Congressional Budget Office
Nonpartisan Analysis for the U.S. Congress

CBO's Model of New Drug Development

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A Model of New Drug Development

CBO's model is:

- Intended to help the Congress understand the effect that legislative proposals would have on the development of new drugs
- Used to produce alternatives to the elasticity estimates reported in the literature that CBO can present along with its estimates of the budgetary cost of legislation

Potential policies that could be analyzed with the model include:

- Allowing the Secretary of Health and Human Services (HHS) to negotiate drug prices
- Placing pricing restrictions on drug manufacturers
- Increasing funding of preclinical drug development
- Reducing requirements for marketing approval
- Providing advanced market commitments
- Allowing easier entry for generic and biosimilar drugs

Background on Drug Price Negotiation

Under current law:

- The Secretary of HHS is not allowed to negotiate prices for drugs purchased by Medicare.
- Medicare Part D provides prescription drug coverage for seniors.
  - Prices are negotiated between manufacturers and insurers.
  - The federal government reimburses insurers.
- Medicare Part B covers provider services, including infused drugs such as chemotherapy.

Changes proposed under Build Back Better (November 2021):

- Prices would be negotiated for Medicare only; an inflation rebate would apply to drug purchases covered by Medicare and commercial insurers.
- Would apply only to drugs that have been on the market for many years.

CBO's previous finding: Allowing price negotiations would not, in and of itself, lead to lower prices.

See Congressional Budget Office, *Negotiation Over Drug Prices in Medicare* (May 2019), www.cbo.gov/publication/55270.

Modeling the Effects of Government Price Negotiations on Prescription Drugs

Changes proposed under H.R. 3, The Elijah E. Cummings Lower Drug Costs Now Act (2019–2020)

- Allow the HHS Secretary to negotiate drug prices for Medicare Part D.
- Price would be available to all parties in the U.S.
- Prices of 25 drugs with highest Medicare spending would be negotiated first.

CBO estimates that:

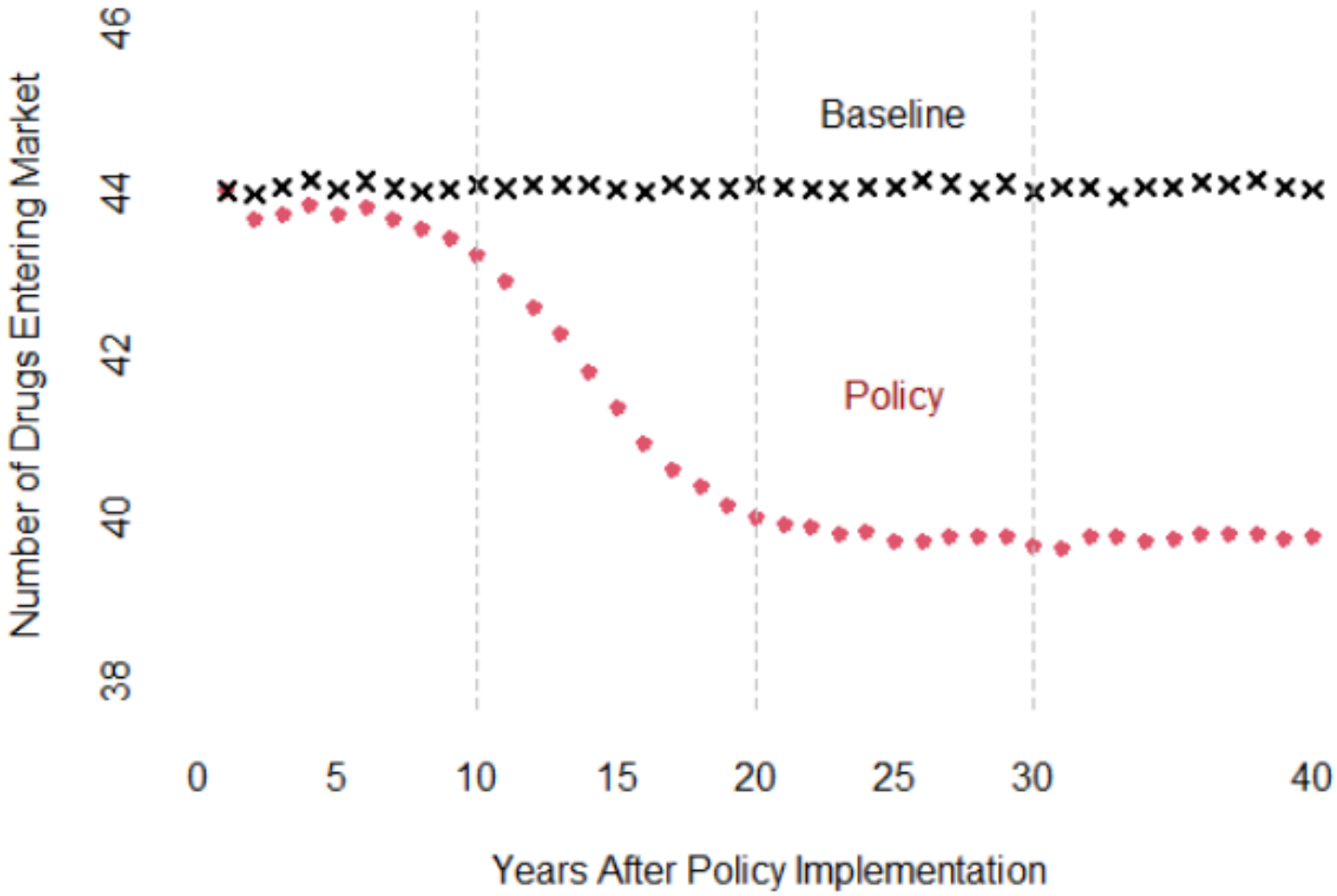
- New (expensive) drugs would be priced at 80% of the price that would have been set under current law.
- Global pharmaceutical revenues would be reduced by 19%.

Modeled policy specifications:

- A reduction in revenues for the top quintile of revenue distribution, increasing from 15% to 25% over the quintile.
- A 200 basis-point increase in financing costs associated with removing an estimated $900 billion from the industry.

See Congressional Budget Office, cost estimate for H.R. 3, Elijah E. Cummings Lower Drug Costs Now Act (December 10, 2019), www.cbo.gov/publication/55936.

Impact of Negotiation on Number of New Drugs Entering the Market



The policy is implemented in year zero, but the full difference is not reached until after year 20. The policy is associated with a long-run reduction of 10% in the number of new drugs.

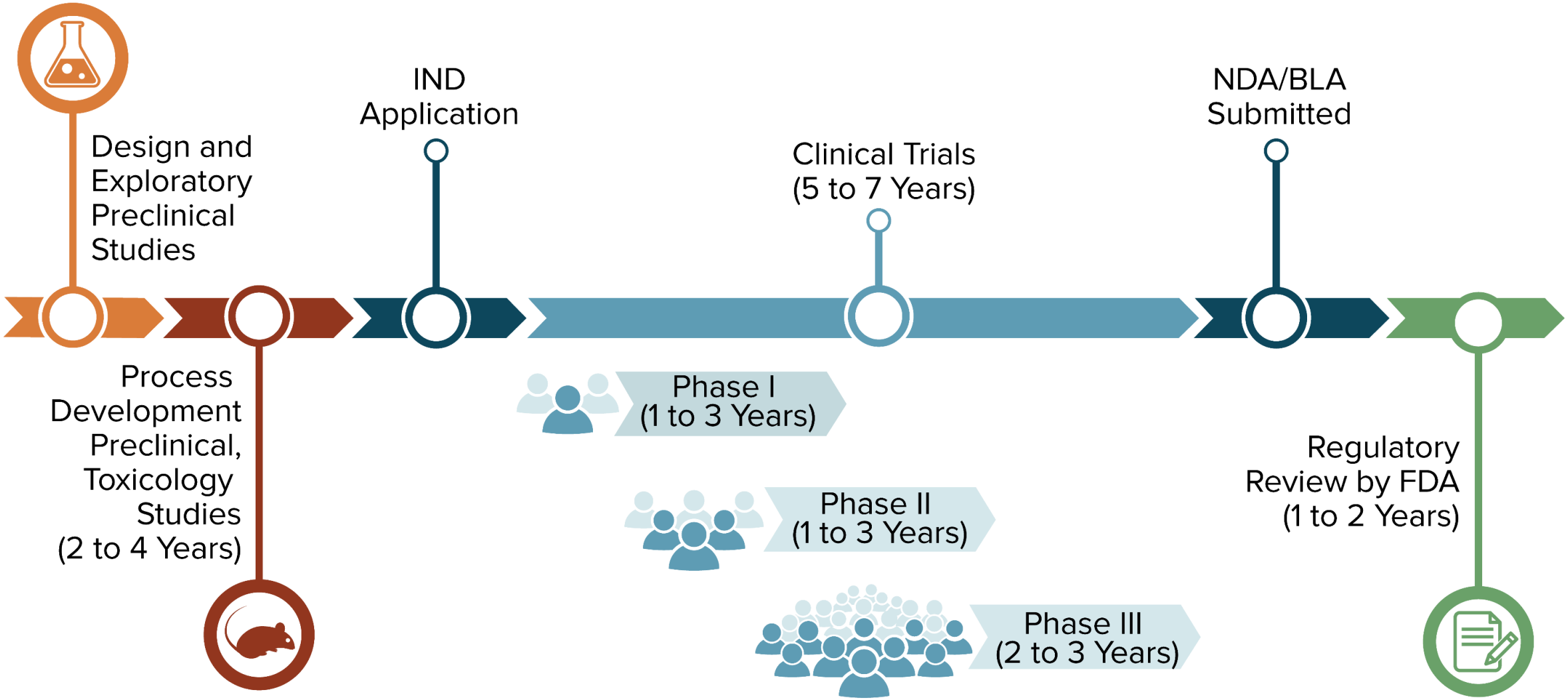
The number of new drugs in year zero is set at the average for 2015 to 2019.

The results differ from the results in the August 2021 working paper because of technical improvements to the model that now allow it to account for these three factors: the policy's effects on financing costs, its effects on decisions made during preclinical development, and an accelerated approval process.

See Christopher P. Adams, *CBO's Simulation Model of New Drug Development*, Working Paper 2021-09 (Congressional Budget Office, August 2021), www.cbo.gov/publication/57010.

Background

The Evaluation and Research Stages of the Drug Development Process



BLA = Biologics License Application; FDA = Food and Drug Administration; IND = Investigational New Drug; NDA = New Drug Application.

The Model

Model Overview

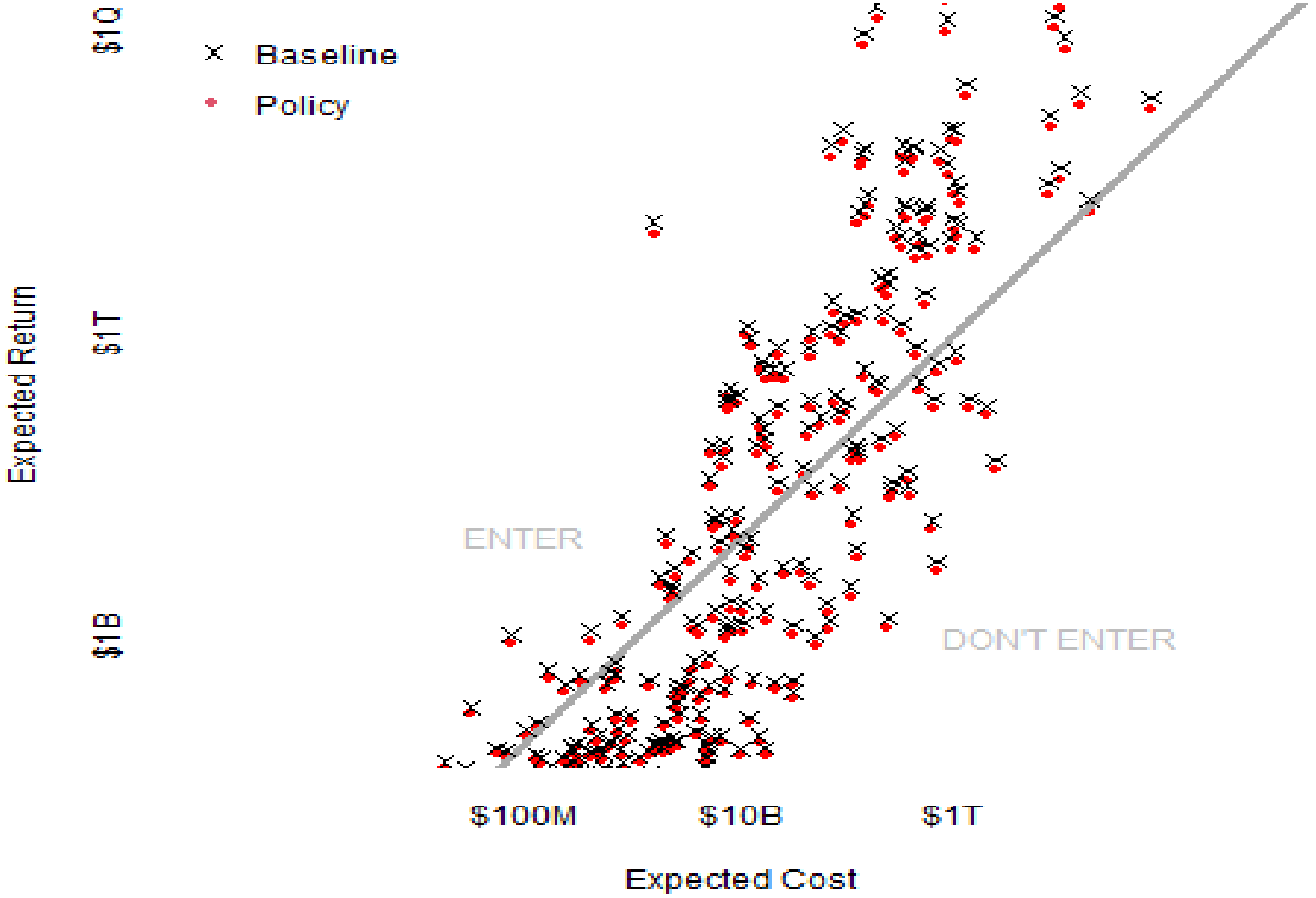
To bring a drug to market, the firm is assumed to have four decision points: phase 0 (preclinical), phase I, phase II, and phase III.

At each decision point, the firm observes expected costs and expected returns for its candidate drug. If expected returns are greater than expected costs, the firm chooses to enter the development stage.

The model works by drawing a large number of simulated drugs from the joint distribution of expected returns and expected costs. Note that the value of each draw is assumed to be independent across the decision points for the same drug candidate.

CBO estimates parameters of the distribution using data on net revenues and survey results on costs reported in the literature.

Joint Distribution of Expected Costs and Returns at Beginning of Phase III



The figure shows, in a log scale, the estimated joint distribution of expected returns and costs with the H.R. 3-like policy (red dots) and without the policy (X marks) for drugs entering phase III. Only drugs above the 40th percentile of the distribution of expected returns are included; for those drugs, the policy leads to a downward shift in expected returns (X mark to red dot). The gray line represents the break-even point. Simulated drugs above and to the left of the line have expected returns greater than expected costs and would enter phase III.

Estimates of Revenues

Estimates of Revenues

Use data on Medicare Part D spending by drug.

- Data from 2010 to 2018
- Net prices (include rebates paid by manufacturers)
- Aggregate NDC-level data up to “ingredient” level

Regress revenues on “time on market.”

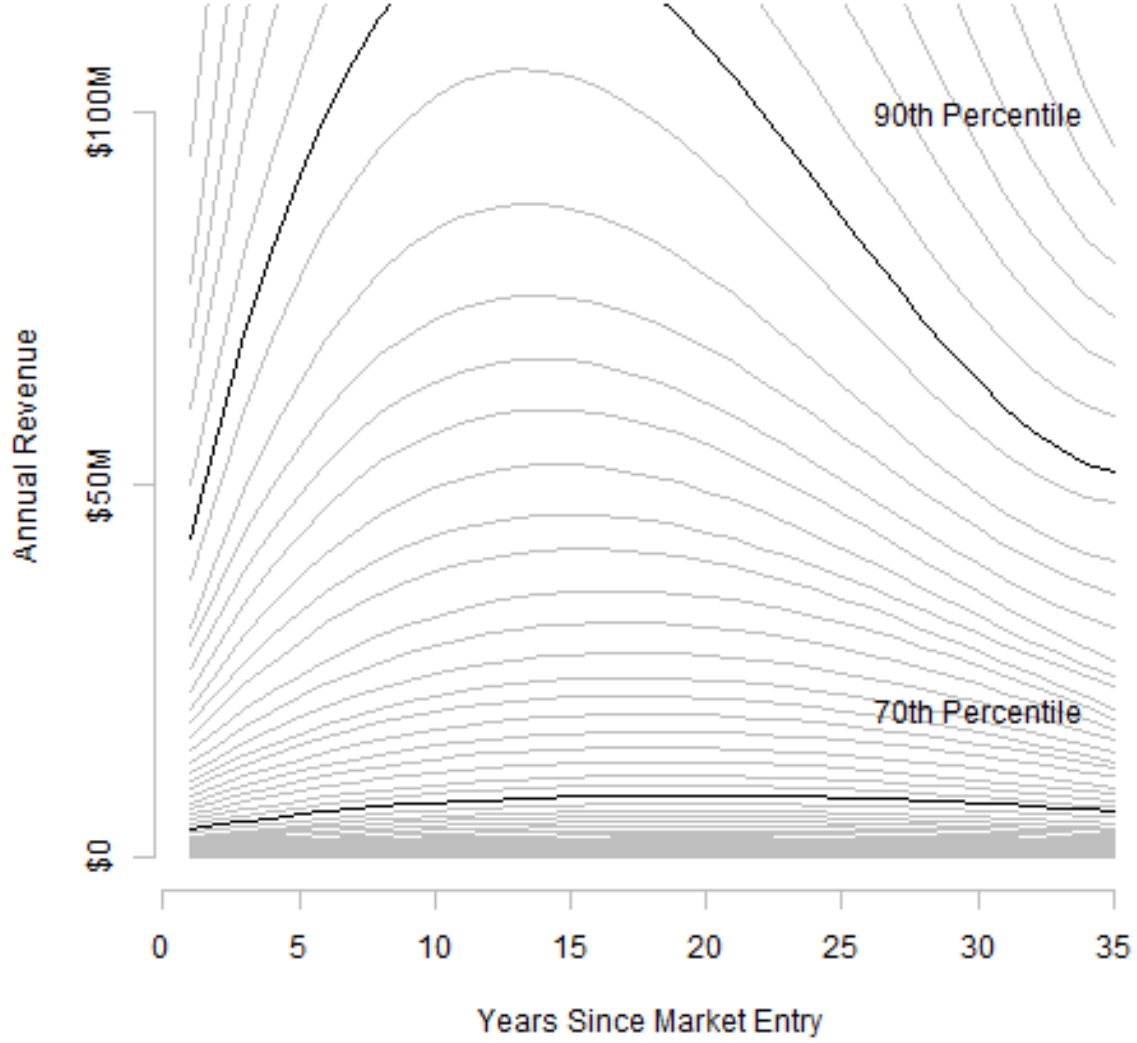
- Quantile regression for each percentile
- Cubic in time on market and a time trend

Estimate the distribution of revenues.

- Use coefficient estimates
- Sum up using weighted average cost of capital (WACC)

Multiply up to global revenues using estimates from the IQVIA Institute for Human Data Science.

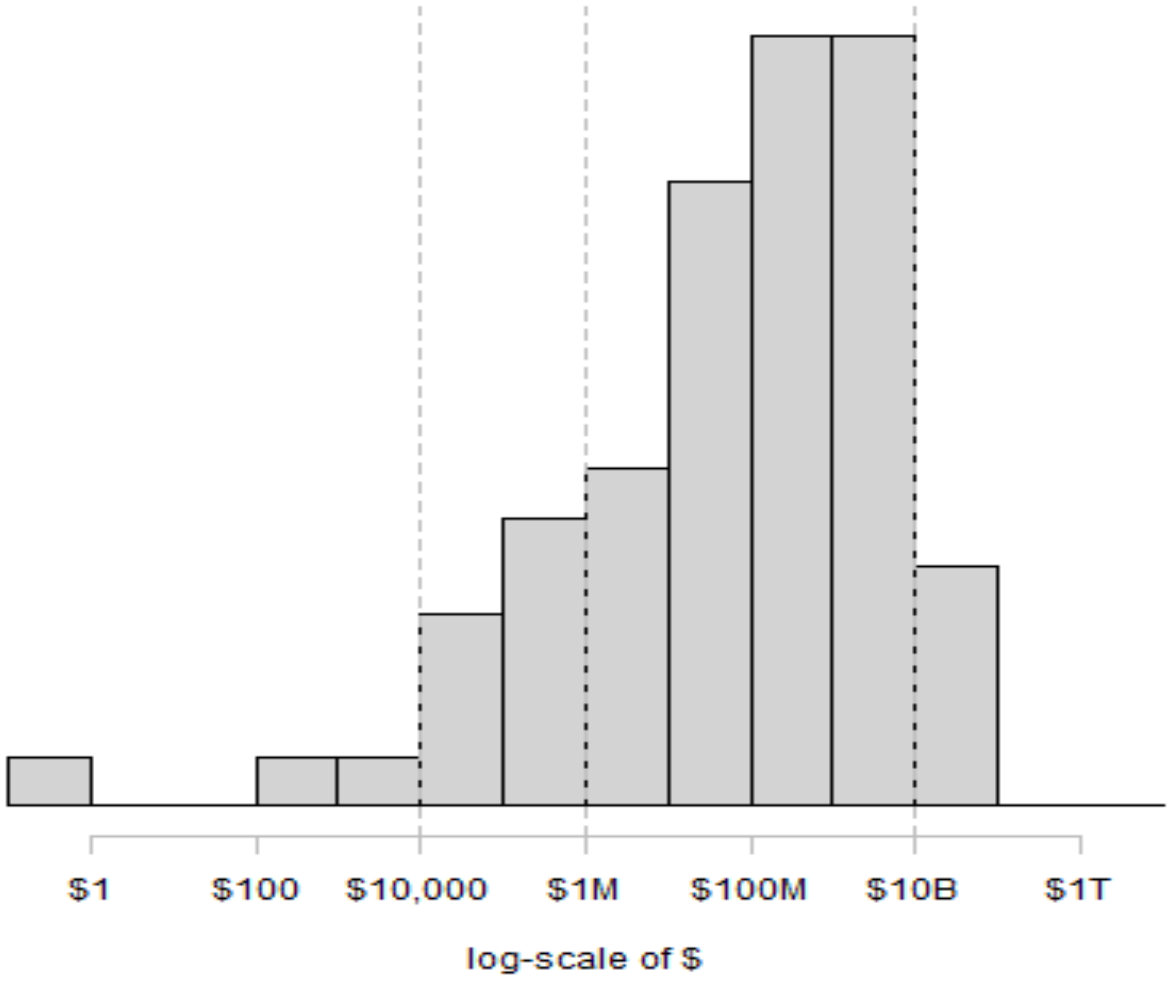
Percentiles of Estimated Lifetime Returns From Medicare Part D



CBO estimates the distribution of revenues over the lifetime of a drug in Medicare Part D. Each line represents the estimated relationship between revenues and the number of years on the market at each percentile.

CBO uses data on revenues net of rebates for Medicare Part D. To estimate the relationship, CBO uses a cubic that includes a term to account for the trend in net prices. Revenues are estimated at the ingredient level.

Estimated Distribution of Lifetime Returns From Medicare Part D



The figure shows CBO's estimate of the distribution of lifetime revenues for Medicare Part D drugs in a log scale of dollars. Using data from 2010 to 2018, CBO found that some drugs (4 percent) earn less than $10,000, most (81 percent) earn more than $1 million, and only a few (7 percent) earn more than $10 billion. The discounted present value of the sum of revenues net of rebates uses a discount rate of 0.086 (the same as the estimated WACC). Revenues are estimated at the ingredient level.

Estimates of Costs

Survey Data From DiMasi et al. (2016)

Authors selected a sample of drugs fully developed by a small set of biotech firms and surveyed those firms about:

- Expenditures on each drug candidate for each phase of development
- The time each drug candidate spent in each phase of development

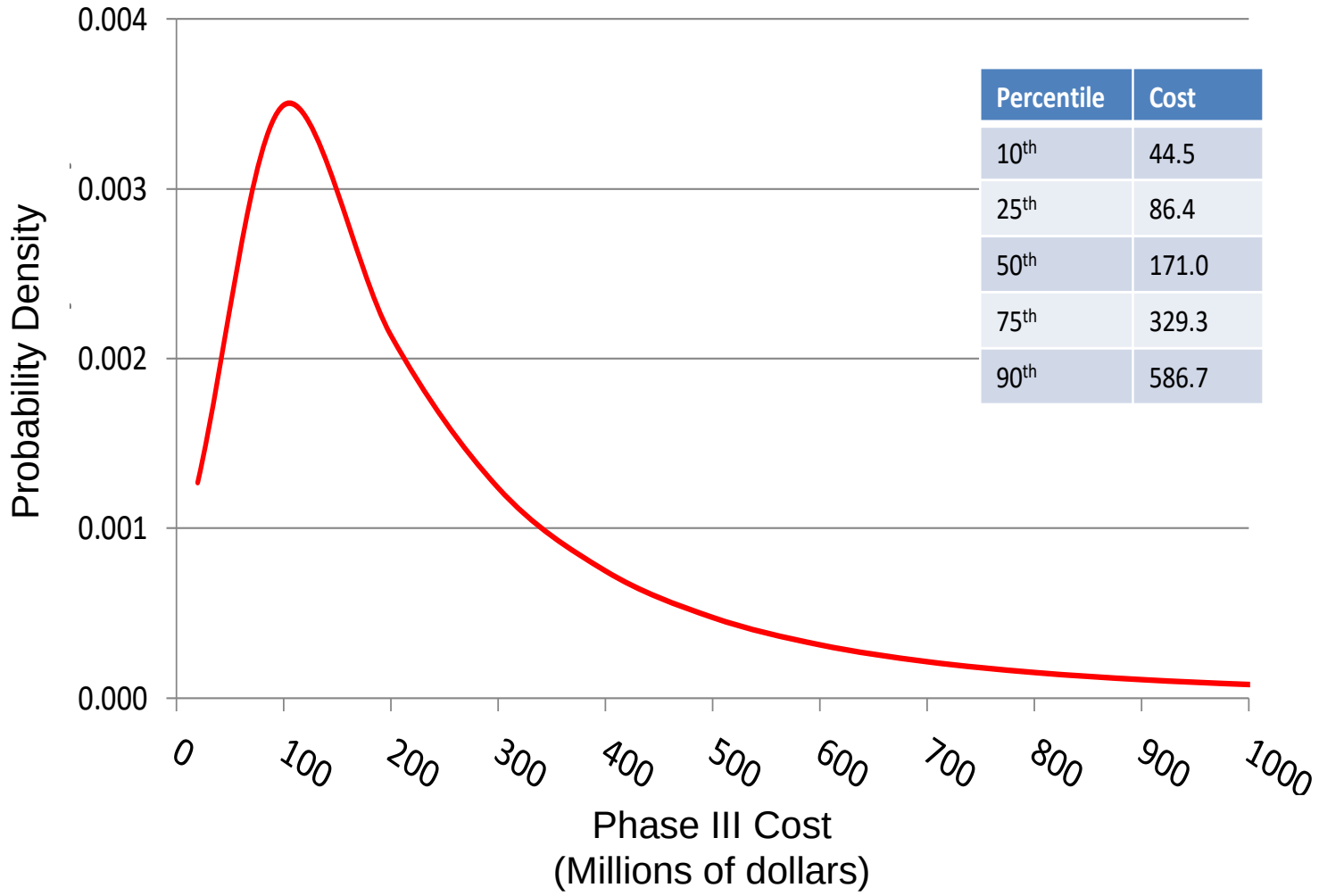
The study reported the following:

- Fitted distributions of expenditures for each phase (I to III) and fitted distributions of time in development for each phase (0 to III)
- Moments of the joint distribution of expenditures and time in development for each phase (I to III)
- Average expenditures per project in phase 0
- Average time from development to market

CBO uses those survey data to estimate costs.

See Joseph A. DiMasi, Henry G. Grabowski, and Ronald W. Hansen, "Innovation in the Pharmaceutical Industry: New Estimates of R&D Costs," *Journal of Health Economics,* vol. 47 (May 2016), pp. 20–33, https://doi.org/10.1016/j.jhealeco.2016.01.012.

Estimated Distribution of Expenditures in Phase III



Percentile	Cost
10th	44.5
25th	86.4
50th	171.0
75th	329.3
90th	586.7

Estimates of expenditures are based on the survey of pharmaceutical manufacturers reported in DiMasi et al. (2016). The authors report the fitted distribution of expenditures.

The figure presents the estimated log-normal distribution of expenditures in phase III.

Distribution parameters: shift = −10.880; scale = 5.204; shape = 0.928

Cost Estimates for Phases 0 to III

Phases I to III:

- Use reported fitted curves and moments to calibrate a joint distribution of expenditures and time in development for each phase.
- Use reported time from development market and WACC (from Damodaran analysis) to draw a simulated set of capitalized costs.

Phase 0:

- Use reported average expenditures, fitted distribution of time in development, and WACC + 200 basis points.
- Based on discussion in DiMasi et al. (2016) and estimates presented in Harrington (2012).

See Aswath Damodaran, “Cost of Capital by Sector (U.S.)” (accessed December 8, 2020), http://tinyurl.com/171f0kqm; and Scott E. Harrington, “Cost of Capital for Pharmaceutical, Biotechnology, and Medical Device Firms,” in Patricia M. Danzon and Sean Nicholson, eds., *The Oxford Handbook of the Economics of the Biopharmaceutical Industry* (Oxford University Press, 2012), pp. 75–99, https://doi.org/10.1093/oxfordhb/9780199742998.013.0004.

Procedure for Estimating Costs of Standard and Accelerated Approval Processes

Standard approval:

- Estimate costs for phase 0 to phase III.
- Estimate time from current phase to entry after phase III.
- Estimate revenues after phase III.

Accelerated approval:

- Estimate costs for phase 0 to phase II.
- Estimate time from current phase to entry after phase II.
- Estimate revenues minus phase III expenditures.

Identifying Model Parameters

Identification: Roy Model

$$R = \begin{cases} R^* & if\ R^* - C^* > 0 \\ . & otherwise \end{cases}$$

$$C = \begin{cases} C^* & if\ R^* - C^* > 0 \\ . & otherwise \end{cases}$$

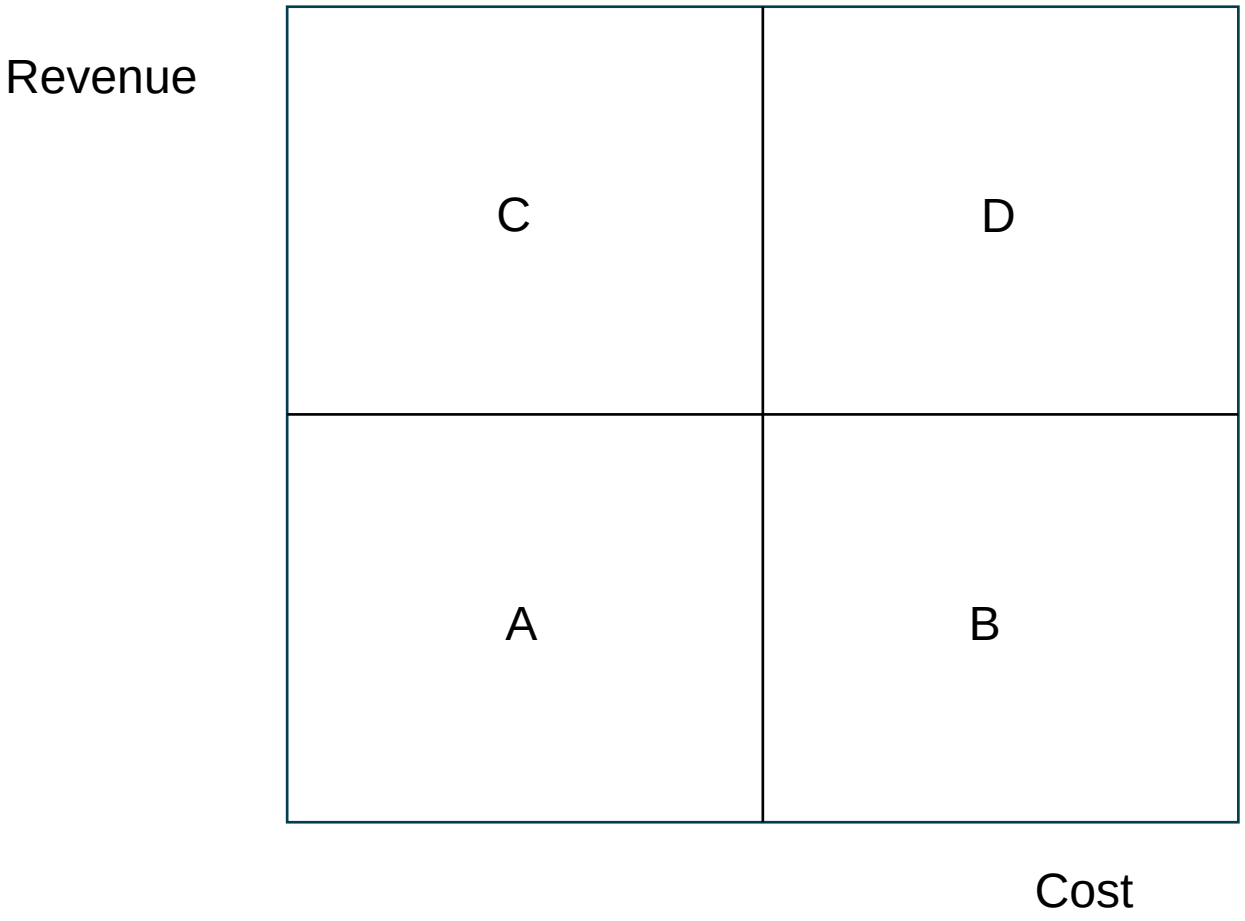
We are interested in determining the distribution of $\{R^*, C^*\}$.

But we observed the distribution of R from one source and the distribution of C from a different source.

Can we determine the distribution of $\{R^*, C^*\}$?

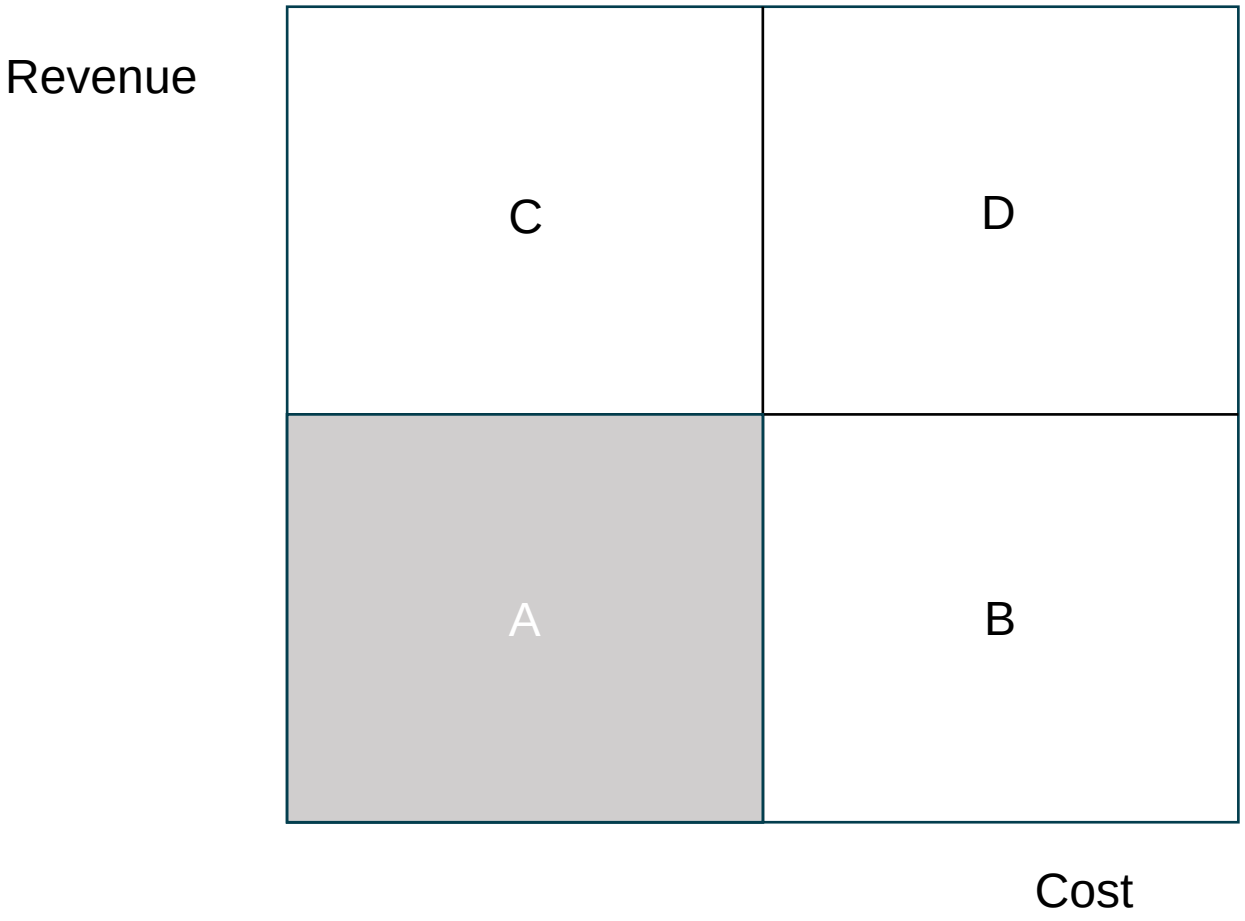
Yes, but we must make structural assumptions and parametric restrictions to do so.

Identification: Example



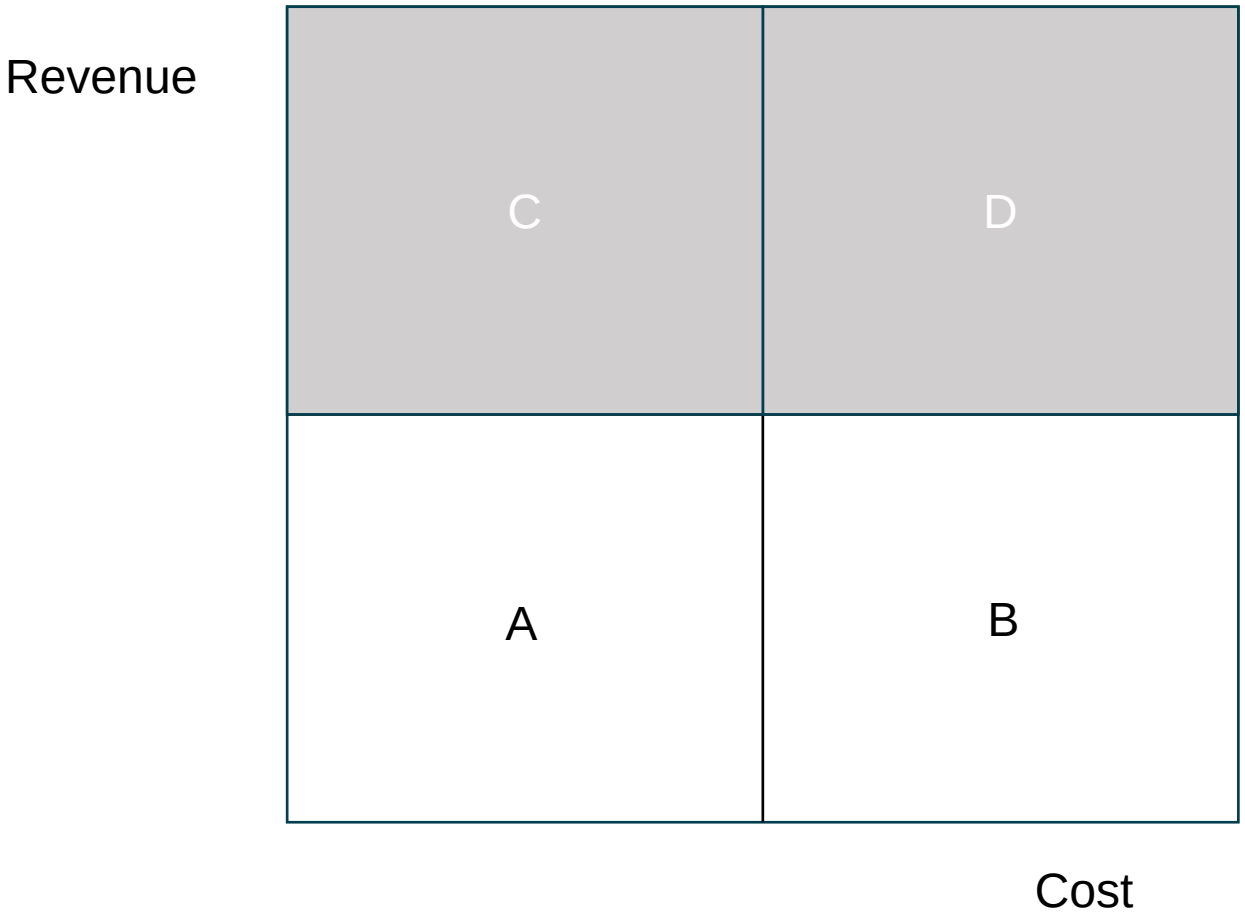
Consider a simple example with four joint probabilities. Can we determine the values A, B, C, and D?

Identification: Example



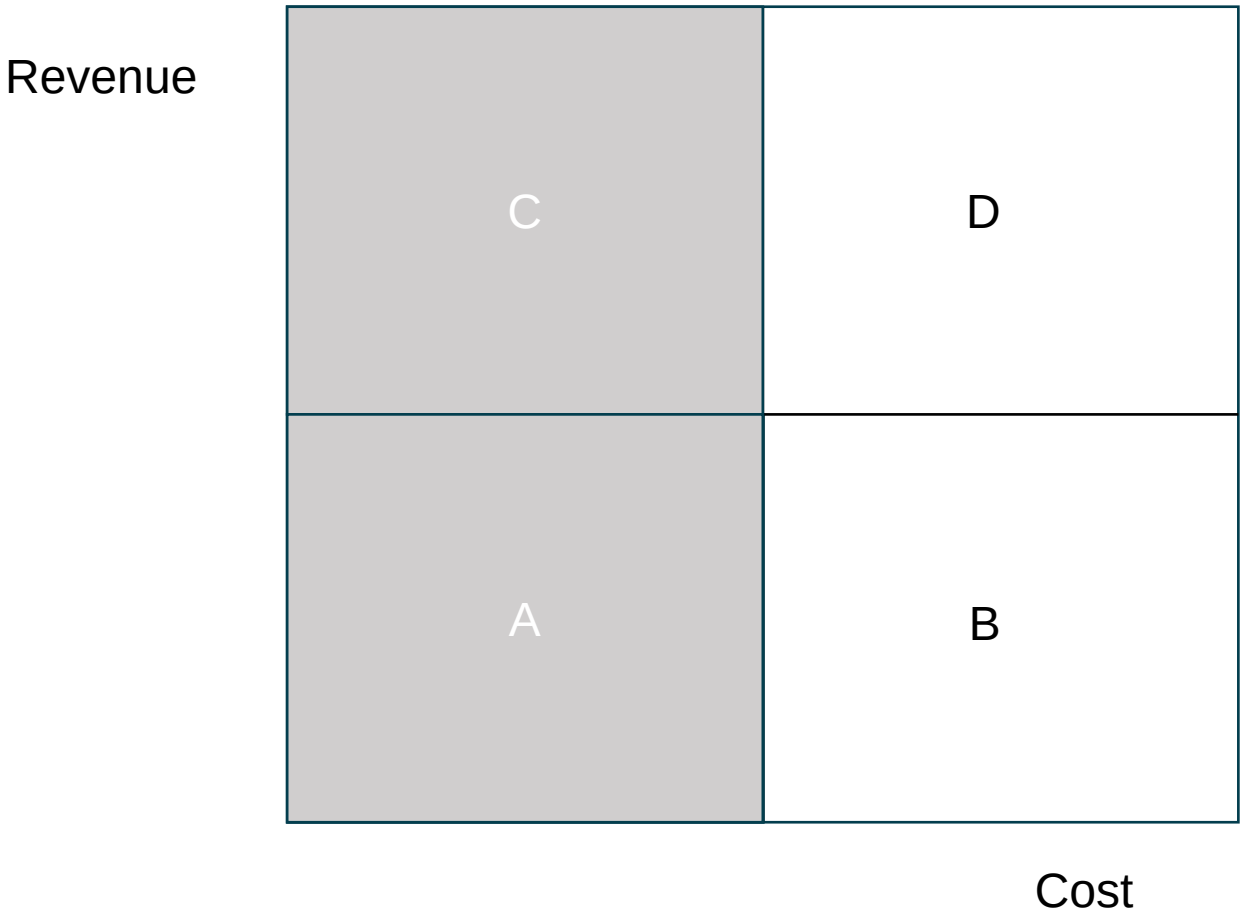
By observing the probability of entry for drugs with low revenues, we can infer that those drugs also had low costs. That observation allows us to determine A.

Identification: Example



By observing the probability of entry for drugs with high revenues, we can determine that they have either low costs or high costs. That allows us to determine the value of the parameters C + D, but not C and D separately.

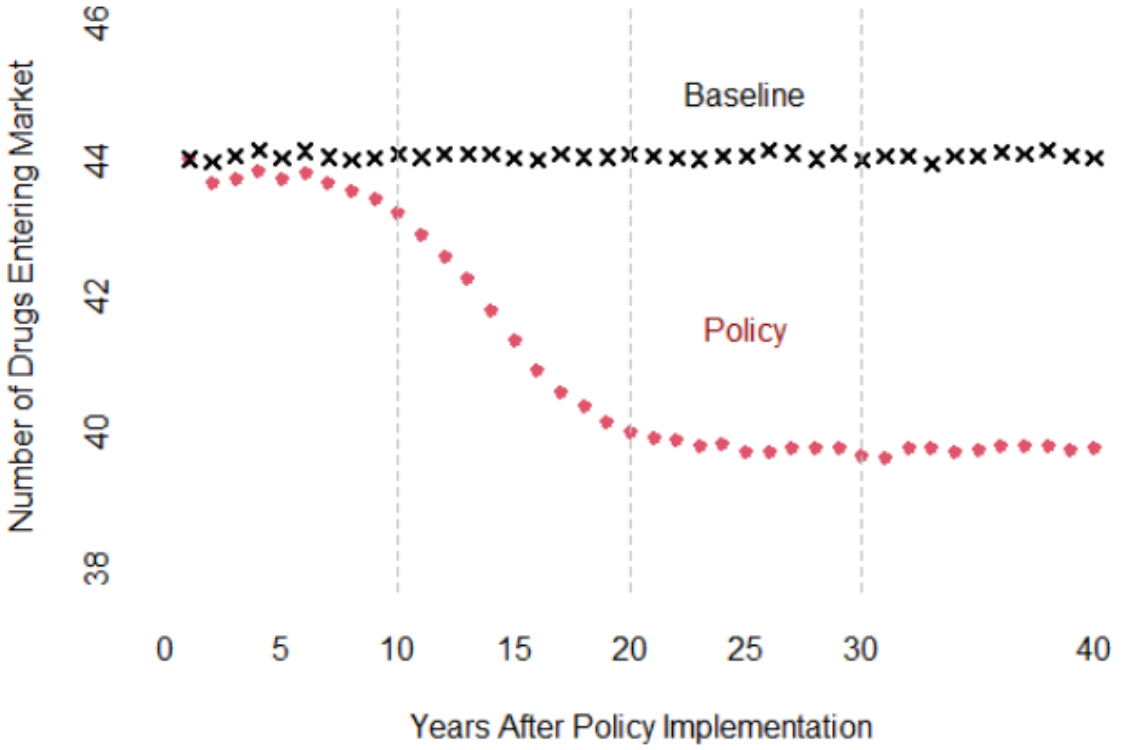
Identification: Example



By observing the probability of entry for drugs with low costs, we cannot tell if they have high revenues or low revenues, but we can determine the value of A + C. Because we already determined A, we can now determine C. We already know C + D, so once we have determined C, we can calculate D. Finally, we can determine B because A + B + C + D = 1.

Policy Simulations

Effects of Price Negotiation Policy on the Number of New Drugs Entering the Market



Phase III trials: 0.7% decrease

Phase II trials:

- Standard approval: 3.4% decrease
- Accelerated approval: 1.2% decrease

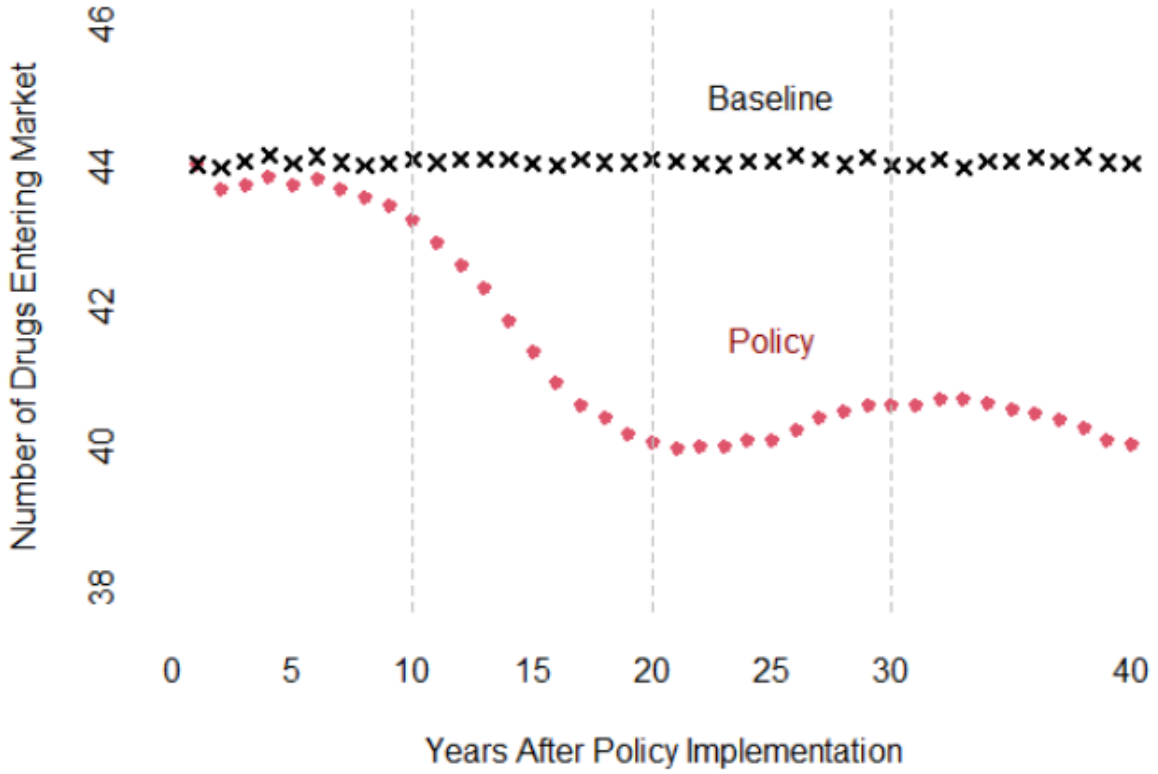
Phase I trials:

- Standard approval: 4.8% decrease
- Accelerated approval: 5.1% decrease
- Expected revenues are 25% lower for all drugs

Phase 0 (preclinical development):

- Standard approval: 1.5% decrease
- Accelerated approval: 2.5% decrease

Effects of Price Negotiation Policy Combined With a $10 Billion Increase in NIH Funding Over 10 Years



Phase I trials: 1.2% increase after 12 years

Estimate of the response to additional NIH funding is based on the elasticity estimate of 0.45 from Blume-Kohout (2012).

NIH funding is assumed to go back to baseline amount after 10 years.

See Margaret E. Blume-Kohout, “Does Targeted, Disease-Specific Public Research Funding Influence Pharmaceutical Innovation?,” *Journal of Policy Analysis and Management*, vol. 31, no. 3 (Summer 2012), pp. 641–660, https://doi.org/10.1002/pam.21640.

Conclusion

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CBO's model of new drug development is intended to help the Congress understand the effect that legislative proposals would have on the development of new drugs.

It is used to produce alternatives to elasticity estimates presented in the literature.

A price negotiation policy would have little effect for the first 10 years, but in the long run, such a policy would decrease the number of new drugs entering the market by 10%, CBO estimates.

Updates Made to CBO's Model Since the Publication of the Working Paper Describing It

Changes made to the model:

- The effects that a policy would have on financing costs are now included in the main model.
- The model can now be used to analyze the effect of a policy on preclinical development (phase 0), which involves higher capital costs than other phases. The process for estimating costs thus differs slightly from that used for other phases.
- The model now accounts for an accelerated approval process (in which phase III is conducted after a drug enters the market).

In the working paper, the sample policy was estimated to result in an 8% reduction in the number of new drugs entering the market. Using the revised model, CBO now estimates that the policy would result in a 10% reduction.

See Congressional Budget Office, "Estimated Budgetary Effects of Title XIII, Committee on Ways and Means, H.R. 5376, the Build Back Better Act, as Posted on the Website of the House Committee on Rules on November 3, 2021 (Rules Committee Print 117-18), as Amended by Yarmuth Amendment 112" (November 18, 2021), note h, www.cbo.gov/publication/57626; and Christopher P. Adams, *CBO's Simulation Model of New Drug Development*, Working Paper 2021-09 (Congressional Budget Office, August 2021), www.cbo.gov/publication/57010.