WHO roadmap on uses of COVID-19 vaccines in the context of Omicron and high population immunity

An approach to optimize the global impact of COVID-19 vaccines at a time when Omicron and its sub-lineages are the dominant circulating variants of concern, based on public health goals, evolving epidemiology, and increasing population-level immunity

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WHO roadmap on uses of COVID-19 vaccines in the context of Omicron and high population immunity

PREAMBLE

This interim guidance constitutes an update of the WHO SAGE roadmap for prioritizing uses of COVID-19 vaccines, first issued in October 2020, with several further updates as the evidence evolved. It is based on deliberations and evidence review conducted by the SAGE Working Group on COVID-19 Vaccines and SAGE members, including consultation with RITAG\(^1\) chairs, and dedicated discussions at the SAGE meeting of the Strategic Advisory Group of Experts (SAGE) on Immunization on 28 September 2023 (1).

On 5 May 2023, the WHO Director-General declared that COVID-19 no longer constitutes a public health emergency of international concern. Given high population-level immunity, estimated at above 90% in most countries due to increasing vaccine coverage rates and infection-induced immunity (2), numbers of hospitalizations and deaths have declined globally.

WHO considers three pandemic scenarios (3): (1) **Base-case scenario**: The virus continues to evolve but does not become more virulent. Periodic spikes in transmission may occur as a result of an increasing proportion of susceptible individuals over time if waning immunity is significant; this may require periodic boosting at least for high-priority populations. (2) **A worst-case scenario**: A more virulent and highly transmissible variant emerges against which vaccines are less effective, and/or immunity against severe disease and death wanes rapidly, especially in the most vulnerable groups. This would require significant alterations to current vaccines and full redeployment and/or broader boosting of all high-priority groups. (3) **Best case scenario**: Future variants that emerge are significantly less virulent, protection against severe disease is maintained without the need for periodic boosting or significant alterations to current vaccines. The recommendations in this document are based on the “base-case” scenario, and these recommendations will be further updated should the situation evolve either into the “best case scenario” or a “worst-case scenario”.

This updated Roadmap addresses evolving public health needs as the Omicron variant and its sub-lineages continue to circulate and provides updates for COVID-19 vaccination in relation to simplified vaccine schedules for programmatic use.

The Roadmap will be further adapted should new variants of concern emerge that do not have the characteristics of Omicron, or in the event of significant changes in COVID-19 disease epidemiology, or if significant changes in vaccine attributes warrant an update to the Roadmap. This Roadmap will not be updated for new variant-updated vaccines, unless characteristics or performance of such vaccines would require a change in policy recommendations in terms of the Roadmap Table.

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. This guidance should be considered along with the broader COVID-19 policy advice to WHO Member States and in particular the advice on how to reach the COVID-19 vaccination targets.

\(^1\) RITAG: Regional Immunization Technical Advisory Group.
EXECUTIVE SUMMARY

The COVID-19 situation towards the end of 2023, almost four years after the start of the pandemic, has changed significantly. Globally, population-level immunity has increased significantly, due to substantial and increasing vaccine use along with infection-induced immunity, or the combination of both (hybrid immunity). Countries have lifted most or all public health and social measures, and while the SARS-CoV-2 virus continues to circulate, the COVID-19 pandemic has seen significant reduction in rates of hospitalization, admission to ICU and deaths across all age groups. Nonetheless, certain subgroups continue to be at greater risk of severe disease and mortality and account for most of the ongoing COVID-19-related mortality.

This Roadmap addresses the evolving public health needs at the present time with Omicron and its sublineages dominating circulation globally and in the context of high population-level immunity, using a base case scenario that assumes that the virus will continue to evolve but cause less severe disease with possible surge in infections that will require booster doses to maintain protection in the high priority groups. In addition to population immunity and the speed of waning vaccine effectiveness, factors such as programmatic ease, community acceptance and cost–effectiveness need to be considered in determining the optimal interval and frequency for booster doses. Furthermore, given that the vast majority of people have experienced at least one SARS-CoV-2 infection, a simplified schedule can be considered for those who have not yet had COVID-19 vaccination (i.e. vaccine-naïve persons).

While currently approved COVID-19 vaccines, e.g those based on the index virus only and the bivalent BA5 vaccines, continue to provide protection against severe disease and death, the TAG-CO-VAC in May 2023 advised moving away from the inclusion of the index virus in future formulations of COVID-19 vaccines.

A number of manufacturers for COVID-19 vaccines are in the process of, or have completed, developing monovalent XBB-based vaccines without the index virus; these should become available in 2023 and 2024. Based on immunogenicity and modelling studies, monovalent variant-containing vaccines containing XBB sub-lineages are likely to have modestly enhanced vaccine effectiveness compared to bivalent variant-containing vaccines and the monovalent index virus-only vaccines at a time when the XBB Omicron sub-lineages predominate. Hence, these vaccines should be used when they become available.

Currently approved COVID-19 vaccines continue to provide protection against severe disease and death. Hence, any of the WHO emergency-use listed or prequalified COVID-19 vaccines can still be used either for the initial series (primary series) or as booster doses when the monovalent XBB vaccines are unavailable. Vaccination should not be delayed in anticipation of access to variant-containing vaccines since there is a greater benefit in ensuring that persons at high risk of developing severe COVID-19 receive a dose of any available vaccination compared to delayed vaccination.

Given that the vast majority of the global population will have been infected at least once, for programmatic purposes, in vaccine-naïve persons, a single dose can be considered for initial vaccination (primary series), except for inactivated vaccines. For inactivated COVID-19 vaccines, two doses are required for the initial vaccine series. The timing for re-vaccination (booster) depends on the time elapsed since the last dose, rather than the number of previous doses.

The table below outlines WHO’s updated interim recommendations for the optimal use of COVID-19 vaccination by priority-use groups.
### HIGH priority--use groups

<table>
<thead>
<tr>
<th>Target population</th>
<th>Vaccination of persons who have never received a COVID-19 vaccine</th>
<th>Revaccination of persons who have received at least one dose of COVID-19 vaccine</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oldest adults(^1)</td>
<td>Single Dose(^6)</td>
<td>6–12 months after previous dose</td>
</tr>
<tr>
<td>Older adults with multiple comorbidities that put them at higher risk of severe COVID–19</td>
<td>Single Dose(^6)</td>
<td>Approximately 12 months after previous dose</td>
</tr>
</tbody>
</table>

### MEDIUM priority--use groups

<table>
<thead>
<tr>
<th>Target population</th>
<th>Vaccination of persons who have never received a COVID-19 vaccine</th>
<th>Revaccination of persons who have received at least one dose of COVID-19 vaccine</th>
</tr>
</thead>
<tbody>
<tr>
<td>Healthy adults(^4)</td>
<td>Single Dose(^6)</td>
<td>Not routinely recommended(^{4,6})</td>
</tr>
<tr>
<td>Children and adolescents aged 6 months to 17 years with severe obesity or a comorbidity that puts them at higher risk of severe COVID–19</td>
<td>Single Dose(^6)</td>
<td>Not routinely recommended(^{4,6})</td>
</tr>
</tbody>
</table>

### LOW priority--use groups

<table>
<thead>
<tr>
<th>Target population</th>
<th>Vaccination of persons who have never received a COVID-19 vaccine</th>
<th>Revaccination of persons who have received at least one dose of COVID-19 vaccine</th>
</tr>
</thead>
<tbody>
<tr>
<td>Healthy children and adolescents aged 6 months to 17 years</td>
<td>If countries opt to vaccinate low priority--use groups(^{4,6}), they could consider single dose for ages 5 years and above; two doses for age 6 months to 4 years(^4)</td>
<td>Not routinely recommended(^{4,6})</td>
</tr>
</tbody>
</table>

### Sub-populations with special considerations

<table>
<thead>
<tr>
<th>Target population</th>
<th>Vaccination of persons who have never received a COVID-19 vaccine</th>
<th>Revaccination of persons who have received at least one dose of COVID-19 vaccine</th>
</tr>
</thead>
<tbody>
<tr>
<td>Persons with moderate and severe immunocompromising conditions (adults, adolescents and children &gt; 6 months)</td>
<td>Two or three doses in consultation with the health care provider</td>
<td>6–12 months after previous dose; optimal time interval should be determined in consultation with the health care provider</td>
</tr>
<tr>
<td>Pregnant adults and pregnant adolescents(^{4,6})</td>
<td>Single dose in each pregnancy regardless of previous vaccination status; ideally during the second trimester or at any opportunity</td>
<td></td>
</tr>
<tr>
<td>Health care workers with direct patient contact</td>
<td>Single dose</td>
<td>Approximately 12 months after previous dose</td>
</tr>
</tbody>
</table>

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1. Age cut-off to be decided by countries; often it is 75 or 80 years. 2. Age cut-off to be decided by countries; often it is 50 or 60 years. 3. In vaccine-- naïve persons, for programmatic purposes, a single dose can be considered for primary vaccination given that the vast majority of the population will have been infected at least once. For inactivated COVID–19 vaccines, two doses are required for the primary vaccine series. 4. Age cut-off to be decided by countries; often it is 18 to 49 or 18 to 59 years. 5. Regulatory approvals or WHO EUL for the age indication differ by vaccine product; refer to the product--specific vaccine recommendations. 6. “Not routinely recommended” means that such vaccines are not recommended because of minimal public health impact and low cost-effectiveness in most settings. However, vaccination may be offered in individual country-specific circumstances where added benefit is expected to be more substantial. This interim recommendation acknowledges that some countries may elect to offer such doses in the routine programme based on population risks, disease epidemiology, or public health priorities. 7. Benefit of vaccinating healthy children and adolescents is substantially lower compared to vaccinating older persons or as compared to other childhood vaccinations. Countries could consider vaccination based on disease burden, cost-effectiveness, and other programmatic priorities. 8. Regulatory approvals or WHO EUL for the use in pregnancy may differ by vaccine product.
HISTORICAL OVERVIEW

To support countries in designing 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 various guidance documents for overall programme optimization, as well as several vaccine-specific recommendations. These included:

(1) **A values framework.** The *WHO SAGE values framework for the allocation and prioritization of COVID-19 vaccination* (4), issued on 14 September 2020, outlined the general principles, objectives, and target groups for prioritizing the use of COVID-19 vaccine when vaccine supplies were limited.

(2) **A roadmap for prioritizing uses of COVID-19 vaccines based on priority-use groups (Prioritization Roadmap) at a time of limited vaccine supply (2020-2021).* Aligned with the *WHO SAGE values framework for the allocation and prioritization of COVID-19 vaccination* (4), and to support countries in planning vaccination programmes, this Roadmap suggested public health strategies and identified target groups (referred to as “priority-use groups”) for optimization of COVID-19 vaccine use 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 sole consideration.

(3) **A roadmap for optimizing uses of COVID-19 vaccines based on priority-use groups beyond the primary vaccination series (2022).* The updated Roadmap of 21 January 2022 was a significant revision to the previous version given increasing vaccine supplies. The focus was the optimization of vaccine use for impact, including a booster dose, and the vaccination of adolescents and children. Additional data from pre- and post-authorization studies was taken into account, as well as lessons learned from COVID-19 vaccine programme implementation.

(4) **This current roadmap for uses of COVID-19 vaccines in the context of Omicron and its sublineages:** The Omicron variant and its more than 600 sub-lineages are currently the dominant circulating COVID-19 virus strains. Although more transmissible than previous variants, Omicron variants in the context of increased population level immunity, are associated with less severe disease, on average, lower fatality rates, and less frequent post-COVID-19 conditions. Whilst there remains a significant risk of further variants of concern emerging, Omicron sub-lineages have remained dominant for more than one year in the context of the currently available vaccines. Therefore, a monovalent Omicron-only vaccine can now be considered for both the initial and booster doses. Given that the vast majority of the population has had at least one SARS-CoV-2 infection, this roadmap also recommends a simplified vaccine schedule. Terms such as “initial doses” instead of primary series are now used to reflect the fact that the vast majority of the population has been primed. Instead of booster doses, WHO now also refers to “re-vaccination”. All these terms can be used interchangeably

(5) **Vaccine-specific recommendations.** Recommendations for the use of each of the WHO Emergency Use Listing (EUL) and WHO prequalified COVID-19 vaccines will continue to be issued based on SAGE’s *Evidence to recommendations for COVID-19: evidence framework* (5). Currently, 11 COVID-19 vaccines have been recommended by WHO for emergency use, and vaccine-specific interim recommendations on the use of these 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 relevant issues (e.g., use of booster doses, variant-containing vaccines) becomes available, and as epidemiological and other contextual conditions evolve. For convenience, these recommendations are being grouped into vaccine platform specific recommendations.
PUBLIC HEALTH GOALS SCENARIOS

The **Strategy to achieve global Covid-19 vaccination by mid-2022** (6) issued by WHO in mid-2021 as vaccine supply increased, highlighted four objectives for vaccination programmes to achieve the overall goal of full recovery from the COVID-19 pandemic: i) to minimize deaths, severe disease and overall disease burden; ii) to curtail health system impact; iii) to fully resume socioeconomic activity; and iv) to reduce the risk of emergence of new variants. The mid-2022 update to the strategy acknowledged the progress made on the disease, health system and socioeconomic goals, and prioritized accelerating toward these achievements while also recognizing the limitations of the vaccines in reducing transmission and therefore the emergence of new variants. The strategy was therefore updated to focus on two goals – the first being to enhance health, socioeconomic and health system protection; and the second to develop COVID-19 vaccines with enhanced performance, including duration of protection, protection against transmission, and reducing the risk of new strains emerging. While progress towards the first goal has been substantial and largely met in many countries, the second is yet to be achieved; efforts to develop vaccines with enhanced performance to prevent mild illness and transmission continue.

Given the robust evidence that currently available vaccines show substantial impact on averting severe disease and deaths, pursuing direct protection of those at high risk of severe disease outcomes remains the highest public health priority. Therefore, vaccination of persons in the high priority-use group, who are at highest risk of severe disease, hospitalizations and death, with both initial series and booster doses will have the greatest public health impact. The decision by countries to procure and use further doses of vaccines needs to be justified with evidence of cost–effectiveness using the same criteria as that used to evaluate other vaccines and health-care interventions. Where possible, cost–effectiveness analyses need to consider the wider socioeconomic benefits of vaccination, such as avoiding productivity loss due to both acute episodes and their long-term sequelae.

Persistent symptoms, complications, and sequelae of COVID-19, such as pulmonary, cardiovascular, neurological, and physical effects, have been reported globally; yet the underlying aetiology, prevalence, and risk factors are still not fully understood (7, 8). Vaccines against SARS-CoV2 are effective against COVID-19 and its progression to severe disease and- may also prevent secondary complications (9). Current COVID-19 vaccines have some impact on reducing post-COVID-19 conditions (7, 10-13), but evidence on the extent of the impact is currently inconsistent in the scientific literature. Nonetheless, reducing post-COVID-19 conditions is one of the arguments to continue offering vaccination to those adults who have not yet received COVID-19 vaccination. Post-COVID-19 conditions are less frequent in healthy children and adolescents. The high incidence of mild to moderate symptomatic COVID-19 illness continues to cause disruptions to society. The impact of currently available vaccines on reducing symptomatic illness and transmission in the context of Omicron is modest. Countries considering methods to reduce the socioeconomic impact due to mild and moderate SARS-CoV2 infections need to take into account rapid waning of vaccine effectiveness against such infections, and number of sequential booster doses required- to restore and sustain vaccine effectiveness, along with cost–effectiveness, affordability, opportunity costs to other vaccination programmes, and community acceptance. Modelling shows that the public health benefit of vaccination is lowest for healthy children and adolescents (14-16).

EVIDENCE CONSIDERED

The evidence considered in this update, in particular Omicron-specific vaccine effectiveness studies, was identified through a living literature review up until 17 March 2023. All data can be accessed on the International Vaccine Access Center (IVAC)’s View-hub website (see: [COVID Vaccines | ViewHub (view-hub.org)]), including weekly literature tables, forest plots, neutralization plots, and methods used.

Systematic reviews and meta-analyses were done for the duration of protection of hybrid immunity, vaccine-and infection-induced immunity over time and considered if they were published up until March 2023. Real-world vaccine effectiveness over time, by vaccine product and by age groups was studied through systematic reviews and meta-analyses. Modelling studies were conducted, including estimates on number needed to vaccinate.
Data on seroprevalence was obtained from the WHO Serotrack (see: SeroTracker).

A comprehensive summary of all the evidence on which this document is based is available in the presentation to SAGE, accessible on the SAGE September 2023 meeting website (see: Strategic Advisory Group of Experts on Immunization).

Evidence to Recommendation Tables and GRADEing on product-specific vaccine performance is available in the Interim recommendations on the use of these vaccines (see: COVID-19 vaccines technical documents: Product specific documentation).

An evidence synthesis on monovalent XBB vaccines and other variant-adapted vaccines is available in the Good Practice Statement.

**OMICRON AND ITS SUBLINEAGES**

There continues to be substantial genetic and antigenic evolution of the spike protein of SARS-CoV-2, and the evolutionary trajectory continues to diverge from the index virus. The available sequencing data indicates that the index virus and other early variants (e.g., Alpha, Beta, Gamma and Delta) are no longer detected in humans.

Omicron emerged in November 2021. Omicron and its sub-lineages (including BA.4, BA.5, XBB, BA.2.86, EG.5, etc.) are now the dominant circulating variants worldwide, with XBB variants having replaced the previous BA.4 and BA.5 variants at the time of writing. The emergence of more sublineages within the Omicron family is likely in the near future. Omicron variants are associated with less severe disease compared to pre-Omicron variants such as Delta in the context of increased seroprevalence (17-19) have a lower risk of post-COVID-19 conditions following infection (20). Of the different viral variants that have caused infection waves, Omicron is antigenically the most distant from the index SARS-CoV-2 virus and is associated with greater immune evasion and consequent lower vaccine effectiveness. Although countries are still experiencing repeated waves of infection, they have not been followed by the same intensity of hospitalizations and deaths, which have generally been declining, as a result of further increasing population-level immunity due to increasing vaccine coverage and infection-induced immunity.

While vaccine effectiveness remains substantial and relatively well maintained over time against severe disease from Omicron, protection against mild disease and infection is lower than against pre-Omicron variants of concern and declines rapidly with time since the last vaccination. Older adults and people with comorbidities continue to be at greatest risk of severe disease and mortality due to Omicron and make up most of the deaths; thus, even a minor decrease in vaccine effectiveness with time in such vulnerable persons translates into a rise in severe disease and deaths. Population seroprevalence levels, reflecting the combined experience of infection and/or vaccination, are now above 90% in most countries (2).

Infection-induced immunity together with vaccine-induced immunity (i.e., hybrid immunity) provide additional benefits against disease. A meta-analysis showed that individuals with hybrid immunity had the highest magnitude and durability of protection against severe disease, and as a result it may be possible to extend the intervals between doses to 12 months for the high priority-se groups (21, 22).

**UPDATES TO COVID-19 VACCINE ANTIGEN COMPOSITION**

There is substantive evidence to support an update to COVID-19 vaccine antigen composition as genetic and antigenic evolution of the spike protein continues, further diverging from the index virus. The XBB variants exhibit high immune evasion, particularly XBB.1.5, which have more than 40 mutations compared to the index virus. Estimates of VE against currently circulating XBB descendent lineages, are very limited in terms of the number of studies, vaccine products evaluated, and populations assessed.
The evidence shows that sera from individuals who have received two, three or four doses of index virus-based vaccines, or a booster dose of a bivalent (BA.1- or BA.4/5- containing) mRNA vaccine show substantially lower neutralizing antibody titres against XBB.1 descendent lineages, as compared to titres specific for the antigens included in the vaccine. Individuals with hybrid immunity due to any SARS-CoV-2 infection show higher neutralizing antibody titres against XBB.1 descendent lineages as compared to responses from vaccinated individuals who had no evidence of infection. There is *in vitro* evidence that immune imprinting, which is a phenomenon in which B cell memory recall responses towards previously encountered antigen reduce the response to new antigens, may be occurring. However, based on observational epidemiological studies to date, the clinical impact remains unclear. Preclinical and clinical data shared with SAGE by vaccine manufacturers show that vaccination with XBB descendent lineage-containing candidate vaccines (including XBB.1.5) elicits higher neutralizing antibody responses to currently circulating SARS-CoV-2 variants, compared to responses elicited by index virus-only vaccines.

While currently approved COVID-19 vaccines, e. g. those based on the index virus only and the bivalent-vaccines, continue to provide protection against severe disease, the TAG-CO-VAC in May 2023 advised moving away from the inclusion of the index virus in future formulations of COVID-19 vaccines ([https://www.who.int/news/item/18-05-2023-statement-on-the-antigen-composition-of-covid-19-vaccines](https://www.who.int/news/item/18-05-2023-statement-on-the-antigen-composition-of-covid-19-vaccines)). This is based on the following reasons: the index virus and antigenically closely related variants no longer circulate in humans; the index virus antigen elicits undetectable or very low levels of neutralizing antibodies against currently circulating SARS-CoV-2 variants, including XBB descendent lineages; inclusion of the index virus in bi- or multivalent vaccines reduces the concentration of the new target antigen(s) as compared to monovalent vaccines, which may decrease the magnitude of the humoral immune response; and immune imprinting due to repeated exposure to the index virus may reduce immune responses to new target antigen(s).

Currently approved COVID-19 vaccines continue to provide protection against severe disease and death. Hence, any of the WHO emergency-use listed or prequalified COVID-19 vaccines can still be used either for the initial series or booster doses when the monovalent XBB vaccines are unavailable. Vaccination should not be delayed in anticipation of access to variant-containing vaccines since there is a greater benefit in ensuring that persons at high risk of developing severe COVID-19 receive a dose of any available vaccination compared to delayed vaccination.

A number of manufacturers for COVID-19 vaccines are now in the process of developing monovalent XBB-based vaccines without the index virus; some are already available in 2023 and others will become available in 2024.

Based on immunogenicity and modelling studies, monovalent variant-containing vaccines containing XBB 1.5 or 1.16 are likely to have modestly enhanced vaccine effectiveness compared to bivalent variant-containing vaccines and the monovalent index virus-only vaccines at a time when the XBB Omicron sub-lineages predominate. Hence, these vaccines should ideally be used when they become available.

The TAG-CO-VAC will continue to make recommendations on changes needed for future COVID-19 vaccines. This Roadmap will not be updated to reflect such changes in vaccine composition, unless new vaccine formulations will require different policy recommendations. The available evidence for the bivalent and monovalent variant-adapted vaccines can be found in the [Good Practice Statement](#).

In light of the extensive population immunity, this roadmap moves away from the notion of primary series and booster doses, and introduces a simplified posology, in accordance with recent regulatory decisions. This Roadmap proposes simplified vaccine schedules for those who have not yet had a COVID-19 vaccine.
CONSIDERATIONS FOR SIMPLIFYING THE VACCINE SCHEDULES

Primary series for vaccine-naïve persons: Neutralizing antibody levels are higher and more durable following vaccination in persons who had a prior infection. Given that four years into the pandemic most people have had at least one SARS-CoV-2 infection, there is now a strong rationale for simplifying the primary vaccine series. Although more than one vaccine dose remains superior to a single dose for the primary series, this additional benefit is marginal. Vaccine acceptance and uptake for a single dose is higher than a two dose, and achieving a higher vaccine coverage with a single dose primary series at this stage of the pandemic is more impactful than a lower vaccine coverage with a two-dose primary series. A 2-dose primary series is now recommended only for inactivated vaccines. Of note, immunogenicity is generally much lower in persons with moderate to severe immunocompromising conditions. For such persons, all efforts should be made to provide two and even three doses for the primary series, in consultation with the health care provider.

As most persons have been “primed”, in the forthcoming, WHO will use the terms “initial doses” instead of primary series. However, these terms can still be used interchangeably.

Interval between doses: With hybrid immunity, protection is higher and more sustained than infection-induced immunity or vaccine-induced immunity alone (22). Programmatically it is not feasible to screen for prior infections and adapt vaccine intervals accordingly. Given that seroprevalence rates are high in almost all countries, intervals between doses can be considered taking into account that most persons would have had a prior infection. Therefore, an interval of 12 months would suffice. There is evidence that VE wanes from 6 months onwards, and for very vulnerable persons such as the very old, frail or those with multiple significant comorbidities, a boosting interval of 6-12 months should be considered, as even minor waning could translate into more severe disease.

“Booster doses” is now often referred to as “re-vaccination” of persons who have received at least one COVID-19 vaccine in the past. The timing of re-vaccination is driven by the time interval to the previous dose, not the number of previous doses. The interval of re-vaccination (previously known as booster doses) is 12 months to the previous dose, except for the very old and those with multiple comorbidities that put them at a significant risk of more severe COVID-19 where an interval of 6 months should ideally be considered, or dependent on the epidemiological setting an interval of 6-12 months. Re-vaccination or booster doses are not recommended for all priority-use groups (see Table).

There is insufficient evidence to conclude that annual boosters will be needed in the longer-term; moreover, it is too early to decide whether seasonality should influence vaccination strategy, although countries with established seasonality for other respiratory infections could consider booster doses to be programmatically delivered prior to the colder season. WHO will continue to monitor the epidemiological and virological situation and update its recommendations accordingly.

In addition to population immunity and the speed of waning vaccine effectiveness, factors such as programmatic ease, community acceptance and cost–effectiveness need to be considered in determining the optimal interval and frequency for booster doses.

The vaccination frequency and intervals are determined by the priority-use groups, as elaborated in the following section and summarized in the table.
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**PRIORITY-USE GROUPS**

**High priority-use group**

High priority-use groups are groups for whom COVID-19 vaccines are of greatest importance to reduce death and severe disease. Vaccination of high priority-use groups remains critical for optimizing the impact of COVID-19 vaccination. Supply and programmatic delivery resources should be prioritized to achieve these goals. As older adults comprise a large fraction of the high priority-use groups, settings unable to access or deliver vaccines to older adults should consider prioritizing new delivery systems specifically in this subgroup. To aid this, WHO has published tools, guidance, national deployment and vaccination plans and training resources (23). Countries should consider the transition from delivery through a campaign mode to integrating COVID-19 vaccine into primary health-care services and other approaches specifically designed to deliver vaccines to those in the high priority groups.

Everyone in the high priority-use group should receive an initial dose (or two doses of the inactivated vaccine) and booster doses as outlined in the Table. The following groups are allocated to the high priority-use group either because of high risk of severe disease outcomes or because of special considerations.

**Higher risk of severe disease outcomes:**

Older adults are at elevated risk of severe COVID-19 disease. Ages 50 or 60 years are commonly used cut-offs for identifying “older adults” but the appropriate age cut-off should be made at the country-level. Adults who have multiple significant comorbidities or severe obesity are at greater risk for severe disease and death than adults in the same age range who do not have these conditions. Significant comorbidities include diabetes, chronic lung diseases, heart, liver and kidney diseases. The risk for severe COVID-19 also rises sharply as body mass index (BMI) increases (24). Severe obesity (BMI >40) is an independent risk factor for mortality in hospitalized adult patients aged younger than 50 years (25).

Oldest adults, e.g., those with advanced age, are at greatest risk of severe disease and death following COVID-19 infection. Because of substantial disparities in life expectancies and burden of disease, the age range best represented as “oldest” in terms of risk category varies across countries. Thus, the Roadmap does not specify an age cut-off for oldest adults but instead leaves that determination to countries. Age cut-offs of 75 or 80 years are common, but countries may have good reasons for selecting another cut-off.

**Groups with special considerations for vaccination**

The following 3 high priority-use subgroups each have distinctive rationales and special considerations for their designation as “high priority”.

**Adults, adolescents, and children older than 6 months with moderate to severe immunocompromising conditions:**

Moderately and severely immunocompromised persons (ICPs) are at greater risk of severe COVID-19, regardless of age, although risk further increases with age. Moderately and severely immunocompromised persons include those with active cancer, transplant recipients, and those who are immunodeficient and being actively treated with immunosuppressives. Also included are people living with HIV with a current CD4 cell count of <200 cells/μl, with evidence of an opportunistic infection, and not on HIV treatment, and/or with a detectable viral load. Available data for WHO EUL COVID-19 vaccines suggest that vaccine effectiveness and immunogenicity are lower in ICPs compared to persons without immunocompromising conditions (26). The emerging evidence suggests that providing an additional dose as part of an extended initial dose series enhances immune responses in some ICPs (27). Available evidence (26) suggests that for ICPs, the initial dose series needs to be expanded, e.g., more doses need to be given compared to persons without immunocompromising conditions. The most appropriate timing for the additional dose may vary

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2 Active cancer: Active immunosuppressive treatment for solid tumour or hematologic malignancy (including leukemia, lymphoma, and myeloma), or within 12 months of ending such treatment. Transplant recipients: Receipt of solid organ transplant and taking immunosuppressive therapy; receipt of stem cell transplant (within 2 years of transplantation or taking immunosuppressive therapy). Immunodeficiency: Severe primary immunodeficiency; chronic dialysis. HIV: with a current CD4 count of <200 cells/μl and/or lacking viral suppression. Immunosuppressives: Active treatment causing significant immunosuppression (including high-dose corticosteroids), alkylating agents, antimitabolites, transplant-related immunosuppressive drugs, cancer chemotherapeutic agents, tumour-necrosis factor (TNF) blockers, and other drugs that are significantly immunosuppressive or have received in the previous 6 months immunosuppressive chemotherapy or radiotherapy.
Health workers: Marketing evidence and observational studies have supported safety and demonstrated effectiveness. For more information, refer to product labels or product specific documents at COVID-19 vaccines technical documents: Product specific documentation. In countries where COVID-19 vaccines have been used in pregnancy, post-marketing evidence and observational studies have supported safety and demonstrated effectiveness. Health workers are all people engaged in work whose primary intent is to improve human health. This includes health service providers, such as doctors, nurses, midwives, public health professionals, laboratory-, health-, and medical and non-medical technicians, personal care workers, community health workers, healers and some practitioners of traditional medicine. It also includes health management and support workers, such as cleaners, drivers, hospital administrators, district health managers and social workers, and other occupational groups in health-related activities. Health workers include not only those who work in acute care facilities but also those employed in long-term care, public health, community-based care, social care and home care and other occupations in the health and social work sectors as defined by the International Standard Industrial Classification of All Economic Activities (ISIC), revision 4, section Q: Human health and social work activities.

Pregnant adults and adolescents: Pregnant adults and adolescents are a high priority-use group because of the potential adverse effects of COVID-19 on the pregnant adult or pregnant adolescent, the foetus, and the infant. Although the risk of severe disease in the Omicron era is less than in the pre-Omicron era (28), pregnant women with COVID-19 continue to be at higher risk of severe maternal morbidity and/or adverse pregnancy outcomes such as preterm birth (29-31). They may also have an increased risk of maternal mortality (29, 30). COVID-19 in pregnancy has also been associated with increased risks of neonates being born with low birth weight and requiring neonatal intensive care (30). Pregnant women who are older (aged 35 years and above), have a high BMI, or have an existing comorbidity such as diabetes or hypertension, are at particularly high risk of severe outcomes from COVID-19. During the Omicron era, COVID-19 vaccination, including booster dose, given to pregnant adults and adolescents protects them against severe disease and hospitalization, particularly when the last dose was received within the previous 4-5 months (32, 33). In addition, the incidence of hospitalization for COVID-19 was lower during the first 6 months of life among infants of vaccinated (and especially boosted) mothers, compared to infants of unvaccinated mothers (33). The burden of severe COVID-19 in infants below the age of 6 months is overall low, but nevertheless higher than in children aged 6 months to 5 years (34).

The recommendation for pregnant adults and adolescents is to receive a single dose during pregnancy. Vaccination in the mid-second trimester is preferred to optimize protection of the pregnant woman, the foetus, and the infant. However, the vaccine can be safely given at any time during pregnancy to avoid missing opportunities to vaccinate.

Many COVID-19 vaccines have received WHO EUL authorization for use in pregnancy; however, product profiles may differ. For more information, refer to product labels or product specific documents at COVID-19 vaccines technical documents: Product specific documentation. In countries where COVID-19 vaccines have been used in pregnancy, post-marketing evidence and observational studies have supported safety and demonstrated effectiveness. Health workers include all people engaged in work whose primary intent is to improve health. The reasons for prioritizing health workers for vaccination early on in the COVID-19 pandemic were, first, that protecting these workers protected the availability of critical essential services; second, evidence suggested that health workers were initially at higher risk of acquiring infection than the general population; and third, there was also a risk of onward transmission to patients who were at higher risk of serious COVID-19 outcomes through their contact with these workers. This prioritization was also supported by the principle of reciprocity: health workers play critical roles in the COVID-19 response, putting not only themselves but potentially also their household members at greater risk for the sake of others (36, 37).

Worldwide vaccine coverage for health workers has increased substantially. Vaccination of health workers, particularly of frontline health workers with direct patient contact and those working in long-term care facilities should be prioritized. As with the general population, COVID-19 fatality rates among health workers increase with age. All health workers who are older, have comorbidities, or moderate to severe immunocompromising conditions, remain in the high-priority use categroy, on the basis of these characteristics.

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3 Some studies on COVID and pregnancy refer to “pregnant women”, and others to “pregnant people”. While most people who are, or can become, pregnant are cisgender women or adolescent girls who were born and identify as female, this guidance is also intended for transgender men and other gender diverse people who can become pregnant. All uses of the terms “pregnant women” and “mothers” in this document are intended to be inclusive of all those who are pregnant or give birth.

4 Health workers are all people engaged in work actions whose primary intent is to improve health. This includes health service providers, such as doctors, nurses, midwives, public health professionals, laboratory-, health-, and medical and non-medical technicians, personal care workers, community health workers, healers and some practitioners of traditional medicine. It also includes health management and support workers, such as cleaners, drivers, hospital administrators, district health managers and social workers, and other occupational groups in health-related activities. Health workers include not only those who work in acute care facilities but also those employed in long-term care, public health, community-based care, social care and home care and other occupations in the health and social work sectors as defined by the International Standard Industrial Classification of All Economic Activities (ISIC), revision 4, section Q: Human health and social work activities.
Given that currently available COVID-19 vaccines confer only limited and short-lived reduction in symptomatic illness and have modest impact on reducing transmission, other infection control measures to reduce transmission and protect vulnerable patients must be in place, such as face masks, hand-washing and other protective measures (38).

**Medium priority-use groups**

Broader access to COVID-19 vaccines beyond the high priority-use groups is intended to optimize protection in the general population, recognizing that severe COVID-19 cases also occur in medium priority-use groups, albeit at much lower frequency compared to the high priority-use group. COVID-19 vaccination may also protect against post-COVID-19 conditions, although the evidence on the extent of such protection remains limited. Modelling evidence suggests that offering booster doses more broadly to medium priority-use groups is less efficient than offering booster doses to the high priority-use groups. This is especially the case for countries with low coverage and high prior transmission (39). Vaccine effectiveness against infections and mild illness wanes rapidly within a few months, thus requiring very frequent boosting which is programmatically not feasible and not acceptable by communities.

**Healthy younger adults:** Healthy younger adults (aged 18 to 59, or age 18 to 49, depending on countries’ age cut-offs) who do not fall into the high priority-use groups benefit from a primary vaccine series to prevent severe disease, although severe disease in this group is far less frequent compared to older adults. Additional objectives include reducing the risk of post-COVID-19 conditions including cardiovascular events (40, 41). However, vaccine effectiveness in preventing post-COVID-19 conditions is only modest (7, 10-13). Younger and healthy adults who have not yet been vaccinated should be offered primary vaccine series. *Booster doses are not routinely recommended at this time.*

**Children and adolescents with severe obesity or comorbidities that put them at higher risk of severe COVID-19:** Severe obesity and certain comorbidities and neurodevelopmental disorders in children and adolescents increase the risk of severe COVID-19 disease (42, 43). Countries should decide on the BMI cut-off for severe obesity. Children and adolescents with severe obesity or comorbidities are included in the medium priority-use group and should be offered primary vaccine series. *Booster doses are not routinely recommended at this time.* It should be noted that not all COVID-19 vaccines have regulatory approval or EUL for use on the very young age groups. The product label should be checked, or COVID-19 vaccines technical documents: Product specific documentation referred to for information.

**Low priority-use groups**

**Healthy children and adolescents aged 6 months to 17 years:**

More than three years into the pandemic at a time of high infection-induced immunity and hybrid immunity, COVID-19 is rarely lethal in healthy children and adolescents. Deaths in children and adolescents due to COVID-19 are now mainly seen in those with comorbidities. Individuals with comorbidities should be offered a primary vaccine series/initial doses (see medium priority-use group); those with moderate to severe immunocompromising conditions should be offered initial series and booster doses (see high priority-use group). Multisystem inflammatory syndrome in children (MIS-C) is a rare condition associated with SAR-CoV-2 infection. In healthy children and adolescents, both MIS-C and post-COVID-19 conditions (44) have decreased in the Omicron era (20, 45).

Several COVID-19 vaccines have been separately licensed for use in children 6 months to 4 years, 5 (or 6) to 11 years and 12 to 17 years based on safety and effectiveness in clinical trials. In countries where COVID-19 vaccines have been used in those aged <18 years, post-marketing experience in all age groups has supported safety and demonstrated effectiveness in preventing infection and MIS-C. While COVID-19 vaccines have been proven to reduce the risk of hospitalization and death in all age groups, currently available COVID-19 vaccines have limited impact on reducing transmission. Therefore, direct vaccine protection of individuals against severe disease in the higher priority-use groups is essential rather than aiming for indirect protection by vaccinating healthy children and adolescents. Vaccine

*“Not routinely recommended” means that such vaccines are not recommended for inclusion in routine programmes because of minimal public health impact and low cost-effectiveness in most settings. However, vaccination may be offered in individual circumstances where added benefit is expected to be more substantial as there are no known additional safety issues associated with additional boosters. This recommendation acknowledges that some countries may elect to offer such doses in the routine programme based on population risks, disease epidemiology, or health priorities.*
effectiveness against infections and illness wanes rapidly within a few months, thus requiring very frequent boosting which is programmatically not feasible and not acceptable by communities. Moreover, a rationale of several countries in the earlier phases of the pandemic to vaccinate children was to avoid school closures. At the present time schools are open around the world.

While there is variability in the relative contribution of COVID-19 mortality compared to other illnesses, in most countries COVID-19 now ranks low in the relative causes of mortality among healthy children and adolescents. Hence, for most countries, vaccinating healthy children is unlikely to be cost–effective in terms of metrics such as the number needed to vaccinate (NNV) to prevent hospitalization or death \((15, 16, 46)\). NNV to prevent severe outcomes is higher compared with other established childhood/adolescent vaccines and manyfold higher compared with vaccinating the high priority groups. A higher NNV equates to lower cost effectiveness.

It is also important to take into consideration that there has been some significant programmatic impact of country COVID-19 immunization campaign efforts on the essential immunization programme which has suffered a historic backsliding from which it is trying to recover. Vaccine policy decisions in all countries involve assessing the human, financial, and programmatic resource tradeoffs relative to other vaccines, as well as community views and opportunity costs of a vaccine recommendation. For example, a recent analysis conducted in the United Kingdom of Great Britain and Northern Ireland found that \(11\,000–76\,000\) older children and adolescents would need to be vaccinated to prevent 1 case of hospitalization due to Omicron infection. In contrast, in the same setting, approximately \(500–1000\) persons over the age of 60 years needed to be vaccinated to prevent 1 hospitalization. In comparison, another study in the United States of America in the same age group reported that approximately \(8000\) older children and adolescents would need to be vaccinated to prevent 1 hospitalization due to influenza \((47)\). WHO recognizes that there is limited information, most often from high income countries.

Conversely in some countries, COVID-19 ranks relatively high as a cause of mortality in children and adolescents – particularly for those in socially vulnerable groups \((34)\). Such countries contemplating vaccinating healthy children should consider benefit–risk, affordability, epidemiological situation, programmatic trade-offs, opportunity costs/cost–effectiveness, seroprevalence rates, equity, and community acceptance for childhood vaccination programmes.

One theoretical rationale in favour of vaccinating children is to prime their T-cell memory, thus preparing them for any new variants of concern that may arise in the future. However, while this hypothesis should be evaluated and must inform innovative research questions, current evidence is insufficient to inform policy at this point. Based on these considerations, introduction of childhood COVID-19 programs is of substantially lower priority compared to the higher priority-use groups and compared with other childhood and adolescent vaccinations. Countries considering vaccination of healthy children and adolescents with COVID-19 vaccines need to take into account that recommendations may vary by age of child as benefit-risk balance is likely different among young children compared to adolescents. Age cut-off will need to be decided by countries. On balance, vaccination of children and adolescents is not routinely recommended. Not all COVID-19 vaccines have regulatory approval or EUL for use in the very young age groups. The product label should be checked, or COVID-19 vaccines technical documents: Product specific documentation referred to for information.

Young infants below the age of 6 months will likely not have had a SARS-CoV2 infection and are therefore immune-naïve, apart from maternally derived antibodies. They can be protected through maternal immunization (see high priority-use groups).
### HIGH priority–use groups

<table>
<thead>
<tr>
<th>Target population</th>
<th>Vaccination of persons who have never received a COVID-19 vaccine</th>
<th>Revaccination of persons who have received at least one dose of COVID-19 vaccine</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oldest adults(^1)</td>
<td>Single Dose(^a)</td>
<td>6–12 months after previous dose</td>
</tr>
<tr>
<td>Older adults with multiple comorbidities that put them at higher risk of severe COVID-19</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Other adults(^2) with severe obesity or a comorbidity that puts them at higher risk of severe COVID-19</td>
<td>Single Dose(^a)</td>
<td>Approximately 12 months after previous dose</td>
</tr>
</tbody>
</table>

### MEDIUM priority–use groups

<table>
<thead>
<tr>
<th>Target population</th>
<th>Vaccination of persons who have never received a COVID-19 vaccine</th>
<th>Revaccination of persons who have received at least one dose of COVID-19 vaccine</th>
</tr>
</thead>
<tbody>
<tr>
<td>Healthy adults(^3)</td>
<td>Single Dose(^a)</td>
<td>Not routinely recommended(^d)</td>
</tr>
<tr>
<td>Children and adolescents aged 6 months to 17 years with severe obesity or a comorbidity that puts them at higher risk of severe COVID-19</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### LOW priority–use groups

<table>
<thead>
<tr>
<th>Target population</th>
<th>Vaccination of persons who have never received a COVID-19 vaccine</th>
<th>Revaccination of persons who have received at least one dose of COVID-19 vaccine</th>
</tr>
</thead>
<tbody>
<tr>
<td>Healthy children and adolescents aged 6 months to 17 years</td>
<td>If countries opt to vaccinate low priority–use groups(^4), they could consider single dose for ages 5 years and above, two doses for age 6 months to 4 years(^4)</td>
<td>Not routinely recommended(^d)</td>
</tr>
</tbody>
</table>

### Sub-populations with special considerations

<table>
<thead>
<tr>
<th>Target population</th>
<th>Vaccination of persons who have never received a COVID-19 vaccine</th>
<th>Revaccination of persons who have received at least one dose of COVID-19 vaccine</th>
</tr>
</thead>
<tbody>
<tr>
<td>Persons with moderate and severe immunocompromising conditions (adults, adolescents and children &gt; 6 months)</td>
<td>Two or three doses in consultation with the health care provider</td>
<td>6–12 months after previous dose; optimal time interval should be determined in consultation with the health care provider</td>
</tr>
<tr>
<td>Pregnant adults and pregnant adolescents(^5)</td>
<td>Single dose in each pregnancy regardless of previous vaccination status; ideally during the second trimester or at any opportunity</td>
<td></td>
</tr>
<tr>
<td>Health and care workers with direct patient contact</td>
<td>Single dose</td>
<td>Approximately 12 months after previous dose</td>
</tr>
</tbody>
</table>

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\(^{1}\) Age cut-off to be decided by countries; often it is 75 or 80 years. \(^{2}\) Age cut-off to be decided by countries; often it is 50 or 60 years. \(^{3}\) In vaccine-naive persons, for programmatic purposes, a single dose can be considered for primary vaccination given that the vast majority of the population will have been infected at least once. For vaccinated COVID-19 vaccines, two doses are required for the primary vaccine series. \(^{4}\) Age cut-off to be decided by countries; often it is 18 to 49 or 18 to 56 years. \(^{5}\) Regulatory approvals or WHO EU, for the age indication differ by vaccine product; refer to the product-specific vaccine recommendations. \(^{d}\) “Not routinely recommended” means that such vaccines are not recommended because of minimal public health impact and low cost-effectiveness in most settings. However, vaccination may be offered in individual country-specific circumstances where added benefit is expected to be more substantial. This interim recommendation acknowledges that some countries may elect to offer such doses in the routine programme based on population risks, disease epidemiology, or public health priorities. \(^{6}\) Interim of vaccinating healthy children and adolescents is substantially lower compared to vaccinating older persons or as compared to other childhood vaccinations. Countries could consider vaccination based on disease burden, cost effectiveness, and other programmatic priorities. \(^{6}\) Regulatory approvals or WHO EU, for the use in pregnancy may differ by vaccine product.
HETEROLOGOUS SCHEDULES

There is increasing evidence that vaccine schedules using different COVID-19 vaccine platforms (mix and match) may provide superior immunogenicity to use of a homologous schedules (48).

For countries considering heterologous schedules, WHO recommends the following on the basis of equivalent or favourable immunogenicity or effectiveness for heterologous versus homologous schedules, depending on product availability:

- countries implementing WHO EUL inactivated vaccines for initial doses may consider using WHO EUL vectored or mRNA vaccines for subsequent doses;
- countries implementing WHO EUL vectored vaccines for initial doses may consider using WHO EUL mRNA vaccines or protein subunit vaccines for subsequent doses;
- countries implementing WHO EUL mRNA vaccines for initial doses may consider using WHO EUL vectored vaccines or protein subunit vaccines for subsequent doses.

When deciding to implement booster doses, each country needs to take into account the age structure of the population; the current and potential burden of severe COVID-19 disease and hospitalizations; the availability and access to vaccines including variant-containing vaccines; as well as opportunity costs, coverage rates with the initial doses, and community acceptance of boosters.

CO-ADMINISTRATION WITH OTHER VACCINES

WHO recommends that countries consider co-administration of COVID-19 vaccines (including variant-containing vaccines) with seasonal influenza vaccines or other respiratory vaccines, whenever epidemiologically justified. Based on several co-administration studies of COVID-19 vaccines and inferred from co-administration studies of other adult vaccines, COVID-19 vaccines may be given concomitantly, or at any time before or after other vaccines for adults and adolescents, including live attenuated, inactivated, adjuvanted, or non-adjuvanted vaccines (49). The same applies to maternal immunization for vaccines recommended during pregnancy.

When administered concomitantly, the vaccines should be injected in separate sites, preferably different extremities. Continued pharmacovigilance monitoring is recommended. WHO aims for a life-course approach for the implementation of all vaccines including COVID-19 vaccines. Such a programmatic approach will help to achieve a higher uptake of vaccines, increase the efficiency of vaccine roll-out and protect stretched health-care systems.

CONSIDERATIONS IN RELATION TO LONGER-TERM PLANNING

Higher levels of population immunity globally due to both infection and vaccination may limit the impact of SARS-CoV-2 on morbidity and mortality in the longer-term, but there is little doubt that this virus will remain an established pathogen in humans and animals for the foreseeable future. While eliminating the virus from human and animal reservoirs is highly unlikely, mitigation of its devastating impact on morbidity and mortality is achievable and should continue to be a prioritized goal.

In the near-term, booster doses are needed within 12 months after the last dose for the high priority-use groups. As part of near-term preparedness planning, countries should consider demand forecasting for booster doses for high priority-use groups for the years 2024 and 2025. Countries should take into account cost–effectiveness, programmatic feasibility, vaccine acceptance and the evolving epidemiological situation when deliberating about timing and frequency of booster doses. Mechanisms for monitoring vaccine uptake that were developed during the earlier stages of the COVID-19
pandemic need to be maintained for the near-term. Furthermore, real-world studies on waning of vaccine effectiveness over time and in relation to new variants need to be maintained.

Longer-term considerations include the significant uncertainties related to the evolution of the virus, the characteristics of future variants, and the trajectory and seasonality of the epidemic given increasing global vaccine- and infection-induced immunity. As of September 2023, the need and timing for further booster doses in the longer-term is unknown, and it remains uncertain whether COVID-19 vaccination needs to be included into routine programmes, such as for seasonal influenza vaccination in the longer-term.

Further adaptations to the composition of COVID-19 vaccines may be needed in order to address future circulating variants; WHO will advise on these (50). Novel approaches to COVID-19 vaccine development, pan-SARS-CoV-2 or pan-sarbecovirus vaccines are urgently needed, as are vaccines with greater impact on virus transmission (i.e. vaccine platforms that elicit strong mucosal immunity).
## ANNEX SUMMARY OF MAJOR UPDATES

### UPDATE OCTOBER 2023

<table>
<thead>
<tr>
<th>Section</th>
<th>Rationale for update</th>
</tr>
</thead>
<tbody>
<tr>
<td>New Recommendations</td>
<td>• Longer interval for booster doses for high priority-use groups;</td>
</tr>
<tr>
<td></td>
<td>• Monovalent XBB vaccines</td>
</tr>
<tr>
<td></td>
<td>• Simplified schedules for vaccine-naive persons</td>
</tr>
</tbody>
</table>

### UPDATE 30 MARCH 2023

<table>
<thead>
<tr>
<th>Section</th>
<th>Rationale for update</th>
</tr>
</thead>
<tbody>
<tr>
<td>Preamble/Introduction</td>
<td>This revised 2023 Roadmap takes into account sufficient vaccine availability, high</td>
</tr>
<tr>
<td></td>
<td>population immunity due to vaccine coverage rates and/or infection-induced immunity,</td>
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<td></td>
<td>and a decoupling of the incidence of deaths compared to the incidence of disease.</td>
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<tr>
<td></td>
<td>It also considers economic considerations and community acceptance.</td>
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<tr>
<td>Public health goals scenarios</td>
<td>Public health goals are now explained in more detail, also taking into account post-</td>
</tr>
<tr>
<td></td>
<td>COVID-19 conditions.</td>
</tr>
<tr>
<td>Priority-use groups</td>
<td>The number of priority-use groups has been reduced to three: “high”, “medium” and</td>
</tr>
<tr>
<td></td>
<td>“low”. Priority-use groups differ by public health impact of vaccination, and need for</td>
</tr>
<tr>
<td></td>
<td>primary series and booster doses.</td>
</tr>
<tr>
<td>Prioritization Table</td>
<td>A new Prioritization Table was created.</td>
</tr>
<tr>
<td>New Recommendations</td>
<td>• Longer interval for additional boosters (i.e. beyond the first booster) for high</td>
</tr>
<tr>
<td></td>
<td>priority-use groups;</td>
</tr>
<tr>
<td></td>
<td>• Medium risk group are no longer routinely recommended for additional boosters</td>
</tr>
<tr>
<td></td>
<td>beyond the first booster;</td>
</tr>
<tr>
<td></td>
<td>• Booster dose during pregnancy if last dose was given more than 6 months ago;</td>
</tr>
<tr>
<td></td>
<td>ideally to be given by the end of the second trimester;</td>
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<tr>
<td></td>
<td>• Additional booster dose for frontline health workers 12 months after the last</td>
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<tr>
<td></td>
<td>dose;</td>
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<tr>
<td></td>
<td>• Primary series in healthy children and adolescents should only be considered in</td>
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<tr>
<td></td>
<td>limited settings based on country context such as disease burden in this age group,</td>
</tr>
<tr>
<td></td>
<td>cost effectiveness, and opportunity costs</td>
</tr>
<tr>
<td>Variant-adapted vaccines</td>
<td>Variant-adapted vaccines have been authorized, and new evidence has emerged on the</td>
</tr>
<tr>
<td></td>
<td>immunogenicity and vaccine effectiveness of such vaccines.</td>
</tr>
</tbody>
</table>
### UPDATE 19 JANUARY 2022

<table>
<thead>
<tr>
<th>Section</th>
<th>Rationale for update</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Title</strong></td>
<td>Shortening of title from: “WHO SAGE roadmap for prioritizing uses of COVID-19 vaccines in the context of limited supply” to: “WHO SAGE roadmap for prioritizing use of COVID-19 vaccines”. Change of subtitle from: “An approach to inform planning and subsequent recommendations based upon epidemiologic setting and vaccine supply scenarios” to: “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”. These changes were made to reflect the increasing vaccine supply globally.</td>
</tr>
<tr>
<td><strong>Preamble/Introduction</strong></td>
<td>This revised 2022 Roadmap took into account increasing vaccine availability and vaccine coverage rates. Scenarios in which vaccination coverage exceeded 50% of the population were considered. Additional topics were considered, such as vaccine use in children and adolescents and the administration of booster doses.</td>
</tr>
<tr>
<td><strong>Definitions</strong></td>
<td>Definitions to guide the user were added (e.g. additional doses, booster doses).</td>
</tr>
<tr>
<td><strong>Epidemiological setting scenarios, including:</strong></td>
<td>The scenarios were revisited in light of the current epidemiology, transmission patterns, variants of concern and their impact on vaccine performance, as well as the increasing population-level immunity from infection.</td>
</tr>
<tr>
<td>variants of concern and</td>
<td></td>
</tr>
<tr>
<td>infection-induced immunity</td>
<td></td>
</tr>
<tr>
<td><strong>Public health goals scenarios</strong></td>
<td>The <em>Strategy to achieve global Covid-19 vaccination by mid-2022</em> was added and referred to.</td>
</tr>
<tr>
<td><strong>Optimized use of COVID-19 vaccines</strong></td>
<td>A major overhaul of this section was conducted. The priority-use groups for COVID-19 vaccination were revisited and reflected in Table 1. Further information on priority-use groups was added in the respective sections on page 9 and in Annex 2. Primary as well as booster dose schedules were considered.</td>
</tr>
<tr>
<td><strong>Heterologous primary vaccination series and</strong></td>
<td>The section was added and current WHO guidance was referenced.</td>
</tr>
<tr>
<td>booster doses</td>
<td></td>
</tr>
</tbody>
</table>

### UPDATE 16 JULY 2021

<table>
<thead>
<tr>
<th>Section</th>
<th>Rationale for update</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Rationale</strong></td>
<td>The new 2021 version stated that while vaccines were now licensed and available, the supply remained limited and unreliable in many settings. It further stated that, while all currently recommended COVID-19 vaccines have similar broad indications for use, countries may decide to consider specific product attributes when prioritizing populations. The updated Prioritization Roadmap did not propose coverage targets for countries. The 2020 version of the Prioritization Roadmap worked with an initial target of 20% population coverage, based on the expected supply of vaccines. The updated Prioritization Roadmap provided guidance up to a level of 50% population coverage.</td>
</tr>
</tbody>
</table>
WHO roadmap on uses of COVID-19 vaccines in the context of Omicron and high population immunity

<table>
<thead>
<tr>
<th>Process of Prioritization Roadmap development</th>
<th>The update reflected the methods and processes used to develop this version of the Prioritization Roadmap.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Key assumptions</td>
<td>A key assumption in 2020 was that COVID-19 vaccines would probably have an impact on transmission. There was now some evidence that supported this statement.</td>
</tr>
<tr>
<td>Key assumptions</td>
<td>Post-COVID-19 condition was noted, but as evidence was still emerging, the impact of vaccines on long-term sequelae from SARS-CoV-2 infection were not included.</td>
</tr>
<tr>
<td>Pregnant women, breastfeeding women and children</td>
<td>Substantive changes were made to these sections to reflect the recent evidence.</td>
</tr>
<tr>
<td>Epidemiological settings</td>
<td>The need to keep a vaccine reserve was removed. Pregnant women were moved to Stage II. Seafarers and air crews were added to Stage II. Settings and geographical locations of high transmission were removed.</td>
</tr>
</tbody>
</table>

**FUNDING SOURCE**

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**ACKNOWLEDGEMENTS**

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External: Current members of the Strategic Advisory Group of Experts (SAGE) on Immunization and the SAGE Working Group on COVID-19 Vaccines.

The drafting of the original Roadmap was led by Ruth Faden, David C. Kaslow, Sonali Kochhar, Saad B. Omer and Sarah Pallas, with input from the members of the Public Health Objectives Subgroup (Muhammed Afolabi, Celia Alpuche-Aranda, Hyam Bashour, David Durrheim, Peter Figueroa, Folake Olayinka, Helen Rees, Peter G. Smith and Yin Zundong), and support from Matthew Crane from the Johns Hopkins University School of Medicine. Hanna Nohynek led the SAGE Working Group on COVID-19 Vaccines at time of publication of the initial Roadmap.

The updates of the Prioritization Roadmaps were led by all members of the SAGE Working Group on COVID-19 vaccines.

WHO secretariat for immunization: Annelies Wilder-Smith, Joachim Hombach, Melanie Marti, Katherine O’Brien.
REFERENCES


WHO roadmap on uses of COVID-19 vaccines in the context of Omicron and high population immunity


WHO continues to monitor the situation closely for any changes that may affect this interim guidance. Should any factors change, WHO will issue a further update. Otherwise, this interim guidance document will expire 2 years after the date of publication.

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