NBER WORKING PAPER SERIES

EVALUATING PHARMACEUTICAL POLICY OPTIONS

Kate Ho
Ariel Pakes

Working Paper 32606
http://www.nber.org/papers/w32606

NATIONAL BUREAU OF ECONOMIC RESEARCH
1050 Massachusetts Avenue
Cambridge, MA 02138
June 2024

We thank Pol Antras, David Cutler, Pierre Dubois, Ali Hortascu, and Chad Syverson for helpful comments. Linda Ouyang provided excellent research assistance. The authors have no relevant or material financial interests that relate to the research described in this paper. The views expressed herein are those of the authors and do not necessarily express the views of the National Bureau for Economic Research.

Evaluating Pharmaceutical Policy Options
Kate Ho and Ariel Pakes
NBER Working Paper No. 32606
June 2024
JEL No. I18,L20

ABSTRACT

Our calculations indicate that currently proposed U.S. policies to reduce pharmaceutical prices, though particularly beneficial for low-income and elderly populations, could dramatically reduce firms' investment in highly welfare-improving R&D. The U.S. subsidizes the worldwide pharmaceutical market. One reason is U.S. prices are higher than elsewhere. If each drug had a single international price across the highest-income OECD countries, and total pharmaceutical firm profits were held fixed, then U.S. prices would fall by half and every other country's prices would increase (by 28 to 300%). International prices would maintain firms' R&D incentives and more equitably share the costs of pharmaceutical research.

Kate Ho
Princeton University
Department of Economics
237 Julis Romo Rabinowitz Building
Princeton, NJ 08544
and NBER
kate.ho@princeton.edu

Ariel Pakes
Department of Economics
Harvard University
Littauer Room 117
Cambridge, MA 02138
and NBER
apakes@fas.harvard.edu

Introduction

There is general agreement that much of the decrease in morbidity and mortality in the U.S. population is the result of new pharmaceuticals. We begin with a quantification of some of these benefits and compare them to the social costs of producing the drugs (some of which are borne by public and some by private institutions). We then consider the likely implications of currently proposed policy options designed to decrease the burden of pharmaceutical costs on the U.S. population. In particular we show that if the policy options that are currently being discussed are actualized, they will have a dramatic impact on pharmaceutical profits. On the other hand, rejecting these policy options would increase the cost of pharmaceuticals to the American economy, likely hurting poor and elderly consumers disproportionately.

If one has the contractarian view that certain basic goods, including a minimal amount of health care that requires less costly access to pharmaceuticals, are a right of consumers who abide by society's rules[1], and also believes that pharmaceutical R&D is as welfare enhancing as it seems to be, then we need to change how the pharmaceutical market works. There have been a lot of proposals on ways to mitigate the tradeoff between incentives to perform R&D and the costs of pharmaceuticals to members of society. In the U.S. these have mostly focused on subsidies (to consumers and/or firms)[2]. We want to draw attention to a characteristic of the market that, though often mentioned, is seldom quantified with this tradeoff in mind: the international dimension of the pharmaceutical market.

Pharmaceuticals, like climate change, are "international products": once a new drug is developed all countries can benefit from it. Yet unlike the attempts to mitigate the impacts of climate change, there are no international agreements on either pharmaceutical pricing, or publicly funded pharmaceutical research. We first explore what would happen to the tradeoff between the cost of pharmaceutical products to the U.S. population and the incentives to do pharmaceutical research were there rules that equalized prices across developed countries. We then consider how the pharmaceutical package adopted by the European Parliament in April 2024 will likely impact our

[1]For more detail on the contractarian argument see Rawls (1971).

[2]There are alternative ways of mitigating this tradeoff which we do not consider here. For example we could try to institute changes which make either the FDA approval process of the R&D process more efficient. An examination of how one would go about increasing the efficiency of these processes is beyond the scope of this paper.

results if it is also adopted by the European Council.

Benefits and Costs

Benefits. Buxbaum et al. (2020) report that between 1990 and 2015 life expectancy increased by 1.32 years per decade. They attribute about 35% of this, or .46 years, to pharmaceuticals. There were 48.9 million live births in the U.S. between 2005 and 2015. If we value a life year at $100,000 (which may be an underestimate, see Neumann, Cohen and Weinstein (2014)), this generates 2.25 trillion dollars in value.

This ignores the improvement in life expectancy of immigrants. Net migration over this period averaged 1.03 million immigrants per annum. If we value the contribution to their welfare at one tenth of the decadal savings for every year they were in the U.S., this adds another .57 trillion dollars of welfare benefits. Harder to quantify, but also important, is the contribution of pharmaceuticals to decreased morbidity over time. If we consider only the over-65 population (about 16% of the U.S. population), Chernew et al. (2016) calculate that their disability-free life expectancy increased by 1.8 years between 1992-2008 or by 1.125 per decade. They find that roughly half of this was due to health improvements and most of that was due to pharmaceuticals[3]. Valuing a healthy life year at $50,000 (half the value of a life year overall) this adds another .25 trillion dollars per decade.

It seems clear, then, that the welfare benefits to the U.S. population from pharmaceutical research exceed three trillion dollars per decade.

Expenditures. U.S. companies spent 747 billion dollars on pharmaceutical research between 2011-2021[4]. US pharmaceutical firms funded about 87% of these expenditures, 7% were funded by companies whose parents were foreign,

[3]Chernew et al. (2016) write: "Our results show that use of effective treatments ... would have led to roughly half the health improvements that we observe. Most of the treatment improvements are pharmaceutical ". The 2010 U.S. over-65 population was 40.6 million.

[4]Source: the OECD Business Enterprise R&D Expenditure by Industry data at `https://stats.oecd.org/Index.aspx?DataSetCode=BERD_INDU`. We focus on the industry defined as "Manufacture of basic pharmaceutical products and pharmaceutical preparations" and the currency measure "2015 constant prices and PPP" so that expenditure in other countries' local currencies (see later in this paper) are converted to US dollars under PPP and years other than 2015 are adjusted for inflation.

3% were funded by other U.S. companies, and the rest were funded by a mix of governments hospitals and universities.

The federal government is also involved in funding pharmaceutical research both directly, through National Institute of Health (NIH), and indirectly through tax and subsidy policies. Here we consider only the NIH expenditures, and we come back to the implications of tax/subsidy policies below. Funding from the NIH "*contributed to* 354 of 356 drugs approved from 2010 to 2019 with expenditure totaling $187 billion ..." (Cleary et al. (2023))[5]. So government institutions (principally the NIH) are involved in some way in the development of most new pharmaceuticals, but they spend much less than pharmaceutical firms on drug development.

Benefit to Expenditure Ratios. Even if we allocate all the government research that "contributed to" new drugs to the R&D of drug development, the U.S. population's welfare benefit-to-expenditure ratio from pharmaceutical company research has recently been extremely high, 4 or more. These simple calculations are obviously subject to caveats. Still, the numbers suggest that it would be socially beneficial to increase pharmaceutical research, not decrease it.

Policies, Incentives, and Company Profits

As long as the vast majority of the funds for research keep being supplied by firms, an increase in pharmaceutical research likely requires increased private incentives to do that research. Two policy changes in the U.S. that impact these incentives have been initiated at a small scale, and are being considered for broader application.

The Inflation Reduction Act of 2022 is allowing bargaining between the Centers for Medicare and Medicaid services (CMS) and drug companies to

[5]The following quote describes how this study was performed (Cleary et al. (2023)). "This study extended these methods by developing an accounting for NIH spending that was comparable with reported investments by the industry. Using a data set of drugs approved from 2010 to 2019 (before the COVID-19 pandemic), this analysis estimated the NIH investment in these drugs, including the cost of published basic and applied research associated with these products, cost of phased clinical trials of failed product candidates, and opportunity cost, using discount rates recommended for government spending"

determine the price Medicare pays for some prescription drugs[6]. Currently the new rules apply to only ten products with about $48 billion in sales. However President Biden's state of the union address (Biden, 2024) included the following statement

"Now it's time to go further and give Medicare the power to negotiate lower prices for 500 drugs over the next decade".

Medicare's share of U.S. sales of pharmaceutical products grew to 30% by 2017. (Source: Kaiser Family Foundation, "10 Essential Facts about Medicare and Prescription Drug Spending", January 29 2019.)

The Congressional Budget Office has estimated a detailed model of the drug research and approval process (Adams, 2021). They predict, and we agree, that the pricing changes inherent in the Inflation Reduction Act of 2022 are unlikely to lead to a substantial reduction in research spending[7]. However the consequences of extending these changes to what is essentially all pharmaceuticals is another matter.

The second change involves allowing importation of pharmaceuticals from Canada. Florida has been approved by the FDA to do so (initially only for 14 drugs and only for people serviced by state agencies (Freed, Neuman and Cubanski, 2024)). Seven other states have applied for similar permissions. Together these states account for about 20% of U.S. pharmaceutical sales, and U.S. sales are over fifty percent of global pharmaceutical sales. More precisely, U.S. sales are on average 55% of sales for the sixteen large pharmaceutical companies listed in Table 1 and used in our calculations below, and 62.5% of the sales in the thirty three OECD countries listed in the RAND (2024) study we come back to below (Mulcahy, Schwam and Lovejoy, 2024).

To get some idea of what the impact of the broader changes would be on company profitability we need a guess at what "bargained prices" would be. If bargaining with Medicare was instituted at a larger scale, the final result would have to be endorsed by a government sanctioned institution

[6]The new pricing process has a price ceiling for the new negotiated price which is not higher than 40-75% of the drug's non-federal average manufacturer price (non-FAMP). The percentage is 75% for small-molecule drugs and vaccines 9-12 years beyond approval, and lower for older drugs. Details of the process are provided in a CMS Memorandum from March 2023 (Seshamani (2023)).

[7]This is due to the small number of drugs included in the new pricing policy; the fact that the new pricing scheme kicks in only after the drug has been on the market for almost a decade; and the fact that price changes apply only to Medicare.

(probably CMS), as is true in most other countries including Canada. The proximity of Canada to the U.S. facilitates importation, and cultural similarities make Canada a natural reference point for bargained outcomes. So we use Canadian prices to evaluate the implications of both CMS bargaining with the pharmaceutical companies and pharmaceutical product importation from Canada. Canadian prices are the second highest prices among developed countries (the U.S. is highest, see below). So moving to Canadian prices would generate a smaller loss in profits than moving to the prices of any other developed country.

Our calculations indicate that, assuming demand was totally inelastic and there were no other mitigating developments, applying the bargained prices to all Medicare demand and allowing for importing drugs from Canada for the eight states currently negotiating with the FDA would cause about a 16% fall in pharmaceutical revenue[8].

Before turning to the implications of the 16% fall in revenues on pharmaceutical company profits, two caveats are in order. First, demand does respond to price, although the elasticities reported in empirical work on pharmaceutical demand are small[9]. More importantly, related studies emphasize that any lowering of prices is likely to have beneficial health effects. For example, in a large scale study of diabetes, cardiovascular, and hypertension patients, Van Alsten and Harris (2020) find that cost is the most common reason for medication non-adherence, with more than two-thirds of patients skipping or delaying medication. Further, cost related non-compliance was associated with 8% to 18% higher disease-specific mortality rates. So were we to adjust our estimates of the revenue reduction to account for the price-induced increase in demand, we would also have to adjust the welfare benefits

[8]We use the data in Mulcahy, Schwam and Lovejoy (2024), Figure 3.6 which specifies that US prescription drug prices, accounting for rebates, were 276% of Canadian prices for retail-dispensed brand-name drugs in 2022. Given this, extending CMS bargaining to all Medicare drugs might reduce total pharmaceutical revenues by 30% (the share of pharma revenues from Medicare) x (1/2.76) = 10.9%. Importing drugs from Canada, if these drugs could be used by the relevant states' entire non-Medicare population, might further reduce pharma revenues by ((100% - 30%) x 20%) x (1/2.76) = 5.1%.

[9]For example, Gatwood et al. (2014) use MarketScan data in a panel data analysis with individual fixed effects to estimate the response to cost sharing incentives for eight categories of medication. They obtain elasticities between -.015 to -.157 for seven of the eight categories and no elasticity at all for anti-platelet agents. The -.157 was for smoking deterrents, and the next highest was -.087 for Proton Pump Inhibitors. This paper also contains an extensive review of the literature on price effects .

for the gains from increased compliance, and the result may well increase the benefit-to-cost ratio.

Perhaps a bigger caveat is that the reduced prices of pharmaceutical products in the U.S. might induce a change in pharmaceutical prices in other countries, and this could mitigate the impact of the proposed policies on pharmaceutical firm revenues overall. The market for pharmaceutical products is international, and other countries, particularly other developed countries, might be induced to change their prices once they realized how the proposed policies would affect the health of their populations in the future. We come back to the issue of the structure of the international pharmaceutical market below, but currently we do not know of any institution in another country that ties their pharmaceutical pricing policies to the incentives to perform pharmaceutical research.

Company Profits. We have gathered data from the SEC reports on 16 of the largest pharmaceutical firms (by capitalization)[10]. The reports provide net profits and net margins. Net profit is computed as pharmaceutical global revenue after rebates minus operating expenses, taxes, interests, and other expenses. Net margins are defined as net profits divided by global revenue after rebates. The data are reported in Table 1.

The weighted average of the global net margins of these firms, weighted by shares of net profit, is 32%. We calculate that a 16% reduction in U.S. revenues would lead to about a 9% reduction in global revenues. If there was no change in costs, net margins would fall from 32% to 25%. That is, the proposed policies could cause an almost 20% decrease in net profits[11].

Of course there is a difference between the average and the marginal welfare benefits of pharmaceutical research, and we have not directly measured the relationship between company funded pharmaceutical research and the

[10]We use 10K reports from the SEC for 2022. For example, the report for Pfizer is at `https://s28.q4cdn.com/781576035/files/doc_financials/2022/ar/PFE-2022-Form-10K-FINAL-(without-Exhibits).pdf`. Our analysis includes the top 18 firms by global market capitalization except CVS Health, which is integrated with a pharmacy chain, a health insurer and a pharmacy benefits manager, and Zoena which is an animal health firm.

[11]If net margin is 32% on average, and is defined as net profit divided by global revenue, then cost is currently 68% of revenue. U.S. revenues make up an average of 55% of global revenues for these firms. So the proposed policies would reduce global revenues to approximately (0.55*0.85 + 0.45)=0.92 of their previous value. Hence new margins would be approximately (0.92-0.68)/0.92 = 0.26, a reduction of (0.32-0.26)/0.32, i.e. 19%.

development of new drugs. There are several reasons for this. In addition to the standard difficulties in production function estimation (De Loecker and Syverson, 2021), there are at least two additional issues that make it difficult to empirically establish the relationship between research expenditures and the production of new pharmaceuticals. First, the outcomes of different research programs designed to mitigate a particular disease are correlated due to the common element of the underlying scientific knowledge in the area. So the disturbances in this R&D-to-new-drug relationship do not average out in the cross section, and are commonly impacted by the increments in scientific knowledge in the time dimension. Second, the relationship between the inputs and the outputs in the pharmaceutical production function involves two distributed lags, one which reflects the production process itself and the other which is a result of the requirements to get FDA approval for the drug. Both of these vary from outcome to outcome[12].

It is also clear that were we not to make the proposed policy changes, U.S. prices would be higher, and this would disproportionately harm older and lower-income people. Still, there is strong evidence that more pharmaceutical research would be beneficial rather than less, and that pharmaceutical companies' response to a 20% cut in margins is likely to be to severely cut pharmaceutical research expenditures.

If one wishes to both: (i) abide by the contractarian view that certain basic goods, including a minimal amount of health care that requires less costly access to drugs, are a right of consumers who abide by society's rules, and (ii) that pharmaceutical R&D is as welfare enhancing as it seems to be, then there needs to be a change in the institutions governing the pharmaceutical market. We present an argument for one possible change below and quantify its likely impact.

[12]We could also ask whether, if firms did change pharmaceutical R&D spending, this would necessarily affect projects with high social value. A number of studies consider this issue using the introduction of Medicare Part D as change that increased firms' market size. Dranove, Garthwaite and Hermosilla (2014) and Dranove, Garthwaite and Hermosilla (2020), for example, provide evidence that while the new program increased development of new medical products and pharmaceuticals for the elderly, they were concentrated among diseases for which treatments already existed rather than more novel innovations. These findings are not directly relevant to our argument, however, because the revenue loss from the policies we consider would impact research for all age groups, and we know that much of the benefit of new medical products is due to an improvement in infant health, with long expected lifespan benefits (Cutler and Meara, 2000).

The international dimension of the market

Our calculations indicate that currently the U.S. provides a substantial subsidy to the worldwide pharmaceutical market. Some of this is due to the size of the U.S. market. We will focus on quantifying the impact of international differences in prices conditional on differences in market size. Before going to those calculations, we briefly consider public funds.

Public funds for pharmaceutical research. A recent OECD report on publicly funded health related research in OECD countries (OECD, 2021) finds that government expenditures were .21% of GDP in the U.S.; .07% of GDP in Europe (that is, in the 21 EU member states that are part of the OECD); and .04% of GDP in the other OECD member countries.

We provide these numbers only to show that if we included differences in direct government support of pharmaceutical research, the inequities in the international distribution of the costs of pharmaceuticals would likely only grow. The numbers on "health related" research relate to a broader category than pharmaceutical research, and were we to do a careful study of this issue we would also need to include the role of tax and subsidy differences across countries. This would include both the subsidies given to privately funded R&D and the impact of tax avoidance policies favoring U.S. companies that offshore profits and production. As discussed in Setser (2023), the implications of the tax avoidance policies would likely dominate, reinforcing the international inequities seen in the differences in pricing regimes across countries.

Prices. Much of the international inequity in funding private incentives to do pharmaceutical research is due to international differences in pharmaceutical prices. A recent RAND report (Mulcahy, Schwam and Lovejoy (2024)) calculates that, using U.S. revenue shares of pharmaceutical products as weights, the indices of U.S. prices for retail-dispensed branded drugs in 2022 were 276% of Canadian prices; 434% of United Kingdom prices, and 381% of a share weighted average of 33 developed countries[13]. These differences have been growing over the last two decades (see Danzon (2018) and

[13]These indices understate the gap between US prices and other countries' prices because they adjust US prices to account for manufacturer rebates but do not adjust prices in other countries for any rebates or other discounts there.

the literature she cites on international price differences).

The Impact of Internationalizing Pharma Prices

We consider the impact of internationalizing the drug prices for only those 21 countries with at least $50,000 in per capita GDP. That is, we ask if (i) there is an international price for each drug that each of these countries abide by, and (ii) we assume total revenue is the same as current total revenue (so incentives to perform R&D would be unchanged),

What would be the weighted average markup or markdown in each country's prices, where the weights are country specific revenue shares?

We do this for both: (i) all retail-dispensed branded pharmaceuticals, and (ii) all pharmaceuticals (including generics). Our data source is the RAND 2024 study discussed above (Mulcahy, Schwam and Lovejoy, 2024). Details of our data and analysis, and a table of results, are provided in the Appendix.

The two indices give similar results. The branded drugs index should be most informative with respect to R&D incentives so we focus on it. As expected given the discussion above, every country except the U.S. has a price increase. The U.S. would pay only 46 cents for every dollar we now spend, whereas the lowest price increase among the other countries would be Canada, with a branded index of 1.28, indicating that its prices would be 128% of its current prices. Some European indices are: 1.48 for Germany; 1.97 for France; 2.00 for the United Kingdom; 2.63 for Italy and 2.87 for Spain. We conclude that the use of international pharmaceutical prices would cut U.S. prices in half, but would cause sharp increases in other countries' prices (of 28% to over 300%).

There would be both obstacles and benefits to proceeding with a single international price for each drug. Benefits would include not having to worry about either the costs of quasi-governmental committees setting and monitoring prices in different countries, or "parallel trade" in pharmaceuticals among the countries that agreed to the single price policy. There are numerous obstacles, including the fact that many countries might have to find alternative ways of providing their citizens the minimal level of health care that they require. We would also need to formulate international prices,

hopefully in a way that led to optimal R&D incentives. Still, any movement in the direction of equating prices would likely lead to less political pressure for the current U.S. policy options and mitigate their negative impacts on pharmaceutical R&D.

The European Parliament's Pharmaceutical Proposal. The package, adopted by the European Parliament in April 2024, needs to be approved by the Council before it is enforced. The two parts of the package that are particularly relevant for the current discussion (Amand-Eeckhout, 2024*a*) are: (i) creation of a single market for medicines for all countries across the EU, and (ii) exclusivity policies which are designed to increase R&D incentives.

The creation of a single market is intended to include concentrating pharmaceutical purchases for all of Europe in a single purchasing agent[14]. This would have administrative, pricing, and R&D incentive effects. Administratively, it would eliminate both free riding in setting prices (see Dubois, Gandhi and Vasserman (2022), for a discussion) and parallel trade among members of the European Union. It may also decrease the cost of negotiating prices with manufacturers because this would only have to be done once for all member states. The impact on R&D incentives depends on how it would affect pharmaceutical prices.

The single purchaser would likely have higher bargaining leverage in negotiations with the pharmaceutical companies than any single member state. As a result, a bargaining model would predict that the change would further lower European prices, accentuating current international inequities. Of course it could also facilitate a negotiation of prices between the U.S. and European nations (since there would be a single European agency to deal with). However this would require the European pricing agent to agree to increase prices in order to foster R&D activity, and as noted above we do not

[14]The new purchasing authority is defined in the legislation as follows. "The Health Emergency Preparedness and Response Authority (hereafter 'HERA' or 'the Authority') is hereby established as a separate structure under the legal personality of the European Centre for Disease Prevention and Control (ECDC). The Authority shall be responsible for creating, coordinating and implementing of the long-term European portfolio of biomedical research and development agenda for medical countermeasures against current and emerging public health threats as well as the, production, procurement, stockpiling and distribution capacity of medical countermeasures and other priority medical products in the EU. (...) (Article 175a new)" (Popp, 2024).

know of a quasi-governmental pricing institution who has done this in the past.

The European Parliament's proposal also extends exclusivity on pharmaceutical products (Amand-Eeckhout, 2024*b*). They i) set a minimum period of 7.5 years of protection after approval (designed for drugs for which there is a long interval between approval and use), ii) guarantee two years of market exclusivity (even if a bio-similar drug appears), and iii) grant other extensions in specific cases[15].

Notice, however, that there is no reference to pharmaceutical prices. Without a lessening of the international price disparities the political pressure on the U.S. government to decrease pharmaceutical prices is unlikely to abate, with potentially serious consequences for pharmaceutical innovation.

Conclusion

There is a worry that the policies directed at the pharmaceutical industry that are currently being discussed would decrease the profits from firms' R&D activities dramatically. These policies are directed at reducing the costs of pharmaceuticals to the American population, particularly to the low income and elderly population. The evidence indicates that the long term welfare benefits to pharmaceutical research greatly exceeds the costs. A change to more equitably share the costs and benefits of pharmaceutical research across developed countries might enable us to mitigate the costs to American consumers while also maintaining current incentives for pharmaceutical R&D.

References

Adams, Christopher P. 2021. "CBO's Simulation Model of New Drug Development." Congressional Budget Office Working Paper 2021-09.

Amand-Eeckhout, Laurence. 2024*a*. "Revision of EU pharmaceutical legislation." European Parliamentary Members' Research Service PE 749.789.

[15]These include: if the drug meets an "unmet" medical need, if much of the R&D is done in Europe, if approval is granted for a second indication.

Amand-Eeckhout, Laurence. 2024*b*. "Revision of the EU's Basic Pharmaceutical Legislation, Including Medicines for Children and for Rare Diseases." European Parliament Legislative Train 04.2024.

Biden, President Joe. 2024. "Remarks of President Joe Biden, State of the Union Address as Prepared for Delivery." https://www.whitehouse.gov/briefing-room/speeches-remarks/2024/03/07.

Buxbaum, Jason D., Michael E. Chernew, A. Mark Fendrick, and David M. Cutler. 2020. "Contribution of Public Health, Pharmaceuticals, And Other Medical Care to US Life Expectancy Changes, 1990-2015." *Health Affairs*, 39(9): 1546–1556.

Chernew, Michael, David M. Cutler, Kaushik Ghosh, and Mary Beth Landrum. 2016. "Understanding the Improvement in Disability-Free Life Expectancy in the US Elderly Population." In *NBER Chapters, Insights in the Economics of Aging*. 161–201. National Bureau of Economic Research, Inc.

Cleary, Ekaterina Galkina, Matthew J. Jackson, Edward W. Zhou, and Fred D. Ledley. 2023. "Comparison of Research Spending on New Drug Approvals by the National Institutes of Health vs the Pharmaceutical Industry, 2010-2019." *JAMA Health Forum*, 4(4). https://doi:10.1001/jamahealthforum.2023.0511.

Cutler, David M., and Ellen Meara. 2000. "The Technology of Birth: Is It Worth It?" In *Frontiers in Health Policy Research Volume 3*. , ed. Alan Garber, 33–67. Cambridge, MA:MIT Press.

Danzon, Patricia. 2018. "Differential Pricing of Pharmaceuticals: Theory, Evidence and Emerging Issues." *PharmacoEconomics*. https://doi.org/10.1007/s40273-018-0696-4.

De Loecker, Jan, and Chad Syverson. 2021. "An Industrial Organization Perspective on Productivity." In *Handbook of Industrial Organization*. Vol. 4, , ed. Kate Ho, Ali Hortacsu and Alessandro Lizzeri, Chapter 3, 141–223. Amsterdam:Elsevier.

Dranove, David, Craig Garthwaite, and Manuel Hermosilla. 2014. "Pharmaceutical Profits and the Social Value of Innovation." NBER Working Paper 20212.

Dranove, David, Craig Garthwaite, and Manuel Hermosilla. 2020. "The Scientific Novelty of Innovation." NBER Working Paper 27093.

Dubois, Pierre, Ashvin Gandhi, and Shoshana Vasserman. 2022. "Bargaining and International Reference Pricing in the Pharmaceutical Industry." NBER Working Paper 30053.

Freed, Meredith, Tricia Neuman, and Juliette Cubanski. 2024. "FAQs on Prescription Drug Importation." Kaiser Family Foundation. https://www.kff.org/health-costs/issue-brief/faqs-on-prescription-drug-importation/#.

Gatwood, J., T.B. Gibson, M.E. Chernew, A.M Farr, E. Vogtmann, and A.M. Fendrick. 2014. "Price elasticity and medication use: cost sharing across multiple clinical conditions." *Journal of managed care & specialty pharmacy*, 20(11): 1102–1107. https://doi.org/10.18553/jmcp.2014.20.11.1102.

Mulcahy, Andrew S, Daniel Schwam, and Susan L Lovejoy. 2024. "International Prescription Drug Price Comparisons, Estimates using 2022 Data." RAND Corporation.

Neumann, Peter J., Joshua T. Cohen, and Milton C. Weinstein. 2014. "Updating Cost Effectiveness: The Curious Resilience of the $50,000-per-QALY Threshold." *New England Journal of Medicine*, 371(9): 796–797.

OECD. 2021. "Pharmaceutical Research and Development." In *Health at a Glance 2021: OECD Indicators*. Paris:OECD Publishing. https://doi.org/10.1787/6e38c622-en.

Popp, Dana. 2024. "Pharmaceutical package: extracts from adopted ENVI reports." European Parliament Press Release 19-03-2024. https://www.europarl.europa.eu/news/en/press-room/20240318IPR19418/pharmaceutical-package-extracts-from-adopted-envi-reports.

Rawls, John. 1971. *A Theory of Justice.* New York:Columbia University Press.

Seshamani, Meena. 2023. "Medicare Drug Price Negotiation Program: Initial Memorandum, Implementation of Sections 1191-1198 of the Social

Security Act for Initial Price Applicability Year 2026, and Solicitation of Comments." Center for Medicare.

Setser, Brad W. 2023. "Cross-Border Rx: Pharmaceutical Manufacturers and U.S. International Tax Policy." Prepared Statement before the Committee on Finance United States Senate.

Van Alsten, S.C, and J.K. Harris. 2020. "Cost-Related Nonadherence and Mortality in Patients With Chronic Disease: A Multiyear Investigation, National Health Interview Survey, 2000–2014." *Preventing Chronic Disease*, 17. http://dx.doi.org/10.5888/pcd17.200244.

Table 1: Large Pharmaceutical Firm Profits, Revenues and R&D Spending

Firm	Country	Global rank in market cap in 2023	Total net-of-discounts global revenue on pharmaceuticals ($ million)	Total net-of-discounts US revenue on pharmaceuticals ($ million)	Share of global revenue that comes from US	R&D spend on pharmaceuticals ($ million)	Net profit ($ million)	Net margin
Eli Lilly	US	1	$28,541	$18,190	63.7%	$7,191	$6,245	21.9%
Novo Nordisk	Denmark	2	$25,057	$11,987	47.8%	$3,405	$7,862	31.4%
Janssen	US	3	$52,563	$28,604	54.4%	$11,622	$17,941	34.1%
Merck	US	4	$52,005	$24,989	48.1%	$7,700	$14,519	27.9%
AbbVie	US	5	$58,054	$45,713	78.7%	$6,510	$11,836	20.4%
Roche	Switzerland	6	$47,742	$21,078	44.2%	$14,736	$14,182	29.7%
AstraZeneca	United Kingdom	7	$44,351	$17,920	40.4%	$9,762	$3,293	7.4%
Novartis	Switzerland	8	$50,545	$17,653	34.9%	$9,996	$6,955	13.8%
Pfizer	US	9	$100,300	$42,126	42.0%	$11,428	$31,372	31.3%
Amgen	US	10	$24,801	$17,743	71.5%	$4,434	$6,552	26.4%
Sanofi	France	11	$32,222	$14,379	44.6%	$5,320	$16,372	50.8%
BMS	US	12	$46,159	$31,850	69.0%	$9,509	$6,327	13.7%
Gilead	US	13	$27,281	$18,884	69.2%	$4,977	$4,592	16.8%
Vertex	US	14	$8,931	$5,699	63.8%	$2,540	$3,322	37.2%
Regeneron	US	16	$12,173	$6,825	56.1%	$3,593	$4,338	35.6%
GSK	United Kingdom	18	$36,271	$17,987	49.6%	$6,788	$19,322	53.3%

Notes: We include the top 18 firms by global rank in market capitalization in 2023 other than CVS Health (which is integrated with a large pharmacy chain, a health insurer and a Pharmacy Benefit Manager) and Zoetis (an animal health company).
Source of all data is firm annual reports 2022. For Janssen we include only pharmaceuticals. For Merck we consider only the human health segment (animal health is excluded). Net margin is net profit / total net-of-discounts global revenue.

Appendix: Price Comparisons

We use 2022 data from Andrew S, Schwam and Lovejoy (2024). We include countries whose GDP per capita is over $\$50,000$, and we add Japan and Spain whose GDP per capita are in the $(\$45,000, \$50,000)$ range but which have total pharmaceutical revenues in the top 15 countries worldwide.

The RAND report provides data on each non-U.S. country k's price index relative to the U.S., weighted by U.S. drug market shares. It also includes data on total pharmaceutical drug revenues, and total revenues for retail-dispensed branded drugs, for each country. Our method, which uses all these data, is as follows.

Define

- $v_d^k \equiv$ volume of branded drug d in country k,
- $p_d^k \equiv$ price of branded drug d in country k,
- $R^k = \sum_d v_d^k p_d^k$, i.e. revenue of drug sales in country k,
- $R^* \equiv \sum_k R^k$, i.e. total sales revenue.

We make the simplifying assumption that the ratio of U.S. to country k prices is constant across drugs and equal to P^k. Then the U.S. share-weighted index of prices reported in RAND (2024) is the ratio of U.S. prices to country k's prices share-weighted with U.S. revenue shares is $(P^k)^{-1}$.

Let $p^* = \{p_d^*\}_d$ be a vector of international prices that generate total revenues across drugs (d) and countries (k) equal to R^* as defined above. We find a uniform markup (or markdown) on each country's prices that makes

$$\sum_k \sum_d p_d^* v_d^k = R^*.$$

Under our assumptions this can be rewritten as

$$\sum_d p_d^* v_d^k = \sum_d (p_d^u / p_d^k)(p_d^* / p_d^u) p_d^k v_d^k = \sum_d P^k P^{*,u} p_d^k v_d^k = P^k P^{*,u} R^k,$$

where P^u is the constant ratio of international to U.S. prices. This will ensure we maintain global sales if

$$P^{*,u} \sum_k P^k R^k = R^* \;\Rightarrow\; P^{*,u} = (R^* / (\sum_k P^k R^k)$$

which defines the ratio of international to U.S. prices. The markup for country k is then $P^k P^{*,u}$.

Results are given in Appendix Table 1.

References

Andrew S, Mulcahy, Daniel Schwam, and Susan L. Lovejoy. 2024. "International Prescription Drug Price Comparisons, Estimates using 2022 Data." RAND Corporation.

Appendix Table 1: Price Comparisons Across Countries

	Sales (bn USD)	Volume (bn)	GDP (PPP) per capita 2022	Price index (retail dispensed brand-name)	Price index (all drugs)	Revenue weighted by price (brand-name)	Revenue weighted by price (all drugs)	Markup (retail-dispensed brand-name)	Markup (all drugs)	Markup by country (brand-name)	Markup by country (all drugs)
Total								0.46	0.58		
United States	617.2	261.6	$76,399	100.00	100.00	617.20	617.20			0.46	0.58
Japan	64.9	219.8	$45,573	390.57	347.07	253.48	225.25			1.80	2.02
Germany	46.5	63.9	$63,150	320.30	294.18	148.94	136.79			1.48	1.72
France	37.5	51.1	$55,493	426.01	326.41	159.75	122.40			1.97	1.90
Italy	33.0	44.3	$51,865	568.77	268.03	187.69	88.45			2.63	1.56
United Kingdom	31.6	66.8	$54,603	434.47	270.04	137.29	85.33			2.01	1.58
Spain	27.4	48.6	$45,825	620.93	284.22	170.13	77.88			2.87	1.66
Canada	26.6	30.6	$58,400	276.03	228.92	73.42	60.89			1.28	1.34
Korea	15.3	54.9	$50,070	707.92	391.29	108.31	59.87			3.27	2.28
Australia	10.9	15.6	$62,625	437.95	369.89	47.74	40.32			2.02	2.16
Belgium	7.3	8.8	$65,027	434.95	320.61	31.75	23.40			2.01	1.87
Switzerland	6.5	5.8	$83,598	293.30	218.87	19.06	14.23			1.35	1.28
Austria	5.7	6.5	$67,936	377.21	276.24	21.50	15.75			1.74	1.61
Sweden	4.7	9.1	$64,578	392.85	333.19	18.46	15.66			1.81	1.94
Netherlands	3.6	13.5	$69,577	432.88	333.17	15.58	11.99			2.00	1.94
Norway	3.2	4.7	$114,899	408.35	248.17	13.07	7.94			1.89	1.45
Finland	2.7	5.4	$59,027	444.07	322.81	11.99	8.72			2.05	1.88
Ireland	2.6	4.5	$126,905	396.00	291.64	10.30	7.58			1.83	1.70
New Zealand	1.2	5.0	$51,967	378.05	288.07	4.54	3.46			1.75	1.68
Slovenia	0.8	1.6	$50,032	518.86	423.92	4.15	3.39			2.40	2.47
Luxembourg	0.2	0.4	$142,214	442.69	413.56	0.89	0.83			2.04	2.41

Notes: GDP (PPP) per capita is from worldometer. All other data are from the RAND 2024 study cited in the text. Method is explained in Appendix 1.