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COMMENTARY

Beyond The High Prices Of Prescription Drugs: A Framework To Assess Costs, Resource Allocation, And Public Funding

ABSTRACT **During the past century, an accumulation of laws, organizations, and policy mechanisms has led to increasing transfers of public funds to private drug manufacturers, straining budgets and enabling industry revenues beyond what markets could ordinarily sustain. Tax benefits and fee waivers subsidize industry research, while public institutions and charities help fund the creation of new products and pay for their use once they are approved. New exclusivities increase prices by delaying competition, and payment programs such as Medicare Part D help guarantee that prices will be paid no matter how high they rise. Members of the public thus pay for pharmaceuticals in more ways than is commonly recognized. This article provides a more comprehensive framework for legislators and scholars to use in assessing the total societal costs of drugs. Greater transparency is needed to clarify individual drug costs, facilitate appropriate resource allocation, and ensure that the amount of public funding is justified by the value of the drugs. Congress should direct the Government Accountability Office to study public contributions underlying the highest-cost drugs and should require periodic reporting by drug manufacturers of the direct and indirect public funding they receive.**

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Governments and patients in many countries have expressed concern over high drug prices and the threat they pose to public and household budgets. In the US, Sen. Ron Wyden (D-OR) has called high drug prices "morally repugnant."[1] Cancer medicines and gene therapies have been launched at prices as high as $2.1 million per patient for a standard course of treatment.[2] Pharmaceutical manufacturers counter that drug prices reflect the manufacturers' costs, risks, and added value.

By focusing on prices, however, both critics and industry have overlooked a growing array of policy mechanisms that, although well intentioned, have greatly increased the amounts paid for drugs by federal and state governments through direct research funding, tax incentives, and insurance programs ("government funding"), as well as by patients, private insurers, and other members of the public (collectively "public funding," a broader term that includes all forms of government funding). These policy mechanisms not only help explain how industry revenue has reached an estimated $323–$477 billion per year but also demonstrate that the total cost of pharmaceuticals extends well beyond these nominal amounts.[3]

This article provides a more comprehensive framework for legislators and scholars to use

as they assess the total societal costs of drugs, looking beyond prices and direct research funding. The expanded framework is based on our experience in this area and our review of the evidence, including supplemental source material not listed in the endnotes (see the online appendix).[4]

Hidden Drug Costs And Modest Benefits

It is often recognized that government funding for basic research means that the public actually pays twice for many drugs: once when publicly funded research institutions support basic and translational research and again when governments and individuals pay high prices for the resulting drugs.[5] For example, federal funding related to chimeric antigen receptor (CAR) T-cell therapy, an immunotherapy technology underlying several new and emerging cancer treatments, has been estimated at $204 million.[6] Yet new therapies based on this technology were launched at up to $475,000 per patient for a standard course of treatment,[7] including a $1,340 (0.3 percent) copayment contributed by patients covered by Medicare Part B.[8]

But the public actually "pays thrice," thanks to additional policies that indirectly increase wealth transfers to pharmaceutical companies. For example, the public underwrites manufacturers' research costs through tax credits and deductions, props up prices as part of innovation incentive programs, and contributes to public and private insurance schemes that guarantee payment for new drugs regardless of price. Most of these policies result from specific legislative provisions that have accumulated over time (exhibit 1), gradually increasing total societal expenditures on pharmaceuticals.

Increasing prices have diverted attention not only from these policy mechanisms but also from questions of therapeutic benefit, making it difficult to evaluate whether expenditures are justified. Although manufacturers may work to develop breakthrough technologies that improve patients' lives, 58 percent of drugs that emerged from the development pipeline in 2019 (28 of 48 drugs) were not first-in-class, suggesting minimal innovative contribution.[9] Even for first-in-class drugs, the technical innovation underlying that status does not necessarily translate into patient benefit. Reviews have found that only about 2–31 percent of new drugs offer meaningful incremental benefits to patients.[10] Given that 78 percent of direct pharmaceutical spending is devoted to new drugs,[11] this suggests that substantial public funds are expended to develop and purchase the 69–98 percent of new medicines that are clinically unimportant.[12]

No federal law requires tracking or measuring how much the public pays to manufacturers of these drugs through indirect subsidies and postapproval support. Yet doing so is essential so that patients, payers, and policy makers can know the true extent of public funding of pharmaceuticals.

EXHIBIT 1

Organizations and policy mechanisms supporting drug expenditures in the US

Public funding types/mechanisms	Year established[a]
DIRECT PUBLIC FUNDING OF PHARMACEUTICALS	
Government	
State funding	Various
NIH funding, intramural	1944
NIH funding, extramural (for example, academic)	1944
FDA funding of orphan drug research	1983
Nonprofit	
Charitable and foundation funding	Various
INDIRECT PUBLIC FUNDING OF PHARMACEUTICALS	
Federal income tax deductions for donations to charities	1917
Training and education (for example, National Science Foundation)	1950
Expensing of research costs	1954
20% research tax credit[b]	1981
25% research tax credit (rare disease)[c]	1983
FDA application fee waiver (rare disease)	1997
State or local tax breaks and incentives	Various
MECHANISMS THAT INCREASE POSTAPPROVAL DRUG REVENUES	
Exclusion of competitors to enable high prices	
Patent system	1790
Bayh-Dole Act (patent retention rights)	1980
Orphan Drug Act exclusivity[d]	1983
Hatch-Waxman exclusivities[d]	1984
Pediatric exclusivity	1997
Qualified Infectious Disease Product exclusivity	2012
Guaranteed or buoyed market of buyers	
Department of Veterans Affairs coverage	1811[e]
Medicare Part B coverage	1965
Medicaid drug coverage	1965
Private prescription drug insurance	~1970[f]
Children's Health Insurance Program	1997
Medicare Part D coverage	2003
State/federal laws mandating drug coverage	Various
Transferable priority review vouchers	
Tropical disease voucher	2007
Rare pediatric disease voucher	2012
Medical countermeasure voucher	2016

SOURCE Authors' analysis of federal and state laws. **NOTES** NIH is National Institutes of Health. FDA is Food and Drug Administration. [a]Years show the accumulation of public funding mechanisms over time. [b]25% from 1981 to 1986. [c]50% from 1983 to 2017. [d]Before these laws, protection of proprietary data was not time limited. [e]An act establishing Navy hospitals, Pub. L. No. 11-26, 2 Stat. 650 (1811). [f]Problems of third-party prepaid prescription programs: a report of the Subcommittee on Environmental Problems Affecting Small Business of the Permanent Select Committee on Small Business, H.R. Rep. 93-730 (1973 Dec 13).

Direct Public Funding Of Pharmaceuticals

Government funding and tax benefits supporting research and training represent "push" in-

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centives, which benefit manufacturers before products reach the market. The largest source of direct federal research funds is the National Institutes of Health, which had a budget of $36 billion in 2018 (in comparison, members of Pharmaceutical Research and Manufacturers of America reported global research and development expenditures of $80 billion in 2018).[13] Through federal agencies, taxpayers funded 776 interventional drug trials initiated in 2019 alone, as revealed in a search of ClinicalTrials.gov. Taxpayers fund research on pharmaceuticals through agencies such as the Food and Drug Administration (FDA), which has awarded more than $320 million in research grants for rare disease ("orphan") products,[14] defined as those intended to treat US patient populations of fewer than 200,000 people. Since the Orphan Drug Act of 1983, such grants have helped fund more than seventy approved products.[15] Another initiative, the Department of Defense's Congressionally Directed Medical Research Programs, has administered $15.9 billion in appropriations since 1992 and conducts research on diseases such as amyotrophic lateral sclerosis, tickborne disease, and cancer.[16]

Federal funding has supported several transformative innovations such as the cancer drug imatinib (Gleevec).[17] Although public funding supports some drugs more than others, government funding contributed in some way to each of the 210 new drugs approved by the FDA from 2010 to 2016, subsidizing more than $100 billion of mostly foundational research.[18] Yet prices of new drugs have soared. Median monthly launch prices of anticancer medicines, for example, increased from less than $2,000 in 1995–99 to approximately $10,000 in 2010–14.[19]

State governments also contribute to pharmaceutical research. For example, California has devoted more than $280 million since 1994 to breast cancer research alone.[20] In 2007 Texas established a state research fund that has awarded $2.6 billion for cancer research and prevention.[21] Twenty-one states provide matching grants to support bioscience research, and fourteen make direct investments in biosciences companies.[22]

Public donations fund hundreds of disease-related charities that support pharmaceutical research and help patients pay for the treatments that result. As of December 29, 2020, Charity Navigator, a nonprofit organization, listed 266 charities that seek cures for particular diseases or support medical research or advocacy; 308 that provide patient support such as travel assistance; and 146 directly involved in medical research, including 36 with expenses of $13.5 million or more.[23]

Indirect Public Funding Of Pharmaceuticals

Since the passage of the Economic Recovery Tax Act of 1981, pharmaceutical manufacturers and other businesses in the US have enjoyed a 20 percent basic research tax credit (25 percent from 1981 to 1986) on increases to their research budgets. Because tax credits reduce a manufacturer's taxes dollar for dollar, they are quite valuable. The pharmaceutical industry earned $1.24 billion from 1981 to 1990 in credits under this provision.[24] More recent figures are unavailable.

The Orphan Drug Act created a tax credit to offset clinical trial costs by 50 percent (reduced to 25 percent in 2017), providing a tax benefit unavailable to other industries. Orphan status also exempts manufacturers in the US from the $2.9 million FDA fee required to review each new drug application.[25]

A less obvious means by which the public funds drug development stems from the ability to deduct research costs in the year they occur instead of amortizing them over time, which increases the deduction's value (see note A in the appendix).[4] Although tax credits and deductions apply generally to all businesses, they are especially important in the pharmaceutical industry (see note B in the appendix),[4] where the costs of research constitute large current expenditures yielding drugs that typically generate revenues for decades into the future. Manufacturers with no current revenue can carry forward net operating losses to reduce taxes on future revenues. Loss carryforwards are particularly beneficial in the pharmaceutical industry, where extended research and development periods mean that small

pharmaceutical companies sometimes accumulate years of expenditures before their first product begins generating taxable income (see note C in the appendix).[4] The federal government does not track the aggregate amount of these subsidies, which likely reaches into the billions of dollars.

States and cities also offer incentives intended to attract business, including thirty-eight states with analogues to the national research tax credit.[22] Additional programs are targeted specifically to the bioscience sector. San Francisco, for example, offered a payroll tax exclusion for biotechnology companies from 2004 to 2015.[26] Since 2009 Massachusetts has administered an incentive program that has provided more than $221 million in tax benefits to companies engaged in life sciences research.[27] In 2017 New York authorized a 20 percent tax credit for qualified life sciences companies as part of a $620 million funding initiative that also included support for laboratory space and investment capital for early-stage life sciences firms.[28] Other incentives directed specifically at the biotechnology sector include sales tax exemptions on purchases of equipment (nine states), tax credits for angel investors (eight states),[22] state-sponsored loans or loan guarantees (five states), and incentives for new jobs (four states).[29] These benefits indirectly subsidize drug development costs by contributing to labor, equipment, and capital inputs.

Federal sponsorship of the education and training of scientists and clinical investigators constitutes another type of indirect government support of drug development. Founded in 1950, the National Science Foundation annually provides $145 million through its Division of Molecular and Cellular Biosciences, including support for more than 4,000 graduate students and postdoctoral associates.[30] Funding initiated under the 1965 Medicare law now provides approximately $16 billion per year in graduate medical education and training, helping prepare many of the physician-investigators needed to conduct the more than 362,000 research studies registered at ClinicalTrials.gov.[31] The Government Accountability Office has found that comprehensive information on the total number of residents supported by federal programs is lacking.[32]

Donations to disease-related charities are generally tax-deductible (26 U.S.C. Sec. 170 [2020]), reducing taxable income according to the donor's marginal tax rate (as much as 37 percent in 2020, not including state taxes). The total value of public donations therefore includes not only the amounts donated but also the value of the tax deductions, which constitute indirect federal and state funding. Similarly, premiums for employer-sponsored prescription drug insurance are generally paid with pretax dollars.

Statutory Mechanisms That Increase Drug Revenues

"Pull" incentives offer financial rewards after drug approval, including mechanisms that allow prices or revenue to rise in excess of what free-market dynamics would ordinarily allow. Patents represent the most long-standing pull incentive, enabling drug manufacturers to temporarily charge higher prices by excluding competitors. Although patents nominally last twenty years from the date of patent application filing (with potential extensions of up to five additional years for time lost due to the trial and FDA approval process), key patents are generally filed many years before drug approval (see note D in the appendix),[4] using up some of the exclusivity period. As a result, the median time between brand-name drug approval and generic entry has been measured to be approximately 13.6 years,[33] a period that has remained relatively constant since the 1960s.[34]

Over time, pull incentives have been increasingly layered onto push incentives or onto other pull incentives, creating a thicket of government-facilitated mechanisms to increase drug prices and the amount society expends to procure its medicines. For example, the Patent and Trademark Law Amendments Act (Bayh-Dole Act) of 1980 established a uniform policy by which recipients of federal grants (a push incentive) could retain the patent rights to their inventions (a pull incentive), supporting cash inflows both before and after drug approval.[35]

Pull incentives that overlap with or extend patent rights were created by legislation beginning in the 1980s, such as the seven-year exclusivity provided by the Orphan Drug Act. The Drug Price Competition and Patent Term Restoration Act (Hatch-Waxman Act) of 1984 provided three- and five-year exclusivity periods for variations of existing drugs and new drugs, respectively (formally, these periods truncated existing trade secret rights that prevented generic drug manufacturers from relying on the original drug manufacturer's safety and efficacy data—rights that were not previously time limited).[36] In 1997 Congress provided a six-month exclusivity extension in return for conducting studies in pediatric patients, added to the end of other patent or nonpatent exclusivities. The Biologics Price Competition and Innovation Act of 2009 instituted a twelve-year exclusivity period for biologic drugs, analogous to the Hatch-Waxman exclusivities. Except for pediatric exclusivity and a five-year exclusivity add-on for Qualified Infectious Dis-

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ease Products authorized in 2012, these periods run concurrently with any patent protection, so the extent to which they yield additional revenues depends in part on the strength and expiration dates of the associated patents. Because patents can sometimes be invalidated as obvious over known technology whereas nonpatent exclusivities cannot be, the latter provide greater certainty of protected revenues.

A recent mechanism that Congress created to increase postapproval rewards at public expense is the transferable priority review voucher,[37] which can be sold to third parties and used to expedite FDA review of unrelated drugs. These vouchers incentivize three categories of treatments: tropical diseases (2007); rare pediatric diseases (2012); and chemical, biological, or nuclear threats ("medical countermeasures," 2016). Since 2018 at least five vouchers have sold for between $80 million and $105 million each, providing cash to the voucher recipient and earlier revenues to the purchaser.[38] Although another manufacturer directly pays for the voucher, this manufacturer is likely to seek expedited review of a high-price product lacking additional benefit over existing products, as products that offer additional benefit will be eligible for priority review without a voucher.[39] The cost of the voucher is thus passed along to the public in the form of higher prices.

Nonstatutory Pull Mechanism: Insurance

A critical pull mechanism that increases public support of pharmaceutical development and use is prescription drug insurance,[40] which paid for just 12 percent of retail prescription drug expenditures in 1970 but 86 percent in 2017.[41] From 1990 to 2017 inflation-adjusted out-of-pocket expenditures on retail prescription drugs remained relatively constant at $43–$64 billion (constant 2017 dollars) per year despite a rising US population, whereas Medicare, Medicaid, and private insurance coverage collectively increased more than eightfold during the same period, from $33 billion to $287 billion.[41] In all fields of technology, patents limit the threat of competition and thereby allow manufacturers to increase prices at their discretion, which is tempered by knowledge that sales volume will decrease if prices rise excessively. Insurance coverage intentionally dampens this relationship between price and volume for the purpose of ensuring access, but by doing so, it frees prices to rise virtually without limit.

Untoward Synergies: Insurance And Patents

The layering of a prescription drug insurance system over an existing patent regime has led to dramatic price increases in the US, where manufacturers can now charge patent-protected prices that regularly exceed $100,000 per patient per year, even when much of the research was funded by the public. State and federal coverage mandates further raise expenditures by decreasing the negotiating power of insurers.[42]

As prices of pharmaceuticals rise, attempts by health insurers to control costs have shifted additional monetary and nonmonetary burdens to the public. The most common cost control measure is step therapy, by which less expensive options must be tried first (73.2 percent of cases),[43] followed by restrictions that limit coverage to certain prescriber types such as specialists (31.2 percent of cases).[44] These measures can result in additional patient visits and, in the case of step therapy, additional prescriptions, thereby imposing direct costs in time and copayments on patients who advance to the next therapeutic step. Additional office visits also impose indirect costs on all patients, as the insurance-paid portion of these visits is distributed among policyholders in the form of higher premiums.

Health insurers also address rising list prices by negotiating rebates or other nontransparent discounts. Although rebates reduce the amount insurers pay relative to the list price and potentially allow savings to be passed along to patients, they also reduce incentives for insurers to oppose list price increases.[45] Because patient cost sharing is based on the list price rather than the undisclosed net price, the direct effect of a rebate is to increase the share of costs borne by the patient.[46] For example, a patient with 30 percent coinsurance on a drug with a $100 list price would expect to pay 30 percent of the drug cost but would actually pay 50 percent if undisclosed rebates reduced the net price to $60. Uninsured patients generally pay the list price.

Discussion

As new policies to control drug costs are considered, government leaders must have an accounting not only of industry revenue and direct public research funding but also of the direct and indirect public funding mechanisms that increase the total costs of pharmaceuticals borne by the public. Both legislators and commentators should engage in more critical review of the accumulating incentives to determine whether the costs paid are commensurate with the value of the products that emerge.[47] This novel, expanded framework provides a more comprehensive approach for analyzing pharmaceutical expenditures to reveal how a growing list of push and pull incentives has contributed to the rising costs of prescription drugs.

Policy makers should also attempt to predict how markets will react to well-intentioned but costly new incentives. For example, priority review vouchers have incentivized some manufacturers to seek FDA approval of drugs long used overseas, such as miltefosine (Impavido) for leishmaniasis, rather than the truly new treatments this program was intended to promote.[39] Qualified Infectious Disease Product exclusivity has similarly yielded many low-value variations of existing products because of its lax eligibility requirements.[48] Rare disease incentives have motivated manufacturers to divide large disease categories into smaller ones based on genetic subtype, a practice referred to as "salami slicing" (see notes E, F, and G in the appendix).[4] Although this strategy is based in part on an improved understanding of the genetic origins of disease, the drugs that emerge sometimes receive multiple rare disease indications that collectively address large and diverse patient populations. For example, nivolumab (Opdivo) has received Orphan Drug Act designations for eleven cancer indications, including melanoma, hepatocellular carcinoma, and lung and esophageal cancers. In 2018 and 2019, 51 percent of novel new drugs (55 of 107) received an Orphan Drug Act designation.[9,49]

Policy makers could take a number of steps to increase the transparency of public expenditures on pharmaceuticals. For example, Congress could require manufacturers to develop an accounting system to track the direct public funding they receive, such as research grants, Orphan Drug Act and other federal research tax credits, drug submission fee waivers, state and local financial incentives, and priority review vouchers, and to report these amounts in their annual public filings with the Securities and Exchange Commission or on a company website. For costs that cannot easily be measured by manufacturers, legislators could direct the Government Accountability Office or the Centers for Medicare and Medicaid Services to more comprehensively study the direct and indirect public funding of specified drugs, such as the ten drugs generating the greatest expenditures for Medicare. These government analyses could use historical data to estimate incremental revenues derived from patents and other exclusivities and the increase in use and spending that results from government and private insurance programs (see notes H and I in the appendix).[4]

Congress should consider options for improving transparency as it prepares to reauthorize the Prescription Drug User Fee Act in 2022.

Congress should consider these and other options for improving transparency as it prepares to reauthorize the Prescription Drug User Fee Act in 2022. The law, first enacted in 1992, authorizes the FDA to collect user fees from the drug industry to help the FDA fund its drug review activities.[50] The lengthy negotiations between the FDA, industry, and other stakeholders in the months and years leading up to each five-year renewal provide an opportunity to consider larger issues of drug policy that can then be included in reauthorizing legislation.

Until Congress acts, state legislatures can consider adding or expanding disclosure requirements. Massachusetts, for example, enacted a law in 2019 authorizing the state Medicaid commission to require that manufacturers disclose company-level research and development expenditures.[51] In implementing this law, the commission developed a standard reporting form that requires manufacturers to report all outside funding or grants, including any public funding or tax credits received.[52]

Conclusion

Public support of the development of and access to new drugs helps satisfy an ethical imperative

to reduce suffering and prolong life (see note J in the appendix).[4] But the accumulation of taxpayer-funded incentive mechanisms warrants recognition and transparency. Better disclosure of the amount of this funding would provide essential information to inform future resource allocation decisions, including whether proposed new incentives would duplicate or be incompatible with older ones and whether the amount of public investment in existing incentives is justified by the value of the drugs that result. ■

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