The Government and Pharmaceutical Innovation: Looking Back and Looking Ahead

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Abstract: Current debates about the roles of the public and private sectors in pharmaceutical innovation have a long history. The extent to which, and ways in which, the public sector supports drug innovation has implications for assessments of the returns to public research funding, taxpayer rights in drugs, the argument the high prices are needed to support drug innovation, and the desirability of patenting publicly funded research.

1. Background

The concern that taxpayers contribute significant funds to support pharmaceutical innovation, but drug companies then obtain rights to the patents and have free reign on pricing, is once again prominent in health policy debates. From the debates about controlling high drug prices in 2019, to discussions about about Covid-19 therapeutics and vaccines in 2020, there is widespread concern that taxpayers effectively "pay twice" for drugs, once by funding the research, and then again through high prices. If there were evidence that public sector did most of the important work, this could challenge the pharmaceutical industry's argument that measures to lower prices (limiting patents, increasing competition, negotiation, price controls) would have detrimental effects on drug innovation. If the bulk of the important R&D were being done by the public sector, after all, private sector financial incentives would seem to be less important.

This paper puts the present debates in historical context, summarizes the current state of knowledge on the main arguments, and suggests an agenda for future research. Section 2 traces the history of the debates and discusses what's at stake. Section 3 reviews empirical evidence on the role of the public sector in drug development. Building on this, Section 4 suggests several questions where additional evidence is needed in order to advance the debate. Section 5 concludes.

2. The History of the Debate

2.1 Roots in World War II

Debates about taxpayer rights in government funded technologies date back to World War II, when the government first started to seriously fund extramural

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research at firms and universities.[1] During the war, a central question was who should own patents resulting from government funded research? On one side of the debate, Vannevar Bush, the head of the Office of Scientific Research and Development, argued that allowing contractors, rather than the government, to retain patent rights was important for incentivizing participation by firms in the wartime effort and facilitating development of the technologies. Doing so was crucial, since in many fields firms had capabilities, processes, and facilities needed that were lacking in the public sector. A paid-up license for government use during the crisis was viewed as sufficient to protect taxpayer interests. Countering this argument, liberal critics led by Harley Kilgore, a New Deal Democrat from West Virginia, argued that this represented a giveaway of technologies generated through taxpayer dollars, and would promote concentration of economic power during and after the war.

Most of this debate was about warfighting technologies, and not about medicine at all. The OSRD's Committee on Medical Research (CMR) had a crucial role in winning the war, supporting research on a range of wartime problems including infectious diseases, trauma, wound treatment, and blood preservation. Unlike OSRD overall, CMR's contracts were mainly awarded to academic institutions, where there were at the time strong norms militating against patenting, particularly strong in the context of medical research.[2] Reflecting this, the CMR typically had contracts giving the government presumptive ownership of any patents that resulted from the funded R&D. During the war, the CMR and other government agencies also directly supported much of the clinical research and development needed to get drugs into use, most prominently in the natural pencillin development and scale-up effort.[3] This weakened the argument (that is prominent today, see below) that private sector control of patents is needed to support these activities.

The question of who retains patent rights from government funded research was also a central one in the famous debates between Bush and Kilgore about the postwar governance of science. Both Bush and Kilgore envisioned a single major funder of research after the war (though differed on what that agency's patent policy should be, political versus scientific governance, funding of basic versus applied research, and other matters). Ironically, while they were debating, a myriad of agencies absorbed wartime R&D contracts. Each would have its own patent policy. CMR contracts were taken over by the NIH, which (through its parent agency) had a general policy of not permitting patents at all, or, when doing so, requiring government ownership of the patents. Again, this may reflect the continuing force of the norm that academic medical research — most of what NIH funded — should not be patented but rather "for the public." Other agencies (including the Department of Defense) had policies allowing funding recipients (which were primarily industrial contractors) to retain patent rights, justified with the same rationale as offered by Bush during the war.

During and after the war, the debates on who should control the patents were mainly around balancing private incentives for participation in government research efforts versus the public interest in low prices, competition, and access once a technology is developed. That continues to be one of the key issues in the debate to this day.

2.2 Kefhauver Hearings

During and after the war, the debates on who should control the patents were mainly around balancing private incentives for participation in government research efforts versus the public interest in low prices, competition, and access once a technology is developed. That continues to be one of the key issues in the debate to this day.

Another issue in today's debates was raised during the "Kefauver" hearings during the late 1950s and early 1960s that eventually would produce the legislation creating the modern FDA. Building on the technological capabilities and opportunities created through the wartime medical research effort, by the 1950s, drug companies became active in research, and also in using patents and other strategies to ward off competition.[4] The resulting high prices attracted scrutiny from antitrust authorities and legislators, including Senator Kefauver. Then as now, representatives of the pharmaceutical industry touted high drug prices as necessary to create research incentives for these valuable drugs. To combat this claim, Senator

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Kefauver and other critics of the industry marshaled evidence that a large share of drugs were discovered not by pharmaceutical companies, but rather by academic and government laboratories. Economist William Comonor characterized this saga as "the battle of the lists" with different sides in the debate producing different lists of "important" drugs, each with different estimates of the public and private sector contributions.[5]

The Kefauver pricing and patent proposals did not find support in Congress or by the Kennedy administration.[6] Nonetheless, the hearings firmly established one of the key themes in the pharmaceutical policy discussions: if the real source of innovation were the public sector, this would undermine the justification that monopoly prices (and policies that sustain them such as patent protection) are needed.Though the specific patent and pricing provisions that originally motivated the Kevhauver bill were dropped,[7] the aspects of the bill that did survive paradoxically changed the stakes and contours of the debate. Following the thalidomide tragedy in Europe, the impetus grew to add pre-marketing approval and efficacy testing to the FDA's powers. The pre-marketing approval provisions institutionalized a formal clinical trial process, which today accounts for a large share of private sector R&D costs for drugs.[8]

Thus by the 1960s several of the key questions in today's pharmaceutical policy debates had already been well-established. First, is allowing the performers of government R&D to retain patent rights necessary to incentivize participation and commercialization, or does this effectively mean taxpayers are to "pay twice" for the same technology. Second, does the role of the government in funding R&D, especially for important drugs, undermine drug companies' claims that high prices and restrictions on competition are essential for innovation?

2.3 Bayh-Dole and Beyond

During the 1960s and 1970s there was considerable policy debate about the lack of "uniformity" of government patent policy across agencies, with some alleging this created confusion for grant and contract recipients, and others countering that different contexts (defense vs. medicine) called for different policies. In the medical research context, several observers and reports raised concerns that the DHEW/NIH's emphasis on keeping medical research in the public domain may have disincentivized drug companies from collaborating with public sector researchers and thus hindered commercialization of federally funded research.[9]

The argument that patents on government research are needed to promote commercialization, and that "uniformity" of government R&D policy across agencies is an important policy goal, supported the passage of Bayh-Dole in 1980.[10] Bayh-Dole allowed universities and small businesses blanket rights to retain patent rights from federally funded grants and contracts. (The exclusion of large businesses was to alleviate concerns that such a policy would lead to concentration of economic benefits from publicly funded research, though this was dropped by executive order several years later.) As noted, universities had historically avoided active involvement in patenting and licensing, especially in medicine. Bayh-Dole provided cover for doing so, endorsing the idea that this would promote technology transfer and the movement of ideas from lab to marketplace, from bench to bedside. The fact that a number of commercially important biotechnology inventions were bubbling up in university laboratories led academic institutions — desperate for revenues — to support passage of the legislation as well. Under Bayh-Dole, universities could take out patents, and exclusively license them to firms for development. In medicine, the idea was that drug companies would be incentivized to develop embryonic pharmaceuticals, and take them through costly clinical trial processes.

In addition to the original exclusion of large businesses (and limits on university licenses to large businesses), each eventually scrapped, Bayh-Dole included a "march-in" provision allowing the government to circumvent patents on a taxpayer developed invention if the licensee did not achieve practical application, or meet health and safety requirements, among other circumstances.[11] Other provisions (including "recoupment" of profits over a certain level, time limits on exclusive licenses) were considered during the hearings, but not included in the final legislation.[12]

Since Bayh-Dole, NIH funded researchers at universities have patented tens of thousands of inventions.[13] These include patents associated with several hundred commercial drugs.[14] Some argue this is prima facie evidence — that allowing universities to retain rights, license exclusively, and let firms charge what the market bears — is basically working.[15] Going back to the pricing of HIV/AIDS drugs in the 1980s, others have argued that the fact that the government is subsidizing much of the work should be accounted for in pricing, and that "march-in" is one way to do so.[16] More generally, echoing some of the arguments during the Kefhauver hearings, critics of high prices in general have argued that the public sector role in drug development undermines the drug industry's justi-

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fication that high prices are needed to sustain drug innovation.[17]

3. What We Know: A High-Level Summary

The debate has gone on, along the same lines for the past 75 years. Over this period a considerable body of empirical research has been done, assessing the respective roles of the public and private sector. What does the evidence say?

- One strand of research examines who funds what. The most comprehensive research on funding suggests that the U.S. government, primarily through the National Institutes of Health (NIH), provides about one-third of total U.S. biomedical research funding, pharmaceutical and biotechnology companies about 50 percent, with the medical device industry, state and local governments, and foundations accounting for the rest.[18] However, there is a rough division of labor, with the vast majority of pharmaceutical R&D focused on clinical research, and the majority of NIH funding focused on "basic" research.
- Cross-industry firm surveys consistently suggest stronger linkages between public sector and private sector research activities in pharmaceuticals than in other sectors.[19] In the largest such survey, Cohen and colleagues suggest that in the drug industry 41 percent of R&D projects used research findings from the public sector, 35 percent instruments and techniques from public science, and 12 percent were based on prototypes from public sector research.[20] Overall, the surveys suggest a larger enabling role for the public sector in drugs than other industries, though only 10-15 percent of projects are based directly on public sector research, or build on public sector prototypes.
- Another approach uses detailed case studies of important drugs to assess, through histories and/or interviews, the role of the public sector.[21] Each of these studies suggests the public sector has a role in the vast majority of important drugs. However, very rarely is the public or private sector solely responsible.
- Analyses of drugs' key patents suggest that the public sector did enough work to obtain a patent associated with the final product (listed on the FDA's Orange Book, see below) for about 20 percent of "important" drugs.[22] This "direct" role of the public sector in principle can be traced through government interest statements which must list any government grants or contracts directly supporting the research on the invention.[23]
- Bibliometric analyses tracing publication inputs for FDA approved drugs[24] and publications cited in the patents on FDA approved drugs[25] suggest that nearly all important drugs have publication links to NIH or other government funded research.
- Econometric analyses relating variation in NIH funding to drug development suggest a statistically significant increase in drugs in trials[26] and approved drugs[27] following increases in NIH funding in the relevant area.

Collectively, the research belies any simple arguments that the public or private sector are primarily responsible for drug innovation. One can squarely reject the argument that the public sector role or the private sector roles are zero; indeed both seem to be qualitatively large, important, and complementary.

What are the implications of this for the longstanding policy debates surveyed earlier? One is that (at least in its extreme) the argument that patents and high prices are not needed for innovation, because the public sector contributes the drug development, seems wrong. Even at the high end of existing estimates, for only 20 percent of drugs does the public sector seems to be involved in enough late stage development to have a key patent on the final product. This is what I have previously called the "direct" role of the public sector. For the other 80 percent of drugs, the private sector appears to be doing important work as well.[28] Other reasonable ways to measure the direct role may yield slightly higher figures,[29] say 30-35 percent, but the basic point remains.

Another reason the direct role is important is that it is for these drugs that Bayh-Dole march-in and other rights resulting from government funding apply. There have been various calls to use these tools to bring down drug prices and promote access in general.[30] However if the numbers on the direct share surveyed above are right, they would only apply to a minority of drugs. March-in is not a comprehensive solution to influencing drug prices, even if it could have an impact in specific, important cases.

Third, even for the ~20 percent of drugs where the government does have a direct role, in the sense of owning a key patent, we cannot just assume that the private sector contribution is negligible. After all, the whole point of Bayh-Dole is that patent exclusivity is needed to facilitate additional investment. For drugs, someone still has to pay for the expensive clinical tri-

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als. Seen this way, the important question is what is the right level of exclusivity (or the right level of prices/profits) needed to incentivize firms to license the public sector technology and invest in the needed additional work. Or, are there other models beyond Bayh-Dole we might use to achieve the same goal? I discuss this and other questions in the next section, where I lay out an agenda for research.

4. What We Don't Know: Data and Research Needs

There have been strong views in this policy debate for the past 75 years, especially in the four decades since Bayh-Dole. Indeed, it is striking how little the debate has changed. This section discusses several types of additional data and analysis that may help advance the debate going forward.

4.1 Better Data on the Direct Role

Even the high-end estimates on the "direct" role suggest that for the vast majority of marketed drugs, there are no Orange Book listed patents with a government interest statement or government ownership. If patents can accurately be linked to drugs (see below) the government interest statements provide fir a full accounting of the direct role of the government in drug development.[31] However, universities and other grant recipients have not always diligently listed government interest statements in the final patents. Perhaps more surprisingly, grantees also do not always report back patents to the funding agency, which they are also required to do under Bayh-Dole.[32] There do appear to be important omissions.[33] Through in-depth qualitative examinations, for a number of important drugs scholars and civil society groups have identified patents that "should have" included government interest statements.[34] Typically, this process involves comparing inventors on drug patents to authors of publications, and looking at publications by the same authors (e.g. in PubMed) that acknowledge government funding or grants to the inventors in similar areas. While this is inherently a subjective process, one promising approach to do this at scale, would be to match patents to "paired" papers[35] using natural language processing and other computational techniques. Alternatively, Congress or the NIH could impose harsher penalties for non-compliance than currently exist, or better enforce existing penalties.[36]

4.2 Patent Landscapes for Biologics

Suppose we had accurate links between NIH grants and patents they funded. The next step to measuring the direct linkages would be to link the patents to drugs. In most contexts, this is hard to do: there is no established method for linking patents to products at scale. In pharmaceuticals, FDA regulations designed to link generic drug approvals to patent status unintentionally created a way to do so. Under the 1984 Hatch-Waxman Act, drug makers are required to list patents covering drug's active ingredients, formulations, or methods of use (for an approved indication) on the Orange Book,[37] to provide notice of potentially binding patents to prospective generic entrants. There are strong incentives to list any relevant patents on the Orange Book, since doing so provides advantages in litigation.[38] While the current version of the Orange Book includes only unexpired patents, numerous sources now include archival versions as well.[39]

Taking the Orange Book patent list as the full set of patents on a drug, one can then assess the share of drugs linked to a government grant or contract, using the approaches outlined in the previous section. One issue that would arise, is which of the several patents on the Orange Book (the average is about 3) is the main patent, and how to attribute a drug where some of the patents result from government funding and others do not.[40] This relates to the cruciality question that will be discussed below.

A more fundamental issue is that biologic drugs approved under Biological License Agreements (BLAs), accounting for a large share of top-selling drugs in recent years,[41] are not subject to Orange Book listing requirements which apply only to drugs approved by New Drug Application (NDA) route. In general, getting patent "landscapes" for biologic drugs is difficult to do at scale, at least with public data. The current "Purple Book" does not require patent listing of relevant patents for biologics, as the Orange Book does for small-molecule drugs. There have been various legislative initiatives to create more transparency around patents for biologics,[42] mainly as a way to promote biosimilar entry. Such data would also be useful for assessing the public sector role.

It might also be useful to try to use other countries' registers of patents and products , or data on litigated patents for biologic drugs, to assemble patent landscapes for biologics to enable the types of analyses that are now common for small molecule drugs.[43] One could also look at the extended patent for a given drug, plausibly the most important one,[44] using FDA data that is available for biologics as well. There may also be administrative solutions, for example the NIH or other funding agencies requiring notifying the agency when any patent (for small molecule drugs or biologics) is associated with a marketed drug and making this information public.

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4.3 Validation of Bibliometric Linkages

The links between grants, patents and products described above would be most useful for understanding the "direct" public sector role. The broader enabling role of the public sector has typically been measured through "bibliometric" measures such as NIH funded publications on a drug, or patents citing NIH-funded publications.[45]

Analyses of publications on a molecule are possible through PubMed,[46] and, as mentioned, have found nearly all approved drugs to have at least one NIH funded publication. Future work might explore the types of publications funded by the NIH versus others, including classifying by timing of publication and MeSH keywords.[47] (Along these lines, Cleary and colleagues show that most of the publications were related to the drug target.[48]) This would allow for assessment of the division of labor between the public and private sector in drug research. One major issue here is that while PubMed does include a flag for whether the article acknowledges U.S. government funding source, articles without this flag do not necessarily come from industry.[49] One might be able to get better data on affiliations of authors on non-NIH funded articles from Web of Science, Microsoft Academic Graph, or other sources. A more important question is cruciality. For most molecules the majority of publications are probably not government funded. In such contexts, we need to better understand whether the public sector contribution was necessary to the development of the drug, i.e. what would have happened absent the NIH research?

Another bibliometric approach involving publications starts with Orange Book patents on drugs (using the techniques discussed in the previous section), but looks not at whether the patent was directly funded by the government but instead whether it cites a publication that was funded by the government. Publications are cited in patents as part of the "prior art" against which a patent application is evaluated. Under U.S. law, if a patent examiner is convinced that an application is "novel" and "non-obvious" relative to the prior art, and meets other criteria, s/he will grant the patent and the patents and publications against which this assessment was made will be listed in the patent. As noted, Sampat and Lichtenberg show the majority of important drugs have an Orange Book listed patent that cites at least one government funded publication, providing support for a large indirect role.[50] However, the same cruciality question raised earlier applies here too. In almost all cases, the drug patents cite non-NIH funded publications as well. How do we divvy up the relative contribution in determining whether a drug counts as a public sector drug?

Another issue with this approach is that patent citations to prior art are made for legal reasons (by applicants and examiners). Despite how they are typically used, it is unclear that all cited publications are important for generating the subject patent, or all important publications are cited. This is an area of active research.[51]

4.4 Drug Specific R&D Measures

Another thing we don't know is the level of funding provided by the public and private sector, beyond the very broad aggregates cited in Section 3. On the private sector side, drug specific R&D costs are not typically revealed or reported. The oft-quoted Tufts study cites a figure of $2.6 billion in private investment on average for approved drugs, after accounting for failures and capitalizing investment dollars.[52] This figure has been questioned since it is based on proprietary data provided by industry, and thus not replicable. However, other efforts to estimate the costs of developing drugs using more public data report similar orders of magnitude.[53] More importantly, the Tufts study ignores in-licensed compounds, so does not tell us the extent of private sector investment in contexts where the public sector has done enough to get the key patent.[54]

We also lack information on public sector (NIH) R&D spending associated with marketed drugs. There are knotty questions here, especially if much of the relevant public sector work is not on the molecule itself, but mechanisms of action, targets, techniques, or basic knowledge. While all NIH grant data are available through RePORTER (together with titles and abstracts) there is a question of how to associate a specific grant with a specific drug. How much of the background research on HIV should count for a given HIV drug, for example? What about cancer research that informed the HIV work? The public sector side raises its own accounting difficulties, including how to deal with indirect costs that account for a quarter of NIH funding.[55] Most importantly, even where we see considerable public sector expenditure, the relevant question from a policy perspective may still be the level of prices/exclusivity needed to incentivize the needed incremental contribution (e.g. clinical trials) from the private sector. Even where the public sector research is necessary (and even a large share of total R&D) is it sufficient? One margin on which we may be able to make more progress, is the public sector role in funding clinical trials. In principle, the pivotal clinical trials for all drugs should be obtainable from FDA review documents[56] and clinicaltrials.gov should indicate funding sources. One could link these data to RePORTER data to look at not just the share of

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drugs where the government is paying for clinical trials, but also the total amounts of expenditures. In the cases where the government is funding trials as well as one of the main patents, presumably a small share of all drugs, the argument that patents/high prices are needed to stimulate additional private sector spending is obviously weaker.

patent term at time of license. The high prices are baked in and completely unsurprising. An alternative "end to end" approach would be for the government to directly fund the clinical trials as well, and then distribute the drugs at cost.[61] I could imagine several lines of opposition to this approach, including inability of the government to "pick winners," the lack of government capabilities/incentives to do

First, we need evidence on the key empirical parameter in these debates, the sensitivity of commercialization to prices (or to patent protection). The proponents of Bayh-Dole come close to arguing that there would be no commercialization absent academic patents and exclusive licenses. In most fields, this is unlikely to be true. But in pharmaceuticals, the case is strongest, since, under the current system, we rely on profit oriented firms to take products through expensive clinical trials.

4.5 Broader Questions

Beyond the specific measurement issues raised above, there are two higher level questions too, where more thinking and evidence is needed.

First, we need evidence on the key empirical parameter in these debates, the sensitivity of commercialization to prices (or to patent protection). The proponents of Bayh-Dole come close to arguing that there would be no commercialization absent academic patents and exclusive licenses.[57] In most fields, this is unlikely to be true. But in pharmaceuticals, the case is strongest, since, under the current system, we rely on profit oriented firms to take products through expensive clinical trials. And there is a sixty year empirical legacy in economics suggesting that drug companies' R&D incentives are responsive to the extent of patent protection.[58] To my knowledge this has not been directly examined in the context of publicly funded research: how would the level of licensing of university technology, participation in development, and ultimate commercialization change with more/less patent term or higher/lower expected prices? While there are anecdotes (e.g. the impact of the NIH "reasonable pricing" clauses on participation in CRADA agreements[59]), none are quite on point. Careful, systematic empirical research on this question is needed.

The second question is broader. As I have argued elsewhere[60] one reason this policy debate is hard is that under Bayh-Dole we rely on the private sector to do the expensive clinical trials needed to get a drug to market. They are compensated through the ability to charge monopoly prices during the remaining the trials and development work as efficiently as the pharmaceutical industry does, crowding out of basic research, etc. Against these, it has the major benefit of potentially delinking commercialization incentives from prices. Experimentation along these lines could be useful, as would be careful evaluations of "natural" experiments (including end-to-end approaches the government has employed during crises such as World War II and COVID).

5. Conclusions

Today's policy debates regarding the roles of the public sector in drug innovation have a long history. Many of the themes in the current debate, including whether high prices (sustained by patents) are needed for innovation, and whether taxpayers unnecessarily "pay twice" for drugs developed by the public sector, echo those in previous debates. A large body of empirical evidence suggests both the public and private sector have important roles in drug innovation. Still, it is apparent that more nuanced evidence and thinking is now needed to advance the policy debate.

Note

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28. One possibility is that the public sector actually does the key work but does not patent it. But in such cases the private sector Orange Book listed patents should be vulnerable to validity challenges. Given strong incentives to challenge patents on important drugs (Hemphill and Sampat 2012, *infra* note 38) one would expect to see many active ingredient patents on drugs invalidated because of public sector prior art. To my knowledge, this is rare.
29. R. K. Nayak, J. Avorn, and A. S. Kesselheim, "Public Sector Financial Support for Late Stage Discovery of New Drugs in the United States: Cohort Study," *BMJ* 367 (2019): l5766, *available at* <https://www.bmj.com/content/367/bmj.l5766> (last visited February 22, 2021).
30. D. Scott, "How a Democratic president could reduce drug prices without Congress," Vox, *available at* <https://www.vox.com/policy-and-politics/2019/11/25/20982374/2020-democratic-presidential-candidates-prescription-drug-prices> (last visited December 18, 2020).
31. Government interest data are available from the USPTO PatentsView database, *available at* <https://www.patentsview.org/download/> (last visited December 18, 2020).
32. A. K. Rai and B. N. Sampat, "Accountability in Patenting of Federally Funded Research," *Nature Biotechnology* 30, no. 10 (2012): 953-956.
33. In principal, the federal iEdison database ought to provide a full listing of all patents resulting from federal grants. The NIH is the only agency that provides iEdison patent data publicly, through its RePORTER system, *available at* <https://exporter.nih.gov/ExPORTER_Catalog.aspx?sid=0&index=3> (last visited December 18, 2020), but its listings appear to be incomplete. RePORTER notes "Patent information in RePORTER is incomplete. The patents in RePORTER come from the iEdison database. Not all recipients of NIH funding are compliant with the iEdison reporting requirements, particularly after their NIH support has ended." Compliance appears to have improved over time, at least if we use RePORTER to gauge accuracy of government interest statements and vice versa. (In principle, the two sources should completely overlap.) However, we don't know what patents were not reported in either source. A. K. Rai and B. N. Sampat, "Accountability in Patenting of Federally Funded Research," *Nature Biotechnology* 30, no. 10 (2012): 953-956.
34. A. K. Rai and B. N. Sampat, "Accountability in Patenting of Federally Funded Research," *Nature Biotechnology* 30, no. 10 (2012): 953-956. See also See also J. Hughes and A. K. Rai, "Acknowledging the public role in private drug development: lessons from remdesivir," Stat News, *available at* <https://www.statnews.com/2020/05/08/acknowledging-public-role-drug-development-lessons-remdesivir/> (last visited December 18, 2020). James Love and colleagues have found that a number of government interest statements are not on the front-page of patents but rather buried in "certificates of

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correction" available only in PDF format. It is unclear how large the magnitude of this problem is. One fix to this problem would be for the PTO or other agency to OCR the CoC and extract any missing government interest statements. See J. Love, "Errors in Patent Grants: More Common in Medical Patents," Bill of Health blog, *available at* <https://blog.petrie-flom.law.harvard.edu/2017/10/21/errors-in-patent-grants-more-common-in-medical-patents/> (last visited December 18, 2020).

35. F. Murray and S. Stern, "Do Formal Intellectual Property Rights Hinder the Free Flow of Scientific Knowledge? An Empirical Test of the Anti-Commons Hypothesis," *Journal of Economic Behavior & Organization* 63, no. 4 (2007): 648-687.
36. For some empirical questions one could also use other approaches to bound effects. For example if one assumed all drug patents with an academic assignee were government funded, this would provide an upper bound on the share of drugs with a government funded patent.
37. Orange Book: Approved Drug Products with Therapeutic Equivalence Evaluations, *available at* <https://www.accessdata.fda.gov/scripts/cder/ob/index.cfm> (last visited December 18, 2020).
38. C. S. Hemphill and B. N. Sampat, "Evergreening, Patent Challenges, and Effective Market Life in Pharmaceuticals," *Journal of Health Economics* 31, no. 2 (2012): 327-339.
39. US Food and Drug Administration (FDA) *Orange Book* patent and exclusivity data, *available at* <https://heidi-williams.humsci.stanford.edu/data> (last visited December 18, 2020).
40. One reasonable thing to do would be to look at the active ingredient patent, the main patent on a drug, versus others. See C. S. Hemphill and B. N. Sampat, "Evergreening, Patent Challenges, and Effective Market Life in Pharmaceuticals," *Journal of Health Economics* 31, no. 2 (2012): 327-339.
41. A. Roy, "Biologic Medicines: The Biggest Driver Of Rising Drug Prices," *Forbes*, *available at* <https://www.forbes.com/sites/theapothecary/2019/03/08/biologic-medicines-the-biggest-driver-of-rising-drug-prices/#2e38c46b18b0> (last visited December 18, 2020).
42. W. N. Price and A. K. Rai, "How Logically Impossible Patents Block Biosimilars," *Nature Biotechnology* 37 (2019): 862–863.
43. Patent Register, Government of Canada, *available at* <https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/patent-register.html> (last visited December 18, 2020).
44. "Patent Terms Extended Under 35 USC §156," United States Patent and Trademark Office, *available at* <https://www.uspto.gov/patent/laws-and-regulations/patent-term-extension/patent-terms-extended-under-35-usc-156> (last visited December 18, 2020); See C. S. Hemphill and B. N. Sampat, "Evergreening, Patent Challenges, and Effective Market Life in Pharmaceuticals," *Journal of Health Economics* 31, no. 2 (2012): 327-339.
45. E. G. Cleary et al., "Contribution of NIH Funding to New Drug Approvals 2010–2016," *Proceedings of the National Academy of Sciences* 115, no. 10 (2018): 2329-2334; B. N. Sampat and F. R. Lichtenberg, "What are the Respective Roles of the Public and Private Sectors in Pharmaceutical Innovation?" *Health Affairs* 30, no. 2 (2011): 332-339.
46. Cleary, *supra* note 45.
47. Medical Subject Headings, *available at* <https://www.ncbi.nlm.nih.gov/mesh/> (last visited December 18, 2020).
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54. It is possible that the development expenses are less in such contexts; one way to examine this might be through looking at development times for Orange Book drugs with and without a public sector patent, using development time data from the patent term extension records discussed in the previous section, which document the length of the clinical trial process. See S. Keyhani, M. Diener-West, and N. Powe, "Do Drug Prices Reflect Development Time and Government Investment?" *Medical Care* 43, no. 8 (2005): 753-762.
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