

The Optimal Budget Generator: A Causal Inference Protocol for Maximizing Median Health and Wealth Through Public Goods Funding

Generating Integrated Public Budget Recommendations Using Diminishing Returns Modeling and Cost-Effectiveness Analysis

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Abstract

20-40% of public goods funding is misallocated relative to outcome-maximizing benchmarks, representing trillions annually in foregone welfare gains. Budget processes respond to lobbying intensity and historical precedent rather than causal evidence of effectiveness.

The Optimal Budget Generator (OBG) applies causal inference, diminishing returns modeling, and cost-effectiveness analysis to determine optimal public goods funding levels that maximize two welfare metrics: real after-tax median income growth and median healthy life years. For each spending category, OBG estimates an Optimal Spending Level (OSL) identifying where marginal returns equal opportunity cost.

The Budget Impact Score (BIS) measures confidence in each OSL estimate based on study quality, statistical precision, and temporal recency of the underlying causal evidence. The result is a gap analysis showing which categories are over- or underfunded relative to evidence-based benchmarks, enabling systematic reallocation from low-return to high-return public investments.

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Abstract

This specification describes the **Optimal Budget Generator (OBG)** framework, a systematic approach to generating integrated budget recommendations that maximize welfare as measured by two metrics: **real after-tax median income growth** and **median healthy life years**.

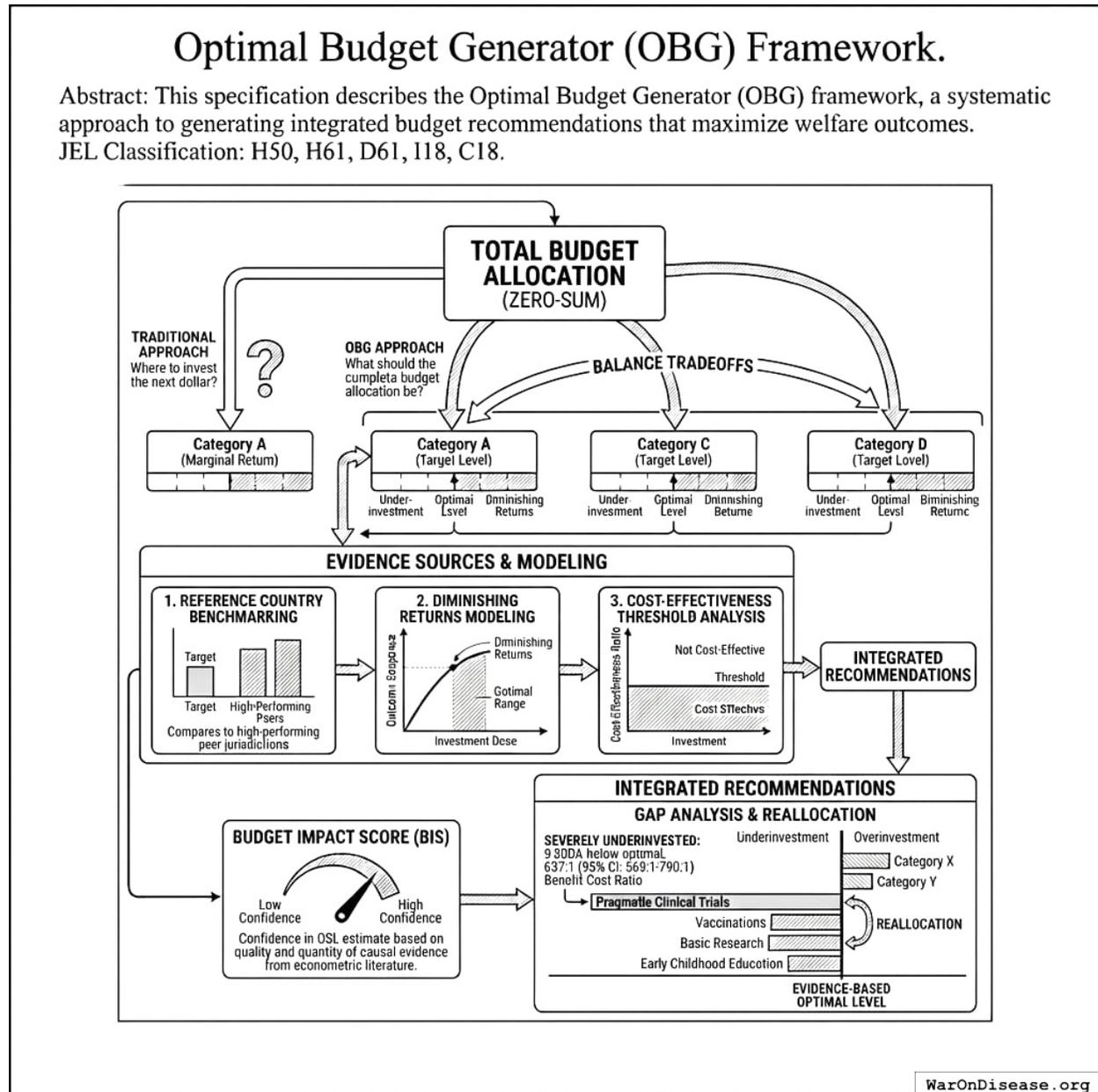


Figure 1: A conceptual diagram of the Optimal Budget Generator (OBG) framework showing how three evidence sources (benchmarking, returns modeling, and threshold analysis) integrate to create a gap analysis between current and evidence-based optimal funding levels.

JEL Classification: H50, H61, D61, I18, C18

Unlike marginal-return frameworks that ask “where should we invest the next dollar?”, OBG asks “what should the complete budget allocation be?” Each category has a target level - too little means underinvestment, too much means diminishing returns. But unlike the Recommended Daily Allowance for nutrients (where you can meet all targets simultaneously), budget allocation is zero-sum: spending more on one category means less for others. OBG generates integrated recommendations that balance these tradeoffs.

The framework combines two evidence sources: (1) **diminishing returns modeling** from cross-country dose-response studies, and (2) **cost-effectiveness threshold analysis** from health economics. The **Budget Impact Score (BIS)** measures our *confidence* in each category’s OSL estimate based on the quality and quantity of causal evidence from the econometric literature.

The result is a gap analysis showing which categories are underfunded relative to evidence-based optimal levels, enabling systematic reallocation from overinvestment to underinvestment. Applied to the US federal budget, the framework identifies pragmatic clinical trials as the most severely underinvested category (9,900% below optimal with 637:1 (95% CI: 569:1-790:1) benefit-cost ratio), followed by vaccinations, basic research, and early childhood education.

1 System Overview

1.1 What Policymakers See

A dashboard showing spending gaps by category, with clear recommendations:

i Illustrative Example: US Federal Budget Gap Analysis							
The following table demonstrates how OBG output would appear. OSL estimates for fully derived categories (pragmatic trials, vaccinations) come from the worked examples in Sections 6-7. Remaining OSL estimates are preliminary and based on cross-country benchmarking; full derivations are future work.							
Category	Current	OSL	Gap	Evidence	Income Effect	Health Effect	Action
Pragmatic clinical trials	\$0.5B	\$50B	+\$49.5B	A (RCTs)	++	+++	Scale 100x
Vaccinations	\$8B	\$35B	+\$27B	A (RCTs)	+	+++	Increase
Basic research	\$45B	\$90B	+\$45B	B (spillovers)	++	++	Increase
Early childhood (0-5)	\$50B	\$70B	+\$20B	A (RCTs)	+++	+	Increase
Military (discretionary)	\$850B	\$459B	-\$391B	C (benchmarks)	—	—	Decrease

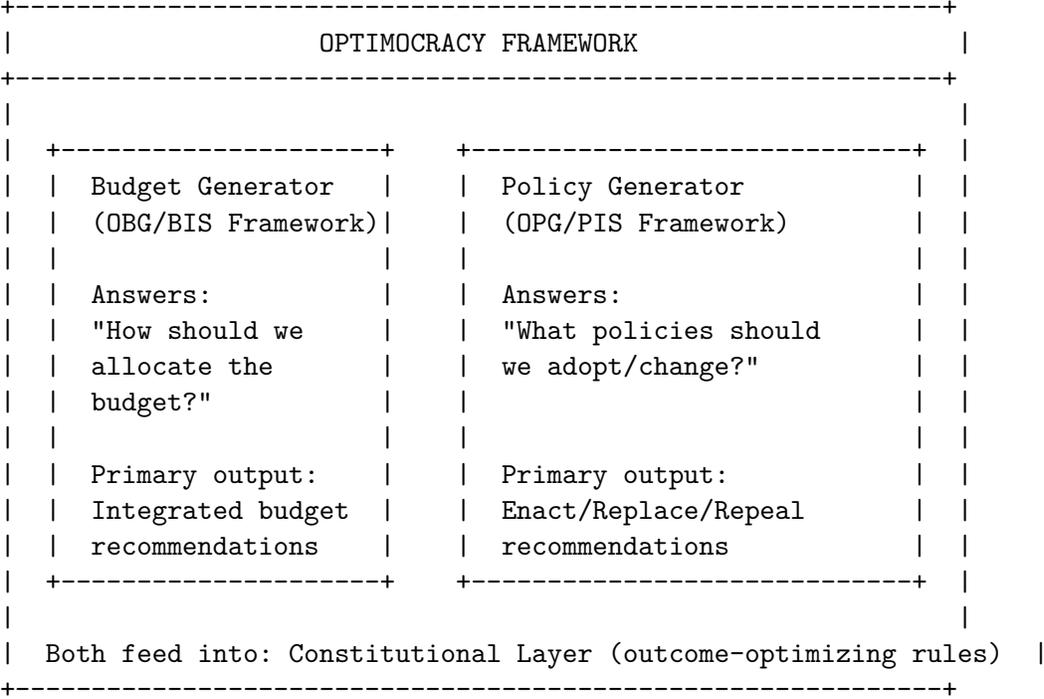
Agricultural subsidies	\$25B	\$0B	-	A (welfare analysis)	-	-	Eliminate
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Positive gaps indicate underinvestment; negative gaps indicate overinvestment. Income Effect: impact on real after-tax median income growth. Health Effect: impact on median healthy life years. Scale: +++ strong positive, ++ moderate positive, + weak positive, - negative.

1.2 What Budget Analysts See

- **OSL estimates** with confidence intervals and methodology notes
- **Cross-country spending data** showing spending-outcome relationships
- **Diminishing returns curves** identifying optimal spending levels
- **Evidence quality scores (BIS)** for each category
- **Sensitivity analysis** showing how OSL changes with different assumptions
- **Priority rankings** by gap size weighted by evidence confidence

1.3 Where This Fits



The OBG/BIS framework answers: “Given what we know about returns to spending, what are the optimal allocation levels?”

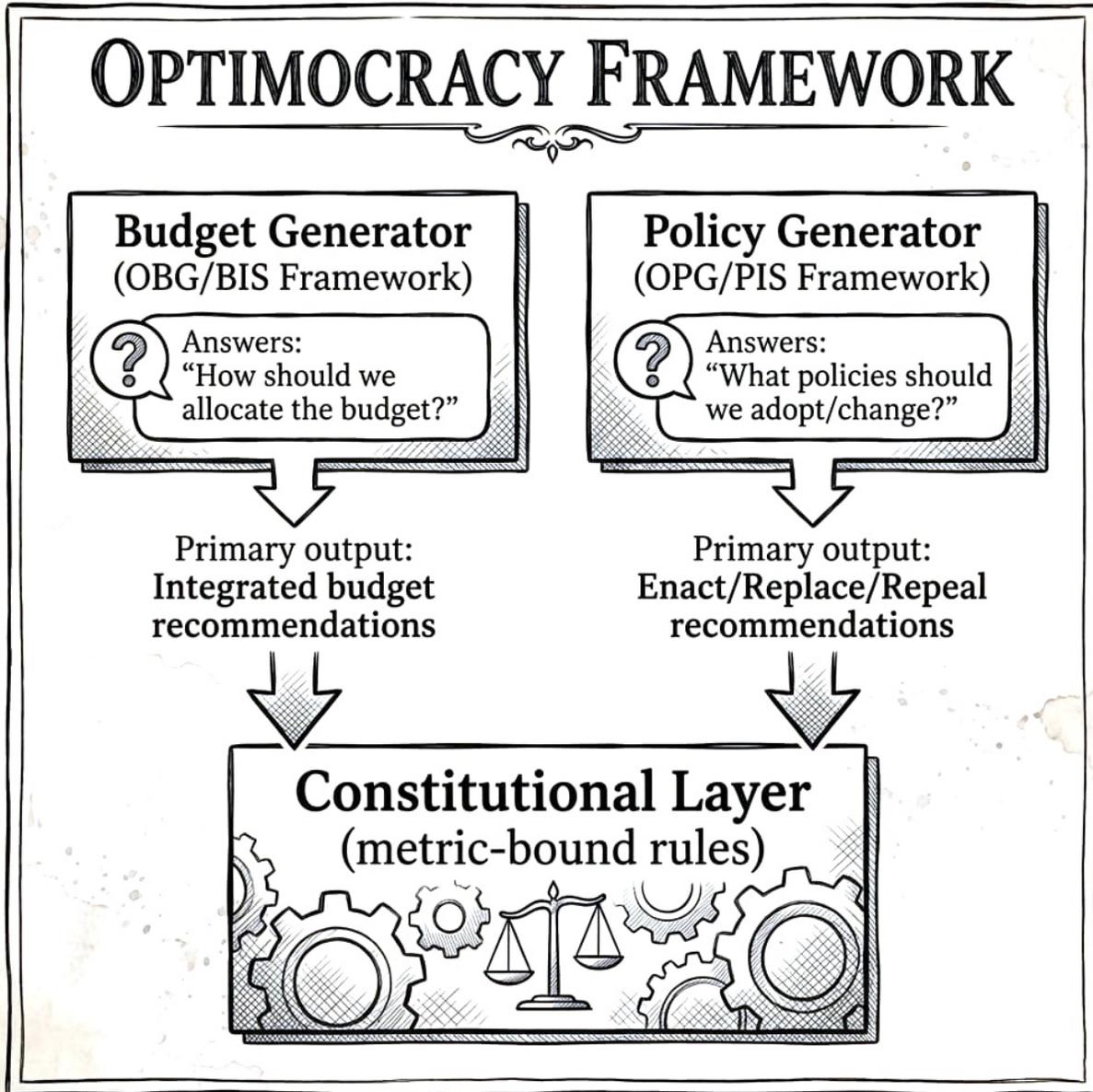


Figure 2: Architecture of the Optimocracy Framework showing the parallel inputs of budget (OBG) and policy (OPG) generators feeding into the Constitutional Layer.

The OPG framework (see [Optimal Policy Generator Specification](#)) answers: “Which policy reforms beyond budget allocation would most improve welfare?”

1.4 Implementation Mechanism

This specification focuses on generating evidence-based budget recommendations. Political implementation mechanisms are discussed separately in [Incentive Alignment Bonds](#).

2 Introduction

2.1 Why Budget Allocation Fails Today

Budget allocation is fundamentally a problem of social choice under uncertainty¹³². The challenge is not simply technical but institutional: current budget processes systematically diverge from welfare-optimal allocations due to political economy dynamics^{133,134}.

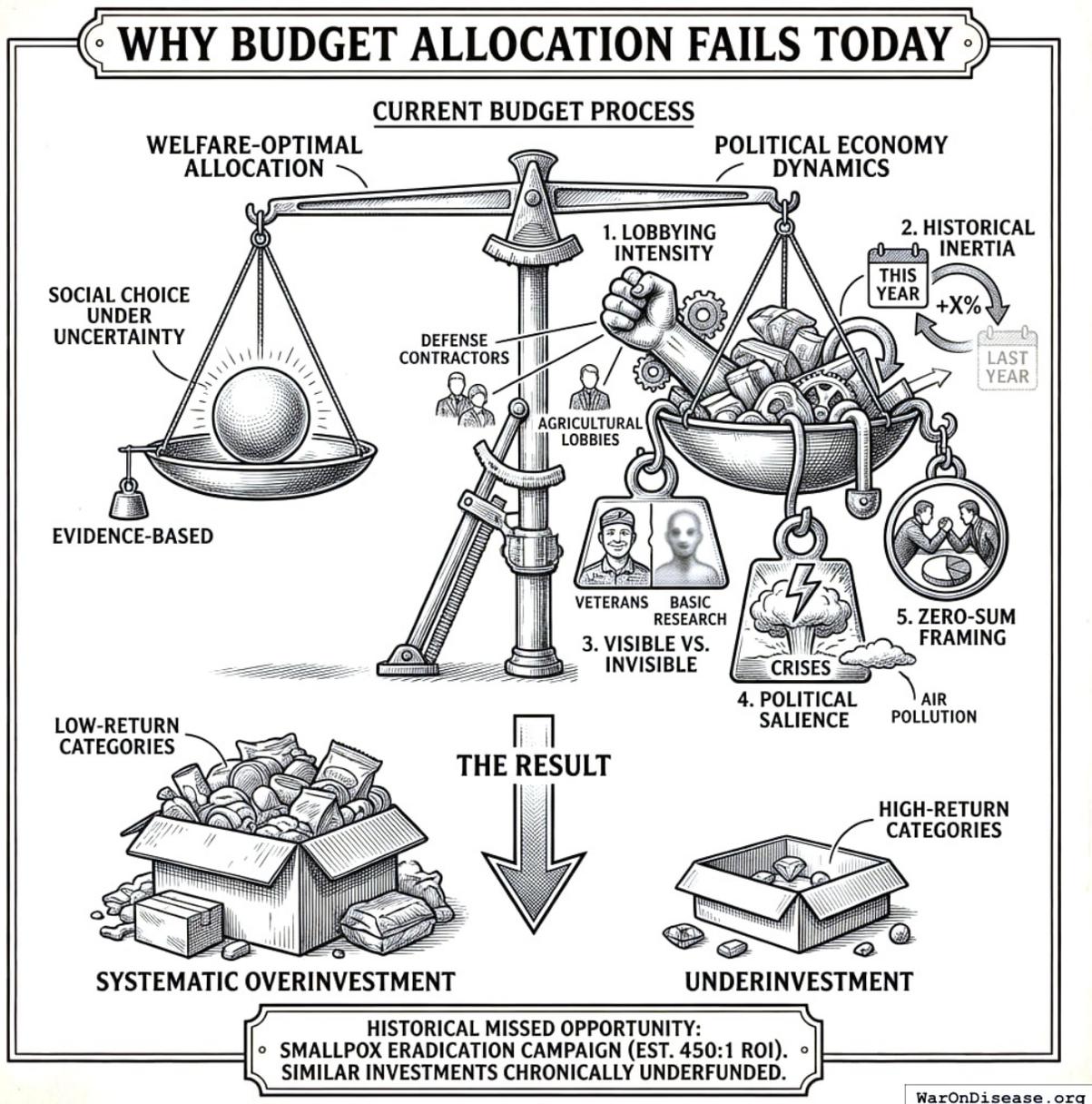


Figure 3: A comparison between the political drivers of current budget allocation (such as lobbying and historical inertia) and the resulting gap between low-return and high-return public investments.

Current budget allocation follows a process dominated by:

1. **Lobbying intensity:** Categories with organized beneficiaries (military contractors, agricultural lobbies) receive disproportionate funding regardless of evidence
2. **Historical inertia:** This year's budget is last year's budget plus a percentage, not a fresh optimization
3. **Visible vs. invisible beneficiaries:** Programs with identifiable beneficiaries (veterans) outcompete programs with diffuse beneficiaries (basic research)
4. **Political salience:** Crises drive spending regardless of cost-effectiveness (terrorism vs. air pollution)
5. **Zero-sum framing:** Budget debates treat all categories as competing rather than asking which ones are at optimal levels

The result: systematic overinvestment in low-return categories and underinvestment in high-return categories. Historical examples demonstrate the scale of missed opportunities: the smallpox eradication campaign returned an estimated 450:1 ROI⁸⁹, yet similar high-return public health investments remain chronically underfunded.

2.2 The RDA Analogy: Optimal Levels, Not Just Marginal Returns

Nutrition science doesn't just say "eat more vitamins." It specifies **Recommended Daily Allowances** - target intake levels where:

- **Below RDA:** Deficiency symptoms, reduced function
- **At RDA:** Optimal health benefits
- **Above RDA:** Diminishing returns, potential toxicity

Budget allocation should work the same way. For each spending category:

- **Below OSL:** Foregone welfare gains (underinvestment)
- **At OSL:** Optimal welfare return per dollar
- **Above OSL:** Diminishing or negative returns (overinvestment)

infinite spending on any category doesn't make sense, even one with high returns. Early childhood education has excellent returns - but spending \$10 trillion on it wouldn't produce 10x the benefits of spending \$1 trillion. There's an optimal level.

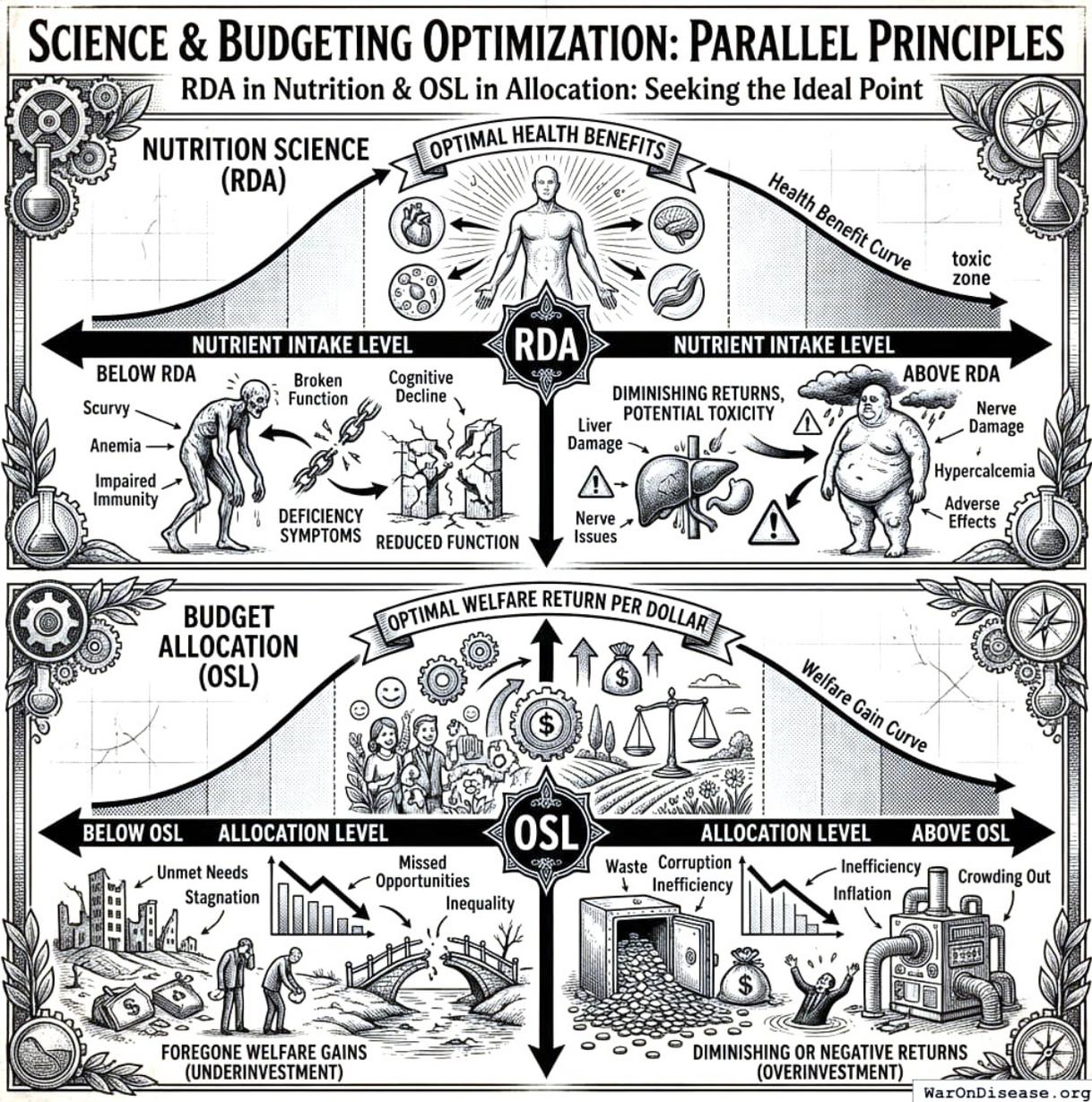


Figure 4: Conceptual comparison between Recommended Daily Allowances (RDA) in nutrition and Optimal Spending Levels (OSL) in public finance.

2.3 What This Framework Provides

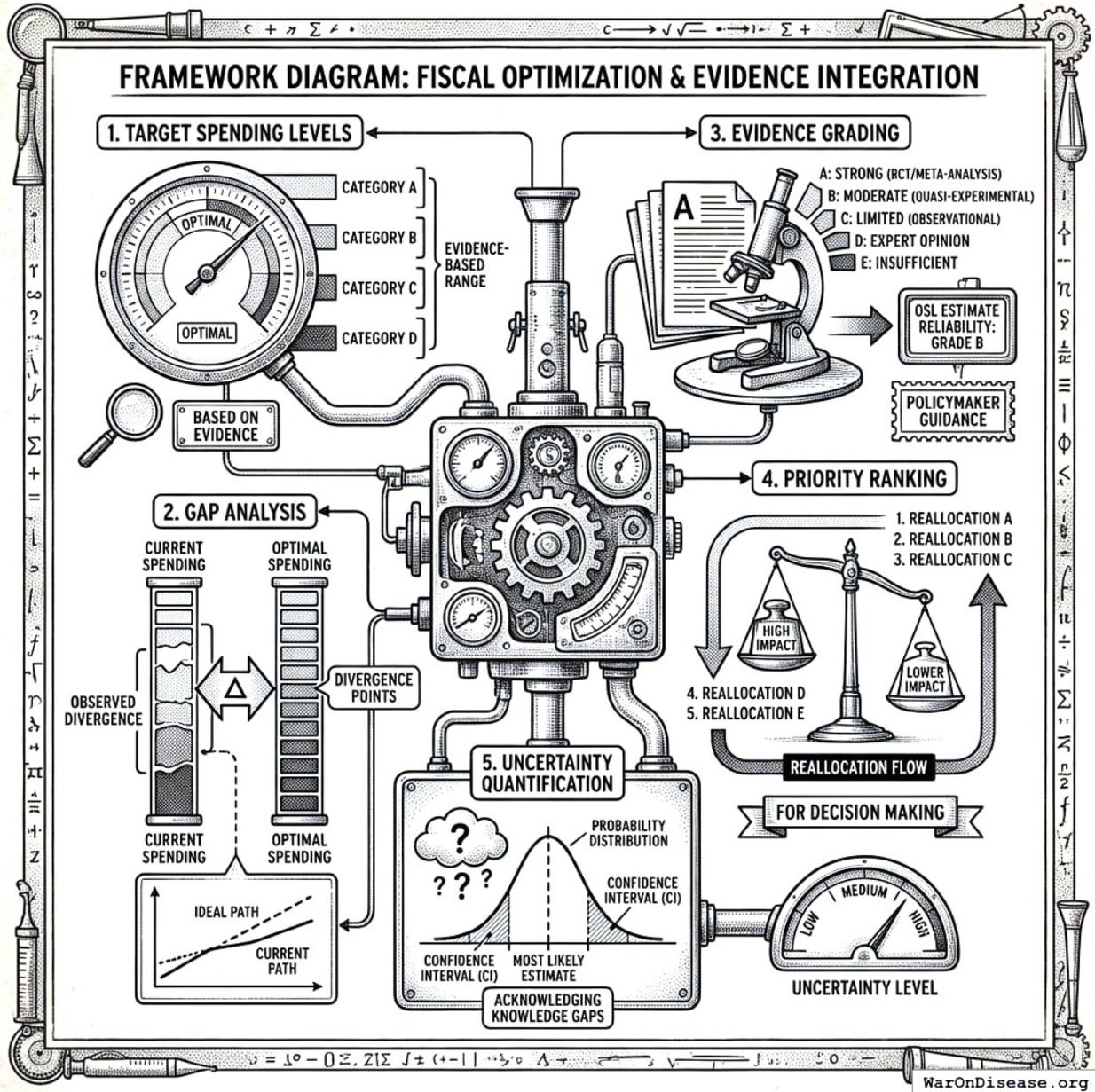


Figure 5: A conceptual diagram showing the five core components of the budget framework, illustrating how evidence-based targets and gap analysis inform priority ranking and uncertainty assessment.

1. **Target spending levels** for each budget category based on evidence
2. **Gap analysis** showing where current spending diverges from optimal
3. **Evidence grading** so policymakers know which OSL estimates are reliable
4. **Priority ranking** for reallocation decisions
5. **Uncertainty quantification** acknowledging what we don't know

2.4 Outcome Metrics: What We’re Optimizing

All OBG recommendations ultimately aim to maximize two welfare metrics:

1. **Real after-tax median income growth** (pp/year): Year-over-year percentage change in inflation-adjusted, post-tax median household income. Sources: Census Bureau, BLS.
2. **Median healthy life years** (years): Expected years of life in good health at the population median. Sources: WHO Global Health Observatory, national health surveys.

The welfare function combines these with equal weight by default:

$$W = 0.5 \cdot \text{IncomeGrowth} + 0.5 \cdot \text{HealthyYears}$$

Why these two metrics? Most policy effects eventually show up in one or both. Economic policies (taxes, regulations, trade) primarily affect income growth. Health policies (healthcare access, public health, safety) primarily affect healthy life years. Education and infrastructure affect both. See [Two-Metric Welfare Function](#) for the complete framework.

Every spending category’s OSL is ultimately justified by its expected impact on these two metrics. The gap analysis and priority rankings reflect which reallocations would most improve the combined welfare function.

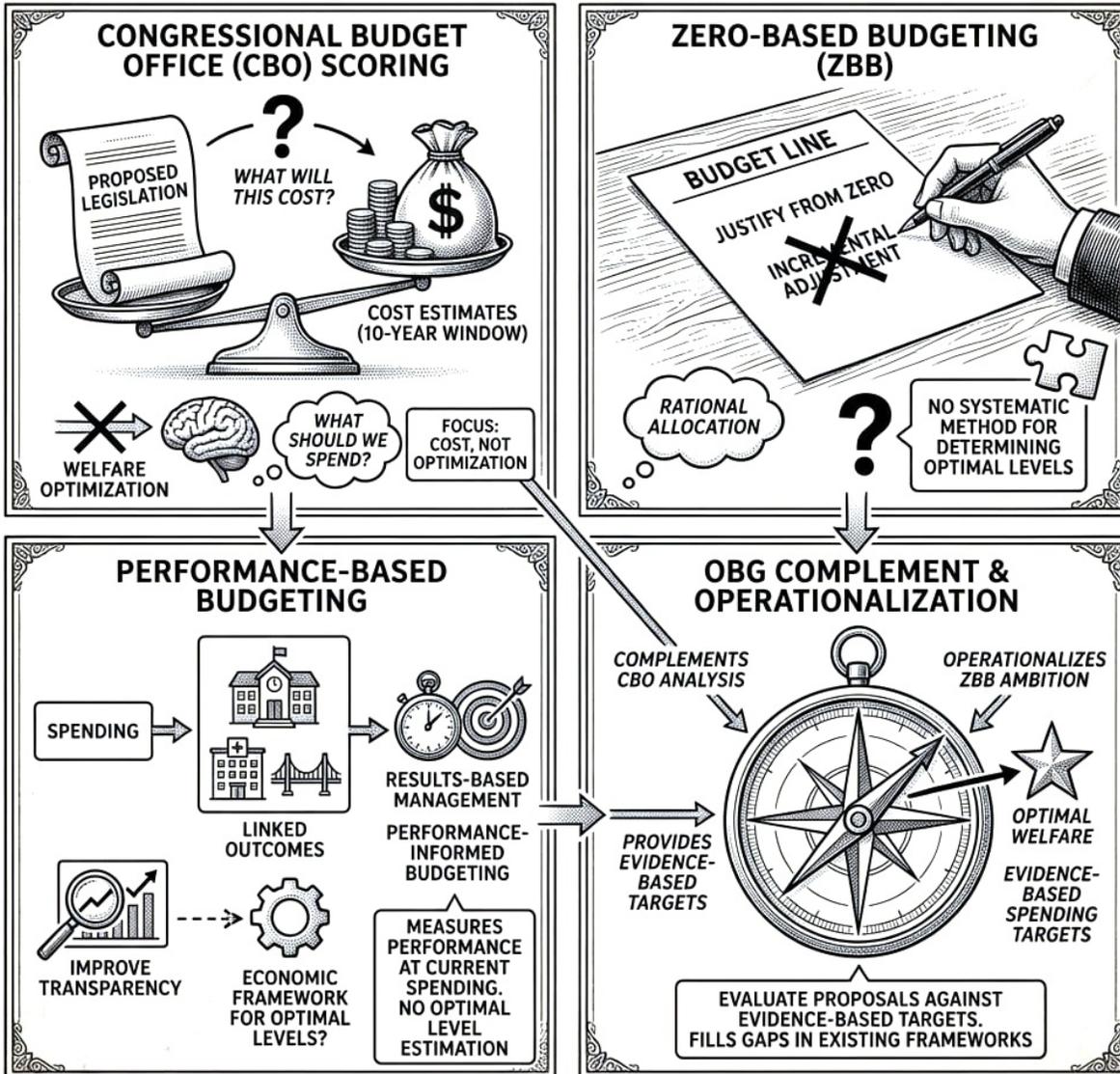
3 Related Work

The OBG framework builds on and extends several established traditions in public finance and evidence-based policy.

3.1 Budget Analysis Frameworks

Congressional Budget Office (CBO) Scoring. The CBO provides cost estimates for proposed legislation, projecting fiscal impacts over 10-year windows¹³⁵. However, CBO scoring focuses on *cost* rather than *welfare optimization* - it answers “what will this cost?” not “what should we spend?” OBG complements CBO analysis by providing evidence-based spending targets against which proposals can be evaluated.

BUDGET ANALYSIS FRAMEWORKS



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Figure 6: A comparison matrix of budget analysis frameworks showing the focus of CBO Scoring, Performance-Based Budgeting, and Zero-Based Budgeting relative to the evidence-based targets of the OBG framework.

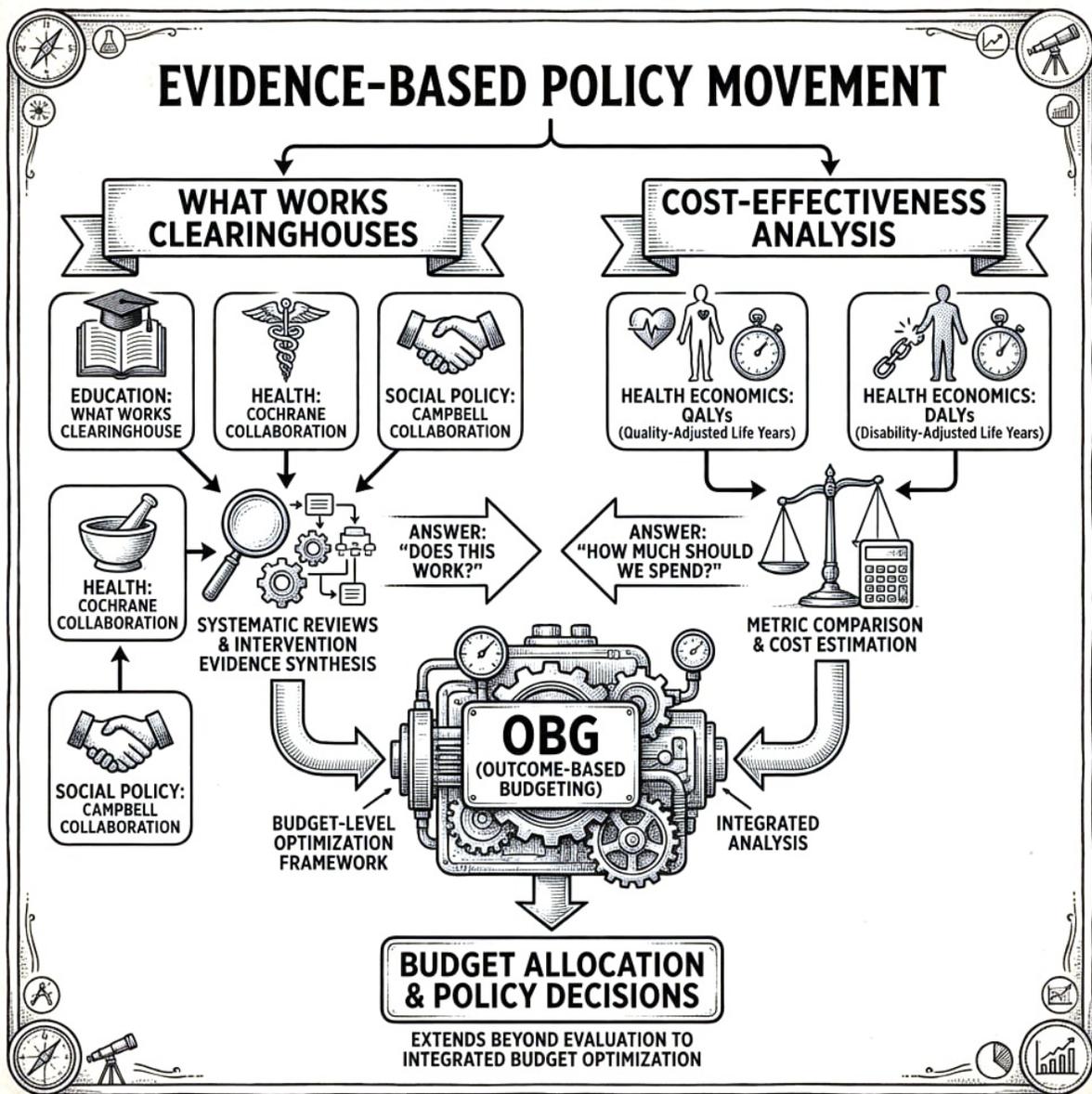
Performance-Based Budgeting. Since the Planning-Programming-Budgeting System (PPBS) of the 1960s, governments have attempted to link spending to outcomes. Modern variants include Results-Based Management and Performance-Informed Budgeting. These approaches improve transparency but typically lack the economic framework for determining *optimal* levels - they measure performance at current spending without estimating what spending *should* be.

Zero-Based Budgeting. ZBB requires justifying each budget line from zero rather than incremental adjustment. While philosophically aligned with OBG’s goal of rational allocation, ZBB provides

no systematic method for determining optimal levels. OBG operationalizes ZBB's ambition with evidence-based targets.

3.2 Evidence-Based Policy Movement

What Works Clearinghouses. Organizations like the What Works Clearinghouse (education), Cochrane Collaboration (health), and Campbell Collaboration (social policy) synthesize intervention evidence through systematic reviews. OBG draws on these evidence bases but extends beyond intervention evaluation to budget-level optimization. While clearinghouses answer “does this work?”, OBG answers “how much should we spend?”



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Figure 7: A comparison showing how Outcome-Based Governance (OBG) builds upon traditional evidence synthesis and cost-effectiveness analysis by shifting from intervention evaluation to budget-level optimization.

Cost-Effectiveness Analysis. Health economics has developed methods for comparing interventions using metrics like QALYs (Quality-Adjusted Life Years) and DALYs (Disability-Adjusted Life Years)¹³⁶. OBG incorporates cost-effectiveness as one of two estimation methods but applies it within an integrated budget optimization framework rather than intervention-by-intervention.

3.3 Comparative Public Finance

OECD Government Spending Analysis. The OECD publishes extensive cross-country spending comparisons and outcome data^{95,112}. OBG leverages this data infrastructure for diminishing returns analysis while adding the conceptual framework of optimal levels and evidence-weighted confidence.

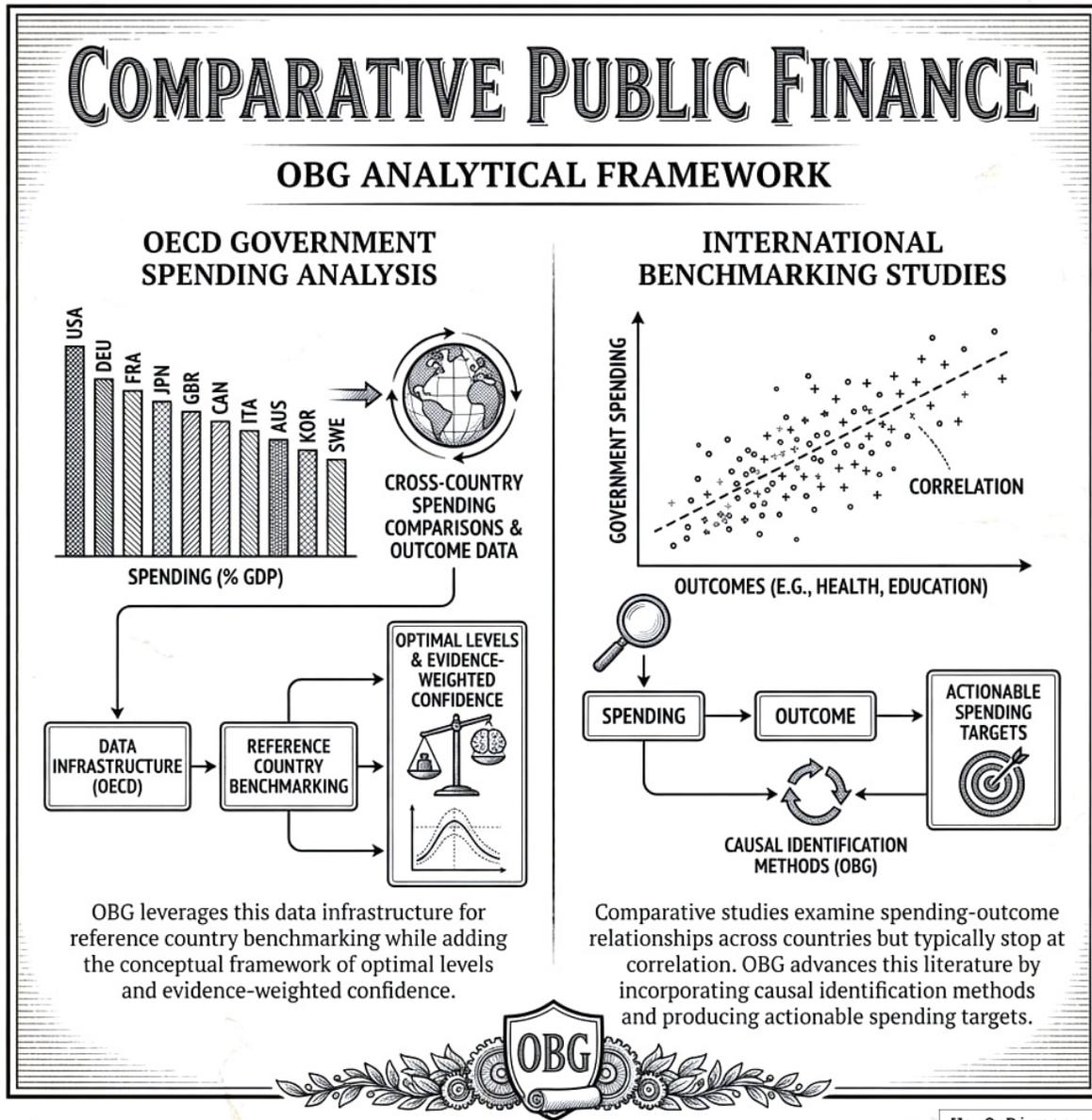


Figure 8: A conceptual model showing the methodological progression from standard OECD benchmarking to OBG’s causal identification framework and actionable spending targets.

International Benchmarking Studies. Comparative studies examine spending-outcome relationships across countries but typically stop at correlation. OBG advances this literature by incorporating causal identification methods and producing actionable spending targets.

3.4 How OBG Differs

The OBG framework advances existing approaches in three key ways:

1. **Integrated multi-method estimation.** Rather than relying on a single approach, OBG combines OSL estimates from diminishing returns modeling and cost-effectiveness analysis. This provides robustness and identifies where methods agree or conflict.

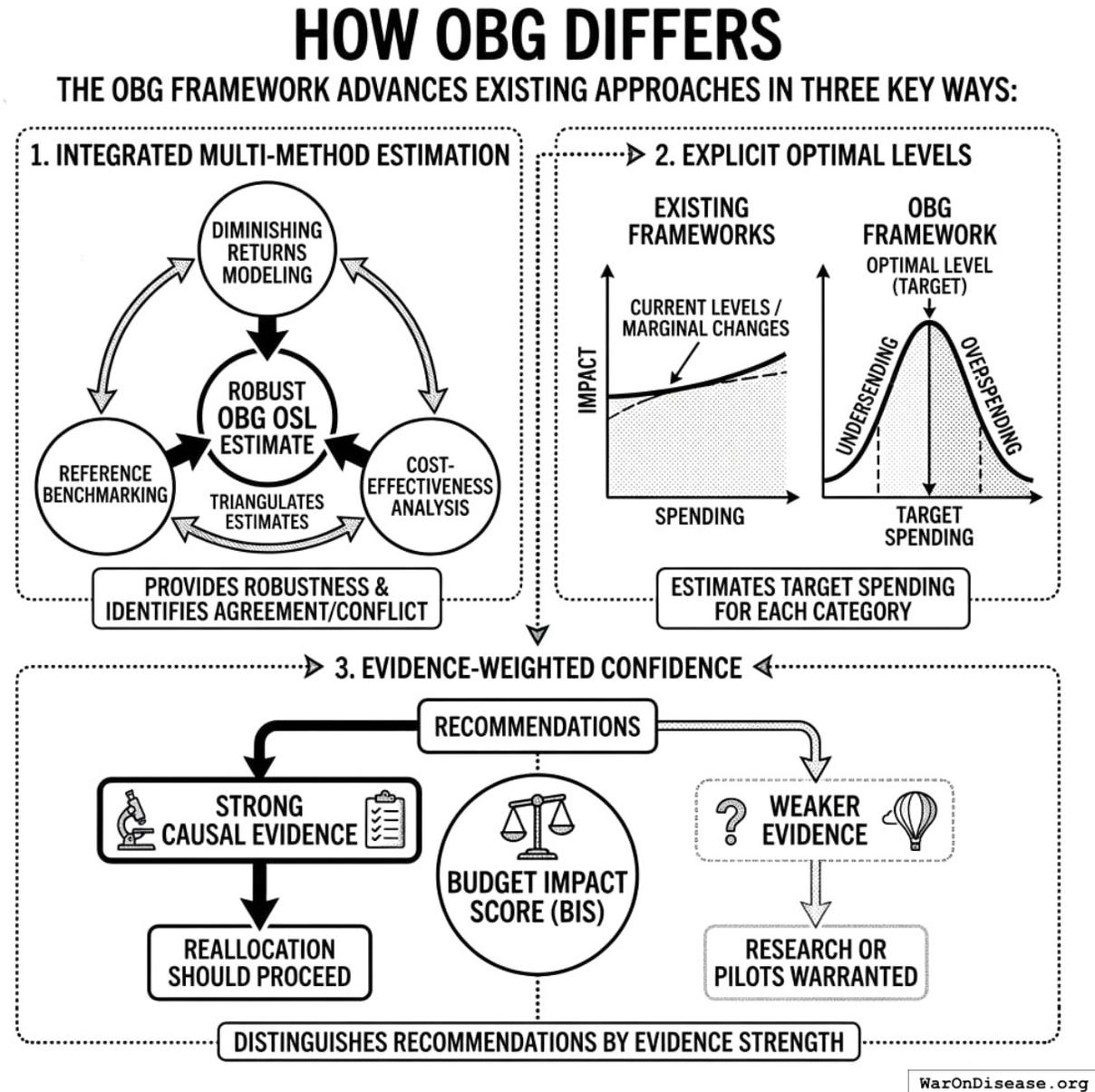


Figure 9: A conceptual overview of the OBG framework illustrating the triangulation of estimation methods, the identification of optimal spending targets, and the categorization of recommendations based on evidence strength via the Budget Impact Score.

2. **Explicit optimal levels.** Unlike frameworks that analyze spending at current levels or propose marginal changes, OBG estimates target spending levels for each category - acknowledging

that both underspending and overspending are suboptimal.

3. **Evidence-weighted confidence.** The Budget Impact Score (BIS) distinguishes recommendations supported by strong causal evidence (where reallocation should proceed) from those based on weaker evidence (where research or pilots are warranted).

4 Theoretical Framework

This section formalizes the OBG framework as a social planner's optimization problem, establishing the theoretical foundations for optimal spending levels and evidence-weighted allocation.

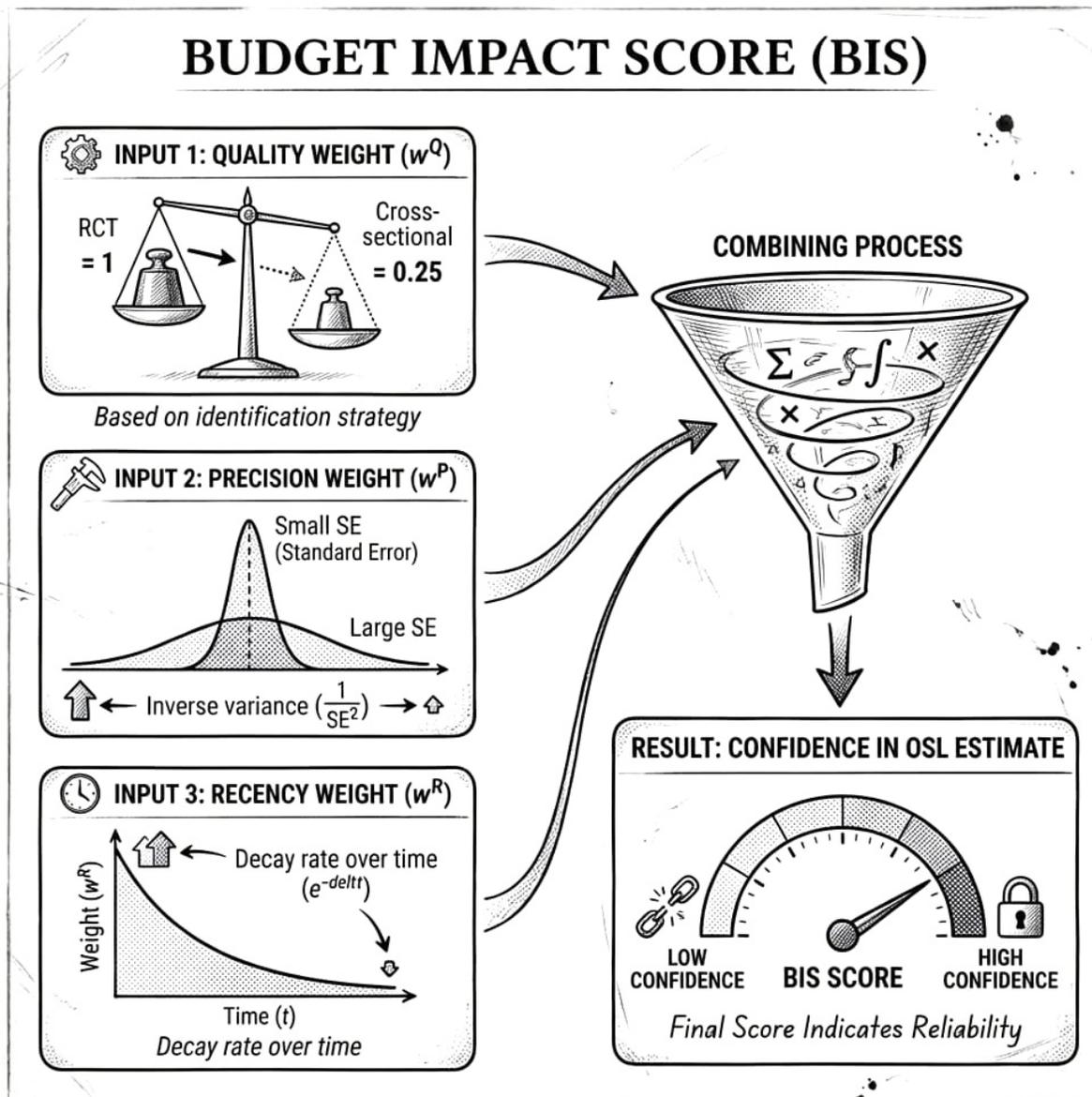


Figure 10: A conceptual diagram illustrating the social planner's optimization process, showing how evidence-weighted inputs lead to optimal spending levels and resource allocation within the OBG framework.

4.1 The Social Planner's Problem

Consider a benevolent social planner allocating a fixed budget B across n spending categories. Each category generates welfare measured using the [two-metric framework](#): **real after-tax median income growth** and **median healthy life years**.

Why these specific metrics? They are universal instrumental goods: virtually everyone wants higher purchasing power and longer healthy life, regardless of other values. They are hard to game (improving them requires actually helping typical citizens), measured by independent statistical

agencies, and capture most policy effects. GDP can rise while median income stagnates; this framework correctly identifies such outcomes as low-welfare.

Let s_i denote spending on category i , with $\sum_{i=1}^n s_i = B$. Each category produces effects on both welfare metrics:

- $\beta_i^{inc}(s_i)$: Effect on real after-tax median income growth (pp/year)
- $\beta_i^{hlth}(s_i)$: Effect on median healthy life years (years)

Total welfare from category i follows the two-metric welfare function:

$$W_i(s_i) = \alpha \cdot \beta_i^{inc}(s_i) + (1 - \alpha) \cdot \beta_i^{hlth}(s_i)$$

where $\alpha = 0.5$ by default (equal weight to economic and health welfare). All welfare calculations in this framework flow through these two metrics.

Assumption 1 (Diminishing Returns). For each category i , both effect functions β_i^{inc} and β_i^{hlth} are twice continuously differentiable with positive first derivatives and negative second derivatives for all $s > 0$.

The social planner maximizes aggregate welfare:

$$\max_{\{s_i\}_{i=1}^n} \sum_{i=1}^n W_i(s_i) \quad \text{subject to} \quad \sum_{i=1}^n s_i = B, \quad s_i \geq 0 \quad \forall i$$

Proposition 1 (Equimarginal Principle). *At the optimal allocation $\{s_i^*\}$, marginal welfare is equalized across all categories with positive spending:*

$$W'_i(s_i^*) = \lambda^* \quad \forall i \text{ with } s_i^* > 0$$

where λ^* is the shadow price of the budget constraint.

Proof. The Lagrangian is $\mathcal{L} = \sum_i W_i(s_i) - \lambda(\sum_i s_i - B)$. First-order conditions yield $W'_i(s_i^*) = \lambda$ for interior solutions. By strict concavity of W_i , the second-order conditions are satisfied. \square

4.2 Optimal Spending Levels Under Uncertainty

In practice, the welfare functions $W_i(\cdot)$ are not known with certainty. Let $\hat{W}_i(s)$ denote the planner's estimate of welfare, with associated uncertainty $\sigma_i^2(s)$.

Definition 1 (Optimal Spending Level). The Optimal Spending Level for category i is:

$$\text{OSL}_i \equiv \arg \max_{s_i} \mathbb{E}[\hat{W}_i(s_i)] - \frac{\rho}{2} \text{Var}[\hat{W}_i(s_i)]$$

where $\rho \geq 0$ is the planner's risk aversion parameter.

For risk-neutral planners ($\rho = 0$), OSL reduces to the spending level that maximizes expected welfare. For risk-averse planners, OSL accounts for estimation uncertainty.

Proposition 2 (OSL Characterization). *Under Assumption 1, with estimated marginal welfare $\hat{W}'_i(s)$ and estimation variance $\sigma_i^2(s)$, the OSL satisfies:*

$$\mathbb{E}[\widehat{W}'_i(\text{OSL}_i)] = r + \rho \cdot \left. \frac{\partial \sigma_i^2}{\partial s} \right|_{s=\text{OSL}_i}$$

where r is the social discount rate (opportunity cost of public funds).

Proof. The first-order condition for the uncertainty-adjusted maximization problem yields the result. The term r represents the marginal value of funds in alternative uses; the second term adjusts for risk. \square

4.3 Budget Impact Score as Precision Weighting

The Budget Impact Score formalizes the precision of OSL estimates, enabling evidence-weighted reallocation decisions.

Definition 2 (Budget Impact Score). For category i with n_i effect estimates $\{\widehat{\beta}_{ij}\}_{j=1}^{n_i}$, the Budget Impact Score is:

$$\text{BIS}_i = \min \left(1, \frac{1}{K} \sum_{j=1}^{n_i} w_j^Q \cdot w_j^P \cdot w_j^R \right)$$

where:

- $w_j^Q \in (0, 1]$ = quality weight based on identification strategy (RCT = 1, cross-sectional = 0.25)
- $w_j^P = 1/\text{SE}(\widehat{\beta}_j)^2$ = precision weight (inverse variance)
- $w_j^R = e^{-\delta(t_{\text{now}} - t_j)}$ = recency weight with decay rate δ
- K = calibration constant

Proposition 3 (BIS as Inverse Variance). Under standard meta-analytic assumptions, BIS is proportional to the precision of the pooled effect estimate:

$$\text{BIS}_i \propto \frac{1}{\text{Var}(\widehat{\beta}_i^{\text{pooled}})}$$

where $\widehat{\beta}_i^{\text{pooled}}$ is the quality-weighted pooled estimate of spending effects.

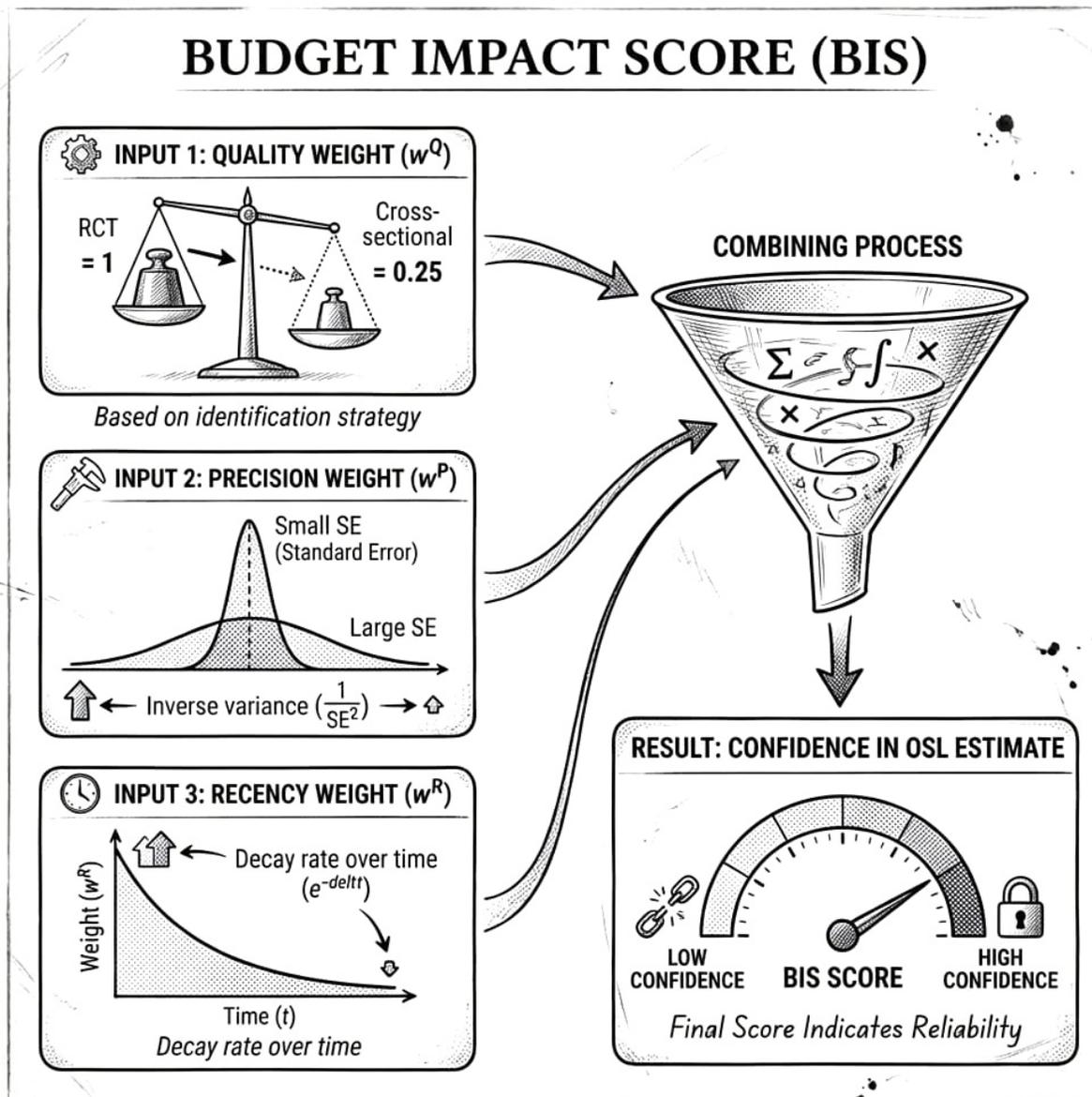


Figure 11: Breakdown of the Budget Impact Score (BIS) components, showing how quality, precision, and recency weights combine to quantify confidence.

4.4 Gap Analysis and Welfare Gains

Definition 3 (Spending Gap). The spending gap for category i is:

$$\text{Gap}_i = \text{OSL}_i - s_i^{\text{current}}$$

Proposition 4 (Welfare Gains from Gap Closure). For small gaps, the welfare gain from moving spending from current level to OSL is approximately:

$$\Delta W_i \approx W'_i(s_i^{current}) \cdot \text{Gap}_i - \frac{1}{2} |W''_i(\bar{s})| \cdot \text{Gap}_i^2$$

where \bar{s} is between $s_i^{current}$ and OSL_i .

Proof. Taylor expansion of $W_i(OSL_i) - W_i(s_i^{current})$ around $s_i^{current}$. \square

Corollary 1 (Priority Ranking). *Categories should be prioritized for reallocation in order of:*

$$\text{Priority}_i = |\text{Gap}_i| \times \text{BIS}_i \times |W'_i(s_i^{current})|$$

This ranks categories by expected welfare gain adjusted for estimation confidence.

Note: In the simplified implementation (Section 10.2), we normalize by setting $|W'_i(s_i^{current})| = 1$ for all categories, reducing the priority formula to $\text{Priority}_i = |\text{Gap}_i| \times \text{BIS}_i$. This assumes equal marginal welfare weights across categories as a first approximation. Future iterations could incorporate category-specific marginal welfare estimates.

4.5 Welfare Bounds Under Model Uncertainty

When the functional form of $W_i(\cdot)$ is uncertain, we can establish bounds on welfare gains.

Proposition 5 (Welfare Bounds). *Let \underline{W}_i and \overline{W}_i denote lower and upper bounds on the welfare function consistent with available evidence. Then:*

$$\underline{\Delta W} = \sum_{i:\text{Gap}_i>0} \underline{W}'_i(s_i) \cdot \text{Gap}_i \leq \Delta W \leq \sum_{i:\text{Gap}_i>0} \overline{W}'_i(s_i) \cdot \text{Gap}_i = \overline{\Delta W}$$

The OBG framework reports both point estimates and these bounds via sensitivity analysis.

4.6 Summary of Theoretical Results

Result	Implication for OBG
Proposition 1	Optimal allocation equalizes marginal returns
Proposition 2	OSL accounts for both expected returns and uncertainty
Proposition 3	BIS captures estimation precision
Proposition 4	Gap closure yields quantifiable welfare gains
Corollary 1	Priority ranking optimizes reallocation sequence
Proposition 5	Welfare bounds enable robust recommendations

5 Core Methodology

5.1 Spending Category Data Structure

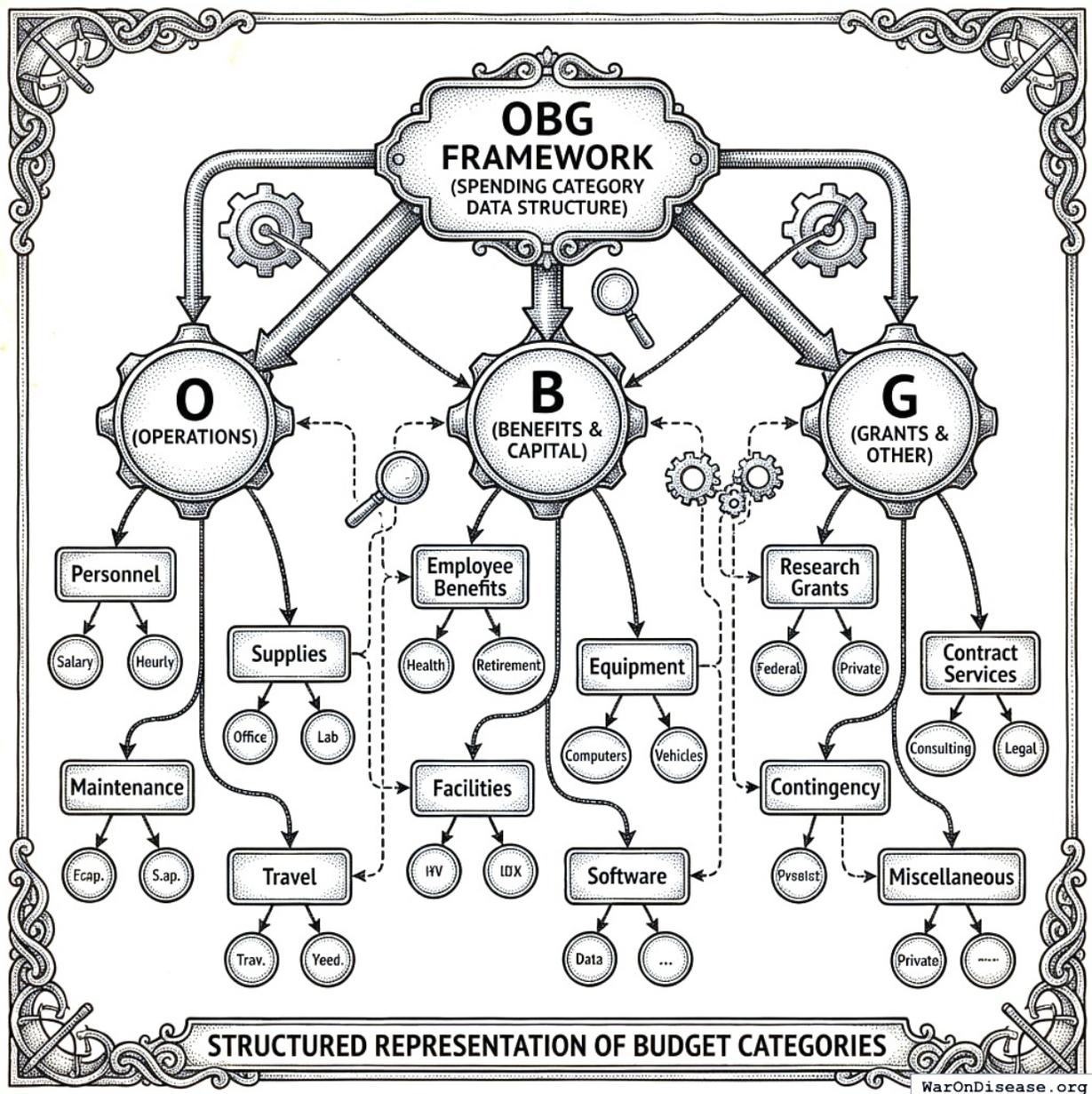


Figure 12: An entity-relationship diagram illustrating the data structure of the OBG framework, connecting spending categories to reference data, optimal estimates, and gap analysis.

The OBG framework uses a structured representation of budget categories:

```
-- Spending categories
spending_categories (
  id, name, parent_category_id,
  spending_type, -- 'program', 'transfer', 'investment', 'regulatory'
```

```

outcome_categories, -- which welfare outcomes this affects
current_spending_usd, fiscal_year,
data_source, last_updated
)

-- Cross-country spending data
reference_spending (
category_id, country_code, year,
spending_usd, spending_per_capita,
spending_pct_gdp, population, gdp,
data_source
)

-- Optimal spending level estimates
osl_estimates (
category_id, estimation_method,
osl_usd, osl_per_capita, osl_pct_gdp,
confidence_interval_low, confidence_interval_high,
evidence_grade, bis_score,
methodology_notes, last_updated
)

-- Gap analysis
spending_gaps (
category_id, current_spending_usd,
osl_usd, gap_usd, gap_pct,
priority_score, -- gap * BIS confidence
recommended_action
)

```

5.2 Two Methods for OSL Estimation

Method	Use Case	Data Required	Strengths	Limitations
Diminish- ing returns modeling	Categories with cross-country spending-outcome data	Effect estimates at multiple spending levels	Theoretically grounded, finds optimal “knee”	Requires sufficient country variation
Cost- effectiveness threshold	Health/life-saving interventions	Cost per QALY/DALY, willingness-to-pay	Links to standard health economics ²⁴	Limited to monetizable outcomes

Each method is detailed below.

6 Diminishing Returns Modeling

6.1 The Core Concept

The fiscal multiplier literature establishes that spending effects vary systematically with scale^{137,138}. At low spending levels, each additional dollar produces substantial welfare gains. At high spending levels, marginal returns diminish. The OSL is where marginal return equals opportunity cost.

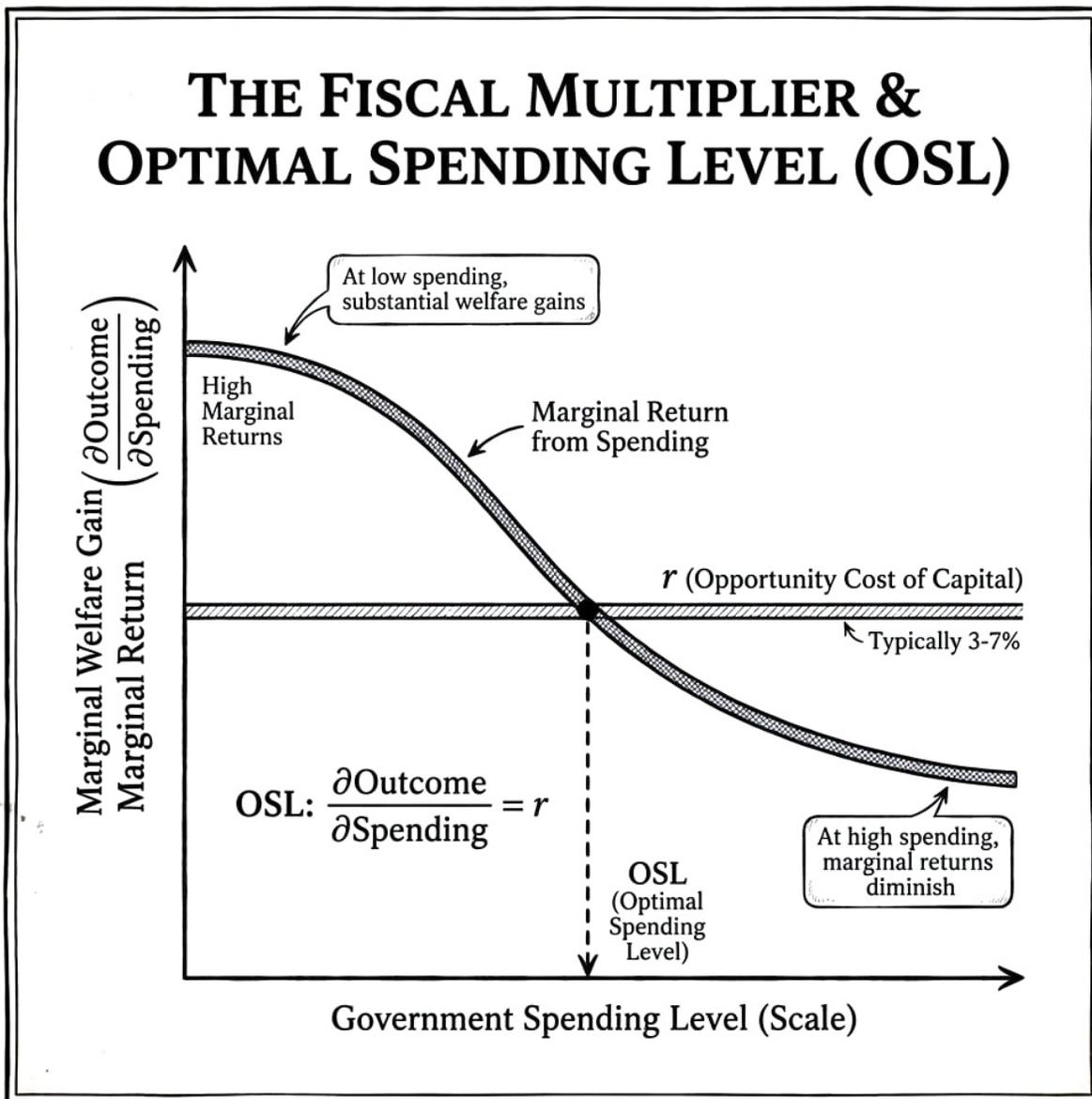


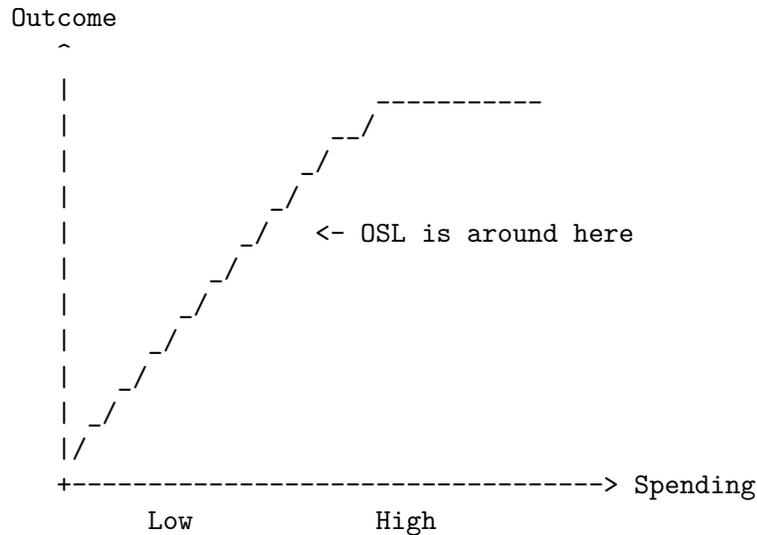
Figure 13: A graph showing a downward-sloping marginal return curve intersecting with a horizontal line representing the opportunity cost (r) to identify the Optimal Spending Level (OSL).

$$\text{OSL} : \frac{\partial \text{Outcome}}{\partial \text{Spending}} = r$$

Where r is the discount rate or opportunity cost of capital (typically 3-7%).

6.2 Finding the “Knee” of the Curve

Empirically, we look for the point where the outcome-spending relationship flattens:



6.3 Estimation Methods

1. Nonlinear regression on cross-country data

Fit diminishing returns functions:

$$\text{Outcome} = \alpha + \beta \cdot \log(\text{Spending}) + \epsilon$$

Or with saturation:

$$\text{Outcome} = \alpha + \beta \cdot \frac{\text{Spending}}{\text{Spending} + \gamma}$$

Where γ is the half-saturation constant.

2. Piecewise linear estimation

Estimate separate slopes for different spending ranges to identify where returns diminish.

3. Meta-regression of effect estimates

If multiple studies estimate effects at different spending levels, meta-regression can identify how effects vary with baseline spending. The credibility of such estimates depends critically on identification strategy¹³⁹.

6.4 Worked Example: K-12 Education Spending

Primary metric affected: Real after-tax median income growth (via higher wages from improved skills).

¹⁴⁰ exploited court-ordered school finance reforms to estimate causal effects of K-12 spending. Key finding: a 10% increase in per-pupil spending increases adult earnings by 7% for students from low-income families.

Does this effect diminish at higher spending levels?

Evidence from cross-state variation suggests:

Baseline spending (per pupil)	Effect of 10% increase	Implied marginal return
\$8,000	+8% earnings	\$0.80 per \$1
\$12,000	+5% earnings	\$0.50 per \$1
\$16,000	+3% earnings	\$0.30 per \$1
\$20,000	+1% earnings	\$0.10 per \$1

OBG estimation: At \$16,000/pupil, the marginal return (~0.30) roughly equals the social discount rate. This suggests:

- Current US average: ~\$15,000/pupil
- OSL: ~\$16,000-\$18,000/pupil (modest underinvestment)
- Gap: ~\$50B nationally

Evidence grade: B (strong causal identification, moderate extrapolation uncertainty)

7 Worked Example: Pragmatic Clinical Trials

7.1 The Highest-Return Public Investment

Metrics affected: Both real after-tax median income growth (via reduced healthcare costs and improved productivity) and median healthy life years (via better treatments). This dual impact contributes to the exceptionally high returns.

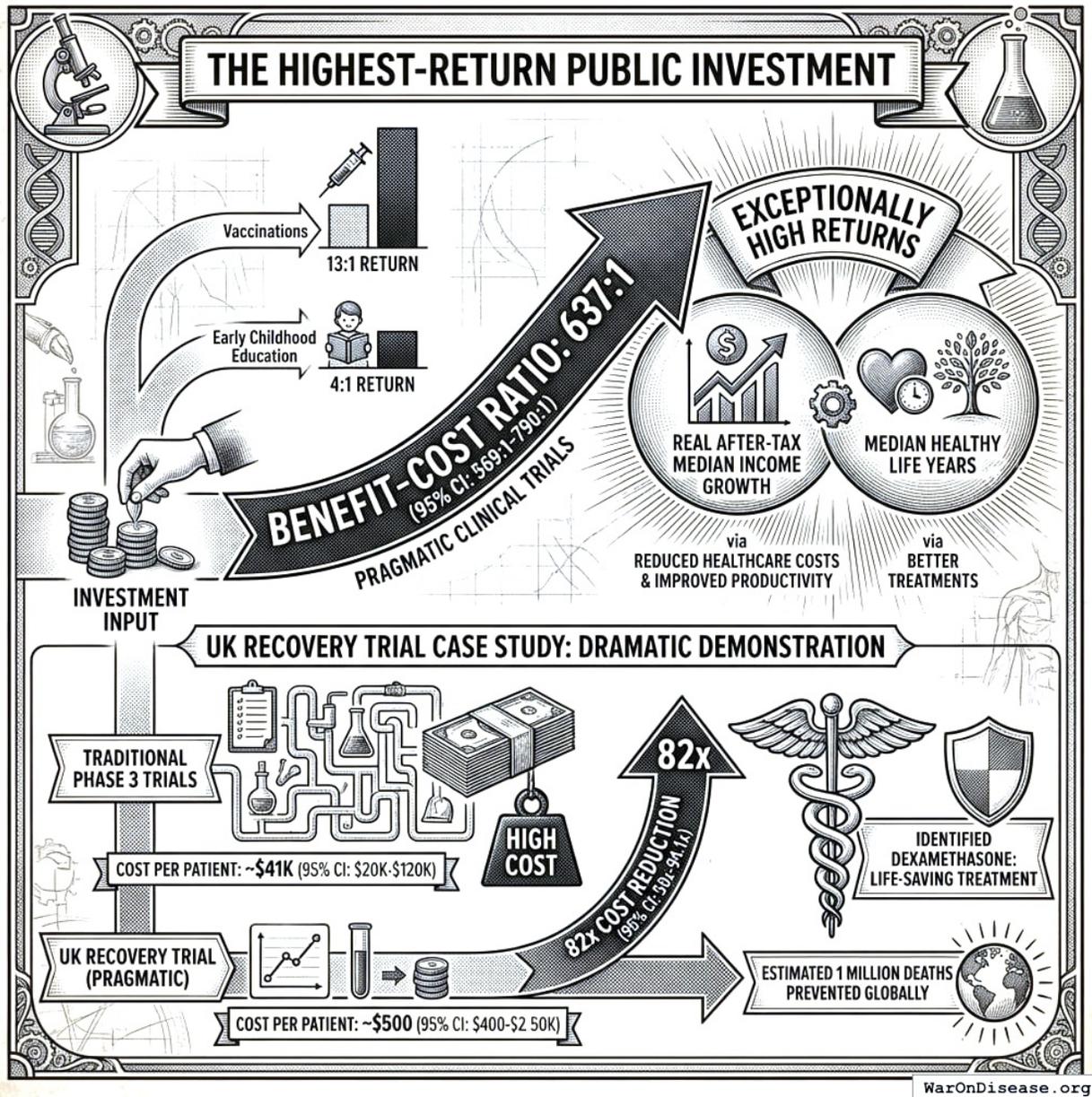


Figure 14: A comparison of return on investment across different public sectors and a cost-efficiency breakdown between pragmatic and traditional clinical trials.

Pragmatic clinical trials represent perhaps the single highest-return category of public investment identified in the literature. While vaccinations return 13:1 and early childhood education returns 4:1, pragmatic trials demonstrate benefit-cost ratios of **637:1 (95% CI: 569:1-790:1)**¹⁴¹.

The UK's RECOVERY trial demonstrated this dramatically during COVID-19: it cost approximately \$500 (95% CI: \$400-\$2.50K) versus \$41K (95% CI: \$20K-\$120K) for traditional Phase 3 trials, a **82x (95% CI: 50x-94.1x)** cost reduction¹⁴². This single trial identified dexamethasone as a life-saving treatment, preventing an estimated 1 million deaths globally.

7.2 OSL Estimation

Pragmatic trials represent an *innovation frontier* where no country has achieved optimal investment. We estimate OSL from cost-effectiveness analysis:

1. **Unmet medical need:** Approximately 2.88 billion DALYs/year (95% CI: 2.63 billion DALYs/year-3.13 billion DALYs/year) DALYs annually from conditions lacking adequate treatment
2. **Cost per DALY averted:** Pragmatic trials cost \$929 (95% CI: \$929-\$1.40K) (ADAPTABLE trial) vs. \$41K (95% CI: \$20K-\$120K) traditional
3. **Scale-up potential:** Current global clinical trial spending is approximately \$60B (95% CI: \$50B-\$75B)/year, but only ~\$500M goes to pragmatic/embedded designs

Data Point	Value	Source
Current pragmatic trial spending (US)	~\$500M	NIH Common Fund
Traditional trial spending (global)	\$60B (95% CI: \$50B-\$75B)	Industry + NIH
Cost per patient (pragmatic)	\$929 (95% CI: \$929-\$1.40K)	ADAPTABLE trial
Cost per patient (traditional Phase 3)	\$41K (95% CI: \$20K-\$120K)	Industry average
Cost reduction factor	44.1x (95% CI: 39.4x-89.1x)	Calculated

7.3 Diminishing Returns Analysis

Unlike most spending categories, pragmatic trials show **increasing returns at current spending levels** due to:

1. **Network effects:** Each additional participant improves statistical power for all trials
2. **Infrastructure leverage:** Platform trials amortize fixed costs across multiple interventions
3. **Learning effects:** Evidence accumulation improves trial design efficiency

The “knee” of the diminishing returns curve is estimated at **\$50-100B annually** (vs. current ~\$500M), suggesting we are operating far below optimal.

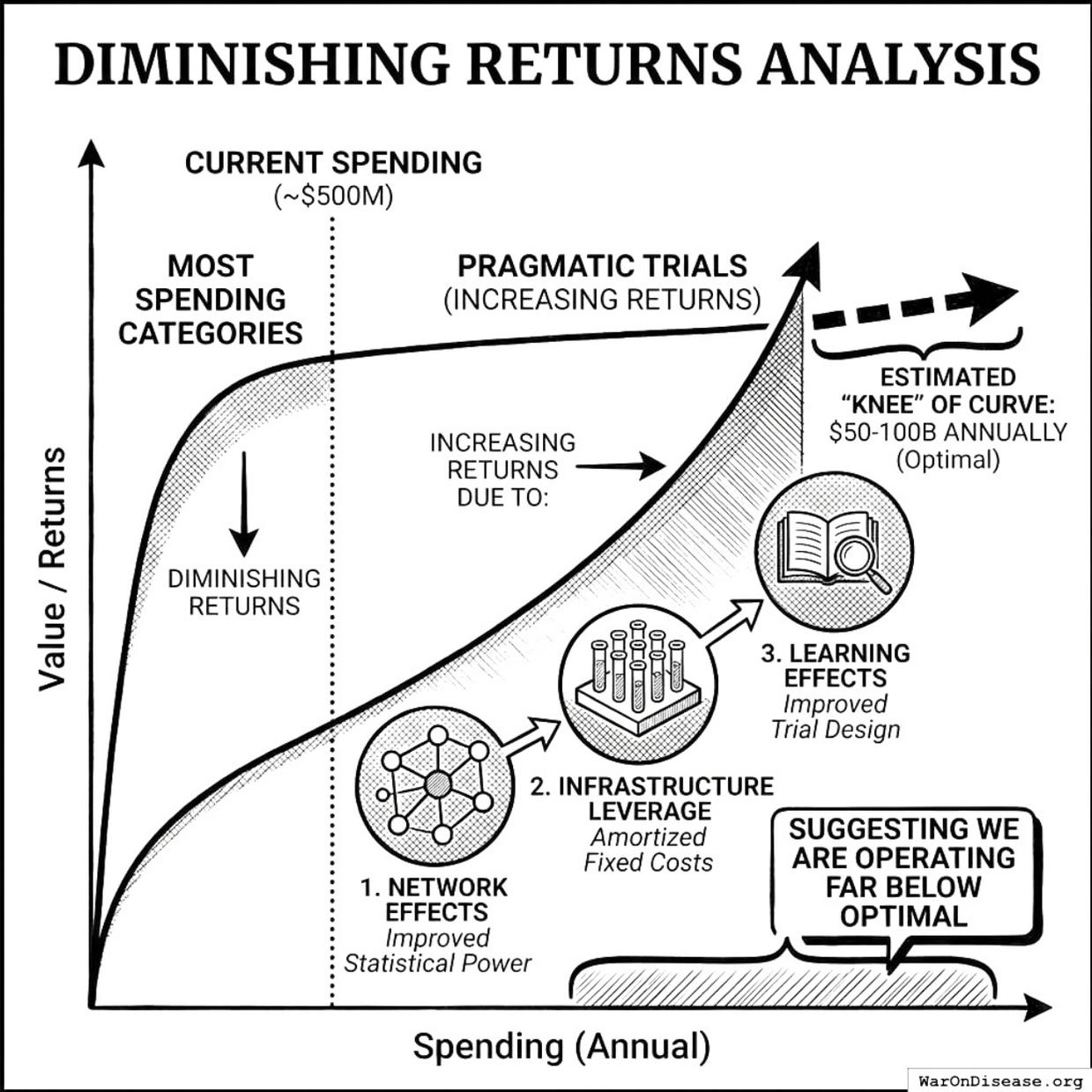


Figure 15: A conceptual line graph showing returns versus spending for pragmatic trials, highlighting the ‘knee’ of the curve at 50-100B and the current position at 500M within the increasing returns phase.

7.4 Cost-Effectiveness Calculation

Using standard health economics methodology:

Component	Value	Calculation
Cost per pragmatic trial participant	\$929 (95% CI: \$929-\$1.40K)	ADAPTABLE benchmark
QALYs gained per participant	0.05-0.2	Evidence generation value

Component	Value	Calculation
Cost per QALY	\$4,600-\$18,600	Well below \$50K threshold
Scale-up population	50M patients/year	10% of treatable conditions
OSL estimate	\$50B/year	Conservative

7.5 Gap Analysis

Metric	Value
Current spending (pragmatic trials)	~\$500M
OSL	\$50B
Gap	+\$49.5B (99x underinvestment)
Gap % of current	+9,900%
Opportunity cost	637:1 (95% CI: 569:1-790:1) foregone returns

Evidence grade: A (RCT evidence from RECOVERY, ADAPTABLE; strong theoretical foundation)

7.6 Why This Category Dominates

Pragmatic clinical trials have the highest priority score of any category analyzed:

$$\text{Priority} = |\text{Gap}| \times \text{BIS} = \$49.5B \times 0.90 = 44.6$$

Among categories requiring increased investment, this is the highest priority score, exceeding basic research (31.5), vaccinations (25.7), and early childhood (17.0). Military spending has a larger absolute priority score (195.5) due to its massive gap, but represents overinvestment requiring reduction.

8 Cost-Effectiveness Threshold Analysis

8.1 The Standard Health Economics Approach

Cost-effectiveness analysis has become the standard framework for health resource allocation decisions¹³⁶. The QALY (Quality-Adjusted Life Year) metric enables comparison across diverse health interventions by monetizing health outcomes at a consistent threshold¹⁴³.

For health interventions, cost-effectiveness analysis provides OSL estimates:

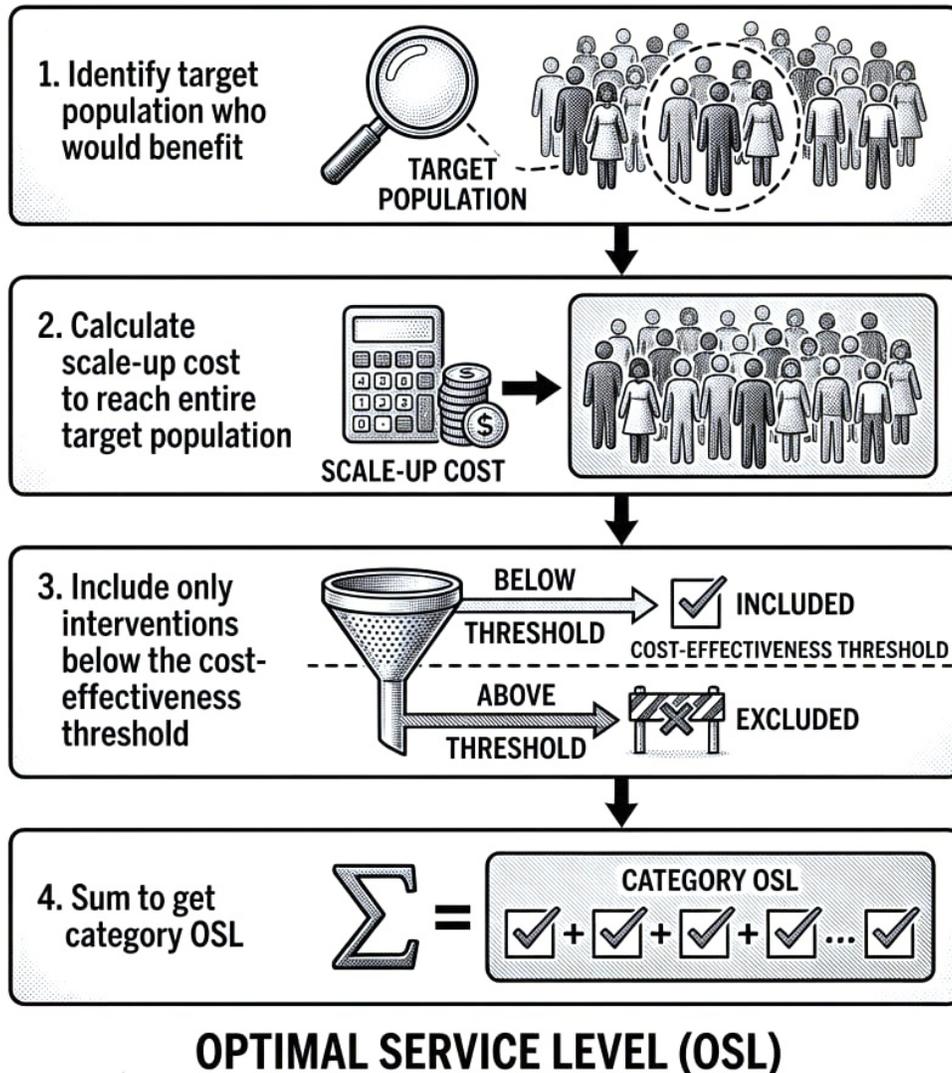
$$\text{OSL} = \sum_{\text{interventions}} \text{Scale}_i \times \text{Cost}_i \quad \text{where} \quad \frac{\text{Cost}_i}{\text{QALY}_i} < \text{WTP}$$

Where:

- Scale_i = target population for intervention i
- Cost_i = per-person cost of intervention i
- QALY_i = QALYs gained per person from intervention i
- WTP = willingness-to-pay threshold (typically \$50K-\$150K per QALY)

8.2 Building Up from Intervention-Level Data

BUILDING UP FROM INTERVENTION-LEVEL DATA



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Figure 16: A sequential flowchart illustrating the four-step process of aggregating intervention-level data into a category-level Optimal Service Level (OSL).

For each health intervention with cost-effectiveness data:

1. **Identify target population** who would benefit
2. **Calculate scale-up cost** to reach entire target population
3. **Include only interventions** below the cost-effectiveness threshold
4. **Sum to get category OSL**

8.3 Worked Example: Vaccinations

Primary metric affected: Median healthy life years (via disease prevention and mortality reduction).

Vaccinations represent one of the highest-return public health investments, with estimated returns of 44:1 for routine childhood immunization^{8,144}. The economic benefits include avoided medical costs, productivity gains, and reduced mortality⁷.

Cost-effectiveness estimates from CEA Registry and CDC vaccination cost studies. QALY estimates reflect average health gains across target populations; costs include vaccine acquisition, administration, and program overhead.

Intervention	Target pop.	Cost/person	QALY/per- son	Cost/QALY	Source	Include?
Childhood routine	4M births	\$500	0.1	\$5,000	CDC VFC	Yes
HPV vaccination	4M teens	\$300	0.05	\$6,000	CEA Registry	Yes
Flu (elderly)	50M elderly	\$40	0.01	\$4,000	CDC	Yes
Shingles	40M eligible	\$200	0.02	\$10,000	CEA Registry	Yes
COVID boosters	100M adults	\$30	0.005	\$6,000	CDC	Yes

All interventions fall well below the conventional \$50,000-\$150,000 per QALY cost-effectiveness threshold, indicating strong economic justification for full scale-up.

OBG calculation:

- Childhood routine: $4M \times \$500 = \$2.0B$
- HPV: $4M \times \$300 = \$1.2B$
- Flu (elderly): $50M \times \$40 = \$2.0B$
- Shingles: $40M \times \$200 = \$8.0B$
- COVID boosters: $100M \times \$30 = \$3.0B$
- **Total OSL: ~\$16B** (vs. current ~\$8B)

Gap: +\$8B (underinvestment)

Evidence grade: A (RCT evidence for most vaccines, well-established cost-effectiveness)

9 Budget Impact Score (BIS)

The Budget Impact Score measures **confidence** in each category’s OSL estimate based on the quality and quantity of causal evidence. The scoring methodology draws on the established evidence hierarchy from the econometrics literature^{139,145}.

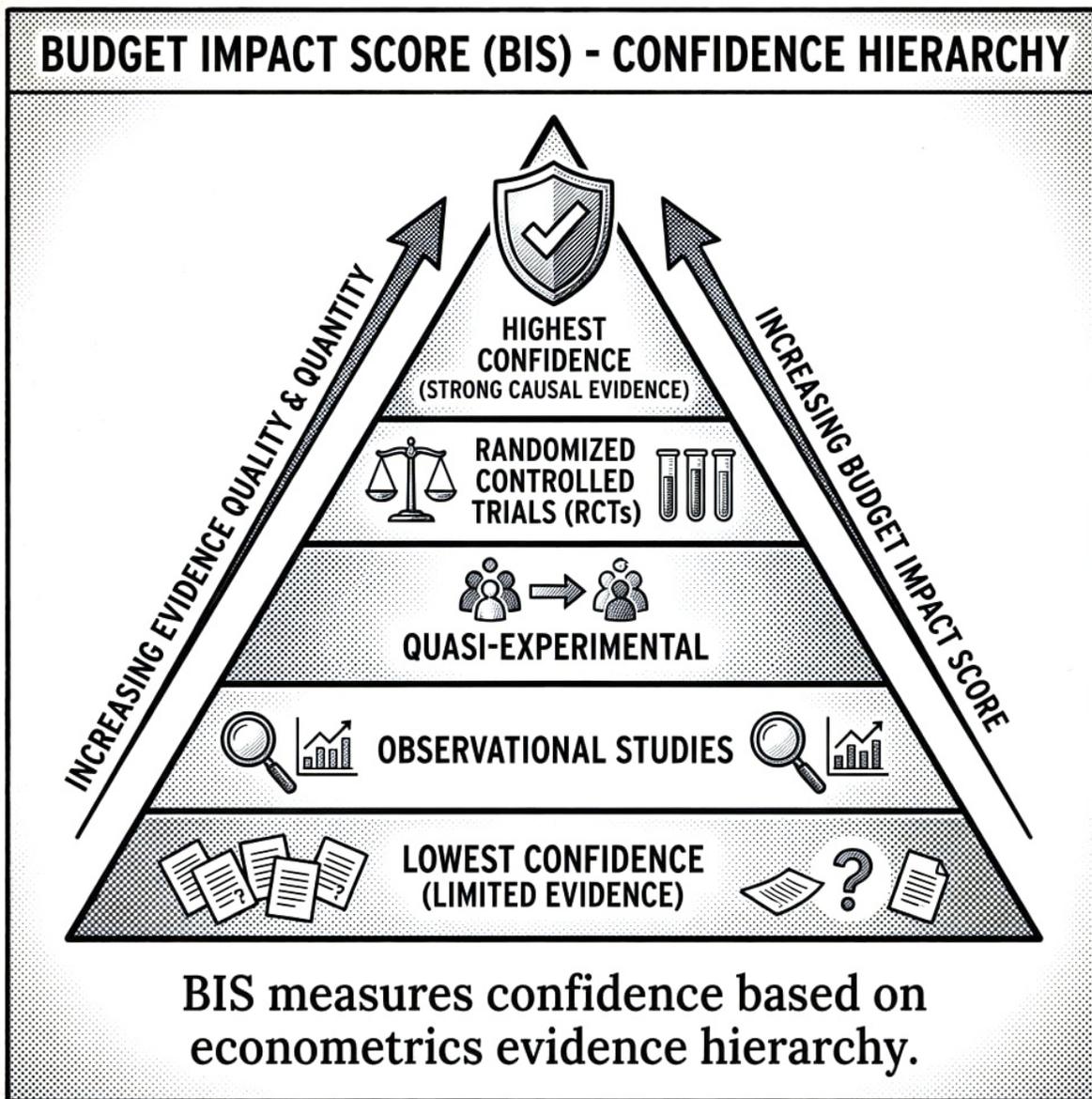


Figure 17: A diagram illustrating the hierarchy of causal evidence, showing how different levels of evidence quality determine the Budget Impact Score and overall confidence levels.

9.1 BIS Calculation

For each spending category i :

Step 1: Gather effect estimates

Collect all available causal effect estimates $\{\beta_{i,1}, \beta_{i,2}, \dots, \beta_{i,n_i}\}$ from the econometric literature.

Step 2: Compute quality weights

Identification Method	Quality Weight (w^Q)
Randomized controlled trial	1.00
Natural experiment (difference-in-differences, regression discontinuity)	0.85
Instrumental variables	0.70
Panel with fixed effects	0.55
Cross-sectional regression	0.25

Step 3: Compute precision weights

$$w_j^P = \frac{1}{\text{SE}(\beta_j)^2}$$

Step 4: Compute recency weights

$$w_j^R = e^{-0.03(t_{now} - t_j)}$$

Step 5: Compute confidence score

$$\text{BIS}_i = \min \left(1, \frac{\sum_j w_j^Q \cdot w_j^P \cdot w_j^R}{K} \right)$$

Where K is a calibration constant.

9.2 Evidence Grading from BIS

BIS Range	Grade	Interpretation	OSL Confidence
0.80 - 1.00	A	Strong causal evidence	High - proceed with reallocation
0.60 - 0.79	B	Good evidence	Moderate - consider with caveats
0.40 - 0.59	C	Mixed evidence	Low - pilot before scaling
0.20 - 0.39	D	Weak evidence	Very low - research priority
0.00 - 0.19	F	Insufficient evidence	Unknown - cannot estimate OSL

10 Gap Analysis and Priority Ranking

10.1 Computing Gaps

For each category i :

$$\text{Gap}_i = \text{OSL}_i - \text{Current}_i$$

- **Gap > 0:** Underinvestment (increase spending)
- **Gap = 0:** At optimal (maintain)
- **Gap < 0:** Overinvestment (decrease spending)

10.2 Priority Score

Prioritize reallocation by gap size weighted by confidence:

$$\text{Priority}_i = |\text{Gap}_i| \times \text{BIS}_i$$

Categories with large gaps AND high confidence should be addressed first.

10.3 Illustrative Example: Priority Ranking

The following uses the same illustrative data from the dashboard example above. OSL estimates for pragmatic trials, vaccinations, and K-12 education are derived in Sections 5-7. Other OSL values are preliminary estimates based on cross-country benchmarking and should be treated as order-of-magnitude approximations. BIS scores reflect the author’s assessment of available causal evidence quality rather than formal calculation from the BIS formula.

Category	Current	OSL	Gap	BIS	Inc	Hlth	Priority	Action
Pragmatic trials	\$0.5B	\$50B	+\$49.5B	0.90	++	+++	44.6	Scale 100x
Basic research	\$45B	\$90B	+\$45B	0.70	++	++	31.5	Increase
Vaccinations	\$8B	\$35B	+\$27B	0.95	+	+++	25.7	Increase
Early childhood	\$50B	\$70B	+\$20B	0.85	+++	+	17.0	Increase
Military	\$850B	\$459B	-\$391B	0.50	–	–	195.5	De-crease
Ag subsidies	\$25B	\$0B	-\$25B	0.90	–	–	22.5	Elimi-nate

Inc = effect on real after-tax median income growth. Hlth = effect on median healthy life years. Scale: +++ strong, ++ moderate, + weak, – negative.

Reallocation plan: Cut military discretionary (-\$391B) and agricultural subsidies (-\$25B) to fund pragmatic clinical trials (+\$49.5B), basic research (+\$45B), vaccinations (+\$27B), and early childhood (+\$20B). Pragmatic trials have the highest priority score among positive-gap categories due to extreme underinvestment combined with strong evidence, and they improve both welfare metrics.

11 Multi-Unit Reporting

11.1 The Problem with Abstract Scores

Composite scores (like 0-1 BIS values) obscure interpretability. Policymakers and citizens understand dollars, lives, and years - not abstract indices.

11.2 Reporting at Multiple Levels

Level	Units	Use Case	Example
0. Core metrics	pp/year income growth, healthy life years	Primary welfare outcomes	“+0.1 pp income growth, +0.05 healthy years”
1. Natural	Domain-specific	Interpretation within domain	“Education: \$2,100/student gap”
2. Monetized	\$ equivalent	Cross-domain comparison	“Expected welfare gain: \$4.00 per \$1”
3. Health	QALYs/DALYs	Health-weighted comparison	“12,000 QALYs per \$1B invested”
4. Composite	0-1 score	Ranking when monetization uncertain	“BIS = 0.85”

Level 0 (Core Metrics) reports expected changes to the two welfare metrics directly. All other levels are derived from or convertible to these core outcomes. QALYs (Level 3) translate directly to median healthy life years. Monetized values (Level 2) combine income effects with health effects valued at standard rates.

11.3 Conversion Factors

Conversion	Value	Source	Notes
Value of Statistical Life (VSL)	~\$10M	EPA, DOT	US regulatory standard
Value per QALY	\$50K-\$150K	ICER, WHO	Context-dependent
QALY → \$	\$100K/QALY	Mid-range estimate	For cross-domain
Life-year → QALY	~0.8-1.0	Age/health adjusted	Quality weighting

11.4 Worked Example: Multi-Unit Output

Category: Early Childhood Education

Unit Level	Value	Interpretation
Natural	+\$20B gap	Current: \$50B, OSL: \$70B
Per-child	+\$833/child gap	24M children
Monetized ROI	4:1 NPV return	146
Health (QALYs)	+8K QALYs/year	Per \$1B additional
Composite (BIS)	0.85	High-quality RCT evidence

Recommendation: Moderate underinvestment with strong evidence. Closing the gap would yield ~\$80B in NPV returns.

12 Quality Requirements and Validation

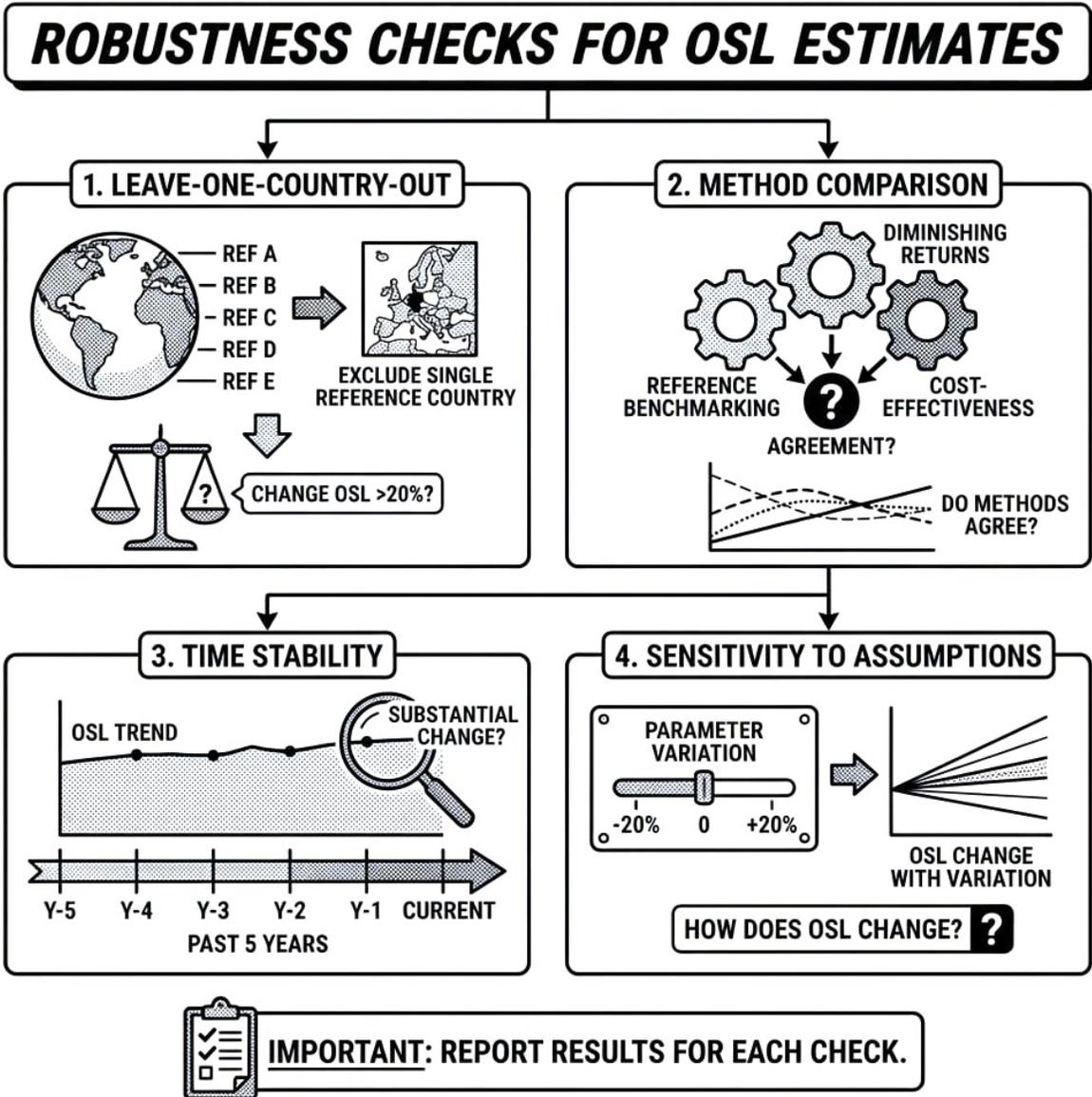
12.1 Minimum Thresholds for OBG Estimation

Criterion	Minimum	Rationale
Reference countries	5+	Avoid outlier bias
Dose-response studies	3+	Identify diminishing returns
Causal effect estimates	2+	Cross-validate
Data recency	Within 10 years	Relevance
BIS for reallocation	> 0.40	Sufficient confidence

12.2 Robustness Checks

For each OSL estimate, report:

1. **Leave-one-country-out:** Does excluding any single country change OSL by >20%?
2. **Method comparison:** Do diminishing returns and cost-effectiveness methods agree?
3. **Time stability:** Has OSL changed substantially over past 5 years?
4. **Sensitivity to assumptions:** How does OSL change with $\pm 20\%$ parameter variation?



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Figure 18: A conceptual framework illustrating the four essential robustness checks for OSL estimates: outlier analysis, methodological consistency, temporal stability, and parameter sensitivity.

13 Interpreting Results

13.1 Gap Ranges and Recommended Actions

Gap (% of current)	Interpretation	Recommended Action
> +50%	Severe underinvestment	Immediate scale-up
+20% to +50%	Moderate underinvestment	Phased increase
-10% to +20%	Near optimal	Monitor, fine-tune

Gap (% of current)	Interpretation	Recommended Action
-50% to -10%	Moderate overinvestment	Gradual reduction
< -50%	Severe overinvestment	Urgent reallocation

13.2 What the Algorithm Cannot Tell You

Factor	OBG Captures	OBG Does Not Capture
Evidence-optimal spending level	Yes	
Confidence in estimates	Yes	
Direction of reallocation	Yes	
Political feasibility		No
Implementation capacity		No
Transition costs		No
Distributional effects		No
Novel interventions		No

OBG provides evidence-based targets. Political judgment is still required for implementation strategy.

14 Pilot Program Prioritization

14.1 Value of Information for Uncertain Categories

Categories with low BIS but potentially high returns warrant research investment:

$$VOI_i = \text{Potential Gap}_i \times (1 - BIS_i) \times P(\text{high return})$$

High-VOI categories should receive pilot funding to generate better evidence.

14.2 Recommended Pilot Designs

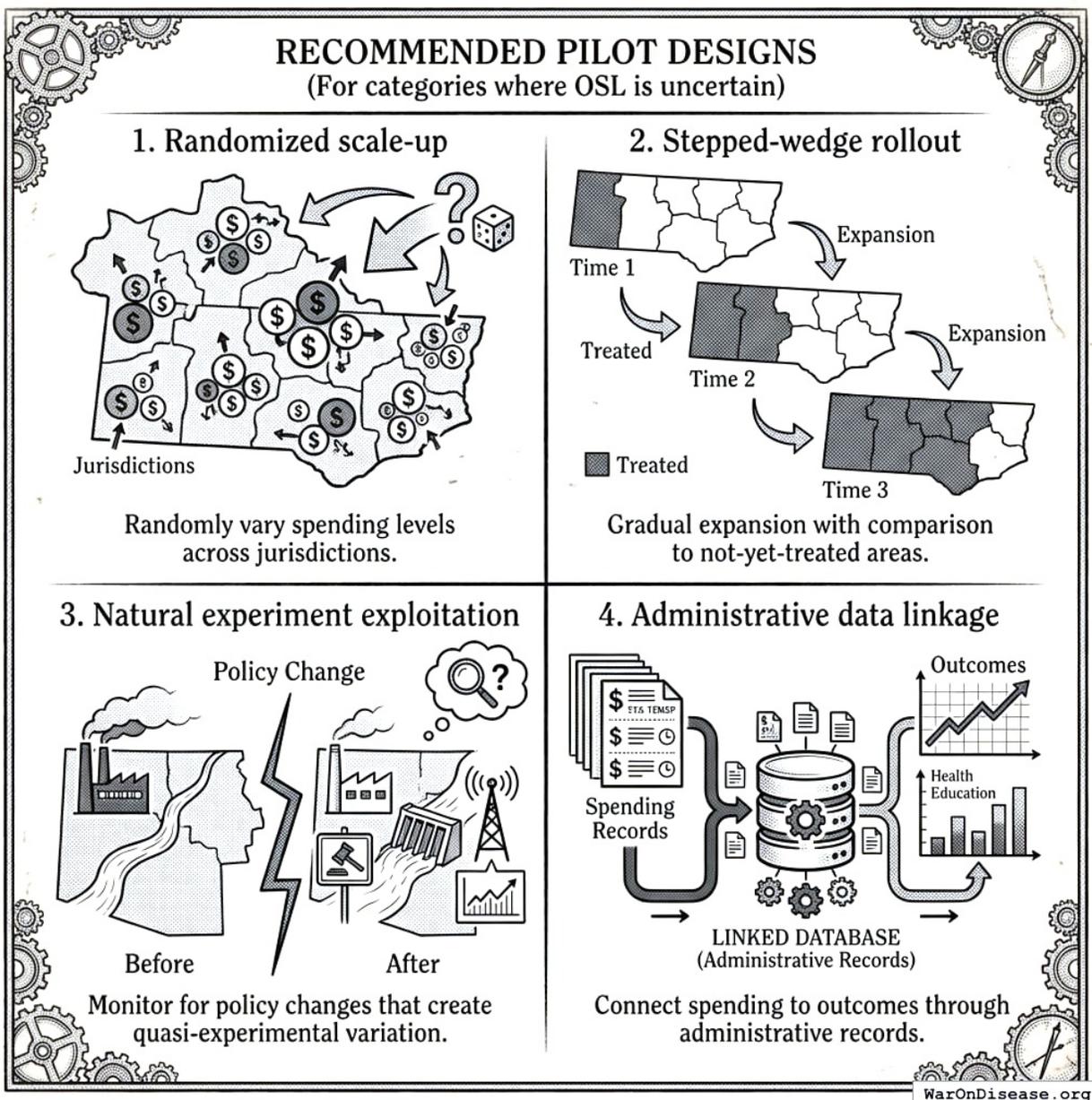


Figure 19: A conceptual comparison of four pilot design strategies: randomized scale-up, stepped-wedge rollout, natural experiment exploitation, and administrative data linkage.

For categories where OSL is uncertain:

1. **Randomized scale-up:** Randomly vary spending levels across jurisdictions
2. **Stepped-wedge rollout:** Gradual expansion with comparison to not-yet-treated areas
3. **Natural experiment exploitation:** Monitor for policy changes that create quasi-experimental variation
4. **Administrative data linkage:** Connect spending to outcomes through administrative

14.3 Learning Feedback Loop

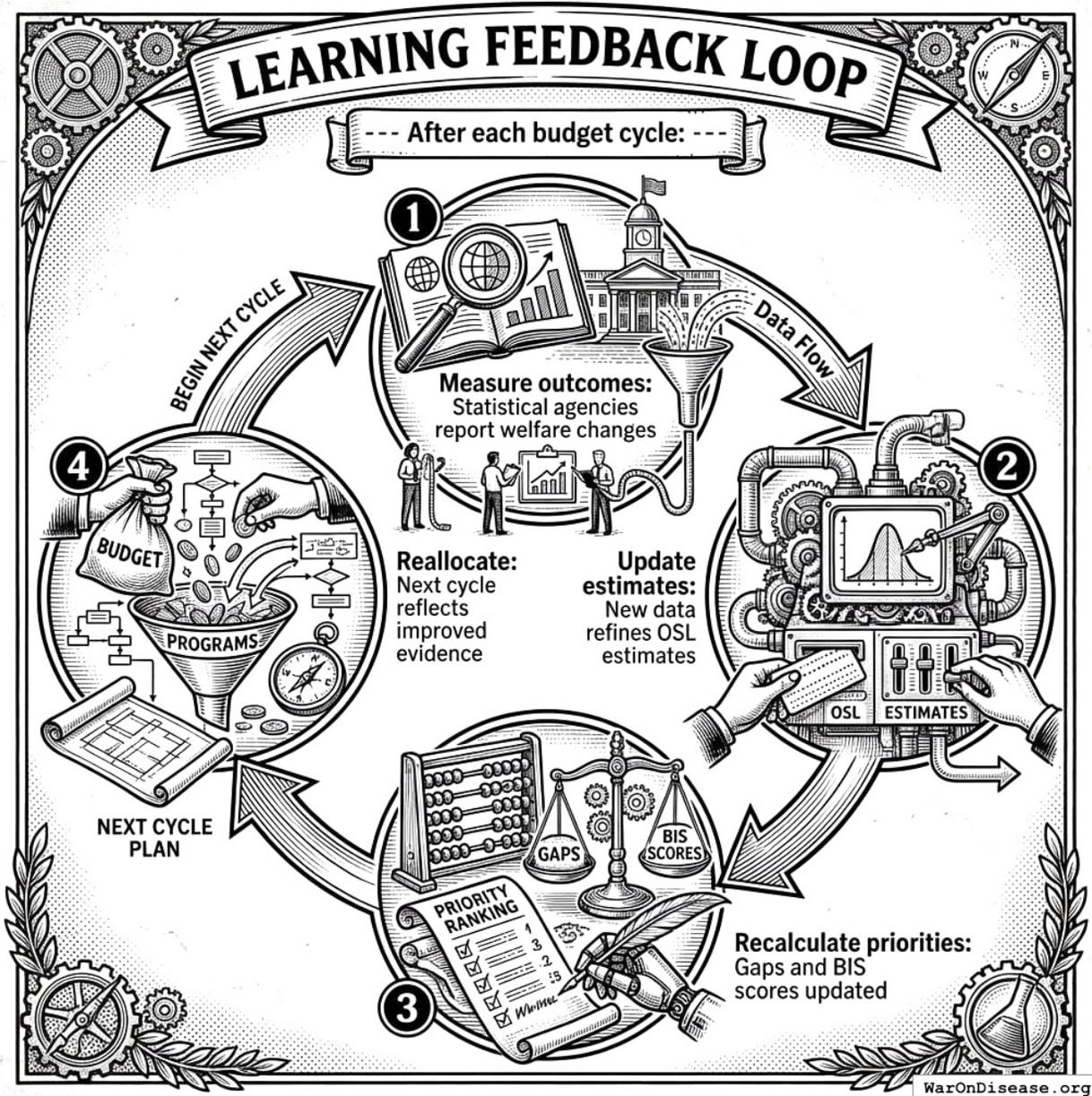


Figure 20: A circular diagram illustrating the continuous four-step learning feedback loop used to refine budget priorities based on statistical outcomes and updated data.

After each budget cycle:

1. **Measure outcomes:** Statistical agencies report welfare changes
2. **Update estimates:** New data refines OSL estimates
3. **Recalculate priorities:** Gaps and BIS scores updated

4. **Reallocate:** Next cycle reflects improved evidence

15 Data Sources

15.1 Cross-Country Databases

International organizations maintain standardized cross-country spending and outcome data essential for diminishing returns analysis. The OECD provides the most comprehensive harmonized data for high-income countries⁹⁵.

Database	Coverage	URL	Use Case
OECD iLibrary	38 OECD members	oecd-ilibrary.org	Education, health, social spending
World Bank WDI	217 countries	data.worldbank.org	Broad spending and outcomes
SIPRI	Global	sipri.org	Military spending
WHO GHED	194 countries	who.int/data/globe	Health expenditure
UNESCO UIS	Global	uis.unesco.org	Education spending

15.2 Cost-Effectiveness Databases

Database	Coverage	URL	Use Case
CEA Registry	8,000+ analyses	cearegistry.org	Health cost-effectiveness
Disease Control Priorities	LMICs	dcp-3.org	Global health priorities
Cochrane Library	8,000+ reviews	cochranelibrary.com	Health intervention effects
Copenhagen Consensus	Development	copenhagenconsensus.com	Development priorities

These databases enable systematic ranking of interventions by cost-effectiveness. For example, deworming programs consistently rank among the most cost-effective health interventions, with costs as low as \$30-50 per DALY averted¹⁸.

15.3 US Budget Data

Source	Coverage	URL	Use Case
OMB Historical Tables	1789-present	whitehouse.gov/omb	Federal spending
CBO Budget Analyses	Federal	cbo.gov	Fiscal impact scoring ¹³⁵

Source	Coverage	URL	Use Case
USASpending	Federal awards	usaspending.gov	Program-level detail
Census of Governments	State & local	census.gov	Subnational spending

16 Limitations

16.1 Diminishing Returns Uncertainty

- **Functional form:** True relationship may not match assumed function
- **Extrapolation:** Estimating returns outside observed spending range
- **Interaction effects:** Returns may depend on other spending categories

Mitigation: Report confidence intervals, use multiple functional forms, acknowledge extrapolation limits.

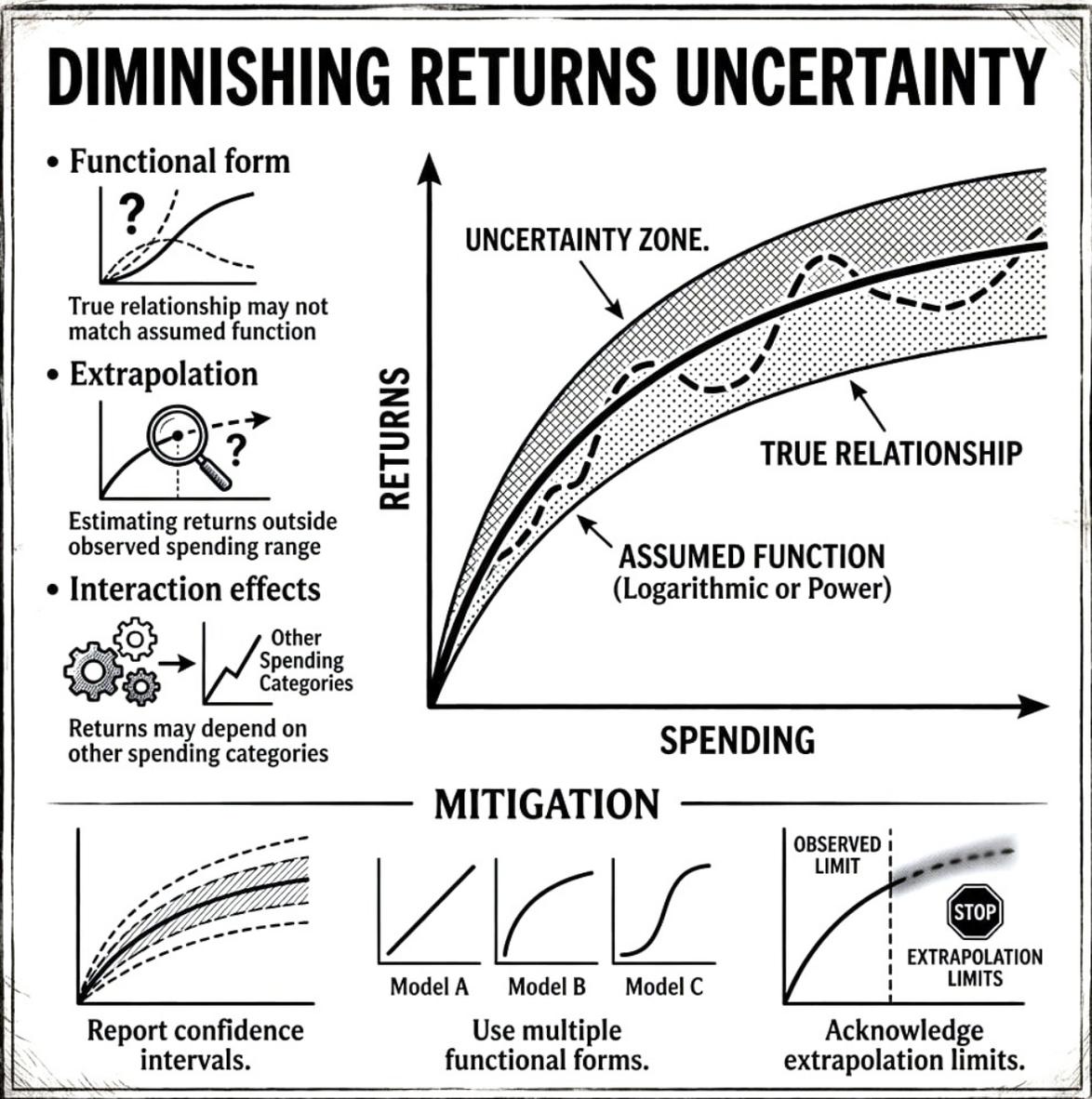


Figure 21: A line graph illustrating diminishing returns with a curve flattening out, featuring shaded confidence intervals and a dashed line representing the risks of extrapolation beyond historical data points.

16.2 Implementation Capacity

Higher spending may not translate to outcomes if implementation capacity is lacking.

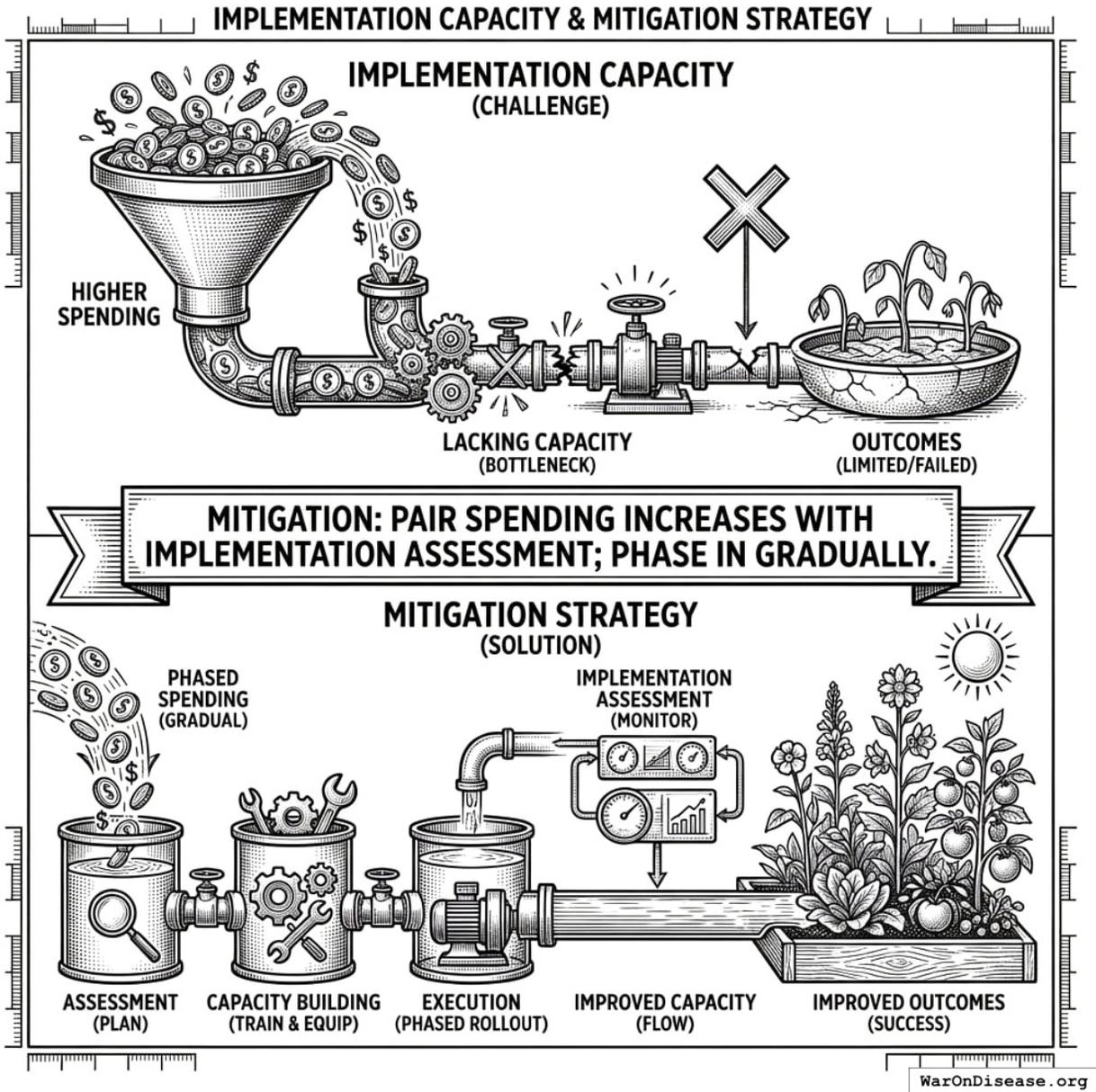


Figure 22: A flow diagram illustrating how spending is successfully converted to outcomes by passing through the filters of implementation assessment and gradual phasing.

Mitigation: Pair spending increases with implementation assessment; phase in gradually.

17 Validation Framework

Rigorous validation is essential for any framework that claims to identify optimal spending levels. This section outlines the validation approach, acknowledging that comprehensive empirical validation remains future work.

17.1 Retrospective Validation

Question: Did jurisdictions that moved toward OSL achieve better outcomes than those that diverged?

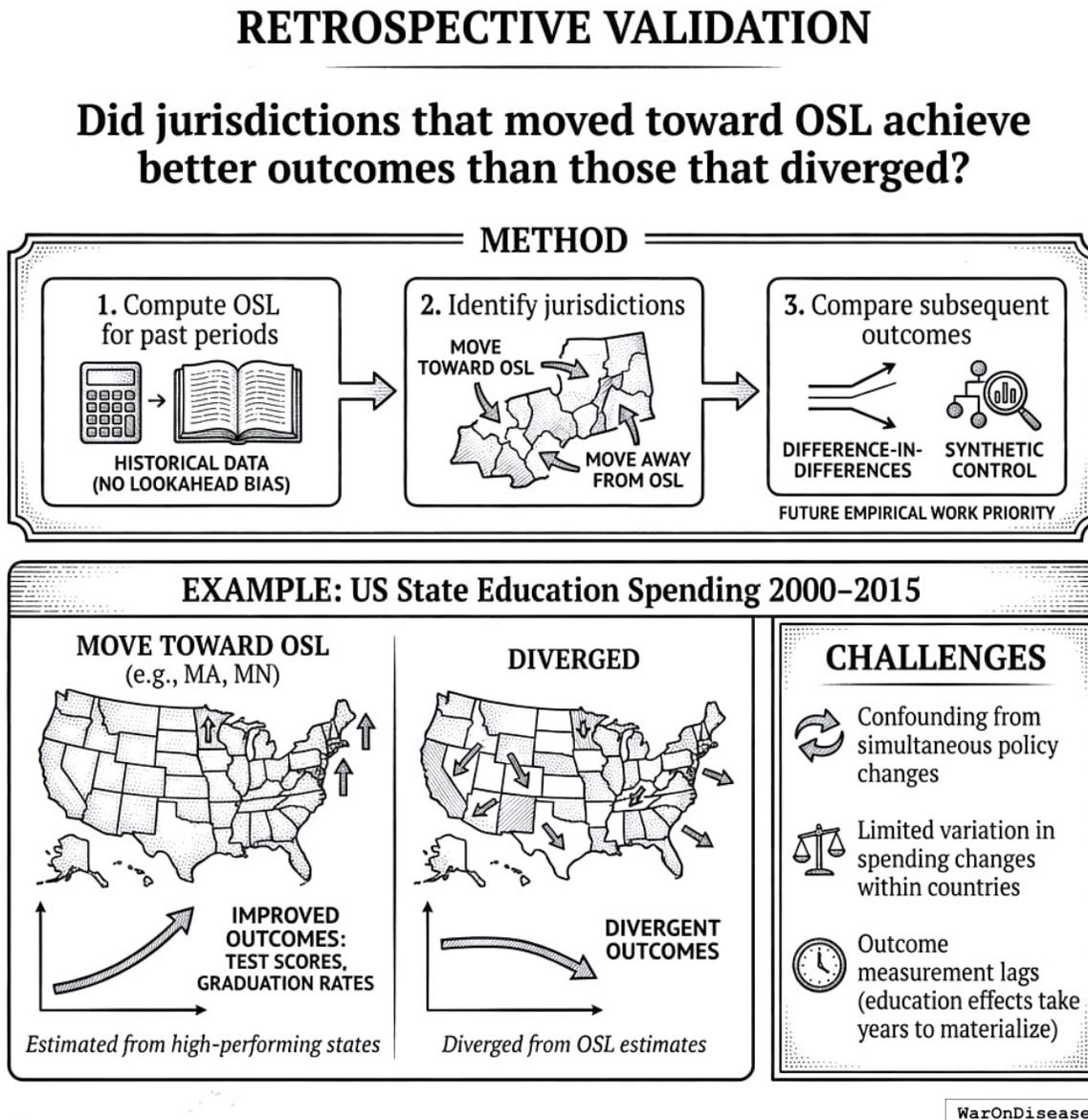


Figure 23: A flowchart outlining the three-step methodology for retrospective validation, showing the sequence from historical OSL calculation to the comparative analysis of jurisdiction outcomes.

Method: 1. Compute OSL for past periods using only data available at that time (to avoid lookahead bias) 2. Identify jurisdictions that moved toward/away from OSL 3. Compare subsequent outcomes using difference-in-differences or synthetic control methods¹⁴⁷

Example: US State Education Spending 2000-2015

A preliminary retrospective analysis could examine whether states that moved toward education OSL (estimated from high-performing states like Massachusetts and Minnesota) subsequently showed improved test scores and graduation rates relative to states that diverged. This analysis is noted as a priority for future empirical work.

Challenges:

- Confounding from simultaneous policy changes
- Limited variation in spending changes within countries
- Outcome measurement lags (education effects take years to materialize)

17.2 Prospective Validation

Question: Do OBG-guided reallocations improve outcomes going forward?

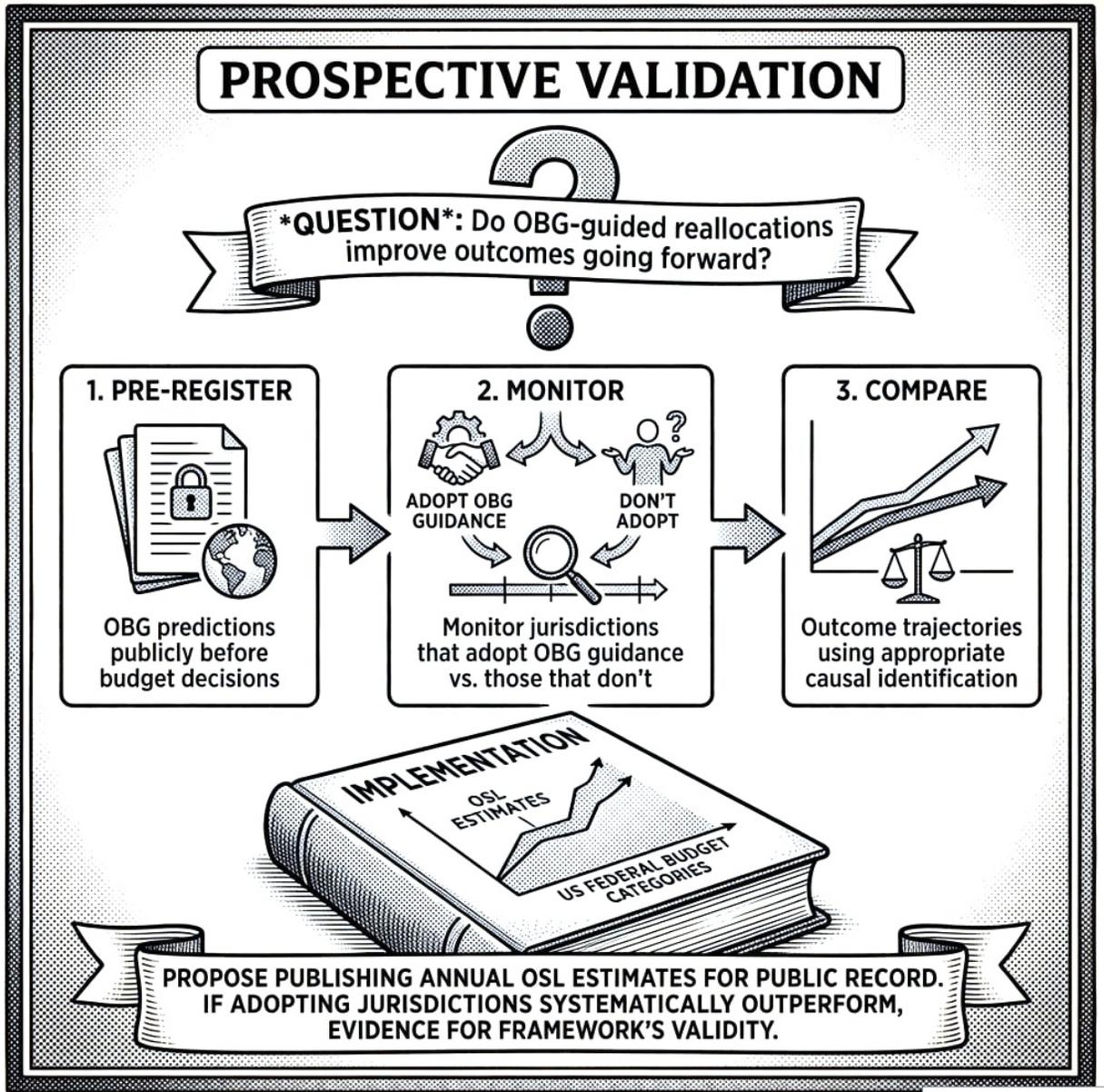


Figure 24: A flowchart illustrating the prospective validation process, from public pre-registration of predictions to the comparative analysis of outcome trajectories between jurisdictions.

Method: 1. Pre-register OBG predictions publicly before budget decisions 2. Monitor jurisdictions that adopt OBG guidance vs. those that don't 3. Compare outcome trajectories using appropriate causal identification

Implementation: We propose publishing annual OSL estimates for US federal budget categories, creating a public record that enables future validation. If jurisdictions that adopt OBG guidance systematically outperform those that don't, this provides evidence for the framework's validity.

17.3 Success Metrics

Metric	Definition	Target	Interpretation
Gap reduction	Did spending move toward OSL?	> 50% of gap closed in 10 years	Tests political feasibility
Outcome improvement	Did welfare metrics improve more in OBG-following jurisdictions?	> 10% relative improvement	Tests welfare prediction accuracy
Prediction accuracy	Did estimated returns match actual returns?	Correlation $r > 0.5$	Tests underlying model
Cross-method consistency	Do diminishing returns and cost-effectiveness methods converge?	Agreement within 30%	Tests methodological robustness

17.4 Validation Status

This working paper presents the OBG *methodology*. Comprehensive empirical validation is future work requiring:

1. **Data collection:** Longitudinal spending and outcome data across jurisdictions
2. **Historical OSL estimation:** Computing past OSL using only contemporaneously available data
3. **Causal analysis:** Rigorous identification of spending \rightarrow outcome effects
4. **Publication:** Peer-reviewed validation study with pre-registered analysis plan

The framework's current evidence base consists of the underlying studies cited throughout (e.g.,¹⁴⁰ for education,¹⁴⁴ for vaccinations), not direct validation of OBG itself.

18 Sensitivity Analysis

18.1 Parameter Sensitivity

Parameter	Default	Test Range	Impact on OSL
Country data set	All OECD	OECD + G20, High-income only	$\pm 15\%$
Discount rate	5%	3-7%	$\pm 20\%$
BIS confidence threshold	0.40	0.30-0.60	Category inclusion
Recency decay rate	0.03/year	0.01-0.05	Estimate weights

18.2 Scenario Analysis

Optimistic scenario: All uncertain categories have high returns **Pessimistic scenario:** Uncertain categories have low/zero returns **Base case:** Use point estimates

Report OSL range across scenarios for policy guidance.

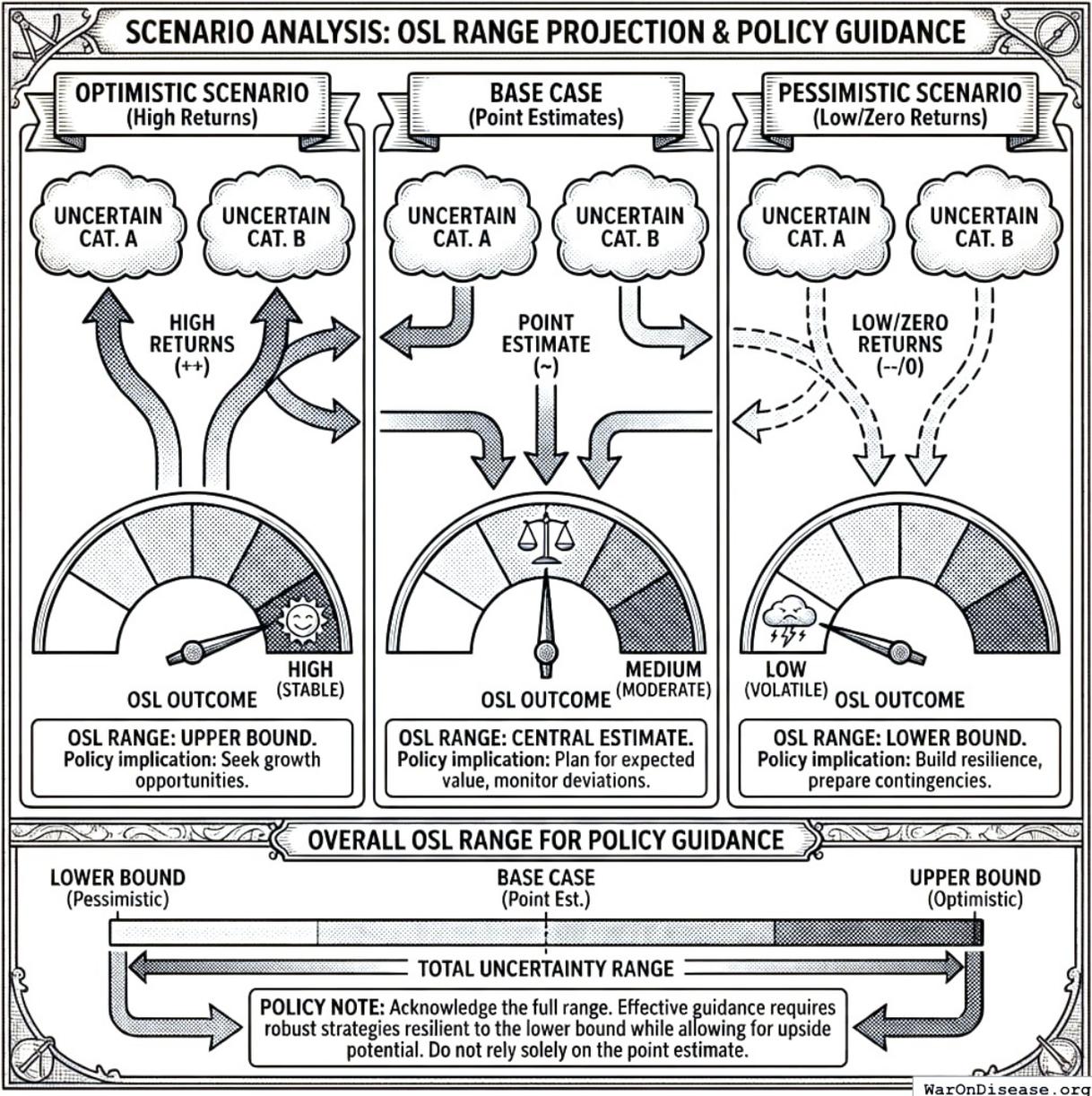


Figure 25: A comparison chart showing the projected OSL range across pessimistic, base case, and optimistic scenarios based on varying return estimates.

19 Conclusion

The Optimal Budget Generator framework provides a systematic, evidence-based approach to budget allocation. Unlike marginal-return frameworks that can justify infinite spending on high-return categories, OBG recognizes that every category has an optimal level - like the Recommended Daily Allowance for nutrients.

The framework answers three questions:

1. **What is the target?** OBG provides evidence-based spending levels for each category

2. **How far are we?** Gap analysis shows where current spending diverges from optimal
3. **How confident are we?** BIS scores evidence quality so policymakers know which OSL estimates are reliable

Even with imperfect evidence, systematically moving from severe misallocation (military 100% above OSL, vaccinations 75% below OSL) toward evidence-based targets should produce substantially larger welfare gains than current lobbying-driven allocation achieves.

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20 References

1. NIH Common Fund. NIH pragmatic trials: Minimal funding despite 30x cost advantage. *NIH Common Fund: HCS Research Collaboratory* <https://commonfund.nih.gov/hcscollaboratory> (2025)
The NIH Pragmatic Trials Collaboratory funds trials at \$500K for planning phase, \$1M/year. for implementation-a tiny fraction of NIH's budget. The ADAPTABLE trial cost \$14 million for 15,076 patients (= \$929/patient) versus \$420 million for a similar traditional RCT (30x cheaper), yet pragmatic trials remain severely underfunded. PCORnet infrastructure enables real-world trials embedded in healthcare systems, but receives minimal support compared to basic research funding. Additional sources: <https://commonfund.nih.gov/hcscollaboratory> | https://pcornet.org/wp-content/uploads/2025/08/ADAPTABLE_Lay_Summary_21JUL2025.pdf | <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5604499/>
2. NIH. Antidepressant clinical trial exclusion rates. *Zimmerman et al.* <https://pubmed.ncbi.nlm.nih.gov/26276679/> (2015)
Mean exclusion rate: 86.1% across 158 antidepressant efficacy trials (range: 44.4% to 99.8%) More than 82% of real-world depression patients would be ineligible for antidepressant registration trials Exclusion rates increased over time: 91.4% (2010-2014) vs. 83.8% (1995-2009) Most common exclusions: comorbid psychiatric disorders, age restrictions, insufficient depression severity, medical conditions Emergency psychiatry patients: only 3.3% eligible (96.7% excluded) when applying 9 common exclusion criteria Only a minority of depressed patients seen in clinical practice are likely to be eligible for most AETs Note: Generalizability of antidepressant trials has decreased over time, with increasingly stringent exclusion criteria eliminating patients who would actually use the drugs in clinical practice Additional sources: <https://pubmed.ncbi.nlm.nih.gov/26276679/> | <https://pubmed.ncbi.nlm.nih.gov/26164052/> | <https://www.wolterskluwer.com/en/news/antidepressant-trials-exclude-most-real-world-patients-with-depression>
3. CNBC. Warren buffett's career average investment return. *CNBC* <https://www.cnbc.com/2025/05/05/warren-buffetts-return-tally-after-60-years-5502284percent.html> (2025)
Berkshire's compounded annual return from 1965 through 2024 was 19.9%, nearly double the 10.4% recorded by the S&P 500. Berkshire shares skyrocketed 5,502,284% compared to the S&P 500's 39,054% rise during that period. Additional sources: <https://www.cnbc.com/2025/05/05/warren-buffetts-return-tally-after-60-years-5502284percent.html> | <https://www.slickcharts.com/berkshire-hathaway/returns>

4. World Health Organization. WHO global health estimates 2024. *World Health Organization* <https://www.who.int/data/gho/data/themes/mortality-and-global-health-estimates> (2024) *Comprehensive mortality and morbidity data by cause, age, sex, country, and year Global mortality: 55-60 million deaths annually Lives saved by modern medicine (vaccines, cardiovascular drugs, oncology): 12M annually (conservative aggregate) Leading causes of death: Cardiovascular disease (17.9M), Cancer (10.3M), Respiratory disease (4.0M) Note: Baseline data for regulatory mortality analysis. Conservative estimate of pharmaceutical impact based on WHO immunization data (4.5M/year from vaccines) + cardiovascular interventions (3.3M/year) + oncology (1.5M/year) + other therapies. Additional sources: https://www.who.int/data/gho/data/themes/mortality-and-global-health-estimates*
5. GiveWell. GiveWell cost per life saved for top charities (2024). *GiveWell: Top Charities* <https://www.givewell.org/charities/top-charities> *General range: \$3,000-\$5,500 per life saved (GiveWell top charities) Helen Keller International. (Vitamin A): \$3,500 average (2022-2024); varies \$1,000-\$8,500 by country Against Malaria Foundation: \$5,500 per life saved New Incentives (vaccination incentives): \$4,500 per life saved Malaria Consortium (seasonal malaria chemoprevention): \$3,500 per life saved VAS program details: \$2 to provide vitamin A supplements to child for one year Note: Figures accurate for 2024. Helen Keller VAS program has wide country variation (\$1K-\$8.5K) but \$3,500 is accurate average. Among most cost-effective interventions globally Additional sources: https://www.givewell.org/charities/top-charities | https://www.givewell.org/charities/helen-keller-international | https://ourworldindata.org/cost-effectiveness*
6. AARP. Unpaid caregiver hours and economic value. *AARP 2023* <https://www.aarp.org/caregiving/financial-legal/info-2023/unpaid-caregivers-provide-billions-in-care.html> (2023) *Average family caregiver: 25-26 hours per week (100-104 hours per month) 38 million caregivers providing 36 billion hours of care annually Economic value: \$16.59 per hour = \$600 billion total annual value (2021) 28% of people provided eldercare on a given day, averaging 3.9 hours when providing care Caregivers living with care recipient: 37.4 hours per week Caregivers not living with recipient: 23.7 hours per week Note: Disease-related caregiving is subset of total; includes elderly care, disability care, and child care Additional sources: https://www.aarp.org/caregiving/financial-legal/info-2023/unpaid-caregivers-provide-billions-in-care.html | https://www.bls.gov/news.release/elcare.nr0.htm | https://www.caregiver.org/resource/caregiver-statistics-demographics/*
7. MMWR, C. Childhood vaccination economic benefits. *CDC MMWR* <https://www.cdc.gov/mmwr/volumes/73/wr/mm7331a2.htm> (1994) *US programs (1994-2023): \$540B direct savings, \$2.7T societal savings (\$18B/year direct, \$90B/year societal) Global (2001-2020): \$820B value for 10 diseases in 73 countries (\$41B/year) ROI: \$11 return per \$1 invested Measles vaccination alone saved 93.7M lives (61% of 154M total) over 50 years (1974-2024) Additional sources: https://www.cdc.gov/mmwr/volumes/73/wr/mm7331a2.htm | https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(24)00850-X/fulltext*
8. CDC. Childhood vaccination (US) ROI. *CDC* <https://www.cdc.gov/mmwr/preview/mmwrhtml/mm6316a4.htm> (2017).
9. Labor Statistics, U. S. B. of. *CPI inflation calculator*. (2024) *CPI-U (1980): 82.4 CPI-U (2024): 313.5 Inflation multiplier (1980-2024): 3.80× Cumulative inflation: 280.48% Average annual inflation rate: 3.08% Note: Official U.S. government inflation data using Consumer Price Index for All Urban Consumers (CPI-U). Additional sources: https://www.bls.gov/data/inflation_calculator.htm*

10. ClinicalTrials.gov API v2 direct analysis. ClinicalTrials.gov cumulative enrollment data (2025). *Direct analysis via ClinicalTrials.gov API v2* <https://clinicaltrials.gov/data-api/api> *Analysis of 100,000 active/recruiting/completed trials on ClinicalTrials.gov (as of January 2025) shows cumulative enrollment of 12.2 million participants: Phase 1 (722k), Phase 2 (2.2M), Phase 3 (6.5M), Phase 4 (2.7M). Median participants per trial: Phase 1 (33), Phase 2 (60), Phase 3 (237), Phase 4 (90). Additional sources: <https://clinicaltrials.gov/data-api/api>*
11. CAN, A. Clinical trial patient participation rate. *ACS CAN: Barriers to Clinical Trial Enrollment* <https://www.fightcancer.org/policy-resources/barriers-patient-enrollment-therapeutic-clinical-trials-cancer>
Only 3-5% of adult cancer patients in US receive treatment within clinical trials About 5% of American adults have ever participated in any clinical trial Oncology: 2-3% of all oncology patients participate Contrast: 50-60% enrollment for pediatric cancer trials (<15 years old) Note: 20% of cancer trials fail due to insufficient enrollment; 11% of research sites enroll zero patients Additional sources: <https://www.fightcancer.org/policy-resources/barriers-patient-enrollment-therapeutic-clinical-trials-cancer> | https://hints.cancer.gov/docs/Briefs/HINTS_Brief_48.pdf
12. ScienceDaily. Global prevalence of chronic disease. *ScienceDaily: GBD 2015 Study* <https://www.sciencedaily.com/releases/2015/06/150608081753.htm> (2015)
2.3 billion individuals had more than five ailments (2013) Chronic conditions caused 74% of all deaths worldwide (2019), up from 67% (2010) Approximately 1 in 3 adults suffer from multiple chronic conditions (MCCs) Risk factor exposures: 2B exposed to biomass fuel, 1B to air pollution, 1B smokers Projected economic cost: \$47 trillion by 2030 Note: 2.3B with 5+ ailments is more accurate than "2B with chronic disease." One-third of all adults globally have multiple chronic conditions Additional sources: <https://www.sciencedaily.com/releases/2015/06/150608081753.htm> | <https://pmc.ncbi.nlm.nih.gov/articles/PMC10830426/> | <https://pmc.ncbi.nlm.nih.gov/articles/PMC6214883/>
13. C&EN. Annual number of new drugs approved globally: 50. *C&EN* <https://cen.acs.org/pharmaceuticals/50-new-drugs-received-FDA/103/i2> (2025)
50 new drugs approved annually Additional sources: <https://cen.acs.org/pharmaceuticals/50-new-drugs-received-FDA/103/i2> | <https://www.fda.gov/drugs/development-approval-process-drugs/novel-drug-approvals-fda>
14. Williams, R. J., Tse, T., DiPiazza, K. & Zarin, D. A. *Terminated trials in the ClinicalTrials.gov results database: Evaluation of availability of primary outcome data and reasons for termination.* *PLOS One* **10**, e0127242 (2015)
Approximately 12% of trials with results posted on the ClinicalTrials.gov results database (905/7,646) were terminated. Primary reasons: insufficient accrual (57% of non-data-driven terminations), business/strategic reasons, and efficacy/toxicity findings (21% data-driven terminations).
15. Report, I. Global trial capacity. *IQVIA Report: Clinical Trial Subjects Number Drops Due to Decline in COVID-19 Enrollment* <https://gmdpacademy.org/news/iqvia-report-clinical-trial-subjects-number-drops-due-to-decline-in-covid-19-enrollment/>
1.9M participants annually (2022, post-COVID normalization from 4M peak in 2021) Additional sources: <https://gmdpacademy.org/news/iqvia-report-clinical-trial-subjects-number-drops-due-to-decline-in-covid-19-enrollment/>

16. Research & Markets. Global clinical trials market 2024. *Research and Markets* <https://www.globenewswire.com/news-release/2024/04/19/2866012/0/en/Global-Clinical-Trials-Market-Research-Report-2024-An-83-16-Billion-Market-by-2030-AI-Machine-Learning-and-Blockchain-will-Transform-the-Clinical-Trials-Landscape.html> (2024)
Global clinical trials market valued at approximately \$83 billion in 2024, with projections to reach \$83-132 billion by 2030. Additional sources: https://www.globenewswire.com/news-release/2024/04/19/2866012/0/en/Global-Clinical-Trials-Market-Research-Report-2024-An-83-16-Billion-Market-by-2030-AI-Machine-Learning-and-Blockchain-will-Transform-the-Clinical-Trials-Landscape.html | https://www.precedenceresearch.com/clinical-trials-market
17. OpenSecrets. Lobbying spend (defense). *OpenSecrets* <https://www.opensecrets.org/industries/lobbying?ind=D> (2024).
18. GiveWell. Cost per DALY for deworming programs. <https://www.givewell.org/international/technical/programs/deworming/cost-effectiveness>
Schistosomiasis treatment: \$28.19-\$70.48 per DALY (using arithmetic means with varying disability weights) Soil-transmitted helminths (STH) treatment: \$82.54 per DALY (mid-point estimate) Note: GiveWell explicitly states this 2011 analysis is "out of date" and their current methodology focuses on long-term income effects rather than short-term health DALYs Additional sources: https://www.givewell.org/international/technical/programs/deworming/cost-effectiveness
19. Transportation, U. S. D. of. [Departmental guidance on valuation of a statistical life in economic analysis](#). (2024).
20. Think by Numbers. Pre-1962 drug development costs and timeline (think by numbers). *Think by Numbers: How Many Lives Does FDA Save?* <https://thinkbynumbers.org/health/how-many-net-lives-does-the-fda-save/> (1962)
Historical estimates (1970-1985): USD \$226M fully capitalized (2011 prices) 1980s drugs: \$65M after-tax R&D (1990 dollars), \$194M compounded to approval (1990 dollars) Modern comparison: \$2-3B costs, 7-12 years (dramatic increase from pre-1962) Context: 1962 regulatory clampdown reduced new treatment production by 70%, dramatically increasing development timelines and costs Note: Secondary source; less reliable than Congressional testimony Additional sources: https://thinkbynumbers.org/health/how-many-net-lives-does-the-fda-save/ | https://en.wikipedia.org/wiki/Cost_of_drug_development | https://www.statnews.com/2018/10/01/changing-1962-law-slash-drug-prices/
21. (BIO), B. I. O. BIO clinical development success rates 2011-2020. *Biotechnology Innovation Organization (BIO)* https://go.bio.org/rs/490-EHZ-999/images/ClinicalDevelopmentSuccessRates2011_2020.pdf (2021)
Phase I duration: 2.3 years average Total time to market (Phase I-III + approval): 10.5 years average Phase transition success rates: Phase I→II: 63.2%, Phase II→III: 30.7%, Phase III→Approval: 58.1% Overall probability of approval from Phase I: 12% Note: Largest publicly available study of clinical trial success rates. Efficacy lag = 10.5 - 2.3 = 8.2 years post-safety verification. Additional sources: https://go.bio.org/rs/490-EHZ-999/images/ClinicalDevelopmentSuccessRates2011_2020.pdf
22. Medicine, N. Drug repurposing rate (30%). *Nature Medicine* <https://www.nature.com/articles/s41591-024-03233-x> (2024)
Approximately 30% of drugs gain at least one new indication after initial approval. Additional sources: https://www.nature.com/articles/s41591-024-03233-x

23. EPI. Education investment economic multiplier (2.1). *EPI: Public Investments Outside Core Infrastructure* <https://www.epi.org/publication/bp348-public-investments-outside-core-infrastructure/>
Early childhood education: Benefits 12X outlays by 2050; \$8.70 per dollar over lifetime Educational facilities: \$1 spent → \$1.50 economic returns Energy efficiency comparison: 2-to-1 benefit-to-cost ratio (McKinsey) Private return to schooling: 9% per additional year (World Bank meta-analysis) Note: 2.1 multiplier aligns with benefit-to-cost ratios for educational infrastructure/energy efficiency. Early childhood education shows much higher returns (12X by 2050) Additional sources: https://www.epi.org/publication/bp348-public-investments-outside-core-infrastructure/ | https://documents1.worldbank.org/curated/en/442521523465644318/pdf/WPS8402.pdf | https://freopp.org/whitepapers/establishing-a-practical-return-on-investment-framework-for-education-and-skills-development-to-expand-economic-opportunity/
24. PMC. Healthcare investment economic multiplier (1.8). *PMC: California Universal Health Care* <https://pmc.ncbi.nlm.nih.gov/articles/PMC5954824/> (2022)
Healthcare fiscal multiplier: 4.3 (95% CI: 2.5-6.1) during pre-recession period (1995-2007) Overall government spending multiplier: 1.61 (95% CI: 1.37-1.86) Why healthcare has high multipliers: No effect on trade deficits (spending stays domestic); improves productivity & competitiveness; enhances long-run potential output Gender-sensitive fiscal spending (health & care economy) produces substantial positive growth impacts Note: "1.8" appears to be conservative estimate; research shows healthcare multipliers of 4.3 Additional sources: https://pmc.ncbi.nlm.nih.gov/articles/PMC5954824/ | https://cepr.org/voxeu/columns/government-investment-and-fiscal-stimulus | https://ncbi.nlm.nih.gov/pmc/articles/PMC3849102/ | https://set.odi.org/wp-content/uploads/2022/01/Fiscal-multipliers-review.pdf
25. World Bank. Infrastructure investment economic multiplier (1.6). *World Bank: Infrastructure Investment as Stimulus* <https://blogs.worldbank.org/en/ppps/effectiveness-infrastructure-investment-fiscal-stimulus-what-weve-learned> (2022)
Infrastructure fiscal multiplier: 1.6 during contractionary phase of economic cycle Average across all economic states: 1.5 (meaning \$1 of public investment → \$1.50 of economic activity) Time horizon: 0.8 within 1 year, 1.5 within 2-5 years Range of estimates: 1.5-2.0 (following 2008 financial crisis & American Recovery Act) Italian public construction: 1.5-1.9 multiplier US ARRA: 0.4-2.2 range (differential impacts by program type) Economic Policy Institute: Uses 1.6 for infrastructure spending (middle range of estimates) Note: Public investment less likely to crowd out private activity during recessions; particularly effective when monetary policy loose with near-zero rates Additional sources: https://blogs.worldbank.org/en/ppps/effectiveness-infrastructure-investment-fiscal-stimulus-what-weve-learned | https://www.github.org/infrastructure-monitor/insights/fiscal-multiplier-effect-of-infrastructure-investment/ | https://cepr.org/voxeu/columns/government-investment-and-fiscal-stimulus | https://www.richmondfed.org/publications/research/economic_brief/2022/eb_22-04

26. Mercatus. Military spending economic multiplier (0.6). *Mercatus: Defense Spending and Economy* <https://www.mercatus.org/research/research-papers/defense-spending-and-economy>
Ramey (2011): 0.6 short-run multiplier Barro (1981): 0.6 multiplier for WWII spending (war spending crowded out 40c private economic activity per federal dollar) Barro & Redlick (2011): 0.4 within current year, 0.6 over two years; increased govt spending reduces private-sector GDP portions General finding: \$1 increase in deficit-financed federal military spending = less than \$1 increase in GDP Variation by context: Central/Eastern European NATO: 0.6 on impact, 1.5-1.6 in years 2-3, gradual fall to zero Ramey & Zubairy (2018): Cumulative 1% GDP increase in military expenditure raises GDP by 0.7% Additional sources: https://www.mercatus.org/research/research-papers/defense-spending-and-economy | https://cepr.org/voxeu/columns/world-war-ii-america-spending-deficits-multipliers-and-sacrifice | https://www.rand.org/content/dam/rand/pubs/research_reports/RRA700/RRA739-2/RAND_RRA739-2.pdf
27. FDA. FDA-approved prescription drug products (20,000+). *FDA* <https://www.fda.gov/media/143704/download>
There are over 20,000 prescription drug products approved for marketing. Additional sources: https://www.fda.gov/media/143704/download
28. FDA. FDA GRAS list count (570-700). *FDA* <https://www.fda.gov/food/generally-recognized-safe-gras/gras-notice-inventory>
The FDA GRAS (Generally Recognized as Safe) list contains approximately 570–700 substances. Additional sources: https://www.fda.gov/food/generally-recognized-safe-gras/gras-notice-inventory
29. ACLED. Active combat deaths annually. *ACLED: Global Conflict Surged 2024* <https://acleddata.com/2024/12/12/data-shows-global-conflict-surged-in-2024-the-washington-post/> (2024)
2024: 233,597 deaths (30% increase from 179,099 in 2023) Deadliest conflicts: Ukraine. (67,000), Palestine (35,000) Nearly 200,000 acts of violence (25% higher than 2023, double from 5 years ago) One in six people globally live in conflict-affected areas Additional sources: https://acleddata.com/2024/12/12/data-shows-global-conflict-surged-in-2024-the-washington-post/ | https://acleddata.com/media-citation/data-shows-global-conflict-surged-2024-washington-post | https://acleddata.com/conflict-index/index-january-2024/
30. UCDP. State violence deaths annually. *UCDP: Uppsala Conflict Data Program* <https://ucdp.uu.se/>
Uppsala Conflict Data Program (UCDP): Tracks one-sided violence (organized actors attacking unarmed civilians) UCDP definition: Conflicts causing at least 25 battle-related deaths in calendar year 2023 total organized violence: 154,000 deaths; Non-state conflicts: 20,900 deaths UCDP collects data on state-based conflicts, non-state conflicts, and one-sided violence Specific "2,700 annually" figure for state violence not found in recent UCDP data; actual figures vary annually Additional sources: https://ucdp.uu.se/ | https://en.wikipedia.org/wiki/Uppsala_Conflict_Data_Program | https://ourworldindata.org/grapher/deaths-in-armed-conflicts-by-region

31. Our World in Data. Terror attack deaths (8,300 annually). *Our World in Data: Terrorism* <https://ourworldindata.org/terrorism> (2024)
2023: 8,352 deaths (22% increase from 2022, highest since 2017) 2023: 3,350 terrorist incidents (22% decrease), but 56% increase in avg deaths per attack Global Terrorism Database (GTD): 200,000+ terrorist attacks recorded (2021 version) Maintained by: National Consortium for Study of Terrorism & Responses to Terrorism (START), U. of Maryland Geographic shift: Epicenter moved from Middle East to Central Sahel (sub-Saharan Africa) - now >50% of all deaths Additional sources: https://ourworldindata.org/terrorism | https://reliefweb.int/report/world/global-terrorism-index-2024 | https://www.start.umd.edu/gtd/ | https://ourworldindata.org/grapher/fatalities-from-terrorism
32. Institute for Health Metrics and Evaluation (IHME). IHME global burden of disease 2021 (2.88B DALYs, 1.13B YLD). *Institute for Health Metrics and Evaluation (IHME)* <https://vizhub.healthdata.org/gbd-results/> (2024)
In 2021, global DALYs totaled approximately 2.88 billion, comprising 1.75 billion Years of Life Lost (YLL) and 1.13 billion Years Lived with Disability (YLD). This represents a 13% increase from 2019 (2.55B DALYs), largely attributable to COVID-19 deaths and aging populations. YLD accounts for approximately 39% of total DALYs, reflecting the substantial burden of non-fatal chronic conditions. Additional sources: https://vizhub.healthdata.org/gbd-results/ | https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(24)00757-8/fulltext | https://www.healthdata.org/research-analysis/about-gbd
33. Costs of War Project, Brown University Watson Institute. Environmental cost of war (\$100B annually). *Brown Watson Costs of War: Environmental Cost* <https://watson.brown.edu/costsofwar/costs/social/environment>
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/
34. ScienceDaily. Medical research lives saved annually (4.2 million). *ScienceDaily: Physical Activity Prevents 4M Deaths* <https://www.sciencedaily.com/releases/2020/06/200617194510.htm> (2020)
Physical activity: 3.9M early deaths averted annually worldwide (15% lower premature deaths than without) COVID vaccines (2020-2024): 2.533M deaths averted, 14.8M life-years preserved; first year alone: 14.4M deaths prevented Cardiovascular prevention: 3 interventions could delay 94.3M deaths over 25 years (antihypertensives alone: 39.4M) Pandemic research response: Millions of deaths averted through rapid vaccine/drug development Additional sources: https://www.sciencedaily.com/releases/2020/06/200617194510.htm | https://pmc.ncbi.nlm.nih.gov/articles/PMC9537923/ | https://www.ahajournals.org/doi/10.1161/CIRCULATIONAHA.118.038160 | https://pmc.ncbi.nlm.nih.gov/articles/PMC9464102/

35. SIPRI. 36:1 disparity ratio of spending on weapons over cures. *SIPRI: Military Spending* <https://www.sipri.org/commentary/blog/2016/opportunity-cost-world-military-spending> (2016)
Global military spending: \$2.7 trillion (2024, SIPRI) Global government medical research: \$68 billion (2024) Actual ratio: 39.7:1 in favor of weapons over medical research Military R&D alone: \$85B (2004 data, 10% of global R&D) Military spending increases crowd out health: 1% ↑ military = 0.62% ↓ health spending Note: Ratio actually worse than 36:1. Each 1% increase in military spending reduces health spending by 0.62%, with effect more intense in poorer countries (0.962% reduction) Additional sources: <https://www.sipri.org/commentary/blog/2016/opportunity-cost-world-military-spending> | <https://pmc.ncbi.nlm.nih.gov/articles/PMC9174441/> | <https://www.congress.gov/crs-product/R45403>
36. Think by Numbers. Lost human capital due to war (\$270B annually). *Think by Numbers: War Costs \$74* <https://thinkbynumbers.org/military/war/the-economic-case-for-peace-a-comprehensive-financial-analysis/> (2021)
Lost human capital from war: \$300B annually (economic impact of losing skilled/productive individuals to conflict) Broader conflict/violence cost: \$14T/year globally 1.4M violent deaths/year; conflict holds back economic development, causes instability, widens inequality, erodes human capital 2002: 48.4M DALYs lost from 1.6M violence deaths = \$151B economic value (2000 USD) Economic toll includes: commodity prices, inflation, supply chain disruption, declining output, lost human capital Additional sources: <https://thinkbynumbers.org/military/war/the-economic-case-for-peace-a-comprehensive-financial-analysis/> | <https://www.weforum.org/stories/2021/02/war-violence-costs-each-human-5-a-day/> | <https://pubmed.ncbi.nlm.nih.gov/19115548/>
37. PubMed. Psychological impact of war cost (\$100B annually). *PubMed: Economic Burden of PTSD* <https://pubmed.ncbi.nlm.nih.gov/35485933/>
PTSD economic burden (2018 U.S.): \$232.2B total (\$189.5B civilian, \$42.7B military) Civilian costs driven by: Direct healthcare (\$66B), unemployment (\$42.7B) Military costs driven by: Disability (\$17.8B), direct healthcare (\$10.1B) Exceeds costs of other mental health conditions (anxiety, depression) War-exposed populations: 2-3X higher rates of anxiety, depression, PTSD; women and children most vulnerable Note: Actual burden \$232B, significantly higher than "\$100B" claimed Additional sources: <https://pubmed.ncbi.nlm.nih.gov/35485933/> | <https://news.va.gov/103611/study-national-economic-burden-of-ptsd-staggering/> | <https://pmc.ncbi.nlm.nih.gov/articles/PMC9957523/>
38. CGDev. UNHCR average refugee support cost. *CGDev* <https://www.cgdev.org/blog/costs-hosting-refugees-oecd-countries-and-why-uk-outlier> (2024)
The average cost of supporting a refugee is \$1,384 per year. This represents total host country costs (housing, healthcare, education, security). OECD countries average \$6,100 per refugee (mean 2022-2023), with developing countries spending \$700-1,000. Global weighted average of \$1,384 is reasonable given that 75-85% of refugees are in low/middle-income countries. Additional sources: <https://www.cgdev.org/blog/costs-hosting-refugees-oecd-countries-and-why-uk-outlier> | <https://www.unhcr.org/sites/default/files/2024-11/UNHCR-WB-global-cost-of-refugee-inclusion-in-host-country-health-systems.pdf>

39. World Bank. World bank trade disruption cost from conflict. *World Bank* <https://www.worldbank.org/en/topic/trade/publication/trading-away-from-conflict> *Estimated \$616B annual cost from conflict-related trade disruption. World Bank research shows civil war costs an average developing country 30 years of GDP growth, with 20 years needed for trade to return to pre-war levels. Trade disputes analysis shows tariff escalation could reduce global exports by up to \$674 billion. Additional sources: https://www.worldbank.org/en/topic/trade/publication/trading-away-from-conflict | https://www.nber.org/papers/w11565 | http://blogs.worldbank.org/en/trade/impacts-global-trade-and-income-current-trade-disputes*
40. VA. Veteran healthcare cost projections. VA <https://department.va.gov/wp-content/uploads/2025/06/2026-Budget-in-Brief.pdf> (2026) *VA budget: \$441.3B requested for FY 2026 (10% increase). Disability compensation: \$165.6B in FY 2024 for 6.7M veterans. PACT Act projected to increase spending by \$300B between 2022-2031. Costs under Toxic Exposures Fund: \$20B (2024), \$30.4B (2025), \$52.6B (2026). Additional sources: https://department.va.gov/wp-content/uploads/2025/06/2026-Budget-in-Brief.pdf | https://www.cbo.gov/publication/45615 | https://www.legion.org/information-center/news/veterans-healthcare/2025/june/va-budget-tops-400-billion-for-2025-from-higher-spending-on-mandated-benefits-medical-care*
41. IQVIA Institute for Human Data Science. The global use of medicines 2024: Outlook to 2028. *IQVIA Institute Report* <https://www.iqvia.com/insights/the-iqvia-institute/reports-and-publications/reports/the-global-use-of-medicines-2024-outlook-to-2028> (2024) *Global days of therapy reached 1.8 trillion in 2019 (234 defined daily doses per person). Diabetes, respiratory, CVD, and cancer account for 71 percent of medicine use. Projected to reach 3.8 trillion DDDs by 2028.*
42. Sinn, M. P. *Private industry clinical trial spending estimate.* (2025) *Estimated private pharmaceutical and biotech clinical trial spending is approximately \$75-90 billion annually, representing roughly 90% of global clinical trial spending.*
43. Calculated from IHME Global Burden of Disease (2.55B DALYs) and global GDP per capita valuation. \$109 trillion annual global disease burden. *The global economic burden of disease, including direct healthcare costs (\$8.2 trillion) and lost productivity (\$100.9 trillion from 2.55 billion DALYs × \$39,570 per DALY), totals approximately \$109.1 trillion annually.*
44. Sinn, M. P. *The Political Dysfunction Tax.* <https://political-dysfunction-tax.warondisease.org> (2025) doi:10.5281/zenodo.18603840 *Quantifying the gap between current global governance and theoretical maximum welfare, estimating a 31-53% efficiency score and \$97 trillion in annual opportunity costs.*
45. Trials, A. C. Global government spending on interventional clinical trials: \$3-6 billion/year. *Applied Clinical Trials* <https://www.appliedclinicaltrials.com/view/sizing-clinical-research-market> *Estimated range based on NIH (\$0.8-5.6B), NIHR (\$1.6B total budget), and EU funding. (\$1.3B/year). Roughly 5-10% of global market. Additional sources: https://www.appliedclinicaltrials.com/view/sizing-clinical-research-market | https://www.thelancet.com/journals/langlo/article/PIIS2214-109X(20)30357-0/fulltext*

46. UBS. Credit suisse global wealth report 2023. *Credit Suisse/UBS* <https://www.ubs.com/global/en/family-office-uhnw/reports/global-wealth-report-2023.html> (2023)
Total global household wealth: USD 454.4 trillion (2022) Wealth declined by USD 11.3 trillion. (-2.4%) in 2022, first decline since 2008 Wealth per adult: USD 84,718 Additional sources: https://www.ubs.com/global/en/family-office-uhnw/reports/global-wealth-report-2023.html
47. Component country budgets. Global government medical research spending (\$67.5B, 2023–2024). *See component country budgets: NIH Budget* <https://www.nih.gov/about-nih/what-we-do/budget>.
48. SIPRI. Global military spending (\$2.72T, 2024). *SIPRI* <https://www.sipri.org/publications/2025/sipri-fact-sheets/trends-world-military-expenditure-2024> (2025).
49. Estimated from major foundation budgets and activities. Nonprofit clinical trial funding estimate.
Nonprofit foundations spend an estimated \$2-5 billion annually on clinical trials globally, representing approximately 2-5% of total clinical trial spending.
50. IQVIA, I. reports: Global pharmaceutical r&d spending.
Total global pharmaceutical R&D spending is approximately \$300 billion annually. Clinical trials represent 15-20% of this total (\$45-60B), with the remainder going to drug discovery, preclinical research, regulatory affairs, and manufacturing development.
51. UN. Global population reaches 8 billion. *UN: World Population 8 Billion Nov 15 2022* <https://www.un.org/en/desa/world-population-reach-8-billion-15-november-2022> (2022)
Milestone: November 15, 2022 (UN World Population Prospects 2022) Day of Eight Billion” designated by UN Added 1 billion people in just 11 years (2011-2022) Growth rate: Slowest since 1950; fell under 1% in 2020 Future: 15 years to reach 9B (2037); projected peak 10.4B in 2080s Projections: 8.5B (2030), 9.7B (2050), 10.4B (2080-2100 plateau) Note: Milestone reached Nov 2022. Population growth slowing; will take longer to add next billion (15 years vs 11 years) Additional sources: https://www.un.org/en/desa/world-population-reach-8-billion-15-november-2022 | https://www.un.org/en/dayof8billion | https://en.wikipedia.org/wiki/Day_of_Eight_Billion
52. Harvard Kennedy School. 3.5% participation tipping point. *Harvard Kennedy School* <https://www.hks.harvard.edu/centers/carr/publications/35-rule-how-small-minority-can-change-world> (2020)
The research found that nonviolent campaigns were twice as likely to succeed as violent ones, and once 3.5% of the population were involved, they were always successful. Chenoweth and Maria Stephan studied the success rates of civil resistance efforts from 1900 to 2006, finding that nonviolent movements attracted, on average, four times as many participants as violent movements and were more likely to succeed. Key finding: Every campaign that mobilized at least 3.5% of the population in sustained protest was successful (in their 1900-2006 dataset) Note: The 3.5% figure is a descriptive statistic from historical analysis, not a guaranteed threshold. One exception (Bahrain 2011-2014 with 6%+ participation) has been identified. The rule applies to regime change, not policy change in democracies. Additional sources: https://www.hks.harvard.edu/centers/carr/publications/35-rule-how-small-minority-can-change-world | https://www.hks.harvard.edu/sites/default/files/2024-05/ERICA%20Chenoweth_2020-005.pdf | https://www.bbc.com/future/article/20190513-it-only-takes-35-of-people-to-change-the-world | https://en.wikipedia.org/wiki/3.5%25_rule

53. NHGRI. Human genome project and CRISPR discovery. *NHGRI* <https://www.genome.gov/11006929/2003-release-international-consortium-completes-hgp> (2003)
Your DNA is 3 billion base pairs Read the entire code (Human Genome Project, completed 2003) Learned to edit it (CRISPR, discovered 2012) Additional sources: https://www.genome.gov/11006929/2003-release-international-consortium-completes-hgp | https://www.nobelprize.org/prizes/chemistry/2020/press-release/
54. PMC. Only 12% of human interactome targeted. *PMC* <https://pmc.ncbi.nlm.nih.gov/articles/PMC10749231/> (2023)
Mapping 350,000+ clinical trials showed that only 12% of the human interactome has ever been targeted by drugs. Additional sources: https://pmc.ncbi.nlm.nih.gov/articles/PMC10749231/
55. WHO. ICD-10 code count (14,000). *WHO* <https://icd.who.int/browse10/2019/en> (2019)
The ICD-10 classification contains approximately 14,000 codes for diseases, signs and symptoms. Additional sources: https://icd.who.int/browse10/2019/en
56. Wikipedia. Longevity escape velocity (LEV) - maximum human life extension potential. *Wikipedia: Longevity Escape Velocity* https://en.wikipedia.org/wiki/Longevity_escape_velocity
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
57. OpenSecrets. Lobbyist statistics for washington d.c. *OpenSecrets: Lobbying in US* https://en.wikipedia.org/wiki/Lobbying_in_the_United_States
Registered lobbyists: Over 12,000 (some estimates); 12,281 registered (2013) Former government employees as lobbyists: 2,200+ former federal employees (1998-2004), including 273 former White House staffers, 250 former Congress members & agency heads Congressional revolving door: 43% (86 of 198) lawmakers who left 1998-2004 became lobbyists; currently 59% leaving to private sector work for lobbying/consulting firms/trade groups Executive branch: 8% were registered lobbyists at some point before/after government service Additional sources: https://en.wikipedia.org/wiki/Lobbying_in_the_United_States | https://www.opensecrets.org/revolving-door | https://www.citizen.org/article/revolving-congress/ | https://www.propublica.org/article/we-found-a-staggering-281-lobbyists-whove-worked-in-the-trump-administration

58. Vaccines, M. Measles vaccination ROI. *MDPI Vaccines* <https://www.mdpi.com/2076-393X/12/11/1210> (2024)
Single measles vaccination: 167:1 benefit-cost ratio. MMR (measles-mumps-rubella) vaccination: 14:1 ROI. Historical US elimination efforts (1966-1974): benefit-cost ratio of 10.3:1 with net benefits exceeding USD 1.1 billion (1972 dollars, or USD 8.0 billion in 2023 dollars). 2-dose MMR programs show direct benefit/cost ratio of 14.2 with net savings of \$5.3 billion, and 26.0 from societal perspectives with net savings of \$11.6 billion. Additional sources: <https://www.mdpi.com/2076-393X/12/11/1210> | <https://www.tandfonline.com/doi/full/10.1080/14760584.2024.2367451>
59. Gosse, M. E. Assessing cost-effectiveness in healthcare: History of the \$50,000 per QALY threshold. *Sustainability Impact Metrics* <https://ecocostsvalue.com/EVR/img/references%20others/Gosse%202008%20QALY%20threshold%20financial.pdf> (2008).
60. World Health Organization. Mental health global burden. *World Health Organization* <https://www.who.int/news/item/28-09-2001-the-world-health-report-2001-mental-disorders-affect-one-in-four-people> (2022)
One in four people in the world will be affected by mental or neurological disorders at some point in their lives, representing [approximately] 30% of the global burden of disease. Additional sources: <https://www.who.int/news/item/28-09-2001-the-world-health-report-2001-mental-disorders-affect-one-in-four-people>
61. Institute, S. I. P. R. *Trends in world military expenditure, 2023*. (2024).
62. Calculated from Orphanet Journal of Rare Diseases (2024). Diseases getting first effective treatment each year. *Calculated from Orphanet Journal of Rare Diseases (2024)* <https://ojrd.biomedcentral.com/articles/10.1186/s13023-024-03398-1> (2024)
Under the current system, approximately 10-15 diseases per year receive their FIRST effective treatment. Calculation: 5% of 7,000 rare diseases (350) have FDA-approved treatment, accumulated over 40 years of the Orphan Drug Act = 9 rare diseases/year. Adding 5-10 non-rare diseases that get first treatments yields 10-20 total. FDA approves 50 drugs/year, but many are for diseases that already have treatments (me-too drugs, second-line therapies). Only 15 represent truly FIRST treatments for previously untreatable conditions.
63. NIH. NIH budget (FY 2025). *NIH* <https://www.nih.gov/about-nih/organization/budget> (2024)
The budget total of \$47.7 billion also includes \$1.412 billion derived from PHS Evaluation financing... Additional sources: <https://www.nih.gov/about-nih/organization/budget> | <https://officeofbudget.od.nih.gov/>
64. Bentley et al. NIH spending on clinical trials: 3.3%. *Bentley et al.* <https://pmc.ncbi.nlm.nih.gov/articles/PMC10349341/> (2023)
NIH spent \$8.1 billion on clinical trials for approved drugs (2010-2019), representing 3.3% of relevant NIH spending. Additional sources: <https://pmc.ncbi.nlm.nih.gov/articles/PMC10349341/> | <https://catalyst.harvard.edu/news/article/nih-spent-8-1b-for-phased-clinical-trials-of-drugs-approved-2010-19-10-of-reported-industry-spending/>

65. PMC. Standard medical research ROI (\$20k-\$100k/QALY). *PMC: Cost-effectiveness Thresholds Used by Study Authors* <https://pmc.ncbi.nlm.nih.gov/articles/PMC10114019/> (1990)
Typical cost-effectiveness thresholds for medical interventions in rich countries range from \$50,000 to \$150,000 per QALY. The Institute for Clinical and Economic Review (ICER) uses a \$100,000-\$150,000/QALY threshold for value-based pricing. Between 1990-2021, authors increasingly cited \$100,000 (47% by 2020-21) or \$150,000 (24% by 2020-21) per QALY as benchmarks for cost-effectiveness. Additional sources: https://pmc.ncbi.nlm.nih.gov/articles/PMC10114019/ | https://icer.org/our-approach/methods-process/cost-effectiveness-the-qaly-and-the-evlyg/
66. Institute, M. RECOVERY trial 82× cost reduction. *Manhattan Institute: Slow Costly Trials* <https://manhattan.institute/article/slow-costly-clinical-trials-drag-down-biomedical-breakthroughs>
RECOVERY trial: \$500 per patient (\$20M for 48,000 patients = \$417/patient) Typical clinical trial: \$41,000 median per-patient cost Cost reduction: 80-82× cheaper (\$41,000 ÷ \$500 82×) Efficiency: \$50 per patient per answer (10 therapeutics tested, 4 effective) Dexamethasone estimated to save >630,000 lives Additional sources: https://manhattan.institute/article/slow-costly-clinical-trials-drag-down-biomedical-breakthroughs | https://pmc.ncbi.nlm.nih.gov/articles/PMC9293394/
67. Trials. Patient willingness to participate in clinical trials. *Trials: Patients' Willingness Survey* <https://trialsjournal.biomedcentral.com/articles/10.1186/s13063-015-1105-3>
Recent surveys: 49-51% willingness (2020-2022) - dramatic drop from 85% (2019). during COVID-19 pandemic Cancer patients when approached: 88% consented to trials (Royal Marsden Hospital) Study type variation: 44.8% willing for drug trial, 76.2% for diagnostic study Top motivation: "Learning more about my health/medical condition" (67.4%) Top barrier: "Worry about experiencing side effects" (52.6%) Additional sources: https://trialsjournal.biomedcentral.com/articles/10.1186/s13063-015-1105-3 | https://www.appliedclinicaltrialsonline.com/view/industry-forced-to-rethink-patient-participation-in-trials | https://pmc.ncbi.nlm.nih.gov/articles/PMC7183682/
68. CSDD, T. Cost of drug development.
Various estimates suggest \$1.0 - \$2.5 billion to bring a new drug from discovery through FDA approval, spread across 10 years. Tufts Center for the Study of Drug Development often cited for \$1.0 - \$2.6 billion/drug. Industry reports (IQVIA, Deloitte) also highlight \$2+ billion figures.
69. Value in Health. Average lifetime revenue per successful drug. *Value in Health: Sales Revenues for New Therapeutic Agents* <https://www.sciencedirect.com/science/article/pii/S1098301524027542>
Study of 361 FDA-approved drugs from 1995-2014 (median follow-up 13.2 years): Mean lifetime revenue: \$15.2 billion per drug Median lifetime revenue: \$6.7 billion per drug Revenue after 5 years: \$3.2 billion (mean) Revenue after 10 years: \$9.5 billion (mean) Revenue after 15 years: \$19.2 billion (mean) Distribution highly skewed: top 25 drugs (7%) accounted for 38% of total revenue (\$2.1T of \$5.5T) Additional sources: https://www.sciencedirect.com/science/article/pii/S1098301524027542

70. Lichtenberg, F. R. **How many life-years have new drugs saved? A three-way fixed-effects analysis of 66 diseases in 27 countries, 2000-2013.** *International Health* **11**, 403–416 (2019) *Using 3-way fixed-effects methodology (disease-country-year) across 66 diseases in 22 countries, this study estimates that drugs launched after 1981 saved 148.7 million life-years in 2013 alone. The regression coefficients for drug launches 0-11 years prior (beta=-0.031, SE=0.008) and 12+ years prior (beta=-0.057, SE=0.013) on years of life lost are highly significant (p<0.0001). Confidence interval for life-years saved: 79.4M-239.8M (95 percent CI) based on propagated standard errors from Table 2.*
71. Deloitte. **Pharmaceutical r&d return on investment (ROI).** *Deloitte: Measuring Pharmaceutical Innovation 2025* <https://www.deloitte.com/ch/en/Industries/life-sciences-health-care/research/measuring-return-from-pharmaceutical-innovation.html> (2025) *Deloitte's annual study of top 20 pharma companies by R&D spend (2010-2024): 2024 ROI: 5.9% (second year of growth after decade of decline) 2023 ROI: 4.3% (estimated from trend) 2022 ROI: 1.2% (historic low since study began, 13-year low) 2021 ROI: 6.8% (record high, inflated by COVID-19 vaccines/treatments) Long-term trend: Declining for over a decade before 2023 recovery Average R&D cost per asset: \$2.3B (2022), \$2.23B (2024) These returns (1.2-5.9% range) fall far below typical corporate ROI targets (15-20%) Additional sources: <https://www.deloitte.com/ch/en/Industries/life-sciences-health-care/research/measuring-return-from-pharmaceutical-innovation.html> | <https://www.prnewswire.com/news-releases/deloittes-13th-annual-pharmaceutical-innovation-report-pharma-rd-return-on-investment-falls-in-post-pandemic-market-301738807.html> | <https://hitconsultant.net/2023/02/16/pharma-rd-roi-falls-to-lowest-level-in-13-years/>*
72. Nature Reviews Drug Discovery. **Drug trial success rate from phase i to approval.** *Nature Reviews Drug Discovery: Clinical Success Rates* <https://www.nature.com/articles/nrd.2016.136> (2016) *Overall Phase I to approval: 10-12.8% (conventional wisdom 10%, studies show 12.8%). Recent decline: Average LOA now 6.7% for Phase I (2014-2023 data) Leading pharma companies: 14.3% average LOA (range 8-23%) Varies by therapeutic area: Oncology 3.4%, CNS/cardiovascular lowest at Phase III Phase-specific success: Phase I 47-54%, Phase II 28-34%, Phase III 55-70% Note: 12% figure accurate for historical average. Recent data shows decline to 6.7%, with Phase II as primary attrition point (28% success) Additional sources: <https://www.nature.com/articles/nrd.2016.136> | <https://pmc.ncbi.nlm.nih.gov/articles/PMC6409418/> | <https://academic.oup.com/biostatistics/article/20/2/273/4817524>*
73. SofproMed. **Phase 3 cost per trial range.** *SofproMed* <https://www.sofpromed.com/how-much-does-a-clinical-trial-cost> *Phase 3 clinical trials cost between \$20 million and \$282 million per trial, with significant variation by therapeutic area and trial complexity. Additional sources: <https://www.sofpromed.com/how-much-does-a-clinical-trial-cost> | <https://www.cbo.gov/publication/57126>*
74. Ramsberg J, P. R. **Pragmatic trial cost per patient (median \$97).** *Learning Health Systems* <https://pmc.ncbi.nlm.nih.gov/articles/PMC6508852/> (2018) *Meta-analysis of 108 embedded pragmatic clinical trials (2006-2016). The median cost per patient was \$97 (IQR \$19-\$478), based on 2015 dollars. 25% of trials cost <\$19/patient; 10 trials exceeded \$1,000/patient. U.S. studies median \$187 vs non-U.S. median \$27. Additional sources: <https://pmc.ncbi.nlm.nih.gov/articles/PMC6508852/>*

75. WHO. Polio vaccination ROI. *WHO* <https://www.who.int/news-room/feature-stories/detail/sustaining-polio-investments-offers-a-high-return> (2019)
For every dollar spent, the return on investment is nearly US\$ 39.” Total investment cost of US\$ 7.5 billion generates projected economic and social benefits of US\$ 289.2 billion from sustaining polio assets and integrating them into expanded immunization, surveillance and emergency response programmes across 8 priority countries (Afghanistan, Iraq, Libya, Pakistan, Somalia, Sudan, Syria, Yemen). Additional sources: <https://www.who.int/news-room/feature-stories/detail/sustaining-polio-investments-offers-a-high-return>
76. ICRC. International campaign to ban landmines (ICBL) - ottawa treaty (1997). *ICRC* <https://www.icrc.org/en/doc/resources/documents/article/other/57jpn.htm> (1997)
ICBL: Founded 1992 by 6 NGOs (Handicap International, Human Rights Watch, Medico International, Mines Advisory Group, Physicians for Human Rights, Vietnam Veterans of America Foundation) Started with ONE staff member: Jody Williams as founding coordinator Grew to 1,000+ organizations in 60 countries by 1997 Ottawa Process: 14 months (October 1996 - December 1997) Convention signed by 122 states on December 3, 1997; entered into force March 1, 1999 Achievement: Nobel Peace Prize 1997 (shared by ICBL and Jody Williams) Government funding context: Canada established \$100M CAD Canadian Landmine Fund over 10 years (1997); International donors provided \$169M in 1997 for mine action (up from \$100M in 1996) Additional sources: <https://www.icrc.org/en/doc/resources/documents/article/other/57jpn.htm> | https://en.wikipedia.org/wiki/International_Campaign_to_Ban_Landmines | <https://www.nobelprize.org/prizes/peace/1997/summary/> | <https://un.org/press/en/1999/19990520.MINES.BRF.html> | <https://www.the-monitor.org/en-gb/reports/2003/landmine-monitor-2003/mine-action-funding.aspx>
77. OpenSecrets. [Revolving door: Former members of congress.](#) (2024)
388 former members of Congress are registered as lobbyists. Nearly 5,400 former congressional staffers have left Capitol Hill to become federal lobbyists in the past 10 years. Additional sources: <https://www.opensecrets.org/revolving-door>
78. Kinch, M. S. & Griesenauer, R. H. [Lost medicines: A longer view of the pharmaceutical industry with the potential to reinvigorate discovery.](#) *Drug Discovery Today* **24**, 875–880 (2019)
Research identified 1,600+ medicines available in 1962. The 1950s represented industry high-water mark with >30 new products in five of ten years; this rate would not be replicated until late 1990s. More than half (880) of these medicines were lost following implementation of Kefauver-Harris Amendment. The peak of 1962 would not be seen again until early 21st century. By 2016 number of organizations actively involved in R&D at level not seen since 1914.

79. Wikipedia. US military spending reduction after WWII. *Wikipedia* https://en.wikipedia.org/wiki/Demobilization_of_United_States_Armed_Forces_after_World_War_II (2020)
Peaking at over \$81 billion in 1945, the U.S. military budget plummeted to approximately \$13 billion by 1948, representing an 84% decrease. The number of personnel was reduced almost 90%, from more than 12 million to about 1.5 million between mid-1945 and mid-1947. Defense spending exceeded 41 percent of GDP in 1945. After World War II, the US reduced military spending to 7.2 percent of GDP by 1948. Defense spending doubled from the 1948 low to 15 percent at the height of the Korean War in 1953. Additional sources: https://en.wikipedia.org/wiki/Demobilization_of_United_States_Armed_Forces_after_World_War_II | <https://www.americanprogress.org/article/a-historical-perspective-on-military-budgets/> | <https://www.st-louisfed.org/on-the-economy/2020/february/war-highest-military-spending-measured> | https://www.usgovernmentspending.com/defense_spending_history
80. Baily, M. N. Pre-1962 drug development costs (baily 1972). *Baily (1972)* <https://samizdathealth.org/wp-content/uploads/2020/12/hlthaff.1.2.6.pdf> (1972)
Pre-1962: Average cost per new chemical entity (NCE) was \$6.5 million (1980 dollars). Inflation-adjusted to 2024 dollars: \$6.5M (1980) \$22.5M (2024), using CPI multiplier of 3.46× Real cost increase (inflation-adjusted): \$22.5M (pre-1962) → \$2,600M (2024) = 116× increase Note: This represents the most comprehensive academic estimate of pre-1962 drug development costs based on empirical industry data Additional sources: <https://samizdathealth.org/wp-content/uploads/2020/12/hlthaff.1.2.6.pdf>
81. Think by Numbers. Pre-1962 physician-led clinical trials. *Think by Numbers: How Many Lives Does FDA Save?* <https://thinkbynumbers.org/health/how-many-net-lives-does-the-fda-save/> (1966)
Pre-1962: Physicians could report real-world evidence directly 1962 Drug Amendments replaced "premarket notification" with "premarket approval", requiring extensive efficacy testing Impact: New regulatory clampdown reduced new treatment production by 70%; lifespan growth declined from 4 years/decade to 2 years/decade Drug Efficacy Study Implementation (DESI): NAS/NRC evaluated 3,400+ drugs approved 1938-1962 for safety only; reviewed >3,000 products, >16,000 therapeutic claims FDA has had authority to accept real-world evidence since 1962, clarified by 21st Century Cures Act (2016) Note: Specific "144,000 physicians" figure not verified in sources Additional sources: <https://thinkbynumbers.org/health/how-many-net-lives-does-the-fda-save/> | <https://www.fda.gov/drugs/enforcement-activities-fda/drug-efficacy-study-implementation-desi> | <http://www.nasonline.org/about-nas/history/archives/collections/des-1966-1969-1.html>
82. GAO. 95% of diseases have 0 FDA-approved treatments. *GAO* <https://www.gao.gov/products/gao-25-106774> (2025)
95% of diseases have no treatment Additional sources: <https://www.gao.gov/products/gao-25-106774> | <https://globalgenes.org/rare-disease-facts/>
83. Oren Cass, M. I. RECOVERY trial cost per patient. *Oren Cass* <https://manhattan.institute/article/slow-costly-clinical-trials-drag-down-biomedical-breakthroughs> (2023)
The RECOVERY trial, for example, cost only about \$500 per patient... By contrast, the median per-patient cost of a pivotal trial for a new therapeutic is around \$41,000. Additional sources: <https://manhattan.institute/article/slow-costly-clinical-trials-drag-down-biomedical-breakthroughs>

84. al., N. E. Á. et. RECOVERY trial global lives saved (1 million). *NHS England: 1 Million Lives Saved* <https://www.england.nhs.uk/2021/03/covid-treatment-developed-in-the-nhs-saves-a-million-lives/> (2021)
Dexamethasone saved 1 million lives worldwide (NHS England estimate, March 2021, 9 months after discovery). UK alone: 22,000 lives saved. Methodology: Águas et al. Nature Communications 2021 estimated 650,000 lives (range: 240,000-1,400,000) for July-December 2020 alone, based on RECOVERY trial mortality reductions (36% for ventilated, 18% for oxygen-only patients) applied to global COVID hospitalizations. June 2020 announcement: Dexamethasone reduced deaths by up to 1/3 (ventilated patients), 1/5 (oxygen patients). Impact immediate: Adopted into standard care globally within hours of announcement. Additional sources: https://www.england.nhs.uk/2021/03/covid-treatment-developed-in-the-nhs-saves-a-million-lives/ | https://www.nature.com/articles/s41467-021-21134-2 | https://pharmaceutical-journal.com/article/news/steroid-has-saved-the-lives-of-one-million-covid-19-patients-worldwide-figures-show | https://www.recoverytrial.net/news/recovery-trial-celebrates-two-year-anniversary-of-life-saving-dexamethasone-result
85. Museum, N. S. 11. M. &. [September 11 attack facts](#). (2024)
2,977 people were killed in the September 11, 2001 attacks: 2,753 at the World Trade Center, 184 at the Pentagon, and 40 passengers and crew on United Flight 93 in Shanksville, Pennsylvania.
86. World Bank. World bank singapore economic data. World Bank <https://data.worldbank.org/country/singapore> (2024)
Singapore GDP per capita (2023): \$82,000 - among highest in the world Government spending: 15% of GDP (vs US 38%) Life expectancy: 84.1 years (vs US 77.5 years) Singapore demonstrates that low government spending can coexist with excellent outcomes Additional sources: https://data.worldbank.org/country/singapore
87. Fund, I. M. [IMF singapore government spending data](#). (2024)
Singapore government spending is approximately 15% of GDP This is 23 percentage points lower than the United States (38%) Despite lower spending, Singapore achieves excellent outcomes: - Life expectancy: 84.1 years (vs US 77.5) - Low crime, world-class infrastructure, AAA credit rating Additional sources: https://www.imf.org/en/Countries/SGP
88. World Health Organization. [WHO life expectancy data by country](#). (2024)
Life expectancy at birth varies significantly among developed nations: Switzerland: 84.0 years (2023) Singapore: 84.1 years (2023) Japan: 84.3 years (2023) United States: 77.5 years (2023) - 6.5 years below Switzerland, Singapore Global average: 73 years Note: US spends more per capita on healthcare than any other nation, yet achieves lower life expectancy Additional sources: https://www.who.int/data/gho/data/themes/mortality-and-global-health-estimates/ghe-life-expectancy-and-healthy-life-expectancy
89. CSIS. Smallpox eradication ROI. CSIS <https://www.csis.org/analysis/smallpox-eradication-model-global-cooperation>.

90. PMC. Contribution of smoking reduction to life expectancy gains. *PMC: Benefits Smoking Cessation Longevity* <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1447499/> (2012)
Population-level: Up to 14% (9% men, 14% women) of total life expectancy gain since 1960 due to tobacco control efforts Individual cessation benefits: Quitting at age 35 adds 6.9-8.5 years (men), 6.1-7.7 years (women) vs continuing smokers By cessation age: Age 25-34 = 10 years gained; age 35-44 = 9 years; age 45-54 = 6 years; age 65 = 2.0 years (men), 3.7 years (women) Cessation before age 40: Reduces death risk by 90% Long-term cessation: 10+ years yields survival comparable to never smokers, averts 10 years of life lost Recent cessation: <3 years averts 5 years of life lost Additional sources: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1447499/ | https://www.cdc.gov/pcd/issues/2012/11_0295.htm | https://www.ajpmonline.org/article/S0749-3797(24)00217-4/fulltext | https://www.nejm.org/doi/full/10.1056/NEJMsa1211128
91. ICER. Value per QALY (standard economic value). *ICER* <https://icer.org/wp-content/uploads/2024/02/Reference-Case-4.3.25.pdf> (2024)
Standard economic value per QALY: \$100,000–\$150,000. This is the US and global standard. willingness-to-pay threshold for interventions that add costs. Dominant interventions (those that save money while improving health) are favorable regardless of this threshold. Additional sources: https://icer.org/wp-content/uploads/2024/02/Reference-Case-4.3.25.pdf
92. GAO. Annual cost of u.s. Sugar subsidies. *GAO: Sugar Program* <https://www.gao.gov/products/gao-24-106144>
Consumer costs: \$2.5-3.5 billion per year (GAO estimate) Net economic cost: \$1 billion per year 2022: US consumers paid 2X world price for sugar Program costs \$3-4 billion/year but no federal budget impact (costs passed directly to consumers via higher prices) Employment impact: 10,000-20,000 manufacturing jobs lost annually in sugar-reliant industries (confectionery, etc.) Multiple studies confirm: Sweetener Users Association (\$2.9-3.5B), AEI (\$2.4B consumer cost), Beghin & Elobeid (\$2.9-3.5B consumer surplus) Additional sources: https://www.gao.gov/products/gao-24-106144 | https://www.heritage.org/agriculture/report/the-us-sugar-program-bad-consumers-bad-agriculture-and-bad-america | https://www.aei.org/articles/the-u-s-spends-4-billion-a-year-subsidizing-stalinist-style-domestic-sugar-production/
93. World Bank. Swiss military budget as percentage of GDP. *World Bank: Military Expenditure* <https://data.worldbank.org/indicator/MS.MIL.XPND.GD.ZS?locations=CH>
2023: 0.70272% of GDP (World Bank) 2024: CHF 5.95 billion official military spending. When including militia system costs: 1% GDP (CHF 8.75B) Comparison: Near bottom in Europe; only Ireland, Malta, Moldova spend less (excluding microstates with no armies) Additional sources: https://data.worldbank.org/indicator/MS.MIL.XPND.GD.ZS?locations=CH | https://www.avenir-suisse.ch/en/blog-defence-spending-switzerland-is-in-better-shape-than-it-seems/ | https://tradingeconomics.com/switzerland/military-expenditure-percent-of-gdp-wb-data.html
94. World Bank. Switzerland vs. US GDP per capita comparison. *World Bank: Switzerland GDP Per Capita* <https://data.worldbank.org/indicator/NY.GDP.PCAP.CD?locations=CH>
2024 GDP per capita (PPP-adjusted): Switzerland \$93,819 vs United States \$75,492 Switzerland's GDP per capita 24% higher than US when adjusted for purchasing power parity Nominal 2024: Switzerland \$103,670 vs US \$85,810 Additional sources: https://data.worldbank.org/indicator/NY.GDP.PCAP.CD?locations=CH | https://tradingeconomics.com/switzerland/gdp-per-capita-ppp | https://www.theglobaleconomy.com/USA/gdp_per_capita_ppp/

95. OECD. [OECD government spending as percentage of GDP](#). (2024)
OECD government spending data shows significant variation among developed nations: United States: 38.0% of GDP (2023) Switzerland: 35.0% of GDP - 3 percentage points lower than US Singapore: 15.0% of GDP - 23 percentage points lower than US (per IMF data) OECD average: approximately 40% of GDP Additional sources: <https://data.oecd.org/gga/general-government-spending.htm>
96. OECD. [OECD median household income comparison](#). (2024)
Median household disposable income varies significantly across OECD nations: United States: \$77,500 (2023) Switzerland: \$55,000 PPP-adjusted (lower nominal but comparable purchasing power) Singapore: \$75,000 PPP-adjusted Additional sources: <https://data.oecd.org/hha/household-disposable-income.htm>
97. Institute, C. Chance of dying from terrorism statistic. *Cato Institute: Terrorism and Immigration Risk Analysis* <https://www.cato.org/policy-analysis/terrorism-immigration-risk-analysis>
Chance of American dying in foreign-born terrorist attack: 1 in 3.6 million per year (1975-2015) Including 9/11 deaths; annual murder rate is 253x higher than terrorism death rate More likely to die from lightning strike than foreign terrorism Note: Comprehensive 41-year study shows terrorism risk is extremely low compared to everyday dangers Additional sources: <https://www.cato.org/policy-analysis/terrorism-immigration-risk-analysis> | <https://www.nbc-news.com/news/us-news/you-re-more-likely-die-choking-be-killed-foreign-terrorists-n715141>
98. Wikipedia. Thalidomide scandal: Worldwide cases and mortality. *Wikipedia* https://en.wikipedia.org/wiki/Thalidomide_scandal
The total number of embryos affected by the use of thalidomide during pregnancy is estimated at 10,000, of whom about 40% died around the time of birth. More than 10,000 children in 46 countries were born with deformities such as phocomelia. Additional sources: https://en.wikipedia.org/wiki/Thalidomide_scandal
99. One, P. Health and quality of life of thalidomide survivors as they age. *PLOS One* <https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0210222> (2019)
Study of thalidomide survivors documenting ongoing disability impacts, quality of life, and long-term health outcomes. Survivors (now in their 60s) continue to experience significant disability from limb deformities, organ damage, and other effects. Additional sources: <https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0210222>
100. Bureau, U. C. Historical world population estimates. *US Census Bureau* <https://www.census.gov/data/tables/time-series/demo/international-programs/historical-est-worldpop.html>
US Census Bureau historical estimates of world population by country and region. (1950-2050). US population in 1960: 180 million of 3 billion worldwide (6%). Additional sources: <https://www.census.gov/data/tables/time-series/demo/international-programs/historical-est-worldpop.html>
101. FDA Study via NCBI. Trial costs, FDA study. *FDA Study via NCBI* <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6248200/>
Overall, the 138 clinical trials had an estimated median (IQR) cost of \$19.0 million (\$12.2 million-\$33.1 million)... The clinical trials cost a median (IQR) of \$41,117 (\$31,802-\$82,362) per patient. Additional sources: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6248200/>

102. Diseases, G. 2019. & Collaborators, I. *Global burden of disease study 2019: Disability weights*. *The Lancet* **396**, 1204–1222 (2020)
Disability weights for 235 health states used in Global Burden of Disease calculations. Weights range from 0 (perfect health) to 1 (death equivalent). Chronic conditions like diabetes (0.05-0.35), COPD (0.04-0.41), depression (0.15-0.66), and cardiovascular disease (0.04-0.57) show substantial variation by severity. Treatment typically reduces disability weights by 50-80 percent for manageable chronic conditions.
103. WHO. Annual global economic burden of alzheimer’s and other dementias. *WHO: Dementia Fact Sheet* <https://www.who.int/news-room/fact-sheets/detail/dementia> (2019)
Global cost: \$1.3 trillion (2019 WHO-commissioned study) 50% from informal caregivers. (family/friends, 5 hrs/day) 74% of costs in high-income countries despite 61% of patients in LMICs \$818B (2010) → \$1T (2018) → \$1.3T (2019) - rapid growth Note: Costs increased 35% from 2010-2015 alone. Informal care represents massive hidden economic burden Additional sources: <https://www.who.int/news-room/fact-sheets/detail/dementia> | <https://alz-journals.onlinelibrary.wiley.com/doi/10.1002/alz.12901>
104. Oncology, J. Annual global economic burden of cancer. *JAMA Oncology: Global Cost 2020-2050* <https://jamanetwork.com/journals/jamaoncology/fullarticle/2801798> (2020)
2020-2050 projection: \$25.2 trillion total (\$840B/year average) 2010 annual cost: \$1.16 trillion (direct costs only) Recent estimate: \$3 trillion/year (all costs included) Top 5 cancers: lung (15.4%), colon/rectum (10.9%), breast (7.7%), liver (6.5%), leukemia (6.3%) Note: China/US account for 45% of global burden; 75% of deaths in LMICs but only 50.0% of economic cost Additional sources: <https://jamanetwork.com/journals/jamaoncology/fullarticle/2801798> | <https://www.nature.com/articles/d41586-023-00634-9>
105. CDC. U.s. Chronic disease healthcare spending. *CDC* <https://www.cdc.gov/chronic-disease/data-research/facts-stats/index.html>
Chronic diseases account for 90% of U.S. healthcare spending (\$3.7T/year). Additional sources: <https://www.cdc.gov/chronic-disease/data-research/facts-stats/index.html>
106. Care, D. Annual global economic burden of diabetes. *Diabetes Care: Global Economic Burden* <https://diabetesjournals.org/care/article/41/5/963/36522/Global-Economic-Burden-of-Diabetes-in-Adults>
2015: \$1.3 trillion (1.8% of global GDP) 2030 projections: \$2.1T-2.5T depending on scenario IDF health expenditure: \$760B (2019) → \$845B (2045 projected) 2/3 direct medical costs (\$857B), 1/3 indirect costs (lost productivity) Note: Costs growing rapidly; expected to exceed \$2T by 2030 Additional sources: <https://diabetesjournals.org/care/article/41/5/963/36522/Global-Economic-Burden-of-Diabetes-in-Adults> | [https://doi.org/10.1016/S2213-8587\(17\)30097-9](https://doi.org/10.1016/S2213-8587(17)30097-9)
107. CBO. *The 2024 Long-Term Budget Outlook*. <https://www.cbo.gov/publication/60039> (2024).
108. World Bank, B. of E. A. US GDP 2024 (\$28.78 trillion). *World Bank* <https://data.worldbank.org/indicator/NY.GDP.MKTP.CD?locations=US> (2024)
US GDP reached \$28.78 trillion in 2024, representing approximately 26% of global GDP. Additional sources: <https://data.worldbank.org/indicator/NY.GDP.MKTP.CD?locations=US> | <https://www.bea.gov/news/2024/gross-domestic-product-fourth-quarter-and-year-2024-advance-estimate>

109. Group, E. W. US farm subsidy database and analysis. *Environmental Working Group* <https://farm.ewg.org/> (2024)
US agricultural subsidies total approximately \$30 billion annually, but create much larger economic distortions. Top 10% of farms receive 78% of subsidies, benefits concentrated in commodity crops (corn, soy, wheat, cotton), environmental damage from monoculture incentivized, and overall deadweight loss estimated at \$50-120 billion annually. Additional sources: https://farm.ewg.org/ | https://www.ers.usda.gov/topics/farm-economy/farm-sector-income-finances/government-payments-the-safety-net/
110. Alliance, D. P. **The drug war by the numbers.** (2021)
Since 1971, the war on drugs has cost the United States an estimated \$1 trillion in enforcement. The federal drug control budget was \$41 billion in 2022. Mass incarceration costs the U.S. at least \$182 billion every year, with over \$450 billion spent to incarcerate individuals on drug charges in federal prisons.
111. Fund, I. M. **IMF fossil fuel subsidies data: 2023 update.** (2023)
Globally, fossil fuel subsidies were \$7 trillion in 2022 or 7.1 percent of GDP. The United States subsidies totaled \$649 billion. Underpricing for local air pollution costs and climate damages are the largest contributor, accounting for about 30 percent each.
112. Papanicolas, I. et al. Health care spending in the united states and other high-income countries. *Papanicolas et al.* <https://jamanetwork.com/journals/jama/article-abstract/2674671> (2018)
The US spent approximately twice as much as other high-income countries on medical care (mean per capita: \$9,892 vs \$5,289), with similar utilization but much higher prices. Administrative costs accounted for 8% of US spending vs 1-3% in other countries. US spending on pharmaceuticals was \$1,443 per capita vs \$749 elsewhere. Despite spending more, US health outcomes are not better. Additional sources: https://jamanetwork.com/journals/jama/article-abstract/2674671
113. Hsieh, C.-T. & Moretti, E. Housing constraints and spatial misallocation. *American Economic Journal: Macroeconomics* <https://www.aeaweb.org/articles?id=10.1257/mac.20170388> (2019)
We quantify the amount of spatial misallocation of labor across US cities and its aggregate costs. Tight land-use restrictions in high-productivity cities like New York, San Francisco, and Boston lowered aggregate US growth by 36% from 1964 to 2009. Local constraints on housing supply have had enormous effects on the national economy. Additional sources: https://www.aeaweb.org/articles?id=10.1257/mac.20170388
114. Lab, Y. B. **The fiscal, economic, and distributional effects of all u.s. tariffs.** (2025)
Accounting for all the 2025 US tariffs and retaliation implemented to date, the level of real GDP is persistently -0.6% smaller in the long run, the equivalent of \$160 billion 2024\$ annually.
115. Foundation, T. Tax compliance costs the US economy \$546 billion annually. <https://taxfoundation.org/data/all/federal/irs-tax-compliance-costs/> (2024)
Americans will spend over 7.9 billion hours complying with IRS tax filing and reporting requirements in 2024. This costs the economy roughly \$413 billion in lost productivity. In addition, the IRS estimates that Americans spend roughly \$133 billion annually in out-of-pocket costs, bringing the total compliance costs to \$546 billion, or nearly 2 percent of GDP.

116. Cook, C., Cole, G., Asaria, P., Jabbour, R. & Francis, D. P. Annual global economic burden of heart disease. *International Journal of Cardiology* [https://www.internationaljournalofcardiology.com/article/S0167-5273\(13\)02238-9/abstract](https://www.internationaljournalofcardiology.com/article/S0167-5273(13)02238-9/abstract) (2014)
Heart failure alone: \$108 billion/year (2012 global analysis, 197 countries) US CVD: \$555B. (2016) → projected \$1.8T by 2050 LMICs total CVD loss: \$3.7T cumulative (2011-2015, 5-year period) CVD is costliest disease category in most developed nations Note: No single \$2.1T global figure found; estimates vary widely by scope and year Additional sources: https://www.ahajournals.org/doi/10.1161/CIR.0000000000001258
117. Source: US Life Expectancy FDA Budget 1543-2019 CSV. [US life expectancy growth 1880-1960: 3.82 years per decade.](#) (2019)
Pre-1962: 3.82 years/decade Post-1962: 1.54 years/decade Reduction: 60% decline in life expectancy growth rate Additional sources: https://ourworldindata.org/life-expectancy | https://www.mortality.org/ | https://www.cdc.gov/nchs/nvss/mortality_tables.htm
118. Source: US Life Expectancy FDA Budget 1543-2019 CSV. [Post-1962 slowdown in life expectancy gains.](#) (2019)
Pre-1962 (1880-1960): 3.82 years/decade Post-1962 (1962-2019): 1.54 years/decade Reduction: 60% decline Temporal correlation: Slowdown occurred immediately after 1962 Kefauver-Harris Amendment Additional sources: https://ourworldindata.org/life-expectancy | https://www.mortality.org/ | https://www.cdc.gov/nchs/nvss/mortality_tables.htm
119. Centers for Disease Control and Prevention. [US life expectancy 2023.](#) (2024)
US life expectancy at birth was 77.5 years in 2023 Male life expectancy: 74.8 years Female life expectancy: 80.2 years This is 6-7 years lower than peer developed nations despite higher healthcare spending Additional sources: https://www.cdc.gov/nchs/fastats/life-expectancy.htm
120. Bureau, U. C. [US median household income 2023.](#) (2024)
US median household income was \$77,500 in 2023 Real median household income declined 0.8% from 2022 Gini index: 0.467 (income inequality measure) Additional sources: https://www.census.gov/library/publications/2024/demo/p60-282.html
121. Statista. US military budget as percentage of GDP. [Statista https://www.statista.com/statistics/262742/countries-with-the-highest-military-spending/](https://www.statista.com/statistics/262742/countries-with-the-highest-military-spending/) (2024)
U.S. military spending amounted to 3.5% of GDP in 2024. In 2024, the U.S. spent nearly \$1 trillion on its military budget, equal to 3.4% of GDP. Additional sources: https://www.statista.com/statistics/262742/countries-with-the-highest-military-spending/ | https://www.sipri.org/sites/default/files/2025-04/2504_fs_milx_2024.pdf
122. Bureau, U. C. Number of registered or eligible voters in the u.s. [US Census Bureau https://www.census.gov/newsroom/press-releases/2025/2024-presidential-election-voting-registration-tables.html](https://www.census.gov/newsroom/press-releases/2025/2024-presidential-election-voting-registration-tables.html) (2024)
73.6% (or 174 million people) of the citizen voting-age population was registered to vote in 2024 (Census Bureau). More than 211 million citizens were active registered voters (86.6% of citizen voting age population) according to the Election Assistance Commission. Additional sources: https://www.census.gov/newsroom/press-releases/2025/2024-presidential-election-voting-registration-tables.html | https://www.eac.gov/news/2025/06/30/us-election-assistance-commission-releases-2024-election-administration-and-voting

123. Senate, U. S. Treaties. *U.S. Senate* <https://www.senate.gov/about/powers-procedures/treaties.htm>
The Constitution provides that the president 'shall have Power, by and with the Advice, and Consent of the Senate, to make Treaties, provided two-thirds of the Senators present concur' (Article II, section 2). Treaties are formal agreements with foreign nations that require two-thirds Senate approval. 67 senators (two-thirds of 100) must vote to ratify a treaty for it to take effect. Additional sources: <https://www.senate.gov/about/powers-procedures/treaties.htm>
124. Commission, F. E. **Statistical summary of 24-month campaign activity of the 2023-2024 election cycle.** (2023)
Presidential candidates raised \$2 billion; House and Senate candidates raised \$3.8 billion, and spent \$3.7 billion; PACs raised \$15.7 billion and spent \$15.5 billion. Total federal campaign spending approximately \$20 billion. Additional sources: <https://www.fec.gov/updates/statistical-summary-of-24-month-campaign-activity-of-the-2023-2024-election-cycle/>
125. OpenSecrets. **Federal lobbying hit record \$4.4 billion in 2024.** (2024)
Total federal lobbying reached record \$4.4 billion in 2024. The \$150 million increase in lobbying, continues an upward trend that began in 2016. Additional sources: <https://www.opensecrets.org/news/2025/02/federal-lobbying-set-new-record-in-2024/>
126. Hutchinson & Kirk. **Valley of death in drug development.** (2011)
The overall failure rate of drugs that passed into Phase 1 trials to final approval is 90%. This lack of translation from promising preclinical findings to success in human trials is known as the "valley of death." Estimated 30-50% of promising compounds never proceed to Phase 2/3 trials primarily due to funding barriers rather than scientific failure. The late-stage attrition rate for oncology drugs is as high as 70% in Phase II and 59% in Phase III trials.
127. DOT. DOT value of statistical life (\$13.6M). *DOT: VSL Guidance 2024* <https://www.transportation.gov/office-policy/transportation-policy/revised-departmental-guidance-on-valuation-of-a-statistical-life-in-economic-analysis> (2024)
Current VSL (2024): \$13.7 million (updated from \$13.6M) Used in cost-benefit analyses for transportation regulations and infrastructure Methodology updated in 2013 guidance, adjusted annually for inflation and real income VSL represents aggregate willingness to pay for safety improvements that reduce fatalities by one Note: DOT has published VSL guidance periodically since 1993. Current \$13.7M reflects 2024 inflation/income adjustments Additional sources: <https://www.transportation.gov/office-policy/transportation-policy/revised-departmental-guidance-on-valuation-of-a-statistical-life-in-economic-analysis> | <https://www.transportation.gov/regulations/economic-values-used-in-analysis>
128. ONE, P. Cost per DALY for vitamin a supplementation. *PLOS ONE: Cost-effectiveness of "Golden Mustard" for Treating Vitamin A Deficiency in India (2010)* <https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0012046> (2010)
India: \$23-\$50 per DALY averted (least costly intervention, \$1,000-\$6,100 per death, averted) Sub-Saharan Africa (2022): \$220-\$860 per DALY (Burkina Faso: \$220, Kenya: \$550, Nigeria: \$860) WHO estimates for Africa: \$40 per DALY for fortification, \$255 for supplementation Uganda fortification: \$18-\$82 per DALY (oil: \$18, sugar: \$82) Note: Wide variation reflects differences in baseline VAD prevalence, coverage levels, and whether intervention is supplementation or fortification Additional sources: <https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0012046> | <https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0266495>
129. News, U. Clean water & sanitation (LMICs) ROI. *UN News* <https://news.un.org/en/story/2014/11/484032> (2014).

130. PMC. Cost-effectiveness threshold (\$50,000/QALY). *PMC* <https://pmc.ncbi.nlm.nih.gov/articles/PMC5193154/>
The \$50,000/QALY threshold is widely used in US health economics literature, originating from dialysis cost benchmarks in the 1980s. In US cost-utility analyses, 77.5% of authors use either \$50,000 or \$100,000 per QALY as reference points. Most successful health programs cost \$3,000-10,000 per QALY. WHO-CHOICE uses GDP per capita multiples ($1 \times \text{GDP/capita} = \text{"very cost-effective"}$, $3 \times \text{GDP/capita} = \text{"cost-effective"}$), which for the US ($\$70,000 \text{ GDP/capita}$) translates to $\$70,000\text{-}\$210,000/\text{QALY}$ thresholds. Additional sources: <https://pmc.ncbi.nlm.nih.gov/articles/PMC5193154/> | <https://pmc.ncbi.nlm.nih.gov/articles/PMC9278384/>
131. Institute, I. B. Chronic illness workforce productivity loss. *Integrated Benefits Institute 2024* <https://www.ibiweb.org/resources/chronic-conditions-in-the-us-workforce-prevalence-trends-and-productivity-impacts> (2024)
78.4% of U.S. employees have at least one chronic condition (7% increase since 2021). 58% of employees report physical chronic health conditions 28% of all employees experience productivity loss due to chronic conditions Average productivity loss: \$4,798 per employee per year Employees with 3+ chronic conditions miss 7.8 days annually vs 2.2 days for those without Note: 28% productivity loss translates to roughly 11 hours per week (28% of 40-hour workweek) Additional sources: <https://www.ibiweb.org/resources/chronic-conditions-in-the-us-workforce-prevalence-trends-and-productivity-impacts> | <https://www.onemedical.com/mediacenter/study-finds-more-than-half-of-employees-are-living-with-chronic-conditions-including-1-in-3-gen-z-and-millennial-employees/> | <https://debeaumont.org/news/2025/poll-the-toll-of-chronic-health-conditions-on-employees-and-workplaces/>
132. Arrow, K. J. *Social Choice and Individual Values*. (Kenneth J. Arrow, 1951).
Arrow's Impossibility Theorem proves that no rank-order voting system can satisfy all of four "fairness" criteria: unrestricted domain, non-dictatorship, Pareto efficiency, and independence of irrelevant alternatives. This foundational result in social choice theory demonstrates that there is no perfect method for aggregating individual preferences into collective decisions—all voting systems involve tradeoffs. The theorem has profound implications for democratic theory, welfare economics, and mechanism design, showing that preference aggregation is irreducibly political. Additional sources: <https://www.amazon.com/Social-Choice-Individual-Values-Monograph/dp/0300013647>
133. Myerson, R. B. *Optimal auction design*. *Mathematics of Operations Research* **6**, 58–73 (1981)
This seminal paper establishes the Revenue Equivalence Theorem and introduces the "virtual valuation" concept for mechanism design. Myerson shows how to design auctions that maximize expected revenue given incentive-compatible reporting constraints. The paper, along with the Revelation Principle, provides foundational tools for designing mechanisms where agents truthfully report private information. Essential for understanding incentive-compatible oracle design in algorithmic governance systems.
134. Kydland, F. E. & Prescott, E. C. *Rules rather than discretion: The inconsistency of optimal plans*. *Journal of Political Economy* **85**, 473–492 (1977)
Time-inconsistency describes situations where, with the passing of time, policies that were determined to be optimal yesterday are no longer perceived to be optimal today and are not implemented... This insight shifted the focus of policy analysis from the study of individual policy decisions to the design of institutions that mitigate the time consistency problem.

135. Office, C. B. [Estimated impact of the american recovery and reinvestment act on employment and economic output in 2014.](#) (2015).
136. ICER. ICER QALY methodology and standards. *ICER* <https://icer.org/our-approach/methods-process/cost-effectiveness-the-qaly-and-the-evlyg/> (2024)
The quality-adjusted life year (QALY) is the academic standard for measuring how well all different kinds of medical treatments lengthen and/or improve patients' lives, and therefore the metric has served as a fundamental component of cost-effectiveness analyses in the US and around the world for more than 30 years. ICER's health benefit price benchmark (HBPB) will continue to be reported using the standard range from \$100,000 to \$150,000 per QALY and per evLYG. Additional sources: https://icer.org/our-approach/methods-process/cost-effectiveness-the-qaly-and-the-evlyg/ | https://icer.org/wp-content/uploads/2024/02/Reference-Case-4.3.25.pdf
137. Batini, N., Di Serio, M., Fragetta, M., Melina, G. & Waldron, A. [Building back better: How big are green spending multipliers?](#) *Ecological Economics* **193**, 107305 (2021).
138. Barro, R. J. & Redlick, C. J. [Macroeconomic effects from government purchases and taxes.](#) *The Quarterly Journal of Economics* **126**, 51–102 (2011).
139. Angrist, J. D. & Pischke, J.-S. [The credibility revolution in empirical economics: How better research design is taking the con out of econometrics.](#) *Journal of Economic Perspectives* **24**, 3–30 (2010)
The primary engine driving improvement has been a focus on the quality of empirical research designs. Additional sources: https://www.aeaweb.org/articles?id=10.1257/jep.24.2.3
140. Jackson, C. K., Johnson, R. C. & Persico, C. [The effects of school spending on educational and economic outcomes: Evidence from school finance reforms.](#) *The Quarterly Journal of Economics* **131**, 157–218 (2016)
Using exogenous variation from court-ordered school finance reforms, finds that a 10% increase in per-pupil spending throughout all 12 years of public school leads to 0.31 more completed years of education, 7.25% higher wages, and a 3.67 percentage-point reduction in adult poverty. This is one of the most credible causal estimates of the effect of education spending on adult outcomes, using natural experiments to address reverse causality concerns.
141. Sinn, M. P. [A Decentralized FDA: How to Prevent a Year of Death and Suffering for 84 Cents.](#) <https://dfda-impact.warondisease.org> (2025) doi:10.5281/zenodo.18243914
Only 15 diseases/year get their first treatment each year. With 6.65 thousand diseases lacking effective treatments, the backlog would take 443 years to clear. Integrating pragmatic trials into standard healthcare increases trial capacity 12.3x, cutting that timeline from 443 years to 36 years. The average untreated disease gets a treatment 212 years earlier, saving 10.7 billion deaths at \$0.841 per year of healthy life saved.
142. News, O. U. [RECOVERY trial summary quote.](#) *Oxford University News* <https://www.ox.ac.uk/news/features/recovery-trial-two-years>
One trial. Over 47,000 participants. Nearly 200 hospital sites, across six countries. Ten results. Four effective COVID-19 treatments... Through discovering four treatments that effectively reduce deaths from COVID-19, it is certain that the study has saved thousands – if not millions – of lives worldwide. Additional sources: https://www.ox.ac.uk/news/features/recovery-trial-two-years

- +-- Pull spending data from OECD, World Bank
- +-- Include all comparable countries
- +-- Normalize to per-capita and % GDP
- +-- Prepare for regression analysis

3. Effect estimate data

- +-- Search systematic reviews and meta-analyses
- +-- Extract effect sizes with standard errors
- +-- Code study quality (RCT, natural experiment, etc.)
- +-- Build literature database by category

Phase 2: OSL ESTIMATION

4. Diminishing returns modeling

- +-- Fit nonlinear spending-outcome functions
- +-- Identify "knee" of curve
- +-- Calculate marginal returns at current spending
- +-- Estimate optimal level

5. Cost-effectiveness analysis (health/life-saving)

- +-- Identify interventions below CE threshold
- +-- Calculate scale-up costs
- +-- Sum to category OSL
- +-- Document assumptions

6. Method reconciliation

- +-- Compare OSL estimates across methods
- +-- Weight by method reliability
- +-- Produce consensus OSL estimate
- +-- Flag discrepancies

Phase 3: EVIDENCE QUALITY

7. BIS calculation

- +-- Compute quality weights per study
- +-- Compute precision weights
- +-- Compute recency weights
- +-- Aggregate to category BIS

8. Evidence grading

- +-- Assign A-F grade based on BIS
- +-- Document key evidence
- +-- Identify research gaps
- +-- Flag high-uncertainty categories

Phase 4: GAP ANALYSIS

9. Compute gaps

- +-- Gap = OSL - Current
- +-- Calculate % gap
- +-- Classify as under/over/optimal
- +-- Apply BIS weighting

10. Priority ranking

- +-- Priority = |Gap| × BIS
- +-- Rank categories
- +-- Identify reallocation pairs
- +-- Estimate welfare gains

Phase 5: OUTPUT GENERATION

11. Multi-unit reporting

- +-- Natural units (\$/capita, % GDP)
- +-- Monetized (ROI, opportunity cost)
- +-- Health units (QALYs where applicable)
- +-- Composite (BIS, evidence grade)

12. Sensitivity analysis

- +-- Vary key parameters
- +-- Test country data subsets
- +-- Report OSL ranges
- +-- Identify robust conclusions

13. Documentation

- +-- Generate category reports
- +-- Create methodology audit trail
- +-- Version control estimates
- +-- Publish to dashboard/API

22 Appendix B: Glossary

22.1 Core Concepts

- **Optimal Budget Generator (OBG):** The framework/methodology for generating integrated budget recommendations based on evidence of spending-outcome relationships. OBG accounts for the zero-sum nature of budget allocation and produces Optimal Spending Level (OSL) estimates for each category.

FRAMEWORK FOR EVIDENCE-BASED BUDGET ALLOCATION: THE OPTIMAL BUDGET GENERATOR (OBG) & RELATED CONCEPTS

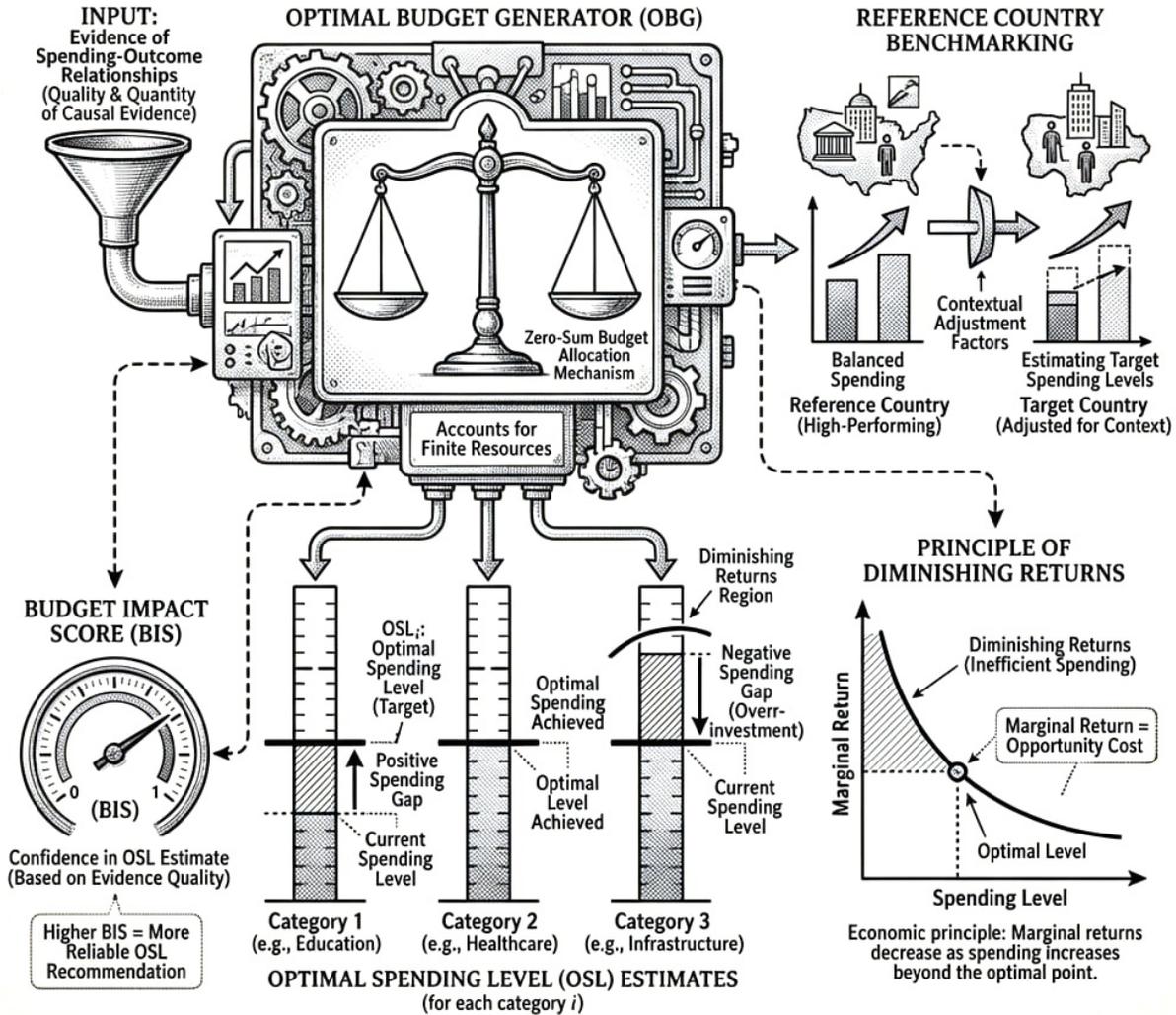


Figure 26: A conceptual framework illustrating the Optimal Budget Generator process, showing how evidence and benchmarking result in OSL and BIS outputs to identify spending gaps.

- **Optimal Spending Level (OSL):** The evidence-based target spending level for each category, produced by the OBG framework. OSL_i represents the optimal spending level for category i . Below OSL indicates underinvestment; above OSL indicates diminishing returns.
- **Budget Impact Score (BIS):** A 0-1 score measuring confidence in each category's OSL estimate based on the quality and quantity of causal evidence. Higher BIS indicates more reliable OSL recommendations.
- **Spending Gap:** The difference between current spending and the evidence-based target for each category. Positive gaps indicate underinvestment; negative gaps indicate overinvestment.

- **Diminishing Returns:** The economic principle that marginal returns to spending decrease as spending increases. The optimal level is where marginal return equals opportunity cost.

22.2 Estimation Methods

- **Cost-Effectiveness Threshold:** The maximum acceptable cost per QALY (or other health outcome) for including an intervention in target calculations. Typically \$50K-\$150K per QALY.
- **Dose-Response Curve:** The relationship between spending level (dose) and outcome (response). Used to identify diminishing returns and estimate optimal spending levels.

22.3 Evidence Quality

- **Quality Weight (w^Q):** Weight assigned to a study based on identification strategy. RCTs receive 1.0; cross-sectional studies receive 0.25.
- **Precision Weight (w^P):** Weight assigned based on standard error. More precise estimates receive higher weight.
- **Recency Weight (w^R):** Weight assigned based on publication date. More recent studies receive higher weight via exponential decay.
- **Evidence Grade:** Letter grade (A-F) summarizing confidence in each category’s target estimate. A = strong evidence; F = insufficient evidence.

22.4 Output Concepts

- **Priority Score:** Product of gap magnitude and BIS. Used to rank categories for reallocation priority.
- **Value of Information (VOI):** Expected benefit of additional research on uncertain categories. High-VOI categories warrant pilot funding.
- **Multi-Unit Reporting:** Presenting results in natural units, monetized equivalents, health units, and composite scores for interpretability.

23 Appendix C: Illustrative Comparison to US Budget

This appendix applies the OBG methodology to the US discretionary budget as an illustrative exercise. “Current” figures reflect approximate FY2024 budget authority. OSL estimates for pragmatic trials, vaccinations, and K-12 education are derived from the worked examples in Sections 5-7. Other OSL values are preliminary estimates based on cross-country benchmarking and published cost-effectiveness evidence; they have not undergone the full OBG estimation pipeline and should be treated as order-of-magnitude approximations pending rigorous analysis. BIS scores reflect the author’s qualitative assessment of causal evidence quality.

23.1 Illustrative US Discretionary Budget vs. OSL Targets

Category	Current (B) OSL(B)	Gap (\$B)	Gap %	BIS	Inc	Hlth	Prior- ity	
Military (discretionary)	850	459	-391	-46%	0.50	—	—	195
Non-military discretionary	915	1,350	+435	+48%	0.65	++	++	283
- Pragmatic clinical trials	0.5	50	+49.5	+9,900%	0.90	++	+++	44.6
-	80	120	+40	+50%	0.75	+++	+	30
<i>Education</i>								
- <i>Health (research)</i>	50	100	+50	+100%	0.80	+	+++	40
- <i>Vaccinations</i>	8	35	+27	+338%	0.95	+	+++	26
- <i>Basic research</i>	45	90	+45	+100%	0.70	++	++	32
- <i>Infras- tructure</i>	100	150	+50	+50%	0.60	++	+	30
- <i>Early childhood</i>	50	70	+20	+40%	0.85	+++	+	17
Agricultural subsidies	25	0	-25	-100%	0.90	—	—	23

Inc = effect on real after-tax median income growth. *Hlth* = effect on median healthy life years. Scale: +++ strong positive, ++ moderate, + weak, — negative.

Illustrative findings (subject to the caveats above):

1. **Extreme underinvestment in pragmatic trials:** At 9,900% below OSL with 637:1 (95% CI: 569:1-790:1) BCR, this appears to be the single largest misallocation in the federal budget (see Section 6 for full derivation)
2. **Apparent overinvestment:** Military spending is ~\$391B (46%) above preliminary OSL estimates based on cross-country benchmarking
3. **Apparent underinvestment:** Vaccinations, basic research, and health research appear far below evidence-optimal levels
4. **Negative-return spending:** Agricultural subsidies produce negative welfare effects per the cost-effectiveness literature
5. **Reallocation potential:** The direction of reallocation (from military and subsidies toward research, health, and education) is robust even if precise OSL magnitudes shift with better data

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Data Availability: All data sources referenced in this paper are publicly available: OECD iLibrary (education, health spending), World Bank WDI (cross-country indicators), SIPRI Military Expenditure Database (defense spending), and CDC vaccination cost data. URLs are provided in the Data Sources section. A complete replication package including analysis code, data extraction scripts, and worked example calculations will be deposited in a public repository (GitHub/Zenodo) upon publication.

Ethics Statement: This is a methodological specification. No human subjects research was conducted.

Preprint: This working paper has not undergone peer review.