WHO SAGE ROADMAP FOR PRIORITIZING USE OF COVID-19 VACCINES

An approach to optimize the global impact of COVID-19 vaccines, based on public health goals, global and national equity, and vaccine access and coverage scenarios

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Preamble

This interim guidance constitutes a major revision of the *WHO SAGE roadmap for prioritizing uses of COVID-19 vaccines*, first issued October 2020, and updated in November 2020 and July 2021. It is based on work conducted by the SAGE Working Group on COVID-19 Vaccines and SAGE members, from October 2021 to January 2022, including consultation with RITAG[1] chairs, and dedicated discussions at extraordinary meetings of the Strategic Advisory Group of Experts (SAGE) on Immunization on 7 December 2021 and 19 January 2022 *(1)*.

This revised Roadmap takes into account increasing vaccine availability, vaccine coverage rates, and the evolving epidemiological situation including COVID-19 variants of concern. Scenarios in which vaccination coverage exceeds 50% of the population are considered, as are topics such as vaccine use in children and adolescents and prioritization of additional and booster doses in relation to vaccination coverage rates. To assist countries in developing recommendations for optimized use of vaccines against COVID-19, priority-use groups for vaccination (both primary series and booster doses) are identified based on epidemiological scenarios, public health goals, and vaccine coverage scenarios (in accordance with *WHO SAGE values framework for the allocation and prioritization of COVID-19 vaccination (2)*).

This Roadmap is complementary to the *Strategy to achieve global Covid-19 vaccination by mid-2022 (3)* issued in September 2021, which was developed by WHO in collaboration with its COVAX partners and key regional and national stakeholders, and which specifies national vaccine coverage categories. The Roadmap emphasizes the importance of prioritizing the distribution of increasingly available vaccine supply to optimize impact on health, socioeconomic conditions, and equity, and focuses on in-country vaccine policies.

Declarations of interests were collected from all external contributors and assessed for any conflicts of interest. Summaries of the reported interests can be found on the SAGE meeting webpage and SAGE Working Group webpage.

[1] RITAG: Regional Immunization Technical Advisory Group

Executive summary

By the end of December 2021, about 12 months after the first COVID-19 vaccine received WHO Emergency Use Listing (EUL), more than 9 billion COVID-19 vaccine doses had been administered globally and 48% of the global population had received the primary vaccination series. However, profound inequities in vaccine access and coverage remain worldwide, with some countries reporting vaccination coverage rates below 5%, and others above 80%. Because millions of people in many countries have been left behind in completing a primary vaccination series, globally-coordinated efforts and funding must be strengthened to achieve equitable distribution to, and uptake of, vaccines in all countries. In 2022, more vaccine doses will become available, enabling many countries to achieve high vaccination coverage by mid-2022. Achieving high vaccine access and coverage rates depends not only on vaccine supplies, but also vaccine acceptance and a country's capacity to roll out available supply.

This Roadmap builds on WHO's *Strategy to achieve global Covid-19 vaccination by mid-2022 (3)* which highlights four objectives for vaccination programmes to achieve the overall goal of full recovery from the COVID-19 pandemic to: i) minimize deaths, severe disease and overall disease burden; ii) curtail the health system impact; iii) fully resume socioeconomic activity; and iv) reduce the risk of new variants. These four objectives are interdependent, and each is important. Currently available COVID-19 vaccines have a modest impact on reducing transmission in the context of SARS-CoV-2 Variants of Concern (VoCs), particularly Omicron. Therefore, averting severe disease and deaths, and protecting health systems remain the primary objectives of vaccine use in the context of the global COVID-19 response, while also reducing morbidity including post COVID conditions. This Roadmap also considers vaccine use in resuming socioeconomic recovery, particularly the priority of maintaining uninterrupted education to keep children connected and learning.

Countries are in different stages of the pandemic and vaccine roll-out, and have different population age structures. To guide country decision-making on how to optimize the public health and social impact of available vaccine supplies and absorptive capacity to administer primary vaccination series and booster doses while attending to equity considerations, the Roadmap identifies priority-use groups and accounts for vaccination coverage rates of the primary series and time since the start of the vaccination programme, in accordance with the *WHO SAGE values framework for the allocation and prioritization of COVID-19 vaccination (2)*.

In most countries, groups at higher risk of severe disease and death were first to receive the primary vaccine series; these groups are therefore among the first to show evidence of declining vaccine effectiveness over time. Emerging evidence indicates that vaccine effectiveness against SARS-CoV-2 infection and any symptomatic COVID-19 declines significantly over a period of six months after completion of the primary series, likely resulting from waning protective vaccine-induced immunity, compounded by lower vaccine-induced neutralizing antibody activity against VoCs, including the Delta and Omicron variants. By contrast, vaccine-induced protection against severe COVID-19 outcomes remains relatively better maintained for at least six months after completion of the primary vaccination series, with some declines from maximum protection after completion depending on vaccine platform and VoC. In the short-term, a third dose (booster dose) may fully or partially restore vaccine effectiveness. Variant-adapted COVID-19 vaccines, while in development, are not yet available, hence their potential use is not considered in this Roadmap.

Given that achieving high rates of primary series coverage among the groups at higher risk of severe disease and death remains a critical priority to optimize the impact of available COVID-19 vaccine supply, this Roadmap is built upon two key findings derived from modelling and vaccine effectiveness data:

1. ***Within a priority-use group*, increasing the primary vaccination series coverage rate has a greater impact on reducing hospitalizations and deaths per dose than use of equivalent vaccine supply to increase the booster dose coverage rate**.

2. ***Across priority-use groups*, increasing the booster dose coverage rate for higher priority-use groups will usually[†] yield greater reductions in severe disease and death than use of equivalent vaccine supply to increase the primary vaccination series coverage rates of lower priority-use groups.**

[†]In some circumstances, there may be a relatively close trade-off in optimizing the impact of vaccine use between offering booster doses to older adults to avert more hospitalizations and deaths versus offering primary series doses to the remaining adults, adolescents, and children, that depend on country conditions, including supply and rollout timelines, past epidemic dynamics and infection-induced immunity, vaccine product, vaccine effectiveness, and waning of protection.

WHO recommends for low, moderate, and high primary series coverage rates in higher priority-use groups (see also **Table 1** below) that:

1. ***Countries with low rates of primary series coverage* should first achieve high primary series coverage rates among the higher priority-use groups before offering vaccine doses to lower priority-use groups.[†]**

Note: As older adults comprise a large fraction of the highest priority-use group, settings unable to access or deliver vaccines to older adults should consider prioritizing new delivery systems specifically to achieve high coverage rates in this subgroup.

[†]As more vaccine becomes available, lower priority-use groups should be offered vaccine, taking into account national epidemiological data and other relevant considerations. Lower priority-use groups should not be offered primary series doses before higher priority-use groups have been offered primary series doses, unless vaccine programmes encounter significant vaccine delivery or acceptability obstacles to uptake in higher priority-use groups that would result in vaccine wastage. In such cases, community engagement and social mobilization efforts to reach higher priority-use groups should be prioritized.

2. ***Countries with moderate-to-high rates of primary series coverage* in higher priority-use groups should usually[‡] prioritize available resources to first achieve high booster dose coverage rates in higher priority-use groups before offering vaccine doses to lower priority-use groups.**

[‡] In some circumstances, there may be a relatively close trade-off in optimizing the impact of vaccine use between offering booster doses to older adults to avert more hospitalizations and deaths versus offering primary series doses to the remaining adults, adolescents, and children, that depend on country conditions, including supply and rollout timelines, past epidemic dynamics and infection-induced immunity, vaccine product, vaccine effectiveness, and waning of protection.

Table 1: Prioritized use of primary series and booster doses by vaccine coverage rates in higher priority-use (I & II) groups

Priority-use groups†	Vaccine coverage rates of *higher priority-use* (I & II) groups ††
	Low → Moderate → High → Very high
I. *Highest priority-use* Older adults Health workers Immunocompromised persons	**Primary series + Additional dose* / Booster****
II. *High priority-use* Adults with comorbidities Pregnant persons Teachers and other essential workers Disadvantaged sociodemographic subpopulations at higher risk of severe COVID-19	**Primary series + Booster**
III. *Medium priority-use* Remaining adults Children and adolescents with comorbidities	**Primary series + Booster**
IV. *Lowest priority-use* Healthy children and adolescents	**Primary series + Booster** (booster doses in children below the age of 12 years have not yet been assessed)

†*Priority-use groups*: The extent of risk of severe disease and death is the main determinant for assignment of a subgroup (or subpopulation) to a priority-use group. This criterion aligns with a specification of the human well-being principle in the *WHO SAGE values framework for the allocation and prioritization of COVID-19 vaccines*. In addition, other specifications of that principle, including reducing societal and economic disruption and protecting essential health services, as well as of the national equity and reciprocity principles, are also used to justify assignment of some of the subgroups to a priority-use group.

†† *Vaccine coverage rates: The coverage rates relate to the very high and high priority-use groups. Specific thresholds are not provided as countries may have different abilities to reach these populations. As general guidance, very high coverage in the very high and high priority groups would be above 70%, and low coverage below 10%.*

**Additional dose:* Persons with moderate to severe immunocompromising conditions should receive an *expanded primary vaccination series* through an additional dose about 1–3 months after completion of the primary series (see *Interim recommendations for an extended primary series with an additional vaccine dose for COVID-19 vaccination in immunocompromised persons (4)*. Such persons are also a high priority-use group for a subsequent (booster) dose.

***Booster dose:* The optimal interval between completion of a primary series and administration of a booster dose has yet to be determined, and depends on epidemiological setting, vaccine product, targeted age groups, background seroprevalence, and circulation of specific variants of concern. As a general principle, dependent on vaccine product, an interval of 4–6 months since completion of the primary series could be considered for countries experiencing significant loss of vaccine effectiveness against severe disease in the context of an impending or ongoing major surge of cases, while a longer interval could be considered for those countries currently not experiencing, or at low risk of, an increasing incidence of cases.

Healthy children and adolescents belong to the lowest priority-use group because of their relatively low risk of severe disease, hospitalization, and death. Vaccinating this age group is less urgent than vaccinating adults, particularly older adults. However, there are benefits of vaccinating children and adolescents that go beyond the direct health benefits, such as minimizing school disruptions. The decision to vaccinate healthy children and adolescents must account for prioritization to first fully protect higher priority-use groups (e.g., older adults and health workers) through primary vaccination series, and, as vaccine effectiveness declines with time, through booster doses. As such, before considering implementing a primary vaccination series in adolescents and children, using the vaccine supply to attain high coverage rates of primary series – and booster doses as needed based on evidence of waning and optimizing vaccination impact – in higher priority-use groups, such as older adults, must be considered.

Homologous schedules (both for primary series and booster doses) are considered standard practice based on substantial safety, immunogenicity, and efficacy data available for each WHO EUL COVID-19 vaccine. Nonetheless, increasing evidence shows that, for some vaccines, heterologous schedules may offer superior immunogenicity. WHO supports a flexible approach to the use of either homologous or heterologous vaccination schedules and boosters. WHO considers two heterologous doses of any EUL COVID-19 vaccine to be a complete primary series. Heterologous vaccination schedules should be implemented only after careful consideration of current vaccine supply, vaccine supply projections, and other access considerations, alongside the potential benefits and risks of the specific products being used.

The need for and optimal timing of the primary vaccination series and booster dose may be different in an individual who has had a prior SARS-CoV-2 infection or who has experienced a breakthrough infection after initiation of the primary series when compared to a previously uninfected individual. On a population level, the number of doses and interdose interval, as well as the need for booster doses, may differ in settings with high seroprevalence from infection-induced immunity. However, seroprevalence rates observed in population-based studies may not be representative of the entire population or certain subpopulations and age groups, and may also differ by population density. While there may be some benefit to account for the variations in population seropositivity rates in different priority-use groups and the degree of infection-induced protective immunity within countries or communities that may already have experienced high levels of community transmission, basing national vaccination policies on seroprevalence rates or individual pre-vaccination screening is currently not recommended. When more evidence is available, advice on if and how infection-induced immunity should be considered in national vaccination policies will be updated accordingly.

As there is modest impact of vaccines on transmission, and substantially less impact for the newly emerged Omicron variant, public health and social measures must continue, including use of effective face masks, physical distancing, handwashing, and other measures based on the epidemiology of SARS-CoV-2 and vaccine coverage rates. This advice will be updated as information on the impact of vaccination on virus transmission and indirect protection in the community accrues. Countries' strategies related to COVID-19 control should be designed to facilitate participation of children and adolescents in education and other aspects of social life, regardless of vaccination.

Introduction

To support countries in implementing their respective vaccination programmes against coronavirus disease (COVID-19), the Strategic Advisory Group of Experts (SAGE) on Immunization of the World Health Organization (WHO) developed a three-step process to provide guidance for overall programme optimization, as well as vaccine-specific recommendations.

Step 1: A values framework. The *WHO SAGE values framework for the allocation and prioritization of COVID-19 vaccination (2)*, issued on 14 September 2020, outlines the general principles, objectives, and target groups for prioritizing the use of COVID-19 vaccine supplies.

Step 2: A roadmap for optimizing uses of COVID-19 vaccines based on priority-use groups (Prioritization Roadmap). This Prioritization Roadmap remains fully aligned with the *WHO SAGE values framework for the allocation and prioritization of COVID-19 vaccination (2)*. To support countries in planning vaccination programmes, this Roadmap suggests public health strategies and identifies target groups for optimization of COVID-19 vaccine use (referred to as "priority-use groups") in the context of different epidemiological settings, public health goals, and levels of vaccine access and coverage. The initial Roadmap, entitled *WHO SAGE roadmap for prioritizing uses of COVID-19 vaccines in the context of limited supply* (first published on 7 October 2020 and updated on 13 November 2020 and 16 July 2021), considered priority uses of vaccines at a time when vaccine supply was limited and deployment of the primary vaccination series was the only consideration. The focus of this current Roadmap is the optimization of vaccine use, including as a booster dose, and vaccination of adolescents and children. This update also reflects additional data from pre- and post-authorization studies, as well as lessons learned from COVID-19 vaccine programme implementation. The Roadmap will be updated, as necessary, to accommodate the dynamic nature of the pandemic, greater availability of vaccines, and evolving evidence about vaccine use and impact.

Step 3: Evidence to vaccine-specific recommendations. Specific recommendations for the use of EUL and WHO prequalified vaccines will be issued based on SAGE's *Evidence to recommendations for COVID-19: evidence framework (5)*. Currently, eight vaccines have been recommended by WHO for emergency use, and vaccine-specific interim recommendations on the use of these EUL vaccines have been issued (see: COVID-19 vaccines technical documents: Product specific documentation). These recommendations are updated as additional evidence on effectiveness, safety, and other needs (e.g., use of additional and booster doses) becomes available, and as epidemiological and other contextual conditions evolve.

Definitions

Throughout this Roadmap, "optimization" refers to policy considerations and decisions that aim to make the most effective and efficient use of COVID-19 vaccine supplies in specific epidemiological settings to achieve global and local public health goals.

The following definitions and terminology for additional doses and booster doses are used by WHO throughout its policy recommendations on COVID-19 vaccination.

- *Additional doses* of a vaccine may be needed as part of an *extended primary vaccination series* for target populations where the immune response rate following the standard primary series is deemed insufficient. The objective of an additional dose in the primary series is to optimize or enhance the immune response to establish a sufficient level of effectiveness against disease. In particular, immunocompromised individuals often fail to mount a protective immune response after a standard primary series. In addition, older adults may also respond poorly to a standard primary series with some vaccines.
- *Booster doses* are administered to a population that has completed a *primary vaccination series* (including additional doses in an extended primary series). The objective of a booster dose is to restore vaccine effectiveness when, with time, the

immunity and clinical protection of a primary vaccination series has fallen below a rate deemed sufficient in that population.

Epidemiological setting scenarios

The epidemiological settings used in this Roadmap take into consideration the relative benefits and potential risks of COVID-19 vaccine use (i.e., both primary vaccination series and booster dose). The public health strategy for optimizing vaccine use depends on the burden of disease and the local epidemiology, including transmission patterns, seroprevalence from infection-induced immunity in the target population, circulation of specific variants of concern (VoCs), and the incidence rate of infection in the specific setting at the time vaccination is being contemplated.

Transmission patterns

WHO uses seven categories[2] to describe transmission patterns at national and subnational levels to guide decisions for preparedness, readiness and response activities (see: WHO's *Critical preparedness, readiness and response actions for COVID-19*). Although countries are in different epidemiological phases with different transmission patterns, essentially all are experiencing at least one of the four community transmission levels, which share common COVID-19 response aims: to slow transmission; to reduce case numbers; and to end community outbreaks. Hence, this Roadmap considers a single epidemiological scenario, community transmission.

Infection-induced immunity

Immunity derived from SARS-CoV-2 infection may provide variable protection against re-infection and severe disease. Infection-induced protective immunity may wane over time and be lower against new VoCs. Uncertainty remains as to the relative protection afforded by infection-induced, versus vaccine-induced, immunity, although initial evidence suggests that some COVID-19 vaccines provide higher levels of protective immunity than does infection, and that vaccination increases protective immunity in those with a prior infection. Preliminary evidence suggests that infection/vaccination-induced hybrid immunity from three exposures to Spike protein (i.e., one or more exposures from vaccination and one or more from SARS-CoV-2 infection, the latter either before or after vaccination) may provide superior neutralization capacity against VoCs, including Omicron, compared with two doses of vaccination, or previous natural SARS-CoV-2 infection without vaccination *(6)*.

As such, the need for, and optimal timing of, the primary vaccination series and booster dose may be different in an individual