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COVAX – Time to reconsider the strategy and its target

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ABSTRACT

COVAX, the international initiative supporting COVID-19 vaccination campaigns globally, is budgeted to be the costliest public health initiative in low- and middle-income countries, with over 16 billion US dollars already committed. While some claim that the target of vaccinating 70% of people worldwide is justified on equity grounds, we argue that this rationale is wrong for two reasons. First, mass COVID-19 vaccination campaigns do not meet standard public health requirements for clear expected benefit, based on costs, disease burden and intervention effectiveness. Second, it constitutes a diversion of resources from more cost-effective and impactful public health programmes, thus reducing health equity. We conclude that the COVAX initiative warrants urgent review.

1. Introduction

Mass vaccination is a well-evidenced strategy for reducing infectious disease burden and was critical to the eradication of smallpox, and regional elimination of polio and measles. Routine vaccination programs also have an important role in reducing infant and child mortality. With its population-wide approach to a new pathogen, the response to the COVID-19 outbreak is the most rapidly and widely implemented example of a global disease control strategy. A major part of this strategy is the Access to COVID-19 Tools Accelerator (ACT-A), and particularly its vaccine pillar, known as COVAX, which involves financial and policy coordination between donors, the World Health Organization (WHO), GAVI, the Coalition for Epidemic Preparedness Innovations (CEPI), and their implementing partner UNICEF [1]. As part of COVAX, the global public health community, led by the WHO, established an 'ambitious' objective: to vaccinate at least 70% of the population in low- and middle-income countries (LMICs) against COVID-19, including those in sub-Saharan Africa. This global target was updated and prioritized in July 2022 in order to achieve "the underpinning targets of vaccinating 100% of health care workers and 100% of the most vulnerable groups, including older populations (over 60s) and those who are immunocompromised or have underlying conditions" [2]. This approach is promoted as 'vaccine equity', a novel concept grounded on the huge discrepancies in national COVID-19 vaccination rates. In terms of proposed cost, COVAX is probably the highest-cost international initiative targeting an infectious disease in history, with over US$ 16 billion already committed, roughly equivalent to three-year's worth of commitment to the Global Fund [3,4], and an estimated cost of universal vaccination with three doses of an mRNA vaccine in low- and lower-middle income countries of US$61 billion [5].

The 70% target might have been relevant at the time it was set up – it is important to remember that ACT-A was launched in April 2020, very early in the pandemic [6] – as an accelerated way of reaching herd immunity without incurring too many human losses. Nevertheless, the situation has changed, our knowledge about COVID-19 immu-

Abbreviations: ACT-A, Access to COVID-19 Tools Accelerator; CEPI, Coalition for Epidemic Preparedness Innovations; DALY, Disability-Adjusted Life Year; LMIC, Low- and middle-income country; ODA, Official Development Assistance; OECD-DAC, Development Assistance Committee of the Organization for Economic Cooperation and Development; UHC, Universal Health Coverage; WHO, World Health Organization.

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nity has evolved, and thus policies should evolve accordingly [7]. Appropriate prioritization of the COVID-19 response in sub-Saharan African countries should be based on the relative impact (direct and indirect) of the pandemic in comparison to populations elsewhere and on other regional health priorities [8]. Many authors defend current COVAX strategies, urging the international community to 'achieve global COVID-19 vaccine equity' through mass vaccination [9-11], pointing notably to the higher case fatality rate of COVID-19 in LMICs [12] as well as to the relatively high burden of COVID-19 in terms of excess death in LMICs, particularly in South-East Asia and Latin America [13]. However, by late 2021, Africa had a similar number of COVID-19 infections to that of the rest of the world, but with far fewer reported deaths [14]. In the first week of January 2023, even if figures are probably under-reported, the African Region of WHO only recorded 7 deaths from COVID-19 in the past week [15]. Some authors suggest to limit vaccination to higher-risk adults and vulnerable children and adolescents [16]. Evidence of relatively high burden of COVID-19 among pregnant women in Africa [17] has also prompted calls to prioritize their vaccination [18].

Based on a targeted literature review, this perspective paper complements existing critiques of COVAX, notably on its governance and ownership [6,19], by arguing that the internationally supported target of mass vaccinating LMIC populations against COVID-19, including the 1.3 billion sub-Saharan African population, is unjustified on health grounds and likely to result in net harm (reduced health equity). We argue that previous analyses have overlooked two important areas: the very limited actual benefit that most people can now accrue through vaccination, and the opportunity costs of resource diversion in achieving this. We conclude that in Africa, orthodox public health decision criteria suggest that the COVID-19 vaccination strategy should be targeted at those most at-risk – which may not equate to 100% of health workers – and not based on the prevailing logic of mass vaccination campaigns.

2. COVID-19 mass vaccination in Africa does not meet standard public health decision criteria

Public health policies should reflect a population's need to attain the best possible health status for those targeted. This also requires responsiveness to people's expectations, equity, financial sustainability, and efficiency [20]. To be justified from a public health standpoint, strategies and interventions must be prioritised through an inclusive policy dialogue that weighs relevant decision criteria, including disease burden, the intervention's potential effectiveness, its costs, and its overall impacts on equity [21,22]. In most cases, such as in the case of malaria, this is the prevailing logic, where interventions are meant to target specific country disease burdens [23].

In the case of COVID-19, the reported disease burden in sub-Saharan Africa is low [24] and arguments that this is due to under-reporting comparted to high-income countries remains weak [9]. Differences in population age distributions and the very high age-related heterogeneity in vulnerability to severe COVID-19 predict far lower mortality in most LMICs [25,26], with 50% of the sub-Saharan population under 19 years of age [27]. In contrast, lockdowns, interrupted supply lines and economic decline are expected to disproportionately increase mortality, accounting for much of any all-cause mortality increase [28,29]. The reasons WHO previously advised against interruptions to economic closure was to prevent such collateral deaths [30]. Yet, even when allowing for gross under-reporting, COVID-19 is not one of the dominating disease burdens for African populations based on disability adjusted life years (DALYs), a metric advocated by WHO [31]. Moreover, most people in sub-Saharan Africa have already acquired post-infection immunity, especially since the arrival of the highly-transmissible Omicron variant [14,32,33]. Countries such as Senegal and Burkina Faso have shown, via national seroprevalence surveys, that more than 90% of the population had been in contact with the coronavirus by the end of 2021. Post-infection immunity is more effective in blocking infection than the current mRNA vaccines, and there is minimal benefit from vaccinating on top of post-infection immunity [34,35]. There is also emerging evidence suggesting that mRNA vaccines have a more limited effect on overall mortality than previously assumed, again requiring a rethink of existing vaccination strategies [36,37]. Therefore, with the possible exception of South Africa with its older population and higher comorbidities, the sub-Saharan population is at low risk of developing a severe form of COVID-19. By contrast, African populations are faced with increased risk from malnutrition and endemic infectious diseases including malaria, tuberculosis and HIV/AIDS [25,27,38,39], which impart far higher burdens than COVID-19.

Public health interventions must be demonstrably effective, both for the recipient and the community. We have argued above that the young, healthy and naturally immune population of Africa is at low overall risk of severe COVID-19. They therefore will accrue limited personal benefits from COVID-19 vaccination. Where a large proportion of recipients are at low risk of the disease being prevented, mass vaccination may still be justified [9], but only if it is transmission-blocking (reducing infection in other, high-risk, people). This strategy could also reduce the pool of circulating virus from which variants may arise. However, the COVID-19 vaccines currently available do not block transmission [40-42], and in some populations recorded infections in vaccinated individuals are more frequent than in unvaccinated individuals [43]. Vaccination of non-vulnerable people is therefore not expected to impart substantial protection on the vulnerable.

Public health interventions must have sufficiently lasting impact. While post-infection immunity is well sustained [44], a large body of evidence shows that vaccine-induced protection against COVID-19 infection wanes after several months [35,45]. Protection against severe disease in the previously non-immune wanes more slowly, but reduces with time, with boosters offering limited recovery of immunity [35,46,47]. Mass vaccination therefore will not provide strong long-term vaccine-derived protection to the recipient population without, at least, frequent population-wide boosters, adding significant cost and thereby raising questions of sustainability [48].

Good public health practice requires that total health gains from the intervention must outweigh its costs. This means that significantly fewer recipients will be put at higher health risk from the vaccine than they would be from the pathogen. Net benefit must be even clearer for mass prevention interventions. Due to the extreme heterogeneity of risk for severe COVID-19 [25], such assessments must consider the varying risk profiles of each population and vaccine type [36,49,50]. The safety of COVID-19 vaccines is a complex area and dealt with extensively elsewhere [51-55]. It is clear that they are not free of severe side-effects, and that voluntary reporting systems register associated adverse events at a rate higher than other vaccines [56-58]. In particular, significant rates of myocarditis are recorded in young males [59-61] and important associated mortality is recorded in the VAERS [60] and EudraVigilance [57] databases. While causality is in dispute, the associated rate is far higher than reported for influenza vaccines. Being of a pharmaceutical class not previously used widely in humans, the mRNA vaccines also have no vaccine-specific or class-specific safety data. This, together with the reduced capacity in LMICs to monitor and manage adverse events, raises medical ethics questions concerning use of such a pharmaceutical in individuals who will accrue minimal direct benefit. As the expected benefit of COVID-19 vaccination in already-immune young African populations is very limited, the risk–benefit balance of COVID-19 vaccines is at best unclear [61].

Some voices have presented COVID-19 "vaccine equity" as a step towards decolonisation and the advancement of human rights [62-66]. These are important concepts in global health and should be taken seriously. Nevertheless, in the case of COVID-19 vaccines, these voices are seemingly most concerned with existing inequalities in terms of access to medicines (writ large) as a symptom of unfair distributive models. What these voices ignore, however, is the difference between *access to medicines* (as a general problem in global health) with *access to the right medicines* (an intervention that will actually advance general health equity). Consequently, COVAX and COVID-19 vaccines have seemingly become a battlefield for the much larger and necessary fight about access, but in doing so, have failed to recognize that access should reflect needs and expected health outcomes, especially we argue, in the case of COVID-19 in Africa.

Moreover, it is also important to consider that other human rights need to be strongly considered when examining potential knock-on effects of promoting broad inoculation targets and their associated enforcement mechanisms, including the need for informed consent and absence of legal or social coercion [65]. For example, in Benin, Ghana and Nigeria, there have been categories of people (e.g. civil servants, medical, paramedical, pharmacist and nursing staff, administrative staff of public and private health facilities) pressured or obliged to get vaccinated against COVID-19 [66-70]. Without going back over the history of medicine in Africa, one has to note the coercive approach used during colonialism, which did not respect human rights and which is still remembered [69]. With few exceptions, modern vaccine programmes have been voluntary and do not restrict participation in society, yet there have been at times a worrying imbalance in soft and hard regulatory coercion measures as well as social stigma / exclusion associated with incentivising COVID-19 vaccinations in the face of vaccine hesitancy.

Human rights are a complex but important area, and are not dealt with here beyond noting that as COVID-19 vaccination will not protect others, arguments for imposition under emergency conditions for that purpose are very weak, and we must be aware of the potential harmful impacts of legal and social stigmatisation [70]. Moreover, ethical considerations in public health emphasize the precautionary principle and stress locally-tailored approaches in mass vaccinations [71]. It is perhaps from this perspective that we can understand the important discrepancies observed in countries such as Benin and Senegal, where the levels of (declarative) intention to vaccinate against COVID-19 are very high (around 70%), but the actual uptake of vaccination is very low (around 10%) [72].

3. The opportunity cost of COVID-19 mass vaccination runs against health equity

It is of crucial importance not to consider the resources dedicated to COVID-19 vaccination, both financial and human, in isolation. Each could have been invested in alternatives; what economists refer to as 'opportunity costs'. The choice of the appropriate mix of health interventions to be included in a national strategy must be decided on a case-by-case basis, normally considering these costs, and relative disease burden, through a policy dialogue with the stakeholders [21]. Mass COVID-19 vaccination will not only involve diverting resources from interventions targeting greater health burdens (including routine children vaccination programmes), but also from 'horizontal' strengthening of health systems necessary for these interventions to succeed [73].

For example, each year the entire global budget for malaria is approximately US$3 billion [74]. Africa CDC estimated that US$10 billion would be required to support two COVID-19 vaccination campaigns on the continent [75]. As of November 22, 2022, US$16.2 billion had been allocated to the vaccine pillar of ACT-A for all LMICs [3]. Other estimates suggest US$35.5 billion would be needed to vaccinate everyone in LMICs, increasing to over $60 billion with a booster [5]; or that US$74 billion would be needed to reach presumed herd immunity through vaccination in LMICs [76]. These are staggering sums, and in the case of COVID-19, for a short-term intervention. By contrast, the entire Global Fund annual dispersal is currently slightly above US$5 billion per year for malaria, tuberculosis and HIV/AIDS combined [4], the estimated burden of each of which dwarfs the COVID-19 burden in these populations [38]. A study in Kenya estimates the total economic cost of procurement and delivery of COVID-19 vaccines, per person vaccinated with 2-doses, between US $29.7-US$24.68 for 30% and 100% population coverage respectively [77]. This amounts to about one third of the current total annual health expenditure per capita [78]. WHO and UNICEF recently warned that pandemic disruptions and diversion of resources from routine immunization leave millions of children worldwide without protection against measles and other vaccine-preventable diseases [79]. In terms of cost-effectiveness, a recent study estimated a cost-per-COVID-19 death averted through universal mRNA vaccination in LMICs of US $40,800 (US$7,400–US$81,500], with several likely factors (lower infection fatality ratios, lower vaccine effectiveness or uptake) leading to higher estimates [5]. This is considerably higher than acceptable cost-effectiveness thresholds in LMICs [80]. By comparison, in Zambia, active case finding of tuberculosis is estimated to incur an incremental cost of US$2,284 per death averted [81].

In addition, there are worrying signs that financial and resource reallocations to COVID-19 vaccine strategies are already significantly short-changing other health subsystems, threatening universal health coverage (UHC). For example, the Development Assistance Committee of the Organization for Economic Cooperation and Development (OECD-DAC) annual data on Overseas Development Assistance (ODA) saw a total donor disbursement of US$4.4 billion on COVID-19 related activities in 2020, representing the largest increase of ODA in history. Yet, despite this overall increase, when compared to 2019, OECD-DAC ODA for basic health care dropped by 34.5% and basic nutrition by 10.1% [82,83]. Other studies suggest that total development spending for COVID-19 exceeded US$13.7 billion, with an estimated US$1.4 billion 'repurposed' from existing health sector commitments, again confirming that a level of resource reallocation has taken place [84]. Further evidence suggests that funds are being diverted from other high-burden diseases, such as malaria [85], TB [86], and HIV [87], while a study in Ghana determined that COVID-19 prioritizations and reallocations have had an adverse effect on overall health financing and the national strategic plan [88]. Moreover, there are a number of reported secondary effects on health systems and outcomes due to COVID-19 vaccine prioritizations, particularly related to malaria [89], TB [90], sexual and reproductive health and HIV [91], noncommunicable diseases [92], and neglected tropical diseases [93]. Lastly, there is clear evidence of task-shifting, where medical personnel are being reassigned from other health subsystems to COVID-19 vaccination activities. In the case of Indonesia, the diversion of human resources to pandemic response efforts disrupted polio immunisation services, putting the country's polio-free status at risk [94].

These costs raise significant questions in terms of cost-effectiveness and health equity. In our case, this consists in comparing the benefits of COVID-19 vaccination (in terms of avoided COVID-19 deaths and/or hospitalisations) to the total costs of vaccination, including in terms of resource use (vaccine procurement and health system-related), resource reallocations, diversions in health financing, secondary effects on health systems, and opportunity costs. It also consists in comparing the population health benefits of COVID-19 vaccination to overall population health access, outcomes and quality of care. When taken as a whole, we argue that the proposed costs for COVID-19 mass vaccination are greatly disproportionate to the disease burden, with significant cost to other health initiatives and health system needs. Taken with the limited duration for protection the vaccines offer against COVID-19, and the small proportion of the population who remain non-immune and are intrinsically susceptible, mass vaccination appears to constitute poor resource stewardship that threatens wider population health needs and UHC vulnerabilities.

4. Conclusion

On orthodox public health criteria (need, impact, efficiency, equity), the case for mass-vaccination of populations against COVID-19 in Africa is weak. Most people in these populations already have immunity as effective as that which vaccination could provide. The vaccines do not prevent transmission to the relatively small pool of highly vulnerable people who may still be non-immune and at high risk. The diversion of resources, far higher than allocated to any other disease, or to general health system strengthening or universal health coverage, will inevitably impose (and already have imposed) a large opportunity cost on health system capacities and thus on management of other diseases, and potentially on the economies on which future disease control will depend.

The COVAX programme is being touted as promoting 'equity', but equal access to a pharmaceutical product is not health equity. The latter requires equal access to an opportunity for a healthy life [95]. Moreover, it is important not to confuse the clear unfairness associated with 'vaccine nationalism' (which we strongly deplore) and persistent blockages to medicines writ large (which underwrite feelings of injustice at the heart of most COVAX 'equity' arguments) with the fact that, in this particular case, a population-wide COVID-19 vaccine programme will not contribute to the equitable promotion of public health. COVAX therefore appears misdirected, and a return to the principles of public health, including resource allocation based on disease burden and actual risk would bring better health outcomes for the populations to whom it is directed. Consequently, in re-considering the strategies and targets for COVAX in the lens of public health equity and opportunity costs, country-wide mandatory COVID-19 vaccinations across population groups is unwarranted, unsustainable and will degrade already weakened health systems. This has implications for reflections about current and future COVAX policy as well as for ongoing debates about its future or its replacement by a different COVID-19 vaccine pooling mechanism. Within these policy debates we believe that allowing space for a more case-by-case approach is preferrable in LMIC settings, where country stakeholder dialogue is paramount, especially much of Africa, where COVID-19 mass vaccination makes little sense, yet comes at great cost.

Declaration of Competing Interest

Elisabeth Paul (last/corresponding author) is an active member of the Technical Review Panel of the Global Fund and of the Independent Review Committee of Gavi. However, this paper was written in total independence from these institutions. The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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