[1] Epidemiology, Biostatistics and Prevention Institute, University of Zurich, Hirschengraben 84, 8001 Zurich, Switzerland

[2] Population Heath Laboratory (#PopHealthLab), University of Fribourg, Fribourg, Switzerland

[3] School of Population and Global Health, McGill University, Montreal, Canada

miloalan.puhan@uzh.ch

Cite this as: *BMJ* 2021;373:n917
http://dx.doi.org/10.1136/bmj.n917
Published: 12 April 2021

COVID ANTIBODIES FROM INFECTION OR VACCINATION

Overcoming spectrum bias for accurate SARS-CoV-2 seroprevalence estimates

Milo A Puhan, [1] Arnaud Chiolero, [2,3] Jan Fehr, [1] Stéphane Cullati[2], On behalf of the Corona Immunitas Research Group

Repeated population based SARS-CoV-2 seroprevalence studies provide evidence on how immunity develops in a population. They are especially relevant now, as we are at a turning point with vaccines that greatly accelerate the development of immunity.

A surprisingly low seroprevalence of 14% was recently reported for the UK.[1] The cumulative proportion of confirmed infected people in the UK (6.3%) is very close to that of Switzerland (6.6%).[2] Assuming that only around one in 3-4 infected people are diagnosed,[3] a seroprevalence of 20-25% would be expected, without people who have been vaccinated. This is consistent with what has been observed for different cantons of Switzerland in the Corona Immunitas programme.[4] Switzerland is experiencing a slow start to its vaccination programme, and the effect of vaccination on seroprevalence estimates is negligible. In the UK, however, with 33 doses given per 100 people[2] and the cumulative proportion of infected people, the seroprevalence should be higher than 14%.

One possible reason for this low estimate is the use of self-administered lateral flow tests in the React-2 study, so seroprevalence estimates were adjusted for the sensitivity (84.4%) and specificity (98.6%) of these tests.[2] The test performance estimates were based on the analyses of clinically ill people with SARS-CoV-2 infection (cases) and pre-pandemic samples (controls), leading to a substantial spectrum bias.[5] This is a major problem for population based studies as many people with past infections have had a mild or asymptomatic course, which is more difficult to detect than moderate to severe infections.

Commercially available tests based on venous blood miss up to 40% of infections,[6] and lateral flow tests are clearly even less accurate and probably have a sensitivity lower than 84.4% in population based samples. In Switzerland, Corona Immunitas chose a sophisticated test, with test performance estimates based on a population based sample.[6] This is more laborious and costlier but gives a more accurate picture of immunity development in a population.

Competing interests: None declared.

Full response at: https://www.bmj.com/content/372/bmj.n561/rr.

1 Wise J. Covid-19: One in seven people in England have antibodies from infection or vaccination, finds study. *BMJ* 2021;372:n561. doi: 10.1136/bmj.n561 pmid: 33632718

2 Our World in Data. United Kingdom: coronavirus pandemic country profile. https://ourworldindata.org/coronavirus/country/united-kingdom?country=GBR~CHE.

3 Office for National Statistics. Coronavirus (covid-19) infection survey antibody data for the UK, March 2, 2021, https://www.ons.gov.uk/peoplepopulationandcommunity/healthandsocialcare/conditionsanddiseases/articles/coronaviruscovid19infectionsurveyantibodydatafortheuk/2march2021.

4 Corona Immunitas programme of the Swiss School of Public Health. https://www.corona-immunitas.ch/en/.

5 Deeks JJ, Dinnes J, Takwoingi Y, etalCochrane COVID-19 Diagnostic Test Accuracy Group. Antibody tests for identification of current and past infection with SARS-CoV-2. *Cochrane Database Syst Rev* 2020;6:CD013652. doi: 10.1002/14651858.CD013652. pmid: 32584464

6 Fenwick C, Croxatto A, Coste AT, etal. Changes in SARS-CoV-2 spike versus nucleoprotein antibody responses impact the estimates of infections in population-based seroprevalence studies. *J Virol* 2021;95:e01828-20.doi: 10.1128/JVI.01828-20. pmid: 33144321