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Application of excess event estimation to investigate mortality and infection spread during the COVID-19 pandemic

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Introduction

- In the COVID-19 pandemic (C19P), official COVID-19 mortality rate was a more reliable indicator of the virus spread compared to the count of positive cases.
- However biases affect ascertainment of COVID-19 deaths too and this is why methods based on the estimation of excess mortality are used [1,2]. We show the use of excess event estimation as a useful tool in two instances:

1) using past national statistics mortality (NSM) data to evaluate retrospectively the actual impact of the C19P in different areas of Italy (North, Centre, South) and in different pandemic waves and

2) using time series of past Accidents and Emergency (A&E) calls to highlight signals of extraordinary events in Lombardy, where the pandemic started in Europe

Methods

- **1)** In the first application, National Statistics Mortality data from 2015 to 2019 were used to estimate a Poisson regression model of the pre-pandemic mortality pattern (PMP):

$$b_i = offset * (1 + slope * i) +$$

$$+ amplitude * cos\left((i + phase) * \frac{2\pi}{365}\right)$$

where b_i is the estimated number of deaths for day *i* from 01/01/2015 to 30/11/2019; the seasonal component is parameterized by a cosine curve with a period of one year, and the amplitude, the phase, and the offset are estimated from data. The offset is multiplied by a linear function to account for possible year-dependent mortality variations due to changes in the age structure of the population [3].

The excess COVID-19 deaths were derived as the difference between the NSM data and the extrapolation of the PMP to the COVID-19 pandemic period considered (23/02/2020–30/04/2022), separately for North/Centre/South regions.

- **2)** In the second application, A&E calls in Lombardy were first filtered to include only those reporting respiratory and cardiological issues, and via the same type of Poisson regression model as above were used to estimate the pre-pandemic A&E call pattern; once more the excess calls were then derived as the difference between the actual calls during the pandemic period (2020 and 2021) and the estimated call pattern before the pandemic (2015-2019).

Results 1: Nation-wide COVID-19 mortality

The gap between the estimated excess and the official COVID-19 mortality shows (**Figure 1**) that :

- during the 1st wave there was an underestimation of deaths , largest in absolute numbers for the North but in relative terms highest for the South (**Table1**).
- In the 2nd and 3rd wave there is a reasonable match between estimated and official COVID-19 mortality.
- During the 4th wave (late 2021 and 2022), a substantial discrepancy appears again, driven by the South.

		Estimates of COVID-19 excess of deaths (± uncertainty)*	Official deaths	Estimated COVID-19 mortality rates (per 1000) (± uncertainty)*	Official mortality rates (per 1000)	Ratio between estimated and official rates (± uncertainty)*
First wave	North	44790 ± 400	24148	1.60 ± 0.02	0.86	1.85 ± 0.02
	Center	3410 ± 230	2367	0.28 ± 0.02	0.20	1.44 ± 0.10
	South	4600 ± 300	1619	0.22 ± 0.02	0.08	2.84 ± 0.19
	Italy	52610 ± 550	28133	0.87 ± 0.01	0.47	1.87 ± 0.02
Second and third waves	North	55940 ± 680	48804	2.00 ± 0.02	1.74	1.15 ± 0.01
	Center	17570 ± 440	16235	1.47 ± 0.04	1.36	1.08 ± 0.03
	South	32530 ± 560	23749	1.62 ± 0.03	1.19	1.37 ± 0.02
	Italy	105410 ± 980	88789	1.75 ± 0.02	1.47	1.19 ± 0.01
Fourth wave	North	19870 ± 570	15277	0.71 ± 0.02	0.55	1.30 ± 0.04
	Center	7680 ± 380	6095	0.64 ± 0.03	0.51	1.26 ± 0.06
	South	19450 ± 490	10232	0.97 ± 0.02	0.51	1.90 ± 0.04
	Italy	46530 ± 840	31604	0.77 ± 0.01	0.52	1.47 ± 0.03

Table 1: Estimated, Official mortality rates and their ratio by region and wave

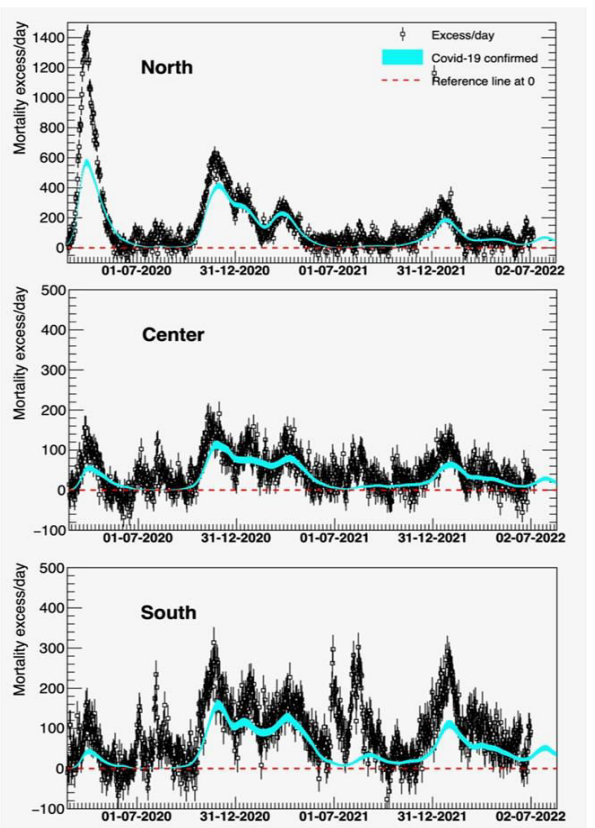

Figure 1. Plot showing the gap between the estimated excess and the official Covid19Pandemic (C19P) mortality

Results 2: Accident and Emergency calls in Lombardy

- The time-series of the excess of relevant respiratory and cardiologic A&E calls (2015-2022) in Lombardy after subtraction of the estimated baseline pattern shows peaks corresponding to the major waves (**Figure 2**).
- The excess relevant calls in the COVID-19 period plotted alongside the confirmed COVID-19 cases in Lombardy (**Figure 3**) suggest a large underestimation of covid cases in the 1st wave but a similar trend thereafter.

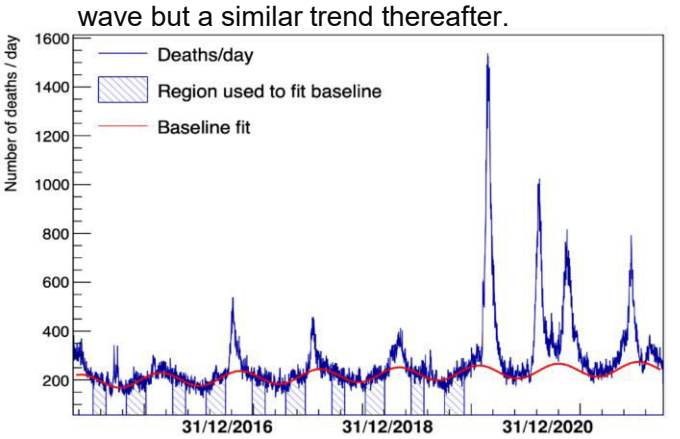

Figure 2: :number of relevant calls as a function of time. In red and overlaid, baseline contribution fitted with the parameterization described in the text.

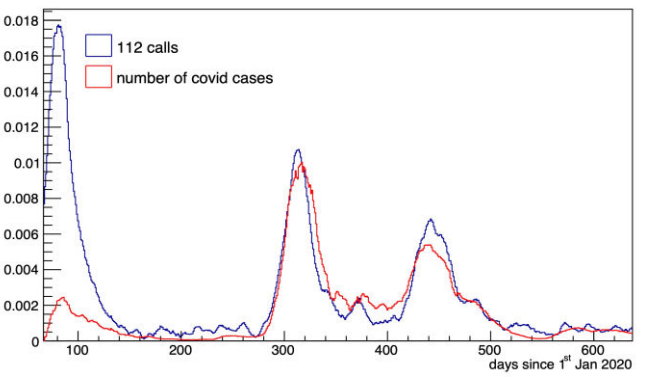

Figure 3: Number of calls for respiratory and cardiologic issues as a function of time and subtracted of the fitted baseline contribution compared with the official number of positive COVID-19 cases in Lombardy

Conclusions

The results confirm the underestimation of cases and deaths in the first wave of the pandemic. Excess event methods

- Provide an unbiased estimate of Italian mortality rates and indicate an issue of underestimation specific to the South in late 2021 and 2022;
- show the usefulness of A&E relevant calls as a proxy for COVID-19 cases in monitoring the spread of the COVID-19 pandemic, after the initial period.

Overall, excess event estimation methods are useful as monitoring tools to investigate the public health system performance and resilience during an epidemic. In future work, when additional individual data is present, Machine Learning may highlight who is at greater risk in various settings.

References

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