Global Covid-19 Case Fatality Rates

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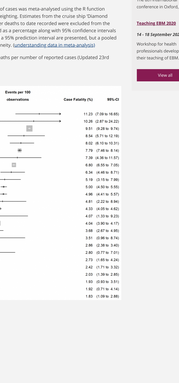
Updated 23 March

The total number of cases and the total number of deaths from COVID-19 outbreak data was drawn down (scraped) from: https://www.worldometers.info/coronavirus/.

The proportion of deaths to the total numbers of cases was meta-analysed using the R function *metaprop*, using fixed effect inverse-variance weighting. Estimates from the cruise ship 'Diamond Princess' as well as countries with three or fewer deaths to date recorded were excluded from the analysis. County-level case fatality is presented as a percentage along with 95% confidence intervals in a forest plot. Estimates of heterogeneity and a 95% prediction interval are presented, but a pooled overall estimate is suppressed due to heterogeneity (understanding data in meta-analysis).

*case fatality rate is the number of reported deaths per number of reported cases (Updated 23rd March)



Between countries, case Fatality rates vary significantly, and over time, which suggests considerable uncertainty over the exact case fatality rates. See: Prediction intervals for CFR over time pdf.

What is affecting the case fatality rate?

- The number of cases detected by testing will vary considerably by country;
- Selection bias can mean those with severe disease are being preferentially tested;
- There may be delays between symptoms onset and deaths which can lead to underestimation of the CFR;
- There may be factors that account for increased death rates such as coinfection, poorer healthcare, patient demographics (i.e., older patients might be more prevalent in countries such as Italy);
- There may be increased rates of smoking or comorbidities amongst the fatalities.
- Differences in how deaths are attributed to coronavirus; dying with the disease (association) is not the same as dying form the disease (causation).

China

In China, CFR was higher in the early stages of the outbreak (17% for cases from 1 to 10 January) and reduced to 0.7% for patients symptom onset after 1 February.

Update 21st March:

Summary of a Report of 72,314 Cases from the Chinese Center for Disease Control and Prevention. The data is also reported in the Epidemiological Characteristics of an Outbreak of 2019 Novel Coronavirus Diseases (COVID-19) in China. 2020 (China CDC weekly).

The epidemic curve of onset of symptoms peaked around January 23rd to 26th, then began to decline up to February 11th. Most cases were aged 30 to 79 years of age (87%), 1% aged ≤9 years, 1% aged 10 to 19 years, and 3% 80 years or older.

The CFR was 2.3% (1023 deaths/44,672 confirmed cases).

Reported CFRs by age were

Age (deaths/cases)	CFR (95% CI)
≤9 years (0/416)	0%
10 to 19 years (1/549)	0.18% (0.03 to 1.02%)
20 to 49 years (63/17790)	0.32% (0.25% to 0.41%)
50 to 59 years (130/10,008)	1.3% (1.1% to 1.5%)
60 to 69, years (309/9583)	3.6% (3.2% to 4.0%)
70 to 79 years (312/3918)	8.0% (7.2% to 8.9%)
≥80 years (208/1408)	14.8% (13.0% to 16.7%)

Patients with comorbid conditions had much higher CFR rates:

Condition*	CFR
Cardiovascular disease	10.5%
Diabetes	7.3%
Chronic respiratory disease	6.3%
Hypertension	6.0%
Cancer	5.6%
No comorbidities	0.9%

*Critical cases had a CFR of 49.0%, no deaths occurred among those with mild or even severe symptoms.

- Critical cases were classified as those that exhibited respiratory failure, septic shock, and/or multiple organ dysfunction/failure.
- Severe characterized by dyspnea, respiratory rate ≥30/minute, oxygen saturation ≤93%, PaO_2/FiO_2 ratio <300, and/or lung infiltrates >50% within 24–48 hours

1716 case were health workers (1.8%), 254 cases (14.8%) were classified as severe or critical and 5 health workers (0.3%) died.

Limitation: some variables of interest (i.e., comorbid condition, and case severity) are not required fields in the Chinese CDC Infectious Disease Information System, and some records have missing data.

Why is cardiovascular disease (CVD) so prevalent in those who died with COVID-19?

Most acute viral infections have three short-term effects on the CVD: system:

- Increase the risk of acute coronary syndromes due to the inflammatory response.
- Depression of the myocardium leading to worsening heart failure.
- The inflammatory process can unmask heart arrhythmias.

Seasonal influenza infections have been shown to contribute to an increase in CVD deaths significantly. Community-level rises in influenza-like illness (ILI) were associated with and predictive of CVD mortality: deaths from ischaemic heart disease rose from 2.3% to 6.2% when emergency department visits with ILI rose from the 25th to the 75th centile.

Nature Medicine: Estimating the clinical severity of COVID-19 from the transmission dynamics in Wuhan, China.

- In those with coronavirus symptoms in Wuhan, China, had a 14% (95% CI, 5.9% to 23.1% chance of dying.
- As of 29th February, the crude CFR case risk, outside Hubei was 0.85%.
- Risk of symptomatic infection increases with age, but this may be preferential ascertainment of older and more severe cases. 'One largely unknown factor at present is the number of asymptomatic, undiagnosed infections.'

Because Wuhan prioritized the admission of more severe cases, the sCFR will be substantially lower than the hFR*

*sCFR (s for symptomatic) defines a case as someone who is infected and shows certain symptoms; HFR (hospitalized) defines a case as someone who is infected and hospitalized.

Italy

In Italy, there are several reasons why CFR might be higher: the age structure of the Italian population (2nd oldest population in the world); highest rates of antibiotic resistance deaths in Europe which might contribute to increased pneumonia deaths (Italy tops the EU for antibiotic-resistance deaths with nearly 3 times all Member States) in the ECDC ranking also seems to be a factor associated with poor survival – in Italy, 24% smoke, 28% men. In the UK, for instance, 15% are current smokers.

Update 20 March: Coronavirus: Is Covid-19 the cause of all the fatalities in Italy?

Sarah Newy reports: Italy's death-rate might be higher because of how fatalities are recorded. In Italy, all those who die in hospitals with Coronavirus will be included in the death numbers. In the article, Professor Walter Ricciardi, Scientific Adviser to, Italy's Minister of Health, reports, "On re-evaluation by the National Institute of Health, only 12 per cent of death certificates have shown a direct causality from coronavirus, while 88 per cent of patients who have died have at least one pre-morbidity – many had two or three."

Recording the numbers of those who die **with** Coronavirus will inflate the CFR as opposed to those that died **from** Coronavirus, which will reduce the CFR.

17th March 2020: Report from the Italian National Institute of Health: analysed 355 fatalities and found only three patients (0.8%) had no prior medical conditions. See Table 1 in the paper; (99% who died had one pre-existing health condition):

- 49% had three or more health conditions
- 26% had two other 'pathologies',
- 25% had one.

The most common problems in the 355 who died were:

- 76% high blood pressure,
- 36% diabetes,
- 33% ischemic heart disease.

The average age of deceased and COVID-19 positive patients was 79.5 years (median 80.5, range 31-103, InterQuartile – IQR 74.3-85.9). The median age of the patients who died was > 15 years higher than that of patients who contracted the infection (median age: patients who died 80.5 years - patients with infection 63 years). Women who died after contracting COVID-19 infection were older than men (median age: women 83.7 – men 78.5).

UK assessment: Impact assessment of non-pharmaceutical interventions (NPIs) to reduce COVID-19 mortality and healthcare demand

Neil Ferguson's team at Imperial College, London, modelled the impact of COVID-19, interventions to reduce the spread and their effects on case fatality.

See the summary of their assumptions: Impact assessment of non-pharmaceutical interventions (NPIs) to reduce COVID-19 mortality and healthcare demand pdf

Their Infection Fatality Rate estimates were based on from Verity et al, and adjusted to account for a non-uniform attack rate giving an overall IFR of 0.9% (95% credible interval 0.4%-1.4%).

Published in: Medrxiv (preprint and not been peer reviewed) Verity estimated age-stratified CFR estimates from cumulative death data in China, and from individual data on 1,334 cases identified outside of mainland China. Verity et al estimated an overall IFR for China of 0.66% (0.39%,1.33%), that increased with age.

Comparison with Swine Flu

The overall case fatality rate as of 16 July 2009, (10 weeks after the first international alert) with pandemic H1N1 influenza varied from 0.1% to 5.1% depending on the country. The WHO reported in 2019 that swine flu ended up with a fatality rate of 0.02%. Evaluating CFR during a pandemic is a hazardous exercise, and high-end estimates and be treated with caution as the H1N1 pandemic highlights that original estimates were not by a factor greater than 10.

Effect of concurrent infections

Highest peak rate ratios for admissions are in those years where the confirmed simultaneous circulation of Influenza Like Illness (ILI) and acute bronchitis occur. Between 1995-97 to 2004-05 respiratory admissions of ≥65 years in England and Wales were analysed. The ILI peaked was highly variable the earliest during mid-November (week 46, 1993-94) and the latest, late February/early March (week 7, 1997-98).

Diamond Princess Cruise Ship

On the *Diamond Princess*, six deaths occurred out of 705 who tested positive constituting a CFR of 0.85%. All six deaths six occurred in patients > 70. No one under 70 died.

Estimating the infection and case fatality ratio for COVID-19 using age-adjusted data from the outbreak on the Diamond Princess cruise ship. Comparing deaths unbiased with expected deaths based on naive CFR estimates using China data, they estimated CFR 1.1% (95% CI: 0.3-2.4%) IFR 0.5% (95% CI: 0.2-1.2%).

Updated 23rd March: Estimating COVID-19 Case Fatality Rates (CFR) and Infection Rate Fatality (IFR)

The Infection Rate Fatality (IFR) differs from the CFR in that aims to estimate the fatality rate in all those with infection the detected disease (cases) and those with an undetected disease (asymptomatic and not tested group). If tested, this group would be counted as infected and at least temporarily be immune.

Our current best assumption, as of the 22nd March, is the IFR is approximate 0.20% (95% CI, 0.17 to 0.25).*

In the elderly, co-morbidities have a significant impact on the CFR: those with a 3 comorbidities are at much higher risk, particularly those with cardiovascular conditions. Modelling the data on the prevalence of comorbidities is essential to understand the CFR and IFR by age. In those without pre-existing health conditions, and over 70, the data is reassuring that the IFR will likely not be above 1%. The prevalence of comorbidities is highly age-dependent and is higher in socially deprived.

How do we arrive at this estimated IFR figure?

The current COVID outbreak seems to be following previous pandemics in that initial CFRs start high and then trend downward. In Wuhan, for instance, the CFR has gone down from 17% in the initial phase to near 1% in the late stage. Current testing strategies are not capturing everybody. At least 50% of those on the Diamond Princess was, asymptomatic, who usually wouldn't get a test.

In South Korea, considerable numbers who tested positive were also asymptomatic. Asymptomatic people and mild cases are likely driving the rapid worldwide spread.

Early IFR rates are subject to selection bias as more severe cases are tested - generally those in the hospital settings or those with more severe symptoms. Mortality in children seems to be near zero (unlike flu) which will drive down the IFR significantly. In Swine flu, the IFR was fivefold less than the lowest estimate in the 1st two weeks (0.1%)

Therefore, to estimate the IFR, we used the estimate from Germany's current data 22nd March (59 deaths 23129 cases) CFR 0.26% (95% CI, 0.33% to 0.49%) and halved this for the IFR of 0.20% (95% CI, 0.17% to 0.25%) based on the assumption that half the cases go undetected by testing and none of this group dies. Our assumptions, however, do not account for some exceptional cases, as in Italy, where the population is older, smoking rates are higher, comorbidities may be higher, and antibiotic resistance is the highest in Europe, which all can act to increase the CFR and the subsequent IFR.

Given the estimated mortality in over 80s is higher (CFR near 15%) there is considerable uncertainty over the IFR rates in this group. It is currently not clear what the excess mortality is in this group.

It is essential to understand whether the elderly are dying with or from the disease (see the Sarah Newy report). It is also not clear if the presence of other circulating influenza viruses act to increase the CFR (testing for co-pathogens is not occurring), and whether certain populations (e.g., those with heart conditions) are more at risk. Understanding this issue is now critical. If, for instance, 80% of those over 80 died with the disease (20% from it) then the CFR in >80s would be near 3% as opposed to 15%. This would lower the overall IFR substantially.

What matters is now is how many people get infected in a short space of time – to what extent this overwhelms healthcare services and whether they can manage – the impact of measures to reduce spread are crucial in the upward phase of a pandemic that can affect a significant number of people at any one time.

*Estimating CFR and IFR in the early stages of outbreaks is subject to considerable uncertainties; the estimates are likely to change as more data emerges. The current prediction interval based on the available has a wide-ranging estimate of the CFR from 0.60 to 7.1%; the corresponding IFR estimate based on this data would be 0.30 to 3.60.

See Lancet report: CFRs on mortality rate estimates can be misleading if the CFR is based on the number of deaths per number of confirmed cases at the same time. Using the denominator of the mortality rate as the total number of patients infected at the same time as those who died would lead to much higher CFRs. However, they report the full denominator remains unknown as asymptomatic with mild symptoms might not be tested and will not be identified, particularly in the early stages of an outbreak.

Acknowledgements:

Thanks to David Bernstein (George Mason University) for posing the question of how we arrived at the CFR estimates.

We welcome more critiques/questions on this article, and we keeping the CFR under daily review.

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What's on

Preventing Overdiagnosis 2020
14 - 16 September 2020
The 8th international conference in Oxford, UK.

Teaching EBM 2020
14 - 18 September 2020
Workshop for health professionals developing their teaching of EBM.

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