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Supplementary appendix

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Seroprevalence of anti-SARS-CoV-2 antibodies after the second pandemic peak: Supplementary Appendix

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S1. SARS-CoV-2 epidemic waves in Geneva, serosurvey dates and seroprevalence estimates

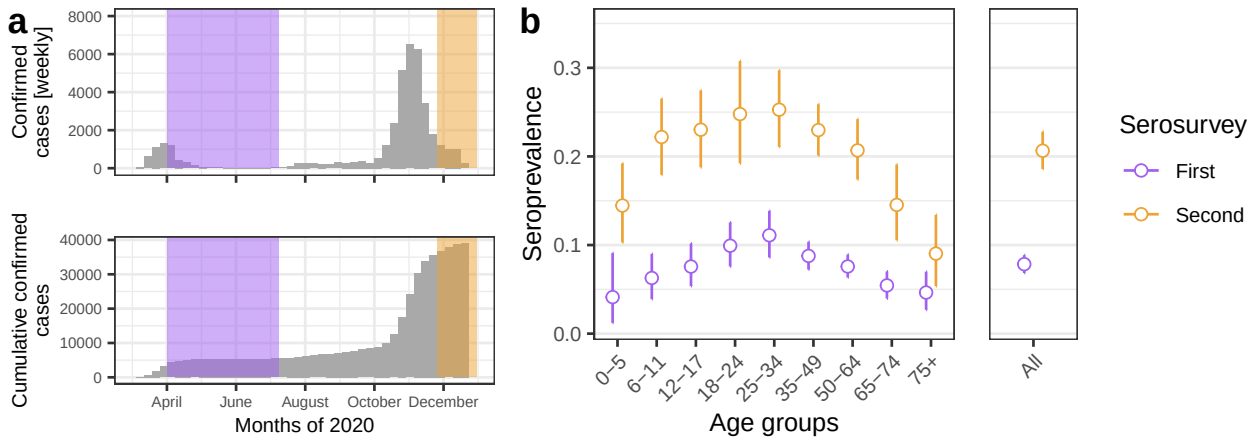

Figure S1: a) Confirmed COVID-19 cases in the canton of Geneva during 2020 and serosurvey timings. b) Seroprevalence estimates by age category. Seroprevalence estimates for the 0-5 age category in the first serosurvey are based only on children aged 5 given our sampling protocol.

Table S1: Seroprevalence estimates and relative risk of seropositivity by age and sex. Data are n (%) unless otherwise stated. Age 25-34 years and female are the reference groups, with which other groups are compared. Estimates are given in terms of the mean and 95% Credible interval (CrI). p values are Bayesian p values. SARS-CoV-2: severe acute respiratory syndrome coronavirus 2. Children (0-17 years) could participate in the study with their family members; analyses account for household clustering[1].

	SARS-CoV-2 serology test result				
	Positive	Negative	**Seroprevalence (95% CrI)**	**Relative risk (95% CrI)**	**p value**
Age groups, years					
0-5 (n=219)	32 (14.6%)	187 (85.4%)	14.9 (10.7-19.6)	0.57 (0.41-0.77)	<0.0001
6-11 (n=395)	86 (21.8%)	309 (78.2%)	22.8 (18.7-27.1)	0.88 (0.70-1.10)	0.27
12-17 (n=400)	87 (21.8%)	313 (78.2%)	23.6 (19.6-28.0)	0.92 (0.73-1.14)	0.41
18-24 (n=206)	56 (27.2%)	150 (72.8%)	25.4 (19.8-31.5)	0.99 (0.75-1.28)	0.88
25-34 (n=336)	89 (26.5%)	247 (73.5%)	25.9 (21.8-30.2)	1 (ref)	–
35-49 (n=1237)	274 (22.2%)	963 (77.8%)	23.6 (20.8-26.4)	0.91 (0.76-1.09)	0.32
50-64 (n=729)	145 (19.9%)	584 (80.1%)	21.2 (18.1-24.6)	0.82 (0.66-1.01)	0.06
65-74 (n=276)	37 (13.4%)	239 (86.6%)	14.9 (10.9-19.5)	0.58 (0.41-0.78)	<0.0001
≥ 75 (n=202)	14 (6.9%)	188 (93.1%)	9.3 (5.5-13.7)	0.36 (0.21-0.54)	<0.0001
Sex					
Male (n=1866)	387 (20.7%)	1479 (79.3%)	21.9 (19.6-24.3)	1.05 (0.95-1.16)	0.34
Female (n=2134)	433 (20.3%)	1701 (79.7%)	20.4 (18.3-22.5)	1 (ref)	–
All					
All (n=4000)	820 (20.5%)	3180 (79.5%)	21.1 (19.2-23.1)	–	–

S2. Study participation rates

Random samples of children under the age of 18 and adults aged 65 or over were invited to participate by letter. Of letters sent, 17% of children under 18 participated in the study and 19% of those aged 65 or over.

We invited participants 18-64 years old from our previous population-based serosurvey, the SEROCoV-POP study[1], to participate in this survey with 69% of those invited participating. A comparison of canton of Geneva's and participant age pyramids is given in Figure S2.

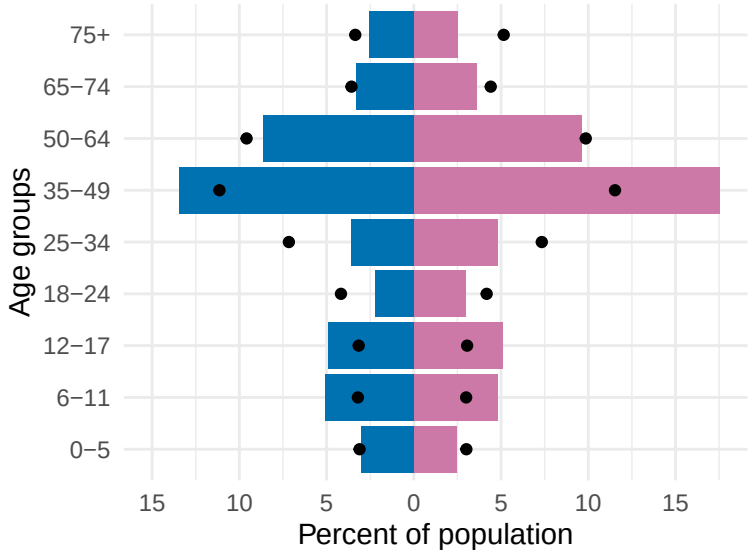

Figure S2: Comparison of sex and age of study sample (bars) and the canton of Geneva's 2019 age pyramid (dots). Blue represents men and purple represents women. Note that seroprevalence estimates are post-stratified to correct for imbalances between the sample and target populations.

S3. Estimation of case to infection ratio

We follow the methods in[1] to estimate the ratio of implied infections (seroprevalence) to the number of virologically-confirmed SARS-CoV-2 infections. It should be noted that in our first estimate of this ratio, most positive tests were from medically attended symptomatic individuals due to testing policy and availability in the first wave. With significantly increased testing and no restrictions on getting tested related to clinical symptoms, tests in this second wave represent a mix of actual COVID-19 cases and mild/asymptomatic infections.

We used the daily number of virologically confirmed SARS-CoV-2 infections from the Canton of Geneva (https://www.ge.ch/document/covid-19-situation-epidemiologique-geneve) and adjusted this time series by assumed times from symptom onset to test result and from symptom onset to seroconversion. While not all positive tests are a result of a symptomatic infection, our approach assumes this adjustment from test date to seroconversion date is equivalent for all infections.

We estimated the time from symptom onset to seroconversion based on validation data from a cohort of 172 PCR-confirmed SARS-CoV-2 infections in adults in Geneva (100 hospitalised and 72 outpatient) tested with the same Roche immunoassay using a parametric accelerated failure time model accounting for right censoring of observations using the `icenReg` package in R. We fit a log-normal model giving a log-mean of 1.48 and a log-standard deviation of 0.97 (Figure S3).

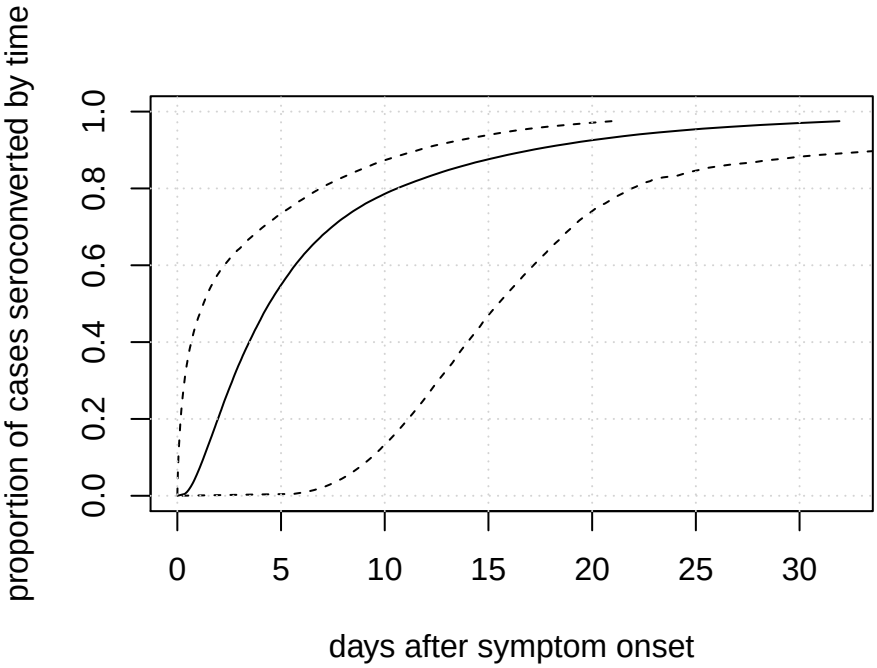

Figure S3: Estimated time to seroconversion after symptom onset assuming a log-normal distribution.

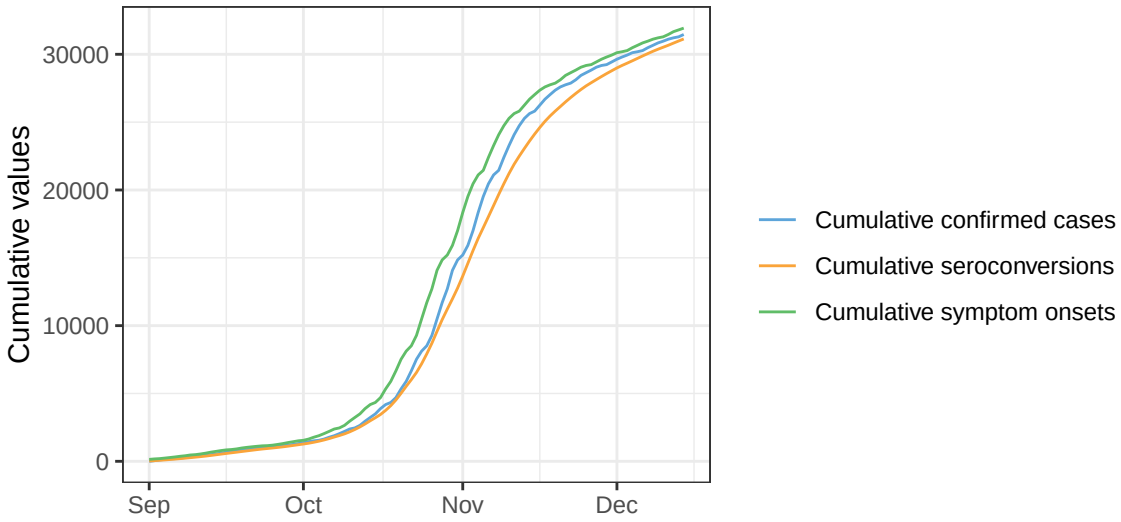

Figure S4: Curves of cumulative reported cases, symptom onsets, and sero-conversions

To obtain the number of infections of the second wave we subtracted the seroprevalence estimates of the first wave in[1] to the ones of the second wave presented in the main text. To estimate the time of seroconversion for each virologically-confirmed infection, we first shifted back the time series of virologically-confirmed infections (time of confirmation) by 3 days, assuming that reporting delays decreased by roughly 50% with respect to the first wave.[2] We then convoluted this time series with the time from symptom onset to seroconversion (truncated at 40 days) (Figure S4). In these calculations we assume that the second wave started on 2020-09-01.

To calculate the ratio of serology-implied infections to virologically-confirmed infections we then divided

the implied number of infections during the second wave by the number of virologically-confirmed infections that have seroconverted up until the mid-point of the second serosurvey (2020-12-08, a mean estimate of 81492 infections versus 30220 reported cases).

We find that for each virologically-confirmed infection reported there were 2.7 (95% CrI: 2.3-3.1) infections in the community. This is a significant decrease from the estimate in our previous serosurvey of 11.6.[1]

S4. Study limitations

Participants between 18 and 64 years of age were invited from a stratified random sample of our previous serosurvey[1] including randomly selected participants as well as members of their households, making this sample not fully randomly selected. Participants < 18 and ≥ 65 were randomly selected from lists of residents obtained from the Swiss Federal Office of Statistics. Index participants under the age of 18 could participate in the study with their household members. In general, both samples only include participants registered as residents in the Canton of Geneva.

Our seroprevalence estimates do not account for possible seroreversions which could lead to lower sensitivity for participants infected during the first wave. While some assays are likely to have this issue, evidence from a recent study in Geneva following infected health workers showed that anti-RBD total Ig antibodies measured with the Elecsys® anti-SARS-CoV-2 S immunoassay (Roche Diagnostics) did not significantly decay over a 6 month period.[3] This is consistent with unpublished data from our group showing those who were seropositive in our first serosurvey almost all remained seropositive when sampled again after 6-8 months.

S5. Funding

This study was funded by the Swiss Federal Office of Public Health, the General Directorate of Health of the Department of Safety, Employment and Health of the canton of Geneva, the Private Foundation of the Geneva University Hospitals, the Swiss School of Public Health (Corona Immunitas Research Program) and the Fondation des Grangettes.

S6. Specchio-COVID19 study group

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References

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2 Sciré J, Nadeau SA, Vaughan TG *et al.* Reproductive number of the COVID-19 epidemic in Switzerland with a focus on the Cantons of Basel-Stadt and Basel-Landschaft. *Swiss Medical Weekly* 2020; **150**: w20271.

3 L'Huillier A, Meyer B, Andrey DO *et al.* Antibody Persistence in the Six Months Following SARS-CoV-2 Infection Among Hospital Workers. *SSRN* DOI:10.2139/ssrn.3720734.