## Coronavirus Pandemic

## Estimating case fatality ratio during COVID-19 epidemics: Pitfalls and alternatives

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We read with great interest the paper by Porcheddu et al. [1], who showed the similarity (2.3%) in Case Fatality Ratio (CFR) of COVID-19 in Italy and China. However, we believe that both the calculation and comparison of the two mentioned CFRs are deeply biased. Indeed, the formula used by authors for calculating the CFR, i.e. the total number of known deaths divided by the total number of confirmed cases, expressed as a percent, is reliable once an epidemic has ended, but it does not represent the true case fatality rate while the epidemic is still ongoing [2]. Moreover, authors compared data drawn by two time intervals with different lengths, i.e. 21-28 February in Italy (8 days), and 19 January-11 February in China (24 days). We agree with Battegay et al. [3], that a precise estimate of the case fatality rate is impossible at present, and, for this reason, we should be cautious when research findings and strategies are taken on the basis of these estimates. To date, there is lack of coordination and resources for an integrated and homogeneous epidemiological surveillance worldwide, which does not allow comparisons to be made between countries. The degree of underreporting COVID-19 cases varies over time as well as between countries. Thus, the CFR may be overestimated, when mild or asymptomatic cases are unrecognized, or may be underestimated, when unclear deaths are not attributed to the SARS-CoV-2 [3]. In confirmation of this, while the 2003 SARS epidemic was still going, the World Health Organization (WHO) reported a CFR of 4%, that became equal to 9.6% at the end of the epidemics. However, as suggested by Worldometer [2], a reference website that provides real-time world statistics, at the present time, the well-known formula proposed by Ghani et al. [4] for calculating the CFR of the 2003 SARS epidemics could be applicable to the current SARS-CoV 2 epidemics as well, as it is needed to divide cases and deaths belonging to the same group of patients. In other words, it would be more accurate to calculate the ratio between the deaths at time T1 (e.g. day 15) and confirmed cases at time T0 (e.g. day 9), where T0 precedes T1 (e.g. 6 days) and depends on the incubation period ("the time between exposure to the virus and the onset of symptoms") of the infection, i.e. that for SARS-CoV2 is ranged from 2 to 7 days, with a mean incubation period of 6.4 days. [5]. Therefore, the formu la modified would be as follows:

CFR = deaths at  $T_1$ /(cases at  $T_0 - T$ )

Where T is the average time period from case confirmation to death.

An alternative and simple method proposed by Ghani *et al.* [4] would follow the formula: CFR = deaths / (deaths + recovered).

In any case, whatever the calculation and the formula used, if we want to compare CFR between countries, the most important requirement is the effectiveness and homogeneity of the surveillance systems.

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