

Supplementary material: Surveillance of SARS-CoV-2 prevalence from repeated pooled testing: application to Swiss routine data

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1 Methods

1.1 Pool-positivity

We derive the probability that a single pooled test returns positive, given the pool size M_t (at time t), the sensitivity S_e and the specificity S_p . Following the approach from Daon et al. [1], we denote $\lambda^t \in \{0, 1\}^{M_t}$ the true infection state at time t , i.e., individual i is infected if $\lambda_i^t = 1$. As shown in Eq. 2.2 of [1], the probability $\theta(t)$ that the pooled test returns positive is:

$$\theta(t) = 1 - S_p (1 - S_e)^{\sum_i \lambda_i^t}$$

The sensitivity is adjusted at the individual level and the specificity at the pool level. We then define the random variable $X_t := \sum_i \lambda_i^t$ as the number of truly infected individuals in the pooled test at time t and assume that X_t follows a binomial distribution with the probability parameter being the prevalence:

$$X_t \sim \text{Bin}(M_t, \pi(t)).$$

Then,

$$\begin{aligned} \theta(t) &= \sum_{k=0}^{M_t} S_p (1 - S_e)^k P(X_t = k) \\ &= \sum_{k=0}^{M_t} S_p (1 - S_e)^k \binom{M_t}{k} \pi(t)^k (1 - \pi(t))^{M_t - k} \\ &= S_p \sum_{k=0}^{M_t} \binom{M_t}{k} ((1 - S_e)\pi(t))^k (1 - \pi(t))^{M_t - k} \\ &= S_p (1 - S_e \pi(t))^{M_t}, \end{aligned} \tag{1}$$

where the last equality follows from the binomial theorem.

1.2 Prior distributions

We assumed that the parameter representing the average prevalence has a logit-normal prior, with default mean of -4 and standard deviation of 2. This corresponds to an average prevalence of 1.8% with 95%

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confidence intervals (CI) of (0.3%,48%). The prior of the overdispersion κ was obtained by adding 2 to an exponential distribution with default mean of 10.

The sensitivity parameter S_e had a beta prior distribution whose hyperparameters were respectively 190 and 40. This corresponds to a mean of approximately 82.6% and with 95% CI of (77.5%, 87.2%).

The specificity S_p was fixed at 100% due to the following reason. From the very low proportion of positive RT-PCR tests in the United Kingdom in summer 2020, we know that the specificity is close to 100% [2]. When assuming that all the positive tests are false positive, a lower bound of 99.9% is achieved. It is however very likely that some of the positive tests are indeed true positive and therefore, the specificity should be even higher. That is why for simplicity, we thus assumed a perfect specificity.

In addition, two parameters determined the Gaussian process used in the GP model: the lengthscale and the output standard deviation. The lengthscale had truncated normal prior distribution with default mean of 0 and standard deviation of 2. The output standard deviation had a truncated normal prior with default mean of 0 and standard deviation of 2.

1.3 Simulation study

We simulated pool test results over 30 weeks in five regions in order to assess the ability of two different models to retrieve the underlying prevalence. We considered four scenarios that mimic various dynamics of SARS-CoV-2 prevalence over time (Figure 1A). The prevalence over time $\pi(t)$ is obtained from a SEIR model, assuming a preinfectious period of 2 days, an infectious period of 10 days and a time-varying reproduction number. To represent the heterogeneity in prevalence between the five regions, we perturbed the prevalence simulated in the four scenarios using a beta distribution:

$$\pi_i(t) \sim \text{Beta}(\pi(t)\kappa, (1 - \pi(t))\kappa)$$

where $\pi_i(t)$ is the prevalence of region i and where κ is fixed to 1000 to reflect an acceptable heterogeneity (see points in Figure 1A). When simulating the pool test results from the prevalence, we considered three different pool sizes ($M = 5, 10$ or 20) and four different number of individuals tested (100, 500, 1000 or 5000) equally distributed over the five regions. For a given region i , the number of positive pools K_i were simulated using a binomial distribution:

$$K_i \sim \text{Binomial}(P, \theta_i(t))$$

where $\theta_i(t) = 1 - S_p(1 - S_e\pi_i(t))^M$ is the probability that a single pooled test in region i returns positive (given a prevalence $\pi_i(t)$ and a pool size M) and P is the number of pools in the region. We assumed a sensitivity S_e of 85% and a specificity S_p of 100%.

For each scenario, pool size and sample size, we generated 100 simulated pool test datasets.

1.4 Imputation of missing data

For 0 (0 %) pool test results, the pool size was missing. We used Multiple Imputation by Chained Equations (MICE) to impute these missing values, adjusting for the type of population, the canton and time [3]. We run five chains.

April 2021 and 29 August 2022 in three settings: schools (panel A), healthcare centers (panel B) and selected workplaces (panel C). The lines represent the posterior means, and the colored areas the 95% credible intervals. The white bars show the weekly number of reported cases of SARS-CoV-2 infections in corresponding age groups (0-20 for schools, above 60 for healthcare centers, and 21-60 for selected workplaces).

2.2 Correlations

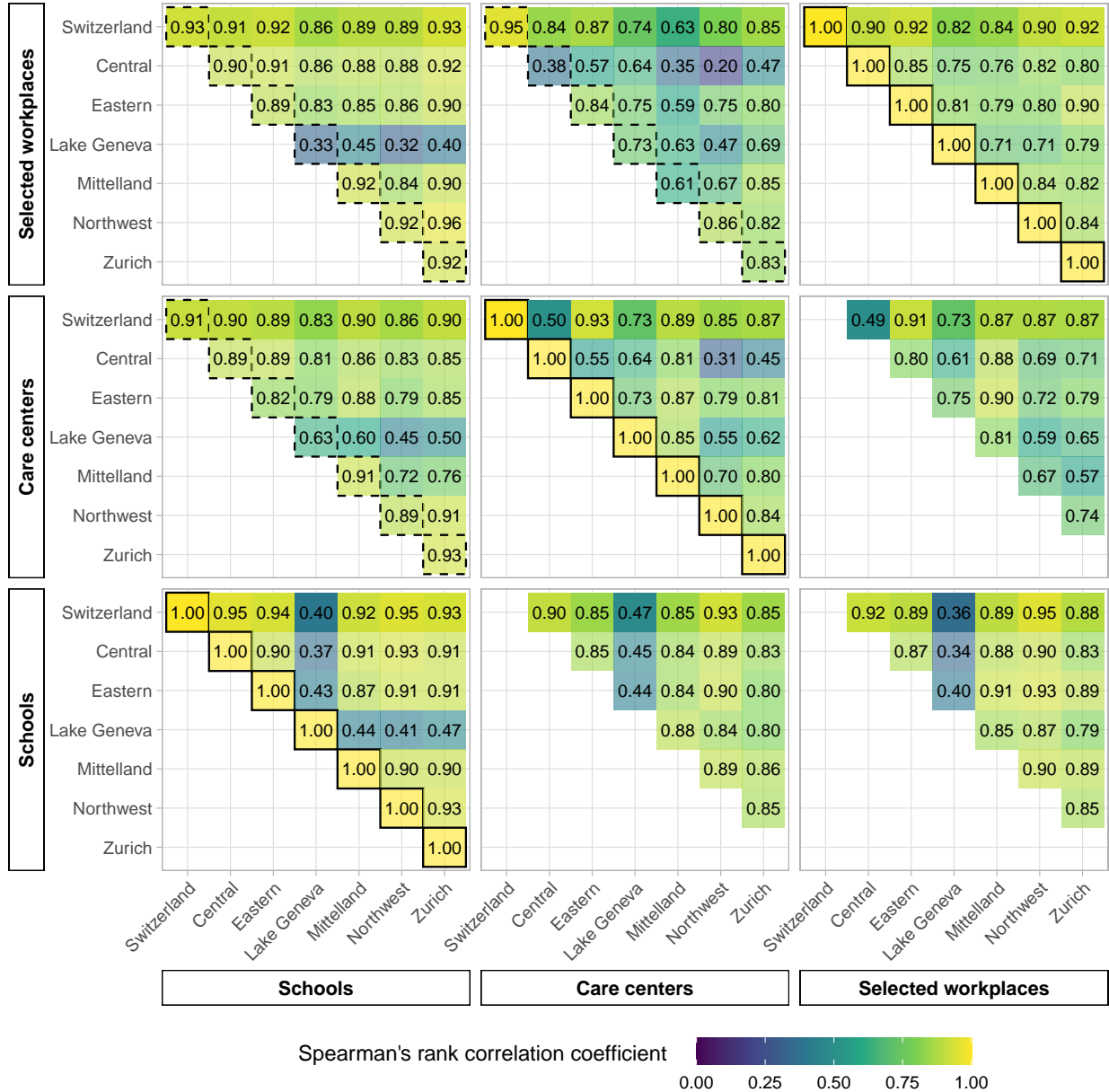


Figure S2. Correlation between SARS-CoV-2 prevalence estimated from pooled test data across the different geographical levels and across settings.

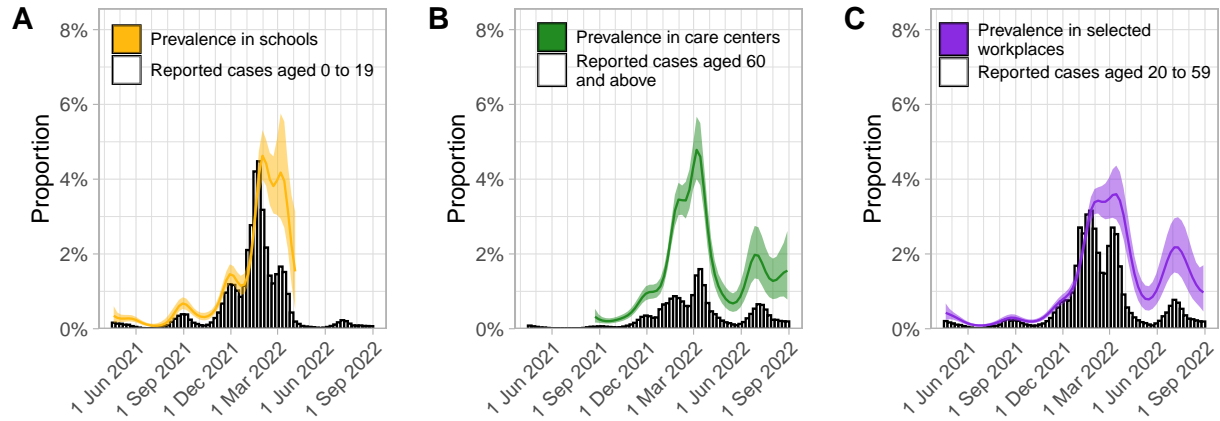
2.3 Additional analyses

In the main analysis, we assumed a perfect RT-PCR test specificity and used the dataset from Marando et al. [4] to estimate the sensitivity of RT-PCR tests and propagate its uncertainty on the results. In two additional analyses, we explored the impact of these assumptions on the prevalence estimates. First, we investigated

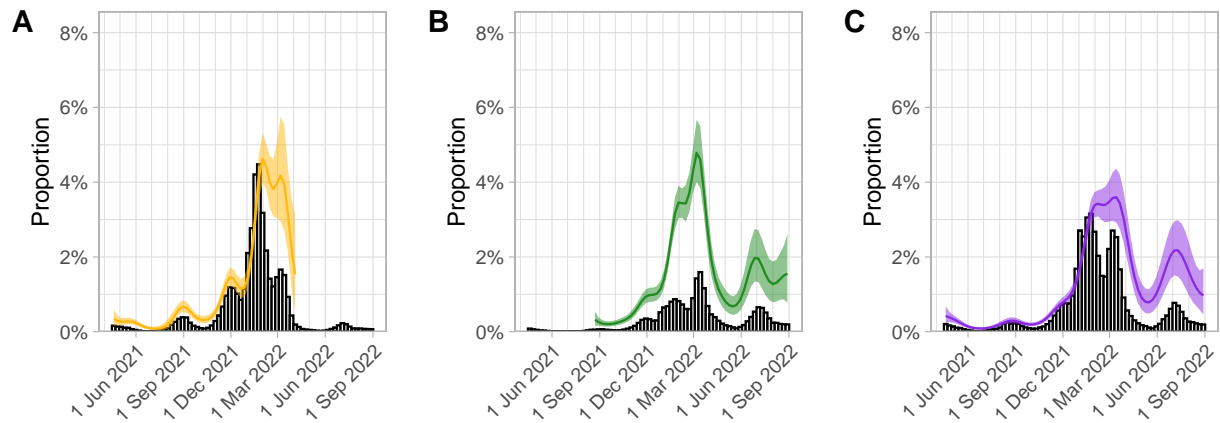
the impact of a lower test specificity. The assumption of perfect specificity was motivated by the very low proportion of positive RT-PCR tests observed in the United Kingdom in summer 2020, where only 159 of the 208,730 RT-PCR tests returned positive. Assuming that all the positive tests are false positive, we can derive a lower bound for specificity of 99.9%. The specificity is likely might be even higher, as some positive tests are likely to be true positive. For this reason and for the sake of simplicity, we assumed a perfect specificity. Here, we assessed the impact of assuming a specificity of 99.9% on the prevalence estimates. The results displayed in Figure S3 (“Imperfect specificity”) are almost indistinguishable from the main analysis (“Main results”), showing the very limited impact of the uncertainty about test specificity.

Second we investigated the impact of using an alternative dataset to inform the model about test sensitivity. Rather than using the dataset from Marando et al. [4], we used the dataset from Mair et al. [5], which gathers data from 11 studies, with a total sample size of 1,208, resulting in a mean sensitivity of 90.6%. The prevalence estimates obtained when using this alternative dataset (see Figure S3 “Alternative sensitivity dataset”) look very similar to the main analysis.

Main results



Imperfect specificity



Alternative sensitivity dataset

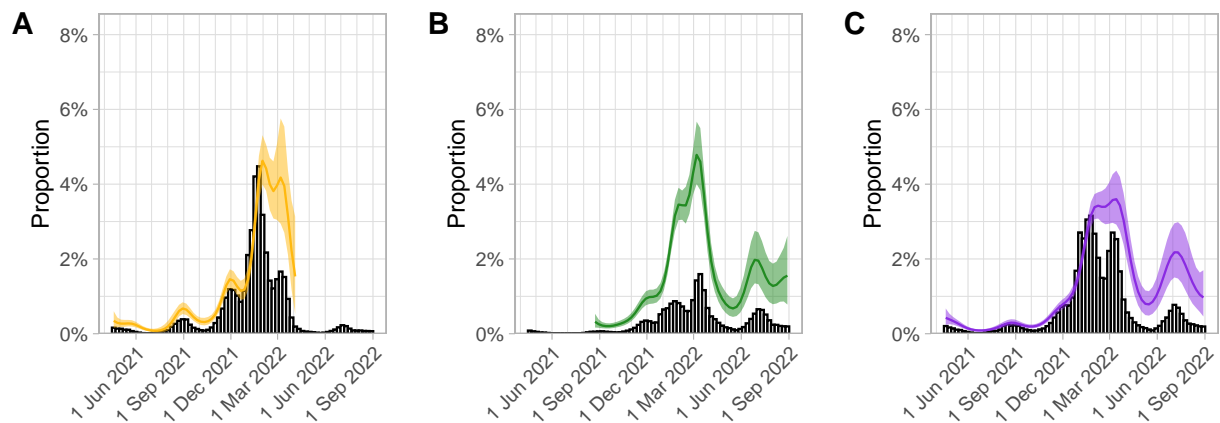


Figure S3. SARS-CoV-2 prevalence estimated from pooled test data in Switzerland between 19 April 2021 and 29 August 2022 in three settings: schools (panels A), care centers (panels B) and selected workplaces (panels C), according to different assumptions regarding test specificity and sensitivity. The first row (“Main results”) displays the prevalence estimates when assuming perfect specificity and using dataset from [4] to

estimate test sensitivity. The second row (“Imperfect specificity”) shows the prevalence estimates when assuming a test specificity of 99.9%. The third row shows the prevalence estimates when using an alternative dataset (from [5]) to estimate test sensitivity.

References

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