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A LECTURE DELIVERED BY ADRIAN TOWSE ON
25TH JUNE 2020 DRAFT PAPER INCLUDING
EXTENSIVE FOOTNOTES

How should the world pay for a COVID-19 vaccine?

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How should the world pay for a COVID-19 vaccine?

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DRAFT

“How should the world pay for a COVID-19 vaccine?”

[slide 5]

1. INTRODUCTION

Thank you for the introduction. I want to address “How should the world pay for a COVID-19 vaccine?”

[slide 6]

I want to begin very briefly with some important acknowledgements:

- Co-author of the paper Isobel Firth of the OHE
- Kalipso Chalkidou, Rachel Silverman and Ganesh Ramakrishnan from the Center for Global Development, and Hannah Kettler from PATH
- My OHE colleagues.

And a disclaimer - all errors of fact and analysis, and the value judgements (especially those you disagree with) are my responsibility alone

So moving on

[Slide 7]

My agenda is to:

- set out the **objective** we are trying to achieve from a payment or financing mechanism and the **context**
- set a **framework** for understanding **what works** and how we can apply it to getting a vaccine for COVID-19
- particular challenges of COVID-19
- focus on two schemes The Gavi COVAX AMC and the BBAMC
- next steps – putting it all together
- and finally, think about some lessons for pandemic preparedness

Where will I get to?

I want to argue that we need

(i) **the right payment mechanism**

Creating a market for a vaccine with an advance market mechanism based on paying for value is the best way forward. We are currently locking ourselves into a COVID-19 paradigm of publicly funded development and manufacturing, with companies offering to price on a cost-plus basis. I do not think, for reasons I will discuss, that this is the best paradigm for

both getting a vaccine and making it available at cost to LICs. We need to use something closer to the normal paradigm of paying for value and mobilising the private sector to invest at risk, in the expectation that they will get a return if they deliver the health gain that society wants.

and (ii) we need **the money** to resource it to get to where we want to be. A serious commitment of money on the part of the higher income countries to fund the key global initiative to pay for vaccines for the nearly 50% of the world's population who will in Lower income countries (LICs) and lower middle income countries (LMICs).

2. SET OUT THE **OBJECTIVE** WE ARE TRYING TO ACHIEVE FROM A FINANCING MECHANISM AND THE **CONTEXT**

“What is our objective?”

[Slide 8]

What are we trying to achieve from designing a payment and financing mechanism?

We want two things:

- (1) to get one or more vaccines that work¹;
- (2) to give the world's population access to it. That means
 - vaccines developed and manufactured **at speed**,
 - manufactured **at scale** and **delivered** for populations across the world,
 - **affordable** to the low income populations of the world and **cost-effective**², i.e. a good use of scarce resources, in very different health care settings around the world.

So, to the global context

[Slide 9]

The first point to make is that a lot of people have been infected and a lot of people have died. These are the latest numbers from the John Hopkins website. We also have a lot of “collateral” loss of life, as other treatable conditions go untreated because health systems

¹ The WHO has set out a Target Product Profile (TPP) for a COVID-19 vaccine.

² I will discuss whether we need a mechanism that involves paying prices that reflect the “value” of the vaccine or one that pays prices that reflect the “cost” of researching, developing and making the vaccine. But two questions, which are both lectures in their own right, I do not plan to cover today – namely “what is the value of a vaccine?” and “how much of the value should we give to the manufacturer?”

are overwhelmed or because patients are too frightened of getting infected to seek medical help³.

And we have massive economic damage. With consequential effects on people's livelihoods, and their health and education. The World Bank is forecasting a much deeper global recession than we had in 2008/9. The IMF has estimated a loss of economic output of \$9 trillion⁴ for 2020 and 2021.

We already know of the global health and economic benefits of vaccines⁵.

In the words of Bill Gates "Vaccines have saved more lives than any other tool in history. Smallpox, which used to kill millions of people every year, was eradicated with a vaccine. New vaccines have played a key role in reducing childhood deaths from 10 million per year in 2000 to fewer than 5 million per year today."⁶

The cornucopia of schemes to get a vaccine

[Slide 10]

Not unsurprisingly, there are a large number of schemes underway or being proposed to get vaccines developed, manufactured and delivered to people.

A non-exhaustive list is as follows⁷

³ For example see <https://www.bbc.com/future/article/20200528-why-most-covid-19-deaths-wont-be-from-the-virus?ocid=ww.social.link.twitter>

⁴ See <https://blogs.imf.org/2020/04/14/the-great-lockdown-worst-economic-downturn-since-the-great-depression/> The AcceleratingHT proposal we consider later turns this into an estimated loss of \$375 billion per month.

⁵ Immunization is one of the most cost-effective public health interventions, averting an estimated 2 to 3 million deaths every year. As a direct result of immunization, the world eradicated small pox and is closer than ever to eradicating polio. Through vaccination, deaths from measles, a major child killer, declined by 80 per cent worldwide between 2000 and 2017 preventing an estimated 21.1 million deaths. For a review see <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4024226/pdf/rstb20130433.pdf>

⁶ See <https://www.gatesnotes.com/Health/Pandemic-Innovation>

⁷ Proposals that we have not listed include (i) Patent buy out proposals (from Elias Mossialos for the EU and from Aidan Hollis for a form of the Health Impact Fund, based on Kremer 1998) [add references]. (ii) Yamey et al. Funding the Development and Manufacturing of COVID-19 Vaccines. Duke Global Working Paper 20, April 2020. Available at https://papers.ssrn.com/sol3/papers.cfm?abstract_id=3575660 and (iii) we have also seen proposals for compulsory licensing, which is permitted by international agreement under the TRIPS agreement of 1995 (clarified for use in Public Health In 2001 the Doha Declaration) but there are two big problems:

(1) If you license something that you cannot manufacture, then you are no further forward. So proposals for compulsory licensing also suffer from the need for investment in enough global manufacturing capacity that someone is able and willing to supply you

(2) Talking about expropriating someone's intellectual property if they invest and succeed in developing a product, makes it less likely that they will invest. And the reality is that IP is not going to be an issue for LICs with COVID-19 vaccines. The People's Vaccine movement (endorsed by traditionally pro-market institutions such as [the World Bank](#)) are responsive to advocacy demands but multinational pharma companies are [pushing back](#) against the idea of pooling intellectual property (IP) for fear of setting a dangerous precedent which will undermine future innovation. The World IP Organization Director General has stated that "[Focusing on access to non-existent vaccines, treatments or cures, rather than the encouragement of needed innovation, at this stage, may not only represent a misunderstanding of the sequencing of innovation and access, but also create a disincentive to investment in needed innovation.](#)"

1. The US Operation WARP Speed⁸

which aims to deliver 300m doses of a safe and effective vaccine by January 2021.⁹ Congress has set aside \$10billion in the CARES Act to fund this and related measures.

2. The UK government

while the UK government has pledged money to organisations like CEPI, it is also focussing on supporting the development of two national vaccine candidates. It has provided direct R&D funding for two UK academic-led vaccine candidates, at the University of Oxford (in partnership with AstraZeneca), and at Imperial College, University of London. It has also agreed to invest at risk in a manufacturing facility that can be used by AstraZeneca to manufacture the University of Oxford vaccine¹⁰.

3. The Coalition for Epidemic Preparedness (CEPI)¹¹

CEPI launched a call in May to fund covid-19 vaccine development and scale-up manufacturing capacity. It was specifically for vaccines that could be available for licensure in 12-18 months. They have 9 candidates, 5 of which are in clinical testing (as of 23 June)¹². They are aiming to raise \$2 billion to support this and have raised \$1.6 billion so far. In addition, they are estimating manufacturing scale up will cost \$1 billion¹³.

4. The WHO Access to Covid Tools (ACT) Accelerator

([https://www.who.int/publications/m/item/access-to-covid-19-tools-\(act\)-accelerator](https://www.who.int/publications/m/item/access-to-covid-19-tools-(act)-accelerator))

⁸ See <https://www.whitehouse.gov/briefings-statements/remarks-president-trump-vaccine-development/> and Explaining Operation Warp Speed available at <https://www.hhs.gov/about/news/2020/06/16/fact-sheet-explaining-operation-warp-speed.html>

⁹ The mechanism is to run stages in parallel and at risk in order to speed up the process. Accelerated development is being achieved by direct federal government investment to support the clinical development of preferred candidates. There is also federal government investment in manufacturing capacity at risk. 14 candidates were initially chosen from the 100+ candidates and this has now been reduced to five (see <https://www.nytimes.com/2020/06/03/us/politics/coronavirus-vaccine-trump-moderna.html>) Moderna; University of Oxford and Astra Zeneca; J&J; Pfizer; and Merck. Federal investment is also taking place to expand domestic supplies of specialised materials including glass vials. It is unclear what has been agreed in terms of manufacturing and supply commitment by companies receiving funding or if any price or pricing policy has been agreed.

¹⁰ need to reference this

¹¹ CEPI's mission is to stimulate and accelerate the development of vaccines against emerging infectious diseases and enable access to these vaccines for people during outbreaks and was developed as a collaboration between WT and Gates Foundation in 2017. Before covid-19, it had given grants to teams developing vaccines for MERS, Nipah and Lassa, specifically and grants for developing vaccine technology for rapid development against unknown pathogens in general.

¹² The vaccines in the CEPI pipeline are Curevac, Inovio, Moderna, Novavax, Uni of Hong Kong, Uni of Oxford, Uni of Queensland, Institut Pasteur and Clover Pharmaceuticals.

¹³ Towards this scale up, they signed a deal with AZ to manufacture 300 million doses of their vaccine candidate ringfenced for COVAX if it is found to be effective. The \$383 million partnership will support tech transfer to sites mainly in Europe, purchase manufacturing materials and reserve manufacturing slots. AZ will supply the vaccine to COVAX not for profit bound by an MOU between themselves, CEPI and Gavi.

The WHO ACT Accelerator and has three pillars relating to therapeutics, testing and vaccines¹⁴. Their action plan is being launched on 27th June. The vaccine pillar will be the responsibility of CEPI and of Gavi¹⁵.

Funding has, so far, been focused on R&D, most recently through a \$8 billion EU-driven pledging drive.

5. AcceleratingHT

The AcceleratingHT Initiative¹⁶ is an academic initiative led by Michael Kremer, the nobel prize winning economist and a key driver of the establishment of the Advance Market Commitment (AMC) (about which more later). This AMC initiative is focused on speeding up the manufacture and delivery of any approved vaccine¹⁷. It does not address vaccine development¹⁸

They propose \$137bn investment in manufacturing capacity for 18 vaccine candidates¹⁹.

¹⁴ This was initially a platform for collaboration between global health actors (Gates Foundation, Wellcome, GAVI, Global Fund, UNITAID, CEPI, Gavi, WHO)

¹⁵ The ACT Accelerator will be releasing its action plan in the next few days to coincide with an ACT Accelerator pledging summit on the 27th of June. The ACT Accelerator action plan will include costings (likely to be in the \$10s of billions), an investment case for a pooled approach and a plan for engaging with vaccine manufacturers (led by CEPI). At the core of this partnership is a commitment to the WHO access conditions and a vision to supply vaccines equitably to Health Care Workers as a priority. Gavi and CEPI are responsible for the vaccine pillar under the ACT Accelerator and the COVAX Facility is the AMC model that is being proposed to pool procurement, mainly for Gavi eligible, LMIC countries. The European Commission is thought to be planning a pooled procurement approach to compliment the COVAX model designed for HICs and UMICs not covered by the Gavi model. The vaccines involved in COVAX are mainly the CEPI candidates that have signed up to the access conditions that are a prerequisite for inclusion the COVAX Facility.

¹⁶ See <https://www.acceleratinght.org/home>

¹⁷ They propose to do this in two ways:

- a. Manufacturing capacity is built speculatively for vaccine candidates
- b. "Excess" manufacturing capacity is built such that all global need is supplied in a short window of time.

The logic is addressing perceived market failure that "vaccine firms do not capture all of the gains from early supply and so produce slower than optimally". This and other quotes are taken from the presentation *Incentive Design to Accelerate a COVID-19 Vaccine*, available at <https://drive.google.com/file/d/1JPNiV7LGNsUUDcXY0sK3VdgpJnR2XH2t/view>.

¹⁸ Benefit calculations are "conditioned on approval of a vaccine". They argue for innovation in clinical development but their proposal is not intended to achieve this. A social cost-benefit calculation is made, using the IMF estimate of \$375 billion monthly loss to the world economy due to COVID-19. The objective is to accelerate access to a successful vaccine by six months. The economic and health benefits of this justify public "at risk" investment in manufacturing capacity for potentially successful vaccine candidates.

¹⁹ Of this:

- \$92bn (two thirds) is push funding with governments financing 85% of the cost of capacity installation. They argue that direct push funding is more efficient than incentivising companies to invest at risk with a higher price via a pull incentive.
- \$45bn (one third) is pull with governments guaranteeing to spend a certain amount on vaccines in the first 18 months at an agreed price of 3bn doses at an average of \$15 per dose (\$35 per dose for first bn and \$5 per dose for next 2bn.)

6. The Gates Foundation

The Gates Foundation's priorities and approach has been reported in an internal White Paper²⁰ to be advocating for a mix of funding totalling \$38 billion to \$74 billion. The White Paper states that:

"The scope and urgency of the current pandemic is also such that at-risk decisions to scale manufacturing capacity will need to be made early in the R&D process, which will in turn require assurances of demand and availability of funding for procurement to pay for finished products."²¹.

7. The EU proposals

The EU is proposing²² use of its joint procurement powers to secure sufficient production of vaccines in the EU and thereby sufficient supplies for its Member States through Advance Purchase Agreements (APAs) with vaccine producers via the Emergency Support Instrument

²⁰ See the Lancet [https://www.thelancet.com/pdfs/journals/lancet/PIIS0140-6736\(20\)31354-4.pdf](https://www.thelancet.com/pdfs/journals/lancet/PIIS0140-6736(20)31354-4.pdf)

²¹ This includes:

- \$2 billion push for CEPI to support vaccine development
- \$12 billion push to scale up capacity to manufacture bulk vaccine and package it
- \$24 to \$60 billion in grants to cover procurement costs to assure suppliers of LMIC market demand.

The mix of push and pull is quite different to that of the AcceleratingHT proposal with push at between 19% - 37% of the total. No specific proposal for procurement is put forward, but Gavi is the preferred candidate to organise procurement (with the UNICEF Supply Division). The assumption is that "In any scenario, at least \$24 billion should be pledged upfront to send a clear market signal, though it may be disbursed over the next 2-4 years". The White Paper states that the high-end of the range would enable procurement of 5 billion doses, which is estimated as sufficient, assuming a two-dose regimen, to vaccinate enough of the population in LMICs to ensure population-level immunity based on current understanding of the science. The high-end estimate also assumes costs of up to \$10 per dose.

²² EU Strategy for COVID-19 vaccines. Published 17th June 2020. Available at https://ec.europa.eu/info/sites/info/files/communication-eu-strategy-vaccines-covid19_en.pdf

(ESI)²³. There is EUR 2.7bn available under that scheme. A further major announcement from the EU is expected, also on June 27th.^{24 25 26}

8. As we noted in the WHO Accelerator, Gavi is proposing a Gavi Advance Market Commitment for COVID-19 Vaccines (Gavi Covax AMC²⁷). Relabelled a “**COVAX Facility**”²⁸ this is a “pull” design complementing CEPI’s push funding into promising vaccine candidates.

²³ It also refers to “Adapting the EU’s regulatory framework to the current urgency and making use of existing regulatory flexibility to accelerate the development, authorisation and availability of vaccines while maintaining the standards for vaccine quality, safety and efficacy.)” Early engagement between the EMA and manufacturers is already underway.

²⁴ An alliance between France, Germany, Italy and the Netherlands was seen as a step towards EU-wide joint action.

²⁵ The Joint Action will involve:

- A central procurement process giving all member states the option to purchase vaccines through this route. It avoids competition between member states and increases EU leverage when negotiating with industry. Vaccine policy remains the responsibility of member states.
- Commission will enter into advance purchase agreements (APAs) with individual vaccine manufacturers which will comprise (i) right to buy a specified number of doses at a given price in a given timeframe in return for (ii) funding part of the upfront costs faced by them (via the ESI). It goes on to say:
- These payments will de-risk necessary investments relating to both vaccine development and clinical trials and preparation of at-scale production capacity.
- “The conditions of the contract will reflect the balance between the prospect of the producer providing a safe and effective vaccine quickly and the investment needed to deploy the vaccine on the European market.”
- APAs can include other “relevant conditions (such a production capacity in the EU, possible availability of production facilities for the manufacturing of other vaccines or medicines in case of failure, or liability arrangements.)”
- Once a vaccine is successful member states can acquire under the terms of the APA.
- Allocations between member states would be according to a “population -based distribution key.”
- The Commission will enter into an agreement with participating member states to formalise their reciprocal commitments.
- The unprecedented circumstances in which the EU finds itself requires a bold response.
- “Though steps will be taken to mitigate the risk – for example, by investing in a portfolio of companies covering different technologies - the failure rate of vaccine development is high. There is a very real risk that none of the supported candidates will be successful. However, the value of earlier access to a vaccine is enormous, in terms of lives saved and economic damage avoided. This makes the risk worth taking.”
- “This proposed framework is therefore an insurance policy, which transfers some of the risk from industry to the public authorities in return for assuring Member States equitable and affordable access to a vaccine, should one become available.”
- The “Commission is ready to support the development and operation of an inclusive international COVID-19 procurement mechanism that facilitates early and affordable access to vaccines and other tools for all who need it across the world. With sufficient scale and scope, such international mechanism could become the world’s insurance policy against pandemics.

²⁶ The Commission also supports voluntary pooling and licensing of intellectual property related to COVID-19 therapeutics and vaccines, in line with the recent resolution of the World Health Assembly (World Health Assembly Resolution 73.1), to promote equitable global access as well as a fair return on investments.

²⁷ See (<https://www.gavi.org/news/media-room/gavi-launches-innovative-financing-mechanism-access-covid-19-vaccines>)

²⁸ It has the full title “The COVID-19 Vaccine Global Access Facility”. See COVID-19 Vaccine Global Access (COVAX) Facility. Discussion Document 11th June 2020. Gavi.

9. **The BBAMC.** The global health policy team at CGD, have, together with several of us from the Office of Health Economics and Hannah Kettler from PATH, developed a concept we refer to as a benefit-based advanced market commitment (BBAMC),

The simplest way of making sense of these is to group them according to whether they are push or pull or both. I am going to build on this in a moment.

But we can also note that a lot of money is being proposed or spent. Over \$230bn. Although much of it is duplication. But we can compare that with the IMF estimate of economic damage alone, which is \$375 billion a month!

[Slide 11]

So lets move on to explain “push” and “pull”.

3. A framework for understanding what works and how we can apply it to getting a vaccine for COVID-19

[Slide 12]

We make a basic distinction between “push” and “pull” incentives.

In the market for a vaccine in a high income country (HIC) pharmaceutical companies research and develop, at risk, with some public research funding, vaccines for diseases affecting HIC populations in the expectation that, if they work, they will be able to sell them to HIC health care systems. Payers (whether governments or insurers) will buy if they offer value. There may, of course, be competition and there may be negotiation on price. But buying power in the market “pulls” investment through development, manufacture, and distribution.²⁹

Introducing these same vaccines to low income countries (LICs) is more difficult, because many of these countries do not have money to buy vaccines. Hence the creation of The Vaccine Alliance, known by the shorthand Gavi, buying on behalf of LICs³⁰. Buying power from Gavi (in this case from donors funding Gavi³¹) pulls investment through³².

Some diseases do not have a big enough HIC disease burden to provide an R&D incentive to invest. Malaria and TB are good examples. There are other neglected tropical diseases.

²⁹ There will be academic research in understanding the disease, and in understanding whether different approaches to developing a vaccine are possible. This has the effect of reducing the costs of pharmaceutical industry research and development by reducing likely failures, which is a major source of cost. We can think of this as early stage “push” which, although not direct funding (Indeed this research has public good attributes), so potentially reduces costs for all companies.

³⁰ Add footnote on Gavi origins Global Alliance for Vaccination and Immunisation and role and UNICEF

³¹ Add footnote on current Gavi replenishment round.

³² Two other policies have been key: (i) differential pricing, so prices paid are close to manufacturing cost – returns on R&D are obtained from HICs and some MICs and (ii) organising Gavi’s procurement programme to reduce the time period between launch in HIC markets and vaccines being available in LICs.

Vaccines for pandemics (such as Ebola) and for biological warfare agents (such as Anthrax) also fit into the same economic category. Here we see both “push” and “pull” funding. We can reposition our nine schemes according to their push and pull attributes.

There has been a debate as to the appropriate balance of push (which reduces research and development costs and failure rates, so reducing scientific risk) and pull (creating the market and so reducing commercial risk)³³. There is no reason why a large enough market will not stimulate R&D risk taking investment by the private sector. The question has been, in the global health arena, what is the most cost-effective use of donor resources? The reality has been that budget constraints rather than efficiency may have held sway. A pull commitment requires a bigger commitment and more cross-organisation coordination, even though it does not have to be spent immediately – we have to wait for the products – whereas push can be done one bit at a time.

A plus with push funding in a pandemic for which we were not prepared is, of course, speed. The problem with push funding, once it goes beyond investment in the early stage public good of creating knowledge about disease mechanisms, is that it involves the donor picking winners³⁴.

[Slide 13]

In the case of Ebola³⁵, Gavi promised an advanced purchase commitment for any vaccine in at least phase 1 during the 2014-16 outbreak. The pull mechanism used by Gavi in 2016

³³ We can think of this simply as “can I develop a product that works?” (the scientific risk) and “can I sell it if I do?” (the commercial risk).

³⁴ The Gates Foundation set up product development partnerships (PDPs) in neglected disease areas in order for them to develop portfolios of pipeline products³⁴. It sought to deal with the product selection challenge by expecting the PDPs to behave as venture capitalists with a social purpose, i.e. build a portfolio of candidates that offered potential. They had the capital at risk and were seeking to leverage the private sector to help deliver value. But the consequence has been some challenges in making sure that products that do get to market are taken up and used by governments, because the emphasis is on “what can we push through to market?” rather than “what do health systems actually want to use?”

³⁵ Development of the Ebola vaccines up to 2014 was led by governments because of the national security concern about the bio-weapon threat of Ebola (1). These candidates were then licensed or acquired by companies. There were three main commercial players at the time of the first outbreak (Merck, Janssen & GSK).

- The Merck vaccine was developed by the Canadian Institute of Public Health in 2007 and the Canadian Government then sold marketing rights to a small biotech (NewLink Genetics) in 2010 (2). Merck then licensed the vaccine from NewLink for \$50 million in 2014 at the start of the West Africa Ebola epidemic (3).
- The GSK vaccines were initially developed by the US NIH and Okairos which was acquired by GSK in 2013 (4). GSK had 3 candidate Ebola vaccines that were tested in 2013-2016 but GSK licensed their Ebola vaccines to the Sabin Vaccine Institute in August 2019 (4).
- The Janssen vaccine is a prime boost vaccine with first dose (Ad26.ZEBOV) and second dose (MVA-BN-Filo) 8 weeks later. Early development was funded by US NIH. The Ad26 component was developed by Janssen using their AdVac vaccine platform-technology and the second component was based on a different vaccine platform-technology developed by Bavarian Nordic. It was in pre-clinical development at the start of the West Africa outbreak. In 2015, Janssen committed \$200m and IMI (Innovative Medicines Initiative) committed \$100m to the clinical development, along with other funders e.g. BARDA and US HSS.

All three vaccines were used through emergency-use licences during the 2014-2016 West Africa Ebola outbreak and received substantial funding for clinical trials during the outbreak. The GSK and Merck vaccines were tested in Liberia and Sierra Leone and the WHO and MSF ran another trial in Guinea co-sponsored by the Guinean government and co-funded

ensured there was a stockpile of vaccine candidates ready for a subsequent outbreak in 2019³⁶. At the start of this outbreak, stockpile doses were licensed for compassionate use³⁷. At the end of 2019, a Gavi pull fund³⁸ funded a stockpile of 500,000 doses available for free to LMIC countries ready for the next outbreak.

[Slide 14]

The AMC was conceived as an idea to promote research and development for both early stage and late stage products.^{39 40}

The pneumococcal AMC was for a vaccine already developed for HICs. The key objective was to shorten the typical 10-15-year gap before a vaccine was available in LICs⁴¹. \$1.5 billion was raised by 6 donor countries towards the AMC and two suppliers, GSK and Pfizer, were given AMC contracts. Companies could see the \$1.5bn market commitment and the pressing need for the vaccine. Hence, they had a high expectation that they would be

by Wellcome. The Guinean vaccine trial of the Merck vaccine was the only trial to be completed (3). BARDA also gave \$175 million to support production and supported Merck's manufacturing plants in Germany. Janssen's vaccine trials in 2016 were funded by the European Commission and the Innovative Medicines Initiative (IMI) and they had funding from BARDA to develop manufacturing capacity. In 2017 Janssen received \$44.7 million funding from BARDA to continue to develop their prime-boost vaccine

Gavi promised an advanced purchase commitment for any vaccine in at least phase 1 during the 2014-16 outbreak (5,6). Merck signed an advanced purchase commitment with Gavi in Jan 2016 and received \$5 million in exchange for seeking regulatory approval by 2017 and ensuring there was a stockpile of 300,000 doses (5,7). Gavi was also 'working with' Janssen and GSK on their Ebola candidates at this point.

At the start of the 2019 outbreak, Merck and Janssen 'donated' doses from the stockpile licensed for compassionate use in an implementation trial with significant push funding (Gates Foundation, Wellcome, NIH and Gavi etc) and run by implementation partners (e.g. MSF and WHO). At the end of 2019, Gavi set up another pull fund of \$173m (to run from 2019-2025) to pay for a stockpile of 500,000 doses that will be available for free for any LMIC countries a combination of the Janssen vaccine and Merck vaccine.

The pull mechanism used by Gavi in 2016 ensured there was a stockpile of vaccine candidates ready for a subsequent outbreak and allowed them to leverage push funding to de-risk clinical trials. Some (e.g. MSF, academics etc.) took issue with the way that the Ebola vaccine was funded saying that more money was going to industry than it deserved (having taken very little risk in the development of the vaccines and so much of the development being co-funded by funders/governments).

³⁶ Companies were in effect being paid to take on the risk of regulatory approval, manufacturing and managing the stockpile

³⁷ This was an implementation trial with significant push funding (Gates Foundation, Wellcome, NIH and Gavi etc) and run by implementation partners (e.g. MSF and WHO)

³⁸ Of \$173m (to run from 2019-2025). The stockpile includes both the Janssen vaccine and Merck vaccine.

³⁹ See Levine Kremer and Albright. 2005 Making Markets for Vaccines. Ideas into action. Available at <https://www.cgdev.org/sites/default/files/archive/doc/books/vaccine/MakingMarkets-complete.pdf>

⁴⁰ The key difference is in the nature of the contract between the buyer (in this case pooled by Gavi) and the vaccine developer'. With early stage it is a framework agreement. With later stage, when the product exists, there is a procurement tender. The AMC did not envisage bilateral contingent contracts conditioned on a product being invented of the sort that we have for COVID-19 vaccines.

⁴¹ See Kremer, Levin and Snyder 2020. Advance Market Commitments: Insights from Theory and Experience. AEA Papers and Proceedings, 110():269-73.

contracted to supply^{42,43} The Serum Institute of India has now joined, with a pneumococcal vaccine that secured a share of the AMC in the most recent tender^{44,45}.

Commitments ensured that manufacturers had to provide the PCV at a price no higher than \$3.50 per dose (referred to as the tail price ceiling) which was paid by the GAVI general fund. Manufacturers also received a \$3.50 'top-up subsidy' on the first 21% of doses in each contract which was paid through the \$1.5 billion AMC fund.⁴⁶ So they were paid \$7 per dose. This concept is illustrated in the slide.

The AMC used a Target Product Profile (TPP) to ensure that participants met a certain quality standard. The TPP was, however, used as a qualifying threshold instead of a tool to differentially reward better quality vaccines.⁴⁷

Overall, the mechanism was effective. More than 150m children have been immunised, saving an estimated 700,000 lives⁴⁸.

The essence of this AMC pull concept was originally intended is to:

⁴² See: (Dalberg 2013 AMC Process Design and Evaluation Report <https://www.gavi.org/our-impact/evaluation-studies/pneumococcal-amc-process-and-design>). Although a choice was made to allow for a 3rd entrant by holding back some of the volume. It took 10 years before the Serum Institute got a product pre-qualified by WHO and able to meet the AMC qualifying TPP. A BCG evaluation from 2015 suggests that this choice to hold back some of the volume sent a conservative demand signal to the companies that in turn may have contributed to the 2012-2014 supply gaps.

⁴³ See: (Dalberg 2013 AMC Process Design and Evaluation Report <https://www.gavi.org/our-impact/evaluation-studies/pneumococcal-amc-process-and-design>). In the event, the advance purchase commitments (rather than advance market commitments) were limited. The AMC was delivered through price-volume agreements between GAVI and the vaccine suppliers. However, while the price was set, only 6% of the value of the contract was guaranteed. This was designed to give flexibility for countries to opt-out of existing agreements and source through other suppliers if they were brought onto the scheme. This assumed that lower-cost suppliers would have been able to rapidly build manufacturing capacity and join the AMC, which was not the case. The Serum institute in India, took 10 years and considerable support from funders to be in a position to join the AMC. It is also unclear the extent to which the AMC incentivised GSK and Pfizer to develop manufacturing capacity to supply AMC-eligible countries. GSK for example began planning a manufacturing facility in Singapore before the AMC began.

Purchase guarantees would have provided a stronger incentive for suppliers to invest in building capacity as the returns would have been more reliable. In the end, companies were expected to commit to providing hundreds of millions of doses over a 10-year time frame with no guarantee that those contracts would be kept by countries. By guaranteeing so little of the contract, there was only a weak incentive for manufacturing investment from Pfizer and GSK.

⁴⁴ (See: <https://www.gavi.org/sites/default/files/document/2018-pneumococcal-amc-annual-reportpdf.pdf>) By the end of 2019, 17.5% of the AMC funds remained and \$1.238 billion has been given to GSK and Pfizer. Annual production of the PCV vaccines have increased year on year from 7 million doses in the year 2010 to 161 million doses in the year 2019. The Serum Institute will supply 10m doses per annum for each of the next 10 years.

⁴⁵ The remaining \$167m that had not been allocated was recently transferred to the Gavi COVAX AMC pot.

⁴⁶ The tail price ceiling, intended to be an upper limit, initially became the de-facto price as both companies set the price at the ceiling for the first two tender rounds. However there had been price reductions of around 17% below the initial \$3.50 tail price ceiling following pressure from organisations like MSF and Gates Foundation. Experts involved believe that price competition would have been greater if there were more than two suppliers. The Serum Institute price represents a 43 per cent reduction from the initial Gavi tail price of USD 3.50.

⁴⁷ There was however a quality difference between the two vaccines. The planned co-payment from countries procuring the vaccines through the AMC was dropped. For this reason, most countries requested the Pfizer vaccine as it was the superior vaccine and there was no differential in price to them.

⁴⁸ Kremer et al. AEA Papers 2020

- (1) Create a market for a new vaccine with guaranteed advance market commitments, i.e. not to any specific company, which is the case with advance purchase contracts.
- (2) Ensure entry into the scheme requires meeting a minimum TPP
- (3) Guarantee (to the companies) a price above cost to provide a return on innovation
- (4) Guarantee (to the buyers) a tail price close to marginal cost once appropriate returns on R&D and manufacturing investment have been made.
- (5) LICs supplied at the tail price (which in practice is paid for by Gavi donors)

I want to argue that AMC style pull mechanisms are better than reliance on push, because it means that those making the investment only get a return if the product is successful. But, as noted, there are occasions on which the need for speed means that some initial push finding is required.

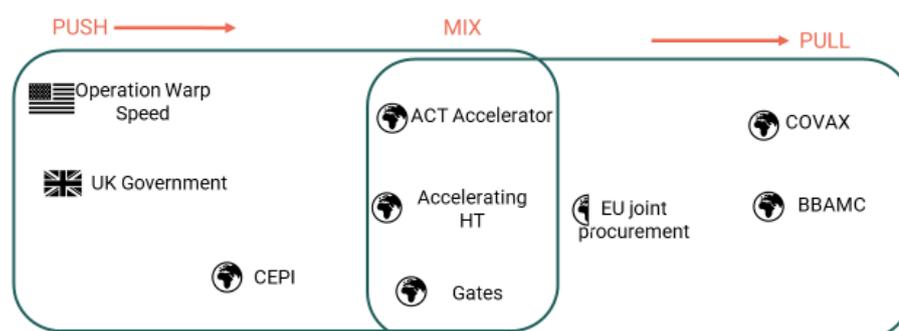
More generally, we can note that Kremer and others have argued that the AMC mechanism may be most effective when it is promoting research and development as well as manufacturing and distribution.⁴⁹ This is important as I want to argue that the schemes creating an Advance Market Commitment for COVID-19 vaccines provide the most useful buying mechanism for us to consider.

[Slide 15]

We can show the nine proposals grouped according to whether they are push, pull, or a combination. We see this below.

What does the vaccine context look like with this analytical framework?

We can group the COVID-19 schemes into 'push' and 'pull'



But in order to design the right AMC for the covid-19 vaccine, we have to understand the specific challenges in developing and manufacturing a COVID-19 vaccine- and they are very different to the pneumococcal challenge.

⁴⁹ Reference / discuss Kremer et al 2019 Paper and his DFID paper with Williams and Towse. available at https://www.who.int/intellectualproperty/submissions/MichealKremerKTW_CIPIH_submit_2.pdf?ua=1

4. Challenges of COVID-19

[Slide 16]

There are two.

Firstly, it is not easy to get a vaccine. Full stop.

We don't have a COVID-19 vaccine. And we might never have one. If we look at the top 3 infectious killer diseases in the world, despite a lot of donor and private investment:

[Slide 17]

1. We don't have a vaccine against HIV, despite looking for one since the 1980s (more than 30 years ago)⁵⁰
2. We only recently got a vaccine against malaria. A major achievement after more than 20 years of development⁵¹, but unfortunately it has limited effectiveness^{52,53}.
3. And we still only have the old BCG vaccine for TB despite years of trying to get a new one^{54, 55}

[Slide 18]

We can note in passing that **SARS** and **MERS** are coronaviruses and we do not have vaccines against these⁵⁶. There are several challenges including:

⁵⁰ See <https://www.avert.org/professionals/hiv-science/developing-vaccine#The%20need%20for%20a%20vaccine%20against%20HIV> and <https://journals.plos.org/plosone/article/file?id=10.1371/journal.pone.0146387&type=printable>. The first large HIV vaccine trial reported results in 2003, 17 years ago.

⁵¹ RTS'S first showed efficacy in a challenge study in 1997 and undertook a pivotal trial in 2009 that enrolled 15,000 infants and young children and was finally approved by the EMA in 2015.

⁵² However due to limited lasting efficacy in young children (for example 30% of cases of severe malaria in small children), the WHO did not include it in the Expanded Programme of Immunisations after it received EMA approval. The WHO is still trying to understand how best to advise use of it by malaria endemic countries and some potential for increased meningitis risk see <https://www.who.int/malaria/media/malaria-vaccine-implementation-qa/en/>

⁵³ RTS'S has been the front-runner in the malaria pipeline for the last 20 years but there are other candidates in clinical development, the next most advanced is in phase 2. See <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3146776/>.

⁵⁴ See <https://cmr.asm.org/content/33/1/e00100-19>. The only vaccine for TB, Bacille Calmette-Guerin (BCG), was developed in 1921. BCG is a very limited vaccine, both in terms of efficacy in preventing pulmonary disease (key for interrupting transmission) and safety particularly in high-risk groups (e.g. HIV coinfecting patients). Vaccine development for TB has been delayed by poor understanding of the immune response to natural infection and a lack of good correlates of protection in humans. They have been 20 candidates that have been evaluated in clinical trials and there are currently 14 active candidates in the pipeline.

⁵⁵ Of course, it is a bit circular – if we had effective vaccines that were widely available they would not be the top 3 killer infectious diseases and of course these are not infectious diseases with close similarities to COVID-19.

⁵⁶ This is part because they have disappeared, and funding disappeared. But research suggested that they are not diseases which induce strong immunity, i.e. they are more like a common cold than measles. This makes vaccine development more difficult for because it is not clear what immune response the vaccine should stimulate to generate long lasting protection (i.e. correlates of protection are unknown). Vaccine development for coronaviruses has also been delayed by vaccine-induced enhancement, where the vaccine makes infection

- Coronaviruses do not generally induce long-term immunity.
- The vaccine needs to generate immunity in older people which is difficult.
- There may be safety concerns around vaccine-induced enhancement with coronaviruses.

Safety issues can emerge as happened recently with a Dengue vaccine where life threatening safety problems were only discovered after a million children in the Philippines had been vaccinated⁵⁷.

It is hard to get portfolio diversification

[Slide 19]

There is also the question of how diversified the global portfolio of candidate vaccines is? Jack Scannell writing in the FT⁵⁸ on May 10th (2020) contrasts:

- “a bunch of mediocre vaccines, each with a mere 10 per cent chance of working, but they were likely to fail for entirely different reasons.” If we put 20 into trials and they are all independent, the likelihood of failure is 0.9^{20} (= 0.12158), i.e. we have an 88% chance of success.

[Slide 20]

- He goes on to say “Contrast this with a set of excellent vaccine candidates, each with a 40 per cent chance of working, but all likely to fail for the same reason. Here, we would be stuck with a 60 per cent chance of failure no matter how many we tried.”

An example of this might be if they are all aiming at the same target and it turns out not to be the right one.

He and, separately, McDonnell et al.⁵⁹ have argued that the current portfolio may contain too much emphasis on candidates with ease (speed) of development plus [Scannell] “Diversification is also undermined by therapeutic nationalism whether in a weak form

more severe. Finally, there is a lack of good animal models for coronaviruses which means results from in vivo testing may not be transferrable to humans. Vaccine development is not impossible and several leading vaccine candidates propose to do exactly this. See: <https://coronavirusexplained.ukri.org/en/article/vdt0002/>
See: <http://www.sciencedirect.com/science/article/pii/S1074761320301205>

⁵⁷ Dengue is a virus for which vaccine development has been complicated by the natural history of the disease. There are four serotypes of dengue that co-circulate in endemic areas. The majority of dengue infections cause Dengue Fever (DF) characterised by mild, flu-like symptoms. Dengue infection can also cause much more serious Dengue Haemorrhagic Fever (DHF) and the risk of this haemorrhagic form of the disease increases if someone has had a prior infection by a different serotype. In 2017, 1 million children in the Philippines were given a Dengue vaccine, Dengvaxia produced by Sanofi. It took years to discover that the vaccine increased the risk of DHF particularly in sero-negative children. See: <https://www.sciencemag.org/news/2019/11/new-dengue-vaccine-performs-well-large-trial-safety-remains-key-concern>

⁵⁸ See <https://www.ft.com/content/3bb6f5d4-8e14-11ea-af59-5283fc4c0cb0>

⁵⁹ See <https://www.cgdev.org/blog/what-does-success-look-covid-19-vaccine-improving-portfolio-level-understanding>

(such as the well-intentioned backing of national winners) or a strong one (a bias to supplying the domestic market)."⁶⁰

[Slide 21]

Scannell went on to say

*"If we look at the Covid-19 front-runners, **individually rational choices may have concentrated risk** in terms of the vaccine platforms that are being used and the specific pieces of viral machinery targeted. ... An overt move towards diversity is necessary, even if individual projects look less attractive"*

This is a good point to turn to Candidates

[Slide 22]

We may find that none of the lead candidates are successful or meet all requirements, such that more clinical development is needed. The timelines in that case will go out well beyond 2 years. But it is possible that the lead candidates deliver vaccines. And it is very important to be optimistic.

As of the 22nd of June, there are 13 candidates in clinical development and 129 candidates in preclinical evaluation. These vaccines are being developed mainly by academic groups (e.g. Oxford, Imperial) and small biotech companies (e.g. Moderna, Inovio) however, the large multi-national pharmaceutical companies (e.g. GSK/Sanofi) are also represented. Crucially they cover 9 different vaccine technologies ranging from established technologies, like adenovirus-based vaccines, to novel technologies, like mRNA vaccines⁶¹.

And the demand required is potentially large in the short term, but much more uncertain in the middle-long term. Here are estimates from Gavi of potential demand. It is not 7 or 14 billion doses on day 1, but the numbers are large.

[Slide 23]

Second, Manufacturing scale up is hard

This raises the crucial question of manufacture.

⁶⁰ Of course, we also have Coalition for Epidemic Preparedness Innovations (CEPI), the Wellcome Trust, and the Gates Foundation involved in investment decisions. But, as Scannell puts it "If we look at the Covid-19 front-runners, individually rational choices may have concentrated risk in terms of the vaccine platforms that are being used and the specific pieces of viral machinery targeted. ... An overt move towards diversity is necessary, even if individual projects look less attractive" The science is not my area of expertise, but we need to consider the possible consequences of being in an environment when the key R&D funding decisions are largely not being made by biotech and pharmaceutical companies thinking of the returns they can get from developing and introducing an effective vaccine, but by international agencies and governments for reasons like speed of development and ease of manufacture or (understandable) political preference which may not lead to an optimal portfolio. I am not saying that the private sector always gets the balance right. Of course it doesn't. My point is that finding a vaccine among the current lead candidates may not be straightforward.

⁶¹ See: <https://www.who.int/publications/m/item/draft-landscape-of-covid-19-candidate-vaccines>

[Slide 24]

The world needs this vaccine quickly at an unprecedented speed and scale. There is already a shortage of supply for established global vaccines and only a small number of large-scale and established vaccine manufacturers. Vaccine manufacturing is a challenging and expensive industry for a number of reasons⁶²:

- High process variability-
 - Vaccine manufacturing is predominantly based on biological not synthetic processes which are highly variable⁶³.
 - Because of this potential variability there is also high regulatory complexity⁶⁴
⁶⁵.
- Long lead-times-
 - Lead times can vary from 6 months (for egg-based influenza) to 3 years (pentavalent combination vaccines⁶⁶) and demand for vaccines is usually estimated 3 years in advance to allow for managing production⁶⁷.
 - New vaccine technologies could theoretically be produced much quicker because of the smaller amounts of antigen needed and the possibility for fully synthetic manufacturing processes⁶⁸.
- High up-front and ongoing costs-
 - facilities in HICs can cost between \$50M and \$500M depending for example, on the vaccine and the complexity of the process, and the level of automation⁶⁹.
- Low fungibility- Vaccine production platforms are diverse. While components in the process may be common (for example bioreactors, filters, chromatography, fill and finish) the arrangement of components in the process may be different and the scale

⁶² <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5518734/pdf/main.pdf>

⁶³ The raw materials for vaccines are also often produced through biological processes potentially adding additional variability. To ensure consistency, highly skilled workers and strict Quality Control (QC) are needed.

⁶⁴ Changes to manufacturing processes (e.g. new raw materials, new equipment etc) usually require regulatory approval and may require clinical trials. This means there is a trade-off between speed to market and optimising the manufacturing process to save costs over the long life of the vaccine in the market.

⁶⁵ In addition, Manufacturers who want to sell through pooled procurement mechanisms (e.g. PAHO/UNICEF) also must go through WHO prequalification.

⁶⁶ Emmanuel Vidor & Benoit Soubeyrand (2016) Manufacturing DTaP-based combination vaccines: industrial challenges around essential public health tools, *Expert Review of Vaccines*, 15:12, 1575-1582, DOI: [10.1080/14760584.2016.1205492](https://doi.org/10.1080/14760584.2016.1205492)

⁶⁷ While the short-term demand for a covid-19 vaccine is significant, for manufacturers who are used to forecasting demand three years ahead, the demand for a covid-19 vaccine is anything but certain in the medium to long-term. Like its cousins MERS and SARS, covid-19 could simply die out. Alternatively, herd immunity could build over time as the vaccine is developed and governments who were initially keen to vaccinate their whole population might become less committed to buying a vaccine. This uncertainty prevents existing manufacturers from feeling confident enough to build capacity at risk.

⁶⁸ Kis, Z., Shattock, R., Shah, N. and Kontoravdi, C. (2019), Emerging Technologies for Low-Cost, Rapid Vaccine Manufacture. *Biotechnol. J.*, 14: 1800376. doi:10.1002/biot.201800376

⁶⁹ While up-front costs can be lower in low resource settings, other ongoing costs can be higher (e.g. cost of importing raw materials, cost of paying highly skilled expat employees). Raw materials are usually expensive and scarce.

of each component may vary, which all lower fungibility. Adapting a bioreactor for a different vaccine may be technically possible but will be time consuming⁷⁰.

While COVID-19 highlights that there has been transformation in vaccine development⁷¹, the specific requirements for a COVID -19 vaccine further complicate this challenge:

- We need vaccines at unprecedented speed- Normally ‘we’ accept a longer wait for delivery of innovation (certainly for LMICs). Even in HICs, we often trade off taking time negotiating price versus the health gain we could get from immediate use⁷².
- There are no related vaccines- it may be an obvious point but there are no existing coronavirus vaccines there is no capacity to rapidly repurpose for covid-19. If we were in the middle of a H1N1 pandemic, manufacturing capacity would not be as much of a challenge given the investment in manufacturing capacity for seasonal influenza⁷³.
- There is large diversity of vaccine platforms in the COVID-19 pipeline- Given low fungibility of vaccine manufacturing, the diversity of vaccine technologies in development adds additional complexity⁷⁴. The pipeline contains candidates

⁷⁰ For example, combination vaccines are usually manufactured across several facilities and then combined later See: Emmanuel Vidor & Benoit Soubeyrand (2016) Manufacturing DTaP-based combination vaccines: industrial challenges around essential public health tools, Expert Review of Vaccines, 15:12, 1575-1582, DOI: [10.1080/14760584.2016.1205492](https://doi.org/10.1080/14760584.2016.1205492)

⁷¹ This transformation centres around the development of platform technologies that are more general than traditional vaccines and some of those platform technologies allow for fully synthetic vaccines. These two breakthroughs, along with preparedness investment in coronavirus vaccines from CEPI, enabled the covid-19 pipeline to be filled with potential candidates just weeks after the genome was shared with the world.

Platforms allow a ‘plug and play’ approach to vaccine development, where the core vaccine framework is standardised, and the disease specific component can be added very quickly. This means that one platform can be the backbone of lots of products. This is exemplified by Janssen’s AdVac technology which is being trialled for covid-19 but which is also the backbone of their licensed Ebola vaccine and phase II HIV candidate. This means that the benefit of huge gains in speed of development, is off-set by a more complex picture of intellectual property for each individual product. Janssen’s covid-19 vaccine is very linked to the commercial value of their other AdVac products, so global health initiatives that focus on delinkage and more open IP sharing have wider commercial implications than for vaccines not based on these generalisable platforms.

The second innovation is in synthetic vaccines such as RNA/DNA vaccines that can be manufactured using synthetic RNA/DNA synthesis techniques. Thanks to the revolution in genomics, these processes now rely much less on the biological processes fundamental to other vaccine types. This means that there is a potential to manufacture billions of vaccines very quickly to satisfy global demand. However, ~70% of the global vaccines are produced by developing country vaccine manufacturers. The expertise for manufacturing these very novel vaccines is very limited globally, but especially with developing country manufactures, many of whom are unable to develop combination vaccines using more traditional technology. In addition, relying on these novel technologies that have never been licensed for human vaccines means there is more regulatory uncertainty which can add additional delays.

Therefore, while these transformations make it theoretically possible to develop and manufacture significant quantities of vaccine quickly, there are other practical barriers which limit their potential. The commercial and IP ‘baggage’ that platform vaccines bring means that the traditional access paradigm based on IP sharing to supply LMIC markets is more costly for developers of platform technologies. And the complexity of these novel vaccine technologies that are theoretically very promising, means that in practice the pool of manufacturers able to manufacture this vaccine is much smaller.

⁷² This is usually because there are competing claims on the health budget. Companies therefore have time to build up manufacturing capacity and the innovator has an incentive to ensure that it has enough of a drug or vaccine available to be used when payers decide to adopt. In some cases where we do need an instant response we can stockpile – as we do with Ebola vaccine and with Anthrax vaccine.

⁷³ There is already significant existing infrastructure for vaccine development and manufacturing. The flu vaccine is manufactured by more than 30 manufacturers around the world with a capacity of around 1.5 billion doses See:

<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5357707/>

⁷⁴ See: <https://www.nature.com/articles/d41573-020-00073-5>

covering 9 different vaccine technologies and there is very low fungibility across them^{75 76}. Building manufacturing capacity at risk that are entirely ‘platform agnostic’ is not possible, therefore it will either be extremely expensive or require some ‘hedging’ (i.e. picking) of winners.

- There is little experience globally for manufacturing novel vaccine platforms. Expertise is not widespread for manufacturing the novel vaccines like mRNA and DNA based platforms (e.g. mRNA/DNA/VLP based)⁷⁷.

We want companies to start manufacturing the vaccine before they know if it works. Hence the buying mechanism has to cover a mechanism for getting vaccines developed, *and a mechanism for getting them manufactured.*

[Slide 25]

5. Exploring the proposals for an AMC: two schemes

The Gavi COVAX AMC and the BBAMC

We are seeing an outbreak of vaccine nationalism with countries going it alone and seeking to make deals on price and volume, using any push funding to get access rights. We see willingness to take away intellectual property rights, such as threatening compulsory licensing. Whatever means are deemed necessary to get citizens access to a vaccine.

Getting global or regional co-ordination or consistency of approach will send clearer signals to developers, and while there has been a significant delay in global coordination, things are starting to change (e.g. with both the WHO ACT accelerator and EU announcements expected in a couple of days).

Why should countries collaborate?

- Countries may find that backing the national vaccine ‘horse’ is not successful⁷⁸;
- Most countries are not funding their own vaccine candidates, have no manufacturing capability and don’t have the buying power to get to the front of the queue on their own.⁷⁹

⁷⁵ See: Kis, Z., Shattock, R., Shah, N. and Kontoravdi, C. (2019), Emerging Technologies for Low-Cost, Rapid Vaccine Manufacture. *Biotechnol. J.*, 14: 1800376. doi:[10.1002/biot.201800376](https://doi.org/10.1002/biot.201800376)

⁷⁶ See:<https://www.nature.com/articles/d41573-020-00073-5>

⁷⁷ There are likely to be very few LMIC manufacturers who have expertise or capability to manufacture these vaccines and the companies developing these vaccines (mainly small biotechs) are not experienced in working with manufacturers outside of HICs.

⁷⁸ Indeed, we have argued that not cooperating on developing a global portfolio may increase the risk of failure of the entire vaccine portfolio

⁷⁹ Other reasons may include:

- Opting out of collaboration gives countries no flex room to use different/more effective/safer vaccines that come through the pipeline later or in other countries.

At a minimum we need a coordinated response for vaccine provision for the 3.7 billion people (50% of the global population) who live in LICs or LMICs⁸⁰

We need to pull vaccines through the pipeline to complement the push funding going into R&D and manufacturing. I want to set out:

The elements of the Gavi COVAX AMC and, how, in my view the concept of the BBAMC and how the Gavi COVAX AMC could move towards it.

For ease I do so using this table (below) which sets out elements of the AMC and how each compares.

[Slide 25]

-
- Most countries (even manufacturing countries) rely on international supply chains- they de-risk their own manufacturing by collaborating even merely strategically with relevant countries.
 - If countries act selfishly, measures taken by those further down the queue are likely to be more aggressive, for example in the use of compulsory licensing.
 - Countries that benefit from, and/ or believe in, international institutions need to show that those institutions are viable in crisis as well as “business as usual” (EU, WHO, World Bank, UN) as a counter argument to (most likely) nationalistic agendas in the US and China and in the UK (the UK’s decision not to join in joint procurement with the EU for PPE and ventilators was seen as a political/Brexit choice).

⁸⁰ Of the world’s population 9% (~705 million) live in low-income countries, 40% (~3 billion) live in lower-middle income countries, 35% (~2.7 billion) live in upper-middle income countries and 16% (~1.2 billion) live in high-income countries. See: <http://data.worldbank.org/data-catalog/world-development-indicators>

Attribute	COVAX
Incentivise private capital to invest in development	No, push needed
Incentivise private capital to invest in manufacturing capacity	No, push needed
Contingent Advance Purchase contracts	Yes
Advance Market Commitment	No (Phase 1 is not a market commitment, planned phase 2 includes unspecified market commitment)
Incentivise follow-on vaccines	Only if AMC component put in place
Countries to participate	LICs, LMICs but HICs, MLICs welcome
Quality hurdle	WHO TPP
Cost-based Pricing	Yes, flat price (allows for other options after first 12 months)
Value-based pricing	No
Differential pricing	Reference to tiered pricing
Account taken of push funding	Yes, in price
Donor support for LICs / LMICs	Yes
Prioritising allocations of vaccines	Secretariat

Taking the **The Gavi COVAX AMC**⁸¹ first

The COVAX pull is intended to complement CEPI push. It is not intended to motivate risk capital, at least initially, for either development or manufacture. This pull involves “two types of pull mechanisms”:

- “**manufacturer-specific contingent volume guarantees** to procure vaccines that meet the agreed WHO Target Product Profile”⁸².

⁸¹ My comments are based on the COVID-19 Vaccine Global Access (COVAX) Facility. Discussion Document 11th June 2020. Gavi.

⁸² Self-financing HICs and UMICs would “make a binding financial commitment to purchase doses” and make some up front “down-payments against future vaccine supply” which “will enable the Facility to enter into advance purchase commitments for future vaccine supply” The UMICs would have access to multilateral development bank (MDB) loans to support their participation.

- “a market-wide demand guarantee, i.e. an AMC.”⁸³

However, the emphasis seems to be on the short term “manufacturer-specific volume guarantee”, rather than the longer term “market-wide demand guarantee”^{84 85} This is despite the discussion document stating that

“in addition to securing supply, the COVAX Facility intends to support a continued pipeline of improved products coming to market.” and that “pull incentives generally encourage successful development and focus on addressing commercial risk.”

Hence we have said it is underspecified. If the AMC component is put in place, it will only incentivise follow-on vaccines.

Additionally:

- It is global “all countries are invited to participate”⁸⁶ but it is a scheme aimed at LICs and LMICs.
- We have already touched on the need to achieve the WHO TPP
- Pricing will “be negotiated under the expectation that manufacturers seek minimal returns in the near term”⁸⁷ [i.e. cost-based] and “there could be a flat price from manufacturers”⁸⁸
- So there is no value-based pricing but
- the paper says that “Beyond the near term, pricing would evolve to a traditional tiered pricing approach.”⁸⁹

⁸³ “Which could provide continued incentives and assurances to manufacturers to expand production capacity and to bring products to market meeting e.g. preferred characteristics of the WHO target product profile (TPP)”

⁸⁴ The document goes on to say “The pull instrument will be structured as a market-wide demand guarantee, out of which multiple manufacturer-specific volume guarantees will be made. For the initial period (2021-2022), the majority of this market-wide demand guarantee will be issued as volume guarantees on specific products to individual suppliers. For the later phase (after 2022), it is expected that the majority of the guarantee would remain unallocated, allowing introduction of improved products over time.”

⁸⁵ This may reflect the perceived importance of getting investment in manufacturing capacity, which clearly will be easier with bilateral guarantees to buy certain volumes but it neglects the need to get more candidates coming through.

⁸⁶ It is “a risk management mechanism” designed to allow countries “to enter a joint pool for securing and procuring vaccine doses” and “reducing risk for manufacturers concerned about investing without assured demand.” The working assumption is that some countries will have bilateral agreements with manufacturers. But these candidates may fail. Access to the Facility would come on top of bilateral agreements for both countries and manufacturers.

⁸⁷ “Being part of a pool ...would bring countries more sustainable vaccine prices, thanks to economies of scale and reduced transaction prices.”

⁸⁸ “with a cross-subsidisation mechanism to establish differential pricing for countries to account for varying ability to pay. The Facility may accommodate manufacturer requests for tiered pricing if the price levels offered for each tier are considered appropriate.”

⁸⁹ “the Facility will adopt the following **pricing principles**:

- Vaccine prices may reflect **the range of cost of goods (COGS), vaccine profiles, developer and manufacturer profiles, levels of support received and risk incurred** during development.
- Vaccine prices may reflect different **time periods in the disease evolution and associated variations in market conditions and commercial opportunity**. This acknowledges the broad willingness from suppliers to consider the vaccine as a global public good in the short-term, to meet global requirements for priority populations, and to evolve later to a more market-based approach. Given the pressing public health need, it is expected that manufacturers would

- and will take into consideration any other direct financial support received by manufacturers” (i.e. push funding).
- Donor financial support for LICs and some LMICs would be available via Gavi⁹⁰.
- Rules about the priorities for allocation of vaccine would follow WHO policy recommendations.

So how will it work? The financing structure, legal agreements and governance mechanism have still to be developed but the Facility will negotiate with manufacturers for volumes and prices via an Expression of Interest. It looks as if there would be legally binding commitments made by Gavi to purchase from specific manufacturers. These would be backed by commitments made to Gavi by purchasers such as UNICEF, PAHO and individual countries⁹¹. It is possible that the EU could be another regional grouping operating under the scheme. However, it does not create a market. To do this Gavi would need to be guaranteeing an overall market size given the country commitments on its “book”, not making large contingent volume commitments to each individual manufacturer.

Additional comments are set out in a footnote to the paper accompanying this lecture that will be available on the OHE website ⁹².

seek **minimal returns**. Such a model could provide incentives to as wide a range of countries as possible to join the COVAX Facility for the short-term period, while establishing a blueprint for a future lower price for LICs/LMICs.

- Vaccine prices may be tiered, reflecting countries’ varying **ability to pay**.
 - Both the Facility and suppliers are expected to adhere to **transparency principles**. The Facility will expect from manufacturers to provide full visibility on other external funding received and will provide countries with the pricing of all participating vaccine candidates’ (to the extent that such information can be shared).
- Based on these pricing principles, the Facility proposes a **mixed pricing approach that will evolve over time**:
- Short-term period to reach priority populations and control the pandemic: **A flat pricing strategy (with firms able to set their own price, which then applies across countries participating in the Facility) will be encouraged**, given existing bilateral agreements between a number of countries and manufacturers and broad expectations to price the vaccine as a global good during the short-term period. Such a pricing structure should incentivize broad country participation in the Facility. However, some manufacturers may prefer tiered pricing; **the Facility will accommodate that request** if the price levels offered for each tier are considered suitable. If a flat pricing strategy is proposed by manufacturers, **a cross-subsidization mechanism may be applied** to establish differential pricing charged to countries to account for varying ability to pay.
 - **Beyond this initial short-term period, the market is expected to evolve towards a traditional, market-led, tiered pricing approach** (noting that the Facility, itself, will be time-limited).

⁹⁰ Seed funding from OECD country ODAs of USD \$500m was pledged at the 4th June launch. Much more is needed.

⁹¹ “Upon availability of doses, vaccines will be procured via **existing procurement mechanisms** (eg UNICEF Supply Division, PAHO Revolving Fund, EC, individual country procurement mechanisms).” It is not clear what this means, but it may mean that these groupings agree the commitments on behalf of their members and are legally responsible to Gavi for honouring them.

⁹² Challenges with the COVAX Facility are:

1. **It does not incentivise development.** It assumes that the push funding model via CEPI (and others) can deliver a vaccine of the required quality. According to Annex D, the CEPI worst case scenario is that one vaccine hits the target. With 9 candidates, 1/9 is over a 10% probability of success which is [twice](#) what a recent NBER paper calculated that public sector push has achieved in previous emerging infectious disease research investments.
2. **It does not incentivise development of better vaccines.** It is cost-based rather than value-based. It assumes that prices will be at cost even if they are tiered in some way (presumably around a weighted average cost price). There is no differential reward for better vaccines. Indeed there is no mention of using HTA to assess the value of any vaccine to participating COVAX countries. As long as (all or some part of) the WHO TPP is met then a cost-based price is paid. But success is not linear. A vaccine that achieved the WHO TPP lower end of 50% efficacy (and which is apparently not necessarily the WHO TPP’s efficacy floor—see footnote 3 [here](#)) would require [unrealistic](#) assumptions re roll out timing and coverage rates, for example in the USA, to achieve immunity.

The BBAMC ⁹³

BBAMC (can be accessed <https://www.cgdev.org/sites/default/files/BB-AMC-May-2020-ppt.pdf>) ⁹⁴ We set out the attributes of the BBAMC below.

[slide 27]

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3. **It is not at all clear that a market is being created that reduces risk for both countries and (successful) manufacturers.** Although it takes the pragmatic view that countries will sign manufacturer specific bilateral deals outside of the Gavi Facility, it is not at all clear that a market is being created that reduces risk for both countries and (successful) manufacturers outside of these bilateral deals. Instead we seem to have a series of bilateral agreements (termed “advance purchase commitments with manufacturers”) within a framework set out by Gavi and at prices negotiated by Gavi. Gavi does not seem to be playing the role of an intermediary that is making a market by holding a “book” of country commitments to purchase vaccine and a corresponding “book” of offers to supply volumes with timelines, contingent on obtaining a product licence and meeting the WHO TPP criteria. Holding a book may be the intention, but it is not conveyed in the text as written. Gavi should be guaranteeing an overall market size given the country commitments on its “book”, not making large volume commitments to each individual manufacturer. Not unsurprisingly it goes on to say “it may be the case that volume guarantees cover volumes in excess of the targeted demand in order to hedge the Facility against failure of certain vaccine candidates. Appropriate financing instruments or risk transfer solutions will need to be considered to ensure that no unfunded liabilities arise from this approach and that financial losses would be minimised should vaccine candidate success rates be significantly different from their anticipated levels.” It also states that “Fully self-financing countries that join the Facility before early deals with manufacturers are concluded (date to be determined) will be able to access the ring-fenced volume for self-financing countries, while those that commit after this point would not have this assurance.”

⁹³ The BBAMC is based on the MVAC proposed for new drugs for TB, and in turn is an adaptation of the pneumococcal AMC with some important adaptations, the most important of which are that:

- (i) It uses value-based pricing rather than the cost-based AMC with a single price and purchaser.
- (ii) It is designed to stimulate R&D (as well as manufacturing) investment

⁹⁴ A summary of the BBAMC in slide form can be accessed <https://www.cgdev.org/sites/default/files/BB-AMC-May-2020-ppt.pdf> . Additional material includes:

- “Leave No One Behind: Using a Benefit-Based Advance Market Commitment to Incentivise Development and Global Supply of COVID-19 Vaccines” available at <https://www.cgdev.org/publication/leave-no-one-behind-using-benefit-based-advance-market-commitment-covid-vaccine>
- “The Race for a COVID-19 Vaccine: An Overview of Current Proposals and Our Contribution in Bringing in the Missing Middle” available at <https://www.cgdev.org/blog/race-covid-19-vaccine-overview-current-proposals-and-our-contribution-bringing-missing-middle>
- “In the Race to Develop A Vaccine For COVID-19, Is A Pull For R&D Essential Or Optional?” available at <https://www.cgdev.org/blog/race-develop-vaccine-covid-19-pull-rd-essential-or-optional>

Attribute	BBAMC
Incentivise private capital to invest in development	Yes but compatible with Push
Incentivise private capital to invest in manufacturing capacity	Yes, but separate push needed also
Contingent Advance Purchase contracts	No
Advance Market Commitment	Yes
Incentivise follow-on vaccines	Yes, a major objective is to have more than one vaccine
Countries to participate	HICs, MICs, LICs (via Gavi) to give overall market commitment
Quality hurdle	WHO TPP, with a minimum and maximum for setting value-based prices
Cost-based Pricing	No, except for the LIC/ LMIC tail-price
Value-based pricing	Yes, using HTA to assess value
Differential pricing	Yes, prices reflect local HTA and affordability results
Account taken of push funding	Yes, in price, or reduced volume commitment
Donor support for LICs / LMICs	Yes
Prioritising allocations of vaccines	Pre-agreed, implemented by the Secretariat

The benefit-based advanced market commitment (BBAMC) in our view builds on the strengths of the COVAX⁹⁵ proposals:

- (i) It incentivises both the clinical development of a vaccine as well as manufacturing supply investments. The BBAMC proposal is distinct in its focus on “pull” incentives for product development. We do not assume that current push funding mechanisms will necessarily be sufficient to bring the portfolio of safe and effective vaccines we need to market. The challenges inherent in vaccine development have largely been overshadowed by an emphasis on the need to scale up manufacturing rapidly⁹⁶.

⁹⁵ And also a manufacturing push such as from CEPI or from Accelerating HT

⁹⁶ Attracting in private capital invested at-risk, but with manageable risk and the prospect of a commercial return. This needs to be done through pull funding. Push funding for early stage research can indeed be cheap and efficient; but the

- (ii) We are however likely to need complementary push investment to bring forward at risk manufacturing capacity investment by companies⁹⁷. This can be accommodated.
- (iii) Creating an AMC rather than a network of conditional contracts is key.
- (iv) Recognising that we are likely to need a number of different vaccines. Assuming more than one vaccine proves sufficiently efficacious, the vaccine that best meets the preferred product characteristics (as detailed in the WHO Target Product Profile or TPP) would receive a greater share of the total revenue commitment⁹⁸. There would be competition, as in a normal vaccine market.
- (v) Attracting HICs and MICs as well as LICs is key and not optional, building an advanced commitment that is not just funded by donor aid. This brings clarity on the size of a very uncertain overall global market.
- (vi) Using the TPP as an entry requirement, plus a basis for assessing value is key.
- (vii) Rewarding companies with prices that reflect value rather than cost is key.
- (viii) The poorest countries would not pay a value-based price but the tailprice.
- (ix) There is differential pricing as the advance commitments are built on value assessments done by national payers that are based on products' expected health and health related benefit and countries' health budgets which impact ability to pay for a new product.

As with the COVAX Facility

- (x) Push funding can be taken into account by either adjusting the price or adjusting the size of the advance market commitment made by the country⁹⁹.
- (xi) LIC / LMIC contributions are met with donor support through Gavi.

costs and risks grow for funders. There is also a risk of funders pursuing the sunk costs fallacy - "we've paid for it so far, let's just keep going" leading to "we paid for it to be developed so now we ought to buy and use it."

⁹⁷ We need manufacturing capacity to be built at risk. This can be done through a higher price for early entry. But this risks complicating setting a VBP for the vaccine, and may incentivise accelerated development and introduction of a vaccine that is easier to manufacture, but less effective. We are therefore likely to need push investment to bring forward at risk capacity investment by companies.

⁹⁸ In terms of target performance, companies are working towards the fairly widely defined WHO Target Product Profile (TPP), without explicit incentives to address market or population specific needs, including differential safety, effectiveness and cost-effectiveness of different vaccine profiles in different populations and geographies. But such performance attributes may well make all the difference in how quickly and effectively we can control the pandemic. The BBAMC mechanism would allow inclusion of more than one product meeting minimal TPP requirements. Provision will be made for a product offering more suitable characteristics for implementation in different contexts and populations. It also takes account of the likelihood that the first vaccine to get a product license may not meet all needed criteria (in terms of overall efficacy, or method of administration or safety) and multiple vaccines may ultimately be necessary to address challenges of efficacy and tolerability in sub populations or to address field conditions. The value assessment element of the BBAMC allows for the same product or indeed different products to command different prices and hence market share across different country contexts and epidemiological realities as they may meet local needs at differing levels (perhaps because of a differential safety profile; their effect on younger vs elderly multi-morbid populations; the need for cold chain; or administration complexity).

⁹⁹ Push funding (R&D push or manufacturing push or both) for successful vaccine candidates only could count against a countries market commitment. Governments backing the wrong candidates have not partially met their commitment. It does not count. This will add to the incentive for governments to choose carefully and also to consider cross-government collaboration. Alternatively, early R&D push and early manufacturing push are taken into account in the arrangements for locking in value ex ante. This is an area that will need further discussion, but which can in principle be incorporated in a BBAMC.

- (xii) Allocation rules of some form will need to be developed to ensure manufacturers are able to distribute product across the countries making up the commitment

It could be argued that it is obvious that there is a market for a COVID-19 vaccine in enough HICs and UMICs to ensure a market incentive for private investors – especially with the push funding already invested. In our view, significant commercial uncertainty remains and an AMC is needed^{100 101}. In particular we are likely to need a number of vaccines.

It needs to be a value-based price rather than cost-based to incentivise the development of better vaccines and to avoid incentivising high cost low quality vaccines at the expense of lower cost but better quality ones.

Current speed-focused models imply a winner-takes-all approach, especially to those who are not in the lead and there is little discussion of what would happen to second (and perhaps better performing or safer) entrants.

A BBAMC for a COVID-19 vaccine would work in the following:

1. **Early health technology assessment (HTA) establishes a value-based price on the assumption that the TPP was met¹⁰²:**
 - a. The price would be “locked in” to provide overall market predictability.
 - b. The early HTA assessment would enable the size (price x volume) of each country’s advance commitment to be identified.
2. **The AMC is the aggregation of the individual commitments.**
 - a. These need to be guaranteed by a third party (such as the World Bank). This may be difficult in the case of a major HIC. However, a credible mechanism is needed to ensure that market commitments are honoured.
 - b. The BBAMC will offer value-based entry market commitments (country-specific tiered prices for guaranteed volumes) to developers that meet the minimum effectiveness threshold (as per the WHO TPP) as an incentive to keep many different potential innovators in the game post launch. This would hedge risk against late failure of one or more early candidates and against the possibility of

¹⁰⁰ Epidemiologically, the disease could either become endemic or fizzle away; here the SARS and MERS precedents are not encouraging. The economic recession could lead to drastic cuts in aid and domestic healthcare budgets that might lead governments to shirk their earlier commitments, while other technological breakthroughs (e.g. a cost-effective cure) could undermine the anticipated size and nature of a market. These uncertainties are more pronounced the longer it takes to develop a vaccine.

¹⁰¹ In our mind, credible pull incentives for development, alongside research push, are needed to further de-risk the development process for both payers (governments and donors) and suppliers (industry and investors), to crowd in private investments reducing the cost to HICs taxpayers, to share the risk of development between the government and the companies, and to inject payer accountability to the process.

¹⁰² This would also determine the vaccination strategy, i.e. the volumes required. The resulting value-based price could be adjusted downwards for relevant public push R&D and manufacturing funding (depending on the arrangements governing the funding)

safety risks after widespread deployment requiring restricted use or withdrawal from the market of the first entrant.

- c. To access the purchase commitment, the successful innovator must agree that any volumes beyond the guaranteed commitment pool—up to a pre-agreed maximum or for a pre-agreed time period—will either receive a heavily discounted price (e.g., a 70 percent discount), close to cost (plus a margin), or be made available to local licensees.

3. A mechanism to deliver manufactured vaccines around the world:

- a. As a condition of accessing this guaranteed market, governments would require the successful innovator(s) to license their vaccines out to other suppliers at low or zero cost, helping facilitate widespread scale-up across to LICs.

In addition, effective governance arrangements will be needed¹⁰³.

I don't have time to illustrate how this might work in practice but this is contained in the [MVAC report proposing an AMC for new TB drugs](#) which is accessible via both the CGD and OHE websites¹⁰⁴.

so let's try and pull this all together

[slide 28]

6. Putting it all together: A Tale of Two Paradigms

We have a clash of paradigms which is inhibiting our ability to get the right buying mechanism and in particular to move from cost-based bilateral contracts to value-based market commitments.

[Slide 29]

In brief:

- As I set out the current business paradigm for pharmaceuticals including vaccines which for HICs, is that the market pulls products through. It is a spot market characterised by an expectation (although not without dispute) on the part of the

¹⁰³ There are four key parties, (i) the governments who make commitments (ii) the guarantor who will sign agreements with the governments and so provide credible commitments to the market (iii) the secretariat / coordinator, who will be funded by a small levy on the governments and (iv) the developers who will register to participate in the scheme and agree (in contracts with the guarantor) that they will supply vaccines at the pre-set value-based price. Subsequently they will contract with governments to do this.

¹⁰⁴ This is Chalkidou K, Garau M, Silverman, R M, et al. 2020 blueprint for a Market-Driven value-based advance commitment (MVAC) for tuberculosis. Center for Global Development and the Office of Health Economics. Available: <https://www.cgdev.org/publication/blueprintmarket-driven-value-based-advance-commitment-tuberculosis> See also Chalkidou K, Towse A, Silverman R, et al. (2020). Market-driven, value-based, advance commitment (MVAC): accelerating the development of a pathbreaking universal drug regimen to end TB. *BMJ Global Health* 2020;5:e002061. available at <https://gh.bmj.com/content/5/4/e002061>

private sector that investment at risk will lead to a return if a product that improves health is delivered. And that price will reflect value rather than cost. (Although the determination of value may be disputed.)

- For LICs, tiered or differential pricing delivers drugs and vaccines developed for HICs at or near cost, but donor support is needed to buy them – donor led-pull. For diseases without a HIC market then donor push and pull is needed. However, with the exception of the pneumo-AMC, the emphasis has been on push.
- In MICs, including those graduating from Gavi and Global Fund support, we have seen a growth of spot purchasing (including contracting) with an expectation of tiered/ differential pricing, and a desire not to pay above cost if possible. There is, arguably, no credible mechanism to develop drugs and vaccines for which there is no HIC market, other than to push fund domestic institutes and companies.^{105 106}

[Slide 30]

- We are in a COVID-19 paradigm characterised by:
 - Government direction and intervention in all sectors, reflecting in the vaccine hunt by (i) push support for early and late stage development and (ii) for manufacturing with (iii) contingent procurement options as part payment for the push funding.
 - Companies exercising corporate social responsibility and recognising that resources need to be committed without a necessary expectation of profit. This is reflected in the vaccine hunt by statements that vaccines will be supplied at cost for the first year (i.e. the pandemic period)¹⁰⁷.

¹⁰⁵ For MICs arguably we are moving (slowly) towards (at least for UMICs) markets that look more like HIC ones. However, most MICs want to pay costs, not pay for value. This is changing with the growth of HTA or value assessment in many MICs, but there is a lack of expectation on the part of global and local companies that R&D investment will be rewarded with prices that reflect value. Arguably we need a stage of advance market commitments of the sort we have set out in the BBAMC to get these markets working in a way that they can transition to an HIC style spot market. There will still be an issue of income per capita in terms of ability to pay value-based prices that are high enough to reward R&D, but as we showed with the MVAC proposal for new TB drugs, there is enough of a market in MICs to reward R&D investment if it can be mobilised through the right mechanism.

¹⁰⁶ Both the COVAX and BBAMC involve (or can involve) HICs and UMICs. The R&D based industry will be very concerned about encouraging a new way of doing business that could become the new normal which is not a viable business model for them to research, develop and deliver profitable innovative vaccines for the future. The BBAMC was derived from the MVAC proposal for new TB drugs and was explicitly intended to be a transitional mechanism to a spot market where MICs paid value-based prices for new drugs which enabled companies to get a return on their R&D investment.

¹⁰⁷ The R&D based industry are very aware that in the current pandemic with economies under pressure, all businesses (whether in pharmaceuticals or any other sector of the economy) have to do what society expects, whether they make or lose money from it. And society looks to the academic science base and to the private sector industries' research and development skills for treatments and vaccines to tackle COVID-19. Hence the substantial investments being made and the statements from a number of R&D-based companies that they will supply, at least initially, on a "not-for-profit" basis. This commitment has to be time limited, private investors expect a return. The sector cannot commit large amounts of capital without making profits. One model proposed is that initial development and production of a COVID-19 vaccine is on a not-for-profit basis but subsequent years of production are supplied on a normal commercial basis.

- Donors identifying the need to find substantial resources to enable LICs to buy the vaccines and other health technologies they will need to tackle COVID-19
- MICs falling through the gaps with most not in a position to push fund vaccine candidates or manufacturing capacity.
- A current lack of global coordination and commitment (in sharp contrast for example to the handling of the 2008 economic crash).

We should pause at this point and note that there is not one global vaccine industry, but three (i) the large multinational R&D-based vaccine manufacturers who have about 80% of the value of the global vaccine market but only 20% of the volume (ii) the Developing Country Vaccine Manufacturers (DCVMs) and (iii) small HIC biotechs and niche manufacturers. The last two groups have the other 20% of the value and deliver 80% of volume primarily manufacturing large volumes of established vaccines at low cost. As we saw, DCVMs from China have COVID-19 vaccines in clinical development. Many DCVMs are able to manufacture under license¹⁰⁸. They offer a potential route to enable a COVID-19 vaccine to be manufactured at scale around the world.

[Slide 31]

What is missing in the present COVID-19 paradigm, in my view, is a recognition of the need:

1. **for greater global co-operation** and a move away from vaccine nationalism or every country for themselves.
2. **the need to get private capital mobilised to address the challenge.** The pharmaceutical industry has to provide a return to investors; its commitment to a “charitable” enterprise is likely to be far lower than its investment in a project with high [profit potential](#). As Craig Garthwaite put it [“to develop the science we need to get us out of the pandemic, we must convince biotechnology firms that we will pay for the value they create. We can’t just hope that they will follow the better angels of their nature and risk tens of millions of dollars with little hope of a return.”](#)

But specifically three ways in which the COVAX Facility could be improved.

1. **to move from cost to value**
2. **to ensure benefits exceed costs before adopting a vaccine**
3. **to move from bilateral contingent contracts to a pull mechanism that creates a market,**

¹⁰⁸ The R&D based industry is not necessarily going to want to manufacture billions of doses of a new vaccine to supply at cost. That is not their core business. Innovators’ willingness to take-on responsibility for global manufacturing may therefore be limited, so they may well welcome initiatives by Gavi and Gates Foundation and others to invest in manufacture aimed at LICs and LMICs, and recognise the need to “hand-off” manufacture of their products to others, subject of course to addressing quality of manufacture concerns and competitive issues (some technologies are proprietary).

More specific details are provided in a footnote to the published text¹⁰⁹.

How do we move the COVAX Facility towards a BBAMC?

It could be argued that timing is key here. If manufacturers and governments and international funders are already “locked” into push funding and contingent advance purchasing contracts, then it is too late to step back and change the buying mechanism at least for the current leading vaccine candidates.

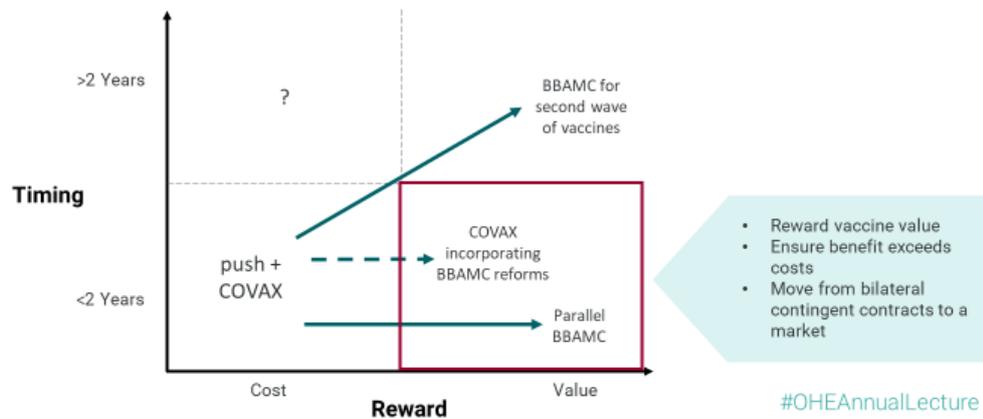
We illustrate this point below in Figure 2 using greater or less than 2 years to have a vaccine as an indicator of how radical the changes can be.

[slide 32]

¹⁰⁹ The challenge for the current proposals notably the COVAX AMC is threefold:

1. **The need to reward Vaccine Value.** This is to avoid countries getting locked into purchasing low-efficacy vaccines. Deals with manufacturers should incorporate value assessment. At a minimum, the deal is only valid *or* commands a higher price if vaccine meets WHO target product profile characteristics based on modelling against epidemiological, health system delivery and demographic characteristics. Ideally Price/total deal amount for vaccines scale progressively with vaccine effectiveness
2. **Ensure Benefits Exceed Costs.** This is to avoid countries rolling-out low-efficacy vaccines because of sunk cost fallacy (“we paid for them, so we may as well use them”) even though the costs of roll-out exceed the benefits. We need to ensure use of a vaccine in any patient group passes the “do benefits exceed the cost?” challenge. We need to ensure health technology assessment (HTA) is conducted before rolling out a vaccine (even if the vaccine price is a sunk cost) and also use HTA processes to ensure accountability and due process around vaccine adoption decision-making.
3. **Move from Bilateral “Deals” to Market Commitments.** This is to avoid countries being locked into purchasing low-efficacy vaccines even if better vaccines become available; bilateral deals crowd out private sector investment in other promising candidates and lower overall probability of successful vaccine development. This can be done by
 - Beyond or instead of bilateral deals, maintain “pull” for R&D by committing unallocated pool of funds to a market-wide advance commitment
 - Link value of commitment to vaccine performance through HTA process
 - Clearly communicate that countries will be open to procuring any effective vaccine in years 2-3 and will respect IP/pay prices commensurate with product value

How can the BBAMC can be implemented for COVID-19? COVAX can be adapted or BBAMC run in parallel to pull candidates through



It is feasible to introduce a BBAMC for a potential second wave of candidates but also to implement incremental change to current proposals and mechanisms in place.

We have three non-mutually exclusive options

- Add elements of BBAMC to existing deals; moving you right along the X axis (COVAX incorporating BBAMC)
- Run a parallel BBAMC, a belt and braces approach, in which countries already committed to bilateral deals can also join. This can be moving us to value and can sit to the right of the first option.
- Scope out/scale up a BBAMC for post first launches, i.e. a second wave of development. COVAX becomes a BBAMC scheme.

Before we move on, we need also to go back to the money. We cannot make a COVAX AMC work, whether or not it is adapted to have elements of a BBAMC without resources. There are two key announcements on the 27th - from WHO and from the EU. They are both likely to set out potential commitments and identify the size of the gap needed to pay for vaccines for LICs and LMICs.

[Slide 33]

So, finally a quick look at lessons for the future

7. Lessons for the future

[Slide 34]

We need to avoid some of the mistakes that are being made this time. In particular, with preparation it may be possible to avoid the government push / industry cost-pricing paradigm we are in with the potential consequences for the composition of the global portfolio and the degree of engagement of private capital.

Preparedness for a repeat of an H1N1 virus-based pandemic was built up with WHO monitoring and seeking to maintain influenza vaccine capacity. A more comprehensive set of market mechanisms now need to be developed.

CEPI has worked and shown that we can get early stage research underway very quickly and some candidates into the pipeline quickly¹¹⁰. But we also need to build market mechanisms in advance, i.e. plan for a (benefit-based) AMC.

The distributive issues will always be an issue in a pandemic and work can take place in advance to get countries to sign up to a realistic set of rules (which may include an element of vaccine nationalism, i.e. countries that host successful candidates get some preferential access.)¹¹¹

The financing arrangements to pay for LIC vaccines and for some LMICs could be pre-agreed and automatically triggered by a pre-set hurdle (e.g. WHO declaring a pandemic).

[Slide 35]

And, finally, let us not forget that COVID-19 is causing a health and economic disaster. Let us wish success to those in academia and in industry involved in researching, developing, or planning the manufacture of a COVID-19 vaccine.

¹¹⁰ In part because of genuine innovation in vaccine technology over the past 20 years.

¹¹¹ Ref Miller - There are three different and conflicting principles of justice:

1. Rights based – Government A has a contract for the vaccine, it has a right to that vaccine for its citizens
2. Desert based – Government B has funded the research and the capacity that has enabled this vaccine to be developed and produced - it deserves to access that vaccine for its citizens
3. Needs based – Government C has a highly vulnerable population - it needs that vaccine for its citizens

We can prioritise health care workers on all three principles. We can make trade-offs e.g. using Eric Nord's person trade-off (PTO) approach. How many of your country's vulnerable citizens are you prepared to sacrifice so that health care workers in another country can get the vaccine? This gets us into principles of global justice, beyond social justice in terms (primarily) of scope. The point is that we need to be having these discussions and going beyond bland statements or lists that way exceed conceivable short term supply availability and so do not make serious trade-offs.