Public Sector Replacement of Privately Funded Pharmaceutical R&D: Cost and Efficiency Considerations

Neumann U[1], Proudman D[2], Martin S[1], Grabowski H[3]

[1]Johnson & Johnson, Titusville, NJ, USA, [2]Analysis Group, Inc., Menlo Park, CA, USA, [3]Duke University, Durham, NC, USA

Background

- Economic studies demonstrate that funding for the US National Institute for Health (NIH) yields substantial returns for society, stimulating job creation and subsequent private sector R&D.[1,2]
- Currently, NIH and the biopharmaceutical industry perform complementary roles in the R&D ecosystem: 90% of NIH funding goes towards basic biomedical science, while private investment drives the development of medicines from pre-clinical research to FDA-approved therapies.[3,4]
- Policy suggestions advocating for partial or full government replacement of industry funding for drug development recently emerged from think tanks, the media, and some economists.[5–10]
- There is a need to investigate the private sector R&D expenditures undertaken for recent new drug approvals, as well as scholarly discussion on the economic efficiency implications of transitioning R&D financing and oversight to the public sector.

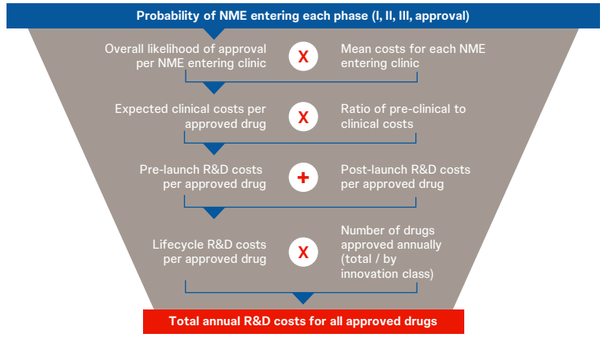
Research objectives

- Estimate pharmaceutical industry R&D spending on FDA-approved drugs to quantify how much public sector financing would be required to substitute for all private sector R&D funding.
- Complement the quantitative model with considerations for important changes in different types of economic efficiencies that warrant further investigation for replacement as a policy option.

Methods

- We developed a model to update R&D cost estimates for each phase of developing one molecule through to FDA approval, risk adjust for current clinical stage failure rates, and scale to the number of drug approvals between 2018 and 2022 stratified across FDA approval categories (**Figure 1**).
- Following a targeted literature review, model inputs for clinical research (Phase I–III trials in humans) are based on a study of publicly available product-level R&D costs in SEC filings.[11] For pre-clinical (e.g. drug discovery, lead candidate generation, and animal studies) and post-approval R&D costs (e.g. FDA-mandated pharmacovigilance, new indications and formulations), we sourced the most reliable measure from a survey-based study of large-to-midsize firms that yields a fixed ratio of pre-clinical to clinical cost and an indirect undiscounted estimate for post-approval cost. Likelihood of approval data was sourced from IQVIA.[12]
- All USD figures were inflation-adjusted to 2022 values using NIH's Biomedical Research and Development Price Index (BRDPI) for input cost in NIH activities.
- Total annual development costs of approved drugs were compared to the entire 2022 NIH budget ($46.2Bn)[13] and the 2017–2021 average annual NIH funding for clinical pharmaceutical trials ($5.6Bn) as estimated by the U.S. Government Accountability Office (GAO).[14]
- A supplementary literature review yielded qualitative insights into economic efficiency changes.

FIGURE 1: Simplified model structure



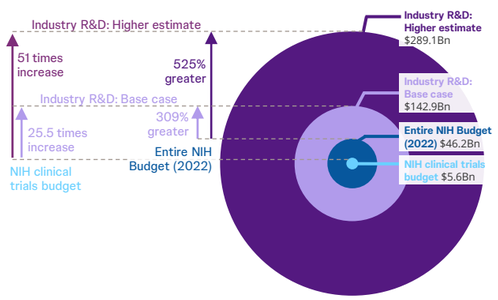
Results

TABLE 1: Key model parameters and outputs for total annual cost of development for approved drugs ($USD 2022)

Parameter	Scenario	Input value	Model Output: Total annual cost of development for all approved drugs	Source
Annualized inflation for clinical costs (2018–2022)	*Base case*	*2.72%*	*$142,855*[49]	*NIH Office of Budget, BRDPI*[65]
	Alternate high	10.34%	$177,298[41,49]	NIH Office of Budget, BRDPI + 8.5%[62]
	Alternate low	1.84%	$139,332[55]	Consumer Price Index[16]
Overall likelihood of approval	*Base case*	*8.57%*	*$142,855*[47]	*IQVIA*[17] *(2018-2022 average success rate)*
	Alternate high	6.67%	$172,456[57]	Dowden et al.[18] (2010-2017 average)
	Alternate low	11.60%	$115,695[56]	Smietana et al.[19] (2012-2014 average)
Average clinical trials costs for investigational compounds (non-capitalized)	*Base case*	*$119.5*	*$142,855*[42,47]	*Wouters et al.*[11] *(not capitalized) and IQVIA*[17] *(2018-2022 average success rates by phase)*
	Alternate high	$114.2	$138,232[41]	*DiMasi et al.*[12]
	Alternate low	$91.4	$127,871[41]	*DiMasi et al.*[12] -20%
Cost of Capital: average clinical period costs for investigational compounds	*Base case*	*Not capitalized*		
	Alternate high	$194.7	$195,395[42,47]	Wouters et al.[11] (capitalized at 10.5% per year) and *IQVIA*[17] (2018-2022 average)
	Alternate low	$168.9	$172,954[42,47]	Wouters et al.[11] (capitalized at 7.0% per year) and *IQVIA*[17] (2018-2022 average)
Proportion of clinical development cost per approved molecule dedicated to preclinical activity	*Base case*	*0.45*	*$142,855*[41]	*DiMasi et al.*[12]
	Alternate high	0.53	$152,250[41]	*DiMasi et al.*[12] +20%
	Alternate low	0.36	$133,832[41]	*DiMasi et al.*[12] -20%
Post-launch R&D costs, per approved drug, in millions	*Base case*	*$581*	*$142,855*[41]	*DiMasi et al.*[12]
	Alternate high	$697	$150,636[41]	*DiMasi et al.*[12] +20%
	Alternate low	$465	$135,075[41]	*DiMasi et al.*[12] -20%
Number of approvals/year		*Number of approvals per year*	*$142,855*[30-34]	*FDA*[20]
First in class		*21*		
Advance in class		*10*		
Addition in class		*18*		
Sum of all categories		*49*		

- Estimated non-capitalized, risk-adjusted clinical trial costs averaged $1.55Bn per approved compound (assuming an overall likelihood of approval of 8.57%; **Table 1**).
- Total R&D expenditures, including pre-clinical and post-approval research were on average $2.83Bn per approved drug (2022 USD).
- Accounting for cost of capital, total lifecycle R&D expenditures per approved drug averaged $3.56Bn (7% cost of capital) or $4.04Bn (10.5% cost of capital).
- When maintaining the same level of FDA approvals, uncapitalized replacement cost of private sector R&D funding are estimated at $142.9Bn in the base case, which is 309% greater than NIH's entire budget and approximately 25.5 times its recent clinical research expenses (**Figure 2**).
- Between 2018 and 2022, an average of 63% of newly approved drugs received first-in-class designation or FDA priority review — incurring replacement costs of $56.1Bn and $25.7Bn, respectively— equivalent to 177% of NIH's total budget or 14.6 times its clinical trials budget.
- Literature-driven scenario analyses indicate results are most sensitive to assumptions on inflation for R&D costs, probability of success, and cost of capital: A scenario based on research estimating a 6.67% success probability, 10.34% R&D cost inflation, and 7.0% cost of capital illustrates the upper bound of a plausible range of replacement cost — resulting in an estimate of $289.1Bn.

FIGURE 2: Visual comparison of model outputs



Unquantified efficiency impacts

- Performance & cost control
- Serendipitous discovery
- Long-run dynamic efficiency
- Asymmetric information
- Adverse selection
- Yardstick competition
- Hold-up/contracting issues
- Political rent-seeking

Discussion

- Our model suggests increased annual cost of R&D in recent years, primarily driven by a higher risk of failure and a greater number of molecules in clinical research. Non-capitalized R&D expenses rose to $2.83Bn per approved drug compared to DiMasi et al.'s (2016) $1.86Bn estimate[12] — a 26% increase after inflation.
- The estimated $142.9Bn cost of shifting funding to the public sector greatly exceed previous estimates of $50.9Bn per year (for drugs that received approval between 2003 and 2011).[4]
- Our replacement cost estimates for drug development may be conservative, considering several other factors that would be inherent in transitioning from private to public sector funding:
  - A. Our estimates do not account for required costs for manufacturing, distribution, or medical education, and they may miss expenditure for R&D platform development and operational administration.
  - B. Our calculations assume that the government supplants private funding through contracts or prizes, not by transferring research execution to government facilities. The additional administrative burden of creating a required R&D financing and monitoring regime remains unquantified, but it is likely substantial.
  - C. Our inputs for pre-clinical cost may only partially capture all early-stage R&D investment of private-sector VC firms, which account for a substantial part of R&D ecosystem funding, resulting in targets pharmaceutical firms can investigate as potential drug candidates.
  - D. Inflation adjustments are based on NIH's current input costs for basic science, which may not adequately reflect price changes in conducting FDA clinical trials for drug approval.
  - E. Estimated post-approval R&D costs, constituting roughly 20% of lifecycle expenses in our base case, might be underestimated. Available input data precede a recent increase in post-approval observational studies and indication expansions, especially for oncology and the most widely used drugs (e.g. a recent analysis estimated 61% of lifecycle R&D for Medicare's top 10 drugs occurred post-FDA approval).[21]
  - F. In the interest of research reproducibility, all clinical period data were derived from a study of product-level R&D costs readily identifiable in public filings, offering a sample of companies that may only imperfectly reflect all R&D expenses for the entire industry.
  - G. Our base case does not include any opportunity costs of capital, but the high failure rate in drug development makes the time value of money a critical factor in R&D expenses, some of which plausibly affects government financing as well.

Further considerations of associated economic implications

- The notion of large-scale government-driven drug development is principally underexplored in mainstream academic discourse, offering insufficient empirical evidence for further quantitative estimation of associated replacement impacts.
- Beyond the scale of quantifiable expenditures required to replace industry, the core assumption that public and private sectors can functionally replace each other warrants critical examination.
- A targeted review of conceptual literature indicates the need to address key factors that could significantly impact economic incentives, associated efficiencies, and welfare effects (**Table 2**).

TABLE 2: Tensions to investigate for proposals of government-directed R&D

Hold-up problem and contracting efficiency:

Once R&D costs become sunk, bargaining power and leverage shift, and rewards may be significantly reduced. Absence of predictability and coordination between parties is known to cause efficiency losses while contracting issues emerge from the tension to pre-align both outcome specificity and operational flexibility of unpredictably complex R&D with optimal risk-sharing.[22–24]

Performance measurement and cost control:

Ex-ante government criteria can lead to adverse selection and diminish innovation quality. With limited monitoring on behalf of the R&D payer, "yardstick competition," has been known to occur where payoffs hinge on costs without incentivizing efficiency or innovation. Approaches such as "cost-plus" have thus often been rejected as viable models for drug innovation.[25–29]

Centralized funding:

Replacing private at-risk capital deployed via the competitive, de-centralized market provision with centrally directed capital allocations could alter collective drug development efforts, for example potentially diminishing the nuanced local knowledge that diverse independent entities contribute within the current dispersed R&D ecosystem. This may under-reward advances core to the iterative process of scientific discovery.[30–34]

Political rent-seeking:

Central funding decisions of the required magnitude may also lead to rent-seeking fueled by short-run political cycles, clashing with the extended timelines of often failure-prone drug R&D. Evidence suggests party political agendas, connections, and lobbying rather than clinical unmet need, can bias science funding. New health equity issues may arise if political majority choices fail to integrate demand for continued research into heterogeneous patient needs across many conditions.[35–40]

Dynamic long-run efficiencies:

As recently experienced with the Inflation Reduction Act (IRA), concerns can arise over the government's limited appreciation of the established value of incentivizing follow-on innovation after initial first-in-class entrants or drug development needs for additional indications.[41] The prospect of public financing of uncertainties and budget constraints might lead to under-rewarding of uncertain and distant biomedical innovations, reduce incentives for earlier-stage clinical research, and lead to fewer new drug introductions.[42,43]

Additional potential effects:

Various further considerations of a scenario for government-directed R&D would also require critical investigation, such as free-riding by ex-US payers in international patenting, impact on the broader US biomedical R&D landscape, or changes in market timing and disease area targets.[44–46]

- Our review of theoretical economic literature and relevant case studies finds scant support for efficiency gains from substituting government for private R&D funding in our policy scenario.
- In turn, substantial evidence supports that public and private roles in drug development are distinct and complementary, indicating replacement could lead to unforeseen changes in welfare.

Conclusions

- Our examination reveals that simply substituting direct R&D expenditures does not nearly encompass the full cost of delivering medicines to patients: Substantial additional expenses, currently covered by the private sector, would either remain or require additional financing.
- To address the substitution costs for the loss of private sector R&D investment without a decline in approvals, policy makers would need to allocate additional funding equivalent to at least three entire NIH budgets solely for drug R&D (in addition to maintaining current NIH funding obligations within the federal budget).
- This study reveals a significant gap between recent private pharmaceutical R&D investments and the relatively more reserved funding of the U.S. government: For every $100 of industry R&D spending in our conservative base case, NIH commits less than $4 to clinical drug research.
- While substitution costs would present a substantial new burden for taxpayers, we find that policies seeking to grow government-funding only to replace already available private capital have generally not been shown to deliver welfare gains in terms of either allocative static or long-run dynamic efficiency.
- Policymakers are well advised to interrogate R&D funding replacement proposals for empirical evidence, considering the numerous uncertainties around economic incentives and efficiencies.
- In view of the risk of undermining existing societal benefits generated from the functional complementarity of private and public R&D, a more pragmatic policy approach may be to calibrate government involvement for disease areas currently underserved by private capital.

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