Summary

Modelling *gambiense* human African trypanosomiasis infection in villages using Kolmogorov forward equations

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Abstract

Stochastic methods for modelling disease dynamics enables the direct computation of the probability of elimination of transmission (EOT). For the low-prevalence disease of human African trypanosomiasis (gHAT), we develop a mechanistic model for gHAT infection that determines the full probability distribution of the gHAT infection using Kolmogorov forward equations. The methodology allows the analytical investigation of the probabilities of gHAT elimination in the spatially-connected villages of the Kwamouth and Mosango health zones of the Democratic Republic of Congo (DRC). We predict that, if current active and passive screening continue at current levels, local elimination of infection for each health zone would occur after 2040 in Kwamouth and in 2029 for Mosango respectively. Our method generates results similar to previous health-zone-level models, yet captures small-scale interactions, with some local importations of infection between villages. The forward Kolmogorov equation model retains both the stochastic properties of event-driven models, but also provides the novel flexibility of modelling the infection of villages, the scale at which control interventions are applied. This development in gHAT modelling will provide a framework in which the impact of village-level decisions – in particular possible future strategies of test-and-treat or treatment of individuals living in villages where cases have been found using acoziborole – could be explored.

Motivation

Kolmogorov forward equations have been utilised in several epidemiological contexts and discussed as a powerful tool, but are not widely used due to constraints on computer memory [1]. This approach captures the stochastic events of infection, recovery and elimination of infection in a way where we can ask questions such as "what is the probability there are currently ≥ 5 infections, or zero infections?". Instead of simulating a stochastic model thousands of times and approximating such probability distributions, the Kolmogorov approach allows us to directly and exactly solve the equations and compute the full probability distribution. Every possible infection state must be explicitly tracked and, if a population is large (and particularly as an individual can be in any of a large number of infection states), the number of these states quickly becomes prohibitive to the method, as the number of required computations becomes infeasible. However for a disease with a relatively small number of cases, the approach becomes more practical. One such disease is *gambiense* human African trypanosomiasis (gHAT). Here, we have developed a model of *gambiense* human African trypanosomiasis (gHAT) infection – a very low prevalence infection – using the Kolmogorov forward equations through which village transmission with some movement between villages are included.

Results

Applying the full Kolmogorov forward equation model to the health zone of Kwamouth, we obtain a full probability distribution in time for each village (Figure 1). Our model results indicate that the expected number of infections in all villages decreases in time, such that by 2030 most of the probability is centred around no infection. We predict that for the smallest villages, there is a large probability of local gHAT elimination by 2030 (> 0.99 for the village of size $N_H = 100$) as there are initially few or no cases, which are

then identified by active screening, or passive screening and treatment or death. However, for the largest villages, such as the one with a population of $N_H = 20,697$, there is a high probability of continued infection with a probability of just 0.26 that elimination of infection will be met in that village by 2030.

The decline in the expected infection in all of individual villages is also evident in total infection of the health zone (Figure 2). This is calculated as the sum of the expected infection in each village. By 2030, the expected number of infected people have greatly decreased, yet persist in low number. This is mirrored in the probability of elimination of infection, calculated as the product of achieving elimination of infection in all villages of the health zone, which is predicted to be $< 0.01\%$ by 2030 if this active screening coverage remains constant, with the expected year of elimination after 2040. Using parameter values in the model matched to WHO HAT Atlas data for the low-incidence health zone of Mosango, we observe an earlier expected year of elimination of infection in 2029.

Discussion

The Kolmogorov forward equation model facilitates a powerful and efficient way to analyse the dynamics of a low-prevalence infection such as gHAT. This method with a simpler model structure than commonly used models is fast to compute (with sufficiently small populations) and yet maintains a good correspondence with more biologically complex approaches. The nature of the implementation means that various interesting properties can easily be explored, with exact methods for calculating extinction times and expected dynamics [1]. This approach has also allowed the model to be easily extended to consider the interaction of multiple villages and even to consider the dynamics of persistence at the health zone level by linking the total number of infected individuals to the rate of infectious imports into the villages.

Using this model, we conclude that based upon the strategy of active screening at the mean level, the expected year of elimination of infection is after 2040 for Kwamouth and in 2029 for Mosango. This is in line with deterministic predictions using this parameterisation; Huang *et al.* [2] predicted that the year of elimination of infection would be after 2040 for Kwamouth and in 2031 for Mosango, using the mean coverage of active screening and continuing passive screening.

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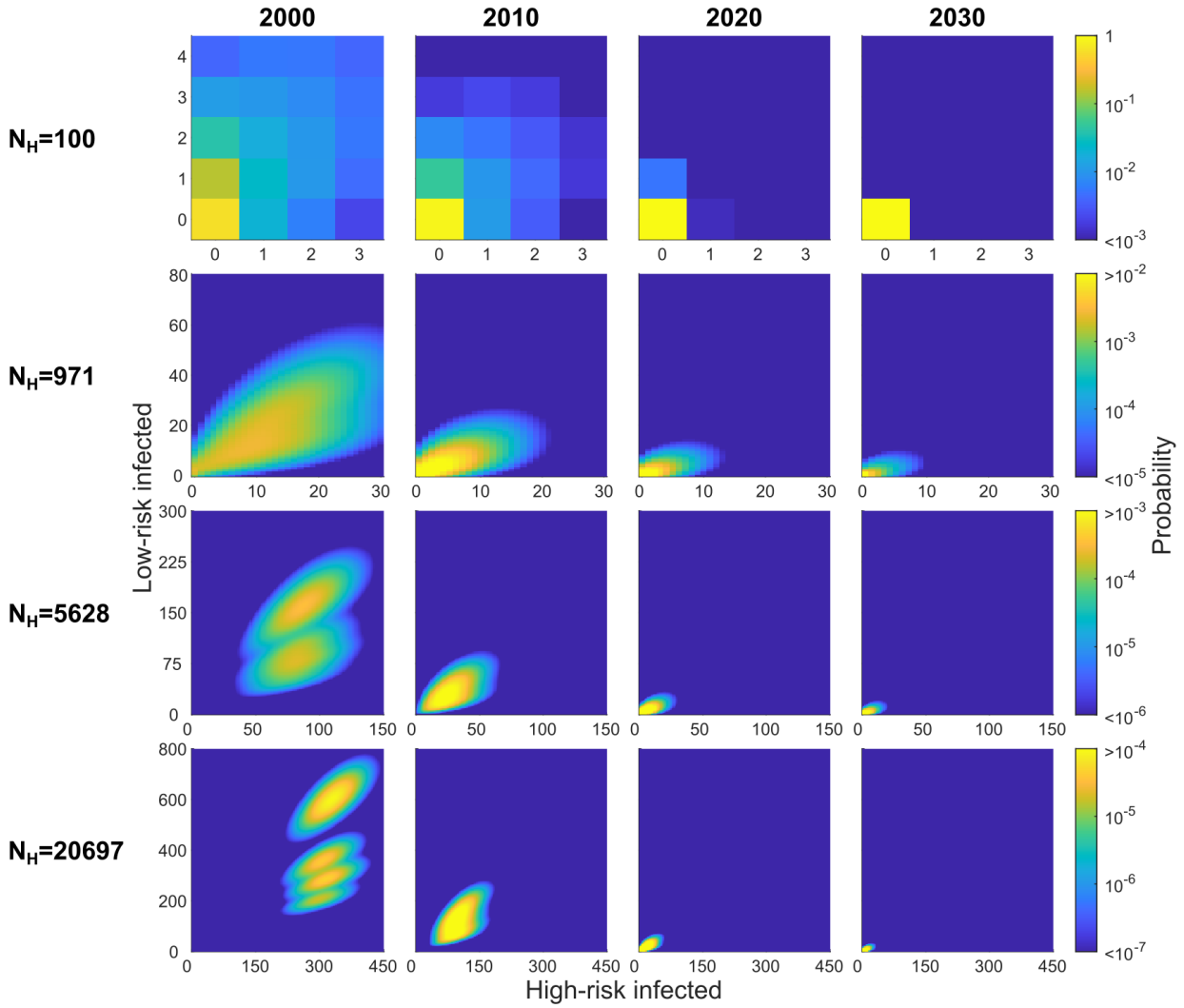

Figure 1: The risk distribution of infection in selected villages of Kwamouth at different time points (the years 2000, 2010, 2020 and 2030); the first possible active screening of each village was in 1998. There are 418 villages with populations ranging between 3 and 20,697 of which we present the probability distribution of infected people in four villages (N_H = 100, 971, 5,628 and 20,697). On each subplot the x-axis represents the number of high-risk people infected, and the y-axis, the number of low-risk people infected. The risk distribution of infection for the alternative health zone of Mosango are presented in the full paper supplementary material.

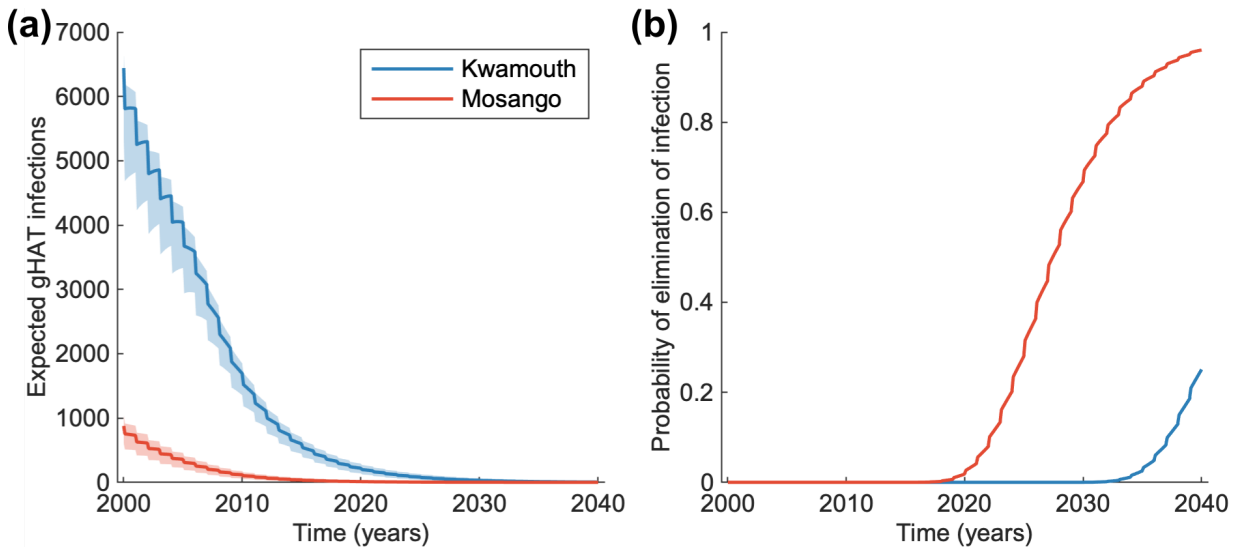

Figure 2: The total infection in the health zones of Kwamouth and Mosango. (A) The expected number of infections across all villages in time. The shaded region shows the 95% prediction intervals. (B) The probability of zero infections in time and hence elimination of infection for all villages in each health zone together.