

Coronavirus Disease 2019 (COVID-19) Vaccine Prioritization in Low- and Middle-Income Countries May Justifiably Depart From High-Income Countries' Age Priorities

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In high-income countries that were first to roll out coronavirus disease 2019 (COVID-19) vaccines, older adults have thus far usually been prioritized for these vaccines over younger adults. Age-based priority primarily resulted from interpreting evidence available at the time, which indicated that vaccinating the elderly first would minimize COVID-19 deaths and hospitalizations. The World Health Organization counsels a similar approach for all countries. This paper argues that some low- and middle-income countries that are short of COVID-19 vaccine doses might be justified in revising this approach and instead prioritizing certain younger persons when allocating current vaccines or future variant-specific vaccines.

Keywords. COVID-19; vaccines; healthcare rationing; developing countries; age-based prioritization.

High-income countries (HICs) are still hoarding coronavirus disease 2019 (COVID-19) vaccines for their populations. Multilateral measures for expanding production thus far remain insufficient and fail to address harmful, inefficient, and unfair global vaccine distribution. One dimension of such unfairness is that, throughout 2022 and beyond, many low- and middle-income countries (LMICs) will lack the vaccines needed to cover their entire adult populations. The COVAX Facility has yet to accelerate distribution of vaccines in LMICs, and new variants like Omicron may mean both that HICs keep more doses for their own and that new products are needed, worsening vaccine scarcity in LMICs. What prioritization principles would be fairest and most rational in LMICs given dose constraints and acute health and development needs? This paper addresses 1 dimension of this question-namely, the complex relation of age to vaccine allocation.

An October 2021 World Health Organization (WHO) strategy recommends that step 1 of rationing should be "targeted vaccination of all older adults, health workers, and high-risk

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groups [ie, individuals with important comorbidities] of all ages, in every country..." [1]. This strategy, and similar earlier advice by WHO's advisory group [2], seems thus far to have a major influence on LMICs. For example, the websites of health ministries in Indonesia, Nigeria, Pakistan, and Vietnam indicate that they prioritize in broad agreement with that framework. As we explain, this is in lockstep with HICs' COVID-19 vaccine allocation, which largely prioritized older adults over younger ones, all else being equal. However, HICs' prioritization schemes should not simply be assumed to be optimal for LMICs; instead, some LMICs may have good reasons to adopt alternative strategies that prioritize subsets of their younger populations over their older populations.

AGE PRIORITIES IN HIGH-INCOME COUNTRIES

High-income countries' COVID-19 vaccine distribution typically prioritizes older adults. Younger adults received early priority for the vaccine and the booster only if they counted as high risk due to medical conditions or worked in highly specific designated professions (eg, as health personnel) [3]. The UK Joint Committee on Vaccination and Immunisation stated that its advice "largely prioritises based on age" [4]. Many other HICs adopted similar COVID-19 guidelines. Such approaches favored older adults, sometimes over designated essential workers. While other considerations, like priority to health

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personnel, also informed allocations, priority based on older age remains central.

The WHO strategy states that this vaccine prioritization scheme, including the priority to older individuals, would "achieve the greatest gains from this expanded vaccination goal" [1]. In HICs, 2 key considerations seem to motivate prioritizing the elderly. First, minimizing the number of COVID-19 deaths was the primary goal of vaccine distribution. The UK's Joint Committee pointed out that evidence "strongly indicates that the single greatest risk of mortality from COVID is increasing age and that the risk increases exponentially with age" [5, 6]. Likewise, according to an influential US model, "in almost all circumstances, reducing fatalities required distributing the vaccine to those who are most at risk of death, usually persons over 60 years of age and those with comorbidities" [7–9].

A second reason why HICs prioritized the elderly was to protect healthcare systems from high hospitalization rates—for example, in the United Kingdom, to "protect the NHS [National Health Service]" [10]. Advanced age is correlated with a higher likelihood of hospitalization. Governments became concerned that healthcare workers are pushed to their limits, affecting their health and well-being and those of their families, and ultimately, the availability and quality of COVID-19 and non– COVID-19 healthcare [11].

We shall argue, however, that similar prioritization may be less appropriate for some LMICs. Three factors may justify different priorities: new scientific evidence and vaccine developments, alternate ethical assumptions, and variation in local circumstances.

First, LMICs could benefit from more updated scientific evidence as they start or expand their vaccine rollout. When HICs developed their strategies, it was not yet known whether available vaccines would reduce community spread. Early modeling work recommending that the United States prioritize older adults made it clear that "indirect effects on transmission are not considered... because vaccine effects on transmission are just beginning to be studied" [8]. Subsequent work shows that authorized vaccines can sometimes significantly reduce community spread of early variants by reducing onward transmission rates [12], or at least by reducing infection rates [13].

We recognize that currently authorized vaccines reduce the transmission of Omicron and its subvariants much less effectively, and that this problem is now familiar. For example, Omicron BA1 is reported to have an average basic reproduction number (R_0) of 8.2 and an effective reproduction number (R) of 3.6, suggesting 3.8 and 2.5 times higher transmissibility than with the Delta variant [14]. As a result, compared with the Delta spike, the Omicron spikes have evaded neutralization by antibodies from convalescent patients and from recipients of the Pfizer vaccine with a 12- to 44-fold higher efficiency [15]. Generally, vaccines (and especially some vaccines common in LMICs) are also less effective at mitigating the risks of severe

illness and death from new variants than they were for old variants, limiting their benefits for older adults as well. Still, it would be too hasty to conclude that effects on transmission should never influence decisions about vaccine allocation between age groups. The inference is invalid because strong protection against future variants might require the production and global distribution of new variant-specific vaccines. These new vaccines will ideally reduce onward transmission of future variants (in line with WHO's important recent recommendation to develop COVID-19 vaccine products that curb transmission more than disease [16]). If so, LMICs will then clearly need to consider how the benefits of reduced transmission should inform their overall vaccine distribution strategy.

Another issue currently under investigation is whether the concentration of COVID-19 mortality among older individuals is as clear in LMICs as it is in richer countries. In LMICs, there was underreporting of COVID-19 mortality due to flawed civil registration systems, insufficient capacity to diagnose COVID-19, limited access to care, and mortality at home without notification. That casts some doubt on the age distribution of that mortality between younger and older adults, although we are unaware of factors that should bias one of those more than the other [17]. Some evidence suggests that "both COVID-19 and excess death agemortality curves are flatter in countries with lower incomes" [18]. Depending on the measure used, across countries the rate of increase in mortality risk rises per year of age by 0.10% to 0.12% for each US\$1000 of gross national income [18]. Of course, this result could be explained by other factors if, for instance, in LMICs COVID-19 deaths are recognized and recorded at much lower rates than in HICs. If, however, a consensus was to emerge that the risks of COVID-19 are not as concentrated in elderly populations in LMICs compared with HICs, vaccine distribution policy should also take this into account.

Second, HICs' priorities rested on various ethical assumptions, some of which are debatable. One controversial assumption was that what matters most is saving the largest number of lives from COVID-19 in the short run. LMICs, and HICs in the future, could reasonably adopt competing assumptions. They might judge, for example, that it is also very important to prevent resulting premature deaths from causes other than COVID-19, to save the highest number of life-years, and to avoid as many years with illness or disability as possible. These assumptions recommend prioritizing younger populations, whose members have more life-years to lose in case of short- and middle-term death or who would suffer from long COVID and from other long-term effects for more years than older individuals. Evidence on long-term effects is still emerging and might be important for LMICs' prioritization strategies. Another controversial assumption underlying HICs' prioritization is that it matters just as much to add a period of equivalent value to an adult's life when she/he is very old as when she/he is young or middle-aged. LMICs and HICs might instead assume that the moral importance of extending life often increases the younger an adult person is.

Third, the social, economic, and political conditions in some LMICs vary greatly from those in HICs (as well as between LMICs). Even if many of these differences are unjust, responsible vaccine allocation will need to heed them. LMICs' economies, for instance, may be less able to withstand (prolonged) lockdowns. The consequences could include not only widespread mortality but also large increases in abject poverty. Accordingly, vaccine distributors might need to enable crucial forms of economic activity to continue, or resume, especially when long-term vaccine shortages are expected. This necessity might support giving priority to (subsets of) the working population rather than to the older population at large, even if in a more just world LMICs might have greater capacity to withstand prolonged lockdowns.

In the next section, we expand on the following: (1) one factor arising from new scientific evidence, (2) a range of reasons for reconsidering certain ethical commitments, and (3) reasons arising from various economic challenges facing LMICs and the need for immediate economic recovery. These reasons challenge the top priority given to older populations and instead favor prioritizing subsets of the younger population in LMICs. Which of these younger subgroups should receive priority depends on further considerations, some of which we also briefly discuss. Decision makers should follow the emerging evidence on vaccine efficacy against transmission and the modeling of outcomes of vaccine distribution under specific country or regional circumstances. They should also consult with ethicists and the wider public. Accordingly, our argument is the beginning of a discussion, not the end. Our main contention is that LMICs have reasons to consider reducing the emphasis on old age.

REASONS TO PRIORITIZE YOUNGER POPULATIONS IN LOW- AND MIDDLE-INCOME COUNTRIES

Potential Indirect Protection of All

At least for LMICs yet to distribute vaccines on a mass scale, the opportunity exists to consider the capacity of vaccines to reduce the spread of infection, already an explicit reason in HICs for vaccinating children. In some circumstances that capacity may justify adopting the prevention of onward transmission as a goal for vaccine distribution. Such an "indirect protection" strategy gives priority to individuals not merely because of their personal need for vaccination but also because of their likelihood of infecting others, especially others at high personal risk or with a prospect of onward transmission. Hence, instead of prioritizing vaccine access for those most vulnerable to illness, an indirect protection strategy will prioritize those in contact (and especially, unprotected contact) with large numbers of people [19–21].

Generally, in LMICs, high-contact individuals are less likely to be old. Young and middle-aged adults are more often in the workforce, which, as in HICs, includes "essential workers," as well as workers who are not "essential" but who interact with many at work. Indeed, in LMICs, many more workers than in HICs are under overwhelming pressure to earn a living outside the home even when a lockdown is imposed [22-24]. Many of them also face greater difficulties to socially distance at crowded workplaces that lack the financial cushion to protect workers. Younger people more often reside in dense urban centers where spread is less avoidable than in rural areas [18]. And, as in HICs, young people may be less inclined to keep social distance or wear masks. In addition, in many LMICs, young and middle-aged people live in multigenerational households with older people [18]. Young and middle-aged women are particularly likely to be primary caretakers of both children and elderly persons. All of this raises the probability of these high-contact individuals transmitting the virus, including to those most vulnerable to COVID-19.

In the United States, given the excessively low rates of vaccine uptake among the young, prioritizing younger adults may unnecessarily delay vaccination. But this problem varies between countries. Recent evidence suggests that populations in LMICs are far more willing to be vaccinated than in HICs, and some LMICs have no statistically significant difference between age groups in this respect [25].

In addition to the question of vaccine uptake, whether it makes sense for an LMIC to even consider the indirect protection strategy will obviously depend on key empirical facts, such as the level of community spread, the number of vaccines available for distribution, and the efficacy of those vaccines in containing the spread of the specific strains that are driving infection at the time. Our intention is not to make specific recommendations as to which LMIC should adopt an indirect protection strategy and when. What we are suggesting is that, in some LMICs, indirect protection may make sense (currently or soon) provided certain key facts obtain, and that under such conditions the strategy should be given more serious consideration than HICs seem to have given it.

If successful, an indirect protection strategy would potentially minimize deaths over time (thus protecting the elderly among others), by reducing the number of cases and opportunities for new variants to emerge [19]. Nevertheless, it is unknown under what conditions (if any) an indirect protection strategy would save more lives than direct protection. New modeling is needed, reflecting the increased transmission rates and partial vaccine evasion of new variants, as well as variable country or regional circumstances (eg, demographics, economic and geographic factors, urban and housing density, patterns of mobility, the spread of COVID-19 infection, vaccine hesitancy, and existing vaccine coverage). But, even if it turned out that direct protection through vaccines remains the better strategy (for a particular LMIC at a particular time) in terms of reducing COVID-19 deaths, it is not obvious that it should be adopted. One reason is that avoiding the most COVID-19 deaths might not be the only, or the most important, moral goal for a vaccine distribution strategy. We turn to this possibility next.

Fewer Life-Years Lost, Fewer Years With Disability, Less Grossly Premature Mortality

A controversial ethical position that underlies HICs' vaccination strategy is that what matters most is the number of lives saved from COVID-19. For one thing, the number of lives saved is not the only thing that truly matters but also (or even instead) the number of life-years saved [26]. In the United States, saving the most life-years was set aside [9], partly because modeling suggested that the difference between lives saved and life-years saved would remain small under various distributions, given how much more common death from COVID-19 is among older people than among younger ones [7]. Maybe the same holds true in some LMICs. But in many LMICs, expected survival after the age at which vulnerability to death from COVID-19 increases is short. Consequently, few expected life-years are saved by each death averted among the elderly. If so, in some LMICs, the twin goals of saving lives and saving life-years may diverge to a greater degree than they do in HICs.

Minimizing the number of years with disability rather than in full health is another straightforward principle of preventive medicine. It is yet another morally weighty consideration pointing in favor of prioritizing the young. COVID-19 infections, even short of hospitalizations, can cause substantial harms to COVID-19 survivors, particularly when they suffer from long COVID. Moreover, necessary but harsh isolation measures may induce or aggravate mental illnesses and risks for domestic violence [27]. Crucially, when a younger person develops morbidities due to long COVID or harsh isolation measures, they may last for decades and could sometimes translate into premature death. This very rarely happens to very old individuals, with lower life expectancy. Reducing the overall incidence of COVID-19 infections in the community via indirect protection would reduce these substantial harms, including the risks for later mortality (as well as reduce future demand for scarce healthcare resources in LMICs).

As we argued, there is a case for saving the most life-years (without disability) over saving the most lives. A utilitarian calculus might support this case. Yet, public health policy need not be utilitarian. Many oppose such a purely aggregative approach because of its insensitivity towards the distribution of health between different lives. Incorporating such distributive concerns might further strengthen the case for prioritizing younger populations. This is so if the moral significance of averting a death varies with the age at which that death occurs independently of how many life-years are saved. Plausibly, it is a greater tragedy if a young adult dies without having had the chance to experience the joys and challenges that come with different life phases than if an older adult dies after having experienced them. Persons who have already lived a long life are in this respect better off. This suggests that extending life sometimes has diminishing moral importance with increased age [28]. Other things being equal, extending the life of a 30-year-old is morally more important than extending the life of a 90-year-old by the same time [29]. This is one more ground for prioritizing younger adults over older ones in LMICs (as well as in HICS).

Granted certain key facts, and depending on the ethical approach taken, these normative considerations could rival the moral importance of directly preventing COVID-19 deaths in older populations through vaccination in some LMICs.

Reducing Unfair Social Impact

Here, we shall elaborate on curbing economic devastation for patients, their families, and society, as well as the pandemic's toll on patients' dependents.

First, like other public health measures, mass COVID-19 vaccinations produce nonmedical benefits that should sometimes influence macrolevel resource allocation [30]. If much of the value of health consists in what it enables us to do, it makes sense to guide the allocation of health resources by its likely effects on some non-health dimensions of life, and not only when economic effects improve health by, for example, increasing investment in medical care.

Some LMICs will have especially weighty reasons to heed some non-health benefits because the COVID-19 pandemic has such grave economic consequences in LMICs. These economic outcomes do not pertain to luxuries. They are casting vast populations into poverty (and the related widespread morbidity and mortality) [31, 32]. When basic economic needs are at stake and government resources for welfare relief and debt protection are scant, the severe effects of the pandemic and of mitigation measures on the economic standing of some populations must inform vaccination priorities. Thus, to the extent that vaccinating working-age individuals helps to remove the need for lockdown measures that disrupt economic activity, this counts in favor of prioritizing working-age adults over other adults in some LMICs.

From a distributive standpoint, the economic devastation expected to affect many in LMICs would typically be concentrated among their poorer and otherwise vulnerable segments. In many LMICs, older adults are less likely to hail from the worst-off segments of the population than younger adults. As is also true in some HICs [9], a policy that prioritizes older over younger individuals thereby risks unfairly prioritizing individuals who are relatively advantaged (by virtue of living longer, typically because of socioeconomic privilege) compared with their co-citizens.

Second, over 1.5 million children have so far lost at least 1 caregiver to COVID-19. Scholars talk about a "hidden pandemic" of orphanhood [33]. Young and middle-aged people are more likely than older adults to have dependents. For child dependents, prioritizing young adults would minimize orphaning, which arguably tends to be economically and psychologically harsher for children than losing a grandparent [33]. In addition, older adults also depend on young adults (their family or nursing professionals) more than the reverse. It may appear as though an indirect protection strategy would have offsetting bad effects on third parties who are not dependents. If, for example, that strategy increased hospitalizations, it might have bad effects on hospital workers and on anyone relying on wellfunctioning hospitals (see above). However, in some models for HICs, under certain specified conditions, the indirect protection strategy of prioritizing high-contact individuals would reduce hospitalizations compared with vaccinating older populations [20]. We are not familiar with models for LMICs on this matter.

CONCLUSIONS: AGE AND POLICY

The arguments developed here speak against automatic priority for older individuals in all LMICs. However, the WHO strategy will clearly remain relevant for many LMICs. Age is often a strong predictor for severe COVID-19 outcomes. Some permutations of future variants and the vaccines available in LMICs would make it rational, all things considered, to prioritize direct protection of older individuals. How the factors that we mentioned weigh together will also depend on facts about transmission patterns, COVID-19 prevalence and distribution, societal age structures, housing, urbanization, labor market conditions, etc. These facts differ from country to country. In addition, which ethical approach is democratically endorsed remains key. As a result, even assuming that the WHO is correct to claim that there is some utility in uniform policies across countries that simplify operations [1], we remain convinced that priority for older adults is not obviously appropriate in all LMICs. Our contribution is meant to trigger discussion, data collection, and modeling that shed light on what would be best for specific LMICs at particular times when their governments doubt that the "default" priority for older adults best serves the public interest.

Notes

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