Designing Pull Funding

For A COVID-19 Vaccine

ABSTRACT

A widely accessible vaccine is essential to mitigate the health and economic ravages of coronavirus disease 2019 (COVID-19). Without appropriate incentives and coordination, however, firms may not respond at sufficient speed or scale, and competition among countries for limited supply may drive up prices and undercut efficient allocation. Programs relying on "push" incentives (direct cost reimbursement) can be complicated by the funder's inability to observe firms' private cost information. To address these challenges, we propose a "pull" program that incentivizes late-stage development (Phase III trials and manufacturing) for COVID-19 vaccines by awarding advance purchase commitments to bidding firms. Using novel cost and demand data, we calculate the optimal size and number of awards. In baseline simulations, the optimal program induces the participation of virtually all ten viable vaccine candidates, spending an average of $110 billion to generate net benefits of $2.8 trillion, nearly double that generated by the free market.

A widely accessible vaccine is essential to mitigate the health and economic ravages of coronavirus disease 2019 (COVID-19). Forecasts indicate that the pandemic could claim forty million lives[1] and reduce global economic output by $9 trillion.[2] Despite the urgent global need for a vaccine, there is a perennial concern that private markets fail to adequately incentivize vaccine investments,[3] particularly at the speed or scale required to mitigate this pandemic.

Public funds from governments, philanthropies, and partnerships such as the Coalition for Epidemic Preparedness Innovations provide resources to reduce the cost and risk of early-stage research and development, but optimal mechanisms to incentivize firms to bring candidates through licensure, scale up capacity, and manufacture vaccine doses at risk are lacking.

Absent public support for these later stages, one concern is that firms will underinvest in manufacturing capacity to produce large quantities of vaccine rapidly because they reap more profit if they serve demand for a longer period of time with less capacity. Firms may also hesitate to scale up manufacturing in a timely fashion. Typically, capacity is installed only after a candidate has proven effective in Phase III trials. To best respond in a pandemic, however, manufacturing capacity investments must be made in parallel with trials, requiring companies to build facilities and purchase supplies for a vaccine that may fail in clinical trials.

Absent global coordination, there is also concern that countries may bid against one another, driving up the price of vaccines. In addition to depleting public resources, a free market approach will allocate vaccines to the highest bidders, leaving the most vulnerable unprotected and therefore failing to end the pandemic in the shortest period possible.

Public support can come in the form of “push” funding (up-front reimbursement of research, development, and production expenditures) or “pull” funding (payment for successful products). The Coalition for Epidemic Preparedness Innovations, the Biomedical Advanced Research and Development Authority, and the National Institutes of Health, which together account for a large portion of publicly funded COVID-19

vaccine research, have largely employed push funding. Looking ahead to later stages of COVID-19 vaccine development, exclusive reliance on push funding may have drawbacks, requiring the funder to predict “winners” in advance (before it is known whether they can in fact produce safe and effective vaccines), elicit accurate cost information from these firms, and micromanage the development process.[4]

To overcome these challenges, we propose an advance purchase commitment to reward the development and manufacture of vaccines that meet specifications for safety, efficacy, and suitability. Because this pull program only pays for successful products, it puts the onus on firms to assess their prospects for success before putting their own capital at risk. Because the reward is a set ex-post payment, not a cost reimbursement, it relieves the funder from having to elicit firms’ cost information.

A variety of advance purchase commitments have been used to stimulate private sector vaccine investment. The Vaccines for Children fund, which provides a standing federal purchase order for recommended pediatric vaccines, has functioned as a pull incentive for new vaccine development in the United States since 1994.[5] An advance market commitment, a particular form of advance purchase commitment that ties the award to volume supplied,[4,5] was piloted for pneumococcal disease, the leading vaccine-preventable killer of children younger than five in developing countries. This advance market commitment sped the development and rollout of vaccines according to several studies.[6–8]

Several pull-funding programs have been proposed to stimulate investment and coordinate the purchase and distribution of a COVID-19 vaccine globally,[9,10] including the $18 billion COVAX facility launched by Gavi, the Vaccine Alliance.[11] Proposals differ

somewhat in the recommended mix of incentives, regional scope, and overall funding amounts.[12] In all cases, key questions remain regarding the size of the fund and the number of candidates that should be funded to ensure wide access to an effective vaccine.

Our analysis can answer these questions for a range of parameters. Using novel demand and cost data, we calculate the number of candidates that should receive purchase commitments and the size of commitments required to induce optimal firm participation. These calculations depend on the value of the health and economic benefits that derive from accelerating vaccine development, the number of firms competing for the award, the distribution of their costs, and the probability that they succeed.

Study Data And Methods

We provide design principles for an optimal pull mechanism under general demand and cost conditions in the presence of "frictions" (including the funder's inability to observe firms' private cost information) that preclude efficient push funding. Operations research has produced a rich literature on procurement under demand risk[13] and supply risk.[14] Our article draws on a relevant article characterizing optimal procurement from multiple suppliers facing a risk of performance failure,[15] translating this abstract characterization into a concrete mechanism, which we use to determine the number of investing suppliers and their award.

We also collect and analyze data from several sources to estimate demand and costs in the market for a COVID-19 vaccine. These estimates are put into Monte Carlo simulations of the performance of our proposed funding mechanism. We gauge

baseline performance against benchmarks ranging from an idealized mechanism operating in a frictionless environment at one extreme to a free market in the absence of coordinated funding at the other. We analyze the sensitivity of the simulation results to variations in the baseline parameters.

Model

We adopt the same time frame as the International Monetary Fund forecasts behind our demand estimates, spanning two years from January 2020, the start of the pandemic, to December 2021, the end of the forecast horizon. As of July 6, 2020, eight vaccine candidates have progressed into Phase II trials and two into Phase III trials.[16] The baseline scenario thus assumes ten promising vaccine candidates. Completing Phase III trials and scaling up manufacturing will require, optimistically, an additional six months, leaving months 13–24 as the potential time frame for a vaccine to become available.

We assume that funding from agencies and foundations is available in the form of grants to defray all costs of bringing candidates through Phase II trials. However, no widely supported mechanism has been proposed to fund the remaining costs—the costs of Phase III trials and manufacturing.

Under the model, a funder representing international interests designs a program to incentivize firms to take vaccine candidates through these later stages. The funder seeks to maximize net benefits—global harm avoided with a vaccine- minus program expenditures—on average across uncertain states of the world. For simplicity, suppose that all countries participate in the program and all commit to obtaining the vaccine solely through the program rather than through side deals with firms.

When push funding (funding with up-front grant payments) is provided, firms' incentives to follow through with a successful product are diminished. Firms with unrealistic chances at success, knowing their costs are covered, may also be drawn into the program. These challenges are magnified in later stages because the associated costs are typically larger.[17] We assume that these challenges are severe enough that push funding would be less efficient to fund late-stage investment and production than pull funding (that is, payment for successful delivery of product). To have a realistic prospect of having a vaccine ready for months 13–24, we assume that the firm must install manufacturing capacity "at risk," in parallel with clinical trials, as opposed to after efficacy had been established, as is typical. Thus, although the firm must self-fund late-stage development, the relevant probability of success that the firm should use to determine whether to undertake this investment is the cumulative probability over the whole development pipeline.

Data

Global Demand:

We estimate global demand for a COVID-19 vaccine by combining estimates of economic output losses and mortality losses. Our estimate of economic output losses is based on International Monetary Fund projections of growth decline in twenty-six global subregions during 2020–21 caused by COVID-19.[2] Translating these growth projections into levels using World Bank data on per capita gross domestic product in every country[18] and dividing by the twenty-four months in 2020–21 provides an estimate of monthly economic harm per capita from COVID-19 in each country.

Our mortality loss estimates are based on projections by the Imperial College COVID-19 Response Team of deaths by country.[1] The online appendix details the steps undertaken to express these losses in monetary terms.[19]

Descriptive statistics for harm from economic output losses, mortality losses, and their sum are provided in exhibit A1 in the appendix.[19] On average, mortality losses constitute about a quarter of a country's total losses

Health and economic harm from COVID-19 can be translated into a global demand curve for a vaccine that would allow this harm to be avoided. The appendix provides a series of exhibits graphing the resulting global demand curve.[19] Appendix exhibit A2 provides a static picture of global demand for a month of avoided harm, assuming constant harm during the pandemic.[19] Appendix exhibit A3 provides an enhanced demand diagram illustrating demand dynamics as pandemic intensity varies over the time frame considered.[19] The baseline scenario assumes that the arrival of mitigating factors (that is, herd immunity, an effective treatment, or improved transmission mitigation measures) generate a 5 percent chance that the pandemic ends each month. The resulting dynamic demand curve in appendix exhibit A3 shrinks over time because the demand for avoiding expected future harm (harm × the probability that it is experienced) declines.[19]

Cost Distribution:

To determine market supply, we need to determine the number of firms that the program induces to participate. We compute the number of participants via simulation, checking whether the firm's return from the program exceeds its draw from the cost distribution, implying participation is profitable. To conduct these simulations requires

information not just on the average value of costs but also on the shape of the cost distribution (mean and variance).

Previous estimates of cost distributions for various stages of pharmaceutical research and development do not directly apply to our context.[17,20–22] We are not aware of any published estimates of the cost of manufacturing capacity or production. Existing cost estimates for Phase III trials, with few exceptions,[18,21] apply to drugs rather than vaccines. Some estimates cover only clinical trial management,[22] not the cost of manufacturing the doses used in the trials. Other estimates adjust for the risk for project failure.[18,20] Because we directly account for failure in our simulations, risk adjusting firms' costs in our context would amount to double counting.

We provide new estimates of the cost distribution using proprietary data from a Coalition for Epidemic Preparedness Innovations survey of more than four hundred firms identified from clinical trial registries of vaccine firms. The first wave of this survey was analyzed by Dimitrios Gouglas and colleagues.[21] Their analysis focused on the cost of early-stage vaccine development (preclinical, Phase I, and Phase II trials). Here, we analyze survey responses for later stages (Phase III trials, capacity installation, and variable manufacturing costs, referred to in the industry as cost of goods sold or COGS) and include the most recent wave of data surveying potential COVID-19 vaccine manufacturers. The appendix provides details on the survey methods and descriptive statistics for the final sample (see appendix exhibit A4).[19]

We assume that the distribution of a firm's costs in each of the three relevant stages is lognormal. Lognormality is a standard assumption for investment costs, applied in contexts ranging from new drug entry[23] to manufacturing research and

development,[24] and has been empirically tested in a study of seven industrial sectors across six countries.[25] We estimate the best-fitting lognormal distribution for the three relevant stages by applying the maximum likelihood method to the Coalition for Epidemic Preparedness Innovations survey data. Details on this method and parameter estimates are provided in the appendix.[19]

Exhibit 1 shows the estimated cost distributions. The colored curved lines are the distributions for separate stages. Although Phase III costs do not depend on the scale of production, both capacity and COGS do. In the exhibit, they are drawn for the baseline scenario in which a firm is assumed to produce 750 million doses annually. The cost distributions for Phase III trials and capacity installation are concentrated at relatively low values, with medians of $30 million and $60 million, respectively. In contrast, the distribution for COGS spreads over much higher values, with a median value of $5.1 billion.

The distribution of combined costs sums the three component distributions. Details behind the method used to aggregate lognormals (the Felton-Wilkinson approximation) are provided in the appendix.[19]

The distribution of combined costs reflects one other adjustment, expressing all costs in terms of ex-ante expectations. This is the relevant number firms would use to compare against expected program rewards to decide whether to participate in the program. In contrast to at-risk investments, which are undertaken with certainty by an investing firm, COGS are only expended if the firm has a successful vaccine, and therefore need to be weighted by the probability of success when added into the combined distribution. This explains why the peak of the combined distribution is below

that for the COGS component. We construe a firm's survey response as building in enough of a profit margin that if these combined costs were covered, the firm would participate in the overall program.

In the baseline scenario underlying the exhibit, with firms assumed to produce 750 million doses in a year, the combined cost distribution has a mean of $3.1 billion and a standard deviation of $3.1 billion. Combined costs for this scale of production are thus high and widely variable.

Other Parameters:

We set the probability that a vaccine candidate succeeds to 30 percent in the baseline scenario, an estimate from a recent, comprehensive study of the probability that a vaccine successfully moves from Phase I trials through approval.[26] This is the relevant probability for our application because the modal COVID-19 vaccine candidate has yet to complete Phase I trials and because investment in our model is undertaken at risk, when the results from these early trials are still in doubt.

The value for a firm's capacity assumed in the baseline scenario is based on the most recent Coalition for Epidemic Preparedness Innovations survey data, which asked potential COVID-19 manufacturers about production schedules; 750 million doses is the closest round number to the mean of firms' forecasted production (data not shown).

Limitations

Our analysis has several limitations. Although the model allows firms to have different costs, firms are assumed to have the same capacities and probabilities of success and success draws are assumed to be independent. This turns out to be a minor limitation in our baseline scenario, as we determine that virtually all firms

participate in the optimal mechanism. Future research may consider a mechanism that would allow more nuanced candidate selection within the portfolio.

Another limitation is that we rule out push funding of the later investment stages, assuming it is prohibitively inefficient. Solving for the optimal balance between push and pull when both are possible would require more detailed modeling of the moral hazard and adverse selection problems that pull funding helps solve. Even so, we find that our mechanism delivers 96 percent of the net benefit of an idealized mechanism in a frictionless world (given baseline parameters), leaving little conceivable scope for a mechanism optimally balancing push and pull to improve on our mechanism.

Study Results

Optimal Funding Mechanism

This section presents the derivation of the optimal funding mechanism. Certain features of the mechanism involve complex formulas (provided in the appendix),[19] but the qualitative structure of the mechanism can be described here, using textbook concepts of demand and supply.

The funder's demand reflects the funder's value for the marginal firm's participation (exhibit 2). If no other participants have successful vaccines, then the marginal firm's capacity is used to vaccinate the highest-harm countries in month twelve, erasing the harm they would have experienced in that and following months. Once these countries are protected, the firm's capacity is devoted to protecting the next highest-harm countries, and so on. The sum of erased harms over time, weighted by the intensity of the pandemic during those months, constitutes the funder's benefit from the marginal firm's capacity.

This benefit is probabilistic because it is conditional on the success of the firm's vaccine and dependent on the number of other successful vaccines. The more other successful vaccines there are, the lower the value of the marginal one because the highest-harm countries remaining each month can be protected by other vaccines. Demand falls as the number of participating firms increases, shifting the distribution toward more rival successes.

In a textbook competitive market, the intersection between supply and demand determines equilibrium. Here, because the funder controls market design, it can retain more surplus by setting a "reserve price." In the present setting of a procurement auction, the reserve price is a ceiling set by the funder above which firms' bids are excluded as nonviable, thus capping the funder's maximum payout. The "Reserve price" curve graphs the optimal reserve price in the baseline scenario according to the formula derived in the appendix (see equation 16).[19] This formula achieves the optimal balance between saving money and expanding firm participation.

First, the funder posts the reserve price schedule. Then each firm reports its cost, drawn from the combined cost distribution in exhibit 1. The schedule of firms' reported costs in ascending order is shown as "Suppliers' costs" in exhibit 2. The mechanism selects the greatest number of firms willing to participate at the reserve price specified for that number of firms. Geometrically, this is given by the intersection between the reserve price schedule and cost schedule, indicated in the exhibit by the circle. In the exhibit, the mechanism optimally selects nine firms to participate, offering an award equal to the $11.6 billion reserve price (in the same ex-ante terms as costs).

Although a firm's cost is private information, the mechanism elicits truthful reporting because the firm's cost report only determines whether it wins; how much it wins depends on the posted reserve price schedule. Truthful reporting ensures the firm wins exactly when this is profitable—that is, when the award exceeds its cost.

In rare cases (3 percent of simulations), the reserve price and cost schedules can intersect in such a way that a rejected supplier would be willing to participate at the reserve price offered to accepted suppliers. In such cases, the optimal mechanism reduces the award below the reserve price down to this losing firm's cost report. The funder saves money while preserving truthful cost reporting.

Simulation Results

Exhibit 3 reports the results from one million simulations for a variety of scenarios. The first row reports the baseline scenario (baseline assumptions are listed for reference in appendix exhibit A6 and summarized in the exhibit 3 notes).[19] The mechanism selects virtually all available firms to participate, an average of 9.8 across simulations, leading to an average of 2.9 successful vaccines. Only successful firms receive an award, averaging $37.7 billion.

Although this may seem high, its expected value from the perspective of an investing firm, which only receives it 30 percent of the time, is $11.3 billion. This amount is close to the simulation average of the highest of the ten cost draws, $9.0 billion, but enough above to induce even the costliest firm's participation 78 percent of the time (data not shown). Average program spending is $110.4 billion, and net funder benefit from the program is $2.8 trillion. This enormous net benefit reflects the urgent need for

vaccine and rationalizes the considerable sums spent to secure the participation of all but those firms with the most exorbitant cost draws.

The next series of scenarios in exhibit 3 analyzes the results from changing one baseline assumption at a time. Program spending and net benefits both increase when firm capacity, probability of success, and the number of candidate firms increase and when the probability the pandemic ends each month decreases. A consistent finding across these scenarios is that the mechanism seeks the participation of almost all available firms. Even with twenty candidates, the mechanism induces the participation of an average of 19.0 firms across simulations.

The next set of scenarios in exhibit 3 varies modeling assumptions related to the manufacturing process. When immunity requires two doses, the program continues to seek the participation of virtually all firms but now the induced capacity only immunizes half the number of people, yielding substantially lower net program benefits. When more expenditure must be made at risk (that is, with no guarantee that it will be recovered), program spending increases slightly, but not enough to measurably reduce net program benefits.

The next scenario in exhibit 3 demonstrates the impact of allocation strategies on social benefit. If instead of efficiently allocating the vaccine to the highest-priority populations first, the vaccine is randomly allocated across countries, most program benefits are lost.

In our model, the funder is limited to pull funding because the nontransparency of firms' costs renders reimbursement of their costs—push funding—infeasible. The next scenario in exhibit 3 analyzes how much better the funder could do in an idealized

setting without push-funding constraints, allowing the funder to procure the vaccine from firms at their cost. Despite the constraints our practical proposal must contend with, it still manages to achieve 96 percent of the net benefit of the idealized, push-funding program ($2.8 versus $3.0 trillion). Our proposal is more than three times as expensive as the idealized push funding model, but because it procures a similar quantity of vaccine, the benefits still dwarf the extra spending.

Our proposal compares favorably with a free-market scenario, which we model assuming the combined capacity of successful firms is auctioned off to countries that remain in the market each month (following the Cournot competition model, standard in the economics literature). A complication is that countries would reduce bids in anticipation of price declines in later months after high bidders had been “skimmed” from the market. Even after accounting for such price dynamics, countries spend $1,375 billion in a bidding war for vaccine.

The last set of scenarios in exhibit 3 changes the baseline model by introducing heterogeneity within countries, assuming that some subpopulations are more vulnerable (more exposed, suffer more severe effects, or spread the disease more widely) than others. To quantify this heterogeneity, assume two thirds of each country’s total harm from the pandemic is concentrated in its vulnerable subpopulation, which constitutes one third of its population. Our proposal becomes even more valuable in this scenario, providing net benefits of $3.2 trillion, because scarce capacity can be allocated to relieve more concentrated harm.

The penultimate row allocates vaccine to vulnerable subpopulations first even if vaccinating vulnerable subpopulations in some low-harm countries provides less benefit

than vaccinating some less-vulnerable subpopulations in high-harm countries. This departure from the efficient allocation causes program benefits to fall by 12 percent, a measurable loss, but one much smaller than from the move to random allocation.

In the last scenario in exhibit 3, the free market performs no better in the within-country heterogeneity model: Each country bids for the vaccine as a unit, so the country's per capita harm determines its bid regardless of how this harm is distributed within the country. The free market fails to obtain an efficient allocation because vulnerable people in lower-income countries lack an agent to voice their value for a vaccine.

Discussion

In baseline simulations, the optimal pull program spends an average of $50 per dose to obtain an average of 2.2 billion doses—$110.4 billion in total. The size of our pull program is driven by the enormous estimated benefit from COVID-19 vaccination, leading the optimal program to induce nearly all firms to participate (average of 9.8 out of 10), installing nearly all available capacity, and allowing more people to be vaccinated with less delay. To secure this level of participation requires the award to cover all but the most exorbitant cost draws. On average, 2.9 participating firms develop a successful vaccine, generating a social benefit (net of program costs) of $2.8 trillion.

This recommendation exceeds funding levels proposed for international and national procurement programs. Gavi proposed $18 billion to procure 2 billion doses to vaccinate priority populations via the COVAX facility.[11] Operation Warp Speed, which seeks to expand and coordinate existing US-based efforts to procure three hundred million doses, has not announced the details of its procurement program, but the $19.5

billion directed to the effort[27] suggests an upper limit on funds. The proportion of push and pull incentives, dose amounts, timelines, and regions served vary among specific proposals, so our results cannot be directly compared with these programs. Rather, we seek to provide quantitative insights that can inform these initiatives and a simulation tool that can readjust parameters to fit these programs as they develop.

In simulations, our proposed mechanism can generate more than 1.8 times the net benefit of the free market in which countries bid for vaccines after they are produced. Our mechanism offers two advantages over the free market. First, it dramatically lowers cost—by a factor of thirteen—by averting a bidding war. Given our program's larger size compared with other policy proposals, it is ironic that its advantage would be to lower costs compared with the private market. Second, it allows for more efficient allocation, moving some vulnerable people in lower-income countries up in the queue ahead of some from richer countries experiencing lower harm. A conjectured third benefit of our mechanism—enhancing investment in more candidates and more capacity—did not materialize in baseline simulations. Demand for a COVID-19 vaccine is so high that every firm in every simulation finds investing profitable under a free market scenario. This third benefit does materialize in scenarios with substantially more per firm capacity than in the baseline.

Our analysis omits several other possible advantages of a collaborative international agreement relative to the free market. We assume the free market self-organizes without delay and country leaders are perfect agents of their citizens. If these ideals are not met, the free market would perform worse than we estimate. An international agreement could also reduce the risk for supply chain disruptions. Vaccine

production is highly globalized, and any protectionist measures on the part of any one country could hamper all producers.[28]

Questions of how to implement this award mechanism must be addressed in a wider forum to give scope to a broad set of political and practical considerations: What is the best way to mobilize resources, who should administer the fund, and who should coordinate development? Potential candidates include the World Bank, Gavi, the Coalition for Epidemic Preparedness Innovations, or another international body.[29] This designated coordinator will have to negotiate policies for candidate selection, liability protection, intellectual property, access, and allocation.

NOTES

<eref>1. Walker PGT, Whittaker C, Watson O, Baguelin M, Ainslie KEC, Bhatia S, et al. The global impact of COVID-19 and strategies for mitigation and suppression [Internet]. London: Imperial College COVID-19 Response Team; 2020 Mar 26 [cited 2020 Jul 30]. Available from: https://www.imperial.ac.uk/media/imperial-college/medicine/sph/ide/gida-fellowships/Imperial-College-COVID19-Global-Impact-26-03-2020v2.pdf</eref>

<unknown>2. International Monetary Fund. World economic outlook. Washington (DC): IMF; 2020 Apr. Table 1.1, Overview of the world economic outlook projections; p. 7–8.</unknown>

<jrn>3. Kremer M, Snyder CM. Preventives versus treatments. Q J Econ. 2015;130(3):1167–239.</jrn>

<edb>4. Kremer M. Creating markets for new vaccines part I: rationale. In: Jaffe A, Lerner J, Stern S, editors. Innovation Policy and the Economy (volume 1). Cambridge (MA): MIT Press; 2001.</edb>

<bok>5. Kremer M, Glennerster R. Strong medicine: creating incentives for pharmaceutical research on neglected diseases. Princeton (NJ): Princeton University Press; 2004.</bok>

<jrn>6. Snyder CM, Begor W, Berndt ER. Economic perspectives on the advance market commitment for pneumococcal vaccines. Health Aff (Millwood). 2011;30(8):1508–17 PubMed.</jrn>

<eref>7. Chau V, Hausman V, Deelder W, Rastegar A, De Monte M, Aizenman Y, et al. The Advance Market Commitment for pneumococcal vaccine: process and design evaluation [Internet]. Geneva: Gavi; 2013 Feb 13 [cited 2020 Jul 30]. Available from: https://www.gavi.org/sites/default/files/document/amc-process-and-design-evaluation-full-reportpdf.pdf</eref>

<jrn>8. Kremer M, Levin J, Snyder CM. Advance market commitments: insights from theory and experience. AEA Pap Proc. 2020;110:269–73.</jrn>

<eref>9. Athey S, Kremer M, Snyder C, Tabarrok A. In the race for a coronavirus vaccine, we must go big. Really, really big. New York Times [serial on the Internet]. 2020 May 4 [cited 2020 Jul 30]. Available from: https://www.nytimes.com/2020/05/04/opinion/coronavirus-vaccine.html</eref>

<eref>10. Chalkidou K, Kettler H, Ramakrishnan G, Silverman R, Towse A. Leave no one behind: using a benefit-based Advance Market Commitment to incentivise development and global supply of COVID-19 vaccines [Internet]. Washington (DC): Center for Global Development; 2020 May 7 [cited 2020 Jul 30]. Available from: https://www.cgdev.org/publication/leave-no-one-behind-using-benefit-based-advance-market-commitment-covid-vaccine</eref>

<eref>11. Gavi. COVAX, the ACT-Accelerator vaccines pillar: insuring accelerated vaccine development and manufacture [Internet]. Geneva: Gavi; 2020 [cited 2020 Jul

30]. Available from: https://www.gavi.org/sites/default/files/document/2020/COVAX-Pillar-backgrounder_3.pdf</eref>

<eref>12. Silverman R, Ramakrishnan G, Towse A, Kettler H, Chalkidou K. The race for COVID-19 vaccine: an overview of current proposals and our contribution in bringing in the missing middle [Internet]. Washington (DC): Center for Global Development; 2020 May 21 [cited 2020 Jul 30]. Available from: https://www.cgdev.org/blog/race-covid-19-vaccine-overview-current-proposals-and-our-contribution-bringing-missing-middle</eref>

<jrn>13. Chen F. Auctioning supply contracts. Manage Sci. 2007;53(10):1562–76.</jrn>

<jrn>14. Anupindi R, Akella R. Diversification under supply uncertainty. Manage Sci. 1993;39(8):944–63.</jrn>

<jrn>15. Chaturvedi A, Martínez-de-Albéniz V. Optimal procurement design in the presence of supply risk. Manuf Serv Oper Manag. 2011;13(2):227–43.</jrn>

<eref>16. World Health Organization. Draft landscape of COVID-19 candidate vaccines [Internet]. Geneva: WHO; 2020 Jul 28 [cited 2020 Jul 30]. Available from: https://www.who.int/publications/m/item/draft-landscape-of-covid-19-candidate-vaccines</eref>

<jrn>17. DiMasi JA, Grabowski HG, Hansen RW. Innovation in the pharmaceutical industry: New estimates of R&D costs. J Health Econ. 2016;47:20–33 PubMed.</jrn>

<eref>18. World Bank. GDP per capita (current US$) [Internet]. Washington (DC): World Bank; [cited 2020 Jul 30]. Available from: https://data.worldbank.org/indicator/NY.GDP.PCAP.CD</eref>

<unknown>19. To access the appendix, click on the Details tab of the article online.</unknown>

<jrn>20. DiMasi JA, Grabowski HG. The cost of biopharmaceutical R&D: is biotech different? Manage Decis Econ. 2007;28(4–5):469–79.</jrn>

<jrn>21. Gouglas D, Thanh Le T, Henderson K, Kaloudis A, Danielsen T, Hammersland NC, et al. Estimating the cost of vaccine development against epidemic infectious diseases: a cost minimisation study. Lancet Glob Health. 2018;6(12):e1386–96 PubMed.</jrn>

<jrn>22. Sertkaya A, Wong H-H, Jessup A, Beleche T. Key cost drivers of pharmaceutical clinical trials in the United States. Clin Trials. 2016;13(2):117–26 PubMed.</jrn>

<jrn>23. Ellison G, Ellison SF. Strategy entry deterrence and the behavior of pharmaceutical incumbents prior to patent expiration. Am Econ J Microecon. 2011;3(1):1–36.</jrn>

<jrn>24. Bøler EA, Moxnes A, Ulltveit-Moe KH. R&D, international sourcing, and the joint impact on firm performance. Am Econ Rev. 2015;105(12):3704–39.</jrn>

<jrn>25. Lee C-Y. Industry R&D intensity distributions: regularities and underlying determinants. J Evol Econ. 2002;12(3):307–41.</jrn>

<eref>26. Wong CH, Siah KW, Lo AW. Estimating probabilities of success of clinical trials for vaccines and other anti-infective therapeutics. MedRxiv [serial on the Internet]. 2020 Apr 14 [cited 2020 Jul 30]. Available from: https://www.medrxiv.org/content/10.1101/2020.04.09.20059600v1</eref>

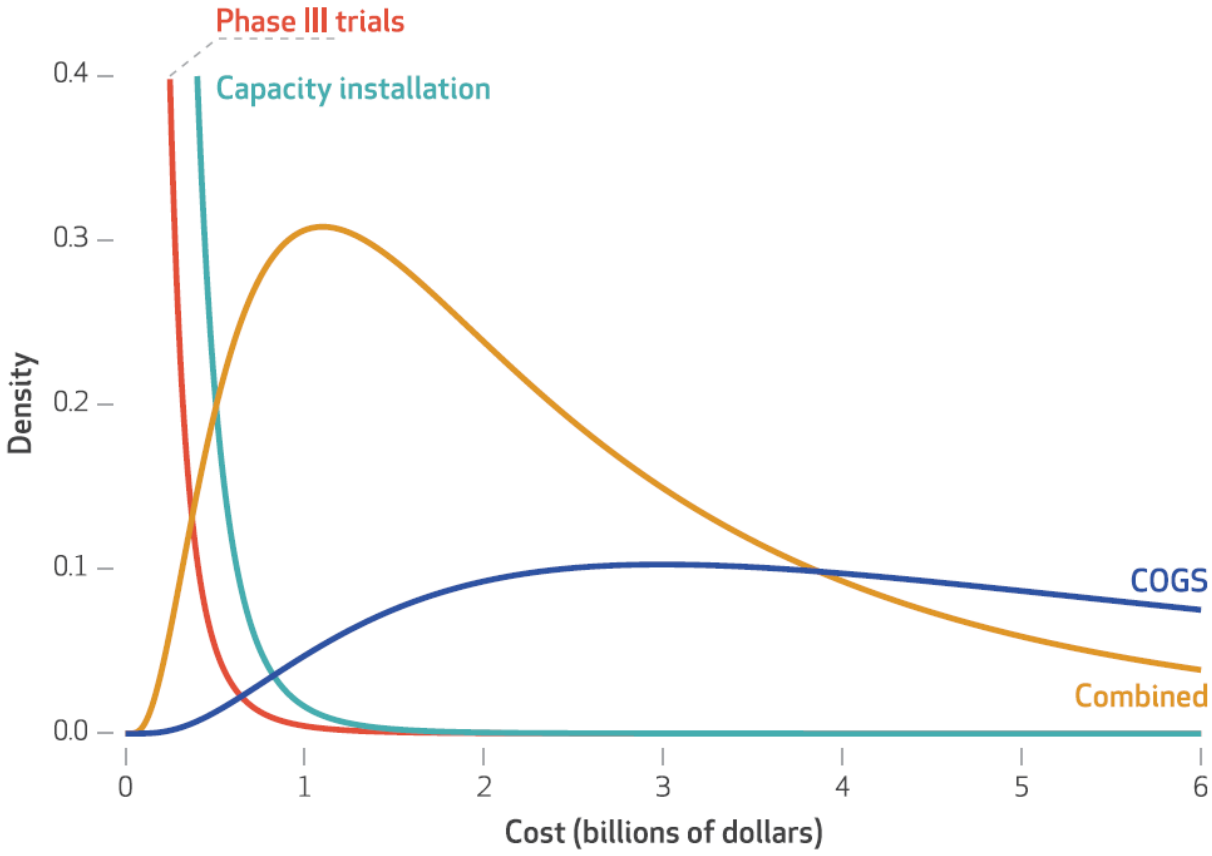
<eref>27. Mahshie A. Operation Warp Speed sets “goal” of 300M coronavirus vaccines by January. Washington Examiner [serial on the Internet]. 2020 May 15 [cited 2020 Jul 30]. Available from: https://www.washingtonexaminer.com/policy/defense-national-security/operation-warp-speed-sets-goal-of-300-million-coronavirus-vaccines-by-january-2021</eref>

<eref>28. Athey S, Hoyt K, Kremer M. Everyone wins from vaccine cooperation. Project Syndicate [serial on the Internet]. 2020 May 14 [cited 2020 Jul 30]. Available from: https://www.project-syndicate.org/commentary/covid19-vaccine-global-diversified-portfolio-by-susan-athey-et-al-2020-05</eref>

<jrn>29. Yamey G, Schäferhoff M, Hatchett R, Pate M, Zhao F, McDade KK. Ensuring global access to COVID-19 vaccines. Lancet. 2020;395(10234):1405–6 PubMed.</jrn>

EXHIBIT 1

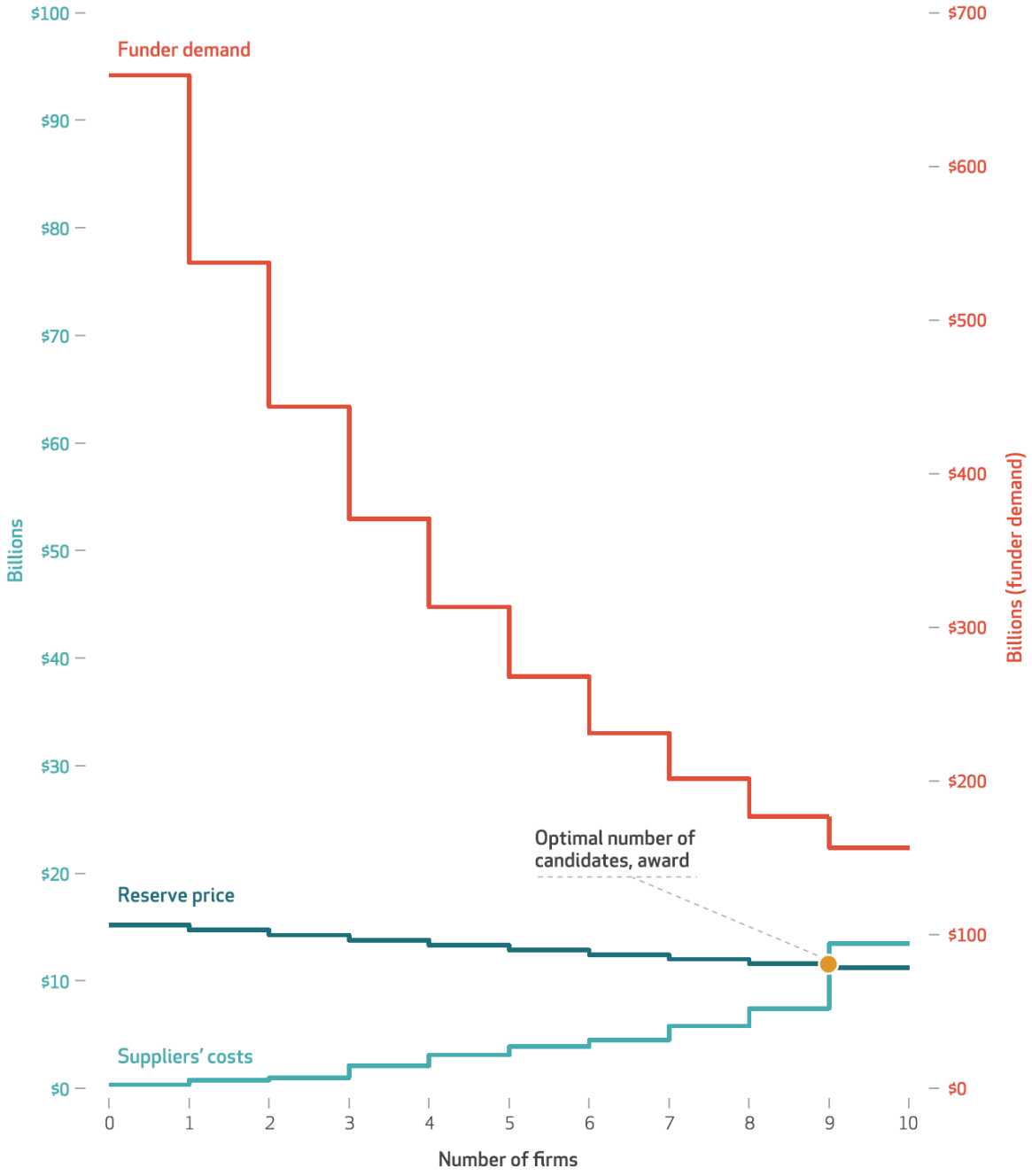
Estimated cost distributions in modeling of push-funding mechanisms for COVID-19 vaccine development



SOURCE Authors' analysis of Coalition for Epidemic Preparedness Innovations survey data. **NOTES** Lognormal distributions of investment costs for separate stages (Phase III trials, capacity installation, and cost of goods sold [COGS] curves) are estimated via maximum likelihood from survey samples for each stage. Lognormal distribution of combined costs was obtained by aggregating the separate lognormals via the Fenton-Wilkinson approximation. The lognormal distribution of combined costs is expressed in terms of ex ante expected costs. Because COGS are not expended at risk but are expended only if the firm has a successful vaccine, they must be weighted by the probability that costs will be expended (that is, probability of success) when added into the distribution of combined costs. All curves were drawn for the baseline scenario in which a firm produces 750 million vaccine doses in a year.

EXHIBIT 2

An example illustrating the inner workings of a pull-funding mechanism for COVID-19 vaccine development



SOURCE Authors' calculations. **NOTES** Funder demand reflects the social value of incremental supplier capacity. The downward steps capture the declining value of using incremental capacity to serve lower-harm countries. The optimal funding mechanism sets a reserve price below funder demand. The intersection between the reserve price and the ascending schedule of suppliers' investment costs (relating to the left-hand *y* axis) determines the optimal number of candidates and supplier award, indicated by the circle. The steps of "suppliers' costs" are drawn accurately for a simulated draw of costs in the baseline scenario. Funder demand is so relatively high that it requires a scale an order of magnitude larger (right-hand *y* axis) to preserve the other curves' legibility.

EXHIBIT 3

Simulated outcomes in COVID-19 vaccine development scenarios

Scenario	Mean of outcome variable across simulations: Selected firms (count)	Completed projects (count)	Award for success (billions)	Spending (billions)	Net program benefit (trillions)
Baseline	9.8	2.9	$37.7	$110.4	$2.8
Firm capacity					
Reduced to 375 million doses	9.9	3.0	22.5	66.6	2.0
Increased to 1.5 billion doses	9.6	2.9	60.6	173.7	3.6
Probability of firm success					
Reduced to 10%	9.9	1.0	48.6	48.0	1.3
Increased to 50%	9.6	4.8	31.0	148.7	3.6
Number of candidate firms					
Reduced to five	4.9	1.5	44.5	65.7	1.8
Increased to twenty	19.0	5.7	29.1	166.3	3.8
Probability pandemic ends each month					
Reduced to 0%	9.8	2.9	41.0	120.6	3.9
Increased to 10%	9.7	2.9	34.8	101.2	2.0
Alternative modeling assumptions					
Two doses for immunity	9.7	2.9	36.5	106.4	1.9
10% of COGS invested at risk	9.7	2.9	43.4	126.3	2.8
50% of capacity invested at risk	9.8	2.9	37.4	109.5	2.8
Alternative mechanisms					
Pull funding, random allocation	9.7	2.9	33.5	97.0	0.7
Idealized push funding	10.0	3.0	—[a]	31.1	3.0
Free market without mechanism	10.0	3.0	—[a]	1,375.0	1.8
Add within-country heterogeneity in vulnerability					
Pull funding, efficient allocation	9.7	2.9	37.1	108.4	3.2
Pull funding, vulnerable first	9.7	2.9	34.8	101.1	2.8
Free market without mechanism	10.0	3.0	—[a]	1,375.0	1.8

SOURCE Authors' calculations based on one million simulations. **NOTES** In the baseline scenario, ten firms each have a yearly capacity of 750 million doses, a 30 percent chance of success, all capacity invested at risk, and no cost of goods sold (COGS) expended at risk; a single dose provides full immunity; the pandemic ends each month with probability 5 percent; and populations are homogeneous within countries. In the baseline scenario, a pull-funding mechanism involving efficient allocation (doses allocated in order of consumer value) is offered. Appendix exhibit A7 provides histograms for outcome variables in the baseline scenario (see note 19 in text). [a]Award entry omitted because scenario does not involve pull funding.

Acknowledgment

A preliminary version of this article was presented in the Dickey Center International Relations and Foreign Policy Seminar on May 22, 2020, and the Masters in Healthcare Delivery Sciences Seminar on June 18, 2020, both at Dartmouth College, Hanover, New Hampshire. Kendall Hoyt and Christopher Snyder are grateful for funding from the Nuclear Threat Initiative for initial research on this topic. Snyder receives textbook royalties from Cengage Learning. The authors thank Sophie Smith and Blake Dignes for excellent research assistance; Amrita Misha for editorial assistance; and Susan Athey, Michael Kremer, Alex Tabarrok and the other members of the Accelerate Health Technologies research group for helpful conversations. The authors are grateful to the editors (including Don Metz) and anonymous reviewers at the journal for extensive, insightful comments, which substantially improved the manuscript.

BIOS for 2020-00646_Snyder

Bio1: Christopher M. Snyder (chris.snyder@dartmouth.edu) is the Hyatt Professor of Economics, Department of Economics, Dartmouth College, in Hanover, New Hampshire.

Bio2: Kendall Hoyt is an Assistant Professor of Medicine at the Geisel School of Medicine at Dartmouth.

Bio3: Dimitrios Gouglas is a Senior Portfolio Manager at the Coalition for Epidemic Preparedness Innovations (CEPI) in Oslo, Norway.

Bio4: Thomas Johnston is a Senior Consultant, Business Development, at the Coalition for Epidemic Preparedness Innovations (CEPI) in Washington, D.C.

Bio5: James Robinson is a Senior CMC Consultant and Vice Chair of the Scientific Advisory Committee at the Coalition for Epidemic Preparedness Innovations (CEPI) in Washington, D.C.