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Abstract

Background To date the European experience with COVID-19 mortality has been different to the observed in China and Asia. We aimed to forecast mortality trends in the 27 countries of the European Union (EU), plus Switzerland and the United Kingdom (UK), where lockdown dates and confinement interventions have been heterogeneous, and to explore its determinants.

Methods: We have adapted our predictive model of COVID-19-related mortality, which rested on the observed mortality within the first weeks of the outbreak and the date of the respective lockdown in each country. It was applied in a training set of three countries (Italy, Germany and Spain), and then applied to the EU plus the UK and Switzerland. In addition, we explored the effects of timeliness and rigidity of the lockdown (on a five-step scale) and population density in our forecasts. We report r^2, and percent variation of expected versus observed deaths, all following TRIPOD guidance.

Results: We identified a homogeneous distribution of deaths, and found a median of 24 days after lockdown adoption to reach the maximum daily deaths. Strikingly, cumulative deaths up to April 25th, 2020 observed in Europe separated countries in three waves, according to the time lockdown measures were adopted following the onset of the outbreak: after a week, within a week, or even prior to the outbreak (r^2= 0.876). In contrast, no correlation neither with lockdown rigidity nor population density were observed.

Conclusions: The European experience confirms that early, effective interventions of lockdown are fundamental to minimizing the COVID-19 death toll.

Abstract word count: 247 words (maximum 250 words)

Key words: COVID-19; Europe; Lockdown; Mortality

Introduction

The unprecedented, rapid spread of SARS-Cov-2 epidemic urgently requires new, timely epidemiological evidence to help mitigate the population burden. Since the safety alert on Tuesday, December 31, 2019 reported in Wuhan, Hubei Province, China due to a cluster of pneumonia of unknown etiology,[1] it took ten days, on January 9, 2020, for China's CDC to report that a novel coronavirus was the causative agent of that local outbreak.[2] Indeed, appropriate epidemiological indicators associated with COVID-19 are necessary steps to reduce the negative consequences of this ongoing pandemic.[3,45] Several countries responded belatedly, with considerable heterogeneity and with different political and healthcare approaches to containment.[6]

Initially focused on an innovative and robust data mining approach based on Chinese and Italian data to forecast SARS-Cov-2-related mortality,[7] our model concluded that SARS-Cov-2-related mortality is closely correlated to early events after the onset of the outbreak, and to the timing of regional/national interventions on social distancing and lockdown, as well as the occurrence of superspreading events (e.g., Italy, Germany, and Spain).[8]

To date the European COVID-19 mortality trends have been largely different to those observed in China and Asia.[9] We aimed to forecast mortality trends up to May 31st, 2020, in the 27 countries of the European Union (EU), plus Switzerland and the United Kingdom (UK), where lockdown timeliness and confinement interventions are highly variable, as well as the effect of that diversity.

Methods

Publicly available data from official data sources on the timing and distribution of deaths related with COVID-19 by country were retrieved.[10,11,12] Our algorithm was fed with data up to April 25th, 2020, and forecasted mortality up to May 31st, 2020.

Our initial model was proven to be accurate in predicting COVID-19 deaths in Italy, Germany, and Spain. [7] This was adapted to forecast COVID-19 mortality in 29 European countries (EU, plus Switzerland and the UK). The model takes into consideration the following variables: the observed mortality distribution within the first 17 days of the outbreak and the date of the national lockdown. This was modelled firstly with a 3rd degree polynomial curve, secondly by a five-parameter logistic (5PL) asymmetrical sigmoidal curve following a parametric growth. Its application was performed to a training set of the 29 countries, both individually and aggregated. Given that lockdown rigidity and population density could be considered determinant factors affecting the death toll, we explored their effects on the forecasts.

Lockdown rigidity was defined by five steps based on increasing levels of closing of commercial and non-commercial activities, namely: 0 without any measures other than travelling ban; 1 gathering ban only; 2 schools closing; 3 plus closure of restaurants and bars; 4 also including non-essential shops; and 5 lockdown extended to non-essential factories. Lockdown dates were chosen when at least a lockdown step 3 was adopted; if no such lockdown occurred, we selected the date where the next stricter lockdown was adopted. Outbreak onset was defined as the first day when at least one death was recorded with ≥3 deaths in the following two days. Of note, Cyprus, Latvia, and Slovakia (respectively 19, 12, and 17 deaths) were not included in the predictive model because of not fulfilling this definition during the first 17 days of outbreak.

Being our algorithm a test prediction model for individual prognosis or diagnosis, r^2 and variation of expected versus observed deaths (percentage) were reported following Transparent Reporting of a multivariable prediction model for Individual Prognosis Or Diagnosis (TRIPOD) guidance.[13]

Results

Information on the national distribution of deaths within the first 17 days of the outbreak, lockdown date and rigidity, and days from lockdown to the onset of the epidemic was obtained in 29 European countries (**Table 1**).

A homogeneous distribution of observed versus expected deaths was found, with a median of 24 days after after lockdown adoption to reach maximum daily deaths in all EU countries, the UK, and Switzerland, with an arithmetic r^2 of 0.917, (**Figure 1a**) and an aggregated r^2 of 0.998 (**Figure 1b**) .

Cumulative deaths up to April 25th, 2020, showed a pattern which depends on the timing of the lockdown adoption (**Figure 2**). Namely, countries which implemented lockdown after a week from outbreak onset (i.e., 9 days in the UK, 10 days in Spain, 12 days in France, or 15 days in Italy) experienced the greatest mortality, ranging from 20,319 up to 26,384 deaths, whereas countries which implemented lockdown within a week experienced an intermediate mortality, from 601 up to 6,917 deaths; on the contrary, those countries which implemented lockdown before the onset of the national outbreak (i.e., -30 days in Slovakia, -20 days in Latvia, or -19 days in Bulgaria) experienced the lowest mortality, from 4 up to 536 deaths.

Cumulative deaths up to April 25th, 2020, computed in EU countries, Switzerland, and the UK were tightly linked to the timing of the lockdown adoption (**Figure 3**), with a high correlation (r^2= 0.876), with an exponential fitting.

Finally, we explored the effect of lockdown rigidity and population density on these trends. We found no correlation of neither lockdown rigidity with number of days needed to reach the maximum daily deaths, nor of population density and observed deaths. (**Online Appendix, eFigures I and II**).

Discussion

Our study highlights the key role played by early events and earlier interventions in the reduction of COVID-19 mortality. Regrettably, late adoption of effective national lockdown was associated with a higher mortality, particularly if the lockdown occurred after one week from the outbreak onset (first day when at least one death occurred with at least three deaths in the following two days). This suggests that for non-European countries (not included in this analysis), where the spread has been slower or later, delaying or avoiding lockdown interventions might be detrimental.

Literature review on COVID-19 forecasting

A number of modelling and forecasting tools quantifying the future COVID-19 burden are available elsewhere.[14,15,16,17,18,19,20]
Sebastiani, et al.,[20] described the trends of Covid-19 spread in Italy, studying the positive cases cumulative incidence, and found similar conclusions of our study about the importance of early containment measures to counteract the epidemic diffusion. We accept the nihilistic conclusion that all outbreak forecasting is subject to errors; however, we followed TRIPOD to cover our model development when limited data were available.[21] We envisage that the eventual pooling of estimates from independent forecasts performed by independent groups will be the closest to reality,[22,23] likely to be observed both in the immediate- and distant future of the ongoing COVID-19 outbreak.[24]

Strengths and limitations

The strengths of our model are its virtual immediacy; parsimony, being the algorithm based on two entry variables, namely dates of outbreak onset and lockdown, and distribution of deaths within the first 17 days from that date; and easy replicability and testing. However, a number of limitations must be discussed: up-to-date, official counting and distribution of deaths by country were retrieved. But, accuracy and completeness of national statistics, reluctance on data sharing, heterogeneous definitions, changes in coding practices, and other technical issues can affect the reliability of country estimates.[25] Without a established lockdown date no forecasting curve can be fit. No significant correlations were found when COVID-related lockdown rigidity and population density were included in the analysis; however, more specific analyses might target any population effect of these crucial variables.

Implications of our research

SARS-Cov-2 is a novel virus and COVID-19 is still a mostly unknown disease, with already differences compared with other coronavirus-related medical conditions (e.g.: SARS and MERS).[26] Many enigmas remain at both the individual and societal level of the COVID-19 outbreak, including how factors such as weather and climate, herd immunity, individual and ethnic susceptibility, health systems quality, new treatments and therapeutic regimes, and effective vaccines could affect globally and nationally the COVID-19 epidemic. Our research may have public health implications which can help mitigate the national COVID-19 burden. Individual country leaders such as in Brazil, Nicaragua[27] or elsewhere, have actively neglected lockdown initiatives suggested by the WHO and implemented in many countries. New models might take into account the interaction of demography and current age-specific mortality for COVID-19, as well as social distancing and other containment policies, age composition of local and national contexts, and intergenerational interactions. We join the call for countries to provide case and fatality data disaggregated by age and gender to improve real-time targeted forecasting of hospitalization and critical care needs.[28] Beyond Europe, given intrinsic difficulties and variable political decisions against this pandemic, the expected death toll might become significantly higher.

Conclusions

Early adoption of effective lockdown measures in European countries was correlated with a reduced death toll, and was most effective in those countries which implemented them before the onset of the outbreak.

Table 1. COVID-19-related containment and lockdown measurements with dates in the 27 European Union countries, plus Switzerland and the UK

Country	17 days range	Lockdown date	Lockdown rigidity	R^2	Delta
Austria	21/03 - 06/04	17/03	4	0.964	-8.0%
Belgium	16/03 - 01/04	18/03	4	0.988	-0.2%
Bulgaria	01/04 - 17/04	13/03	4		-25.5%
Croatia	02/04 - 18/04	17/03	4	0.734	-14.8%
Cyprus	27/03 - 12/04	15/03	0		
Czechia	24/03 - 09/04	16/03	4	0.967	4.6%
Denmark	19/03 - 04/04	13/03	3	0.931	0.2%
Estonia	31/03 - 16/04	13/03	2	0.536	-8.7%
Finland	25/03 - 10/04	16/03	2	0.752	-53.8%
France	05/03 - 21/03	17/03	4	0.997	-6.1%
Germany	13/03 - 29/03	16/03	3	0.957	-4.8%
Greece	21/03 - 06/04	10/03	4	0.893	4.6%
Hungary	20/03 - 05/04	16/03	2.5	0.878	-46.3%
Ireland	22/03 - 07/04	27/03	5	0.974	-11.1%
Italy	23/02 - 10/03	09/03	5	0.993	6.0%
Latvia	03/04 - 19/04	14/03	1		
Lithuania	04/04 - 20/04	12/03	2		-9.8%
Luxembourg	26/03 - 11/04	16/03	2	0.803	27.1%
Malta	08/04 - 24/04	16/03	3		
Netherlands	13/03 - 29/03	13/03	1	0.953	10.8%
Poland	23/03 - 08/04	20/03	3	0.928	11.3%
Portugal	18/03 - 03/04	18/03	4	0.989	11.6%
Romania	22/03 - 07/04	24/03	3	0.972	-19.8%
Slovakia	15/04 - 01/05	16/03	4		
Slovenia	25/03 - 10/04	16/03	3	0.956	8.6%
Spain	05/03 - 21/03	15/03	5	0.978	31.2%
Sweden	16/03 - 01/04	17/03	1	0.976	-4.9%
Switzerland	13/03 - 29/03	16/03	4	0.992	18.3%
UK	14/03 - 30/03	23/03	4	0.986	7.3%

Figure 1. Robustness of the predictive model to forecast COVID-19-related mortality in the EU, Switzerland and the UK

Figure 1a) Expected vs observed percent death ratio associated with days since outbreak onset in each EU country, Switzerland and the UK

Figure 1a footnote. The x axis represents the number of days needed to reach a maximum daily deaths peak after lockdown adoption (as per our algorithm). The y axis represents the death ratio percentage: (expected – observed)/observed). For each country, we mined data from the first 17 days since the onset of the outbreak (first COVID-19 deaths detected) to prove correlation and robustness of the model from day 18 onwards (histograms).
The red line shows the arithmetic average of the values of all countries, which intercepts y axis in the interval (24 - 25 days), closer to 24 days. The blue line shows the arithmetic average of all absolute values of all countries, which has the lower value with 24 days.

Figure 1b) Observed and expected cumulative deaths in all 29 European countries

Figure 1b footnote: Observed and expected aggregated data for the EU27, Switzerland and the UK. The grey line shows expected deaths assuming 24 days, according to Figure 1a.

Figure 2. Map of cumulative deaths up to April 25th, 2020 observed in European countries (EU, Switzerland and the UK) according to the timing of the lockdown adoption.

a) After one week; b) within a week; and c) before outbreak onset

Figure 3. Correlation of cumulative deaths up to April 25th, 2020 observed in European countries (EU, Switzerland and the UK) according to the timing of the lockdown adoption ($r^2 = 0.878$)

Online Appendix:

Online Appendix eFigure I. Lack of direct correlation among lockdown rigidity (five steps) and deaths and days to reach daily peak.

Online Appendix eFigure II. Association of population density and total population with observed deaths ($r^2 = 0.626$).

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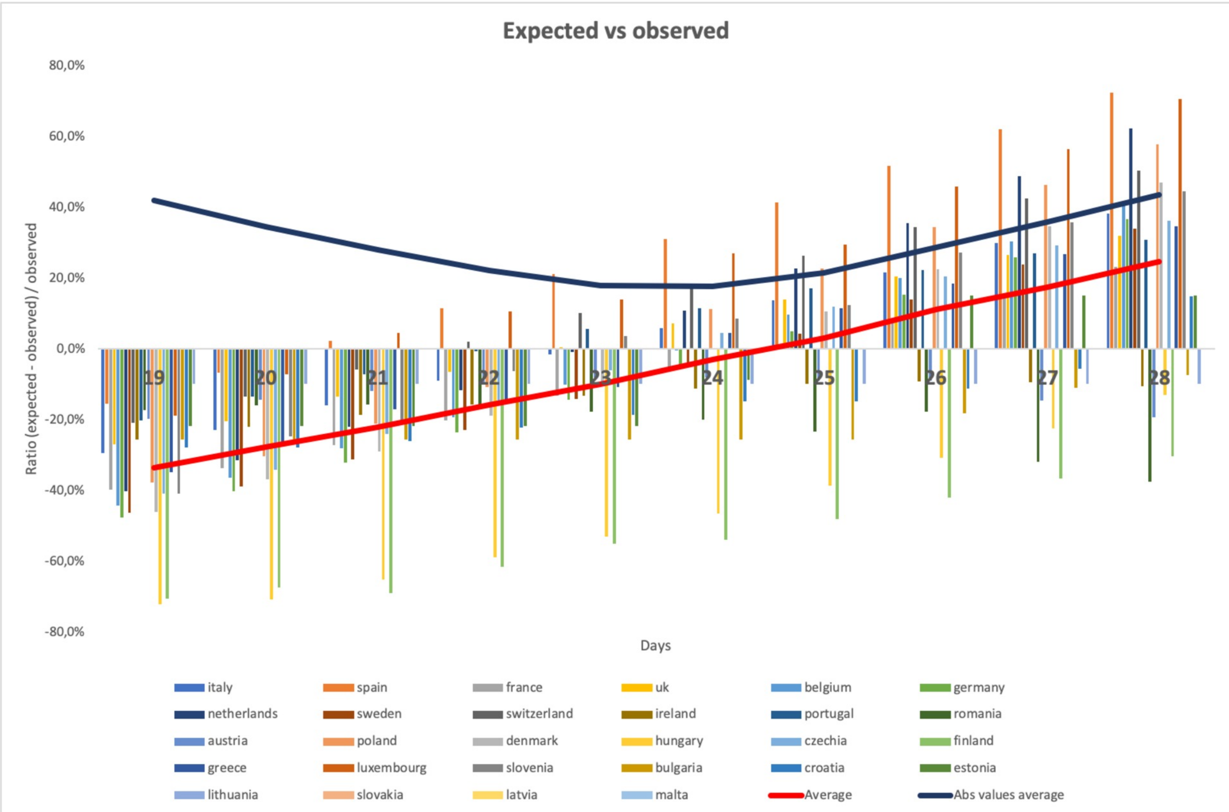

Expected vs observed
80,0%
60,0%
40,0%
20,0%
0,0%
-20,0%
-40,0%
-60,0%
-80,0%
Ratio (expected - observed) / observed
19
20
21
22
23
24
25
26
27
28
Days
italy
spain
france
uk
belgium
germany
netherlands
sweden
switzerland
ireland
portugal
romania
austria
poland
denmark
hungary
czechia
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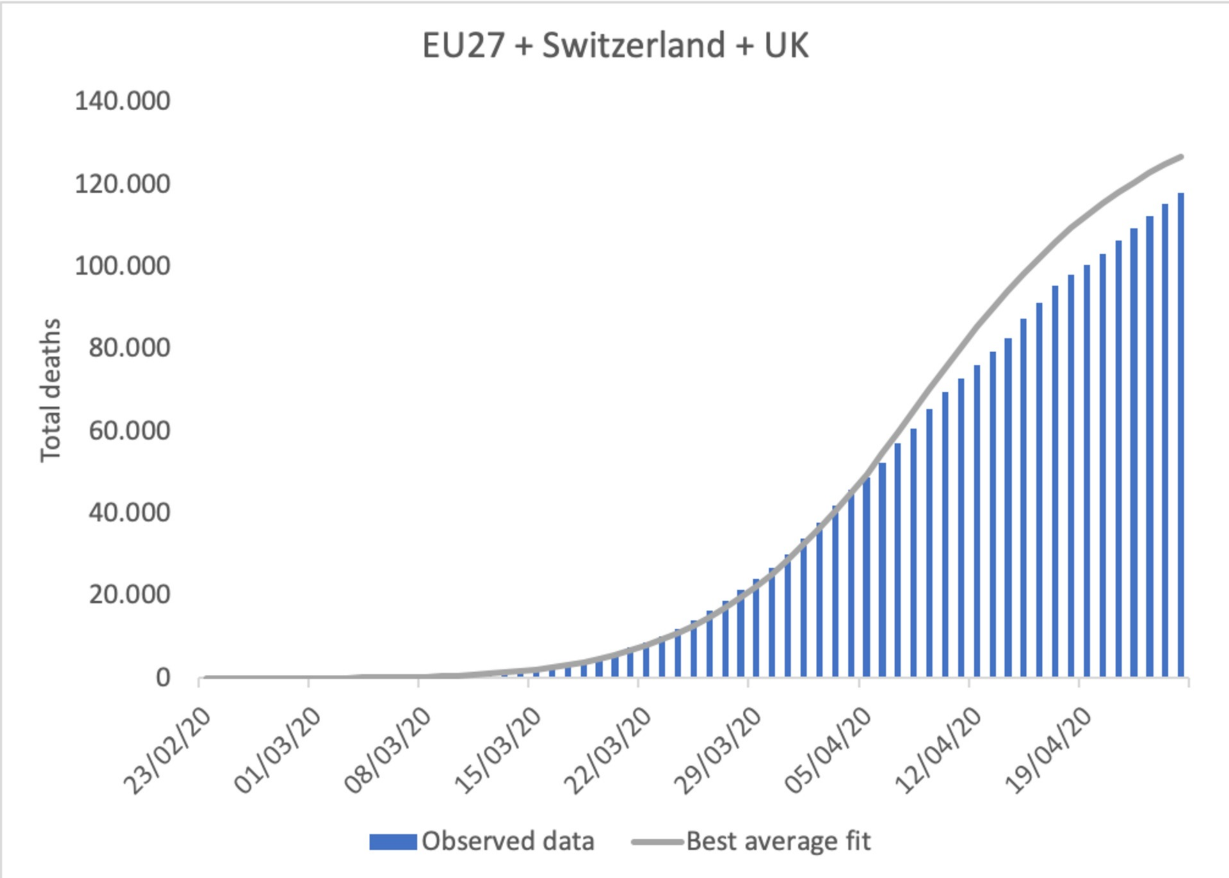
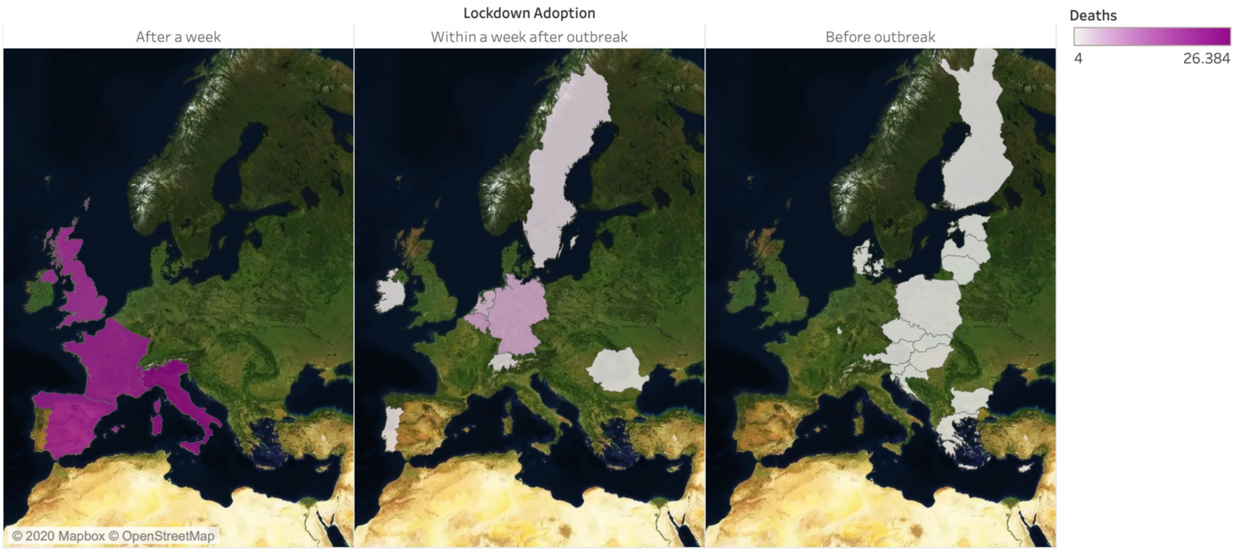
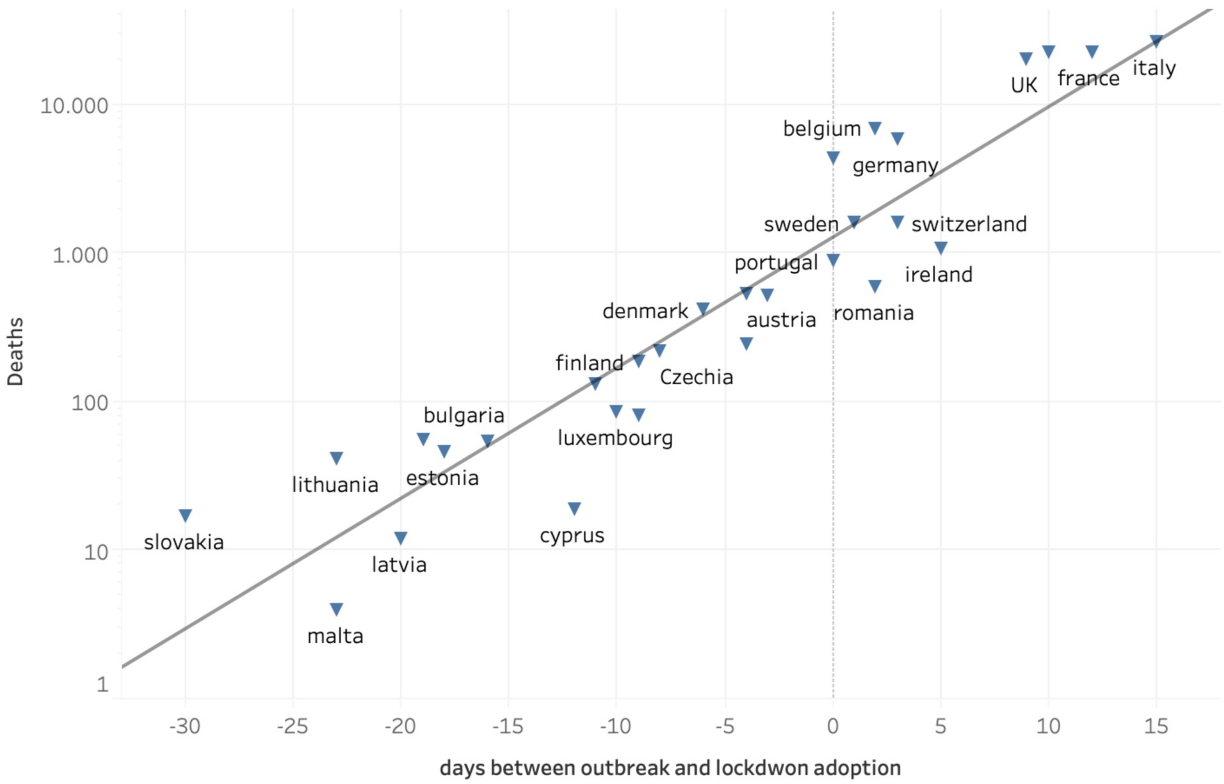
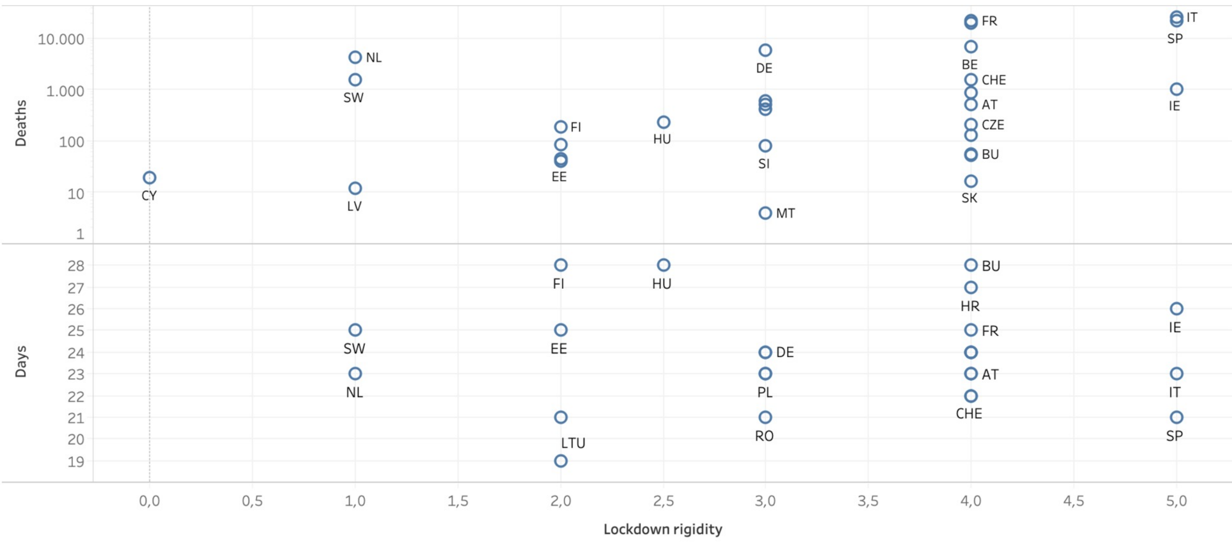
latvia
malta
Average
Abs values average


EU27 + Switzerland + UK
Total deaths
140.000
120.000
100.000
80.000
60.000
40.000
20.000
0
23/02/20
01/03/20
08/03/20
15/03/20
22/03/20
29/03/20
05/04/20
12/04/20
19/04/20
Observed data
Best average fit


Lockdown Adoption
After a week
Within a week after outbreak
Before outbreak
Deaths
4
26.384
© 2020 Mapbox © OpenStreetMap



Deaths
10.000
1.000
100
10
1
-30
-25
-20
-15
-10
-5
0
5
10
15
days between outbreak and lockdwon adoption
UK
france
italy
belgium
germany
sweden
switzerland
portugal
ireland
denmark
austria
romania
finland
Czechia
bulgaria
luxembourg
lithuania
estonia
slovakia
cyprus
latvia
malta


Deaths
10.000
1.000
100
10
1
Days
28
27
26
25
24
23
22
21
20
19
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0,5
1,0
1,5
2,0
2,5
3,0
3,5
4,0
4,5
5,0
Lockdown rigidity
CY
NL
SW
LV
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IE
LTU
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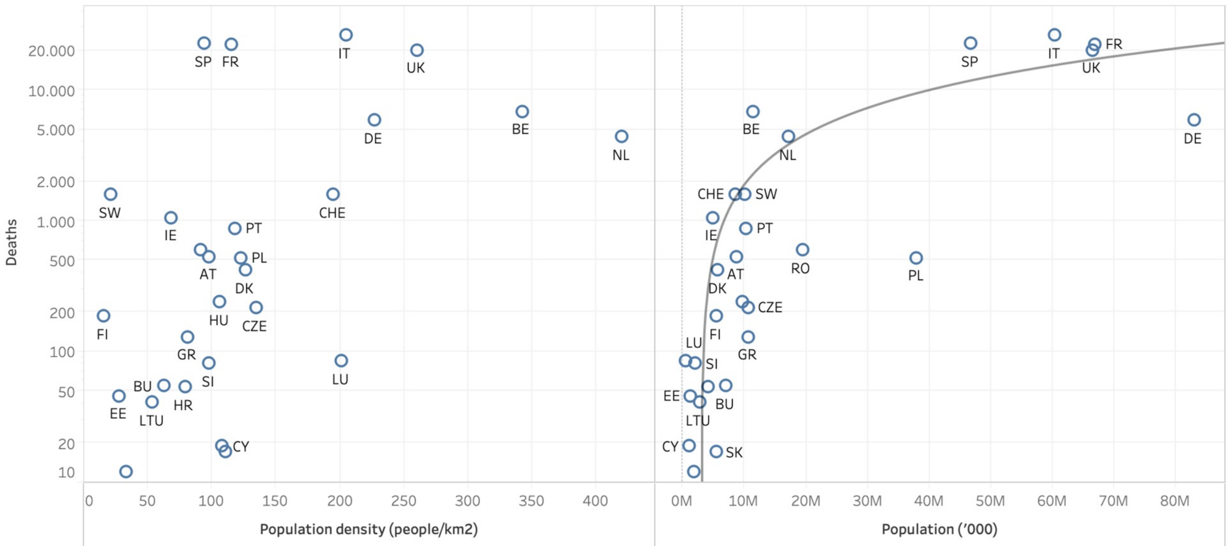
Deaths
20.000
10.000
5.000
2.000
1.000
500
200
100
50
20
10
Population density (people/km2)
Population ('000)
0M
10M
20M
30M
40M
50M
60M
70M
80M
SP
FR
IT
UK
DE
BE
NL
SW
CHE
IE
PT
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