



OPINION ARTICLE

Public research funding and pharmaceutical prices: do Americans pay twice for drugs? [version 1; peer review: 2 approved]

Rena M. Conti^{1,2}, Frank S. David ^{3,4}

¹Questrom School of Business, Boston University, Boston, MA, 02215, USA

²Institute for Health System Innovation and Policy, Boston University, Boston, MA, 02215, USA

³Pharmagellan LLC, Milton, MA, 02186, USA

⁴Harvard-MIT Center for Regulatory Science, Boston, MA, 02115, USA

V1 First published: 15 Jul 2020, 9:707
<https://doi.org/10.12688/f1000research.24934.1>
 Latest published: 15 Jul 2020, 9:707
<https://doi.org/10.12688/f1000research.24934.1>

Abstract

In the debate over prescription drug pricing, some pharmaceutical industry critics claim that U.S. taxpayers pay twice for costly therapies, because publicly supported research is a major contributor to drug discovery and American taxpayers are inadequately rewarded for their research investment due to high drug prices. In fact, the empirical evidence supporting these claims is weak, and the pay twice argument distracts from important efforts to ensure that impactful new drugs continue to be developed and made widely available to patients who need them.

Keywords

Pharmaceutical, drug, price, access, research, development, funding, patents

Open Peer Review

Reviewer Status ✓ ✓

	Invited Reviewers	
	1	2
version 1	✓	✓
15 Jul 2020	report	report

- Fred D. Ledley** , Bentley University, Waltham, USA
- Jacob Sherkow** , University of Illinois at Urbana-Champaign, Champaign, USA

Any reports and responses or comments on the article can be found at the end of the article.

Corresponding author: Frank S. David (frank@pharmagellan.com)

Author roles: **Conti RM:** Conceptualization, Investigation, Writing – Original Draft Preparation, Writing – Review & Editing; **David FS:** Conceptualization, Funding Acquisition, Investigation, Writing – Original Draft Preparation, Writing – Review & Editing

Competing interests: FSD derives most of his income from providing consulting services to drug and device manufacturers, and is also a part-time employee of Brigham and Women's Hospital. FSD's spouse is employed by and expects to receive equity in Sanofi Genzyme. RMC has no competing interests to disclose.

Grant information: Dr. David's work on this manuscript was supported by a research grant from BIO (Biotechnology Industry Organization, Inc.). Dr. Conti's effort on this manuscript was unfunded.

The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript.

Copyright: © 2020 Conti RM and David FS. This is an open access article distributed under the terms of the [Creative Commons Attribution License](#), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

How to cite this article: Conti RM and David FS. **Public research funding and pharmaceutical prices: do Americans pay twice for drugs? [version 1; peer review: 2 approved]** F1000Research 2020, 9:707 <https://doi.org/10.12688/f1000research.24934.1>

First published: 15 Jul 2020, 9:707 <https://doi.org/10.12688/f1000research.24934.1>

Introduction

Do pharmaceutical companies unfairly bilk American patients when they charge exorbitant prices for drugs developed based on publicly funded research? In a [hearing of the House Committee on Oversight and Reform in January, 2019](#), U.S. Representative Alexandria Ocasio-Cortez of New York argued that “the public is acting as early investor, putting tons of money into the development of drugs that then become privatized, and then they receive no return on the investment that they have made” (see [video recording from Twitter](#)).

Embedded in this “pay twice” argument are three key questions. First, to what extent is public funding responsible for the invention of most new drugs? Second, are U.S. taxpayers inadequately rewarded for their contribution to new drug development? And third, how are these claims salient to the national debate over drug prices?

In this piece, we summarize the available evidence regarding each of these questions as follows: First, although public funds support a significant amount of important biomedical research, the vast majority of the credit for translating this research into new therapies is due to private companies. Second, the contention that taxpayers receive “no return” on their research investment is incorrect, as it fails to account for the massive health and wealth benefits that Americans receive from new drugs. And finally, the pay twice claim distracts attention from far more impactful and feasible efforts to balance innovation and access across the entire pharmaceutical sector.

Are new drugs invented by publicly funded researchers?

There is little debate that public funding of basic science is a critical enabler of drug development^{1,2}. The [National Institutes of Health \(NIH\)](#) is the world’s largest government funder of biomedical research, and makes financial and practical contributions to all stages of it, including pre-clinical scientific investigations, translational medicine, and clinical trials. Detailed case studies reveal that public support has played at least some role in virtually all of the 26 most clinically and commercially significant drugs and drug classes approved over the past several decades³. And [several important medicines](#) were solely invented by academic researchers, including the lung cancer therapy pemetrexed, the vitamin D analog doxercalciferol, the inhaled pulmonary vasodilator nitrous oxide, and the vaccine for *Haemophilus influenzae* type b⁴.

But in a large majority of cases, the public sector’s contribution to new drugs has been in the form of early scientific findings, unrelated to current or potential applications. The public sector supported key basic research for 19 of the 26 “transformative” drugs and drug classes cited above, contributed to the actual discovery of a new therapy in just 11, and could claim sole discovery credit in only four cases⁵. More broadly, although NIH funding supported at least one publication related to each of the 210 new medicines approved by the Food and Drug Administration (FDA) from 2010 to 2016, over 90 percent of those papers were related to the underlying drug target, not the actual therapy itself⁶.

Comprehensive reviews of the genesis of approved drugs confirm that while publicly funded science often characterizes important pathologic processes and identifies potential drug targets, the private sector is the main inventor of most new therapies. A recent study found that for only 25 percent of drugs approved from 2008 to 2017 was there any documented contribution, of any magnitude, to a drug’s initial discovery, synthesis, or key intellectual property by a public sector research institution or academic “spin-off” company⁷. This finding corroborated a review of approvals from 1998 to 2007, which found that publicly funded research helped either identify the chemical structure of the final compound or its direct antecedents or demonstrated therapeutic proof-of-concept for the target for only about a third of new drugs⁸. If one uses a more stringent definition of “contribution” based solely on intellectual property, then taxpayers’ role in drug discovery is even smaller; less than 15 percent of new medicines are covered by even a single patent that was either directly issued to a public entity or contains a “government interest statement” acknowledging public funding^{7,9,10}.

Government funding makes enormous contributions to medicine by generating novel insights into biology and disease. But accumulated evidence demonstrates that in the majority of cases, it is the private sector, not academia, which translates those insights into new therapeutics.

Are U.S. taxpayers inadequately rewarded for their investment in drug development?

A key component of the pay twice argument is that Americans receive an insufficient return from the funds they allot to biomedical research that enables new drug development. But although it is technically true that direct returns to the NIH from licensing royalties comprise a miniscule fraction of the agency’s budget, this strictly transactional assessment ignores the health and wealth benefits that accrue to taxpayers from publicly funded science.

In fact, the main return on investment American taxpayers expect from supporting biomedical research is in the form of direct benefits to morbidity and mortality – which have largely been realized. Therapies enabled by publicly funded science have extended and improved human lives, and enabled patients to avoid hospitalizations and other costly interventions that yield worse outcomes^{11–13}. In specific therapeutic areas, like hypertension¹⁴, mental illness¹⁵, some cancers¹⁶, HIV¹⁷, and routine childhood vaccinations¹⁸, biomedical research has generated enormous surplus economic value for the American public, far in excess of the sum of all public and private investments in research and development¹⁹. These savings increase further when exclusivity ends, generics enter the market, and low-priced therapies become available to users of both the branded agent and other expensive medicines in the same class²⁰. Many new medicines also generate other valuable health and welfare benefits that are difficult to quantify, such as improving employment and social engagement for both patients and caregivers²¹.

Public research and development investments have also been a significant growth driver for the U.S. economy and a wealth creator for taxpayers. This funding has yielded millions of

relatively well-paid jobs and billions of dollars of taxes paid into the coffers of local communities, states, and the federal government²², although these benefits **take a long time to accrue** and are often unevenly distributed across geographies.

An important caveat to these studies and conclusions is that just because publicly funded biomedical research yields large returns to taxpayers, does not mean that the current system for realizing those benefits is optimal. As discussed above, about 15 percent of new drugs are based on at least one patent that relied on public funding. In almost all cases, those patents were licensed to pharmaceutical firms under the Bayh-Dole Act, which was passed in 1980 to encourage the commercialization of taxpayer-funded research that might otherwise lie dormant²³. Since its passage, detractors have argued that academic patenting insufficiently rewards U.S. taxpayers for their contributions, and imposes costs that reduce its net social benefit²⁴. But even in light of possible opportunities to improve Bayh-Dole to create even more social value, the pharmaceutical industry is one of the clearest examples where exclusive intellectual property rights are critical to convert taxpayer-funded research into useful new products, because of the high cost and risk of drug development²⁵.

Calculating the net returns from publicly funded science is complicated, and it is unlikely that economists will ever explicitly quantify them in a way that satisfies all stakeholders. For this reason, it is impossible to determine objectively whether or not the extent of public support for drug development is appropriately accounted for in their prices. But this challenge notwithstanding, it is empirically false to argue that Americans “receive no return on the investment that they have made” in biomedical research.

How is the “pay twice” claim relevant to the debate over high drug prices?

Recent proposals to limit drug prices are motivated by the worthy goal of ensuring that clinically valuable new drugs are not only developed, but also maximally available to the patients who need them²⁶. The pay twice critique has played an increasingly prominent role in justifying these legislative and administrative remedies, fueled by expensive medicines that owe at least some indisputable scientific debt to public research.

From a rhetorical standpoint, the pay twice argument certainly brings attention to the challenge of drug access and affordability. But practically speaking, prior experience suggests it would be difficult to link drug prices to the receipt of public support for basic biomedical research. NIH established a “**reasonable pricing clause**” in 1989 for products developed through some collaborative public-private research grants, which authorized the government to “require ... reasonable evidence” of “a reasonable relationship between the pricing of a licensed product, the public investment in that product, and the health and safety needs of the public.” But the agency eliminated this provision in 1995, amidst concerns about how to define “reasonable pricing,” enforce restrictions and penalties, and

mitigate potential negative effects on innovation²⁷. These concerns remain relevant today, in light of the persistent challenges outlined above in quantifying these factors, and would likely preclude adoption of a similar policy, especially if it were intended to apply to an even wider set of therapies.

Similarly, the feasibility of limiting drug prices via existing “**march-in**” rights is also limited. Bayh-Dole allows the government to obtain a nonexclusive, royalty-free license to patents developed with public funds, for its own use or that of a third party, if the patent holder fails to adequately commercialize the invention. The NIH has denied all of the march-in petitions it has received to date, maintaining that high prices per se are insufficient rationale to claim inadequate commercialization. (A **petition related to Exondys 51**, a therapy for Duchenne muscular dystrophy, is still under review.) But even if this obstacle were surmounted, the practical impact of march-in rights would be limited, because almost all drugs covered by Bayh-Dole patents are also covered by additional privately held patents, to which the government has no claim²⁸.

Beyond the practical challenge of how to operationalize a link between a drug’s price and the extent to which public funds contributed to its development lies a more fundamental question: why should it matter? If one’s primary concern is that corporate profiteering limits affordable and equitable access to medicines with proven clinical benefits, then the pay twice argument undercuts the potential impact of broader proposals to improve access to all drugs, regardless of their provenance. **Recent suggestions discussed by lawmakers** and others include revoking monopoly pricing power once a certain profit threshold is exceeded; “**delinking**” patents from innovation and **rewarding innovators instead with prizes**; awarding the government more direct control over drug pricing via international reference price or cost-effectiveness benchmarks; and expanding government’s use of so-called “Section 1498” to use or manufacture any patented product²⁹. In parallel, proposals to eliminate out-of-pocket costs and ensure the availability of cheap generics after patent expiry could also improve access to drugs by reducing patient-borne expenses³⁰. These ideas all entail significant tradeoffs related to innovation that are incompletely understood, and reasonable stakeholders can disagree about how to weigh these tradeoffs given this inherent uncertainty³¹. But importantly, they share a common focus on improving access to *all* clinically important therapies, irrespective of their origin, while ensuring that new drugs continue to be developed.

It is superficially attractive to argue that Americans are entitled to pay a lower price for a new drug that was substantially enabled by taxpayer-funded research. But the implication of that claim – that there is no such entitlement to affordability, or far less of one, for a drug mostly developed by a for-profit company – runs counter to the overarching goal of ensuring that all Americans have equitable access to beneficial therapies. Proposals to control a therapy’s price based on the degree to which public funds contributed to its development are not just unfeasible to implement, but also a distraction from more

far-reaching efforts to improve the affordability of all medicines. Attention should instead be focused on developing practical solutions that ensure that clinically valuable new drugs **continue to be developed and are accessible by all patients in need.**

Data availability

Underlying data

No data are associated with this article.

Acknowledgements

We thank Amitabh Chandra, Yevgeniy Feyman, Rachel Sachs, and Rebecca Wolitz for helpful comments on earlier drafts of this manuscript, and Gabriela Gracia for expert research assistance on manuscript preparation. We also thank the anonymous reviewers at *Annals of Internal Medicine*, whose helpful suggestions on an earlier version of this manuscript led us to make substantial improvements.

References

- Flier JS: **Academia and industry: allocating credit for discovery and development of new therapies.** *J Clin Invest.* 2019; **129**(6): 2172–2174. [PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
- Spector JM, Harrison RS, Fishman MC: **Fundamental science behind today's important medicines.** *Sci Transl Med.* 2018; **10**(438): eaaq1787. [PubMed Abstract](#) | [Publisher Full Text](#)
- Kesselheim AS, Tan YT, Avorn J: **The roles of academia, rare diseases, and repurposing in the development of the most transformative drugs.** *Health Aff (Millwood).* 2015; **34**(2): 286–293. [PubMed Abstract](#) | [Publisher Full Text](#)
- Schneerson R, Porter A, Smith DH: **Prevention of systemic infections, especially meningitis, caused by Haemophilus influenzae type b: impact on public health and implications for other polysaccharide-based vaccines.** *JAMA.* 1996; **276**(14): 1181–1185. [PubMed Abstract](#) | [Publisher Full Text](#)
- Chakravarthy R, Cotter K, DiMasi J, et al.: **Public-and private-sector contributions to the research and development of the most transformational drugs in the past 25 years: From theory to therapy.** *Ther Innov Regul Sci.* 2016; **50**(6): 759–768. [PubMed Abstract](#) | [Publisher Full Text](#)
- Cleary EG, Beierlein JM, Khanuja NS, et al.: **Contribution of NIH funding to new drug approvals 2010 – 2016.** *Proc Natl Acad Sci U S A.* 2018; **115**(10): 2329–2334. [PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
- Nayak RK, Avorn J, Kesselheim AS: **Public sector financial support for late stage discovery of new drugs in the United States: cohort study.** *BMJ.* 2019; **367**: i5766. [PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
- Kneller R: **The importance of new companies for drug discovery: origins of a decade of new drugs.** *Nat Rev Drug Discov.* 2010; **9**(11): 867–882. [PubMed Abstract](#) | [Publisher Full Text](#)
- Sampat BN, Lichtenberg FR: **What are the respective roles of the public and private sectors in pharmaceutical innovation?** *Health Aff (Millwood).* 2011; **30**(2): 332–339. [PubMed Abstract](#) | [Publisher Full Text](#)
- Stevens AJ, Jensen JJ, Wyller K, et al.: **The role of public-sector research in the discovery of drugs and vaccines.** *N Engl J Med.* 2011; **364**(6): 535–541. [PubMed Abstract](#) | [Publisher Full Text](#)
- Lichtenberg FR: **Sources of US longevity increase, 1960–2001.** *Quart Rev Econ Finance.* 2004; **44**(3): 369–389. [Publisher Full Text](#)
- Lichtenberg FR: **Benefits and costs of newer drugs: an update.** *Manag Dec Econ.* 2007; **28**(4–5): 485–490. [Publisher Full Text](#)
- Zhang Y, Soumerai SB: **Do newer prescription drugs pay for themselves? A reassessment of the evidence.** *Health Aff (Millwood).* 2007; **26**(3): 880–886. [PubMed Abstract](#) | [Publisher Full Text](#)
- Cutler DM: **The lifetime costs and benefits of medical technology.** *J Health Econ.* 2007; **26**(6): 1081–1100. [PubMed Abstract](#) | [Publisher Full Text](#)
- Frank RG, Berndt ER, Busch AB, et al.: **Quality-constant “prices” for the ongoing treatment of schizophrenia: an exploratory study.** *Q Rev Econ Finance.* 2004; **44**(3): 390–409. [PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
- Sun EC, Jena AB, Lakdawalla DN, et al.: **An economic evaluation of the war on cancer.** *J Health Econ.* 2010; **29**(3): 333–346. [PubMed Abstract](#) | [Publisher Full Text](#)
- Phillipson TJ, Jena AB: **Who benefits from new medical technologies? Estimates of consumer and producer surpluses for HIV/AIDS drugs.** *Forum for Health Economics & Policy.* 2006; **9**(2): 1–33. [Publisher Full Text](#)
- Phillipson TJ, Snider JT, Chit A, et al.: **The social value of childhood vaccination in the United States.** *Am J Manag Care.* 2017; **23**(1): 41–47. [PubMed Abstract](#)
- Lane J, Bertuzzi S: **Measuring the results of science investments.** *Science.* 2011; **331**(6018): 678–680. [PubMed Abstract](#)
- Padula WV, Larson RA, Dusetzina SB, et al.: **Cost-effectiveness of tyrosine kinase inhibitor treatment strategies for chronic myeloid leukemia in chronic phase after generic entry of imatinib in the United States.** *J Natl Cancer Inst.* 2016; **108**(7): djw003. [PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
- Neumann PJ, Sanders GD, Russell LB, et al.: **Cost-effectiveness in health and medicine.** (Oxford University Press). 2016. [Reference Source](#)
- Gruber J, Johnson S: **Jump-starting America: How breakthrough science can revive economic growth and the American dream.** (Public Affairs). 2019. [Reference Source](#)
- Sampat BN: **Patenting and US academic research in the 20th century: The world before and after Bayh-Dole.** *Research Policy.* 2006; **35**(6): 772–789. [Publisher Full Text](#)
- Mazzucato M: **The entrepreneurial state: Debunking public vs. private sector myths.** (Anthem Press). 2013. [Reference Source](#)
- Ouellette LL, Weires R: **University Patenting: Is Private Law Serving Public Values?** *Michigan State Law Review.* forthcoming; *Stanford Law and Economics*, Olin Working Paper No. 2020; 537. [Reference Source](#)
- Bach PB: **New math on drug cost-effectiveness.** *N Engl J Med.* 2015; **373**(19): 1797–1799. [PubMed Abstract](#) | [Publisher Full Text](#)
- Wolitz RE: **The pay-twice critique, government funding, and reasonable pricing clauses: Georgia State University, College of Law Journal of Legal Medicine Symposium.** *J Legal Med.* 2019; **39**: 177–211.
- Engelberg AB, Kesselheim AS: **Use the Bayh-Dole Act to lower drug prices for government healthcare programs.** *Nat Med.* 2016; **22**(6): 576. [PubMed Abstract](#) | [Publisher Full Text](#)
- Brennan H, Kapczynski A, Monahan CH, et al.: **A prescription for excessive drug pricing: leveraging government patent use for health.** *Yale J Law & Tech.* 2016; **18**: 275. [Reference Source](#)
- Kolchinsky P: **The Great American Drug Deal.** (Evelexa Press). 2020.
- Bagley N, Berger M, Chandra A, et al.: **The Orphan Drug Act at 30.** In: *Innovation Policy and the Economy*, J. Lerner and S. Stern, eds. (University of Chicago Press). 2018.

Open Peer Review

Current Peer Review Status:  

Version 1

Reviewer Report 04 November 2020

<https://doi.org/10.5256/f1000research.27509.r73200>

© 2020 Sherkow J. This is an open access peer review report distributed under the terms of the [Creative Commons Attribution License](#), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.



Jacob Sherkow 

College of Law, University of Illinois at Urbana-Champaign, Champaign, USA

The authors succinctly and clearly explain why the "pay twice" critique regarding drug pricing in the U.S. is misguided using available evidence drawn from the literature. This is important because, as the authors note, critiques regarding "excessive" pricing "run[] counter to the overarching goal of ensuring that all Americans have equitable access to beneficial therapies." An excellent summary of a thorny—and unfortunately, persistent—topic in the literature.

Is the topic of the opinion article discussed accurately in the context of the current literature?

Yes

Are all factual statements correct and adequately supported by citations?

Yes

Are arguments sufficiently supported by evidence from the published literature?

Yes

Are the conclusions drawn balanced and justified on the basis of the presented arguments?

Yes

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: intellectual property, patents, biotechnology, bioethics, regulation

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard.

Reviewer Report 26 October 2020

<https://doi.org/10.5256/f1000research.27509.r73012>

© 2020 Ledley F. This is an open access peer review report distributed under the terms of the [Creative Commons Attribution License](#), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.



Fred D. Ledley 

Center for Integration of Science and Industry, Departments of Natural & Applied Science and Management, Bentley University, Waltham, MA, USA

This is a well written and referenced article and a significant contribution to the discussion about the relationship between public sector funding for biomedical research and drug prices by two accomplished scholars. We believe this is a meaningful contribution to the literature and should be published.

We have several comments and suggestions for the authors and, since this is an open review, we offer these in the context of a more dialectical discussion than we would in a conventional review.

As the author's correctly note, there are two largely unrelated, issues in the "playing twice" policy debates:

1. Is the public actually paying for drug development while the company receives all of the profits based on the premise that they developed the drug?
2. Are taxpayers adequately rewarded for the contribution to new drug development? A corollary to this is the question of the role of Bayh-Dole in providing the public sector with a return.

We will address these arguments separately.

First, we would note that quote from Representative Ocasio-Cortez' relates specifically to the second question, not the question of "paying twice", and recommend that the author clarify this point.

While the authors are absolutely correct in stating that "the vast majority of the credit for translating this research into new therapies is due to private companies," we would point out that the framing of this question as relating solely to "translation" unfairly narrows the question. The problem is that, rhetorically framing the question as one that relates specifically to "translation' or "development," when the public sector contribution focuses primarily on basic biomedical research, makes their argument essentially a tautology.

As the authors note, our research (referenced in the manuscript), demonstrates that >\$100 billion in NIH funding was related to the drugs (or their targets) approved 2010-2016 www.pnas.org/content/115/10/2329, with >90% of this funding focused on basic research. We call the authors attention to a recent follow-on study, which shows that >\$200 billion in NIH funding was related to the 356 drugs approved for the full decade 2010-2019. www.ineteconomics.org/uploads/papers/WP_133-Cleary-et-al-Govt-innovation.pdf, again, with the large majority focused on basic science. If one assumes that industry spends an average of \$1.5 billion in developing each drug, the amount estimated by DiMasi *et al*,¹ pubmed.ncbi.nlm.nih.gov/26928437/ without considering cost of capital, (there is no cost of

capital correction in calculating NIH spending), these data argue that the public sector contribution that enables drug discovery and development is of the same order of magnitude as the contribution of the private sector in the penultimate stages of translation. If one considers the range of drug development costs described by Wouters *et al* jamanetwork.com/journals/jama/fullarticle/2762311², or the substantially lower estimates promulgated by some critics, the contributions of the public and private sectors may be very similar.

The point is that BOTH the public sector investment in the enabling science AND the private sector investments in translation are required for drugs to reach the market, and that the overall investment needed to translate a scientific insight into an approved product is much greater than generally appreciated. In this context, public DOES contribute a significant fraction of the overall cost of developing a drug, and DOES pay for the drug itself. Taking this value chain one step further, inasmuch as the revenues from sale of the drug provides the revenue for the large majority of industrial R&D, taxpayers are paying the FULL cost of both the basic research and the applied/translational research and development. Despite this, the public is ALSO paying for the profits of biopharmaceutical companies (<https://jamanetwork.com/journals/jama/fullarticle/2762308>), and the price of drugs is, in fact, titrated to the desired profit rather than the cost of bringing drugs to market.

It is important to recognize that capital investments by shareholders contribute only a small fraction of the costs of research and development. The large pharmaceutical companies, which are primarily responsible for the costs of most drug development, distribute substantially more capital to shareholders in the form of dividends and stock buybacks than they raise in the form of stock sales (www.ineteconomics.org/perspectives/blog/financialization-us-pharma-industry).

Shareholders play a more significant role in funding R&D expenditures of emerging biotechnology companies. While capital investments in biotechnology companies have increased dramatically since 2015, annual investments in biotechnology companies are historically a small fraction of total R&D spending and not greater than public sector support through the NIH.

We have several final suggestions for the authors (i) While we agree with the authors that taxpayers are not technically “paying twice,” we encourage the authors to acknowledge the limited frame of this question. (ii) We encourage the authors to recognize that the public sector is paying the large majority of the costs for R&D through taxes and drug prices, and ALSO subsidizing the distribution of cash to shareholders, who speculate in the success or failure of biopharmaceutical companies, but make little contribution to the development of new drugs.

Second, the argument that the public should receive a return on its investment in basic science, which was the basis of Representative Ocasio-Cortez’ question, arises from the work of Dr. Marianna Mazzucato (Dr. Mazzucato has consulted with Representative Ocasio-Cortez). As the authors reference, these arguments are articulated in her book *The Entrepreneurial State* (referenced in the article), and numerous articles in the academic literature. (e.g. hbr.org/2016/10/an-entrepreneurial-society-needs-an-entrepreneurial-state) Her argument is that government serves as the “investor of first resort” in innovation, investing even before angel or venture investors, who expect high returns on their “risk investments.” Inasmuch as taxpayers are making even earlier investments with implicitly higher risk, Mazzucato argues that the public is similarly entitled to a proportionate return on investment. These arguments are increasingly

important in public policy discussions and warrant further elaboration in the article. While the authors are technically correct in calling out the statement that taxpayers “receive no return” on investment as untrue, we would encourage them to refrain from rhetorically limiting the question to the issue of “NO” return.

The authors correctly quote an extensive literature demonstrating the health value of effective medicines. We would note, however, that much of this work (particularly the series of landmark papers by Lichtenberg), largely reflect advances made in preventing and treating cardiovascular and infectious diseases, and there is increasing concern about the health value of many recently approved drugs, particularly those approved through expedited pathways. The authors also correctly note that job creation, taxes, and economic growth arising from pharmaceutical innovation constitute a public good and an indirect return on taxpayer investments. We would, however, encourage the authors to use more modest language than “...enormous surplus economic value...” in describing these benefits. We would also note that reference #19 does not appear to be relevant to this statement.

We would, however, encourage the authors to recognize that these arguments are undercut by social inequities. The benefits of new drugs are not available to those without adequate insurance/government coverage due to their high price; the jobs created by the biopharmaceutical industry are disproportionately available in selected geographic areas and to individuals with access to higher education; companies go to extraordinary lengths to minimize the taxes they pay to the US government; and the profits generated by high drug prices are often distributed to shareholders who are disproportionately in the highest socioeconomic classes and who also go to great lengths to minimize their taxes. In this context, while the returns may not be as high as anticipated by policy makers due to tax avoidance strategies, and the aggregate or average benefits may not reflect the returns to most taxpayers.

The authors should also recognize that the Bayh Dole Act captures a very small fraction of the value created by taxpayer investments in basic science and that the direct returns to the public sector are very limited. By design, Bayh-Dole is relevant only to “subject inventions” and the licenses that provide returns to nonprofit, academic organizations are predicated on patentable subject matter. The problem is that the legal definitions of an “invention” and patentable subject matter require that the inventor establish utility and the ability to reduce their advances to practice. In contrast, the primary focus of taxpayer-funded research is on basic science, which does not require recognized utility, though it may be “use inspired” (Stokes, Pasteur’s Quadrant: Basic Science and Technological Innovation, Brookings, 1997) and is, by definition, not focused on enabling reduction to practice. Thus, the vast majority of government funded biomedical research is not covered by the Bayh-Dole Act and there is no formal mechanism for the public sector to receive a direct return on investment.

References

1. DiMasi JA, Grabowski HG, Hansen RW: Innovation in the pharmaceutical industry: New estimates of R&D costs. *J Health Econ.* 2016; **47**: 20-33 [PubMed Abstract](#) | [Publisher Full Text](#)
2. Wouters OJ, McKee M, Luyten J: Estimated Research and Development Investment Needed to Bring a New Medicine to Market, 2009-2018. *JAMA.* 2020; **323** (9): 844-853 [PubMed Abstract](#) | [Publisher Full Text](#)
3. Ledley F, McCoy S, Vaughan G, Cleary E: Profitability of Large Pharmaceutical Companies Compared With Other Large Public Companies. *JAMA.* 2020; **323** (9). [Publisher Full Text](#)

Is the topic of the opinion article discussed accurately in the context of the current literature?

Yes

Are all factual statements correct and adequately supported by citations?

Yes

Are arguments sufficiently supported by evidence from the published literature?

Yes

Are the conclusions drawn balanced and justified on the basis of the presented arguments?

Partly

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: Characterizing systems for translational science including science, public and private sector investments, measures of public value creation, and public policy.

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard.

The benefits of publishing with F1000Research:

- Your article is published within days, with no editorial bias
- You can publish traditional articles, null/negative results, case reports, data notes and more
- The peer review process is transparent and collaborative
- Your article is indexed in PubMed after passing peer review
- Dedicated customer support at every stage

For pre-submission enquiries, contact research@f1000.com

F1000Research