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INSIGHTS FROM INDUSTRY
INTERVIEWS AND EXPERT ELICITATION

The Lower Drug Costs Now Act and Pharmaceutical Innovation

CONSULTING | EXECUTIVE SUMMARY
SEPTEMBER 2021

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OFFICE OF HEALTH ECONOMICS
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1 Background

The Elijah E. Cummings Lower Drug Costs Now Act (commonly referred to as H.R. 3) passed the US House of Representatives in December 2019 and was reintroduced by the House in May 2021. The bill would require manufacturers of high-earning drugs to "negotiate" prices with the Secretary of Health and Human Services (HHS) (who could also unilaterally set prices under some circumstances). The "maximum fair price" for an eligible drug – the price ceiling used in negotiations – would be based on international reference prices, and the negotiated prices would be available to insurers participating in Medicare Part D (the prescription drug programme), insurers in the commercial market, and other direct providers of prescription drugs.

When considering such a policy, it is important for policymakers to understand the likely benefits of the policy (in terms of expenditure savings) and the likely cost (in terms of innovation and ultimately health gains forgone). To inform the debate, the Congressional Budget Office (CBO) performed a quantitative analysis of the impact of the bill on Federal government expenditure and pharmaceutical research and development (R&D).

CBO estimates that the price negotiation provisions in H.R. 3 would lower direct spending by $456 billion over the period 2020-2029. However, on net, H.R. 3 would only lead to a $5 billion reduction in unified federal deficits over that period, mainly due to a significant increase in Medicare dental, vision, and hearing coverage under Title VI of H.R. 3. Against a current background of 30 new drugs approved by the FDA per year on average (a critical assumption), they estimate that the bill would lead to 8-15 fewer drugs developed in the first decade (2021-2030) of the policy and 30 fewer drugs (i.e., a 10% reduction) developed in the second decade (2030-2039). This is based on their estimate that H.R. 3 would reduce the present value of future global revenues from new drugs by 19 per cent.

Other analyses contest the CBO's findings on the impact of the policy on pharmaceutical innovation – the number of drugs forgone in the first two decades of the bill. CBO's estimates are particularly sensitive to three key assumptions: (i) the reduction in global revenue due to H.R. 3, (ii) the baseline number of drugs approved by the FDA annually, and (iii) the impact of a reduction in expected revenues/returns on the number of drugs approved, i.e., the elasticity of innovation.

The estimates of the elasticity of innovation from the academic literature cited by the original CBO study cover a wide range of values, demonstrating significant uncertainty. These estimates come from research with arguably limited relevance to an unprecedented policy shock such as H.R. 3. Dubois et al. (2015), for example, studied the response of new drugs *marketed* in a sample of 14 countries in the period 1997-2007. Acemoglu and Linn (2004), on the other hand, look at data from 1970-2000, so the most recent data points are 20 years prior to the date of policy implementation modelled in the CBO analysis.

To understand the precise channels through which a policy such as H.R. 3 would impact outcomes related to drug innovation and to uncover the magnitude of key parameters such as the elasticity of innovation, OHE completed two complementary workstreams on behalf of PhRMA. Firstly, a set of interviews were conducted with key decision-makers in the pharmaceutical, biotechnology, venture capital and private equity industries (industry interviews). The second workstream was a two-round Delphi expert elicitation exercise with a set of academic economists and industry analysts/consultants. The methods involved in these two workstreams are described here.

2 Methods

2.1 Company interviews

2.1.1 Aims

Semi-structured interviews were aimed at:

1. Understanding the processes behind significant investment decisions related to pharmaceutical research and development (R&D). This includes details about timelines, stakeholders, rules of thumb and quantitative thresholds.

2. Eliciting respondents' expectations about the likely impacts of policies such as H.R. 3 on pharmaceutical R&D inputs and outputs, including the size and composition of R&D budgets.

3. Gathering the most important information that policymakers and analysts *should* be considering when evaluating the total impact of H.R. 3.

2.1.2 Data collection

Figure 2 illustrates the structure of the questionnaire used to interview respondents. Each section covered one of the above three aims outlined above. The first section contained questions about the processes behind R&D investment decisions in normal times, i.e., in the absence of a significant policy shock such as H.R. 3. The second consisted of questions on the likely impacts of H.R. 3 on R&D inputs and outputs. The third section consisted of one open-ended question on the data, perspectives, and historical policy shocks that respondents recommend should be considered in policy analyses.

FIGURE 2: INDUSTRY INTERVIEW SECTIONS

Part I: Processes	Part II: Impacts of H.R. 3	Part III: Guidance for analysts/policymakers
Processes behind investment in new drug development • Overview • Timelines • Decision rules • Differences across therapeutic areas • How government policy factors into decision making	Behavioral responses to estimated price reductions in CBO analysis Expected impacts of H.R. 3 (as currently designed) on pipeline, R&D expenditure, composition of R&D portfolio, etc.	What information and perspectives should analysts and policymakers be considering to understand the total impacts of HR3?

In total, 11 sets of responses were gathered. Nine of these came from virtual one-hour interviews, and two sets of partial written responses were submitted by email. Five respondents were currently working or had significant recent experience in large pharmaceutical companies, three were senior members of biotechnology companies, and three worked in external investment companies (including venture capital and private equity). Eight of the companies represented were headquartered in the US, one in the UK, one in Japan and one in Switzerland. All the respondents had global perspectives.

2.1.3 Data analysis

Interviews were recorded, and transcripts were studied along with the written responses. Based on these text resources and internal debriefs, the most relevant areas of consensus and disagreement were identified. Desk research was then conducted to fully elucidate each of these key themes or insights before gathering precise extracts to support or qualify each.

2.2 Expert elicitation

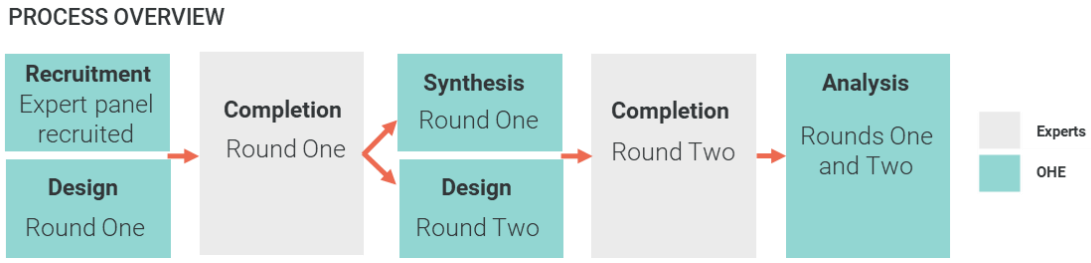
2.2.1 Aims

The main aim of this workstream was to elicit point estimates and confidence intervals for the key parameters used in the CBO analysis, including aggregate elasticities of drug innovation to expected revenues and elasticities stratified by shock size, company type and therapeutic area. The experts were also asked to provide a written rationale for each of their estimates. Both the anonymised numerical estimates and their rationales were shared with the full panel of experts prior to their second-round estimates.

2.2.2 Data collection

The methodology chosen for the expert elicitation exercise was a two-round Delphi survey. This consisted of two sequential survey rounds, where the second questionnaire included summaries of responses from round one. Figure 3 illustrates the process which the project sub-team followed.

FIGURE 3: EXPERT ELICITATION PROCESS



Each survey consisted of four sections:

Section 1: Estimates of key CBO model parameters
Section 2: Variation in elasticity of innovation estimates
Section 3: Review of CBO model main drivers
Section 4: Additional comments on the impact of H.R. 3 and the CBO analysis

Seven experts took part in the Delphi survey. Four were academic economists, and three were industry-oriented consultants or analysts. Five were based in the US and two in Europe.

2.2.3 Data analysis

Point estimates and confidence intervals across the two survey rounds were summarised visually, and the degree of convergence in point estimates (and any change in degrees of confidence) across the two rounds was examined.

3 Results

Six main insights emerged across the two workstreams.

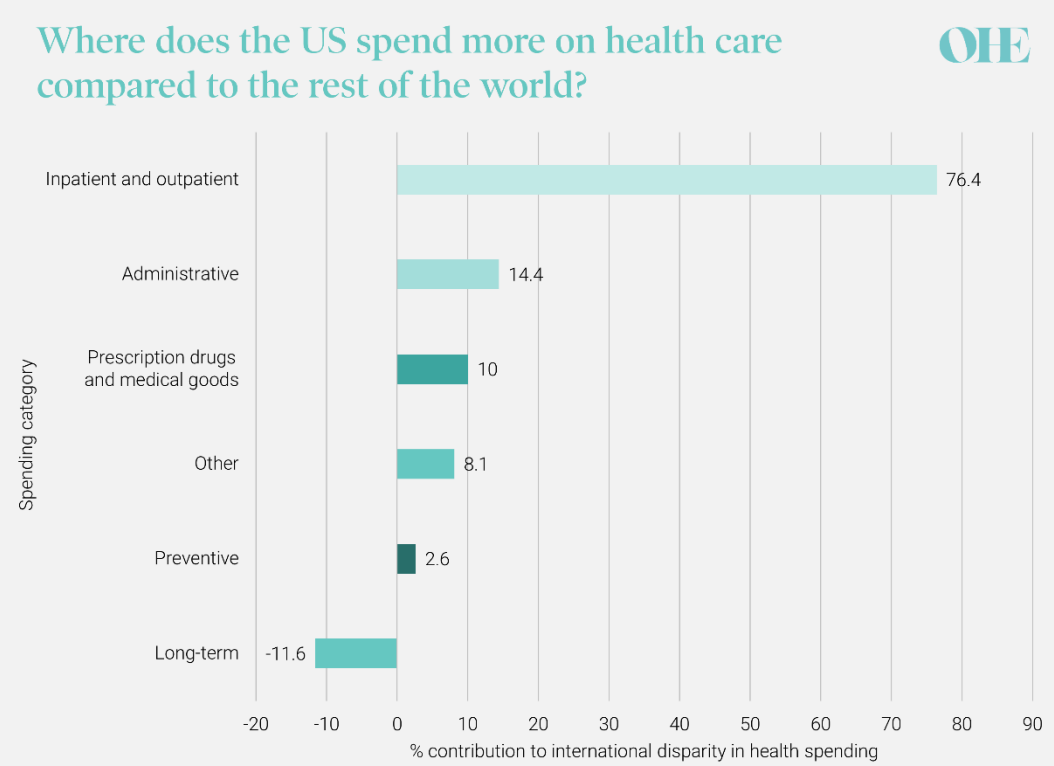
3.1 H.R. 3 is the wrong policy for the wrong problem

"… there's a huge contextual system piece that H.R. 3 doesn't actually address, and price is just one very small part of the puzzle" - industry interview respondent with significant experience in large US- and Europe-based pharmaceutical companies

Many respondents across the expert elicitation and industry interviews were vocal that H.R. 3 would not address the most important problems with the US healthcare system. The *right* problems that health reform should prioritise are high out-of-pocket costs, barriers to insurance, and addressing the cost of chronic disease and preventable use of health services. International reference pricing, which several respondents stressed would involve importing value-based pricing determinations from countries including the UK and Australia with different healthcare contexts, would not address this missing link. It would also have an important detrimental effect on patients globally by reducing expected revenues and hence disincentivising innovation in key therapeutic areas. Several respondents also stressed that the *right solution*, or at least one of them, is a reform of the insurance system. This process needs to be more focused on the health gains that innovative pharmaceuticals create, and this would require some form of homegrown health technology assessment.

Ultimately, H.R. 3 would not address the main causes of the disparity in overall health care spending between the US and other developed nations. As figure 1 shows, prescription drugs and medical goods contribute relatively little to the disparity in total healthcare spending between the US and other developed countries. Resources should be directed elsewhere if the government wishes to bring total healthcare spending in line with international peers.

FIGURE 1: CONTRIBUTIONS OF DIFFERENT HEALTH CATEGORIES TO DISPARITY IN PER CAPITA HEALTH SPENDING BETWEEN US AND INTERNATIONAL COMPARATORS
Notes: Attribution analysis for difference in per capita health spending between the US and comparable countries, by spending category, 2018. Original graph and data: What drives health spending in the U.S. compared to other countries – Peterson-KFF Health System



3.2 Companies would take measures to protect US revenue in response to H.R. 3

"If you can get $400,000 for a rare disease drug in the US and that pricing might be at risk by launching in Australia at a much lower price, the launch in Australia will be delayed at best" - industry interview respondent from the private equity industry

The experts and industry decision-makers believed that companies would attempt to minimise the impact of the policy by delaying new product launches in reference countries. By significantly delaying or completely avoiding launching in countries such as the UK and Australia, the company may avoid a low internationally referenced price in the dominant US market. Although companies would miss out on the ex-US revenues, the US market is typically dominant, and companies could always implement the option of raising US prices to recoup some of this revenue loss.

3.3 H.R. 3 is likely to reduce investment in pharmaceutical R&D by reducing expected revenues.

To the extent that the policy squeezes expected revenues and company R&D budgets, H.R. 3 would likely have a negative effect on the aggregate level of R&D expenditure. As one interview respondent suggested, this would simply be because the company has fewer dollars to invest in new drug development. Due to the length of drug development timelines, this will, in turn, lead to some reduction in the total number of new drug launches, as well as changes in the shares of different therapeutic areas and classes of innovation which we summarise in Section 3.4.

At a more granular level, fewer drug candidates are likely to meet the criteria to be funded as viable assets. Some R&D projects will not be started in the first place, and others may even be scrapped during clinical trials, as one interview respondent suggested. This is assuming that investment committees are constrained by similar criteria and decision rules under H.R. 3 as under the current policy environment as they decide whether to progress individual assets into each stage of development.

While there was agreement that significant R&D cuts would be unavoidable if faced with a sufficiently large persistent demand shock, there was a lack of consensus amongst interviewees regarding the responsiveness of drug development spending in comparison with other areas of business such as marketing.

Respondents from the venture capital and private equity industries emphasised that a policy such as H.R. 3 would significantly squeeze external funding for biotech companies, with one royalty-based private equity fund emphasising that with a version of H.R. 3 in place, investors would require higher shares of profits from commercial activities to compensate for the drop in company valuations.

3.4 Experts and interviewees did not reach a consensus on which therapeutic areas would be most affected by H.R. 3.

To the extent that H.R. 3 impacts investment decisions, some therapeutic areas are likely to be more adversely affected than others. There were two hypotheses advanced:

1. Follow-up treatments in areas with many existing therapy options would be lost partly because of the downward trend in overall willingness to pay for these therapies.

> ***"…one argument could say (sic) that if there was a more restrictive situation in the US, perhaps we get better drugs because companies don't waste their money on kind of minimal innovation."***
> - industry interview respondent with significant experience in US and European pharmaceutical companies

2. High-risk R&D might be lost. Therapeutic areas with high technical and regulatory uncertainty (e.g., neurology) would become less attractive if H.R. 3 reduces expected revenues and investors respond by shifting away from riskier investments.

In contrast to the first view, some respondents suggested that the policy would, in fact, lead to a shift towards not away from the aforementioned "minimal innovation". Higher-risk drug candidates (those with a lower probability of technical and regulatory success) are likely to become less attractive to investment committees, and as a result, there will be fewer transformational or breakthrough pharmaceutical innovations and relatively more follow-on drugs, an example of incremental innovation.

3.5 Experts agreed that the data/assumptions underpinning the CBO model were flawed.

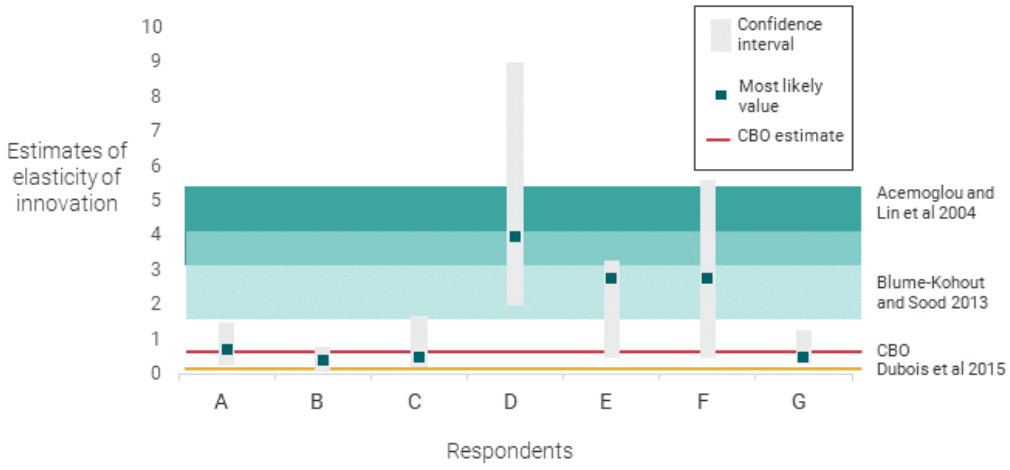
"Here is a place where I think that the CBO is really undercounting, there has been a marked surge in the number of drugs coming to market." – expert elicitation respondent (consultant/analyst)

There was recognition that the CBO had attempted a highly complex task in predicting the long-term impact of a policy like H.R. 3. The analysis is hampered by substantial uncertainty surrounding estimates of the key parameters, including the one characterising the relationship between prices, or industry revenues, and innovation. Experts point out how the uncertainty around both the response of innovation to expected revenue and the impact of the policy on expected revenue create compounded uncertainty which is very difficult to gauge. This situation could be interpreted as one with both ambiguity and compound risk. On top of standard risk aversion, decision-makers in various contexts have been found to be averse to these related but separate phenomena.

3.6 There is significant uncertainty around how to estimate the impact on innovation and, in particular, the relevance of historical estimates of key parameters

Experts were divided on whether the estimates of the magnitude of the relationship between revenue and the number of new medicines (i.e., the elasticity of innovation) from the literature are even applicable to the post-H.R. 3 context. Figure 4 shows the variation and uncertainty in aggregate elasticity estimates. Square icons indicate point estimates, and grey bars indicate confidence intervals.

FIGURE 4: FINAL (AGGREGATE) ELASTICITY ESTIMATES (EXPERT ELICITATION)



- Some academic experts believed that the underlying dynamics are the same, regardless of the size of the market shock under consideration, and therefore the CBO estimate of a 5.3% reduction in new molecular entities (NMEs) approved following a 10% reduction in market size was plausible.

- The more industry-oriented experts believed the elasticity would be substantially higher (>1) than the CBO estimate because the market shock was so unprecedentedly large that at the margin, dynamics would be disrupted, with the impact of H.R. 3 being so focused on US revenue.

Experts were also split on whether historical trends in the number of new medicines approved and marketed each year would continue in the future, even in the absence of H.R. 3. However, experts agreed that, given the trend of reduced patient populations targeted by each NME due to

technological progress in disease characterisation (e.g., genomics), a further decrease in their expected revenue due to the H.R. 3 policy might lead to a displacement of investment in them.

Given the high degree of uncertainty regarding the values of key parameters such as the elasticity of innovation and the relevance of historical data to an unprecedented policy such as H.R. 3, further research is required to understand its full impact on biopharmaceutical innovation.

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- 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

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