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Covid-19: Fever, chills, and aches more common when AstraZeneca and Pfizer vaccines are mixed, early data show

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Mixing doses of the Oxford AstraZeneca and the Pfizer BioNTech covid-19 vaccine leads to more frequent mild to moderate reactions compared with standard dosing schedules, researchers have reported.

Researchers running the University of Oxford led Com-COV study—which is investigating the reactogenicity and immunogenicity from mixing doses of the two vaccines—reported their preliminary results in a peer reviewed research letter in the *Lancet*.[1]

Matthew Snape, associate professor in paediatrics and vaccinology at the University of Oxford and chief investigator on the trial, said, "While this is a secondary part of what we are trying to explore through these studies, it is important that we inform people about these data, especially as these mixed doses schedules are being considered in several countries.

"The results from this study suggest that mixed dose schedules could result in an increase in work absences the day after immunisation, and this is important to consider when planning immunisation of healthcare workers."

The study[2] is comparing all four prime and boost permutations of the AstraZeneca and the Pfizer vaccines (Pfizer followed by AstraZeneca, AstraZeneca followed by Pfizer, AstraZeneca twice unmixed, and Pfizer twice unmixed) both at 28 day and 84 day prime boost intervals.

A total of 830 participants were enrolled and randomised—463 to the four groups with a 28 day prime boost interval, and 367 to groups with an 84 day prime boost interval.

When given at a four week interval, both of the heterologous (or "mixed") schedules created more frequent reactions after the second boost dose than the standard, homologous (or "non-mixed") schedules.

Feverishness was reported by 37 (34%) of 110 recipients who received AstraZeneca for prime and Pfizer for boost, compared with 11 (10%) of 112 recipients of AstraZeneca for both prime and boost (difference 24%, 95% confidence interval 13 to 35%).

Feverishness was reported by 47 (41%) of 114 recipients of Pfizer for prime and AstraZeneca for boost, compared with 24 (21%) of 112 recipients of Pfizer for both prime and boost (difference 21%, 95% CI 8 to 33%).

Similar increases were observed for chills, fatigue, headache, joint pain, malaise, and muscle ache.

Any adverse reactions were short lived and there were no other safety concerns, the study team reported.

Participants were advised that paracetamol might reduce side effects but were not actively directed to medicate prophylactically.

Paracetamol use in the 48 hours post-boost vaccine was reported by 40 (36%) of 112 recipients of AstraZeneca for both prime and boost, 63 (57%) of 110 recipients of AstraZeneca for prime and Pfizer for boost, 48 (41%) of 117 recipients of Pfizer for both prime and boost, and 68 (60%) of 114 recipients of Pfizer for prime and AstraZeneca for boost, thereby mirroring the reactogenicity pattern.

Speaking at a Science Media Centre briefing, Snape said, "Whether or not this will relate to an improved immune response, we don't yet know. We'll be finding out those results in a few weeks' time. That will be an important part of the picture to try and understand what's going on here."

In the meantime, Snape said the team had adapted the ongoing study to assess whether early and regular use of paracetamol reduces the frequency of reactions.

Snape also highlighted the study data only covered participants aged 50 and above, so the impact on younger age groups was not yet known. "We have, in general, seen higher rates of reactions in younger age groups, so reactions might be higher still in younger age groups," he said.

1 Heterologous prime-boost covid-19 vaccination: initial reactogenicity data. May 2021. www.thelancet.com.

2 Heath P, Faust S, Finn A, et al. A single blind, randomised, phase II UK multicentre study to determine reactogenicity and immunogenicity of heterologous prime/boost covid-19 vaccine schedules. 2021. comcovs-tudy.org.uk/files/com-covprotocolv5026-apr-2021finalpdf.