



**Figure: Probability of a major outbreak of Ebola virus disease from a single imported infectious host** Assuming the infectious period follows an exponential or gamma distribution. Parameter values used are consistent with data from the 2014–16 Ebola epidemic in west Africa (appendix p 3). The x-axis range is set to 0–9 to reflect the wide variation in estimated values of reproduction numbers for Ebola outbreaks in different settings.

formula was used to assess the risk of sustained outbreaks in different countries during the 2014–16 west Africa epidemic,<sup>3</sup> and was considered in the context of vaccination.<sup>4</sup> In that epidemic,  $R$  ranged from 1.51 to 2.53 in Guinea, Liberia, and Sierra Leone, leading to major outbreak probabilities of 0.34–0.60 in those locations, with a higher value of  $R$  (9.01) estimated for Nigeria.<sup>3</sup>

However, implicit in these estimates is the common assumption that the infectious period follows an exponential distribution (appendix p 3).<sup>5</sup> For many pathogens, infectious periods are less dispersed than exponential distributions suggest, and gamma distributions characterise epidemiological periods more accurately (appendix p 3).<sup>6</sup> The standard estimate for the major outbreak probability must be altered to account for this difference (more detailed calculations and discussion are in the appendix [pp 1–3]). With this amendment, the risk is larger than the formula  $1 - (1/R)$  suggests. Consequently, in the west African epidemic, the major outbreak probability in Guinea, Liberia, and Sierra Leone would have been 0.52–0.83. In the figure, we show this discrepancy between the standard and more realistic estimates using parameters consistent with

Ebola virus transmission.<sup>2</sup> Our main qualitative result is robust to interventions used during Ebola virus disease epidemics (including vaccination, which has an important role currently); when  $R$  is greater than 1, the assumption of an exponentially distributed infectious period leads to the underestimation of risk.

Control of the ongoing epidemic is being hindered by factors including recurrent violent attacks on health workers and distrust of the government and outside organisations. Our results underline the importance of public health measures, including surveillance and outbreak preparedness in regions without observed cases and fast responses whenever newly imported cases are identified. These measures are vital to minimise the risk of sustained transmission after import of people with Ebola virus disease, and this risk is higher than previously estimated.

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Robin N Thompson, Katri Jalava,  
\*Uri Obolski  
uriobols@tauex.tau.ac.il

Christ Church, Department of Zoology, and Mathematical Institute, University of Oxford, Oxford, UK (RNT); Department of Food Hygiene and Environmental Health, and Department of Mathematics and Statistics, University of Helsinki,

Helsinki, Finland (KJ); and School of Public Health and Porter School of the Environment and Earth Sciences, Tel Aviv University, 69978 Tel Aviv, Israel (UO)

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## Treating Ebola in eastern DRC

Ebola virus has infected more than 3000 people in the Democratic Republic of the Congo (DRC),<sup>1</sup> more than 200 000 people have received an investigational vaccine, and several new treatments are being tested. Nonetheless, the case fatality rate (>65%) remains high. Pierre Rollin notes that Ebola could become endemic in eastern DRC and only “immediate changes...[in]... leadership and coordination...will be able to reverse this trend”, adding that helping health-care providers to “regain the population’s confidence is crucial”.<sup>2</sup>

Confidence could be regained by improving survival of patients with Ebola virus disease. News reports have announced that monoclonal antibody treatment improves survival in patients with low viral loads,<sup>3</sup> but these agents are unlikely to alter the trajectory of the outbreak. Another way to regain people’s confidence might be to treat patients with drugs that target the host response, not the virus. Ebola is associated with endothelial dysfunction and breakdown of vascular barrier integrity.<sup>4</sup> In Sierra Leone, treatment with a statin-angiotensin receptor

See Online for appendix

blocker combination apparently led to “remarkable improvement” in survival of patients with Ebola virus disease.<sup>4</sup> These and other inexpensive generic drugs are widely available in developing countries. We need more convincing evidence that combination treatment is safe and improves survival of patients with Ebola virus disease. Unfortunately, scientists and health officials have shown no interest in testing this idea.<sup>4,5</sup> Until they are willing to do so, the Ebola

case fatality rate and lack of population confidence are unlikely to change.

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**David S Fedson**  
**davidfedson@gmail.com**

Sergy Haut, France

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