The Case for Why Africa Should Host COVID-19 Candidate Vaccine Trials

Jerome Amir Singh
Centre for the AIDS Programme of Research in South Africa, Durban, South Africa

In response to provocative comments by 2 European clinicians and scientists, the World Health Organization Director General has declared that Africa will not host COVID-19 vaccine trials. Such a stance risks stigmatizing COVID-19 vaccine trials in Africa and depriving Africa of critical research. To the contrary, there is a critical need for Africa to host COVID-19 vaccine trials on public health, scientific, and ethics grounds.

**Keywords.** COVID-19; vaccine trials; ethics; public health; global health.

In early April 2020, during a debate on vaccine trials on French television, a senior French clinician suggested that a vaccine trial testing the efficacy of a decades-old tuberculosis vaccine, bacille Calmette-Guérin (BCG), against COVID-19, should be conducted in Africa. His rationale was simple: “...there are no masks, no treatment, no intensive care, a bit like it is done in some studies on AIDS or among prostitutes. We try things because we know they [sex workers] are highly exposed and they don’t protect themselves.” [1] A senior French scientist also being interviewed, concurred. While the scientists, were not, in fact, referring to the testing of a novel COVID-19 candidate vaccine in Africa [1], the damage was done. The remarks provoked global outrage [2, 3]. In his response to the ensuing controversy, the World Health Organization (WHO) Director General, who hails from Africa, was emphatic. Categorizing the remarks as appalling, disgraceful, and racist, the WHO Director General declared: “Africa cannot and will not be a testing ground for any [COVID-19] vaccine.” Further, that “the hangover from a colonial mentality has to stop. We assure you that this will not happen in Africa.” [4] While the WHO Director General may not have intended his comments to mean that Africa was barred from participating in such trials and, further, while the WHO has no authority under international law to block such trials in Africa, the ensuing negative publicity has fueled suspicion about biomedical research and quickly turned public sentiment against COVID-19 vaccine trials across the African continent [5–7]. This is an unfortunate development. To the contrary, because of its particular vulnerabilities, Africa critically needs to host studies trialing novel COVID-19 vaccine candidates, from the outset of the COVID-19 pandemic.

THE PUBLIC HEALTH IMPERATIVE TO TEST NOVEL COVID-19 CANDIDATE VACCINES ON AFRICAN POPULATIONS

While African countries have relatively low numbers of COVID-19 cases compared to settings elsewhere, this is not necessarily indicative of low prevalence or successful containment, but low surveillance. By 21 May 2020, South Africa, which has a population of approximately 59.5 million, had conducted 37 043 tests, including 18 572 tests in the previous 24 hours [8]. By 20 May 2020, Kenya, which has an estimated population in excess of 200 million, had conducted 37 043 tests, including 1812 tests in the previous 24 hours [10]. These statistics speak to the low level of surveillance on the continent and almost certainly mask much higher prevalence in these countries. These settings typify the situation elsewhere on the continent. The low number of documented cases on the continent may also be due to the possibility that the virus is not yet as prevalent in many parts of Africa. However, there is no reason to believe the disease will not eventually spread just as widely as has been the case elsewhere in the world.

Africa is particularly susceptible to COVID-19 because 56% of its urban population is concentrated in overcrowded and poorly serviced slum dwellings [11], and only 34% of households on the continent have access to basic hand washing facilities [12]. Africa also shoulders a disproportionate burden of major diseases, such as HIV/AIDS, tuberculosis, and malaria [13]. With lower ratios of hospital beds and health professionals to its population than other regions [14], and high dependency on imports for its medicinal and pharmaceutical products [15], the United Nations Economic
understanding the underlying genomic vaccine for COVID-19 requires a better immune intervention or preventive of SARS-CoV-2 infection and designing accordingly, controlling current rates complications for viral pathogenesis [21].

Race and ethnicity/geographic ancestry have also been shown to affect vaccine responsiveness [23–26]. For instance, rotavirus vaccine efficacy is considerably lower in Africa as compared to Europe and North America, and has been attributed to host genomics, particularly mutations in genes involved in the immune response, or to the receptor/ligand [27]. Given these factors, it cannot be taken for granted that a vaccine which demonstrates efficacy in Asian or Caucasian populations will demonstrate equivalent efficacy in African populations, or in all African settings. As such, it is crucial for Africans across the continent to participate in COVID-19 vaccine trials, from their outset.

THE SCIENTIFIC RATIONALE TO TEST NOVEL COVID-19 CANDIDATE VACCINES ON AFRICAN POPULATIONS

As of 20 April 2020, there were 5 candidate vaccines in clinical evaluation and a further 71 candidate vaccines in preclinical evaluation [17]. These candidates are being trialed in Asia, North America, and Europe. If novel candidate vaccines are not tested in African settings, the continent has to bank on efficacious vaccines developed and tested elsewhere being effective in African populations. This may turn out not to be the case. Host genomics play a key role in viral susceptibility, disease progression, and clinical outcome after viral exposure [18, 19].

In this regard, the immune response in Africans and Europeans differ, especially in the cases of genes involved in inflammatory and antiviral responses [20]. This is significant as interactions between the innate and adaptive immune responses in COVID-19 have implications for viral pathogenesis [21]. Accordingly, controlling current rates of SARS-CoV-2 infection and designing an immune intervention or preventive vaccine for COVID-19 requires a better understanding of the underlying genomic susceptibility and resistance to COVID-19 [22], including host-pathogen interaction, host immune responses, and the pathogen immune evasion strategies.

The exclusion of African populations in COVID-19 vaccine trials testing novel vaccine candidates could translate to African countries losing precious time in protecting their populations if efficacious vaccines developed elsewhere are later found not to confer protection on African populations. Accordingly, the conduct of COVID-19 vaccine trials in Africa has considerable social value as such research is responsive to the urgent health needs and priorities of African people and will yield critical information towards those ends. It has been argued that inclusion in clinical trials is a moral right and a benefit [28], and the US National Institutes of Health has even made inclusivity a review criterion [29]. Equity speaks to social justice or fairness [30]. As the inclusion of disadvantaged and marginalized groups in research can help global health research advance equity [31], sponsors, scientists, and regulators contemplating host sites for candidate COVID-19 vaccines should consider that the health and well-being of African populations can best be assured by their inclusion in COVID-19 vaccine research. Such inclusion also realizes the notions of solidarity—which requires us to think about how we might stand together to defend the interests of vulnerable groups—and common good—which requires us to share benefits and burdens, and sacrifice for one another, as it will benefit everyone if we do so. Dozens of concurrent COVID-19 vaccine trials testing novel candidates will require the accrual of thousands of participants to meet sample size targets. This need will be expeditiously met if dozens of host sites across multiple regions accrue such numbers concurrently. Africa can play a crucial role in helping to meet such targets in a timely manner.

Africa has a long history of, and considerable experience in, hosting and conducting vaccine trials [32], including phase 1 vaccine trials on a range of major diseases across the continent [33–37]. African scientists are also making valuable contributions to COVID-19 vaccine development [38–41]. Accordingly, the inclusion of suitable African host countries in vaccine trials will honor the principle of collaborative partnership. South Africa is currently the only African country to participate in the SOLIDARITY trial, which aims to assess the efficacy of multiple candidate COVID-19 therapeutics [42]. African countries can play a similar participatory role in novel COVID-19 vaccine trials. The inclusion of African populations in COVID-19 vaccine research could also facilitate their timely post-trial access to efficacious experimental intervention [43, 44], arguably faster than if those settings were not participating in COVID-19 vaccine trials.

Lastly, it would be remis not to acknowledge that the WHO Director General’s strongly expressed sentiments against the testing of vaccines on the African continent may be premised on the belief that Africans could be exploited if they participate in COVID-19 vaccine trials. As is the case with other research conducted in
Africa, including COVID-19 therapeutic trials [42], COVID-19 vaccine trials must be conducted in accordance with local and international ethics guidelines [43, 44], and applicable local regulations. Such an approach is supported by the WHO Director General, who has noted: “We [the WHO] would follow all the rules to test any vaccine or therapeutics all over the world using exactly the same rule, whether it’s in Europe, Africa or wherever.” [1]. Furthermore, COVID-19 vaccine research should involve local investigators and must be underpinned by meaningful stakeholder and community engagement initiatives.

CONCLUSION

The COVID-19 pandemic presents the greatest public health threat to the world since the 1918 H1N1 pandemic. As COVID-19 is now truly a global pandemic, all of humanity shares a common fate. As dozens of COVID-19 vaccine trials commence in the weeks and months ahead, African sites should be central to COVID-19 vaccine trial site mapping. Such an approach is in the interests of public health, scientifically responsible, and realizes key ethics values. Without such an approach, Africa risks being left behind in our response to the COVID-19 pandemic. This would be unconscionable.

Notes

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References

1. Euronews and AP. What French doctors and the WHO really said about Africa and vaccine testing. Euronews and AP, 4 April 2020. https://www.euronews.com/2020/04/07/what-french-doctors-and-the-who-really-said-about-africa-and-vaccine-testing. Accessed 25 April 2020.

2. BBC. Coronavirus: France racism row over doctors’ Africa testing comments. BBC, 3 April 2020. https://www.bbc.com/news/world-europe-52151722. Accessed 25 April 2020.

3. Busari S, Wojazer B. French doctors’ proposal to test Covid-19 treatment in Africa slammed as ‘colonial mentality’. CNN, 7 April 2020. https://edition.cnn.com/2020/04/07/africa/french-doctors-africa-covid-19-intl/index.html. Accessed 25 April 2020.

4. BBC. Coronavirus: Africa will not be testing ground for vaccine, says WHO. BBC, 6 April 2020. https://www.bbc.com/news/world-africa-52192184. Accessed 25 April 2020.

5. Editorial Staff. Kenyans slam BBC journalist over Covid-19 vaccine trial comments. African Briefing, 24 April 2020. https://africabriefing.org/2020/04/kenyans-slam-bbc-journalist-over-covid-19-vaccine-trial-comments/. Accessed 25 April 2020.

6. Namubiru L. Africans facing coronavirus must not suffer the injustices they saw with Aids. Guardian, 18 April 2020. https://www.theguardian.com/commentisfree/2020/apr/18/africans-coronavirus-injustices-aids-big-pharma. Accessed 25 April 2020.

7. Guoussanou W. COVID-19 trials at risk after Africa ‘racism’ backlash. SciDevNet, 24 April 2020. https://www.scidev.net/global/health/news/covid-19-trials-at-risk-after-africa-racism-backlash.html. Accessed 25 April 2020.

8. Department of Health, South Africa. Update on Covid-19, 21 May 2020. https://sacoronavirus.co.za/category/press-releases-and-notices/. Accessed 21 May 2020.

9. Ministry of Health, Kenya. Press statement on COVID-19, 20 May 2020. https://www.health.go.ke/press-releases/. Accessed 21 May 2020.

10. Nigeria National Centre for Disease Control. An update of COVID-19 outbreak in Nigeria, 20 May 2020. https://ncdc.gov.ng/diseases/sitreps/?cat=14&name=An%20update%20of%20COVID-19%20outbreak%20in%20Nigeria. Accessed 21 May 2020.

11. United Nations Habitat. World cities report 2016: urbanization and development - emerging futures. United Nations Human Settlement Programme, 2016. https://unhabitat.org/world-cities-report. Accessed 24 April 2020.

12. World Health Organization (WHO)/ United Nations Children’s Fund (UNICEF). Progress on drinking water, sanitation and hygiene. Update and SDG baselines 2017. WHO/UNICEF, 2017. https://www.who.int/mmediacentre/news/releases/2017/launch-version-report-jmp-water-sanitation-hygiene.pdf. Accessed 24 April 2020.

13. Institute for Health Metrics and Evaluation (IHME). Findings from the global burden of disease study 2017. IHME, 2018. https://www.healthdata.org/sites/default/files/policy_report/2019/GBD_2017_Booklet.pdf. Accessed 24 April 2020.

14. World Health Organization (WHO). World health statistics 2019: monitoring health for the SDGs. WHO, 2019. https://apps.who.int/iris/bitstream/handle/10665/311696/WHO-DAD-2019.1-eng.pdf. Accessed 1 June 2020.
15. United Nations Economic Commission for Africa (UNECA). Trade policies for Africa to tackle COVID-19. UNECA, 27 March 2020. https://www.uneca.org/sites/default/files/PublicationFiles/briefing_paper_on_trade_policies_for_africa_to_tackle_covid-19_20200327.pdf. Accessed 1 June 2020.

16. United Nations Economic Commission for Africa. COVID-19 in Africa. Protecting lives and economies. UNECA, 16 April 2020. https://www.uneca.org/sites/default/files/PublicationFiles/eca_covid_report_en_rev16april_5web.pdf. Accessed 26 April 2020.

17. World Health Organization. Draft landscape of COVID-19 candidate vaccines – 20 April 2020. WHO. https://www.who.int/blueprint/priority-diseases/key-action/novel-coronavirus-landscape-ncov.pdf. Accessed 26 April 2020.

18. Gonzalez E, Bamshad M, Sato N, et al. Race-specific HIV-1 disease-modifying effects associated with CCR5 haplotypes. Proc Natl Acad Sci U S A 1999; 96:12004–9.

19. Peacl K, Goldstein DB, Walley NM, et al; Infectious Disease Clinical Research Program HIV Working Group; National Institute of Allergy and Infectious Diseases Center for HIV/AIDS Vaccine Immunology (CHAVI). Host determinants of HIV-1 control in African Americans. J Infect Dis 2010; 201:1141–9.

20. Quach H, Rotival M, Pothlichet J, et al. Genetic adaptation and Neandertal admixture shaped the immune system of human populations. Cell 2016; 167:643–656. e17.

21. Du SQ, Yuan W. Mathematical modeling of interaction between innate and adaptive immune responses in COVID-19 and implications for viral pathogenesis [published online ahead of print 1 May 2020]. J Med Virol. doi:10.1002/jmv.25866.

22. Godri Pollitt KJ, Peccia J, Ko AI, et al. COVID-19 vulnerability: the potential impact of genetic susceptibility and airborne transmission. Hum Genomics 2020; 14:17.

23. Christy C, Pichichero ME, Reed GF, et al. Effect of gender, race, and parental education on immunogenicity and reported reactogenicity of acellular and whole-cell pertussis vaccines. Pediatrics 1995; 96:584–7.

24. Kurupati R, Kossenkov A, Haut L, et al. Race-related differences in antibody responses to the inactivated influenza vaccine are linked to distinct pre-vaccination gene expression profiles in blood. Oncotarget 2016; 7:62898–911.

25. Haralambieva IH, Salk HM, Lambert ND, et al. Associations between race, sex and immune response variations to rubella vaccination in two independent cohorts. Vaccine 2014; 32:1946–53.

26. McQuillan GM, Kruszon-Moran D, Hyde TB, Forghani B, Bellini W, Dayan GH. Seroprevalence of measles antibody in the US population 1999–2004. J Infect Dis 2007; 196:1459–64.

27. Sharma S, Hagbom M, Svensson L, Nordgren J. The impact of human genetic polymorphisms on rotavirus susceptibility, epidemiology, and vaccine take. Viruses 2020; 12:324.

28. Zuckerman D. The ethics of inclusion on the basis of sex/gender, race, ethnicity, and age in clinical research. Revision notes. March 2019. https://grants.nih.gov/grants/peer/guidelines_general/Review_Human_subjects_Inclusion.pdf. Accessed 1 June 2020.

29. National Institutes of Health. Guidelines for the review of inclusion on the basis of sex/gender, race, ethnicity, and age in clinical research. Revision notes. March 2019. https://grants.nih.gov/grants/peer/guidelines_general/Review_Human_subjects_Inclusion.pdf. Accessed 1 June 2020.

30. Braveman P, Gruskin S. Defining equity in health. J Epidemiol Community Health 2003; 57:254–8.

31. Pratt B. Inclusion of marginalized groups and communities in global health research priority-setting. J Empir Res Hum Res Ethics 2019; 14:169–81.

32. Ndwandwe D, Dube K, Mathebula L, Wiysonge CS. Description of vaccine clinical trials in Africa: a narrative review. Hum Vaccin Immunother 2020; 16:972–80.

33. Aponte JJ, Aide P, Renom M, et al. Safety of the RTS,S/AS02D candidate malaria vaccine in infants living in a highly endemic area of Mozambique: a double blind randomised controlled phase I/IIb trial. Lancet 2007; 370:1543–51.

34. Stoute JA, Heppner DG Jr, Mason CJ, et al. Phase 1 safety and immunogenicity trial of malaria vaccine RTS,S/AS02A in adults in a hyperendemic region of western Kenya. Am J Trop Med Hyg 2006; 75:166–70.

35. Thera MA, Dumbo OK, Coulibaly D, et al. Safety and immunogenicity of an AMA-1 malaria vaccine in Malian adults: results of a phase 1 randomized controlled trial. PLoS One 2008; 3:e1465.

36. Bekker LG, Dintwe O, Fiore-Gartland A, et al; HVTN 602/ Aeras A-042 Protocol Team. A phase 1b randomized study of the safety and immunological responses to vaccination with H4:IC31, H56:IC31, and BCG revaccination in Mycobacterium tuberculosis-uninfected adolescents in Cape Town, South Africa. EClinicalMedicine 2020; 21:100313.

37. Hosseinipour MC, Innes C, Naidoo S, et al. Phase 1 HIV vaccine trial to evaluate the safety and immunogenicity of HIV subtype C DNA and MF59-adjuvanted subtype C Env protein [published online ahead of print 4 January 2020]. Clin Infect Dis doi:10.1093/cid/ciz1239.
38. Cleary K. COVID-19: how scientists found the fingerprint behind South Africa’s SARS-CoV-2 virus. Spotlight, 10 April 2020. https://www.spotlightnsp.co.za/2020/04/10/covid-19-how-scientists-found-the-fingerprint-behind-south-africas-sars-cov-2-virus/. Accessed 26 April 2020.

39. Ho U. SA’s first successful genome sequencing of a local SARS-CoV-2 sample will help global fight against the disease. Daily Maverick, 7 April 2020. https://www.dailymaverick.co.za/article/2020-04-07-sas-first-successful-genome-sequencing-of-a-local-sars-cov-2-sample-will-help-global-fight-against-the-disease/. Accessed 26 April 2020.

40. Express. UFS joins vaccine research. Express, 8 April 2020. https://www.news24.com/SouthAfrica/Local/Express-News/ufs-joins-vaccine-research-20200407. Accessed 26 April 2020.

41. Behr M. Cape town trial begins next week - can BCG shot prevent COVID-19 infection? IOL, 25 April 2020. https://www.iol.co.za/weekend-argus/news/cape-town-trial-begins-next-week-can-bcg-shot-prevent-covid-19-infection-47187565. Accessed 26 April 2020.

42. Singh JA. COVID-19: science and global health governance under attack. S Afr Med J 2020; 110.

43. World Medical Association (WMA). WMA declaration of Helsinki - ethical principles for medical research involving human subjects. WMA, 2013. https://www.wma.net/policies-post/wma-declaration-of-helsinki-ethical-principles-for-medical-research-involving-human-subjects/. Accessed 26 April 2020.

44. Council for the International Organization for Medical Sciences (CIOMS) and World Health Organization (WHO). International ethical guidelines for health-related research involving humans. CIOMS/WHO, 2016. https://cioms.ch/publications/product/international-ethical-guidelines-for-health-related-research-involving-humans/. Accessed 26 April 2020.