Limitations of CBO’s Simulation Model of New Drug Development as a Tool for Policymakers
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Executive Summary

In recent years, US policymakers have been considering reforms to reduce drug spending, including allowing the government to directly set prices for branded medicines. Such policies would reduce global pharmaceutical revenues, leading to a reduction in research and development (R&D) expenditure and ultimately to lower levels of innovation. To support policymakers in evaluating the impact of such proposals, the Congressional Budget Office (CBO) has developed models to quantify the loss in pharmaceutical industry revenues and the reduction in the number of new drugs expected to reach the US market.

To date, CBO has taken two different approaches to estimating the impact of pharmaceutical pricing policies on new drug development. The first approach was to estimate a top-down, industry-wide relationship between revenues and new drug development based on historical estimates from the empirical literature (CBO, 2019). Second, in a subsequent working paper (CBO, 2021a), CBO attempted to model the investment decision-making process of a representative pharmaceutical company from the “bottom up” in a product-level simulation.

CBO has utilised a slightly modified version of the second approach to estimate the impact of the drug pricing provisions in the Build Back Better Act (BBBA) – a bill recently passed by the US House of Representatives that would allow the government to set prices for select drugs (CBO, 2021b). This OHE report evaluates CBO’s simulation model of new drug development and assesses whether this methodology provides policymakers with a way of accurately estimating the impact of lower US drug prices on future pharmaceutical innovation.

We conclude that while the model is novel and has academic merit, it is too limited to guide policymaking as it inadequately represents the reality of investment in new drug development. Furthermore, the estimates produced by the model are subject to considerable uncertainty and policymakers should exercise caution in relying on these findings for evaluating the potential impact of real-world policy changes.

The key limitations of the CBO simulation analysis

- The model makes the unrealistic assumption that companies make investment decisions with just the single product in mind rather than its entire drug development portfolio
- The model applies an oversimplified decision rule which states that any positive expected return on investment is sufficient to incentivise clinical development, regardless of magnitude
- The model does not reflect that pharmaceutical companies differ in characteristics such as size and development costs which influence R&D investment decision making
- Expected drug prices and costs of clinical development are assumed to have no impact on preclinical development
- Signals about a drug candidate’s likelihood of success are unrealistically assumed to be independent across phases of clinical development
- The significant uncertainty around the estimated impacts mean policymakers should exercise caution in applying them
- Innovation is measured by the number of new drugs coming to market, but it is the value not volume of innovation that ultimately matters
While policies that reduce drug spending by allowing the government to set prices may initially sound attractive, a focus on poorly targeted short-term savings could have major adverse consequences for patients in the future by causing an immediate decline in R&D spending, resulting in fewer new drugs coming onto the market in subsequent decades.

Two bills recently passed by the US House of Representatives would require the government to directly regulate the prices of certain prescription drugs. In December 2019, the House approved the Lower Drug Prices Now Act (H.R. 3), which would cap the prices of many high-expenditure prescription drugs based on prices in other countries. The FY 2022 reconciliation package, the Build Back Better Act (BBBA), on the other hand, which passed the House in November 2021, would impose government-set ceiling prices for certain brand medicines covered by Medicare, amongst other drug pricing provisions. Both bills would require manufacturers to accept the government’s prices or face an excise tax of up to 95% of the medicine’s total sales.

Prior to the passage of H.R. 3, the Congressional Budget Office (CBO) was asked to estimate the likely effects of the policy on federal spending and pharmaceutical innovation. A December 2019 report by CBO (CBO, 2019) found that H.R. 3 would reduce direct federal spending by $456 billion over the period 2020-29 and result in a 19% drop in the present discounted value of worldwide pharmaceutical revenues.

Despite H.R. 3’s unprecedented impact on the world’s largest pharmaceutical market, CBO estimated that only eight fewer new drugs would be approved by the Food & Drug Administration (FDA) over the first decade of the policy (2020-2029), with up to 30 further new medicines lost over the subsequent ten years (CBO, 2019). This is equivalent to a 2.7% reduction in annual drug approvals in the first decade and a 10% reduction in the second decade. These estimates are surprisingly low given the magnitude of the policy, calling into question the methods and data behind the analysis.

CBO had attempted a highly complex task in predicting the long-term impact of H.R. 3, and academic economists and industry analysts concurred that their analysis was hampered by substantial uncertainty surrounding the key parameters, especially the response of innovation to expected revenue and the impact of the policy on expected revenue (OHE, 2021a). Whereas CBO’s initial analysis of H.R. 3 drew heavily on published literature to estimate the relationship between industry revenues and new drug development, CBO ultimately abandoned this methodology. In August 2021, CBO released a working paper (CBO, 2021a) describing an updated approach to estimating the impact of drug pricing policies likely to affect pharmaceutical revenues and development of new drugs. Subsequent estimates, including CBO’s analysis of the BBBA (CBO, 2021b), would utilise this new methodology.
2 A new method for estimating the impact of drug pricing policies on pharmaceutical innovation

Motivation for CBO’s simulation model

Earlier analysis by OHE and others such as Charles Rivers Associates (2021) have identified several challenges with CBO’s original approach to estimating the impact of H.R. 3 on pharmaceutical innovation. In August 2021, CBO released a working paper describing an alternative methodology – a general simulation model that can be used to evaluate any policy which alters expected returns (e.g., any policy reducing drug prices) or R&D costs (CBO, 2021a). Rather than relying on estimates of the elasticity of innovation from the literature, this new approach attempts to model the investment decision-making process of a hypothetical pharmaceutical company from the “bottom up” to simulate the relationship between expected net revenues and new drug development.

In November 2021, CBO used this simulation approach to estimate the impact of the drug pricing provisions of the BBBA (CBO, 2021b). They estimate that the bill would reduce the number of new drugs introduced to the US market by only 0.7% between 2022 and 2051. This is based on their expectation that 1,300 new drugs would come to market over this period under current law. The policy would take time to have its full effect. CBO estimates that only one fewer drug would come to market in decade one (2022-31), four fewer in decade two (2032-41), and five fewer in decade three (2042-2051). CBO acknowledges that these estimates are subject to uncertainty.

The CBO simulation model is a novel approach and may have academic merit. However, as the model is intended to be used to inform policymaking, it is critical that it provides as accurate a reflection of the real world as is practically possible, i.e., that it is of policy relevance rather than merely academic relevance. It must also be transparent in terms of its methodology, inputs, and assumptions so that the analysis can be fully understood and evaluated by others.

The purpose of this critique is to evaluate the simulation model as a tool for policymakers, who will implicitly rely on its outputs if they accept the findings of CBO’s latest estimations of the impact of the BBBA.

Simulating the pharmaceutical investment decision

CBO describes a simplified economic model of new drug development, which contains several simplifying assumptions outlined below.

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1 Although not directly stated by CBO, these estimates imply that BBBA would reduce industry revenues by 2.6%. This is calculated by dividing the percentage long-run revenue impact by the long-run elasticity of innovation. CBO estimates that five fewer drugs will come to market by the third decade of the policy and the same thereafter from an assumed baseline of 1,300 drugs, a loss of 1.154%. Using the long-run elasticity of innovation of 0.45 taken from CBO’s white paper (2021a) implies a revenue reduction of 2.6% (1.154/0.45=2.564) although nowhere does CBO state their estimated revenue impact of BBBA or how they have arrived at the estimate.
Key assumptions behind the CBO simulation analysis

- There is a single pharmaceutical company that is assumed to be representative of the entire industry; there is no analysis of the impact of biopharmaceutical firm heterogeneity.
- The expected prices of new drugs and expected costs of clinical development have no impact on preclinical development.
- As long as the candidate is expected to make some positive profit, it will be progressed into the next stage of development – the level of expected profit has no impact.
- In the absence of any policy shock, the number of new drug approvals would be constant.

To estimate expected returns, CBO uses confidential Medicare Part D reimbursement data. To estimate expected development costs, CBO uses data from DiMasi et al. (2016), a study that surveyed pharmaceutical companies on their aggregate pharmaceutical R&D expenditures for the period 1990-2010. These development cost data are, therefore, relatively old for modelling the impacts of contemporary policy changes.

The mechanics of the simulation model work as follows. In each phase of clinical development (phase I, II or III), the firm receives a signal (information) about its drug’s likelihood of success, returns once on the market, and costs of development. It then decides whether it expects it to be profitable to progress the drug into the next stage of development. It will do so if and only if expected net returns are positive, i.e., above zero, conditional on the information it has received in that phase. The firm continues to do this through to phase III. The model incorporates uncertainty from the perspective of the representative decision-maker, and the decision-maker is also forward-looking.

Importantly, after calibration or estimation of the relevant parameters using the data described above, the model can be used to project the impact of any hypothetical pharmaceutical policy shock, which impacts expected costs or expected returns.

Evaluating drug pricing policies

In their August 2021 working paper (CBO, 2021a), CBO applied their new simulation model in the evaluation of a hypothetical policy that would reduce expected revenues by 15-25% for drugs in the top 20% of drugs ranked by expected returns. CBO uses the model to estimate the impact of this policy on the probabilities of a drug candidate moving into each phase of clinical development and ultimately on the number of new drugs approved by the FDA (assuming no subsequent policy shock).

The output of the policy evaluation is visualised in figures 1 and 2, where the black line gives the baseline time path for the number of new drugs entering the market in the absence of the policy, and the red line shows the same path but with the policy in place. The baseline is initially set equal to the average number of annual drug approvals by the FDA over the period 2015-2019, which hovers around 44 for the entirety of the 30-year policy evaluation window. The ultimate effect of the hypothetical policy is to reduce the number of new products by only two over the first decade, with a further 23 and 34 products lost over the second and third decades, respectively.

Clearly, it takes time for the policy to have its full effect on new drug approvals because drug development timelines are long, and the model assumes that all historical costs are sunk. Therefore, in each phase, the investment decision is based only on the development costs and revenues in the next phase.
Figure 1 shows the impact of the policy on entry into phase III from phase II for a set of drug candidates varying in expected costs and expected returns. The grey line gives the breakeven line, i.e., all points such that expected returns = expected costs. There is one black cross and one red dot per drug. A black cross gives the combination of expected returns and expected costs for a given drug in the absence of the policy, and the respective red dot gives the same combination but with the policy in place. If the drug is located to the left of the grey line, then expected net returns are positive, and the firm will move the candidate into phase III. If the drug is located to the right of the grey line, expected net returns are negative, and therefore, the drug will not enter phase III.

The impact of the policy on innovation is represented as the total number of drugs that cross the breakeven line. Although no exact quantification is possible, the policy affects only a small number of "marginal" high-expected-return products and firms, i.e., those which were already close to the expected breakeven line before the policy. While those candidates with low initial expected returns could be seen as marginal in financial terms, they could be transformative in terms of health impact.

Figure 2, on the other hand, shows the estimated impacts of the policy on the number of new drugs entering the market over time. The number of new drugs is initially set equal to the average for the period 2015-2019. The policy has essentially zero impact in the first decade, and the full impact of 8% is only realised from the third decade onwards.

This methodology differs from CBO’s original analysis of H.R. 3 (CBO, 2019), in which CBO used three industry average figures to estimate the policy’s impact: the estimated average impact of H.R. 3 on revenues, the estimated relationship between revenue and the number of new drugs developed (the elasticity of innovation), and a baseline estimate of the future annual number of new drugs in the absence of any policy change. All three of these estimates are subject to considerable uncertainty, and indeed all have been contested (OHE, 2021b-f).
The updated methodology put forth in CBO’s August 2021 working paper makes progress on one of these criticisms – estimating the elasticity of innovation. Instead of CBO selecting its own elasticity (0.53) informed by the historic academic economic literature and applying this at an industry level, the primary purpose of the new paper is to build a model from the level of the individual drug candidate and link the expected net returns and R&D decision-making throughout the clinical trial programme.

Prior to the passage of the BBBA in the House of Representatives, CBO used their simulation model to estimate the impact of the bill’s drug pricing provisions on new drug development, albeit with only very limited detail about methodology. Interestingly, accompanying the quantitative estimates, CBO notes that they have made technical improvements to the model, including incorporating preclinical decisions about new drug development. However, there is no detail about how exactly CBO addressed these specific issues. This is a feature that is missing in their August 2021 working paper and one which OHE criticised in the final blog of its five-part series on the impacts of drug pricing policies on pharmaceutical innovation. Aside from this, the model also allows for greater costs of capital for small companies and accelerated approvals for certain drugs. While these small technical changes are welcome improvements, they do not address the key limitations of CBO’s simulation model, or the broader concerns raised in this critique.

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2 The BBBA would allow the federal government to negotiate prices for high-cost drugs covered under Medicare Parts B and D, require inflation rebates to limit annual increases in drug prices in Medicare and private insurance, cap out-of-pocket spending for Medicare Part D enrollees and other Part D benefit design changes, limit cost sharing for insulin for people with Medicare and private insurance, eliminate cost sharing for adult vaccines covered under Part D, and repeal the Trump Administration’s drug rebate rule (KFF, 2021; Congress, 2021)
3 Limitations of the CBO simulation analysis as a tool for policy evaluation

The model makes the unrealistic assumption that investment decisions are based on a single product rather than a given company’s entire drug development portfolio.

A limitation of the original CBO analysis of H.R.3. is that it combined a single elasticity of innovation and predicted change in global pharmaceutical revenues to estimate an industry-level reduction in the number of new drugs coming to market. CBO’s new simulation model goes to the other extreme and attempts to model investment decision-making at the individual product level.

However, this alternative approach is not realistic, as pharmaceutical companies and private equity investors do not make decisions on individual products in a vacuum but rather within the broader context of a portfolio of R&D projects. This was echoed in recent interviews OHE conducted with biopharmaceutical investors (OHE, 2021a). Several individuals with experience making R&D investment decisions within large pharmaceutical companies emphasised the importance of conducting a broad portfolio analysis in addition to product-specific analysis. The expected returns across the portfolio are what influences decision-making in a “blockbuster” model of product innovation like biopharmaceuticals. Investment decisions are made within a budget constraint based upon multi-criteria analysis to optimise the expected performance of a portfolio of assets.

While CBO’s assumption of product independence simplifies the model and makes it tractable, it does not reflect the reality that investors make decisions to maximize returns across a portfolio of pipeline investments. Companies that can afford to do so will typically have multiple drug candidates in their pipeline to increase the probability of producing at least one highly successful and profitable product (a blockbuster). In practice, sharply reducing returns on a large share of all commercially successful drugs will sharply reduce returns for the entire portfolio, making it less able to meet return thresholds and attract high risk high reward investment.

The model applies an oversimplified decision rule which states that any positive expected return on investment is sufficient to incentivise clinical development, regardless of magnitude.

A crude and almost certainly erroneous assumption is that a drug candidate will be advanced into the next stage of clinical development (e.g., from phase II to phase III) if and only if expected returns exceed expected costs, i.e., if expected net returns are above zero. We refer to this as the decision rule, defined as the mapping from observations of expected development costs and returns into a decision about whether to progress the drug candidate into the next phase of development. This implies that the level of (positive) net expected returns is irrelevant. That is, CBO assumes that two drugs with expected net returns of 0.01% and 15% are equally likely to advance into the next stage of clinical development.
This may make the model tractable, but it does not accord with real-world experience where expected returns are required to be a multiple of investment costs, partly to hedge against future uncertainty in achieving clinical and commercial success. Our findings from recent interviews with industry decision-makers (OHE, 2021a) indicate that while thresholds for expected returns are used, these are typically not prescriptive, and committees also consider a range of other factors, such as unmet need and the company’s historical areas of success, as well as expectations for the rest of the portfolio. Aside from the level of expected net returns, some investors require that their initial R&D investment will be recovered within a set timeframe to enable this capital to be redeployed. This suggests that projects with lower expected net returns may be preferred over projects which will only offer a positive return on investment after many years.

Decision rules also vary across the different phases of clinical development. In the early phases, sophisticated financial and commercial analysis is less important than broader analysis relating to patient populations and level of unmet need. It is on the precipice of phase III that investors typically want to see detailed financial analysis, and thresholds for expected returns may be used. Although commercial considerations may become important earlier in the development timeframe under accelerated approval mechanisms, the factors which determine whether an asset progresses to the next phase of development typically differ across the different stages and are not narrowly commercially focused as the CBO model requires.

The model does not reflect that pharmaceutical companies differ in characteristics such as size and development costs which influence R&D investment decisions

CBO’s simulation model only considers a “representative” pharmaceutical company. In reality, biopharmaceutical companies are not homogeneous and differ across many dimensions that may have important implications for R&D investment decisions. One important dimension is size. Due to economies of scale (average costs falling as a company gets bigger), size and development costs may be negatively correlated. A smaller firm would find it more costly to develop the same drug because they must implement more processes and devote a higher share of their budgets to the development. Development costs and timelines may also depend on the company’s years of experience in a disease area or in conducting trials.

Another important dimension is the source of financing. In recent years, there has been a trend of increased innovation generated by smaller, venture-capital-based companies. This has many implications, one being that small biotech companies that rely on external investors – who expect a higher return on investment than is needed for traditional in-house financing by large companies – would find it more difficult to receive funding. In the CBO model, a drug candidate with positive expected net returns, no matter how small, will always go ahead into the next phase of development. However, externally funded companies would likely demand higher expected returns than assumed by CBO.

There are many other limitations in assuming homogeneity of firms within the theoretical model presented in the CBO working paper. Firstly, CBO only considers “in-house” drug development. However, in practice, a large share of innovation is produced by small biotech firms, and the drug candidates are then licensed in and commercialised by larger pharmaceutical companies. CBO’s analysis completely misses this important feature of the innovation supply chain. The representative drug developer is solely responsible for progressing (or not) their drug candidate through the different phases of clinical development. Again, this choice was likely made for tractability or because CBO is reliant on the DiMasi et al. (2016) cost data, which are also based on “in-house” development.
Heterogeneity is a key ingredient that is missing in the CBO simulation model and is further evidence that CBO’s analysis fails to represent the reality of pharmaceutical investment decisions.

**Expected drug prices and costs of clinical development are assumed to have no impact on preclinical development**

A potentially major assumption in the CBO simulation model is that expected development costs and expected market size have no effect whatsoever on the extent of preclinical development and therefore have no effect on the size of the pool of assets companies can take into clinical development. As CBO claims, “The model takes preclinical decision-making as given - that is, outside the model”. However, it is highly unrealistic to assume that preclinical drug development is completely independent of expected clinical development costs and market size. Preclinical development is a substantial investment that is made after the potentially less cost- and revenue-sensitive drug discovery phase involving basic research and in vivo efficacy studies. A policy that shrinks the upper tail of expected returns from new drug development is likely to have adverse effects on the extent of preclinical development, thereby shrinking the pool of potential phase I drug candidates (and hence potential phase II, III and marketable drugs).

This criticism of the simulation model is one that we outlined in our five-part blog series and one that CBO claim to have addressed in their recent analysis of the innovation impacts of the BBBA. They call this a “technical improvement” in their latest publication but are not transparent about their methodology, and results could be highly sensitive to this change. In the absence of further detail on how they have allowed for these effects, we cannot comment further.

**Signals about a drug candidate’s likelihood of success are unrealistically assumed to be independent across phases of clinical development**

As well as the assumed independence of drug candidates within a given company’s R&D portfolio, the model features another form of independence. In each phase, the firm receives a random signal about the drug candidate’s type (which captures its likelihood of success, returns once on the market, and costs of development). For modelling simplicity, these are assumed to be independent across phases. This means – for example – that in phase II, a certain drug candidate may have very high expected returns, but these could fall significantly upon entry into phase III. In general, the signal received in one phase has no bearing on the signal received in the subsequent phase – the signals are independent across phases – and these signals significantly affect firm decision making. CBO admits that this assumption is unrealistic, but again it simplifies the modelling and estimation.

**The significant uncertainty around the estimated impacts mean policymakers should exercise caution in applying them**

As CBO acknowledges, uncertainty exists around both the values of key inputs used in the simulation model (which were calibrated or estimated) and around the impact of the illustrative policy. In line with the degree of uncertainty surrounding the point estimates, policymakers should exercise caution in relying on these for the evaluation of potential real-world policy changes.
Figure 3 depicts the distributions surrounding CBO’s quantitative point estimates of the impact of the hypothetical policy on the probability of entering each phase. A more spread-out distribution indicates greater uncertainty. Clearly, there is significantly more uncertainty around the impacts on earlier stages of clinical development, as shown by the greater spread in the distribution of impacts for phases I and II compared to phase III. Although there is less uncertainty about the impact for phase III, the number of drug candidates in phase III depends on entry into previous phases. More uncertainty around the impacts of the policy on phase I and phase II entry probabilities imply more uncertainty around the impact of the policy on the number of phase III candidates. Policymakers should clearly understand that the findings produced by CBO’s simulation model are subject to considerable uncertainty, which could misrepresent the true impacts of the policy change.

For example, suppose there are 100 potential phase I drugs (successful in preclinical development). Suppose the probability of entering phase I is initially 50%, and it is the same for entering phase II from phase I. We would expect 50 drugs to move into phase I and, consequently, 25 drugs to move into phase II. Twenty-five drugs would therefore be available to potentially enter phase III. If each of these phase entry probabilities is reduced from 50% to 48%, then there would be a 7.8% reduction in the number of drugs available to potentially enter phase III clinical trials. This is despite only a two-percentage-point decrease in the entry probabilities for phase I and phase II. Therefore, small differences in the success rates in early clinical development can have a relatively large downstream and therefore impact the number of new drugs coming to market in a meaningful way.

Figure 4 shows the degree of uncertainty around the time paths of new drug approvals before and after the hypothetical policy. The figure shows that, on average, the policy reduces the number of drugs entering the market, but for any particular year, the same, significantly fewer, or significantly more drugs could enter the market under the policy compared to baseline. This uncertainty is inherent in the model and partially due to the randomness of the signals that the firm receives about its drug candidate.

**FIGURE 3: UNCERTAINTY IN THE ESTIMATED IMPACTS OF THE POLICY ON PHASE ENTRY PROBABILITIES**

**FIGURE 4: PATH OF NUMBERS OF NEW DRUGS ENTERING THE MARKET**

Source: CBO (2021a)
CBO uses numbers of new drugs coming to market as their only measure of innovation

CBO measures the impact of drug pricing policies on innovation by the change in the annual number of new drugs coming to the US market. In their initial analysis of H.R. 3 (CBO, 2019), CBO assumes that 300 new drugs are approved each decade, implying 30 per year on average. This baseline has been disputed. The 10-year average from 2011 was 41 (FDA, 2021), and the median number estimated by the experts we surveyed in our recent study was 45 (OHE, 2021a).

As well as understating the level of baseline new drug approvals, CBO uses a constant rate of new drug approvals over the 20-year policy horizon, but the experts surveyed in our study suggested that developments such as genomics will contribute to an increasing rate of new molecular entities (NMEs) approved each year. These enabling technologies give scientists a better understanding of the biology underpinning disease, making drug development much more targeted because scientists know the structure, sequence, and role of so many molecules involved in diseases. Relying on a static baseline is a simplifying but highly unrealistic assumption.

In their August 2021 working paper (CBO, 2021a), CBO increases their baseline value from 30 to 44 (the average annual number of drugs entering the market for 2015-2019), a 47% increase, without clear justification. Assuming the same elasticity of innovation (the same percentage change in new drug approvals for a given percentage change in expected revenues/returns), this increase in baseline new drugs should have increased CBO’s estimate of the impact of H.R. 3 in their original evaluation by 50%. However, there have been no updates or revisions to that original work incorporating this higher baseline approval figure. Despite the greater level of detail in the CBO simulation analysis, there clearly remains a lack of transparency around many aspects of the modelling exercise, including the assumed baseline number or trend in new drug approvals. This is important because the innovation impacts of a policy depend on what the evolution of new drug approvals would have been in the absence of the policy. Another point which requires greater transparency is whether “new drugs” refers to all new therapeutics including biologics, or just NMEs.

Moreover, while the simulation paper does not state this explicitly, it is likely that the baseline new drug figure of 44 does not include biologics. 44 is the average annual number of Center for Drug Evaluation and Research (CDER) approvals over the period 2015-19. This does not include biological approvals by the Center for Biologics Evaluation and Research (CBER). This should inform the interpretation of the CBO estimates and the lack of transparency on this point is a limitation in and of itself.

More importantly, the number of drugs is too simplistic a measure to capture the true impact of any policy on innovation. It is the value, not the volume of innovation, that is fundamental to patients and wider society. In health care, innovation should generate “value” by (1) improving patients’ quality and/or length of life and/or (2) reducing the costs of achieving these health objectives. A simple count of the annual number of new drugs coming to market is, at best, a correlate of meaningful health innovation. Changes in this number also tell us very little about the size or distribution of the impact on innovation across therapeutic areas/diseases/indications.

This may seem intuitive, but drugs generate different amounts of value. The total value a drug delivers depends on how many patients will benefit and how much health gain the drug generates for each patient. Some drugs target diseases with large patient populations; for example, the antiretroviral therapies developed in the 1990s to treat millions of HIV patients worldwide. Others, like orphan drugs, are more specialized and target rare diseases with small population sizes.
Innovation can also be classified by how much health gain is achieved for each patient, i.e., distinguishing between 'breakthrough' and incremental innovations. A new, lifesaving, curative therapies, such as those for treating a rare disease like spinal muscular atrophy, may provide enormous health gains for each patient. Another innovative treatment may help many patients by preventing unnecessary heart attacks and hospital stays, for example.

CBO does not explore the impact of fewer drugs coming to market on patient health, when clearly scientific advances are affecting both the number and distribution of the types of new medicines across disease areas. New drugs that CBO estimates will be lost may include the fifth treatment on the market for migraines or a cure for Alzheimer's. The former society may be willing to forgo, while the other would be a significant loss because it has so much value for patients and wider society.
4 Conclusion

Projecting the impact of drug pricing policies on future innovation is a challenging task. The simulation model developed by CBO is highly interesting, and the level of effort invested demonstrates the importance of the debate. However, the CBO model suffers from several serious flaws and fails to adequately represent the reality of biopharmaceutical investing. The simulation model may be of academic interest, but it cannot be reliably used to inform policymaking, at least not without significant qualifying information, including a better accounting of the uncertainty around the point estimates.

It is encouraging to see that CBO has addressed a small number of the shortcomings of the model in their evaluation of the BBBA. However, many criticisms remain. In particular, at the time of writing, it is not at all clear how CBO models the link between the BBBA and pharmaceutical revenues, and the impact on the number of new drugs entering the US market will be sensitive to the size of the revenue reduction assumed by the analysts.

Although it does not claim to, CBO’s model cannot project the impact of policy change on population health, which would be required for a complete and thorough policy evaluation. The CBO analysis is rich, but we still do not know what types of innovation would be lost due to the passage of the BBBA or similar policies, nor what the ultimate impact on the average length and quality of life will be for the US and global populations. Buxbaum et al. (2020) find that 35% of the US life expectancy gained over the period 1990-2015 was due to pharmaceuticals.

While policies that reduce drug spending by allowing the government to set prices may initially sound attractive, a focus on poorly targeted short-term savings could have major adverse consequences for patients in the future by causing an immediate decline in R&D spending, resulting in fewer new drugs coming onto the market in the next few decades. Policymakers should clearly understand that the estimates produced by CBO’s simulation model are subject to considerable uncertainty and should exercise caution in relying on these findings for evaluating the potential impact of real-world policy changes.
References


Appendix 1: Key criticisms of CBO’s evaluation of H.R. 3 (CBO, 2019)

1. **Important features of biopharmaceutical investing are ignored**: CBO does not closely model the real decision problems facing biopharmaceutical investors.

2. **Implausibly low elasticity of innovation used**: the value assumed by CBO is too low and as highlighted by experts, there is substantial uncertainty around its value.

3. **Upward trend in number and composition of NME approvals ignored**: CBO assumes a constant baseline number of NMEs approved but experts in our original study (OHE, 2021a) suggested that developments such as genomics will contribute to an acceleration in NME approvals.

4. **Wrong measure of innovation**: measuring innovation in terms of total NMEs is misleading as there is no link between NMEs and the health improvement lost.

5. **Uncertainty around parameters makes precise and reliable estimates hard to achieve**: the lack of consensus on parameter values in our expert elicitation exercise demonstrates this uncertainty, which should reduce confidence in the final point estimates.
About us
Founded in 1962 by the Association of the British Pharmaceutical Society, the Office of Health Economics (OHE) is not only the world’s oldest health economics research group, but also one of the most prestigious and influential.

OHE provides market-leading insights and in-depth analyses into health economics & health policy. Our pioneering work informs health care and pharmaceutical decision-making across the globe, enabling clients to think differently and to find alternative solutions to the industry’s most complex problems.

Our mission is to guide and inform the healthcare industry through today’s era of unprecedented change and evolution. We are dedicated to helping policy makers and the pharmaceutical industry make better decisions that ultimately benefit patients, the industry and society as a whole.

OHE. For better healthcare decisions.

Areas of expertise
- Evaluation of health care policy
- The economics of health care systems
- Health technology assessment (HTA) methodology and approaches
- HTA’s impact on decision making, health care spending and the delivery of care
- Pricing and reimbursement for biologics and pharmaceuticals, including value-based pricing, risk sharing and biosimilars market competition
- The costs of treating, or failing to treat, specific diseases and conditions
- Drivers of, and incentives for, the uptake of pharmaceuticals and prescription medicines
- Competition and incentives for improving the quality and efficiency of health care
- Incentives, disincentives, regulation and the costs of R&D for pharmaceuticals and innovation in medicine
- Capturing preferences using patient-reported outcomes measures (PROMs) and time trade-off (TTO) methodology
- Roles of the private and charity sectors in health care and research
- Health and health care statistics