‘Reply to Uzoigwe: Modeling and the historical record’

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We thank the reader for their provocative response to our work **[1,2].** However the core premise that our findings are “in conflict with some compelling historical evidence” misinterprets our results and places too much stock in historical claims that experts no longer consider credible.

Regarding measles and smallpox, sixteenth century trans-Atlantic transfers are well-documented **[3]** and are entirely consistent with our results. As we noted, sail voyages from Europe to the Americas during this period lasted roughly 35-70 days. Our analyses indicated that smallpox and measles introductions are very plausible on this timeframe; for example, in Table 2 we estimate roughly a 25% risk of smallpox or measles transfer had Christopher Columbus’s ship, the *Santa María*, departed with one infectious person on board. Supplementary analyses indicated that these results were robust across a broad range of conditions.

Regarding influenza, modern scholars widely view the hypothesis of a 1550s influenza outbreak in the Americas as uncertain **[4, p.270;]** and unsubstantiated **[5, p.18; 6, p. 190]**. More generally, there is reason to be skeptical of any influenza diagnosis based solely on written records. In contrast to smallpox and measles, influenza symptoms are highly non-specific and can plausibly result from infection with a broad range of pathogens, including metapneumovirus, adenoviruses, and human coronaviruses **[7].** For this reason, the United States Center for Disease Control requires laboratory confirmation for definitive influenza diagnosis, and uses the more general term “influenza-like illness” to refer to cases based only on the classic symptoms of fever and sore throat **[8]**. Notably, many pathogens causing “influenza-like” symptoms have significantly longer life cycles **[9],** and so, written accounts of influenza-like illness during the fifteenth and sixteenth centuries do not, in themselves, contradict our assessment that early trans-Atlantic transfers of influenza were unlikely.

More generally, our framework was not presented as a definitive statement on global infectious disease history.. As we emphasized, pathogen introduction rates were highly sensitive to a range of factors which are not yet well-characterized in historical systems. These include ship-board transmission rate, population susceptibility, pathogen natural history, and the infection prevalence in ports of origin. Necessarily, we selected a small set of values for illustrative simulations. However, we do not rule out the possibility that different scenarios could have – and possibly did – occur, perhaps resulting from factors such as sexual differences in immunity or epidemiologically-meaningful pathogen evolution. For this reason, we explored a broader range of scenarios in supplementary analyses. In this initial analysis, we explicitly excluded zoonotic involvement for the sake of simplicity.

Theoretical disease modeling necessarily requires broad approximations of complex social and biological processes. Real-world comparisons offer a critical sense of whether our models can usefully approximate the biology of any given system. We consider model validation and parameterization to be a priority in future research, and in future work plan to assess this model’s predictions at several scales. These include validation at the level of a single vessel (using individual ship medical records) as well as at a broader system scale (using port and quarantine station data to examine pathogen arrival rates). Currently, the historical record of past infectious disease outbreaks offers the best available comparison. On this score, we are satisfied that our predictions are consistent with the present-day historical consensus.

Citations

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