

# South African Oxford AstraZeneca vaccine study a global game-changer

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This is a landmark study in so far as being the first to raise the alarm that, despite early successes with COVID-19 vaccines, further research is warranted on a next generation of COVID-19 vaccines.

The results from this study, however, only indicate that the AstraZeneca [vaccine](#) does not have at least 60% efficacy against mild-moderate COVID-19 due to the B.1.351 (N501Y.V2) variant.

Based on a broader body of evidence, the World Health Organization recommends that this vaccine still be deployed in countries where the B.1.351 variant circulates, as it likely still protects against severe infection, hospitalization, and death caused by COVID-19.

Professor Shabir Madhi, Executive Director of the Vaccines and Infectious Diseases Analytics (VIDA) Research Unit at the University of the Witwatersrand, Johannesburg, led the trial in South Africa:

"Despite the disappointing finding that the

AstraZeneca vaccine did not protect against mild COVID infection because of the B.1.351 variant first identified in South Africa, [peer review](#) and publication of our research validates the findings and makes a compelling case for the development of a second-generation vaccines worldwide," says Madhi.

First-generation vaccines refer to those designed to respond to the original SARS-CoV-2 virus. Second-generation vaccines refer to technology and design innovations that can provide protections against the constantly evolving variants that cause COVID-19 disease.

## A rapid response to variant reality

The findings of this study were previously publicized as a preprint on Sunday, 7 February 2021, and concluded that the ChAdOx1 nCoV-19 vaccine provided minimal protection against mild to moderate COVID-19 infection from the B.1.351 [coronavirus](#) variant first identified in South Africa in mid-November 2020.

Prior to the evolution of the B.1.351 and P.1 variants, the South African National Department of Health (NDOH) had ordered and taken delivery of approximately one million doses of the Oxford AstraZeneca vaccine on 1 February 2021, after a published pooled analysis of this vaccine in December 2020 showed an overall vaccine efficacy of 66.7% in the UK and Brazil.

"We were in a state of euphoria about the high efficacy of several COVID-19 vaccines against the original virus, but then the AstraZeneca study threw us a curve-ball," says Madhi. "In this study now published in *NEJM*, we found that two doses of ChAdOx1 nCoV19 had no efficacy against non-hospitalized mild to moderate COVID-19, mainly due to the B.1.351 variant."

## What the SA study published in *NEJM* reveals

The randomized, multi-centre, double-blinded trial enrolled 2026 participants between 24 June and 9 November 2020.

The trial was a phase 1b/11 trial that aimed to evaluate the safety, immunogenicity, and efficacy of the AstraZeneca vaccine ChAdOx1 nCoV19 in preventing symptomatic COVID-19. Immunogenicity refers to the ability of a foreign substance, such as an antigen, to provoke an immune response. Vaccine efficacy refers to the percentage reduction of a disease in a clinical trial.

"A trial enrolling just 2026 participants is considered small, while phase 3 [trials](#) enroll tens of thousands of participants," says Madhi. "Yet the startling data that our small trial generated was irrefutable, and the implications profound."

### **Profile of a South African AstraZenca COVID-19 vaccine trial participant**

The majority of participants enrolled were relatively young (under 65-years-old), generally healthy, and HIV-negative. The median [middle] age of participants was 30 years old. More than half (56.5%) of the trial participants identified as male, 70.5% were Black Africans, 12.8% were white, and 14.9% identified as 'mixed' race.

"These demographics are important because they reflect characteristics of the overall population in South Africa. Conducting [clinical trials](#) in diverse settings like these is critical to understanding how vaccines work in local contexts," says Madhi.

### **Testing a hypothesis**

The primary objective of this trial was to establish this vaccine's efficacy against all-severity COVID-19, irrespective of variants.

A secondary objective was to evaluate the vaccine's efficacy against the B.1.351 variant specifically.

"When this trial began in June 2020, we were testing a vaccine against SARS-CoV-2," says Madhi. "By January 2021, SARS-CoV-2 had spawned variants, including the B.1.351 first

discovered in South Africa. As a secondary objective, we tested a hypothesis: would this vaccine prove at least 60% efficacious in preventing mild to moderate COVID-19 disease? It did not."

The results showed that a two-dose regimen of ChAdOx1-nCov19 did not show protection against mild to moderate COVID-19 due to the B.1.351 variant.

Crucially, Madhi notes that, "This vaccine may still help protect high-risk individuals with co-morbidities from contracting severe COVID-19 disease, having to be hospitalized, mechanically ventilated, or dying. The AstraZeneca vaccine remains essential in the arsenal against this virus, particularly in Africa, which has already received 14 million doses of this vaccine as the COVID-19 immunization program starts in multiple countries."

### **How the WHO took note**

On 15 February 2021, the WHO recommended that the AstraZeneca vaccine still be rolled out, even in countries where the B.1.351 variant or other similar variants of concern are circulating.

A WHO news release says that the vaccine was reviewed on 8 February by the WHO Strategic Advisory Group of Experts on Immunization (SAGE), which makes recommendations for vaccines' use in populations (i.e. recommended age groups, intervals between shots, advice for specific groups such as pregnant and lactating women). The SAGE recommended the vaccine for all age groups 18 years and above.

"While the AstraZeneca vaccine—like many other first-generation COVID-19 vaccines—is unlikely to interrupt transmission of SARS-CoV-2 or protect against mild infection from variants like B.1.351, these first-generation vaccines could still provide the only sustainable option to prevent flooding our hospitals with severe COVID-19 cases, and to mitigate COVID-19 deaths once the third wave hits," says Madhi.

### **Second-generation vaccine innovation**

The development of an Oxford AstraZeneca and other COVID-19 vaccines targeting the B.1351 variant is currently underway.

The South African study increased awareness worldwide of the necessity of developing vaccines that target variants specifically—and even reimagining vaccines entirely.

Innovations in vaccine technologies, platforms and designs suggest exciting advances in this field.

"The finding of our [Oxford AstraZeneca COVID-19 vaccine] study are truly a turning point in COVID vaccine development—and a rude awakening," says Madhi. "This one small South African study has alerted the world to the fact that second generation COVID-19 vaccines will be required to provide protection against inevitable and persistent SARS-COV-2 variants. If we had not conducted this trial in South Africa, the world would be none the wiser."

**More information:** Shabir A. Madhi et al, Efficacy of the ChAdOx1 nCoV-19 Covid-19 Vaccine against the B.1.351 Variant, *New England Journal of Medicine* (2021). [DOI: 10.1056/NEJMoa2102214](https://doi.org/10.1056/NEJMoa2102214)

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