Study supports flexible second dose options following Pfizer or Oxford/AstraZeneca jabs

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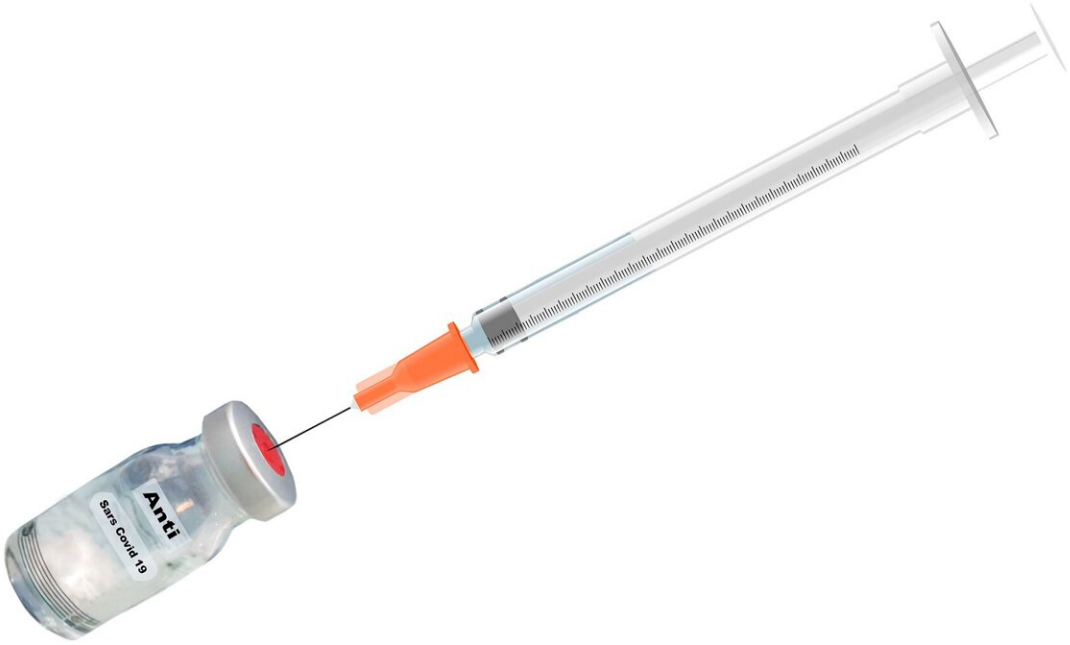

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Following up first doses of the Oxford-AstraZeneca or Pfizer-BioNTech vaccines with second doses of the Moderna or Novavax jabs will generate robust immune responses against COVID-19, according to

researchers running the University of Oxford-led Com-COV study.

In a paper published in *The Lancet*, they report that participants receiving a first dose of Oxford-AstraZeneca or Pfizer-BioNTech generated a robust immune response when immunized nine weeks later with a second dose of COVID-19 vaccines manufactured by Novavax or Moderna. No safety concerns were raised in this study of 1,070 participants, who took part in the study across nine National Institute for Health Research-supported sites.

This study therefore supports flexible use of these vaccines in primary immunization schedules, which is crucial to help rapid deployment of these vaccines, especially in low- and middle-income countries where vaccine supply may be inconsistent.

Professor Matthew Snape, Associate Professor in Paediatrics and Vaccinology at the University of Oxford, and Chief Investigator on the trial, said: "Thanks to studies such as these, we are now getting a more complete picture of how different COVID-19 vaccines can be used together in the same vaccine schedule.

"Encouragingly, all these schedules generated antibody concentrations above that of the licensed and effective two dose Oxford-AstraZeneca schedule. When it comes to cellular immunity, having a first dose of the Oxford-AstraZeneca vaccine followed by any of the other study vaccines generates a particularly robust response.

"It's only through the inspiring efforts of the Com-COV2 participants and study teams that we can generate these data; this will help get the world immunized against COVID-19 as quickly as possible."

Of note is that the primary vaccine made a difference to the immunogenicity of the various schedules:

- Oxford-AstraZeneca followed by Moderna/Novavax schedules both induced higher antibodies and T-cell responses than the licensed and highly effective 'standard' two-dose Oxford-AstraZeneca schedule.
- Pfizer-BioNTech/Moderna induced higher antibody and T-cell responses than the standard two-dose Pfizer-BioNTech schedule
- Pfizer-BioNTech/Novavax induced higher antibodies than the two-dose Oxford-AstraZeneca schedule; this schedule induced lower antibody and T-cell responses than two-dose Pfizer-BioNTech schedule.
- Blood samples taken from participants were tested for their effectiveness against the Wild-Type, Beta and Delta variants—while it was observed that the vaccines' efficacy against the variant strains had decreased, this was a consistent trend across the mixed schedules.

In addition, a significantly higher number of short-lived vaccine reactions were reported in volunteers who received a second dose of Moderna compared to those who received two doses of either Oxford-AstraZeneca or Pfizer-BioNTech.

Professor Matthew Snape said: "Using different types of vaccines within the same schedule as we have done here (for example mRNA vaccines, viral-vector vaccines or protein-based vaccines) is a relatively novel approach to immunization.

"As well as providing evidence for flexibility in deployment, these results suggest this approach can also help generate better immune responses. This has implications beyond COVID-19 and will inform new approaches to immunization against other diseases that are, as yet, not vaccine preventable."

The study was designed as a so-called 'non-inferiority' study—the intent

is to demonstrate that mixing is not substantially worse than the standard schedules—and compares the immune system responses to the gold-standard responses reported in previous clinical trials of each vaccine.

Professor Andrew Ustianowski, National Clinical Lead for the UK NIHR COVID Vaccine Research Programme, said: "We really cannot thank the volunteers and staff involved in studies such as Com-COV2 enough. The continued effort from everyone within the study helps to gather more important information on the immune response of vaccine dose combinations.

"This is another set of positive findings discovered by the UK research community, supported by the NIHR, which could be applied globally. Results such as these will help to shape guidance nationally and internationally, allowing populations to be better protected from COVID-19."

CEO of CEPI Dr. Richard Hatchett said: "We're pleased to have co-funded this crucial area of research, in collaboration with our partners at the University of Oxford and in the UK Government, supporting excellent science conducted in the UK that advances vaccine research for the benefit of all. This is yet another example of the impact that funding innovative R&D can have on our hopes of ending the COVID-19 pandemic.

"With COVID-19 cases continuing to rise and the emergence of new variants like Omicron, it is imperative that we rapidly protect as many people as possible from this devastating virus. As has long been said, no one is safe until everybody is safe, and we hope that today's trial findings will contribute to our work to achieve this vital goal.

"This is extremely encouraging and valuable data on the potential to mix-and-match COVID-19 vaccines in primary immunization schedules.

Knowing that a second dose of a different COVID-19 vaccine can generate a robust immune response is advantageous in helping the rollout of COVID-19 vaccines through COVAX, especially in populations still urgently waiting for their primary immunization or in those partially vaccinated."

More information: Arabella S V Stuart et al, Immunogenicity, safety, and reactogenicity of heterologous COVID-19 primary vaccination incorporating mRNA, viral-vector, and protein-adjuvant vaccines in the UK (Com-COV2): a single-blind, randomised, phase 2, non-inferiority trial, *The Lancet* (2021). DOI: 10.1016/S0140-6736(21)02718-5

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