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Global COVID-19 vaccine inequality: An overview of critical factors and possible solutions

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Abstract

The effectiveness of the vaccines, as well as global distribution and intervention strategies in order to deal with vaccine hesitancy, remain a challenge in both developing and developed countries. Even though several COVID-19 vaccines are used globally in population-wide vaccination campaigns, it has been difficult to achieve population-wide immunity. This paper examines select factors within and between nations that have hampered the ability to achieve this level of immunity, including inequalities in production and distribution among low-, middle- and high-income countries and suggests some possible solutions or policies to address global vaccine hesitancy and the unequal distribution of COVID-19 vaccines. The allocation of COVID-19 vaccines should be based on ethical principles to ensure fair and timely administration. Better health education and communication, as well as planning and equitable vaccine allocation strategies, should be carried out by public health policymakers and stakeholders. A globally coordinated strategy that tackles vaccine inequity may reduce hospitalization and death rates, promote vaccine-induced population-wide immunity, and curb the spread of SARS-CoV-2 before the onset of new SARS-CoV-2 strains that might render ongoing mass vaccination campaigns ineffective.

Take-home message: Equity in the distribution and interventions of COVID-19 vaccination remains a challenge and may be decisive to reach the goals of COVID-19 mass vaccination campaigns.

Keywords: COVID-19; distribution; ethics; equitable allocation; health policies; inequalities; SARS-CoV-2; misinformation, supply chain; vaccine hesitancy.

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INTRODUCTION

As the world approaches the three-year mark since SARS-CoV-2 was initially identified on January 7, 2020, the continued rapid spread of variants of this virus is evidence of the impact of the Coronavirus disease 2019 (COVID-19) pandemic on the global population. To date (August 16, 2022), SARS-CoV-2 has infected 596 million individuals globally and caused 6.46 million deaths [1]. The pandemic has stressed healthcare systems in many countries [2,3]. Lockdown strategies, social isolation, and quarantine measures [2,4,5], in combination with new therapies, including oxygen therapy, anticoagulation therapy, steroids, antivirals, or immunosupressive drugs on special indications, have been helpful in curbing the letality and, partially, the contagion [6]. The bulk of efforts to date has focused on vaccines, which are currently the most effective weapon against transmission and disease caused by existing strains of the SARS-CoV-2 virus [7].

Early in 2021, wealthy nations initiated COVID-19 mass vaccination campaigns after the World Health Organization (WHO) released recommendations for implementing a mass vaccination campaign against COVID-19 [8]. Such a complex campaign requires careful design and implementation strategies and also depends on the ability of nations to carry out such mass events, although experience and knowledge gained from previous vaccination campaigns may increase its likelihood of success [9].

All COVID-19 vaccines that received WHO emergency use authorization (EUA) status passed through randomized clinical trials to test their quality, safety, and efficacy [10]. Even though vaccines offer protection against severe disease, hospitalization, and deaths, the longitudinal assessment of vaccine participants is critical because it provides information on whether vaccination can achieve long-lasting immunity [11]. A recent study published in JAMA found that individuals vaccinated with three doses of mRNA vaccine were more protected than unvaccinated or vaccinated individuals with two doses against both the Omicron and Delta variants [12]. In another study, a fourth dose of the BNT162b2 vaccine effectively reduced the short-term risk of COVID-19-related outcomes among persons who had received a third dose at least 4 months earlier [13].

Given that an effective vaccine should confer long-term protection, be cost-effective, counteract a waning natural immune response, and be adaptable to new variants, a pan-coronavirus vaccine should be developed in the future [14]. Although vaccinated individuals may have lower viral loads or a more rapid viral decline and thus perhaps less potential for onward transmission [15,16], it cannot be excluded that vaccinated individuals spread the virus [17,18], while unvaccinated people may facilitate the emergence of new SARS-CoV-2 mutations [19–21]. During a mass vaccination campaign, a limited number of COVID-19 carriers, either asymptomatic or symptomatic, may be responsible for a high proportion of cases (i.e., “super-spreaders”), so their identification is key for the success of strategies against the virus [22]. On the other hand, some have claimed that COVID-19 vaccines are very unlikely to result in a state of population-worldwide immunity since the onset of new variants of concern remains very likely, so effective COVID-19 vaccines will be a future determinant for learning to live with the virus [23]. Recently, Koelle et al. argued that SARS-CoV-2 may become an endemic pathogen in the human population with a higher transmissibility in the population, thus vaccinations might make the COVID-19 infection less severe in terms of health impact [24].

However, differences between natural and vaccine-induced immunity responses remain still poorly understood, including if they offer strong protection against new SARS-CoV-2 variants or if permanent immunity can be induced [25]. For this reason, non-pharmaceutical interventions, including social distancing, quarantine, as well as testing and contact-tracing strategies, should be followed during a mass vaccination campaign and until the end of the COVID-19 pandemic [4,18,26]. Furthermore, heterogeneity in vaccination responses might not generate robust antibody responses in some individuals, including those who are immunodepressed [27]. For this reason, a mass vaccination campaign, by reaching population-worldwide immunity, may effectively contribute to protect the most vulnerable categories of the populace.

Yet, this ambitious objective may be hampered by some critical factors within and between nations, which this paper attempts to address. First, there are challenges related to the large-scale manufacturing of vaccines and the supply chain [28]. Second, priorities in the distribution of vaccines within nations must be addressed [29]. Third, misinformation and vaccine hesitancy within nations hamper the achievement of population-wide immunity [30]. Finally, vaccine inequity across nations may provide only short-term benefits to high-income countries (HICs) [31,32]. Although there are strong arguments for a more equitable distribution of vaccines globally, it is important to note that rich nations seem to have suffered the most in tems of costs of premature mortality from the pandemic [33]. Testing and early policy enactments will save lives and reduce the transmission rate especially in the absence of a vaccination campaign [34]. Extreme vaccine inequity and injustice are not only moral failures that have a negative impact on economic and human rights [35], they can make the objective of reaching population-worldwide immunity difficult because COVID-19 transmission is borderless and global [32], and because SARS-CoV-2 may become endemic [36], despite the emergence of new variants. As stated by the WHO Director, the unequal distribution of vaccines is not only a moral failure but is “an epidemiological failure, which is creating the ideal conditions for new variants to emerge” [37].

Global vaccination coverage depends on the capacity of countries to manufacture cost-effective vaccines and to export large vaccine consignments worldwide [38] because only HICs have their own advanced vaccine-producing resources. An exception to this is India, a lower middle-income country that is also considered as the “vaccine manufacturing hub of the world" due to their ability to manufacture large consignments of vaccines at low cost [38,39]. This capacity requires a global cooperation mechanism that supports fair vaccine allocation and ensures equitable distribution, which are key to overcoming health inequity and disparities between low-income countries (LICs) and HICs [40], and even between different groups or races within the same population [41].

The aim of this paper is to provide an overview of some of the main challenges that have been faced during global mass vaccination campaigns against COVID-19, primarily covering limitations to large-scale manufacturing and distribution of COVID-19 vaccines and, more briefly, misinformation and vaccine hesitancy, and possible solutions. These findings might be useful for global public health stakeholders to promote better global cooperation and equality in distribution and access to current or future COVID-19 vaccines.

DISCUSSION

Large-scale manufacturing of vaccines, intellectual property, and supply chain challenges

Unless a very high percentage of the worldwide population gains population-wide immunity, as high as 90% [42], which can only be achieved through mass vaccinations, COVID-19 will continue to be a medical challenge [43]. However, vaccination should prevent the onset of severe disease in vaccinated individuals, easing the burden on healthcare systems [44]. To achieve this goal, the large-scale production and distribution of vaccines is needed, although there are logistic limitations in manufacturing, distribution, and regulation, which collectively cause delays [45].

Since November 2020, when mass vaccination campaigns started, China produced the most vaccines (4.95 billion), second was the EU (2.46 billion), followed by India (1.81 billion) and the US (1.13 billion), with a total of 11.72 billion as of January 31, 2022 [46]. This confirms that large-scale production accelerated and that by the end of 2021, production was close to what was expected, reaching 12 billion doses, enough to vaccinate the world population with one dose [46]. IFPMA (2021) also expected this to double to 24 billion by mid-2022 [46]. However, vaccine production in LICs is absent, and LICs tend to rely on donations from HICs, which want first to secure their population to be fully vaccinated with booster shots, while LICs depend on the charity of HICs [47]. Hence, the large-scale production of vaccines is not a challenge. Rather, the challenge is to establish production facilities in LICs so that their populations do not rely on donations by HICs to be vaccinated.

An important challenge to global vaccine equity and production is intellectual property since pharmaceutical companies welcome any interested company and country to license their intellectual property for COVID-19 vaccines. Most LICs lack vaccine-producing resources, including health policies and planning capacity, as well as vaccinologists, organized laboratories, industries for research and development, and government funding [48]. In countries such as Nepal, Buthan, Pakistan, and Afghanistan, it is difficult to physically reach rural populations, and this poses many challenges to vaccine campaigners and staff when distributing vaccines, while the situation may be worse in conflict-affected or war-torn zones [48], including in Ukraine caused by the ongoing Russo-Ukrainian war [49].

In a summit of European Union (EU) and African Union nations, it was revealed that Egypt, Kenya, Nigeria, Senegal, South Africa, and Tunisia obtained intellectual property rights to produce mRNA vaccines, signaling the reduction in worldwide inequality of vaccine distribution [50]. However, this does not necessarily imply that rights to patents have been waived.

Supply chain challenges include few vaccine manufacturing firms not located in LICs, coordination in the distribution of vaccines within and between countries, insufficient vaccine monitoring bodies, costs and financial support issues with LICs, and temperature storage requirements [51]. Expanding on the storage temperature requirements, the low-cost manufacturing technology used for the Oxford COVID-19 vaccine candidate, ChAdOx1 nCoV-19, requires “normal refrigeration temperatures” compared to the supercooling storage requirement of the Pfizer-BioNTech vaccine, resulting in a lower price per dose of the former [38]. As another example, the Sinopharm product (Sinovac-CoronaVac), which is less effective than mRNA vaccines [52,53], has easy storage requirements, making it suitable for low-resource settings, and it also has a vial monitor that indicates to healthcare workers (HCWs) when the vaccine has been exposed to heat and thus cannot be safe [54].

Addressing priorities in the distribution of vaccines within nations

Prioritizing access to a vaccine for specific categories of the population is needed, for example, HCWs, as the first line of defense to prevent direct harm and avoid the spread of SARS-CoV-2 from healthcare facilities to vulnerable patients [55–57]. HCWs represent a case of perfect ethical convergence due to their deontological and utilitarian considerations [58].

When vaccine supply is limited, consideration is given to specific groups or settings that may have a high risk of exposure to SARS-CoV-2 [59]. In the COVID-19 pandemic, individual vulnerability, as well as occupational risk factors, may constitute guidance for promoting vaccination campaigns, including in workplaces [57,60,61]. Workplaces may represent an opportunity for workplace health promotion programs targeted to the educational level of workers in order to increase vaccine confidence and tackle misinformation and fake news [62]. Such programs should be carried out by employers, supported by occupational physicians, and built on evidence-based and trusted information to ensure that as many workers as possible are vaccinated [63]. This is an example of effective collaboration between occupational and public health stakeholders [62,64].

In the future, clinical and serological tests, as well as "frailty" (i.e., immunosuppressed individuals), should be considered by health policies to prioritize populations at greatest risk to create fair vaccine-allocation systems [65–68]. Generally, the first targets to be tested should be high-risk categories such as patients, the elderly, and HCWs at hospitals, followed by asymptomatic people in infected local areas. The third group should be those in hospitals, including essential workers [56,69].

Furthermore, during the pandemic, racial and ethnic minority communities experienced a high economic and health burden from the COVID-19 pandemic [70]. This confirms the need to ensure equitable access to COVID-19 vaccination in African American and Latino adults in the US, who tend to show high levels of vaccine hesitancy [71]. Information about, and access to, vaccines are also needed in underrepresented strata of the population, such as refugees and migrants, which tend to be irregular and undocumented groups [72]. A relevant barrier to vaccine acceptance within minority groups is the lack of trust of governments, pharmaceutical companies, and the process of vaccine development [73]. In the US and the UK, systemic racism and structural inequalities are claimed to be high within ethnic minorities, hampering vaccine uptake, so eradicating racism and providing information to religious leaders are tools to improving vaccine uptake [74].

Addressing vaccine hesitancy and misinformation within nations

Members of the public may sometimes witness confusing or conflicting information by scientists and/or media about COVID-19 vaccines, and the spread of misinformation may increase vaccine hesitancy and hinder the effective control of COVID-19 [75]. During the current COVID-19 pandemic, evidence-based research should serve as the basis to inform the decisions of stakeholders and policymakers, but disagreements among healthcare professionals [76], media spreading fear and uncertainty about the side-effects of COVID-19 vaccines [77,78], and poorly vetted or low-quality literature [79] may promote vaccine hesitancy in populations.

Predictors of lower vaccine acceptance in LICs were lower education and socio-economic status, suggesting that exposure to misinformation about COVID-19 vaccines and public concerns over the safety of vaccines may contribute to lower acceptance rates [80]. In HICs, the most relevant predictors of vaccine hesitancy were vaccination conspiracy beliefs, paranoid concerns about the pandemic,

COVID-19 anxiety, high-perceived risk of infection, low perceived social rank, lower income, and lower age [81].

If a large sector of society is skeptical [82] and includes anti-vaccination views, even among HCWs, such as nurses [83], then in such a case, a mass vaccination campaign will not succeed in achieving population-wide immunity [84]. Rather, the desire or intent to obtain the COVID-19 vaccine is offset by concerns about its side effects [85].

One way to stimulate skeptics who are afraid of the risks and those who cannot afford vaccines is to use a "carrot", and pay them to be vaccinated to compensate them for the risk they take [86]. An alternative method is to use a "stick" and deprive them from social and commercial activities, such as the use of a vaccine passport [87,88]. Both methods have been used with some success, but skeptics remain, even with carrots or sticks.

Since "erosion of public trust and a sense of helplessness" is the perfect mix of conditions for spreading "harmful misinformation that begins a vicious circle", vaccine education campaigns should enlist cultural leaders outside of traditional medical and public health communities as vaccination proponents [89]. To this end, research ethics committees could be a forum among scientists, editors, and policymakers for shared solutions to address vaccine hesitancy, fake news and misinformation [90,91].

Addressing priorities in the distribution of vaccines across nations

Concerns about prioritization and equitable distribution are raised not only within a nation but across nations [92,93]. Currently, HICs are focusing on booster doses rather than immunizing LICs, which are currently struggling to provide a first dose to their populations. The COVID-19 Vaccine Global Access (COVAX) scheme, which is run by the Vaccine Alliance (GAVI), the Coalition for Epidemic Preparedness Innovations (CEPI), and WHO is expected to support fair vaccine allocation under a distributive scheme in which COVID-19 vaccines should be made available globally [40]. As of August 4, 2022, the US and EU donated the most doses to COVAX, including those shipped to recipient countries by COVAX. Total doses shipped by COVAX to a recipient country and donated to COVAX are 1.4651 billion, but if these include new levels announced but not yet donated, the total increases to 2.3042 billion [94]. In comparison, booster doses as of July 28, 2022 are 2.2568 billion, 82.4% of which have been administered to the citizens of HICs and upper middle-income countries (Tables 1, 2).

Table 1. COVID-19 vaccine doses administered and cases by income group (Retrieved: August 4, 2022).

Income group	Total vaccinations (in millions)	%	Population, (in millions)	Vaccines per 100 people	Cumulative cases (in millions)	%	New cases	%
High income nations	2,541.0	20.6%	1241.37	205	344.1	59.9%	869,415	82.8%
Upper middle income	5,271.8	42.7%	2501.43	211	136.0	23.7%	142,982	13.6%
Lower middle income	4,321.5	35.0%	3363.20	128	92.8	16.1%	36,355	3.5%
Low income nations	200.0	1.6%	701.93	28	1.9	0.3%	984	0.1%
World	12,334.4	100.0%	7909.30	156	574.9	100.0%	1,049,722	100.0%

Sources: Our World in Data at https://ourworldindata.org/covid-vaccinations. All income groups data are from July 28 2022 except for low income nations which is from July 19 2022. For a list of countries by income group classification see: https://datahelpdesk.worldbank.org/knowledgebase/articles/906519-world-bank-country-and-lending-groups

Table 2. People vaccinated and booster administered by income group (updated: August 4, 2022).

Income group	Total vaccinations (in millions)	People Vaccinated (in millions)	People fully vaccinated (in millions)	In percent	Total booster doses (in millions)	In percent
High income nations	2,541.0	974.3	913.2	18.8%	675.1	29.9%
Upper middle income	5,271.8	2,087.2	1,973.8	40.5%	1,184.0	52.5%
Lower middle income	4,321.5	2,100.7	1,868.6	38.4%	388.9	17.2%
Low income nations	200.0	139.4	113.2	2.3%	8.7	0.4%
World	12,334.4	5,301.7	4,868.8	100.0%	2,256.8	100.0%

Sources: https://ourworldindata.org/covid-vaccinations. All income groups data are from July 28 2022 except for low income nations which is from July 19 2022

Had the 2.257 billion booster doses been supplied to LICs, the inequality between rich and poor would diminish significantly. In HICs, where vaccination programs are at an advanced stage, much attention is paid to waning immunity [53]. In contrast, in LICs, two-dose coverage in the unvaccinated may have a greater effect than booster doses in fully vaccinated people at low risk of severe diseases [95].

Despite these unprecedented efforts, as well as the administration of 12.33 billion shots as of July 28, 2022 worldwide, allowing 67% of the global population to receive at least one shot, although country-based population coverage varies widely (Tables 1,2) [96]. There are still huge disparities between rich and poorer nations. Most of the COVID-19 vaccine doses have been administered to HICs and upper middle-income nations, and as of July 28, 2022, only 1.6% of the total vaccinations have been received to people in LICs, and only 2.3% of those fully vaccinated are from LICs (Tables 1,2) [94,96]. Disparities can also be observed by continents and, in particular, the rich northern versus poorer southern hemisphere (Table 3).

Table 3. People vaccinated and booster administered by continent (updated: Feb 17, 2022).

Continent	Total cases	Total deaths	Total vaccines	People vaccinated	People fully vaccinated	Total boosters	New Vaccines	Pop	% Vaccinated	% fully vaccinated
Africa	12.3	0.26	595.3	367.1	288.7	34.9	0.07	1,392.4	26.4%	20.7%
Asia	164.2	1.45	8,409.8	3,579.4	3,344.6	1,437.0	6.73	4,693.2	76.3%	71.3%
Europe	217.1	1.88	1,307.5	516.0	494.0	314.4	0.42	748.7	68.9%	66.0%
North America	108.1	1.48	1,037.7	441.1	382.6	230.8	0.16	596.3	74.0%	64.2%
Oceania	11.3	0.02	74.5	29.0	27.8	17.6	0.03	44.5	65.3%	62.6%
South America	62.0	1.31	909.5	368.9	331.1	222.0	0.22	434.0	85.0%	76.3%
World	574.9	6.40	12,334.4	5,301.7	4,868.8	2,256.8	7.63	7,909.3	67.0%	61.6%

All continent data are from July 28 2022 at : https://ourworldindata.org/covid-vaccinations (expressed in millions)

Several countries procured early stocks of COVID-19 vaccines, hindering the availability of a vaccine to LICs in terms of supply in coming years and affordability in terms of paying for the vaccines [97]. Rich nations have pre-emptively secured millions of vaccine doses from pharmaceutical companies, while the African continent has limited capacity for vaccine manufacturing, even in countries such as South Africa [45,98]. To ensure the fair and timely distribution and administration of COVID-19 vaccines, allocation should be based on ethical principles of a public health policy that is coordinated in a global way to avoid differences between rich and poor nations [99], to allow global mass immunization to become a reality, with the ultimate

goal of controlling SARS-CoV-2 [100].

Ensuring equitable access to COVID-19 vaccines has become more challenging in the present scenario, especially when rich nations are focusing on providing booster doses to fully vaccinated individuals to boost their immunity [101]. For this reason, WHO warned countries to balance their public health benefits of vaccine booster programs with global equity in vaccine doses needed to address the pandemic's impact [102]. Another factor that should be considered to ensure access to COVID-19 vaccines by vulnerable communities is strategic deployment based on the risk of resurgence and severity at the district level [103], especially in areas with low rates of vaccination. However, many open questions remain on the changing epidemiology of COVID-19 that may be answered in coming years [24].

CONCLUSION

Possible solutions or policies to address global vaccine hesitancy and the equal distribution of COVID-19 vaccines

In the context of current mass vaccination campaigns against COVID-19, vaccine effectiveness in high-risk and vulnerable groups, misinformation and vaccine hesitancy, and the global and equal distribution of vaccines are the main challenges for global public health policymakers and stakeholders.

First, global production and distribution of vaccines should be ensured in an equal and justifiable way so that immunity and protection against the virus is optimum and persistent for the entire population, especially vulnerable individuals at high risk of hospitalization and death [104].

Second, policy- and decision-makers should be equipped with epidemiological tools that can allow them to estimate the prevalence of SARS-CoV-2 because some vaccines might be less effective or ineffective against new variants [10,21,30]. An analysis of available resources (vaccinations and equipment), epidemiological data (e.g., the prevalence of natural protection in local communities), key categories at risk of infection and complications should be considered to prioritize the order of vaccination, so a risk assessment analysis should play a central role within national vaccination programs [105].

Compounding these limitations, excessive debate among scientists on this topic in the media and on social media might confuse the public and be dangerous due to contrarian views, some opinionated, others evidence-based. Thus, to temper expectations, an evidence-based, unbiased, and data-driven approach supported by solid peer-reviewed and critically assessed scientific papers is needed with an open data sharing approach [77,106]. Members of the public also need to be vigilant of fraudulent schemes and scams, such as the illegal sale of vaccines or false products, such as tests and treatments [107].

Finally, another challenge for policymakers covered in this paper is their global distribution and administration, especially in LICs. International cooperation is, therefore crucial for effective vaccine production and distribution in order to contain the COVID-19 pandemic globally. While some might argue that vaccines should be allocated equitably among all countries, others might claim that it is proper for governments to prioritize vaccines nationally, but this inequality in vaccine distribution may leave exposed groups (e.g., HCWs) and high-risk individuals vulnerable [108]. Therefore, the accessibility of COVID-19 vaccines should be guaranteed not only in LICs but also in poor, marginalized and vulnerable individuals within nations, including in HICs [109]. Absent such

caution, this pandemic will only exacerbate pre-existing health and socio-economic disparities [110,111].

The provision of equitable vaccine access to global citizens should not be considered a limitation in the ongoing pandemic. A new international treaty, which will "foster a comprehensive, multi-sectoral approach to strengthen national, regional and global capacities and resilience to future pandemics", is already underway for future pandemic preparedness and response [112–114]. However, the present scenario requires a different approach and could require vaccine manufacturers to align with the principles of the "Doha declaration on the TRIPS Agreement and Public Health" for granting intellectual property waivers [115]. This would enable the rapid scale-up of vaccine production as well as distribution.

The ability to address vaccine hesitancy and promote global and accessible production and distribution of COVID-19 vaccines are important public health interventions that occupational and public health stakeholders need to consider in order to increase vaccine uptake, attempt to reduce vaccine hesitancy and contribute to stable healthcare systems.

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