OPINION ARTICLE

Option-based guarantees to accelerate urgent, high-risk vaccines: a new market-shaping approach [version 2; peer review: 2 approved]

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Abstract

Accelerating the availability of COVID-19 vaccines is critical to preventing further waves and mitigating the impact on society. However, preparations for large-scale manufacturing, such as building production facilities, are typically delayed until a vaccine is proven safe and effective. This makes sense from a commercial perspective, but incurs great costs in terms of lives lost and damage to the economy. Several policy options are available to reduce this delay, all of which involve incentives or subsidies to invest in production facilities. We review existing approaches, then propose a novel alternative using “option-based guarantees” in which the government commits to paying a proportion of the manufacturer’s preparation costs should the product turn out not to be viable. Counterintuitively, this “payment for failure” is appropriate because in the case of success, a company makes a profit from the product itself, and does not need additional money from the government. While other approaches have critical roles, we argue that option-based guarantees are the most promising approach to ensuring a rapid vaccine for COVID-19. Compared to the alternative approaches, they reduce both costs to the government and risk to the companies, while maintaining an incentive to produce a high-quality product quickly and at scale.

Keywords

Vaccines, Advance market commitments, Health economics, Financing mechanisms, Public Policy

This article is included in the Disease Outbreaks gateway.
Introduction
The urgent need for a COVID-19 vaccine was widely recognized, with governments setting ambitious targets for timelines, testing, and approval. Even now that early candidates have been approved, more doses and likely additional vaccines would be useful in accelerating supply. A recent op-ed by Nobel Prize winner Michael Kremer and colleagues\(^1\) noted that “we need multiple shots on goal” because a 90% chance of finding a successful vaccine requires funding 15–20 candidates. While the top candidates were already pushing forward with manufacturing well in advance of clarity about efficacy, longer-term safety cannot yet be evaluated, costs are high, and some are likely to be difficult to deploy to developing countries due to refrigeration requirements.

In addition, there are economic issues that proved to be critical barriers for vaccine development. It is not coincidental that despite hundreds of candidates which were quickly announced, the largest companies were by far the fastest to conduct trials, and to begin manufacturing. Companies with a smaller chance of being first to market have little incentive to invest in very expensive production facilities before their product achieves regulatory approval\(^2\). Even now that top candidates are nearly certain to be deployed, at least for emergency use, scaling up production of alternative vaccine candidates is likely to add months to the overall timeline, costing thousands of lives and many hundreds of billions of dollars of lost GDP – far more than the cost of preparing to manufacture products that do not end up reaching the market.

Many candidates
Perhaps more concerning, the first successful vaccine is not necessarily the best option.

Vaccine efficacy can vary widely. While the world was lucky that mRNA vaccines and other early vaccine candidates proved very effective, it was by no means obvious that one of the front-runner candidates would be approved. The FDA initially announced that it will approve vaccines which are only 50% effective, far short of the level needed for herd immunity, much less near-full protection\(^3\). If early vaccines had been in fact only partially effective, or those vaccines are found to have longer term safety issues that present major drawbacks despite approval, investment in alternatives may still become a priority. And even if none of these problems occur, supplies of the initial groups of vaccine candidates will be in short supply for months, because the delay in investment has led to delays in scaling up. For the same reason, there will be delays in the production of any additional candidates which are found safe and effective.

A more diverse portfolio of options reduces the risk that a small group of vaccines are all insufficient, or that none are safe or effective enough to be approved. Even if this risk were low, the costs of failure would be high enough to warrant additional efforts. A critical task for governments is therefore to reduce delays due to risk-avoidance by firms so that multiple vaccines are developed and manufactured, thereby increasing the probability of finding a viable candidate and accelerating its availability. Before introducing solutions, however, it is worth reviewing part of the current landscape on which these solutions will operate.

Vaccine development funding and market failures
There are a variety of mechanisms by which biomedical research, including vaccines, can be funded. This starts with the funding of basic research by governments, universities, and foundations, and continues through to mechanisms we discuss below for supplementing extant measures. In between, there is translational research, corporate research and development, and production costs. The funding for these stages comes from capital markets or private investments, or from nonprofits, nongovernmental organizations, and governments.

Despite these funding sources, there seem to be market failures, where socially beneficial products like vaccines are not produced because the firm-level incentives are insufficient to overcome the firm-level costs and risks.

It is useful to distinguish between two market failures that are implicated here. The first is a buyer/seller mismatch, where a market would exist for a product, but producers are unaware, or are concerned that the market will not buy sufficient quantity to justify investment. The second is a risk tolerance mismatch, where the socially optimal level of risk-taking is higher than the level for individual firms, so firms will not take risks in developing something that may not be purchased. This mismatch is particularly acute for smaller firms that cannot afford to absorb the loss from failures, but it also applies to larger firms, which may have high opportunity costs of capital.

Potential solutions
For a pressing need like COVID-19 vaccines, a solution to the market failure provided by government or another organization must address multiple economic problems simultaneously. First, it needs to create incentives for companies and investors to take on high-risk projects, many of which have individually low probabilities of success. Second, it needs to create a motivation to scale up production capacity before the success of different approaches is known, to ensure timely availability. Finally, it should do these two things in ways that do not incentivise throwing money at projects that are too unlikely to succeed.
These different issues apply differently to different firm types, of course. Smaller firms have less capital, and less ability to raise capital, as well as a lower ability to diversify against the risk of long-shot projects. They are also far less able to invest in manufacturing. Larger firms, on the other hand, are far better at regulatory capture and finding ways to benefit from programs that could allow wasteful spending.

Several classes of solutions have historically been used to foster innovation: prizes, government programs, guaranteed demand, and for vaccines specifically, advance market commitments. While all are limited in their ability to compress timelines, each has significant advantages in addressing at least one of the market failures, or is useful for some firm types. A new approach we propose, option-based guarantees, seems particularly well suited to mitigating the risk tolerance mismatch for smaller and newer firms, some of which are pursuing novel ideas. This could have been critical to ensure a diversity of COVID-19 vaccine candidates, and could still foster innovation in vaccines more broadly.

Prizes
Governments and private philanthropists can offer financial rewards for breakthroughs or solutions to a scientific problem. In the current scenario, a prize could be offered to companies that have a vaccine approved. Alternatively, companies could compete to offer the best idea for rapidly scaling up vaccines, and a contract to produce them could be part of the prize. By only paying out for successful solutions – or perhaps not any, if certain criteria are unmet – prizes are a fairly inexpensive option that incentivises innovation. This approach has a long history, and has been used by governments recently in the US and abroad.

These cases illustrate that prizes are useful for spurring new areas of research, but primarily attract large firms or well-funded new entrants. This is partly because they require investors to supply and risk capital, while paying nothing to firms that “lose,” thereby failing to address (or worsening) risk tolerance mismatches. This is particularly difficult for smaller firms. The hope is that many firms would participate due to the increased gain in case of success, but there will not be adequate financial incentive for them to do so unless the probability of success is high, the investment is nearly viable without a prize, or the size of the prize makes the investment an expected gain despite the risk. These conditions seem unlikely to be met in the current circumstances, where it is likely that only a few of the many vaccines will ever be made widely available.

Another disadvantage relates to timing. Prizes are often appropriate for early-stage investments in projects that have little short-term chance of profitability, but which have a clear path to success. In the current situation, where speed is critical, the decision would ideally be immediate and certain, rather than contingent and post-success. This means that prizes do not address the risk mismatch issue. Not only this, but unlike the alternatives outlined below, because they are contingent upon success, prizes cannot be used or borrowed against to fund the project.

These drawbacks mean that, in the present case, prizes are unlikely to lead to a diversity of high-risk approaches.

Government programs and public-private partnerships
Another alternative is the “Apollo program” or “Manhattan Project” approach, where the government directly invests massively in projects. Government agencies often enter into agreements, as the US Biomedical Advanced Research and Development Authority and others have done for COVID-19, to develop treatments, vaccines, and diagnostic tools. But this approach requires government expertise, and requires selecting one or a few projects to focus on. As a consequence, projects that are not funded, which are the majority of projects, languish unless and until the primary projects fail. It also favours well-connected and larger firms.

A common variant of direct government investment is public-private partnerships (PPPs). These share the risk between government and private companies, which allows the government to leverage private companies’ expertise. PPPs can be an effective means of achieving social objectives, but such deals generally take a long time to negotiate and implement, are complex in ways that can make regulatory capture a larger problem, and are usually best deployed when a single approach is needed.

Thus, a government-led approach is promising for relatively predictable projects, such as building test-and-trace infrastructure. In contrast, a key goal of higher-risk investments in vaccine candidates is to build a diverse portfolio of investments with an overall high probability of ensuring needs are met more quickly than markets allow on their own. Because multiple approaches are needed and the negotiation and development process is limited by government capacity, neither direct government funding nor PPPs are likely to be the best option for creating a large and diverse portfolio.

Purchase orders and advance market commitments
Another approach is to pre-order vaccines. This has been done successfully by governments in the past, and in this case it could provide capital well before efficacy or safety is established. This would legally guarantee that producers have a market and that the company will supply the product, thereby reducing risk to both parties.

Kremer, Levin, and Snyder (2020) present a version of this called advance market commitments (AMCs), which are purchase orders contingent on successful development. These have been used successfully for “technologically close products,” such as a pneumococcal conjugate vaccine. They are a particularly valuable tool when few of those who would benefit from a vaccine are able to afford it, in which case development is only economically feasible with an outside funder, though this does not apply to COVID-19.

However, this approach has several drawbacks, which the authors identify. First, both purchase orders and AMCs require choosing which approaches to fund or waiting until funding is not necessary to jumpstart production early. Governments’ track
record of “picking winners” is less than stellar, and any such decisions would inevitably be highly politicized. Second, the government or other funder would need to negotiate prices and contractual details before companies would be able to start. Not only might this be a lengthy process, but vaccine manufacturers have a significant advantage in such negotiations, and there is potentially significant room for regulatory capture or windfall profits on the part of companies.

In addition to these problems, for COVID-19 this approach requires the government or other sponsor to commit to purchases of many still-unproven products. For this reason, it would need to contract with many different companies – the more the better, to improve the chances of a viable product – but committing to purchasing many vaccines when only a few will be needed would be very wasteful. In addition, purchase orders would potentially involve commitments to purchasing products not shown to be safe, which may be illegal for government agencies. It also gives far less incentive for producers to improve quality, speed, or cost-effectiveness through innovation. In the present crisis, these shortcomings are especially pressing.

A variant on AMC proposed by Athey et al.5 to address COVID-19 would combine the direct investments (“push”) of PPPs with the typical AMC mechanism of a precommitment to purchase (“pull”) the first resulting product to come to market. This push-pull approach improves on both direct investment and PPPs; but because the government funding for purchasing may be exhausted before it reaches market, it has drawbacks similar to prize competitions in that it leaves companies with the bulk of the risk from overproduction if they are not first to market. This means that AMCs are an option regardless of which “push” option is selected.

Option-based guarantees
In March and April of 2020, we suggested6 a new approach for governments to “push” vaccine production, which is to enter into agreements with companies using put options. A put option (as in “put up for sale”) gives the holder the right, but not the obligation, to sell an asset, by (or on) a specified date, to the provider of the put. In this case, the put option would give companies the right to sell a portion of their investment in vaccine production to the government, i.e. at a guaranteed loss. Because there is no obligation to exercise the put, companies could sell viable products as usual, and would only use the option if their product turns out to be non-viable. If structured well, options can also align incentives in several other ways.

To understand how this would work, we start with an example, then note possible variants on the idea. Following this, we discuss the advantages of the proposal, and the implementation and political challenges it may face.

Illustrative example
Suppose, optimistically, that a manufacturer thinks it will be able to produce 100 million doses of a vaccine within six months, but is delaying investment in production facilities because the vaccine’s Phase 3 trial results will not be available for a year. Once the result is known, it will begin to invest in the production, and if there are no unforeseen obstacles, have the vaccine available six months later.

Under the proposed scheme, the company can approach the government with a budget and a timeline, and the government can agree to provide a put option that allows the company to recoup, say, 90% of its eventual costs, capped at the company’s initial project cost estimate, in exchange for the facility and equipment. If the vaccine is viable, the company would not exercise the option, the government would pay nothing, and the company would be able to sell the vaccine normally. If found non-viable, however, the company would have an incentive to stop production and exercise its option as soon as possible. When the option is exercised, a financial audit of costs would take place, and the government would accept delivery of any items purchased, built, and/or produced in exchange for 90% of costs. Delivery upon contract termination is both a potential avenue for the government to recoup costs, and a means to ensure companies do not gain windfall profits from declaring a program a failure, then selling assets.

Variants
A number of variants of this approach are possible, and three are worth highlighting: declining payouts, priced contracts, and conditions on sales. The first two modify the incentives, while the final variant addresses additional concerns about the availability and price of the vaccine.

First, the payout for the put options could be declining over time, so that the payment is, say, 95% at the outset, and declines by a specified percentage, say 1%, each month. This will incentivize companies to exit as soon as possible if they think the project will fail.

Second, instead of providing options to companies for free, the government could charge for the contracts. This would further dissuade unqualified or undercapitalized companies from taking huge immediate risks with small probabilities of success. Prices for such contracts would still need to be a small fraction of the actuarially fair price, otherwise the scheme does not actually provide the needed incentives.

The last of the variants, conditions on sales, is somewhat different, since it is largely unrelated to the options themselves. Put options do not ensure the final vaccine is available at a reasonable price, but nor do they preclude other policy solutions. Because recipients of these options benefit from the program’s guarantee, in exchange for participation the government may claim priority for purchases, cap the profit margin on sales to the government, or cap the price paid by the government for a product. This is reasonable, but care should be taken not to either significantly reduce the incentive to invest, or greatly slow down the process of agreeing to deals. Note also that governments that took on risk to ensure investment in a product might also want to prioritize domestic
purchases, rather than allowing them to be sold internationally. While posing additional challenges for international cooperation, this does not differ from other solutions, and can be addressed in similar ways, such as through international coalitions and agreements. Finally, we note that it may be less than ideal to pursue multiple goals with a single policy. If price controls or similar constraints are desired, they do not need to be tied to funding mechanisms.

Discussion
The use of put options to accelerate vaccine production is a somewhat novel idea. Though it creates incentives and shapes markets in ways similar to other policy tools, it is worth looking at the unique advantages and drawbacks of this approach.

Advantages
First, commercial companies can continue to use traditional methods for financing and operating their businesses without unnecessary government supervision or contracting. New companies can also use these options to help them secure funding from private investors, making the program more equitable to newer firms without requiring direct government investments.

Second, it provides incentives for starting production earlier, but preserves normal market mechanisms to provide high-quality products. Because the market is competitive, and it will be unclear whether other firms will be earlier to market or have a safer product, perhaps with higher efficacy, having an earlier and/or better product on the market will increase sales, and therefore profit.

Third, this approach is guaranteed to have lower cost than direct investment to pay for high-risk products, while preserving market incentives. Increasing the possible cost savings, the government may also be able to resell some items. For example, a plant or equipment designed to manufacture an ineffective vaccine could be resold and adapted to produce a different one. There have been intermittent shortages of other vaccines, so excess capacity may not be entirely wasted.

Fourth, unlike advance payments or contracts, put options do not subsidize companies to undertake projects that they expect cannot succeed, but do allow them to take additional risks in order to accelerate production.

Lastly, it can be implemented more quickly than the alternatives. Private funding that relies in part on the known risk reduction from the government guarantee could replace direct payment by the government. Not only that, but because the calculation of the payment is deferred, the approach could potentially be implemented without extensive and slow negotiations – a very important consideration in the current circumstances where speed is critical.

Implementation challenges
The most critical decision for option-based guarantees is the structure of the payments. There is a tradeoff between payment amounts and incentives for firms. The ideal percentage of costs to reimburse with such a program requires economic analysis, weighing the cost of such a program, which likely involves payment of all or all but one of the put options, against the public benefit of a more rapidly available vaccine.

However, these challenges are not unique to put options. Any incentive for production requires the government to choose projects to fund, and then pick a level of funding. By guaranteeing the payout will be less than the investment, providing incentives for early termination, and enabling cost-recovery through reselling assets, put options reduce the risk of corporate profiteering relative to direct investment and PPPs. In addition, as noted above, AMCs and prizes are compatible with put options as well as those two alternatives.

Perhaps a greater disadvantage is that this is a novel suggestion: similar programs have not, to our knowledge, been tried before. While the proposal has attempted to consider implementation, unforeseen challenges may arise.

The political challenge
An option-based guarantee is a potential political liability. The program may appear wasteful because, perhaps counter-intuitively, payments are only made for unused products and abandoned projects. This may make the program politically unpopular, especially if no successful vaccines are generated, or if the costs outweigh the value of the successes. In addition, put options do not address pricing or local supply, so they do not guarantee that any viable vaccines would become widely available. This potentially makes options far better for researching or manufacturing capacity, rather than the products themselves.

At least four factors should mitigate the political risk. First, as explained above, the payment structure should help to minimise waste, giving less ammunition to opponents. Second, the program could (quite accurately) be presented as evidence of government action to combat the pandemic, which is likely to be popular in the current climate. Third, the government could of course claim credit for any successful products emerging from the program – products that would save or improve many of their constituents’ lives. Fourth, additional mechanisms or clauses in the contract, such as the variants described above, could ensure that the products are sold at a reasonable price.

Conclusion
The optimal approach – or more likely, combination of approaches – to developing healthcare products will vary by disease, time period, and urgency. For this reason, we conclude with a discussion of a few contexts in which option-based guarantees seem most useful, as well as areas where the other reviewed approaches are likely to be superior.

In the case of vaccines for COVID-19, we think that option-based guarantees for constructing production facilities would have been, and still may be, the best alternative for candidates...
that are promising but whose viability, large-scale manufacturing methods, and/or quantity required are substantially uncertain. These types of guarantees are potentially useful in other areas as well, but the selection of funding mechanisms should be made on the basis of the needs and characteristics of each specific product type and need, both in combating COVID-19 and for future pandemics.

We also think that option-based approaches may be useful for funding very costly Phase 2 and 3 trials, perhaps in place of the current model of directly funding large firms. This is especially true for smaller firms that may otherwise delay or under-power vaccine trials to mitigate risks. In this case, they could be paid part of their costs if the product fails to gain approval.

Based on our review, PPP or direct purchase orders are much more appropriate than option-based guarantees for low-risk products. For example, purchasing a large number of a certain vaccine that is already near approval would be ideal if the safety, accuracy, cost, and quantity required are known, the company is trusted, and the paperwork can be done quickly. Antivirals or antibiotics that are already being produced and are likely to be useful may also fall into this category. This approach can also mitigate the risk that a company will be slow to respond to anticipated but uncertain demand.

Athey et al.’s advance market commitments are useful when products are higher risk, but are close enough to being ready that price and quantity negotiations can take place before the decision is made. In such a case, option-based guarantees are less helpful.

In other contexts, such as when innovative solutions with low capital costs but significant conceptual innovation are likely to be needed, prizes for successful innovation are another useful approach for creating incentives for investments. This would potentially be true for new types of point-of-care tests for active infection and new monitoring technologies. Both AMCs and prizes are also useful in combination with any of the proposed “push” funding approaches, including option-based guarantees.

Over the coming weeks and months, choosing the right funding mechanisms could save tens of thousands of lives. The sooner additional companies start these investments, the sooner their products can reduce economic damage, mitigate ongoing risks to the safety of vulnerable communities, and staunch the very high human costs of the ongoing COVID-19 pandemic.

**Data availability**

No data is associated with this article.

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**References**


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Rino Rappuoli
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Simone Pecetta
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Rino Rappuoli: I have no additional comments.

Simone Pecetta: I also have no additional comments and I believe the manuscript is suitable for indexing.

Competing Interests: No competing interests were disclosed.

We confirm that we have read this submission and believe that we have an appropriate level of expertise to confirm that it is of an acceptable scientific standard.

Version 1

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Rino Rappuoli
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The paper proposes one alternative mechanism to increase the incentives to develop vaccines which do not have an attractive market. The authors call this mechanism “option-based guarantees.” Overall, proposing an additional model to develop vaccines when there is a market failure is fine, because we need as many options as possible.

Here are some comments:

1. This proposal is too late for COVID-19 vaccines, as they have been already developed.

2. The authors argue for an option-based approach to help manufacturers in investing in new vaccines by de-risking eventual failures with public money. This approach might be relevant to incentivize development efforts in areas of high public health and medical need.

3. Overall, the manuscript is well written and brings interesting insights on mechanisms that will likely be at the center of the public attention in the upcoming post-discovery phase of COVID-19 vaccines. However, its content seems to be completely detached from present day issues and it is very theoretical. It is not clear how the proposed solution integrates with - or differentiates from - the dozens of private and public initiatives that support COVID-19 vaccine development. Are there already option-based approaches being used for COVID-19 vaccines? If not, why? Are governments or public entities considering such approaches for some of the vaccines under development?

Minor: the authors should update the introduction session as - as of today - two vaccine candidates have already demonstrated high efficacy in interim ph3 analysis without the need of human challenge trials and with much stringent timelines than reported in this manuscript.

Is the topic of the opinion article discussed accurately in the context of the current literature?
Yes

Are all factual statements correct and adequately supported by citations?
Yes

Are arguments sufficiently supported by evidence from the published literature?
Yes

Are the conclusions drawn balanced and justified on the basis of the presented arguments?
Yes

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: infectious diseases; vaccines

We confirm that we have read this submission and believe that we have an appropriate level of expertise to confirm that it is of an acceptable scientific standard, however we have significant reservations, as outlined above.
David Manheim, University of Haifa, Haifa, Israel

Thank you very much for the helpful notes and concerns. We are in the process of finalizing a revised version of the manuscript that addresses the concerns. We respond to the individual points below.

1. This proposal is too late for COVID-19 vaccines, as they have been already developed.

While there are now approved vaccines, manufacturing for COVID-19 vaccines is not obviously a fulfilled need, and still-unapproved second-generation vaccines may still have an important role in fulfilling global demand. At the same time, we agree that at the current time, the proposal is far less relevant. At the time it was proposed and initially discussed with policymakers, this was not yet true. The current paper is the culmination of an initial idea from the beginning of April [1], a presentation of the idea in mid-April [2], discussions with policymakers, and an initial writeup [3] which was discussed seriously, albeit privately, as a policy approach. We have now cited the writeup in the revision of the paper. The peer reviewed publication process is unfortunately far slower than the policy process, and the current manuscript has been a victim of that delay.

We will note that the developed vaccines are still being manufactured far more slowly than would be ideal. An investment of several billion dollars several months ago, earlier during the trials, would have significantly alleviated the current lack of vaccine production capacity. For that reason, it still seems very relevant to the policy discussion to point out that mechanisms to allow this were being proposed in time for them to have been used.

Moreover, it is clearly relevant as a possible approach for future crises. It would be a shame if promising ideas once again only gained traction in academic and policy circles when it was too late to avert catastrophic outcomes.

2. The authors argue for an option-based approach to help manufacturers in investing in new vaccines by de-risking eventual failures with public money. This approach might be relevant to incentivize development efforts in areas of high public health and medical need.

We certainly agree that this approach is viable in some other contexts, and agree that the paper is useful for that context. As we discussed in the paper, the different approaches are relevant for different needs.

We are skeptical, however, that the approach we suggest for COVID-19 is applicable widely outside of the urgent development of a new and promising technology to meet a widely recognized need. We can certainly envision scenarios where the mechanism would be viable, but because the primary advantage is de-risking capital investment, rather than funding development, it seems unlikely to spur great interest unless and until there is a new need for drastic action, or a niche use case can be found to pioneer the method on a smaller scale via a philanthropic investment.
3. Overall, the manuscript is well written and brings interesting insights on mechanisms that will likely be at the center of the public attention in the upcoming post-discovery phase of COVID-19 vaccines. However, its content seems to be completely detached from present day issues and it is very theoretical. It is not clear how the proposed solution integrates with - or differentiates from - the dozens of private and public initiatives that support COVID-19 vaccine development. Are there already option-based approaches being used for COVID-19 vaccines? If not, why? Are governments or public entities considering such approaches for some of the vaccines under development?

We appreciate the feedback. The paper presents a mechanism, and requires policy-decision making and negotiation if it were used in the future to integrate with other mechanisms. The mechanisms which were used seem to have spurred sufficient investment, though it is unclear how much of the credit for this should go to the financing mechanisms.

While we will not discuss the history and context extensively in the paper, we will make a few observations here in the reply. As the paper discusses, the proposal is novel, and while we think there was promise, we are unaware of any earlier suggestions or current plans for using the novel mechanism. This seems to be due to a combination of factors. First, given the prominent role that the US played in financing vaccines, and the political turmoil of the Trump administration, there was reticence on the part of policymakers to try anything which might draw attention to the potential risks. Second, once funding was made available widely for vaccine development, efficiency of the mechanism was relegated to a minor role.

Given this, we note that despite thinking our proposed mechanism is promising for any future pandemics, over-supply of funding was potentially a better choice, and is certainly simpler. Almost any plausible level of overspending on the vaccines to spur faster development and production would have been worthwhile, post-hoc. At the same time, investment in production of vaccines was not as timely or as large as could have been achieved with this model. Soon after this model was first proposed, in April, the Gates Foundation announced it would fund production of the 7 leading vaccine candidates, and it did so by funding GAVI to enter into advance market commitments.

The EU similarly used AMCs, which were paired with funding for production. Unfortunately, as we discussed in the manuscript, the funds are only useful for providing capital, in these cases, to already-large global firms with existing access to global capital markets. Because the purchases are contingent on approval, they do not decrease risk, and so production has been slow. This makes sense for firms; if the purchase agreement is early, the company bears the risk of it not being approved - as seems to have occurred recently in Australia with the UQ/CSL vaccine, where the advance purchase was cancelled.

Moreover, because AMCs are only used after it seems clear a vaccine has a high chance of success, these were not entered into until after June. The stated rationale was that “this Strategy is therefore similar to an insurance policy, by transferring some of the risks from industry to public authorities in return for assuring Member States of equitable and
affordable access to a vaccine.” The proposal put forward here is a more straightforward way to accomplish the first half. The ethics of ensuring supply to some countries at the expense of others aside, as we noted, this does not preclude also using purchase commitments to guarantee supply. Not only this, but provision of funds was slow. Despite early promises, it took until August for the Gates Foundation to give $150m to increase production in India.

Minor: the authors should update the introduction session as - as of today - two vaccine candidates have already demonstrated high efficacy in interim ph3 analysis without the need of human challenge trials and with much stringent timelines than reported in this manuscript.

This is now edited in the revision to reflect the timing of the publication.

Citations:

1. Manheim, D. (2020, April 2). A Simple Proposal for Jumpstarting Vaccine Production. In about 12 months, the world will need to start producing massive quantities... [Tweet]. Twitter. https://twitter.com/davidmanheim/status/1245810066843983872


Competing Interests: No additional interests are disclosed.
new financing mechanism to speed up investment. Specifically, the government will provide vaccine manufacturers with a put option, that if exercised, will require the government to purchase vaccine manufacturing equipment and facilities for a prespecified amount, for example 90% of the cost of developing the facilities. The paper then compares the proposed financing mechanism with existing financing mechanisms and discusses the relative advantages and disadvantages of the proposed mechanism.

Accelerating the development of a COVID vaccine is one of the most pressing challenges of our times and I commend the authors for inventing and developing a new financial mechanism to aid in this acceleration. Their proposed mechanism is a clever compromise between the direct funding of manufacturing approach taken in the US and the advanced purchase commitment approach taken in Europe.

I have two concerns about the proposed mechanism which I outline below and several minor points which might help the authors improve the article.

The article does not discuss how manufacturers will be chosen to receive this option. Since the authors suggest using this mechanism to fund vaccine trials as well as manufacture, the number of companies that one might reasonably consider as applicants is quite large. The Milken Institute estimated there are 214 Covid-19 vaccines in development. Additionally, the option has no downside for the vaccine developer, so there is no reason they would not apply. The mechanism by which vaccine producers are chosen is essential. Because the option is worth more, the more likely you are to fail, offering the option will select producers with the least viable prospects. Additionally, given the difficulty of separating out project specific costs and costs the firms would have paid anyway, the option would attract firms with lower probabilities of success that see the option as away to increase general funding for their operations. The authors should make clear if and how they intend to limit the number of producers who receive the option.

Another issue that could be discussed is the socially optimal number of vaccines. From a social perspective, we would like a large number of safe and effective vaccines. This is both because increased competition benefits consumers through lower prices and population subgroups may respond differently to various vaccines. This reason is why wealthy countries have invested in a diverse portfolio of vaccine and agreed to advanced purchase commitment. However, even if a vaccine is proven safe and effective, a vaccine manufacturer may exercise the put option if they view the vaccine market as crowded and not profitable enough even if additional vaccines would be socially beneficial.

Some more minor points. [Note the first three points below are why I answered partly to the question “Are all factual statements correct and adequately supported by citations?”]

A citation should be provided for the Michael Kremer op-ed article.

The estimate of the monthly costs of the pandemic “tens or hundreds of billions of dollars of lost GDP,” seems too conservative. It is clearly in the hundred of billions of dollars per month even if you are only counting the US. For example, Cutler and Summers (2020) puts it in excess of 800 billion per month.

The claim that a vaccine with 50% efficacy is far short of the level of protection needed for herd
immunity does not seem to be supported by the literature. See for example, Gomes et al. (2020)\textsuperscript{2} which estimate 60-70% immunity as sufficient for herd immunity.

I found the paragraph on page 4 about the timing of prizes lacking precise reasoning. For example, while they cannot be borrowed against, they can help vaccine developers find investors by increasing their profit if they produce a successful candidate. Additionally, the option the authors propose is both contingent and in the future, so this line of thought doesn't really make a distinction between prizes and the option.

It is incorrect to say AMCs require governments to pick winners. The typical AMC requires the government purchase the vaccine only when it is approved as safe and effective by a regulatory body like the FDA or WHO. As such it tends to select firms who believe they have a high likelihood of success.

On page 5 there is a typographical error. “Put options do not ensure the final vaccine is available at a reasonable price, but nor do they preclude other policy solutions." The word but is not needed.

References

Is the topic of the opinion article discussed accurately in the context of the current literature?
Yes

Are all factual statements correct and adequately supported by citations?
Partly

Are arguments sufficiently supported by evidence from the published literature?
Yes

Are the conclusions drawn balanced and justified on the basis of the presented arguments?
Yes

Competing Interests: “Daniel Tortorice works with Data for Decisions (DfD), a consultancy, where he has performed research for clients including GSK, Merck, and Pfizer."

Reviewer Expertise: Macroeconomics, Finance, Value of Vaccination

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard.
David Manheim, University of Haifa, Haifa, Israel

Thank you for your review and comments. We have responded to the points raised below, and are in the process of posting a revision which clarifies many of these points in the text. We have responded to the two major points, then responded to each of the minor points below.

First, the review notes: "The article does not discuss how manufacturers will be chosen to receive this option. Since the authors suggest using this mechanism to fund vaccine trials as well as manufacture, the number of companies that one might reasonably consider as applicants is quite large. The Milken Institute estimated there are 214 Covid-19 vaccines in development. Additionally, the option has no downside for the vaccine developer, so there is no reason they would not apply. The mechanism by which vaccine producers are chosen is essential. Because the option is worth more, the more likely you are to fail, offering the option will select producers with the least viable prospects. Additionally, given the difficulty of separating out project specific costs and costs the firms would have paid anyway, the option would attract firms with lower probabilities of success that see the option as a way to increase general funding for their operations. The authors should make clear if and how they intend to limit the number of producers who receive the option."

We agree that there is some amount of discretion needed on the part of governments, but as we noted in the paper “these challenges are not unique to put options. Any incentive for production requires the government to choose projects to fund, and then pick a level of funding.” While the existence of 214 candidates seems daunting, it is immediately clear that some are more advanced along the track than others (and at this point, many are finished) so the government's choices can be far better informed. Lastly, as a policy analysis, we think the paper is more helpful explicitly leaving this choice to policymakers and the political process, where it will inevitably happen.

However, the mechanism is not costless for manufacturers, since less than the full cost is paid. The option is more valuable to a less viable candidate, but because they have some portion of the funds at risk, despite a guaranteed partial repayment upon failure, they will be less interested in making an investment that is nearly certain to lose money, even if it is only a fraction of the investment.

Additionally, the put option does not provide money upfront, and this means that most smaller manufacturers would need loans. Because of the very high cost of building manufacturing capacity, an option which repays “90% of costs,” as the paper suggests, would mean that failure is still likely to bankrupt smaller firms. For larger firms, we agree that there is a risk that they use the put option to reduce their cost of capital rather than spend more. For smaller firms, lenders will plausibly be willing to make such loans if there is an option in place, but it by no means suggests that lenders will give money to projects which are near-certain to fail – despite the ability to recover most of their investment due to the option, they are unlikely to be repaid in full in that case.

For this reason, we think that the use of options will be limited to firms with a reasonable chance of success – and since only a finite number of vaccines are needed, the number of
such firms which can succeed is, by nature of the problem, small.

Second, the review notes that "Another issue that could be discussed is the socially optimal number of vaccines. From a social perspective, we would like a large number of safe and effective vaccines. This is both because increased competition benefits consumers through lower prices and population subgroups may respond differently to various vaccines. This reason is why wealthy countries have invested in a diverse portfolio of vaccine and agreed to advanced purchase commitment. However, even if a vaccine is proven safe and effective, a vaccine manufacturer may exercise the put option if they view the vaccine market as crowded and not profitable enough even if additional vaccines would be socially beneficial."

We agree that this could be a concern, but suggest two reasons it is unlikely. First, the manufacturer would be publicly claiming failure in a way that is nearly certain to create public backlash. Second, the public is by no means powerless in such a scenario – any philanthropist or government that wishes to see the vaccine produced has every right, and a significant incentive, to offer funds or contracts to urge a producer of, say, the 5th or 6th vaccine which is found effective and safe to continue despite their otherwise unprofitable situation.

Regarding the more minor points, we have responded below.

**A citation should be provided for the Michael Kremer op-ed article.**

Thank you - this oversight is now corrected.

**The estimate of the monthly costs of the pandemic “tens or hundreds of billions of dollars of lost GDP,” seems too conservative. It is clearly in the hundred of billions of dollars per month even if you are only counting the US. For example, Cutler and Summers (2020)1 puts it in excess of 800 billion per month.**

Thank you for pointing this out - we have clarified. At the time the paper was initially written, the situation was less clear, and the estimate was clearly very conservative/optimistic.

**The claim that a vaccine with 50% efficacy is far short of the level of protection needed for herd immunity does not seem to be supported by the literature. See for example, Gomes et al. (2020) which estimate 60-70% immunity as sufficient for [herd] immunity.**

The occasional discussion of successful immunization with lower numbers of vaccinated individuals rests on a number of very dicey assumptions. While the point is mostly irrelevant to the current paper, it is sufficient to note that, to be generous to the assumptions of those promoting the vaccination of superspreaders, it seems extremely optimistic to think that countries which cannot manage viable test and trace programs will nonetheless be able to identify the future superspreaders prospectively. This also ignores the fact that "superspreader" is a characteristic of the circumstances, and the constantly shifting set of contacts individuals have over time – not simply a property of an individual which can be found in advance. Beyond that, the assumption is that almost all of these (by assumption)
foolhardy individuals – those most likely to contract and spread COVID-19 – would be willing to be vaccinated.

For a very recent preprint that lays out some of these issues, see Fox et al. [1]

I found the paragraph on page 4 about the timing of prizes lacking precise reasoning. For example, while they cannot be borrowed against, they can help vaccine developers find investors by increasing their profit if they produce a successful candidate. Additionally, the option the authors propose is both contingent and in the future, so this line of thought doesn't really make a distinction between prizes and the option.

The key difference between prizes and options is the combination of timing and contingency. As noted, prizes cannot be relied on or borrowed against, so even if they change the overall incentives to succeed, they won't impact overall timelines as significantly. Options, because they are a financial guarantee which can be borrowed against, allow and encourage earlier and larger investments in production; the contingency ensures profitability, rather than enhancing it, as occurs in the case of prizes.

It is incorrect to say AMCs require governments to pick winners. The typical AMC requires the government purchase the vaccine only when it is approved as safe and effective by a regulatory body like the FDA or WHO. As such it tends to select firms who believe they have a high likelihood of success.

We agree that not all AMCs require picking winners, and this is a tradeoff between early funding, and picking winners. We have edited to clarify that this is a tradeoff. By the time a typical AMC can be put in place, market funding is likely available, and it does not reduce risks. If the purchase agreement is early, the company bears the risk of it not being approved - as seems to have occurred recently in Australia with the UQ/CSL vaccine.

On page 5 there is a typographical error. “Put options do not ensure the final vaccine is available at a reasonable price, but nor do they preclude other policy solutions.” The word but is not needed.

Thank you. The British and American usage seem to differ slightly, and it can be used since this contrasts a positive and negative point, but we have amended it to omit the word.


**Competing Interests:** No additional conflicts of interest are reported.
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