ISSUE BRIEF:
THE IMPACT OF HR 5376 ON BIOPHARMACEUTICAL
INNOVATION AND PATIENT HEALTH

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by

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Executive Summary

This issue brief reviews the evidence-base to assess the impact of HR 5376 on drug innovation and patient health. A large academic literature estimates the effect of future drug revenues on R&D spending and finds that on average that a 1 percent reduction in revenue leads to a 1.5 percent reduction in R&D activity. We find that HR 5376 will reduce revenues by 12.0 percent through 2039 and therefore that the evidence base predicts that R&D spending will fall about 18.5 percent, amounting to $663 billion. We find that this cut in R&D activity leads to 135 fewer new drugs. This drop in new drugs is predicted to generate a loss of 331.5 million life years in the US, 31 times as large as the 10.7 million life years lost from COVID-19 in the US to date. These estimated effects on the number of new drugs brought to market are 27 times larger than projected by CBO, which finds only 5 drugs will be lost through 2039, equaling a 0.63 percent reduction.

Section 1: Introduction

 A national debate has emerged again about the effect of price controls on pharmaceutical innovation. Many proponents of price controls for pharmaceutical drugs argue that they have negligible effects on innovation while opponents argue they will lead to significantly fewer new drugs, delaying treatment for millions of Americans. This issue brief attempts to provide insight into the effects of the recent price control proposal in HR 5376 on drug innovation and patient health as implied by basic economics and the prevailing empirical evidence base on innovation.

Section 2: Evidence Base on Revenue Effects on Innovation

 Biopharmaceutical companies routinely project future market size and profits for their products to determine the rate of return on R&D investments. A large body of evidence reviewed here suggests that these market practices translate into a predictable positive relationship between realized revenues and R&D spending in the economy in general, and for biomedical innovation in particular.

 A set of papers looks at the expansion of the Medicare prescription drug benefit, Medicare Part D, which provides the most relevant evidence for assessing the revenue effects of Medicare policy changes. They find that companies recognized this expansion and increased innovation in drugs treating diseases prevalent in the elderly population more so than innovation in non-elderly diseases (Blume-Kohout and Sood 2013). Quantifying that relationship, a 1 percent increase in market size due to Medicare Part D leads to a 2.8 percent increase in new drug approvals.[1] Another often cited paper finds a 1 percent increase in potential market size leads to a 4-6 percent increase in the entry of new drugs (Acemoglu and Linn 2004) in the US. Other studies show that a 1 percent increase in price leads to a 0.22-1.33 percent increase in innovation.[2]

 We synthesized the evidence base by computing the average R&D elasticity with respect to revenue estimated from 10 different studies looking at the effect of a price change, expected market, and overall revenue on R&D. Table 1 illustrates the elasticities used from each paper, and the average elasticity across these 10 studies is 1.54.

Table 1. Elasticities used from the 10 Papers Identified

Paper	Elasticity
Acemoglu and Linn (2004)	5
Dubois et al (2015)	0.23
Finkelstein (2004)	2.75
Blume-Kohout and Sood (2013)	2.8
Filson (2012)	1

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[1] Finkelstein (2004) finds a similar effect of a 1 percent increase in the utilization of preexisting vaccines through public policy increases new clinical trials for new vaccines by 2.5-2.75 percent.
[2] Dubois et al (2015) uses a multi-country sample to look at expected market size innovation. Giacotto, Santerre, and Vernon (2005) look at drug prices and R&D spending, Vernon (2005) look at potential cash flow and R&D spending, Civan and Maloney (2009) look at entry price and drugs in the pipeline, and Abbott and Vernon (2007) look at price and R&D projects undertaken.

Lichtenberg (2005)	1.3
Vernon (2005)	0.22
Giacotto, Santerre, and Vernon (2005)	0.58
Civan and Maloney (2009)	0.5
Abbott and Vernon (2007)	1
Mean	1.54

Note: Acemoglu and Linn (2004) find an elasticity range of 4-6 based on if all approved drugs including generics are included or not. We take the midpoint of this range. Abbott and Vernon (2007) find a price cut of 40 to 50 percent lowers R&D by 30 to 60 percent. Taking the midpoint of these numbers, a 45 percent price cut leads to a 45 percent decrease in R&D, or an elasticity of 1.

The average elasticity is conservative as the entire evidence base is considered and not only the evidence base for the more R&D sensitive US market, where revenue losses impact returns on R&D more because of higher margins.[3]

To assess the impact on the number of new drugs from reductions in R&D spending, a common approach is to divide the reduction in R&D spending by an estimate of the costs of bringing a drug to market. This is a useful approach and implies a proportional reduction in new drugs to the reduction in R&D spending regardless of the cost-per-drug. In other words, using this methodology, a 10 percent reduction in R&D spending leads to 10 percent fewer drugs regardless of the cost per drug estimate used. The elasticity of R&D spending with respect to revenue in this case therefore also represents the elasticity of new drugs to revenue.

Section 3: Calibration of the Impact of US Price Controls on Innovation and Health

This section evaluates what the evidence implies for the innovation effects on new drug approvals of proposed US price controls in HR 5376. We find reduced revenues of 12.0 percent for pharmaceutical companies through 2039. Using the evidence base above on the impact of revenue on R&D we find R&D spending will be about 18.5 percent lower, or $663 billion, under HR 5376 through 2039. This equates to new drug therapies being delayed up to 7 years due to less R&D spending leading to 135 fewer new drug approvals through 2039. The declines in new drug approvals could potentially lead to 331.5 million life years lost through 2039. For comparison, this is 31 times higher than the life years lost due to COVID-19 to date.[4]

3.1 Estimating the Revenue Effects of the Proposed Price Controls

The main provisions of this new agreement will all have a negative impact on manufacturer revenues as outlined in detail in the Appendix. Table 2 illustrates the revenue lost from three major provisions. Overall, the bill will lead to $2.9 trillion foregone revenue through 2039. With our methodology, this would equate to a 12 percent drop in global revenues. The inflation rebates will have the largest impact with 61.2 percent of the loss followed by price negotiations at 34.0 percent.

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[3] Our analysis likely underestimates true innovation effects because the average R&D elasticity of 1.5 used included studies of non-US markets with lower earnings effects than US markets. Given that the US has higher margins, price controls are expected to have a larger impact on earnings.

[4] For clarification, 100% would mean the life years lost would equal the amount of life years lost from COVID-19.

Table 2. Manufacturer Revenue Effects from the Different Provisions in
HR 5376, 2022-2039

Part of Bill	Change in Revenue (billions, $)	Share of Total Revenue Loss
Negotiation	-986.9	34.0%
Inflation	-1,777.6	61.2%
Part D Redesign	-138.1	4.8%
Total	**-2,902.6**	100.0%

We start by creating a counterfactual of drug manufacturer revenue based on current law. The National Health Expenditures Account (NHE) in 2019 estimates total US drug spending to be $369.7 billion.[5] We use a current drug net price increase of 4.5 percent from Hernandez et al (2020) to form the counterfactual price increases.[6] This price increase is applied every year through 2039. We subtract out the current annual manufacturer liability, about $10.1 billion a year, of the benefit design that we calculated using current law and the average spending per beneficiary from CMS' Medicare Part D Data Dashboard.

This counterfactual is compared to our predicted revenue under HR 5376 to obtain the revenue loss of the bill. Using CMS' Medicare Part B and Part D Data Dashboard, we predict the negotiation provision will lower manufacturer revenue by $986.9 billion.

Table 3 illustrates the annual cost of negotiation. The bill starts with 10 negotiated drugs plus all insulins, increasing to 220 by 2039. We combined the Part B and Part D datasets to identify the top 220 drugs in total Medicare drug spending in 2019, the most recent data. We ranked them in order of total Medicare spending to determine when they will be negotiated. We used the Informa data set to provide us the earliest year of approval for these drugs, so we assume the year of earliest approval is the start of their exclusivity period.

For example, the drug Eliquis was the top selling Medicare Part D drug in 2019. It is a small molecule drug that was first approved by the FDA in 2012.[7] This means by the year its negotiated price takes effect in 2025, it will have been 13 years since the start of its exclusivity period, so we assume its max price would be 35 percent lower than it was in 2019.

In year 1, we assume the 10 top selling drug prices will be negotiated, in year 2 the next 15, and so on through 2036 when 220 drugs would be negotiated. We then conservatively assume the maximum prices under

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[5] The National Health Expenditures account has a projected series of total drug spending from 2019 to 2028. We do not use this as the 2019 value is already larger than the projected 2020 drug spending.

[6] Hernandez et al (2020) uses a constant sample of brand drugs to show list prices from 2007 to 2018 grew 9.1 percent annually, but net prices (list price minus manufacturer rebates) only grew 4.5 percent annually. We use this annual growth as it looks at one sample of drugs overtime, so new drug approvals will not affect this estimate. We do note the limitation of this number since generic drugs will most likely not rise this fast. CPI-RX samples the last 20 prescriptions at a pharmacy, so it accounts for price changes for quality adjustments from new drug approvals, but we are trying to isolate price changes from current approved drugs.

[7] Eliquis does have approved but not yet marketed generics due to ongoing patent litigation. Depending on future settlements, they could be exempt from negotiations due to new generics.

the bill through 2039 so that if lower prices are negotiated larger revenue drops occur. As a drug's period since the start of their initial exclusivity increases (from 15 years to 16 years for example), we change their price reduction from negotiation accordingly. Table 3 illustrates how the loss of revenue from negotiations increases over time as more drugs are negotiated.

Table 3. Number of Drugs Negotiated and Revenue Lost from HR 5376, 2025-2039

Year of Negotiation	Total Number of Drugs Negotiated	Actual 2019 Medicare Spending of Negotiated Drugs ($Billion)	Medicare Spending of Negotiated Drugs after Negotiation ($Billion)	Revenue Change from Negotiation ($Billion)	Revenue Change from Negotiation (Percent)
2025	10	38.1	20.6	-17.5	-45.9%
2026	25	67.0	35.4	-31.6	-47.1%
2027	40	85.7	44.7	-41.0	-47.8%
2028	60	99.0	48.6	-50.4	-50.9%
2029	80	109.7	51.4	-58.3	-53.1%
2030	100	118.3	53.8	-64.5	-54.5%
2031	120	123.3	53.0	-70.2	-57.0%
2032	140	127.4	52.8	-74.6	-58.5%
2033	160	131.9	54.0	-77.8	-59.0%
2034	180	135.6	54.5	-81.1	-59.8%
2035	200	138.3	55.3	-83.0	-60.0%
2036	220	140.5	56.2	-84.3	-60.0%
2037	220	140.5	56.2	-84.3	-60.0%
2038	220	140.5	56.2	-84.3	-60.0%
2039	220	140.5	56.2	-84.3	-60.0%
Total	**N/A**	**1,736.1**	**749.1**	**-986.9**	**-56.8%**

Sources: CMS Medicare Part B and D Data Dashboards; Informa; Author calculations.

We find that the second provision of the bill through inflation rebates will cost manufacturers $1.8 trillion through 2039. We assume the inflation caps only apply to the 28.3 percent of total drug spending from Medicare, as calculated in the NHE tables for 2019. Under the bill we assume Medicare prices will increase at a 2 percent annual pace while all other pharmaceutical spending (the other 71.7 percent) increases at a 4.5 percent rate from Hernandez et al (2020). The total cost effect for inflation is the residual between the total cost of the agreement and the sum of the cost of the other two provisions.

This inflation estimate is large because the inflation cap affects all Medicare drugs and the effects compound. We are not only applying a lower inflation rate in HR 5376, but we are also applying it to a lower base annually due to decreases in revenue from negotiations and manufacturer liability. This means as the

inflation rate compounds under current law to have larger revenue increases accumulate in dollar terms, revenues under HR 5376 will have a much smaller increase leading to a growing cost of the inflation cap.[8]

Finally, we find that the third provision of Part D redesign implies a $138.1 billion decline in revenue from HR 5376. We use the average spending per beneficiary for each drug covered under Medicare D. We calculate how much on average a manufacturer contributes to the spending on this drug per beneficiary under current law and HR 5376. Under current law, manufacturers pay 70 percent of the cost during the coverage gap which applies between $4,130 and $10,048 of payments. We calculate for each drug how much the manufacturer would pay per beneficiary and multiply this by the number of beneficiaries each year. From 2024 to 2039, we calculate manufacturer liability would have been $10.1 billion a year for a total cost of $161.6 billion.

HR 5376 eliminates the coverage gap and requires manufacturers to pay 10 percent for brand drugs in the initial coverage phase (between $445 and $7,205 in beneficiary payments) and 20 percent for brand drugs in the catastrophic phase (over $7,205 in beneficiary payments). When summing across all drugs, this leads to $18.7 billion a year for a total cost of $299.7 billion in costs for manufacturers through 2039. This means the new manufacturer liability will increase $138.1 billion in total. We assume this change begins in 2024 as stated in the legislative text.

The total change in U.S pharmaceutical revenues implied by the three provisions is illustrated in figure 1. HR 5376 would lead to a total 31.3 percent drop in U.S. revenues through 2039. Without considering new drug approvals that will increase U.S. revenue, pharmaceutical manufacturer revenue would level out at a lower level of revenue through 2039 as our assumed price increases do not offset the increasing revenue shortfalls from capping Medicare price increases and increased negotiations. Under current law, current revenues would almost reach $600 billion while HR 5376 will limit them to just under $250 billion by 2039. A Torreya industry report illustrates the U.S. makes up 38.3 percent of global drug revenues of the world. If we assume this proportion in the global market, global revenue will fall 12.0 percent. This is less than half of the midpoint estimate for a fall in global revenues from HR 3 in Philipson and Durie (2021).

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[8] For example, assume a company has $100. This grows by 4.5% after a year to $104.5. The next year it grows 4.5% again to $109.2. Assume a 2% growth rate on $100. After a year, this is $102. The next year $104.04. After year 1, the annual cost of the inflation cap was $2.5 then grew to $2.66 the next year. Imagine in year 1 we added a $10 cost, so that the 2% growth rate applied to $92, so in year 2, they had $93.84. The annual cost of inflation in year 2 would be the difference in the growth in dollar terms, so this would be ($4.7 - $1.84)= $2.86. This means inflation would have a larger cost due to the lower base in that year. This accumulates, or compounds, overtime.

Figure 1. Pharmaceutical Manufacturer U.S. Revenues Under Current Law and HR 5376, 2019-2039
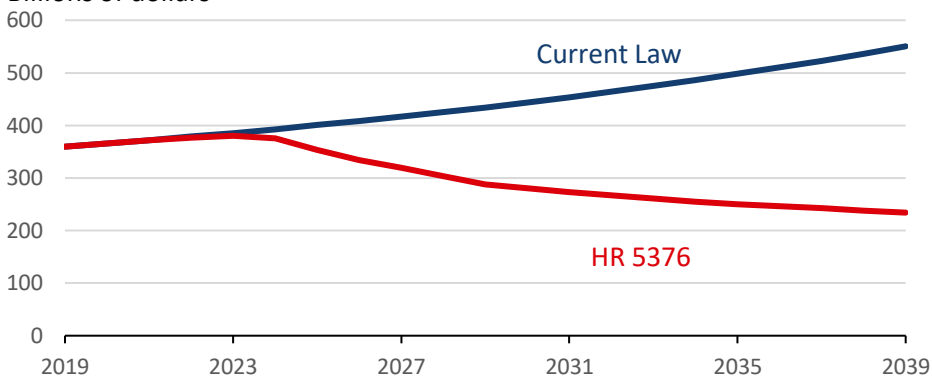
Billions of dollars

Sources: National Heatlh Expenditures; CMS Medicare Part B and D Data Dastboards; Informa; Hernandez et al (2020); Author caluclations.

The revenue effect could be considered a lower bound estimate for several reasons. First, targeting blockbusters with negotiations in Medicare will affect prices of drugs not targeted and non-Medicare drug prices. The top-selling blockbuster drugs fund the rest of the development pipeline where just under 90 percent of drugs fail (Wong et al 2019). HR 5376 will lead to losses in revenues leading pharmaceutical manufacturers to trim down their portfolio of drugs in development.[9]

Second, we assume pricing is the most favorable allowed for the companies. However, the exact magnitude of the price cuts on negotiated drugs is unclear. HR 5376 sets a maximum price but not a minimum. If the manufacturer does not accept the offered price, they would face up to a 95 percent excise tax, so almost all offered prices would be better. One reason the Secretary could do this is the implied strategy of tying prices to mandatorily reported R&D spending of the negotiated drug. The issue is that a company needs to earn a multiple of their R&D spending in order to continue to pay for other drug failures, and those expected high earnings are the incentive to take on the risk to invest in new drug development.[10] These revenue losses lead to fewer future drug approvals, so there are additional revenue costs due to foregone revenue.

Third, negotiated drugs will put downward price pressure on competing non-negotiated drugs in order for them to stay competitive. Fourth, Medicaid pricing is mandated to be 23 percent cheaper than other programs, so lower prices in Medicare will lower Medicaid pricing. Fifth, negotiated prices will affect the hospital prices in the 340B program leading to more revenue losses. Sixth, due to the negotiations taking place independent of current patent exclusivity, manufacturers will no longer have incentives to extend the drug to new diseases or
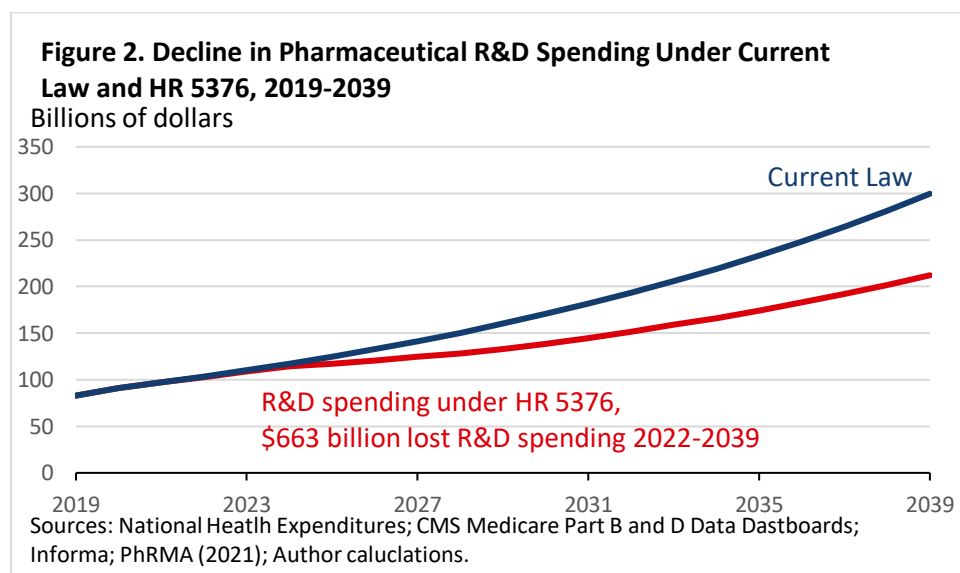
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[9] The agreement will shorten drug's market life by 2-4 years meaning less revenue for future approved drugs moving forward. Manufacturers will take the shorter market life into account when making investment decisions on new drugs which will then add additional reductions in new drug approvals from less expected future revenues.

[10] CBO (2018) finds to have a 4.8 percent return on their portfolio, pharmaceutical companies need a profit margin of 62.2 percent from their successful drugs

stay away from innovating into large diseases.[11] Innovation into large diseases such as diabetes and Alzheimer's will be discouraged due to the price reductions in negotiations. This would also include disincentives to doing pediatric trials as a drug would no longer receive the 6-month exclusivity extension to sponsor such a trial. Seventh, generic or biosimilars, which effectively lower prices dramatically, would be discouraged from entering the market due to the need to compete with forced lower prices of innovator products. Additional limitations are discussed in section 5.

3.2 Innovation Effects of the Proposed Price Controls

The estimated drop in annual global revenues will have an effect on drug innovation. Figure 2 shows the gradual fall in R&D spending through 2039. HR 5376 will lower R&D spending by $663 billion. Put another way, it will take about 7 years for R&D spending to reach R&D spending under current law meaning new drug treatments that would become available without HR 5376 will now be delayed up to 7 years.
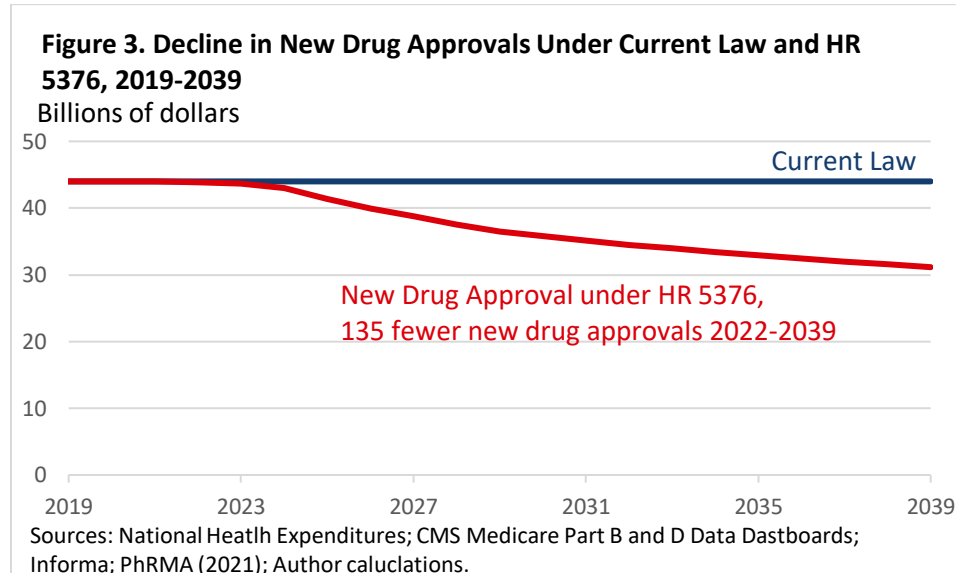

Figure 2. Decline in Pharmaceutical R&D Spending Under Current Law and HR 5376, 2019-2039
Billions of dollars

Sources: National Heatlh Expenditures; CMS Medicare Part B and D Data Dastboards; Informa; PhRMA (2021); Author caluclations.

This is calculated using the methodology of Philipson and Durie (2021). We used PhRMA's 2021 membership survey to find R&D spending and applied the compound annual growth rate from 2000 to 2019 forward to get counterfactual R&D spending. As discussed earlier, a conservatively low estimate of the elasticity of revenue on either R&D or the introduction of new drugs is 1.5 based on current evidence. We apply this elasticity to the annual decline in revenue that we derived from CBO scoring and from our own estimates to calculate a percentage reduction in total R&D spending.

To estimate the impact on new drug approvals, we assume a baseline of 44 annual new drug approvals (2015-2019 average) as noted in CBO's November 18, 2021 scoring of HR 5376.[12] The decline in R&D spending

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[11] Using data from Informa, drugs that have been approved by the FDA have on average 1.4 indications, but the top 25 drugs in Medicare Part B and D spending have 4 indications on average and all eligible drugs to be negotiated have 2.2 on average.

[12] This baseline is higher than the 30 new drug approvals assumed in Philipson and Durie (2021).

will lead to 135 fewer new drug approvals over time (figure 3). The bill will have larger impacts over time because more drugs are negotiated leading to larger corresponding falls in R&D spending. Another reason for larger effects over time is that R&D spending will take time to be reflected in new drug approvals due to long development process.[13]

Figure 3. Decline in New Drug Approvals Under Current Law and HR 5376, 2019-2039
Billions of dollars

Sources: National Heatlh Expenditures; CMS Medicare Part B and D Data Dastboards; Informa; PhRMA (2021); Author caluclations.

We again follow the methodology from Philipson and Durie (2021) by applying the 1.5 elasticity from the literature to the percentage drop in revenue overtime. We apply this to a baseline of 44 annual new drug approvals, the 2015-2019 average annual new drug approval. This is the same baseline as CBO's recent score.

The number of indications treated will also decrease as the agreement disincentives finding new indications for drugs. If you assume the average drug has 1.4 indications, 188 indications will not get new prevention, treatment, or cures through 2039.

Section 3.3: Health Effects of the Proposed Price Controls

As in CEA (2019), we use the existing evidence base to assume every $2,000 in lost R&D spending leads to the loss of 1 statistical life year. We apply this to the $663 billion in lost R&D spending to find HR 5376 will lead to 331.5 million fewer life years through 2039. For comparison, we updated the COVID-19 life year lost estimate from Philipson and Durie (2021) to 10.7 million life years. Thus, the life years lost from the bill are about 31 times larger than from COVID-19 to date.[14]

Section 3.4: Comparison to CBO's Innovation Estimate

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[13] CBO (2019) notes this as well and shows that 18.9 percent of their total estimate will occur through 2029 and 81.1 percent of their total estimate from 2030 to 2039.

[14] The reason the health effects are larger than the ones reported in the abstract of Philipson and Durie (2021) is those health effects were over a 10-year horizon, while we report them here over 18 years.

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Table 4 summarizes CBO's November 18, 2021 scoring of HR 5376 with our estimates of the innovation impact from this bill. We derive a 5.1 percent fall in global revenue from CBO's results.[15] We also use this revenue decline within our methodology to show how many fewer new drug approvals would occur with this smaller revenue impact. CBO had not previously provided any health effects from this bill.

We believe CBO underestimates the drug innovation effects of HR 5376. They find new drug approvals will fall by 5 through 2041, which we conservatively use to compare to our 2039 end year. This implies innovation will fall by 0.6 percent through 2039.[16] Using our preferred methodology, HR 5376 will have a substantial impact on innovation through an 18.5 percent decline meaning our innovation estimates are 27 times larger than CBO's. Even with CBO's lower innovation effect, HR 5376 will still lead to larger losses in life years than COVID-19 to date.

We also estimate the drug innovation impact of CBO's 5.1 percent revenue impact using our methodology. We find new drug approvals would still fall by 61 drugs and the health impacts would be 12 times as large as COVID-19. Due to the black box nature of CBO estimates, and government estimates in general, which only report results and not analysis generating the results, we are not able to discuss the causes of differences in our estimates.

Table 4. Revenue, Innovation, and Health Effects from HR 5376

	CBO November 18, 2021 Estimates	CBO Revenue Estimates using our Innovation Methodology	Our HR 5376 Estimates
Lower Global Revenue	-5.1%*	-5.1%	-12.0%
Impact on R&D (%)	-0.6%*	-7.9%	-18.5%
Impact on R&D Spending (billions of dollars)	-25.3*	-262.1	-663.0
Impact on New Drug Approvals	-5	-61	-135
2022-2029	-1	-10	-27
2030-2039	-4	-50	-107
COVID-19 Million of Life Years Lost	10.7*	10.7	10.7
HR 5376 Million of Life Years Lost	12.6*	131.1	331.5
Ratio of Life Years Lost from HR 5376 and COVID-19 Life Years Lost	1.2*	12.2	30.9

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[15] CBO does not report a fall in global revenue, so we take the federal government budget changes from the cost of the three tenets of this bill through 2031 to find a $129.9 billion reduction in spending: price negotiation at $78.8 billion, inflation caps at $49.4, and Medicare Part D redesign at $1.6 billion. We compared this to their scoring of HR 3 which found a $483.0 billion reduction in spending from 3 similar provisions which they estimate led to a 19 percent decline in global drug revenues. We took the proportion of $129.9 billion and $483.0 billion applied to the 19 percent reduction in global drug revenues to get the 5.1 percent reduction.

[16] We calculate this by dividing the 5 lost new drug approvals through 2039 to the 792 baseline they used over this timeframe (44 annual new drug approvals).

Section 4: Changes to Stakeholder payments in Medicare Part D

Another large aspect of HR 5376 and HR 3 is the redesign of Medicare Part D. Figure 4 illustrates the changing shares of drug spending by stakeholders for brand name drugs for patients not eligible for the low-income subsidy. HR 5376 would put a $2,000 out-of-pocket cap on drug spending for beneficiaries, but the corresponding increase in payer liability in the catastrophic coverage phase is likely to increase premiums for patients. Part D plans operate in a very competitive market which implies any higher costs must be pushed onto patients via higher premiums.

HR 5376 eliminates the coverage gap (doughnut hole) and takes away the beneficiary's contributions in the catastrophic phase. However, the plans pay a much larger share than before after the deductible is met. This ultimately leads to the shifting of the cost burden from the government to patients in the catastrophic phase. About 90 percent of spending below $7,205 in drug spending for brands will be paid for by the beneficiary through premiums or cost sharing. The catastrophic phase is mainly reached by patients with chronic conditions using specialty high-cost drugs, such as e.g. HIV drugs for antivirals.

Figure 4. Share of Brand Drug Copays by Payer under Current Law / Share of Brand Drug Copays by Payer under the New Agreement

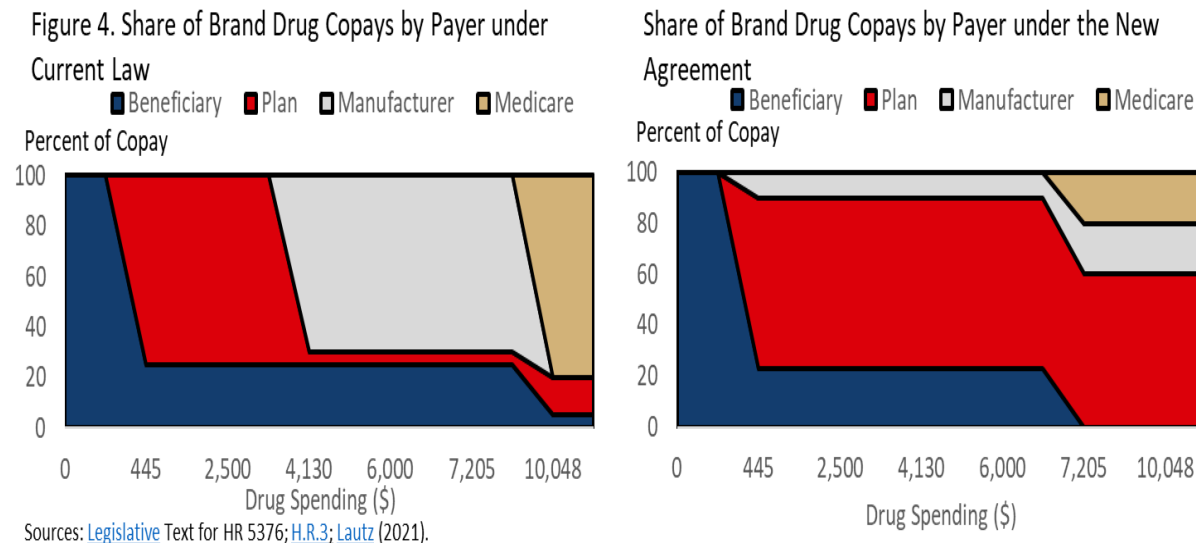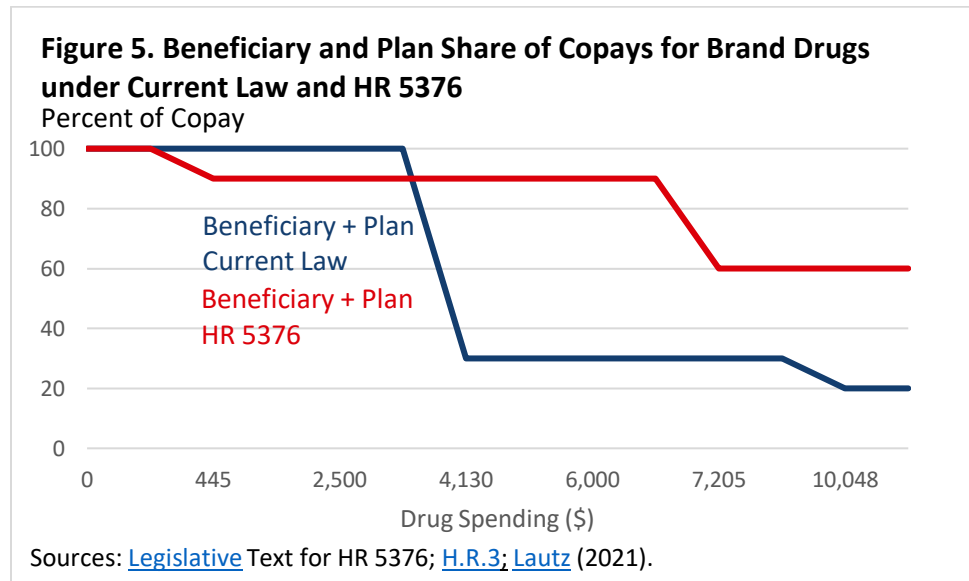Sources: Legislative Text for HR 5376; H.R.3; Lautz (2021).

Figure 5 further illustrates the dramatic changes on high expenses covered by patients, either through cost sharing directly or through premiums. The Figure depicts the share of spending covered by patients or plans

under the status quo and HR 5376. The Medicare reinsurance share of the catastrophic phase changes from 80 percent under current law to 20 percent for brand name drugs.

Figure 5. Beneficiary and Plan Share of Copays for Brand Drugs under Current Law and HR 5376

Sources: Legislative Text for HR 5376; H.R.3; Lautz (2021).

In 2017, the catastrophic phase accounted for about 40 percent of total Part D spending, $59 billion, and growing (Sen et al 2020). If the new design had been law in 2017, Medicare's reinsurance cost burden would have been $35.4 billion lower, going from $47.2 billion down to $11.8 billion. The plan's cost burden just in the catastrophic phase would increase from $8.9 billion to $38.4 billion. The higher cost burden on plans will lead to higher premiums for beneficiaries, reducing savings from the new lower out-of-pocket cap and the elimination of the coverage gap. This will adversely affect innovation through lower demand for more expensive plans.

Patients will most likely see an increase in total spending from this Part D redesign through higher premiums even with the government increasing their subsidy on premiums from 74.5 to 76.5 percent. Figure 6 illustrates the impact of different assumed shares of catastrophic spending. We believe our approach undercounted how much money is spent in the catastrophic phase as this approach says the catastrophic phase only accounts for 25.8 percent of total Medicare Part D spending, compared to about 40 percent in Sen et al (2020). The difference is we used average spending per beneficiary per drug, so we do not count the variance between beneficiaries through full raw totals like in Sen et al (2020). Since the catastrophic phase pays for the most expensive drugs, and the new legislation shifts the cost burden of this phase onto plans, the correct share of spending here is crucial. We decided to show the tradeoff of how much spending occurs in the catastrophic phase due to this uncertainty. The main takeaway is when adjusting total spending by increased utilization, beneficiaries will be paying more with the main reason being the increased premiums despite the out-of-pocket cap and the increase in the government premium subsidy. The catastrophic phase spending estimate from Sen et al (2020) gives up to a 10 percent increase in beneficiary spending depending on utilization changes.

Figure 6. Change in Total Beneficiary Spending at Different Levels of Spending in Catastrophic Phase from HR 5376 Part D Redesign, 2019
Percent Increase in Beneficiary Spending
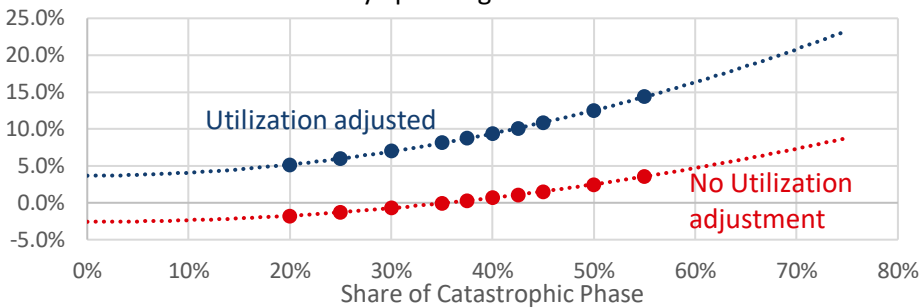
Sources: CMS Medicare Part D Data Dashboard; Author calculations.
Note: Under current law, we assumed the share of spending in other phases would account for 35.5% (deductible), 53.9% (initial coverage phase), and 10.6% (coverage phase) of the remaining spending (1-share of catastrophic spending). Under HR 5376, this would be 36.9% (deductible) and 63.1% (initial coverage phase).

Section 5: Other Considerations and Limitations

We do note other considerations and limitations of this analysis. This analysis provides a macro view of the impact of HR 5376. Certain disease groups will be impacted more than others due to Medicare being the primary focus of HR 5376. Older populations have higher market shares of certain drugs, so these disease groups will have a higher negative impact. Blume-Kohout and Sood (2013) provide a case study in how the number of clinical trials for Alzheimer's disease (86 percent of its drug revenue is in Medicare) increased from 10 to 50 while contraceptives (<1 percent of its drug revenue is in Medicare) had no break in trend at the introduction of Medicare Part D. If the Medicare market had the same medical needs as the rest of the population, then the spending share of the top 220 drugs by disease group would be the same as the entire market. We identified disease groups for just under 200 of the top 220 Medicare drugs, accounting for over 95 percent of their revenue in 2019. We took the disease group share of the total spending of these drugs and compared them to the disease group share of revenue for 2019 revenue in Informa data for the entire U.S. market. Drugs treating diseases in the disease groups Endocrine (9.5 p.p.), Cardiovascular (6.0 p.p.), and Respiratory (2.8 p.p.) have the highest differential when comparing the shares of revenue between the two markets. Oncology and Neurology are other disease groups that will be affected due to their high value and high share of Medicare spending. This matches with CDC's cause of death by age group in 2018 as diabetes (Endocrine), heart disease and cardiovascular issues (Cardiovascular), Chronic Lower Respiratory Disease (Respiratory), Malignant Neoplasms (Oncology), and Alzheimer's and Parkinson's Disease (Neurology) are in the top 10 for people aged 65+. This means these disease groups are going to be hurt more than others due to price negotiations due to their importance to older populations.

Health care spending outside of drugs will be raised because new drugs on average reduce other forms of health care spending through cost offsets. We estimate a 3.7 percent increase in medical services spending due to the decline in new drug approvals. This means that budget savings from this agreement need to take into

account the lack of new drug approvals that will lead to higher spending in other healthcare settings. As patients would have to rely on other ways to receive treatment or cures this would on average raise costs. CBO (2012) estimates a 10 percent increase in drug spending leads to 2 percent lower other medical services spending. We assume foregone drug spending of 18.5 percent, which translates to a 3.7 percent increase in other medical services. These increased costs and worse health outcomes are tied to fewer new drug approvals, meaning the budget savings must be adjusted to account for higher beneficiary spending on other forms of health care.

In addition to other limitations we noted in section 3.1, our global revenue estimate can possibly be thought of as a lower bound with some offsetting effects Foregone new drug approvals are also foregone manufacturer revenue. The issue is that losing revenue leads to less R&D, which leads to fewer new drug approvals, which lead to less revenue compared to the counterfactual. We just look at the revenue impact of current drugs, though we understand more global revenues will be lost due to fewer new drug approvals. Additionally, due to uncertainty in behavioral responses, our estimates could change due to potential behavioral responses, such as how quickly and radically manufacturers react to inflation caps by setting higher list prices at launch, affordability increases from lower patient out-of-pocket costs, and uncertainty around negotiations. Further, we assume a constant average elasticity, though there is most likely a different elasticity in the short and long run. If R&D goes down now it has an impact today and the future, so as more R&D is lost over the years, it will accumulate into a higher R&D elasticity. On the other hand, this methodology likely overestimates the effect of HR 5376 on revenues as the negotiation eligibility criteria likely keep some of the drugs that we assume would be negotiated from actually being negotiated. We did not filter out drugs with already marketed generic competition. This would also lower the cost of inflation due to the compounding dynamic explained in section 3.1. Also, we only looked at retail drug spending and did not take into account non-retail drug spending as the NHE only captures retail spending.

Finally, we do not directly estimate an impact on generic drugs. As stated above, the number of generics and biosimilars will most likely decrease. This is not ideal as more generic competition leads to more price declines. Generics and biosimilars are an effective way to create competition and affordable easy to administer drugs to improve access to these treatments. The agreement will artificially set prices for brands which will lead to generics being priced out of the market and not being developed. A reduction in price for one drug also has an effect on other drugs in the same disease class, leading to more potential price declines further hurting manufacturer revenue.

Further considerations of the differences between HR 3 and HR 5376 as well as changing the incentive structures of HR 5376 can be found in the appendix.

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Appendix: Differences Between HR 3 and HR 5376 and Other Considerations of HR 5376

The United States has fewer restrictions on price than other countries, but the Biden Administration has announced their goal to lower drug prices through greater price regulation, as set forth in a recent bill referred to as HR 3, that was originally a part of the Build Back Better Act. This proposal would change the way certain single-source brand drugs are priced for Medicare beneficiaries by requiring drug manufacturers to "negotiate" drug prices with the Secretary of Health and Human Services starting with 25 drugs in 2024 with 50 new drugs annually starting in 2025. A prohibitive excise tax of 65 to 95 percent would be applied to a company's annual gross sales if they refuse to negotiate, making the requirement largely equivalent to mandatory price controls. Drug prices set by the Secretary may not exceed the prices in specified countries by more than 20 percent and price increases would be capped at the rate of inflation (CBO 2021a). In addition, these price controls would also be extended to private transactions by employer-based plans as stated on August 12, 2021 by President Biden and as implied by the proposed legislation. Private payers can choose the lower prices negotiated by the government, which they presumably will. Additionally, HR 3 also stipulates drug price increases may not increase faster than the rate of inflation with a "look back" provision that would charge a company a one-time payment for price growth faster than inflation since 2016. Finally, the last major change was a redesign of Part D to set an out-of-pocket maximum cap for beneficiaries and eliminate the coverage gap (doughnut hole).

On November 2, 2021, the White House unveiled a new agreement with Congressional Democrats for new provisions on prescription drug pricing in the Build Back Better Legislation with legislative text being passed by the House of Representatives on November 19. This agreement has very similar tenets to the original proposed legislation. The agreement has three main provisions: 1. allows Medicare to negotiate drug prices after a certain number of years of initial exclusivity, 2. drug rebates to make sure drug prices do not increase more than the rate of inflation, and 3. redesign Part D coverage capping patient out-of-pocket costs. They also added carve-outs for small biotech companies.

An overarching theme in both bills is the creation of price controls for blockbuster drugs. The creation of price controls limits revenue of drugs, especially blockbuster drugs, leading to reduced funding for the entire development pipeline. Of the just over 3,500 drugs in the CMS Medicare Part D data dashboard for 2019, the top 200 Medicare Part D drugs account for 72.2 percent of total spending, further illustrating how the revenue from top drugs fund the rest of the portfolio. Of the drugs that start clinical trials, only about 13.8 percent actually make it to the market (Wong et al 2019). Further, Grabowski et al (2002) finds the top 10 percent of drugs that actually do make it to the market make up over half of total earnings and only the top 30 percent will have earnings that exceed their R&D cost. Due to long development periods and high risks of failure, CBO (2018) also finds that to have a 4.8 percent return on their portfolio, pharmaceutical companies need a profit margin of 62.2 percent from their successful drugs. This means the pharmaceutical drug pipeline has high risk of failure and revenue losses in R&D spending despite massive health gains from innovation. The issue is prior to starting the development process, a company does not know if this project will be profitable, so companies cannot just pick the investments for the best drugs. They invest in promising drugs that most of the time do not succeed. Limiting the revenue of top earning drugs will lead to a shrinking development pipeline leading to fewer new drug approvals.

HR 5376 and HR 3 have the same big ideas with different crucial details for drug price negotiations, the inflation cap, and the Medicare Part D redesign. Table 5 illustrates these differences. A key difference is in HR 3 the negotiated price for Medicare would be applied to commercial plans, while under HR 5376, the negotiated price will first affect the Medicare price. This is then incorporated into Medicaid Best Price and the 340B program. Another key difference for the drug price negotiations is a change in the criteria for which drugs can be negotiated. In HR 5376, only drugs that are single-sourced and have passed certain exclusivity thresholds are included, independent of patent and data exclusivity status. Small molecule drugs must have had at least 9 years of exclusivity and biologics at least 13 years. This raises one issue of changing incentives for pharmaceutical company's investment in new drugs. Kolchinsky (2021) discusses how companies will now prioritize biologic drugs over small molecule drugs due to the 13-year market life for biologics. The issue here is small molecule drugs are easier to administer and have lower costs leading to more generics that increase affordability and access. We looked at the patent life and data exclusivity of the top 20 drugs by total Medicare Part B and D spending, finding that this plan will shorten their market life by 2-4 years on average. These drugs will no longer have the advantages of exclusivity by having an artificially lower price, but cheaper generics still will not be able to be developed while they watch the government price them out of the market. This new price control scheme will lead to fewer generics and less competition which has been shown to lead to effective price reductions without undermining innovation.

An unintended consequence with the eligibility for price negotiations is it depends on total amounts of spending, but spending is determined not only by prices but also quantity, here utilization. This implies that the drugs that are negotiated may not have abnormal prices, just abnormal utilization at normal prices. A drug may be a blockbuster due to many patients benefiting from the drug rather than high prices. This will lead marginal companies to attempt to avoid negotiations by limiting quantity, hence lowering the number of patients benefiting from fairly priced drugs. For example, this could either be done through reduced marketing of fairly priced drugs or through not expanding indications of a given drug. More importantly, it may reduce innovation into highly prevalent diseases, such as diabetes, even though that is where innovation does the most good.

This is further exacerbated in HR 5376 from losing exclusivity faster as pharmaceutical companies will no longer have an incentive to expand the use of the drug to new populations like pediatrics or to new diseases, more specifically new indications. A drug can be initially approved by the FDA to treat a certain indication like Rheumatoid Arthritis or Hepatitis-C. Manufacturers have an exclusivity period to market that drug and earn revenues on it without competition to cover the costs of development and distribution. Many times, researchers will continue trials and find other indications for the drug leading to multiple drug-indication pairs. This expands the value of the drug to a new market and typically leads to extensions on exclusivity to cover the additional trials and other costs for further development. Using data from Informa, drugs that have been approved by the FDA have on average 1.4 indications, but the top 25 drugs in Medicare Part B and D spending have 4 indications on average and all eligible drugs to be negotiated have 2.2 on average. By setting hard exclusivity periods independent of patent life, this agreement discourages companies from finding additional uses of approved drugs. Kolchinsky (2021) further notes how manufacturers can receive a 6-month extension to their exclusivity to conduct pediatric clinical trials to determine the right dosage and effectiveness of the drug for children.

Companies would no longer be incentivized to conduct these critical trials and expand needed medication to children.

Table 5. Changes from HR 3 and November 2021 Agreement

	HR 3	November 2021 Agreement
Which drugs can be negotiated?	Single-Source and brand name drugs. Must be either in the top 125 drugs of either national health spending or Medicare spending	Single-Source drugs. Small molecule drugs: must be at least 9 years since the start of the exclusivity period. Biologic drugs: must be at 13 years since the start of the exclusivity period. Drugs with highest total spending for Parts B and D, contributing more than $200 million
What is the Price Cap?	Markup 20% of the average price in 6 foreign countries. CBO	If small molecule and 9-12 years past exclusivity: 75% of 2020 non-federal AMP 13-16 years past exclusivity: 65% of 2020 non-federal AMP 16+ years past exclusivity: 40% of 2020 non-federal AMP
How many drugs can be negotiated per year?	25 in 2024, 50 annually starting in 2025 plus all insulins	10 in 2025, 15 in 2026, 15 in 2027, and 20 annually starting in 2028 plus all insulins
What is the Excise Tax on drug revenue due to failure in agreeing to a price?	Up to 95%	Up to 95%
Who are Small Biotech carve-outs for and what are they?	None.	Companies with 80% or more of Medicare revenue coming from one drug with less than 1% of total Medicare spending. These companies do not have to undergo negotiations from 2025-2027. A 2-year phase in period when they do negotiate. Increased manufacturer liability for Part D redesign is phased in over 6 years.
Does this proposal limit price increases to inflation, and does it have a "look back" provision?	Yes and Yes.	Yes and no.
Part D Redesign	Increases manufacturer cost share in Initial Coverage Phase to 10%. Eliminates the Coverage Gap (donut hole). Eliminates beneficiary share of copay in Catastrophic phase. Increases plan (50%) and manufacturer (30%) share. Decreases Medicare Share (20%).	Increases manufacturer cost share in Initial Coverage Phase for brands to 10%. Eliminates the Coverage Gap (donut hole). Eliminates beneficiary share of copay in Catastrophic phase. Increases plan (60%) and manufacturer (20%) share for brands. Decreases Medicare reinsurance Share (20%) for brands.

Sources: Legislative Text for HR 5376; HR 3; Lautz (2021).

HR 5376 is a restriction on the lifecycle pricing of drugs as opposed to HR 3 which would benchmark prices to an international price. One thing to note is the negotiated prices under HR 3 needed to be between the international price and 20 percent above the international price. HR 5376 does not have an explicit price floor. This means the Secretary of HHS could give take it or leave it offers well below the maximum amount as the 95 percent excise tax would be worse than most price offers from the Secretary. The calculations in this brief are conservative as we assume the maximum price in negotiations despite uncertainty around negotiations. Some provisions in HR 5376 may also allow for the government to start mimicking foreign price control bodies such as the UK's National Institute for Health and Care Excellence (NICE) by starting to use cost-effectiveness thresholds like the ones abroad which adds to the concern of no price floor.

The negotiation process begins 2 years before the eligible drug would face the negotiated price with the Secretary of HHS providing an initial written offer by June 1. The manufacturer has 30 days to counteroffer, then they go back and forth. The negotiated price will be published in the Federal Register by November of that year with a published explanation from the Secretary of HHS by March 1 of the next year. The Secretary must take into account information submitted by the manufacturer like return on R&D costs, distribution of sales across buyers and projected future revenues, production and distribution costs, prior novel therapeutic discovery federal support, existing and pending exclusivity, national sales, and clinical trial information. Other information to be considered can be simplified down to competition from other drugs based on effectiveness on different populations and addresses unmet medical needs.

Another aspect of HR 5376 is the speed at which drug prices can be negotiated. In the old agreement, the Secretary of HHS could negotiate the price of 25 drugs and 50 new drugs annually going forward versus 10 in the first year of HR 5376 rising to 20 new drugs annually after 2 years. This means under HR 3, as many as 225 drugs could be negotiated in the first 5 years versus HR 5376 which would take 12 years to reach a similarnumber of drugs. This will slow down the pace of revenue losses in HR 5376.

The inflation rebate will still apply the same in both bills except HR 5376 gets rid of the "look back" provision. This provision in HR 3 would have made companies have to pay a one-time sum for any price increases faster than inflation going back to 2016. Behavioral responses to the inflation rebate could mean higher initial list prices since later price increases are now limited.

Finally, the small biotech carveouts will have limited effects due to the nature of the industry from the interdependence between smaller and larger firms in the biopharmaceutical pipeline. Typically, smaller biotech firms fund earlier phases of development before larger firms acquire them or create licensing deals to fund later phases and bring the drug to market. Larger companies tend to rely on M&A (41%) and licensing agreements (19%) to fund most of their R&D (Schuhmacher et al 2021).[17] Smaller companies are able to utilize larger companies' size, brand, and expertise in marketing and navigating regulations creating revenue streams for

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[17] Large companies fund the other 40% of their R&D through their own current revenues.

continued accumulation of R&D.[18] The larger companies tend to absorb the smaller companies and/or the product, so these carve outs have limited rewards for smaller companies.

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[18] Petrova (2014) and Wuyts and Dutta (2008) have good discussions on this concept.