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Real-time naive case fatality rates can reflect timeliness of case confirmation during pandemics

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**Abstract**

An objective law was observed that naive case fatality rates (CFRs) of a disease will decrease early and then gradually increase infinitely near the true CFR as time went on during an outbreak. The normal growth of naive CFR was an inherent character rather than indicating the disease was becoming more severe. According to the law, by monitoring real-time naive CFRs, it can help outbreak-controllers know if there were many cases left unconfirmed or undiscovered in the outbreak. We reflected on the use of the naive CFR in the context of COVID-19 outbreaks. The results showed that Hubei Province of China, France and South Korea had cases that were not confirmed in a timely manner during the initial stages of the outbreak. Delayed case confirmations existed for long periods of time in France, Italy, the United Kingdom, the Netherlands and Spain. Monitoring of real-time naive CFRs could be helpful for decision-makers to identify under-reporting of cases during pandemics.

How the naive CFRs theoretically change with time

Naive CFR is an underestimation of true CFR because it does not account for the delay between case confirmation and the outcome of death \cite{6,7}. For exploration of the theoretical trend of naive CFR at any given point in time, we denote \( n \), \( D(n) \), \( C(n) \), \( CFR(n) \), \( T \) and \( r \) as the cumulative number of deaths, cases, naive CFRs at time \( n \), the death delay and the true CFR respectively. The theoretical trend could be studied by CFR(\( n \rightarrow n+1) - CFR(n) \):

\[
CFR(n+1) = CFR(n) + (1 + a(n)/C(n)) \times D(n) / C(n) \times r.
\]

Where \( a(n) \) is the growth rate of cases at time \( n \). Put (\ref{eq:2}), (\ref{eq:3}) and (\ref{eq:4}) into (\ref{eq:1}), then:

\[
CFR(n+1) = CFR(n) + (1 + a(n)/C(n)) \times (D(n+1) - D(n)) / C(n+1) + A(n) \times r.
\]

To compare CFR(\( n \rightarrow n+1 \)) with CFR(\( n \)), it was only needed to compare \((1 + a(n)/C(n)) / (1 + a(n)/C(n)) \times r \) with 1. The cases would not grow endlessly. According to the SIR model (Susceptible, Infectious, or Recovered) \cite{8}, as time passes, the growth in the number of cases would slow down.
down which meant $a(n)$ would become smaller and smaller, resulting in $a(n) < a(n-T)$. Then $(1+a(n-T))/(1+a(n))$ must be greater than 1 and the $CFR(n+1)$ will be greater than $CFR(n)$. This means the real-time naive CFR would continue increasing. A hypothetical example with exponential case growth was shown in Fig. 1. It was found that the real-time naive CFRs would gradually increase infinitely near the true CFR as time went on. The trend has been mentioned in previous epidemics [9]. At the exponential growth stage, the trend of increasing was negligible due to the slowly decreasing $a$. The normal growth of naive CFR with time was an inherent character rather than indicating the disease was becoming more severe.

It’s worth noting that deaths must occur later than cases when outbreaks begin, which would result in a decreasing trend. Thus, theoretically, naive CFRs should decrease early in an outbreak and then increase with time.

**What can outbreak-controllers learn from real-time naive CFRs?**

Based on the theoretical law above, as the number of deaths was a generally unbiased statistic in a pandemic, real-time change of naive CFRs could provide valuable information of the case number. We reflected on the use of the naive CFR statistics in the context of COVID-19 outbreaks. Firstly, COVID-19 in China was analyzed, which was used to confirm the validity of our approach and conclusions. Secondly, the timeliness of case confirmation of COVID-19 in some other countries (where the numbers of deaths were greater than 100 as of Mar 21) was analyzed.

As Fig. 2A shown, the real-time CFRs curve of Chinese regions excluding Hubei Province (non-Hubei regions) decreased early and then continuously increased to a plateau, which was similar in shape to the theoretically expected results. Case confirmation of COVID-19 in non-Hubei regions of China could be regarded as timely. This is due to the Chinese government rapidly taking emergency measures (strict quarantine and screening policies) nationwide immediately following the beginning of the outbreak. The real-time CFR curve of non-Hubei regions presented an expected pattern in line with the theoretical trend, which could be a proof of reliability of this approach.

For Hubei Province (Fig. 2B), rather than a decreasing trend during the early stage, the naive CFRs curve instead increased and almost stabilized. This meant the denominators were smaller than expected for a decreasing trend. Thus, many cases were left unconfirmed at that time. On February 13, the Chinese government
reported many suspected cases in a single day [10]. This could prove definitively that there had been a delay in case confirmation in Hubei at the time, which would be consistent with our analysis. This result proved the validity of the analysis by naive CFR trend.

For other countries as shown in Fig. 2, the curves of France and South Korea kept stable, and then decreased before continuously increasing. Curves for the United Kingdom, the Netherlands and Spain immediately increased since the outbreaks began. For France and South Korea, the presence of stable trends (and increasing trends) at an early stage, which were expected to decrease, meant the denominators of naive CFRs were smaller. It indicated the cases had not been confirmed in a timely manner at the time. Countries with CFRs that skipped the decreasing stage and immediately increased must have experienced delayed reporting and responses to the outbreak, since deaths must occur later than cases when outbreaks begin. After the decreasing stage, curves of the United Kingdom, the Netherlands, France, Italy and Spain had increasing trends, but they were rugged. Decreases during the expected increasing stage indicated that delayed case confirmations still existed (previous unreported cases had accumulated, resulting in smaller CFRs). The United States and Iran had no abnormal trends of CFRs, and it could not be determined whether there had been cases left unconfirmed by real-time naive CFRs.

The limitation in this approach was that statistics of deaths were assumed to be unbiased. When hospitals were overwhelmed, some deaths could happen at home, as reported in Hubei Province of China [11]. However, the existence of unnoticed deaths in itself is evidence of under-reporting. In addition, more real-world data was needed for confirmation of the theoretical law.

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Competing interest

None declared.

Ethical approval

Not required.

CRediT authorship contribution statement

Rui Qi: Methodology, Writing - original draft. Cong Chen: Methodology, Data curation, Formal analysis. Xiao-Bin Hu:
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