Overview
Quantifying epidemiological drivers of gambiense human African Trypanosomiasis across the Democratic Republic of Congo

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Abstract

Gambiense human African trypanosomiasis (gHAT) is a virulent disease declining in burden but still endemic in West and Central Africa. Although it is targeted for elimination of transmission by 2030, there remain numerous questions about the drivers of infection and how these vary geographically.

In this study we focus on the Democratic Republic of Congo (DRC), which accounted for ∼84% of the case burden in 2016, to explore changes in transmission across the country and elucidate factors which may have contributed to the persistence of disease or success of interventions in different regions. We present a state-of-the-art Bayesian fitting methodology which allows for calibration of mechanistic gHAT model to case data (from the World Health Organization HAT Atlas) in a adaptive and automated framework. We focus on 168 endemic health zones (∼100,000 population size).

It was found that the model needed to capture improvements in passive detection to match observed trends in the data within former Bandundu and Bas Congo provinces indicating these regions have substantially reduced time to detection. Health zones in these provinces generally had longer burn in periods during fitting due to additional model parameters.

Previously, it was not clear whether a fall in active case finding in the period contributed to the declining case numbers. The modelling here accounts for variable screening and suggests that underlying transmission has also reduced greatly – on average 96% in former Equateur, 93% in former Bas Congo and 89% in former Bandundu – Equateur and Bandundu having had highest the case burden in 2000.

Posteriors were found for a range of fitted parameters in each health zone; these included the basic reproduction number estimates for 1998 (R_0) which was inferred to be between 1 and 1.19, in line with previous gHAT estimates, with higher median values typically in health zones with more case

reporting in the 2000s. This analysis also sets out a framework to enable future predictions for the country.

Introduction

In this article, we use a state-of-the art statistical fitting methodology to automate calibration of a model of gambiense human African trypanosomiasis (gHAT) to longitudinal data (2000–2016) across endemic health zones of the Democratic Republic of Congo (DRC). Through this process we aim to quantify key underlying factors which contribute to the observational and transmission variation across the country. These factors include: the proportion of the population who are at high-risk of exposure to tsetse, the relative risk of high-risk people, the passive detection rate in stage 1 and stage 2 of disease, the proportion of infections which are not diagnosed (underreported), and the specificity of the diagnostic algorithm. We also estimate the basic reproduction number, R_0, a bundled parameter which also incorportates factors such as the tsetse to human ratio.

Methods

We used a previously developed variant of the Warwick HAT model to predict gHAT dynamics by considering transmission among humans, tsetse and non-reservoir animals. This model with low-risk and high-risk humans captures systematic non-participation high-risk groups in the population.

The model takes into account previous improvements in medical, diagnostic and control systems. Major changes include better PS systems in the entire former province of Bandundu and some health zones in former Bas Congo province (now Kongo Central), improved active case confirmation by video recording of diagnostics in Mosango and Yasa Bonga in Bandundu from 2015, and implementation of VC in Yasa Bonga since mid-2015.

Passive surveillance

- We assume that pre-1998 there was limited access to diagnostics (pre-CATT test) and there was no stage 1 passive detection, and limited stage 2 passive detection.

- In 1998 we assume there was a step change which increased the stage 1 and stage 2 passive detection rates. These rates were computed by fitting to the data.

- In former Bandundu and Bas Congo provinces there is province-level evidence of improved passive detection (increased stage 1 passive reporting proportional to stage 2 during the 2000–2012 period, Lumbala et al. 2015). We use an increasing function (logistic) for the detection rates in these provinces with the shape parameters fitted to data. In Bandundu this change occurs earlier on (around 2008) and is gradual, whereas there is a steep change in Bas Congo, linked to the large increase in RDT health facilities in 2015.

Orientale Province

- MSF were active in Orientale before 2013 and used a different diagnostic algorithm to identify cases.

- A higher fixed sensitivity (MSF sensitivity = 0.95 in contrast to PNLTHA sensitivity = 0.91) and a lower fitted specificity were used for years up to 2012 in this province.

Specificity of diagnostic algorithm in active screening

- Video confirmation was introduced to Mosango and Yasa Bonga in Bandundu in 2015.

- The assumption of no false positives in active screening since 2015 is made for both places.

Vector control

- Vector control started in Yasa Bonga in mid-2015. We simulate this with 90% tsetse reduction. No other vector control was implemented prior to 2017 in DRC and therefore is not simulated.

Results

The fitting process calibrates model outcomes to reported timeseries of actively- and passively-detected cases. Fig 1 shows examples of these trends for two example health zones; Kwamouth (in the former province of Bandundu) and Tandala (Equateur). Fig 1 shows how well the model fits to the timeseries of reported cases both actively and passively detected, and where there has been a change in the passive case detection rate during the data collection period (as in Kwamouth). The results of all 168 health zone level fits are available online (see Fitting GUI).
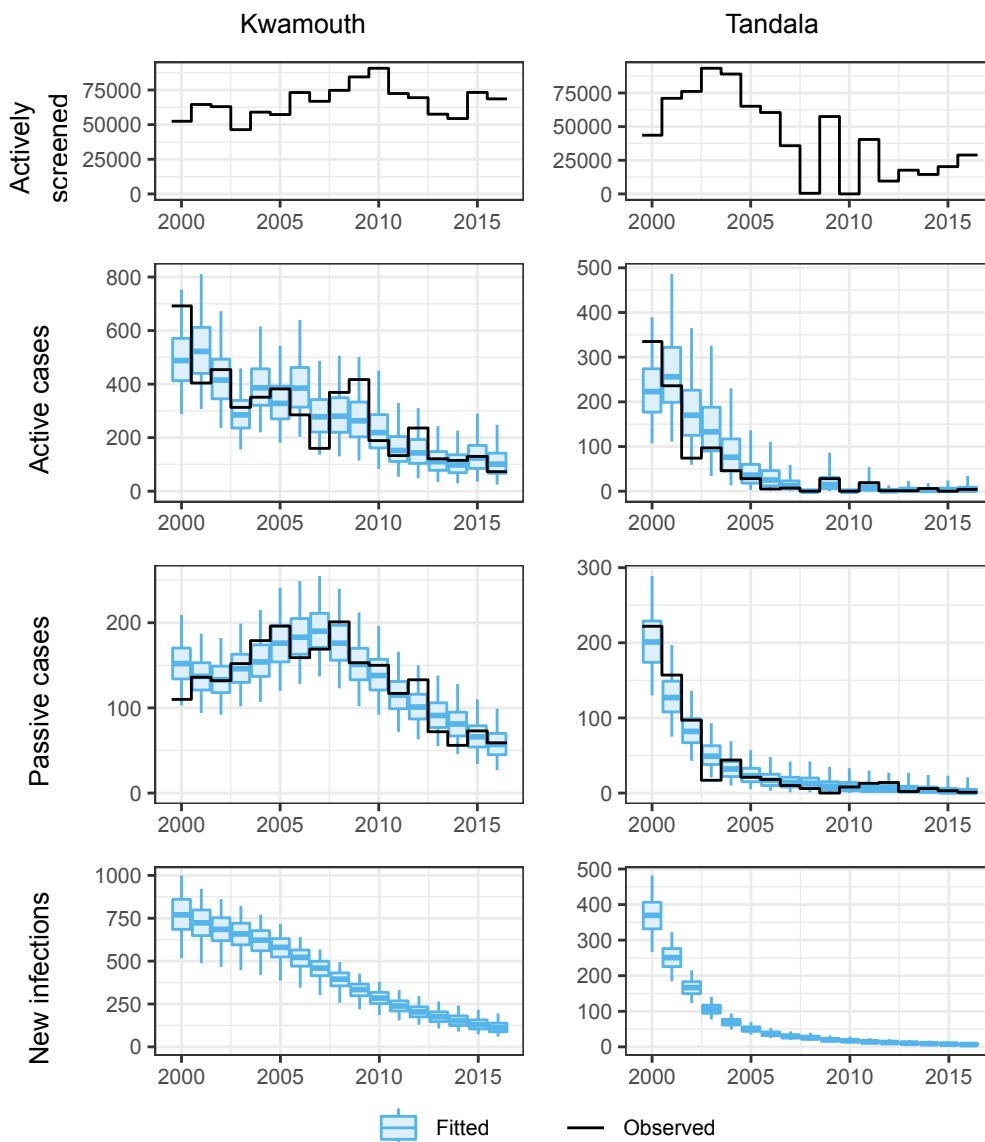

Figure 1: Demonstration of fit to the trends in new case detection over time and predicted numbers of new infections for two example health zones.

Fig 2 shows a map of health zone level estimates for R_0 including uncertainty - the varying colours in each health zone reflect possible parameter values that R_0 could take as estimated through model fitting.

Table 1: Reduction in new gHAT infections by former province. Medians and 95% credible intervals (CIs) of aggregated health zone-level outcomes.

Former province	New infections (median [95% CI])			Percentage reduction	
	2000	2008	2016	2000–2008	2000–2016
Bandundu	7344 [6733, 7977]	3187 [2931, 3466]	808 [684, 950]	57 [55, 58]	89 [87, 90]
Bas Congo	804 [723, 889]	204 [181, 230]	58 [45, 76]	75 [72, 77]	93 [90, 95]
Equateur	4565 [4152, 4980]	446 [404, 490]	161 [136, 189]	90 [89, 91]	96 [96, 97]
Kasai Occidental	701 [601, 825]	312 [270, 362]	163 [133, 198]	55 [51, 60]	77 [71, 81]
Kasai Oriental	4184 [3672, 4740]	2284 [1769, 2840]	1892 [1261, 2583]	45 [39, 53]	55 [44, 66]
Katanga	145 [109, 193]	135 [102, 178]	117 [85, 161]	7 [-3, 17]	20 [-1, 37]
Kinshasa	161 [126, 226]	96 [76, 126]	66 [46, 94]	41 [26, 52]	59 [39, 74]
Maniema	233 [189, 292]	174 [144, 214]	150 [118, 194]	25 [16, 35]	35 [20, 50]
Orientale	1936 [1701, 2194]	1336 [1130, 1547]	672 [531, 833]	31 [22, 40]	65 [58, 72]

Conclusion

In this study the fitting of transmission models for gHAT has been automated allowing health zone-level model fitting across the whole of DRC to be performed for the first time. This is a necessary step towards providing modelling information which can assist in the formulation of policy appropriate to the varying needs across the country; this will be done through modelling future strategies and performing health-economic analysis for the health zones.

The fits here highlight the success of past interventions, both in the obvious decline in the number of reported cases but also through quantification of improvements in surveillance, such as in the case of changes in passive surveillance over time in Bandundu and Bas Congo. Across the country, the fits have been able to provide estimates for reduction in transmission in each health zone which is not directly observable from case data; even in areas where there has been a decline in active screening activity over time, the modelling indicates that there has been a real reduction in transmission, rather than just a decline in reported cases. For example, although there was a reduction in active screening coverage in former Equateur province from a maximum of around 900,000 in 2003 to around 150,000 annual on average between 2012–2016, we still estimate that there is a 96% reduction in transmission from 2000–2016.
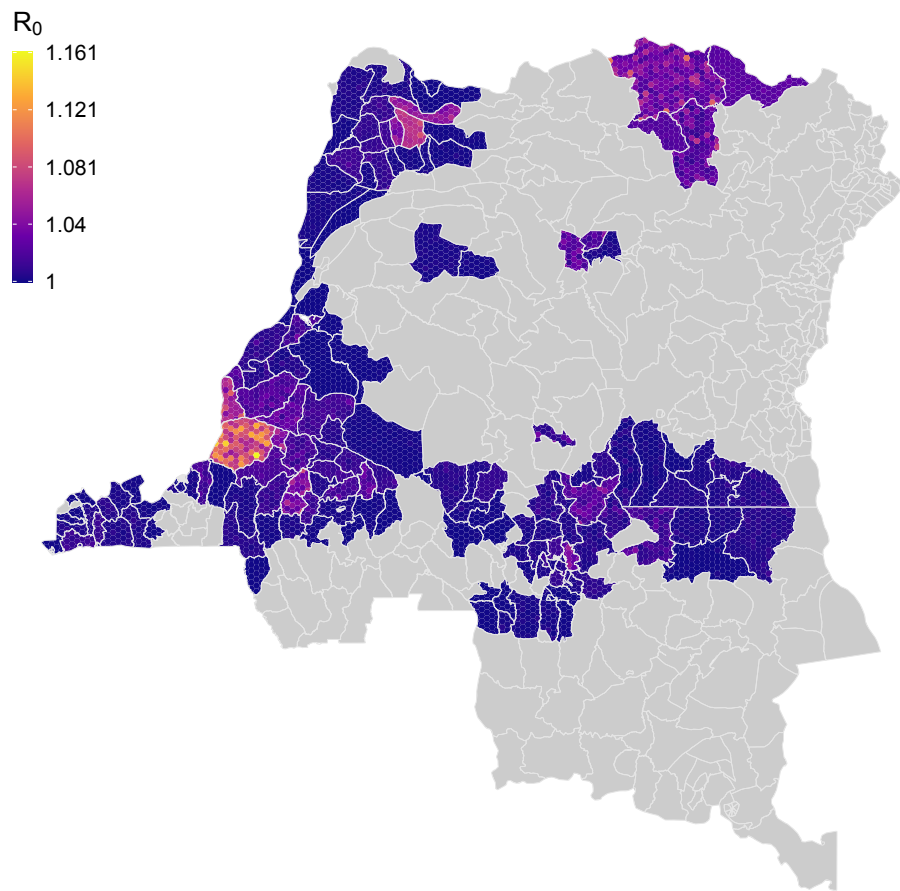
Figure 2: Within health zone posterior distribution of R_0, fill colours are randomly sampled from the posterior distribution of R_0 from the analysis of the health zone.