Economic evaluation of *gambiense* human African trypanosomiasis elimination campaigns in five distinct transmission settings in the Democratic Republic of Congo

Marina Antillon$^{1,2}$, Ching-I Huang$^{3,4}$, Ronald E. Crump$^{3,4}$, Paul E. Brown$^{3,4}$, Rian Snijders$^{1,2,5}$, Erick Mwamba Miaka$^6$, Matt J. Keeling$^{3,4,7}$, Kat S. Rock$^{3,4,*}$ and Fabrizio Tediosi$^{1,2,*}$

$^1$Household Economics and Health Policy Unit, Swiss Tropical and Public Health Institute, Basel, Switzerland  
$^2$University of Basel, Basel, Switzerland  
$^3$Zeeman Institute, University of Warwick, Coventry, UK  
$^4$Mathematics Institute, University of Warwick, Coventry, UK  
$^5$Institute of Tropical Medicine, Antwerp, Belgium  
$^6$Programme National de Lutte contre la Trypanosomie Humaine Africaine, Kinshasa, Democratic Republic of Congo  
$^6$School of Life Sciences, University of Warwick, Coventry, UK  
*Authors contributed equally to this work

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**Abstract**

**Background:** Gambiense human African trypanosomiasis (gHAT) is marked for elimination of transmission (EOT) by 2030, but the disease persists in several low-income countries. We examine the cost-effectiveness of four gHAT elimination strategies in Democratic Republic of Congo (DRC), which has the highest burden of gHAT.

**Methods:** We compared four strategies against gHAT by coupling a transmission model with a health outcomes model in five settings – spanning low- to high-risk. Alongside passive surveillance (PS) in fixed health facilities, the strategies included active screening (AS) at average or high coverage levels, both alone or with vector control (VC). A scale-back algorithm was devised to simulate cessation of AS and VC when no cases were reported for three consecutive years. Outcomes were denominated in disability-adjusted life-years (DALYs) and costs until 2040 were denominated in 2018 US$.

**Results:** In high or moderate-risk settings, costs of gHAT strategies are primarily driven by AS and, if used, VC. Due to the cessation of AS and VC most investments (75-80%) will be made by 2030 and VC might be cost-saving while ensuring EOT. In low-risk settings, costs are driven by PS, and minimum-cost strategies consisting of AS and PS lead to EOT by 2030 with high probability.

**Conclusion:** In many settings, the case for EOT by 2030 is a sensible use of resources, and investments in gHAT will decelerate within this decade in moderate- and low-risk regions.

**Keywords**— sleeping sickness, elimination of transmission, economic evaluation, modelling, Democratic Republic of Congo

**Abstract word count:** 248 words
Research in context

Evidence before this study: The databases PubMed and ScienceDirect were searched on 28 April 2020 to identify previous studies undertaken on cost-effectiveness of strategies to control gHAT. We used an unrestricted language search and dates from January 2000 to focus on contemporary interventions and prevalence. The search terms were “sleeping sickness” OR “trypanosomiasis” AND “cost effective”. We excluded studies on rhodesiense HAT, animal trypanosomiasis and Chagas disease. A few intervention-specific studies have examined the cost-effectiveness of different tools, such as treatment and diagnostic tools or algorithms, but only a cost-effective analysis by Sutherland and colleagues (2017) examines the potential of multi-faceted strategies to avert burden and achieve elimination. Sutherland and colleagues showed that the deployment of emerging technologies - new treatments, new diagnostics, and/or vector control - would make elimination of transmission (EOT) feasible and cost-effective at thresholds below $1500–$1800 per DALY averted in theoretical settings of low, medium, and high prevalence.

Added value of this study: Using a dynamic modelling framework, the present study is the first to perform a DRC-specific cost-effectiveness analysis for gHAT strategies that accounts for local epidemiological and operational characteristics. Using detailed cost-functions and updated information on the impact of interventions, we have projected the epidemiological and health economic implications by 2040 of gHAT control and EOT by 2030. We have simulated four alternative strategies combining passive surveillance with moderate and high coverage levels of active screening by mobile units. We have also simulated strategies with and without vector control. We found that in high-risk settings, strategies that lead to EOT are in line with strategies that aim to minimise costs, but in moderate-risk settings strategies with a high risk to EOT would require a relatively high willingness to pay to be considered cost-effective; this is similar to investments made for other infectious disease elimination programs.

Implications of all the available evidence: gHAT elimination strategies can represent a justifiable use of resources even in resource-constrained settings. Investments in EOT in the near-term will enable a good degree of reduced costs post-2030, and in high-incidence settings, these investments will pay back by 2040.
1 Introduction

*Gambieiene* human African trypanosomiasis (gHAT) has caused three decades-long epidemics in Western, Central, and Eastern-Sub-Saharan Africa during the twentieth century [1]. Caused by the parasite *Trypanosoma brucei gambiense* and transmitted by tsetse, the disease is almost always fatal if untreated. No vaccine exists against gHAT, and treatments are incompatible with mass drug administration strategies, but there is a relatively diverse toolbox available to control the infection [2]: a range of diagnostics for screening in at-risk villages by mobile teams, termed as active screening (AS), or to test symptomatic individuals in fixed health facilities, termed as passive surveillance (PS). A new oral therapeutic became available in 2020, expanding the treatments available for outpatient care [3]. In addition, vector control (VC) can now be deployed across moderate scales to reduce tsetse density [4–7]. This toolbox has enabled a vast reduction in burden from 37,000 reported cases at the peak of the epidemic in 1998 to 977 reported cases in 2018 [8–9].

In 2012, less than a decade and a half after the peak of the last epidemic, gHAT was targeted for elimination of transmission (EOT) by 2030; by 2014 case reduction outpaced the intermediate goals set by the WHO [2] [10]. Consequently, the pursuit of EOT brings new questions to the fore: because gHAT activities take place in settings facing both resource constraints and competing health needs, what are the resource implications of further pursuing gHAT EOT by 2030? Which are the most efficient strategies toward gHAT suppression?

The key economic arguments for and against disease elimination programmes occasionally appear at odds: (i) the long-term benefits of elimination and the subsequent savings borne out of discontinued disease control measures are substantial, yet (ii) the endgame is comprised of increasingly more expensive activities on a per-person basis without the guarantee of success. Smallpox eradication is heralded as an example of (i): elimination activities saved 1.35 billion US$ but had a cost of 100 million US$ [11]. Whereas polio – for which there were 42 cases reported in 2016 – exemplifies (ii), with a cost of 3.3 billion US$ each year, or a one-billion US$ excess over the cost of control strategies [12].

To date, there has been one cost-effectiveness analysis of control and elimination strategies for gHAT, showing that new technologies to facilitate diagnosis, treatment, and curtail vector transmission could make elimination feasible at a moderate cost ($400–1500 per DALY averted) for high- and medium-transmission settings but at high costs for low-transmission settings [13]. However, it is worth reconsidering these questions while taking into account specific, local transmission dynamics, which is now possible thanks to recent developments in model calibration [14]. Moreover, including realistic levels of screening based on regional data allows us to consider expenses and cost-effectiveness in these real-world settings.

In the current study, we undertake an economic evaluation of four gHAT control and elimination strategies in distinct transmission settings in five health zones of the Democratic Republic of Congo (DRC), the country that reported 74% of global cases in 2018 [9]. We adopt a modelling framework in order to examine the interplay of epidemiological, economic and both short- and long-term factors in effective decision-making around strategies of gHAT elimination.

2 Methods

In this study we use the net monetary benefits framework (NMB) to examine the cost-effectiveness of gHAT strategies to avert disease burden, which is dominated in disability-adjusted life years (DALYs; see sections S1.3, S1.5, S1.7).

2.1 Settings and strategies

We selected five health zones in DRC, described in Table 1 and depicted in Figure S1. These five health zones span the spectrum of the WHO’s risk (incidence) categories [2]. For each health zone, we simulated four strategies using a variant of the “Warwick gHAT model”, a deterministic transmission model that explicitly simulates the transmission between humans via tsetse (see supplement S1.2.1). The model was fitted to case data from the health zones and projections were simulated for 2020–2050 [14–15]. The same underlying model framework has also been used to examine the epidemiology of gHAT in DRC and Chad [6–16–19].

The strategies are configurations of the following interventions (see Figure 1 and section S1.2.2 for more details):

- Active screening (AS): at-risk village populations are screened each year by mobile teams and suspected cases are confirmed before treatment. In two strategies (1 and 3, “Mean AS”) the number of people screened annually per health zone is equal to the mean number of individuals screened during 2014–2018 (the last five years for
Table 1: Descriptive summaries of five health zones. For Yasa Bonga and Kwamouth, the amount of vector control performed was informed by current and planned practice. For Mosango, Boma Bungu, and Budjala, assumptions regarding vector control extent and intensity were based on the experience in places of similar incidence. Sensitivity analyses regarding the assumptions around vector control are found in the supplement and in the companion website.

| Characteristic                                      | Yasa Bonga                   | Mosango                     | Kwamouth                     | Boma Bungu                     | Budjala                      |
|-----------------------------------------------------|------------------------------|------------------------------|------------------------------|--------------------------------|------------------------------|
| Former province (new province)                      | Bandundu (Kwilu)             | Bandundu (Kwilu)             | Bandundu (Mai-Ndombe)        | Bas-Congo (Kongo Central)      | Equateur (Sud-Ubangi)        |
| Population (2016 est.)                              | 221,917                      | 125,076                      | 131,022                      | 85,960                         | 133,425                      |
| Area (km²)                                          | 2,606                        | 2,673                        | 14,589                       | 2,866                          | 4,397                        |
| Active screening as a percent of 2016 population     | 57,91                        | 34,60                        | 48,69                        | 7.2, 29                        | 0.41, 36                     |
| gHAT testing centers (2014 est.)                    | 4                            | 1                            | 5                            | 2                              | 2                            |
| Yearly incidence per 10,000 (2012–2016)             | 4.87                         | 2.19                         | 16.79                        | 1.37                           | 0.05                         |
| WHO Incidence category                              | Moderate                     | Moderate                     | High                         | Moderate                       | Very low                     |
| Vector control extent (linear km)                   | 210                          | 100                          | 432                          | 100                            | 100                          |
| Vector control density (targets per linear km)       | 60                           | 40                           | 20                           | 40                             | 40                           |

In all strategies, AS (at either ‘Mean’ or ‘Max’ coverage) and PS are in place, with supplemental VC deployed in Strategies 3 and 4 (see Figure 1). In Yasa Bonga, VC has taken place since mid-2015, so only the two VC strategies (3 and 4) were considered.

The transition between the suppression and post-elimination phases, not included in the previous projections [15], is simulated as the cessation of both AS and VC after three consecutive years of zero detected cases by any screening modality (AS or PS). Should a new case present to fixed health facilities (through PS), reactive screening (RS) begins the following year: equivalent in form and intensity to the previous AS, RS is simulated until there are two consecutive years of zero case detection by any mechanism (either AS or PS). The availability of screening in health facilities (PS) is assumed to remain constant for the duration of our simulations, even after cessation of AS and VC and EOT. Transmission model outputs for each simulated year include cases detected via AS and PS, underlying new infections, person-years spent in stage 1 or stage 2 of disease, and deaths outside the health-care system. Furthermore for each realisation, we record the year that EOT is achieved using a proxy threshold of less than one new infection per year in the health zone.

2.2 Health outcomes

The outputs of the transmission model were inputs in a probability tree model of disease outcomes (see Figure 1). We simulated the treatment process separately for stage 1 and stage 2 disease, sorting patients into the WHO-recommended treatment, treatment success or failure, diagnosis in the event of treatment failure, and progression to rescue treatment (see [S1, 2, 3]). DALYs were calculated according to WHO conventions, and we report cases and deaths for general
Figure 1: Model of strategies and treatment against gHAT in DRC including active screening (AS) by mobile teams, passive surveillance (PS) in fixed health facilities. In two strategies (‘Mean AS’ and ‘Mean AS & VC’) the proportion screened equalled the mean number screened during 2014–2018. In two other strategies (‘Max AS’ and ‘Max AS & VC’), the coverage is the maximum number screened during 2000–2018. In strategies 3 and 4, vector control (VC) is simulated assuming an 80% tsetse density reduction in 1 year. PS is in place under all strategies. The right hand treatment tree shows possible health outcomes for diagnosed gHAT patients including fexinidazole use. Abbreviations: SAE: Serious adverse events, IP: inpatient care, OP: outpatient care.
2.3 Costs and cost-effectiveness analysis

We performed our analysis from the perspective of health-payers collectively. Disease-related costs include confirmation, staging via lumbar puncture (when indicated), and drug administration. Other intervention costs include diagnostics, mobile teams, fixed facilities, and target deployment (more details can be found in section S1.4). Costs were parameterized using values from the literature expressed in 2018 US$ (see Section S5).

We computed incremental cost-effectiveness ratios (ICERs) to account for parameter uncertainty in the economic evaluation, and we adopted the NMB framework, which expresses the probability that an intervention is optimal at a range of willingness-to-pay thresholds (WTP). Optimal strategies are selected based on the highest mean NMB at a given WTP threshold. For further elaboration on the framework and our implementation, see section S1.5.

We examined health impacts and costs in a relatively long-term horizon (2020–2040), discounting at a yearly rate of 3% in accordance with standard conventions [21]. We also performed scenario analyses to examine the impact of our default assumptions around time horizons, discounting, and on the efficacy and cost of VC (see supplemental section S1.8).

3 Results

3.1 Feasibility of gHAT elimination and health impact

The feasibility of EOT and cessation of AS are shown in Table 2. While the risk category of each health zone (Table 1) influences the year when EOT is expected — places with higher incidence likely meeting EOT later than places with lower incidence — the implementation of VC is predicted to substantially expedite EOT across all moderate- and high-risk settings.

In low-risk Budjala, EOT by 2030 appears imminent with any strategy, although exploiting Max AS over Mean AS would reduce the uncertainty. In the moderate-risk settings of Mosango and Boma Bungu, EOT may occur by 2030 even with only Mean AS (79% and >99% probability, respectively) and EOT is almost certain by 2040. With additional AS coverage, the predicted probability of EOT by 2030 increases from 79% to 92% in Mosango, but VC should both ensure EOT by 2030 and bring forward the mean time to elimination by five years. In Yasa Bonga, where VC activities began in 2015 and scaled up completely by 2017, the model predicts that EOT may have been achieved by 2017 if VC was present in all areas of ongoing transmission, although predicted case detection are still expected into the early 2020s followed by AS cessation in 2024 (95% CI: 2021-2028). In high-risk Kwamouth, EOT is predicted to be almost impossible by 2030 (<0.01) in the absence of VC, and unlikely by 2040 (11–13% depending on AS coverage), but adding VC is predicted to bring forward EOT by more than two decades. Zero detections are more informative as an EOT proxy when VC is in situ; if AS is stopped after three years of zero detections, there is up to a 62% probability that RS would be necessary in Kwamouth in the absence of VC, but at most 19% of VC simulations result in RS in Budjala.

The health impact and net costs of each strategy between 2020–2040 are shown in Table S23. Yasa Bonga, Boma Bungu, and Budjala are each predicted to have an average of ≤ 5 cases and ≤ 5 gHAT-related deaths over the next 20 years. Mosango is predicted to have more cases (≤ 23) and deaths (≤ 13) in the absence of VC. Kwamouth has the most predicted cases and deaths, although the burden may be cut by three-quarters with the deployment of VC. In terms of DALYs, Kwamouth sustains the worst burden even under the best strategy (1807 DALYs) compared to the worst strategy in moderate-risk Mosango (443 DALYs in Mosango). Supplemental outcomes of treatment are found in section S1.2.3; 97% of treated stage-1 patients and 93% of treated stage-2 patients will be cured, an additional 1% and 3%, respectively, will be cured after sustaining severe adverse events, and between 2% and 4% of patients will need rescue treatment. Fewer than 1% of all treated cases will die. Further details of the outcomes under different time horizons are found in supplementary sections S24 and S26.

3.2 Costs

The total mean costs in each location vary between $480,000 (Boma Bungu) and $5.26 million (Kwamouth), and on a yearly per-capita basis, costs range from $0.19 (Budjala) to $1.91 (Kwamouth). Cost components are shown in Figure 3; these components are derived from the mean costs and the probability of activity cessation. For all locations except Kwamouth, additional costs in the latter half of the 2030s arise from PS, as most simulations indicate that AS and VC would cease by this period. In Yasa Bonga, Mosango, and Kwamouth, about three-quarters of the cumulative costs are expected to be spent within the first five years of the 2020s and then stabilise when AS and VC cease (Figure S4).
Table 2: Feasibility of elimination (additional scenarios are shown in the supplement). Estimates shown are means and their 95% predictive intervals (PI). Color scheme for years: earlier years are in blue tones and later years are in red tones. Pr. RAS is calculated as a proportion of the iterations when active surveillance must be when active surveillance ceases.
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Costs with the least ambitious (default) strategy in Kwamouth and Mosango are expected to overtake the costs of the same strategy with VC by 2040, indicating that such a strategy would be economically neutral or even cost-saving in 20 years. In Boma Bungu and Budjala, where scant screening is undertaken and VC would cease quickly, costs are slow to accumulate throughout the period of study. The cost breakdowns across different investment horizons are shown in Figure S3.

| Cases detected (95% PI) | Deaths (95% PI) | DALYs (95% PI) | Costs millions USD (95% PI) | Yearly cost per capita USD (95% PI) |
|-------------------------|-----------------|---------------|-----------------------------|-----------------------------------|
| **Yasa Bonga**          |                 |               |                             |                                   |
| Mean AS & VC            | 5 (0, 23)       | 2 (0, 7)      | 67 (1, 255)                | 3.08 (1.59, 5.23)                | 0.66 (0.34, 1.12)                |
| Max AS & VC             | 4 (0, 23)       | 2 (0, 7)      | 66 (1, 252)                | 3.81 (1.82, 6.79)                | 0.82 (0.39, 1.46)                |
| **Mosango**             |                 |               |                             |                                   |
| Mean AS                 | 23 (1, 79)      | 13 (1, 42)    | 441 (33, 1,479)            | 1.26 (0.60, 2.32)                | 0.48 (0.23, 0.88)                |
| Max AS                  | 22 (0, 92)      | 8 (0, 29)     | 295 (5, 1,011)             | 1.67 (0.74, 3.24)                | 0.64 (0.28, 1.23)                |
| Mean AS & VC            | 9 (0, 41)       | 5 (0, 16)     | 175 (3, 528)               | 1.14 (0.62, 1.83)                | 0.43 (0.24, 0.70)                |
| Max AS & VC             | 10 (0, 54)      | 4 (0, 12)     | 137 (2, 440)               | 1.45 (0.74, 2.44)                | 0.55 (0.28, 0.93)                |
| **Kwamouth**            |                 |               |                             |                                   |
| Mean AS                 | 477 (144, 1,081)| 215 (44, 629)| 7,518 (1,622, 21,736)     | 4.01 (2.72, 6.17)                | 1.46 (0.99, 2.24)                |
| Max AS                  | 463 (136, 1,047)| 176 (37, 503)| 6,324 (1,418, 17,773)     | 5.26 (3.48, 8.27)                | 1.91 (1.27, 3.01)                |
| Mean AS & VC            | 116 (41, 235)   | 63 (22, 132)  | 1,969 (684, 4,157)         | 3.71 (2.42, 5.84)                | 1.35 (0.88, 2.12)                |
| Max AS & VC             | 120 (38, 270)   | 51 (17, 108)  | 1,795 (610, 3,813)         | 4.27 (2.72, 6.95)                | 1.55 (0.99, 2.53)                |
| **Boma Bungu**          |                 |               |                             |                                   |
| Mean AS                 | 1 (0, 10)       | 1 (0, 4)      | 18 (0, 153)                | 0.48 (0.31, 0.70)                | 0.27 (0.17, 0.39)                |
| Max AS                  | 1 (0, 10)       | 0 (0, 3)      | 13 (0, 112)                | 0.59 (0.36, 0.92)                | 0.33 (0.20, 0.51)                |
| Mean AS & VC            | 1 (0, 7)        | 0 (0, 3)      | 14 (0, 109)                | 0.62 (0.38, 0.95)                | 0.34 (0.21, 0.53)                |
| Max AS & VC             | 1 (0, 8)        | 0 (0, 3)      | 11 (0, 99)                 | 0.72 (0.42, 1.17)                | 0.40 (0.23, 0.65)                |
| **Budjala**             |                 |               |                             |                                   |
| Mean AS                 | 4 (0, 22)       | 5 (0, 18)     | 166 (0, 614)               | 0.54 (0.34, 0.81)                | 0.19 (0.12, 0.29)                |
| Max AS                  | 4 (0, 24)       | 2 (0, 8)      | 82 (0, 281)                | 0.91 (0.44, 1.51)                | 0.32 (0.16, 0.54)                |
| Mean AS & VC            | 2 (0, 12)       | 3 (0, 8)      | 85 (0, 277)                | 0.68 (0.39, 1.05)                | 0.24 (0.14, 0.38)                |
| Max AS & VC             | 3 (0, 19)       | 2 (0, 6)      | 57 (0, 205)                | 1.00 (0.45, 1.68)                | 0.36 (0.16, 0.60)                |

Table 3: Summary of effects and costs 2020-2040. Two differences should be noted between these estimates and those used for decision analysis shown in table. First, these estimates are not discounted. Second due to asymmetric distributions, a naive difference in mean costs would not equal the mean differences in costs across simulations – the metric we used in decision analysis. Undetected cases are reflected in deaths, as very few deaths (<1 percent) originate from treated cases. Estimates shown are means and their 95% predictive intervals (PI).

### 3.3 Cost-effectiveness

The cost-effectiveness results are displayed in Table and select features are illustrated in Figure. Cost-effectiveness acceptability curves, expressing the same information in a more conventional format, are shown in Figure S9.

In Yasa Bonga, Boma Bungu and Budjala, the predicted minimum-cost strategy has a 97-99% probability of EOT by 2030. After accounting for uncertainty, the current practice (Mean AS & VC) in Yasa Bonga is the optimal strategy across all WTP thresholds under $1,000 in more than 78% of simulations. In Budjala, there is even more support (77–91% of simulations) indicating that the least ambitious intervention (Mean AS) is optimal across all WTP values. It should be noted that, perhaps because of minimal AS coverage, there is a 36% probability that RS would be deployed in Budjala after cessation, and while VC would nearly halve that prospect, it would come at a steep cost of $2,932 per DALY averted.

In Mosango, VC would both raise the probability of achieving EOT, save costs, and minimize the probability of RS. However, the potential for cost savings is contingent on the assumption that an operation across 100 km of riverbank deploying 40 targets per kilometer yields an 80% tsetse reduction in ongoing transmission locations. An operation closer in extent to the one in Yasa Bonga would be optimal at a mean cost of $1,513 to $2,071 per DALY averted (see Figure S6).
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Figure 3: Displayed costs are not discounted. Treatment costs, indicated in purple, are shown here although they are so small as to be hardly visible.

In Kwamouth, more than 64% of simulations favoured the addition of VC to Mean AS for WTP values above $250. In fact, Mean AS & VC costs $37 per DALY averted, and the strategy was cost-saving in 42% of simulations. Importantly, the analysis favours VC activities even if target density must be doubled at a relatively low cost of $269 and $375 per DALY averted (see Figure S5).

The results across shorter (2020–2030) and longer (2020–2050) time horizons are very similar (see Figure S10). The results assuming no discounting on costs or effects (Figure S10) lead to comparable recommended strategies for WTP values < $1500.

4 Discussion

Applying a decision-analytic framework across five health zones of DRC we have assessed current efforts to control gHAT, as well as the efficiency of alternative strategies to transition beyond suppression to EOT. The transmission model predicted substantial declines in observed gHAT cases and the underlying transmission in all locations using any strategy, but the cumulative burden of disease and the capacity to reach EOT by 2030 varied considerably.

In Mosango and Kwamouth the addition of VC to Mean AS is predicted to expedite EOT and be cost-effective for low WTP. However, in Boma Bungu and Budjala current practice appears sufficient to ensure EOT by 2030 despite Boma Bungu’s “moderate” incidence and Budjala’s low AS coverage (<0.5%). Although the mean total costs in each location vary between $480,000 in Boma Bungu to $5.26 million in Kwamouth, the optimal strategies have a mean cost of at most $3.71 million (95% CI: 2.28–5.63) in undiscounted terms. Per person, the optimal strategies would not exceed $1.35 per year per person protected (Table 3) – comparable to many other global health interventions [12]. Notably,
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| Cost-effectiveness analysis without uncertainty | Net benefit (uncertainty) analysis: Pr. that a strategy is optimal (conditional on willingness-to-pay) | Pr EOT by 2030 |
|-----------------------------------------------|-------------------------------------------------------------------------------------------------|-----------------|
| **Mean cost difference** | **Mean DALYs averted** | **ICER** | **Minimum cost** | **250 USD per DALY averted** | **500 USD per DALY averted** | **1,000 USD per DALY averted** | **Pr EOT by 2030** |
| Yasa Bonga | | | | | | | |
| Mean AS & VC | 0 | 0 | 0.78 | 0.78 | 0.78 | 0.78 | >0.99 |
| Max AS & VC | 671,005 | 2,178,454 | 0.22 | 0.22 | 0.22 | 0.22 | >0.99 |
| Mosango | | | | | | | |
| Mean AS | 0 | 0 | Dominated | 0.38 | 0.34 | 0.3 | 0.25 | 0.79 |
| Mean AS & VC | -44,433 | 142 | Min Cost | 0.49 | 0.53 | 0.55 | 0.58 | >0.99 |
| Kwamouth | | | | | | | |
| Mean AS | 0 | 0 | Min Cost | 0.52 | 0.24 | 0.15 | 0.08 | <0.01 |
| Mean AS & VC | 102,208 | 2,751 | 37 | 0.42 | 0.63 | 0.67 | 0.68 | >0.99 |
| Budjala | | | | | | | |
| Mean AS | 0 | 0 | Min Cost | 1 | 0.99 | 0.99 | 0.99 | >0.99 |
| Mean AS & VC | 123,230 | 4 | 91,907 | 0 | 0 | 0 | 0 | >0.99 |

Table 4: Summary of cost-effectiveness, assuming a time horizon of 2020-2040. Cost differences and DALYs averted are relative to the comparator, which is the first strategy listed for each location. DALYs averted and cost differences are discounted at 3 percent per year in accordance with guidelines. In the uncertainty analysis (columns 5-8), the probability that a strategy is optimal is shown (as a proportion of all simulations, accounting for parameter uncertainty). Strategies highlighted in pink are optimal strategies: the strategies for which the mean net monetary benefit (NMB) is highest.

while healthcare costs and disability-adjusted life-years can be considered narrow criteria to justify investments in elimination, we chose to conduct an analysis that would allow us to understand the relative efficiency of these strategies by the same rubric employed to assess the cost-effectiveness of other disease programs; we found that gHAT elimination is possible and efficient at modest economic costs.

Our cost parameters were informed by recent cost studies in Yasa Bonga and Mosango, therefore updating the costs used in the past [13][22], and a decomposition of the costs showed that while there are contributions from varied factors, some broad patterns emerged (Table S23). First, AS costs and, when applicable, VC costs will play a large role in overall costs everywhere except in Budjala, where no more than PS and minimal AS is recommended. Second, cessation of AS and VC activities means costs are expected to decrease during the 2020’s, and in Kwamouth, investments in VC in the early 2020’s could be recovered by the late-2030’s (Fig S4).

Importantly, we have found that our conclusions are quite robust to the choice of time-horizon as well as discount rate, and our framework has accounted for parameter uncertainty. Notably, we have chosen to consider a 20-year horizon with supplemental results for a 10- and 30-year horizon because an intervention with long-term consequences like EOT would be under-appreciated in a short horizon, but conclusions do not differ substantially (see figures S9 and S10). Simulation results presented here suggest that local EOT of gHAT is epidemiologically and operationally feasible across different risk settings with the current toolbox. As expected, higher-burden health zones expect later EOT, but VC raises the possibility and substantially expedites EOT, as seen across DRC [15]. The model utilised here did not explicitly include potential hindrances such as asymptomatic human infection or animal reservoirs [23], however the long-tailed distribution used for disease progression captures possible long-term asymptomatic carriage. Skin-only
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Figure 4: Maps of preferred strategies according to economic or budgetary goals for 2020–2040. Maps A & B show the optimal strategies depending on WTP. The text indicates the probability that the optimal strategy will lead to EOT by 2030. Map C shows the most efficient strategy that has >90% probability of EOT by 2030 and shows the mean ICER vs the comparator (Mean AS for all locations except Yasa Bonga, where it is Mean AS & VC). Maps are not drawn to scale. Maps with time horizons 2020–2030 and 2020–2050 are in the supplement: Figures S7 and S8.

Infections or asymptomatic individuals whose infection may self-resolve would require further model modifications and ongoing modelling work will examine potential risks and impact. Previous modelling analyses indicate that the existence of animal reservoirs may not greatly alter timelines to EOT, especially if VC is implemented [6, 17].
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Although this is the first analysis where fenixinidazole was the default treatment, WHO guidelines propose caution in its use, and 65% of simulated patients were assumed to be treated with NECT on an in-patient basis due to late-stage detection, low body weight, or the young age of the patient (see sections S5.5.10, S5.5.14, and S5.5.15). The prospect of a single-dose oral treatment for gHAT (acoziborole), currently in trials, could further bolster the impact of medical interventions if it allows the treatment of gHAT suspects without confirmation; evaluating the impact of a drug that overcomes the limitations of the current treatment arsenal is beyond the scope of this analysis, and a careful treatment of the matter ought to be pursued [10].

Previous cost-effectiveness analyses have underlined key factors associated with suppression and elimination of gHAT, but this is the first study to confront the question of cost-effectiveness with data from five specific locations [13, 24, 25]. An analysis by Bessel et al shows that RDTs in DRC are cost-effective when employed within AS and PS [24], and an analysis by Davis et al shows that once-per-year AS campaigns within endemic villages are cost-effective to control disease [25]. Only one other analysis, performed by Sutherland et al, examined the combination of multi-faceted strategies, and they found that elimination strategies are likely cost-effective at a WTP of $400-$1500 in high- and moderate-incidence places. One important difference is that we assumed yearly (rather than biennial) AS campaigns at coverage levels that match historical averages (rather than a fixed value of 80% of the population, which would be considered quite high). We also assumed that AS would persist for three years after the last detected case in a health zone, irrespective of the initial incidence of the health zone, whereas Sutherland et al assumed no AS in low-incidence health zones and therefore had to recommend VC activities to reach EOT. In our lower incidence health zones (Boma Bungu and Budjala), the presence of AS meant that EOT could be reached without VC (Table 4).

Our analyses reinforce previous findings that VC would be both an expedited method of achieving EOT and cost-effective in one moderate-incidence health zone (Mosango) and one high-incidence health zone (Kwamouth). However, determining the amount of VC necessary to reach a desired tsetse population reduction is a complicated task, as it depends on local ecology. For transparency, we have shown cost-effectiveness results in a three-way sensitivity analysis in places where VC might be warranted and was not previously in place (Mosango and Kwamouth; see S6 and S5). In Mosango, a modest VC operation could be cost-saving, but these results are contingent on the geographic distribution of current cases as well as on the sensitivity of the tsetse population to targets (see S6). Because Kwamouth is substantially larger than other health zones, the geographic clustering of cases will be important to determine whether all high-risk areas can be addressed in a cost-effective way (see Figure S5).

Our findings took into account historical improvements in PS, which was made possible by more recent data and novel model calibration; this element of the strategies has difficult-to-quantify impacts that might explain some of the difference between our results and previous findings. The fact that our analysis was more optimistic about current practice in lower-incidence health zones underscores the potential of a well-equipped health system that can serve self-presenting gHAT cases. Future analyses on the impact of integrated gHAT surveillance is warranted.

As this paper goes to press, DRC is contending with the emergence of COVID-19, which has triggered the untimely, but hopefully temporary, suspension of AS activities [26]. Elimination strategies would protect the gains that have been made in gHAT control in the twenty-first century [27]. While reported gHAT cases now number under 1000, there remain 54 million people in environments that could sustain gHAT transmission [9]. The epidemic potential of gHAT in locations as resource-constrained as DRC underscores the importance of careful deliberation around strategies of gHAT elimination.

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