Direct and indirect effects of the COVID-19 pandemic on mortality in Switzerland, a population study

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- No conflict of interest

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Aims

1. Estimate the excess all-cause mortality in Switzerland in 2020-2022 by age, canton and epidemic phase (with uncertainty)

2. Examine the interplay between excess mortality and laboratory-confirmed SARS-CoV-2-related deaths

Step 1: estimate the excess all-cause mortality

Definition:

- excess mortality = observed mortality - expected mortality
- counter-factual reasoning: how many deaths would have occurred had the pandemic not occurred?

Extrapolate from:

- historical trends in mortality data (seasonality, yearly trends)
- by location, age, sex
- account for changes in the population (extrapolate from 2010-2019)
- account for key covariates: temperature (ERA5), public holidays
- account for geographical structure (BYM structure[1])

Poisson model fitted in INLA, cross-validated[2]

[1] Besag, York & Mollié (1991)
[2] Konstantinoudis et al (2022)

Results: Excess mortality

Over the full study period (February 24, 2020 to April 3, 2022):

- 156,193 observed deaths from all causes in Switzerland
- 142,408 (95% CrI: 138,044 to 149,125) expected deaths had the pandemic not occurred
- 13,786 (95% CrI: 7,068 to 18,149) excess all-cause deaths
- a relative increase of 9.7% (95%CrI: 4.7 to 13.1)

NB: this includes all sources of uncertainty (population, effect of covariates)

Results: Excess mortality

Break-down by epidemic phase:

Epidemic phase	Dates	Expected all-cause deaths (95% credible interval)	Observed all-cause deaths	Excess all-cause deaths (95% credible interval)	Relative excess all-cause deaths (95% credible interval)	Laboratory-confirmed COVID-19 deaths
1	Feb 24, 2020 to Jun 7, 2020	19,376 (18,767 to 20,033)	20,791	1,415 (758 to 2,024)	7% (4 to 11)	1,725
2	Jun 8, 2020 to Sep 27, 2020	19,180 (18,440 to 20,042)	19,103	-76 (-939 to 663)	-0% (-5 to 4)	104
3	Sep 28, 2020 to Feb 14, 2021	27,004 (25,569 to 28,604)	36,157	9,154 (7,553 to 10,588)	34% (26 to 41)	7,652
4	Feb 15, 2021 to Jun 20, 2021	23,386 (22,320 to 24,834)	22,369	-1,017 (-2,465 to 49)	-4% (-10 to 0)	895
5	Jun 21, 2021 to Oct 10, 2021	19,174 (18,284 to 20,223)	20,007	832 (-216 to 1,723)	4% (-1 to 9)	380
6	Oct 11, 2021 to Dec 19, 2021	13,036 (12,298 to 13,944)	15,105	2,070 (1,161 to 2,807)	16% (8 to 23)	956
7	Dec 20, 2021 to Apr 3, 2022	21,370 (20,067 to 22,894)	22,661	1,291 (-233 to 2,594)	6% (-1 to 13)	1,418

Figure: Number of expected and observed deaths from all causes, estimated excess mortality and laboratory-confirmed COVID-19-related deaths by seven epidemic phases between February 2020 and April 2022.

Results: Excess mortality

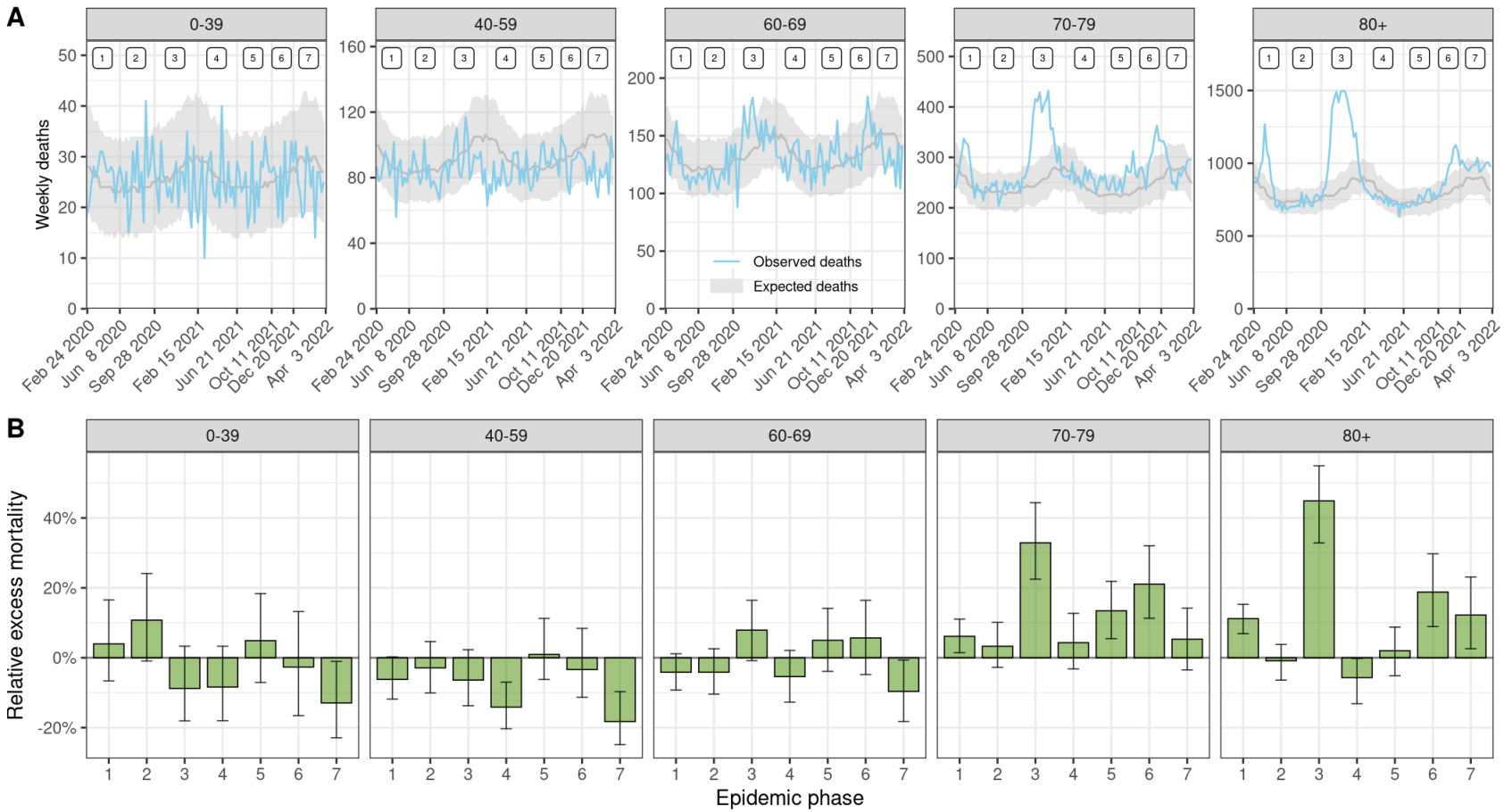
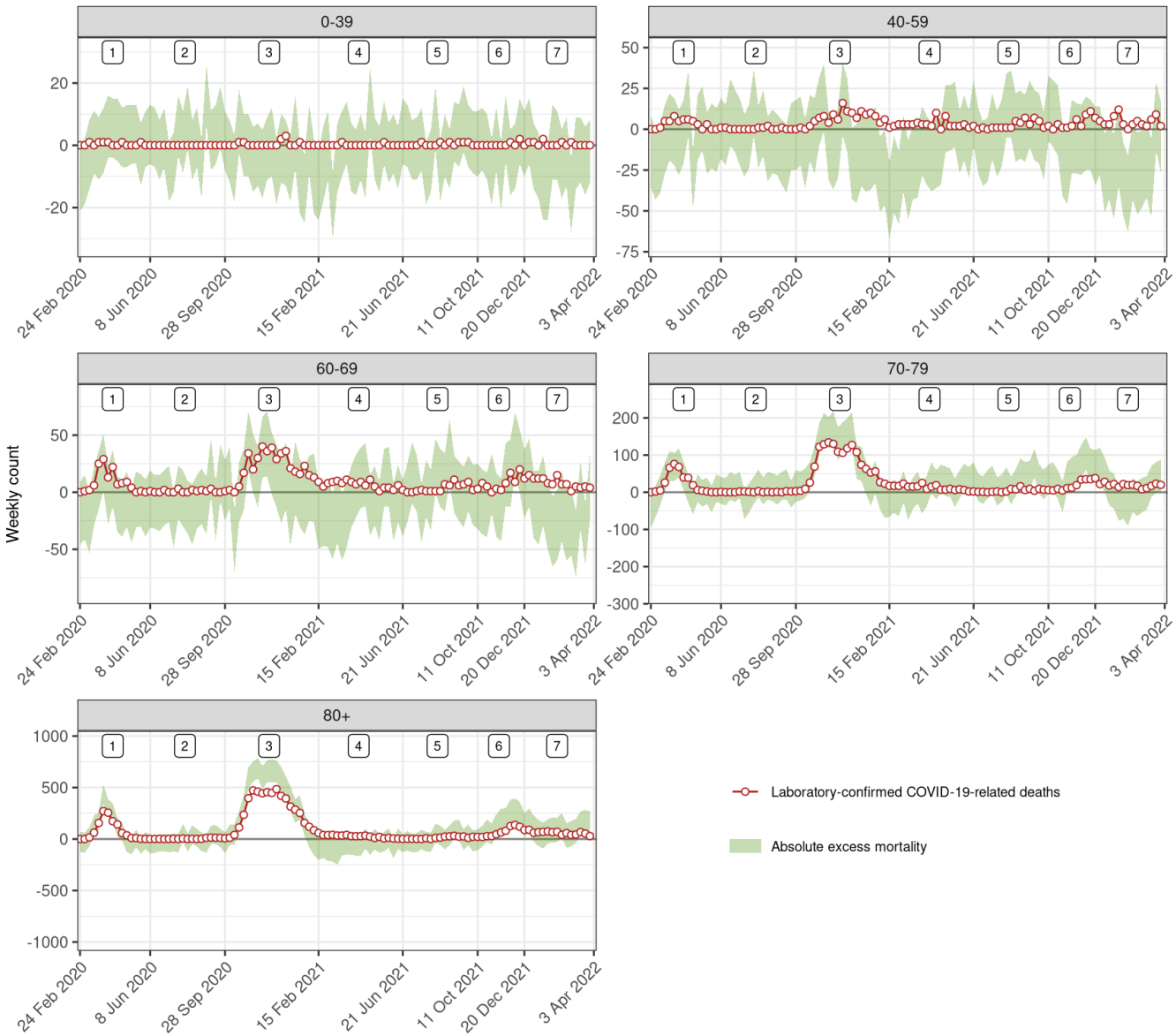


Figure: (A) Observed and expected number of weekly deaths by age group in Switzerland from February 2020 to April 2022. Model-predicted expected deaths are shown with median and 95% credibility interval. Numbers at the top indicate epidemic phases 1 to 7. (B) Estimated relative excess mortality by seven epidemic phases from February 2020 to April 2022 and five age groups. Medians with 95% credible intervals are shown.

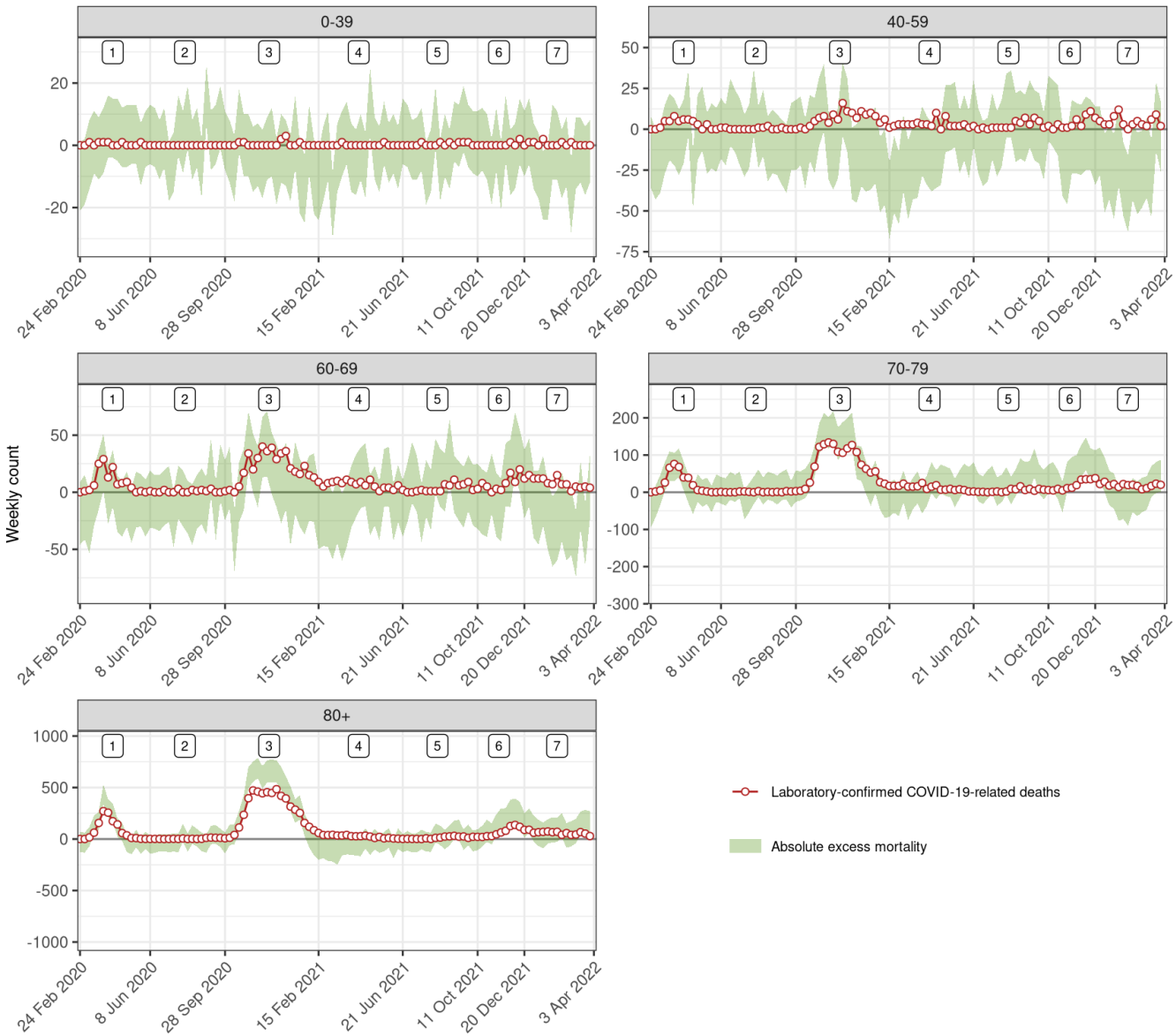
Step 2: excess mortality vs. SARS-CoV-2 deaths

Visual comparison:



Step 2: excess mortality vs. SARS-CoV-2 deaths

Overall correlation coefficient: 0.89 (95%CrI: 0.85 to 0.92)



Step 2: excess mortality vs. SARS-CoV-2 deaths

Statistical approach using modified Poisson regression (no intercept):

$$O_t \sim \text{Poisson}\left(\beta_1 L_t + \beta_2 E_t\right)$$

where:

- O_t is the observed number of all-cause deaths on week t
- L_t is the number of laboratory-confirmed SARS-CoV-2 deaths
- E_t is the expected number of all-cause deaths given historical trends

Step 2: excess mortality vs. SARS-CoV-2 deaths

$$O_t \sim \text{Poisson}\left(\beta_1 L_t + \beta_2 E_t\right)$$

Interpretation: β_1 is the additional number of observed deaths for each unit increase in laboratory-confirmed deaths, controlling for expected deaths:

- if $\beta_1 = 1 \rightarrow$ perfect ascertainment of SARS-CoV-2 deaths
- if $\beta_1 > 1 \rightarrow$ more deaths attributable to SARS-CoV-2 than laboratory-confirmed deaths

$\Rightarrow \beta_1$ measures the direct effect of the pandemic on mortality

$\Rightarrow \beta_1 \times L_t$ is the total number of deaths directly attributable to SARS-CoV-2 infections

$\Rightarrow 1/\beta_1$ corresponds to the ascertainment of SARS-CoV-2-related deaths

Step 2: excess mortality vs. SARS-CoV-2 deaths

$$O_t \sim \text{Poisson}\left(\beta_1 L_t + \beta_2 E_t\right)$$

Interpretation: β_2 is the additional number of observed deaths for each unit increase in the expected number of all-cause deaths, controlling for SARS-CoV-2 deaths:

- if $\beta_2 = 1 \rightarrow$ as many "all-cause-except-SARS-CoV-2" deaths than expected
- if $\beta_2 < 1 \rightarrow$ fewer "all-cause-except-SARS-CoV-2" deaths than expected

$\Rightarrow \beta_2$ measures the indirect effect of the pandemic on mortality

Results: direct effect

Overall β_1 is estimated to 1.38 (1.22 to 1.54):

- 22% to 54% more deaths directly attributable to SARS-CoV-2 than confirmed over the whole period
- or equivalently an ascertainment of 65% to 82% ($1/\beta_1$) of deaths directly attributable to SARS-CoV-2
- given 13,130 laboratory-confirmed deaths, this implies 16,000 to 20,000 COVID-19 deaths directly attributable to COVID-19 in Switzerland over the period

Results: indirect effect

After accounting for deaths directly attributable to COVID-19, the observed number of all-cause deaths was slightly lower than expected

- β_2 estimated to 0.97 (0.93 to 1.01)
- 3% (-1 to 7) fewer all-cause deaths than expected (after accounting for...)
- corresponding to 4,406 (-1,776 to 10,700) fewer deaths overall

Results: variations

Variations of β_1 by age and epidemic phase:

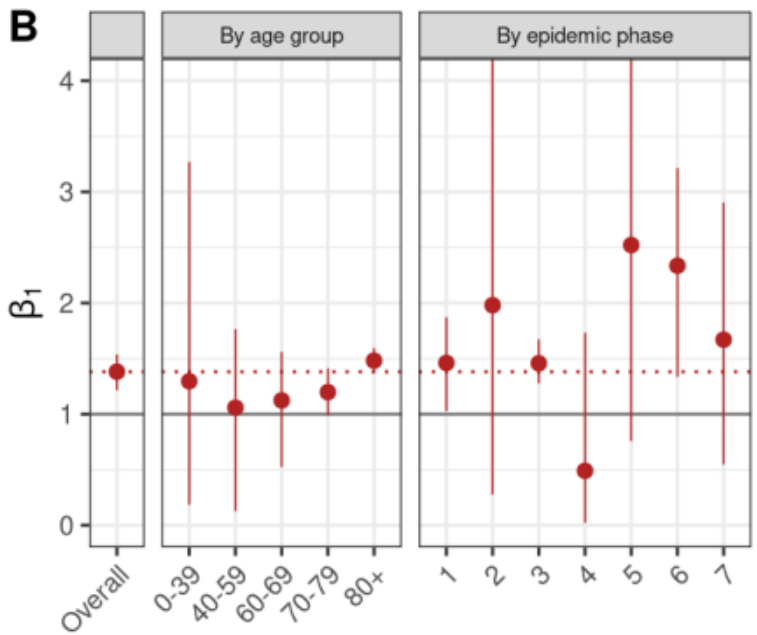


Figure: Estimates of β_1, the additional number of deaths to be observed for each unit increase in laboratory-confirmed deaths, after adjusting for the expected number of all-causes deaths given historical trends.

- more deaths were not ascertained in age groups 70-79 and 80+
- lower ascertainment during phases 1, 3 and 6 (large epidemic waves)

Results: variations

Variations of β_2 by age and epidemic phase:

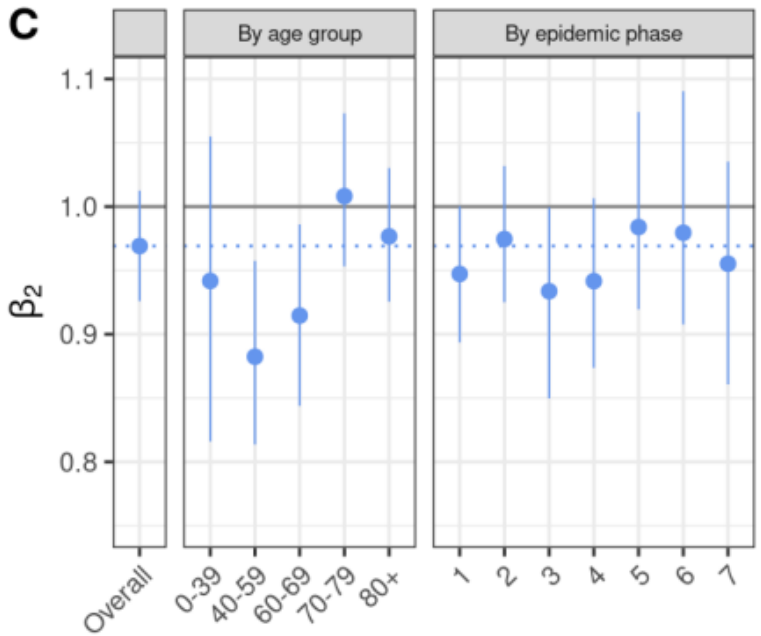


Figure: Estimates of β_2, the additional number of deaths to be observed for each unit increase in the expected number of all-cause deaths, after adjusting for the direct effect of SARS-CoV-2 infections. Estimates of and are shown for the whole period, by phase and by age group.

- deficit in all-cause deaths more pronounced in age groups 40 to 69
- and during phases 1, 3 and 4 (more stringent control measures)

Conclusions

Summary of results and interpretations:

- estimates of excess generally in line with other studies (except WHO)
- 1.2-1.5 times more deaths directly caused by COVID-19 than the number of laboratory-confirmed deaths (or reciprocally only 70% of deaths were ascertained)
  - compatible with recent multi-country study (1.29)[3]
  - cause of deaths 2020: 24-33% more COVID-19 deaths than FOPH
  - lower ascertainment during periods of high epidemic activity
  - concentrated in older age groups, pointing towards nursing homes[4]
- 3% (-1 to 7) fewer all-cause deaths than expected (after accounting for deaths directly caused by COVID-19)
  - concentrated in age groups 40 to 69 and phases 1, 3, 4
  - protective effect of control measures rather than harvesting/influenza
  - mechanism unknown (lower pollution, traffic, contacts, activities...)
  - no argument towards overall harmful effect (does not refute harmful effects from control measures e.g. delays in care, suicide, substance use, violence...)

[3] Wang et al (2022)
[4] Li et al (2020)

Conclusions

Strengths and limitations:

+ statistically rigorous approach
+ accounts for projected population sizes and temperature
+ full uncertainty propagation
- all deaths with a positive test considered caused by COVID-19
- ecological bias
- assumptions about population changes and mortality in 2020-2022 had the pandemic not occurred