Enhanced surveillance of COVID-19 in Scotland: population-based seroprevalence surveillance for SARS-CoV-2 during the first wave of the epidemic

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Abstract

Objectives

The impact of the COVID-19 pandemic in Scotland has been amongst the most severe in Europe. Serological surveillance is critical to determine the overall extent of infection across populations and to inform the public health response. This study aimed to estimate the proportion of people who have antibodies to SARS-CoV-2 ("seroprevalence") in the general population of Scotland and to see if this changes over time.

Study design/Methods

Between ISO week 17 (i.e. week commencing 20th April) and ISO week 25 (week commencing 15 June), 4751 residual blood samples were obtained from regional biochemistry laboratories in six participating regional health authority areas covering approximately 75% of the Scottish population. Samples were tested for the presence of anti-SARS-CoV-2 IgG antibodies using the LIAISON®SARS-CoV-2 S1/S2 IgG assay (DiaSorin, Italy). Seroprevalence rates were adjusted for the sensitivity and specificity of the assay using Bayesian methods.

Results

The combined adjusted seroprevalence across the study period was 4.3% (95% CI 4.2%-4.5%). The proportion varied each week between 1.9% and 6.8% with no difference in antibody positivity by age, sex, or geographical area.

Conclusions

At the end of the first wave of the COVID-19 pandemic, only a small fraction of the Scottish population had antibodies to SARS-CoV-2.

Control of COVID-19 requires the ability to detect asymptomatic and mild infections, that would otherwise remain undetected through existing surveillance systems. This is important to determine the true number of infections within the general population which, in turn, can help to understand transmission, inform control measures, and provide a denominator for the estimation of severity measures such as the proportion of infected people who have been hospitalised and/or have died.

The first COVID-19 diagnosis in Scotland was notified on 1 March 2020. WHO declared COVID-19 a global pandemic on 11 March 2020. On 23 March 2020, lockdown measures for Scotland and the rest of the UK were implemented. By the end of the first wave of the epidemic, Scotland was estimated to have the third highest rate of excess mortality in Europe after England and Spain [1].

Here, that sought to maximise the use of existing residual blood samples from primary care (general practice) settings to estimate the proportion of people who have antibodies to SARS-CoV-2 ("seroprevalence") in the general population of Scotland and to see if this changes over time. The results presented here cover the pilot phase of the project between ISO week 17 and week 25.

Seroprevalence of SARS-CoV-2 antibodies in primary care patients

Since ISO week 17 (i.e. week commencing 20th April), residual blood samples, originally collected for other diagnostic purposes in primary care settings, were obtained from regional biochemistry laboratories in six participating regional health authority areas ('NHS Boards'): Greater Glasgow and Clyde (GGC), Grampian, Highland, Lanarkshire, Lothian, and Tayside. These six health boards account for approximately 75% of the Scottish population [2]. Laboratories identified 500 samples each week according to an age/sex sampling frame, in order to achieve a representative sample based on the age/sex/NHS Board structure of the general population. Samples were anonymised and sent to the Scottish Microbiology Reference Laboratory in Inverness for testing for the presence of anti-SARS-CoV-2 IgG antibodies using the LIAISON®SARS-CoV-2 S1/S2 IgG assay (DiaSorin, Italy). Seroprevalence rates were adjusted for the sensitivity and specificity of the assay using Bayesian methods [3]. We applied a sensitivity of 87.5% (95% CI 78.2%-93.8%) and specificity of 98.6% (95% CI 97.0%-99.5%) based on a local evaluation of the DiaSorin assay.

Samples are processed and analysed anonymously for the purposes of public health surveillance only, therefore the need for informed consent and ethical approval was waived. Public Health Scotland is registered under the General Data Protection Regulation and has an information security policy to safeguard the collection, processing and storage of confidential information. Approval for the COVID-19 serological surveillance work was given by the Head of Information Governance and Statistical Governance on 8th May 2020.

Between week 17 and week 25 a total of 4751 samples had been received from the six participating NHS boards and were available for testing. The combined adjusted seroprevalence across the study period was 4.3% (95% CI 4.2%-4.5%). Week to week fluctuation was evident: 6.8% in week 17, 1.9% in week 21, and 4.4% by week 25 (Table 1). Chi-square test for trend analysis on adjusted data showed no significant difference in prevalence across the study period (p=0.266). Rates among males and females showed similar variation across the study period. For males, the combined adjusted prevalence was 4.1% in week 17, 1.5% in week 21, and 3.8% by week 25 (Table 1). Among females, combined adjusted prevalence was 9.3% in week 17, 4.0% in week 21, and 3.9% by week 25. Trends were slightly less variable by age, in particular among older age groups. For example, for those aged 60+ combined prevalence was 6.3% in week 17, 2.4% in week 21 and 2.4% in week 25. By comparison, in the youngest age group (0-19 years), combined prevalence ranged from 5.8% in week 17, 0.1% in week 21 and 8.1% in week 25.

INSERT TABLE 1

Determinants of SARS-CoV-2 antibody positivity

A logistic regression model was constructed to examine the association between the available data associated with the samples (sex, age, NHS Board where testing took place, and testing week) and SARS-CoV-2 antibody positivity using the crude (unadjusted) data. Multivariable analysis showed no significant differences in the odds of SARS-CoV-2 antibody positivity across the available covariates (Supplementary File 1).

Discussion

Our results suggest that there is likely to have been no appreciable change across the weeks presented to date and that seroprevalence in the Scottish population may lie somewhere between 4.2% and 4.5%. Multivariate analysis showed no difference in results across different strata including age, sex, geographical area, and testing week. These estimates are similar to those reported from samples of Scottish blood donors collected within a similar timeframe [4]. Our results are from a sample of individuals attending primary care between April and June 2020, a period where Scotland was confined to lockdown restrictions on individual movement and social contact. There is uncertainty whether the individuals in our sample are representative of the general population. Further work is underway to understand more about our tested population and prospective data linkage to secondary care data will provide information on the co-morbidities and potential risk factors in this population.

Studies from across Europe have also reported low seroprevalence levels of SARS-CoV-2 antibodies in the general population at the end of the first wave of the epidemic despite its intensity [5,6,7]. It is unclear if antibody testing provides an accurate indicator of current levels of exposure to the virus: not all individuals who are exposed/infected mount an antibody response and, among those who do, antibody levels may wane over time [8,9]. Antibody seroprevalence may therefore underestimate population level exposure, but is nevertheless a critical piece of the puzzle to fully understand of the extent of exposure across different populations, to aid our understanding of the role of antibodies in protective immunity, and to inform vaccine development [10].

The following other limitations are pertinent to our study. Firstly, there is uncertainty around the exact sensitivity and specificity of the Diasorin antibody test. Our adjustment takes into account the range of uncertainty in the values for sensitivity and specificity. Secondly, between weeks 18 and 22, some laboratories were excluding known COVID-19 positive patients and others were not. There are no exclusions of known COVID positive patients from week 23 onwards.

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Table 1: Proportion of individuals testing positive for antibodies to Coronavirus overall, by sex and by age-group: adjusted data from community healthcare blood tests, Scotland, 20 April-21 June 2020

Week commencing	Iso week	No. tested	Overall	Sex		Age-group			
				Male	Female	0-19	20-39	40-59	60+
20 April	17	443	6.8% (3.9%, 10.2%)	4.1% (0.9%, 8.3%)	9.3% (5.2%, 14.6%)	5.8% (1.0%, 13.2%)	4.8% (0.8%, 10.9%)	10.6% (4.6%, 18.9%)	6.3% (1.9%, 12.7%)
27 April	18	543	4.3% (1.9%, 7.0%)	4.6% (1.6%, 8.6%)	4.0% (1.1%, 7.7%)	5.7% (1.4%, 12.1%)	3.1% (0.1%, 7.8%)	4.9% (0.9%, 11.0%)	3.9% (0.5%, 8.7%)
4 May	19	530	3.1% (0.9%, 5.7%)	4.7% (1.6%, 8.6%)	1.6% (0.1%, 4.7%)	1.8% (0.1%, 6.9%)	4.6% (0.7%, 10.4%)	2.3% (0.1%, 7.8%)	3.5% (0.4%, 8.0%)
11 May	20	521	2.6% (0.5%, 5.0%)	2.1% (0.1%, 5.3%)	3.0% (0.4%, 6.4%)	4.2% (0.3%, 10.0%)	3.3% (0.1%, 8.3%)	0.9% (0.1%, 6.0%)	1.9% (0.1%, 6.2%)
18 May	21	547	1.9% (0.1%, 4.0%)	1.5% (0.1%, 4.6%)	2.2% (0.1%, 5.3%)	0.1% (0.1%, 4.8%)	1.5% (0.1%, 6.1%)	4.1% (0.3%, 9.8%)	2.4% (0.1%, 6.7%)
25 May	22	527	2.9% (0.8%, 5.5%)	4.4% (1.3%, 8.3%)	1.5% (0.1%, 4.6%)	4.0% (0.3%, 9.6%)	2.5% (0.1%, 7.5%)	2.7% (0.1%, 7.7%)	2.7% (0.1%, 7.2%)
1 June	23	544	3.7% (1.4%, 6.3%)	2.8% (0.3%, 6.2%)	4.5% (1.5%, 8.3%)	6.1% (1.7%, 12.2%)	1.6% (0.1%, 6.3%)	2.2% (0.1%, 7.6%)	4.3% (0.9%, 9.3%)
8 June	24	553	5.2% (2.7%, 8.2%)	5.3% (2.0%, 9.4%)	5.2% (2.0%, 9.3%)	7.4% (2.8%, 13.8%)	0.2% (0.1%, 5.9%)	5.8% (1.4%, 12.2%)	6.3% (2.2%, 12.0%)
15 June	25	536	4.4% (2.0%, 7.2%)	3.8% (1.0%, 7.6%)	4.9% (1.8%, 8.9%)	8.1% (3.2%, 14.9%)	2.9% (0.1%, 8.1%)	4.6% (0.7%, 10.4%)	2.4% (0.1%, 6.7%)
Total[a]		4,744	4.3% (4.2%, 4.5%)						

a Total sample does not equal 4,751 as seven results were received from samples taken prior to the study start date

References

1. Office for National Statistics. Comparisons of all-cause mortality between European countries and regions: January to June 2020, https://www.ons.gov.uk/peoplepopulationandcommunity/birthsdeathsandmarriages/deaths/articles/comparisonsofallcausemortalitybetweeneuropeancountriesandregions/januarytojune2020 ; 2020 [Accessed 1 September 2020]
2. National Records of Scotland. Mid-2019 Population Estimates Scotland, https://www.nrscotland.gov.uk/statistics-and-data/statistics/statistics-by-theme/population/population-estimates/mid-year-population-estimates/mid-2019 ; 2020 [Accessed 1 September 2020]
3. Diggle P. Estimating prevalence using an imperfect test. *Epidemiology Research International* 2011;608719:1-6
4. Thompson CP, Grayson N, Paton R, Bolton JS, Lourenço J, Penman B, et al. Detection of neutralising antibodies to SARS coronavirus 2 to determine population exposure in Scottish blood donors between March and May 2020. *medRxiv [Preprint]* 2020 [cited 2020 Jul 9]. Available from: https://www.medrxiv.org/content/10.1101/2020.04.13.20060467v2
5. Pollán M, Pérez-Gómez B, Pastor-Barriuso R, Oteo J, Hernán MA, Pérez-Olmeda M, et al. Prevalence of SARS-CoV-2 in Spain (ENE-COVID): a nationwide, population-based seroepidemiological study. *The Lancet* 2020;396(10250):535-544
6. Stringhini S, Wisniak A, Piumatti G, Azman AS, Lauer SA, Baysson H, et al. Seroprevalence of anti-SARS-CoV-2 IgG antibodies in Geneva, Switzerland (SEROCoV-POP): a population-based study. *The Lancet* 2020;396(10247)313-31
7. Snoeck CJ, Vaillant M, Abdelrahman T, Satagopam VP, Turner JD, Beaumont K, et al. Prevalence of SARS-CoV-2 infection in the Luxembourgish population: the CON-VINCE study. *medRxiv [Preprint]* 2020 [cited 2020 May 18]. Available from: https://doi.org/10.1101/2020.05.11.20092916
8. Long Q, Tang X, Shi Q, Qin Li, Deng H, Yuan J, et al. Clinical and immunological assessment of asymptomatic SARS-CoV-2 infections. *Nat Med* 2020;26:1200-1204.
9. Liu T, Wu S, Tao H, Zeng G, Zhou F, Guo F, et al. Prevalence of IgG antibodies to SARS-CoV-2 in Wuhan – implications for the ability to produce long-lasting protective antibodies against SARS-CoV-2. *medRxiv [Preprint]* 2020 [cited Jun 16]. Available from: https://www.medrxiv.org/content/10.1101/2020.06.13.20130252v1.full.pdf
10. Alter G, & Seder R. The Power of Antibody-Based Surveillance. *N Engl J Med* 2020;doi: 10.1056/NEJMe2028079. Online ahead of print.