Adopting an heterologous prime-boost strategy in COVID-19 vaccination: the need for locally generated evidence in Africa

Mary Aigbiremo Oboh, Semeeh Omoleke, Kolawole Salami

Corresponding author: Mary Aigbiremo Oboh, Medical Research Council Unit, The Gambia at London School of Hygiene and Tropical Medicine, Fajara, Banjul, The Gambia. aigbi4god@gmail.com

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Adopting an heterologous prime-boost strategy in COVID-19 vaccination: the need for locally generated evidence in Africa

Mary Aigbiremo Oboh¹,²,³,⁴, Semeeh Omoleke³,⁴, Kolawole Salami⁵

¹Medical Research Council Unit, The Gambia at London School of Hygiene and Tropical Medicine, Fajara, Banjul, The Gambia, ²Malaria Genomic Epidemiology Network, Nigeria, Nigerian Institute of Medical Research, Lagos, Nigeria, ³Field Presence, World Health Organization, Adamawa State Field Office, Adamawa, Nigeria, ⁴Research and Development Blueprint Unit, World Health Organization, Geneva, Switzerland

Corresponding author
Mary Aigbiremo Oboh, Medical Research Council Unit, The Gambia at London School of Hygiene and Tropical Medicine, Fajara, Banjul, The Gambia
Abstract

The reduction in the severity and prevalence of COVID-19 has been largely due to the rapid development and deployment of COVID-19 vaccines. Consequently, WHO, in partnership with the Coalition for Epidemic Preparedness Innovation, GAVI, the Vaccine Alliance, set up the COVID-19 Vaccines Global Access (COVAX) Initiative. The goal of this initiative is to prevent discrimination between high and low-income/middle-income countries and ensure equitable vaccine distribution. The first COVID-19 vaccine sent to most countries in the region through the COVAX initiative was the Oxford AstraZeneca (ChAdOx1 nCoV-19) vaccine. Due to the reduced protection against variants of concern, safety issues, and supply challenges of the AstraZeneca vaccine in some countries, heterologous booster dose with alternative vaccines for individuals who have received a prime dose of AstraZeneca. Moreover, vaccine mixing (heterologous vaccination) due to its superior immunogenicity and enhanced protection is being recommended even for individuals who are yet to be vaccinated. However, it is important that prior adoption, empirical data on immunogenicity, safety, and reactogenicity be locally generated in populations where such heterologous vaccine is to be implemented. Regrettably, such data from our search in all clinical trial databases is not ongoing in Africa as at the time of writing this manuscript. Therefore, this treatise advocates an experimental arm to generate such robust evidence. This will provide empirical evidence to guide this innovative approach aimed at ensuring equity and access to COVID-19 vaccines in LMICs, particularly countries within the African region.

Commentary

The detection of the novel coronavirus disease (COVID-19) in China; in December 2019 and its subsequent declaration as a public health emergency of international concern on 30 January 2020 has significantly impacted global health systems, economies, and travel. The African region has recorded a relatively modest infection rate of infection. As of 2 September 2021, Africa has an estimated 7 849 859 cases and 198 132 mortality, representing 0.04% and 0.04% of the global estimates [1]. In the absence of effective treatment, the rapid development of vaccines using innovative platforms offers a glimmer of hope. The World Health Organisation (WHO) has approved some of the vaccines for emergency use [2]. With the tremendous success of COVID-19 vaccine development, it becomes imperative to set a robust strategic plan for equitable distribution, affordability, and accessibility to every individual regardless of political, racial or cultural background. Consequently, WHO, in partnership with the Coalition for Epidemic Preparedness Innovation (CEPI), GAVI, the Vaccine Alliance, set up the COVID-19 Vaccines Global Access (COVAX) Initiative, which aims to accelerate the manufacture and equitable access of COVID-19 vaccines to all countries irrespective of their economic status. The COVAX initiative proposed to deliver approximately 2 billion doses of COVID-19 vaccines by the end of 2021 to frontline workers and individuals who are > 65 years with or without co-morbidities. At conception, the ultimate goal of this distribution initiative is to prevent discrimination between high and low income/middle income countries (LMICs), and in turn, ensure equitable vaccine distribution. COVAX and the World Bank hopes to accelerate COVID-19 vaccine supply for developing countries through a new financing mechanism that builds on GAVI’s newly designed arthrogryposis multiplex congenita (AMC) cost-sharing arrangement. Therefore, countries within the African region can capitalise on this distribution plan to access the COVID-19 vaccine and effect strategic distribution across the continent and nationwide. However, hoarding and vaccine nationalism by wealthier nations have slowed the COVAX initiatives’ implementation and hindered the realization of its ambitious drive. The first COVID-19 vaccine sent to most countries in the region through the COVAX initiative was the Oxford AstraZeneca (ChAdOx1 nCoV-19) vaccine. However, the supply dwindled due to a decline in
production capacity caused by an upsurge in COVID-19 cases in India, where the manufacturer (Serum Institute of India, Pvt) of AstraZeneca vaccine is located.

As of 9<sup>th</sup> August 2021, reports on COVID-19 vaccination coverage have not been encouraging in countries within the African region. Only 1.56% and 3.71% of the population have received two (2) and one (1) doses of the various COVID-19 vaccines. Only two countries have vaccinated more than 50% of its population (Seychelles - 95% and Mauritius - 75%), and six have vaccinated almost a quarter of its population (Morocco, South Africa, Djibouti, Equatorial Guinea, Eswatini, and Cape Verde), while some (Burundi, Eritrea and Sierra Leone) are yet to provide any vaccination indices [2]. The setbacks in access and coverage would impact on transmission negatively and spread of variants SARS-CoV-2 strains by each country and the continent in general, given the suboptimal adherence to public health and social measures.

As a result of the changing recommendations on the use of the AstraZeneca vaccine regarding its reduced protection against variants of concern in some countries [3], high income countries are now recommending that individuals previously primed with the AstraZeneca vaccine should receive an alternative vaccine as their second (boost) dose. In addition, alternative prime-boost vaccination has been found to provoke superior immunogenicity and enhanced protection against SARS-CoV-2 [4] as well as against Ebola [5]. Messenger Ribonucleic Acid (mRNA) vaccine has been suggested as a reliable boost dose [6]. Hence, a heterologous prime-boost COVID-19 vaccine scenario is gaining prominence. Consequently, with African countries getting various COVID-19 vaccines based on different technology platforms, secured through different initiatives, to ensure as much coverage as possible, (Table 1, Table 1 (suite), Table 1 (suite 1), Table 1 (suite 2)) it is expected and indeed planned by some of these countries that most people who received an incomplete AstraZeneca dose (a single dose of the vaccine), or have not received any vaccination, will receive a second (for complete vaccination) or full dose course of another vaccine. Theoretically, this serves as the booster vaccine.

Although, some studies which evaluated heterologous prime-boost COVID-19 vaccine of different platforms have reported higher frequency of spike-specific CD4+, CD8+ T-cells [4], strong and high titer of neutralising antibodies against B1.1.7 and B.1.351 strains [6,7]. Reactogenicity after heterologous boost was reported as vaccine unrelated in one study (flu-like illness, headache, asthenia) [8], while another [9] attributed increased systemic reactogenicity after boost dose to heterologous manner. The Shaw [9] study which was conducted in individuals >50 years and older in the UK, suggested that reactogenicity might be higher if younger individuals were administered heterologous prime-boost doses. Although the reactogenicity observed is short-term, such trial needs to be replicated in various populations with the different vaccine combinations intended for implementation. All the aforementioned studies were conducted in Germany, Russia, China, and the UK. None has been conducted in any African countries that have or are about to commence implementing heterologous boost dose. A thorough search of clinical trial registries (clinicaltrial.gov, ICTRP, ISRCTN, PACTR, etc.) for COVID-19 heterologous vaccine efficacy regrettably did not return any hit from any African country. The importance of carrying out such a study in different African settings/countries cannot be overemphasised, especially as the emergence of new variants is quite rapid.

**Conclusion**

Globally, heterologous prime-boost vaccines offer enhanced protection in comparison to homologous vaccine, however, it is important that prior adoption, safety and reactogenicity data be locally generated in populations where such heterologous vaccine is to be implemented. Therefore, this treatise advocates an experimental arm to generate robust evidence on immunogenicity, reactogenicity and safety of heterologous prime-booster within the African population, even in
countries that have commenced the roll-out. This will provide an empirical evidence to guide this innovative approach aimed at ensuring equity and access to COVID-19 vaccines in LMICs, particularly countries within the African region.

Competing interests

The authors declare no competing interests.

Authors' contributions

All the authors have read and agreed to the final manuscript.

Tables

Table 1: different COVID-19 in African countries and percentage of population vaccinated
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Table 1 (suite 2): different COVID-19 in African countries and percentage of population vaccinated

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### Table 1: different COVID-19 in African countries and percentage of population vaccinated

| Countries    | COVID-19 vaccines                                      | Number of vaccine supplied | Number of vaccine administered | Percentage of population fully vaccinated |
|--------------|--------------------------------------------------------|-----------------------------|-------------------------------|------------------------------------------|
| South Africa | BNT162b2, Johnson and Johnson                          | 14 408 830                  | 7 567 757                     | 24.3                                     |
| Morocco      | AstraZeneca, Sinopharm, Johnson and Johnson            | 27 109 400                  | 24 751,744                    | 0.57                                     |
| Egypt        | AstraZeneca, Sinopharm                                 | 7 323 200                   | 5 582 316                     | 1.76                                     |
| Nigeria      | AstraZeneca, Moderna                                   | 7 940 000                   | 3 938 945                     | 0.68                                     |
| Tunisia      | AstraZeneca, Sinopharm, Sputnik V, BNT162b2, Moderna   | 3 575 890                   | 2 663 438                     | 8.17                                     |
| Zimbabwe     | Sinopharm, Sputnik V                                   | 4 900 000                   | 2 540 555                     | 5.59                                     |
| Algeria      | AstraZeneca Sinopharm, Sputnik V                       | 3 673 200                   | 2 500 000                     | 0                                         |
| Ethiopia     | AstraZeneca Sinopharm, Johnson and Johnson             | 3 344 800                   | 2 277 783                     | 0.04                                     |
| Kenya        | AstraZeneca                                           | 1 706 100                   | 1 734 013                     | 1.24                                     |
| Angola       | AstraZeneca, Sinopharm, Sputnik V, BNT162b2            | 1 525 240                   | 1 674 157                     | 2.14                                     |
| Senegal      | AstraZeneca Sinopharm, Johnson and Johnson             | 1 476 200                   | 1 388 153                     | 2.92                                     |
| Ghana        | AstraZeneca                                           | 1 331 000                   | 1 271 393                     | 1.31                                     |
| Mauritius    | AstraZeneca Sinopharm, Sputnik V                       | 1 974 000                   | 1 252 974                     | 43.21                                    |
| Uganda       | AstraZeneca Sinopharm                                  | 1 725 28                    | 1 152 874                     | 0                                         |

### Table 1 (suite): different COVID-19 in African countries and percentage of population vaccinated

| Countries       | COVID-19 vaccines                                      | Number of vaccine supplied | Number of vaccine administered | Percentage of population fully vaccinated |
|-----------------|--------------------------------------------------------|-----------------------------|-------------------------------|------------------------------------------|
| Côte d’Ivoire   | AstraZeneca Sinopharm                                  | 1 123 420                   | 976 545                       | 0.44                                     |
| Guinea          | AstraZeneca Sinopharm, Sputnik V Sinovac              | 985 460                     | 904 845                       | 2.59                                     |
| Rwanda          | AstraZeneca BNT162b2 Moderna                           | 1 280 320                   | 868 972                       | 3.02                                     |
| Sudan           | AstraZeneca Sinopharm                                  | 1 050 000                   | 810 560                       | 0.42                                     |
| Libya           | AstraZeneca Sinopharm, Sputnik V                       | 580 190                     | 712 213                       | 0                                         |
| Malawi          | AstraZeneca Johnson and Johnson                        | 876 390                     | 597 862                       | 0.74                                     |
| Togo            | AstraZeneca BNT162b2 Sinovac                           | 576 620                     | 474 776                       | 1.85                                     |
| Zambia          | AstraZeneca Sinopharm, Johnson and Johnson             | 620 800                     | 444 574                       | 0.86                                     |
| Niger           | AstraZeneca Sinopharm, Johnson and Johnson             | 931 400                     | 401 133                       | 0.24                                     |
| Botswana        | AstraZeneca Sinopharm                                  | 492 400                     | 365 137                       | 5.31                                     |
| Cameroon        | AstraZeneca Sinopharm, Johnson and Johnson             | 1 045 900                   | 331 875                       | 0.2                                       |
| Mozambique      | AstraZeneca Sinopharm, Johnson and Johnson             | 1 704 400                   | 318 004                       | 0.25                                     |
| Equatorial Guinea | Sinopharm                                    | 600 000                     | 308 858                       | 9.17                                     |
### Table 1 (suite 1): different COVID-19 in African countries and percentage of population vaccinated

| Country                  | Vaccine(s)                | Population vaccinated | Vaccinated population | Coverage |
|--------------------------|---------------------------|-----------------------|------------------------|----------|
| Somalia                  | AstraZeneca Sinopharm     | 608 000               | 249 790                | 0.55     |
| Mauritania               | AstraZeneca Sinopharm, BNT162b2 Johnson and Johnson | 839 600               | 224 000                | 0.41     |
| Namibia                  | AstraZeneca Sinopharm     | 197 200               | 218 453                | 2.02     |
| Mali                     | AstraZeneca Sinopharm     | 396 000               | 206 562                | 0.28     |
| Congo (Republic)         | Sinopharm Sputnik V      | 172 000               | 198 698                | 1.2      |
| Madagascar               | AstraZeneca Johnson and Johnson | 552 750              | 197 001                | 0        |
| Cabo Verde               | AstraZeneca Sinopharm, BNT162b2 | 211 050              | 183 620                | 3.61     |
| Sierra Leone             | AstraZeneca Sinopharm     | 324 125               | 163 085                | 0.3      |
| Sechelles                | AstraZeneca Sinopharm Sputnik V | 190 000              | 139 625                | 68.14    |
| Comoros                  | AstraZeneca Sinopharm     | 112 000               | 134 020                | 4.79     |
| Gabon                    | Sinopharm                | 300 000               | 103 820                | 1.93     |
| Liberia                  | AstraZeneca Johnson and Johnson | 700 800              | 95 423                 | 0.18     |
| Central African Republic | AstraZeneca Johnson and Johnson | 382 400              | 95 282                 | 0.21     |
| Democratic Republic of Congo | AstraZeneca                  | 351 000               | 86 170                 | 0.01     |

### Table 1 (suite 2): different COVID-19 in African countries and percentage of population vaccinated

| Country                  | Vaccine(s)                | Population vaccinated | Vaccinated population | Coverage |
|--------------------------|---------------------------|-----------------------|------------------------|----------|
| Benin                    | AstraZeneca Johnson and Johnson | 649 400             | 70 323                 | 0.18     |
| Eswatini                 | AstraZeneca Johnson and Johnson | 512 000             | 65 667                 | 2.28     |
| South Sudan              | AstraZeneca               | 132 000               | 56 989                 | 0.04     |
| Djibouti                 | AstraZeneca Johnson and Johnson | 475 200             | 50 509                 | 1.9      |
| Sao Tome and Principe    | AstraZeneca               | 53 850                | 43 960                 | 5.94     |
| Gambia                   | AstraZeneca Johnson and Johnson | 202 200             | 43 557                 | 0.51     |
| Lesotho                  | AstraZeneca Sinopharm Johnson and Johnson | 510 000             | 38 320                 | 0.38     |
| Chad                     | AstraZeneca Sinopharm     | 300 620               | 36 173                 | 0.06     |
| Burkina Faso             | AstraZeneca Johnson and Johnson | 266 400             | 35 402                 | 0        |
| Guinea-Bissau            | AstraZeneca               | 64 800                | 25 872                 | 0.09     |
| Tanzania                 | Johnson and Johnson       | 1 058 400             | 0                      | 0        |
| Sahrawi Republic         | AstraZeneca               | 20 000                | 0                      | 0        |