

Correspondence



Case fatality rate for Ebola virus disease in west Africa

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The case fatality rate (CFR) for the 2014 Ebola outbreak in west Africa has been widely reported to be much lower than for most previous outbreaks.¹ However, this low rate is not necessarily a feature of the infection itself. Rather, it is likely to be the result of a failure to account for delays between disease onset and final outcome. The low reported CFR values were generated from a so-called naive CFR calculation,² in which the total number of deaths reported so far is divided by the total number of cases. Based on WHO reports up to Sept 7, 2014, which include 2226 deaths and 4390 cases,¹ the naive CFR estimate is 51% (95% CI 49–53%).

This naive approach does not account for the delay between onset of Ebola symptoms and disease outcome (ie, recovery or death). During the 1976 outbreak in Yambuku, Democratic Republic of the Congo,³ this delay was 7.5 days on average (appendix). In the middle of the outbreak, cases for which the outcome was as-yet unknown existed (appendix). Because the naive CFR calculation includes these cases—but not their outcomes—it generates a substantial

underestimate of the actual CFR. Halfway through the 1976 outbreak, the naive CFR estimate would have been around 50%; as the outbreak reached its conclusion, this number would have climbed towards the much higher true value (figure). By contrast, if we only consider cases with known outcomes, the realtime estimate of CFR remains consistently high throughout.

If cumulative incidences of cases and deaths are available, and delay from onset to outcome is known, the number of cases with outcomes can be estimated and hence a more accurate estimate of CFR obtained.^{4,5} We estimate that the 2014 infection has an overall CFR of around 70% at present using the 1976 distribution of Ebola onset to outcome and WHO reports on total cases and deaths across all countries in 2014.¹ If the delay is longer than in 1976, this CFR could be even higher.

The widely cited 2014 CFR of around 50% is therefore likely to be a substantial underestimate of the true value, and so the number could apparently rise over the course of the outbreak. With data on individual onsets and outcomes, more precise estimates of CFR could be obtained, and how it varies with setting and availability of treatment could be assessed.

We declare no competing interests.

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Neuraminidase inhibitors for influenza complications

In their Comment (Aug 2, p 386),¹ Jonathan Nguyen-Van-Tam and colleagues suggest that findings from our Cochrane review² and a study of observational data³ are consistent. In our review, which was based on full clinical study reports of all manufacturer-sponsored randomised trials, we did not find evidence that neuraminidase inhibitors improve important outcomes of influenza, whereas the Roche-funded individual analysis of a subset of retrospective case reports suggested that neuraminidase inhibitors do have some beneficial effect. These observational studies were of patients admitted to hospital for influenza, some of whom apparently benefited from neuraminidase inhibitors.³ Most treated patients received oseltamivir, with a minority receiving zanamivir. Similar evidence was cited in a statement from Roche.⁴ Our Cochrane review did not include similar patients, but was based on typical patients with influenza-like illness.

However, the hypothesis that oseltamivir protects against complications of influenza proposed by

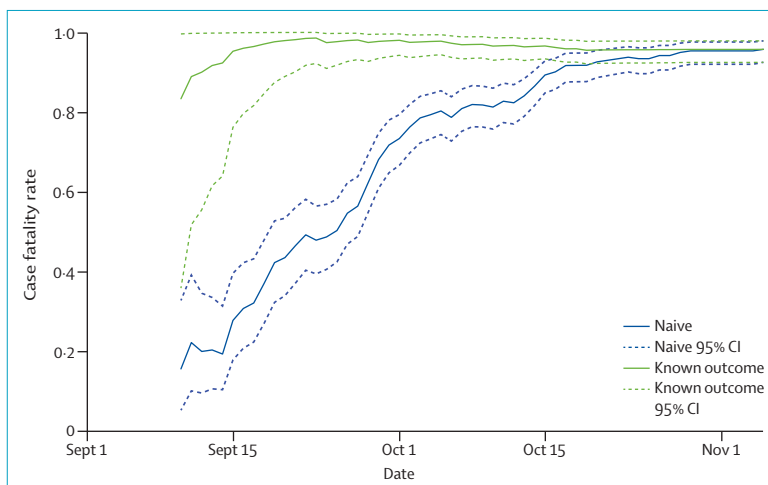


Figure: Realtime estimation of case fatality rate using data from the 1976 Yambuku Ebola outbreak
Data are from reference 3.

See Online for appendix