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.

SARS-CoV-2 seroprevalence in Spain

We read with great interest the Article by Marina Pollán and colleagues.[1] It is remarkable that in the Spanish population, the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) seroprevalence as of May, 2020, appeared to be the same in men (immunoassay positive 4·6%, 95% CI 4·2–5·0) and women (4·6%, 4·2–5·0). Of note, neither Pollán and colleagues nor Eckerle and Meyer's linked Comment[2] mention the sex distribution throughout different age strata. This is a missed opportunity because Spain, among other countries, showed marked age-specific sex differences among confirmed SARS-CoV-2 cases during the first months of the pandemic.[3]

To depict this difference, we used data provided by governmental health authorities from countries in Europe, as well as the USA and Canada (appendix). In all 12 countries with data available on sex distribution across different ages, the proportion of men with confirmed SARS-CoV-2 was lower than for women in the age group older than 80 years, and was similar to the proportion of older men in the general population. Additionally, some countries also showed sex differences in younger age groups. For example in Spain, as of May 5, 2020, the proportion of men aged 20–39 years with confirmed SARS-CoV-2 was only 36% (women accounted for 64%),[3] which was markedly lower than the proportion of men (50%) aged 20–39 years reported in the general population.[4]

See Online for appendix

Nationwide seroepidemiological studies such as ENE-COVID[1] should provide details on age-stratified sex distribution to clarify whether sex differences are due to the testing policies or acceptability, or due to exposure differences (ie, more women in high risk groups such as health-care workers). In countries with large sex differences, such as Belgium, the UK, or Spain, this information might help to elucidate whether SARS-CoV-2 diagnoses have been disproportionately overlooked in specific populations (eg, in young men).

See Online for appendix

We declare no competing interests.

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Marina Pollán and colleagues[1] conclude that herd immunity is difficult to achieve because the seroprevalence by point-of-care testing after the first wave of the epidemic was only 5% (95% CI 4·7–5·4).

Antibodies only neutralise the virus in interstitial fluid and the mucosal surface. The intracellular virus that causes illness is countered by cellular immunity mediated by T cells and macrophages. This process is part of a complex pathway and cannot be measured easily, as shown by a report from Sweden.[2] Thus, measuring antibodies and assuming that a population is susceptible lacks a holistic view because Pollán and colleagues failed to take into account the two essential parts of viral immunology. Reinfection with the same strain of SARS-CoV-2 is very rare and protection is offered by cellular immunity and antibodies working in tandem.

Long and colleagues[3] have shown that the antibody response in asymptomatic COVID-19 cases is weak. Asymptomatic individuals probably have effective cellular immunity that destroys the intracellular virus, even though there is no robust antibody response to neutralise SARS-CoV-2 on the mucosal surface, as the virus enters the respiratory tract or blood stream. A virus has to enter the cell to replicate and cause systemic illness. Cellular immunity is memory-driven, similar to humoral immunity, and might perhaps be more crucial and effective in COVID-19. Pollán and colleagues' findings revealed that relying on SARS-CoV-2 antibodies alone as a test for prevalence and immunity goes against the fundamental tenets of viral immunology.

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Authors' reply

We thank Christian Hoffmann and Eva Wolf for pointing out the contradiction of similar severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) seroprevalence figures between men and women in our nationwide study,[1] compared with the distribution of confirmed COVID-19 cases in the most severely affected countries. Following their suggestion, we provide seroprevalence data stratified by age and sex (appendix) to show that infection rates were similar in men and women during the first epidemic wave in Spain.

According to the consolidated data from the Spanish National Epidemiological Surveillance Network, men account for 43% of COVID-19

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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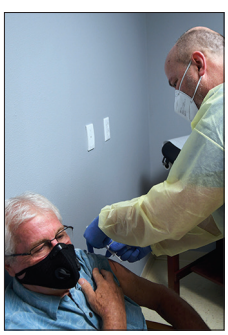
ChAdOx1 nCoV-19 vaccine for SARS-CoV-2


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