An Advance Market Commitment to Incentivize a Universal Coronavirus Vaccine Before the Next Variant

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Abstract: A new booster dose for Covid-19 vaccine, designed to target the currently predominant Omicron variant, became available in the United States in the fall of 2022, nearly a year after the variant was first detected. This pattern of designing, testing, and distributing a variant-specific booster appears to have become the default response to new variants of concern. We argue that an innovation with realistic scientific potential, a universal coronavirus vaccine, effective against existing and future variants of Covid-19 and related viruses, would provide much more value by preempting new variants. We model the social value of a policy called an advance market commitment that could be used to fund the development of a universal coronavirus vaccine and compare it to a default policy of funding new variant-specific boosters. We find that a universal coronavirus vaccine provides around $700 billion more social value within the United States than the default policy on average across Monte Carlo simulations, even under conservative assumptions. We argue that the cost of such an advance market commitment could be under $5 billion.

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Introduction and Rationale

The original Covid-19 vaccines were the key medical countermeasure against the global coronavirus pandemic. Against the original strain, a full series of the vaccines were extremely effective at preventing infection and transmission, as well as serious symptoms and death. Multiple new variants of concern of Covid-19 have emerged. While the original vaccines remain relatively effective in terms of preventing serious symptoms and death, their efficacy has waned over time. In addition, they are much less effective at preventing infection and transmission with new variants.

To address the waning efficacy against newer variants, a bivalent booster targeting both the original strain and the circulating Omicron strain was developed. The short lag between detection of the Omicron strain in November 2021 (World Health Organization, no date) and its integration into a booster approved in the United Kingdom in August 2022 (U.K. Medicines and Healthcare Products Regulatory Agency, 2022) and in the United States shortly after (Food and Drug Administration, 2022) was an historic achievement. Still, the Omicron variant was able to circulate for nearly a year before distribution of the targeted booster began. For previous variants of concern, including Delta, there was no successful release of a variant-specific booster.

The primary weakness of a strategy that reacts to new variants by developing variant-specific boosters is that even under the most favorable timetables, new variants can spread around the world and kill hundreds of thousands before the new vaccine can be distributed. A secondary concern is that this strategy relies on the general population taking vaccine after vaccine after vaccine, an inauspicious approach in the light of vaccine hesitancy and the less than full uptake of even the original booster dose in the United States.

Vaccines designed to work against most or all coronaviruses, including all variants of concern of Covid-19, are in development in several labs across the world. The history of the original Covid vaccines shows that with financial backing that offsets the risk of vaccine development, pharmaceutical companies are capable of rapid clinical testing and mass production of vaccines. The United States is also capable of rapid distribution of vaccines. The original Covid-19 vaccines became available in the United States less than a year after the pandemic started there. A universal coronavirus vaccine has many advantages over a series of specific boosters developed to respond to each new variant of concern. Most importantly, a universal coronavirus vaccine can be produced and distributed before a new variant causes another wave.

We argue that to encourage the rapid production of such a vaccine, the United States should provide an advance market commitment (AMC) to vaccine manufacturers, pledging the federal government or some other consortium of funders to buy courses of a universal coronavirus vaccine at a pre-specified price provided that the vaccine meets pre-specified efficacy thresholds and receives approval by the U.S. Food and Drug Administration (FDA). A guaranteed market for their vaccines reduces manufacturers’ risk. Currently, vaccine manufacturers face uncertainty about the level of demand for any universal coronavirus vaccine due to vaccine fatigue and competition from boosters and therapeutics. Since an AMC only rewards manufacturers if the vaccine is actually effective, the financial risk to the funders is minimized. Our estimates below will show that the value of such an AMC would be over half a trillion dollars to the United States alone.

The theoretical advantages of a universal coronavirus vaccine are easy to appreciate, and such vaccines are far from theoretical. Dozens of universal coronavirus vaccine candidates are already being developed (Dolgin, 2022), including by research teams based at institutions such as Francis Crick Institute (Ng et al., 2022) and Pfizer and BioNTech (Burger, 2022). Perhaps the most advanced current effort, based at Walter Reed Medical Center, is already in early clinical trials (Dolgin, 2022).

Not every potentially desirable innovation is an equally suitable candidate for an AMC. We also analyzed the
case for an AMC to incentivize an intranasal vaccine that would be more effective in reducing coronavirus transmission than an injectable vaccine. While an intranasal vaccine would have some value, we calculate that the reduction in transmission would be marginal compared to a broadly protective vaccine as the uptake of any new vaccine would likely be too low to achieve “herd immunity” and prevent community transmission. Details on the analysis of an AMC for an intranasal vaccine are provided in the appendix.

**Advance Market Commitments**

An AMC is a contract where a sponsor agrees to purchase a specified quantity of a product at a specified price, provided it meets predetermined benchmarks. Because it encourages the creation of a product without directly funding research or development or production of a product, AMCs are considered a type of “pull funding.”

AMCs reduce the risk to the sponsor. The sponsor only pays for a product if it exists and is produced. In contrast, loan guarantees, research grants, subsidies, and other types of “push financing” sometimes result in no value for the sponsor if the funded effort fails. AMCs also help ensure a large quantity of the product is produced because the subsidy is tied to unit sales. The pre-specified price can ensure that if only one or a few manufacturers succeed, they do not exploit their monopoly positions by charging exorbitant prices, which might exhaust the funder’s budget and limit uptake.

AMCs have been advocated for and used in the field of global health for diseases that primarily affect the global poor. Such diseases tend not to attract research and development investment by pharmaceutical companies, as the financial incentives to produce such products are low (World Bank, no date).

Why is there a need for an AMC to produce a universal coronavirus vaccine that could be broadly used in the United States, one of the most lucrative markets for medical products in the world? Why not just rely on typical market incentives and private demand to encourage pharmaceutical companies to produce a universal coronavirus vaccine if it is technologically possible?

The AMC is desirable because the commercial firm’s private value from developing a universal coronavirus vaccine—its revenue earned from sales of the vaccine—would be substantially below the value of the vaccine to society, thus limiting the firm’s investment incentives. Political pressure, whether implicit or explicit, constrains firms to charge prices well below levels judged as repugnant (Roth, 2007). For example, during the initial period of supply shortages, Castillo et al. (2021) estimated a course of the original Covid-19 vaccine to have an average social value of $5,800 globally, eclipsing the $6 to $40 prices manufacturers were charging at the time. Even without political constraints on prices, individuals would not be willing to pay the whole social value for their vaccination since much of that benefit accrues to others. The benefits of reopening the economy after distribution of Covid-19 vaccines are generalized and not captured by individuals in isolation. Another risk is that faced with the expectation of low prices, pharmaceutical companies might go ahead and develop the vaccine but devote relatively little manufacturing capacity to producing such a low-profit product. In this case, a small fraction of the U.S. population may receive the vaccine (and the most vulnerable could be prioritized), but the overall potential benefits of the vaccine would not be maximized.

Other sources of uncertainty for potential vaccine manufacturers include the risk of low vaccine demand due to vaccine fatigue, competition from strain-specific boosters that in the short-term offer equivalent benefits to patients, competition from highly effective and widely available antiviral medicines, or perhaps even widespread natural immunity or potential declines in new Covid-19 infections. To be sure, all of those sources of uncertainty also factor into the social value of an innovative vaccine and should weigh against any decision to pursue a funding program for it. Indeed, we
will factor all such sources of uncertainty into our analysis of the case for an AMC. However, such factors weigh much more heavily in the firm’s private decision because the firm is already on a thin margin, since it obtains so much less private value from innovating than the social value.

**Analytical Model**

The value of a universal coronavirus vaccine depends on several factors. Does it appear before or after the next variant of concern? If it appears after the next variant of concern, can it be developed and distributed more quickly than the alternative response of a variant-specific booster? Further, the value depends on the expected severity of the pandemic wave caused by the next variant of concern and the ability of vaccines to mitigate the next wave.

To produce an estimate of the value generated by a universal coronavirus vaccine, we conduct 10,000 Monte Carlo runs simulating the emergence of a new Covid-19 wave caused by a new variant of concern, the availability of a universal vaccine, and the availability of a variant-specific booster. We model uptake of the new vaccines on the uptake of the first booster dose within the United States. We assume that the path of the Covid-19 pandemic following this new simulated wave follows the course of the pandemic following the Omicron wave.

Across our simulations, we make relatively conservative choices to produce a conservative estimate of the value of a universal vaccine. Still, the expected value of such a vaccine is enormous.

**Emergence of Variants and Products**

Based on the rate of occurrence of new variants since February 2020, we assume there is a 5% chance of a new wave of Covid-19 beginning each month caused by a new variant of concern. To arrive at this estimate, we look at the arrival of variants of concern for Covid-19 to date. Over the 36 months from the declaration of a Covid-19 emergency at the end of January 2020 to date as of this writing (February 2023), there have been two variants of concern causing Covid-19 waves, the Delta and Omicron. Letting \( p \) be the monthly arrival rate of a new variant of concern, the likelihood of observing the number of variants of concern we have seen, which has a binomial distribution, equals

\[
\binom{36}{2} p^2 (1-p)^{34}
\]

This likelihood is maximized for \( p^* = 5.6\% \), which we round down to 5% to be conservative.

We allow for at most one new variant of concern to cause an outbreak during a simulation run. Of course, we may end up being less fortunate; but we choose to be conservative and understate the risks and thus the value of a universal coronavirus vaccine relative to variant-specific boosters. The universal vaccine is meant to work against all new variants, the booster against one. But there is some probability that a variant-specific booster will retain its efficacy against the next variant of concern, especially if the variants are closely related. Limiting the number of new waves to at most one absolves us from having to make assumptions about how much efficacy the variant-specific booster retains.

We assume that if no new wave begins within seven years (84 months) there will never be a new wave. Seven years without a new variant suggests the rate of new variants emerging is very low or conditions have changed such that humanity has successfully suppressed new variants. This could be through cases being kept so low that there is little chance for mutation, by virulent strains of Covid-19 being outcompeted by low-risk strains that cause substantial natural immunity, or by some other mechanism. With a 5% chance of beginning each month, a new wave occurs in over 98% of our simulations.

Both the original Covid-19 vaccine and the Omicron booster became available to the U.S. population within less than 12 months after the original coronavirus and the Omicron booster were widely circulating in the United States. This suggests that a concerted effort to
produce a universal vaccine or to develop a variant-specific booster could produce a new vaccine that was available within 12 months. Vaccines developed under less urgent conditions typically take much longer to become available, and no other variant has received a variant-specific booster, so we will specify a distribution of arrival times so that 12 months is feasible but optimistic. More specifically, we take the arrival time of a new vaccine to be a normal random variable with mean 12 months and a standard deviation of three months but then censor the draws from this distribution at a lower bound of six months. That is, when a simulated vaccine arrives in fewer than six months, we treat it as arriving in six months.

The estimated arrival of the universal vaccine is based on time from the creation of an AMC that incentivizes it; for this model, we assume that it is created today. The earliest hypothetical arrival of the universal vaccine is six months from today. The estimated arrival of the variant-specific booster is based on time from the start of the next wave, since that strategy requires a pathogen from which to develop the vaccine. This means that the universal coronavirus vaccine is likely to arrive earlier than the variant-specific booster since there is only a 5% chance of a new wave beginning in the first month. The universal vaccine sometimes arrives on the market before the new variant emerges, allowing individuals who take it to be protected in advance.

**Product X**

Vaccines are not the only possible response to Covid-19. Perhaps a new antiviral appears, or new affordable air filters that diminish the dangers of a new wave of Covid-19 are developed. Both such cases would diminish the total value of a vaccine. To account for this possibility, in addition to simulating the arrival of new vaccines, we also simulate the arrival of a new and effective product against Covid-19, which we call “Product X.” Implicitly, we think of Product X as a new, effective, and popular antiviral, but it could also be a ubiquitous form of personal protective equipment or air filtration or some unknown technology.

We model the development and approval of Product X after FDA approval of Paxlovid (Food and Drug Administration, 2021). We assume that the emergence of Product X is normally distributed with a mean of 21 months and a standard deviation of three months, bounded at the lower end of six months. We assume that Product X immediately cuts the deaths from Covid-19 by half when it appears and continues to do so until the end of the simulation in which it appears.

For readers who think the emergence of Product X is too optimistic, we present the value of a universal vaccine with and without the existence of Product X.

**Covid-19 Mortality**

We assume that before a new wave caused by a new variant of concern occurs that Covid-19 deaths occur at the same monthly rate as December 2022, the last month for which we have data. Data for Covid-19 deaths comes from the Our World in Data website (Mathieu et al., no date).

After a new variant emerges, we assume deaths follow the course of deaths that began with the Omicron wave of the pandemic, which in the United States began circa December 2021 (World Health Organization, 2022). For our model, we assume that the deaths caused by Covid-19 will follow the same pattern and number of deaths and cases that occurred beginning in December 2021. Because we allow for the next wave to last 24 months and there have not been 24 months since December 2021, we assume that after the next wave completes the post-December 2021 pattern, it continues to generate the number of deaths and new cases of Covid-19 that occurred in December 2022.

**Vaccine Uptake**

How popular would a new vaccine be? What share of the population would seek out a universal vaccine? We use as a benchmark for the popularity of a new and effective Covid-19 vaccine the first set of booster vaccines released in the United States. A universal vaccine
would protect against more variants than the original booster but use this benchmark to be conservative.

Using the first set of booster vaccines provides data from many months on the popularity of a vaccine and data on the popularity of a vaccine for Covid-19 specifically.

Other potential benchmarks include the annual influenza vaccine, the original Covid-19 vaccine, and the new bivalent booster vaccine. We think the annual influenza vaccine is also a realistic benchmark for a universal coronavirus vaccine. Influenza vaccines are an important public health measure, broadly promoted especially to vulnerable populations, and widely available. Such vaccines have become a routine part of healthcare in the United States for many people and are not dependent upon a general sense of crisis nor extraordinary measures to encourage vaccination such as vaccine lotteries or vaccine mandates by employers. As it turns out, the popularity of the influenza vaccine for the most recent flu season (Centers for Disease Control, 2021) was very similar to the popularity of the original Covid-19 booster vaccine (Centers for Disease Control, no date). Roughly half the population received each vaccine. (See Fig. 1) This perhaps suggests that perhaps half of the U.S. population would seek out a high-value and effective vaccine promoted by the U.S. health system.

The most optimistic benchmark for vaccine uptake would be the original Covid-19 vaccines, which were fully taken by two-thirds of the population. This level is likely too optimistic, as subsequent Covid-19 waves did not prompt the same sense of crisis as the original outbreak.

The final benchmark is the vaccination rates of the new bivalent booster vaccine. One downside to this is practical, as there are fewer months of data to use. Another is that a universal coronavirus vaccine would offer much greater benefits than a new booster and should therefore be more valuable. Further, a vaccine that is created and purchased through an AMC would

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**Figure 1**: Vaccination Rates in Recent U.S. Examples
by definition have met clear benchmarks of efficacy to qualify for the AMC which should contribute to public trust and interest. In contrast, the bivalent vaccine drew controversy by skipping human subject trials before its release (Vogel, 2022).

We also note that in the case of a new Covid-19 variant as deadly as the wave caused by the Omicron variant, it is likely that the popularity of vaccines would increase. A universal coronavirus vaccine would be most popular and most sought out in scenarios where it is most valuable. We assume that both a new universal vaccine and a new variant-specific booster would follow the same vaccine course. While it is possible that uptake of a universal vaccine would be higher as it is more valuable, we assume both vaccines take the same route. If we allowed vaccines to take different routes, the value of the universal vaccine would rise.

Consequently, all figures reported are based on the assumption that a new vaccine is as popular over time as the original Covid-19 booster vaccine and plateaus at the vaccination corresponding to the last month for which we have data. Data on booster vaccine uptake comes from the Centers for Disease Control (CDC). To calculate the average vaccination rate for a month, we use the midpoint of the vaccination rate at the beginning and the end of the month.

We model the new vaccine as only offering any benefits over the first 24 months of the new wave. This conservative assumption is meant to capture factors such as increased natural immunity resulting from a new wave, behavioral changes that might reduce the costs of a new wave (behavioral changes are more more likely when a new wave is not mitigated by effective vaccines), or the absence of vaccines prompting the emergence of another successful response after two years—such as widely available and effective antiviral drugs.

Because the universal vaccine can emerge before the new wave, it can begin providing benefits by reducing Covid-19 deaths from the current rate of death as soon as it is released.

Again, to be conservative, we assume that the first vaccine to emerge (the universal vaccine or the variant-specific booster), will take 100% market share. Thus, the universal vaccine will only generate any value in simulations where it emerges first. This happens across most simulations because it is possible to start working on the universal vaccine today rather than waiting passively for a new variant to emerge. The simulations involve some randomness, so the variant-specific vaccine does beat the universal vaccine to market in some simulations.

Valuing Lives
We assume that preventing a single Covid-19 death is worth $7.5 million. This is the figure generally used by the U.S. Federal Emergency Management Administration (Federal Emergency Management Administration, 2020). As our goal is to present a conservative estimate for the value of an AMC, we choose a conservative estimate for the value of a human life. Others have suggested that higher figures are appropriate. Kniesner and Viscusi (2019) calculated that the value of a statistical life in the United States is worth $10 million. Some other federal agencies also internally use a figure higher than $7.5 million. The EPA suggests using a value of $7.4 million in 2006 dollars which inflation-adjusted is $11 million in 2022 dollars. In 2016, the Department of Agriculture and the FDA valued life at $8.9 million and $9.5 million, respectively (Merrill, 2017).

As the United States federal government funded the original Covid-19 vaccines and is likeliest funder for any AMC, we prefer to use a figure for the value of life that comes from U.S. government use rather than other approaches such as years of life lost.

Our estimated value of a vaccine comes solely from the expected number of deaths from Covid-19 prevented. Readers that prefer a more or less generous value assigned to the value of preventing a single death can adjust our results proportionally. For example, if one prefers to value the prevention of single death
from Covid-19 at $10 million rather than $7.5 million, the values presented for a universal vaccine should be multiplied by 1.33.

**Value of Preventing Infection**

We do not directly estimate the value of preventing a non-fatal infection of Covid-19 in this paper, though such costs are certainly substantial. Glennerster, Snyder, and Tan (2022) estimate that the expected annual costs of pandemics in general exceed $800 billion. While some of these costs are due to deaths, significant societal loss arises from declines in economic output and learning. The authors estimate that across pandemics, 62% of the cost of pandemics come from deaths. This paper represents a very conservative estimate of value for a universal coronavirus vaccine as it only accounts for deaths prevented.

**Estimating Deaths Prevented**

The simulated emergence of each product (vaccines and Product X) and the new variant is rounded to the nearest month. Each simulation runs for 84 months or until the new variant occurs, whichever is longer, and then for another 24 months while death rates follow those of the Omicron wave.

We model the vaccine as preventing deaths proportionally to the share of the population that we estimate will have been vaccinated with the new vaccine each month following its release. We estimate that the new vaccine will be 95% effective at preventing death.

**Simulation Results**

The universal vaccine appeared before the variant-specific booster in 93% of the simulations. A new variant occurs in over 98% of simulations. (See Fig. 2.)

Because we assume the first new vaccine captures the entire market, the universal vaccine only provides value in the simulations where it appears before the variant-specific booster. The value it adds in simulations where it appears second is zero. To calculate the value generated by the universal vaccine in simulations where it appears first, we calculate the value generated by lives saved by Product X and the universal vaccine and subtract the value that would have been generated by lives saved by Product X and the variant-specific booster. We then do the same process across all simulations ignoring Product X.

![Figure 2: Arrival of Variants and Products in Simulations](image-url)

Sources: Author calculations based on 10,000 Monte Carlo simulations of model.
Table 1: Net Social Value of Universal Covid-19 Vaccine

<table>
<thead>
<tr>
<th>Average across simulations</th>
<th>With Product X</th>
<th>Without Product X</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean</td>
<td>$692 billion</td>
<td>$1.08 trillion</td>
</tr>
<tr>
<td>Median</td>
<td>$706 billion</td>
<td>$976 trillion</td>
</tr>
</tbody>
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The value generated by the universal vaccine is highest when it occurs substantially before the new variant. In these cases, it can prevent baseline Covid-19 deaths before the next wave and the vaccination rate can even plateau before the new wave emerges.

The mean value of a universal vaccine ranges from approximately $700 billion to $1 trillion, depending on the inclusion of Product X. Even if we cut our estimated value of human life in half, the value of a universal vaccine would be roughly $350 billion.

Design and Cost of an Advance Market Commitment

Basic Design Features

Any AMC depends on a clear statement of what qualities a product needs to demonstrate before the sponsor of the AMC is obligated to purchase the product. This reduces demand risk for the manufacturer and ensures the sponsor gets the product they value. Some of these characteristics can be drawn from a list of “necessary qualifications” for a universal vaccine drawn up by Morens, Taubenberger, and Fauci (2022), which include the prevention of clinical disease, prevents infection by all sarbecoviruses and merbecoviruses and all infection by viral drift and recombination variants, is safe for pregnant women, is safe for all ages, and several other conditions.

However, a key challenge for determining the necessary characteristics not addressed in Morens, Taubenberger and Fauci (2022) is that we want a product effective against strains that have not yet emerged, for which it is not possible to test vaccines against before approval. This matters because the value of the universal vaccine is highest when it is rolled out and popular before a new wave emerges. Ideally, the AMC would incentivize the development and approval of the product far in advance of any new variants. There are several practical approaches to solving this problem. We would recommend a combination of these approaches, allowing vaccines to fulfill some but not all.

1. Require FDA approval that the vaccine is safe and effective in preventing serious disease for strains of Covid-19 and other coronaviruses that are currently found in humans.
2. Require that the vaccine target an agreed number of spike proteins of coronaviruses that are relatively stable across variants.
3. Allow for the vaccine to work through a mechanism that would destroy or make most viruses ineffective.

The sponsor could provide a payment for the initial vaccine based on sufficient evidence that it would work against future strains (1+2 or 1+3 above) but also provide for a bonus payment if and when it is proven to work against a new virulent strain.

Some of the payment per dose could be delayed for a period of time and would only be released contingent on the universal vaccine functioning against any new variants that emerged across the entire time frame. This would incentivize manufacturers to produce vaccines that are, on the basis of scientific knowledge, believed to function against all coronaviruses, rather than simply producing a quadrivalent vaccine closely tailored to current variants.

One way this structure could work in practice would be for the sponsor of the AMC to offer initial payment for the “universal vaccine” and then, if future bench-
marks are achieved several years later, to release the rest of the funding.

The first payment could be based upon the product demonstrating efficacy against current strains of Covid-19 circulating in the population, demonstrating cross-reactivity against other Covid-19 strains, and expert evaluation at the FDA establishing that the vaccine technology has a strong claim to providing universal, or near universal protection against likely Covid-19 variants.

The second payment could be based on real-world performance over several years. For instance, if the efficacy against severe illness and death of the universal vaccine is equivalent or nearly-equivalent (say within 5%) of new boosters released within five years of the universal vaccine’s release, that demonstrates that the universal vaccine did deliver broad protection against future variants of Covid-19.

One concern might be that if the universal vaccine is popular, it disincentives development of new variant-specific boosters in the future. While avoiding the costs of new vaccine development is a social benefit, if no new boosters are developed due to competition from the universal vaccine, it would be impossible to compare the universal vaccine against new boosters. To avoid labeling the awarded vaccine “universal” due to lack of competition, the second payment could be contingent on both performance relative to new boosters and absolute performance against Covid-19 at the end of five years, with the required level of efficacy determined in advance.

While our model suggests that the universal vaccine is most valuable when it arrives before a booster, firms should be able to receive the full value of the AMC even when a booster already exists. One reason is that it lowers the risk for the manufacturer which is the main point of the AMC.

The other reason is that it is socially beneficial. To present a conservative estimate, we assumed only one new variant would emerge so that a universal vaccine would be less valuable. However, in reality we face the risk of multiple new variants emerging. A universal vaccine would have value in administering to preempt a new vaccine, to stockpile in case of a new outbreak, to produce ancillary benefits against non-Covid coronaviruses like colds, or to distribute to other countries that lack access to variant-specific boosters.

Cost of an Advance Market Commitment

The Congressional Research Service (2021) compiled data on Operation Warp Speed contracts that included the number of doses contracted per vaccine, number of recommended doses making up a vaccine course, and the contract value the manufacturer received. The cost per vaccine course was $40 in the Pfizer/BioNTech contract, $33 in the Moderna contract, $8 in the AstraZeneca contract, and $10 in the Johnson and Johnson contract. (AstraZeneca and Johnson & Johnson also received additional development funding.)

If the goal of the AMC was to purchase enough vaccines to vaccinate everyone in the United States who wished to receive the universal vaccine and we assume that roughly a third of the US population (110 million) wished to receive the universal vaccine, and we base the price on the original contract with Pfizer/BioNTech, a funder would have to commit $4.4 billion in funding.

Would this be enough to motivate a pharmaceutical company to prioritize the development and production of such a vaccine? Levine, Kremer, and Albright (2005) argue that an AMC fund has to be large enough to make investing in that particular treatment or countermeasure attractive relative to the pharmaceutical companies other options. By reviewing pharmaceutical company spending on pharmaceuticals marketed to rich countries, the authors suggest that $3 billion would be sufficient to attract pharmaceutical company investment. Adjusted for inflation, the appropriate amount would be $4.7 billion. This is very similar to the $4.4 billion in funding suggested by the original Operation
Warp Speed contracts. If an AMC of the same size were also offered for new therapeutics, the total cost would be approximately $9 billion.

Given that the expected value of such an AMC is (conservatively) near a trillion dollars, funders who wanted to make investing in a universal coronavirus vaccine could offer higher prices per vaccine course or promise to buy more vaccines, perhaps enough to vaccinate the U.S. population, or perhaps enough to vaccinate the U.S. population and some share of the rest of the world population.

The value of any universal vaccine depends on how quickly it arrives. Ahuja et al. (2021) suggested that an AMC designed to respond to a pandemic, should only offer payment for vaccines delivered within a certain time frame to encourage scaling up manufacturing capability. An AMC for a universal coronavirus vaccine should follow this practice.

**Bundling Support for Vaccines and Therapeutics**

Highly effective vaccines and therapeutics are substitutes, not complements. A vaccine that perfectly prevented infection would dramatically shrink the market for therapeutics. Easily available, fast-acting and effective therapeutics such as a new antiviral in turn reduces the value of a vaccine. People who dislike vaccines because of pain, inconvenience, the expressive value of declining a vaccine, or concern about vaccine side effects would have less reason to pursue vaccination if highly effective therapeutics were readily available.

The expected market for vaccines will be larger when the expected success of therapeutics is low. The expected market for therapeutics will be larger when the expected success of vaccines is low. Market uncertainty for one class of products generates market uncertainty for the other class of product.

This dynamic of various medical countermeasures serving as competitors for market share is natural and would occur without any funder providing support for any AMC. Rapid advances in one product line might discourage further investment in other product lines. Expected advances driven by the existence of an AMC could have the same effect of encouraging some forms of innovation and discouraging others.

Both therapeutics and vaccines are important and are likely to be undersupplied by the market and thus worth governments or foundations considering AMCs to support their development. We concentrate here on vaccines partly because there are reasons that vaccines might be particularly undersupplied (Kremer and Snyder, 2015) and are likely to reach more people. People in remote or rural areas of the United States, people with limited access to the healthcare system, and many people in low-income countries may not be able to expect quick access to therapeutics. In contrast, vaccine campaigns, such as the distribution of the original Covid-19 vaccine, reached large shares of the population in countries around the world.

However, the best policy would simultaneously provide support for new vaccines and new therapeutics. The arguments for why an AMC is a good funding structure for vaccines also apply well to new therapeutics. Of course, a funder could provide an AMC for a new vaccine while providing other types of support for therapeutics. For instance, research grants to groups or firms working on new antivirals, or public awareness campaigns about existing therapeutics like Paxlovid.

**Accounting for Cannibalization of Suppliers’ Other Products**

The number of firms that could plausibly produce a universal vaccine is low. During Operation Warp Speed, the federal government provided support to seven different firms or groups of firms to produce the original Covid-19 vaccine. There are of course more than seven potential entrants into the market for a universal coronavirus vaccine, in the United States and abroad. Still, the number is low. Would a manufacturer hesitate to invest resources in a universal vaccine if it were already...
working on a booster vaccine and thought producing a universal vaccine would result in paying for the development costs of two products but only being able to sell one? If that were the case, some manufacturers might still pursue a universal vaccine to benefit from the AMC, but perhaps the single most capable firm would choose not to.

We think this is unlikely for two reasons. First, companies would understand that even if they forgo producing a universal vaccine to protect their booster market another company might produce one and then they would have a reduced booster market and not have captured the benefits of the AMC. Second, the current bivalent booster is relatively small. Only 15% of the eligible population has received the new booster (Simmons-Duffin, 2022), much smaller than the market that would be guaranteed for a universal vaccine through an AMC. A manufacturer should be happy to trade the small booster market for the market guaranteed for a universal vaccine.

If this was still a concern, one approach to overcome manufacturer hesitation from the risk of market cannibalization would be to simply increase the price paid per dose of the universal vaccine such that it would be profitable to cannibalize sales of its own booster. Alternatively, the AMC could be structured to pay any firm that introduced a universal vaccine and a variant-specific booster a sum per dose equal to the payment guaranteed by the AMC plus some other figure to represent the foregone sale of the booster. For simplicity, it could simply be paid twice as much for each dose of the universal vaccine produced. In this case, the AMC could cost approximately $9 billion for the vaccine alone.

While we think the risk that companies will hesitate to engage in the AMC because of a risk of cannibalization is low, given the benefits of a universal vaccine are so high it is important to mitigate any serious risks. We therefore recommend the value of the AMC be somewhat above $5 billion.

Funder Support

Relation to Current Policy Initiatives

While the pandemic continues, the sense of crisis has faded. One challenge to a proposed campaign for a universal coronavirus vaccine would be the claim that, absent the sense of crisis that prevailed early in the pandemic, political or philanthropic support for a universal vaccine might not exist, regardless of how valuable it could be. Another challenge might be lack of awareness that a universal vaccine for a mutating virus is possible. But recent successes in developing a universal flu vaccine, and past and current political support for a universal influenza vaccine, suggest a case for optimism.

The current influenza vaccines that many Americans take each year are intended to target the strains of influenza predicted to be most prevalent in the upcoming flu season. The efficacy of the flu shot varies per year and requires annual vaccination drives to maintain protection. The National Institutes of Health are now running a Phase 1 trial for a universal flu vaccine, the goal being the production of a vaccine that can induce immunity against not just the strains of influenza predicted to be common in the next year, but across all influenza strains (NIH, 2022). This would also eliminate the need for annual vaccinations to maintain protection against the flu.

Several members of Congress have also repeatedly endorsed investing federal resources in a universal influenza vaccine. The Flu Vaccine Act introduced into this Congress, in both the House and the Senate, proposes spending $1 billion over the next five years to support the National Institutes of Health in support of a universal flu vaccine.

There are also other indicators for support for proactive investment in medical countermeasures. Senator Baldwin’s proposed Disease X Act would require Biomedical Advanced Research and Development Authority and the Public Health Emergency Medical Countermeasure Enterprise to develop plans to create medical
countermeasures for unknown viral threats.

The death toll of the Covid-19 pandemic far outstripped recent influenza deaths and caused massive economic disruption. The ability of the scientific establishment to press forward with research on the universal flu vaccine and at least some political support for a universal flu vaccine suggests that advocates for a universal coronavirus vaccine can feasibly mobilize support for such an initiative in Washington, D.C. The ability to point to advances in developing other universal vaccines is also useful.

**Value of Learning**

The value of an AMC that could speed the development of a universal coronavirus vaccine would be immense, just in terms of mitigating the death and illness toll of future waves of Covid-19. However, another urgent reason to pursue this initiative is that an AMC would provide a valuable model for future viral threats and allow policymakers, researchers, and manufacturers to learn more about the process of targeting a specific viral threat and the value of targeted investment to preempt or respond to such a threat.

The rapid development and approval of the original Covid-19 vaccine surprised many. On one hand, it is a clear reason for optimism. Advances in vaccine technology, federal funding, private enterprise, and regulatory streamlining quickly made an effective vaccine together. This is a reason for hope that future viral pandemics may also be responded to with quickly arriving vaccines. Our proposed AMC suggests using similar mechanisms to incentivize the development of a universal coronavirus vaccine that were used to encourage the development of the original Covid-19 vaccines. The results of such an AMC would give us more information on whether we are in a new golden age of vaccines or were incredibly lucky with the original Covid-19 vaccines.

**Potential Funders**

The most obvious funder for an AMC for a universal Covid-19 vaccine would be the U.S. federal government. The federal government funded the development, manufacture, and distribution of the original Covid-19 vaccine. The federal government has also spent substantial amounts of money to offset economic losses of the Covid-19 pandemic and in support of other measures to protect public health. An AMC would not be large relative to the sums routinely expended by the federal government and would only be paid out in the result of a successful vaccine.

It would also be possible for a large philanthropic funder or a consortium of philanthropic funders to provide funding for an AMC. Financial risk to funders could be offset by such funders purchasing prize indemnity or some other form of insurance against the cost of purchasing successfully developed vaccines.

Insurance has been used by private funders in the past to offset the risk of offering funding to reward scientific advances. A $10 million X Prize for space flight was paid by an insurance company—the funder of the X Prize had purchased an insurance contract against that eventuality.

Finally, individual U.S. states or a consortium of them could also fund such an AMC. California could feasibly fund such an AMC and bring an end to the Covid-19 pandemic without support from any other funder. There is a precedent for California to spend billions of dollars on targeted medical research. In 2020, voters in the state authorized $5.5 billion in funding for stem cell and other medical research (Subbaraman, 2020).
Conclusion

The creation of an advance market commitment (AMC) for a universal coronavirus vaccine offers a potentially immense return on investment and the opportunity to save many lives in the United States and around the globe. The structure of AMCs dramatically limits the downside risk of failure to produce a universal coronavirus vaccine. The use of an AMC also would provide insight into the rate at which pharmaceutical companies can develop and produce vaccines for viral threats. The value of this information for planning and preparing for future pandemics is also substantial. An AMC builds upon lessons from the original Covid-19 vaccine development process and offers the best hope for a permanent technological solution to Covid-19.

Appendix: Intranasal Covid-19 Vaccine

Beyond the attraction of a universal coronavirus vaccine, another proposed innovation and a potential target for an advance market commitment (AMC) is an intranasal Covid-19 vaccine that produces mucosal immunity and not only protects vaccinated people from serious illness and death but prevents them from transmitting Covid-19 to others. Another feature of intranasal vaccines that has attracted interest is the potential for more people to seek out vaccination that only requires a nasal spray to vaccination that requires painful injection.

This appendix discusses the possible advantages of an intranasal vaccine that reduces transmission of Covid-19. We focus on the potential advantages that an intranasal vaccine might have in reducing transmission. In theory, advances in non-intranasal vaccines could also achieve reduced transmission, so the analysis could be construed as applying to those advances as well. We also discuss whether intranasal vaccines would prove more popular than injected vaccines and conclude there is little reason to think so.

We estimate the value of a vaccine that prevents the transmission of Covid-19 and argue that a policy, such as an AMC, that led to transmission-reducing Covid-19 booster would be worth roughly $10 billion in terms of deaths prevented, orders of magnitude less than our estimate for a universal coronavirus vaccine. Of course, one could achieve the sum of those benefits by targeting an intranasal version of a universal coronavirus vaccine. The danger in doing so is that it might substantially lower the probability by limiting the potential candidates. The $10 billion additional benefit is not even worth a small chance of losing out on the between $700 billion and $1 trillion benefit of a universal coronavirus vaccine.

A.1. Would Intranasal Vaccines Increase Vaccination Rates?

It is possible that a vaccine that provides mucosal immunity via a nasal spray (an intranasal vaccine) may be more attractive to Americans than a vaccine administered via injection, and thus encourage greater uptake. People who are afraid of needles might be willing to seek out vaccines that come in the form of a nasal spray.

Based on the history of nasal vaccines for influenza, we are skeptical that intranasal vaccines would result in meaningfully greater vaccination rates. First, available nasal spray vaccines do not make up a large share of vaccines administered to adults. If there were a large number of people who would seek out nasal sprays, we would expect many patients to demand such vaccines or vaccine providers to promote them in order to gain market share. This has not happened.

Further, the introduction of nasal spray flu vaccines did not appear to trigger a clear increase in the influenza vaccination rate. Finally, when the CDC recommended against the use of intranasal flu vaccines for a flu season, there is no evidence that vaccination rates fell.

FluMist was originally approved by the FDA in 2003
for healthy children and adults, up to the age of 49 (Food and Drug Administration, 2003). Figure A1 graphs trends in vaccination rates by age group from data provided by Centers for Disease Control (no date [b]). From 2002, the last year before FluMist, to 2004, vaccination rates for adults aged 18-49 for whom FluMist was allowed increased by 1.6%. For adults aged 50-64 for whom it was not, vaccination rates increased by 1.9%.

Covid-19 is far more harmful to older Americans than children. FluMist achieved meaningful market share among children receiving the flu vaccine but did not among adults. Data from before FluMist was recommended against showed that it only had 8% of market share and was disproportionately popular among children (Joy, 2016).

For the 2016-2017 flu season, the Advisory Committee on Immunization Practices recommended against the use of FluMist. Robison, Richards, and Leman (2017) show that the vaccination rate of children within Oregon did not change following the recommendation against FluMist. Jhaveri (2018) criticizes their conclusion, noting that the vaccination rate for children between the ages of 5 to 12 fell by about 2% relative to the previous flu season, with a smaller decline among younger populations. The data source Jhaveri recommends, the CDC’s FluVacView, also shows that vaccination rates for children aged 13–17 increased as did vaccination rates for each age category of adults in the 2016–2017 season relative to the previous season.

The data on FluMist and America’s flu vaccination rates unfortunately does not comport with the intuitive notion that needle-free vaccines would make vaccination more attractive.

A.2. Cautious Immunocompromised People

The CDC acknowledges that the immunocompromised population probably has a weaker immune response to Covid-19 vaccines than the general population (Center for Disease Control, 2022). In addition, immunocompromised people are already at greater risk of severe illness and death. Even generally very effective vaccines may not provide satisfactory protection for this population. Vaccines that prevent transmission could protect immunocompromised people.

It is unlikely that uptake of any Covid-19 vaccine in the United States would be high enough to provide “herd immunity” or eliminate community transmission of Covid-19. This means that immunocompromised patients, assuming that new vaccines are less effective for immunocompromised people just as previous vaccines are, would still face a higher risk of contracting Covid-19 through typical social engagement and in-person work. However, some immunocompromised people might still benefit greatly. If healthcare workers or nursing home workers took this vaccine at high levels, it could protect immunocompromised people. Likewise, immunocompromised people who limit their exposure to a small number of people—such as immediate family—might be protected if their family took the vaccine. The combination of cautious, social distancing and a transmission-preventing vaccine would have value.

How large is the population of cautious immunocompromised people? Harpaz, Dahl, and Dooling (2013) estimate that 2.7% of U.S. adults are immunocompromised. Given a total U.S. adult population of 258 million, that suggests that roughly 7 million U.S. adults are immunocompromised. In September 2022, the analytics company Ipsos reported that 36% of US adults claim to still be social distancing (Jackson et al., 2022).


The clearest source of value for an intranasal vaccine would be that it induces mucosal immunity, perhaps even producing sterilizing immunity. This could reduce the transmission rate of Covid-19, a value that a universal coronavirus vaccine would not be likely to offer. Of course, a non-universal intranasal vaccine lacks one
of the most important qualities of a universal vaccine: the opportunity to arrive before a new variant emerges.

Given the low uptake of previous booster vaccine doses, it is unlikely that even an intranasal vaccine that provides sterilizing immunity would lead to “herd immunity” and successfully prevent community transmission of Covid-19.

This means that people who would choose to not take such a vaccine would eventually be infected. The value of a vaccine that reduces transmission is that in any given time period, the probability of a non-vaccinated person being infected would be lower. By delaying the expected time to infection, extending the amount of time someone has to receive the vaccine before being infected. We can think of the transmission-reducing properties of such a vaccine primarily benefiting the people who without the transmission-reducing properties would be infected before receiving their vaccine, but due to the delay in exposure and possible infection are only exposed to Covid-19 after receiving and gaining protection from the vaccine. Estimating the value of a vaccine that reduces transmission primarily depends on the size of this population.

How valuable would a universal vaccine that also prevented transmission be relative to a universal vaccine that did not prevent transmission? We assume that in each month, a share of deaths among the unvaccinated population are deferred one month equal to the share of the population that is vaccinated at the time. Consider how this would work in a population of 100. If 10% of the population is vaccinated at time , then 10% of the 90% of the population that is unvaccinated, is not infected but rather exposed to the virus in one month’s time. These nine people’s infections and deaths are deferred one month.

How many of these people will go to be vaccinated before they are infected in one month’s time? We assume the same proportion of these people will receive a vaccination in the next month as the overall proportion of the population that is unvaccinated at time but goes on to be vaccinated at time . For example, if the vaccination rate increased from 10% to 15%, that represents 5.5% of the previous unvaccinated population receiving a vaccine in one month.
Of the nine people whose deaths were deferred one month, 5.5% will now be protected by the vaccine before being infected, and assuming a 95% efficacy rate against death, deferring those nine people’s infections will prevent 0.47 deaths.

We return to our previous 10,000 simulations to calculate the value in lives saved of these infections deferred to a transmission-preventing vaccine.

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Table 2: Value Added by a Transmission-Preventing Vaccine

A universal vaccine is worth hundreds of billions more than a variant-specific booster. However, a universal vaccine that also reduces transmission is worth less than $10 billion more than a universal vaccine that does not reduce transmission according to our model. One option would be to include a bonus under the AMC for a vaccine that, in addition to meeting the standard criteria, also reduced transmission. However, the potential risk of obtaining no product and losing out on an expected $700 billion to $1 trillion benefit is too great to require transmission reduction as a necessary condition to receive any funding under an AMC for a universal coronavirus vaccine.
References


Jhaveri, R. (2018) “Letter to the Editor: these findings are not consistent with national data,” *Pediatrics* 141 (2): e20173679A.


