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Achieving path-dependent equity for global COVID-19 vaccine allocation

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Committing to global access for COVID-19 vaccines is key to avoiding a resurgence of the pandemic. However, agreements between countries and vaccine manufacturers have undermined a globally coordinated approach, and the ongoing vaccine rollout highlights long-standing inequities in health. Yet, the surest path out of this pandemic is one toward greater equity.

In a globalizing world, pathogens cross borders readily, as do the expectations of life-saving vaccines, but the products often lag behind. This asymmetry in globalization gives rise to health inequity. Delays in life-saving treatments arriving in low- and middle-income countries (LMICs) years after they have become available in high-income countries is not new, but COVID-19 has shone a spotlight on this.

In fact, the delay between first approval in a high-income country and final approval in Sub-Saharan Africa for products preventing or treating communicable diseases has historically added 4 to 7 years.¹ To bring such products from bench to bedside, product development partnerships and financing mechanisms like advanced market commitments have helped to speed or scale their development; collaborative procedures for accelerated registration have expedited their approval in countries that can take advantage of work already carried out by stringent drug regulatory authorities; and agencies like United Nations

International Children’s Emergency Fund (UNICEF) have worked to procure and scale these products. The key difference now is that there is urgency in delivering COVID-19 vaccines not only to LMICs, but also to the entire globe—both to address humanitarian needs and also to stamp out the risk of pandemic resurgence and of variants emerging.

Just as it has highlighted disparities within countries, COVID-19 has exposed the gulf between countries as well. Before the first vaccine received US FDA Emergency Use Authorization, just over half of pre-market purchase commitments of COVID-19 vaccines were reserved by high-income countries comprising 14% of the world’s population.² Canada, Australia, the United Kingdom, Japan, the European Union, and United States all had reserved more than one vaccine course per person for their respective populations. However, financing for the COVAX Facility—the vaccines pillar of the World Health Organization (WHO)’s Access to COVID-19 Tools (ACT) Accel-

erator—was still coming together then, and 40% of the projected capacity for vaccine production by the end of 2021 among leading manufacturers had not been bought up by that time.² Hedging their bets, countries arguably were responsibly diversifying their risks by investing across a range of candidate vaccines, because no one knew which would eventually succeed.

As vaccines are now administered, this disparity has only widened, and the rift in global solidarity has become glaringly obvious. Opening the WHO’s Executive Board in January, Director-General Tedros Adhanom Ghebreyesus related, “More than 39 million doses of vaccine have now been administered in at least 49 higher-income countries. Just 25 doses have been given in one lowest-income country. Not 25 million; not 25,000; just 25.”³ After three months of COVID-19 vaccine distribution, the United States and China account for nearly half of all vaccinations globally, and nearly 60% of all vaccines have been administered in high-income countries (see [Table S1](#)).

The WHO put forward an approach to equitable allocation based on ensuring COVID-19 vaccine doses proportional to population, prioritizing high-risk

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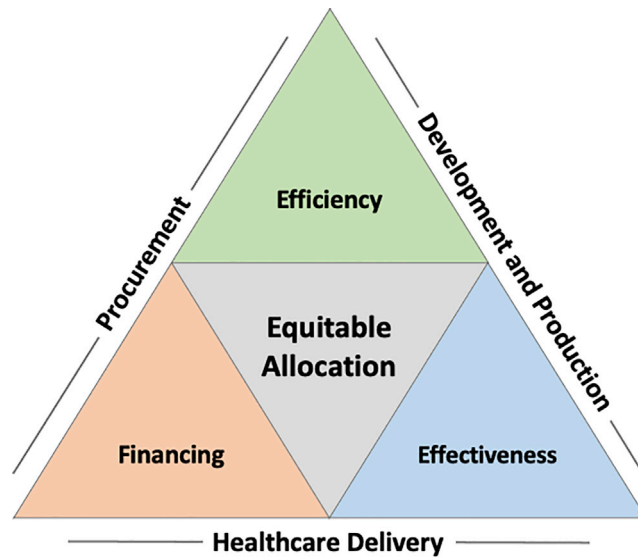


Figure 1. Triangle of equitable allocation for COVID-19 vaccines

individuals and vulnerable populations first within recipient countries.⁴ With over fifty countries not having administered any COVID-19 vaccines, the world seems far from meeting the global demand (<https://covid19.who.int/>). However, efforts are stepping up. Boosted by recent pledges from G7 countries, the COVAX Facility has mobilized US\$6.3 billion for 92 lower-income countries eligible to receive donor-funded doses of COVID-19 vaccines (<https://www.gavi.org/news/media-room/g7-backs-gavis-covax-amc-boost-covid-19-vaccines-worlds-poorest-countries>). Belatedly, the United States, under a new administration, has joined COVAX—pledging US\$4 billion of this total. To date, COVAX has secured over a billion doses and, in the first two quarters of this year, will roll out about 240 million doses, 12% of its end-of-year goal of 2 billion doses (see [Table S2](#)). Still these efforts will leave most lower-income countries considerably short of achieving herd immunity through vaccination.

No country's government can be faulted for wanting to take every domestic measure possible to avoid further tragedy. A year into this pandemic, the United States

has lost over half a million lives—more than the country's lives lost in World War I, World War II, and the Vietnam War combined and a fifth of the world's total toll. However, the boomerang risk of continued transmission and emerging variants should motivate a global response in ways that diseases like HIV/AIDS, malaria, and tuberculosis have not in the past. With only vaccination of those susceptible in advanced economies, the economic toll may mount to trillions more, much of it falling back on these high-income countries.⁵ The surest path out of this pandemic is also the one toward greater equity. Admittedly though, the decisions made by countries to date, the bilateral deals struck, and the lack of global solidarity make this road to equity path dependent.

In bringing COVID-19 vaccines to market, equitable allocation is a function of demonstrating vaccine candidate effectiveness, ensuring financing for healthcare systems, and enabling efficient delivery. As these vaccines become available, three policy levers might help define the triangle of equitable allocation (see [Figure 1](#)): development and production, procurement, and ultimately, healthcare delivery. Development and production shape the supply side; health-

care delivery, the demand side; and procurement, demand against available supply. How do we triangulate these factors to achieve more equitable allocation of COVID-19 vaccines?

Development and production

Development and production of COVID-19 vaccines for global allocation will necessarily unfold in stages. Sustaining the research & development (R&D) pipeline will be important for several reasons. Among the 81 COVID-19 vaccines currently in clinical development, other vaccines may yet come forward, offering just-in-time alternatives tested on variants, options better suited for delivery in resource-limited settings, or longer lasting duration of immunity.⁶ This progress will continue to rely on timely sharing and exchange of data, biospecimens, and research findings. Regulatory review filings and peer-reviewed journal publications have provided much needed transparency over the science behind claims of vaccine efficacy.

Such transparency has provided reassurance to policymakers and the public that vaccine candidates work across a range of ages and diverse populations, protect against severe disease, and have acceptable risk profiles. However, the duration of immunity and effectiveness against variants remain in continuing flux. Already, drops in efficacy have been observed in clinical trials carried out in South Africa—where the B.1.351 variant predominates—for AstraZeneca/Oxford, Novavax, and Johnson & Johnson/Janssen candidates.⁷ Without ramped up diagnostic testing for COVID-19 variants, comparing vaccines tested in different countries will become harder, limiting where we might generalize the findings of clinical trials.

In the near term, a key bottleneck to ensuring global access to these vaccines is production. No single vaccine manufacturer is positioned to produce enough vaccines for global coverage. To meet global demand, multiple

vaccines will have to be scaled, each with a network of partners. The need for investing in these production facilities was anticipated early on. The Coalition for Epidemic Preparedness Innovations (CEPI) had made strategic investments in a global manufacturing network, both reserving capacity for production of the active ingredient for COVID-19 vaccines and securing supplies of glass vials (https://cepi.net/news_cepi/cepi-expands-global-manufacturing-network-reserving-manufacturing-capacity-for-more-than-1-billion-doses-of-covid-19-vaccines/). UNICEF announced plans last October to stockpile over half a billion syringes by the end of 2020.⁸ The COVAX Facility brought together key partners, from the WHO and CEPI to UNICEF and the Pan American Health Organization's (PAHO's) Revolving Fund for Vaccine Access.

Still, these efforts collectively fall significantly short of the capacity needed to meet global demand. Speeding the pace of scale-up will require enlisting more partners. This will entail sharing intellectual property and the technical know-how of manufacturing these vaccines. Some have called for voluntary pledges to share such intellectual property,⁹ others, both from governments led by South Africa and India and from civil society groups led by voices from the People's Vaccine Alliance, for a Trade-Related Aspects of Intellectual Property Rights (TRIPS) waiver suspending patent rights on COVID-19-related technologies to meet the urgent needs during the pandemic. Forty member states joined Costa Rica in calling on WHO to establish a COVID-19 Technology Access Pool (C-TAP) that would facilitate the voluntary sharing of knowledge, data, and intellectual property needed to accelerate the development of products to address COVID-19.

The sharing of intellectual property has already proven critical for several of the leading COVID-19 vaccines that target the coronavirus spike glycoprotein,

which aids the viral membrane to fuse with the human host cell. The antibody response of these COVID-19 vaccines to this target depends on stabilizing the spike protein in its prefusion conformation, and this relies on an approach developed and patented by NIH and academic scientists. Reportedly, at least three mRNA vaccines (Pfizer/BioNTech, Moderna, and CureVac) as well as the vaccine candidates developed by Johnson & Johnson and Novavax rely on this publicly funded, patented invention (https://www.citizen.org/article/leading-covid-19-vaccines-depend-on-nih-technology/?eType=EmailBlastContent&eld=3dbde9f7-8f59-48e0-99d8-78b49ea5e77e#_ftn3). Just as these first-generation vaccines have depended on the ability to license a key patented invention to accelerate their product development, so may be the case for second-generation vaccines, of which there are over 260 candidates in the pipeline.⁶ Over 30 of these vaccines are based on the mRNA vaccine platform. Yet, a patent landscape of the mRNA vaccine space found the intellectual property holdings to be "highly fragmented," with BioNTech, Moderna, CureVac, and GSK collectively owning half of these patent applications.¹⁰ A proposal such as C-TAP was meant to anticipate the challenge of a potential patent thicket, but to date, not one vaccine firm has licensed patents voluntarily as part of this initiative. Such a technology trust can provide needed public-sector stewardship for the building blocks of knowledge that must be widely licensed, so that the development of products to fight COVID-19 can be accelerated from bench to bedside and affordably distributed to those in need.

Public investment will also be needed to facilitate technology transfer, contract existing manufacturing facilities, and build new facilities to scale up vaccines for the current and future pandemics. A key motivation for making this investment should be to ensure the capacity to switch vaccines. With potentially new COVID-19 variants on the way, lead vaccine manufacturers may not be well positioned to

switch to a demonstrably better vaccine, even if their facilities could scale its production. Public investment and control over the manufacturing infrastructure of the supply chain could speed the switch to such a better, second-generation vaccine.

Procurement

Public sector procurement provides assurances to manufacturers of market demand and leverages monopsony buying power to ensure affordable pricing. Effective procurement requires many key elements, but we will focus here on transparency of COVID-19 vaccine arrangements, global coordination of vaccination efforts, an effective sharing and exchange mechanism for COVID-19 vaccine doses, and affordable pricing.

At every stage, from R&D to delivery, there needs to be transparency of the COVID-19 supply chain. Making clinical trial findings available builds public confidence in vaccine performance and in the government's process to ensure effectiveness and safety of these products. Vaccine manufacturers should be keen for this review, for it reflects a partnership and a shared responsibility to bring forward new vaccines should unforeseeable adverse reactions, logistical challenges in delivery, or disinformation efforts require response. Transparency should also extend to the public financing of these vaccines as well as the pricing, licensing, purchase commitments, and scale-up options. Unless vaccine manufacturers can shoulder the responsibility and the public accountability for deciding which country's vaccine orders come first and which countries come last, transparency is a prerequisite to global coordination of vaccination efforts. It should not be the prerogative of any private company to ration a pandemic vaccine for the world. So, country governments, beginning with those home to these vaccine manufacturers, should insist on such transparency and work to make signed vaccine deals transparent.

While the vaccine doses may not yet be in hand, all of the G7 countries—including Canada, Japan, the United States, the United Kingdom, and France, Italy, and Germany as part of the European Union—have secured sufficient approved COVID-19 vaccines to cover their entire populations (see [Table S3](#)). The French government has proposed sharing 5% of its vaccine doses, and the United Kingdom and Germany have indicated a willingness to provide surplus vaccines to COVAX, with timing and quantity to be determined. The critical question is at what level of domestic vaccination efforts are national governments prepared to share available vaccine supplies with other countries. While there remains uncertainty around the duration of immunity and effectiveness against emerging variants, now is the time to make clear, public, and principled commitments to share any surplus and to help mobilize the manufacturing capacity to make up the difference.

The patchwork of bilateral deals has complicated efforts to roll out COVID-19 vaccines. The COVAX Facility recently published their interim distribution forecast of COVID-19 vaccines, based on projected availability of two vaccine candidates approved by the WHO for emergency use: AstraZeneca/Oxford and Pfizer/BioNTech (<https://www.who.int/news/item/03-02-2021-covax-publishes-first-interim-distribution-forecast>). Out of the 140 UN member states included in this distribution, more than 40 countries had also signed bilateral purchase commitments for vaccine doses in addition to those received through the COVAX Facility (see [Table S4](#)). Earlier bilateral purchase commitments had been struck largely by high-income countries, but now many middle-income countries have such arrangements as well. Could some countries be double-dipping, drawing on their COVAX allocation while also receiving doses under bilateral purchase commitments?

Sharing and exchange mechanisms are impeded by limits on the interchangeability of vaccines, on where countries are in the queue for receiving vaccines, and on export restrictions. Not all COVID-19 vaccines are shareable from one country to another, given differences in cold-chain requirements, effectiveness against variants, and other factors. With multiple vaccines coming onto the market, temporal trading of places in the queue might also speed global access. For example, should the United States, which has not yet approved the AstraZeneca/Oxford vaccine, make a temporal trade on its reserved doses with countries waiting and ready to use this vaccine now (<https://www.nytimes.com/2021/03/11/us/politics/coronavirus-astrazeneca-united-states.html?smid=url-share>)? Export restrictions can also thwart efforts to distribute vaccines. The European Union has required that companies receive authorization before exporting COVID-19 vaccine doses. Facing under-delivery from AstraZeneca/Oxford for vaccines destined to the European Union, Italy blocked more than 250,000 of these vaccine doses to Australia.¹¹ While these export controls were set to expire in March, the European Union plans to extend these measures until at least the end of June.¹²

Regional procurement facilities also have the potential of bolstering such sharing and exchange. While the PAHO Revolving Fund for Vaccine Access has long served Latin America and the Caribbean to secure vaccine doses, another regional platform is emerging and could complement COVAX's efforts. The African Union has established the Africa Vaccine Acquisition Task Team to secure sufficient vaccine doses to achieve a target immunization level of 60% (<https://www.afreximbank.com/african-union-member-states-accelerates-online-pre-orders-as-ampsp-adds-300-million-sputnik-v-doses-to-its-covid-19-vaccine-portfolio/>). South Africa has switched from the AstraZeneca/Oxford vaccine, which has

proven less effective against the B.1.351 variant, to other COVID-19 vaccines, and in so doing, has offered the AstraZeneca/Oxford doses to the African Union for use in countries where this variant is not widely circulating. Building such regional capacity may provide needed infrastructure for addressing COVID-19 vaccine supply and perhaps other health commodities over time.

Given limited financing, low-cost pricing of vaccines will be key to enabling countries to secure sufficient vaccine doses for population coverage. However, vaccine prices vary widely, with mRNA vaccines commanding higher prices compared with most other platforms. Such price differentials can have significant impact on budgets: switching from the AstraZeneca/Oxford vaccine to an mRNA vaccine could result in a nearly 3-fold increase in the financing required.¹³ While several vaccine manufacturers have pledged pandemic pricing, some reportedly at no profit, the question remains when pandemic pricing will go away.

Many reasons could explain the range of vaccine prices, including differences in the costs of R&D, manufacturing, distribution, licensing arrangements, and level of public financing. In the end, the costs for developing successful vaccines are covered by the public, either upfront through financing that pays for the inputs of R&D or financing that pays for the outputs through purchase of vaccine doses. In 2019, the World Health Assembly adopted a resolution urging member states to, among other things, “take appropriate measures to publicly share information on the net prices of health products” and “work collaboratively to improve the reporting of information by suppliers on registered health products, such as reports on sales revenues, prices, units sold, marketing costs, and subsidies and incentives.”¹⁴ Now would be an excellent time for member states to follow through on the WHO's transparency

resolution (<http://g2h2.org/wp-content/uploads/2019/12/Session-2-Thiru.pdf>).

Healthcare Delivery

Deployment of vaccines in the healthcare delivery system will present challenges. Lowering R_t (the rate of transmission) below 1 is a goal achievable only if effective herd immunity is reached in the population, population coverage is sufficiently high, and pandemic social distancing measures hold while the other two aims are achieved. High-income countries have shown just how hard this is to achieve even in well-resourced settings. Financing the in-country delivery of vaccines, from cold chain to administration, must also fall into place if last-mile challenges are to be surmounted. As the sprint turns into a marathon, will the financial commitments from multilateral institutions and development banks hold and sustain financing on the road to recovery?

For LMICs, this story of being last in line is not new. In 2009, the emergence of the H1N1 influenza virus prompted a WHO declaration of a global pandemic and led to efforts to develop a vaccine. After a slow start and shortages, vaccine supply began to scale, but not before patient demand began to wane as it typically does with seasonal influenza.¹⁵ Of 229 million vaccine doses bought by the United States, 91 million were used, 71.5 million were possibly discarded, and only 25 million donated to other countries (<https://web.archive.org/web/20100408172009/http://www.washingtonpost.com/wp-dyn/content/article/2010/03/31/AR2010033104201.html>). This time round, governments around the globe should show global solidarity and commit to do better.

The path into this pandemic has sharply reminded us of long-standing health inequities, only made starker because of its toll on livelihoods as well as lives.

When we turn the page on this chapter, perhaps we can do more to ensure that it is remembered for the more equitable path we sought to pave on the way out of this pandemic.

SUPPLEMENTAL INFORMATION

Supplemental information can be found online at <https://doi.org/10.1016/j.medj.2021.03.004>.

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DECLARATION OF INTERESTS

The authors declare no competing interests.

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