **Regulatory delay cost quantification**
   - First comprehensive estimate of the 8.2 years (95% CI: 4.85 years-11.5 years)-year efficacy lag cost
   - $1.19 quadrillion (95% CI: $443T-$2.41 quadrillion) in foregone economic value
   - 416 million deaths (95% CI: 225 million deaths-630 million deaths) lives lost (excludes unavoidable deaths)
   - Uses standard QALY methodology ($150K (95% CI: $100K-$199K)/QALY)
2. **Trial capacity expansion benefits**
   - Quantifies impact of 12.3x (95% CI: 4.19x-61.3x) trial capacity on disease eradication timeline
   - 204 years (95% CI: 123 years-350 years) average acceleration in first treatment discovery
   - Combined with efficacy lag: 212 years (95% CI: 135 years-355 years)-year total timeline shift
   - 10.7 billion deaths (95% CI: 7.39 billion deaths-16.2 billion deaths) total lives saved, $84.8 quadrillion (95% CI: $62.4 quadrillion-$97.3 quadrillion) economic value
3. **Cost-effectiveness under political uncertainty**
   - Risk-adjusted analysis at 1% (95% CI: 0.1%-10%) adoption probability
   - $0.177 (95% CI: $0.029-$3.20)/DALY expected cost-effectiveness
   - Monte Carlo validation across 10,000 scenarios
   - Demonstrates robustness to parameter uncertainty
4. **Self-sustaining funding mechanism**
   - Incentive Alignment Bonds align investors, politicians, patients
   - Converts military spending (0.6x (95% CI: 0.4x-0.9x) economic multiplier) → health research (4.3x (95% CI: 3x-6x) multiplier)
   - Legally-binding treaty with market-based incentives

- No reliance on altruism or bureaucratic mandate

The analysis that follows uses standard cost-benefit methodology (NPV, QALY modeling, ICER analysis) applied to SIPRI military expenditure data, WHO mortality statistics, and published clinical trial cost literature. All parameter uncertainty is quantified through Monte Carlo simulation (10,000 trials) with tornado diagrams identifying key drivers of variance.

Research Hypothesis

Primary Hypothesis: Reallocating 1% of global military spending ($27.2B annually) to fund decentralized pragmatic clinical trials generates return on investment between 637:1 (95% CI: 569:1-790:1) (conservative estimate, R&D savings only) and 84.8M:1 (95% CI: 46.6M:1-144M:1) (complete estimate, including peace dividend and all direct benefits), representing a dominant health intervention that simultaneously reduces costs while improving health outcomes.

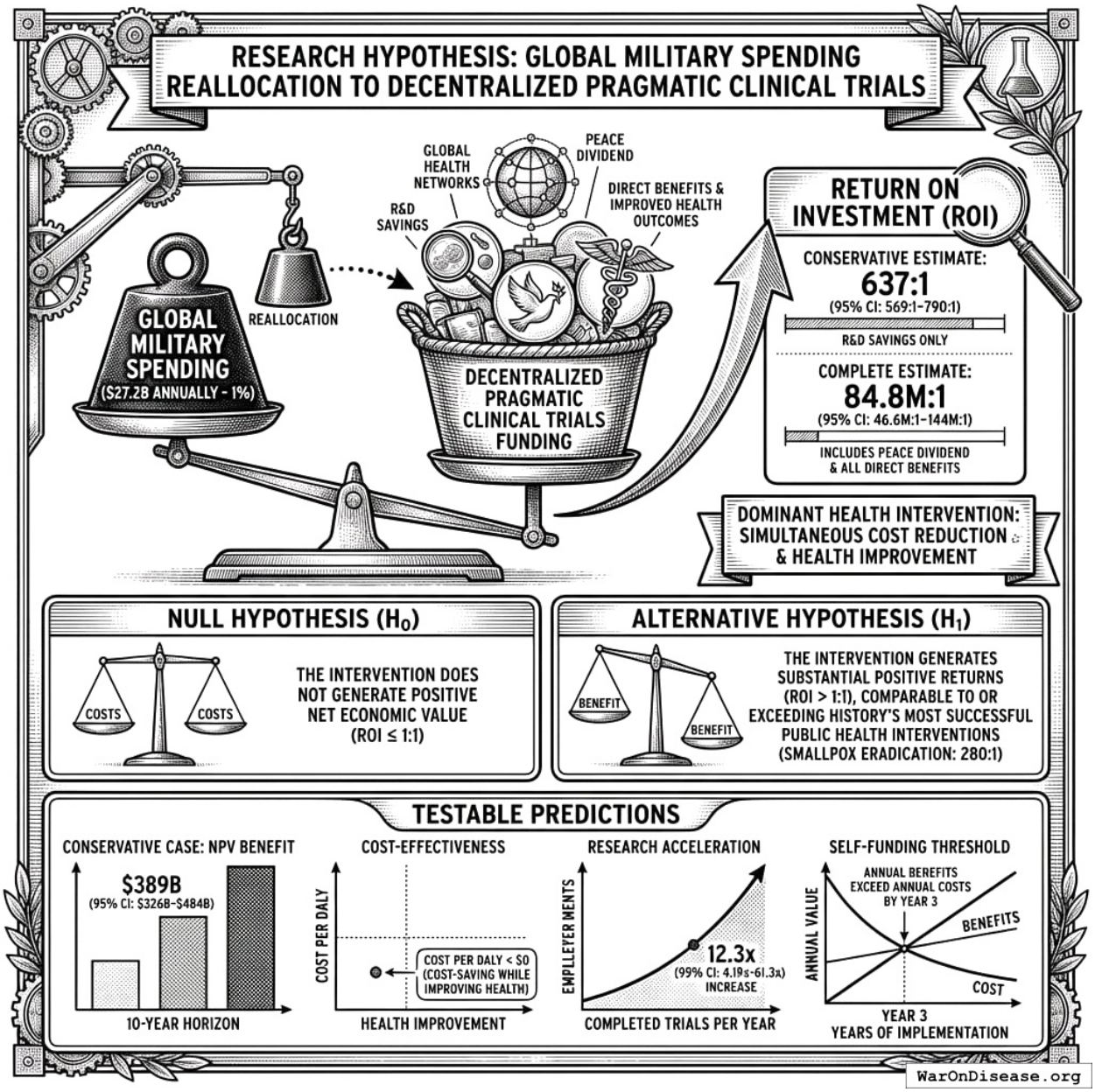


Figure 2: A conceptual visualization comparing the investment of 1% military spending to its projected economic returns, highlighting ROI benchmarks against historical public health successes like smallpox eradication.

Null Hypothesis (H): The intervention does not generate positive net economic value (ROI 1:1)

Alternative Hypothesis (H): The intervention generates substantial positive returns (ROI > 1:1), comparable to or exceeding history's most successful public health interventions (smallpox eradication: 280:1[89])

Testable Predictions:

- Conservative case: NPV benefit of $389B (95% CI: $326B-$484B) over 10 years-year horizon

- Cost-effectiveness: Cost per DALY < $0 (cost-saving while improving health)
- Research acceleration: 12.3x (95% CI: 4.19x-61.3x) increase in completed trials per year
- Self-funding threshold: Annual benefits exceed annual costs by year 3 of implementation

Nomenclature and Key Terms

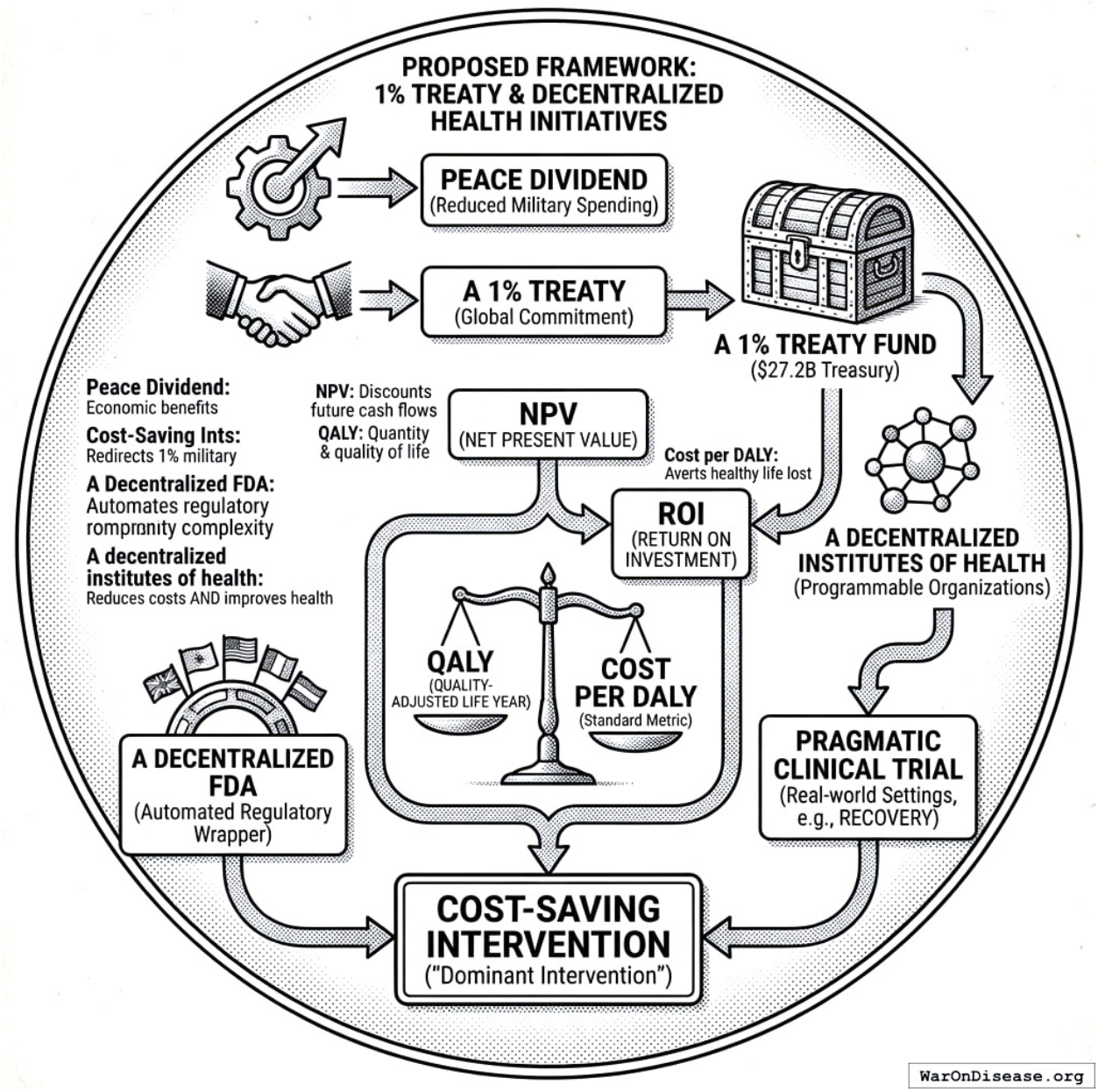


Figure 3: System architecture of the 1% Treaty ecosystem, illustrating the flow of reallocated military funding into a central fund that powers decentralized regulatory frameworks and pragmatic clinical trials.

A Decentralized FDA: A regulatory wrapper that automates trial creation, IRB approval, liability insurance, and simultaneous multi-agency submissions (FDA, EMA, PMDA, etc.) across countries. Like TurboTax abstracts away tax code complexity, the system abstracts away regulatory complexity: researchers define hypotheses, and the system handles compliance. Uses real-world data, electronic health records, and decentralized patient participation. Reduces per-patient costs by 50-95% compared to traditional trials.

A decentralized institutes of health: A pattern for decentralized, programmable, and democratic organizations that implement health initiatives. A decentralized institutes of health can be funded by a 1% Treaty Fund to subsidize patient participation in pragmatic clinical trials.

Peace Dividend: Economic benefits from reduced military spending, including fiscal savings, reduced conflict-related economic damage, and favorable economic multiplier effects from reallocating resources to productive sectors.

Cost-Saving Intervention (technical term: "dominant intervention"): Interventions that both reduce costs AND improve health outcomes. Generally recommended regardless of willingness-to-pay thresholds (e.g., vaccination programs, smoking cessation).

A 1% Treaty: Proposed international agreement where signatory nations commit to reducing military expenditure by 1% and redirecting those funds ($27.2B globally) to pragmatic clinical trials infrastructure.

$$\begin{aligned} & Funding_{treaty} \\ &= Spending_{mil} \times Reduce_{treaty} \\ &= \$2.72T \times 1\% \\ &= \$27.2B \end{aligned}$$

A 1% Treaty Fund: The treasury that receives and allocates the 1% of military spending reallocated by the 1% Treaty. It funds pragmatic clinical trials, which can be implemented through networks of decentralized institutes of health.

Pragmatic Clinical Trial: Trial design using real-world settings and broad eligibility criteria rather than highly controlled laboratory conditions, improving generalizability and dramatically reducing costs. Examples: Oxford RECOVERY (COVID, 47,000 patients), PCORnet ADAPTABLE (cardiovascular, 15.1 thousand patients), and 108+ trials documented in Harvard meta-analysis[132].

Problem Statement

Current Resource Allocation

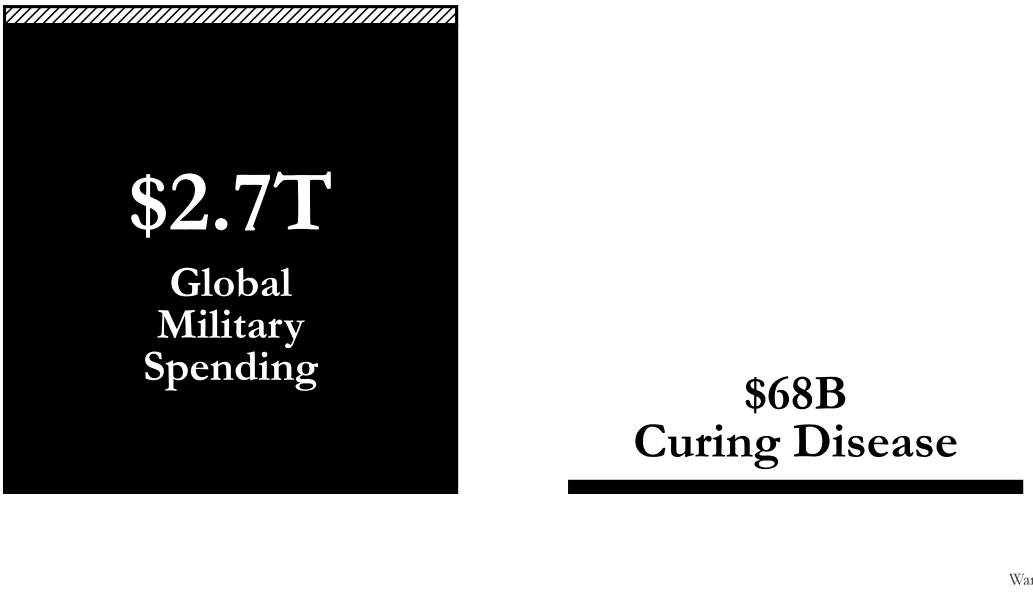
Humanity's budget priorities, explained simply:

- **Military spending**: $2.72T[48]/year (ending life)
- **Government clinical trials spending**: $4.50B (95% CI: $3B-$6B)[45]/year (testing which medicines actually work)
- **Ratio**: 604:1 (95% CI: 453:1-894:1) (global spending on weapons exceeds spending on discovering which drugs treat diseases by 604:1 (95% CI: 453:1-894:1))

$$
\begin{aligned}
&Ratio_{mil:RD} \\
&= \frac{Spending_{mil}}{Spending_{RD}} \\
&= \frac{\$2.72T}{\$67.5B} \\
&= 40.3
\end{aligned}
$$

Understanding the comparison: While total government medical research spending is $67.5B (95% CI: $54B-$81B) (including basic research, translational research, and clinical trials), government clinical trial funding is only $4.50B (95% CI: $3B-$6B). The 1% treaty redirects $27.2B to pragmatic clinical trials, increasing government clinical trial funding ~7-fold.

The bottleneck isn't basic research or laboratory science. It's **clinical trials**. We've tested 0.342% (95% CI: 0.21%-0.514%) of possible drug-disease combinations using existing safe compounds. Not because the science is impossible, but because traditional trials cost $41K (95% CI: $20K-$120K) while pragmatic trials like Oxford RECOVERY run for $500 (95% CI: $400-$2.50K). At current funding levels, testing the remaining 99.7% (95% CI: 99.5%-99.8%) of therapeutic space would take millennia. Meanwhile, military budgets dwarf the funding needed to automate ubiquitous clinical trials and systematically explore what actually helps people.



Disease treatment vs. curing disease

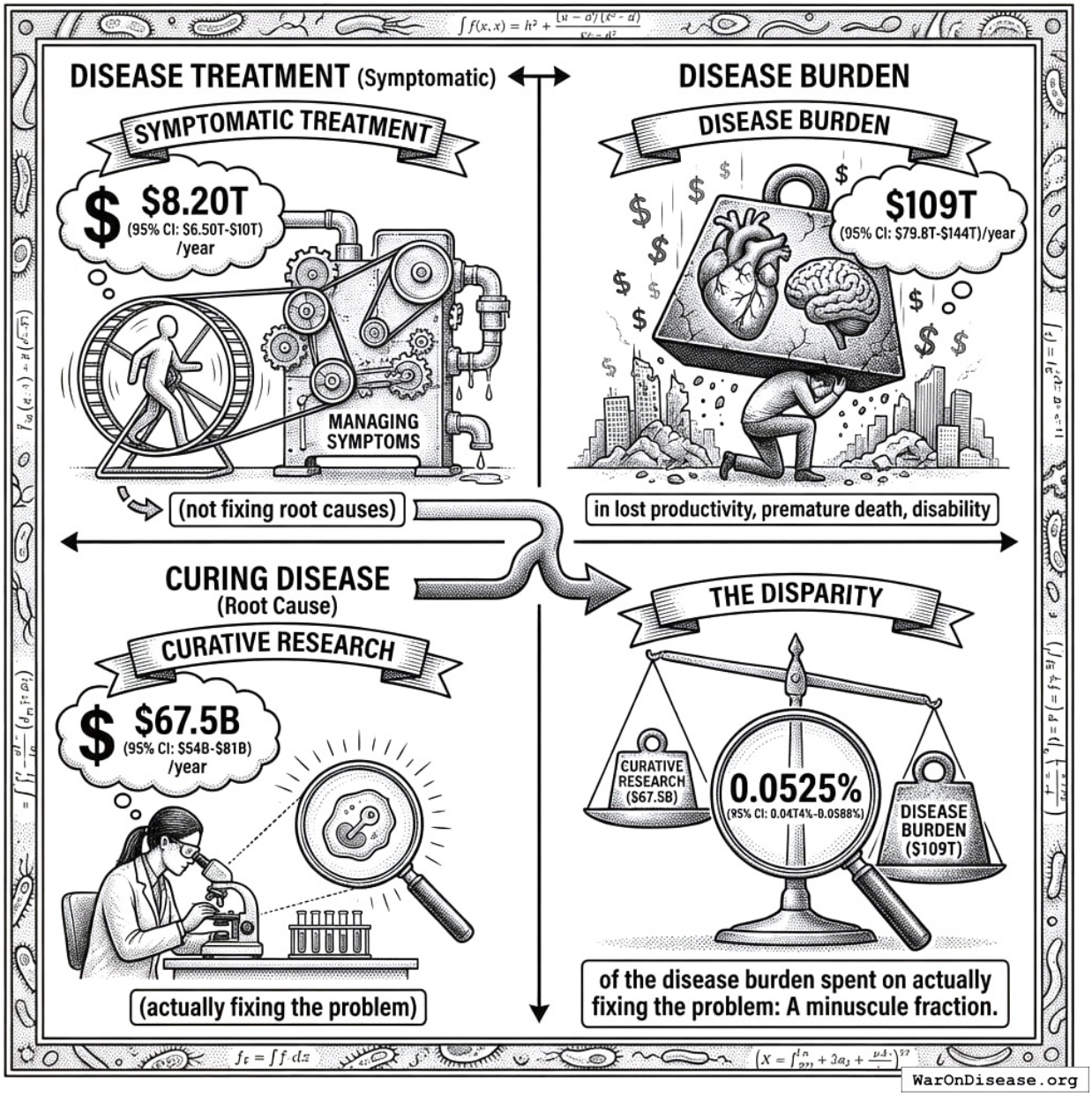


Figure 4: A scale comparison showing the massive annual global disease burden and symptomatic treatment costs relative to the microscopic sliver of funding allocated to curative research.

- **Symptomatic treatment**: $8.20T (95% CI: $6.50T-$10T)[43]/year (managing symptoms, not fixing root causes)
- **Disease burden**: $109T (95% CI: $79.8T-$144T)/year in lost productivity, premature death, disability

$$
\begin{aligned}
&Burden_{disease} \\
&= Cost_{medical,direct} + Loss_{life,disease} \\
&+ Loss_{productivity} \\
&= \$9.9T + \$94.2T + \$5T \\
&= \$109T
\end{aligned}
$$

- **Curative research**: $67.5B (95% CI: $54B-$81B)[47]/year

That's 0.0525% (95% CI: 0.0474%-0.0588%) of the disease burden spent on actually fixing the problem:

$$
\begin{aligned}
&Pct_{RD:burden} \\
&= \frac{Spending_{RD}}{Cost_{health+war}} \\
&= \frac{\$67.5B}{\$129T} \\
&= 0.0525\%
\end{aligned}
$$

$$
\begin{aligned}
&\text{where } Cost_{health+war} \\
&= Cost_{war,total} + Burden_{disease} + Spending_{symptom} \\
&= \$11.4T + \$109T + \$8.2T \\
&= \$129T
\end{aligned}
$$

$$
\begin{aligned}
&\text{where } Cost_{war,total} \\
&= Cost_{war,direct} + Cost_{war,indirect} \\
&= \$7.66T + \$3.7T \\
&= \$11.4T
\end{aligned}
$$

$$
\begin{aligned}
&\text{where } Cost_{war,direct} \\
&= Loss_{life,conflict} + Damage_{infra,total} \\
&+ Disruption_{trade} + Spending_{mil} \\
&= \$2.45T + \$1.88T + \$616B + \$2.72T \\
&= \$7.66T
\end{aligned}
$$

$$
\begin{aligned}
&\text{where } Loss_{life,conflict} \\
&= Cost_{combat,human} + Cost_{state,human} \\
&+ Cost_{terror,human} \\
&= \$2.34T + \$27B + \$83B \\
&= \$2.45T
\end{aligned}
$$

$$
\begin{aligned}
&\text{where } Cost_{combat,human} \\
&= Deaths_{combat} \times VSL \\
&= 234{,}000 \times \$10M \\
&= \$2.34T
\end{aligned}
$$

$$
\begin{aligned}
&\text{where } Cost_{state,human} \\
&= Deaths_{state} \times VSL \\
&= 2{,}700 \times \$10M \\
&= \$27B
\end{aligned}
$$

$$
\begin{aligned}
&\text{where } Cost_{terror,human} \\
&= Deaths_{terror} \times VSL \\
&= 8{,}300 \times \$10M \\
&= \$83B
\end{aligned}
$$

$$
\begin{aligned}
&\text{where } Damage_{infra,total} \\
&= Damage_{comms} + Damage_{edu} + Damage_{energy} \\
&+ Damage_{health} + Damage_{transport} \\
&+ Damage_{water}
\end{aligned}
$$

Mortality and Morbidity Burden

The World Health Organization reports 150 thousand deaths/day[4] daily deaths from disease and aging. Many of these are eventually avoidable with accelerated biomedical progress (55.0 million deaths/year (95% CI: 46.6 million deaths/year-63.2 million deaths/year) annually).

This mortality burden exceeds:

- Annual terrorism deaths[97] by a factor of 18.4k:1 (95% CI: 15.6k:1-21.1k:1)

$$\begin{aligned} & Ratio_{dis:terror} \\ &= \frac{Deaths_{curable,ann}}{Deaths_{9/11}} \\ &= \frac{55M}{3{,}000} \\ &= 18{,}400 \end{aligned}$$

- Annual war deaths[29] by a factor of 225:1 (95% CI: 210:1-239:1) (based on 245 thousand deaths/year (95% CI: 194 thousand deaths/year-302 thousand deaths/year) conflict deaths annually)

$$Ratio_{dis:war} = \frac{Deaths_{curable,ann}}{Deaths_{conflict}} = \frac{55M}{245{,}000} = 225$$

$$\begin{aligned} & \text{where } Deaths_{conflict} \\ &= Deaths_{combat} + Deaths_{state} + Deaths_{terror} \\ &= 234{,}000 + 2{,}700 + 8{,}300 \\ &= 245{,}000 \end{aligned}$$

Despite this disparity in mortality burden, resource allocation heavily favors security spending over medical research and curative interventions.

How It Works

The mechanism is financial, not bureaucratic:

1. **Patient subsidies**: Most treaty funding ($21.7B (95% CI: $21.7B-$21.7B)) goes directly to subsidizing patient participation in trials at ~$929 (95% CI: $97-$3K)[1] per patient, similar to how insurance covers medical procedures
2. **Providers get paid**: Treatment providers can charge for patient participation in trials, making trials profitable rather than costly
3. **Easy enrollment**: A decentralized FDA infrastructure (costing just $40M (95% CI: $27.3M-$55.6M)) makes it easy for anyone to create or join Phase 2/3/4 trials globally
4. **Patient choice**: Patients choose which trials to join; their subsidy follows them. Trials that attract patients get funded. No grant committees deciding what's "worthy."

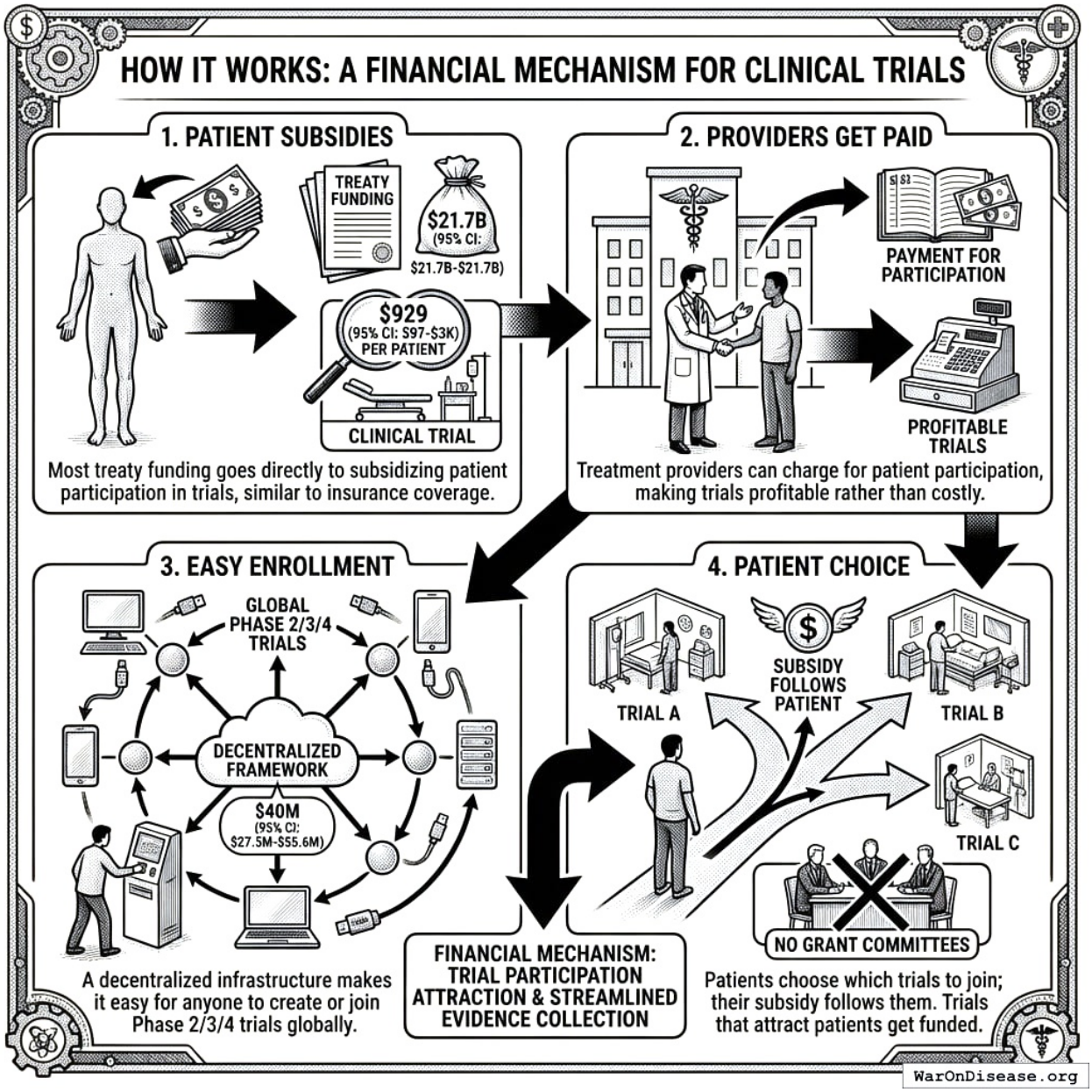


Figure 5: A diagram illustrating the flow of treaty funding from patient subsidies to treatment providers, highlighting how patient choice drives the decentralized clinical trial ecosystem.

The mechanism makes trial participation financially attractive for both patients and providers while streamlining evidence collection through existing healthcare delivery infrastructure.

A Decentralized Framework for Drug Assessment

The economic model assumes integration of pragmatic trial infrastructure into standard healthcare delivery. Every prescription becomes a data point. Every patient visit generates evidence. Every treatment outcome feeds into a continuously-updating system that tells doctors and patients what actually works. Not what pharmaceutical companies claim works (published trials show 94% positive

results while FDA data shows only 51%[133]), but what measurably happens to real humans taking real treatments.

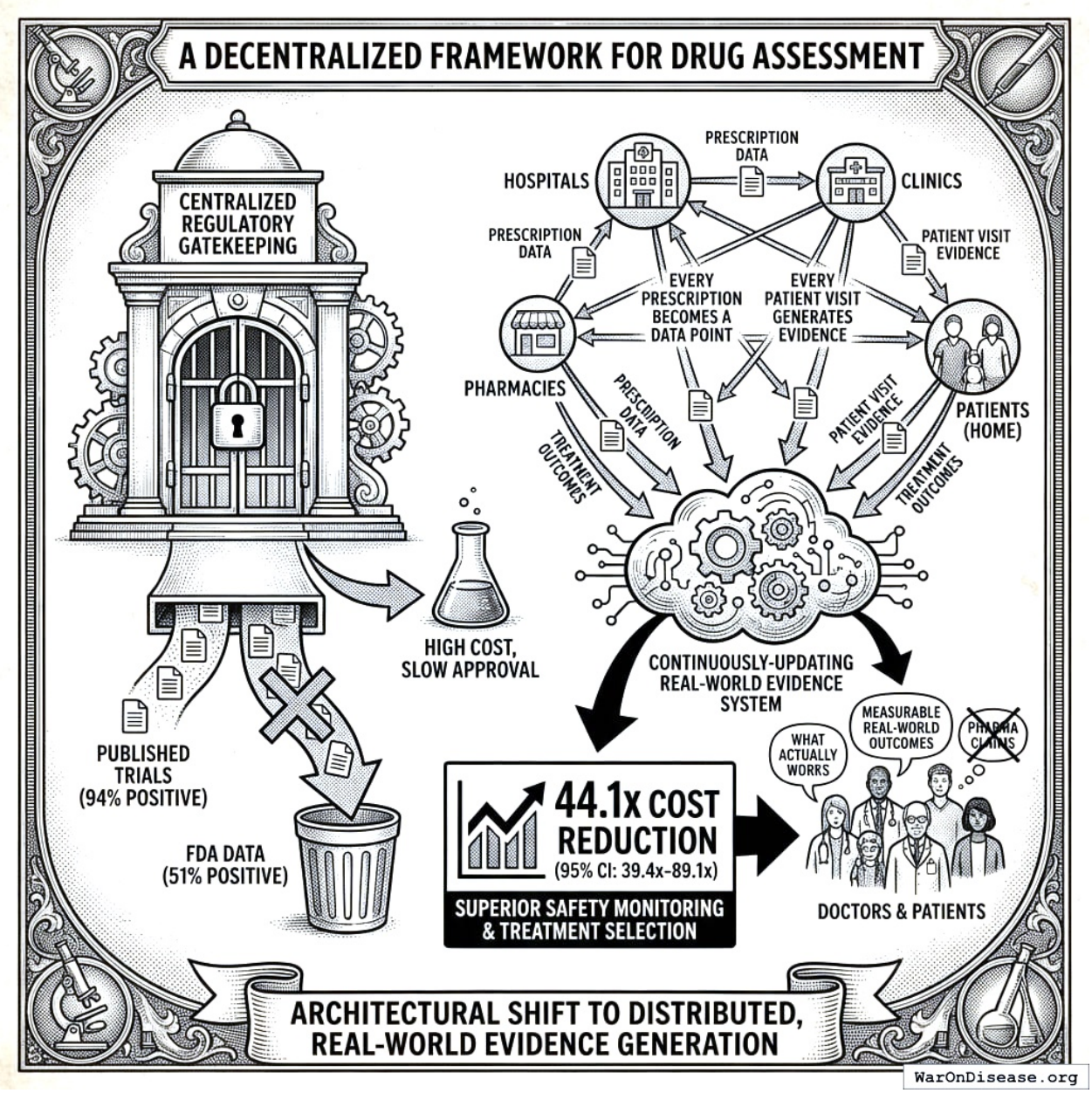


Figure 6: A comparison between the traditional centralized clinical trial model and the proposed decentralized real-world evidence framework, illustrating the shift from linear regulatory gatekeeping to a continuous data-feedback loop within standard healthcare.

This architectural shift from centralized regulatory gatekeeping to distributed, real-world evidence generation achieves a **44.1x (95% CI: 39.4x-89.1x) cost reduction** while providing superior safety monitoring and treatment selection capabilities.

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

Trial Cost Reduction

Traditional FDA Phase 3 trials cost $41K (95% CI: $20K-$120K)[101] per patient because they require dedicated infrastructure: specialized research sites, dedicated research coordinators, custom data collection systems, patient travel reimbursement, and extensive monitoring visits. This overhead exists independent of the actual treatment being tested.

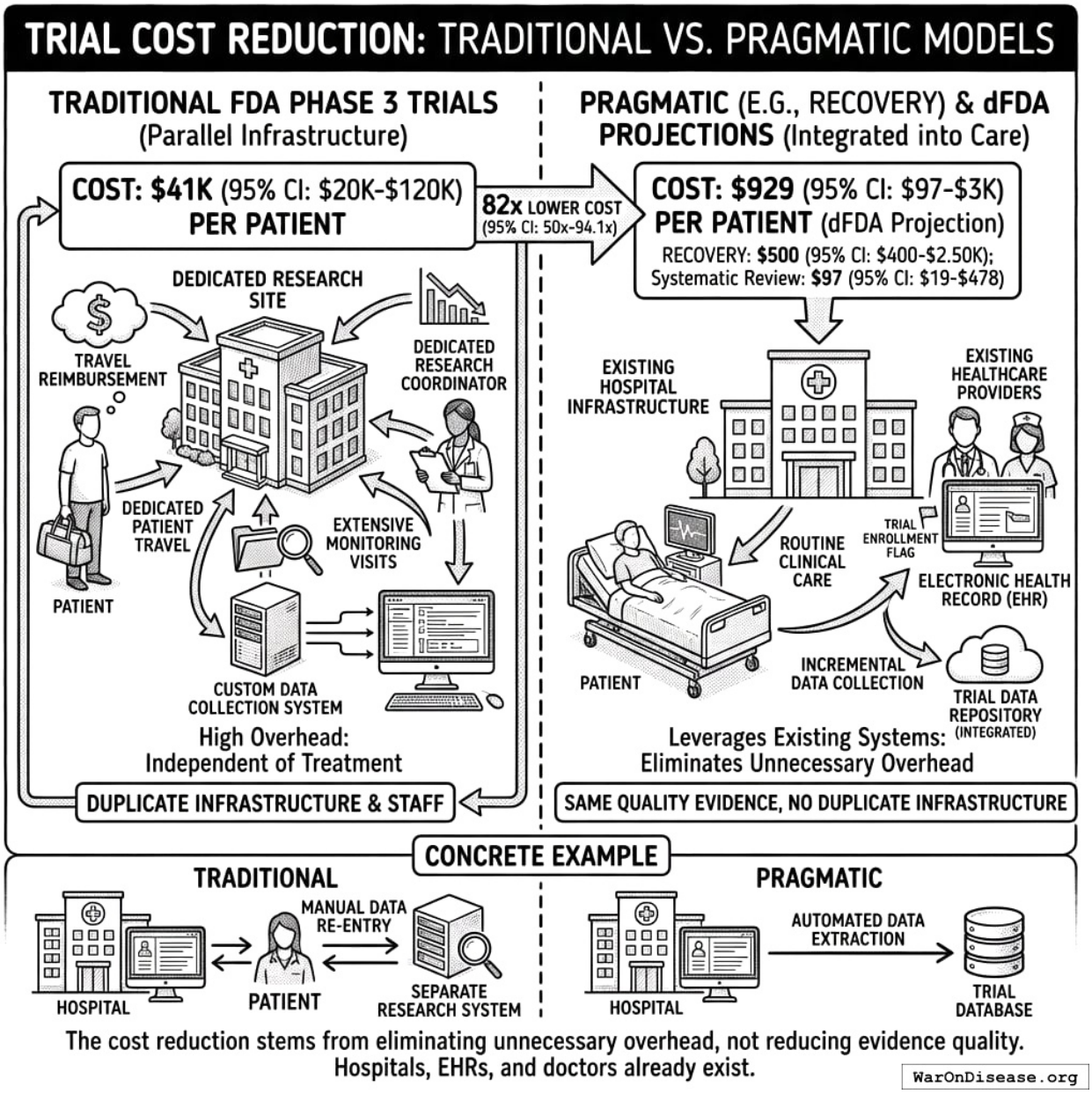


Figure 7: A side-by-side comparison of traditional clinical trials using redundant infrastructure versus pragmatic trials integrated into routine hospital care, illustrating the 82x cost reduction.

The Oxford RECOVERY trial demonstrated an alternative: leverage existing hospital infrastructure, collect only incremental data beyond standard medical records, and integrate evidence generation into routine clinical care. Cost: $500 (95% CI: $400-$2.50K)[83] per patient. (Note: RECOVERY benefited from NHS/COVID conditions; however, a systematic review of 64 pragmatic trials found a median cost of $97 (95% CI: $19-$478)/patient[74], confirming this efficiency is replicable. Our system projections use a conservative $929 (95% CI: $97-$3K)/patient based on the ADAPTABLE trial.) Same quality evidence. 82x (95% CI: 50x-94.1x) lower cost.

Concrete example: A hospital already tracks patient lab results, symptoms, and outcomes in

electronic health records. Traditional trials build a parallel research infrastructure to collect the same information again. Pragmatic trials simply flag which patients are enrolled and automatically extract relevant data from existing systems. No duplicate infrastructure, no dedicated research staff per trial.

The cost reduction stems from eliminating unnecessary overhead, not reducing evidence quality. Hospitals already exist. Electronic health records already exist. Doctors already see patients. The trial infrastructure simply uses what's already there rather than building dedicated research facilities.

$$
\begin{aligned}
& k_{RECOVERY} \\
&= \frac{Cost_{P3,pt}}{Cost_{RECOVERY,pt}} \\
&= \frac{\$41K}{\$500} \\
&= 82
\end{aligned}
$$

Enhanced Safety Monitoring

Current system limitations: If a drug causes liver damage in 1% of patients, this pattern often goes undetected until 100,000+ prescriptions have been written, because adverse event reporting is voluntary. Doctors must notice the problem, remember to file a report, and complete the paperwork. Average reporting rate approximately 6%[134], meaning ~94% of adverse events go unreported.

Concrete failure case: Rofecoxib (Vioxx)[135], approved in 1999 for arthritis pain, increased cardiovascular event risk (heart attacks and strokes) through COX-2 enzyme inhibition. The cardiovascular signal went undetected for 5 years despite 92.8 million U.S. prescriptions (1999-2003)[135]. Voluntary adverse event reporting failed to identify the pattern until dedicated post-market studies confirmed the association in 2004, leading to withdrawal. Estimates of deaths from the delay range from 38,000 (Lancet) to 55,000 (FDA testimony)[135]. Continuous EHR monitoring of cardiovascular events (heart attacks, strokes, ER visits) across millions of patients would have detected the elevated rate within months, not years, as these outcomes are objectively captured in hospital records.

Integrated surveillance alternative: Every prescription automatically becomes a tracked data point. When patients experience cardiovascular events, get lab tests, or visit emergency rooms, the system captures these outcomes via existing EHR infrastructure. No extra paperwork required. Like credit card fraud detection systems that identify suspicious patterns across millions of transactions in real-time, integrated health systems can detect treatment-associated adverse events across millions of patients automatically.

The system automatically aggregates outcomes:

- **10,000 patients prescribed Drug X** → System tracks all subsequent cardiovascular events, ER visits, lab results, and hospitalizations via existing EHR infrastructure
- **120 patients (1.2%) show elevated cardiovascular event rates within 90 days** → Automated statistical flag triggers when pattern exceeds expected background rate for matched controls

- **Pattern detected after 5,000 prescriptions** → Public alert issued to all prescribing physicians and patients, rather than waiting for years and dedicated post-market studies
- **Mass notification system** → All patients currently taking the drug receive automated alerts through patient portals, enabling immediate clinical review and alternative treatment consideration

Detection timeline comparison (Vioxx cardiovascular risk[135]):

- **Actual detection with voluntary reporting**: 5 years from approval (1999) to withdrawal (2004), 38,000-55,000 estimated deaths[135]
- **Projected with ubiquitous EHR monitoring**: 6-12 months from widespread use to pattern detection (automated cardiovascular event surveillance comparing treated patients to matched controls)

This infrastructure is not hypothetical. The[136] currently monitors 128.7 million patients across US health systems for drug safety signals using similar distributed data methodology. The proposed system makes this the default infrastructure for all treatments from day one, rather than a separate monitoring program activated only after problems are suspected. This represents a fundamental safety improvement: continuous, automated, population-scale adverse event detection with immediate mass notification capability, rather than relying on voluntary physician reporting (which captures only ~6% of actual adverse events)[134] and slow manual review processes.

Comparative Effectiveness Rankings

Current decision-making: Doctor prescribes treatments based on pharmaceutical marketing, medical school training from years ago, and whatever clinical experiences they happen to remember. Patient has no access to comparative effectiveness data.



Figure 8: A side-by-side comparison showing the current method of subjective medical decision-making versus an evidence-based system that uses stratified data to rank treatments for specific patient profiles.

Evidence-based alternative: Doctor searches "rheumatoid arthritis treatment" in the integrated evidence system, sees treatments ranked by measured effectiveness in real-world patients:

Rankings show frequency and magnitude of outcome changes across actual patient populations. Filters allow stratification: "Show me effectiveness in women over 50 with my patient's genetic markers and comorbidities." This precision medicine approach shows what works for patients like yours, not what works on average across everyone.

Like Amazon rankings based on verified purchase reviews, except based on measured clinical

outcomes rather than subjective opinions, and stratified by patient characteristics rather than averaged across all users.

Implementation: The system already has prescription records and outcome data from routine care. Ranking is just aggregation and sorting. No new data collection needed, just making existing data actually useful for treatment decisions.

How Comparative Effectiveness Data Is Collected

Traditional RCT limitation: Standard trials compare one treatment vs. placebo (or occasionally one active comparator). To rank 10 treatments for a condition, you would need ~45 separate head-to-head RCTs, each costing $50-100M and taking 3-5 years. This is economically impossible for most conditions.

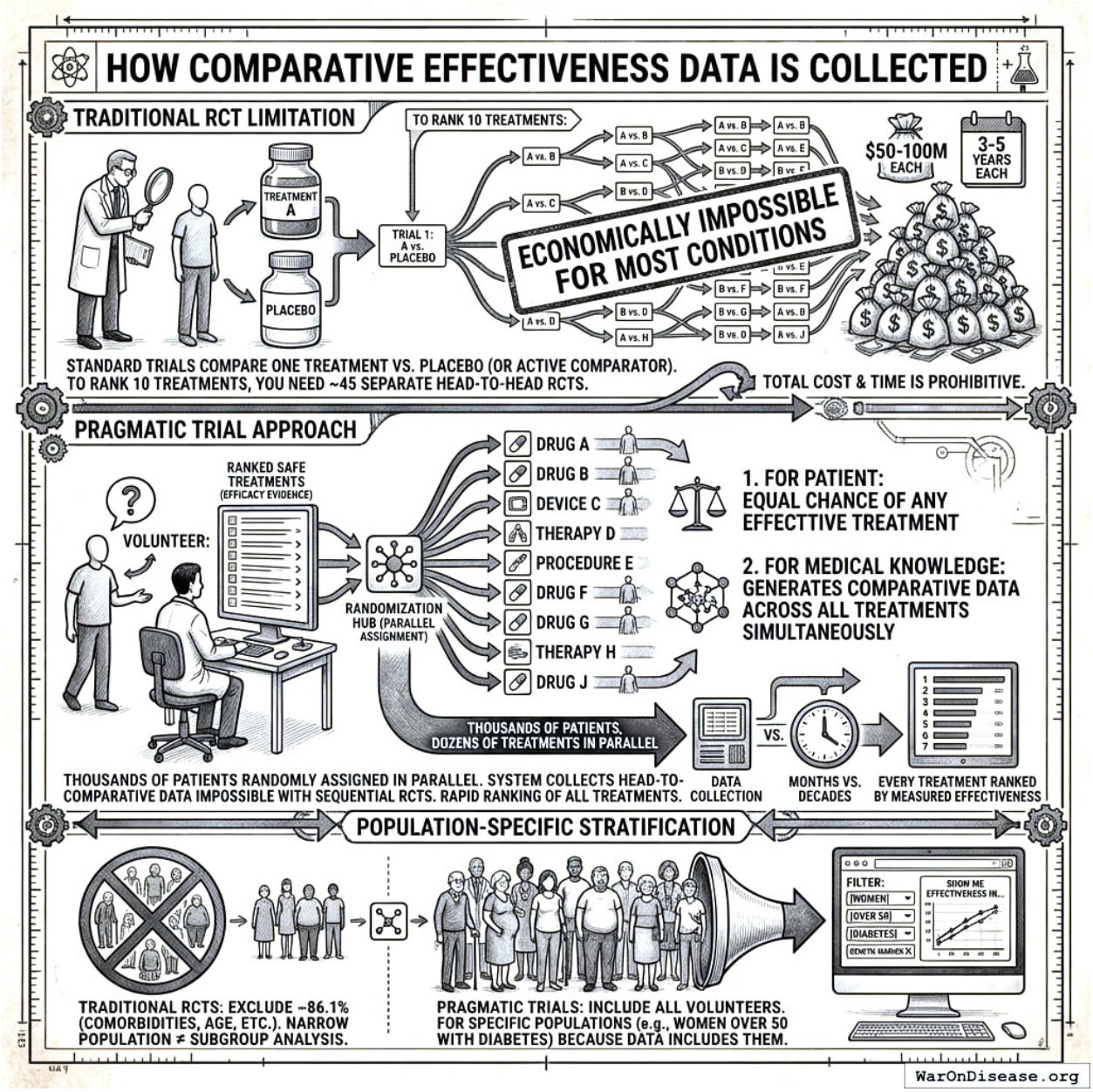


Figure 9: A comparison between the limited, sequential nature of traditional RCTs and the parallel, inclusive structure of pragmatic trials that allow for real-time comparative data and population stratification.

Pragmatic trial approach: When a patient volunteers for treatment of their condition, physicians access a ranked list of all safe treatments with demonstrated or theoretical efficacy based on existing evidence. The patient is then randomly assigned to one of these treatment options. This randomization serves dual purposes:

1. **For the patient**: Equal chance of receiving any potentially effective treatment
2. **For medical knowledge**: Generates comparative effectiveness data across all treatments simultaneously

Because thousands of patients are randomly assigned across dozens of treatments in parallel, the system collects head-to-head comparative data that would be impossible to generate through sequential RCTs. Within months rather than decades, every treatment can be ranked by measured effectiveness.

Population-specific stratification: RCTs typically exclude 86.1% of patients due to comorbidities, age, or concurrent medications. The narrow populations that qualify cannot support subgroup analysis. Pragmatic trials include all volunteers, generating data on "women over 50 with diabetes" or "patients with genetic marker X." The filter capability shown above ("Show me effectiveness in women over 50 with my patient's genetic markers") is only possible because the underlying data includes those populations.

Outcome Labels

Current drug information: 40-page package inserts written by lawyers, listing every possible side effect without quantifying frequencies. Patients have no idea whether "may cause headaches" means 0.1% or 50% of users.

Standardized outcome labels: Quantified summaries of what actually happens to patients taking each treatment, displayed like nutrition labels:

Based on systematic outcome collection across thousands of patients, labels show:

- **Quantified benefits**: "Memory improved 35%, Executive Function improved 22%"
- **Adverse effect frequencies**: "Headache: 9% (8% mild, 1% severe); Fatigue: 7%"
- **Treatment persistence**: "2.3% discontinued due to side effects"
- **Sample size and confidence**: "Based on 4,200 patients, 95% CI"

This is measured data from actual patient outcomes, not marketing claims or lawyer-drafted disclaimers.

Implementation workflow: 1. Patient prescribed new treatment → Automatically enrolled in outcome tracking 2. Patient reports symptoms at routine visits → Data flows into aggregation system 3. Lab results, ER visits, prescription refills → Automatically captured from electronic health records 4. System aggregates outcomes across all patients taking that treatment → Updates outcome label in real-time 5. Next doctor/patient looking at that treatment sees current evidence, not 5-year-old clinical trial results

No extra paperwork. No dedicated research staff. Just making routine clinical data actually useful for evidence generation.

Summary of Results

637:1 (95% CI: 569:1-790:1) to 84.8M:1 (95% CI: 46.6M:1-144M:1) ROI

Total Economic Value

$84.8 quadrillion (95% CI: $62.4 quadrillion-$97.3 quadrillion) in total economic value (cumulative over ~212 years (95% CI: 135 years-355 years)-year timeline shift, conditional on implementation).

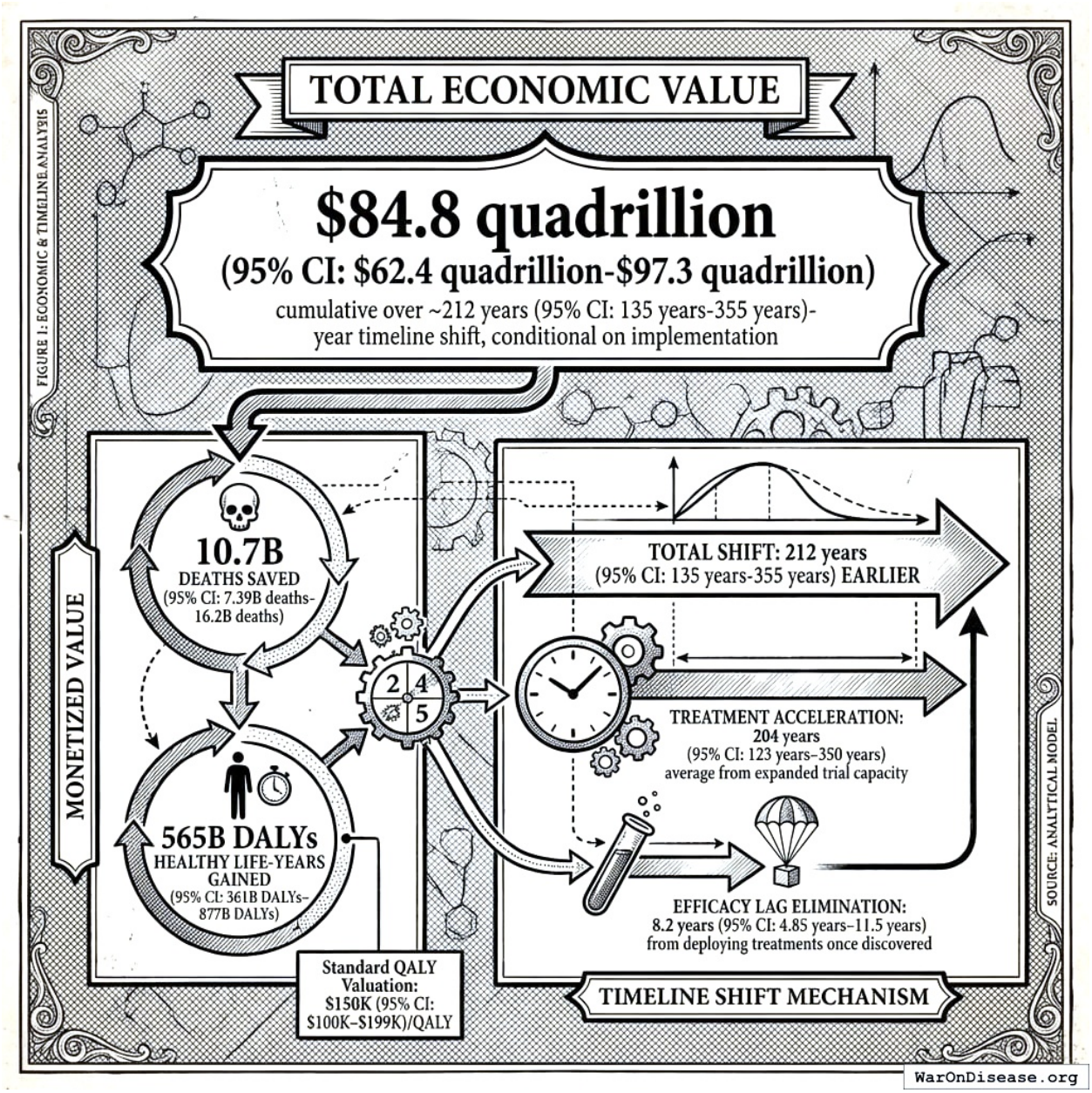
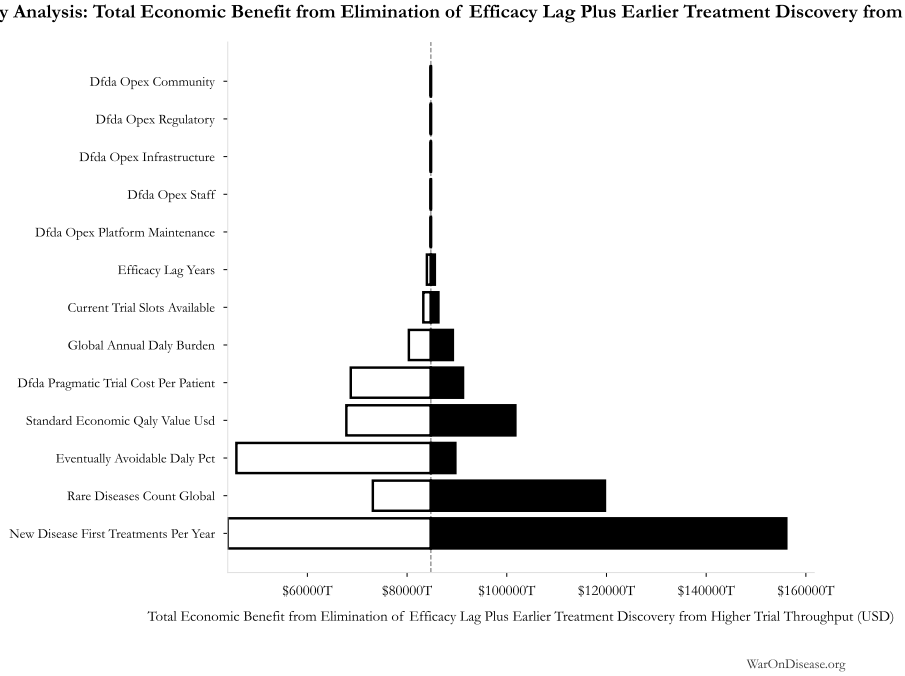


Figure 10: A flow diagram illustrating how treatment acceleration and efficacy lag reduction combine to save billions of lives, resulting in an estimated $84.8 quadrillion in cumulative economic value.

This is the monetized value of 10.7 billion deaths (95% CI: 7.39 billion deaths-16.2 billion deaths) saved and 565 billion DALYs (95% CI: 361 billion DALYs-877 billion DALYs) healthy life-years gained, using standard QALY valuation ($150K (95% CI: $100K-$199K)/QALY). On average, first treatments become available 212 years (95% CI: 135 years-355 years) earlier - combining treatment acceleration (204 years (95% CI: 123 years-350 years) average from expanded trial capacity) and efficacy lag elimination (8.2 years (95% CI: 4.85 years-11.5 years) from deploying treatments once discovered).

Uncertainty Analysis: Total Economic Value



The tornado diagram shows that timeline shift duration and QALY valuation dominate the uncertainty in total economic value. Even under conservative parameter assumptions, the intervention generates quadrillions in cumulative economic value over the timeline shift period (not annually).

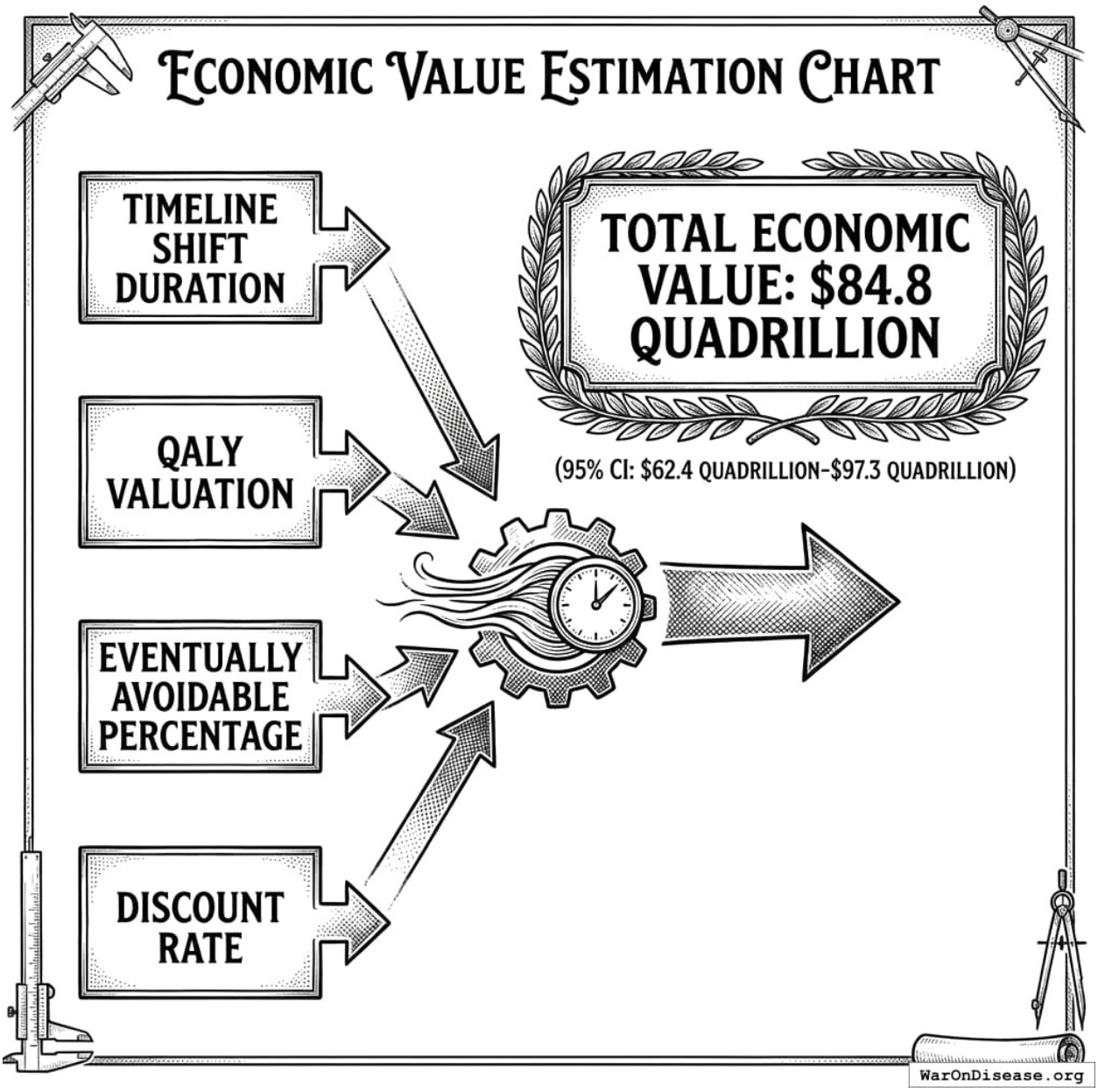


Figure 11: Causal pathway showing how investment in trial capacity leads to accelerated treatment access and massive cumulative economic value.

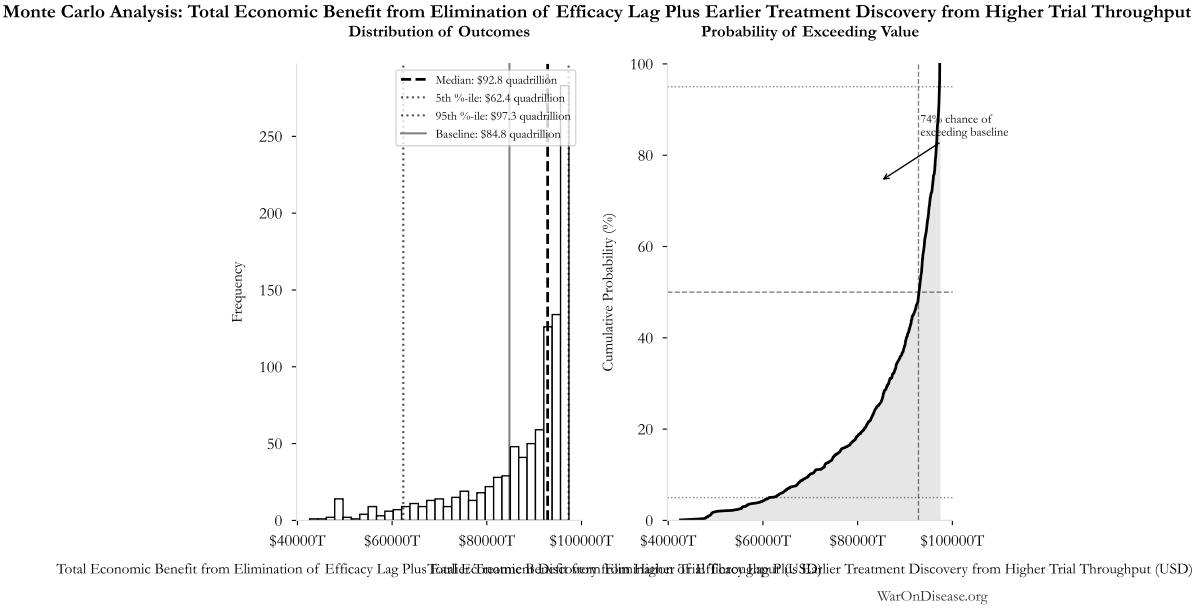


Figure 12: Monte Carlo Distribution: Total Economic Benefit from Elimination of Efficacy Lag Plus Earlier Treatment Discovery from Higher Trial Throughput (10,000 simulations)

Simulation Results Summary: Total Economic Benefit from Elimination of Efficacy Lag Plus Earlier Treatment Discovery from Higher Trial Throughput

Statistic	Value
Baseline (deterministic)	$84.8 quadrillion
Mean (expected value)	$87.8 quadrillion
Median (50th percentile)	$92.8 quadrillion
Standard Deviation	$11.5 quadrillion
90% Range (5th-95th percentile)	[$62.4 quadrillion, $97.3 quadrillion]

The histogram shows the distribution of Total Economic Benefit from Elimination of Efficacy Lag Plus Earlier Treatment Discovery from Higher Trial Throughput 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.

Monte Carlo analysis confirms the 95% confidence interval for total economic value remains in the quadrillions across all plausible scenarios. These are cumulative values representing accelerated access to treatments over ~212 years (95% CI: 135 years-355 years), not annual benefits.

Investment required: $1B

Research Acceleration

12.3x (95% CI: 4.19x-61.3x) more trial capacity (246 years (95% CI: 83.8 years-1.23 thousand years) of medical advancement in 20 years)

Treatment Timeline Acceleration

Under the status quo, 6.65 thousand diseases (95% CI: 5.70 thousand diseases-8.24 thousand diseases) lack treatment. At 15 diseases/year (95% CI: 8 diseases/year-30 diseases/year) new treatments/year, the average disease waits 222 years (95% CI: 162 years-356 years) for a treatment. With the framework's 12.3x (95% CI: 4.19x-61.3x) trial capacity increase, treatments arrive **204 years (95% CI: 123 years-350 years) earlier**.

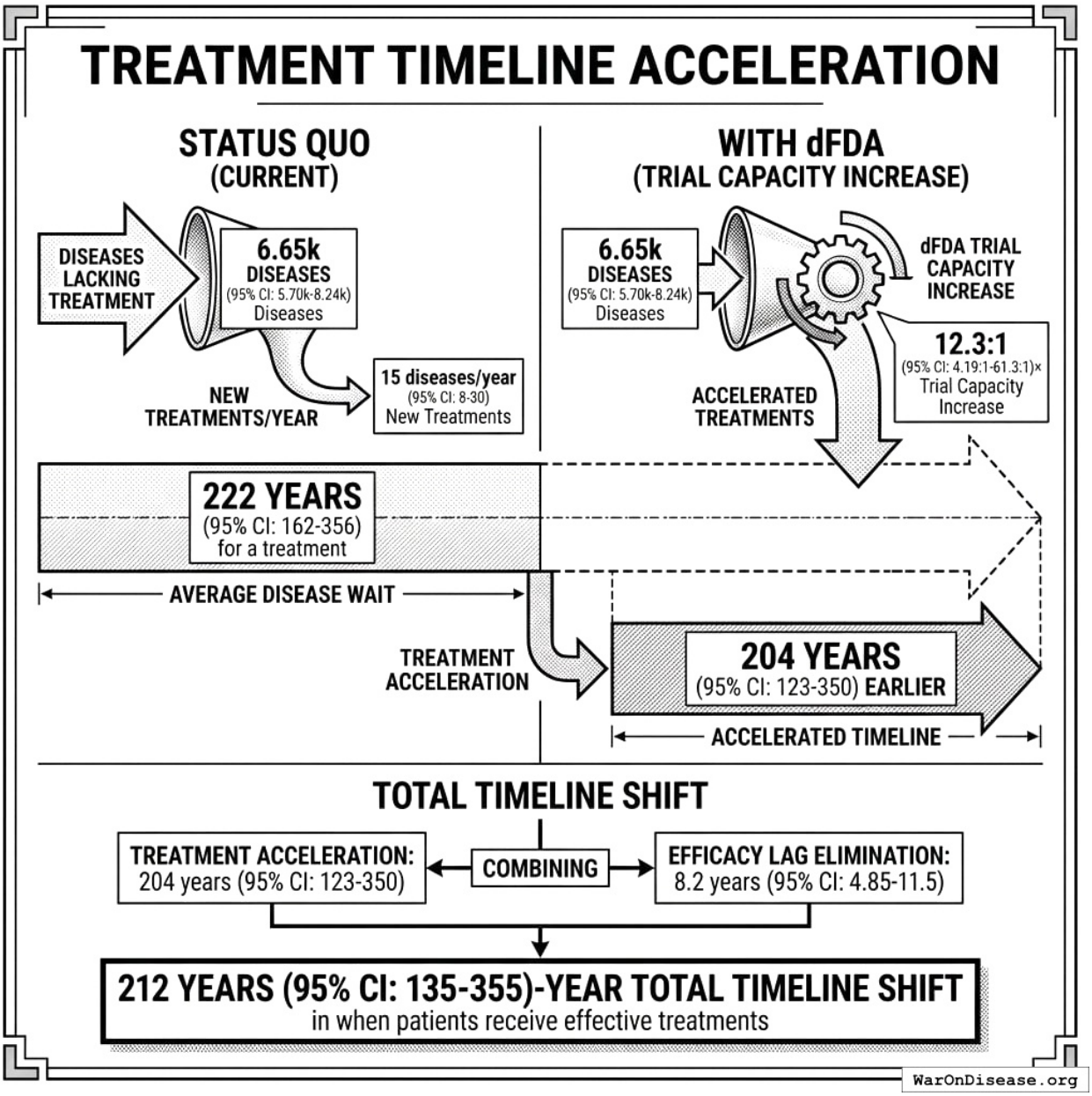


Figure 13: A comparison between the current 222-year average wait time for disease treatments and the accelerated timeline achieved through trial capacity increases and efficacy lag elimination.

Total Timeline Shift: Combining treatment acceleration (204 years (95% CI: 123 years-350

years)) with efficacy lag elimination (8.2 years (95% CI: 4.85 years-11.5 years)) yields a **212 years (95% CI: 135 years-355 years)-year total timeline shift** in when patients receive effective treatments.

Suffering Reduction

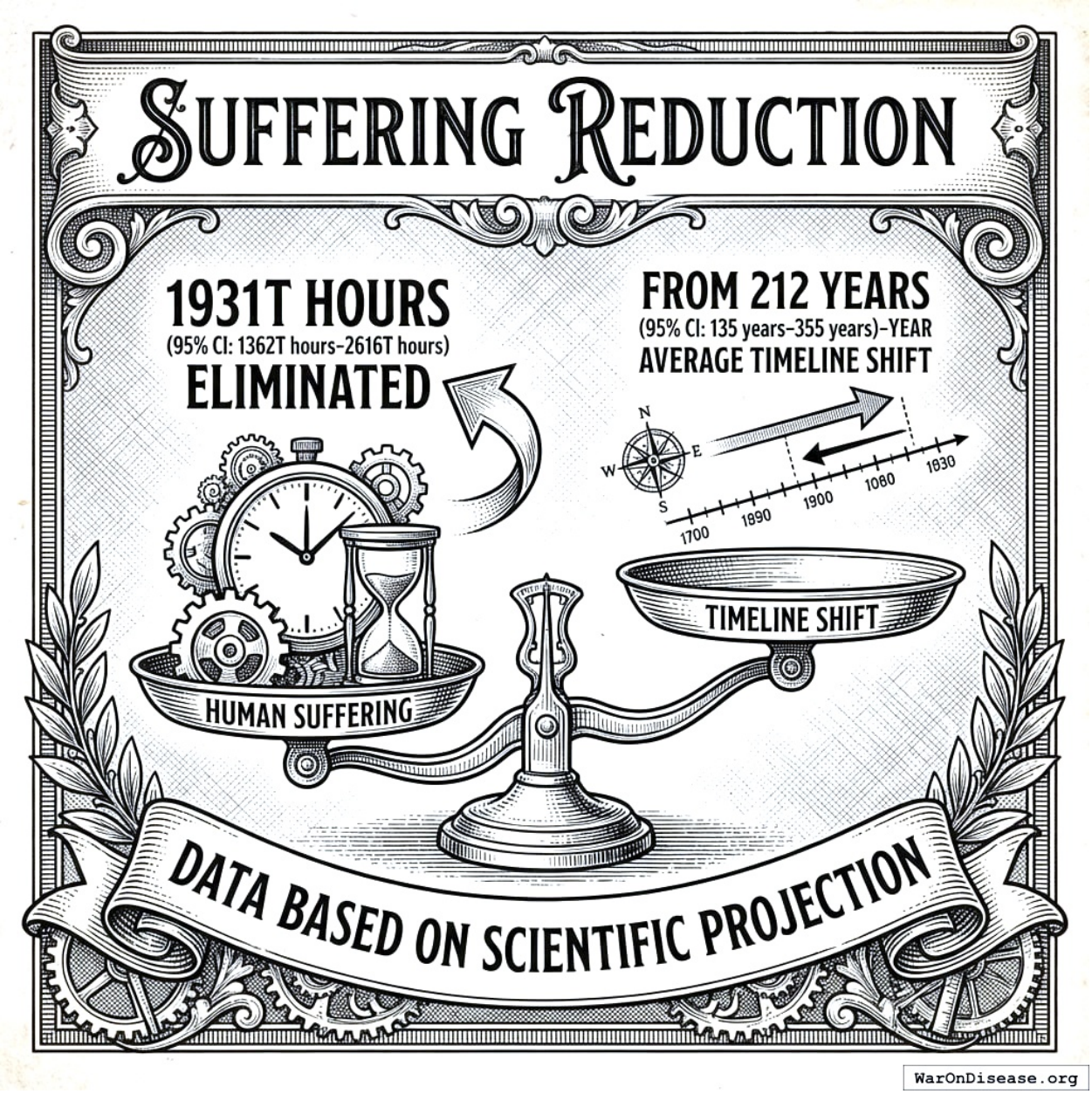


Figure 14: A visualization illustrating the impact of a 212-year timeline shift on human suffering, showing the massive reduction of 1931 trillion hours with associated confidence intervals.

1.93 quadrillion hours (95% CI: 1.36 quadrillion hours-2.62 quadrillion hours) hours of human suffering eliminated (from 212 years (95% CI: 135 years-355 years)-year average timeline shift)

Lives Saved

10.7 billion deaths (95% CI: 7.39 billion deaths-16.2 billion deaths) from 212 years (95% CI: 135 years-355 years)-year average timeline shift

This total combines two effects:

- **Treatment acceleration (204 years (95% CI: 123 years-350 years) on average)**: With 12.3x (95% CI: 4.19x-61.3x) trial capacity, the average disease receives first effective treatment ~204 years (95% CI: 123 years-350 years) earlier
- **Efficacy lag elimination (8.2 years (95% CI: 4.85 years-11.5 years))**: Once discovered, treatments are deployed without post-safety delay

For context: **150 thousand deaths/day people die every day** under the current system.

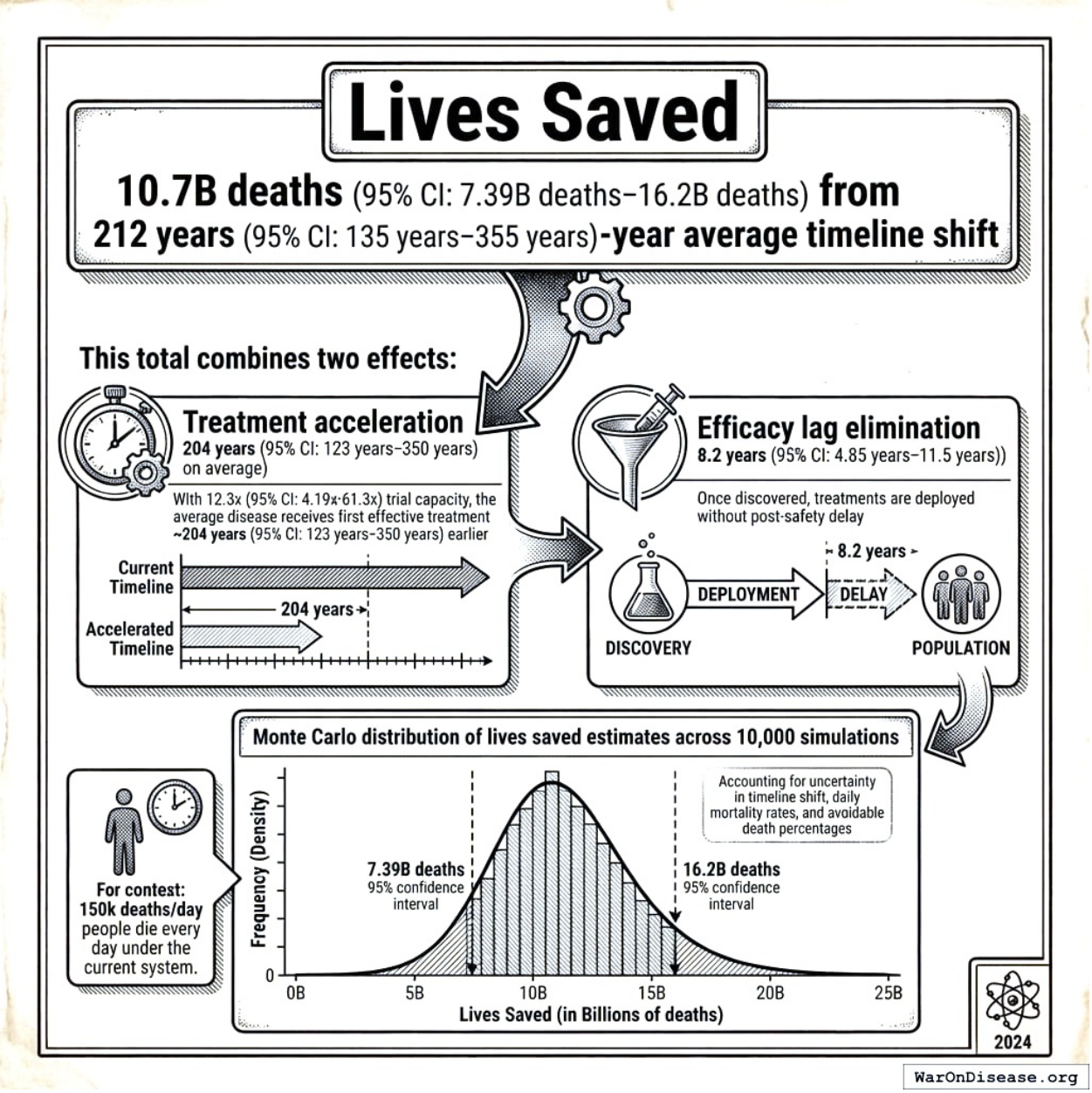


Figure 15: A conceptual diagram showing how increased trial capacity and the elimination of efficacy lags combine to shift treatment timelines forward, resulting in billions of lives saved.

The Monte Carlo distribution below shows the range of lives saved estimates across 10,000 simulations, accounting for uncertainty in timeline shift, daily mortality rates, and avoidable death percentages:

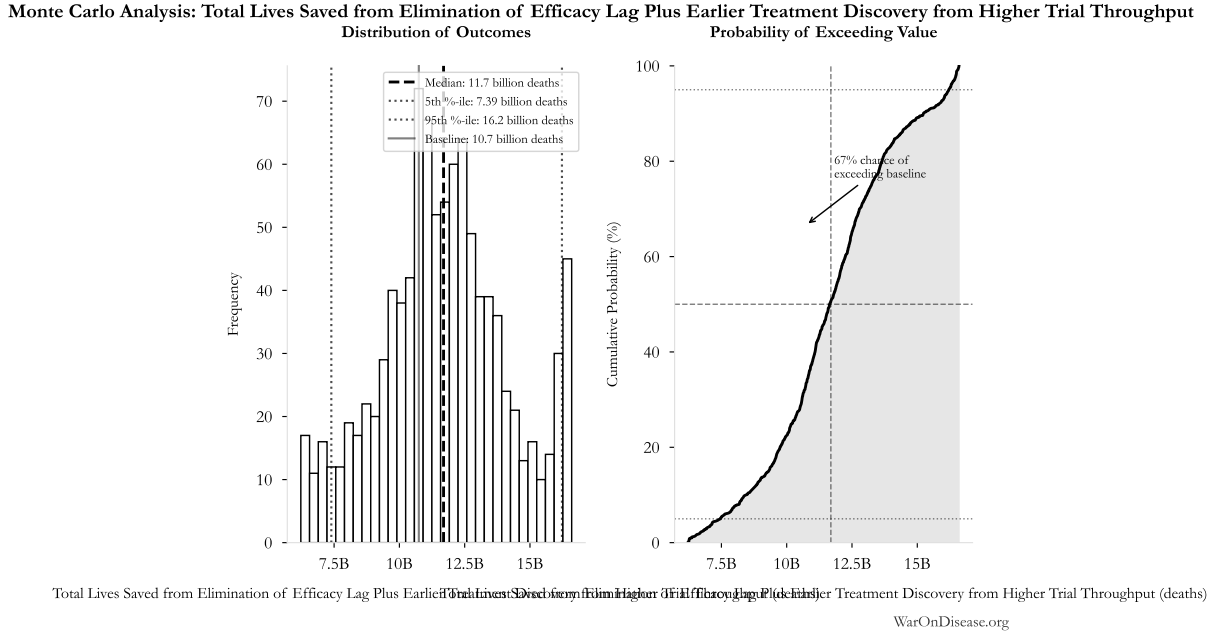


Figure 16: Monte Carlo Distribution: Total Lives Saved from Elimination of Efficacy Lag Plus Earlier Treatment Discovery from Higher Trial Throughput (10,000 simulations)

Simulation Results Summary: Total Lives Saved from Elimination of Efficacy Lag Plus Earlier Treatment Discovery from Higher Trial Throughput

Statistic	Value
Baseline (deterministic)	10.7 billion
Mean (expected value)	11.7 billion
Median (50th percentile)	11.7 billion
Standard Deviation	2.45 billion
90% Range (5th-95th percentile)	[7.39 billion, 16.2 billion]

The histogram shows the distribution of Total Lives Saved from Elimination of Efficacy Lag Plus Earlier Treatment Discovery from Higher Trial Throughput 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.

DALYs Averted

565 billion DALYs (95% CI: 361 billion DALYs-877 billion DALYs) (Disability-Adjusted Life Years) averted from the 212 years (95% CI: 135 years-355 years)-year timeline shift.

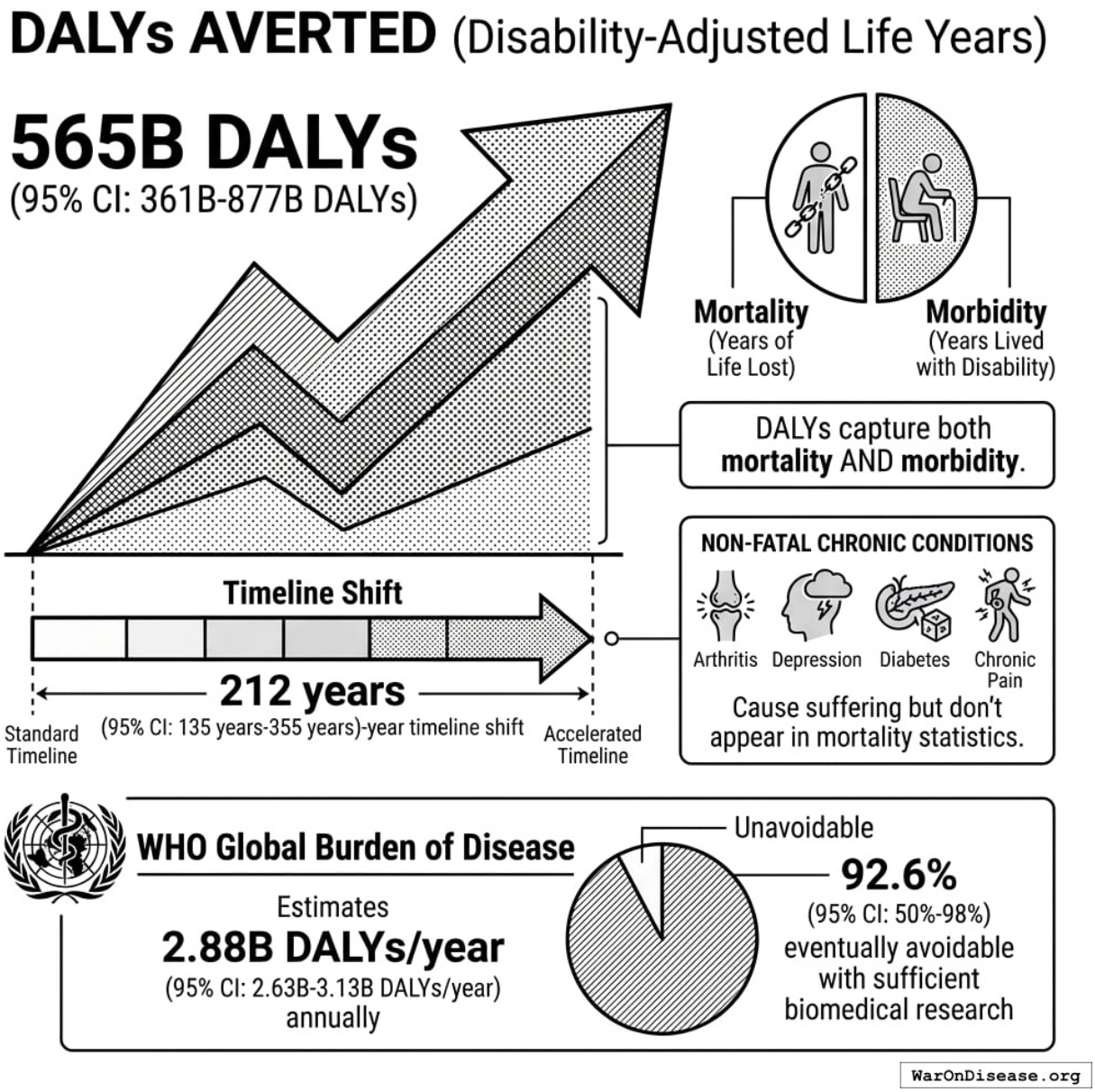


Figure 17: A visual breakdown of Disability-Adjusted Life Years (DALYs), illustrating how they combine Years of Life Lost (mortality) and Years Lived with Disability (morbidity) to measure the total burden of disease.

DALYs capture both mortality (years of life lost) AND morbidity (years lived with disability). This includes non-fatal chronic conditions like arthritis, depression, diabetes, and chronic pain that cause suffering but don't appear in mortality statistics. The WHO Global Burden of Disease estimates 2.88 billion DALYs/year (95% CI: 2.63 billion DALYs/year-3.13 billion DALYs/year) annually, of which 92.6% (95% CI: 50%-98%) are eventually avoidable with sufficient biomedical research.

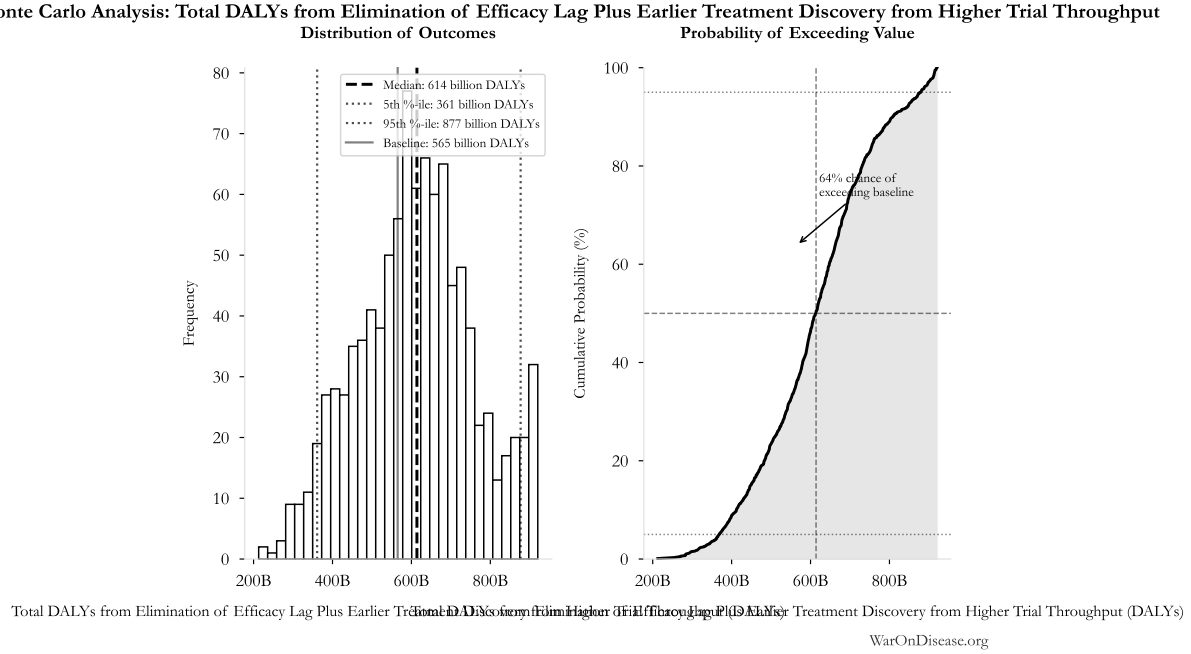


Figure 18: Monte Carlo Distribution: Total DALYs from Elimination of Efficacy Lag Plus Earlier Treatment Discovery from Higher Trial Throughput (10,000 simulations)

Simulation Results Summary: Total DALYs from Elimination of Efficacy Lag Plus Earlier Treatment Discovery from Higher Trial Throughput

Statistic	Value
Baseline (deterministic)	565 billion
Mean (expected value)	610 billion
Median (50th percentile)	614 billion
Standard Deviation	148 billion
90% Range (5th-95th percentile)	[361 billion, 877 billion]

The histogram shows the distribution of Total DALYs from Elimination of Efficacy Lag Plus Earlier Treatment Discovery from Higher Trial Throughput 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.

Why "Eventually Avoidable" Matters

Of 150 thousand deaths/day:

- **92.6% (95% CI: 50%-98%) eventually avoidable** with sufficient biomedical research (gene therapy, AI drug discovery, cellular reprogramming, etc.)
- **7.37% fundamentally unavoidable** (primarily accidents, even with advanced prevention)

This differs from "currently preventable" deaths (20-30M annually via vaccines, sanitation, behavior change). The 92.6% (95% CI: 50%-98%) figure represents maximum achievable with advanced biotechnology over decades, not current interventions.

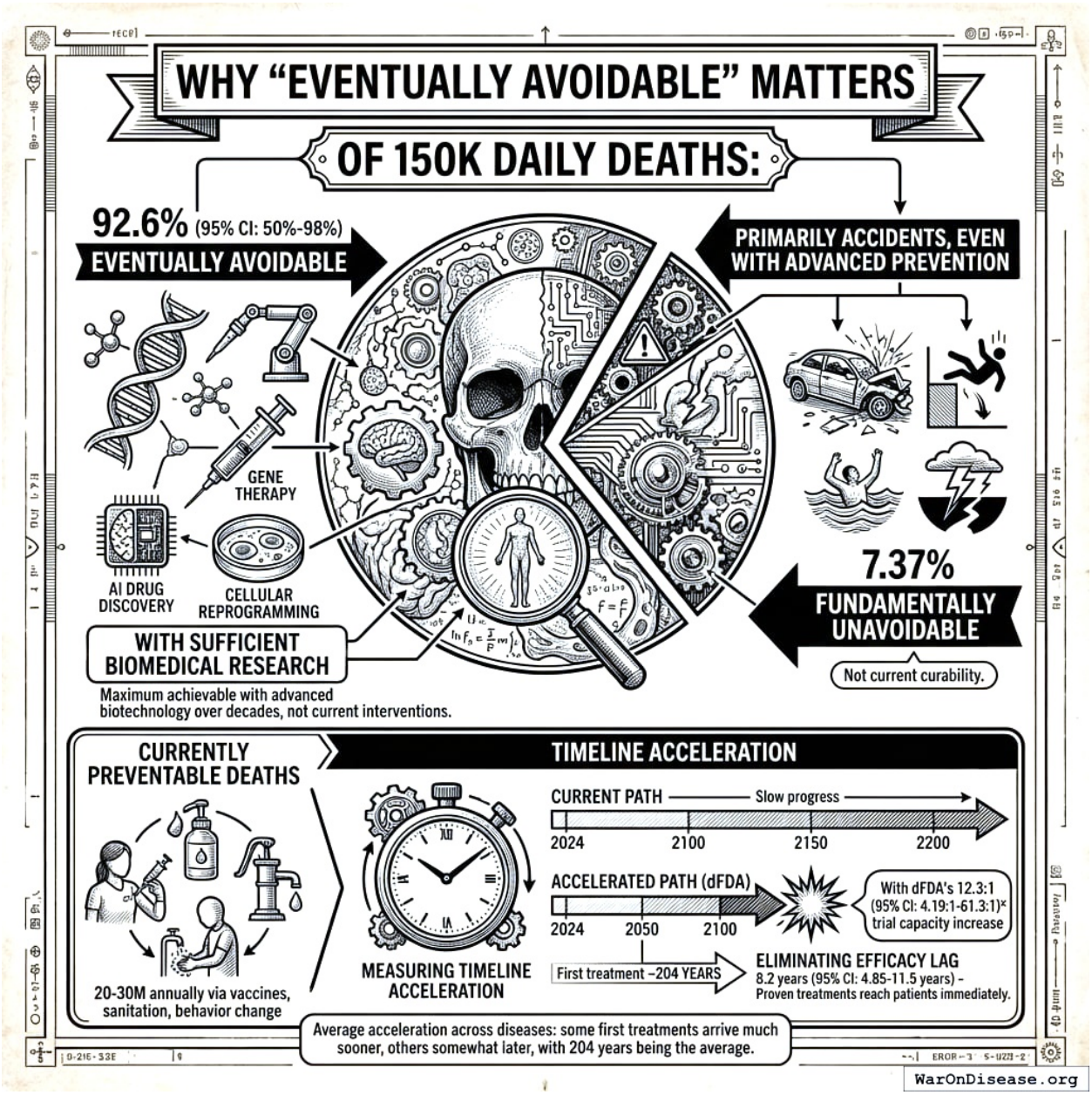


Figure 19: A comparison of daily mortality categories and a timeline visualization showing how increased trial capacity accelerates the arrival of medical treatments by over 200 years.

The lives saved calculation measures **timeline acceleration**, not current curability. With the framework's 12.3x (95% CI: 4.19x-61.3x) trial capacity increase, the average disease receives first treatment ~204 years (95% CI: 123 years-350 years) earlier. Additionally, eliminating the 8.2 years (95% CI: 4.85 years-11.5 years)-year efficacy lag means proven treatments reach patients immediately. This logic applies on average across diseases: some first treatments arrive much sooner (early in the

therapeutic search space), others somewhat later (later in exploration), with 204 years (95% CI: 123 years-350 years) being the average acceleration.

The Leverage Mechanism: Why 1% Is Enough

The protocol exploits two structural inefficiencies in global capital allocation:

1. The Peace Dividend (Multiplier Differential)

$114B (95% CI: $90.1B-$141B)/year

How the peace dividend is calculated:

The peace dividend doesn't assume the treaty prevents wars. It's based on the **economic multiplier effect** of resource reallocation: military spending generates 0.6x (95% CI: 0.4x-0.9x) in economic value per dollar spent, while healthcare research generates 4.3x (95% CI: 3x-6x) per dollar. Redirecting $27.2B from military to medical research produces a net economic gain of $114B (95% CI: $90.1B-$141B)/year simply from the multiplier differential, independent of whether conflicts occur.

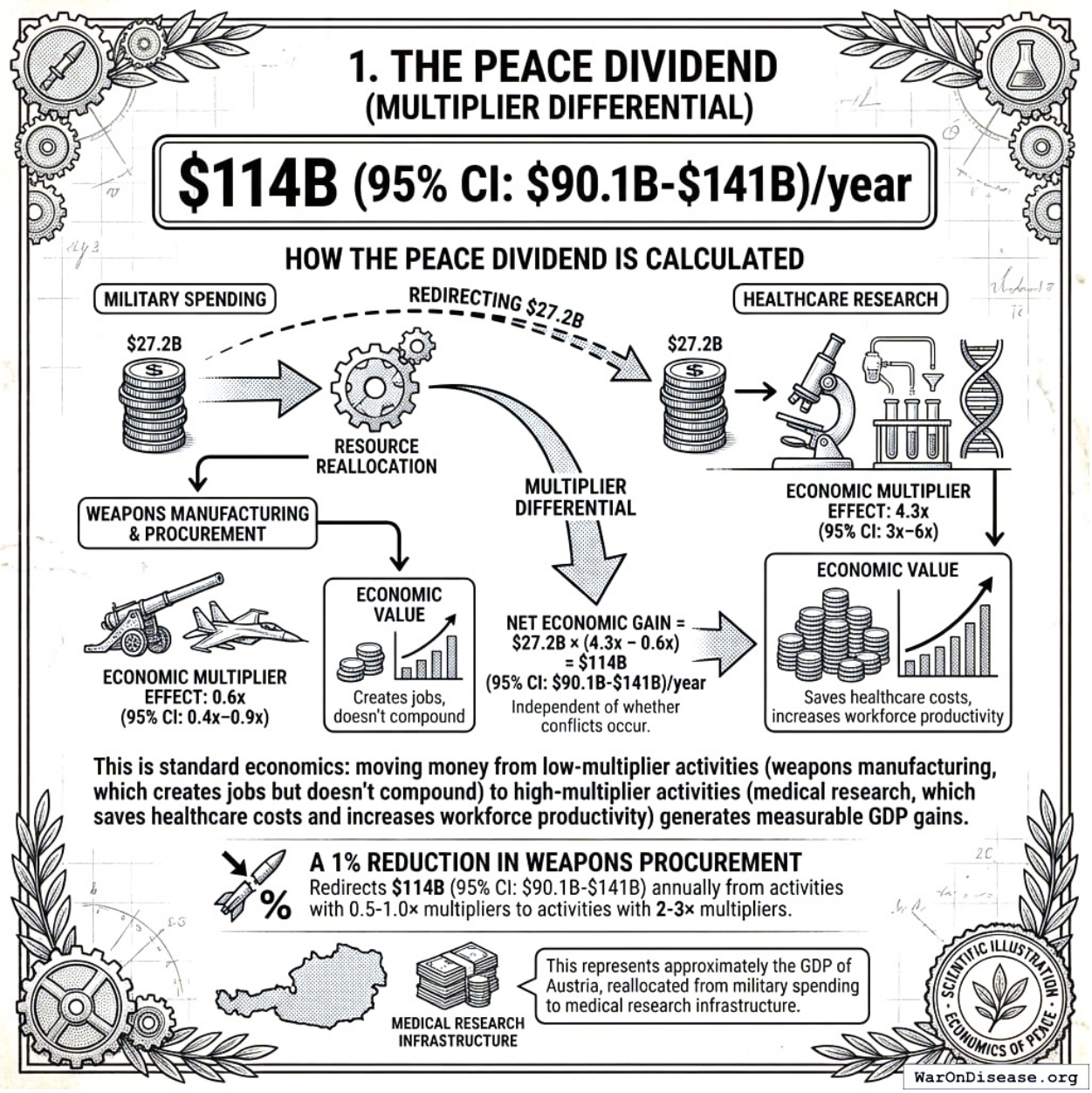


Figure 20: A comparison of the economic multiplier effect showing how redirecting $27.2 billion from military spending (0.6x multiplier) to healthcare research (4.3x multiplier) generates a $114 billion annual peace dividend.

This is standard economics: moving money from low-multiplier activities (weapons manufacturing, which creates jobs but doesn't compound) to high-multiplier activities (medical research, which saves healthcare costs and increases workforce productivity) generates measurable GDP gains.

A 1% reduction in weapons procurement redirects $114B (95% CI: $90.1B-$141B) annually from activities with 0.5-1.0× multipliers to activities with 2-3× multipliers. This represents approximately the GDP of Austria, reallocated from military spending to medical research infrastructure.

2. Research Efficiency Dividend (Infrastructure Leverage)

$58.6B (95% CI: $49.2B-$73.1B)–$60B (95% CI: $50B-$75B)[42]

Traditional trials require:

- Dedicated trial sites with custom infrastructure (pragmatic trials use existing hospitals)
- Extensive source data verification and monitoring visits (pragmatic trials use routine medical records)
- Complex eligibility criteria excluding most patients (pragmatic trials enroll broadly)
- Detailed case report forms capturing hundreds of data points (pragmatic trials collect <10 core outcomes)
- Years of site activation and regulatory approval per country (pragmatic trials activate sites in weeks)

Pragmatic trials eliminate these duplicative overhead costs by leveraging existing infrastructure. The Harvard meta-analysis of 108 embedded trials[132] confirms this efficiency is reproducible: median cost $97 (95% CI: $19-$478)/patient across diverse therapeutic areas. This structural difference explains why costs drop **44.1x (95% CI: 39.4x-89.1x)** instead of 2× or 5×.

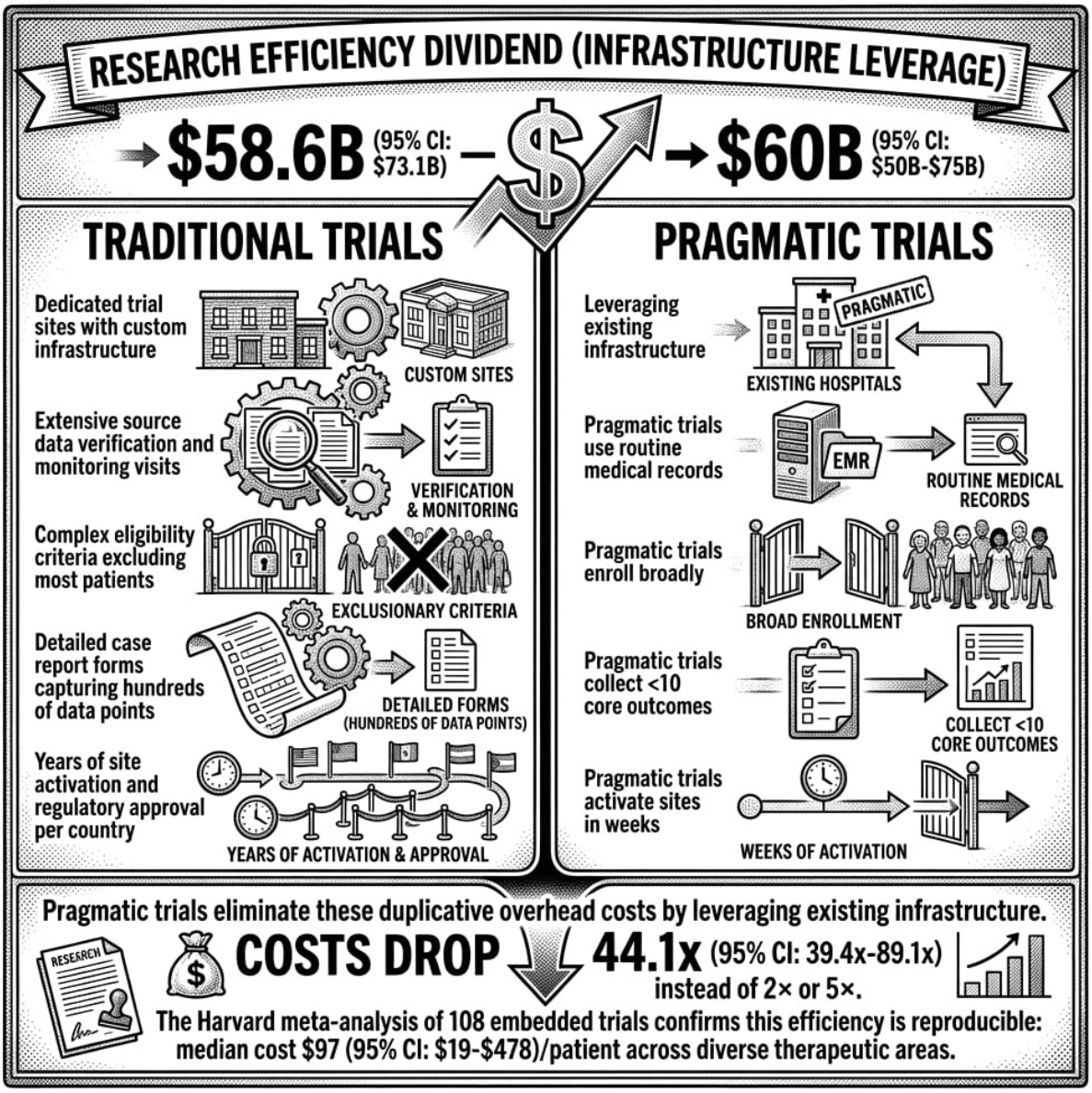


Figure 21: A side-by-side comparison illustrating the structural differences between traditional clinical trial overhead and the streamlined infrastructure leverage of pragmatic trials.

3. 15–40 "NIH equivalents" of new research capacity

Currently, diseases kill people faster than we develop effective treatments. This would change that.

How It Increases National Security

All signatories reduce by 1% simultaneously.

What doesn't change

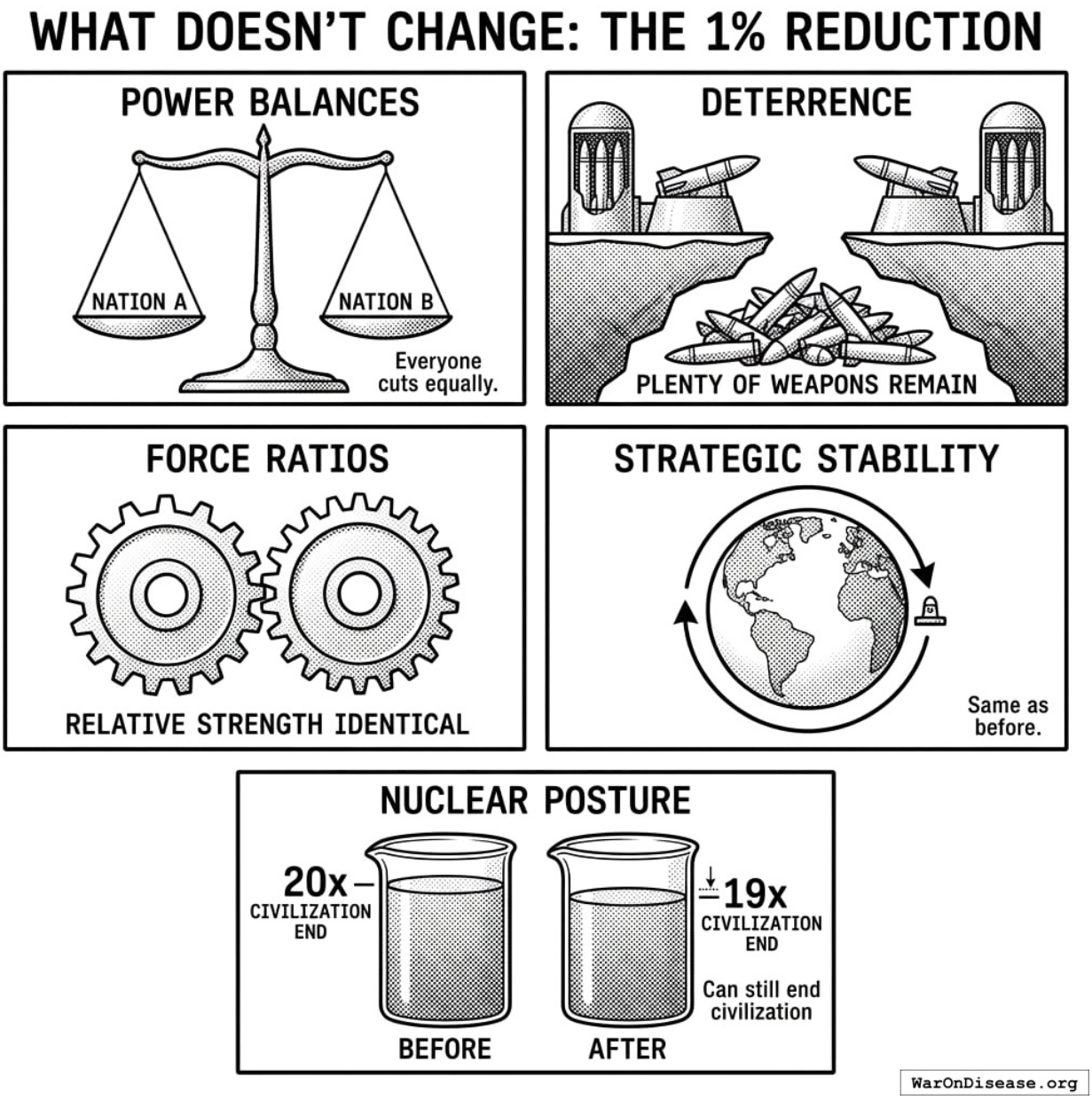


Figure 22: A comparison showing that the relative balance of power and strategic stability remain unchanged despite a 1% reduction in total military resources.

- Power balances (everyone cuts equally)
- Deterrence (still plenty of weapons)
- Force ratios (relative strength identical)
- Strategic stability (same as before, just 1% less apocalyptic)
- Nuclear posture (can still end civilization 19 times instead of 20)

What improves

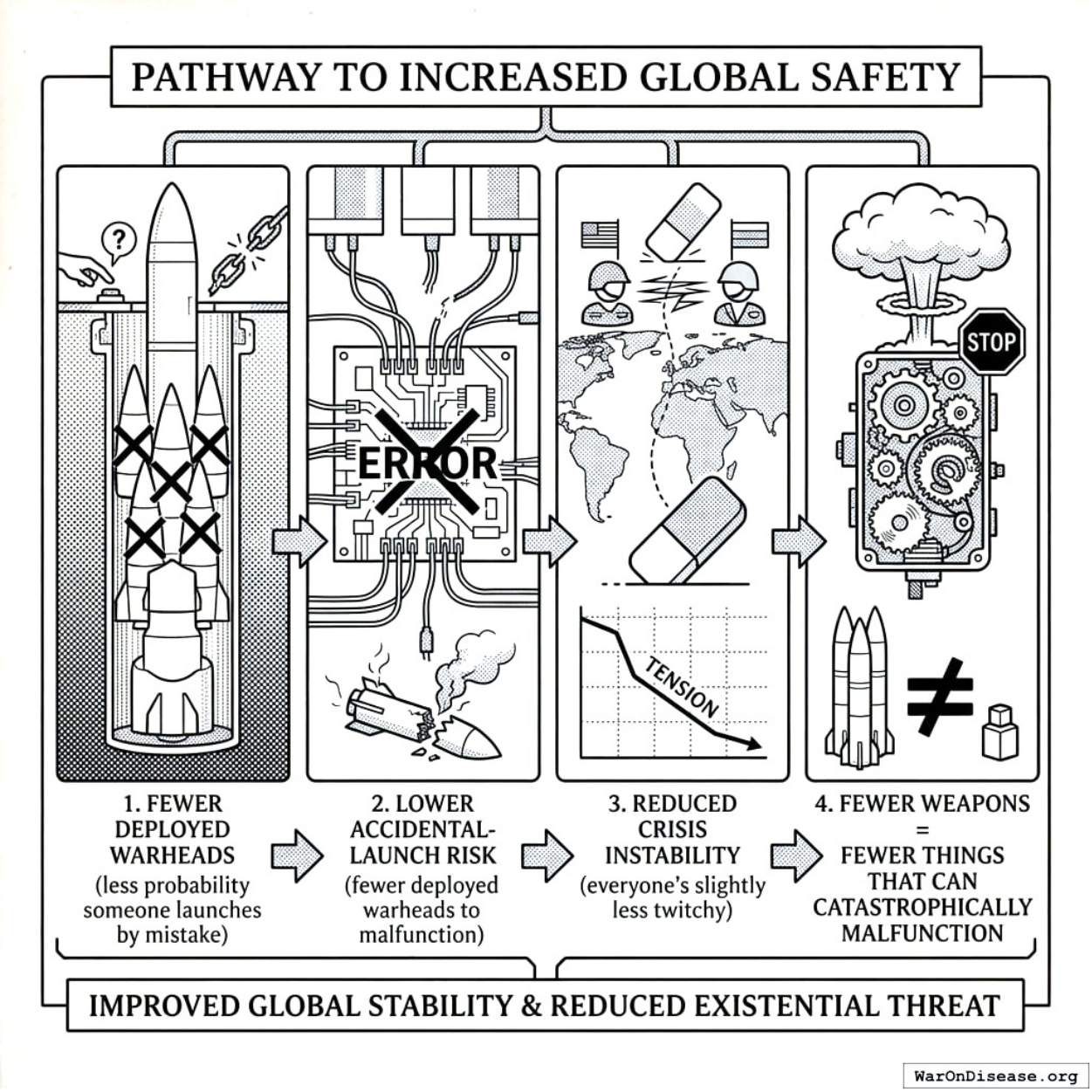


Figure 23: A conceptual diagram showing how a reduction in deployed warheads leads to improved safety outcomes, including lower accidental risk and increased crisis stability.

- Fewer deployed warheads (less probability someone launches by mistake)
- Lower accidental-launch risk (fewer deployed warheads to malfunction)
- Reduced crisis instability (everyone's slightly less twitchy)
- Fewer weapons = fewer things that can catastrophically malfunction

The De-escalation Trajectory

The 1% Treaty is the first step in a **gradual off-ramp from the arms race**.

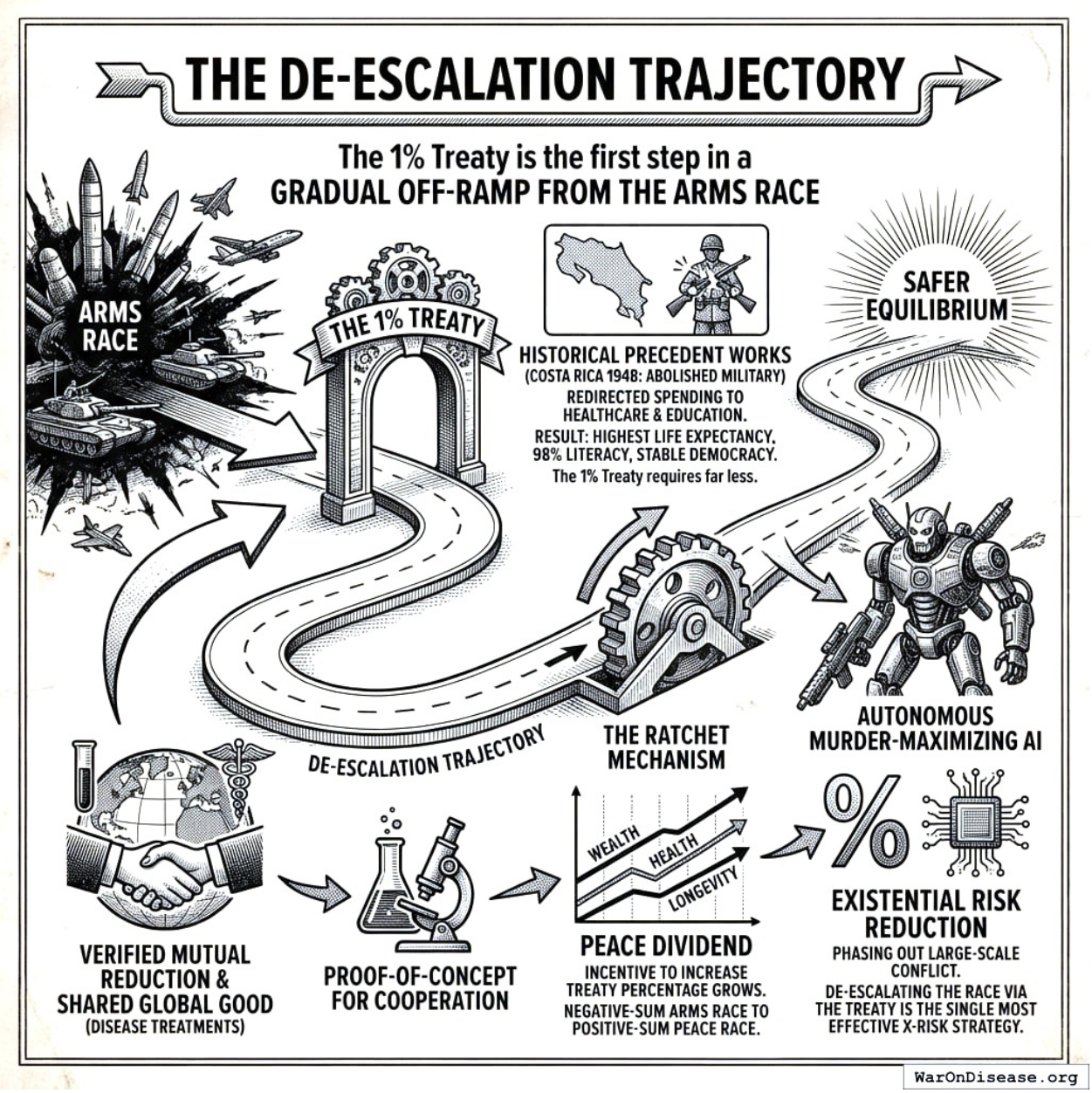


Figure 24: A conceptual diagram illustrating the 'Ratchet Mechanism' where initial military reductions fund health benefits, creating a positive feedback loop that transitions from a negative-sum arms race to a positive-sum peace race.

By successfully executing a verified, mutual reduction in military spending to fund a shared global good (developing disease treatments), humanity establishes a proof-of-concept for cooperation.

1. **Historical precedent works**: Costa Rica abolished its military entirely in 1948, redirecting defense spending to universal healthcare and education. Result: highest life expectancy in Central America (80 years), 98% literacy, and stable democracy for 75+ years. The 1% Treaty requires far less. It maintains virtually all military capacity while redirecting just 1% to health research.

2. **The Ratchet Mechanism**: Once the economic benefits of the "Peace Dividend" (wealth, health, longevity) materialize, the incentive to increase the treaty percentage grows. We move from a negative-sum arms race to a positive-sum "peace race."
3. **Existential Risk Reduction**: Gradually increasing the percentage creates a trajectory toward phasing out large-scale conflict entirely. Since a primary driver of existential risk is **autonomous murder-maximizing AI produced by military arms races**, de-escalating this race via the treaty is arguably the single most effective X-Risk strategy available.

This gradual approach steers nations toward a safer equilibrium, one percentage point at a time.

Why The Ratchet Works: The IAB Scaling Engine

The ratchet mechanism isn't just economic gravity. It's engineered through Incentive Alignment Bonds.

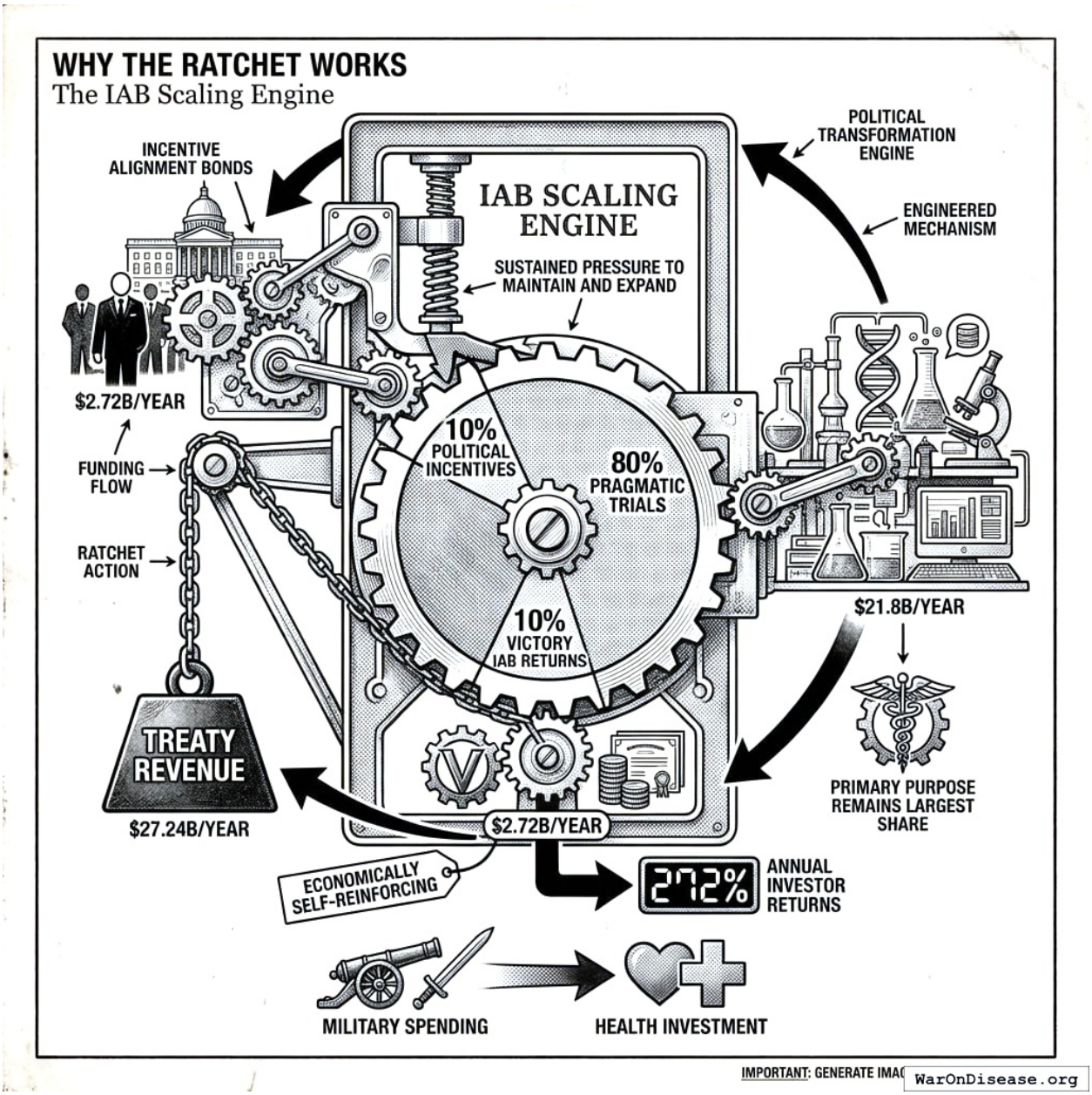


Figure 25: A diagram of the IAB Scaling Engine showing the 80/10/10 split of treaty revenue between pragmatic trials, investor returns, and political incentives to create a self-reinforcing feedback loop.

The mechanism: 10% of treaty revenue ($2.72B/year) funds political incentives while 80% ($21.8B/year) funds pragmatic trials. The remaining 10% funds Incentive Alignment Bond investor returns.

Incentive Alignment Bond investors receive projected 272% on their investment. The 10% allocation to political incentives creates sustained pressure to maintain and expand the treaty, while the 80% allocation ensures the primary purpose (funding pragmatic trials) remains the largest share.

This allocation structure (80% medical research, 10% investor returns, 10% political incentives) functions as a political transformation engine, making the transition from military spending to

health investment economically self-reinforcing.

Treaty Funding Allocation

Total annual treaty funding: $27.2B

Allocation	Percentage	Annual Amount	Purpose
Pragmatic Clinical Trials	80%	$21.8B	Patient subsidies, system operations
IAB Investor Returns	10%	$2.72B	Perpetual investor payments
IAB Political Incentives	10%	$2.72B	Rewards for supporting legislators

Within the 80% allocated to pragmatic clinical trials:

1. **Patient Trial Subsidies** (79.9% (95% CI: 79.8%-79.9%)): $21.7B (95% CI: $21.7B-$21.7B)/year
   - Subsidizes 23.4 million patients/year (95% CI: 9.44 million patients/year-96.8 million patients/year) patients annually at $929 (95% CI: $97-$3K)[1] per patient
   - Patients bring subsidies to trials; providers collect payment when patients enroll
2. **Coordination Framework** (0.147% (95% CI: 0.1%-0.204%)): $40M (95% CI: $27.3M-$55.6M)/year for system infrastructure

Political Economy and Financing

Ideas don't win on merit alone. They win by aligning incentives.

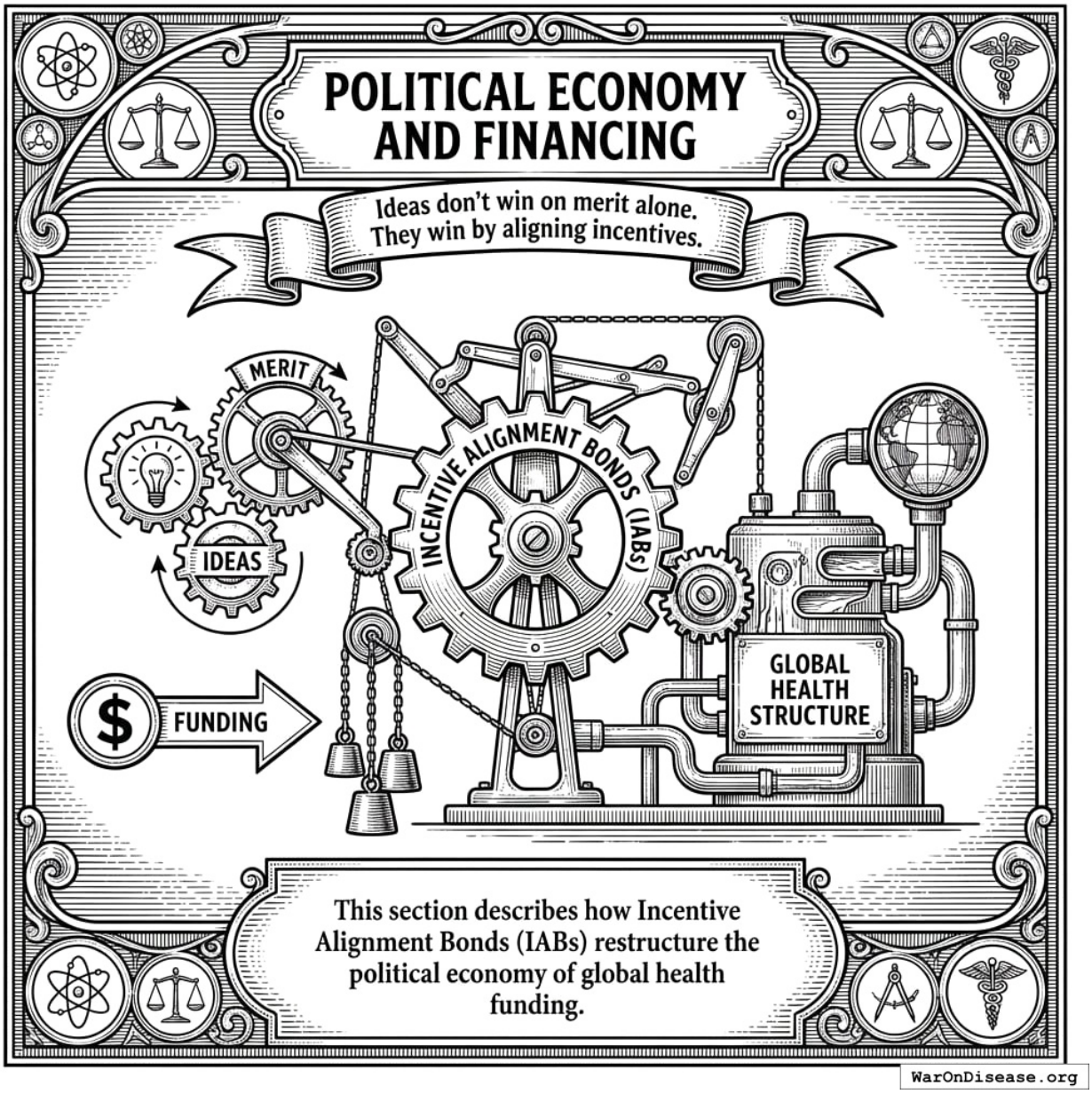


Figure 26: A conceptual model showing how Incentive Alignment Bonds (IABs) synchronize the interests of donors, governments, and investors to prioritize global health outcomes.

This section describes how Incentive Alignment Bonds (IABs) restructure the political economy of global health funding.

Incentive Alignment Bonds

Incentive Alignment Bonds address a fundamental problem: politicians face career penalties for supporting beneficial policies that threaten incumbent industries. IABs restructure these incentives so that supporting effective policy becomes professionally advantageous.

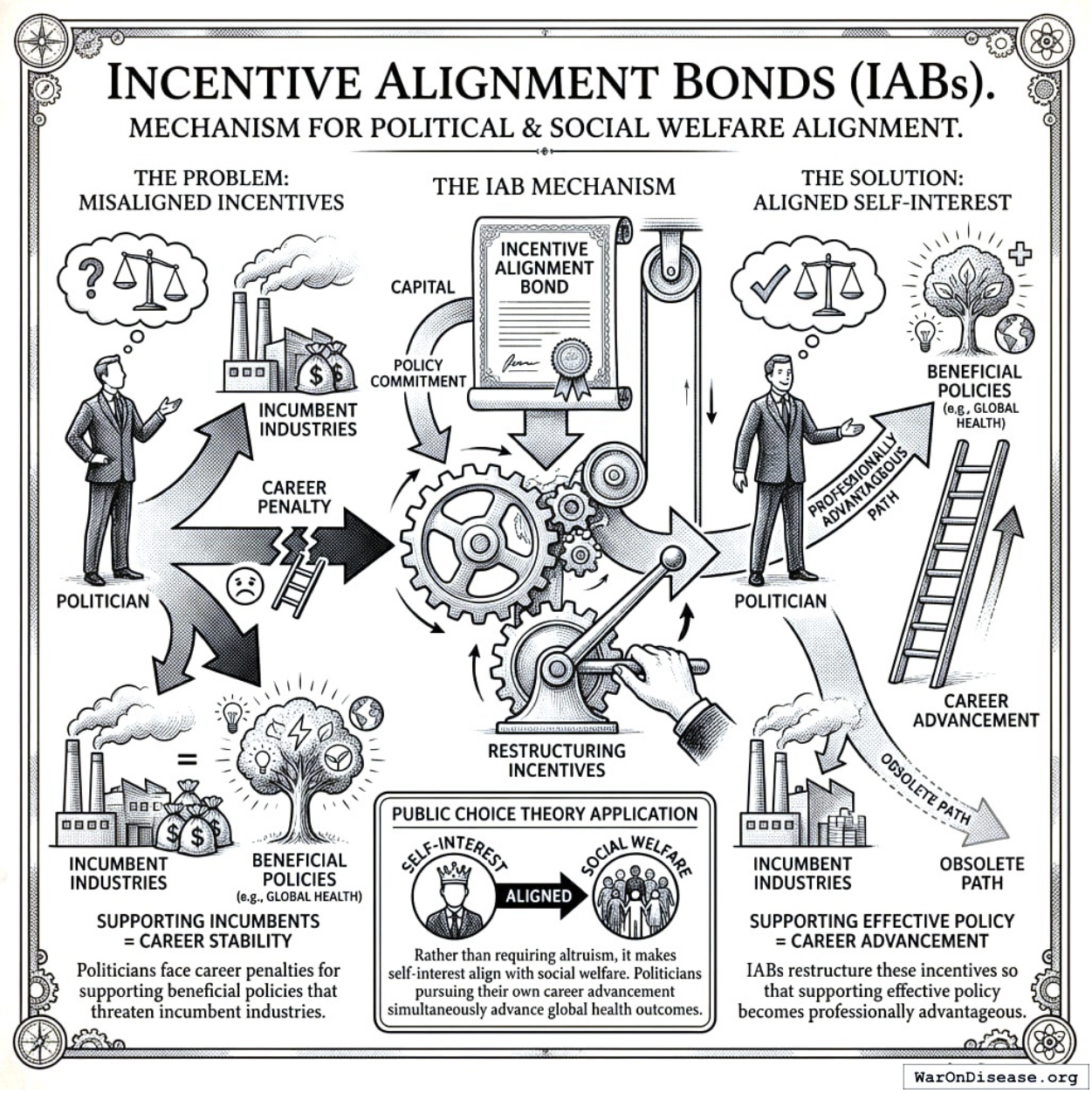


Figure 27: A comparison diagram illustrating the shift in political incentives: from a career penalty for opposing incumbent industries to professional advancement through Incentive Alignment Bonds when achieving social welfare goals.

The mechanism applies public choice theory systematically. Rather than requiring altruism, it makes self-interest align with social welfare. Politicians pursuing their own career advancement simultaneously advance global health outcomes.

Mechanism Architecture

Politicians are evaluated through a **Public Good Score** based on verifiable voting records for treaty funding. This scoring system creates three channels of incentive alignment:

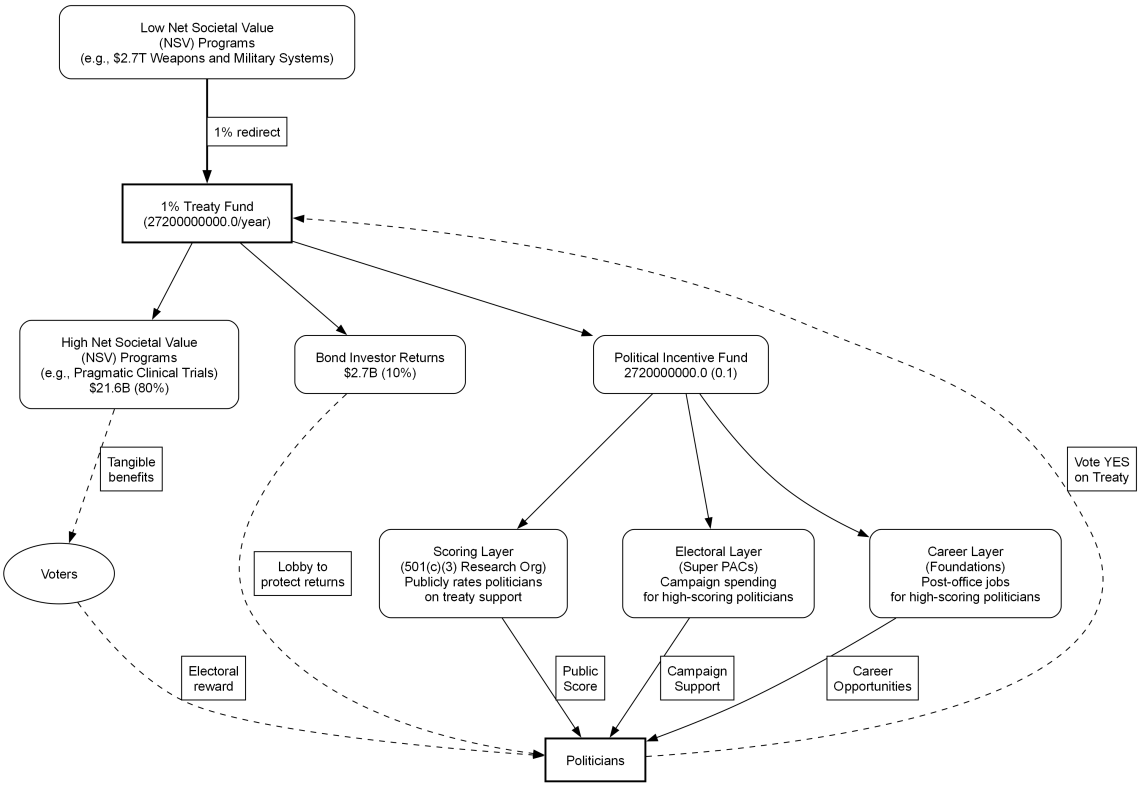

Low Net Societal Value
(NSV) Programs
(e.g., $2.7T Weapons and Military Systems)
1% redirect
1% Treaty Fund
(27200000000.0/year)
High Net Societal Value
(NSV) Programs
(e.g., Pragmatic Clinical Trials)
$21.6B (80%)
Bond Investor Returns
$2.7B (10%)
Political Incentive Fund
2720000000.0 (0.1)
Tangible
benefits
Vote YES
on Treaty
Voters
Lobby to
protect returns
Scoring Layer
(501(c)(3) Research Org)
Publicly rates politicians
on treaty support
Electoral Layer
(Super PACs)
Campaign spending
for high-scoring politicians
Career Layer
(Foundations)
Post-office jobs
for high-scoring politicians
Electoral
reward
Public
Score
Campaign
Support
Career
Opportunities
Politicians

Figure 28

1. **Electoral advantage**: Independent campaign support flows to high-scoring politicians
2. **Reputational benefits**: Public scores create transparency and accountability
3. **Post-office opportunities**: High scorers gain access to prestigious fellowships, advisory positions, and speaking engagements

Critically, no direct monetary transfers to politicians occur. Benefits flow through reputation, electoral support, and career advancement - all based on publicly verifiable voting records that cannot be manipulated.

Comparative Static Analysis: Senator Smith

Consider a legislator's decision calculus regarding the 1% Treaty vote:

Without IABs:

Action	Expected Outcome
Vote Yes	Military lobby attack ads; reduced industry support
Vote No	Retained military contractor funding; no electoral risk

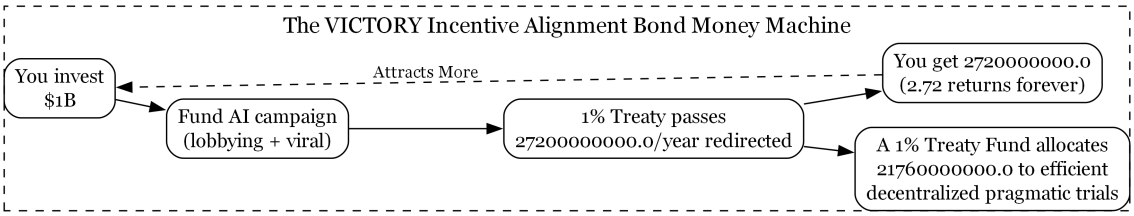
With IABs:

Action	Expected Outcome
Vote Yes	Public Good Score: 45 → 72; P(reelection): 55% → 62%; Expected post-office income: \$200K → \$500K/yr
Vote No	Score: 45 → 30; P(reelection): 55% → 48%; Opposition receives \$2M independent support

The mechanism changes the math. Supporting beneficial policy becomes professionally advantageous rather than requiring self-sacrifice.

Stakeholder Alignment

The IAB mechanism aligns incentives across all key stakeholder groups:



Military Contractors: Retain 99% of current budgets while earning projected 272% returns on Incentive Alignment Bonds. The treaty creates new revenue streams without threatening core business.

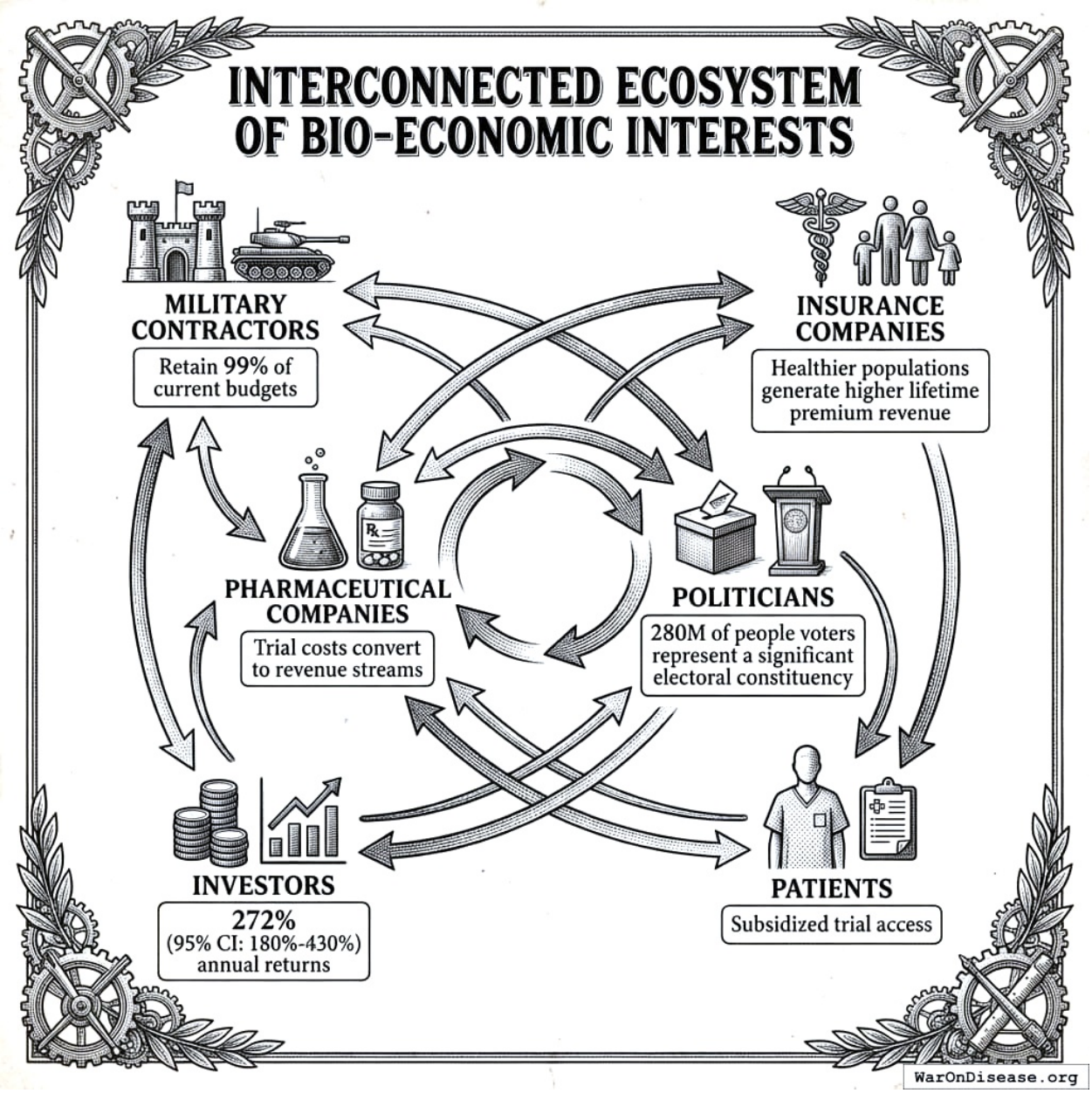


Figure 29: A comparison of current costs and returns versus the projected gains for stakeholders under the Incentive Alignment Bond mechanism, illustrating the shift from zero-sum to positive-sum outcomes.

Insurance Companies: Healthier populations generate higher lifetime premium revenue. Patients living longer with better health outcomes produce better actuarial performance than the current mortality-driven model.

Pharmaceutical Companies: Trial costs convert to revenue streams. Instead of paying \$41K (95% CI: \$20K-\$120K)[101] per trial patient, companies collect \$929 (95% CI: \$97-\$3K)[1] subsidies when patients enroll. This transforms trials from cost centers to profit centers.

Politicians: 280 million of people million voters represent a significant electoral constituency.

Politicians supporting the treaty gain reputation benefits, campaign support, and reduced opposition funding. Those opposing it face well-funded challengers and organized voter blocs.

$$\begin{aligned} & N_{voters,target} \\ &= Pop_{global} \times Threshold_{activism} \\ &= 8B \times 3.5\% \\ &= 280M \end{aligned}$$

Investors: Incentive Alignment Bonds offer projected 272%, substantially exceeding typical market returns of 10%.

$$r_{bond} = \frac{Payout_{bond,ann}}{Cost_{campaign}} = \frac{\$2.72B}{\$1B} = 272\%$$

$$\begin{aligned} &\text{where } Payout_{bond,ann} \\ &= Funding_{treaty} \times Pct_{bond} \\ &= \$27.2B \times 10\% \\ &= \$2.72B \end{aligned}$$

$$\begin{aligned} &\text{where } Funding_{treaty} \\ &= Spending_{mil} \times Reduce_{treaty} \\ &= \$2.72T \times 1\% \\ &= \$27.2B \end{aligned}$$

$$\begin{aligned} &\text{where } Cost_{campaign} \\ &= Budget_{viral,base} + Budget_{lobby,treaty} \\ &\quad + Budget_{reserve} \\ &= \$250M + \$650M + \$100M \\ &= \$1B \end{aligned}$$

Patients: Subsidized access to experimental treatments recommended by physicians. Patients choose which trials to join, with subsidies following their decisions. Additional benefits include lifetime wealth gains and longevity increases from the economic multiplier effect.

The mechanism redirects competitive incentives from zero-sum conflicts toward positive-sum health outcomes.

See Aligning Incentives for complete analysis.

Legal and Ethical Framework

This mechanism differs from bribery in four key ways:

1. **No duty violation**: IABs reward policy support that advances rather than undermines public welfare
2. **Transparent rules**: Scoring criteria are public, announced in advance, and apply equally to all legislators

3. **No direct payments**: Benefits flow through reputation, electoral support, and career opportunities, not cash transfers
4. **Verifiable metrics**: Scores depend entirely on public voting records from official government sources

The mechanism strengthens rather than corrupts the alignment between political success and social outcomes.

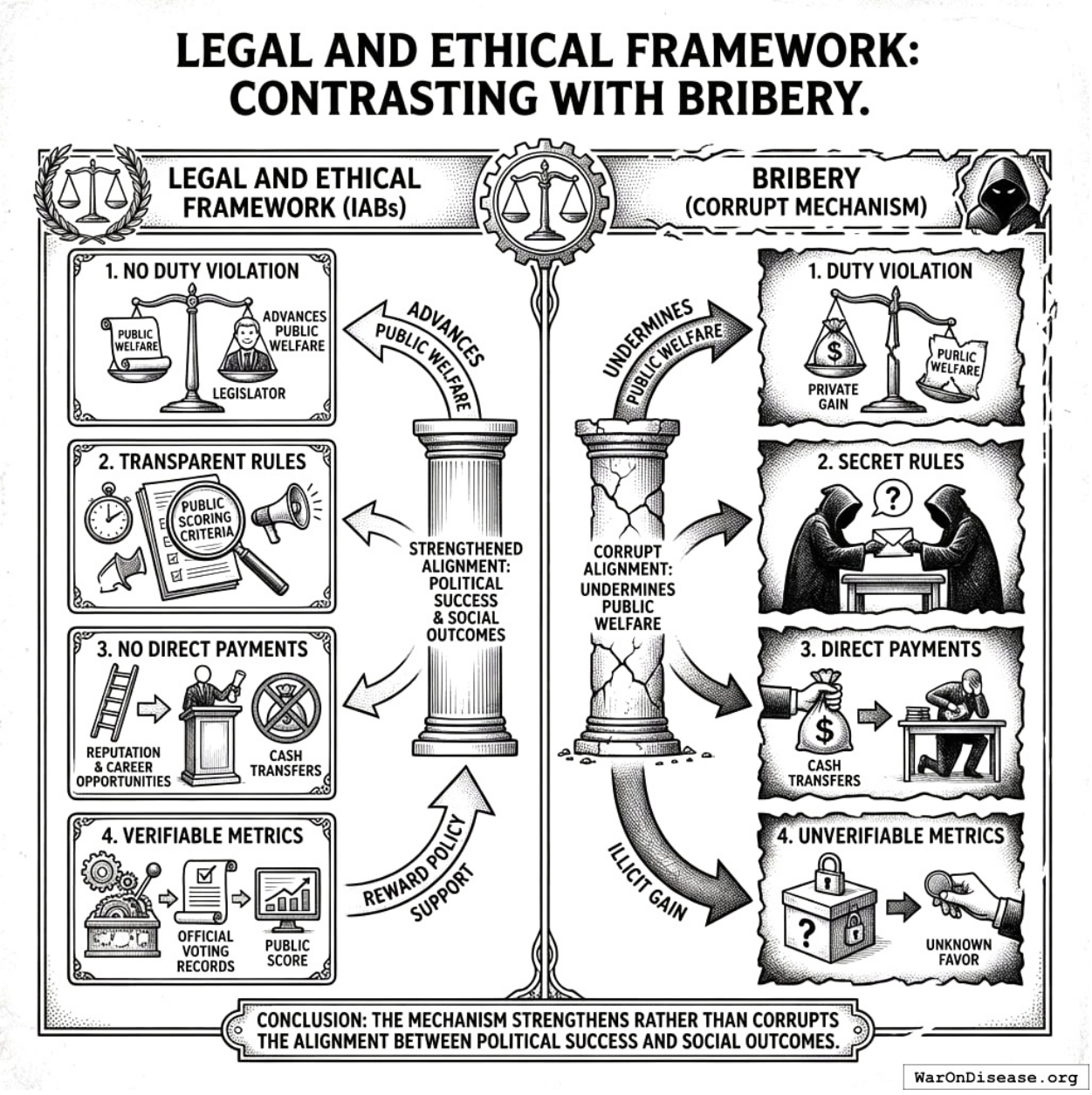


Figure 30: A comparison diagram illustrating the four key legal and ethical distinctions between IABs and bribery across metrics of transparency, duty, payment type, and verifiability.

Dominance Analysis

For objectives including:

- Quality-adjusted life years (QALYs)
- Lifespan
- Productivity
- Economic growth
- National security
- Existential safety
- Not suffering unnecessarily

Redirection of 1% of military spending to pragmatic trials delivers exceptional returns.

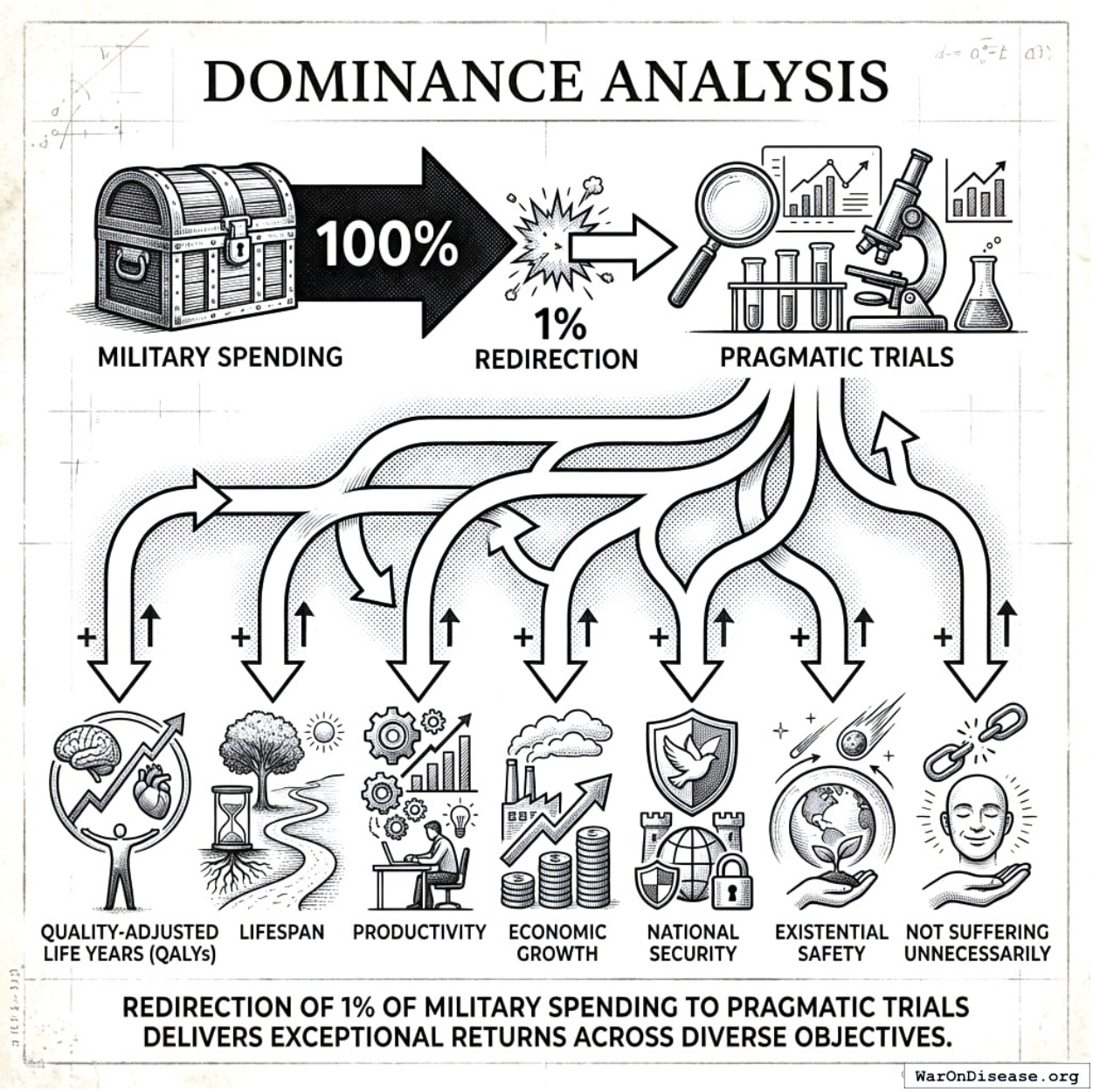


Figure 31: A visual representation showing the redirection of 1% of military spending into pragmatic trials, yielding positive outcomes across health, economic growth, and national security.

Quantitative Comparison

With $1B allocated toward saving lives, here's what each option delivers:

Intervention	Cost per DALY	Scale	Economic Model
1% Treaty (Timeline Shift)	$0.0018 (95% CI: $0.0007-$0.0041)	565 billion DALYs (95% CI: 361 billion DALYs-877 billion DALYs)	Cost-saving
1% Treaty (Expected Value)	$0.177 (95% CI: $0.029-$3.20)	At 1% (95% CI: 0.1%-10%) success probability	503x (95% CI: 29.9x-3.0kx) better than bed nets
Malaria Bed Nets	$89 (95% CI: $78-$100)	Proven, scalable	Linear scaling
Childhood Vaccinations	Self-funding	Annual benefit: ~$15B (95% CI: $8.79B-$23.3B)	Self-funding
GiveWell Top Charities	$3.50K-$5.50K per life saved	Variable	Linear scaling
Cancer Screening	$20,000-$50,000	Variable	Linear scaling
Cardiovascular Prevention	$10,000-$30,000	Variable	Linear scaling

Conservative benefits ($172B (95% CI: $140B-$213B) annually) exceed childhood vaccinations by 11.5x (95% CI: 9x-16.1x).

$$k_{treaty:vax} = \frac{Benefit_{peace+RD}}{Benefit_{vax,ann}} = \frac{\$172B}{\$15B} = 11.5$$

$$\text{where } Benefit_{peace+RD}$$
$$= Benefit_{peace,soc} + Benefit_{RD,ann}$$
$$= \$114B + \$58.6B$$
$$= \$172B$$

$$\text{where } Benefit_{peace,soc}$$
$$= Cost_{war,total} \times Reduce_{treaty}$$
$$= \$11.4T \times 1\%$$
$$= \$114B$$

$$\text{where } Cost_{war,total}$$
$$= Cost_{war,direct} + Cost_{war,indirect}$$
$$= \$7.66T + \$3.7T$$
$$= \$11.4T$$

$$\text{where } Cost_{war,direct}$$
$$= Loss_{life,conflict} + Damage_{infra,total}$$
$$+Disruption_{trade} + Spending_{mil}$$
$$= \$2.45T + \$1.88T + \$616B + \$2.72T$$
$$= \$7.66T$$

$$\text{where } Loss_{life,conflict}$$
$$= Cost_{combat,human} + Cost_{state,human}$$
$$+Cost_{terror,human}$$
$$= \$2.34T + \$27B + \$83B$$
$$= \$2.45T$$

$$\text{where } Cost_{combat,human}$$
$$= Deaths_{combat} \times VSL$$
$$= 234{,}000 \times \$10M$$
$$= \$2.34T$$

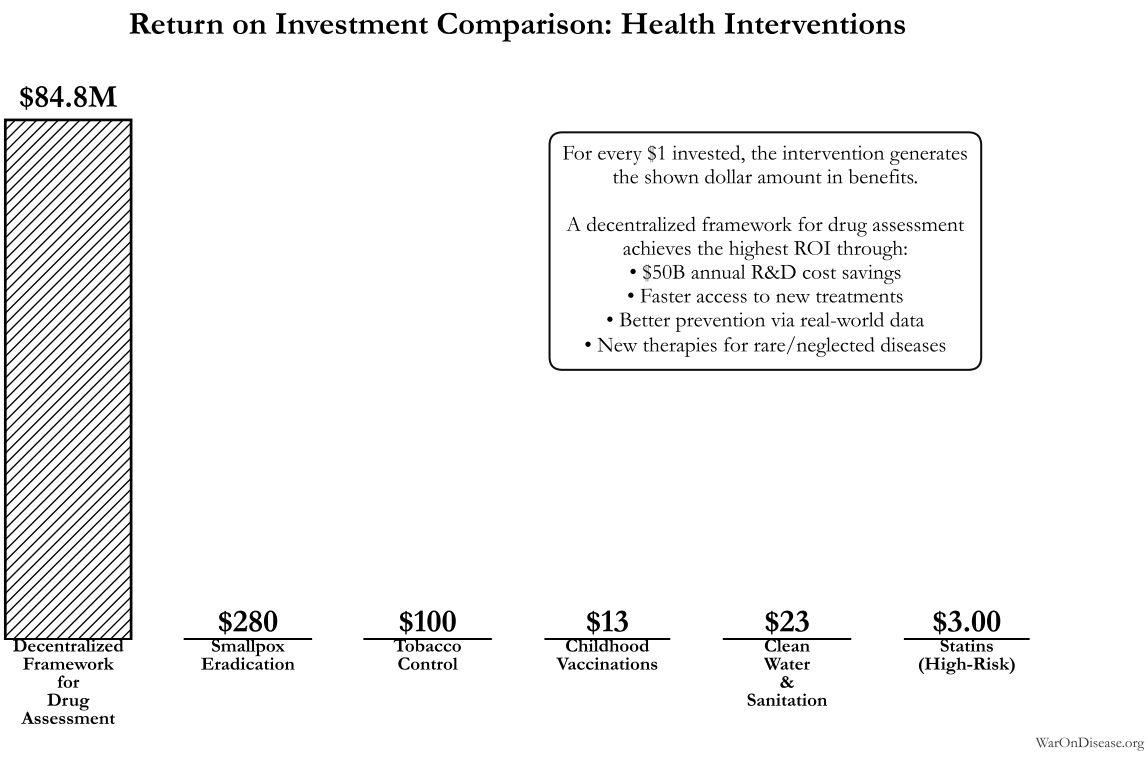
$$\text{where } Cost_{state,human}$$
$$= Deaths_{state} \times VSL$$
$$= 2{,}700 \times \$10M$$
$$= \$27B$$

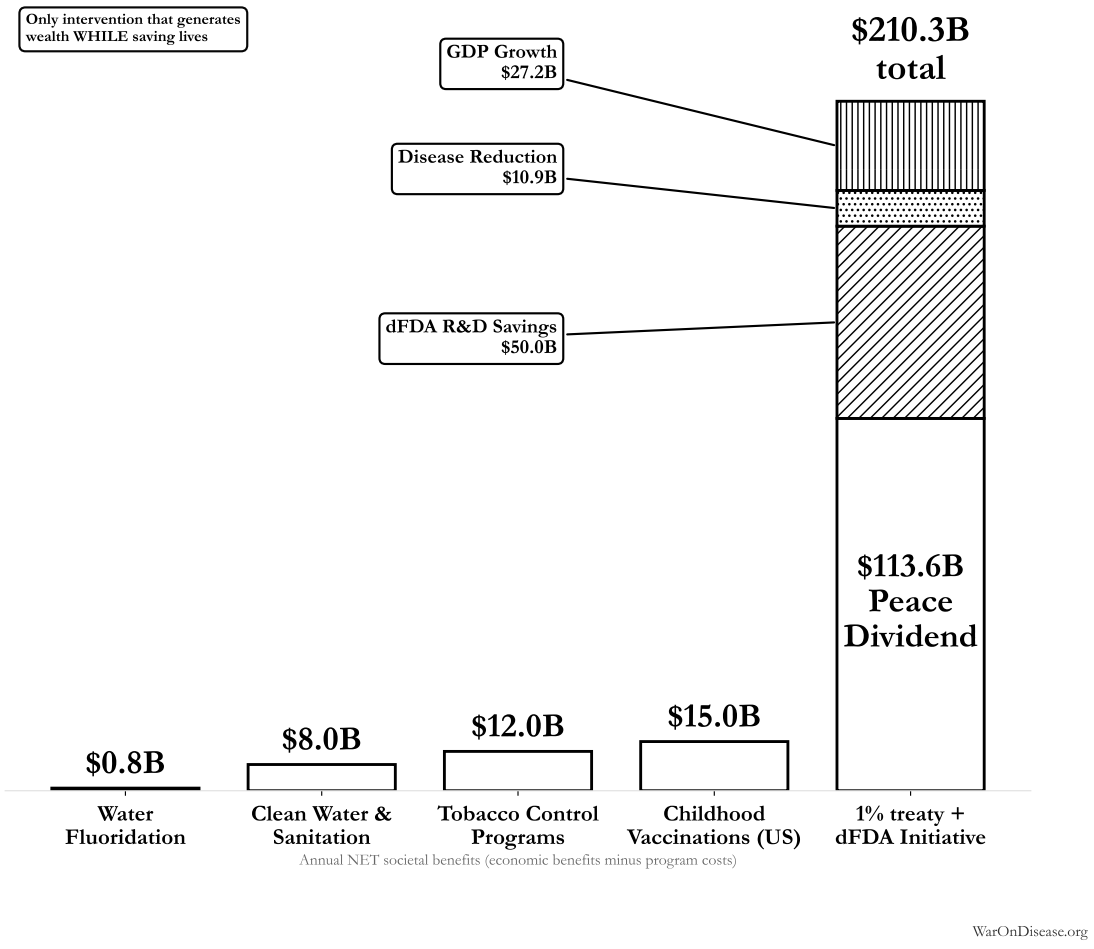
$$\text{where } Cost_{terror,human}$$
$$= Deaths_{terror} \times VSL$$
$$= 8{,}300 \times \$10M$$
$$= \$83B$$

$$\text{where } Damage_{infra,total}$$
$$= Damage_{comms} + Damage_{edu} + Damage_{energy}$$
$$+Damage_{health} + Damage_{transport}$$

GiveWell Top Charities (individual benchmarks):

- **Bed Nets**[5]: $89 (95% CI: $78-$100)/DALY
- **Deworming**[18]: $55/DALY
- **Vitamin A**[128]: $37/DALY





Why the 50.3kx (95% CI: 23.7kx-111.7kx) better cost-effectiveness vs. bed nets is plausible:

Bed nets are **consumable interventions** requiring ongoing replacement every 3-5 years. To save 1,000 lives over 20 years requires purchasing and distributing thousands of bed nets repeatedly. Total cost scales linearly with lives saved.

The 1% Treaty is a **one-time implementation cost** ($1B) that unlocks a **permanent infrastructure shift**. Once the treaty passes, it redirects $27.2B/year in perpetuity, funding millions of trial participants annually. The implementation cost is paid once; the benefits compound indefinitely.

Asset class comparison: Bed nets are **depreciating assets** (consumed, worn out, require replacement). Medical treatments are **appreciating assets**. Once discovered, they compound in value forever; penicillin discovered in 1928 still saves lives today. Military spending creates **depreciating assets** (weapons become obsolete, require replacement). This reallocation shifts capital from depreciating to appreciating asset classes, explaining why ROI can be 50.3kx (95% CI: 23.7kx-111.7kx) better than excellent consumable interventions like bed nets.

$$
\begin{aligned}
&k_{treaty:nets} \\
&= \frac{Cost_{nets}}{Cost_{treaty,DALY}} \\
&= \frac{\$89}{\$0.00177} \\
&= 50{,}300
\end{aligned}
$$

$$\text{where } Cost_{treaty,DALY} = \frac{Cost_{campaign}}{DALYs_{max}} = \frac{\$1B}{565B} = \$0.00177$$

$$
\begin{aligned}
&\text{where } Cost_{campaign} \\
&= Budget_{viral,base} + Budget_{lobby,treaty} \\
&+ Budget_{reserve} \\
&= \$250M + \$650M + \$100M \\
&= \$1B
\end{aligned}
$$

$$
\begin{aligned}
&\text{where } DALYs_{max} \\
&= DALYs_{global,ann} \times Pct_{avoid,DALY} \times T_{accel,max} \\
&= 2.88B \times 92.6\% \times 212 \\
&= 565B
\end{aligned}
$$

$$\text{where } T_{accel,max} = T_{accel} + T_{lag} = 204 + 8.2 = 212$$

$$
\begin{aligned}
&\text{where } T_{accel} \\
&= T_{first,SQ} \times \left(1 - \frac{1}{k_{capacity}}\right) \\
&= 222 \times \left(1 - \frac{1}{12.3}\right) \\
&= 204
\end{aligned}
$$

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

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

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

$$\text{where } k_{capacity} = \frac{N_{fundable,ann}}{Slots_{curr}} = \frac{23.4M}{1.9M} = 12.3$$

$$
\begin{aligned}
&\text{where } N_{fundable,ann} \\
&= \frac{Subsidies_{trial,ann}}{Cost_{pragmatic,pt}} \\
&= \frac{\$21.7B}{\$929} \\
&= 23.4M
\end{aligned}
$$

$$
\begin{aligned}
&\text{where } Subsidies_{trial,ann} \\
&= Treasury_{RD,ann} - OPEX_{dFDA} \\
&= \$21.8B - \$40M \\
&= \$21.7B
\end{aligned}
$$

Methodology

This analysis uses three standard health economics tools:

1. **Net Present Value (NPV)**: Future money is worth less than current money because humans are impatient
2. **Quality-Adjusted Life Years (QALYs)**: Measuring healthy life, not just survival - a year lived in full health scores 1.0, while years with illness or disability score proportionally lower
3. **Return on Investment (ROI)**: Economic value generated per dollar invested

The methodology follows standard health economics practices. All parameters, sources, and uncertainty ranges are documented in Parameters and Calculations.

Cost-Benefit Framework

Cost Components

One spends $1B convincing humans that not dying is preferable to dying. This covers:

- Global referendum campaign to get 280 million of people votes ($250M)
- Professional lobbyists and Super PAC spending ($650M)

This is a one-time cost. Treaty passage is either achieved or it isn't.

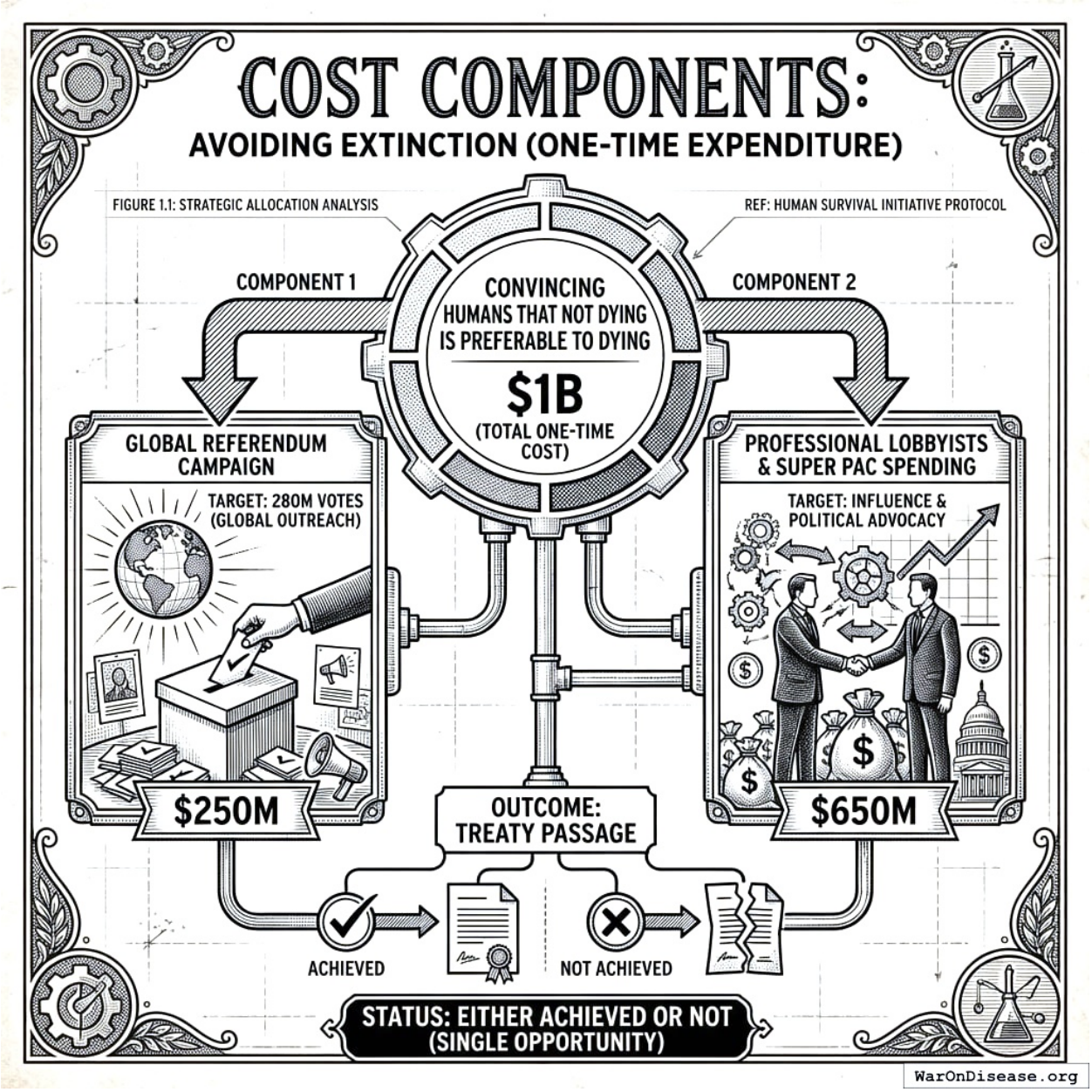


Figure 32: A hierarchical breakdown of the $1 billion political strategy budget, split between a $250 million grassroots referendum campaign and a $650 million top-down lobbying effort.

Benefit Components

The treaty redirects $27.2B annually from military spending to pragmatic clinical trials.

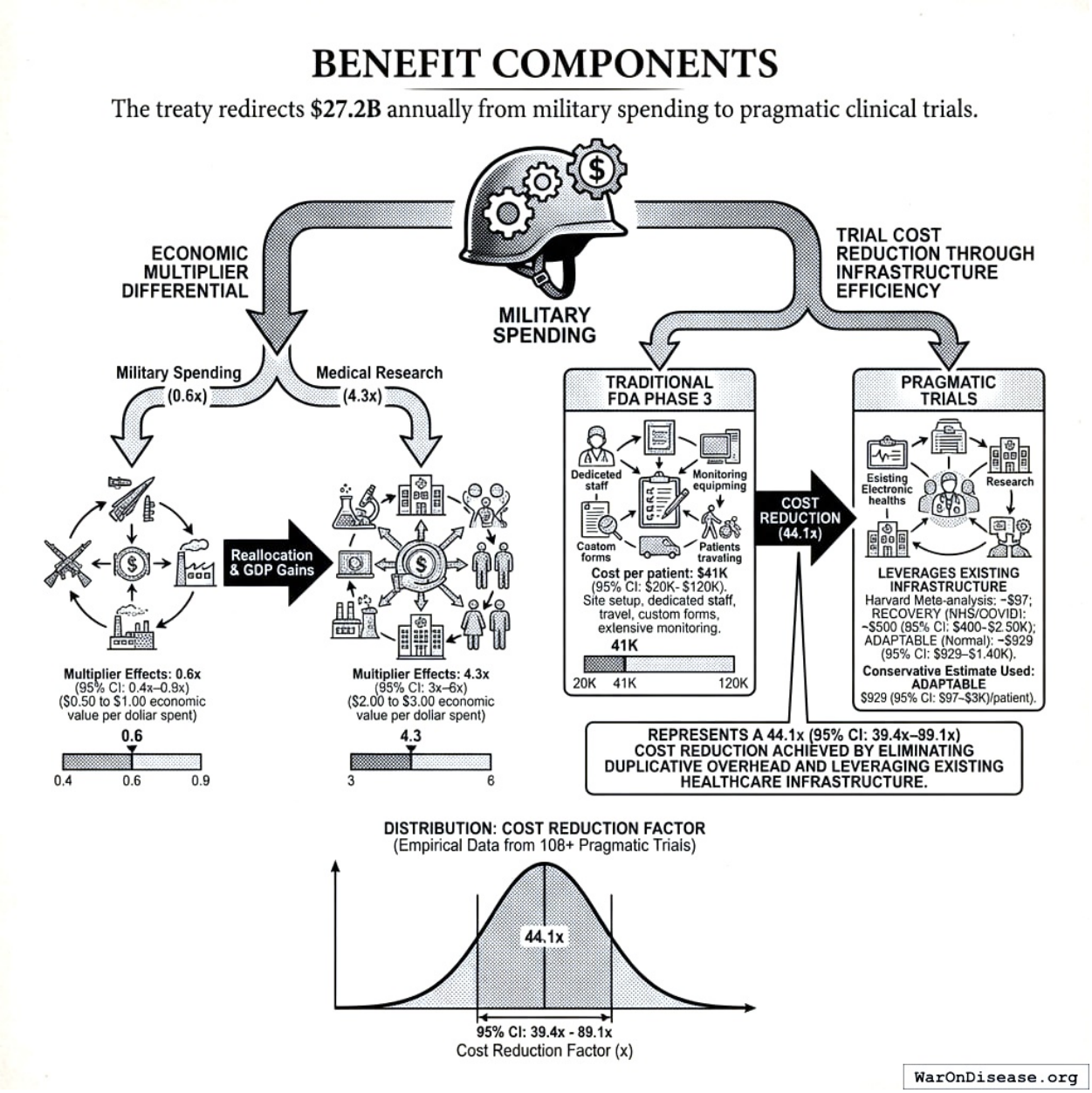


Figure 33: A visual comparison of the economic multipliers and trial efficiency gains achieved by redirecting funds from military spending to pragmatic clinical research.

This generates benefits through two mechanisms:

1. Economic multiplier differential

Military spending generates economic multiplier effects of 0.6x (95% CI: 0.4x-0.9x)[26] (50 cents to $1 of economic value per dollar spent). Medical research generates multiplier effects of 4.3x (95% CI: 3x-6x)[24] ($2-3 of economic value per dollar spent). Reallocating funds from low-multiplier to high-multiplier activities produces measurable GDP gains.

2. Trial cost reduction through infrastructure efficiency

Traditional FDA Phase 3 trials cost $41K (95% CI: $20K-$120K)[101] per patient due to site setup costs, dedicated research staff, patient travel reimbursement, custom case report forms, and extensive monitoring requirements. Pragmatic trials leverage existing infrastructure: the Harvard meta-analysis of 108 embedded pragmatic trials found median costs of $97/patient[132], RECOVERY achieved $500 (95% CI: $400-$2.50K)/patient (NHS/COVID conditions), and ADAPTABLE achieved $929 (95% CI: $929-$1.40K)/patient under normal conditions. Our system projections use the conservative ADAPTABLE estimate ($929 (95% CI: $97-$3K)/patient).

This represents a 44.1x (95% CI: 39.4x-89.1x) cost reduction achieved by eliminating duplicative overhead and leveraging existing healthcare infrastructure.

The distribution below shows the uncertainty range for the cost reduction factor based on empirical data from 108+ pragmatic trials:

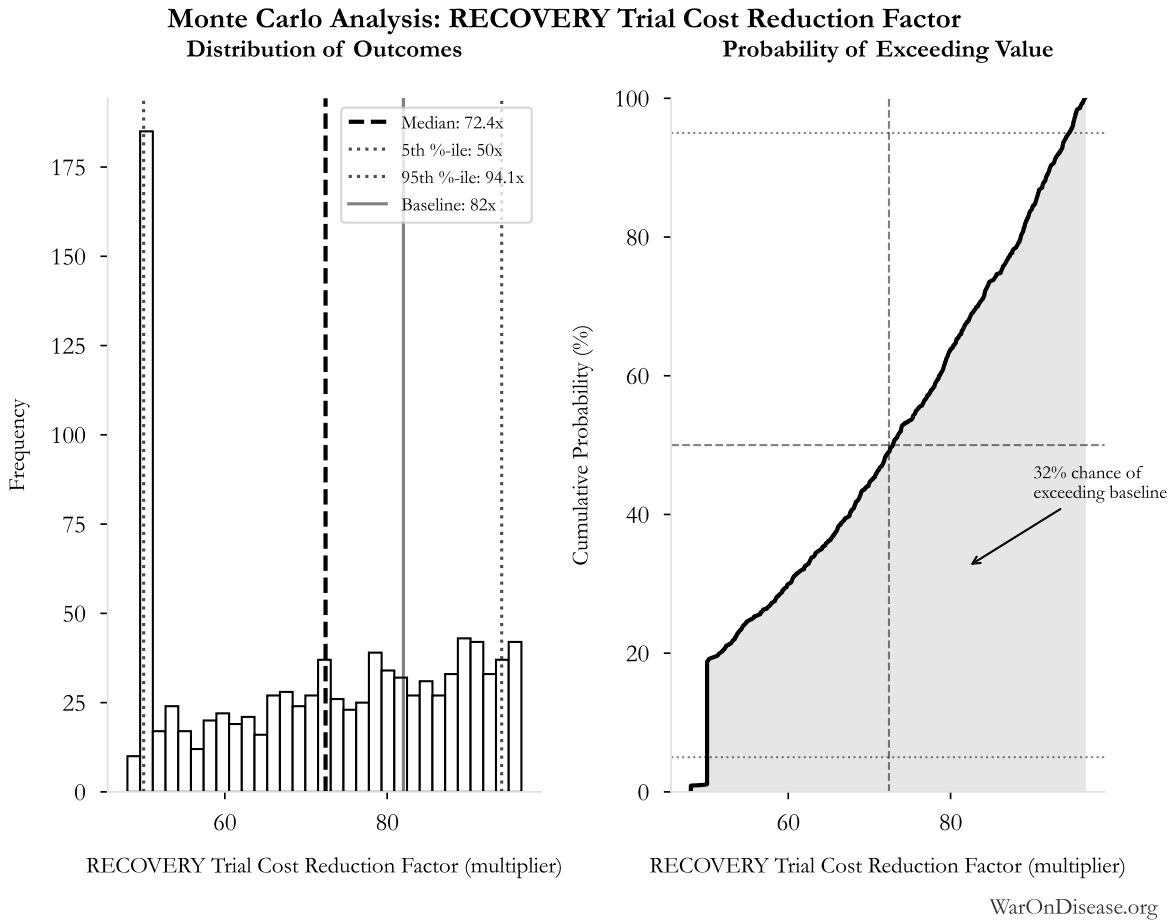


Figure 34: Monte Carlo Distribution: RECOVERY Trial Cost Reduction Factor (10,000 simulations)

Simulation Results Summary: RECOVERY Trial Cost Reduction Factor

Statistic	Value
Baseline (deterministic)	82x
Mean (expected value)	71.2x
Median (50th percentile)	72.4x
Standard Deviation	15.3x
90% Range (5th-95th percentile)	[50x, 94.1x]

The histogram shows the distribution of RECOVERY 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.

ROI Calculation

In human language: "How much value is generated per dollar spent?"

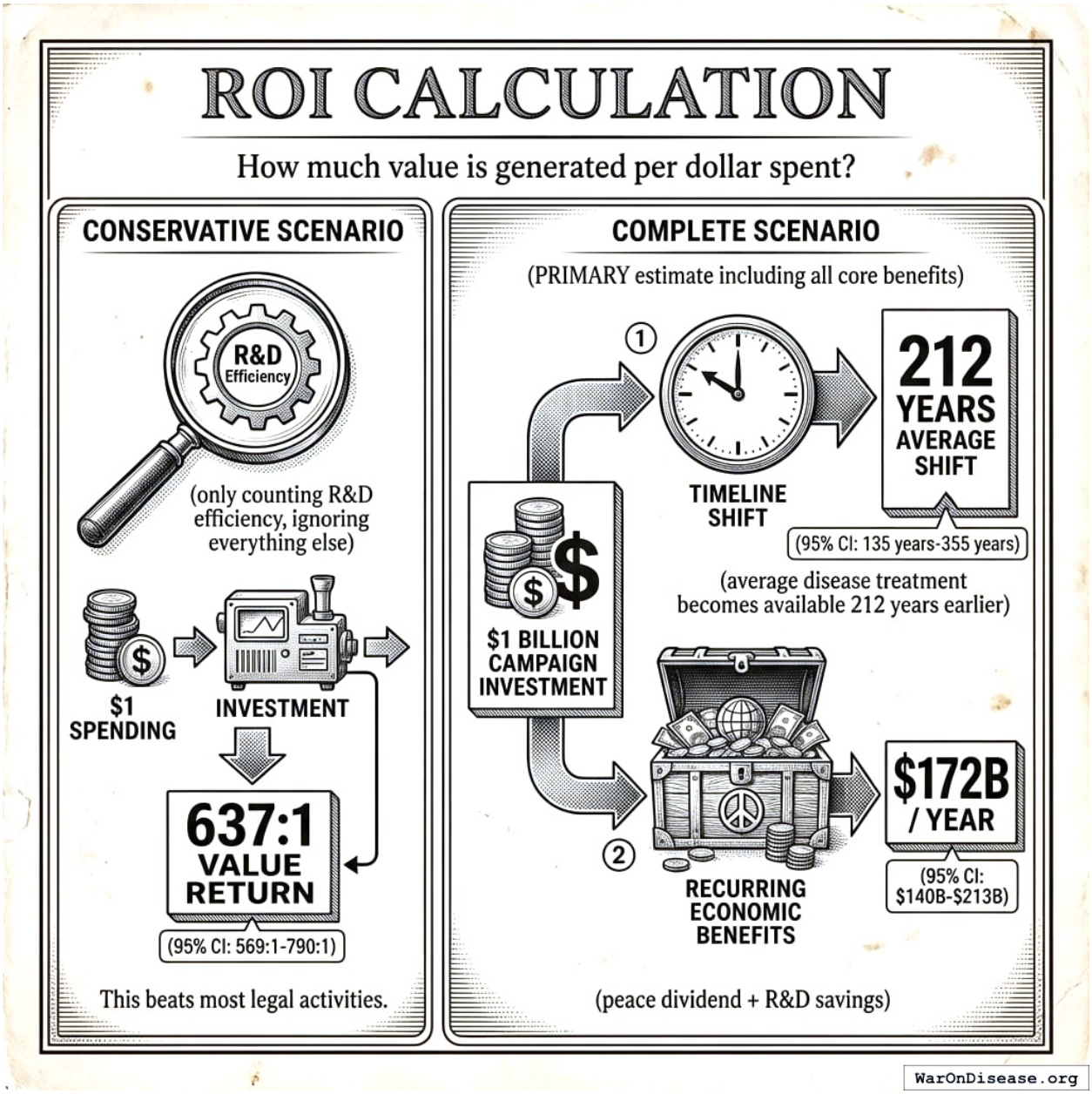


Figure 35: A comparison of ROI scenarios, contrasting the 637:1 return on R&D efficiency with the massive 212-year timeline shift and $172B in annual economic benefits in the complete model.

Conservative scenario (only counting R&D efficiency, ignoring everything else):

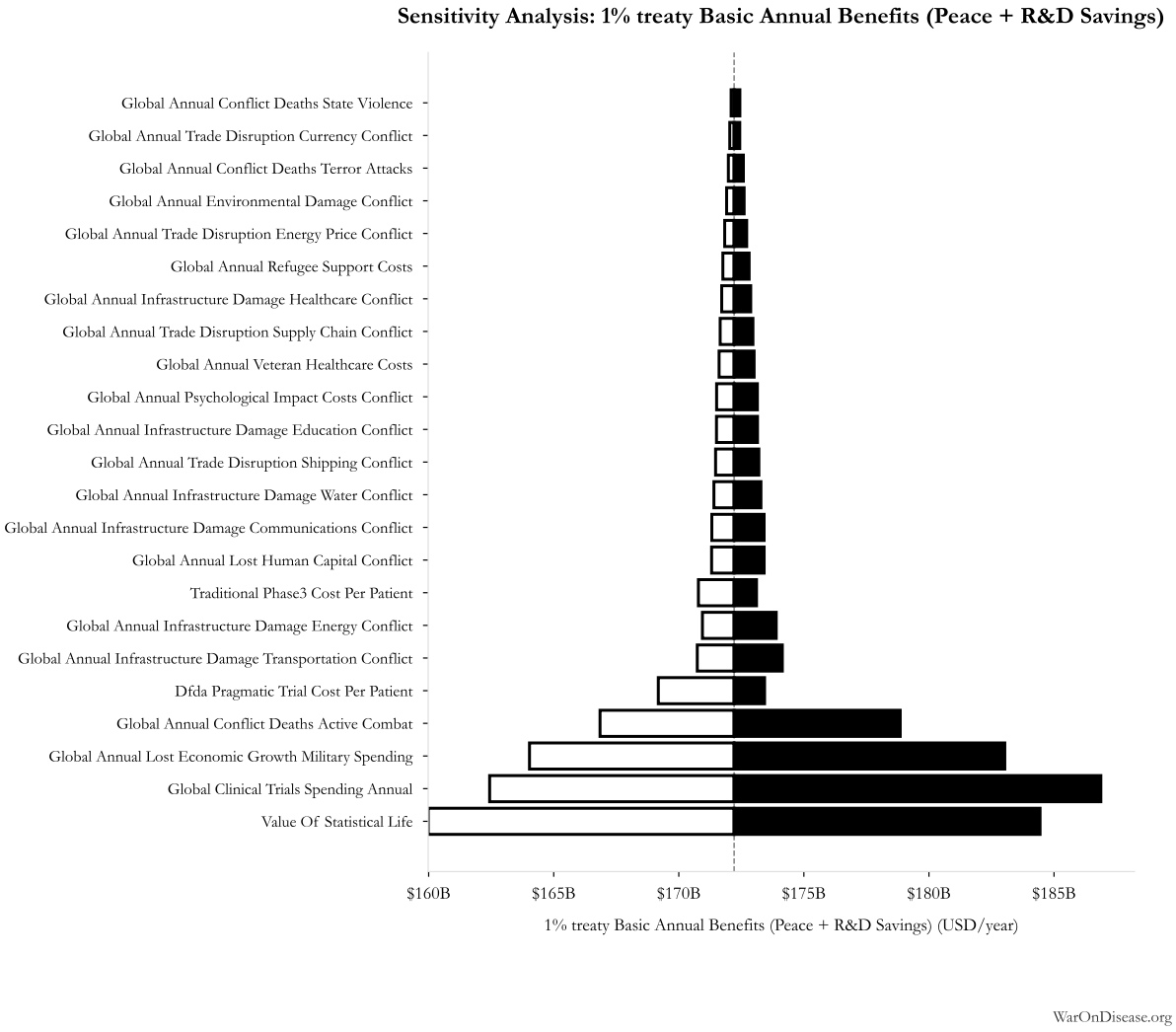
Spending $1 returns 637:1 (95% CI: 569:1-790:1). This beats most legal activities.

Complete scenario (PRIMARY estimate including all core benefits):

A $1 billion campaign investment could plausibly generate: (1) a 212 years (95% CI: 135 years-355 years)-year average timeline shift (the average disease treatment becomes available 212 years (95% CI: 135 years-355 years) earlier), plus (2) $172B (95% CI: $140B-$213B)/year in recurring economic benefits (peace dividend + R&D savings).

Combined Annual Benefits Uncertainty

The recurring annual benefits combine two streams: peace dividend ($114B (95% CI: $90.1B-$141B)/year) and R&D savings ($58.6B (95% CI: $49.2B-$73.1B)/year).



The tornado diagram shows that peace dividend magnitude and R&D savings dominate the uncertainty in combined annual benefits.

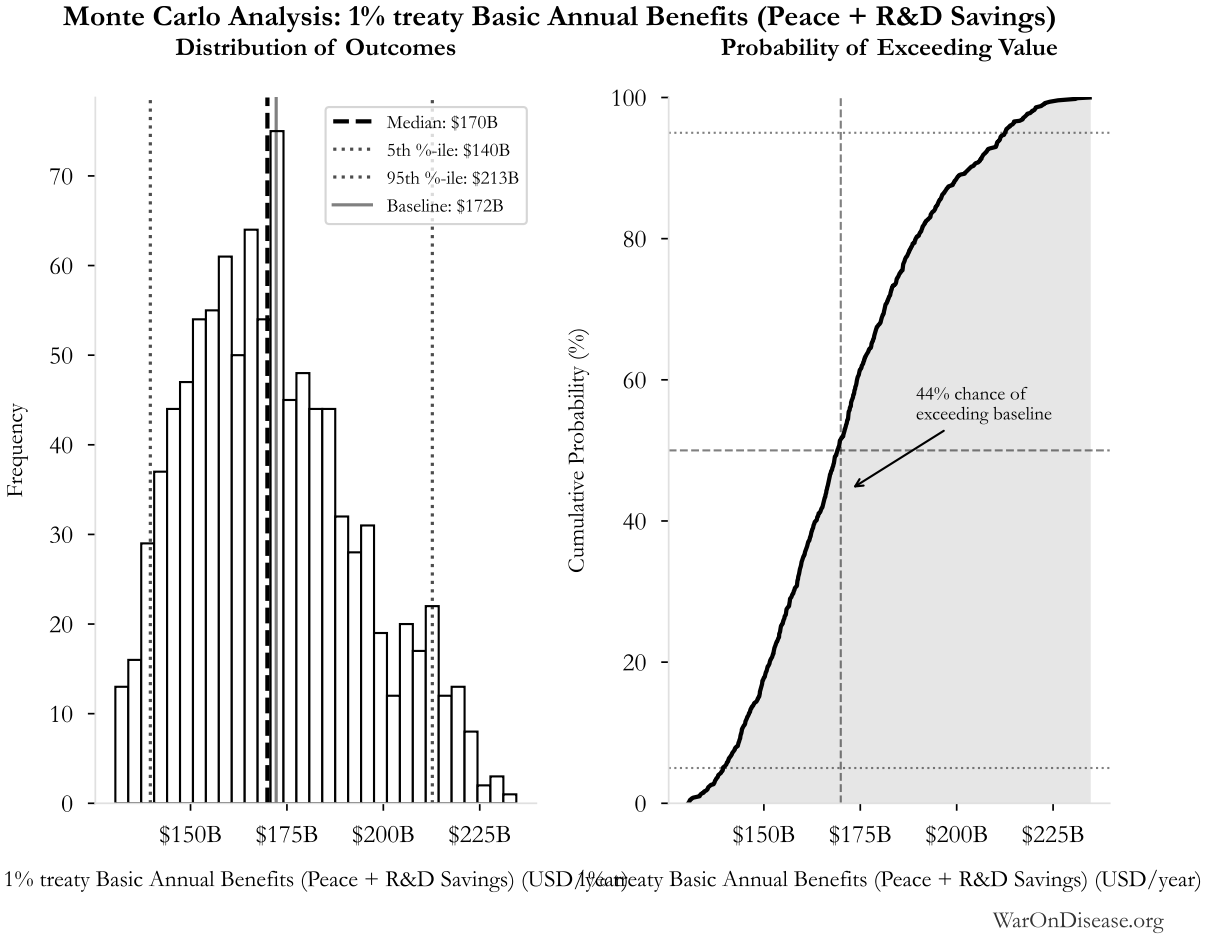


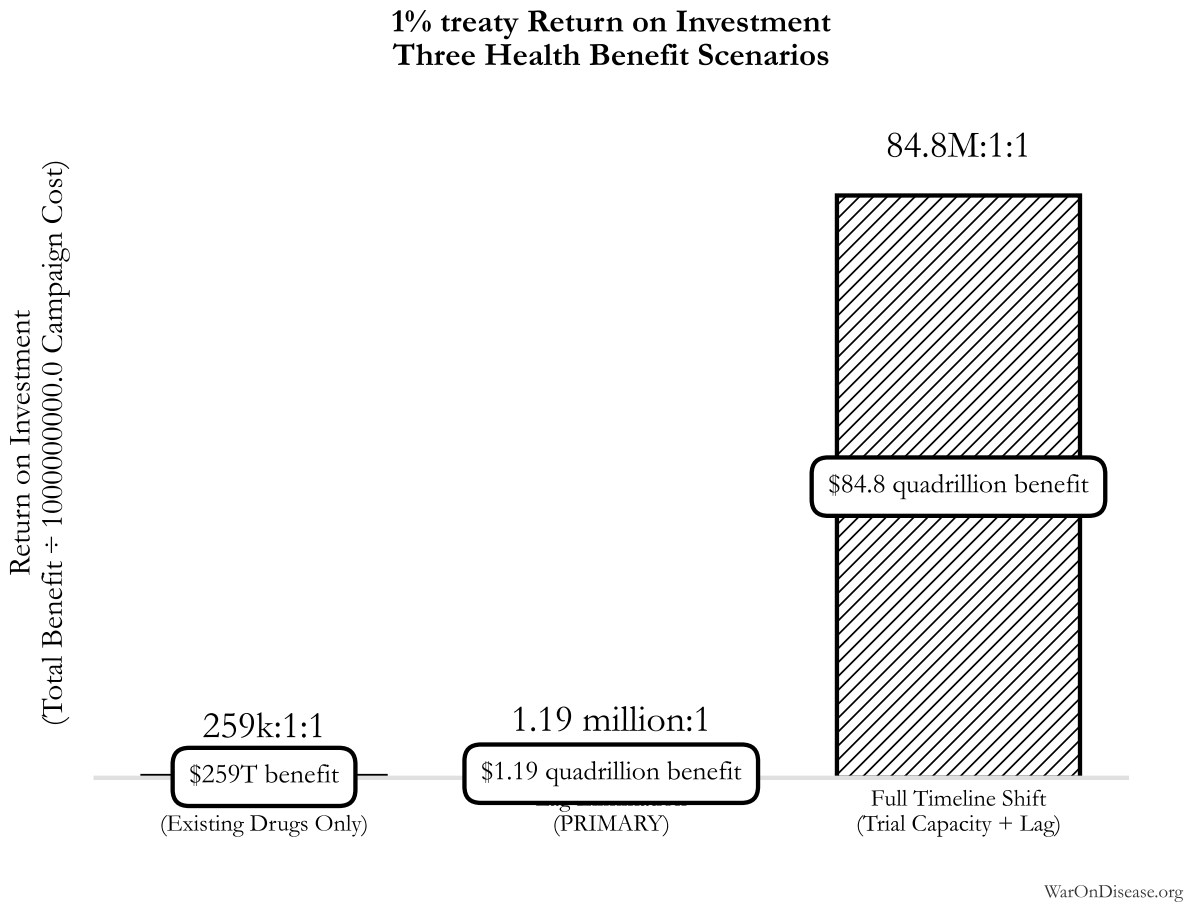
Figure 36: Monte Carlo Distribution: 1% treaty Basic Annual Benefits (Peace + R&D Savings) (10,000 simulations)

Simulation Results Summary: 1% treaty Basic Annual Benefits (Peace + R&D Savings)

Statistic	Value
Baseline (deterministic)	$172B
Mean (expected value)	$172B
Median (50th percentile)	$170B
Standard Deviation	$22.2B
90% Range (5th-95th percentile)	[$140B, $213B]

The histogram shows the distribution of 1% treaty Basic Annual Benefits (Peace + R&D Savings) 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.

Monte Carlo analysis confirms the intervention generates tens of billions in recurring annual value across all plausible scenarios.



Cost-Effectiveness Analysis

Health economists measure cost-effectiveness as **cost per DALY** (Disability-Adjusted Life Year): how much does it cost to avert one year of disease burden?

WHO says interventions under $50K[130] per DALY are "cost-effective." Most successful health programs cost $3,000-10,000[130] per DALY.

This system's upfront cost: **$0.0018 (95% CI: $0.0007-$0.0041) per DALY**

But here's the key: this intervention is **cost-saving**. The upfront implementation cost of $0.0018 (95% CI: $0.0007-$0.0041)/DALY unlocks $172B (95% CI: $140B-$213B)/year in recurring economic benefits.

Technical note: This uses "net present value," which is economist code for "future money is worth less than current money" (3% discount rate). For detailed analysis: full NPV methodology here.

Pragmatic Trials vs. NIH Standard Research

NIH Standard Research (Current Status Quo):

- **Standard NIH Portfolio:** $50K (95% CI: $20K-$100K)/QALY[65]

- **Pragmatic Trials:** $4.00 (95% CI: $1.71-$10)/QALY (from RECOVERY trial: $20M (95% CI: $15M-$25M) spent, 1.00 million lives (95% CI: 500 thousand lives-2.00 million lives) saved; note RECOVERY benefited from NHS/COVID conditions)

Efficiency gap: 12.5kx (95% CI: 2.3kx-51.5kx).

$$Cost_{pragmatic,QALY} = \frac{Cost_{RECOVERY}}{QALY_{RECOVERY}} = \frac{\$20M}{5M} = \$4$$

$$\text{where } QALY_{RECOVERY} = Lives_{RECOVERY} \times QALY_{COVID} = 1M \times 5 = 5M$$

$$k_{pragmatic:NIH} = \frac{Cost_{NIH,QALY}}{Cost_{pragmatic,QALY}} = \frac{\$50K}{\$4} = 12{,}500$$

$$\text{where } Cost_{pragmatic,QALY} = \frac{Cost_{RECOVERY}}{QALY_{RECOVERY}} = \frac{\$20M}{5M} = \$4$$

$$\text{where } QALY_{RECOVERY} = Lives_{RECOVERY} \times QALY_{COVID} = 1M \times 5 = 5M$$

Expected Value Under Political Uncertainty

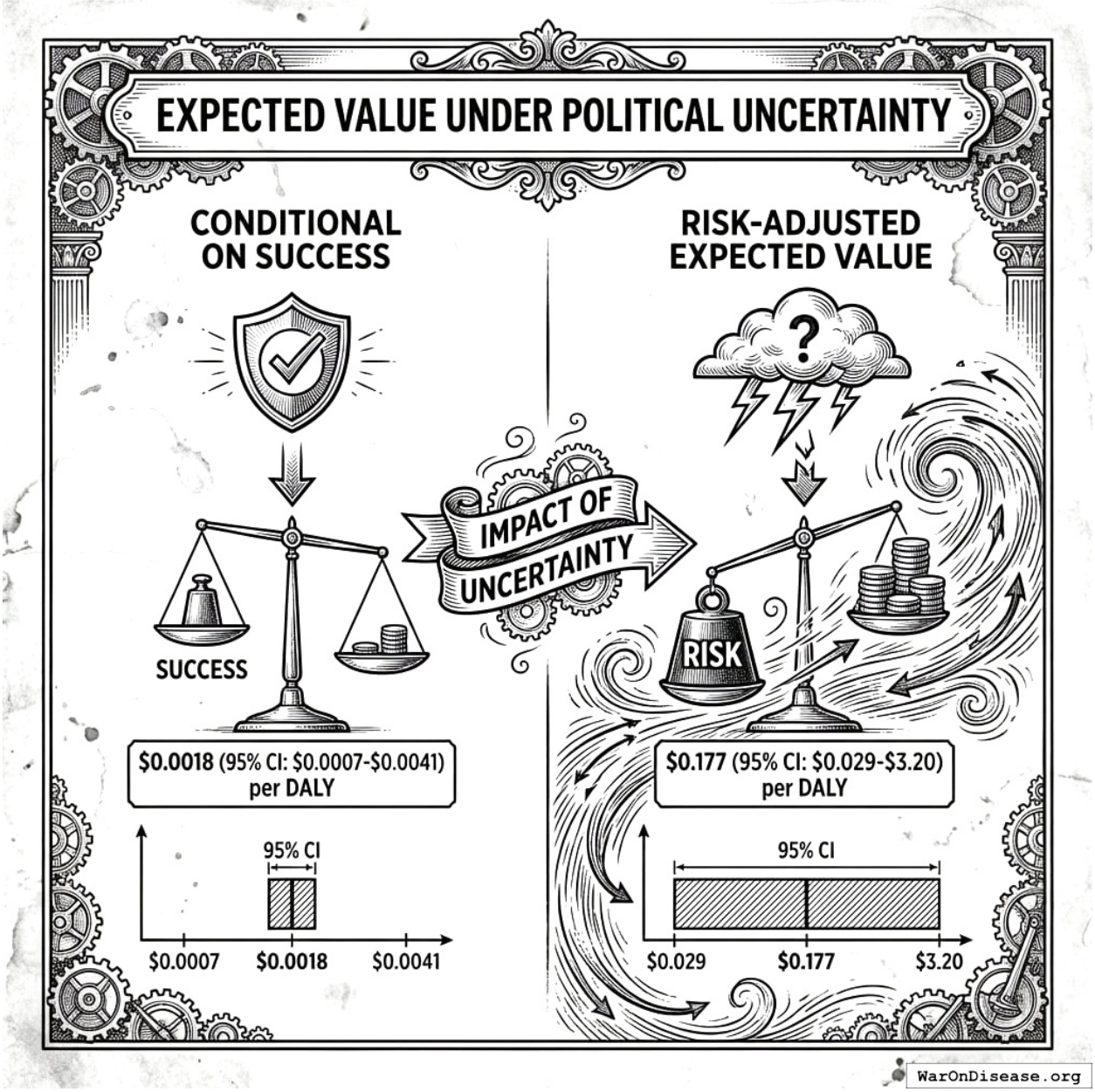
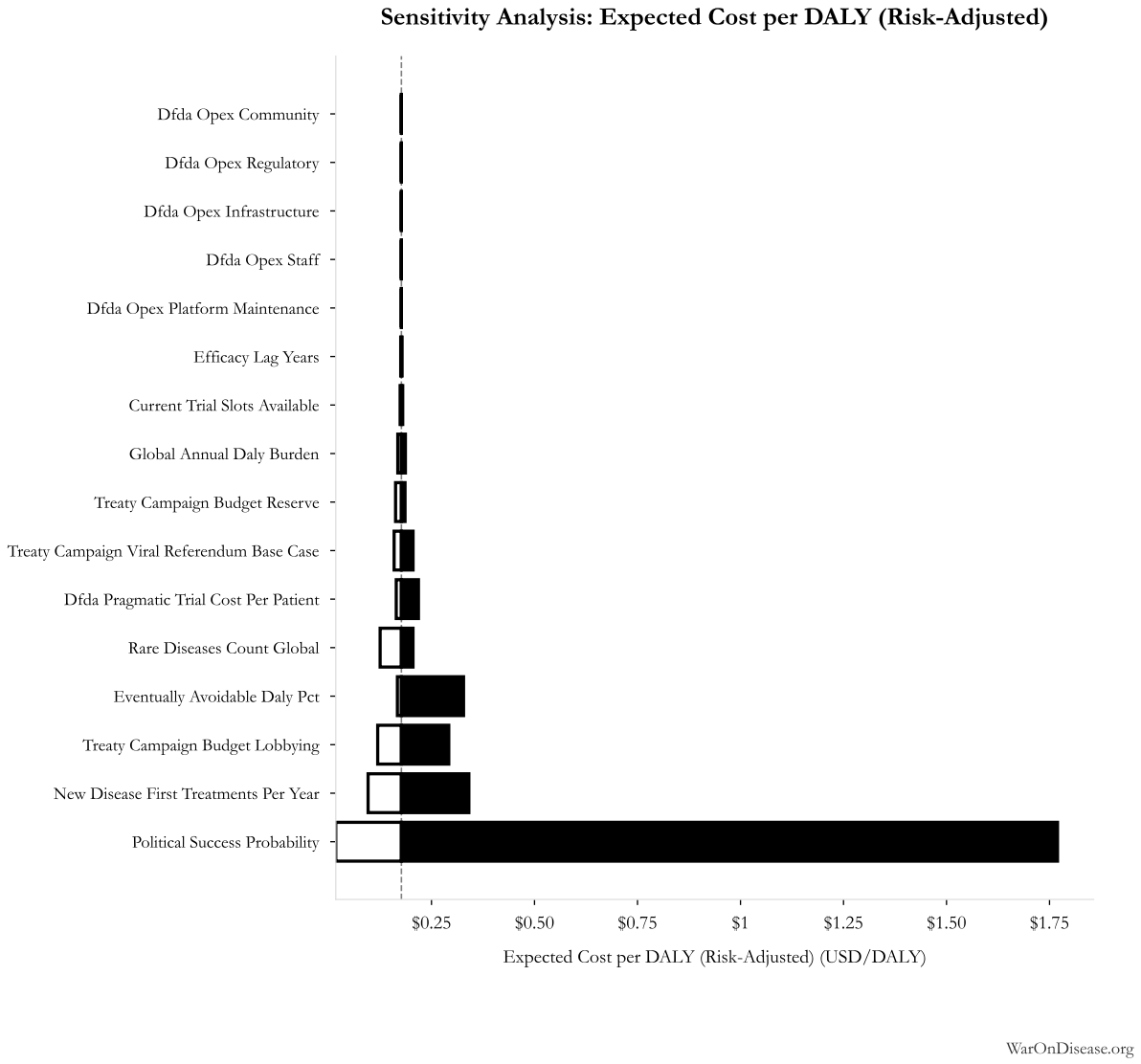


Figure 37: Comparison of expected value per DALY between a conditional success scenario and a risk-adjusted scenario, showing the impact of political uncertainty and 95% confidence intervals.

Conditional on success: $0.0018 (95% CI: $0.0007-$0.0041) per DALY

Risk-adjusted expected value: $0.177 (95% CI: $0.029-$3.20) per DALY

Uncertainty in Risk-Adjusted Cost-Effectiveness



The tornado diagram shows that political success probability dominates uncertainty in risk-adjusted cost-effectiveness. Even at conservative political success estimates, expected cost per DALY remains highly competitive with top global health interventions.

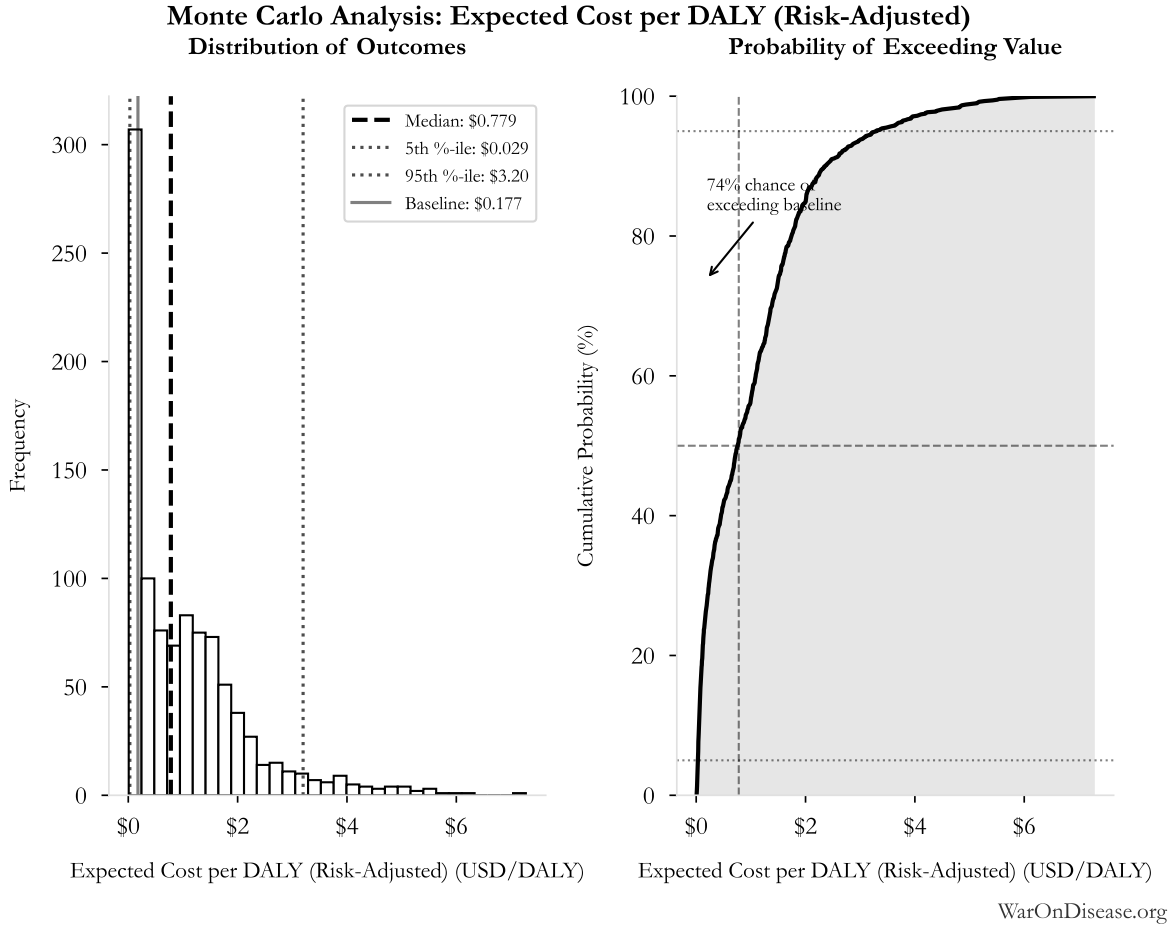


Figure 38: Monte Carlo Distribution: Expected Cost per DALY (Risk-Adjusted) (10,000 simulations)

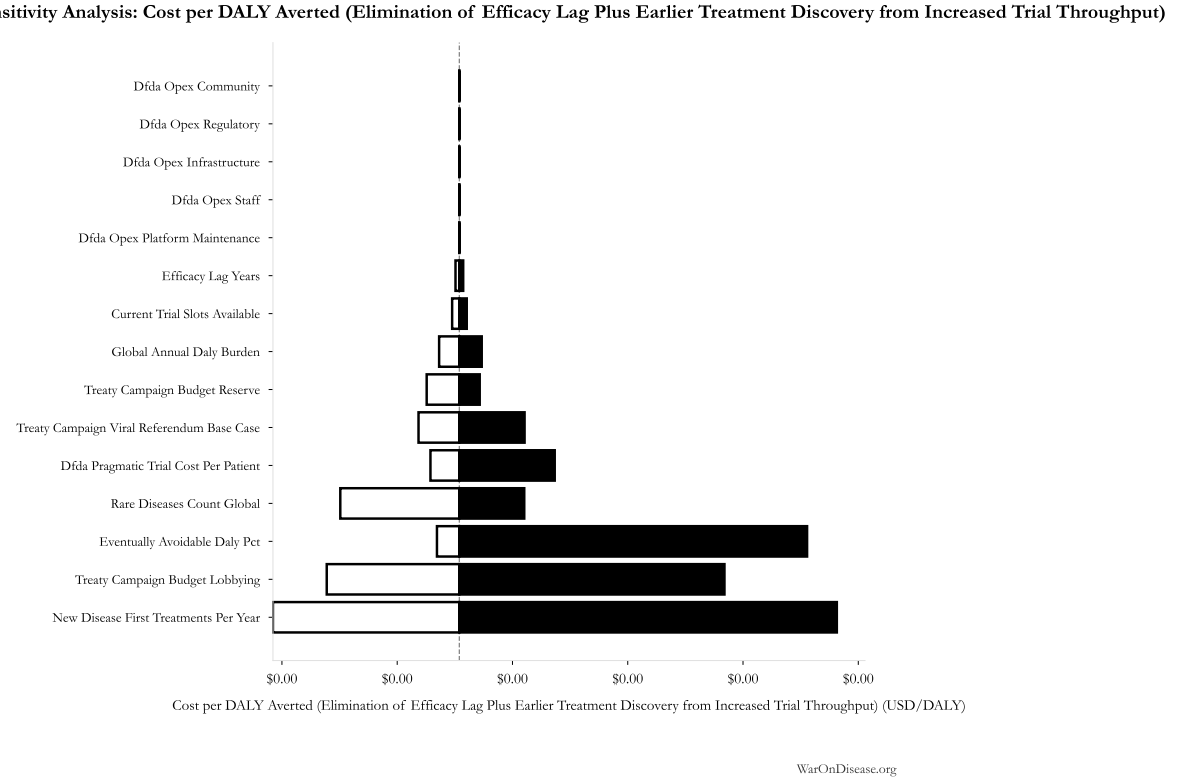
Simulation Results Summary: Expected Cost per DALY (Risk-Adjusted)

Statistic	Value
Baseline (deterministic)	$0.177
Mean (expected value)	$1.06
Median (50th percentile)	$0.779
Standard Deviation	$1.12
90% Range (5th-95th percentile)	[$0.029, $3.20]

The histogram shows the distribution of Expected Cost per DALY (Risk-Adjusted) 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.

Monte Carlo simulation confirms that accounting for political risk, the 95% confidence interval maintains dominance over established interventions.

Uncertainty in Cost-Effectiveness (Conditional on Success)



The tornado diagram shows that timeline shift assumptions and discount rate dominate uncertainty in cost-effectiveness. Even under conservative parameter assumptions, the intervention remains highly cost-effective.

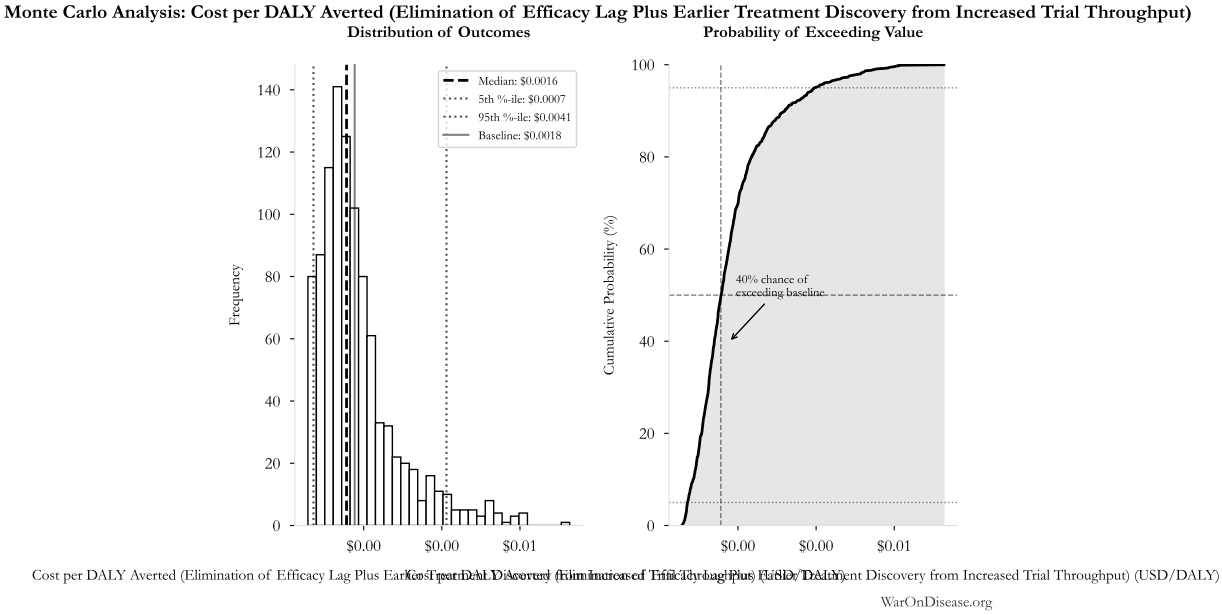


Figure 39: Monte Carlo Distribution: Cost per DALY Averted (Elimination of Efficacy Lag Plus Earlier Treatment Discovery from Increased Trial Throughput) (10,000 simulations)

Simulation Results Summary: Cost per DALY Averted (Elimination of Efficacy Lag Plus Earlier Treatment Discovery from Increased Trial Throughput)

Statistic	Value
Baseline (deterministic)	$0.0018
Mean (expected value)	$0.0019
Median (50th percentile)	$0.0016
Standard Deviation	$0.0011
90% Range (5th-95th percentile)	[$0.0007, $0.0041]

The histogram shows the distribution of Cost per DALY Averted (Elimination of Efficacy Lag Plus Earlier Treatment Discovery from Increased Trial Throughput) 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.

Monte Carlo analysis confirms the 95% confidence interval for cost per DALY remains well below $1/DALY, maintaining dominance.

Accounting for political uncertainty (1% (95% CI: 0.1%-10%)), this remains 503x (95% CI: 29.9x-3.0kx) more cost-effective than bed nets ($89 (95% CI: $78-$100)/DALY) and comparable to deworming, the gold standard.

For context: Ottawa Treaty[76] (landmine ban) was called a "bold gamble" that succeeded with 122 states signing[76] in just 14 months.

Policy Advocacy Leverage vs Direct Funding

A natural question: Why not skip the $1B treaty campaign and simply convince major philanthropists (Gates Foundation, Open Philanthropy) or expand NIH budgets to directly fund $21.8B/year for clinical trials?

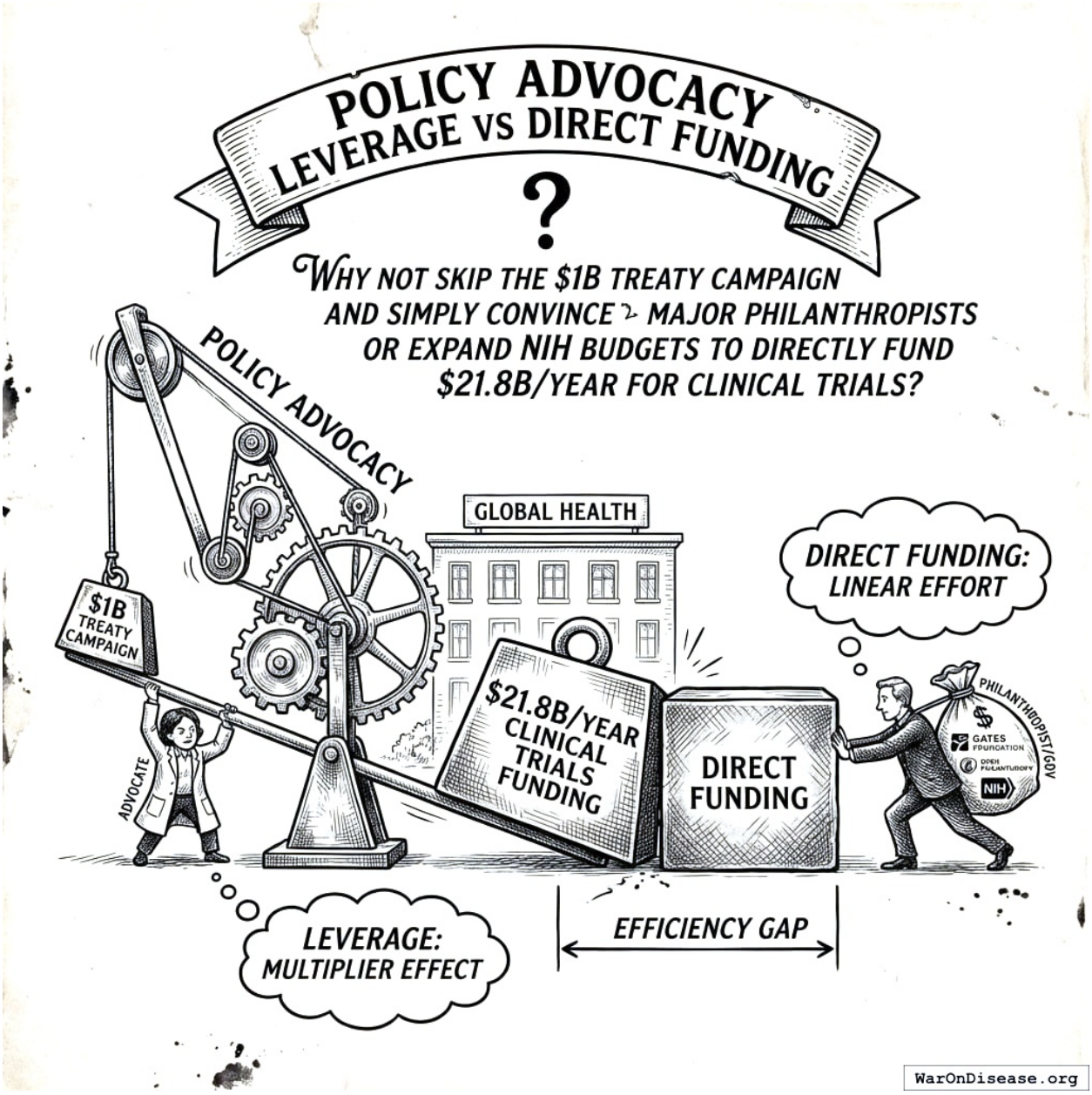


Figure 40: A comparison of two funding models: policy advocacy leverage ($1B campaign for a treaty) versus direct funding ($21.8B/year from existing budgets).

Why Billionaires Buy Lottery Tickets Instead of the Casino

The world's richest people (who will die of cancer, heart disease, or aging just like everyone else) are not exclusively focused on passing this treaty. This is arguably the single most puzzling fact about

modern philanthropy.

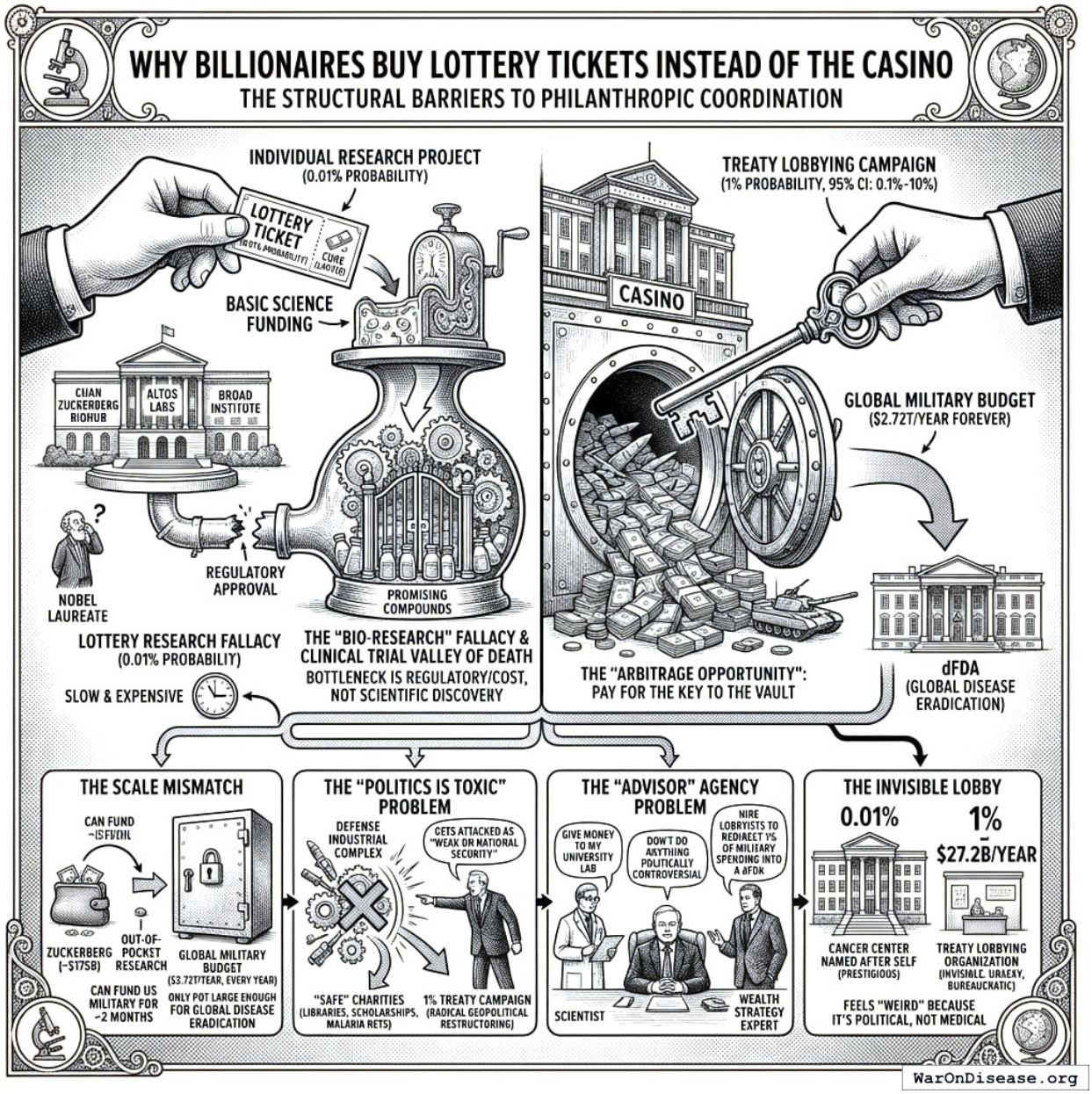


Figure 41: A comparison between the 'Science Bet' (funding individual labs with low success probability) and the 'Lobbying Bet' (using capital to unlock global military budgets via a treaty).

Four structural barriers explain this coordination failure:

1. The "Bio-Research" Fallacy (buying the wrong asset): Billionaires spend billions on health, but on the wrong part of the supply chain. They build labs (Chan Zuckerberg Biohub, Altos Labs, Broad Institute) and hire Nobel laureates, assuming the bottleneck is *scientific discovery*. It isn't. We have thousands of promising compounds on shelves. The real bottleneck is the **Clinical Trial Valley of Death**: proving drugs work costs $100M-$1B per drug. No amount of "basic science" funding solves the regulatory/cost engine being too slow and expensive. Building a lab

wing named after yourself is prestigious; funding a "Treaty Lobbying Organization" is invisible, unsexy, and bureaucratic.

2. The Scale Mismatch: Mark Zuckerberg is worth ~$175B. If he spent *every penny*, he could fund the US military for approximately **2 months**. The only pot of money large enough to fund global disease eradication is the **Global Military Budget** ($2.72T/year, *every year*). Billionaires try to pay for the *research* out of pocket (which runs out) instead of paying for the *key* (the treaty) that unlocks the government's vault.

3. The "Politics is Toxic" Problem: To pass a 1% Treaty, you fight the Defense Industrial Complex. Any billionaire saying "take 1% of military budgets" gets immediately attacked as "weak on national security." Most billionaires are risk-averse regarding public image, preferring "safe" charities (libraries, scholarships, malaria nets) over "radical" geopolitical restructuring.

4. The "Advisor" Agency Problem: Who advises billionaires? Scientists say "give money to my university lab." Wealth managers say "don't do anything politically controversial." Almost no one in a billionaire's inner circle is a "Grand Strategy" expert who would say: *"The most efficient use of your capital is not to hire scientists, but to hire lobbyists to force governments to redirect 1% of military spending into a decentralized clinical trial framework."*

The arbitrage opportunity: Billionaires are buying **lottery tickets** (individual research projects with 0.01% probability of curing cancer) when they should be buying the **casino** (changing the rules via treaty). A billionaire spends $1B on a cancer center with ~0.01% probability of success. The same $1B spent on treaty campaign has ~1% (95% CI: 0.1%-10%) probability of unlocking $27.2B/year forever. The "lobbying" bet is mathematically thousands of times better than the "science" bet, but feels "weird" because it's political, not medical.

Numerical Comparison: Treaty vs Direct Funding

The answer reveals the treaty campaign's massive leverage advantage:

Direct Funding Scenario

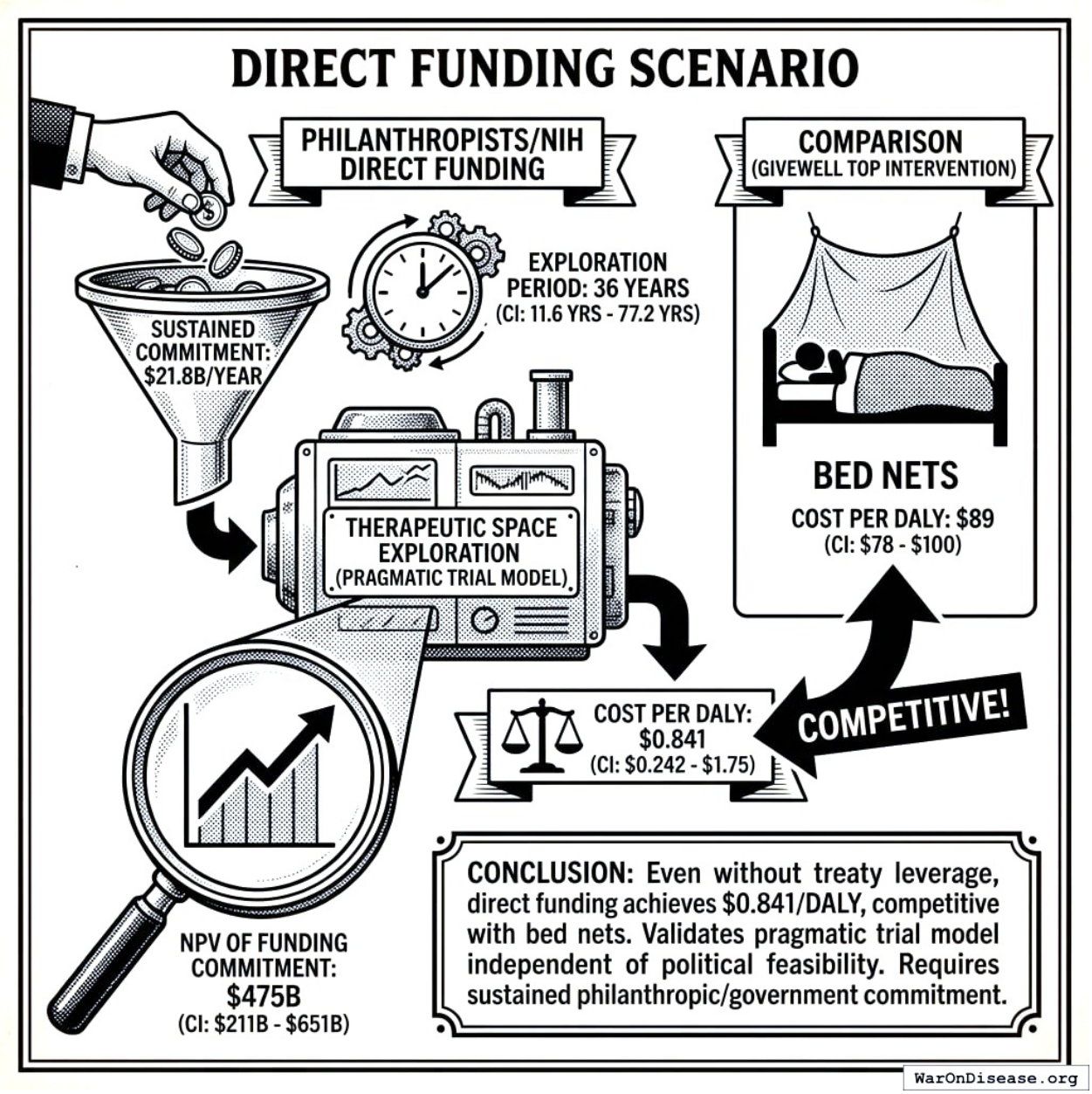


Figure 42: A comparison showing the cost-effectiveness of direct funding for therapeutic exploration ($0.84) versus bed nets ($89) per disability-adjusted life year (DALY), alongside the 36-year funding timeline.

If philanthropists/NIH directly funded $21.8B/year for 36 years (95% CI: 11.6 years-77.2 years) (therapeutic space exploration period):

- **NPV of funding commitment**: $475B (95% CI: $211B-$651B)
- **Cost per DALY**: $0.841 (95% CI: $0.242-$1.75)
- **Still cost-effective** vs bed nets ($89 (95% CI: $78-$100)/DALY), but requires sustained philanthropic/government commitment

$$NPV_{direct} = Funding_{ann} \times \frac{1 - (1 + r)^{-T}}{r}$$

$$Cost_{direct,DALY} = \frac{NPV_{direct}}{DALYs_{max}} = \frac{\$475B}{565B} = \$0.841$$

$$\text{where } NPV_{direct} = Funding_{ann} \times \frac{1-(1+r)^{-T}}{r}$$

$$\text{where } Treasury_{RD,ann}$$
$$= Funding_{treaty} - Payout_{bond,ann} - Funding_{political,ann}$$
$$= \$27.2B - \$2.72B - \$2.72B$$
$$= \$21.8B$$

$$\text{where } Funding_{treaty}$$
$$= Spending_{mil} \times Reduce_{treaty}$$
$$= \$2.72T \times 1\%$$
$$= \$27.2B$$

$$\text{where } Payout_{bond,ann}$$
$$= Funding_{treaty} \times Pct_{bond}$$
$$= \$27.2B \times 10\%$$
$$= \$2.72B$$

$$\text{where } Funding_{treaty}$$
$$= Spending_{mil} \times Reduce_{treaty}$$
$$= \$2.72T \times 1\%$$
$$= \$27.2B$$

$$\text{where } Funding_{political,ann}$$
$$= Funding_{treaty} \times Pct_{political}$$
$$= \$27.2B \times 10\%$$
$$= \$2.72B$$

$$\text{where } Funding_{treaty}$$
$$= Spending_{mil} \times Reduce_{treaty}$$
$$= \$2.72T \times 1\%$$
$$= \$27.2B$$

$$\text{where } T_{queue,dFDA} = \frac{T_{queue,SQ}}{k_{capacity}} = \frac{443}{12.3} = 36$$

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

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

$$\text{where } k_{capacity} = \frac{N_{fundable,ann}}{Slots_{curr}} = \frac{23.4M}{1.9M} = 12.3$$

$$\text{where } N_{fundable,ann}$$
$$= \frac{Subsidies_{trial,ann}}{Cost_{pragmatic,pt}}$$
$$= \frac{\$21.7B}{}$$

Direct Funding Still Excellent

Even without treaty leverage, direct funding achieves **$0.841 (95% CI: $0.242-$1.75)/DALY** - competitive with GiveWell's top interventions (bed nets at $89 (95% CI: $78-$100)/DALY). This validates the pragmatic trial model independent of political feasibility.

Treaty Campaign Advantage

Conditional leverage (if treaty succeeds): 475x (95% CI: 329x-462x)

The $1B treaty campaign unlocks the same $475B (95% CI: $211B-$651B) in government funding ($21.8B/year for 36 years (95% CI: 11.6 years-77.2 years)) that would otherwise require direct philanthropic commitment. Both approaches achieve the same 565 billion DALYs (95% CI: 361 billion DALYs-877 billion DALYs) benefit by exploring the therapeutic space 12.3x (95% CI: 4.19x-61.3x) faster.

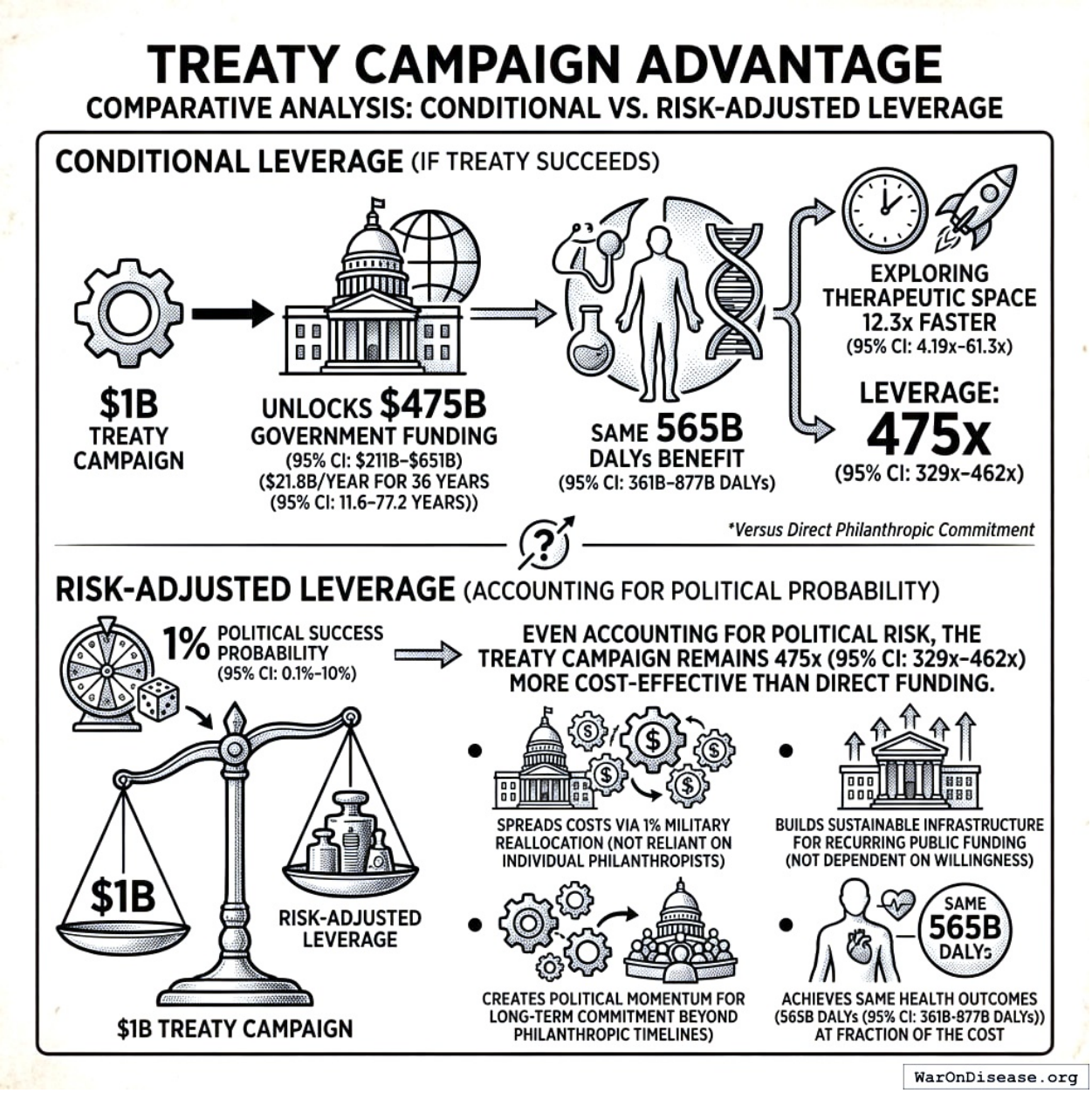


Figure 43: A comparison of the Treaty Campaign versus Direct Funding, illustrating how a $1B investment leverages $475B in government funding to achieve identical health benefits through a 475x leverage mechanism.

Risk-adjusted leverage (accounting for 1% (95% CI: 0.1%-10%) political success probability):

$$
\begin{aligned}
&Leverage_{treaty} \\
&= \frac{Cost_{direct,DALY}}{Cost_{treaty,DALY}} \\
&= \frac{\$0.841}{\$0.00177} \\
&= 475
\end{aligned}
$$

$$\text{where } Cost_{direct,DALY} = \frac{NPV_{direct}}{DALYs_{max}} = \frac{\$475B}{565B} = \$0.841$$

$$\text{where } NPV_{direct} = Funding_{ann} \times \frac{1-(1+r)^{-T}}{r}$$

$$
\begin{aligned}
&\text{where } Treasury_{RD,ann} \\
&= Funding_{treaty} - Payout_{bond,ann} - Funding_{political,ann} \\
&= \$27.2B - \$2.72B - \$2.72B \\
&= \$21.8B
\end{aligned}
$$

$$
\begin{aligned}
&\text{where } Funding_{treaty} \\
&= Spending_{mil} \times Reduce_{treaty} \\
&= \$2.72T \times 1\% \\
&= \$27.2B
\end{aligned}
$$

$$
\begin{aligned}
&\text{where } Payout_{bond,ann} \\
&= Funding_{treaty} \times Pct_{bond} \\
&= \$27.2B \times 10\% \\
&= \$2.72B
\end{aligned}
$$

$$
\begin{aligned}
&\text{where } Funding_{treaty} \\
&= Spending_{mil} \times Reduce_{treaty} \\
&= \$2.72T \times 1\% \\
&= \$27.2B
\end{aligned}
$$

$$
\begin{aligned}
&\text{where } Funding_{political,ann} \\
&= Funding_{treaty} \times Pct_{political} \\
&= \$27.2B \times 10\% \\
&= \$2.72B
\end{aligned}
$$

$$
\begin{aligned}
&\text{where } Funding_{treaty} \\
&= Spending_{mil} \times Reduce_{treaty} \\
&= \$2.72T \times 1\% \\
&= \$27.2B
\end{aligned}
$$

$$\text{where } T_{queue,dFDA} = \frac{T_{queue,SQ}}{k_{capacity}} = \frac{443}{12.3} = 36$$

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

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

Even accounting for political risk, the treaty campaign remains 475x (95% CI: 329x-462x) more cost-effective than direct funding. The treaty approach:

1. **Spreads costs** across governments via 1% military reallocation (not reliant on individual philanthropists)
2. **Builds sustainable infrastructure** for recurring public funding (not dependent on continued philanthropic willingness)
3. **Creates political momentum** for long-term commitment beyond philanthropic timelines
4. **Achieves same health outcomes** (565 billion DALYs (95% CI: 361 billion DALYs-877 billion DALYs)) at fraction of the cost

Detailed NPV Formulas

NPV of Costs

$$\begin{aligned} & Cost_{dFDA,total} \\ &= PV_{OPEX} + Cost_{upfront,total} \\ &= \$342M + \$270M \\ &= \$611M \end{aligned}$$

$$\text{where } PV_{OPEX} = OPEX_{ann} \times \frac{1-(1+r)^{-T}}{r}$$

$$\begin{aligned} & \text{where } OPEX_{total} \\ &= OPEX_{ann} + OPEX_{DIH,ann} \\ &= \$18.9M + \$21.1M \\ &= \$40M \end{aligned}$$

$$\begin{aligned} & \text{where } Cost_{upfront,total} \\ &= Cost_{upfront} + Cost_{DIH,init} \\ &= \$40M + \$230M \\ &= \$270M \end{aligned}$$

where C_0 is upfront costs (platform development, legal structure, data integration), $C_{\text{op}}(t)$ is annual operating costs in year t (maintenance, analysis, administration), r is the discount rate (3%), and T is the time horizon (10 years).

NPV of Benefits

Note: The NPV calculation includes **only annual recurring R&D savings**, not the timeline shift benefits. The full timeline shift (~212 years (95% CI: 135 years-355 years) on average, combining treatment acceleration and efficacy lag elimination) is a separate benefit analyzed below. This section focuses on the efficacy lag component (8.2 years (95% CI: 4.85 years-11.5 years)) for NPV purposes. See Regulatory Mortality Analysis.

Annual benefits $S(t)$ are calculated as:

$$S(t) = p(t)\alpha R_d$$

where $p(t)$ is the adoption rate at year t (gradual ramp-up over 5 years), α is the fraction of R&D costs saved (97.7% (95% CI: 97.5%-98.9%) baseline), and R_d is annual global clinical trial spending ($60B (95% CI: $50B-$75B)[42]).

The NPV of benefits (R&D savings only):

Return on Investment

$$ROI_{RD} = \frac{NPV_{RD}}{Cost_{dFDA,total}} = \frac{\$389B}{\$611M} = 637$$

$$\text{where } NPV_{RD} = \sum_{t=1}^{10} \frac{Savings_{RD,ann} \times \frac{\min(t,5)}{5}}{(1+r)^t}$$

$$\text{where } Savings_{RD,ann}$$
$$= Benefit_{RD,ann} - OPEX_{dFDA}$$
$$= \$58.6B - \$40M$$
$$= \$58.6B$$

$$\text{where } Benefit_{RD,ann}$$
$$= Spending_{trials} \times Reduce_{pct}$$
$$= \$60B \times 97.7\%$$
$$= \$58.6B$$

$$\text{where } Reduce_{pct}$$
$$= 1 - \frac{Cost_{pragmatic,pt}}{Cost_{P3,pt}}$$
$$= 1 - \frac{\$929}{\$41K}$$
$$= 97.7\%$$

$$\text{where } OPEX_{dFDA}$$
$$= Cost_{platform} + Cost_{staff} + Cost_{infra}$$
$$+Cost_{regulatory} + Cost_{community}$$
$$= \$15M + \$10M + \$8M + \$5M + \$2M$$
$$= \$40M$$

$$\text{where } Cost_{dFDA,total}$$
$$= PV_{OPEX} + Cost_{upfront,total}$$
$$= \$342M + \$270M$$
$$= \$611M$$

$$\text{where } PV_{OPEX} = OPEX_{ann} \times \frac{1-(1+r)^{-T}}{r}$$

$$\text{where } OPEX_{total}$$
$$= OPEX_{ann} + OPEX_{DIH,ann}$$
$$= \$18.9M + \$21.1M$$
$$= \$40M$$

$$\text{where } Cost_{upfront,total}$$
$$= Cost_{upfront} + Cost_{DIH,init}$$
$$= \$40M + \$230M$$
$$= \$270M$$

This yields the conservative estimate of 637:1 (95% CI: 569:1-790:1) ROI over 10 years.

Important distinction: The NPV calculation above includes only annual recurring R&D savings. However, the cost per DALY calculations below **do include** the full ~212 years (95% CI: 135 years-355 years)-year average timeline shift (treatment acceleration + efficacy lag elimination), as this represents the primary health benefit. See Regulatory Mortality Analysis.

For the framework's cost per health benefit averted (using the full ~212 years (95% CI: 135 years-355 years)-year average timeline shift):

Cost per DALY averted: $0.0018 (95% CI: $0.0007-$0.0041)

This represents $0.0018 (95% CI: $0.0007-$0.0041) per year of healthy life gained. This extremely low cost per DALY, combined with net economic benefits that exceed costs, qualifies this as a cost-saving intervention under model assumptions. Standard willingness-to-pay thresholds are $50K-$150K (95% CI: $100K-$199K)[91] per QALY; cost-saving interventions are generally prioritized regardless of threshold.

NPV of Regulatory Delay Avoidance

The conservative NPV above excludes the benefit from eliminating the regulatory delay. This section calculates the NPV of just the **efficacy lag component** (8.2 years (95% CI: 4.85 years-11.5 years)) - a subset of the full ~212 years (95% CI: 135 years-355 years)-year timeline shift.

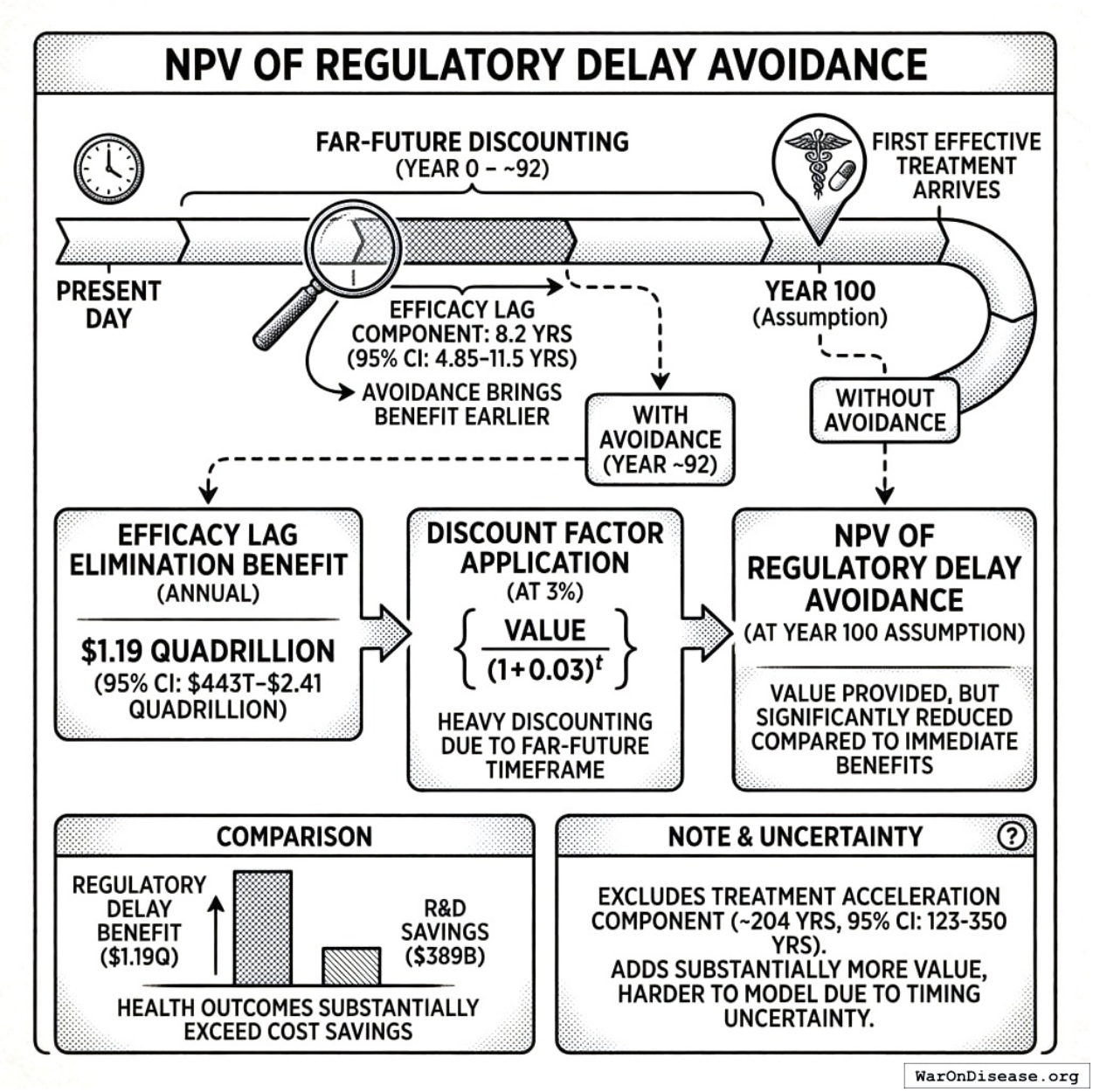


Figure 44: A timeline comparison showing how eliminating an 8.2-year regulatory delay shifts future medical benefits earlier in a 100-year horizon, illustrating the impact of long-term discounting on Net Present Value.

Assumption: We assume diseases receive first effective treatments 100 years in the future on average. If first effective treatments arrive at year 100, eliminating the regulatory delay brings them 8.2 years (95% CI: 4.85 years-11.5 years) earlier. Far-future discounting dramatically reduces NPV compared to immediate benefits, but the delay avoidance still provides value.

The NPV of regulatory delay avoidance (assuming average time to first effective treatment of 100 years):

Using the efficacy lag elimination benefit of $1.19 quadrillion (95% CI: $443T-$2.41 quadrillion),

applied across 8.2 years (95% CI: 4.85 years-11.5 years) with future discounting at 3%.

This yields an NPV assuming first effective treatments are discovered 100 years in the future on average. The discount factor at year ~92 (when benefits begin) makes far-future benefits much smaller than if they occurred immediately.

Note: This NPV calculation covers only the efficacy lag component (8.2 years (95% CI: 4.85 years-11.5 years)). The treatment acceleration component (~204 years (95% CI: 123 years-350 years) on average) would add substantially more value, but is harder to model with NPV due to uncertainty in when each disease receives its first treatment.

Comparison: The regulatory delay avoidance benefit ($1.19 quadrillion (95% CI: $443T-$2.41 quadrillion) annually) is substantially larger than the conservative R&D-only benefit ($389B (95% CI: $327B-$485B):1 ROI), demonstrating that health outcomes substantially exceed cost savings even with far-future discounting. Note: These are separate benefit streams; the delay avoidance benefit does not include R&D savings.

Why this matters: Eliminating the regulatory delay still provides value even if first effective treatments are 100 years away on average, but far-future discounting means the NPV is much smaller. The actual value depends on when diseases actually receive first effective treatments, which varies by disease category. Some may receive treatments in 10-20 years (moderate discounting), others in 50-100+ years (heavy discounting). The 100-year assumption is conservative for many diseases that may take decades to treat effectively.

Quality-Adjusted Life Year (QALY) Valuation

QALYs represent the standard metric in health economics for comparing health interventions across different conditions and treatment modalities. One QALY equals one year of life in perfect health.

QALY Calculation Model

The total DALYs averted (565 billion DALYs (95% CI: 361 billion DALYs-877 billion DALYs)) from the ~212 years (95% CI: 135 years-355 years)-year timeline shift derives from two complementary mechanisms:

1. **Efficacy Lag Elimination** (8.2 years (95% CI: 4.85 years-11.5 years)): Treatments reach patients immediately after Phase I safety, rather than waiting for Phase II/III efficacy trials
2. **Trial Capacity Expansion** (204 years (95% CI: 123 years-350 years) average): 12.3x (95% CI: 4.19x-61.3x) more trials running in parallel accelerates discovery of first treatments for untreated diseases

$$DALYs_{max}$$
$$= DALYs_{global,ann} \times Pct_{avoid,DALY} \times T_{accel,max}$$
$$= 2.88B \times 92.6\% \times 212$$
$$= 565B$$

where $T_{accel,max} = T_{accel} + T_{lag} = 204 + 8.2 = 212$

where T_{accel}
$$= T_{first,SQ} \times \left(1 - \frac{1}{k_{capacity}}\right)$$
$$= 222 \times \left(1 - \frac{1}{12.3}\right)$$
$$= 204$$

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

where $k_{capacity} = \frac{N_{fundable,ann}}{Slots_{curr}} = \frac{23.4M}{1.9M} = 12.3$

where $N_{fundable,ann}$
$$= \frac{Subsidies_{trial,ann}}{Cost_{pragmatic,pt}}$$
$$= \frac{\$21.7B}{\$929}$$
$$= 23.4M$$

where $Subsidies_{trial,ann}$
$$= Treasury_{RD,ann} - OPEX_{dFDA}$$
$$= \$21.8B - \$40M$$
$$= \$21.7B$$

where $OPEX_{dFDA}$
$$= Cost_{platform} + Cost_{staff} + Cost_{infra}$$
$$+ Cost_{regulatory} + Cost_{community}$$
$$= \$15M + \$10M + \$8M + \$5M + \$2M$$
$$= \$40M$$

where $Treasury_{RD,ann}$
$$= Funding_{treaty} - Payout_{bond,ann} - Funding_{political,ann}$$
$$= \$27.2B - \$2.72B - \$2.72B$$
$$= \$21.8B$$

where $Funding_{treaty}$
$$= Spending_{mil} \times Reduce_{treaty}$$
$$= \$2.72T \times 1\%$$
$$= \$27.2B$$

These benefits flow through three distinct channels:

A. Accelerated Development of Existing Pipeline Drugs

Health gains from bringing effective treatments to patients faster through shortened development and approval timelines:

- **Baseline:** Research shows treatment delays significantly increase cancer mortality, with studies indicating approximately 10% increased risk per month of delay (systematic review)
- **Estimate:** 2-year average acceleration across pharmaceutical pipeline
- **Impact:** Significant contribution to the total 565 billion DALYs (95% CI: 361 billion DALYs-877 billion DALYs) averted from the average ~212 years (95% CI: 135 years-355 years)-year timeline shift

B. Improved Preventative Care via Real-World Evidence

Value of using comprehensive data to optimize preventative care and treatment effectiveness:

- **Baseline:** Cancer screenings alone have saved millions of life-years; significant untapped potential remains
- **Mechanism:** Large-scale identification of at-risk populations and real-world effectiveness measurement
- **Impact:** Contributes to the total 565 billion DALYs (95% CI: 361 billion DALYs-877 billion DALYs) averted

C. Enabling Research for Previously Untreatable Diseases

Transformative potential to create viable research pathways for conditions ignored due to high trial costs:

- **Baseline:** 7.00 thousand diseases (95% CI: 6.00 thousand diseases-10.0 thousand diseases)[82]+ rare diseases, 95% lack FDA-approved treatments
- **Mechanism:** Radically lower per-patient costs make rare disease R&D economically feasible
- **Impact:** Major contributor to the total 565 billion DALYs (95% CI: 361 billion DALYs-877 billion DALYs) averted

QALY Valuation: Standard economic valuations range from $50K-$150K (95% CI: $100K-$199K)[91] per QALY. This analysis uses conservative mid-range values.

The distribution below shows the uncertainty range in total DALYs averted from the combined timeline shift (efficacy lag elimination + trial capacity expansion), based on Monte Carlo simulation of input parameter uncertainty:

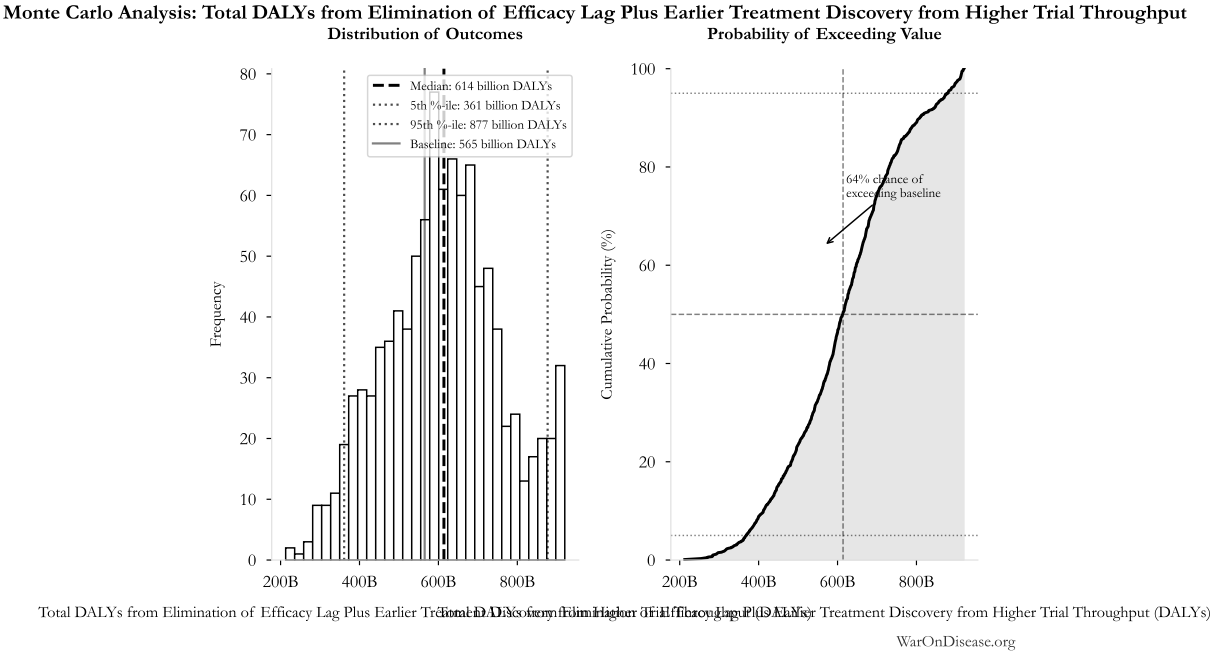


Figure 45: Monte Carlo Distribution: Total DALYs from Elimination of Efficacy Lag Plus Earlier Treatment Discovery from Higher Trial Throughput (10,000 simulations)

Simulation Results Summary: Total DALYs from Elimination of Efficacy Lag Plus Earlier Treatment Discovery from Higher Trial Throughput

Statistic	Value
Baseline (deterministic)	565 billion
Mean (expected value)	610 billion
Median (50th percentile)	614 billion
Standard Deviation	148 billion
90% Range (5th-95th percentile)	[361 billion, 877 billion]

The histogram shows the distribution of Total DALYs from Elimination of Efficacy Lag Plus Earlier Treatment Discovery from Higher Trial Throughput 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 detailed DALY calculation methodology, see Regulatory Mortality Analysis.

Economist Verification: Complete Derivation Chains

This section provides step-by-step derivations for all headline claims, enabling independent verification. All intermediate values are linked to their source parameters in Parameters and Calculations.

1. Trial Capacity Multiplier Derivation (12.3x (95% CI: 4.19x-61.3x))

Current System Baseline:

- 3.30 thousand trials/year (95% CI: 2.64 thousand trials/year-3.96 thousand trials/year)[16] clinical trials initiated per year
- 10.0 thousand trials[10] active trials at any time (3-5 year duration)
- 0.0792% (95% CI: 0.0761%-0.0819%) patient participation (1.90 million patients/year (95% CI: 1.50 million patients/year-2.30 million patients/year) trial slots for 2.40 billion people (95% CI: 2.00 billion people-2.80 billion people) with chronic disease[12])
- 40%[14] abandonment rate (studies never complete)

The trial capacity multiplier determines how many more trials can be run with reallocated funding:

Step 1: Calculate patients fundable annually

$$N_{fundable,ann}$$
$$= \frac{Subsidies_{trial,ann}}{Cost_{pragmatic,pt}}$$
$$= \frac{\$21.7B}{\$929}$$
$$= 23.4M$$

where $Subsidies_{trial,ann}$
$$= Treasury_{RD,ann} - OPEX_{dFDA}$$
$$= \$21.8B - \$40M$$
$$= \$21.7B$$

where $OPEX_{dFDA}$
$$= Cost_{platform} + Cost_{staff} + Cost_{infra}$$
$$+Cost_{regulatory} + Cost_{community}$$
$$= \$15M + \$10M + \$8M + \$5M + \$2M$$
$$= \$40M$$

where $Treasury_{RD,ann}$
$$= Funding_{treaty} - Payout_{bond,ann} - Funding_{political,ann}$$
$$= \$27.2B - \$2.72B - \$2.72B$$
$$= \$21.8B$$

where $Funding_{treaty}$
$$= Spending_{mil} \times Reduce_{treaty}$$
$$= \$2.72T \times 1\%$$
$$= \$27.2B$$

where $Payout_{bond,ann}$
$$= Funding_{treaty} \times Pct_{bond}$$
$$= \$27.2B \times 10\%$$
$$= \$2.72B$$

where $Funding_{treaty}$
$$= Spending_{mil} \times Reduce_{treaty}$$
$$= \$2.72T \times 1\%$$
$$= \$27.2B$$

where $Funding_{political,ann}$
$$= Funding_{treaty} \times Pct_{political}$$
$$= \$27.2B \times 10\%$$
$$= \$2.72B$$

where $Funding_{treaty}$
$$= Spending_{mil} \times Reduce_{treaty}$$
$$= \$2.72T \times 1\%$$
$$= \$27.2B$$

- Treaty redirects $27.2B/year
- Trial subsidies allocation: $21.7B (95% CI: $21.7B-$21.7B) (after IAB and political allocations)
- Pragmatic trial cost: $929 (95% CI: $97-$3K)/patient (ADAPTABLE basis; RECOVERY achieved $500 (95% CI: $400-$2.50K))

Step 2: Compare to current capacity

- Current global trial slots: 1.90 million patients/year (95% CI: 1.50 million patients/year-2.30 million patients/year) patients/year (IQVIA 2022)

Step 3: Calculate multiplier

$$k_{capacity} = \frac{N_{fundable,ann}}{Slots_{curr}} = \frac{23.4M}{1.9M} = 12.3$$

$$\text{where } N_{fundable,ann}$$
$$= \frac{Subsidies_{trial,ann}}{Cost_{pragmatic,pt}}$$
$$= \frac{\$21.7B}{\$929}$$
$$= 23.4M$$

$$\text{where } Subsidies_{trial,ann}$$
$$= Treasury_{RD,ann} - OPEX_{dFDA}$$
$$= \$21.8B - \$40M$$
$$= \$21.7B$$

$$\text{where } OPEX_{dFDA}$$
$$= Cost_{platform} + Cost_{staff} + Cost_{infra}$$
$$+Cost_{regulatory} + Cost_{community}$$
$$= \$15M + \$10M + \$8M + \$5M + \$2M$$
$$= \$40M$$

$$\text{where } Treasury_{RD,ann}$$
$$= Funding_{treaty} - Payout_{bond,ann} - Funding_{political,ann}$$
$$= \$27.2B - \$2.72B - \$2.72B$$
$$= \$21.8B$$

$$\text{where } Funding_{treaty}$$
$$= Spending_{mil} \times Reduce_{treaty}$$
$$= \$2.72T \times 1\%$$
$$= \$27.2B$$

$$\text{where } Payout_{bond,ann}$$
$$= Funding_{treaty} \times Pct_{bond}$$
$$= \$27.2B \times 10\%$$
$$= \$2.72B$$

$$\text{where } Funding_{treaty}$$
$$= Spending_{mil} \times Reduce_{treaty}$$
$$= \$2.72T \times 1\%$$
$$= \$27.2B$$

$$\text{where } Funding_{political,ann}$$
$$= Funding_{treaty} \times Pct_{political}$$
$$= \$27.2B \times 10\%$$
$$= \$2.72B$$

$$\text{where } Funding_{treaty}$$
$$= Spending_{mil} \times Reduce_{treaty}$$

Step 4: Cumulative Research Impact (20-year horizon)

$$Capacity_{20yr} = k_{capacity} \times 20 = 12.3 \times 20 = 246$$

$$\text{where } k_{capacity} = \frac{N_{fundable,ann}}{Slots_{curr}} = \frac{23.4M}{1.9M} = 12.3$$

$$\text{where } N_{fundable,ann}$$
$$= \frac{Subsidies_{trial,ann}}{Cost_{pragmatic,pt}}$$
$$= \frac{\$21.7B}{\$929}$$
$$= 23.4M$$

$$\text{where } Subsidies_{trial,ann}$$
$$= Treasury_{RD,ann} - OPEX_{dFDA}$$
$$= \$21.8B - \$40M$$
$$= \$21.7B$$

$$\text{where } OPEX_{dFDA}$$
$$= Cost_{platform} + Cost_{staff} + Cost_{infra}$$
$$+Cost_{regulatory} + Cost_{community}$$
$$= \$15M + \$10M + \$8M + \$5M + \$2M$$
$$= \$40M$$

$$\text{where } Treasury_{RD,ann}$$
$$= Funding_{treaty} - Payout_{bond,ann} - Funding_{political,ann}$$
$$= \$27.2B - \$2.72B - \$2.72B$$
$$= \$21.8B$$

$$\text{where } Funding_{treaty}$$
$$= Spending_{mil} \times Reduce_{treaty}$$
$$= \$2.72T \times 1\%$$
$$= \$27.2B$$

$$\text{where } Payout_{bond,ann}$$
$$= Funding_{treaty} \times Pct_{bond}$$
$$= \$27.2B \times 10\%$$
$$= \$2.72B$$

$$\text{where } Funding_{treaty}$$
$$= Spending_{mil} \times Reduce_{treaty}$$
$$= \$2.72T \times 1\%$$
$$= \$27.2B$$

$$\text{where } Funding_{political,ann}$$
$$= Funding_{treaty} \times Pct_{political}$$
$$= \$27.2B \times 10\%$$
$$= \$2.72B$$

$$\text{where } Funding_{treaty}$$

2. Timeline Shift Derivation (212 years (95% CI: 135 years-355 years))

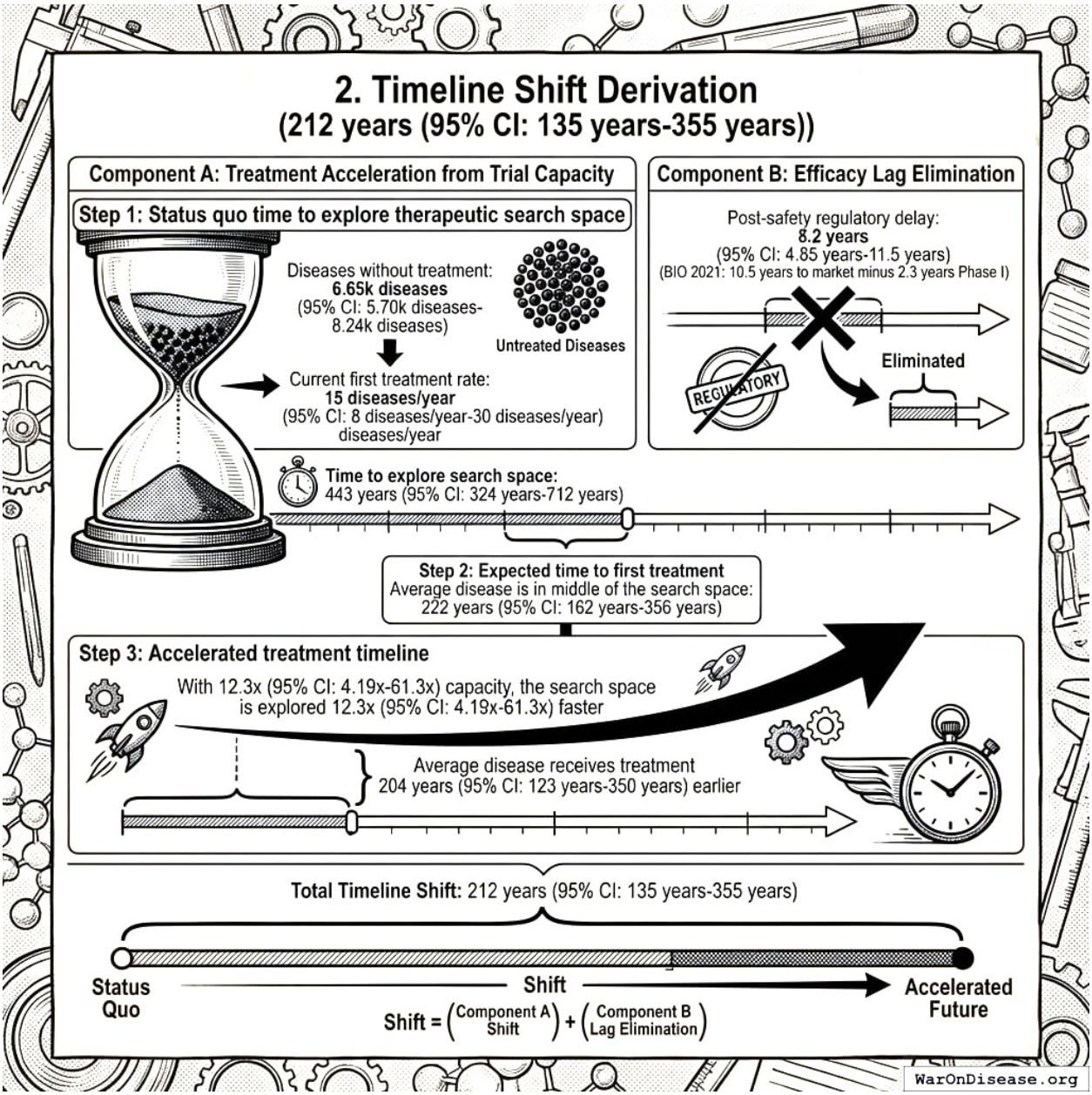


Figure 46: A comparative timeline visualization showing the status quo path to therapeutic discovery versus the accelerated path achieved through trial capacity expansion and efficacy lag elimination.

The timeline shift combines two independent effects:

Component A: Treatment Acceleration from Trial Capacity

Step 1: Status quo time to explore therapeutic search space

- Diseases without treatment: 6.65 thousand diseases (95% CI: 5.70 thousand diseases-8.24 thousand diseases)

- Current first treatment rate: 15 diseases/year (95% CI: 8 diseases/year-30 diseases/year) diseases/year
- Time to explore search space: 443 years (95% CI: 324 years-712 years)

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

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

Step 2: Expected time to first treatment

- Average disease is in middle of the search space: 222 years (95% CI: 162 years-356 years)

Step 3: Accelerated treatment timeline

With 12.3x (95% CI: 4.19x-61.3x) capacity, the search space is explored 12.3x (95% CI: 4.19x-61.3x) faster. The average disease receives treatment 204 years (95% CI: 123 years-350 years) earlier:

$$
\begin{aligned}
&T_{accel} \\
&= T_{first,SQ} \times \left(1 - \frac{1}{k_{capacity}}\right) \\
&= 222 \times \left(1 - \frac{1}{12.3}\right) \\
&= 204
\end{aligned}
$$

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

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

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

$$\text{where } k_{capacity} = \frac{N_{fundable,ann}}{Slots_{curr}} = \frac{23.4M}{1.9M} = 12.3$$

$$
\begin{aligned}
&\text{where } N_{fundable,ann} \\
&= \frac{Subsidies_{trial,ann}}{Cost_{pragmatic,pt}} \\
&= \frac{\$21.7B}{\$929} \\
&= 23.4M
\end{aligned}
$$

$$
\begin{aligned}
&\text{where } Subsidies_{trial,ann} \\
&= Treasury_{RD,ann} - OPEX_{dFDA} \\
&= \$21.8B - \$40M \\
&= \$21.7B
\end{aligned}
$$

$$
\begin{aligned}
&\text{where } OPEX_{dFDA} \\
&= Cost_{platform} + Cost_{staff} + Cost_{infra} \\
&+ Cost_{regulatory} + Cost_{community} \\
&= \$15M + \$10M + \$8M + \$5M + \$2M \\
&= \$40M
\end{aligned}
$$

$$
\begin{aligned}
&\text{where } Treasury_{RD,ann} \\
&= Funding_{treaty} - Payout_{bond,ann} - Funding_{political,ann} \\
&= \$27.2B - \$2.72B - \$2.72B \\
&= \$21.8B
\end{aligned}
$$

$$
\begin{aligned}
&\text{where } Funding_{treaty} \\
&= Spending_{mil} \times Reduce_{treaty} \\
&= \$2.72T \times 1\% \\
&= \$27.2B
\end{aligned}
$$

$$
\begin{aligned}
&\text{where } Payout_{bond,ann} \\
&= Funding_{treaty} \times Pct_{bond} \\
&= \$27.2B \times 10\% \\
&= \$2.72B
\end{aligned}
$$

$$\text{where } Funding$$

Component B: Efficacy Lag Elimination

Post-safety regulatory delay: 8.2 years (95% CI: 4.85 years-11.5 years) (BIO 2021: 10.5 years to market minus 2.3 years Phase I)

Total Timeline Shift

$$T_{accel,max} = T_{accel} + T_{lag} = 204 + 8.2 = 212$$

$$\text{where } T_{accel}$$
$$= T_{first,SQ} \times \left(1 - \frac{1}{k_{capacity}}\right)$$
$$= 222 \times \left(1 - \frac{1}{12.3}\right)$$
$$= 204$$

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

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

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

$$\text{where } k_{capacity} = \frac{N_{fundable,ann}}{Slots_{curr}} = \frac{23.4M}{1.9M} = 12.3$$

$$\text{where } N_{fundable,ann}$$
$$= \frac{Subsidies_{trial,ann}}{Cost_{pragmatic,pt}}$$
$$= \frac{\$21.7B}{\$929}$$
$$= 23.4M$$

$$\text{where } Subsidies_{trial,ann}$$
$$= Treasury_{RD,ann} - OPEX_{dFDA}$$
$$= \$21.8B - \$40M$$
$$= \$21.7B$$

$$\text{where } OPEX_{dFDA}$$
$$= Cost_{platform} + Cost_{staff} + Cost_{infra}$$
$$+Cost_{regulatory} + Cost_{community}$$
$$= \$15M + \$10M + \$8M + \$5M + \$2M$$
$$= \$40M$$

$$\text{where } Treasury_{RD,ann}$$
$$= Funding_{treaty} - Payout_{bond,ann} - Funding_{political,ann}$$
$$= \$27.2B - \$2.72B - \$2.72B$$
$$= \$21.8B$$

$$\text{where } Funding_{treaty}$$
$$= Spending_{mil} \times Reduce_{treaty}$$
$$= \$2.72T \times 1\%$$
$$= \$27.2B$$

$$\text{where } Payout_{bond,ann}$$
$$= Funding_{treaty} \times Pct_{bond}$$
$$= \$27.2B \times 10\%$$
$$= \$2.72B$$

3. DALYs Averted Derivation (565 billion DALYs (95% CI: 361 billion DALYs-877 billion DALYs))

Step 1: Identify annual DALY burden

- Global annual DALY burden: 2.88 billion DALYs/year (95% CI: 2.63 billion DALYs/year-3.13 billion DALYs/year) (WHO GBD 2021)
- This includes both mortality (YLL) and morbidity (YLD: arthritis, depression, chronic pain, etc.)

Step 2: Determine avoidable fraction

- Eventually avoidable with biomedical research: 92.6% (95% CI: 50%-98%)
- Fundamentally unavoidable (accidents): 7.37%

Assumption justification (92.6% (95% CI: 50%-98%) avoidable): This represents the theoretical ceiling of what is biologically addressable, not what is currently preventable. It excludes only fundamentally unavoidable causes (primarily accidents, which cannot be addressed by medical research). Conservative estimates of current preventability (20-30%) are much lower because they measure what we can do today, not what is scientifically possible with sufficient research over decades.

Step 3: Calculate DALYs averted

$$DALYs_{max}$$
$$= DALYs_{global,ann} \times Pct_{avoid,DALY} \times T_{accel,max}$$
$$= 2.88B \times 92.6\% \times 212$$
$$= 565B$$

$$\text{where } T_{accel,max} = T_{accel} + T_{lag} = 204 + 8.2 = 212$$

$$\text{where } T_{accel}$$
$$= T_{first,SQ} \times \left(1 - \frac{1}{k_{capacity}}\right)$$
$$= 222 \times \left(1 - \frac{1}{12.3}\right)$$
$$= 204$$

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

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

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

$$\text{where } k_{capacity} = \frac{N_{fundable,ann}}{Slots_{curr}} = \frac{23.4M}{1.9M} = 12.3$$

$$\text{where } N_{fundable,ann}$$
$$= \frac{Subsidies_{trial,ann}}{Cost_{pragmatic,pt}}$$
$$= \frac{\$21.7B}{\$929}$$
$$= 23.4M$$

$$\text{where } Subsidies_{trial,ann}$$
$$= Treasury_{RD,ann} - OPEX_{dFDA}$$
$$= \$21.8B - \$40M$$
$$= \$21.7B$$

$$\text{where } OPEX_{dFDA}$$
$$= Cost_{platform} + Cost_{staff} + Cost_{infra}$$
$$+Cost_{regulatory} + Cost_{community}$$
$$= \$15M + \$10M + \$8M + \$5M + \$2M$$
$$= \$40M$$

$$\text{where } Treasury_{RD,ann}$$
$$= Funding_{treaty} - Payout_{bond,ann} - Funding_{political,ann}$$
$$= \$27.2B - \$2.72B - \$2.72B$$
$$= \$21.8B$$

$$\text{where } Funding_{treaty}$$
$$= Spending_{mil} \times Reduce_{treaty}$$
$$= \$2.72T \times 1\%$$
$$= \$27.2B$$

4. Cost per DALY Derivation ($0.0018 (95% CI: $0.0007-$0.0041))

Step 1: Identify one-time implementation cost

- Treaty implementation cost: $1B
  - Referendum: $250M
  - Lobbying: $650M
  - Reserve: $100M

Step 2: Calculate cost per DALY

$$Cost_{treaty,DALY} = \frac{Cost_{campaign}}{DALYs_{max}} = \frac{\$1B}{565B} = \$0.00177$$

$$\text{where } Cost_{campaign}$$
$$= Budget_{viral,base} + Budget_{lobby,treaty}$$
$$+ Budget_{reserve}$$
$$= \$250M + \$650M + \$100M$$
$$= \$1B$$

$$\text{where } DALYs_{max}$$
$$= DALYs_{global,ann} \times Pct_{avoid,DALY} \times T_{accel,max}$$
$$= 2.88B \times 92.6\% \times 212$$
$$= 565B$$

$$\text{where } T_{accel,max} = T_{accel} + T_{lag} = 204 + 8.2 = 212$$

$$\text{where } T_{accel}$$
$$= T_{first,SQ} \times \left(1 - \frac{1}{k_{capacity}}\right)$$
$$= 222 \times \left(1 - \frac{1}{12.3}\right)$$
$$= 204$$

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

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

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

$$\text{where } k_{capacity} = \frac{N_{fundable,ann}}{Slots_{curr}} = \frac{23.4M}{1.9M} = 12.3$$

$$\text{where } N_{fundable,ann}$$
$$= \frac{Subsidies_{trial,ann}}{Cost_{pragmatic,pt}}$$
$$= \frac{\$21.7B}{\$929}$$
$$= 23.4M$$

$$\text{where } Subsidies_{trial,ann}$$
$$= Treasury_{RD,ann} - OPEX_{dFDA}$$
$$= \$21.8B - \$40M$$
$$= \$21.7B$$

$$\text{where } OPEX_{dFDA}$$
$$= Cost_{platform} + Cost_{staff} + Cost_{infra}$$
$$+ Cost_{regulatory} + Cost_{community}$$
$$= \$15M + \$10M + \$8M + \$5M + \$2M$$
$$= \$40M$$

$$\text{where } Treasury_{RD,ann}$$

Comparison: Malaria bed nets cost $89 (95% CI: $78-$100)/DALY - this intervention is 50.3kx (95% CI: 23.7kx-111.7kx) more cost-effective.

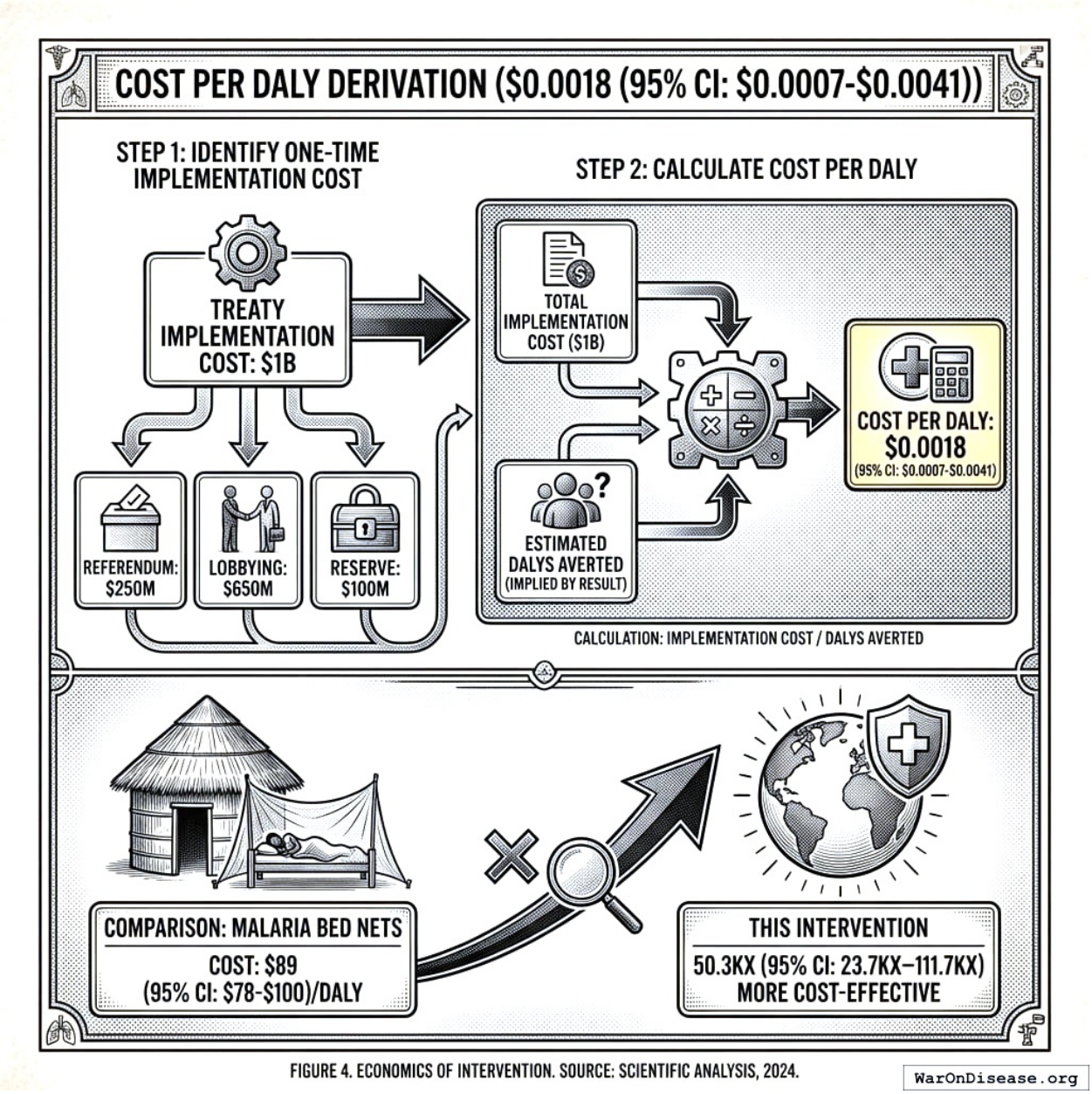


Figure 47: A visual breakdown of the $1 billion implementation budget and a scale comparison showing the intervention's cost-effectiveness relative to malaria bed nets.

5. ROI Derivation (Conservative: 637:1 (95% CI: 569:1-790:1))

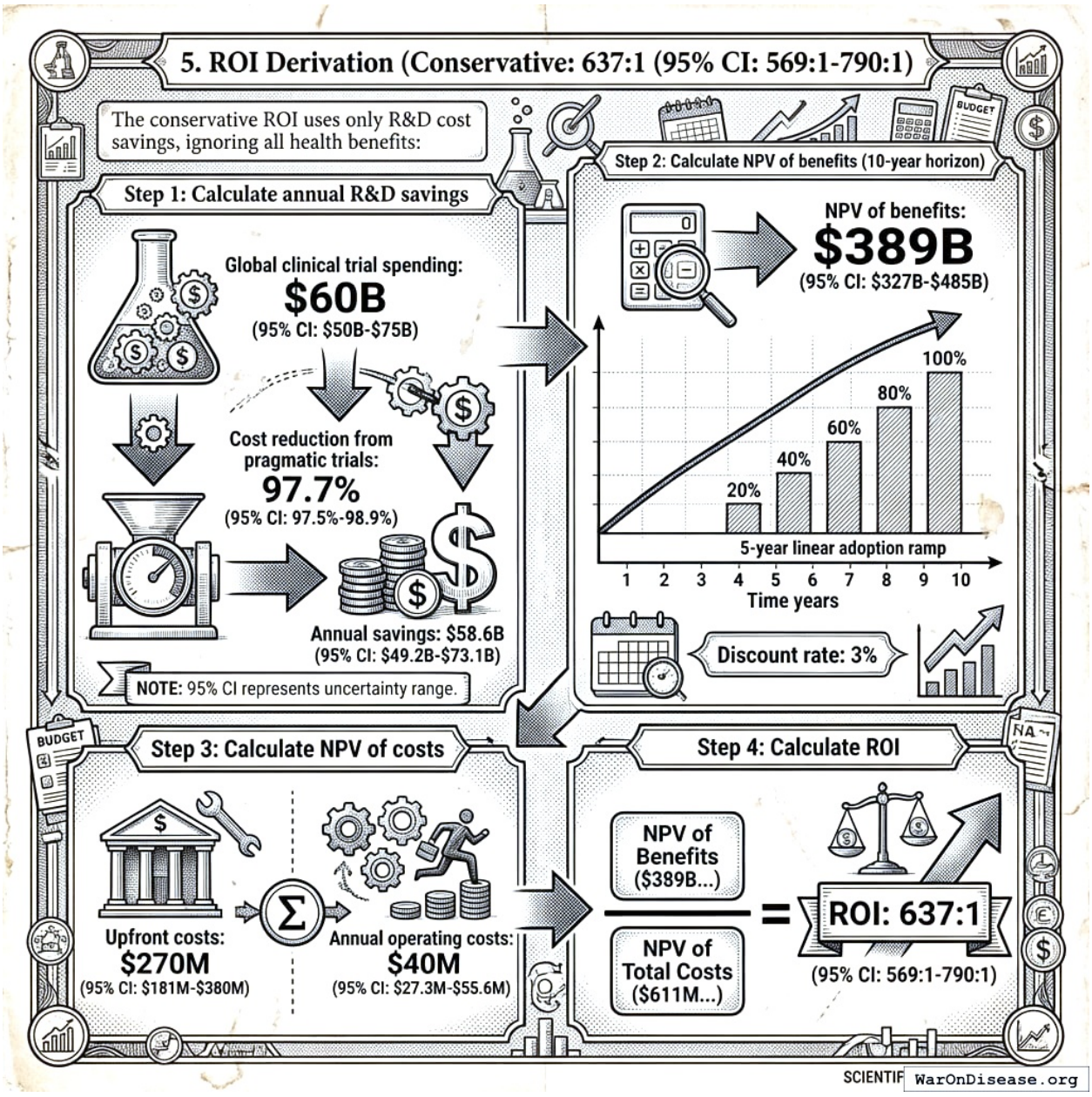


Figure 48: A visual breakdown of the four-step ROI derivation process, illustrating the conversion of global clinical trial spending into R&D savings and the final 637:1 return ratio.

The conservative ROI uses only R&D cost savings, ignoring all health benefits:

Step 1: Calculate annual R&D savings

- Global clinical trial spending: $60B (95% CI: $50B-$75B)[42]
- Cost reduction from pragmatic trials: 97.7% (95% CI: 97.5%-98.9%)
- Annual savings: $58.6B (95% CI: $49.2B-$73.1B)

$$
\begin{aligned}
&Benefit_{RD,ann} \\
&= Spending_{trials} \times Reduce_{pct} \\
&= \$60B \times 97.7\% \\
&= \$58.6B
\end{aligned}
$$

$$
\begin{aligned}
&\text{where } Reduce_{pct} \\
&= 1 - \frac{Cost_{pragmatic,pt}}{Cost_{P3,pt}} \\
&= 1 - \frac{\$929}{\$41K} \\
&= 97.7\%
\end{aligned}
$$

Step 2: Calculate NPV of benefits (10-year horizon)

- Discount rate: 3%
- 5-year linear adoption ramp (20%, 40%, 60%, 80%, 100%)
- NPV of benefits: $389B (95% CI: $327B-$485B)

$$
\begin{aligned}
&NPV_{RD} \\
&= \sum_{t=1}^{10} \frac{Savings_{RD,ann} \times \frac{\min(t,5)}{5}}{(1+r)^t}
\end{aligned}
$$

Step 3: Calculate NPV of costs

- Upfront costs: $270M (95% CI: $181M-$380M)
- Annual operating costs: $40M (95% CI: $27.3M-$55.6M)
- NPV of total costs: $611M (95% CI: $415M-$853M)

Step 4: Calculate ROI

$$ROI_{RD} = \frac{NPV_{RD}}{Cost_{dFDA,total}} = \frac{\$389B}{\$611M} = 637$$

$$\text{where } NPV_{RD} = \sum_{t=1}^{10} \frac{Savings_{RD,ann} \times \frac{\min(t,5)}{5}}{(1+r)^t}$$

$$\text{where } Savings_{RD,ann}$$
$$= Benefit_{RD,ann} - OPEX_{dFDA}$$
$$= \$58.6B - \$40M$$
$$= \$58.6B$$

$$\text{where } Benefit_{RD,ann}$$
$$= Spending_{trials} \times Reduce_{pct}$$
$$= \$60B \times 97.7\%$$
$$= \$58.6B$$

$$\text{where } Reduce_{pct}$$
$$= 1 - \frac{Cost_{pragmatic,pt}}{Cost_{P3,pt}}$$
$$= 1 - \frac{\$929}{\$41K}$$
$$= 97.7\%$$

$$\text{where } OPEX_{dFDA}$$
$$= Cost_{platform} + Cost_{staff} + Cost_{infra}$$
$$+Cost_{regulatory} + Cost_{community}$$
$$= \$15M + \$10M + \$8M + \$5M + \$2M$$
$$= \$40M$$

$$\text{where } Cost_{dFDA,total}$$
$$= PV_{OPEX} + Cost_{upfront,total}$$
$$= \$342M + \$270M$$
$$= \$611M$$

$$\text{where } PV_{OPEX} = OPEX_{ann} \times \frac{1-(1+r)^{-T}}{r}$$

$$\text{where } OPEX_{total}$$
$$= OPEX_{ann} + OPEX_{DIH,ann}$$
$$= \$18.9M + \$21.1M$$
$$= \$40M$$

$$\text{where } Cost_{upfront,total}$$
$$= Cost_{upfront} + Cost_{DIH,init}$$
$$= \$40M + \$230M$$
$$= \$270M$$

6. ROI Derivation (Complete: 84.8M:1 (95% CI: 46.6M:1-144M:1))

The complete ROI includes the full timeline shift health benefits:

Step 1: Economic value of timeline shift

$$
\begin{gathered}
Value_{max} \\
= DALYs_{max} \times Value_{QALY} \\
= 565B \times \$150K \\
= \$84800T
\end{gathered}
$$

$$
\begin{gathered}
\text{where } DALYs_{max} \\
= DALYs_{global,ann} \times Pct_{avoid,DALY} \times T_{accel,max} \\
= 2.88B \times 92.6\% \times 212 \\
= 565B
\end{gathered}
$$

$$\text{where } T_{accel,max} = T_{accel} + T_{lag} = 204 + 8.2 = 212$$

$$
\begin{gathered}
\text{where } T_{accel} \\
= T_{first,SQ} \times \left(1 - \frac{1}{k_{capacity}}\right) \\
= 222 \times \left(1 - \frac{1}{12.3}\right) \\
= 204
\end{gathered}
$$

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

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

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

$$\text{where } k_{capacity} = \frac{N_{fundable,ann}}{Slots_{curr}} = \frac{23.4M}{1.9M} = 12.3$$

$$
\begin{gathered}
\text{where } N_{fundable,ann} \\
= \frac{Subsidies_{trial,ann}}{Cost_{pragmatic,pt}} \\
= \frac{\$21.7B}{\$929} \\
= 23.4M
\end{gathered}
$$

$$
\begin{gathered}
\text{where } Subsidies_{trial,ann} \\
= Treasury_{RD,ann} - OPEX_{dFDA} \\
= \$21.8B - \$40M \\
= \$21.7B
\end{gathered}
$$

$$
\begin{gathered}
\text{where } OPEX_{dFDA} \\
= Cost_{platform} + Cost_{staff} + Cost_{infra} \\
+ Cost_{regulatory} + Cost_{community} \\
= \$15M + \$10M + \$8M + \$5M + \$2M \\
= \$40M
\end{gathered}
$$

$$
\begin{gathered}
\text{where } Treasury_{RD,ann} \\
= Funding_{treaty} - Payout_{bond,ann} - Funding_{political,ann} \\
= \$27.2B - \$2.72B - \$2.72B \\
= \$21.8B
\end{gathered}
$$

QALY Valuation Justification ($150K (95% CI: $100K-$199K)): This uses standard US economic valuations. WHO recommends $50K-$150K (95% CI: $100K-$199K) per QALY for cost-effectiveness thresholds in high-income countries. The $150K (95% CI: $100K-$199K) value reflects revealed preferences from regulatory decisions (EPA, FDA), wage-risk tradeoffs, and health insurance willingness-to-pay studies. International analyses often use lower thresholds ($50-100K), which would reduce the ROI proportionally but not change the cost-saving classification.

Step 2: Calculate ROI

$$ROI_{max} = \frac{Value_{max}}{Cost_{campaign}} = \frac{\$84800T}{\$1B} = 84.8M$$

$$\text{where } Value_{max}$$
$$= DALYs_{max} \times Value_{QALY}$$
$$= 565B \times \$150K$$
$$= \$84800T$$

$$\text{where } DALYs_{max}$$
$$= DALYs_{global,ann} \times Pct_{avoid,DALY} \times T_{accel,max}$$
$$= 2.88B \times 92.6\% \times 212$$
$$= 565B$$

$$\text{where } T_{accel,max} = T_{accel} + T_{lag} = 204 + 8.2 = 212$$

$$\text{where } T_{accel}$$
$$= T_{first,SQ} \times \left(1 - \frac{1}{k_{capacity}}\right)$$
$$= 222 \times \left(1 - \frac{1}{12.3}\right)$$
$$= 204$$

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

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

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

$$\text{where } k_{capacity} = \frac{N_{fundable,ann}}{Slots_{curr}} = \frac{23.4M}{1.9M} = 12.3$$

$$\text{where } N_{fundable,ann}$$
$$= \frac{Subsidies_{trial,ann}}{Cost_{pragmatic,pt}}$$
$$= \frac{\$21.7B}{\$929}$$
$$= 23.4M$$

$$\text{where } Subsidies_{trial,ann}$$
$$= Treasury_{RD,ann} - OPEX_{dFDA}$$
$$= \$21.8B - \$40M$$
$$= \$21.7B$$

$$\text{where } OPEX_{dFDA}$$
$$= Cost_{platform} + Cost_{staff} + Cost_{infra}$$
$$+ Cost_{regulatory} + Cost_{community}$$
$$= \$15M + \$10M + \$8M + \$5M + \$2M$$
$$= \$40M$$

$$\text{where } Treasury_{RD,ann}$$

7. Lives Saved Derivation (10.7 billion deaths (95% CI: 7.39 billion deaths-16.2 billion deaths))

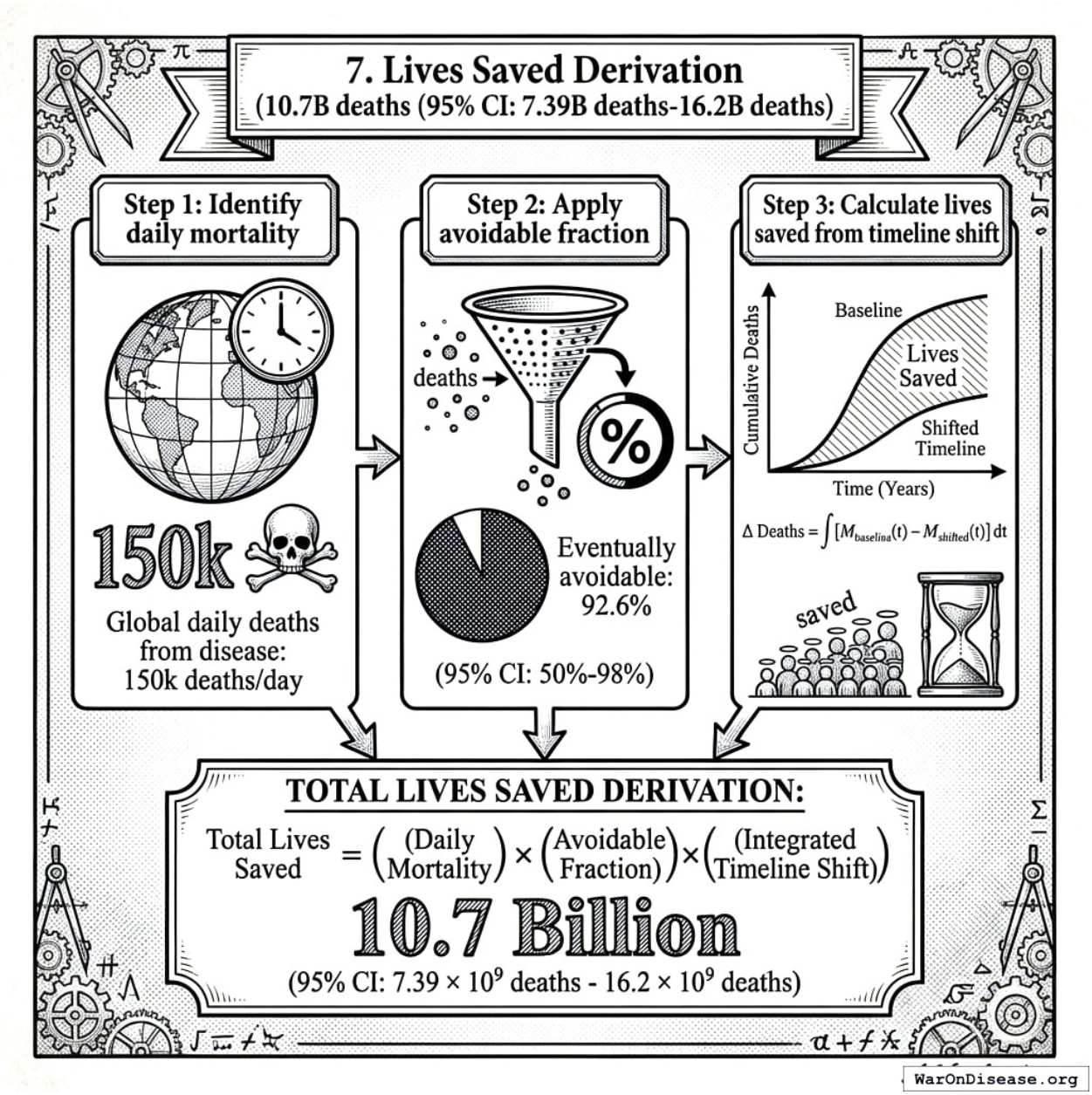


Figure 49: A flowchart illustrating the multi-step derivation of total lives saved, starting from daily global mortality and applying the avoidable fraction and timeline shift variables.

Step 1: Identify daily mortality

- Global daily deaths from disease: 150 thousand deaths/day[4]

Step 2: Apply avoidable fraction

- Eventually avoidable: 92.6% (95% CI: 50%-98%)

Step 3: Calculate lives saved from timeline shift

$$
\begin{aligned}
&Lives_{max} \\
&= Deaths_{disease,daily} \times T_{accel,max} \times 338 \\
&= 150{,}000 \times 212 \times 338 \\
&= 10.7B
\end{aligned}
$$

$$\text{where } T_{accel,max} = T_{accel} + T_{lag} = 204 + 8.2 = 212$$

$$
\begin{aligned}
&\text{where } T_{accel} \\
&= T_{first,SQ} \times \left(1 - \frac{1}{k_{capacity}}\right) \\
&= 222 \times \left(1 - \frac{1}{12.3}\right) \\
&= 204
\end{aligned}
$$

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

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

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

$$\text{where } k_{capacity} = \frac{N_{fundable,ann}}{Slots_{curr}} = \frac{23.4M}{1.9M} = 12.3$$

$$
\begin{aligned}
&\text{where } N_{fundable,ann} \\
&= \frac{Subsidies_{trial,ann}}{Cost_{pragmatic,pt}} \\
&= \frac{\$21.7B}{\$929} \\
&= 23.4M
\end{aligned}
$$

$$
\begin{aligned}
&\text{where } Subsidies_{trial,ann} \\
&= Treasury_{RD,ann} - OPEX_{dFDA} \\
&= \$21.8B - \$40M \\
&= \$21.7B
\end{aligned}
$$

$$
\begin{aligned}
&\text{where } OPEX_{dFDA} \\
&= Cost_{platform} + Cost_{staff} + Cost_{infra} \\
&+ Cost_{regulatory} + Cost_{community} \\
&= \$15M + \$10M + \$8M + \$5M + \$2M \\
&= \$40M
\end{aligned}
$$

$$
\begin{aligned}
&\text{where } Treasury_{RD,ann} \\
&= Funding_{treaty} - Payout_{bond,ann} - Funding_{political,ann} \\
&= \$27.2B - \$2.72B - \$2.72B \\
&= \$21.8B
\end{aligned}
$$

$$
\begin{aligned}
&\text{where } Funding_{treaty} \\
&= Spending_{mil} \times Reduce_{treaty} \\
&= \$2.72T \times 1\% \\
&= \$27.2B
\end{aligned}
$$

8. Regulatory Delay Elimination Derivation

Step 1: Lives Saved from Lag Elimination

$$
\begin{aligned}
&Deaths_{lag} \\
&= T_{lag} \times Deaths_{disease,daily} \times 338 \\
&= 8.2 \times 150{,}000 \times 338 \\
&= 416M
\end{aligned}
$$

Step 2: Economic Value of Lag Elimination

$$
\begin{aligned}
&Value_{lag} \\
&= DALYs_{lag} \times Value_{QALY} \\
&= 7.94B \times \$150K \\
&= \$1190T
\end{aligned}
$$

$$\text{where } DALYs_{lag} = YLL_{lag} + YLD_{lag} = 7.07B + 873M = 7.94B$$

$$
\begin{aligned}
&\text{where } YLL_{lag} \\
&= Deaths_{lag} \times (LE_{global} - Age_{death,delay}) \\
&= 416M \times (79 - 62) \\
&= 7.07B
\end{aligned}
$$

$$
\begin{aligned}
&\text{where } Deaths_{lag} \\
&= T_{lag} \times Deaths_{disease,daily} \times 338 \\
&= 8.2 \times 150{,}000 \times 338 \\
&= 416M
\end{aligned}
$$

$$
\begin{aligned}
&\text{where } YLD_{lag} \\
&= Deaths_{lag} \times T_{suffering} \times DW_{chronic} \\
&= 416M \times 6 \times 0.35 \\
&= 873M
\end{aligned}
$$

$$
\begin{aligned}
&\text{where } Deaths_{lag} \\
&= T_{lag} \times Deaths_{disease,daily} \times 338 \\
&= 8.2 \times 150{,}000 \times 338 \\
&= 416M
\end{aligned}
$$

9. Annual Recurring Benefits Derivation

$$
\begin{gathered}
Benefit_{peace+RD} \\
= Benefit_{peace,soc} + Benefit_{RD,ann} \\
= \$114B + \$58.6B \\
= \$172B
\end{gathered}
$$

$$
\begin{gathered}
\text{where } Benefit_{peace,soc} \\
= Cost_{war,total} \times Reduce_{treaty} \\
= \$11.4T \times 1\% \\
= \$114B
\end{gathered}
$$

$$
\begin{gathered}
\text{where } Cost_{war,total} \\
= Cost_{war,direct} + Cost_{war,indirect} \\
= \$7.66T + \$3.7T \\
= \$11.4T
\end{gathered}
$$

$$
\begin{gathered}
\text{where } Cost_{war,direct} \\
= Loss_{life,conflict} + Damage_{infra,total} \\
+ Disruption_{trade} + Spending_{mil} \\
= \$2.45T + \$1.88T + \$616B + \$2.72T \\
= \$7.66T
\end{gathered}
$$

$$
\begin{gathered}
\text{where } Loss_{life,conflict} \\
= Cost_{combat,human} + Cost_{state,human} \\
+ Cost_{terror,human} \\
= \$2.34T + \$27B + \$83B \\
= \$2.45T
\end{gathered}
$$

$$
\begin{gathered}
\text{where } Cost_{combat,human} \\
= Deaths_{combat} \times VSL \\
= 234{,}000 \times \$10M \\
= \$2.34T
\end{gathered}
$$

$$
\begin{gathered}
\text{where } Cost_{state,human} \\
= Deaths_{state} \times VSL \\
= 2{,}700 \times \$10M \\
= \$27B
\end{gathered}
$$

$$
\begin{gathered}
\text{where } Cost_{terror,human} \\
= Deaths_{terror} \times VSL \\
= 8{,}300 \times \$10M \\
= \$83B
\end{gathered}
$$

$$
\begin{gathered}
\text{where } Damage_{infra,total} \\
= Damage_{comms} + Damage_{edu} + Damage_{energy} \\
+ Damage_{health} + Damage_{transport} \\
+ Damage_{water} \\
= \$298B + \$234B + \$422B + \$166B + \$487B + \$268B
\end{gathered}
$$

Verification Summary

Claim	Value	Derivation	Inputs
Trial Capacity	12.3x (95% CI: 4.19x-61.3x)	Patients fundable ÷ current slots	Funding, trial cost, current capacity
Timeline Shift	212 years (95% CI: 135 years-355 years)	Treatment acceleration + efficacy lag	Discovery capacity model, multiplier, regulatory data
DALYs Averted	565 billion DALYs (95% CI: 361 billion DALYs-877 billion DALYs)	DALY burden × avoidable × shift	WHO GBD, avoidability assumption
Cost/DALY	$0.0018 (95% CI: $0.0007-$0.0041)	Implementation cost ÷ DALYs	Implementation budget, DALYs
ROI (Conservative)	637:1 (95% CI: 569:1-790:1)	NPV benefits ÷ NPV costs	Trial savings, discount rate
ROI (Complete)	84.8M:1 (95% CI: 46.6M:1-144M:1)	Economic value ÷ implementation cost	QALY valuation, timeline shift
Lives Saved	10.7 billion deaths (95% CI: 7.39 billion deaths-16.2 billion deaths)	Daily deaths × avoidable × shift	WHO mortality, timeline shift
Delay Lives	416 million deaths (95% CI: 225 million deaths-630 million deaths)	Daily deaths × lag × avoidable	WHO mortality, lag years
Delay Value	$1.19 quadrillion (95% CI: $443T-$2.41 quadrillion)	Delay DALYs × QALY Value	Delay DALYs, QALY ($150k)

Sensitivity to key assumptions: The tornado diagrams throughout this document show that results are most sensitive to: (1) timeline shift duration, (2) QALY valuation, and (3) eventually avoidable percentage. Even under conservative parameter assumptions (lower timeline shift, lower QALY values, lower avoidability), the intervention remains cost-saving.

For complete parameter definitions, uncertainty ranges, and Monte Carlo distributions, see Parameters and Calculations.

Counterfactual Baseline Specification

This cost-effectiveness analysis uses the **status quo** as the baseline counterfactual: military spending continues at current levels ($2.72T[48] annually) and is allocated to traditional military purposes. Under this baseline, the $27.2B redirected to pragmatic clinical trials infrastructure would otherwise remain in military budgets.

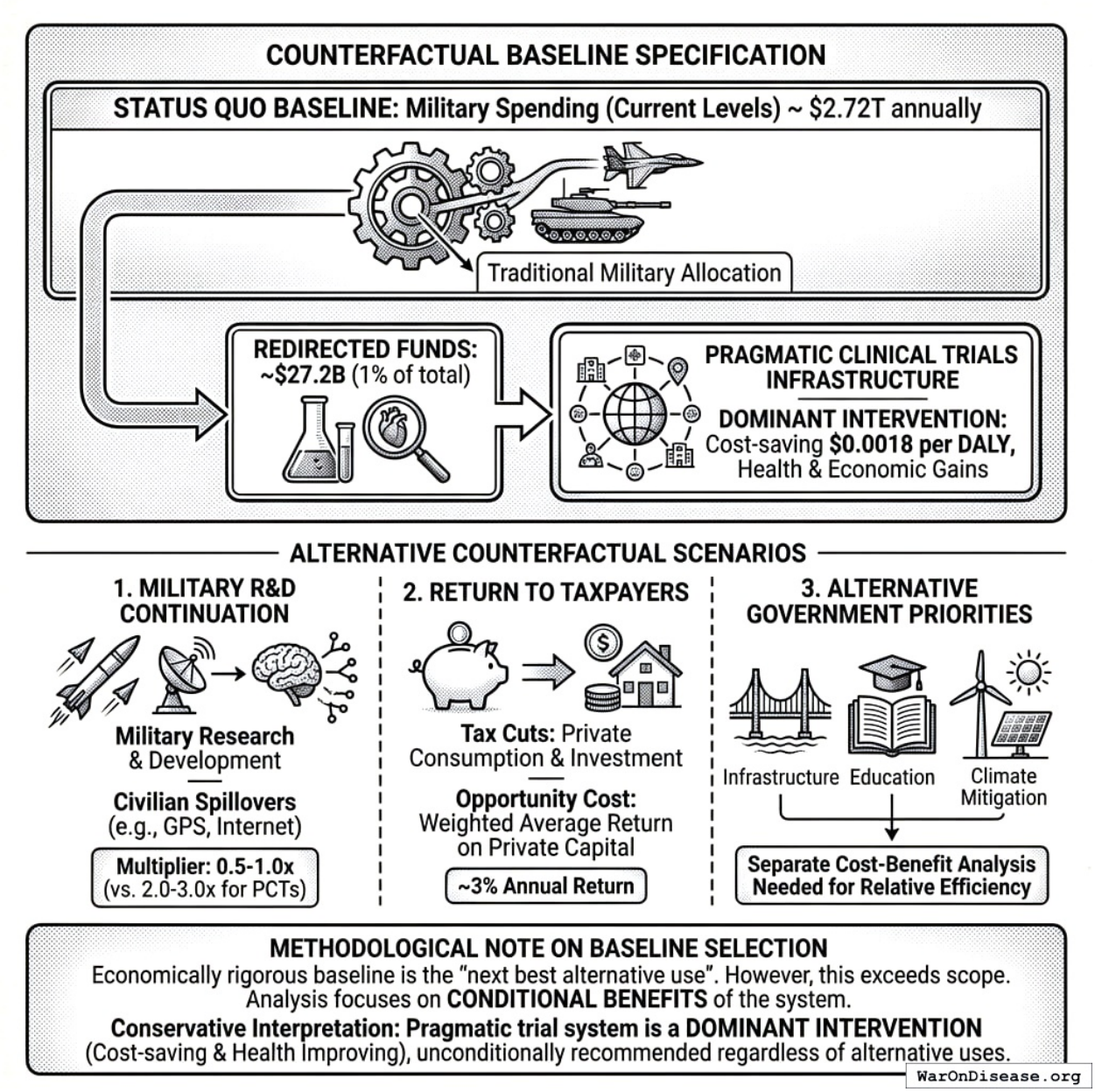


Figure 50: A comparison of the proposed $27.2B reallocation toward clinical trial infrastructure versus alternative counterfactual scenarios, illustrating differences in economic multipliers and health impacts.

Alternative counterfactual scenarios include:

1. **Military R&D continuation**: The $27.2B continues funding military research and development, potentially yielding civilian technology spillovers (e.g., GPS, internet protocols, materials science advances). This scenario is partially addressed in the peace dividend calculations, which acknowledge that military spending generates economic multiplier effects of 0.5-1.0× compared to pragmatic clinical trial multipliers of 2.0-3.0×.
2. **Return to taxpayers**: Funds are returned via tax cuts, enabling private consumption and

investment. Under this scenario, the opportunity cost equals the weighted average return on private capital (approximately 3% annually in developed economies).

3. **Alternative government priorities**: Reallocation to other public investments such as infrastructure, education, or climate mitigation. Each alternative use would require separate cost-benefit analysis to determine relative efficiency.

Methodological note on baseline selection: The economically rigorous baseline is the "next best alternative use" rather than "status quo continuation." However, identifying the single next-best alternative requires comprehensive comparison across all possible uses of public funds, which exceeds the scope of this analysis. This analysis therefore focuses on the **conditional benefits of the system**: the health and economic gains achievable by redirecting $27.2B from military to medical research infrastructure.

Conservative interpretation: Even if alternative uses generate positive economic value, a global pragmatic trial system exhibits **dominant intervention** characteristics (cost-saving: $0.0018 (95% CI: $0.0007-$0.0041) per DALY), indicating it saves costs while improving health outcomes. Under standard cost-effectiveness frameworks, dominant interventions are unconditionally recommended regardless of alternative uses, as they represent free gains in both dimensions (reduced costs and improved health).

Peace Dividend Calculation Methodology

> **i** Relative Importance
>
> The peace dividend ($114B (95% CI: $90.1B-$141B)/year) represents <0.01% of the timeline shift value ($84.8 quadrillion (95% CI: $62.4 quadrillion-$97.3 quadrillion)). We include the full methodology for transparency and funder due diligence, not because it materially affects the case.

The peace dividend represents economic benefits from reduced military spending. The 1% Treaty redirects 1% of global military spending ($2.72T[48] in 2024) = $27.2B annually.

Economic benefits of reduced military spending

1. **Direct fiscal savings (Cash):** $27.2B available for productive investment. This is the floor.
2. **Diplomatic De-escalation (Upside):** Reduced conflict-related economic damage (trade disruption, infrastructure destruction, refugee costs).

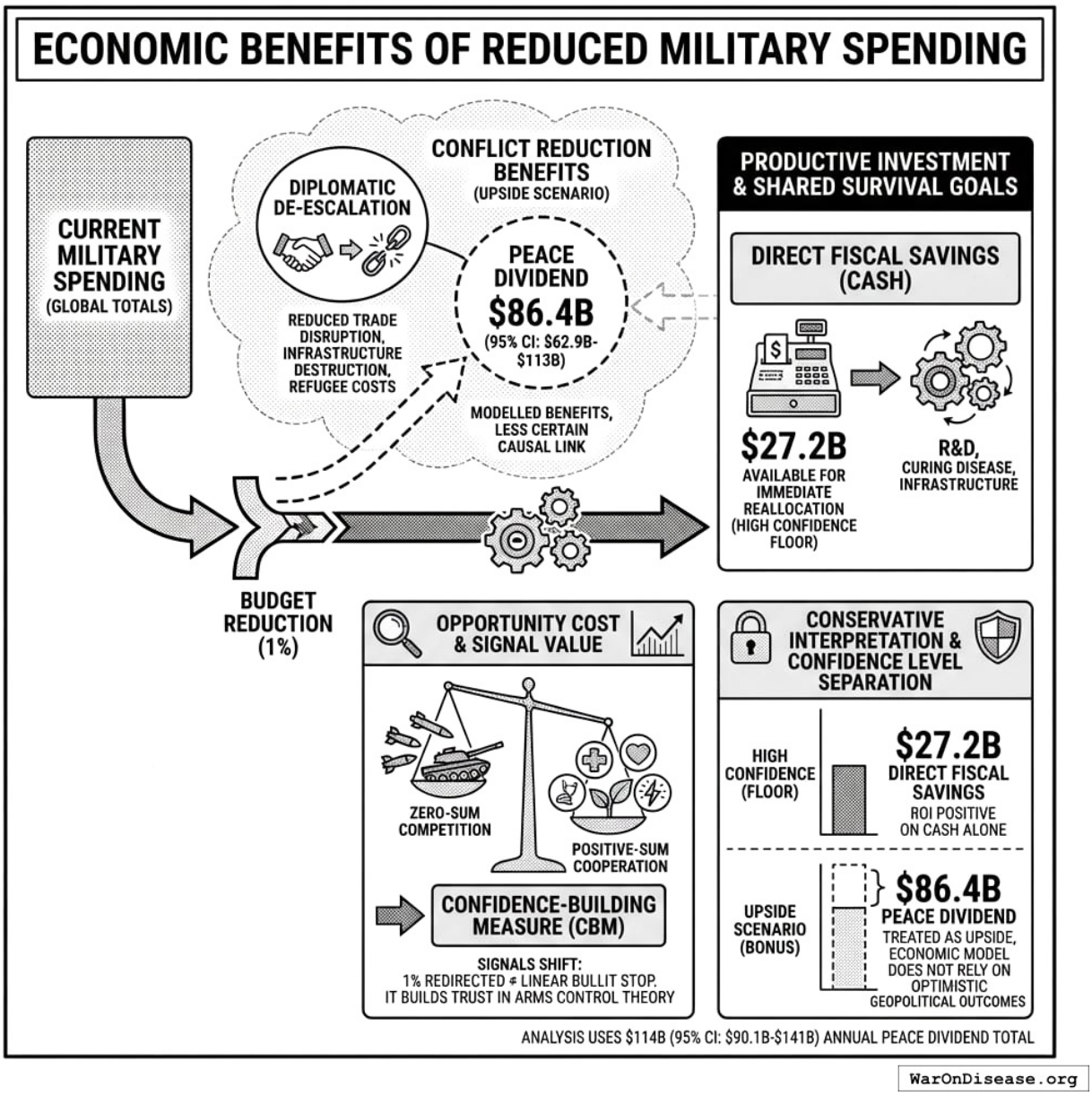


Figure 51: A breakdown of the peace dividend components, showing the guaranteed 27.2 billion dollar fiscal floor compared to the 86.4 billion dollar upside scenario from conflict reduction.

Opportunity Cost & Signal Value: The argument isn't just that 1% less budget stops 1% of bullets linearly. It's that 1% *redirected* to shared survival goals (curing disease) acts as a **confidence-building measure** (CBM) in arms control theory. It signals a shift from zero-sum competition to positive-sum cooperation.

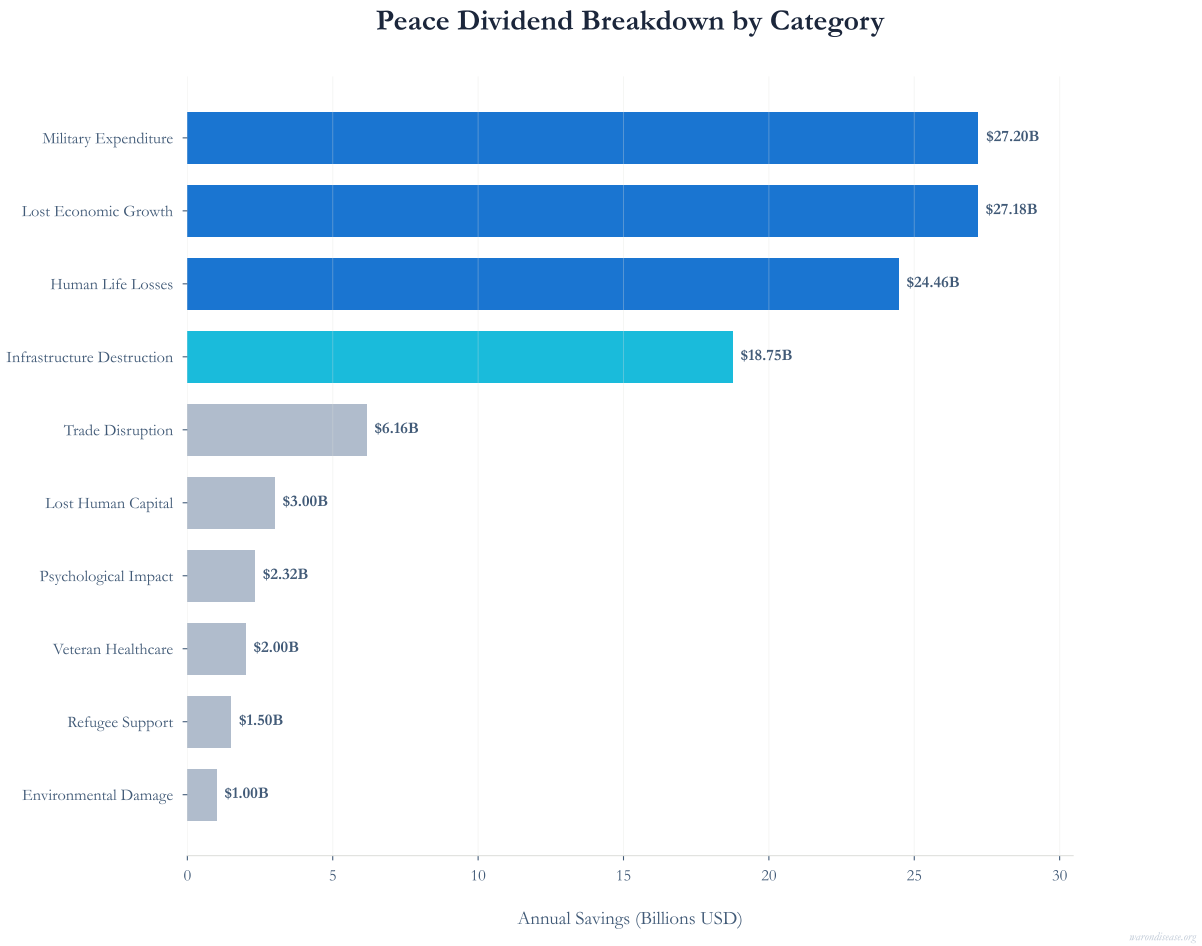
Conservative estimate: Analysis uses $114B (95% CI: $90.1B-$141B) annual peace dividend. Even if conflict intensity doesn't drop linearly, the $27.2B annual cash reallocation is real. The ROI works on the cash alone; peace is a massive bonus.

War Costs Breakdown

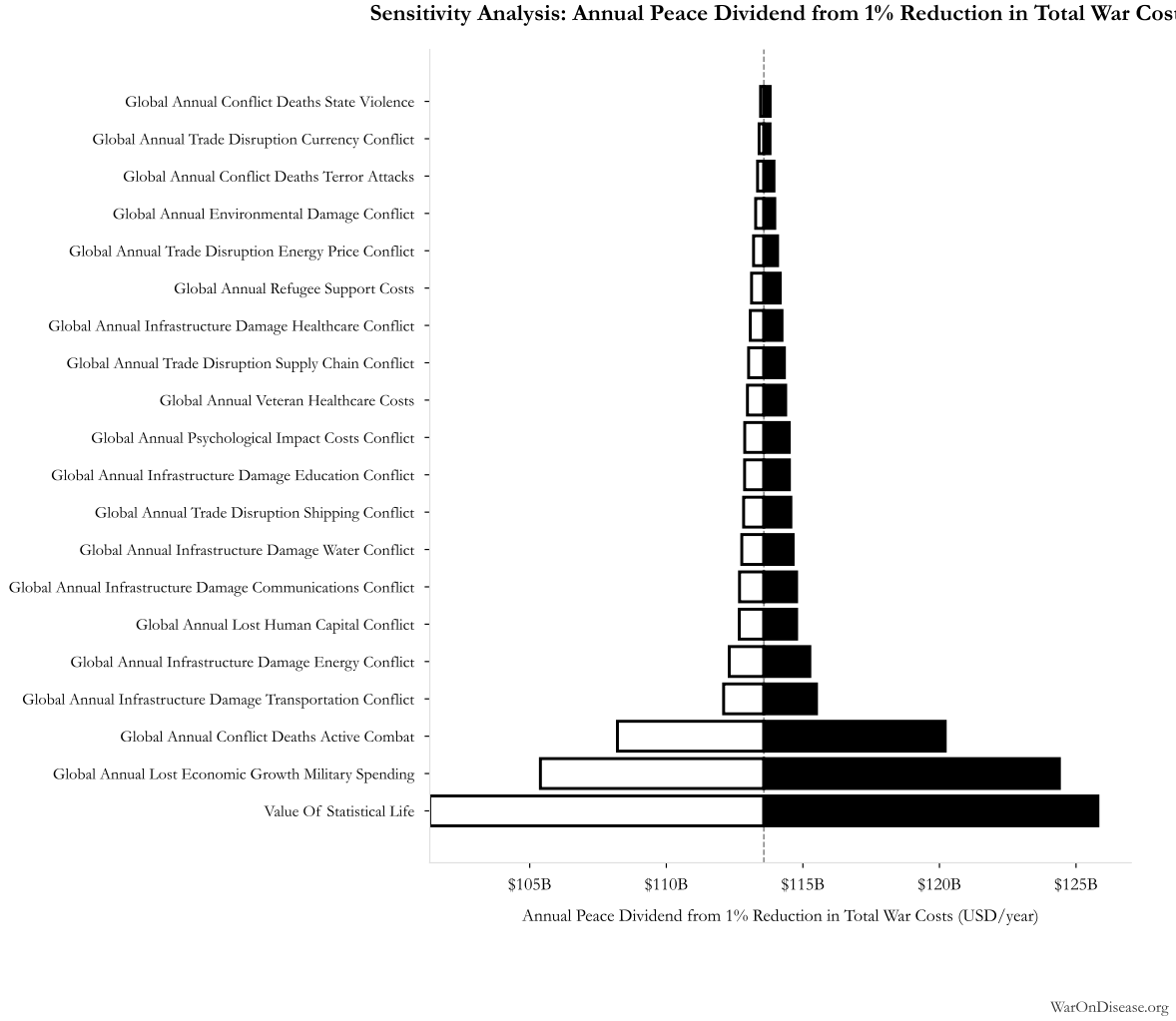
Cost Category	Annual Amount	Components
Direct Military Spending	$2.72T[48]	SIPRI 2024 global military budgets (source)[61]
Infrastructure Destruction	$1.88T (95% CI: $1.37T-$2.47T)	Transportation, energy, communications, water, education, healthcare facilities
Human Life Losses	$2.45T (95% CI: $1.31T-$3.75T)	245 thousand deaths/year (95% CI: 194 thousand deaths/year-302 thousand deaths/year) conflict deaths × $10M (95% CI: $5M-$15M)[127] value of statistical life (conservative estimate)
Trade Disruption	$616B (95% CI: $450B-$812B)	Shipping, supply chains, energy prices, currency volatility
Lost Economic Growth	$2.72T (95% CI: $1.90T-$3.80T)[35]	Opportunity cost of military spending vs. productive investment
Veteran Healthcare	$200B (95% CI: $140B-$280B)[40]	Long-term medical care for conflict-related injuries
Refugee Support	$150B (95% CI: $105B-$210B)[38]	108.4M displaced persons[137] × $1,384/year[38]
Environmental Damage	$100B (95% CI: $70B-$140B)[33]	Environmental destruction, toxic contamination, restoration costs
Psychological Impact	$232B (95% CI: $162B-$325B)[37]	PTSD treatment, mental health services, productivity loss
Lost Human Capital	$300B (95% CI: $210B-$420B)[36]	Productive capacity lost from casualties and displacement
Total War Costs	**$11.4T (95% CI: $9.01T-$14.1T)**	Combined direct and indirect annual costs
1% Reduction	**$114B (95% CI: $90.1B-$141B)**	Peace dividend from 1% treaty implementation

This calculation methodology follows standard cost-of-conflict analysis frameworks used by the World Bank, IMF, and academic conflict economics research.

Note on confidence levels: The direct military spending reduction ($27.2B) has high confidence. The remaining conflict cost reductions assume proportional scaling (1% military spending → 1% conflict reduction) which lacks empirical validation. Conservative scenarios should use only direct fiscal savings; optimistic scenarios can include full peace dividend effects.



Sensitivity of peace dividend estimate: The tornado chart below shows which cost components have the largest impact on the total peace dividend. The primary drivers are infrastructure destruction costs and lost economic growth:



Confidence level separation: The peace dividend calculation separates into two components:

1. **Direct fiscal savings (high confidence)**: $27.2B - The 1% reduction in military budgets ($27.2B) represents direct fiscal savings with high certainty. These funds are immediately available for reallocation.

2. **Conflict reduction benefits (upside scenario)**: $86.4B (95% CI: $62.9B-$113B) - The remaining $86.4B (95% CI: $62.9B-$113B) models the benefits if conflict costs reduce proportionally. While the causal link between marginal budget cuts and conflict intensity is complex, the *directionality* is positive.

$$Savings_{conflict}$$
$$= Benefit_{peace,soc} - Funding_{treaty}$$
$$= \$114B - \$27.2B$$
$$= \$86.4B$$

where $Benefit_{peace,soc}$
$$= Cost_{war,total} \times Reduce_{treaty}$$
$$= \$11.4T \times 1\%$$
$$= \$114B$$

where $Cost_{war,total}$
$$= Cost_{war,direct} + Cost_{war,indirect}$$
$$= \$7.66T + \$3.7T$$
$$= \$11.4T$$

where $Cost_{war,direct}$
$$= Loss_{life,conflict} + Damage_{infra,total}$$
$$+ Disruption_{trade} + Spending_{mil}$$
$$= \$2.45T + \$1.88T + \$616B + \$2.72T$$
$$= \$7.66T$$

where $Loss_{life,conflict}$
$$= Cost_{combat,human} + Cost_{state,human}$$
$$+ Cost_{terror,human}$$
$$= \$2.34T + \$27B + \$83B$$
$$= \$2.45T$$

where $Cost_{combat,human}$
$$= Deaths_{combat} \times VSL$$
$$= 234{,}000 \times \$10M$$
$$= \$2.34T$$

where $Cost_{state,human}$
$$= Deaths_{state} \times VSL$$
$$= 2{,}700 \times \$10M$$
$$= \$27B$$

where $Cost_{terror,human}$
$$= Deaths_{terror} \times VSL$$
$$= 8{,}300 \times \$10M$$
$$= \$83B$$

where $Damage_{infra,total}$
$$= Damage_{comms} + Damage_{edu} + Damage_{energy}$$
$$+ Damage_{health} + Damage_{transport}$$
$$+ Damage_{water}$$
$$= \$298B + \$234B + \$422B + \$166B + \$487B + \$268B$$

Conservative interpretation: The direct fiscal savings ($27.2B annually) are certain. The "peace dividend" is treated as an **upside scenario** in the conservative case, ensuring the economic model doesn't rely on optimistic geopolitical outcomes. The ROI remains positive on R&D savings alone.

Research Acceleration Mechanism

The 12.3x (95% CI: 4.19x-61.3x) research acceleration multiplier comes from the combination of multiple proven accelerators:

Faster Recruitment: The Oxford RECOVERY trial recruited 47,000+ patients across nearly 200 hospitals[138], while 80% of traditional trials fail to meet enrollment timelines[139]. This speed comes from pragmatic eligibility (minimal exclusions[140] vs. 86.1% excluded traditionally) and embedded recruitment in routine care.

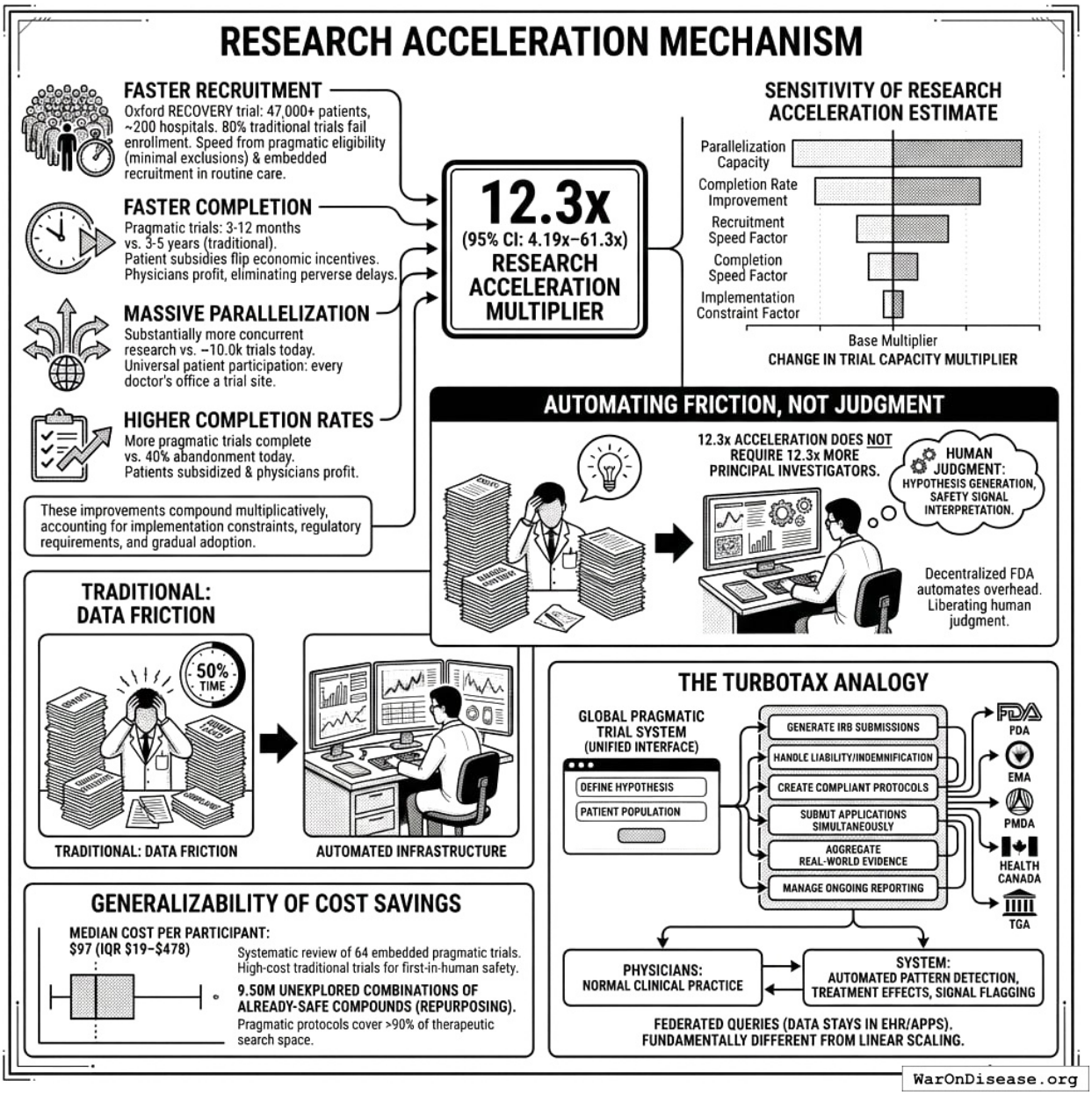


Figure 52: A flowchart contrasting the manual, linear bottlenecks of traditional clinical trials with the automated, parallelized infrastructure of a decentralized pragmatic trial system.

Faster Completion: Pragmatic trials complete in 3-12 months instead of 3-5 years because patient subsidies flip economic incentives. Physicians gain revenue from trial participation rather than losing it, eliminating the perverse incentives that delay traditional trials.

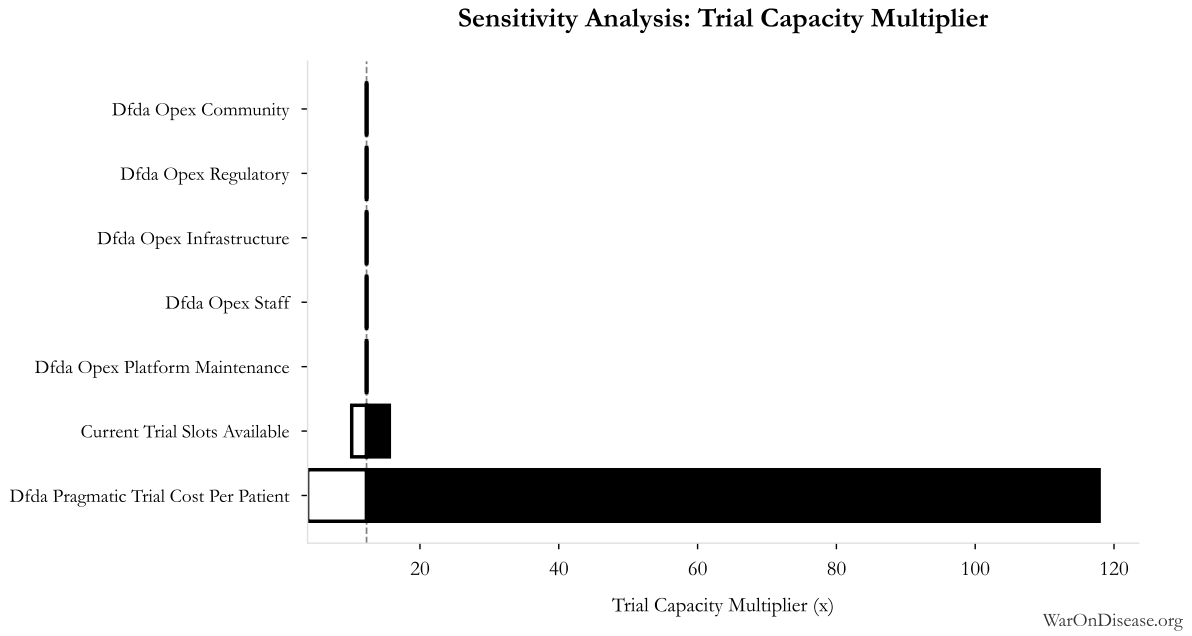
Massive Parallelization: With more trials running simultaneously (vs. 10.0 thousand trials[10] today), the framework achieves substantially more concurrent research. Universal patient participation makes this possible, as every doctor's office becomes a trial site.

Higher Completion Rates: More of pragmatic trials complete (vs. 40%[14] abandonment rate today) because patients are subsidized and physicians profit from participation.

These improvements compound multiplicatively to produce the 12.3x (95% CI: 4.19x-61.3x) acceleration used in this analysis. This is a conservative estimate accounting for implementation constraints, regulatory requirements, and gradual adoption.

Generalizability of Cost Savings: Critics regarding RECOVERY and ADAPTABLE as outliers should note that a systematic review of 64 embedded pragmatic clinical trials[74] found a median cost per participant of just **$97** (IQR $19–$478). High-cost traditional trials are necessary only for first-in-human safety testing. For the **9.50 million combinations** unexplored combinations of *already-safe* compounds (repurposing), pragmatic protocols are sufficient, covering the vast majority (>90%) of the therapeutic search space.

Sensitivity of research acceleration estimate: The tornado chart below shows which input parameters have the largest impact on the trial capacity multiplier. The width of each bar shows how much the multiplier changes when that parameter varies across its uncertainty range:



Automating Friction, Not Judgment: The system operates as automated infrastructure analyzing time-series EHR data from electronic health records, wearables, and apps. The 12.3x (95% CI: 4.19x-61.3x) research acceleration does **not** require 12.3x (95% CI: 4.19x-61.3x) more Principal Investigators.

The bottleneck in clinical research isn't "scientific genius", we have plenty of underemployed PhDs. The bottleneck is **"Data Friction"**.

Currently, researchers spend up to 50% of their time[141] on grants and administrative tasks. A decentralized FDA automates this overhead, liberating human judgment to focus on hypothesis generation and complex safety signal interpretation.

The TurboTax Analogy: Just as TurboTax wraps the complexity of federal, state, and local tax codes into a simple interface (users answer questions, it generates compliant filings), a global pragmatic trial system wraps the complexity of global regulatory bodies (FDA, EMA, PMDA,

Health Canada, TGA, etc.) into a unified system. Researchers define their hypothesis and patient population; the system automatically:

- Generates IRB submissions for each jurisdiction
- Handles liability insurance and indemnification
- Creates compliant protocol documents for each agency
- Submits applications simultaneously to multiple regulatory bodies
- Aggregates real-world evidence into agency-specific formats
- Manages ongoing reporting requirements across jurisdictions

The system uses federated queries (data stays in EHR and consumer health app systems) rather than centralized databases, enabling analysis without data movement. Physicians continue normal clinical practice; the system automatically detects patterns, identifies treatment effects, and flags signals for peer review. This is fundamentally different from traditional research models that scale linearly with researcher headcount.

Treatment Discovery Through Therapeutic Space Exploration

The 12.3x (95% CI: 4.19x-61.3x) research acceleration transforms our ability to explore the vast therapeutic space where undiscovered treatments already exist.



Figure 53: A visual comparison showing the expansion of searchable therapeutic space, contrasting traditional research speed with the 12.3x acceleration in discovery capacity.

The Unexplored Therapeutic Frontier

The fundamental problem isn't that effective treatments are hard to discover. It's that we're barely looking. As documented in The Untapped Therapeutic Frontier:

- **9.50 million combinations** plausible drug-disease combinations exist (9.50 thousand compounds (95% CI: 7.00 thousand compounds-12.0 thousand compounds) safe compounds × 1.00 thousand diseases (95% CI: 800 diseases-1.20 thousand diseases))
- **<1%** of these combinations have been tested
- **Only 12%** of the human interactome has ever been targeted by drugs

- **30%** of approved drugs gain new indications, proving undiscovered uses exist

$$\begin{aligned} & N_{combos} \\ & = N_{safe} \times N_{diseases,trial} \\ & = 9{,}500 \times 1{,}000 \\ & = 9.5M \end{aligned}$$

Effective treatments likely already exist among tested-safe compounds. We just haven't looked.

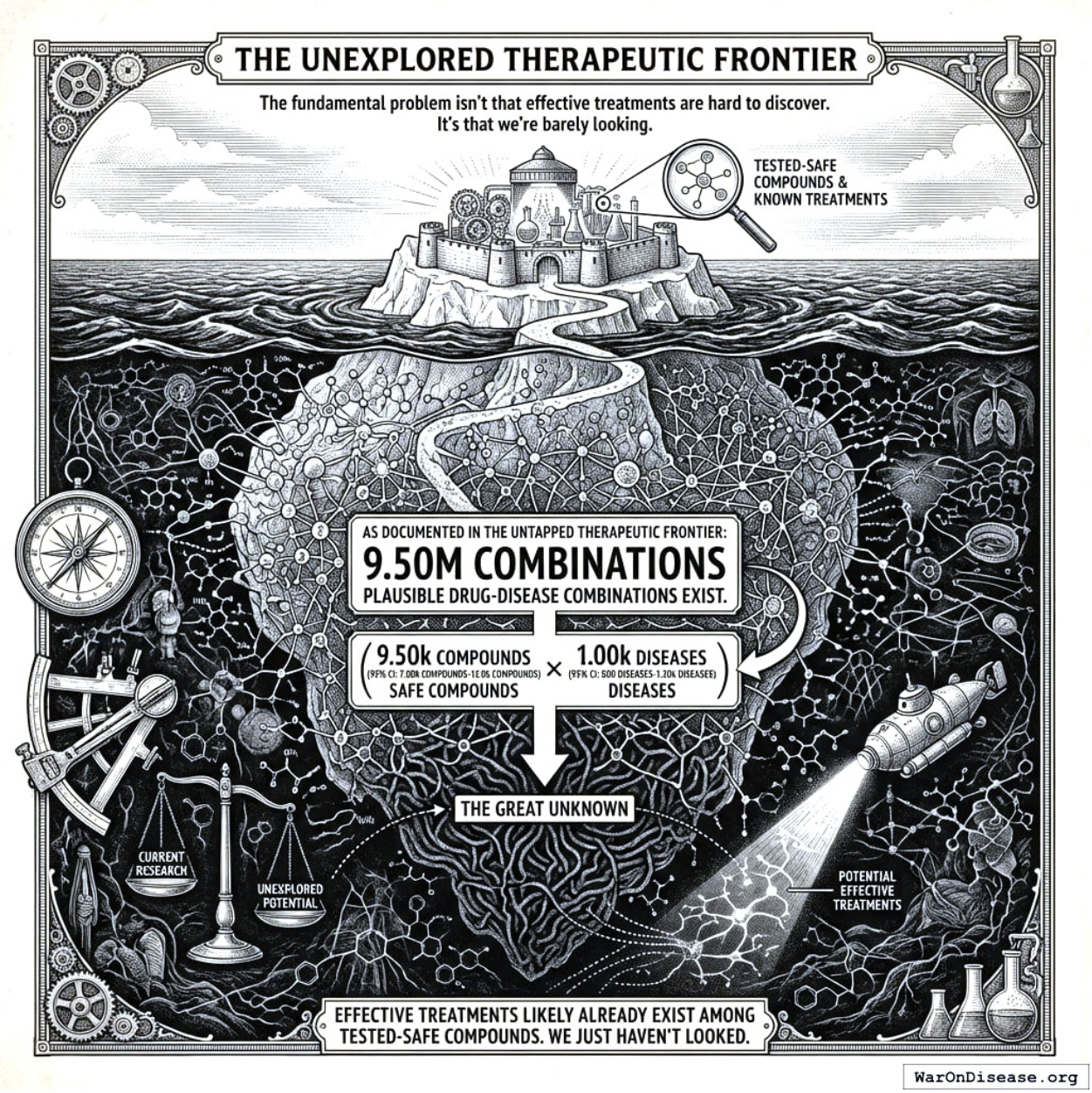


Figure 54: A visualization of the vast drug-disease search space, contrasting the 9.5 million possible therapeutic combinations against the tiny fraction currently explored.

Current Exploration Rate vs. Therapeutic Space

Under the status quo:

- **6.65 thousand diseases (95% CI: 5.70 thousand diseases-8.24 thousand diseases)** currently lack effective treatment
- **15 diseases/year (95% CI: 8 diseases/year-30 diseases/year) diseases/year** receive their first effective treatment
- At this exploration rate, systematically searching the remaining 99%+ of therapeutic space would take ~**443 years (95% CI: 324 years-712 years)**
- **222 years (95% CI: 162 years-356 years)** average wait for a randomly selected disease to receive its first treatment

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

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

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

This calculation is empirically grounded: only ~5% of the 7.00 thousand diseases (95% CI: 6.00 thousand diseases-10.0 thousand diseases) rare diseases have FDA-approved treatments after 40+ years of the Orphan Drug Act. At the current rate of 15 diseases/year (95% CI: 8 diseases/year-30 diseases/year) diseases/year getting first treatments, most of the therapeutic space remains permanently unexplored.

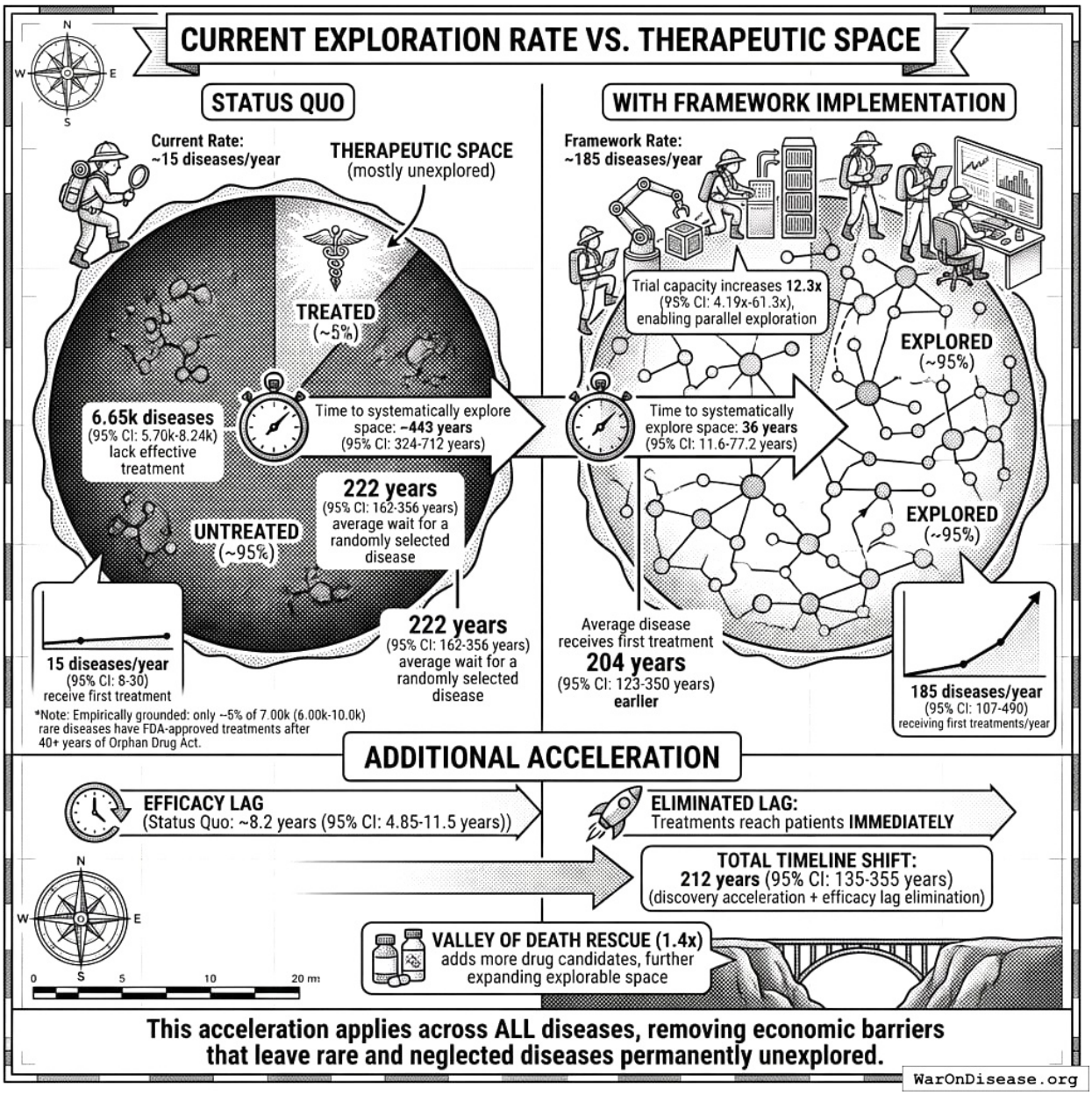


Figure 55: A side-by-side comparison of drug discovery efficiency showing the shift from a 443-year exploration timeline to a 36-year timeline under the proposed framework.

With framework implementation:

- Trial capacity increases 12.3x (95% CI: 4.19x-61.3x), enabling parallel exploration of the therapeutic space
- Exploration rate: **185 diseases/year (95% CI: 107 diseases/year-490 diseases/year) diseases receiving first treatments/year** (vs 15 diseases/year (95% CI: 8 diseases/year-30 diseases/year)/year status quo)
- Time to systematically explore disease space: **36 years (95% CI: 11.6 years-77.2 years)** (vs 443 years (95% CI: 324 years-712 years))

- Average disease receives first treatment **204 years (95% CI: 123 years-350 years) earlier**

$$
\begin{aligned}
&Treatments_{dFDA,ann} \\
&= Treatments_{new,ann} \times k_{capacity} \\
&= 15 \times 12.3 \\
&= 185
\end{aligned}
$$

$$
\text{where } k_{capacity} = \frac{N_{fundable,ann}}{Slots_{curr}} = \frac{23.4M}{1.9M} = 12.3
$$

$$
\begin{aligned}
&\text{where } N_{fundable,ann} \\
&= \frac{Subsidies_{trial,ann}}{Cost_{pragmatic,pt}} \\
&= \frac{\$21.7B}{\$929} \\
&= 23.4M
\end{aligned}
$$

$$
\begin{aligned}
&\text{where } Subsidies_{trial,ann} \\
&= Treasury_{RD,ann} - OPEX_{dFDA} \\
&= \$21.8B - \$40M \\
&= \$21.7B
\end{aligned}
$$

$$
\begin{aligned}
&\text{where } OPEX_{dFDA} \\
&= Cost_{platform} + Cost_{staff} + Cost_{infra} \\
&+ Cost_{regulatory} + Cost_{community} \\
&= \$15M + \$10M + \$8M + \$5M + \$2M \\
&= \$40M
\end{aligned}
$$

$$
\begin{aligned}
&\text{where } Treasury_{RD,ann} \\
&= Funding_{treaty} - Payout_{bond,ann} - Funding_{political,ann} \\
&= \$27.2B - \$2.72B - \$2.72B \\
&= \$21.8B
\end{aligned}
$$

$$
\begin{aligned}
&\text{where } Funding_{treaty} \\
&= Spending_{mil} \times Reduce_{treaty} \\
&= \$2.72T \times 1\% \\
&= \$27.2B
\end{aligned}
$$

$$
\begin{aligned}
&\text{where } Payout_{bond,ann} \\
&= Funding_{treaty} \times Pct_{bond} \\
&= \$27.2B \times 10\% \\
&= \$2.72B
\end{aligned}
$$

$$
\begin{aligned}
&\text{where } Funding_{treaty} \\
&= Spending_{mil} \times Reduce_{treaty} \\
&= \$2.72T \times 1\% \\
&= \$27.2B
\end{aligned}
$$

$$
\begin{aligned}
&\text{where } Funding_{political,ann} \\
&= Funding_{treaty} \times Pct_{political}
\end{aligned}
$$

$$T_{queue,dFDA} = \frac{T_{queue,SQ}}{k_{capacity}} = \frac{443}{12.3} = 36$$

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

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

$$\text{where } k_{capacity} = \frac{N_{fundable,ann}}{Slots_{curr}} = \frac{23.4M}{1.9M} = 12.3$$

$$\begin{gathered}\text{where } N_{fundable,ann} \\ = \frac{Subsidies_{trial,ann}}{Cost_{pragmatic,pt}} \\ = \frac{\$21.7B}{\$929} \\ = 23.4M\end{gathered}$$

$$\begin{gathered}\text{where } Subsidies_{trial,ann} \\ = Treasury_{RD,ann} - OPEX_{dFDA} \\ = \$21.8B - \$40M \\ = \$21.7B\end{gathered}$$

$$\begin{gathered}\text{where } OPEX_{dFDA} \\ = Cost_{platform} + Cost_{staff} + Cost_{infra} \\ + Cost_{regulatory} + Cost_{community} \\ = \$15M + \$10M + \$8M + \$5M + \$2M \\ = \$40M\end{gathered}$$

$$\begin{gathered}\text{where } Treasury_{RD,ann} \\ = Funding_{treaty} - Payout_{bond,ann} - Funding_{political,ann} \\ = \$27.2B - \$2.72B - \$2.72B \\ = \$21.8B\end{gathered}$$

$$\begin{gathered}\text{where } Funding_{treaty} \\ = Spending_{mil} \times Reduce_{treaty} \\ = \$2.72T \times 1\% \\ = \$27.2B\end{gathered}$$

$$\begin{gathered}\text{where } Payout_{bond,ann} \\ = Funding_{treaty} \times Pct_{bond} \\ = \$27.2B \times 10\% \\ = \$2.72B\end{gathered}$$

$$\begin{gathered}\text{where } Funding_{treaty} \\ = Spending_{mil} \times Reduce_{treaty} \\ = \$2.72T \times 1\% \\ = \$27.2B\end{gathered}$$

$$\text{where } Funding_{political,ann}$$

Additionally, eliminating the 8.2 years (95% CI: 4.85 years-11.5 years)-year efficacy lag means discovered treatments reach patients immediately. The **total timeline shift** is 212 years (95% CI: 135 years-355 years) (discovery acceleration + efficacy lag elimination).

$$T_{accel,max} = T_{accel} + T_{lag} = 204 + 8.2 = 212$$

$$\text{where } T_{accel}$$
$$= T_{first,SQ} \times \left(1 - \frac{1}{k_{capacity}}\right)$$
$$= 222 \times \left(1 - \frac{1}{12.3}\right)$$
$$= 204$$

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

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

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

$$\text{where } k_{capacity} = \frac{N_{fundable,ann}}{Slots_{curr}} = \frac{23.4M}{1.9M} = 12.3$$

$$\text{where } N_{fundable,ann}$$
$$= \frac{Subsidies_{trial,ann}}{Cost_{pragmatic,pt}}$$
$$= \frac{\$21.7B}{\$929}$$
$$= 23.4M$$

$$\text{where } Subsidies_{trial,ann}$$
$$= Treasury_{RD,ann} - OPEX_{dFDA}$$
$$= \$21.8B - \$40M$$
$$= \$21.7B$$

$$\text{where } OPEX_{dFDA}$$
$$= Cost_{platform} + Cost_{staff} + Cost_{infra}$$
$$+Cost_{regulatory} + Cost_{community}$$
$$= \$15M + \$10M + \$8M + \$5M + \$2M$$
$$= \$40M$$

$$\text{where } Treasury_{RD,ann}$$
$$= Funding_{treaty} - Payout_{bond,ann} - Funding_{political,ann}$$
$$= \$27.2B - \$2.72B - \$2.72B$$
$$= \$21.8B$$

$$\text{where } Funding_{treaty}$$
$$= Spending_{mil} \times Reduce_{treaty}$$
$$= \$2.72T \times 1\%$$
$$= \$27.2B$$

$$\text{where } Payout_{bond,ann}$$
$$= Funding_{treaty} \times Pct_{bond}$$
$$= \$27.2B \times 10\%$$
$$= \$2.72B$$

Note: Valley of death rescue (1.4x) adds more drug candidates to the pipeline, further expanding the explorable therapeutic space.

$$k_{rescue} = Attrition_{valley} + 1 = 40\% + 1 = 1.4$$

This acceleration applies across *all* diseases, not just well-funded ones. The current system prioritizes diseases with commercial potential; the framework's universal trial infrastructure removes economic barriers that leave rare and neglected diseases permanently unexplored.

Addressing the Returns Question: Diminishing, Linear, or Compounding?

A common objection is that "more trials won't produce proportionally more treatments," the diminishing returns hypothesis. This deserves serious consideration, but the evidence suggests the opposite may be true.

Important distinction: Bloom et al. (2020)[142] document declining research productivity (~5% annually across industries), but this measures **idea productivity** (breakthroughs per researcher-year). This intervention targets a different margin: **trial execution efficiency** (cost per patient enrolled, completion rates, recruitment speed). Streamlining data collection is not the same as discovering new biology.

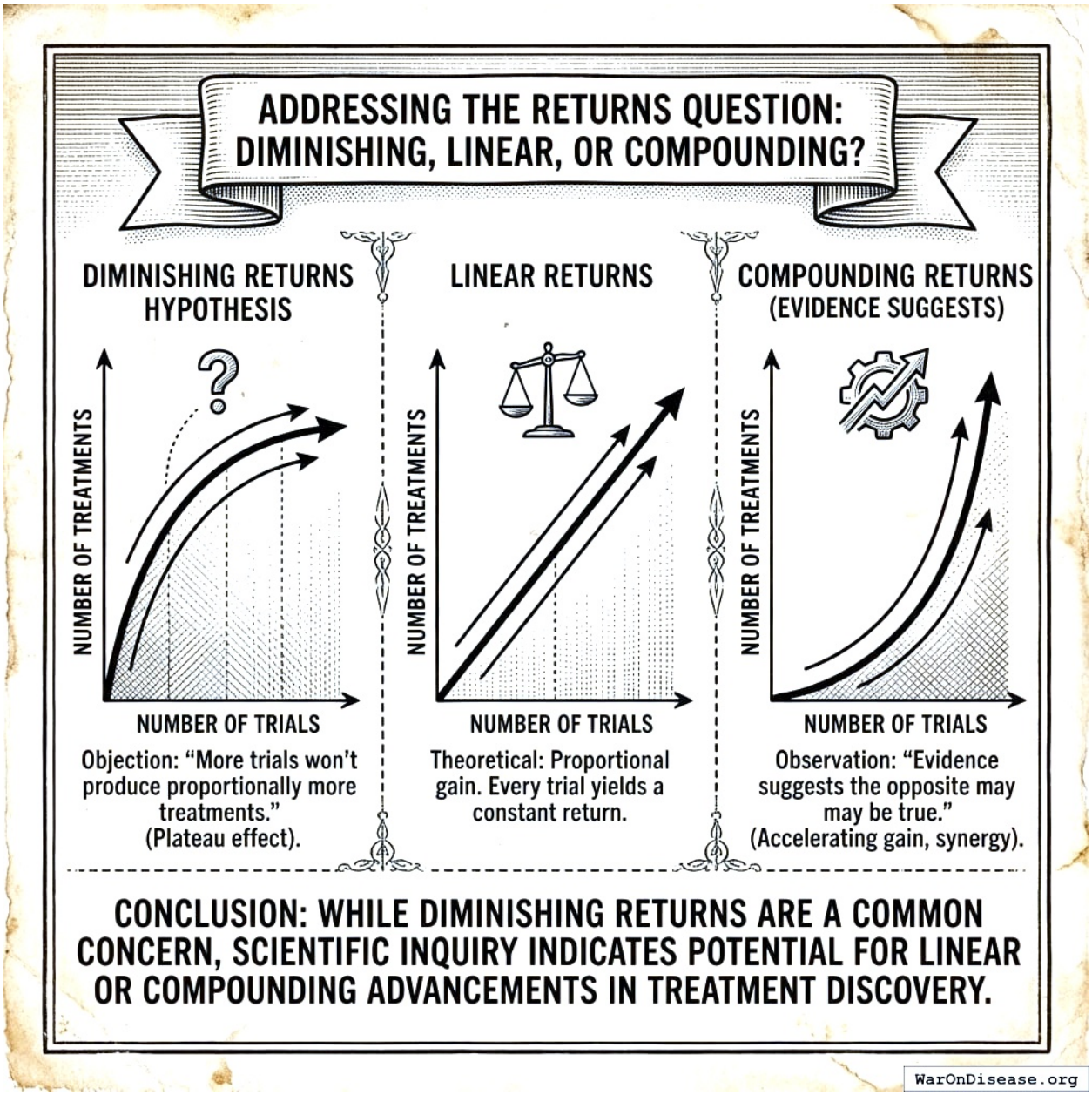


Figure 56: A comparison of three growth trajectories (diminishing, linear, and compounding) illustrating how the volume of treatments scales relative to the number of trials.

Why Diminishing Returns Is Unlikely (We Haven't Started Looking)

The diminishing returns objection assumes we've exhausted low-hanging fruit. But we've barely begun:

1. **Single compounds alone**: 9.50 million combinations possible combinations of known safe compounds × diseases. At current trial capacity, systematically testing these would take **2.88 thousand years (95% CI: 2.45 thousand years-3.43 thousand years)**. We won't finish until the year 5000.

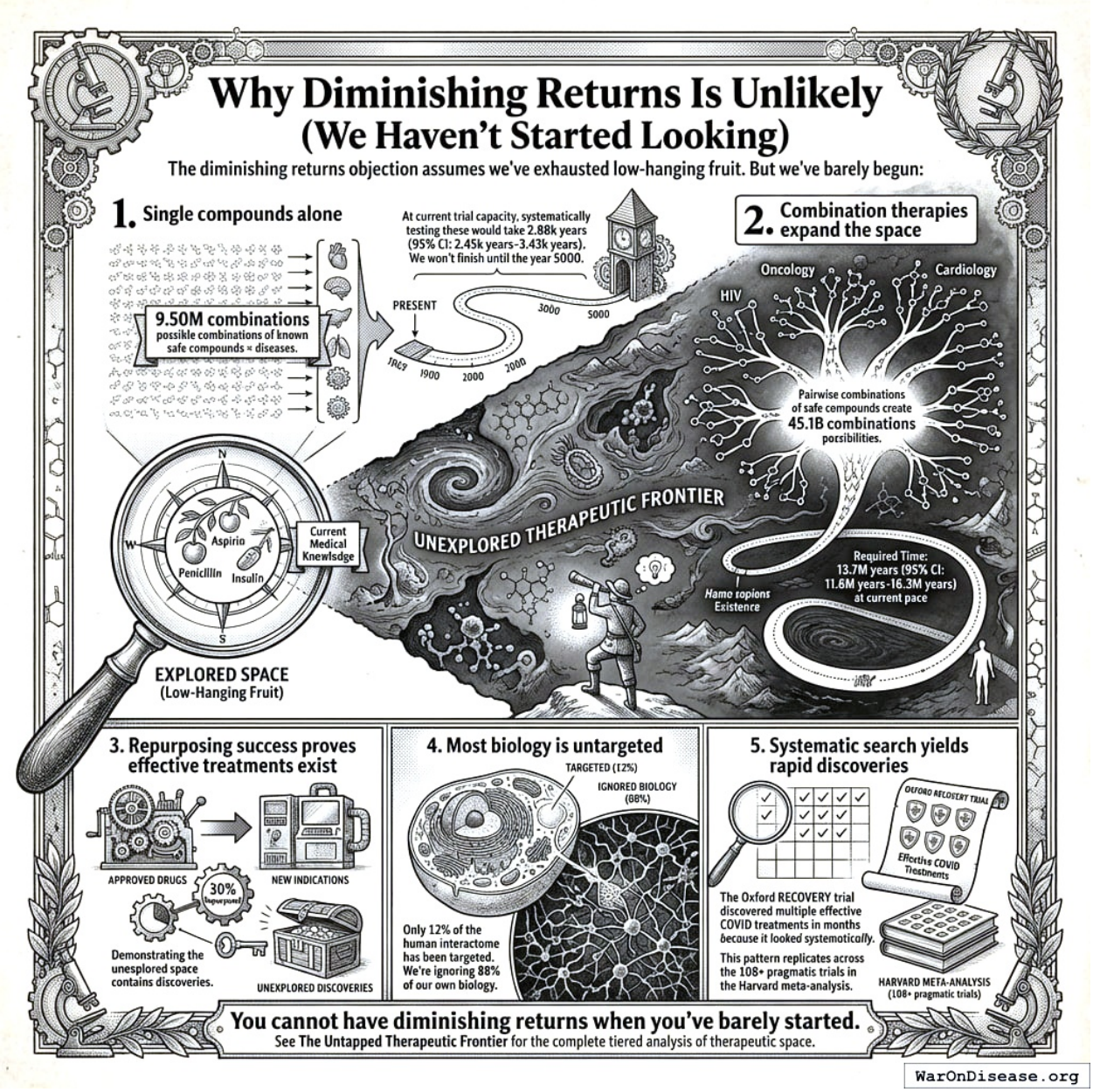


Figure 57: A comparison of the small fraction of explored therapeutic space versus the massive, untapped potential of compound combinations and the human interactome.

$$
\begin{aligned}
&T_{explore,safe} \\
&= \frac{N_{combos}}{Trials_{ann,curr}} \\
&= \frac{9.5M}{3{,}300} \\
&= 2{,}880
\end{aligned}
$$

$$
\begin{aligned}
&\text{where } N_{combos} \\
&= N_{safe} \times N_{diseases,trial} \\
&= 9{,}500 \times 1{,}000 \\
&= 9.5M
\end{aligned}
$$

2. **Combination therapies expand the space**: Modern medicine relies on multi-drug regimens (oncology, HIV, cardiology). Pairwise combinations of safe compounds create **45.1 billion combinations** possibilities, requiring **13.7 million years (95% CI: 11.6 million years-16.3 million years)** at current pace, longer than *Homo sapiens* has existed.

$$
\begin{aligned}
&Space_{combo} \\
&= N_{combo} \times N_{diseases,trial} \\
&= 45.1M \times 1{,}000 \\
&= 45.1B
\end{aligned}
$$

3. **Repurposing success proves effective treatments exist**: 30% of approved drugs gain new indications, demonstrating the unexplored space contains discoveries.
4. **Most biology is untargeted**: Only 12% of the human interactome has been targeted. We're ignoring 88% of our own biology.
5. **Systematic search yields rapid discoveries**: The Oxford RECOVERY trial discovered multiple effective COVID treatments in months *because it looked systematically*. This pattern replicates across the 108+ pragmatic trials in the Harvard meta-analysis[132].

See The Untapped Therapeutic Frontier for the complete tiered analysis of therapeutic space.

You cannot have diminishing returns when you've barely started.

The Case for Compounding Returns

Platform technologies may actually produce *increasing* returns per trial over time:

Expanding the candidate pipeline:

- **mRNA platforms**: COVID vaccines demonstrated mRNA can be designed in days. This platform applies to cancer, infectious diseases, and potentially genetic disorders, vastly expanding testable candidates
- **AI drug discovery**: Machine learning models increasingly predict drug-target interactions, enabling smarter trial selection. DeepMind's AlphaFold solved protein structure prediction; similar approaches will prioritize high-probability combinations

- **Epigenetic reprogramming**: Yamanaka factors demonstrated cellular reprogramming. As this technology matures, entirely new therapeutic modalities become testable
- **Gene therapy platforms**: AAV vectors, plasmid delivery, and CRISPR-based approaches create thousands of new candidate therapies annually

Learning effects that improve success rates:

- **Predictive analytics**: Each completed trial generates data that improves predictions for future trials. As the framework accumulates outcomes across millions of patients, machine learning models will increasingly identify which drug-disease combinations merit testing
- **Network pharmacology**: Understanding how drugs affect biological networks (not just single targets) reveals unexpected therapeutic applications. More data = better network models = higher hit rates
- **Biomarker discovery**: Large-scale trial data identifies patient subpopulations who respond to specific treatments, enabling precision targeting that increases trial success rates
- **Failure analysis**: Systematically studying why trials fail (wrong dose, wrong population, wrong endpoint) improves future trial design
- **Biological model refinement**: Every trial (success or failure) teaches us how human biology responds to interventions. This cumulative knowledge improves our mechanistic understanding of disease pathways, enabling increasingly accurate prediction of which candidates will work. The ratio of effective treatments per trial should *increase* over time, not decrease.

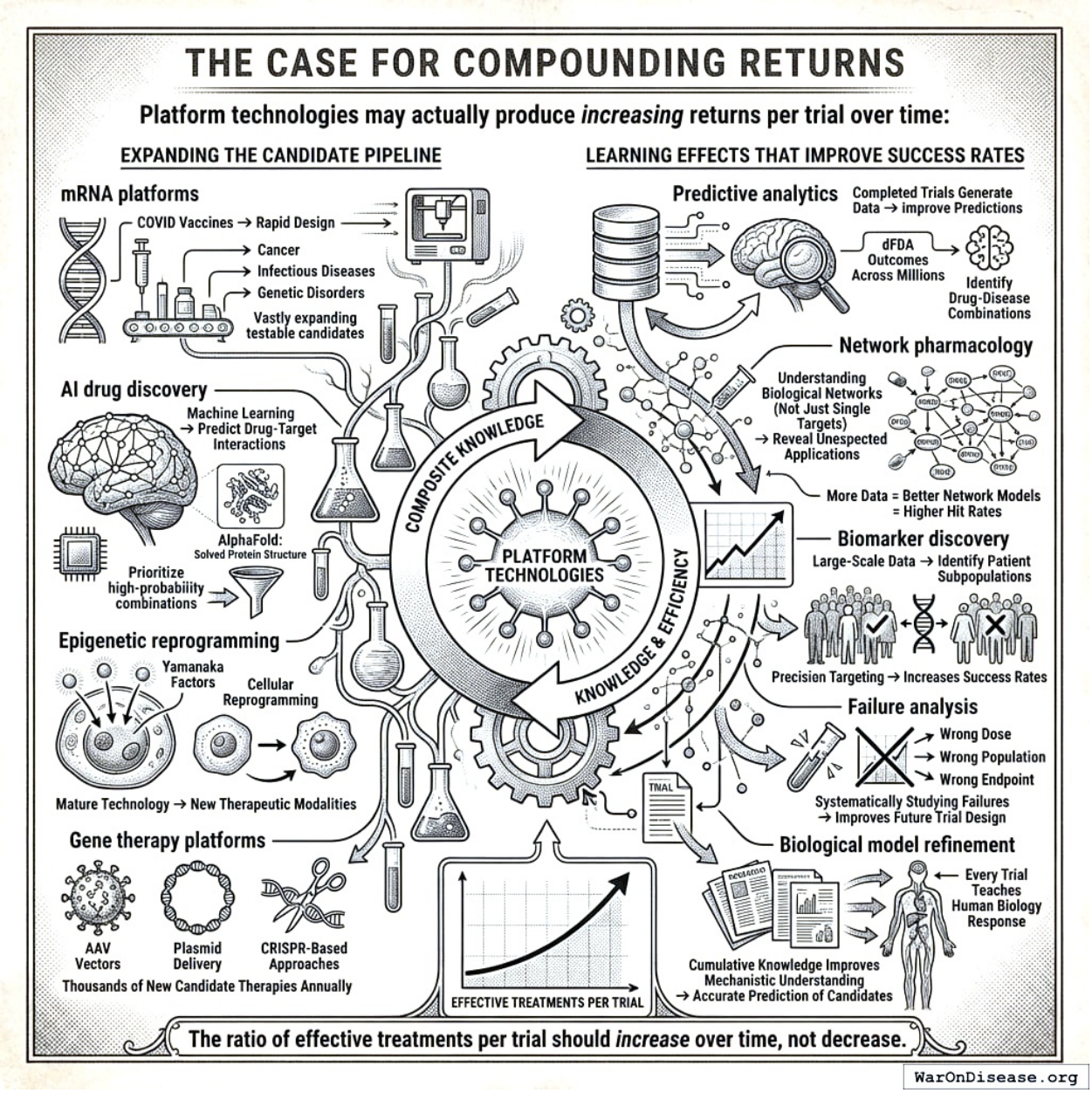


Figure 58: A virtuous cycle diagram showing how platform technologies and trial data create a flywheel effect of expanding candidate pipelines and improved success rates through cumulative learning.

Mathematical Framework: When Would Diminishing Returns Dominate?

We can formalize the competing models to identify when diminishing returns would actually matter.

Model 1: Linear (Baseline)

$$T_{discovered} = k_0 \cdot N_{trials}$$

Where k_0 is the constant discovery rate (effective treatments per trial). This assumes the therapeutic

space is sampled uniformly at random.

Model 2: Diminishing Returns (Pessimistic)

As we exhaust the therapeutic space, the hit rate decreases:

$$k_{dim}(s) = k_0 \cdot (1 - s)$$

Where $s = S_{explored}/S_{total}$ is the fraction of therapeutic space already tested. At current exploration ($s < 0.01$), this gives $k_{dim} \approx 0.99 \cdot k_0$, virtually identical to linear.

Model 3: Learning/Compounding (Optimistic)

Each trial improves our biological models, increasing future hit rates:

$$k_{learn}(n) = k_0 \cdot (1 + \alpha \cdot \ln(1 + n))$$

Where α is the learning coefficient and n is cumulative trials completed. Even modest learning ($\alpha = 0.1$) with 100,000 trials yields $k_{learn} \approx 2.15 \cdot k_0$.

Model 4: Combined (Realistic)

Both effects operate simultaneously:

$$k_{combined}(s, n) = k_0 \cdot (1 - s) \cdot (1 + \alpha \cdot \ln(1 + n))$$

The Crossover Point: When Does Depletion Dominate Learning?

Diminishing returns dominates when the depletion factor exceeds the learning factor:

$$(1 - s) < \frac{1}{1 + \alpha \cdot \ln(1 + n)}$$

Solving for the critical exploration fraction:

$$s_{crossover} = 1 - \frac{1}{1 + \alpha \cdot \ln(1 + n)}$$

Numerical Analysis:

Learning Coefficient (α)	Trials Completed (n)	Crossover Exploration ($s_{crossover}$)
0.05 (weak)	100,000	37%
0.10 (modest)	100,000	53%
0.15 (strong)	100,000	63%
0.10 (modest)	1,000,000	61%

Interpretation: Even with weak learning effects, diminishing returns only dominates after exploring 37%+ of therapeutic space. With modest learning, the crossover occurs at 53%+ exploration.

Timeline to Crossover:

At current exploration of 0.342% (95% CI: 0.21%-0.514%) (<1%), reaching the 53% crossover would require:

- **Current pace** (3.30 thousand trials/year (95% CI: 2.64 thousand trials/year-3.96 thousand trials/year)): ~1,500 years for single compounds
- **With framework** (40.6 thousand trials/year (95% CI: 16.3 thousand trials/year-170 thousand trials/year)): ~125 years

For combination therapies (45.1 billion combinations), reaching 53% exploration would take:

- **Current pace**: ~7 million years
- **With framework**: ~600,000 years

Conclusion: For any plausible planning horizon, learning effects dominate. Diminishing returns is a theoretical concern for civilizations operating on multi-century timescales, not a practical constraint for the next 100+ years of medical research.

The Conservative Default: Linear Assumption

Given genuine uncertainty about whether returns are diminishing or compounding, our analysis assumes a **linear relationship** between trial capacity and treatment discoveries. This is the conservative choice because:

1. **It's the neutral prior**: Without strong evidence for either diminishing or compounding returns, linearity is the least assumptive model
2. **It may underestimate benefits**: If platform technologies and learning effects produce compounding returns, our projections are conservative
3. **It's empirically defensible**: The RECOVERY trial's success (multiple treatments found with increased search) is consistent with linear or better returns
4. **It avoids both failure modes**: Assuming diminishing returns would justify inaction; assuming compounding returns might overstate benefits. Linearity is the responsible middle ground

Bottom line: Even under the conservative linear assumption, 12.3x (95% CI: 4.19x-61.3x) more trials produces 12.3x (95% CI: 4.19x-61.3x) more discoveries from a space that is 99%+ unexplored. The expected value calculation remains overwhelmingly positive.

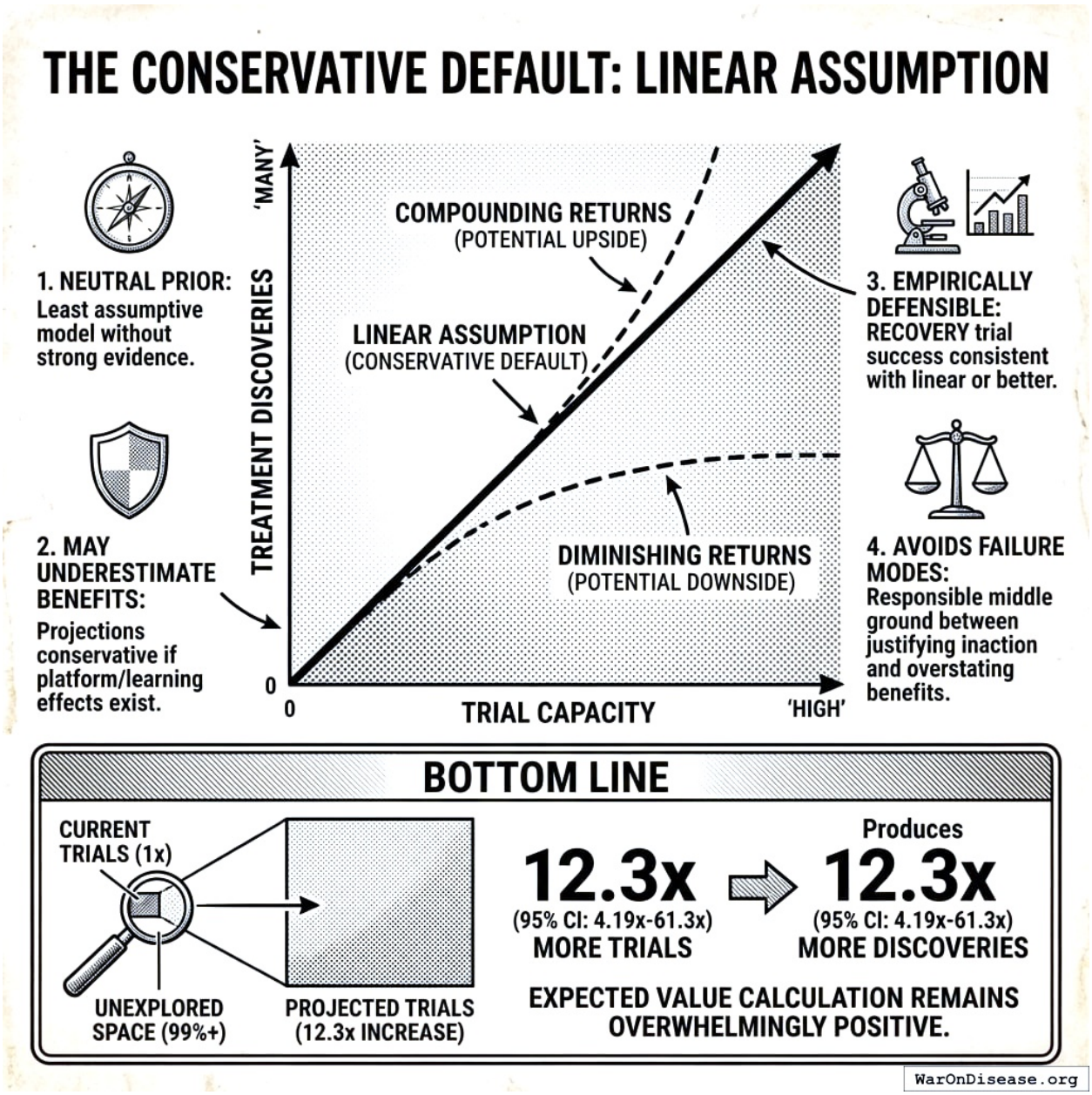


Figure 59: A comparison of three mathematical models (diminishing, linear, and compounding) showing how trial capacity translates to discoveries and why linearity is the conservative middle ground.

Data Sources and Primary Inputs

Military and Conflict Data

- Global military spending: SIPRI Military Expenditure Database[48] ($2.72T[48] annually)
- Conflict deaths: Armed Conflict Location & Event Data Project (ACLED)[29], Global Terrorism Database (GTD)[31], Uppsala Conflict Data Program (UCDP)[30]

Clinical Trial Economics

- Global trial market: Global Clinical Trials Market Report 2024[16] ($60B (95% CI: $50B-$75B)[42] annually)
- Cost reduction benchmarks: Oxford RECOVERY Trial (82x (95% CI: 50x-94.1x) cost reduction demonstrated)
- Trial completion rates: ClinicalTrials.gov database[10] (3.30 thousand trials/year (95% CI: 2.64 thousand trials/year-3.96 thousand trials/year)[16] trials initiated annually, 40%[14] completion rate)

Health Economics

- QALY valuations:[143], NBER working papers (Glied & Lleras-Muney, Philipson et al.)
- Disease burden: WHO Global Health Observatory[4]
- Rare diseases: National Organization for Rare Disorders (NORD)[144]

Economic Parameters

- Discount rate: 3% (standard health economics practice)
- Time horizon: 10 years (standard for infrastructure investments)
- Value of statistical life: $10M (95% CI: $5M-$15M)[127] (EPA/DOT standard)

All data sources include confidence levels and last-update dates. See References for complete bibliography.

Sensitivity Analysis Approach

The analysis employs comprehensive sensitivity testing across multiple scenarios to assess robustness of findings:

Conservative Scenario (637:1 (95% CI: 569:1-790:1) ROI):

- R&D cost reduction: 97.7% (95% CI: 97.5%-98.9%)
- QALY gains: 7.94 billion DALYs (95% CI: 4.43 billion DALYs-12.1 billion DALYs) annually
- Adoption timeline: 5 years to full adoption
- Includes only R&D efficiency savings (excludes peace dividend and six additional benefit categories)

Optimistic Scenario (84.8M:1 (95% CI: 46.6M:1-144M:1) ROI):

- R&D cost reduction: 97.7% (95% CI: 97.5%-98.9%) (RECOVERY trial-like efficiency)
- QALY gains: 565 billion DALYs (95% CI: 361 billion DALYs-877 billion DALYs) (total from ~212 years (95% CI: 135 years-355 years)-year timeline shift)
- Faster adoption and broader scope

Complete Case (84.8M:1 (95% CI: 46.6M:1-144M:1) ROI):

- Includes all eight quantifiable benefit categories
- Peace dividend: $114B (95% CI: $90.1B-$141B)
- Earlier treatment access, research acceleration, rare disease treatments, drug price reductions, prevention medicine, mental health benefits

Probabilistic sensitivity analysis: We ran 10,000 Monte Carlo simulations where each uncertain parameter was randomly sampled from probability distributions. The chart below shows the resulting ROI distributions with 95% confidence intervals.

What we varied: Cost reduction (50-95%), political success probability, adoption timeline (3-8 years), discount rate (1-7%), and QALY gains (0.7-1.3× baseline).

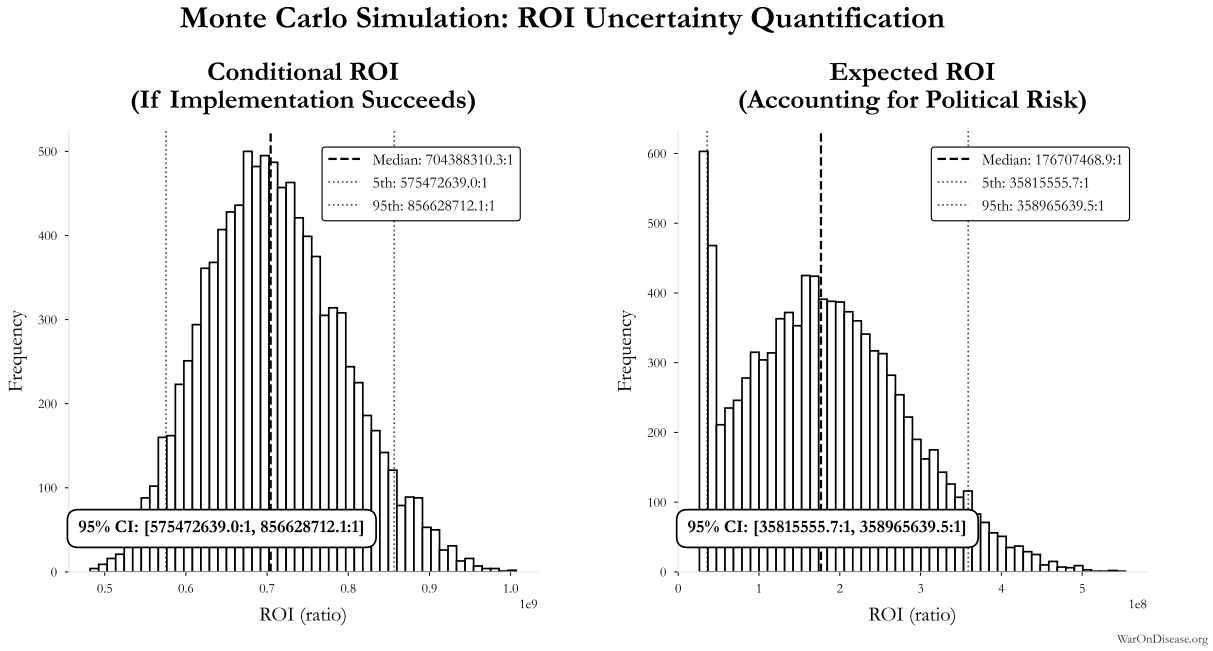
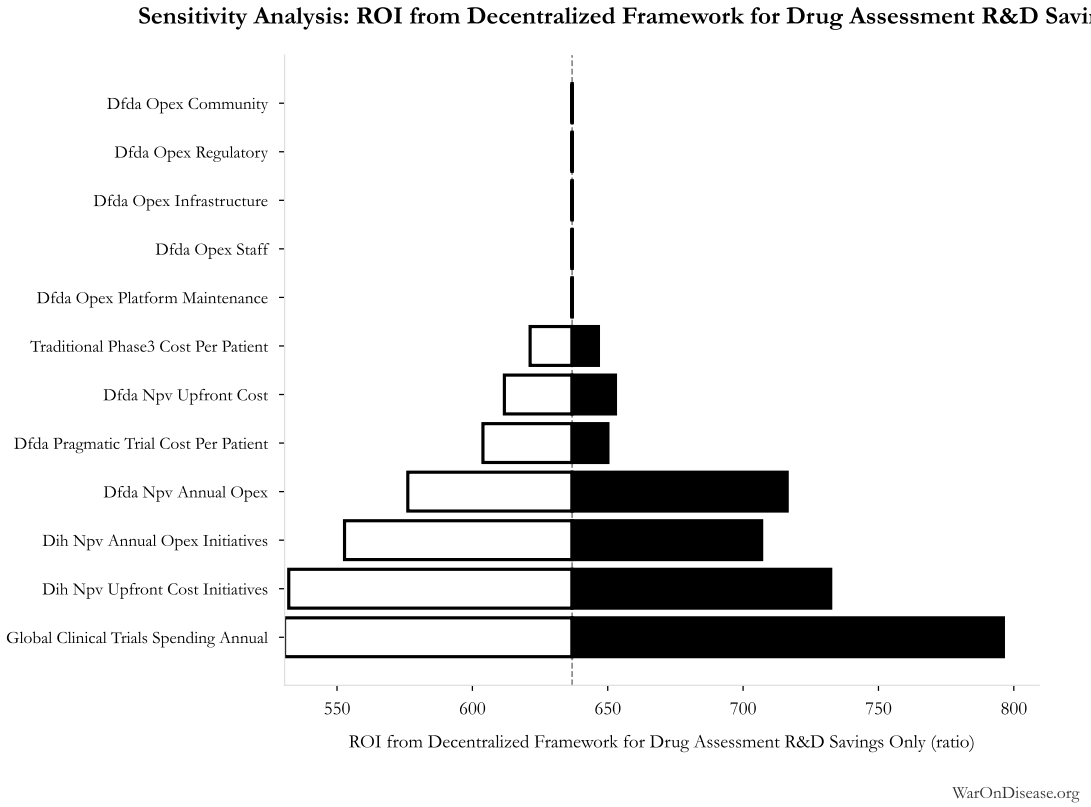


Figure 60: Monte Carlo Simulation: ROI Uncertainty Distribution (10,000 iterations)

Economic interpretation: ROI > 1:1 means benefits exceed costs. All simulations produce ROI > 1:1, meaning there is effectively zero probability (within the modeled uncertainty) that this intervention loses money. Even the most conservative scenario (R&D savings only at 637:1 (95% CI: 569:1-790:1)) generates positive returns. This qualifies as a **dominant intervention** in health economics: it should be implemented regardless of budget constraints, as it generates net economic surplus while improving health outcomes.

Which parameters matter most for conservative ROI? The tornado chart below shows the sensitivity of the R&D-only ROI estimate to each input parameter. Parameters at the top have the largest impact on the final result:



For comprehensive sensitivity analysis including tornado charts for all calculated parameters, see Parameters and Calculations.

Key Analytical Assumptions

This analysis rests on several core assumptions that should be made explicit for academic transparency:

Strategic Stability Assumption

Assumption: A coordinated 1% reduction in military spending across all nations maintains relative power balances and strategic deterrence capabilities.

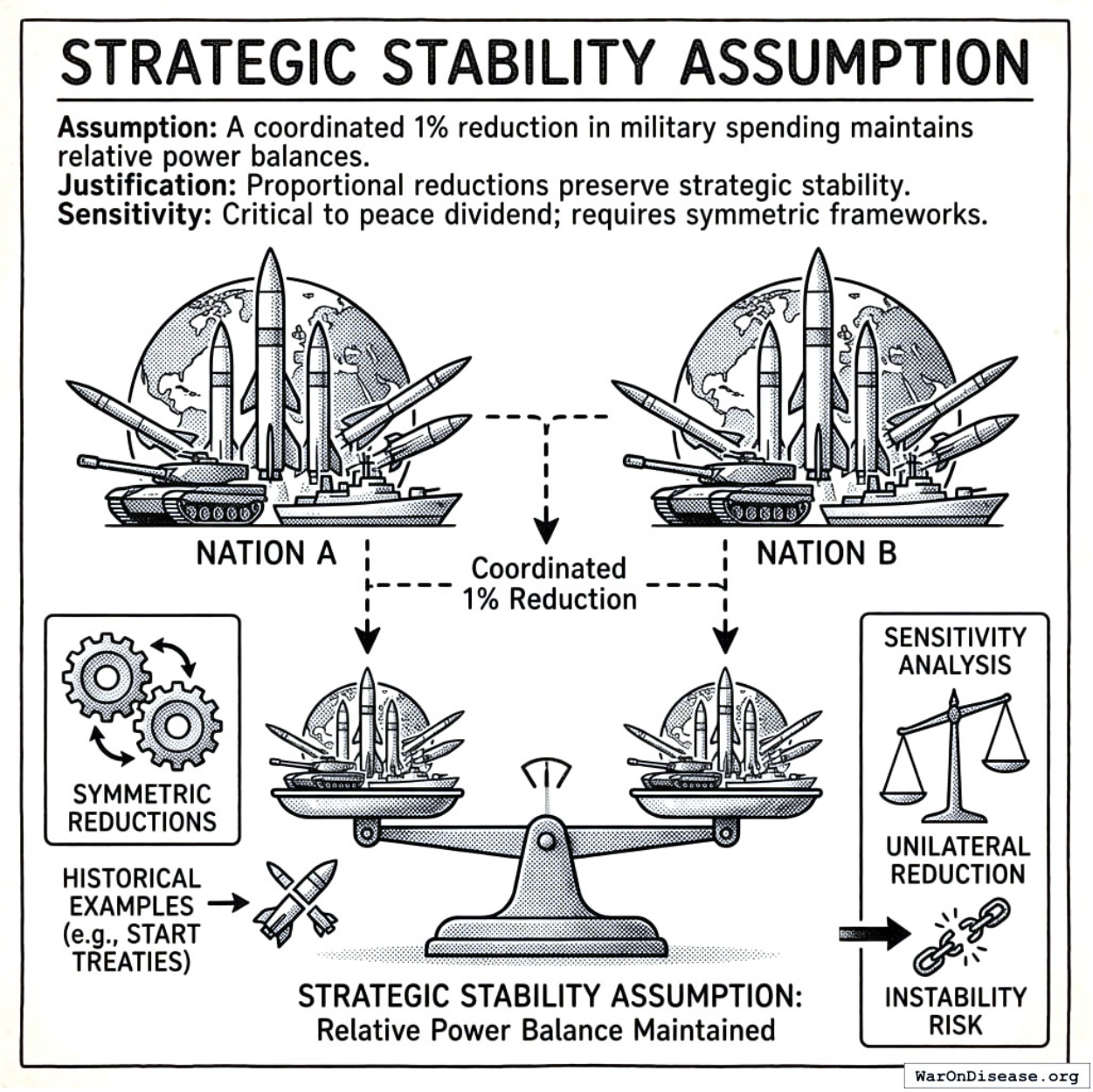


Figure 61: A diagram illustrating how proportional spending reductions across different nations maintain a constant balance of power and strategic deterrence.

Justification: The 1% Treaty explicitly requires proportional reductions from all signatories. Since relative military capabilities remain unchanged, strategic stability is preserved. Historical analysis shows that symmetric reductions in military tensions (e.g., START treaties, naval treaties between world wars) maintained deterrence while reducing absolute expenditure.

Sensitivity: This assumption is critical to the peace dividend calculation. Alternative scenarios modeling unilateral reductions would require different political economy frameworks.

Linear Scaling Assumption

Assumption: Economic benefits and costs scale approximately linearly with program scope and adoption rates.

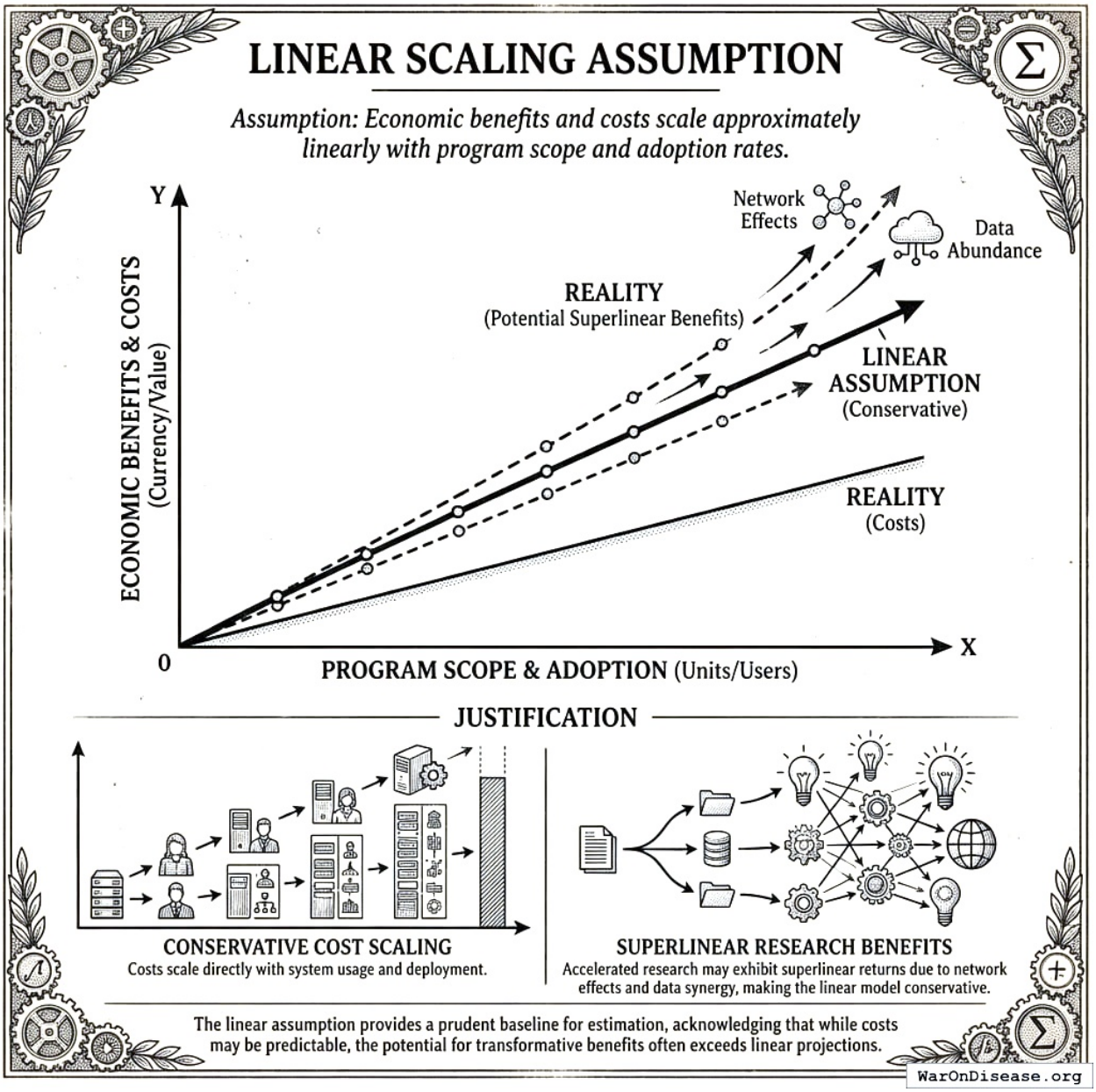


Figure 62: A line chart comparing a linear growth model for costs and benefits against a superlinear curve representing potential network effects and data abundance.

Justification: Conservative assumption that costs scale with system usage. Research acceleration benefits may exhibit superlinear returns (network effects, data abundance), making this assumption conservative.

Adoption Rate Assumptions

Assumption: The framework achieves gradual adoption following a 5 years linear ramp to 50%-80% participation rate among eligible trials.

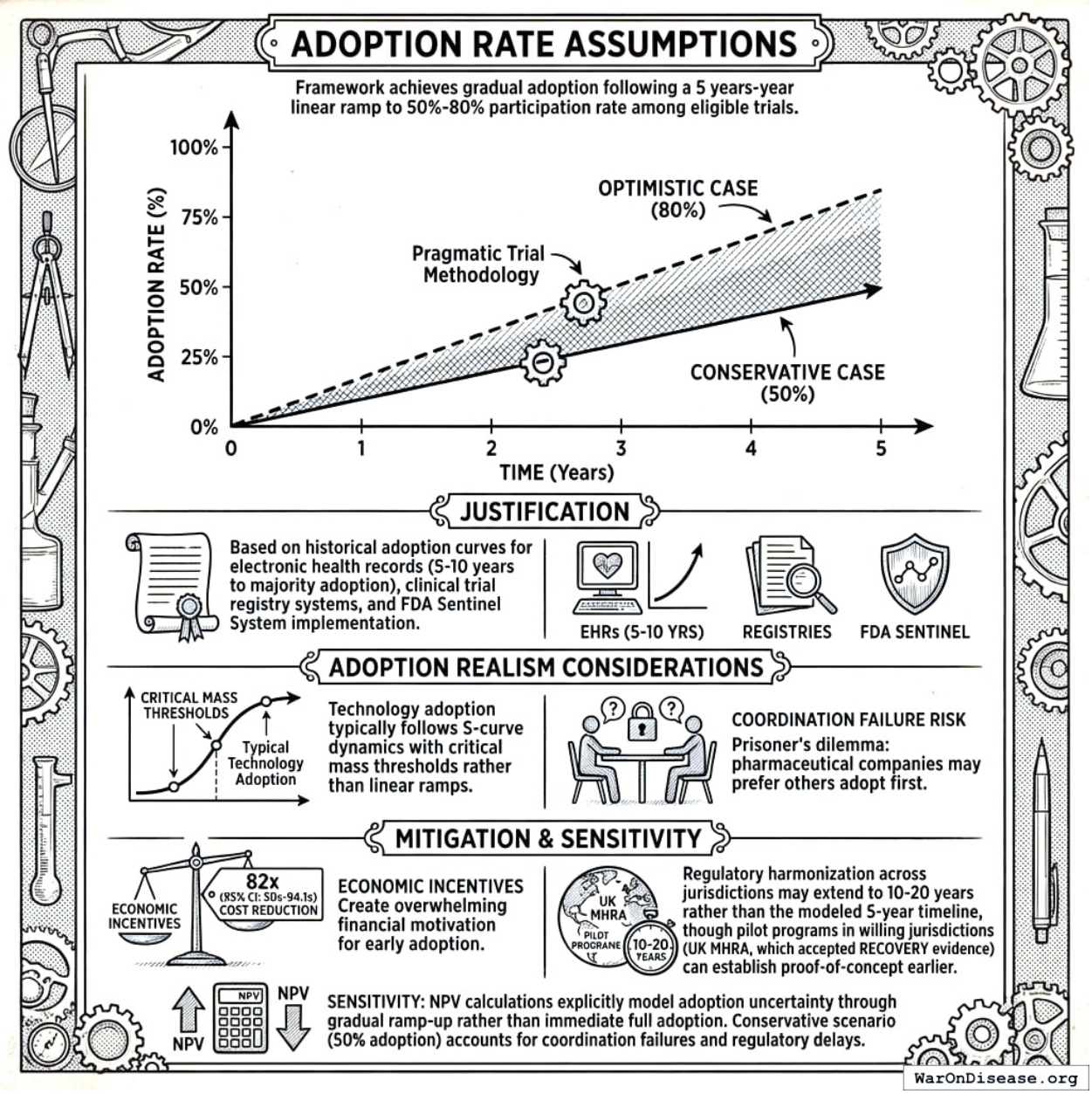


Figure 63: A comparison of the conservative and optimistic adoption scenarios showing the 5-year linear ramp to 50% and 80% participation rates respectively.

Conservative case: 50% of trials adopt the pragmatic trial methodology **Optimistic case:** 80% adoption rate

Justification: Based on historical adoption curves for electronic health records (5-10 years to majority adoption), clinical trial registry systems, and FDA Sentinel System implementation.

Adoption realism considerations: Technology adoption typically follows S-curve dynamics with critical mass thresholds rather than linear ramps. Coordination failure risk exists (prisoner's dilemma: pharmaceutical companies may prefer others adopt first). Mitigation: Economic incentives (82x (95% CI: 50x-94.1x) cost reduction) create overwhelming financial motivation for early adoption. Regulatory harmonization across jurisdictions may extend to 10-20 years rather than the modeled 5-year timeline, though pilot programs in willing jurisdictions (UK MHRA, which accepted RECOVERY evidence) can establish proof-of-concept earlier.

Sensitivity: NPV calculations explicitly model adoption uncertainty through gradual ramp-up rather than immediate full adoption. Conservative scenario (50% adoption) accounts for coordination failures and regulatory delays.

Cost Reduction Assumptions

Assumption: The methodology of a decentralized FDA reduces per-patient trial costs by 97.7% (95% CI: 97.5%-98.9%) (conservative) to 95% (optimistic) compared to traditional randomized controlled trials.

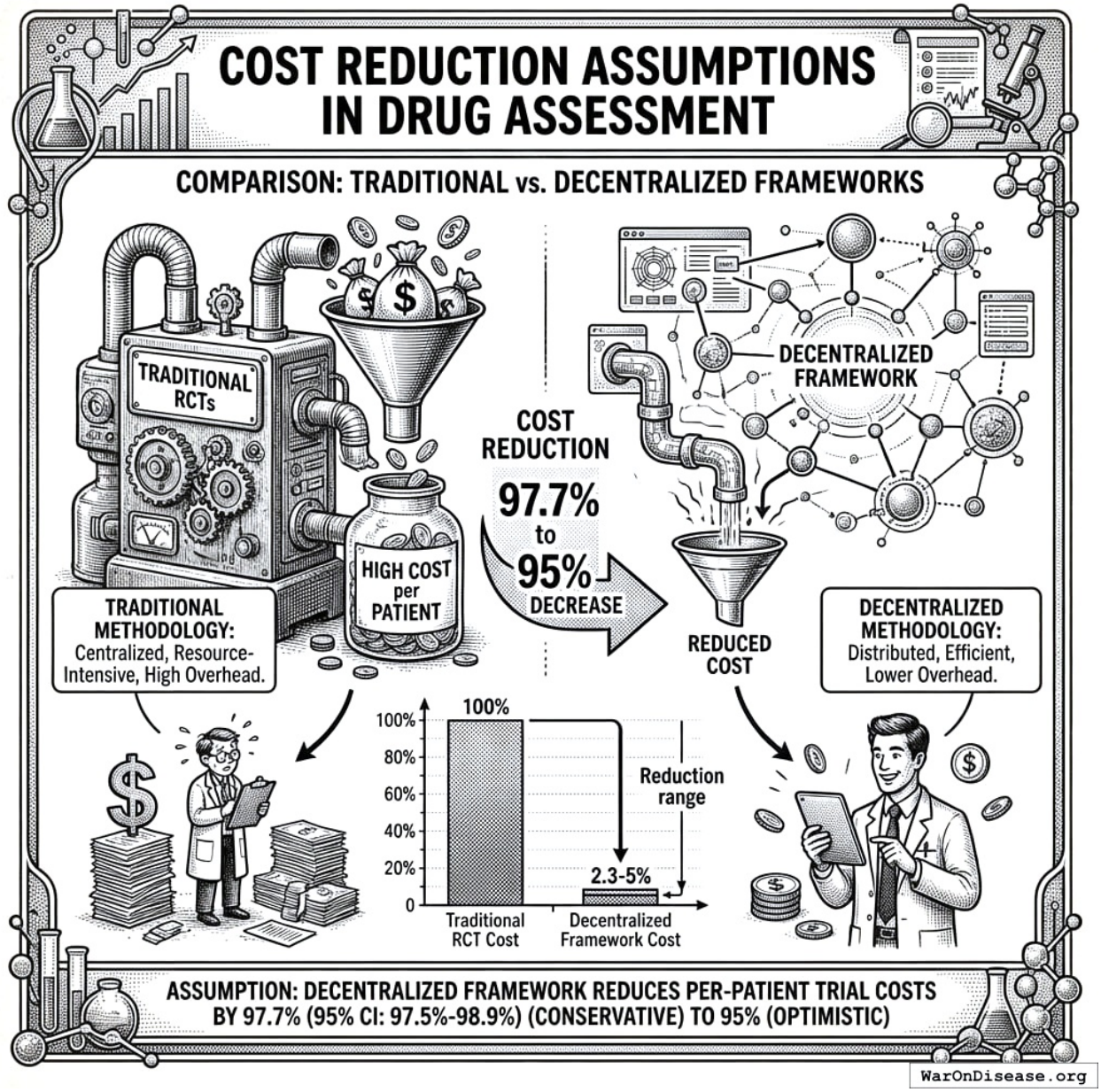


Figure 64: A comparison bar chart illustrating the dramatic cost reduction per patient when moving from traditional randomized controlled trials to a decentralized FDA methodology.

Empirical basis

- Oxford RECOVERY trial: 82x (95% CI: 50x-94.1x) cost reduction ($500 (95% CI: $400-$2.50K) vs. $41K (95% CI: $20K-$120K) traditional). Note: RECOVERY benefited from NHS infrastructure and COVID emergency conditions.
- ADAPTABLE trial: $14M (95% CI: $14M-$20M) / 15.1 thousand patients = $929 (95% CI: $929-$1.40K)/patient using PCORnet pragmatic design, more representative of typical pragmatic trial costs.
- Our system projections use $929 (95% CI: $97-$3K)/patient based on ADAPTABLE. Con-

fidence interval ($500-$3,000) captures range from RECOVERY-like efficiency to complex chronic disease trials.
- Literature on pragmatic trials consistently shows 50-95% cost reductions

Sensitivity: Conservative scenario (637:1 (95% CI: 569:1-790:1) ROI) uses 97.7% (95% CI: 97.5%-98.9%) reduction; optimistic case uses 95%.

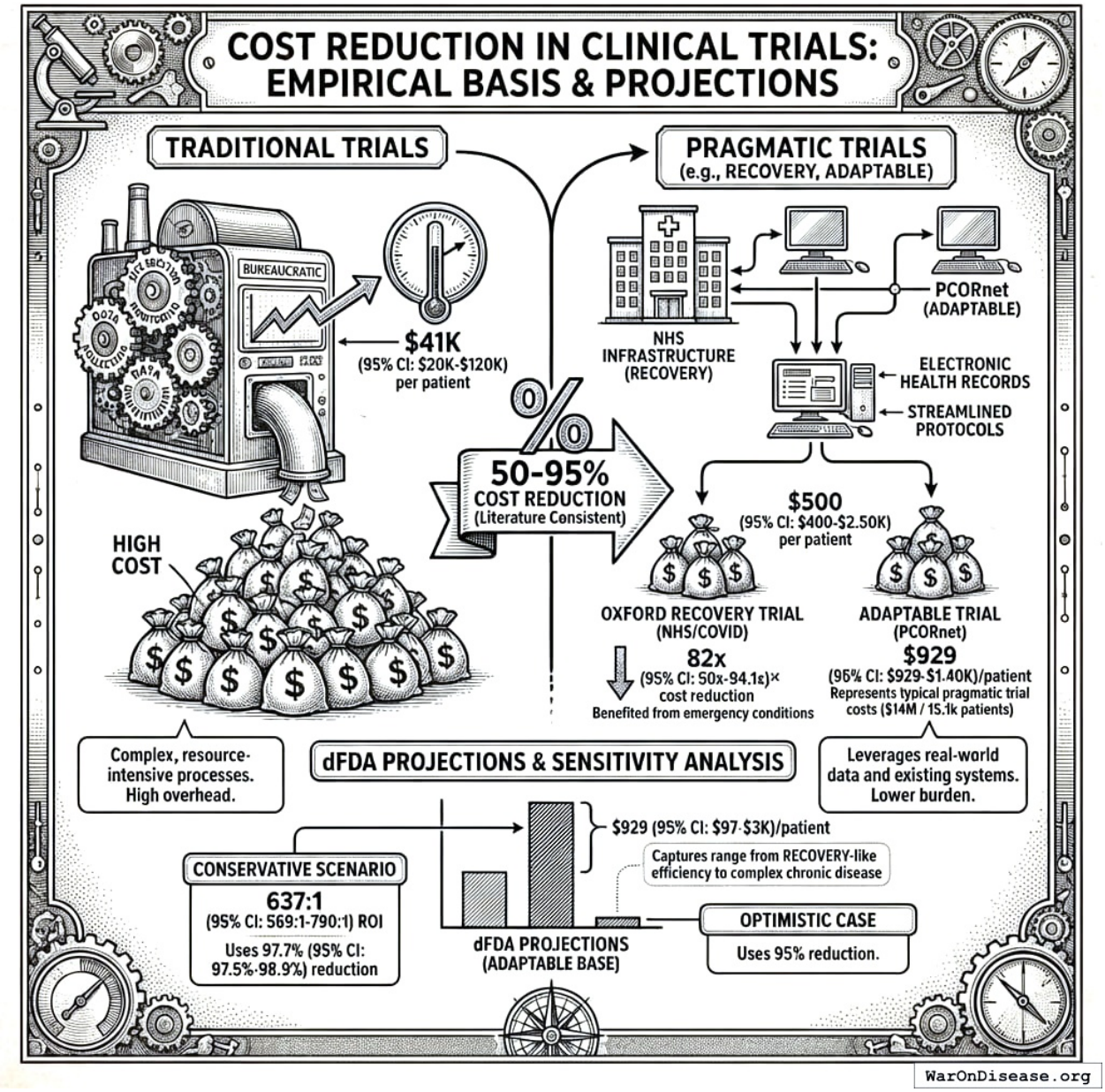


Figure 65: Comparison of per-patient costs between traditional clinical trials and pragmatic trial models like RECOVERY and ADAPTABLE, highlighting the 50-95% cost reduction.

Historical Precedent: Pre-1962 Physician-Led Efficacy Trials

Context: A decentralized FDA approach is not an untested innovation extrapolated from a single case study. The Harvard meta-analysis of 108 embedded pragmatic trials[132] demonstrates that cost reductions are reproducible across therapeutic areas, not unique to RECOVERY's COVID emergency conditions. Moreover, this approach represents a return to the physician-led, real-world evidence model that operated successfully from 1883 to 1960 before being replaced by the current centralized system.

Cost structure comparison demonstrates dramatic efficiency difference:

- **Pre-1962 system**: $24.7M (95% CI: $19.5M-$30M)[80] per drug (2024 inflation-adjusted) for safety testing; efficacy determined through decentralized physician case reports
- **Post-1962 system**: $2.60B (95% CI: $1.50B-$4B) per drug average, a **105x (95% CI: 90.6x-119x) cost increase**; drug companies conduct both safety and efficacy trials internally
- **Pragmatic trial model**: Return to decentralized physician-led efficacy testing with modern automation (electronic health records, AI-assisted analysis, real-time data aggregation), targeting **50-95% cost reductions**

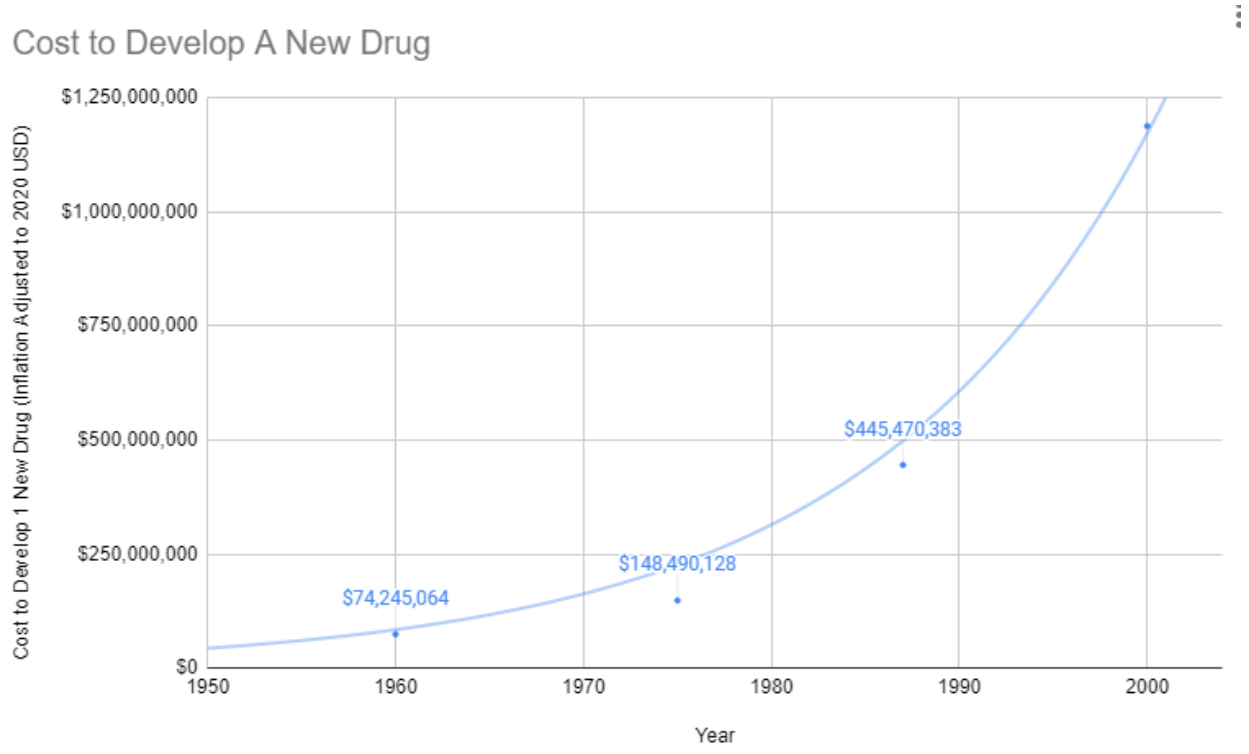


Figure 66: Drug development costs exploded after 1962 regulations

The cost explosion began exactly when efficacy testing was centralized within pharmaceutical companies. This wasn't a natural evolution of drug development or increasing drug complexity. It was a regulatory mandate that increased costs 105x (95% CI: 90.6x-119x)-fold while slowing innovation.

The regulatory causation is clear: The same types of compounds (small molecules, biologics) that cost $24.7M (95% CI: $19.5M-$30M) to develop in 1960 now cost $2.60B (95% CI: $1.50B-$4B).

The molecules didn't get more complex; the regulatory requirements did. Aspirin, if discovered today under current regulations, would cost billions to approve despite being chemically identical to the version approved for pennies in the pre-1962 era.

Historical operational model

From 1883 to 1960, 144 thousand physicians across America tested drug efficacy on real patients in routine clinical practice. The Journal of the American Medical Association (JAMA)[145] compiled these observational reports, leading medical experts peer-reviewed the aggregated data, and effective treatments received endorsement.

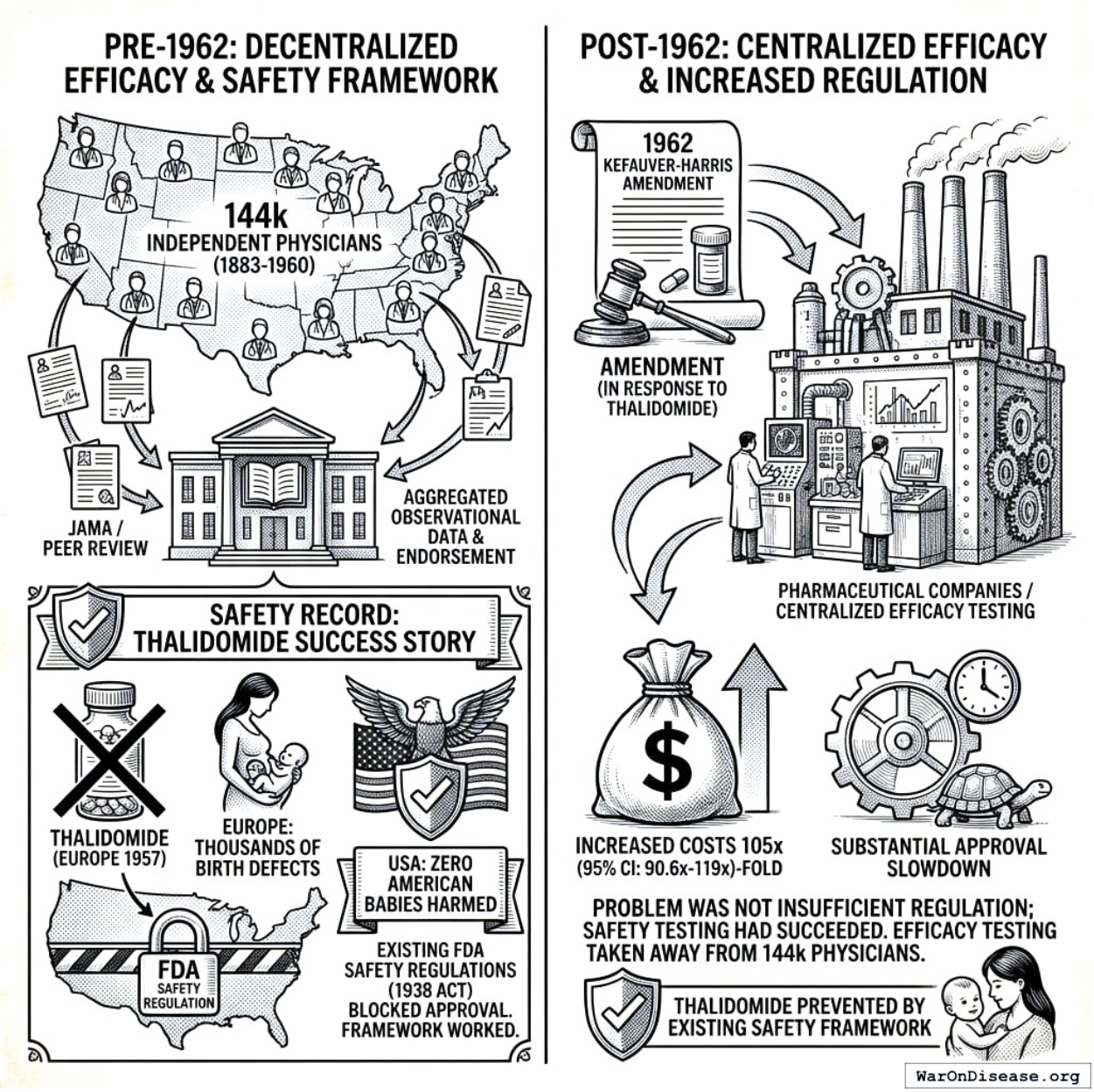


Figure 67: Comparison of the decentralized pre-1962 medical testing model versus the centralized post-1962 regulatory framework, highlighting the shift in efficacy testing and cost impact.

Safety record, the thalidomide success story: The pre-1962 safety testing framework successfully prevented the thalidomide disaster[146] that devastated Europe with thousands of horrific birth defects[147]. When thalidomide was marketed in Europe starting in 1957 for morning sickness, existing FDA safety regulations (1938 Food, Drug, and Cosmetic Act) blocked the drug from approval in the United States. **Zero American babies were harmed** - the safety testing framework worked exactly as intended.

The 1962 Kefauver-Harris Amendment added extensive efficacy requirements *in response to thalidomide*, despite the fact that the US had already been fully protected by existing safety regulations. The problem was not insufficient regulation; safety testing had succeeded. The response was to take efficacy testing away from 144 thousand physicians independent physicians and centralize it within pharmaceutical companies, increasing costs 105x (95% CI: 90.6x-119x)-fold while slowing approvals substantially.

Implications for generalizability

The RECOVERY trial ($500 (95% CI: $400-$2.50K)[83] per patient) demonstrates that modern infrastructure enables even greater efficiency than the pre-1962 system. (Our system projections use $929 (95% CI: $97-$3K)/patient based on the ADAPTABLE trial.) However, the fundamental approach, physicians testing treatments on real patients in clinical practice settings, has 77 years of empirical validation (1883-1960), not merely one case study.

The cost reduction estimates are conservative relative to historical costs. 1980s drugs cost approximately $194M (95% CI: $146M-$242M) (compounded, 1990 dollars)[20] compared to modern $2.60B (95% CI: $1.50B-$4B) costs[20], representing a 13.4x (95% CI: 11.9x-14.7x)-fold increase. Modern technology (EHRs, wearables, automated data collection) suggests efficiency gains could exceed historical precedent while maintaining the safety protections that successfully prevented disasters like thalidomide.

Political Feasibility Assumption

Assumption: The 1% Treaty achieves ratification by sufficient nations within a 3-5 year campaign timeline.

Justification: Historical treaty adoption timelines vary (Nuclear Non-Proliferation Treaty: 3 years; Paris Climate Agreement: 5 years). This analysis focuses on economic value *conditional* on implementation, not probability of political success.

Important caveat: This analysis does not model the probability distribution over political outcomes. The economic case (637:1 (95% CI: 569:1-790:1) to 84.8M:1 (95% CI: 46.6M:1-144M:1) ROI) holds *if implemented*, but political economy barriers to implementation are substantial and outside the scope of this cost-benefit analysis.

Expected Value Analysis Accounting for Political Risk

Standard economic practice: Cost-benefit analysis for interventions with implementation uncertainty requires expected value calculation:

$$E[ROI] = ROI_{conditional} \times P_{success}$$

The preceding analysis presents *conditional* benefits (returns IF implementation succeeds). Expected value analysis incorporates the probability of achieving political ratification and sustained commitment.

Political success probability: We model political success as uncertain (1% (95% CI: 0.1%-10%)) reflecting geopolitical uncertainty. The distribution below shows the assumed probability range:

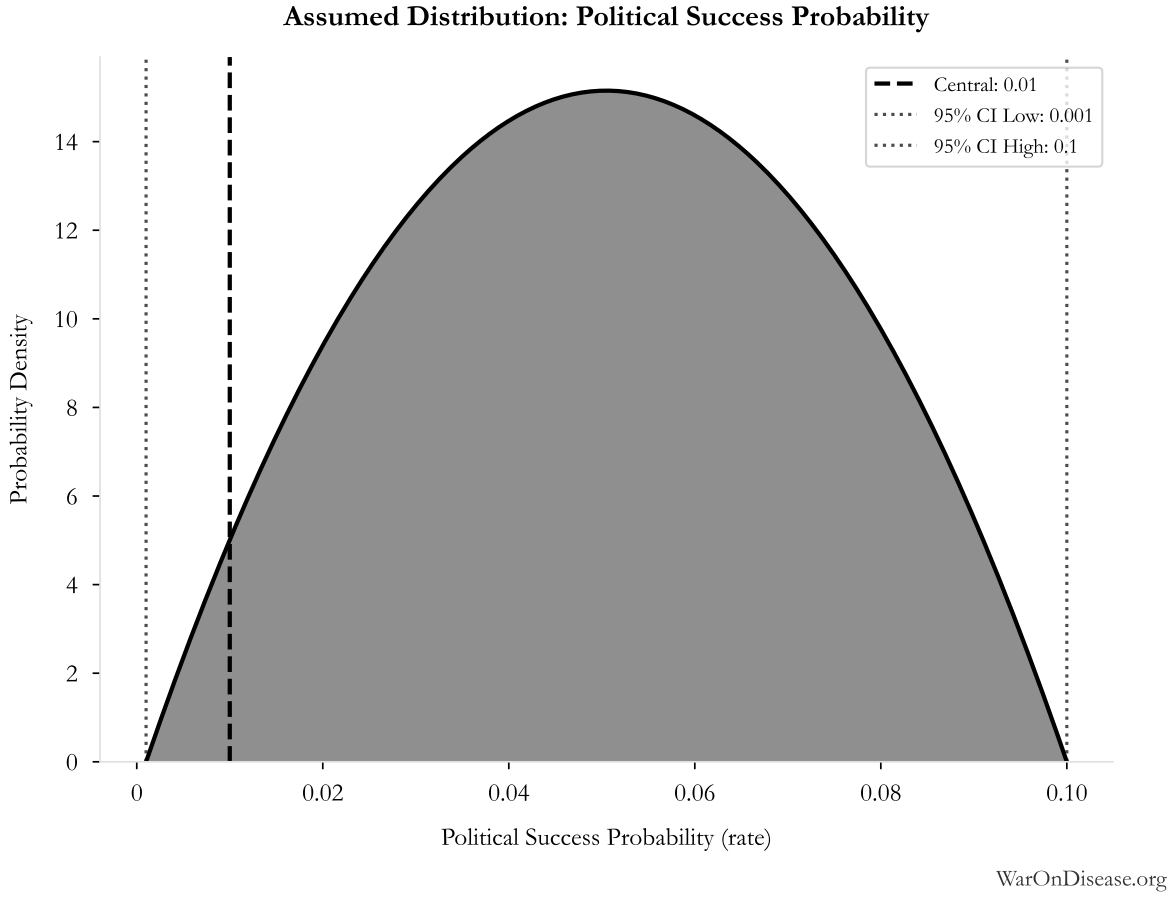


Figure 68: Probability Distribution: Political Success Probability

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.

Risk-adjusted expected ROI: 848k:1 (95% CI: 58.0k:1-4.76M:1)

$$
\begin{aligned}
&E[ROI_{max}] \\
&= ROI_{max} \times P_{success} \\
&= 84.8M \times 1\% \\
&= 848{,}000
\end{aligned}
$$

$$\text{where } ROI_{max} = \frac{Value_{max}}{Cost_{campaign}} = \frac{\$84800T}{\$1B} = 84.8M$$

$$
\begin{aligned}
&\text{where } Value_{max} \\
&= DALYs_{max} \times Value_{QALY} \\
&= 565B \times \$150K \\
&= \$84800T
\end{aligned}
$$

$$
\begin{aligned}
&\text{where } DALYs_{max} \\
&= DALYs_{global,ann} \times Pct_{avoid,DALY} \times T_{accel,max} \\
&= 2.88B \times 92.6\% \times 212 \\
&= 565B
\end{aligned}
$$

$$\text{where } T_{accel,max} = T_{accel} + T_{lag} = 204 + 8.2 = 212$$

$$
\begin{aligned}
&\text{where } T_{accel} \\
&= T_{first,SQ} \times \left(1 - \frac{1}{k_{capacity}}\right) \\
&= 222 \times \left(1 - \frac{1}{12.3}\right) \\
&= 204
\end{aligned}
$$

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

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

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

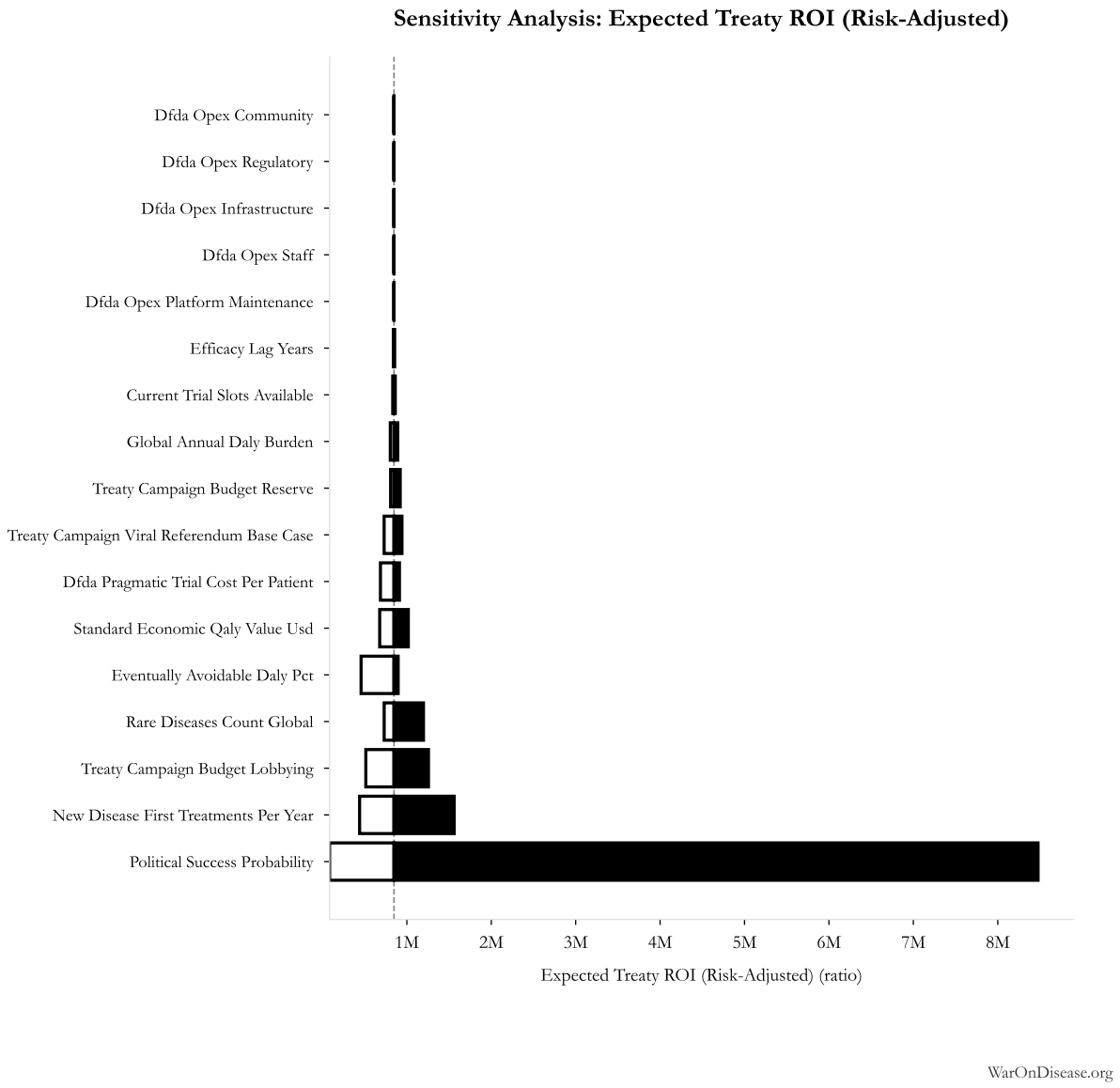
$$\text{where } k_{capacity} = \frac{N_{fundable,ann}}{Slots_{curr}} = \frac{23.4M}{1.9M} = 12.3$$

$$
\begin{aligned}
&\text{where } N_{fundable,ann} \\
&= \frac{Subsidies_{trial,ann}}{Cost_{pragmatic,pt}} \\
&= \frac{\$21.7B}{\$929} \\
&= 23.4M
\end{aligned}
$$

$$
\begin{aligned}
&\text{where } Subsidies_{trial,ann} \\
&= Treasury_{RD,ann} - OPEX_{dFDA} \\
&= \$21.8B - \$40M \\
&= \$21.7B
\end{aligned}
$$

$$
\begin{aligned}
&\text{where } OPEX_{dFDA} \\
&= Cost_{platform} + Cost_{staff} + Cost_{infra} \\
&+ Cost \qquad + Cost
\end{aligned}
$$

The tornado chart below shows how expected ROI varies with political success probability - this is the primary driver of uncertainty:



The Monte Carlo distribution shows the full range of expected ROI outcomes when sampling political success probability from its uncertainty distribution:

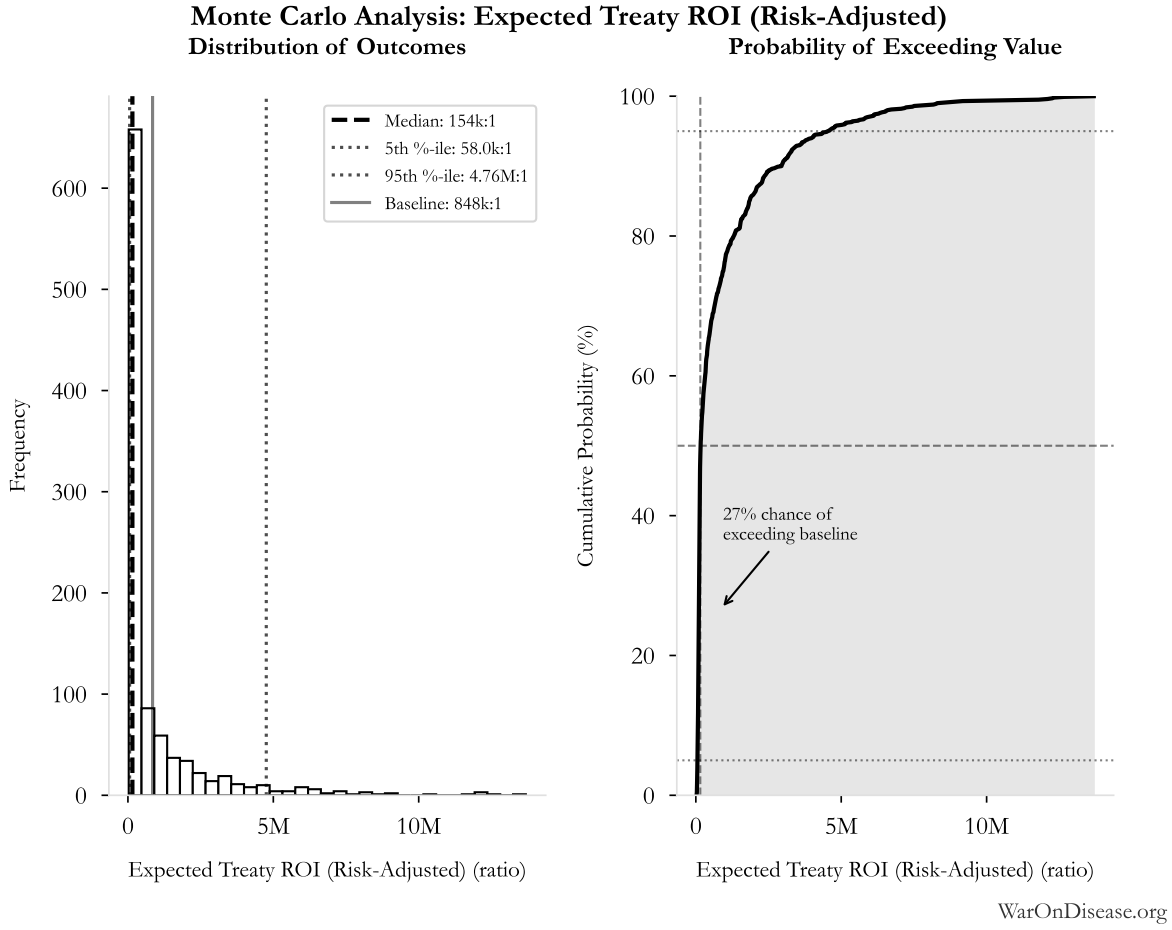


Figure 69: Monte Carlo Distribution: Expected Treaty ROI (Risk-Adjusted) (10,000 simulations)

Simulation Results Summary: Expected Treaty ROI (Risk-Adjusted)

Statistic	Value
Baseline (deterministic)	848k:1
Mean (expected value)	962k:1
Median (50th percentile)	154k:1
Standard Deviation	1.80M:1
90% Range (5th-95th percentile)	[58.0k:1, 4.76M:1]

The histogram shows the distribution of Expected Treaty ROI (Risk-Adjusted) 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.

Comparison to traditional interventions (assuming 100% implementation probability):

- Childhood vaccination programs: 13:1[8]:1 ROI with P 1.0

- Against Malaria Foundation: ~8:1 equivalent ROI
- **1% treaty (central estimate, P=1% (95% CI: 0.1%-10%))**: 848k:1 (95% CI: 58.0k:1-4.76M:1) expected ROI

Interpretation: The high conditional ROI (84.8M:1 (95% CI: 46.6M:1-144M:1)) means that even modest implementation probabilities yield expected values competitive with best-in-class health interventions that have near-certain implementation.

Note: The uncertainty analysis samples political probability from its full distribution (1% (95% CI: 0.1%-10%)). Actual probability depends on campaign execution, geopolitical conditions, and public support mobilization. The campaign strategy allocates $1B over 4 years specifically to maximize ratification probability.

Time Inconsistency and Commitment Credibility

Political economy challenge: Even if the treaty achieves initial ratification, sustained commitment over the 10 years analytical horizon faces time inconsistency problems. Political business cycles (2-6 year terms) create incentives to raid the pragmatic clinical trials budget for short-term priorities.

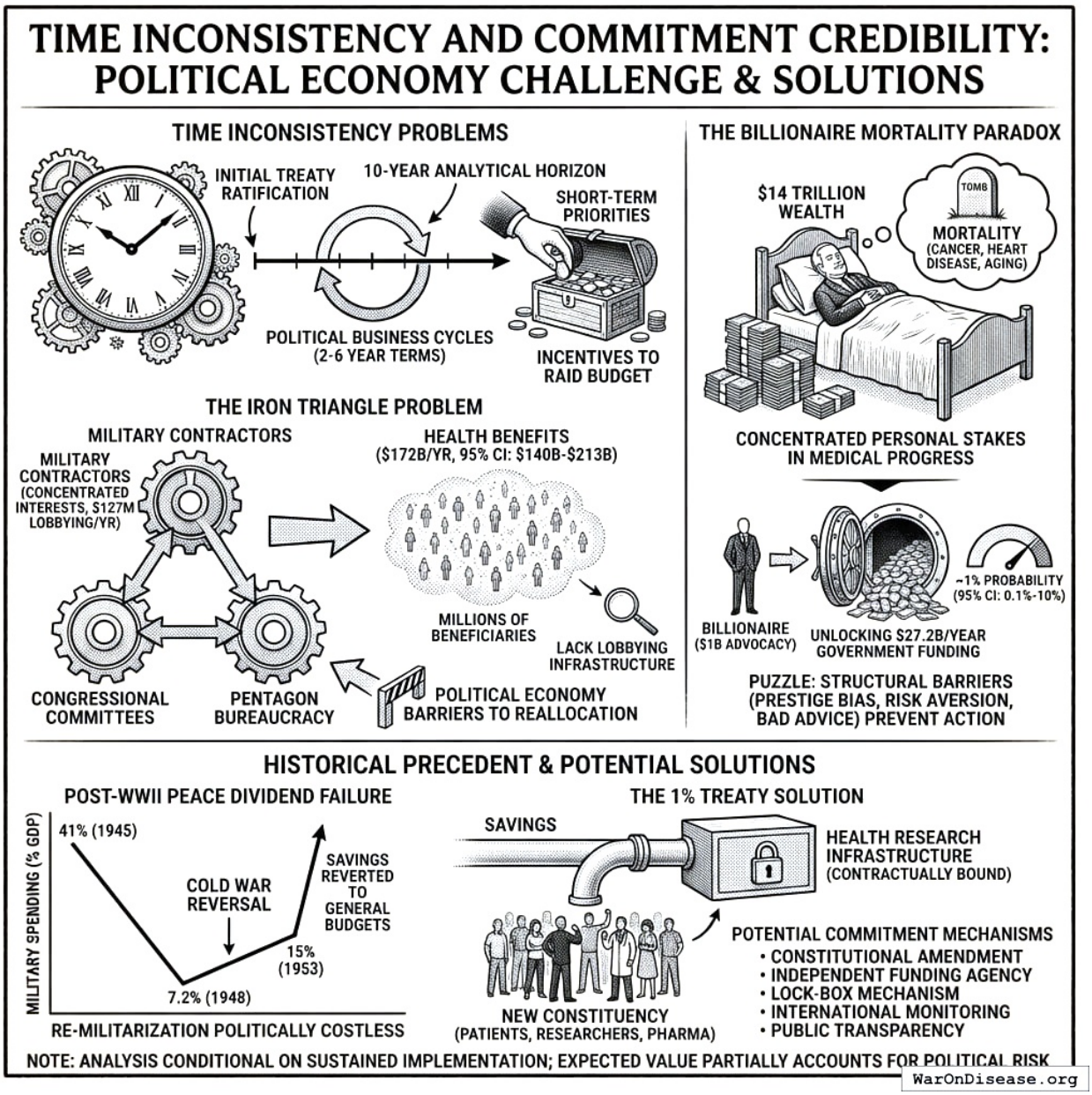


Figure 70: A conceptual diagram illustrating the political asymmetry between the concentrated defense 'Iron Triangle' and diffuse health beneficiaries, contrasted with the proposed treaty mechanism that binds savings to a new medical-research constituency.

The Iron Triangle problem: Military contractors have concentrated interests with substantial lobbying capacity ($127M[17] annually), creating tight coordination between defense industry, congressional committees, and Pentagon bureaucracy. Health benefits, while larger in aggregate ($172B (95% CI: $140B-$213B) annually), are diffuse across millions of beneficiaries who lack equivalent lobbying infrastructure. This asymmetry (concentrated producer benefits vs. diffuse consumer benefits) creates political economy barriers to reallocation even when aggregate welfare gains are enormous.

The billionaire mortality paradox: This diffusion argument has a critical exception. The world's ~3,000 billionaires (with combined wealth exceeding $14 trillion) are themselves patients who will die of cancer, heart disease, or aging. Unlike defense contractors who profit regardless of personal health outcomes, billionaires have **concentrated personal stakes** in medical progress: their own mortality and that of everyone they love. A single billionaire spending $1B on treaty advocacy has ~1% (95% CI: 0.1%-10%) probability of unlocking $27.2B/year in government funding. The personal benefit (years of additional life expectancy, treatments for diseases that would otherwise kill them and their families) is worth far more than $1B to someone with $100B+ who cannot currently buy immortality or treatments that don't exist. The puzzle isn't that benefits are truly diffuse. Billionaires face the same mortality as everyone else, and their wealth becomes worthless when they're dead. The puzzle is why structural barriers (prestige bias toward labs over lobbying, political risk aversion, bad advice from scientists saying "fund my lab" rather than "hire lobbyists") prevent them from acting on their concentrated personal interest in not dying.

Historical precedent: Why past peace dividends failed: The post-World War II "peace dividend" saw military spending fall from 41% of GDP (1945) to 7.2% (1948)[79], with expectations of permanent reductions. However, the Cold War reversed this within 3 years. Military spending returned to 15% of GDP by 1953. Similar patterns occurred post-Vietnam (1970s) and post-Cold War (1990s): initial reductions followed by reversals within 5-10 years. The critical failure: **savings weren't bound to a substitute industry**. Money reverted to general budgets, making re-militarization politically costless. The 1% Treaty solves this by **contractually binding savings to health research infrastructure**, creating a new constituency (patients, researchers, pharmaceutical companies) with incentives to defend the reallocation.

Treaty ratification sustained funding: The Paris Climate Agreement provides a cautionary example: 196 parties ratified, but many failed to meet funding commitments. As of 2024, developed countries have not met the $100B annual climate finance pledge despite treaty obligations. Treaty ratification creates moral commitment but weak enforcement mechanisms for sustained budgetary allocations.

Implication for expected value: The political success probabilities used in expected value analysis (1% (95% CI: 0.1%-10%)) implicitly incorporate time inconsistency risk. The expected value analysis partially addresses this through probability discounting, but time inconsistency (commitment erosion over time) represents an additional risk factor beyond initial political feasibility.

Potential commitment mechanisms (not modeled):

- Constitutional amendment (very high barrier, very high credibility)
- Independent funding agency with statutory protections
- Lock-box mechanism with supermajority requirement to redirect funds
- International monitoring and reputation costs
- Public transparency: all spending and trial outcomes publicly auditable

Note: The analysis acknowledges this limitation. Results should be interpreted as conditional on sustained implementation, with expected value analysis providing probability-adjusted estimates that partially account for political risk.

Technology Constancy Assumption

Assumption: Analysis does not incorporate potential advances in AI, automation, or biotechnology that could further accelerate research.

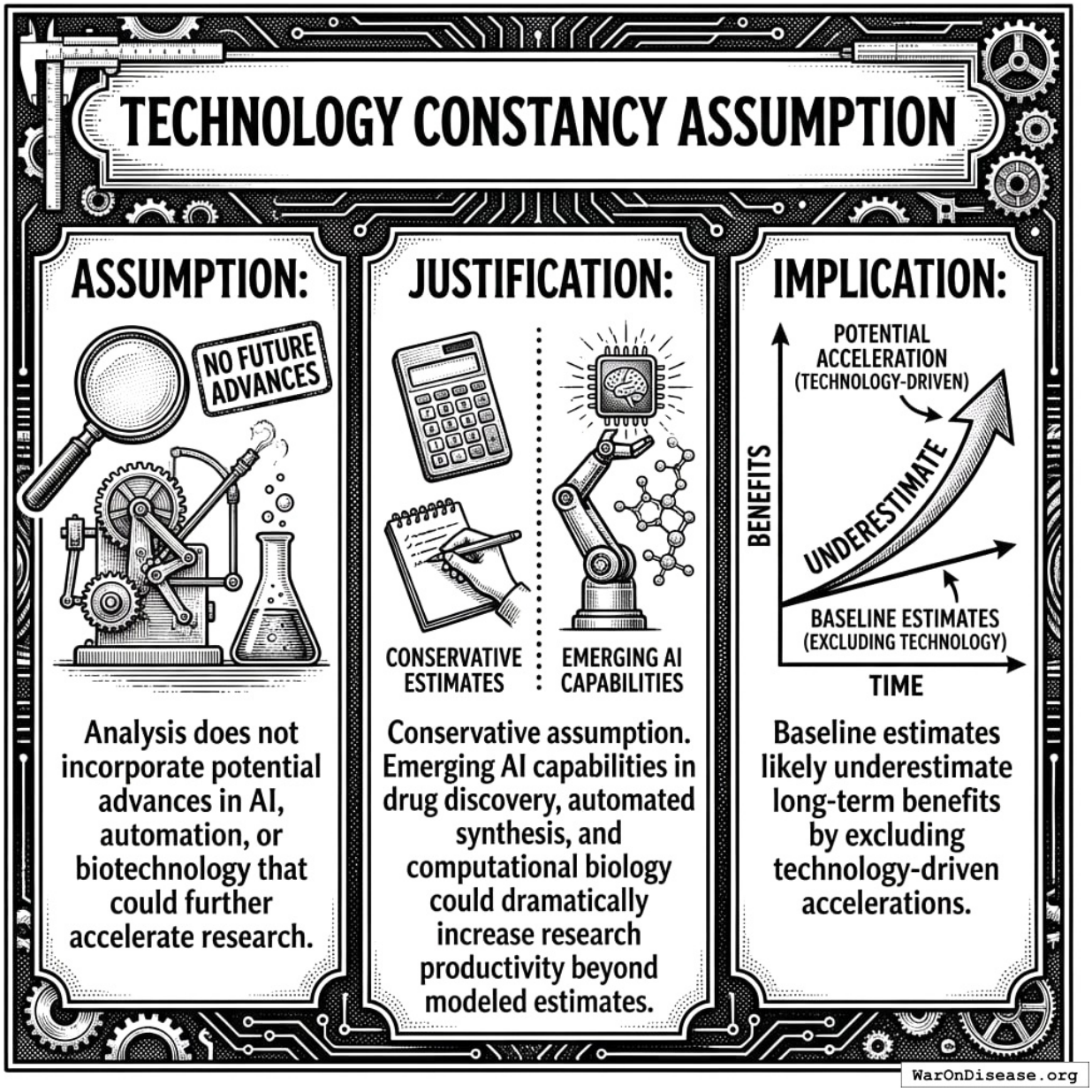


Figure 71: A comparison between a conservative baseline estimate and an accelerated trajectory driven by AI and biotechnology advancements.

Justification: Conservative assumption. Emerging AI capabilities in drug discovery, automated synthesis, and computational biology could dramatically increase research productivity beyond modeled estimates.

Implication: Baseline estimates likely underestimate long-term benefits by excluding technology-driven accelerations.

Data Quality and Availability

All primary data sources are documented in References with confidence levels:

- **High confidence** (78%): SIPRI military expenditure, WHO mortality statistics, ClinicalTrials.gov data
- **Medium confidence** (17%): Peace dividend estimates, QALY valuations (wide range in literature)
- **Conservative bounds**: Where uncertainty exists, analysis uses conservative estimates favoring underestimation of benefits

For complete parameter documentation with confidence indicators and peer-review status, see Parameters and Calculations Reference.

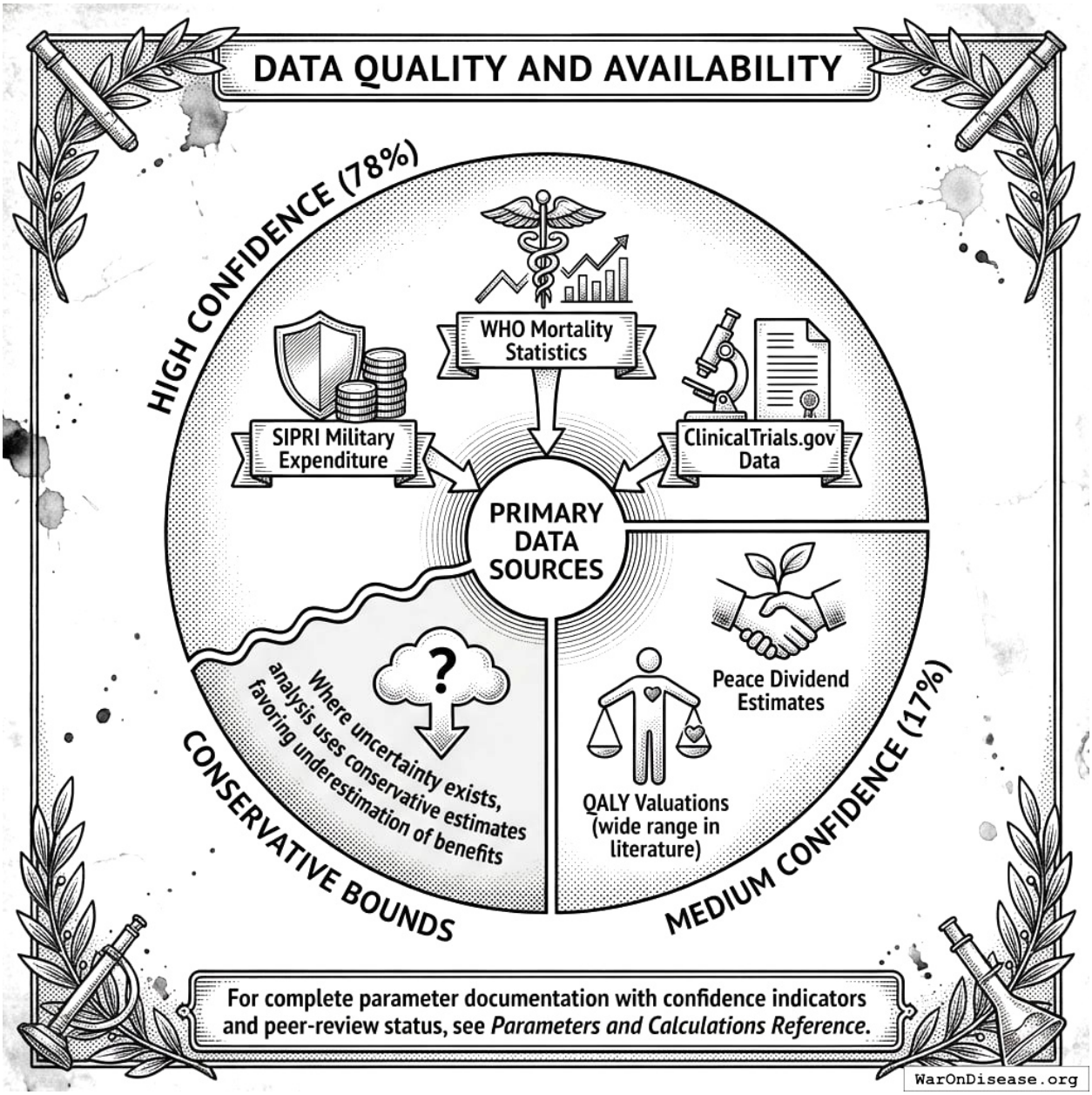


Figure 72: A breakdown of data source confidence levels, illustrating the high percentage of reliable data supporting the analysis.

Scenario Analysis: Complete Case

84.8M:1 (95% CI: 46.6M:1-144M:1) ROI

The conservative scenario counted only R&D efficiency gains. This section includes all quantifiable benefit categories.

Timeline Shift Value

The recurring benefits ($172B (95% CI: $140B-$213B)/year) are trivial compared to the timeline shift: $84.8 quadrillion (95% CI: $62.4 quadrillion-$97.3 quadrillion) from treatments arriving ~212 years (95% CI: 135 years-355 years) earlier on average.

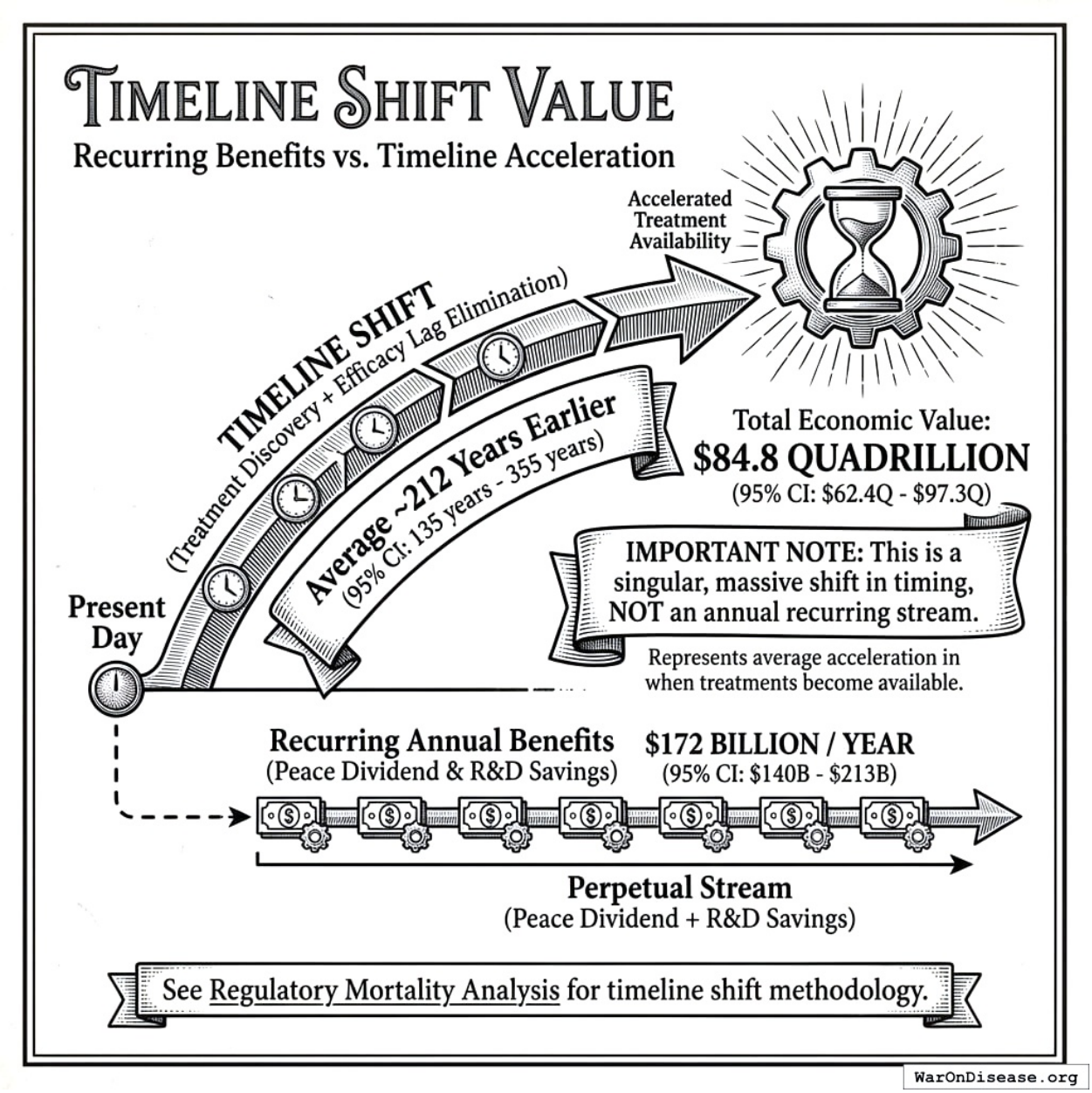


Figure 73: A visualization comparing the standard medical discovery timeline with an accelerated 212-year shift, highlighting the massive difference between $172B in annual recurring benefits and the $84.8 quadrillion total value of the timeline acceleration.

Important Note: The system provides an average ~212 years (95% CI: 135 years-355 years)-year timeline shift (treatment discovery acceleration + efficacy lag elimination) in when diseases receive first effective treatments, not an annual recurring benefit. This timeline shift benefit is massive ($84.8 quadrillion (95% CI: $62.4 quadrillion-$97.3 quadrillion) total economic value) but represents an average acceleration in when treatments become available, not an annual stream. The recurring annual benefits above ($172B (95% CI: $140B-$213B)/year) represent only the peace dividend and R&D savings, which continue perpetually. See Regulatory Mortality Analysis for timeline shift methodology.

Complete Case ROI

$$ROI_{max} = \frac{Value_{max}}{Cost_{campaign}} = \frac{\$84800T}{\$1B} = 84.8M$$

$$\text{where } Value_{max}$$
$$= DALYs_{max} \times Value_{QALY}$$
$$= 565B \times \$150K$$
$$= \$84800T$$

$$\text{where } DALYs_{max}$$
$$= DALYs_{global,ann} \times Pct_{avoid,DALY} \times T_{accel,max}$$
$$= 2.88B \times 92.6\% \times 212$$
$$= 565B$$

$$\text{where } T_{accel,max} = T_{accel} + T_{lag} = 204 + 8.2 = 212$$

$$\text{where } T_{accel}$$
$$= T_{first,SQ} \times \left(1 - \frac{1}{k_{capacity}}\right)$$
$$= 222 \times \left(1 - \frac{1}{12.3}\right)$$
$$= 204$$

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

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

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

$$\text{where } k_{capacity} = \frac{N_{fundable,ann}}{Slots_{curr}} = \frac{23.4M}{1.9M} = 12.3$$

$$\text{where } N_{fundable,ann}$$
$$= \frac{Subsidies_{trial,ann}}{Cost_{pragmatic,pt}}$$
$$= \frac{\$21.7B}{\$929}$$
$$= 23.4M$$

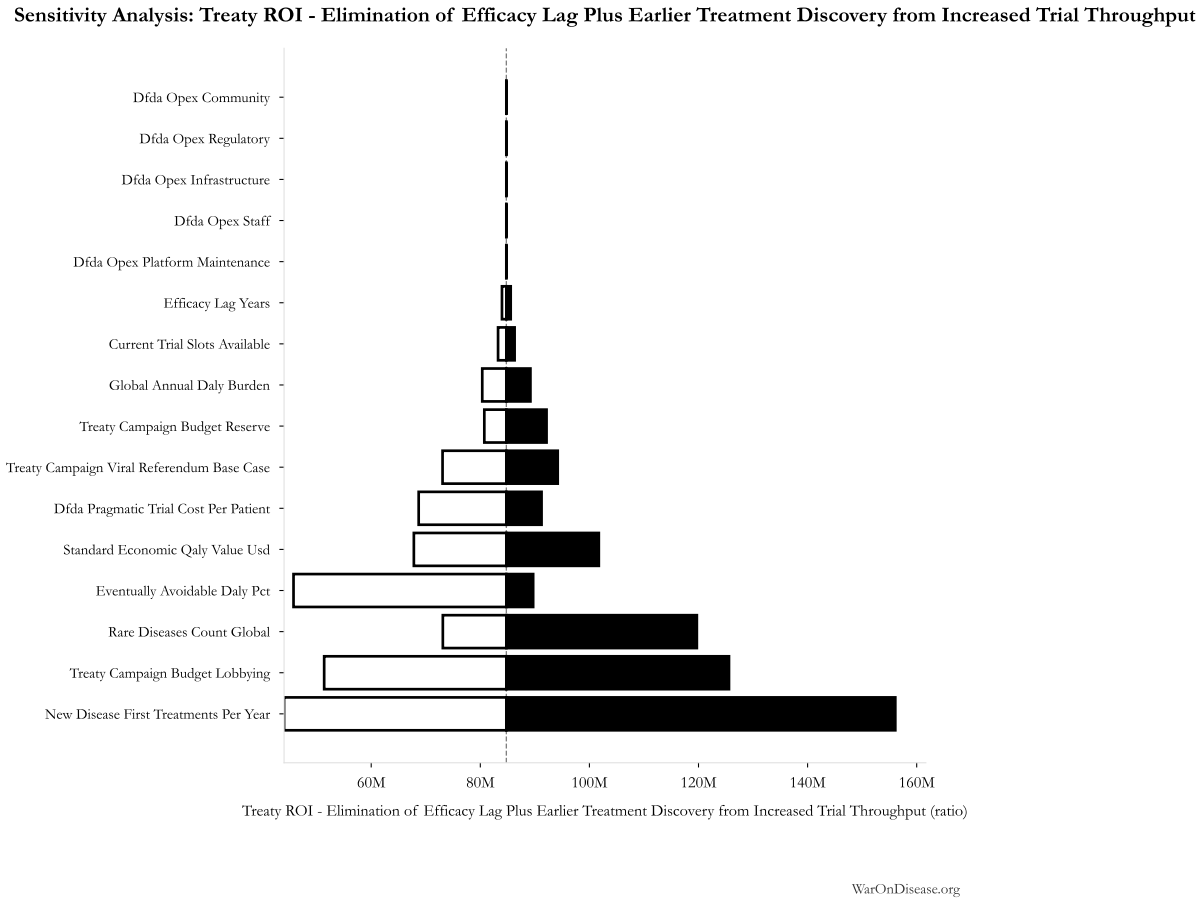
$$\text{where } Subsidies_{trial,ann}$$
$$= Treasury_{RD,ann} - OPEX_{dFDA}$$
$$= \$21.8B - \$40M$$
$$= \$21.7B$$

$$\text{where } OPEX_{dFDA}$$
$$= Cost_{platform} + Cost_{staff} + Cost_{infra}$$
$$+ Cost_{regulatory} + Cost_{community}$$
$$= \$15M + \$10M + \$8M + \$5M + \$2M$$
$$= \$40M$$

$$\text{where } Treasury_{RD,ann}$$

Translation: Every $1 invested returns $84.8M:1 (95% CI: 46.6M:1-144M:1) in **recurring annual benefits** (peace dividend + R&D savings), plus a ~212 years (95% CI: 135 years-355 years)-year average timeline shift in disease eradication (not included in annual figure).

Sensitivity of complete ROI: The tornado chart below shows which parameters most affect the complete ROI estimate:



These estimates derive from:

- Proven trial costs (RECOVERY: 82x (95% CI: 50x-94.1x) cost reduction demonstrated)
- Disease prevalence data (WHO Global Health Observatory)
- Standard QALY valuations (health economics consensus thresholds)

Critical distinction - the two benefit categories are different things:

Benefit Category	Type	Value	Frequency	Description
Timeline Shift	Average	$84.8 quadrillion (95% CI: $62.4 quadrillion-$97.3 quadrillion)	Per disease	Average ~212 years (95% CI: 135 years-355 years)-year timeline acceleration: treatment discovery acceleration (~204 years (95% CI: 123 years-350 years) yrs from 12.3x (95% CI: 4.19x-61.3x) trial capacity) + efficacy lag elimination (~8.2 years (95% CI: 4.85 years-11.5 years) yrs). Saves 10.7 billion deaths (95% CI: 7.39 billion deaths-16.2 billion deaths) and 565 billion DALYs (95% CI: 361 billion DALYs-877 billion DALYs).
Peace Dividend	Recurring	$114B (95% CI: $90.1B-$141B)/year	Perpetual	1% reduction in global military spending redirected to pragmatic clinical trials
R&D Savings	Recurring	$58.6B (95% CI: $49.2B-$73.1B)/year	Perpetual	82x (95% CI: 50x-94.1x) trial cost reduction from pragmatic trial model
Total Recurring	Recurring	$172B (95% CI: $140B-$213B)/year	Perpetual	Peace dividend + R&D savings (makes system self-funding)

Benefit Category	Type	Value	Frequency	Description
Total Value	Combined	$84.8 quadrillion (95% CI: $62.4 quadrillion-$97.3 quadrillion) + recurring	Average + perpetual	Average timeline shift + perpetual annual benefits

Investment required: $1B (one-time implementation cost)

Efficacy lag uncertainty: The timeline shift depends on the efficacy lag parameter, which represents years of regulatory delay after safety is established. The distribution below shows the uncertainty range:

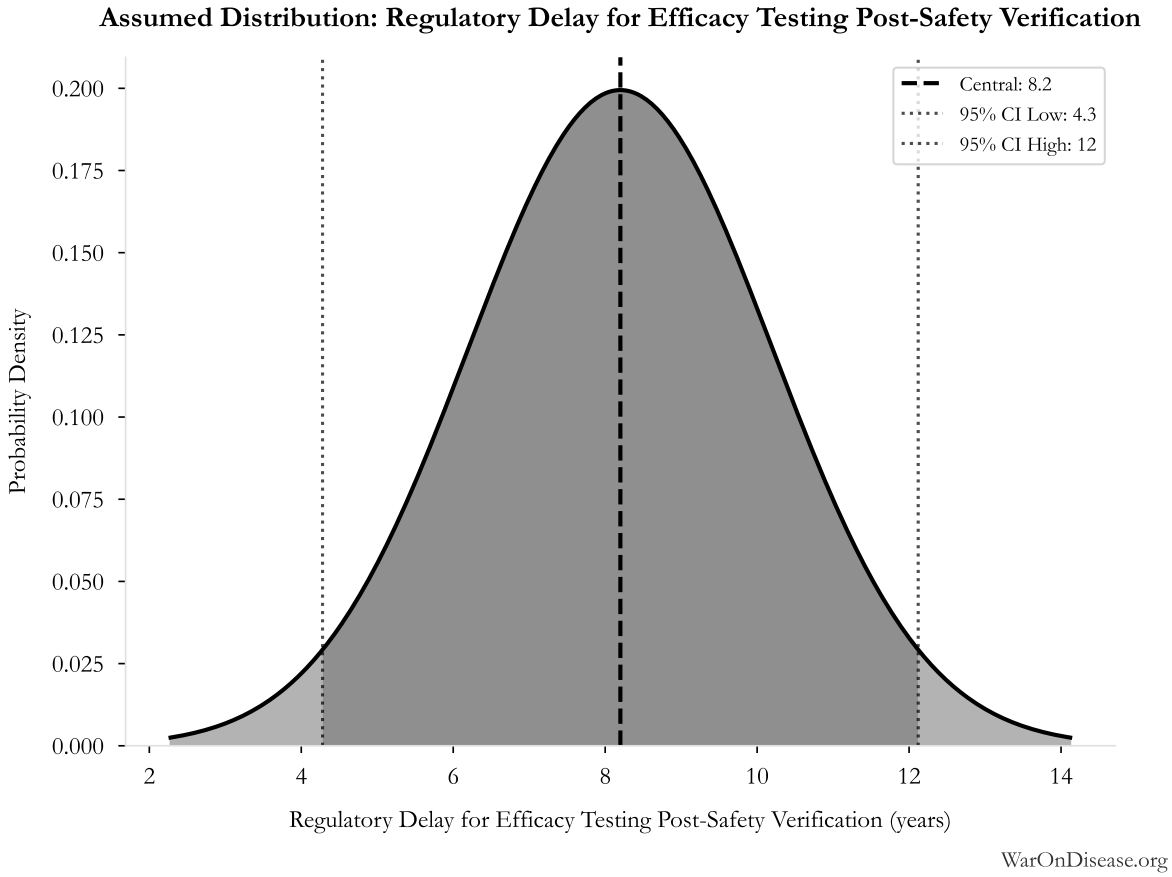
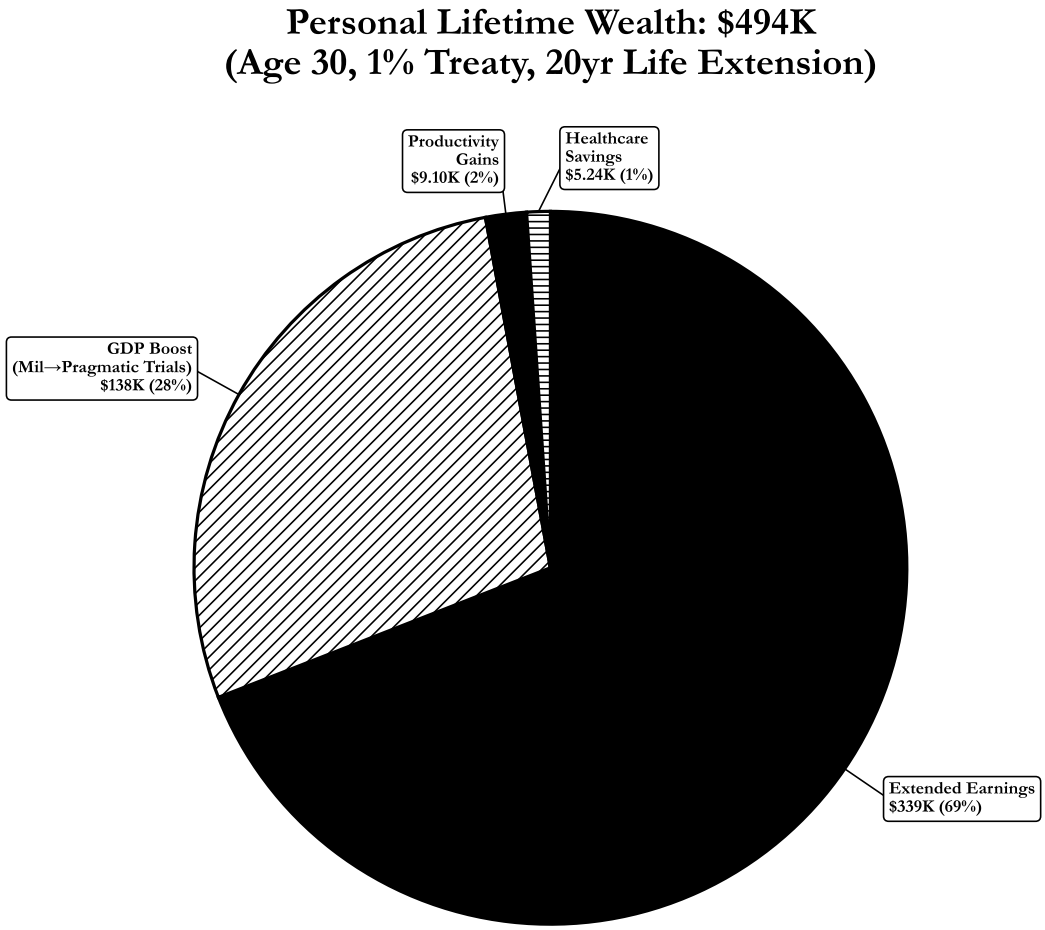


Figure 74: Probability Distribution: Regulatory Delay for Efficacy Testing Post-Safety Verification

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.

Individual-Level Economic Impact

The aggregate societal benefits ($172B (95% CI: $140B-$213B)-$172B (95% CI: $140B-$213B) annually) result from individual economic gains multiplied across billions of people. Understanding individual impact helps explain both the scale and the equity of the Disease Eradication Model.



With 20 years of life extension, extended earnings from living longer dominate the benefit calculation.

WarOnDisease.org

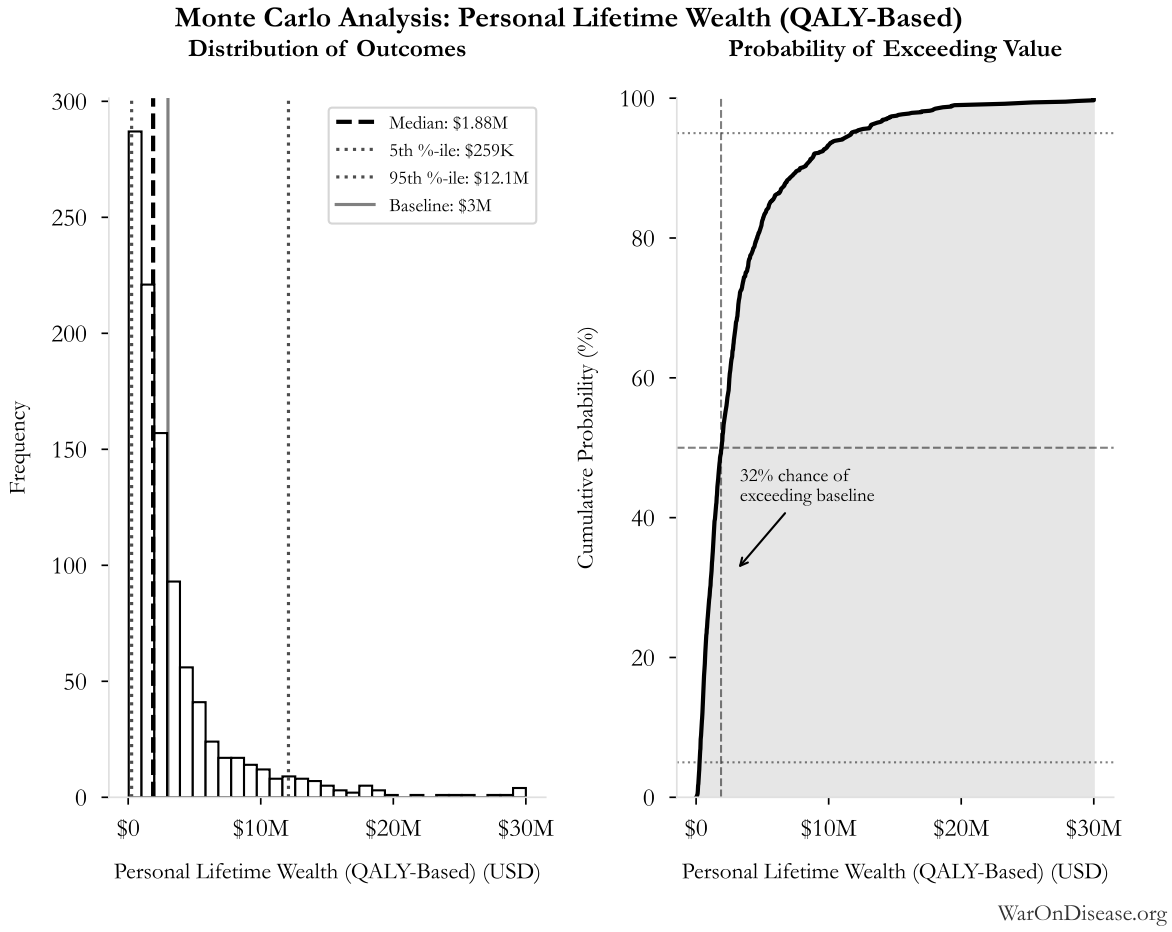


Figure 75: Monte Carlo Distribution: Personal Lifetime Wealth (QALY-Based) (10,000 simulations)

Simulation Results Summary: Personal Lifetime Wealth (QALY-Based)

Statistic	Value
Baseline (deterministic)	$3M
Mean (expected value)	$3.41M
Median (50th percentile)	$1.88M
Standard Deviation	$4.41M
90% Range (5th-95th percentile)	[$259K, $12.1M]

The histogram shows the distribution of Personal Lifetime Wealth (QALY-Based) 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 detailed analysis of personal wealth calculations, see Disease Eradication Model: Personal Lifetime Wealth.

Who Benefits and How

The 1% Treaty creates positive economic incentives across all major groups, eliminating traditional opposition to healthcare system reform. This alignment makes it politically feasible and sustainable.

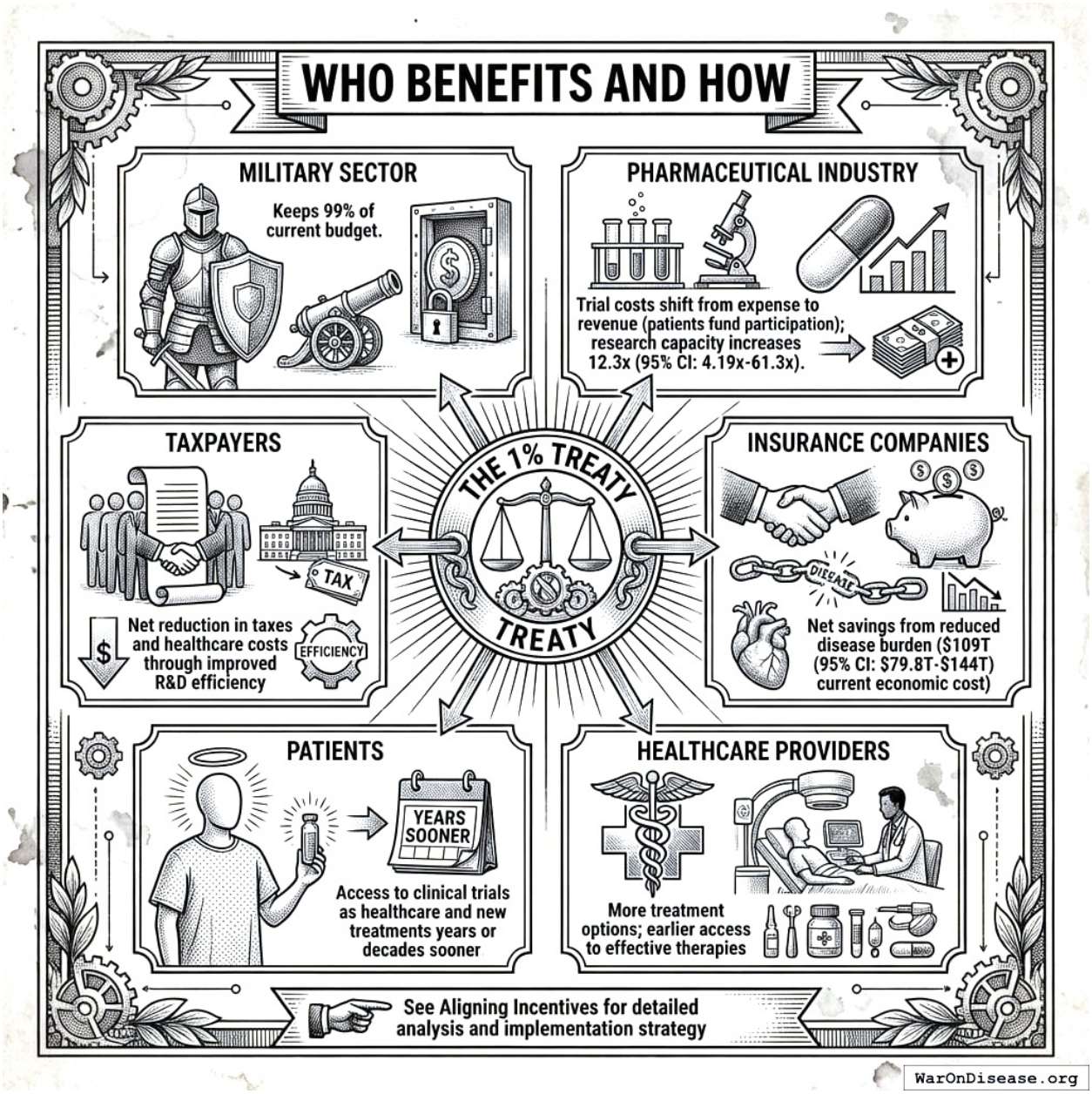


Figure 76: A stakeholder benefit map illustrating how the 1% Treaty aligns incentives across the military, pharmaceutical industry, insurance companies, healthcare providers, patients, and taxpayers.

Who Gets What (see Aligning Incentives for details):

- **Military sector**: Keeps 99% of current budget

- **Pharmaceutical industry**: Trial costs shift from expense to revenue (patients fund participation); research capacity increases 12.3x (95% CI: 4.19x-61.3x)
- **Insurance companies**: Net savings from reduced disease burden[43] ($109T (95% CI: $79.8T-$144T) current economic cost)
- **Healthcare providers**: More treatment options; earlier access to effective therapies
- **Patients**: Access to clinical trials as healthcare and new treatments years or decades sooner
- **Taxpayers**: Net reduction in taxes and healthcare costs through improved R&D efficiency

See Aligning Incentives for detailed analysis and implementation strategy.

Adoption Dynamics: Game-Theoretic Analysis

Western economies are facing a solvency crisis driven by healthcare inflation and aging populations. Traditional approaches face severe constraints: austerity programs cutting benefits generate political backlash, while monetary expansion through Modern Monetary Theory risks inflation. Technological deflation through dramatically reduced clinical trial costs offers an alternative path.

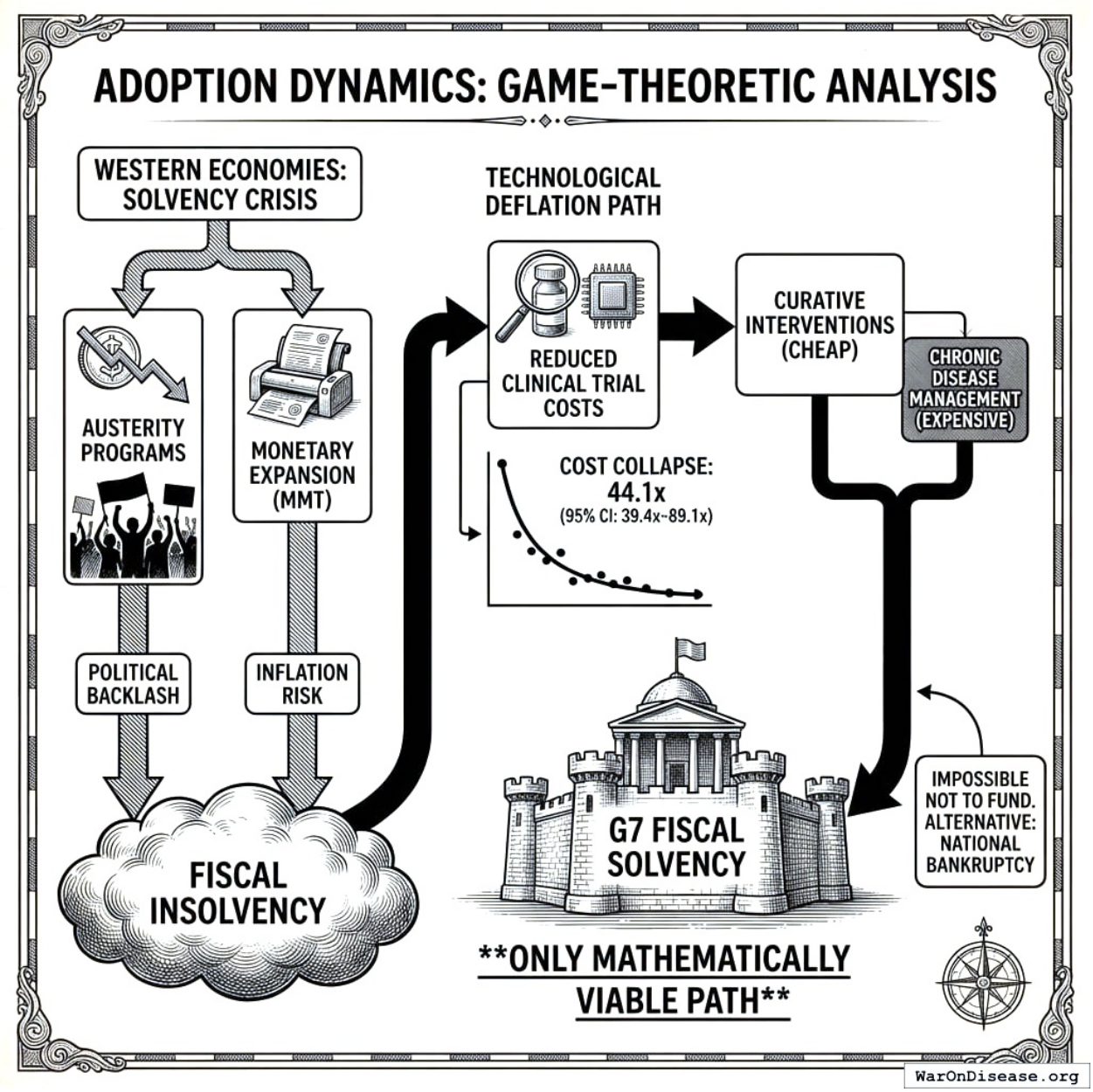
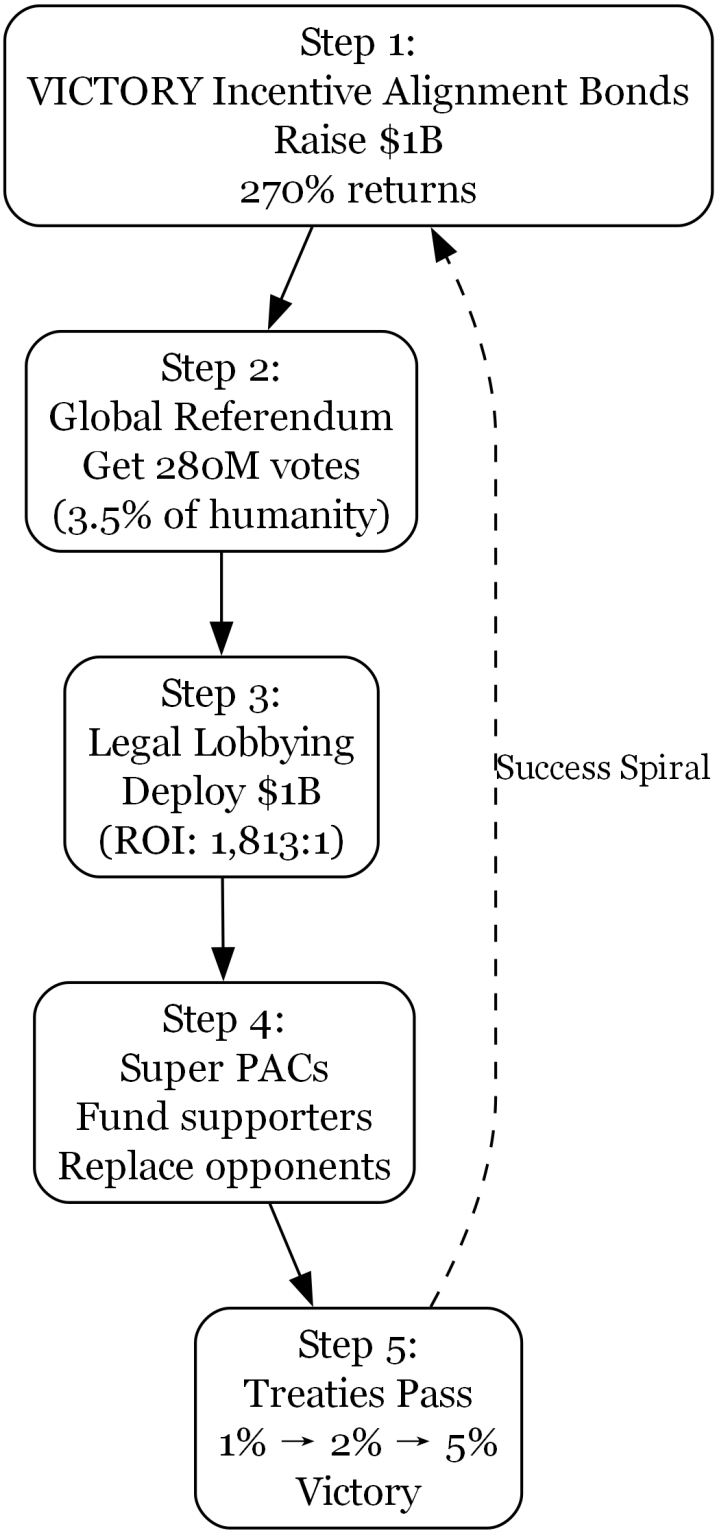


Figure 77: A comparison of three fiscal pathways for G7 nations: Austerity and Monetary Expansion leading to failure, versus Technological Deflation through reduced clinical trial costs leading to national solvency.

By collapsing the cost of clinical trials by 44.1x (95% CI: 39.4x-89.1x), we fundamentally alter the cost structure of healthcare. We replace expensive "chronic disease management" with cheap "curative interventions." This is the **only mathematically viable path** to long-term fiscal solvency for G7 nations. It is impossible *not* to fund this, because the alternative is national bankruptcy.

Implementation Strategy

The economic benefits outlined above demonstrate the value proposition of the 1% Treaty system. Implementation requires political mobilization to achieve treaty adoption:


Step 1:
VICTORY Incentive Alignment Bonds
Raise $1B
270% returns
Step 2:
Global Referendum
Get 280M votes
(3.5% of humanity)
Step 3:
Legal Lobbying
Deploy $1B
(ROI: 1,813:1)
Step 4:
Super PACs
Fund supporters
Replace opponents
Step 5:
Treaties Pass
1% → 2% → 5%
Victory
Success Spiral

Step 1: Global Mandate (The Philanthropic Catalyst)

Goal: Survey **3.5% of the global population** (280 million of people people).

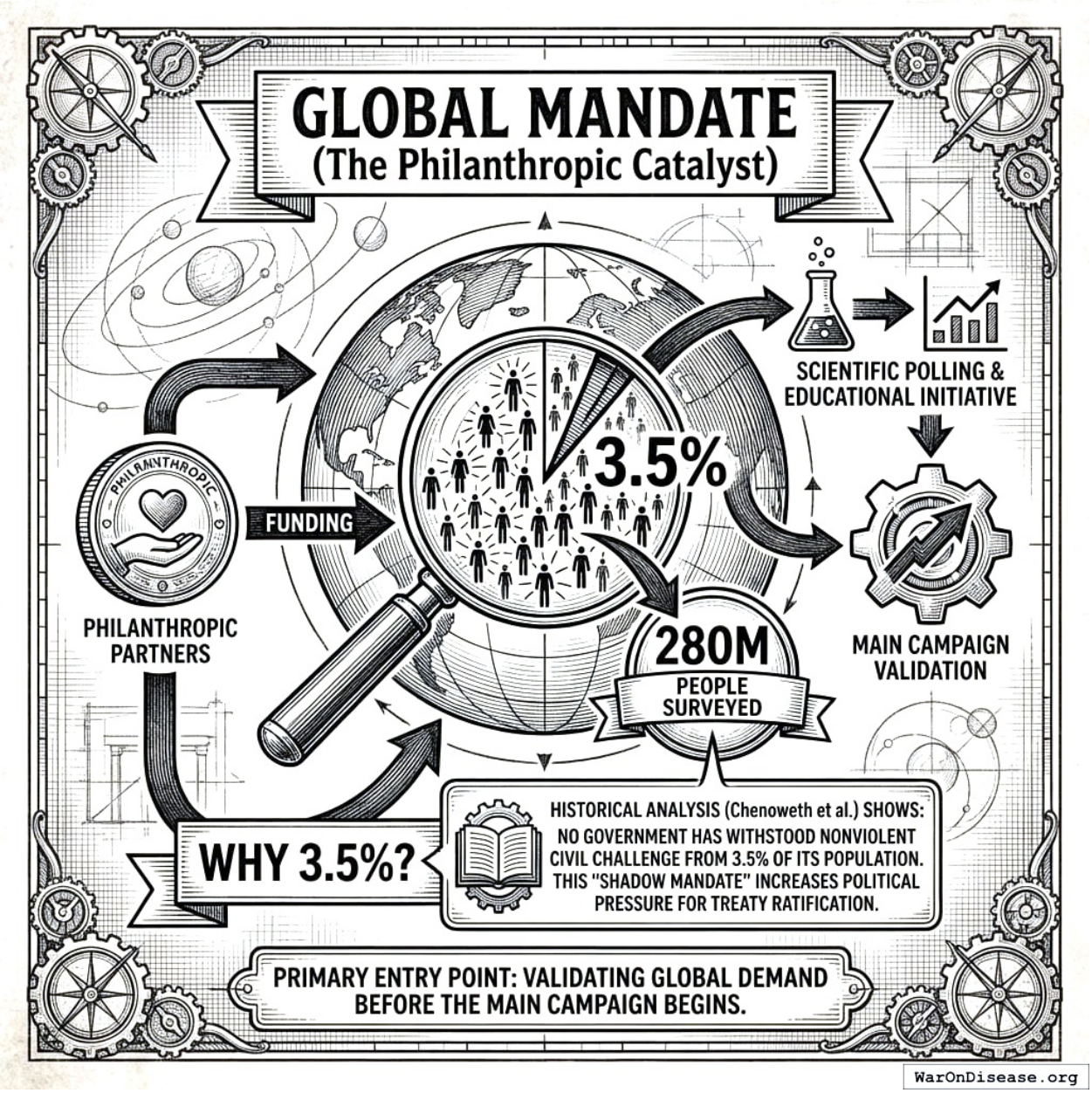


Figure 78: A visual representation of the 3.5% threshold for social change, illustrating how reaching 280 million people creates a tipping point for global political pressure.

Why 3.5%?: Historical analysis (Chenoweth et al.) shows that no government has withstood nonviolent civil challenge from 3.5% of its population. This "Shadow Mandate" would increase political pressure for treaty ratification.

Funding: This educational and scientific polling initiative is the primary entry point for **philanthropic partners**, validating global demand before the main campaign begins.

Step 2: Capitalization via Incentive Alignment Bonds (IABs)

A Special Purpose Vehicle (SPV) issues Incentive Alignment Bonds to capitalize the advocacy roadmap. By front-loading the cost of political change, investors capture the arbitrage gap between lobbying costs ($1B) and sovereign flows ($27.2B/year). Financial modeling projects a risk-adjusted IRR of ~272%.

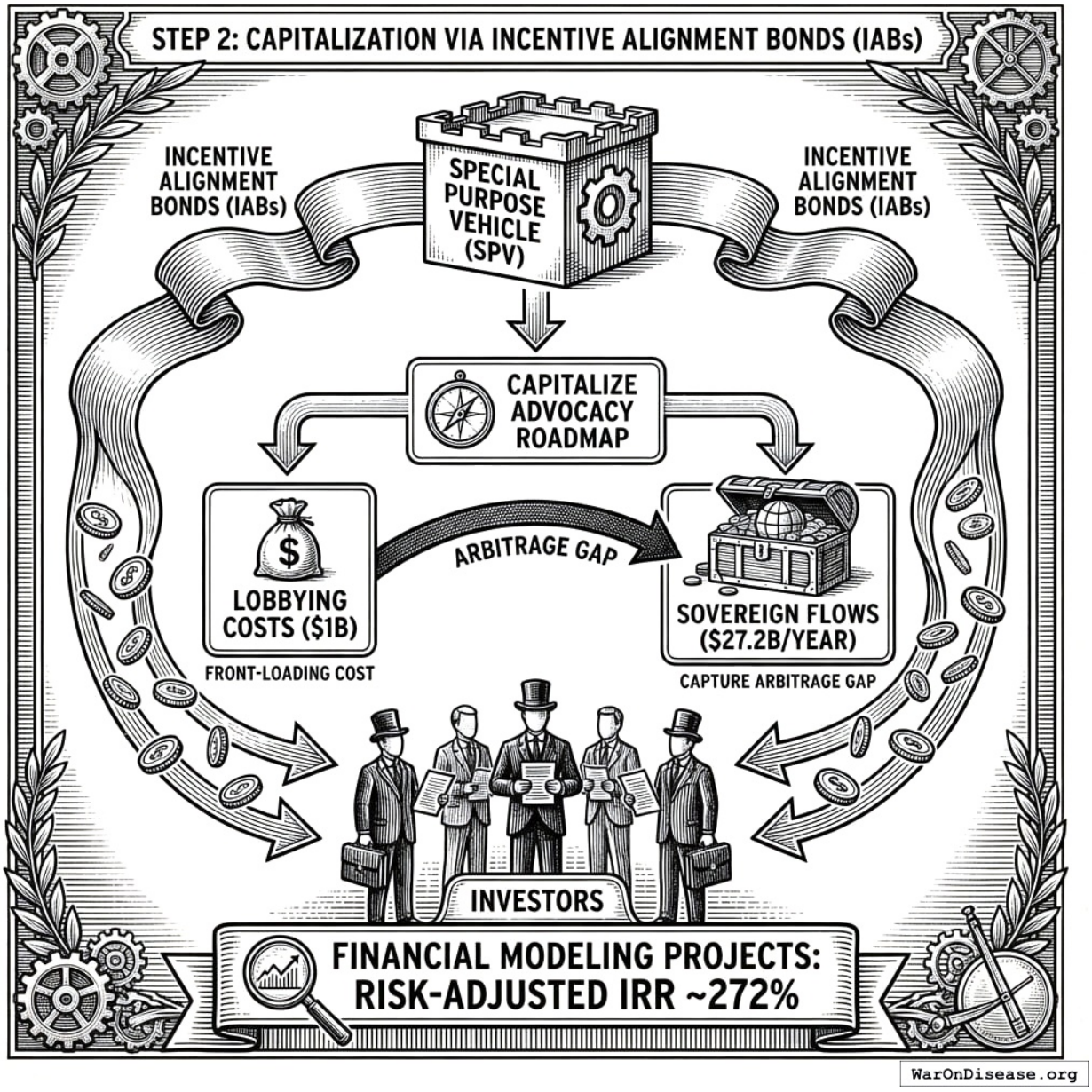


Figure 79: A diagram showing the flow of capital from Incentive Alignment Bonds issued by an SPV to bridge the arbitrage gap between lobbying costs and sovereign revenue flows.

Step 3: Implement the Legislative Strategy

Deploy Incentive Alignment Bond proceeds to translate public support into legislative action.

Step 4: Build the Infrastructure

The 1% shift funds globally scaled pragmatic trial infrastructure modeled on RECOVERY's approach. Thousands of neglected treatments finally get tested. Effective ones scale instantly.

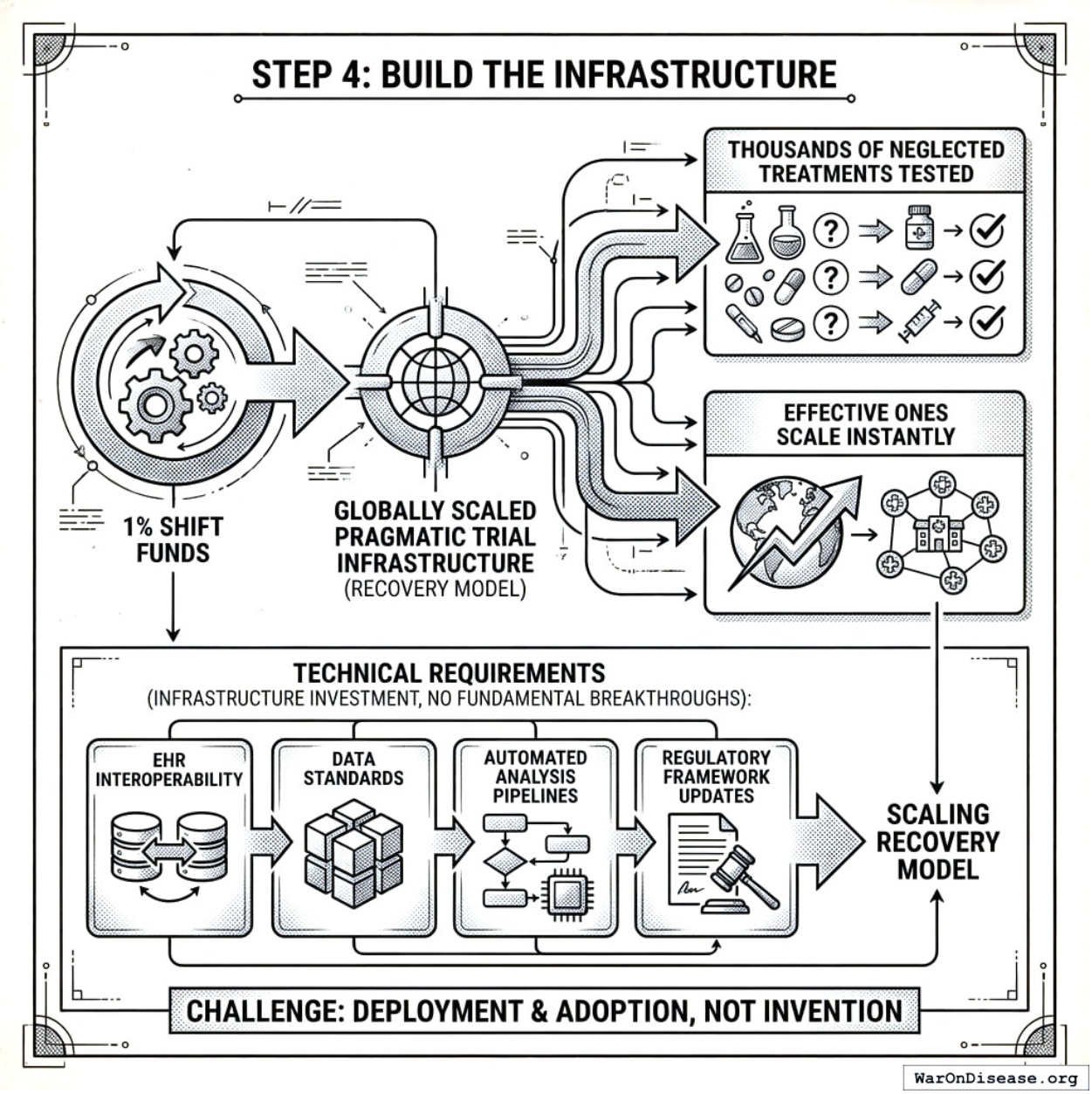


Figure 80: A flow diagram showing how funding creates global trial infrastructure, leading to the testing of neglected treatments and the rapid scaling of effective results.

Technical requirements: Building this requires EHR interoperability, data standards, automated analysis pipelines, and regulatory framework updates. RECOVERY demonstrated the core model works; scaling requires infrastructure investment but no fundamental technical breakthroughs. The challenge is deployment and adoption, not invention.

Step 5: The Statutory Administration Utility

The Treaty mandates that the Fund be managed by a private Central Counterparty to ensure operational efficiency and accountability.

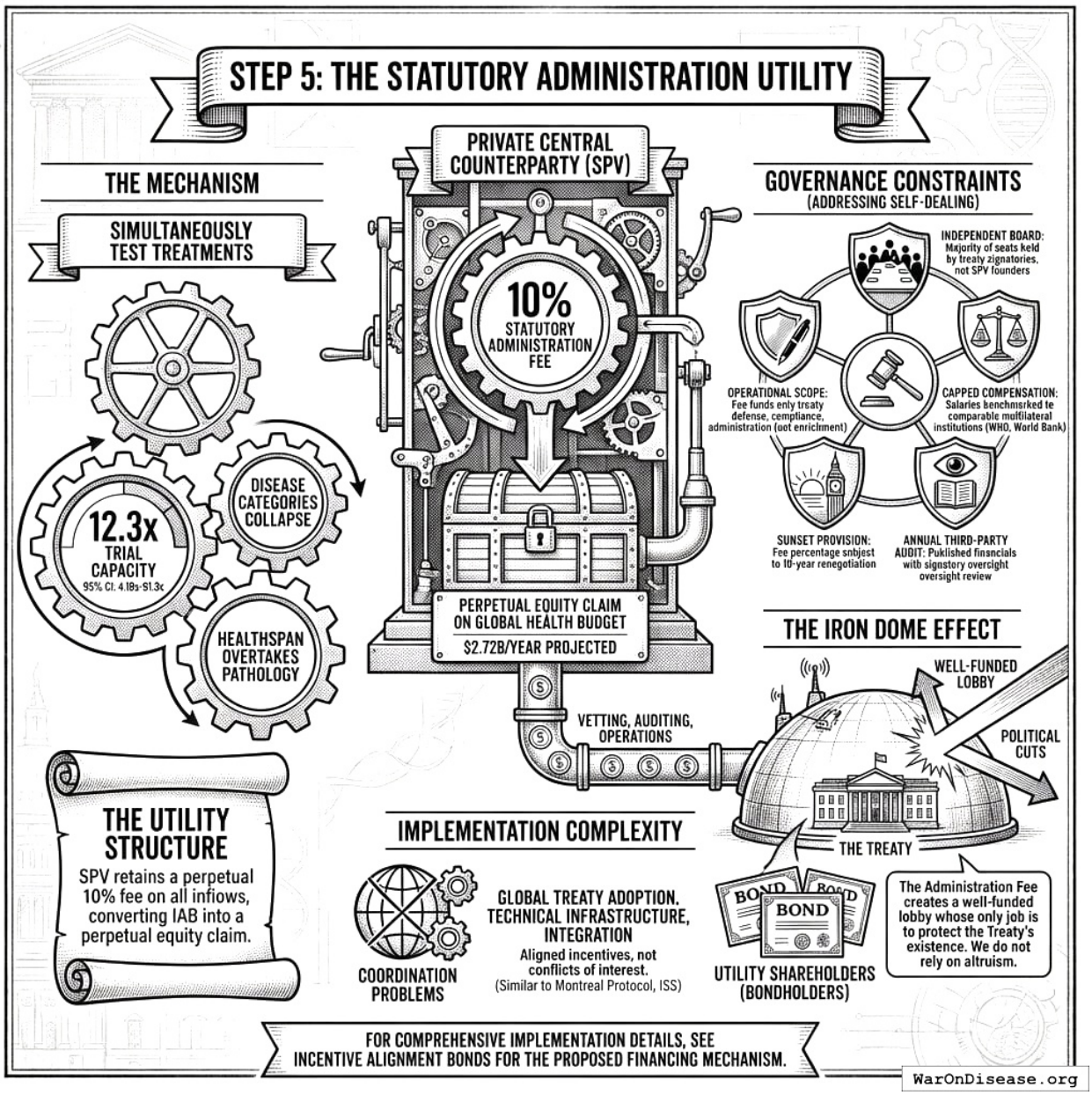


Figure 81: A conceptual diagram showing the flow of the Statutory Administration Fee from treaty inflows to fund operations, dividends, and the 'Iron Dome' lobbying mechanism that protects the treaty's longevity.

The mechanism:

- 12.3x (95% CI: 4.19x-61.3x) more trial capacity to test treatments simultaneously
- Disease categories collapse as effective treatments scale

- Healthspan overtakes pathology

The utility structure: The SPV retains a perpetual 10% Statutory Administration Fee on all inflows ($2.72B/year projected) to cover vetting, auditing, and operations. This converts the IAB from a debt instrument into a perpetual equity claim on the Global Health Budget.

Governance constraints (addressing self-dealing concerns):

- **Independent board**: Majority of seats held by treaty signatory representatives, not SPV founders
- **Capped compensation**: Administrator salaries benchmarked to comparable multilateral institutions (WHO, World Bank)
- **Annual third-party audit**: Published financials with signatory oversight committee review
- **Sunset provision**: Fee percentage subject to 10-year renegotiation by signatory majority
- **Operational scope**: Fee funds only treaty defense lobbying, compliance monitoring, and fund administration (not founder enrichment)

Utility shareholders (bondholders) receive dividends from the Administration Fee, creating a permanent constituency to defend the Treaty against political cuts. We do not rely on altruism. We rely on the "Iron Dome" effect: The Administration Fee creates a well-funded lobby whose only job is to protect the Treaty's existence.

Implementation complexity: Coordinating global treaty adoption, building technical infrastructure, and integrating with existing health systems presents significant logistical challenges. However, these are coordination problems with aligned incentives, not conflicts of interest. Similar to how nations coordinated on the Montreal Protocol (ozone layer) or the International Space Station despite complexity, the economic case makes cooperation rational even for self-interested actors.

For comprehensive implementation details, see **Incentive Alignment Bonds** for the proposed financing mechanism.

Implementation Budget Breakdown

The $1B implementation cost (used as denominator in complete case 84.8M:1 (95% CI: 46.6M:1-144M:1) ROI) allocates funds across three strategic categories:

Budget Category	Amount	Purpose
Global Referendum	$250M	Global direct democracy campaign (280 million of people votes). Creates a **"Shadow Mandate"** and political cost for non-adoption. Not legally binding, but politically coercive.
Legislative Advocacy	$650M	Legislative outreach (US/EU/G20), policy education, military industry conversion, legal/compliance, opposition research. Outspends pharma + MIC combined

Budget Category	Amount	Purpose
Reserve Fund	\$100M	Post-victory transition, treaty implementation support, contingency buffer
Total Implementation Cost	**\$1B**	4-year implementation timeline

$$\begin{aligned} &Cost_{campaign} \\ &= Budget_{viral,base} + Budget_{lobby,treaty} \\ &+ Budget_{reserve} \\ &= \$250M + \$650M + \$100M \\ &= \$1B \end{aligned}$$

Philanthropic Leverage: For a philanthropic partner, the leverage works in two phases:

1. **Phase 1 (The Catalyst):** A **\$250M grant** for the Global Survey provides the proof-of-demand that de-risks the private capital raise, unlocking the **\$1B** bond market
2. **Phase 2 (Policy Change):** That \$1B campaign convinces governments to redirect **\$27.2B/year** from military to pragmatic clinical trials

Total Leverage: The **\$250M** philanthropic catalyst + **\$650M** campaign investment unlocks **\$27.2B/year** in redirected government spending.

Why such high leverage is achievable: This isn't a traditional financial return. It's **policy leverage**. Philanthropic capital funds advocacy that shifts existing government budgets. Similar mechanisms:

- Gates Foundation's \$10B vaccine pledge leveraged \$200B+ in government commitments (20x policy leverage)
- Climate advocacy: \$50M campaigns regularly shift billions in energy policy
- Tobacco control: Bloomberg's \$1B unlocked \$15B+ in government tobacco control spending (15x leverage)

The 1% Treaty targets a much larger budget reallocation (1% of \$11.4T (95% CI: \$9.01T-\$14.1T) global military spending), making the leverage ratio proportionally higher. The key difference: military budgets are ~1000x larger than typical philanthropic targets, enabling proportionally higher leverage when successfully redirected.

This budget is designed for a 3-5 year campaign to achieve treaty ratification by major powers, representing less than 4% of the first year's conservative benefits (\$172B (95% CI: \$140B-\$213B)). The referendum component isn't a "magic wand"; it's a mechanism to generate the **political capital** required to force the treaty onto the agenda of sovereign nations.

This economic analysis focuses on the return on investment once the framework is operational, demonstrating that the intervention generates 637:1 (95% CI: 569:1-790:1) to 84.8M:1 (95% CI: 46.6M:1-144M:1) returns regardless of the specific path to adoption.

Detailed Technical References

For the rigorous analysis:

- **Decentralized FDA Cost-Benefit Analysis** - The complete 637:1 (95% CI: 569:1-790:1) ROI breakdown with NPV calculations
- **Economic Value of Accelerated Treatments** - The 7-year access acceleration math
- **Economic Models Notebook** - All calculations available for independent verification
- **1% Treaty Cost-Effectiveness** - Why this is a dominant health intervention

Risk Analysis and Mitigation

This section addresses common objections and potential failure modes, along with specific mitigation strategies.

The "But Politicians Won't Do It" Problem

What could go wrong: Politicians refuse to redirect 1% of military spending to pragmatic clinical trials because military contractors oppose the change.

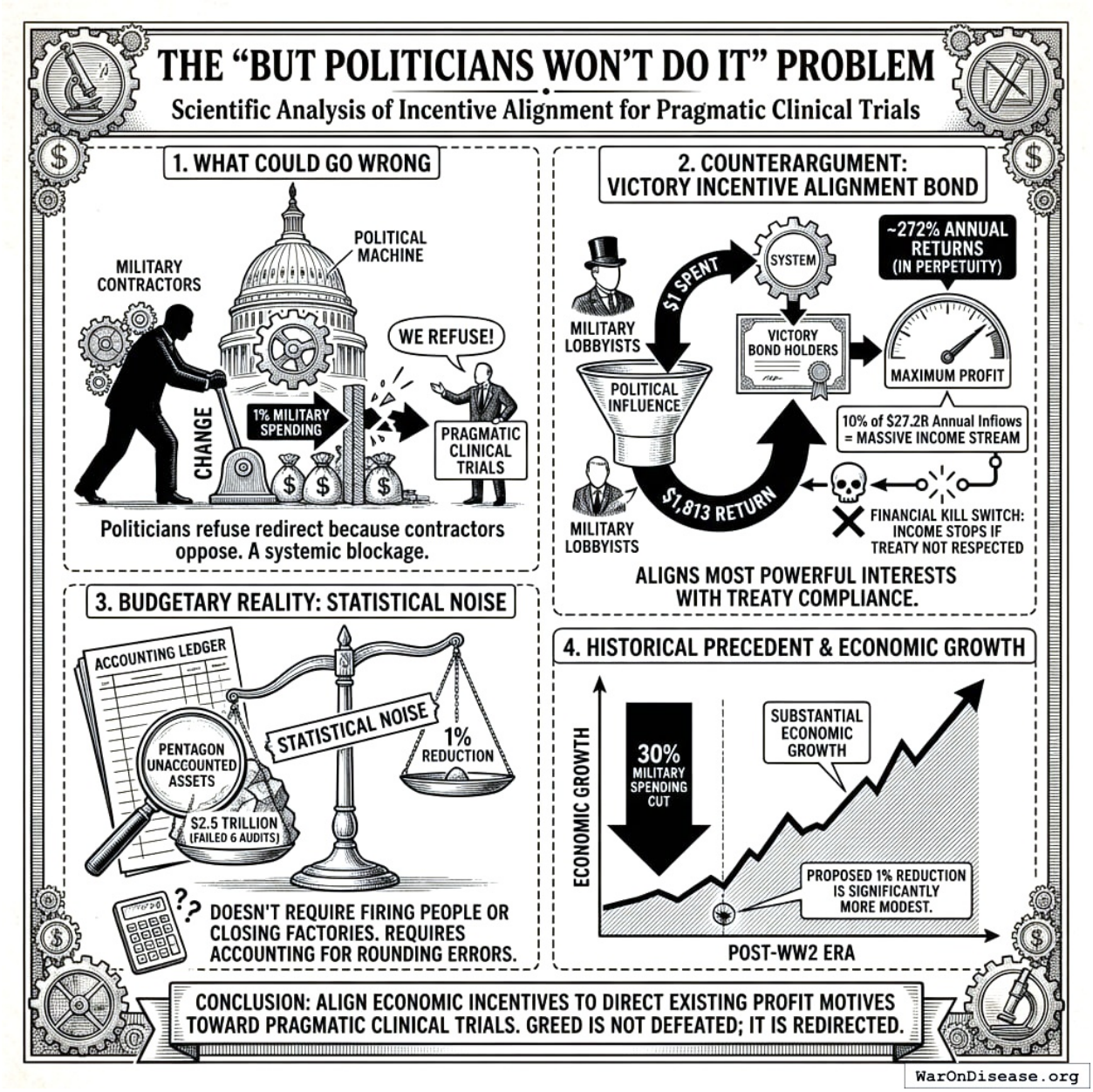


Figure 82: A visualization comparing the proposed 1% military spending reduction against the scale of unaccounted Pentagon assets, alongside a logic flow showing how Incentive Alignment Bonds create a financial 'kill switch' for treaty compliance.

Counterargument:

Military lobbyists currently get $1,813 back for every $1 spent[148] on political influence. The proposed model offers Incentive Alignment Bond holders ~**272%** in perpetuity (allocating 10% of the $27.2B annual inflows to bond payouts).

This creates a financial "kill switch": if the treaty is not respected, this massive income stream stops. This aligns the most powerful interests on earth with treaty compliance.

Budgetary Reality: The Pentagon has failed its sixth consecutive audit and cannot account for **$2.5 trillion** in assets. A 1% reduction is statistical noise in a system that can't locate trillions. It doesn't require firing people or closing factories; it requires accounting for rounding errors.

This doesn't defeat greed. It aligns economic incentives to direct existing profit motives toward pragmatic clinical trials.

Historical precedent: After WW2, military spending was cut by 30%[79], contributing to substantial economic growth. The proposed 1% reduction is significantly more modest.

Safety Concerns

Objection: Pragmatic trials with lower costs may compromise safety by missing dangerous side effects.

Response: The empirical evidence indicates the opposite. The proposed system provides superior safety monitoring compared to traditional trials across multiple dimensions: sample size, population diversity, monitoring duration, publication completeness, and adverse event detection speed.

Current system limitations:

- Voluntary adverse event reporting captures an estimated 1-10% of actual events (FDA assessment)
- Traditional Phase III trials test 100-300 patients for 3-12 months, then monitoring stops
- Approximately 50% of trial results go unpublished, with publication bias favoring positive findings 3:1
- 86.1% of patients excluded from trials due to age, comorbidities, or concurrent medications, meaning safety signals in these populations remain undetected
- Long-term effects (>1 year) are rarely captured in pre-approval trials

Proposed system safety advantages:

1. **Mandatory universal data collection**: The system automatically collects and publishes outcome data on all treatments and all health outcomes using existing EHR infrastructure. This is not currently done systematically for approved drugs.

2. **Continuous population-scale monitoring**: Pragmatic trials with 10,000-100,000+ participants monitored continuously through EHR integration detect safety problems faster and more reliably than small, time-limited traditional trials. The RECOVERY trial identified both effective treatments (dexamethasone) and harmful ones (hydroxychloroquine) in under 100 days with 47,000 patients - faster and more definitively than traditional trial timelines.

3. **Preserved Phase I safety testing**: The proposal retains rigorous Phase I safety testing (~2.3 years), which successfully prevented the thalidomide disaster in the United States. What changes is eliminating the 8.2 years (95% CI: 4.85 years-11.5 years)-year efficacy delay after safety is verified. Phase I safety assessment remains mandatory.

4. **Ubiquitous adverse event detection**: The Vioxx cardiovascular risk[135] took 5 years to detect through voluntary reporting and dedicated post-market studies (1999-2004), resulting in 38,000-55,000 estimated deaths[135]. Automated EHR monitoring comparing cardiovascular event rates in treated patients versus matched controls would have detected the elevated risk within 6-12 months. The proposed system implements ubiquitous automated monitoring from day one, not years later.

5. **Immediate mass notification**: When safety signals are detected, all patients currently taking the drug receive automated alerts through patient portals, enabling immediate clinical review and discontinuation if warranted. Current voluntary reporting systems lack this capability.

Comparative safety surveillance:

Safety Dimension	Traditional Phase III Trials	Pragmatic Trials + EHR Monitoring
Sample size	100-300 patients	10,000-100,000+ patients
Patient selection	86.1% excluded (comorbidities, age, medications)	All volunteers included (real-world populations)
Monitoring duration	3-12 months (then stops)	Continuous through EHR integration (indefinite)
Publication rate	~50% unpublished[133]; positive results 3× more likely published	100% automatically published (automated data aggregation)
Subpopulation safety	Excludes elderly, children, pregnant patients	Tests all populations, detects subpopulation-specific risks
Long-term effects	Rarely captured (<1 year observation)	Continuous multi-year tracking via EHR linkage
Adverse event detection	Voluntary physician reporting (1-10% capture rate)	Automated statistical surveillance (100% capture of recorded events)
Mass notification	Manual, slow, incomplete	Automated, immediate, comprehensive
Comparative effectiveness	Single treatment vs. placebo (or one comparator)	Multiple treatments randomized simultaneously; enables ranking
Population stratification	Not possible (86.1% excluded; narrow population)	Full subgroup analysis by demographics, genetics, comorbidities

Type II error dominance: Regulatory mortality analysis quantifies the harm ratio at 3.07k:1 (95% CI: 2.88k:1-3.12k:1). For every person protected from an unsafe drug approval (Type I error prevention), 3.07k:1 (95% CI: 2.88k:1-3.12k:1) people die from delayed access to beneficial treatments (Type II errors). The current regulatory framework successfully prevents toxic compounds from reaching patients through Phase I safety testing - as demonstrated by thalidomide's prevention in the United States - but the barriers placed between patients and beneficial treatments after safety verification cause 3.07k:1 (95% CI: 2.88k:1-3.12k:1) more deaths than they prevent.

$$Ratio_{TypeII} = \frac{DALYs_{lag}}{DALY_{TypeI}} = \frac{7.94B}{2.59M} = 3{,}070$$

where $DALYs_{lag} = YLL_{lag} + YLD_{lag} = 7.07B + 873M = 7.94B$

where YLL_{lag}
$= Deaths_{lag} \times (LE_{global} - Age_{death,delay})$
$= 416M \times (79 - 62)$
$= 7.07B$

where $Deaths_{lag}$
$= T_{lag} \times Deaths_{disease,daily} \times 338$
$= 8.2 \times 150{,}000 \times 338$
$= 416M$

where YLD_{lag}
$= Deaths_{lag} \times T_{suffering} \times DW_{chronic}$
$= 416M \times 6 \times 0.35$
$= 873M$

where $Deaths_{lag}$
$= T_{lag} \times Deaths_{disease,daily} \times 338$
$= 8.2 \times 150{,}000 \times 338$
$= 416M$

where $DALY_{TypeI} = DALY_{thal} \times 62 = 41{,}800 \times 62 = 2.59M$

where $DALY_{thal}$
$= YLD_{thal} + YLL_{thal}$
$= 13{,}000 + 28{,}800$
$= 41{,}800$

where YLD_{thal}
$= DW_{thal} \times N_{thal,survive} \times LE_{thal}$
$= 0.4 \times 540 \times 60$
$= 13{,}000$

where $N_{thal,survive}$
$= N_{thal,US,prevent} \times (1 - Rate_{thal,mort})$
$= 900 \times (1 - 40\%)$
$= 540$

where $N_{thal,US,prevent}$
$= N_{thal,global} \times Pct_{US,1960}$
$= 15{,}000 \times 6\%$
$= 900$

where $YLL_{thal} = Deaths_{thal} \times 80 = 360 \times 80 = 28{,}800$

where $Deaths_{thal}$

Quantified mortality from efficacy delay: The 8.2 years (95% CI: 4.85 years-11.5 years)-year delay between Phase I safety verification and final approval has resulted in an estimated 416 million deaths (95% CI: 225 million deaths-630 million deaths) from 1962-2024 by delaying patient access to beneficial treatments that had already passed safety testing. This figure represents the cumulative mortality from requiring patients to wait ~8 years for efficacy confirmation after treatments are confirmed non-toxic, when those patients could have voluntarily participated in efficacy trials immediately following Phase I completion.

$$\begin{aligned} & Deaths_{lag} \\ &= T_{lag} \times Deaths_{disease,daily} \times 338 \\ &= 8.2 \times 150{,}000 \times 338 \\ &= 416M \end{aligned}$$

Cost reduction does not imply quality reduction: The 82x (95% CI: 50x-94.1x) cost reduction achieved by the RECOVERY trial came from eliminating duplicative infrastructure (using existing hospitals instead of building dedicated trial sites, using existing EHR data instead of parallel data collection systems), not from reducing sample sizes, shortening observation periods, or relaxing safety standards. Lower cost reflects infrastructure efficiency, not reduced scientific rigor.

For detailed mortality analysis, see Regulatory Mortality Analysis.

Patient Agency and Autonomy

A decentralized institutes of health puts patients in control through trial participation, not committee votes.

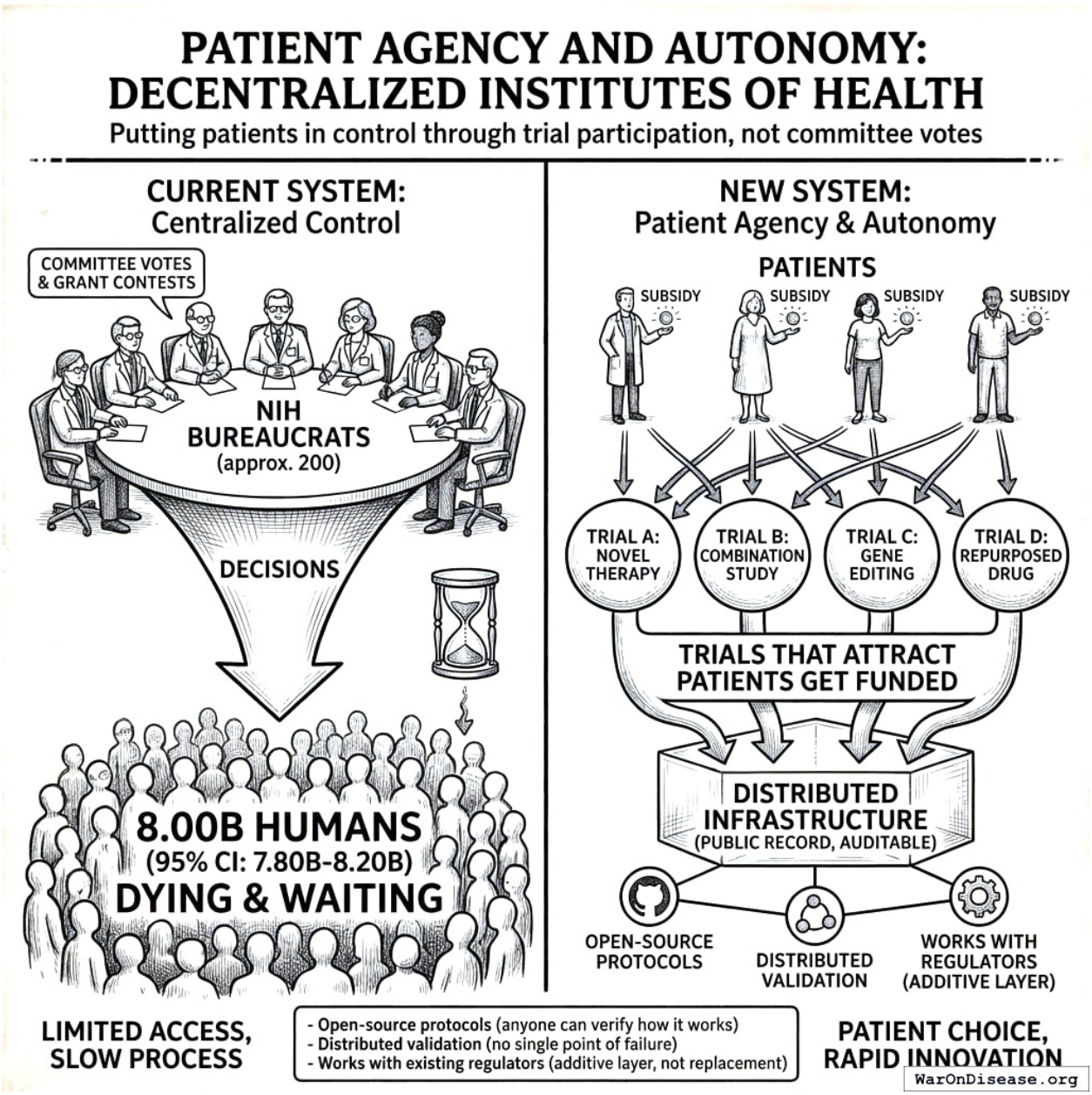


Figure 83: A comparison between the current centralized NIH funding model, where bureaucrats act as a bottleneck, and a decentralized model where patient participation directly drives funding to clinical trials.

Current system: 200 NIH bureaucrats[149] decide what 8.00 billion of people (95% CI: 7.80 billion of people-8.20 billion of people) humans can try when dying

New system: Patients choose which trials to join. Trials that attract patients get funded. Trials that don't, die.

Patient subsidies follow them to whichever trial they join. Researchers compete to design trials that patients actually want to participate in. No committees, no grant-writing contests, no bureaucrats deciding what's "worthy" of study.

All transactions publicly recorded. All spending transparent. All decisions auditable.

Patients select which trials to join. Trials that attract participants receive funding. Researchers compete for patient participation rather than committee grants.

The system operates through distributed infrastructure:

- Open-source protocols (anyone can verify how it works)
- Distributed validation (no single point of failure)
- Works with existing regulators (additive layer, not replacement)

Accountability measures

- Annual third-party audits of 1% Treaty Fund and system operations
- Public reporting of all spending and outcomes
- Milestone-based funding (money releases when targets hit)

See Anti-Capture Design and Legal Architecture for accountability mechanisms designed to prevent administrative delays and ensure timely fund deployment.

Limitations and Uncertainties

This analysis acknowledges several important limitations and sources of uncertainty inherent in modeling a transformative policy intervention of this scale.

Adoption Timeline Uncertainty

The base case assumes gradual adoption over 5 years to full implementation. Actual adoption may be faster or slower depending on:

- **Regulatory harmonization:** International coordination requirements may extend implementation timelines
- **Technical infrastructure readiness:** EHR interoperability, data standardization, and privacy compliance vary significantly across jurisdictions
- **Industry cooperation:** Pharmaceutical companies, regulators, and healthcare providers will resist or accelerate adoption based on whether they profit from it

Sensitivity analysis addresses this: Worst-case scenario models extended timelines with ROI remaining positive (66:1) even under pessimistic assumptions.

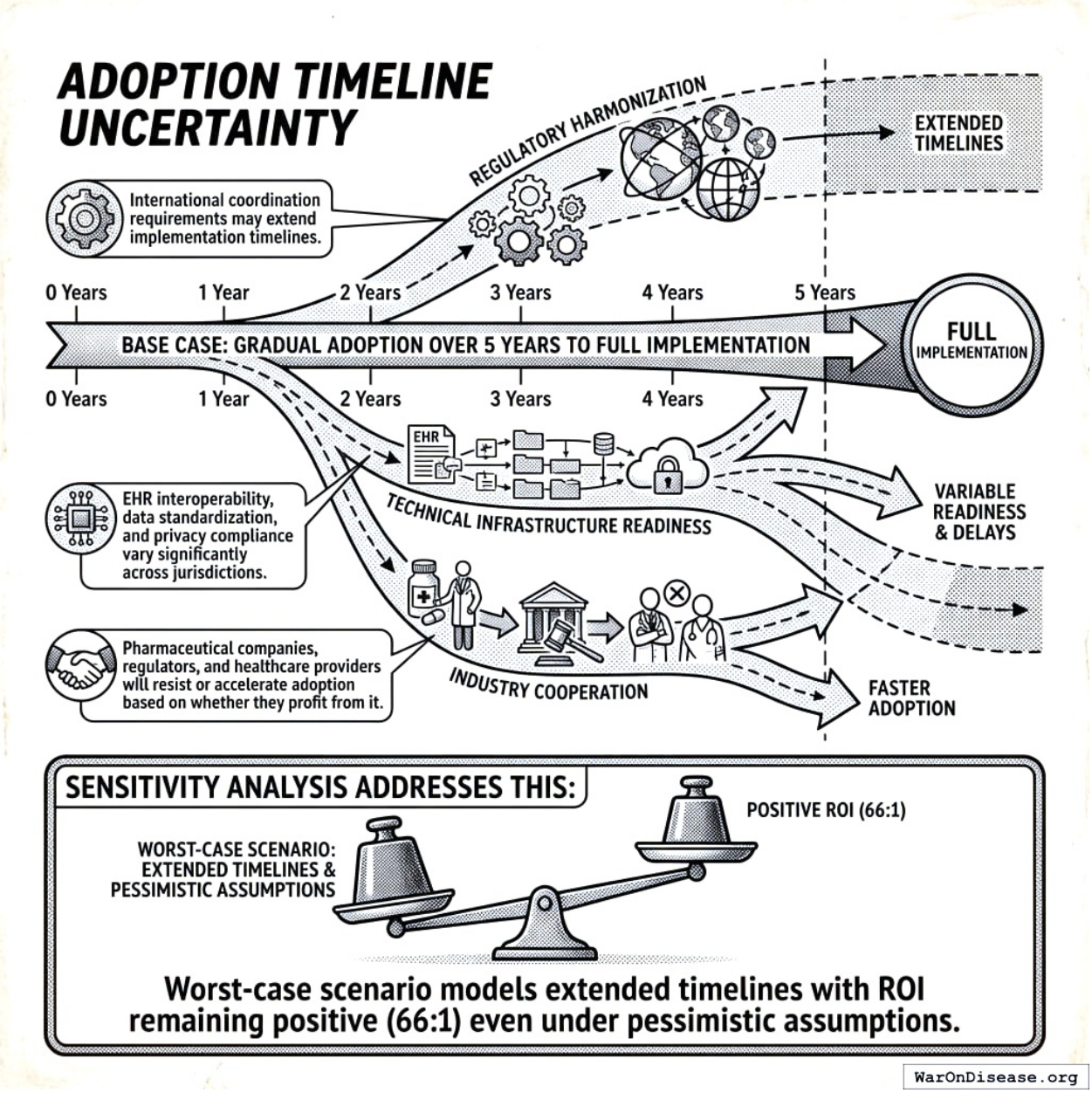


Figure 84: A visual comparison of the 5-year base case adoption timeline versus an extended implementation scenario, highlighting how factors like regulatory coordination and technical readiness shift the speed of rollout.

Pragmatic Trial Internal Validity and Selection Bias

Decentralized trials with broad eligibility criteria face potential selection bias concerns. Traditional randomized controlled trials use restrictive eligibility *precisely* to control confounding and establish internal validity.

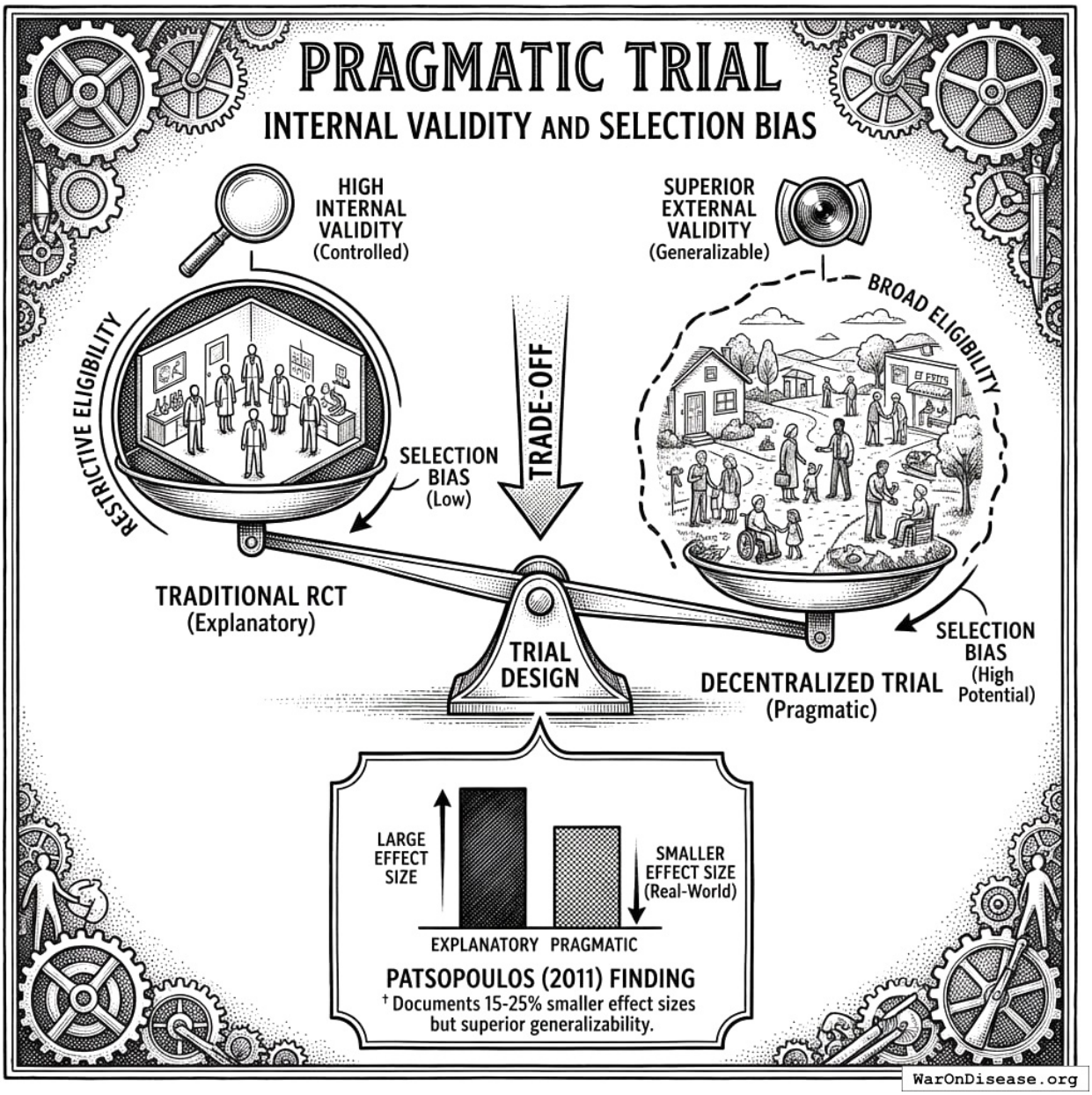


Figure 85: A conceptual diagram showing the inverse relationship between internal and external validity across explanatory and pragmatic clinical trials.

Trade-off between internal and external validity: Patsopoulos (2011)[150] documents that pragmatic trials often find 15-25% smaller effect sizes than explanatory trials but offer superior external validity (generalizability to real-world populations).

Mitigation strategies

- **Randomization preserved:** The global pragmatic trial system maintains random treatment assignment (the core causal identification strategy)
- **Large sample sizes:** Decentralized recruitment enables 10-100× larger trials, improving

statistical power and subgroup analysis
- **Covariate adjustment:** Electronic health record data enables controlling for confounders ex-post using propensity score matching and instrumental variables
- **Replication at scale:** Lower costs enable rapid replication across diverse populations, testing robustness

Empirical evidence, observational studies produce valid results: A meta-analysis in the New England Journal of Medicine compared effect sizes from high-quality observational studies to randomized controlled trials across multiple interventions. The findings demonstrate that well-designed observational studies produce results statistically indistinguishable from expensive RCTs.

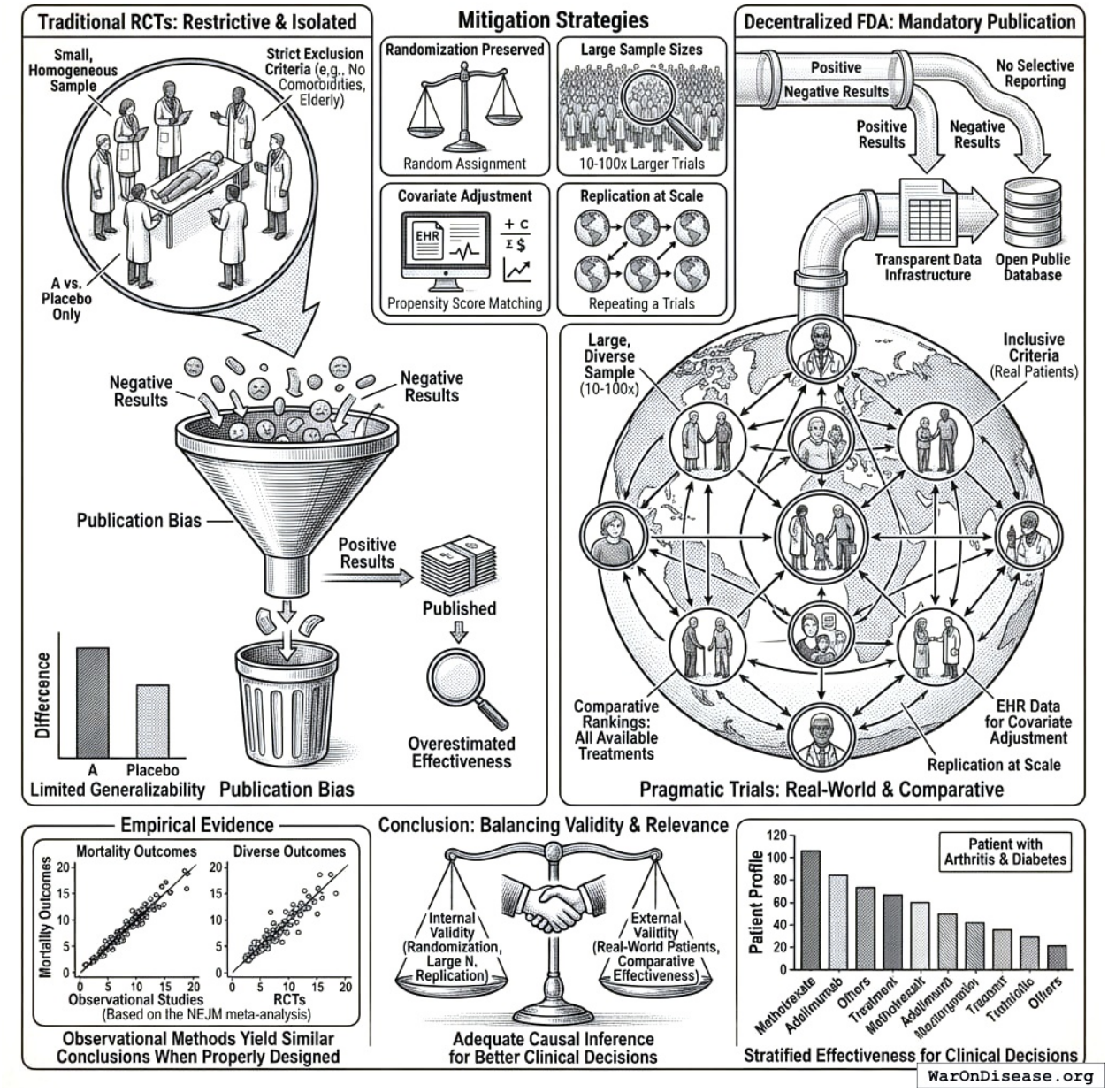


Figure 86: Comparison of traditional RCTs versus pragmatic trials, illustrating the shift from binary 'Treatment vs. Placebo' tests in restricted populations to comparative rankings of all treatments in diverse, real-world patient groups.

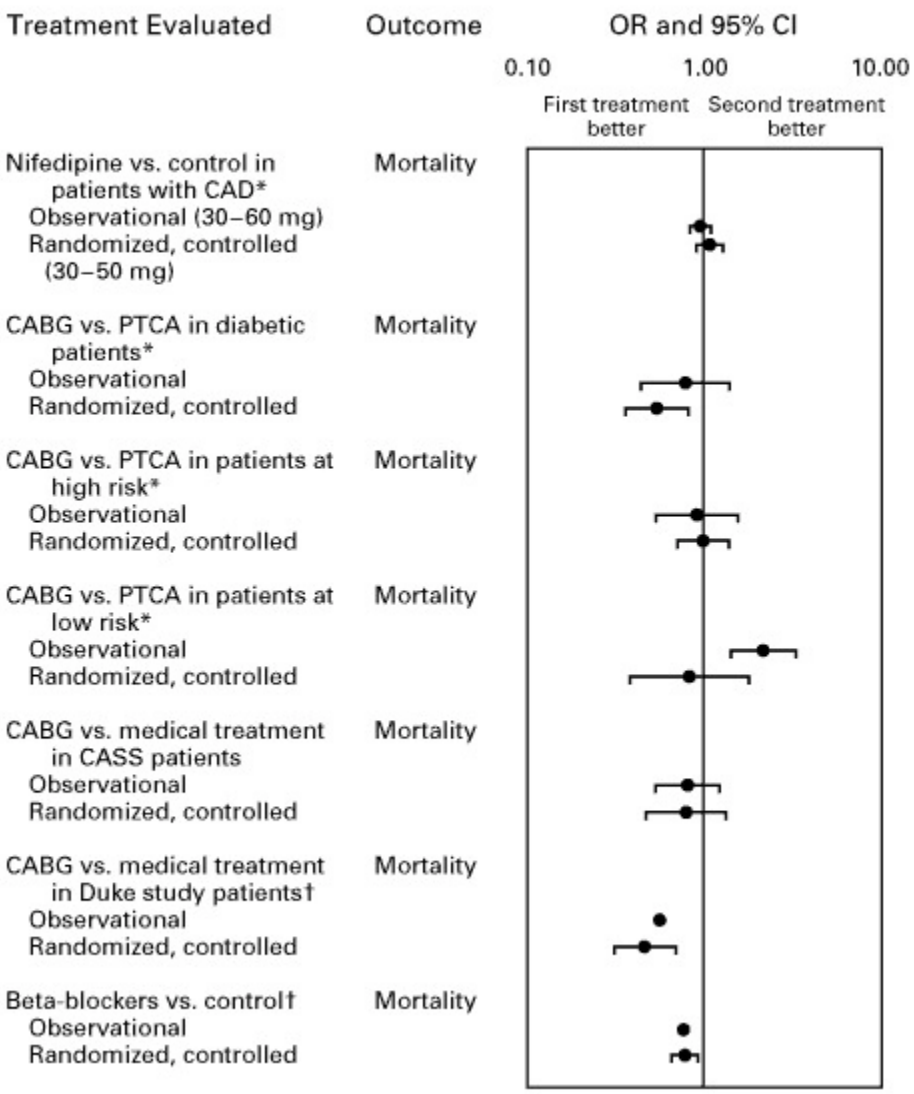


Figure 87: Comparison of effect sizes from observational studies versus randomized trials for mortality outcomes, showing strong concordance between methodologies.

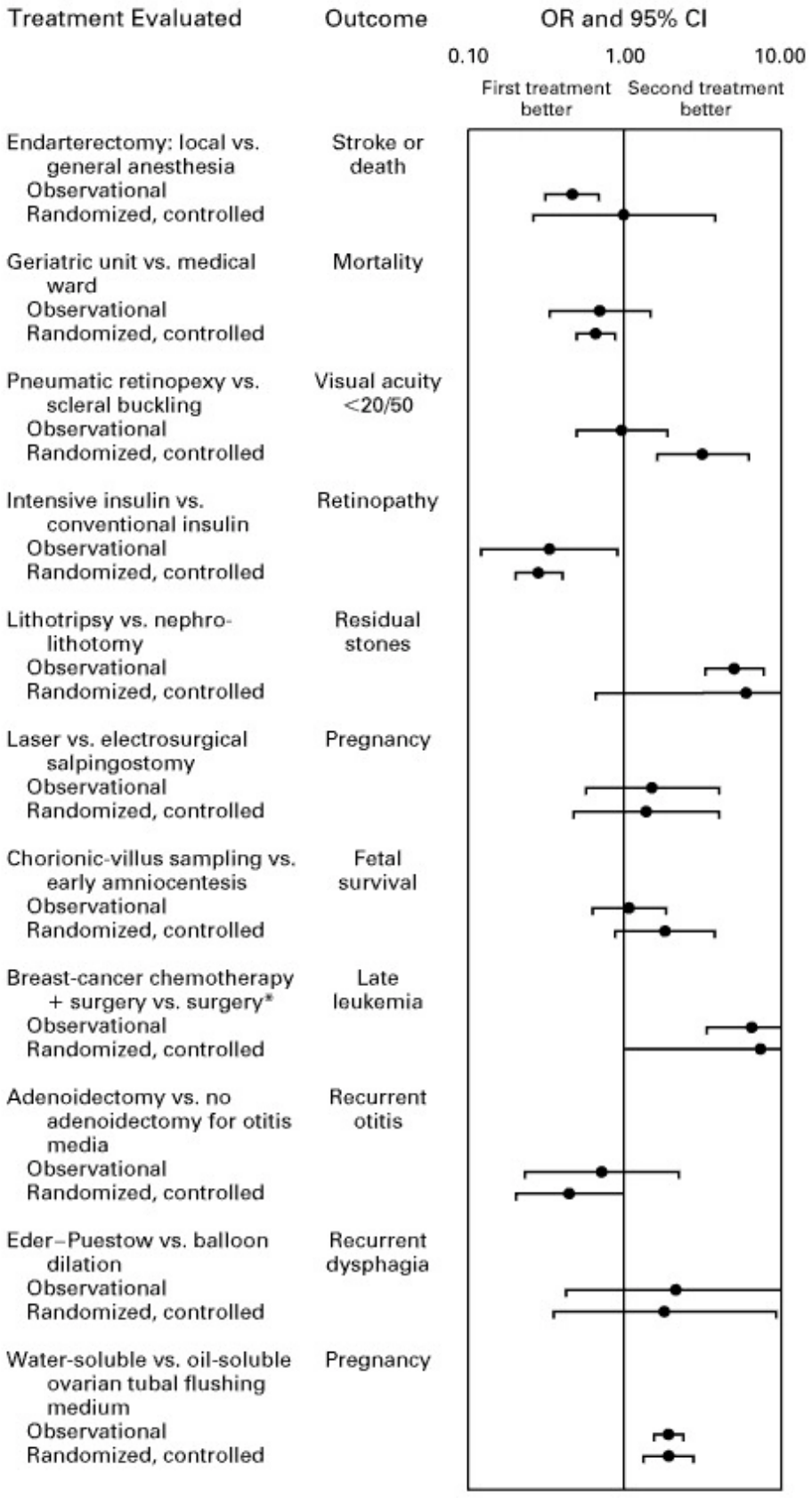


Figure 88: Comparison of effect sizes from observational studies versus randomized trials across diverse outcomes, demonstrating that observational methods yield similar conclusions when properly designed.

These meta-analytic findings support the validity of pragmatic trial designs used in this system. Modern statistical methods, large sample sizes, and proper covariate adjustment enable observational and quasi-experimental designs to achieve causal inference comparable to traditional RCTs at a fraction of the cost.

Why pragmatic trial data is more valuable than RCT data for clinical decisions:

Traditional RCTs answer: "Is treatment A better than placebo?" Pragmatic trials answer: "How do ALL available treatments rank for patients like mine?"

This distinction is crucial for clinical decision-making. A physician facing a patient with rheumatoid arthritis has 15+ approved treatment options. Traditional evidence provides isolated A-vs-placebo studies; the physician cannot determine whether methotrexate or adalimumab is superior for their specific patient. Pragmatic trials, by randomly assigning patients across all options simultaneously and including diverse populations, generate the comparative rankings clinicians actually need.

Furthermore, RCTs' restrictive eligibility criteria (excluding patients with comorbidities, elderly patients, patients on multiple medications) mean their results don't generalize to real patients. A 73-year-old with diabetes and hypertension was excluded from the original trials; the physician is guessing how results might apply. Pragmatic trials include these patients, enabling stratified effectiveness rankings by actual patient characteristics.

Historical precedent: Pre-1962 physician-led system successfully identified effective treatments (antibiotics, vaccines, surgical techniques) despite lacking modern randomization, suggesting real-world evidence can establish causality when combined with peer review and replication.

Publication bias: Traditional trials face severe publication bias: only 37% of negative results are published compared to 94% of positive results[133], leading to overestimation of treatment effectiveness and ~$100 billion annually wasted on repeating failed experiments[151]. A decentralized FDA addresses this by design: all trials are registered in the public database, all results (positive and negative) are automatically published through the transparent data infrastructure, and the open data architecture ensures no selective reporting. Unlike traditional systems where researchers choose what to publish, mandatory publication of all registered trials eliminates publication bias as a concern.

Conclusion: Internal validity concerns are acknowledged, but the combination of randomization, large samples, and replication capacity provides adequate causal inference even with broader eligibility criteria.

QALY Calculation Uncertainties

The 565 billion DALYs (95% CI: 361 billion DALYs-877 billion DALYs) estimate aggregates benefits from the average ~212 years (95% CI: 135 years-355 years)-year timeline shift across three benefit streams with varying levels of empirical support.

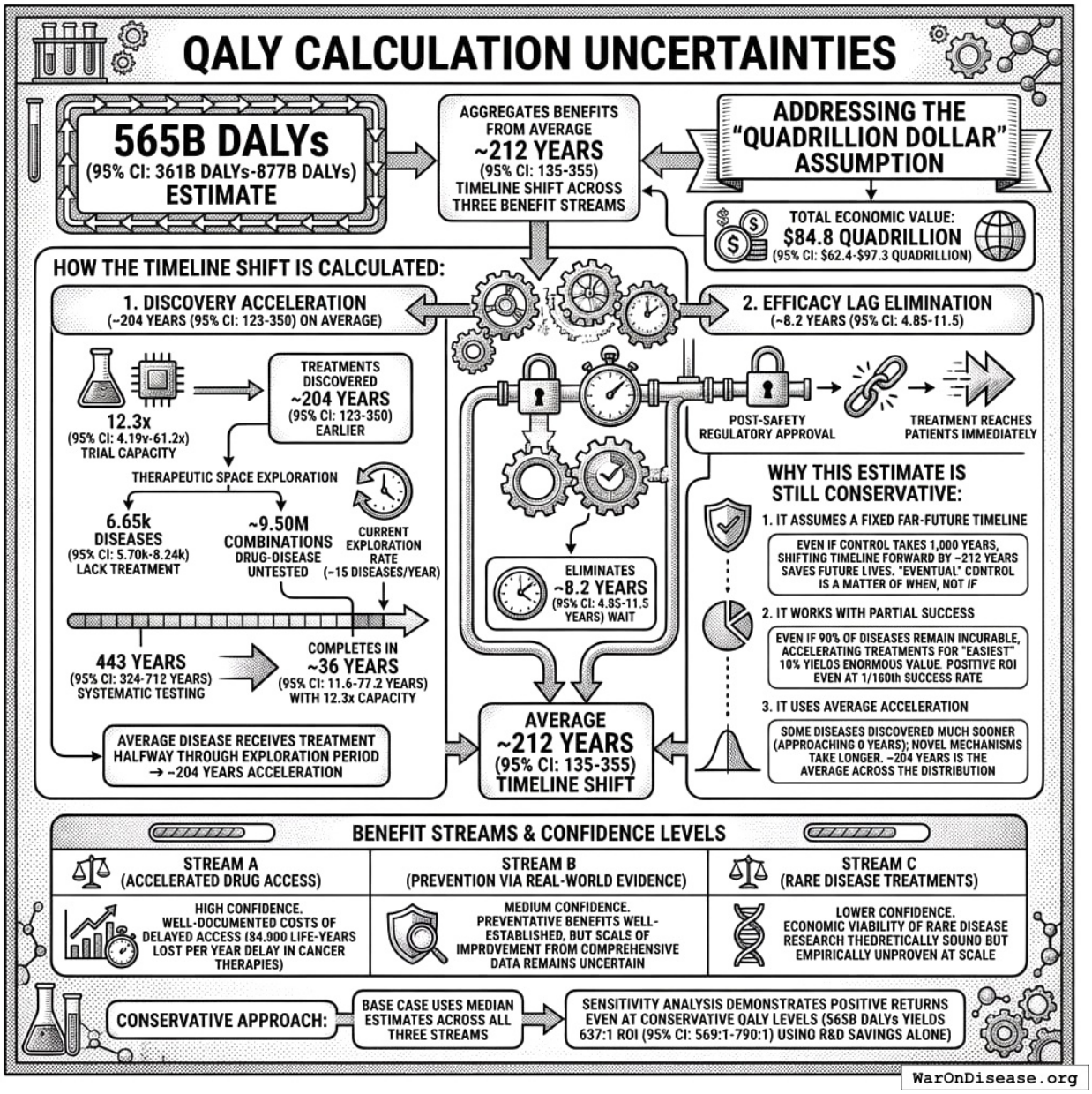


Figure 89: A visual comparison of medical discovery timelines showing the reduction in disease exploration time from 443 years to 36 years through increased trial capacity, resulting in a 212-year average acceleration.

Addressing the "Quadrillion Dollar" Assumption: The total economic value of $84.8 quadrillion (95% CI: $62.4 quadrillion-$97.3 quadrillion) derives from the average ~212 years (95% CI: 135 years-355 years)-year timeline shift in disease eradication.

How the timeline shift is calculated:

1. **Discovery acceleration (~204 years (95% CI: 123 years-350 years) on average)**: With 12.3x (95% CI: 4.19x-61.3x) trial capacity, treatments are discovered ~204 years (95% CI: 123 years-350 years) earlier on average. This is based on therapeutic space exploration: 6.65

thousand diseases (95% CI: 5.70 thousand diseases-8.24 thousand diseases) lack treatment, with ~9.50 million combinations drug-disease combinations untested. At current exploration rate (~15 diseases/year getting first treatments), systematically testing this space would take 443 years (95% CI: 324 years-712 years). With 12.3x (95% CI: 4.19x-61.3x) capacity, exploration completes in ~36 years (95% CI: 11.6 years-77.2 years). Average disease receives treatment halfway through exploration period, yielding ~204 years (95% CI: 123 years-350 years) acceleration.

2. **Efficacy lag elimination (~8.2 years (95% CI: 4.85 years-11.5 years))**: Once a treatment is discovered, it reaches patients immediately instead of waiting ~8.2 years (95% CI: 4.85 years-11.5 years) for post-safety regulatory approval.

Why this estimate is still conservative:

1. **It assumes a fixed far-future timeline**: Even if full biological control takes 1,000 years, shifting that timeline forward by ~212 years (95% CI: 135 years-355 years) on average saves that many years' worth of future lives. Given the trajectory of biotechnology, "eventual" control over biology is a matter of *when*, not *if*.
2. **It works with partial success**: Even if we assume 90% of diseases remain biologically incurable (a massive discount), accelerating treatments for just the "easiest" 10% of the burden (e.g., cardiovascular disease, metabolic disorders) still yields enormous value. The ROI is positive even at 1/100th of the projected success rate.
3. **It uses average acceleration**: Some diseases with existing-but-untested treatments would be discovered much sooner (approaching 0 years wait); diseases requiring novel mechanisms would take longer. The 204 years (95% CI: 123 years-350 years)-year figure is the average across the distribution.

Stream A (Accelerated Drug Access): High confidence, based on well-documented costs of delayed access (84,000 life-years lost per year delay in cancer therapies alone).

Stream B (Prevention via Real-World Evidence): Medium confidence, preventative care benefits are well-established, but scale of improvement from comprehensive data remains uncertain.

Stream C (Rare Disease Treatments): Lower confidence, economic viability of rare disease research is theoretically sound but empirically unproven at scale.

Conservative approach: Base case uses median estimates across all three streams; sensitivity analysis demonstrates positive returns even at conservative QALY levels (565 billion DALYs (95% CI: 361 billion DALYs-877 billion DALYs) yields 637:1 (95% CI: 569:1-790:1) ROI using R&D savings alone).

Data Limitations

Military Spending Data

Global military expenditure data ($2.72T, SIPRI 2024) is well-documented but:

- **Off-budget spending:** Some military expenditures may be classified or categorized elsewhere
- **Exchange rate fluctuations:** Multi-year projections require currency assumptions
- **Conflict zones:** Military spending in active conflict regions may be less fungible for redirection

Clinical Trial Market Sizing

The $60B (95% CI: $50B-$75B)[42] global clinical trials market estimate derives from industry reports, which:

- **Industry variation:** Methodologies vary across market research firms
- **Private vs. public trials:** Some trial spending may be unreported or proprietary
- **Non-pharmaceutical trials:** Medical device and digital health trials may have different cost structures

QALY Valuation Thresholds

Standard willingness-to-pay thresholds ($50K-$150K (95% CI: $100K-$199K)[91] per QALY) vary by jurisdiction:

- **Geographic variation:** WHO recommends 1-3× GDP per capita; high-income countries use higher thresholds
- **Ethical considerations:** Monetary QALY valuations raise equity concerns
- **Discount rates:** Future health benefits discounted at 3% may undervalue long-term gains

Generalizability Constraints

Political Feasibility

This analysis models economic returns conditional on treaty ratification. Political feasibility depends on:

- **Geopolitical stability:** International cooperation requirements may face challenges during periods of global tension
- **Domestic politics:** Military budget reductions face constituency resistance in military-dependent regions
- **Lobbying influence:** Military industry opposition may impede adoption

Risk assessment: The 1% reduction is intentionally modest to minimize political resistance. Historical precedents (military-to-civilian conversions post-Cold War) demonstrate feasibility.

Institutional Capacity

Implementation requires substantial institutional development:

- **Regulatory expertise:** The framework requires experienced personnel (FDA, EMA, other regulators) to enable integration with existing regulatory frameworks
- **Technical infrastructure:** Data systems, AI/ML capabilities, cybersecurity at global scale
- **Legal frameworks:** International treaties, data privacy compliance, intellectual property harmonization

Mitigation: Phased implementation allows capacity building concurrent with scale-up.

Healthcare System Integration

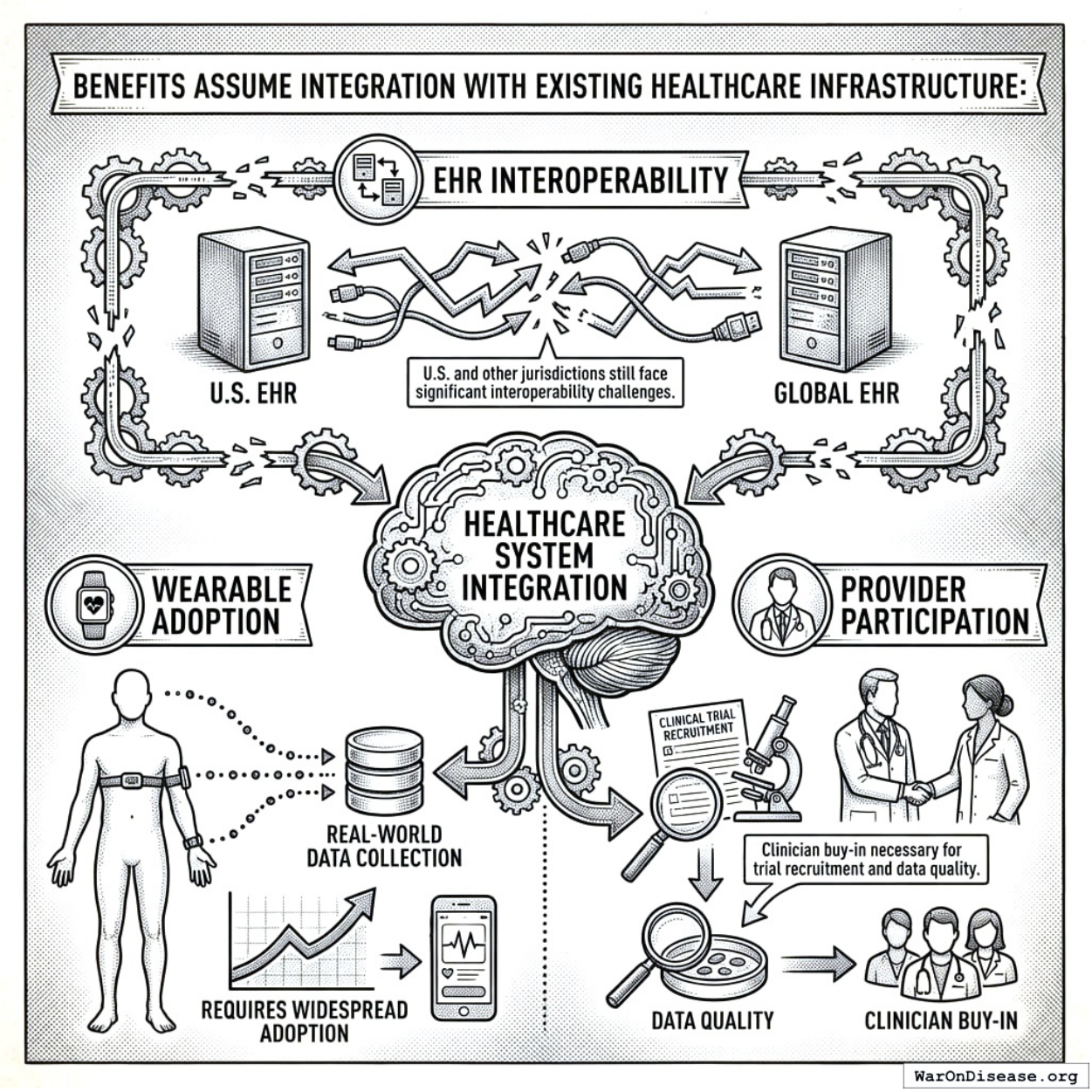


Figure 90: A conceptual diagram showing the three pillars required for healthcare system integration: EHR interoperability, wearable adoption, and provider participation.

Benefits assume integration with existing healthcare infrastructure:

- **EHR interoperability:** U.S. and other jurisdictions still face significant interoperability challenges
- **Wearable adoption:** Real-world data collection requires widespread wearable/digital health adoption
- **Provider participation:** Clinician buy-in necessary for trial recruitment and data quality

Uncertainty Quantification

Primary Risk Factors

The following table summarizes key risk factors and their mitigation strategies:

Risk Factor	Level	Primary Uncertainty	Mitigation Strategy
Political Risk	VERY HIGH	Treaty ratification dependent on international coordination	Modest 1% reduction; precedent from military-industrial lobbying ROI (1,813:1)
Execution Risk	HIGH	Complex global legal/technical coordination required	Phased implementation; leverage existing regulatory expertise
Regulatory Risk	MEDIUM-HIGH	Harmonization across jurisdictions varies	Pilot programs in willing jurisdictions first
Market Risk	VERY LOW	$2.72T[48] military spending already allocated	Redirection rather than new appropriation
Technical Risk	MEDIUM	Data interoperability, AI/ML accuracy	Build on proven platforms (DCT platforms collectively raising $1B+ in VC funding)

Scenario Analysis Robustness

Comprehensive sensitivity analysis across multiple scenarios demonstrates:

- **Risk-adjusted (848k:1 (95% CI: 58.0k:1-4.76M:1) expected ROI):** Central estimate with political success probability uncertainty (1% (95% CI: 0.1%-10%)), intervention generates substantial positive returns
- **Conservative (637:1 (95% CI: 569:1-790:1) ROI):** R&D savings only, excludes peace dividend, intervention is dominant
- **Complete (84.8M:1 (95% CI: 46.6M:1-144M:1) ROI):** All quantifiable benefits, intervention transforms global health economics

Robustness: Even under pessimistic assumptions with multiple adverse conditions simultaneously occurring, the intervention generates positive returns exceeding most established public health programs. The tornado chart for `DFDA_EXPECTED_ROI` shows that political success probability is the primary driver of uncertainty.

General Equilibrium Effects

This analysis employs partial equilibrium methodology, holding prices and market structures constant while evaluating the intervention's direct effects. General equilibrium analysis would account for

market adjustments to the $27.2B annual reallocation from military to pragmatic clinical trials spending.

Unmodeled general equilibrium effects include:

1. **Data infrastructure scaling costs**: Decentralized trial infrastructure uses automated software (federated queries, not centralized databases), scaling through technology rather than labor. Unlike traditional research that faces researcher supply constraints, the framework leverages existing EHR systems and adds coordination protocols. Marginal scaling costs are low relative to traditional models.

2. **Clinical trial market price effects**: Increasing trial demand by 12.3x (95% CI: 4.19x-61.3x) could affect equilibrium prices for clinical research services. However, the pragmatic trial approach *reduces* per-trial costs (82x (95% CI: 50x-94.1x) cheaper via automation), suggesting supply constraints may not bind. Traditional trials cost $41K (95% CI: $20K-$120K); decentralized trials target $929 (95% CI: $97-$3K) by eliminating overhead, not by increasing demand for scarce inputs.

3. **Crowding out effects**: Do billions in new pragmatic clinical trials displace existing research funding, or does it add incrementally? Conservative assumption: fully additive. If partially substitutive (e.g., governments reduce NIH funding in response), net research increase would be lower than modeled.

4. **Quality versus quantity trade-off**: 12.3x (95% CI: 4.19x-61.3x) more trials may not yield proportional breakthroughs if resources spread thin or trial quality declines. The analysis assumes quality maintenance through peer review and replication; actual quality effects remain uncertain.

Conservative treatment in base case: The analysis excludes general equilibrium effects from benefit calculations, providing a lower bound estimate.

Methodological limitation acknowledged: Full general equilibrium modeling (computable general equilibrium models with labor markets, international trade, and technology diffusion) would require substantial additional complexity beyond this analysis scope. The partial equilibrium approach follows standard cost-benefit analysis methodology for policy interventions.

Conditional Benefits Interpretation

The ROI estimates (637:1 (95% CI: 569:1-790:1) conservative, 84.8M:1 (95% CI: 46.6M:1-144M:1) complete) are **conditional on successful implementation**, they represent returns *if* the system operates as designed. Expected value analysis (see "Expected Value Analysis Accounting for Political Risk" section) incorporates probability-weighted scenarios. This section examines operational and technical failure modes that could occur even after political success, complementing the Investor Risk Analysis focus on political barriers. Pilot implementations should monitor false positive rates, adverse event detection sensitivity, regulatory acceptance rates, and industry adoption velocity to enable early course corrections.

Limitations Summary

Despite these limitations, several factors support the analysis's robustness:

1. **Conservative assumptions throughout:** Base case uses median estimates; optimistic scenarios excluded from primary ROI (637:1 (95% CI: 569:1-790:1))
2. **Empirical grounding:** Cost reductions based on meta-analysis of 108 pragmatic trials[132] plus large-scale implementations (RECOVERY, ADAPTABLE), not theoretical models
3. **Sensitivity analysis:** Wide range of scenarios tested; positive returns maintained across all plausible parameter combinations
4. **Dominant intervention status:** Cost-saving intervention ($0.0018 (95% CI: $0.0007-$0.0041) per DALY) means it saves money even if health benefits are substantially overstated

Transparency commitment: All parameters, data sources, and calculation methodologies are publicly documented with confidence levels and last-update dates in Parameters and Calculations Reference and References.

Future research priorities include prospective data collection during pilot implementations, real-world validation of cost reduction estimates, and longitudinal assessment of QALY gains across diverse populations and disease contexts.

Why This Differs from Failed Megaprojects

Large-scale interventions face legitimate skepticism. The development economics literature documents numerous failures: infrastructure megaprojects that exceed budgets by 50-100%, foreign aid programs with negative or negligible returns, and "grand challenges" that fail to materialize promised benefits.

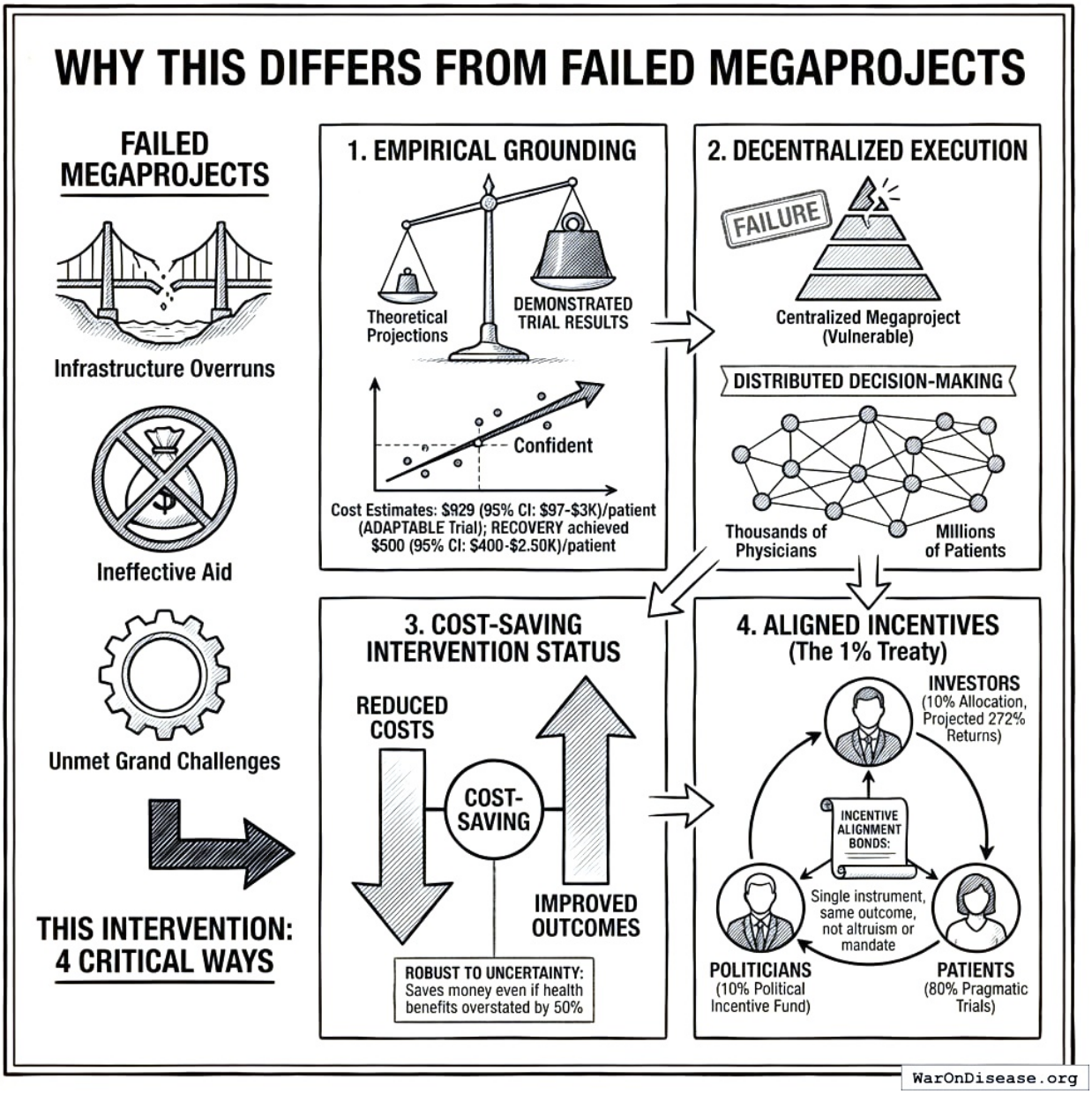


Figure 91: A conceptual diagram contrasting centralized megaprojects with the decentralized, incentive-aligned structure of the 1% Treaty and its bond mechanism.

This intervention differs in four critical ways:

1. **Empirical grounding**: Cost estimates based on demonstrated pragmatic trial results, not theoretical projections. Our projections use \$929 (95% CI: \$97-\$3K)/patient based on the ADAPTABLE trial. (RECOVERY achieved \$500 (95% CI: \$400-\$2.50K)/patient under exceptional NHS/COVID conditions; confidence interval captures this range.)

2. **Decentralized execution**: Unlike centralized megaprojects vulnerable to corruption and bureaucratic failure, pragmatic trials distribute decision-making across thousands of physicians and millions of patients. No single point of failure.

3. **Cost-saving intervention status**: Cost-saving interventions (reducing costs while improving outcomes) are robust to uncertainty in ways that cost-effective interventions are not. Even if health benefits are overstated by 50%, the intervention still saves money.

4. **Aligned incentives**: The 1% Treaty proposes Incentive Alignment Bonds: a single instrument that aligns investors (10% allocation, projected 272% returns), politicians (10% political incentive fund), and patients (80% pragmatic trials) with the same outcome, rather than relying on altruism or bureaucratic mandate.

Policy Implications

This analysis has direct implications for resource allocation decisions across multiple policy domains:

National Health Budgets

Traditional health budgets face impossible trade-offs: every dollar spent on cancer treatment is a dollar not spent on heart disease prevention. This intervention eliminates that constraint by redirecting funds from outside the health sector.

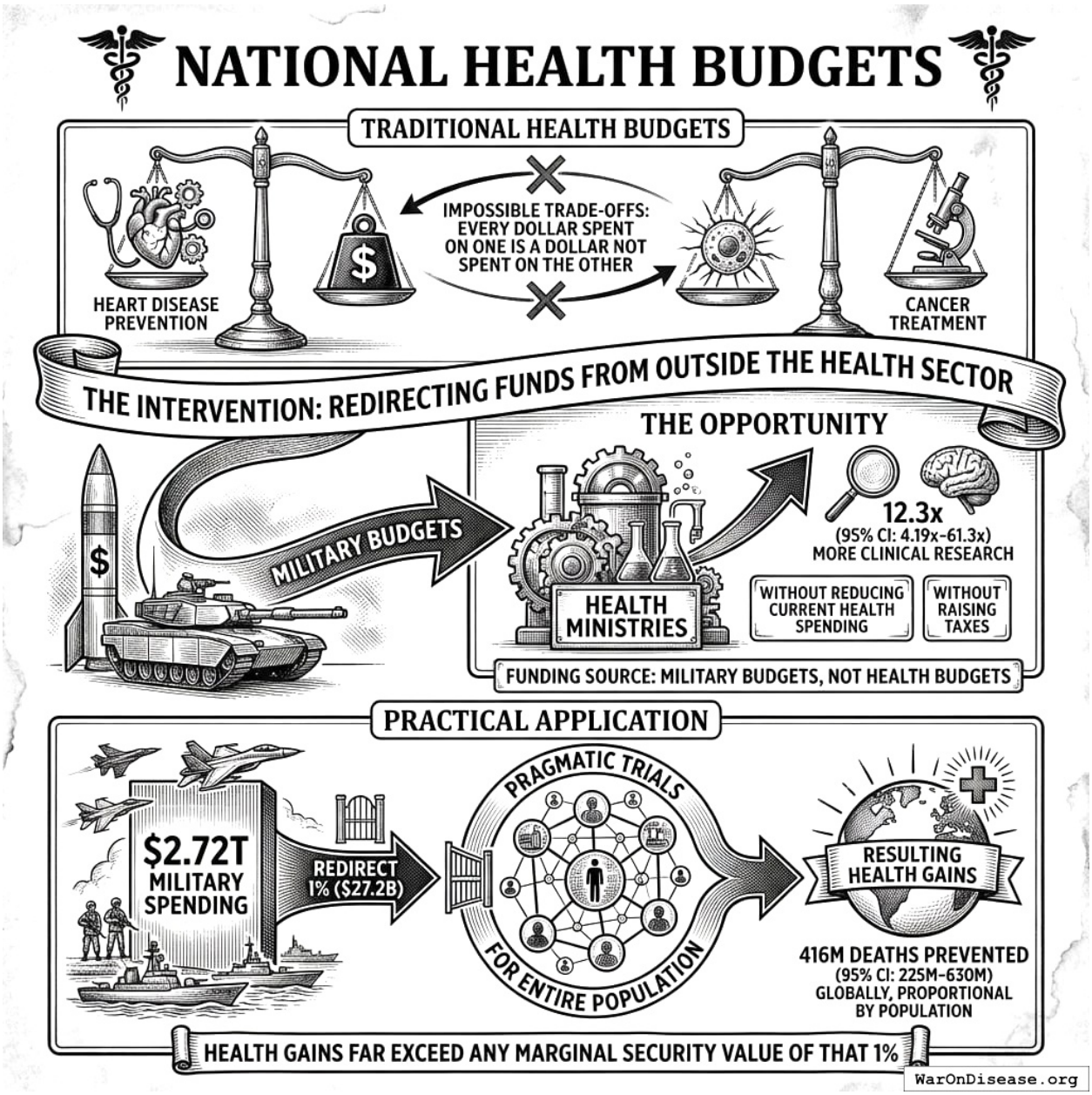


Figure 92: Infographic showing how a 1% redirection of military funds eliminates traditional health budget trade-offs and achieves a 12.3x increase in clinical research capacity.

The opportunity: Health ministries can achieve 12.3x (95% CI: 4.19x-61.3x) more clinical research without reducing current health spending or raising taxes. The funding comes from military budgets, not health budgets.

Practical application: A nation spending $2.72T on military could redirect 1% ($27.2B) to fund pragmatic trials for its entire population while maintaining virtually all of its military capacity. The resulting health gains (416 million deaths (95% CI: 225 million deaths-630 million deaths) lives saved globally, proportional by population) far exceed any marginal security value of that 1%.

International Development Priorities

Development agencies face a fundamental problem: the most cost-effective interventions (bed nets at \$89 (95% CI: \$78-\$100)/DALY, vaccines) can only scale linearly. Doubling impact requires doubling spending.

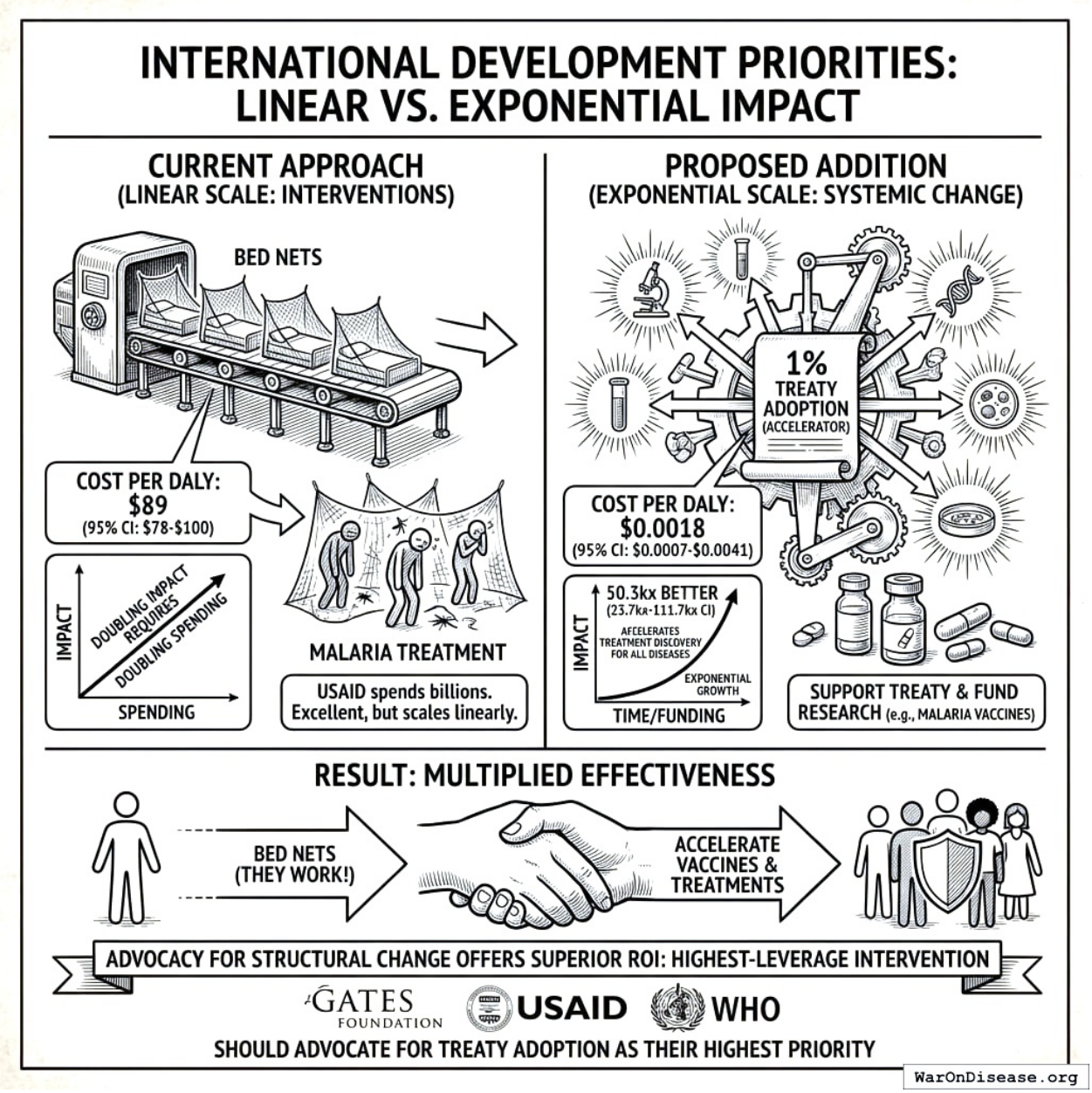


Figure 93: A comparison between linear scaling of direct interventions like bed nets and the exponential leverage of structural treaty adoption, illustrating the 'multiplier effect' on international development funding.

The difference: This intervention scales exponentially through systemic change. It doesn't compete with existing development programs; it accelerates treatment discovery for all diseases affecting developing nations.

Practical application:

- **Current approach**: USAID spends billions on malaria bed nets (excellent intervention, $89 (95% CI: $78-$100)/DALY)
- **Proposed addition**: Support 1% treaty adoption, which delivers $0.0018 (95% CI: $0.0007-$0.0041)/DALY (50.3kx (95% CI: 23.7kx-111.7kx) better) *while also* funding research to eradicate malaria
- **Result**: Keep funding bed nets (they work!) AND accelerate development of malaria vaccines and treatments through massively expanded trial capacity

The Gates Foundation, USAID, and WHO should advocate for treaty adoption as their highest-leverage intervention: it multiplies the effectiveness of everything else they fund. The Gates Foundation's historical pattern (spending billions on individual disease programs when the same capital could lobby for treaty passage and unlock $27.2B/year in government funding) exemplifies the "lottery tickets vs casino" problem described earlier. Advocacy for structural change offers superior ROI to direct program spending.

Military Budget Allocation

Military planners optimize for national security. This analysis demonstrates that 1% of military spending provides near-zero marginal security value while generating enormous economic returns when redirected.

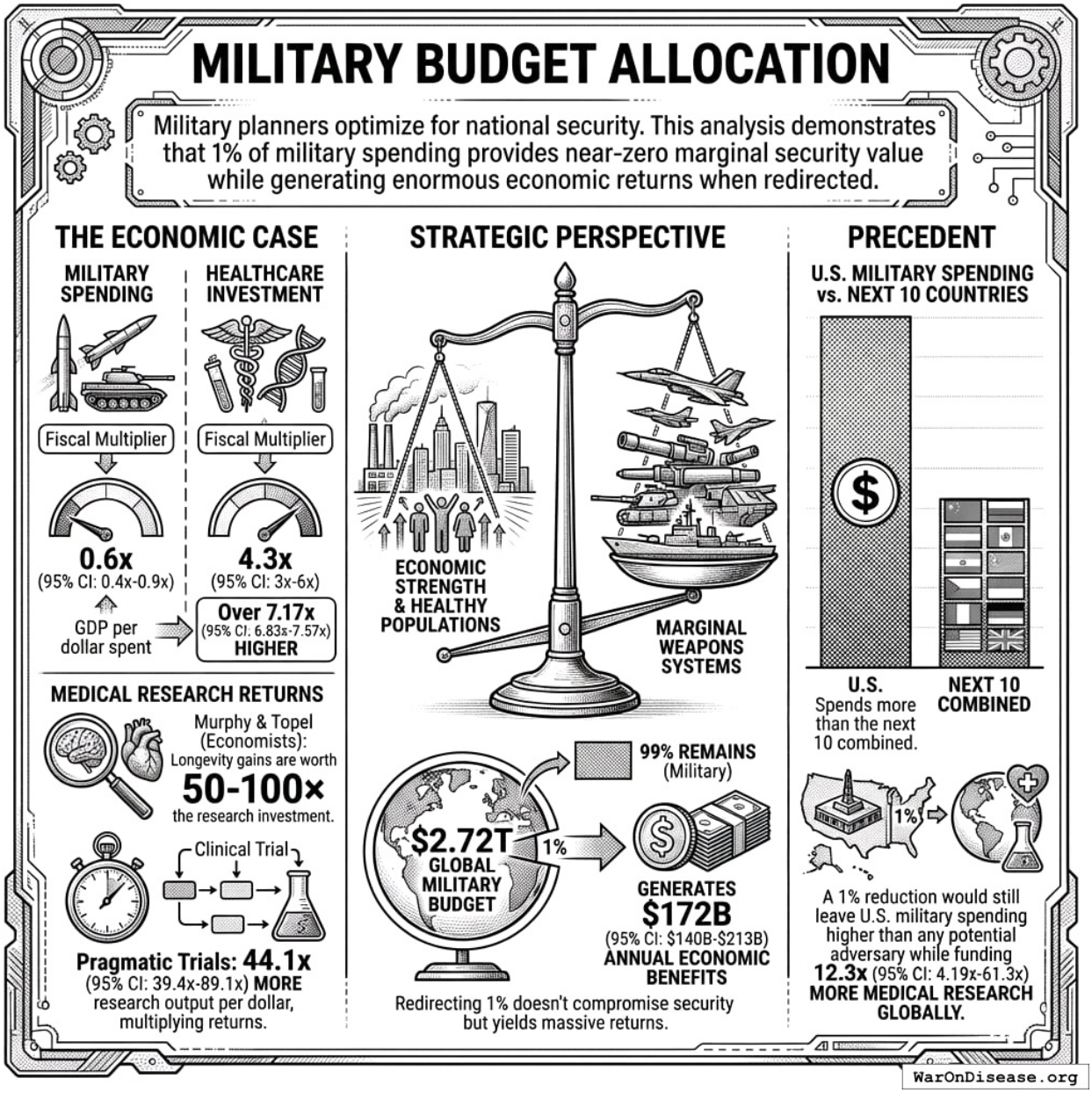


Figure 94: A comparison of economic fiscal multipliers and investment returns showing the impact of redirecting 1% of military spending toward healthcare and medical research.

The economic case: The fiscal multiplier (GDP generated per dollar spent) for military spending is 0.6x (95% CI: 0.4x-0.9x)[26]. Healthcare investment generates 4.3x (95% CI: 3x-6x)[24], over 7.17x (95% CI: 6.83x-7.57x) higher. Beyond fiscal multipliers, medical research generates extraordinary health returns: economists Murphy and Topel found that longevity gains from medical advances are worth **50-100× the research investment**[152]. Pragmatic trials, which produce 44.1x (95% CI: 39.4x-89.1x) more research output per dollar, multiply these already-massive returns.

Strategic perspective: A nation's long-term security depends more on economic strength and healthy populations than on marginal weapons systems. Redirecting 1% from the $2.72T global

military budget doesn't compromise military (99% remains) but generates $172B (95% CI: $140B-$213B) in annual economic benefits.

Precedent: The U.S. spends more on military than the next 10 countries combined. A 1% reduction would still leave U.S. military spending higher than any potential adversary while funding 12.3x (95% CI: 4.19x-61.3x) more medical research globally.

Global Health Funding Mechanisms

Current global health funding relies on unpredictable philanthropic donations and limited government aid budgets. Total official development assistance for health: ~$40B/year. This intervention creates a $27.2B/year permanent funding stream.

Why this works: This is not charity; it's profitable. Investors can purchase Incentive Alignment Bonds offering projected 272% backed by the peace dividend, making health funding financially attractive rather than dependent on altruism.

Mechanism design: The 1% Treaty Fund allocates:

- 80% ($21.8B) → pragmatic trials
- 10% ($2.72B) → bond investor returns
- 10% ($2.72B) → political incentive alignment

This creates a self-sustaining funding mechanism where: 1. **Investors profit** from peace dividend returns 2. **Politicians profit** from voter support and campaign funding 3. **Pharma companies profit** from massively reduced R&D costs 4. **Patients benefit** from 8.2 years (95% CI: 4.85 years-11.5 years)-year faster access to treatments 5. **Governments benefit** from healthier, more productive populations

Contrast with current system: WHO's annual budget (~$6B) depends on voluntary contributions that can be cut at any time. The 1% Treaty creates a $27.2B/year legally-binding funding stream that grows automatically with military budgets.

Implementation Pathway

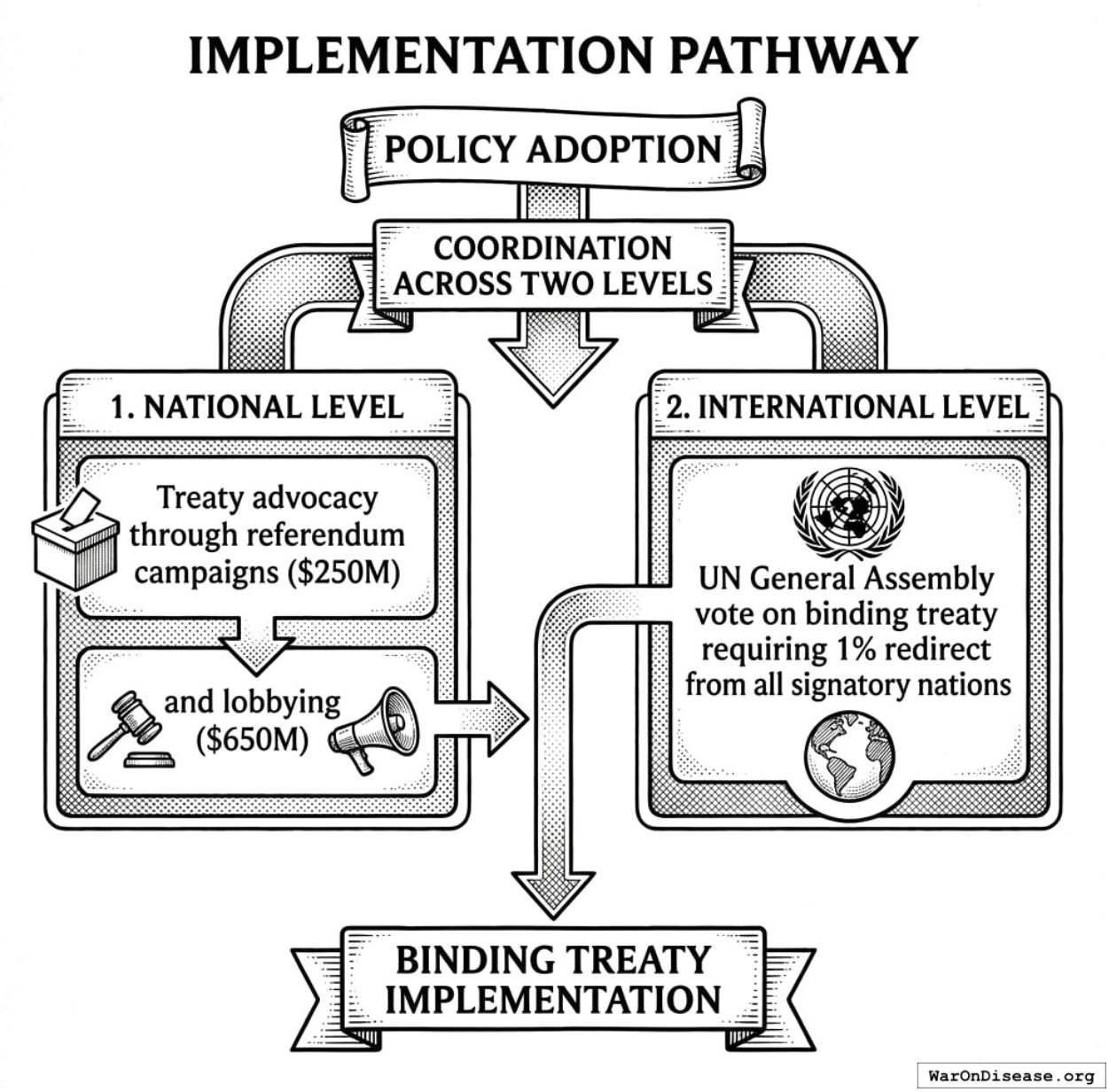


Figure 95: A dual-level implementation pathway showing national referendum and lobbying tracks coordinating with international UN treaty processes to redirect military spending.

Policy adoption requires coordination across two levels:

1. **National level**: Treaty advocacy through referendum campaigns ($250M) and lobbying ($650M)
2. **International level**: UN General Assembly vote on binding treaty requiring 1% redirect from all signatory nations

Bottom Line for Policymakers

This intervention is **cost-saving**, making it one of the rarest findings in health economics. It doesn't require:

- New taxes
- Reduced health spending
- Cuts to popular programs
- Technological breakthroughs

It requires only a 1% reallocation from the least cost-effective government spending (military) to the most cost-effective health intervention (pragmatic trials at $929 (95% CI: $97-$3K)/patient).

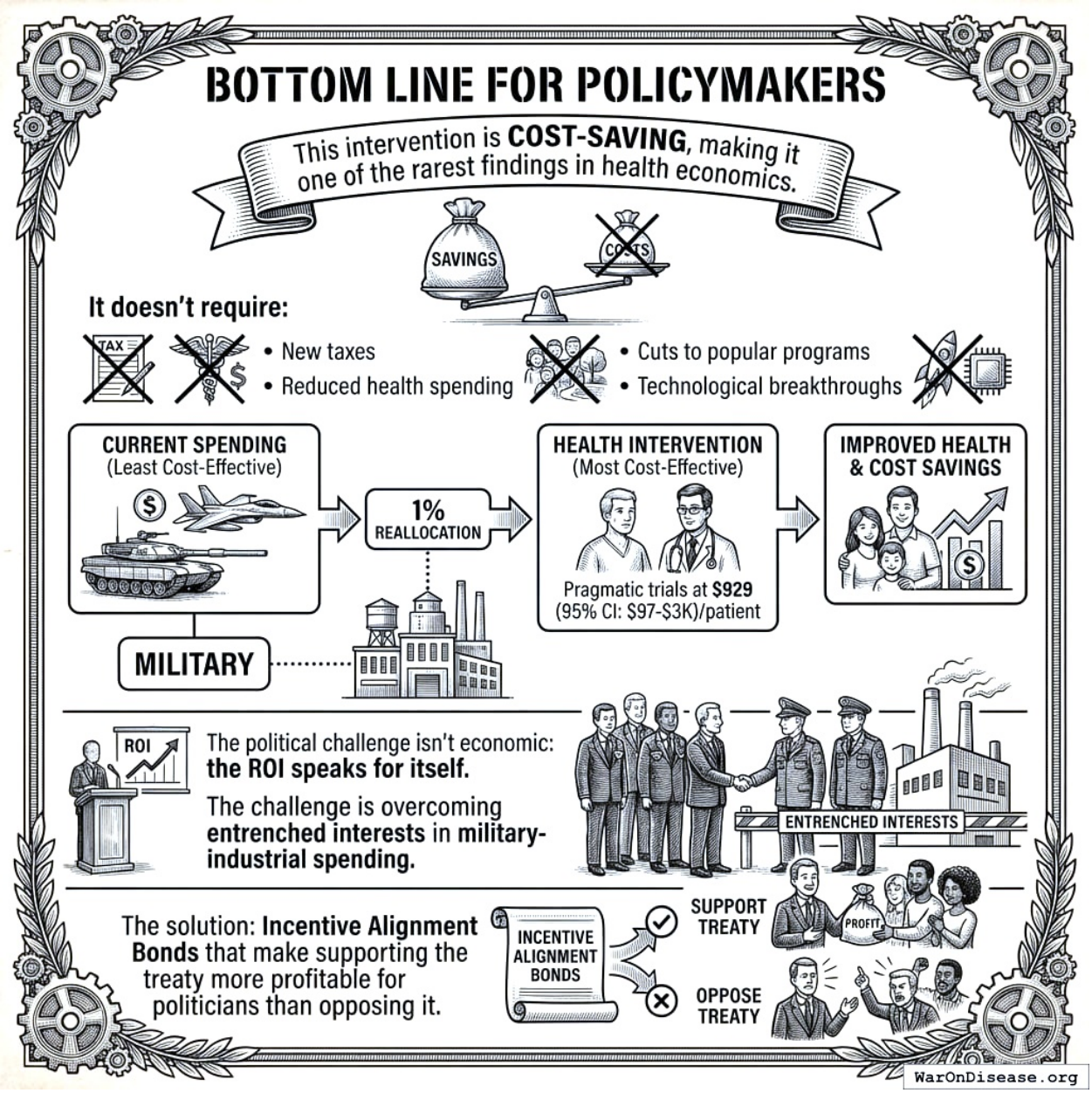


Figure 96: A visual comparison showing a 1% reallocation of military spending toward high-ROI pragmatic trials, contrasted with the political solution of Incentive Alignment Bonds to overcome entrenched interests.

The political challenge isn't economic: the ROI speaks for itself. The challenge is overcoming entrenched interests in military-industrial spending. The solution: Incentive Alignment Bonds that make supporting the treaty more profitable for politicians than opposing it.

Treaty Adoption: Political Will and Diplomatic Strategy

International treaty adoption is fundamentally a political and diplomatic process, not a technical implementation timeline. The 1% Treaty's viability depends on **simultaneous multilateral**

commitment: no nation reduces military spending unilaterally, creating security vulnerabilities or free-rider problems. All signatories reduce together.

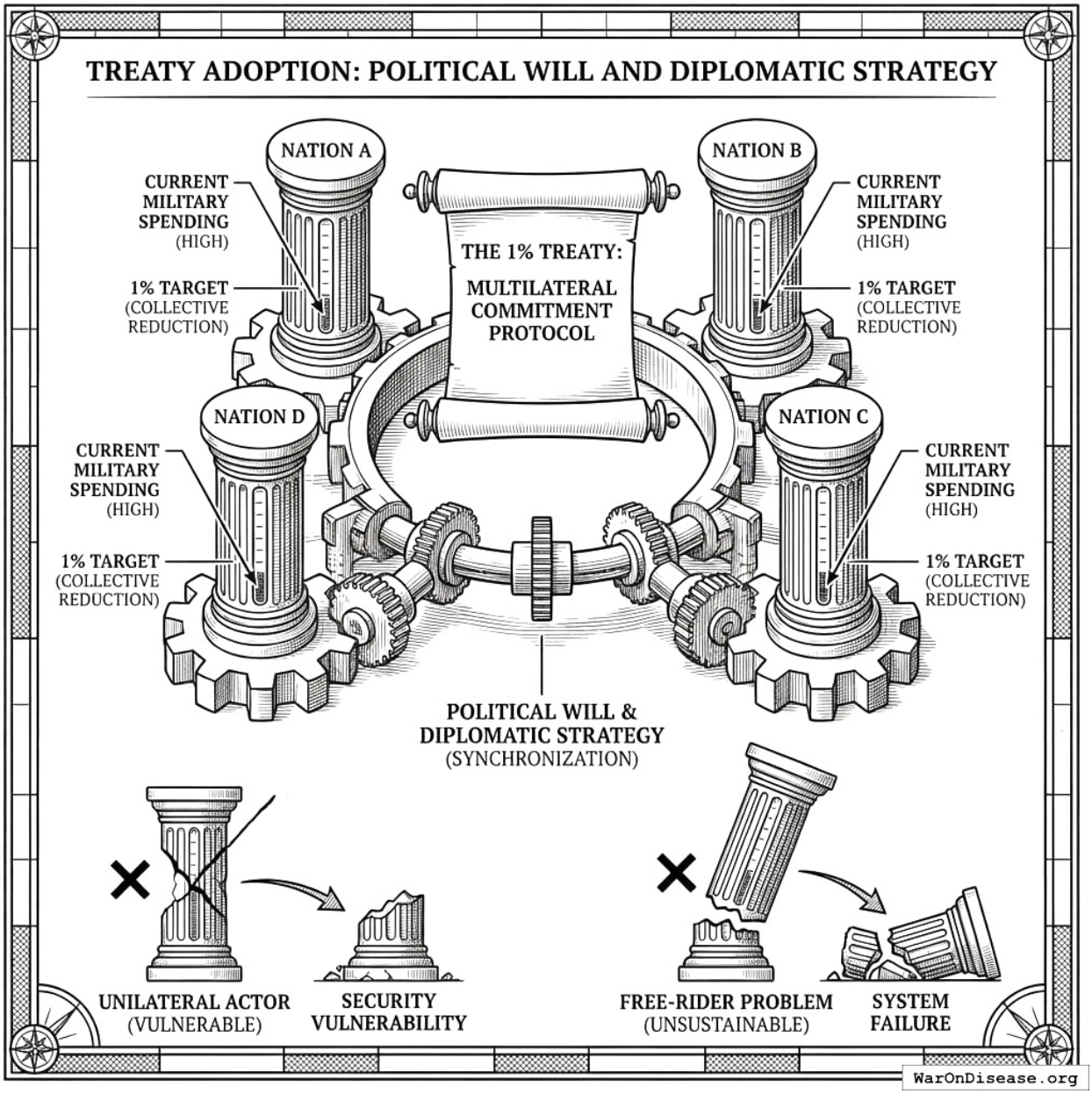


Figure 97: A conceptual diagram illustrating the multilateral commitment process where multiple nations reduce military spending simultaneously to maintain a balanced security environment.

Why Simultaneous Commitment Works: Escaping the Prisoner's Dilemma

Unilateral military reduction is politically infeasible. This is a classic **Prisoner's Dilemma**:

- **If I reduce alone**: Security vulnerability while others maintain full capacity (worst outcome)
- **If I don't reduce but others do**: Free-ride on reduced conflict risk (tempting but unsustainable)

- **If nobody reduces**: Arms race continues, all players worse off (current equilibrium)
- **If all reduce together**: Maintain relative balance, redirect savings to health (optimal Nash equilibrium)

Simultaneous binding commitment solves the coordination problem: All signatories reduce 1% together, maintaining relative military balance while collectively redirecting $27.2B/year to health research that benefits all participants. The treaty converts a Prisoner's Dilemma (where rational self-interest produces suboptimal outcomes) into a coordination game with enforceable commitments.

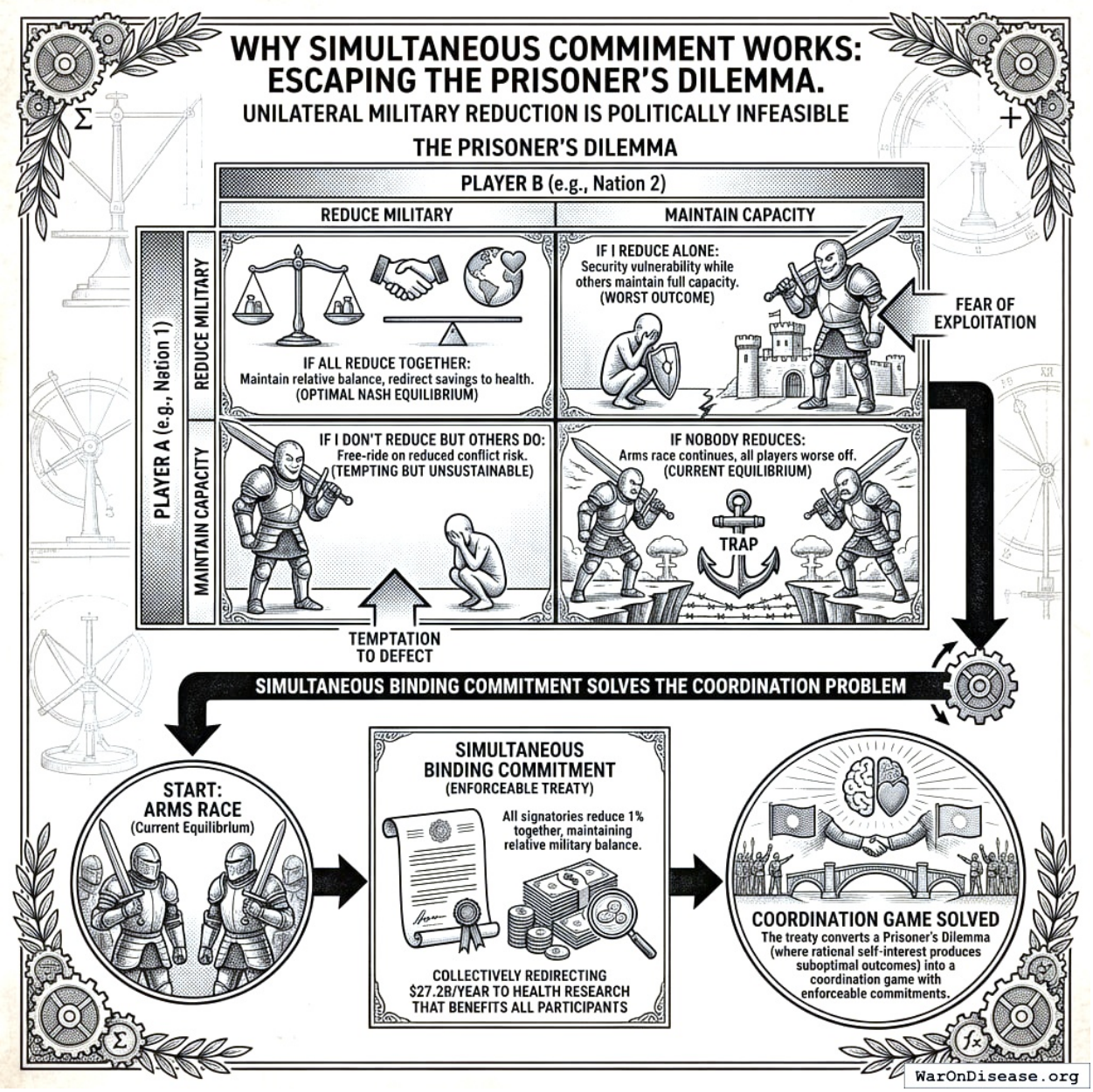


Figure 98: A conceptual diagram showing the transition from a Prisoner's Dilemma arms race to a coordination game where simultaneous military reductions maintain balance while funding global health.

Historical Treaty Precedents

Successful international treaties achieved rapid adoption through diplomatic coalition-building, not phased pilots:

- **Ottawa Landmine Ban Treaty (1997)**: Diplomatic push → international negotiation → 122 nations signed in 2 years
- **Paris Climate Agreement (2015)**: Built on existing framework, achieved 195 signatories through coordinated diplomatic effort
- **Chemical Weapons Convention (1993)**: International negotiation process, 193 state parties

Common pattern: Political will + coalition of willing nations + diplomatic negotiation → treaty adoption

The 1% Treaty follows this model, with the advantage that it offers immediate economic returns (637:1 (95% CI: 569:1-790:1) ROI minimum) rather than requiring sacrifice.

Adoption Pathway

Treaty adoption depends on: 1. **Political coalition**: Build support among health ministries, fiscal conservatives seeking budget efficiency, and populations demanding better healthcare 2. **Economic case**: 637:1 (95% CI: 569:1-790:1) ROI makes this profitable, not charitable 3. **Incentive Alignment Bonds**: Fund $1B advocacy phase, align investor and political incentives 4. **Diplomatic negotiation**: UN General Assembly or coalition of willing nations

Timeline: Highly variable depending on political momentum. Successful precedents range from 18 months (rapid consensus) to 5+ years (extended negotiation). The self-funding nature and aligned incentives favor faster adoption than typical treaties requiring sacrifice.

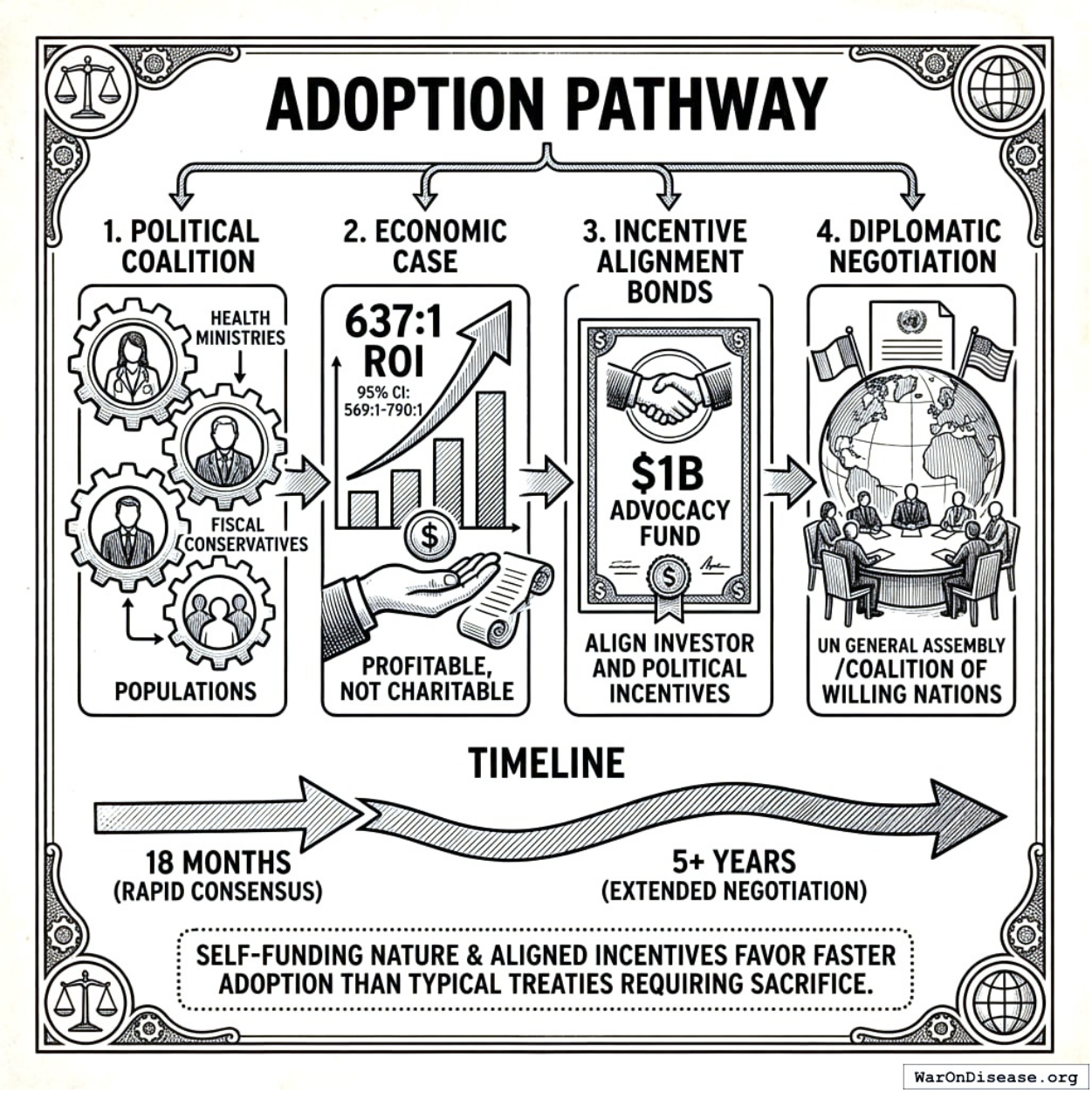


Figure 99: A visualization of the four pillars of the treaty adoption pathway (political, economic, financial, and diplomatic) mapped against a variable implementation timeline.

Conclusion

Redirecting 1% of global military spending to pragmatic clinical trials delivers 637:1 (95% CI: 569:1-790:1) to 84.8M:1 (95% CI: 46.6M:1-144M:1) ROI using standard health economics methodology (NPV, QALYs, ICER). The intervention qualifies as cost-saving and requires no new taxes, only reallocation of existing budgets to higher-ROI activities.

Methodology, Parameters, and Calculations

Overview

This appendix documents all 214 parameters used in the analysis, organized by type:

- External sources (peer-reviewed): 88
- Calculated values: 97
- Core definitions: 29

Quick Navigation

Calculated Values (97 parameters) • External Data Sources (88 parameters) • Core Definitions (29 parameters)

Calculated Values

Parameters derived from mathematical formulas and economic models.

Combination Therapy Space: 45.1 billion combinations

Details

Total combination therapy space (pairwise drug combinations × diseases). Standard in oncology, HIV, cardiology.

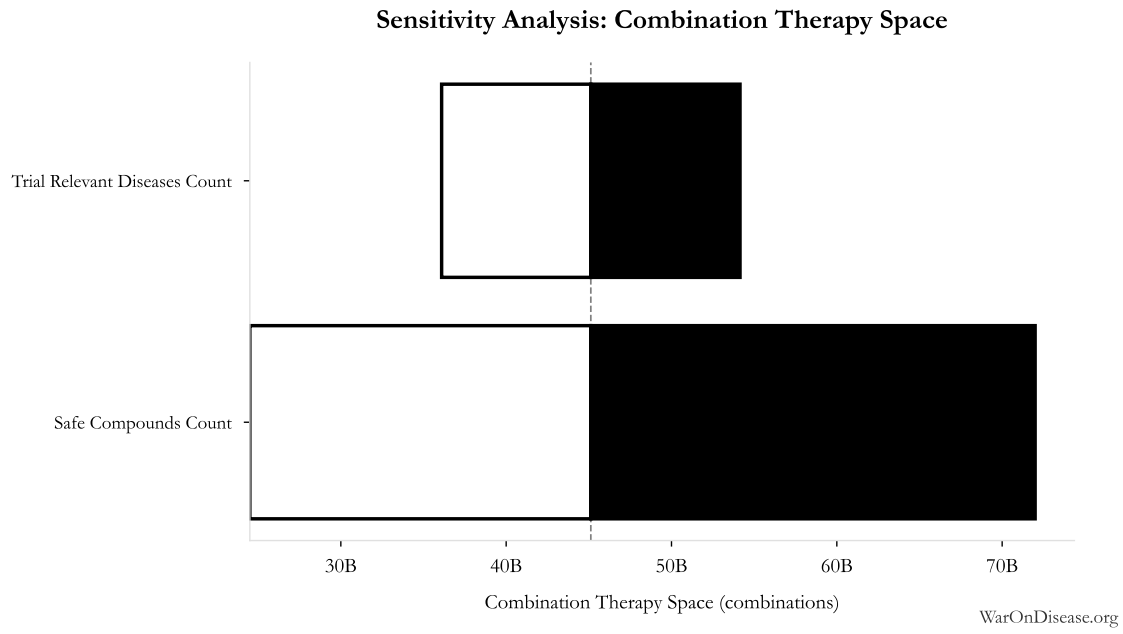
Inputs:

- Pairwise Drug Combinations : 45.1 million combinations
- Trial-Relevant Diseases: 1.00 thousand diseases (95% CI: 800 diseases - 1.20 thousand diseases)

$$\begin{aligned} & Space_{combo} \\ &= N_{combo} \times N_{diseases,trial} \\ &= 45.1M \times 1{,}000 \\ &= 45.1B \end{aligned}$$

High confidence

Sensitivity Analysis



Pairwise Drug Combinations: 45.1 million combinations

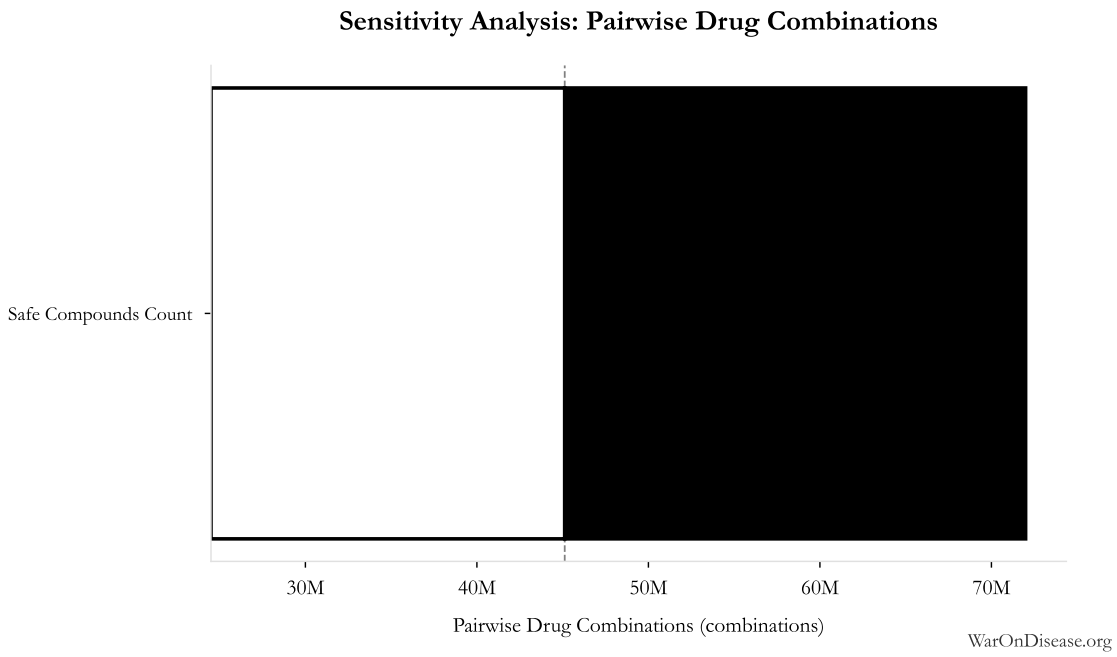
Details

Unique pairwise drug combinations from known safe compounds (n choose 2)
Inputs:

- Safe Compounds Available for Testing: 9.50 thousand compounds (95% CI: 7.00 thousand compounds - 12.0 thousand compounds)

Formula: `SAFE_COMPOUNDS × (SAFE_COMPOUNDS - 1) ÷ 2`
High confidence

Sensitivity Analysis



Combination Therapy Exploration Time (Current): 13.7 million years

Details

Years to test all pairwise drug combinations at current trial capacity. Combination therapy is standard in oncology, HIV, cardiology.

Inputs:

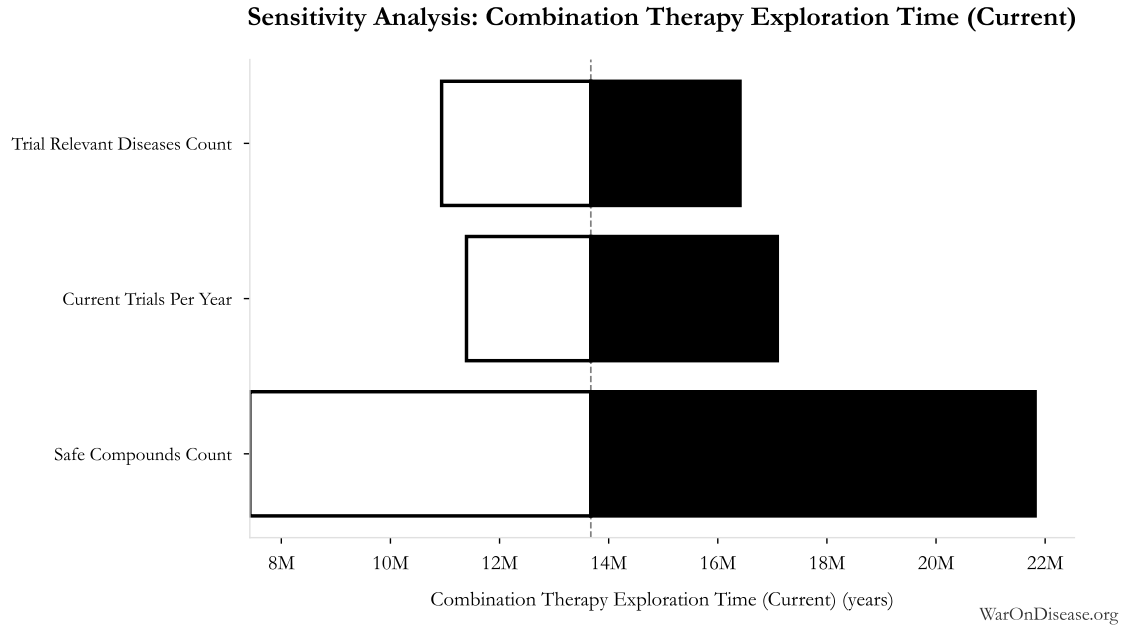
- Combination Therapy Space : 45.1 billion combinations
- Current Global Clinical Trials per Year : 3.30 thousand trials/year (95% CI: 2.64 thousand trials/year - 3.96 thousand trials/year)

$$
\begin{aligned}
&T_{explore,combo} \\
&= \frac{Space_{combo}}{Trials_{ann,curr}} \\
&= \frac{45.1B}{3{,}300} \\
&= 13.7M
\end{aligned}
$$

$$
\begin{aligned}
&\text{where } Space_{combo} \\
&= N_{combo} \times N_{diseases,trial} \\
&= 45.1M \times 1{,}000 \\
&= 45.1B
\end{aligned}
$$

High confidence

Sensitivity Analysis



Sensitivity Indices for Combination Therapy Exploration Time (Current)
Regression-based sensitivity showing which inputs explain the most variance in the output.

Input Parameter	Sensitivity Coefficient	Interpretation
Current Trials Per Year	-0.9931	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

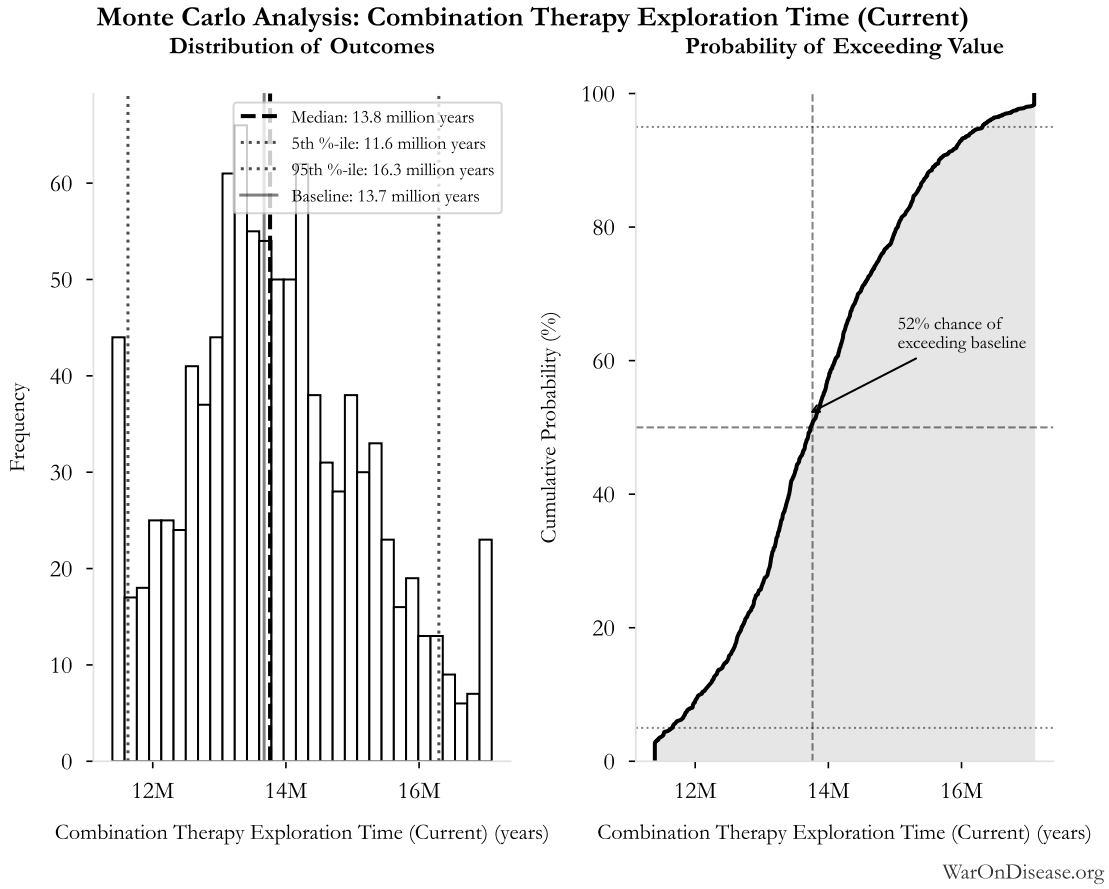


Figure 100: Monte Carlo Distribution: Combination Therapy Exploration Time (Current) (10,000 simulations)

Simulation Results Summary: Combination Therapy Exploration Time (Current)

Statistic	Value
Baseline (deterministic)	13.7 million
Mean (expected value)	13.8 million
Median (50th percentile)	13.8 million
Standard Deviation	1.36 million
90% Range (5th-95th percentile)	[11.6 million, 16.3 million]

The histogram shows the distribution of Combination Therapy Exploration Time (Current) 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

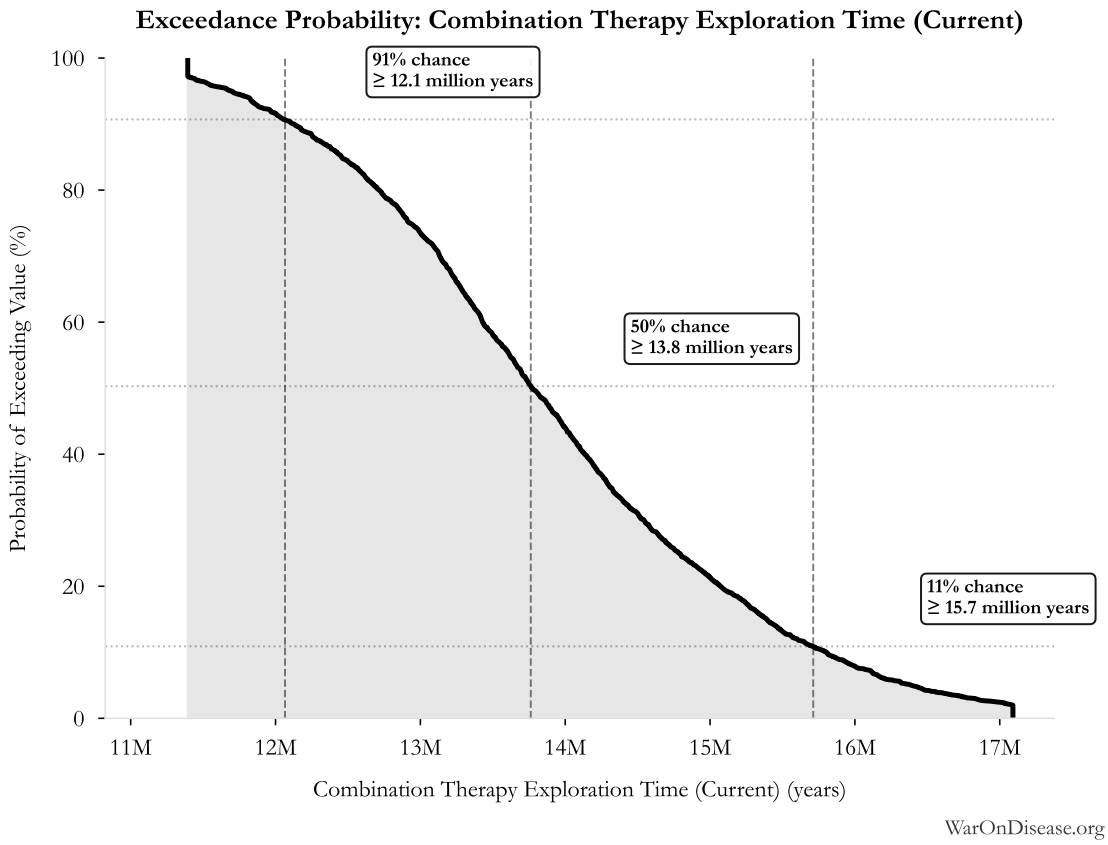


Figure 101: Probability of Exceeding Threshold: Combination Therapy Exploration Time (Current)

This exceedance probability chart shows the likelihood that Combination Therapy Exploration Time (Current) will exceed any given threshold. Higher curves indicate more favorable outcomes with greater certainty.

Known Safe Exploration Time (Current): 2.88 thousand years

Details

Years to test all known safe drug-disease combinations at current global trial capacity
Inputs:

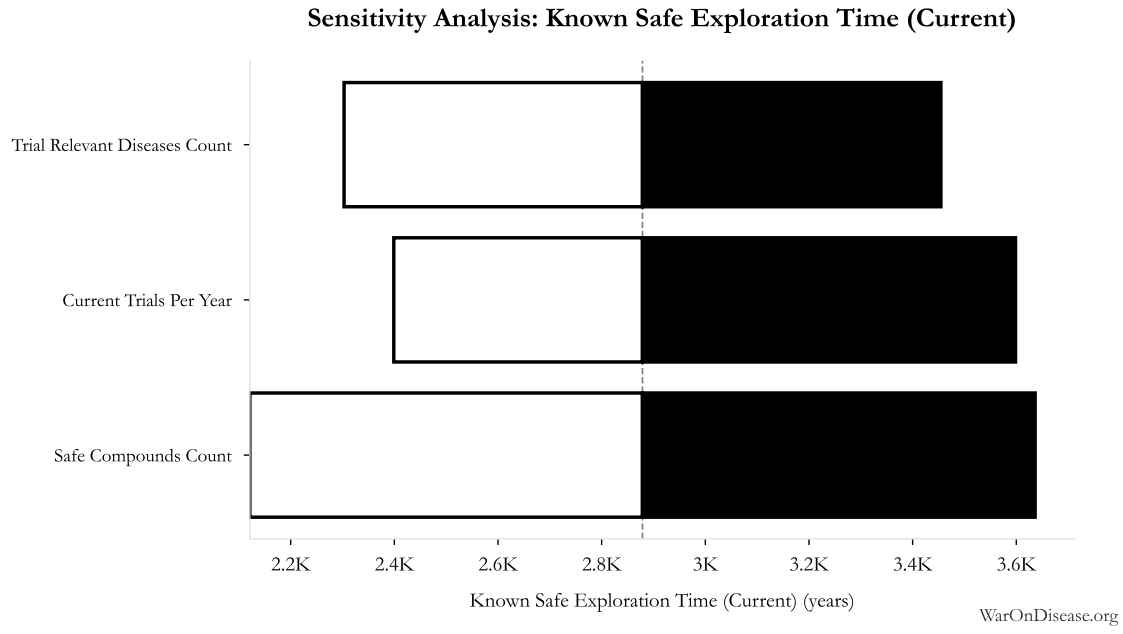
- Possible Drug-Disease Combinations : 9.50 million combinations
- Current Global Clinical Trials per Year : 3.30 thousand trials/year (95% CI: 2.64 thousand trials/year - 3.96 thousand trials/year)

$$
\begin{aligned}
&T_{explore,safe} \\
&= \frac{N_{combos}}{Trials_{ann,curr}} \\
&= \frac{9.5M}{3{,}300} \\
&= 2{,}880
\end{aligned}
$$

$$
\begin{aligned}
&\text{where } N_{combos} \\
&= N_{safe} \times N_{diseases,trial} \\
&= 9{,}500 \times 1{,}000 \\
&= 9.5M
\end{aligned}
$$

High confidence

Sensitivity Analysis



Sensitivity Indices for Known Safe Exploration Time (Current)

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

Input Parameter	Sensitivity Coefficient	Interpretation
Current Trials Per Year	-0.9931	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

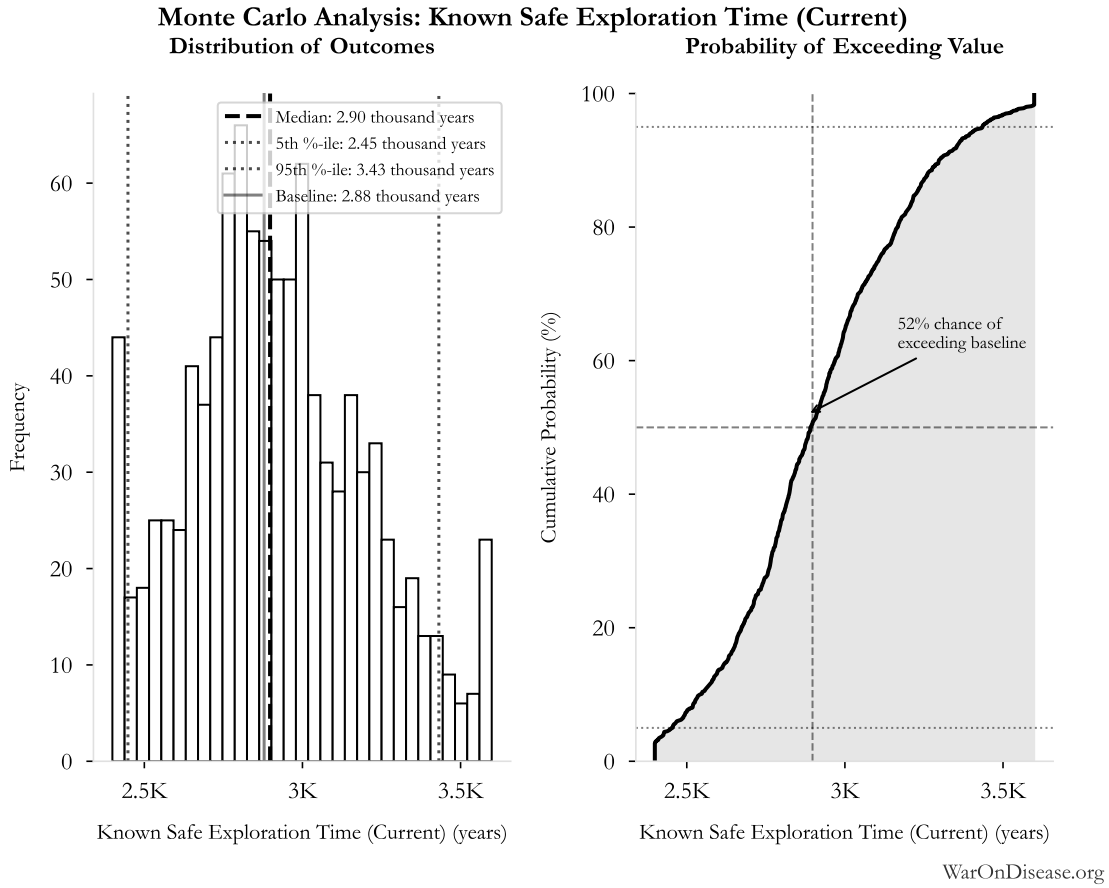


Figure 102: Monte Carlo Distribution: Known Safe Exploration Time (Current) (10,000 simulations)

Simulation Results Summary: Known Safe Exploration Time (Current)

Statistic	Value
Baseline (deterministic)	2.88 thousand
Mean (expected value)	2.91 thousand
Median (50th percentile)	2.90 thousand
Standard Deviation	286
90% Range (5th-95th percentile)	[2.45 thousand, 3.43 thousand]

The histogram shows the distribution of Known Safe Exploration Time (Current) 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

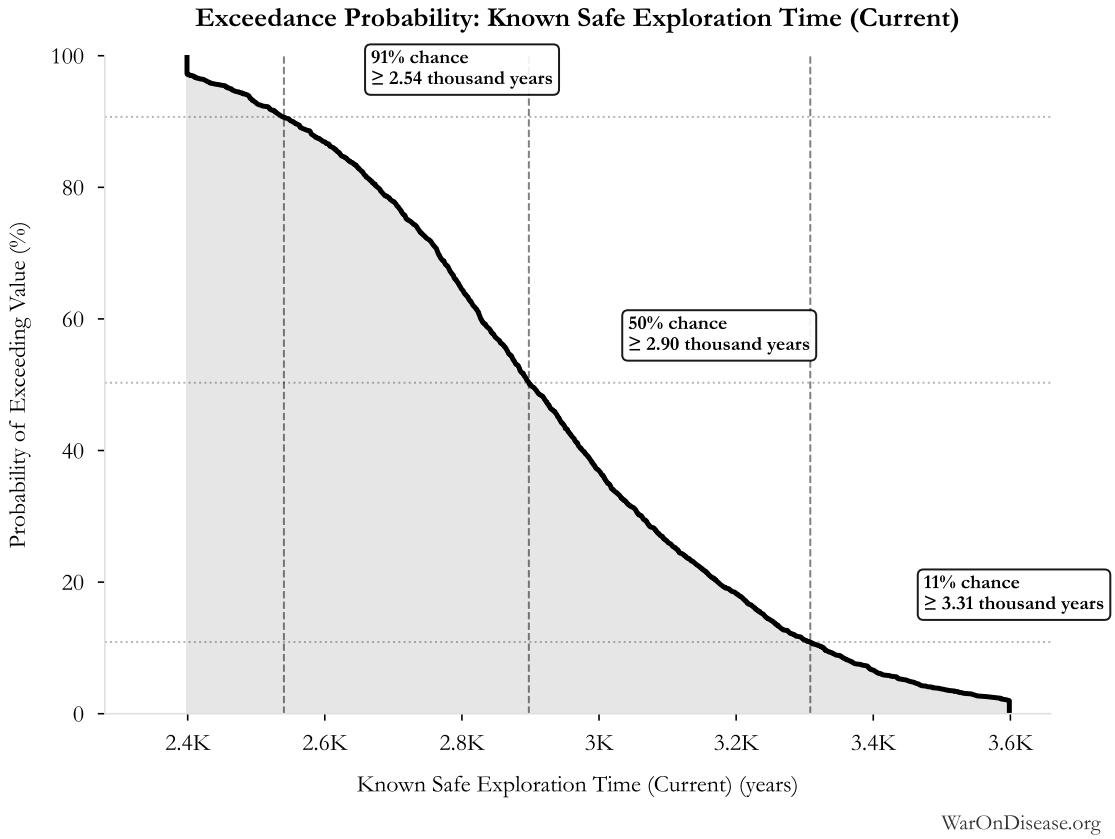


Figure 103: Probability of Exceeding Threshold: Known Safe Exploration Time (Current)

This exceedance probability chart shows the likelihood that Known Safe Exploration Time (Current) will exceed any given threshold. Higher curves indicate more favorable outcomes with greater certainty.

Current Patient Participation Rate in Clinical Trials: 0.0792%

Details

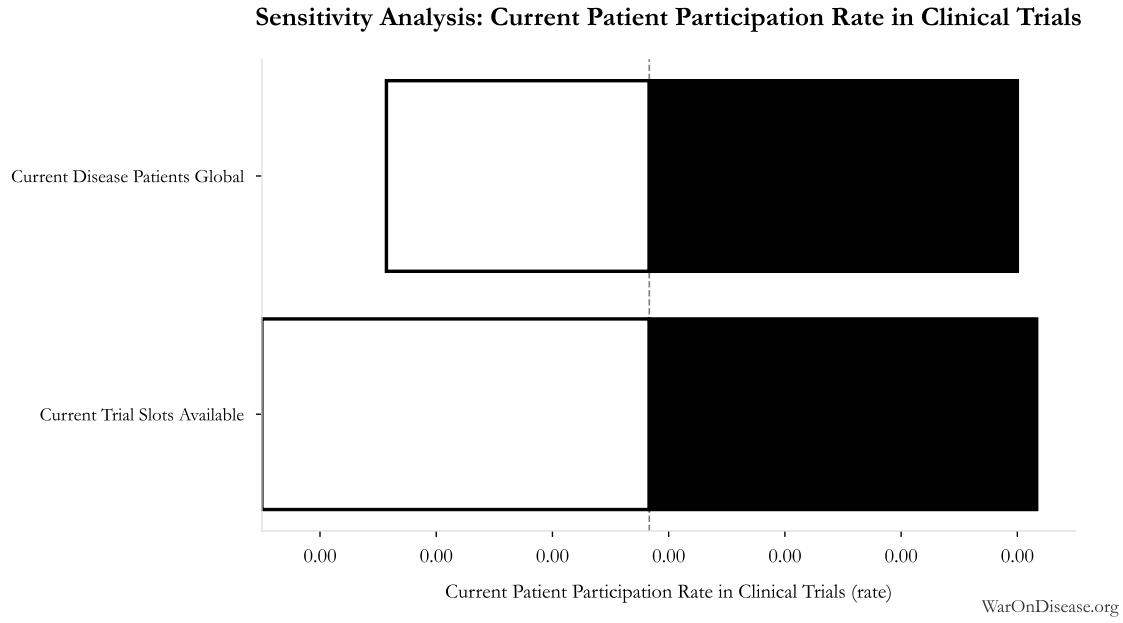
Current patient participation rate in clinical trials (0.08% = 1.9M participants / 2.4B disease patients)
Inputs:

- Annual Global Clinical Trial Participants : 1.90 million patients/year (95% CI: 1.50 million patients/year - 2.30 million patients/year)
- Global Population with Chronic Diseases : 2.40 billion people (95% CI: 2.00 billion people - 2.80 billion people)

$$\begin{aligned} & Rate_{part} \\ &= \frac{Slots_{curr}}{N_{patients}} \\ &= \frac{1.9M}{2.4B} \\ &= 0.0792\% \end{aligned}$$

Methodology:[11]
High confidence

Sensitivity Analysis



Sensitivity Indices for Current Patient Participation Rate in Clinical Trials
Regression-based sensitivity showing which inputs explain the most variance in the output.

Input Parameter	Sensitivity Coefficient	Interpretation
Current Disease Patients Global	4.1698	Strong driver
Current Trial Slots Available	-3.1720	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

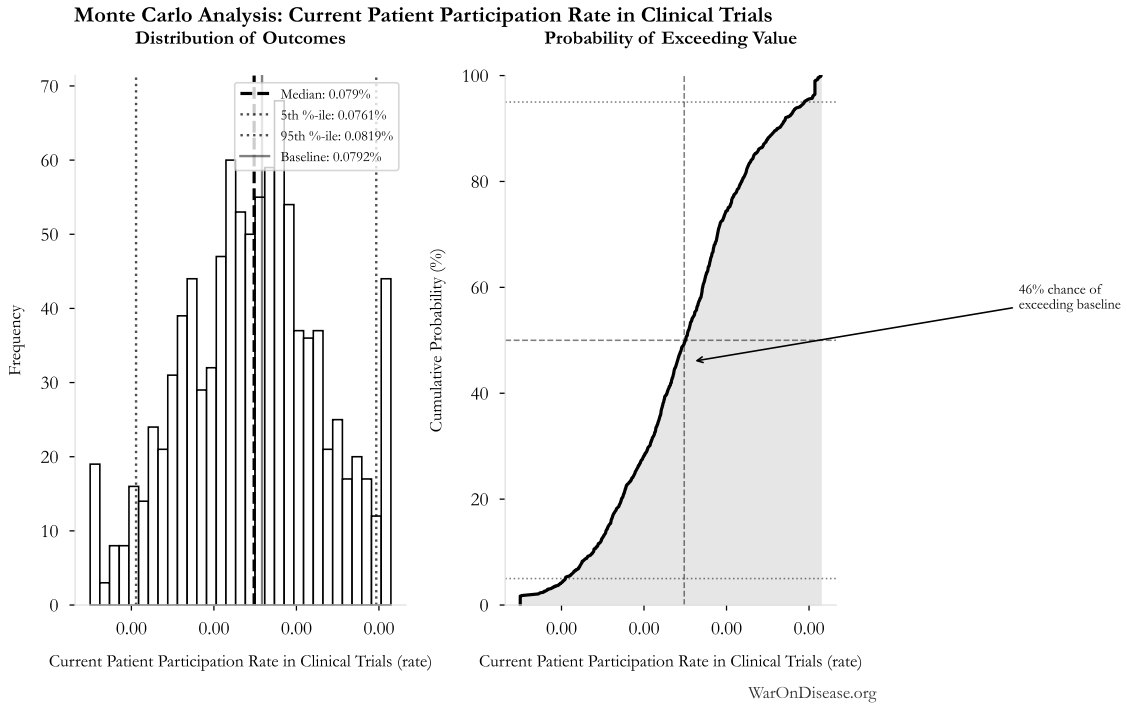


Figure 104: Monte Carlo Distribution: Current Patient Participation Rate in Clinical Trials (10,000 simulations)

Simulation Results Summary: Current Patient Participation Rate in Clinical Trials

Statistic	Value
Baseline (deterministic)	0.0792%
Mean (expected value)	0.079%
Median (50th percentile)	0.079%
Standard Deviation	0.00169%
90% Range (5th-95th percentile)	[0.0761%, 0.0819%]

The histogram shows the distribution of Current Patient Participation Rate in Clinical Trials 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

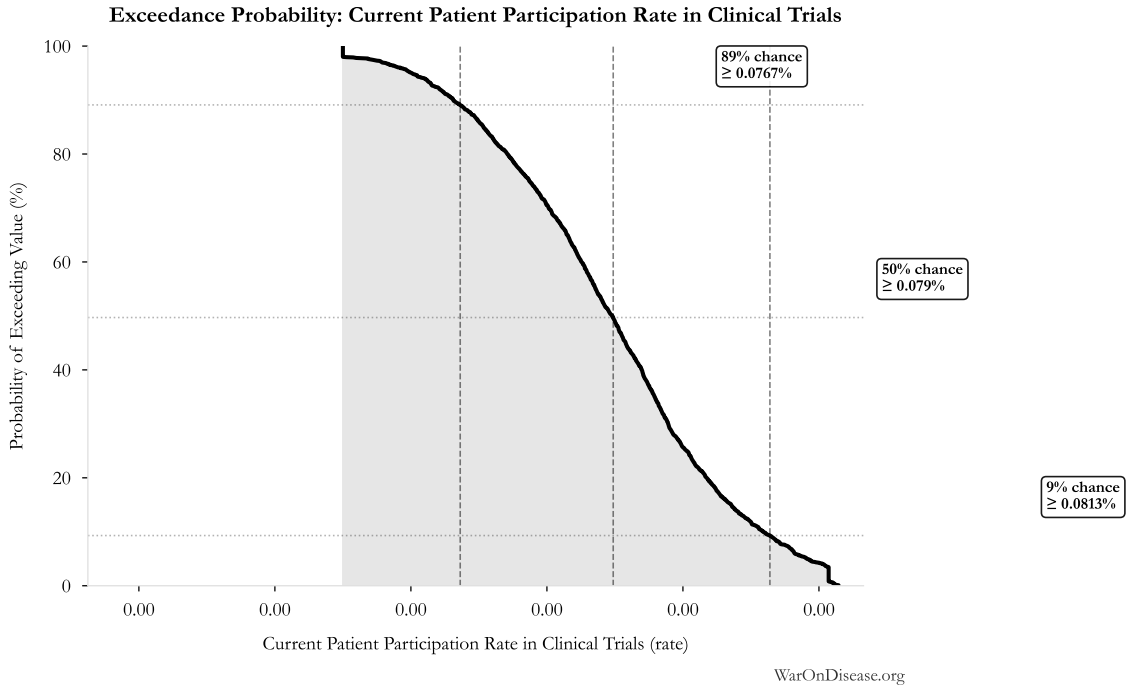


Figure 105: Probability of Exceeding Threshold: Current Patient Participation Rate in Clinical Trials

This exceedance probability chart shows the likelihood that Current Patient Participation Rate in Clinical Trials will exceed any given threshold. Higher curves indicate more favorable outcomes with greater certainty.

Total Annual Decentralized Framework for Drug Assessment Operational Costs: $40M

Details

Total annual Decentralized Framework for Drug Assessment operational costs (sum of all components: $15M + $10M + $8M + $5M + $2M)
Inputs:

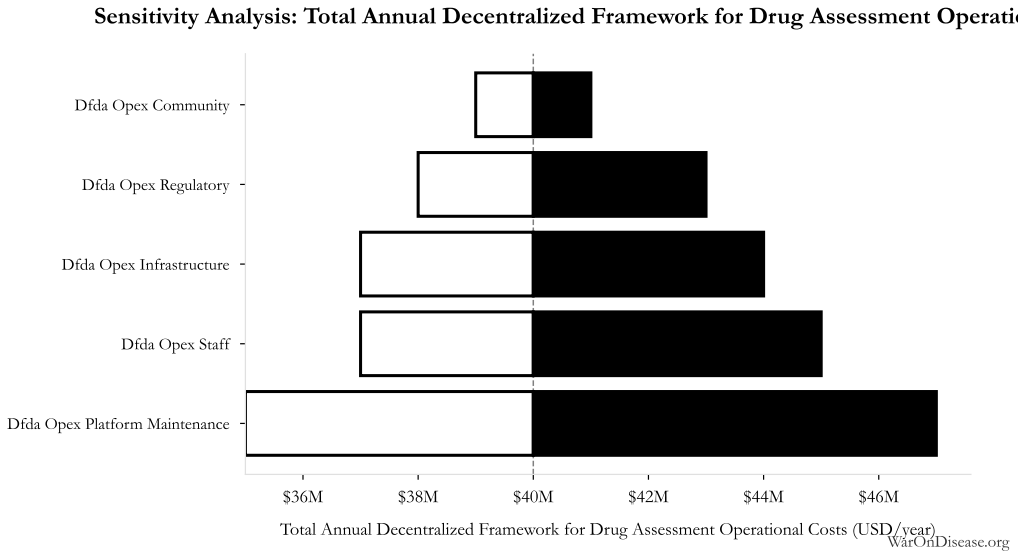
- Decentralized Framework for Drug Assessment Maintenance Costs: $15M (95% CI: $10M - $22M)
- Decentralized Framework for Drug Assessment Staff Costs: $10M (95% CI: $7M - $15M)

- Decentralized Framework for Drug Assessment Infrastructure Costs: $8M (95% CI: $5M - $12M)
- Decentralized Framework for Drug Assessment Regulatory Coordination Costs: $5M (95% CI: $3M - $8M)
- Decentralized Framework for Drug Assessment Community Support Costs: $2M (95% CI: $1M - $3M)

$$\begin{aligned} & OPEX_{dFDA} \\ &= Cost_{platform} + Cost_{staff} + Cost_{infra} \\ &+ Cost_{regulatory} + Cost_{community} \\ &= \$15M + \$10M + \$8M + \$5M + \$2M \\ &= \$40M \end{aligned}$$

High confidence

Sensitivity Analysis



Sensitivity Indices for Total Annual Decentralized Framework for Drug Assessment Operational Costs

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

Input Parameter	Sensitivity Coefficient	Interpretation
dFDA OPEX Platform Maintenance	0.3542	Moderate driver
dFDA OPEX Staff	0.2355	Weak driver
dFDA OPEX Infrastructure	0.2060	Weak driver
dFDA OPEX Regulatory	0.1469	Weak driver
dFDA OPEX Community	0.0576	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.

Monte Carlo Distribution

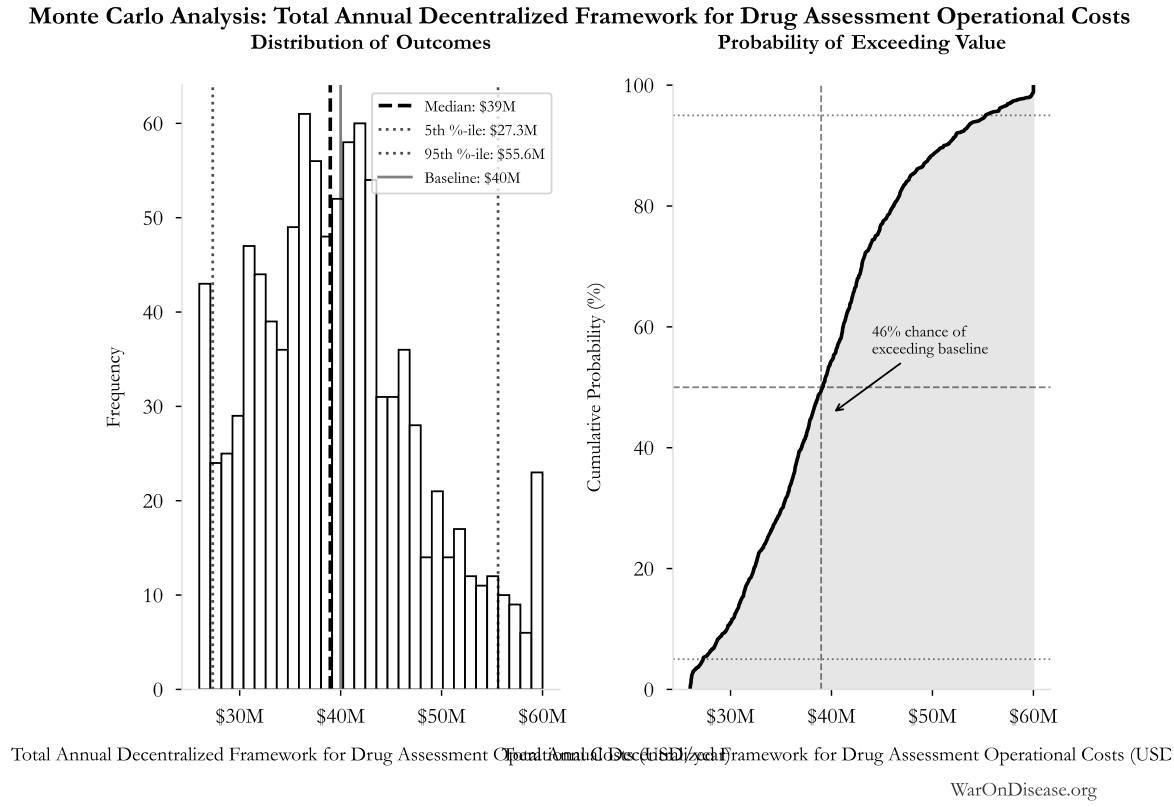


Figure 106: Monte Carlo Distribution: Total Annual Decentralized Framework for Drug Assessment Operational Costs (10,000 simulations)

Simulation Results Summary: Total Annual Decentralized Framework for Drug Assessment Operational Costs

Statistic	Value
Baseline (deterministic)	$40M
Mean (expected value)	$39.9M
Median (50th percentile)	$39M
Standard Deviation	$8.21M
90% Range (5th-95th percentile)	[$27.3M, $55.6M]

The histogram shows the distribution of Total Annual Decentralized Framework for Drug Assessment Operational Costs 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

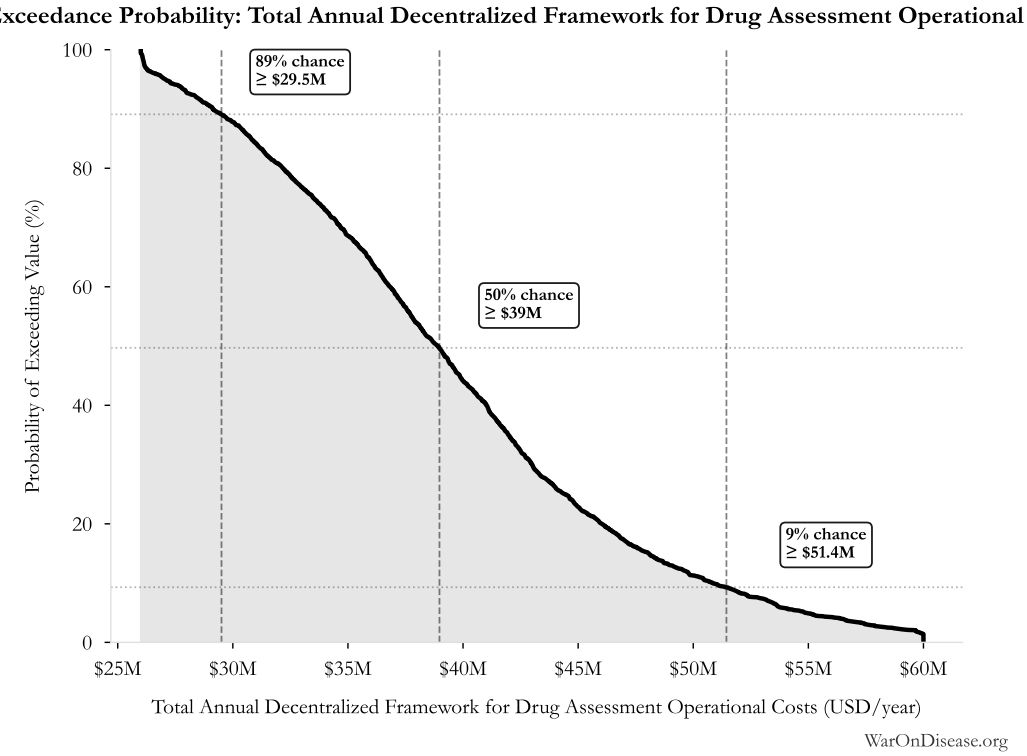


Figure 107: Probability of Exceeding Threshold: Total Annual Decentralized Framework for Drug Assessment Operational Costs

This exceedance probability chart shows the likelihood that Total Annual Decentralized Framework for Drug Assessment Operational Costs will exceed any given threshold. Higher curves indicate more favorable outcomes with greater certainty.

Decentralized Framework for Drug Assessment Annual Benefit: R&D Savings: $58.6B

Details

Annual Decentralized Framework for Drug Assessment benefit from R&D savings (trial cost reduction, secondary component)

Inputs:

- Annual Global Spending on Clinical Trials : $60B (95% CI: $50B - $75B)

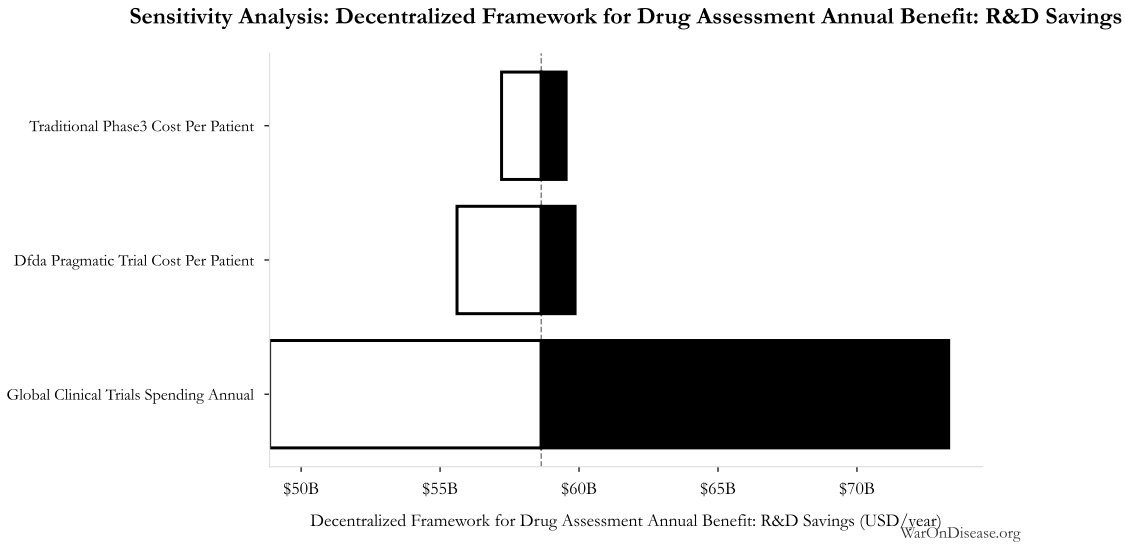
- dFDA Trial Cost Reduction Percentage : 97.7%

$$
\begin{aligned}
&Benefit_{RD,ann} \\
&= Spending_{trials} \times Reduce_{pct} \\
&= \$60B \times 97.7\% \\
&= \$58.6B
\end{aligned}
$$

$$
\begin{aligned}
&\text{where } Reduce_{pct} \\
&= 1 - \frac{Cost_{pragmatic,pt}}{Cost_{P3,pt}} \\
&= 1 - \frac{\$929}{\$41K} \\
&= 97.7\%
\end{aligned}
$$

High confidence

Sensitivity Analysis



Sensitivity Indices for Decentralized Framework for Drug Assessment Annual Benefit: R&D Savings

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

Input Parameter	Sensitivity Coefficient	Interpretation
Global Clinical Trials Spending Annual	1.0205	Strong driver
dFDA Trial Cost Reduction %	0.0244	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.

Monte Carlo Distribution

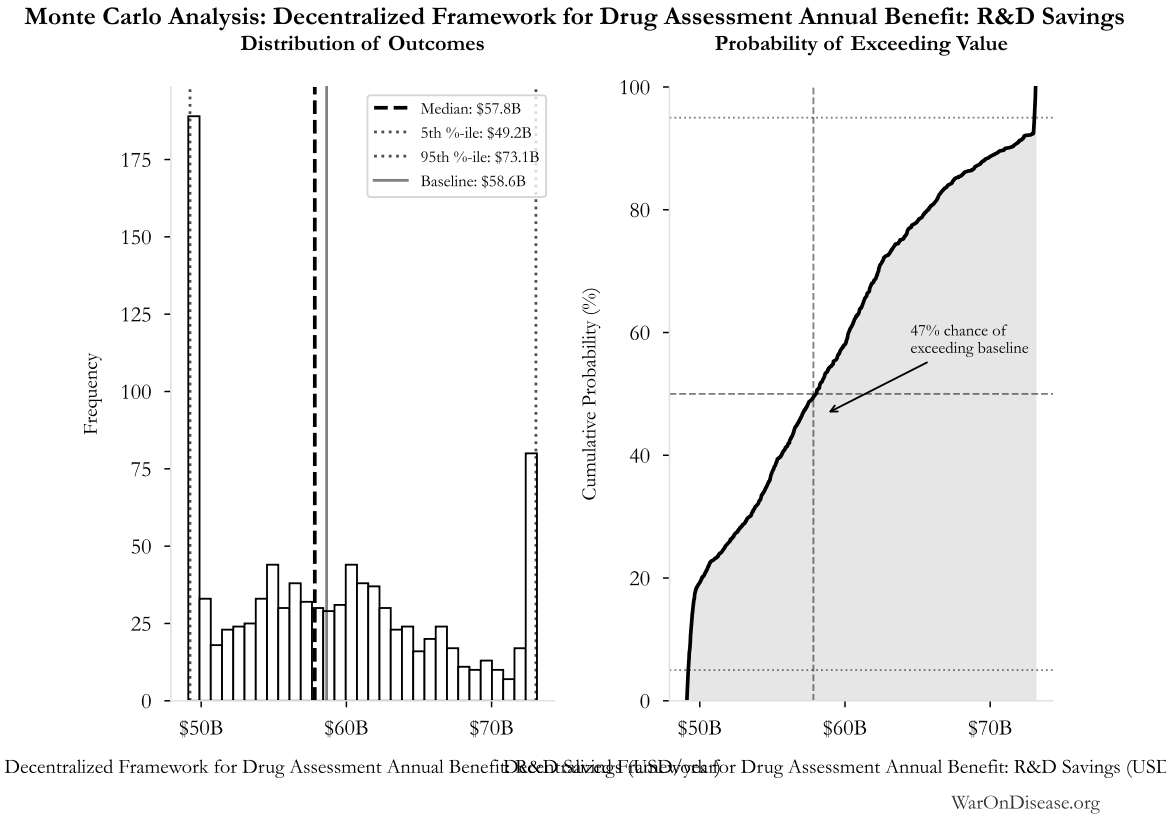


Figure 108: Monte Carlo Distribution: Decentralized Framework for Drug Assessment Annual Benefit: R&D Savings (10,000 simulations)

Simulation Results Summary: Decentralized Framework for Drug Assessment Annual Benefit: R&D Savings

Statistic	Value
Baseline (deterministic)	$58.6B
Mean (expected value)	$58.8B
Median (50th percentile)	$57.8B
Standard Deviation	$7.66B
90% Range (5th-95th percentile)	[$49.2B, $73.1B]

The histogram shows the distribution of Decentralized Framework for Drug Assessment Annual Benefit: R&D Savings 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

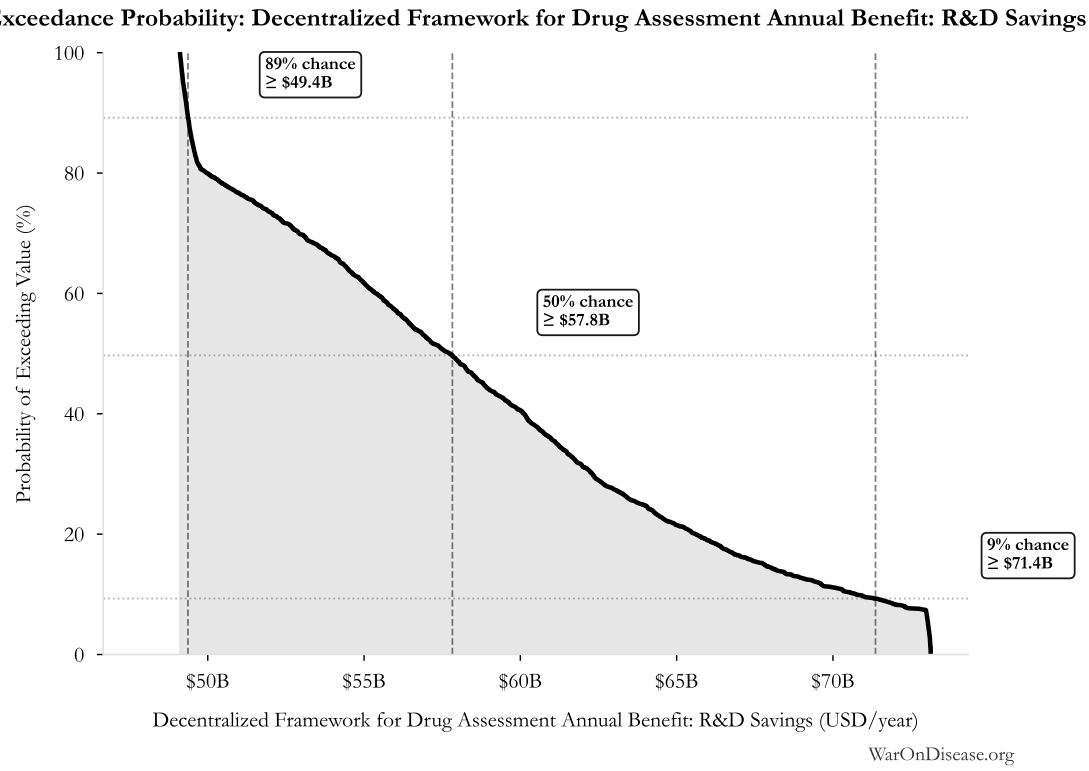


Figure 109: Probability of Exceeding Threshold: Decentralized Framework for Drug Assessment Annual Benefit: R&D Savings

This exceedance probability chart shows the likelihood that Decentralized Framework for Drug Assessment Annual Benefit: R&D Savings will exceed any given threshold. Higher curves indicate more favorable outcomes with greater certainty.

dFDA Direct Funding Cost per DALY: $0.841

Details

Cost per DALY if philanthropists/governments directly funded $21.76B/year for ~46.5 years (therapeutic space exploration period, NPV: ~$541.9B) instead of treaty campaign ($1B). Treaty achieves 542× leverage: $1B campaign unlocks government funding for 46.5 years (NPV: $541.9B), avoiding direct philanthropic commitment. Both achieve same 200B DALY timeline

shift benefit. Still cost-effective vs bed nets ($89.0/DALY).
Inputs:

- dFDA Direct Funding NPV (Exploration Period) : $475B
- Total DALYs from Elimination of Efficacy Lag Plus Earlier Treatment Discovery from Higher Trial Throughput : 565 billion DALYs

$$Cost_{direct,DALY} = \frac{NPV_{direct}}{DALYs_{max}} = \frac{\$475B}{565B} = \$0.841$$

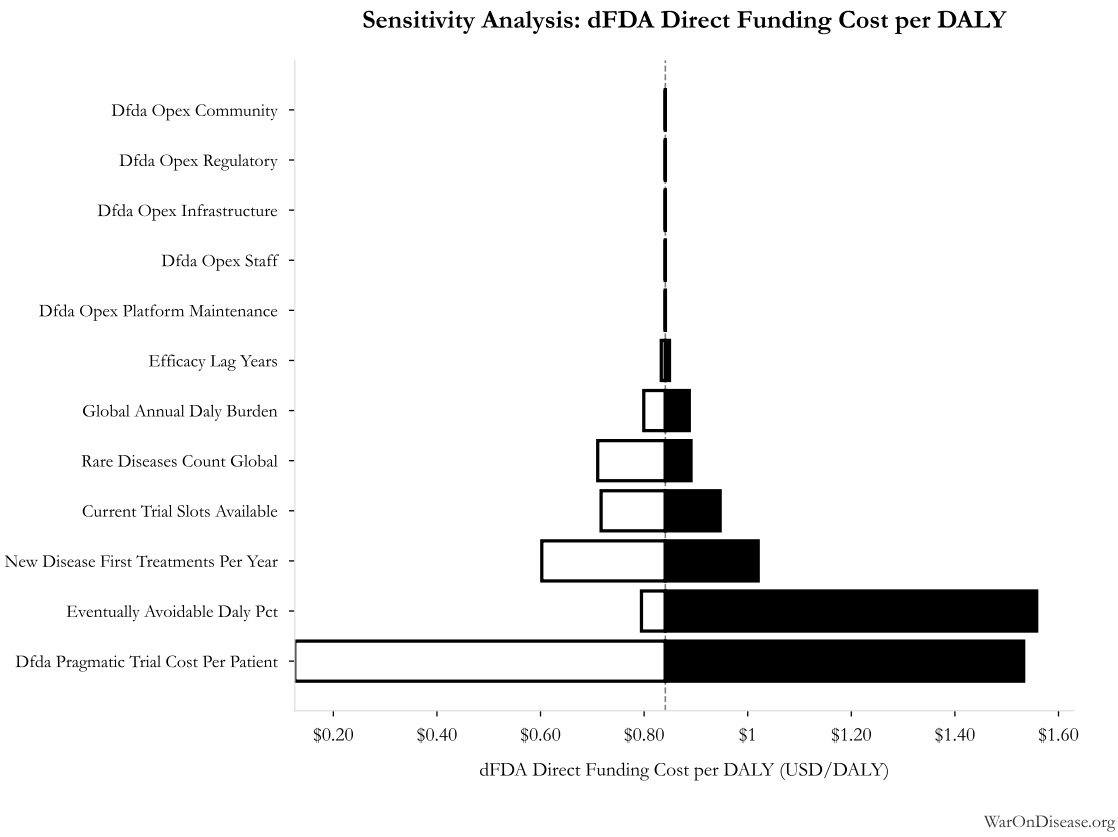
$$\text{where } NPV_{direct} = Funding_{ann} \times \frac{1-(1+r)^{-T}}{r}$$

$$\text{where } Treasury_{RD,ann}$$
$$= Funding_{treaty} - Payout_{bond,ann} - Funding_{political,ann}$$
$$= \$27.2B - \$2.72B - \$2.72B$$
$$= \$21.8B$$

$$\text{where } Funding_{treaty}$$

~ *Medium confidence*

Sensitivity Analysis



Sensitivity Indices for dFDA Direct Funding Cost per DALY
Regression-based sensitivity showing which inputs explain the most variance in the output.

Input Parameter	Sensitivity Coefficient	Interpretation
dFDA Trial Capacity Plus Efficacy Lag DALYs	-0.5182	Strong driver
dFDA Direct Funding Queue Clearance NPV	0.4583	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

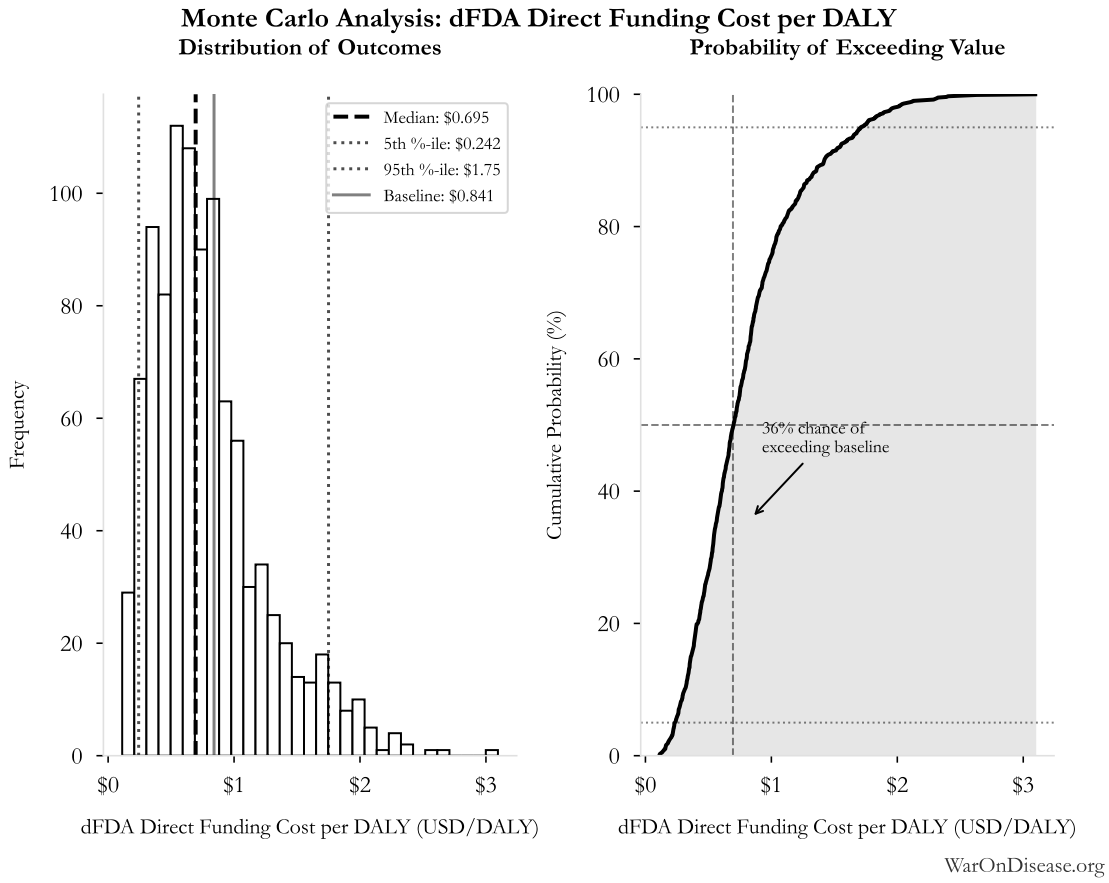


Figure 110: Monte Carlo Distribution: dFDA Direct Funding Cost per DALY (10,000 simulations)

Simulation Results Summary: dFDA Direct Funding Cost per DALY

Statistic	Value
Baseline (deterministic)	$0.841
Mean (expected value)	$0.800
Median (50th percentile)	$0.695
Standard Deviation	$0.466
90% Range (5th-95th percentile)	[$0.242, $1.75]

The histogram shows the distribution of dFDA Direct Funding 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

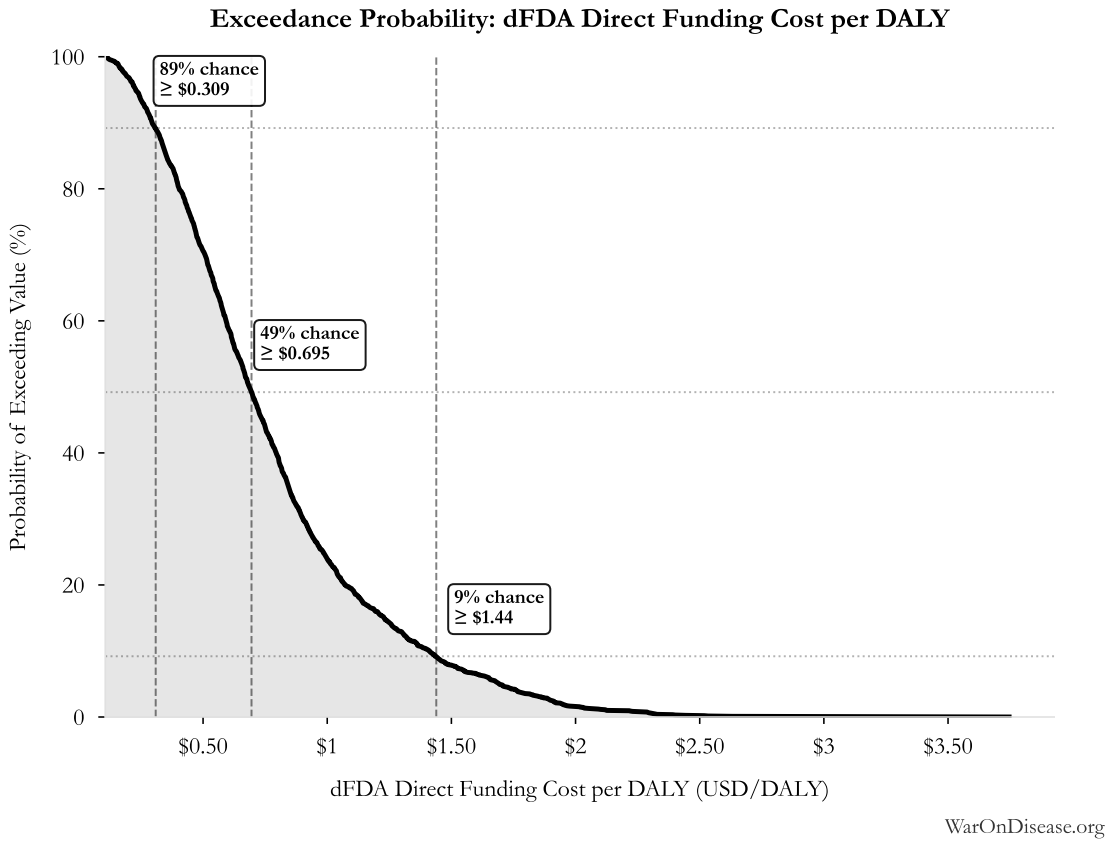


Figure 111: Probability of Exceeding Threshold: dFDA Direct Funding Cost per DALY

This exceedance probability chart shows the likelihood that dFDA Direct Funding Cost per DALY will exceed any given threshold. Higher curves indicate more favorable outcomes with greater certainty.

dFDA Direct Funding NPV (Exploration Period): $475B

Details

NPV of direct funding ($21.76B/year for medical research after bond/IAB allocations) for the ~46.5-year therapeutic space exploration period. Alternative scenario: instead of $1B treaty campaign to unlock government funding, philanthropists/NIH directly fund clinical trials until the therapeutic space is fully explored. Funding period is exploration time (46.5 years with 9.5× trial capacity), not timeline shift amount (207 years). After exploration completes, the timeline shift benefit (200B DALYs) is fully realized.

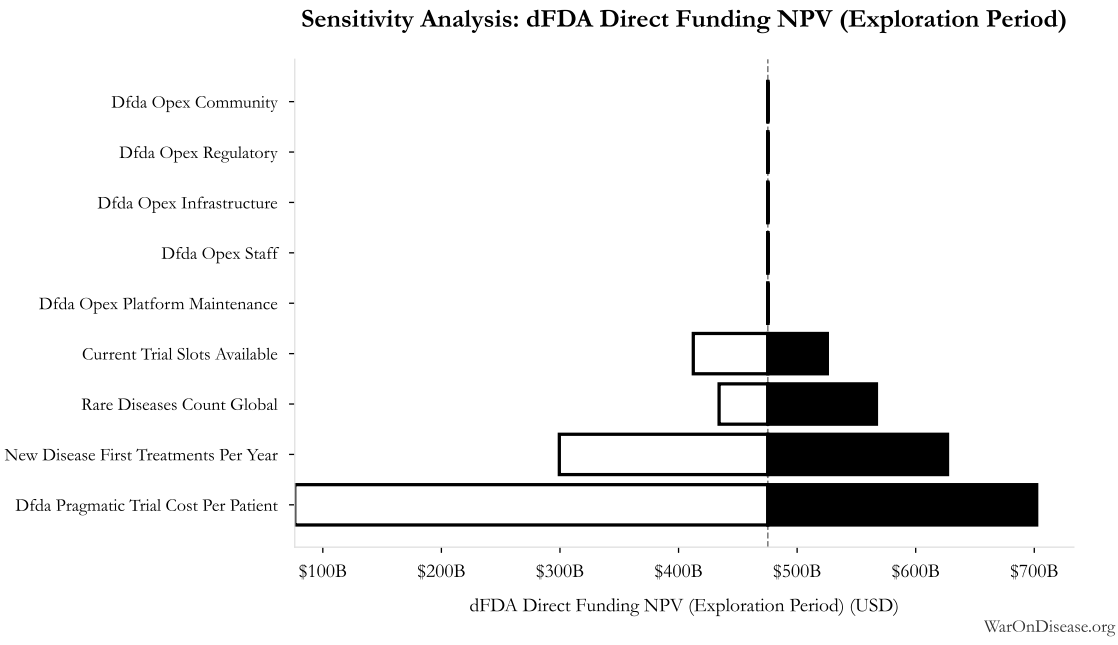
Inputs:

- Annual Funding for Pragmatic Clinical Trials : $21.8B
- Standard Discount Rate for NPV Analysis: 3%
- dFDA Therapeutic Space Exploration Time : 36 years

$$NPV_{direct} = Funding_{ann} \times \frac{1 - (1 + r)^{-T}}{r}$$

High confidence

Sensitivity Analysis



Sensitivity Indices for dFDA Direct Funding NPV (Exploration Period)

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

Input Parameter	Sensitivity Coefficient	Interpretation
dFDA Queue Clearance Years	0.9443	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

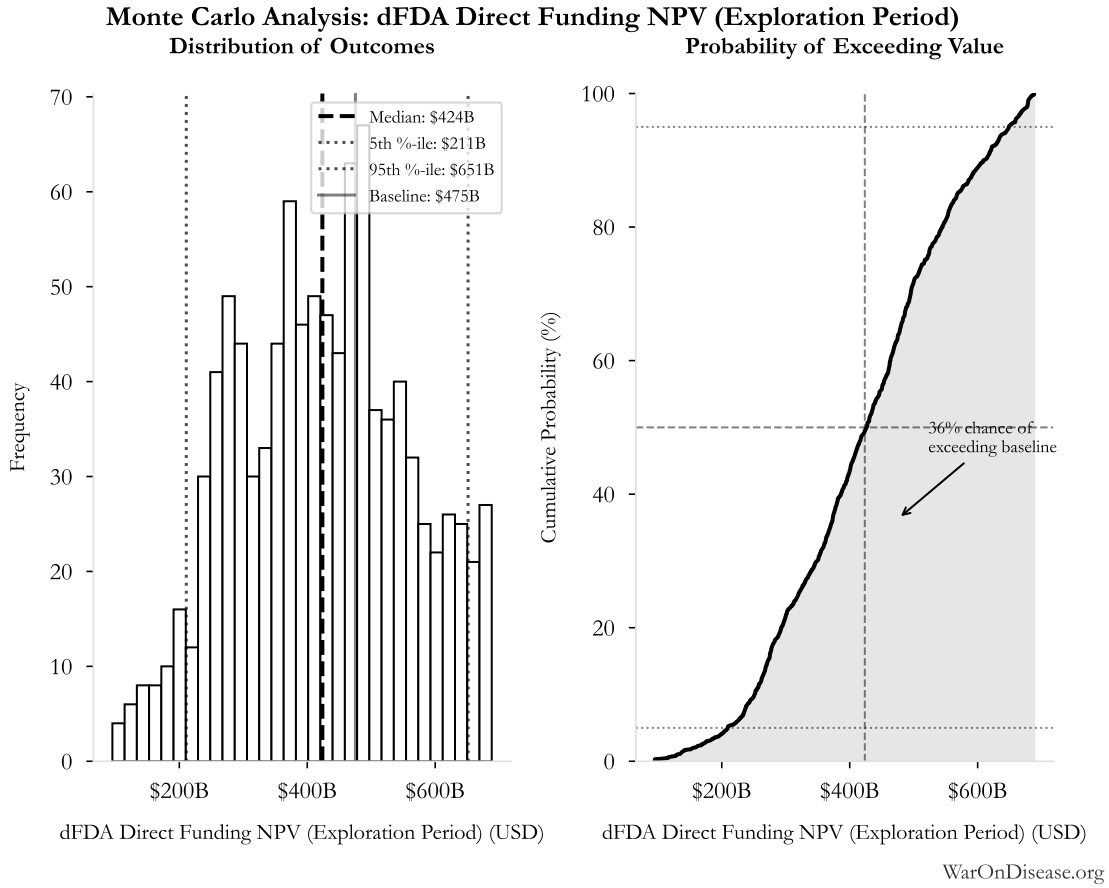


Figure 112: Monte Carlo Distribution: dFDA Direct Funding NPV (Exploration Period) (10,000 simulations)

Simulation Results Summary: dFDA Direct Funding NPV (Exploration Period)

Statistic	Value
Baseline (deterministic)	$475B
Mean (expected value)	$425B
Median (50th percentile)	$424B
Standard Deviation	$135B
90% Range (5th-95th percentile)	[$211B, $651B]

The histogram shows the distribution of dFDA Direct Funding NPV (Exploration Period) 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

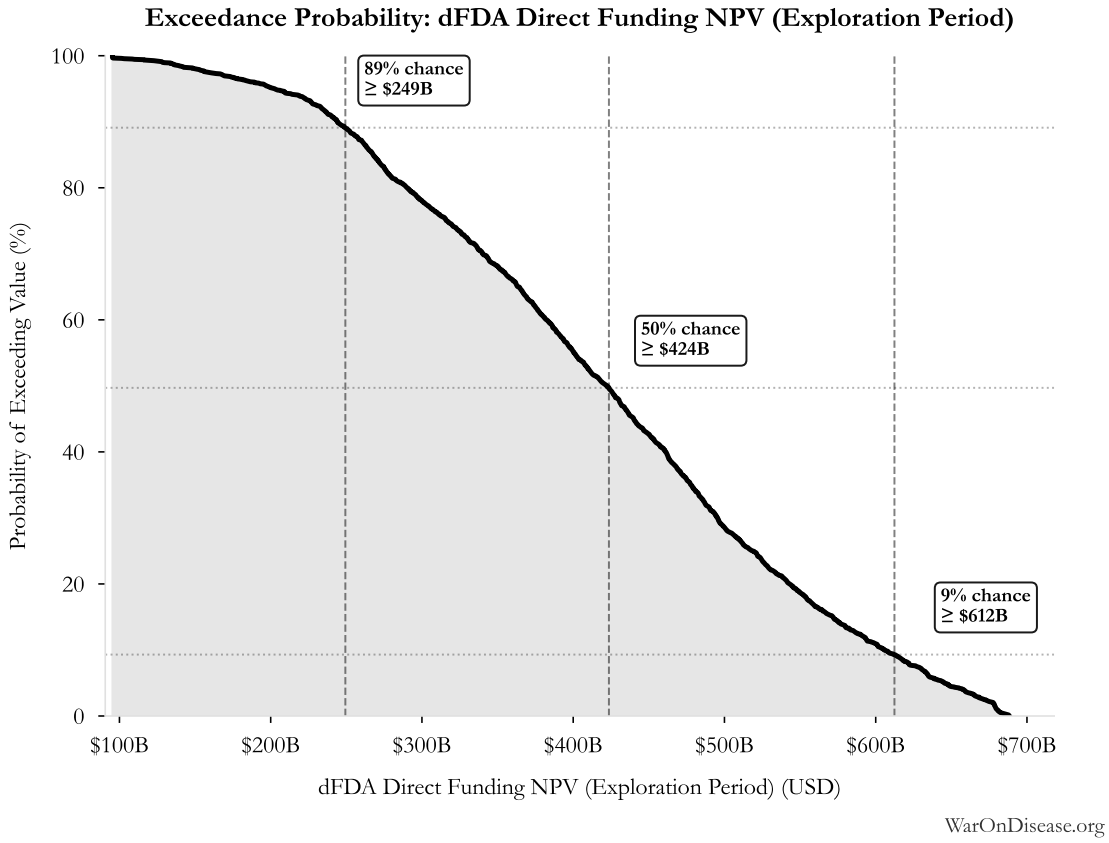


Figure 113: Probability of Exceeding Threshold: dFDA Direct Funding NPV (Exploration Period)

This exceedance probability chart shows the likelihood that dFDA Direct Funding NPV (Exploration Period) will exceed any given threshold. Higher curves indicate more favorable outcomes with greater certainty.

Total DALYs Lost from Disease Eradication Delay: 7.94 billion DALYs

Details

Total Disability-Adjusted Life Years lost from disease eradication delay (PRIMARY estimate)
Inputs:

- Years of Life Lost from Disease Eradication Delay : 7.07 billion years
- Years Lived with Disability During Disease Eradication Delay : 873 million years

$$DALYs_{lag} = YLL_{lag} + YLD_{lag} = 7.07B + 873M = 7.94B$$

$$\text{where } YLL_{lag}$$
$$= Deaths_{lag} \times (LE_{global} - Age_{death,delay})$$
$$= 416M \times (79 - 62)$$
$$= 7.07B$$

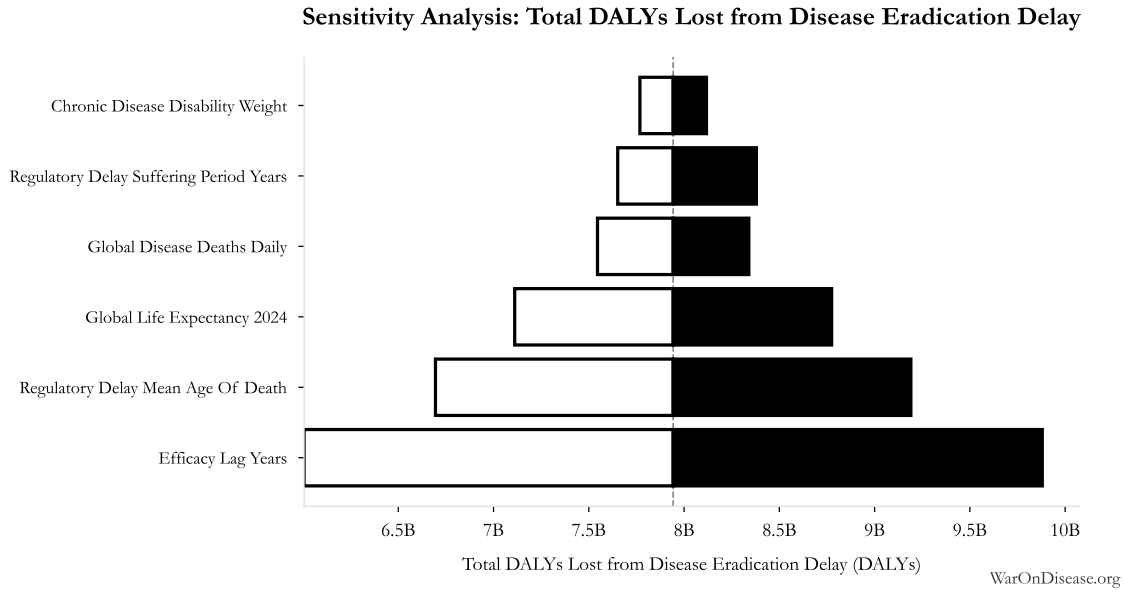
$$\text{where } Deaths_{lag}$$
$$= T_{lag} \times Deaths_{disease,daily} \times 338$$
$$= 8.2 \times 150{,}000 \times 338$$
$$= 416M$$

$$\text{where } YLD_{lag}$$
$$= Deaths_{lag} \times T_{suffering} \times DW_{chronic}$$
$$= 416M \times 6 \times 0.35$$
$$= 873M$$

$$\text{where } Deaths_{lag}$$
$$= T_{lag} \times Deaths_{disease,daily} \times 338$$
$$= 8.2 \times 150{,}000 \times 338$$
$$= 416M$$

~ *Medium confidence*

Sensitivity Analysis



Sensitivity Indices for Total DALYs Lost from Disease Eradication Delay
Regression-based sensitivity showing which inputs explain the most variance in the output.

Input Parameter	Sensitivity Coefficient	Interpretation
dFDA Efficacy Lag Elimination Yll	0.7043	Strong driver
dFDA Efficacy Lag Elimination Yld	0.3107	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

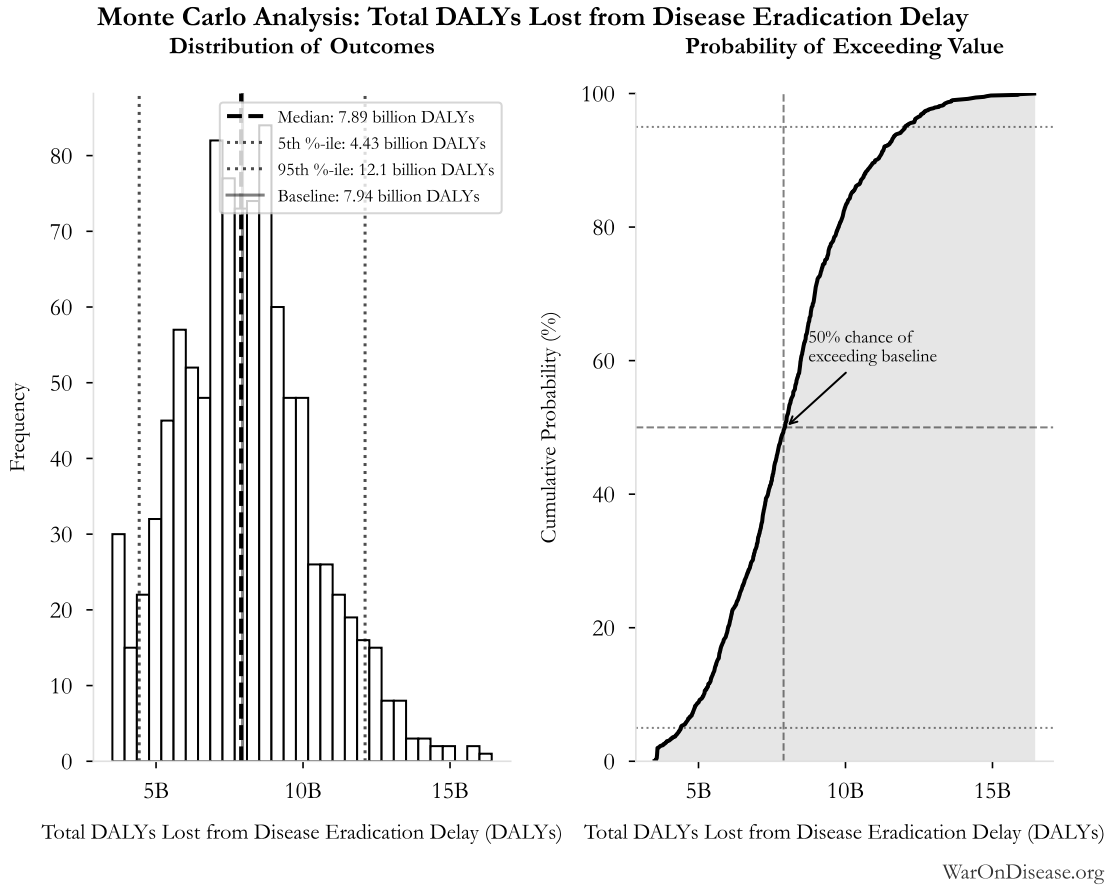


Figure 114: Monte Carlo Distribution: Total DALYs Lost from Disease Eradication Delay (10,000 simulations)

Simulation Results Summary: Total DALYs Lost from Disease Eradication Delay

Statistic	Value
Baseline (deterministic)	7.94 billion
Mean (expected value)	8.05 billion
Median (50th percentile)	7.89 billion
Standard Deviation	2.31 billion
90% Range (5th-95th percentile)	[4.43 billion, 12.1 billion]

The histogram shows the distribution of Total DALYs Lost from Disease Eradication Delay 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

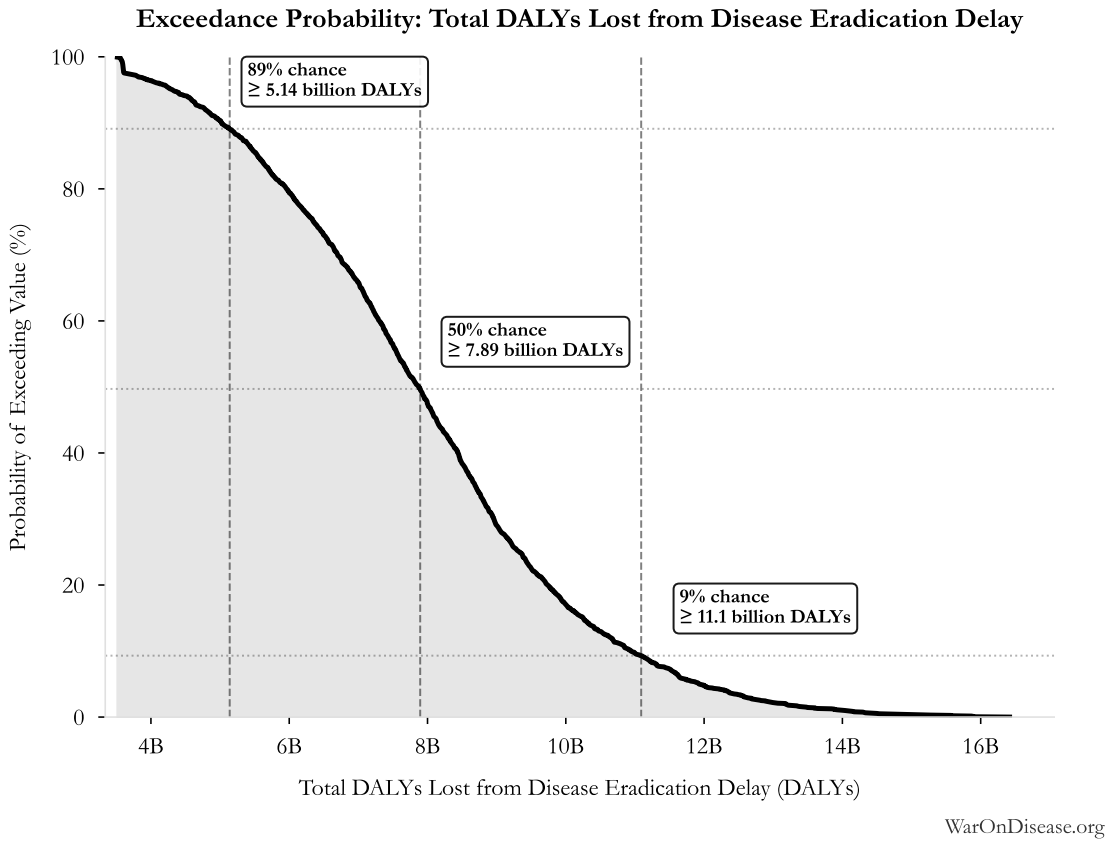


Figure 115: Probability of Exceeding Threshold: Total DALYs Lost from Disease Eradication Delay

This exceedance probability chart shows the likelihood that Total DALYs Lost from Disease Eradication Delay will exceed any given threshold. Higher curves indicate more favorable outcomes with greater certainty.

Total Deaths from Disease Eradication Delay: 416 million deaths

Details

Total eventually avoidable deaths from delaying disease eradication by 8.2 years (PRIMARY estimate, conservative). Excludes fundamentally unavoidable deaths (primarily accidents ~7.9%).

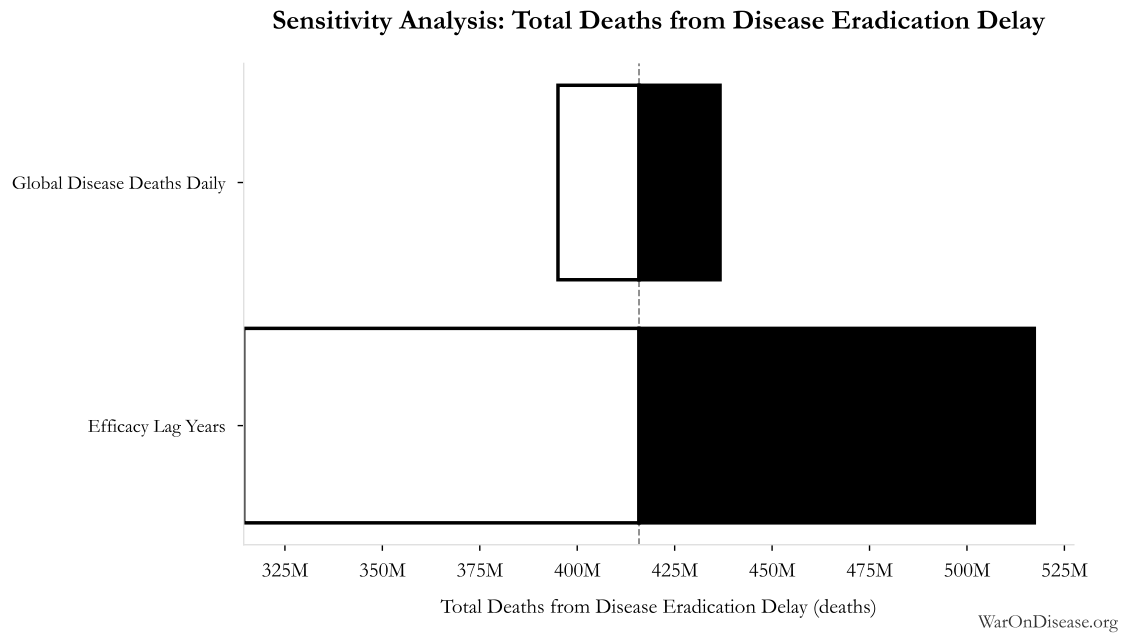
Inputs:

- Regulatory Delay for Efficacy Testing Post-Safety Verification : 8.2 years (SE: ±2 years)
- Global Daily Deaths from Disease and Aging : 150 thousand deaths/day (SE: ±7.50 thousand deaths/day)

$$\begin{aligned} & Deaths_{lag} \\ &= T_{lag} \times Deaths_{disease,daily} \times 338 \\ &= 8.2 \times 150{,}000 \times 338 \\ &= 416M \end{aligned}$$

~ *Medium confidence*

Sensitivity Analysis



Sensitivity Indices for Total Deaths from Disease Eradication Delay

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

Input Parameter	Sensitivity Coefficient	Interpretation
Efficacy Lag Years	1.1404	Strong driver
Global Disease Deaths Daily	-0.1422	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

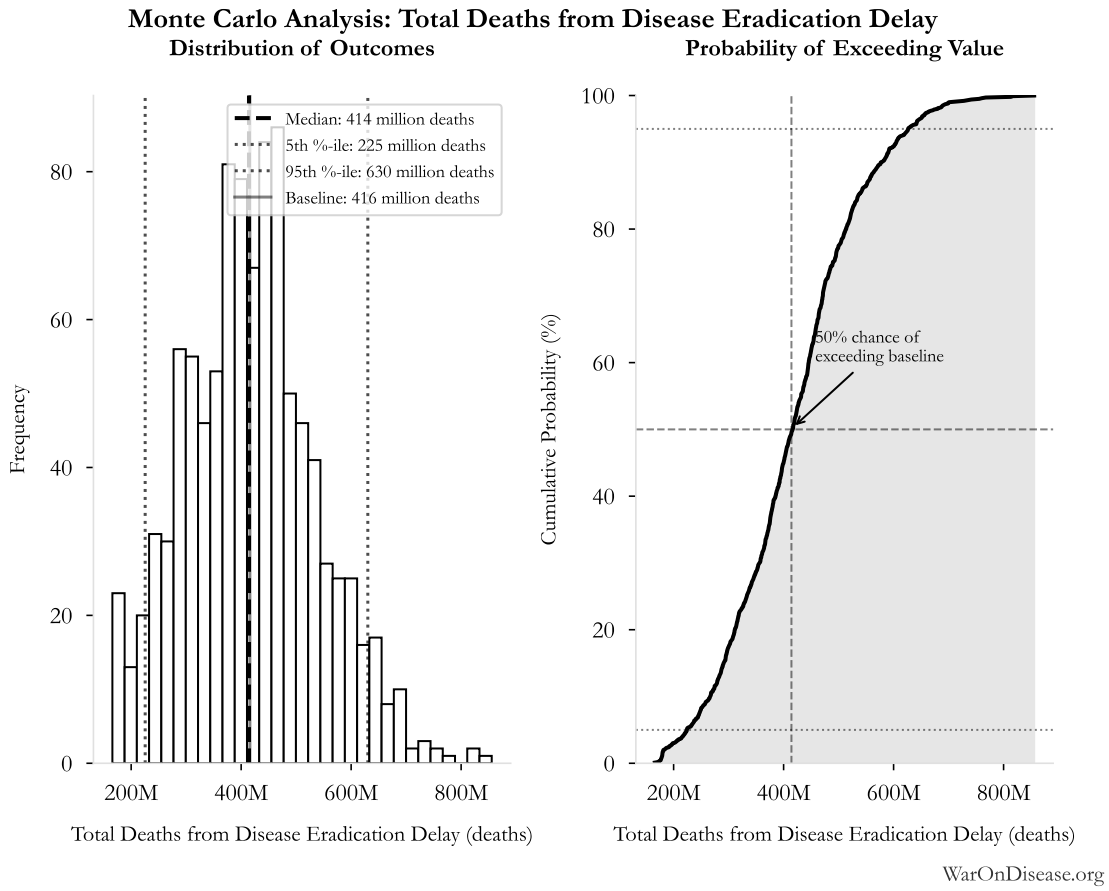


Figure 116: Monte Carlo Distribution: Total Deaths from Disease Eradication Delay (10,000 simulations)

Simulation Results Summary: Total Deaths from Disease Eradication Delay

Statistic	Value
Baseline (deterministic)	416 million
Mean (expected value)	420 million
Median (50th percentile)	414 million
Standard Deviation	122 million
90% Range (5th-95th percentile)	[225 million, 630 million]

The histogram shows the distribution of Total Deaths from Disease Eradication Delay 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

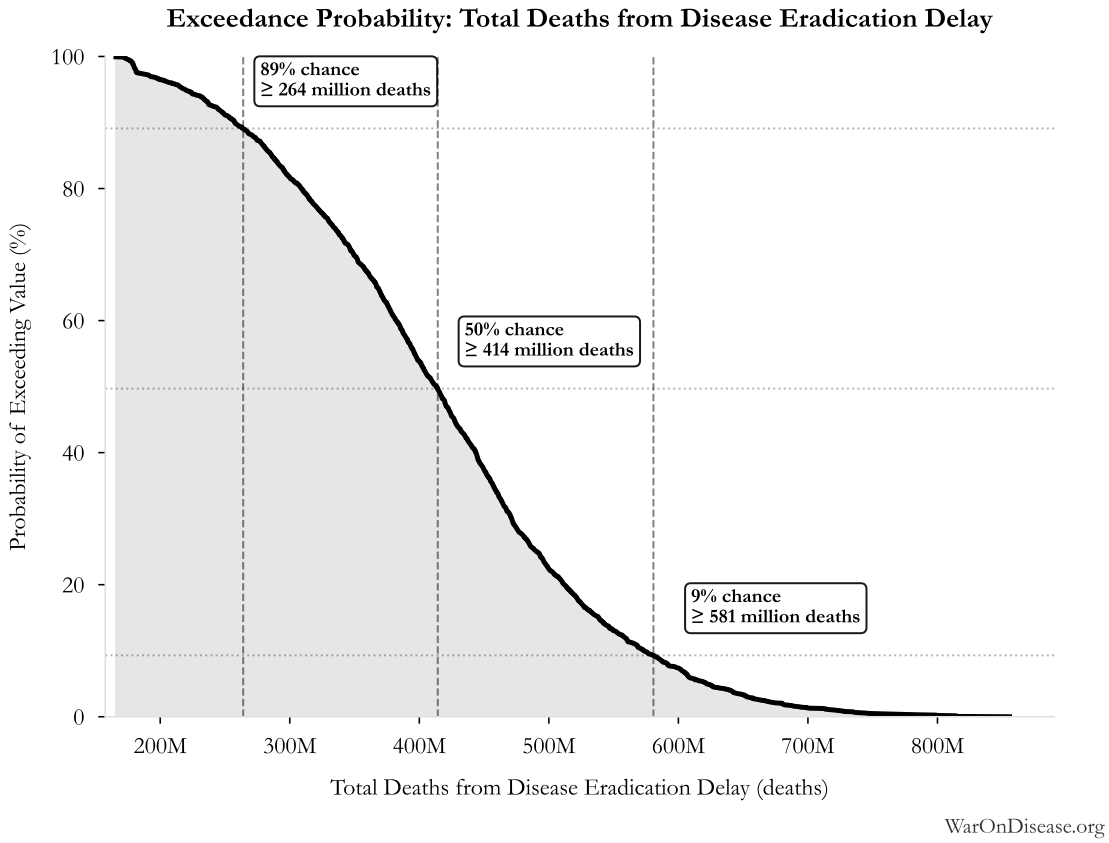


Figure 117: Probability of Exceeding Threshold: Total Deaths from Disease Eradication Delay

This exceedance probability chart shows the likelihood that Total Deaths from Disease Eradication Delay will exceed any given threshold. Higher curves indicate more favorable outcomes with greater certainty.

Total Economic Loss from Disease Eradication Delay: $1.19 quadrillion

Details

Total economic loss from delaying disease eradication by 8.2 years (PRIMARY estimate, 2024 USD). Values global DALYs at standardized US/International normative rate ($150k) rather than local ability-to-pay, representing the full human capital loss.

Inputs:

- Total DALYs Lost from Disease Eradication Delay : 7.94 billion DALYs
- Standard Economic Value per QALY : $150K (SE: ±$30K)

$$
\begin{aligned}
&Value_{lag} \\
&= DALYs_{lag} \times Value_{QALY} \\
&= 7.94B \times \$150K \\
&= \$1190T
\end{aligned}
$$

$$\text{where } DALYs_{lag} = YLL_{lag} + YLD_{lag} = 7.07B + 873M = 7.94B$$

$$
\begin{aligned}
&\text{where } YLL_{lag} \\
&= Deaths_{lag} \times (LE_{global} - Age_{death,delay}) \\
&= 416M \times (79 - 62) \\
&= 7.07B
\end{aligned}
$$

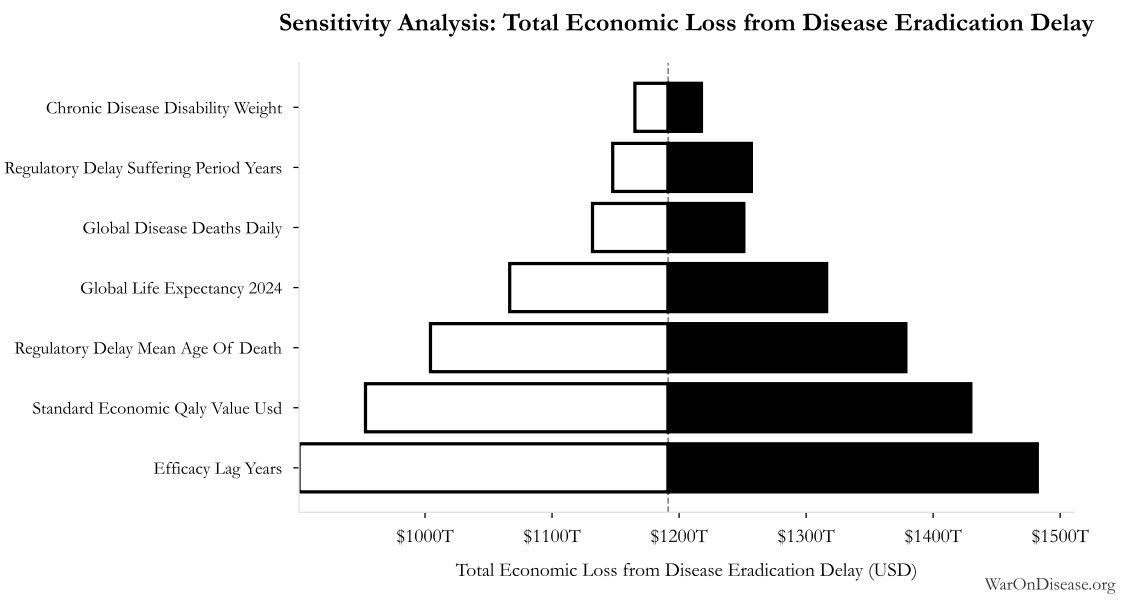
$$
\begin{aligned}
&\text{where } Deaths_{lag} \\
&= T_{lag} \times Deaths_{disease,daily} \times 338 \\
&= 8.2 \times 150{,}000 \times 338 \\
&= 416M
\end{aligned}
$$

$$
\begin{aligned}
&\text{where } YLD_{lag} \\
&= Deaths_{lag} \times T_{suffering} \times DW_{chronic} \\
&= 416M \times 6 \times 0.35 \\
&= 873M
\end{aligned}
$$

$$
\begin{aligned}
&\text{where } Deaths_{lag} \\
&= T_{lag} \times Deaths_{disease,daily} \times 338 \\
&= 8.2 \times 150{,}000 \times 338 \\
&= 416M
\end{aligned}
$$

~ *Medium confidence*

Sensitivity Analysis



Sensitivity Indices for Total Economic Loss from Disease Eradication Delay
Regression-based sensitivity showing which inputs explain the most variance in the output.

Input Parameter	Sensitivity Coefficient	Interpretation
dFDA Efficacy Lag Elimination DALYs	1.0671	Strong driver
Standard Economic QALY Value Usd	-0.0733	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.

Monte Carlo Distribution

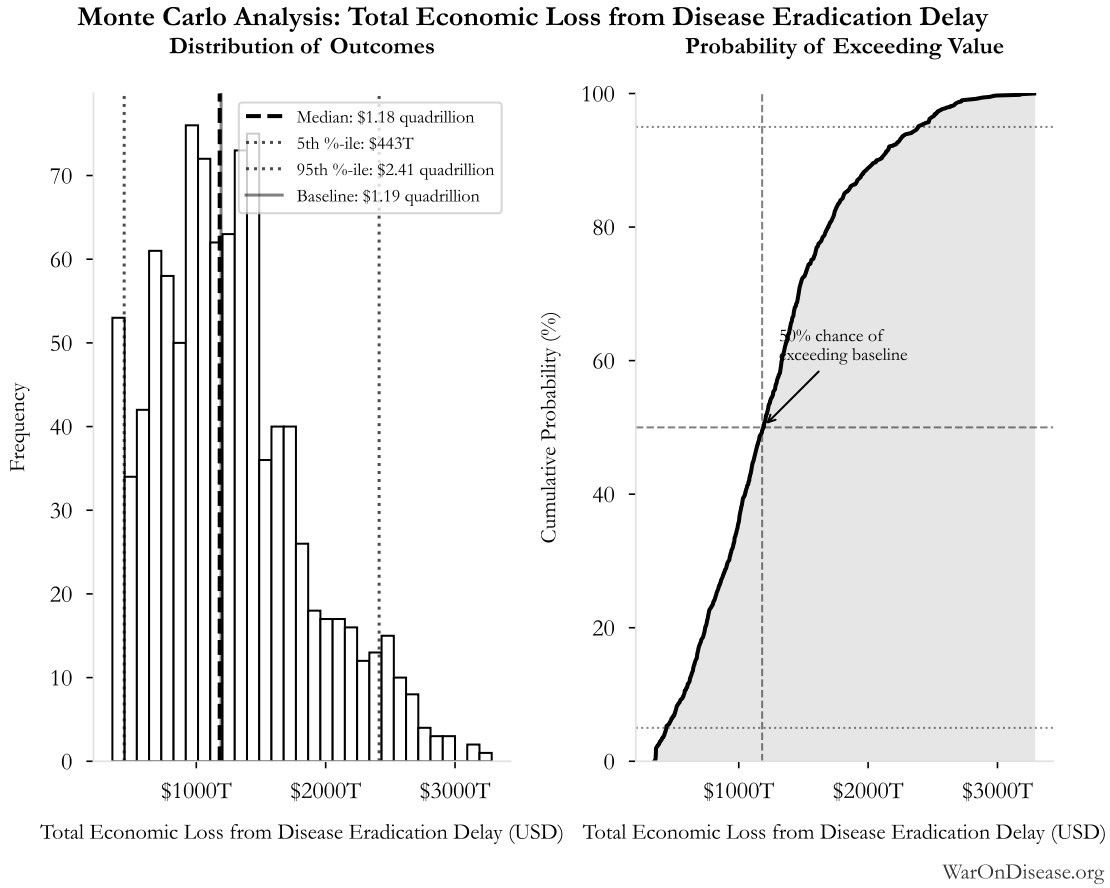


Figure 118: Monte Carlo Distribution: Total Economic Loss from Disease Eradication Delay (10,000 simulations)

Simulation Results Summary: Total Economic Loss from Disease Eradication Delay

Statistic	Value
Baseline (deterministic)	$1.19 quadrillion
Mean (expected value)	$1.27 quadrillion
Median (50th percentile)	$1.18 quadrillion
Standard Deviation	$581T
90% Range (5th-95th percentile)	[$443T, $2.41 quadrillion]

The histogram shows the distribution of Total Economic Loss from Disease Eradication Delay 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

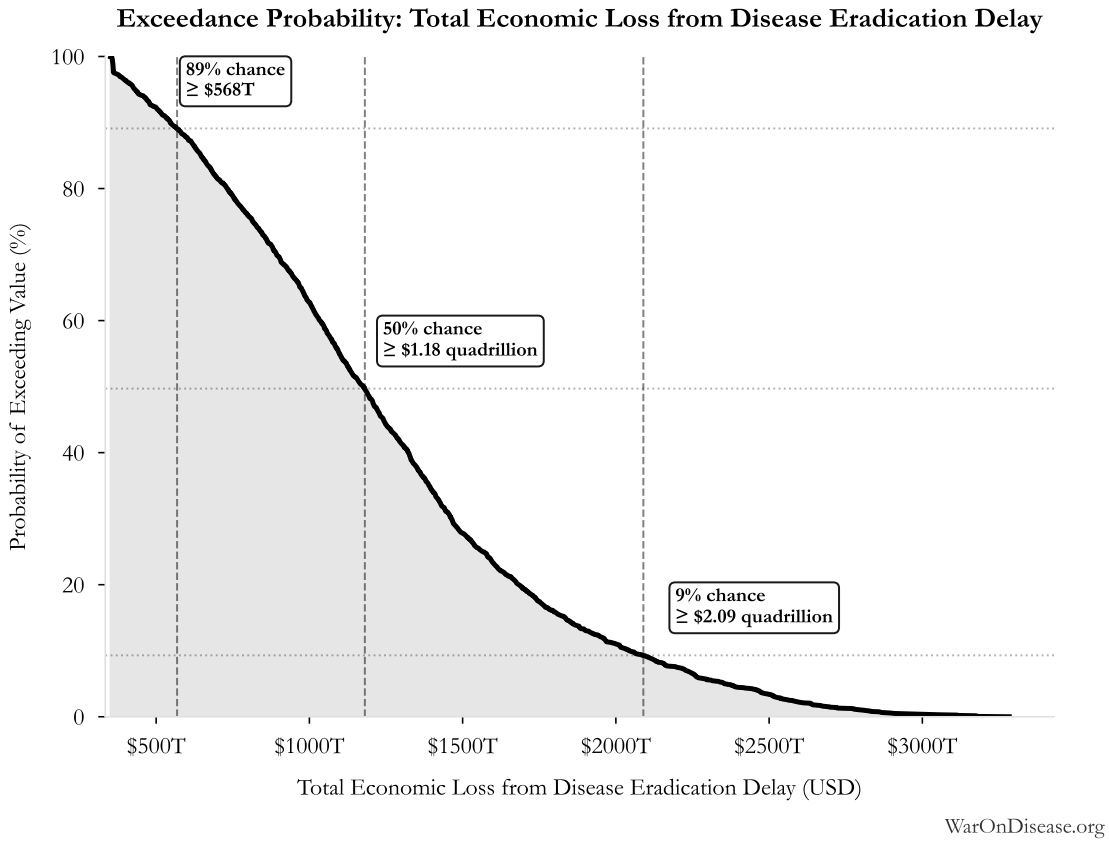


Figure 119: Probability of Exceeding Threshold: Total Economic Loss from Disease Eradication Delay

This exceedance probability chart shows the likelihood that Total Economic Loss from Disease Eradication Delay will exceed any given threshold. Higher curves indicate more favorable outcomes with greater certainty.

Years Lived with Disability During Disease Eradication Delay: 873 million years

Details

Years Lived with Disability during disease eradication delay (PRIMARY estimate)
Inputs:

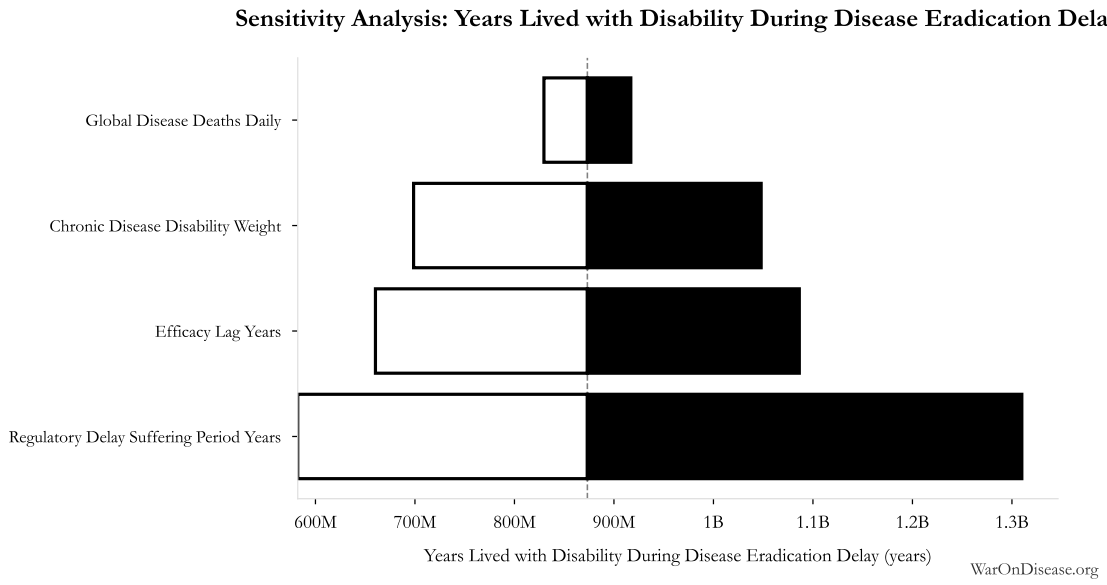
- Total Deaths from Disease Eradication Delay : 416 million deaths
- Pre-Death Suffering Period During Post-Safety Efficacy Delay : 6 years (95% CI: 4 years - 9 years)
- Disability Weight for Untreated Chronic Conditions : 0.35 weight (SE: ±0.07 weight)

$$
\begin{aligned}
&YLD_{lag} \\
&= Deaths_{lag} \times T_{suffering} \times DW_{chronic} \\
&= 416M \times 6 \times 0.35 \\
&= 873M
\end{aligned}
$$

$$
\begin{aligned}
&\text{where } Deaths_{lag} \\
&= T_{lag} \times Deaths_{disease,daily} \times 338 \\
&= 8.2 \times 150{,}000 \times 338 \\
&= 416M
\end{aligned}
$$

~ *Medium confidence*

Sensitivity Analysis



Sensitivity Indices for Years Lived with Disability During Disease Eradication Delay

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

Input Parameter	Sensitivity Coefficient	Interpretation
Regulatory Delay Suffering Period Years	2.0883	Strong driver
Chronic Disease Disability Weight	-0.9003	Strong driver
dFDA Efficacy Lag Elimination Deaths Averted	-0.2255	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

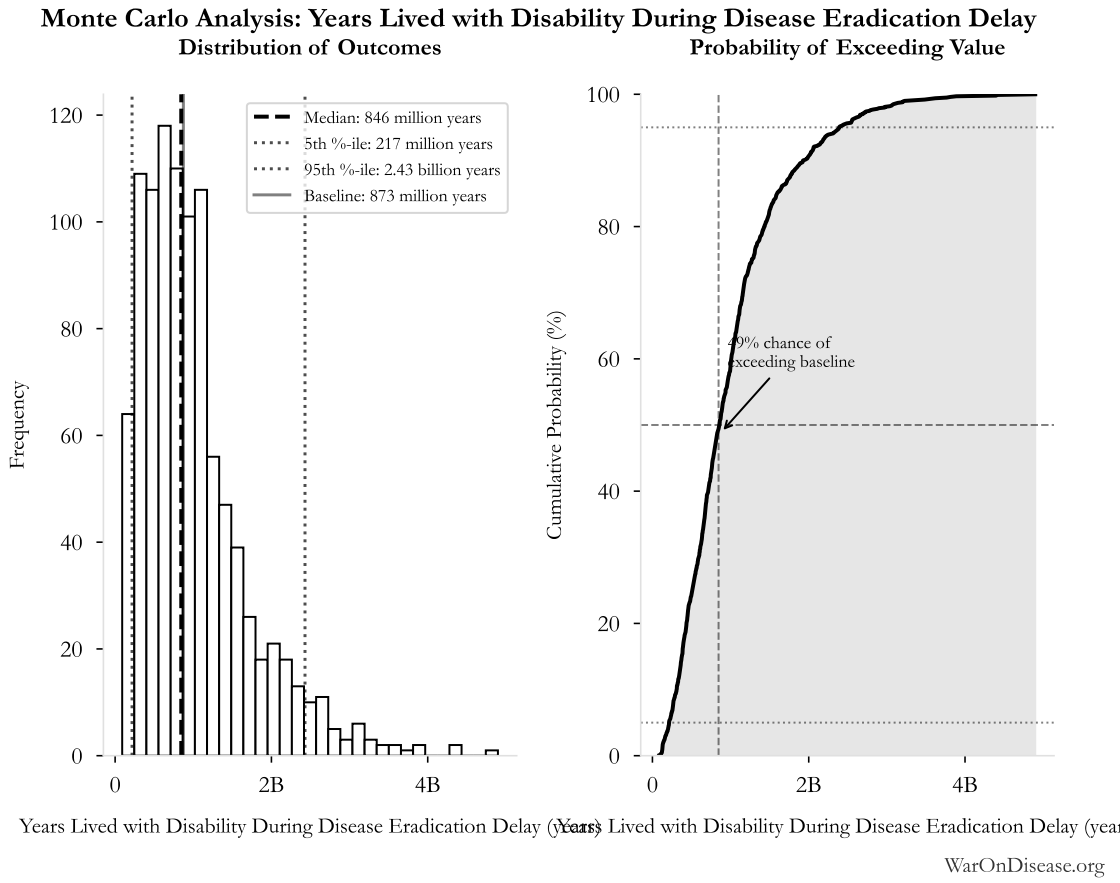


Figure 120: Monte Carlo Distribution: Years Lived with Disability During Disease Eradication Delay (10,000 simulations)

Simulation Results Summary: Years Lived with Disability During Disease Eradication Delay

Statistic	Value
Baseline (deterministic)	873 million
Mean (expected value)	1.02 billion
Median (50th percentile)	846 million
Standard Deviation	716 million
90% Range (5th-95th percentile)	[217 million, 2.43 billion]

The histogram shows the distribution of Years Lived with Disability During Disease Eradication Delay 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

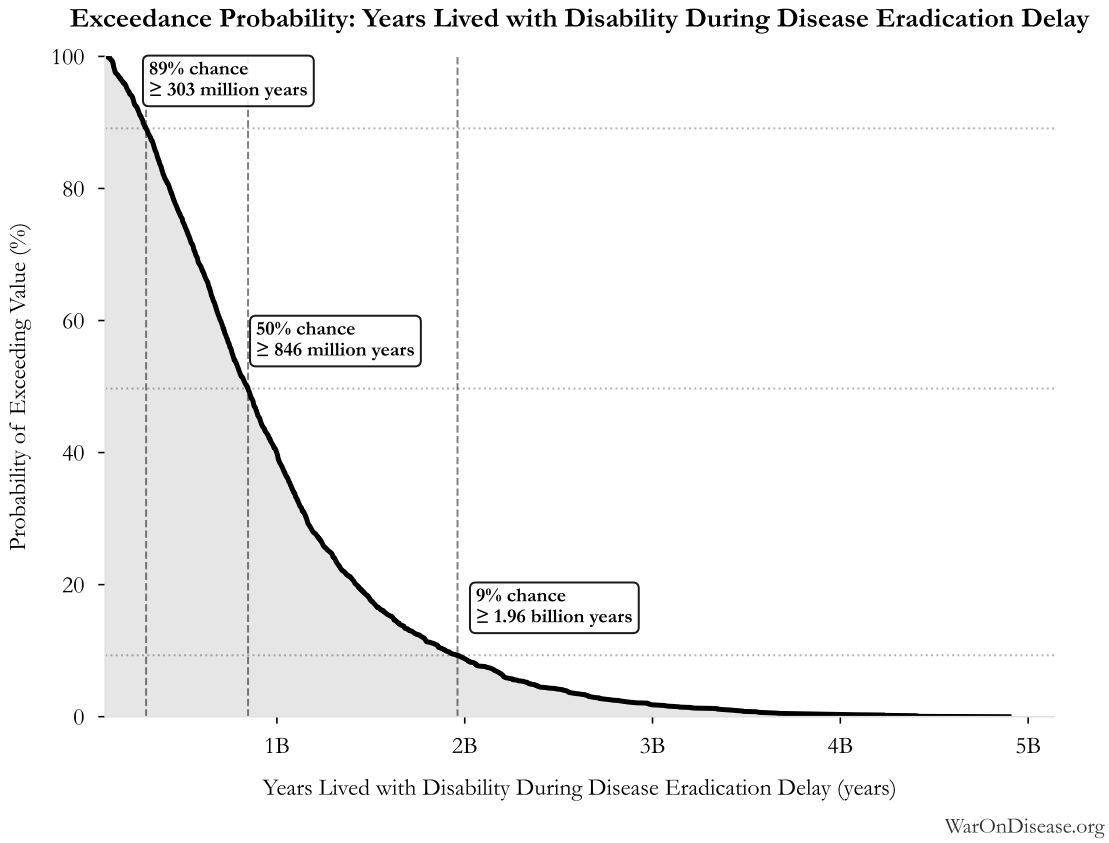


Figure 121: Probability of Exceeding Threshold: Years Lived with Disability During Disease Eradication Delay

This exceedance probability chart shows the likelihood that Years Lived with Disability During Disease Eradication Delay will exceed any given threshold. Higher curves indicate more favorable outcomes with greater certainty.

Years of Life Lost from Disease Eradication Delay: 7.07 billion years

Details

Years of Life Lost from disease eradication delay deaths (PRIMARY estimate)
Inputs:

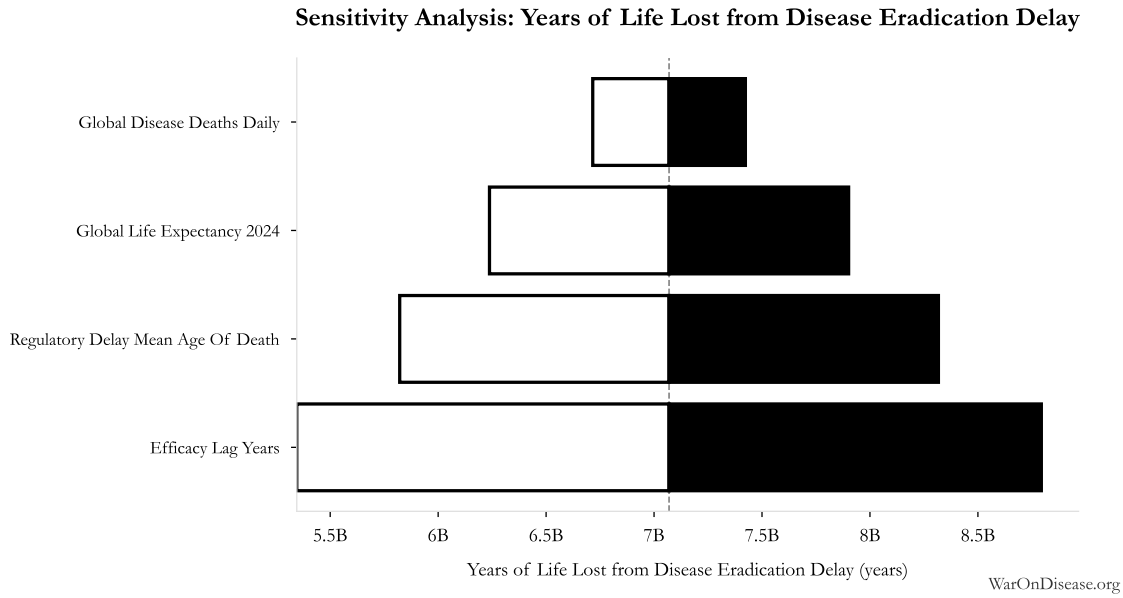
- Total Deaths from Disease Eradication Delay : 416 million deaths
- Global Life Expectancy (2024) : 79 years (SE: ±2 years)
- Mean Age of Preventable Death from Post-Safety Efficacy Delay : 62 years (SE: ±3 years)

$$
\begin{aligned}
&YLL_{lag} \\
&= Deaths_{lag} \times (LE_{global} - Age_{death,delay}) \\
&= 416M \times (79 - 62) \\
&= 7.07B
\end{aligned}
$$

$$
\begin{aligned}
&\text{where } Deaths_{lag} \\
&= T_{lag} \times Deaths_{disease,daily} \times 338 \\
&= 8.2 \times 150{,}000 \times 338 \\
&= 416M
\end{aligned}
$$

~ *Medium confidence*

Sensitivity Analysis



Sensitivity Indices for Years of Life Lost from Disease Eradication Delay
Regression-based sensitivity showing which inputs explain the most variance in the output.

Input Parameter	Sensitivity Coefficient	Interpretation
Global Life Expectancy 2024	2.0066	Strong driver
Regulatory Delay Mean Age Of Death	-1.3852	Strong driver
dFDA Efficacy Lag	0.3779	Moderate driver
Elimination Deaths Averted		

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

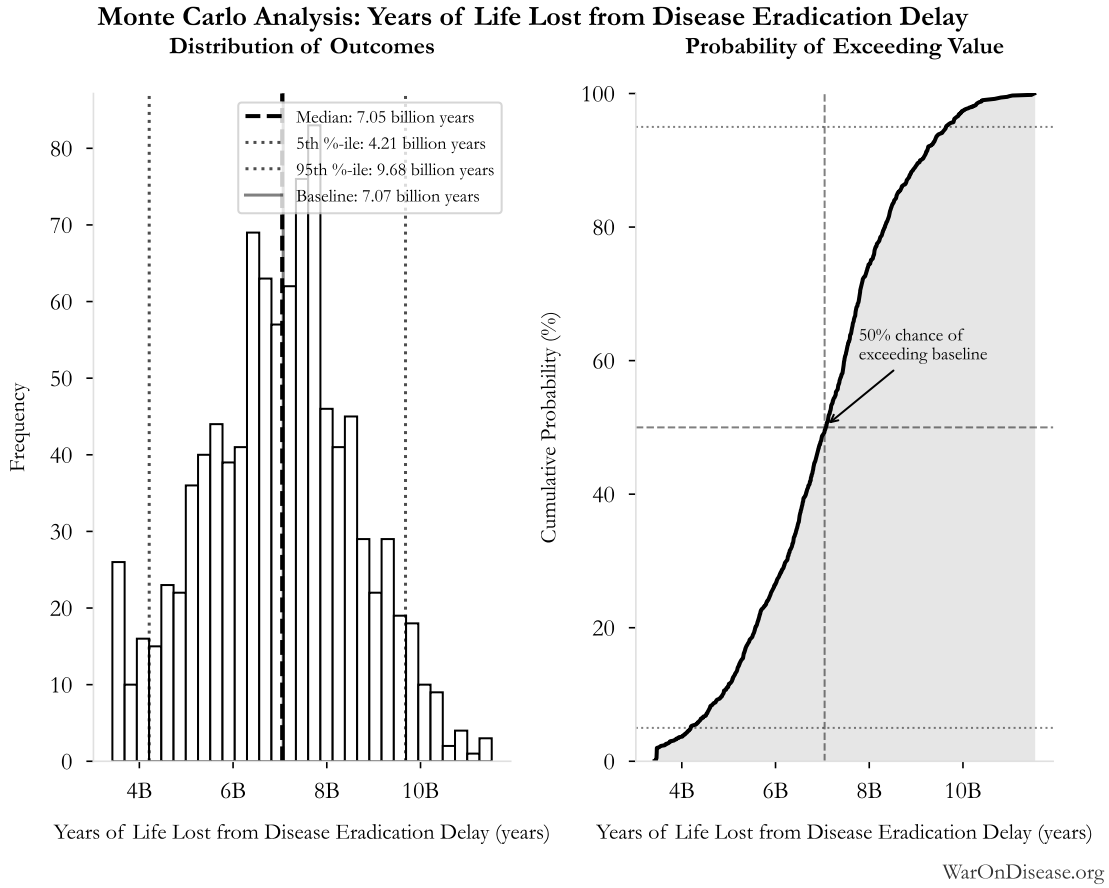


Figure 122: Monte Carlo Distribution: Years of Life Lost from Disease Eradication Delay (10,000 simulations)

Simulation Results Summary: Years of Life Lost from Disease Eradication Delay

Statistic	Value
Baseline (deterministic)	7.07 billion
Mean (expected value)	7.03 billion
Median (50th percentile)	7.05 billion
Standard Deviation	1.62 billion
90% Range (5th-95th percentile)	[4.21 billion, 9.68 billion]

The histogram shows the distribution of Years of Life Lost from Disease Eradication Delay 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

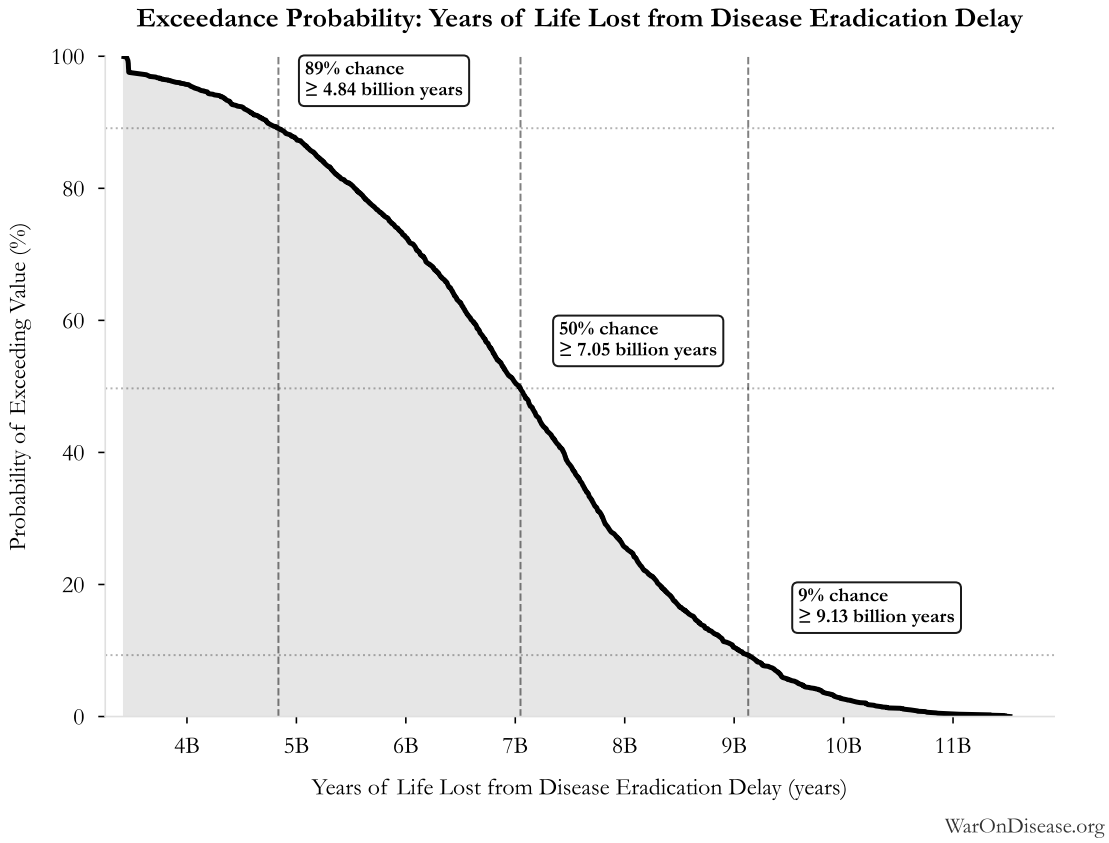


Figure 123: Probability of Exceeding Threshold: Years of Life Lost from Disease Eradication Delay

This exceedance probability chart shows the likelihood that Years of Life Lost from Disease Eradication Delay will exceed any given threshold. Higher curves indicate more favorable outcomes with greater certainty.

dFDA New Treatments Per Year: 185 diseases/year

Details

Diseases per year receiving their first effective treatment with dFDA. Scales proportionally with trial capacity multiplier.

Inputs:

- Diseases Getting First Treatment Per Year : 15 diseases/year (95% CI: 8 diseases/year - 30 diseases/year)
- Trial Capacity Multiplier : 12.3x

$$Treatments_{dFDA,ann}$$
$$= Treatments_{new,ann} \times k_{capacity}$$
$$= 15 \times 12.3$$
$$= 185$$

$$\text{where } k_{capacity} = \frac{N_{fundable,ann}}{Slots_{curr}} = \frac{23.4M}{1.9M} = 12.3$$

$$\text{where } N_{fundable,ann}$$
$$= \frac{Subsidies_{trial,ann}}{Cost_{pragmatic,pt}}$$
$$= \frac{\$21.7B}{\$929}$$
$$= 23.4M$$

$$\text{where } Subsidies_{trial,ann}$$
$$= Treasury_{RD,ann} - OPEX_{dFDA}$$
$$= \$21.8B - \$40M$$
$$= \$21.7B$$

$$\text{where } OPEX_{dFDA}$$
$$= Cost_{platform} + Cost_{staff} + Cost_{infra}$$
$$+Cost_{regulatory} + Cost_{community}$$
$$= \$15M + \$10M + \$8M + \$5M + \$2M$$
$$= \$40M$$

$$\text{where } Treasury_{RD,ann}$$
$$= Funding_{treaty} - Payout_{bond,ann} - Funding_{political,ann}$$
$$= \$27.2B - \$2.72B - \$2.72B$$
$$= \$21.8B$$

$$\text{where } Funding_{treaty}$$
$$= Spending_{mil} \times Reduce_{treaty}$$
$$= \$2.72T \times 1\%$$
$$= \$27.2B$$

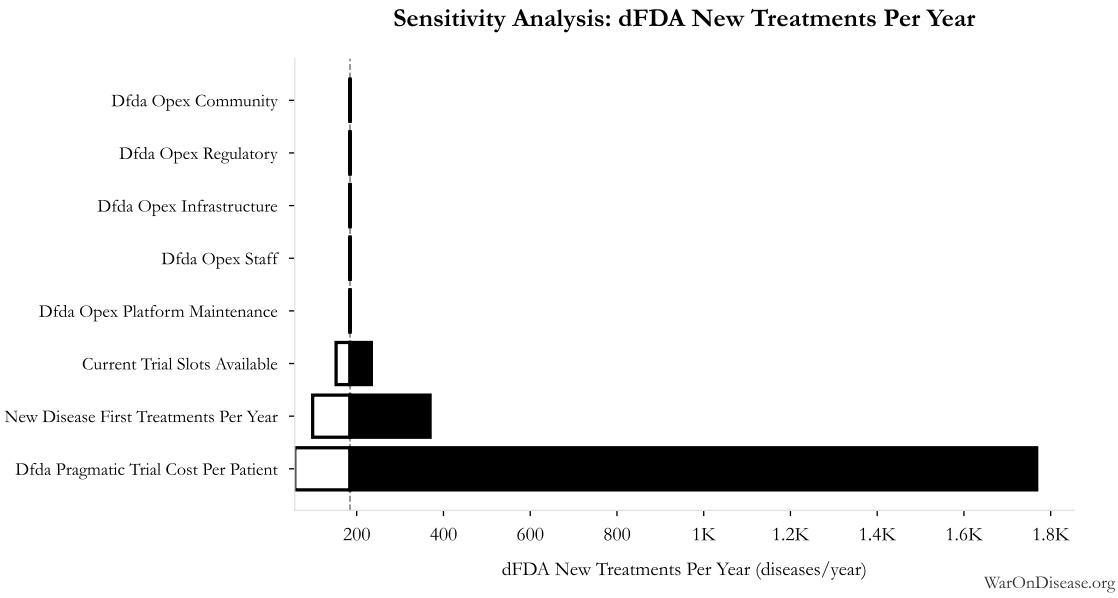
$$\text{where } Payout_{bond,ann}$$
$$= Funding_{treaty} \times Pct_{bond}$$
$$= \$27.2B \times 10\%$$
$$= \$2.72B$$

$$\text{where } Funding_{treaty}$$
$$= Spending_{mil} \times Reduce_{treaty}$$
$$= \$2.72T \times 1\%$$
$$= \$27.2B$$

$$\text{where } Funding_{political,ann}$$
$$= Funding_{treaty} \times Pct_{political}$$
$$= \$27.2B \times 10\%$$

? Low confidence

Sensitivity Analysis



Sensitivity Indices for dFDA New Treatments Per Year
Regression-based sensitivity showing which inputs explain the most variance in the output.

Input Parameter	Sensitivity Coefficient	Interpretation
dFDA Trial Capacity Multiplier	0.9380	Strong driver
New Disease First Treatments Per Year	-0.0784	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.

Monte Carlo Distribution

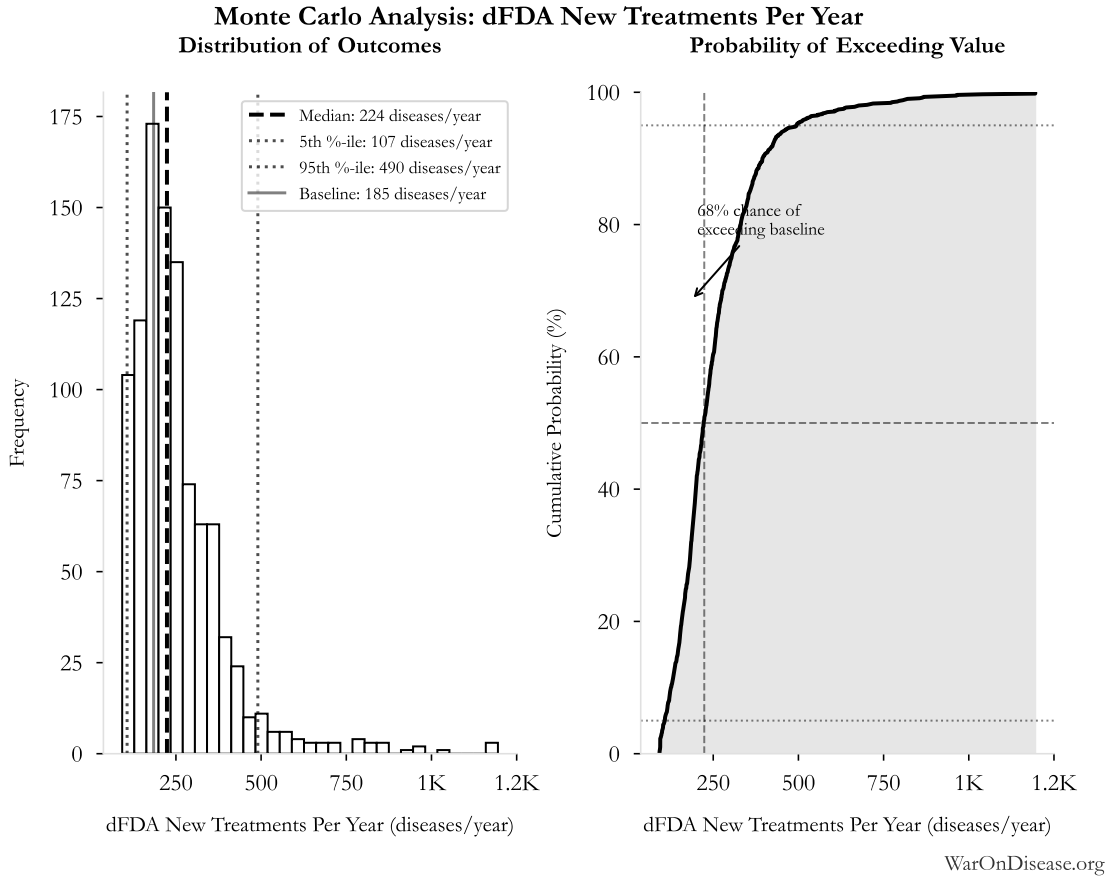


Figure 124: Monte Carlo Distribution: dFDA New Treatments Per Year (10,000 simulations)

Simulation Results Summary: dFDA New Treatments Per Year

Statistic	Value
Baseline (deterministic)	185
Mean (expected value)	254
Median (50th percentile)	224
Standard Deviation	140
90% Range (5th-95th percentile)	[107, 490]

The histogram shows the distribution of dFDA New Treatments Per Year 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

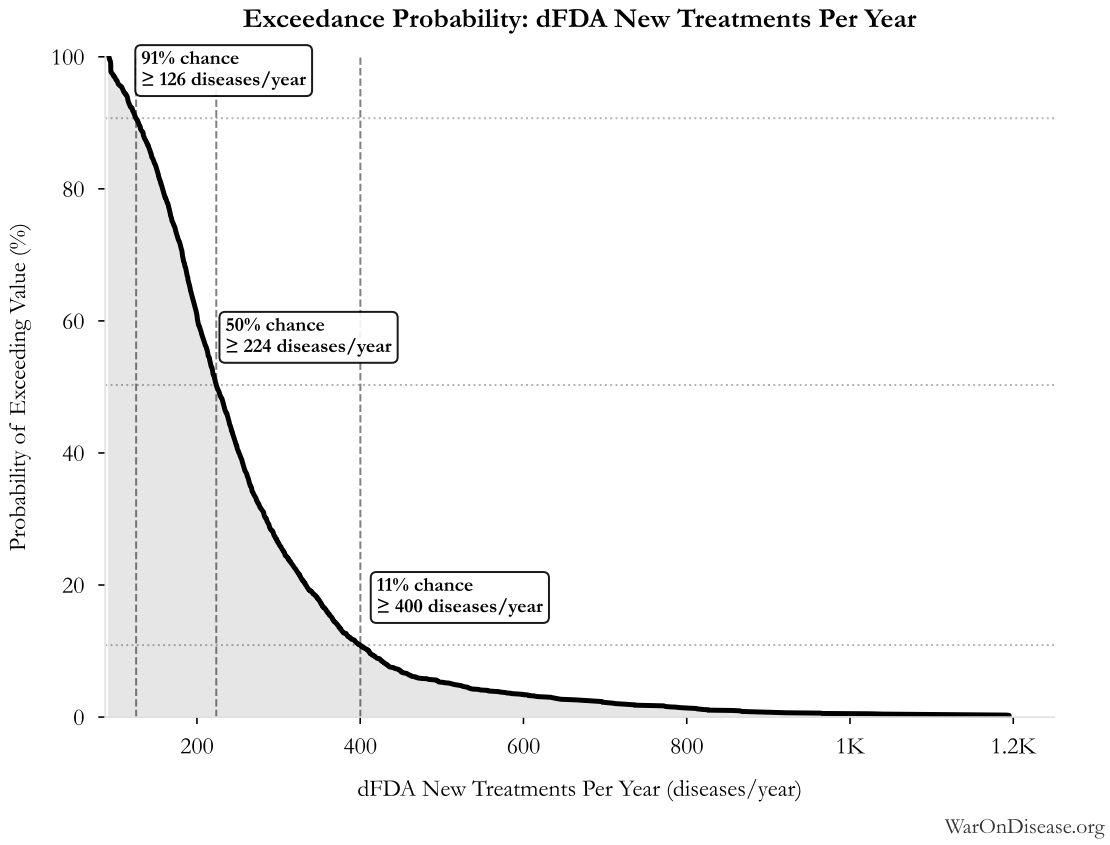


Figure 125: Probability of Exceeding Threshold: dFDA New Treatments Per Year

This exceedance probability chart shows the likelihood that dFDA New Treatments Per Year will exceed any given threshold. Higher curves indicate more favorable outcomes with greater certainty.

Decentralized Framework for Drug Assessment Annual Net Savings (R&D Only): $58.6B

Details

Annual net savings from R&D cost reduction only (gross savings minus operational costs, excludes regulatory delay value)

Inputs:

- Decentralized Framework for Drug Assessment Annual Benefit: R&D Savings : $58.6B
- Total Annual Decentralized Framework for Drug Assessment Operational Costs : $40M

$$
\begin{aligned}
&Savings_{RD,ann} \\
&= Benefit_{RD,ann} - OPEX_{dFDA} \\
&= \$58.6B - \$40M \\
&= \$58.6B
\end{aligned}
$$

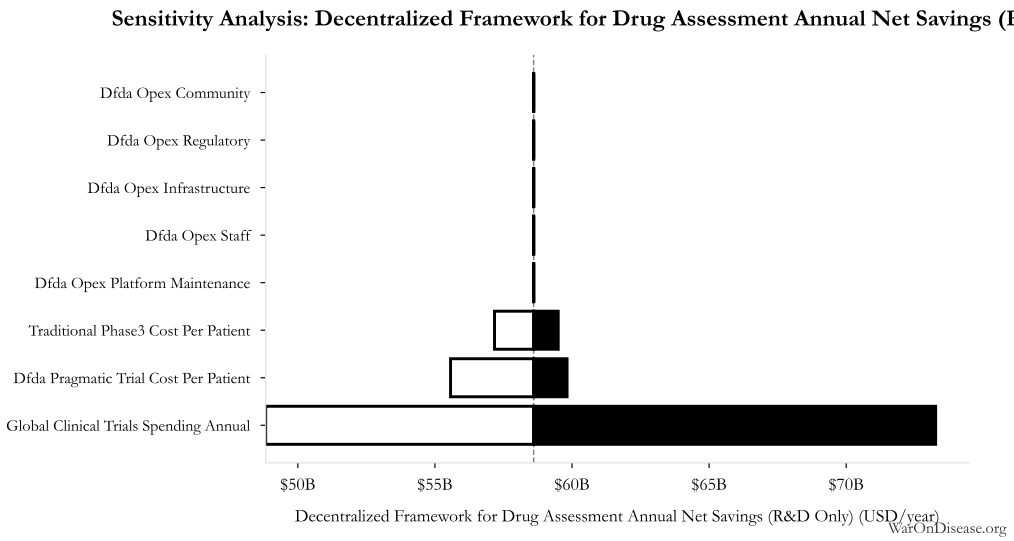
$$
\begin{aligned}
&\text{where } Benefit_{RD,ann} \\
&= Spending_{trials} \times Reduce_{pct} \\
&= \$60B \times 97.7\% \\
&= \$58.6B
\end{aligned}
$$

$$
\begin{aligned}
&\text{where } Reduce_{pct} \\
&= 1 - \frac{Cost_{pragmatic,pt}}{Cost_{P3,pt}} \\
&= 1 - \frac{\$929}{\$41K} \\
&= 97.7\%
\end{aligned}
$$

$$
\begin{aligned}
&\text{where } OPEX_{dFDA} \\
&= Cost_{platform} + Cost_{staff} + Cost_{infra} \\
&+ Cost_{regulatory} + Cost_{community} \\
&= \$15M + \$10M + \$8M + \$5M + \$2M \\
&= \$40M
\end{aligned}
$$

High confidence

Sensitivity Analysis



Sensitivity Indices for Decentralized Framework for Drug Assessment Annual Net Savings (R&D Only)

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

Input Parameter	Sensitivity Coefficient	Interpretation
dFDA Benefit R&D Only Annual	1.0011	Strong driver
dFDA Annual OPEX	-0.0011	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.

Monte Carlo Distribution

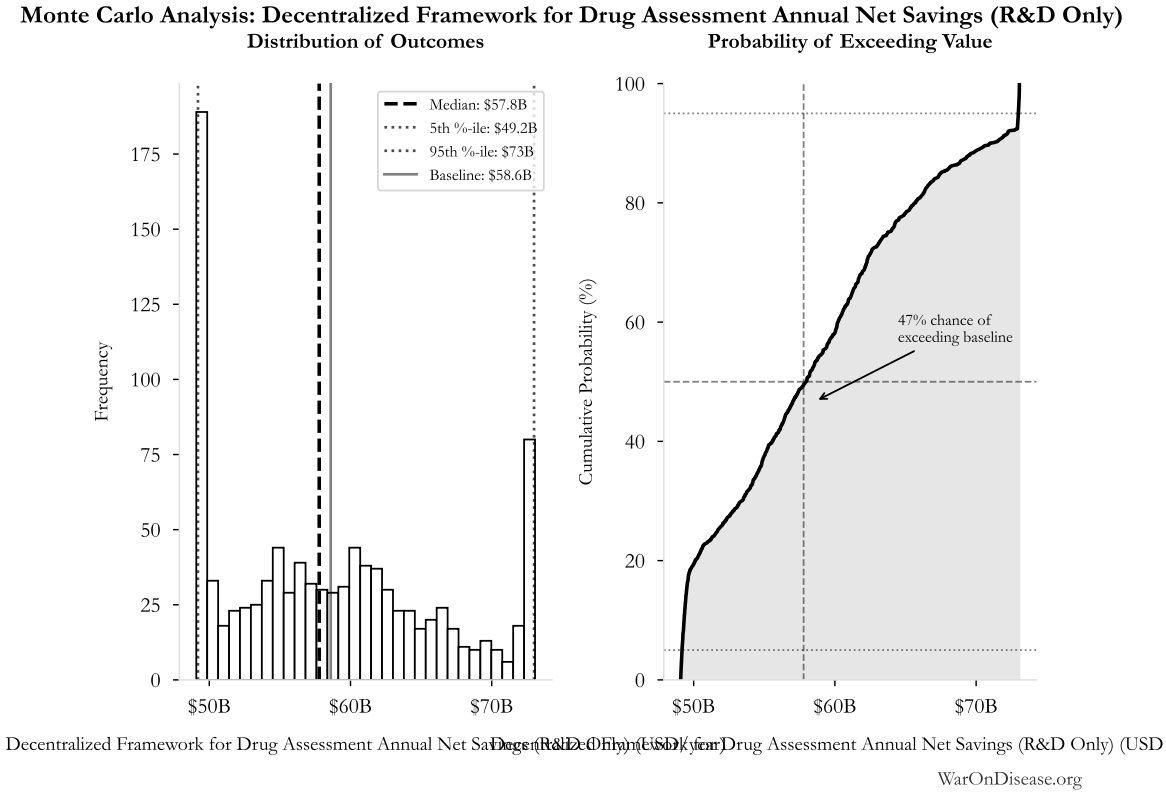


Figure 126: Monte Carlo Distribution: Decentralized Framework for Drug Assessment Annual Net Savings (R&D Only) (10,000 simulations)

Simulation Results Summary: Decentralized Framework for Drug Assessment Annual Net Savings (R&D Only)

Statistic	Value
Baseline (deterministic)	$58.6B
Mean (expected value)	$58.8B
Median (50th percentile)	$57.8B
Standard Deviation	$7.66B
90% Range (5th-95th percentile)	[$49.2B, $73B]

The histogram shows the distribution of Decentralized Framework for Drug Assessment Annual Net Savings (R&D Only) 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

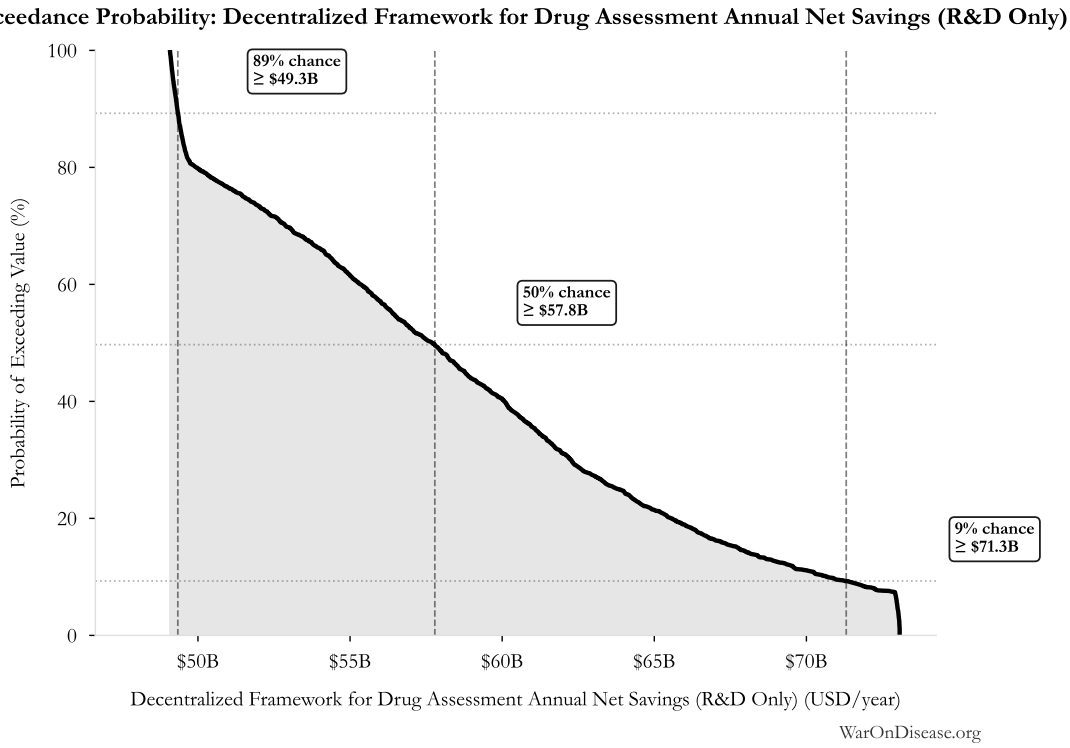


Figure 127: Probability of Exceeding Threshold: Decentralized Framework for Drug Assessment Annual Net Savings (R&D Only)

This exceedance probability chart shows the likelihood that Decentralized Framework for Drug Assessment Annual Net Savings (R&D Only) will exceed any given threshold. Higher curves indicate more favorable outcomes with greater certainty.

Decentralized Framework for Drug Assessment Total NPV Annual OPEX: $40M

Details

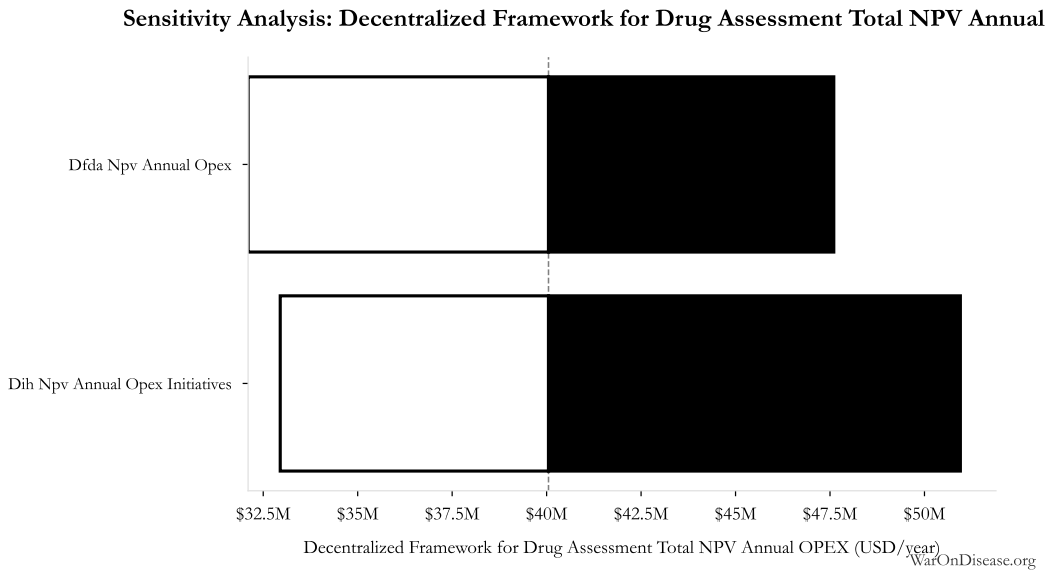
Total NPV annual opex (Decentralized Framework for Drug Assessment core + DIH initiatives)
Inputs:

- Decentralized Framework for Drug Assessment Core framework Annual OPEX: $18.9M (95% CI: $11M - $26.5M)
- DIH Broader Initiatives Annual OPEX: $21.1M (95% CI: $14M - $32M)

$$
\begin{aligned}
&OPEX_{total} \\
&= OPEX_{ann} + OPEX_{DIH,ann} \\
&= \$18.9M + \$21.1M \\
&= \$40M
\end{aligned}
$$

High confidence

Sensitivity Analysis



Sensitivity Indices for Decentralized Framework for Drug Assessment Total NPV Annual OPEX

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

Input Parameter	Sensitivity Coefficient	Interpretation
DIH NPV Annual OPEX Initiatives	0.5419	Strong driver
dFDA NPV Annual OPEX	0.4592	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

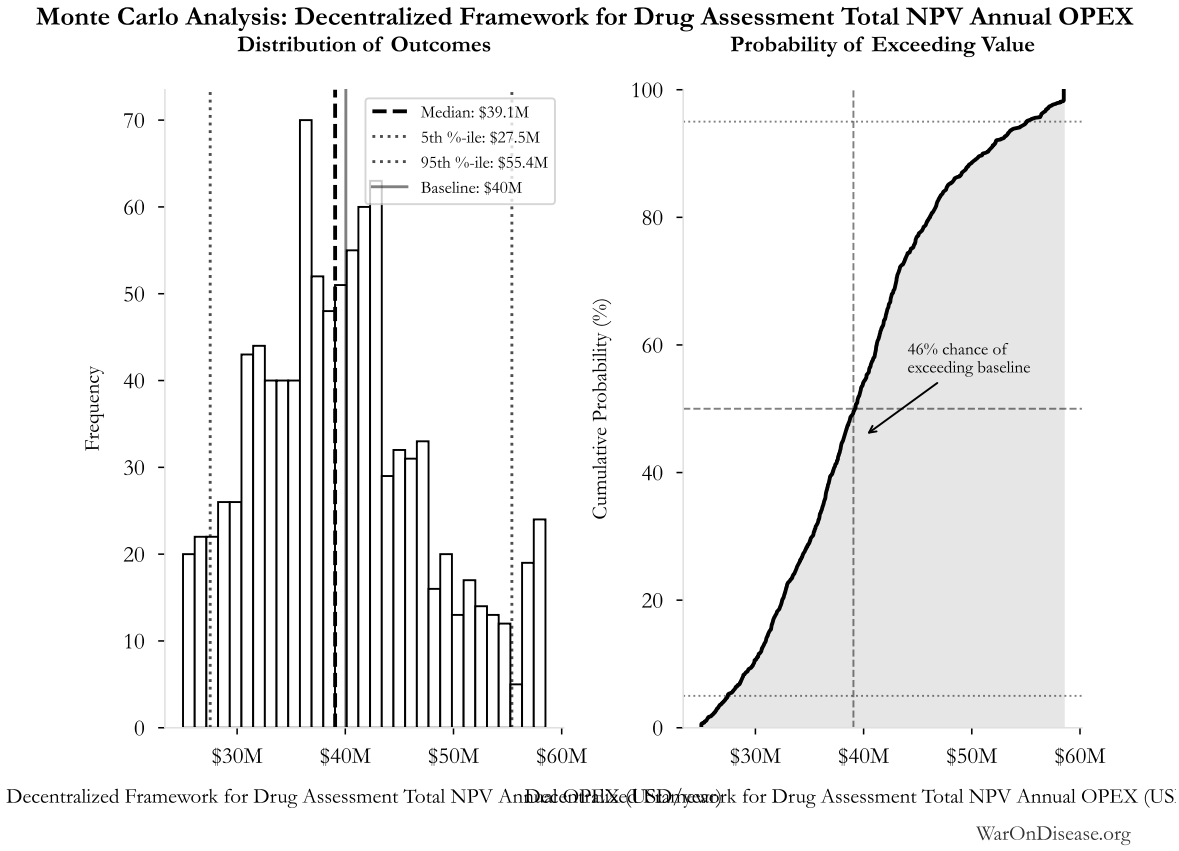


Figure 128: Monte Carlo Distribution: Decentralized Framework for Drug Assessment Total NPV Annual OPEX (10,000 simulations)

Simulation Results Summary: Decentralized Framework for Drug Assessment Total NPV Annual OPEX

Statistic	Value
Baseline (deterministic)	$40M
Mean (expected value)	$39.9M
Median (50th percentile)	$39.1M
Standard Deviation	$8.04M
90% Range (5th-95th percentile)	[$27.5M, $55.4M]

The histogram shows the distribution of Decentralized Framework for Drug Assessment Total NPV Annual OPEX 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

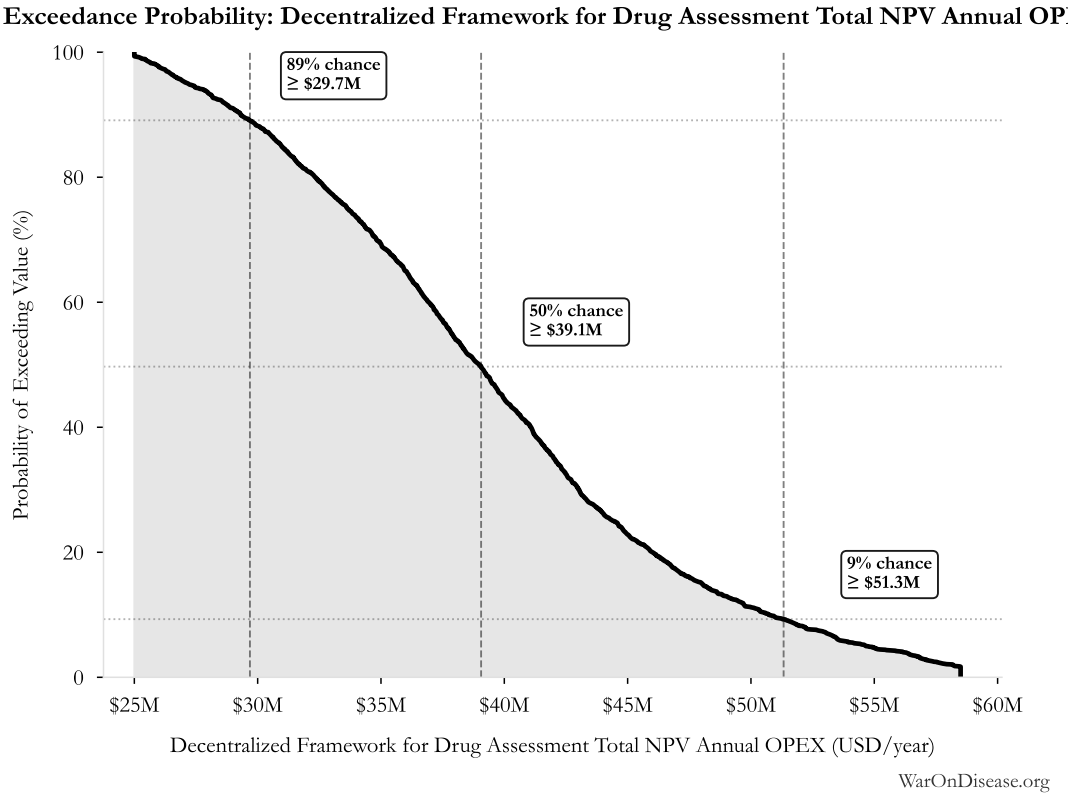


Figure 129: Probability of Exceeding Threshold: Decentralized Framework for Drug Assessment Total NPV Annual OPEX

This exceedance probability chart shows the likelihood that Decentralized Framework for Drug Assessment Total NPV Annual OPEX will exceed any given threshold. Higher curves indicate more favorable outcomes with greater certainty.

NPV of Decentralized Framework for Drug Assessment Benefits (R&D Only, 10-Year Discounted): $389B

Details

NPV of Decentralized Framework for Drug Assessment R&D savings only with 5-year adoption ramp (10-year horizon, most conservative financial estimate)

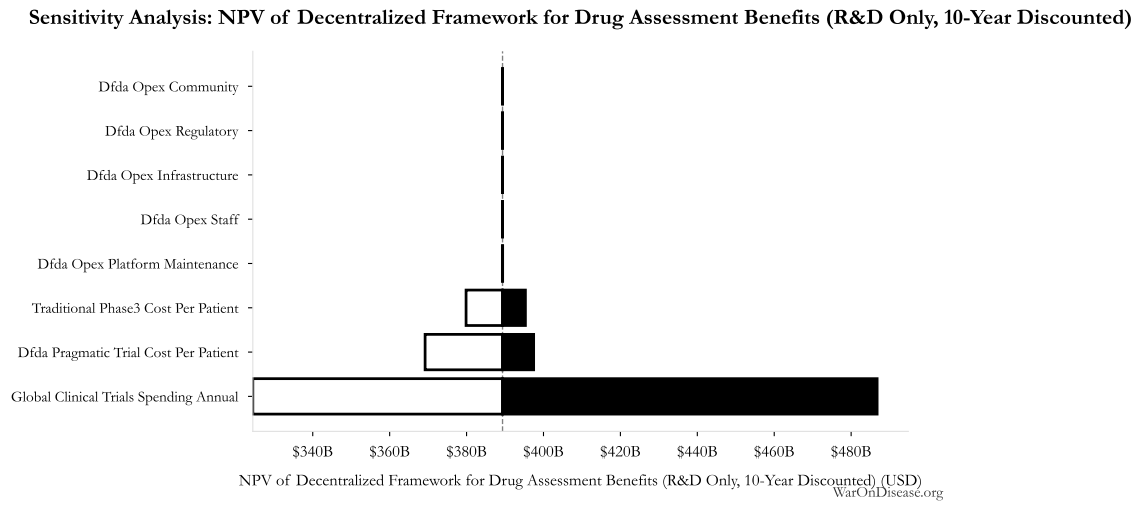
Inputs:

- Decentralized Framework for Drug Assessment Annual Net Savings (R&D Only) : $58.6B
- Standard Discount Rate for NPV Analysis: 3%

$$NPV_{RD} = \sum_{t=1}^{10} \frac{Savings_{RD,ann} \times \frac{\min(t,5)}{5}}{(1+r)^t}$$

High confidence

Sensitivity Analysis



Sensitivity Indices for NPV of Decentralized Framework for Drug Assessment Benefits (R&D Only, 10-Year Discounted)

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

Input Parameter	Sensitivity Coefficient	Interpretation
dFDA Net Savings R&D Only Annual	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

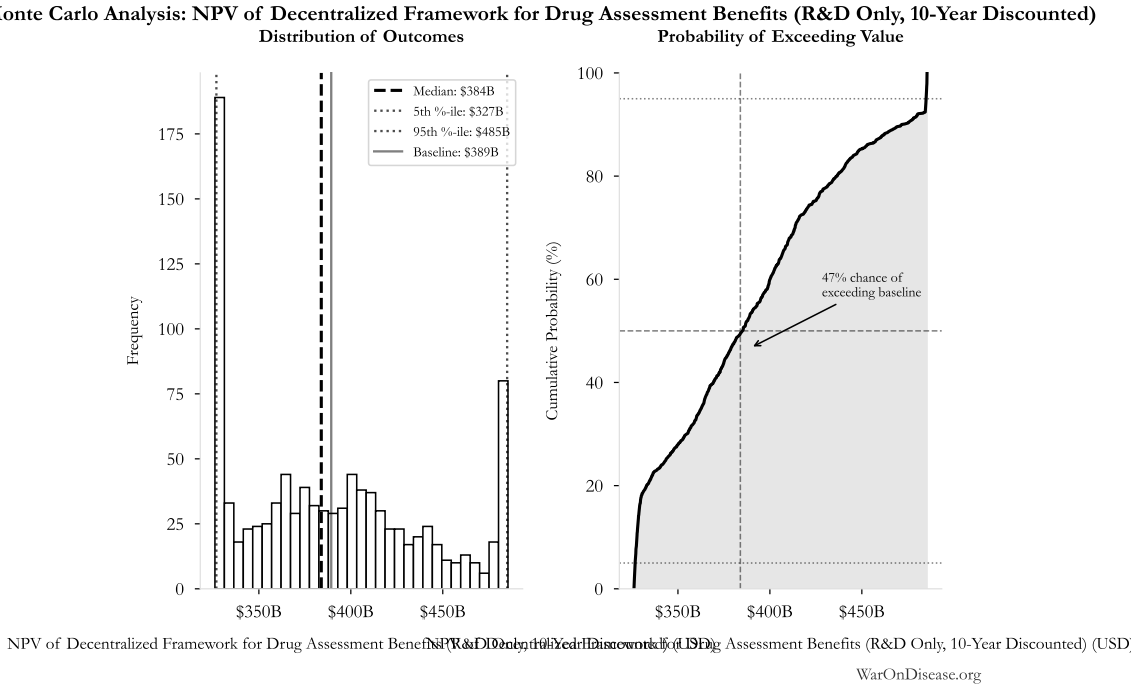


Figure 130: Monte Carlo Distribution: NPV of Decentralized Framework for Drug Assessment Benefits (R&D Only, 10-Year Discounted) (10,000 simulations)

Simulation Results Summary: NPV of Decentralized Framework for Drug Assessment Benefits (R&D Only, 10-Year Discounted)

Statistic	Value
Baseline (deterministic)	$389B
Mean (expected value)	$391B
Median (50th percentile)	$384B
Standard Deviation	$50.9B
90% Range (5th-95th percentile)	[$327B, $485B]

The histogram shows the distribution of NPV of Decentralized Framework for Drug Assessment Benefits (R&D Only, 10-Year Discounted) 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

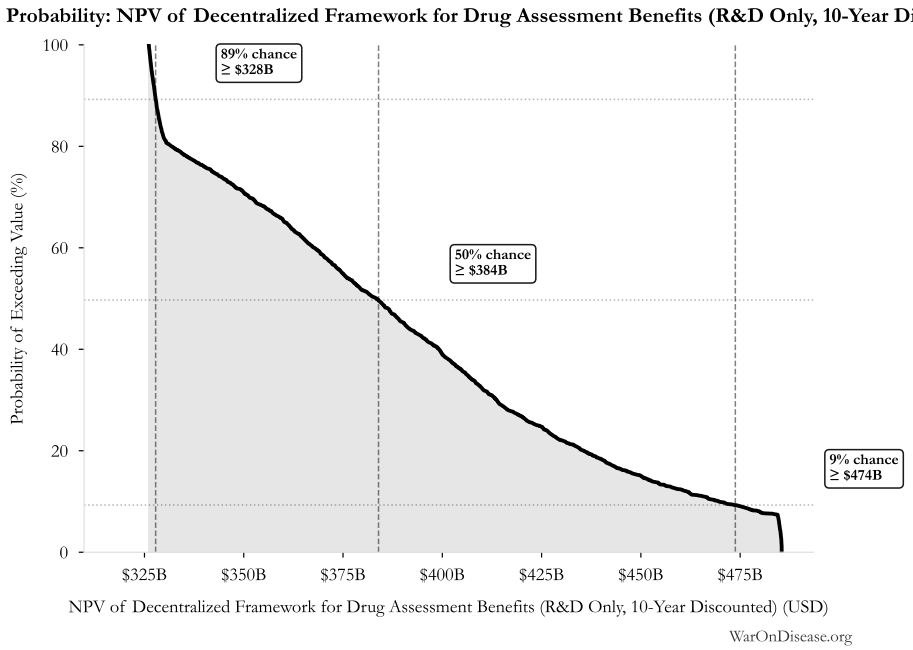


Figure 131: Probability of Exceeding Threshold: NPV of Decentralized Framework for Drug Assessment Benefits (R&D Only, 10-Year Discounted)

This exceedance probability chart shows the likelihood that NPV of Decentralized Framework for Drug Assessment Benefits (R&D Only, 10-Year Discounted) will exceed any given threshold. Higher curves indicate more favorable outcomes with greater certainty.

NPV Net Benefit (R&D Only): $389B

Details

NPV net benefit using R&D savings only (benefits minus costs)
Inputs:

- NPV of Decentralized Framework for Drug Assessment Benefits (R&D Only, 10-Year Discounted) : $389B
- Decentralized Framework for Drug Assessment Total NPV Cost : $611M

$$NPV_{net,RD}$$
$$= NPV_{RD} - Cost_{dFDA,total}$$
$$= \$389B - \$611M$$
$$= \$389B$$

$$\text{where } NPV_{RD} = \sum_{t=1}^{10} \frac{Savings_{RD,ann} \times \frac{\min(t,5)}{5}}{(1+r)^t}$$

$$\text{where } Savings_{RD,ann}$$
$$= Benefit_{RD,ann} - OPEX_{dFDA}$$
$$= \$58.6B - \$40M$$
$$= \$58.6B$$

$$\text{where } Benefit_{RD,ann}$$
$$= Spending_{trials} \times Reduce_{pct}$$
$$= \$60B \times 97.7\%$$
$$= \$58.6B$$

$$\text{where } Reduce_{pct}$$
$$= 1 - \frac{Cost_{pragmatic,pt}}{Cost_{P3,pt}}$$
$$= 1 - \frac{\$929}{\$41K}$$
$$= 97.7\%$$

$$\text{where } OPEX_{dFDA}$$
$$= Cost_{platform} + Cost_{staff} + Cost_{infra}$$
$$+ Cost_{regulatory} + Cost_{community}$$
$$= \$15M + \$10M + \$8M + \$5M + \$2M$$
$$= \$40M$$

$$\text{where } Cost_{dFDA,total}$$
$$= PV_{OPEX} + Cost_{upfront,total}$$
$$= \$342M + \$270M$$
$$= \$611M$$

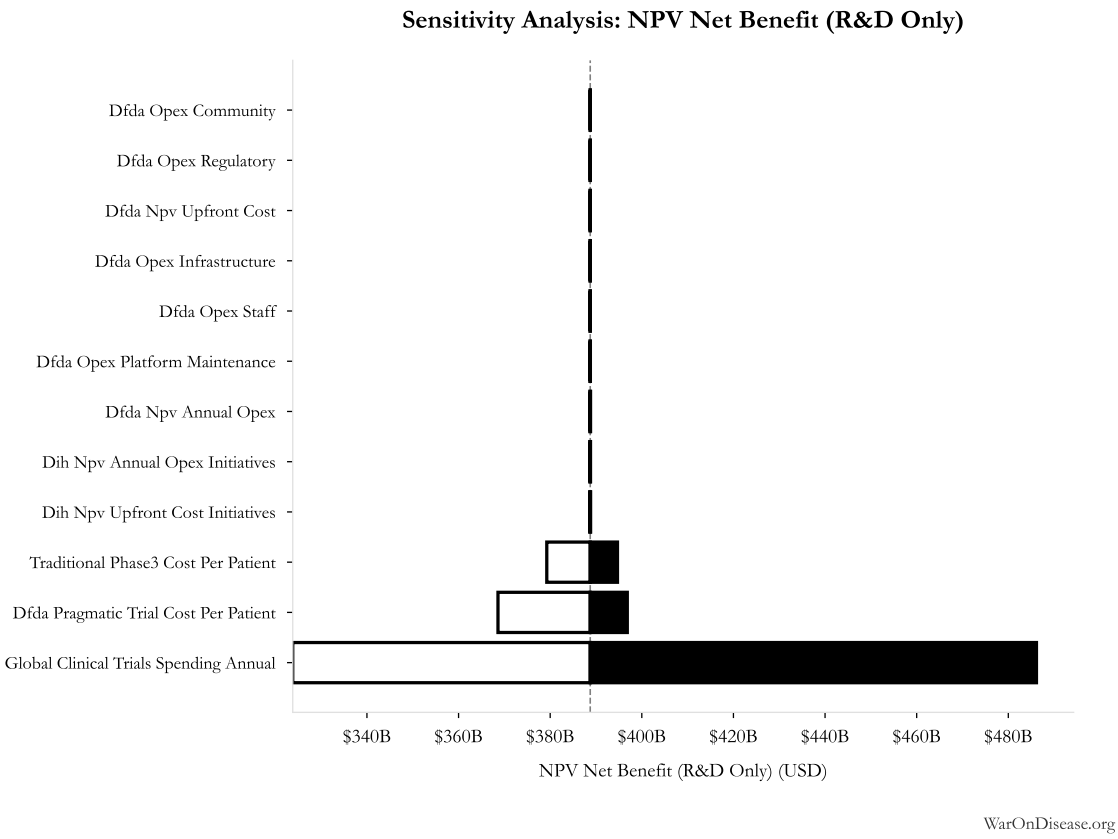
$$\text{where } PV_{OPEX} = OPEX_{ann} \times \frac{1-(1+r)^{-T}}{r}$$

$$\text{where } OPEX_{total}$$
$$= OPEX_{ann} + OPEX_{DIH,ann}$$
$$= \$18.9M + \$21.1M$$
$$= \$40M$$

$$\text{where } Cost_{upfront,total}$$
$$= Cost_{upfront} + Cost_{DIH,init}$$
$$= \$40M + \$230M$$
$$= \$270M$$

High confidence

Sensitivity Analysis



Sensitivity Indices for NPV Net Benefit (R&D Only)

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

Input Parameter	Sensitivity Coefficient	Interpretation
dFDA NPV Benefit R&D Only	1.0025	Strong driver
dFDA NPV Total Cost	-0.0025	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.

Monte Carlo Distribution

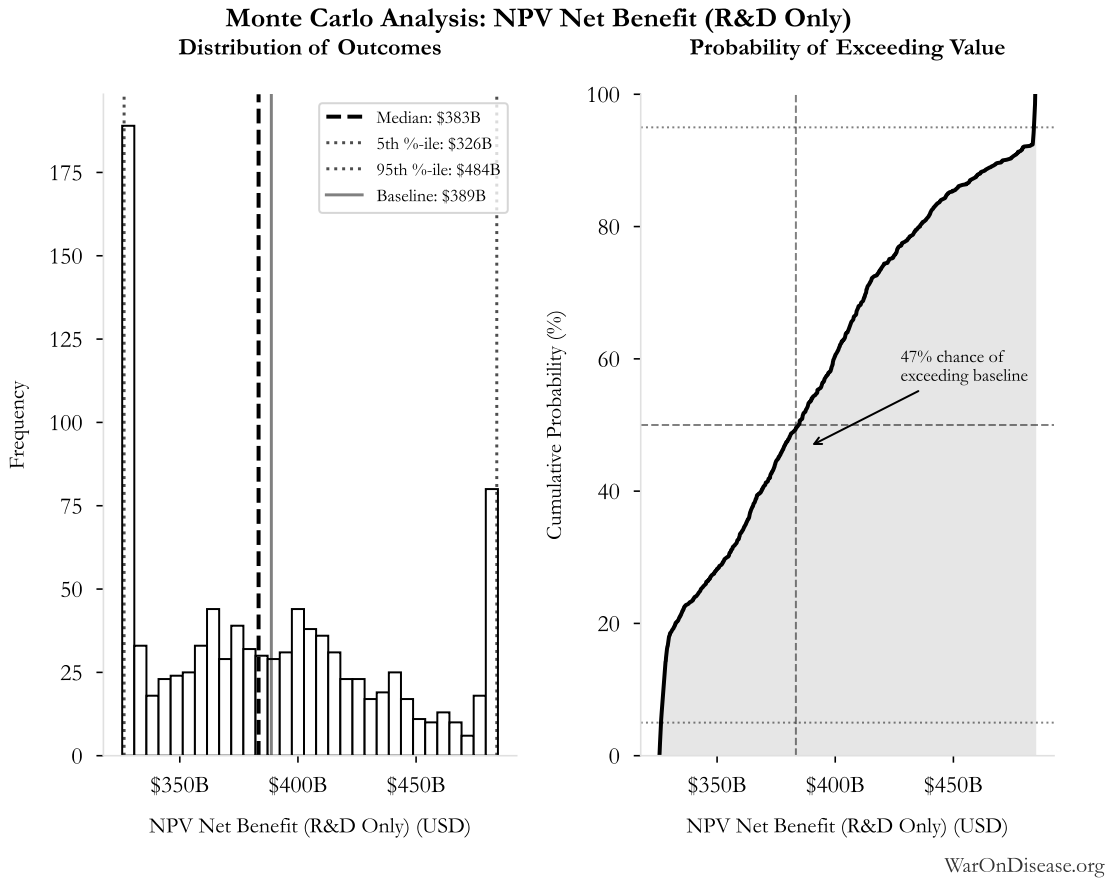


Figure 132: Monte Carlo Distribution: NPV Net Benefit (R&D Only) (10,000 simulations)

Simulation Results Summary: NPV Net Benefit (R&D Only)

Statistic	Value
Baseline (deterministic)	$389B
Mean (expected value)	$390B
Median (50th percentile)	$383B
Standard Deviation	$50.7B
90% Range (5th-95th percentile)	[$326B, $484B]

The histogram shows the distribution of NPV Net Benefit (R&D Only) 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

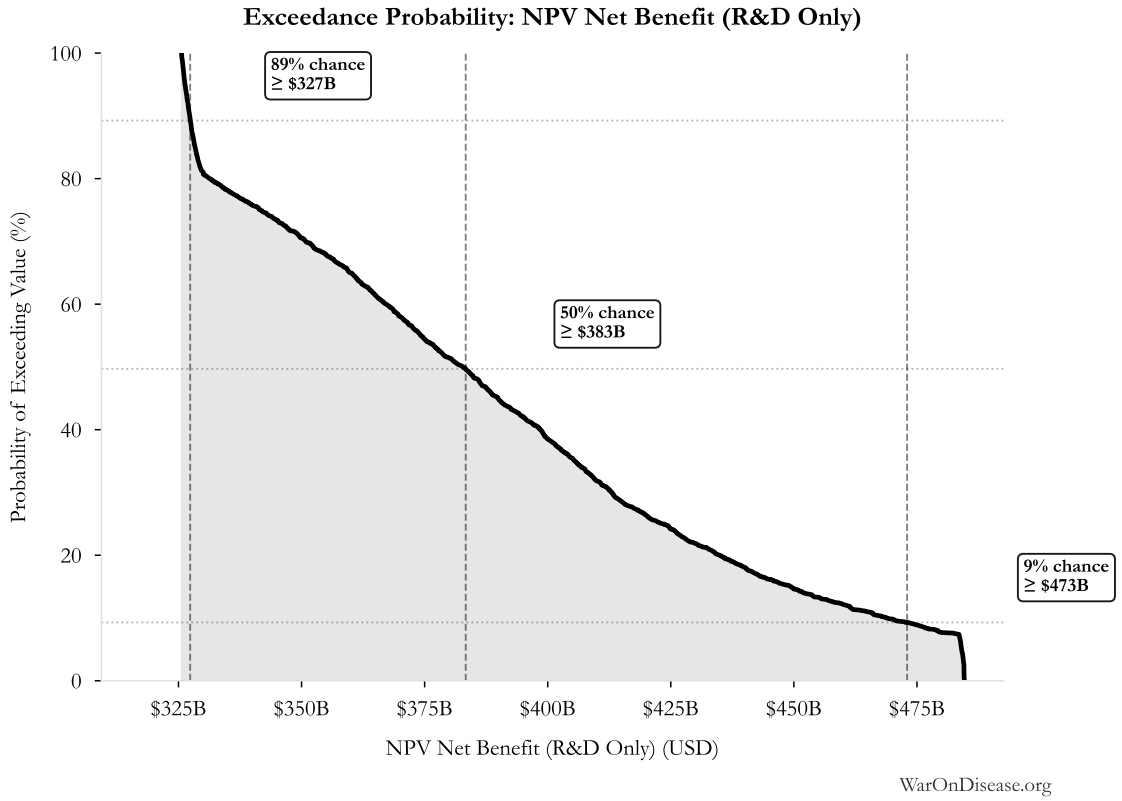


Figure 133: Probability of Exceeding Threshold: NPV Net Benefit (R&D Only)

This exceedance probability chart shows the likelihood that NPV Net Benefit (R&D Only) will exceed any given threshold. Higher curves indicate more favorable outcomes with greater certainty.

Decentralized Framework for Drug Assessment Present Value of Annual OPEX Over 10 Years: $342M

Details

Present value of annual opex over 10 years (NPV formula)
Inputs:

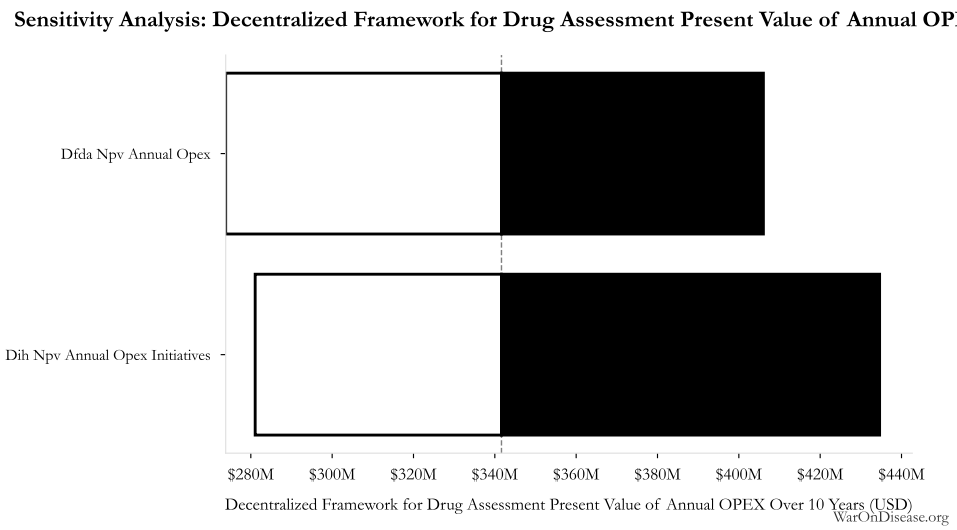
- Decentralized Framework for Drug Assessment Total NPV Annual OPEX : $40M
- Standard Discount Rate for NPV Analysis: 3%

- Standard Time Horizon for NPV Analysis: 10 years

$$PV_{OPEX} = OPEX_{ann} \times \frac{1-(1+r)^{-T}}{r}$$

High confidence

Sensitivity Analysis



Sensitivity Indices for Decentralized Framework for Drug Assessment Present Value of Annual OPEX Over 10 Years

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

Input Parameter	Sensitivity Coefficient	Interpretation
dFDA NPV Annual OPEX Total	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

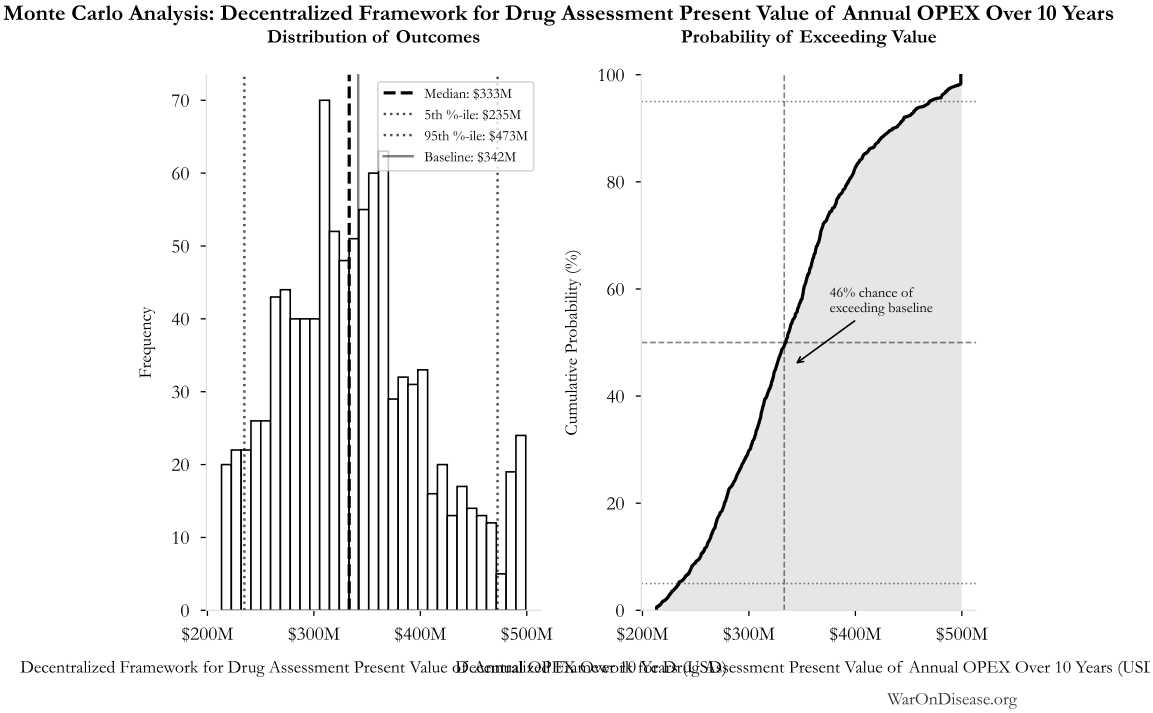


Figure 134: Monte Carlo Distribution: Decentralized Framework for Drug Assessment Present Value of Annual OPEX Over 10 Years (10,000 simulations)

Simulation Results Summary: Decentralized Framework for Drug Assessment Present Value of Annual OPEX Over 10 Years

Statistic	Value
Baseline (deterministic)	$342M
Mean (expected value)	$340M
Median (50th percentile)	$333M
Standard Deviation	$68.6M
90% Range (5th-95th percentile)	[$235M, $473M]

The histogram shows the distribution of Decentralized Framework for Drug Assessment Present Value of Annual OPEX Over 10 Years 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

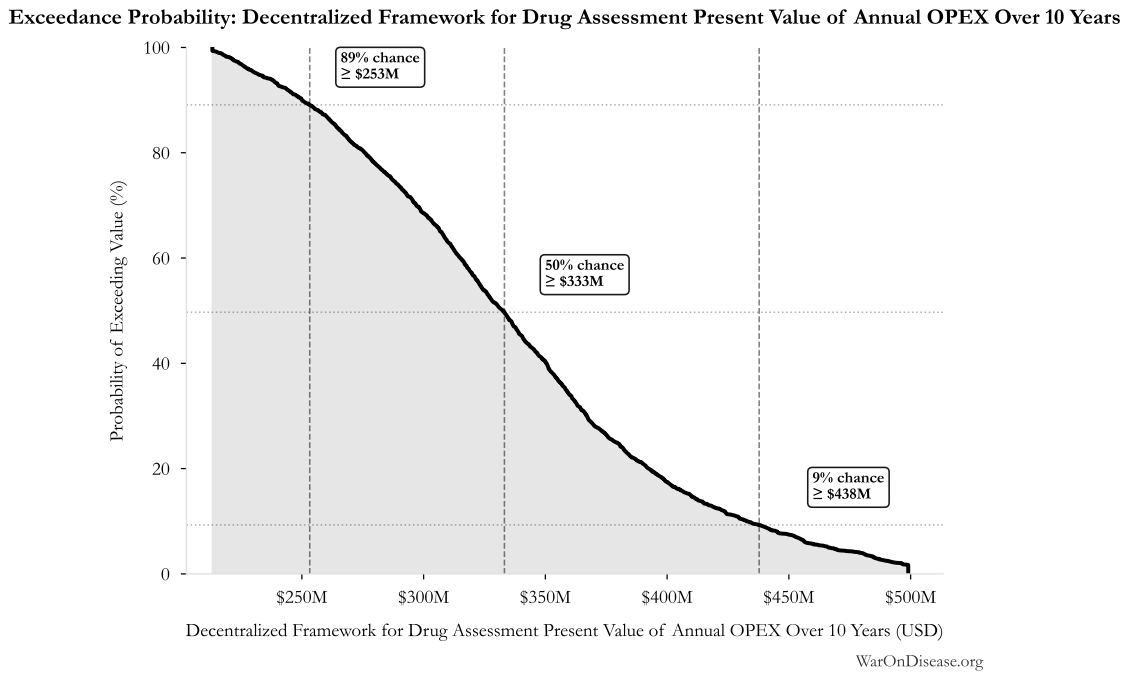


Figure 135: Probability of Exceeding Threshold: Decentralized Framework for Drug Assessment Present Value of Annual OPEX Over 10 Years

This exceedance probability chart shows the likelihood that Decentralized Framework for Drug Assessment Present Value of Annual OPEX Over 10 Years will exceed any given threshold. Higher curves indicate more favorable outcomes with greater certainty.

Decentralized Framework for Drug Assessment Total NPV Cost: $611M

Details

Total NPV cost (upfront + PV of annual opex)
Inputs:

- Decentralized Framework for Drug Assessment Present Value of Annual OPEX Over 10 Years : $342M
- Decentralized Framework for Drug Assessment Total NPV Upfront Costs : $270M

$$
\begin{aligned}
&Cost_{dFDA,total} \\
&= PV_{OPEX} + Cost_{upfront,total} \\
&= \$342M + \$270M \\
&= \$611M
\end{aligned}
$$

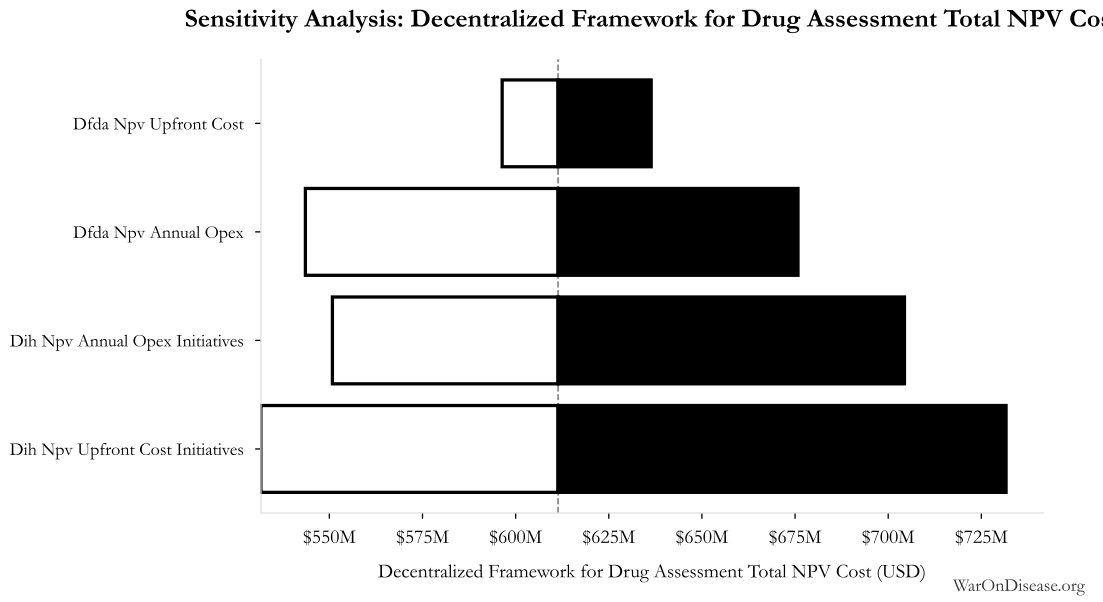
$$
\text{where } PV_{OPEX} = OPEX_{ann} \times \frac{1-(1+r)^{-T}}{r}
$$

$$
\begin{aligned}
&\text{where } OPEX_{total} \\
&= OPEX_{ann} + OPEX_{DIH,ann} \\
&= \$18.9M + \$21.1M \\
&= \$40M
\end{aligned}
$$

$$
\begin{aligned}
&\text{where } Cost_{upfront,total} \\
&= Cost_{upfront} + Cost_{DIH,init} \\
&= \$40M + \$230M \\
&= \$270M
\end{aligned}
$$

High confidence

Sensitivity Analysis



Sensitivity Indices for Decentralized Framework for Drug Assessment Total NPV Cost

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

Input Parameter	Sensitivity Coefficient	Interpretation
dFDA NPV Pv Annual OPEX	0.5417	Strong driver
dFDA NPV Upfront Cost Total	0.4585	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

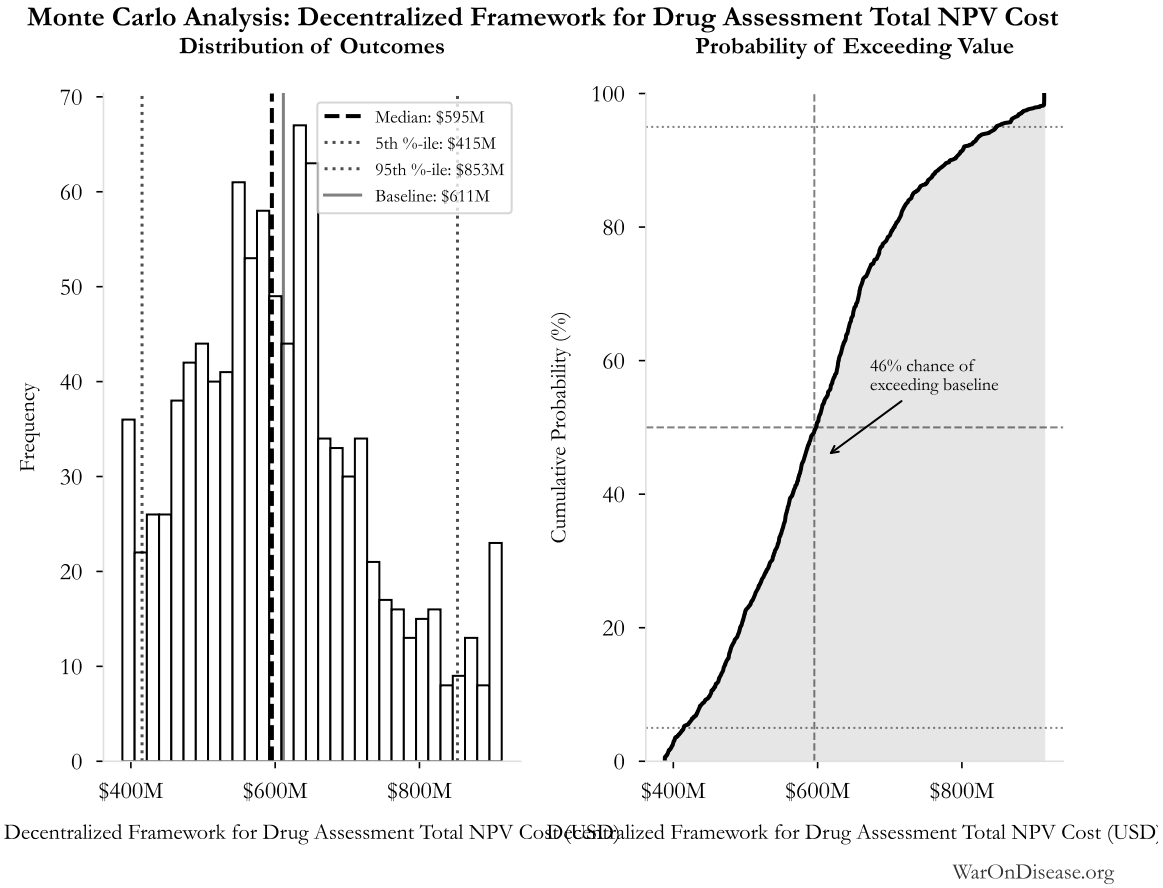


Figure 136: Monte Carlo Distribution: Decentralized Framework for Drug Assessment Total NPV Cost (10,000 simulations)

Simulation Results Summary: Decentralized Framework for Drug Assessment Total NPV Cost

Statistic	Value
Baseline (deterministic)	$611M
Mean (expected value)	$609M
Median (50th percentile)	$595M
Standard Deviation	$127M
90% Range (5th-95th percentile)	[$415M, $853M]

The histogram shows the distribution of Decentralized Framework for Drug Assessment Total NPV Cost 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

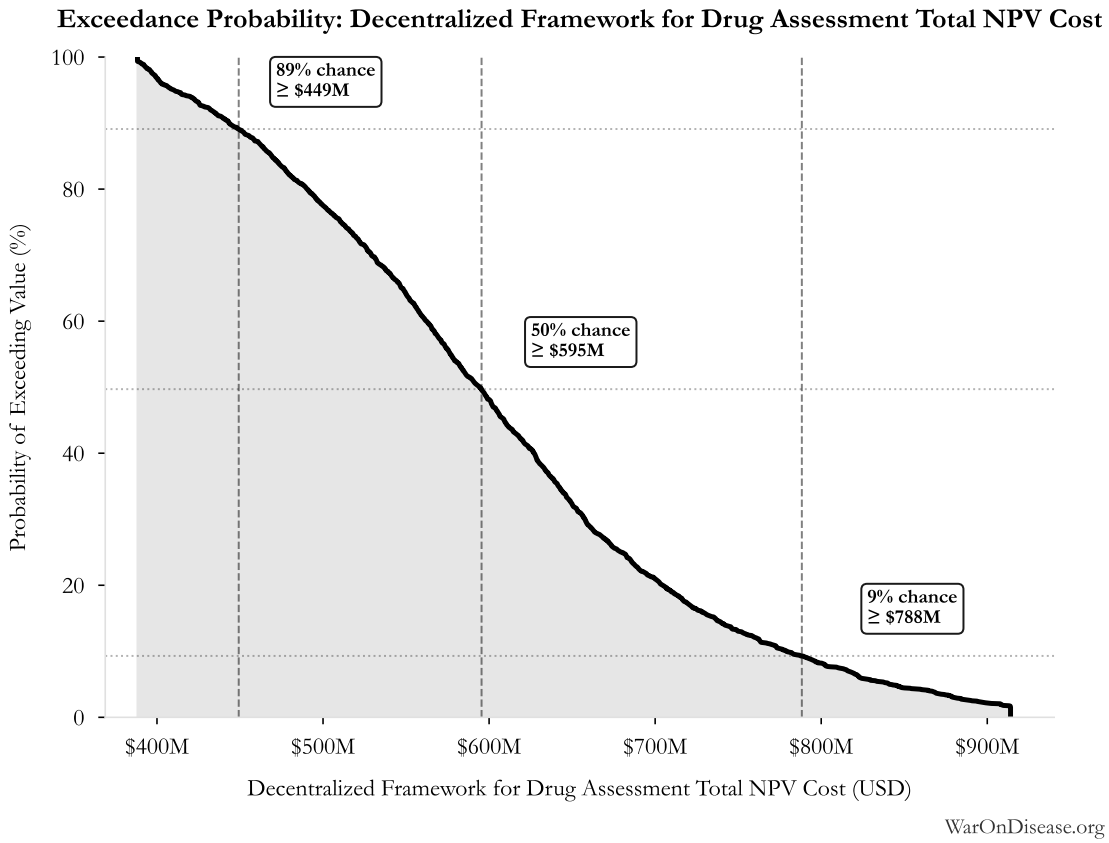


Figure 137: Probability of Exceeding Threshold: Decentralized Framework for Drug Assessment Total NPV Cost

This exceedance probability chart shows the likelihood that Decentralized Framework for Drug Assessment Total NPV Cost will exceed any given threshold. Higher curves indicate more favorable outcomes with greater certainty.

Decentralized Framework for Drug Assessment Total NPV Upfront Costs: $270M

Details

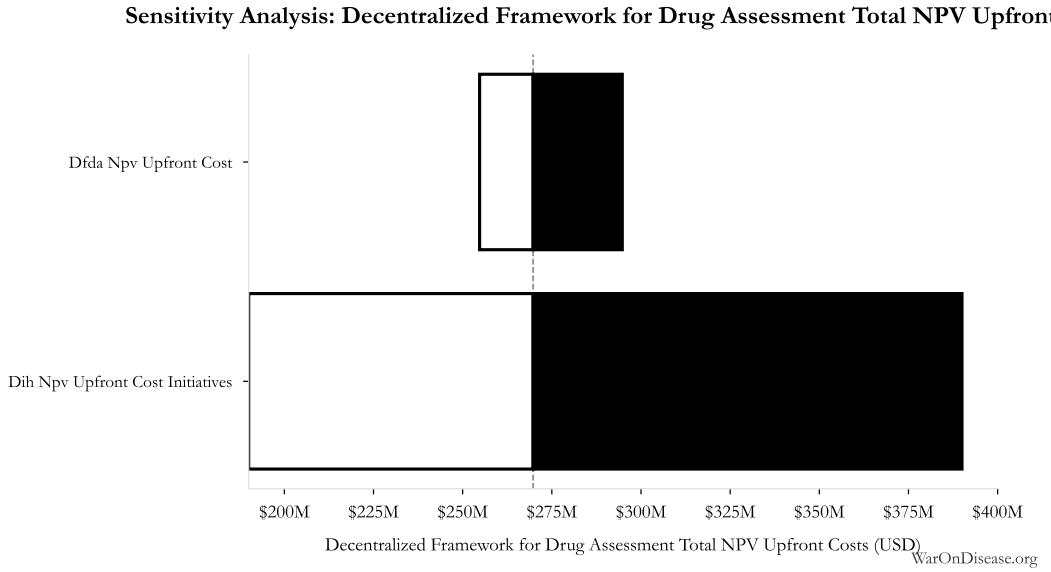
Total NPV upfront costs (Decentralized Framework for Drug Assessment core + DIH initiatives)
Inputs:

- Decentralized Framework for Drug Assessment Core framework Build Cost: $40M (95% CI: $25M - $65M)
- DIH Broader Initiatives Upfront Cost: $230M (95% CI: $150M - $350M)

$$\begin{aligned} & Cost_{upfront,total} \\ &= Cost_{upfront} + Cost_{DIH,init} \\ &= \$40M + \$230M \\ &= \$270M \end{aligned}$$

High confidence

Sensitivity Analysis



Sensitivity Indices for Decentralized Framework for Drug Assessment Total NPV Upfront Costs

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

Input Parameter	Sensitivity Coefficient	Interpretation
DIH NPV Upfront Cost Initiatives	0.8338	Strong driver
dFDA NPV Upfront Cost	0.1662	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

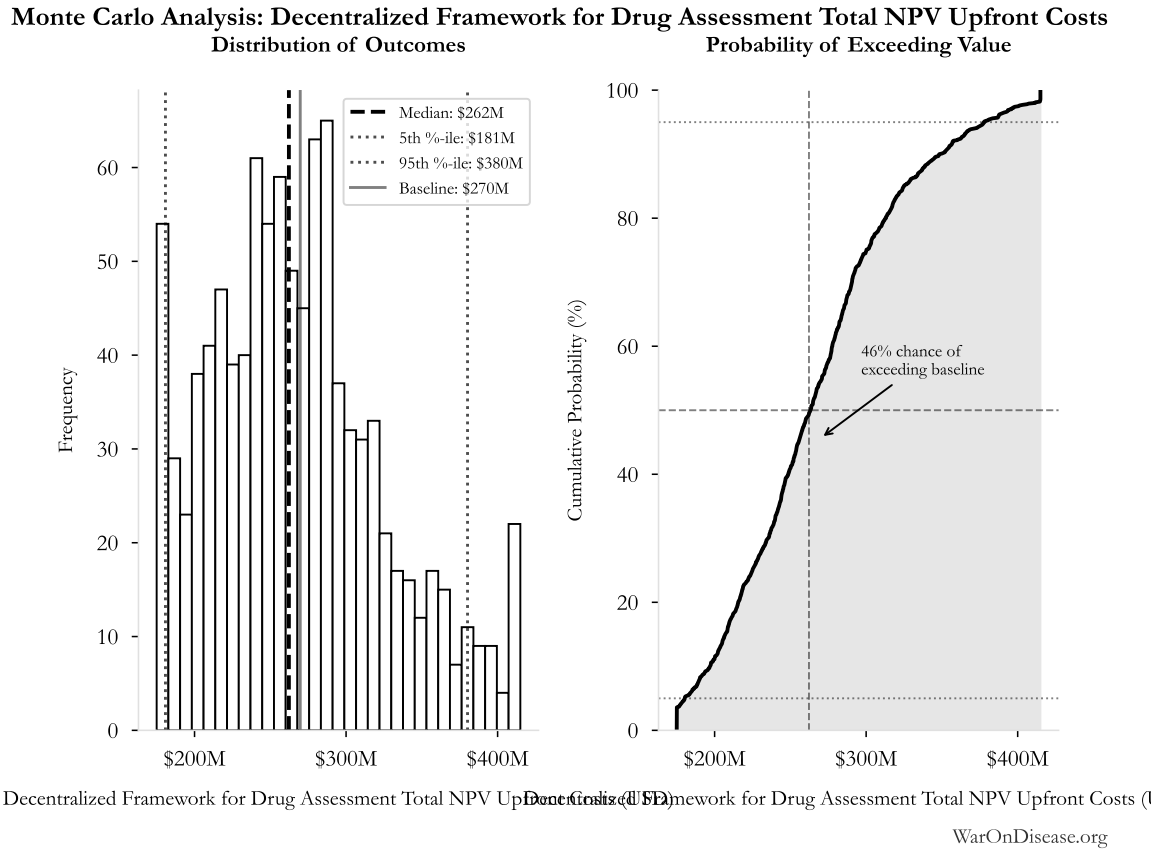


Figure 138: Monte Carlo Distribution: Decentralized Framework for Drug Assessment Total NPV Upfront Costs (10,000 simulations)

Simulation Results Summary: Decentralized Framework for Drug Assessment Total NPV Upfront Costs

Statistic	Value
Baseline (deterministic)	$270M
Mean (expected value)	$269M
Median (50th percentile)	$262M
Standard Deviation	$58.1M
90% Range (5th-95th percentile)	[$181M, $380M]

The histogram shows the distribution of Decentralized Framework for Drug Assessment Total NPV Upfront Costs 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

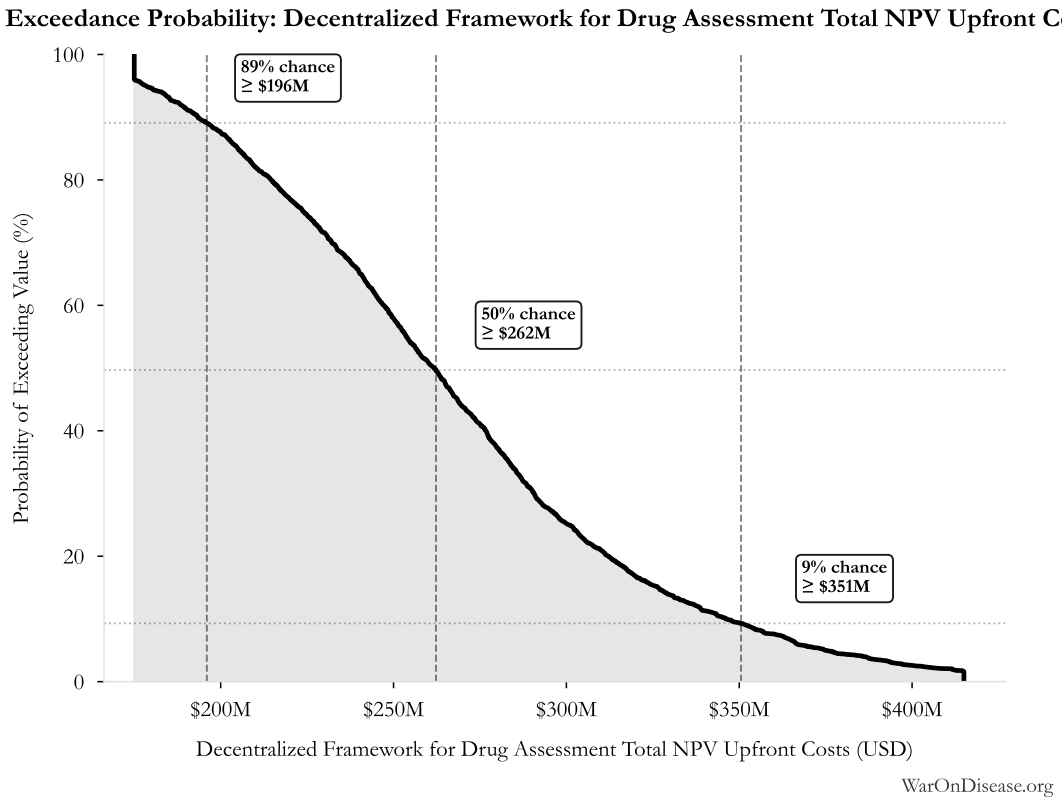


Figure 139: Probability of Exceeding Threshold: Decentralized Framework for Drug Assessment Total NPV Upfront Costs

This exceedance probability chart shows the likelihood that Decentralized Framework for Drug Assessment Total NPV Upfront Costs will exceed any given threshold. Higher curves indicate more favorable outcomes with greater certainty.

Decentralized Framework for Drug Assessment Overhead Percentage of Treaty Funding: 0.147%

Details

Percentage of treaty funding allocated to Decentralized Framework for Drug Assessment framework overhead

Inputs:

- Total Annual Decentralized Framework for Drug Assessment Operational Costs : $40M
- Annual Funding from 1% of Global Military Spending Redirected to DIH : $27.2B

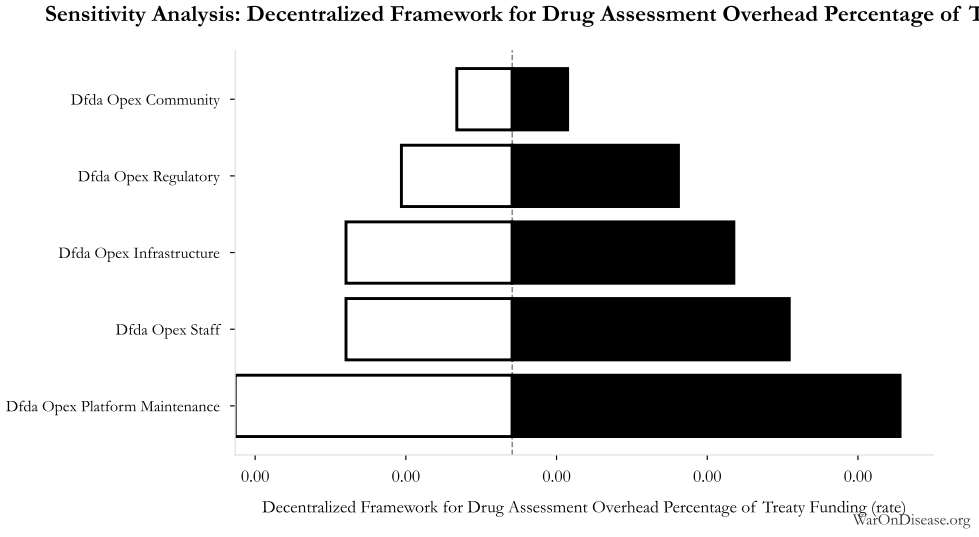
$$OPEX_{pct} = \frac{OPEX_{dFDA}}{Funding_{treaty}} = \frac{\$40M}{\$27.2B} = 0.147\%$$

$$\begin{aligned} &\text{where } OPEX_{dFDA} \\ &= Cost_{platform} + Cost_{staff} + Cost_{infra} \\ &+ Cost_{regulatory} + Cost_{community} \\ &= \$15M + \$10M + \$8M + \$5M + \$2M \\ &= \$40M \end{aligned}$$

$$\begin{aligned} &\text{where } Funding_{treaty} \\ &= Spending_{mil} \times Reduce_{treaty} \\ &= \$2.72T \times 1\% \\ &= \$27.2B \end{aligned}$$

High confidence

Sensitivity Analysis



Sensitivity Indices for Decentralized Framework for Drug Assessment Overhead Percentage of Treaty Funding

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

Input Parameter	Sensitivity Coefficient	Interpretation
dFDA Annual OPEX	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

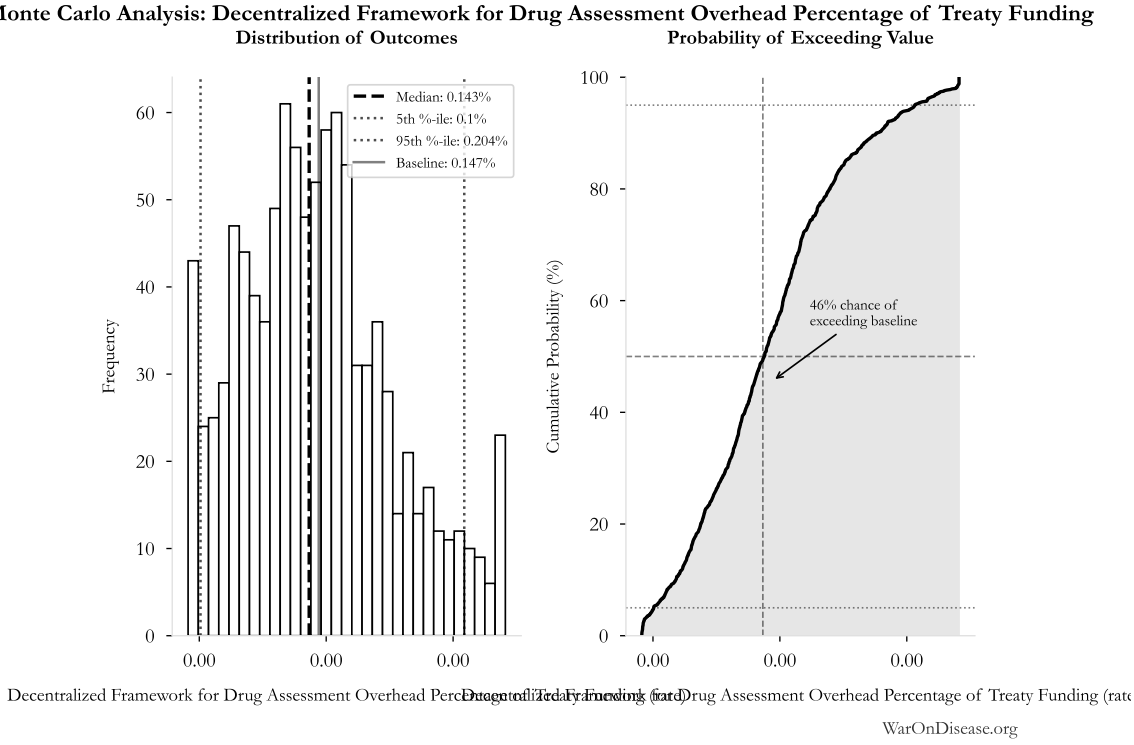


Figure 140: Monte Carlo Distribution: Decentralized Framework for Drug Assessment Overhead Percentage of Treaty Funding (10,000 simulations)

Simulation Results Summary: Decentralized Framework for Drug Assessment Overhead Percentage of Treaty Funding

Statistic	Value
Baseline (deterministic)	0.147%
Mean (expected value)	0.147%
Median (50th percentile)	0.143%
Standard Deviation	0.0302%
90% Range (5th-95th percentile)	[0.1%, 0.204%]

The histogram shows the distribution of Decentralized Framework for Drug Assessment Overhead Percentage of Treaty Funding 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

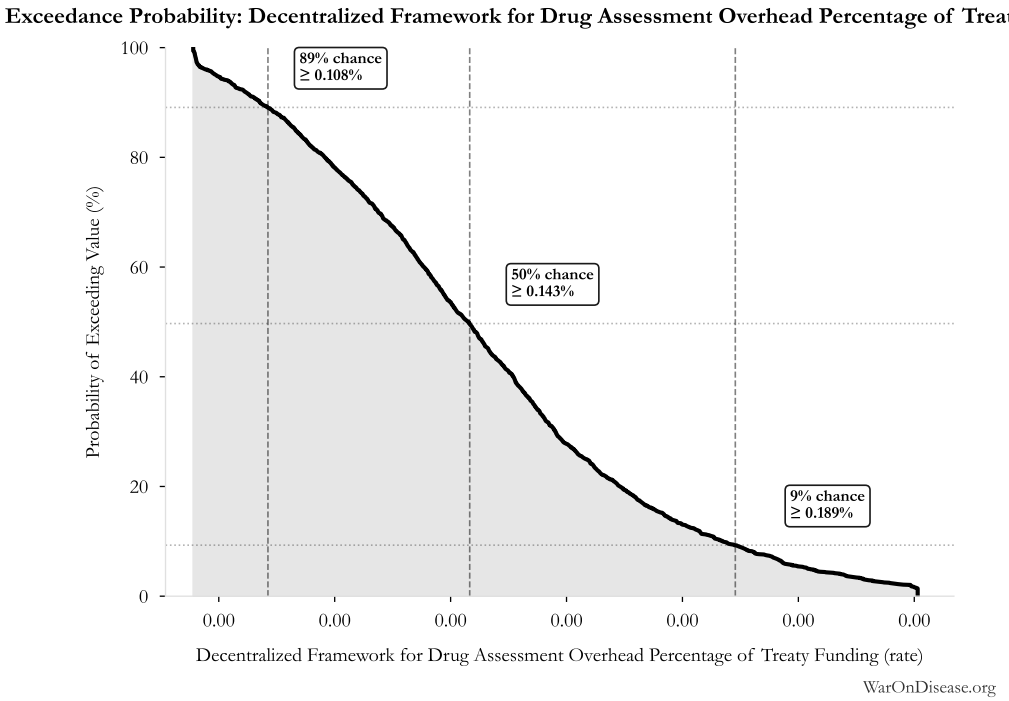


Figure 141: Probability of Exceeding Threshold: Decentralized Framework for Drug Assessment Overhead Percentage of Treaty Funding

This exceedance probability chart shows the likelihood that Decentralized Framework for Drug Assessment Overhead Percentage of Treaty Funding will exceed any given threshold. Higher curves indicate more favorable outcomes with greater certainty.

dFDA Therapeutic Space Exploration Time: 36 years

Details

Years to explore the entire therapeutic search space with dFDA implementation. At increased discovery rate, finding first treatments for all currently untreatable diseases takes ~36 years instead of ~443.

Inputs:

- Status Quo Therapeutic Space Exploration Time : 443 years
- Trial Capacity Multiplier : 12.3x

$$T_{queue,dFDA} = \frac{T_{queue,SQ}}{k_{capacity}} = \frac{443}{12.3} = 36$$

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

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

$$\text{where } k_{capacity} = \frac{N_{fundable,ann}}{Slots_{curr}} = \frac{23.4M}{1.9M} = 12.3$$

$$\begin{gathered}\text{where } N_{fundable,ann} \\ = \frac{Subsidies_{trial,ann}}{Cost_{pragmatic,pt}} \\ = \frac{\$21.7B}{\$929} \\ = 23.4M\end{gathered}$$

$$\begin{gathered}\text{where } Subsidies_{trial,ann} \\ = Treasury_{RD,ann} - OPEX_{dFDA} \\ = \$21.8B - \$40M \\ = \$21.7B\end{gathered}$$

$$\begin{gathered}\text{where } OPEX_{dFDA} \\ = Cost_{platform} + Cost_{staff} + Cost_{infra} \\ + Cost_{regulatory} + Cost_{community} \\ = \$15M + \$10M + \$8M + \$5M + \$2M \\ = \$40M\end{gathered}$$

$$\begin{gathered}\text{where } Treasury_{RD,ann} \\ = Funding_{treaty} - Payout_{bond,ann} - Funding_{political,ann} \\ = \$27.2B - \$2.72B - \$2.72B \\ = \$21.8B\end{gathered}$$

$$\begin{gathered}\text{where } Funding_{treaty} \\ = Spending_{mil} \times Reduce_{treaty} \\ = \$2.72T \times 1\% \\ = \$27.2B\end{gathered}$$

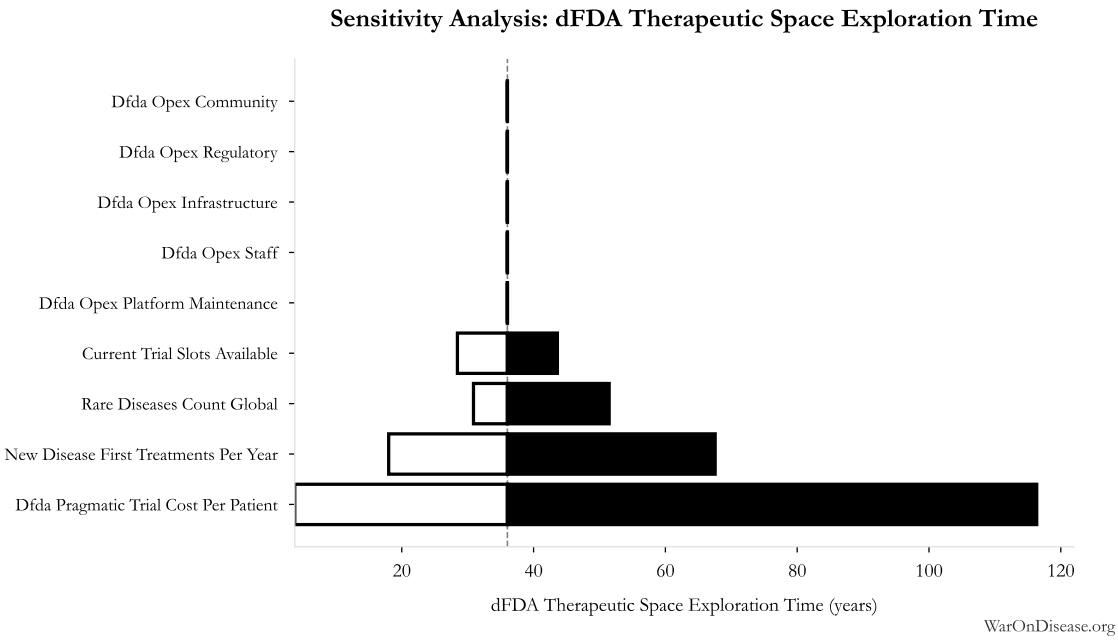
$$\begin{gathered}\text{where } Payout_{bond,ann} \\ = Funding_{treaty} \times Pct_{bond} \\ = \$27.2B \times 10\% \\ = \$2.72B\end{gathered}$$

$$\begin{gathered}\text{where } Funding_{treaty} \\ = Spending_{mil} \times Reduce_{treaty} \\ = \$2.72T \times 1\% \\ = \$27.2B\end{gathered}$$

$$\text{where } Funding_{political,ann}$$

? Low confidence

Sensitivity Analysis



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

Input Parameter	Sensitivity Coefficient	Interpretation
Status Quo Queue Clearance Years	-1.3321	Strong driver
dFDA Trial Capacity Multiplier	0.4867	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

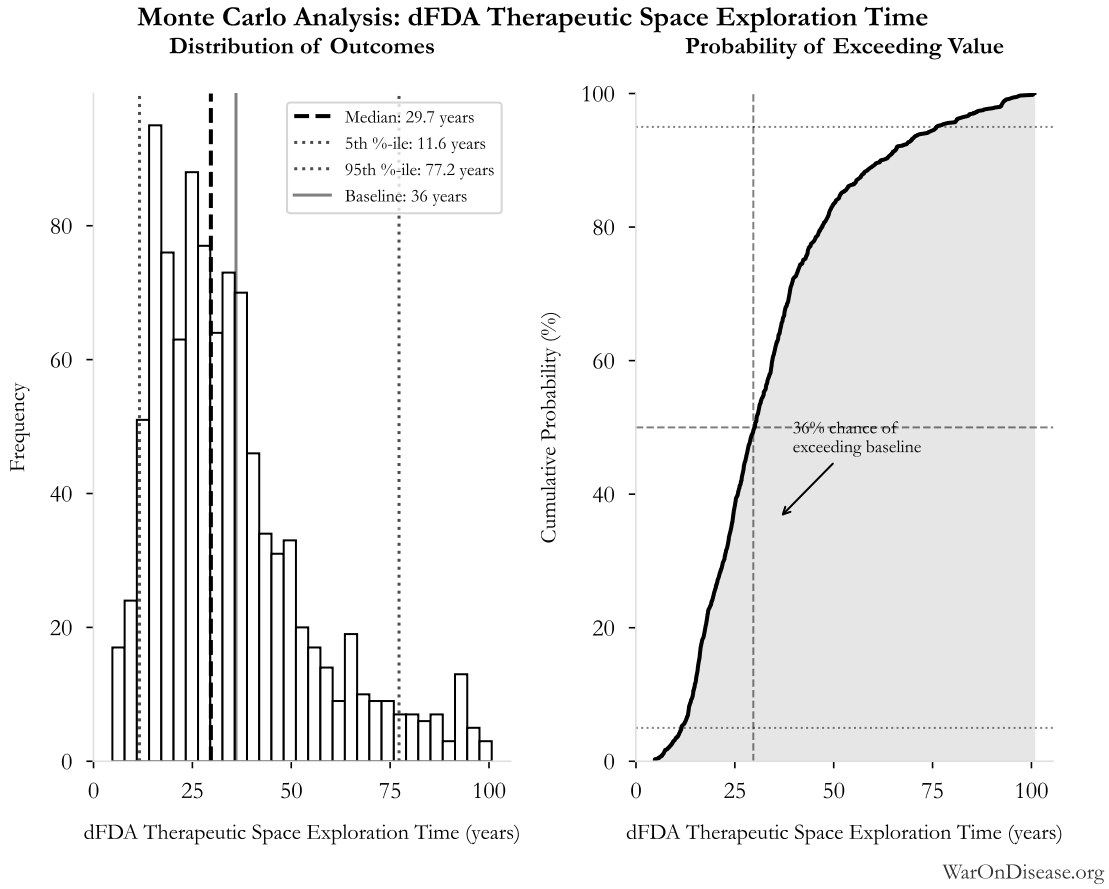


Figure 142: Monte Carlo Distribution: dFDA Therapeutic Space Exploration Time (10,000 simulations)

Simulation Results Summary: dFDA Therapeutic Space Exploration Time

Statistic	Value
Baseline (deterministic)	36
Mean (expected value)	34.6
Median (50th percentile)	29.7
Standard Deviation	19.9
90% Range (5th-95th percentile)	[11.6, 77.2]

The histogram shows the distribution of dFDA 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

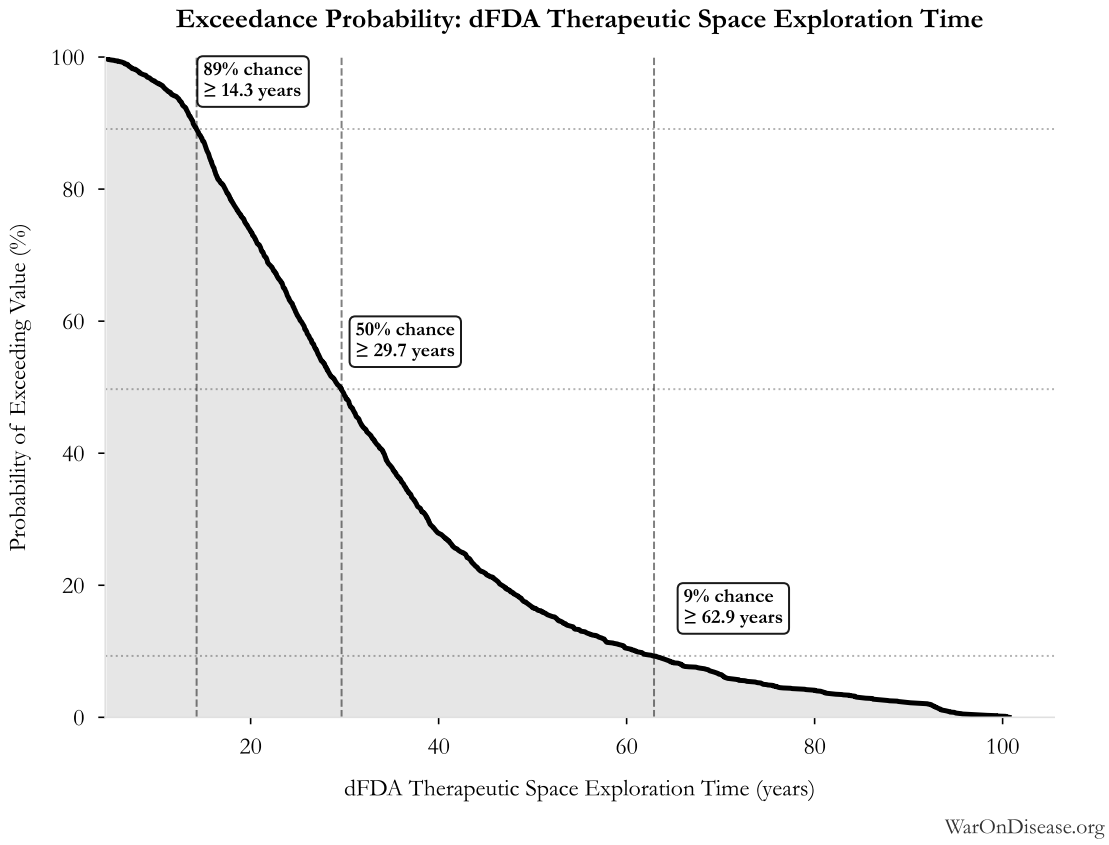


Figure 143: Probability of Exceeding Threshold: dFDA Therapeutic Space Exploration Time

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

ROI from Decentralized Framework for Drug Assessment R&D Savings Only: 637:1

Details

ROI from Decentralized Framework for Drug Assessment R&D savings only (10-year NPV, most conservative estimate)

Inputs:

- NPV of Decentralized Framework for Drug Assessment Benefits (R&D Only, 10-Year Discounted) : $389B
- Decentralized Framework for Drug Assessment Total NPV Cost : $611M

$$ROI_{RD} = \frac{NPV_{RD}}{Cost_{dFDA,total}} = \frac{\$389B}{\$611M} = 637$$

$$\text{where } NPV_{RD} = \sum_{t=1}^{10} \frac{Savings_{RD,ann} \times \frac{\min(t,5)}{5}}{(1+r)^t}$$

$$\text{where } Savings_{RD,ann}$$
$$= Benefit_{RD,ann} - OPEX_{dFDA}$$
$$= \$58.6B - \$40M$$
$$= \$58.6B$$

$$\text{where } Benefit_{RD,ann}$$
$$= Spending_{trials} \times Reduce_{pct}$$
$$= \$60B \times 97.7\%$$
$$= \$58.6B$$

$$\text{where } Reduce_{pct}$$
$$= 1 - \frac{Cost_{pragmatic,pt}}{Cost_{P3,pt}}$$
$$= 1 - \frac{\$929}{\$41K}$$
$$= 97.7\%$$

$$\text{where } OPEX_{dFDA}$$
$$= Cost_{platform} + Cost_{staff} + Cost_{infra}$$
$$+ Cost_{regulatory} + Cost_{community}$$
$$= \$15M + \$10M + \$8M + \$5M + \$2M$$
$$= \$40M$$

$$\text{where } Cost_{dFDA,total}$$
$$= PV_{OPEX} + Cost_{upfront,total}$$
$$= \$342M + \$270M$$
$$= \$611M$$

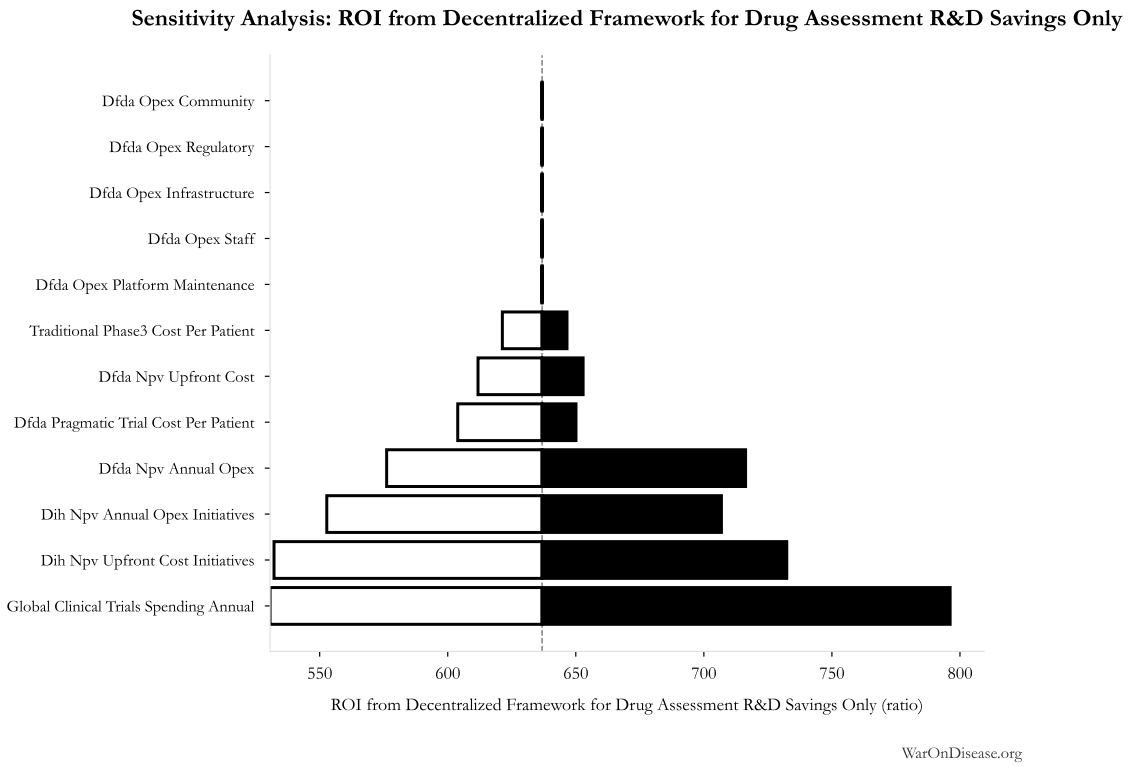
$$\text{where } PV_{OPEX} = OPEX_{ann} \times \frac{1-(1+r)^{-T}}{r}$$

$$\text{where } OPEX_{total}$$
$$= OPEX_{ann} + OPEX_{DIH,ann}$$
$$= \$18.9M + \$21.1M$$
$$= \$40M$$

$$\text{where } Cost_{upfront,total}$$
$$= Cost_{upfront} + Cost_{DIH,init}$$
$$= \$40M + \$230M$$
$$= \$270M$$

High confidence

Sensitivity Analysis



Sensitivity Indices for ROI from Decentralized Framework for Drug Assessment R&D Savings Only

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

Input Parameter	Sensitivity Coefficient	Interpretation
dFDA NPV Total Cost	-2.6305	Strong driver
dFDA NPV Benefit R&D Only	1.7615	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

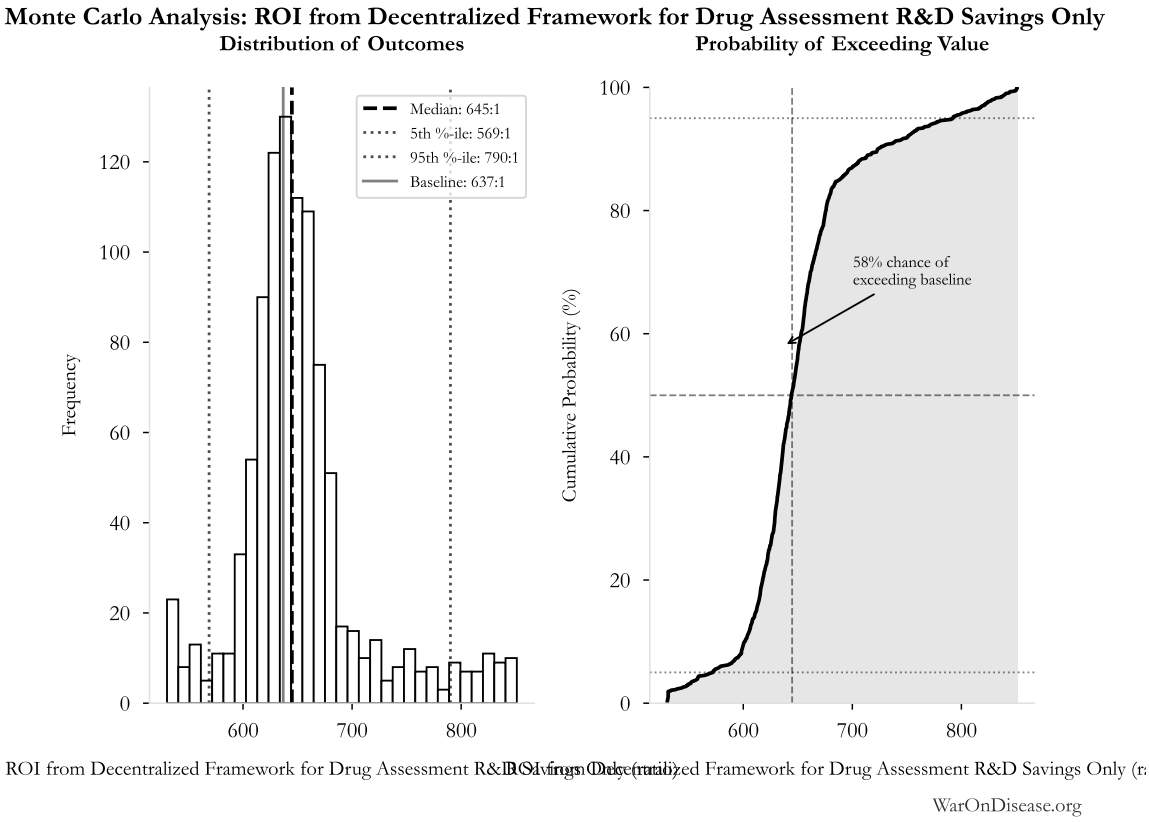


Figure 144: Monte Carlo Distribution: ROI from Decentralized Framework for Drug Assessment R&D Savings Only (10,000 simulations)

Simulation Results Summary: ROI from Decentralized Framework for Drug Assessment R&D Savings Only

Statistic	Value
Baseline (deterministic)	637:1
Mean (expected value)	653:1
Median (50th percentile)	645:1
Standard Deviation	58.4:1
90% Range (5th-95th percentile)	[569:1, 790:1]

The histogram shows the distribution of ROI from Decentralized Framework for Drug Assessment R&D Savings Only 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

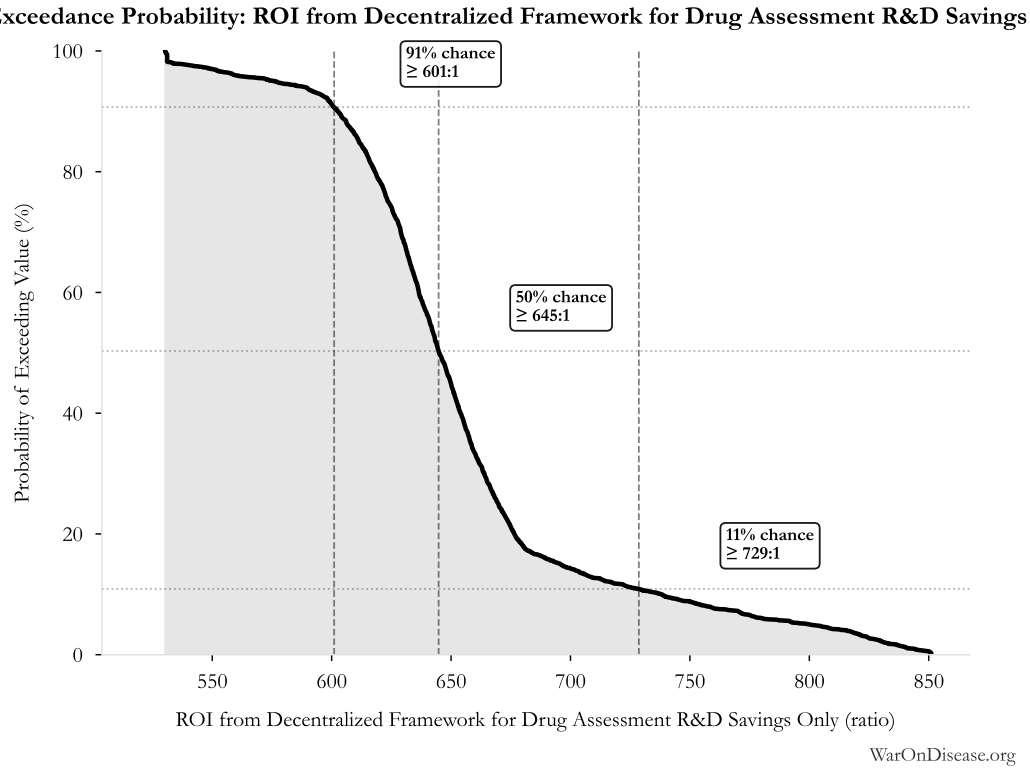


Figure 145: Probability of Exceeding Threshold: ROI from Decentralized Framework for Drug Assessment R&D Savings Only

This exceedance probability chart shows the likelihood that ROI from Decentralized Framework for Drug Assessment R&D Savings Only will exceed any given threshold. Higher curves indicate more favorable outcomes with greater certainty.

Decentralized Framework for Drug Assessment Maximum Trials per Year: 40.6 thousand trials/year

Details

Maximum trials per year possible with trial capacity multiplier
Inputs:

- Current Global Clinical Trials per Year : 3.30 thousand trials/year (95% CI: 2.64

thousand trials/year - 3.96 thousand trials/year)
- Trial Capacity Multiplier : 12.3x

$$
\begin{aligned}
&Capacity_{trials} \\
&= Trials_{ann,curr} \times k_{capacity} \\
&= 3{,}300 \times 12.3 \\
&= 40{,}600
\end{aligned}
$$

$$
\text{where } k_{capacity} = \frac{N_{fundable,ann}}{Slots_{curr}} = \frac{23.4M}{1.9M} = 12.3
$$

$$
\begin{aligned}
&\text{where } N_{fundable,ann} \\
&= \frac{Subsidies_{trial,ann}}{Cost_{pragmatic,pt}} \\
&= \frac{\$21.7B}{\$929} \\
&= 23.4M
\end{aligned}
$$

$$
\begin{aligned}
&\text{where } Subsidies_{trial,ann} \\
&= Treasury_{RD,ann} - OPEX_{dFDA} \\
&= \$21.8B - \$40M \\
&= \$21.7B
\end{aligned}
$$

$$
\begin{aligned}
&\text{where } OPEX_{dFDA} \\
&= Cost_{platform} + Cost_{staff} + Cost_{infra} \\
&+ Cost_{regulatory} + Cost_{community} \\
&= \$15M + \$10M + \$8M + \$5M + \$2M \\
&= \$40M
\end{aligned}
$$

$$
\begin{aligned}
&\text{where } Treasury_{RD,ann} \\
&= Funding_{treaty} - Payout_{bond,ann} - Funding_{political,ann} \\
&= \$27.2B - \$2.72B - \$2.72B \\
&= \$21.8B
\end{aligned}
$$

$$
\begin{aligned}
&\text{where } Funding_{treaty} \\
&= Spending_{mil} \times Reduce_{treaty} \\
&= \$2.72T \times 1\% \\
&= \$27.2B
\end{aligned}
$$

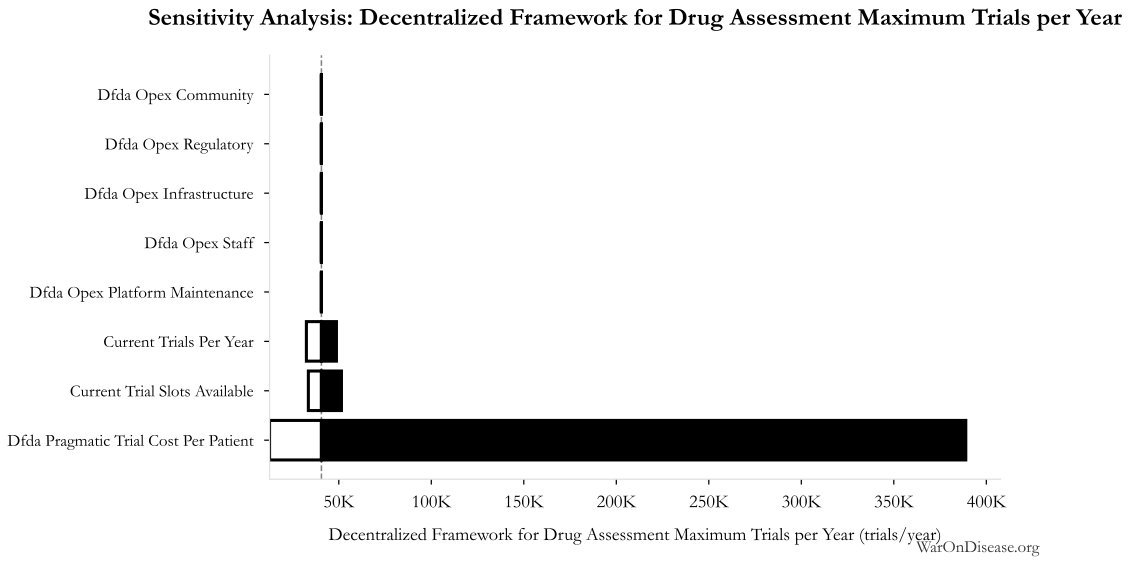
$$
\begin{aligned}
&\text{where } Payout_{bond,ann} \\
&= Funding_{treaty} \times Pct_{bond} \\
&= \$27.2B \times 10\% \\
&= \$2.72B
\end{aligned}
$$

$$
\begin{aligned}
&\text{where } Funding_{treaty} \\
&= Spending_{mil} \times Reduce_{treaty} \\
&= \$2.72T \times 1\% \\
&= \$27.2B
\end{aligned}
$$

$$
\begin{aligned}
&\text{where } Funding_{political,ann} \\
&= Funding_{treaty} \times Pct_{political} \\
&= \$27.2B \times 10\%
\end{aligned}
$$

High confidence

Sensitivity Analysis



Sensitivity Indices for Decentralized Framework for Drug Assessment Maximum Trials per Year

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

Input Parameter	Sensitivity Coefficient	Interpretation
dFDA Trial Capacity Multiplier	0.9321	Strong driver
Current Trials Per Year	-0.0802	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.

Monte Carlo Distribution

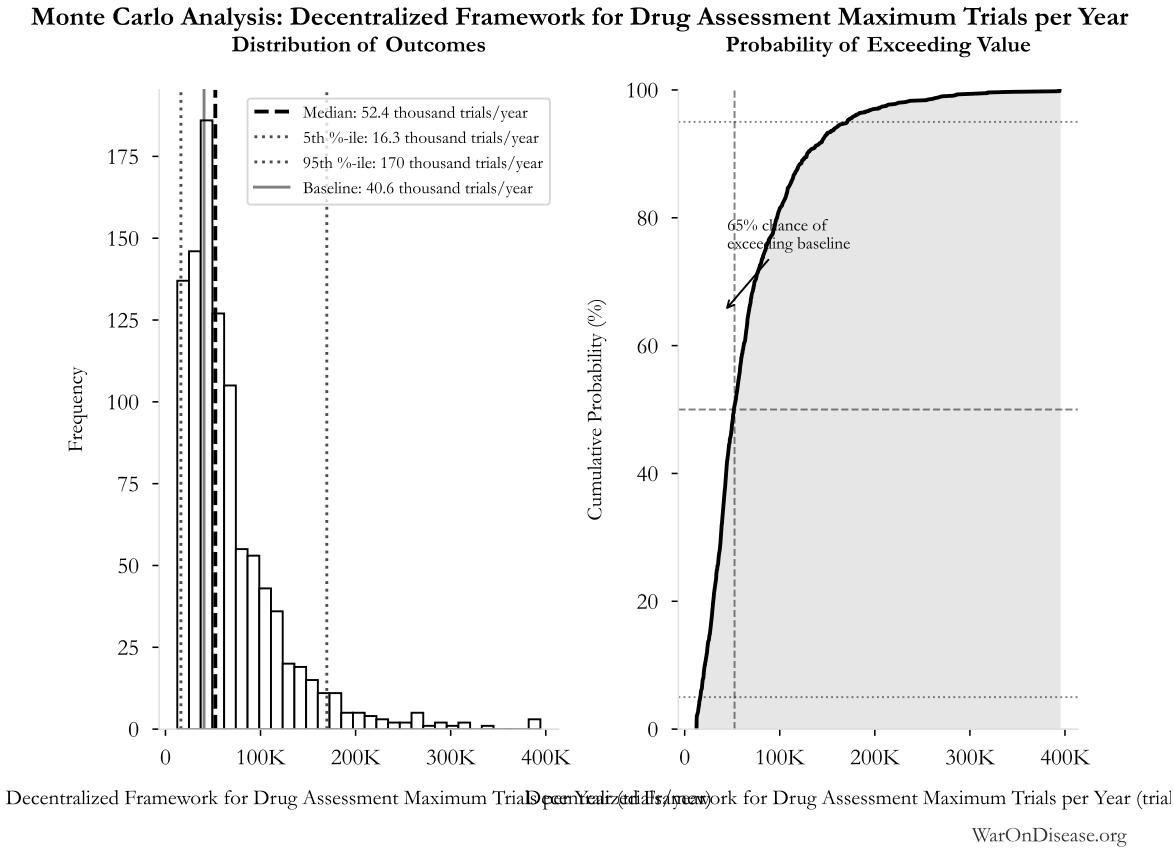


Figure 146: Monte Carlo Distribution: Decentralized Framework for Drug Assessment Maximum Trials per Year (10,000 simulations)

Simulation Results Summary: Decentralized Framework for Drug Assessment Maximum Trials per Year

Statistic	Value
Baseline (deterministic)	40.6 thousand
Mean (expected value)	67.3 thousand
Median (50th percentile)	52.4 thousand
Standard Deviation	53.1 thousand
90% Range (5th-95th percentile)	[16.3 thousand, 170 thousand]

The histogram shows the distribution of Decentralized Framework for Drug Assessment Maximum Trials per Year 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

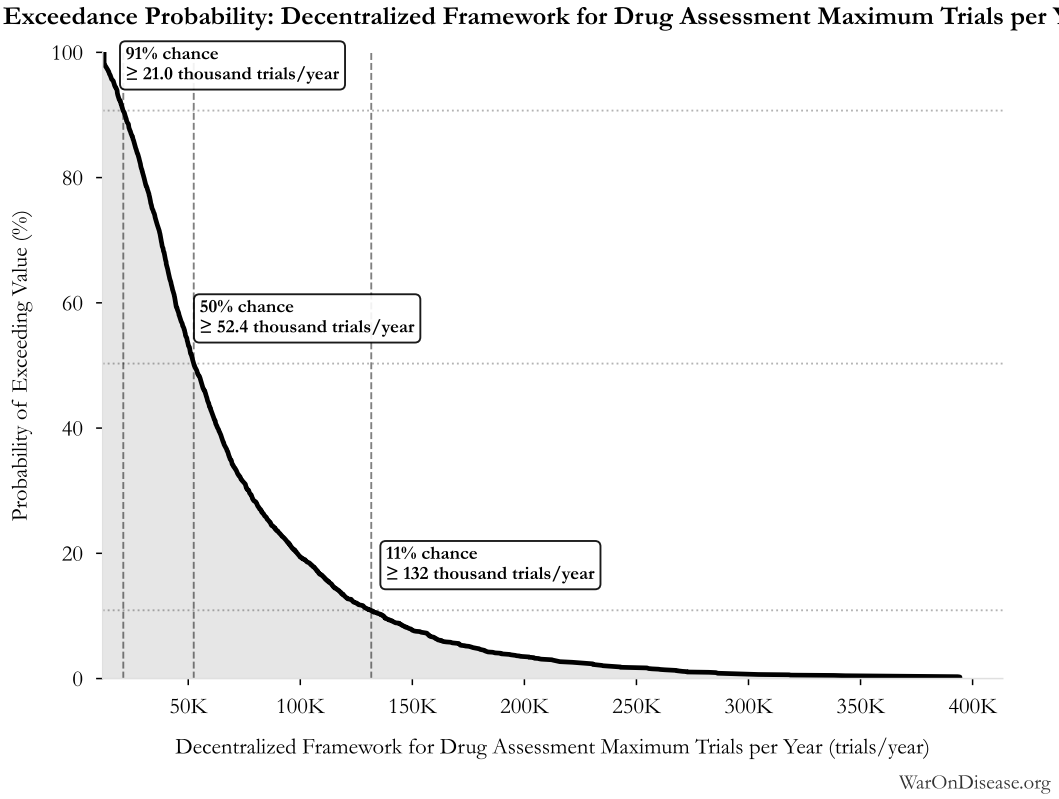


Figure 147: Probability of Exceeding Threshold: Decentralized Framework for Drug Assessment Maximum Trials per Year

This exceedance probability chart shows the likelihood that Decentralized Framework for Drug Assessment Maximum Trials per Year will exceed any given threshold. Higher curves indicate more favorable outcomes with greater certainty.

Trial Capacity Multiplier: 12.3x

Details

Trial capacity multiplier from DIH funding capacity vs. current global trial participation
Inputs:

- Annual Global Clinical Trial Participants : 1.90 million patients/year (95% CI: 1.50

million patients/year - 2.30 million patients/year)
- Patients Fundable Annually : 23.4 million patients/year

$$k_{capacity} = \frac{N_{fundable,ann}}{Slots_{curr}} = \frac{23.4M}{1.9M} = 12.3$$

$$\text{where } N_{fundable,ann}$$
$$= \frac{Subsidies_{trial,ann}}{Cost_{pragmatic,pt}}$$
$$= \frac{\$21.7B}{\$929}$$
$$= 23.4M$$

$$\text{where } Subsidies_{trial,ann}$$
$$= Treasury_{RD,ann} - OPEX_{dFDA}$$
$$= \$21.8B - \$40M$$
$$= \$21.7B$$

$$\text{where } OPEX_{dFDA}$$
$$= Cost_{platform} + Cost_{staff} + Cost_{infra}$$
$$+Cost_{regulatory} + Cost_{community}$$
$$= \$15M + \$10M + \$8M + \$5M + \$2M$$
$$= \$40M$$

$$\text{where } Treasury_{RD,ann}$$
$$= Funding_{treaty} - Payout_{bond,ann} - Funding_{political,ann}$$
$$= \$27.2B - \$2.72B - \$2.72B$$
$$= \$21.8B$$

$$\text{where } Funding_{treaty}$$
$$= Spending_{mil} \times Reduce_{treaty}$$
$$= \$2.72T \times 1\%$$
$$= \$27.2B$$

$$\text{where } Payout_{bond,ann}$$
$$= Funding_{treaty} \times Pct_{bond}$$
$$= \$27.2B \times 10\%$$
$$= \$2.72B$$

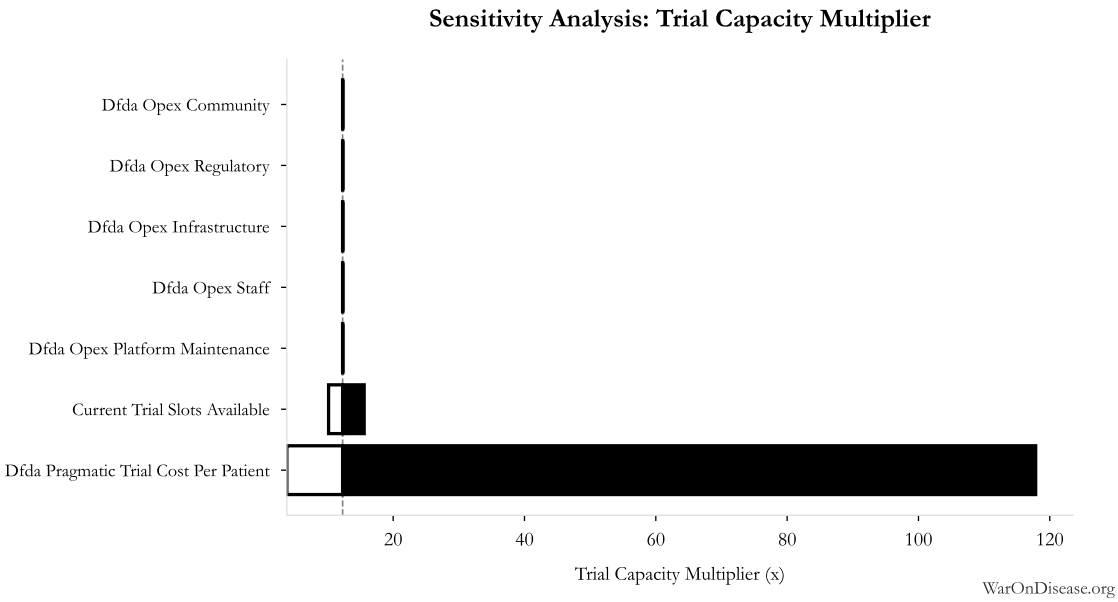
$$\text{where } Funding_{treaty}$$
$$= Spending_{mil} \times Reduce_{treaty}$$
$$= \$2.72T \times 1\%$$
$$= \$27.2B$$

$$\text{where } Funding_{political,ann}$$
$$= Funding_{treaty} \times Pct_{political}$$
$$= \$27.2B \times 10\%$$
$$= \$2.72B$$

$$\text{where } Funding_{treaty}$$
$$= Spending_{mil} \times Reduce_{treaty}$$
$$= \$2.72T \times 1\%$$

High confidence

Sensitivity Analysis



Sensitivity Indices for Trial Capacity Multiplier
Regression-based sensitivity showing which inputs explain the most variance in the output.

Input Parameter	Sensitivity Coefficient	Interpretation
DIH Patients Fundable Annually	1.0768	Strong driver
Current Trial Slots Available	0.0910	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.

Monte Carlo Distribution

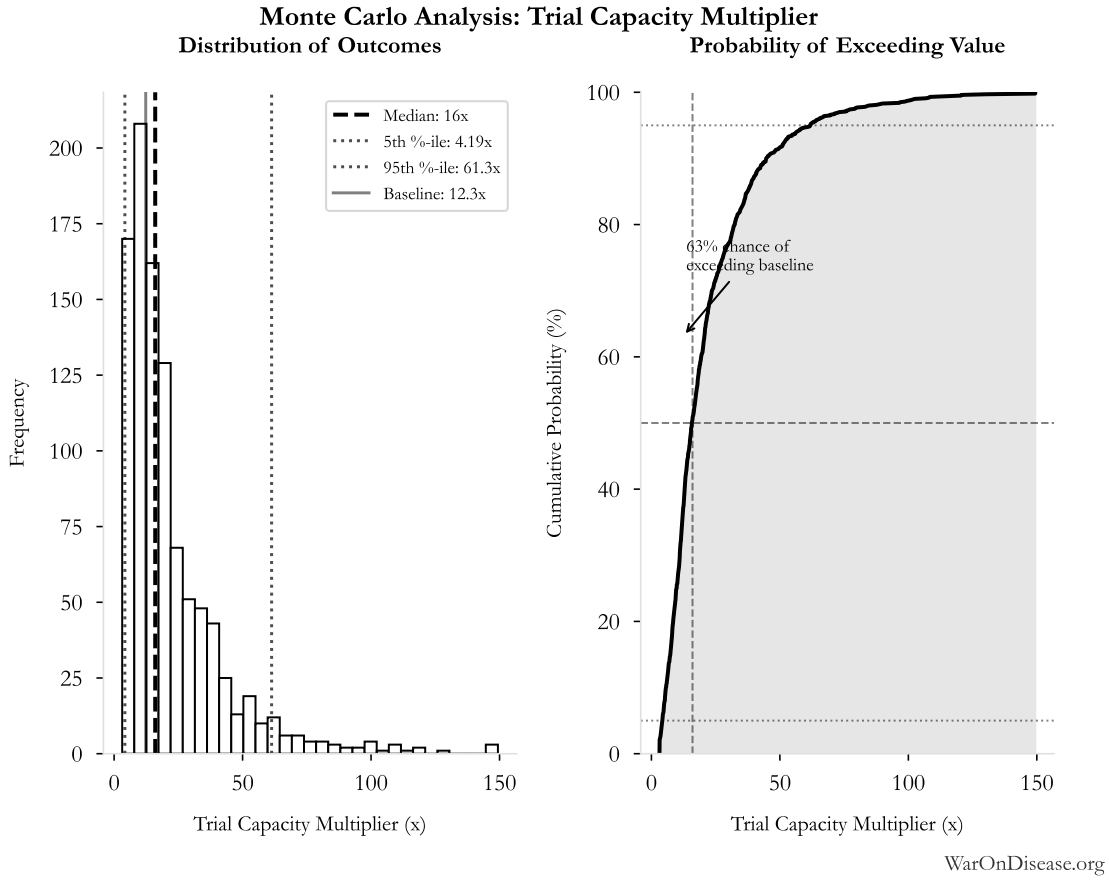


Figure 148: Monte Carlo Distribution: Trial Capacity Multiplier (10,000 simulations)

Simulation Results Summary: Trial Capacity Multiplier

Statistic	Value
Baseline (deterministic)	12.3x
Mean (expected value)	22.1x
Median (50th percentile)	16x
Standard Deviation	20.2x
90% Range (5th-95th percentile)	[4.19x, 61.3x]

The histogram shows the distribution of Trial Capacity Multiplier 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

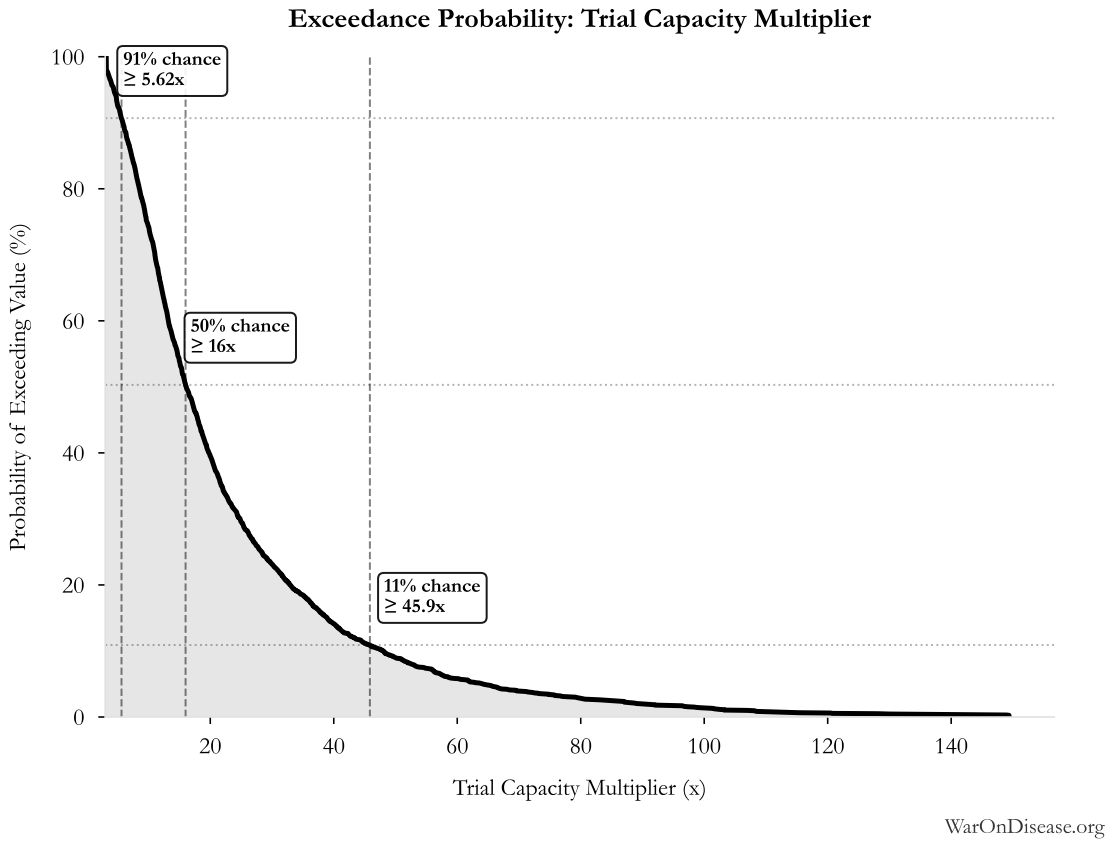


Figure 149: Probability of Exceeding Threshold: Trial Capacity Multiplier

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

Total DALYs from Elimination of Efficacy Lag Plus Earlier Treatment Discovery from Higher Trial Throughput: 565 billion DALYs

Details

Total DALYs averted from the combined dFDA timeline shift. Calculated as annual global DALY burden × eventually avoidable percentage × timeline shift years. Includes both fatal and non-fatal diseases (WHO GBD methodology).

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%)
- dFDA Average Total Timeline Shift : 212 years

$$DALYs_{max}$$
$$= DALYs_{global,ann} \times Pct_{avoid,DALY} \times T_{accel,max}$$
$$= 2.88B \times 92.6\% \times 212$$
$$= 565B$$

$$\text{where } T_{accel,max} = T_{accel} + T_{lag} = 204 + 8.2 = 212$$

$$\text{where } T_{accel}$$
$$= T_{first,SQ} \times \left(1 - \frac{1}{k_{capacity}}\right)$$
$$= 222 \times \left(1 - \frac{1}{12.3}\right)$$
$$= 204$$

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

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

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

$$\text{where } k_{capacity} = \frac{N_{fundable,ann}}{Slots_{curr}} = \frac{23.4M}{1.9M} = 12.3$$

$$\text{where } N_{fundable,ann}$$
$$= \frac{Subsidies_{trial,ann}}{Cost_{pragmatic,pt}}$$
$$= \frac{\$21.7B}{\$929}$$
$$= 23.4M$$

$$\text{where } Subsidies_{trial,ann}$$
$$= Treasury_{RD,ann} - OPEX_{dFDA}$$
$$= \$21.8B - \$40M$$
$$= \$21.7B$$

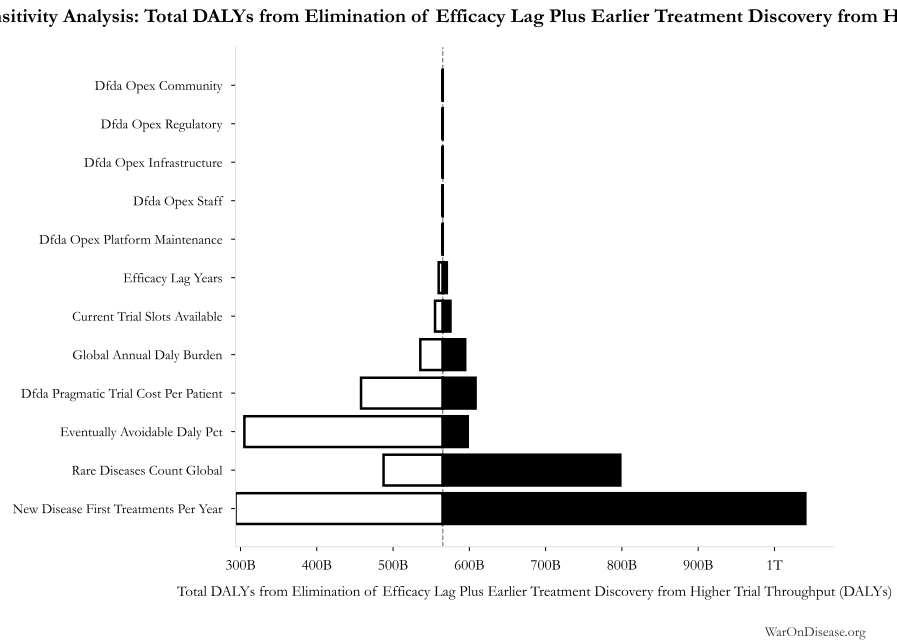
$$\text{where } OPEX_{dFDA}$$
$$= Cost_{platform} + Cost_{staff} + Cost_{infra}$$
$$+ Cost_{regulatory} + Cost_{community}$$
$$= \$15M + \$10M + \$8M + \$5M + \$2M$$
$$= \$40M$$

$$\text{where } Treasury_{RD,ann}$$
$$= Funding_{treaty} - Payout_{bond,ann} - Funding_{political,ann}$$
$$= \$27.2B - \$2.72B - \$2.72B$$
$$= \$21.8B$$

$$\text{where } Funding_{treaty}$$
$$= Spending_{mil} \times Reduce_{treaty}$$
$$= \$2.72T \times 1\%$$
$$= \$27.2B$$

? Low confidence

Sensitivity Analysis



Sensitivity Indices for Total DALYs from Elimination of Efficacy Lag Plus Earlier Treatment Discovery from Higher Trial Throughput
Regression-based sensitivity showing which inputs explain the most variance in the output.

Input Parameter	Sensitivity Coefficient	Interpretation
dFDA Trial Capacity Plus Efficacy Lag Years	0.9001	Strong driver
Eventually Avoidable DALY %	0.4864	Moderate driver
Global Annual DALY Burden	0.0433	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.

Monte Carlo Distribution

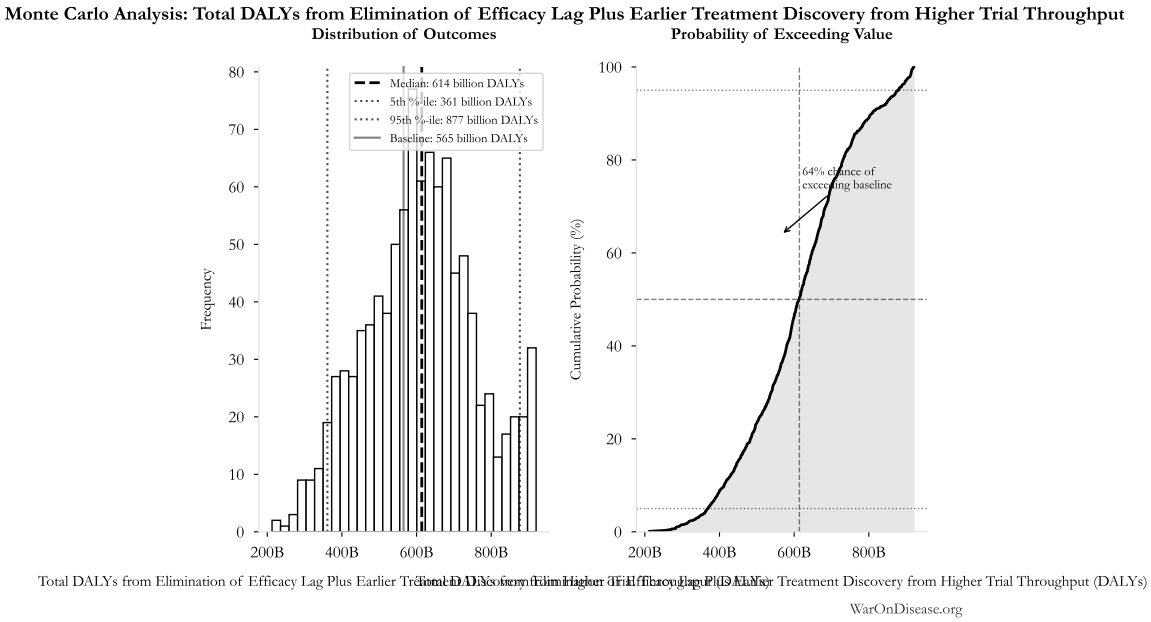


Figure 150: Monte Carlo Distribution: Total DALYs from Elimination of Efficacy Lag Plus Earlier Treatment Discovery from Higher Trial Throughput (10,000 simulations)

Simulation Results Summary: Total DALYs from Elimination of Efficacy Lag Plus Earlier Treatment Discovery from Higher Trial Throughput

Statistic	Value
Baseline (deterministic)	565 billion
Mean (expected value)	610 billion
Median (50th percentile)	614 billion
Standard Deviation	148 billion
90% Range (5th-95th percentile)	[361 billion, 877 billion]

The histogram shows the distribution of Total DALYs from Elimination of Efficacy Lag Plus Earlier Treatment Discovery from Higher Trial Throughput 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

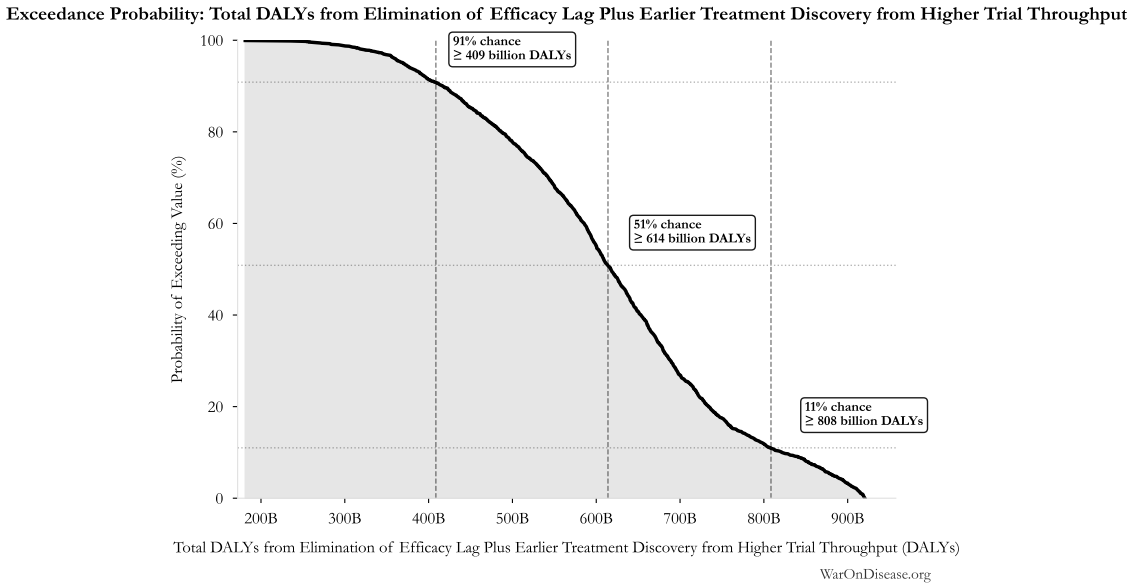


Figure 151: Probability of Exceeding Threshold: Total DALYs from Elimination of Efficacy Lag Plus Earlier Treatment Discovery from Higher Trial Throughput

This exceedance probability chart shows the likelihood that Total DALYs from Elimination of Efficacy Lag Plus Earlier Treatment Discovery from Higher Trial Throughput will exceed any given threshold. Higher curves indicate more favorable outcomes with greater certainty.

Total Economic Benefit from Elimination of Efficacy Lag Plus Earlier Treatment Discovery from Higher Trial Throughput: $84.8 quadrillion

Details

Total economic value from the combined dFDA timeline shift. DALYs valued at standard economic rate.

Inputs:

- Total DALYs from Elimination of Efficacy Lag Plus Earlier Treatment Discovery from Higher Trial Throughput : 565 billion DALYs
- Standard Economic Value per QALY : $150K (SE: ±$30K)

$$
\begin{aligned}
&Value_{max} \\
&= DALYs_{max} \times Value_{QALY} \\
&= 565B \times \$150K \\
&= \$84800T
\end{aligned}
$$

$$
\begin{aligned}
&\text{where } DALYs_{max} \\
&= DALYs_{global,ann} \times Pct_{avoid,DALY} \times T_{accel,max} \\
&= 2.88B \times 92.6\% \times 212 \\
&= 565B
\end{aligned}
$$

$$\text{where } T_{accel,max} = T_{accel} + T_{lag} = 204 + 8.2 = 212$$

$$
\begin{aligned}
&\text{where } T_{accel} \\
&= T_{first,SQ} \times \left(1 - \frac{1}{k_{capacity}}\right) \\
&= 222 \times \left(1 - \frac{1}{12.3}\right) \\
&= 204
\end{aligned}
$$

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

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

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

$$\text{where } k_{capacity} = \frac{N_{fundable,ann}}{Slots_{curr}} = \frac{23.4M}{1.9M} = 12.3$$

$$
\begin{aligned}
&\text{where } N_{fundable,ann} \\
&= \frac{Subsidies_{trial,ann}}{Cost_{pragmatic,pt}} \\
&= \frac{\$21.7B}{\$929} \\
&= 23.4M
\end{aligned}
$$

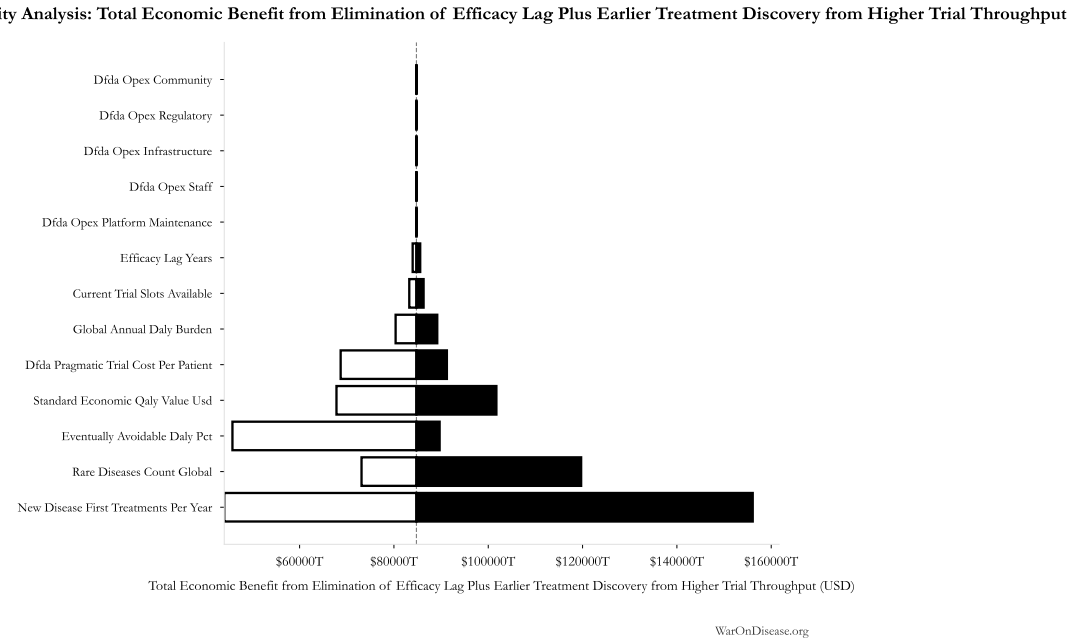
$$
\begin{aligned}
&\text{where } Subsidies_{trial,ann} \\
&= Treasury_{RD,ann} - OPEX_{dFDA} \\
&= \$21.8B - \$40M \\
&= \$21.7B
\end{aligned}
$$

$$
\begin{aligned}
&\text{where } OPEX_{dFDA} \\
&= Cost_{platform} + Cost_{staff} + Cost_{infra} \\
&+ Cost_{regulatory} + Cost_{community} \\
&= \$15M + \$10M + \$8M + \$5M + \$2M \\
&= \$40M
\end{aligned}
$$

$$
\begin{aligned}
&\text{where } Treasury_{RD,ann} \\
&= Funding_{treaty} - Payout_{bond,ann} - Funding_{political,ann} \\
&= \$27.2B - \$2.72B - \$2.72B \\
&= \$21.8B
\end{aligned}
$$

? Low confidence

Sensitivity Analysis



Sensitivity Indices for Total Economic Benefit from Elimination of Efficacy Lag Plus Earlier Treatment Discovery from Higher Trial Throughput
Regression-based sensitivity showing which inputs explain the most variance in the output.

Input Parameter	Sensitivity Coefficient	Interpretation
dFDA Trial Capacity Plus Efficacy Lag DALYs	1.7790	Strong driver
Standard Economic QALY Value Usd	1.3377	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

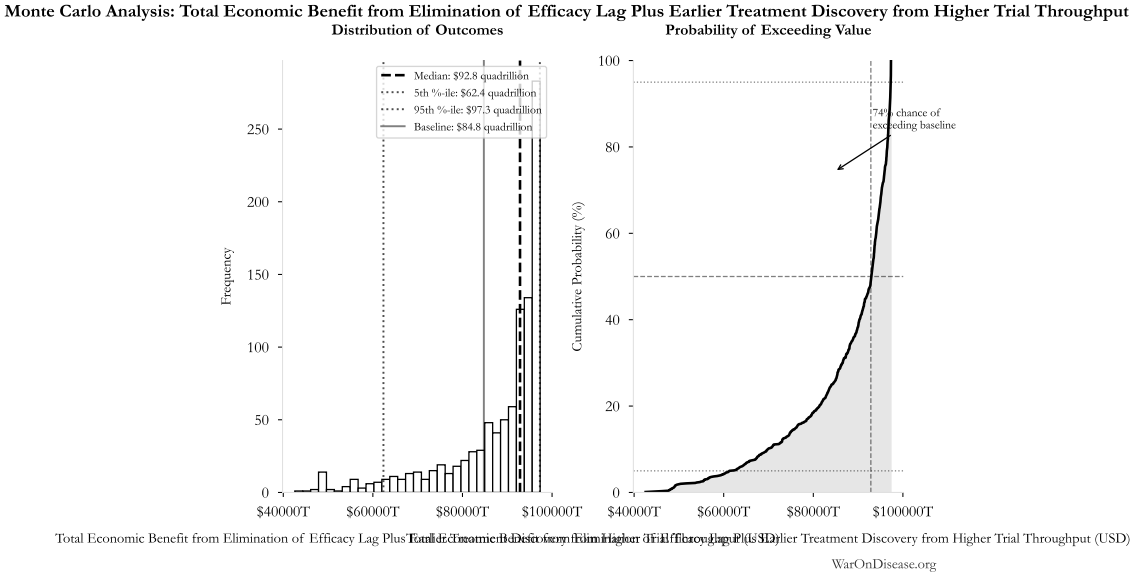


Figure 152: Monte Carlo Distribution: Total Economic Benefit from Elimination of Efficacy Lag Plus Earlier Treatment Discovery from Higher Trial Throughput (10,000 simulations)

Simulation Results Summary: Total Economic Benefit from Elimination of Efficacy Lag Plus Earlier Treatment Discovery from Higher Trial Throughput

Statistic	Value
Baseline (deterministic)	$84.8 quadrillion
Mean (expected value)	$87.8 quadrillion
Median (50th percentile)	$92.8 quadrillion
Standard Deviation	$11.5 quadrillion
90% Range (5th-95th percentile)	[$62.4 quadrillion, $97.3 quadrillion]

The histogram shows the distribution of Total Economic Benefit from Elimination of Efficacy Lag Plus Earlier Treatment Discovery from Higher Trial Throughput 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

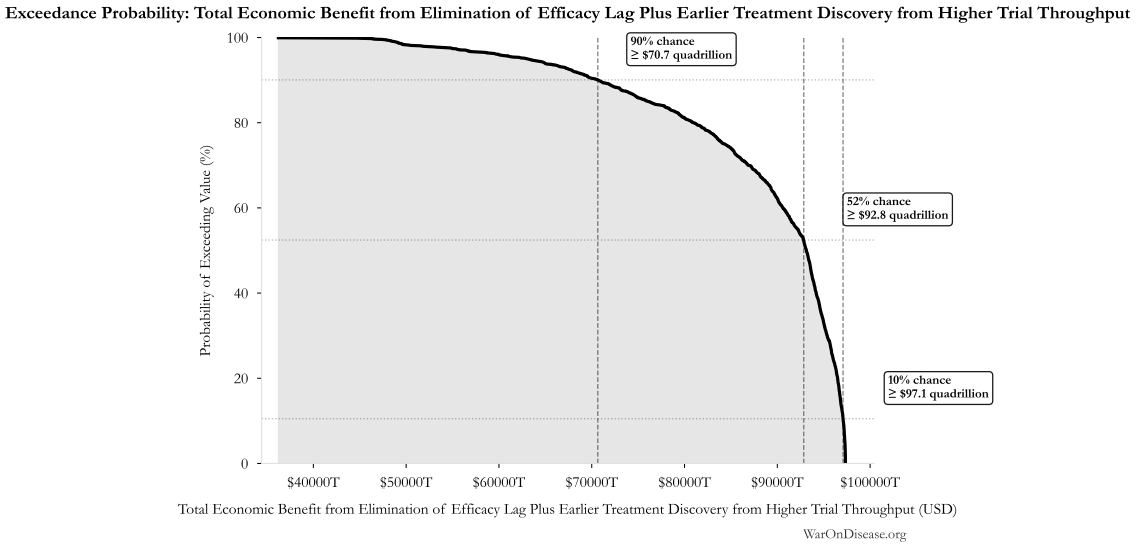


Figure 153: Probability of Exceeding Threshold: Total Economic Benefit from Elimination of Efficacy Lag Plus Earlier Treatment Discovery from Higher Trial Throughput

This exceedance probability chart shows the likelihood that Total Economic Benefit from Elimination of Efficacy Lag Plus Earlier Treatment Discovery from Higher Trial Throughput will exceed any given threshold. Higher curves indicate more favorable outcomes with greater certainty.

Total Lives Saved from Elimination of Efficacy Lag Plus Earlier Treatment Discovery from Higher Trial Throughput: 10.7 billion deaths

Details

Total eventually avoidable deaths from the combined dFDA timeline shift. Represents deaths prevented when cures arrive earlier due to both increased trial capacity and eliminated efficacy lag.

Inputs:

- Global Daily Deaths from Disease and Aging : 150 thousand deaths/day (SE: ±7.50 thousand deaths/day)
- dFDA Average Total Timeline Shift : 212 years

$$Lives_{max}$$
$$= Deaths_{disease,daily} \times T_{accel,max} \times 338$$
$$= 150{,}000 \times 212 \times 338$$
$$= 10.7B$$

where $T_{accel,max} = T_{accel} + T_{lag} = 204 + 8.2 = 212$

where T_{accel}
$$= T_{first,SQ} \times \left(1 - \frac{1}{k_{capacity}}\right)$$
$$= 222 \times \left(1 - \frac{1}{12.3}\right)$$
$$= 204$$

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

where $k_{capacity} = \frac{N_{fundable,ann}}{Slots_{curr}} = \frac{23.4M}{1.9M} = 12.3$

where $N_{fundable,ann}$
$$= \frac{Subsidies_{trial,ann}}{Cost_{pragmatic,pt}}$$
$$= \frac{\$21.7B}{\$929}$$
$$= 23.4M$$

where $Subsidies_{trial,ann}$
$$= Treasury_{RD,ann} - OPEX_{dFDA}$$
$$= \$21.8B - \$40M$$
$$= \$21.7B$$

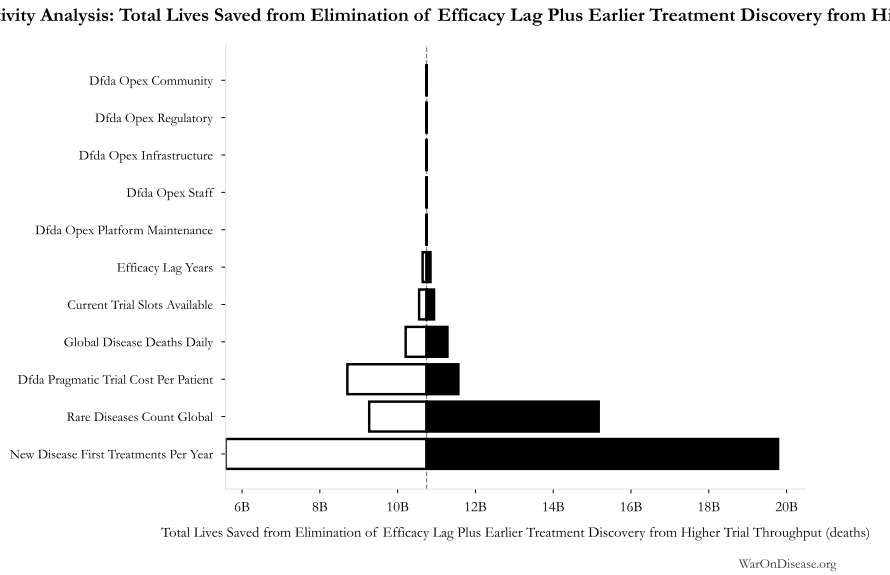
where $OPEX_{dFDA}$
$$= Cost_{platform} + Cost_{staff} + Cost_{infra}$$
$$+ Cost_{regulatory} + Cost_{community}$$
$$= \$15M + \$10M + \$8M + \$5M + \$2M$$
$$= \$40M$$

where $Treasury_{RD,ann}$
$$= Funding_{treaty} - Payout_{bond,ann} - Funding_{political,ann}$$
$$= \$27.2B - \$2.72B - \$2.72B$$
$$= \$21.8B$$

where $Funding_{treaty}$
$$= Spending_{mil} \times Reduce_{treaty}$$
$$= \$2.72T \times 1\%$$
$$= \$27.2B$$

? Low confidence

Sensitivity Analysis



Sensitivity Indices for Total Lives Saved from Elimination of Efficacy Lag Plus Earlier Treatment Discovery from Higher Trial Throughput
Regression-based sensitivity showing which inputs explain the most variance in the output.

Input Parameter	Sensitivity Coefficient	Interpretation
dFDA Trial Capacity Plus Efficacy Lag Years	1.0375	Strong driver
Global Disease Deaths Daily	0.0407	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.

Monte Carlo Distribution

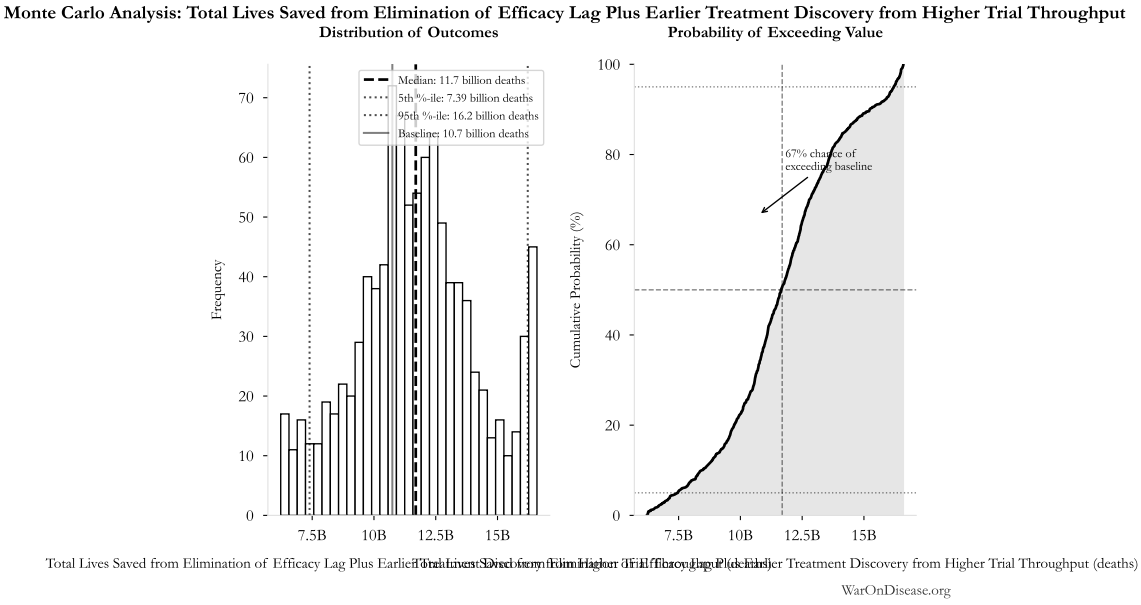


Figure 154: Monte Carlo Distribution: Total Lives Saved from Elimination of Efficacy Lag Plus Earlier Treatment Discovery from Higher Trial Throughput (10,000 simulations)

Simulation Results Summary: Total Lives Saved from Elimination of Efficacy Lag Plus Earlier Treatment Discovery from Higher Trial Throughput

Statistic	Value
Baseline (deterministic)	10.7 billion
Mean (expected value)	11.7 billion
Median (50th percentile)	11.7 billion
Standard Deviation	2.45 billion
90% Range (5th-95th percentile)	[7.39 billion, 16.2 billion]

The histogram shows the distribution of Total Lives Saved from Elimination of Efficacy Lag Plus Earlier Treatment Discovery from Higher Trial Throughput 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

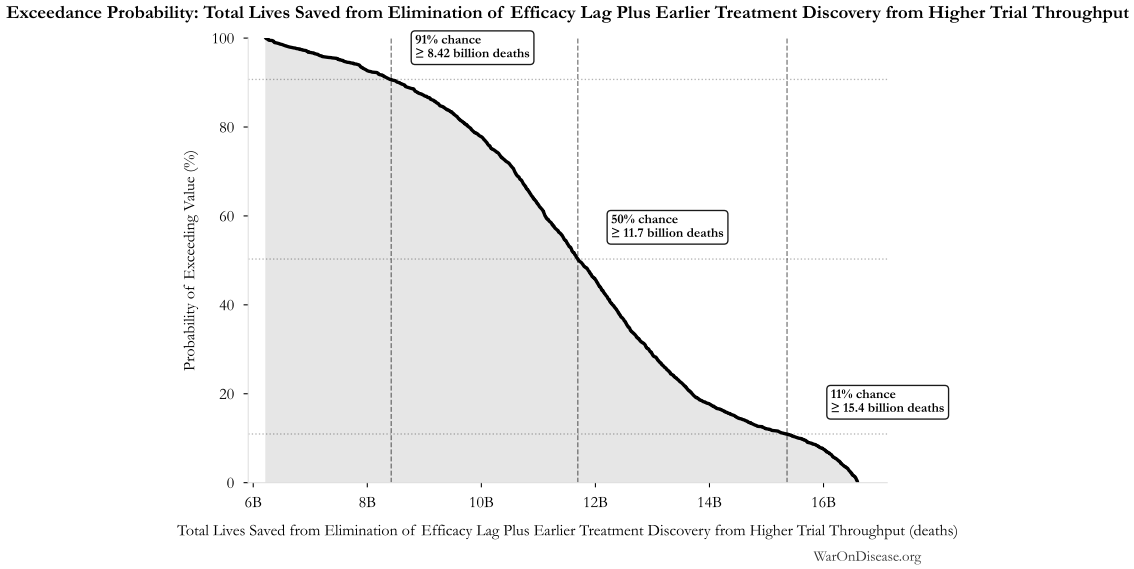


Figure 155: Probability of Exceeding Threshold: Total Lives Saved from Elimination of Efficacy Lag Plus Earlier Treatment Discovery from Higher Trial Throughput

This exceedance probability chart shows the likelihood that Total Lives Saved from Elimination of Efficacy Lag Plus Earlier Treatment Discovery from Higher Trial Throughput will exceed any given threshold. Higher curves indicate more favorable outcomes with greater certainty.

Suffering Hours Eliminated from Elimination of Efficacy Lag Plus Earlier Treatment Discovery from Higher Trial Throughput: 1.93 quadrillion hours

Details

Hours of suffering eliminated from the combined dFDA timeline shift. Calculated from YLD component of DALYs (39% of total DALYs × hours per year). One-time benefit, not annual recurring.

Inputs:

- Total DALYs from Elimination of Efficacy Lag Plus Earlier Treatment Discovery from Higher Trial Throughput : 565 billion DALYs
- YLD Proportion of Total DALYs : 0.39 proportion (SE: ±0.03 proportion)

$$Hours_{suffer,max}$$
$$= DALYs_{max} \times Pct_{YLD} \times 8760$$
$$= 565B \times 0.39 \times 8760$$
$$= 1930T$$

$$\text{where } DALYs_{max}$$
$$= DALYs_{global,ann} \times Pct_{avoid,DALY} \times T_{accel,max}$$
$$= 2.88B \times 92.6\% \times 212$$
$$= 565B$$

$$\text{where } T_{accel,max} = T_{accel} + T_{lag} = 204 + 8.2 = 212$$

$$\text{where } T_{accel}$$
$$= T_{first,SQ} \times \left(1 - \frac{1}{k_{capacity}}\right)$$
$$= 222 \times \left(1 - \frac{1}{12.3}\right)$$
$$= 204$$

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

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

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

$$\text{where } k_{capacity} = \frac{N_{fundable,ann}}{Slots_{curr}} = \frac{23.4M}{1.9M} = 12.3$$

$$\text{where } N_{fundable,ann}$$
$$= \frac{Subsidies_{trial,ann}}{Cost_{pragmatic,pt}}$$
$$= \frac{\$21.7B}{\$929}$$
$$= 23.4M$$

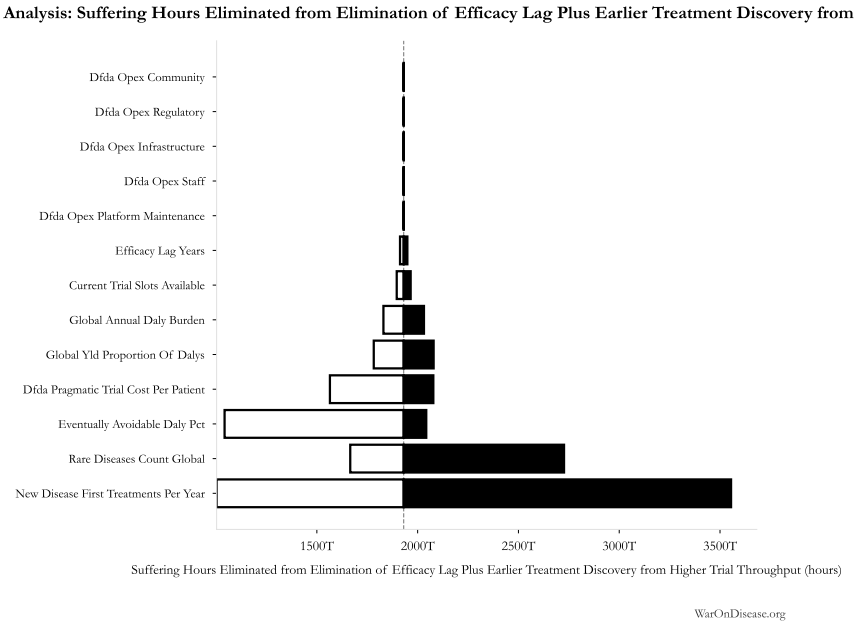
$$\text{where } Subsidies_{trial,ann}$$
$$= Treasury_{RD,ann} - OPEX_{dFDA}$$
$$= \$21.8B - \$40M$$
$$= \$21.7B$$

$$\text{where } OPEX_{dFDA}$$
$$= Cost_{platform} + Cost_{staff} + Cost_{infra}$$
$$+ Cost_{regulatory} + Cost_{community}$$
$$= \$15M + \$10M + \$8M + \$5M + \$2M$$
$$= \$40M$$

$$\text{where } Treasury_{RD,ann}$$
$$= Funding_{treaty} - Payout_{bond,ann} - Funding_{political,ann}$$
$$= \$27.2B - \$2.72B - \$2.72B$$
$$= \$21.8B$$

? Low confidence

Sensitivity Analysis



Sensitivity Indices for Suffering Hours Eliminated from Elimination of Efficacy Lag Plus Earlier Treatment Discovery from Higher Trial Throughput
Regression-based sensitivity showing which inputs explain the most variance in the output.

Input Parameter	Sensitivity Coefficient	Interpretation
dFDA Trial Capacity Plus Efficacy Lag DALYs	1.3101	Strong driver
Global Yld Proportion Of DALYs	0.3975	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

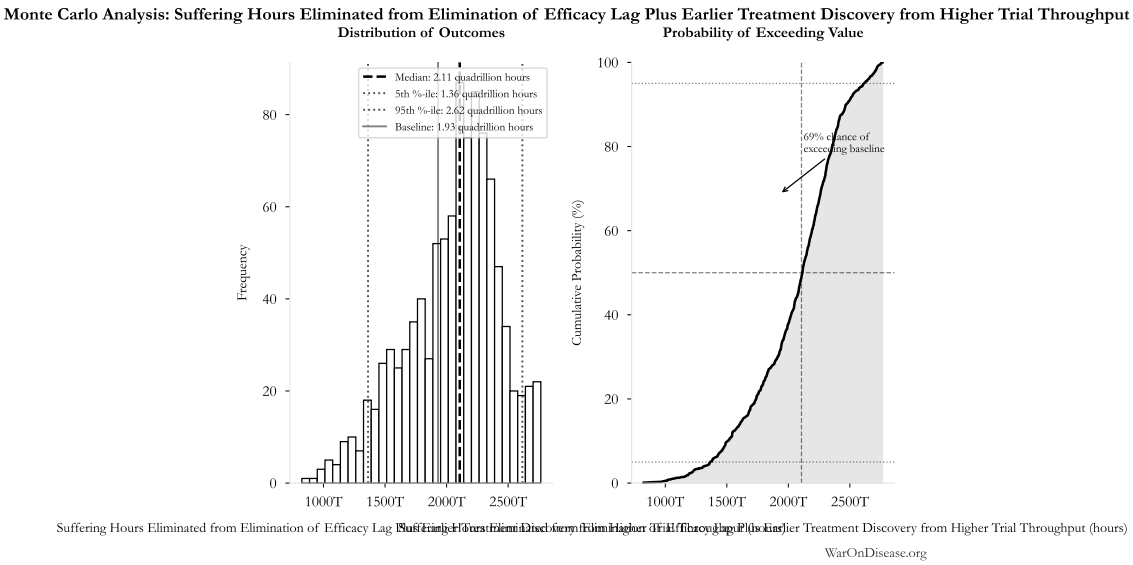


Figure 156: Monte Carlo Distribution: Suffering Hours Eliminated from Elimination of Efficacy Lag Plus Earlier Treatment Discovery from Higher Trial Throughput (10,000 simulations)

Simulation Results Summary: Suffering Hours Eliminated from Elimination of Efficacy Lag Plus Earlier Treatment Discovery from Higher Trial Throughput

Statistic	Value
Baseline (deterministic)	1.93 quadrillion
Mean (expected value)	2.05 quadrillion
Median (50th percentile)	2.11 quadrillion
Standard Deviation	374 trillion
90% Range (5th-95th percentile)	[1.36 quadrillion, 2.62 quadrillion]

The histogram shows the distribution of Suffering Hours Eliminated from Elimination of Efficacy Lag Plus Earlier Treatment Discovery from Higher Trial Throughput 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

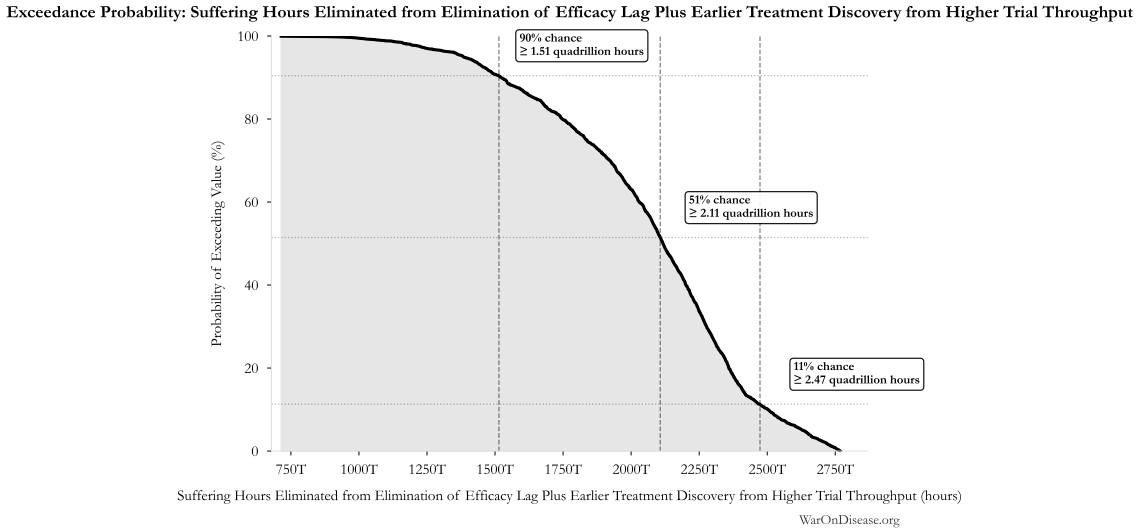


Figure 157: Probability of Exceeding Threshold: Suffering Hours Eliminated from Elimination of Efficacy Lag Plus Earlier Treatment Discovery from Higher Trial Throughput

This exceedance probability chart shows the likelihood that Suffering Hours Eliminated from Elimination of Efficacy Lag Plus Earlier Treatment Discovery from Higher Trial Throughput will exceed any given threshold. Higher curves indicate more favorable outcomes with greater certainty.

dFDA Average Total Timeline Shift: 212 years

Details

Average years earlier patients receive treatments due to dFDA. Combines treatment timeline acceleration from increased trial capacity with efficacy lag elimination for treatments already discovered.

Inputs:

- dFDA Treatment Timeline Acceleration : 204 years
- Regulatory Delay for Efficacy Testing Post-Safety Verification : 8.2 years (SE: ±2 years)

$$T_{accel,max} = T_{accel} + T_{lag} = 204 + 8.2 = 212$$

$$\text{where } T_{accel} = T_{first,SQ} \times \left(1 - \frac{1}{k_{capacity}}\right) = 222 \times \left(1 - \frac{1}{12.3}\right) = 204$$

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

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

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

$$\text{where } k_{capacity} = \frac{N_{fundable,ann}}{Slots_{curr}} = \frac{23.4M}{1.9M} = 12.3$$

$$\text{where } N_{fundable,ann} = \frac{Subsidies_{trial,ann}}{Cost_{pragmatic,pt}} = \frac{\$21.7B}{\$929} = 23.4M$$

$$\text{where } Subsidies_{trial,ann} = Treasury_{RD,ann} - OPEX_{dFDA} = \$21.8B - \$40M = \$21.7B$$

$$\text{where } OPEX_{dFDA} = Cost_{platform} + Cost_{staff} + Cost_{infra} + Cost_{regulatory} + Cost_{community} = \$15M + \$10M + \$8M + \$5M + \$2M = \$40M$$

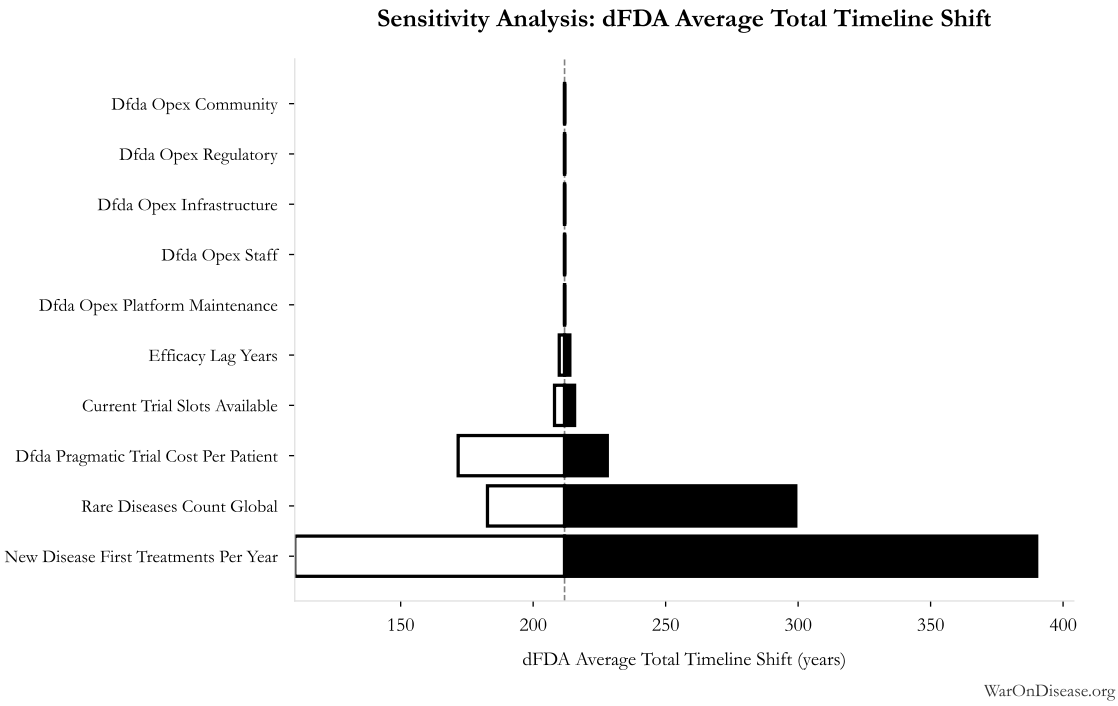
$$\text{where } Treasury_{RD,ann} = Funding_{treaty} - Payout_{bond,ann} - Funding_{political,ann} = \$27.2B - \$2.72B - \$2.72B = \$21.8B$$

$$\text{where } Funding_{treaty} = Spending_{mil} \times Reduce_{treaty} = \$2.72T \times 1\% = \$27.2B$$

$$\text{where } Payout_{bond,ann} = Funding_{treaty} \times Pct_{bond} = \$27.2B \times 10\% = \$2.72B$$

? Low confidence

Sensitivity Analysis



Sensitivity Indices for dFDA Average Total Timeline Shift
Regression-based sensitivity showing which inputs explain the most variance in the output.

Input Parameter	Sensitivity Coefficient	Interpretation
dFDA Trial Capacity	1.0325	Strong driver
Treatment Acceleration Years		
Efficacy Lag Years	0.0327	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.

Monte Carlo Distribution

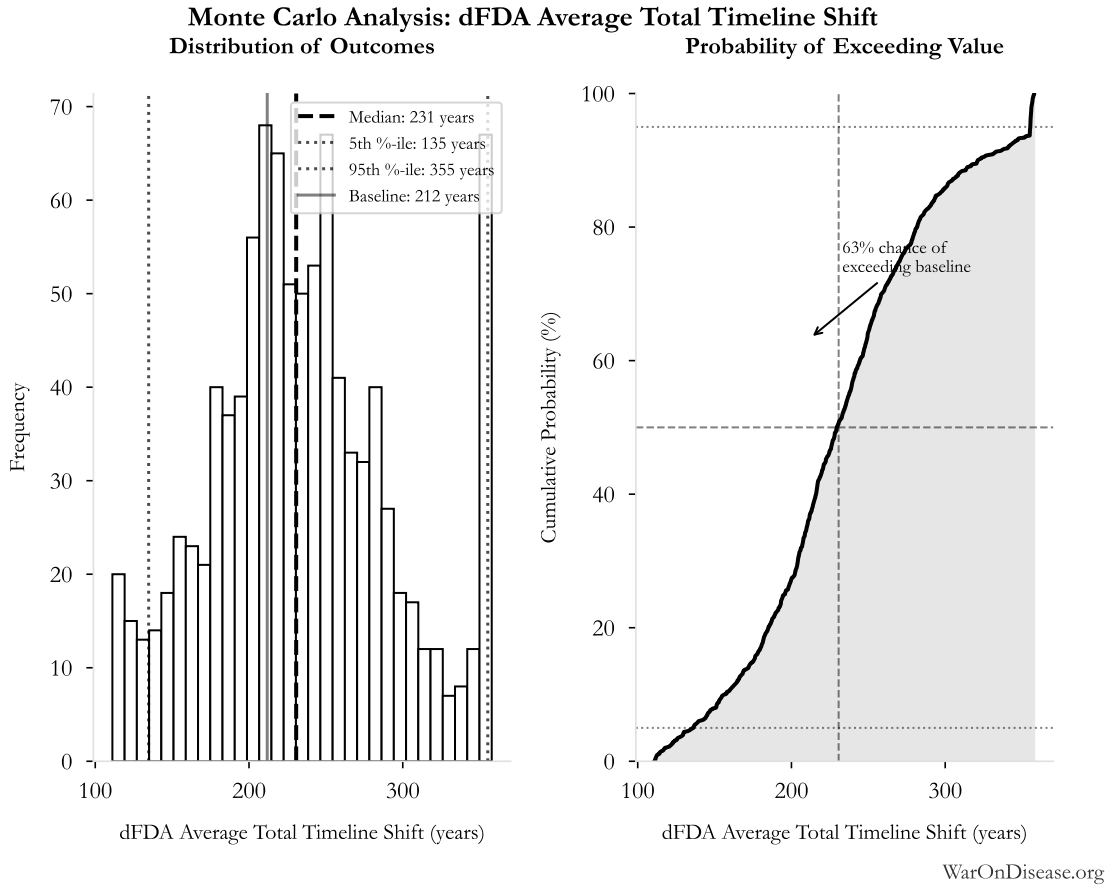


Figure 158: Monte Carlo Distribution: dFDA Average Total Timeline Shift (10,000 simulations)

Simulation Results Summary: dFDA Average Total Timeline Shift

Statistic	Value
Baseline (deterministic)	212
Mean (expected value)	233
Median (50th percentile)	231
Standard Deviation	60.3
90% Range (5th-95th percentile)	[135, 355]

The histogram shows the distribution of dFDA Average Total Timeline Shift 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

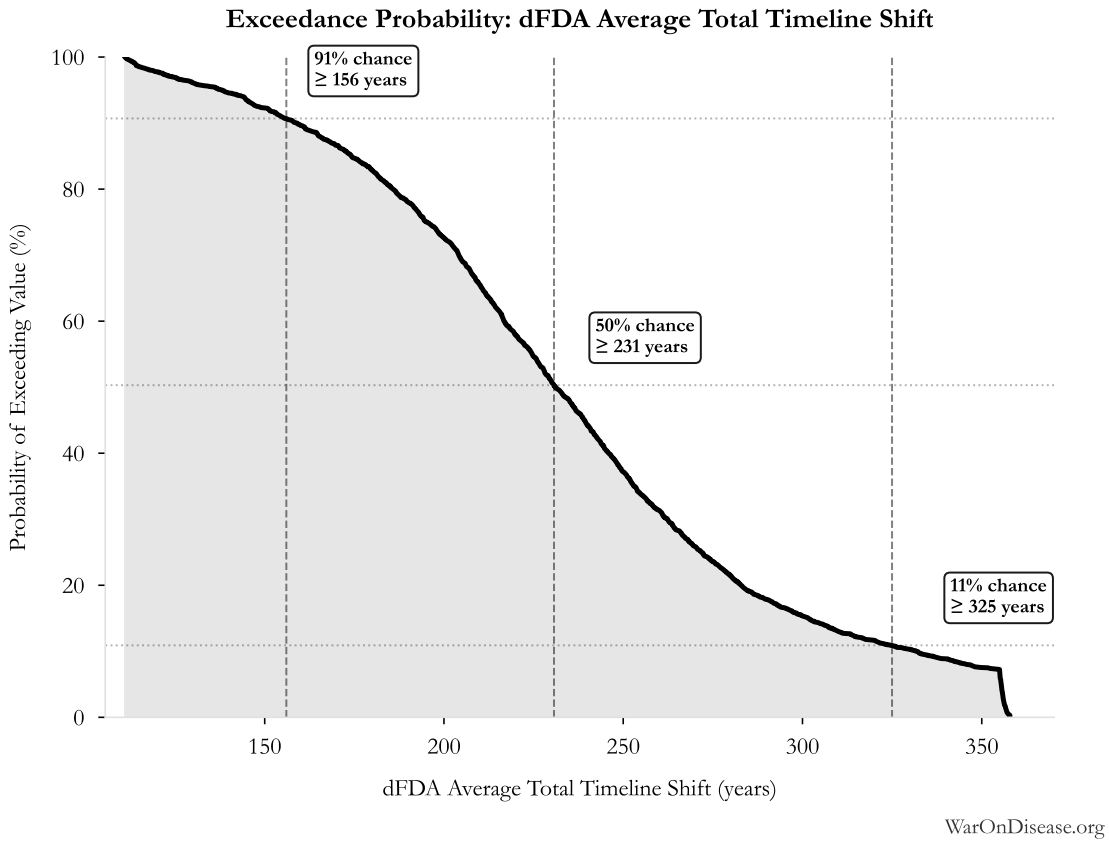


Figure 159: Probability of Exceeding Threshold: dFDA Average Total Timeline Shift

This exceedance probability chart shows the likelihood that dFDA Average Total Timeline Shift will exceed any given threshold. Higher curves indicate more favorable outcomes with greater certainty.

dFDA Treatment Timeline Acceleration: 204 years

Details

Years earlier the average first treatment arrives due to dFDA's trial capacity increase. Calculated as the status quo timeline reduced by the inverse of the capacity multiplier. Uses only trial capacity multiplier (not combined with valley of death rescue) because additional candidates don't directly speed therapeutic space exploration.

Inputs:

- Status Quo Average Years to First Treatment : 222 years
- Trial Capacity Multiplier : 12.3x

$$
\begin{aligned}
&T_{accel} \\
&= T_{first,SQ} \times \left(1 - \frac{1}{k_{capacity}}\right) \\
&= 222 \times \left(1 - \frac{1}{12.3}\right) \\
&= 204
\end{aligned}
$$

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

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

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

$$\text{where } k_{capacity} = \frac{N_{fundable,ann}}{Slots_{curr}} = \frac{23.4M}{1.9M} = 12.3$$

$$
\begin{aligned}
&\text{where } N_{fundable,ann} \\
&= \frac{Subsidies_{trial,ann}}{Cost_{pragmatic,pt}} \\
&= \frac{\$21.7B}{\$929} \\
&= 23.4M
\end{aligned}
$$

$$
\begin{aligned}
&\text{where } Subsidies_{trial,ann} \\
&= Treasury_{RD,ann} - OPEX_{dFDA} \\
&= \$21.8B - \$40M \\
&= \$21.7B
\end{aligned}
$$

$$
\begin{aligned}
&\text{where } OPEX_{dFDA} \\
&= Cost_{platform} + Cost_{staff} + Cost_{infra} \\
&+ Cost_{regulatory} + Cost_{community} \\
&= \$15M + \$10M + \$8M + \$5M + \$2M \\
&= \$40M
\end{aligned}
$$

$$
\begin{aligned}
&\text{where } Treasury_{RD,ann} \\
&= Funding_{treaty} - Payout_{bond,ann} - Funding_{political,ann} \\
&= \$27.2B - \$2.72B - \$2.72B \\
&= \$21.8B
\end{aligned}
$$

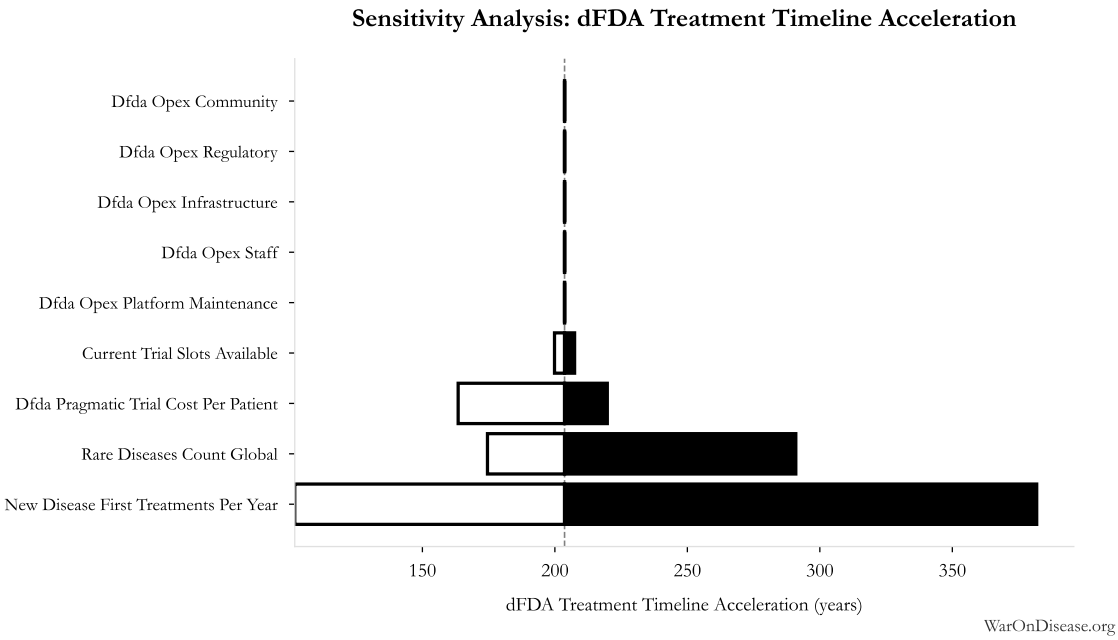
$$
\begin{aligned}
&\text{where } Funding_{treaty} \\
&= Spending_{mil} \times Reduce_{treaty} \\
&= \$2.72T \times 1\% \\
&= \$27.2B
\end{aligned}
$$

$$
\begin{aligned}
&\text{where } Payout_{bond,ann} \\
&= Funding_{treaty} \times Pct_{bond} \\
&= \$27.2B \times 10\% \\
&= \$2.72B
\end{aligned}
$$

$$\text{where } Funding_{\quad\quad} \quad ,$$

? Low confidence

Sensitivity Analysis



Sensitivity Indices for dFDA Treatment Timeline Acceleration
Regression-based sensitivity showing which inputs explain the most variance in the output.

Input Parameter	Sensitivity Coefficient	Interpretation
Status Quo Avg Years To First Treatment	1.0665	Strong driver
dFDA Trial Capacity Multiplier	-0.0779	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.

Monte Carlo Distribution

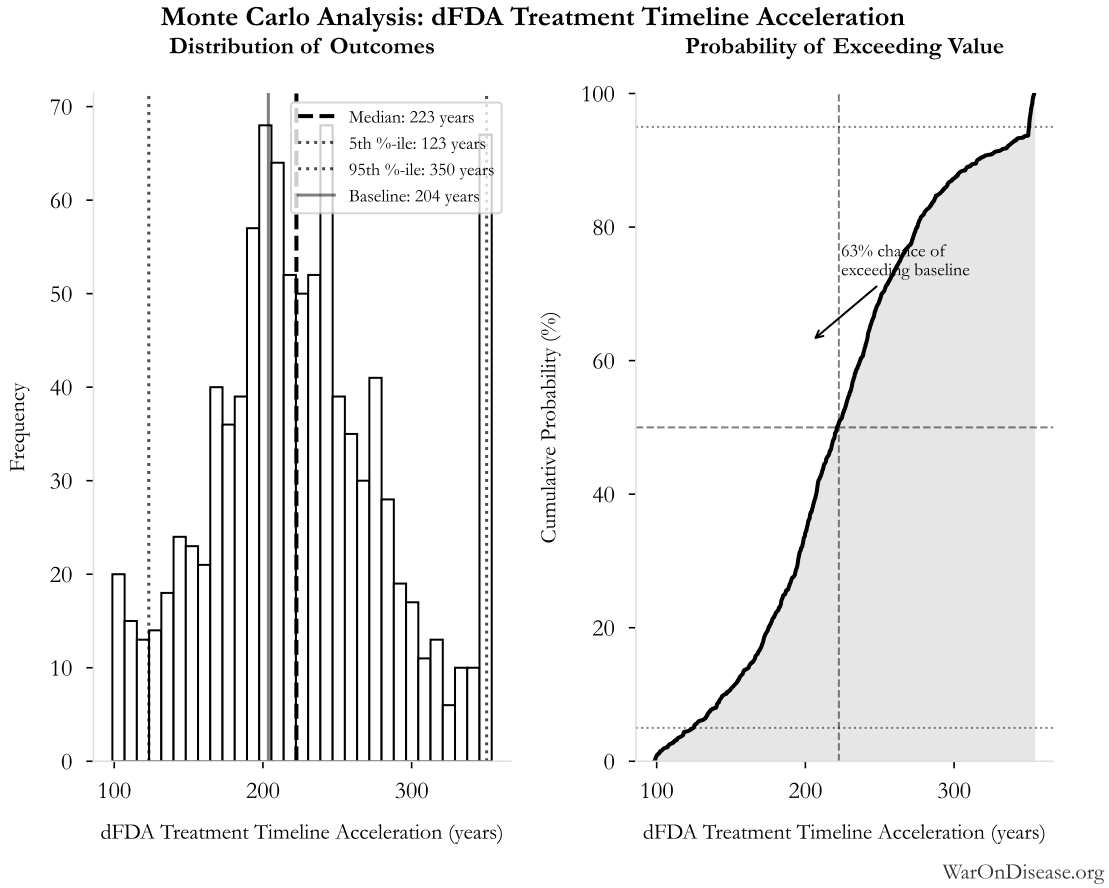


Figure 160: Monte Carlo Distribution: dFDA Treatment Timeline Acceleration (10,000 simulations)

Simulation Results Summary: dFDA Treatment Timeline Acceleration

Statistic	Value
Baseline (deterministic)	204
Mean (expected value)	225
Median (50th percentile)	223
Standard Deviation	62.3
90% Range (5th-95th percentile)	[123, 350]

The histogram shows the distribution of dFDA Treatment Timeline Acceleration 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

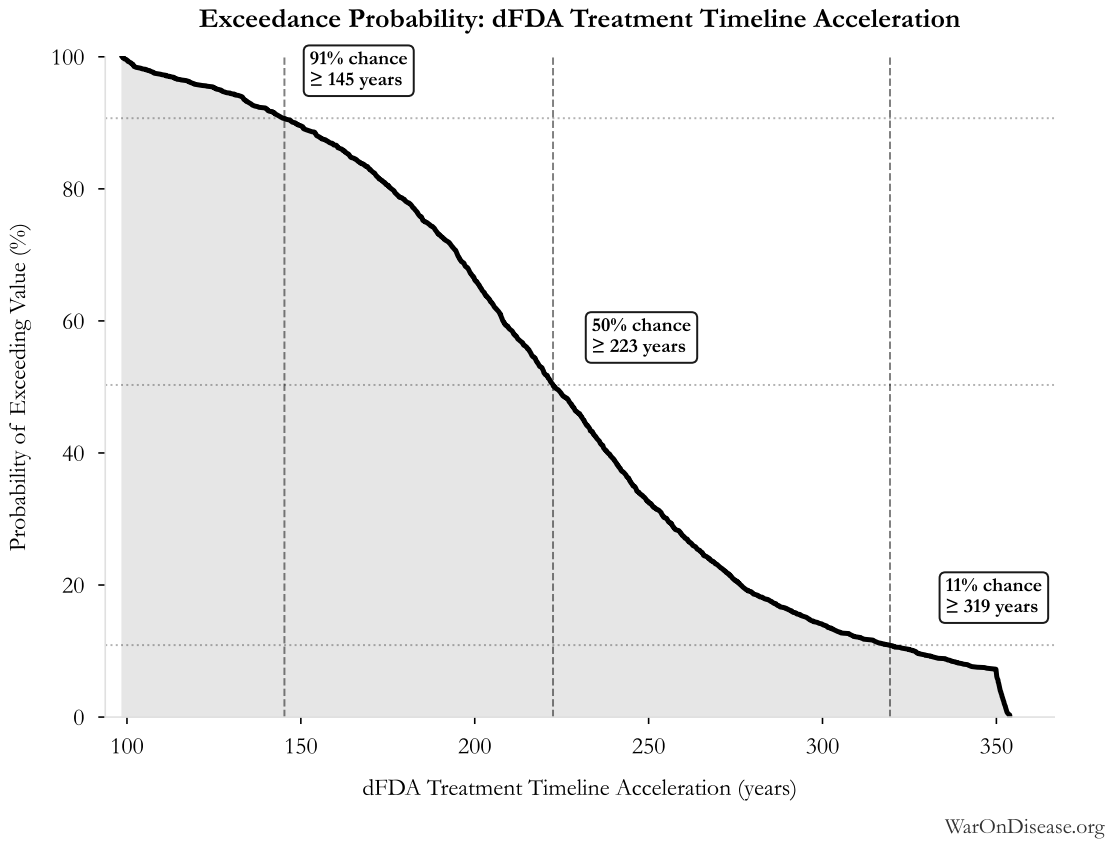


Figure 161: Probability of Exceeding Threshold: dFDA Treatment Timeline Acceleration

This exceedance probability chart shows the likelihood that dFDA Treatment Timeline Acceleration will exceed any given threshold. Higher curves indicate more favorable outcomes with greater certainty.

dFDA Trial Cost Reduction Factor: 44.1x

Details

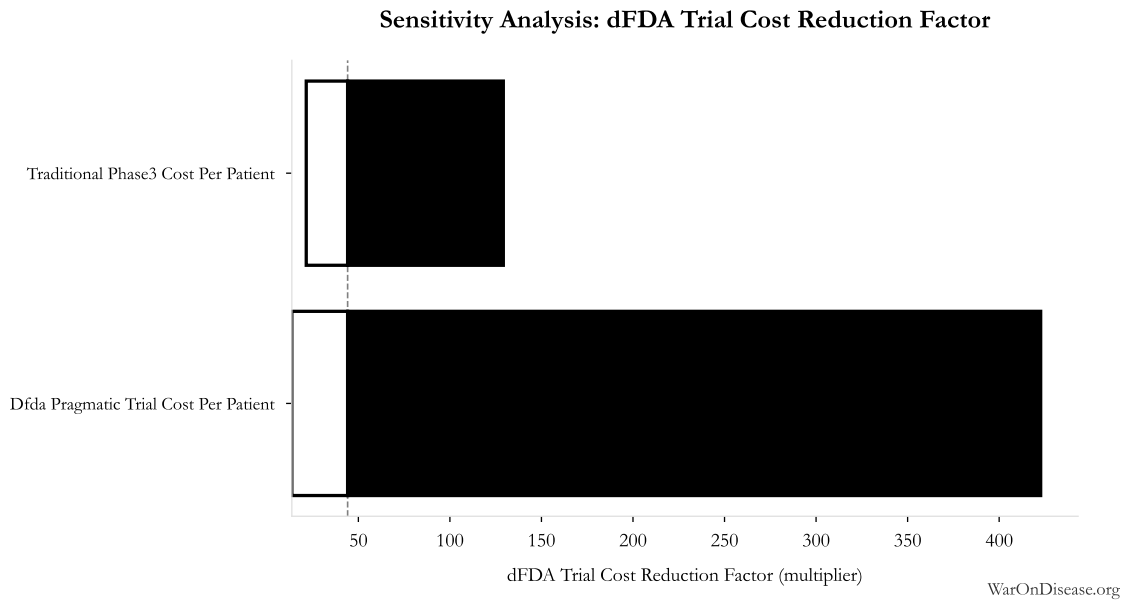
Cost reduction factor projected for dFDA pragmatic trials ($41K traditional / $1,200 dFDA = 34x)
Inputs:

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

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

High confidence

Sensitivity Analysis



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

Input Parameter	Sensitivity Coefficient	Interpretation
dFDA Pragmatic Trial Cost Per Patient	-8.8326	Strong driver
Traditional Phase3 Cost Per Patient	8.3341	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

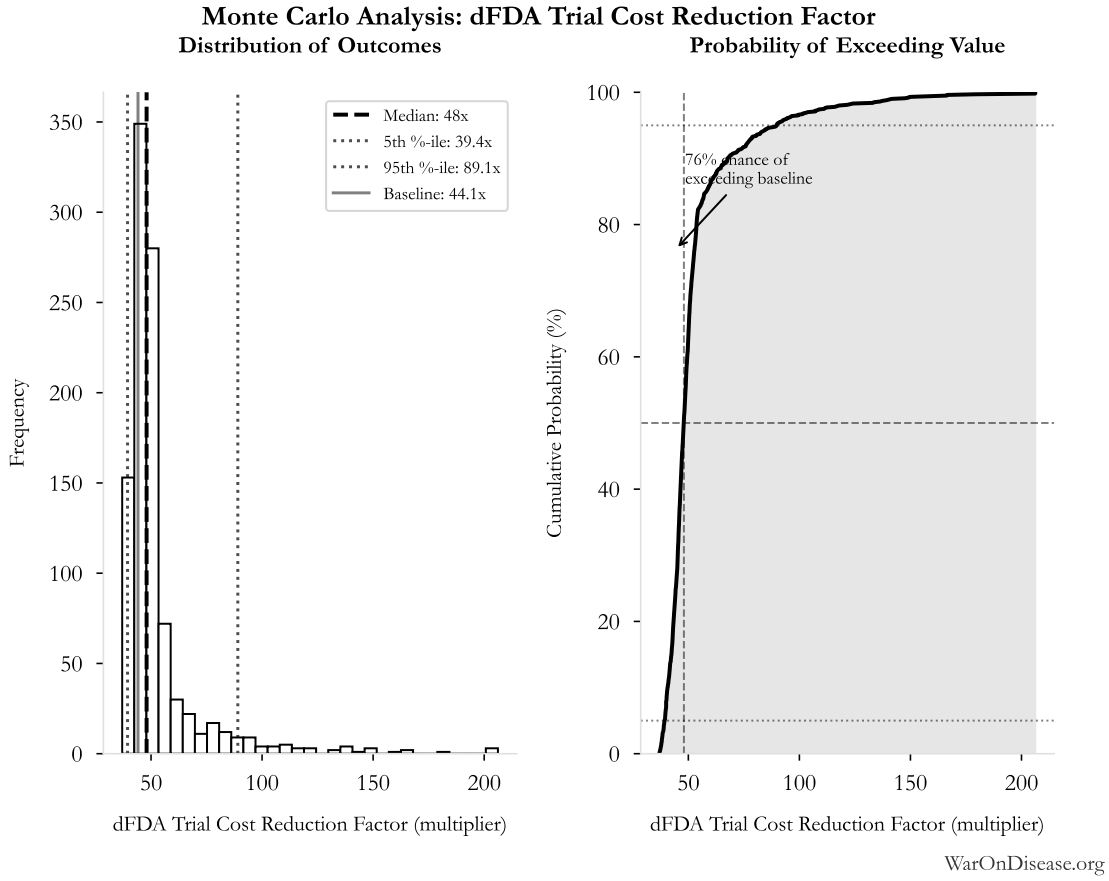


Figure 162: Monte Carlo Distribution: dFDA Trial Cost Reduction Factor (10,000 simulations)

Simulation Results Summary: dFDA Trial Cost Reduction Factor

Statistic	Value
Baseline (deterministic)	44.1x
Mean (expected value)	52.8x
Median (50th percentile)	48x
Standard Deviation	19.5x
90% Range (5th-95th percentile)	[39.4x, 89.1x]

The histogram shows the distribution of dFDA 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

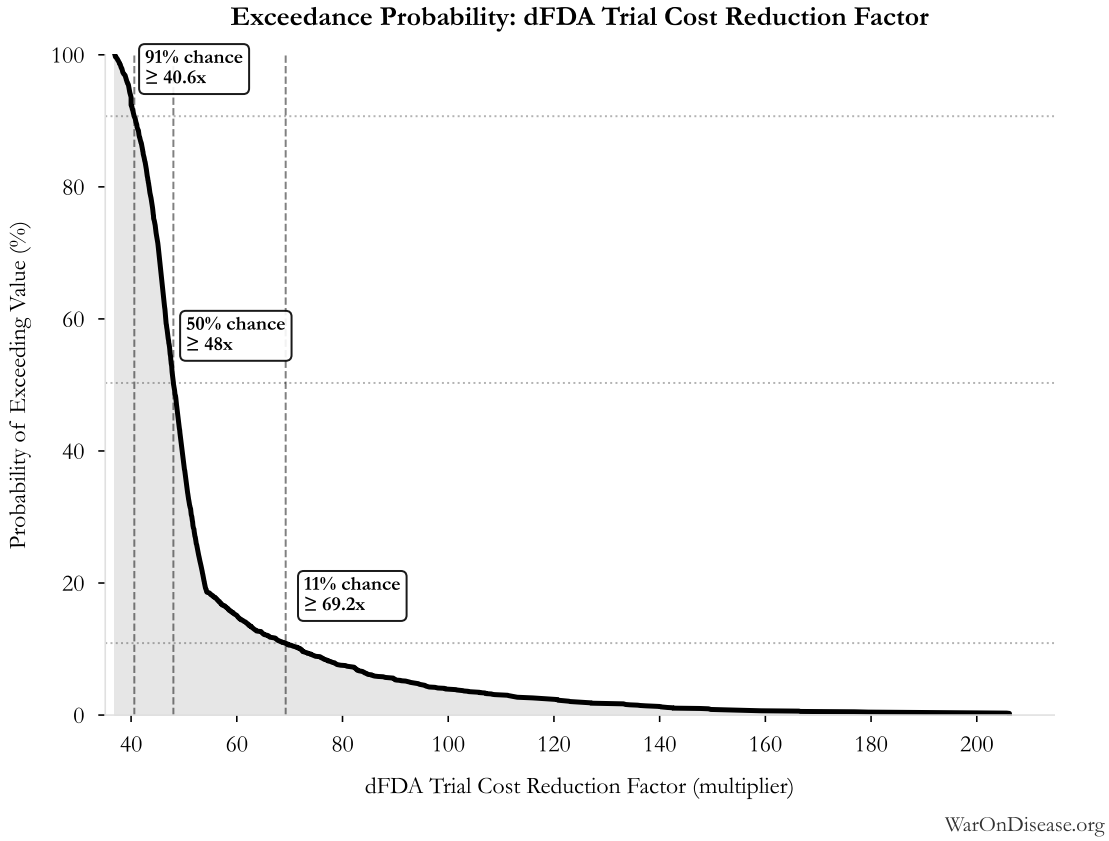


Figure 163: Probability of Exceeding Threshold: dFDA Trial Cost Reduction Factor

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

dFDA Trial Cost Reduction Percentage: 97.7%

Details

Trial cost reduction percentage: (traditional - dFDA) / traditional = ($41K - $1.2K) / $41K = 97%

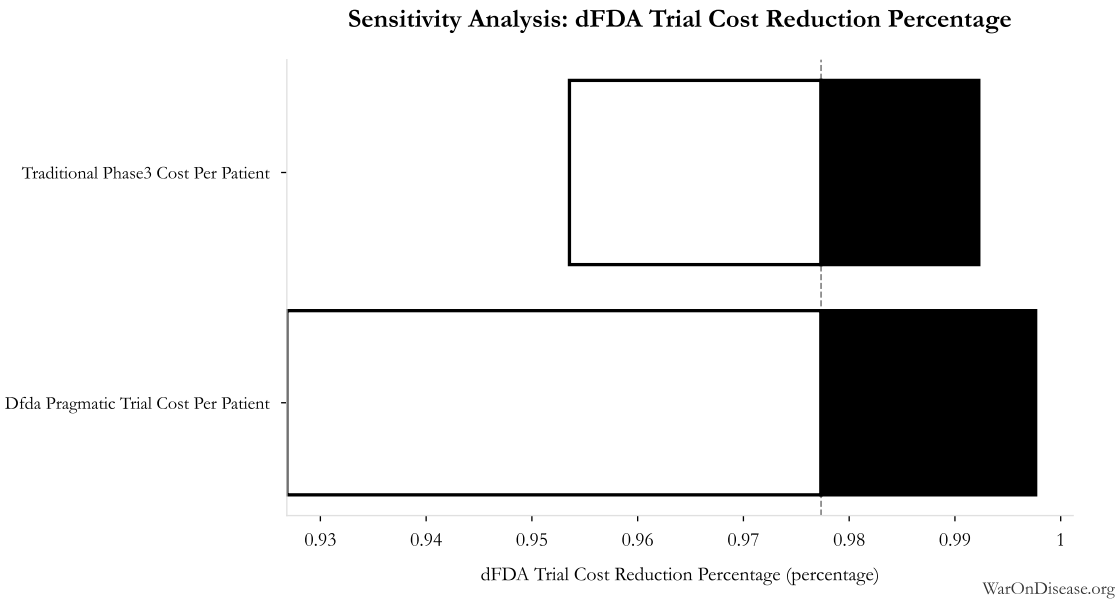
Inputs:

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

$$
\begin{aligned}
& Reduce_{pct} \\
&= 1 - \frac{Cost_{pragmatic,pt}}{Cost_{P3,pt}} \\
&= 1 - \frac{\$929}{\$41K} \\
&= 97.7\%
\end{aligned}
$$

High confidence

Sensitivity Analysis



Sensitivity Indices for dFDA Trial Cost Reduction Percentage

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

Input Parameter	Sensitivity Coefficient	Interpretation
dFDA Pragmatic Trial Cost Per Patient	-6.4207	Strong driver
Traditional Phase3 Cost Per Patient	5.6539	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

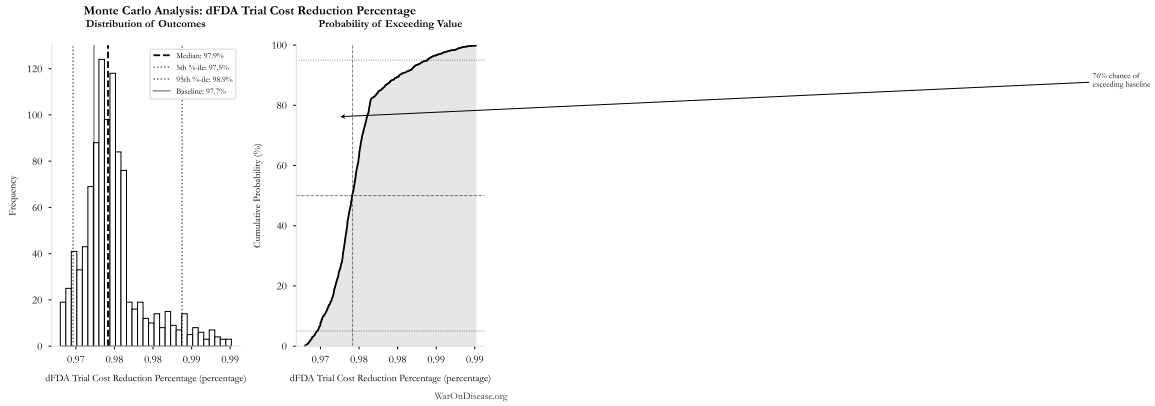


Figure 164: Monte Carlo Distribution: dFDA Trial Cost Reduction Percentage (10,000 simulations)

Simulation Results Summary: dFDA Trial Cost Reduction Percentage

Statistic	Value
Baseline (deterministic)	97.7%
Mean (expected value)	98%
Median (50th percentile)	97.9%
Standard Deviation	0.401%
90% Range (5th-95th percentile)	[97.5%, 98.9%]

The histogram shows the distribution of dFDA Trial Cost Reduction Percentage 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

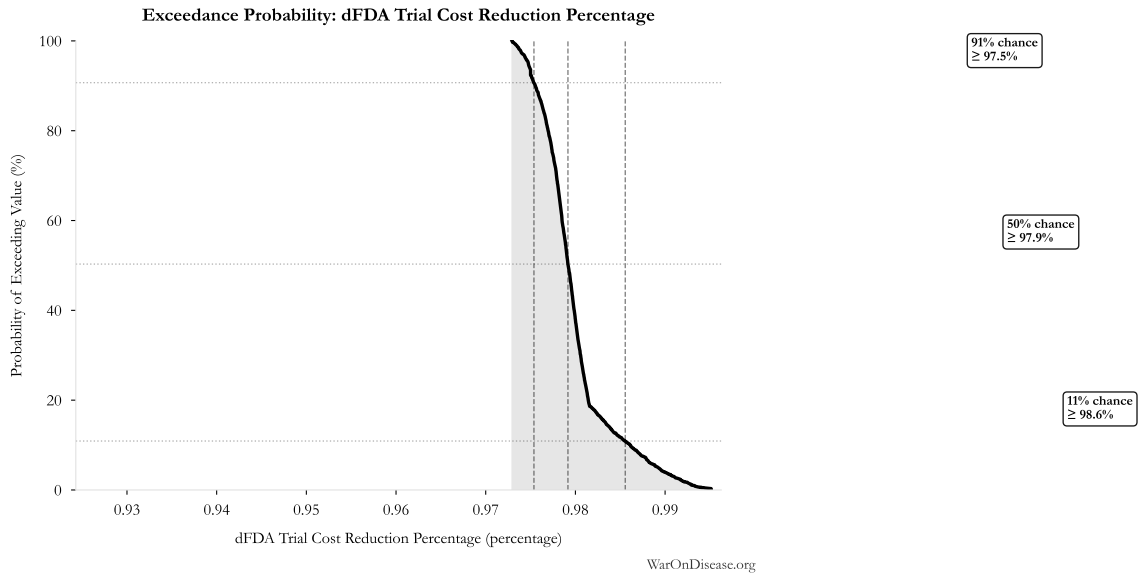


Figure 165: Probability of Exceeding Threshold: dFDA Trial Cost Reduction Percentage

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

dFDA Valley of Death Rescue Multiplier: 1.4x

Details

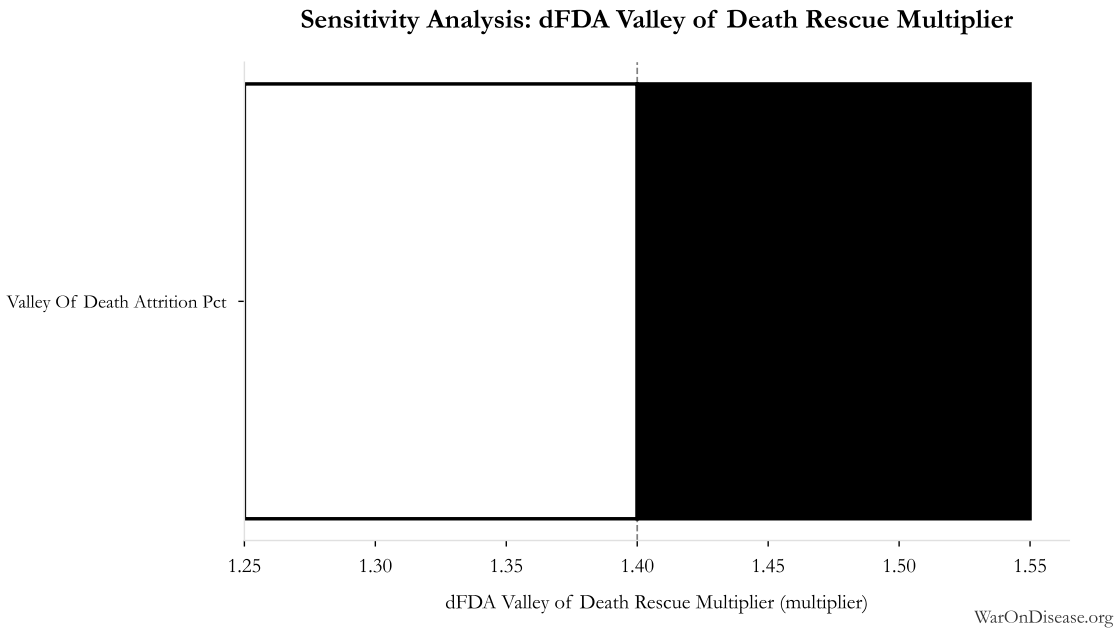
Factor increase in drugs entering development when dFDA eliminates Phase 2/3 cost barrier. Valley-of-death attrition (40%) becomes new drugs, so 1 + 0.40 = 1.4× more drugs.
Inputs:

- Valley of Death Attrition Rate : 40% (95% CI: 25% - 55%)

$$k_{rescue} = Attrition_{valley} + 1 = 40\% + 1 = 1.4$$

~ *Medium confidence*

Sensitivity Analysis



Monte Carlo Distribution

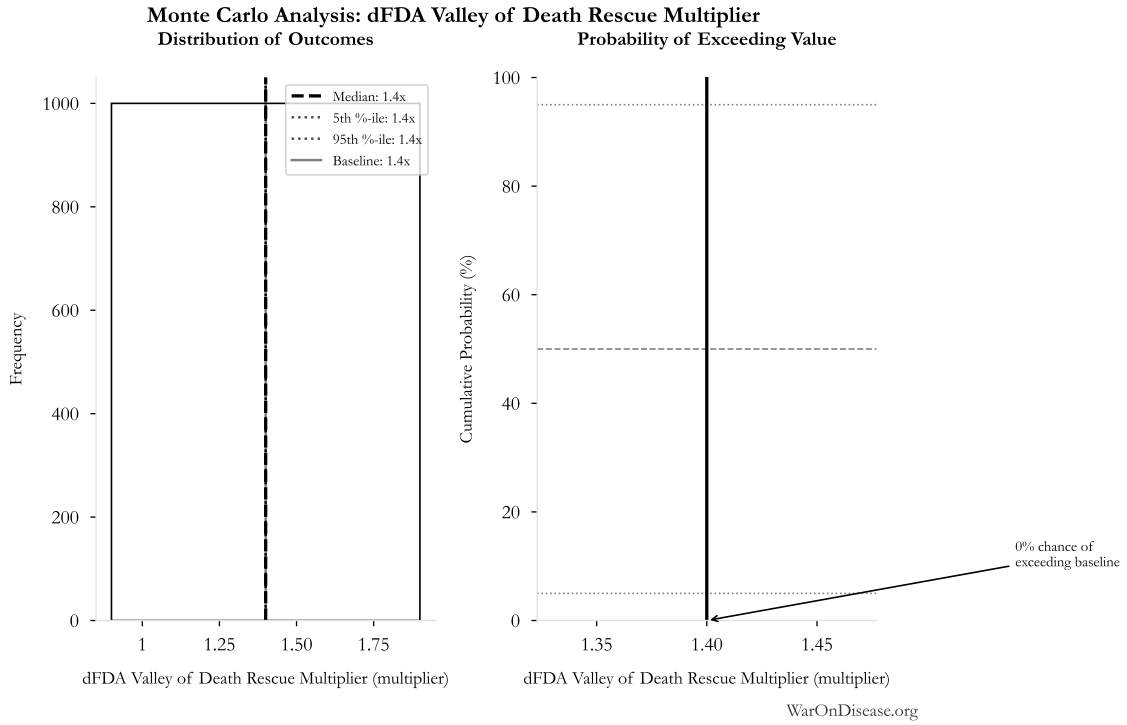


Figure 166: Monte Carlo Distribution: dFDA Valley of Death Rescue Multiplier (10,000 simulations)

Simulation Results Summary: dFDA Valley of Death Rescue Multiplier

Statistic	Value
Baseline (deterministic)	1.4x
Mean (expected value)	1.4x
Median (50th percentile)	1.4x
Standard Deviation	2.22e-16x
90% Range (5th-95th percentile)	[1.4x, 1.4x]

The histogram shows the distribution of dFDA Valley of Death Rescue Multiplier 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

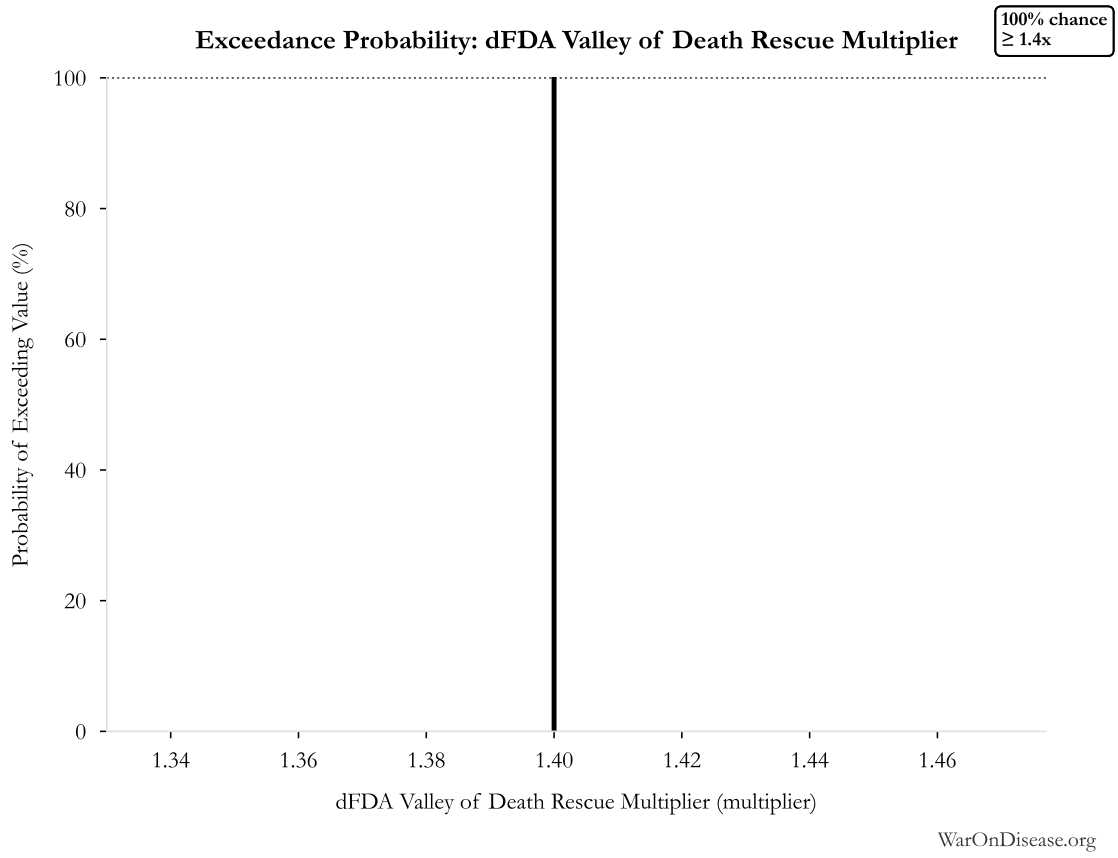


Figure 167: Probability of Exceeding Threshold: dFDA Valley of Death Rescue Multiplier

This exceedance probability chart shows the likelihood that dFDA Valley of Death Rescue Multiplier will exceed any given threshold. Higher curves indicate more favorable outcomes with greater certainty.

Patients Fundable Annually: 23.4 million patients/year

Details

Number of patients fundable annually at dFDA pragmatic trial cost ($1,200/patient). Based on empirical pragmatic trial costs (RECOVERY to PCORnet range).

Inputs:

- Annual Clinical Trial Patient Subsidies : $21.7B
- dFDA Pragmatic Trial Cost per Patient : $929 (95% CI: $97 - $3K)

$$N_{fundable,ann}$$
$$= \frac{Subsidies_{trial,ann}}{Cost_{pragmatic,pt}}$$
$$= \frac{\$21.7B}{\$929}$$
$$= 23.4M$$

where $Subsidies_{trial,ann}$
$$= Treasury_{RD,ann} - OPEX_{dFDA}$$
$$= \$21.8B - \$40M$$
$$= \$21.7B$$

where $OPEX_{dFDA}$
$$= Cost_{platform} + Cost_{staff} + Cost_{infra}$$
$$+Cost_{regulatory} + Cost_{community}$$
$$= \$15M + \$10M + \$8M + \$5M + \$2M$$
$$= \$40M$$

where $Treasury_{RD,ann}$
$$= Funding_{treaty} - Payout_{bond,ann} - Funding_{political,ann}$$
$$= \$27.2B - \$2.72B - \$2.72B$$
$$= \$21.8B$$

where $Funding_{treaty}$
$$= Spending_{mil} \times Reduce_{treaty}$$
$$= \$2.72T \times 1\%$$
$$= \$27.2B$$

where $Payout_{bond,ann}$
$$= Funding_{treaty} \times Pct_{bond}$$
$$= \$27.2B \times 10\%$$
$$= \$2.72B$$

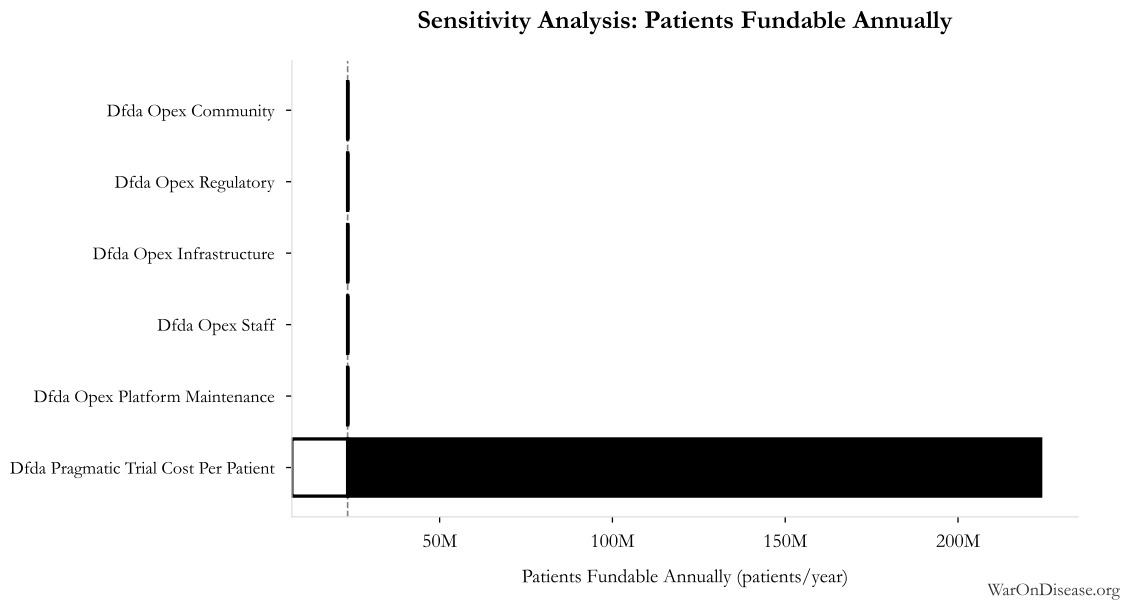
where $Funding_{treaty}$
$$= Spending_{mil} \times Reduce_{treaty}$$
$$= \$2.72T \times 1\%$$
$$= \$27.2B$$

where $Funding_{political,ann}$
$$= Funding_{treaty} \times Pct_{political}$$
$$= \$27.2B \times 10\%$$
$$= \$2.72B$$

where $Funding_{treaty}$
$$= Spending_{mil} \times Reduce_{treaty}$$
$$= \$2.72T \times 1\%$$
$$= \$27.2B$$

High confidence

Sensitivity Analysis



Sensitivity Indices for Patients Fundable Annually
Regression-based sensitivity showing which inputs explain the most variance in the output.

Input Parameter	Sensitivity Coefficient	Interpretation
DIH Treasury Trial Subsidies Annual	2.3351	Strong driver
dFDA Pragmatic Trial Cost Per Patient	1.5755	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

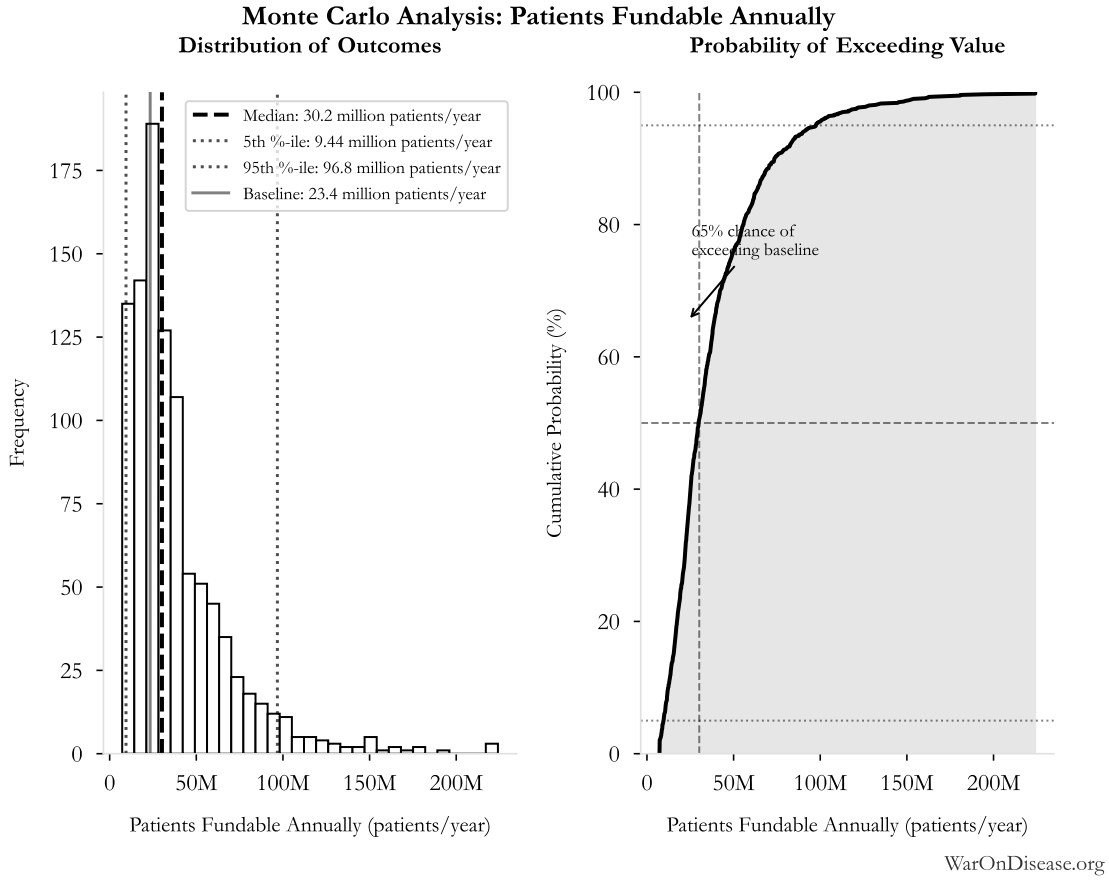


Figure 168: Monte Carlo Distribution: Patients Fundable Annually (10,000 simulations)

Simulation Results Summary: Patients Fundable Annually

Statistic	Value
Baseline (deterministic)	23.4 million
Mean (expected value)	38.6 million
Median (50th percentile)	30.2 million
Standard Deviation	30.2 million
90% Range (5th-95th percentile)	[9.44 million, 96.8 million]

The histogram shows the distribution of Patients Fundable Annually 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

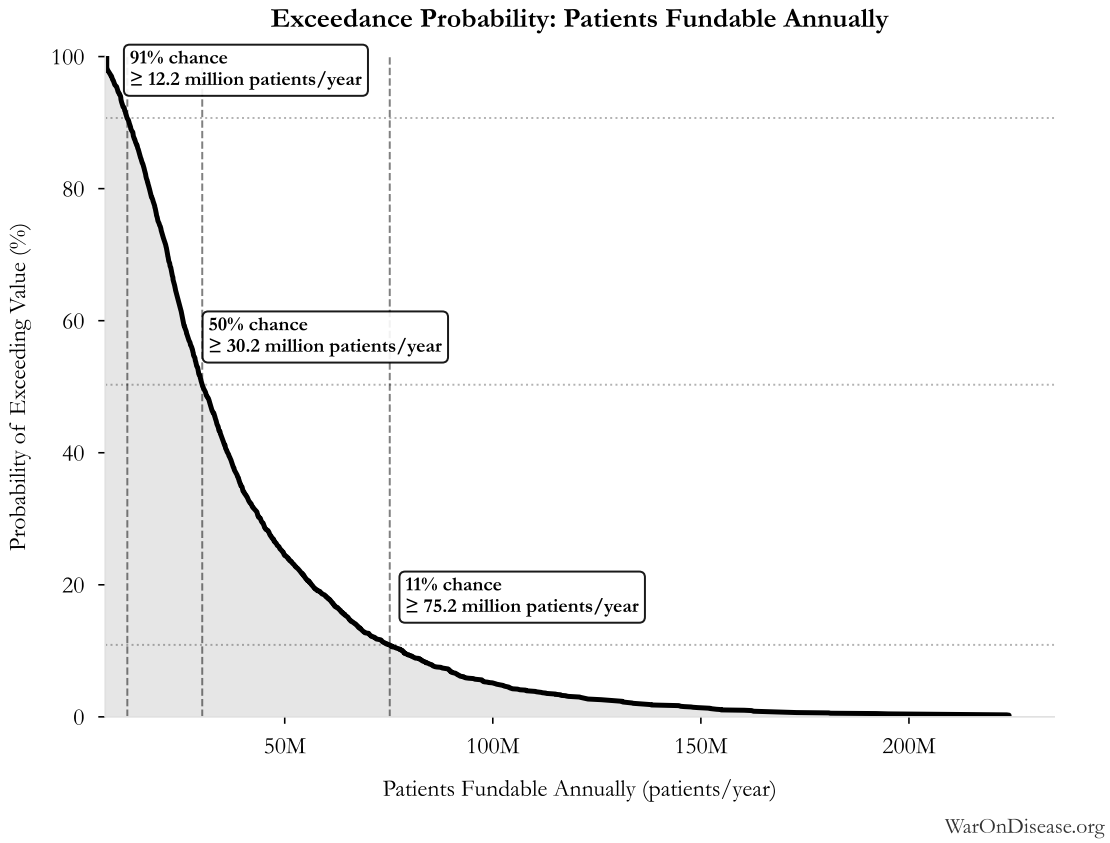


Figure 169: Probability of Exceeding Threshold: Patients Fundable Annually

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

Medical Research Percentage of Treaty Funding: 80%

Details

Percentage of treaty funding allocated to medical research (after bond payouts and IAB incentives)

Inputs:

- Annual Funding for Pragmatic Clinical Trials : $21.8B
- Annual Funding from 1% of Global Military Spending Redirected to DIH : $27.2B

$$Pct_{treasury,RD} = \frac{Treasury_{RD,ann}}{Funding_{treaty}} = \frac{\$21.8B}{\$27.2B} = 80\%$$

$$\text{where } Treasury_{RD,ann}$$
$$= Funding_{treaty} - Payout_{bond,ann} - Funding_{political,ann}$$
$$= \$27.2B - \$2.72B - \$2.72B$$
$$= \$21.8B$$

$$\text{where } Funding_{treaty}$$
$$= Spending_{mil} \times Reduce_{treaty}$$
$$= \$2.72T \times 1\%$$
$$= \$27.2B$$

$$\text{where } Payout_{bond,ann}$$
$$= Funding_{treaty} \times Pct_{bond}$$
$$= \$27.2B \times 10\%$$
$$= \$2.72B$$

$$\text{where } Funding_{treaty}$$
$$= Spending_{mil} \times Reduce_{treaty}$$
$$= \$2.72T \times 1\%$$
$$= \$27.2B$$

$$\text{where } Funding_{political,ann}$$
$$= Funding_{treaty} \times Pct_{political}$$
$$= \$27.2B \times 10\%$$
$$= \$2.72B$$

$$\text{where } Funding_{treaty}$$
$$= Spending_{mil} \times Reduce_{treaty}$$
$$= \$2.72T \times 1\%$$
$$= \$27.2B$$

$$\text{where } Funding_{treaty}$$
$$= Spending_{mil} \times Reduce_{treaty}$$
$$= \$2.72T \times 1\%$$
$$= \$27.2B$$

High confidence

Monte Carlo Distribution

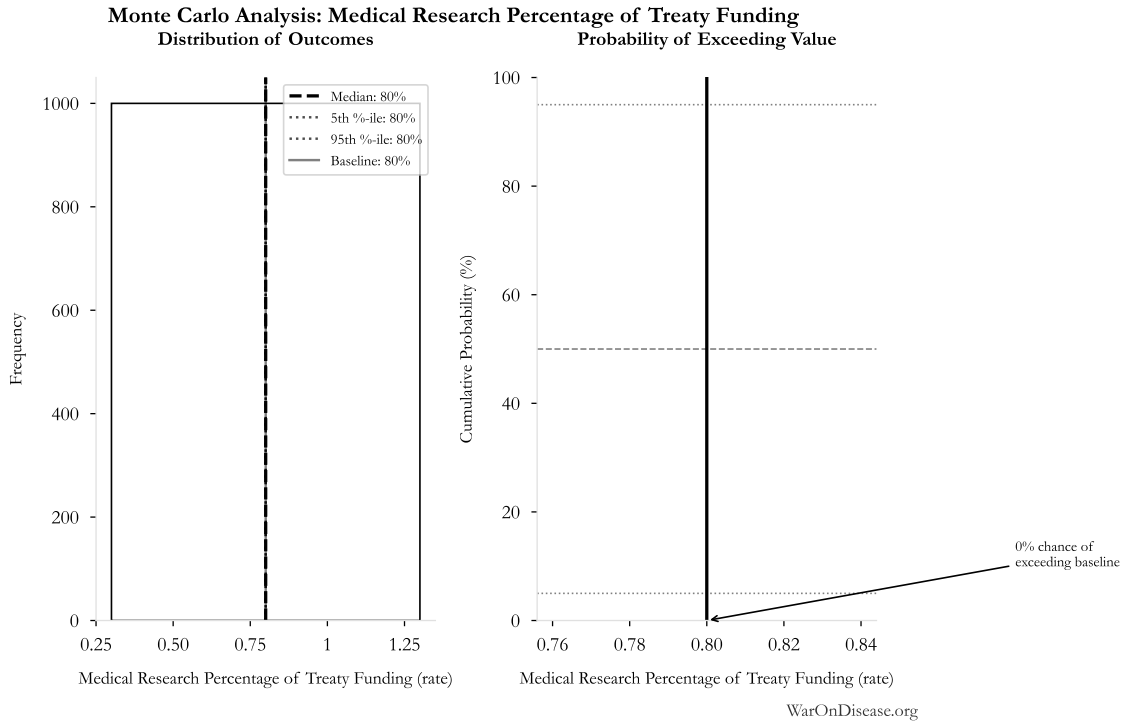


Figure 170: Monte Carlo Distribution: Medical Research Percentage of Treaty Funding (10,000 simulations)

Simulation Results Summary: Medical Research Percentage of Treaty Funding

Statistic	Value
Baseline (deterministic)	80%
Mean (expected value)	80%
Median (50th percentile)	80%
Standard Deviation	1.11e-14%
90% Range (5th-95th percentile)	[80%, 80%]

The histogram shows the distribution of Medical Research Percentage of Treaty Funding 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

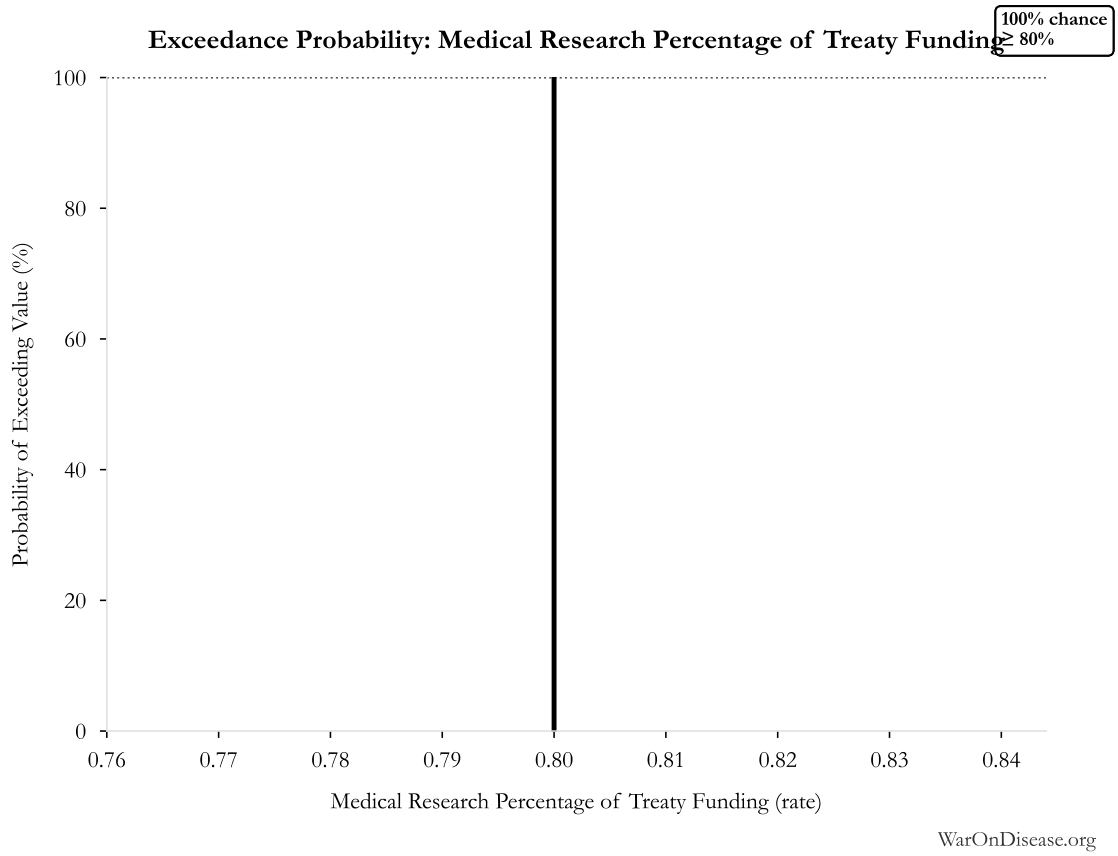


Figure 171: Probability of Exceeding Threshold: Medical Research Percentage of Treaty Funding

This exceedance probability chart shows the likelihood that Medical Research Percentage of Treaty Funding will exceed any given threshold. Higher curves indicate more favorable outcomes with greater certainty.

Annual Funding for Pragmatic Clinical Trials: $21.8B

Details

Annual funding for pragmatic clinical trials (treaty funding minus VICTORY Incentive Alignment Bond payouts and IAB political incentive mechanism)

Inputs:

- Annual Funding from 1% of Global Military Spending Redirected to DIH : $27.2B
- Annual VICTORY Incentive Alignment Bond Payout : $2.72B
- Annual IAB Political Incentive Funding : $2.72B

$$
\begin{aligned}
&Treasury_{RD,ann} \\
&= Funding_{treaty} - Payout_{bond,ann} - Funding_{political,ann} \\
&= \$27.2B - \$2.72B - \$2.72B \\
&= \$21.8B
\end{aligned}
$$

$$
\begin{aligned}
&\text{where } Funding_{treaty} \\
&= Spending_{mil} \times Reduce_{treaty} \\
&= \$2.72T \times 1\% \\
&= \$27.2B
\end{aligned}
$$

$$
\begin{aligned}
&\text{where } Payout_{bond,ann} \\
&= Funding_{treaty} \times Pct_{bond} \\
&= \$27.2B \times 10\% \\
&= \$2.72B
\end{aligned}
$$

$$
\begin{aligned}
&\text{where } Funding_{treaty} \\
&= Spending_{mil} \times Reduce_{treaty} \\
&= \$2.72T \times 1\% \\
&= \$27.2B
\end{aligned}
$$

$$
\begin{aligned}
&\text{where } Funding_{political,ann} \\
&= Funding_{treaty} \times Pct_{political} \\
&= \$27.2B \times 10\% \\
&= \$2.72B
\end{aligned}
$$

$$
\begin{aligned}
&\text{where } Funding_{treaty} \\
&= Spending_{mil} \times Reduce_{treaty} \\
&= \$2.72T \times 1\% \\
&= \$27.2B
\end{aligned}
$$

High confidence

Annual Clinical Trial Patient Subsidies: $21.7B

Details

Annual clinical trial patient subsidies (all medical research funds after Decentralized Framework for Drug Assessment operations)

Inputs:

- Total Annual Decentralized Framework for Drug Assessment Operational Costs : $40M
- Annual Funding for Pragmatic Clinical Trials : $21.8B

$$Subsidies_{trial,ann}$$
$$= Treasury_{RD,ann} - OPEX_{dFDA}$$
$$= \$21.8B - \$40M$$
$$= \$21.7B$$

where $OPEX_{dFDA}$
$$= Cost_{platform} + Cost_{staff} + Cost_{infra}$$
$$+Cost_{regulatory} + Cost_{community}$$
$$= \$15M + \$10M + \$8M + \$5M + \$2M$$
$$= \$40M$$

where $Treasury_{RD,ann}$
$$= Funding_{treaty} - Payout_{bond,ann} - Funding_{political,ann}$$
$$= \$27.2B - \$2.72B - \$2.72B$$
$$= \$21.8B$$

where $Funding_{treaty}$
$$= Spending_{mil} \times Reduce_{treaty}$$
$$= \$2.72T \times 1\%$$
$$= \$27.2B$$

where $Payout_{bond,ann}$
$$= Funding_{treaty} \times Pct_{bond}$$
$$= \$27.2B \times 10\%$$
$$= \$2.72B$$

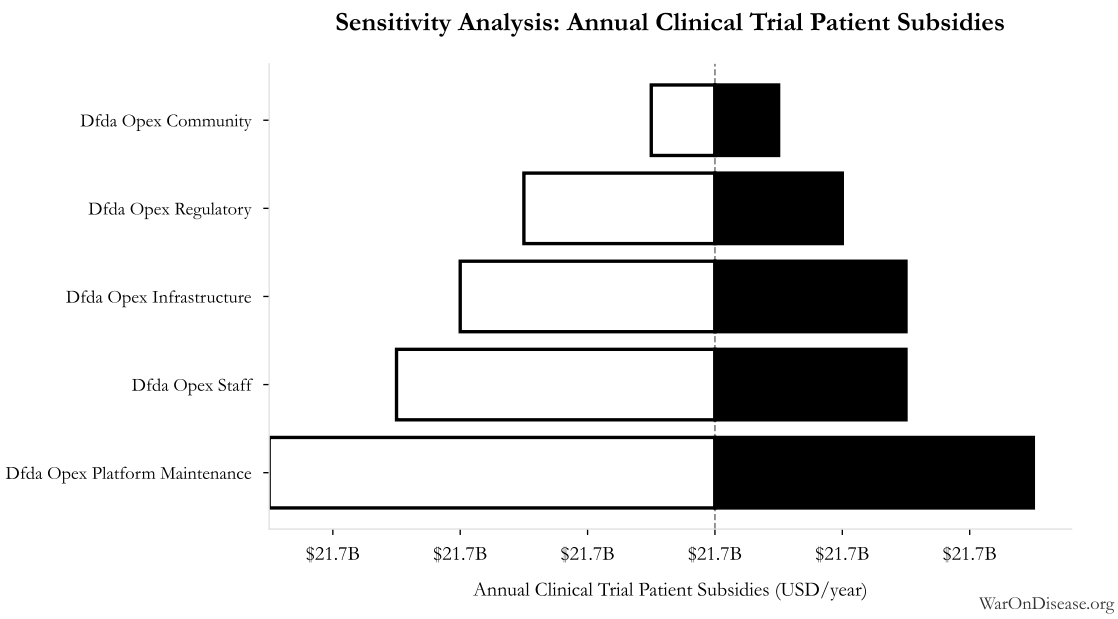
where $Funding_{treaty}$
$$= Spending_{mil} \times Reduce_{treaty}$$
$$= \$2.72T \times 1\%$$
$$= \$27.2B$$

where $Funding_{political,ann}$
$$= Funding_{treaty} \times Pct_{political}$$
$$= \$27.2B \times 10\%$$
$$= \$2.72B$$

where $Funding_{treaty}$
$$= Spending_{mil} \times Reduce_{treaty}$$
$$= \$2.72T \times 1\%$$
$$= \$27.2B$$

High confidence

Sensitivity Analysis



Sensitivity Indices for Annual Clinical Trial Patient Subsidies
Regression-based sensitivity showing which inputs explain the most variance in the output.

Input Parameter	Sensitivity Coefficient	Interpretation
dFDA Annual OPEX	-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 172: Monte Carlo Distribution: Annual Clinical Trial Patient Subsidies (10,000 simulations)

Simulation Results Summary: Annual Clinical Trial Patient Subsidies

Statistic	Value
Baseline (deterministic)	$21.7B
Mean (expected value)	$21.7B
Median (50th percentile)	$21.7B
Standard Deviation	$8.21M
90% Range (5th-95th percentile)	[$21.7B, $21.7B]

The histogram shows the distribution of Annual Clinical Trial Patient Subsidies 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

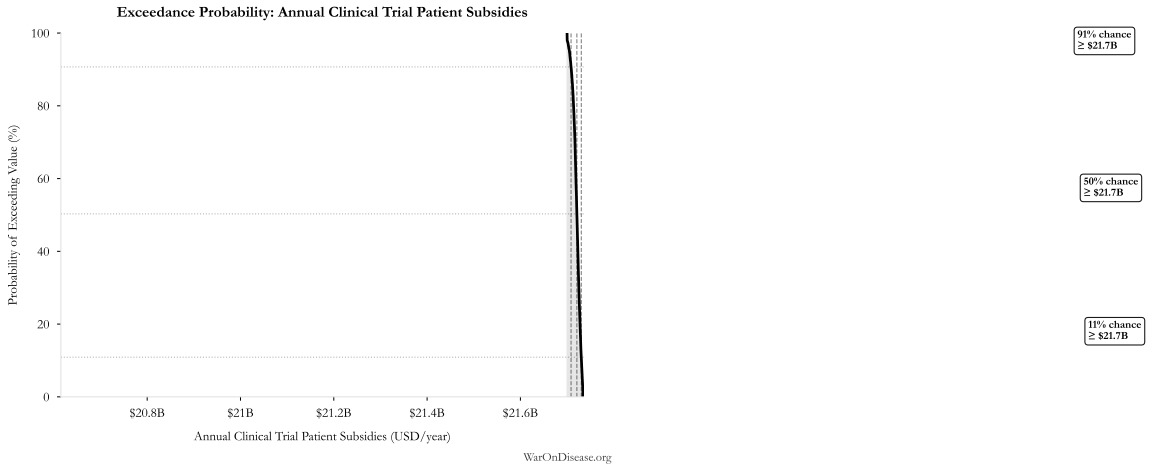


Figure 173: Probability of Exceeding Threshold: Annual Clinical Trial Patient Subsidies

This exceedance probability chart shows the likelihood that Annual Clinical Trial Patient Subsidies will exceed any given threshold. Higher curves indicate more favorable outcomes with greater certainty.

Patient Trial Subsidies Percentage of Treaty Funding: 79.9%

Details

Percentage of treaty funding going directly to patient trial subsidies
Inputs:

- Annual Clinical Trial Patient Subsidies : $21.7B
- Annual Funding from 1% of Global Military Spending Redirected to DIH : $27.2B

$$Pct_{subsidies} = \frac{Subsidies_{trial,ann}}{Funding_{treaty}} = \frac{\$21.7B}{\$27.2B} = 79.9\%$$

$$\text{where } Subsidies_{trial,ann}$$
$$= Treasury_{RD,ann} - OPEX_{dFDA}$$
$$= \$21.8B - \$40M$$
$$= \$21.7B$$

$$\text{where } OPEX_{dFDA}$$
$$= Cost_{platform} + Cost_{staff} + Cost_{infra}$$
$$+Cost_{regulatory} + Cost_{community}$$
$$= \$15M + \$10M + \$8M + \$5M + \$2M$$
$$= \$40M$$

$$\text{where } Treasury_{RD,ann}$$
$$= Funding_{treaty} - Payout_{bond,ann} - Funding_{political,ann}$$
$$= \$27.2B - \$2.72B - \$2.72B$$
$$= \$21.8B$$

$$\text{where } Funding_{treaty}$$
$$= Spending_{mil} \times Reduce_{treaty}$$
$$= \$2.72T \times 1\%$$
$$= \$27.2B$$

$$\text{where } Payout_{bond,ann}$$
$$= Funding_{treaty} \times Pct_{bond}$$
$$= \$27.2B \times 10\%$$
$$= \$2.72B$$

$$\text{where } Funding_{treaty}$$
$$= Spending_{mil} \times Reduce_{treaty}$$
$$= \$2.72T \times 1\%$$
$$= \$27.2B$$

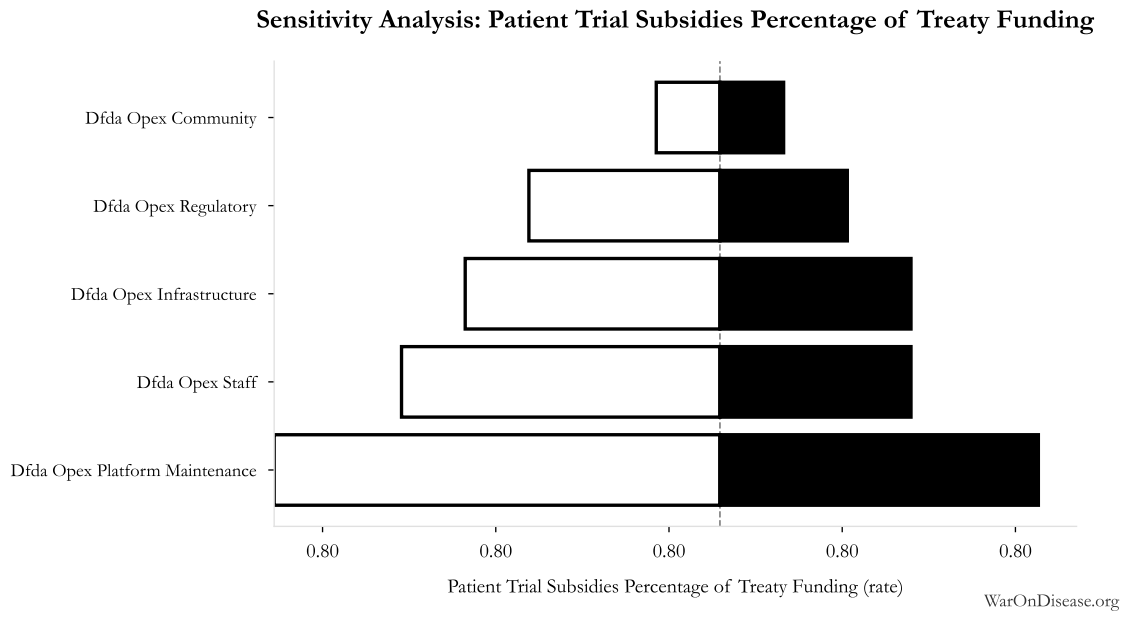
$$\text{where } Funding_{political,ann}$$
$$= Funding_{treaty} \times Pct_{political}$$
$$= \$27.2B \times 10\%$$
$$= \$2.72B$$

$$\text{where } Funding_{treaty}$$
$$= Spending_{mil} \times Reduce_{treaty}$$
$$= \$2.72T \times 1\%$$
$$= \$27.2B$$

$$\text{where } Funding_{treaty}$$
$$= Spending_{mil} \times Reduce_{treaty}$$
$$= \$2.72T \times 1\%$$
$$= \$27.2B$$

High confidence

Sensitivity Analysis



Sensitivity Indices for Patient Trial Subsidies Percentage of Treaty Funding
Regression-based sensitivity showing which inputs explain the most variance in the output.

Input Parameter	Sensitivity Coefficient	Interpretation
DIH Treasury Trial Subsidies Annual	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 174: Monte Carlo Distribution: Patient Trial Subsidies Percentage of Treaty Funding (10,000 simulations)

Simulation Results Summary: Patient Trial Subsidies Percentage of Treaty Funding

Statistic	Value
Baseline (deterministic)	79.9%
Mean (expected value)	79.9%
Median (50th percentile)	79.9%
Standard Deviation	0.0302%
90% Range (5th-95th percentile)	[79.8%, 79.9%]

The histogram shows the distribution of Patient Trial Subsidies Percentage of Treaty Funding 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

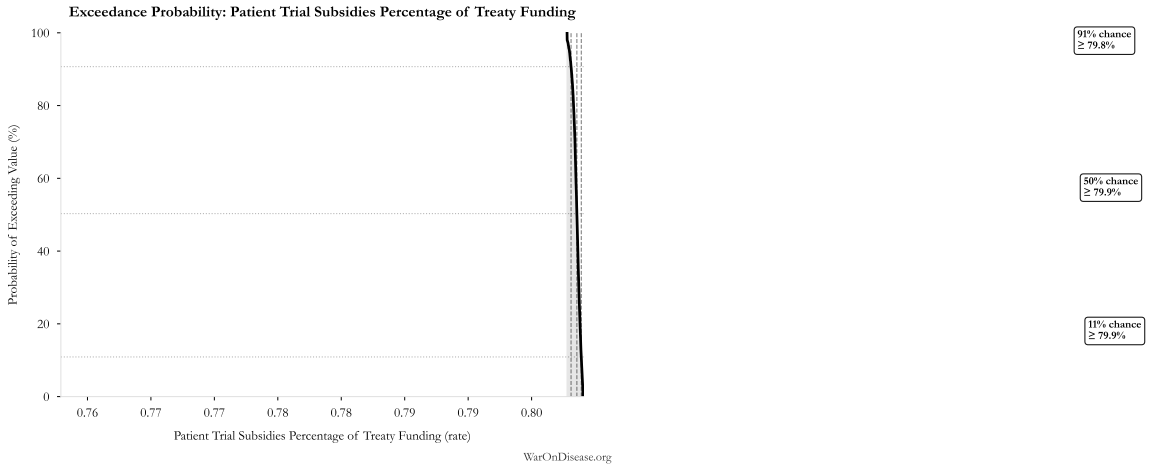


Figure 175: Probability of Exceeding Threshold: Patient Trial Subsidies Percentage of Treaty Funding

This exceedance probability chart shows the likelihood that Patient Trial Subsidies Percentage of Treaty Funding will exceed any given threshold. Higher curves indicate more favorable outcomes with greater certainty.

Diseases Without Effective Treatment: 6.65 thousand 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.

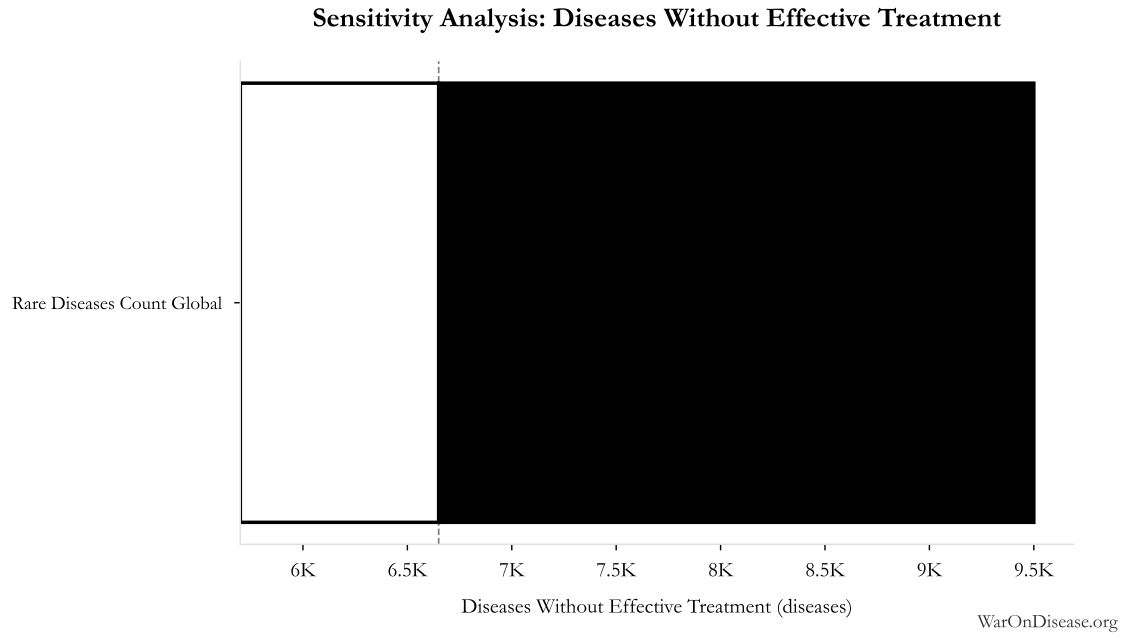
Inputs:

- Total Number of Rare Diseases Globally : 7.00 thousand diseases (95% CI: 6.00 thousand diseases - 10.0 thousand diseases)

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

Methodology:[153]
~ *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
Rare Diseases Count Global	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

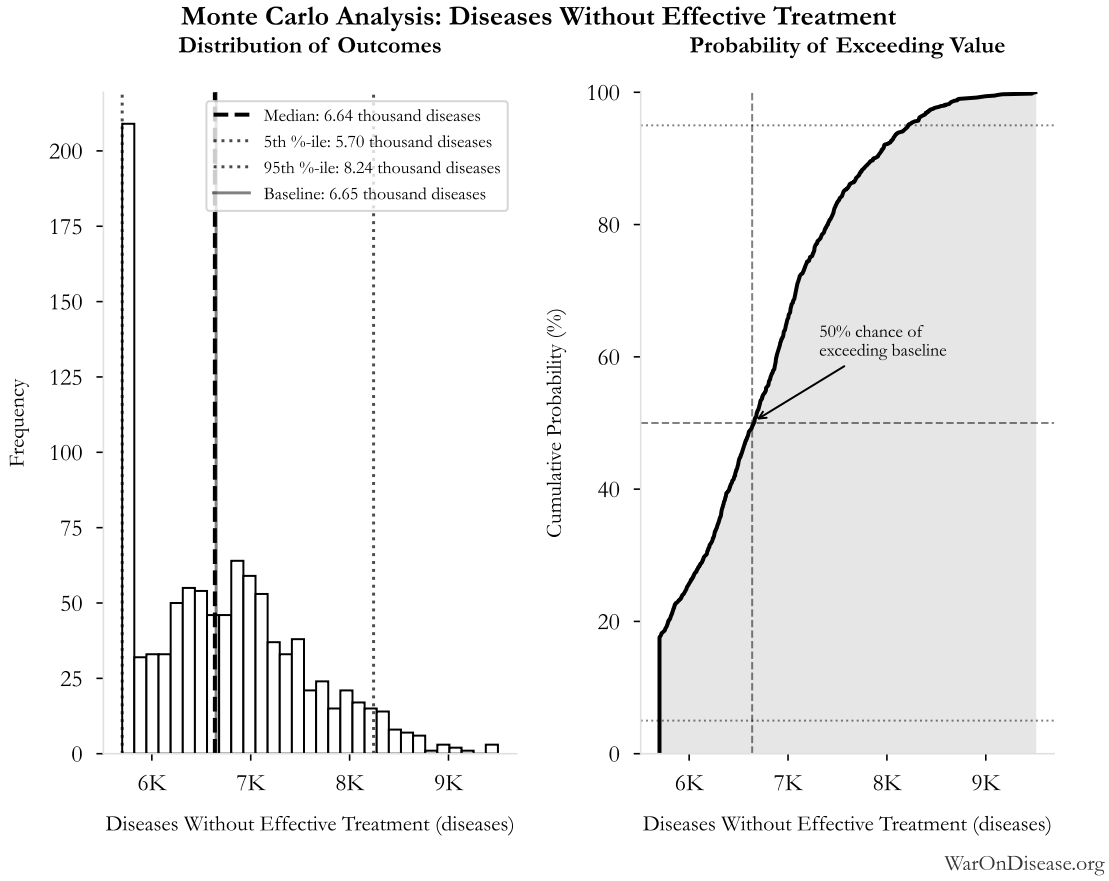


Figure 176: Monte Carlo Distribution: Diseases Without Effective Treatment (10,000 simulations)

Simulation Results Summary: Diseases Without Effective Treatment

Statistic	Value
Baseline (deterministic)	6.65 thousand
Mean (expected value)	6.73 thousand
Median (50th percentile)	6.64 thousand
Standard Deviation	835
90% Range (5th-95th percentile)	[5.70 thousand, 8.24 thousand]

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

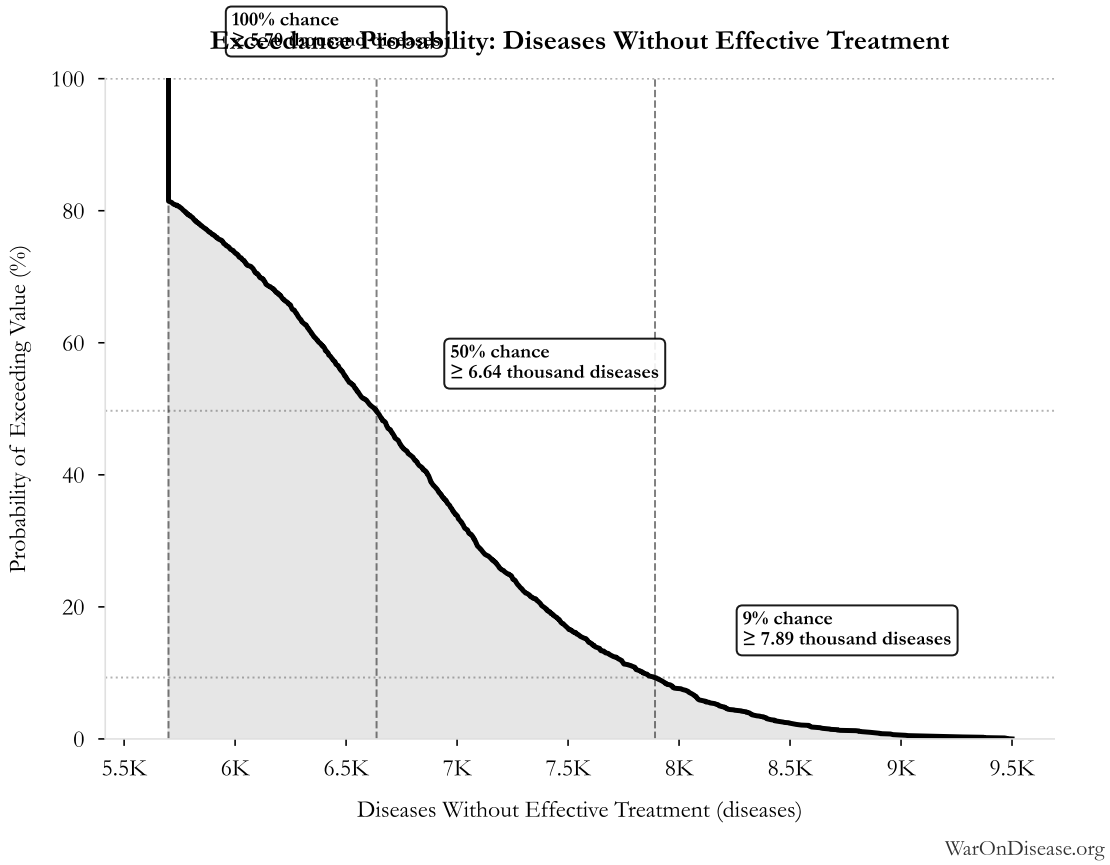


Figure 177: Probability of Exceeding Threshold: Diseases Without Effective Treatment

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.

Ratio of Annual Disease Deaths to 9/11 Terrorism Deaths: 18.4k:1

Details

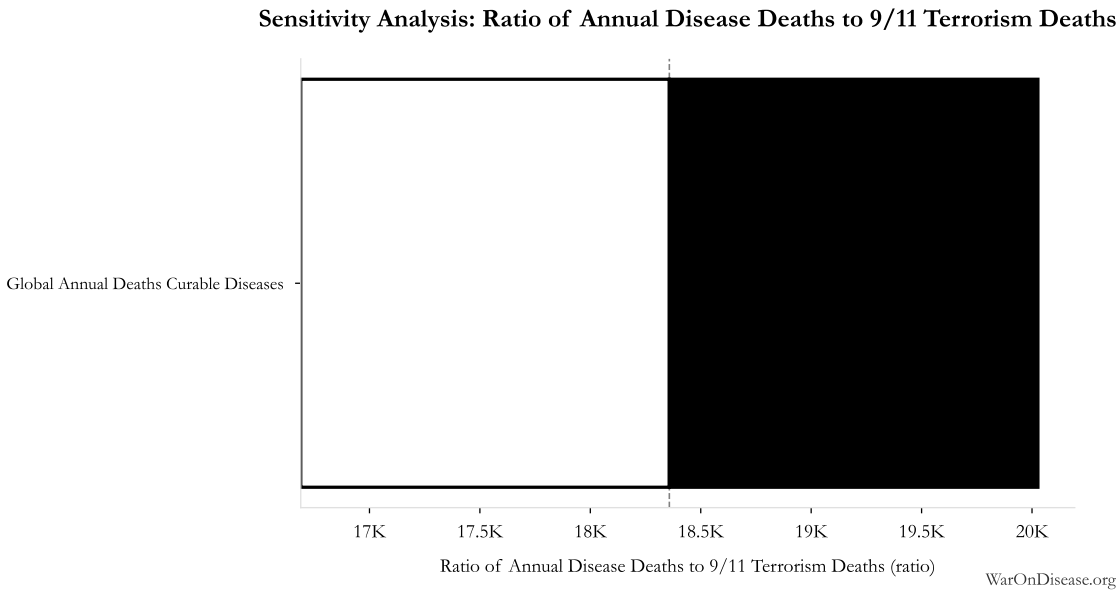
Ratio of annual disease deaths to 9/11 terrorism deaths
Inputs:

- Annual Deaths from All Diseases and Aging Globally : 55.0 million deaths/year (SE: ±5.00 million deaths/year)
- Deaths from 9/11 Terrorist Attacks : 3.00 thousand deaths

$$\begin{aligned} & Ratio_{dis:terror} \\ &= \frac{Deaths_{curable,ann}}{Deaths_{9/11}} \\ &= \frac{55M}{3{,}000} \\ &= 18{,}400 \end{aligned}$$

High confidence

Sensitivity Analysis



Sensitivity Indices for Ratio of Annual Disease Deaths to 9/11 Terrorism Deaths

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

Input Parameter	Sensitivity Coefficient	Interpretation
Global Annual Deaths Curable 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

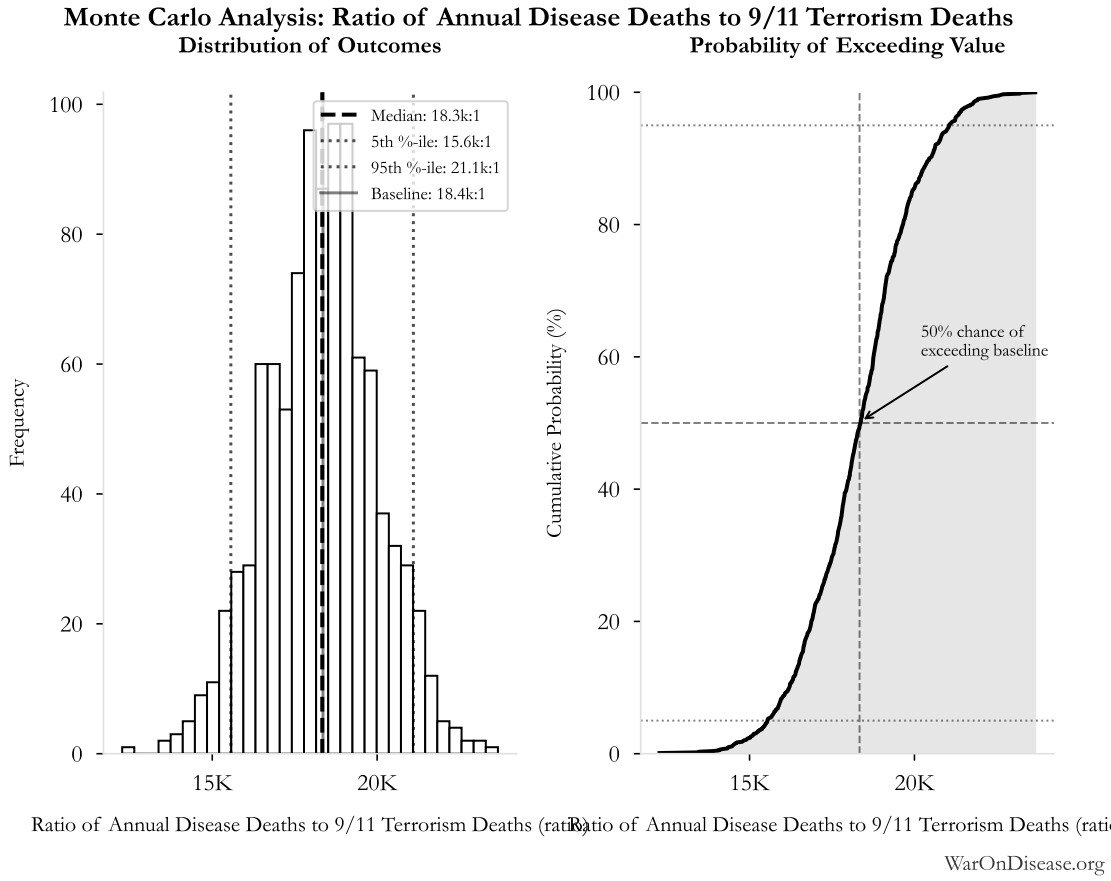


Figure 178: Monte Carlo Distribution: Ratio of Annual Disease Deaths to 9/11 Terrorism Deaths (10,000 simulations)

Simulation Results Summary: Ratio of Annual Disease Deaths to 9/11 Terrorism Deaths

Statistic	Value
Baseline (deterministic)	18.4k:1
Mean (expected value)	18.3k:1
Median (50th percentile)	18.3k:1
Standard Deviation	1.68k:1
90% Range (5th-95th percentile)	[15.6k:1, 21.1k:1]

The histogram shows the distribution of Ratio of Annual Disease Deaths to 9/11 Terrorism Deaths 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

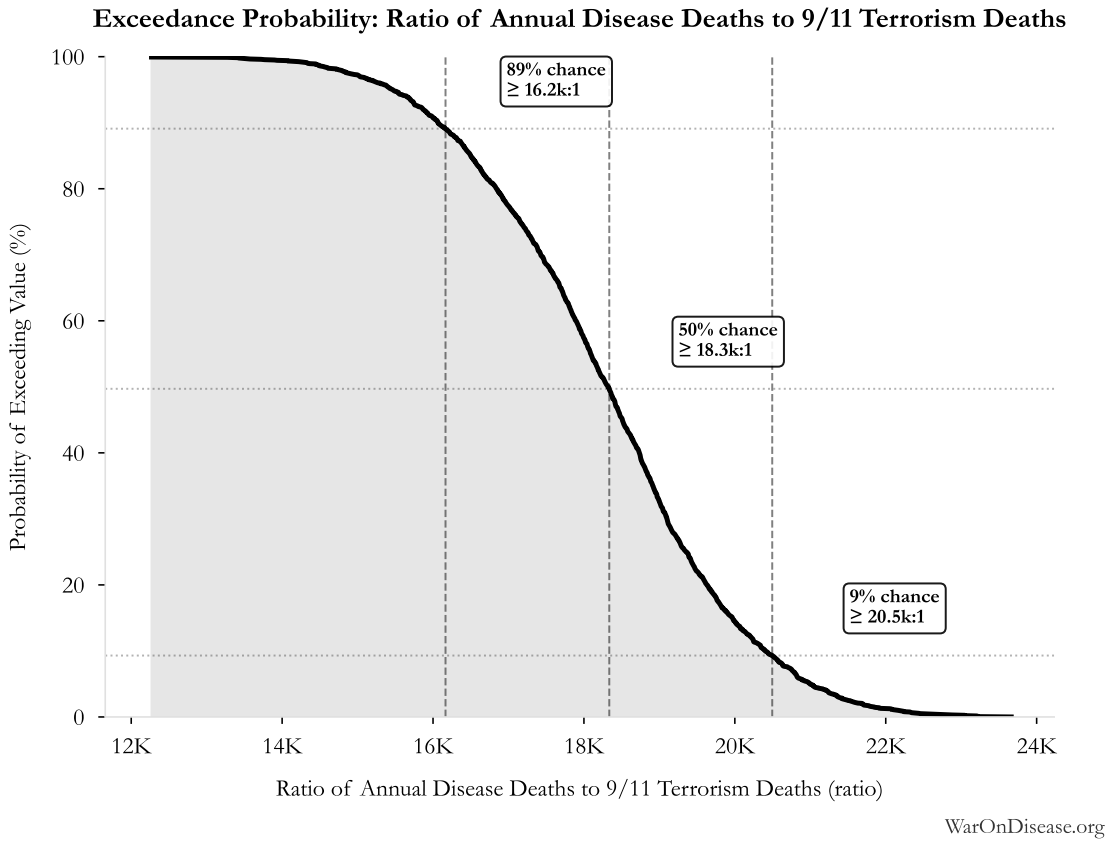


Figure 179: Probability of Exceeding Threshold: Ratio of Annual Disease Deaths to 9/11 Terrorism Deaths

This exceedance probability chart shows the likelihood that Ratio of Annual Disease Deaths to 9/11 Terrorism Deaths will exceed any given threshold. Higher curves indicate more favorable outcomes with greater certainty.

Ratio of Annual Disease Deaths to War Deaths: 225:1

Details

Ratio of annual disease deaths to war deaths

Inputs:

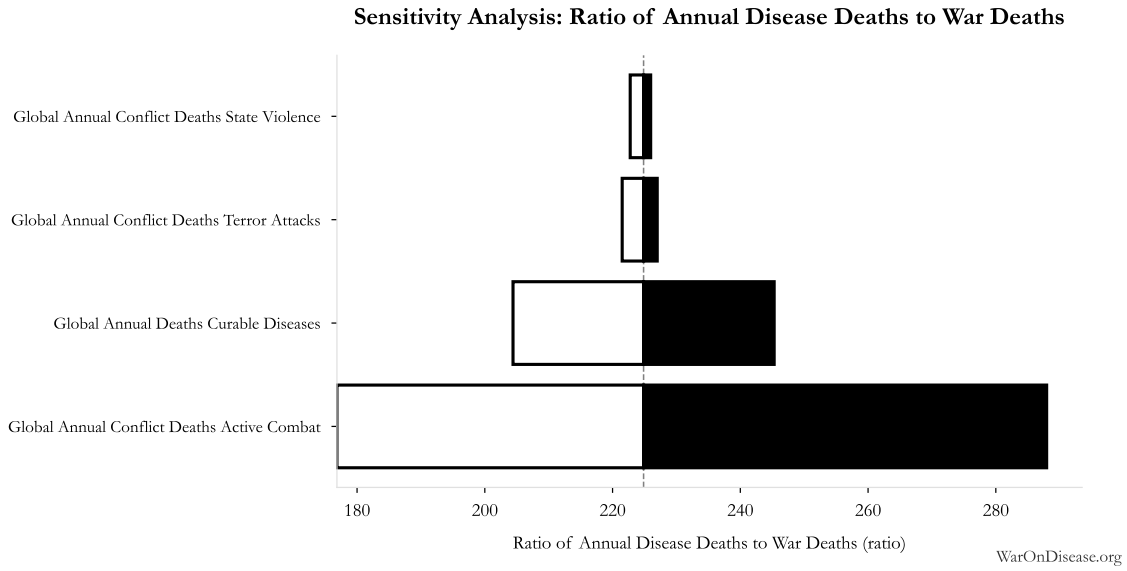
- Annual Deaths from All Diseases and Aging Globally : 55.0 million deaths/year (SE: ±5.00 million deaths/year)
- Total Annual Conflict Deaths Globally : 245 thousand deaths/year

$$Ratio_{dis:war} = \frac{Deaths_{curable,ann}}{Deaths_{conflict}} = \frac{55M}{245{,}000} = 225$$

$$\begin{aligned} &\text{where } Deaths_{conflict} \\ &= Deaths_{combat} + Deaths_{state} + Deaths_{terror} \\ &= 234{,}000 + 2{,}700 + 8{,}300 \\ &= 245{,}000 \end{aligned}$$

High confidence

Sensitivity Analysis



Sensitivity Indices for Ratio of Annual Disease Deaths to War Deaths

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

Input Parameter	Sensitivity Coefficient	Interpretation
Global Annual Conflict Deaths Total	-2.9115	Strong driver
Global Annual Deaths Curable Diseases	1.9792	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

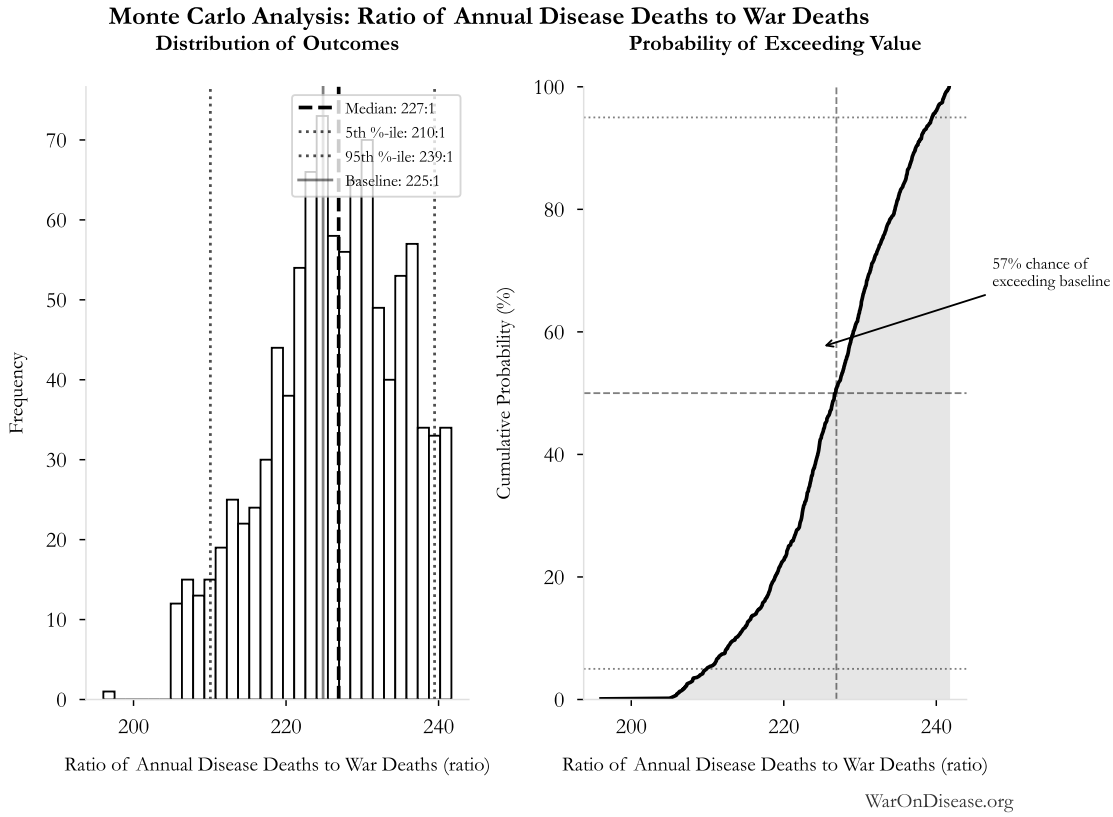


Figure 180: Monte Carlo Distribution: Ratio of Annual Disease Deaths to War Deaths (10,000 simulations)

Simulation Results Summary: Ratio of Annual Disease Deaths to War Deaths

Statistic	Value
Baseline (deterministic)	225:1
Mean (expected value)	226:1
Median (50th percentile)	227:1
Standard Deviation	8.8:1
90% Range (5th-95th percentile)	[210:1, 239:1]

The histogram shows the distribution of Ratio of Annual Disease Deaths to War Deaths 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

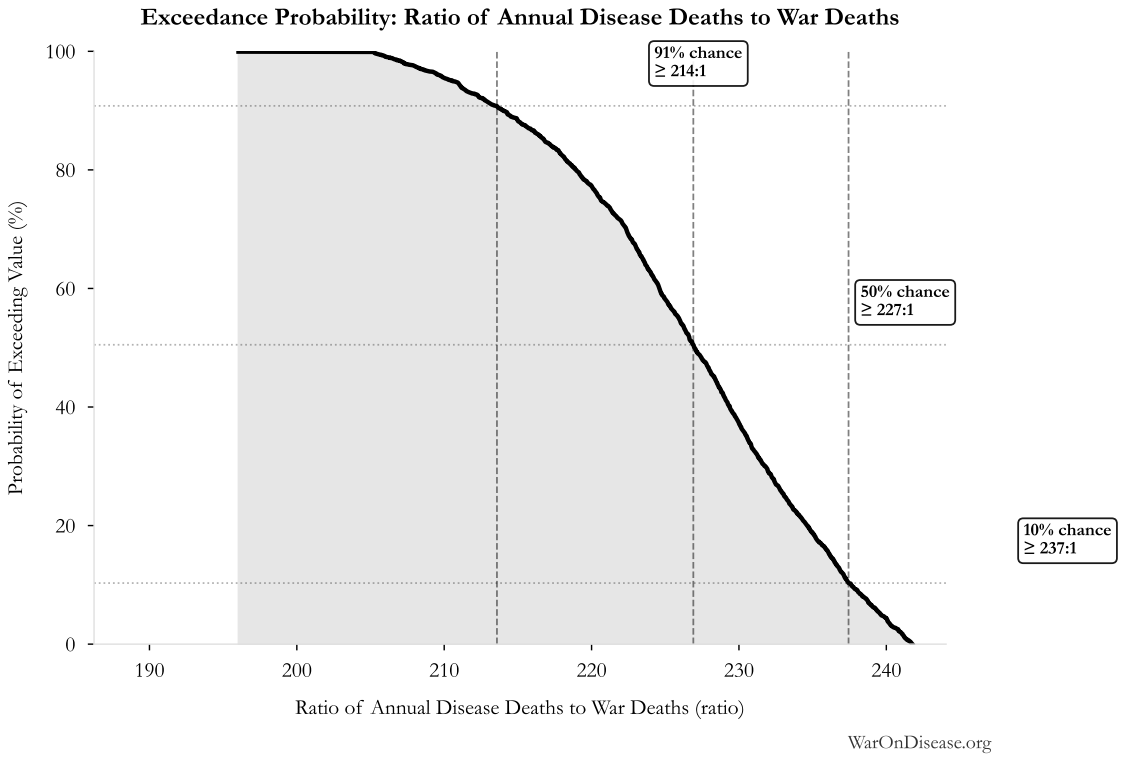


Figure 181: Probability of Exceeding Threshold: Ratio of Annual Disease Deaths to War Deaths

This exceedance probability chart shows the likelihood that Ratio of Annual Disease Deaths to War Deaths will exceed any given threshold. Higher curves indicate more favorable outcomes with greater certainty.

Drug Cost Increase: 1980s to Current: 13.4x

Details

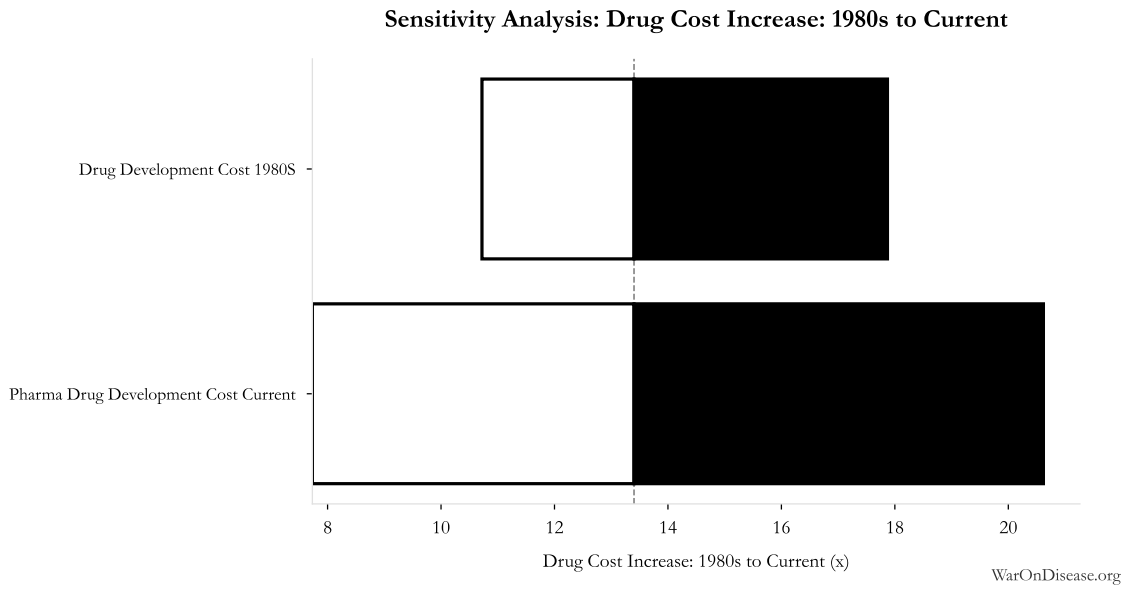
Drug development cost increase from 1980s to current ($194M → $2.6B = 13.4x)
Inputs:

- Drug Development Cost (1980s) : $194M (95% CI: $146M - $242M)
- Pharma Drug Development Cost (Current System) : $2.60B (95% CI: $1.50B - $4B)

$$
\begin{aligned}
& k_{cost,80s} \\
&= \frac{Cost_{dev,curr}}{Cost_{dev,80s}} \\
&= \frac{\$2.6B}{\$194M} \\
&= 13.4
\end{aligned}
$$

Methodology:[20]
High confidence

Sensitivity Analysis



Sensitivity Indices for Drug Cost Increase: 1980s to Current
Regression-based sensitivity showing which inputs explain the most variance in the output.

Input Parameter	Sensitivity Coefficient	Interpretation
Pharma Drug Development Cost Current	1.6909	Strong driver
Drug Development Cost 1980s	-0.7048	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

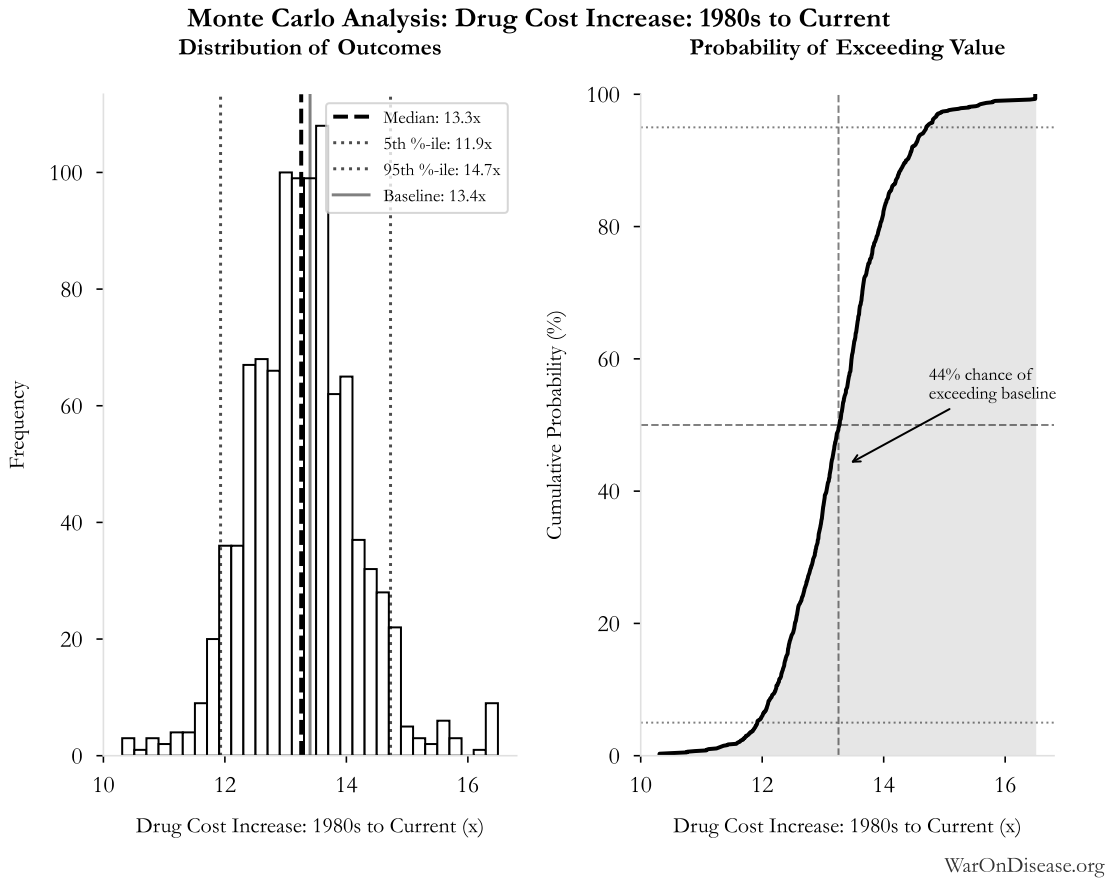


Figure 182: Monte Carlo Distribution: Drug Cost Increase: 1980s to Current (10,000 simulations)

Simulation Results Summary: Drug Cost Increase: 1980s to Current

Statistic	Value
Baseline (deterministic)	13.4x
Mean (expected value)	13.3x
Median (50th percentile)	13.3x
Standard Deviation	0.915x
90% Range (5th-95th percentile)	[11.9x, 14.7x]

The histogram shows the distribution of Drug Cost Increase: 1980s to Current 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

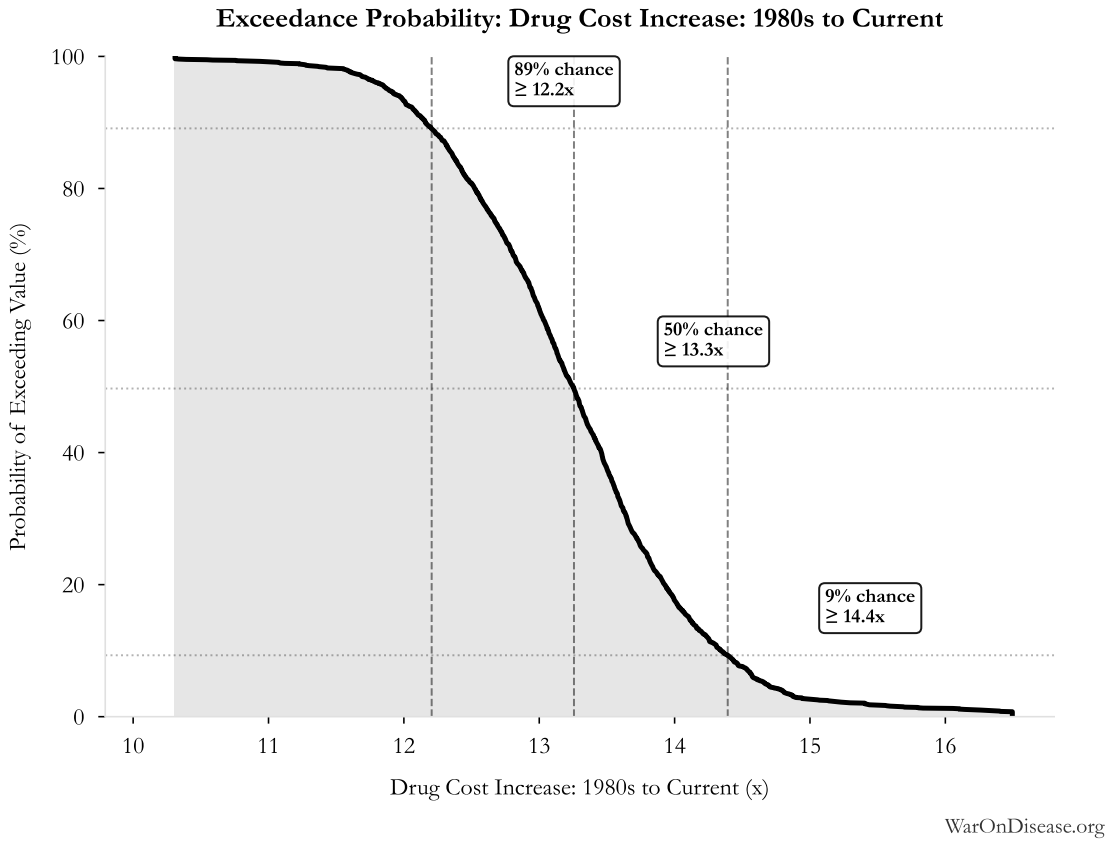


Figure 183: Probability of Exceeding Threshold: Drug Cost Increase: 1980s to Current

This exceedance probability chart shows the likelihood that Drug Cost Increase: 1980s to Current will exceed any given threshold. Higher curves indicate more favorable outcomes with greater certainty.

Drug Cost Increase: Pre-1962 to Current: 105x

Details

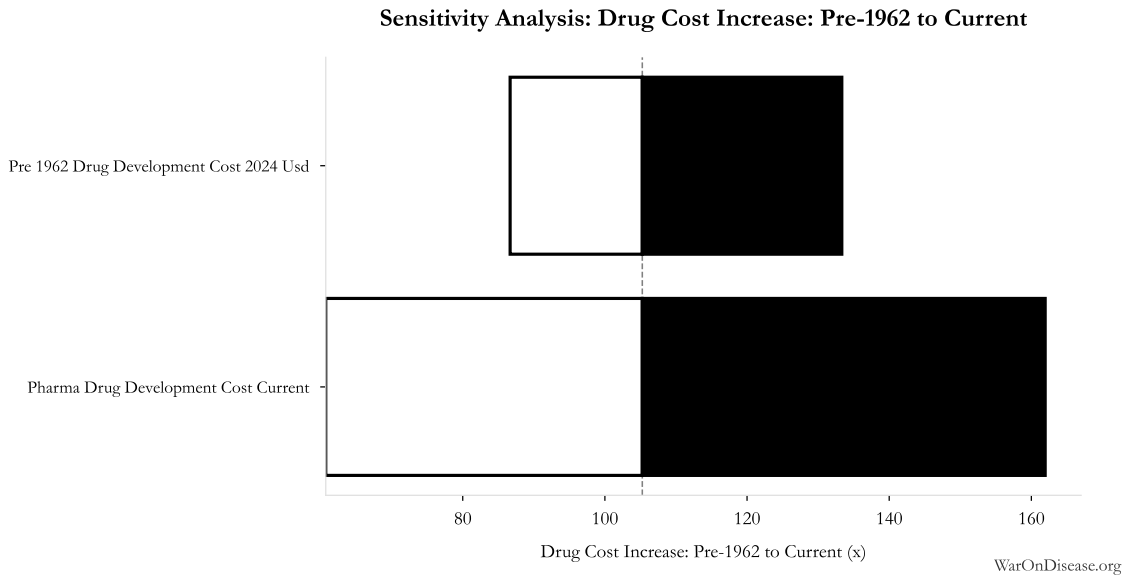
Drug development cost increase from pre-1962 to current ($24.7M → $2.6B = 105×)
Inputs:

- Pharma Drug Development Cost (Current System) : $2.60B (95% CI: $1.50B - $4B)
- Pre-1962 Drug Development Cost (2024 Dollars) : $24.7M (95% CI: $19.5M - $30M)

$$\begin{aligned} & k_{cost,pre62} \\ &= \frac{Cost_{dev,curr}}{Cost_{pre62,24}} \\ &= \frac{\$2.6B}{\$24.7M} \\ &= 105 \end{aligned}$$

Methodology:[80]
High confidence

Sensitivity Analysis



Sensitivity Indices for Drug Cost Increase: Pre-1962 to Current

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

Input Parameter	Sensitivity Coefficient	Interpretation
Pharma Drug Development Cost Current	1.3110	Strong driver
Pre 1962 Drug Development Cost 2024 Usd	-0.3181	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

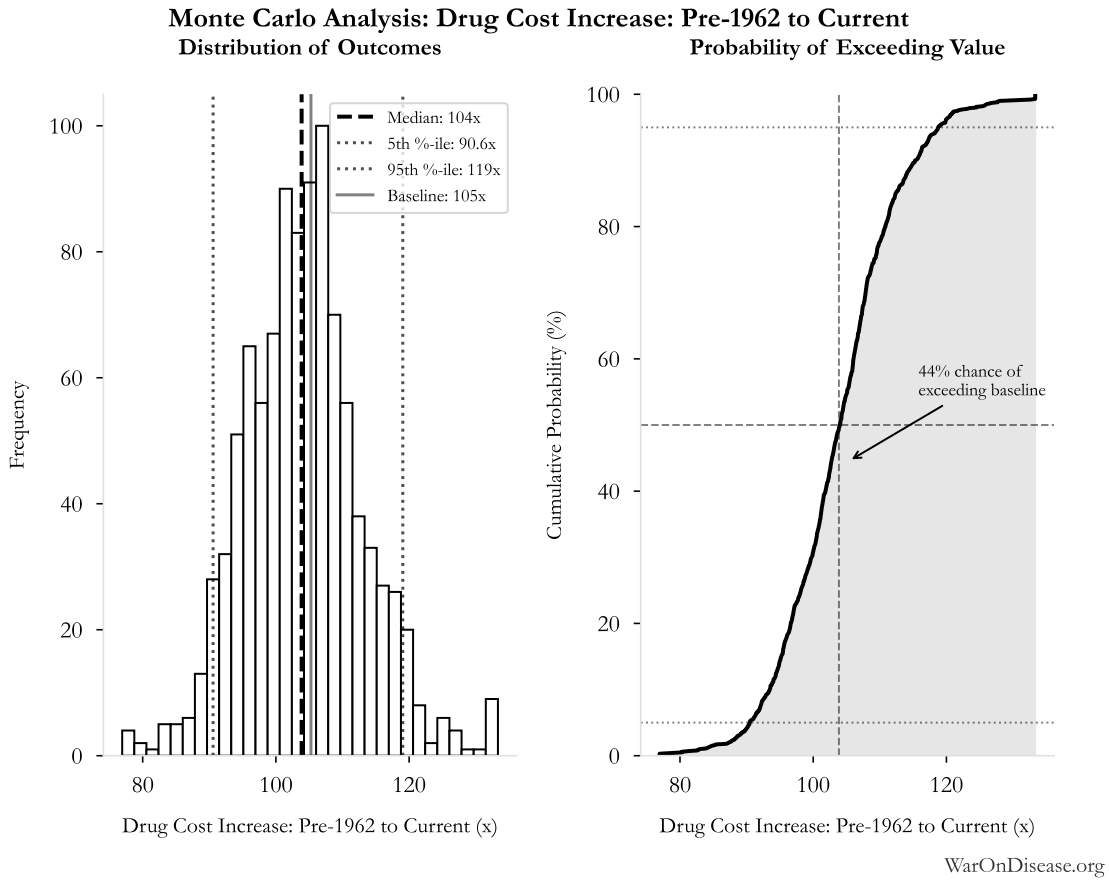


Figure 184: Monte Carlo Distribution: Drug Cost Increase: Pre-1962 to Current (10,000 simulations)

Simulation Results Summary: Drug Cost Increase: Pre-1962 to Current

Statistic	Value
Baseline (deterministic)	105x
Mean (expected value)	104x
Median (50th percentile)	104x
Standard Deviation	9.03x
90% Range (5th-95th percentile)	[90.6x, 119x]

The histogram shows the distribution of Drug Cost Increase: Pre-1962 to Current 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

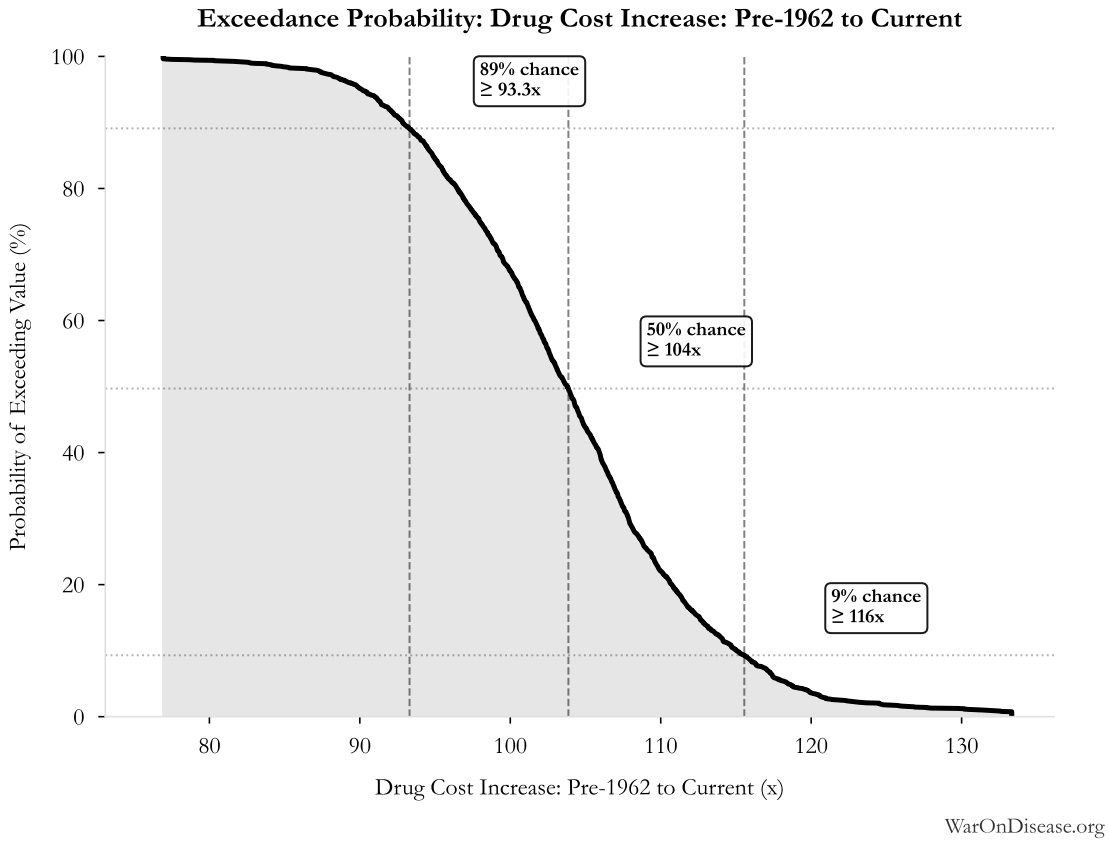


Figure 185: Probability of Exceeding Threshold: Drug Cost Increase: Pre-1962 to Current

This exceedance probability chart shows the likelihood that Drug Cost Increase: Pre-1962 to Current will exceed any given threshold. Higher curves indicate more favorable outcomes with greater certainty.

Possible Drug-Disease Combinations: 9.50 million combinations

Details

Total possible drug-disease combinations using existing safe compounds
Inputs:

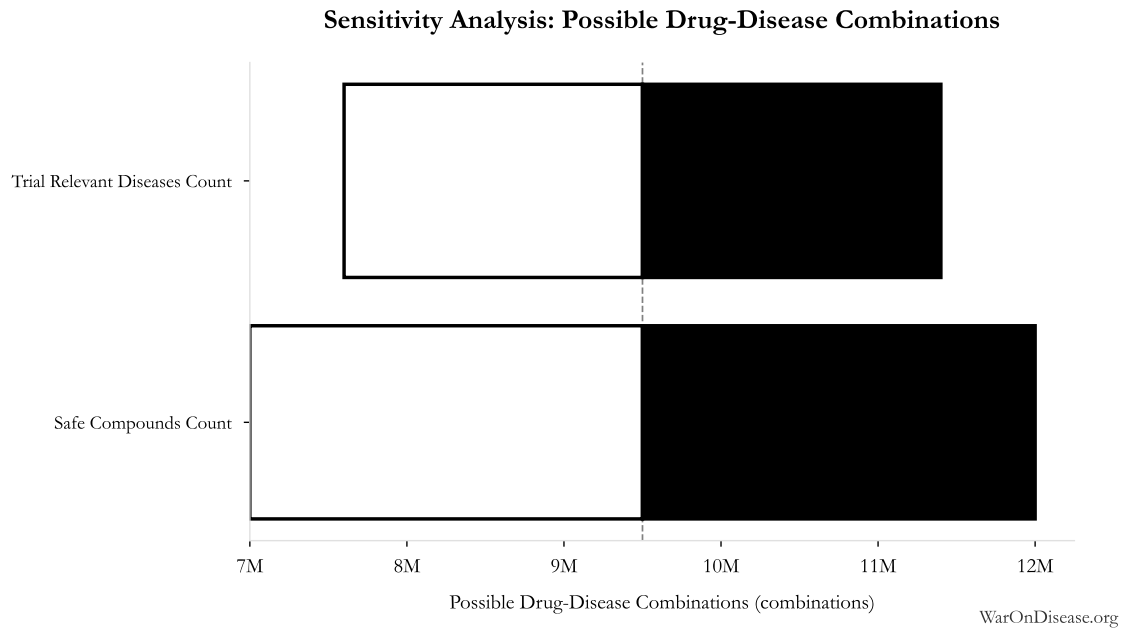
- Safe Compounds Available for Testing: 9.50 thousand compounds (95% CI: 7.00 thousand

compounds - 12.0 thousand compounds)
- Trial-Relevant Diseases: 1.00 thousand diseases (95% CI: 800 diseases - 1.20 thousand diseases)

$$\begin{aligned} & N_{combos} \\ & = N_{safe} \times N_{diseases,trial} \\ & = 9{,}500 \times 1{,}000 \\ & = 9.5M \end{aligned}$$

High confidence

Sensitivity Analysis



Therapeutic Frontier Exploration Ratio: 0.342%

Details

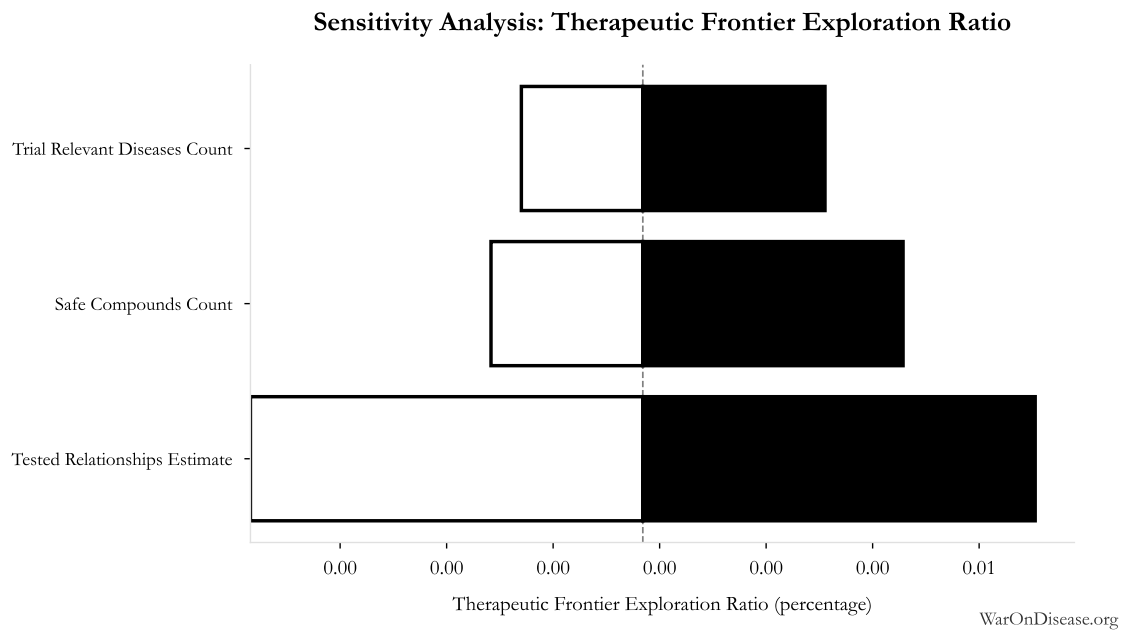
Fraction of possible drug-disease space actually tested (<1%)
Inputs:
- Tested Drug-Disease Relationships: 32.5 thousand relationships (95% CI: 15.0 thousand relationships - 50.0 thousand relationships)
- Possible Drug-Disease Combinations : 9.50 million combinations

$$Ratio_{explore} = \frac{N_{tested}}{N_{combos}} = \frac{32{,}500}{9.5M} = 0.342\%$$

$$\text{where } N_{combos} = N_{safe} \times N_{diseases,trial} = 9{,}500 \times 1{,}000 = 9.5M$$

High confidence

Sensitivity Analysis



Sensitivity Indices for Therapeutic Frontier Exploration Ratio
Regression-based sensitivity showing which inputs explain the most variance in the output.

Input Parameter	Sensitivity Coefficient	Interpretation
Tested Relationships Estimate	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

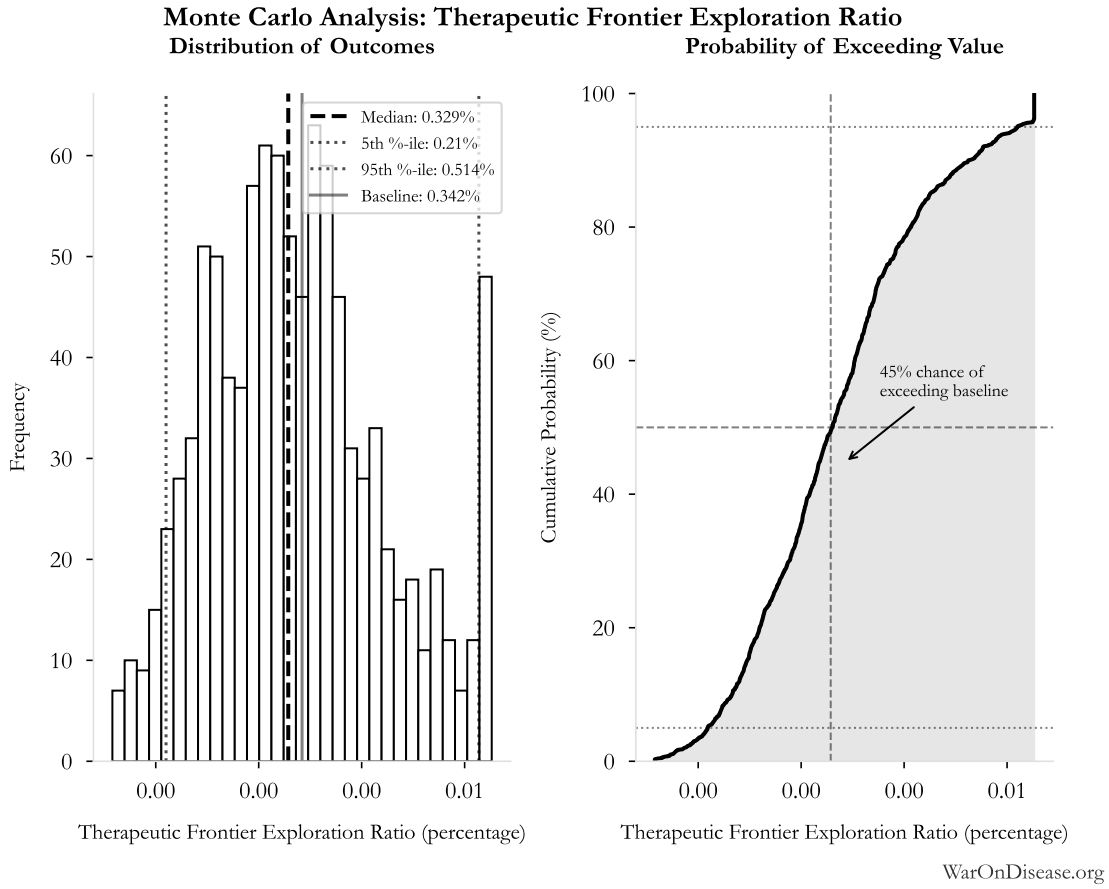


Figure 186: Monte Carlo Distribution: Therapeutic Frontier Exploration Ratio (10,000 simulations)

Simulation Results Summary: Therapeutic Frontier Exploration Ratio

Statistic	Value
Baseline (deterministic)	0.342%
Mean (expected value)	0.339%
Median (50th percentile)	0.329%
Standard Deviation	0.0868%
90% Range (5th-95th percentile)	[0.21%, 0.514%]

The histogram shows the distribution of Therapeutic Frontier Exploration Ratio 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

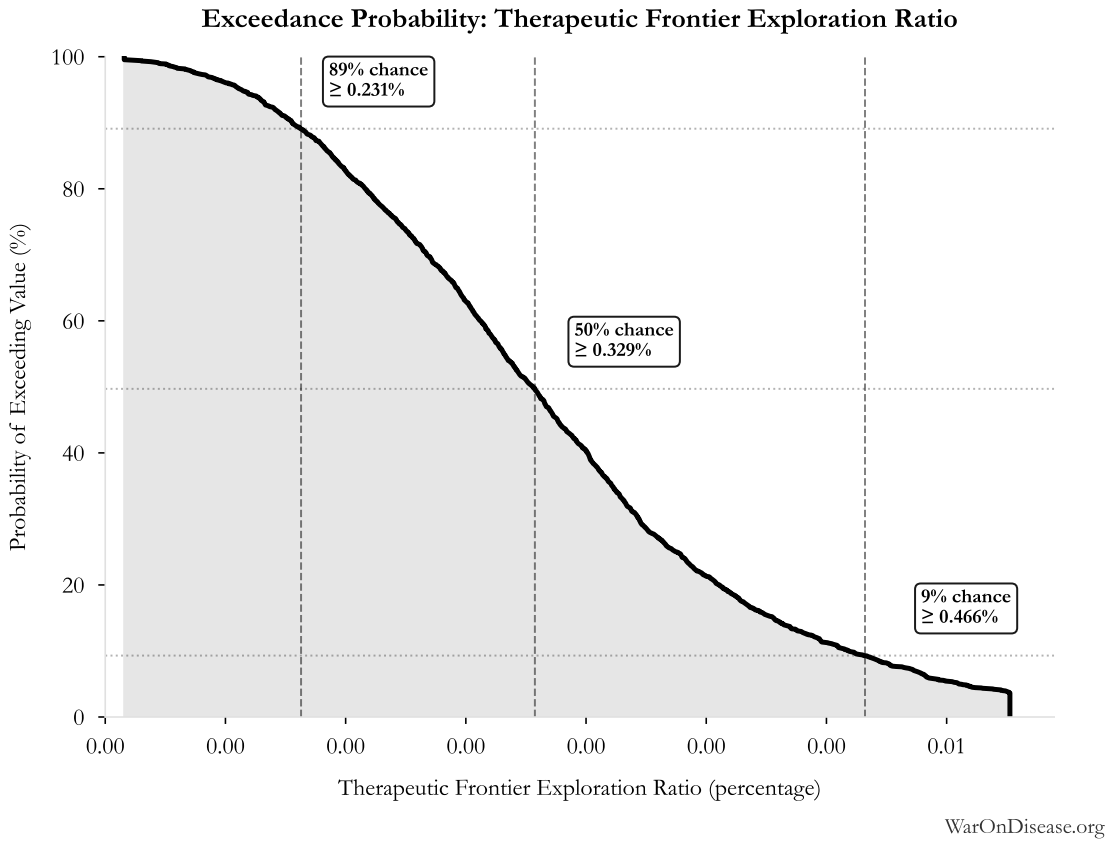


Figure 187: Probability of Exceeding Threshold: Therapeutic Frontier Exploration Ratio

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

Total Annual Conflict Deaths Globally: 245 thousand deaths/year

Details

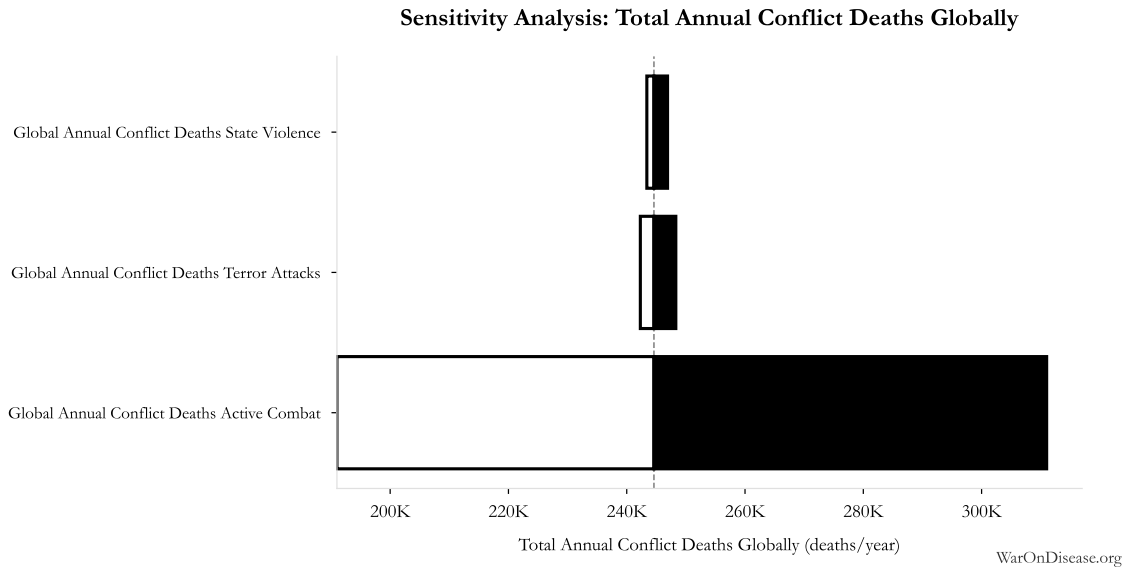
Total annual conflict deaths globally (sum of combat, terror, state violence)
Inputs:

- Annual Deaths from Active Combat Worldwide : 234 thousand deaths/year (95% CI: 180 thousand deaths/year - 300 thousand deaths/year)
- Annual Deaths from State Violence : 2.70 thousand deaths/year (95% CI: 1.50 thousand deaths/year - 5.00 thousand deaths/year)
- Annual Deaths from Terror Attacks Globally : 8.30 thousand deaths/year (95% CI: 6.00 thousand deaths/year - 12.0 thousand deaths/year)

$$\begin{aligned} & Deaths_{conflict} \\ &= Deaths_{combat} + Deaths_{state} + Deaths_{terror} \\ &= 234{,}000 + 2{,}700 + 8{,}300 \\ &= 245{,}000 \end{aligned}$$

High confidence

Sensitivity Analysis



Sensitivity Indices for Total Annual Conflict Deaths Globally

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

Input Parameter	Sensitivity Coefficient	Interpretation
Global Annual Conflict Deaths Active Combat	0.9276	Strong driver
Global Annual Conflict Deaths Terror Attacks	0.0461	Minimal effect

Global Annual Conflict Deaths State Violence	0.0266	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.

Monte Carlo Distribution

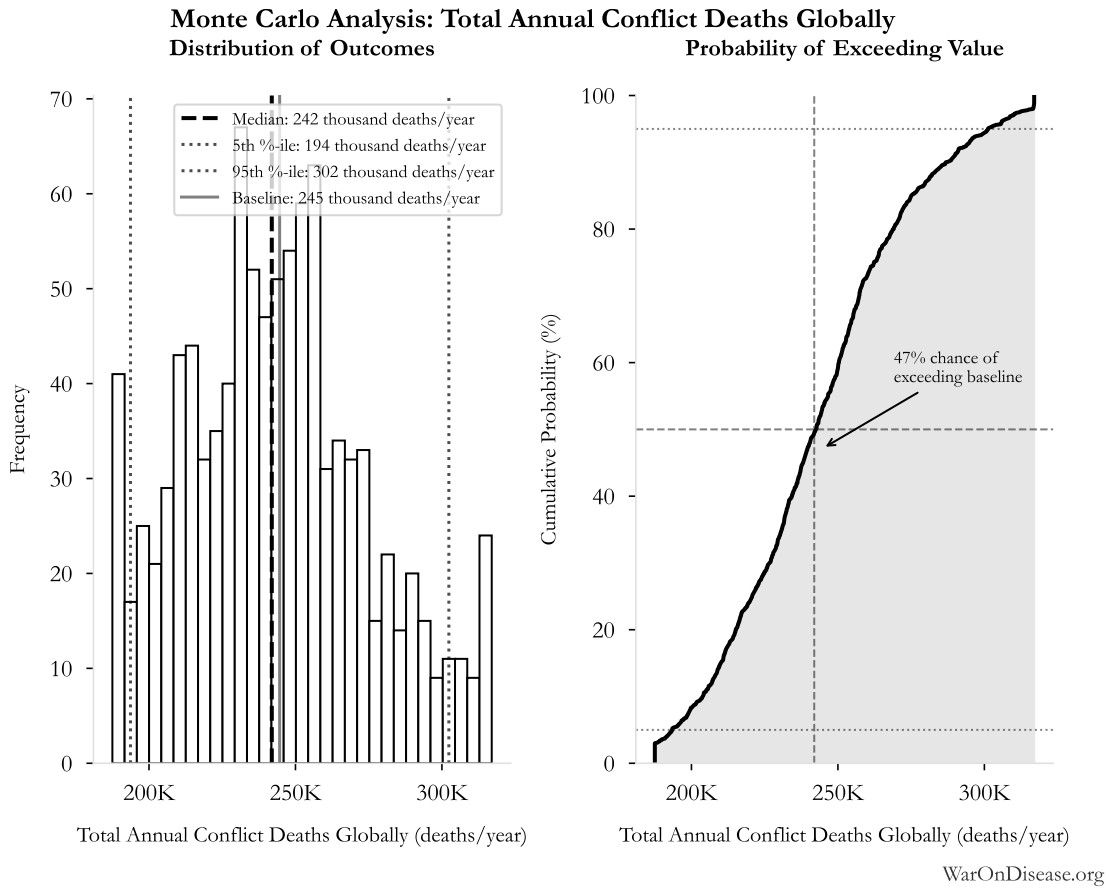


Figure 188: Monte Carlo Distribution: Total Annual Conflict Deaths Globally (10,000 simulations)

Simulation Results Summary: Total Annual Conflict Deaths Globally

Statistic	Value
Baseline (deterministic)	245 thousand
Mean (expected value)	244 thousand
Median (50th percentile)	242 thousand
Standard Deviation	31.5 thousand
90% Range (5th-95th percentile)	[194 thousand, 302 thousand]

The histogram shows the distribution of Total Annual Conflict Deaths Globally 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

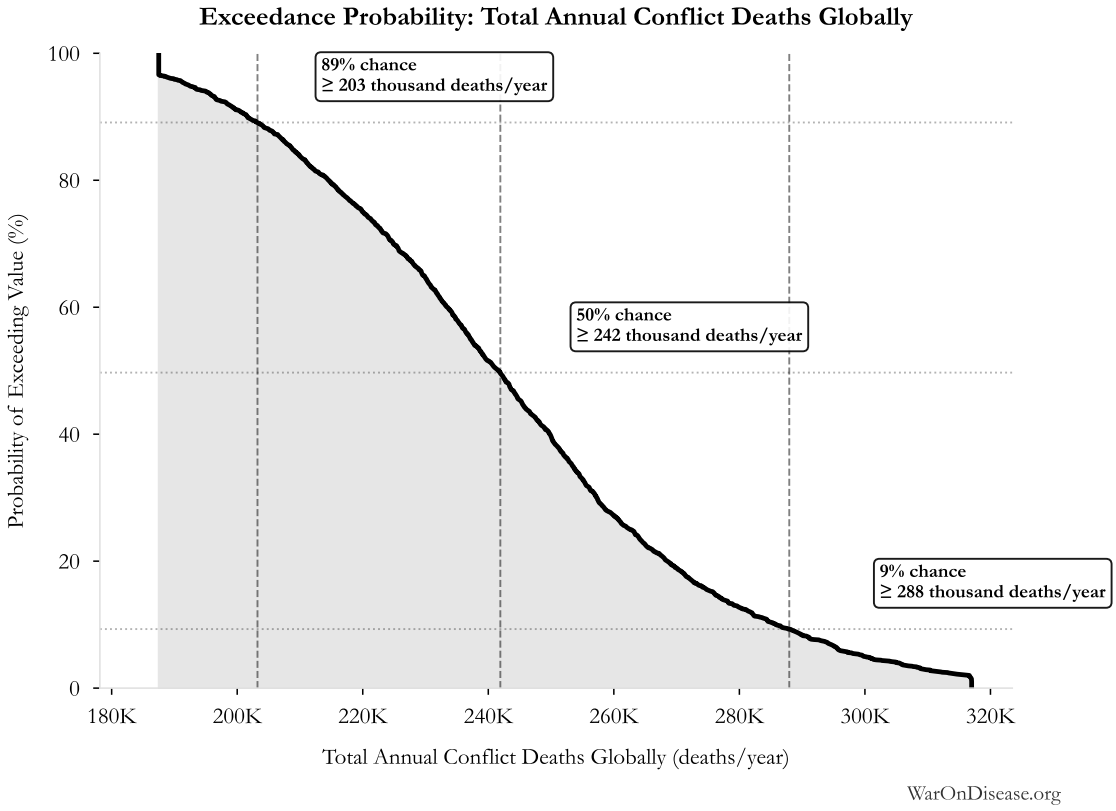


Figure 189: Probability of Exceeding Threshold: Total Annual Conflict Deaths Globally

This exceedance probability chart shows the likelihood that Total Annual Conflict Deaths Globally will exceed any given threshold. Higher curves indicate more favorable outcomes with greater certainty.

Total Annual Cost of War Worldwide: $11.4T

Details

Total annual cost of war worldwide (direct + indirect costs)
Inputs:

- Total Annual Direct War Costs : $7.66T
- Total Annual Indirect War Costs : $3.70T

$$Cost_{war,total}$$
$$= Cost_{war,direct} + Cost_{war,indirect}$$
$$= \$7.66T + \$3.7T$$
$$= \$11.4T$$

where $Cost_{war,direct}$
$$= Loss_{life,conflict} + Damage_{infra,total}$$
$$+Disruption_{trade} + Spending_{mil}$$
$$= \$2.45T + \$1.88T + \$616B + \$2.72T$$
$$= \$7.66T$$

where $Loss_{life,conflict}$
$$= Cost_{combat,human} + Cost_{state,human}$$
$$+Cost_{terror,human}$$
$$= \$2.34T + \$27B + \$83B$$
$$= \$2.45T$$

where $Cost_{combat,human}$
$$= Deaths_{combat} \times VSL$$
$$= 234{,}000 \times \$10M$$
$$= \$2.34T$$

where $Cost_{state,human}$
$$= Deaths_{state} \times VSL$$
$$= 2{,}700 \times \$10M$$
$$= \$27B$$

where $Cost_{terror,human}$
$$= Deaths_{terror} \times VSL$$
$$= 8{,}300 \times \$10M$$
$$= \$83B$$

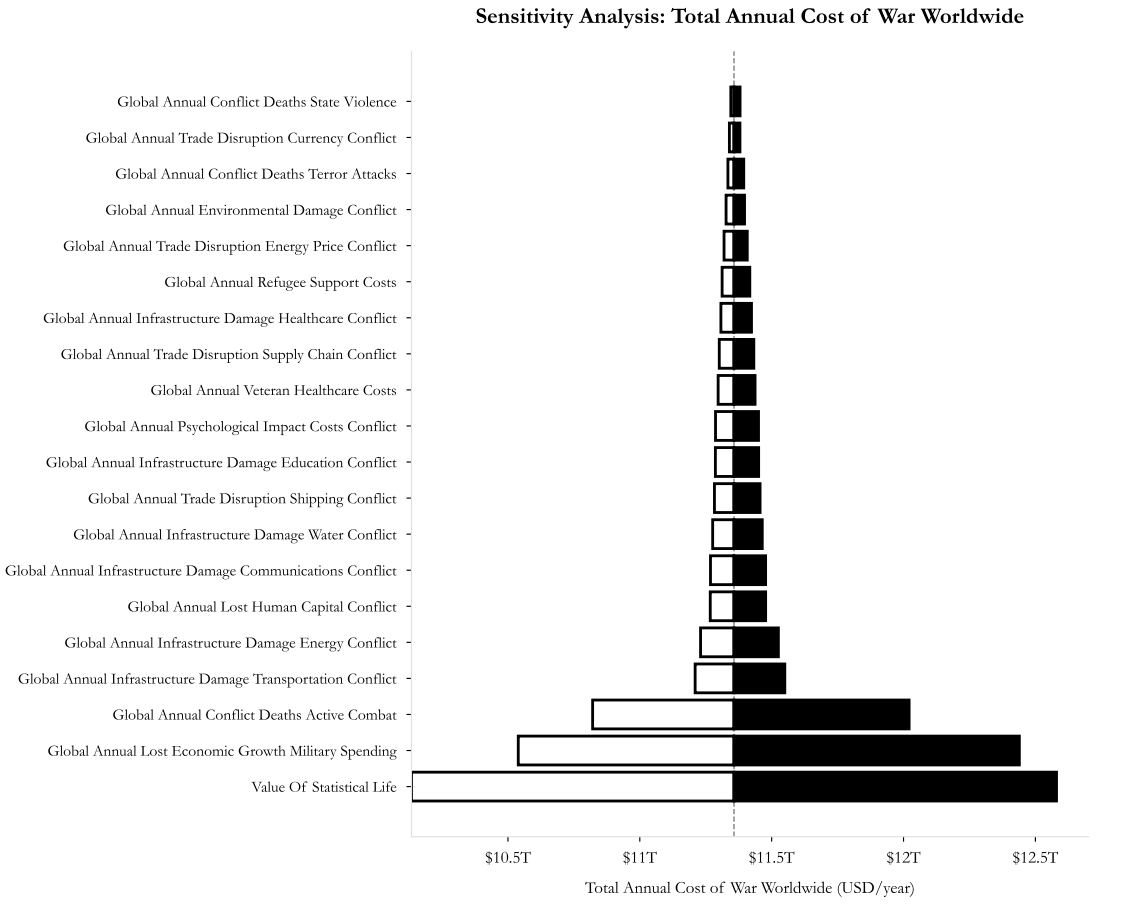
where $Damage_{infra,total}$
$$= Damage_{comms} + Damage_{edu} + Damage_{energy}$$
$$+Damage_{health} + Damage_{transport}$$
$$+Damage_{water}$$
$$= \$298B + \$234B + \$422B + \$166B + \$487B + \$268B$$
$$= \$1.88T$$

where $Disruption_{trade}$
$$= Disruption_{currency} + Disruption_{energy}$$
$$+Disruption_{shipping} + Disruption_{supply}$$
$$= \$57.4B + \$125B + \$247B + \$187B$$
$$= \$616B$$

where $Cost_{war,indirect}$
$$= Damage_{env} + Loss_{growth,mil}$$

High confidence

Sensitivity Analysis



Sensitivity Indices for Total Annual Cost of War Worldwide

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

Input Parameter	Sensitivity Coefficient	Interpretation
Global Annual War Direct Costs Total	0.6553	Strong driver
Global Annual War Indirect Costs Total	0.4150	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

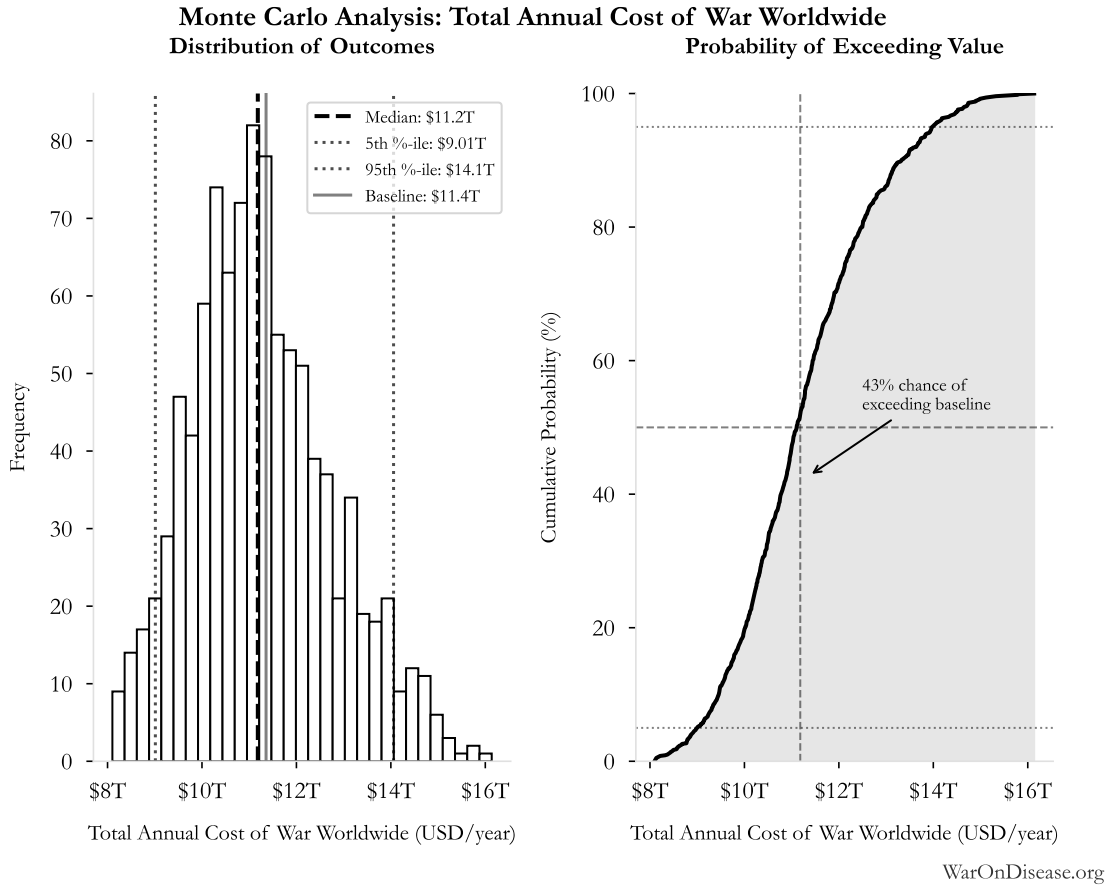


Figure 190: Monte Carlo Distribution: Total Annual Cost of War Worldwide (10,000 simulations)

Simulation Results Summary: Total Annual Cost of War Worldwide

Statistic	Value
Baseline (deterministic)	$11.4T
Mean (expected value)	$11.3T
Median (50th percentile)	$11.2T
Standard Deviation	$1.51T
90% Range (5th-95th percentile)	[$9.01T, $14.1T]

The histogram shows the distribution of Total Annual Cost of War Worldwide 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

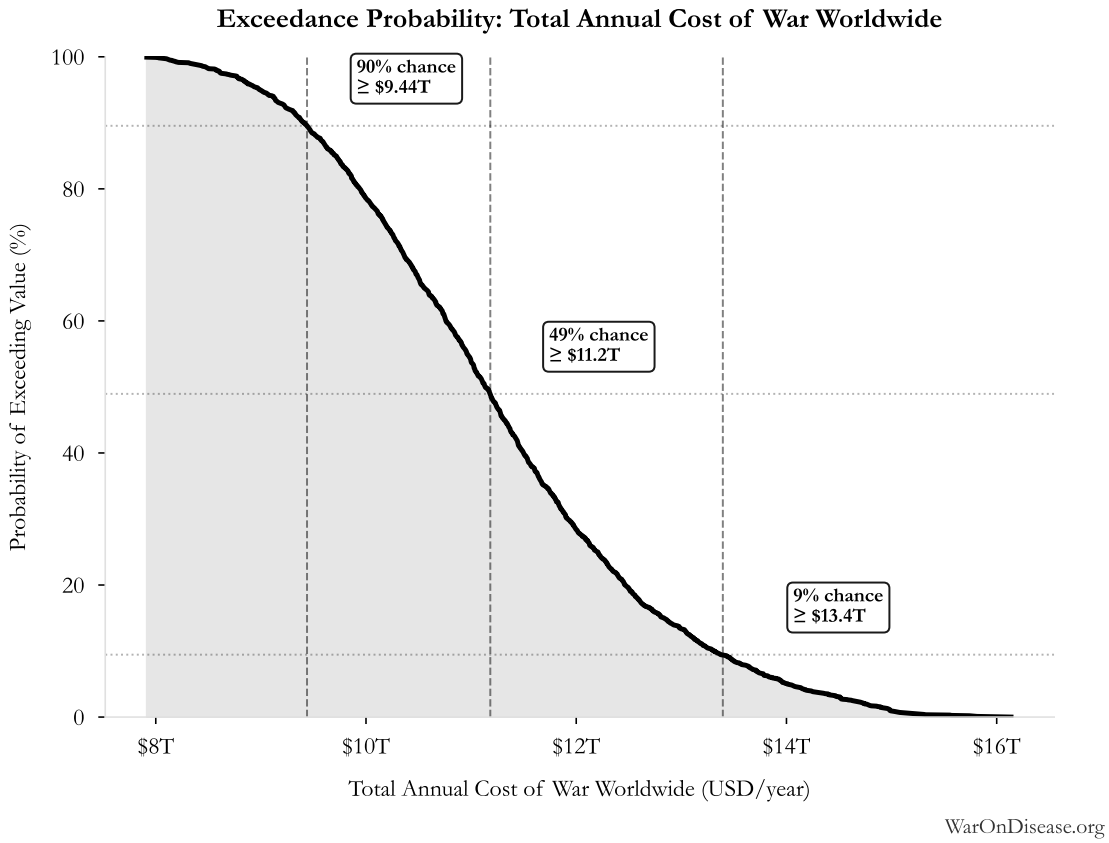


Figure 191: Probability of Exceeding Threshold: Total Annual Cost of War Worldwide

This exceedance probability chart shows the likelihood that Total Annual Cost of War Worldwide will exceed any given threshold. Higher curves indicate more favorable outcomes with greater certainty.

Annual Cost of Combat Deaths: $2.34T

Details

Annual cost of combat deaths (deaths × VSL)
Inputs:

- Annual Deaths from Active Combat Worldwide : 234 thousand deaths/year (95% CI:

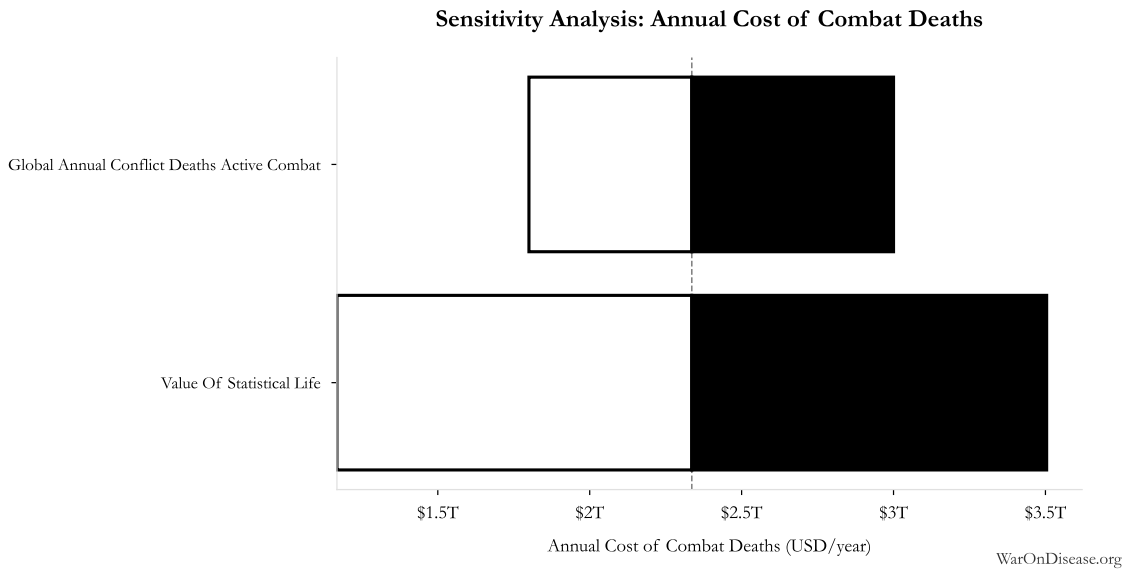
180 thousand deaths/year - 300 thousand deaths/year)

- Value of Statistical Life : $10M (95% CI: $5M - $15M)

$$\begin{aligned} & Cost_{combat,human} \\ &= Deaths_{combat} \times VSL \\ &= 234{,}000 \times \$10M \\ &= \$2.34T \end{aligned}$$

High confidence

Sensitivity Analysis



Sensitivity Indices for Annual Cost of Combat Deaths
Regression-based sensitivity showing which inputs explain the most variance in the output.

Input Parameter	Sensitivity Coefficient	Interpretation
Value Of Statistical Life	0.9096	Strong driver
Global Annual Conflict Deaths Active Combat	0.4115	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

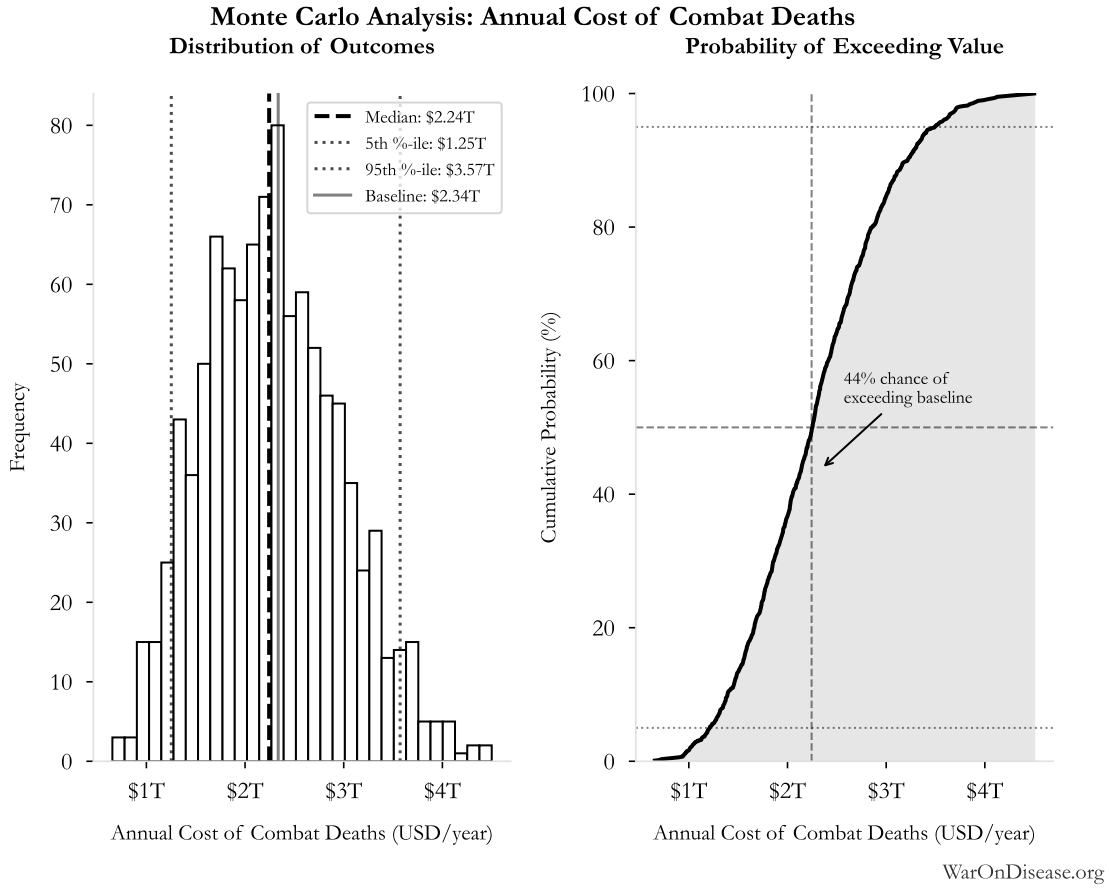


Figure 192: Monte Carlo Distribution: Annual Cost of Combat Deaths (10,000 simulations)

Simulation Results Summary: Annual Cost of Combat Deaths

Statistic	Value
Baseline (deterministic)	$2.34T
Mean (expected value)	$2.31T
Median (50th percentile)	$2.24T
Standard Deviation	$703B
90% Range (5th-95th percentile)	[$1.25T, $3.57T]

The histogram shows the distribution of Annual Cost of Combat Deaths 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

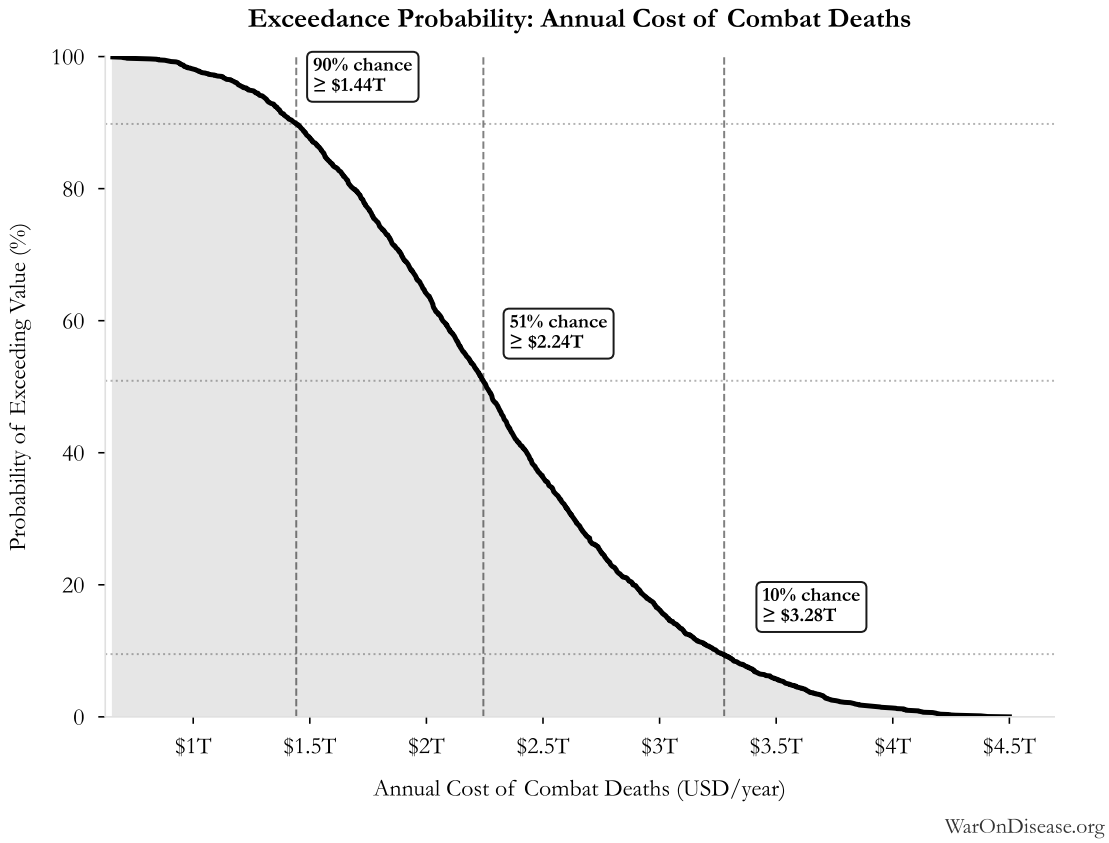


Figure 193: Probability of Exceeding Threshold: Annual Cost of Combat Deaths

This exceedance probability chart shows the likelihood that Annual Cost of Combat Deaths will exceed any given threshold. Higher curves indicate more favorable outcomes with greater certainty.

Annual Cost of State Violence Deaths: $27B

Details

Annual cost of state violence deaths (deaths × VSL)
Inputs:

- Annual Deaths from State Violence : 2.70 thousand deaths/year (95% CI: 1.50 thousand

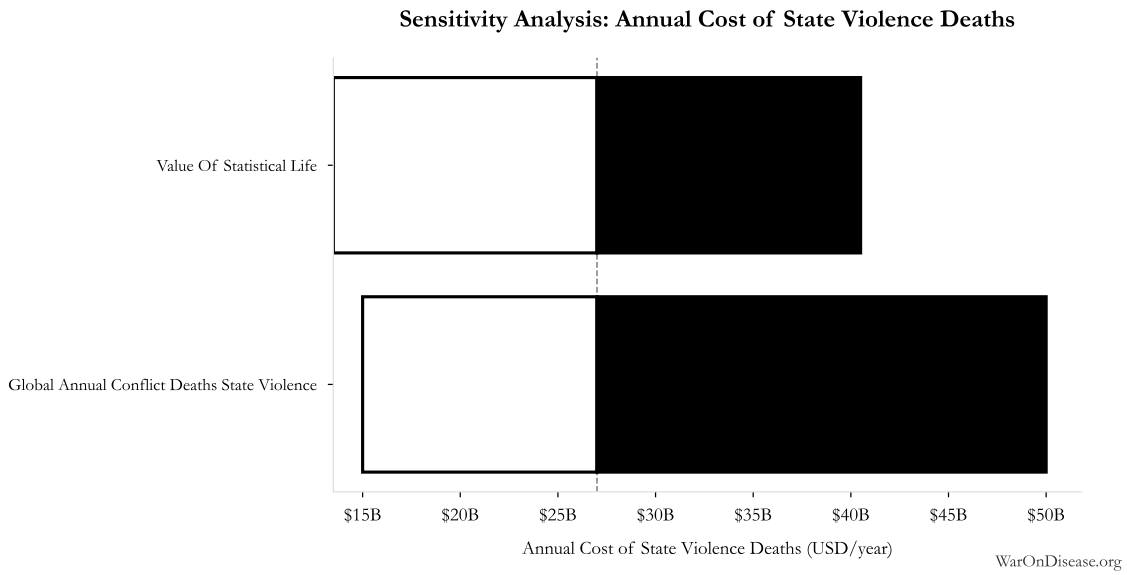
deaths/year - 5.00 thousand deaths/year)

- Value of Statistical Life : $10M (95% CI: $5M - $15M)

$$
\begin{aligned}
&Cost_{state,human} \\
&= Deaths_{state} \times VSL \\
&= 2{,}700 \times \$10M \\
&= \$27B
\end{aligned}
$$

High confidence

Sensitivity Analysis



Sensitivity Indices for Annual Cost of State Violence Deaths
Regression-based sensitivity showing which inputs explain the most variance in the output.

Input Parameter	Sensitivity Coefficient	Interpretation
Global Annual Conflict Deaths State Violence	0.7358	Strong driver
Value Of Statistical Life	0.6553	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

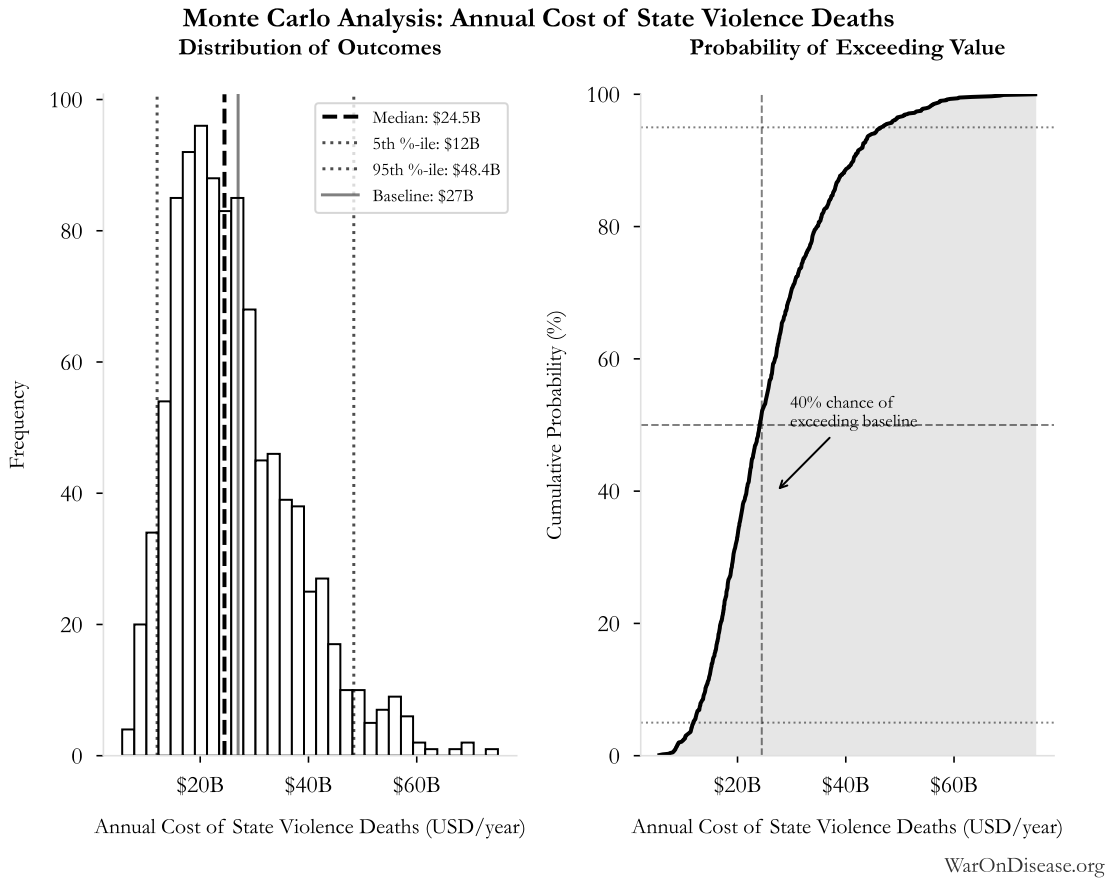


Figure 194: Monte Carlo Distribution: Annual Cost of State Violence Deaths (10,000 simulations)

Simulation Results Summary: Annual Cost of State Violence Deaths

Statistic	Value
Baseline (deterministic)	$27B
Mean (expected value)	$26.6B
Median (50th percentile)	$24.5B
Standard Deviation	$11.3B
90% Range (5th-95th percentile)	[$12B, $48.4B]

The histogram shows the distribution of Annual Cost of State Violence Deaths 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

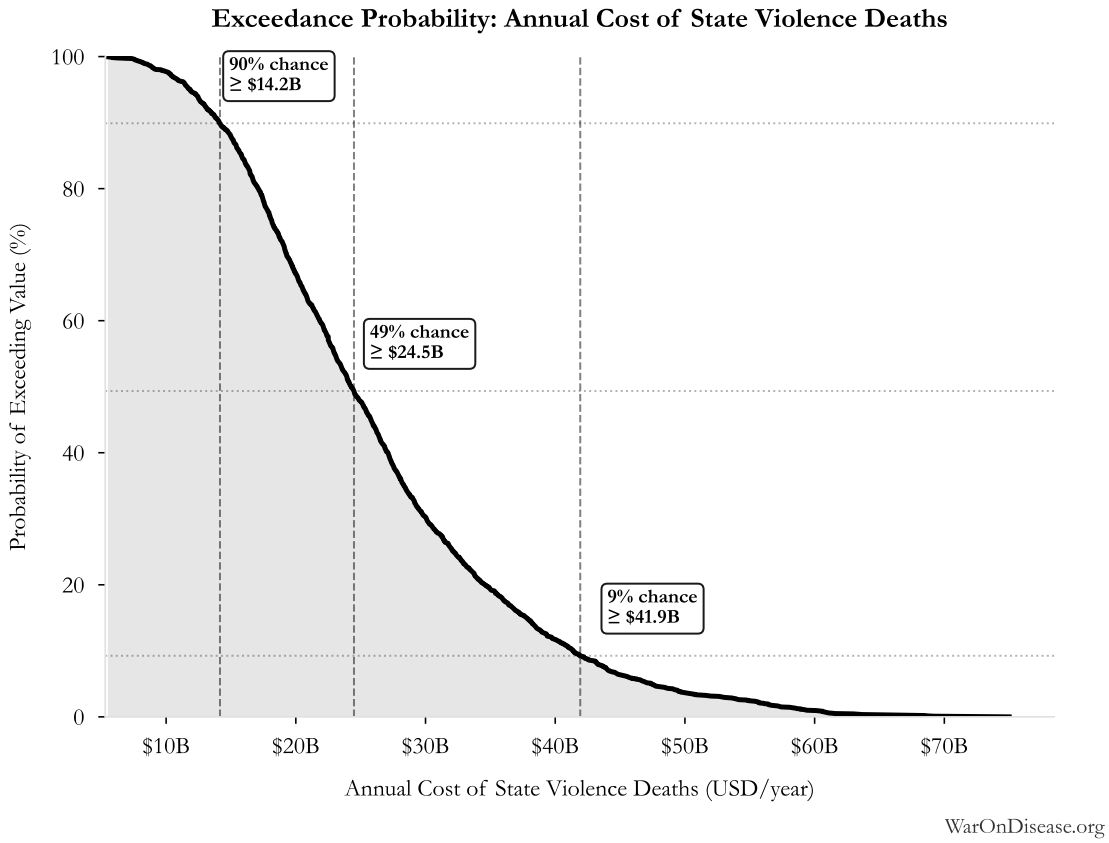


Figure 195: Probability of Exceeding Threshold: Annual Cost of State Violence Deaths

This exceedance probability chart shows the likelihood that Annual Cost of State Violence Deaths will exceed any given threshold. Higher curves indicate more favorable outcomes with greater certainty.

Annual Cost of Terror Deaths: $83B

Details

Annual cost of terror deaths (deaths × VSL)
Inputs:

- Annual Deaths from Terror Attacks Globally : 8.30 thousand deaths/year (95% CI: 6.00

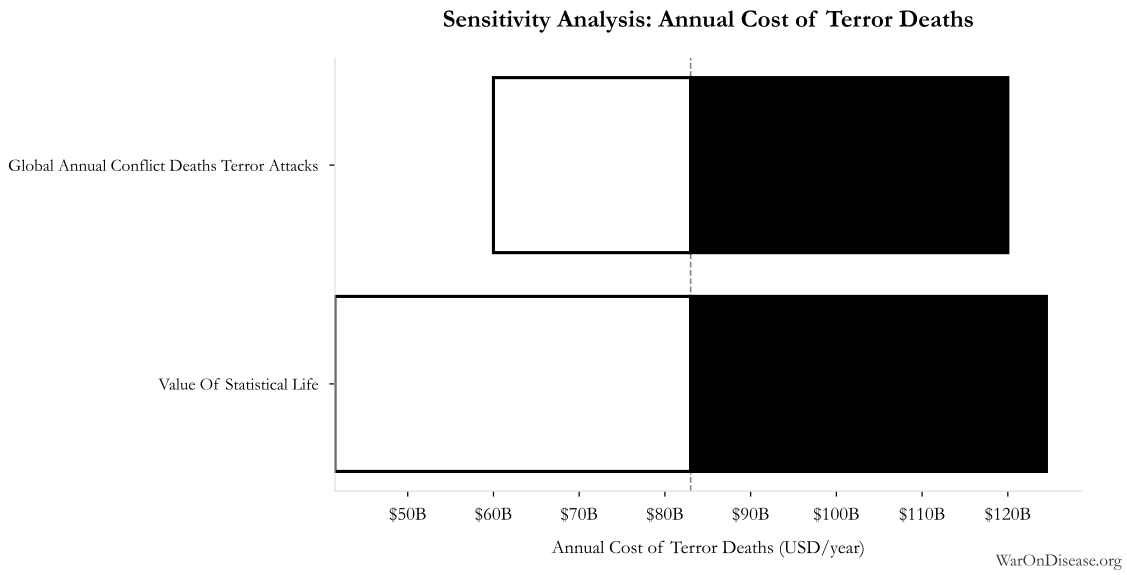
thousand deaths/year - 12.0 thousand deaths/year)

- Value of Statistical Life : $10M (95% CI: $5M - $15M)

$$
\begin{aligned}
&Cost_{terror,human} \\
&= Deaths_{terror} \times VSL \\
&= 8{,}300 \times \$10M \\
&= \$83B
\end{aligned}
$$

High confidence

Sensitivity Analysis



Sensitivity Indices for Annual Cost of Terror Deaths

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

Input Parameter	Sensitivity Coefficient	Interpretation
Value Of Statistical Life	0.8410	Strong driver
Global Annual Conflict Deaths Terror Attacks	0.5319	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

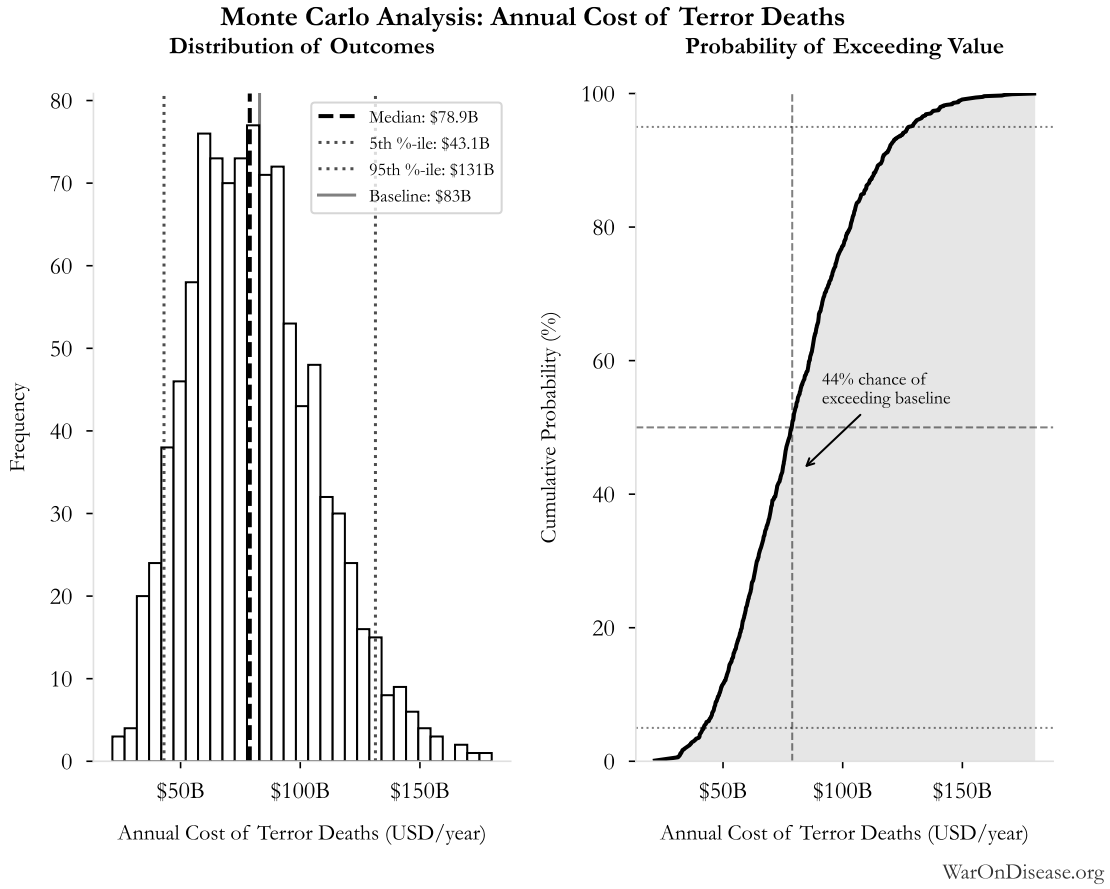


Figure 196: Monte Carlo Distribution: Annual Cost of Terror Deaths (10,000 simulations)

Simulation Results Summary: Annual Cost of Terror Deaths

Statistic	Value
Baseline (deterministic)	$83B
Mean (expected value)	$82.1B
Median (50th percentile)	$78.9B
Standard Deviation	$27B
90% Range (5th-95th percentile)	[$43.1B, $131B]

The histogram shows the distribution of Annual Cost of Terror Deaths 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

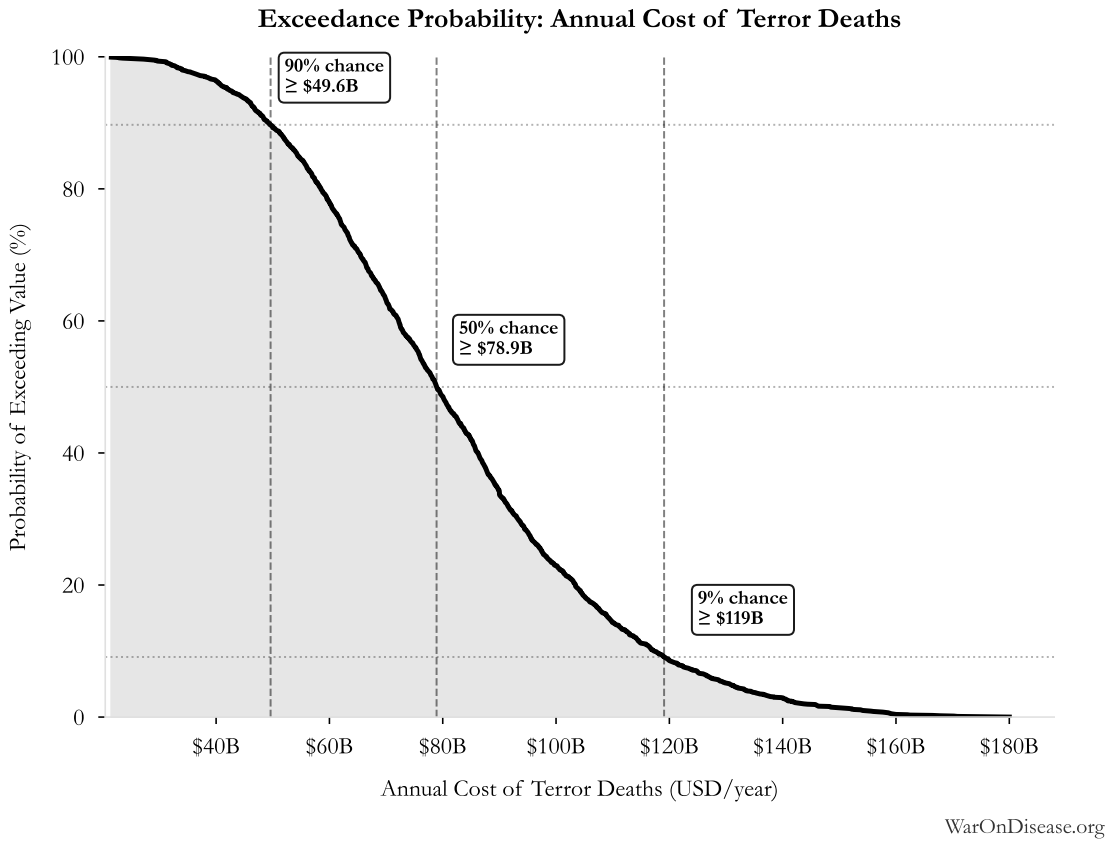


Figure 197: Probability of Exceeding Threshold: Annual Cost of Terror Deaths

This exceedance probability chart shows the likelihood that Annual Cost of Terror Deaths will exceed any given threshold. Higher curves indicate more favorable outcomes with greater certainty.

Total Annual Human Life Losses from Conflict: $2.45T

Details

Total annual human life losses from conflict (sum of combat, terror, state violence)
Inputs:

- Annual Cost of Combat Deaths : $2.34T

- Annual Cost of State Violence Deaths : $27B
- Annual Cost of Terror Deaths : $83B

$$
\begin{aligned}
&Loss_{life,conflict} \\
&= Cost_{combat,human} + Cost_{state,human} \\
&+ Cost_{terror,human} \\
&= \$2.34T + \$27B + \$83B \\
&= \$2.45T
\end{aligned}
$$

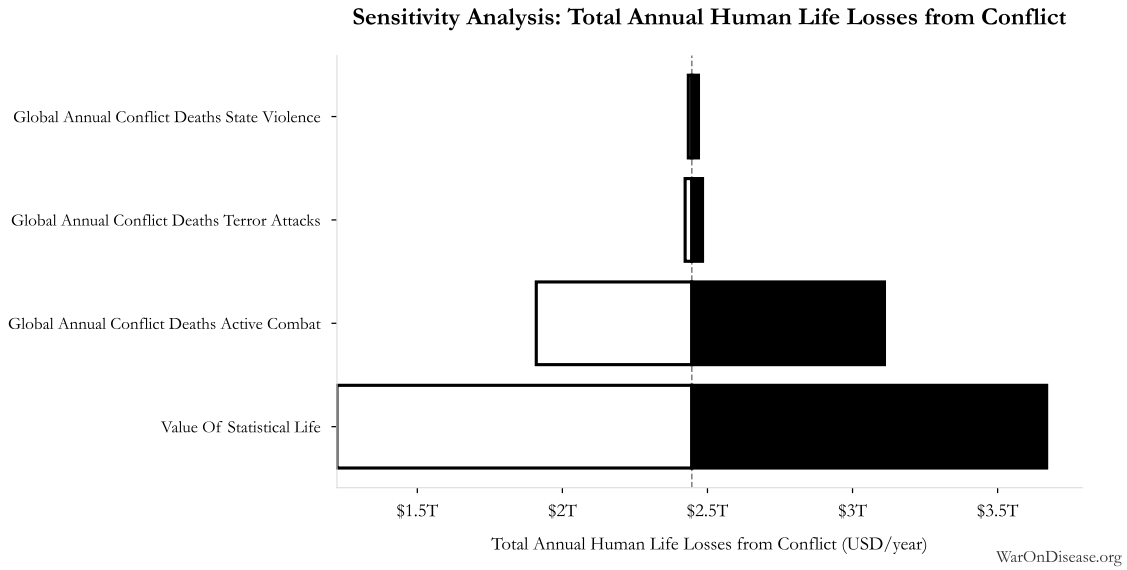
$$
\begin{aligned}
&\text{where } Cost_{combat,human} \\
&= Deaths_{combat} \times VSL \\
&= 234{,}000 \times \$10M \\
&= \$2.34T
\end{aligned}
$$

$$
\begin{aligned}
&\text{where } Cost_{state,human} \\
&= Deaths_{state} \times VSL \\
&= 2{,}700 \times \$10M \\
&= \$27B
\end{aligned}
$$

$$
\begin{aligned}
&\text{where } Cost_{terror,human} \\
&= Deaths_{terror} \times VSL \\
&= 8{,}300 \times \$10M \\
&= \$83B
\end{aligned}
$$

High confidence

Sensitivity Analysis



Sensitivity Indices for Total Annual Human Life Losses from Conflict
Regression-based sensitivity showing which inputs explain the most variance in the output.

Input Parameter	Sensitivity Coefficient	Interpretation
Global Annual Human Cost Active Combat	0.9500	Strong driver
Global Annual Human Cost Terror Attacks	0.0365	Minimal effect
Global Annual Human Cost State Violence	0.0152	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.

Monte Carlo Distribution

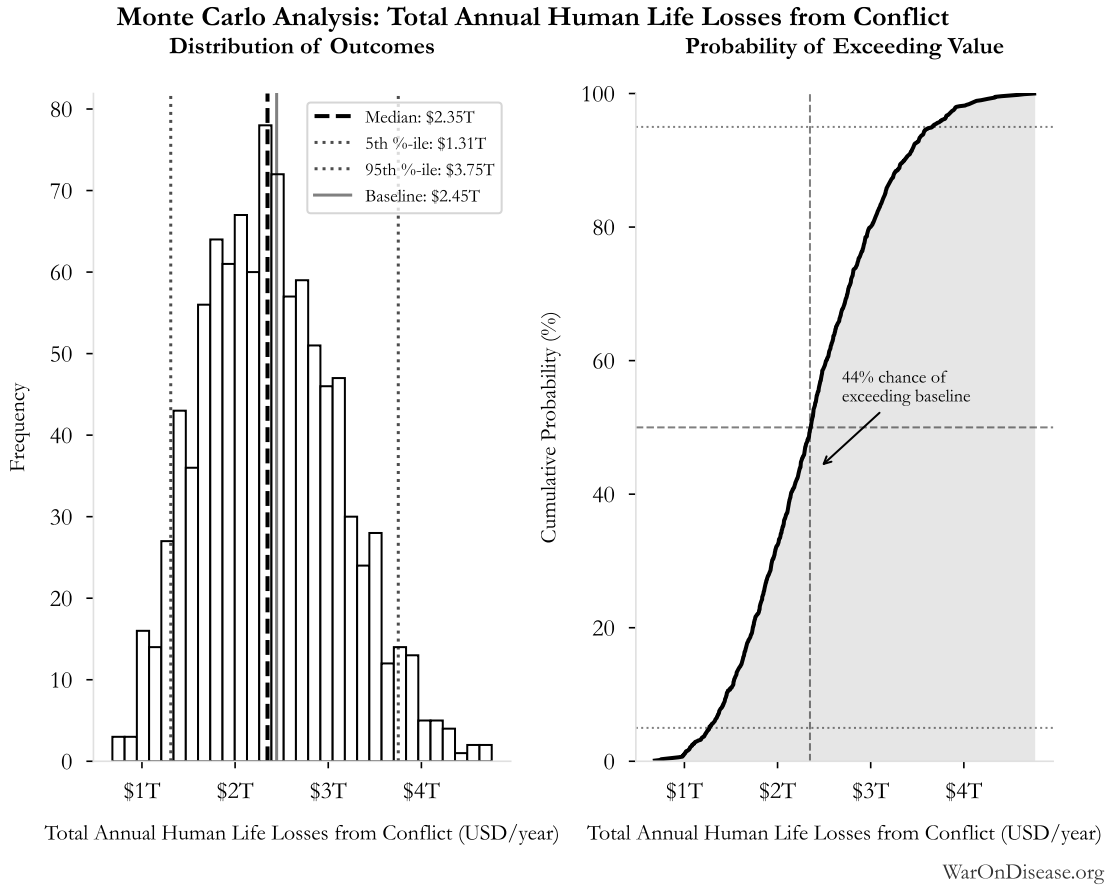


Figure 198: Monte Carlo Distribution: Total Annual Human Life Losses from Conflict (10,000 simulations)

Simulation Results Summary: Total Annual Human Life Losses from Conflict

Statistic	Value
Baseline (deterministic)	$2.45T
Mean (expected value)	$2.42T
Median (50th percentile)	$2.35T
Standard Deviation	$740B
90% Range (5th-95th percentile)	[$1.31T, $3.75T]

The histogram shows the distribution of Total Annual Human Life Losses from Conflict 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

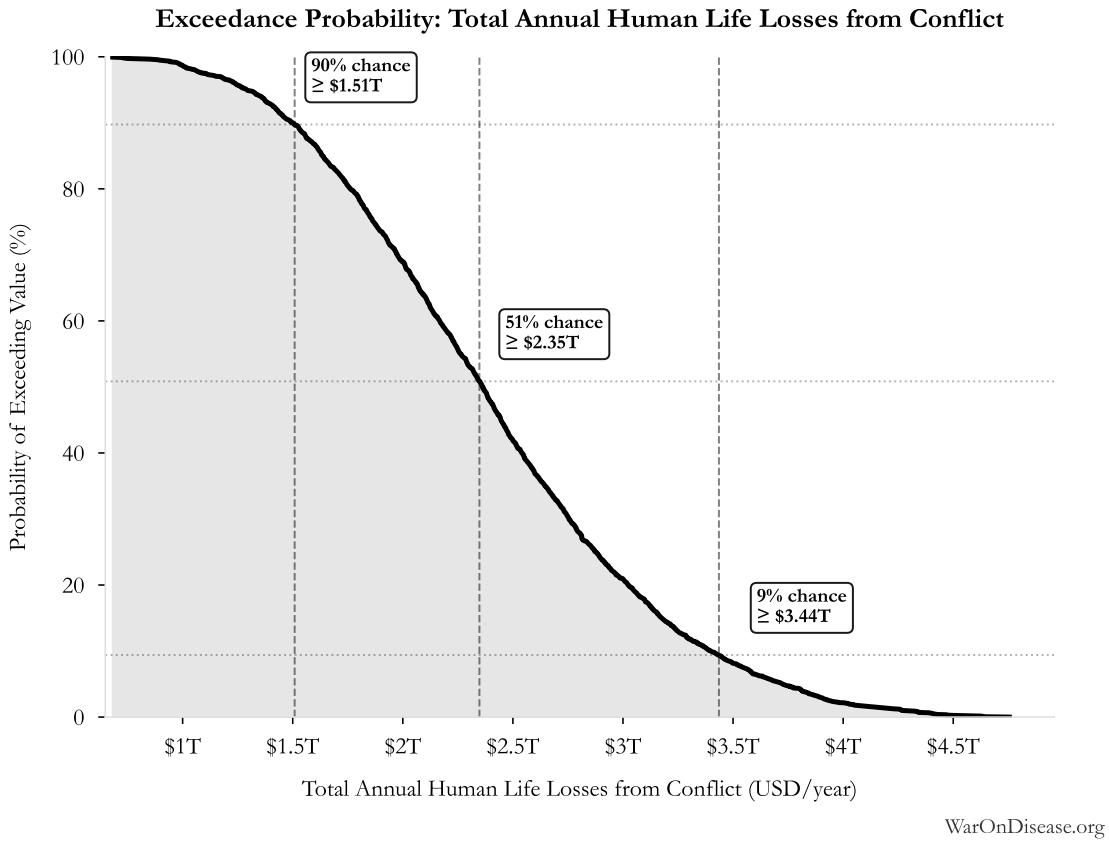


Figure 199: Probability of Exceeding Threshold: Total Annual Human Life Losses from Conflict

This exceedance probability chart shows the likelihood that Total Annual Human Life Losses from Conflict will exceed any given threshold. Higher curves indicate more favorable outcomes with greater certainty.

Total Annual Infrastructure Destruction: $1.88T

Details

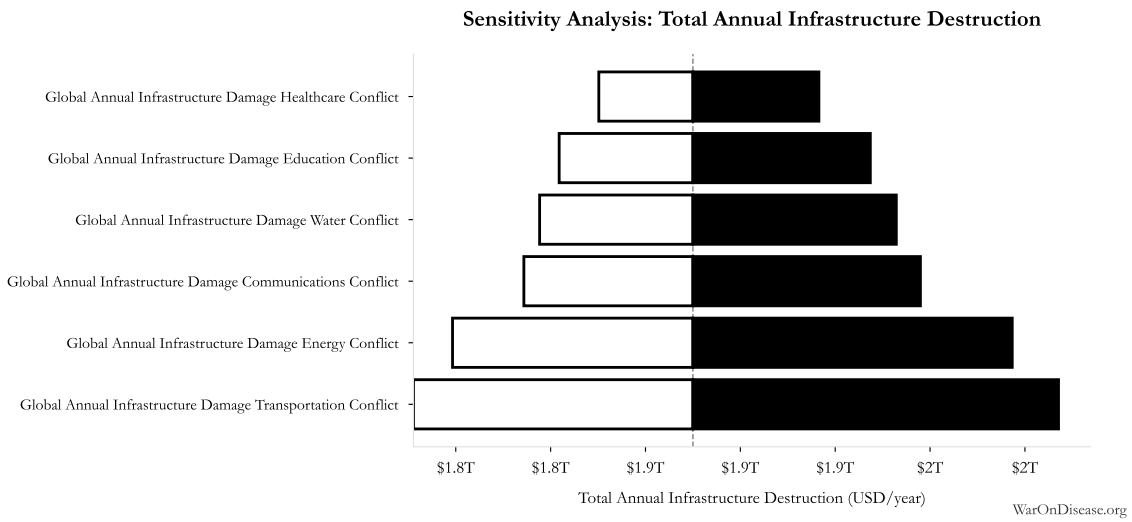
Total annual infrastructure destruction (sum of transportation, energy, communications, water, education, healthcare)
Inputs:

- Annual Infrastructure Damage to Communications from Conflict : $298B (95% CI: $209B - $418B)
- Annual Infrastructure Damage to Education Facilities from Conflict : $234B (95% CI: $164B - $328B)
- Annual Infrastructure Damage to Energy Systems from Conflict : $422B (95% CI: $295B - $590B)
- Annual Infrastructure Damage to Healthcare Facilities from Conflict : $166B (95% CI: $116B - $232B)
- Annual Infrastructure Damage to Transportation from Conflict : $487B (95% CI: $340B - $680B)
- Annual Infrastructure Damage to Water Systems from Conflict : $268B (95% CI: $187B - $375B)

$$\begin{aligned} &Damage_{infra,total} \\ &= Damage_{comms} + Damage_{edu} + Damage_{energy} \\ &+ Damage_{health} + Damage_{transport} + Damage_{water} \\ &= \$298B + \$234B + \$422B + \$166B + \$487B + \$268B \\ &= \$1.88T \end{aligned}$$

High confidence

Sensitivity Analysis



Sensitivity Indices for Total Annual Infrastructure Destruction
Regression-based sensitivity showing which inputs explain the most variance in the output.

Input Parameter	Sensitivity Coefficient	Interpretation
Global Annual Infrastructure Damage Transportation Conflict	0.2591	Weak driver

Global Annual Infrastructure Damage Energy Conflict	0.2249	Weak driver
Global Annual Infrastructure Damage Communications Conflict	0.1593	Weak driver
Global Annual Infrastructure Damage Water Conflict	0.1433	Weak driver
Global Annual Infrastructure Damage Education Conflict	0.1250	Weak driver
Global Annual Infrastructure Damage Healthcare Conflict	0.0884	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.

Monte Carlo Distribution

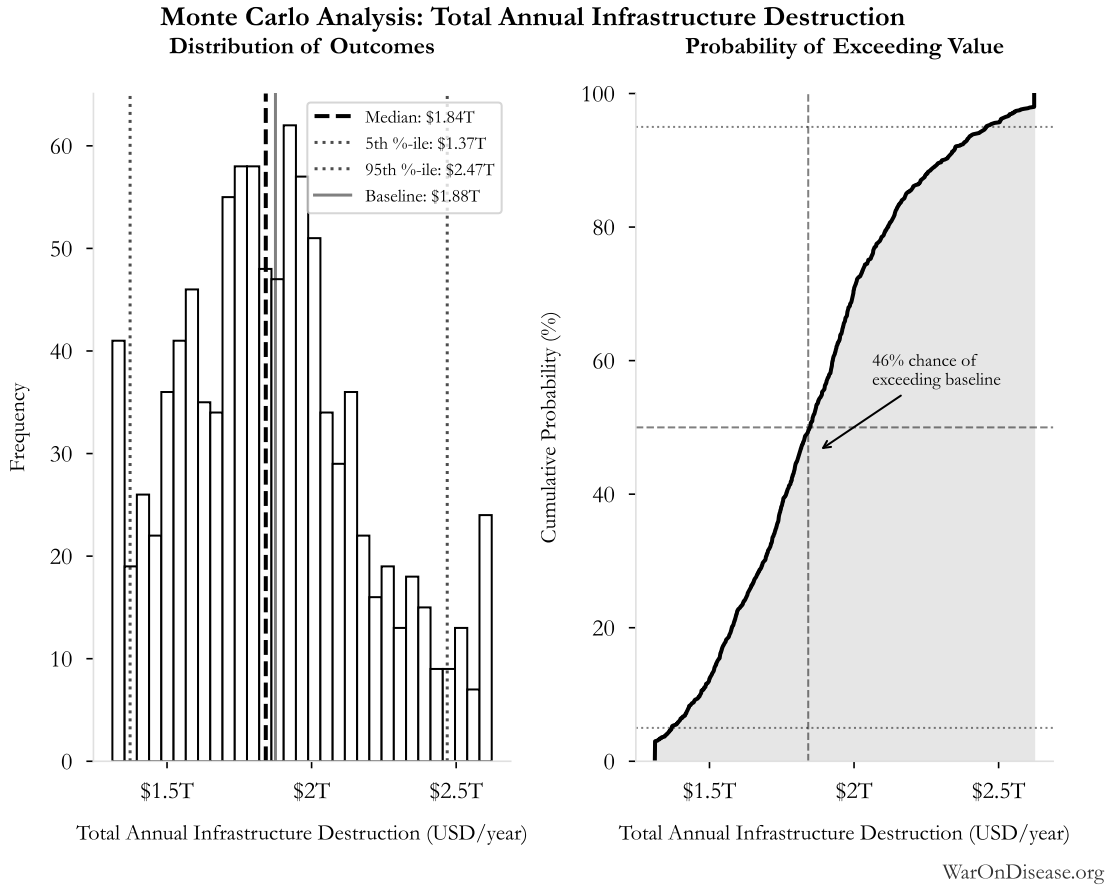


Figure 200: Monte Carlo Distribution: Total Annual Infrastructure Destruction (10,000 simulations)

Simulation Results Summary: Total Annual Infrastructure Destruction

Statistic	Value
Baseline (deterministic)	$1.88T
Mean (expected value)	$1.87T
Median (50th percentile)	$1.84T
Standard Deviation	$319B
90% Range (5th-95th percentile)	[$1.37T, $2.47T]

The histogram shows the distribution of Total Annual Infrastructure Destruction 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

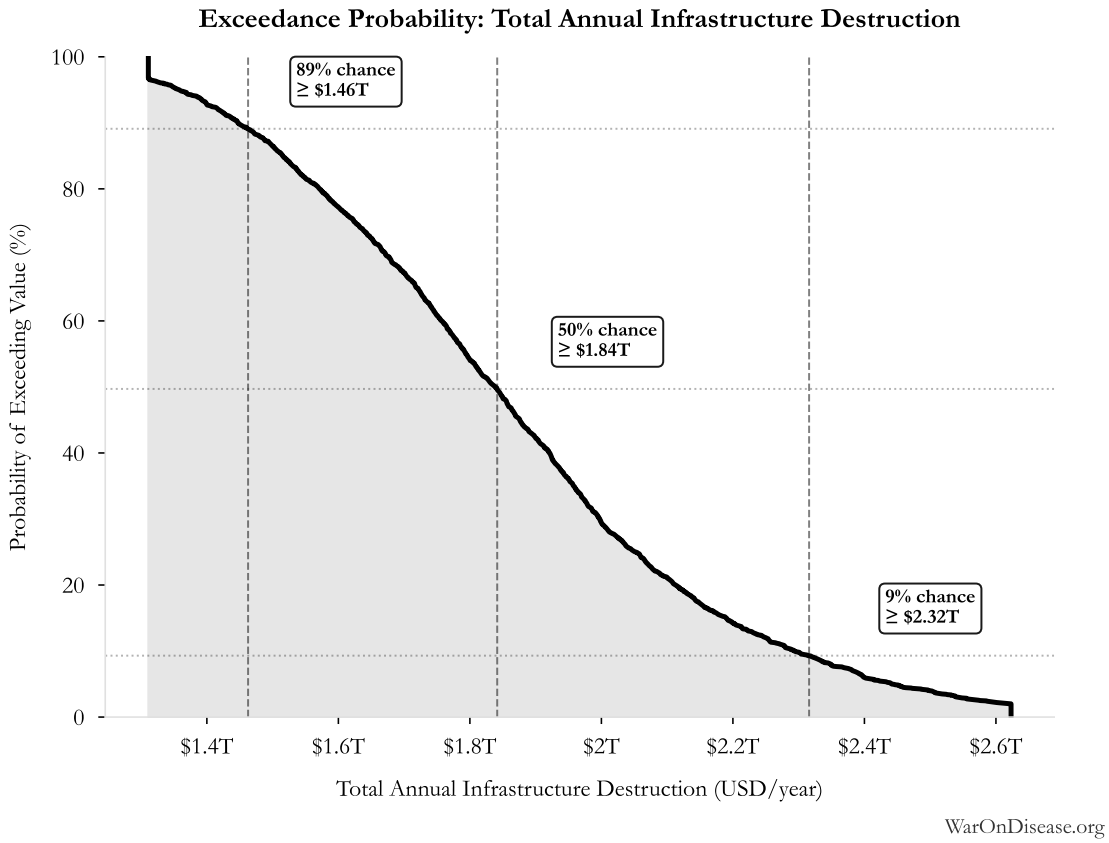


Figure 201: Probability of Exceeding Threshold: Total Annual Infrastructure Destruction

This exceedance probability chart shows the likelihood that Total Annual Infrastructure Destruction will exceed any given threshold. Higher curves indicate more favorable outcomes with greater certainty.

Total Annual Trade Disruption: $616B

Details

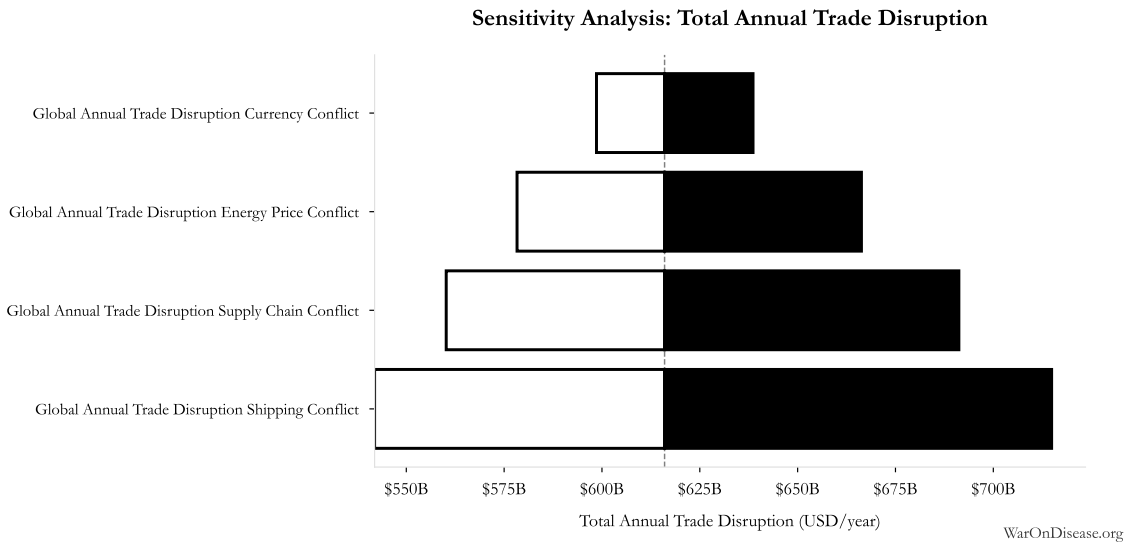
Total annual trade disruption (sum of shipping, supply chain, energy prices, currency instability)
Inputs:

- Annual Trade Disruption Costs from Currency Instability : $57.4B (95% CI: $40B - $80B)
- Annual Trade Disruption Costs from Energy Price Volatility : $125B (95% CI: $87B - $175B)
- Annual Trade Disruption Costs from Shipping Disruptions : $247B (95% CI: $173B - $346B)
- Annual Trade Disruption Costs from Supply Chain Disruptions : $187B (95% CI: $131B - $262B)

$$\begin{aligned} &Disruption_{trade} \\ &= Disruption_{currency} + Disruption_{energy} \\ &+ Disruption_{shipping} + Disruption_{supply} \\ &= \$57.4B + \$125B + \$247B + \$187B \\ &= \$616B \end{aligned}$$

High confidence

Sensitivity Analysis



Sensitivity Indices for Total Annual Trade Disruption

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

Input Parameter	Sensitivity Coefficient	Interpretation
Global Annual Trade Disruption Shipping Conflict	0.4005	Moderate driver
Global Annual Trade Disruption Supply Chain Conflict	0.3033	Moderate driver
Global Annual Trade Disruption Energy Price Conflict	0.2037	Weak driver
Global Annual Trade Disruption Currency Conflict	0.0926	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.

Monte Carlo Distribution

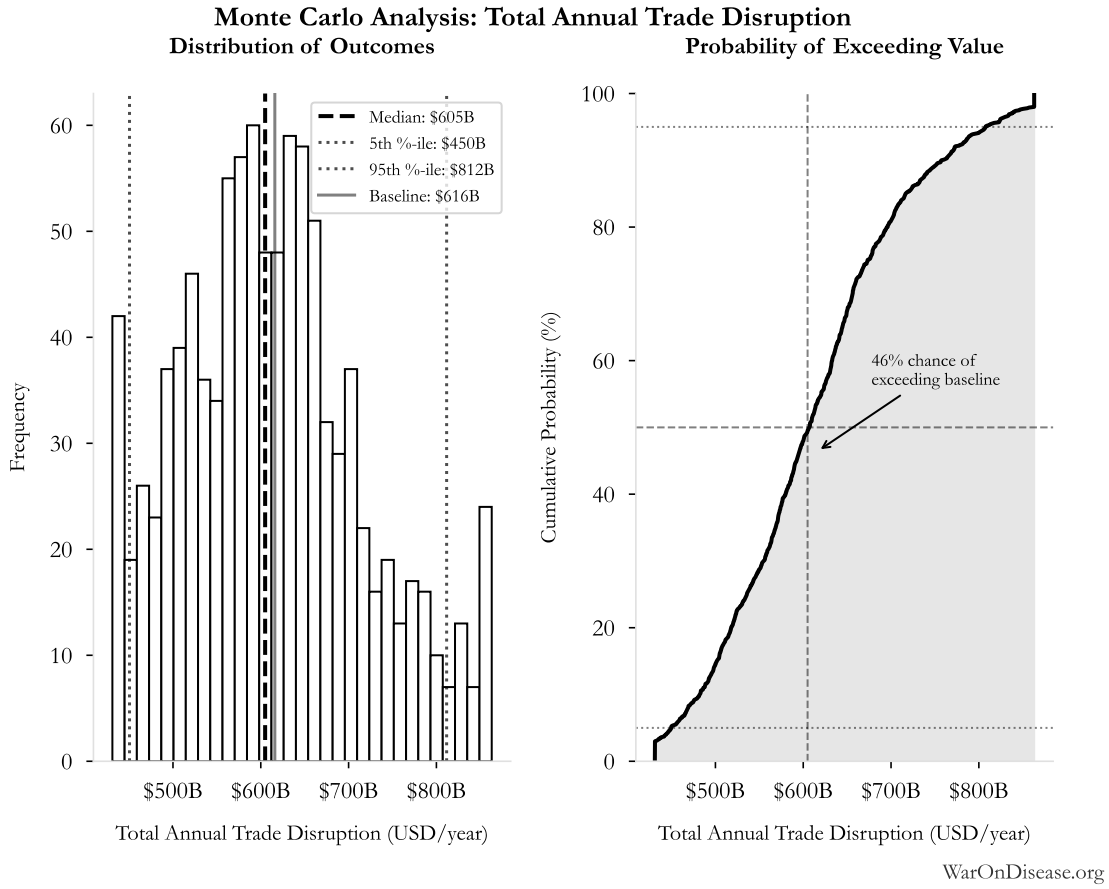


Figure 202: Monte Carlo Distribution: Total Annual Trade Disruption (10,000 simulations)

Simulation Results Summary: Total Annual Trade Disruption

Statistic	Value
Baseline (deterministic)	$616B
Mean (expected value)	$614B
Median (50th percentile)	$605B
Standard Deviation	$105B
90% Range (5th-95th percentile)	[$450B, $812B]

The histogram shows the distribution of Total Annual Trade Disruption 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

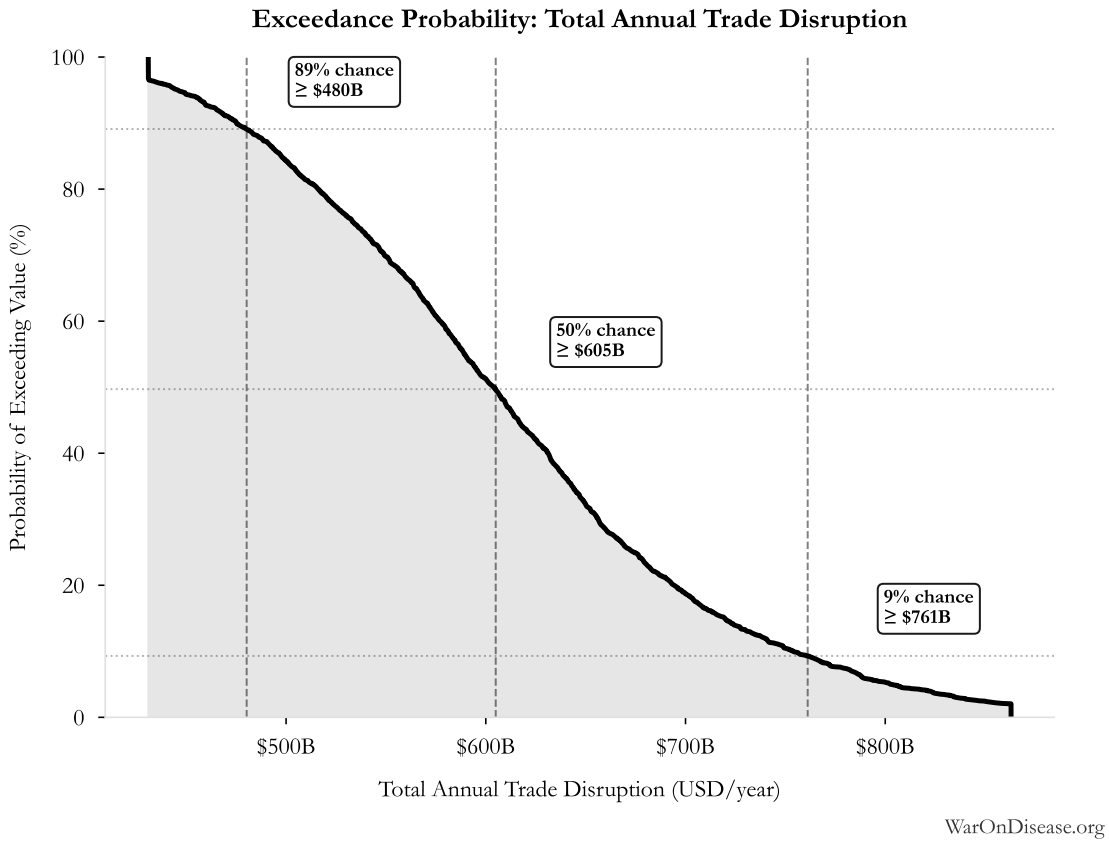


Figure 203: Probability of Exceeding Threshold: Total Annual Trade Disruption

This exceedance probability chart shows the likelihood that Total Annual Trade Disruption will exceed any given threshold. Higher curves indicate more favorable outcomes with greater certainty.

Total Annual Direct War Costs: $7.66T

Details

Total annual direct war costs (military spending + infrastructure + human life + trade disruption)
Inputs:

- Total Annual Human Life Losses from Conflict : $2.45T
- Total Annual Infrastructure Destruction : $1.88T
- Total Annual Trade Disruption : $616B
- Global Military Spending in 2024 : $2.72T

$$
\begin{aligned}
&Cost_{war,direct} \\
&= Loss_{life,conflict} + Damage_{infra,total} \\
&+ Disruption_{trade} + Spending_{mil} \\
&= \$2.45T + \$1.88T + \$616B + \$2.72T \\
&= \$7.66T
\end{aligned}
$$

$$
\begin{aligned}
&\text{where } Loss_{life,conflict} \\
&= Cost_{combat,human} + Cost_{state,human} \\
&+ Cost_{terror,human} \\
&= \$2.34T + \$27B + \$83B \\
&= \$2.45T
\end{aligned}
$$

$$
\begin{aligned}
&\text{where } Cost_{combat,human} \\
&= Deaths_{combat} \times VSL \\
&= 234{,}000 \times \$10M \\
&= \$2.34T
\end{aligned}
$$

$$
\begin{aligned}
&\text{where } Cost_{state,human} \\
&= Deaths_{state} \times VSL \\
&= 2{,}700 \times \$10M \\
&= \$27B
\end{aligned}
$$

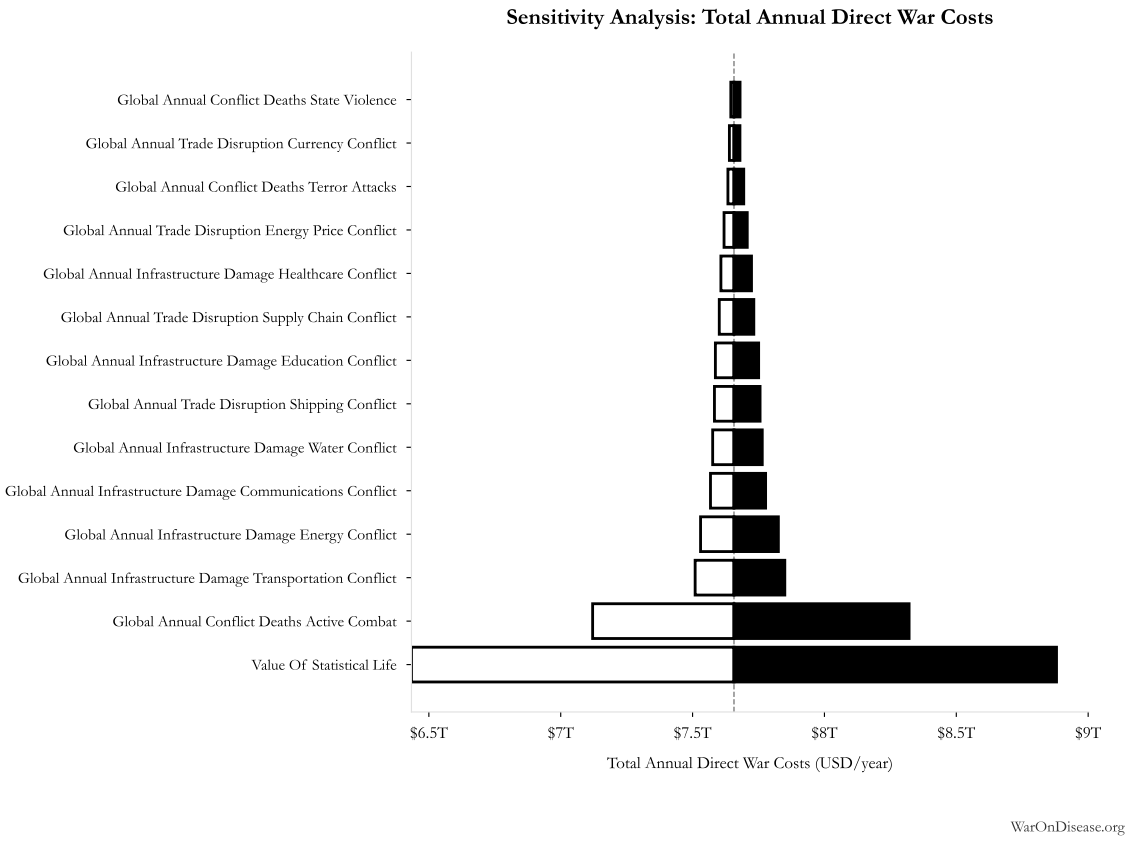
$$
\begin{aligned}
&\text{where } Cost_{terror,human} \\
&= Deaths_{terror} \times VSL \\
&= 8{,}300 \times \$10M \\
&= \$83B
\end{aligned}
$$

$$
\begin{aligned}
&\text{where } Damage_{infra,total} \\
&= Damage_{comms} + Damage_{edu} + Damage_{energy} \\
&+ Damage_{health} + Damage_{transport} \\
&+ Damage_{water} \\
&= \$298B + \$234B + \$422B + \$166B + \$487B + \$268B \\
&= \$1.88T
\end{aligned}
$$

$$
\begin{aligned}
&\text{where } Disruption_{trade} \\
&= Disruption_{currency} + Disruption_{energy} \\
&+ Disruption_{shipping} + Disruption_{supply} \\
&= \$57.4B + \$125B + \$247B + \$187B \\
&= \$616B
\end{aligned}
$$

High confidence

Sensitivity Analysis



Sensitivity Indices for Total Annual Direct War Costs

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

Input Parameter	Sensitivity Coefficient	Interpretation
Global Annual Human Life Losses Conflict	0.7463	Strong driver
Global Annual Infrastructure Destruction Conflict	0.3211	Moderate driver
Global Annual Trade Disruption Conflict	0.1057	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

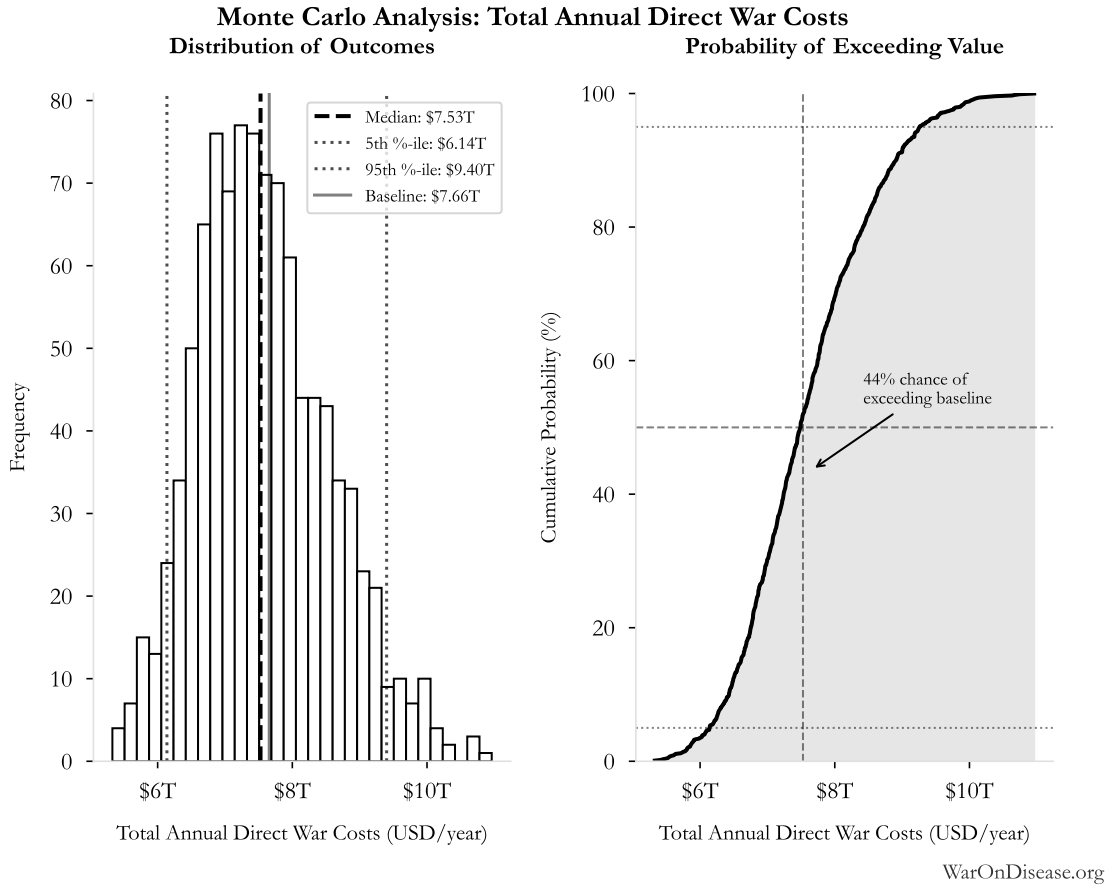


Figure 204: Monte Carlo Distribution: Total Annual Direct War Costs (10,000 simulations)

Simulation Results Summary: Total Annual Direct War Costs

Statistic	Value
Baseline (deterministic)	$7.66T
Mean (expected value)	$7.62T
Median (50th percentile)	$7.53T
Standard Deviation	$992B
90% Range (5th-95th percentile)	[$6.14T, $9.40T]

The histogram shows the distribution of Total Annual Direct War Costs 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

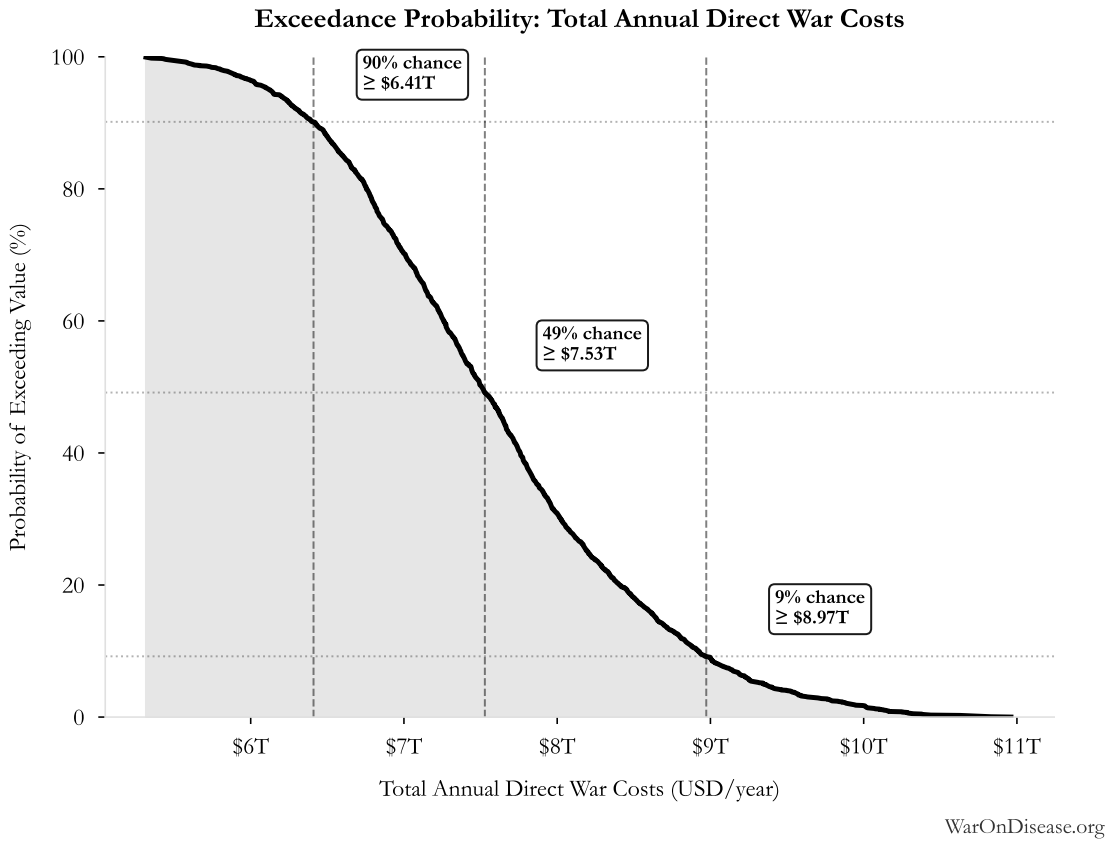


Figure 205: Probability of Exceeding Threshold: Total Annual Direct War Costs

This exceedance probability chart shows the likelihood that Total Annual Direct War Costs will exceed any given threshold. Higher curves indicate more favorable outcomes with greater certainty.

Total Annual Indirect War Costs: $3.70T

Details

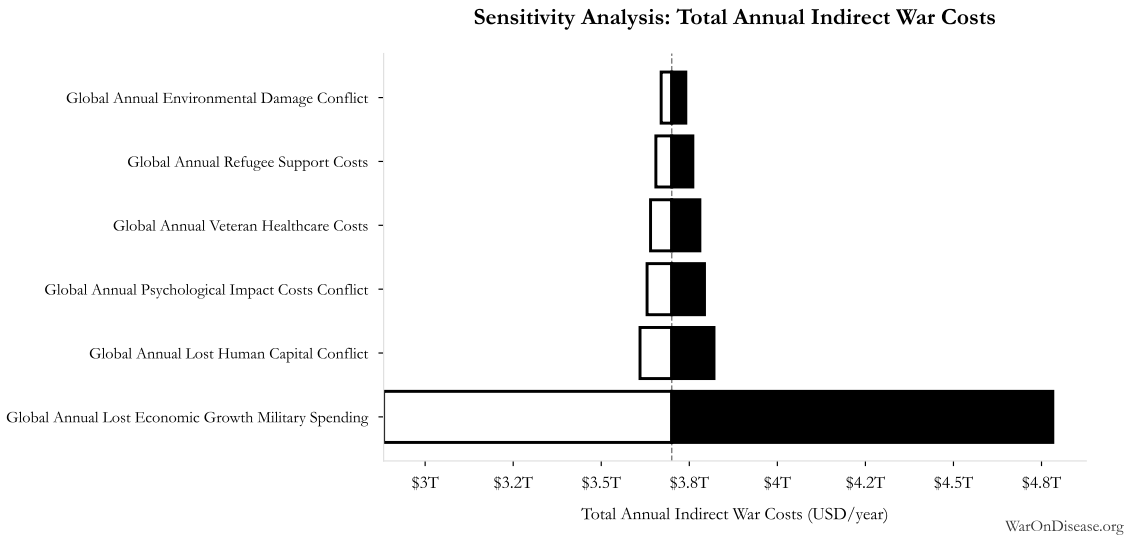
Total annual indirect war costs (opportunity cost + veterans + refugees + environment + mental health + lost productivity)
Inputs:

- Annual Environmental Damage and Restoration Costs from Conflict : $100B (95% CI: $70B - $140B)
- Annual Lost Economic Growth from Military Spending Opportunity Cost : $2.72T (95% CI: $1.90T - $3.80T)
- Annual Lost Productivity from Conflict Casualties : $300B (95% CI: $210B - $420B)
- Annual PTSD and Mental Health Costs from Conflict : $232B (95% CI: $162B - $325B)
- Annual Refugee Support Costs : $150B (95% CI: $105B - $210B)
- Annual Veteran Healthcare Costs : $200B (95% CI: $140B - $280B)

$$
\begin{aligned}
&Cost_{war,indirect} \\
&= Damage_{env} + Loss_{growth,mil} + Loss_{capital,conflict} \\
&+ Cost_{psych} + Cost_{refugee} + Cost_{vet} \\
&= \$100B + \$2.72T + \$300B + \$232B + \$150B + \$200B \\
&= \$3.7T
\end{aligned}
$$

High confidence

Sensitivity Analysis



Sensitivity Indices for Total Annual Indirect War Costs
Regression-based sensitivity showing which inputs explain the most variance in the output.

Input Parameter	Sensitivity Coefficient	Interpretation
Global Annual Lost Human Capital Conflict	5.0931	Strong driver
Global Annual Refugee Support Costs	-2.5522	Strong driver
Global Annual Environmental Damage Conflict	-2.3922	Strong driver

Global Annual Lost Economic Growth Military Spending	0.7342	Strong driver
Global Annual Psychological Impact Costs Conflict	0.0630	Minimal effect
Global Annual Veteran Healthcare Costs	0.0541	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.

Monte Carlo Distribution

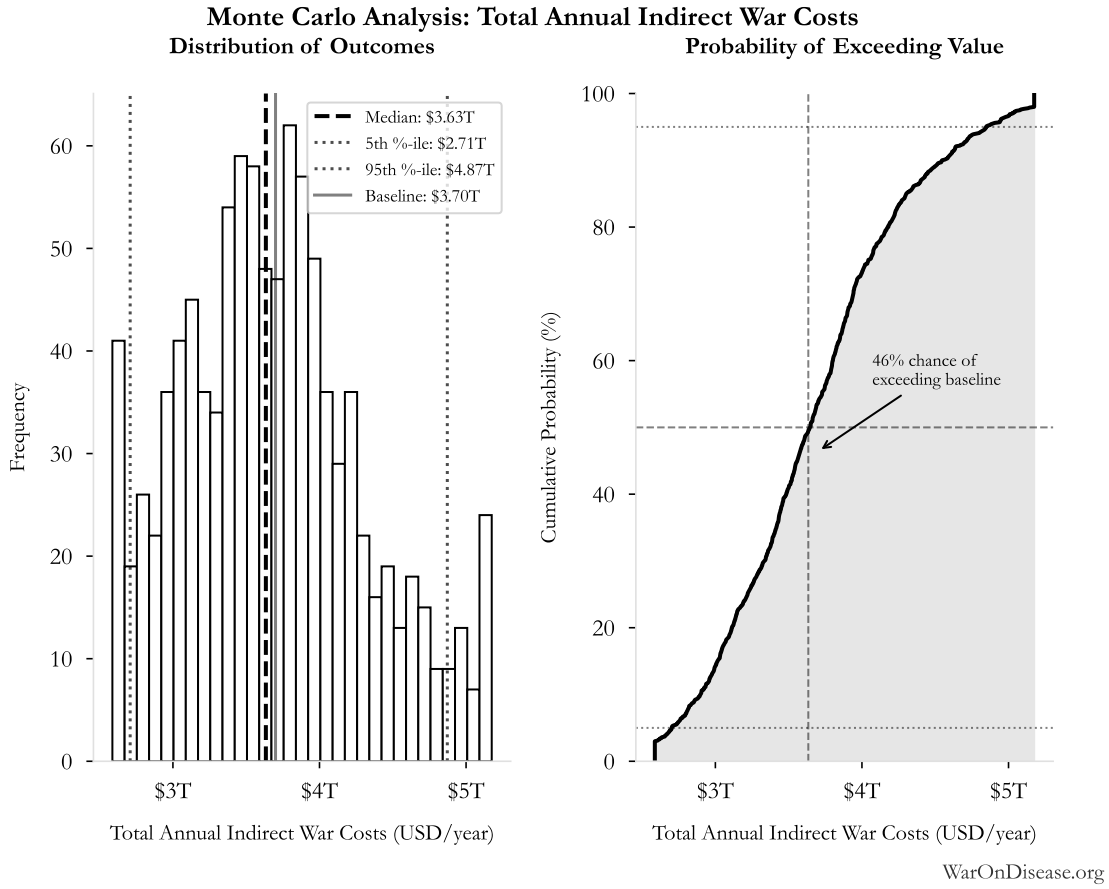


Figure 206: Monte Carlo Distribution: Total Annual Indirect War Costs (10,000 simulations)

Simulation Results Summary: Total Annual Indirect War Costs

Statistic	Value
Baseline (deterministic)	$3.70T
Mean (expected value)	$3.69T
Median (50th percentile)	$3.63T
Standard Deviation	$628B
90% Range (5th-95th percentile)	[$2.71T, $4.87T]

The histogram shows the distribution of Total Annual Indirect War Costs 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

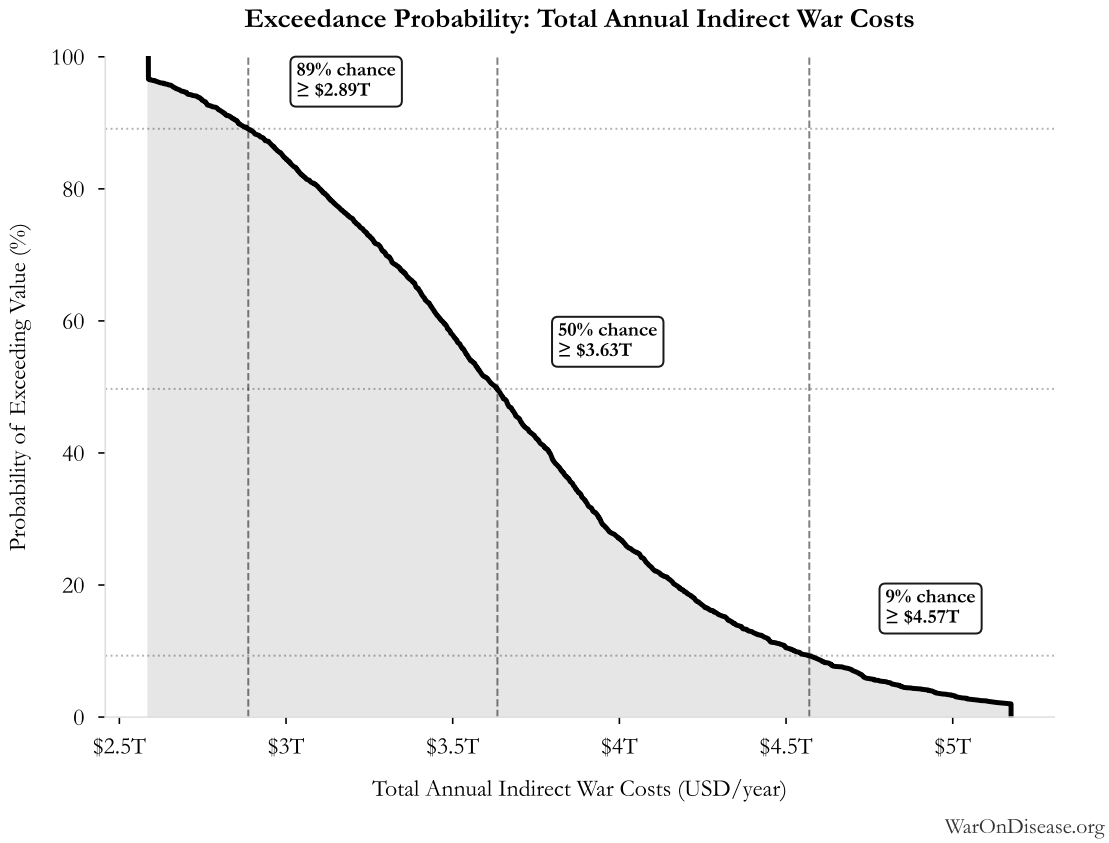


Figure 207: Probability of Exceeding Threshold: Total Annual Indirect War Costs

This exceedance probability chart shows the likelihood that Total Annual Indirect War Costs will exceed any given threshold. Higher curves indicate more favorable outcomes with greater certainty.

Total Economic Burden of Disease Globally: $109T

Details

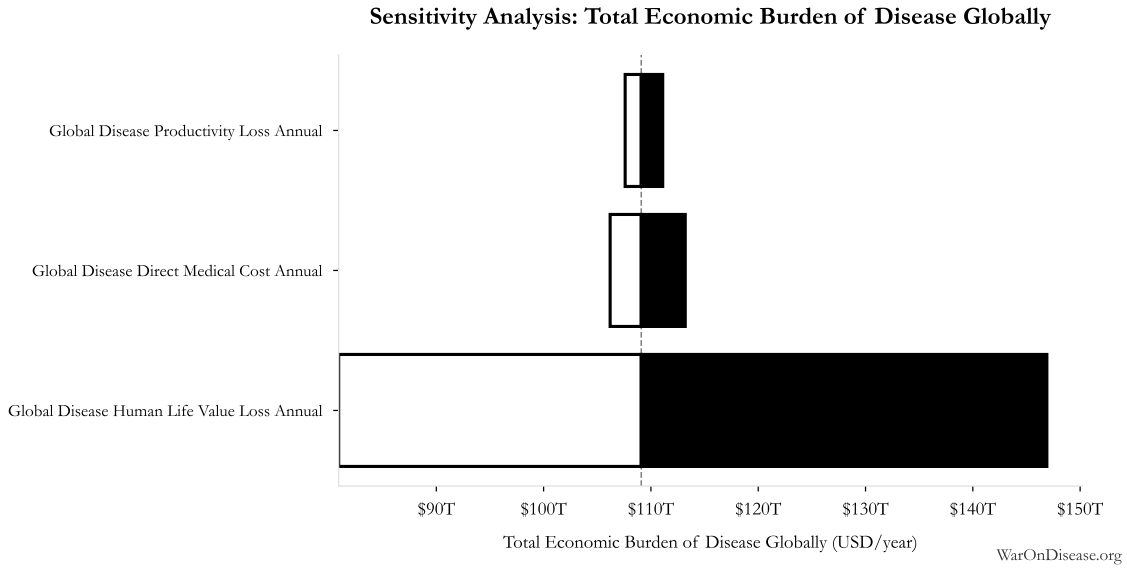
Total economic burden of disease globally (medical + productivity + mortality)
Inputs:

- Global Annual Direct Medical Costs of Disease : $9.90T (95% CI: $7T - $14T)
- Global Annual Economic Value of Human Life Lost to Disease : $94.2T (95% CI: $66T - $132T)
- Global Annual Productivity Loss from Disease : $5T (95% CI: $3.50T - $7T)

$$\begin{aligned} &Burden_{disease} \\ &= Cost_{medical,direct} + Loss_{life,disease} \\ &+ Loss_{productivity} \\ &= \$9.9T + \$94.2T + \$5T \\ &= \$109T \end{aligned}$$

Methodology:[43]
High confidence

Sensitivity Analysis



Sensitivity Indices for Total Economic Burden of Disease Globally

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

Input Parameter	Sensitivity Coefficient	Interpretation
Global Disease Human Life Value Loss Annual	0.8628	Strong driver
Global Disease Direct Medical Cost Annual	0.0915	Minimal effect
Global Disease Productivity Loss Annual	0.0458	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.

Monte Carlo Distribution

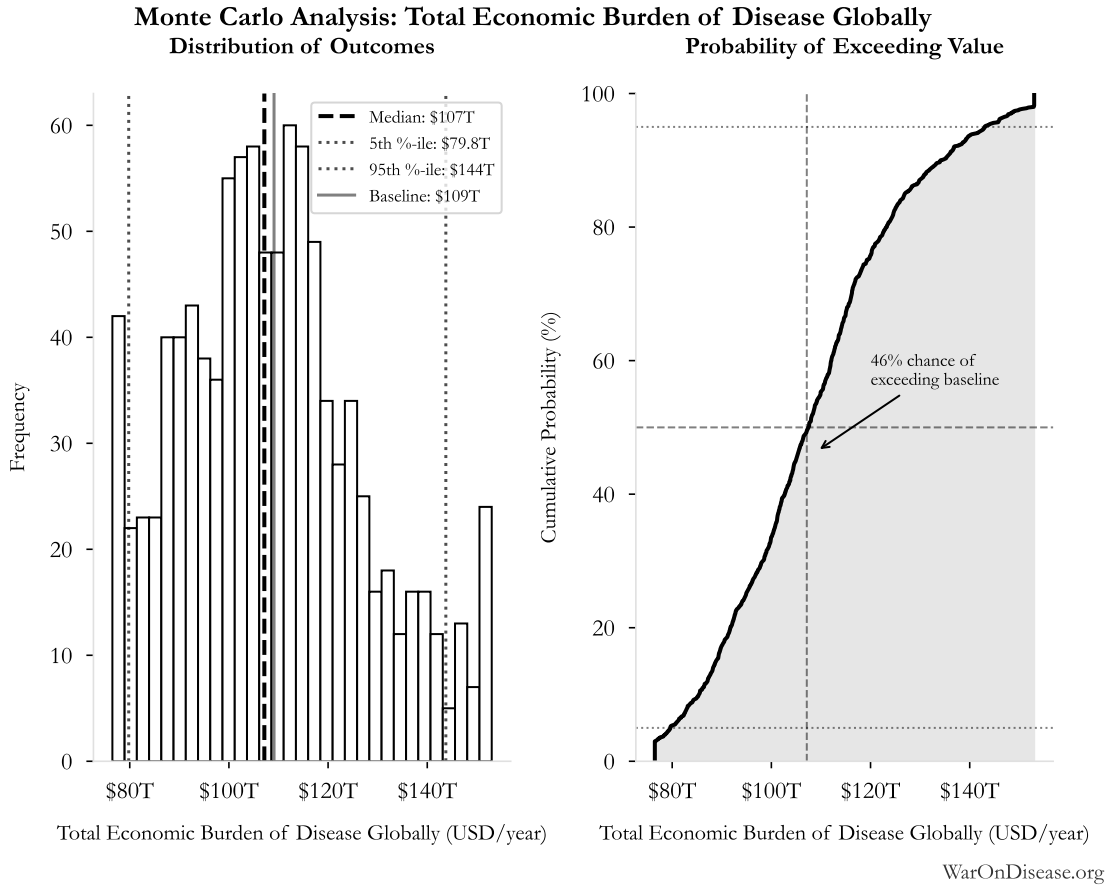


Figure 208: Monte Carlo Distribution: Total Economic Burden of Disease Globally (10,000 simulations)

Simulation Results Summary: Total Economic Burden of Disease Globally

Statistic	Value
Baseline (deterministic)	$109T
Mean (expected value)	$109T
Median (50th percentile)	$107T
Standard Deviation	$18.6T
90% Range (5th-95th percentile)	[$79.8T, $144T]

The histogram shows the distribution of Total Economic Burden of Disease Globally 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

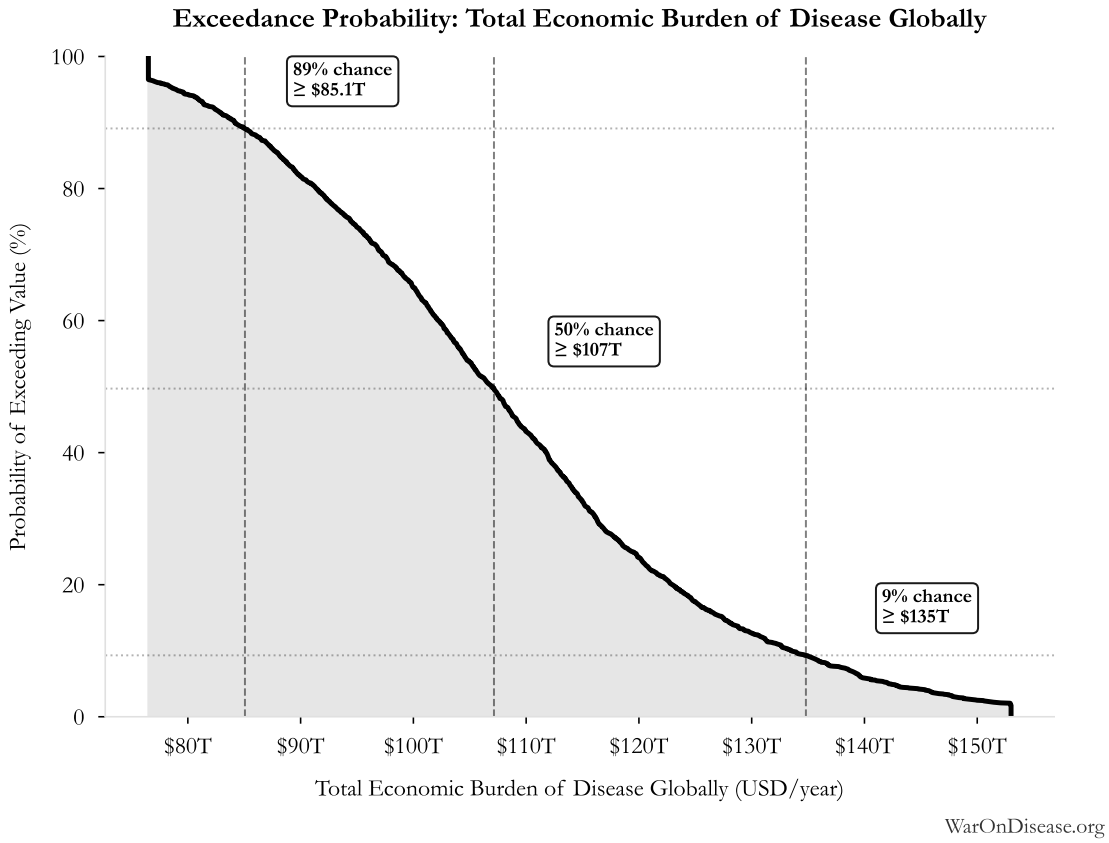


Figure 209: Probability of Exceeding Threshold: Total Economic Burden of Disease Globally

This exceedance probability chart shows the likelihood that Total Economic Burden of Disease Globally will exceed any given threshold. Higher curves indicate more favorable outcomes with greater certainty.

Total Annual Cost of War and Disease with All Externalities: $129T

Details

Total annual cost of war and disease with all externalities (direct + indirect costs for both)
Inputs:

- Total Annual Cost of War Worldwide : $11.4T

- Total Economic Burden of Disease Globally : $109T
- Annual Global Spending on Symptomatic Disease Treatment : $8.20T (95% CI: $6.50T - $10T)

$$
\begin{aligned}
&Cost_{health+war} \\
&= Cost_{war,total} + Burden_{disease} + Spending_{symptom} \\
&= \$11.4T + \$109T + \$8.2T \\
&= \$129T
\end{aligned}
$$

$$
\begin{aligned}
&\text{where } Cost_{war,total} \\
&= Cost_{war,direct} + Cost_{war,indirect} \\
&= \$7.66T + \$3.7T \\
&= \$11.4T
\end{aligned}
$$

$$
\begin{aligned}
&\text{where } Cost_{war,direct} \\
&= Loss_{life,conflict} + Damage_{infra,total} \\
&+ Disruption_{trade} + Spending_{mil} \\
&= \$2.45T + \$1.88T + \$616B + \$2.72T \\
&= \$7.66T
\end{aligned}
$$

$$
\begin{aligned}
&\text{where } Loss_{life,conflict} \\
&= Cost_{combat,human} + Cost_{state,human} \\
&+ Cost_{terror,human} \\
&= \$2.34T + \$27B + \$83B \\
&= \$2.45T
\end{aligned}
$$

$$
\begin{aligned}
&\text{where } Cost_{combat,human} \\
&= Deaths_{combat} \times VSL \\
&= 234{,}000 \times \$10M \\
&= \$2.34T
\end{aligned}
$$

$$
\begin{aligned}
&\text{where } Cost_{state,human} \\
&= Deaths_{state} \times VSL \\
&= 2{,}700 \times \$10M \\
&= \$27B
\end{aligned}
$$

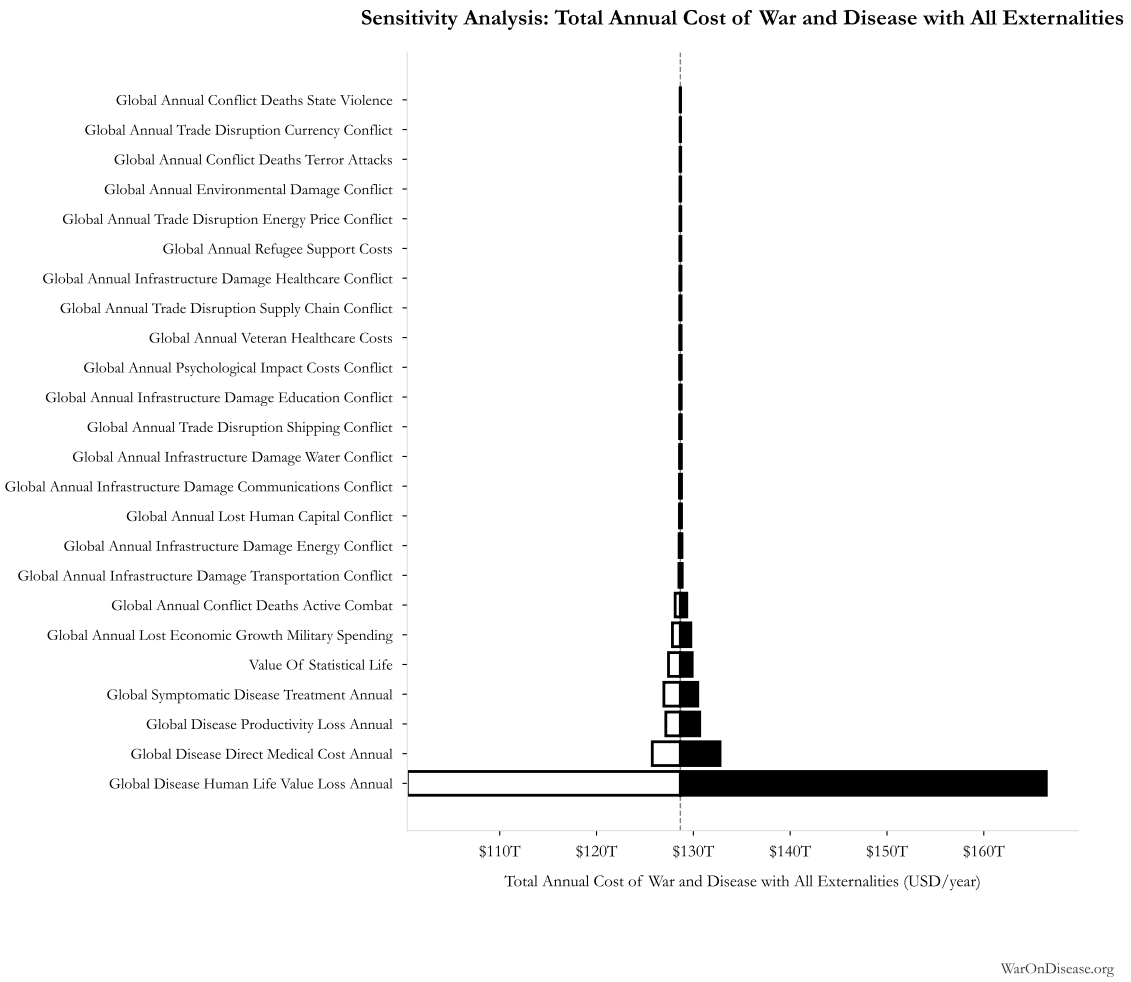
$$
\begin{aligned}
&\text{where } Cost_{terror,human} \\
&= Deaths_{terror} \times VSL \\
&= 8{,}300 \times \$10M \\
&= \$83B
\end{aligned}
$$

$$
\begin{aligned}
&\text{where } Damage_{infra,total} \\
&= Damage_{comms} + Damage_{edu} + Damage_{energy} \\
&+ Damage_{health} + Damage_{transport} \\
&+ Damage_{water} \\
&= \$298B + \$234B + \$422B + \$166B + \$487B + \$268B \\
&= \$1.88T
\end{aligned}
$$

$$
\begin{aligned}
&\text{where } Disruption_{trade} \\
&= Disruption_{currency} + Disruption_{energy} \\
&+ Disruption_{shipping} + Disruption_{supply} \\
&= \$57.4B + \$125B + \$247B + \$187B
\end{aligned}
$$

High confidence

Sensitivity Analysis



Sensitivity Indices for Total Annual Cost of War and Disease with All Externalities
Regression-based sensitivity showing which inputs explain the most variance in the output.

Input Parameter	Sensitivity Coefficient	Interpretation
Global Disease Economic Burden Annual	0.8934	Strong driver
Global Annual Direct Indirect War Cost	0.0728	Minimal effect
Global Symptomatic Disease Treatment Annual	0.0410	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.

Monte Carlo Distribution

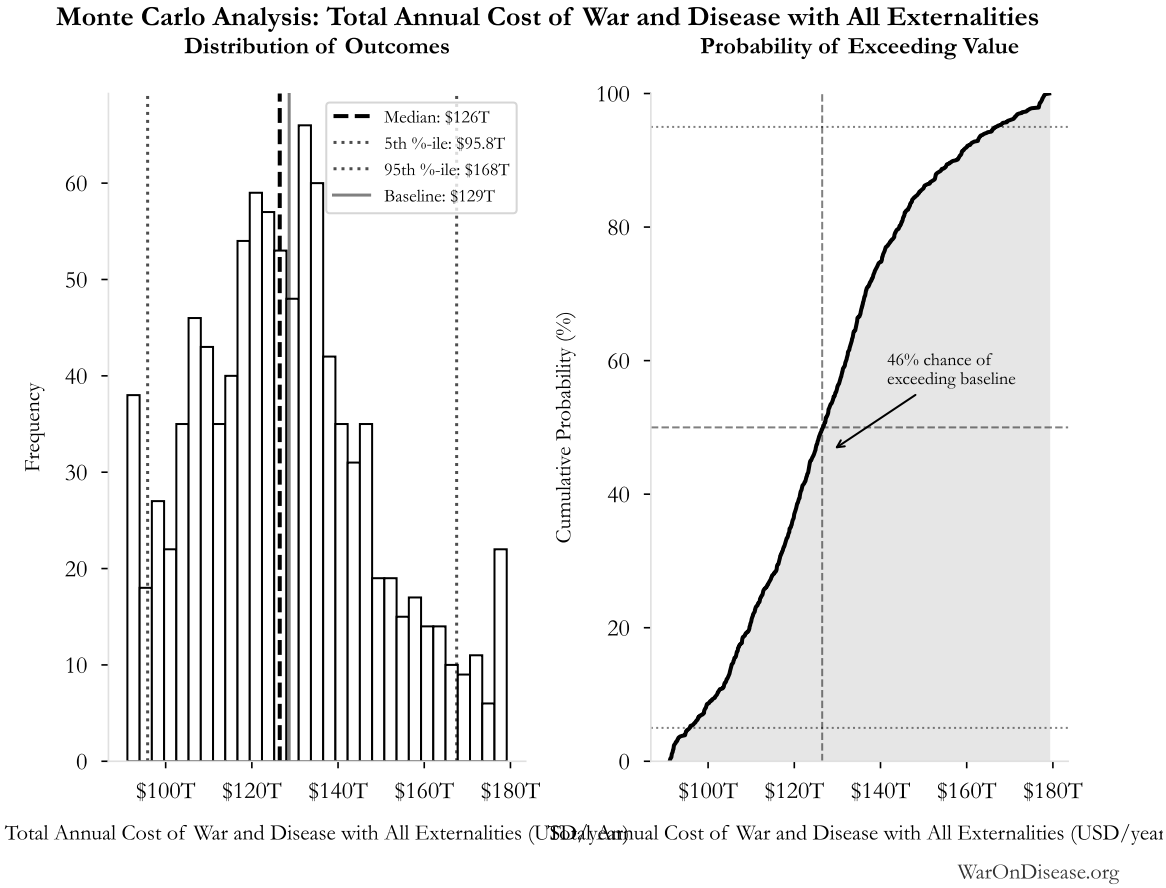


Figure 210: Monte Carlo Distribution: Total Annual Cost of War and Disease with All Externalities (10,000 simulations)

Simulation Results Summary: Total Annual Cost of War and Disease with All Externalities

Statistic	Value
Baseline (deterministic)	$129T
Mean (expected value)	$128T
Median (50th percentile)	$126T
Standard Deviation	$20.8T
90% Range (5th-95th percentile)	[$95.8T, $168T]

The histogram shows the distribution of Total Annual Cost of War and Disease with All Externalities 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

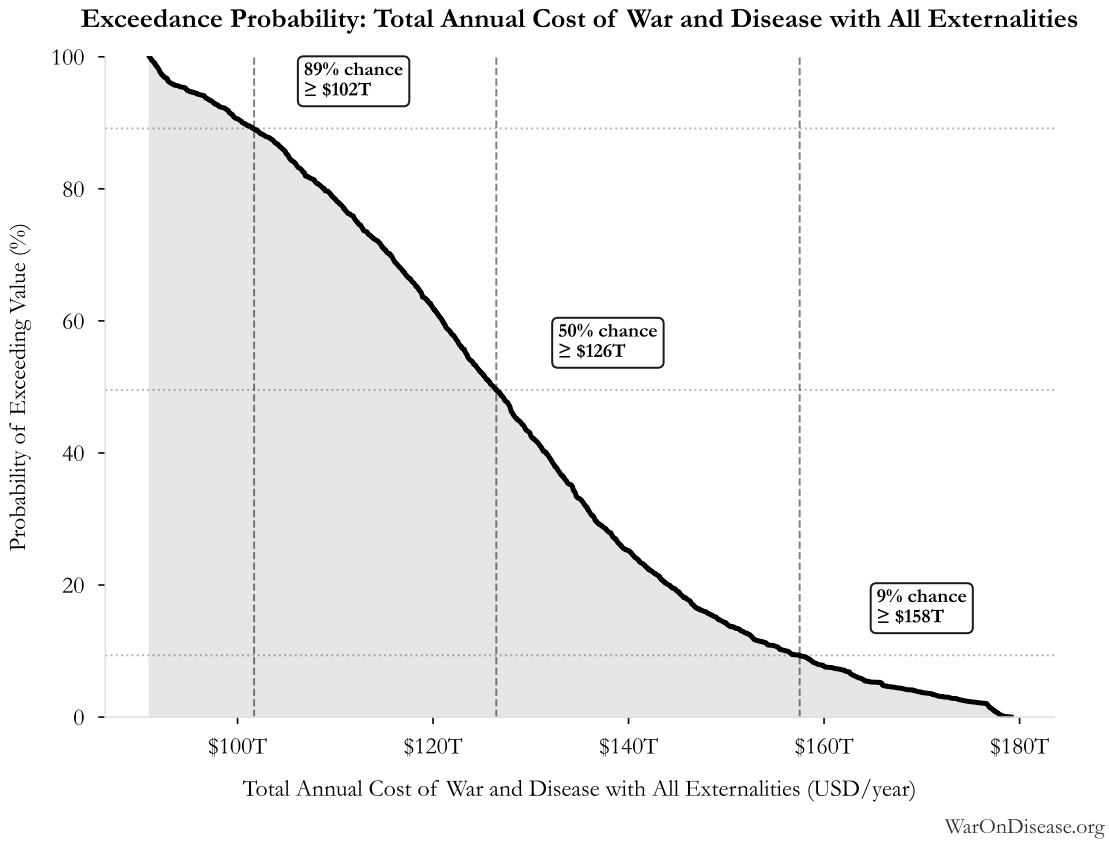


Figure 211: Probability of Exceeding Threshold: Total Annual Cost of War and Disease with All Externalities

This exceedance probability chart shows the likelihood that Total Annual Cost of War and Disease with All Externalities will exceed any given threshold. Higher curves indicate more favorable outcomes with greater certainty.

Healthcare vs Military Multiplier Ratio: 7.17x

Details

Ratio of healthcare to military fiscal multipliers. Healthcare investment generates 7× more economic activity per dollar than military spending.

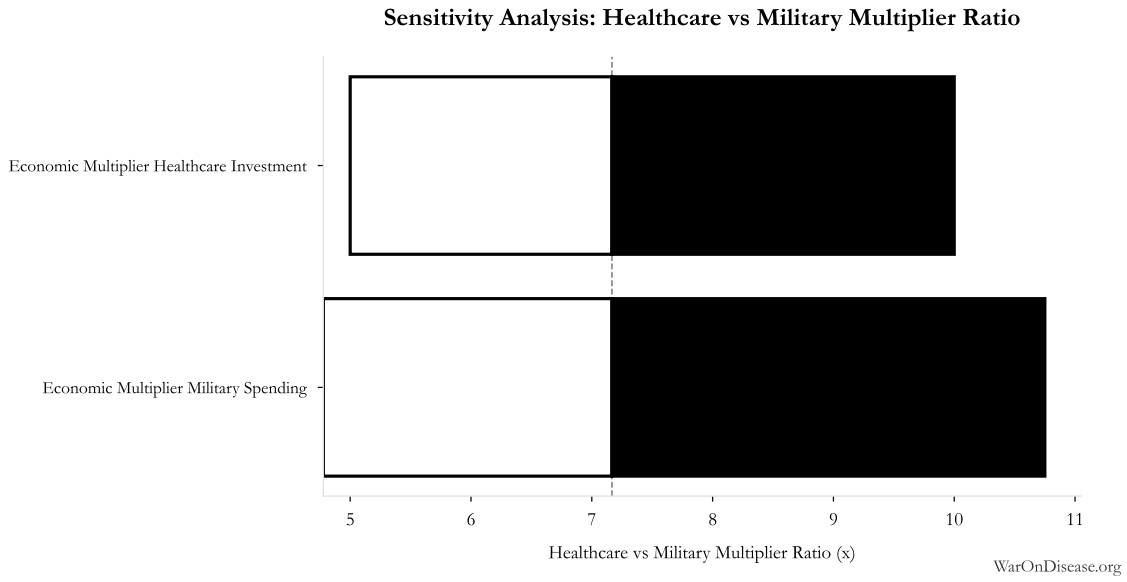
Inputs:

- Economic Multiplier for Healthcare Investment : 4.3x (95% CI: 3x - 6x)
- Economic Multiplier for Military Spending : 0.6x (95% CI: 0.4x - 0.9x)

$$
\begin{aligned}
r_{health/mil} &= \frac{k_{health}}{k_{mil}} \\
&= \frac{4.3}{0.6} \\
&= 7.17
\end{aligned}
$$

High confidence

Sensitivity Analysis



Sensitivity Indices for Healthcare vs Military Multiplier Ratio

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

Input Parameter	Sensitivity Coefficient	Interpretation
Economic Multiplier Military Spending	-0.5163	Strong driver
Economic Multiplier Healthcare Investment	-0.4760	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

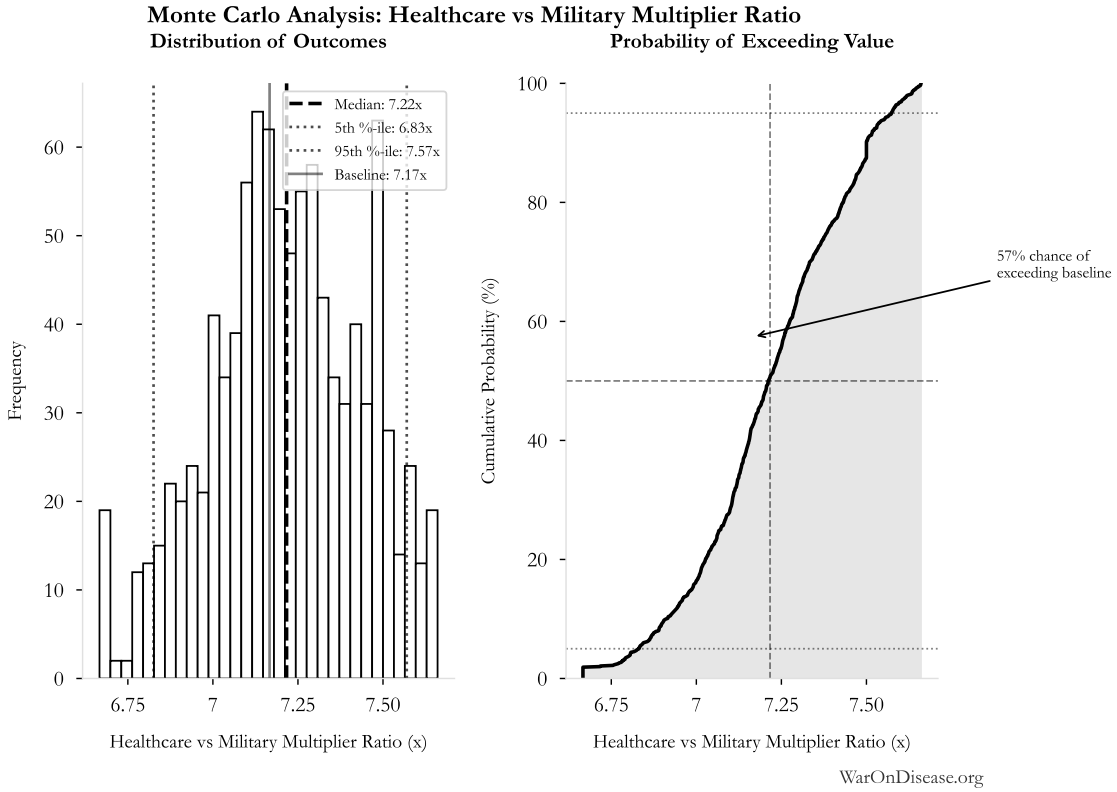


Figure 212: Monte Carlo Distribution: Healthcare vs Military Multiplier Ratio (10,000 simulations)

Simulation Results Summary: Healthcare vs Military Multiplier Ratio

Statistic	Value
Baseline (deterministic)	7.17x
Mean (expected value)	7.21x
Median (50th percentile)	7.22x
Standard Deviation	0.227x
90% Range (5th-95th percentile)	[6.83x, 7.57x]

The histogram shows the distribution of Healthcare vs Military Multiplier Ratio 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

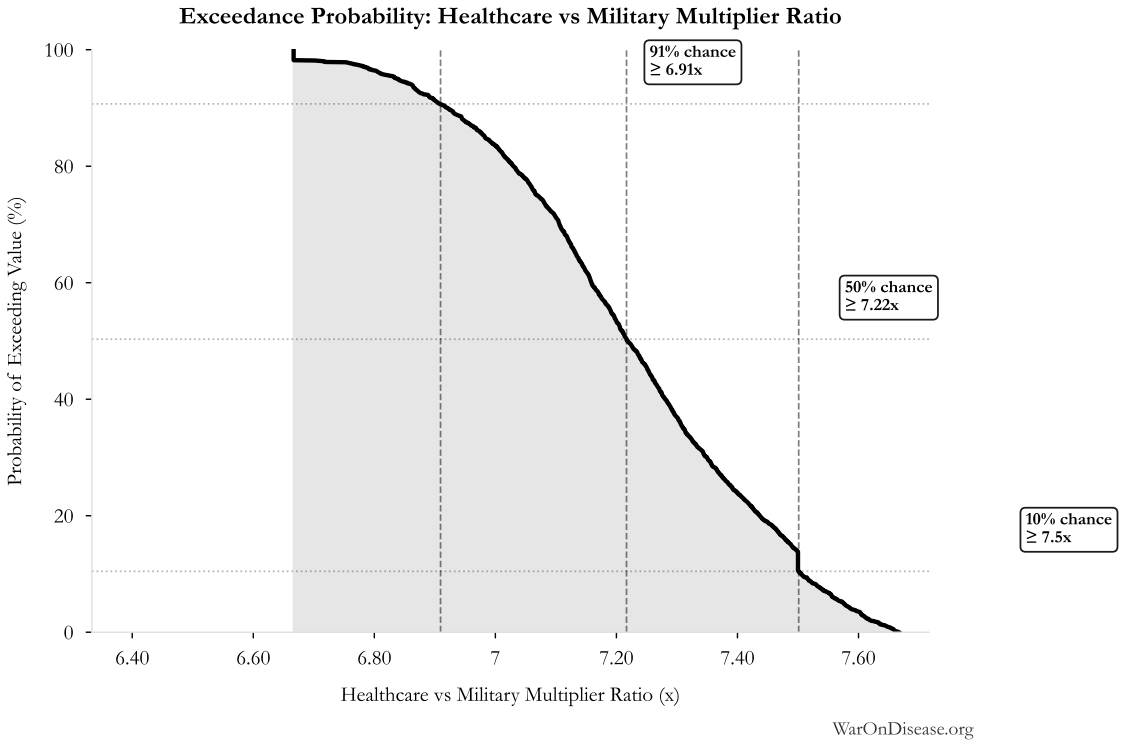


Figure 213: Probability of Exceeding Threshold: Healthcare vs Military Multiplier Ratio

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

Annual IAB Political Incentive Funding: $2.72B

Details

Annual funding for IAB political incentive mechanism (independent expenditures supporting high-scoring politicians, post-office fellowship endowments, Public Good Score infrastructure)
Inputs:

- Annual Funding from 1% of Global Military Spending Redirected to DIH : $27.2B
- IAB Political Incentive Funding Percentage: 10%

$$Funding_{political,ann}$$
$$= Funding_{treaty} \times Pct_{political}$$
$$= \$27.2B \times 10\%$$
$$= \$2.72B$$

where $Funding_{treaty}$
$$= Spending_{mil} \times Reduce_{treaty}$$
$$= \$2.72T \times 1\%$$
$$= \$27.2B$$

High confidence

Medical Research Spending as Percentage of Total Disease Burden: 0.0525%

Details

Medical research spending as percentage of total disease burden
Inputs:

- Global Government Medical Research Spending : $67.5B (95% CI: $54B - $81B)
- Total Annual Cost of War and Disease with All Externalities : $129T

$$Pct_{RD:burden} = \frac{Spending_{RD}}{Cost_{health+war}} = \frac{\$67.5B}{\$129T} = 0.0525\%$$

where $Cost_{health+war} = Cost_{war,total} + Burden_{disease} + Spending_{symptom} = \$11.4T + \$109T + \$8.2T = \$129T$

where $Cost_{war,total} = Cost_{war,direct} + Cost_{war,indirect} = \$7.66T + \$3.7T = \$11.4T$

where $Cost_{war,direct} = Loss_{life,conflict} + Damage_{infra,total} + Disruption_{trade} + Spending_{mil} = \$2.45T + \$1.88T + \$616B + \$2.72T = \$7.66T$

where $Loss_{life,conflict} = Cost_{combat,human} + Cost_{state,human} + Cost_{terror,human} = \$2.34T + \$27B + \$83B = \$2.45T$

where $Cost_{combat,human} = Deaths_{combat} \times VSL = 234{,}000 \times \$10M = \$2.34T$

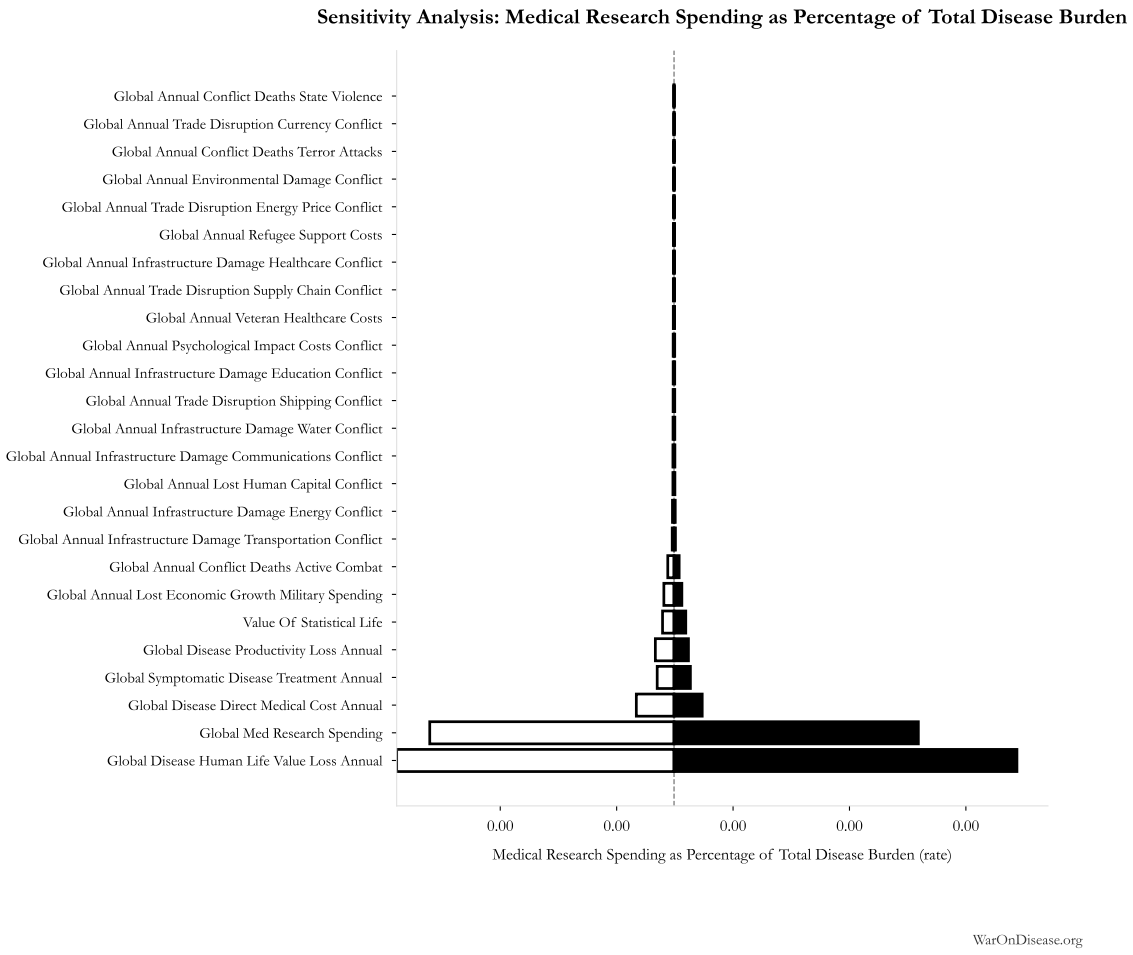
where $Cost_{state,human} = Deaths_{state} \times VSL = 2{,}700 \times \$10M = \$27B$

where $Cost_{terror,human} = Deaths_{terror} \times VSL = 8{,}300 \times \$10M = \$83B$

where $Damage_{infra,total} = Damage_{comms} + Damage_{edu} + Damage_{energy} + Damage_{health} + Damage_{transport} + Damage_{water}$

High confidence

Sensitivity Analysis



Sensitivity Indices for Medical Research Spending as Percentage of Total Disease Burden

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

Input Parameter	Sensitivity Coefficient	Interpretation
Global Total Health And War Cost Annual	-0.5152	Strong driver
Global Med Research Spending	-0.4795	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

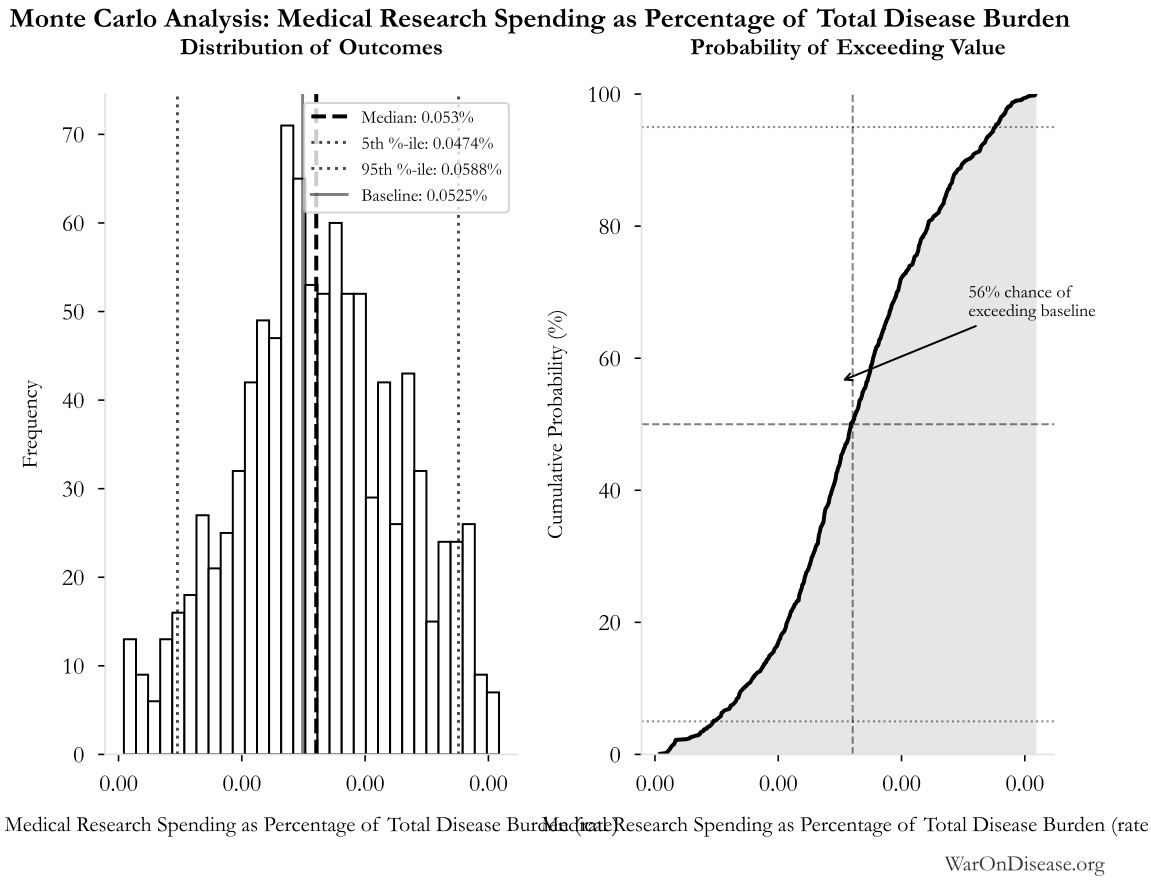


Figure 214: Monte Carlo Distribution: Medical Research Spending as Percentage of Total Disease Burden (10,000 simulations)

Simulation Results Summary: Medical Research Spending as Percentage of Total Disease Burden

Statistic	Value
Baseline (deterministic)	0.0525%
Mean (expected value)	0.053%
Median (50th percentile)	0.053%
Standard Deviation	0.00337%
90% Range (5th-95th percentile)	[0.0474%, 0.0588%]

The histogram shows the distribution of Medical Research Spending as Percentage of Total Disease Burden 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

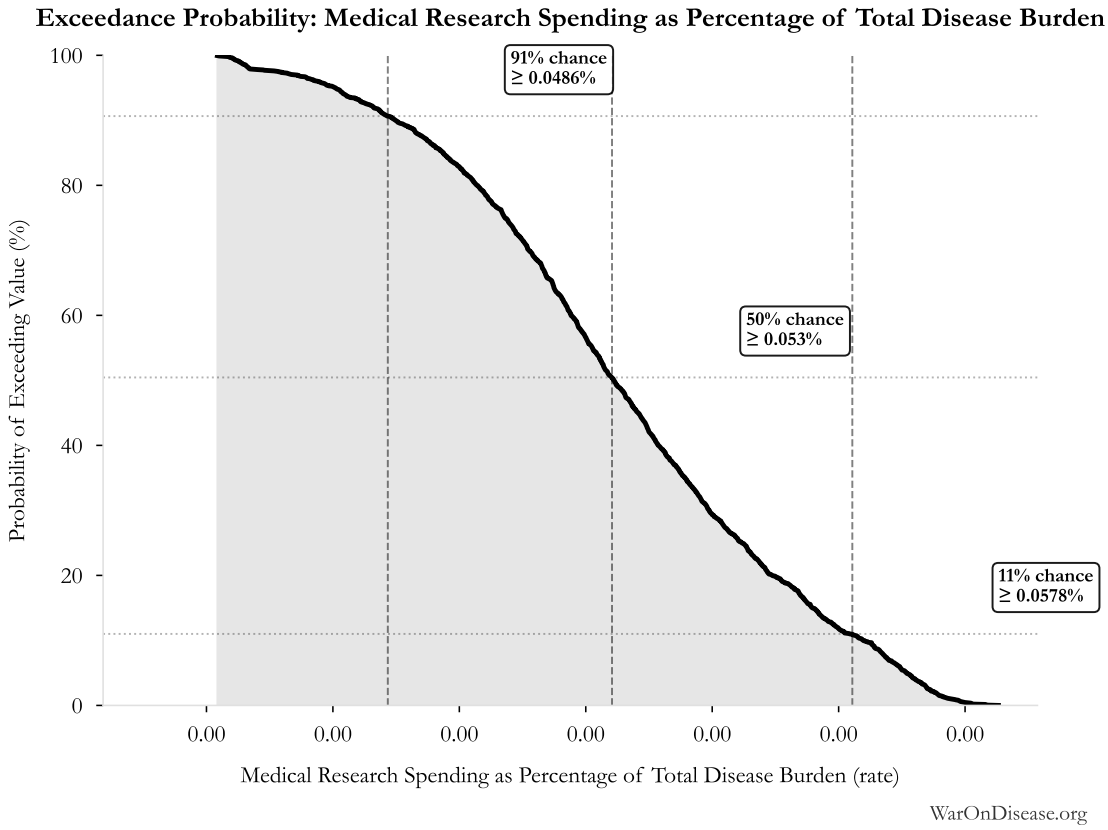


Figure 215: Probability of Exceeding Threshold: Medical Research Spending as Percentage of Total Disease Burden

This exceedance probability chart shows the likelihood that Medical Research Spending as Percentage of Total Disease Burden will exceed any given threshold. Higher curves indicate more favorable outcomes with greater certainty.

Ratio of Military to Government Clinical Trials Spending: 604:1

Details

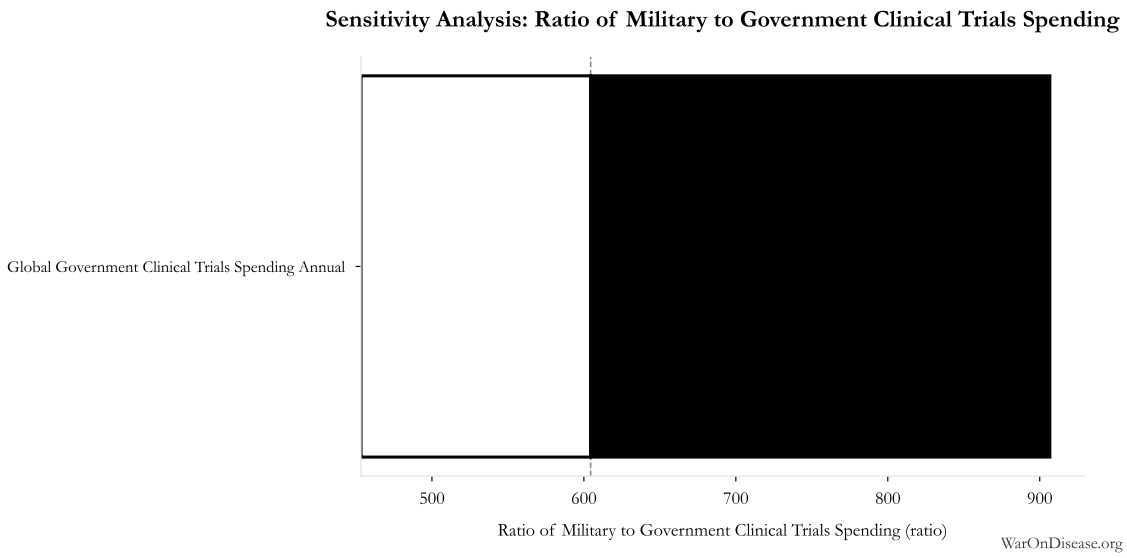
Ratio of global military spending to government clinical trials spending
Inputs:

- Global Military Spending in 2024 : $2.72T
- Annual Global Government Spending on Clinical Trials : $4.50B (95% CI: $3B - $6B)

$$\begin{aligned} & Ratio_{mil:gov} \\ &= \frac{Spending_{mil}}{Spending_{trials,gov}} \\ &= \frac{\$2.72T}{\$4.5B} \\ &= 604 \end{aligned}$$

High confidence

Sensitivity Analysis



Sensitivity Indices for Ratio of Military to Government Clinical Trials Spending
Regression-based sensitivity showing which inputs explain the most variance in the output.

Input Parameter	Sensitivity Coefficient	Interpretation
Global Government Clinical Trials Spending Annual	-0.9786	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

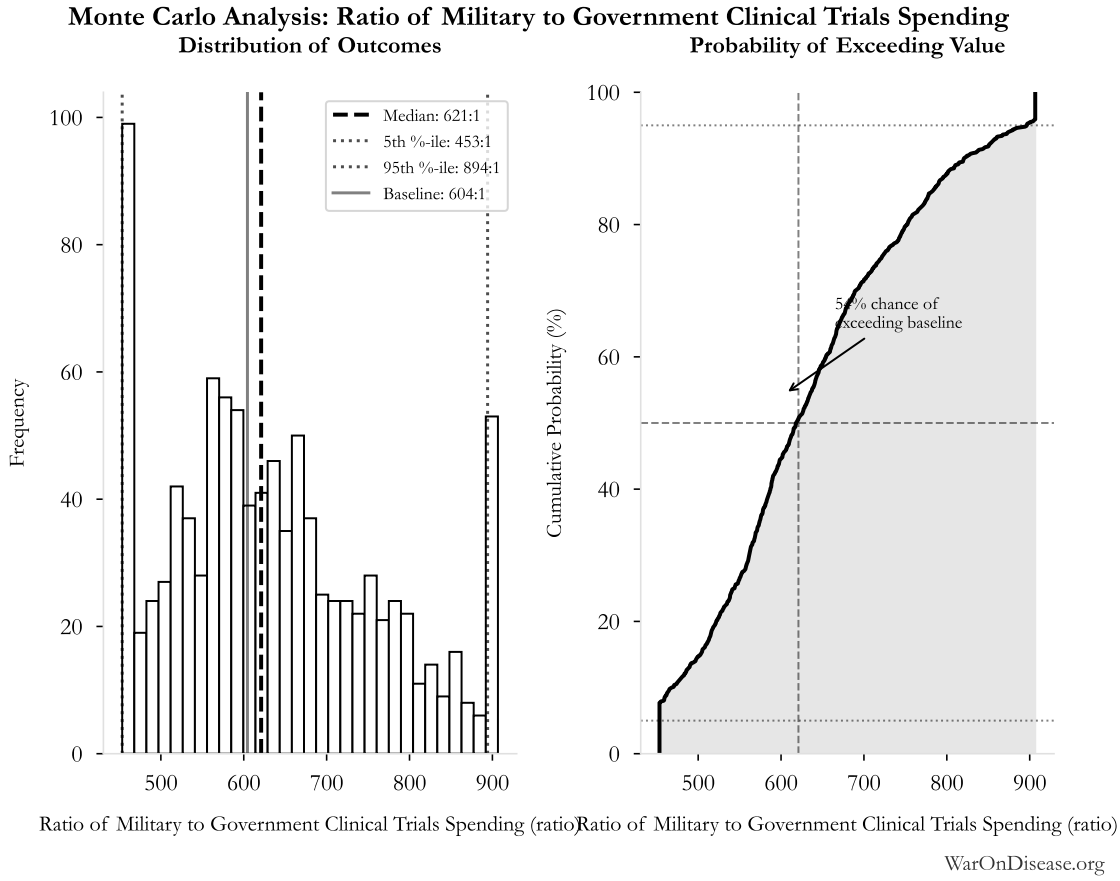


Figure 216: Monte Carlo Distribution: Ratio of Military to Government Clinical Trials Spending (10,000 simulations)

Simulation Results Summary: Ratio of Military to Government Clinical Trials Spending

Statistic	Value
Baseline (deterministic)	604:1
Mean (expected value)	635:1
Median (50th percentile)	621:1
Standard Deviation	127:1
90% Range (5th-95th percentile)	[453:1, 894:1]

The histogram shows the distribution of Ratio of Military to Government Clinical Trials Spending 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

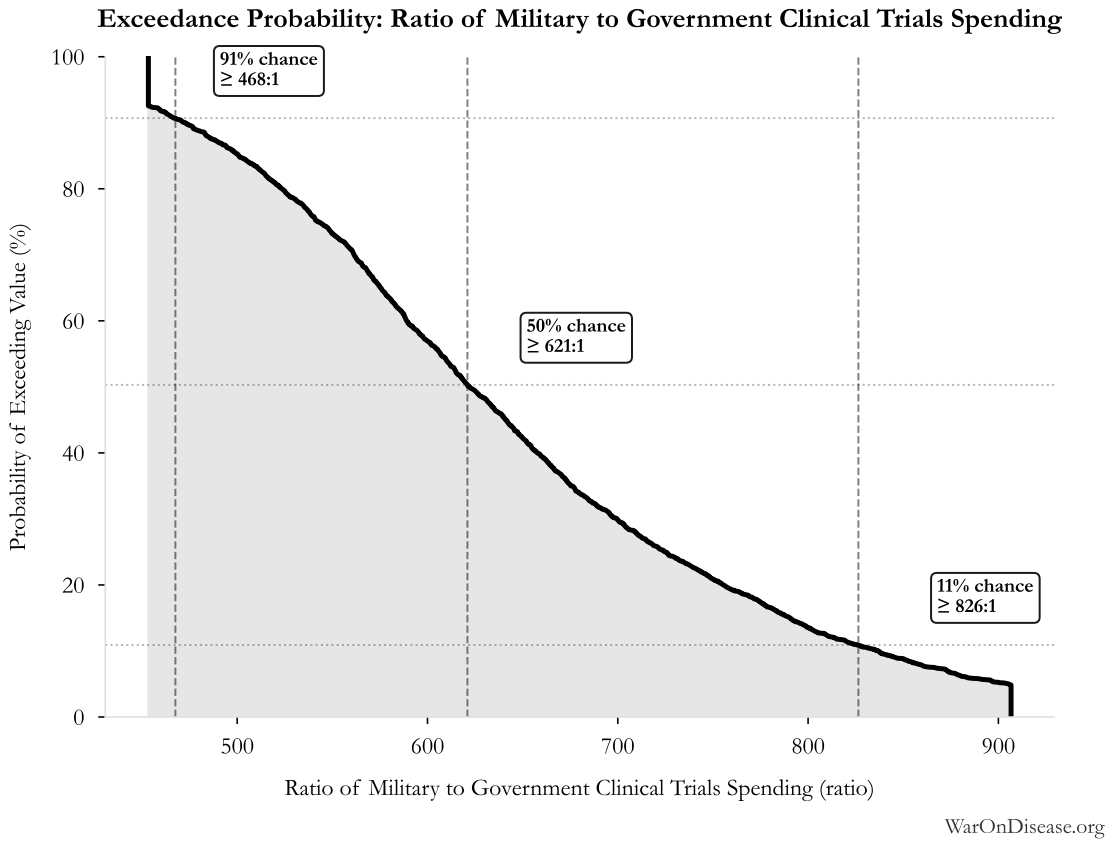


Figure 217: Probability of Exceeding Threshold: Ratio of Military to Government Clinical Trials Spending

This exceedance probability chart shows the likelihood that Ratio of Military to Government Clinical Trials Spending will exceed any given threshold. Higher curves indicate more favorable outcomes with greater certainty.

Ratio of Military Spending to Medical Research Spending: 40.3:1

Details

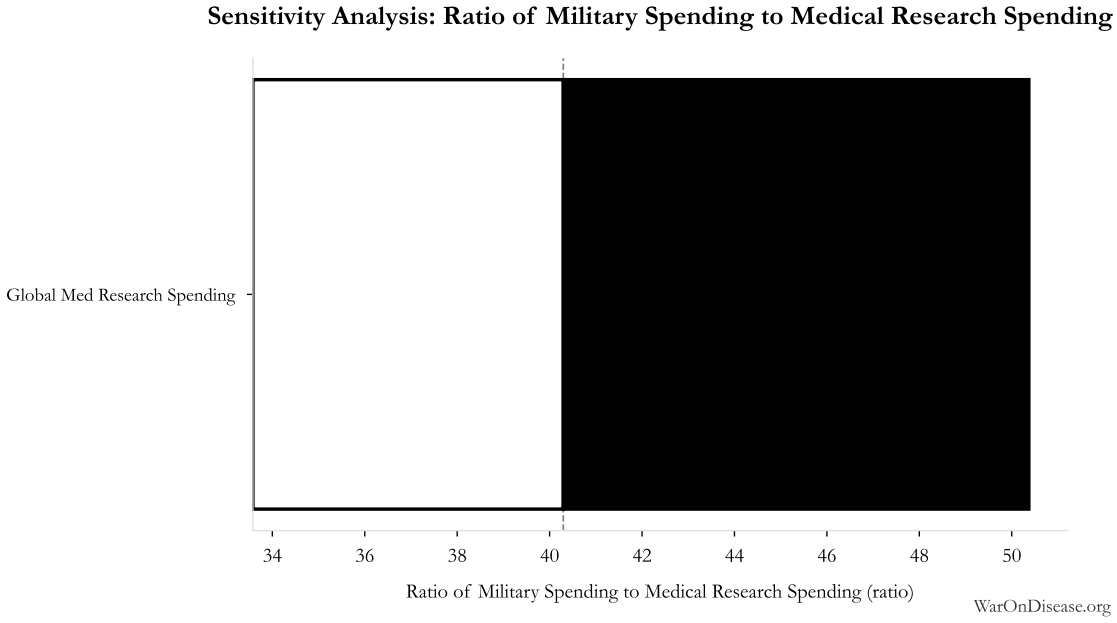
Ratio of military spending to medical research spending
Inputs:

- Global Government Medical Research Spending : $67.5B (95% CI: $54B - $81B)
- Global Military Spending in 2024 : $2.72T

$$\begin{aligned} & Ratio_{mil:RD} \\ &= \frac{Spending_{mil}}{Spending_{RD}} \\ &= \frac{\$2.72T}{\$67.5B} \\ &= 40.3 \end{aligned}$$

High confidence

Sensitivity Analysis



Sensitivity Indices for Ratio of Military Spending to Medical Research Spending
Regression-based sensitivity showing which inputs explain the most variance in the output.

Input Parameter	Sensitivity Coefficient	Interpretation
Global Med Research Spending	-0.9931	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

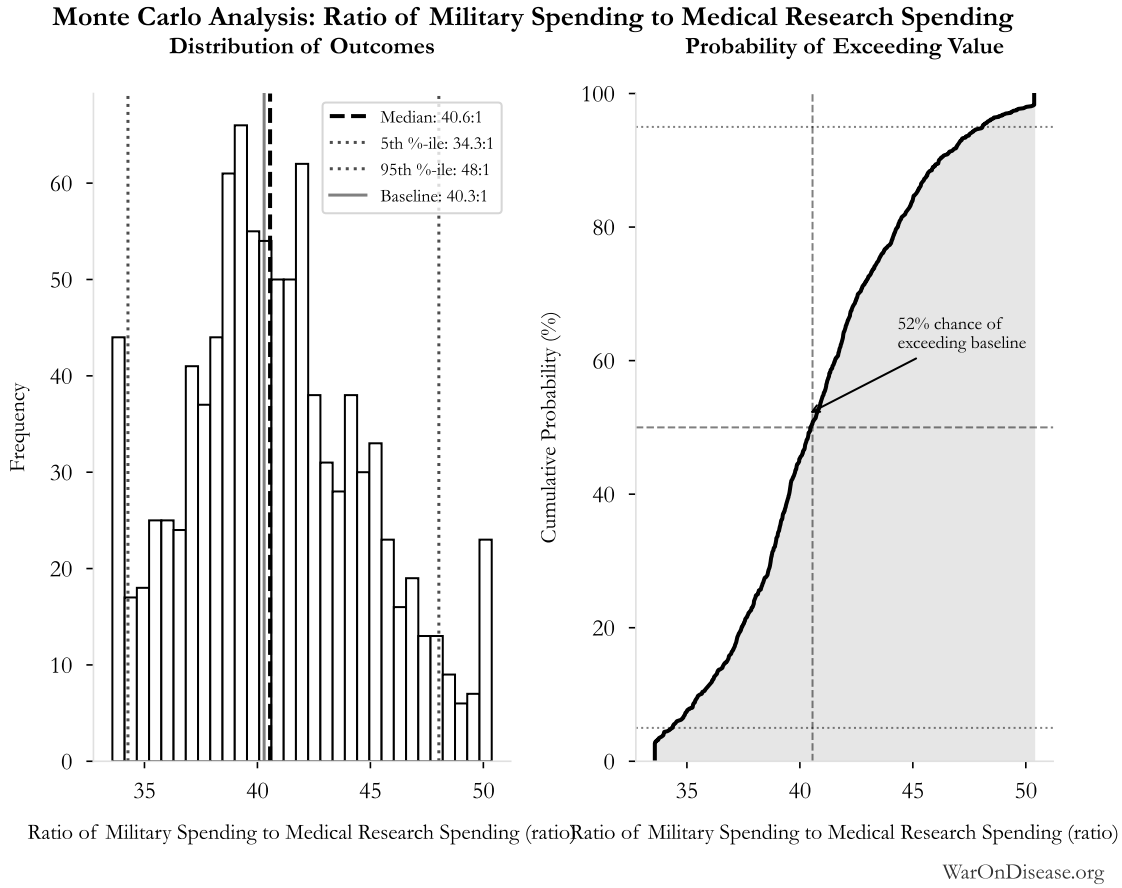


Figure 218: Monte Carlo Distribution: Ratio of Military Spending to Medical Research Spending (10,000 simulations)

Simulation Results Summary: Ratio of Military Spending to Medical Research Spending

Statistic	Value
Baseline (deterministic)	40.3:1
Mean (expected value)	40.8:1
Median (50th percentile)	40.6:1
Standard Deviation	4:1
90% Range (5th-95th percentile)	[34.3:1, 48:1]

The histogram shows the distribution of Ratio of Military Spending to Medical Research Spending 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

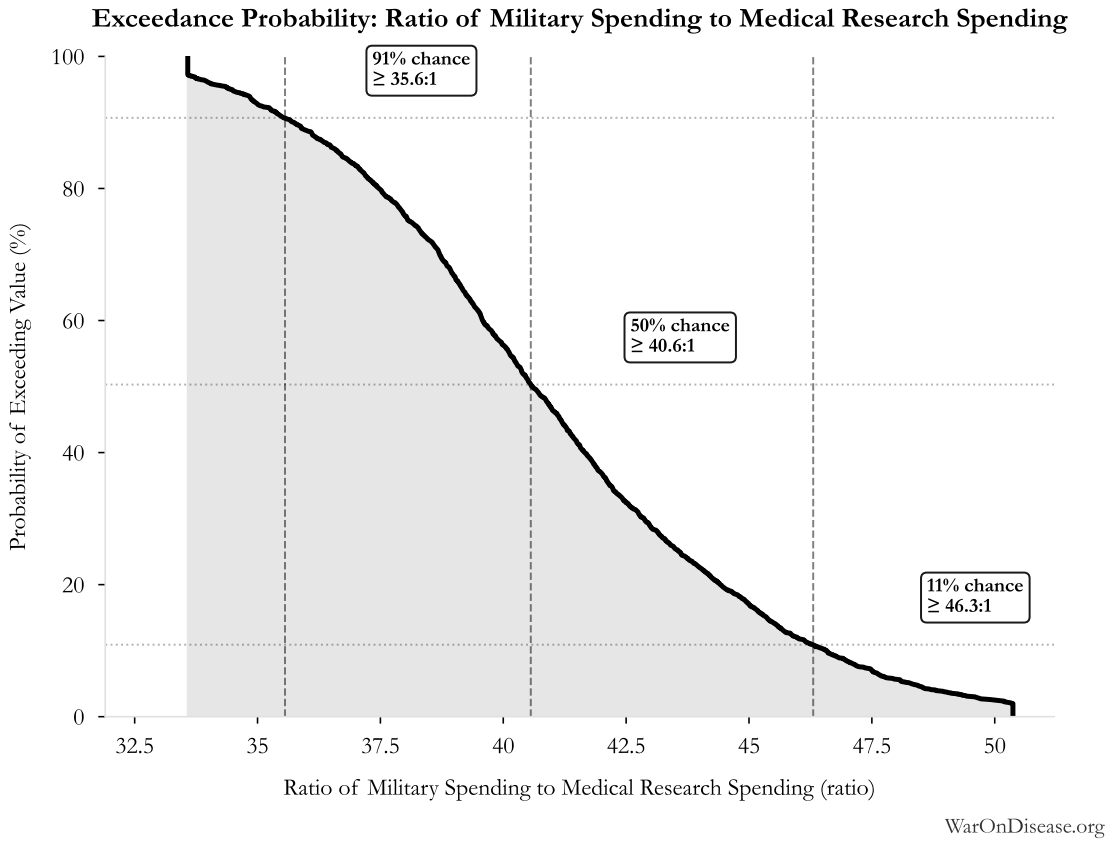


Figure 219: Probability of Exceeding Threshold: Ratio of Military Spending to Medical Research Spending

This exceedance probability chart shows the likelihood that Ratio of Military Spending to Medical Research Spending will exceed any given threshold. Higher curves indicate more favorable outcomes with greater certainty.

Annual Peace Dividend from 1% Reduction in Total War Costs: $114B

Details

Annual peace dividend from 1% reduction in total war costs (theoretical maximum at =1.0)
Inputs:

- Total Annual Cost of War Worldwide : $11.4T
- 1% Reduction in Military Spending/War Costs from Treaty: 1%

$$Benefit_{peace,soc}$$
$$= Cost_{war,total} \times Reduce_{treaty}$$
$$= \$11.4T \times 1\%$$
$$= \$114B$$

where $Cost_{war,total}$
$$= Cost_{war,direct} + Cost_{war,indirect}$$
$$= \$7.66T + \$3.7T$$
$$= \$11.4T$$

where $Cost_{war,direct}$
$$= Loss_{life,conflict} + Damage_{infra,total}$$
$$+Disruption_{trade} + Spending_{mil}$$
$$= \$2.45T + \$1.88T + \$616B + \$2.72T$$
$$= \$7.66T$$

where $Loss_{life,conflict}$
$$= Cost_{combat,human} + Cost_{state,human}$$
$$+Cost_{terror,human}$$
$$= \$2.34T + \$27B + \$83B$$
$$= \$2.45T$$

where $Cost_{combat,human}$
$$= Deaths_{combat} \times VSL$$
$$= 234{,}000 \times \$10M$$
$$= \$2.34T$$

where $Cost_{state,human}$
$$= Deaths_{state} \times VSL$$
$$= 2{,}700 \times \$10M$$
$$= \$27B$$

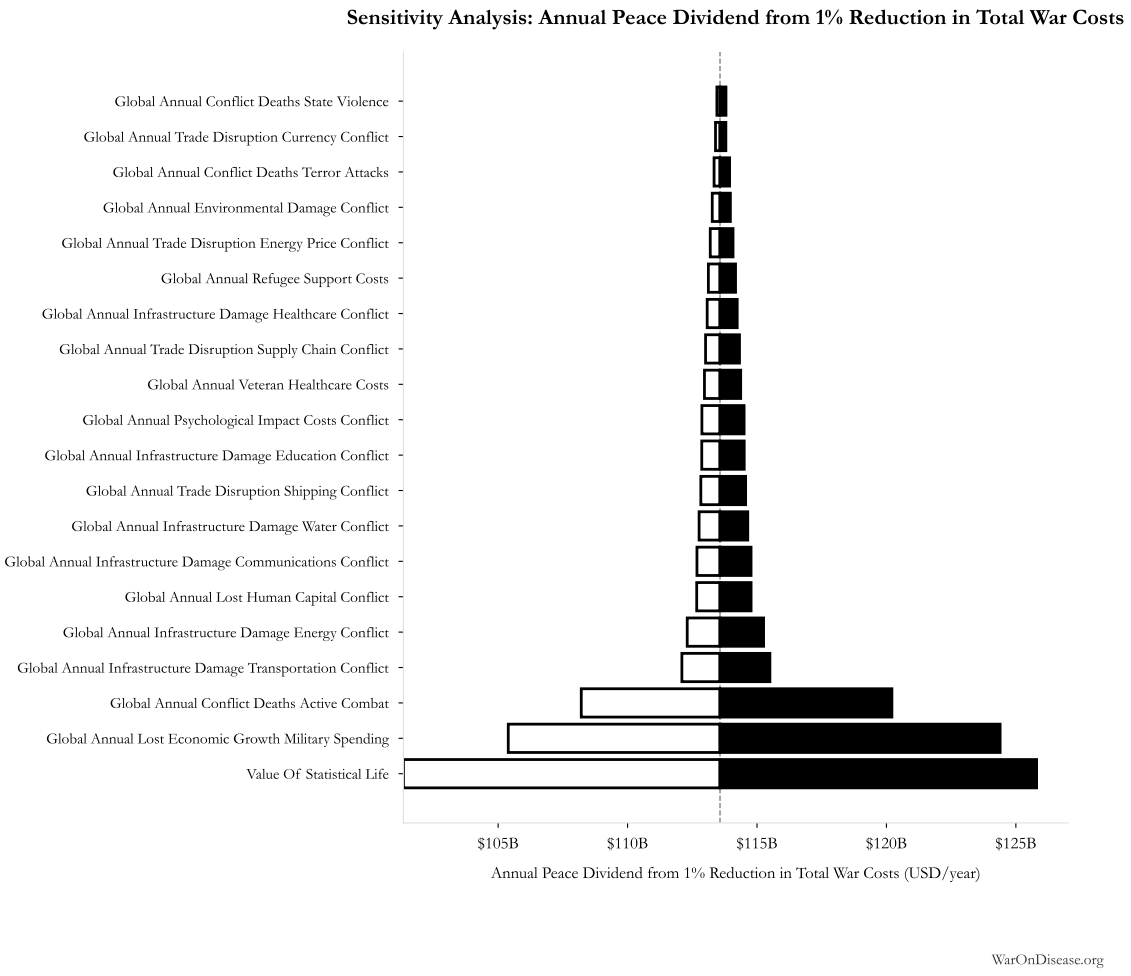
where $Cost_{terror,human}$
$$= Deaths_{terror} \times VSL$$
$$= 8{,}300 \times \$10M$$
$$= \$83B$$

where $Damage_{infra,total}$
$$= Damage_{comms} + Damage_{edu} + Damage_{energy}$$
$$+Damage_{health} + Damage_{transport}$$
$$+Damage_{water}$$
$$= \$298B + \$234B + \$422B + \$166B + \$487B + \$268B$$
$$= \$1.88T$$

where $Disruption_{trade}$
$$= Disruption_{currency} + Disruption_{energy}$$
$$+Disruption_{shipping} + Disruption_{supply}$$

High confidence

Sensitivity Analysis



Sensitivity Indices for Annual Peace Dividend from 1% Reduction in Total War Costs

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

Input Parameter	Sensitivity Coefficient	Interpretation
Global Annual Direct Indirect War Cost	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

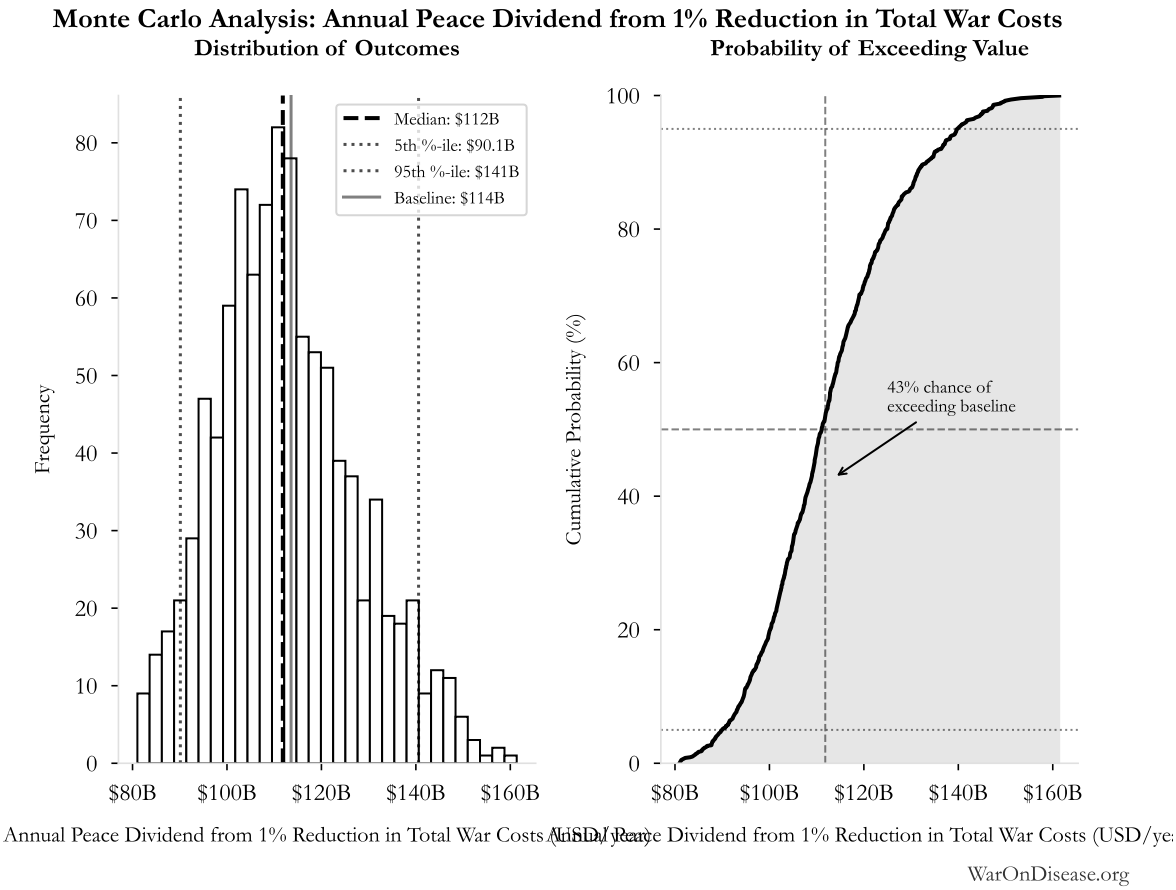


Figure 220: Monte Carlo Distribution: Annual Peace Dividend from 1% Reduction in Total War Costs (10,000 simulations)

Simulation Results Summary: Annual Peace Dividend from 1% Reduction in Total War Costs

Statistic	Value
Baseline (deterministic)	$114B
Mean (expected value)	$113B
Median (50th percentile)	$112B
Standard Deviation	$15.1B
90% Range (5th-95th percentile)	[$90.1B, $141B]

The histogram shows the distribution of Annual Peace Dividend from 1% Reduction in Total War Costs 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

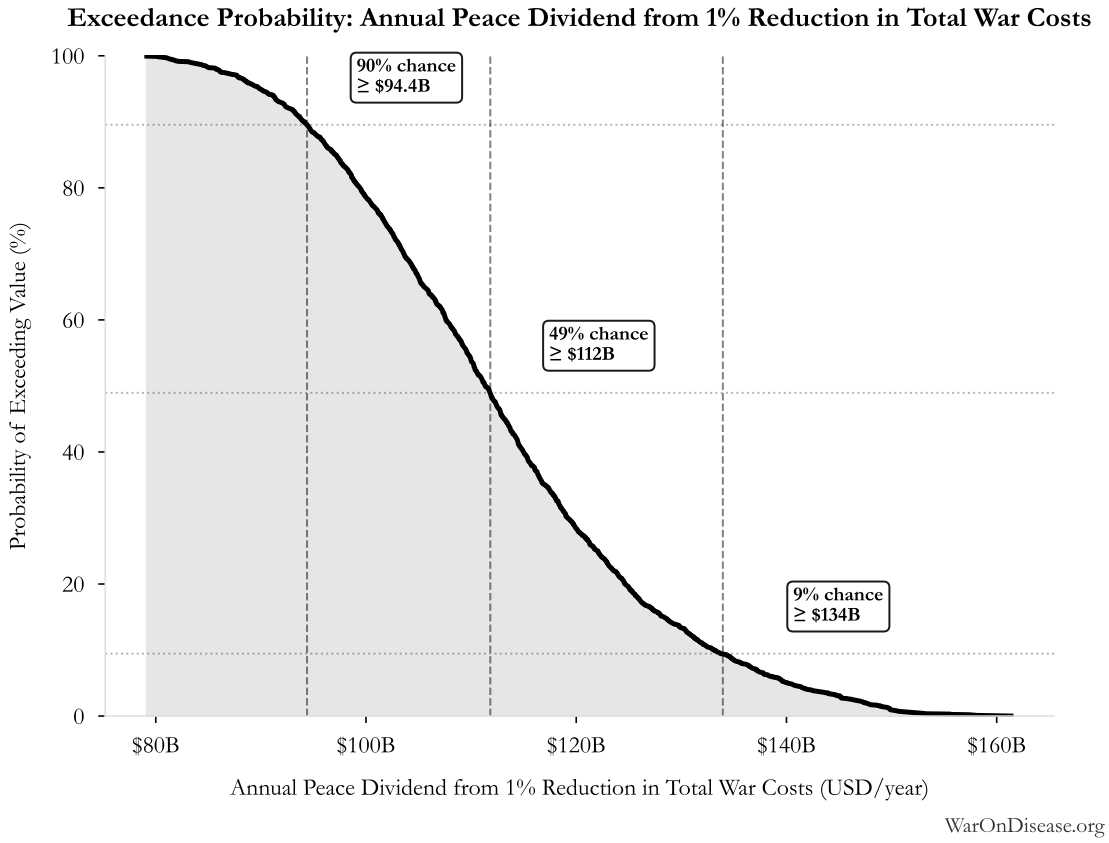


Figure 221: Probability of Exceeding Threshold: Annual Peace Dividend from 1% Reduction in Total War Costs

This exceedance probability chart shows the likelihood that Annual Peace Dividend from 1% Reduction in Total War Costs will exceed any given threshold. Higher curves indicate more favorable outcomes with greater certainty.

Conflict Reduction Benefits from 1% Less Military Spending: $86.4B

Details

Conflict reduction benefits from 1% less military spending (lower confidence - assumes proportional relationship)

Inputs:

- Annual Peace Dividend from 1% Reduction in Total War Costs : $114B
- Annual Funding from 1% of Global Military Spending Redirected to DIH : $27.2B

$$Savings_{conflict}$$
$$= Benefit_{peace,soc} - Funding_{treaty}$$
$$= \$114B - \$27.2B$$
$$= \$86.4B$$

where $Benefit_{peace,soc}$
$$= Cost_{war,total} \times Reduce_{treaty}$$
$$= \$11.4T \times 1\%$$
$$= \$114B$$

where $Cost_{war,total}$
$$= Cost_{war,direct} + Cost_{war,indirect}$$
$$= \$7.66T + \$3.7T$$
$$= \$11.4T$$

where $Cost_{war,direct}$
$$= Loss_{life,conflict} + Damage_{infra,total}$$
$$+Disruption_{trade} + Spending_{mil}$$
$$= \$2.45T + \$1.88T + \$616B + \$2.72T$$
$$= \$7.66T$$

where $Loss_{life,conflict}$
$$= Cost_{combat,human} + Cost_{state,human}$$
$$+Cost_{terror,human}$$
$$= \$2.34T + \$27B + \$83B$$
$$= \$2.45T$$

where $Cost_{combat,human}$
$$= Deaths_{combat} \times VSL$$
$$= 234{,}000 \times \$10M$$
$$= \$2.34T$$

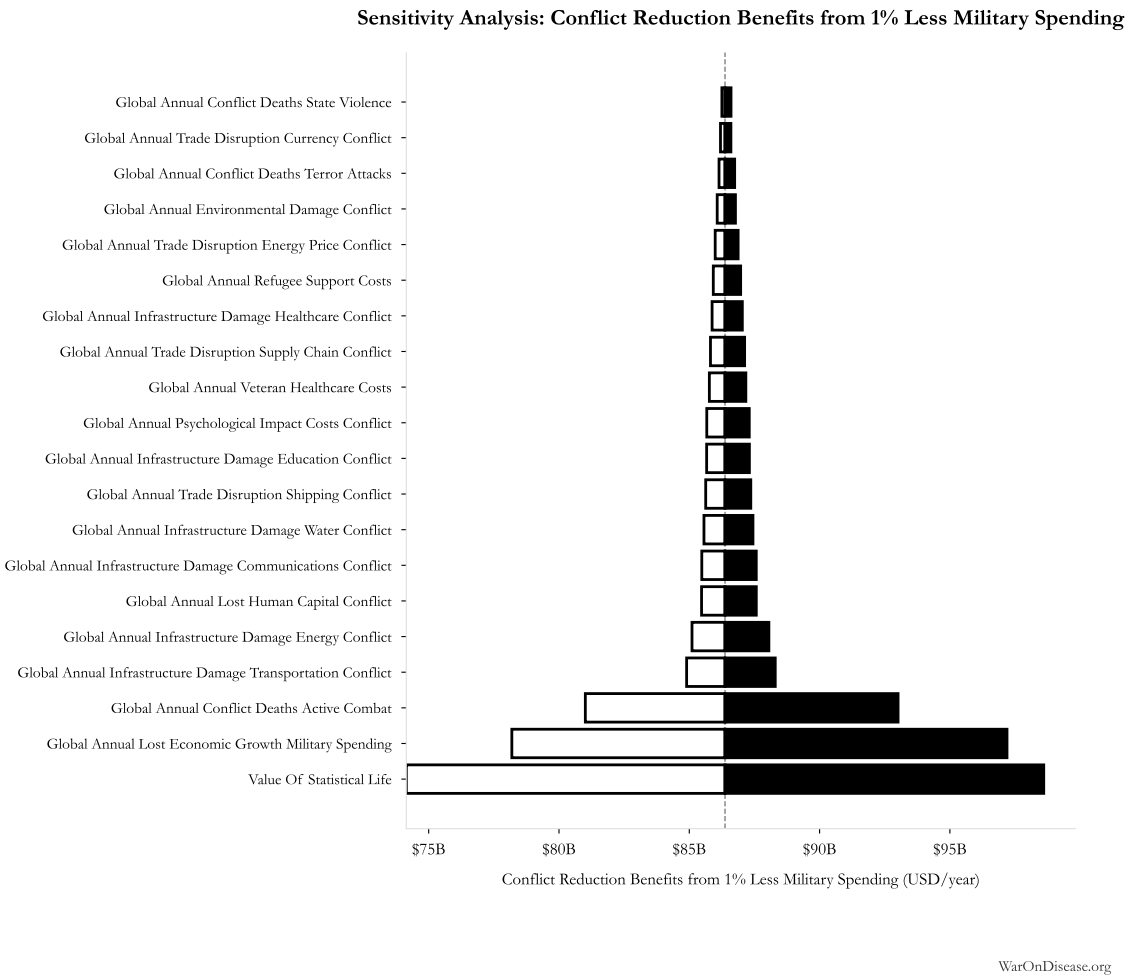
where $Cost_{state,human}$
$$= Deaths_{state} \times VSL$$
$$= 2{,}700 \times \$10M$$
$$= \$27B$$

where $Cost_{terror,human}$
$$= Deaths_{terror} \times VSL$$
$$= 8{,}300 \times \$10M$$
$$= \$83B$$

where $Damage_{infra,total}$
$$= Damage_{comms} + Damage_{edu} + Damage_{energy}$$
$$+Damage_{health} + Damage_{transport}$$
$$+Damage_{water}$$
$$= \$298B + \$234B + \$422B + \$166B + \$487B + \$268B$$

Methodology: Direct Calculation
? Low confidence

Sensitivity Analysis



Sensitivity Indices for Conflict Reduction Benefits from 1% Less Military Spending
Regression-based sensitivity showing which inputs explain the most variance in the output.

Input Parameter	Sensitivity Coefficient	Interpretation
Peace Dividend Annual Societal Benefit	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

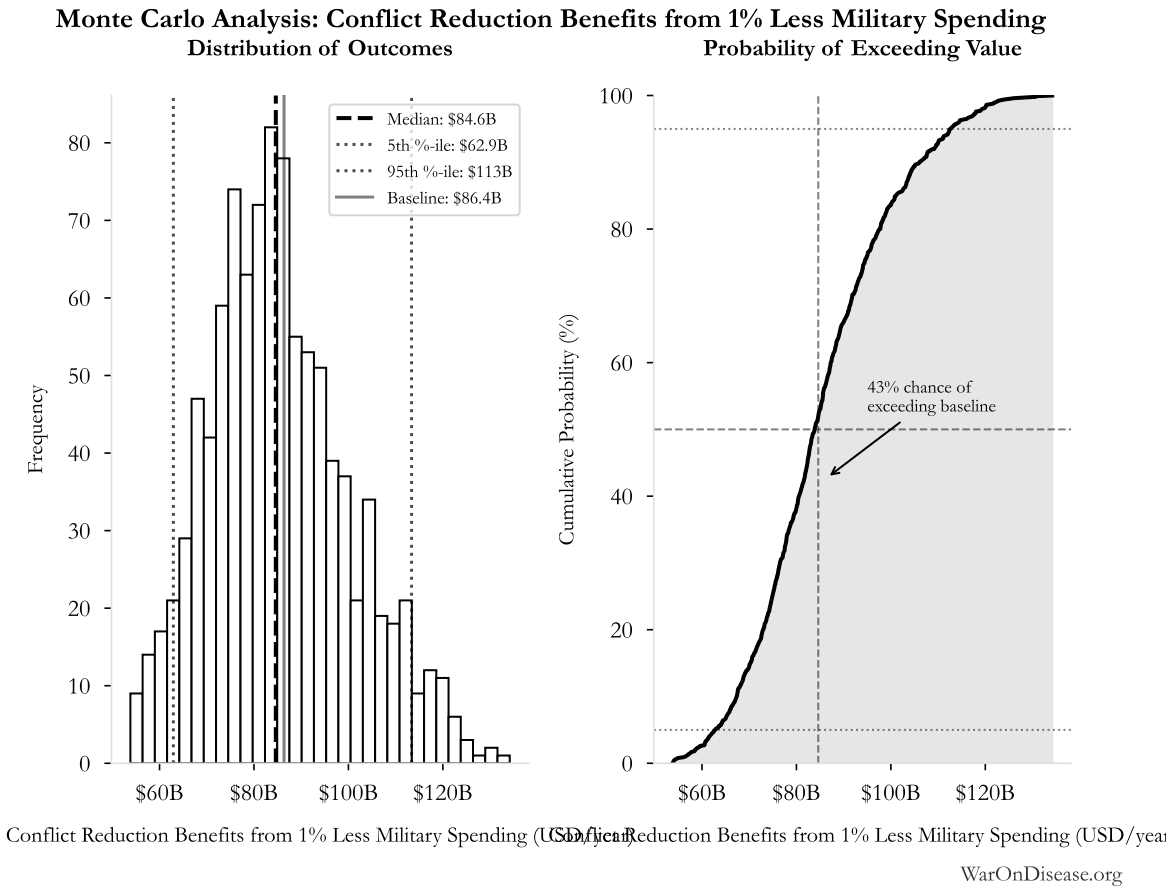


Figure 222: Monte Carlo Distribution: Conflict Reduction Benefits from 1% Less Military Spending (10,000 simulations)

Simulation Results Summary: Conflict Reduction Benefits from 1% Less Military Spending

Statistic	Value
Baseline (deterministic)	$86.4B
Mean (expected value)	$85.9B
Median (50th percentile)	$84.6B
Standard Deviation	$15.1B
90% Range (5th-95th percentile)	[$62.9B, $113B]

The histogram shows the distribution of Conflict Reduction Benefits from 1% Less Military Spending 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

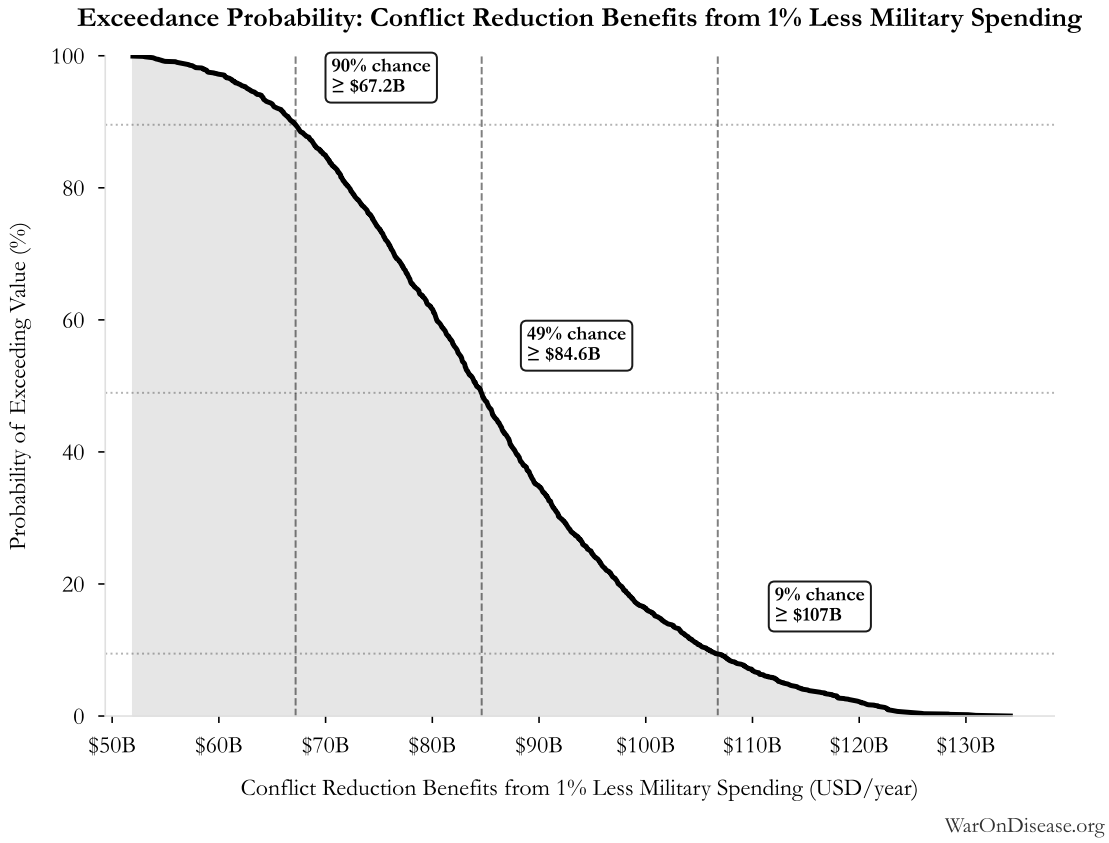


Figure 223: Probability of Exceeding Threshold: Conflict Reduction Benefits from 1% Less Military Spending

This exceedance probability chart shows the likelihood that Conflict Reduction Benefits from 1% Less Military Spending will exceed any given threshold. Higher curves indicate more favorable outcomes with greater certainty.

Pragmatic Trial Cost per QALY (RECOVERY): $4.00

Details

Cost per QALY for pragmatic platform trials, calculated from RECOVERY trial data. Uses global impact methodology: trial cost divided by total QALYs from downstream adoption. This measures research efficiency (discovery value), not clinical intervention ICER.

Inputs:

- RECOVERY Trial Total Cost : $20M (95% CI: $15M - $25M)
- RECOVERY Trial Total QALYs Generated : 5.00 million QALYs

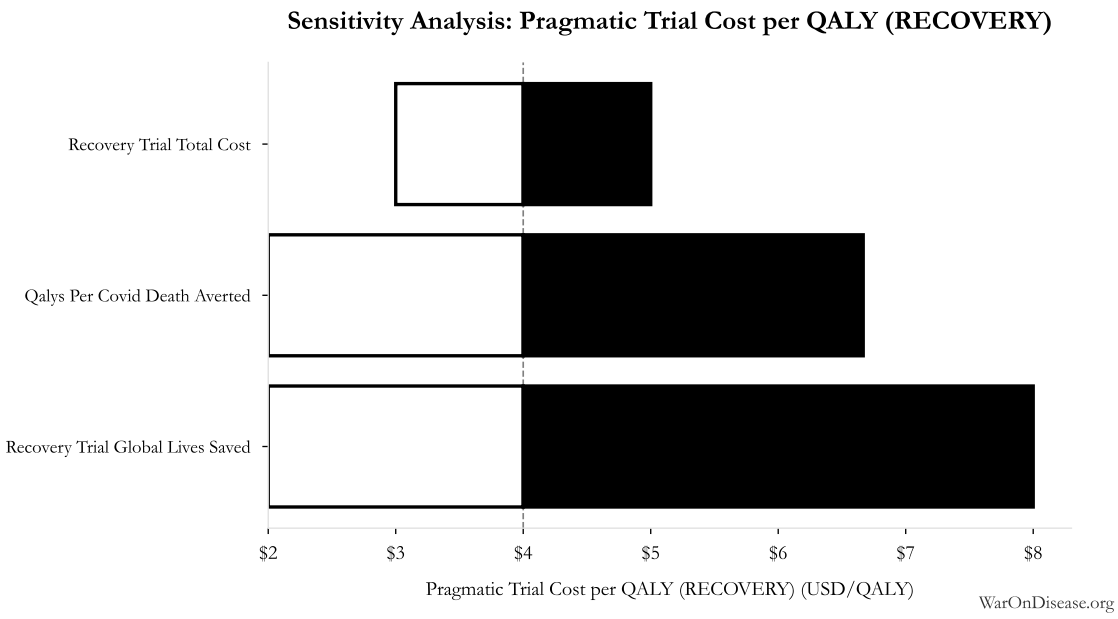
$$Cost_{pragmatic,QALY} = \frac{Cost_{RECOVERY}}{QALY_{RECOVERY}} = \frac{\$20M}{5M} = \$4$$

$$\begin{aligned} &\text{where } QALY_{RECOVERY} \\ &= Lives_{RECOVERY} \times QALY_{COVID} \\ &= 1M \times 5 \\ &= 5M \end{aligned}$$

Methodology:[66]

~ *Medium confidence*

Sensitivity Analysis



Sensitivity Indices for Pragmatic Trial Cost per QALY (RECOVERY)

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

Input Parameter	Sensitivity Coefficient	Interpretation
Recovery Trial Total Cost	-1.4871	Strong driver

Recovery Trial Total QALYs Generated	0.5682	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

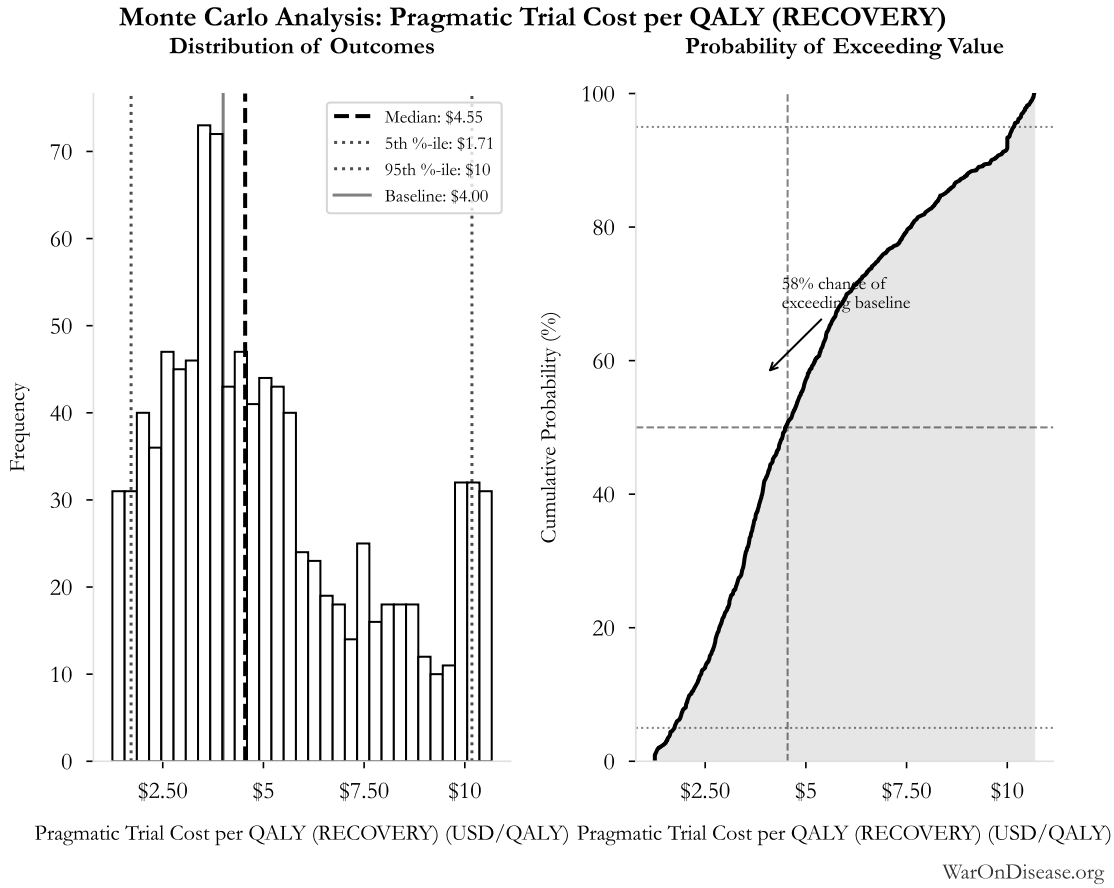


Figure 224: Monte Carlo Distribution: Pragmatic Trial Cost per QALY (RECOVERY) (10,000 simulations)

Simulation Results Summary: Pragmatic Trial Cost per QALY (RECOVERY)

Statistic	Value
Baseline (deterministic)	$4.00
Mean (expected value)	$5.10
Median (50th percentile)	$4.55
Standard Deviation	$2.59
90% Range (5th-95th percentile)	[$1.71, $10]

The histogram shows the distribution of Pragmatic Trial Cost per QALY (RECOVERY) 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

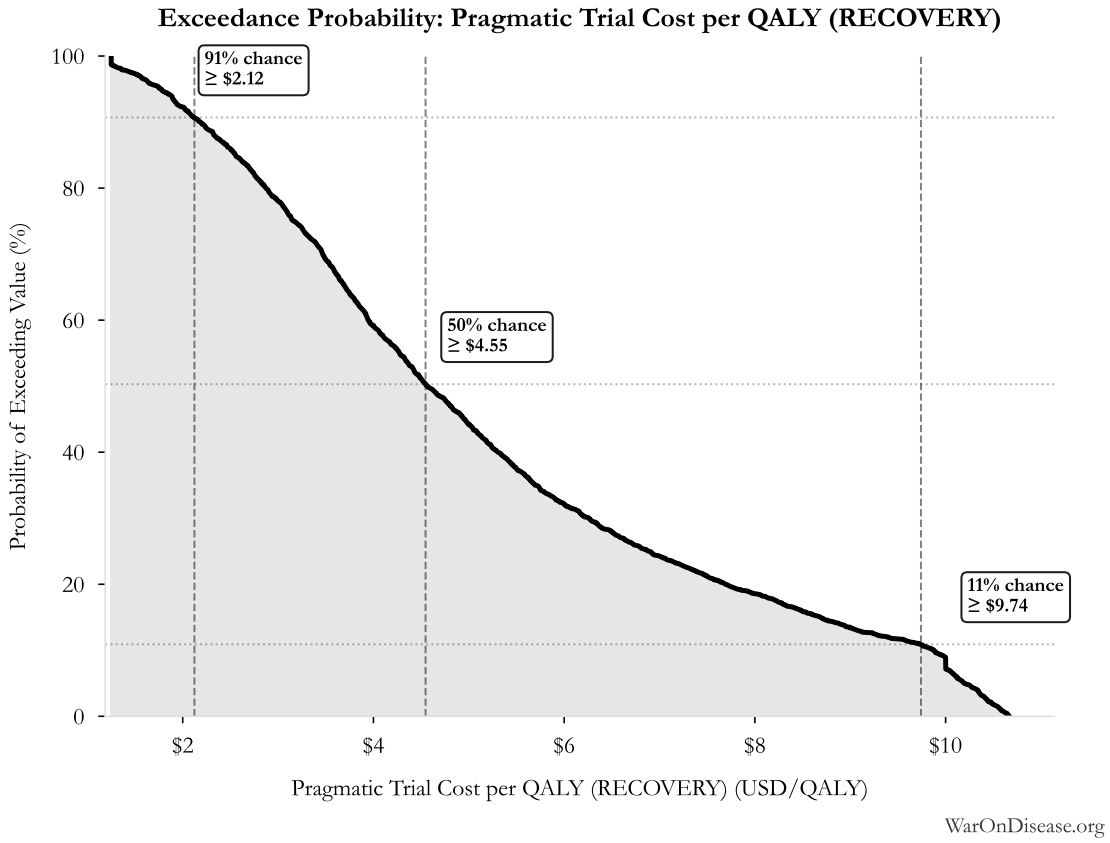


Figure 225: Probability of Exceeding Threshold: Pragmatic Trial Cost per QALY (RECOVERY)

This exceedance probability chart shows the likelihood that Pragmatic Trial Cost per QALY (RECOVERY) will exceed any given threshold. Higher curves indicate more favorable outcomes with greater certainty.

Pragmatic Trial Efficiency Multiplier vs NIH: 12.5kx

Details

How many times more cost-effective pragmatic trials are vs standard NIH research. Calculated using global impact methodology (NIH cost per QALY / pragmatic cost per QALY). Shows orders-of-magnitude efficiency gap between discovery-focused pragmatic trials and standard research.

Inputs:

- NIH Standard Research Cost per QALY : $50K (95% CI: $20K - $100K)
- Pragmatic Trial Cost per QALY (RECOVERY) : $4.00

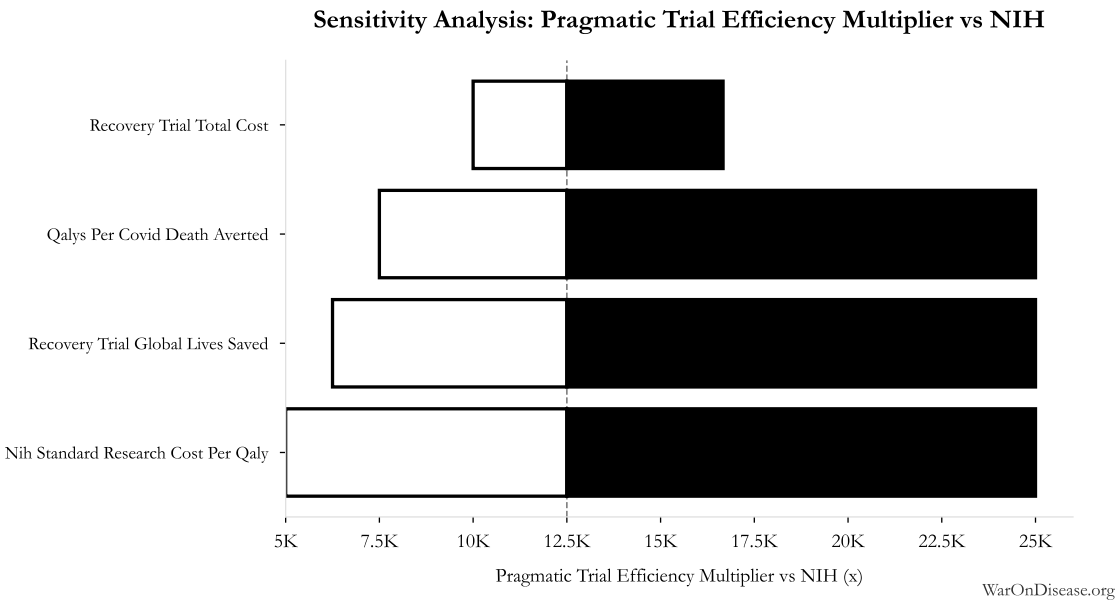
$$
\begin{aligned}
&k_{pragmatic:NIH} \\
&= \frac{Cost_{NIH,QALY}}{Cost_{pragmatic,QALY}} \\
&= \frac{\$50K}{\$4} \\
&= 12{,}500
\end{aligned}
$$

$$\text{where } Cost_{pragmatic,QALY} = \frac{Cost_{RECOVERY}}{QALY_{RECOVERY}} = \frac{\$20M}{5M} = \$4$$

$$
\begin{aligned}
&\text{where } QALY_{RECOVERY} \\
&= Lives_{RECOVERY} \times QALY_{COVID} \\
&= 1M \times 5 \\
&= 5M
\end{aligned}
$$

~ *Medium confidence*

Sensitivity Analysis



Sensitivity Indices for Pragmatic Trial Efficiency Multiplier vs NIH
Regression-based sensitivity showing which inputs explain the most variance in the output.

Input Parameter	Sensitivity Coefficient	Interpretation
NIH Standard Research Cost Per QALY	1.5607	Strong driver
Pragmatic Trial Cost Per QALY	0.6777	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

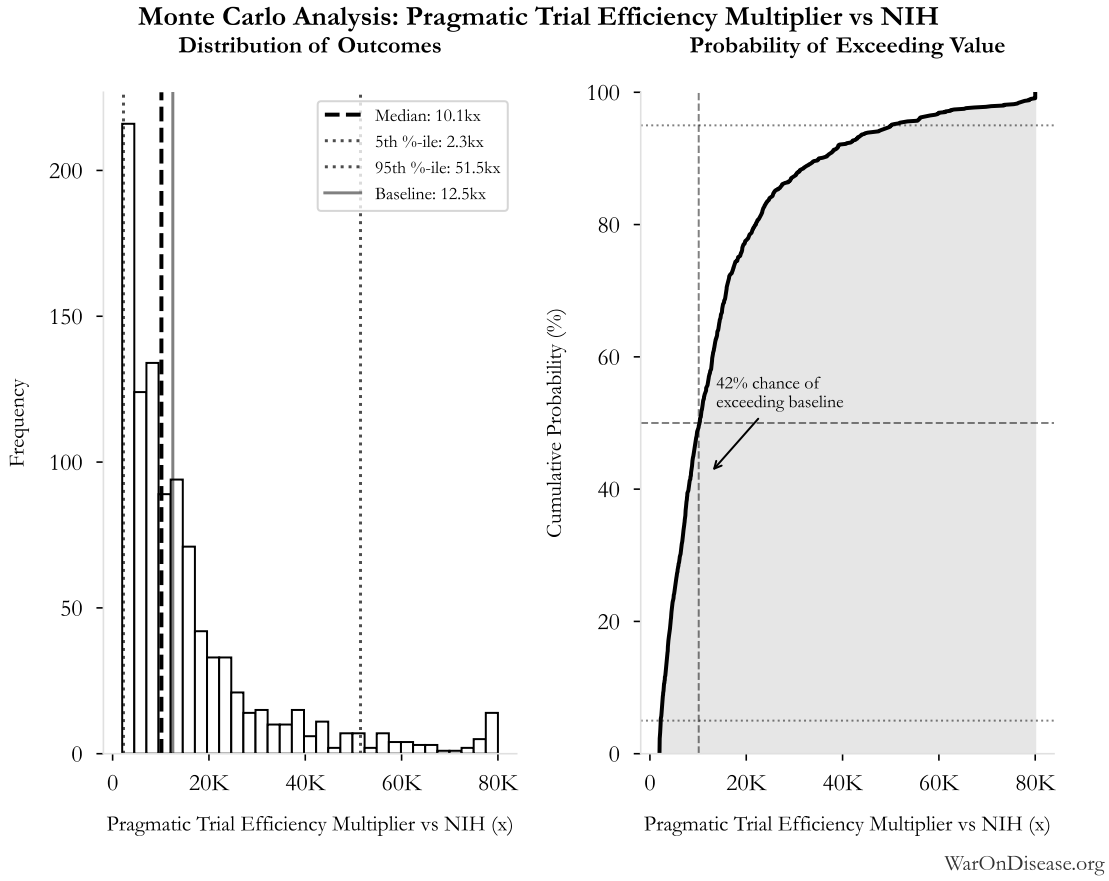


Figure 226: Monte Carlo Distribution: Pragmatic Trial Efficiency Multiplier vs NIH (10,000 simulations)

Simulation Results Summary: Pragmatic Trial Efficiency Multiplier vs NIH

Statistic	Value
Baseline (deterministic)	12.5kx
Mean (expected value)	15.8kx
Median (50th percentile)	10.1kx
Standard Deviation	16.2kx
90% Range (5th-95th percentile)	[2.3kx, 51.5kx]

The histogram shows the distribution of Pragmatic Trial Efficiency Multiplier vs NIH 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

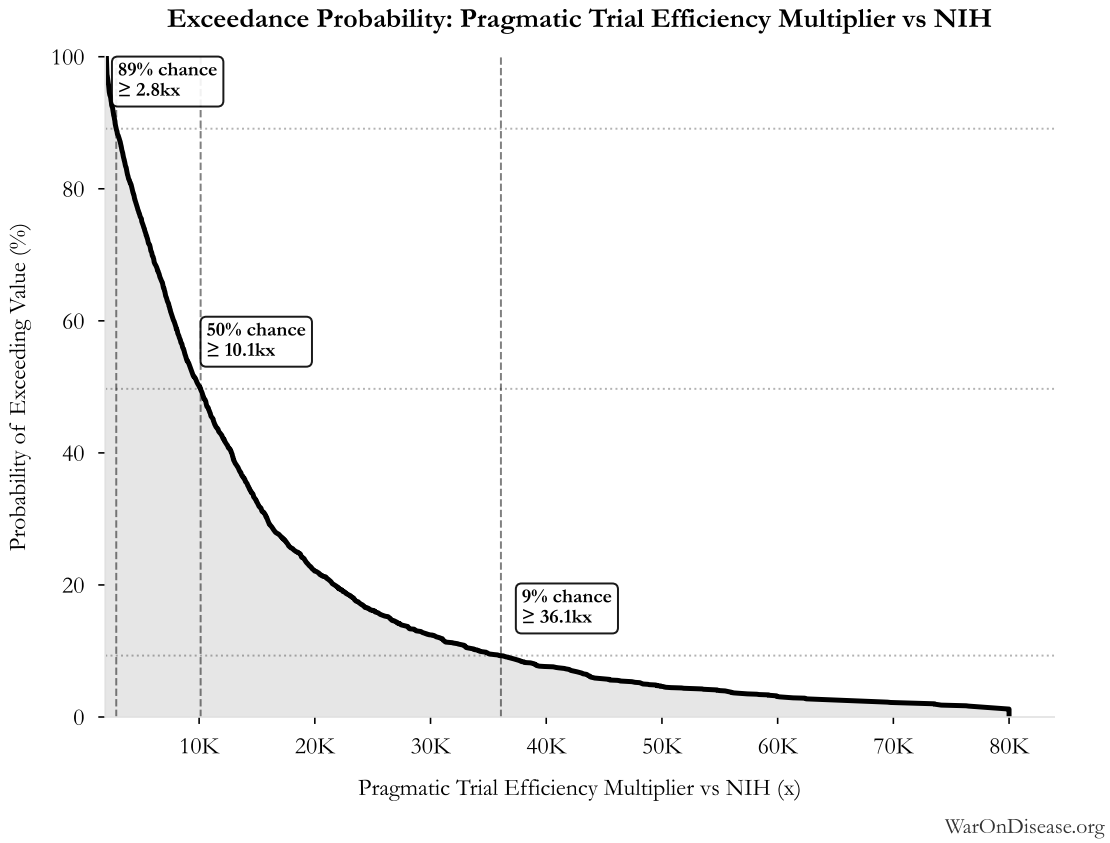


Figure 227: Probability of Exceeding Threshold: Pragmatic Trial Efficiency Multiplier vs NIH

This exceedance probability chart shows the likelihood that Pragmatic Trial Efficiency Multiplier vs NIH will exceed any given threshold. Higher curves indicate more favorable outcomes with greater certainty.

RECOVERY Trial Cost Reduction Factor: 82x

Details

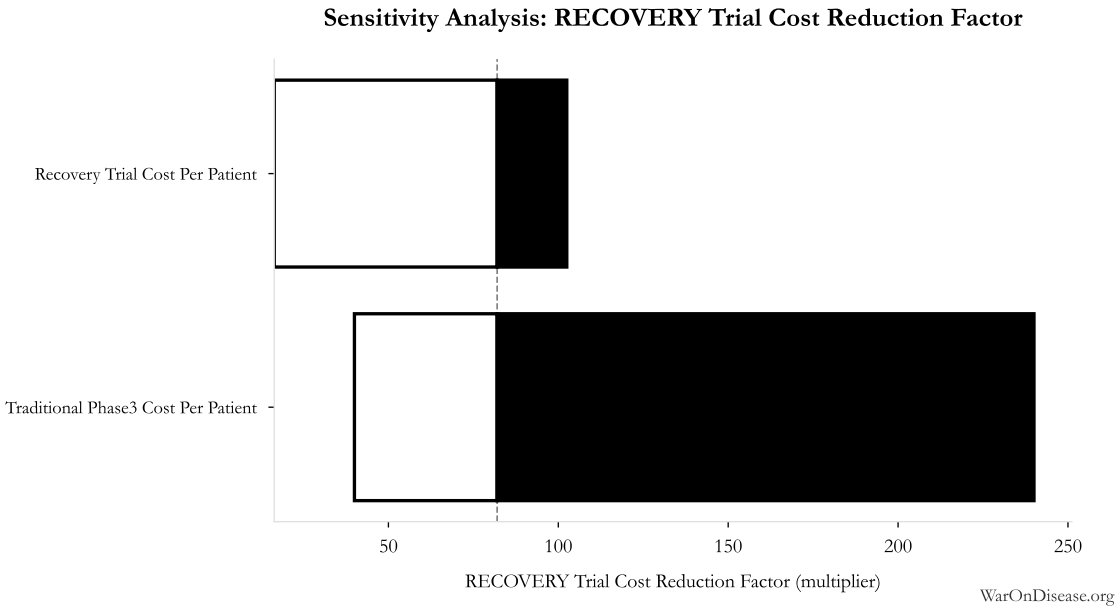
Cost reduction factor demonstrated by RECOVERY trial ($41K traditional / $500 RECOVERY = 82x)
Inputs:

- Phase 3 Cost per Patient : $41K (95% CI: $20K - $120K)
- Recovery Trial Cost per Patient : $500 (95% CI: $400 - $2.50K)

$$
\begin{aligned}
k_{RECOVERY} &= \frac{Cost_{P3,pt}}{Cost_{RECOVERY,pt}} \\
&= \frac{\$41K}{\$500} \\
&= 82
\end{aligned}
$$

Methodology:[66]
High confidence

Sensitivity Analysis



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

Input Parameter	Sensitivity Coefficient	Interpretation
Recovery Trial Cost Per Patient	-2.4783	Strong driver
Traditional Phase3 Cost Per Patient	2.4635	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

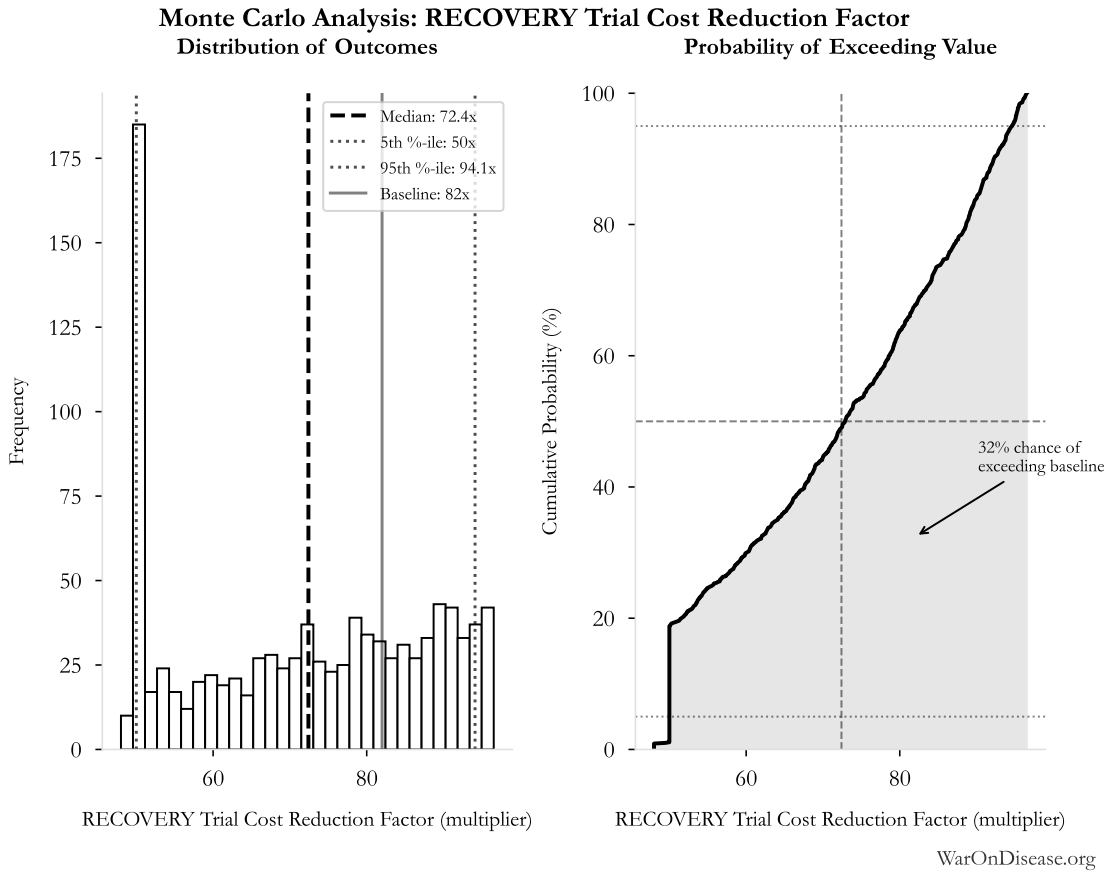


Figure 228: Monte Carlo Distribution: RECOVERY Trial Cost Reduction Factor (10,000 simulations)

Simulation Results Summary: RECOVERY Trial Cost Reduction Factor

Statistic	Value
Baseline (deterministic)	82x
Mean (expected value)	71.2x
Median (50th percentile)	72.4x
Standard Deviation	15.3x
90% Range (5th-95th percentile)	[50x, 94.1x]

The histogram shows the distribution of RECOVERY 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

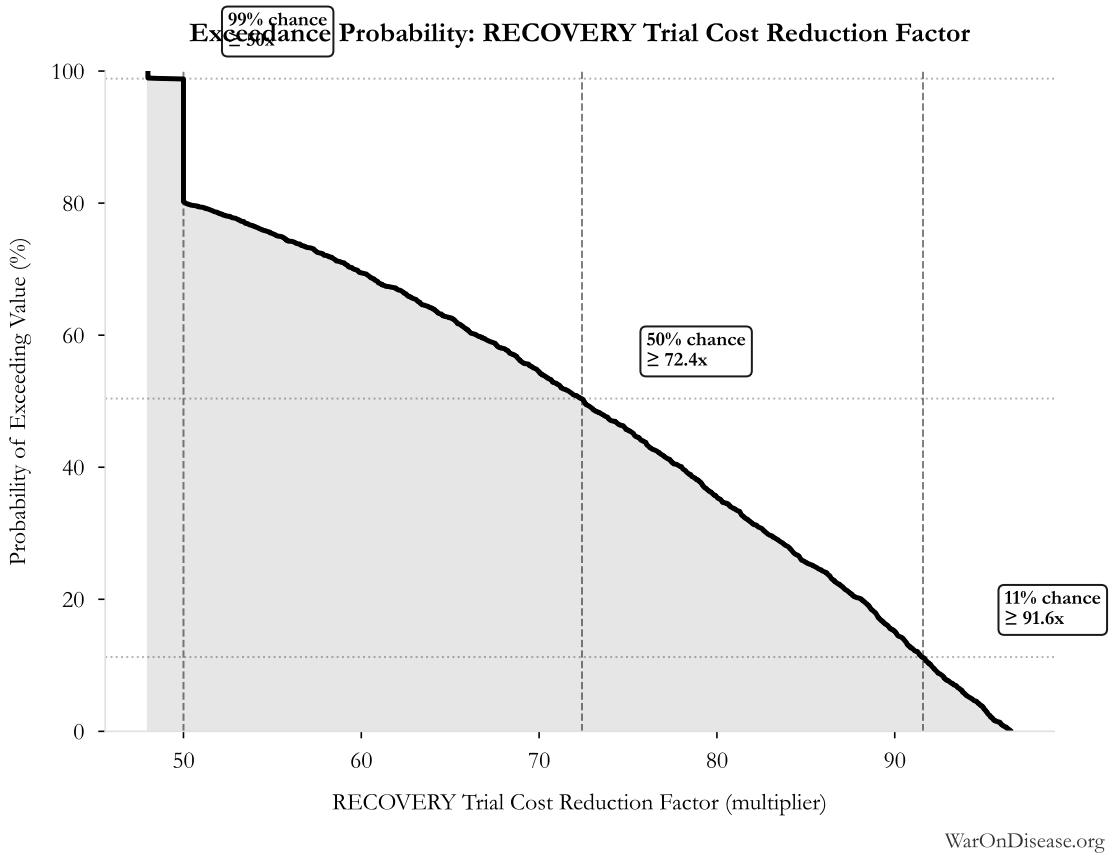


Figure 229: Probability of Exceeding Threshold: RECOVERY Trial Cost Reduction Factor

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

RECOVERY Trial Total QALYs Generated: 5.00 million QALYs

Details

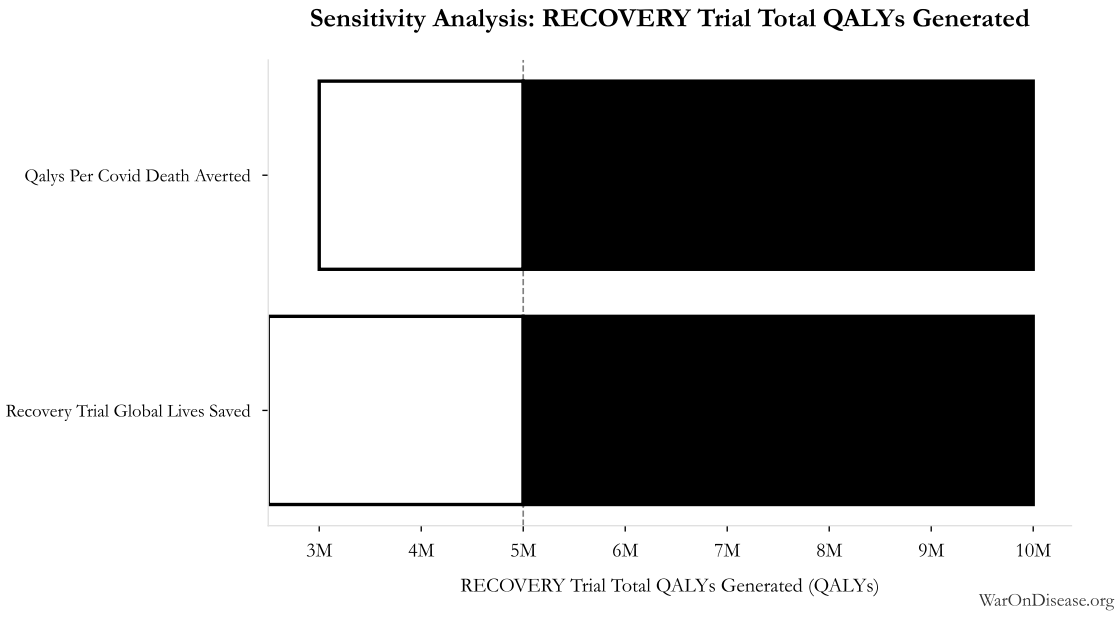
Total QALYs generated by RECOVERY trial's discoveries (lives saved × QALYs per life). Uses global impact methodology: counts all downstream health gains from the discovery.
Inputs:

- RECOVERY Trial Global Lives Saved : 1.00 million lives (95% CI: 500 thousand lives - 2.00 million lives)
- QALYs per COVID Death Averted: 5 QALYs/death (95% CI: 3 QALYs/death - 10 QALYs/death)

$$
\begin{aligned}
&QALY_{RECOVERY} \\
&= Lives_{RECOVERY} \times QALY_{COVID} \\
&= 1M \times 5 \\
&= 5M
\end{aligned}
$$

~ *Medium confidence*

Sensitivity Analysis



Sensitivity Indices for RECOVERY Trial Total QALYs Generated

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

Input Parameter	Sensitivity Coefficient	Interpretation
QALYs Per Covid Death Averted	2.2404	Strong driver
Recovery Trial Global Lives Saved	-1.2571	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

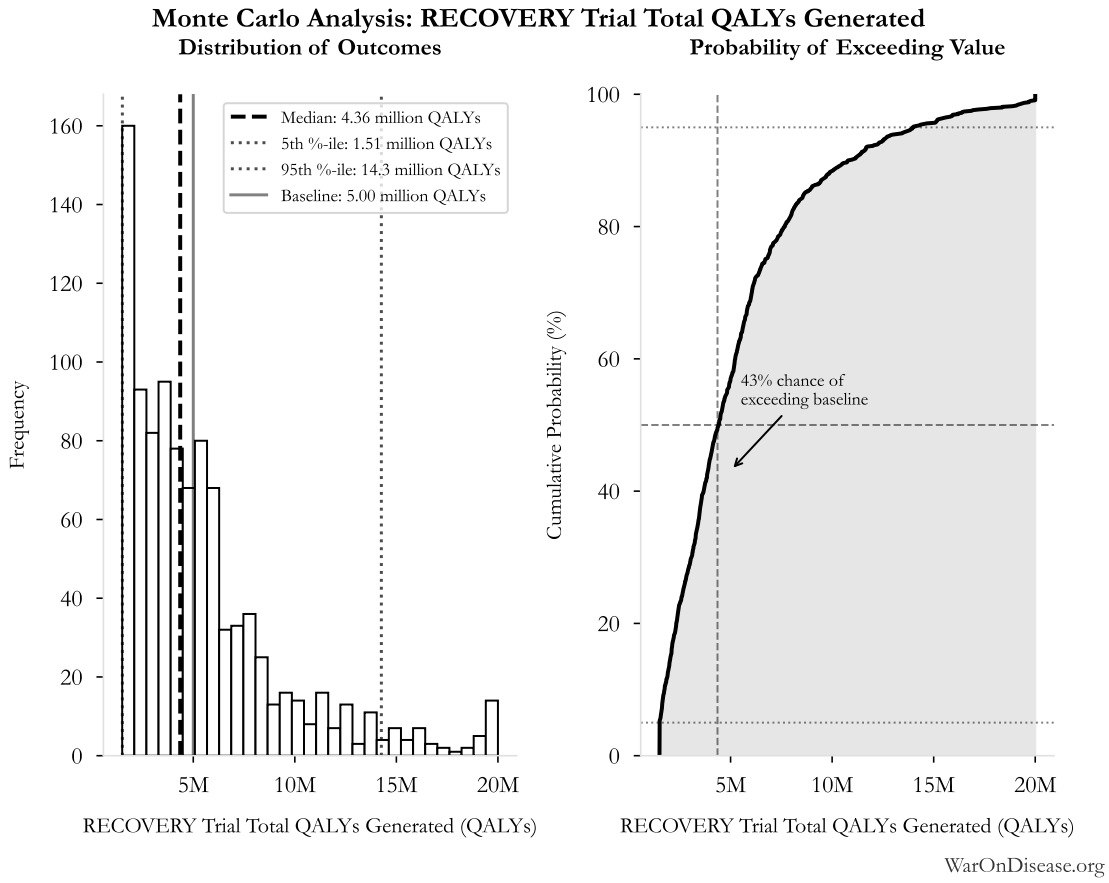


Figure 230: Monte Carlo Distribution: RECOVERY Trial Total QALYs Generated (10,000 simulations)

Simulation Results Summary: RECOVERY Trial Total QALYs Generated

Statistic	Value
Baseline (deterministic)	5.00 million
Mean (expected value)	5.57 million
Median (50th percentile)	4.36 million
Standard Deviation	4.03 million
90% Range (5th-95th percentile)	[1.51 million, 14.3 million]

The histogram shows the distribution of RECOVERY Trial Total QALYs Generated 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

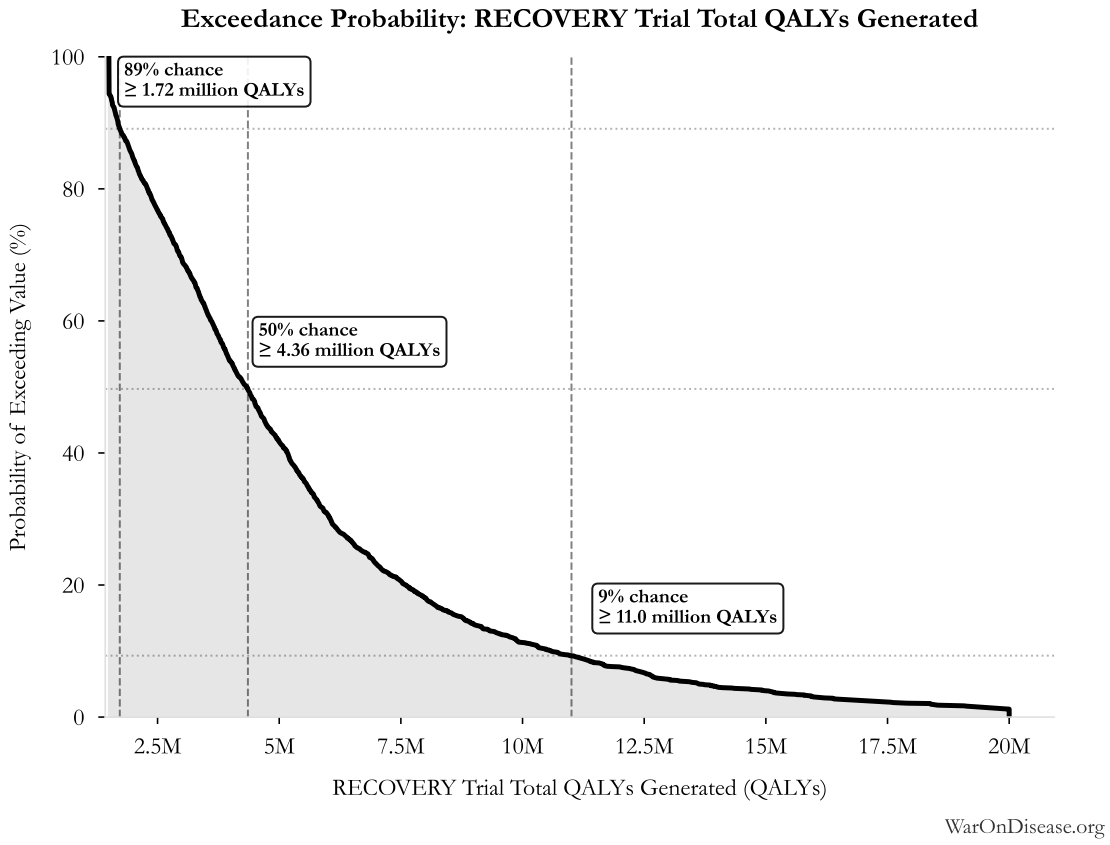


Figure 231: Probability of Exceeding Threshold: RECOVERY Trial Total QALYs Generated

This exceedance probability chart shows the likelihood that RECOVERY Trial Total QALYs Generated 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

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

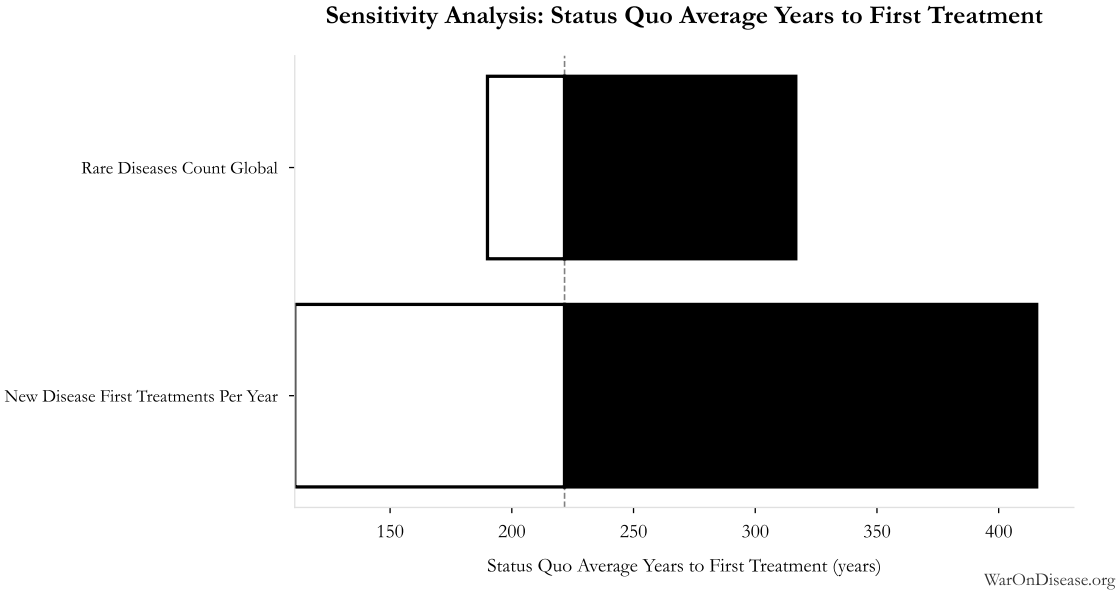
$$\text{where } T_{queue,SQ} = \frac{N_{untreated}}{Treatments_{new,ann}} = \frac{6{,}650}{15} = 443$$

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

Methodology:[154]

? 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 Queue Clearance 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

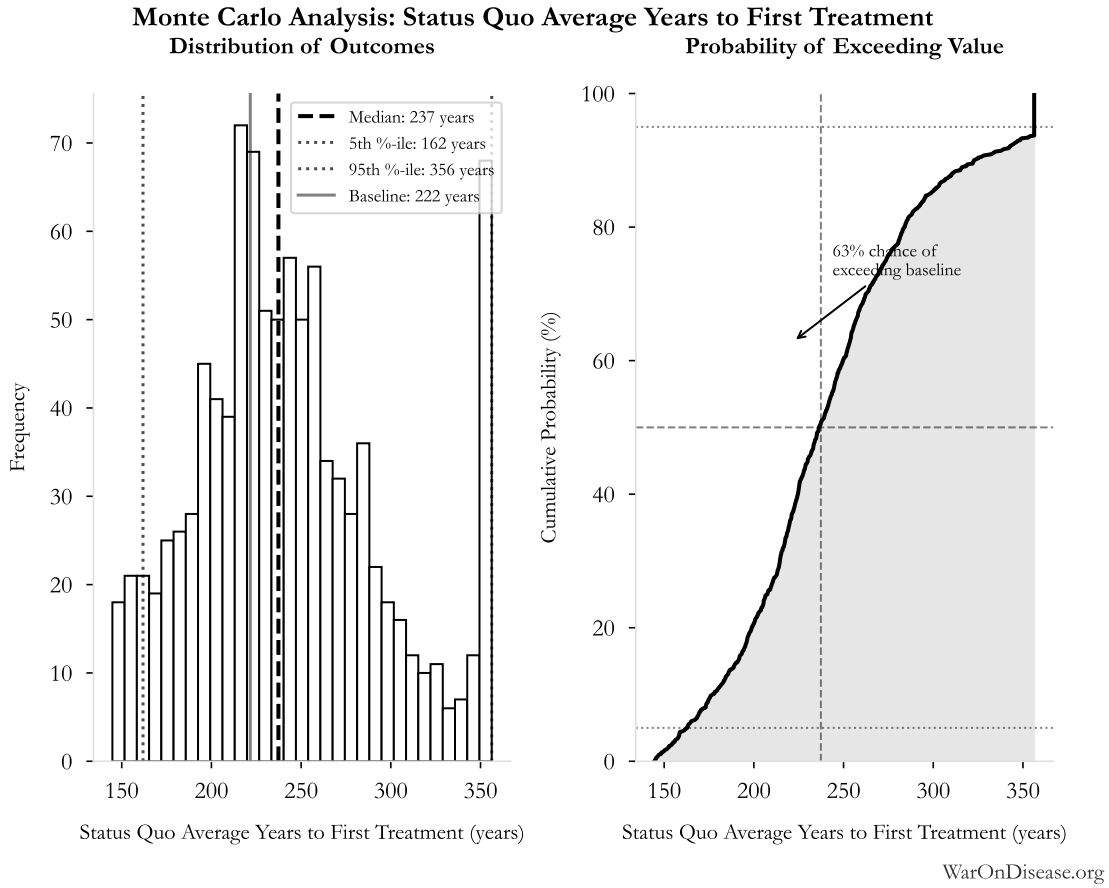


Figure 232: Monte Carlo Distribution: Status Quo Average Years to First Treatment (10,000 simulations)

Simulation Results Summary: Status Quo Average Years to First Treatment

Statistic	Value
Baseline (deterministic)	222
Mean (expected value)	242
Median (50th percentile)	237
Standard Deviation	53.2
90% Range (5th-95th percentile)	[162, 356]

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

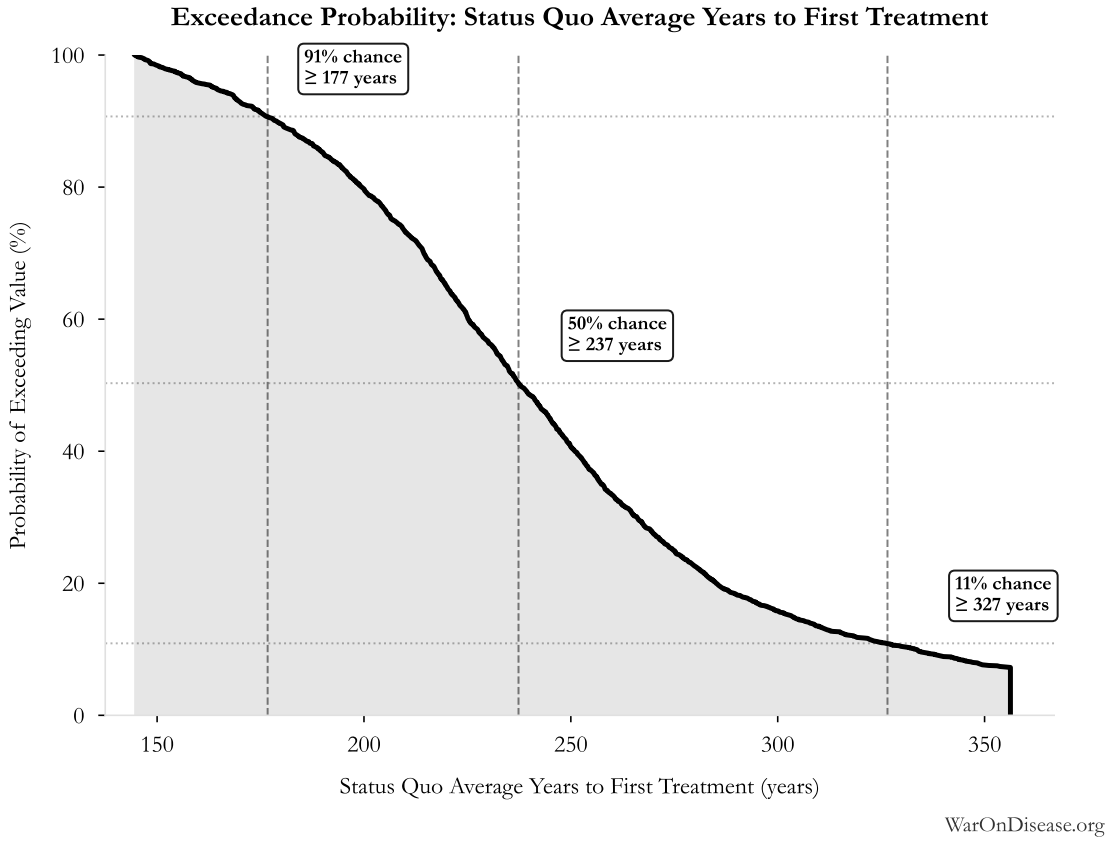


Figure 233: Probability of Exceeding Threshold: Status Quo Average Years to First Treatment

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 : 6.65 thousand diseases
- Diseases Getting First Treatment Per Year : 15 diseases/year (95% CI: 8 diseases/year - 30 diseases/year)

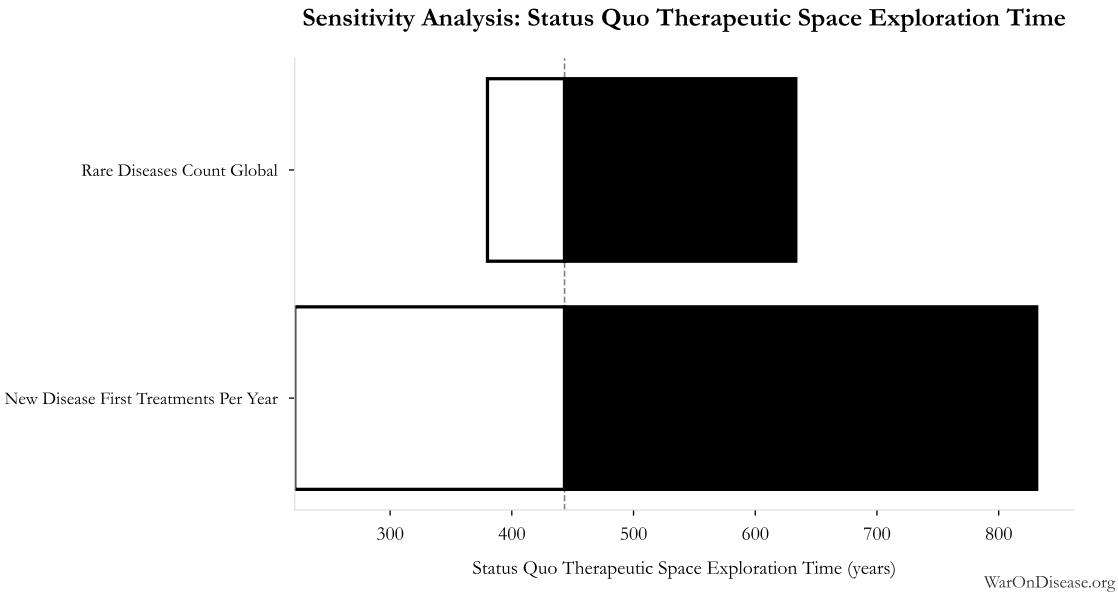
$$T_{queue,SQ} = \frac{N_{untreated}}{Treatments_{new,ann}} = \frac{6{,}650}{15} = 443$$

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

Methodology:[154]

? 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 Without Effective Treatment	-0.7011	Strong driver
New Disease First Treatments Per Year	-0.2360	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

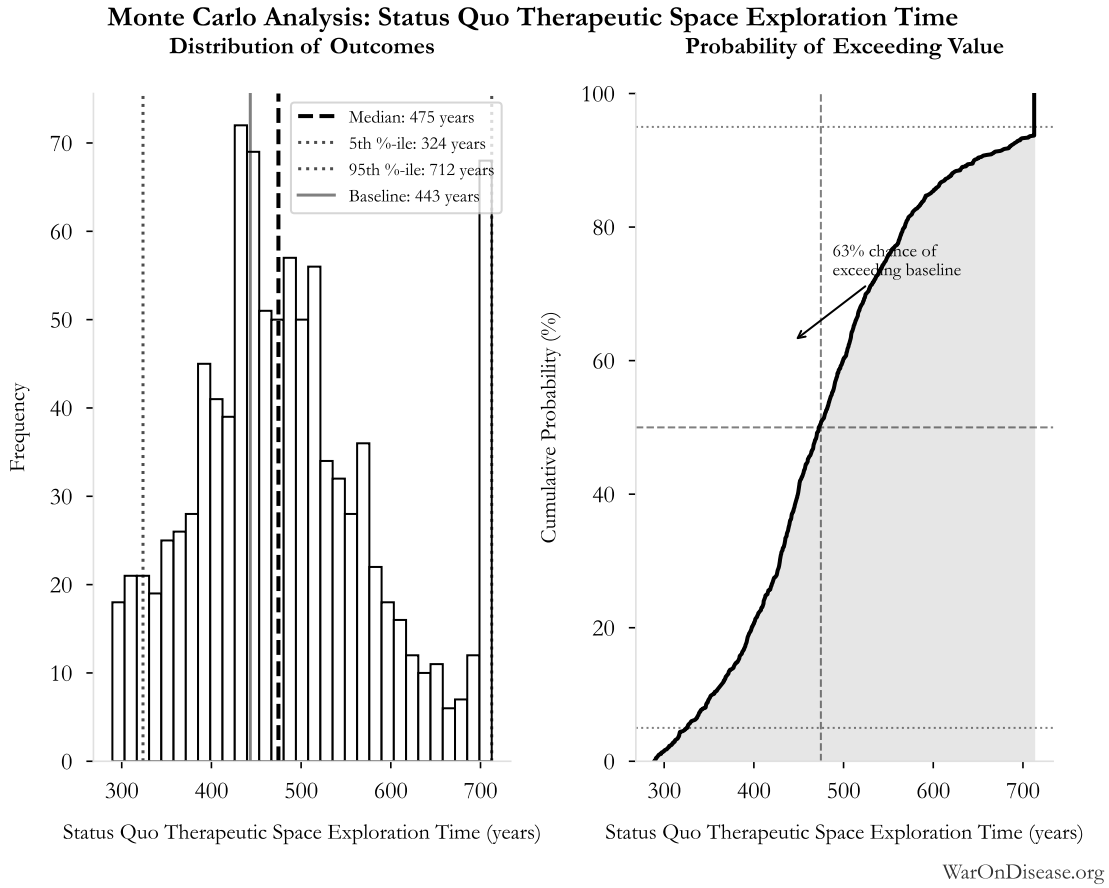


Figure 234: Monte Carlo Distribution: Status Quo Therapeutic Space Exploration Time (10,000 simulations)

Simulation Results Summary: Status Quo Therapeutic Space Exploration Time

Statistic	Value
Baseline (deterministic)	443
Mean (expected value)	485
Median (50th percentile)	475
Standard Deviation	106
90% Range (5th-95th percentile)	[324, 712]

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

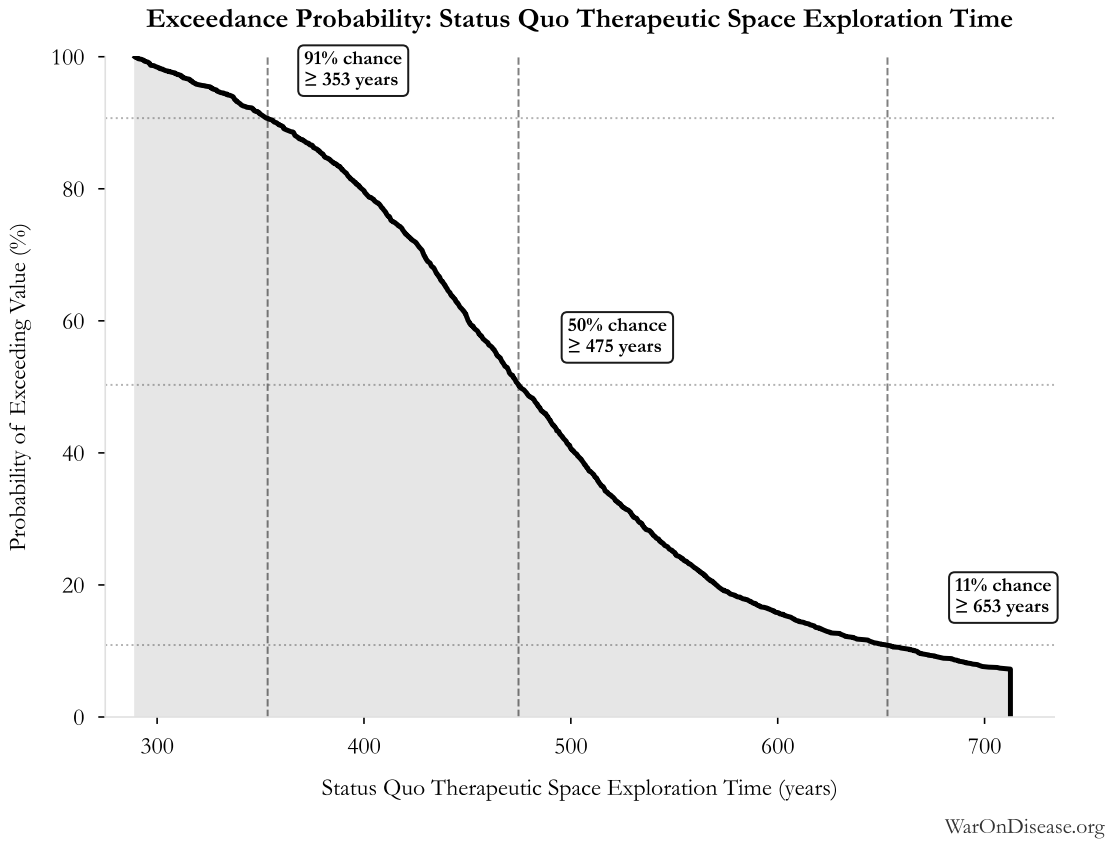


Figure 235: Probability of Exceeding Threshold: Status Quo Therapeutic Space Exploration Time

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.

Thalidomide DALYs Per Event: 41.8 thousand DALYs

Details

Total DALYs per US-scale thalidomide event (YLL + YLD)
Inputs:

- Thalidomide YLD Per Event : 13.0 thousand years
- Thalidomide YLL Per Event : 28.8 thousand years

$$
\begin{aligned}
&DALY_{thal} \\
&= YLD_{thal} + YLL_{thal} \\
&= 13{,}000 + 28{,}800 \\
&= 41{,}800
\end{aligned}
$$

$$
\begin{aligned}
&\text{where } YLD_{thal} \\
&= DW_{thal} \times N_{thal,survive} \times LE_{thal} \\
&= 0.4 \times 540 \times 60 \\
&= 13{,}000
\end{aligned}
$$

$$
\begin{aligned}
&\text{where } N_{thal,survive} \\
&= N_{thal,US,prevent} \times (1 - Rate_{thal,mort}) \\
&= 900 \times (1 - 40\%) \\
&= 540
\end{aligned}
$$

$$
\begin{aligned}
&\text{where } N_{thal,US,prevent} \\
&= N_{thal,global} \times Pct_{US,1960} \\
&= 15{,}000 \times 6\% \\
&= 900
\end{aligned}
$$

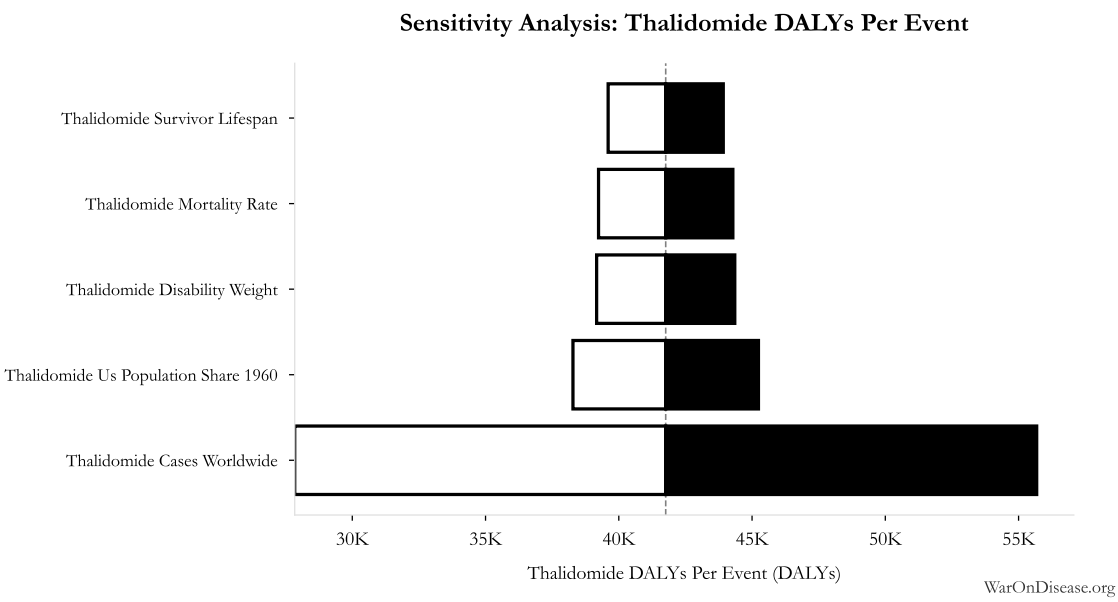
$$\text{where } YLL_{thal} = Deaths_{thal} \times 80 = 360 \times 80 = 28{,}800$$

$$
\begin{aligned}
&\text{where } Deaths_{thal} \\
&= Rate_{thal,mort} \times N_{thal,US,prevent} \\
&= 40\% \times 900 \\
&= 360
\end{aligned}
$$

$$
\begin{aligned}
&\text{where } N_{thal,US,prevent} \\
&= N_{thal,global} \times Pct_{US,1960} \\
&= 15{,}000 \times 6\% \\
&= 900
\end{aligned}
$$

~ *Medium confidence*

Sensitivity Analysis



Sensitivity Indices for Thalidomide DALYs Per Event

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

Input Parameter	Sensitivity Coefficient	Interpretation
Thalidomide Yll Per Event	0.6300	Strong driver
Thalidomide Yld Per Event	0.3701	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

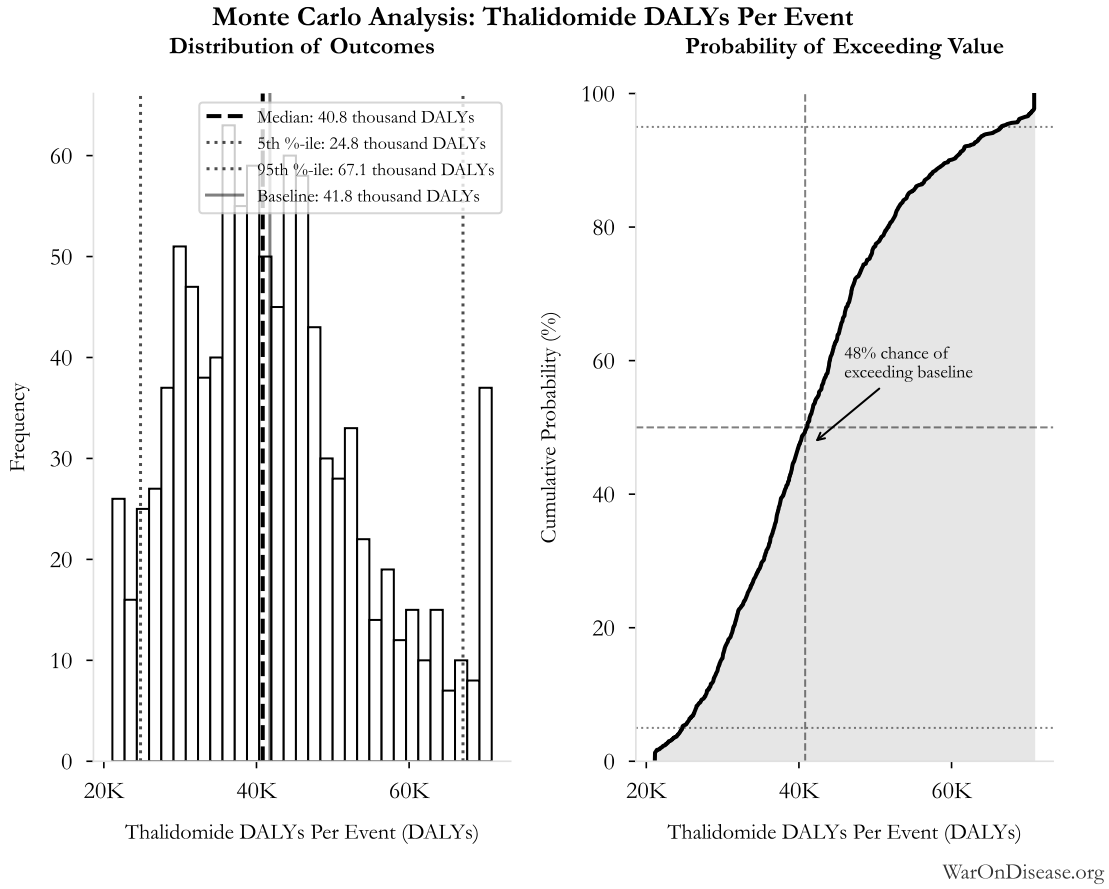


Figure 236: Monte Carlo Distribution: Thalidomide DALYs Per Event (10,000 simulations)

Simulation Results Summary: Thalidomide DALYs Per Event

Statistic	Value
Baseline (deterministic)	41.8 thousand
Mean (expected value)	42.5 thousand
Median (50th percentile)	40.8 thousand
Standard Deviation	12.2 thousand
90% Range (5th-95th percentile)	[24.8 thousand, 67.1 thousand]

The histogram shows the distribution of Thalidomide DALYs Per Event 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

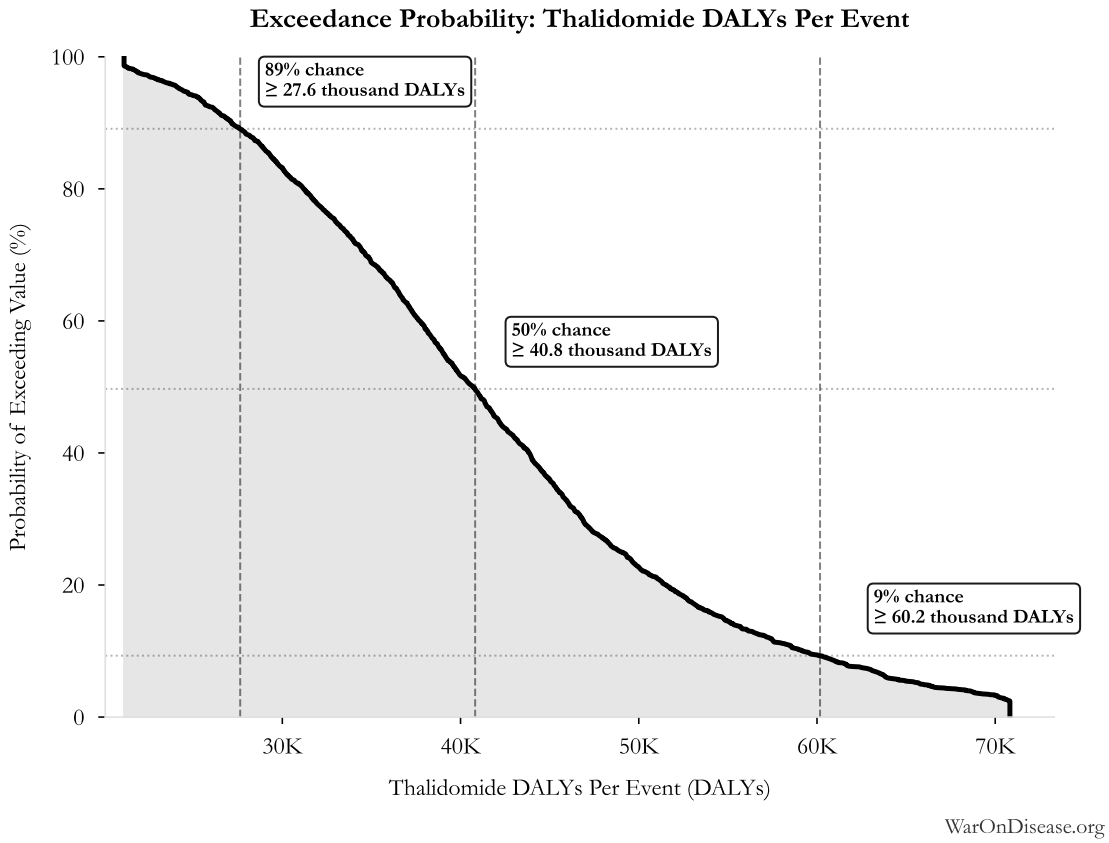


Figure 237: Probability of Exceeding Threshold: Thalidomide DALYs Per Event

This exceedance probability chart shows the likelihood that Thalidomide DALYs Per Event will exceed any given threshold. Higher curves indicate more favorable outcomes with greater certainty.

Thalidomide Deaths Per Event: 360 deaths

Details

Deaths per US-scale thalidomide event
Inputs:

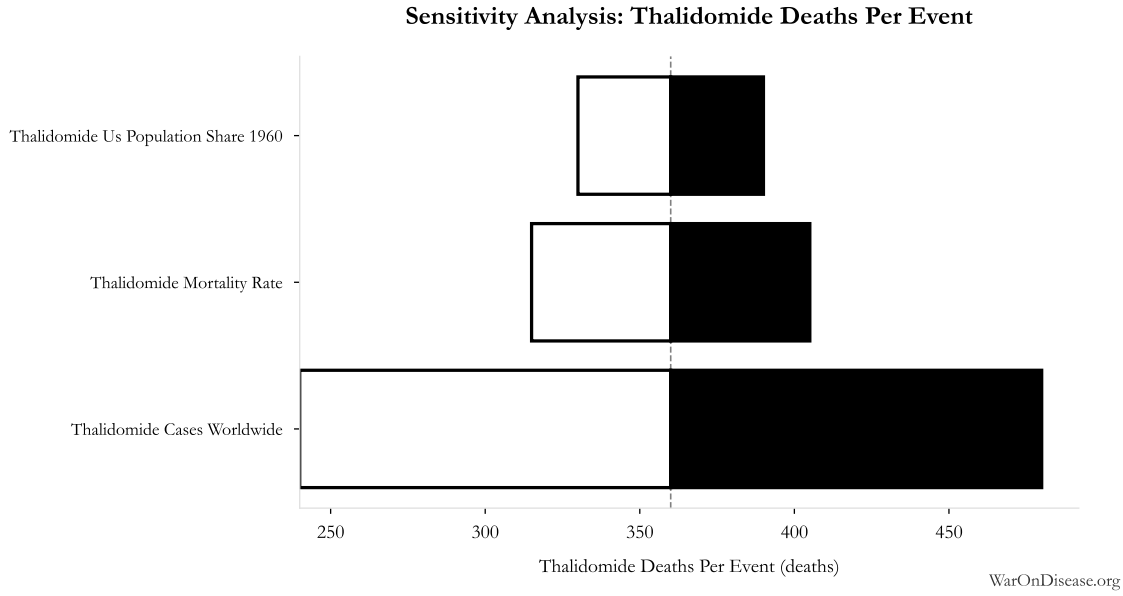
- Thalidomide Mortality Rate : 40% (95% CI: 35% - 45%)
- Thalidomide US Cases Prevented : 900 cases

$$
\begin{aligned}
&Deaths_{thal} \\
&= Rate_{thal,mort} \times N_{thal,US,prevent} \\
&= 40\% \times 900 \\
&= 360
\end{aligned}
$$

$$
\begin{aligned}
&\text{where } N_{thal,US,prevent} \\
&= N_{thal,global} \times Pct_{US,1960} \\
&= 15{,}000 \times 6\% \\
&= 900
\end{aligned}
$$

~ Medium confidence

Sensitivity Analysis



Sensitivity Indices for Thalidomide Deaths Per Event
Regression-based sensitivity showing which inputs explain the most variance in the output.

Input Parameter	Sensitivity Coefficient	Interpretation
Thalidomide US Cases Prevented	1.5027	Strong driver
Thalidomide Mortality Rate	-0.5048	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

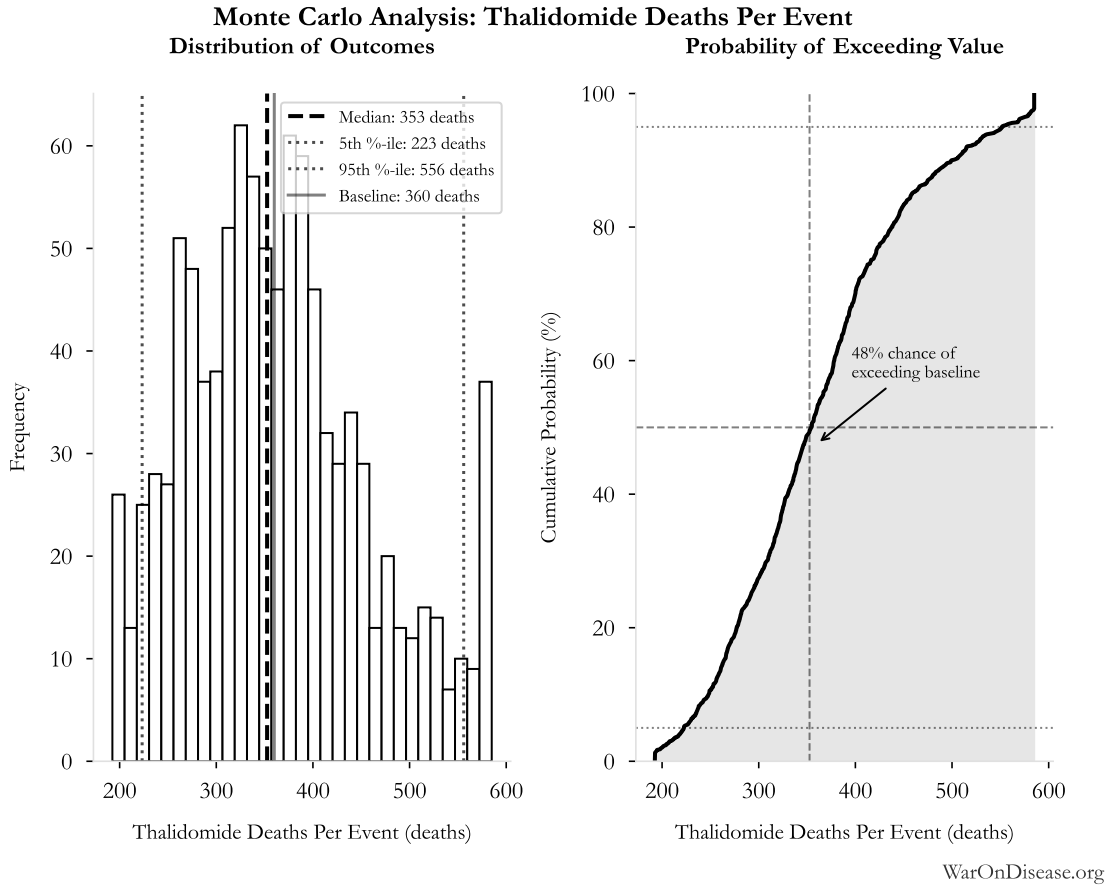


Figure 238: Monte Carlo Distribution: Thalidomide Deaths Per Event (10,000 simulations)

Simulation Results Summary: Thalidomide Deaths Per Event

Statistic	Value
Baseline (deterministic)	360
Mean (expected value)	364
Median (50th percentile)	353
Standard Deviation	95.8
90% Range (5th-95th percentile)	[223, 556]

The histogram shows the distribution of Thalidomide Deaths Per Event 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

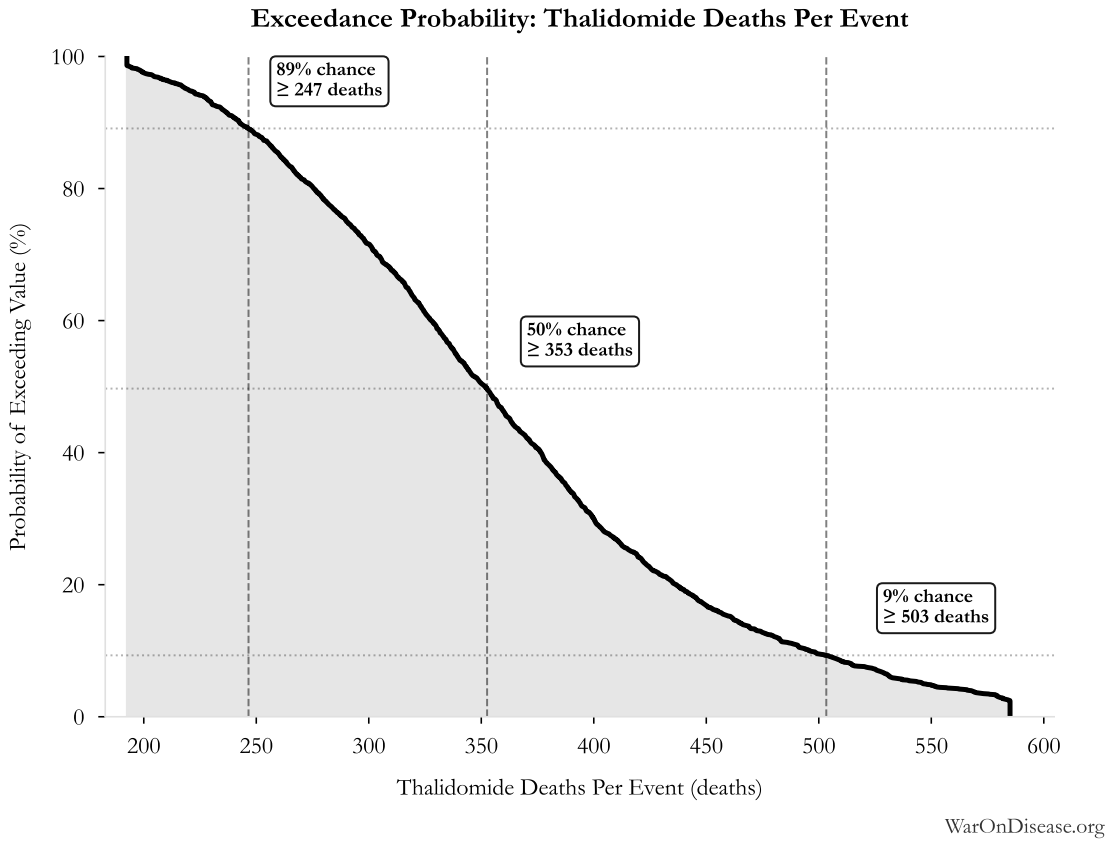


Figure 239: Probability of Exceeding Threshold: Thalidomide Deaths Per Event

This exceedance probability chart shows the likelihood that Thalidomide Deaths Per Event will exceed any given threshold. Higher curves indicate more favorable outcomes with greater certainty.

Thalidomide Survivors Per Event: 540 cases

Details

Survivors per US-scale thalidomide event

Inputs:

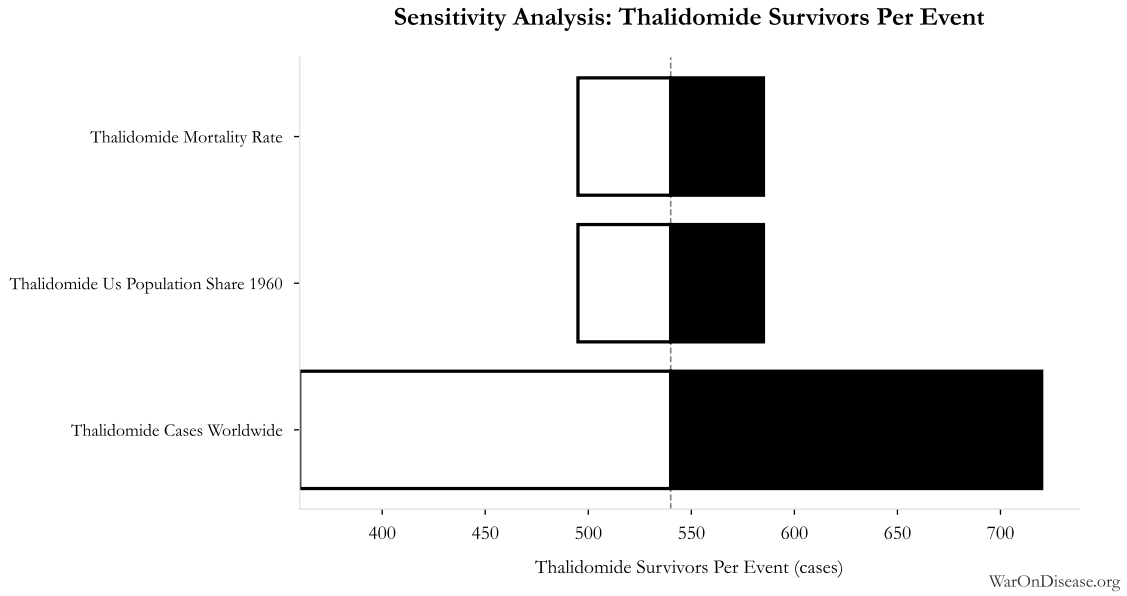
- Thalidomide Mortality Rate : 40% (95% CI: 35% - 45%)
- Thalidomide US Cases Prevented : 900 cases

$$
\begin{aligned}
&N_{thal,survive} \\
&= N_{thal,US,prevent} \times (1 - Rate_{thal,mort}) \\
&= 900 \times (1 - 40\%) \\
&= 540
\end{aligned}
$$

$$
\begin{aligned}
&\text{where } N_{thal,US,prevent} \\
&= N_{thal,global} \times Pct_{US,1960} \\
&= 15{,}000 \times 6\% \\
&= 900
\end{aligned}
$$

~ Medium confidence

Sensitivity Analysis



Sensitivity Indices for Thalidomide Survivors Per Event
Regression-based sensitivity showing which inputs explain the most variance in the output.

Input Parameter	Sensitivity Coefficient	Interpretation
Thalidomide Mortality Rate	0.5607	Strong driver
Thalidomide US Cases Prevented	0.4398	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

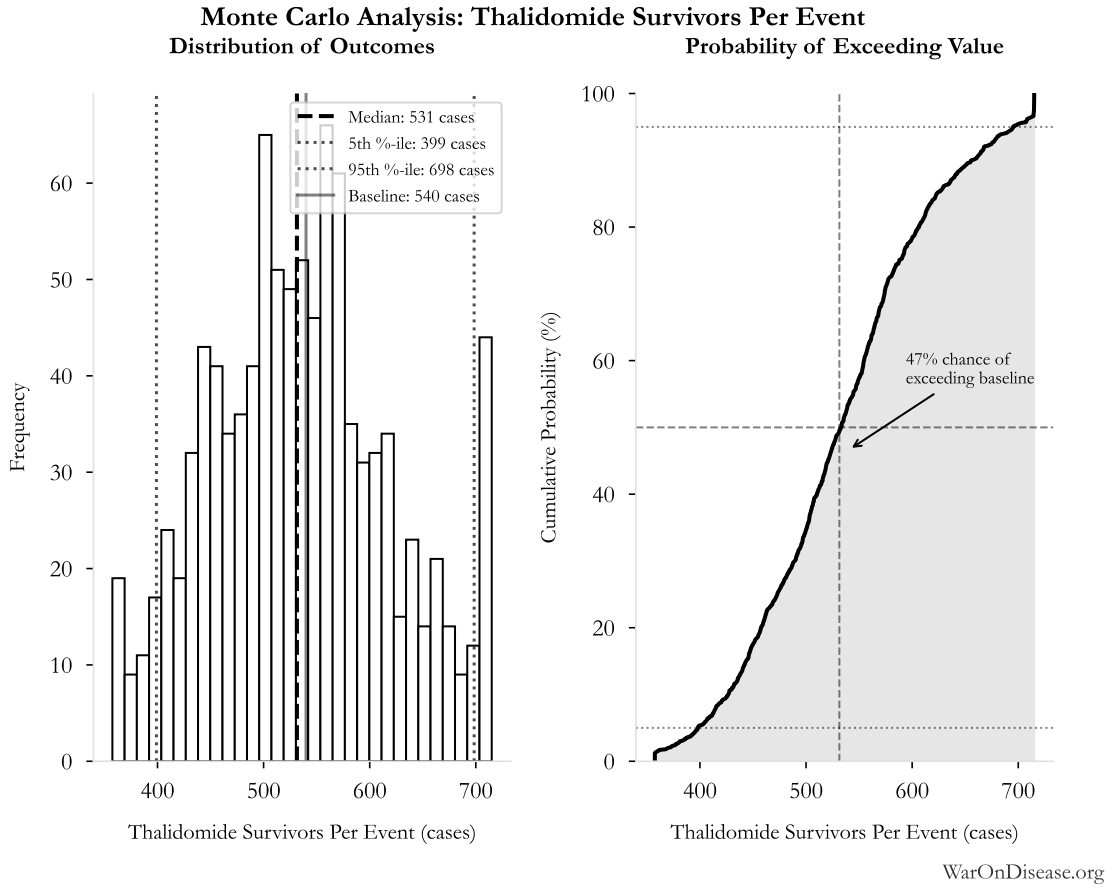


Figure 240: Monte Carlo Distribution: Thalidomide Survivors Per Event (10,000 simulations)

Simulation Results Summary: Thalidomide Survivors Per Event

Statistic	Value
Baseline (deterministic)	540
Mean (expected value)	537
Median (50th percentile)	531
Standard Deviation	86.3
90% Range (5th-95th percentile)	[399, 698]

The histogram shows the distribution of Thalidomide Survivors Per Event 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

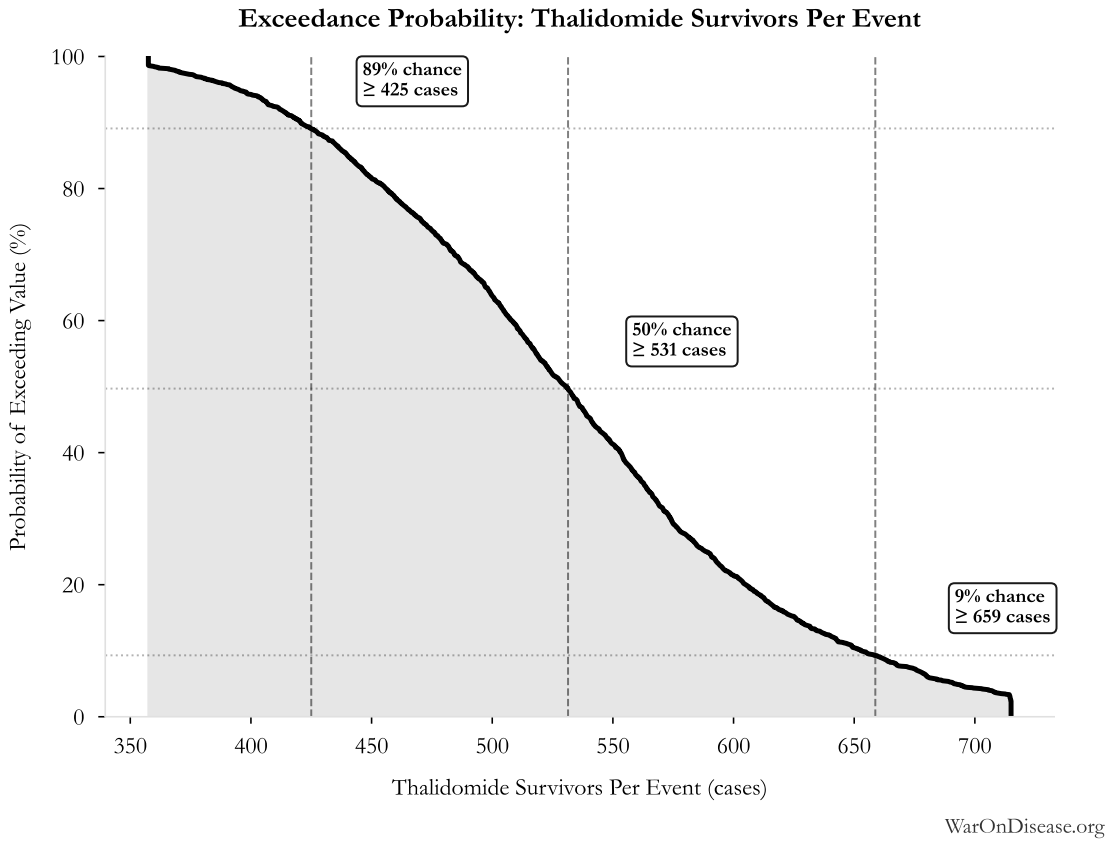


Figure 241: Probability of Exceeding Threshold: Thalidomide Survivors Per Event

This exceedance probability chart shows the likelihood that Thalidomide Survivors Per Event will exceed any given threshold. Higher curves indicate more favorable outcomes with greater certainty.

Thalidomide US Cases Prevented: 900 cases

Details

Estimated US thalidomide cases prevented by FDA rejection
Inputs:

- Thalidomide Cases Worldwide : 15.0 thousand cases (95% CI: 10.0 thousand cases -

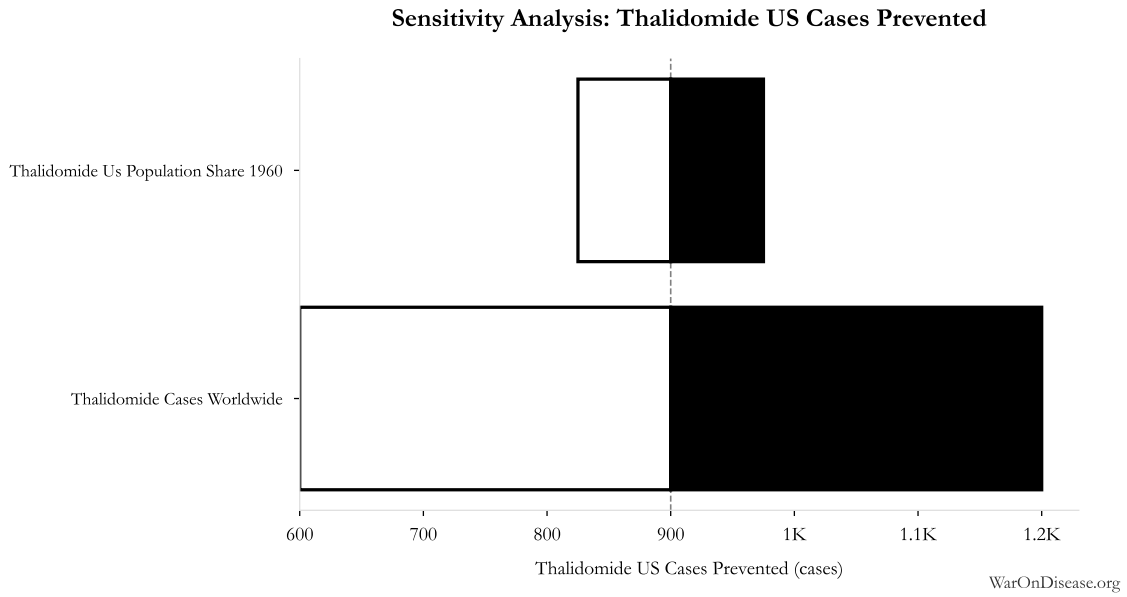
20.0 thousand cases)

- US Population Share 1960 : 6% (95% CI: 5.5% - 6.5%)

$$
\begin{aligned}
&N_{thal,US,prevent} \\
&= N_{thal,global} \times Pct_{US,1960} \\
&= 15{,}000 \times 6\% \\
&= 900
\end{aligned}
$$

~ *Medium confidence*

Sensitivity Analysis



Sensitivity Indices for Thalidomide US Cases Prevented

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

Input Parameter	Sensitivity Coefficient	Interpretation
Thalidomide Cases Worldwide	1.3746	Strong driver
Thalidomide US Population Share 1960	-0.3756	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

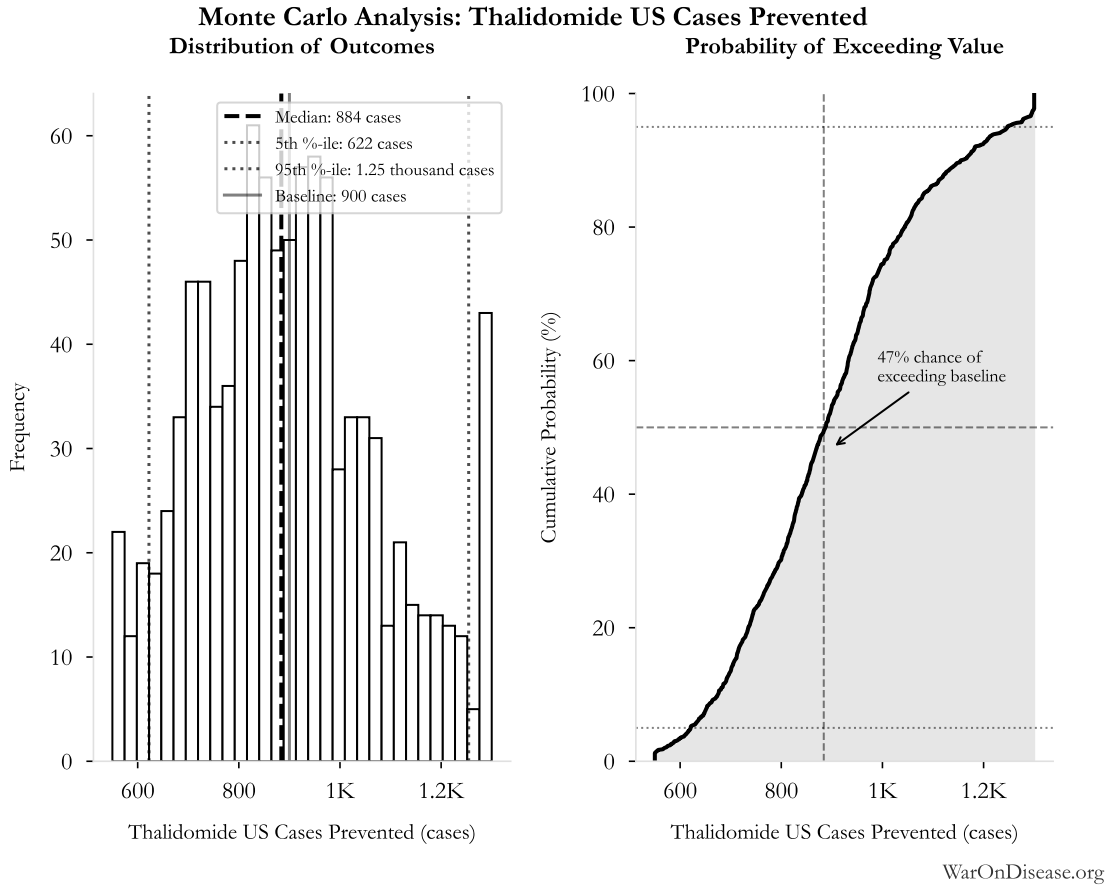


Figure 242: Monte Carlo Distribution: Thalidomide US Cases Prevented (10,000 simulations)

Simulation Results Summary: Thalidomide US Cases Prevented

Statistic	Value
Baseline (deterministic)	900
Mean (expected value)	901
Median (50th percentile)	884
Standard Deviation	182
90% Range (5th-95th percentile)	[622, 1.25 thousand]

The histogram shows the distribution of Thalidomide US Cases Prevented 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

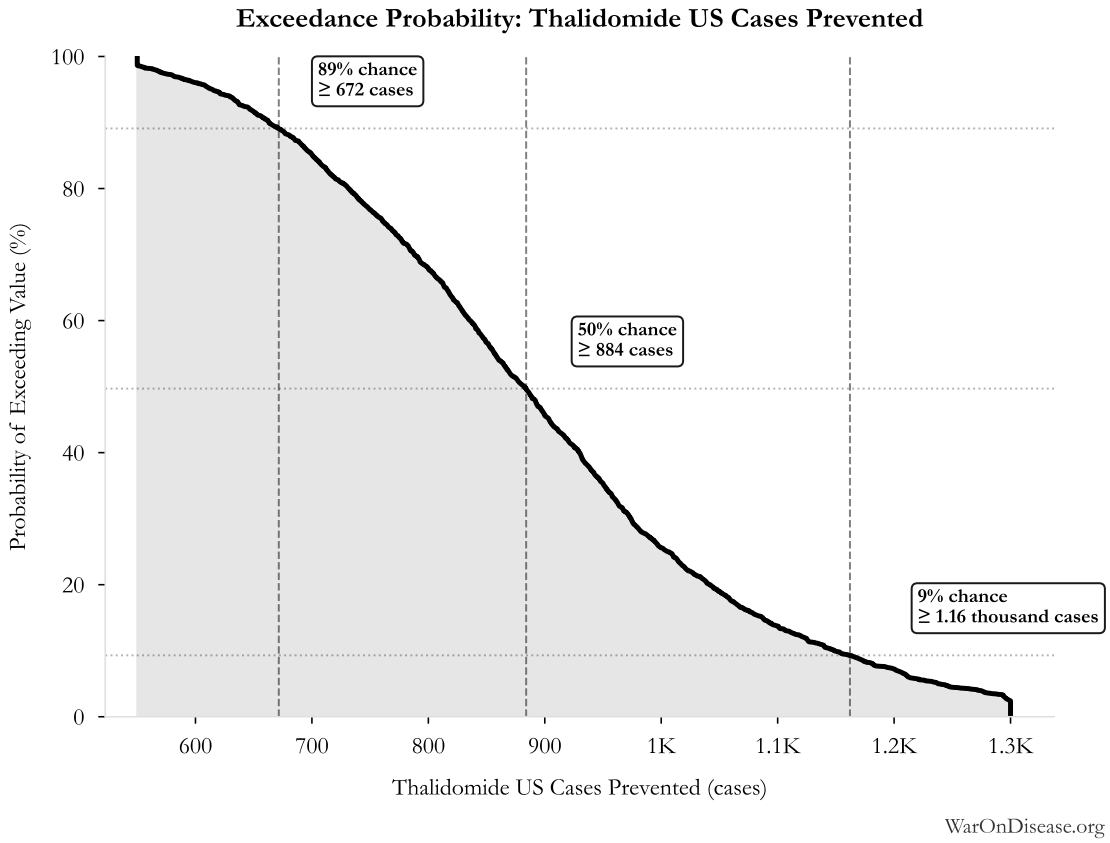


Figure 243: Probability of Exceeding Threshold: Thalidomide US Cases Prevented

This exceedance probability chart shows the likelihood that Thalidomide US Cases Prevented will exceed any given threshold. Higher curves indicate more favorable outcomes with greater certainty.

Thalidomide YLD Per Event: 13.0 thousand years

Details

Years Lived with Disability per thalidomide event

Inputs:

- Thalidomide Disability Weight : 0.4:1 (95% CI: 0.32:1 - 0.48:1)
- Thalidomide Survivors Per Event : 540 cases
- Thalidomide Survivor Lifespan : 60 years (95% CI: 50 years - 70 years)

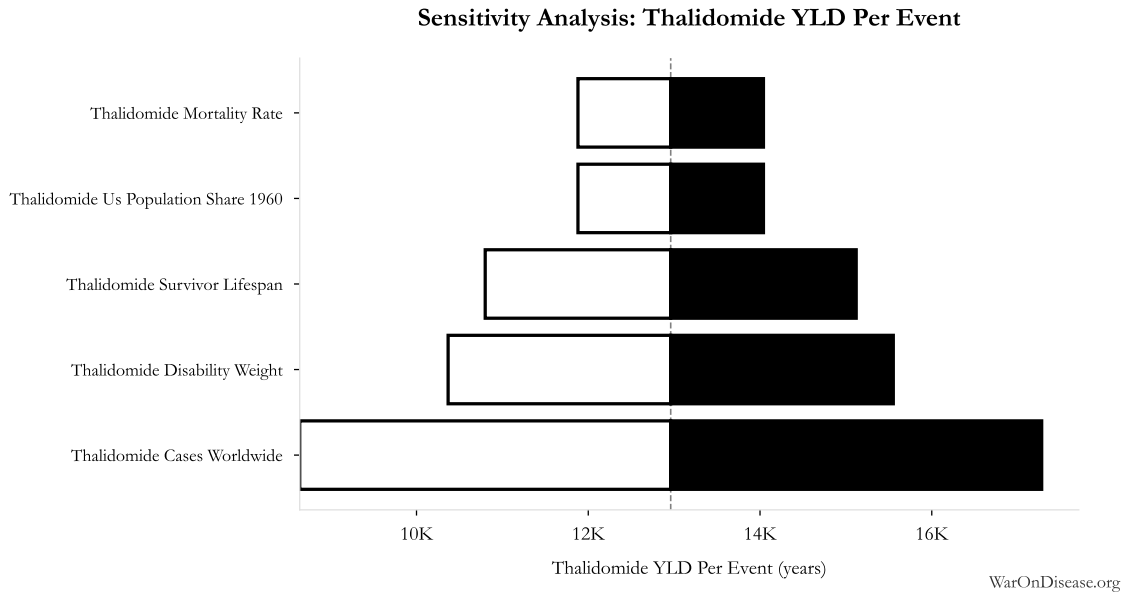
$$
\begin{aligned}
&YLD_{thal} \\
&= DW_{thal} \times N_{thal,survive} \times LE_{thal} \\
&= 0.4 \times 540 \times 60 \\
&= 13{,}000
\end{aligned}
$$

$$
\begin{aligned}
&\text{where } N_{thal,survive} \\
&= N_{thal,US,prevent} \times (1 - Rate_{thal,mort}) \\
&= 900 \times (1 - 40\%) \\
&= 540
\end{aligned}
$$

$$
\begin{aligned}
&\text{where } N_{thal,US,prevent} \\
&= N_{thal,global} \times Pct_{US,1960} \\
&= 15{,}000 \times 6\% \\
&= 900
\end{aligned}
$$

~ *Medium confidence*

Sensitivity Analysis



Sensitivity Indices for Thalidomide YLD Per Event
Regression-based sensitivity showing which inputs explain the most variance in the output.

Input Parameter	Sensitivity Coefficient	Interpretation
Thalidomide Disability Weight	28.4785	Strong driver
Thalidomide Survivor Lifespan	-23.4440	Strong driver
Thalidomide Survivors Per Event	-4.0444	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

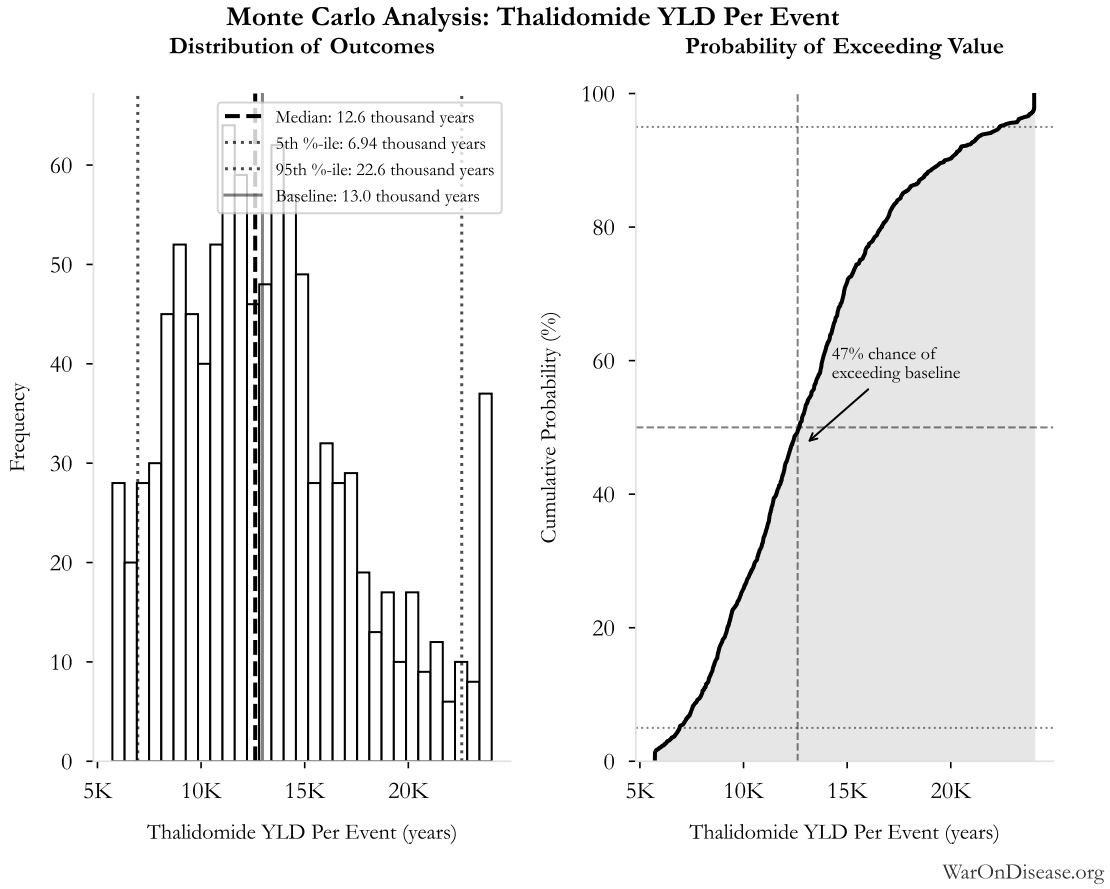


Figure 244: Monte Carlo Distribution: Thalidomide YLD Per Event (10,000 simulations)

Simulation Results Summary: Thalidomide YLD Per Event

Statistic	Value
Baseline (deterministic)	13.0 thousand
Mean (expected value)	13.3 thousand
Median (50th percentile)	12.6 thousand
Standard Deviation	4.50 thousand
90% Range (5th-95th percentile)	[6.94 thousand, 22.6 thousand]

The histogram shows the distribution of Thalidomide YLD Per Event 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

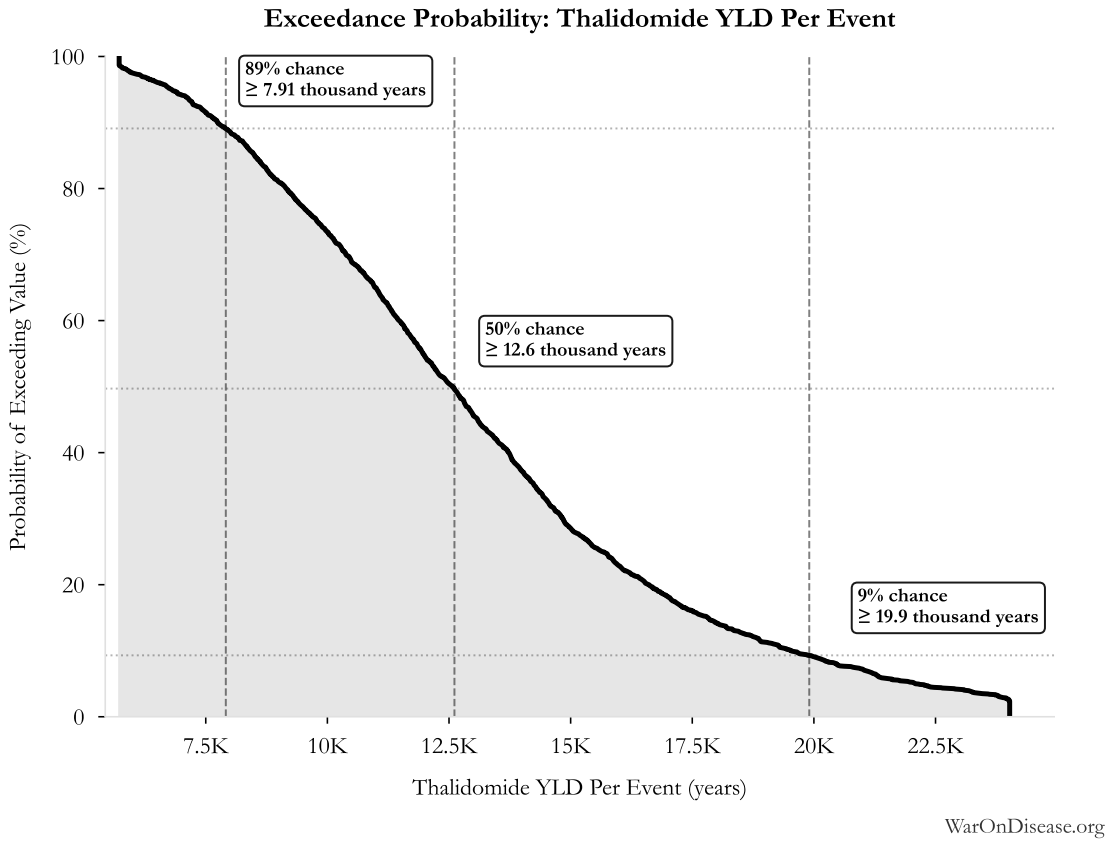


Figure 245: Probability of Exceeding Threshold: Thalidomide YLD Per Event

This exceedance probability chart shows the likelihood that Thalidomide YLD Per Event will exceed any given threshold. Higher curves indicate more favorable outcomes with greater certainty.

Thalidomide YLL Per Event: 28.8 thousand years

Details

Years of Life Lost per thalidomide event (infant deaths)
Inputs:

- Thalidomide Deaths Per Event : 360 deaths

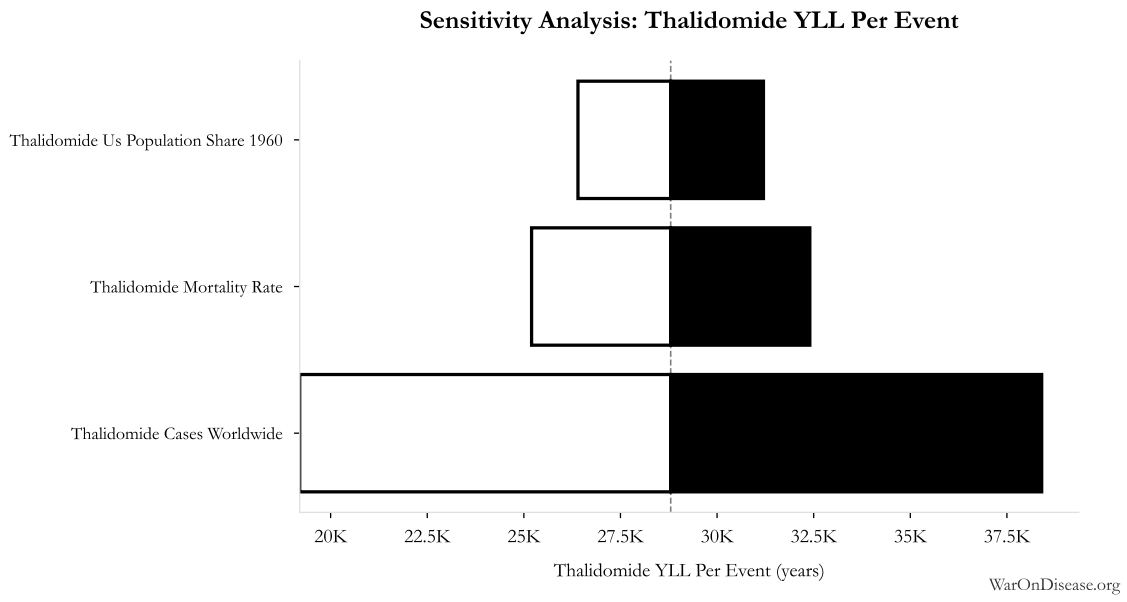
$$YLL_{thal} = Deaths_{thal} \times 80 = 360 \times 80 = 28{,}800$$

$$\text{where } Deaths_{thal} = Rate_{thal,mort} \times N_{thal,US,prevent} = 40\% \times 900 = 360$$

$$\text{where } N_{thal,US,prevent} = N_{thal,global} \times Pct_{US,1960} = 15{,}000 \times 6\% = 900$$

~ *Medium confidence*

Sensitivity Analysis



Sensitivity Indices for Thalidomide YLL Per Event

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

Input Parameter	Sensitivity Coefficient	Interpretation
Thalidomide Deaths Per Event	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

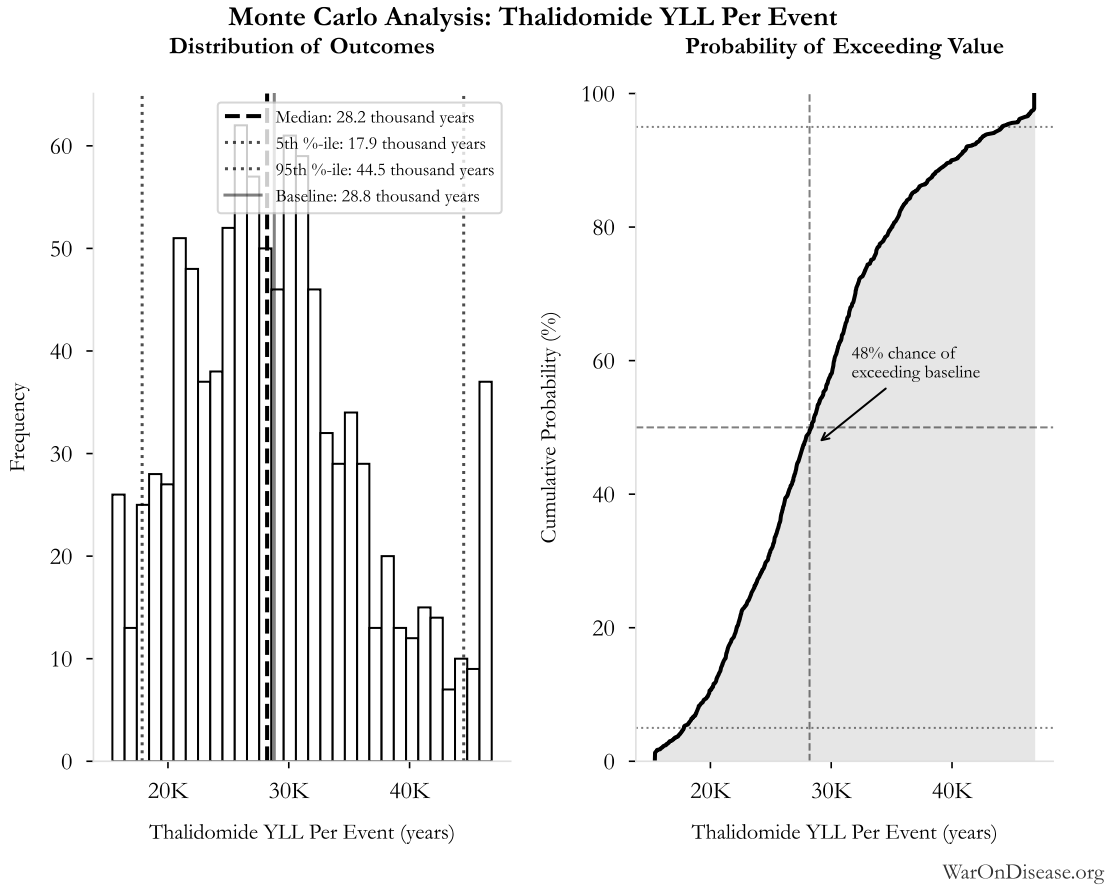


Figure 246: Monte Carlo Distribution: Thalidomide YLL Per Event (10,000 simulations)

Simulation Results Summary: Thalidomide YLL Per Event

Statistic	Value
Baseline (deterministic)	28.8 thousand
Mean (expected value)	29.2 thousand
Median (50th percentile)	28.2 thousand
Standard Deviation	7.67 thousand
90% Range (5th-95th percentile)	[17.9 thousand, 44.5 thousand]

The histogram shows the distribution of Thalidomide YLL Per Event 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

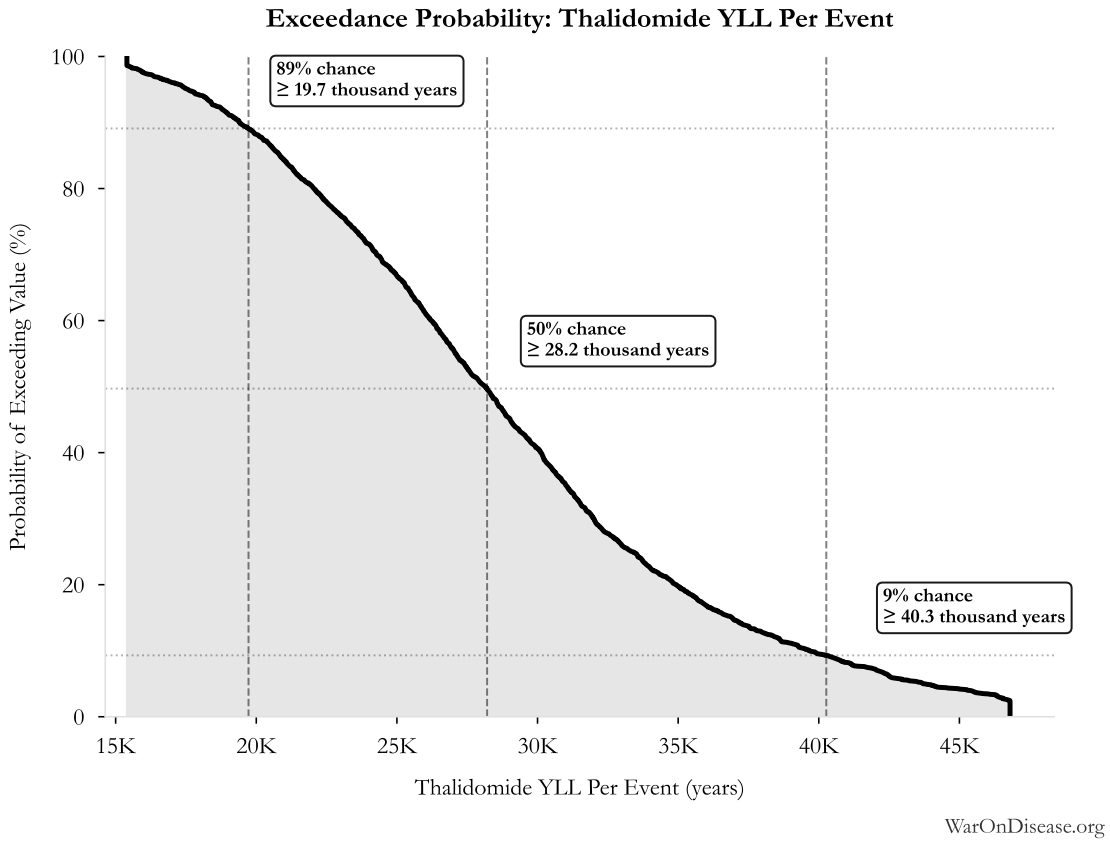


Figure 247: Probability of Exceeding Threshold: Thalidomide YLL Per Event

This exceedance probability chart shows the likelihood that Thalidomide YLL Per Event will exceed any given threshold. Higher curves indicate more favorable outcomes with greater certainty.

Annual Funding from 1% of Global Military Spending Redirected to DIH: $27.2B

Details

Annual funding from 1% of global military spending redirected to DIH
Inputs:

- Global Military Spending in 2024 : $2.72T

- 1% Reduction in Military Spending/War Costs from Treaty: 1%

$$\begin{aligned} & Funding_{treaty} \\ &= Spending_{mil} \times Reduce_{treaty} \\ &= \$2.72T \times 1\% \\ &= \$27.2B \end{aligned}$$

High confidence

Treaty System Benefit Multiplier vs Childhood Vaccination Programs: 11.5x

Details

Treaty system benefit multiplier vs childhood vaccination programs
Inputs:

- Estimated Annual Global Economic Benefit from Childhood Vaccination Programs : $15B (SE: ±$4.50B)
- 1% treaty Basic Annual Benefits (Peace + R&D Savings) : $172B

$$k_{treaty:vax} = \frac{Benefit_{peace+RD}}{Benefit_{vax,ann}} = \frac{\$172B}{\$15B} = 11.5$$

$$\text{where } Benefit_{peace+RD}$$
$$= Benefit_{peace,soc} + Benefit_{RD,ann}$$
$$= \$114B + \$58.6B$$
$$= \$172B$$

$$\text{where } Benefit_{peace,soc}$$
$$= Cost_{war,total} \times Reduce_{treaty}$$
$$= \$11.4T \times 1\%$$
$$= \$114B$$

$$\text{where } Cost_{war,total}$$
$$= Cost_{war,direct} + Cost_{war,indirect}$$
$$= \$7.66T + \$3.7T$$
$$= \$11.4T$$

$$\text{where } Cost_{war,direct}$$
$$= Loss_{life,conflict} + Damage_{infra,total}$$
$$+Disruption_{trade} + Spending_{mil}$$
$$= \$2.45T + \$1.88T + \$616B + \$2.72T$$
$$= \$7.66T$$

$$\text{where } Loss_{life,conflict}$$
$$= Cost_{combat,human} + Cost_{state,human}$$
$$+Cost_{terror,human}$$
$$= \$2.34T + \$27B + \$83B$$
$$= \$2.45T$$

$$\text{where } Cost_{combat,human}$$
$$= Deaths_{combat} \times VSL$$
$$= 234{,}000 \times \$10M$$
$$= \$2.34T$$

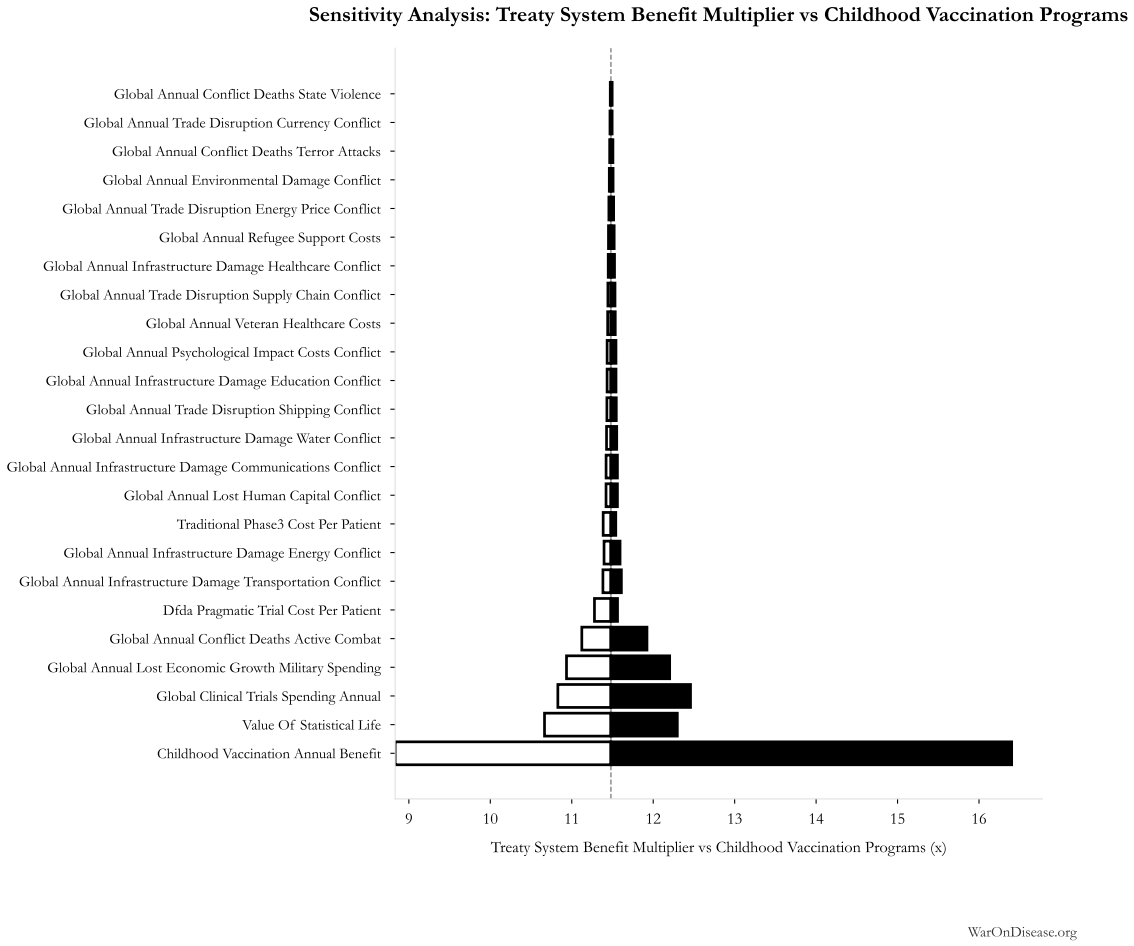
$$\text{where } Cost_{state,human}$$
$$= Deaths_{state} \times VSL$$
$$= 2{,}700 \times \$10M$$
$$= \$27B$$

$$\text{where } Cost_{terror,human}$$
$$= Deaths_{terror} \times VSL$$
$$= 8{,}300 \times \$10M$$
$$= \$83B$$

$$\text{where } Damage_{infra,total}$$
$$= Damage_{comms} + Damage_{edu} + Damage_{energy}$$
$$+Damage_{health} + Damage_{transport}$$

High confidence

Sensitivity Analysis



Sensitivity Indices for Treaty System Benefit Multiplier vs Childhood Vaccination Programs

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

Input Parameter	Sensitivity Coefficient	Interpretation
Childhood Vaccination Annual Benefit	-1.1963	Strong driver
Treaty Peace Plus R&D Annual Benefits	0.3259	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

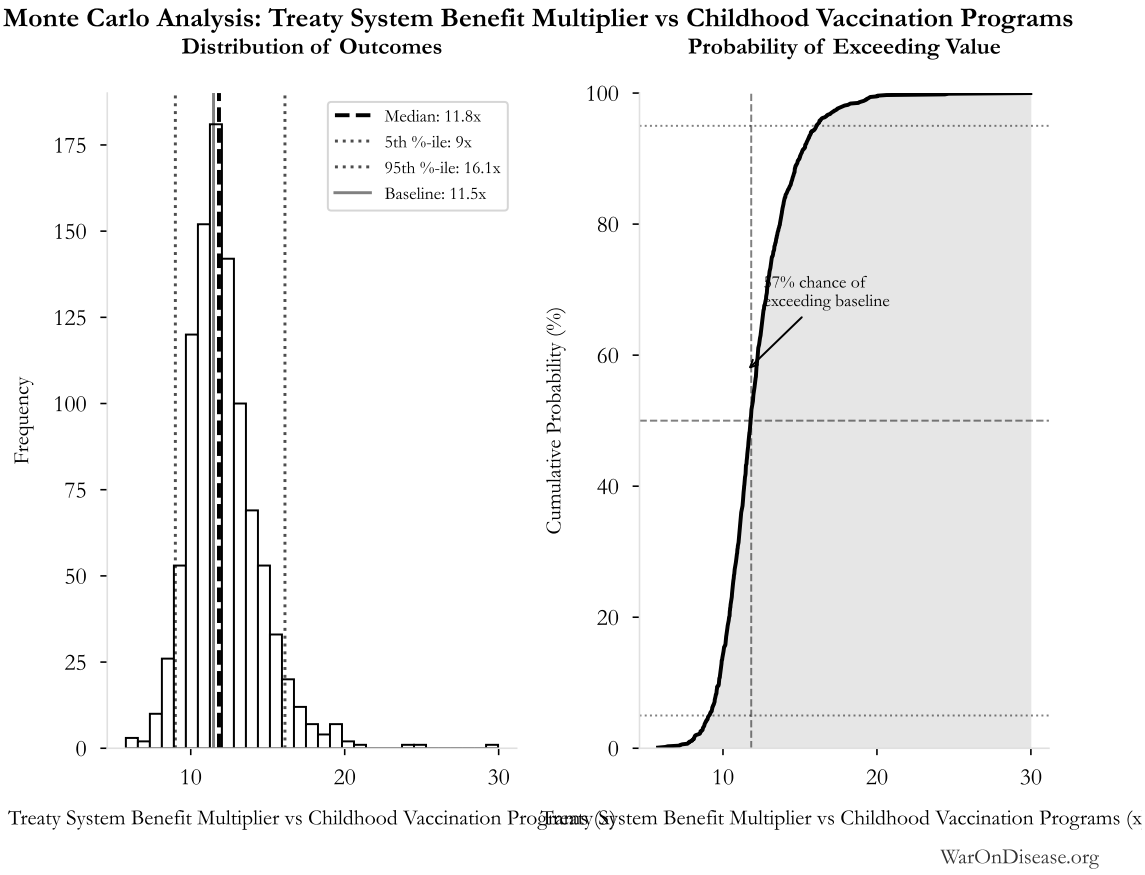


Figure 248: Monte Carlo Distribution: Treaty System Benefit Multiplier vs Childhood Vaccination Programs (10,000 simulations)

Simulation Results Summary: Treaty System Benefit Multiplier vs Childhood Vaccination Programs

Statistic	Value
Baseline (deterministic)	11.5x
Mean (expected value)	12.1x
Median (50th percentile)	11.8x
Standard Deviation	2.28x
90% Range (5th-95th percentile)	[9x, 16.1x]

The histogram shows the distribution of Treaty System Benefit Multiplier vs Childhood Vaccination Programs 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

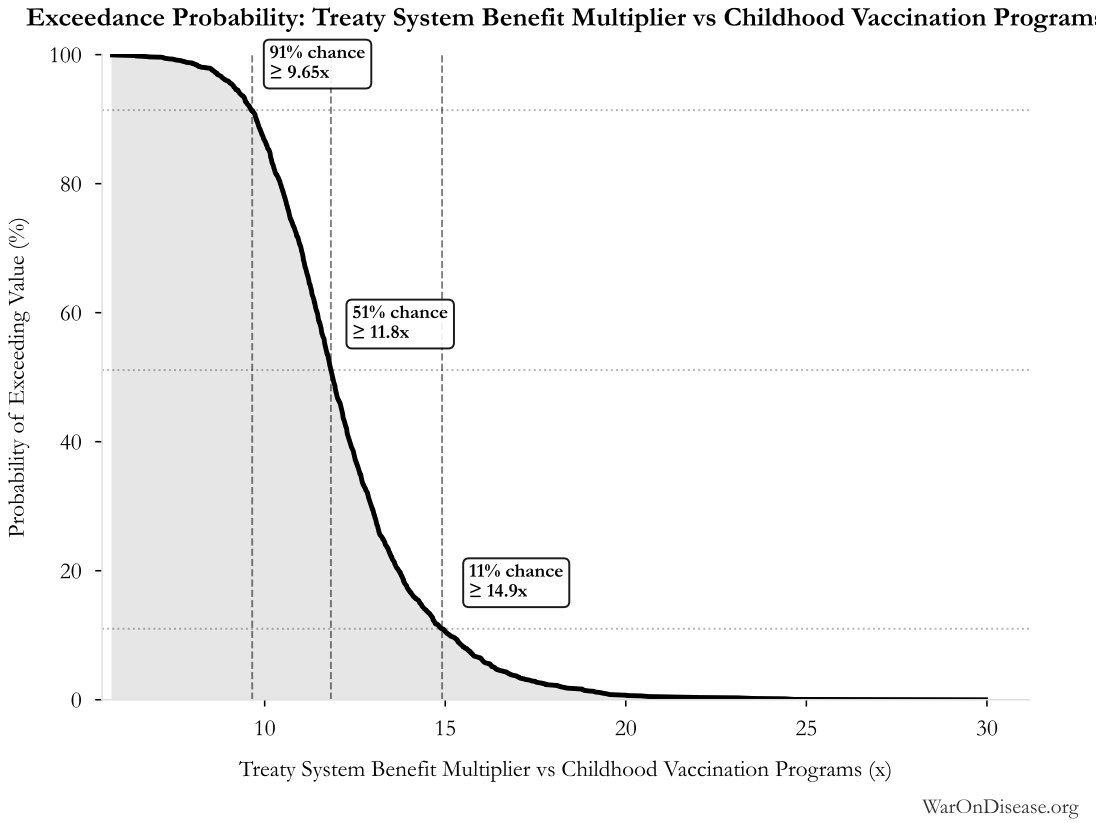


Figure 249: Probability of Exceeding Threshold: Treaty System Benefit Multiplier vs Childhood Vaccination Programs

This exceedance probability chart shows the likelihood that Treaty System Benefit Multiplier vs Childhood Vaccination Programs will exceed any given threshold. Higher curves indicate more favorable outcomes with greater certainty.

Total 1% Treaty Campaign Cost: $1B

Details

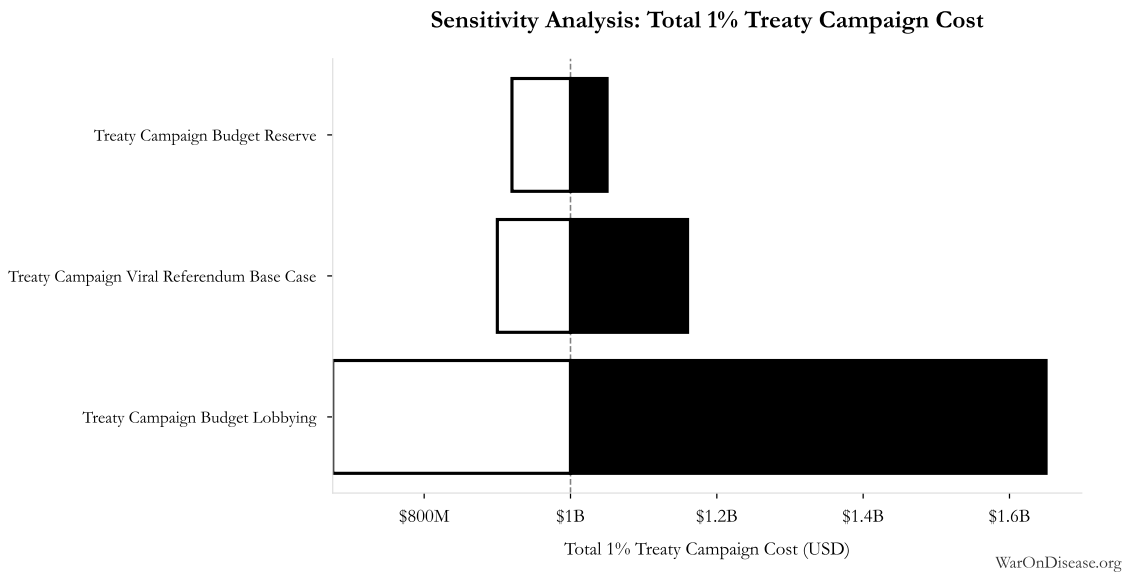
Total treaty campaign cost (100% VICTORY Incentive Alignment Bonds)
Inputs:

- Viral Referendum Budget: $250M (95% CI: $150M - $410M)
- Political Lobbying Campaign: Direct Lobbying, Super Pacs, Opposition Research, Staff, Legal/Compliance: $650M (95% CI: $325M - $1.30B)
- Reserve Fund / Contingency Buffer: $100M (95% CI: $20M - $150M)

$$\begin{aligned} & Cost_{campaign} \\ & = Budget_{viral,base} + Budget_{lobby,treaty} \\ & + Budget_{reserve} \\ & = \$250M + \$650M + \$100M \\ & = \$1B \end{aligned}$$

High confidence

Sensitivity Analysis



Sensitivity Indices for Total 1% Treaty Campaign Cost

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

Input Parameter	Sensitivity Coefficient	Interpretation
Treaty Campaign Budget Lobbying	0.9016	Strong driver
Treaty Campaign Budget Reserve	0.1026	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

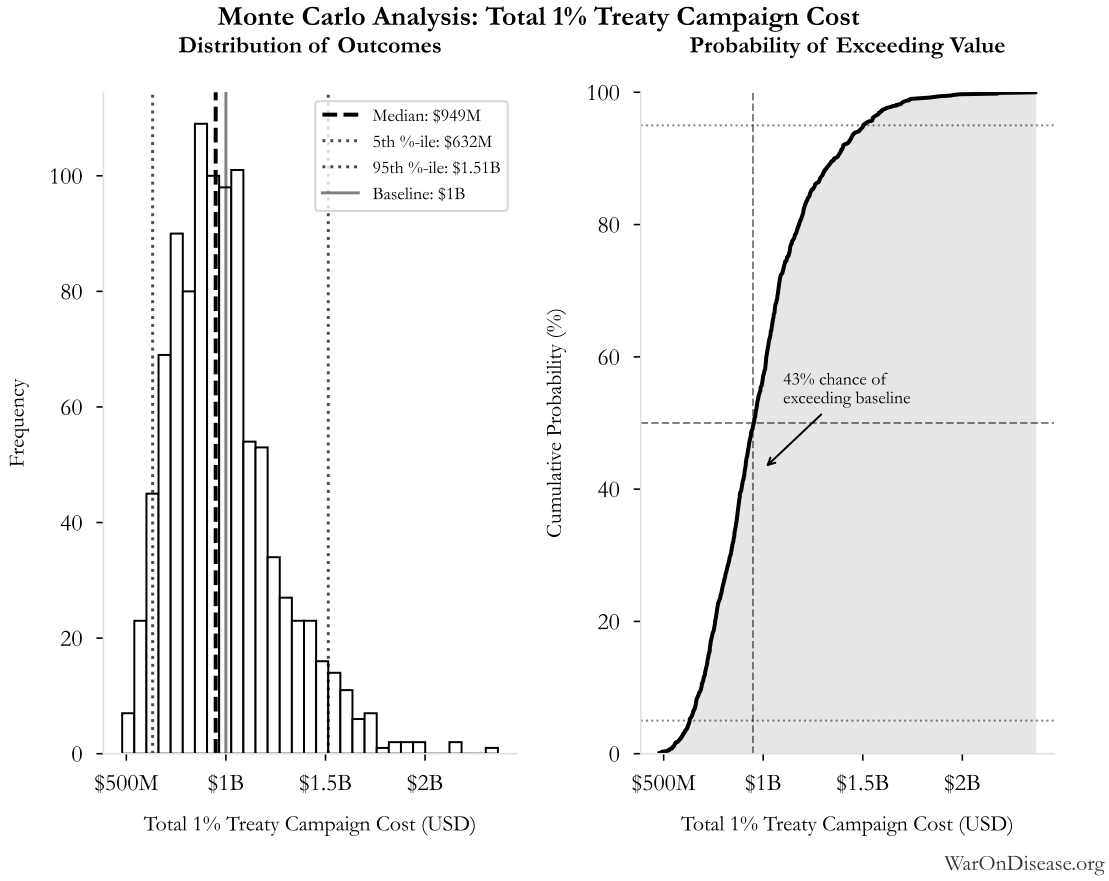


Figure 250: Monte Carlo Distribution: Total 1% Treaty Campaign Cost (10,000 simulations)

Simulation Results Summary: Total 1% Treaty Campaign Cost

Statistic	Value
Baseline (deterministic)	$1B
Mean (expected value)	$996M
Median (50th percentile)	$949M
Standard Deviation	$276M
90% Range (5th-95th percentile)	[$632M, $1.51B]

The histogram shows the distribution of Total 1% Treaty Campaign Cost 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

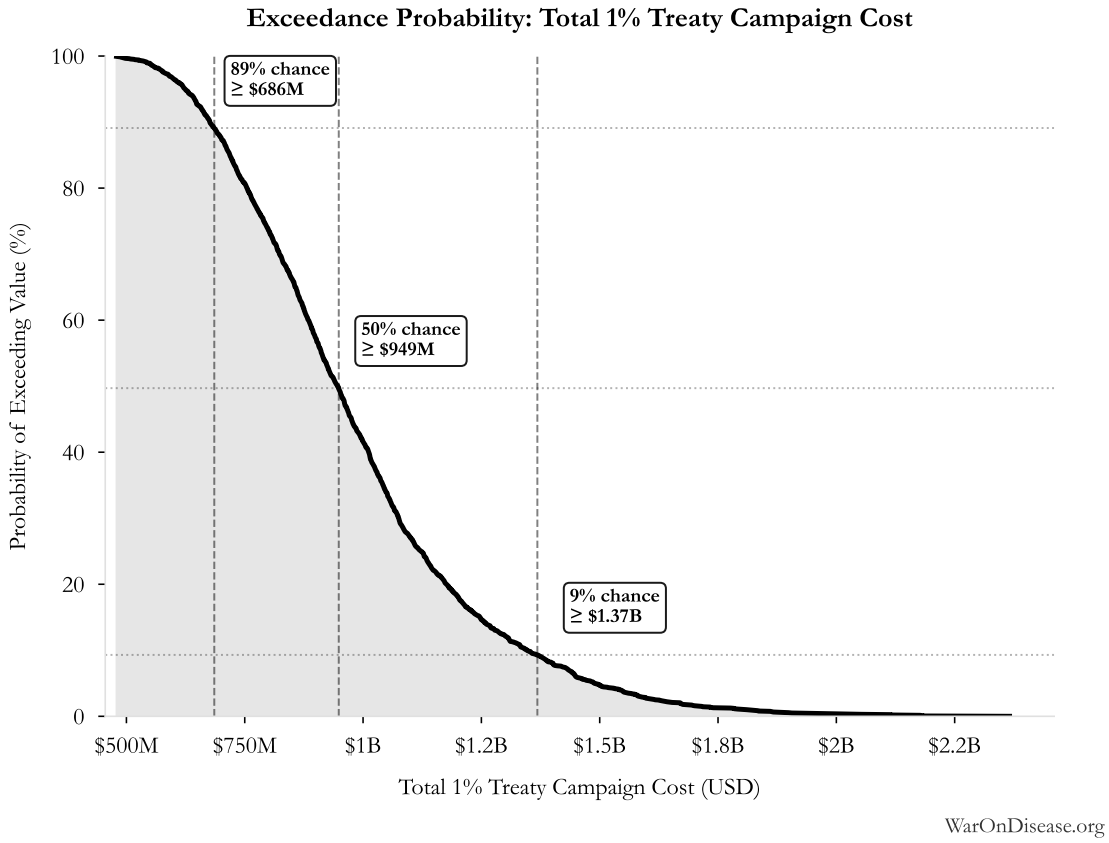


Figure 251: Probability of Exceeding Threshold: Total 1% Treaty Campaign Cost

This exceedance probability chart shows the likelihood that Total 1% Treaty Campaign Cost will exceed any given threshold. Higher curves indicate more favorable outcomes with greater certainty.

Target Voting Bloc Size for Campaign: 280 million of people

Details

Target voting bloc size for campaign (3.5% of global population - critical mass for social change)

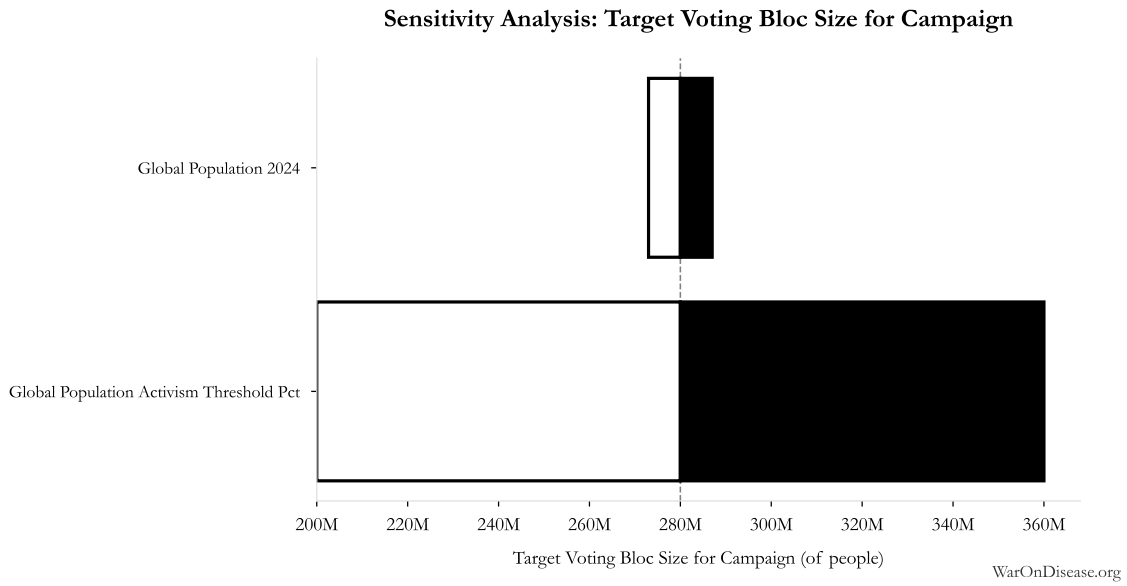
Inputs:

- Global Population in 2024 : 8.00 billion of people (95% CI: 7.80 billion of people - 8.20 billion of people)
- Critical Mass Threshold for Social Change : 3.5% (95% CI: 2.5% - 4.5%)

$$
\begin{aligned}
&N_{voters,target} \\
&= Pop_{global} \times Threshold_{activism} \\
&= 8B \times 3.5\% \\
&= 280M
\end{aligned}
$$

High confidence

Sensitivity Analysis



Sensitivity Indices for Target Voting Bloc Size for Campaign

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

Input Parameter	Sensitivity Coefficient	Interpretation
Global Population Activism Threshold %	1.1097	Strong driver
Global Population 2024	-0.1099	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

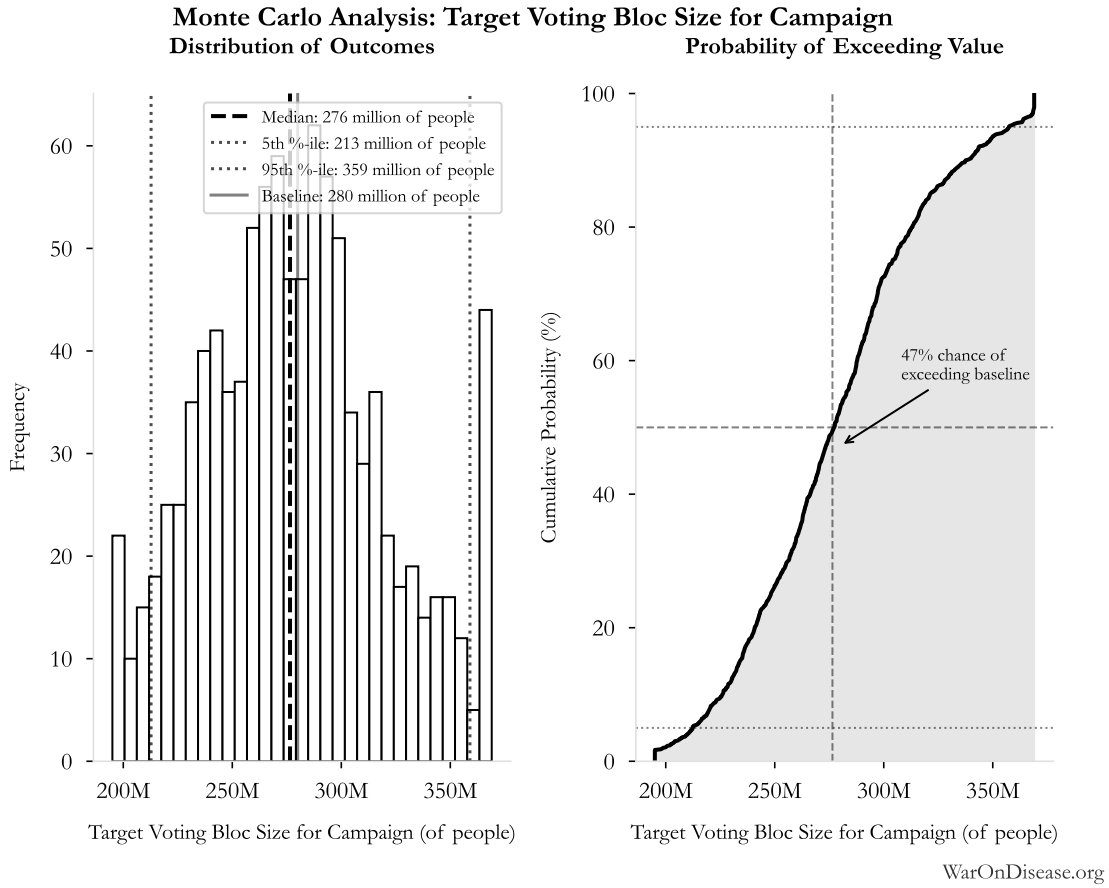


Figure 252: Monte Carlo Distribution: Target Voting Bloc Size for Campaign (10,000 simulations)

Simulation Results Summary: Target Voting Bloc Size for Campaign

Statistic	Value
Baseline (deterministic)	280 million
Mean (expected value)	279 million
Median (50th percentile)	276 million
Standard Deviation	42.1 million
90% Range (5th-95th percentile)	[213 million, 359 million]

The histogram shows the distribution of Target Voting Bloc Size for Campaign 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

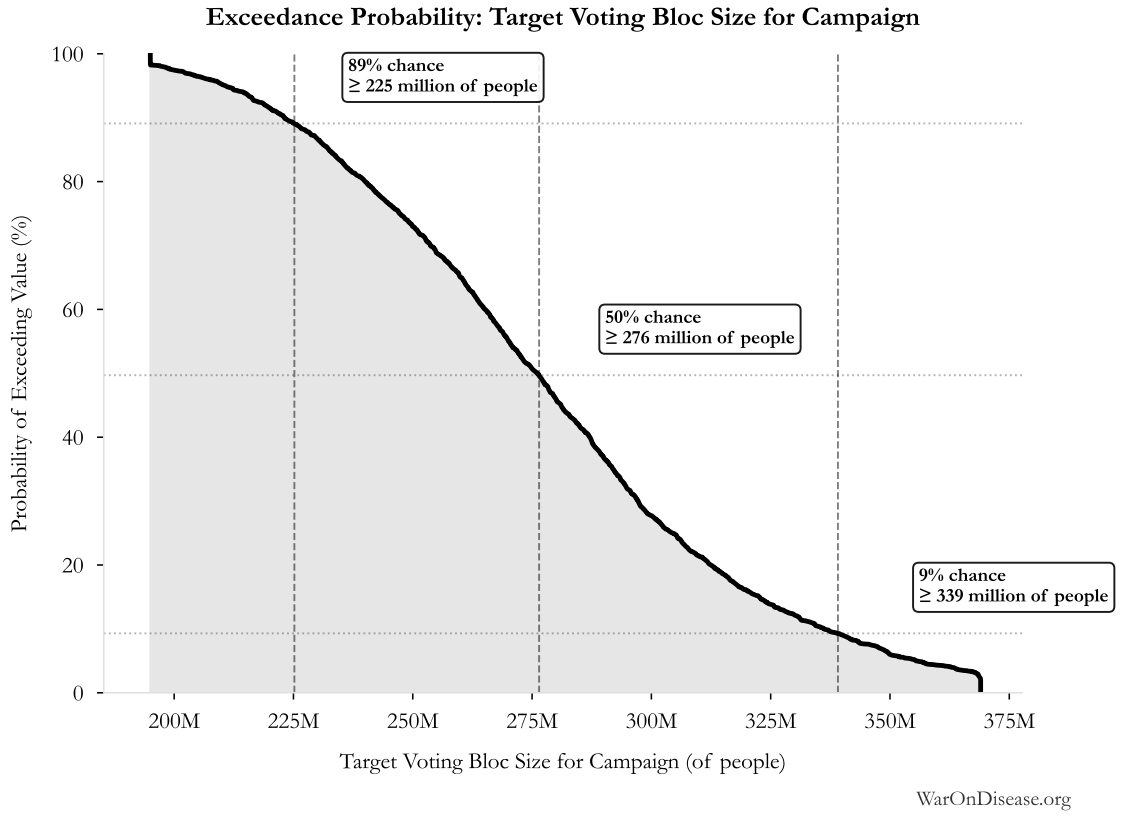


Figure 253: Probability of Exceeding Threshold: Target Voting Bloc Size for Campaign

This exceedance probability chart shows the likelihood that Target Voting Bloc Size for Campaign will exceed any given threshold. Higher curves indicate more favorable outcomes with greater certainty.

Cost per DALY Averted (Elimination of Efficacy Lag Plus Earlier Treatment Discovery from Increased Trial Throughput): $0.0018

Details

Cost per DALY averted from elimination of efficacy lag plus earlier treatment discovery from increased trial throughput. Only counts campaign cost; ignores economic benefits from funding and R&D savings.

Inputs:

- Total 1% Treaty Campaign Cost : $1B
- Total DALYs from Elimination of Efficacy Lag Plus Earlier Treatment Discovery from Higher Trial Throughput : 565 billion DALYs

$$Cost_{treaty,DALY} = \frac{Cost_{campaign}}{DALYs_{max}} = \frac{\$1B}{565B} = \$0.00177$$

$$\text{where } Cost_{campaign}$$
$$= Budget_{viral,base} + Budget_{lobby,treaty}$$
$$+ Budget_{reserve}$$
$$= \$250M + \$650M + \$100M$$
$$= \$1B$$

$$\text{where } DALYs_{max}$$
$$= DALYs_{global,ann} \times Pct_{avoid,DALY} \times T_{accel,max}$$
$$= 2.88B \times 92.6\% \times 212$$
$$= 565B$$

$$\text{where } T_{accel,max} = T_{accel} + T_{lag} = 204 + 8.2 = 212$$

$$\text{where } T_{accel}$$
$$= T_{first,SQ} \times \left(1 - \frac{1}{k_{capacity}}\right)$$
$$= 222 \times \left(1 - \frac{1}{12.3}\right)$$
$$= 204$$

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

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

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

$$\text{where } k_{capacity} = \frac{N_{fundable,ann}}{Slots_{curr}} = \frac{23.4M}{1.9M} = 12.3$$

$$\text{where } N_{fundable,ann}$$
$$= \frac{Subsidies_{trial,ann}}{Cost_{pragmatic,pt}}$$
$$= \frac{\$21.7B}{\$929}$$
$$= 23.4M$$

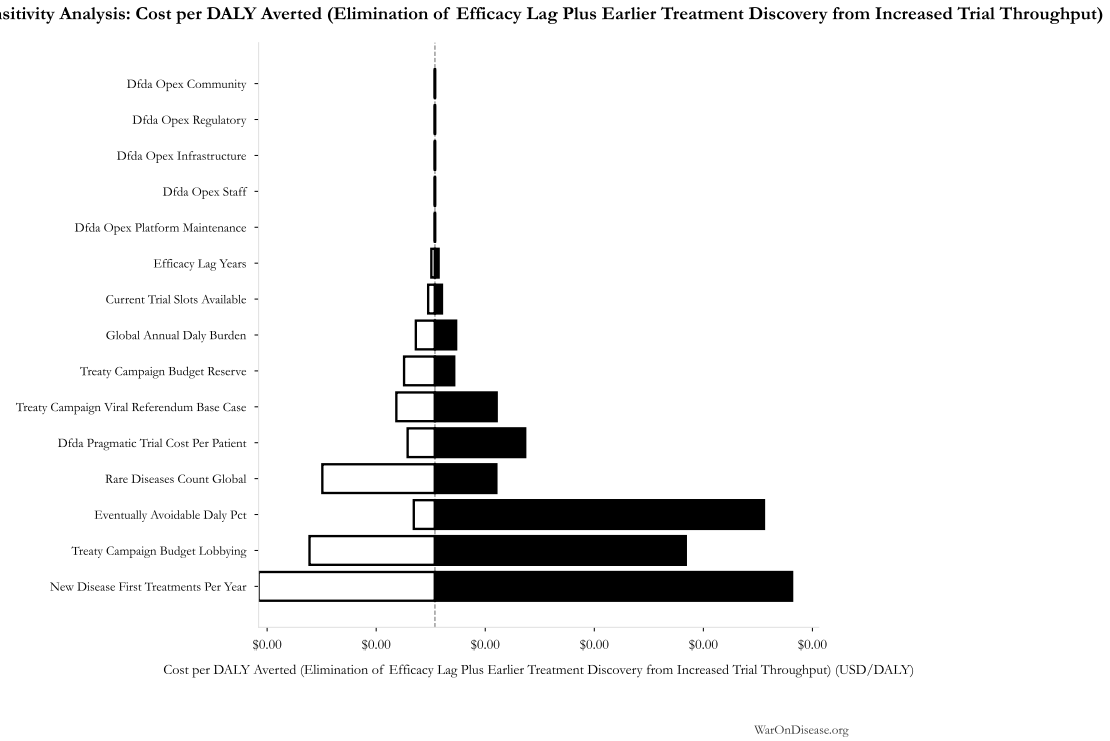
$$\text{where } Subsidies_{trial,ann}$$
$$= Treasury_{RD,ann} - OPEX_{dFDA}$$
$$= \$21.8B - \$40M$$
$$= \$21.7B$$

$$\text{where } OPEX_{dFDA}$$
$$= Cost_{platform} + Cost_{staff} + Cost_{infra}$$
$$+ Cost_{regulatory} + Cost_{community}$$
$$= \$15M + \$10M + \$8M + \$5M + \$2M$$
$$= \$40M$$

$$\text{where } Treasury_{RD}$$

High confidence

Sensitivity Analysis



Sensitivity Indices for Cost per DALY Averted (Elimination of Efficacy Lag Plus Earlier Treatment Discovery from Increased Trial Throughput)
Regression-based sensitivity showing which inputs explain the most variance in the output.

Input Parameter	Sensitivity Coefficient	Interpretation
Treaty Campaign Total Cost	0.6489	Strong driver
dFDA Trial Capacity Plus Efficacy Lag DALYs	-0.3320	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

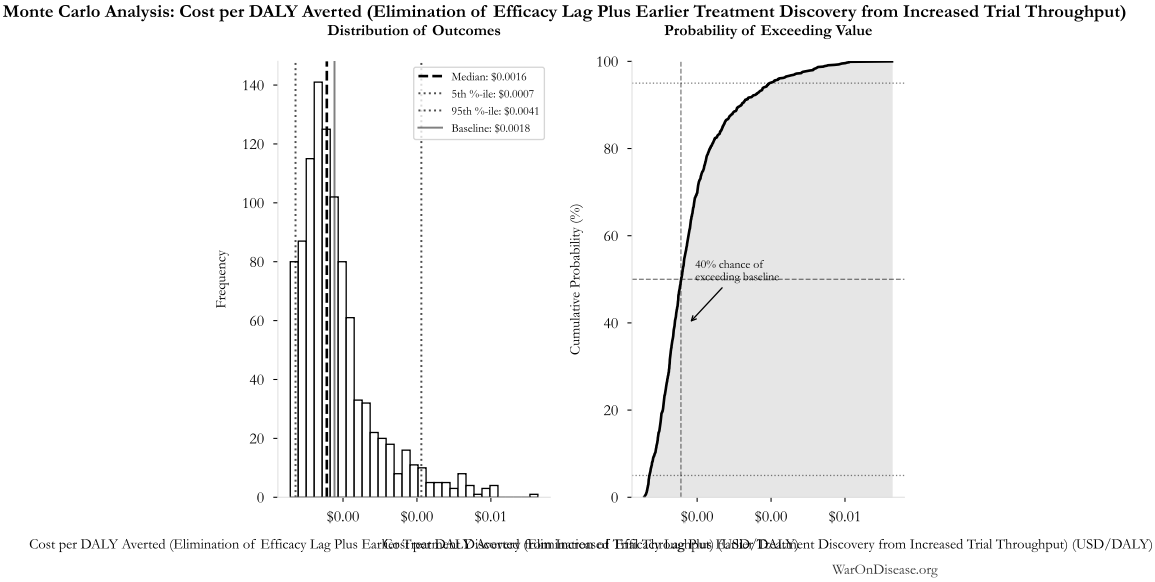


Figure 254: Monte Carlo Distribution: Cost per DALY Averted (Elimination of Efficacy Lag Plus Earlier Treatment Discovery from Increased Trial Throughput) (10,000 simulations)

Simulation Results Summary: Cost per DALY Averted (Elimination of Efficacy Lag Plus Earlier Treatment Discovery from Increased Trial Throughput)

Statistic	Value
Baseline (deterministic)	$0.0018
Mean (expected value)	$0.0019
Median (50th percentile)	$0.0016
Standard Deviation	$0.0011
90% Range (5th-95th percentile)	[$0.0007, $0.0041]

The histogram shows the distribution of Cost per DALY Averted (Elimination of Efficacy Lag Plus Earlier Treatment Discovery from Increased Trial Throughput) 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

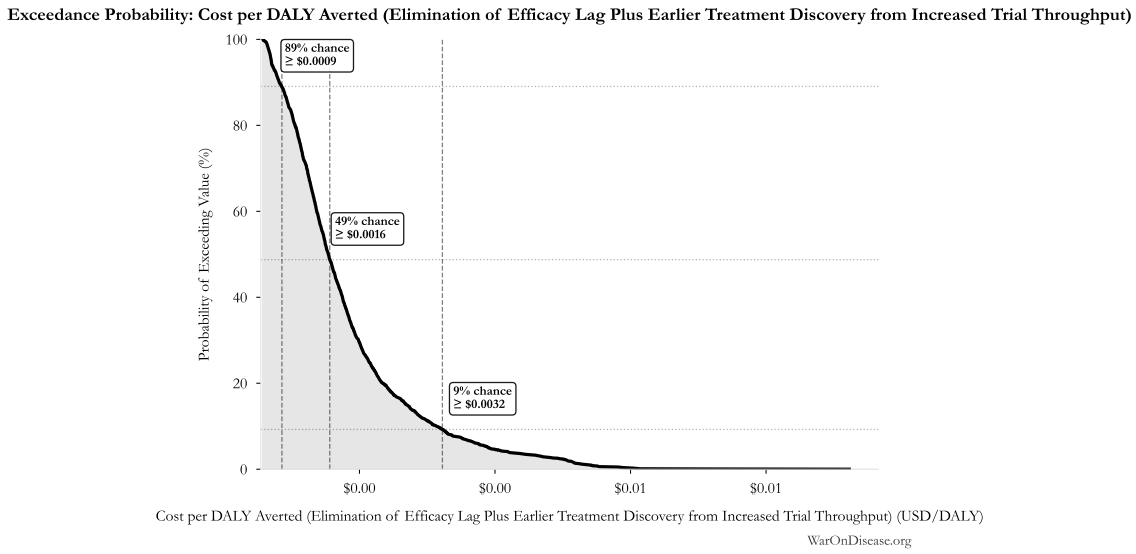


Figure 255: Probability of Exceeding Threshold: Cost per DALY Averted (Elimination of Efficacy Lag Plus Earlier Treatment Discovery from Increased Trial Throughput)

This exceedance probability chart shows the likelihood that Cost per DALY Averted (Elimination of Efficacy Lag Plus Earlier Treatment Discovery from Increased Trial Throughput) will exceed any given threshold. Higher curves indicate more favorable outcomes with greater certainty.

Expected Cost per DALY (Risk-Adjusted): $0.177

Details

Expected cost per DALY accounting for political success probability uncertainty. Monte Carlo samples from beta(0.1%, 10%) distribution. At the conservative 1% estimate, this is still more cost-effective than bed nets ($89.0/DALY).

Inputs:

- Cost per DALY Averted (Elimination of Efficacy Lag Plus Earlier Treatment Discovery from Increased Trial Throughput) : $0.0018
- Political Success Probability : 1% (95% CI: 0.1% - 10%)

$$E[Cost_{DALY}] = \frac{Cost_{treaty,DALY}}{P_{success}} = \frac{\$0.00177}{1\%} = \$0.177$$

$$\text{where } Cost_{treaty,DALY} = \frac{Cost_{campaign}}{DALYs_{max}} = \frac{\$1B}{565B} = \$0.00177$$

$$\begin{aligned}\text{where } Cost_{campaign} \\ = Budget_{viral,base} + Budget_{lobby,treaty} \\ + Budget_{reserve} \\ = \$250M + \$650M + \$100M \\ = \$1B\end{aligned}$$

$$\begin{aligned}\text{where } DALYs_{max} \\ = DALYs_{global,ann} \times Pct_{avoid,DALY} \times T_{accel,max} \\ = 2.88B \times 92.6\% \times 212 \\ = 565B\end{aligned}$$

$$\text{where } T_{accel,max} = T_{accel} + T_{lag} = 204 + 8.2 = 212$$

$$\begin{aligned}\text{where } T_{accel} \\ = T_{first,SQ} \times \left(1 - \frac{1}{k_{capacity}}\right) \\ = 222 \times \left(1 - \frac{1}{12.3}\right) \\ = 204\end{aligned}$$

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

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

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

$$\text{where } k_{capacity} = \frac{N_{fundable,ann}}{Slots_{curr}} = \frac{23.4M}{1.9M} = 12.3$$

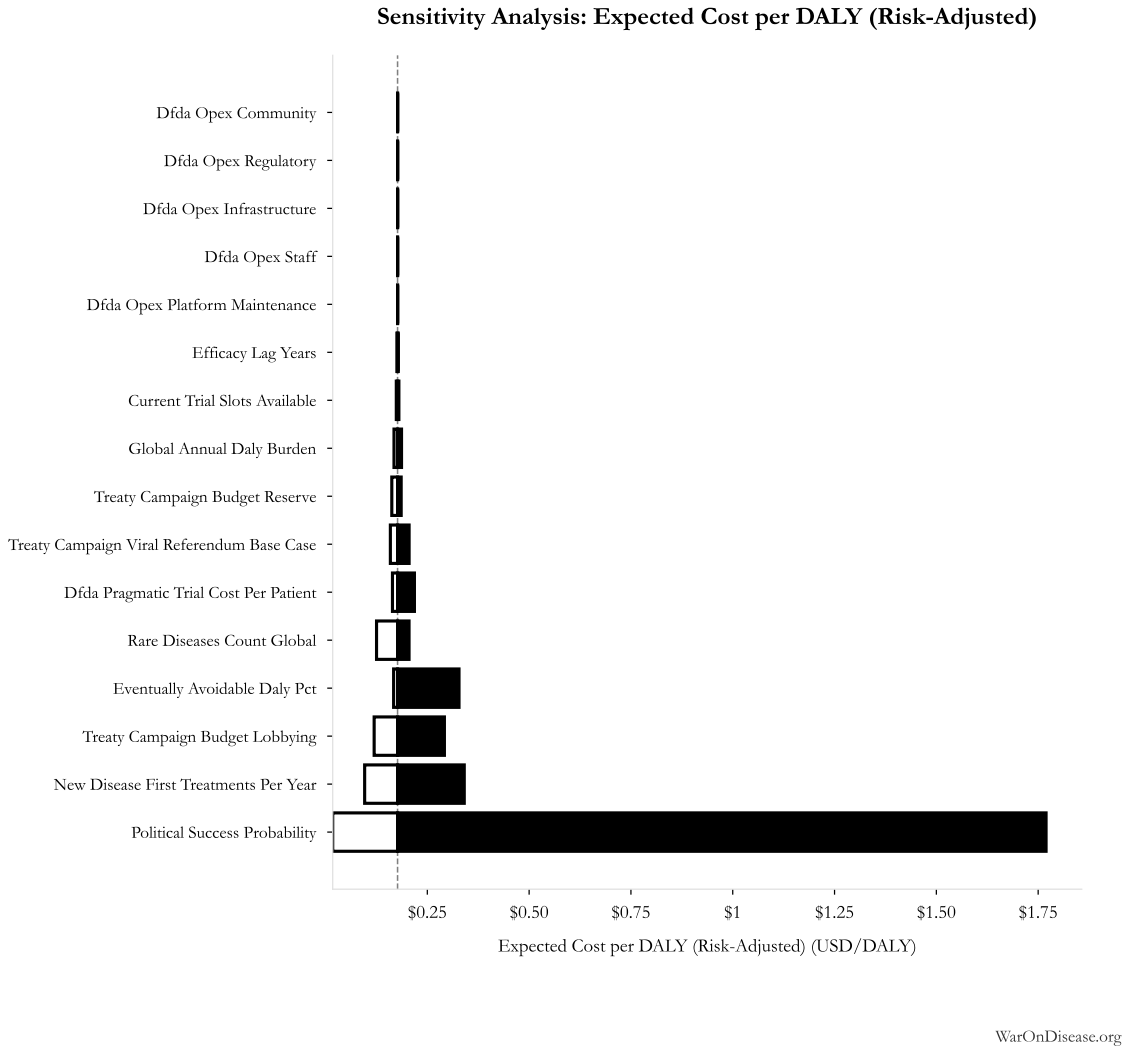
$$\begin{aligned}\text{where } N_{fundable,ann} \\ = \frac{Subsidies_{trial,ann}}{Cost_{pragmatic,pt}} \\ = \frac{\$21.7B}{\$929} \\ = 23.4M\end{aligned}$$

$$\begin{aligned}\text{where } Subsidies_{trial,ann} \\ = Treasury_{RD,ann} - OPEX_{dFDA} \\ = \$21.8B - \$40M \\ = \$21.7B\end{aligned}$$

$$\begin{aligned}\text{where } OPEX_{dFDA} \\ = Cost_{platform} + Cost_{staff} + Cost_{infra} \\ + Cost_{regulatory} + Cost_{community} \\ = \$15M + \$10M + \$8M + \$5M + \$2M\end{aligned}$$

? Low confidence

Sensitivity Analysis



Sensitivity Indices for Expected Cost per DALY (Risk-Adjusted)
Regression-based sensitivity showing which inputs explain the most variance in the output.

Input Parameter	Sensitivity Coefficient	Interpretation
Treaty Cost Per DALY Trial Capacity Plus Efficacy Lag	0.5669	Strong driver
Political Success Probability	-0.4438	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

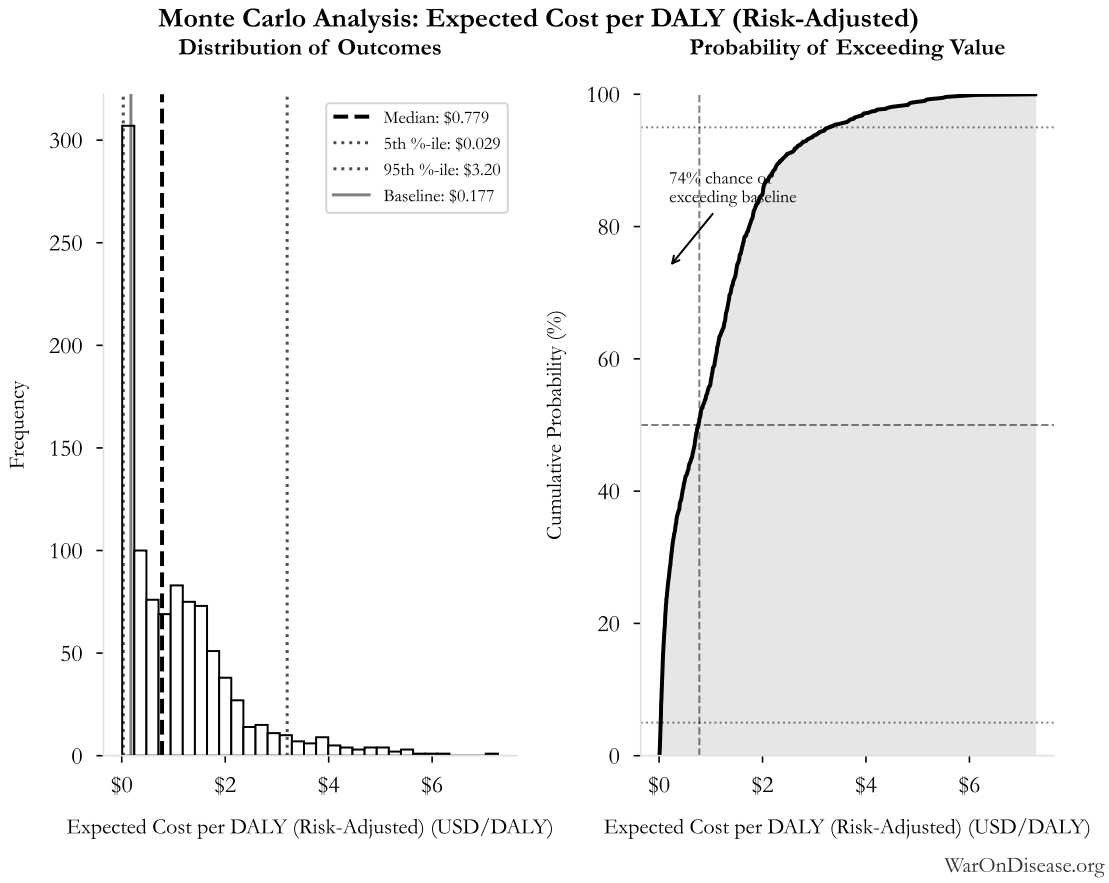


Figure 256: Monte Carlo Distribution: Expected Cost per DALY (Risk-Adjusted) (10,000 simulations)

Simulation Results Summary: Expected Cost per DALY (Risk-Adjusted)

Statistic	Value
Baseline (deterministic)	$0.177
Mean (expected value)	$1.06
Median (50th percentile)	$0.779
Standard Deviation	$1.12
90% Range (5th-95th percentile)	[$0.029, $3.20]

The histogram shows the distribution of Expected Cost per DALY (Risk-Adjusted) 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

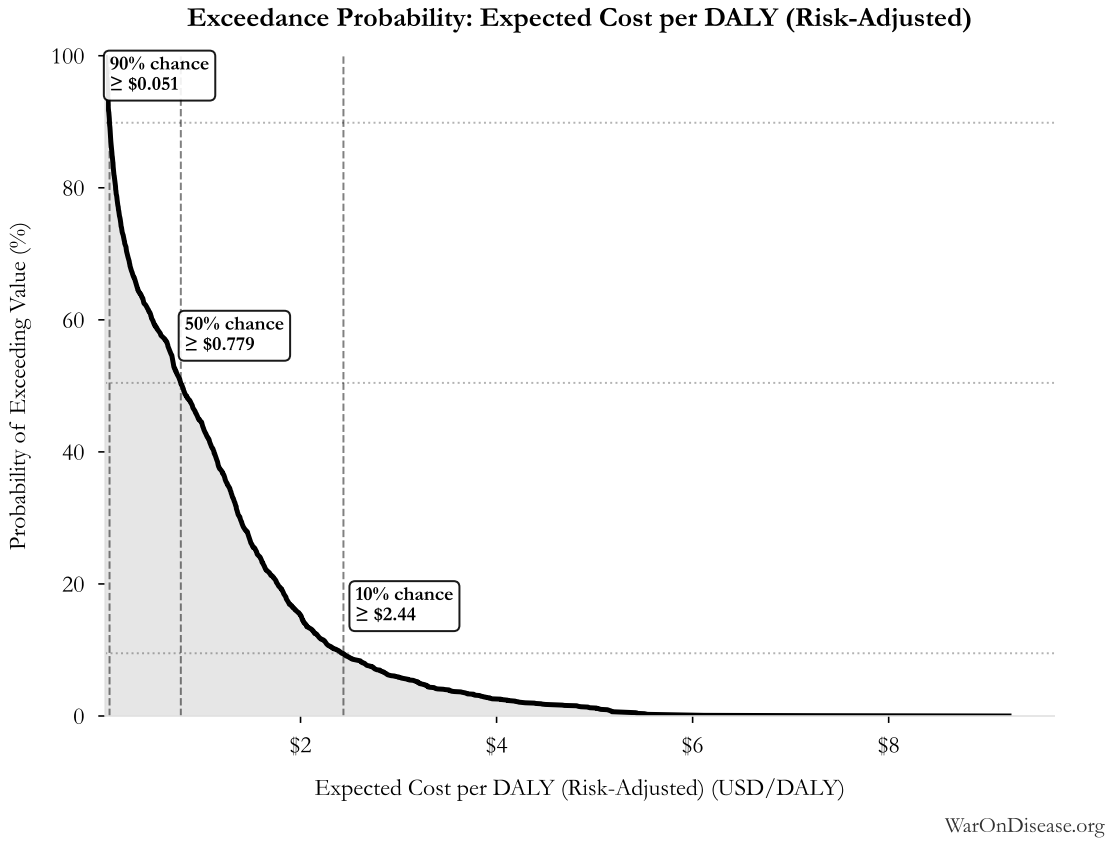


Figure 257: Probability of Exceeding Threshold: Expected Cost per DALY (Risk-Adjusted)

This exceedance probability chart shows the likelihood that Expected Cost per DALY (Risk-Adjusted) will exceed any given threshold. Higher curves indicate more favorable outcomes with greater certainty.

Expected Treaty ROI (Risk-Adjusted): 848k:1

Details

Expected ROI for 1% treaty accounting for political success probability uncertainty. Monte Carlo samples POLITICAL_SUCCESS_PROBABILITY from beta(0.1%, 10%) distribution to generate full expected value distribution. Central value uses 1% probability.

Inputs:

- Treaty ROI - Elimination of Efficacy Lag Plus Earlier Treatment Discovery from Increased Trial Throughput : 84.8M:1
- Political Success Probability : 1% (95% CI: 0.1% - 10%)

$$
\begin{aligned}
&E[ROI_{max}] \\
&= ROI_{max} \times P_{success} \\
&= 84.8M \times 1\% \\
&= 848{,}000
\end{aligned}
$$

$$\text{where } ROI_{max} = \frac{Value_{max}}{Cost_{campaign}} = \frac{\$84800T}{\$1B} = 84.8M$$

$$
\begin{aligned}
&\text{where } Value_{max} \\
&= DALYs_{max} \times Value_{QALY} \\
&= 565B \times \$150K \\
&= \$84800T
\end{aligned}
$$

$$
\begin{aligned}
&\text{where } DALYs_{max} \\
&= DALYs_{global,ann} \times Pct_{avoid,DALY} \times T_{accel,max} \\
&= 2.88B \times 92.6\% \times 212 \\
&= 565B
\end{aligned}
$$

$$\text{where } T_{accel,max} = T_{accel} + T_{lag} = 204 + 8.2 = 212$$

$$
\begin{aligned}
&\text{where } T_{accel} \\
&= T_{first,SQ} \times \left(1 - \frac{1}{k_{capacity}}\right) \\
&= 222 \times \left(1 - \frac{1}{12.3}\right) \\
&= 204
\end{aligned}
$$

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

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

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

$$\text{where } k_{capacity} = \frac{N_{fundable,ann}}{Slots_{curr}} = \frac{23.4M}{1.9M} = 12.3$$

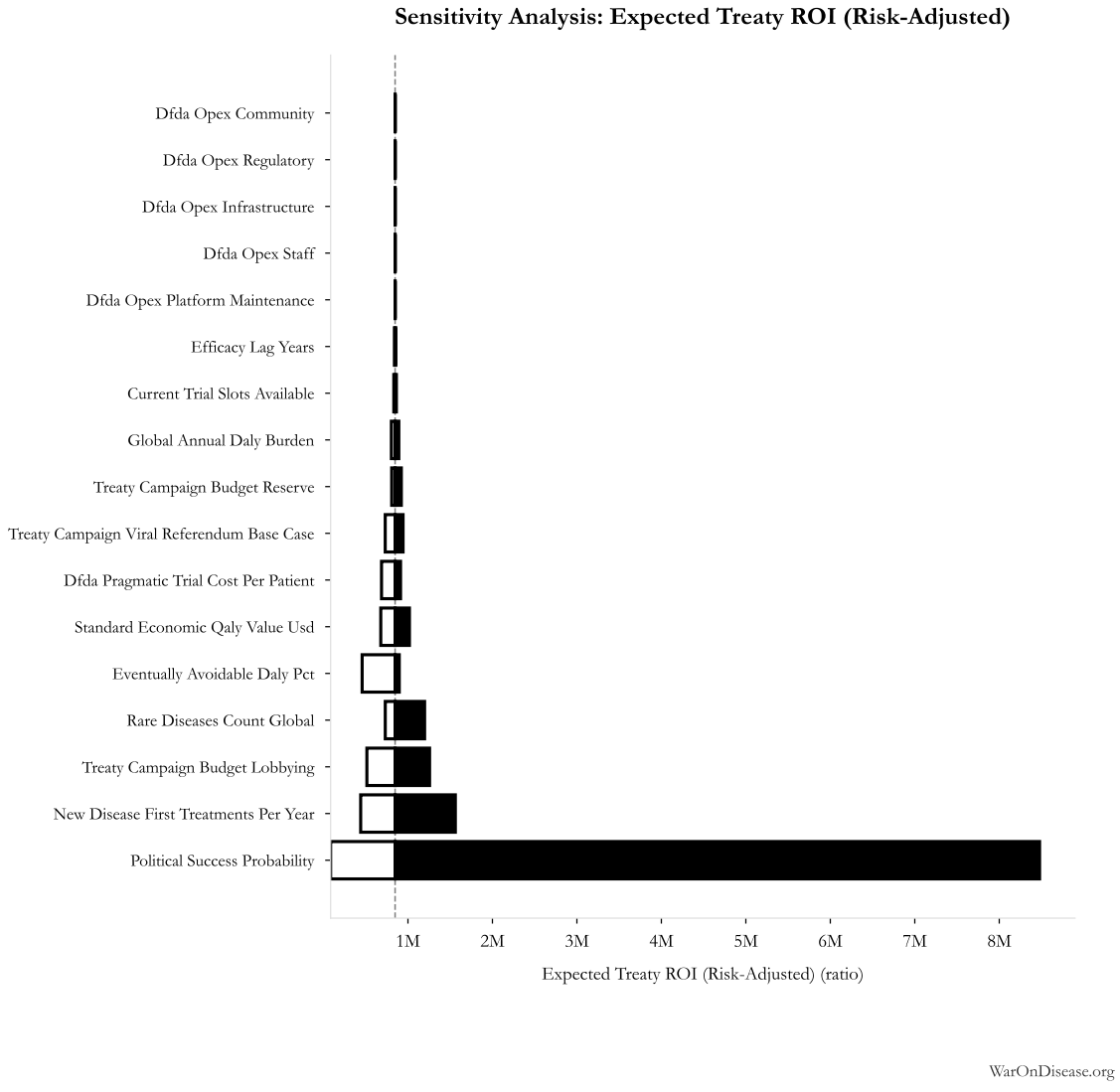
$$
\begin{aligned}
&\text{where } N_{fundable,ann} \\
&= \frac{Subsidies_{trial,ann}}{Cost_{pragmatic,pt}} \\
&= \frac{\$21.7B}{\$929} \\
&= 23.4M
\end{aligned}
$$

$$
\begin{aligned}
&\text{where } Subsidies_{trial,ann} \\
&= Treasury_{RD,ann} - OPEX_{dFDA} \\
&= \$21.8B - \$40M \\
&= \$21.7B
\end{aligned}
$$

$$
\begin{aligned}
&\text{where } OPEX_{dFDA} \\
&= Cost_{platform} + Cost_{staff} + Cost_{infra} \\
&+ Cost_{\quad} + Cost_{\quad}
\end{aligned}
$$

Methodology: Direct Calculation
? Low confidence

Sensitivity Analysis



Sensitivity Indices for Expected Treaty ROI (Risk-Adjusted)

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

Input Parameter	Sensitivity Coefficient	Interpretation
Political Success Probability	0.9453	Strong driver
Treaty ROI Trial Capacity Plus Efficacy Lag	0.1601	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

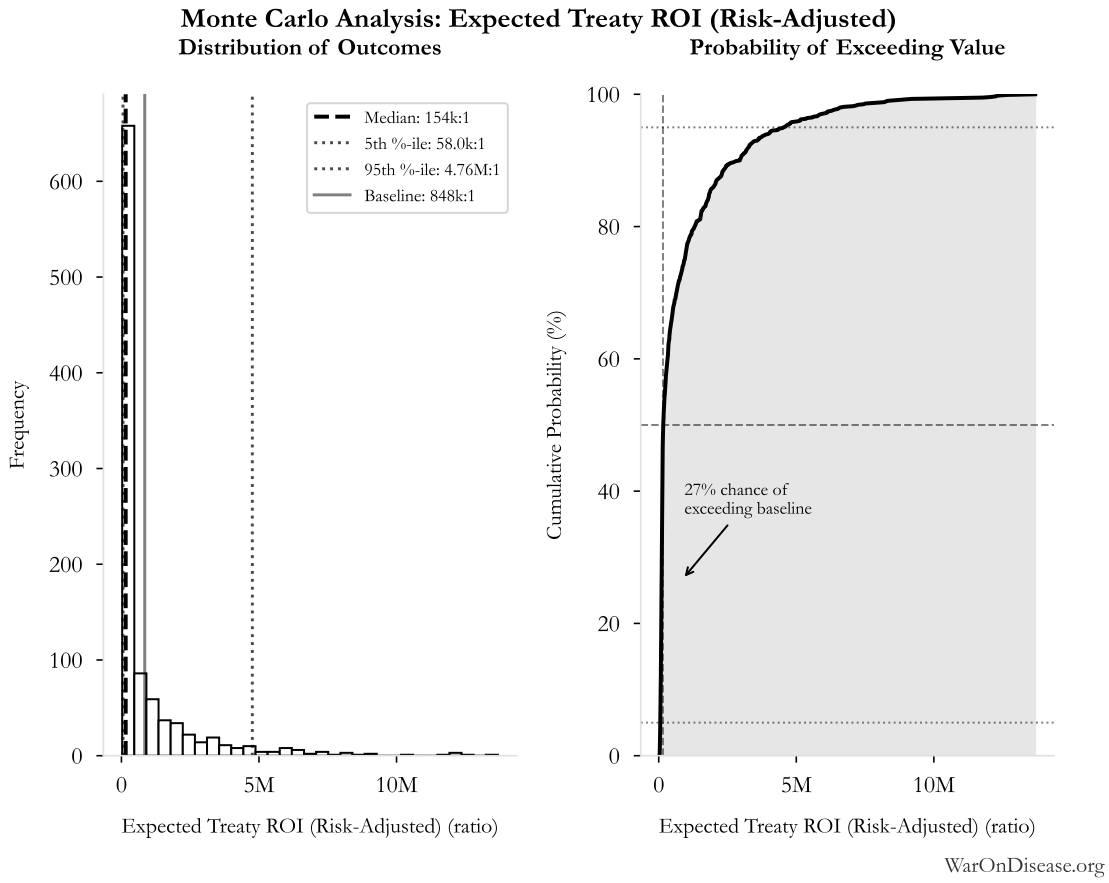


Figure 258: Monte Carlo Distribution: Expected Treaty ROI (Risk-Adjusted) (10,000 simulations)

Simulation Results Summary: Expected Treaty ROI (Risk-Adjusted)

Statistic	Value
Baseline (deterministic)	848k:1
Mean (expected value)	962k:1
Median (50th percentile)	154k:1
Standard Deviation	1.80M:1
90% Range (5th-95th percentile)	[58.0k:1, 4.76M:1]

The histogram shows the distribution of Expected Treaty ROI (Risk-Adjusted) 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

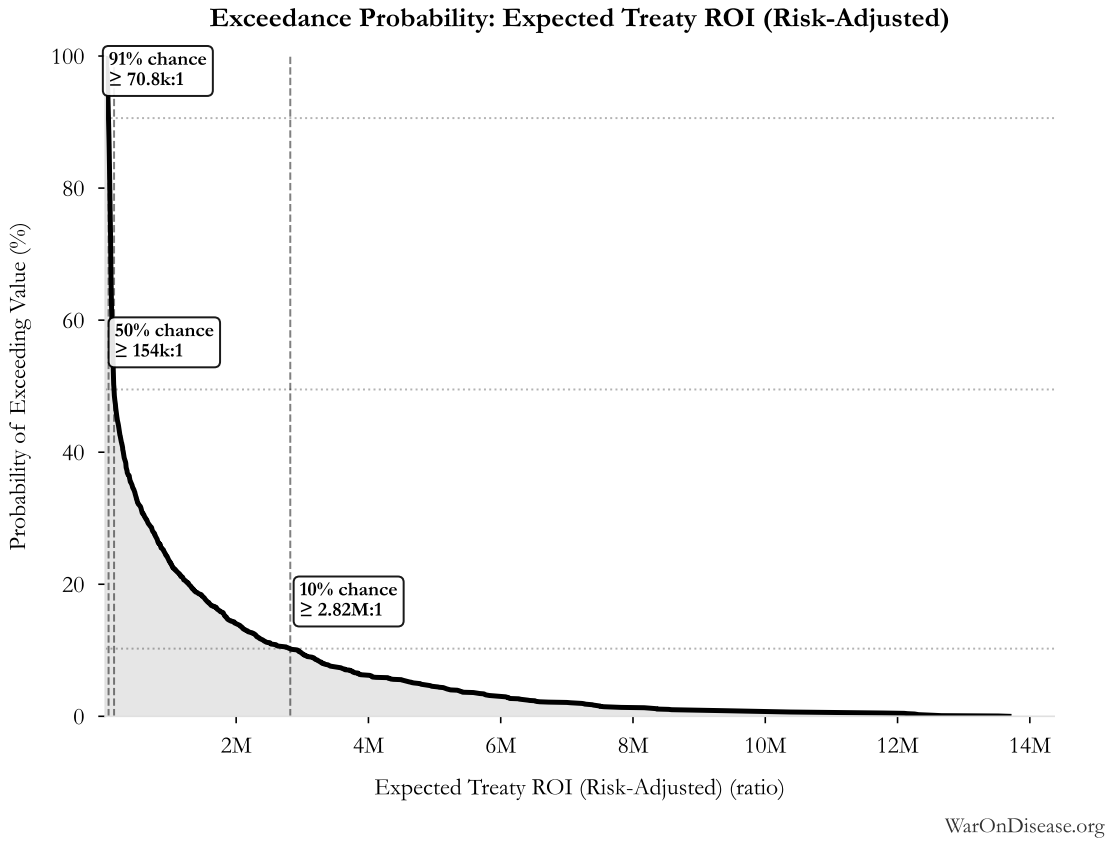


Figure 259: Probability of Exceeding Threshold: Expected Treaty ROI (Risk-Adjusted)

This exceedance probability chart shows the likelihood that Expected Treaty ROI (Risk-Adjusted) will exceed any given threshold. Higher curves indicate more favorable outcomes with greater certainty.

Expected Cost-Effectiveness vs Bed Nets Multiplier: 503x

Details

Expected value multiplier vs bed nets (accounts for political uncertainty at 1% success rate)
Inputs:

- Bed Nets Cost per DALY : $89 (95% CI: $78 - $100)
- Expected Cost per DALY (Risk-Adjusted) : $0.177

$$E[k_{nets}] = \frac{Cost_{nets}}{E[Cost_{DALY}]} = \frac{\$89}{\$0.177} = 503$$

$$\text{where } E[Cost_{DALY}] = \frac{Cost_{treaty,DALY}}{P_{success}} = \frac{\$0.00177}{1\%} = \$0.177$$

$$\text{where } Cost_{treaty,DALY} = \frac{Cost_{campaign}}{DALYs_{max}} = \frac{\$1B}{565B} = \$0.00177$$

$$\begin{gathered}\text{where } Cost_{campaign} \\ = Budget_{viral,base} + Budget_{lobby,treaty} \\ + Budget_{reserve} \\ = \$250M + \$650M + \$100M \\ = \$1B\end{gathered}$$

$$\begin{gathered}\text{where } DALYs_{max} \\ = DALYs_{global,ann} \times Pct_{avoid,DALY} \times T_{accel,max} \\ = 2.88B \times 92.6\% \times 212 \\ = 565B\end{gathered}$$

$$\text{where } T_{accel,max} = T_{accel} + T_{lag} = 204 + 8.2 = 212$$

$$\begin{gathered}\text{where } T_{accel} \\ = T_{first,SQ} \times \left(1 - \frac{1}{k_{capacity}}\right) \\ = 222 \times \left(1 - \frac{1}{12.3}\right) \\ = 204\end{gathered}$$

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

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

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

$$\text{where } k_{capacity} = \frac{N_{fundable,ann}}{Slots_{curr}} = \frac{23.4M}{1.9M} = 12.3$$

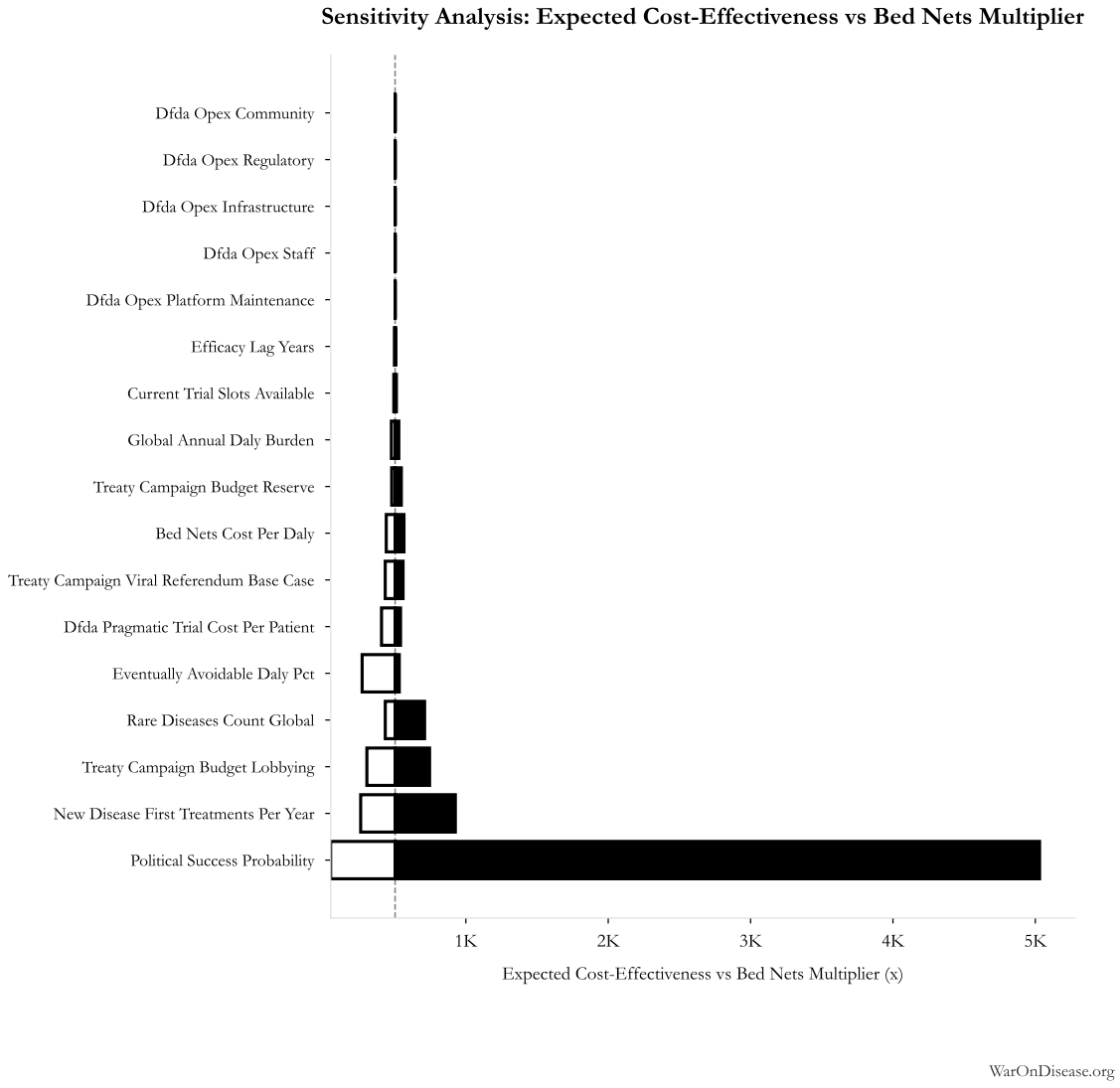
$$\begin{gathered}\text{where } N_{fundable,ann} \\ = \frac{Subsidies_{trial,ann}}{Cost_{pragmatic,pt}} \\ = \frac{\$21.7B}{\$929} \\ = 23.4M\end{gathered}$$

$$\begin{gathered}\text{where } Subsidies_{trial,ann} \\ = Treasury_{RD,ann} - OPEX_{dFDA} \\ = \$21.8B - \$40M \\ = \$21.7B\end{gathered}$$

$$\begin{gathered}\text{where } OPEX_{dFDA} \\ = Cost_{platform} + Cost_{staff} + Cost_{infra}\end{gathered}$$

? Low confidence

Sensitivity Analysis



Sensitivity Indices for Expected Cost-Effectiveness vs Bed Nets Multiplier
Regression-based sensitivity showing which inputs explain the most variance in the output.

Input Parameter	Sensitivity Coefficient	Interpretation
Treaty Expected Cost Per DALY	-0.4156	Moderate driver
Bed Nets Cost Per DALY	0.0039	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.

Monte Carlo Distribution

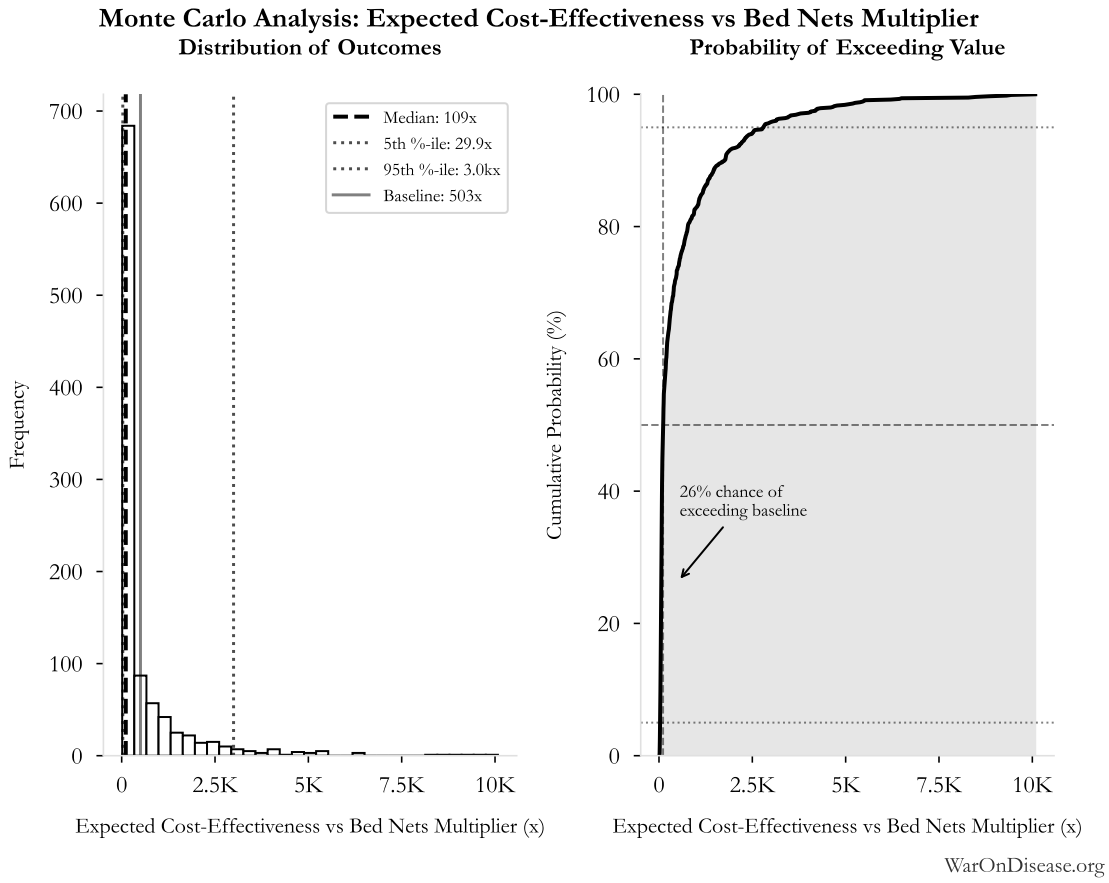


Figure 260: Monte Carlo Distribution: Expected Cost-Effectiveness vs Bed Nets Multiplier (10,000 simulations)

Simulation Results Summary: Expected Cost-Effectiveness vs Bed Nets Multiplier

Statistic	Value
Baseline (deterministic)	503x
Mean (expected value)	605x
Median (50th percentile)	109x
Standard Deviation	1.2kx
90% Range (5th-95th percentile)	[29.9x, 3.0kx]

The histogram shows the distribution of Expected Cost-Effectiveness vs Bed Nets Multiplier 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

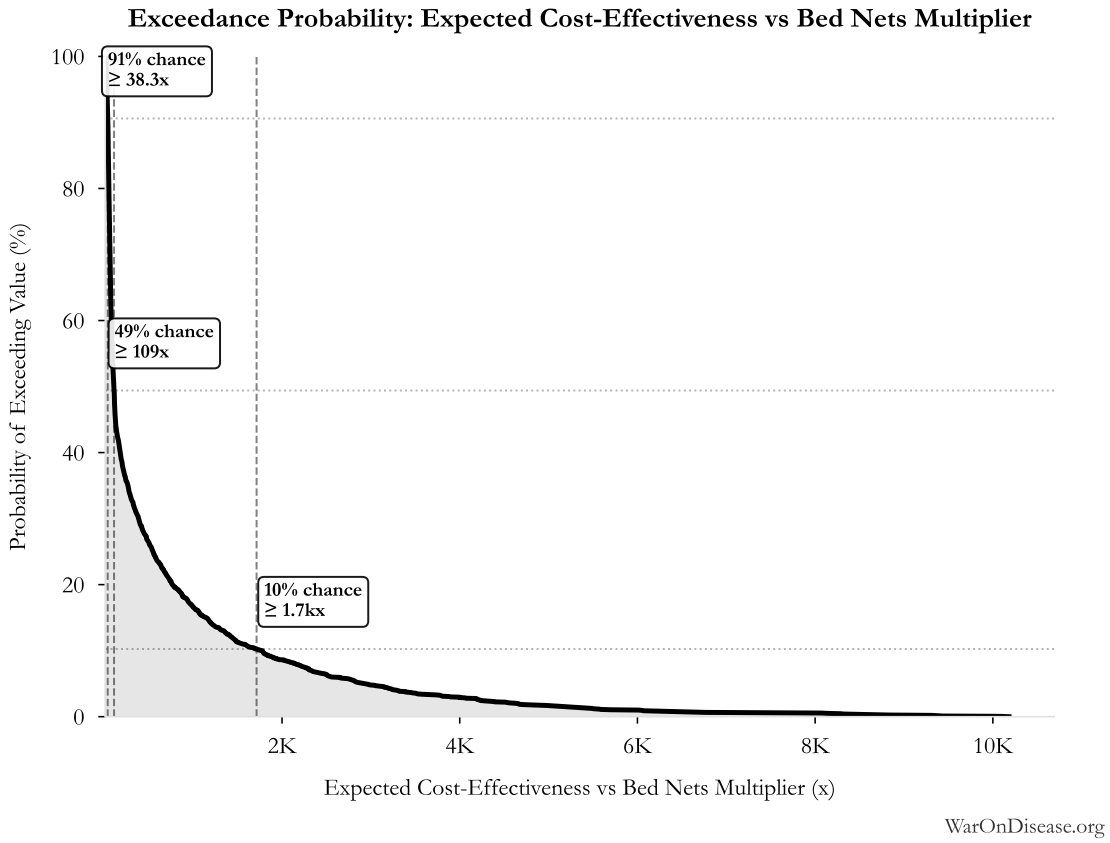


Figure 261: Probability of Exceeding Threshold: Expected Cost-Effectiveness vs Bed Nets Multiplier

This exceedance probability chart shows the likelihood that Expected Cost-Effectiveness vs Bed Nets Multiplier will exceed any given threshold. Higher curves indicate more favorable outcomes with greater certainty.

1% treaty Basic Annual Benefits (Peace + R&D Savings): $172B

Details

Basic annual benefits: peace dividend + Decentralized Framework for Drug Assessment R&D savings only (2 of 8 benefit categories, excludes regulatory delay value)

Inputs:

- Annual Peace Dividend from 1% Reduction in Total War Costs : $114B
- Decentralized Framework for Drug Assessment Annual Benefit: R&D Savings : $58.6B

$$Benefit_{peace+RD}$$
$$= Benefit_{peace,soc} + Benefit_{RD,ann}$$
$$= \$114B + \$58.6B$$
$$= \$172B$$

where $Benefit_{peace,soc}$
$$= Cost_{war,total} \times Reduce_{treaty}$$
$$= \$11.4T \times 1\%$$
$$= \$114B$$

where $Cost_{war,total}$
$$= Cost_{war,direct} + Cost_{war,indirect}$$
$$= \$7.66T + \$3.7T$$
$$= \$11.4T$$

where $Cost_{war,direct}$
$$= Loss_{life,conflict} + Damage_{infra,total}$$
$$+Disruption_{trade} + Spending_{mil}$$
$$= \$2.45T + \$1.88T + \$616B + \$2.72T$$
$$= \$7.66T$$

where $Loss_{life,conflict}$
$$= Cost_{combat,human} + Cost_{state,human}$$
$$+Cost_{terror,human}$$
$$= \$2.34T + \$27B + \$83B$$
$$= \$2.45T$$

where $Cost_{combat,human}$
$$= Deaths_{combat} \times VSL$$
$$= 234{,}000 \times \$10M$$
$$= \$2.34T$$

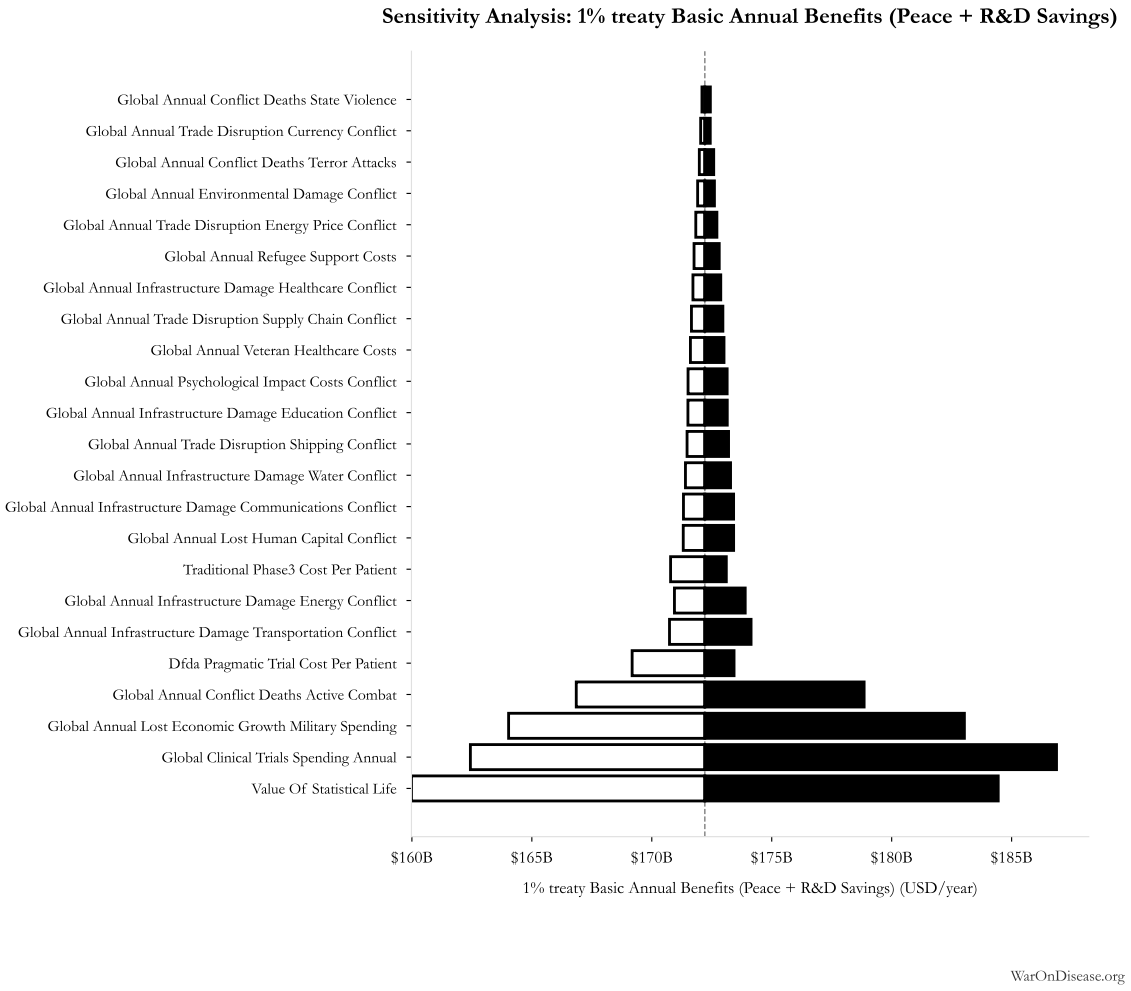
where $Cost_{state,human}$
$$= Deaths_{state} \times VSL$$
$$= 2{,}700 \times \$10M$$
$$= \$27B$$

where $Cost_{terror,human}$
$$= Deaths_{terror} \times VSL$$
$$= 8{,}300 \times \$10M$$
$$= \$83B$$

where $Damage_{infra,total}$
$$= Damage_{comms} + Damage_{edu} + Damage_{energy}$$
$$+Damage_{health} + Damage_{transport}$$
$$+Damage_{water}$$
$$= \$298B + \$234B + \$422B + \$166B + \$487B + \$268B$$

High confidence

Sensitivity Analysis



Sensitivity Indices for 1% treaty Basic Annual Benefits (Peace + R&D Savings)
Regression-based sensitivity showing which inputs explain the most variance in the output.

Input Parameter	Sensitivity Coefficient	Interpretation
Peace Dividend Annual Societal Benefit	0.6828	Strong driver
dFDA Benefit R&D Only Annual	0.3457	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

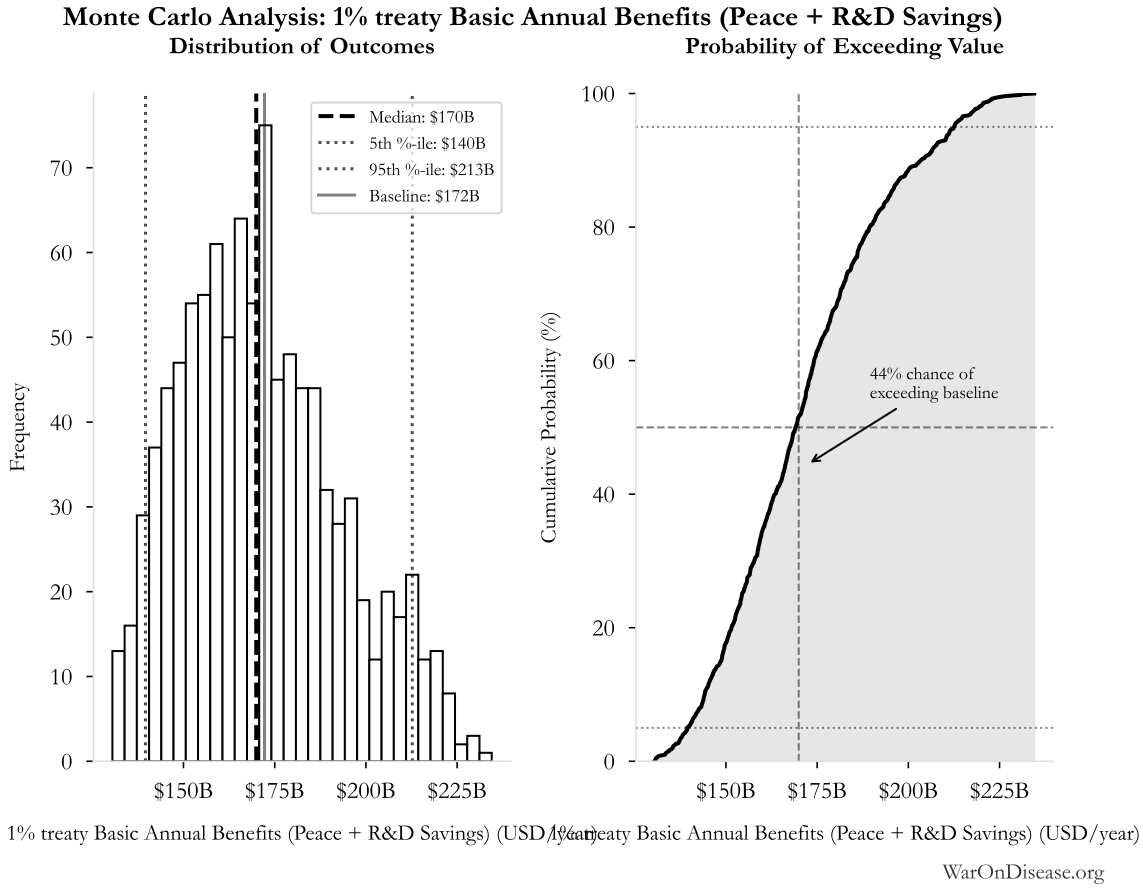


Figure 262: Monte Carlo Distribution: 1% treaty Basic Annual Benefits (Peace + R&D Savings) (10,000 simulations)

Simulation Results Summary: 1% treaty Basic Annual Benefits (Peace + R&D Savings)

Statistic	Value
Baseline (deterministic)	$172B
Mean (expected value)	$172B
Median (50th percentile)	$170B
Standard Deviation	$22.2B
90% Range (5th-95th percentile)	[$140B, $213B]

The histogram shows the distribution of 1% treaty Basic Annual Benefits (Peace + R&D Savings) 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

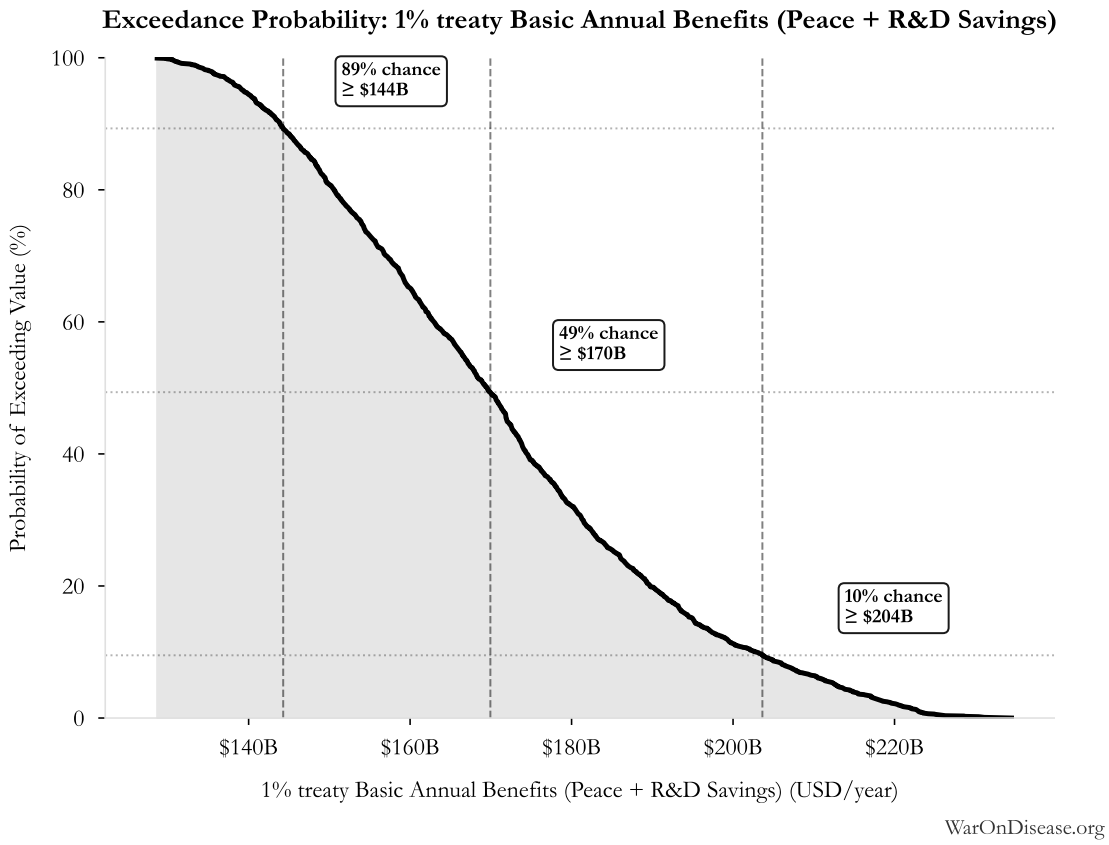


Figure 263: Probability of Exceeding Threshold: 1% treaty Basic Annual Benefits (Peace + R&D Savings)

This exceedance probability chart shows the likelihood that 1% treaty Basic Annual Benefits (Peace + R&D Savings) will exceed any given threshold. Higher curves indicate more favorable outcomes with greater certainty.

Treaty ROI - Elimination of Efficacy Lag Plus Earlier Treatment Discovery from Increased Trial Throughput: 84.8M:1

Details

Treaty ROI from elimination of efficacy lag plus earlier treatment discovery from increased trial throughput. Total one-time benefit divided by campaign cost. This is the primary ROI estimate for total health benefits.

Inputs:

- Total Economic Benefit from Elimination of Efficacy Lag Plus Earlier Treatment Discovery from Higher Trial Throughput : $84.8 quadrillion
- Total 1% Treaty Campaign Cost : $1B

$$ROI_{max} = \frac{Value_{max}}{Cost_{campaign}} = \frac{\$84800T}{\$1B} = 84.8M$$

$$\text{where } Value_{max} = DALYs_{max} \times Value_{QALY} = 565B \times \$150K = \$84800T$$

$$\text{where } DALYs_{max} = DALYs_{global,ann} \times Pct_{avoid,DALY} \times T_{accel,max} = 2.88B \times 92.6\% \times 212 = 565B$$

$$\text{where } T_{accel,max} = T_{accel} + T_{lag} = 204 + 8.2 = 212$$

$$\text{where } T_{accel} = T_{first,SQ} \times \left(1 - \frac{1}{k_{capacity}}\right) = 222 \times \left(1 - \frac{1}{12.3}\right) = 204$$

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

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

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

$$\text{where } k_{capacity} = \frac{N_{fundable,ann}}{Slots_{curr}} = \frac{23.4M}{1.9M} = 12.3$$

$$\text{where } N_{fundable,ann} = \frac{Subsidies_{trial,ann}}{Cost_{pragmatic,pt}} = \frac{\$21.7B}{\$929} = 23.4M$$

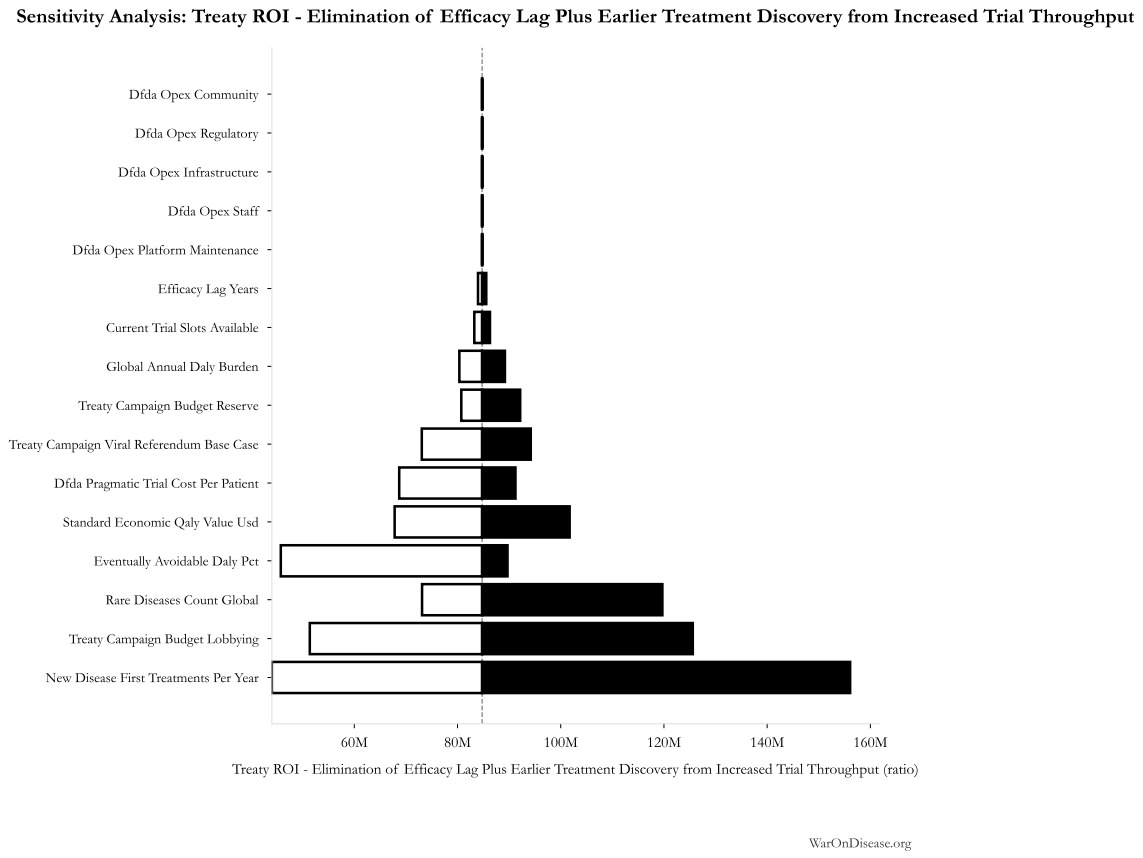
$$\text{where } Subsidies_{trial,ann} = Treasury_{RD,ann} - OPEX_{dFDA} = \$21.8B - \$40M = \$21.7B$$

$$\text{where } OPEX_{dFDA} = Cost_{platform} + Cost_{staff} + Cost_{infra} + Cost_{regulatory} + Cost_{community} = \$15M + \$10M + \$8M + \$5M + \$2M = \$40M$$

$$\text{where } Treasury_{RD,ann} = Funding_{...} = Payout_{...} = Funding_{...}$$

~ Medium confidence

Sensitivity Analysis



Sensitivity Indices for Treaty ROI - Elimination of Efficacy Lag Plus Earlier Treatment Discovery from Increased Trial Throughput
Regression-based sensitivity showing which inputs explain the most variance in the output.

Input Parameter	Sensitivity Coefficient	Interpretation
Treaty Campaign Total Cost	-0.7928	Strong driver
dFDA Trial Capacity Plus Efficacy Lag Economic Value	0.3363	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

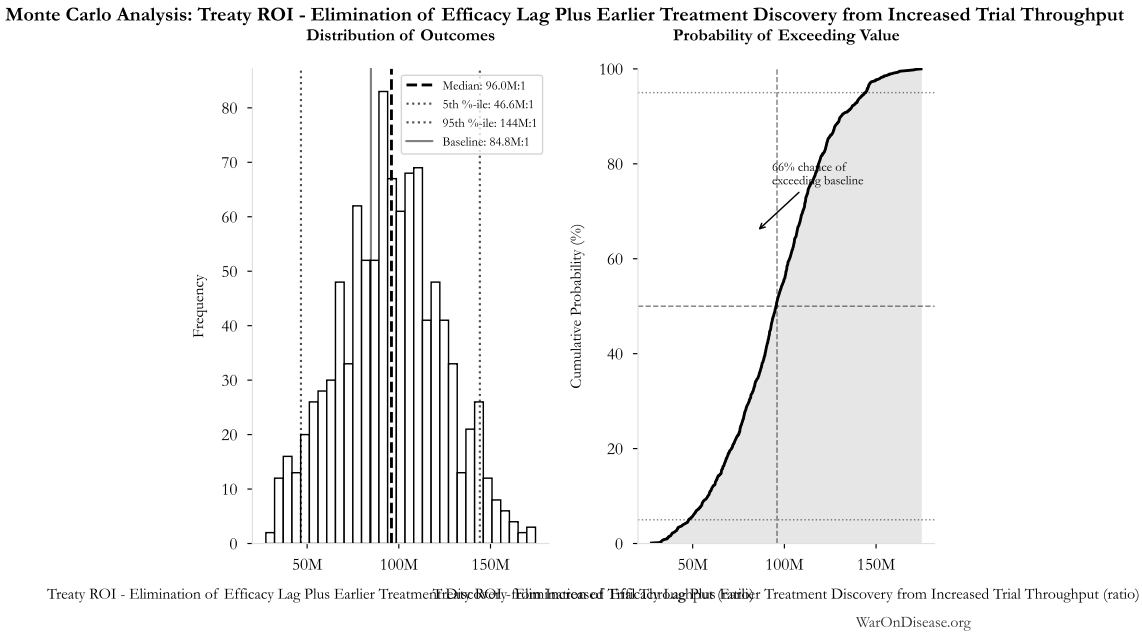


Figure 264: Monte Carlo Distribution: Treaty ROI - Elimination of Efficacy Lag Plus Earlier Treatment Discovery from Increased Trial Throughput (10,000 simulations)

Simulation Results Summary: Treaty ROI - Elimination of Efficacy Lag Plus Earlier Treatment Discovery from Increased Trial Throughput

Statistic	Value
Baseline (deterministic)	84.8M:1
Mean (expected value)	95.1M:1
Median (50th percentile)	96.0M:1
Standard Deviation	28.2M:1
90% Range (5th-95th percentile)	[46.6M:1, 144M:1]

The histogram shows the distribution of Treaty ROI - Elimination of Efficacy Lag Plus Earlier Treatment Discovery from Increased Trial Throughput 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

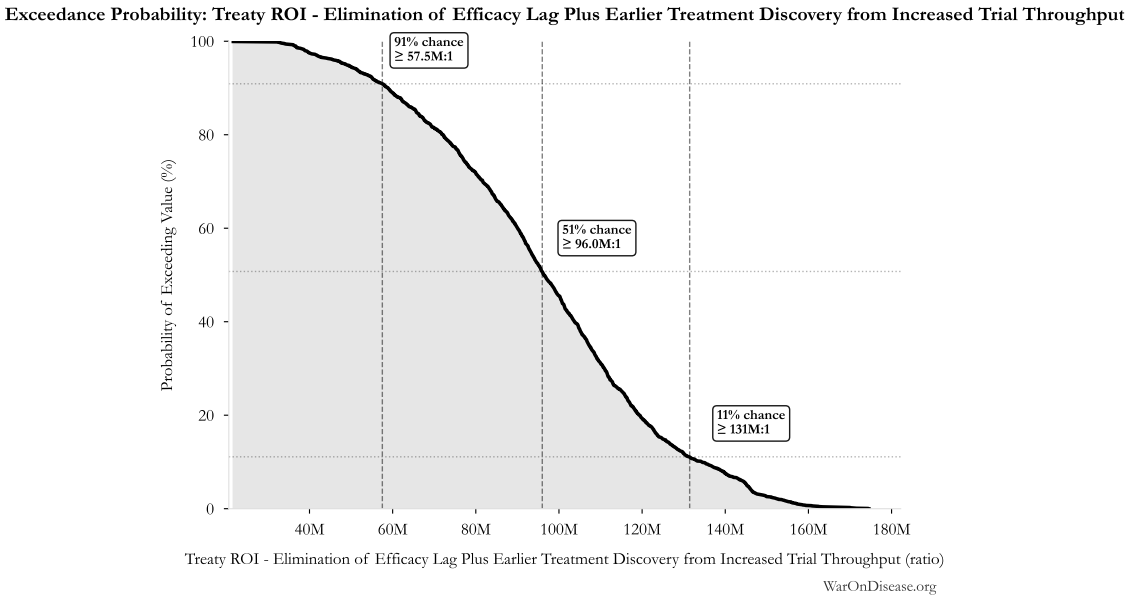


Figure 265: Probability of Exceeding Threshold: Treaty ROI - Elimination of Efficacy Lag Plus Earlier Treatment Discovery from Increased Trial Throughput

This exceedance probability chart shows the likelihood that Treaty ROI - Elimination of Efficacy Lag Plus Earlier Treatment Discovery from Increased Trial Throughput will exceed any given threshold. Higher curves indicate more favorable outcomes with greater certainty.

Cost-Effectiveness vs Bed Nets Multiplier: 50.3kx

Details

How many times more cost-effective than bed nets (using $89/DALY midpoint estimate)
Inputs:

- Bed Nets Cost per DALY : $89 (95% CI: $78 - $100)
- Cost per DALY Averted (Elimination of Efficacy Lag Plus Earlier Treatment Discovery from Increased Trial Throughput) : $0.0018

$$k_{treaty:nets} = \frac{Cost_{nets}}{Cost_{treaty,DALY}} = \frac{\$89}{\$0.00177} = 50{,}300$$

where $Cost_{treaty,DALY} = \frac{Cost_{campaign}}{DALYs_{max}} = \frac{\$1B}{565B} = \$0.00177$

where $Cost_{campaign} = Budget_{viral,base} + Budget_{lobby,treaty} + Budget_{reserve} = \$250M + \$650M + \$100M = \$1B$

where $DALYs_{max} = DALYs_{global,ann} \times Pct_{avoid,DALY} \times T_{accel,max} = 2.88B \times 92.6\% \times 212 = 565B$

where $T_{accel,max} = T_{accel} + T_{lag} = 204 + 8.2 = 212$

where $T_{accel} = T_{first,SQ} \times \left(1 - \frac{1}{k_{capacity}}\right) = 222 \times \left(1 - \frac{1}{12.3}\right) = 204$

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

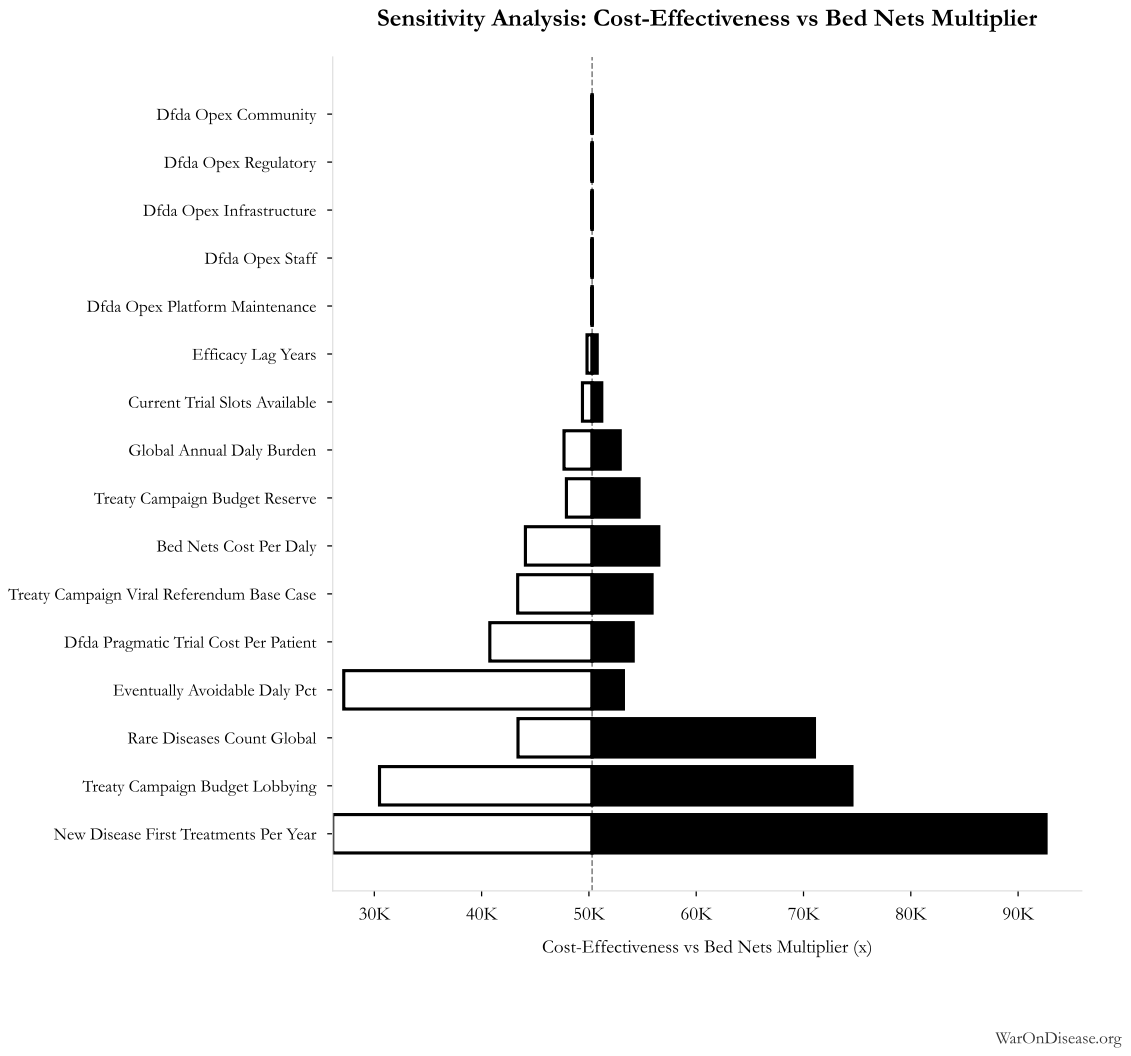
where $k_{capacity} = \frac{N_{fundable,ann}}{Slots_{curr}} = \frac{23.4M}{1.9M} = 12.3$

where $N_{fundable,ann} = \frac{Subsidies_{trial,ann}}{Cost_{pragmatic,pt}} = \frac{\$21.7B}{\$929} = 23.4M$

where $Subsidies_{trial,ann} = Treasury_{RD,561} - OPEX_{dFDA} = \$21.8B - \$40M = \$21.7B$

High confidence

Sensitivity Analysis



Sensitivity Indices for Cost-Effectiveness vs Bed Nets Multiplier
Regression-based sensitivity showing which inputs explain the most variance in the output.

Input Parameter	Sensitivity Coefficient	Interpretation
Bed Nets Cost Per DALY	-0.8686	Strong driver
Treaty Cost Per DALY	-0.0847	Minimal effect
Trial Capacity Plus Efficacy Lag		

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

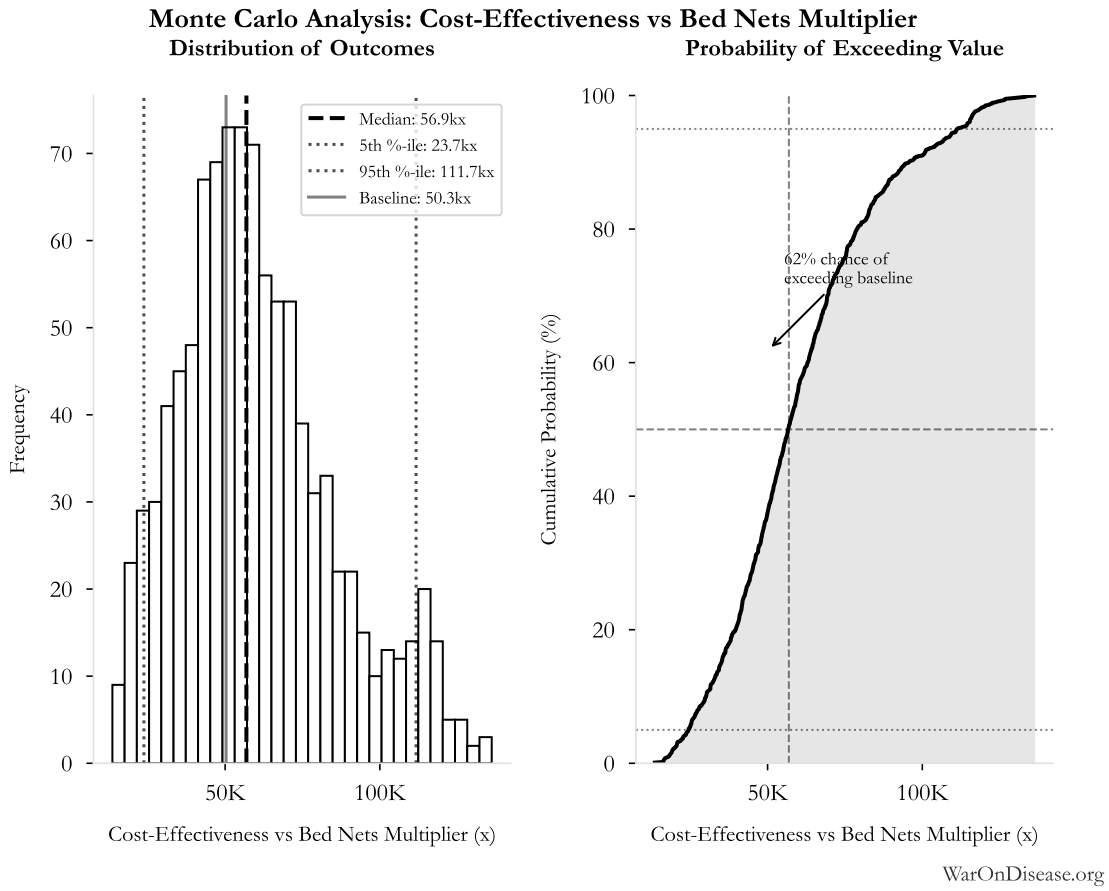


Figure 266: Monte Carlo Distribution: Cost-Effectiveness vs Bed Nets Multiplier (10,000 simulations)

Simulation Results Summary: Cost-Effectiveness vs Bed Nets Multiplier

Statistic	Value
Baseline (deterministic)	50.3kx
Mean (expected value)	59.9kx
Median (50th percentile)	56.9kx
Standard Deviation	25.0kx
90% Range (5th-95th percentile)	[23.7kx, 111.7kx]

The histogram shows the distribution of Cost-Effectiveness vs Bed Nets Multiplier 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

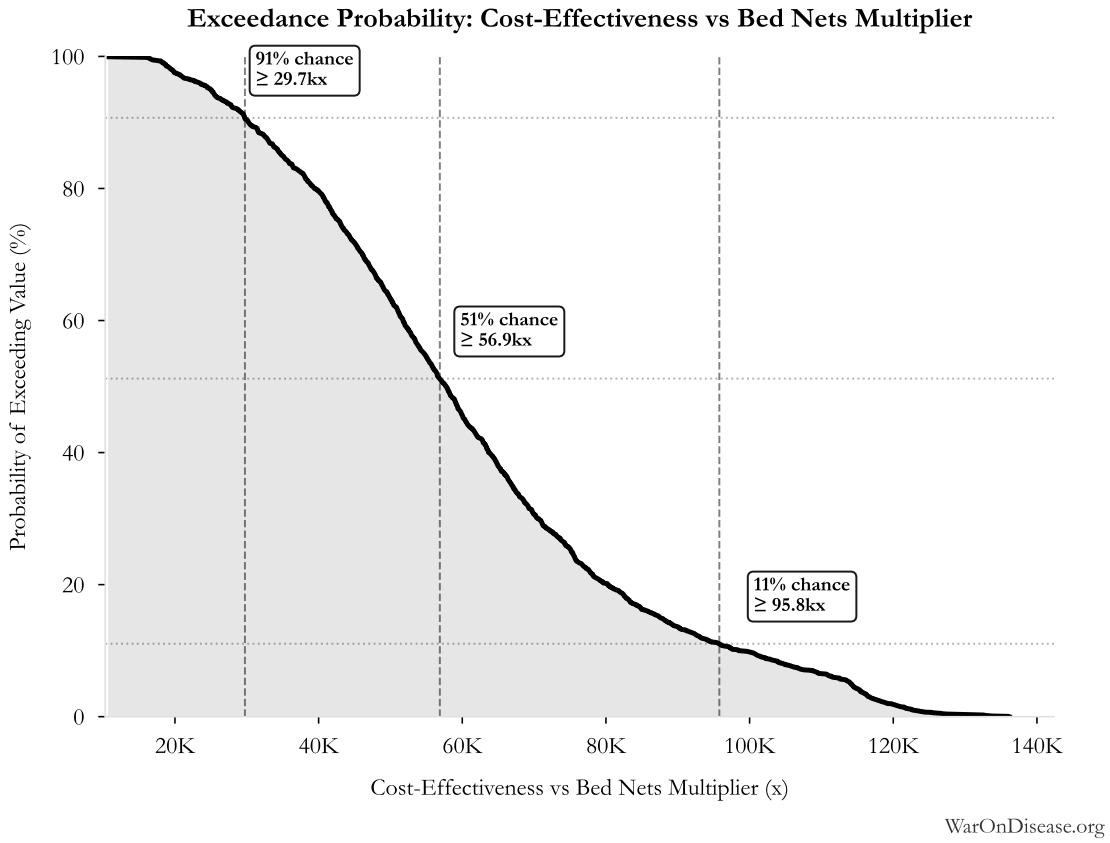


Figure 267: Probability of Exceeding Threshold: Cost-Effectiveness vs Bed Nets Multiplier

This exceedance probability chart shows the likelihood that Cost-Effectiveness vs Bed Nets Multiplier will exceed any given threshold. Higher curves indicate more favorable outcomes with greater certainty.

Treaty Campaign Leverage vs Direct Funding: 475x

Details

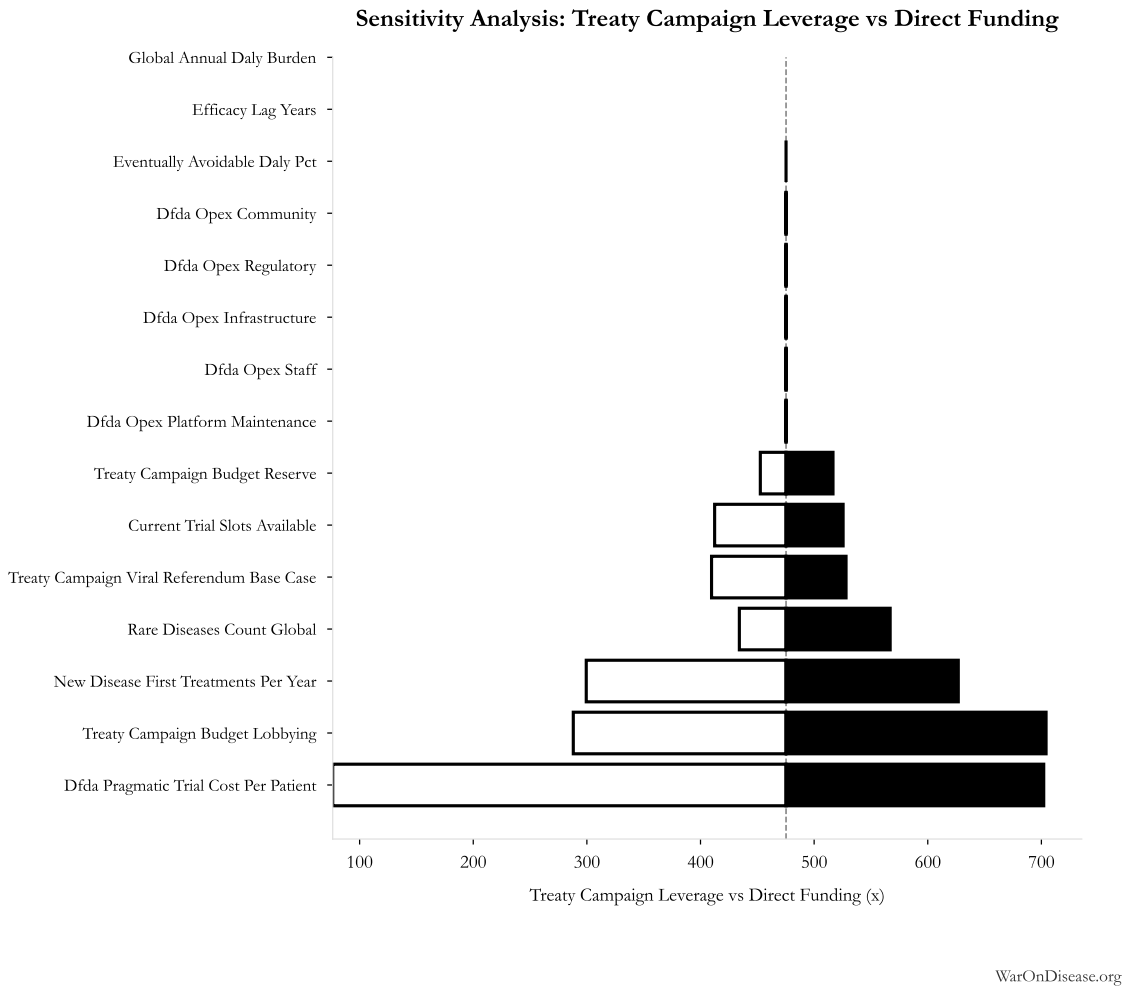
How many times more cost-effective the treaty campaign is vs direct funding. Treaty achieves 542× leverage: $1B campaign unlocks $27.2B/year government funding for 46.5 years (exploration period, NPV: $541.9B), avoiding need for philanthropists/NIH to directly commit this amount. Both approaches achieve same 200B DALY timeline shift benefit by exploring the therapeutic space 9.5× faster. Treaty spreads cost across governments while building sustainable public funding infrastructure.

Inputs:

- dFDA Direct Funding Cost per DALY : $0.841
- Cost per DALY Averted (Elimination of Efficacy Lag Plus Earlier Treatment Discovery from Increased Trial Throughput) : $0.0018

High confidence

Sensitivity Analysis



Sensitivity Indices for Treaty Campaign Leverage vs Direct Funding
Regression-based sensitivity showing which inputs explain the most variance in the output.

Input Parameter	Sensitivity Coefficient	Interpretation
dFDA Direct Funding Cost Per DALY	4.1716	Strong driver
Treaty Cost Per DALY	-3.7769	Strong driver
Trial Capacity Plus Efficacy Lag		

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

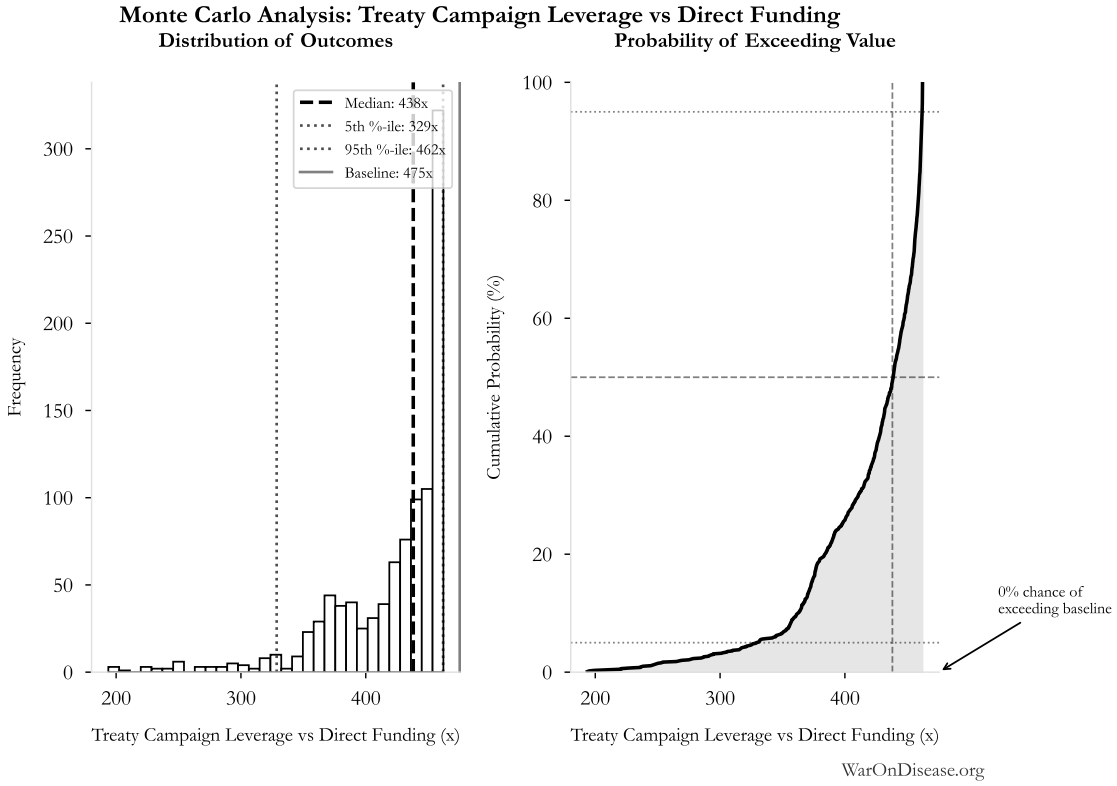


Figure 268: Monte Carlo Distribution: Treaty Campaign Leverage vs Direct Funding (10,000 simulations)

Simulation Results Summary: Treaty Campaign Leverage vs Direct Funding

Statistic	Value
Baseline (deterministic)	475x
Mean (expected value)	421x
Median (50th percentile)	438x
Standard Deviation	47.4x
90% Range (5th-95th percentile)	[329x, 462x]

The histogram shows the distribution of Treaty Campaign Leverage vs Direct Funding 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

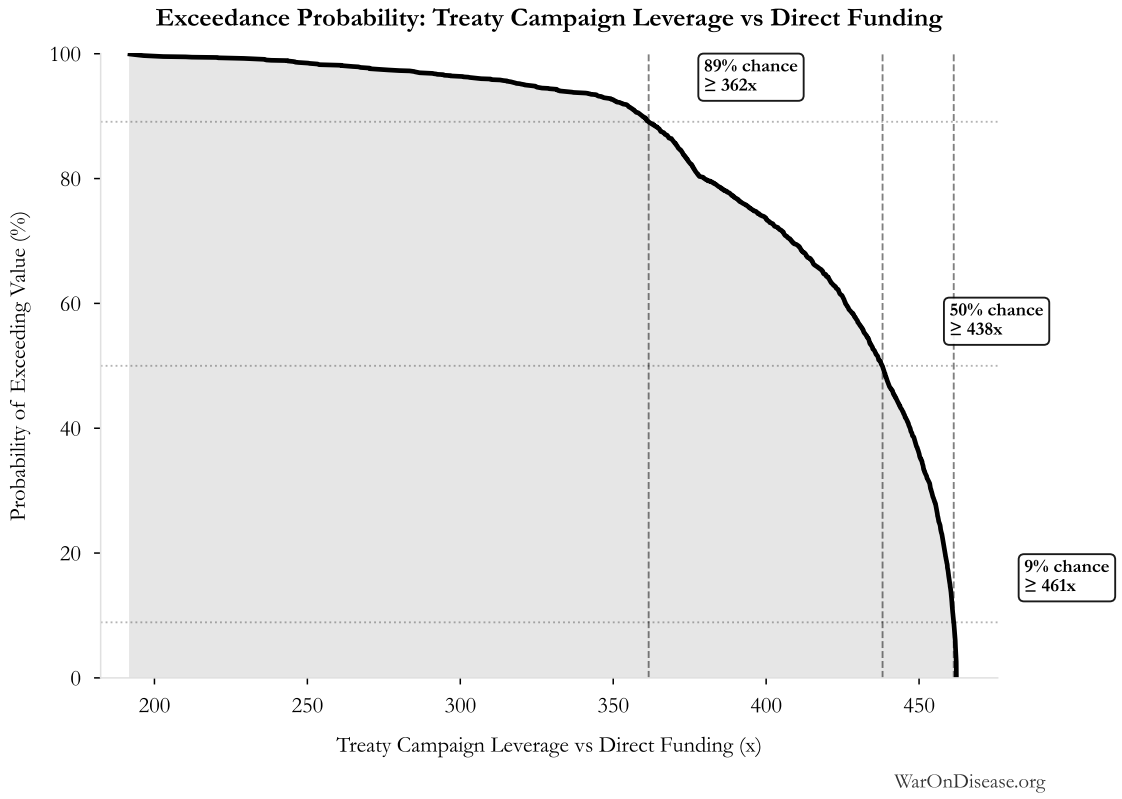


Figure 269: Probability of Exceeding Threshold: Treaty Campaign Leverage vs Direct Funding

This exceedance probability chart shows the likelihood that Treaty Campaign Leverage vs Direct Funding will exceed any given threshold. Higher curves indicate more favorable outcomes with greater certainty.

Cumulative Trial Capacity Years Over 20 Years: 246 years

Details

Cumulative trial-capacity-equivalent years over 20-year period
Inputs:

- Trial Capacity Multiplier : 12.3x

$$Capacity_{20yr} = k_{capacity} \times 20 = 12.3 \times 20 = 246$$

$$\text{where } k_{capacity} = \frac{N_{fundable,ann}}{Slots_{curr}} = \frac{23.4M}{1.9M} = 12.3$$

$$\begin{gathered}\text{where } N_{fundable,ann} \\ = \frac{Subsidies_{trial,ann}}{Cost_{pragmatic,pt}} \\ = \frac{\$21.7B}{\$929} \\ = 23.4M\end{gathered}$$

$$\begin{gathered}\text{where } Subsidies_{trial,ann} \\ = Treasury_{RD,ann} - OPEX_{dFDA} \\ = \$21.8B - \$40M \\ = \$21.7B\end{gathered}$$

$$\begin{gathered}\text{where } OPEX_{dFDA} \\ = Cost_{platform} + Cost_{staff} + Cost_{infra} \\ + Cost_{regulatory} + Cost_{community} \\ = \$15M + \$10M + \$8M + \$5M + \$2M \\ = \$40M\end{gathered}$$

$$\begin{gathered}\text{where } Treasury_{RD,ann} \\ = Funding_{treaty} - Payout_{bond,ann} - Funding_{political,ann} \\ = \$27.2B - \$2.72B - \$2.72B \\ = \$21.8B\end{gathered}$$

$$\begin{gathered}\text{where } Funding_{treaty} \\ = Spending_{mil} \times Reduce_{treaty} \\ = \$2.72T \times 1\% \\ = \$27.2B\end{gathered}$$

$$\begin{gathered}\text{where } Payout_{bond,ann} \\ = Funding_{treaty} \times Pct_{bond} \\ = \$27.2B \times 10\% \\ = \$2.72B\end{gathered}$$

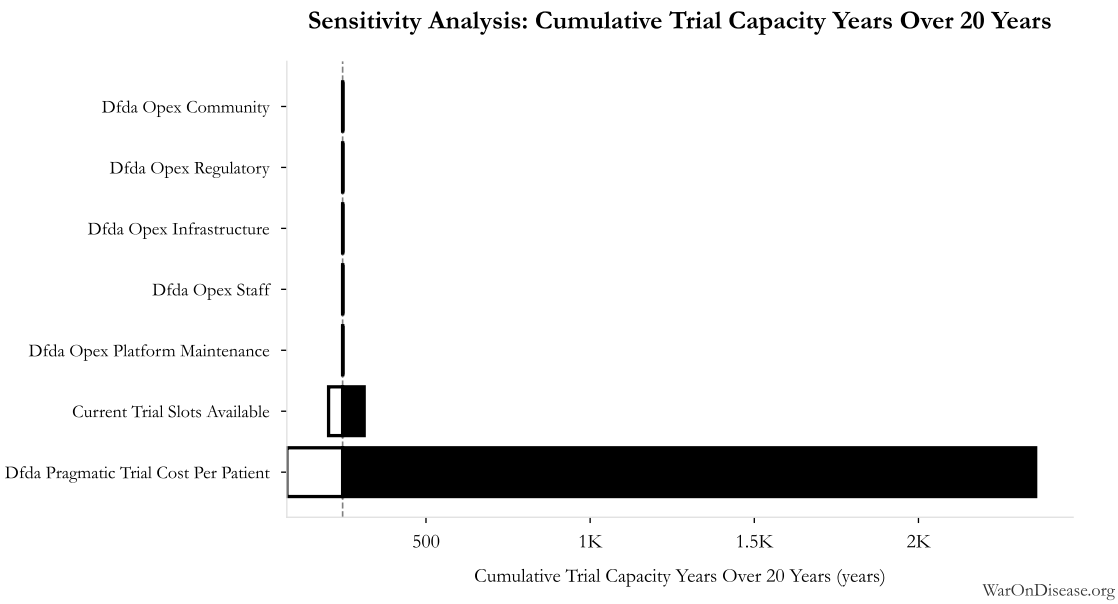
$$\begin{gathered}\text{where } Funding_{treaty} \\ = Spending_{mil} \times Reduce_{treaty} \\ = \$2.72T \times 1\% \\ = \$27.2B\end{gathered}$$

$$\begin{gathered}\text{where } Funding_{political,ann} \\ = Funding_{treaty} \times Pct_{political} \\ = \$27.2B \times 10\% \\ = \$2.72B\end{gathered}$$

$$\text{where } Funding_{treaty}$$

High confidence

Sensitivity Analysis



Sensitivity Indices for Cumulative Trial Capacity Years Over 20 Years
Regression-based sensitivity showing which inputs explain the most variance in the output.

Input Parameter	Sensitivity Coefficient	Interpretation
dFDA Trial Capacity Multiplier	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

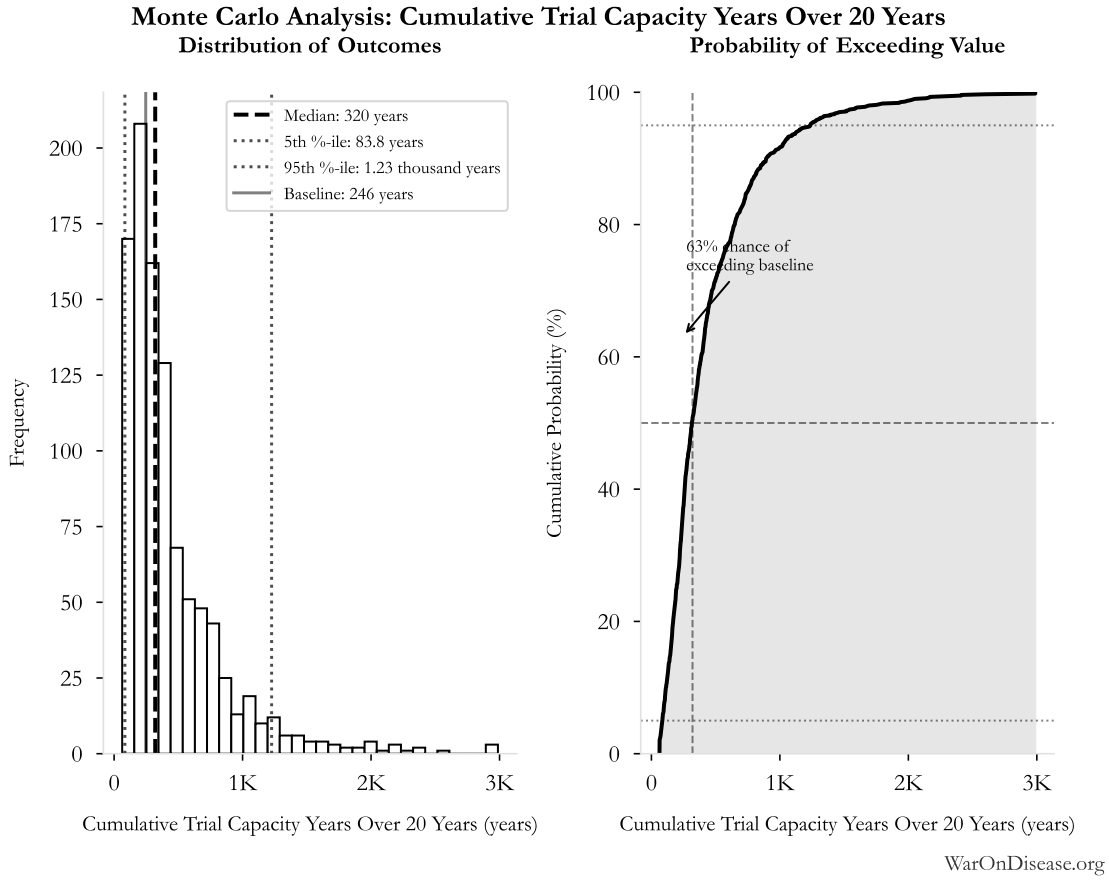


Figure 270: Monte Carlo Distribution: Cumulative Trial Capacity Years Over 20 Years (10,000 simulations)

Simulation Results Summary: Cumulative Trial Capacity Years Over 20 Years

Statistic	Value
Baseline (deterministic)	246
Mean (expected value)	441
Median (50th percentile)	320
Standard Deviation	404
90% Range (5th-95th percentile)	[83.8, 1.23 thousand]

The histogram shows the distribution of Cumulative Trial Capacity Years Over 20 Years 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

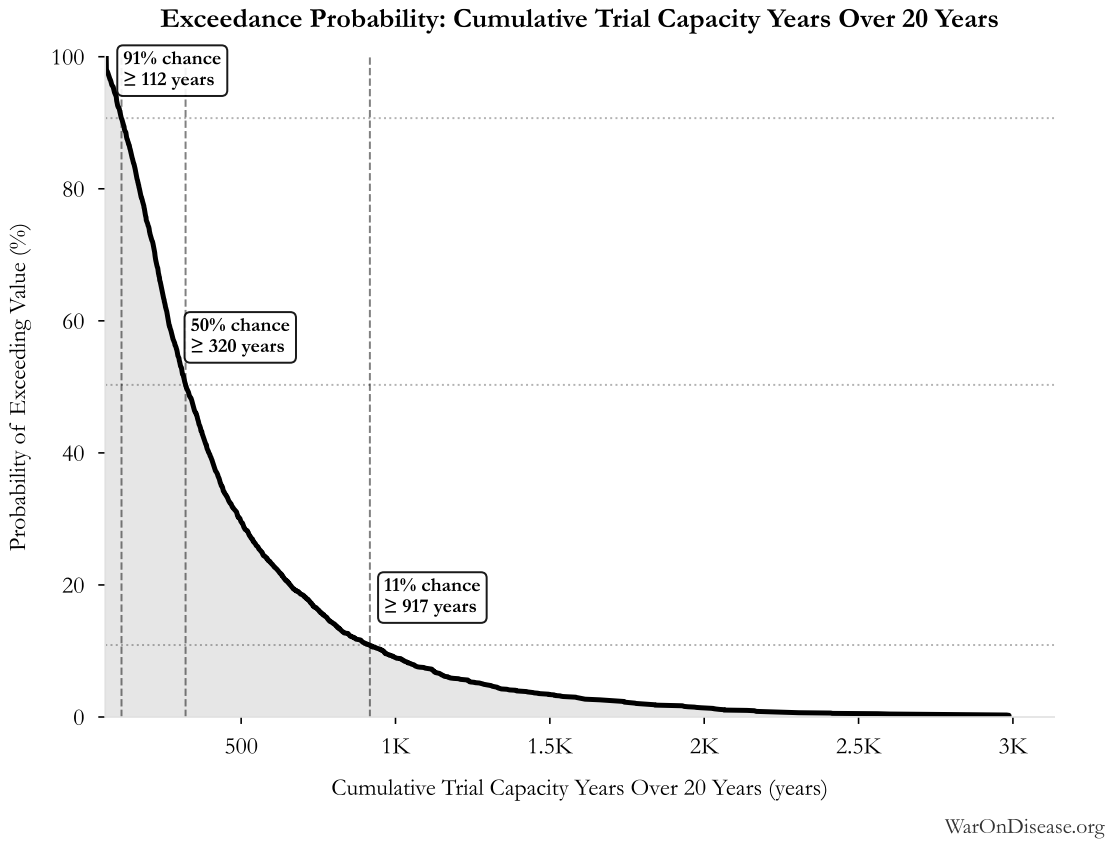


Figure 271: Probability of Exceeding Threshold: Cumulative Trial Capacity Years Over 20 Years

This exceedance probability chart shows the likelihood that Cumulative Trial Capacity Years Over 20 Years will exceed any given threshold. Higher curves indicate more favorable outcomes with greater certainty.

Ratio of Type II Error Cost to Type I Error Benefit: 3.07k:1

Details

Ratio of Type II error cost to Type I error benefit (harm from delay vs. harm prevented)
Inputs:

- Total DALYs Lost from Disease Eradication Delay : 7.94 billion DALYs
- Maximum DALYs Saved by FDA Preventing Unsafe Drugs (1962-2024) : 2.59 million DALYs

$$Ratio_{TypeII} = \frac{DALYs_{lag}}{DALY_{TypeI}} = \frac{7.94B}{2.59M} = 3{,}070$$

where $DALYs_{lag} = YLL_{lag} + YLD_{lag} = 7.07B + 873M = 7.94B$

where YLL_{lag}
$= Deaths_{lag} \times (LE_{global} - Age_{death,delay})$
$= 416M \times (79 - 62)$
$= 7.07B$

where $Deaths_{lag}$
$= T_{lag} \times Deaths_{disease,daily} \times 338$
$= 8.2 \times 150{,}000 \times 338$
$= 416M$

where YLD_{lag}
$= Deaths_{lag} \times T_{suffering} \times DW_{chronic}$
$= 416M \times 6 \times 0.35$
$= 873M$

where $Deaths_{lag}$
$= T_{lag} \times Deaths_{disease,daily} \times 338$
$= 8.2 \times 150{,}000 \times 338$
$= 416M$

where $DALY_{TypeI} = DALY_{thal} \times 62 = 41{,}800 \times 62 = 2.59M$

where $DALY_{thal}$
$= YLD_{thal} + YLL_{thal}$
$= 13{,}000 + 28{,}800$
$= 41{,}800$

where YLD_{thal}
$= DW_{thal} \times N_{thal,survive} \times LE_{thal}$
$= 0.4 \times 540 \times 60$
$= 13{,}000$

where $N_{thal,survive}$
$= N_{thal,US,prevent} \times (1 - Rate_{thal,mort})$
$= 900 \times (1 - 40\%)$
$= 540$

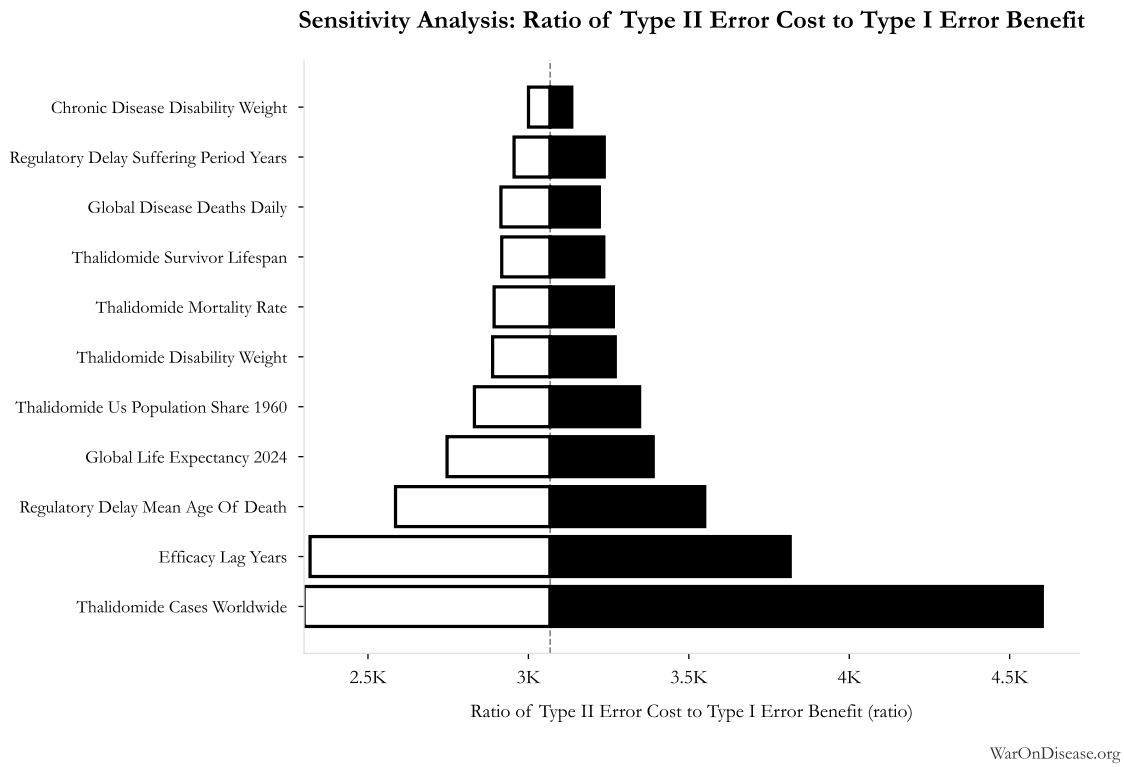
where $N_{thal,US,prevent}$
$= N_{thal,global} \times Pct_{US,1960}$
$= 15{,}000 \times 6\%$
$= 900$

where $YLL_{thal} = Deaths_{thal} \times 80 = 360 \times 80 = 28{,}800$

where $Deaths_{thal}$

~ *Medium confidence*

Sensitivity Analysis



Sensitivity Indices for Ratio of Type II Error Cost to Type I Error Benefit
Regression-based sensitivity showing which inputs explain the most variance in the output.

Input Parameter	Sensitivity Coefficient	Interpretation
dFDA Efficacy Lag Elimination DALYs	7.2872	Strong driver
Type I Error Benefit DALYs	-7.1207	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

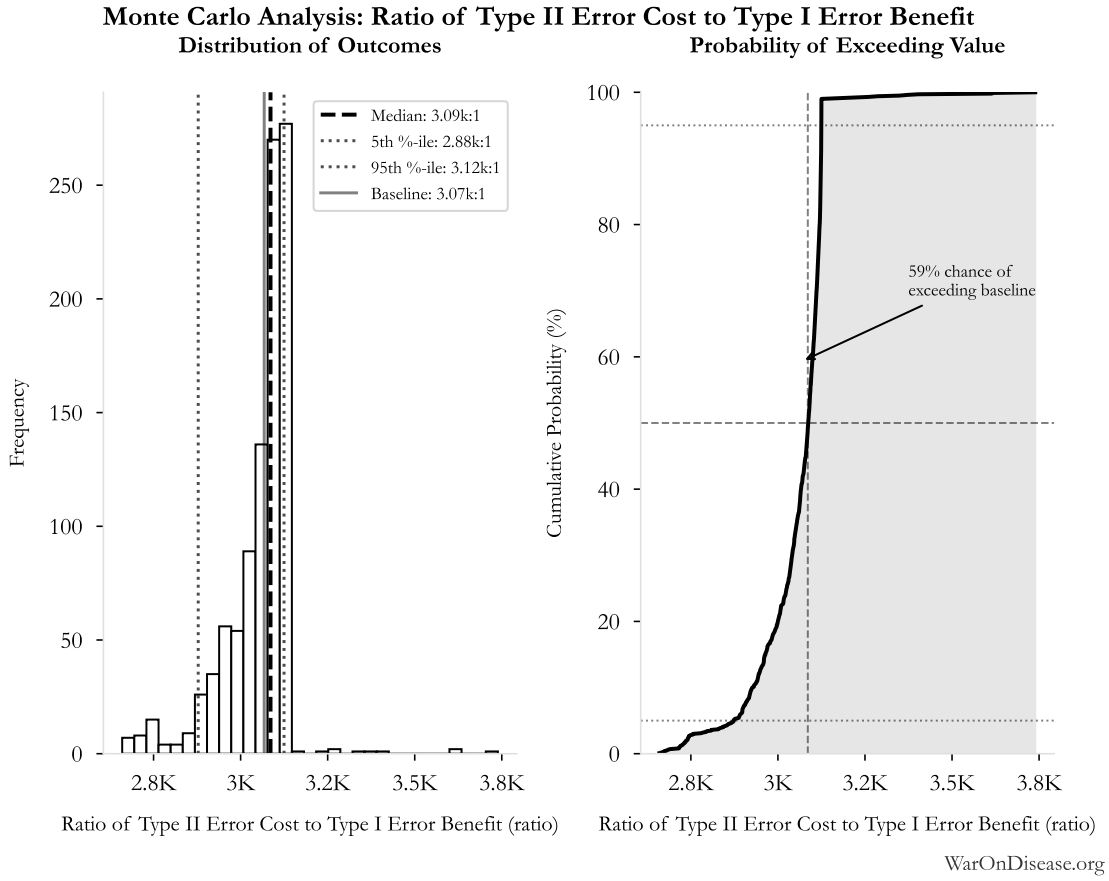


Figure 272: Monte Carlo Distribution: Ratio of Type II Error Cost to Type I Error Benefit (10,000 simulations)

Simulation Results Summary: Ratio of Type II Error Cost to Type I Error Benefit

Statistic	Value
Baseline (deterministic)	3.07k:1
Mean (expected value)	3.05k:1
Median (50th percentile)	3.09k:1
Standard Deviation	101:1
90% Range (5th-95th percentile)	[2.88k:1, 3.12k:1]

The histogram shows the distribution of Ratio of Type II Error Cost to Type I Error Benefit 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

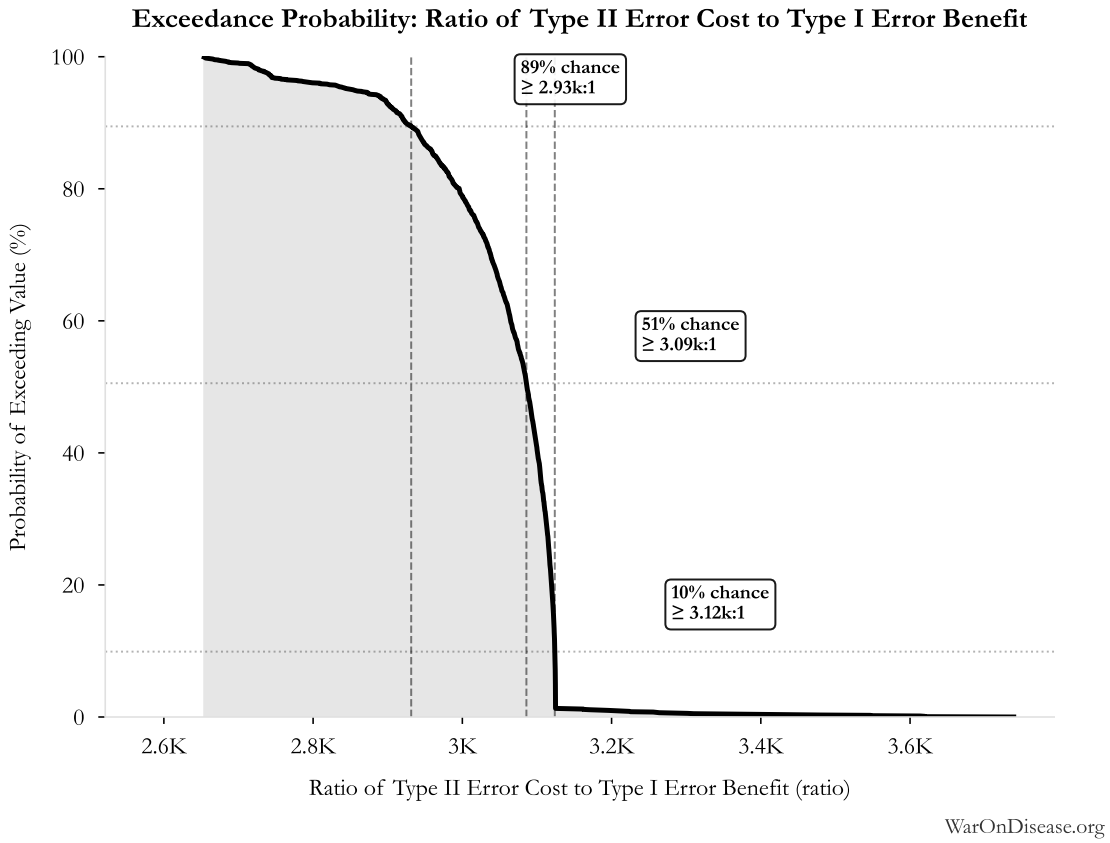


Figure 273: Probability of Exceeding Threshold: Ratio of Type II Error Cost to Type I Error Benefit

This exceedance probability chart shows the likelihood that Ratio of Type II Error Cost to Type I Error Benefit will exceed any given threshold. Higher curves indicate more favorable outcomes with greater certainty.

Maximum DALYs Saved by FDA Preventing Unsafe Drugs (1962-2024): 2.59 million DALYs

Details

Maximum DALYs saved by FDA preventing unsafe drugs over 62-year period 1962-2024 (extreme overestimate: one Thalidomide-scale event per year)

Inputs:

- Thalidomide DALYs Per Event : 41.8 thousand DALYs

$$DALY_{TypeI} = DALY_{thal} \times 62 = 41{,}800 \times 62 = 2.59M$$

$$\begin{gathered}\text{where } DALY_{thal} \\ = YLD_{thal} + YLL_{thal} \\ = 13{,}000 + 28{,}800 \\ = 41{,}800\end{gathered}$$

$$\begin{gathered}\text{where } YLD_{thal} \\ = DW_{thal} \times N_{thal,survive} \times LE_{thal} \\ = 0.4 \times 540 \times 60 \\ = 13{,}000\end{gathered}$$

$$\begin{gathered}\text{where } N_{thal,survive} \\ = N_{thal,US,prevent} \times (1 - Rate_{thal,mort}) \\ = 900 \times (1 - 40\%) \\ = 540\end{gathered}$$

$$\begin{gathered}\text{where } N_{thal,US,prevent} \\ = N_{thal,global} \times Pct_{US,1960} \\ = 15{,}000 \times 6\% \\ = 900\end{gathered}$$

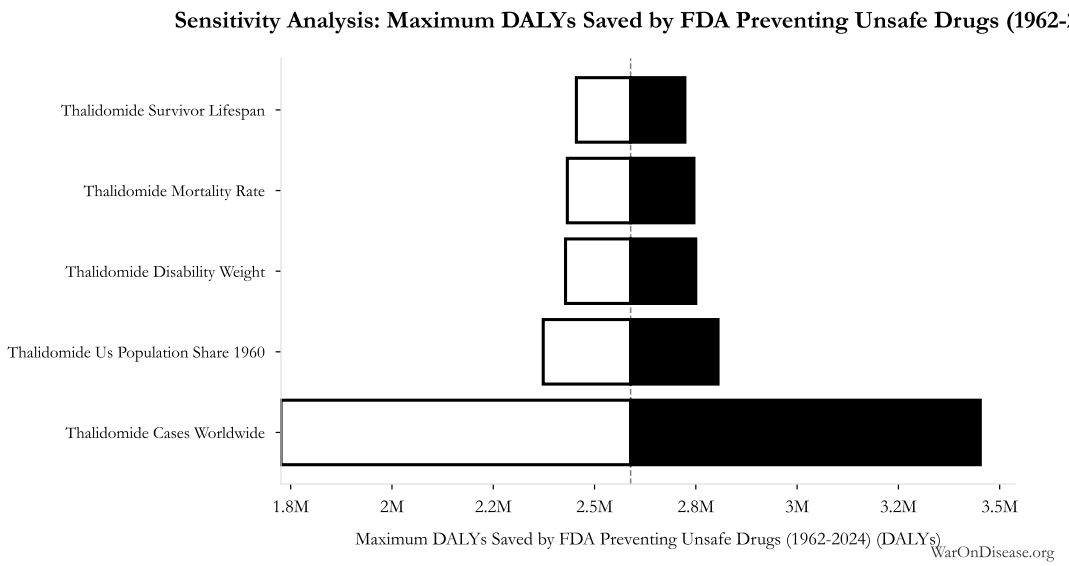
$$\text{where } YLL_{thal} = Deaths_{thal} \times 80 = 360 \times 80 = 28{,}800$$

$$\begin{gathered}\text{where } Deaths_{thal} \\ = Rate_{thal,mort} \times N_{thal,US,prevent} \\ = 40\% \times 900 \\ = 360\end{gathered}$$

$$\begin{gathered}\text{where } N_{thal,US,prevent} \\ = N_{thal,global} \times Pct_{US,1960} \\ = 15{,}000 \times 6\% \\ = 900\end{gathered}$$

? Low confidence

Sensitivity Analysis



Sensitivity Indices for Maximum DALYs Saved by FDA Preventing Unsafe Drugs (1962-2024)

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

Input Parameter	Sensitivity Coefficient	Interpretation
Thalidomide DALYs Per Event	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

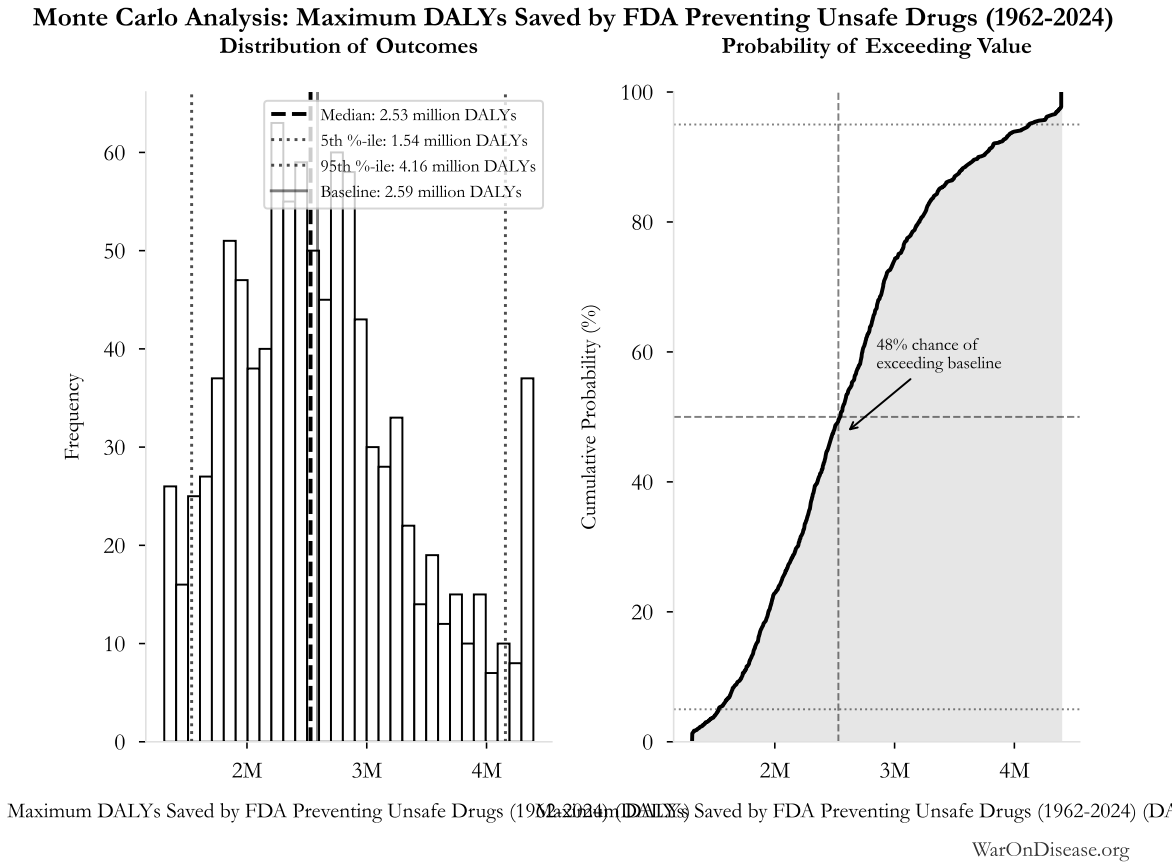


Figure 274: Monte Carlo Distribution: Maximum DALYs Saved by FDA Preventing Unsafe Drugs (1962-2024) (10,000 simulations)

Simulation Results Summary: Maximum DALYs Saved by FDA Preventing Unsafe Drugs (1962-2024)

Statistic	Value
Baseline (deterministic)	2.59 million
Mean (expected value)	2.63 million
Median (50th percentile)	2.53 million
Standard Deviation	754 thousand
90% Range (5th-95th percentile)	[1.54 million, 4.16 million]

The histogram shows the distribution of Maximum DALYs Saved by FDA Preventing Unsafe Drugs (1962-2024) 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

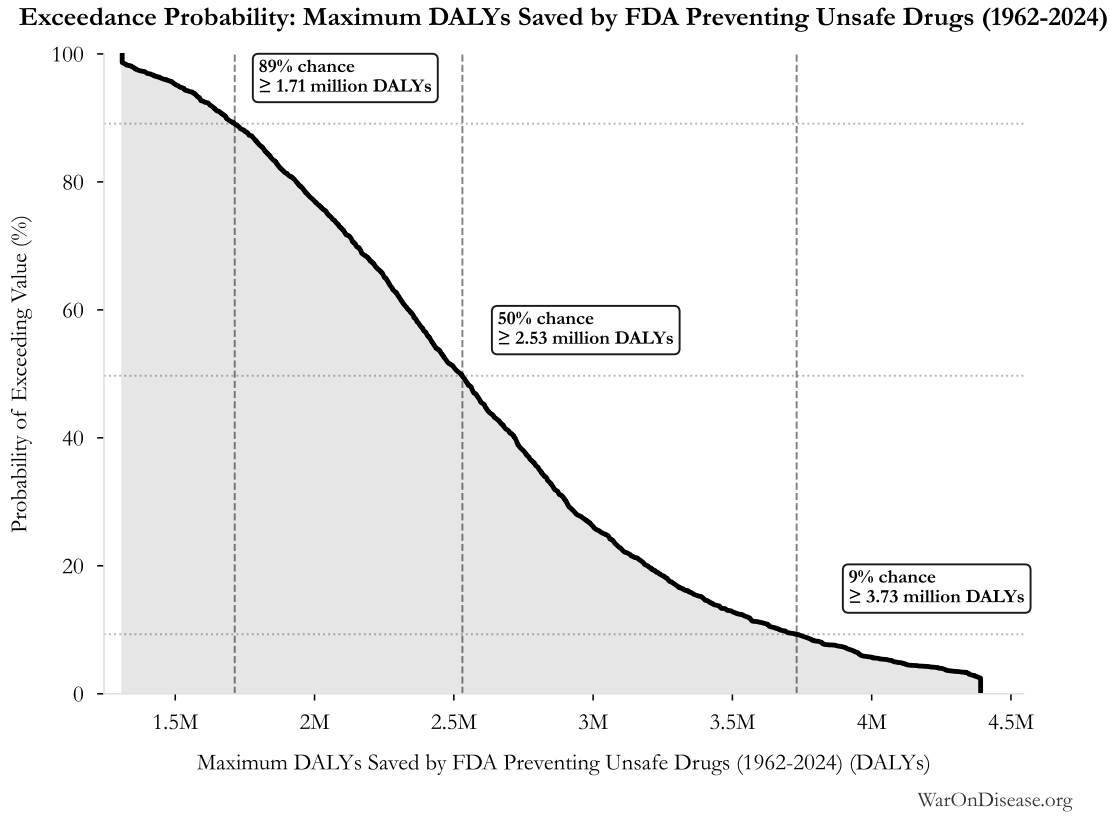


Figure 275: Probability of Exceeding Threshold: Maximum DALYs Saved by FDA Preventing Unsafe Drugs (1962-2024)

This exceedance probability chart shows the likelihood that Maximum DALYs Saved by FDA Preventing Unsafe Drugs (1962-2024) will exceed any given threshold. Higher curves indicate more favorable outcomes with greater certainty.

Unexplored Therapeutic Frontier: 99.7%

Details

Fraction of possible drug-disease space that remains unexplored (>99%)
Inputs:

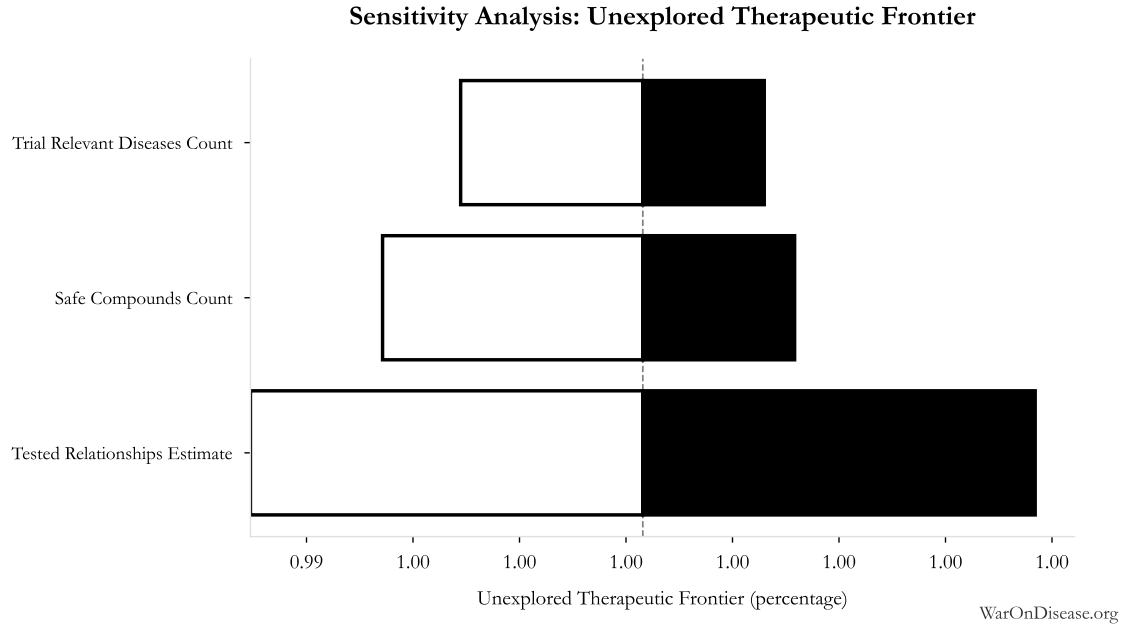
- Tested Drug-Disease Relationships: 32.5 thousand relationships (95% CI: 15.0 thousand relationships - 50.0 thousand relationships)
- Possible Drug-Disease Combinations : 9.50 million combinations

$$
\begin{aligned}
&Ratio_{unexplored} \\
&= 1 - \frac{N_{tested}}{N_{combos}} \\
&= 1 - \frac{32{,}500}{9.5M} \\
&= 99.7\%
\end{aligned}
$$

$$
\begin{aligned}
&\text{where } N_{combos} \\
&= N_{safe} \times N_{diseases,trial} \\
&= 9{,}500 \times 1{,}000 \\
&= 9.5M
\end{aligned}
$$

High confidence

Sensitivity Analysis



Sensitivity Indices for Unexplored Therapeutic Frontier

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

Input Parameter	Sensitivity Coefficient	Interpretation
Tested Relationships Estimate	-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 276: Monte Carlo Distribution: Unexplored Therapeutic Frontier (10,000 simulations)

Simulation Results Summary: Unexplored Therapeutic Frontier

Statistic	Value
Baseline (deterministic)	99.7%
Mean (expected value)	99.7%
Median (50th percentile)	99.7%
Standard Deviation	0.0868%
90% Range (5th-95th percentile)	[99.5%, 99.8%]

The histogram shows the distribution of Unexplored Therapeutic Frontier 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

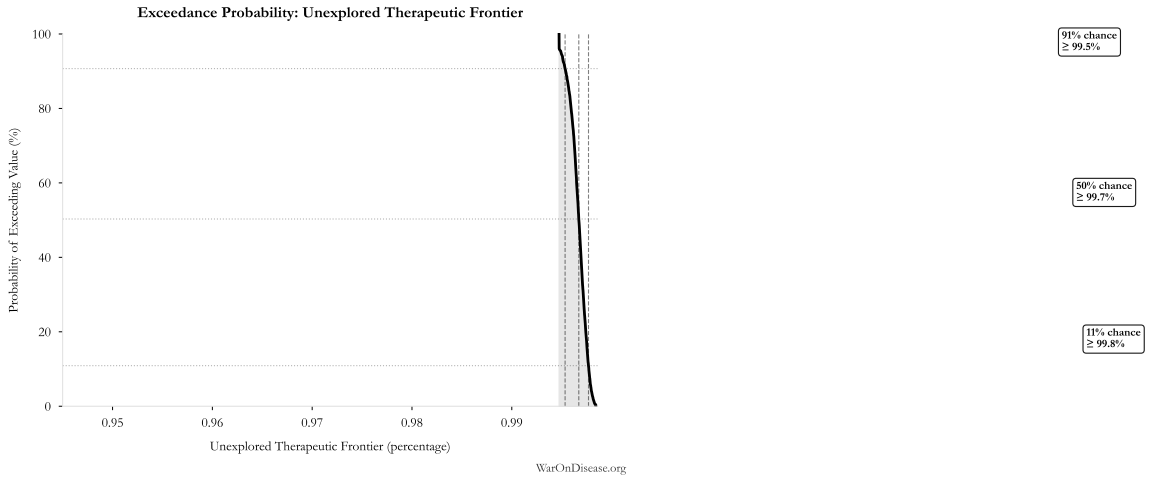


Figure 277: Probability of Exceeding Threshold: Unexplored Therapeutic Frontier

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

Annual VICTORY Incentive Alignment Bond Payout: $2.72B

Details

Annual VICTORY Incentive Alignment Bond payout (treaty funding × bond percentage)
Inputs:

- Annual Funding from 1% of Global Military Spending Redirected to DIH : $27.2B
- Percentage of Captured Dividend Funding VICTORY Incentive Alignment Bonds: 10%

$$Payout_{bond,ann}$$
$$= Funding_{treaty} \times Pct_{bond}$$
$$= \$27.2B \times 10\%$$
$$= \$2.72B$$

$$\text{where } Funding_{treaty}$$
$$= Spending_{mil} \times Reduce_{treaty}$$
$$= \$2.72T \times 1\%$$
$$= \$27.2B$$

High confidence

Annual Return Percentage for VICTORY Incentive Alignment Bondholders: 272%

Details

Annual return percentage for VICTORY Incentive Alignment Bondholders
Inputs:

- Annual VICTORY Incentive Alignment Bond Payout : $2.72B
- Total 1% Treaty Campaign Cost : $1B

$$r_{bond} = \frac{Payout_{bond,ann}}{Cost_{campaign}} = \frac{\$2.72B}{\$1B} = 272\%$$

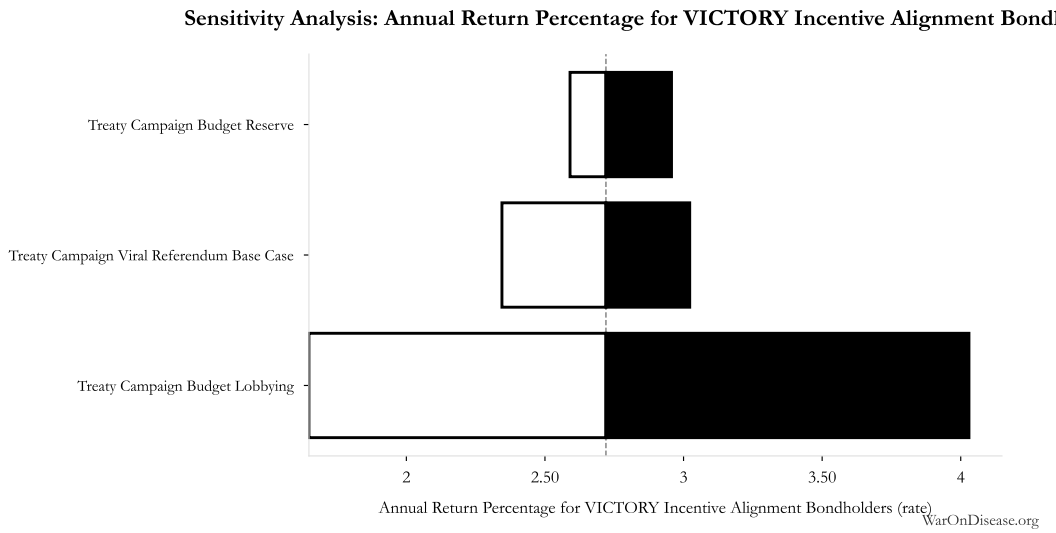
$$\text{where } Payout_{bond,ann}$$
$$= Funding_{treaty} \times Pct_{bond}$$
$$= \$27.2B \times 10\%$$
$$= \$2.72B$$

$$\text{where } Funding_{treaty}$$
$$= Spending_{mil} \times Reduce_{treaty}$$
$$= \$2.72T \times 1\%$$
$$= \$27.2B$$

$$\text{where } Cost_{campaign}$$
$$= Budget_{viral,base} + Budget_{lobby,treaty}$$
$$+Budget_{reserve}$$
$$= \$250M + \$650M + \$100M$$
$$= \$1B$$

High confidence

Sensitivity Analysis



Sensitivity Indices for Annual Return Percentage for VICTORY Incentive Alignment Bondholders

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

Input Parameter	Sensitivity Coefficient	Interpretation
Treaty Campaign Total Cost	-0.9366	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

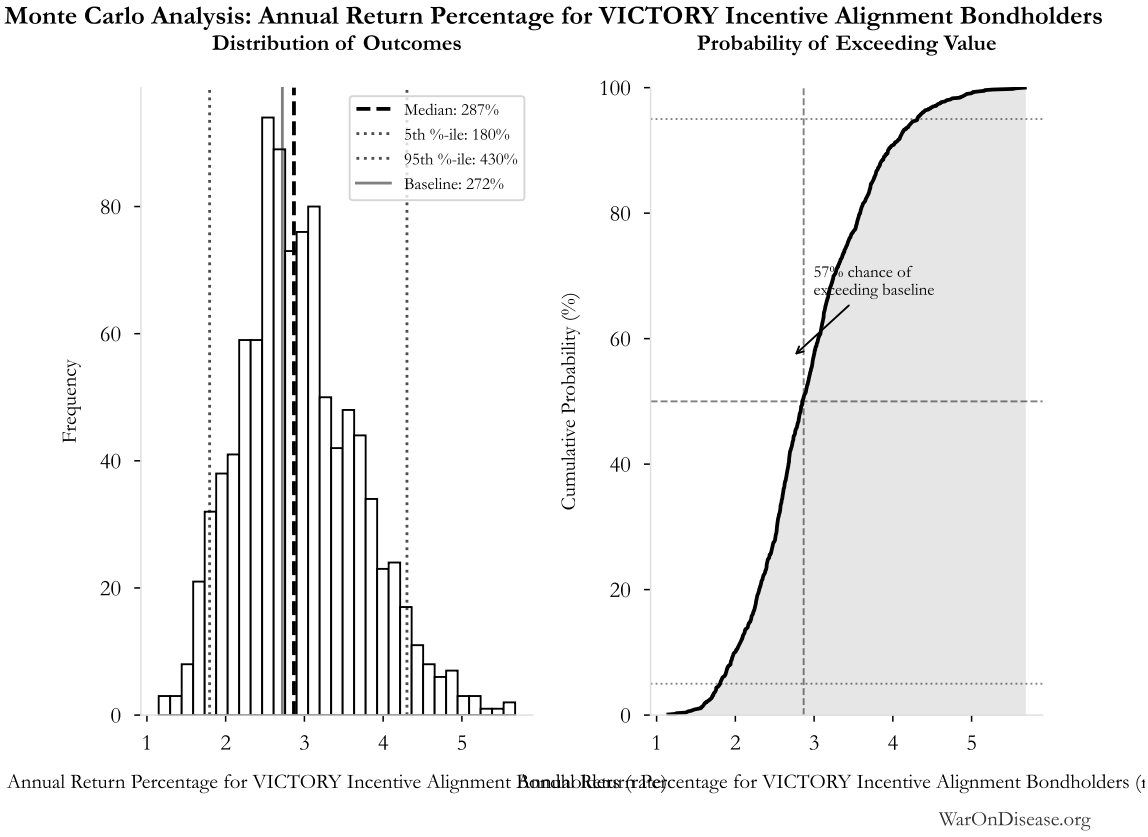


Figure 278: Monte Carlo Distribution: Annual Return Percentage for VICTORY Incentive Alignment Bondholders (10,000 simulations)

Simulation Results Summary: Annual Return Percentage for VICTORY Incentive Alignment Bondholders

Statistic	Value
Baseline (deterministic)	272%
Mean (expected value)	293%
Median (50th percentile)	287%
Standard Deviation	76.3%
90% Range (5th-95th percentile)	[180%, 430%]

The histogram shows the distribution of Annual Return Percentage for VICTORY Incentive Alignment Bondholders 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

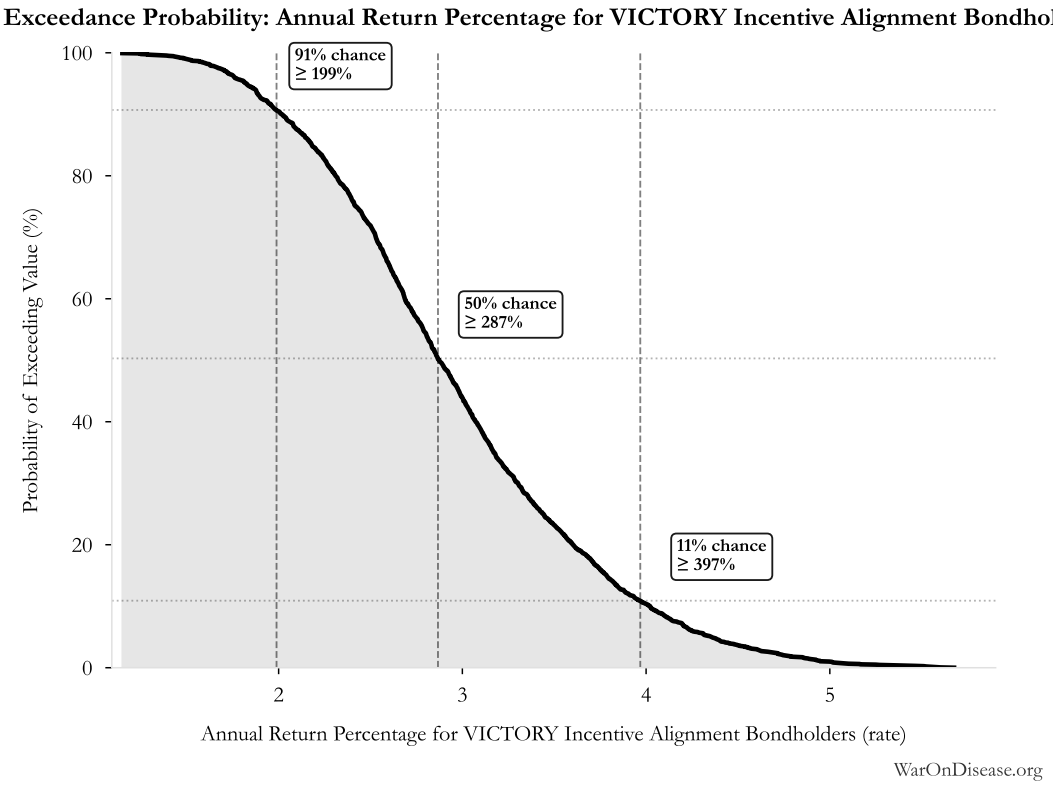


Figure 279: Probability of Exceeding Threshold: Annual Return Percentage for VICTORY Incentive Alignment Bondholders

This exceedance probability chart shows the likelihood that Annual Return Percentage for VICTORY Incentive Alignment Bondholders 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.

ADAPTABLE Trial Cost per Patient: $929

Details

Cost per patient in ADAPTABLE trial ($14M PCORI grant / 15,076 patients). Note: This is the direct grant cost; true cost including in-kind may be 10-40% higher.
Source:[1]

Uncertainty Range

Technical: 95% CI: [$929, $1.40K] • Distribution: Lognormal
What this means: There's significant uncertainty here. The true value likely falls between $929 and $1.40K (±25%). This represents a 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

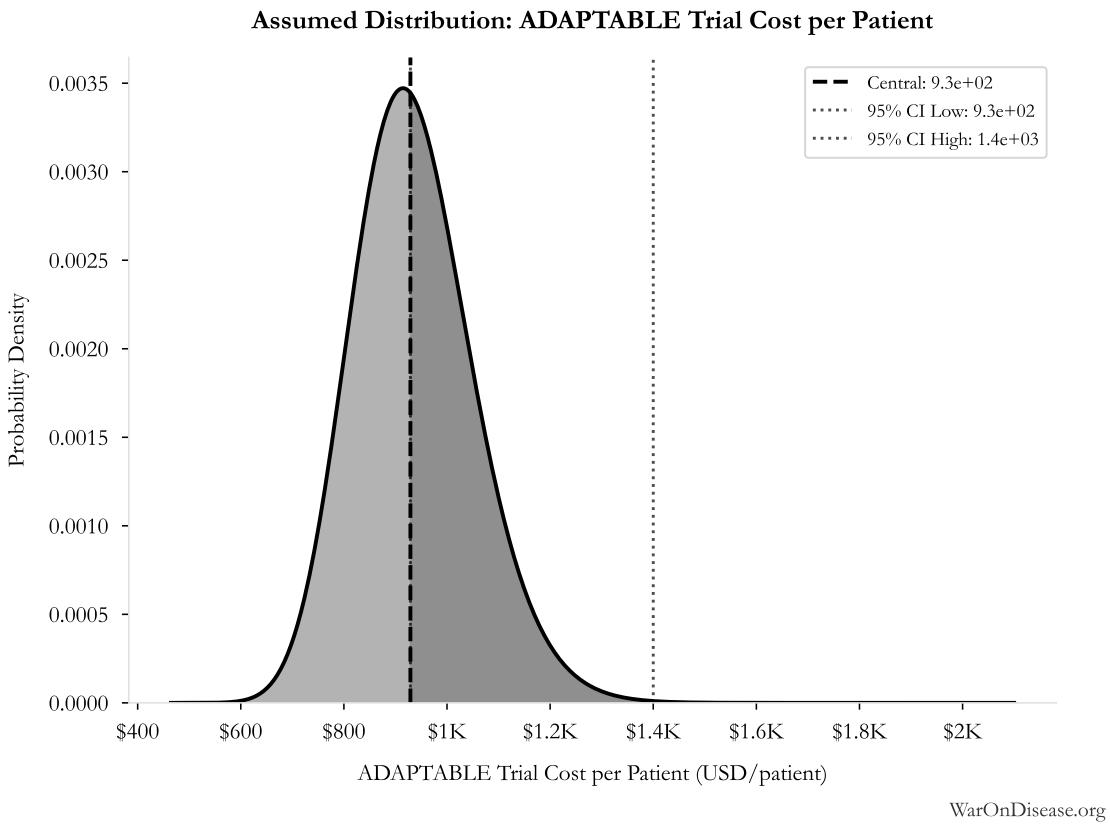


Figure 280: Probability Distribution: ADAPTABLE Trial Cost per Patient

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

ADAPTABLE Trial Total Cost: $14M

Details

PCORI grant for ADAPTABLE trial (2016-2019). Note: Direct funding only; total costs including site overhead and in-kind contributions from health systems may be higher.
Source:[1]

Uncertainty Range

Technical: 95% CI: [$14M, $20M] • Distribution: Lognormal
What this means: This estimate has moderate uncertainty. The true value likely falls between $14M and $20M (±21%). This represents a reasonable 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

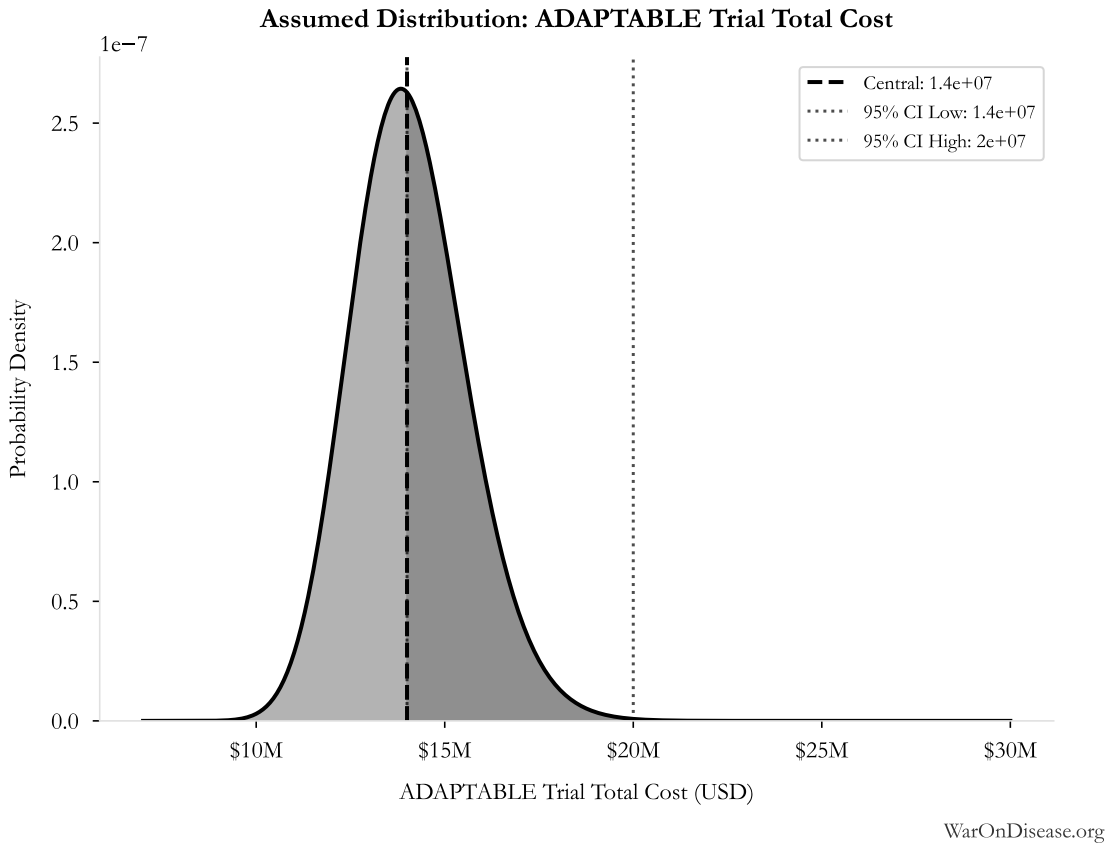


Figure 281: Probability Distribution: ADAPTABLE Trial Total Cost

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.
~ Medium confidence

Antidepressant Trial Exclusion Rate: 86.1%

Details

Mean exclusion rate in antidepressant trials (86.1% of real-world patients excluded)
Source:[2]
High confidence

Average Annual Stock Market Return: 10%

Details

Average annual stock market return (10%)
Source:[3]
High confidence

Bed Nets Cost per DALY: $89

Details

GiveWell cost per DALY for insecticide-treated bed nets (midpoint estimate, range $78-100). DALYs (Disability-Adjusted Life Years) measure disease burden by combining years of life lost and years lived with disability. Bed nets prevent malaria deaths and are considered a gold standard benchmark for cost-effective global health interventions - if an intervention costs less per DALY than bed nets, it's exceptionally cost-effective. GiveWell synthesizes peer-reviewed academic research with transparent, rigorous methodology and extensive external expert review.
Source:[5]

Uncertainty Range

Technical: 95% CI: [$78, $100] • Distribution: Normal
What this means: This estimate has moderate uncertainty. The true value likely falls between $78 and $100 (±12%). 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.

Input Distribution

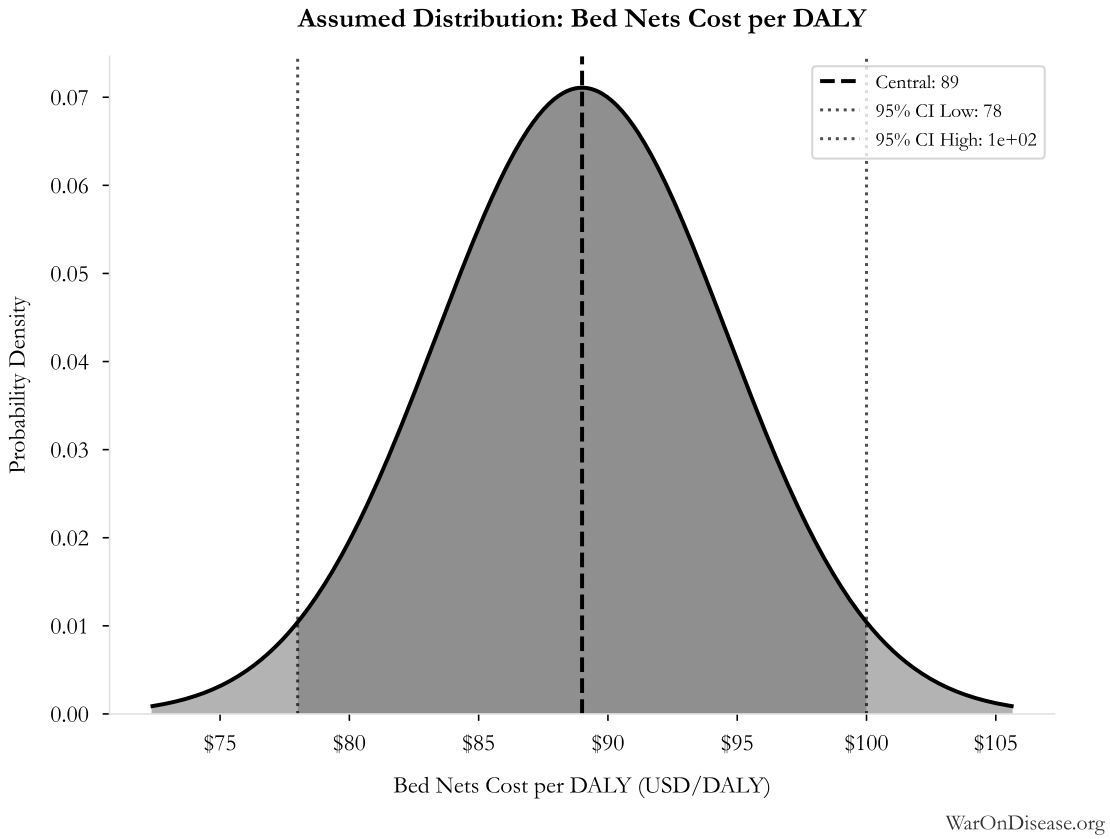


Figure 282: Probability Distribution: Bed Nets Cost per DALY

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*

Estimated Annual Global Economic Benefit from Childhood Vaccination Programs: $15B

Details

Estimated annual global economic benefit from childhood vaccination programs (measles, polio, etc.)
Source:[7]

Uncertainty Range

Technical: Distribution: Lognormal (SE: $4.50B)

Input Distribution

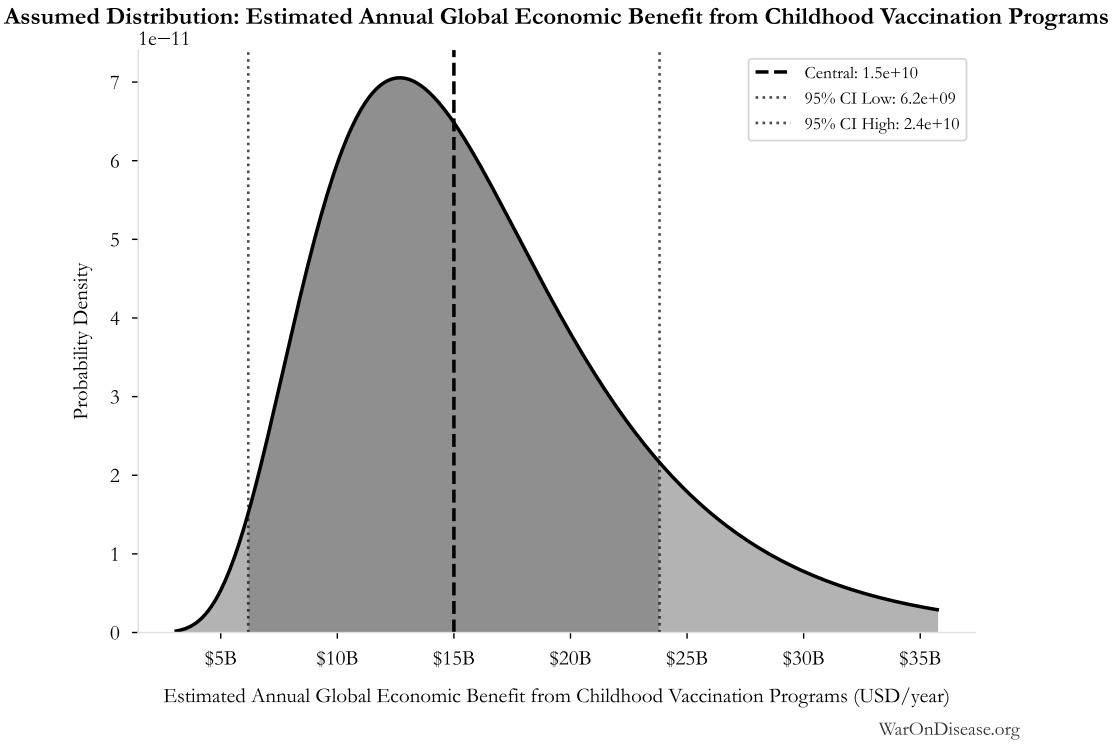


Figure 283: Probability Distribution: Estimated Annual Global Economic Benefit from Childhood Vaccination Programs

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

Return on Investment from Childhood Vaccination Programs: 13:1

Details

Return on investment from childhood vaccination programs
Source:[8]
High confidence

Disability Weight for Untreated Chronic Conditions: 0.35 weight

Details

Disability weight for untreated chronic conditions (WHO Global Burden of Disease)
Source:[4]

Uncertainty Range

Technical: Distribution: Normal (SE: 0.07 weight)

Input Distribution

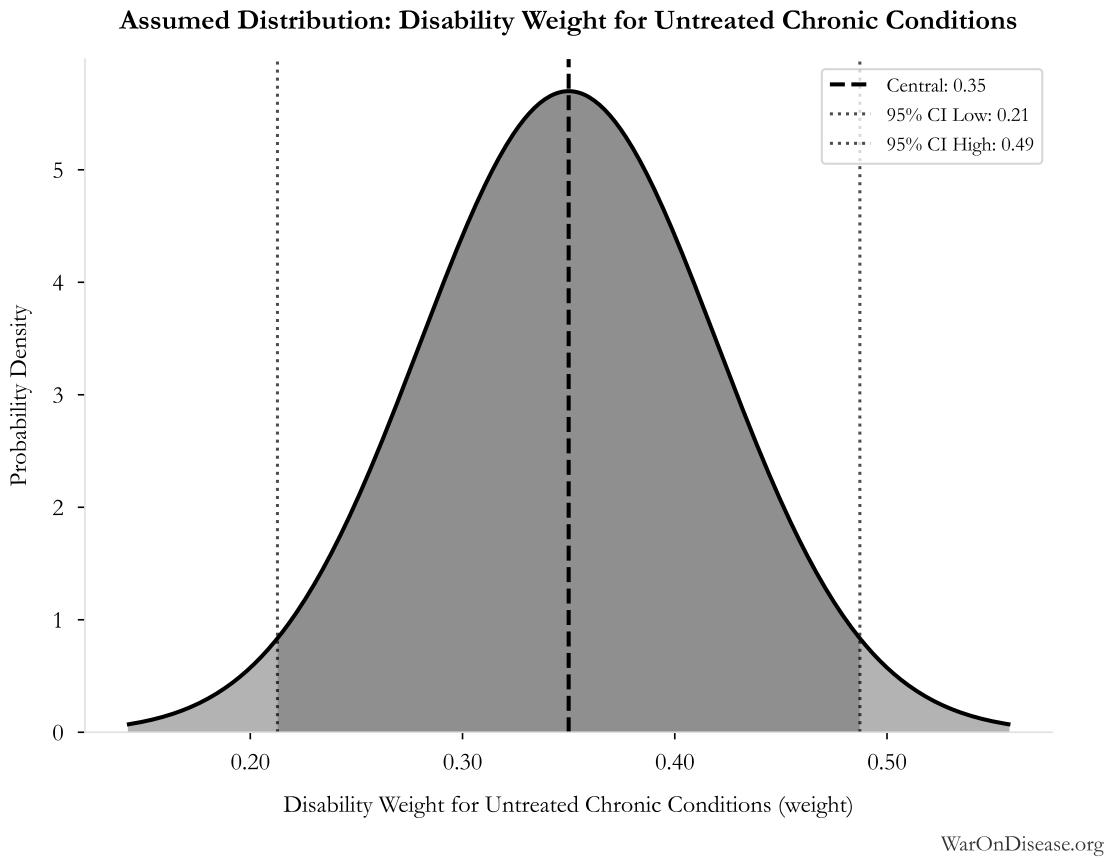


Figure 284: Probability Distribution: Disability Weight for Untreated Chronic Conditions

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 • Peer-reviewed

Current Active Trials at Any Given Time: 10.0 thousand trials

Details

Current active trials at any given time (3-5 year duration)
Source:[10]
High confidence

Current Clinical Trial Participation Rate: 0.06%

Details

Current clinical trial participation rate (0.06% of population)
Source:[11]
High confidence

Global Population with Chronic Diseases: 2.40 billion people

Details

Global population with chronic diseases
Source:[12]

Uncertainty Range

Technical: 95% CI: [2.00 billion people, 2.80 billion people] • Distribution: Lognormal
What this means: This estimate has moderate uncertainty. The true value likely falls between 2.00 billion people and 2.80 billion people (±17%). This represents a reasonable 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

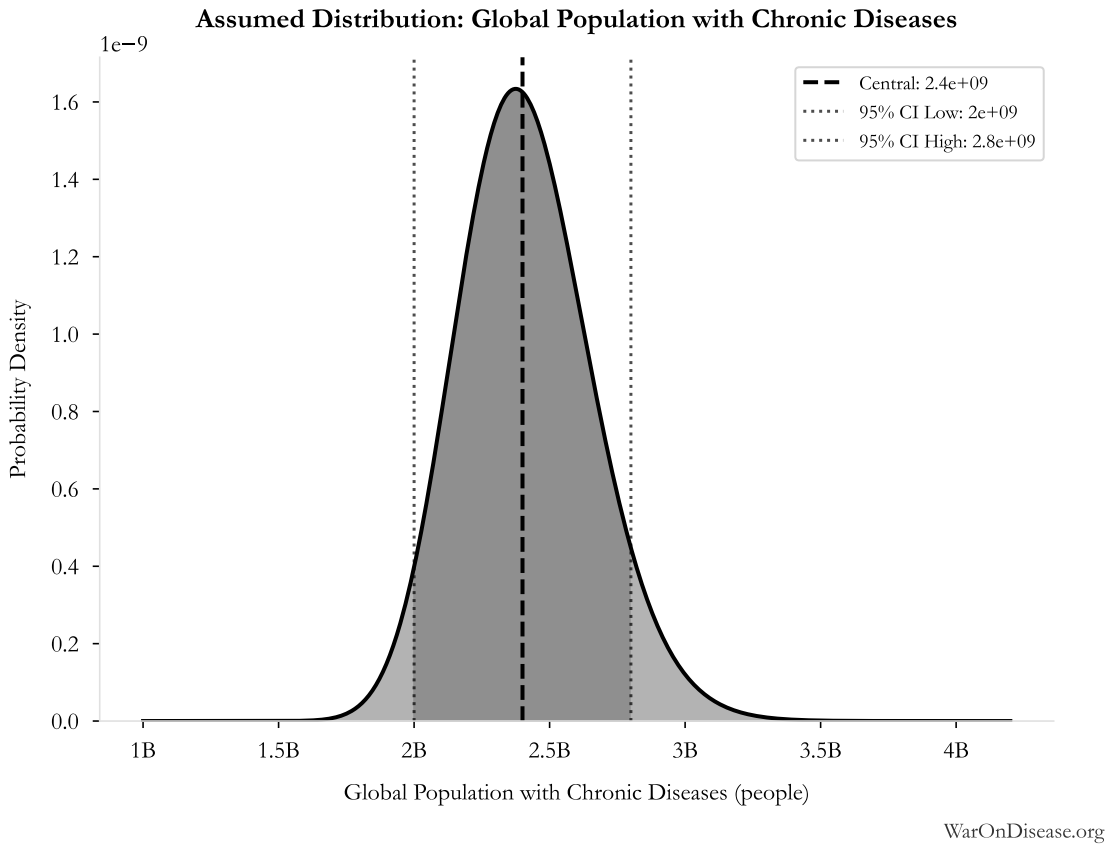


Figure 285: Probability Distribution: Global Population with Chronic Diseases

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

Current Global Clinical Trials per Year: 3.30 thousand trials/year

Details

Current global clinical trials per year
Source:[16]

Uncertainty Range

Technical: 95% CI: [2.64 thousand trials/year, 3.96 thousand trials/year] • Distribution: Lognormal
What this means: This estimate has moderate uncertainty. The true value likely falls

between 2.64 thousand trials/year and 3.96 thousand trials/year (±20%). This represents a reasonable 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

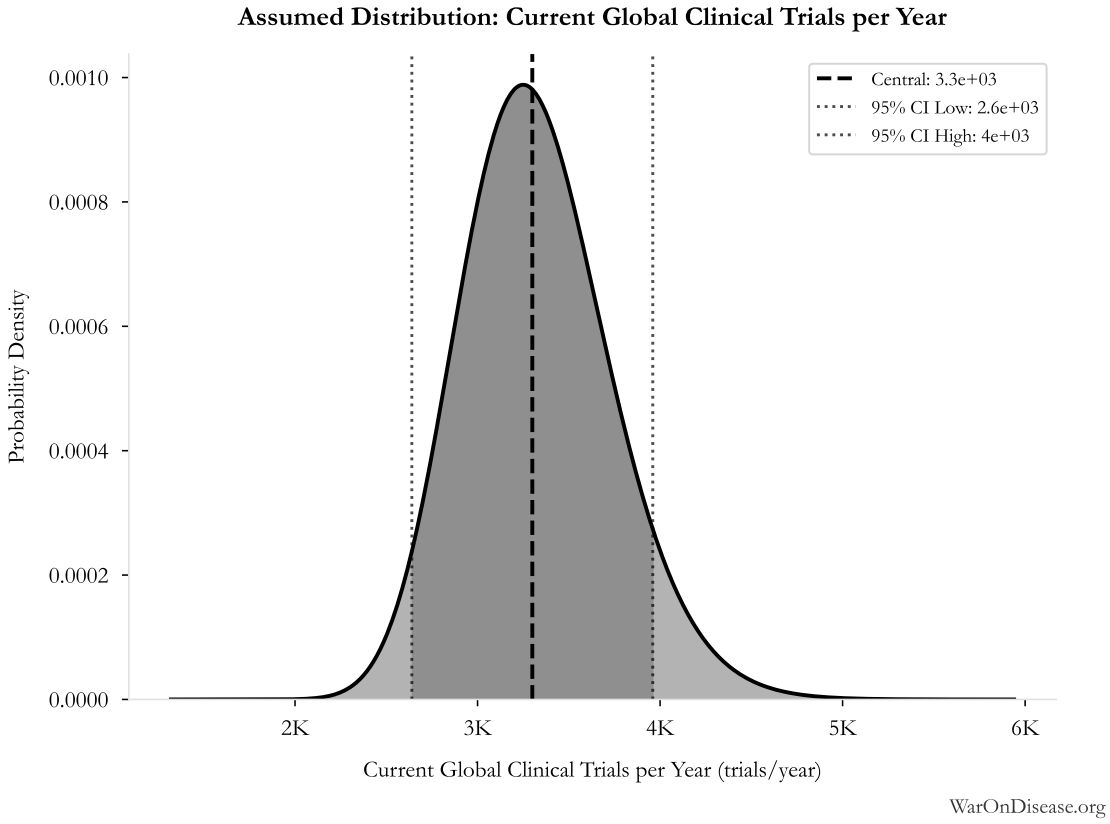


Figure 286: Probability Distribution: Current Global Clinical Trials per Year

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.
High confidence

Current Trial Abandonment Rate: 40%

Details

Current trial abandonment rate (40% never complete)
Source:[14]
High confidence

Annual Global Clinical Trial Participants: 1.90 million patients/year

Details

Annual global clinical trial participants (IQVIA 2022: 1.9M post-COVID normalization)
Source:[15]

Uncertainty Range

Technical: 95% CI: [1.50 million patients/year, 2.30 million patients/year] • Distribution: Lognormal
What this means: This estimate has moderate uncertainty. The true value likely falls between 1.50 million patients/year and 2.30 million patients/year (±21%). This represents a reasonable 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

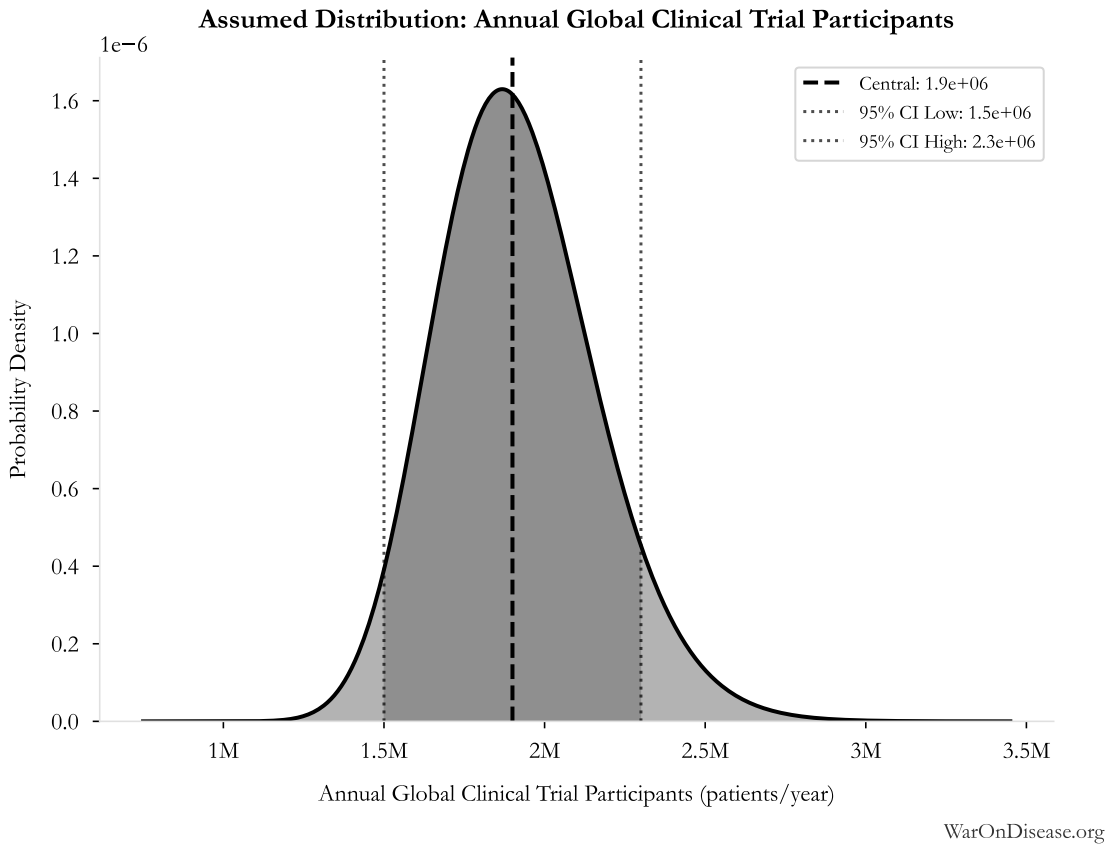


Figure 287: Probability Distribution: Annual Global Clinical Trial Participants

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

Annual Defense Industry Lobbying Spending: $127M

Details

Annual defense industry lobbying spending
Source:[17]
High confidence • *Peer-reviewed* • *Updated 2024*

Deworming Cost per DALY: $55

Details

Cost per DALY for deworming programs (range $28-82, midpoint estimate). GiveWell notes this 2011 estimate is outdated and their current methodology focuses on long-term income effects rather than short-term health DALYs.
Source:[18]
? Low confidence

dFDA Pragmatic Trial Cost per Patient: $929

Details

dFDA pragmatic trial cost per patient. Uses ADAPTABLE trial ($929) as DELIBERATELY CONSERVATIVE central estimate. Harvard meta-analysis of 108 trials found median of only $97/patient - our 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, $3K] • Distribution: Lognormal
What this means: This estimate is highly uncertain. The true value likely falls between $97 and $3K (±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

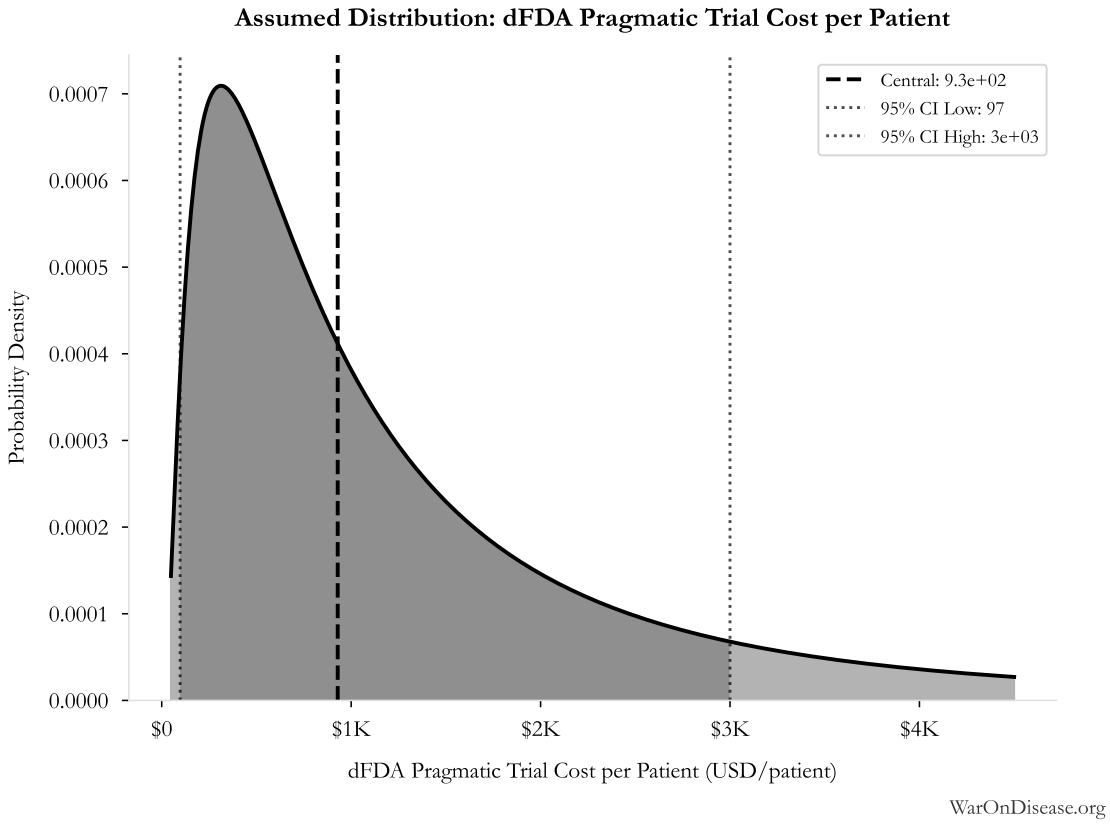


Figure 288: Probability Distribution: dFDA Pragmatic Trial Cost per Patient

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

Drug Development Cost (1980s): $194M

Details

Drug development cost in 1980s (compounded to approval, 1990 dollars)
Source:[20]

Uncertainty Range

Technical: 95% CI: [$146M, $242M] • Distribution: Lognormal
What this means: This estimate has moderate uncertainty. The true value likely falls between $146M and $242M (±25%). This represents a reasonable 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

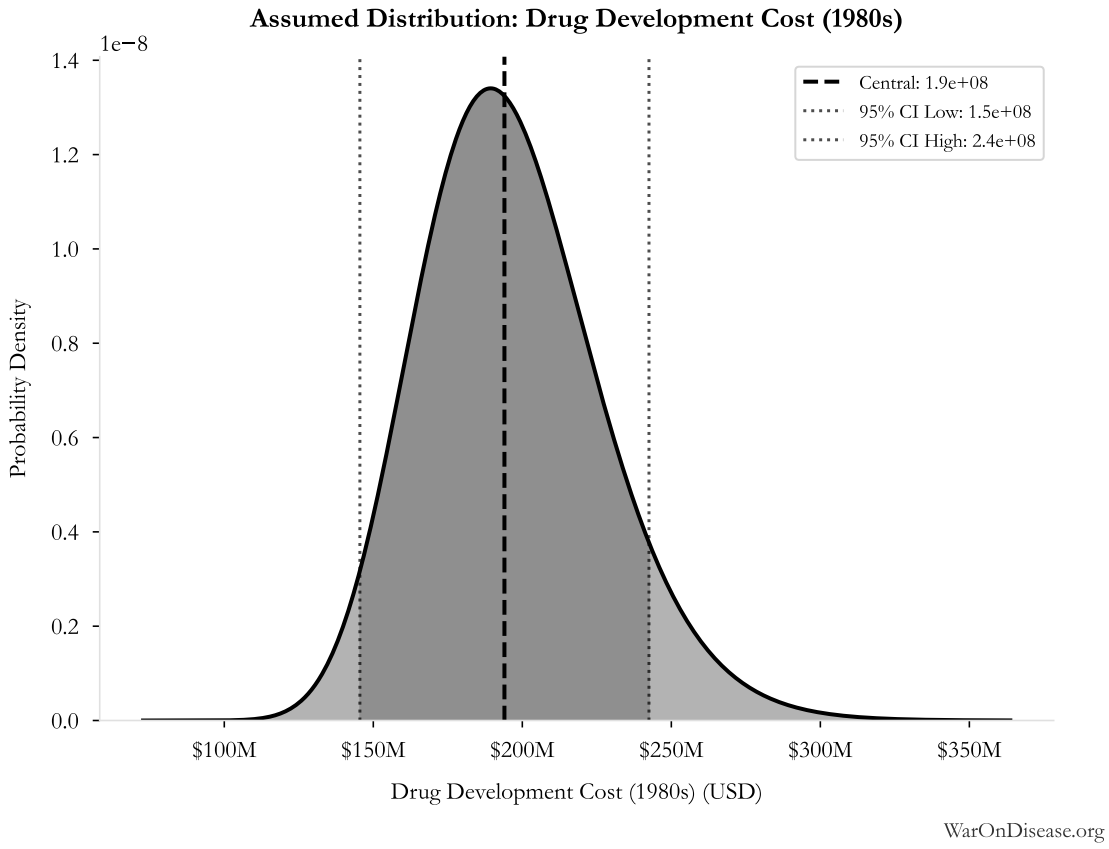


Figure 289: Probability Distribution: Drug Development Cost (1980s)

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

Drug Repurposing Success Rate: 30%

Details

Percentage of drugs that gain at least one new indication after initial approval
Source:[22]
High confidence

Economic Multiplier for Healthcare Investment: 4.3x

Details

Economic multiplier for healthcare investment (4.3x ROI). Literature range 3.0-6.0×.
Source:[24]

Uncertainty Range

Technical: 95% CI: [3x, 6x] • Distribution: Lognormal
What this means: There's significant uncertainty here. The true value likely falls between 3x and 6x (±35%). This represents a 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

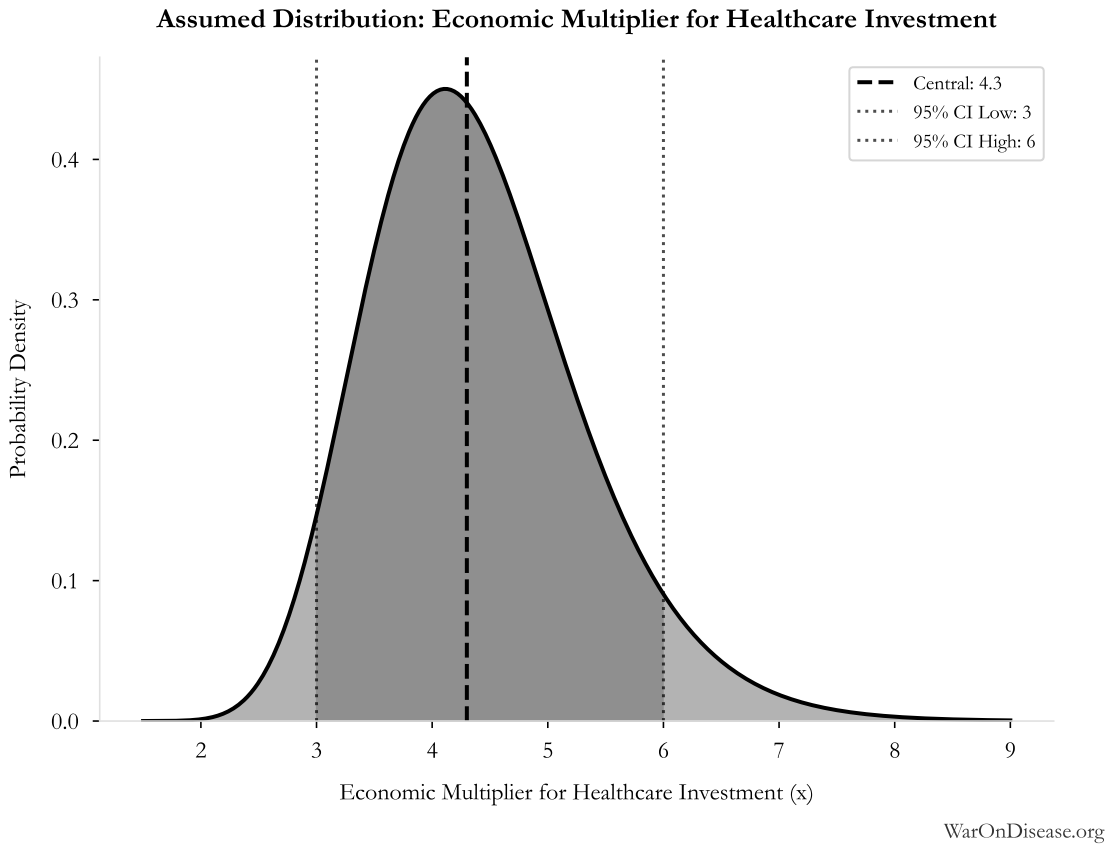


Figure 290: Probability Distribution: Economic Multiplier for Healthcare Investment

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

Economic Multiplier for Military Spending: 0.6x

Details

Economic multiplier for military spending (0.6x ROI). Literature range 0.4-1.0×.
Source:[26]

Uncertainty Range

Technical: 95% CI: [0.4x, 0.9x] • Distribution: Lognormal
What this means: There's significant uncertainty here. The true value likely falls between 0.4x and 0.9x (±42%). This represents a 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

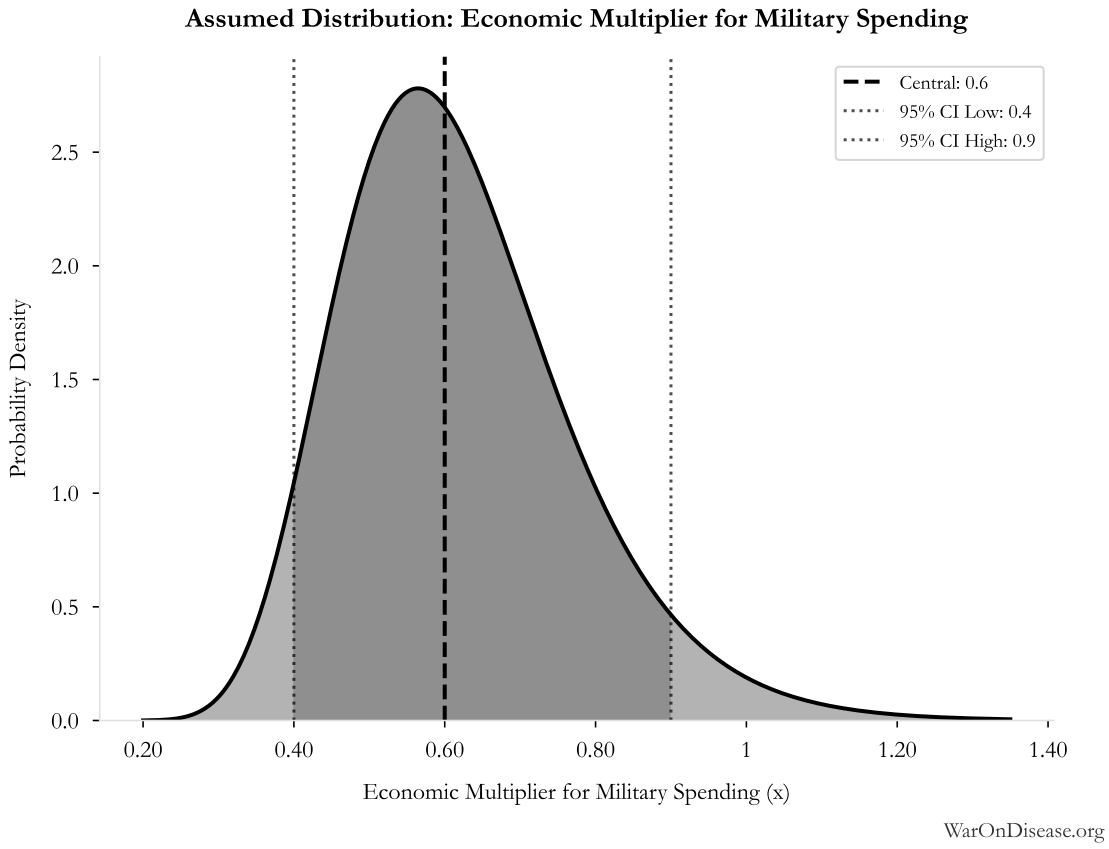


Figure 291: Probability Distribution: Economic Multiplier for Military Spending

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

Regulatory Delay for Efficacy Testing Post-Safety Verification: 8.2 years

Details

Regulatory delay for efficacy testing (Phase II/III) post-safety verification. Based on BIO 2021 industry survey. Note: This is for drugs that COMPLETE the pipeline - survivor bias means actual delay for any given disease may be longer if candidates fail and must restart.
Source:[21]

Uncertainty Range

Technical: Distribution: Normal (SE: 2 years)

Input Distribution

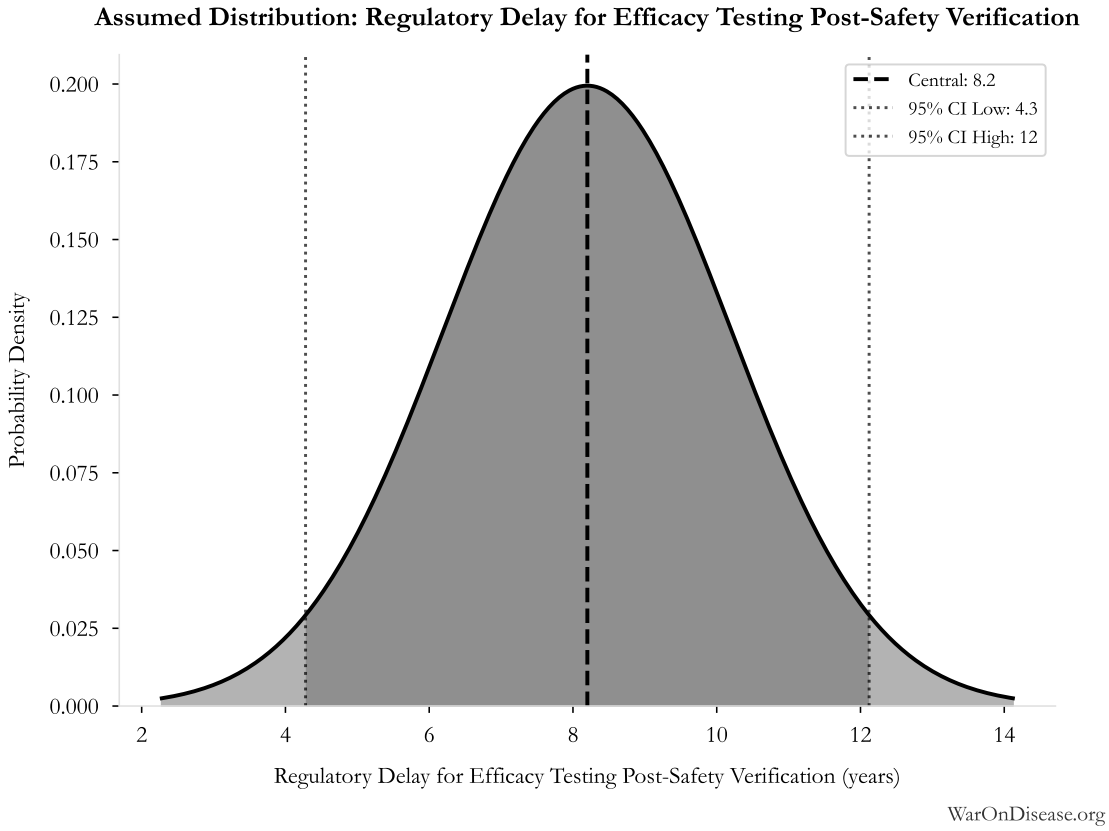


Figure 292: Probability Distribution: Regulatory Delay for Efficacy Testing Post-Safety Verification

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 • Peer-reviewed • Updated 2021

Givewell Cost per Life Saved (Maximum): $5.50K

Details

GiveWell cost per life saved (Against Malaria Foundation)
Source:[5]
High confidence

Givewell Cost per Life Saved (Minimum): $3.50K

Details

GiveWell cost per life saved (Helen Keller International)
Source:[5]
High confidence

Annual Deaths from Active Combat Worldwide: 234 thousand deaths/year

Details

Annual deaths from active combat worldwide
Source:[29]

Uncertainty Range

Technical: 95% CI: [180 thousand deaths/year, 300 thousand deaths/year] • Distribution: Lognormal
What this means: There's significant uncertainty here. The true value likely falls between 180 thousand deaths/year and 300 thousand deaths/year (±26%). This represents a 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

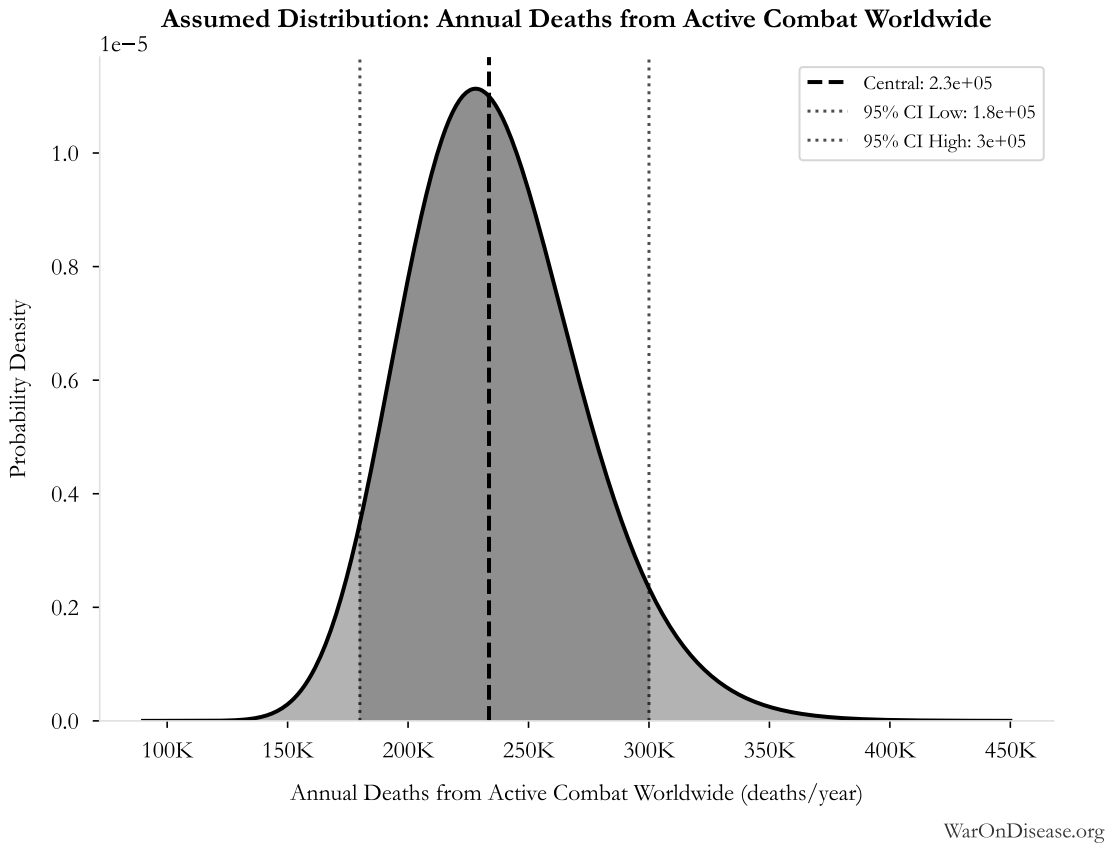


Figure 293: Probability Distribution: Annual Deaths from Active Combat Worldwide

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

Annual Deaths from State Violence: 2.70 thousand deaths/year

Details

Annual deaths from state violence
Source:[30]

Uncertainty Range

Technical: 95% CI: [1.50 thousand deaths/year, 5.00 thousand deaths/year] • Distribution: Lognormal
What this means: This estimate is highly uncertain. The true value likely falls between 1.50

thousand deaths/year and 5.00 thousand deaths/year (±65%). 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

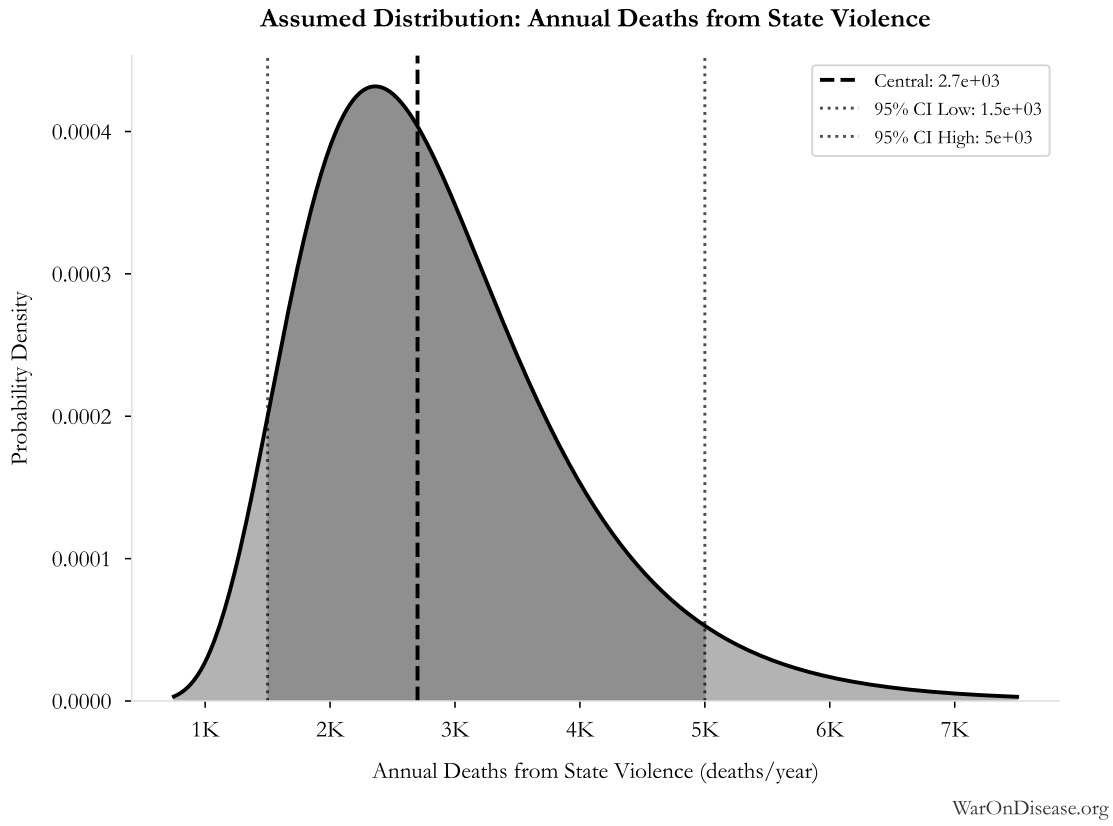


Figure 294: Probability Distribution: Annual Deaths from State Violence

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

Annual Deaths from Terror Attacks Globally: 8.30 thousand deaths/year

Details

Annual deaths from terror attacks globally
Source:[31]

Uncertainty Range

Technical: 95% CI: [6.00 thousand deaths/year, 12.0 thousand deaths/year] • Distribution: Lognormal
What this means: There's significant uncertainty here. The true value likely falls between 6.00 thousand deaths/year and 12.0 thousand deaths/year (±36%). This represents a 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

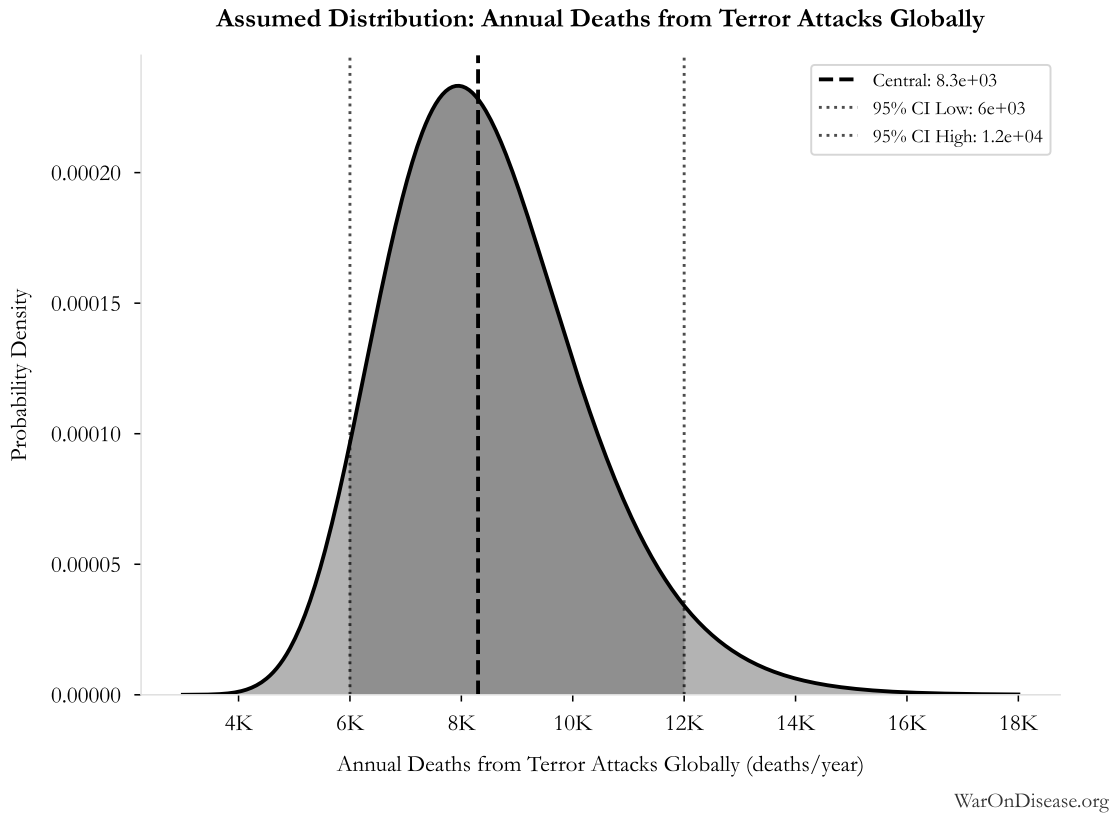


Figure 295: Probability Distribution: Annual Deaths from Terror Attacks Globally

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

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:[32]

Uncertainty Range

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

Input Distribution

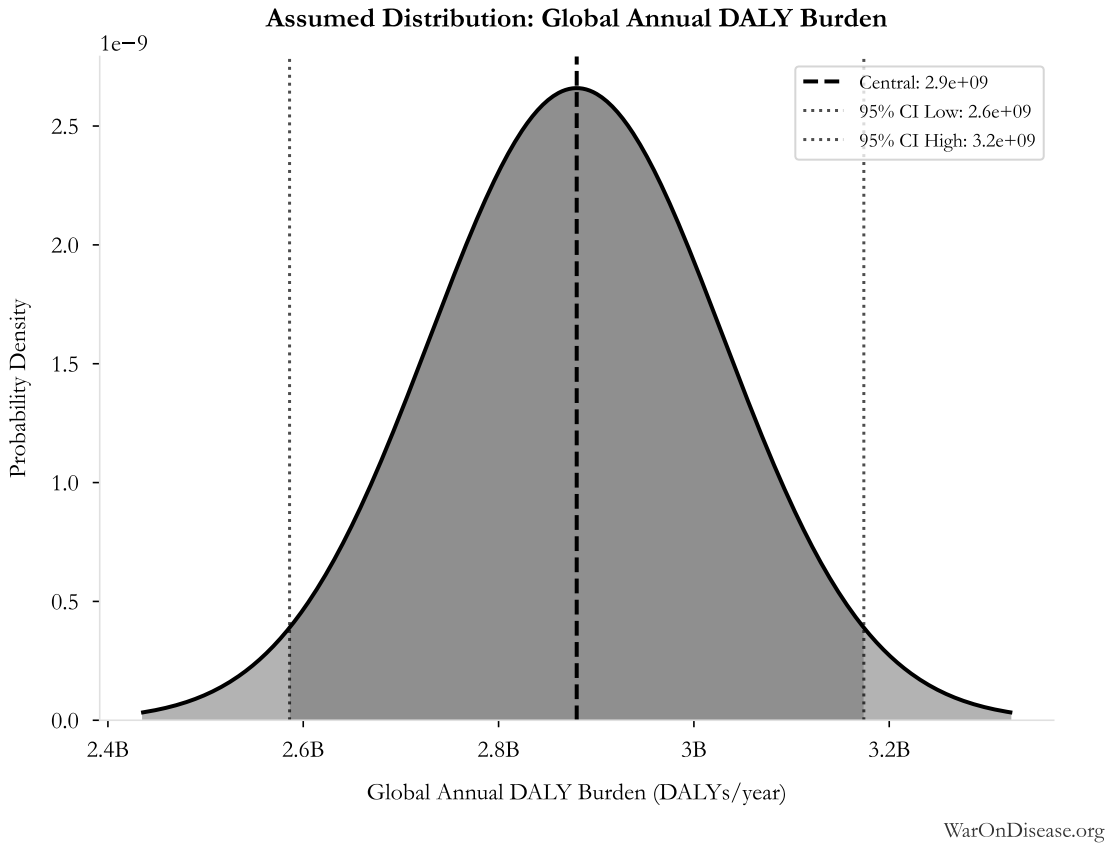


Figure 296: Probability Distribution: Global Annual DALY Burden

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*

Annual Deaths from All Diseases and Aging Globally: 55.0 million deaths/year

Details

Annual deaths from all diseases and aging globally
Source:[4]

Uncertainty Range

Technical: Distribution: Normal (SE: 5.00 million deaths/year)

Input Distribution

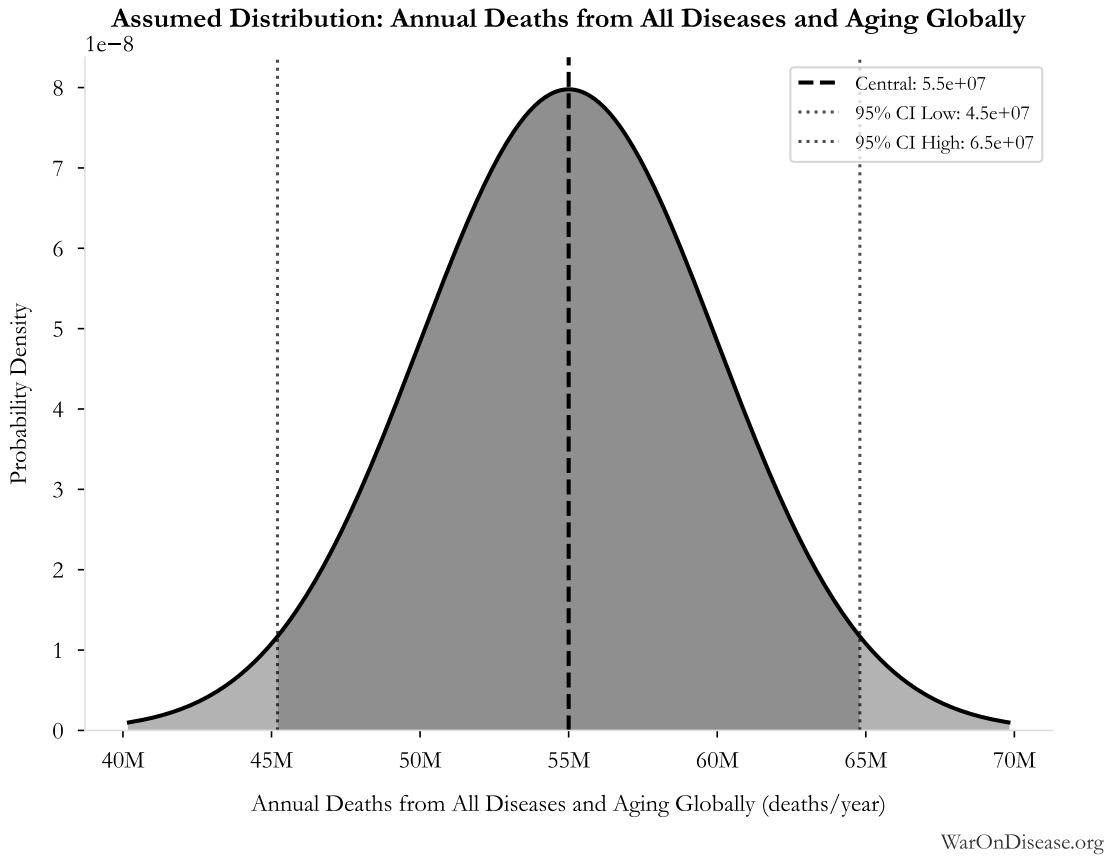


Figure 297: Probability Distribution: Annual Deaths from All Diseases and Aging Globally

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

Annual Environmental Damage and Restoration Costs from Conflict: $100B

Details

Annual environmental damage and restoration costs from conflict
Source:[33]

Uncertainty Range

Technical: 95% CI: [$70B, $140B] • Distribution: Lognormal
What this means: There's significant uncertainty here. The true value likely falls between $70B and $140B (±35%). This represents a 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

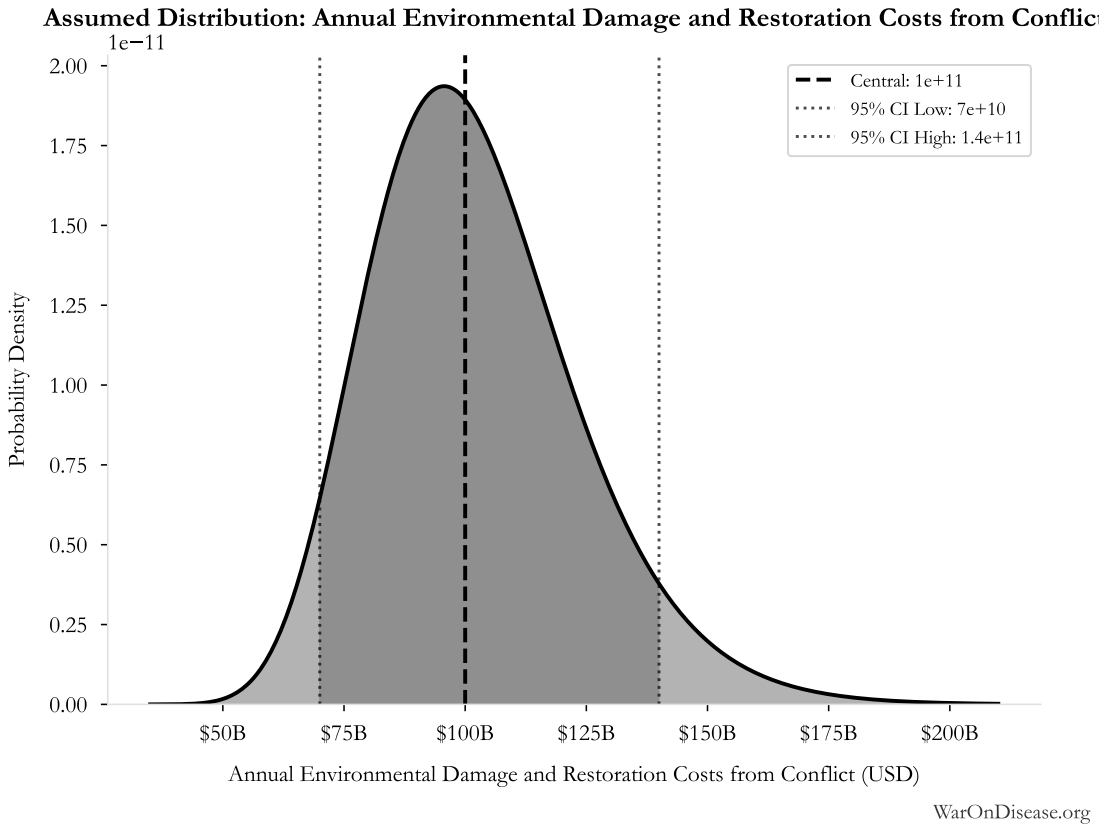


Figure 298: Probability Distribution: Annual Environmental Damage and Restoration Costs from Conflict

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

Annual Infrastructure Damage to Communications from Conflict: $298B

Details

Annual infrastructure damage to communications from conflict
Source:[33]

Uncertainty Range

Technical: 95% CI: [$209B, $418B] • Distribution: Lognormal
What this means: There's significant uncertainty here. The true value likely falls between

$209B and $418B (±35%). This represents a 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

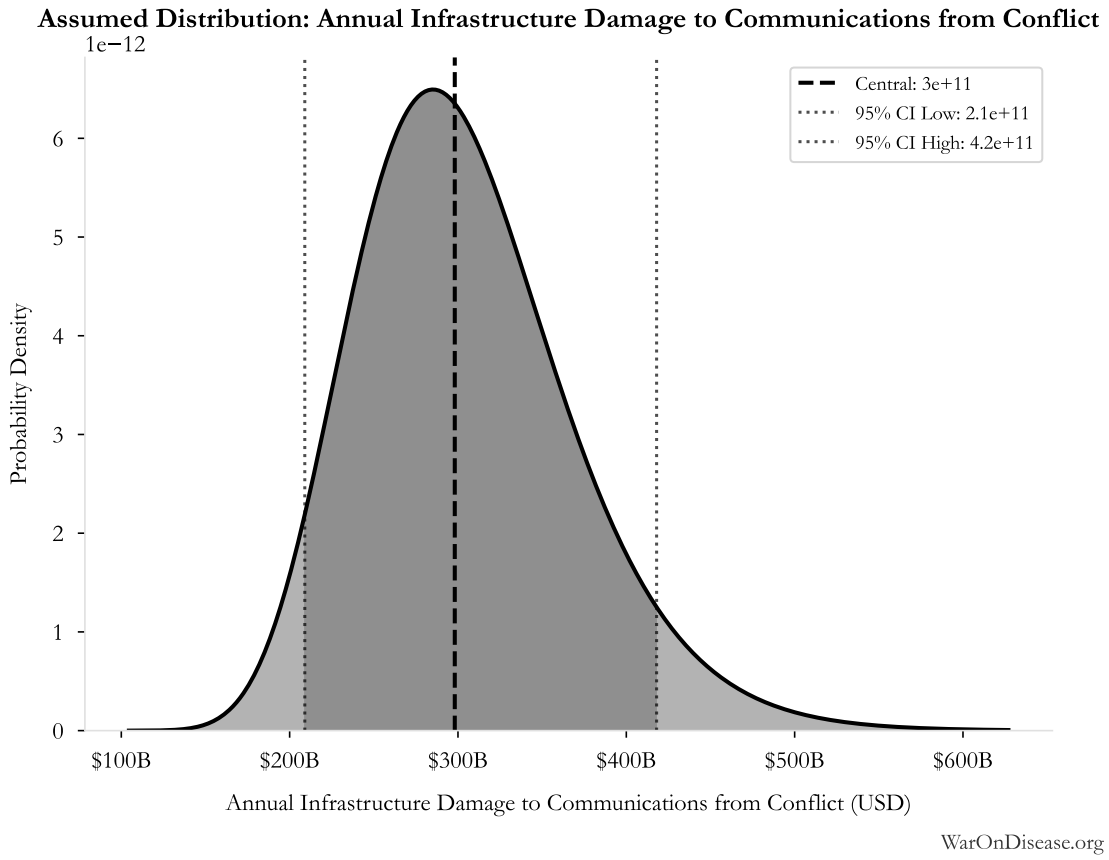


Figure 299: Probability Distribution: Annual Infrastructure Damage to Communications from Conflict

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

Annual Infrastructure Damage to Education Facilities from Conflict: $234B

Details

Annual infrastructure damage to education facilities from conflict
Source:[33]

Uncertainty Range

Technical: 95% CI: [$164B, $328B] • Distribution: Lognormal
What this means: There's significant uncertainty here. The true value likely falls between $164B and $328B (±35%). This represents a 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

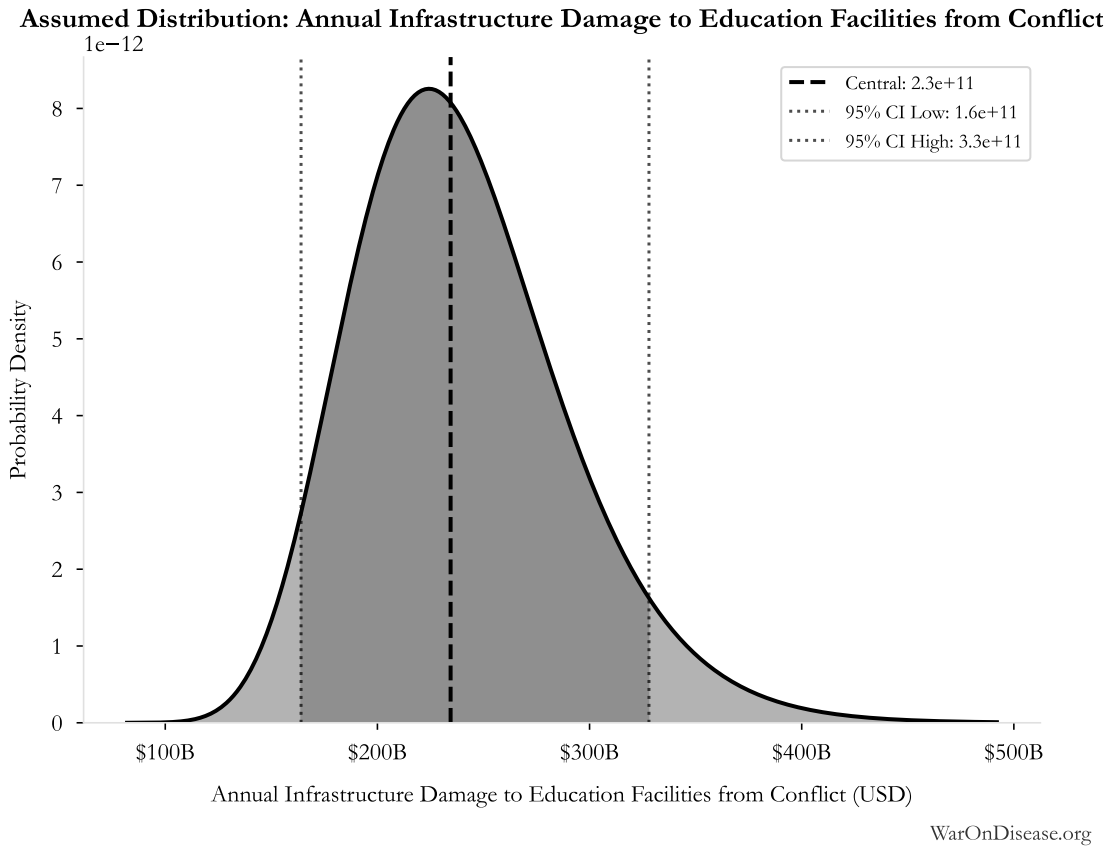


Figure 300: Probability Distribution: Annual Infrastructure Damage to Education Facilities from Conflict

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

Annual Infrastructure Damage to Energy Systems from Conflict: $422B

Details

Annual infrastructure damage to energy systems from conflict
Source:[33]

Uncertainty Range

Technical: 95% CI: [$295B, $590B] • Distribution: Lognormal
What this means: There's significant uncertainty here. The true value likely falls between $295B and $590B (±35%). This represents a 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

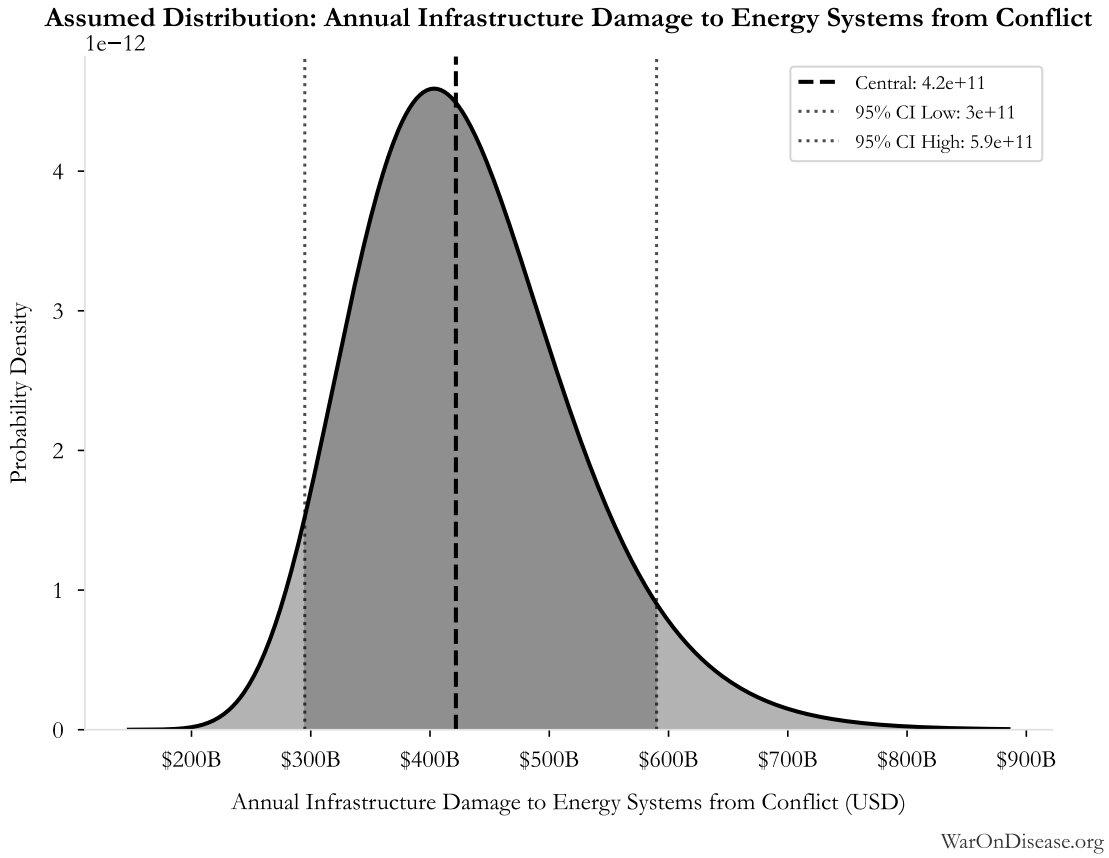


Figure 301: Probability Distribution: Annual Infrastructure Damage to Energy Systems from Conflict

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

Annual Infrastructure Damage to Healthcare Facilities from Conflict: $166B

Details

Annual infrastructure damage to healthcare facilities from conflict
Source:[33]

Uncertainty Range

Technical: 95% CI: [$116B, $232B] • Distribution: Lognormal

What this means: There's significant uncertainty here. The true value likely falls between $116B and $232B (±35%). This represents a 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

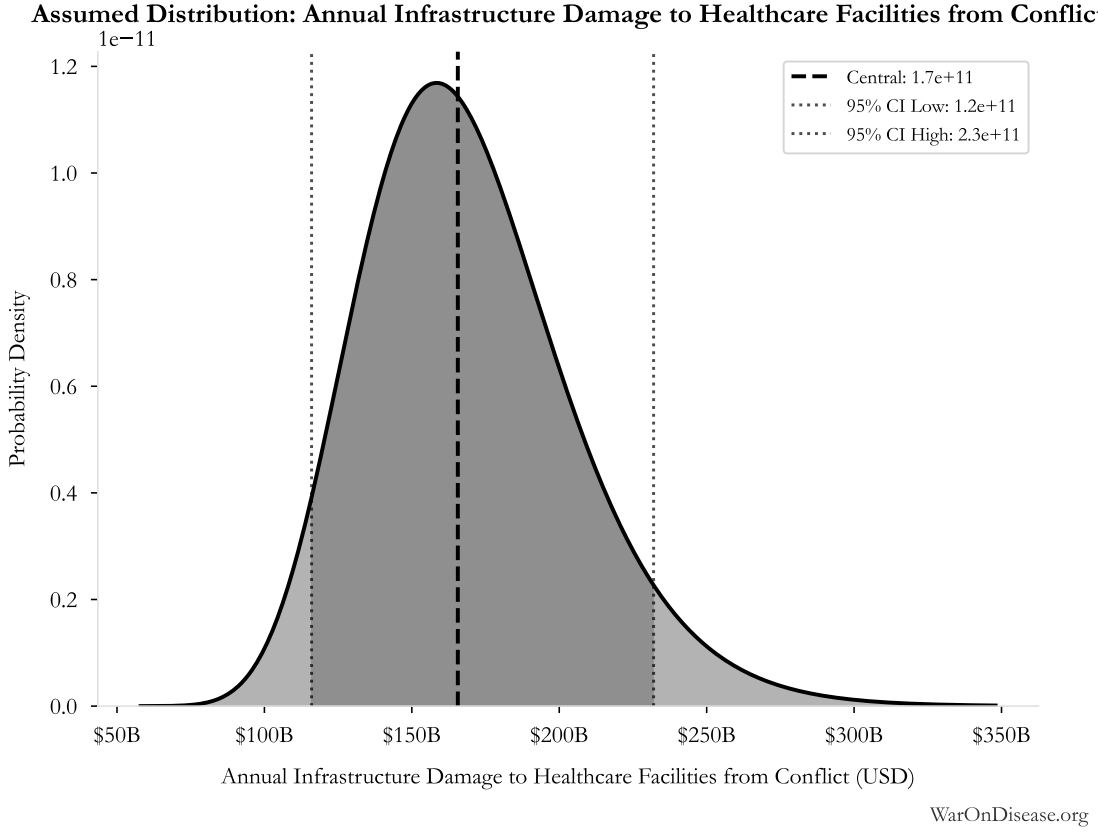


Figure 302: Probability Distribution: Annual Infrastructure Damage to Healthcare Facilities from Conflict

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

Annual Infrastructure Damage to Transportation from Conflict: $487B

Details

Annual infrastructure damage to transportation from conflict
Source:[33]

Uncertainty Range

Technical: 95% CI: [$340B, $680B] • Distribution: Lognormal
What this means: There's significant uncertainty here. The true value likely falls between $340B and $680B (±35%). This represents a 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

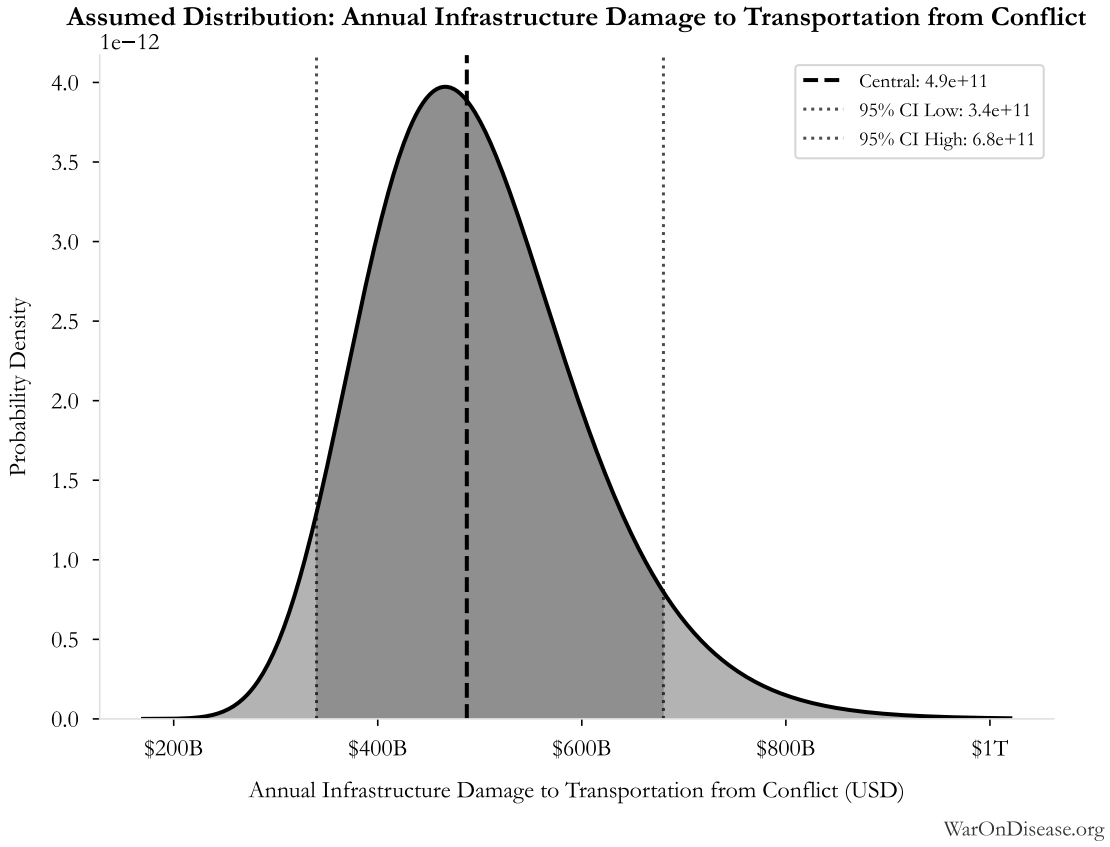


Figure 303: Probability Distribution: Annual Infrastructure Damage to Transportation from Conflict

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

Annual Infrastructure Damage to Water Systems from Conflict: $268B

Details

Annual infrastructure damage to water systems from conflict
Source:[33]

Uncertainty Range

Technical: 95% CI: [$187B, $375B] • Distribution: Lognormal
What this means: There's significant uncertainty here. The true value likely falls between $187B and $375B (±35%). This represents a 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

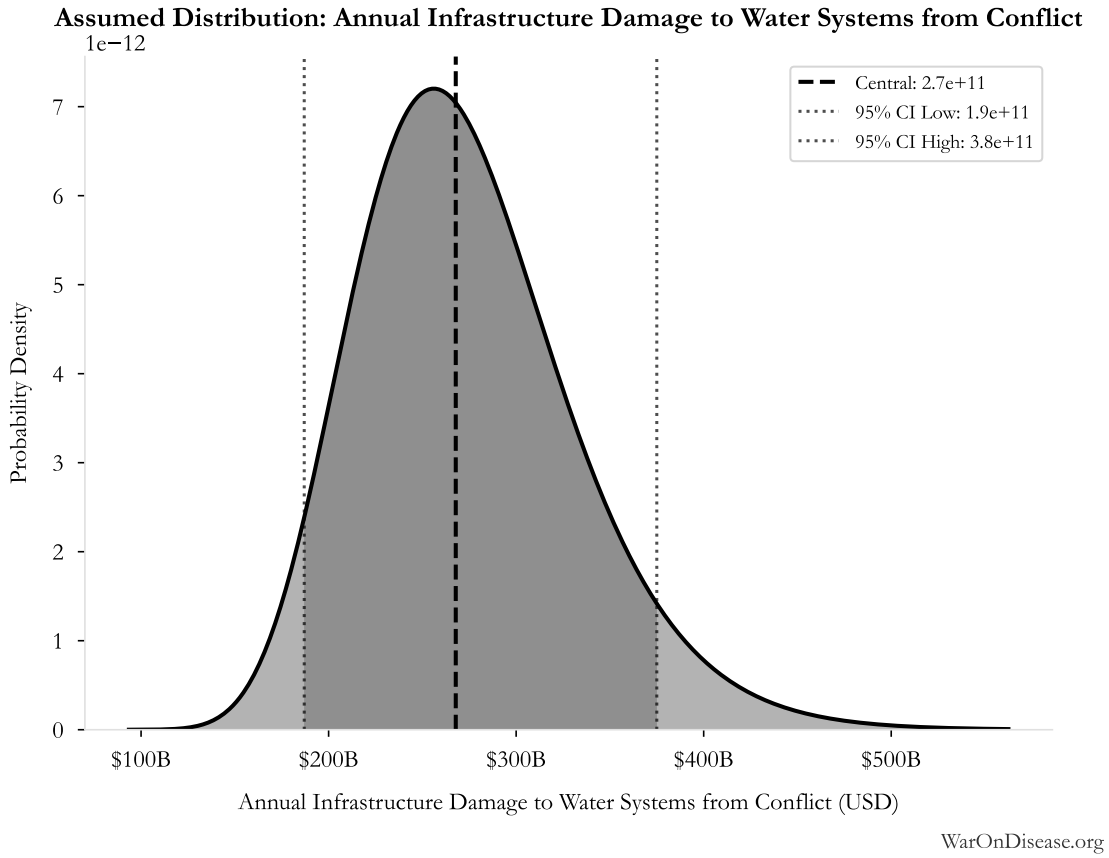


Figure 304: Probability Distribution: Annual Infrastructure Damage to Water Systems from Conflict

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

Annual Lost Economic Growth from Military Spending Opportunity Cost: $2.72T

Details

Annual foregone economic output from military spending vs productive alternatives. This estimate implicitly captures fiscal multiplier differences (military ~0.6x vs healthcare ~4.3x GDP multiplier). Do not add separate GDP multiplier adjustment to avoid double-counting. **Source**:[35]

Uncertainty Range

Technical: 95% CI: [$1.90T, $3.80T] • Distribution: Lognormal
What this means: There's significant uncertainty here. The true value likely falls between $1.90T and $3.80T (±35%). This represents a 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

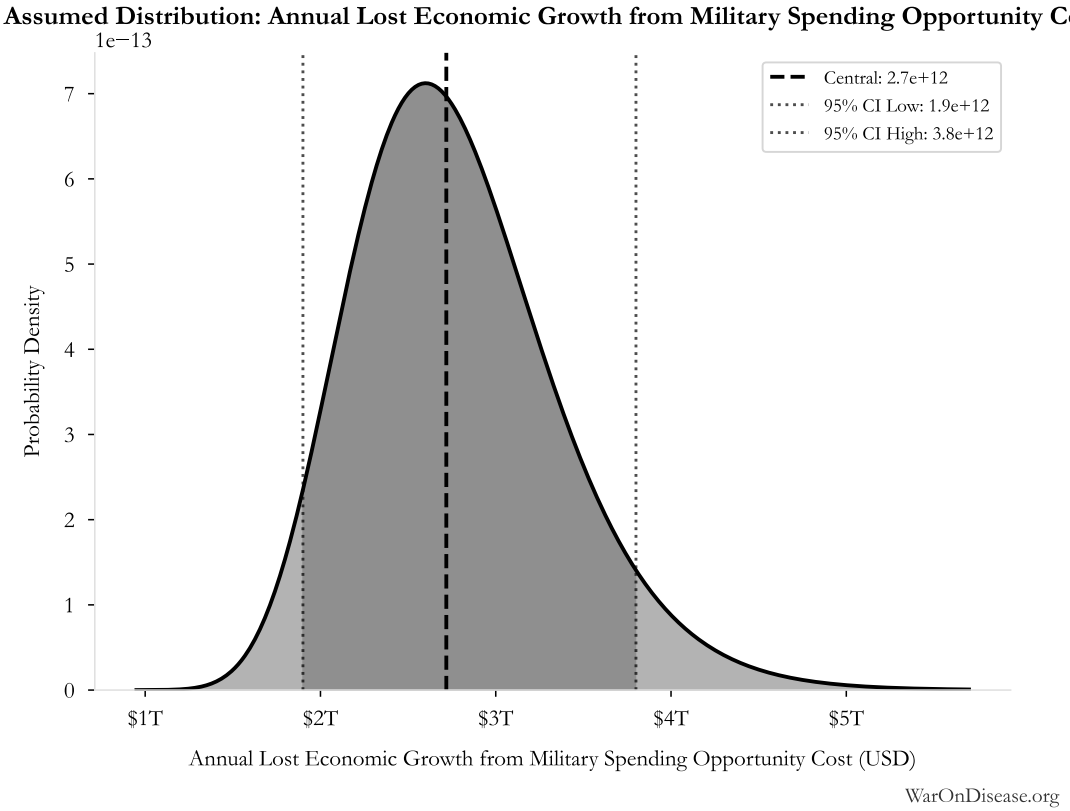


Figure 305: Probability Distribution: Annual Lost Economic Growth from Military Spending Opportunity Cost

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.
High confidence

Annual Lost Productivity from Conflict Casualties: $300B

Details

Annual lost productivity from conflict casualties
Source:[36]

Uncertainty Range

Technical: 95% CI: [$210B, $420B] • Distribution: Lognormal
What this means: There's significant uncertainty here. The true value likely falls between $210B and $420B (±35%). This represents a 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

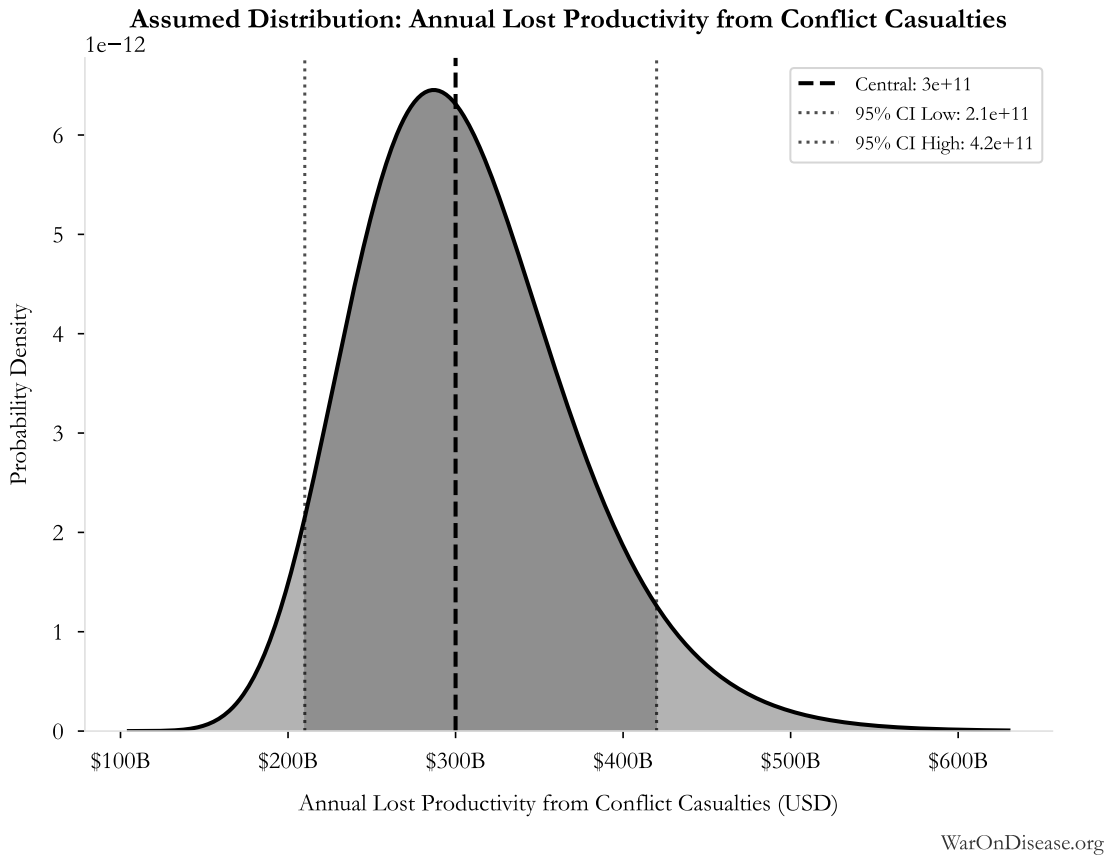


Figure 306: Probability Distribution: Annual Lost Productivity from Conflict Casualties

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

Annual PTSD and Mental Health Costs from Conflict: $232B

Details

Annual PTSD and mental health costs from conflict
Source:[37]

Uncertainty Range

Technical: 95% CI: [$162B, $325B] • Distribution: Lognormal
What this means: There's significant uncertainty here. The true value likely falls between $162B and $325B (±35%). This represents a 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

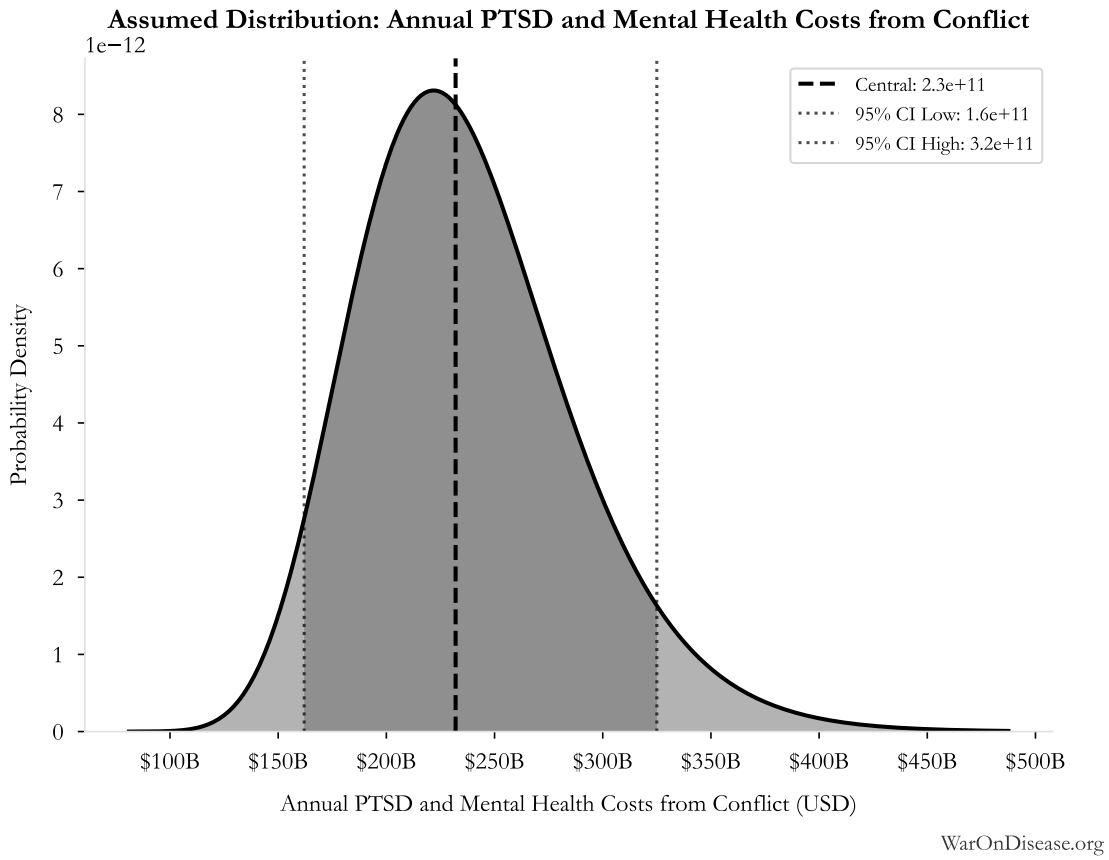


Figure 307: Probability Distribution: Annual PTSD and Mental Health Costs from Conflict

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

Annual Refugee Support Costs: $150B

Details

Annual refugee support costs (108.4M refugees × $1,384/year)
Source:[38]

Uncertainty Range

Technical: 95% CI: [$105B, $210B] • Distribution: Lognormal
What this means: There's significant uncertainty here. The true value likely falls between

$105B and $210B (±35%). This represents a 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

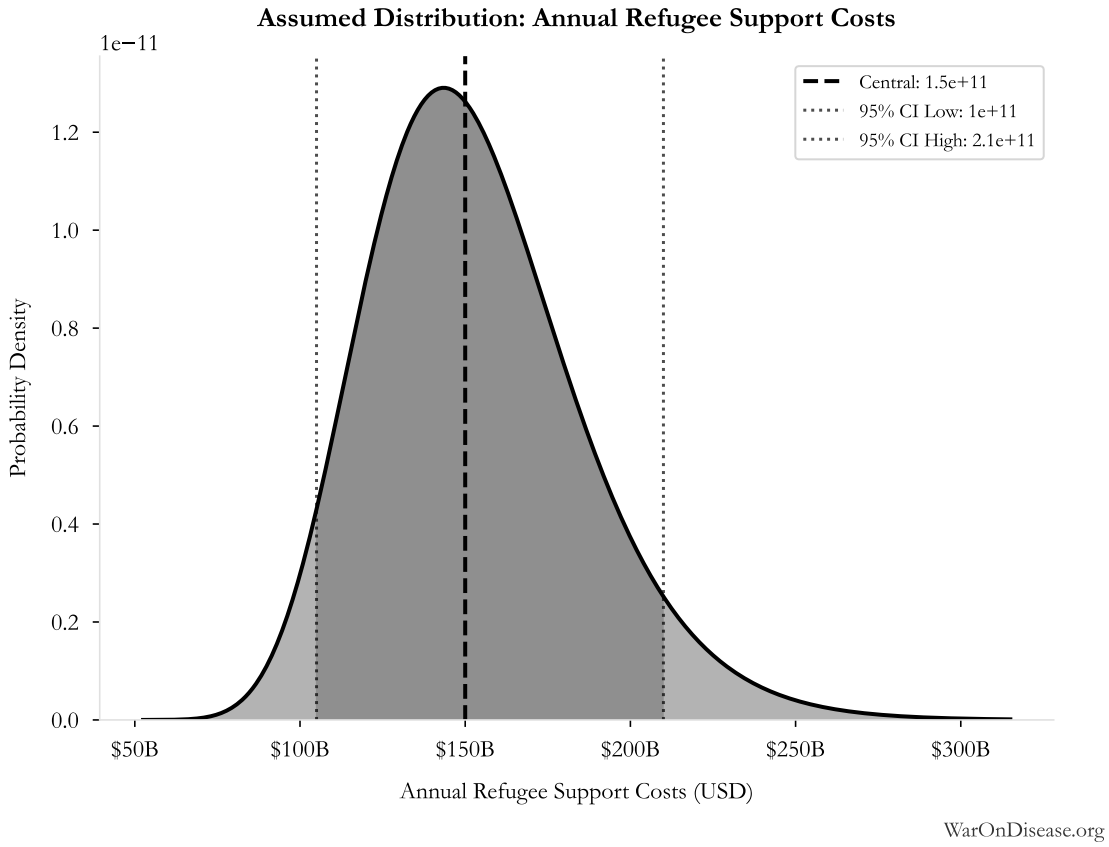


Figure 308: Probability Distribution: Annual Refugee Support Costs

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

Annual Trade Disruption Costs from Currency Instability: $57.4B

Details

Annual trade disruption costs from currency instability
Source:[39]

Uncertainty Range

Technical: 95% CI: [$40B, $80B] • Distribution: Lognormal
What this means: There's significant uncertainty here. The true value likely falls between $40B and $80B (±35%). This represents a 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

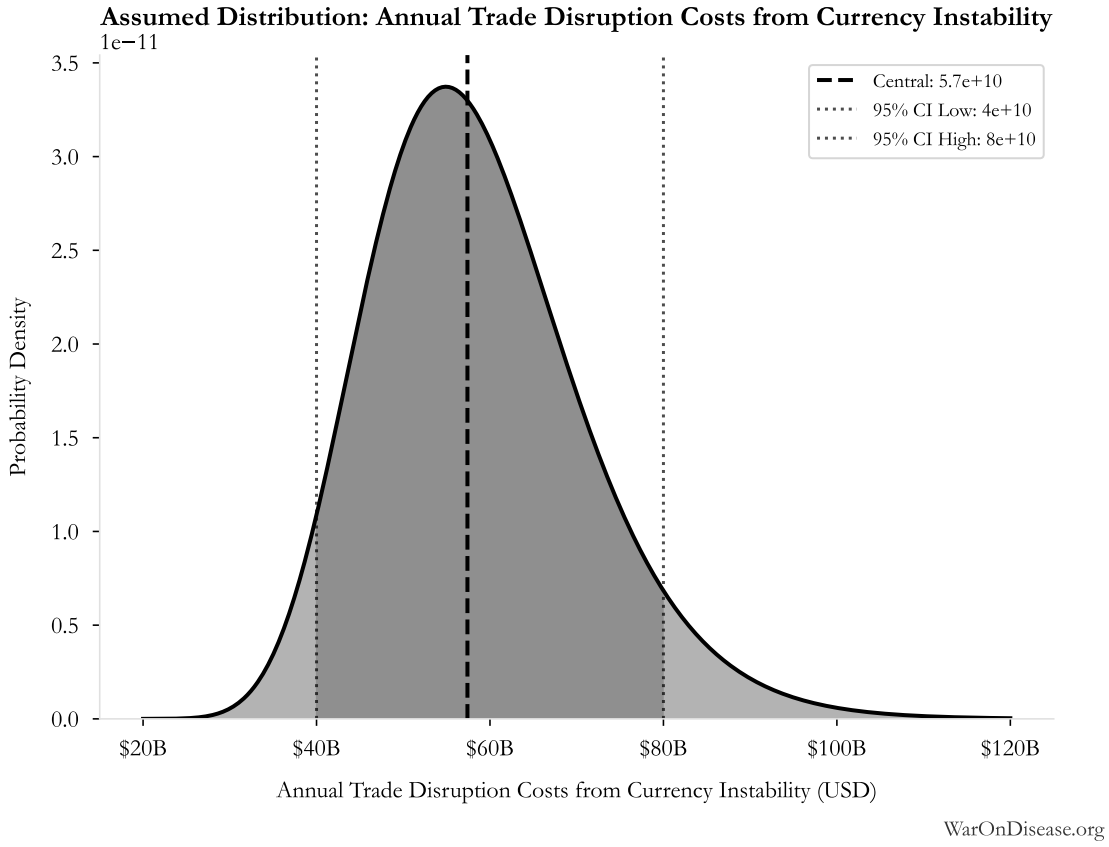


Figure 309: Probability Distribution: Annual Trade Disruption Costs from Currency Instability

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

Annual Trade Disruption Costs from Energy Price Volatility: $125B

Details

Annual trade disruption costs from energy price volatility
Source:[39]

Uncertainty Range

Technical: 95% CI: [$87B, $175B] • Distribution: Lognormal
What this means: There's significant uncertainty here. The true value likely falls between $87B and $175B (±35%). This represents a 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

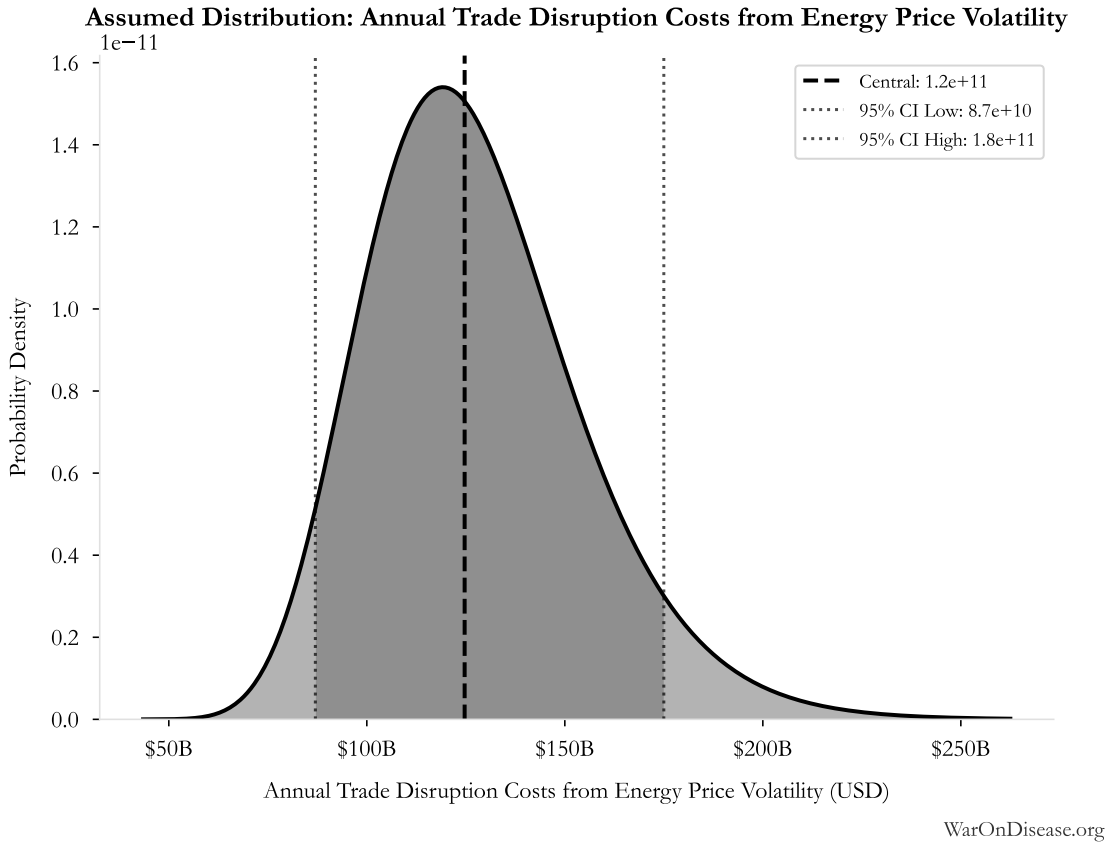


Figure 310: Probability Distribution: Annual Trade Disruption Costs from Energy Price Volatility

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

Annual Trade Disruption Costs from Shipping Disruptions: $247B

Details

Annual trade disruption costs from shipping disruptions
Source:[39]

Uncertainty Range

Technical: 95% CI: [$173B, $346B] • Distribution: Lognormal
What this means: There's significant uncertainty here. The true value likely falls between

$173B and $346B (±35%). This represents a 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

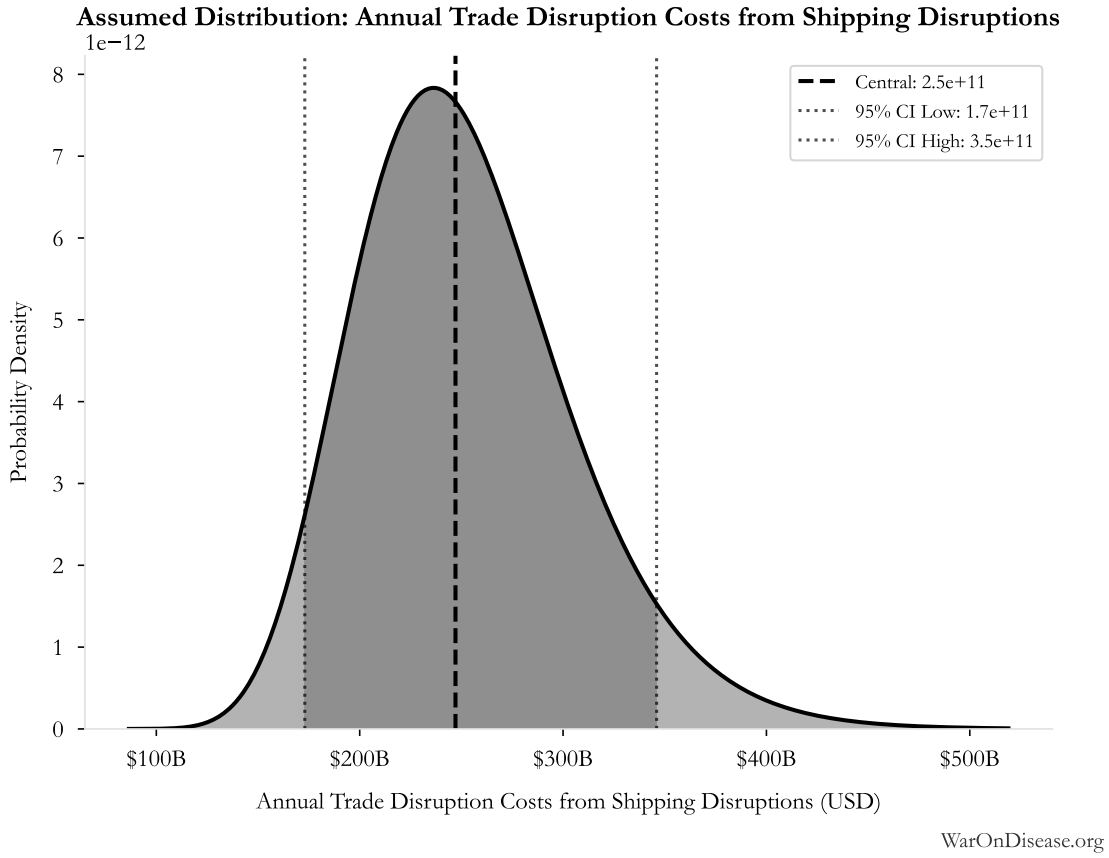


Figure 311: Probability Distribution: Annual Trade Disruption Costs from Shipping Disruptions

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

Annual Trade Disruption Costs from Supply Chain Disruptions: $187B

Details

Annual trade disruption costs from supply chain disruptions
Source:[39]

Uncertainty Range

Technical: 95% CI: [$131B, $262B] • Distribution: Lognormal
What this means: There's significant uncertainty here. The true value likely falls between $131B and $262B (±35%). This represents a 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

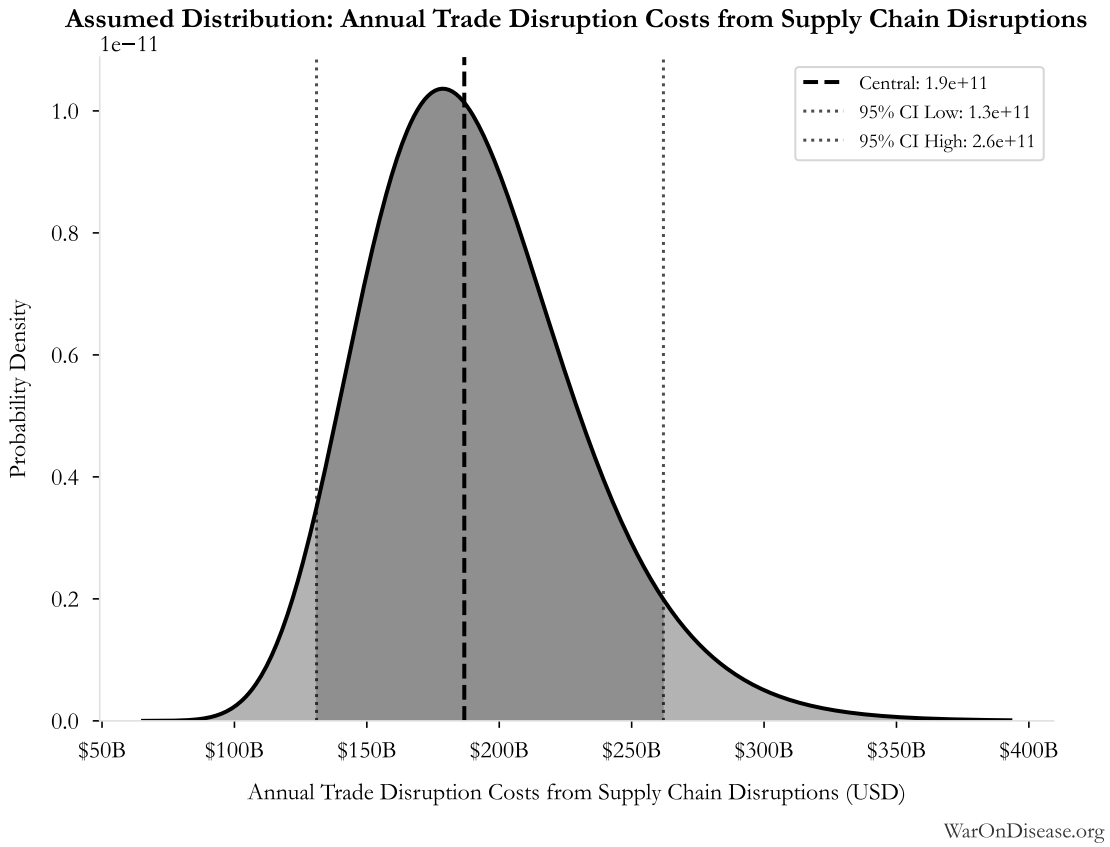


Figure 312: Probability Distribution: Annual Trade Disruption Costs from Supply Chain Disruptions

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

Annual Veteran Healthcare Costs: $200B

Details

Annual veteran healthcare costs (20-year projected)
Source:[40]

Uncertainty Range

Technical: 95% CI: [$140B, $280B] • Distribution: Lognormal
What this means: There's significant uncertainty here. The true value likely falls between $140B and $280B (±35%). This represents a 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

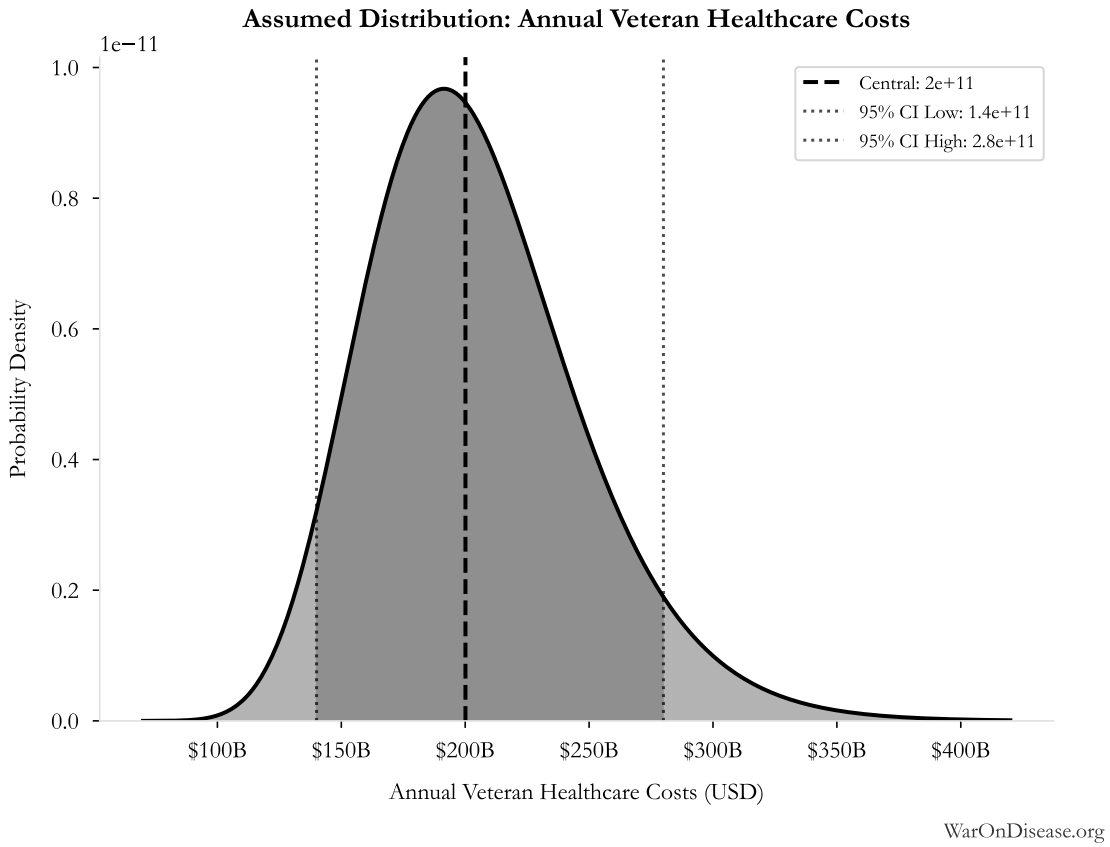


Figure 313: Probability Distribution: Annual Veteran Healthcare Costs

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

Annual Global Spending on Clinical Trials: $60B

Details

Annual global spending on clinical trials (Industry: $45-60B + Government: $3-6B + Nonprofits: $2-5B). Conservative estimate using 15-20% of $300B total pharma R&D, not inflated market size projections.
Source:[42]

Uncertainty Range

Technical: 95% CI: [$50B, $75B] • Distribution: Lognormal (SE: $10B)

What this means: This estimate has moderate uncertainty. The true value likely falls between $50B and $75B (±21%). This represents a reasonable 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

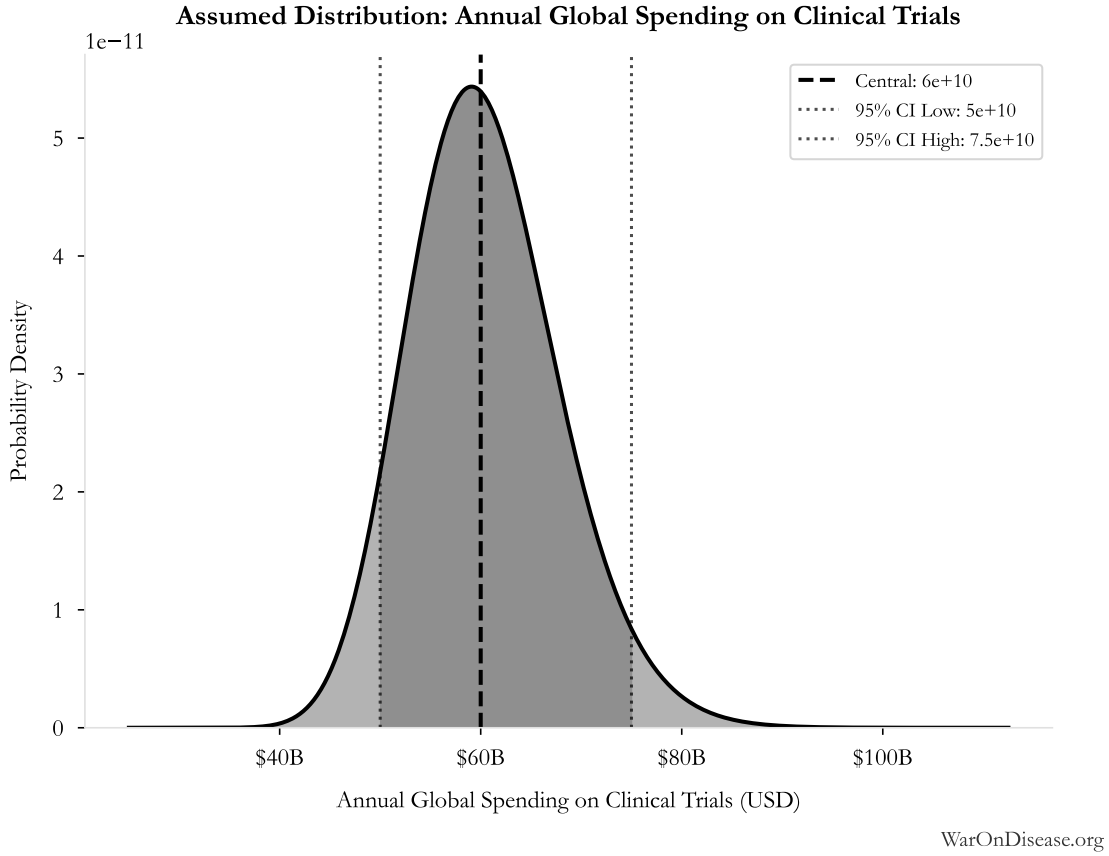


Figure 314: Probability Distribution: Annual Global Spending on Clinical Trials

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

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**:[4]

Uncertainty Range

Technical: Distribution: Normal (SE: 7.50 thousand deaths/day)

Input Distribution

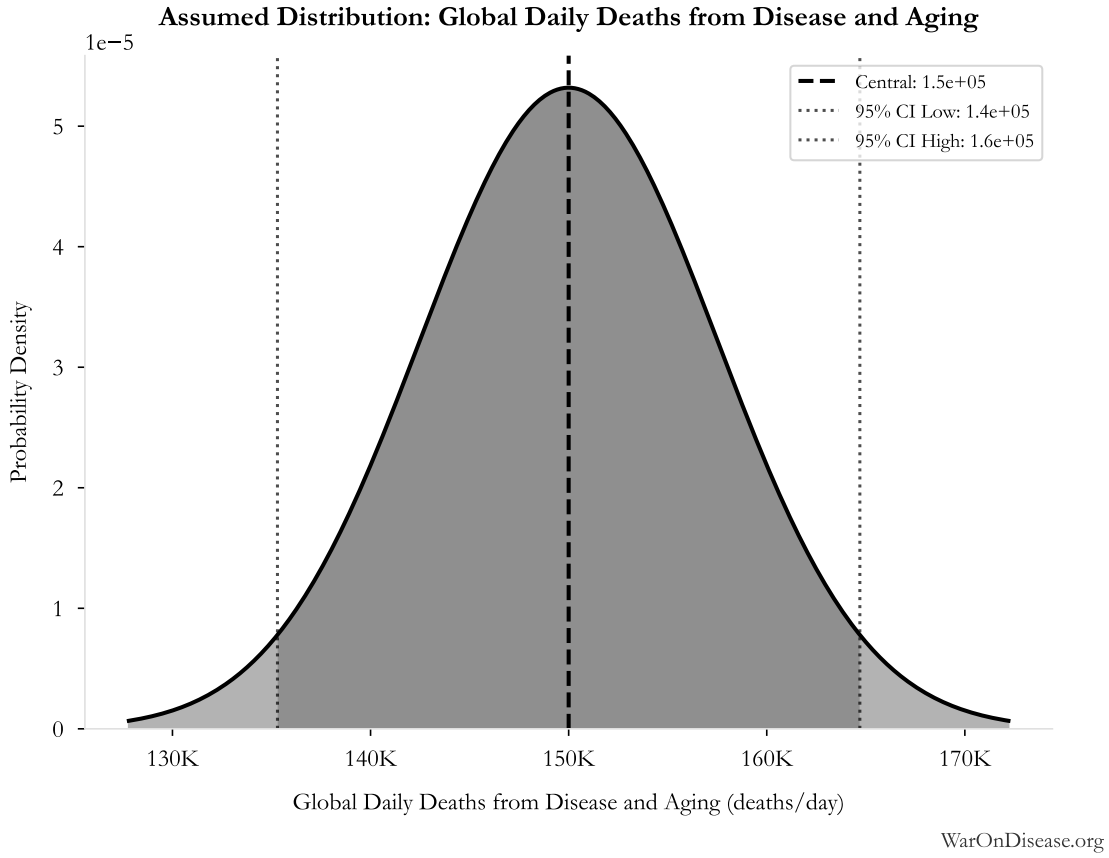


Figure 315: Probability Distribution: Global Daily Deaths from Disease and Aging

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*

Global Annual Direct Medical Costs of Disease: $9.90T

Details

Direct medical costs of disease globally (treatment, hospitalization, medication)
Source:[43]

Uncertainty Range

Technical: 95% CI: [$7T, $14T] • Distribution: Lognormal
What this means: There's significant uncertainty here. The true value likely falls between $7T and $14T (±35%). This represents a 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

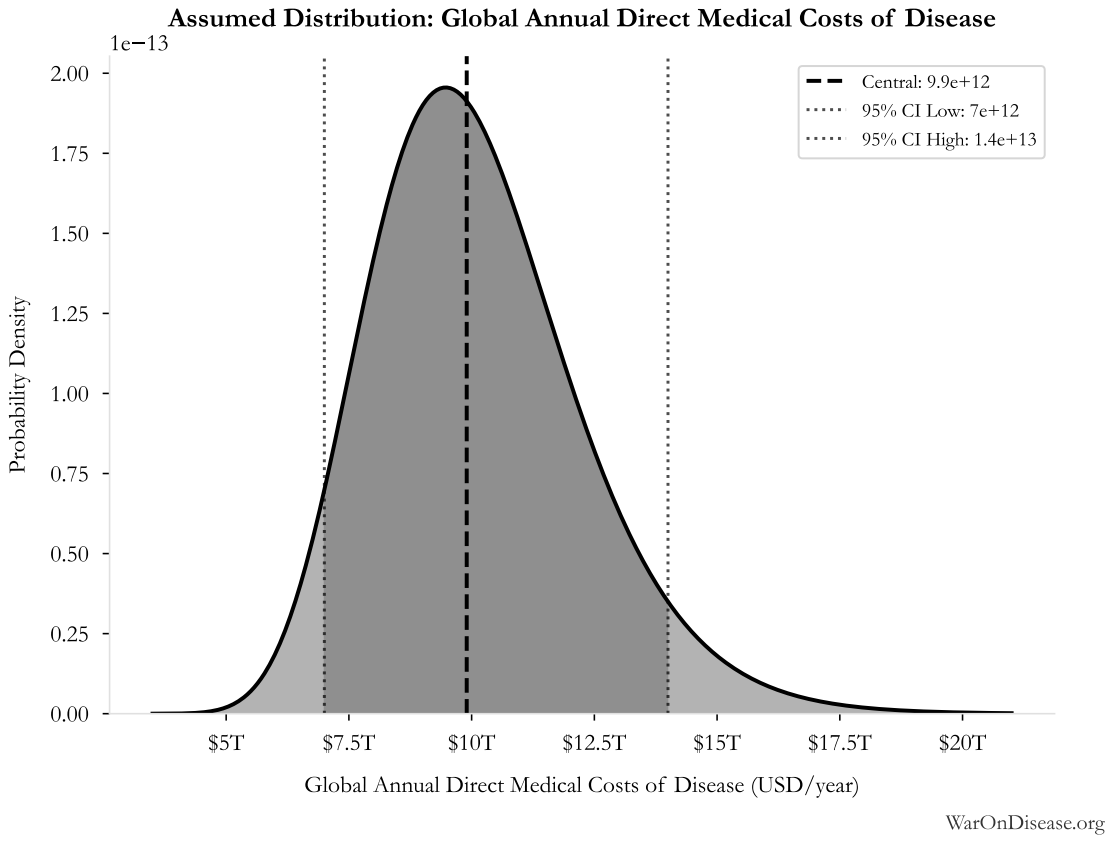


Figure 316: Probability Distribution: Global Annual Direct Medical Costs of Disease

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

Global Annual Economic Value of Human Life Lost to Disease: $94.2T

Details

Economic value of human life lost to disease annually (mortality valuation)
Source:[43]

Uncertainty Range

Technical: 95% CI: [$66T, $132T] • Distribution: Lognormal
What this means: There's significant uncertainty here. The true value likely falls between $66T and $132T (±35%). This represents a 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

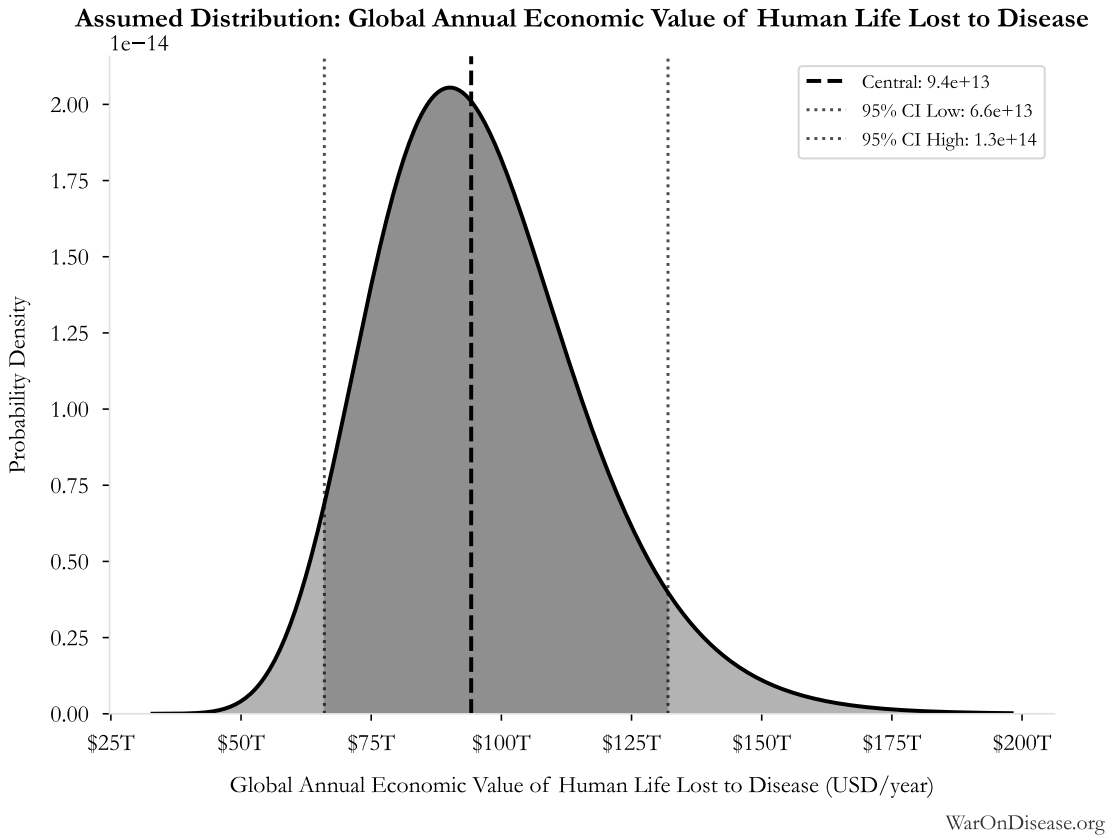


Figure 317: Probability Distribution: Global Annual Economic Value of Human Life Lost to Disease

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

Global Annual Productivity Loss from Disease: $5T

Details

Annual productivity loss from disease globally (absenteeism, reduced output)
Source:[43]

Uncertainty Range

Technical: 95% CI: [$3.50T, $7T] • Distribution: Lognormal
What this means: There's significant uncertainty here. The true value likely falls between

$3.50T and $7T (±35%). This represents a 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

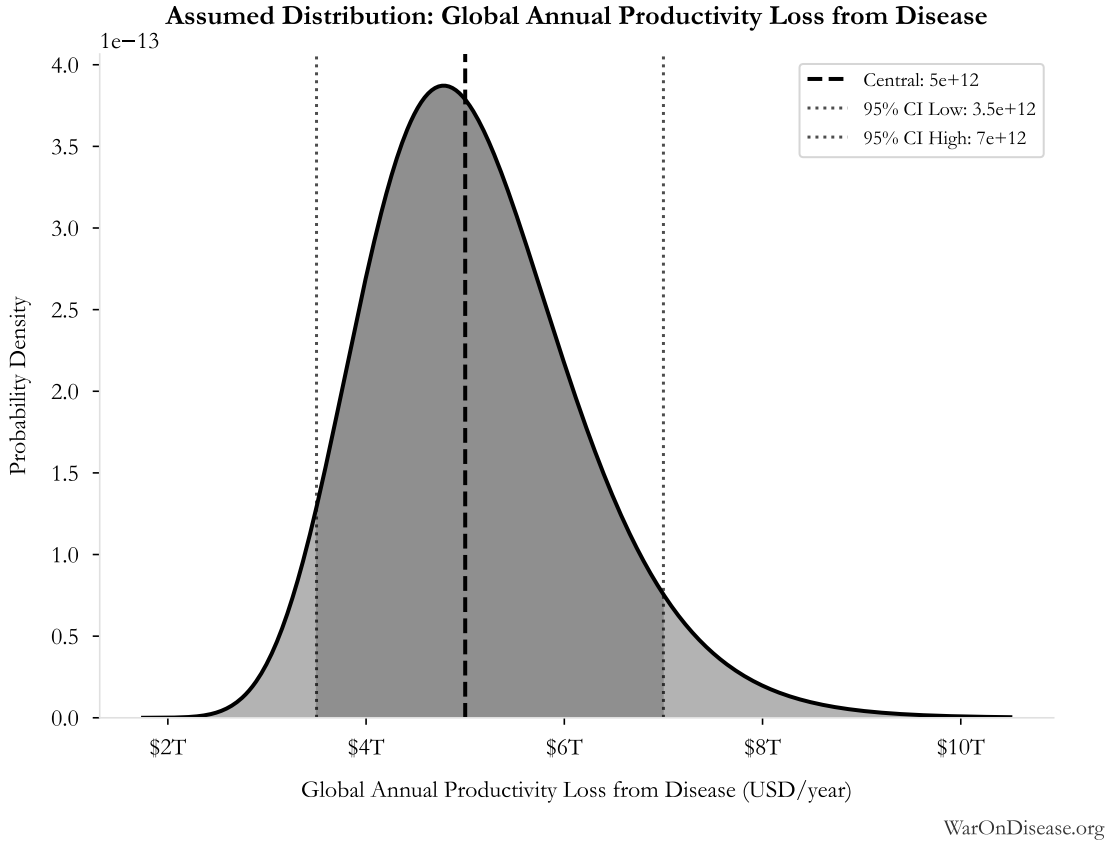


Figure 318: Probability Distribution: Global Annual Productivity Loss from Disease

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

Annual Global Government Spending on Clinical Trials: $4.50B

Details

Annual global government spending on interventional clinical trials (~5-10% of total)
Source:[45]

Uncertainty Range

Technical: 95% CI: [$3B, $6B] • Distribution: Lognormal (SE: $1B)
What this means: There's significant uncertainty here. The true value likely falls between $3B and $6B (±33%). This represents a 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

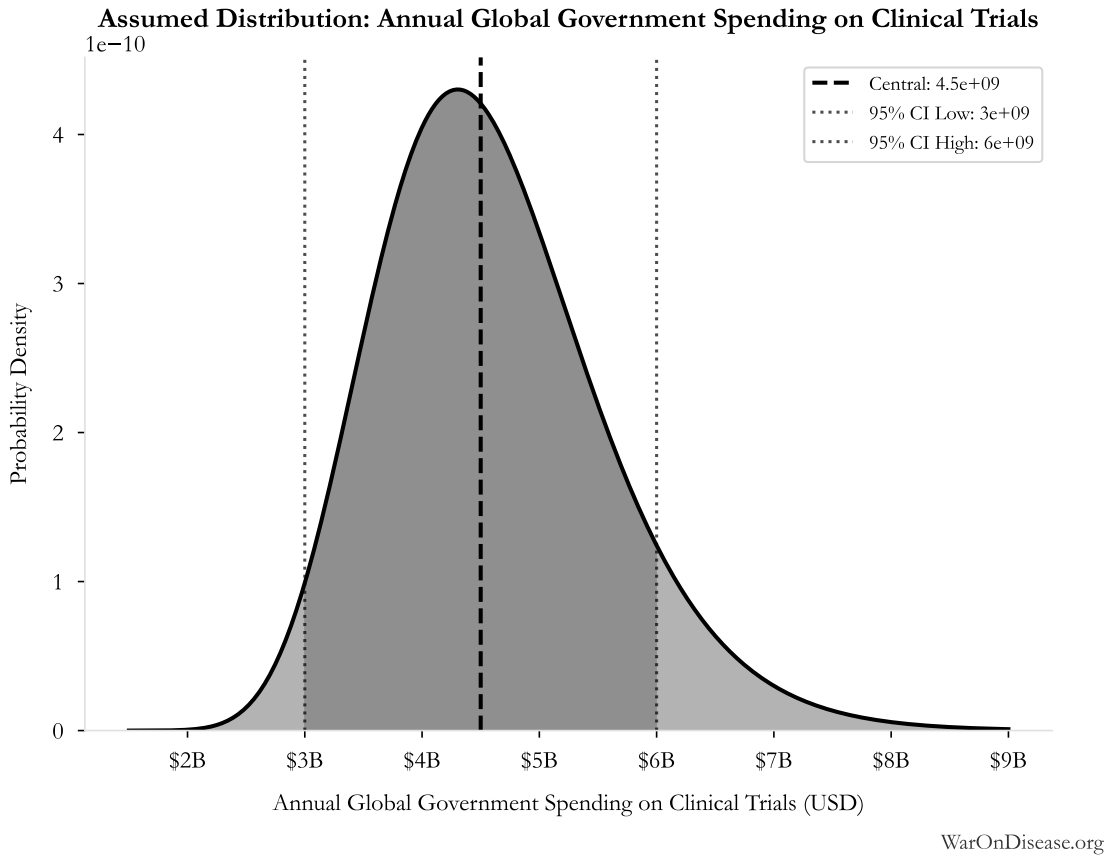


Figure 319: Probability Distribution: Annual Global Government Spending on Clinical Trials

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

Global Life Expectancy (2024): 79 years

Details

Global life expectancy (2024)
Source:[4]

Uncertainty Range

Technical: Distribution: Normal (SE: 2 years)

Input Distribution

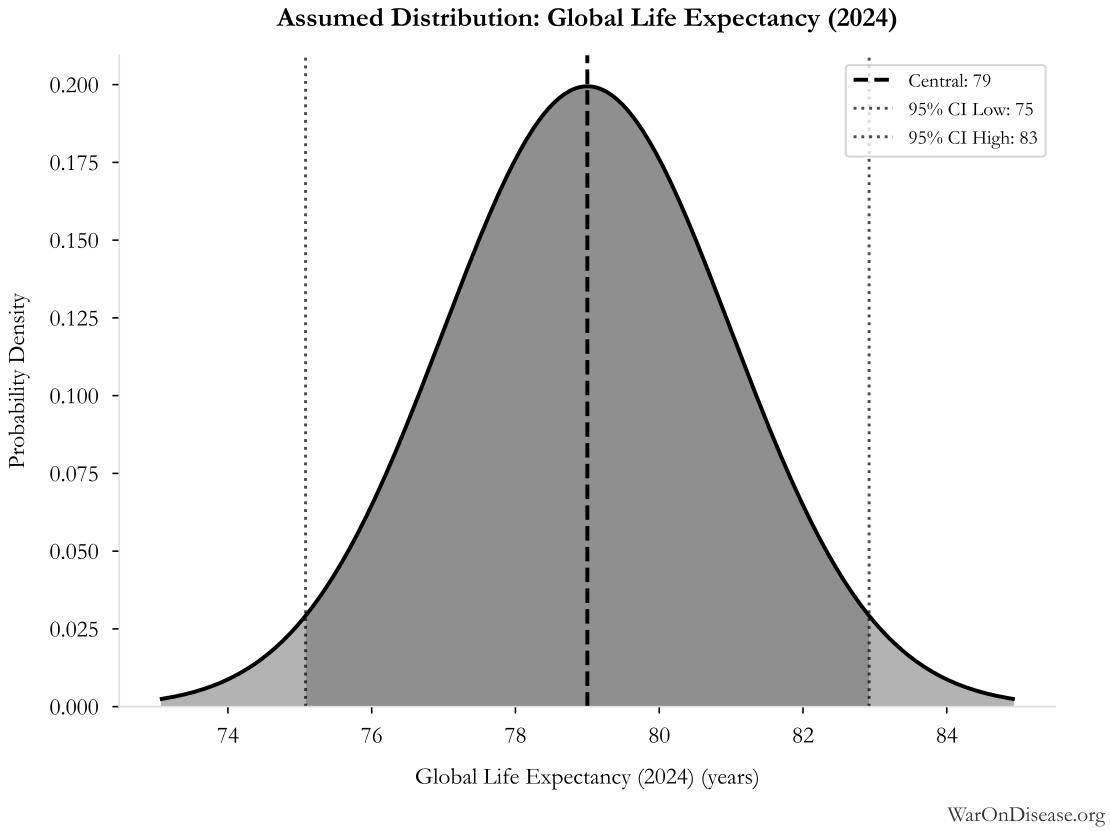


Figure 320: Probability Distribution: Global Life Expectancy (2024)

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* • *Updated 2024*

Global Government Medical Research Spending: $67.5B

Details

Global government medical research spending
Source:[47]

Uncertainty Range

Technical: 95% CI: [$54B, $81B] • Distribution: Lognormal
What this means: This estimate has moderate uncertainty. The true value likely falls between $54B and $81B (±20%). This represents a reasonable 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

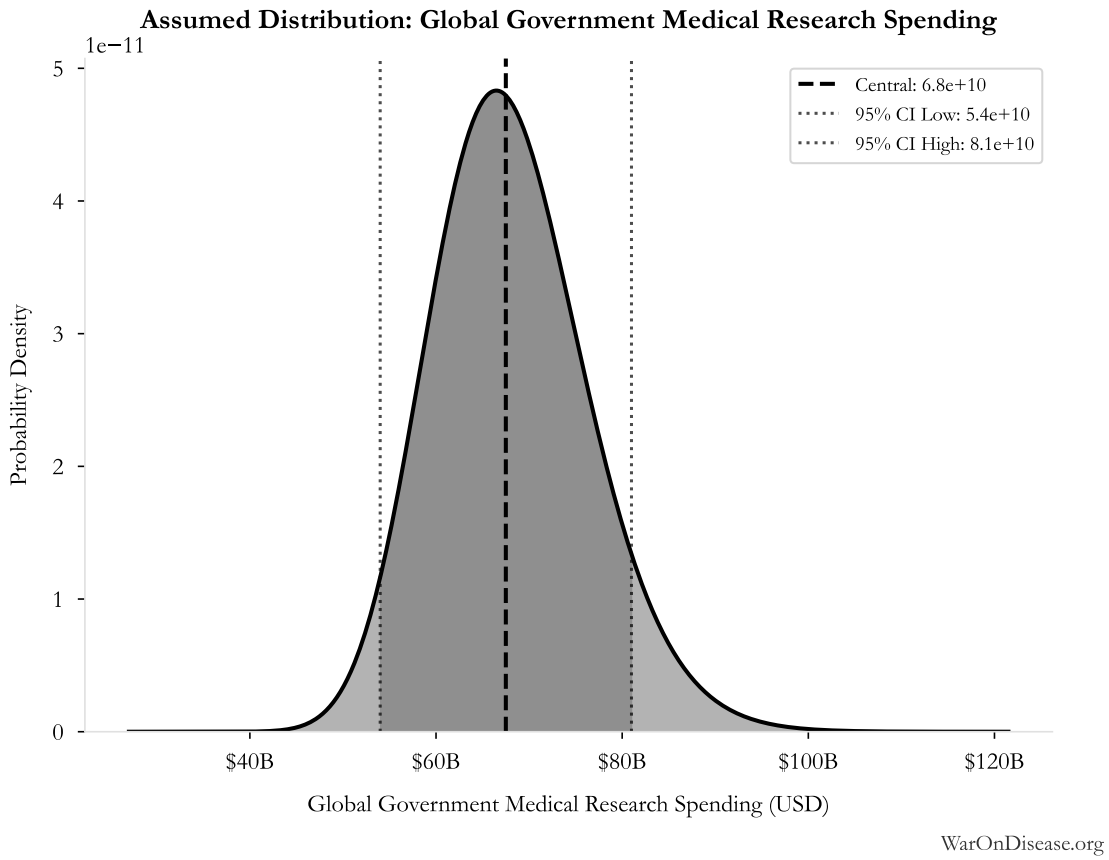


Figure 321: Probability Distribution: Global Government Medical Research Spending

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

Global Military Spending in 2024: $2.72T

Details

Global military spending in 2024
Source:[48]

Uncertainty Range

Technical: Distribution: Fixed
High confidence

Global Population in 2024: 8.00 billion of people

Details

Global population in 2024
Source:[51]

Uncertainty Range

Technical: 95% CI: [7.80 billion of people, 8.20 billion of people] • Distribution: Lognormal
What this means: We're quite confident in this estimate. The true value likely falls between 7.80 billion of people and 8.20 billion of people (±2%). This represents a narrow 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

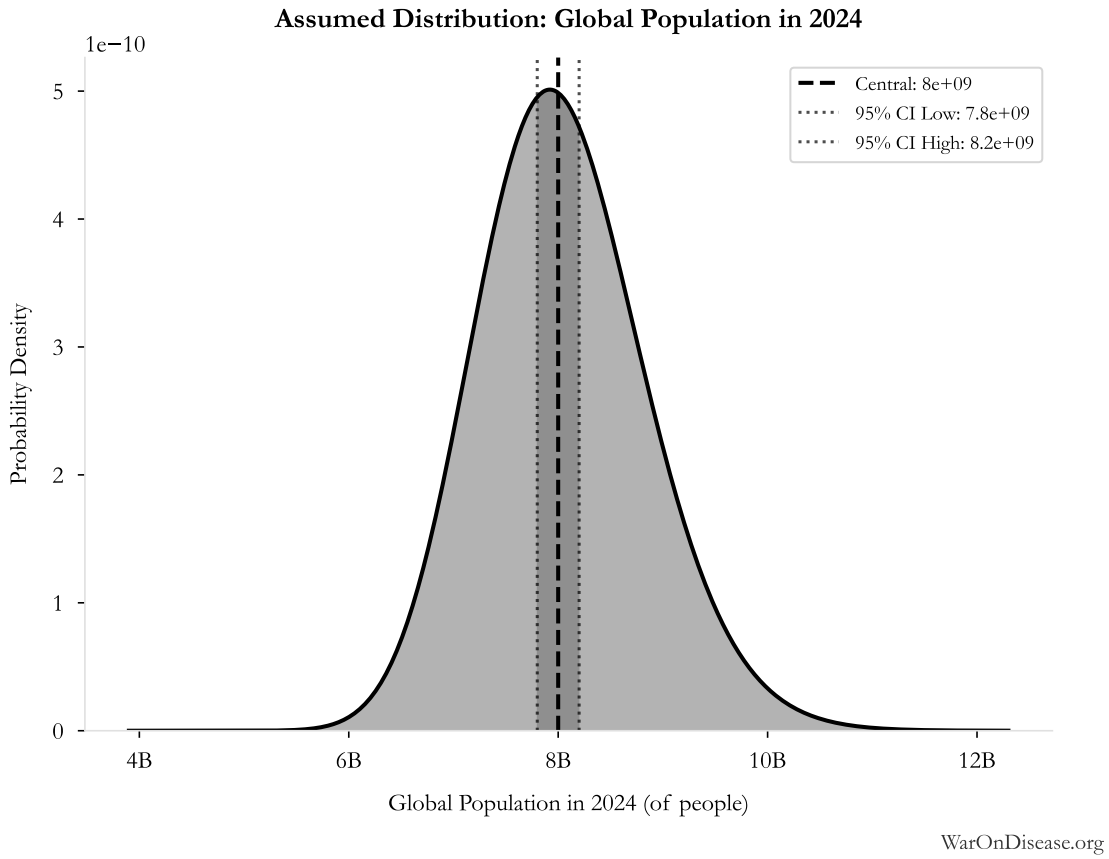


Figure 322: Probability Distribution: Global Population in 2024

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

Critical Mass Threshold for Social Change: 3.5%

Details

Critical mass threshold for social change (3.5% rule)
Source:[52]

Uncertainty Range

Technical: 95% CI: [2.5%, 4.5%] • Distribution: Lognormal
What this means: There's significant uncertainty here. The true value likely falls between 2.5% and 4.5% (±29%). This represents a 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

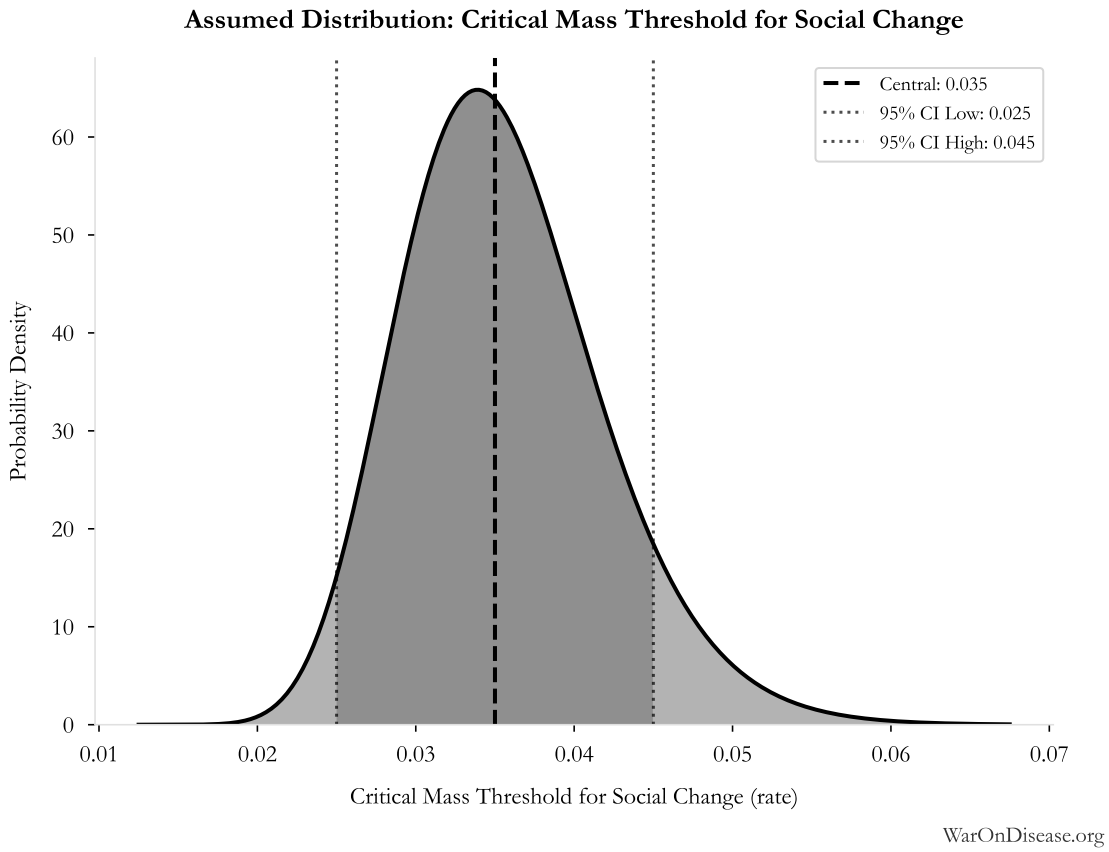


Figure 323: Probability Distribution: Critical Mass Threshold for Social Change

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

Annual Global Spending on Symptomatic Disease Treatment: $8.20T

Details

Annual global spending on symptomatic disease treatment
Source:[43]

Uncertainty Range

Technical: 95% CI: [$6.50T, $10T] • Distribution: Lognormal
What this means: This estimate has moderate uncertainty. The true value likely falls between $6.50T and $10T (±21%). This represents a reasonable 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

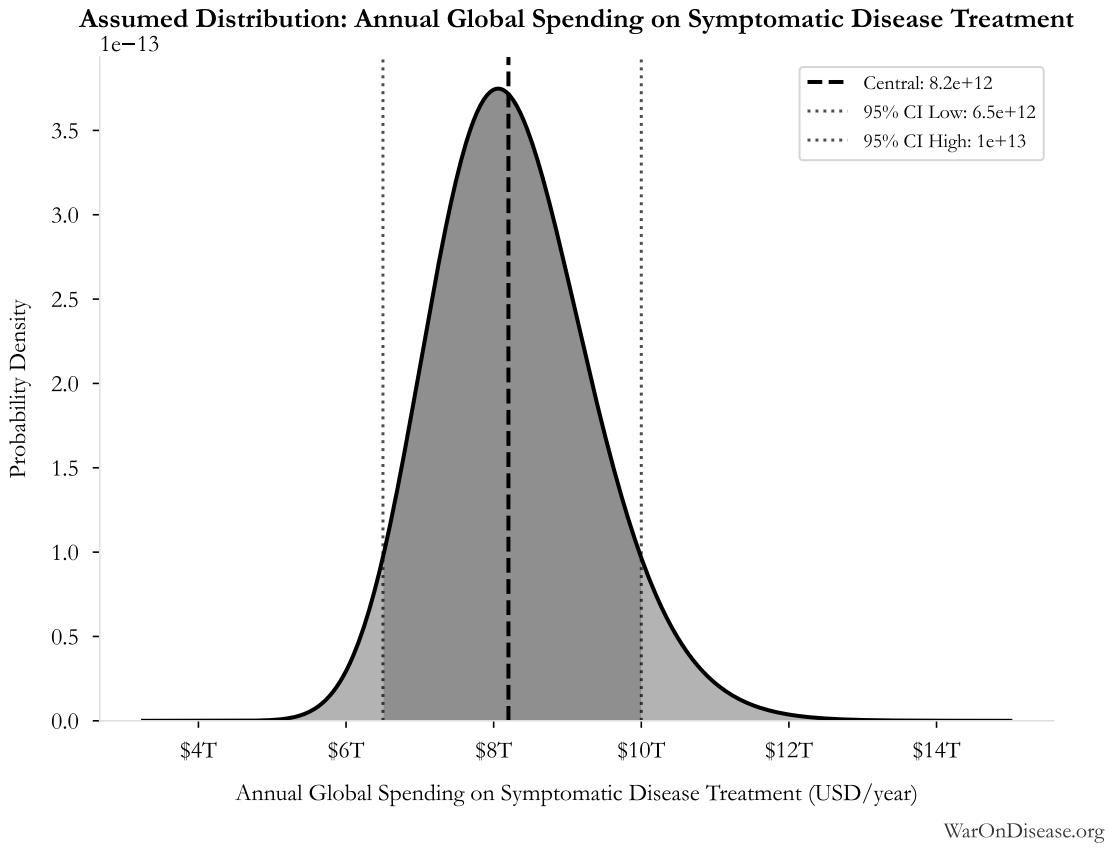


Figure 324: Probability Distribution: Annual Global Spending on Symptomatic Disease Treatment

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

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:[32]

Uncertainty Range

Technical: Distribution: Normal (SE: 0.03 proportion)

Input Distribution

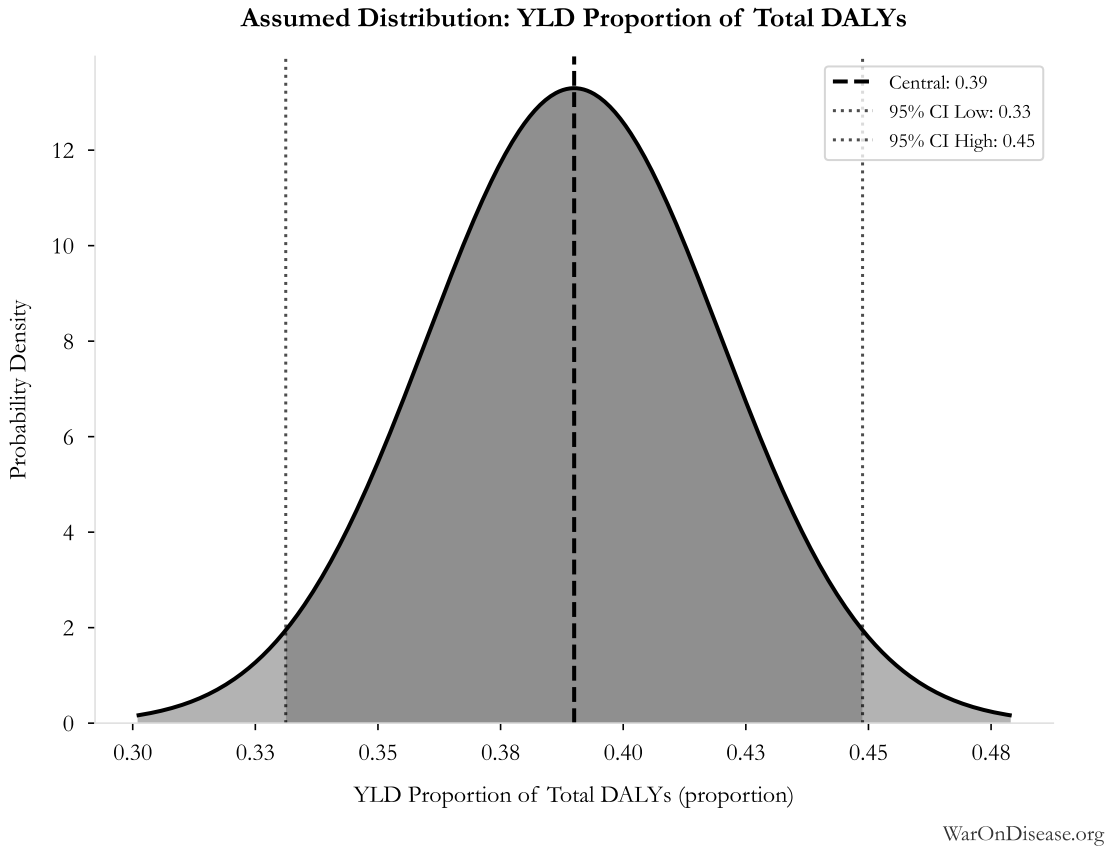


Figure 325: Probability Distribution: YLD Proportion of Total DALYs

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

Human Interactome Targeted by Drugs: 12%

Details

Percentage of human interactome (protein-protein interactions) targeted by drugs
Source:[54]
High confidence

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:[62]

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

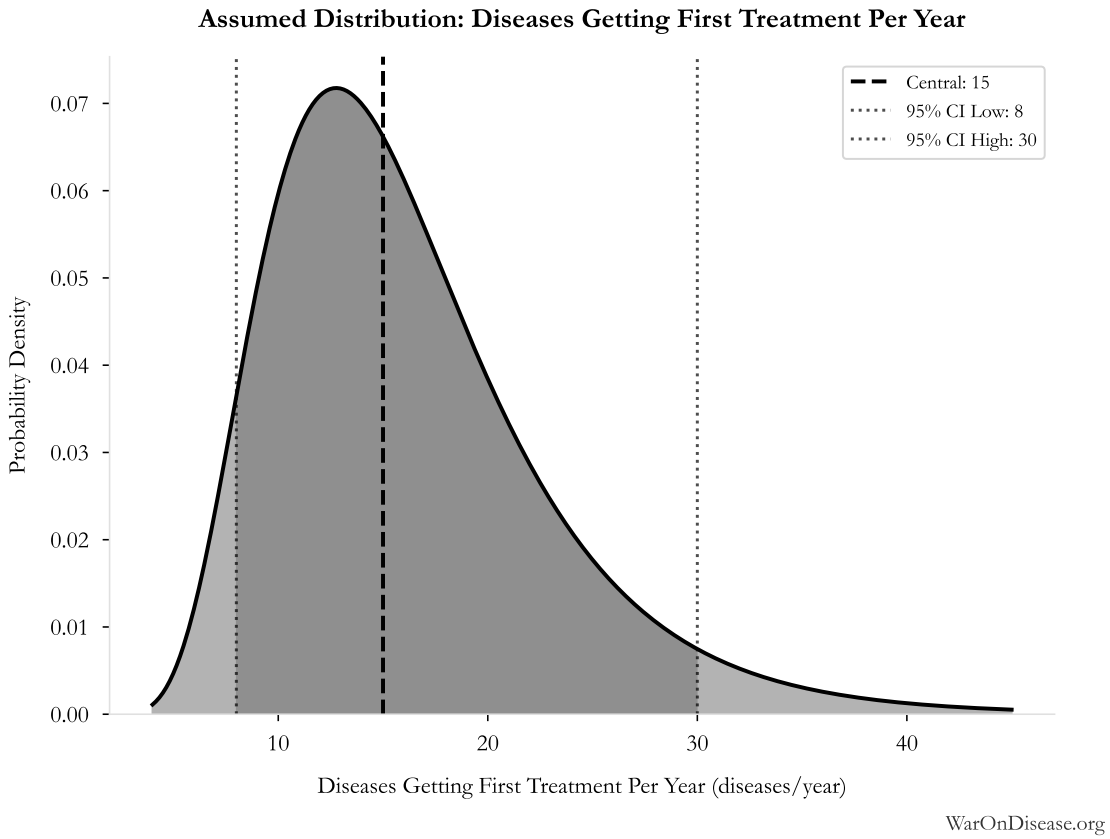


Figure 326: Probability Distribution: Diseases Getting First Treatment Per Year

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

NIH Standard Research Cost per QALY: $50K

Details

Typical cost per QALY for standard NIH-funded medical research portfolio. Reflects the inefficiency of traditional RCTs and basic research-heavy allocation. See confidence_interval for range; ICER uses higher thresholds for value-based pricing.
Source:[65]

Uncertainty Range

Technical: 95% CI: [$20K, $100K] • Distribution: Lognormal

What this means: This estimate is highly uncertain. The true value likely falls between $20K and $100K (±80%). 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

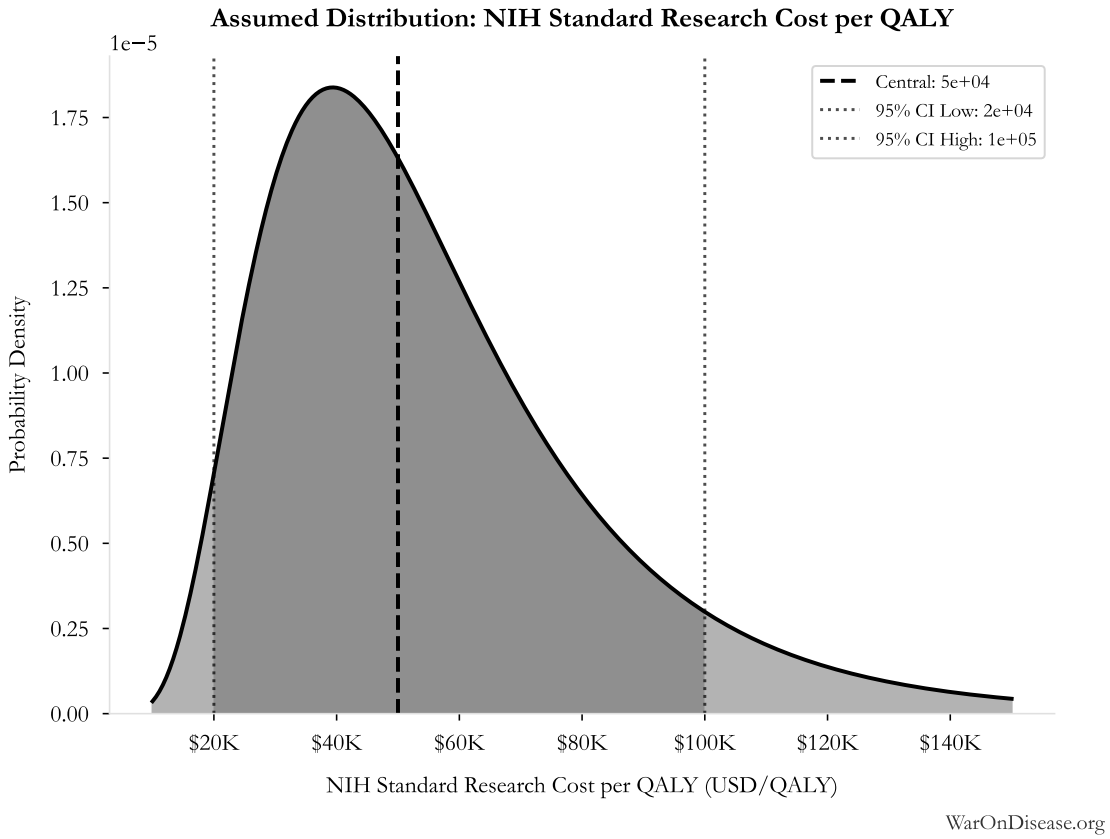


Figure 327: Probability Distribution: NIH Standard Research Cost per QALY

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

Pharma Drug Development Cost (Current System): $2.60B

Details

Average cost to develop one drug in current system
Source:[68]

Uncertainty Range

Technical: 95% CI: [$1.50B, $4B] • Distribution: Lognormal (SE: $500M)
What this means: There's significant uncertainty here. The true value likely falls between $1.50B and $4B (±48%). This represents a 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

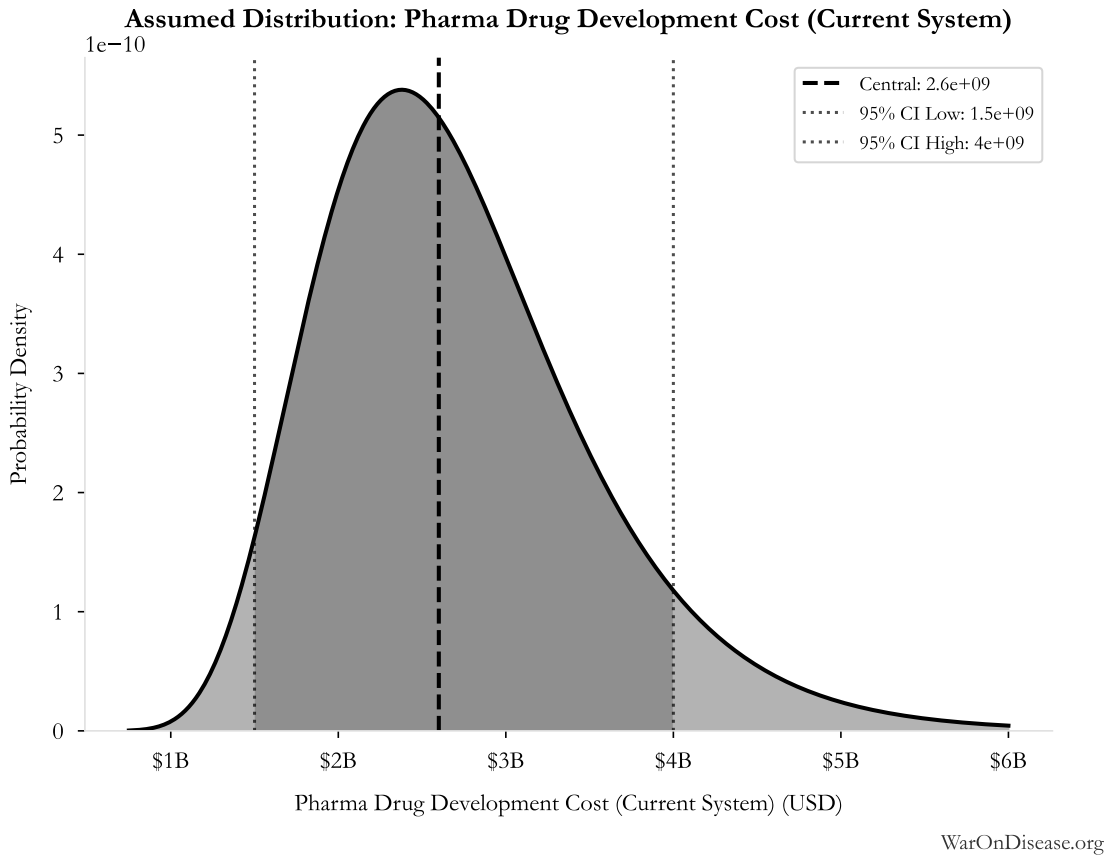


Figure 328: Probability Distribution: Pharma Drug Development Cost (Current System)

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*

Phase I Safety Trial Duration: 2.3 years

Details

Phase I safety trial duration
Source:[21]
High confidence • *Peer-reviewed* • *Updated 2021*

Pragmatic Trial Median Cost per Patient (PMC Review): $97

Details

Median cost per patient in embedded pragmatic clinical trials (systematic review of 64 trials). IQR: $19-$478 (2015 USD).
Source:[74]

Uncertainty Range

Technical: 95% CI: [$19, $478] • Distribution: Lognormal
What this means: This estimate is highly uncertain. The true value likely falls between $19 and $478 (±237%). 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

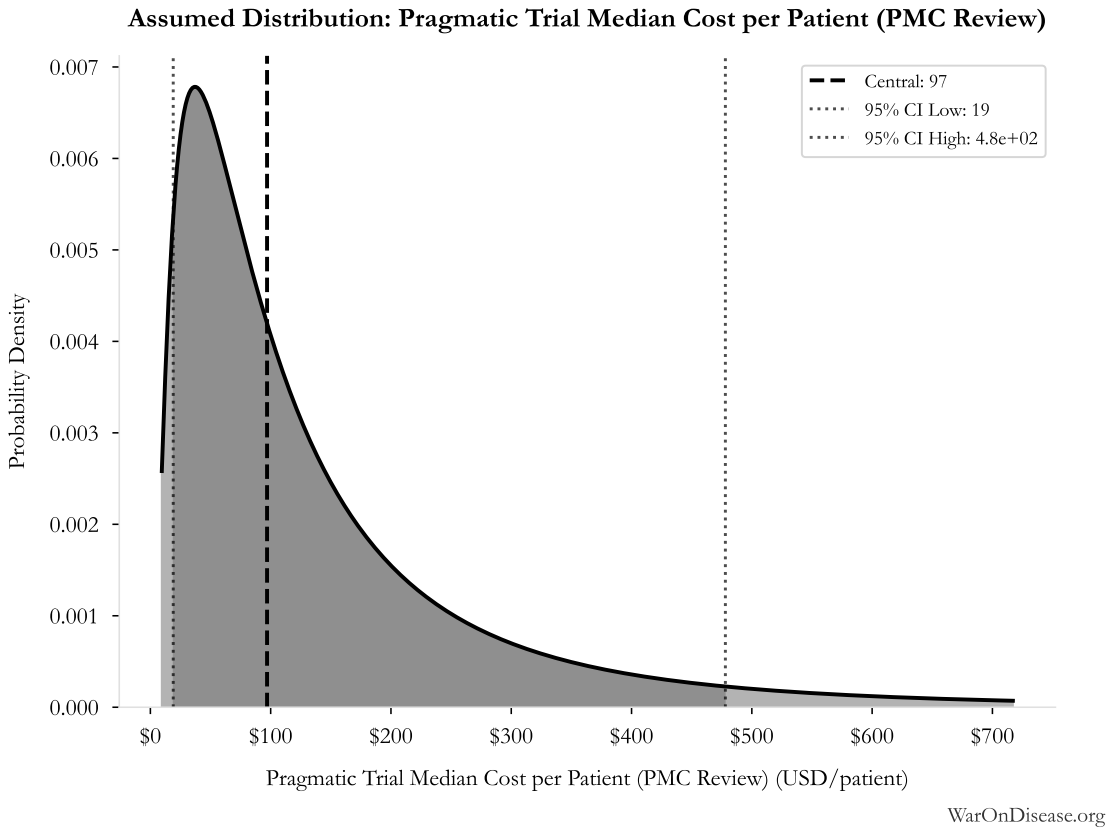


Figure 329: Probability Distribution: Pragmatic Trial Median Cost per Patient (PMC Review)

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

Political Success Probability: 1%

Details

Estimated probability of treaty ratification and sustained implementation. Central estimate 1% is conservative. This assumes 99% chance of failure.
Source:[76]

Uncertainty Range

Technical: 95% CI: [0.1%, 10%] • Distribution: Beta (SE: 2%)
What this means: This estimate is highly uncertain. The true value likely falls between

0.1% and 10% (±495%). This represents a very 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

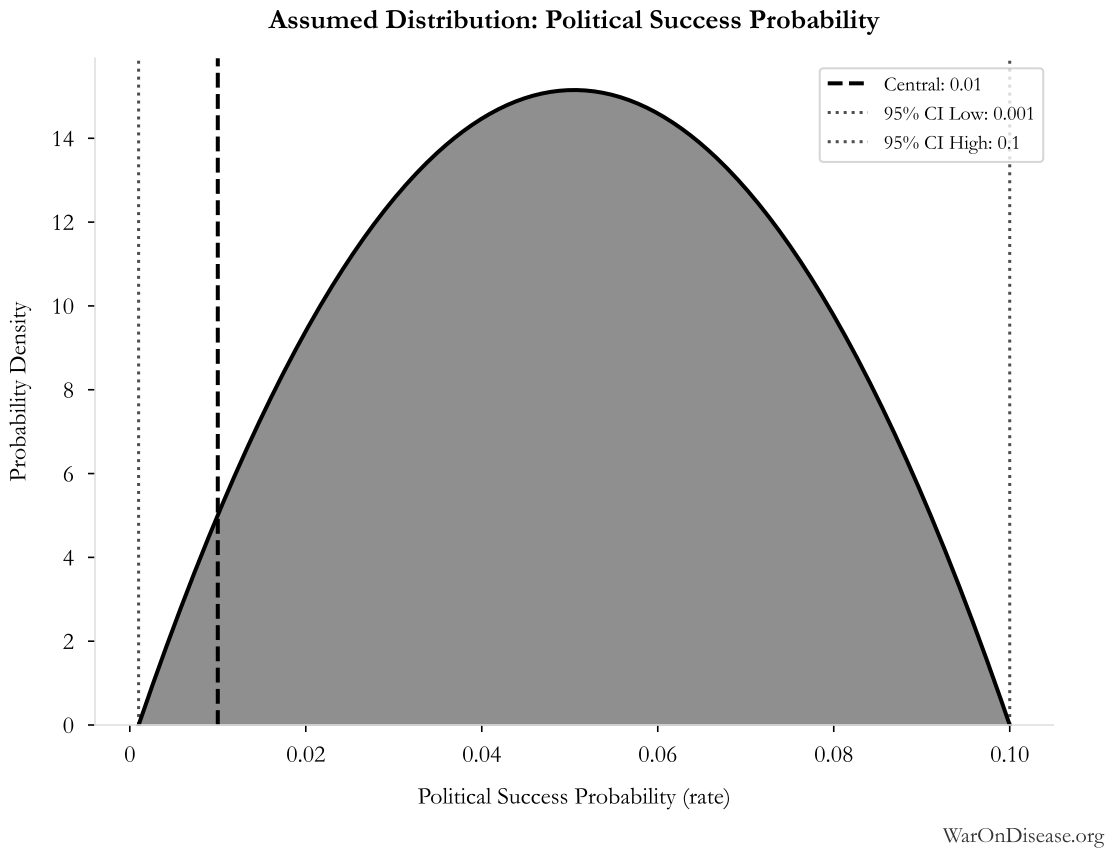


Figure 330: Probability Distribution: Political Success Probability

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

Percentage Military Spending Cut After WW2: 30%

Details

Percentage military spending cut after WW2 (historical precedent)
Source:[79]
High confidence

Pre-1962 Drug Development Cost (2024 Dollars): $24.7M

Details

Pre-1962 drug development cost adjusted to 2024 dollars ($6.5M × 3.80 = $24.7M, CPI-adjusted from Baily 1972)
Source:[80]

Uncertainty Range

Technical: 95% CI: [$19.5M, $30M] • Distribution: Lognormal
What this means: This estimate has moderate uncertainty. The true value likely falls between $19.5M and $30M (±21%). This represents a reasonable 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

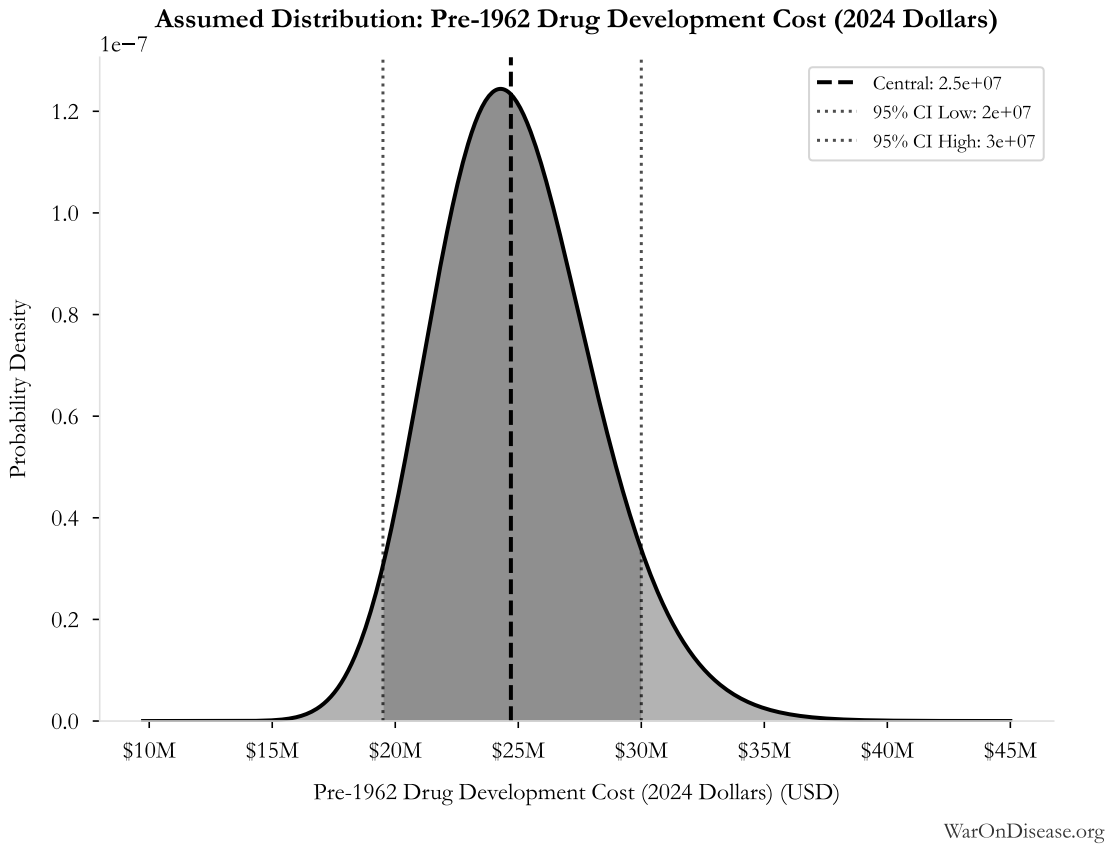


Figure 331: Probability Distribution: Pre-1962 Drug Development Cost (2024 Dollars)

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*

Pre-1962 Physician Count (Unverified): 144 thousand physicians

Details

Estimated physicians conducting real-world efficacy trials pre-1962 (unverified estimate)
Source:[81]
? Low confidence

Total Number of Rare Diseases Globally: 7.00 thousand diseases

Details

Total number of rare diseases globally
Source:[82]

Uncertainty Range

Technical: 95% CI: [6.00 thousand diseases, 10.0 thousand diseases] • Distribution: Normal
What this means: There's significant uncertainty here. The true value likely falls between 6.00 thousand diseases and 10.0 thousand 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

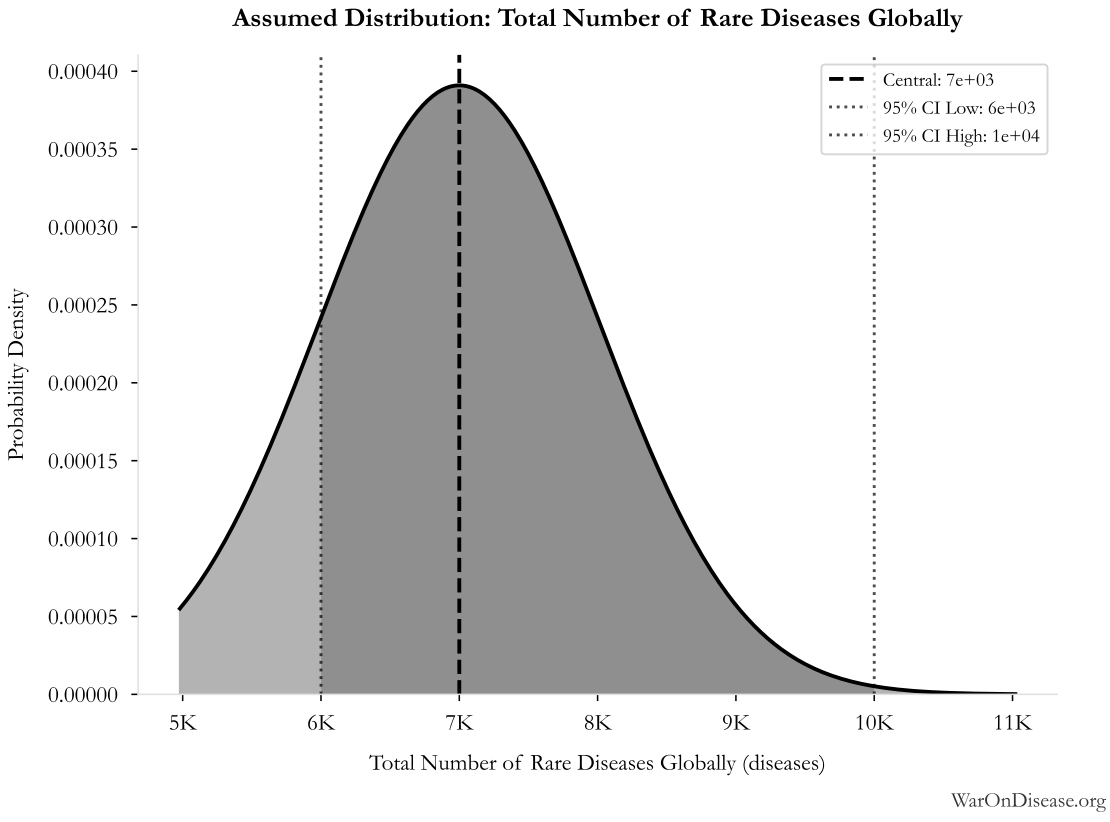


Figure 332: Probability Distribution: Total Number of Rare Diseases Globally

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

Recovery Trial Cost per Patient: $500

Details

RECOVERY trial cost per patient. Note: RECOVERY was an outlier - hospital-based during COVID emergency, minimal extra procedures, existing NHS infrastructure, streamlined consent. Replicating this globally will be harder.
Source:[83]

Uncertainty Range

Technical: 95% CI: [$400, $2.50K] • Distribution: Lognormal
What this means: This estimate is highly uncertain. The true value likely falls between $400 and $2.50K (±210%). 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

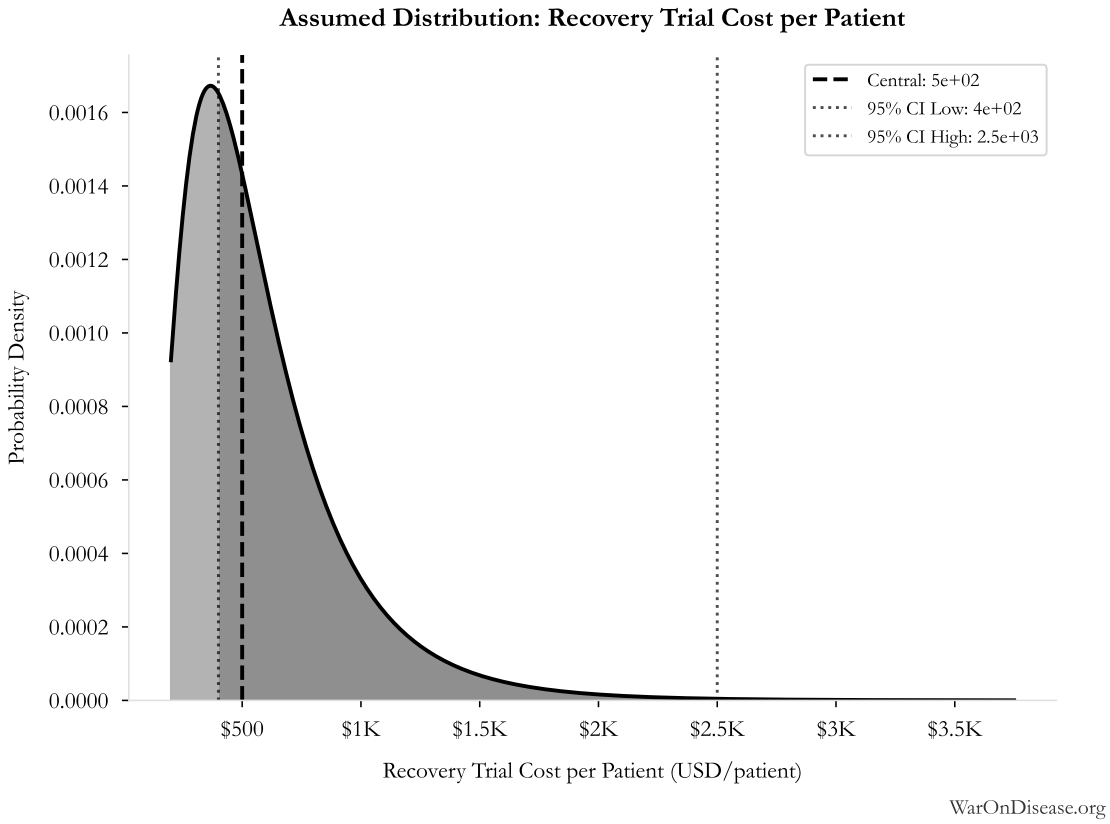


Figure 333: Probability Distribution: Recovery Trial Cost per Patient

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.
High confidence

RECOVERY Trial Global Lives Saved: 1.00 million lives

Details

Estimated lives saved globally by RECOVERY trial's dexamethasone discovery. NHS England estimate (March 2021). Based on Águas et al. Nature Communications 2021 methodology applying RECOVERY trial mortality reductions (36% ventilated, 18% oxygen) to global COVID hospitalizations. Wide uncertainty range reflects extrapolation assumptions.
Source:[84]

Uncertainty Range

Technical: 95% CI: [500 thousand lives, 2.00 million lives] • Distribution: Lognormal

What this means: This estimate is highly uncertain. The true value likely falls between 500 thousand lives and 2.00 million lives (±75%). 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

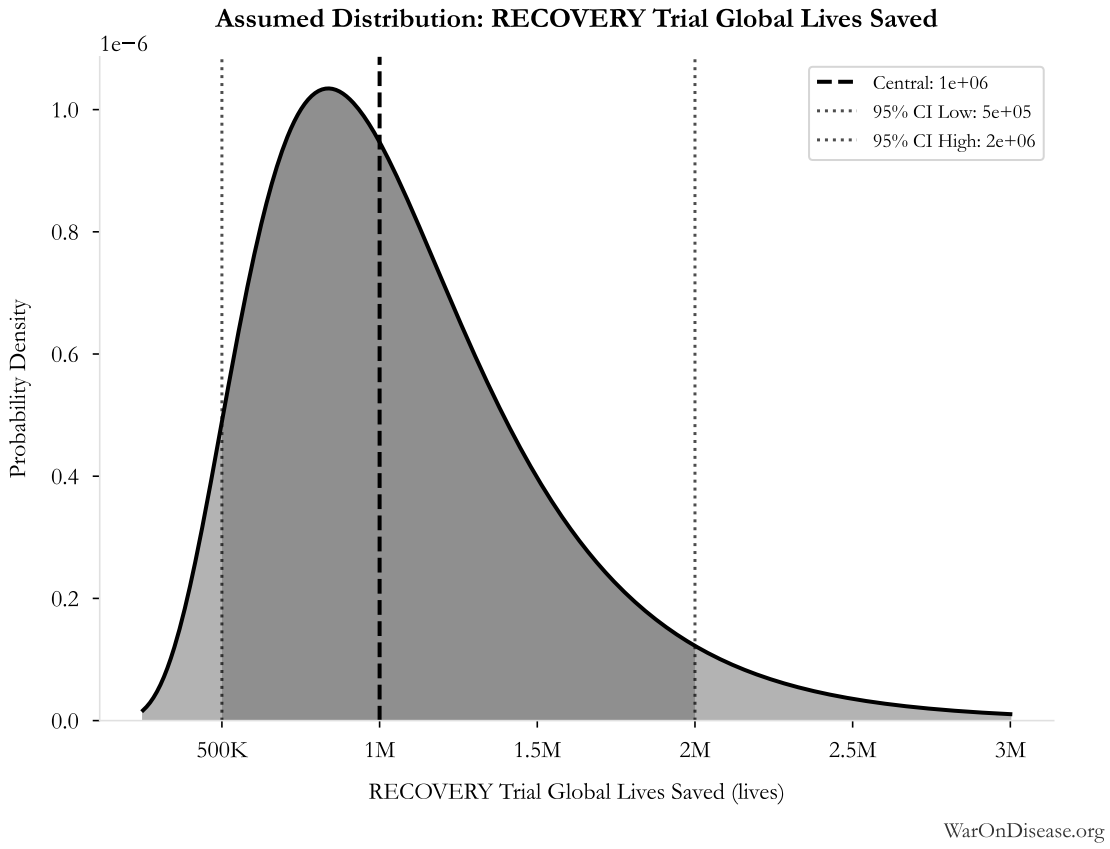


Figure 334: Probability Distribution: RECOVERY Trial Global Lives Saved

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

RECOVERY Trial Total Cost: $20M

Details

Total cost of UK RECOVERY trial. Enrolled tens of thousands of patients across multiple treatment arms. Discovered dexamethasone reduces COVID mortality by ~1/3 in severe cases. **Source**:[66]

Uncertainty Range

Technical: 95% CI: [$15M, $25M] • Distribution: Lognormal
What this means: This estimate has moderate uncertainty. The true value likely falls between $15M and $25M (±25%). This represents a reasonable 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

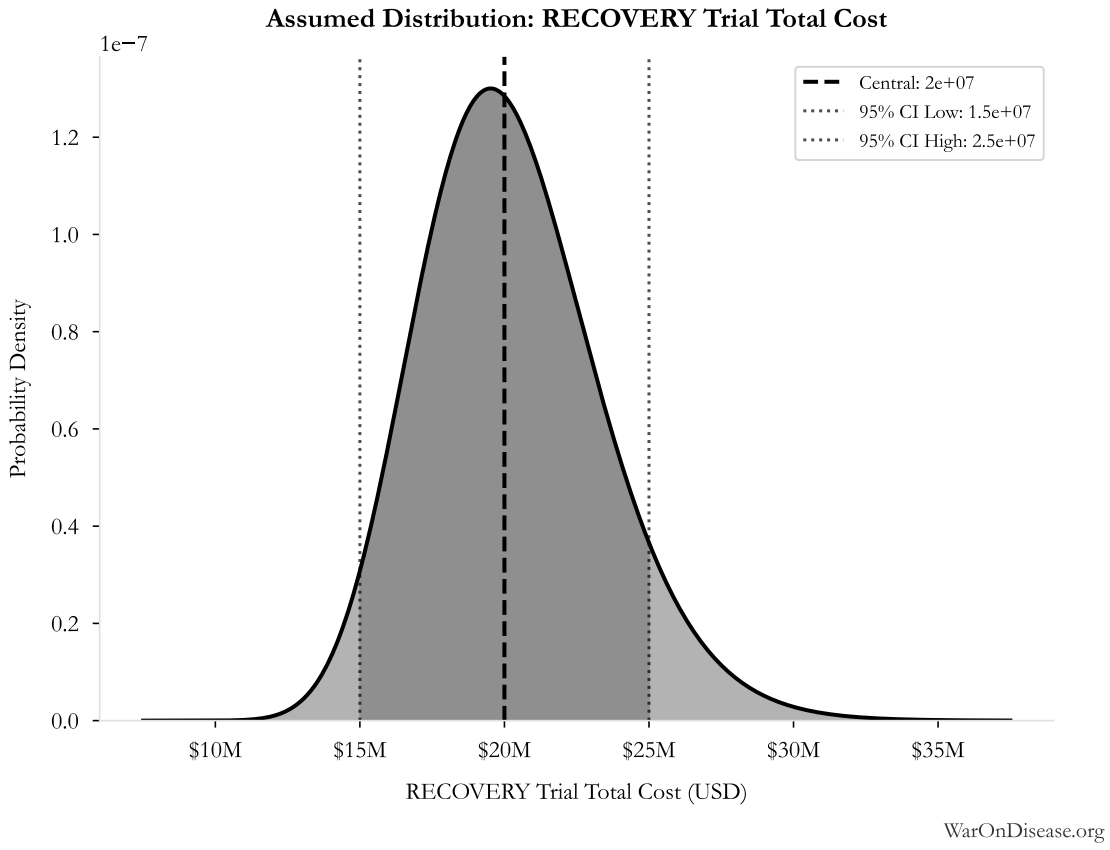


Figure 335: Probability Distribution: RECOVERY Trial Total Cost

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.
High confidence

Mean Age of Preventable Death from Post-Safety Efficacy Delay: 62 years

Details

Mean age of preventable death from post-safety efficacy testing regulatory delay (Phase 2-4)
Source:[4]

Uncertainty Range

Technical: Distribution: Normal (SE: 3 years)

Input Distribution



Figure 336: Probability Distribution: Mean Age of Preventable Death from Post-Safety Efficacy Delay

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 • Peer-reviewed

Pre-Death Suffering Period During Post-Safety Efficacy Delay: 6 years

Details

Pre-death suffering period during post-safety efficacy testing delay (average years lived with untreated condition while awaiting Phase 2-4 completion)
Source:[4]

Uncertainty Range

Technical: 95% CI: [4 years, 9 years] • Distribution: Lognormal
What this means: There's significant uncertainty here. The true value likely falls between 4 years and 9 years (±42%). This represents a 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

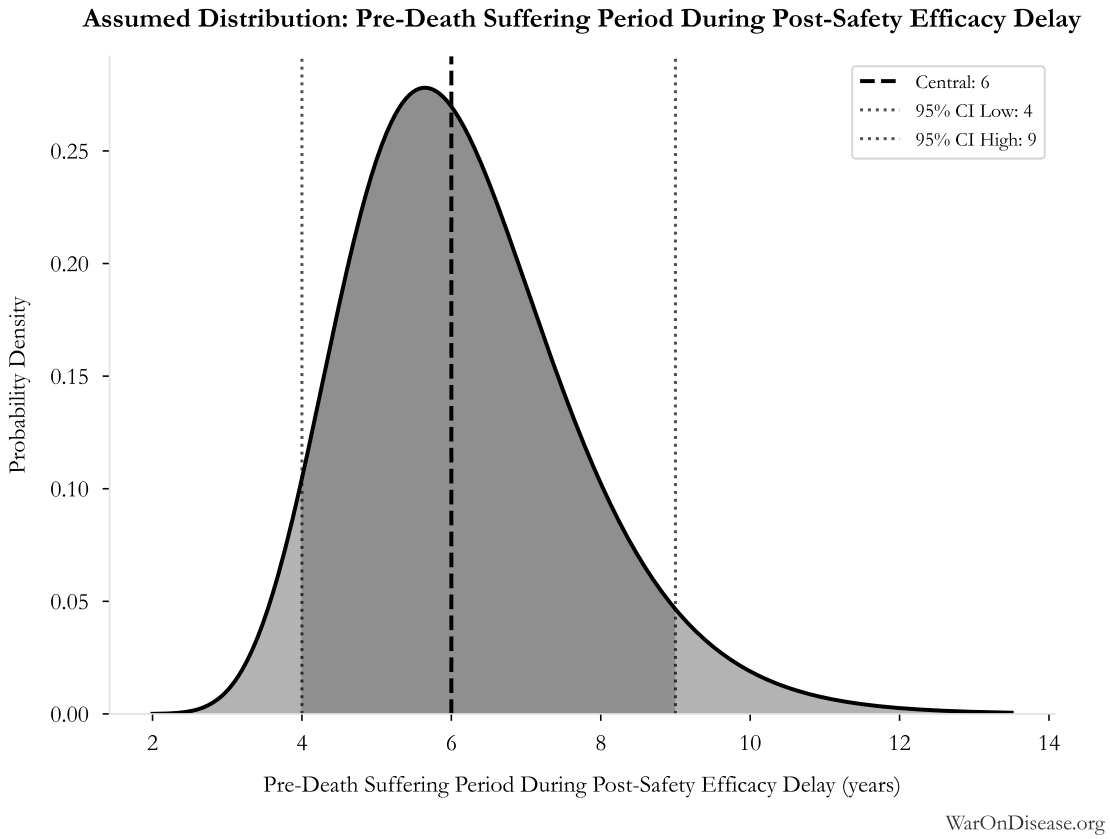


Figure 337: Probability Distribution: Pre-Death Suffering Period During Post-Safety Efficacy Delay

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 • Peer-reviewed

Return on Investment from Smallpox Eradication Campaign: 280:1

Details

Return on investment from smallpox eradication campaign
Source:[89]
High confidence

Standard Economic Value per QALY: $150K

Details

Standard economic value per QALY
Source:[91]

Uncertainty Range

Technical: Distribution: Normal (SE: $30K)

Input Distribution

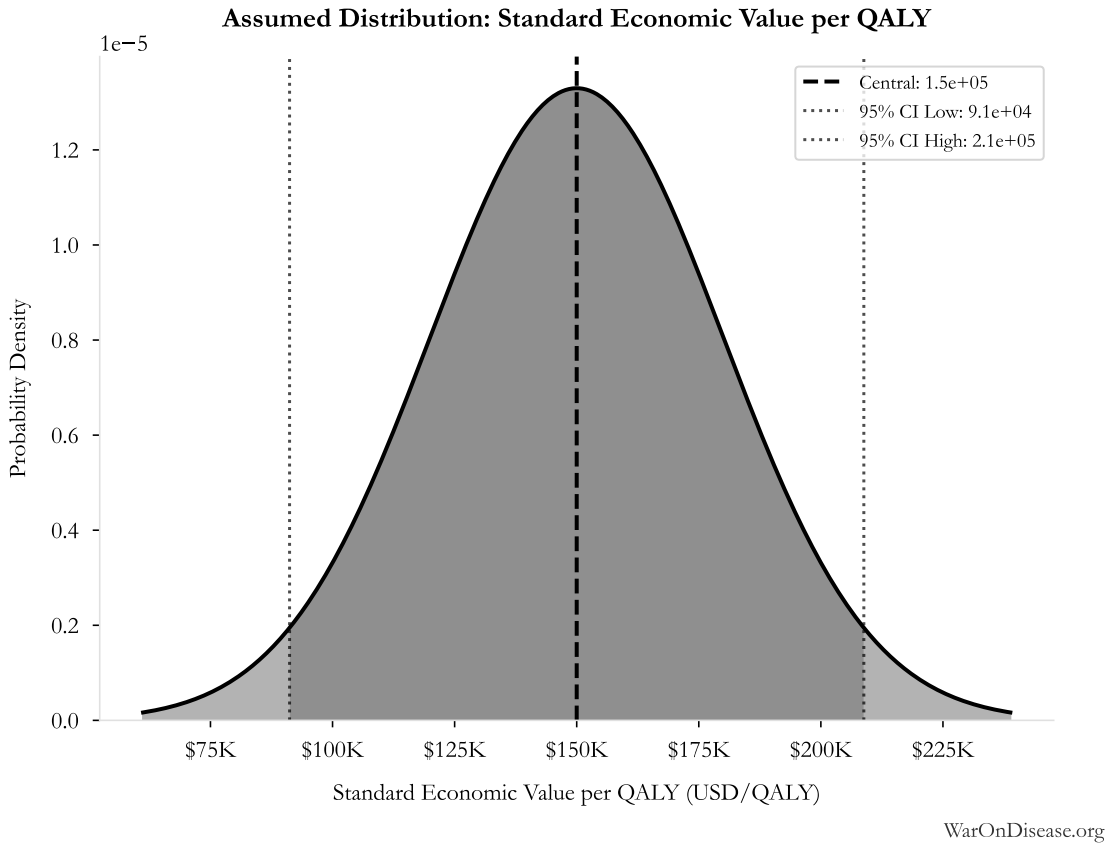


Figure 338: Probability Distribution: Standard Economic Value per QALY

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

Deaths from 9/11 Terrorist Attacks: 3.00 thousand deaths

Details

Deaths from 9/11 terrorist attacks
Source:[97]

Uncertainty Range

Technical: Distribution: Fixed
High confidence

Thalidomide Cases Worldwide: 15.0 thousand cases

Details

Total thalidomide birth defect cases worldwide (1957-1962)
Source:[98]

Uncertainty Range

Technical: 95% CI: [10.0 thousand cases, 20.0 thousand cases] • Distribution: Lognormal
What this means: There's significant uncertainty here. The true value likely falls between 10.0 thousand cases and 20.0 thousand cases (±33%). This represents a 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

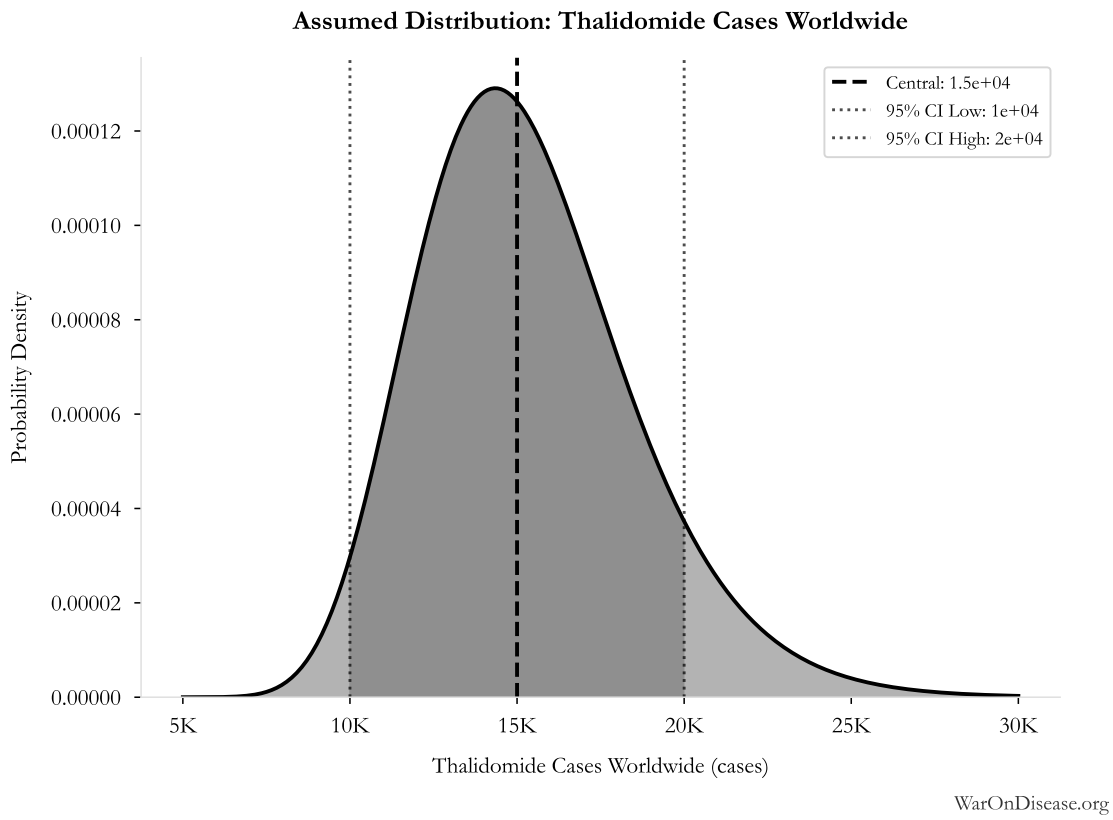


Figure 339: Probability Distribution: Thalidomide Cases Worldwide

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

Thalidomide Disability Weight: 0.4:1

Details

Disability weight for thalidomide survivors (limb deformities, organ damage)
Source:[99]

Uncertainty Range

Technical: 95% CI: [0.32:1, 0.48:1] • Distribution: Lognormal
What this means: This estimate has moderate uncertainty. The true value likely falls between 0.32:1 and 0.48:1 (±20%). This represents a reasonable 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

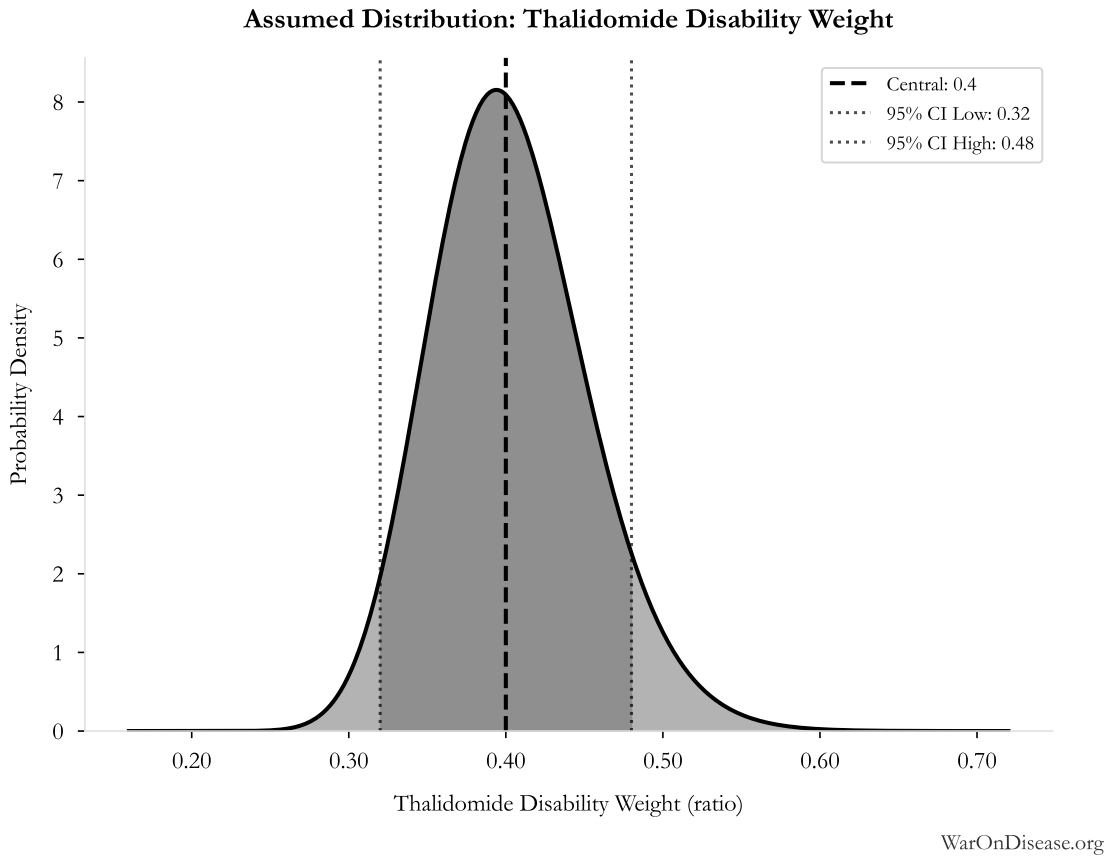


Figure 340: Probability Distribution: Thalidomide Disability Weight

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

Thalidomide Mortality Rate: 40%

Details

Mortality rate for thalidomide-affected infants (died within first year)
Source:[98]

Uncertainty Range

Technical: 95% CI: [35%, 45%] • Distribution: Lognormal
What this means: This estimate has moderate uncertainty. The true value likely falls between 35% and 45% (±13%). This represents a reasonable 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

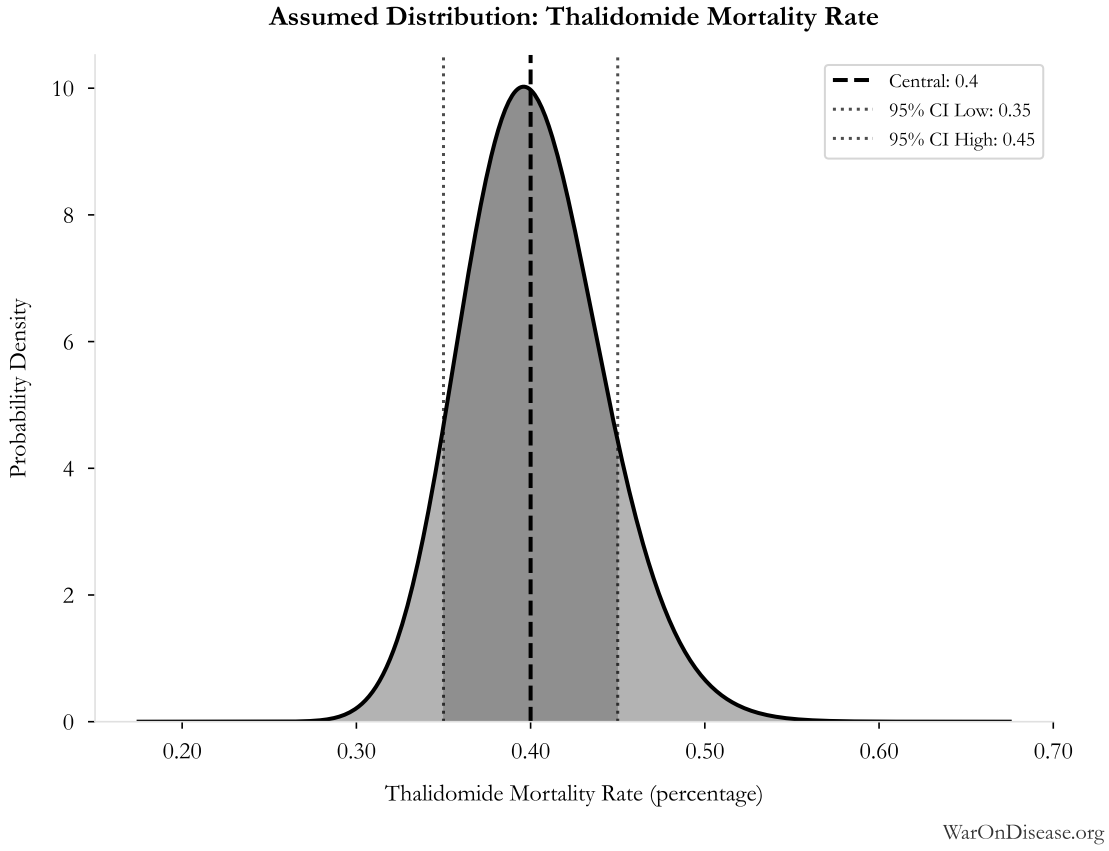


Figure 341: Probability Distribution: Thalidomide Mortality Rate

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

Thalidomide Survivor Lifespan: 60 years

Details

Average lifespan for thalidomide survivors
Source:[99]

Uncertainty Range

Technical: 95% CI: [50 years, 70 years] • Distribution: Lognormal
What this means: This estimate has moderate uncertainty. The true value likely falls between 50 years and 70 years (±17%). This represents a reasonable 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

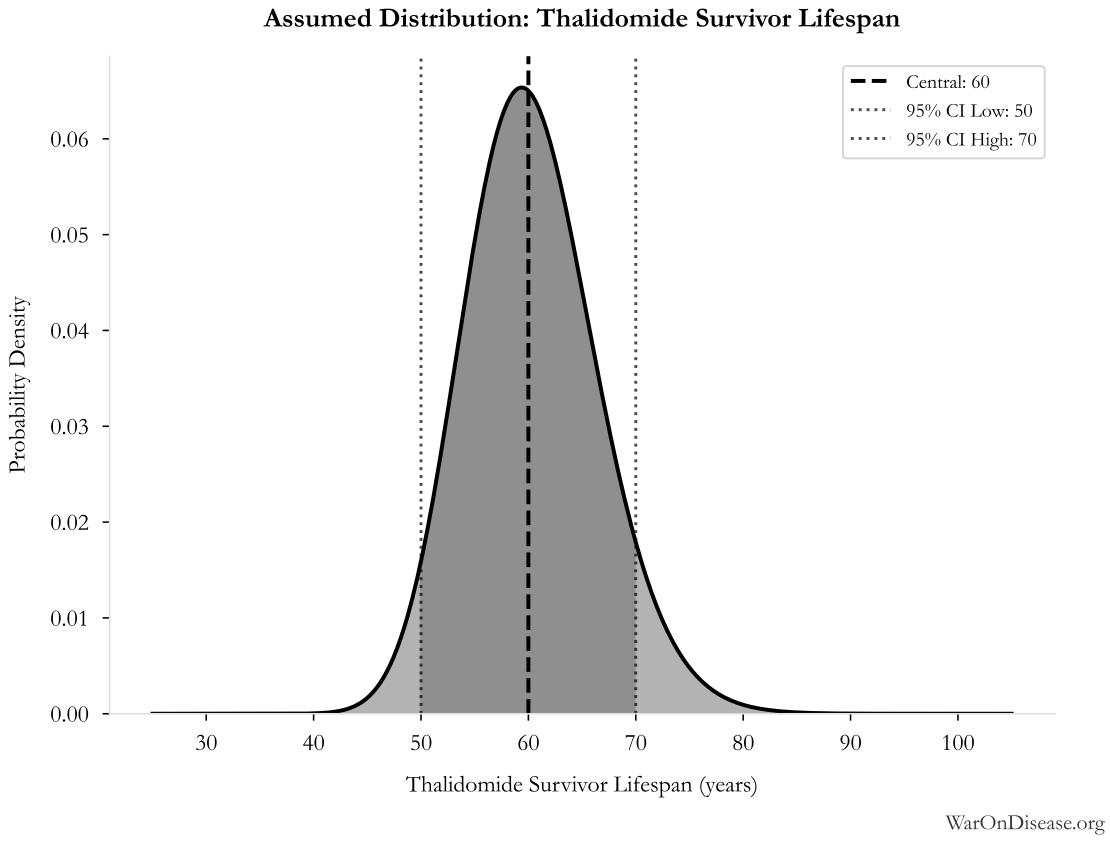


Figure 342: Probability Distribution: Thalidomide Survivor Lifespan

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

US Population Share 1960: 6%

Details

US share of world population in 1960
Source:[100]

Uncertainty Range

Technical: 95% CI: [5.5%, 6.5%] • Distribution: Lognormal
What this means: We're quite confident in this estimate. The true value likely falls between 5.5% and 6.5% (±8%). This represents a narrow 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

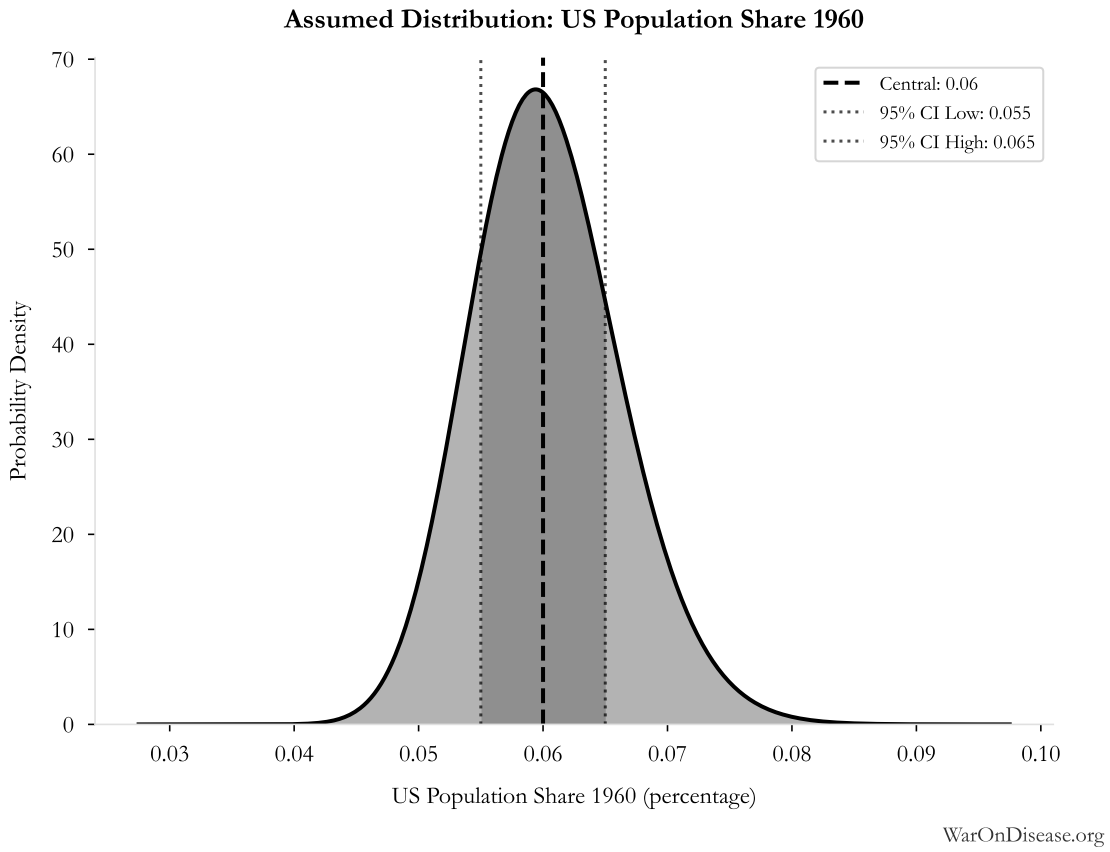


Figure 343: Probability Distribution: US Population Share 1960

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: $41K

Details

Phase 3 cost per patient (median from FDA study)
Source:[101]

Uncertainty Range

Technical: 95% CI: [$20K, $120K] • Distribution: Lognormal
What this means: This estimate is highly uncertain. The true value likely falls between $20K and $120K (±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

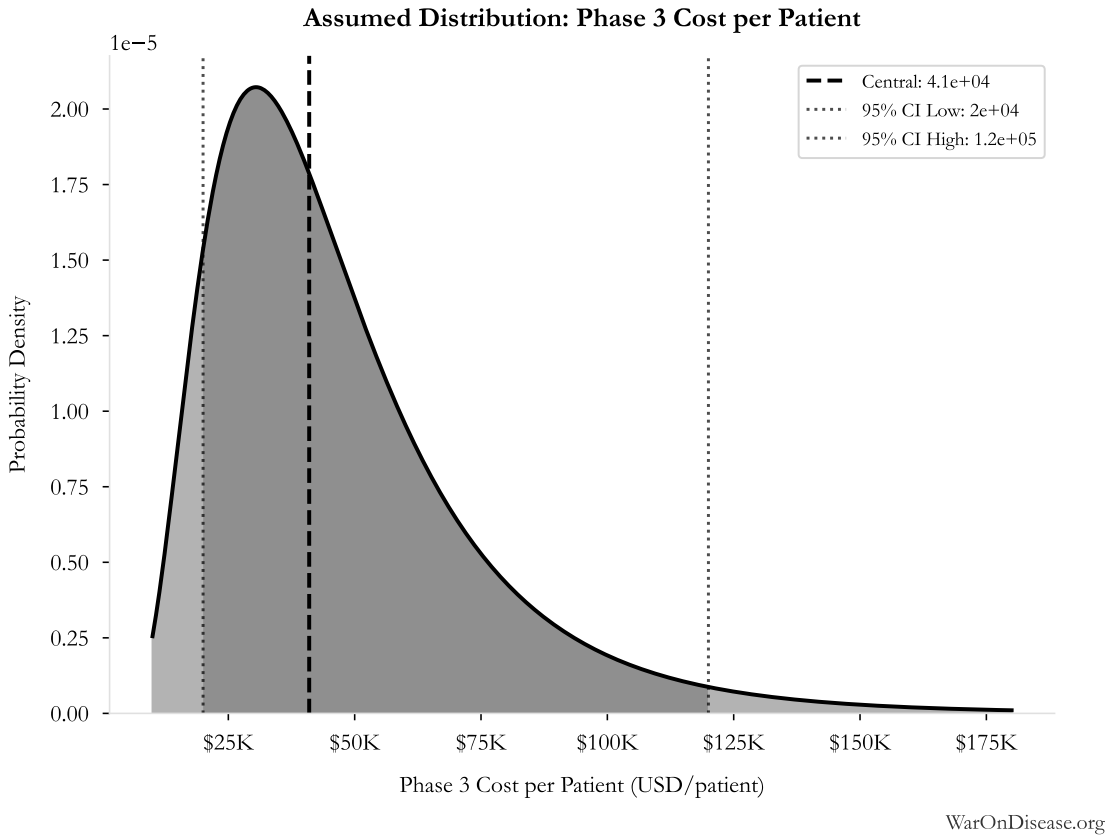


Figure 344: Probability Distribution: Phase 3 Cost per Patient

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

Valley of Death Attrition Rate: 40%

Details

Percentage of promising Phase 1-passed compounds abandoned primarily due to Phase 2/3 cost barriers (not scientific failure). Conservative estimate: many rare disease, natural compound, and low-margin drugs never tested.
Source:[126]

Uncertainty Range

Technical: 95% CI: [25%, 55%] • Distribution: Uniform
What this means: There's significant uncertainty here. The true value likely falls between 25% and 55% (±38%). This represents a wide range that our Monte Carlo simulations account for when calculating overall uncertainty in the results.
The uniform distribution means any value in the range is equally likely.

Input Distribution

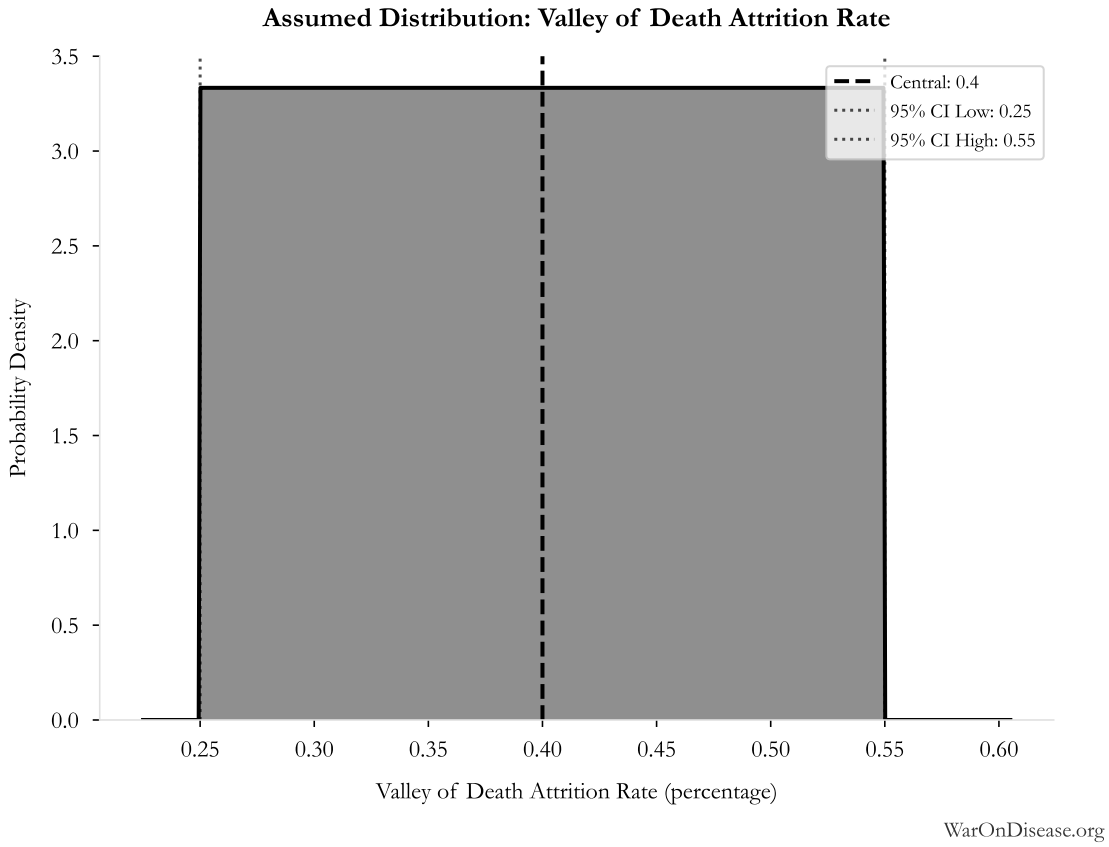


Figure 345: Probability Distribution: Valley of Death Attrition Rate

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

Value of Statistical Life: $10M

Details

Value of Statistical Life (conservative estimate)
Source:[127]

Uncertainty Range

Technical: 95% CI: [$5M, $15M] • Distribution: Gamma (SE: $3M)
What this means: There's significant uncertainty here. The true value likely falls between $5M and $15M (±50%). This represents a wide range that our Monte Carlo simulations account for when calculating overall uncertainty in the results.
The gamma distribution means values follow a specific statistical pattern.

Input Distribution

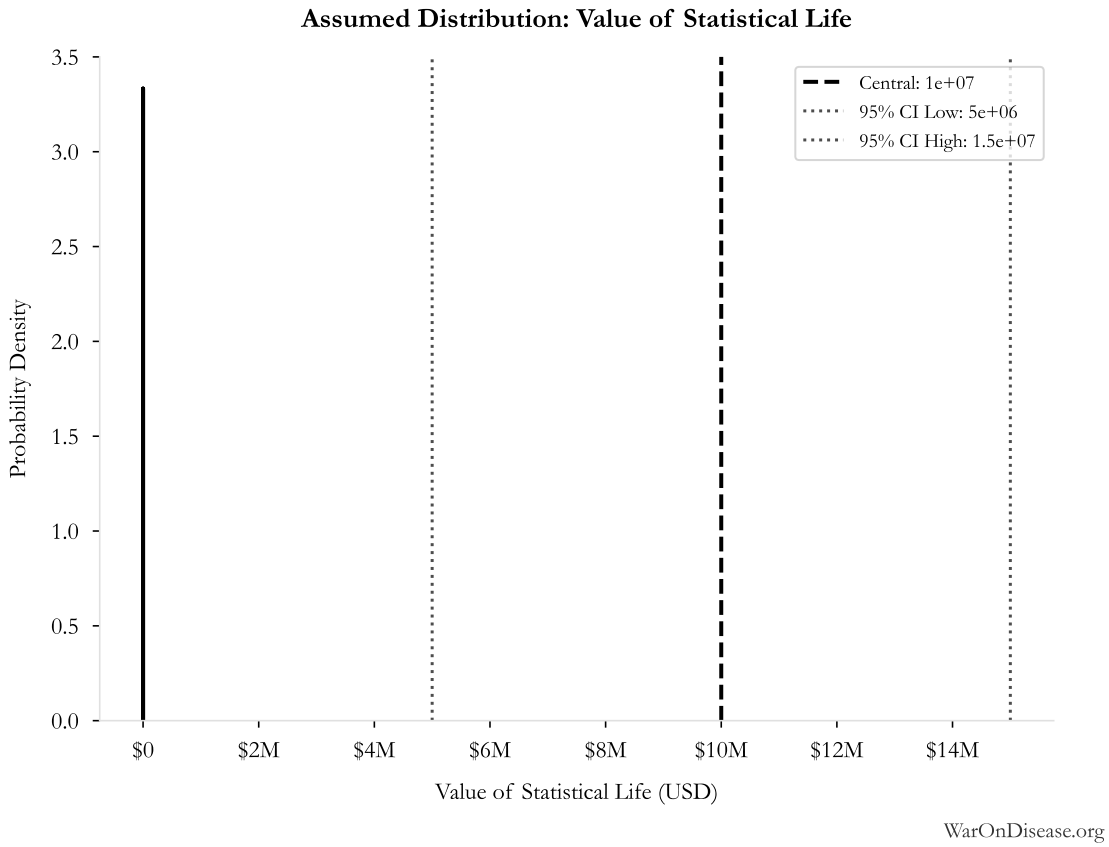


Figure 346: Probability Distribution: Value of Statistical Life

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

Vitamin A Supplementation Cost per DALY: $37

Details

Cost per DALY for vitamin A supplementation programs (India: $23-50; Africa: $40-255; wide variation by region and baseline VAD prevalence). Using India midpoint as conservative estimate.
Source:[128]
~ *Medium confidence*

Return on Investment from Water Fluoridation Programs: 23:1

Details

Return on investment from water fluoridation programs
Source:[129]
High confidence

Cost-Effectiveness Threshold ($50,000/QALY): $50K

Details

Cost-effectiveness threshold widely used in US health economics ($50,000/QALY, from 1980s dialysis costs)
Source:[130]
High confidence

Core Definitions

Fundamental parameters and constants used throughout the analysis.

ADAPTABLE Trial Patients Enrolled: 15.1 thousand patients

Details

Patients enrolled in ADAPTABLE trial (PCORnet 2016-2019). Enrolled across 40 clinical sites. Precise count from trial completion records.
Core definition

Percentage of Budget Defense Sector Keeps Under 1% treaty: 99%

Details

Percentage of budget defense sector keeps under 1% treaty
Core definition

Years to Reach Full Decentralized Framework for Drug Assessment Adoption: 5 years

Details

Years to reach full Decentralized Framework for Drug Assessment adoption
Core definition

Decentralized Framework for Drug Assessment Core framework Annual OPEX: $18.9M

Details

Decentralized Framework for Drug Assessment Core framework annual opex (midpoint of $11-26.5M)

Uncertainty Range

Technical: 95% CI: [$11M, $26.5M] • Distribution: Lognormal
What this means: There's significant uncertainty here. The true value likely falls between $11M and $26.5M (±41%). This represents a 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

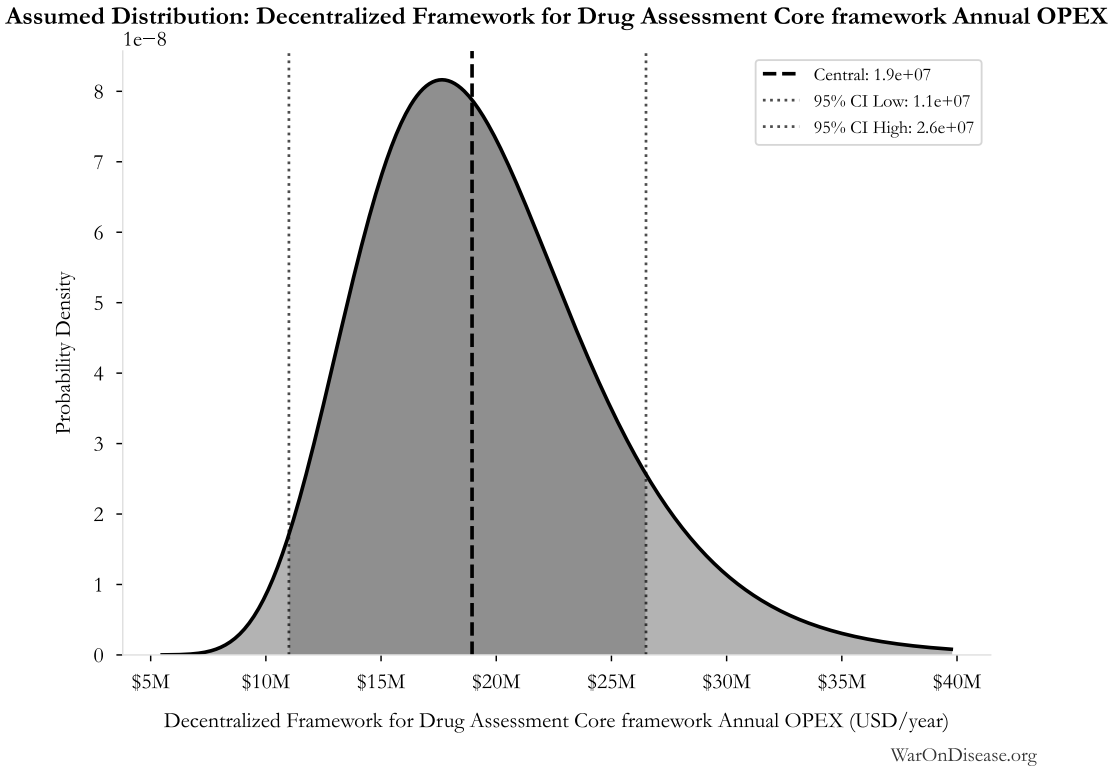


Figure 347: Probability Distribution: Decentralized Framework for Drug Assessment Core framework Annual OPEX

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

Decentralized Framework for Drug Assessment Core framework Build Cost: $40M

Details

Decentralized Framework for Drug Assessment Core framework build cost

Uncertainty Range

Technical: 95% CI: [$25M, $65M] • Distribution: Lognormal
What this means: There's significant uncertainty here. The true value likely falls between $25M and $65M (±50%). This represents a 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

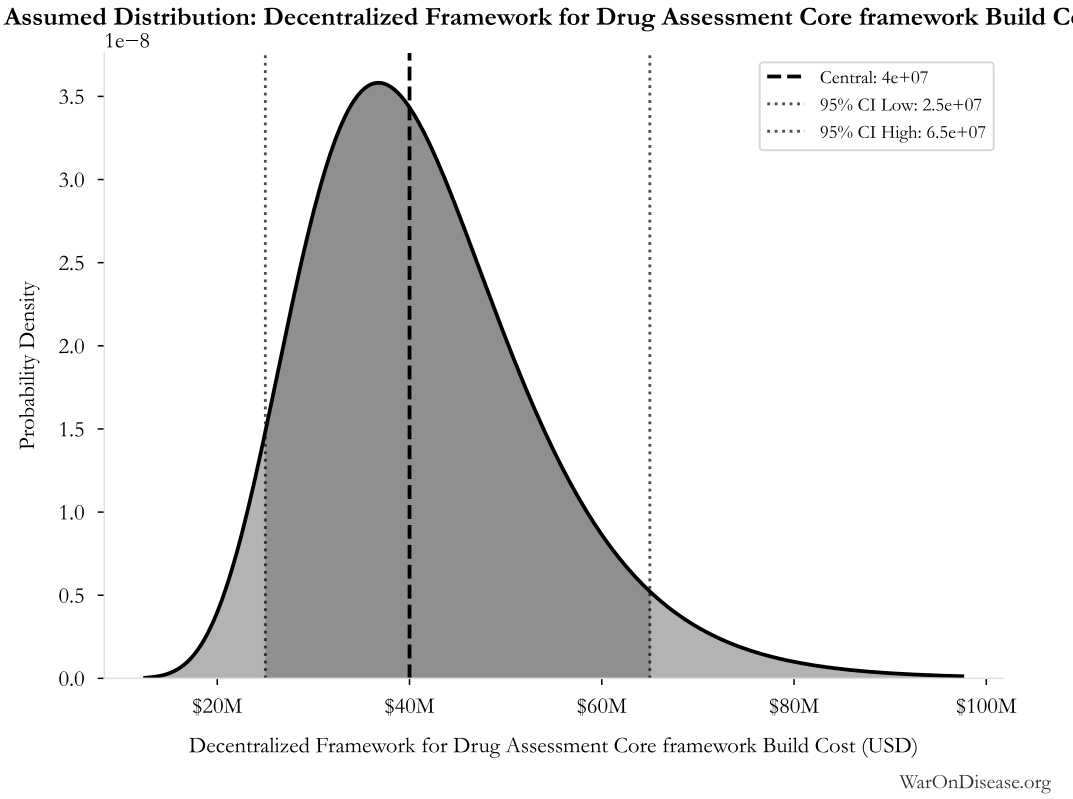


Figure 348: Probability Distribution: Decentralized Framework for Drug Assessment Core framework Build Cost

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

Decentralized Framework for Drug Assessment Community Support Costs: $2M

Details

Decentralized Framework for Drug Assessment community support costs

Uncertainty Range

Technical: 95% CI: [$1M, $3M] • Distribution: Lognormal

What this means: There's significant uncertainty here. The true value likely falls between $1M and $3M (±50%). This represents a 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

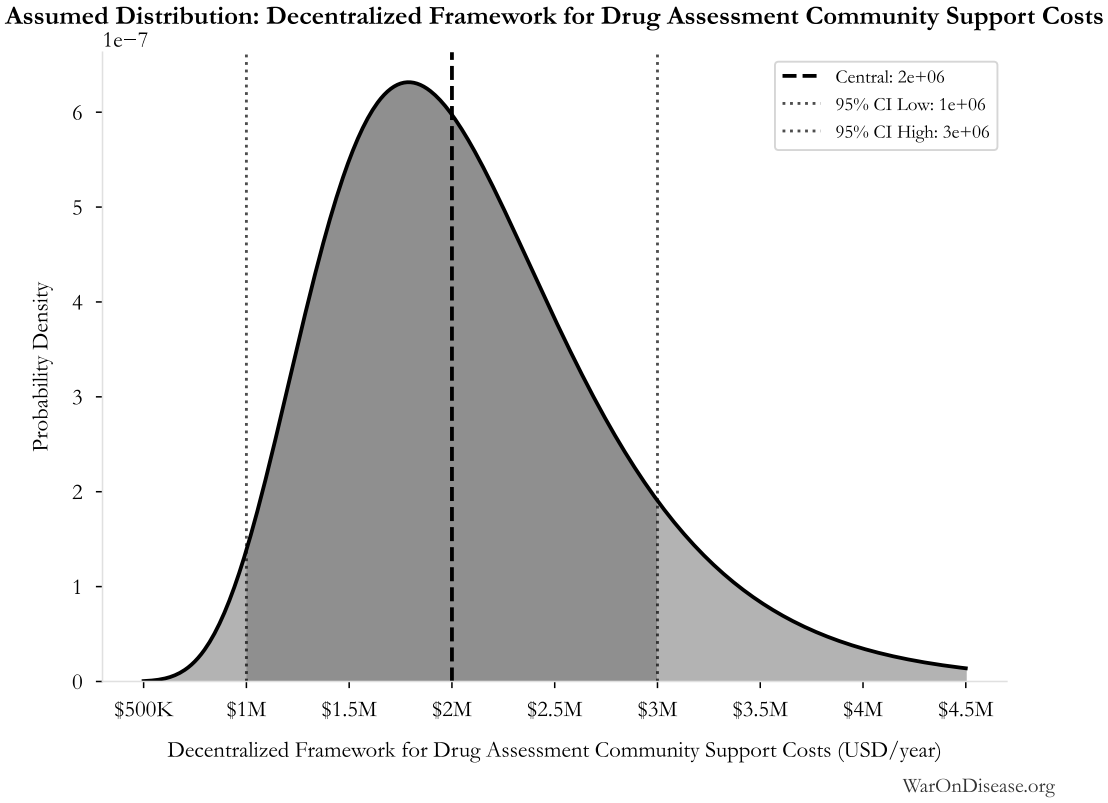


Figure 349: Probability Distribution: Decentralized Framework for Drug Assessment Community Support Costs

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

Decentralized Framework for Drug Assessment Infrastructure Costs: $8M

Details

Decentralized Framework for Drug Assessment infrastructure costs (cloud, security)

Uncertainty Range

Technical: 95% CI: [$5M, $12M] • Distribution: Lognormal
What this means: There's significant uncertainty here. The true value likely falls between $5M and $12M (±44%). This represents a 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

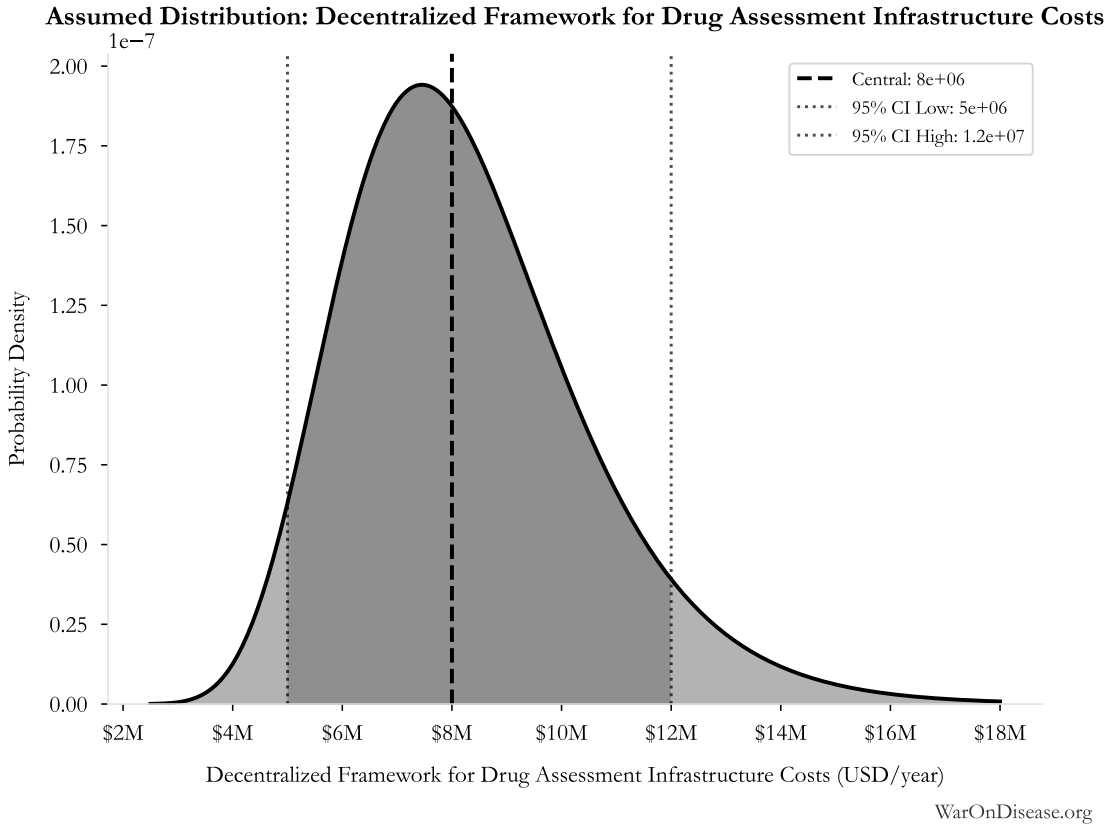


Figure 350: Probability Distribution: Decentralized Framework for Drug Assessment Infrastructure Costs

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

Decentralized Framework for Drug Assessment Maintenance Costs: $15M

Details

Decentralized Framework for Drug Assessment maintenance costs

Uncertainty Range

Technical: 95% CI: [$10M, $22M] • Distribution: Lognormal
What this means: There's significant uncertainty here. The true value likely falls between $10M and $22M (±40%). This represents a 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

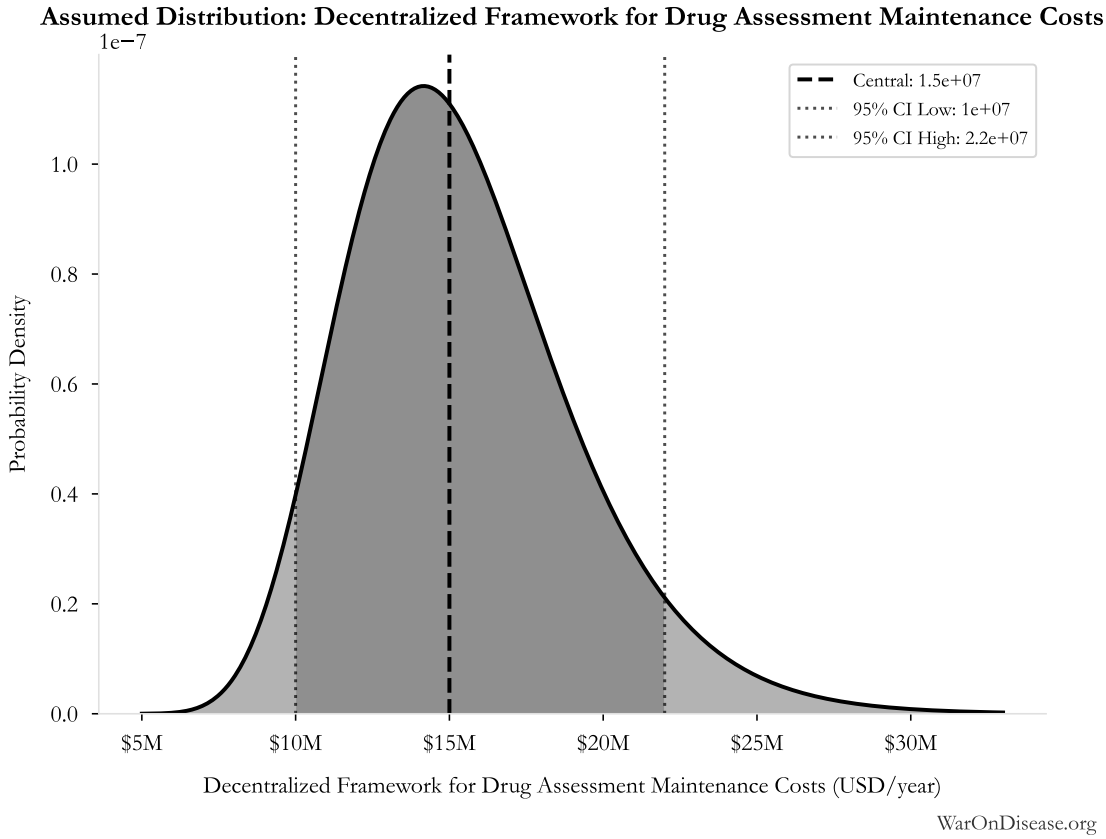


Figure 351: Probability Distribution: Decentralized Framework for Drug Assessment Maintenance Costs

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

Decentralized Framework for Drug Assessment Regulatory Coordination Costs: $5M

Details

Decentralized Framework for Drug Assessment regulatory coordination costs

Uncertainty Range

Technical: 95% CI: [$3M, $8M] • Distribution: Lognormal
What this means: There's significant uncertainty here. The true value likely falls between

$3M and $8M (±50%). This represents a 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

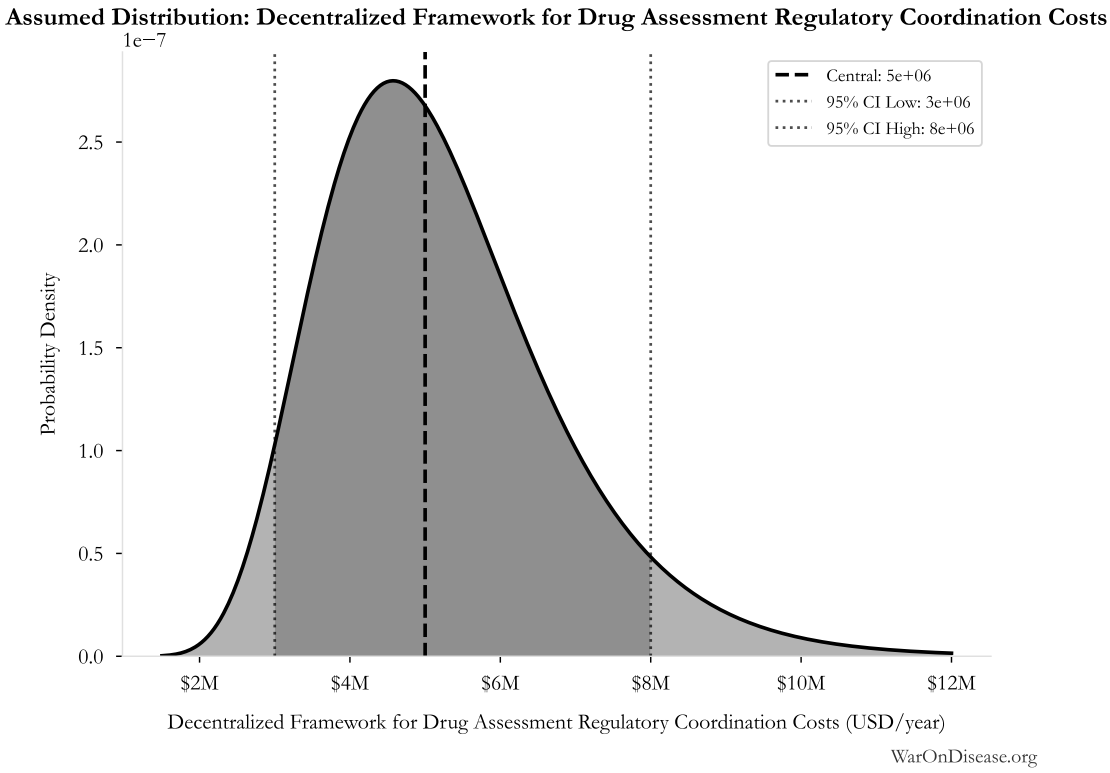


Figure 352: Probability Distribution: Decentralized Framework for Drug Assessment Regulatory Coordination Costs

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

Decentralized Framework for Drug Assessment Staff Costs: $10M

Details

Decentralized Framework for Drug Assessment staff costs (minimal, AI-assisted)

Uncertainty Range

Technical: 95% CI: [$7M, $15M] • Distribution: Lognormal
What this means: There's significant uncertainty here. The true value likely falls between $7M and $15M (±40%). This represents a 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

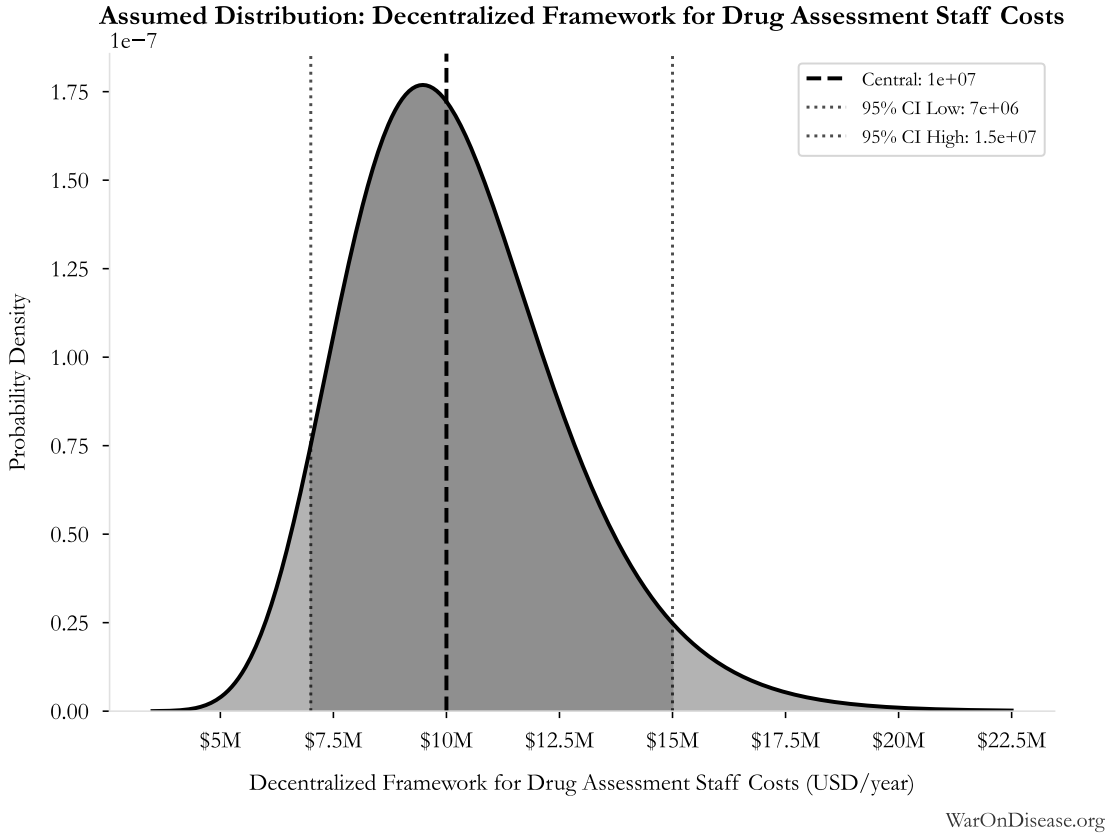


Figure 353: Probability Distribution: Decentralized Framework for Drug Assessment Staff Costs

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

DIH Broader Initiatives Annual OPEX: $21.1M

Details

DIH broader initiatives annual opex (medium case)

Uncertainty Range

Technical: 95% CI: [$14M, $32M] • Distribution: Lognormal
What this means: There's significant uncertainty here. The true value likely falls between $14M and $32M (±43%). This represents a 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

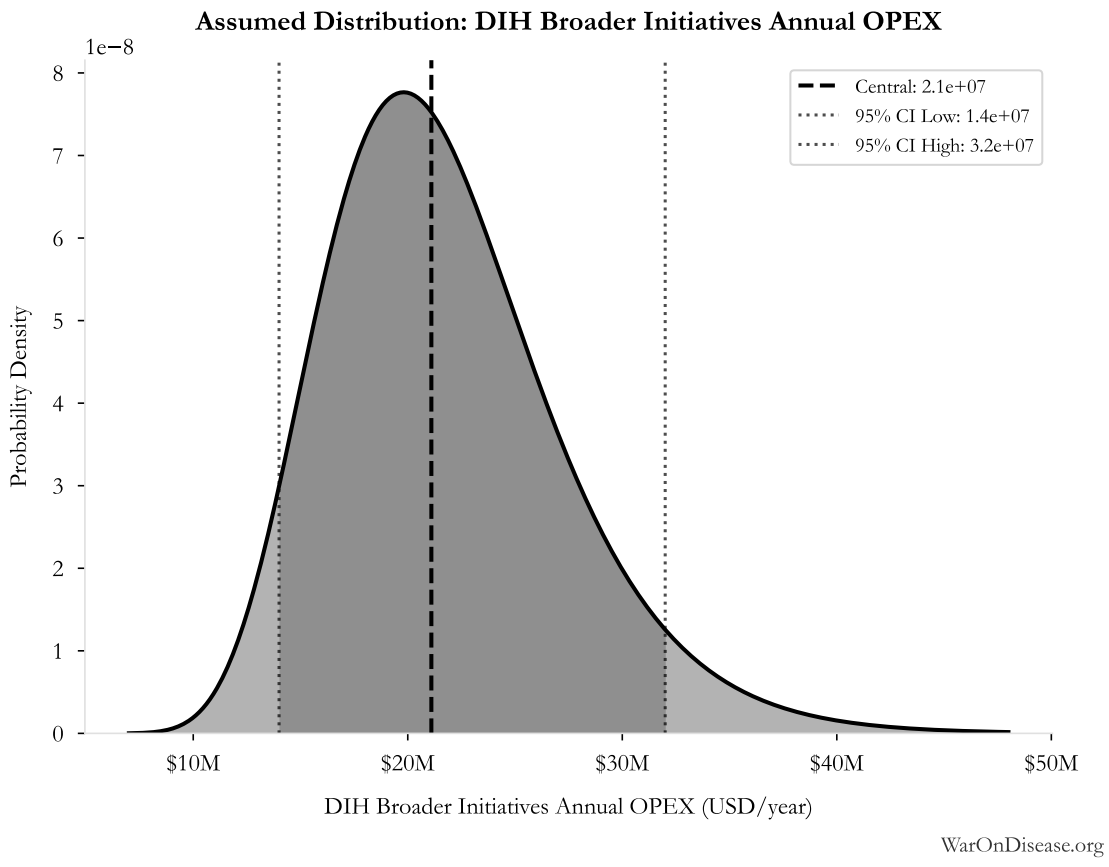


Figure 354: Probability Distribution: DIH Broader Initiatives Annual OPEX

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

DIH Broader Initiatives Upfront Cost: $230M

Details

DIH broader initiatives upfront cost (medium case)

Uncertainty Range

Technical: 95% CI: [$150M, $350M] • Distribution: Lognormal
What this means: There's significant uncertainty here. The true value likely falls between $150M and $350M (±44%). This represents a 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

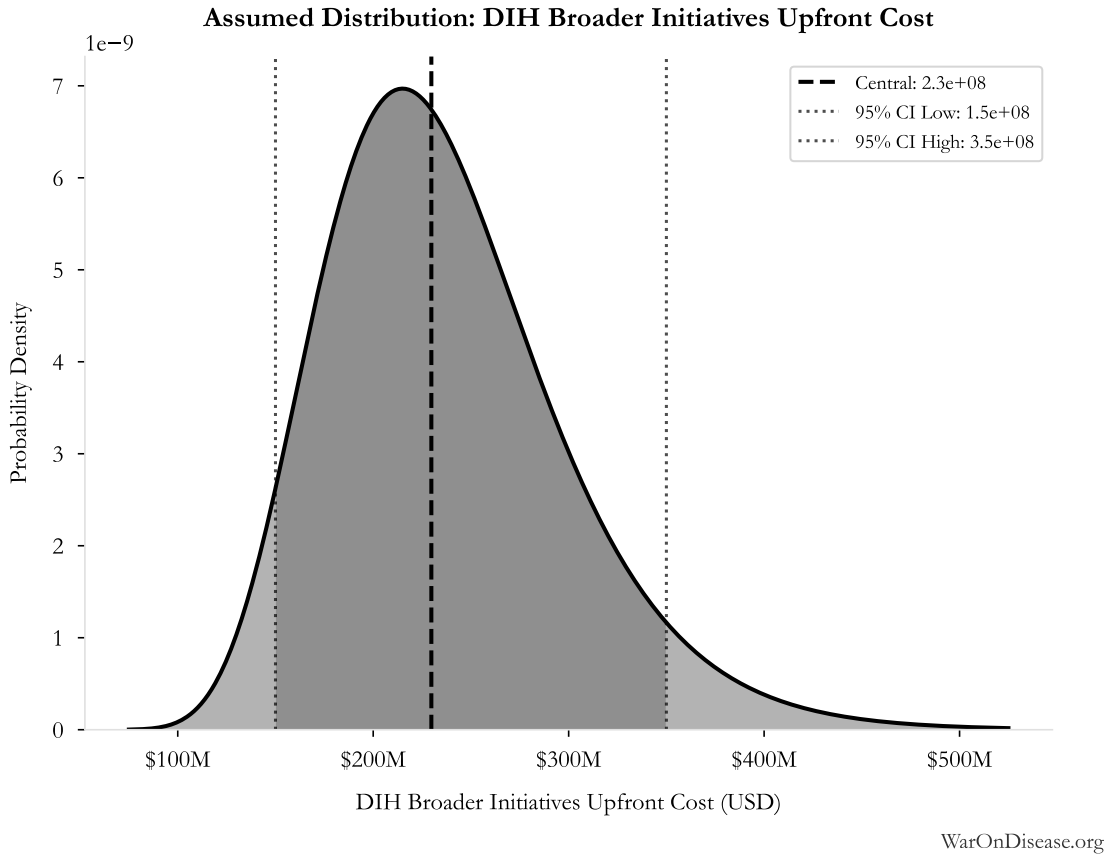


Figure 355: Probability Distribution: DIH Broader Initiatives Upfront Cost

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

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

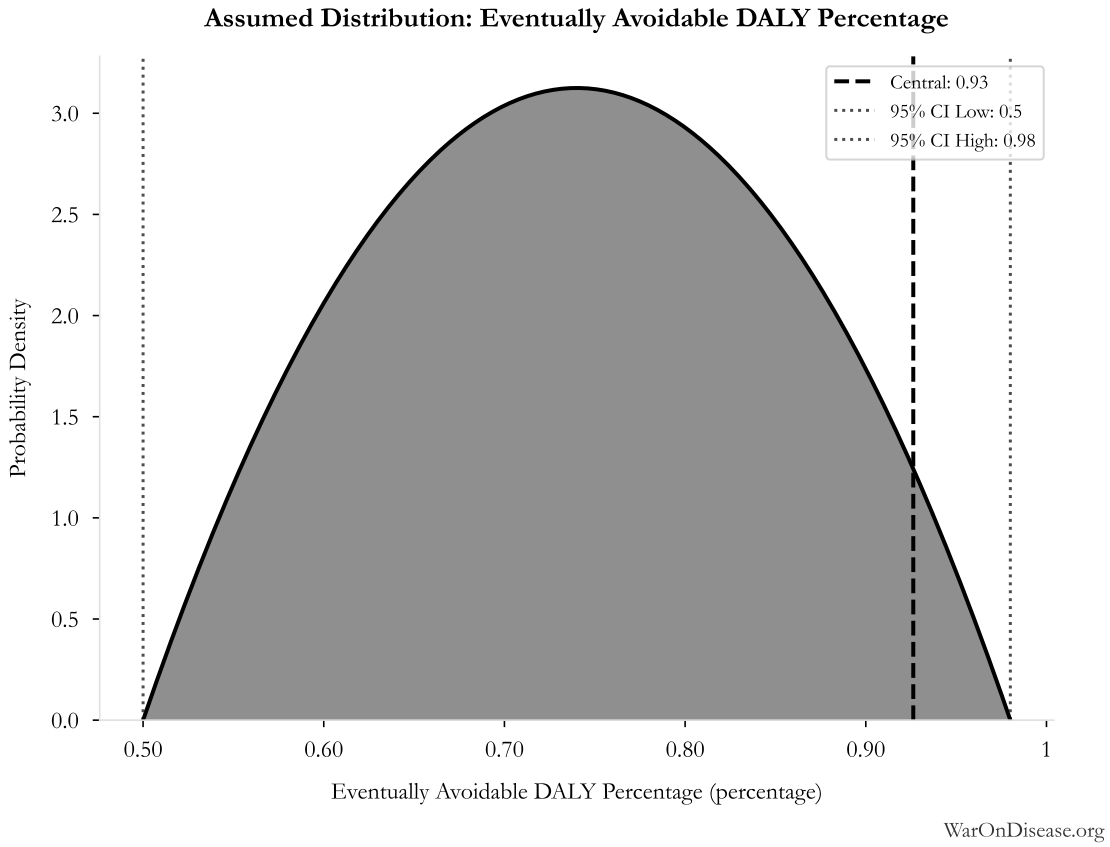


Figure 356: Probability Distribution: Eventually Avoidable DALY Percentage

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

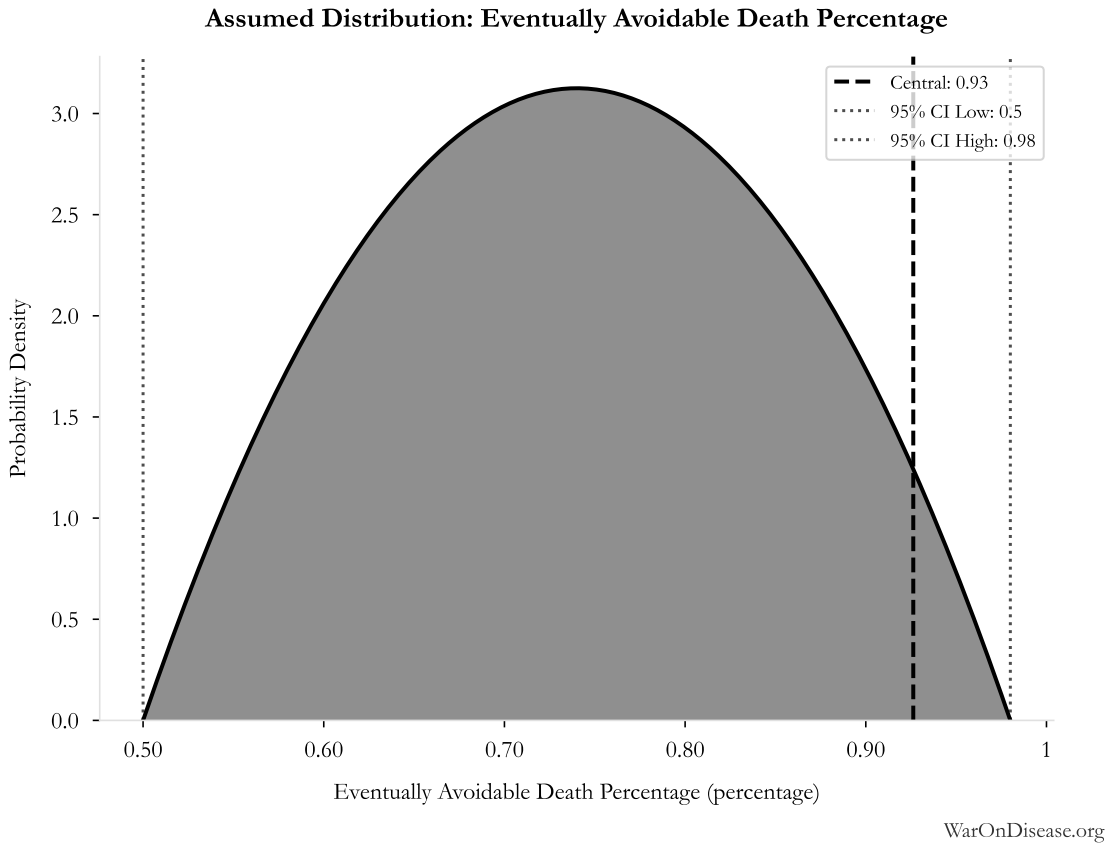


Figure 357: Probability Distribution: Eventually Avoidable Death Percentage

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

Fundamentally Unavoidable Death Percentage: 7.37%

Details

Percentage of deaths that are fundamentally unavoidable even with perfect biotechnology (primarily accidents). Calculated as Σ(disease_burden × (1 - max_cure_potential)) across all disease categories.
Core definition

IAB Political Incentive Funding Percentage: 10%

Details

Percentage of treaty funding allocated to Incentive Alignment Bond mechanism for political incentives (independent expenditures/PACs, post-office fellowships, Public Good Score infrastructure)

Uncertainty Range

Technical: Distribution: Fixed
Core definition

Standard Discount Rate for NPV Analysis: 3%

Details

Standard discount rate for NPV analysis (3% annual, social discount rate)

Uncertainty Range

Technical: Distribution: Fixed
Core definition

Standard Time Horizon for NPV Analysis: 10 years

Details

Standard time horizon for NPV analysis

Uncertainty Range

Technical: Distribution: Fixed

Core definition

Direct Fiscal Savings from 1% Military Spending Reduction: $27.2B

Details

Direct fiscal savings from 1% military spending reduction (high confidence)
Core definition

Pre-1962 Validation Years: 77 years

Details

Years of empirical validation for physician-led pragmatic trials (1883-1960)
Core definition

QALYs per COVID Death Averted: 5 QALYs/death

Details

Average QALYs gained per COVID death averted. Conservative estimate reflecting older age distribution of COVID mortality. See confidence_interval for range.

Uncertainty Range

Technical: 95% CI: [3 QALYs/death, 10 QALYs/death] • Distribution: Lognormal
What this means: This estimate is highly uncertain. The true value likely falls between 3 QALYs/death and 10 QALYs/death (±70%). 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

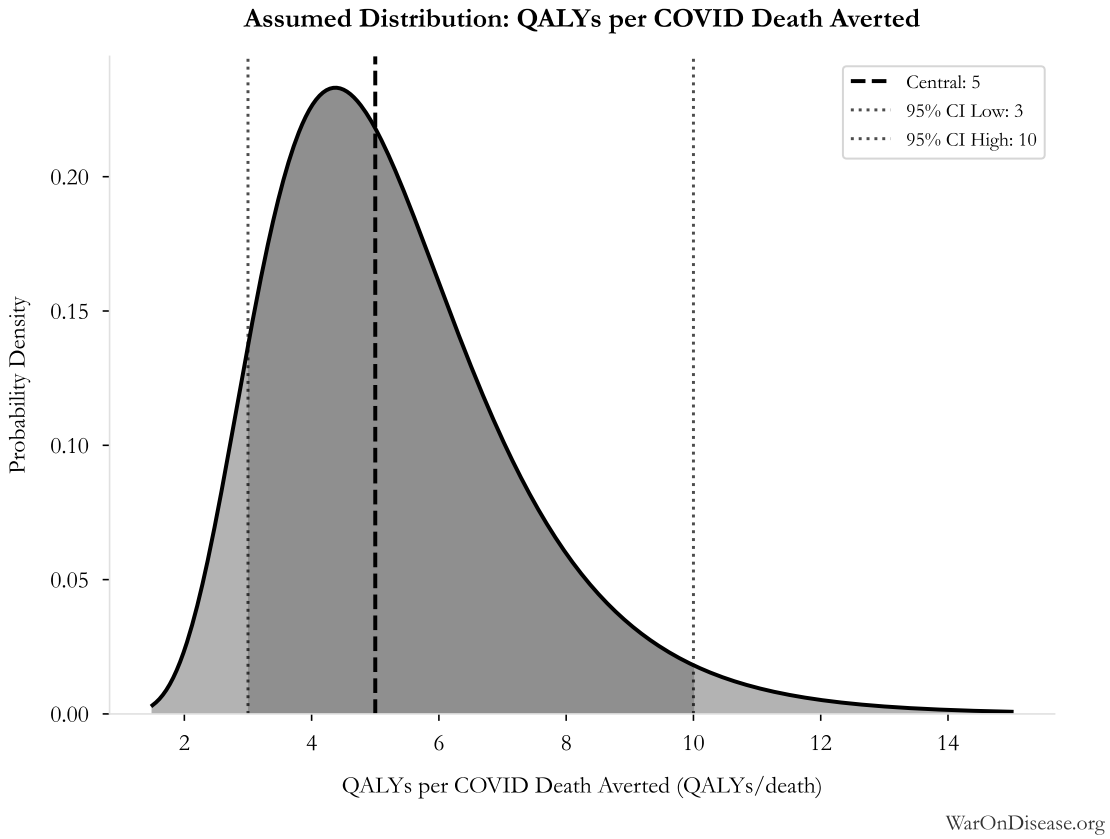


Figure 358: Probability Distribution: QALYs per COVID Death Averted

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

Safe Compounds Available for Testing: 9.50 thousand compounds

Details

Total safe compounds available for repurposing (FDA-approved + GRAS substances, midpoint of 7,000-12,000 range)

Uncertainty Range

Technical: 95% CI: [7.00 thousand compounds, 12.0 thousand compounds] • Distribution: Uniform
What this means: There's significant uncertainty here. The true value likely falls between

7.00 thousand compounds and 12.0 thousand compounds (±26%). This represents a wide range that our Monte Carlo simulations account for when calculating overall uncertainty in the results.
The uniform distribution means any value in the range is equally likely.

Input Distribution

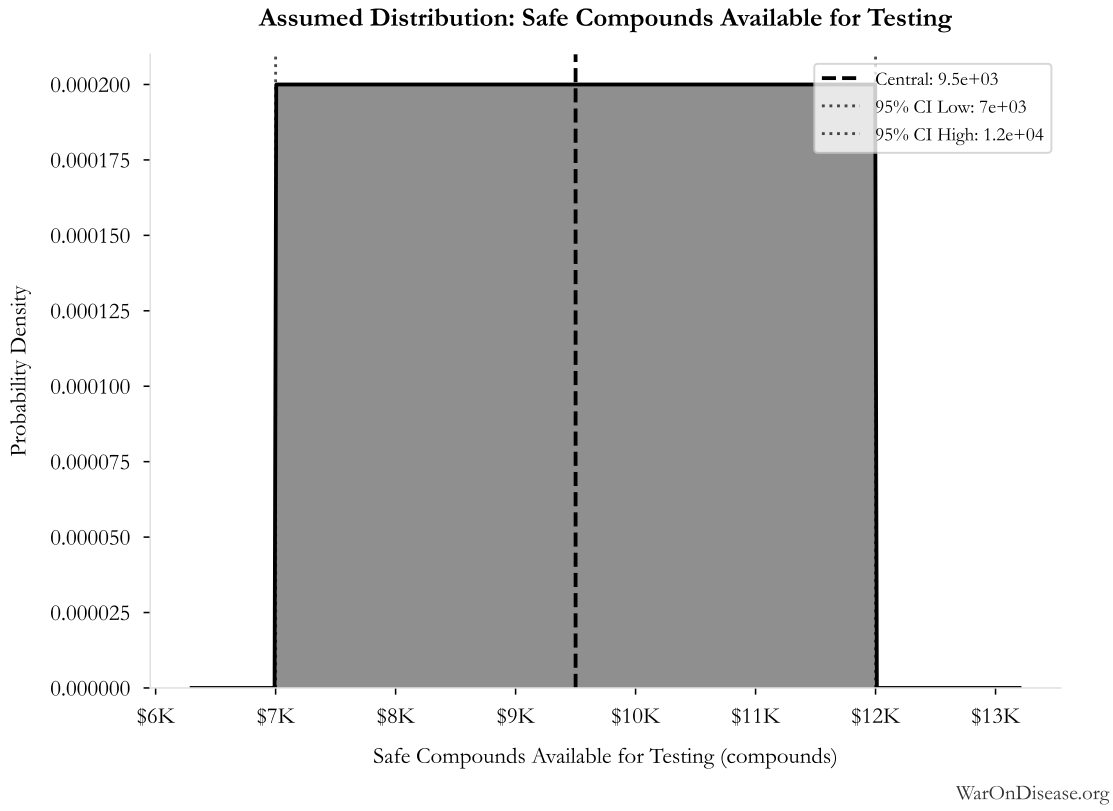


Figure 359: Probability Distribution: Safe Compounds Available for Testing

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

Tested Drug-Disease Relationships: 32.5 thousand relationships

Details

Estimated drug-disease relationships actually tested (approved uses + repurposed + failed trials, midpoint of 15,000-50,000 range)

Uncertainty Range

Technical: 95% CI: [15.0 thousand relationships, 50.0 thousand relationships] • Distribution: Lognormal
What this means: This estimate is highly uncertain. The true value likely falls between 15.0 thousand relationships and 50.0 thousand relationships (±54%). 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

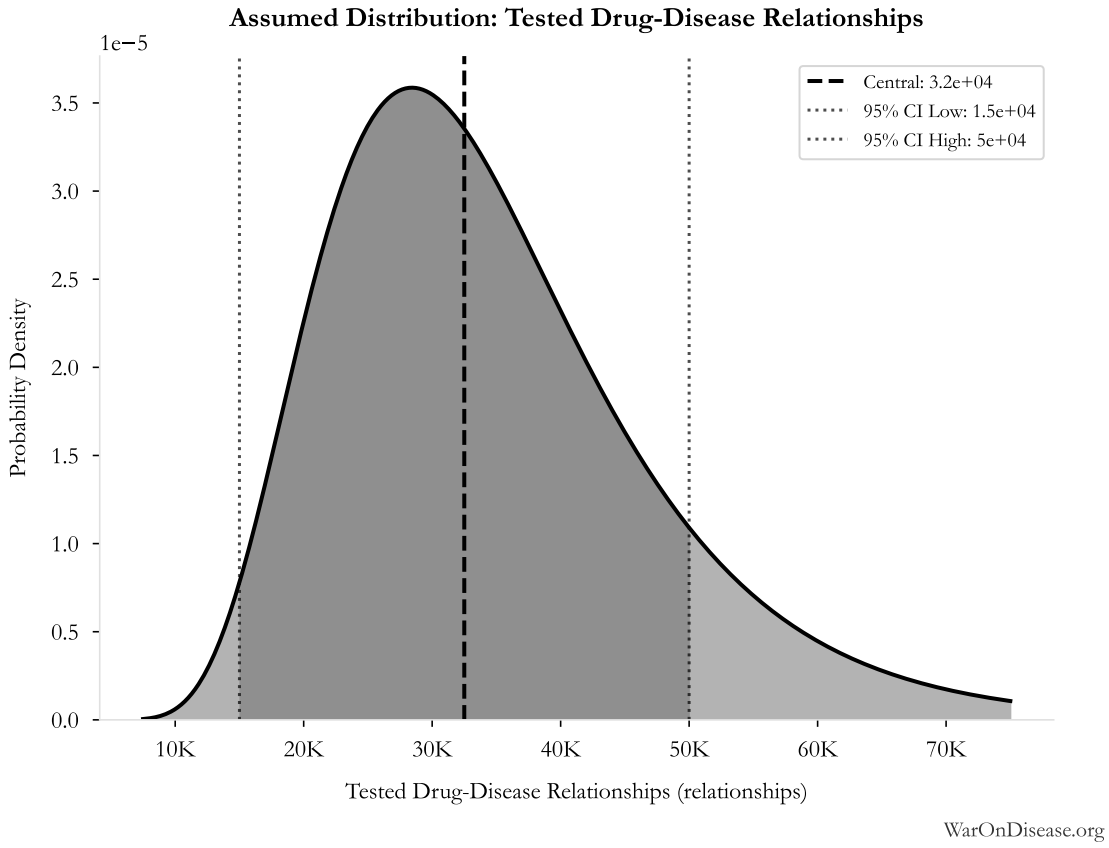


Figure 360: Probability Distribution: Tested Drug-Disease Relationships

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

Political Lobbying Campaign: Direct Lobbying, Super Pacs, Opposition Research, Staff, Legal/Compliance: $650M

Details

Political lobbying campaign: direct lobbying (US/EU/G20), Super PACs, opposition research, staff, legal/compliance. Budget exceeds combined pharma ($300M/year) and military-industrial complex ($150M/year) lobbying to ensure competitive positioning. Referendum relies on grassroots mobilization and earned media, while lobbying requires matching or exceeding opposition spending for political viability.

Uncertainty Range

Technical: 95% CI: [$325M, $1.30B] • Distribution: Lognormal
What this means: This estimate is highly uncertain. The true value likely falls between $325M and $1.30B (±75%). 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

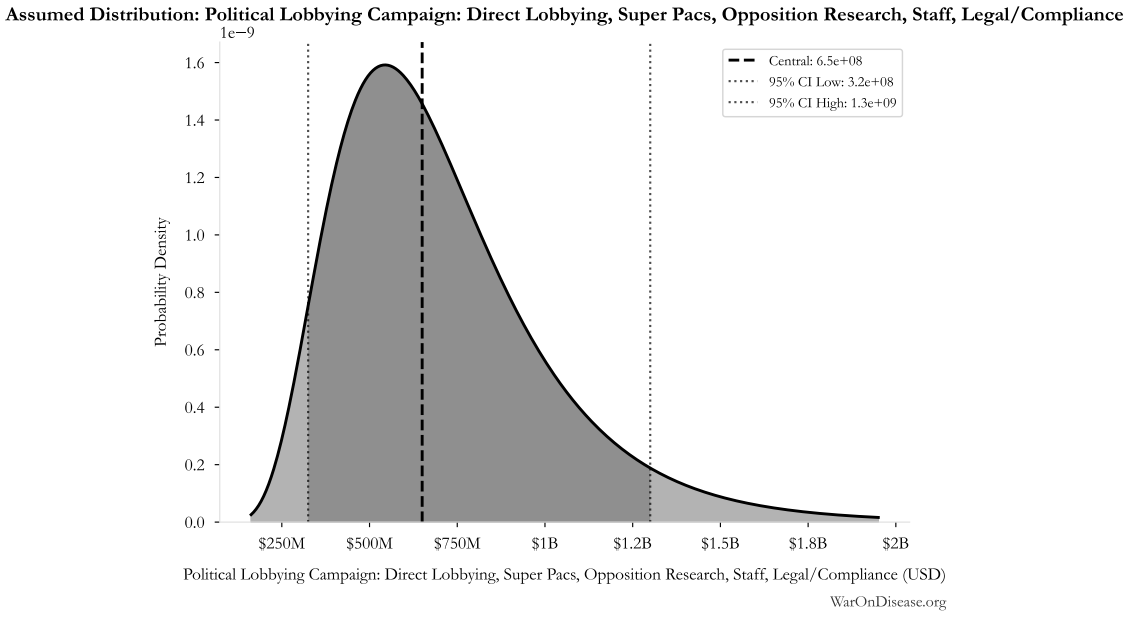


Figure 361: Probability Distribution: Political Lobbying Campaign: Direct Lobbying, Super Pacs, Opposition Research, Staff, Legal/Compliance

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

Reserve Fund / Contingency Buffer: $100M

Details

Reserve fund / contingency buffer (10% of total campaign cost). Using industry standard 10% for complex campaigns with potential for unforeseen legal challenges, opposition response, or regulatory delays. Conservative lower bound of $20M (2%) reflects transparent budget allocation and predictable referendum/lobbying costs.

Uncertainty Range

Technical: 95% CI: [$20M, $150M] • Distribution: Lognormal
What this means: This estimate is highly uncertain. The true value likely falls between $20M and $150M (±65%). 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

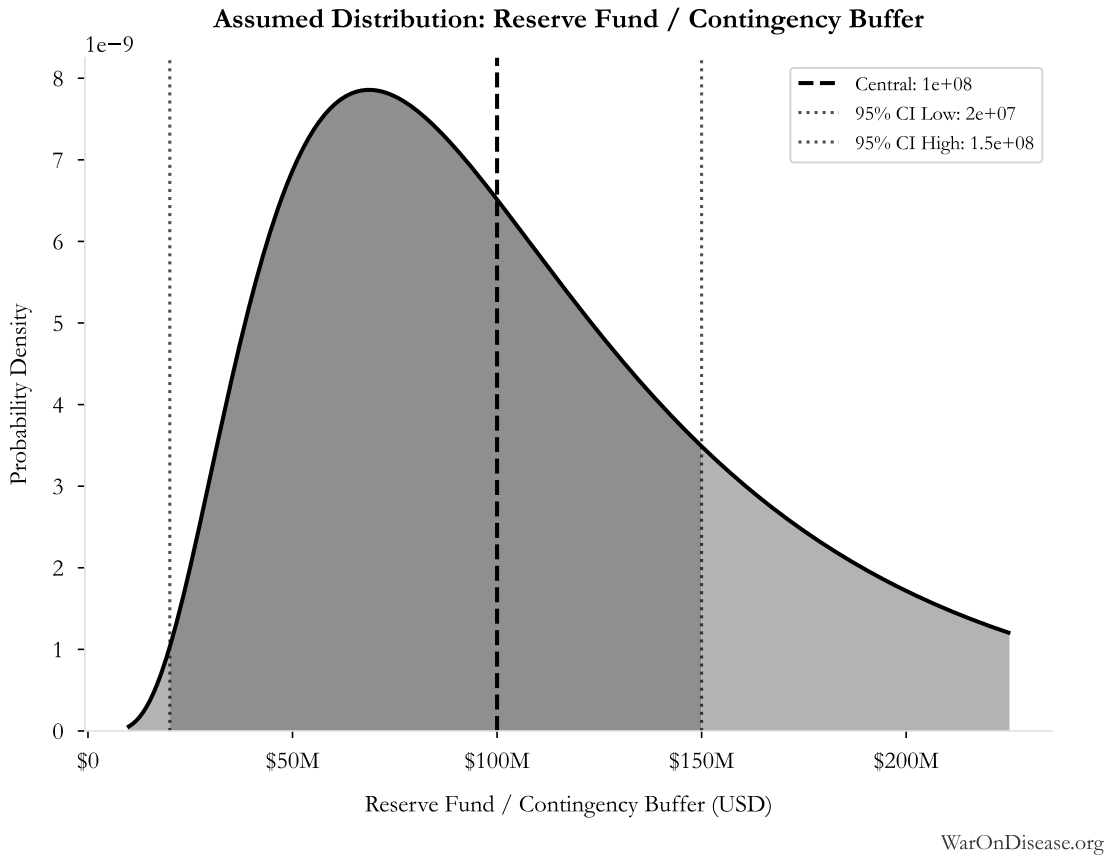


Figure 362: Probability Distribution: Reserve Fund / Contingency Buffer

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

Viral Referendum Budget: $250M

Details

Viral referendum budget for 280M verified votes (base: $250M realistic with $0.50/vote avg, range: $150M optimistic $0.20/vote to $410M worst-case $1.05/vote). Components: platform ($35M), verification infrastructure (280M × friction × $0.18-0.20), tiered referral payments (varies by virality and marginal cost curve per diffusion theory), marketing seed ($5-15M). Based on PayPal referral economics ($18-36 inflation-adjusted) and biometric verification pricing ($0.15-0.25 at 300M+ scale).

Uncertainty Range

Technical: 95% CI: [$150M, $410M]
What this means: This estimate is highly uncertain. The true value likely falls between $150M and $410M (±52%). This represents a very wide range that our Monte Carlo simulations account for when calculating overall uncertainty in the results.

Input Distribution

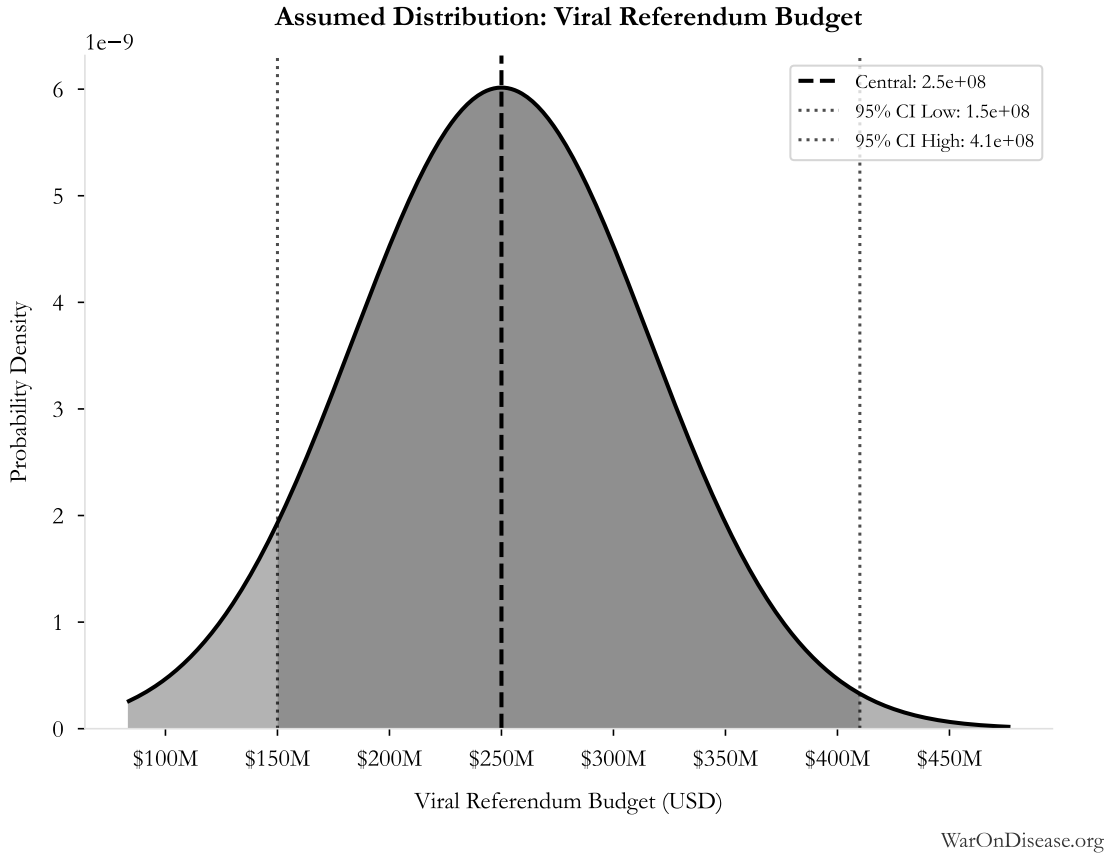


Figure 363: Probability Distribution: Viral Referendum Budget

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.
Core definition

1% Reduction in Military Spending/War Costs from Treaty: 1%

Details

1% reduction in military spending/war costs from treaty

Uncertainty Range

Technical: Distribution: Fixed
Core definition

Trial-Relevant Diseases: 1.00 thousand diseases

Details

Consolidated count of trial-relevant diseases worth targeting (after grouping ICD-10 codes)

Uncertainty Range

Technical: 95% CI: [800 diseases, 1.20 thousand diseases] • Distribution: Uniform
What this means: This estimate has moderate uncertainty. The true value likely falls between 800 diseases and 1.20 thousand diseases (±20%). This represents a reasonable range that our Monte Carlo simulations account for when calculating overall uncertainty in the results.
The uniform distribution means any value in the range is equally likely.

Input Distribution

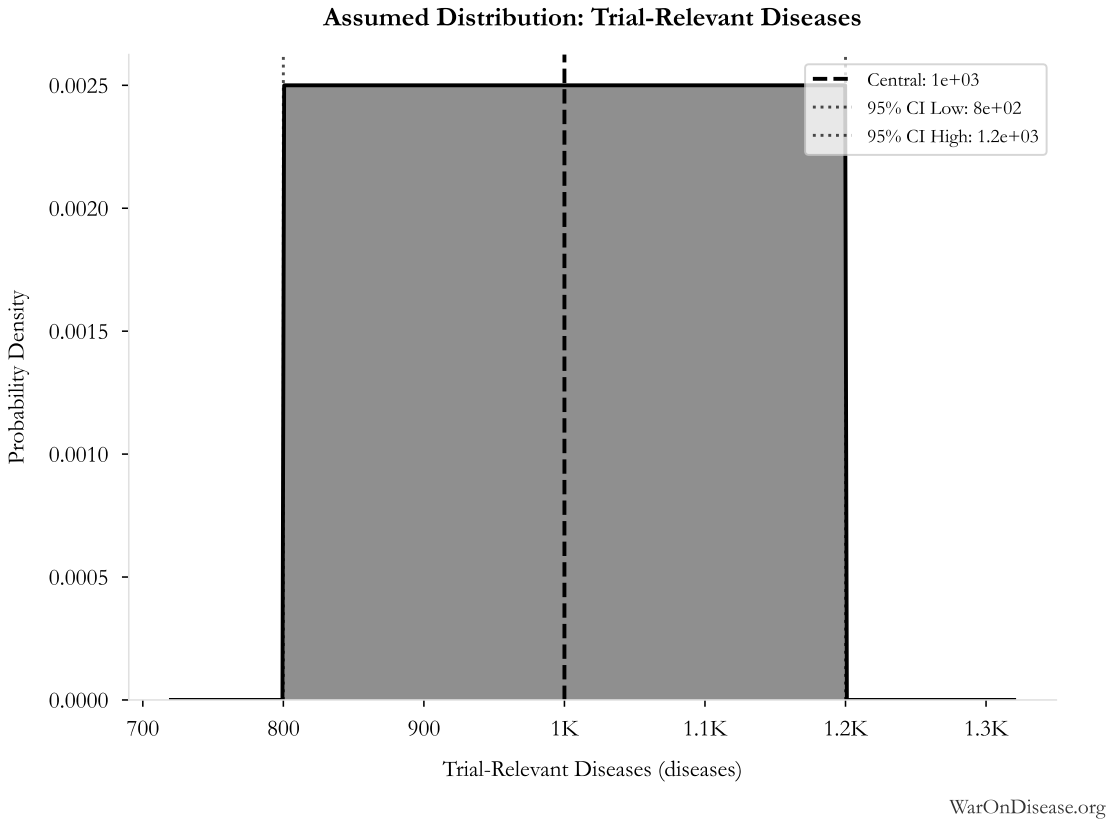


Figure 364: Probability Distribution: Trial-Relevant Diseases

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

Percentage of Captured Dividend Funding VICTORY Incentive Alignment Bonds: 10%

Details

Percentage of captured dividend funding VICTORY Incentive Alignment Bonds (10%)

Uncertainty Range

Technical: Distribution: Fixed
Core definition

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War on Terror emissions: 1.2B metric tons GHG (equivalent to 257M cars/year) Military:. 5.5% of global GHG emissions (2X aviation + shipping combined) US DoD: World's single largest institutional oil consumer, 47th largest emitter if nation Cleanup costs: $500B+ for military contaminated sites Gaza war environmental damage: $56.4B; landmine clearance: $34.6B expected Climate finance gap: Rich nations spend 30X more on military than climate finance Note: Military activities cause massive environmental damage through GHG emissions, toxic contamination, and long-term cleanup costs far exceeding current climate finance commitments Additional sources: https://watson.brown.edu/costsofwar/costs/social/environment | https://earth.org/environmental-costs-of-wars/ | https://transformdefence.org/transformdefence/stats/

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Longevity escape velocity: Hypothetical point where medical advances extend life expectancy. faster than time passes Term coined by Aubrey de Grey (biogerontologist) in 2004 paper; concept from David Gobel (Methuselah Foundation) Current progress: Science adds 3 months to lifespan per year; LEV requires adding >1 year per year Sinclair (Harvard): "There is no biological upper limit to age" - first person to live to 150 may already be born De Grey: 50% chance of reaching LEV by mid-to-late 2030s; SENS approach = damage repair rather than slowing damage Kurzweil (2024): LEV by 2029-2035, AI will simulate biological processes to accelerate solutions George Church: LEV "in a decade or two" via age-reversal clinical trials Natural lifespan cap: 120-150 years (Jeanne Calment record: 122); engineering approach could bypass via damage repair Key mechanisms: Epigenetic reprogramming, senolytic drugs, stem cell therapy, gene therapy, AI-driven drug discovery Current record: Jeanne Calment (122 years, 164 days) - record unbroken since 1997 Note: LEV is theoretical but increasingly plausible given demonstrated age reversal in mice (109% lifespan extension) and human cells (30-year epigenetic age reversal) Additional sources: https://en.wikipedia.org/wiki/Longevity_escape_velocity | https://pmc.ncbi.nlm.nih.gov/articles/PMC423155/ | https://www.popularmechanics.com/science/a36712084/can-science-cure-death-longevity/ | https://www.diamandis.com/blog/longevity-escape-velocity

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Empirical estimation: Average reporting rate approximately 6%, meaning 94% of adverse. events are underreported Variability: 0.01% to 44% for statin events; 0.002% to >100% for biological drugs; 20% to >100% for narrow therapeutic index (NTI) drugs Selective reporting: Serious, unusual events more likely reported than mild or expected ones Newly marketed drugs: Higher reporting rates due to heightened awareness Older drugs: Events often under-reported Note: FAERS voluntary reporting system captures only "tip of the iceberg" of drug safety problems. Under-reporting introduces inherent biases and limitations in pharmacovigilance data Additional sources: https://pubmed.ncbi.nlm.nih.gov/28447485/ | https://pmc.ncbi.nlm.nih.gov/articles/PMC12393772/

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Most frequent exclusions: Pregnancy, lactation/breastfeeding, renal/hepatic abnormalities,. specific infectious diseases Pregnant/lactating women: >90% of trials exclude Older adults: 27% exclude based on age (arbitrary upper limits) Patients with organ dysfunction: Excluded due to adverse impact concerns from comorbidities/concomitant meds Multiple chronic conditions: Often exclusion criterion despite being common in target population Children/adolescents: Excluded due to ethical considerations High-risk patients: Prior malignancy history, active brain metastases, suboptimal hepatic/renal function, HIV+ FDA guidance: Working to broaden eligibility; "exclusions based on age alone rarely appropriate Note: Exclusion criteria often eliminate patients who would actually use the drug, reducing real-world applicability of trial results Additional sources: https://www.fda.gov/media/134754/download | https://www.sciencedirect.com/science/article/abs/pii/S1551714421002512 | https://ascopubs.org/doi/10.1200/EDBK_155880

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Top researchers can spend up to 50% of their time writing grants. Additional. sources: https://acquisitiontalk.com/2021/12/top-researchers-spend-50-of-their-time-writing-grants-how-to-fix-it-and-what-it-means-for-dod/

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Conservative estimate: 300 million people (3.5-5.9% of world population of 7.5B) Range:. 263-446 million people globally Based on Orphanet database analysis of 3,585 rare diseases Note: Excludes rare cancers and infectious diseases, so actual number likely higher Additional sources: https://www.rarediseasesinternational.org/new-scientific-paper-confirms-300-million-people-living-with-a-rare-disease-worldwide/ | https://sciencedaily.com/releases/2019/10/191024075007.htm | https://pmc.ncbi.nlm.nih.gov/articles/PMC9632971/

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Dr. Frances Kelsey (FDA reviewer) resisted pressure to approve thalidomide September. 1960-November 1961 Worldwide: 8,000 infants born with missing/malformed limbs; 5,000-7,000 perished in utero United States: 17 confirmed phocomelia cases + 9 likely cases (vs. 8,000 worldwide) Kelsey insisted on hard evidence, refused to be browbeaten; repeatedly requested more information every 60 days Merrell complained to her bosses, calling her "petty bureaucrat" - she persisted Recognition: President's Award for Distinguished Federal Civilian Service (JFK, 1962) Led to 1962 Kefauver-Harris Amendments requiring drugs prove both safety AND effectiveness Additional sources: https://www.fda.gov/about-fda/fda-history-exhibits/frances-oldham-kelsey-medical-reviewer-famous-averting-public-health-tragedy | https://www.uchicagomedicine.org/forefront/biological-sciences-articles/courageous-physician-scientist-saved-the-us-from-a-birth-defects-catastrophe | https://www.smithsonianmag.com/science-nature/woman-who-stood-between-america-and-epidemic-birth-defects-180963165/

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Pragmatic trials evaluate the effectiveness of interventions in real-life routine practice. conditions, whereas explanatory trials determine the efficacy of interventions under ideal situations. Pragmatic trials produce results that can be generalized and applied in routine practice settings. Note: Pragmatic trials often find smaller effect sizes than explanatory trials but have higher external validity (generalizability to real-world populations) Additional sources: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3181997/

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Up to 50.0% of published preclinical research is irreproducible, with an estimated annual cost of $28 billion in the U.S. alone. This is based on $56B annual spending on preclinical research × 50.0% irreproducibility rate. Main causes: reagents/materials (36%), study design (28%), data analysis (25%), protocols (11%). Additional sources: https://www.science.org/content/article/study-claims-28-billion-year-spent-irreproducible-biomedical-research | https://www.idbs.com/2020/11/replicating-science-28-billion-is-wasted-every-year-in-the-us-alone/

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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.

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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.