# WHO SAGE roadmap on uses of COVID-19 vaccines in the context of OMICRON and substantial 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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World Health Organization

## PREAMBLE

This interim guidance constitutes a major revision of the *WHO SAGE roadmap for prioritizing uses of COVID-19 vaccines*, first issued in October 2020, and updated in November 2020, July 2021 and January 2022. 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 meeting of the Strategic Advisory Group of Experts (SAGE) on Immunization on 21 March 2023 *(1)*.

This revised Roadmap also replaces the *Good Practice Statement on COVID-19 boosters* published in August 2022.[2] It takes into account sufficient availability of COVID-19 vaccines, and high population-level seroprevalence, currently estimated at above 90% in most countries due to increasing vaccine coverage rates and infection-induced immunity *(2)*. It further addresses evolving public health needs as the Omicron variant and its sublineages continue to circulate and provides updates for COVID-19 vaccination in relation to:

- new priority-use groupings;
- specific recommendations for primary series and boosters according to priority-use groups;
- need and frequency for boosters beyond the first booster dose;
- variant-containing vaccines;
- vaccination during pregnancy; and
- post-COVID-19 conditions[3]

The Roadmap will be further adapted should new variants of concern emerge that do not have characteristics of Omicron, in the event of significant changes in COVID-19 disease epidemiology, or changes in vaccine attributes that are relevant to the Roadmap.

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.

[2] See: https://www.who.int/publications/i/item/WHO-2019-nCoV-vaccines-SAGE-good-practice-statement-second-booster.

[3] Post COVID-19 condition occurs in individuals with a history of probable or confirmed SARS-CoV-2 infection, usually 3 months from the onset of COVID-19 with symptoms and that last for at least 2 months and cannot be explained by an alternative diagnosis. Common symptoms include fatigue, shortness of breath, cognitive dysfunction but also others and generally have an impact on everyday functioning. Symptoms may be new onset following initial recovery from an acute COVID-19 episode or persist from the initial illness. Symptoms may also fluctuate or relapse over time. A separate definition may be applicable for children.

## EXECUTIVE SUMMARY

The COVID-19 situation in early 2023, more than three 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). Most countries have lifted most or all public health and social measures, and while the SARS-CoV-2 virus continues to circulate, the third year of the COVID-19 pandemic has been marked by significant reduction in rates of hospitalization, admission to ICU and deaths across all age groups. This is due to a number of factors including increasing population level immunity from infection and/or vaccination, and earlier testing and access to COVID-19 therapeutics. 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; thus, even a minor decrease in vaccine effectiveness with time in vulnerable subgroups translates into a rise in cases of severe disease and death.

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 periodic booster doses of the vaccine to protect the high priority groups. Consideration has been given to high population immunity, ample vaccine supply, declining risk of mortality and severe disease, global dominance of Omicron and its subvariants, differential vaccine performance against infection and severe disease outcomes, and post COVID-19 conditions.

Based on an extensive evidence review including systematic reviews and meta-analyses, the Roadmap provides updates on new priority-use groupings (reducing from four to three strata); specific recommendations for primary series and boosters according to priority-use groups; variant-containing vaccines; heterologous schedules; and vaccination during pregnancy. Specifically, this Roadmap suggests:

- Longer interval for additional boosters (i.e. beyond the first booster) for high priority-use groups;
- Medium risk groups are no longer routinely recommended for additional boosters beyond the first booster;
- Additional booster dose during pregnancy if last dose was given more than 6 months ago; ideally to be given by mid-second trimester;
- Additional booster dose for frontline health workers 12 months after the last dose;
- Primary series in healthy children and adolescents could be considered, based on country context such as disease burden in this age group, cost effectiveness, other health or programmatic priorities and opportunity costs;

The table below outlines WHO's updated interim recommendations for the optimal use of COVID-19 vaccination for primary series and booster doses at the present time of dominant Omicron circulation and high population-level immunity. The recommendations in this Roadmap will be updated should the epidemiology or vaccine characteristics change.

## WHO Interim Recommendations[a] for the optimal use of COVID-19 vaccination: primary series and booster doses in the context of Omicron and high population-level immunity

### HIGH priority-use groups

| Target population | Primary series and booster[b] | Additional booster doses | Remarks |
|---|---|---|---|
| **Groups with the highest risk of death from COVID-19** | | | |
| Older adults[c]<br>Younger adults with significant comorbidities or severe obesity | Recommended | Recommended *(12 months after previous dose)* | Most efficient use of COVID-19 vaccines with greatest impact on reducing deaths. |
| Subgroup of older adults:<br>Oldest adults[d]<br>Older adults with multiple significant comorbidities | Recommended | Recommended *(6 months after previous dose)* | |
| **Groups with special considerations for vaccination** | | | |
| Adults, adolescents and children 6 months and older with moderate to severe immunocompromising conditions | Recommended as extended primary series[e] | Recommended *(Approximately 6 months after previous dose; optimal time interval should be discussed with the treating physician)* | Vaccine effectiveness is lower for persons with immunocompromising conditions. For additional protection, personal protective measures, vaccinating close contacts, and early treatment in case of a SARS-CoV-2 infection is recommended. |
| Pregnant adults and adolescents[f] | Recommended | Recommended once during a pregnancy *(If previous dose was >6 months ago)* | Rationale for immunization during pregnancy is three-fold: to protect the pregnant person, the foetus, and the infant up to age 6 months. |
| Frontline health workers | Recommended | Recommended *(12 months after previous dose)* | Rationale is to maintain health care system resilience. |

### MEDIUM priority-use groups

| Target population | Primary series and booster[b] | Additional booster doses | Remarks |
|---|---|---|---|
| Healthy younger adults[g]<br>Children and adolescents aged 6 months to 17 years with severe obesity or comorbidities that put them at higher risk of severe COVID[i] | Recommended | Not routinely recommended.[h] | Benefit of additional boosters is marginal. |

### LOW priority-use groups

| Target population | Primary series and booster[b] | Additional booster doses | Remarks |
|---|---|---|---|
| Healthy children and adolescents aged 6 months to 17 years[i] | Countries could consider based on disease burden, cost effectiveness, and other health or programmatic priorities and opportunity costs. | Not routinely recommended.[h] | Benefit and cost-effectiveness of vaccinating healthy children and adolescents is substantially lower compared to high and medium priority-use groups and compared to most other vaccine preventable diseases in childhood. |

**a.** These recommendations are time-limited and apply only to the current situation and may need to be revisited when new variants of concern emerge or the epidemiology changes. WHO currently does not recommend regular annual boosters on a long-term basis until more evidence becomes available. **b.** First booster is recommended 6-12 months after the completion of the primary series. **c.** Age cut-off to be decided by countries: often it is 50 or 60 years. **d.** Age cut-off to be decided by countries; often it is 75 or 80 years. **e.** Extended primary series means one additional dose to the two-dose series, given about 3-6 months after the second dose. **f.** Regulatory approvals or WHO EUL for the use in pregnancy may differ by vaccine product. **g.** Age cut-off to be decided by countries: often it is 18 to 49 or 18 to 59 years. **h.** "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. **i.** Regulatory approvals or WHO EUL for the age indication differ by vaccine product; refer to the Product-specific vaccine recommendations.

## INTRODUCTION

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 (3)*, 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* (3), 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 at the present time:** The Omicron variant and its more than 600 sublineages 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. With increasing vaccine coverage and infection-induced immunity, population immunity has increased and most countries have relaxed or abandoned their public health and social measures against COVID-19. The consequent rises in community infection/re-infection rates have led to increased rates of severe disease and death, but of a comparatively lower magnitude than those of infection rates because of the broad population immunity, especially in countries with high vaccine coverage in older populations. This Roadmap addresses the epidemiological transition and evolution of COVID-19 from an emergency phase to an endemic situation. Whilst there remains a significant risk of further variants of concern emerging, Omicron sublineages have remained dominant for more than one year in the context of the currently available vaccines. Consideration has been given to recognize that countries vary in their COVID-19 vaccine policy development as the pandemic has evolved. For countries as yet without policies addressed in this roadmap, the recommendations are broadly applicable. For countries with existing policies concerning the topics considered in this update, future policy review in light of the recommendations is advised, considering the evolving virus, vaccine effectiveness, and programmatic priorities. This Roadmap will be updated as needed, should new variants emerge that are associated with more severe disease or that present more immune evasion from currently available COVID-19 vaccines, or if the characteristics of available vaccines change substantially.

**(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 (4)*. 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 additional and booster doses, variant-containing vaccines) becomes available, and as epidemiological and other contextual conditions evolve.

## THE ERA OF OMICRON AND HIGH POPULATION-LEVEL IMMUNITY

The variant of concern, Omicron, emerged in November 2021. Omicron and its sub-lineages (including BA.1, BA.2, BA.4, BA.5, XBB, BQ.1 etc.) are now the dominant circulating variants worldwide. Omicron and its sub-lineages are associated with less severe disease, on average, compared to pre-Omicron variants such as Delta in the context of increased seroprevalence *(5-7)*, and have a lower risk of post-COVID-19 conditions following infection *(8)*. 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. Given the high transmissibility of Omicron, incidence of Omicron infections was extremely high during most of 2022; however, a decoupling of incidence of infection from incidences of hospitalization and death due to COVID-19 was consistently observed around the world. Countries that achieved high levels of vaccine uptake in priority-use groups and of infection-induced immunity and hybrid immunity have seen large reductions in rates of COVID-19-related hospitalizations and death, even with relaxation or abandonment of most or all public health and social measures. It is important to note that when community transmission is high, it can be difficult to distinguish hospital admissions that are specifically due to SARS-CoV-2, from admissions in which SARS-CoV-2 is detected incidentally, particularly in health-care systems that routinely conduct COVID-19 screening at the time of hospital admission. Towards the beginning of 2023, countries are still experiencing repeated waves of infection, but 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 period before booster vaccinations are needed compared to individuals who have never been infected *(9, 10)*.

With regards to programming, pre-vaccination screening for past infections would be impractical, costly, and would most likely impede vaccine access and uptake. This Roadmap assumes that, globally, at the present time, there is a high proportion of the population with hybrid immunity or immunity from either vaccination or infection, and therefore, for most populations, a longer interval between the last vaccine dose and boosters is appropriate. 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.

This Roadmap focuses on optimizing the use of currently available COVID-19 vaccines in the context of Omicron and its sub-lineages at a time of high population immunity and an uncertain virus trajectory. Should new variants arise with substantially different characteristics than Omicron, revisions to the Roadmap may be needed.

## PUBLIC HEALTH GOALS SCENARIOS

The *Strategy to achieve global Covid-19 vaccination by mid-2022 (11)* 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.

Current COVID-19 vaccines have some impact on reducing post-COVID-19 conditions *(12-16)*, but evidence on the extent of the impact is currently inconsistent in the scientific literature. Nonetheless, reducing post-COVID-19 conditions is a possible argument to continue offering primary series vaccination.

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 which are at highest risk of severe disease, hospitalizations and death with both primary series and booster doses will have the greatest public health impact.

Throughout 2021 and part of 2022, vaccine supply was severely constrained (particularly in low- and middle-income countries). The health, social, and economic justification for mass vaccination was to protect people from severe disease while population immunity was increasing and reduced the need for the most stringent public health and social measures. In 2023, vaccines are no longer supply-constrained and the economic benefit of vaccination, while still substantial, is not as large since countries have been able to curtail most public health and social measures. For this reason, 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 increasingly reported globally; yet the underlying aetiology, prevalence, and risk factors are still not clearly understood *(16, 17)*. Vaccines against SARS-CoV-2 are effective against COVID-19 and its progression to severe disease, and may also prevent secondary complications *(18)*. Vaccination both before and after having COVID-19 infection decreased post–COVID-19 conditions for the circulating variants although vaccine effectiveness was low.

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-CoV-2 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 *(19-21)*.

## PANDEMIC SCENARIOS

WHO considers three pandemic scenarios *(22)*: (1) Base-case scenario: The virus continues to evolve but does not become more virulent. Severity remains relatively low over time due to sustained and sufficient immunity against severe disease and death, with further decoupling of incidence of cases and severe disease leading to progressively less severe outbreaks. 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: a seasonal pattern of peaks in transmission in temperate zones may emerge. (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. Vaccine policies will need to be adapted to such future scenarios.

The recommendations in this document are based on the "base-case" scenario. Surveillance of COVID-19 needs to be optimized to rapidly determine any change in scenario, and this Roadmap will be adapted accordingly.

## 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: *https://view-hub.org/vaccine/covid*), 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 (up until March 2023) was obtained from the WHO Serotracker (see: *www.serotracker.com*).

A comprehensive summary of all the evidence on which this document is based is available in the presentation to SAGE, accessible on the SAGE March 2023 meeting website (see: *www.who.int/news-room/events/detail/2023/03/20/default-calendar/sage_meeting_march_2023*).

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*).

## PRIORITY-USE GROUPS

The principles outlined in the previous Prioritization Roadmap were developed to address the optimal use of limited available vaccine supplies, reduce inequities and protect health-care systems *(23)*. This Roadmap simplifies the four priority-use groups (highest, high, medium and lowest) that were specified in previous Roadmaps, to three priority-use groups (high, medium and low) in the current context of sufficient vaccine supply, and an epidemiology in many countries that is increasingly settling into periodic waves of relatively high incidence of infections, but overall decreasing deaths and hospitalizations.

Given the characteristics of currently available COVID-19 vaccines, the rationale for primary series vaccination, and need for and frequency of booster doses, is based largely on risk of severe disease, hospitalization, and death, while taking into account cost–effectiveness, programmatic considerations and community acceptance. The three priority-use groups are described below and presented in the Table.

**High priority-use groups**

High priority-use groups are groups for whom COVID-19 vaccines are of greatest importance to reduce death and severe disease.

**Older adults:** 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. The recommendation for "older adults" is for primary series and booster vaccination, with ***additional boosters 12 months after the last dose.***

**Older adults with multiple significant comorbidities:** Older adults who have multiple significant comorbidities are at greater risk for severe disease and death than adults in the same age range who do not have these conditions. The recommendation for older adults with multiple significant comorbidities or severe obesity (BMI >40) is for primary series and booster vaccination, ***with additional boosters 6 months after the last dose.***

**Oldest adults:** Those in the extreme old age range 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. The recommendation for "oldest adults" is for primary series and booster vaccination, with ***additional boosters 6 months after the last dose.***

**Younger adults with significant comorbidities or severe obesity:** The age range for individuals classified as "younger adults" will vary (for example, 18–49 years or 18–59 years). Although this subgroup is generally less likely to experience severe disease or death from COVID-19 infection compared to older adults, there remains substantial risk for morbidity/mortality in those with significant comorbidities. 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)*. The recommendation for this subgroup is for primary series and booster vaccination, with ***additional boosters 12 months*** after the last dose.

**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.[4] 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 primary series enhances immune responses in some ICPs *(27)*. Available evidence *(26)* suggests that for ICPs, an additional (third) dose should be given 1–3 months after the second dose in the standard primary series in order to increase protection as quickly as possible. The most appropriate timing for the

[4] **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, antimetabolites, 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.

additional dose may vary depending on the epidemiological setting and the extent and timing of immune suppressive therapy, and should be discussed with the treating physician. A first booster dose given 4–6 months after the previous dose is recommended for all ICPs. The frequency and interval of additional booster doses beyond the first booster should also be discussed with the treating physician, but given the vulnerability of ICPs, ***6 months should be considered***. Additional personal protective measures for immunocompromised persons to reduce exposure are warranted depending on the local epidemic circumstances, as is early institution of treatment once such a patient acquires a SARS-CoV-2 infection.

**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 adults and adolescents,[5] 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 adults and adolescents 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 low birth weight and requiring neonatal intensive care *(30)*. Pregnant adults 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.

Growing evidence shows that 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 the primary series and booster vaccination as soon as possible. ***An additional booster dose should be given once in pregnancy if the last dose was more than 6 months prior. For this additional booster dose, vaccination in the mid-second trimester is preferred to optimize protection of the pregnant adult or adolescent, the foetus, as well as 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 pregnant adults and adolescents, post-marketing evidence has supported safety and demonstrated effectiveness *(35)*.

**Health workers:** Health workers[6] include all people engaged in work whose primary intent is to improve human 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)*.

[5] The terms "pregnant adults" and "adolescents" are intended to be inclusive of all those who give birth. While most people who are or can give birth are cisgender women or adolescents, who were born and identify as female, this guidance is also inclusive of the experiences of transgender men and other gender diverse people who can give birth.

[6] 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.

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 category, on the basis of these characteristics.

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)*.

***A booster 12 months following the last booster dose is recommended for frontline health workers***, the objective being to maintain health system resilience, although the evidence is not robust. The consequences of disruptions to the health system can be substantial, especially during seasonal surges of other respiratory infections. Ideally, booster doses should be administered at a time of surge of infections, but often such surges are not predictable. As with all recommendations in this Roadmap, at this present time this does not equate to a future recommendation for annual boosters.

**Medium priority-use groups**

WHO recommends vaccination with primary series and first booster. ***Additional boosters are not routinely recommended at this time.*** Countries that already have a policy in place for additional boosters should assess the evolving need based on national disease burden, cost effectiveness and opportunity costs.

**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 *(39, 40)*. However, vaccine effectiveness in preventing post-COVID-19 conditions is only modest *(12-16)*. Younger and healthy adults who have not yet been vaccinated should be offered primary vaccine series and a first booster. ***Additional booster doses are not routinely recommended at this time.***[7]

**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 *(41, 42)*. 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 and a first booster. ***Additional booster doses are not routinely recommended at this time.***[7] 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:** Between November 2021 to present, Omicron has been the dominant variant in circulation. During this time, fewer deaths were reported compared to the first two years of the pandemic. The case fatality rate (CFR) in children aged less than 5 years has substantially declined from 0.08% in the pre-Omicron era to 0.02% in the Omicron era, and from 0.02% in children aged 5–14 years in the pre-Omicron era to 0.004% in the Omicron era *(43)*, although WHO acknowledges that CFR is an imperfect measure. Omicron

[7]"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.

variant infection in children and adolescents appears to be associated with less severe disease than pre-Omicron variant infections as measured by hospitalization rates and need for intensive unit care or mechanical ventilation, although other factors such as increasing population immunity also play a major role *(5)*. Risk of severe disease and death due to COVID-19 is lowest in people less than 18 years of age, and becomes lower as age decreases, with the possible exception of very young infants below the age of 1 year.

More than three years into the pandemic, and with 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. Such individuals should be offered a primary vaccine series and first booster (see medium priority-use group); those with moderate to severe immunocompromising conditions should be offered primary series and additional boosters (see high priority-use group). Multisystem inflammatory syndrome in children (MIS-C) is a rare condition associated with SARS-CoV-2 infection. In healthy children and adolescents, both MIS-C and post-COVID-19 conditions *(44)* have decreased in the Omicron era *(8, 45)*. Although children can still experience significant morbidity, most infections are self-limiting, and only a small proportion of children require hospitalization.

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 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 *(20, 21, 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 rrecommendations 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.

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.

## PROGRAMMATIC EFFORTS BY PRIORITY-USE GROUP

**High priority-use groups:**
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 *(48)*.
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.

**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 *(49)*. Children with comorbidities and severe obesity are included in the medium priority-use group and should be offered primary series vaccination and a first booster dose.

**Low priority-use groups:**
Countries should prioritize vaccination of higher priority-use groups. With increasing infection-induced immunity globally in younger age groups, the number of severe COVID-19 cases in healthy children has decreased substantially. In most countries globally, the benefit of vaccinating healthy children and adolescents is substantially lower compared to higher priority-use groups and compared to most other vaccine preventable diseases in childhood *(19, 20)*. In most country settings therefore, vaccinating healthy children and adolescents should be weighed up against other health priorities, programmatic and equity issues, opportunity costs/cost–effectiveness, and account resources (supply, programmatic and financial), so that a broader programme does not detract from efforts to vaccinate the high-priority groups or from other vaccinations. All countries must prioritize programmatic efforts to ensure that all children receive routine childhood vaccinations.

## CONSIDERATIONS FOR A LONGER INTERVAL FOR BOOSTER DOSES

Waning of clinical vaccine effectiveness over time has been demonstrated after the primary series and first booster dose for all WHO EUL vaccine products. Waning vaccine effectiveness is in the range of 11% over 9 months for severe disease, hospitalizations and death, but greater for SARS-CoV-2 infections and symptomatic COVID-19 disease *(50)*. The administration of additional booster doses improves protection against severe disease above the level achieved post-primary and first booster doses, and transiently also restores protection against mild infections. Offering regular booster doses to the highest-risk populations, particularly older adults, has the potential to be cost–effective even for countries with high population-level infection-induced immunity; however, the preventable burden and cost–effectiveness depend on the timing of boosting in respect to SARS-CoV-2 peak circulation and the emergence of immune-escape variants *(49)*.

With hybrid immunity, protection is higher and more sustained than infection-induced immunity or vaccine-induced immunity alone *(10)*. 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 are considered taking into account that most persons would have had a prior infection.

WHO recommends that for all older adults and adults with significant comorbidities or severe obesity, second and additional booster doses should be given at an interval of 12 months after the prior dose; an interval of 12 months may lead to higher community acceptance and hence higher uptake. For persons with the highest risk of severe disease and death, such as those who are very old and frail, those with multiple significant comorbidities, those with severe immunocompromising conditions, and those in long-term care facilities, an interval of 6 months should be considered given that even a minor reduction in vaccine effectiveness after 6 months could translate into substantial mortality.

The recommendation for additional boosters applies to the current situation and is not a recommendation for continued annual booster doses. There is insufficient evidence to conclude that annual boosters will be needed in the long-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.

The Table below summarizes WHO recommendations for primary series and booster vaccination for the three priority-use groups.

## WHO Interim Recommendations[a] for the optimal use of COVID-19 vaccination: primary series and booster doses in the context of Omicron and high population-level immunity

### HIGH priority-use groups

| Target population | Primary series and booster[b] | Additional booster doses | Remarks |
|---|---|---|---|
| **Groups with the highest risk of death from COVID-19** | | | |
| Older adults[c]<br>Younger adults with significant comorbidities or severe obesity | Recommended | Recommended *(12 months after previous dose)* | Most efficient use of COVID-19 vaccines with greatest impact on reducing deaths. |
| Subgroup of older adults:<br>Oldest adults[d]<br>Older adults with multiple significant comorbidities | Recommended | Recommended *(6 months after previous dose)* | |
| **Groups with special considerations for vaccination** | | | |
| Adults, adolescents and children 6 months and older with moderate to severe immunocompromising conditions | Recommended as extended primary series[e] | Recommended *(Approximately 6 months after previous dose; optimal time interval should be discussed with the treating physician)* | Vaccine effectiveness is lower for persons with immunocompromising conditions. For additional protection, personal protective measures, vaccinating close contacts, and early treatment in case of a SARS-CoV-2 infection is recommended. |
| Pregnant adults and adolescents[f] | Recommended | Recommended once during a pregnancy *(If previous dose was >6 months ago)* | Rationale for immunization during pregnancy is three-fold: to protect the pregnant person, the foetus, and the infant up to age 6 months. |
| Frontline health workers | Recommended | Recommended *(12 months after previous dose)* | Rationale is to maintain health care system resilience. |

### MEDIUM priority-use groups

| Target population | Primary series and booster[b] | Additional booster doses | Remarks |
|---|---|---|---|
| Healthy younger adults[g]<br>Children and adolescents aged 6 months to 17 years with severe obesity or comorbidities that put them at higher risk of severe COVID[i] | Recommended | Not routinely recommended.[h] | Benefit of additional boosters is marginal. |

### LOW priority-use groups

| Target population | Primary series and booster[b] | Additional booster doses | Remarks |
|---|---|---|---|
| Healthy children and adolescents aged 6 months to 17 years[i] | Countries could consider based on disease burden, cost effectiveness, and other health or programmatic priorities and opportunity costs. | Not routinely recommended.[h] | Benefit and cost-effectiveness of vaccinating healthy children and adolescents is substantially lower compared to high and medium priority-use groups and compared to most other vaccine preventable diseases in childhood. |

**a.** These recommendations are time-limited and apply only to the current situation and may need to be revisited when new variants of concern emerge or the epidemiology changes. WHO currently does not recommend regular annual boosters on a long-term basis until more evidence becomes available. **b.** First booster is recommended 6-12 months after the completion of the primary series. **c.** Age cut-off to be decided by countries: often it is 50 or 60 years. **d.** Age cut-off to be decided by countries; often it is 75 or 80 years. **e.** Extended primary series means one additional dose to the two-dose series, given about 3-6 months after the second dose. **f.** Regulatory approvals or WHO EUL for the use in pregnancy may differ by vaccine product. **g.** Age cut-off to be decided by countries: often it is 18 to 49 or 18 to 59 years. **h.** "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. **i.** Regulatory approvals or WHO EUL for the age indication differ by vaccine product; refer to the Product-specific vaccine recommendations.

## CONSIDERATIONS WITH REGARDS TO VARIANT-CONTAINING BOOSTERS

The composition of currently available COVID-19 vaccines is being updated to offer broader protection against new variants of concern *(51)*. Despite the potential benefit of variant-containing vaccines, current vaccines, based on the index virus, maintain high vaccine effectiveness against severe disease in the context of the Omicron variant and its sub-lineages based on an assessment by the WHO Technical Advisory Group on COVID-19 Vaccine Composition (TAG-CO-VAC) *(52)*.

As of March 2023, the following variant-containing vaccines have been authorized for use as a booster vaccine: the original/BA.1 and original/BA.5 bivalent mRNA vaccines by Pfizer-BioNTech and Moderna; and the monovalent Sanofi-GSK Vidprevtyn Beta (CoV2 preS dTM-AS03 (B.1.351)) vaccine against COVID-19 *(53)*. Countries can also consider using BA.5 bivalent mRNA vaccine for the primary series. It should be noted that the preponderance of data for variant-containing vaccines is driven by mRNA vaccines. Globally there is much diversity in platforms used for COVID-19 vaccination; the extent to which findings with mRNA vaccines can be generalized to other platforms is unknown.

WHO recommends using any of the WHO EUL COVID-19 vaccines or authorized mRNA bivalent variant-containing vaccines for booster vaccination. The TAG-CO-VAC has and will continue to make recommendations on changes needed for future COVID-19 vaccines *(52, 53)*.

Bivalent variant-containing vaccines used as booster doses may have modestly enhanced vaccine effectiveness over monovalent variant-containing vaccines at a time of circulating Omicron sub-lineages. However, there are no head-to-head comparisons for the extent to which vaccine effectiveness is enhanced with bivalent mRNA vaccines compared with other platforms or heterologous schedules. When deciding which vaccine to use as a booster, each country needs to take into account access to different vaccines and costs. Countries should not delay implementing booster doses. Generally there is greater benefit in ensuring that persons at high risk of developing severe COVID-19 receive a booster than in delaying vaccination in anticipation of access to a variant-containing vaccine.

There is increasing evidence that boosters using a different COVID-19 vaccine platform from that used for the primary series (heterologous boosting) may provide superior immunogenicity to use of a homologous booster *(54)*.

For countries considering heterologous boosters, 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 additional boosters, 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 primary series, 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, 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 *(55)*. 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, additional 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 2023 and 2024. 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 March 2023, the need and timing for additional boosters in the longer-term is unknown, and it remains uncertain whether COVID-19 vaccination needs to be included into routine programmes in the long-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 *(52)*. 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 30 MARCH 2023

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

## UPDATE 19 JANUARY 2022

| Section | Rationale for update |
|---|---|
| Title | 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".*<br><br>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*".<br><br>These changes were made to reflect the increasing vaccine supply globally. |
| Preamble/Introduction | 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.<br><br>Additional topics were considered, such as vaccine use in children and adolescents and the administration of booster doses. |
| Definitions | Definitions to guide the user were added (e.g. additional doses, booster doses). |
| Epidemiological setting scenarios, including:<br>- variants of concern and<br>- infection-induced immunity | 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. |
| Public health goals scenarios | The *Strategy to achieve global COVID-19 vaccination by mid-2022* was added and referred to. |
| Optimized use of COVID-19 vaccines | 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.<br><br>Primary as well as booster dose schedules were considered. |
| Heterologous primary vaccination series and booster doses | The section was added and current WHO guidance was referenced. |

## UPDATE 16 JULY 2021

| Section | Rationale for update |
|---|---|
| Rationale | 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. |
| Process of Prioritization Roadmap development | The update reflected the methods and processes used to develop this version of the Prioritization Roadmap. |
| Key assumptions | 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. |
| Key assumptions | 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. |
| Pregnant women, breastfeeding women and children | Substantive changes were made to these sections to reflect the recent evidence. |
| Epidemiological settings | 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. |

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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.

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The drafting of the current version of the Roadmap was led by the chair, Sonali Kochhar, and members of the SAGE Working Group on COVID-19 vaccines, namely Ruth Faden, Saad B. Omer and Peter Smith, with additional input from other members of the SAGE Working Group on COVID-19 vaccines.

WHO secretariat for immunization: Annelies Wilder-Smith, Joachim Hombach, Melanie Marti, Shalini Desai, Katherine O`Brien.

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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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