The Underappreciated Value of Biopharmaceutical Innovation: A Conservative Benefit-Cost Estimate of Long-Run Returns

Louis P. Garrison, Jr., The CHOICE Institute, University of Washington
Jelena Zurovac, Independent Consultant

Note to conference reviewers. This paper has been prepared for submission to *Health Affairs Forefront*, which publishes short articles of about 2,200 words with embedded hyperlinks in place of an abstract and reference list. For the convenience of conference reviewers, we have added an abstract in the style of a regular *Health Affairs* article and a numbered reference list corresponding to the hyperlinks in the text; neither will be part of the *Forefront* submission. A technical methods note documenting data sources, calculations, and sensitivity analyses is appended.

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Abstract

Debates over prescription drug prices rarely set the long-run health returns to biopharmaceutical innovation against the resources society invested to produce them. We estimated a conservative benefit-cost ratio for US biopharmaceutical research and development (R&D). Building on evidence attributing 35 percent of the 3.3-year gain in US life expectancy during 1990–2015 to pharmaceuticals, we valued the resulting discounted life-years at $100,000 each and compared them with cumulative public, private, and nonprofit biomedical R&D during 1960–2005, expressing all values in 2024 dollars discounted to 1960 at 3 percent. Pharmaceutical-attributable health benefits had a present value of approximately $1.4 trillion, compared with $0.24 trillion in industry R&D and $0.53 trillion in total societal R&D, implying returns of roughly 6:1 on private investment and 2.7:1 on the combined investment. One-way sensitivity analyses, reported in the appended technical note, yield societal ratios above 1:1 in every case, and illustrative adjustments for omitted costs yield about 1.8:1 to 2.4:1. Because the estimate excludes quality-of-life gains, contributions of other medical technologies, and benefits accruing outside the United States or after 2015, it likely understates the true return. Policies that reduce expected returns to R&D should weigh these long-run benefits against near-term savings.

Why rising healthcare costs obscure the value of pharmaceutical innovation

The economic value of biopharmaceutical innovation is widely acknowledged in the academic literature but remains poorly understood among the public and in health policy debates. The magnitudes involved are difficult to grasp: United States (U.S.) prescription drug spending reached approximately $467 billion in 2024. Against this backdrop, a large body of research has documented substantial improvements in population health—particularly longevity—associated with advances in medical care, including pharmaceuticals. Yet these gains are rarely framed in economic terms that allow comparison with the resources required to generate them.

At the same time, concerns about rising healthcare costs are both real and salient. Patients encounter drug costs directly through cost sharing and coverage restrictions, while the key drivers of spending—hospital care, physician services, and system inefficiencies—are less visible. This asymmetry contributes to a persistent focus on drug prices in policy discussions, often without a corresponding accounting of the long-term value generated by pharmaceutical innovation.

This disconnect reflects a deeper issue: the economic value of biopharmaceutical innovation is inherently difficult to perceive. Research and development (R&D) costs are incurred upfront over decades, while health gains materialize gradually thereafter, often as diffuse reductions in mortality risk rather than discrete, observable events. The link between investment and outcomes is therefore distant and hard to evaluate with conventional policy frameworks. Drug development is a multi-decade process: research[1] on the origins of recently approved drugs shows that foundational research on drug targets typically precedes approval by decades, with cumulative R&D investments spanning many years before a new medicine reaches patients. This motivates our choice of a 45-year investment window (1960–2005) to capture the R&D that plausibly generated the health gains observed over the 26-year period between 1990 and 2015.

In this short paper, building on previous research[2] that attributes 35 percent of U.S. life expectancy gains in 1990-2015 to pharmaceutical innovation, we apply a long-term benefit-cost framework to estimate the value of those health benefits relative to the historical cumulative investment required to generate them. Our approach is deliberately conservative, incorporating realistic time lags, partial attribution, and discounting of both costs and benefits.

Our denominator is the real resource cost of creating medicines—the scientists, laboratories, and clinical trials devoted to biomedical research—not what Americans spend at the pharmacy. Spending on drugs is largely a transfer from purchasers to

producers rather than a resource society consumes, so it does not belong on the cost side of a social benefit-cost ratio. The question we ask is whether society's investment in creating new medicines—from basic science through clinical development—has paid off. That is also the question current policy turns on, because the major levers now under debate operate by changing expected returns to research and development.

Research shows immense value generated by drugs

Murphy and Topel[3] show that mortality reductions generate very large social value under willingness-to-pay frameworks. Hall and Jones[4] find rising health spending consistent with welfare maximization as the value of longevity rises with income. Lichtenberg[5] links newer drugs to longer life expectancy at a cost per life-year well below common value-of-life thresholds.

Large-scale analyses[6] of U.S. cost-effectiveness studies find that health gains account for most of the value generated by medical innovation. More recent work[7] argues that such approaches still understate value by omitting insurance value, option value, and productivity gains.

Estimating the health benefits of pharmaceutical innovation

The estimated health benefits realized between 1990 and 2015 leverage the results of a comprehensive, condition-by-condition study by Buxbaum et al. (2020),[2] who analyzed vital statistics data across the conditions most responsible for changing longevity to estimate that pharmaceuticals accounted for approximately 35 percent of the 3.3-year increase in U.S. life expectancy at birth over this period.

We translate this life expectancy gain into economic value using the complete period life tables for 1990 and 2015 to capture the full age-specific pattern of mortality improvement. We compute the change in discounted life expectancy at birth—the present value of expected future life-years, discounted at 3 percent within each lifetime to reflect the diminishing present value of gains at older ages. This yields an increase of approximately 0.50 discounted life-years per person. Separately, we discount the resulting benefits across calendar years at 3 percent back to 1960, the base year used for costs. Applying the 35 percent pharmaceutical attribution implies a gain of 0.17 discounted life-years per person. Scaled to 285 million people and valued at $100,000 per life-year, this corresponds to approximately $5.0 trillion in contemporaneous health value. Discounting to the common base year of 1960 yields approximately $1.4 trillion in present value (2024 dollars).

Both windows are truncated: basic science before 1960 contributed to later drugs, and health gains from R&D in our cost window continue beyond 2015, biasing the ratio in opposite directions.

Return on private biopharmaceutical R&D

We first compare these health benefits to the private-sector biopharmaceutical R&D investment that directly produced the drugs generating them. Using National Science Foundation surveys of R&D performed by U.S. biopharmaceutical manufacturers (NAICS 3254), we estimate cumulative industry R&D from 1960 to 2005 at approximately $600 billion in constant 2024 dollars, or about $240 billion in present value when discounted to 1960 at 3 percent. This measure covers preclinical research, clinical development, and regulatory activities required to bring new therapies to market. Compared with $1.4 trillion in pharmaceutical-attributable health benefits, this implies a return on private R&D investment of approximately 6:1—each dollar of industry R&D helped to generate roughly six dollars in discounted health value.

The full societal investment: a more conservative estimate

This 6:1 ratio attributes to industry R&D alone the output of a cumulative process that builds on upstream basic and translational science. To construct a more complete denominator that recognizes the role advances in disease biology and target identification play in informing private industry investment, we aggregate three complementary streams, reported as undiscounted cumulative totals for 1960–2005 in constant 2024 dollars. First, the private-sector biopharmaceutical R&D described above (~$600 billion). Second, public-sector research funding, measured using annual NIH appropriations (~$600 billion), which primarily supports basic research on the biology of disease and early translational research to identify and validate therapeutic targets. Third, nonprofit biomedical research funding (~$65 billion) from disease foundations and mission-driven organizations.

These three streams reflect sequential and complementary stages of a cumulative innovation process. Public and nonprofit funding is concentrated in upstream discovery of disease mechanisms and targets; private investment is concentrated downstream, in medicinal chemistry, preclinical testing, clinical development, and regulatory review. All spending flows are converted to constant 2024 dollars and discounted to 1960 at 3 percent, yielding an aggregate present value of approximately $530 billion in R&D over 1960–2005. The denominator omits research that universities and research institutes fund from their own resources, including indirect costs of federally funded projects that grants do not cover. Research!America[8] estimates this institutional funding at about $30 billion in 2025; it was likely a smaller factor during our 1960–2005 window, and including it would modestly lower the ratio.

This societal benefit–cost ratio is approximately 2.7:1 (Exhibit 2). Put differently, every dollar of combined public, private, and nonprofit R&D generated roughly $2.70 in health benefits through medicines alone.

This estimate is intentionally conservative. It charges the full cost of the publicly funded research enterprise, including all NIH appropriations for training and infrastructure, to pharmaceutical innovation while counting only health gains delivered through medicines, even though the same research also advances diagnostics, devices, and public health.

In undiscounted constant 2024 dollars, cumulative health benefits of approximately $5 trillion compare to cumulative R&D investment of approximately $1.3 trillion. The undiscounted ratio exceeds the discounted one because costs are incurred well before benefits are realized.

Notably, these public and private investments are complementary,[9] not perfect substitutes. Public funding addresses the public-goods problem in basic science, whose findings firms cannot readily patent or appropriate; private investment finances the capital-intensive, high-attrition work of converting that knowledge into approved medicines. As Lakdawalla[10] notes, NIH funding contributed to every drug[1] approved in 2010–2016, but more than 90 percent of it built basic knowledge about biological targets rather than the drugs themselves; industry, which funds about two-thirds of U.S. biomedical R&D, concentrates on developing them. Summing these public and private streams values the output of a joint and sequential enterprise; it does not imply that the inputs are interchangeable, nor that a share of cost confers a share of claim on the resulting medicines.

Society's commitment has grown not merely in absolute terms but as a share of a growing economy. Combined public, private, and nonprofit biomedical R&D rose from roughly 0.15 percent of U.S. GDP in 1960 to more than 0.6 percent today (Exhibit 1). Even broader measures that add device R&D and institutions' own funds put the total at only about 1 percent. The composition also shifted: public funding predominated early, while industry investment grew faster, overtook it in the late 1980s, and is now roughly two and a half times as large.

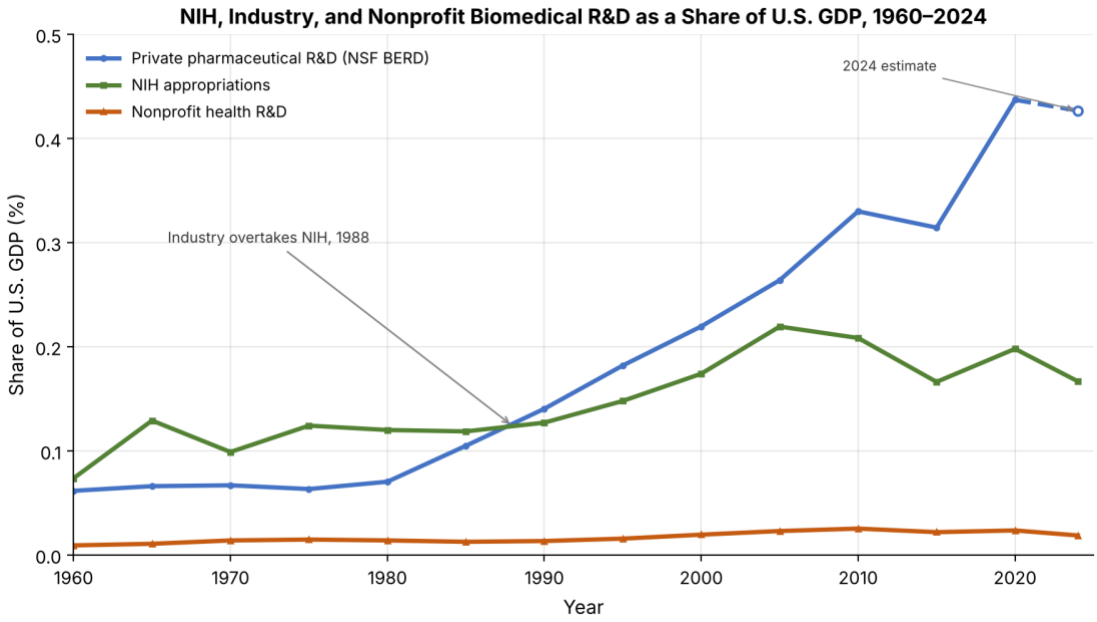


Exhibit 1. NIH, Industry, and Nonprofit Biomedical R&D as a Share of U.S. GDP, 1960–2024. Annual spending by the three investment streams—NIH, private-sector pharmaceutical R&D (NSF BERD), and nonprofit health research—expressed as a percentage of U.S. gross domestic product. Industry R&D for 2024 is estimated (dashed segment); nonprofit values are interpolated estimates. Source: Authors' analysis of data from the NIH Almanac, National Science Foundation Business Enterprise R&D surveys, and U.S. Bureau of Economic Analysis.

Exhibit 2. Benefit-Cost Estimates of U.S. Biopharmaceutical R&D Investment

Component	Estimate	Basis or source
Benefits		
Gain in life expectancy at birth, 1990–2015	3.3 years	Period life tables
Discounted life-expectancy gain	0.50 years	Discounted at 3% within lifetimes
Pharmaceutical-attributable share (35%)	0.17 years	Buxbaum et al. (2020)
Population base	285 million	Average U.S. population
Aggregate discounted life-years gained	50 million	
Value of life-years, undiscounted (2024 $)	$5.0 trillion	At $100,000 per life-year
Present value of benefits	$1.4 trillion	Discounted to 1960 at 3%
Costs: present value of R&D, 1960–2005 (2024 $, discounted to 1960 at 3%)		
Industry R&D	$0.24 trillion	NSF BERD (NAICS 3254)
All societal R&D	$0.53 trillion	NIH + industry + nonprofit
Benefit–cost ratios		
Return on private R&D	**~6:1**	Benefits ÷ industry R&D
Return on societal investment	**~2.7:1**	Benefits ÷ all societal R&D

Notes: Benefits reflect biopharmaceutical-attributable gains in life expectancy between 1990 and 2015, discounted both within lifetimes and across time. Costs reflect cumulative biomedical R&D investment from 1960 to 2005 discounted to 1960. *Source:* Authors' analysis of data from Buxbaum et al. (2020), SSA and NCHS life tables, the NIH Almanac, and National Science Foundation Business Enterprise R&D surveys.

Comparison with broader estimates and the conservatism of our approach

Recent work[11] by Tomas Philipson and colleagues estimates substantially larger societal returns to medical innovation—often exceeding 20:1—chiefly by valuing life-years at a value of a statistical life-year of $558,812 (2020 dollars), drawn from values used by five U.S. government agencies, rather than the $100,000 we use here. Applying that valuation to our framework would yield a benefit–cost ratio on the order of 15:1. Our 2.7:1 figure should be read as a conservative estimate.

Moreover, the 35 percent pharmaceutical attribution is itself conservative. Buxbaum et al. attribute an additional 13 percent of life expectancy gains to "other medical care"—including cancer screening, cardiac surgery, and neonatal interventions—all products of the biomedical R&D included in our cost denominator but not credited in our numerator. Furthermore, the 44 percent that Buxbaum et al. attribute to "public health"—principally reductions in cholesterol, hypertension, and smoking—rested on publicly funded science, such as the NIH-supported Framingham Heart Study and the epidemiological evidence linking smoking to cancer. Crediting that research would yield a higher benefit–cost ratio.

Finally, because our measure counts only longevity, it omits the value of medicines whose benefits are primarily improvements in quality of life or productivity rather than survival.

The decade since 2015 reinforces these returns

U.S. life expectancy fell sharply from 78.7 years in 2015 to 76.4 in 2021, driven first by "deaths of despair"[12] and then catastrophically by COVID-19, which Cutler and Summers[13] estimated to impose approximately $16 trillion in total costs on the U.S. economy. Recovery to pre-pandemic levels by 2024 was enabled largely by mRNA vaccines, built on decades of publicly funded basic science in lipid nanoparticles, mRNA modification, and pre-fusion spike protein research. The federal investment in COVID-19 vaccine R&D and procurement—approximately $32 billion—helped curtail that loss, illustrating how far the returns to biopharmaceutical R&D can exceed its costs.

Policy implications

Our analysis suggests that biopharmaceutical innovation represents a highly productive long-term investment in population health—not simply a contemporaneous cost. Yet the frameworks used to evaluate proposed pharmaceutical policies often rely on short time horizons, static budget constraints, and highly visible prices at launch, while discounting or ignoring the long-term benefits that accrue to patients and society.

Moreover, by counting only U.S. health gains, our analysis understates the full return to biomedical R&D: the U.S. funds approximately 55 percent[14] of global biopharmaceutical R&D, yet the resulting medicines benefit populations many times larger. A global accounting would yield a substantially higher benefit–cost ratio.

A related question—whether what Americans pay for medicines is justified by the health they deliver—has been examined separately. Research on how the social surplus from pharmaceuticals is divided consistently finds that patients capture the large majority of it even during patent exclusivity: Philipson and Jena[15] estimate that innovators appropriated roughly 5 percent of the social surplus generated by HIV/AIDS therapies. Once generic entry occurs, patients capture nearly all of it. Our estimate speaks to the prior question of whether the underlying investment was worth making.

Our estimate is an average realized return across all research undertaken, not the return on the next dollar invested. For current investment to be excessive, marginal returns would have to have fallen from this average to the private cost of capital—a collapse for which there is no evidence. If anything, the pressure runs the other way: patents expire, prices then fall, and the health benefits continue indefinitely, so developers capture only a fraction of the value their medicines create. Private investment decisions therefore understate the social return.

Returns may nonetheless be diminishing. The number of new drugs approved per dollar of R&D fell for six decades, and the easiest therapeutic problems were solved first, though that trend appears to have reversed[16] since 2010. And cost per approval is not cost per life-year gained: a single modern approval can deliver far more health than one from 1985. The value of health is itself rising, since willingness to pay for longevity grows faster than income across a global population growing wealthier. Whether returns at the margin are rising or falling is an open question this paper does not answer. It establishes only that what has been achieved should not be underestimated.

Policies that narrowly target drug prices without accounting for their effects on innovation incentives risk trading large, delayed benefits for relatively small near-term savings. Failing to account for these long-term dynamics of societal health investment risks repeating a familiar policy error: treating visible costs as real while deeply discounting invisible—but far larger—benefits.

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Appendix: Technical Methods Note

Benefit–Cost Analysis of U.S. Biopharmaceutical R&D: Investment 1960–2005, Health Benefits 1990–2015

All figures are computed in a supporting workbook, available from the authors on request.

Component 1: NIH Appropriations. Annual NIH program-level appropriations for fiscal years 1960 through 2005 are taken directly from the NIH Almanac, "Historical Budget Information," Section 2, "Total" column (https://www.nih.gov/about-nih/nih-almanac/appropriations-section-1). Published in thousands of dollars, the values are converted to nominal millions, then deflated to constant 2024 dollars using the BEA GDP implicit price deflator (NIPA Table 1.1.9, 2017=100), and finally discounted to 1960 at a 3 percent real rate. This is complete administrative data requiring no estimation. The series understates total federal health R&D by approximately 15–20 percent because it excludes other federal health research funders (CDC, AHRQ, VA, DoD health programs, BARDA). A discontinuity in FY1993 reflects the organizational return of NIMH, NIDA, and NIAAA from ADAMHA to NIH. The cumulative present value of NIH appropriations over 1960–2005 is approximately $261 billion (in 2024 dollars, discounted to 1960); the corresponding undiscounted cumulative total in constant 2024 dollars is approximately $599 billion.

Component 2: Private-Sector Pharmaceutical R&D. Annual pharmaceutical industry R&D is drawn from National Science Foundation Business Enterprise Research and Development (BERD) surveys for firms classified under SIC 283 (Drugs, pre-1998) and NAICS 3254 (Pharmaceutical and Medicine Manufacturing, 1998 onward). The data are available from the NSF NCSES website (https://ncses.nsf.gov/surveys/business-enterprise-research-development). For 2008–2022, values come from BERD Table 59 (NSF 24-335); for 1960–2007, from the historical Survey of Industrial Research and Development (SIRD) and its successor series. The measure captures domestic R&D performed by all firms in the industry classification, funded by all sources (company, federal, and other). This series closely tracks the PhRMA Annual Membership Survey (average ratio 0.97 over 1983–2022), providing independent corroboration from a federal statistical source. Nominal values are deflated and discounted using the same procedure as the NIH series. The cumulative present value over 1960–2005 is approximately $237 billion; the corresponding undiscounted cumulative total in constant 2024 dollars is approximately $604 billion. Because NAICS 3254 classifies firms by primary activity, R&D performed by research-intensive biotechnology firms classified in scientific research and development services (NAICS 5417), or elsewhere, falls outside the series. Research!America's industry estimates, which build on BERD but allocate part of this R&D to the biopharmaceutical sector, are correspondingly larger; its biopharmaceutical figure for 2024 is approximately

$168 billion (https://www.researchamerica.org/wp-content/uploads/2026/09/2026-ResearchAmerica-Investment-Report-September-2026.pdf). If our historical series understated industry R&D by as much as one-third throughout 1960–2005, the industry present value would rise to about $316 billion, the return on industry R&D would fall from about 6.1:1 to about 4.6:1, and the societal ratio would fall from about 2.7:1 to about 2.4:1.

Component 3: Nonprofit Health R&D. No continuous annual series exists for nonprofit health R&D. We construct estimates by interpolating linearly between anchor points drawn from several sources: the NSF NCSES surveys of nonprofit R&D (conducted in 1957, 1960, 1973, and 1996–97); the 1991 Institute of Medicine report "Funding Health Sciences Research" (NCBI Bookshelf), which reports an NIH estimate of approximately $700 million in nonprofit health R&D in 1988; and the Research!America "U.S. Investments in Medical and Health R&D" reports, which provide estimates of $3.5–4.7 billion annually for 2013–2018 and, in the September 2026 edition (https://www.researchamerica.org/wp-content/uploads/2026/09/2026-ResearchAmerica-Investment-Report-September-2026.pdf), $2.9–4.4 billion annually for 2021–2025 (current dollars) for foundations, voluntary health associations, and professional societies. Our 1960–2005 series averages roughly $1.4 billion a year in constant 2024 dollars, consistent with the sector's growth over time. Anchor points include $50 million in 1960, $150 million in 1970, $400 million in 1980, $700 million in 1988, $1.2 billion in 1995, $2.0 billion in 2000, and $3.0 billion in 2005. These estimates carry uncertainty of approximately ±30 percent but contribute only about 5 percent of the total denominator, so even substantial errors have modest impact on the benefit–cost ratio. The cumulative present value over 1960–2005 is approximately $29 billion; the corresponding undiscounted cumulative total in constant 2024 dollars is approximately $65 billion.

Component 4: Value of Pharmaceutical-Attributable Longevity Gains. The numerator measures the economic value of the improvement in U.S. mortality between 1990 and 2015 attributable to pharmaceutical innovation. Using the 1990 U.S. period life table (SSA Actuarial Study No. 116, Table 6, combined male and female average, ages 0–100) and the 2015 NCHS annual complete life table (ages 0–100), we compute discounted life expectancy at birth for each year by summing age-specific person-years (Lx) each divided by (1.03)^a, where a is age. The difference in discounted life expectancy between 2015 and 1990 is 0.50 years. Following Buxbaum et al. (2020, *Health Affairs*, doi:10.1377/hlthaff.2020.00284), we attribute 35 percent of this gain to pharmaceutical innovation, yielding 0.17 discounted life-years per person. Scaling to the average U.S. population over 1990–2015 (approximately 285 million) gives 50 million discounted life-years gained. Valued at $100,000 per life-year (constant 2024 dollars) — a deliberately conservative figure relative to standard value-of-statistical-life estimates — this yields

approximately $5.0 trillion in contemporaneous health value. To discount this benefit stream to 1960 for comparison with the R&D denominator, we approximate the midpoint of realized benefits at 2002 and divide by (1.03)^42, yielding a present value of approximately $1.4 trillion. A year-by-year valuation using interpolated annual life tables confirms that the midpoint approximation is accurate to within 3.3 percent.

Benefit–Cost Ratio. The total present value of the three R&D investment streams (1960–2005) is approximately $527 billion in constant 2024 dollars, discounted to 1960 at 3 percent real: NIH $261 billion (49.6%), private-sector pharmaceutical R&D $237 billion (45.0%), and nonprofit health R&D $29 billion (5.4%). NIH and industry contributed comparable amounts on both an undiscounted and a discounted basis. Undiscounted, the industry total is marginally the larger of the two ($604 billion versus $599 billion); in present value, NIH is about 10 percent larger, reflecting the somewhat greater concentration of its spending in the earlier decades, when discounting has less effect. The present value of pharmaceutical-attributable health benefits (1990–2015) is approximately $1.4 trillion. Set against the private-sector component alone ($237 billion), this implies a return on industry R&D of approximately 6.1:1. Set against the full societal denominator of $527 billion, the benefit–cost ratio is approximately 2.7:1, meaning that each dollar of societal R&D investment generated approximately $2.70 in discounted health value. In undiscounted constant 2024 dollars — the comparison most intuitive for scale — cumulative health benefits of approximately $5.0 trillion compare to cumulative R&D investment of approximately $1.3 trillion, for a ratio of 3.9:1. To put these magnitudes in perspective, the $5 trillion in cumulative health benefits is roughly one-sixth of current U.S. GDP. The benefit–cost ratio is not sensitive to any single alternative assumption. Varying the pharmaceutical attribution share alone yields 2.0:1 at 25 percent and 3.5:1 at 45 percent; varying the value per life-year alone yields 1.4:1 at $50,000, 4.1:1 at $150,000, and 5.5:1 at $200,000; the return on industry R&D scales in the same proportion (about 9:1 at $150,000 and 12:1 at $200,000). Applying the government-agency-derived value of a statistical life-year of $558,812 (Durie and Philipson, 2021) yields approximately 15.3:1; because that figure is expressed in 2020 dollars while our benefits are in constant 2024 dollars, this understates the resulting ratio. These are one-way sensitivities. Imposing the two most adverse assumptions jointly—25 percent attribution together with $50,000 per life-year—would bring the ratio to approximately 0.98:1. We regard that combination as implausible, since $50,000 per life-year is roughly one-fifth of the value used by U.S. federal agencies, and Buxbaum et al. attribute a further 13 percent of life expectancy gains to other medical care also produced by the R&D in our denominator. Under every other specification examined, the societal return on biopharmaceutical R&D investment exceeds 1:1.

Sensitivity to NIH Budget Mechanism. The base case uses total NIH appropriations. Because those appropriations fund activities beyond research itself—research training, research management and support, and buildings and facilities—a narrower measure of public research investment is defensible. NIH's composition by mechanism has been stable across recent decades: approximately 82 percent of appropriations fund extramural activity through grants, contracts, and other awards; approximately 11 percent funds intramural research; and approximately 6 percent covers research support, administration, and facilities (NIH, "Budget," based on FY2022 actual obligations; Congressional Research Service R43341; HHS FY2016 Budget in Brief). The detailed FY2009 mechanism table (Congressional Research Service RL33695) apportions the total as research project grants 53.2 percent, research centers 10.2 percent, other research 6.1 percent, R&D contracts 10.2 percent, research training 2.7 percent, intramural research 10.7 percent, research management and support 2.2 percent, and all other including buildings and facilities 4.7 percent. Excluding training, management, and facilities removes approximately 10 percent of the total, reducing the NIH present value to about $235 billion and raising the benefit–cost ratio to approximately 2.9:1. Additionally excluding intramural research—a more aggressive adjustment, since NIH laboratories conduct research directly—removes approximately 20 percent, reducing the NIH present value to about $209 billion and raising the ratio to approximately 3.0:1. We retain the full NIH total in the base case because it is the most conservative choice, and because applying mechanism-level adjustments to NIH but not to the NSF BERD industry series, which likewise includes overhead and administration, would introduce asymmetry.

Omitted Cost Components. Three omissions bias the denominator downward and therefore the ratio upward. First, as noted under Component 1, NIH appropriations exclude other federal health research funders (CDC, AHRQ, VA, DoD health programs, BARDA), understating federal health R&D by approximately 15–20 percent. Second, the denominator excludes research that universities, independent research institutes, and research hospitals finance from their own resources, including indirect costs of federally funded projects that grants do not cover, cost sharing, and institutionally financed research such as faculty start-up packages. Research!America estimates this institutional funding at $29.9 billion in 2025, about 65 percent of NIH's $46.0 billion (https://www.researchamerica.org/wp-content/uploads/2026/09/2026-ResearchAmerica-Investment-Report-September-2026.pdf); it was likely a smaller share during 1960–2005, and historical NSF Higher Education R&D data could be used to quantify it. If institutional funding averaged 25–50 percent of NIH spending over our window, adding it would raise the denominator by about $65–130 billion in present value and lower the societal ratio to about 2.4:1–2.2:1. Third, the industry series is narrower in scope than broader measures of

biopharmaceutical R&D, as discussed under Component 2. These adjustments are illustrative rather than estimated, and some of the omitted spending supported research unrelated to medicines. Combining the upper ends of all three (other federal funders at 20 percent of NIH, institutional funds at 50 percent of NIH, and industry R&D one-third higher) would lower the societal ratio to about 1.8:1; the lower ends together yield about 2.3:1. In every case the return remains well above 1:1.