The interplay between excess mortality and laboratory-confirmed COVID-19-related deaths in Switzerland

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# Introduction

There are two main approaches to quantify the impact of COVID-19 mortality at the population level. The first approach relies upon the reporting of laboratory-confirmed deaths, i.e. deaths of people with a recent confirmed positive SARS-CoV-2 RT-PCR or rapid antigen test. This has the advantage of being available in real-time, but depends on the quality and comprehensiveness of the country’s deaths registration system and on the testing availability. It is therefore almost never exhaustive, as some deaths will remain unidentified because of a lack of test (e.g. due to testing practices, test shortages or overwhelmed health systems) [1]. Laboratory-confirmed deaths also do not include deaths that have been indirectly caused (or averted) by the SARS-CoV-2 pandemic (e.g. in consequence of control measures). The second approach is based on excess mortality, and relies upon all-cause mortality data and counter-factual reasoning [2]. The idea is to compare the observed number of deaths to what would have been expected had the SARS-CoV-2 pandemic not occurred, based on mortality data from the previous years, demographic changes and a set of covariates. Excess mortality has the advantage of summing all the negative and positive effects of the occurrence of the COVID-19 pandemic on mortality, at the cost of not being able to disentangle them [3]. It is also highly dependent on model assumptions and methodological choices, such as for instance age-specific population trends [4].

There have been many attempts at estimating excess mortality associated with COVID-19 in various settings [3], but new approaches are needed to distinguish the proportion of excess mortality that can be directly attributed to SARS-CoV-2 infections [3]. While data on laboratory-confirmed COVID-19-related deaths are incomplete, more information can be gained by linking their variations across time, space and population groups with variations in excess mortality. Excesses of deaths observed during peaks of epidemic activity, when laboratory-confirmed deaths are high, may serve to estimate the total number of deaths that can be directly attributed to SARS-CoV-2 infections, together with the proportion that was confirmed in laboratories (the ascertainment proportion). On the other hand, deficits or excesses in mortality observed between epidemic waves, when there is no or a weak epidemic activity, may provide estimates of the indirect effect of the COVID-19 pandemic on mortality. Deficits in deaths observed in the weeks following large epidemic waves may be attributed to mortality displacement (sometimes called the “harvesting” effect). Variations in mortality distributed more uniformly across the pandemic period may be attributed to mandated or spontaneous changes in behaviors that led to a reduction or an increase of the risk of death. Examples include a diminution of social contacts preventing the spread of other pathogens such as influenza, work from home limiting traffic and thus road accidents, or in the other direction a general increase in anxiety levels or substance abuse.

In this nationwide study in Switzerland in 2020 and 2021, we aimed to characterize the similarities and discrepancies between laboratory-confirmed COVID-19-related deaths and excess mortality by time period, location and age group. We used a validated statistical approach to compute the expected number of all-cause deaths in 2020 and 2021 by week, age group and location using historical data from 2014-2019, accounting for the effect of temperature and population changes. We then developed a statistical method to decompose all-cause deaths into death excesses directly attributable to SARS-CoV-2 infections and deaths excesses or deficits indirectly attributable to the pandemic, and use this decomposition to study specific phenomenon such as death ascertainment, mortality displacement and other indirect effects of COVID-19 on all-cause mortality during different time periods of the pandemic.

# Methods

## Data sources

We retrieved population data for the prepandemic years 2014 to 2019 from the Federal Statistical Office (FSO) in Switzerland [6]. Estimates are available for 31 December of each year by age (5 groups: 0-39, 40-59, 60-69, 70-79 and 80 and older), sex (2 groups) and administrative region (26 cantons). These were used to predict population sizes in each stratum for each week of the entire study period. Data on all-cause deaths was also obtained from the FSO [7]. These consisted of counts of deaths from any cause by age, sex and canton for each week of 2014 to 2019, and afterwards up to 03 April 2022. Details about the cause of death as listed in the death certificate are encoded with a delay of several months and were not available for this analysis. Data from the prepandemic years were used to compute expected death counts per stratum during the pandemic period. These predictions were supported by covariates related with ambient temperature (obtained from MeteoSwiss [8]) and national holidays (obtained from nager.date [9]). Daily mean ambient temperature between 2014 and 2022 at 1km grid was aggregated by taking means per week and canton. National holidays were considered as dummy variables, and defined on a weekly basis for each canton, being 1 if there was at least 1 cantonal holiday in that week. The declaration of laboratory-confirmed SARS-CoV-2-related deaths has been mandatory in Switzerland since February 2020. All collected data at the individual are centralized at the Federal Office of Public Health (FOPH), and are available on motivated request [10]. Available information include age, sex, canton of residence, and the date and type of the positive SARS-CoV-2 test.

## Statistical methods

### Population model

Data on population size on 31 December 2014-2019 by age group, sex and canton was used to predict population sizes in each stratum for each week of the entire study period (01 January, 2014 to 03 April 2022) with a two-step procedure. First, we fitted a Poisson regression model to population data from 2014 to 2019. This model included a linear yearly trend, a fixed effect by sex, and independent random effects by week (seasonality), by age group, by sex and by canton. We validated this model with cross-validation and determined that the best model also included two-way and three-way interactions between canton, age and week. This model was used to obtain posterior distributions of the population in each stratum for 31 December 2020, 2021 and 2022, under the counter-factual scenario that the pandemic did not occur. In a second step, we used linear interpolation to obtain weekly estimates of population size (with uncertainty).

### Expected deaths model

We estimated the expected number of all-cause deaths for each week between 24 February 2020, the day of the first confirmed SARS-CoV-2 case in Switzerland, and 03 April 2022 by age, sex and canton of residence using historical data (2014-2019) and expanding a previously proposed model [11]. Briefly, we used Bayesian spatio-temporal models accounting for population trends and including covariates related with temperature and national holidays. To account for uncertainty in population estimates, we applied the model multiple times over the posterior distributions of the population predictions. Since the effect of temperature on all-cause mortality is expected to be U-shaped, we used a random walk of order 2 to allow flexible fits. We accounted for seasonality using a random walk of order 1 at the weekly level, for long-term trends using a white noise process at the yearly level, and for spatial autocorrelation using conditional autoregressive priors. In particular, we modeled spatial autocorrelation using an extension of the BYM model, allowing for a mixing parameter which measures the proportion of the marginal variance explained by the spatial autocorrelation term [REF]. The model has been internally validated and found to have high predictive accuracy in the older groups, whereas the results were less reliable in for people years old [11]. The fitted model was used to obtain posterior distributions of the expected number of all-cause deaths by age group, sex and canton in each week between 24 February 2020 and 03 April 2022.

### Decomposition model

We developed a method to decompose the observed all-cause deaths into 1) the number that can be expected given historical trends and 2) the number of deaths attributed to the COVID-19 pandemic. We used a Poisson regression model with an identity link and no intercept term of the form:

where is the observed number of all-cause deaths on week , is the number of laboratory-confirmed SARS-CoV-2-related deaths, is the expected number of all-cause deaths given historical trends, and is a normally-distributed overdispersion term centered at zero.

Within this formulation, is the number of all-cause deaths for each unit increase in laboratory-confirmed deaths, after adjusting for the expected number of all-cause deaths given historical trends. That means that under perfect case ascertainment . If , then we observe a greater number of deaths attributed to SARS-CoV-2 infections compared with the number of laboratory-confirmed deaths. The ascertainment proportion of SARS-CoV-2-related deaths is obtained by . This relies on the assumption that when there is at least one laboratory-confirmed death in a given week, then the excess in observed all-cause deaths can be directly attributed to SARS-CoV-2. In a similar way, is the number of all-cause deaths for each unit increase in the expected number of all-cause deaths, after adjusting for the direct effect of SARS-CoV-2. We expect when the net effect of the pandemic-related behavioral, societal and health system changes on all-cause deaths is zero. The estimate of can thus be interpreted as a measure of the indirect effect of the pandemic on mortality. If , then there were fewer all-cause deaths than expected after removing the direct effect of SARS-CoV-2, which implies an indirect protective effect of all changes and control measures associated with the pandemic. Estimates of and thus provide a way to understand the interplay between laboratory-confirmed SARS-CoV-2-related deaths and excess all-cause deaths, and allow to differentiate between direct and indirect consequences of the SARS-CoV-2 pandemic on mortality.

Going beyond the general case at the country level for the whole period, we extended the model presented above to examine these associations by phase (from 1 to 6 as defined by the Federal Office of Public Health), by age group (0-39, 40-59, 60-69, 70-79 and 80+), and by area (26 cantons). To this end, we introduced multiple and for each phase, each age group or each area separately, with the additional constraint of a multilevel structure allowing a smoothing towards the global mean of the estimator [12].

# Results

In Switzerland, there were 155,924 observed all-cause deaths and 13,130 laboratory-confirmed COVID-19 from 24 February 2020 to 03 April 2022 (Table 1). Figure 1A shows the relative excess mortality in Switzerland compared to what would have been expected had the pandemic not occurred. We observe that during the pandemic period there was overall increase in excess mortality of [TO UPDATE] 3.1% (95% CrI: -4.3, 11.2), with phase 3 (covering the period between 28 September 2020 and 15 February 2021) being the period with the highest relative excess mortality ([TO UPDATE]24.4, 95% CrI: 14.7, 35.5). We find evidence suggesting a harvesting effect during phase 4 (covering the period between 15 February 2021 and 21 June 2021) with the relative excess mortality being [TO UPDATE]-11.7 (95% CrI: -20.0, -2.5), and weaker evidence during phases 2 and 5. The age groups affected most by the pandemic were the ones over 70, whereas the cantons affected the most were Glarus and Jura. During the first phase of the pandemic the areas hit the most were the ones near the borders with France and Italy (cantons of Ticino, Geneva and Vaud), whereas excess mortality was more homogeneous during phase 3, and focused more on the northern and eastern regions during phase 6 (Figure 1B).

Weekly counts of laboratory-confirmed SARS-CoV-2-related deaths were aligned with estimates of excess all-cause mortality in Switzerland during most of the time (Figure 2). Quantitatively, the number of excess all-cause deaths was greater than the counts of laboratory-confirmed deaths during epidemic waves (phases 1, 3 and 6). This was translated into an overall estimate of of 1.39 (95%CrI: 1.21 to 1.58), suggesting that there were on average 39% (95%CrI: 21 to 58) more deaths directly attributable to SARS-CoV-2 than laboratory-confirmed deaths during the period (Table 1). Given that there have been 13,130 laboratory-confirmed SARS-CoV-2-related deaths over the period, this implies that the total number of deaths directly attributable to SARS-CoV-2 in Switzerland up to 03 April 2022 is 18,313 (15,843 to 20,757).

Outside of large epidemic waves (phases 2, 4, 5 and 7), the observed number of all-cause deaths was generally lower than expected based on historical trends. The overall estimate of was 0.92 (95%CrI: 0.86 to 1.01), suggesting that there were 8% (95%CrI: -1 to 14) fewer all-cause deaths than expected during the COVID-19 pandemic (after adjusting for the direct effects of SARS-CoV-2 infection on mortality).

Looking at the variation of these indicators across phases brings further insights. The relative number of deaths directly attributable to SARS-CoV-2 for each laboratory-confirmed death () was estimated around 1.5 during phases 1 and 3 and around 2 during phases 5 and 6, suggesting an ascertainment proportion of COVID-19 deaths ranging between 50 and 66% (Figure 1B). This estimate is less precise during periods where counts of laboratory-confirmed cases were low (phases 2, 4 and 7). The relative deficit in deaths indirectly attributable to the COVID-19 pandemic () also varied by phase. It was comparatively lower during large epidemic waves (phases 1 and 3), but also in the period following epidemic waves (phases 4 and 7), suggesting short-term mortality displacement.

Variation of by age group suggests that more deaths were not ascertained in age group 80+, while the data was compatible with 100% ascertainment () in other age groups. Estimates of show a different gradient by age, with a reduction in all-cause mortality () in age groups 40-59 and 60-69. Below 40 and above 70, the data was compatible with no or a small reduction in all-cause mortality. Estimates by canton show generally homogeneous results for the whole of Switzerland, bringing more weight to our results. There were a few exceptions with higher estimates of , potentially signaling an issue in the local reporting system.

# Discussion

Summary of main results and of the model:

* total excess deaths, total laboratory confirmed deaths
* general alignment between excess deaths and laboratory-confirmed deaths
* estimated total deaths directly due to COVID-19, comment on ascertainment
* estimated reduction on other-than-COVID deaths

Comment on beta\_1:

* Variation of by age group suggests that more deaths were not ascertained in age group 80+, which points toward nursing homes as the place where incomplete ascertainment occurs, confirming other reports [1]
* Christian: You might want to add that this was particularly pronounced during the second wave and the most recent time periods when testing was probably reduced due the availability of the vaccines.

Comment on beta\_2:

* This can be explained by a combination of three different phenomena. First, the model based on historical trends may have overestimated the expected all-cause mortality, which would lead to an underestimation of but would not impact . Second, it could be explained by some level of mortality displacement, whereby SARS-CoV-2 precipitated deaths that would have occurred during the period anyway. Third, the deficit could be attributed to the indirect effect of the pandemic, including prevention and control measures and a large array of changes such as reductions in mobility and traffic, social contacts and activities, or air pollution levels.
* Christian: Maybe worth hypothesizing how many deaths can be averted by missing two annual influenza epidemics. I would say this can be easily 1,000-3,000.
* Estimates of also show a gradient by age, with the groups most affected by SARS-CoV-2 mortality also being the ones that show a deficit of all-cause deaths, an argument in favor of mortality displacement, but also pointing towards the protective effects of the non-pharmaceutical interventions in the older age groups (for instance resulting in a lack of influenza season).

Limitations:

* lack cause of deaths
* Estimates restricted on time periods defined by FOPH

Comparisons:

* Compare numbers to ref. 3 and <https://elifesciences.org/articles/69336> (see <https://github.com/dkobak/excess-mortality>). Karlinsky et al. report an excess mortality of 12,000 (18% of baseline annual deaths) and 90% ascertainment.

# Conclusions

# Table and figures

**Table 1.** Summary of mortality patterns in Switzerland between February 2020 and December 2021.

table1 %>%   
 kableExtra::kable(col.names = c("Quantity","Value (95% uncertainty interval where applicable)")) %>%   
 kableExtra::add\_footnote(c("adjusted for expected all-cause deaths","adjusted for deaths directly caused by SARS-CoV-2")) %>%   
 kableExtra::kable\_paper()

Quantity

Value (95% uncertainty interval where applicable)

Laboratory-confirmed COVID-19 deaths

13,130

Observed all-cause deaths

155,924

Expected all-cause deaths

148,932 (137,523 to 160,716)

Excess all-cause deaths

6,992 (-4,792 to 18,401)

Deaths directly attributable to SARS-CoV-2 for each laboratory-confirmed death ()

1.39 (1.21 to 1.58)

Observed all-cause deaths for each expected all-cause deaths ()

0.92 (0.86 to 1.01)

Deaths directly attributable to SARS-CoV-2

18,313 (15,843 to 20,757)

Ascertainment of deaths directly attributable to SARS-CoV-2

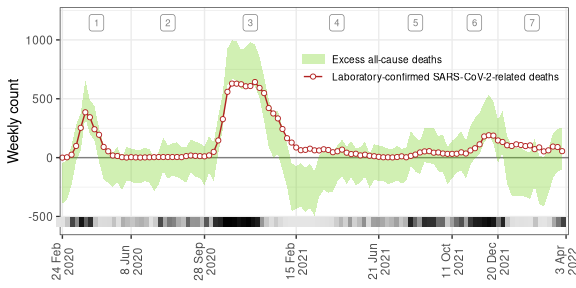
72% (63 to 83)

a adjusted for expected all-cause deaths

b adjusted for deaths directly caused by SARS-CoV-2

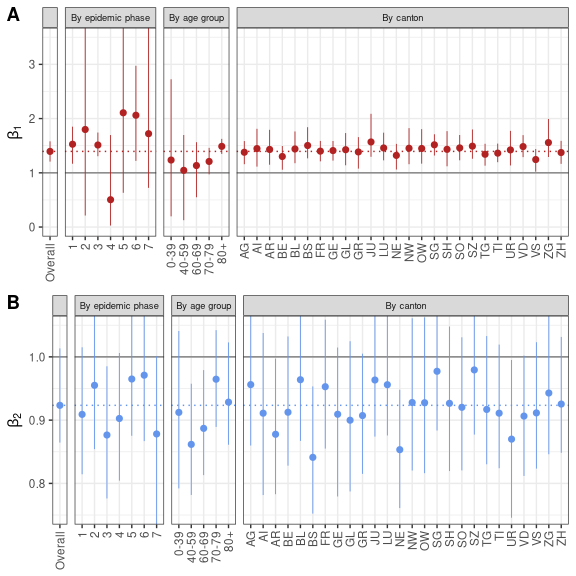
**Figure 1.** (A) Relative excess mortality in Switzerland between 24 February 2020 and 03 April 2022 overall, by epidemic phase, by age group and by canton. (B) Weekly relative excess mortality in Switzerland between 24 February 2020 and 03 April 2022 by canton.

da\_301\_summary\_plot(summ\_week\_temp)



**Figure 2.** Weekly counts of excess all-cause deaths (95% uncertainty intervals) and of laboratory-confirmed SARS-CoV-2-related deaths between 24 February 2020 and 03 April 2022 in Switzerland. The bar at the bottom shows the probability that excess all-cause deaths is greater than laboratory-confirmed SARS-CoV-2-related deaths (light gray is 0, black is 1). Numbers at the top indicate phases 1 to 7.

da\_404\_plot\_regbma(summ\_regbma,panel\_labels = c("A","B"))



**Figure 3.** (A) Posterior estimates of , the additional number of deaths to be observed for each unit increase in laboratory-confirmed deaths, after adjusting for the expected number of all-causes deaths given historical trends. (B) Posterior estimates of , the additional number of deaths to be observed for each unit increase in the expected number of all-cause deaths, after adjusting for the direct effect of SARS-CoV-2 infections. Estimates of and are shown for the whole period, by phase, by age group and by canton.

**References**

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