Stanford's Contrasting Fatality Estimates

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COVID-19 Actuaries Response Group – Learn. Share. Educate. Influence

Summary

Over the past couple of days Stanford academics have published greatly contrasting estimates of the Infection Fatality Rate (IFR) of COVID-19. We briefly examine both papers and consider them in the context of other work done in this area (including our related work using Italian data).

We conclude that the study by Grewelle and De Leo, with its estimate of 1.0% for the IFR globally, looks plausible and in line with much other work in this area.

"Estimating the Global Infection Fatality Rate of COVID-19" – Grewelle, De Leo[i]

The authors have sought to provide a first estimate of the global IFR using a novel method and data from multiple countries. It seems a clever approach, which works around the lack of knowledge of true infection numbers. Their approach is, broadly, as follows:

- Because the true number of cases is unknown, a 'testing capacity' parameter C is estimated. This is defined as tests conducted per positive case, so C=1 would mean all tests are positive. As C gets larger, the country's IFR estimate improves.
- Using that parameter, the authors develop a relationship between sample prevalence and the reported Case Fatality Rate (CFR).
- The relationship hypothesised showed a medium-strong correlation (55% correlation – where 0% would mean no relationship, 100% a perfect relationship).
- The method allows for false negatives in testing but not explicitly for differences in demographic profiles across countries (they contend the method allows for this implicitly).

With this approach, the authors estimate IFR at 1.0% (with 0.8% to 1.4% as the 95% range).

The results are tested (i.e. comparing what their model predicts against what is known about CFRs) to look at outliers – the two extremes were Italy (much higher than expected CFR) and Singapore (much lower). Some of the variation between countries may be explained by difference in approach for attribution of deaths to COVID-19, or large differences in testing protocol.

The authors also examined whether countries' GDP (per capita) or high-age profiles might affect their findings, concluding that these aspects did not seem significant.

The authors examined the question of whether victims were dying from COVID-19 or from comorbidities and concluded "the vast majority of SARS-COV-2 positive deaths are due in whole or primarily to COVID-19". We would note however that the method they applied to reach that conclusion may not be appropriate for deaths of those in care homes.

A key consideration in assessing the innovative method used is whether it incorporates bias – i.e. whether some artefact of the assumptions made means the result is likely to be too high or too low. We do not think the method has introduced any obvious bias, although some elements require deeper investigation, such as the "decay constant" *k*. Of course the estimate is uncertain, hence the confidence intervals, but crucially it appears that the real and currently unknown IFR is equally likely to be higher or lower than their estimate of 1.0%.

"The infection fatality rate of COVID-19 inferred from seroprevalence data", Ioannides[ii]

The author considers twelve papers that examine IFR from seroprevalence studies. The studies were selected for sample size (> 500) and reference to other criteria. Each study estimated the IFR as number of COVID-19 deaths at a relevant time point by the number of estimated people infected. Adjustments were made to allow for antibody types that were not assessed in some of the studies.

The paper appears to have introduced a selection bias towards lower IFRs – for example, it has included studies of blood donors, who are typically younger and fitter than the wider population and has excluded studies of healthcare workers. Studies have been included which have been shown to have used calculation methods which underestimate the IFR. One of the studies is the IFR only for people aged 18-72 (clearly an underestimate of the IFR for the population as a whole). Another is the author's own widely-criticised Santa Clara study.

The paper concludes that IFRs worldwide ranged from 0.02% to 0.40%. The lower end of the range is demonstrably too low based on observed deaths in locations such as New York City.

Other reference points

A recent paper was released by Meyerowitz-Latz and Merone[iii], based on a search of Pubmed and Medrxiv for IFR studies published between February and April 2020. They conducted a meta-analysis on thirteen studies, giving an estimate of IFR of 0.75% (confidence interval 0.5 to 1.0%).

However, the authors note that very high heterogeneity in the meta-analysis makes it difficult to know how representative their estimate is – in particular, different countries will experience different IFRs.

Our own earlier work[iv]

Back in March we used data from Italy only (a reasonable choice at the time) to estimate – via necessary assumptions about aspects such as proportions of unknown cases, and time lags – that the IFR was in the range of 1.0-2.0%.

Having regard to the other studies done on the IFR, although this result looks on the high side, that seems to reflect the particularly tragic impact of the first wave of infection on Italy. The Grewelle paper notes that the CFR in Italy is exceptionally high.

Conclusion

The uncertainties inherent in estimating the IFR are still with us today to a material extent, even if we have, unfortunately, many more tests, cases and deaths than we did two months ago. We are still in a position of uncertainty.

The above results, in particular the variety of results, shows that this remains the case. However, the study by Grewelle and De Leo does look both reasonable in its (admittedly unusual) method, and reasonable in the overall result – an IFR of around 1%.

As countries start to emerge from lockdown, proper appreciation of the IFR is necessary to make the right decisions over the remainder of the year. One of the biggest risks is that of false security, and thinking that the IFR may be only one-tenth or so of what it really is (admitting that we are still unsure as to 'what it really is') would be a dangerous mistake.

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[i] https://www.medrxiv.org/content/10.1101/2020.05.11.20098780v1

[ii] https://www.medrxiv.org/content/10.1101/2020.05.13.20101253v1

[iii] https://www.medrxiv.org/content/10.1101/2020.05.03.20089854v2.full.pdf

[iv] https://www.theactuary.com/2020/04/14/quantifying-coronavirus