COVID-19 vaccine equity: a health systems and policy perspective

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ABSTRACT

Introduction: The global COVID-19 vaccine rollout has highlighted inequities in the accessibility of countries to COVID-19 vaccines. Populations in low- and middle-income countries have found it difficult to have access to COVID-19 vaccines.

Areas covered: This perspective provides analyses on historical and contemporary policy trends of vaccine development and immunization programs, including the current COVID-19 vaccination drive, and governance challenges. Moreover, we also provide a comparative health system analysis of the COVID-19 vaccine deployment in some countries from different continents. It recommends that the international Access to COVID-19 Tools Accelerator (ACT-A) partnership requires a strong governance mechanism and urgent financial investment.

Expert opinion: All WHO member states should agree on technology transfer and voluntary license-sharing via a commonly governed technology access pool and supported by a just Intellectual Property regime. Contextualized, dynamic understandings and country-specific versions of health systems strengthening are needed to improve vaccine equity in a sustainable matter.

1. The COVID-19 pandemic and its vaccine race

At the time of writing, the world is over a year into the COVID-19 pandemic and the origin, drivers, and course of the pandemic as well as public health and broader policy responses to contain it have been extensively debated [1]. While non-pharmaceutical interventions were initially the mainstay to control this pandemic, vaccines have been developed surprisingly fast, and are now globally the most powerful immediate strategy to allow societal and economic activity to resume. Vaccines have historically been critical tools in controlling, eliminating, or even eradicating infectious diseases, but many steps in the trajectory from prioritization for development, licensing, costing, availability, manufacture, and global distribution have invariably led to unequal or delayed access to these across global populations. The rapid development of highly effective and broadly safe COVID-19 vaccines is laudable and scientifically unprecedented in scope and speed. However, this development has been driven largely by the need and financing in high-income countries (HICs)1 where the COVID-19 disease had initially struck especially hard. Moreover, the SARS-CoV-2 virus is highly transmissible, with a high fatality rate among risk groups, and new variants rapidly emerging, leading to unpredictable surges with an overload of hospital and primary health-care facilities. This high burden and uncertainty has resulted in governments focusing primarily on their national electorates, whereas equitable need-based global distribution of vaccines, is not only fair, but also makes all safer. Despite early policy commitments by the European Union (EU) and its member states to ensure that COVID-19 vaccines become a global public good, by 9 April 2021, 40% of the 726 million doses of COVID-19 vaccines administered globally have been in 27 wealthy nations representing only 11% of the global population. In contrast, people in countries making up the least-wealthy 11% have been administered only 1.6% of COVID-19 vaccines so far [2]. This discrepancy is in part since the reported burden of COVID-19 has been higher in some countries. As of 1 May 2021, the US, UK, and EU had reported 1,392,249 (44%) of all 3,192,782 global fatalities [3] while comprising 10% of the world’s 7.67 billion population – likely due to an older population than less-resourced countries. However, less wealthy countries do not have doses to vaccinate even the most high-risk populations such as health-care workers and most vulnerable older adults, comprising 1–10% of the population as estimated by the WHO in the most basic scenario of very limited vaccine availability [4]. Meanwhile, some HICs have started vaccinating less vulnerable younger people; moreover, as insurance for future needs, these countries have secured enough vaccine doses and manufacturing capacity to vaccinate their population several times over. Yet, the surge in India and the predominance of younger adults hospitalized in Brazil demonstrates the capricious nature of this virus and the need for vaccination can suddenly become...
urgent in previously less-affected countries [5]. This inequity led the WHO Director-General (DG) Dr. Tedros Adhanom Ghebreyesus to state at the WHO’s Executive Board meeting in 2021 that ‘the world is on the brink of a catastrophic moral failure – and the price of this failure will be paid with lives and livelihoods in the world’s poorest countries’ [6].

Not only is there polarization between the global North and the global South [7], but ‘vaccine nationalism’ has also led to fierce competition among HICs. For instance, Italy blocked the export of 250,000 vaccines produced by AstraZeneca (AZ) to Australia in March 2021 [8]. This was an unprecedented step at the time as the EU is a regional economic entity that promotes free trade. The main argument provided was that the EU and Italy had experienced shortages of supplies and delays from AZ [9]. Serum Institute of India, the world’s largest vaccine manufacturer [10], is a major producer of the AZ vaccine for the COVAX COVID-19 vaccine initiative also had halted vaccine exports given a surge of the epidemic in India from April 2021. Prioritizing India’s domestic needs delays the delivery of this COVISHIELD vaccine and puts 64 low- (LICs) and lower-middle-income countries (LMICs) at risk [11]. Meanwhile, the EU and its member states, while also prioritizing and protecting their own populations, sued AZ over vaccine delivery delay [12] in a move that further demonstrates the intricate implications of a fragile global vaccine supply system.

The Access to COVID-19 Tools Accelerator (ACT-A) partnership was established by the WHO and partners in April 2020 to facilitate global availability to COVID-19 testing, preventive, and therapeutic tools [13]. ACT-A is mandated to coordinate the strategy, financing, and work of several global health partners under four pillars: diagnostics, therapeutics, vaccines, and health systems. The vaccine pillar (COVAX [14]) aims to make 2 billion doses of the COVID-19 vaccine globally available by the end of 2021. Unfortunately, not only considerable funding gaps but also the political realities of many countries prioritizing domestic vaccination coverage over international cooperation are hampering its success. Only 69 million doses have been made available through COVAX as of May 2021 [15]. While ACT-A is a laudable multilateral partnership that was quickly established to respond to the COVID-19 emergency, it has flaws. Its funding follows an international aid model that depends on the benevolence of rich multilateral, bilateral, and philanthropic donors that has proved fickle in these difficult times. There are several suggestions that this setup is unfit to respond to a pandemic, and that it must be rethought, especially as massive public funding has been invested in vaccine development and procurement, including for its COVAX facility [16,17]. At a minimum, it could be expected that transparent and fair price-setting mechanisms are established and that intellectual property, technology, and knowledge are publicly shared to make COVID-19 vaccines a global public good [18].

1.1. Immunization campaigns in a historical perspective

Of relevance is a historical perspective, and an examination of the large international immunization campaigns in the second half of the 20th century. The smallpox eradication campaign is hailed as one of the WHO’s biggest successes and considered one of the victories of Cold War cooperation. Still, the WHO’s DG Halfdan Malher, who oversaw the final stages of smallpox eradication in the 1970s, considered it a unique exception rather than an example for other worldwide disease eradication campaigns: ‘That idea is tempting but illusory’ given the financial and logistic burden of those campaigns on health systems [19]. The WHO’s Expanded Program of Immunization (EPI) was initiated in 1974, aiming to ensure all children were vaccinated. Centralized procurement by UNICEF led to low costs of oral polio, measles, BCG, and DTP vaccines in the original basic EPI scheme, ranging between USD 0.1–0.4/dose including procurement, supply chain, and service delivery costs [20].

In the last 20 years, inequity of routine vaccination has further decreased, in large part because of new financing frameworks and procurement mechanisms, and the establishment of Gavi, the Vaccine Alliance, in 2000, bringing together private and public partners. The Gavi Alliance, via its Advanced Market Mechanism (AMC) and partnership model, has driven down prices for the procurement of routine vaccines. In 2002, Gavi funded three ‘Accelerated Development and Introduction Plans’ for rotavirus, pneumococcus (PCV), and Haemophilus influenzae type b (Hib) vaccines to reduce the time lag between their introduction in rich countries and poor
countries and increasing coverage. These plans have supported the introduction of four vaccines in 43 countries since 2002 [21]. Of note are the newer vaccines such as rotavirus, human papillomavirus (HPV), pentavalent (diphtheria, pertussis, tetanus, hepatitis B, and Hib), and PCV vaccines. Although these have prices ranging from USD 1.6-14.0/dose – a price range that is often over 10 times as those in the original EPI scheme [20] – global expansion of the use of these vaccines continues because of public subsidies and international aid.

The development, manufacture, and delivery of vaccines for pandemics is a relatively new concept. The world has been thinking about global pandemic vaccination for over 20 years; especially since 1997 when the emergence of the deadly bird flu H5N1 in Asia stimulated the development of pre-pandemic vaccines. Equity issues arose at that time as companies needed access to the virus for vaccine production. In 2007, Indonesia stopped sharing flu virus strains until they were assured access to the benefits of vaccine production [22]. It led to the creation of the WHO’s Pandemic Influenza Preparedness Framework in 2011 intending to create ‘a fair, transparent, equitable, efficient, effective system for access to vaccines and sharing of other benefits’ [23]. In response to the H1N1 pandemic in April 2009, the WHO started the Vaccine Deployment Initiative [24]. Despite the initial commitment of 100 million doses, the initiative had to deal with several legal, planning, and certification delays. The pandemic was not as serious as initially feared and enthusiasm for vaccination waned in many countries. Although the COVID-19 pandemic is more deadly and impactful, the current vaccine equity debate, however, feels much a déjà vu.

Vaccine inequity is a long-standing public health challenge. For instance, inequities between HICs and LICs/LMICs in access to vaccines have been discussed in relation to rabies [25]. Inequity also exists within countries where often the most affected sections of society are also the least vaccinated, especially for adult immunization [26]. This is known as the inverse care law: the availability of good medical care tends to vary inversely with the need of the population served [27]. This was observed for HPV vaccination [28] and also for influenza vaccines in the US where vaccination rates in 2009 for both seasonal and pandemic H1N1 influenza among non-Hispanic White adults were higher than in Black, Hispanic, and other groups [29,30]. These patterns have repeated themselves across US states for COVID-19 vaccination [31].

1.2. The policy imperatives for vaccine equity

Vaccine inequity is an increasingly important matter in public health and foreign policy debates, for both ethical and pragmatic reasons. First, access to essential medicines and vaccines is a prerequisite for the fundamental human right to health for all [32]. Second, pandemics come in waves, with devastating effects on health systems, particularly (but not exclusively) those in LICs/LMICs [33]. Third, the longer a pandemic virus circulates globally, the more opportunity there is for the emergence of more transmissible or virulent variants, which may evade existing vaccine formulations and put the global population at risk, thereby delaying global economic recovery. The International Chamber of Commerce estimates that in today’s era of global supply chains and commerce, uncoordinated COVID-19 vaccination will risk global gross domestic product (GDP) losses of as much as USD 9.2 trillion, approximately half of which will be in advanced economies [34]. Ensuring a mechanism for equitable global need-based pandemic vaccination is, therefore, an urgent matter [35].

In this perspective, we will not only look at the current global policy debate but also consider the difficulties that especially LICs/LMICs face in organizing their national health systems in such a way as to prioritize, procure, and deliver COVID-19 vaccines. While currently much attention is, rightfully, focused on international policy and coordination mechanisms such as COVAX and the impact of the 1995 World Trade Organization (WTO) Agreement on Trade-Related Aspects of Intellectual Property Rights (TRIPS) [36] on access to vaccines, it should not distract from the need to address the other, related health inequities between and within countries. Notably, after over a decade under the WHO’s revised International Health Regulations (IHR) from 2005, only a third of Member States meet the core capacities of public health systems required to fulfill the obligations to guarantee basic health security and essential public health functions [37]. The failure to strengthen fragile and under-funded health systems is among the major reasons that vaccination coverage for several infectious diseases, including COVID-19, remains far from optimal for the majority of the world population [38].

2. Vaccine equity

We apply a ‘shortfall equality’ working definition to global COVID-19 vaccination (see Text Box 1) as the entry point to improve equity [39]. This concept can be applied between and within countries and populations using the ‘standard expected years of life lost’ averted per dose as a metric. This principle raises several questions and complexities. First, in most countries, vaccines are being prioritized for the elderly and other risk groups, such as those with important comorbidities. Second, the COVAX allocation plan uses a threshold allocation norm: vaccine doses would initially be allocated to participating LICs/LMICs in proportion to their population size. Only after each country receives vaccine doses for 20% of its population (the pre-stated threshold, to date) would countries’ COVID-19 risk profiles be considered in a subsequent phase of vaccine distribution. Scholars have argued that such an allocation would contradict the WHO’s Strategic Advisory Group of Experts’ (SAGE’s) own ethical framework for COVID-19 vaccine allocation [6]. They propose instead a Fair Priority model, which takes into consideration premature mortality; serious economic and social harm, measured through loss of Gross National Income and reduction in absolute poverty gap; and how much transmission was ongoing in a country [40]. In-country analysis has little relevance as long as vaccines are hardly available in many LICs/LMICs. Pursuing vaccine equity
also requires having a closer look at the global governance of trade and intellectual property rights (IPR).

**Text Box 1: A vaccine equity definition: Shortfall equality**

We apply the definition that is used for health equity that is known as the ‘health capability paradigm’ [39]. This states that health equity can be constructed along three principal lines. The first is the principle of equality: are vaccines across and within countries allocated in an equal matter to ensure population coverage? The second is the *prioritarian* principle: this justifies the allocation of vaccines to the worst-off first and foremost, above all others. This principle aims to improve the situation for the most deprived. Thirdly, there is the principle of the threshold view: this states that international allocation of vaccine resources is based on an agreed minimally adequate health status. These three aspects combined lead to the construct of ‘shortfall equality’; this takes into account a norm and threshold vaccine allocation to the worst-off as well as the need for proportional allocation. Equality, from a societal viewpoint, can then be assessed quantitatively by how much a given society has realized its health potential and how much remains unrealized.

3. Intellectual property, local production, and access to vaccines

The TRIPS Agreement has extended the Western concept of intellectual property to all WTO Member States, who have to consistently adopt a patent system with minimum standards that do not allow the exemption of pharmaceuticals and vaccines anymore. Developing countries were requested to become TRIPS-compliant by 2005, while for least developed countries, there was a separate deadline of 2016, further extended to 2021.

In the 1990s and early 2000s, the TRIPS rules delayed access to HIV antiretrovirals for millions of people in LICs/LMICs, which continued until WHO pre-qualified, cheaper generic medicines were marketed by companies in India as the obligation to patent innovative medicines there would have only started in 2005. Meanwhile, following pressure from civil society, the 2001 WTO Doha ministerial conference issued a Declaration on the TRIPS Agreement and Public Health, stating that TRIPS ‘does not and should not prevent countries from taking measures to safeguard public health and to promote access to essential medicines for all’ [41]. The Doha Declaration also reminded that under certain situations, and particularly in case of a public health emergency, TRIPS ‘flexibilities’ allow for countries to produce pharmaceuticals and vaccines under a compulsory license, even for export purposes, so that countries with no manufacturing capacities could also benefit [42]. However, the process is quite burdensome and time-consuming, and not fit for the urgency of responding to a pandemic. It is noteworthy that article 7 of the Doha Declaration also reaffirmed ‘the commitment of developed-country members to provide incentives to their enterprises and institutions to promote and encourage technology transfer to least-developed country members.’ This would be extremely important under the current circumstances, where COVID-19 vaccine manufacturing appears seriously insufficient to address global needs.

A WHO-mandated thematic review from 2006 concluded that it is unlikely that the TRIPS Agreement will have a positive effect on actual innovation in the investments of pharmaceutical products that are needed but for which there is no strong financial incentive, e.g. products for neglected tropical diseases or orphan drugs. The current intellectual property governance mechanism seems to disincentivize the expansion of R&D in innovative medicines, including vaccines, for the developing world [43]; a phenomenon that has been described as a ‘tragedy of the anti-commons’ [42]. Furthermore, it reflects an older context, whereby investments in pharmaceutical R&D mainly or exclusively came from the private sector whereas the response to the pandemic has been characterized by massive investment from the public sector, which is neither acknowledged nor rewarded by the patent system.

In principle, market forces could help to resolve such problems, among others, via cross-licensing or voluntary patent pooling, such as now proposed via the WHO-governed COVID-19 Technology Access Pool (C-TAP) [44]. However, actual commitment and outcomes of such patent pools have proven to be limited, with the notable exception of the Medicines Patent Pool (MPP) that was initially set up to provide access to HIV antiretrovirals in low-income settings, and further expanded to antivirals against hepatitis C [45]. The successful experience of the Geneva-based MPP prompted a recommendation from the Lancet Commission on Essential Medicines that the international community should create ‘a general Essential Medicines Patent Pool’ [46].

Unfortunately, the Lancet recommendation was left unheard, as was article 7 of the 2001 Doha Declaration. Also, the question is would a patent pool targeting pandemic vaccines work under the conditions related to essential medicines? The MPP already expanded its mandate in March 2020 to include any health technology, including vaccines, that could contribute to the global response to COVID-19 [45]. Would the TRIPS agreement then hinder access to vaccines? A WHO bulletin series’ review from 2006 states that there is no direct evidence as such and that IPR to protect technology does not have an immediate impact on vaccine use. The commission, however, did foresee that there may be negative impacts on vaccine availability in the future [42].

In October 2020, the governments of South Africa and India proposed a temporary TRIPS waiver to ramp up global supply chains of COVID-19 vaccines. India and South Africa referred in their proposal to Article IX of the Marrakesh Agreement (which formally established the WTO in 1994), that ‘in exceptional circumstances, the Ministerial Conference may decide to waive an obligation imposed on a Member by this Agreement or any of the Multilateral Trade Agreements ... ’; and that a decision granting a waiver shall state ‘the exceptional circumstances justifying the decision ... ’ [47]. There is certainly is international consensus that COVID-19 has triggered an exceptional crisis. For these reasons, mid-April 2021, a high-level group of 170 former heads of state and government and Nobel laureates wrote a letter to US President Biden, arguing that intellectual property is the utmost artificial barrier to vaccine supply, that a global multi-year burden-sharing plan is required to finance vaccines for the poorest countries, and that commitment to technology transfer is key [48]. At a WTO-organized event on COVID-19 and vaccine equity, Dr. Tedros, DG WHO, stated: *We must leave no stone untumed. We must explore every option for increasing production, including voluntary licenses, technology pools, the use of TRIPS flexibilities and the waiver of certain intellectual property provisions* [49]. Political lines have shifted with the US Biden government announcing in May 2021
support for waiving intellectual property protections for COVID-19 vaccines [50].

Technology transfer of vaccine production to LICs/LMICs is key to enabling rapid and sustainable scale of production. The WHO and its partners have now established a ‘COVAX manufacturing task force’ not only to increase short-term supply but also to build a platform for sustainable vaccine manufacturing to support regional health security. Under the leadership of countries such as Rwanda, Senegal, and South Africa, which have some local production capacity, there is now a push to investing in sustainable and secure domestic manufacturing capacity in Africa. To provide for a sustainable business plan, this manufacturing capacity needs to anticipate long-term market analysis forecasting needs for other vaccines addressing a broader range of diseases including influenza, malaria, yellow fever, and others [51].

Middle-income countries (MICs) such as India, Brazil, Thailand, Indonesia, Egypt, and Morocco have already burgeoning or developed pharmaceutical industries and could be explored as sites to develop manufacturing under a TRIPS waiver or a pooled voluntary licensing mechanism such as C-TAP. However, there is still a dearth of vaccine producers on the African continent, which currently only produces 1% of what it needs. Of the 140 companies that currently manufacture vaccines, just one of these sites is in Sub-Saharan Africa [52]. The waiver by itself will not solve the many problems that national health systems have in making vaccines available given the complex issue of technology transfer and maintaining quality of production, which requires expertise and a commitment from existing producers.

However, it is an important, temporary, and legitimate legal option and urgent step to take among other measures that should be available for governments to use [53].

Regional production should play a key role in expanding access to COVID-19 vaccines, and it could also help to fill gaps in equitable access to other vaccines and health technologies in the future [54]. However, it should be accompanied by strengthening national regulatory capacities [55] and pharmaceutical systems (to ensure adequate quality, accurate forecast of the demand, timely distribution, and adequate policies for universal health coverage). Furthermore, it should have a regional scope, to allow economies of scale, while building solidarity and avoiding new forms of nationalism; it should be supported by explicit advanced market commitments, hopefully through COVAX; and it needs a flexible and fair intellectual property environment, fine-tuned with global health needs.

3.1. Governing national health systems

To paraphrase Julio Frenk: ‘In a world of sovereign nation states, once vaccines are available at the national level, design and implementation of vaccination strategies are primarily a national responsibility.’ He further states: ‘In the absence of a world government, there is an inherent tension between the reality of national sovereignty and the imperative of international collective action to properly manage interdependence’ [56].

Consequently, global vaccine equity critically depends on how national health systems perform toward COVID-19 vaccine coverage, including within-country vaccine equity. Despite the advocacy and rhetoric for increased attention for strengthening national health systems over the past decade [57], many countries, especially LICs/LMICs, will need international support, not only in the form of vaccine supply but also for sustainable mobilization of financial and technical resources for their vaccination strategies [57].

While attention is obviously mostly on vaccinating the population at risk, it is the leadership and governance in the national health system, which is critical. This is especially the case with a new disease, such as COVID-19, which requires a strategy: mass vaccination of adults, which is quasi nonexistent in many countries. Moreover, COVID-19 has rapidly become an issue of high politics requiring a prompt whole-of-society response, at a moment of much international pressure and emerging global vaccine diplomacy [58]. National governance of the health system is then key not only to develop and implement a national COVID-19 vaccination strategy but also to manage the relationship with the myriad actors in the global health system [59], all of which are now mobilized in tackling the COVID-19 pandemic.

And for the national COVID-19 vaccination strategy, obviously, not only are vaccines needed but also a strategic vision to lead the complex process of designing and implementing an appropriate nationwide vaccination campaign, without precedent in recent history, adapted to the country-specific burden and epidemiology of COVID-19 [60]. This will need the massive mobilization of health workers, and material resources, hence requiring important financial means [61].

In such processes, the national absorption capacity and the many bottlenecks that national health systems invariably will have to face have been relatively neglected in global discourses on COVID-19 vaccination. These will, however, be critical for obtaining the required COVID-19 vaccination coverage, with due attention to within-country vaccine equity, which will need to overcome significant levels of vaccine hesitancy in many countries.

3.2. Bottlenecks in national health systems

Based on our longstanding and current involvement in health systems R&D in different regions in the world (notably in Guinea, the Democratic Republic of the Congo (DRC), India, Peru, and Italy), we provide in this part a comparative analysis (see Table 1 for key indicators), by applying the Tanahashi framework, of the issues faced by national governments rolling out COVID-19 vaccination. In 1978, the WHO scientist Tanahashi published on the limitations that national health systems may face when expanding healthcare and services [62]. He proposed a framework that considers the following elements of health service coverage: availability, accessibility, acceptability, contact, and effectiveness coverage. We have slightly amended this framework and hence identify consecutive six health systems coverage issues that ought to be considered for improving COVID-19 vaccination coverage and hence overcoming inherent systematic inequities (see Text Box 2).
Table 1. Comparative selected health systems indicators for respective countries.

| Country   | Classification | Domestic government health expenditure per capita in USD | Nursing and midwifery personnel/10,000 population | COVID-19 mortality/100,000 inhabitants | COVID-19 full vaccination rate/100,000 inhabitants (%) | DPT3-vaccination coverage among 1 year olds (%) |
|-----------|----------------|--------------------------------------------------------|-----------------------------------------------|-------------------------------------|---------------------------------------------------------|-------------------------------------------------|
| The DRC   | LIC            | 2.79                                                   | 11.1                                          | 0.16                                | Not available                                           | 57.0                                            |
| India     | LMIC          | 19.63                                                  | 23.88                                         | 21.47                               | 14.0                                                    | 91.0                                            |
| Italy     | HIC           | 2209.00                                               | 58.87                                         | 207.2                               | 17.2                                                    | 95.0                                            |
| Guinea    | LIC           | 6.3                                                    | 4.20                                          | 1.17                                | 0.57                                                    | 47.0                                            |
| Peru      | UMIC          | 231.11                                                 | 29.77                                         | 208.1                               | 2.7                                                     | 88.0                                            |

Data sources: World Bank Income Classification, WHO Global Health Observatory, John Hopkins Coronavirus Resource Center, United Nations world population database. Data as available on 21 May 2021.

LIC: low-income country; HIC: high-income country; LMIC: lower-middle-income country; UMIC: upper-middle-income country.

Text Box 2: Tanahashi health system framework adapted to vaccination coverage

1. **Applicability**: Does a country have an evidence base to inform vaccine introduction? Inequity of access to diagnostics and poorly developed surveillance will lead to unreliable estimation of burden and risk groups and challenge articulation of needs.

2. **Appropriateness**: Is the vaccine appropriately designed for the national context? For example, cold-chain requirements (ultracold-chain) or the use of several doses will require more complex vaccine administration and logistics.

3. **Availability**: Are there sufficient vaccine doses actually available to allow the rollout of a program? If production capacity is limited or if there are no quality-assured supply chain or supplies reserved, there simply may not be enough vaccines to go around? Are there sufficient trained and decently paid health workers to conduct a vaccination campaign?

4. **Affordability**: Are vaccines affordable considering domestic government health expenditure and fiscal limitations in guaranteeing essential health services. Novel programs to reach populations such as the elderly – who are not usually vaccinated in many countries – will be needed as well as trained health-care staff to administer doses and systems to record vaccination?

5. **Acceptability**: Are vaccines trusted by the population and has the government adequate communication strategies to promote vaccination? Can the government provide leadership on real or perceived issues such as safety and overall immunization purpose? COVID-19 vaccine hesitancy is a major issue worldwide but in some countries and communities, it is much more present than in others.

6. **Efficacy and effectiveness**: Are these effective and do they produce the desired results? Are they actually safe? Are regulatory authorities in place and how are liability practices organized in case of serious vaccine side effects?

Reconstructing health systems bottlenecks point to many issues that require attention and policy action. The first element in the Tanahashi framework is *applicability*, in many countries, evidence is not available to guide the vaccination strategy. Which areas and who are most vulnerable and will need to be prioritized for vaccination? This is especially challenging when vaccine supply is limited, as is invariably the case till now. Surveillance systems may be poorly developed and diagnostic tools may not be available to yield the relevant information. In India, the rapid surge of the virus in April 2021 has surprised researchers and policymakers alike. Early 2021, seroprevalence studies estimated that more than 50% of the population in some areas of India’s large cities had already been exposed to SARS-CoV-2. But limited access to testing and regular surveillance missed the emergence of a new, highly transmissible variant and underestimated the impact of superspreading events [63]. Even in a HIC like Italy, where early warning systems and disease surveillance are expected to be well developed, the health system was not prepared and was overwhelmed during the first wave of the pandemic. Health-care infrastructures at the community level have gotten weakened over the years [64]. In the African region, there are likewise worries that limited testing capacity and surveillance lead to underestimates of the impact of the COVID-19 pandemic, which may fuel complacency. Many African Union (AU) member states had over 10% test positive rates during the second wave. With cases surging around the world, and new variants emerging, the director of the Africa Centers for Disease Control and Prevention (CDC) urged AU states to use evidence-based strategies to manage COVID-19 [65]. In Guinea and the DRC, the large majority of notified cases are in larger cities. While this may reflect reality, it is feared that it also indicates serious underreporting. Peru has one of the highest mortality rates (208 deaths per 100,000 population [3]) in the world but RT-PCR testing availability remains insufficient, especially outside the larger cities. These country cases indicate that surveillance capacity requires strengthening to guide COVID-19 immunization campaigns.

A second element is the *appropriateness* of the vaccines. For many LICs/LMICs vaccination strategies, mRNA vaccines would face serious challenges mainly because of restricted availability of the ultracold chain. Guinea and the DRC already have relevant experience from Ebola vaccination, but not on a nationwide scale. The Sinovac, Gamaleya, AZ, and COVAX vaccines being used in several LICs/LMICs require two doses, months apart posing a serious challenge, certainly in countries with limited civil registration and often high mobility [66]. India seems to be in a particularly paradoxical logic of decentralizing vaccine procurement while at the same time centralizing vaccine administration operations through a smartphone app that is heavily exclusionary [67]. This provides risks for vaccine efficiency and the potential emergence of new variants. Therefore, many LICs/LMICs prefer using the Johnson & Johnson (J&J) vaccine that only requires only one dose. A European country, like Italy, can manage the cold-chain, administrative, and logistics requirements, but even then, vaccine wastage has been of concern. This is partly linked to the rare side effects of the AZ and J&J vaccines detected through pharmacovigilance and several countries restricting its use for a population above 60 years only [68] and partly also because supporting equipment such as dead-space syringes to extract more doses from vaccine vials were not available [69].
A major challenge remains the availability of the vaccine. The COVAX facility still has considerable challenges to scale up vaccine production, procurement, and deployment to the 92 LICs/LMICs in need. This is (May 2021) partly because the Indian government is prioritizing vaccination of its population given the escalating epidemic and variants, and not exporting the licensed AZ COVISHIELD vaccine to other countries anymore. Reliance on a single supplier is never a good strategic choice in pharmaceutical procurement. While USD 15 billion has been pledged by countries and other actors to match the needs of ACT-A and COVAX, the funding gap for 2021 is about USD 18.5 billion. The G20 summit in May 2021 will indicate to what extent the largest economies globally will be able to cover that gap. It is noteworthy that the health systems pillar of ACT-A is most seriously underfunded, with only three state donors providing for the USD 280 million allocated so far [70]. Many LICs/LMICs will undoubtedly need foreign aid for implementing nationwide vaccination campaigns for the high-risk adult population, something unprecedented in most HICs.

Despite finalized agreements by many LICs/LMICs not only with COVAX but also bilaterally for the Sinopharm, Sinovac, and Gamaleya vaccines, only small quantities have arrived slowly. For instance, while Peru has a deal for the procurement of 48 million vaccines, only 2% of the population (650,000 people) had been vaccinated till May 2021. The DRC has received 1.7 million doses of the AZ vaccine through COVAX, and while there may have been enough health-care workers to conduct the immunization, there are several security obstacles, and financial incentives and logistics for distributing vaccines across the country are lacking. Guinea has received about 7% of 9 million doses it has secured via COVAX, the AU’s African Vaccine Acquisition Task Team (AVTT) [71], and bilateral cooperation with the Russian Federation and the People’s Republic of China. In India, about 10% of the population (140 million people) has received at least one dose of a vaccine [72,73], but that was only possible through its vaccine manufacturing capacity in the Serum Institute of India and Bharat Biotech (COVAXIN vaccine) and export restrictions. Meanwhile, Italy has, late April 2021, already fully (two doses) vaccinated 13.5% (8 million people) of its population and has administered 25.5 million injections in total. Italy has (in theory) and stockpiled 255 million vaccine doses [74,75]. Some MICs have local production capacity, e.g. the Cuban government has developed its vaccines called ‘Soberana’ [76]. Given the long-standing dependence on medical technologies, Africa’s leaders have in a high-level meeting called for the ‘development of a vibrant and innovative African medical supplies manufacturing capability’ and ‘the need to expand existing capabilities into regional hubs that serve the continent as a whole’ [77]. Political, technological, and economic cooperation to enable the capabilities of African regional manufacturing hubs will become a priority global health matter in the near future.

Currently, many countries across different regions apply more or less the same criteria for the allocation of vaccines. Some countries, like Peru, have established specific ethical committees for this. Guinea and the DRC follow the recommendations from the WHO and Africa CDC. These provide considerations for an ‘equitable and timely allocation of COVID-19 vaccine based on African indigenous values’ [78]. In times of vaccine scarcity, one has to find a balance between protecting those that ensure community survival, those at high risk for severe infection, and the general population. The actual allocation of vaccines suffers from entrenched inequities in health systems configurations that will make it difficult in many LICs/LMICs to deliver vaccines beyond health centers in (provincial) urban environments, especially in many informal settlements with many people being undocumented.

The affordability for vaccine acquisition is yet another matter. Globally, USD 112 billion has been invested in developing and procuring the COVID-19 vaccines. The vast majority of these funds are public, with 69% of this coming from the US, EU, and its member states, Japan, and South Korea [79]. With the relative scarcity and bilateral procurement deals (advanced market commitments) of HICs, vaccines’ price per dose, especially for the mRNA vaccines, has been driven up. These cost now somewhere between USD 10–20/dose. The European Commission announced in May 2021 that it made a massive vaccine deal; 1.8 billion doses of the Pfizer vaccine to be procured over the period 2021–2023, with the price likely to be around USD 23.75/dose [80]. This enormous public commitment raises questions over how much of the market share will be still available for LICs/LMICs and whether part of these vaccines will be rerouted via the COVAX facility. Moreover, it has led to questions on the legitimacy of the private profits generated via these deals as the pharmaceutical company in case also has avoided paying tax on these profits via its branch in the Netherlands [81]. At the same time do LICs/LMICs struggle to afford these vaccines? India, with its vaccine manufacturing capacity, can, technically, impose price regulation. Nevertheless, this investment will be a considerable burden on the public health-care budget, with current health expenditure (CHE) being about 3.5% of the GDP and of which 63% is out-of-pocket spending. Peru, Guinea, and the DRC cannot finance such expenses with domestic resources and have to rely on COVAX, AVTT, and bilateral partnerships. This generates vulnerability, dependency, and possibly further indebtedness. Fiscal capacity for absorbing the vaccines in the public health-care system is limited with the countries’ CHE being only 4.5%, 3.7%, and 4% of the GDP, respectively (for comparison, in Germany this is 10.5% of the GDP). A risk exists that the current priority given to COVID-19 immunization campaigns may crowd out, from the public budget, other much-needed health services such as for HIV, TB, and malaria [82].

Acceptability of the vaccines seems to be partly related to the COVID-19 disease burden in a country as well as the overall state of trust that the population has in the government to manage the epidemic effectively. But vaccine hesitancy is influenced by many factors and is certainly not directly related to a country’s GDP. A survey conducted in October–December 2020 indicated that vaccine acceptance was about 91% in India and 72% in Peru but only 44% in France and 38% in Serbia [83]. Rather, there is an indication that existing social inequities, as well as a relative lack of government communication strategies and presence on social media, public television, and in the printed press, have considerable impacts on vaccine acceptance.
Sub-Saharan African countries seems considerable [83]. This is partly related to relatively low disease burden and the very young population, but as elsewhere is a complex mix of factors such as access to reliable sources of information, distrust of government, safety concerns with the AZ and J&J vaccine in HICs, existing belief systems on health, and a historical suspicion due to colonial legacies, notably in francophone Africa. The DRC received 1.7 million AZ COVID-19 vaccines via COVAX but had to return a major part of it due to low vaccine uptake. This may improve over time, but context-specific studies are required to understand the drivers of vaccine hesitancy among different parts of the population. Anecdotal reports from Guinea, for instance, indicate that people are hesitant to take the Chinese vaccines but have relative confidence in the Russian vaccines.

**Effectiveness and safety:** the WHO has a vaccine prequalification team that ensures that vaccines used in national immunization programs are safe and effective. As of May 2021, the WHO has approved six COVID-19 vaccines as safe and effective (an Emergency Use Listing, EUL), including the Sinopharm vaccine [84]. China has supplied over 100 million doses of the Sinovac and Sinopharm vaccines to 69 countries including Cambodia, Serbia, and Indonesia. More than 75 million of those doses have been delivered to 10 countries in Latin America [85]. With this WHO listing, Sinopharm vaccines likely become more dominant in LICs/LMICs. The emergence of new variants, especially the B.1.617 ‘double mutation’ one in India, raises questions on the efficacy of existing vaccines. The Sinovac vaccine has been reported to be only 56% effective against mild disease after two doses [86]. Continuous vaccine ‘rolling reviews’ of the safety and effectiveness of COVID-19 vaccines are crucial. While in Europe, the European Medicines Agency takes this role, such a regulatory agency will have to be strengthened for the regional manufacturing hubs in Africa. Capacity development and a governance structure to do so need to be developed in close collaboration with the AU, the African CDC, and the, to be established, African Medicines Agency (AMA) [87].

### 4. Expert opinion: transforming pandemic preparedness and response

Reflecting on the ‘shortfall equality’ concept of vaccine allocation across as well within countries, three key issues come to the fore. The first consideration is that after decades of pandemic viral vaccine development there is still no global, institutional, and legal framework that regulates R&D, manufacturing, pricing, procurement, and allocation. The ACT-A accelerator and COVAX facility are much-needed international partnership mechanisms but require to be embedded in a structured, democratic, multilateral governance framework on pandemic preparedness and response, whereby the interests of all of the WHO’s 194 member states are being transparently and equitably guaranteed. The current global partnership models are failing in this regard. Not only LICs, which have to rely on international assistance, do not receive a fair share of the vaccines, MICs like Peru, India, Brazil, Indonesia, Mexico, etc., also face great difficulties in ensuring a rapid scale-up of vaccine production and roll-out. In these countries, the epidemiological transition to chronic noncommunicable diseases, a risk factor for developing severe COVID-19, has already (partly) taken place. The focus of vaccine and treatment deployment should hence for a part as well consider the needs of these MICs.

HICs like Israel, the US, the UK, and the EU have managed to quickly ramp up their national vaccination campaigns and population coverage, but the dramatic escalation of the pandemic in MICs in Latin American and South Asian countries in the first half of 2021 is an indication that current international cooperation mechanisms are far from sufficient and equitable.

Secondly, there are strong moral, economic, and security foreign policy imperatives that currently converge and that could enable a diplomatic and political multilateral international agreement on pandemic response and preparedness, including considerations of vaccine equity. It is noteworthy that the WHO’s revised IHR from 2005 were negotiated and established in reaction to the Severe Acute Respiratory Syndrome (SARS) pandemic in 2003 [88]. The deep impact of the SARS-CoV-2 pathogen and its COVID-19 pandemic in 2021 requires the international community to consider the developments of such an international agreement. With the new US administration, there seems to be momentum for policy negotiations toward the agreement of an international pandemic treaty, which ideally ought to be established in 2022. The WHO’s DG, 25 heads of government, and international agencies, representing countries from the six WHO’s Regions, have spoken out for the development of such a treaty, which would be underpinned by the current IHR [89]. The COVID-19 pandemic could be the trigger that creates the momentum prompting states to overcome their domestic dilemmas and effectively taking international responsibility and collective action [90]. The negotiation of such a treaty should consider the needs and perspectives of countries at different levels of development.

Lastly, in all of this, a contextualized, differentiated approach is needed in which national strategic priorities and local public health needs and constraints are being considered. The COVID-19 pandemic has unfolded in many unexpected ways across different countries and contexts and will continue to do so [60]. The (in)direct impact on health services and its resilience capabilities to address the epidemic varies greatly per country. Health systems bottlenecks for vaccine uptake, and how to overcome them, hence need to be fully considered, not only at the national level but also more granularly at the local level [91], and decided upon in a deliberative inclusive manner. COVID-19 has led governments to impose unpopular, often draconian, measures. A delicate balance needs to be struck between developing and implementing national vaccination strategies that are effective and similarly should receive sufficient popular and participatory support by people to overcome vaccine hesitancy [92].

These reflections would then lead to the following recommendations advancing vaccine equity both across and within countries and communities for the coming years. We follow the policy advice from the Independent Panel for Pandemic Preparedness and Response (IPPR) [93]. From these broad recommendations, we want to emphasize three more explicitly.
Firstly, G7 countries should commit to providing 60% of the USD 19 billion required for ACT-A in 2021. ACT-A must develop into a truly global end-to-end platform for vaccines, diagnostics, therapeutics, and essential supplies, shifting from a model where innovation is left to the market to a model aimed at delivering global public goods and make them available for all. This platform must be democratically and multilaterally governed, with an augmented role for the WHO and, in secondary line, the Gavi Alliance, Coalition for Epidemic Preparedness Innovations (CEPI), and other global health organizations. The overall goal must be to achieve rapid, equitable, and effective access to pandemic tools including vaccines [15].

Secondly, the WTO and the WHO should immediately convene major vaccine-producing countries, including those with potential manufacturers and patent holders, to agree on technology transfer and voluntary license-sharing via a commonly governed technology access pool, preferably such as the C-TAP mechanism [94]. In the mid-long term, national governments should ensure that technology transfer and commitment to voluntary licensing will be included in all agreements where public funding is invested in R&D. International cooperation should focus on larger manufacturing hubs in each region. Shared financing and regional capacities for manufacturing, regulation, and procurement of tools for equitable and effective access to vaccines and other medical products need to be pursued [93]. Medical technology that has been developed for the most part with public financing should be global goods to benefit humanity. For this, governments should incentivize COVID-19 vaccine companies to help make mechanisms such as C-TAP work, including concrete proof-of-concept projects [95]. C-TAP could set up tech hubs around the world, where selected manufacturers would gain the start-to-finish production know-how. Vaccine companies would maintain more control over the scale-up than they would through the proposed intellectual property waivers and allow them to collect fair royalties [96]. Regardless, an intellectual property waiver remains an important, temporary, legitimate policy action to take amongst other measures and that should become available for governments to use [53].

Thirdly, the international pandemic treaty that is under consideration should not only envisage ramping up current vaccine allocation and a funding framework but likewise ensure international financial commitments for future pandemic preparedness and response. The IPPR calls for the creation of an International Pandemic Financing Facility to raise additional reliable financing. It mentions an ability-to-pay formula whereby larger and wealthier economies will pay the most, preferably from non-Official Development Assistance budget lines, as to avoid dependency on volatile and unpredictable aid budgets [93]. Several new proposals have been put on the table to finance pandemic-vaccine R&D and the capabilities and tools for pandemic response and preparedness. This could be established by ensuring a sustained source of revenue through a mix of national, global, and regional taxation [97]. A wealth tax for global public goods could be another option. For instance, a global tax of 2% on fortunes over USD 12 million could raise an estimated USD 1.2 trillion per year or approximately 1.4% of global GDP [98].

Finally, such a transformative, improved global governance regime strengthening essential public health functions, the resilience of health systems across the world, and the R&D landscape of global public goods such as pandemic vaccines must make sense and be effective across and in very different contexts and countries. A dignified, human security approach is required when new global health security elements such as pandemic vaccines are introduced in societies. There are long-standing tensions between biosecurity-focused, authoritarian approaches to public health, and, in contrast, comprehensive, participatory, and rights-based-oriented public health programs that focus on the social determinants of health. Inclusive and adaptive public health approaches, with their use of diverse sources of knowledge, disciplines, and capabilities, will be more effective to meet the 21st-century challenges of pandemic diseases and other upcoming crises. A contextualized, dynamic understanding and country-specific version of health systems strengthening are needed to improve vaccine and health equity in a sustainable matter [99].

In conclusion, COVID-19 vaccine equity has become a major test case for Global Health cooperation, science, and diplomacy including for the legitimacy of the main actors, countries, and institutions involved. The historian Yuval Harari summarizes it very well: ‘Humanity needs to make a choice. Will we travel down the route of disunity, or will we adopt the path of global solidarity? If we choose disunity, this will not only prolong the crisis, but will probably result in even worse catastrophes in the future. If we choose global solidarity, it will be a victory not only against the coronavirus, but against all future epidemics and crises that might assail humankind in the 21st century’ [100].

Note
1. World Bank country income classifications are applied throughout the article: https://datahelpdesk.worldbank.org/knowledgebase/articles/906519-world-bank-country-and-lending-groups

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