## Supplements to COVID-19 Confirmed Cases Prediction This version: April 15, 2020

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This document contains material supplementing the prediction analysis in daily reports published on <u>https://er.ethz.ch/Covid-19</u>.

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## 1-Daily growth rate of hospitalization, ICU admittance and mortality in Belgium: insight on the problems with death numbers

In each daily report, we focus on the number of confirmed cases, which is the single metric that is **available** on a daily basis for a wide range of countries and regions. We have mentioned, however, that, for a thorough understanding of the Covid-19 epidemic, it is essential to

- 1. keep track of other key variables such as **mortality, hospitalizations** and **ICU admittance**;
- 2. and make a serious effort to relate **reported** to **actual** numbers (which, for the confirmed number of cases indicates a careful consideration of testing rates).

Figure 1 reports the daily growth rate of hospitalization, ICU admittance and mortality in Belgium. Looking at the data on confirmed cases only, Belgium followed exponential growth with stable daily growth rate until recently. This, however, is heavily influenced by the varying number of tests conducted. On the other hand, the daily growth rates of hospitalization, ICU admittance and mortality have been decreasing throughout, and provide a much clearer picture of Belgium approaching the peak of the epidemic. As of 14 April 2020's data, it seems that Belgium has reached the peak in hospitalizations and ICU admittance roughly one week ago.



Figure 1. Daily growth rate of mortality, hospitalization and ICU admittance in Belgium.

Over the last days, we have seen daily corrections of the numbers of reported deaths in Belgium up to one month back in time (this is not reflected in the graph above, which is based on the most recent update).

- This increase in mortality is due to the fact that it was decided to add all the deaths from elderly homes, even the ones where a Covid-19 infection was not formally tested, but was based on a general practitioners' diagnosis.
- 2/3 of newly reported deaths are from elderly homes, about half of the deaths in the historical data are from elderly homes.

- The gravity and scale of the impact of Covid-19 infections in elderly homes in Belgium seems to have been underestimated for some time: personnel has not been wearing mouth masks, was not well-trained for the situation, sometimes people from elderly homes were not admitted in the hospitals.

To allow for intra-country comparison, it thus seems essential to further analyze and correct for this reporting standards.

# 2-Relation between the number of confirmed positive cases in the US to the number of tests conducted

Numbers in this section are updated from the last report on April 8, but conclusions remain the same.

Based on the findings for Belgium, in Figure 2, we try to relate the number of confirmed positive cases in the US to the number of tests conducted.<sup>1</sup> In particular, we normalize the number of reported cases with the number of tests to get a better understanding of the growth rate of actual infections in the population. We find that a large part of the exponential growth of reported cases may be due to an exponential increase in testing. To make such an analysis more reliable, random testing (polling) in the general population would be necessary (and is highly recommended).





Figure 2. Upper plot: Growth rates of confirmed cases and of total tests in the US; lower plot: daily fraction of confirmed cases per number of tests and daily growth rate of confirmed cases.

<sup>&</sup>lt;sup>1</sup> Using data from https://covidtracking.com.



### 3-Death per capita in countries from different regions of the world

Figure 3. Total deaths per million population for selected countries ranked by deaths per million on 14 April 2020. Log scale top and linear scale bottom. The countries are subjectively divided into 4 groups: Rich Cool North countries (dark blue), Hot North countries (dark red), Southern Hemisphere countries (pink), and the East Block countries (Russia, China and East Europe) in green.

- 1. One of our favored metrics for following the epidemic is recorded deaths per million population. Figure 3 displays countries in rank order and categorises them according to Rich Cool North, Hot North, East Block and Southern Hemisphere. We have added a number of new countries since the last report. The overall picture has not changed dramatically since we first produced this graph on 19<sup>th</sup> March. Finland marks the mid-point being number 28 out of 55 countries. Finland is the rich cool north country with lowest death rate so far. It currently has 7 deaths / mil equivalent to a rate of 0.0007% of the population who have died so far from Covid 19. All countries to the right of Finland have a lower death rate than that. There is no serious Covid 19 epidemic throughout most of the world.
- 2. Note that the epidemic is at varying stages throughout these countries and this impacts the numbers recorded on 14<sup>th</sup> April. Adjustments for stage of outbreak are quite small, but need to be monitored. We adjust for this variable in the following section.
- 3. We observe that all of the Rich Cool North countries lie to the left of Finland and cluster far to the left. The Covid 19 epidemic is mainly a disease of the Rich Cool North and we need to ask why this is so. This is particularly evident on the lower linear scale chart. Why is it that the Rich Cool North, with their expensive and advanced health care systems are being hit hardest?
- 4. It is difficult to make sense out of the order in the East Block, Hot North and Southern Hemisphere countries. These tend to be quite randomly mixed in the rank order. We can hypothesise that this respiratory illness thrives in the cold North since outbreaks in the Hot North are at a considerably lesser scale. And we can hypothesise that the Southern Hemisphere has done well so far because it is mainly remote and is just entering autumn as the North enters spring. But we can observe that Ecuador that lies on the equator has the worst record of all southern hemisphere countries (for convenience we class Ecuador as southern hemisphere). And we are very puzzled by the fact that east European countries and Russia are mainly doing significantly better that the Rich Cool North. Why is Poland doing so

much better than Germany, one of the best performing Rich Cool North group members? Below we go on to examine possible links to BCG vaccination policies.

- 5. We continue to monitor Sweden with great interest. Sweden, and the Swedish Prime Minister, have followed a courageous path. Sweden remains the only west European country to have no lockdown. Primary schools remain open as do shops, bars and cafes. Many places of work remain open. Some were predicting Armageddon. Well, it hasn't happened yet in Sweden, but it has happened in the UK where thousands of businesses have failed, millions have lost their jobs, the government has forced millions of pensioners into solitary confinement and introduced economic measures with hugely unpredictable outcomes. As discussed below, Sweden should be compared to Denmark and not Norway. And sure Sweden is doing not so well as Denmark so far (Sweden 102 deaths / mil compared with Denmark 51.6 deaths / mil). Sweden has one big ace up its sleeve. It does not need to worry about the consequence of coming out of lockdown. And by protecting its economy, it will be able to fund health care and to care for the elderly in the future. It is not clear that this will be so in many other west European nations. Sweden's rank position has slipped to 10 from 12 but there are signs from mortality statistics that the epidemic is abating in Sweden. Sweden will provide a vital reference point in the years ahead when the post-mortem examination is held.
- 6. Greece remains an interesting case, located one place to the left of Finland. We classified Greece as Hot North and it does not have an epidemic. Being a hot Island archipelago Greece's main concern remains mainly economic. Greece already had a very weak economy, and its main source of revenue (tourism) has just been destroyed, with no clear pathway to recovery.
- 7. China continues to march to the right through the ranks. The horror story of January and February that everyone in the west watched is going to turn out to be a fairy tale for China, while the rich north countries wither on the vine. Understanding the astonishingly different dynamics between Hubei Province and the rest of China is a priority for our group research.
- 8. The southern hemisphere remains mainly hot. If the epidemic comes in the Southern hemisphere winter, they have time to prepare. Locations like S Chile, Patagonia and S Island New Zealand could be most at risk.
- 9. The large epidemic lies in Rich Cool North countries where land locked San Marino is by far the hardest hit with 1059 deaths / million. With 36 deaths, the population is reduced from 34,000 to 33,964 (0.11%).
- 10. Iran is the only hot north country to have had a large epidemic. It was cold over Teheran during the early stage and a large part of the population lives in high plateaus and mountains where the weather is cold. And we speculate that old men sharing bubble pipes may have spread the virus among the vulnerable who then imported it to the family home.
- 11. India, Pakistan and Bangladesh are all big countries that should have been in the thick of it early on given their location. They might not have enough resources to test and find the cause of death. But they appear to be seeing something going on now since India and Pakistan have gone into lockdown. We speculate that the very low death rate in India, Pakistan and Bangladesh is in part because there populations lack large cohorts in the over 65 groups where most deaths in the Rich North occur (Figure 4).
- 12. It is important not to forget the "follow-up" cost of Covid-19 in the sense of longer term damage to organs that is not reflected in current death statistics.



Figure 4. Demographics of India and distribution of Covid-19 deaths in the UK.

## 4-Discussion of the hypothesis of a correlation between Covid 19 deaths and BCG vaccination policies

We now move on to examine links between Covid 19 deaths and BCG vaccination policies that have already received much academic scrutiny and media attention. We base our analysis on the map shown in Figure 5 [https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3062527/].



Figure 5. Reproduced from The BCG World Atlas: A Database of Global BCG Vaccination Policies and Practices.

There are three main categories of BCG vaccination strategies, 1) never had, 2) had but lapsed and 3) on going. It was immediately apparent to us that the Rich Cool North countries corresponded in large part with countries that had either never had or had lapsed BCG programs. There are four main outliers in Ecuador, Israel, Australia and New Zealand. All once had BCG vaccination programs that have lapsed, mainly in the late 90s and early 00s. In Europe, notably Italy, Belgium and The Netherlands have never had BCG vaccination program. In North America, the USA and Canada never had vaccination programs.



Figure 6. Same rank order as Figure 3 but colour coded according to BCG never had (red), BCG lapsed (blue) and BCG on going (green).

Our median point Finland has a lapsed BCG program. All countries with lapsed or never had BCG, bar Australia, lie to the left. Australia can be viewed as a special case being a large, isolated, hot island continent. There seems little doubt that countries that never had, or have lapsed BCG programs are those that have been hardest hit by Covid 19. And many of these countries correspond to the Rich Cool North.

But now we need to mention a number of cautionary notes. There seems to be little difference between countries that never had BCG vaccination and those that once had but let the program lapse. Countries that have lapsed programs allowed them to lapse in the period 1980 (Denmark) to 2007 (France). In Denmark 40 to 74 year olds are inoculated, in France 13 to 70 year olds are inoculated (based on Wikipedia [https://en.wikipedia.org/wiki/BCG\_vaccine]. And so in the lapsed inoculation group, there is a cohort of variable duration in the middle of the population that are inoculated while younger and older cohorts are not. This pattern does not seem to be discriminated against those populations that never were inoculated. We have not yet managed to make sense of these findings and report these as preliminary, not yet understood observations.

The BCG World Atlas (Figure 5) presents a number of binary case examples where we can compare adjacent countries where one country has on-going vaccination and the other either has lapsed or no vaccination. Figure 7 illustrates the relationship where arrows point from on-going towards lapsed or never.



Figure 7. Same as Figure 6 where countries with ongoing BCG vaccination link to adjacent peers where BCG vaccination was never implemented or where it has lapsed.

In each of 9 pairs of adjacent countries where on-going BCG inoculation may be compared with a contrasting peer, the contrasting peer country is doing substantially worse when it comes to deaths / mil during the Covid 19 outbreak. These pairs of countries are as follows, the numbers = displacement in rank order and normalised death rate ratio:

South Africa – Australia (13 / 5.2)

Russia – Finland (20 / 6.32)

Columbia – Ecuador (20 / 9.4)

Mexico – USA (23 / 28)

Lebanon – Israel (9 / 4.40)

Poland –Germany (12 / 4.39)

Norway – Denmark (4 / 2.0)

Portugal – Spain (12 / 6.95)

Ireland – UK (5 / 2.41)

We can conclude that our analysis of Covid 19 mortality statistics provides strong support to the theory that countries with on-going and current BCG vaccination programs have significantly lower mortality rates than those that don't. It is a puzzle, however, to understand why countries with lapsed programs appear to fare little better than those that never had a BCG program at all. It is also a puzzle to understand why the BCG vaccine, designed to combat tuberculosis, a bacterial infection of the lungs, should have efficacy, combating the SARS-CoV-2 virus. We are not yet in a position to draw any firm conclusions and point to large epidemological studies that are planned. We also draw attention to the cautionary advice offered by Professor Madhukar Pai [1]. The empirical evidence, however, may help us to understand why, for example, western Europe has been struck so much harder than eastern Europe.

[1] <u>https://www.forbes.com/sites/madhukarpai/2020/04/12/bcg-against-coronavirus-less-hype-and-more-evidence-please/#31bf37256b4f</u>

### 5-Per Capita Mortality Trends

**Summary:** Figure 8 presents an analysis of cumulative mortality trends for 18 countries. See our report on Supplements to Covid 19 confirmed cases prediction from April 8 for a description of methods.

https://ethz.ch/content/dam/ethz/special-interest/mtec/chair-of-entrepreneurial-risksdam/documents/Covid-19/Covid\_Supplements\_8April2020repl07.pdf

In short, mortality statistics are reduced to deaths per million population. We then normalise for the different stages of outbreak in various countries by aligning the curves on 4 deaths / million. The result is shown in Figure 8.



Figure 8. Population normalised cumulative mortality curves time shifted to account for the different stage of outbreak between countries. Time shifting is based on aligning data on 4 deaths / mil (the datum).

We can observe that there is a very large range in outcomes between countries. The focus of our research is to try and understand the factors leading to this range of outcomes. We acknowledge that it is probably too late for this information to impact during the current epidemic, but hope that this analysis may guide response to similar future events.

It needs to be noted that many countries with the best outcomes are not plotted because they have yet to reach 4 deaths / mil. The countries with best outcomes (S Korea, Hungary, Poland) are going to track along the X-axis.

At face value, Norway currently has the best outcome and Belgium the worst outcome of the European countries. However, we caution against using only the gradients of these curves as a measure of final performance. As the outbreaks mature, and the rise in daily death toll slows, we should see a flattening of the curves as may be evident in the USA, Sweden, Switzerland and the Netherlands.

To read this chart properly, one needs to read along a vertical line since this gives a constant time of outbreak from the datum. The values for day from datum equal to + 17 days are summarised in Table 1. We have also fitted logistics to the mortality curves for certain countries that estimates final total deaths. These are also shown in Table 1.

			Final deaths	Final deaths
	14-Apr	datum + 17 days	estimates	estimates
	Total deaths	deaths / mil	1000s	deaths/mil
Spain	18056	181	19.9 to 21.6	442
Portugal	567	49.4	0.87 to 5.94	128
France	14967	115.8	17 to 19	274
Germany	3220	38.4	3.72 to 4.28	47
UK	12107	104.5	15.9 to 21.2	259
Belgium	4157	175.6	6.65 to 15.7	759
Switzerland	1162	77	1.01 to 1.63	134
Italy	20465	112.8	23.9 to 25.4	408
USA	23765	69	32.6 to 37.7	105
Sweden	1033	87.8	1.11 to 1.66	127
Netherlands	2945	122.6	3.45 to 3.82	212
Poland	251			
Norway	139	25.6		
Hungary	122			
Denmark	299	42.65		
Iran	4683	30	5.74 to 7.02	75
S Korea	222			
Austria	384	38.9	0.53 to 2.73	81

Table 1. Column 1 & 2 = Total deaths on April 14 and deaths/ mil on datum + 17 days. Column 3 & 4 = estimates of final deaths in thousands and deaths /mil from logistic fit to the per capita mortality curves. The values reported are the range of medium estimates.

For details and a comprehensive table of our estimates of final deaths, we refer to our daily updated document:

https://ethz.ch/content/dam/ethz/special-interest/mtec/chair-of-entrepreneurial-risks-dam/documents/Covid-19/Covid\_daily-forecasts\_ETH\_14April2020.pdf

#### Discussion

We are still at an early stage of trying to quantify the key variables that control the severity of outbreak from one country to the next.

To understand the controlling variables within the Rich Cool North group, we draw attention to the analysis presented in the next section, where we see a good correlation between Stringency measures within the European group.

Qualitatively, it seems that being a hot country is better than being a cold country and we hope that the Northern hemisphere summer may abate or kill the epidemic.

It is worth noting that Sweden, the only country with no lockdown is performing well and a flattening of the curve could indicate the outbreak is coming to an end, although there are large variations in the reported numbers from day to day.

The USA is also performing well relative to many European peers.

Mortality within the Rich Cool North group is overwhelmingly concentrated in the aging cohorts > 70 years old (see section on age distribution below). If you are a poor country with few people living into old age, you may perform much better than a rich country where populations have large numbers of very old, often with co-morbidities.

Another feature of Rich Cool North Countries is obesity where obesity rates typically fall in the range 20 to 25%. We have heard reports that the majority of younger people in intensive care are obese.

An active BCG vaccination program seems to correlate with low mortality. If so, the causal relationship is still not understood.

As we begin to make sense of the controlling factors, we now see it as less likely that large variations between countries comes down to different reporting standards. However, we need to caution that there are significant problems with data reliability and variations in reliability from one country to the next.

So far mortality in most countries is relatively low. Estimated final totals are within the range of a bad flu season, although we caution that there may be significant underestimates since many countries, like the UK, are only counting hospital deaths so far.

Sweden continues to perform well compared to European peers. Sweden will have minimised the social and economic costs that are likely to be very high in countries like the UK and France that have imposed strict lockdowns on their populations. Viable elderly people have been forced into solitary confinement with untold physical and mental harm being done.

#### 6-Efficiency of lockdown strategies

Here, we take a first look at different lockdown strategies across countries and their impact on subsequent number of deaths. As above, we align countries at 4 deaths/million population and look mainly at European countries (many other countries have not reached this threshold, yet).

#### Methodology:

1) To classify the different lockdown strategies, we use the data from [2], where the authors collect information on seven different policy measures<sup>2</sup> and calculate a *Stringency Index* between 0 and 100, which averages over these policy measures. This gives an indication of the severity of lockdown in each country for a given data.

2) As discussed in the last section, we align the countries at the **datum** where the country reaches 4 deaths/million. We then calculate the total deaths in an interval [datum,datum+T] for each country, where T is the same for every country and is chosen as large as possible.

3) Finally, we calculate the average stringency index in an interval that is chosen based on the *reported time from infection to death*, which is around 13 to 20 days according to [3].

#### Discussion

As expected (see Figure 9), we see a negative correlation between the number of deaths and lockdown measures in the respective intervals. There seem to be two group of countries, with Spain, Belgium, France and Italy showing roughly twice as many deaths as other countries with the same stringency level. Following our analysis on Belgium above, we hypothesise that this could be related to the situation in elderly homes, in particular, a lack of recording deaths outside of hospitals and/or handling the delicate situation within these risk group clusters.

Going forward, we hope this type of analysis helps to assess the efficiency, cost and benefits of various lockdown measures.

<sup>&</sup>lt;sup>2</sup> School closing, Workplace closing, Cancel public events, Close public transport, Public info campaigns, Restrictions on internal movement, International travel controls



Deaths aligned at 4 deaths/mill, summed over largest possible time-frame (15 days)

Average Stringency in [datum - 20, datum + 15 - 13], datum = 4 death/mill

Figure 9. Efficiency of lockdown strategies in various countries, using deaths per million and a time shift to datum=4 deaths/mill to account for different stages of the epidemic. To choose the interval to calculate the average stringency, we use the reported time from infection to death [4].

[2] <u>https://www.bsg.ox.ac.uk/research/research-projects/oxford-covid-19-government-response-tracker</u>

[3] https://wwwnc.cdc.gov/eid/article/26/7/20-0282 article

### 7-Age distribution of deaths

Numbers in this section are updated from the last report on April 8, but conclusions remain the same.

The UK has begun to report the demographic profiles of those dying from Covid 19 (https://www.ons.gov.uk). The first report was for week 12 (ending 20 March), see Figure 10. There is promise of more detailed reports to come. It has to be noted that week 12 is a very early stage of the epidemic in the UK. Similar to other countries, Covid 19 is killing the elderly to very elderly in the UK. The mean age of death is computed to be 80.2 years compared with life expectancy in the UK of 81 years. In this calculation, an age of 90 years is assumed for the 85+ cohort



Figure 10. Age distribution of confirmed deaths in England and Wales (different from UK) (Mean: 80.2), Source: <u>https://www.ons.gov.uk</u>

and