SUMMARY

Comparison of stochastic and deterministic models for *gambiense* sleeping sickness at different spatial scales: A health area analysis in the DRC

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Abstract

The intensification of intervention activities against the fatal vector-borne disease *gambiense* human African trypanosomiasis (gHAT, sleeping sickness) in the last two decades has led to a large decline in the number of annually reported cases. However, while we move closer to achieving the ambitious target of elimination of transmission (EoT) to humans, pockets of infection remain, and it becomes increasingly important to quantitatively assess if different regions are on track for elimination, and where intervention efforts should be focused.

We present a previously developed stochastic mathematical model for gHAT in the Democratic Republic of Congo (DRC), and show that this same formulation is able to capture the dynamics of gHAT observed at the health area level (approximately 10,000 people). This analysis was the first time any stochastic gHAT model has been fitted directly to case data, and allows us to better quantify the uncertainty in our results. The analysis focuses on utilising a particle filter Markov chain Monte Carlo (MCMC) methodology to fit the model to the data from 16 health areas of Mosango health zone in Kwilu province as a case study.

The spatial heterogeneity in cases is reflected in modelling results, where we predict that under the current intervention strategies, the health area of Kinzamba II, which has approximately one third of the health zone's cases, will have the latest expected year for EoT. We also find that fitting the analogous deterministic version of the gHAT model using MCMC has substantially faster computation times than fitting the stochastic model using pMCMC, but produces virtually indistinguishable posterior parameterisation. This suggests that further health area fitting, to cover a larger region of the DRC, should be done with deterministic fits for efficiency, but with stochastic projections used to capture both the parameter and stochastic variation in case reporting and elimination year estimations.

Methods

Previous models have considered gHAT transmission at health zone level in the Democratic Republic of Congo (DRC), populations of approximately 150,000 people, but smaller scale models are useful to better reflect the distribution of transmission dynamics across larger regions, as well as to simulate more spatially targeted interventions. In this manuscript, we present models for health areas, populations of approximately 10,000

people. These smaller scale models require a stochastic modelling approach, which captures chance events particularly prominent in small populations or with extremely low infection levels, and a large increase in the number of locations that need model fitting.

We show how a stochastic model for gHAT can be directly calibrated to data from the Mosango health area of the DRC (see Figure A) with a particle Markov chain Monte Carlo (pMCMC) method. This stochastic model fitting approach allows us to understand drivers of transmission in different health areas and subsequently model targeted control interventions within these different health areas, at the cost of significantly greater computation time.

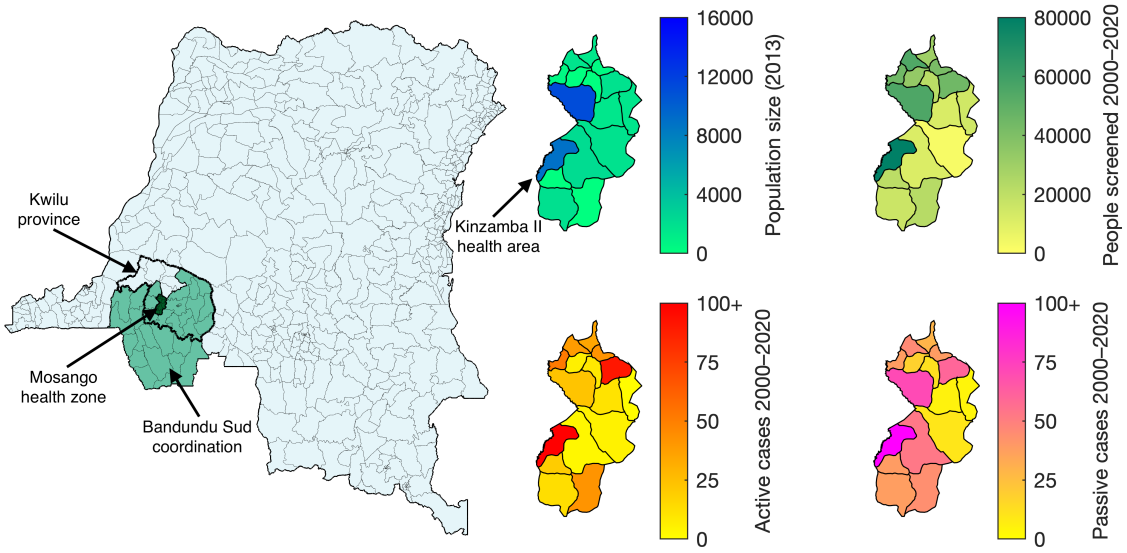

Fig A: **Data for Mosango health areas.**
A map of the location of Mosango, in the Kwilu province and Bandundu Sud coordination of the DRC (coordinations are the large geographic units, similar to provinces, for the organisation of gHAT activities). The map is divided into health area units, where possible, and health zone units otherwise. The Kwilu province is shown by the thick black border, the Bandundu coordination is shown in green and Mosango is dark green. Shown in smaller maps to the right are the distribution of the population (data provided by UCLA), the number of people screened (2000–2020) and the number of active and passive cases (2000–2020) across the health areas of Mosango (extracted from the WHO HAT Atlas [2]). The largest number of active and passive cases is 220 and 208 respectively, both in the health area of Kinzamba II. Shape files were provided by American Red Cross under a CC BY licence [1].

Results

Results for the health areas within the Mosango health zone show that the trend in reported cases for health areas is well captured by the stochastic model (Figure B). The fitted parameters indicate where the most transmission is likely to be occurring in the full health zone and where passive screening is performing better or worse than might be expected.

By aggregating health area results back to the full health zone, we show the health area modelling approach corresponds well to results for larger scale modelling, but also provides greater detail in the locations where cases occur (Figure C). These new results validate the previous results modelled at the health zone level, but in particular highlight the importance of using stochastic model projections, which better reflect our uncertainty and so provide better estimates of when elimination of transmission (EoT) for gHAT may occur.

Results suggest that there is little difference in obtaining parameter estimates using the stochastic versus the original deterministic variant. Therefore, we propose that future analyses will fit health area models using a deterministic method, but simulate projections with the stochastic model. This will save on computation time in calibrating the models, but retain the useful stochastic model properties of measuring EoT with more realistic uncertainty.

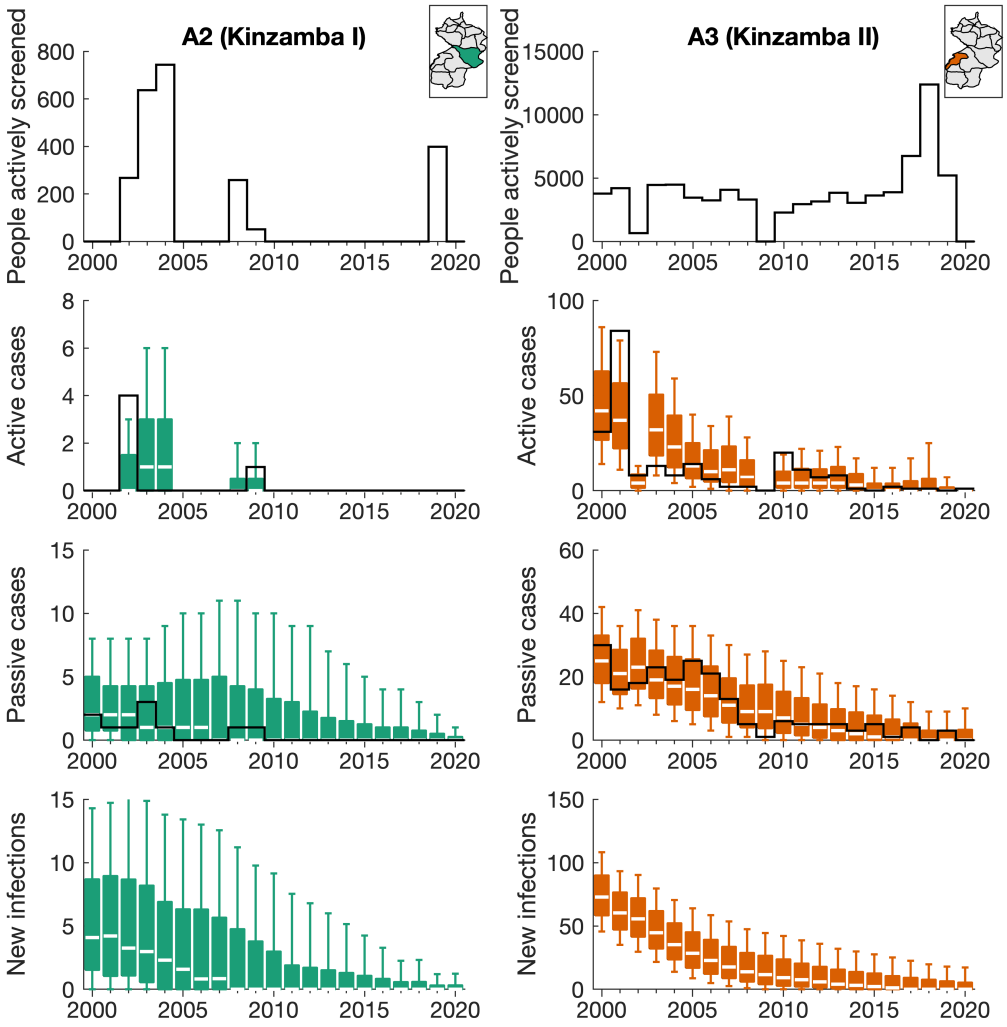

Fig B: **Model fitting outputs in example health areas.**
Data for the number of people actively screened and the active and passive cases reported are displayed as solid black lines for two health areas: Kinzamba I and Kinzamba II (labelled as A2 and A3 respectively in this analysis). This is compared with modelling outputs for active and passive cases and the number of new infections in each year given as coloured box plots. The median value of the box plots is shown as a white line, with outer boxes and whiskers representing 50% and 95% credible intervals respectively. No data line is shown for new infections, since this cannot be directly observed. Maps of the health area locations with the Mosango health zone are shown in the top right of each column.

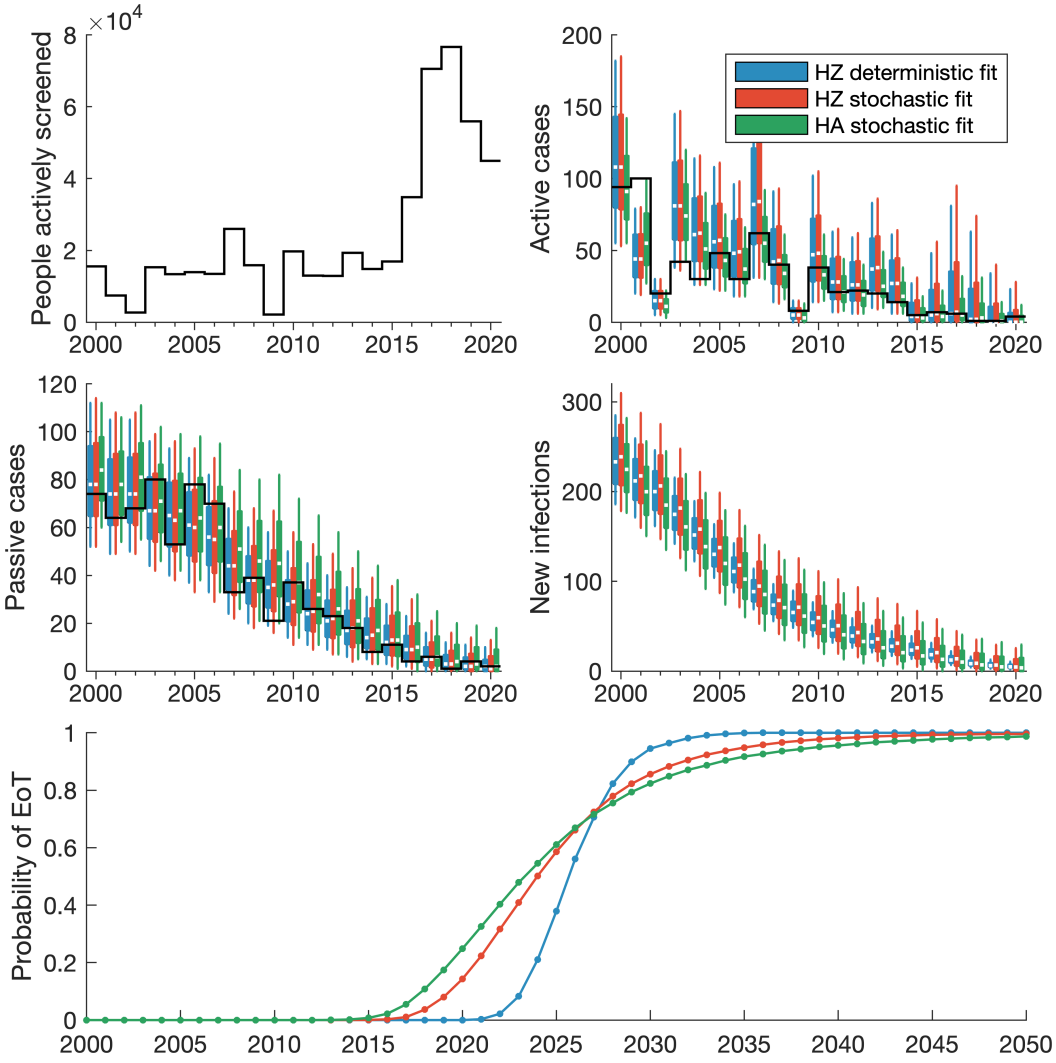

Fig C: **Model fitting outputs for Mosango health zone.**
Data for the number of people actively screened and the active and passive cases reported is displayed as solid black lines. The coloured box plots show annual model outputs for different fitting approaches, where blue boxes show the deterministic health zone model, red shows the stochastic health zone model, and green shows the aggregated stochastic health area models. The median value of the box plots is shown as a white line, with box plot whiskers representing 95% credible intervals.

Conclusions

By better reflecting the real-world situation in the models by exploring smaller spatial scales, we aim to achieve improved recommendations in how and where to focus efforts and achieve elimination of gHAT transmission. We plan for future work to scale up these results to cover all analysable health areas (those with sufficient data) for the DRC.

References

[1] American Red Cross. Drc health zone and health area boundaries, 2022. URL `https://data.humdata.org/dataset/drc-health-data`. (accessed May 20, 2022).

[2] J. R. Franco, G. Cecchi, M. Paone, A. Diarra, L. Grout, A. Kadima Ebeja, P. P. Simarro, W. Zhao, and D. Argaw. The elimination of human african trypanosomiasis: Achievements in relation to who road map targets for 2020. *PLoS neglected tropical diseases*, 16(1):e0010047, 2022.