Supplementary Appendix

This appendix has been provided by the authors to give readers additional information about their work.

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Supplementary Appendix

Humoral Immune response to SARS-CoV-2 in Iceland

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Supplementary Methods

Ethical considerations

The study was approved by the National Bioethics Committee of Iceland (Approvals no. VSN-20-070 and VSN-20-076) following evaluation of the Icelandic Data Protection Authority. The healthcare sample were collected on behalf of Icelandic health authorities in agreement with the Act no. 19/1997 on Health Security and Communicable Diseases, as notified to the Icelandic Data Protection Authority. The personal identities of participants other than from the healthcare collection were encrypted using a third-party system approved and monitored by the Icelandic Data Protection Authority

Serum samples and antibody measurements

Blood was collected and allowed to clot for 30 minutes and centrifuged for 10 minutes at 3000 x g at 4°C. Serum samples were frozen in aliquots at -80°C. We allowed serum aliquots to thaw on ice and kept away from light during defrosting. The aliquots were mixed by inverting the tubes several times and then centrifuged for 1 minute at 1000 x g, at 4°C. Antibody levels should be stable as the sera were aliquoted and stored at -80°C without freeze/thaw.

SARS-CoV-2 specific antibodies were measured with six different assays, targeting: pan-Ig (IgM, IgG and IgA) antibodies against the nucleoprotein (N) (anti-N; Roche Elecsys chemiluminescence assay, ECLIA, Roche International, Basel, Switzerland), pan-Ig antibodies against the receptor binding domain (RBD) in the S1 subunit of the spike protein (pan-Ig anti-S1-RBD; Wantai ELISA, Wantai /Nordic BioSite, Täby, Sweden), IgG or IgM antibodies against the nucleocapsid protein (IgM anti-N or IgG anti-N, respectively, EDI ELISAs, EDI/Eagle Biosciences, Amherst, NH, United States) and IgG or IgA against S1 subunit of the spike protein (IgG anti-S1 or IgA anti-S1, respectively, Euroimmun ELISAs, Euroimmun AG, Luebeck, Germany). Sera were tested undiluted in the Roche ECLIA (20 ul of undiluted serum was mixed in the instrument with the reagent solution) and Wantai ELISA (undiluted serum added to the antigen-coated well), at 1/100 in the Euroimmun and IgG EDI ELISA, and 1/10 in the IgM EDI ELISA. All measurements were done according to manufacturer’s instructions. The ELISA results are expressed as optical density (OD) and the ECLIA results as log light emission. For the IgG and IgM anti-N assays, we ran four negative controls per 96 well plate and subtracted the mean OD of the negative controls from the OD. The manufacturer recommended OD thresholds for positive results were 1 (0 for log(OD)) for the pan-Ig anti-N assay and 0.19 for the pan-Ig anti-S1-RBD assay. After subtraction of the negative controls, the manufacturer recommended OD thresholds for positive results were 0.198 for the IgG anti-N assay and 0.11 for the IgM anti-N assay. For the IgG and IgA anti-S1 assays, the manufacturer recommends using two negative controls and two calibrator
samples per plate and declaring samples positive if they have greater OD than the difference of the mean OD for the calibrator samples minus the mean OD for the negative control samples. The mean threshold was 0.33 for the IgG anti-S1 assay and 0.36 for the IgA anti-S1 assay.

Both assays measuring pan-Ig antibodies, against N and S1-RBD, had low false positive rates among samples collected in 2017: 0 and 1 out of 472, respectively. These results are consistent with the reported high specificity of the pan Ig anti-N assay (N=5,262, 99.8%, 95% confidence interval (CI): 99.7%, 99.9%) and for the pan-Ig anti-S1-RBD assay (N=333, 100.0%, 95%CI: 99.4%, 100.0%)².

Of the 1,120 recovered persons who were positive for pan-Ig anti-N, 1,107 (98.8%) were also positive for pan-Ig anti-S1-RBD. Conversely, of the 1,143 persons who tested positive for pan-Ig anti-S1-RBD, 1,107 (96.9%) also tested positive for pan-Ig anti-N. There was substantially worse concordance between the two measurements in the healthcare collection; 35 out of 58 (60.3%) positive for pan-Ig anti-N were also positive for pan-Ig anti-S1-RBD, and conversely 35 out of 79 (44.3%) positive for pan-Ig anti-S1-RBD were also positive for pan-Ig anti-N. Moreover, for the persons with discrepant results, the positive tests were mostly marginally positive and the negative tests tended to show very little signal, a pattern that is almost never seen among recovered COVID-19 cases (Figure S1). These results indicate the presence of false positive measurements by both pan-Ig antibody assays that are common relative to the low fraction of true positives being assessed here and that false positive results are not positively correlated for the two pan-Ig antibody assays. Based on these findings, we estimated the population prevalence of SARS-CoV-2 antibodies on positivity for both pan-Ig anti-N and pan-Ig anti-S1-RBD antibodies.

To improve the antibody level quantification of the pan-Ig antibody assays for qPCR-diagnosed persons, we combined results from measuring undiluted, 1:4 and 1:16 diluted samples (diluted with 1x reagent diluent concentrate 2 (R&D Systems Europe Ltd, Abingdon, United Kingdom)). The pan-Ig anti-N assay yielded much more consistent results between undiluted and diluted samples than the pan-Ig anti-S1-RBD assay (Figure S6), indicating that it gives better quantification of antibody levels. To obtain a single antibody level from the three sample dilutions we searched for a limit of antibody level where there was an approximately linear relationship between the undiluted and 1:4 diluted samples and the 1:4 diluted and 1:16 diluted samples and used the undiluted measurement when the 1:4 diluted sample was below the limit and a transformed 1:16 diluted measurement if it was above the limit. For the pan-Ig anti-N assay we worked with the logarithm of the optical density, and if the logarithm of the 1:4 diluted level was below 1.5 we used the undiluted value, and otherwise used the logarithm of the 1:16 diluted value plus 3.4. For the pan-Ig anti-S1-RBD assay we used the
undiluted measurement if the 1:4 diluted level was below 0.8 and otherwise used the 1:16 diluted measurement plus 1.15.

**Testing of samples for SARS-COV-2 using qPCR**

Testing for SARS-CoV-2 was performed either at Landspitali – The National University Hospital of Iceland (LUH) or deCODE using similar qPCR methods. The assay at LUH is based on the WHO recommended screening method ([https://www.who.int/docs/default-source/coronaviruse/wuhan-virus-assay-v1991527e5122341d99287a1b17c111902.pdf](https://www.who.int/docs/default-source/coronaviruse/wuhan-virus-assay-v1991527e5122341d99287a1b17c111902.pdf)), which involves a single probe pan-screening assay for betacoronaviruses, followed by confirmatory measurements for all positive samples using an nCoV-2019 specific assay. The broad betacoronavirus assay is based on probes for a conserved region of the E-gene, whereas confirmatory testing assays were done using either nCoV-2019 specific probes for the RdRp gene or the TaqMan™ Fast Virus 1-step Master Mix, 2019-nCoV Assay kits v1 from Thermo Fisher (see Method 1 below for details). All labelled probes and primers for the E-and -RdRP genes were from TAG (Copenhagen, Denmark). Superscript™ III One-Step RT-PCR assay mix with Platinum™ Taq DNA polymerase was from Thermo Fisher. 2019 E gene control and SARS-CoV Frankfurt 1 positive controls were obtained from EVAg ([https://www.european-virus-archive.com/bundle/diagnostics-controls-wuhan-coronavirus-2019-2019-ncov](https://www.european-virus-archive.com/bundle/diagnostics-controls-wuhan-coronavirus-2019-2019-ncov)). Each assay was done in a 25 µL total sample volume with FAM™ dye labelled probes in addition to VIC™ dye labelled probes for human RNase P as internal control. Plates (96 well) were scanned in an AB-7500 Fast real-time PCR thermocycler for 40 cycles of amplification following the manufacturer’s instructions (Thermo Fisher). Samples in the E-gene screening assay with $C_T < 35$ were considered strong positive and went for confirmatory testing using RdRp, whereas samples with $C_T$ values between 35-37 were considered weak positive and were confirmed using the TaqMan™ Fast Virus method. Samples with $C_T$ values from 37-40 were classified as inconclusive and were tested again to confirm their status.

SARS-CoV-2 screening at deCODE was performed using qPCR assays in either a singleplex (Method 1) or a multiplex (Method 2) format, respectively. Method 1 uses the three probe TaqMan™ Fast Virus 1-step Master Mix, 2019-nCoV Assay kits v1 and 2019-nCov control kit from Thermo Fisher. Assay mix A, B and C were prepared containing FAM™ dye labelled probes for the SARS-CoV-2 specific genes ORF1ab, S-gene and N-gene, respectively. In addition, each assay mix contained VIC™ dye labelled probes for human RNase P as internal control. Samples from 96-well RNA sample plates were dispensed into three wells each in a 384 plate layout, in addition to three negative (no template) and three positive controls. Assay mix was added in a total reaction volume of 12.5 µL per sample. All sample aliquoting and mixing was performed with an automated Hamilton STARlet 8-channel liquid handler and the assay plates were scanned in an ABI 7900 HT RT-PCR system following manufacturer’s instructions with a total of 40 cycles of amplification. Samples with FAM™ dye $C_T$
values <37 in at least two of three assays were classified as positive. Samples with FAM™ dye \( C_t \) values between 37 and 40 were classified as inconclusive and their testing repeated. If repeated testing gave the same result with at least two probes the sample was classified as positive. If repeated testing gave positive results for only one probe the test was considered inconclusive and a new sample from the subject was requested. The frequency of inconclusive results was 0.04% (data not shown). Samples with undetected FAM™ dye \( C_t \) values or values equal to 40 in all three assays were classified as negative if the human RNaseP assay was positive (VIC™ dye \( C_t <40 \)). The sensitivity of the assay was evaluated by serial dilution of the positive control and was estimated at 6 copies per reaction (data not shown).

Method 2 uses the TaqPath™ COVID-19 CE-IVD RT-PCR kit from Thermo Fisher (Catalog# A48067). TaqPath™ COVID-19 is a multiplexed assay that contains three primer/probe sets specific to different SARS-CoV-2 genomic regions and primers/probes for bacteriophage MS2 as a control, all measured in the same reaction well. The SARS-CoV-2 targets are the same as in Method 1, however each target and the MS2 control contain probes with different reporter dyes (ORF1ab, FAM™; N-gene, VIC™; S-gene, ABY™; MS2, JUN™). The MS2 was used as an internal control and was added to each viral swab sample to assess the efficacy of the sample preparation. All reactions were performed in 384-well plate layout in a total reaction volume of 6.25 µL per sample using an 8-channel Hamilton STARlet liquid handler for dispensing and mixing. A negative control (no template) and a positive control (COVID-19 Control, 25 copies/reaction) was run on each plate. Assay plates were scanned in a QuantStudio 7 Pro System Real-Time PCR instrument following the manufacturer’s instruction to a total of 40 cycles of amplification. Result criteria were the same as described for Method 1 above.

**Follow-up of qPCR-diagnosed cases**

From February 28 to May 1, 1,797 patients were found to be SARS-CoV-2 positive by qPCR. Of those, 1,746 were enrolled in the telehealth service at the COVID Outpatient Clinic of LUH while the remaining 51 patients were admitted to hospital at the time of diagnosis. Those enrolled in the telehealth monitoring service underwent an initial interview. A physician documented clinical symptoms, past medical history and medications using a standardized data entry form. Patients were categorized into one of three stages of clinical severity: (1) low severity, defined as mild symptoms; (2) moderate severity, defined as mild dyspnea, cough or fever for less than five days; or (3) high severity, defined as severe dyspnea, worsening cough, high or persistent fever for five days or longer, or severe fatigue. Follow-up interviews were conducted every one to four days based on the clinical severity. Patients reporting severe or worsening symptoms were referred for an in-person clinical evaluation at the COVID-19 Outpatient Clinic. A discharge phone call was made by a physician when
the patient fulfilled two predetermined criteria; 14 days had passed from their first positive test and they had been symptom-free for seven days.

**Questionnaire for recovered cases**

We invited those who had recovered from confirmed COVID-19 illness to answer an online questionnaire on general health, COVID-19 symptoms and suggested COVID-19 risk factors. The questionnaire was introduced in the second week of May. By July 1, 545 of the 1,215 (45%) recovered persons included in the study had answered the questionnaire.

**Hospitalized COVID-19 cases**

We collected longitudinal series of serum samples from 48 out of 101 (48%) hospitalized Icelandic COVID-19 patients during their hospital admission (Table S1). All cases were qPCR-positive. Serum samples for antibody measurements were drawn between once and 17 times (median 4), between 2 and 35 days after diagnosis with qPCR. The most common reason for missing samples was that the patient had been discharge before commencement of the study, followed by the patient not consenting to participate in the study.

**Recovered COVID-19 cases**

We invited all qPCR-positive persons to give a blood sample after recovery (defined as at least two weeks from qPCR diagnosis and one week after end of symptoms) and again on July 1, on average 100 days after diagnosis with qPCR (Table S1, Figure S2). From April 8, we collected serum samples from 1,215 out of 1,797 (68%) qPCR-positive persons. Non-participation was because of refusal or inability to participate because of health or geographic constraints.

To assess if the antibody test results from recovered persons changed with time after the acute phase, we compared early and latest antibody test results where the early sample was collected at least 3 weeks after the qPCR diagnosis, and the latest one at least one month after the first sample. We had samples from 489 persons satisfying these criteria. The early sample was collected an average of 32 days (SD=11 days) and the latest sample an average of 102 days (SD=11 days) after the qPCR diagnosis, yielding an average of 70 days (SD=14 days) between sampling times (Figure S4)

**Samples from 2017**

We used 472 serum samples from persons collected in the year 2017 to estimate the specificity of the pan-Ig anti-N, pan-Ig anti-S1-RBD, IgM anti-N and IgG anti-N antibody assays. These samples were collected from persons participating in the deCODE health study (Table S1).
Samples from February and early March 2020
We used 470 samples from persons participating in the deCODE health study from February 18 through March 9 2020 to assess if there was evidence for early spread of the virus (Table S1).

Healthcare sample collection
On behalf of the Icelandic health authorities, we screened for antibodies reactive to SARS-CoV-2 in serum samples from 18,609 Icelanders who sought service from the healthcare system for various reasons and had blood drawn between May 5 and June 12 2020 (Table S1). We restricted the collection to persons who had not tested positive with SARS-CoV-2 qPCR and who had not been quarantined because of exposure to the virus.

Because of the nature of the healthcare sample collection, it was skewed towards older people. We therefore stratified the dataset based on region, sex, and 10 year age bins and weighted the sample from each stratum by the size of the stratum in the population. More precisely, let \( s_i \) be the number of persons in strata \( i \), sharing legal residence in the same zip code, sex, and 10 year age bin (0-10, 11-20, 21-30, ...), who had neither tested positive with qPCR nor been quarantined. Let \( n_i \) be the number of persons sampled from stratum \( i \) and let \( x_i \) be how many of those tested positive for both pan-Ig antibody assays. Then we estimated the seroprevalence in each region from the set, \( R \), of strata with zip codes in the region:

\[
\frac{\sum_{i \in R} s_i x_i}{\sum_{i \in R} s_i}
\]

To estimate the seroprevalence over the whole of Iceland, we used the set of all strata.

Reykjavik sample collection
We invited a random sample of Icelanders living in the greater Reykjavik area (Reykjavik, Kopavogur, Hafnarfjordur, Gardabaer, Seltjarnarnes, and Mosfellsbaer), home to 64% of the Icelandic population, to have their blood tested for antibodies against SARS-CoV-2 from April 27 through June 5 2020 (Table S1). The sample consisted mostly of 20-65 years old adults. This collection allowed us to get a second estimate of seroprevalence in the Reykjavik area and therefore evaluate how representative the antibody test results are from persons seeking service from Iceland’s healthcare system. The invited persons were selected from a pool of persons who had at some point participated in deCODE studies, but had not previously been invited to participate in studies related to COVID-19. A total of 13,086 persons were invited with a phone text message between April 25 and June 3. Of those persons, 46.1% were male.
Vestmannaeyjar sample collection

Vestmannaeyjar were one of the two main locations of SARS-CoV-2 outbreaks in Iceland identified with qPCR (Table S1). We invited residents of Vestmannaeyjar to have their blood tested for antibodies and collected serum samples from 447 out of 597 (75%) quarantined persons and 663 qPCR negative persons outside quarantine. The purpose of this collection was to evaluate the effectiveness of quarantine in managing the outbreak.

Quarantine sample collection

By April 30 2020, 20,766 Icelanders (6% of the population) had been quarantined because of exposure to the SARS-CoV-2 virus. Of those who had been in quarantine, 1088 (5%) later tested positive with qPCR. Between April 14 and July 8, we invited those who had completed their quarantine to be tested for SARS-CoV-2 antibodies and 4,023 (19%) persons accepted (Table S1). We had information on clinical symptoms for 1,198 of those. All persons in quarantine were classified by whether they had household exposure or non-household exposure. Information on those in quarantine was obtained from the Directorate of Health.
Figure S1. Comparison of pan-Ig antibody levels. The first panel shows samples from 2017 (N=472) and early 2020 (N=470), both from before the pandemic. The second panel shows samples from hospitalized (249 samples from 48 persons) and recovered COVID-19 cases (1,853 samples from 1,215 persons). The third panel shows samples from quarantined persons (N=4,222) and persons from the Reykjavik sample collection from outside quarantine (N=4,843). The log(pan-Ig anti-N) levels are shown on the x-axis and pan-Ig anti-S1-RBD levels on the y-axis. The dashed lines show the thresholds for a sample being considered positive for antibodies.
Figure S2. Time from qPCR-diagnosis to antibody testing and fraction of persons positive for two pan-Ig SARS-CoV-2 assays among qPCR-positive persons. Time from diagnosis is expressed in days. In red, the count or fraction of samples among persons during their hospitalization (249 samples from 48 persons). In blue, the count or fraction of samples for persons after being declared recovered (1,853 samples from 1,215 persons). The whiskers correspond to 95% confidence intervals around the estimate. Shown are the count of samples as a function of time from diagnosis and the fraction of positive samples as a function of time with the pan-Ig anti-N and anti-S1-RBD assays.
Figure S3. Trajectories of SARS-CoV-2 antibody measurements among hospitalized COVID-19 cases. Each trajectory corresponds to one of 48 cases. Circles represent samples taken at the hospital. Crosses represent samples taken after recovery. The dashed horizontal line shows the threshold for a sample being considered positive for antibodies. Results of the pan-Ig anti-N assay are shown as log light emission or optical density (OD) for the ELISAs. The dotted lines represent the cutoff for positive values.
Figure S4. Time from qPCR diagnosis to early sample and the latest sample. The early sample was collected at least 21 days from qPCR diagnosis. The distribution of the time from early sample to the latest sample is also shown. All samples were collected after recovery from the infection was declared.
Figure S5. Change in antibody levels between early and latest samples of recovered cases. Up to 487 recovered cases had repeated measurements. The early sample was collected at least 21 days from qPCR diagnosis. Time from diagnosis is expressed in days. The dashed lines indicate the thresholds required for a test to be declared positive. The solid diagonal lines correspond to no difference between early and latest samples. The Pearson correlation (R) between the antibody levels early and latest antibody levels for each antibody assay is shown.
Figure S6. Correlation between SARS-CoV-2 antibody levels measured at different serum dilutions in the two pan-Ig SARS-CoV-2 antibody assays. Results of pan-Ig anti-N (Roche ECLIA) are presented as log light emission and results of pan-Ig anti-S1-RBD as OD (Wantai ELISA) at different serum dilutions (undiluted, ¼ and 1/16). Each dot represents one sample.
### Supplementary Tables

| Study population | qPCR        | Recruitment period     | N   | N samples | qPCR test% | Male % | Age (SD) |
|------------------|-------------|------------------------|-----|-----------|------------|--------|----------|
| 2017             | Neg/NA      | 2017: Jan 2-Des 4     | 472 | 473       | 0%         | 41%    | 57 (16)  |
| Early 2020       | Neg/NA      | 2020: Feb 18-Mar 9    | 470 | 470       | 0%         | 51%    | 58 (14)  |
| Healthcare       | Neg/NA      | 2020: May 5-Jun 12    | 18,609 | 18,609 | 15%       | 44%    | 56 (20)  |
| Reykjavik        | Neg/NA      | 2020: April 27-Jun 5  | 4,843 | 4,843 | 5%        | 38%    | 48 (13)  |
| Vestmannaejar    | Neg/NA      | 2020: Apr 27-May 9    | 663 | 663       | 60%       | 47%    | 52 (18)  |
| Quarantine       | Neg/NA      | 2020: Apr 14-Jul 8    | 4,222 | 4,251 | 32%       | 41%    | 47 (17)  |
| Hospitalized     | Positive    | 2020: Apr 3-Apr 30    | 48  | 249       | 100%      | 60%    | 66 (12)  |
| Recovered        | Positive    | 2020: Apr 3-Jul 8     | 1,215 | 1,853 | 100%      | 48%    | 43 (16)  |

**Table S1.** An overview of sample collections tested for both pan-Ig assays. qPCR indicates the inclusion criteria which is either that the person had not been tested positive with qPCR (Neg/NA) or that the person had been positive with qPCR assay (Positive). qPCR test% indicates the fraction of the study population that had been tested with a qPCR assay prior to donation of serum sample. N corresponds to the number of persons tested and had results for both pan-Ig assays. SD: Standard deviation.
| Source       | Protein target                  | Ig      | Dilution |
|--------------|---------------------------------|---------|----------|
| Roche        | Nucleocapsid (anti-N)           | pan-Ig  | Undiluteda |
| Wantai       | Spike 1 RBD (anti-S1-RBD)       | pan-Ig  | Undiluted |
| EDI/Eagle    | Nucleocapsid (anti-N)           | IgG     | 1:10     |
| EDI/Eagle    | Nucleocapsid (anti-N)           | IgM     | 1:10     |
| Euroimmun    | Spike subunit 1 (anti-S1)       | IgG     | 1:100    |
| Euroimmun    | Spike subunit 1 (anti-S1)       | IgA     | 1:100    |

Table S2. Overview of SARS-CoV-2 antibody assays. a20 ul of undiluted serum was mixed in the instrument with the reagent solution.
| Sample collection | IgG anti-N | IgM anti-N |
|------------------|------------|------------|
|                  | N/N pos    | Frequency (95 %CI) | N/N pos    | Frequency (95 %CI) |
| 2017             | 437/8      | 1.8% (0.8%, 3.4%)  | 434/8      | 1.8% (0.8%, 3.4%)  |
| Early 2020       | 424/7      | 1.7% (0.7%, 3.2%)  | 411/2      | 0.5% (0.1%, 1.5%)  |
| Hospitalized     | 42/40      | 95.2% (86.0%, 99.2%) | 42/29      | 69.0% (54.2%, 81.6%) |
| Recovered        | 1,134/539  | 47.5% (44.6%, 50.4%) | 1,145/57   | 5.0% (3.8%, 3.6%)  |

**Table S3.** Prevalence of SARS-CoV-2 antibodies by sample collection as measured by IgG and IgM anti-N assays. For the hospitalized and recovered persons, the latest available sample was used.
| Sample collection | N     | N pos | Frequency (95 %CI) | N pos | Frequency (95 %CI) | N pos | Frequency (95 %CI) | N pos | Frequency (95 %CI) |
|-------------------|-------|-------|--------------------|-------|--------------------|-------|--------------------|-------|--------------------|
| 2017              | 472   | 0     | 0.0% (0.0%, 0.4%) | 1     | 0.2% (0.0%, 0.9%) | 0     | 0.0% (0.0%, 0.4%) | 1     | 0.2% (0.0%, 0.9%) |
| Early 2020        | 470   | 4     | 0.9% (0.3%, 2.0%) | 0     | 0.0% (0.0%, 0.4%) | 0     | 0.0% (0.0%, 0.4%) | 4     | 0.9% (0.3%, 2.0%) |
| Healthcare a       | 18,609| 56    | 0.3% (0.2%, 0.4%) | 102   | 0.5% (0.4%, 0.7%) | 39    | 0.2% (0.2%, 0.3%) | 119   | 0.6% (0.5%, 0.8%) |
| Reykjavik a       | 4,843 | 28    | 0.6% (0.4%, 0.8%) | 31    | 0.6% (0.4%, 0.9%) | 21    | 0.4% (0.3%, 0.6%) | 38    | 0.8% (0.6%, 1.1%) |
| Vestmannaeyjar a  | 663   | 5     | 0.8% (0.3%, 1.6%) | 5     | 0.8% (0.3%, 1.6%) | 3     | 0.5% (0.1%, 1.2%) | 7     | 1.1% (0.5%, 2.0%) |
| Quarantine        | 4,222 | 109   | 2.6% (2.1%, 3.1%) | 119   | 2.8% (2.3%, 3.3%) | 97    | 2.3% (1.9%, 2.8%) | 131   | 3.1% (2.6%, 3.7%) |
| Hospitalized      | 48    | 46    | 95.8% (87.7%, 99.3%) | 46    | 95.8% (87.7%, 99.3%) | 45    | 93.8% (84.6%, 98.4%) | 47    | 97.9% (91.1%, 99.9%) |
| Recovered         | 1,215 | 1,120 | 92.2% (90.6%, 93.6%) | 1,143 | 94.1% (92.7%, 95.3%) | 1,107 | 91.1% (89.4%, 92.6%) | 1,156 | 95.1% (93.8%, 96.3%) |

**Table S4.** Prevalence of SARS-CoV-2 antibodies by sample collection as measured by two pan-Ig antibody assays. The latest available sample was used. N corresponds to the number of persons tested and had results for both pan-Ig assays. 95% CI: 95% confidence interval. Pos = positive. See Figure 1 for overview of the different sample collections. aSampling restricted to persons who had not tested qPCR-positive and who had not been quarantined.
| Assay               | pan-Ig anti-N | Pan-Ig anti-S1-RBD | IgG anti-N | IgM anti-N | IgG anti-S1 | IgA anti-S1 |
|---------------------|---------------|-------------------|-----------|-----------|-----------|-----------|
| pan-Ig anti-N       | 0.54          |                   | 0.74      | 0.27      | 0.67      | 0.41      |
| pan-Ig anti-S1-RBD  | 0.51          |                   | 0.57      | 0.22      | 0.68      | 0.57      |
| IgG anti-N          | 0.65          |                   | 0.48      | 0.39      | 0.71      | 0.47      |
| IgM anti-N          | 0.36          |                   | 0.27      | 0.27      | 0.27      | 0.16      |
| IgG anti-S1         | 0.60          |                   | 0.54      | 0.73      | 0.14      | 0.69      |
| IgA anti-S1         | 0.59          |                   | 0.55      | 0.75      | 0.18      | 0.75      |

Table S5. Pairwise correlation between levels obtained in different antibody assays. The correlation between recovered persons are shown in the upper triangle (N up to 1,215) and between hospitalized persons in the lower triangle (N up to 48). For persons with multiple measurements, we used the latest available measurement.
Table S6. The prevalence of qPCR-positivity, seroprevalence, and estimated infection fraction in Iceland. Stratified by region and overall. *Seroprevalence estimated by weighting the sample based on the sex and 10-year age bins. 95% CI: 95% confidence interval. Pos = positive.
| Age range | Infected persons | N qPCR positive | Estimated from quarantine | Estimated from outside quarantine | Total | Deaths | Infection fatality rate (95% CI) |
|-----------|------------------|----------------|--------------------------|-------------------------------|-------|--------|--------------------------------|
| All       | 1796             | 447.3          | 933.9                    | 3177.3                        | 10    | 0.3% (0.2%, 0.6%)               |
| 0-70      | 1716             | 411.8          | 884.1                    | 3011.9                        | 3     | 0.1% (0.0%, 0.3%)               |
| >70       | 80               | 35.5           | 49.8                     | 165.4                         | 7     | 4.4% (1.9%, 8.3%)               |
| 70-80     | 57               | 28.8           | 41.9                     | 127.7                         | 3     | 2.4% (0.6%, 6.2%)               |
| >80       | 23               | 6.7            | 8.0                      | 37.7                          | 4     | 11.2% (3.6%, 24.0%)             |

*Table S7.* SARS-CoV-2 infection fatality rate stratified by age.
(in Excel file)

**Table S8.** Pre-existing conditions clinical outcomes among SARS-CoV-2 qPCR-positive cases and their associations with SARS-CoV-2 antibody levels. All associations were performed without adjustment for any covariates and all associations except the age and sex associations were performed adjusting for age, age squared, sex, and time from diagnosis. Information was available on up to 1,215 recovered cases with at least one antibody measurement. Of these, 545 answered an online questionnaire.
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