Interim recommendations for use of the ChAdOx1-S [recombinant] vaccine against COVID-19 (AstraZeneca COVID-19 vaccine AZD1222 Vaxzevria™, SII COVISHIELD™)

Interim guidance

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World Health Organization

Background

This interim guidance has been developed on the basis of the advice issued by the Strategic Advisory Group of Experts (SAGE) on Immunization at its extraordinary meeting on 8 February 2021 *(1)* and updated on 21 April 2021 and 30 July 2021. It was further updated based on additional discussions at the extraordinary SAGE meeting on 19 January 2022 with regards to the revised WHO Prioritization Roadmap which now also includes considerations for booster doses. A summary of the updates are presented in a table at the end of this document.

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 website and SAGE Working Group website.

These interim recommendations[1] refer to a generic group of COVID-19 vaccines (ChAdOx1-S [recombinant]) which all rely on the AstraZeneca core clinical data for regulatory evaluation for AZD1222 and are authorized under the emergency use listing procedure by WHO. The most commonly used trade names are AstraZeneca COVID-19 vaccine Vaxzevria, and COVISHIELD. Consequently, these vaccines are considered fully equivalent, even if produced at different manufacturing sites or assigned different product names; the interim recommendations here apply universally to all ChAdOx1-S vaccines.

The guidance is based on the initial evidence summarized in the *Background document on the AZD1222 vaccine against COVID-19 developed by Oxford University and AstraZeneca (2)*.

Annexes which include GRADE and evidence-to-recommendations (ETR) tables have also been updated to reflect the updated recommendations *(3)*.

All referenced documents are available on the SAGE COVID-19 webpage: https://www.who.int/groups/strategic-advisory-group-of-experts-on-immunization/covid-19-materials.

[1] The recommendations contained in this publication are based on the advice of independent experts who have considered the best available evidence, a risk–benefit analysis, and other factors, as appropriate. This publication may include recommendations on the use of medicinal products for an indication, in a dosage form, dose regimen, population or other use parameters that are not included in the approved labelling. Relevant stakeholders should familiarize themselves with applicable national, legal, and ethical requirements. WHO does not accept any liability for the procurement, distribution and/or administration of any product for any use.

Methods

SAGE applies the principles of evidence-based medicine and has set in place a thorough methodological process for issuing and updating recommendations *(4)*. A detailed description of the methodological processes as they apply to COVID-19 vaccines may be found in the SAGE evidence framework for COVID-19 vaccines *(5)*. This framework contains guidance on considering data emerging from clinical trials and post-introduction effectiveness and safety monitoring.

General goal and strategy for the use of the vaccine against COVID-19

The COVID-19 pandemic has caused significant morbidity and mortality throughout the world, as well as major social, educational and economic disruptions. There is an urgent global need to make COVID-19 vaccines available at scale and equitably across all countries.

As sufficient vaccine supply will not be immediately available to immunize all who could benefit from it, countries are recommended to use the WHO Prioritization Roadmap (6) and the WHO Values Framework *(7)* as guidance for their prioritization of target groups. As long as vaccine supplies are very limited, the WHO Prioritization Roadmap recommends that vaccine use be prioritized initially to health workers and older people with and without comorbidities. As more vaccine becomes available, additional priority-use groups should be vaccinated as outlined in the WHO Prioritization Roadmap (6), taking into account national epidemiological data and other relevant considerations.

Vaccine performance

The global phase 3 trial (conducted in Chile, Peru and the United States of America) enrolled 32 451 participants, with approximately 20% of the trial population aged 65 years or older *(8)*. The vaccine efficacy against symptomatic SARS-CoV-2 infection was 74% (95% confidence interval [CI]: 65.3–80.5%). No severe or critically ill cases occurred in the vaccinated group; 8 cases occurred in the placebo group. Vaccine efficacy in trial participants aged 65 years or older was 83.5% (95% CI: 54.2–94.1%) *(8)*. More detailed data on the efficacy and safety of this vaccine may be found in the 1 March 2021 Background document on the AZD1222 vaccine *(2)*.

Based on the phase 3 trials, the ChAdOx1-S [recombinant] vaccine against COVID-19 has an efficacy of 72% (95% CI: 63–79%) against symptomatic SARS-CoV-2 infection, as shown by the primary analysis of data irrespective of interdose interval (data cut-off, 14 January 2021) from trial participants who received 2 standard doses with an interval varying from about 4 to 12 weeks *(9)*. Vaccine efficacy tended to be higher when the interval between doses was longer. This, together with the finding of higher antibody levels with increasing interdose interval, supports the conclusion that longer dose intervals within the 4–12 week range are associated with greater vaccine efficacy against COVID-19.

Duration of protection and booster doses, including in the context of variants of concern

Studies of antibodies following immunization with ChAdOx1-S [recombinant] vaccine against Beta (B.1.351), Gamma (P.1), and Delta (B.1.617.2) show that neutralizing activity is variably lower than against the ancestral strain *(10-12)*. A 2-dose regimen of the ChAdOx1 nCoV-19 vaccine did not show protection against mild-to-moderate COVID-19 due to the Beta (B.1.351) variant in a trial in South Africa *(13)*. The young age group (median 30 years) and low prevalence of underling medical conditions did not allow a specific assessment of vaccine efficacy against severe COVID-19. Recent estimates of vaccine effectiveness against hospitalization with Delta (B.1.617.2) were 71% (95% CI 51–83%) after 1 dose of ChAdOx1-S [recombinant] vaccine; and 92% (95% CI: 75–97%) after 2 doses. Vaccine effectiveness against hospitalization with Alpha was 76% (95% CI: 61–85%) after 1 dose of ChAdOx1-S [recombinant] vaccine; and 86% (95% CI: 53–96%) after 2 doses *(14)*. Among those who had received 2 doses of ChAdOx1-S [recombinant] vaccine, there was no effect against Omicron from 20 weeks after the second dose *(15)*. There are no data currently on Lambda or other newer variants of interest.

Vaccine effectiveness against symptomatic COVID-19 of the Delta variant peaked in the early weeks after receipt of the second dose of ChAdOx1-S [recombinant] vaccine and then decreased by 20 weeks to 44% (95% CI: 43–45%). Waning of vaccine effectiveness was greater in persons aged 65 years or older than in those aged 40–64 years. Limited waning of vaccine effectiveness was noted with regard to protection against hospitalization at 20 weeks or more after vaccination. Vaccine effectiveness against hospitalization with infection with the Delta variant was 80% (95% CI, 77–83%) *(16)*.

Homologous booster: In a small study, antibody levels to the ancestral strain were 2-fold higher after the third dose of ChAdOx1-S [recombinant] vaccine than after the second dose *(17)*. Third dose boosters of ChAdOx1-S [recombinant] vaccine also increased neutralizing antibody responses to other variants, including the Omicron variant, compared to the primary series *(18)*.

Heterologous booster: In the COV-Boost trial in the United Kingdom, a booster dose with a heterologous vaccine (i.e an mRNA vaccine) resulted in improved immunogenicity compared to a homologous booster dose *(19)*. The relative effectiveness (compared to only a 2-dose primary series at least 175 days after the second dose) against symptomatic disease 14–34 days after a BNT162b2 or mRNA-1273 booster after ChAdOx1-S [recombinant] vaccine as a primary series, ranged from around 85% to 95%, and absolute vaccine effectiveness (compared to unvaccinated) ranged from 94% to 97% and was similar in all age groups. Limited waning was seen 10+ weeks after the booster dose *(20)*.

Use of a booster dose of ChAdOx1-S [recombinant] vaccine following a primary vaccination series with another EUL COVID-19 vaccine platform: A large cohort study in Chile compared the vaccine effectiveness of ChAdOx1-S [recombinant] vaccine when given as a third dose booster following a 2-dose primary vaccination schedule with CoronaVac in 11.2 million people. ChAdOx1-S [recombinant] vaccine as a third dose following a primary series of CoronaVac resulted in a higher vaccine effectiveness against hospitalizations, ICU admissions, and deaths compared with using CoronaVac as the homologous third dose *(21)*. A phase 4 randomized, single-blind, two-centre safety and immunogenicity study of a third heterologous booster dose of either ChAdOx1-S [recombinant] vaccine, compared with a third homologous booster dose of CoronaVac who had received 2 doses of CoronaVac 6 months previously in Brazil, found that the heterologous boost resulted in superior immunogenicity and effectiveness *(22).*

Intended use

Persons aged 18 years and older (for prioritization of subpopulations by age and other considerations, see the WHO Prioritization Roadmap *(6)*).

Administration

The recommended schedule is 2 doses (0.5 ml) given intramuscularly into the deltoid muscle. According to the manufacturer's product label, the vaccine can be administered with an interval of 4–12 weeks *(23)*. In light of the observation that 2-dose efficacy and immunogenicity increase with a longer interdose interval, WHO recommends an interval of 8–12 weeks between the 2 doses. If administration of the second dose is inadvertently delayed beyond 12 weeks, it should be given at the earliest possible opportunity.

Booster doses

Booster doses are administered to a vaccinated population that has completed a *primary vaccination series* when, with time, the immunity and clinical protection has fallen below a rate deemed sufficient in that population. The objective of a booster dose is to restore vaccine effectiveness.

In accordance with the WHO Prioritization Roadmap *(23)*, a booster dose is recommended for the highest and high priority-use groups (e.g. older adults, health workers, persons with comorbidities), administered 4–6 months after completion of the primary series. Countries with moderate-to-high rates of primary series coverage in higher priority-use groups should usually prioritize available resources to first achieve high booster dose coverage rates in higher priority-use groups before offering vaccine doses to lower priority-use groups.[2]

If more than 6 months have elapsed since completion of the primary series, a booster dose should be given at the earliest opportunity.

Interchangeability with other COVID-19 vaccines (heterologous schedules)

Primary series: WHO supports a flexible approach to using different EUL COVID-19 vaccine products for different doses (heterologous schedule), and considers a total of 2 doses of any combination of EUL COVID-19 vaccines (e.g. 1 dose of ChAdOx1-S [recombinant] vaccine, and 1 dose of another EUL COVID-19 vaccine) to be a complete primary series. Studies to date show that immune responses after a first dose of ChAdOx1-S [recombinant] products followed by a second dose of mRNA

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

vaccine (i.e. BNT162b2 or mRNA-1273) show higher neutralizing antibody levels and higher T-cell mediated immune responses than with 2 doses of the ChAdOx1-S [recombinant] products; similar levels to those of 2 doses of mRNA vaccine; and higher levels than a first dose of mRNA vaccine followed by a second dose of ChAdOx1-S [recombinant] vaccine *(24-28)*.

Heterologous booster following primary vaccine series with the ChAdOx1-S [recombinant] vaccine: A heterologous booster with other EUL COVID-19 vaccines (BNT162b2, mRNA 1273 or NVX-COV2373), 4–6 months after completion of the primary series with the ChAdOx1-S [recombinant] vaccine, resulted in superior immunogenicity or vaccine effectiveness compared to a homologous booster with ChAdOx1-S. Evidence to date is insufficient to recommend an inactivated vaccine as a booster (third) dose.

ChAdOx1-S [recombinant] vaccine as heterologous booster following a completed primary vaccination series with another COVID-19 platform: The ChAdOx1-S [recombinant] vaccine may be used as a booster dose following a completed primary series using any other EUL COVID-19 vaccine platform *(28)*. Data are not available on the risk of thrombosis with thrombocytopenia syndrome (TTS) with ChAdOx1-S [recombinant] vaccine used as a booster following the completion of a primary vaccination series with another WHO EUL COVID-19 vaccine.

Heterologous vaccination (primary series or booster doses) should only be implemented with careful consideration of current vaccine supply, vaccine supply projections, and other access considerations, alongside the potential benefits and risks of the specific products being used.

Co-administration with other vaccines

For adults, 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 any time before or after, other adult vaccines including live-attenuated, inactivated, adjuvanted, or non-adjuvanted vaccines *(29)*. When administered concomitantly, the vaccines should be injected in separate sites, preferably different extremities. For children and adolescents, evidence from co-administration studies is currently insufficient to make a recommendation for concomitant administration with COVID-19 vaccines.

Contraindications

A history of anaphylaxis to any component of the vaccine is a contraindication to vaccination. People who have an anaphylactic reaction following the first dose of this vaccine should not receive a second dose of the same vaccine. People who have had TTS (a very rare syndrome of blood clotting combined with low platelet counts) following the first dose of this vaccine should not receive a second dose of the same vaccine.

Precautions

A history of anaphylaxis to any other vaccine or injectable therapy (i.e. intramuscular, intravenous, or subcutaneous vaccines or therapies) is not a contraindication to vaccination. For such persons, a risk assessment should be conducted by a health professional. It is uncertain if there is an increased risk of anaphylaxis, but counselling should be given about the potential risk of anaphylaxis and the risks should be weighed against the benefits of vaccination. Such persons should be observed for 30 minutes after vaccination in health-care settings where anaphylaxis can be immediately treated.

In general, persons with an immediate non-anaphylactic allergic reaction to the first dose (i.e. urticaria, angioedema without respiratory signs or symptoms that occur within 4 hours of administration) should not receive additional doses, unless recommended after review by a health professional with specialist expertise. Subject to individual risk–benefit assessment, ChAdOx1-S [recombinant] vaccine could be provided under close medical supervision if it is the only available vaccine for persons at high risk of severe COVID-19. If a second dose is offered, the patient should be observed closely for 30 minutes after vaccination in a health-care setting where severe allergic reactions can be immediately treated.

No severe allergic reactions or anaphylaxis caused by ChAdOx1-S [recombinant] vaccine have been recorded in the context of clinical trials, but rare cases have been reported following use in national vaccination programmes. As for all vaccines, ChAdOx1-S [recombinant] vaccine should be given under health-care supervision, with the appropriate medical treatment available in case of allergic reactions. As for any other vaccine, an observation period of 15 minutes after vaccination should be ensured.

Thrombosis with thrombocytopenia syndrome *(30)* has been reported around 3–21 days following vaccination with the ChAdOx1-S [recombinant] vaccine *(31)*. A causal relationship between the vaccine and TTS is considered plausible although the biological mechanism for this syndrome is still being investigated. Most of these cases were reported from the United Kingdom and the European Union (EU). There is considerable geographical variation with regards to the reported incidence, with very few cases reported from non-European countries, despite extensive use of the vaccine in these countries. Data from the United Kingdom (as of 14 June 2021) *(32)* and the EU suggest that the risk of TTS is estimated to be approximately 1 case per 100 000 vaccinated adults.

Current data from Europe and other countries, such as Australia, suggest a higher risk in younger adults compared with older adults; no additional risk factors have yet been identified *(31)*. An estimation of the risk in other countries needs further data collection and analysis. Based on the AstraZeneca global safety database, TTS reporting rates (cases per 1 million doses administered per 21 days) ranged from 17.6 in Nordic countries to 0.2 in Asian countries and Brazil (estimated background rate, pre-pandemic population: 5.6–10.7 events per 1 million persons per 21 days), suggesting geographical differences in TTS risk *(33)*.

In countries with ongoing SARS-CoV-2 transmission, the benefit of vaccination in protecting against COVID-19 far outweighs the risks. However, benefit–risk assessments may differ from country to country, and countries should consider their epidemiological situation, individual and population-level risks, availability of other vaccines, and alternative options for risk mitigation. The benefit–risk ratio is greatest in older age groups as the risk of severe COVID-19 disease outcomes, including COVID-19 related thromboembolic events, increase with age.

The attributable risk of TTS in the United Kingdom was 16.1 per 1 million doses for individuals aged 15–39 years, and 3.2 per 1 million doses for individuals aged 40–64 years *(34)*. The risk of TTS was lower following the second dose of ChAdOx1-S vaccine than after the first dose. There was no evidence of a gender effect for any outcomes after a first dose. It is currently unknown whether there is a risk of TTS following a third dose. As data from additional studies become available, enabling better understanding of the pathophysiology of TTS and its relationship to the vaccine, recommendations on vaccination will be updated, as appropriate.

Anyone with an acute febrile illness (body temperature over 38.5 ºC) should postpone vaccination until they are afebrile.

Guillain-Barré syndrome (GBS) has been reported very rarely following vaccination with ChAdOx1-S [recombinant] vaccine *(35)*. However, a causal relationship with the vaccine has neither been confirmed nor ruled out and more rigorous studies are needed to fully assess the significance of these events. Based on the available data, the potential benefits of the ChAdOx1-S [recombinant] vaccine continue to outweigh any potential risk of GBS, particularly given the increase in the more transmissible Delta (B.1.617.2) variant. Health workers should be alert to possible signs and symptoms of GBS to ensure timely and accurate diagnosis (or to rule out other causes) and management of potential cases.

Vaccination of specific populations

Persons aged 65 years and over

The risk of severe COVID-19 and death increases steeply with age. Phase 3 clinical trials demonstrated an efficacy against symptomatic COVID-19 of 83.5% (95% CI: 54.2–94.1%) in individuals aged 65 years and older *(8)*. The trial data also indicate that the vaccine is safe for this age group. Post-introduction vaccine effectiveness studies from the United Kingdom show high rates of protection against hospitalizations, severe COVID-19 and death in older persons, including those over the age of 80 years *(36, 37)*. WHO recommends the vaccine for use in persons aged 65 years and older. In accordance with the WHO Prioritization Roadmap *(23)*, a booster dose is recommended for the highest and high priority-use groups such as older adults, administered 4–6 months after completion of the primary series.

Persons with comorbidities

Certain comorbidities and health states such as diabetes mellitus, cardiovascular and respiratory disease, neurodegenerative disease and obesity have been identified as increasing the risk of severe COVID-19 disease and death. Data for vaccine effectiveness after 2 doses suggests a similar safety and effectiveness profile for persons with comorbidities *(38)*. WHO recommends vaccination of persons with comorbidities. In accordance with the WHO Prioritization Roadmap *(23)*, a booster dose is recommended for the highest and high priority-use groups such as persons with comorbidities, administered 4–6 months after completion of the primary series.

Children and adolescents below 18 years of age

There are limited data on efficacy or safety for persons below the age of 18 years for the ChAdOx1-S [recombinant] vaccine. Until more data are available, vaccination of individuals in this age range with this vaccine is not routinely recommended.

Pregnant women

Pregnant women with COVID-19 are at higher risk of developing severe disease, with increased risk of intensive care unit admission and invasive ventilation, compared to non-pregnant women of reproductive age. COVID-19 in pregnancy is also associated with an increased risk of preterm birth, and of neonates requiring neonatal intensive care. It may also be associated with an increased risk

of maternal mortality *(39, 40)*. Pregnant women who are older (aged ≥35 years), or have high body mass index, or have an existing comorbidity such as diabetes or hypertension are at particular risk of serious outcomes from COVID-19.

Developmental and reproductive toxicology (DART) studies have not shown harmful effects of the vaccine in pregnant animals and their offspring. Available data from clinical trials are insufficient to assess vaccine efficacy or vaccine-associated risks in pregnancy; studies in pregnant women are ongoing, including a pregnancy registry. Based on previous experience with other vaccine use during pregnancy, the effectiveness of the ChAdOx1-S [recombinant] vaccine in pregnant women is expected to be comparable to that observed for non-pregnant women in similar age groups. Of note, compared with non-pregnant women, pregnancy is associated with higher rates of thrombosis, thrombocytopenia, and haemorrhage. However, current evidence does not suggest that pregnant women are at any greater risk of TTS than nonpregnant women. As data become available, recommendations on vaccination will be updated accordingly.

WHO has identified pregnant women as a priority-use group for COVID-19 vaccination, given their increased risk of severe outcomes. WHO recommends the use of ChAdOx1-S [recombinant] vaccine in pregnant women when the benefits of vaccination to the pregnant woman outweigh the potential risks. To help pregnant women make this assessment, they should be provided with information about the risks of COVID-19 in pregnancy, the likely benefits of vaccination in the local epidemiologic context, and the current limitations of the safety data in pregnant women. WHO does not recommend pregnancy testing prior to vaccination. WHO does not recommend delaying pregnancy or terminating pregnancy because of vaccination.

Breastfeeding women

WHO recommends the same use of ChAdOx1-S [recombinant] vaccine in breastfeeding and non-breastfeeding women. This is based on the following considerations: breastfeeding offers substantial health benefits to breastfeeding women and their breastfed children; vaccine effectiveness is expected to be similar in breastfeeding women as in non-breastfeeding individuals. Data are not available on the potential benefits or risks of the vaccine to breastfed children. However, as ChAdOx1-S [recombinant] vaccine is not a live virus vaccine, it is biologically and clinically unlikely to pose a risk to the breastfeeding child. WHO does not recommend discontinuing breastfeeding because of vaccination.

Moderately and severely immunocompromised persons, including persons living with HIV with CD4 cell count of <200 cells/µl

Moderately and severely immunocompromised persons (ICPs) are at higher risk of severe COVID-19, regardless of age, although increasing age remains an important co-factor. For purposes of this interim recommendation, moderately and severely ICPS include those with active cancer, transplant recipients, immunodeficiency, and active treatment with immunosuppressives. It also includes people living with HIV with a current CD4 cell count of <200 cells/µl, evidence of an opportunistic infection, not on HIV treatment, and/or with a detectable viral load (i.e. advanced HIV disease).[3] For more details, see the WHO Interim recommendations for an extended primary vaccination series in immunocompromised persons *(41)*.

Available data for WHO EUL COVID-19 vaccine products suggest that vaccine effectiveness and immunogenicity are lower in ICPs compared to persons without immunocompromising conditions *(41)*. Emerging evidence suggests that an additional dose included in an extended primary series enhances immune responses in some ICPs *(42)*. Reactogenicity data of an additional (third) dose given to ICPs, where reported, have generally been similar to those observed for the standard primary series. Given the significant risk of severe COVID-19 for ICPs, if infected, WHO recommends an extended primary series including an additional (third) dose for ICPs and considers that the benefits of an additional (third) dose outweigh the risks based on available data, although additional safety monitoring is required.

Available evidence *(41)* suggests that in order to increase protection as quickly as possible in ICPs, the additional (third) dose should be administered 1–3 months after the second dose in the standard primary series. The most appropriate timing for the additional

[3] **Active cancer:** Active immunosuppressive treatment for solid tumour or hematologic malignancy (including leukaemia, 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, tumor-necrosis factor (TNF) blockers, and other drugs that are significantly immunosuppressive or have received in the previous 6 months immunosuppressive chemotherapy or radiotherapy

dose may vary depending on the epidemiological setting and the extent and timing of immune suppressive therapy and course of the disease, and should be discussed with the treating physician.

Given the limited vaccine effectiveness in this population, a booster (fourth) dose administered 3–6 months after the additional (third) dose should be considered.

Information and, where possible, counselling about the limitations around the data on administration of an additional dose to ICPs should be provided to inform individual benefit–risk assessment.

Given that protection may remain inadequate in a portion of ICPs even after the administration of an additional dose, WHO further recommends that close contacts (in particular caregivers) of such individuals should be vaccinated if eligible (according to the product-specific vaccines that have received EUL). Additional public health and social measures at household level to protect ICPs are also warranted depending on the local epidemic circumstances.

Persons living with HIV who are stable on antiretroviral therapy

Persons living with HIV (PLWH) may be at higher risk of severe COVID-19. Among the phase 3 clinical trial participants with well-controlled HIV, there were no reported differences in safety signals. PLWH who are well controlled on highly active antiretroviral therapy and are part of a group recommended for vaccination, can be vaccinated. Available data on administration of the vaccine are currently insufficient to allow assessment of vaccine efficacy or safety for PLWH who are not well controlled on therapy. Humoral and cell mediated immunogenicity have been evaluated in subgroups of PLWH who are stable on antiretroviral therapy (undetectable viral load and CD4 counts >350). Similar anti-Spike IgG responses and T-cell responses were observed in PLWH as compared to an HIV negative cohort *(43)*. In the interim, given that the vaccine is not a live virus, PLWH who are part of a group recommended for vaccination may be vaccinated. Information and, where possible, counselling about vaccine safety and efficacy profiles in ICPs should be provided to inform individual benefit–risk assessment. It is not necessary to test for HIV infection prior to vaccine administration.

Persons who have previously had SARS-CoV-2 infection

Vaccination should be offered regardless of a person's history of symptomatic or asymptomatic SARS-CoV-2 infection. Viral or serological testing for prior infection is not recommended for the purpose of decision-making about vaccination. Data from the pooled analyses indicate that the vaccine is safe in people with evidence of prior SARS-CoV-2 infection. With the emergence of Omicron, reinfections after prior infection appear to be more common. Hybrid immunity is superior to immunity induced by vaccine or infection alone *(44)*. The optimal time interval between infection and vaccination is not yet known. Persons with laboratory-confirmed SARS-CoV-2 infection before primary series vaccination may choose to delay vaccination for 3 months. Persons with breakthrough infections following any dose could also consider delaying the next dose by 3 months. When more data on duration of immunity after natural infection become available, the length of this time period may be revised as well as the number of doses needed.

Persons with current acute COVID-19

Persons with acute PCR-confirmed COVID-19, including persons who are in-between doses, should not be vaccinated until after they have recovered from acute illness and the criteria for discontinuation of isolation have been met as per government advice. The optimal minimum interval between a natural infection and vaccination is not yet known. An interval of 3 months could be considered.

Persons who previously received passive antibody therapy for COVID-19

In people who have previously received monoclonal antibodies or convalescent plasma as part of COVID-19 treatment, vaccination does not need to be delayed. Although some reduction in vaccine-induced antibody titers was observed in people who previously received antibody products, the clinical significance of this reduction is unknown, and the balance of benefits versus risks favours proceeding with vaccination even considering the possibility of diminished vaccine effectiveness in this situation*(45)*.

Special settings

Persons in settings such as refugee and detention camps, prisons, slums, and other settings with high population densities, where physical distancing is not implementable, should be prioritized for vaccination as outlined in the WHO Prioritization Roadmap*(6)*, taking into account national epidemiological data, vaccine supply and other relevant considerations.

As noted in the WHO Prioritization Roadmap, national programmes should give special consideration to groups that are disproportionately affected by COVID-19, or that face health inequities as a result of social or structural inequities. Such groups should be identified, barriers to vaccination should be addressed, and programmes should be developed to enable equitable access to vaccines.

Other considerations

SARS-CoV-2 tests

Prior receipt of the vaccine will not affect the results of SARS-CoV-2 nucleic acid amplification or antigen tests for diagnosis of acute/current SARS-CoV-2 infection. However, it is important to note that currently available antibody tests for SARS-CoV-2 assess levels of IgM and/or IgG to the spike or the nucleocapsid protein. The vaccine contains the spike protein; thus, a positive test for spike protein IgM or IgG could indicate either prior infection or prior vaccination. To evaluate for evidence of prior infection in an individual who has received the vaccine, a test that specifically evaluates IgM or IgG to the nucleocapsid protein should be used. A positive nucleocapsid protein-based assay indicates prior infection, while a negative nucleocapsid protein-based assay is expected after vaccination (unless a natural infection has occurred). Antibody testing at an individual level is currently not recommended to assess immunity to COVID-19 following ChAdOx1-S [recombinant] vaccination.

Role of vaccines among other preventive measures

As recent data suggest limited effect of the vaccine on transmission, particularly against Omicron, it is advisable that public health and social measures to reduce SARS-CoV-2 transmission continue, including use of face masks, physical distancing, handwashing, appropriate ventilation and other measures as appropriate in particular settings, depending on the COVID-19 epidemiology and potential risks of emerging variants. Each country is facing a different situation in the pandemic depending on several factors including the intensity of SARS-CoV-2 circulation, amount of population level immunity, capacities to respond and agility to adjust measures. As the pandemic continues and the virus evolves, policy adjustments related to SARS-CoV-2 public health and social measures, will be needed. Government advice on public health and social measures should continue to be followed by vaccinated individuals, as well as those who have not yet been vaccinated.

Country strategies related to COVID-19 control should be designed to facilitate the participation of children in education and other aspects of social life, regardless of vaccination *(46)*.

Community engagement, and effective communication

Community engagement and effective communication (including risk communication) are essential to the success of COVID-19 vaccination programmes. The decisions and processes regarding prioritization should be transparent and based on shared values, the best available scientific evidence, and appropriate representation and input by affected parties. Furthermore, communication needs to be strengthened on the mechanism of action of vector-based vaccines; efficacy and safety data derived from clinical trials and post-marketing studies; background mortality, maternal and neonatal outcomes; and rates of adverse events of special interest (AESIs) in groups prioritized for vaccination. Strategies should include: (i) culturally acceptable and linguistically accessible communications regarding COVID-19 vaccination made freely available; (ii) active community engagement and involvement of