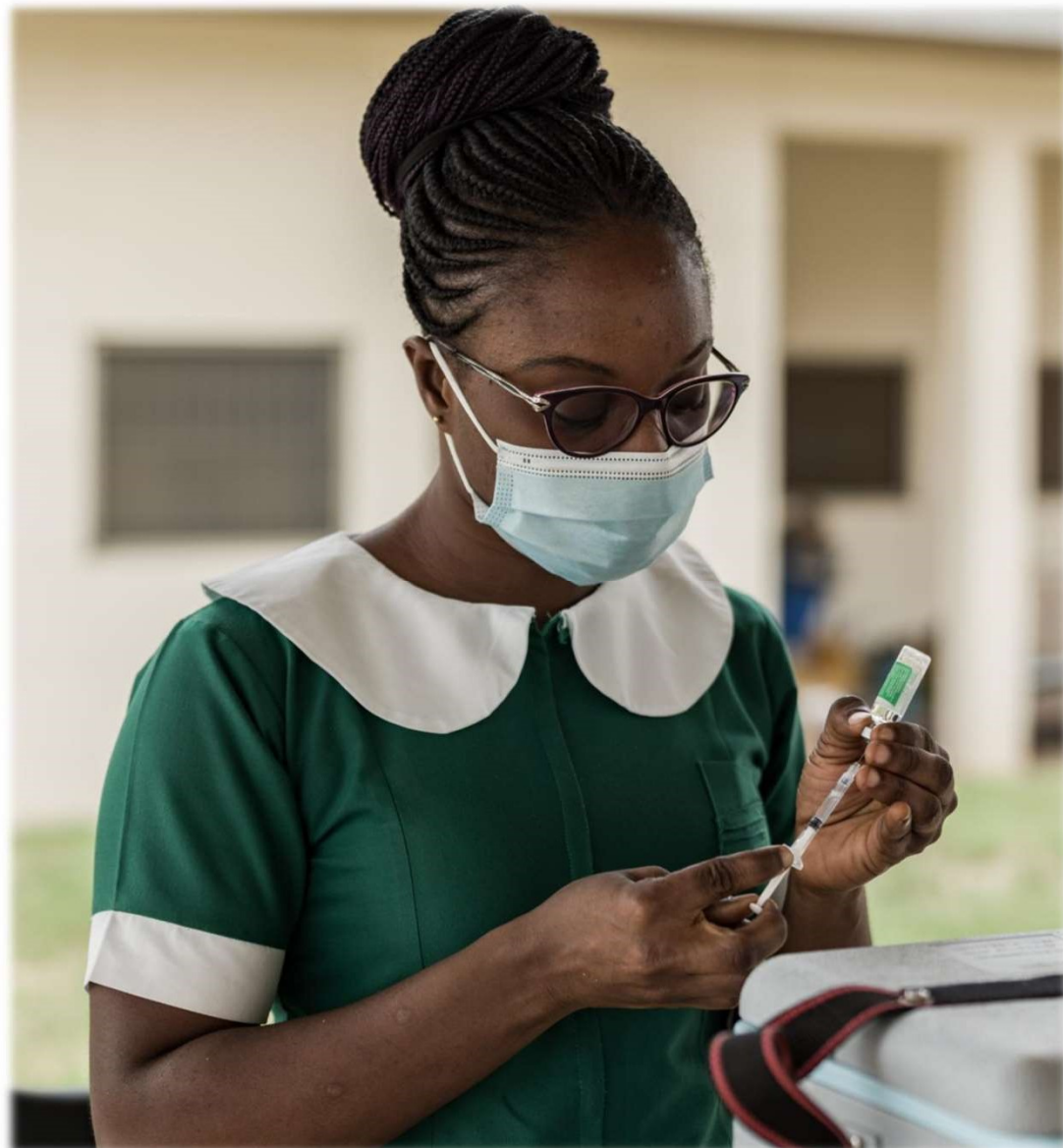


**Considerations for optimizing
deployment of ChAdOx1-S
[recombinant] vaccines in a time-
limited constrained supply situation**
(AstraZeneca/AZD1222-Vaxzevria,
AstraZeneca/SK Bioscience and SII/Covishield
vaccines)

30 April 2021
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Context



- WHO EUL was granted for ChAdOx1-S [recombinant] vaccine products against COVID-19 on February 15, 2021
 - Astra Zeneca/AZD1222, produced by Astra Zeneca-SKBio
 - SII/Covishield, produced by Serum Institute of India
 - New manufacturing sites have been approved since EUL
- ChAdOx1-S vaccines are the primary vaccines provided under the COVAX Facility
- **Currently, the global market supply of these vaccines does not fully meet global demand**
- While supply is expected to increase through the second half of 2021, the frequency and size of future shipments to countries remains uncertain and unpredictable
- Shelf-life at the time of deliveries received in country may be as short as 3 months

Context

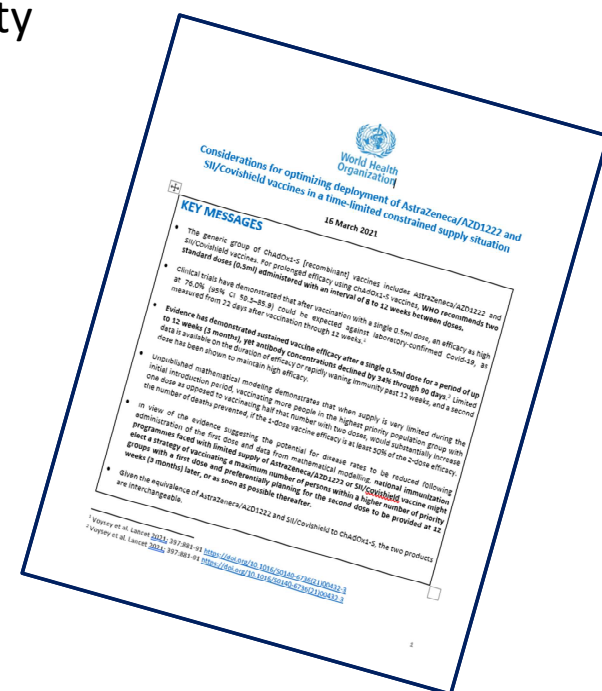


Countries need to find balance across key objectives:

- Maximizing immunity against COVID-19 in the highest priority groups according to the recommended 2-dose schedule;
- Reaching as many people within as many priority groups as quickly as possible, with at least one dose; and
- Fully administering all doses available prior to their lot expiration date.

Considerations for optimizing deployment of ChAdOx1-S [recombinant] vaccines in a time-limited constrained supply situation

- Evidence base
- Mathematical modelling
- Programmatic Considerations



Evidence base



- For prolonged efficacy using ChAdOx1-S vaccines, **WHO recommends two standard (0.5ml) doses administered with an interval of 8-12 weeks between doses¹**
- Efficacy against symptomatic SARS-CoV-2 infection after **two doses is 66.7%²**
 - Vaccine efficacy increases significantly when the interval between doses is >4 weeks and immunogenicity data also shows an antibody response 2x higher with an interval of ≥12 weeks
- Vaccine efficacy after **one dose has been shown to be as high as 76%³**, as measured from 22 days after vaccination through 12 weeks
 - Observational studies also show a 80-94% effect against hospitalization after 1 dose⁴
- Evidence demonstrates **sustained vaccine efficacy after one dose, up to 12 weeks** (although antibody concentrations declined by 34% through this period)
 - Data on duration of efficacy or rapidly waning immunity beyond 12 weeks is limited, and a second dose has been shown to maintain high efficacy

1. https://www.who.int/publications/i/item/WHO-2019-nCoV-vaccines-SAGE_recommendation-AZD1222-2021.1

2. (95% CI 57.4-74.0), Voysey et al. Lancet 2021; 397:881-91 [https://doi.org/10.1016/S0140-6736\(21\)00432-3](https://doi.org/10.1016/S0140-6736(21)00432-3)

3. (95% CI 59.3-85.9), Voysey et al. Lancet 2021; 397:881-91 [https://doi.org/10.1016/S0140-6736\(21\)00432-3](https://doi.org/10.1016/S0140-6736(21)00432-3)

4. Lopez Bernal J, et al. MedRxiv preprint. <https://doi.org/10.1101/2021.03.01.21252652>; Hyams C, et al. Lancet preprint. https://papers.ssrn.com/sol3/papers.cfm?abstract_id=3796835; Vasileiou et al, Lancet preprint. https://papers.ssrn.com/sol3/papers.cfm?abstract_id=3789264

Mathematical modelling



- Unpublished mathematical modeling demonstrates that when supply is very limited during the initial introduction period, **vaccinating more people in the highest priority population group with one dose as opposed to vaccinating half that number with two doses, would substantially increase the number of deaths prevented, if the 1-dose vaccine efficacy is at least 50% of the 2-dose efficacy.**
- Prioritizing first dose administration at the outset of the programme to highest priority groups is expected to provide **greater benefit when supply is very limited**; this holds true even when supply is insufficient to administer the second dose in a timely manner, as long as waning of first dose immunity is not very rapid.

Programmatic considerations

Countries receiving fewer doses than required to fully vaccinate all highest priority groups may need to consider modifying their planned vaccination strategies, with support of NITAGs in decision-making

Size of highest priority groups to vaccinate

- If supply is insufficient to cover the target population with 2 doses, countries should consider:
 - Option A:** Stratifying risk within the priority groups to provide a smaller “highest priority group” with 2 doses, or
 - Option B:** Stretching all available doses to vaccinate priority groups with at least one dose until supply is replenished

Programmatic considerations

Shelf life of first shipments

- COVID-19 vaccines have shorter shelf-lives than other EPI vaccines, and some shipments may arrive within 3 months of the expiration dates.

Vaccine delivery strategy and speed at which doses can be administered

- To ensure the second dose can be provided within the 8-12 interval, target populations will have to be reached very quickly with the first dose.
- If vaccine administration rate is expected to be slower, then administration of one dose to a larger group of people may be necessary to maximize consumption of vaccine before expiry.

Interval between dose 1 and dose 2

- Since vaccine efficacy increases with a longer duration between doses, it can be advantageous to extend the inter-dose interval up to 12 weeks.

Programmatic considerations

Interchangeability

- All ChAdOx1-S products covered in this presentation (AstraZeneca AZD1222, SII Covishield, and SK Bioscience) are considered equivalent and interchangeable for both doses
- Currently, WHO recommends that both doses should be administered with ChAdOx1-S products. Studies are underway to assess whether COVID-19 vaccines using a different platform can be used interchangeably in the dosing schedule. WHO recommendations may be updated as further information becomes available

Timing of future shipments

- The timing of future vaccine shipments and quantities may be uncertain and may result in a delivery schedule that does not allow timely implementation of a country's initial vaccination plans
- Recognizing that even with one dose, vaccine efficacy of 76% can be expected for at least 12 weeks, prudent to maximizing the interval to accommodate uncertain arrival

Programmatic considerations

Recording and communication

- All vaccinees should be given a date to return for the second dose. If stocks are limited and resupply uncertain, vaccinees should be advised to return in 12 weeks
- Countries should establish a mechanism for contacting these individuals if the second dose will be delayed beyond 12 weeks.
- Communication strategies should be adapted to clearly explain the vaccine schedule to the public as necessary – health workers must clearly understand rationale

Programmatic considerations



COVAX No Fault Compensation Program for AMC Eligible Economies

- AMC eligible economies should be aware that administering a vaccine received through the COVAX Facility in a manner that is not in accordance with relevant WHO SAGE recommendations and other guidance provided by WHO and otherwise in accordance with the Vaccine's label as approved by the NRA of reference, may result in eligible individuals who suffer a serious AEFI resulting in permanent impairment or death following the administration of such a vaccine, having their application for compensation under the COVAX NFC Program rejected
- In the case of the AstraZeneca vaccines, the WHO guidance acknowledges that delays beyond 12 weeks are possible under the current supply circumstances
- Applications for compensation by eligible individuals who have received the second dose of AstraZeneca vaccine beyond 12 weeks, will be considered in light of the above

Programmatic considerations



Indemnification and Liability

- For AMC eligible economies that are supplied vaccines through the COVAX Facility, special consideration must be given to the implications of the indemnification and liability agreement for the specific product
- The terms of the indemnity for a dose procured and distributed outside the COVAX Facility are likely to be different from the terms applicable to those procured and distributed through the COVAX Facility
- Countries should consider the potential complexity of managing any legal issues that arise following administration of such doses
- It is therefore critical that country supply and logistics systems accommodate careful tracking and tracing of batch numbers of vaccines supplied through the COVAX Facility

Conclusion



- In view of the evidence suggesting the potential for disease rates to be reduced following administration of the first dose, **national immunization programmes faced with limited supply of any time of ChAdOx1-S [recombinant] might elect a strategy of vaccinating a maximum number of persons within the highest number of priority groups with a first dose and preferentially planning for the second dose to be provided at 12 weeks (3 months) later, or as soon as possible thereafter.**