Estimating clinical severity of COVID-19 amongst symptomatic cases from the transmission dynamics in Wuhan

Professors Gabriel Leung and Joseph Wu

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*In collaboration with Professor Marc Lipsitch*

*Harvard T. H. Chan School of Public Health*
Crude or naïve CFR = cumulative deaths/cumulative cases = 3354/98243 = 3.4%
Approximator = cumulative deaths/cumulative deaths+recoveries = 3354/(3354+54021) = 5.8%
Lessons learnt a decade apart: direction of bias through epidemic stage

SARS-CoV

A(H7N9)

Date of analysis

- Observed case fatality ratio
- Simple estimate 1
- Simple estimate 2
- KM-like method
- Range from KM-like method
- Gamma mixture model

Ghani et al. *Am J Epidemiol* 2005
Yu et al. *Lancet* 2013
Definitions of clinical severity

**Infection fatality risk (IFR):** IFR defines a case as a person who would if tested be counted as infected and rendered (at least temporarily) immune, as usually demonstrated by seroconversion or other immune response. Such cases may or may not be symptomatic.

**Symptomatic case fatality risk (sCFR):** sCFR defines a case as someone who is infected and shows certain symptoms.

**Hospitalization fatality risk (HFR):** HFR defines a case as someone who is infected and hospitalized. It is typically assumed in such estimates that the hospitalization is for treatment rather than isolation purposes.
Challenge of estimating CFR in A(H1N1)pdm

pH1N1 2009: problem with **numerator and denominator**

Numerator of “confirmed” deaths likely to underestimate impact on the elderly
Denominator of confirmed cases led to overestimation of CFR by several orders of magnitude

Wong et al *Epidemiology* 2013
The COVID-19 clinical iceberg

Cases detected in Wuhan?
Source of COVID-19 data

Singapore confirms first case of Wuhan virus

Japan and Thailand Confirm New Cases of Chinese Coronavirus

The two new patients will add to fears that the virus will spread further outside China’s borders.

Coronavirus: German evacuation flight lands in Frankfurt

A German military plane carrying citizens escaping the coronavirus in China has touched down in Frankfurt. Countries around the world are taking action to protect citizens as cases increase.

3 CASES CONFIRMED IN EVACUEES FROM WUHAN
Source of COVID-19 data

- H2H cases in Wuhan before 3 Jan
- No. of cases outside mainland China (date of arrival before 19 Jan)
- Proportion of cases on charter flights before 5 Feb

Deaths in Wuhan

No. of deaths in Wuhan
Assumption:

1. Detection sensitivity $p_{det}$
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2. Infection-symptomatic probability $p_{sym}$
sCFR increase with age

- $P_{sym} = 0.50$, overall sCFR = 1.4% (0.9% - 2.1%)
- $P_{sym} = 0.75$, overall sCFR = 1.3% (0.8% - 2.3%)
- $P_{sym} = 0.95$, overall sCFR = 1.2% (0.7% - 1.9%)
# Severity estimates of SARS (2002-3), MERS (2014-), 1918 influenza pandemic (1918-20) and 2009 influenza pandemic (2009-10)

<table>
<thead>
<tr>
<th>Parameter</th>
<th>SARS*</th>
<th>MERS†</th>
<th>1918 influenza pandemic</th>
<th>2009 influenza pandemic</th>
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</thead>
<tbody>
<tr>
<td>Infection fatality risk (IFR) (risk of death among all infections)</td>
<td>Worldwide (WHO)** 9.6% (774/8096)</td>
<td>Worldwide 2.5%</td>
<td>Hong Kong</td>
<td>Hong Kong</td>
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<td>Mainland China** 6.4% (343/5327)</td>
<td>Copenhagen 1.7%</td>
<td>&lt;60 yrs: &lt;0.1%</td>
<td>≥60 yrs: 1.1% (0.2-4.7)</td>
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<tr>
<td>Symptomatic case fatality risk (sCFR) (risk of death among symptomatic infections)</td>
<td>Hong Kong*** Overall: 17.2% (302/1755) &lt;60 yrs: 13.2% (9.8-16.8) ≥60 yrs: 43.3% (35.2-52.4)</td>
<td>--</td>
<td>United Kingdom</td>
<td>North America</td>
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<td></td>
<td>Taiwan*** Overall: 27.6% (180/664) &lt;60 yrs: 15.3% (72/470) ≥60 yrs: 48.6% (88/181)</td>
<td>Worldwide (WHO)*** 34.4% (858/2494)</td>
<td>Overall: 0.026% (0.011-0.066)</td>
<td>Overall: 2.6% (1.6, 3.9)</td>
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<td>Saudi Arabia*** 40.7% (726/1783)</td>
<td>5-14 yrs: 0.011% (0.003-0.036)</td>
<td>≤19 yrs: 0.8% (0.5, 1.1)</td>
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<td>South Korea*** 20.4% (38/186)</td>
<td>≥65 yrs: 5.4% (3.5, 7.5)</td>
<td>20-64 yrs: 10.7% (5.3, 17.6)</td>
</tr>
</tbody>
</table>

* IFR=CFR=HFR given virtually every infected person required hospitalization and seroprevalence amongst close contacts and in general community approximated zero
** Among probable cases
*** Among laboratory-confirmed cases
† There are more infections “undetected” in MERS compared with SARS. The seroprevalence amongst individuals exposed to camels was estimated as 6.2% in Arabian Peninsula.
Susceptibility increase with age
Caveats

• Precise fatality risk estimates may not generalize to those outside of Wuhan especially during subsequent phases of the epidemic
  • experience gained from managing initial patients and increasing availability of newer, and potentially better, treatment modalities
  • public health control measures since the Wuhan alert have also kept case numbers down elsewhere such that their health systems are not nearly as overwhelmed beyond surge capacity, thus again perhaps leading to better outcomes
• One largely unknown factor at present is the number of asymptomatic, undiagnosed infections. These do not enter our estimates of the symptomatic CFR, but if such asymptomatic or clinically very mild cases existed and were not detected, the infection fatality risk would be lower than the sCFR. Further clarifying this requires new data sources not yet available, specifically including age-stratified serologic studies.

• Our prevalence estimates relying on travelers are based on those well enough to travel, so may slightly underestimate prevalence in Wuhan due to not including those who are already in serious condition and for example hospitalized. We have accounted for the possibility that travelers may underestimate the prevalence of infection at the source by using as our best estimate from a separate analysis of the probability of detection for international travelers.

• On the other hand, the numerator of the number of deaths could also have been undercounted although much less likely so by comparison to enumerating the denominator, for the same surge capacity reason or due to imperfect test sensitivity especially during the first month of the outbreak. If deaths in Wuhan were under-ascertained, this would bias our severity estimates downward.