Online Supplement: "The interplay between excess mortality and laboratory-confirmed COVID-19-related deaths in Switzerland, a nationwide study."

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S1.1 Population models

S1.1.1 Model specification

Let P_{ijkl} be the population for the i-th sex (male-female), j-th age-group (<40, 40-59, 60-69, 70-79, $\geq$ 80), k-th year (2010-2019) and l-th canton. Let X_{1i} be the sex and X_{2k} be the year covariate. To predict populations for the years 2020-2023, had the COVID-19 pandemic not occurred, we considered 6 models of the following formulation:

$$P_{ijkl} \sim \text{Poisson}(\mu_{ijkl})$$

$$\log(\mu_{ijkl}) = \beta_0 + \beta_1 X_{1i} + \beta_2 X_{2k} + b_{ikl}$$

where b_{ikl} is a random effect that has an age, temporal and spatial structure, see Table S1. All random effects were assigned an iid structure: $w_j, v_k, u_l, \xi_{jkl}, \beta_{2jkl}, \sim N(0, \sigma_g^2), g = 1, \ldots, 5$ and for σ_t^2 we considered penalised complexity priors [1]. In particular, we selected a prior so that $\Pr(\sigma_t > 10) = 0.1$, implying that it is unlikely to have population counts larger than exp(10) based solely on the selected structure of the random effects. All the models were fit using the Integrated Nested Laplace Approximation (INLA) for quick computation [2].

Model	Abbreviation	b_{ikl}
1	BASE	$w_j + v_k + u_l$
2	OV	$w_j + v_k + u_l + \xi_{jkl}$
3	OV_INT	$w_j + v_k + u_l + w_j \otimes v_k + w_j \otimes u_l + v_k \otimes u_l + \xi_{jkl}$
4	VC	$w_j + v_k + u_l + \beta_{2jkl} X_{2k}$
5	VC_OV	$w_j + v_k + u_l + \xi_{jkl} + \beta_{2jkl} X_{2k}$
6	VC_OV_INT	$w_j + v_k + u_l + w_j \otimes v_k + w_j \otimes u_l + v_k \otimes u_l + \xi_{jkl} + \beta_{2jkl} X_{2k}$

Table S1: Specification of the random effects of the different population models. The notation $\otimes$ defines for the Kronecker product.

S1.1.2 Cross validation

To mimic the scenario we want to reproduce, we selected to leave out the past 3 years all-together and examine the model prediction. To compare model prediction we calculated the coverage proportion, root mean square error (RMSE) and the mean bias. The coverage proportion is defined as the probability that the true population

value lies in the 95% model based credible intervals, the MSE as $E[(\tilde{Y}_{ijkl} - Y_{ijkl})^2]$ and the mean bias as $E[\tilde{Y}_{ijkl} - Y_{ijkl}]$, where $\tilde{Y}_{ijkl}$ are the predictions and Y_{ijkl} the true values of the population.

S1.1.3 Results

Table S2, shows the results of the cross validation and it is apparent that model 3, performs best, and this was the model selected for the subsequent analysis of excess deaths.

Model	Coverage	RMSE	mean bias
BASE	0.08	6198	15
OV	0.96	7481	145
OV_INT	0.98	6009	9
VC	0.38	7415	175
VC_OV	0.55	6265	17
VC_OV_INT	0.61	7694	139

Table S2: Coverage, root mean square error (RMSE) and mean bias for the different models based on the leave out the past 3 years cross validation scheme.

S1.2 Expected mortality model

S1.2.1 Model specification

We used a Bayesian hierarchical model to predict deaths in 2020-2022, under the counterfactual scenario of absence of the COVID-19 pandemic. Let Y_{jtkl} be the number of all-cause deaths, P_{jtkl} be the population at risk (for the weeks during 2010-2019 this is fixed, whereas we used 200 samples to propagate the model based uncertainty from the population model for the weeks during 2020-2022) and r_{jtkl} the risk in the j-th age-sex group (male-female and <40, 40-59, 60-69, 70-79, ≥ 80), t-th week of the k-th year ($t = 1, \ldots, 13$ with year 1 corresponding to 2010) and l-th canton ($s = 1, \ldots, S$). We assume a Poisson distribution for the number of deaths Y_{jtkl} and specified the following model:

$$Y_{jtkl} \sim \text{Poisson}\big(r_{jtkl} P_{jtkl}\big)$$

$$\log\left(r_{jtkl}\right) = \beta_{0j} + \beta_1 X_{1t} + \beta_2 X_{2j} + \beta_3 X_{3k} + f(x_{jtl}) + v_t + u_l,$$

where β_{0t} is a week specific intercept given by $\beta_{0t} = \beta_0 + \epsilon_t$, with β_0 being the global intercept and $\epsilon_t \sim \text{Normal}(0, \sigma_\epsilon^2)$ an unstructured random effect representing the deviation of each week from the global intercept, with σ_ϵ^2 denoting the variance of ϵ_t. The term β_1 represents the effect of public holidays, β_2 the effect of age and β_3 a linear term to capture the long-term trend of the mortality. The effect of (mean weekly and cantonal) temperature on the all-cause mortality is captured in the flexible functions $f(\cdot)$. We define $f(\cdot)$ as a second-order random walk:

$$x_{jtl} \mid x_{(t-1)jl}, x_{(t-2)jl}, \sigma_x^2 \sim \text{Normal}\left(2x_{(t-1)jl} + x_{(t-2)jl}, \sigma_x^2\right), \tag{1}$$

with σ_x^2 denoting the variance.

We accounted for seasonality using a non-linear weekly effect v_t with a first order random walk (RW1) structure:

$$v_t \mid v_{t-1}, \sigma_t^2 \sim \text{Normal}(v_{t-1}, \sigma_t^2),$$

where σ_t^2 is the variance of v_t.

The term u_l is defined as a reparametrisation of the Besag-York-Mollié model given by the sum of an unstructured random effect, $\gamma_l \sim \text{Normal}(0, \sigma_\gamma^2)$, and a spatially structured effect δ_l [3, 4]. In particular u_l is defined as:

$$u_l = \sigma_u^2 \left(\sqrt{1-\theta}\gamma_l^\star + \sqrt{\theta}\delta_l^\star\right),$$

where $\gamma_l^\star$ and $\delta_l^\star$ are standardised version of γ_l and δ_l to have variance equal to 1 [1]. The term $0 \leq \theta \leq 1$ is a mixing parameter which measures the proportion of the marginal variance explained by the structured effect

and σ_u^2 the variance of the spatial field.

S1.2.2 Prior specification

We specified uninformative priors for the fixed effects β_0, β_1 and β_2. For the hyperparameters of the random effects we considered priors that tend to regularise inference while not providing too strong information [1]. For the standard deviation of the spatial field we defined a prior so that $\Pr(\sigma_u > 1) = 0.01$, implying that it is unlikely to have a spatial relative risk higher than exp(2) based solely on spatial variation. For θ we set $\Pr(\theta < 0.5) = 0.5$ reflecting our lack of knowledge about which spatial component, the unstructured or structured, should dominate the field u. For the rest of the standard deviations we defined the priors as $\Pr(\sigma_* > 1) = 0.01$.

S1.2.3 Cross validation

To examine the predictive ability of the above-mentioned model we defined a cross validation scheme, leaving the past 2 years out (we did not leave a third year out, as our predictions for 2022 are only for the first 3 months). We used metrics regarding the coverage proportion, bias, and correlation between predicted and true value of deaths. The results of the cross validation are shown on Figures S1-5 and Table S3.

Figure S1 shows the correlation between predicted and true value of deaths by age, sex and year (across the weeks and cantons). We see that the correlation is highest for the older groups and is not modified by year or sex. Figure S2 shows the bias by age, sex and year (across the weeks and cantons) and we see that it is always centred in 0. Figure S3 shows the coverage proportion by age, sex and year and we see that is pretty high for all groups, with the lowest (0.95) being for the older age groups. We also calculated the relative bias (truth-predicted / truth) by canton and and week and we can see that there the model is overall unbiased, Figure S4 and S5. Table S3 calculated the relative bias in the totals by age, sex in 2018, 2019 and 2018 and 2019 combined. We observed higher relative bias in females in general, but the overall relative bias for the totals is 0.

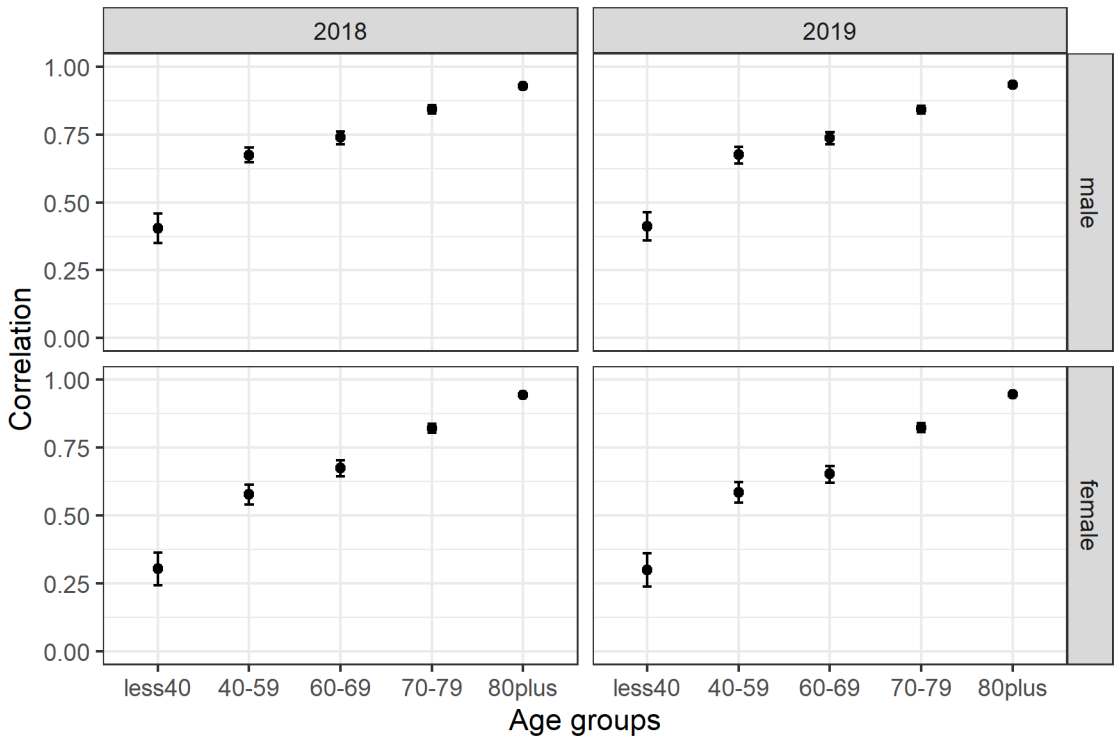

Figure S1: Correlation between the predicted and observed weekly and cantonal number of deaths by year, age and sex.

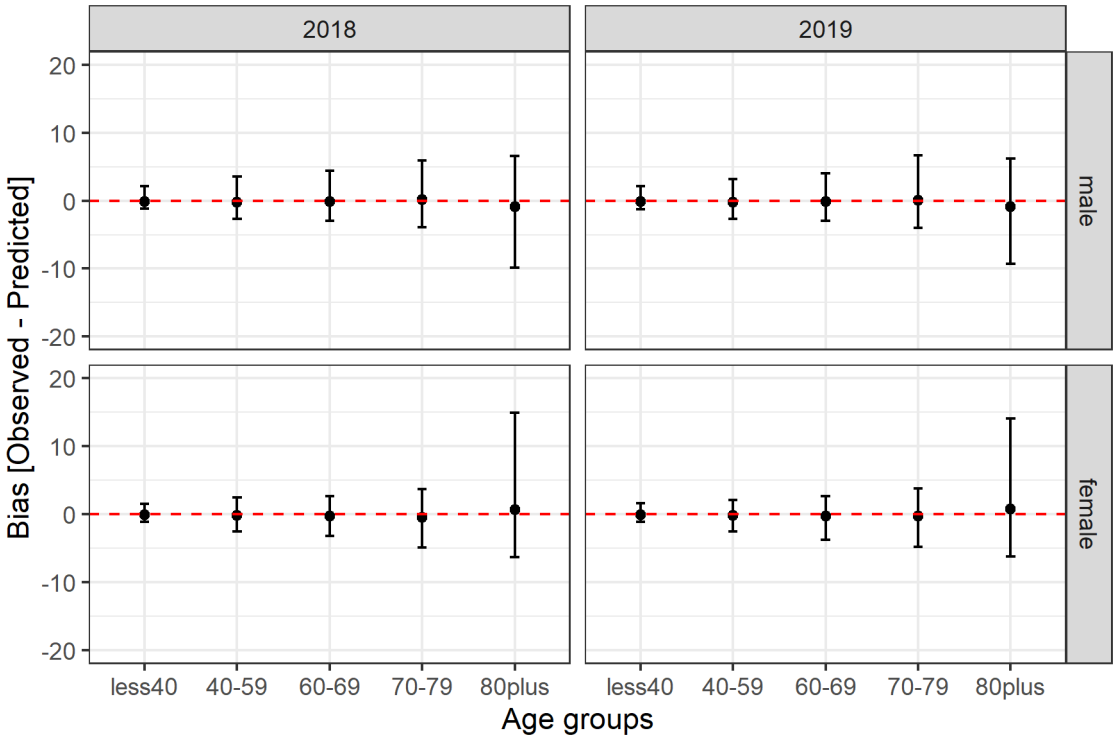

Figure S2: Bias between the predicted and observed weekly and cantonal number of deaths by year, age and sex.

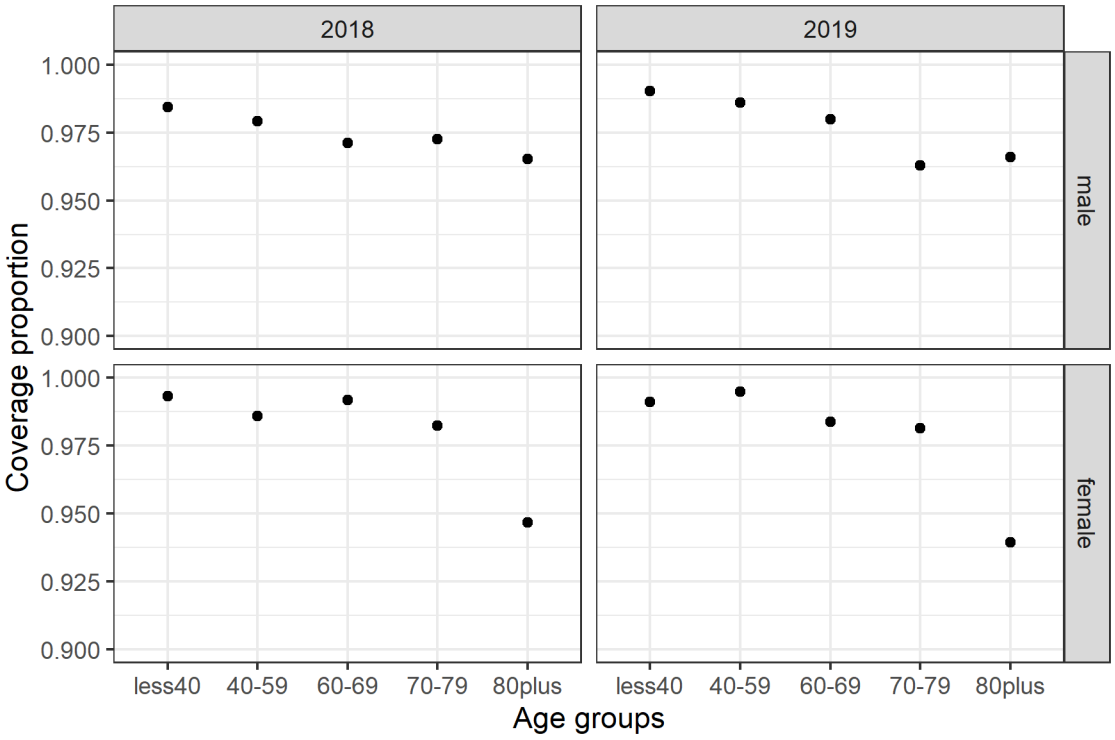

Figure S3: Coverage proportion by year, age and sex.

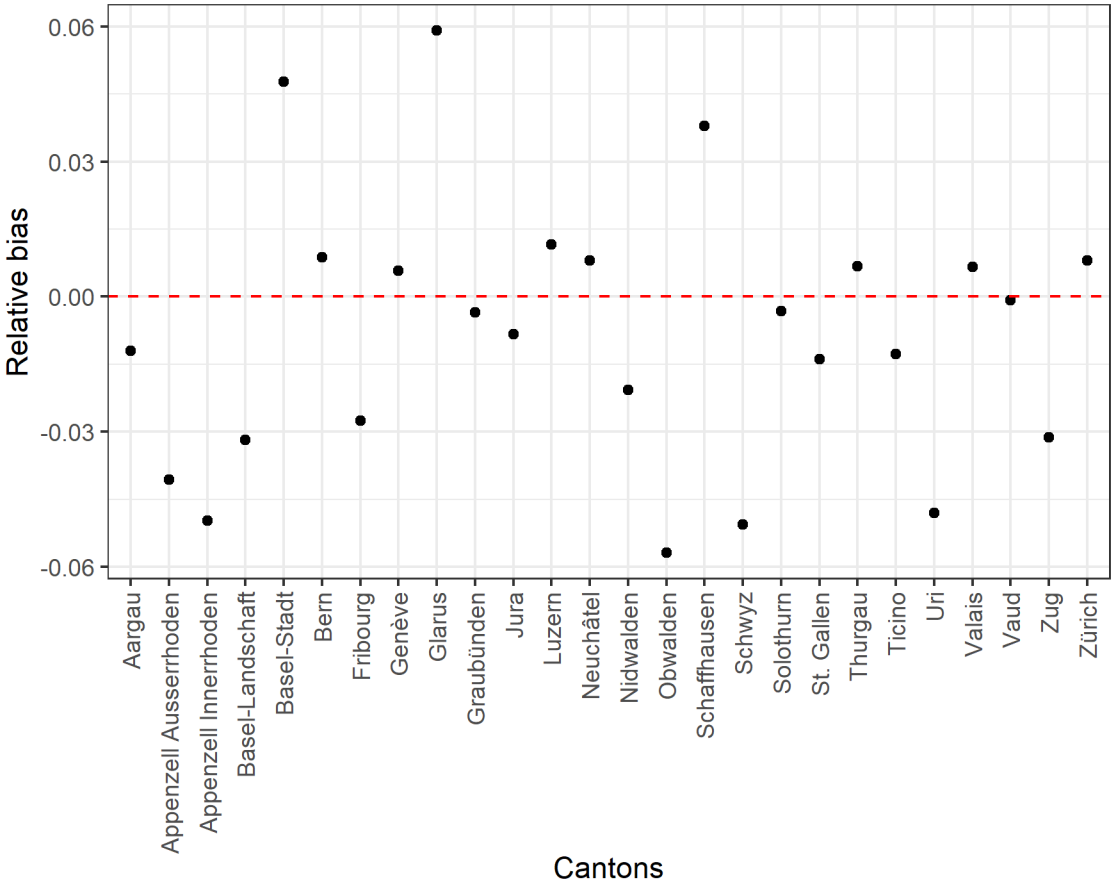

Figure S4: Relative bias by canton.

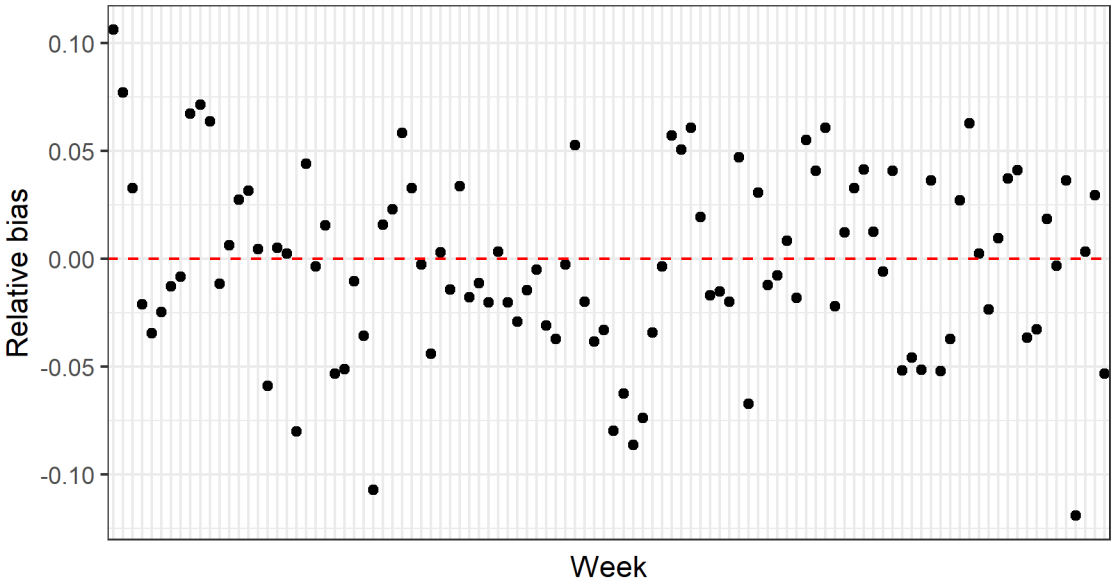

Figure S5: Relative bias by week.

age	sex	2018	2019	2018-2019
less40	male	0.05	0.01	0.04
40-59	male	0.04	0.00	0.02
60-69	male	0.07	0.04	0.05
70-79	male	0.06	0.07	0.07
80plus	male	-0.09	-0.10	-0.10
less40	female	-0.13	-0.22	-0.18
40-59	female	-0.11	-0.19	-0.15
60-69	female	-0.16	-0.19	-0.17
70-79	female	-0.11	-0.08	-0.10
80plus	female	0.08	0.09	0.08
less40	Total	-0.02	-0.07	-0.04
40-59	Total	-0.01	-0.07	-0.04
60-69	Total	-0.02	-0.05	-0.03
70-79	Total	-0.01	0.01	-0.00
80plus	Total	0.01	0.01	0.01
Total	Total	0.00	-0.00	-0.00

Table S3: Relative bias by age, sex and year.

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