Dynamic IgG seropositivity after rollout of CoronaVac and BNT162b2 COVID-19 vaccines in Chile: a sentinel surveillance study

Denis Sauré, Miguel O'Ryan, Juan Pablo Torres, Marcela Zuniga, Emilio Santelices, Leonardo J Basso

Summary

Background By July 14, 2021, 81·3 % of adults (aged ≥18 years) in Chile had received a first SARS-CoV-2 vaccine and 72·3% had received a second SARS-CoV-2 vaccine, with the majority of people given Sinovac's inactivated CoronaVac vaccine (75·3% of vaccines dispensed) or Pfizer–BioNTech's mRNA BNT162b2 vaccine (20·9% of vaccines dispensed). Due to the absence of simultaneous real-world data for these vaccines, we aimed to compare SARS-CoV-2 IgG positivity between vaccines using a dynamic national monitoring strategy.

Methods From March 12, 2021, 28 testing stations for SARS-CoV-2 IgG detection were installed in hotspots based on cellular-phone mobility tracking within the most populated cities in Chile. Individuals voluntarily approaching the testing stations were invited to do a lateral flow test by finger prick and respond to a questionnaire on sociodemographic characteristics, vaccination status (including type of vaccine if one was received), variables associated with SARS-CoV-2 exposure, and comorbidities. We compared the proportion of individuals testing positive for anti-SARS-CoV-2 IgG across sites by week since vaccination between recipients of CoronaVac and BNT162b2. Unvaccinated participants served as a control population and were matched to vaccinated individuals on the basis of date of presentation to the testing station, gender, and age group. Individuals were excluded from the analysis if they were younger than 18 years, had no declared gender, had an invalid IgG test result, had previously tested positive for SARS-CoV-2 infection on PCR, could not recall their vaccination status, or had been immunised against COVID-19 with vaccines other than CoronaVac or BNT162b2. Here, we report data collected up to July 2, 2021.

Findings Of 64 813 individuals enrolled, 56 261 were included in the final analysis, of whom 33 533 (59·6%) had received at least one dose of the CoronaVac vaccine, 8947 (15·9%) had received at least one dose of the BNT162b2 vaccine, and 13 781 (24·5%) had not received a vaccine. SARS-CoV-2 IgG positivity during week 4 after the first dose of CoronaVac was 28·1% (95% CI 25·0–31·2; 220 of 783 individuals), reaching a peak of 77·4% (75·5–79·3; 1473 of 1902 individuals) during week 3 after the second dose. SARS-CoV-2 IgG positivity during week 4 after the first dose of the BNT162b2 vaccine was 79·4% (75·7–83·1; 367 of 462 individuals), increasing to 96·5% (94·9–98·1; 497 of 515 individuals) during week 3 after the second dose and remaining above 92% until the end of the study. For unvaccinated individuals, IgG seropositivity ranged from 6·0% (4·4–7·6; 49 of 810 individuals) to 18·7% (12·5–24·9; 28 of 150 individuals) during the 5 month period. Regression analyses showed that IgG seropositivity was significantly lower in men than women and in people with diabetes or chronic diseases for CoronaVac vaccine recipients ($p<0·0001$), and for individuals aged 60 years and older compared with people aged 18–39 years for both vaccines ($p<0·0001$), 3–16 weeks after the second dose.

Interpretation IgG seropositivity was lower after CoronaVac than after BNT162b2 and declined over time since vaccination for CoronaVac recipients but not BNT162b2 recipients. Prolonged IgG monitoring will allow further evaluation of seropositivity overtime, providing data, in conjunction with effectiveness studies, for possible future re-assessment of vaccination strategies.

Funding Instituto Sistemas Complejos de Ingeniería and Ministerio de Salud Chile.

Lancet Infect Dis 2021

Published Online September 9, 2021 https://doi.org/10.1016/S1473-3099(21)00479-5

See Online/Comment https://doi.org/10.1016/S1473-3099(21)00561-2

For the Spanish translation of the abstract see Online for appendix 1

Departamento de Ingeniería Industrial (D Sauré PhD) **and Departamento de Ingeniería Civil** (Prof L J Basso PhD), **Universidad de Chile, Santiago, Chile; Instituto Sistemas Complejos de Ingeniería, Santiago, Chile** (D Sauré, Prof L J Basso); **Programa de Microbiología y Micología, Instituto de Ciencias Biomédicas and Instituto Milenio de Inmunidad e Inmunoterapia** (Prof M O'Ryan MD), **Departamento de Pediatría y Cirugía Infantil** (J P Torres MD), **and Departamento de Salud Pública** (E Santelices MD), **Universidad de Chile, Santiago, Chile; Ministerio de Salud, Santiago, Chile** (M Zuniga MBA)

Correspondence to: Prof Leonardo J Basso, Departamento de Ingeniería Civil, Instituto Sistemas Complejos de Ingeniería, Universidad de Chile, Santiago 8370456, Chile **lbasso@ing.uchile.cl**

Introduction

COVID-19 vaccination coverage in Chile is one of the highest globally: by July 14, 2021, approximately 5 months after the launch of the vaccination campaign,[1] 81·3% of 15 200 840 eligible adults (aged ≥18 years) had received at least one dose, and 72·3% had received two doses, of a COVID-19 vaccine. Sinovac's inactivated SARS-CoV-2 CoronaVac vaccine represented 75·3% of the vaccine doses dispensed (18·0 million doses) and Pfizer–BioNTech's mRNA vaccine BNT162b2 represented 20·9% (5·0 million doses).[1] Since the introduction of adenoviral-vectored vaccines (Oxford–AstraZeneca's ChAdOx1 nCoV-19 and CanSino Biologics' Ad5-nCoV) on June 1, 2021, and April 28, 2021, respectively, nearly 874 000 doses of these vaccines have been dispensed in Chile. According to Chile's vaccination plan, health-care personnel were

Research in context

Evidence before this study

Vaccination is crucial for the control of COVID-19 and to date several vaccines have been deployed. It is important to assess and compare the real-life immunogenicity and effectiveness of the licensed vaccines. We searched PubMed and medRxiv for articles published up to July 14, 2021, using the search terms ("COVID-19" OR "SARS-CoV-2" OR "2019-nCoV") AND ("vaccine" OR "vaccination") AND ("immunogenicity" OR "efficacy" OR "effectiveness"); we then repeated the search by replacing the ("immunogenecity" OR "efficacy" OR "effectiveness) with "rollout" in an attempt to identify more studies. Our search yielded two studies of vaccine effectiveness, including one from Israel that assessed the effectiveness of Pfizer–BioNTech's mRNA BNT162b2 vaccine against symptomatic infection and one study from Scotland that compared the effectiveness of BNT162b2 with that of Oxford–AstraZeneca's ChAdOx1 nCoV-19. In this study from Scotland, a single dose of the BNT162b2 vaccine was 91% effective (95% CI 85–94) and of the ChAdOx1 vaccine was 88% effective (95% CI 75–94) in reducing COVID-19 hospital admissions 28–34 days after vaccination. The combined vaccine effect against hospital admission due to COVID-19 was 83% (95% CI 72–89) for people aged 80 years and older at 28–34 days after vaccination. For inactivated vaccines, we found no studies comparing immunogenicity, one underpowered study assessing the effectiveness of Sinovac's CoronaVac in health-care workers, and one non-peer-reviewed study in older individuals done in a setting with substantial SARS-CoV-2 gamma (P.1) variant circulation, which showed a decline in Coronavac vaccine effectiveness against RT-PCR confirmed SARS-CoV-2 infection from 62% (95% CI 35–78) in people aged 70–74 years to 28% (0·6–48) in people aged 80 years and older. Population-based studies simultaneously assessing the performance of two or more vaccines are scarce.

Added value of this study

To the best of our knowledge, this is the only study to date to compare population IgG immunity after vaccination with CoronaVac (Sinovac Life Sciences, Beijing, China) and BNT162b2 vaccine in nearly 60 000 individuals in a country with rapid vaccine rollout. 4 weeks after one dose, the IgG seropositivity among CoronaVac recipients was 28·1% (95% CI 25·0–31·2) and among BNT162b2 recipients was 79·4% (75·7–83·1%). 3 weeks after the second vaccine dose, the IgG positivity was 77·4% (75·5–79·3) for the CoronaVac vaccine and 96·5% (94·9–98·1) for the BNT162b2 vaccine. A steady decrease in IgG seropositivity was observed in CoronaVac recipients 4–16 weeks after the second dose, whereas seropositivity remained high and stable in people who had received the BNT162b2 vaccine. IgG seropositivity was significantly lower in participants aged 60 years and older than in adults aged 18–39 years for both vaccines and significantly lower in men than women for the CoronaVac vaccine.

Implications of all the available evidence

Overall, IgG positivity for CoronaVac recipients reached 77% after two doses, and a single dose led to low IgG positivity levels (ie, seropositivity of 28%). Seropositivity in BNT162b2 vaccine recipients surpassed 95% after two doses and 80% after one vaccine dose. A steady decline in IgG seropositivity was observed for the CoronaVac vaccine from 4 weeks after full vaccination; however, this effect was not observed in people who had the BNT162b2 vaccine. Prolonged IgG monitoring will enable further evaluation of seropositivity over time, providing data in conjunction with effectiveness studies, for possible future reassessment of vaccination strategies.

vaccinated first, followed by an age-descending strategy, in addition to teachers and school staff, and essential workers. At the time of writing, individuals aged 12–17 years are elegible for vaccination as well. By early July, 2021, nearly 88% of adults aged 60 years and older in Chile had received their first vaccine dose (appendix 2 p 17).

See Online for appendix 2

Results from a non-peer reviewed study of Brazilian health-care workers indicated that efficacy of the inactivated CoronaVac vaccine was 50% for PCR-positive SARS-CoV-2 infections requiring medical intervention and 78% for PCR-positive SARS-CoV-2 infections not requiring medical intervention.[2] For the BNT162b2 vaccine, a multinational trial reported 95% efficacy for COVID-19 in people aged 16 years and older.[3] The Chilean Health Ministry reported that the CoronaVac vaccine had 65·9% effectiveness for symptomatic infection and 87·5% effectiveness for hospital admission in people aged 16 years and older.[4]

In March, 2021, when variants of concern were emerging (appendix 2 p 18), we initiated COVID-19 IgG surveillance in large cities in Chile to enable dynamic tracking of IgG positivity rates,[5] based on the implementation of strategically located testing stations, to obtain a geographically diverse representation within each city. In this study, we report results from the first 64 813 people tested up to July 2, 2021.

Methods

Study design and participants

From March 12, 2021, all 29 health services in the Chilean public health-care system were invited to participate in the surveillance programme, of which 28 had agreed by the cutoff date (July 2, 2021); the remaining service began data collection on July 8, 2021. As of July 2, 2021, 28 testing stations strategically located in public open spaces had been implemented (Araucanía Sur Health Service participated with two stations, and the Metropolitan Central, Occidente, and Norte Health Services chose to operate two stations jointly). These stations were deployed in the most populated cities in Chile, aiming to replicate the diverse geographical

distribution of the population of such cities. We used an optimisation model (mixed-integer program) based on weekly analysis of national mobile phone mobility data, facilitated by Chile's largest telecommunications agency (Empresa Nacional de Telecomunicaciones, Santiago, Chile), to select sites with high traffic volume and wide county-level distribution of people, and to correct deviations from the target geographical distribution (elicited from census data;[6] appendix 2 p 1).

Between March 12 and July 2, 2021, adults (aged ≥18 years) approaching the testing sites were invited to participate. Testing stations included lateral flow tests, a laptop computer with internet access, and two study personnel among whom there was at least one trained health-care worker who did the test and read the result. Personnel selection and training were done by staff from Subsecretaria de Redes Asistenciales (Health Ministry, Santiago, Chile). After written informed consent had been obtained, participants were asked to provide a blood sample by finger prick, which was immediately applied to the lateral flow test. During the 15-min interval required for the test, the second study person completed an online questionnaire on behalf of the participant, including data on sociodemographic characteristics, vaccination status and type of vaccine, commuting habits, variables associated with SARS-CoV-2 exposure, and comorbidities (appendix 2 p 2). Results were instantly uploaded to a centralised database harboured on the servers of the Instituto Sistemas Complejos de Ingeniería, where the data were stored in an anonymised format.

The study was approved by the Comité de Ética de Investigación en Seres Humanos (Universidad de Chile, Santiago, Chile).

SARS-CoV-2 IgG testing

The COVID-19 IgG/IgM Rapid Test kit (CTK Biotech, San Diego, CA, USA) was used according to the manufacturer's specifications (96·7% sensitivity and 98·1% specificity for detection of SARS-CoV-2 IgG[7]). Test results were read in 15 min by trained study personnel and entered on the electronic platform. Results were categorised as positive (visible bands on the IgG and test control positions), negative (visible band only on the test control position), or invalid (absence of any visible band); where possible, invalid outcomes were re-tested on-site and such outcomes were registered only when re-testing was not feasible. For this study, we only considered IgG results; individuals with a positive IgM result were advised to have PCR testing.

Statistical analysis

Data are presented as counts, percentages, and 95% CIs. Comparisons between groups were done using standard two proportion Z tests. Data from all participants with complete records were included in the analysis, with the exception of people younger than 18 years, with no declared gender, with a previous positive PCR test result, or with an invalid lateral flow assay result. Participants who did not recall their vaccination status, or were immunised with vaccines other than CoronaVac or BNT162b2, were also excluded from the analysis. Analyses were done using the open-source Julia programming language;[8] the integer programs for the optimal location of testing sites were solved using the Gurobi solver.[9] Time periods are presented in terms of the number of weeks elapsed since vaccination: week 1, therefore, included days 0–6 after vaccination, and week 2 included days 7–13 days. We also performed multivariate logistic regression analysis to analyse IgG positivity starting from week 3 after the second dose.

Seropositivity for the different weeks after a dose of either vaccine included individuals tested on different dates; thus, to obtain an unbiased comparison with unvaccinated individuals, we adjusted these groups of vaccinated individuals tested on different dates (grouped by testing date) by matching them with the distribution of the vaccinated participants according to date of presentation to the testing station, gender, and age group (≤39 years, 40–49 years, 50–59 years, or ≥60 years; appendix 2 p 3). Our analysis pertains to proportions of individuals testing positive for IgG across all test sites, and not to antibody titres.

Role of the funding source

The funders of the study had no role in the study design, data collection, data analysis, data interpretation, or writing of the report.

Results

64 813 individuals were enrolled, of whom 59 987 were eligible for inclusion in the study. Reasons for exclusion were incomplete information on vaccination status (n=3921), immunisation with SARS-CoV-2 vaccines other than CoronaVac or BNT162b2 (n=533), undeclared gender (n=54), age younger than 18 years (n=251), invalid test result (n=39), or a combination of these (n=28; appendix 2 p 5). Compared with unvaccinated participants, vaccinated individuals were older and had more comorbidities (table 1), an expected outcome due to the national vaccination priority groups. A higher proportion of vaccinated participants were female and Chilean than were unvaccinated participants. Baseline characteristics were similar between the CoronaVac and BNT162b2 vaccine recipients, although the CoronaVac group had a higher proportion of individuals aged 60 years or older than did the other groups, which was also expected since early vaccination efforts started among older age groups, using mostly CoronaVac. All counties within each of the 28 participating health services were reasonably well represented in the study population (appendix 2 p 19). Information on the contribution of each testing site to the overall population study and a comparison between the sample and the national population are available in appendix 2 (pp 6–8).

	Overall (n=59 987)	Unvaccinated (n=14 739)	CoronaVac (n=35 696)	BNT162b2 (n=9552)
Age, years				
18–39	27 289 (45·5%)	9708 (65·9%)	13 469 (37·7%)	4112 (43·0%)
40–49	12 532 (20·9%)	2967 (20·1%)	7197 (20·2%)	2368 (24·8%)
50–59	10 824 (18·0%)	1576 (10·7%)	6667 (18·7%)	2581 (27·0%)
≥60	9342 (15·6%)	488 (3·3%)	8363 (23·4%)	491 (5·1%)
Gender				
Male	24 652 (41·1%)	6589 (44·7%)	14 285 (40·0%)	3778 (39·6%)
Female	35 335 (58·9%)	8150 (55·3%)	21 411 (60·0%)	5774 (60·4%)
Nationality				
Chilean	57 599 (96·0%)	13 758 (93·3%)	34 662 (97·1%)	9179 (96·1%)
Other	2388 (4·0%)	981 (6·7%)	1034 (2·9%)	373 (3·9%)
Previous positive COVID-19 PCR	3726 (6·2%)	958 (6·5%)	2163 (6·1%)	605 (6·3%)
Previous positive COVID-19 IgG	876 (1·5%)	82 (0·6%)	659 (1·8%)	135 (1·4%)
Times leaving home per week				
<3	19 443 (32·4%)	5187 (35·2%)	11 179 (31·3%)	3077 (32·2%)
3–5	20 939 (34·9%)	4963 (33·7%)	12 688 (35·5%)	3288 (34·4%)
6–7	15 324 (25·5%)	3519 (23·9%)	9297 (26·0%)	2508 (26·3%)
>7	4281 (7·1%)	1070 (7·3%)	2532 (7·1%)	679 (7·1%)
Comorbidities				
Obesity	2834 (4·7%)	615 (4·2%)	1746 (4·9%)	473 (5·0%)
High blood pressure	9285 (15·5%)	831 (5·6%)	7087 (19·9%)	1367 (14·3%)
Diabetes	4626 (7·7%)	457 (3·1%)	3418 (9·6%)	751 (7·9%)
Cancer	650 (1·1%)	69 (0·5%)	484 (1·4%)	97 (1·0%)
Chronic pulmonary disease	2737 (4·6%)	531 (3·6%)	1784 (5·0%)	422 (4·4%)
Chronic cardiovascular disease	1532 (2·6%)	201 (1·4%)	1138 (3·2%)	193 (2·0%)

Data are n (%).

Table 1: **Baseline characteristics of study population by vaccination status**

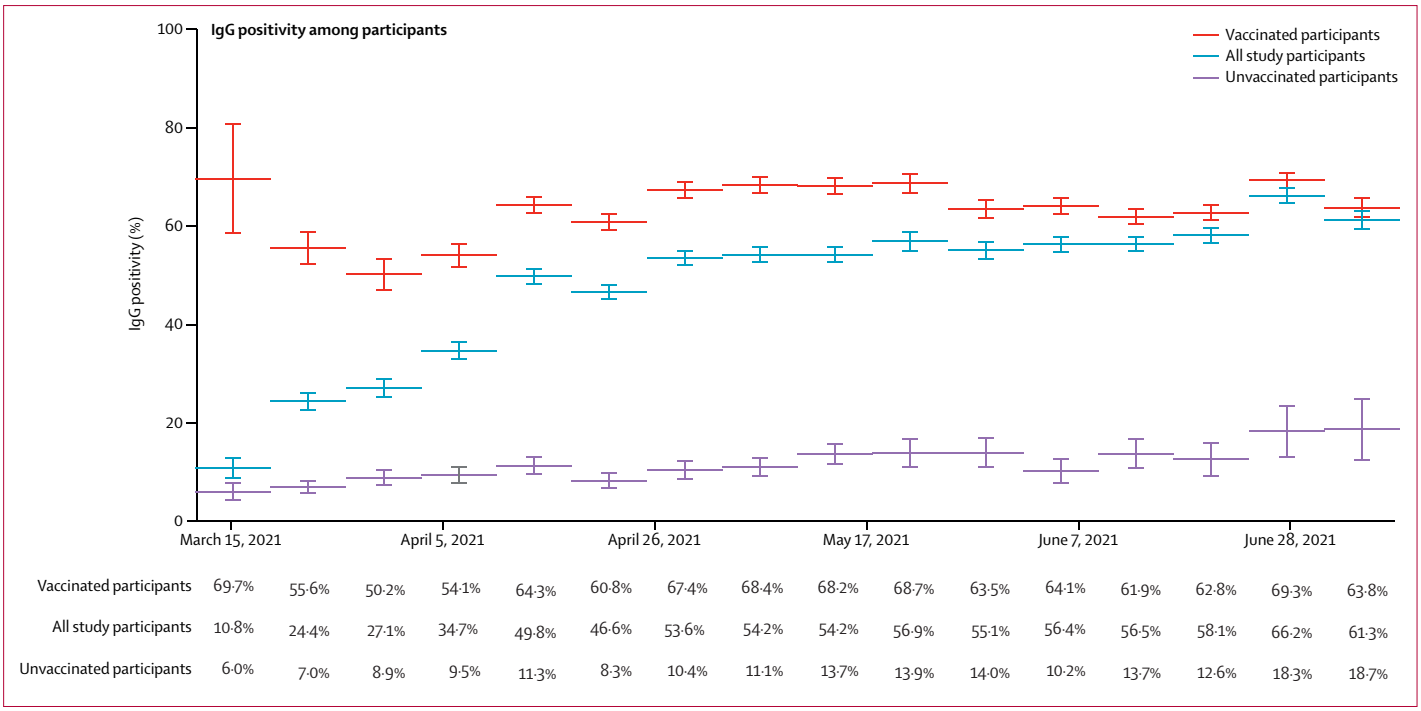
Among 59 987 eligible individuals, 3726 (6·2%) had a previous PCR positive result and were excluded from the final analysis (appendix 2 pp 9, 23). Of 56 261 individuals included in the analysis, 33 533 (59·6%) had received at least one dose of the CoronaVac vaccine, 8947 (15·9%) had received at least one dose of the BNT162b2 vaccine, and 13 781 (24·5%) had not received a vaccine. 3519 individuals had received one dose of the CoronaVac vaccine and 30 014 had received a second dose. 2192 individuals had received one dose of BNT162b2 and 6755 had received two doses.

Overall, weekly SARS-CoV-2 IgG positivity ranged from 10·8% (95% CI 8·7–12·9; 95 of 876 individuals) to 66·2% (64·6–67·8; 2297 of 3470 individuals) during the study period (figure 1). For unvaccinated individuals, weekly seropositivity ranged from 6·0% (4·4–7·6; 49 of 810 individuals) to 18·7% (12·5–24·9; 28 of 150 individuals). For individuals who received any vaccine, weekly SARS-CoV-2 IgG positivity ranged from 50·2% (47·1–53·3; 508 of 1012 individuals) to 69·7% (58·4–80·0; 46 of 66 individuals).

Participants who received their second vaccine dose 5 weeks or more after the first dose (175 [0·52%] of 33 533 CoronaVac recipients and 85 [0·95%] of 8947 BNT162b2 recipients) were not considered in the analysis that follows; appendix 2 p 10). The SARS-CoV-2 IgG positivity among CoronaVac vaccine recipients during week 4 after the first dose was 28·1% (95% CI 25·0–31·2; 220 of 783 individuals), increasing to a peak of 77·4% (75·5–79·3; 1473 of 1902 individuals) during week 3 after the second dose and decreasing to 47·3% (95% CI 44·9–49·7; 793 of 1677 individuals) during week 16 after the second dose (figure 2A). The SARS-CoV-2 IgG positivity among BNT162b2 vaccine recipients during week 4 after the first dose was 79·4% (75·7–83·1; 367 of 462 individuals), increasing to 96·5% (94·9–98·1; 497 of 515 individuals) during week 3 after the second dose and remaining above 92% until the end of the study (figure 2B). Seropositivity during the first week after vaccination was similar for both vaccines; the difference was not statistically significant (Z test p=0·29). The adjusted IgG seropositivity among matched unvaccinated individuals, was low, ranging from 11·5% (95% CI 10·6–12·4) to 17·0% (11·1–22·9; figure 2A, B). For any given number of weeks elapsed since vaccination, the difference in adjusted IgG positivity among matched individuals between CoronaVac and Pfizer did not surpass 3%.

Overall, IgG positivity in BNT162b2 vaccine recipients was significantly higher than that for CoronaVac vaccine recipients during weeks 1–4 after the first dose (21·1% [95% CI 19·6–22·6] for CoronaVac *vs* 47·7% [45·4–49·9] for BNT162b2; p<0·0001) and weeks 5–9 after the second dose (68·5% [67·6–69·3] for CoronaVac *vs* 95·7% [94·9–96·6] for BNT162b2; p<0·0001; table 2; appendix 2 pp 11–12). In the 4-week period after the first dose, cross-sectional SARS-CoV-2 IgG positivity by gender was similar for both vaccines (Z test p=0·081 for CoronaVac and p=0·092 for BNT162b2; and p values for weeks 5–9 after the second dose were p<0·0001 for CoronaVac and 0·052 for Pfizer). Seropositivity decreased with increasing age among CoronaVac vaccine recipients, whereas for BNT162b2 vaccine recipients, there was no difference in seropositivity among individuals aged 40 years and older in weeks 1–4 after the first dose and in seropositivity among individuals aged 18–59 years in weeks 5–9 after the second dose (appendix 2 p 13).

To further study and perform comparisons of the period after the second dose, we did multivariate logistic regression analyses starting at week 3 after the second dose, when overall positivity reached its maximum for CoronaVac. This regression analysis showed a significant decrease in seropositivity over time among CoronaVac vaccine recipients (weekly decrease in the log odds ratio coefficient –0·031, 95% CI –0·034 to –0·027). Furthermore, seropositivity was significantly lower among people aged 60 years and older than those aged 18–39 years (coefficient –0·086, –0·128 to –0·044) and among men than women (0·176, 0·146 to 0·206) for the CoronaVac vaccine (appendix 2 p 14). Diabetes and chronic diseases were associated with reduced seropositivity among CoronaVac recipients (appendix 2 p 14). No significant



Vaccinated participants	69·7%	55·6%	50·2%	54·1%	64·3%	60·8%	67·4%	68·4%	68·2%	68·7%	63·5%	64·1%	61·9%	62·8%	69·3%	63·8%
All study participants	10·8%	24·4%	27·1%	34·7%	49·8%	46·6%	53·6%	54·2%	54·2%	56·9%	55·1%	56·4%	56·5%	58·1%	66·2%	61·3%
Unvaccinated participants	6·0%	7·0%	8·9%	9·5%	11·3%	8·3%	10·4%	11·1%	13·7%	13·9%	14·0%	10·2%	13·7%	12·6%	18·3%	18·7%

Figure 1: **Seropositivity over time by vaccination status**
Vaccinated participants included individuals who had received one or two doses of CoronaVac or BNT162b2. Error bars show 95% CIs, horizontal lines show weekly positivity. Absolute numbers (ie, number of positive tests divided by number of tests overall) are presented in appendix 2 (p 15).

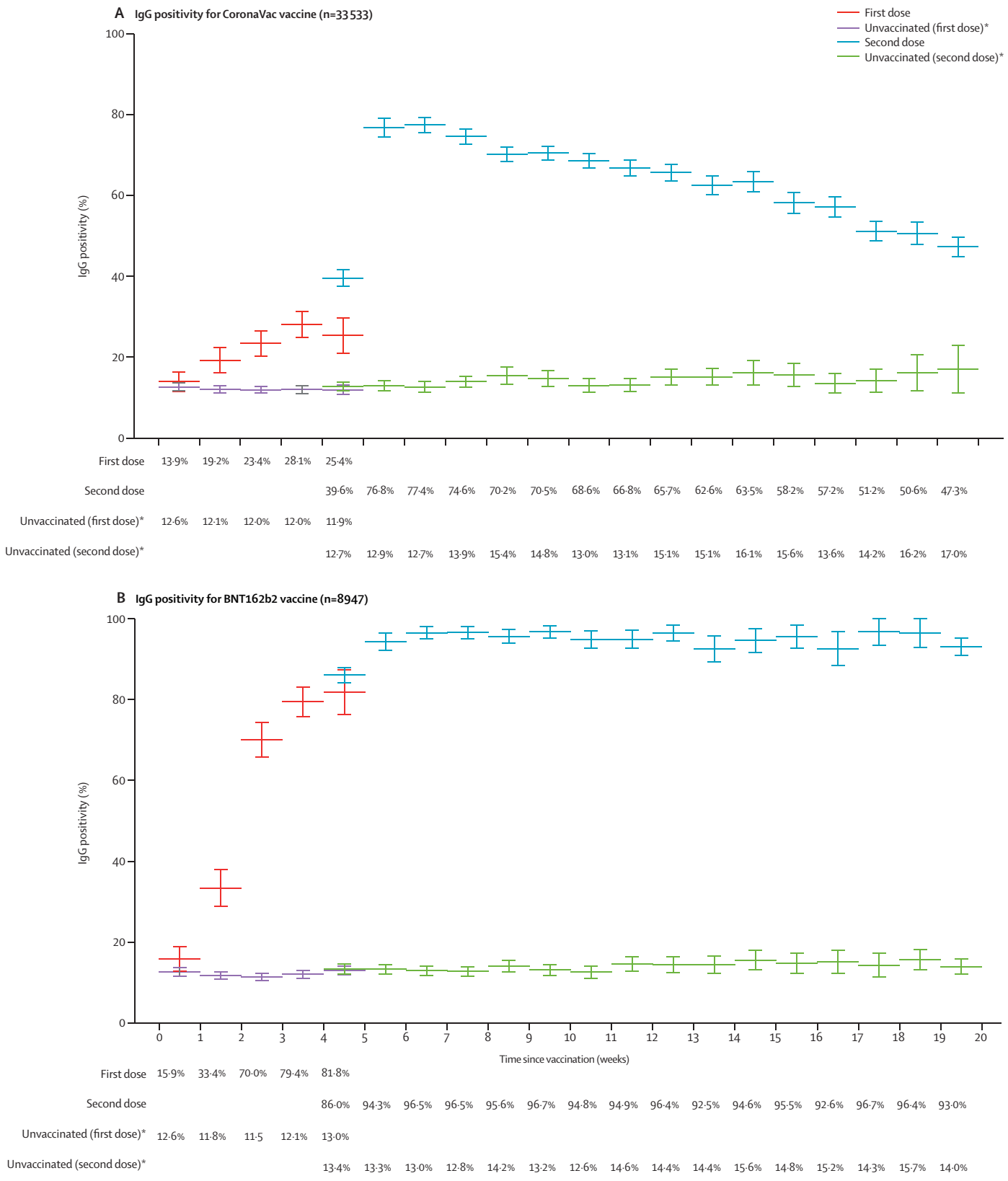
decreases in seropositivity over time, nor by gender or comorbidities, was observed among BNT162b2 vaccine recipients; however, lower seropositivity was observed among participants aged 60 years and older than those aged 18–39 years (–0·677, –0·857 to –0·497; appendix 2 p 14).

Discussion

COVID-19 IgG antibody testing with rapid lateral flow tests implemented in mobility hotspots throughout Chile seems to be an efficient strategy to compare population humoral immunity to different vaccines. In this study of data obtained 5 months after initiation of the vaccination campaign in Chile, IgG positivity reached 77·4% for recipients of the CoronaVac vaccine and 96·5% for recipients of the BNT162b2 vaccine, 3 weeks after receiving the second dose, when the adjusted seroprevalence among unvaccinated individuals was estimated to be no greater than 13%.

IgG positivity was lower in men than in women for the CoronaVac vaccine. Seropositivity was lower in individuals aged 60 years and older than in younger individuals for both vaccines. Seropositivity declined in CoronaVac recipients from 3 weeks after the second dose. The between-gender difference observed is not novel and has been reported for other vaccines.[10] The finding that seropositivity was lower in older individuals than in younger individuals was not reported in the phase 2 and 3 trials for these vaccines. The BNT162b2 vaccine induced high levels of humoral and T-cell responses, with robust interferon-γ T-cell responses to a peptide pool including the receptor-binding domain in both younger (<65 years) and older Chinese adults (aged ≥65 years), and geometric mean neutralising titres were 1·3 times higher in older participants than in a panel of COVID-19 convalescent human sera obtained at least 14 days after a positive SARS-CoV-2 PCR test.[11] An inverse association between age and neutralising responses after the first dose has been reported, with a more rapid decline observed in individuals aged 80 years and older.[12] Conversely, when the CoronaVac vaccine was tested in older adults (aged ≥60 years) in a dose-escalation study with a two-dose vaccination schedule (days 0 and 28), neutralising antibody responses to live SARS-CoV-2 were not reduced in this population and were similar to the responses observed among adults aged 18–59 years.[13] Results from a non-peer reviewed study done during a period of high P.1 SARS-CoV-2 variant circulation in Brazil[14] showed that, for CoronaVac, vaccine effectiveness 14 days or more after the second dose declined with increasing age (61·8% among individuals aged 70–74 years, 48·9% among individuals aged 75–79 years, and 28·0% among individuals aged ≥80 years).

A decline in seropositivity over time might prove important if associated with an increase in cases among vaccinated individuals, thus suggesting reduced protection. On the basis of our results, this decline might


A IgG positivity for CoronaVac vaccine (n=33 533)
First dose
Unvaccinated (first dose)*
Second dose
Unvaccinated (second dose)*
IgG positivity (%)
100
80
60
40
20
0
First dose 13·9% 19·2% 23·4% 28·1% 25·4%
Second dose 39·6% 76·8% 77·4% 74·6% 70·2% 70·5% 68·6% 66·8% 65·7% 62·6% 63·5% 58·2% 57·2% 51·2% 50·6% 47·3%
Unvaccinated (first dose)* 12·6% 12·1% 12·0% 12·0% 11·9%
Unvaccinated (second dose)* 12·7% 12·9% 12·7% 13·9% 15·4% 14·8% 13·0% 13·1% 15·1% 15·1% 16·1% 15·6% 13·6% 14·2% 16·2% 17·0%
B IgG positivity for BNT162b2 vaccine (n=8947)
IgG positivity (%)
100
80
60
40
20
0
0 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20
Time since vaccination (weeks)
First dose 15·9% 33·4% 70·0% 79·4% 81·8%
Second dose 86·0% 94·3% 96·5% 96·5% 95·6% 96·7% 94·8% 94·9% 96·4% 92·5% 94·6% 95·5% 92·6% 96·7% 96·4% 93·0%
Unvaccinated (first dose)* 12·6% 11·8% 11·5 12·1% 13·0%
Unvaccinated (second dose)* 13·4% 13·3% 13·0% 12·8% 14·2% 13·2% 12·6% 14·6% 14·4% 14·4% 15·6% 14·8% 15·2% 14·3% 15·7% 14·0%

	First dose (week 1–4)			Second dose (week 5–9)		
	CoronaVac	BNT162b2	p value*	CoronaVac	BNT162b2	p value*
Overall	21·1% (19·6–22·6); 624/2958	47·7% (45·4–49·9); 915/1920	<0·0001	68·5% (67·6–69·3); 8322/12 157	95·7% (94·9–96·6); 2160/2256	<0·0001
Gender						
Male	19·5% (17·3–21·8); 241/1233	49·9% (46·5–53·3); 410/822	<0·0001	64·7% (63·3–66·0); 3152/4875	94·7% (93·2–96·2); 801/846	<0·0001
Female	22·2% (20·2–24·2); 383/1725	46·0% (43·0–48·9); 505/1098	<0·0001	71·0% (70·0–72·0); 5170/7282	96·4% (95·4–97·4); 1359/1410	<0·0001
Age, years						
18–39	24·6% (22·4–26·8); 359/1458	51·6% (48·5–54·6); 524/1016	<0·0001	72·2% (70·9–73·6); 3098/4289	97·7% (96·6–98·7); 794/813	<0·0001
40–49	20·1% (17·3–22·9); 154/766	43·9% (39·5–48·4); 210/478	<0·0001	69·4% (67·6–71·3); 1597/2300	96·5% (94·9–98·0); 520/539	<0·0001
50–59	16·3% (13·3–19·4); 93/569	42·8% (37·9–47·8); 164/383	<0·0001	70·3% (68·4–72·2); 1597/2272	96·7% (95·5–98·0); 739/764	<0·0001
≥60	10·9% (6·2–15·7); 18/165	39·5% (24·9–54·1); 17/43	<0·0001	61·6% (59·9–63·3); 2030/3296	76·4% (69·4–83·5); 107/140	0·0002

Data are seropositivity (95% CI); n/N. *Comparison of CoronaVac versus BNT162b2, using a one-sided two proportion Z test.

Table 2: **Seropositivity after first and second vaccination for CoronaVac and BNT162b2 vaccines, by gender and age**

become important for CoronaVac, but a more prolonged observation period is required. Investigation of the correlation between IgG positivity measured by the lateral flow test used in this study and neutralising antibodies is ongoing[15,16] and will be highly relevant since neutralising antibodies are considered a more likely correlate of protective immunity than IgG. If a further decline over time is observed and is paralleled with increasing cases, a booster vaccine might have to be considered in the future.

Consistent with antibody prevalence results from clinical trials,[17] IgG positivity was low with one dose of the inactivated CoronaVac vaccine, which did not exceed 29% at 4 weeks after the first dose, whereas IgG positivity had reached 79% with the BNT162b2 vaccine at the same timepoint. This observation might also have programmatic implications, supporting the consideration of using one dose of BNT162b2 as a strategy to increase coverage in countries with low vaccine supply.

We found no studies comparing the immunogenicity of two or more vaccines, and population-based studies comparing the effectiveness of two or more vaccines were scarce. In Scotland, effectiveness of the first dose of the BNT162b2 mRNA vaccine was 91% (95% CI 85–94) and of ChAdOx1 was 88% (75–94) against COVID-19 hospital admission at 28–34 days after vaccination. As a result of the overall vaccination programme, combined vaccine effects against hospital admission due to COVID-19 was 83% (95% CI 72–89) at 28–34 days post-vaccination for individuals aged 80 years and older.[18,19]

The immunogenicity results of our study are consistent with preliminary effectiveness results for both vaccines. At 3–16 weeks after the second dose of CoronaVac vaccine, the IgG positivity was 64·5%, compared with an effectiveness against symptomatic infection of 65·9% 14 days or more after the second dose, as reported in a study in Chile.[4] For the BNT162b2 vaccine, 2–16 weeks after the second dose, IgG positivity was 95·2% compared with an estimated effectiveness against symptomatic infection of 94% in a study from Israel, 7 or more days after the second dose.[20]

Our study has several limitations. SARS-CoV-2 IgG detected by the lateral flow test used in this study does not assure protection, and therefore, a correlation study with neutralisation antibody testing is warranted. Although the lateral flow test used (COVID-19 IgG/IgM Rapid Test kit) had not been evaluated for response to vaccination, this test showed high IgG positivity for the two vaccines used in Chile. The test had reported high sensitivity and specificity for detection of SARS-CoV-2 infection.[21,22] It is unclear if the test will perform similarly well for other vaccines that have been recently introduced in Chile. Importantly, considerable variability exists among lateral flow tests[23] and interpretations might be misleading if a test with with low sensitivity and specificity is used. Thus, we chose to use a high-yield test for targeting the nucleocapsid and spike proteins. Additional limitations are those associated with self-selection and recall biases (eg, vaccination dates) arising in part because of the self-reported nature of our data. Although we cannot fully assure general population

Figure 2: **Seropositivity after first or second dose for recipients of the CoronaVac or BNT162b2 vaccines and unvaccinated individuals over time**
(A) CoronaVac vaccine. (B) BNT162b2 vaccine. Error bars show 95% CIs, horizontal lines show weekly positivity. Absolute numbers (ie, number of positive tests divided by number of tests overall) are presented in appendix 2 (p 16). *IgG positivity for unvaccinated individuals was adjusted for the specific time periods, by matching with the distribution of the vaccinated subset according to date of presentation to a testing station, gender, and age group (appendix 2 p 1).

representability in terms of socio-demographic covariates, we believe that biases in this dimension would not significantly affect comparison of seropositivity over time or across vaccines. We did not include a control group matched by gender and age; however, we adjusted for age, gender, and timepoint when comparing vaccine groups with unvaccinated individuals. The ethnicity of participants was not recorded, thus the observed results do not allow any inferences about immune responses by ethnic group.

In conclusion, IgG positivity remained below 29% after the first dose for CoronaVac recipients, peaking at 77% 3 weeks after the second dose and decreasing thereafter. By contrast, among BNT162b2 recipients, IgG positivity was high (>70%) from 3 weeks after the first dose, even higher (>96%) 3 weeks after the second dose, and remained above 92% until the end of the study. This dynamic monitoring system can be replicated in other regions to longitudinally characterise population IgG positivity to SARS-CoV-2 in the presence or absence of vaccination and determine antibody waning over time, providing data, in conjunction with effectiveness studies, for possible future reassessment of vaccination strategies.

Contributors

DS, MO'R, JPT, MZ, ES, and LJB conceived the study. DS and LJB directed the Instituto Sistemas Complejos de Ingeniería team who worked on the testing site optimisation module and the web-based platform for collecting data. MZ led the teams for the field work. DS was responsible for database cleaning and data analysis, generating tables and figures. DS, MO'R, JPT, and LJB drafted the original manuscript. All authors provided important input to methods of the study, revised the manuscript, and approved the final version. LJB and MZ led the funding acquisition efforts. LJB, DS, and MZ had full access to and verified all data. All authors had full access to the study results and had final responsibility for the decision to submit for publication.

Declaration of interests

We declare no competing interests.

Data sharing

To have access to the data collected for the study, researchers need to apply to the Ministerio de Salud (Santiago, Chile). The informed consent, the approval from the Ethics Committee, and the Julia software code are available upon request to the corresponding author.

Acknowledgments

This work was supported in part by a grant from Instituto Sistemas Complejos de Ingeniería (ANID PIA AFB 180003); these funds were used to hire research assistants for the information systems, data management, and training of field staff. Field work was funded by the Ministerio de Salud (Santiago, Chile). We thank Digital Entel Ocean, Empresa Nacional de Telecomunicaciones, and Julio Covarrubia, for processing and sharing fine granular mobility data since the beginning of the pandemic. We thank the Servicio de Salud Metropolitano Centro, the Ministry of Sciences, and BHP for their support in setting up the pilot scheme for the dynamic COVID-19 IgG monitoring system. We thank Sergio Contreras, Simon Grass, Ignasi Neira, Matias Moscoso, and Ignacia Segura for their hard work in setting up and operating the information systems used in this project. We also thank all individuals involved in the field work throughout Chile.

References

1 Department of Statistics and Information, Ministry of Health Chile. Official figures COVID-19 Chile. 2021. https://deis.minsal.cl/ (accessed July 15, 2021; in Spanish).

2 Palacios R, Batista AP, Albuquerque CSN, et al. Efficacy and safety of a COVID-19 inactivated vaccine in healthcare professionals in Brazil: the PROFISCOV study. *SSRN* 2021; published online April 14. https://doi.org/10.2139/ssrn.3822780 (preprint).

3 Polack FP, Thomas SJ, Kitchin N, et al. Safety and efficacy of the BNT162b2 mRNA Covid-19 vaccine. *N Engl J Med* 2020; **383:** 2603–15.

4 Jara A, Undurraga EA, González C, et al. Effectiveness of an inactivated SARS-CoV-2 vaccine in Chile. *N Engl J Med* 2021; published online July 7. https://doi.org/110.1056/NEJMoa2107715.

5 Instituto Sistemas Complejos de Ingeniería. Seroprevalence. 2021. https://covidanalytics.isci.cl/seroprevalencia/ (accessed July 15, 2021).

6 Instituto Nacional de Estadísticas. Population projections. https://www.ine.cl/estadisticas/sociales/demografia-y-vitales/proyecciones-de-poblacion, (accessed July 23, 2021).

7 CTK Biotech. Onsite COVID-19 IgG/IgM Rapid test. Instructions for use. https://drive.google.com/file/d/1ATIHN4yKm_X9GPgJZER46e9YSJZfuO6R/view?usp=sharing (accessed July 15, 2021).

8 Bezanson J, Edelman A, Karpinski S, Shah VB. Julia: a fresh approach to numerical computing. *SIAM Rev* 2017; **59:** 65–98.

9 Gurobi Optimization. Gurobi Optimizer reference manual. https://www.gurobi.com/documentation/9.1/refman/index.html (accessed July 15, 2021).

10 Fischinger S, Boudreau CM, Butler AL, Streeck H, Alter G. Sex differences in vaccine-induced humoral immunity. *Semin Immunopathol* 2019; **41:** 239–49.

11 Li J, Hui A, Zhang X, et al. Safety and immunogenicity of the SARS-CoV-2 BNT162b1 mRNA vaccine in younger and older Chinese adults: a randomized, placebo-controlled, double-blind phase 1 study. *Nat Med* 2021; **27:** 1062–70.

12 Collier DA, Ferreira IATM, Kotagiri P, et al. Age-related immune response heterogeneity to SARS-CoV-2 vaccine BNT162b2. *Nature* 2021; published online June 30. https://doi.org/10.1038/s41586-021-03739-1.

13 Wu Z, Hu Y, Xu M, et al. Safety, tolerability, and immunogenicity of an inactivated SARS-CoV-2 vaccine (CoronaVac) in healthy adults aged 60 years and older: a randomised, double-blind, placebo-controlled, phase 1/2 clinical trial. *Lancet Infect Dis* 2021; **21:** 803–12.

14 Ranzani O, Hitchings M, Dorion M, et al. Effectiveness of the CoronaVac vaccine in the elderly population during a P.1 variant-associated epidemic of COVID-19 in Brazil: a test-negative case-control study. *medRxiv* 2021; published online May 21. https://doi.org/10.1101/2021.05.19.21257472 (preprint).

15 Khoury DS, Cromer D, Reynaldi A, et al. Neutralizing antibody levels are highly predictive of immune protection from symptomatic SARS-CoV-2 infection. *Nat Med* 2021; **27:** 1205–11.

16 Earle KA, Ambrosino DM, Fiore-Gartland A, et al. Evidence for antibody as a protective correlate for COVID-19 vaccines. *Vaccine* 2021; **39:** 4423–28.

17 Zhang Y, Zeng G, Pan H, et al. Safety, tolerability, and immunogenicity of an inactivated SARS-CoV-2 vaccine in healthy adults aged 18-59 years: a randomised, double-blind, placebo-controlled, phase 1/2 clinical trial. *Lancet Infect Dis* 2021; **21:** 181–92.

18 Sim F. Early Covid-19 vaccination rollout: a commentary from England. *Isr J Health Policy Res* 2021; **10:** 18.

19 Vasileiou E, Simpson CR, Shi T, et al. Interim findings from first-dose mass COVID-19 vaccination roll-out and COVID-19 hospital admissions in Scotland: a national prospective cohort study. *Lancet* 2021; **397:** 1646–57.

20 Dagan N, Barda N, Kepten E, et al. BNT162b2 mRNA Covid-19 vaccine in a nationwide mass vaccination setting. *N Engl J Med* 2021; **384:** 1412–23.

21 Instituto de Salud Publica, Ministerio de Salud. Informe Evaluación de Ensayos Comerciales Subdepartamento de Enfermedades Virales. https://covidanalytics.isci.cl/wp-content/uploads/2021/03/Informe_ISP.pdf (accessed Sept 2, 2021).

22 Department of Health and Human Services, Food and Drug Administration. Serology test evaluation report for "OnSite COVID-19 IgG/IgM Rapid Test" from CTK Biotech, Inc. Sept 11, 2020. https://www.accessdata.fda.gov/cdrh_docs/presentations/maf/maf3355-a001.pdf (accessed Sept 2, 2021).

23 Moshe M, Daunt A, Flower B, et al. SARS-CoV-2 lateral flow assays for possible use in national Covid-19 seroprevalence surveys (React 2): diagnostic accuracy study. *BMJ* 2021; **372:** n423.