## Lower Bounds for COVID-19 Mortality Based on Towns in

## **Northern Italy**

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Circumstance in northern Italy allow estimation of lower bounds for excess mortality resulting from COVID-19 – a proxy for the Infection Fatality Rate (IFR). Some towns were heavily infected in the first few months of 2020 and experienced substantially more deaths compared to the same period in 2019, and thus high all-cause excess mortality:

- Nembro, 147 more 2020 deaths, population 11,526, excess mortality 1.275 percent
- Alzano Lombardo, 102 more 2020 deaths, population 13,655, excess mortality 0.75 percent

If the towns had been fully infected during 2020 the excess mortality would provide an estimate of mortality due to COVID-19 (IFR). Since the towns may have been less than fully infected these provide lower bounds.

In the four northern provinces of Milano, Bergamo, Brescia, and Lodi there are 612 towns with data published by ISTAT for age- and sex-specific deaths for January through April 15 for the years 2017-2020<sup>5</sup>. These towns account for 98 percent of the regional population of 5,529,147. To generalize the calculation of excess mortality from one to many towns we use a generalized linear mixed (Poisson count) model<sup>6,2</sup>. We control for differences across towns in pre-2020 mortality using a pre-2020 random effect, and for town differences in 2020 mortality by a 2020 random effect. Mortality for baseline 2017-2019 by sex and age (using categories shown in Table 1) is estimated using fixed effect estimators. Differences in mortality for 2020 are captured by 2020 age and sex fixed effects.

The upper tail (99th percentile) of the 2020 town distribution represents the most-infected towns. The 99<sup>th</sup> percentile of the excess mortality (calculated by interacting the 2020 town

random effect with the age-sex fixed effects) provides a lower bound for age-specific COVID-19 mortality and by extension the Infection Fatality Rate (IFR). Table 1 shows overall excess mortality (weighted by region-wide population) for the 99th percentile town of 1.09 percent (95% CI 1.02-1.16). This is higher than many published IFR estimates (e.g. a survey of studies<sup>4</sup> reports 0.02 percent to 0.40 percent; a global study<sup>3</sup> estimates a higher global IFR (1.04 percent), but this is equal to our lower bound). There are dramatic age and sex differences with higher mortality for older men: mortality for men age 65-74 is 3.7-times higher than younger men and 2.7-times higher than women of the same age. In all cases mortality is estimated with narrow confidence intervals.

Our estimates provide a lower bound for an "initial response" Infection Fatality Rate (IFR) that measures mortality due not only to mortality under ideal clinical conditions but also real-world treatment challenges in fighting a new disease. Measuring all-cause excess mortality has the benefit (relative to some methods) that the overall number of deaths is easy to measure and does not depend on accurately determining cause of death or the proportion of asymptomatic infections.

|         | Male      |           | Female    |           | Male & Female |           | Male-to-Female |           |
|---------|-----------|-----------|-----------|-----------|---------------|-----------|----------------|-----------|
|         | Mortality | CI        | Mortality | CI        | Mortality     | CI        | Ratio          | CI        |
| 0-14yr  | 0.01%     | 0.01-0.02 | 0.01%     | 0-0.01    | 0.01%         | 0-0.01    |                |           |
| 15-54yr | 0.06%     | 0.05-0.07 | 0.04%     | 0.03-0.04 | 0.05%         | 0.04-0.06 | 1.65           | 1.4-1.91  |
| 55-64yr | 0.59%     | 0.54-0.64 | 0.22%     | 0.19-0.25 | 0.40%         | 0.37-0.43 | 2.65           | 2.34-3.14 |
| 65-74yr | 2.10%     | 1.94-2.28 | 0.80%     | 0.74-0.87 | 1.41%         | 1.3-1.52  | 2.62           | 2.47-2.8  |
| 75+     | 8.95%     | 8.36-9.52 | 6.47%     | 6.02-6.89 | 7.42%         | 6.93-7.88 | 1.38           | 1.34-1.45 |
| TOTAL   | 1.14%     | 1.07-1.21 | 1.04%     | 0.97-1.11 | 1.09%         | 1.02-1.16 | 1.09           | 1.06-1.14 |

Table 1: Estimated Excess Mortality, 99th Percentile of Town Infection Distribution

Using data on deaths and population for January - April 15<sup>th</sup> for the years 2017-2020 for 612 towns in the northern provinces of Milano, Bergamo, Brescia, Lodi. Estimated using Poisson count mixed model with fixed age-sex effects, random town effects. Bootstrap confidence intervals.<sup>2</sup>

The estimates in Table 1 provide a benchmark for parameters used in epidemiological modeling. Examining recent CDC simulations<sup>1</sup> is an example. "Current best estimate" simulations (scenario 5) assume 35 percent asymptomatic cases and case fatality rates of 0.4 percent overall and 1.3 percent for age 65+, implying IFR of 0.26 percent overall and 0.845 percent age 65+. These are substantially lower than the observations from northern Italy: Re-

weighting our age-specific estimates using US population we find 0.73 percent overall and 3.95 percent for age 65+.

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