Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

cases confirmed by PCR and for 56% of patients admitted to hospital.[2] Women represent 64% of cases among young adults aged 15–39 years, reflecting better access to PCR testing among milder cases in women. The most plausible explanation for the lower percentage of men among confirmed cases is the larger proportion of women among the essential health-care personnel. Women represent 74% of workers in the Spanish health sector, one of the highest in the world, with 56% of doctors and 85% of nurses being women.[3] During the first epidemic wave, there was a shortage in personal protective equipment for health-care workers, and our findings[1] reveal that the seroprevalence values were two times higher in health-care personnel than in the general population.

Seroprevalence studies are useful to determine the spread of infectious disease for asymptomatic infections or incomplete ascertainment of those who are symptomatic,[4] two circumstances that are present in the COVID-19 pandemic. Particular limitations might hamper the results: (1) the representativeness of the sample, which should not be an issue in our study,[1] given the population-based design and high participation rates; (2) the sensitivity and specificity of new tools, which was something we tried to overcome when choosing immunoassays against two different targets and combining results to provide a specificity–sensitivity range; (3) timing of the serological survey, because the humoral response declines 2–3 months after infection,[5] ENE-COVID started 4 weeks after the peak of the first epidemic wave, with second and third study rounds providing similar results; and (4) the existence of a group of infected individuals who have recovered, and in whom antibodies are not detected. We agree with T Paulose George that this information is not sufficient to characterise the immunological status of the population. The correlation between serological assays and the presence of neutralising antibodies against SARS-CoV-2 is not completely understood.[6–8] Indeed, cellular immunity seems to have a substantial role,[8,9] but the duration and protective nature of the T-cell response is unknown. However, T-cell reactivity in people who are not exposed to SARS-CoV-2 suggests the possibility of pre-existing immune memory.[10] Despite all these considerations, the intensity of the second epidemic wave that Spain and other countries are experiencing is a clear indication of the absence of herd immunity against SARS-CoV-2.

We declare no competing interests.

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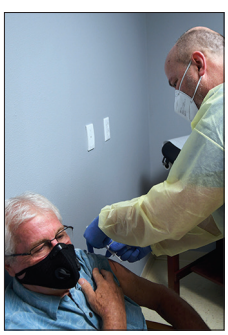
ChAdOx1 nCoV-19 vaccine for SARS-CoV-2


NurPhoto/Getty Images

The ChAdOx1 nCoV-19 vaccine against severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), described by Pedro Folegatti and colleagues,[1] was an important milestone in vaccine development to contain the ongoing pandemic. The vaccine is one of several SARS-CoV-2 vaccines that have entered the human trial phase, and the phase 1/2 trial showed encouraging results. This trial has focused on the most relevant clinical outcomes of safety, reactogenicity, and immunogenicity of the vaccine. The recruited participants (ie, healthy adults aged 18–55 years who were negative for SARS-CoV-2) were randomly assigned to receive either the vaccine (ie, ChAdOx1 nCoV-19 at a dose of 5×10^4 viral particles) or an active control (ie, a meningococcal conjugate vaccine; MenACWY) as a single intramuscular injection. The study showed the safety, reactogenicity, and immunogenicity of the ChAdOx1 nCoV-19 vaccine.

Although the outcomes were meticulously planned, an important outcome, anaphylactic reaction, was not mentioned. Anaphylaxis is important to consider while a new vaccine is being tested.[2] Additionally, the selection criteria for ten participants in group 3, who were recruited in a non-randomised way, needs to be described. The trial is labelled as a randomised controlled trial and the criteria for recruiting participants in

a non-randomised method should be made available. While we looked at the immunogenicity outcomes in figure 3,[1] we noted that the number of participants who were analysed was different at each follow-up stage. Some explanation for this difference needs to be given to make the findings more applicable. In the trial, participants with high titres of neutralising antibodies at baseline were also included in the same analysis, but whether the rise in their antibody titres affected the overall results and whether the non-randomised recruitment of the participants influenced the comparison is unclear. In the group of participants receiving ChAdOx1 nCoV-19 and paracetamol, the adverse event of itching was higher than in participants receiving ChAdOx1 nCoV-19 without paracetamol, which needs to be investigated.

Although phase 2 trials are usually underpowered for reporting of efficacy outcomes,[3] Folegatti and colleagues have planned to assess them. We hope to read about the results of the vaccine trial soon.

We declare no competing interests.

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As a participant in the ChAdOx1 nCoV-19 vaccine trial, I was particularly excited to read the preliminary report by Pedro Folegatti and colleagues[1] and congratulate the team on their promising results.

However, glancing at the summary of adverse reactions in figure 1 of the Article,[1] I was uncomfortably surprised to discover that I had unmasked myself. I self-reported moderate feverishness, which was experienced by 21% (12 of 56) of the ChAdOx1 nCoV-19 paracetamol group and none of the associated control group.

Other symptoms might also provide insight to participants: the presence of malaise and myalgia were predictive of allocation to the experimental group (positive predictive value of 78% for malaise and 71% for myalgia, calculated for the combined cohort of participants who received ChAdOx1 nCoV-19 vaccine with and without paracetamol). The positive predictive values increase if the timing or severity of symptoms is considered. These symptoms were common in participants who received the ChAdOx1 nCoV-19 vaccine (59% [323 of 543] of participants had malaise and 59% [321 of 543] of participants had myalgia) so many participants could have at least partly unmasked themselves.

In most trials, this unmasking might have been inconsequential as few participants would analyse preliminary results in detail. However, this trial is different. Recruitment was targeted at scientifically literate health-care workers near academic centres. The article was emailed by the study team to all participants, who have substantial personal interests in the results. The charts showing side-effects are prominent and easy to interpret. I fear that I am not the only person with an inappropriate insight into my allocation.

Relaxation of prophylactic measures (eg, physical distancing) due to perceived immunity by participants who had severe side-effects could cause a false-negative trial result with substantial consequences for public health and the economy. Although there is clearly public interest in interim publication of trial data, this interest should be balanced against the risk of compromising the integrity of the trial.

I am a participant in the ChAdOx1 nCoV-19 vaccine trial.

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Authors' reply

We agree with Anil Chauhan and colleagues that recording of anaphylaxis is important when testing a new vaccine. All participants in the trial were observed in the clinic for at least 30 min after they were vaccinated, and no cases of anaphylaxis occurred.[1]

1067 participants in the trial were randomly assigned (1:1) to receive either ChAdOx1 nCoV-19 or the control meningococcal conjugate vaccine (MenACWY), with an additional ten participants enrolled into a non-randomised subgroup, who all received two doses of the ChAdOx1 nCoV-19 vaccine. There were no additional criteria for the selection of participants for this group, other than their willingness to receive two doses of vaccine and attend additional study visits for blood sampling.

Chauhan and colleagues emphasise the different numbers of participants analysed at different timepoints in figure 3.[1] The variation in numbers is due to the timing of blood sampling for different groups in the trial. Only a subset of participants enrolled in group 1 or group 3 had blood samples taken at days 7, 14, and 56. All participants had baseline and day 28 samples taken but, due to low laboratory capacity, not all samples had been tested at the time of publication and so we reported the data that were available at the time of publication. Further data on immunogenicity will be available in the future.

Receipt of prophylactic paracetamol with the ChAdOx1 nCoV-19 vaccine did not result in higher rates of