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Assessing the implications of centralized drug price setting to investment in clinical development for HIV treatments

A study for Gilead Sciences

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Executive Summary

The Build Back Better Act, which is under consideration for passage into law includes price controls in Medicare Part B and D, and price caps more broadly. In this report we explore how the introduction of this type of a federal price setting policy in the United States would impact the size of the pharmaceutical market and investment in research and development (R&D). Although price controls would not target medicines in specific therapy areas, the wording in the proposed legislation may mean that price controls would impact certain medicines disproportionately. Less investment in R&D would mean fewer clinical trials. In this paper we consider the impact of such a policy on future medicines and potential cures for Human Immunodeficiency Virus and Acquired Immune Deficiency Syndrome (HIV) by developing a quantitative model. We find that there have been over 3,000 clinical trials for potential treatments for HIV since 1990 and 57 medicines for HIV have been approved by the FDA since 1987. Our model identifies HIV drugs that would be placed under price control as specified by the Build Back Better Act as:

- Innovative HIV medicines that have a budget impact of more than $200 million
- Small molecules and biologics for HIV that have been on the market for 9 or 12 years, respectively

Based on the Build Back Better Act, we estimate that price control for a segment of the HIV market would reduce future revenues for HIV medicines by 16.8% to 17.2% and, as a result, in 2021-2035 we project that R&D investment spending could decline by **21.6% to 22.0%.** If this were the case, there would be **537 to 551** fewer HIV clinical trials relative to what would have otherwise occurred in that period. The implications for drug development could be significant, given that currently around 610 HIV clinical trials are ongoing in the United States.[1] While this paper considers the implications on clinical trials, this would ultimately impact the likelihood of new treatments coming to market, the prospect of a cure, the development of knowledge about treatment in specific populations, vaccine or other transformational therapy for HIV, and the health of patients.

Introduction

The United States (U.S.) leads the world in the development of innovative medicines that have delivered significant benefits to patients and the healthcare system domestically and globally. However, there is intense debate in the U.S. on whether the federal government should set drug prices, both in programs like Medicare, where there is a government subsidy, and across the private insurer market. Price setting proposals from the Biden Administration and Congressional leaders would introduce reforms that effectively determine prices for many medicines.[2,3]

The most recent proposal is the Build Back Better (BBB) Act (H.R. 5736), which is under consideration for passage into law and would allow the federal government to set the price of certain prescription drugs in Medicare Part B and D.[4] Although the proposal describes the pricing process as a “negotiation”, the price will be set equal to a percentage of the non-federal average manufacturer price and manufacturers who do not accept the government’s

price would face an excise tax penalty. Therefore, the described process is effectively price setting by the federal government (rather than the status quo where there is a private negotiation between manufacturers and individual health insurers to establish net prices).

Specifically, the Act authorizes the government, through the Department of Health and Human Services (HHS), to establish a Drug Negotiation Program which would set prices for a selection of medicines to be determined at HHS discretion. The process would be focused on the largest medicines as measured by the financial impact on the Medicare program. The proposed text suggests that the medicines placed under price control will be selected by the HHS in the following manner:[5]

- Brand name drugs that "lack price competition" and with Medicare Parts B and D expenditures greater than $200 million.
- Small molecule and biological drugs that have been on the market for at least 9 years and 12 years, respectively.
- "From that list, the Secretary [of the HHS] will negotiate up to 10 drugs in 2025, 15 drugs in 2026 and 2027, and [up to] 20 drugs thereafter.

The Congressional Budget Office's (CBO) score of the BBB Act follows an approach akin to that employed to estimate the impact of similar legislation (H.R.3) on the federal budget and the number of drugs developed. However, there have been several reports from government, academia and one issued by Charles River Associates (CRA), that find the CBO's approach is flawed and likely under-estimates the impact that H.R.3 would have on new drugs, in part because there are no relevant analogues for a policy change of this size in the U.S., the world's largest biopharmaceutical market.[6,7,8]

Among other limitations that lead to an under-estimate of the total impact of a price setting policy, the CBO failed to consider the implications on innovation in specific therapy areas or the impact on innovative activity. For example, the CBO did not estimate the change in the number of clinical trials expected as a result of price setting or the impact this would have. Clinical trials generate evidence on new medicines or expanding the use of existing medicines, as well as continuing to inform the use of medicines, for example, in specific populations such as people with co-morbid diseases. Reflecting this, Gilead Sciences (Gilead) asked CRA to consider the impact of price setting as defined by the BBB Act in the U.S. on R&D of medicines for Human Immunodeficiency Virus and Acquired Immune Deficiency Syndrome (HIV).[9] From this assessment we infer the impact on clinical trials for new and expanded uses of HIV drugs.

Background

Access to HIV medicine in the U.S. through Medicare Part D

Medicare Part D supports the coverage of HIV prevention and treatment. Part D has played an important role in supporting the development of drugs for seniors as seen through an increase in the number of clinical trials for therapeutic areas particularly important for seniors since the introduction of Medicare Part D.[10] When Congress created Part D, it recognized the importance of ensuring coverage of certain medicines used to treat particularly vulnerable

patients with life threatening conditions. To prevent plans from discouraging enrollment of these patients, CMS established six protected classes to avoid interruptions in therapy for these conditions.[11] To achieve this, Part D requires plans to cover all drugs in the six protected classes: antidepressants, antineoplastics, immunosuppressants, antipsychotics, anticonvulsants and antiretrovirals (including medicines for HIV).[12]

There is evidence that drug costs are controlled in Part D:

- Average premiums in Medicare Part D have been stable over time and are lower than they were when the program started.[13]
- The U.S. Government Accountability Office (GAO) found that Part D plans negotiated rebates and discounts for 99%t of the most used Part D medicines, and the rebates and discounts for the top 200 Part D drugs nearly doubled from 2014 to 2016.[14]

The introduction of the BBB Act will impact prices. Given this, we sought to investigate the impact of introducing a price setting process.

Prior to examining the impact of price-setting on clinical trials, it is useful to set out some background on HIV.

HIV in the U.S.

The first diagnosis of HIV in the U.S. occurred in 1980 and although it is estimated that there were approximately 42,000 people unknowingly living with HIV infections at that time. By 1985, 420,000 people in the U.S. were infected. Today, there are an estimated 1.2 million living with HIV, with 37,000 new infections every year.[15,16] New infections have dropped by more than 70% from 1984 to present, with the mortality rate declining by more than 80% since its peak in 2010.[17] Medicines and specifically antiretroviral therapy (ART) introduced in the years following the emergence of the disease have contributed significantly to, and continue to play, a critical role in controlling and reducing HIV-related mortality and in improving long term health for people with HIV.[18]

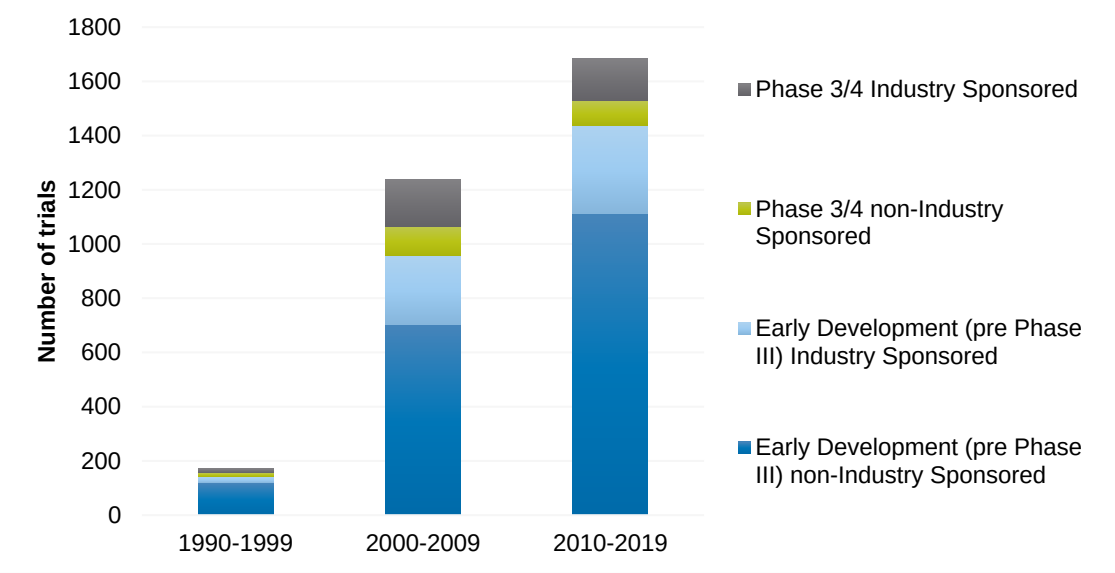
The HIV therapy area has evolved from one where there were mostly treatment-naïve infected individuals to an environment where there are more than a million people living with HIV in the U.S. While there is not a cure for HIV, the disease can be controlled with medicines and broad access and adherence to effective HIV medication remains critical to ending the epidemic.[19] With proper adherence to medication, the virus can be suppressed to undetectable levels, where the risk of transmission through sex is extremely low.[20] In addition, people with HIV in the U.S. that initiate ART can currently expect to live nearly as long as people without HIV and are in otherwise good health.[21]

The development of HIV medicines

The medicines that people with HIV have been taking for the last ten years were in development twenty and thirty years ago. Figure 1 shows that the number of clinical trials for HIV medicines and related conditions increased dramatically from 1990 to 2019. These are a result of research by academia, non-governmental organizations, and the pharmaceutical industry. A significant number of clinical trials in the earliest stages of clinical development are without industry sponsorship. Even though only a minority of therapies make it through to the

later stages of development, these trials are significantly larger in terms of patient enrolment and more expensive (clinical development costs for Phase III are up to eight times more than those for Phase I).[22] The biopharma industry sponsors most later stage clinical development. To illustrate the challenges to sustaining investment in R&D for HIV, consider that when an infectious disease drug candidate (the broader class that includes HIV) enters early human clinical development (Phase I), there is a 79.9% chance that the drug will never be approved for use by patients.[23] This expectation of revenue from the few drugs that are approved sustains interest in such a high-risk investment where failure is far more common than success.

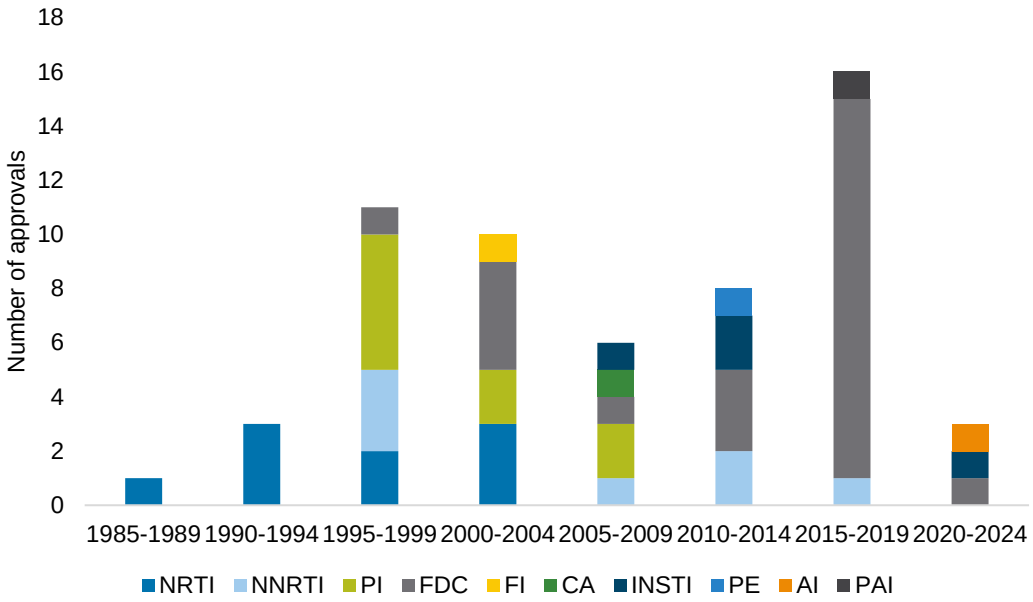
Figure 1: Number of Clinical Trials for HIV in the U.S.



Source: CRA analysis based on data from ClinicalTrials.gov[24]

As a result of investment in clinical development, there have been 57 medicines for HIV approved in the U.S. since 1987 when the first nucleoside reverse transcriptase inhibitor was approved. As clinical guidelines have evolved, nine of those approved HIV drugs are no longer in use although some are currently available in fixed dose combinations. Figure 2 shows the numbers of FDA approvals for HIV medicines, as well as the shift in technology and dose administration.

Figure 2: Timeline of Medicines Approved for HIV in the U.S.



Source: CRA analysis based on data from NIH [25]
NRTI=nucleoside reverse transcriptase inhibitor, NNRTI non-nucleoside reverse transcriptase inhibitor, PI=protease inhibitor, FDC=fixed dose combination, FI=fusion inhibitor, CA=CCR4 agonist, INSTI=integrase inhibitor, PE=pharmacokinetic enhancer, AI=attachment inhibitor, PAI=post attachment inhibitor

HIV recent developments and pipeline

Investment in R&D for HIV has resulted in new and improved medications that independently and in combination have been crucial building blocks in the fight against the disease.[26] While there is still no cure, the value of these incremental investments to patients and society has been substantial. Innovation in HIV has taken multiple forms, in addition to transforming mortality, innovation has made drugs easier to take with fixed dose combinations improving adherence and addressing resistance issues associated with patients who have taken drug therapy for a long time.[27]

R&D in HIV continues to evaluate potential drugs and drug targets for combatting resistance, preventing infection, improving drug tolerability, and developing curative therapies. As a result, the treatment modalities and goals of medicine development are evolving to meet the unmet needs of patients. Examples of medicines in early and mid to late-stage development for HIV prevention and treatment indicate ongoing innovation that could enhance the lives of people living with HIV:

- In 2020, a first-in-class HIV treatment for heavily treatment-experienced (HTE) adults who failed other antiretroviral therapies due to resistance and intolerance or safety considerations, was introduced into the market.[28] Furthermore, in 2021, the first long-acting injectable pre-exposure prophylaxis (PrEP) treatment is being reviewed by the FDA.[29]

- Recent (June 2021) trial data of a long-acting injectable HIV treatment has shown it achieves undetectable viral load (over 80%) and viral suppression (over 90%) in a significant proportion of patients tested.[30] This indicates the potential for long-acting injectables to support patients that have previously struggled to achieve viral suppression.[31]
- HIV vaccines have an increasing presence in the pipeline, though failure rates have been high.[32] As of September 2021, there were over 20 vaccine trials for HIV. Most recently, the International AIDS Vaccine Initiative (IAVI) and Center for Family Health Research are partnering to conduct a research study for a potential HIV vaccine. The study will draw from an mRNA vaccine study with the aim to overcome a significant barrier – producing enough neutralizing antibodies that defend cells from pathogens.[33,34]
- Today in the U.S. there are seven clinical trials ongoing investigating potential curative therapies for HIV.[35] A number of these trials are testing cell-based and DNA modifying therapies. Others are evaluating new uses of existing drugs. None of these studies are in the later stage (Phase III) of development. Investment and time are still needed to advance the science of a potential curative treatment to market approval in the U.S. by the FDA.

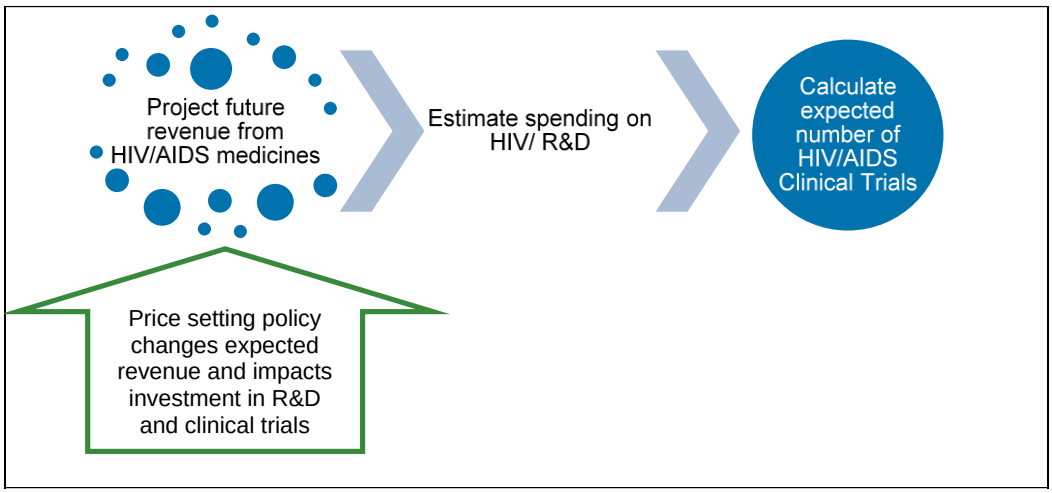
Significant advances over the past few decades have dramatically improved HIV treatment for many people. However, unmet patient need and the lack of a cure indicate that ongoing innovation remains crucial.

Estimated impact of price control policy on HIV innovation

To estimate the impact of a centralized price setting policy in the U.S. as defined by the BBB Act on investment in R&D for HIV medications, we considered how it would affect the number of clinical trials that develop evidence for new and improved treatments, vaccines, and cures.

The decision to invest in a given clinical trials program is complex. It is based on the expected cost of clinical development, the likelihood of success and the degree to which it will address patient needs and hence be commercially successful in the market.[36] However, to estimate the impact of price-setting on clinical trials, we start by adopting a similar approach to academics who have observed the relationship between R&D spend from revenue from medicines and clinical trials.[37] Philipson and Durie (2021) studied the effect of a price change, expected market size, and overall revenue on R&D and associated impact on new drug approvals.[38] Our approach to estimating the impact of price setting regulation on revenues and how the corresponding change in the amount invested in R&D is based on the methods employed by Philipson and Durie. A simple overview of our approach is illustrated in Figure 3.

Figure 3: Simplified overview of approach to estimating the impact of price setting policy on HIV R&D investment and clinical trials



Source: CRA illustration

We first look at the future nominal revenues from HIV medicines in 2021-2035 by extrapolating from a revenue forecast published by Global Data. Forecasted annual sales for HIV medicines range from $22.2 billion to $28.0 billion per year from 2021 to 2029.[39] We project the annual revenue in 2030-2035 using trend analysis.[40]

We then calculate expected R&D investment in HIV for this amount of revenue. We use an estimate from the CBO's evaluation of H.R.3, which found that pharmaceutical companies on average spend 19% of their revenue on R&D.[41,42] Making the simplifying assumption that HIV medicine manufacturers invest the same share of their revenue on R&D, we apply this ratio to our HIV revenue estimate. We estimate **$64.5 billion** R&D investment in HIV from 2021-2035.

We then forecast the number of clinical trials expected for HIV. We consider the publicly available number of clinical trials in HIV compared to R&D investments for HIV in 2016-2020 (810 clinical trials).[43,44] The R&D investment per clinical trial ranged $17 million to $27 million; we used the average across the 5 years of $20.7 million from 2016-2020. To forecast the future R&D investment per clinical trial, we applied the price growth rate for medical goods and services at 2.4% (as measured by the personal health care deflator in 2019-2028).[45] Based on our estimate of R&D spending, we project **2591** clinical trials for HIV between 2021-2035.[46]

Then we consider how a price setting policy would change the amount of expected revenue from HIV medications from 2021-2035. Based on the proposal of the BBB Act, we estimate that price control would affect a segment of the entire HIV medicines market. Our model identifies HIV drugs that would be placed under price control as:

- Innovative HIV medicines that have a budget impact of more than $200 million
- Small molecules and biologics for HIV that have been on the market for 9 or 12 years, respectively

Accordingly, we estimate that the segment potentially eligible for price control under the BBB Act to be 76% of the HIV market.

We assume a two-fold impact of price setting policy on innovation: First, Sood et al. (2009) considered the average impact of price regulation in nineteen countries and found that price setting would reduce revenue in the country with price setting by 13.7% in the year of introduction, and 1.1% additional reduction every year afterwards.[47] We use this to estimate the impact of price setting policy on HIV revenue from 2022-2035[48] and find that all HIV revenues would be reduced by **16.8%** as a result of price setting imposed on the segment of HIV medicines subject to the BBB Act. In the same research, Sood et al. (2009) also estimate a second (non-linear) model; using this estimate, we estimate that HIV revenue would be reduced by **17.2%**.[49] Next, given the change in revenue, we wanted to determine the impact on R&D spending and clinical trials. Shaikh (2020) examined the impact of R&D relative to sales (i.e. R&D investment intensity) with price regulation. [50] Shaikh (2020) suggested that R&D investment would decrease by 7.96% in response to price control, compared to a non-price control environment. Hence, we assume R&D investment would be approximately 17.5% of revenue under a price setting environment, instead of the 19% of revenue that we apply in a non-price control setting.

We apply the change in R&D investment intensity from Shaikh (2020) and the reduction in R&D investment in a price control environment (Sood et al. 2009) to the segment of the HIV market that could be placed under price control. From this, we estimate the loss of R&D investment in HIV medicine and estimate how many clinical trials would be foregone if prices were controlled. We are therefore assuming the same impact on all clinical trials, whether they are sponsored by the industry or not.

The impact of price setting policy on HIV clinical trials

As described above, we estimate that price control of the segment of HIV medicines as specified by the BBB Act would see all revenue from HIV medicines reduced between 16.8% and 17.2%. As a result of the revenue reduction, we estimate that R&D investment would decline by **21.6% to 22.0%** which would be associated with a loss of **537 to 551** HIV clinical trials initiated between 2022-2035. These results are bound by two key inputs, the anticipated R&D investment as a percentage of expected revenue, and the change in revenue expected from a price setting policy.[51]

One limitation of our study is that we assume that all HIV medicines eligible for price control under the BBB Act will be price controlled. In practice, given that the BBB Act will imply price control for only a subset of eligible drugs across Medicare Part B and Part D, it is unlikely that all HIV medicines eligible for price control, will be price controlled. To account for this reality, we implemented a sensitivity check which assumes that the drugs with the largest total spending on Part B and Part D would be impacted by the price negotiation.[52] Three HIV drugs appear on the list of top 50 drugs on Part B and Part D. Accordingly, we assume that three HIV drugs currently marketed will be price controlled. The sales of these three drugs are expected to account for approximately 50% of the entire HIV market between 2023-2029 but 66% of the segment we judged as potentially affected by BBB Act.[53] Assuming that price control would be applied to the three HIV drugs, we estimate that market revenue would drop

by a range of **10.5% to 10.9%**, leading to a loss of **341 to 349** HIV clinical trials initiated between 2022-2035.

Conclusions

It is notable that while there have been significant advances in HIV treatment and prevention and there are new therapies coming to market for HIV, there remains clear unmet need for transformative therapies, including a possible vaccine or cure. Investment in R&D for new treatments needs to continue. The science of a cure for HIV is early in development and will require substantial additional time and investment. A significant reduction in the size of the U.S. market will discourage private companies from making this investment.

In this paper, we have attempted to quantify how an expected reduction in HIV medicines' revenue under a price setting policy as defined by the BBB Act could affect investment in R&D and clinical trials for new medications or curative therapies using a simple model. We have chosen to estimate the impact on clinical trials to illustrate the potential implications of price control on patient access to innovation and find that reducing revenue from all medicines for HIV potentially eligible for centralized price setting will result in **537 to 551** fewer clinical trials between 2022-2035.[54] The implications for drug development could be significant, given that currently around 610 HIV clinical trials are ongoing.[55]

However, we recognize that there are many impacts of price control that we have not quantified. A reduction in clinical trials would reduce the scientific knowledge and understanding of the disease accrued from clinical trials and could have a knock-on impact on basic research. In addition, we have not accounted for the potential multiplier effects from foregone clinical trials, such as the loss of university and academic center employment and income of those involved in research. We also do not consider the potential cost implications associated with clinical needs that otherwise may have been addressed but for the foregone clinical research because of the price setting associated with the BBB Act.

Ultimately the impact of reduced innovation is on patients. It has been estimated that HIV medicines have generated far more value to society, roughly $1.4 trillion between 1980 and 2000, than their cost which is roughly 5% of that benefit.[56] Introducing price setting policies for medicines for any disease, but particularly for a life-threatening disease such as HIV, deserves careful consideration.

[1] Clinicaltrials.gov, search for HIV in “Conditions”, U.S. for “Locations”, Active, recruiting or currently enroll for “Status”, accessed in November 2021, https://clinicaltrials.gov/ct2/results?cond=Hiv&term=&cntry=US&state=&city=&dist=&recrs=a&recrs=d&recrs=f.

[2] Lower Costs, More Cures Act, H.R.19.

[3] Lower Drug Costs Now Act, H.R.3.

[4] Build Back Better Act, H.R.5376.

[5] Build Back Better Act - Rules Committee Print 117-18 Section-By-Section. Available at: https://rules.house.gov/sites/democrats.rules.house.gov/files/Section_by_Section_BBB_RCP117-18_.pdf.

[6] “Government scorekeepers likely underestimate the impact of lower drug costs now act (h.r.3) on investment in innovative medicines May 2021,” https://www.crai.com/insights-events/publications/government-scorekeepers-likely-underestimate-the-impact-of-lower-drug-costs-now-act-h-r-3-on-investment-in-innovative-medicines/.

[7] Issue Brief: The Evidence Base on The Impact of Price settings on Medical Innovation by Tomas J. Philipson Troy Durie September 2021, https://bfi.uchicago.edu/wp-content/uploads/2021/09/BFI_WP_2021-108.pdf.

[8] White House Counsel of Economic Advisors Report posted on Energy and Commerce Committee Republicans website, report issued in 2019, https://republicans-energycommerce.house.gov/news/in-the-news/100-fewer-lifesaving-drugs/.

[9] Human immunodeficiency virus (“HIV”) is a virus that attacks the body’s immune system. If the HIV virus is not adequately suppressed HIV progresses into acquired immunodeficiency syndrome (“AIDS”).

[10] M. Blume-Kohout and N Sood. Market size and innovation: effects of Medicare Part D on pharmaceutical research and development. Journal of Public Economics. 27 May 2011.

[11] Medicare Prescription Drug Benefit Manual. Chapter 6 – Part D Drugs and Formulary Requirements (Rev. 18, January 2016), https://www.cms.gov/Medicare/Prescription-Drug-Coverage/PrescriptionDrugCovContra/Downloads/Part-D-Benefits-Manual-Chapter-6.pdf.

[12] Medicare Advantage and Part D Drug Pricing Final Rule (CMS-4180-F), https://www.cms.gov/newsroom/fact-sheets/medicare-advantage-and-part-d-drug-pricing-final-rule-cms-4180-f.

[13] 2012 Medicare Trustee Report, Table V.E2., p.229; See: CMS Office of the Actuary Memos, “Release of Part D National Average Monthly Bid Amount.” The annual CMS/OACT memos for 2006-2020 are available at https://www.cms.gov/files/document/july-29-2020-parts-c-d-announcement.pdf.

[14] Government Accountability Office. “Use of Pharmacy Benefit Managers and Efforts to Manage Drug Expenditures and Utilization.” July 2019, https://www.gao.gov/assets/710/700259.pdf.

[15] “HIV and AIDS Timeline,” CDC, https://npin.cdc.gov/pages/hiv-and-aids-timeline#1980.

[16] "HIV in the United States and Dependent Areas," CDC, https://www.cdc.gov/hiv/statistics/overview/ataglance.html.

[17] "The HIV/AIDS Epidemic in the United States: The Basics," KFF, https://www.kff.org/hivaids/fact-sheet/the-hivaids-epidemic-in-the-united-states-the-basics/.

[18] "HIV-Related Death Rate in U.S. Fell by Half From 2010 to 2017," CDC, https://www.cdc.gov/nchhstp/newsroom/2020/hiv-related-death-rate-press-release.html.

[19] "About HIV," CDC, https://www.cdc.gov/hiv/basics/whatishiv.html.

[20] "The science is clear, with HIV, undetectable equals untransmittable," National Institution of Health, January 10, 2019, https://www.nih.gov/news-events/news-releases/science-clear-hiv-undetectable-equals-untransmittable.

[21] Marcus JL, Leyden WA, Alexeeff SE, et al., "Comparison of Overall and Comorbidity-Free Life Expectancy Between Insured Adults With and Without HIV Infection, 2000-2016," JAMA Netw Open, June 2020, 2020;3(6):e207954, https://jamanetwork.com/journals/jamanetworkopen/article-abstract/2767138.

[22] Sertkaya A, Wong HH, Jessup A, Beleche T. Key cost drivers of pharmaceutical clinical trials in the United States. Clin Trials. 2016 Apr;13(2):117-26. doi: 10.1177/1740774515625964. Epub 2016 Feb 8. PMID: 26908540., https://journals.sagepub.com/doi/abs/10.1177/1740774515625964.

[23] "Clinical Development Success Rates 2006 – 2015," Biotechnology Innovation Organization, June 2016, pp. 7, 9.

[24] Search of clinicaltrials.gov, search term HIV Acquired Immunodeficiency Syndrome and Human Immunodeficiency Virus trials conducted in the United States, accessed 10/2021.

[25] NIH HIVinfo FDA approval of HIV medicines timelines https://hivinfo.nih.gov/understanding-hiv/infographics/fda-approval-hiv-medicines.

[26] European Pharmaceutical Review, New report shows impressive innovation in HIV first-in-class pipeline, https://www.europeanpharmaceuticalreview.com/news/111195/new-report-shows-impressive-innovation-in-hiv-first-in-class-pipeline/.

[27] Kauf, T. L., Davis, K. L., Earnshaw, S. R., & Davis, E. A. (2012). Spillover adherence effects of fixed-dose combination HIV therapy. Patient preference and adherence, 6, 155–164. https://doi.org/10.2147/PPA.S28482.

[28] 2020 Drug Trials Snapshots FDA, and "ViiV Healthcare announces U.S. FDA approval for Rukobia (fostemsavir), a first-in-class treatment for HIV in adults with few treatment options available," ViiV Healthcare, https://viivhealthcare.com/hiv-news-and-media/news/press-releases/2020/july/viiv-healthcare-announces-us-fda-approval-for-rukobia/ ("ViiV Press Release").

[29] ViiV Press Release.

[30] Clinicaltrials.gov, https://clinicaltrials.gov/ct2/show/NCT04150068.

[31] Rosenberg, Jaime, “Gilead Reports Positive Results for Lenacapavir, Semiannual HIV Treatment,” Managed Healthcare Executive, August 2021, https://www.managedhealthcareexecutive.com/view/gilead-reports-positive-results-for-lenacapavir-semiannual-hiv-treatment.

[32] “HIV: First-in-class Therapies Target Major Unmet Needs Including Drug Resistance and Latency Reversal,” Global data, December 2019, p.6.

[33] “A Safety, Tolerability and Immunogenicity Study of 2 Different Regimens of Tetravalent AD26.Mos4.HIV Prime Followed by Boost with Tetravalent ad26.mos.4.HIV along with Either Clade C gp140 plus Adjuvant or with a Combination of Mosaic and Clade C gp140 plus Adjuvant in Healthy HIV Uninfected Adults,” ClinicalTrials.gov, https://clinicaltrials.gov/ct2/show/NCT02935686?term=HPX2003&rank=1.

[34] Rosenberg, Jaime, “One HIV Vaccine Fails While a First-of-its-Kind mRNA Vaccine Trial is Set to Begin,” Managed Healthcare Executive, September 2021, https://www.managedhealthcareexecutive.com/view/one-hiv-vaccine-fails-while-a-first-of-its-kind-mrna-vaccine-trial-is-set-to-begin.

[35] Clinicaltrials.gov, search terms HIV and cure, included trials recruiting in the U.S. from 2015 to 2021.

[36] ASPE (2014) Examination of Clinical Trial Costs and Barriers for Drug Development, https://aspe.hhs.gov/reports/examination-clinical-trial-costs-barriers-drug-development-0.

[37] Goldman, D. and Lakdawalla, D. (2018) The Global Burden of Medical Innovation. USC Schaeffer.

[38] Issue Brief: The Evidence Base on The Impact of Price settings on Medical Innovation by Tomas J. Philipson Troy Durie September 2021, https://bfi.uchicago.edu/wp-content/uploads/2021/09/BFI_WP_2021-108.pdf.

[39] “HIV Therapeutics: Global Drug Forecast and Market Analysis to 2029 - Forecast Update," GlobalData, August 2021, "U.S. forecast".

[40] Assuming the sales trend and market behavior resume same during 2030-2035 comparing 2021-2029.

[41] Smaller companies and earlier stage biotech often spend far more than their revenue on R&D and there is broad variability between biopharma companies. Companies with a large generics portfolio for example spend a lower percentage on R&D.

[42] "Research and Development in the Pharmaceutical Industry," Congressional Budget Office, April 2021 Figure 1.

[43] Historical sales for HIV, retrieved from Evaluate Pharma. Again, 19% of the historical sales were assumed invested in R&D.

[44] “HIV,” Clinicaltrials.gov, retrieved in October 2021.

[45] "NHE Fact Sheet," https://www.cms.gov/Research-Statistics-Data-and-Systems/Statistics-Trends-and-Reports/NationalHealthExpendData/NHE-Fact-Sheet#:~:text=Projected%20NHE%2C%202019%2D2028%3A&text=Price%20growth%20for%20medical%20goods,growth%20in%20health%20sector%20wages.

[46] This includes industry and non-industry sponsored trials.

[47] Sood, Neeraj, et al., "The effect of regulation on pharmaceutical revenues: experience in nineteen countries," Health Aff (Millwood), 28:1, 2009, p. 9, Exhibit 7.

[48] We eliminate 2021 assuming the policy would be implemented in 2022.

[49] Sood finds Effect of price controls in years 1–3 after introduction −0.203 (0.041)***, in years 4–6 after introduction −0.179 (0.042)*** and in 6 years after introduction −0.239 (0.043)***

[50] Shaikh, Mujaheed et al., "Revisiting the Relationship Between Price Regulation and Pharmaceutical R&D Investment," Applied Health Economics and Health Policy, July 2020, Table 2.

[51] Our model is available upon request.

[52] Per total spending in 2019, "Medicare Part D Drug Spending Dashboard & Data," CMS.gov, https://www.cms.gov/Research-Statistics-Data-and-Systems/Statistics-Trends-and-Reports/Information-on-Prescription-Drugs/MedicarePartD; "Medicare Part D Drug Spending Dashboard & Data," CMS.gov, https://www.cms.gov/Research-Statistics-Data-and-Systems/Statistics-Trends-and-Reports/Information-on-Prescription-Drugs/MedicarePartB.

[53] "HIV Therapeutics: Global Drug Forecast and Market Analysis to 2029 - Forecast Update," GlobalData, August 2021, "US forecast". See also, "Medicare Part D Drug Spending Dashboard & Data," CMS.gov, https://www.cms.gov/Research-Statistics-Data-and-Systems/Statistics-Trends-and-Reports/Information-on-Prescription-Drugs/MedicarePartD.

[54] We likely underestimate the impact of price controls on HIV clinical trials since our approach relies on industry averages of the relationship of R&D investment to revenue applied to the anticipated revenue from HIV/AIDS.

[55] Clinicaltrials.gov, search for HIV in "Conditions", U.S. for "Locations", Active, recruiting or currently enroll for "Status", accessed in November 2021, https://clinicaltrials.gov/ct2/results?cond=Hiv&term=&cntry=US&state=&city=&dist=&recrs=a&recrs=d&recrs=f.

[56] Philipson, Tomas J and Jena, Anupam B. "Who Benefits from New Medical Technologies? Estimates of Consumer and Producer Surpluses for HIV/AIDS Drugs" Forum for Health Economics & Policy, vol. 9, no. 2, 2006. https://doi.org/10.2202/1558-9544.1005.