UNEDITED TRANSCRIPT

Preparing for a Pandemic: Accelerating Vaccine Availability

FEATURING

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MICHAEL KREMER
Some of us were involved in proposing the idea of advance market commitments for vaccines in the early 2000s, and we helped design an advance market commitment for pneumococcus, which is a leading cause of child mortality. And that focused on trying to create incentives for the development of a vaccine that would cover the strains common in developing countries, and also to help make sure that that would be affordable once it was developed.

And that program was funded. Several of us were highly involved in the design. And two vaccines have been developed and have now saved an estimated 700,000 lives. So when this pandemic came around, it was approached by policy makers who were asking could we establish similar advance market commitments for COVID-19 vaccines. And thinking about it, quickly I realized there are some similarities, but also some differences.

We reached out to the leading experts like Susan and others, and we established an informal group called Accelerating Health Technologies with Incentive Design to help think about the financing of health technology for COVID-19 and help expedite the development of vaccines and drug treatments.

So we've been advising governments in the US and abroad throughout the pandemic, and today, I'd like to talk about the working paper that was circulated, but I will also say a little bit of two other papers that are in progress. One covers similar issues of how to stimulate production of vaccines, another one is just thinking about how can we get more out of the existing supply of vaccines. Those two other papers aren't quite ready, but I hope they'll be ready soon.
Let me start out by saying a little bit about Biden's plan. This is pushing on many fronts, vaccine delivery, vaccine production, testing, masks, investing in clinical trials for repurposed therapeutics. I think that's broadly very, very appropriate.

Our work is focused on vaccines, and there I'd note that investments in production and delivery are complements. Vaccines are more valuable the faster we can get the shots in arms, but I think we can we can do a lot more to accelerate vaccination. And just to give a sense of how important speed is, if the US could increase the rate of vaccination from one million per day to two million per day, rough calculations suggest we'd prevent 20% to 35% of future COVID-19 infections and 15% to 20% of future deaths.

We think about this from a global perspective, and adding in the economic perspective, every month, the world is losing $500 billion in short-run GDP alone. If you take a more comprehensive measure of harm that includes long-run health costs, costs in education, you get much, much bigger numbers. So Cutler and Summers, just for the US, estimate $800 billion each month for the US alone. That's actually $16 trillion over a longer period, but if you convert it to monthly, it's $800 billion a month.

So that suggests that if we can-- given those huge monthly costs, the social benefit of expanding manufacturing capacity and delivery capacity is immense. And that's really the starting observation for our analysis and the analysis of this paper.

The time to complete vaccination is just the total population to be vaccinated, whatever that is, divided by the capacity, the annual capacity or monthly capacity. And that means that the putting in more capacity early, and putting-- so in advance of the completion of trials and parallel with trials, which we did to a large extent-- would have been nice to have done more, but we did to some extent-- and putting it in a very large scale is incredibly valuable.

So our estimate is that the last billion courses of annual capacity that have been installed, that the global benefits of that are about $1.740 trillion. Or another way to think about that is what's the value per course of-- and it's $1,700, $1,750 is what we would estimate.

So the sooner this is available, the more it's worth. So having a billion of courses of annual capacity available today rather than six months from now-- imagine we'd waited until the testing was finished before we started the construction process or start installing the capacity. That saved the world $1.2 trillion, or almost $1,200 per course.

So another finding-- so one of our first findings is the early investments we did were incredibly valuable from an economic perspective, as well as a health perspective-- but another conclusion is that even at this late stage, it's still worth investing more in capacity.
So if we think about the world as a whole-- and it's particularly true for the world as a whole, as opposed to just for the US-- if the vaccines could be ready in-- if we could get another billion doses of our annual capacity-- if it would take three months to put that in place, which would be optimistic, they'd be worth $376 billion. But even if it took six months, it would still be worth $165 billion. So tremendous-- it's worth to society a vast amount to put in this additional capacity.

Now here's where the standard issue in economics comes in, which is the social value of this is immense. The private value to a vaccine manufacturer is large, but much smaller.

So if you think about the price of a course of vaccine-- two doses-- that might be for the low-cost vaccines, that's as little $6, or higher costs, we have $30, $40. That's probably because there's social, ethical constraints on pricing, implicit political constraints on pricing. And that's a decision society has to make.

We're not saying that this should necessarily be priced at the social value. But in a setting where the social value is so much greater than the private value, the purely commercial incentives to do things that are quite expensive, to increase capacity or speed capacity, and thus speed the time for vaccination, don't reflect the full social benefits.

And that suggests there's at least a case for governments-- and I think we would all support-- the idea that governments should try to procure that capacity, should try to help pay for companies to put in that capacity. And whether that's-- that's often actually a matter of repurposing savings from existing purposes, not necessarily starting straight into construction. So that's our first set of conclusions.

The second paper that I mentioned earlier-- which is not yet ready to distribute, but I hope will be soon-- it's going to be very important, given that in the short run, since it takes so much time to put additional capacity in place, in the short run, we need to do everything we can to try to get more doses out of the existing capacity.

And there's several possibilities here, and a little bit of analysis suggests there are potential huge benefits. Obviously this is something where health professionals would need to be making the final decision on changing the administration to try to get more people vaccinated with the existing capacity. But so modeling suggests they're worth considering.

So one approach is first doses first. So the UK is allowing up to three months between the first and second doses, and models suggest that will reduce infections and deaths by allowing more people to be vaccinated, even if the first dose isn't quite as effective as two doses.
A second approach is a lower dosing regimen, especially for less vulnerable groups. That's another way to potentially increase the number of people vaccinated. And just the logic of that is if you had half the dose, to take an extreme, you could vaccinate potentially twice as many people. There's some evidence from Moderna and AstraZeneca suggesting some possibilities that they could work.

Obviously this type of idea would have to be subject to medical decisions, but I think a key point here is if we want to have the option of doing this, the option of doing this could be incredibly valuable in terms of the number of additional people that could be vaccinated and the reductions in infections and mortality.

To get that option, we could learn-- we could do things to learn about whether this would work. So if we did large scale trials, we could compare the status quo approach to approaches of having a longer gap between the first and second dose or reducing the dosage.

If you were comparing the existing procedure to these modified procedures, I think there would be lots of people who would sign up for such a trial-- wouldn't it be a problem getting people to sign up-- and you could piggyback on existing distribution. Maybe you wouldn't do this for the highest priority of people, but for somewhat lower priority people, you could do this.

That's not necessarily going to generate a lot of additional revenue for firms because they're not going to make more money if we give two doses-- if we go with first doses first, for example. So we can't expect the firms to necessarily pay for this. It's another case where there's a difference between the social value of learning about this and the private value. So this may make sense for the government to support these types of trials.

And so other approaches to get more out of existing doses could include giving people opportunities to take antibody tests to find out whether they've already been infected, and then to say, those who've been found not to have already been infected would be prioritized for early vaccination, those who'd already been vaccinated might go further back in the queue and get vaccinated later.

Another element-- which might not be so relevant for the US, but it's relevant for many countries-- is there might be vaccines with different efficacies. Some modeling suggests that the benefits from using a 70% effective vaccine that's available now are greater than those than waiting three months for a 95% effective vaccine.

Let me say a few things from an international perspective before handing this over to Susan. My firm has done a lot of work on vaccines R&D, but I'm an economist who specializes in the economics of developing countries, and there was a lot of concern that purchases like the ones the US did would have a negative effect on the rest of the world.

And I think some people probably had a mental model where there was a fixed supply, a certain amount of capacity. The US buys up the doses, somebody else can't use them. I think what we've seen is that the capacity is much greater than some people anticipated early on in the epidemic. So I think there's at least-- I don't want to write off those concerns altogether-- but there's at least some ability to increase the amount of capacity.

And if you do that, then-- if you write contracts appropriately so you actually get capacity increased-- that can not just have the negative effects that some people have focused on, but it can potentially have positive effects in the long run because if we get more global manufacturing capacity, that benefits the rest of the world. At some level, if one country doubles its capacity and vaccinates their population in half the time, that capacity then can move on to work in other countries.

Obviously that depends on how fast-- how much capacity can be put in place, and depends on the nature of the contracts. One lesson-- and I think Susan will pick up on this again-- is we want to make sure if there's another pandemic in the future that we've got lots of capacity in place so we don't have a situation where moves by one country are going to hurt other countries, moves to increase capacity.

Final thing I'll say on the international side-- and I'll conclude here and turn it over to Susan-- is the importance of setting up some mechanism for donation and for exchange of vaccines. So some countries took this sort of approach that we were advocating of before we knew which vaccines were working, putting in orders so that many different companies would-- or multiple companies-- would start building out the capacity.

So they put in orders, in some cases-- I think Canada is the extreme of this-- they actually now are entitled to many more doses than they'll need to vaccinate the population. So this is a situation where they'll be able to make some donations down the road, and even the COVAX facility, which is purchasing on behalf of poor countries, also ordered multiple vaccines.

Now it's easier, technically, to administer just a single or small number of vaccines, so part of our group is working on thinking about how do you set up an exchange, and COVAX, the international body, has announced it's planning to set up such an exchange. And that would allow countries to get the type of vaccines they need in exchange with each other, but would also create an opportunity for high-income countries that have bought vaccines in advance from multiple companies and that have excess doses to donate them, and for those doses to go where they can have a tremendous impact. So I certainly hope that that will be taking place in the future. Why don't I turn it over to Susan to say a few words, and then we can open up for questions.

SUSAN ATHEY

Great, thanks. So just a few more topics. One concern people might have about trying to expand capacity is that maybe we can't absorb that capacity, and I think that's been the narrative for the last couple of weeks in the US, that our capacity-- that we weren't able to deliver.

But in the end, Israel vaccinated 30% of its population in under four weeks, and the US, we expect, should be able to speed up substantially now that they're going and they've set up these large scale sites, and that federal resources are available. And so it seems likely that vaccine production will be the limiting factor, not distribution in most places.

One month matters, so other countries should certainly learn from the US about losing a few weeks where you're not vaccinating as fast as you can is costly. But ultimately, when we're planning for these things, the vaccines themselves are the limiting factor.

A second point just to kind of flesh out a little bit more about contracting, in the paper that we sent you, we talked about how earlier in the pandemic, we were pushing countries very hard to invest at risk. So to install the manufacturing capacity in advance of approvals. There are still things going through approval, so that analysis still matters now, and because of this huge social benefit, investing at risk for something that even has a pretty low chance of success, if it accelerates vaccination of a country's population, that will be worthwhile.

Now we also talk about how we want to contract on capacity rather than doses. So if you think about one example of a contract would be just, give me $100 million doses by the end of March. And that's the way a lot of these things are talked about in the press. Now we don't actually know exactly what the full contracts look like, and so there can be more behind the scenes, and in some cases, you get the idea that there is more behind the scenes, like the contracts are about specific production facilities. But in general, if you just say, deliver me a certain number of doses by a certain date, and you make that contract before approval, the company can make a smaller facility, stockpile doses in advance, still meet its delivery requirements, but then there won't be as much capacity left over for the rest of the world if anything goes wrong in the timeline. The pipe that's spitting out the vaccines is narrower, and that smaller pipe is not as desirable from a social perspective.

Another thing is that if you just contract for doses, a company doesn't base that much problem if they overpromise. So if they promise 100 million to one country and 100 million to another country and there's a setback, everybody just has to wait longer. If they contract for one country first and then another country comes later and then there's a setback, then the country who contracted first won't get what they were initially promised unless the contracts specify that more clearly.

So if a country really specifies the amount of capacity that's getting built, and that it will, say, get the first in-lots off that capacity, they can ensure that the company will actually do what it is that they want them to do and actually have enough capacity to serve the needs. Because in the end of the day, we don't have a lot of recourse. There's not enough vaccines in the world, and so if the company hasn't built enough capacity, there's not that much we can do about it.

Another point that we made was that, in general, we-- in Michael's previous work, they had promoted advance market commitments, which is sort of a market-wide commitment to pay a premium for vaccines, and that would induce firms to incur the development costs at the firm's risk. What we propose in this pandemic is more like direct procurement for the things that you want.

Because the gap between the social benefits and the private cost is so large, it's easier just to tell people what you want if you can observe it, like you can observe they build capacity, that's going to be a more direct way to make sure you get what you want, and in addition, the government bearing the risk is efficient given the large social value here.

And another factor is that all the firms are different from one another, so some firms might be fairly certain they're going to get across the finish line, while other firms are higher risk. And so if you're trying to get lots and lots of firms to invest, a market-wide commitment didn't make as much sense because it would have to be really big to get the vaccines that were less sure that they were going to make it across the finish line to invest.

So it could be very expensive and give too much profits to certain firms-- the firms that had a higher probability of success-- so both from a cost perspective, and just from a making sure you actually get what you need perspective, we advocated for directly reimbursing capacity.

Michael already talked about another topic which is super important, but I just really want to reiterate it. We need to keep learning and developing. We're mass vaccinating people. There's a bunch of people who want the vaccine who can't get it. This is a great opportunity to continue to learn and test.

The pharmaceutical companies don't have the incentive to do that. In fact, there's a disincentive to do that, and so the government should be playing a major role in figuring out things like how long does immunity last, how good or vaccines at stopping transmission, can you mix and match vaccines, how effective are lower doses. And it would be pretty easy to send a set of people home after vaccination with rapid testing kits to accelerate our learning, rather than just measuring symptoms like they did in some of the trials.

Another point about learning we need to keep in development is we need to keep investing in mRNA. We want the cost to come down. It's amazing that we got here. So many people early in the pandemic we're skeptical about mRNA because it had never been done before. There are risks not just in safety and efficacy, but also in manufacturing at scale, trying to manufacture hundreds of millions of doses of something that's never been done.

But the mRNA, in general, is very fast. And so once we now know that it can work, and once we can build the manufacturing capacity, then it's going to be able to respond to mutations and things like that. It can be applicable to other diseases in the future. So we suggest that we should-- investments in capacity from for mRNA are not going to be wasted in any case, so we should be scaling that up as much as possible.

In terms of preparing for the next pandemic, in general, we've seen that every-- one thing after the other. You think we'd learn the first time, but just as we roll from one issue to the next, it can be hard to have enough supply quickly. Economics-- the market tends to work in the long run when prices can reflect value and when supply chains have a chance to adjust, but when there's shortages, markets can get incredibly chaotic.

And so in general, if there's social constraints on pricing, there won't be enough supply. So we both see not enough supply, but also, perhaps, people being afraid to take big financial risks and create that supply because they're not sure if they'll be rewarded, and that uncertainty makes it hard-- especially CEO of a firm producing one thing, they're going to give up known profits, and they don't really know for sure what the environment will look like by the time they repurpose or whether they'll get financially rewarded for their costs.

So we generally want to invest more in spare manufacturing capacity and supply chains. The US already has programs to do this, but they were too small scale, and so we should make them larger. Standardization also can make a big difference. Standardizing inputs like vials can reduce the cost of expanding capacity, especially at the time when you're at risk. You don't know which candidates will succeed, you don't know which candidates will have a manufacturing problem and have to shut down for a while, so the more the supply chain is interchangeable, the more we can shift around and make sure we don't slow down total output.

If we don't have enough capacity, there can be these prisoner dilemmas problems where there's just a bidding war. One country's trying to use emergency authorization or something else to grab stuff for themselves, while if we instead focus on building more capacity, when one country has more capacity, they get finished faster, and then that larger capacity is available to also vaccinate the rest of the world faster. So basically, if one country spends money on jumping to the top of the queue, that doesn't benefit the world as a whole, but if they spend money expanding capacity, they vaccinate themselves faster and the rest of the world.

Last point, Biden's executive orders promoted investment in therapeutics, as well. I have a blog in Health Affairs that you can look at that laid out the need for that, outlining some of the failures we had in 2020, especially around coordinating clinical trials, and also having the right government agencies to make those investments and what institutional changes would better prepare us. So the executive order was for the short term, but a lot of that could be expanded in the long term so that in the next pandemic, we are learning quickly, we are running the experiments so we know what works much faster.