NEUBERGER BERMAN

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How Deadly Is COVID-19?

On April 18, the *Wall Street Journal* opinion page included a description of how new work from Stanford University using antibody screening presents evidence that the SARS-COV2 virus (that causes the COVID-19 disease) is much more widespread than previously thought, and therefore less dangerous.

The medRxiv preprint of the paper in question (Bendavid et al) showed that, of 3,300 subjects tested in Santa Clara County, 50 were found with antibodies for SARS-COV2. The authors concluded that the Infection Fatality Rate (IFR) is between 0.12% and 0.25%.

The IFR (deaths divided by infected) is different from the Case Fatality Rate (CFR), which is the deaths divided by positive cases, and there is general agreement that the number of infections are likely larger than the number of positive cases, although in most instances there has been insufficient testing.

There is less agreement about the precise ratio between infections and positive cases, however. Our models are based on evidence that the ratio is between two and four—that is, there are between two and four times as many actual infections as there are recorded positive cases. The Bendavid et al paper suggests that the ratio is between 50 and 85, which appears to make the denominator much larger, and therefore the IFR much smaller. As the table below indicates, an IFR of 0.12% — 0.25% is comparable to influenza.

Disease	Estimated case fatality rate (CFR)
SARS-CoV	10% Venkatesh and Memish (2004) Munster et al. (2020)
MERS-CoV	34% Munster et al. (2020)
Seasonal flu (US)	0.1-0.2% US CDC
Ebola	50% 40% in the 2013-16 outbreak WHO (2020) Shultz et al. (2016)

So Many Different Views

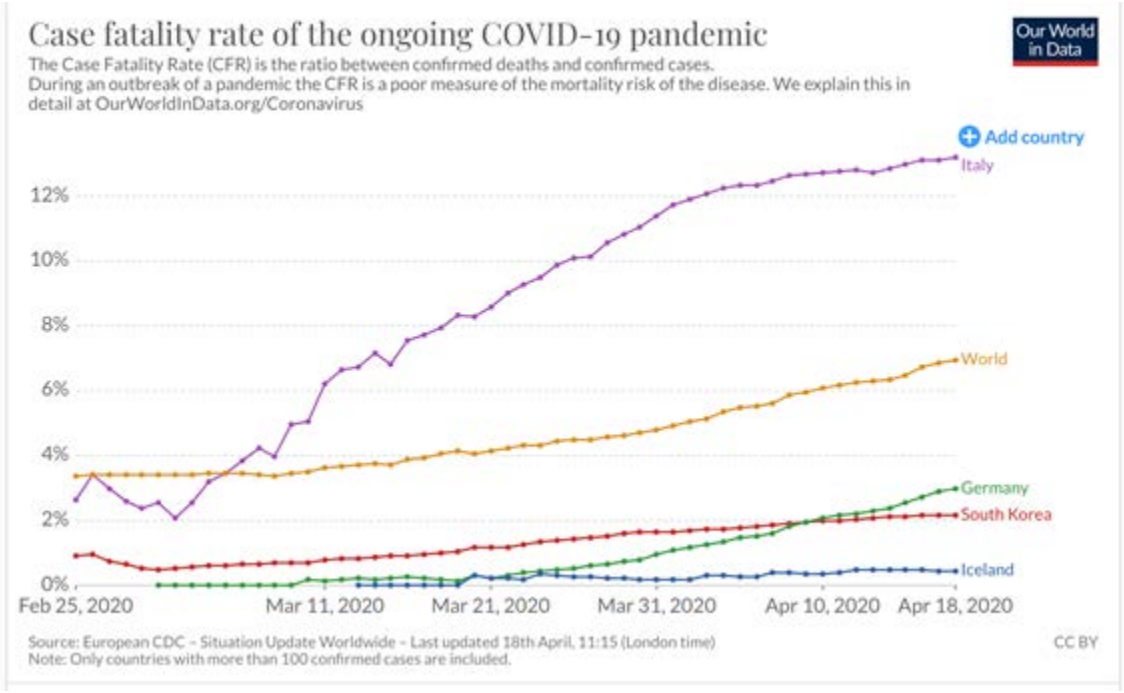
As antibody tests have started, the key metrics to watch are their sensitivity and specificity.[1] In the Bendavid et al paper, the specificity of the antibody test to the COV-SARS2 virus is measured using 371 blood samples that predated this virus. Two of the 371 blood samples were false positives (perhaps revealing antibodies to a similar, older virus), resulting, they wrote, in a 95% confidence interval of 98% to 99.9% specificity. In other words the test could produce, with this confidence, up to 2% false positives.

The authors describe antibody tests on 3,300 volunteers, who all presumably suspected they had the disease. In fact, had none of them been infected, a 2% false positive rate would have returned 66 positive results. The fact that they found 50 positive cases, a number within their confidence bounds, leaves us with a wide range of possible interpretations of the data. In addition, the authors may have given 50 people a potentially incorrect belief in their immunity to the disease, which may have changed their behavior.

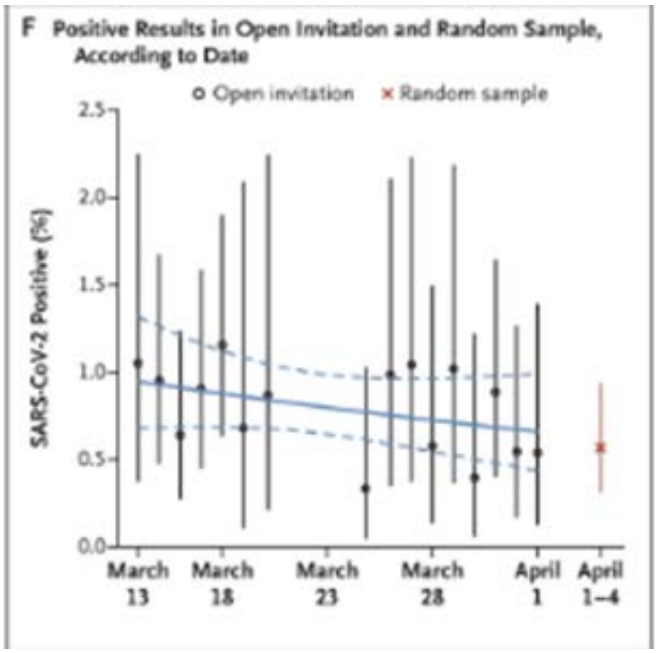
The measured value of CFR varies by larger than a factor of 10 from region to region (shown as of April 18, in the figure below). As the pandemic has spread, the overall CFR changes, in aggregate and for individual countries. Note that the CFR from Italy is 25 times that of

[1] See Terri Towers, "What Could Get Us Out of the COVID-19 Pandemic Beyond Current Measures?", March 29, 2020

Iceland, and since Iceland is among the most comprehensive in testing, this example is also used as evidence that the true IFR could be much smaller than the CFR.



Another recent paper (Gudbjartsson et al, NEJM, April 14, 2020) describes the testing that was performed in Iceland—both targeted screening of 9,199 people (of whom 13.3% tested positive) and random screening of 13,080 people (of whom 0.8% tested positive). In total, 6% of the population of Iceland was screened. Most of the people who tested positive had recently traveled internationally and were isolated. Note that in the figure below, reproduced from the Gudbjartsson et al paper, the percentage of positive tests in the random samples of the population did not change over time, which could indicate that the virus was not spreading rapidly due to the containment process put in place. The low CFR may also have been partly due to successfully blocking the infection of vulnerable groups with a higher risk of fatality.



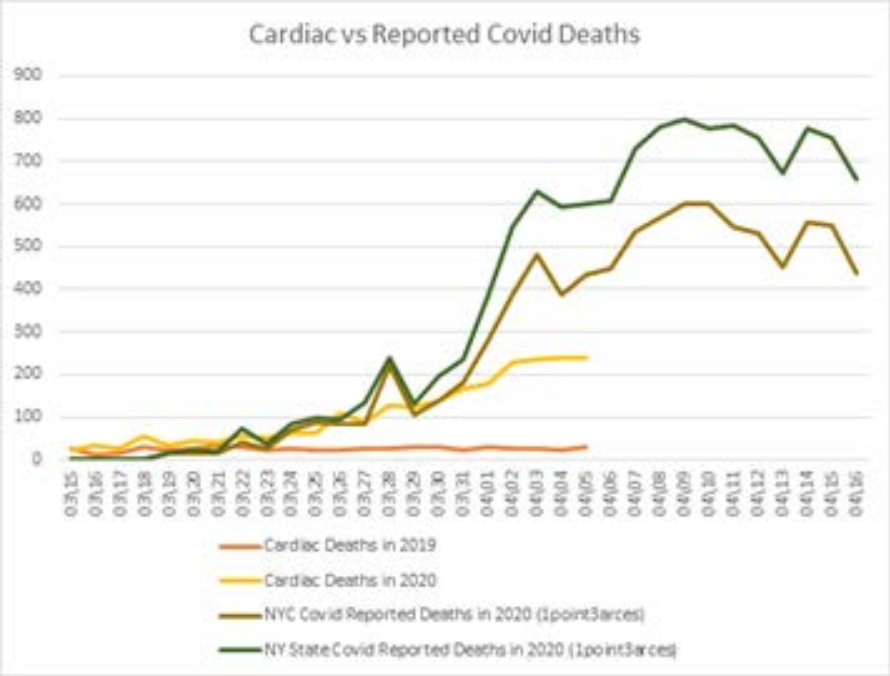
Source: New England Journal of Medicine. Apr 14, 2020. DOI:10.1056/NEJMoa2006100 [e-pub ahead of print].

In addition to changes in the denominator of the CFR, calculating the true probability of death is also complicated by the rate of growth of positive cases, the rate of growth of deaths, and the duration of the disease. Many studies calculate the death rate divided by the number of cases two weeks prior, but inconsistent testing also makes this calculation a challenge.

Undercounting

In all of these calculations of CFR the rate is a small percentage, so while it is sensitive to changes in the denominator, the rate is much more sensitive to changes in the numerator, and we believe that deaths are being undercounted.

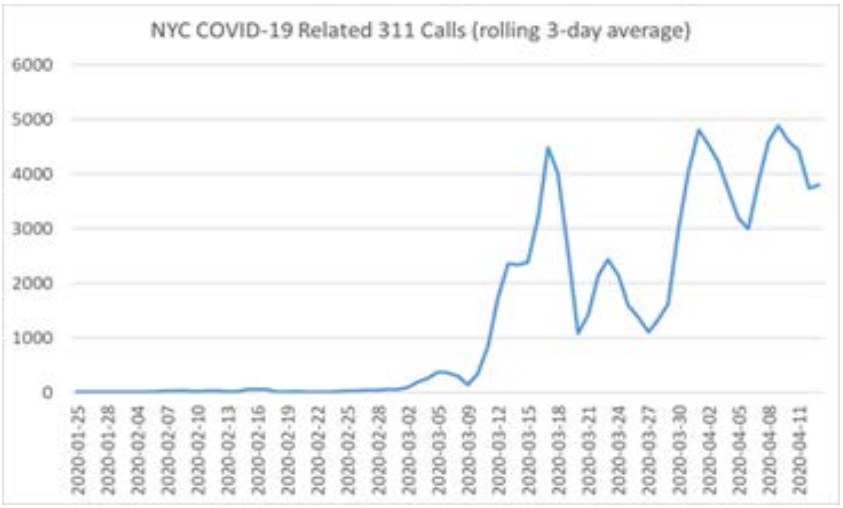
The number of deaths in New York City was increased by over 4,000 to correct for probable COVID-19 deaths that had been previously not reported. As of April 16, according to nyc.gov, the total deaths has increased to 12,109, which includes 7,890 confirmed COVID-19 deaths and 4,309 probable COVID- 19 deaths.



Source: Neuberger Berman, data from FDNY as of April 15

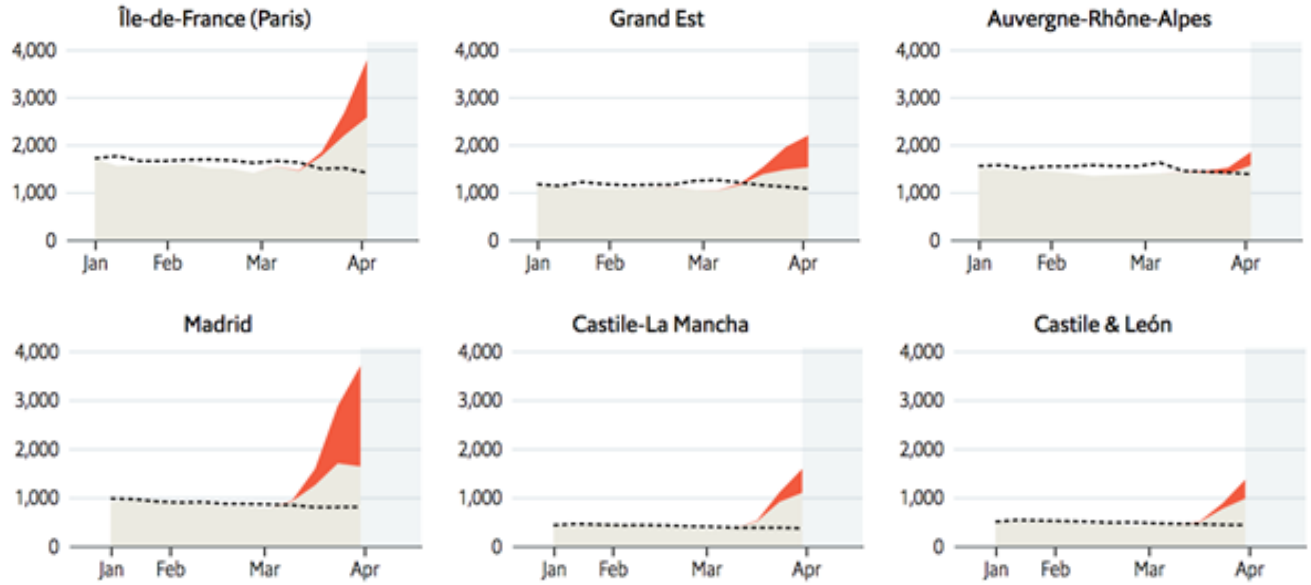
The graph above shows the deaths that had previously been reported in New York City and New York State, as well as additional deaths occurring following 911 calls, relative to the same period last year. The additional deaths are from data recorded by the New York City Fire Department (FDNY), and counted as cardiac arrest deaths. The graph shows the number of deaths from cardiac arrest recorded this time last year as 25 to 30 per day. This year the number has been over 200 per day. The FDNY data also show that, whereas normally only 40% of people die after these calls, deaths are now trending at 80%. This data is normally only released annually, but data up to April 5 was released to the press on April 15.

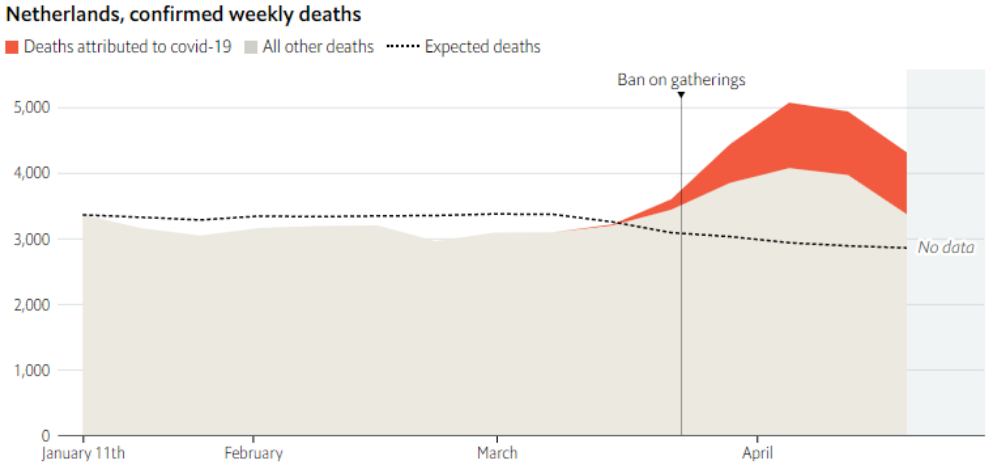
Recall that the paper on antibody testing by Bendavid et al discussed above predicts an IFR of 0.12% to 0.25%. For New York City's population of 8.4 million, this corresponds to 10,080 to 21,000 deaths should everyone become infected. The models only predict that 75% of the population will eventually be infected, thus reducing the upper bound to 15,750. The predictions of this antibody study does not appear to be consistent with the number of deaths already observed in New York City—and, as the chart below shows, calls to the special COVID-19 311 line remain high in New York.



Source: Neuberger Berman, data from ny.gov as of April 18

The issue with unattributed deaths is not unique to New York. Data has been published by *The Economist* show that in France, Spain, and the Netherlands there are also large numbers of unattributed deaths.



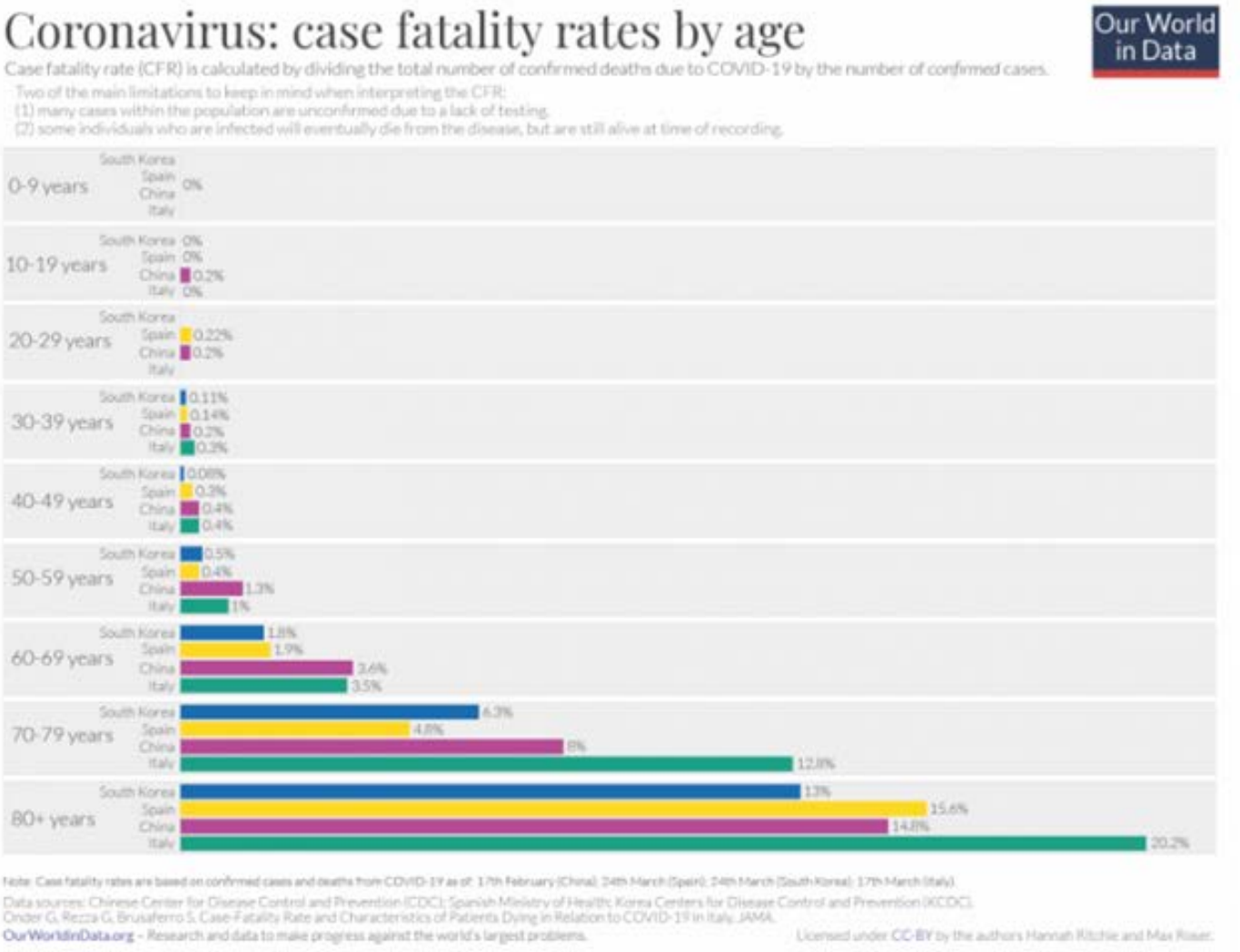


Source: *The Economist,* as of April 18

The Age and Comorbidity Impact

Differences in CFR and IFR occur not only due to uncounted deaths, but also due to variation in population demographics, population density, the groups that were initially infected prior to non-medical interventions, the medical system in individual regions, and many other factors. The largest of these factors are age and the presence of comorbidities.

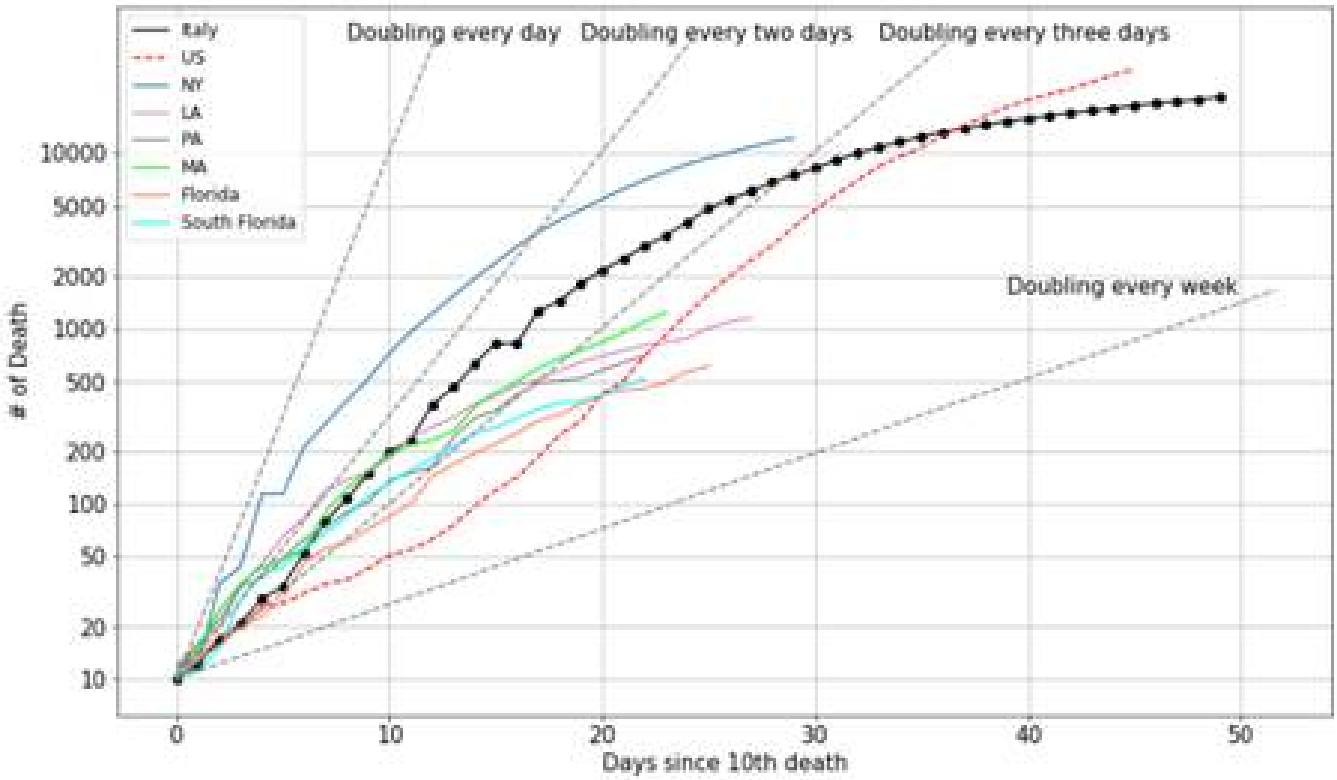
The CFR for people under 40 years old is comparable to influenza, but it has increased exponentially with age, as shown in the figure below. The figure also shows, if the disease has not reached the highest risk part of a population the CFR is lower. If the disease spreads through the entire population, the CFR values appear more comparable if weighted by the size of the population in each age range.



Unlike the Spanish Flu in 1918, COVID-19 produces worse outcomes in people that have weaker immune systems. A NEJM paper (Baum et al, April 3) reported that the comorbidities that led to the worst outcomes in 7,162 hospitalizations for COVID-19 in the U.S. were diabetes, chronic lung disease and cardiac disease. In this case, 71% of the patients hospitalized had one or more of these comorbidities. Similarly, a medRxiv preprint of a paper by Petrilli et al, from April 11, shows that, of 4,103 COVID-19 patients in New York City, 48.7% were hospitalized, 49.1% were discharged home and 14.6% died. Out of the 445 patients requiring mechanical ventilation, 162 (36.4%) died. An analysis of variance indicated that being over 65, a BMI>40 and heart failure were most correlated with death, in that order.

Does Weather Matter?

One of the most actively debated factors in predicting the spread of COVID-19 is the impact of the weather (temperature and humidity). The two most similar diseases, SARS and MERS, were not affected by weather, and so far we have not found convincing evidence in the data or published scientific literature to support an impact of weather on COVID-19. For example, in the chart below the doubling rate of deaths in Louisiana and South Florida are not significantly different from other areas in the U.S. with lower temperatures.



Source: Neuberger Berman, Data from Johns Hopkins as of April 18

Conclusion

We are seeing some epidemiological research that indicates the fatality rate of COVID-19 is much lower than currently feared. However, we would note that these results are often clouded by variation in the population samples examined—variations in local disease-control policy, demographics and comorbidity. Existing data indicates that the lowest estimates of the fatality rate are not consistent with already observed data on reported COVID-19 deaths, even where a very high rate of infection is assumed.