Estimating the time to extinction of infectious diseases in mean-field approaches

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For many infectious diseases the eventual aim of control measures is elimination of transmission. Theoretical models can help to study and predict the time to eradication in different circumstances. Deterministic models present an average ("mean-field") approximation of infection dynamics and are very practical being computationally efficient and therefore allow relatively straightforward matching to available data. However, the elimination of an infection is ambiguous in deterministic models since the number of infections is a continuous number that cannot reach zero (although it can get very close including < 1 infection). In practice, a proxy threshold is needed to determine when extinction may occur in deterministic models, but it is not clear how such a threshold should be defined. Aside from deterministic model, we can also use stochastic models. Stochastic models incorporate chance events at very low infection numbers and only take integer numbers of infections. A stochastic model can reach zero infections, and at this point no further infection occur without importation (e.g. from another region without elimination of transmission). Unfortunately stochastic models are typically more computationally demanding (the can take a long time to simulate, and are complex to match to data), however, they are more helpful for studying the extinction of diseases. See the summary Table 1.

Deterministic	Stochastic
Quick to simulate and match to data	Slow to simulate and hard to match to data
Average dynamics (same output each simulation using the same parameters)	Chance events (different outputs from each simulation using the same parameters)
Infections are a positive number (average expected value). This is often not an integer	Infections are positive integers
The number of infections can become infinitely small but not reach zero	The number of infections can become zero
We need to select a "proxy threshold" to estimate when elimination of transmission has been achieved (e.g. < 1 new infection per year in a health zone)	Elimination of transmission is achieved when there are zero new infections

Table 1: Summary of deterministic and stochastic models

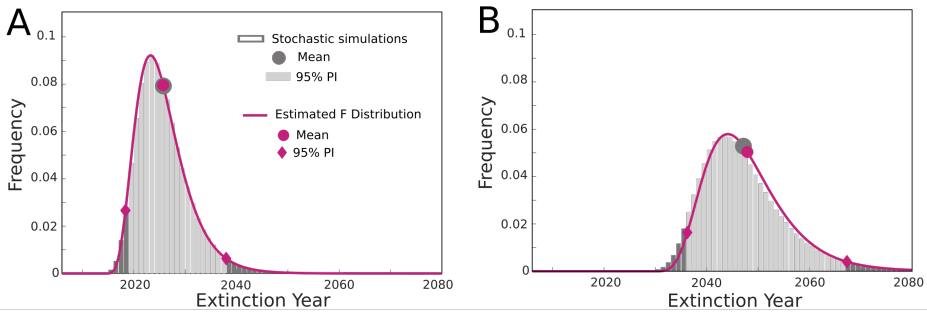

Figure 1: Probability distribution of extinction year for the full gHAT model for two health zones, (A) Mosango and (B) Kwamouth with 30% AS. Gray bars represent the solutions of one million stochastic simulations (light gray specifies 95% prediction interval). The purple line shows the estimate based on the simplified birth-death process approach. Corresponding mean values and 95% prediction intervals are plotted for each data set.

To study local elimination of transmission (the "extinction problem"), we develop a framework based on the simple "birth-death" process for infections, where "birth" corresponds to a new infection occurring and "death" refers to their recovery. This model helps us to estimate the mean and the distribution of extinction times for a birth-death process. We show these predictions agree very well with the results of simple stochastic infection models. This has considerable implications for the robustness of predictions made in deterministic frameworks. Moreover, this analysis allows us to introduce a threshold value for the deterministic model that equates to the mean extinction time of the associated stochastic model.

We further investigate how well our theory holds against more realistic, and hence more complex, simulation models by using our previously developed model for gHAT dynamics that takes into account vectors and two human risk groups. This model was previously fitted to the human case incidence data recorded in different health zones across DRC to estimate the free parameters of the deterministic model. The deterministic equations can be numerically solved to find the disease dynamics including the number of humans infected and new transmission each year. Such analysis allows us to determine appropriate values of the "birth-death" process, and therefore generate the distribution of extinction times with our new method. This analysis confirms the predicted intervals are in very good agreement with the solutions of full stochastic simulations of the gHAT model (Figure 1).

This work can be used in the future to enable more robust predictions for time to local elimination of transmission when using deterministic models.

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