Summary: Cost-effectiveness of sleeping sickness elimination campaigns in five settings of the Democratic Republic of Congo

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Abstract

Gambiense *human African trypanosomiasis (gHAT) is marked for elimination of transmission by 2030, but the disease persists in several low-income countries. We couple transmission and health outcomes models to examine the cost-effectiveness of four gHAT elimination strategies in five settings – spanning low- to high-risk – of the Democratic Republic of Congo. Alongside passive screening in fixed health facilities, the strategies include active screening at average or intensified coverage levels, alone or with vector control with a scale-back algorithm when no cases are reported for three consecutive years. In high or moderate-risk settings, costs of gHAT strategies are primarily driven by active screening and, if used, vector control. Due to the cessation of active screening and vector control, most investments (75-80%) are made by 2030 and vector control might be cost-saving while ensuring elimination of transmission. In low-risk settings, costs are driven by passive screening, and minimum-cost strategies consisting of active screening and passive screening lead to elimination of transmission by 2030 with high probability.*

E1 Introduction

In the current study, we undertake an economic evaluation of four gHAT control and elimination strategies in five health zones of the Democratic Republic of Congo (DRC). We adopt a modelling framework in order to examine the interplay of epidemiological, economic and temporal factors in effective decision-making around gHAT strategies for elimination of transmission (EOT). We aim to answer the following questions:

- What are the resource implications of further pursuing gHAT EOT by 2030?
- Which of the considered strategies has the highest probability of being cost-effective in these different settings?

E2 Methods

E2.1 Settings and strategies

- We selected five health zones in DRC described in Table E1 and depicted in Figure E1.
- In each health zone, we simulated four strategies (see Figure E2) with interventions including: either mean or maximum active screening (AS) coverage (Mean AS or Max AS) (see Table E1), and whether or not to deploy vector control (VC). In Yasa Bonga, VC has taken place since mid-2015, so only two strategies were modelled: Mean AS & VC and Max AS & VC.

- All strategies feature continuation of current passive surveillance (PS).
- Cessation was modelled as stopping AS and VC after three consecutive years of zero detected cases by any screening modality. Reactive screening (RS) is started in the event that a new case presents to the fixed health facilities (PS). PS is assumed to remain constant for the duration of our simulations, even after cessation of AS and VC and presumed EOT.

E2.2 Model

The original model fitting (2000–2016) and projections (2017–2050) [1, 2] were modified to simulate costs and outcomes for health zones across DRC for the period of 2020–2050. We used a variant of the "Warwick gHAT model", a previously published model that uses a mechanistic, deterministic modelling framework to explicitly simulate transmission between humans via tsetse vectors.

E2.3 Health outcomes

We used the outputs of the transmission model as inputs in a probability tree model of disease outcomes (see Figure E2). We simulated the disease process separately for stage 1 and stage 2 of the disease, including steps to sort patients into the type of care indicated by the WHO, treatment success or failure, diagnosis in the event of treatment failure, and progression to rescue treatment. For stage 2, an additional step is included to simulate serious adverse events.

Health burden is denominated in disability-adjusted life years (DALYs), but we report cases and deaths for the benefit of the reader (see further discussion of DALYs). We assumed that the mean age of death from gHAT is 26.6 years (95% CI: 22.4-31.8) (see SI section G.6.4).

E2.4 Costs

We developed a cost function that incorporates inputs from the transmission and the treatment models (see SI section A.4). Costs include fixed and variable costs of operation. Disease costs include diagnosis, confirmation, and staging via lumbar puncture, as well as the cost of the drug itself and the administration. We performed our analysis from the perspective of health- or intervention-delivery payers collectively.

E2.5 Economic evaluation and investment horizon

We computed incremental cost-effectiveness ratios (ICERs) by taking the mean difference in costs and health effects (DALYs). As per recent recommendations from the WHO, we refrained from selecting a specific ICER that would be considered "cost-effective", and we aimed to make recommendations after accounting for uncertainty. Therefore, we adopted the net-benefits framework, which expresses the probability that an intervention is optimal at a range of thresholds, known as the willingness-to-pay (WTP) thresholds.

We examined health and cost impacts in the long-term (2020–2040) to assess the returns on investments in both augmented disease control and elimination. Both costs and health outcomes are discounted at a yearly rate of 3%.
A glossary of epidemiology and health economic terms is found in section E5.

E3 Results

E3.1 The impact of strategies on elimination, health, and net costs

Feasibility of elimination. The feasibility of EOT and the cessation of AS are shown in Table E2. While the incidence category of each health zone (Table E1) influences the year when EOT is expected — with higher incidence places likely taking more time than lower incidence places to meet EOT — the implementation of VC is predicted to substantially expedite EOT across all moderate- and high-risk settings considered.
Safe cessation of activities. As cessation of AS (and VC if used) is based on observed cases, it can occur before EOT in some simulations, but on average, cessation occurs after EOT; usually infected cases still remain to be diagnosed and treated once transmission chains have been interrupted. The deployment of VC reduces the probability of RS; when VC is not deployed, up to 62% of our simulations had RS occur (in Boma Bungu and Kwamouth), but with VC, at most 19% of simulations had RS occur in Boma Bungu.

E3.1.1 Health outcomes and costs

Health impact. The health impact and net costs of each strategy between 2020–2040 are shown in Table E3.

- Yasa Bonga, Boma Bungu, Budjala are predicted to have an average of ≤5 reported cases and ≤5 deaths for the next 20 years.
- Mosango is predicted to have a few dozen cases (9–23) and deaths (4–12) in the absence of VC and only slightly higher cases and deaths as Yasa Bonga and Budjala with VC.
- Kwamouth is predicted to have the most cases (116–477) and deaths (49–207), although the burden in terms of DALYs may be cut by three-quarters with VC.

Costs. Cost components are shown in Figure E3.

- AS costs and, when applicable, VC costs played a large role in overall costs, but in Boma Bungu and in Budjala, the relative cost of PS is higher.
- Although strategies with VC incur higher costs at first, much of this is recovered by early cessation of AS activities, thus yielding cumulative costs that are similar to the strategies without VC.
- Cost trends (undiscounted) are shown in Figure E4 - cumulative costs are expected to rise within the first five years of the 2020 decade and then stabilize due AS cessation, and when applicable, the cessation of VC as well.
- For all locations except in Kwamouth under strategies that do not include VC, the additional costs in the 2040s are expenditures in PS.

E3.2 Economic evaluation

The decision analyses are displayed in Table E4 and select features of the table are illustrated in Figure E5.

- In all places but Kwamouth, the optimal strategy (in terms of minimum costs) is in line with strategies predicted to meet the goal of EOT by 2030.
  - In Mosango the current strategy (Mean AS) has a 79% probability of achieving EOT by 2030, and the addition of VC is predicted to both raise the probability of EOT by 2030 and lower costs. However, the potential for cost savings is contingent on the assumption that an operation across 100 km of riverbank deploys 40 targets per kilometer; an operation closer in size to the one in Yasa Bonga would be optimal at a mean cost of $1,488 to $2,051 per DALY averted (see SI Figure 11).
- In Kwamouth, the strategy that ensures EOT by 2030 (Mean AS & VC) is optimal above WTP values of $4 per DALY averted, and was even cost-saving in 44% of simulations. Importantly, the analysis favours VC activities even if target density must be doubled at mean cost of $236 to $343 per DALY averted (see SI Figure 12).

E4 Discussion

E4.1 Key findings

The model predicted substantial decline 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. Although mean total costs in each location vary between $490,000 in Boma Bungu to $5.43 million in Kwamouth, in high-risk areas such as Kwamouth, the additional investments in VC are even potentially cost-saving in 44% of the iterations of our models, with a mean cost of $3.78 million with VC vs $4.19 million (undiscounted) for the same strategy without VC (Table E3).

Yearly costs of interventions range from $0.19-$1.91 per person protected, but optimal strategies would not exceed $1.37 per year – comparable to many other global health interventions (SI Section B.3).

The potential to cease AS and VC activities means that costs are expected to stabilize by the middle or latter part of the 2020's, and in Kwamouth, investments in VC in the early part of the 2020's could be recovered by the mid-2030's Figure E4.

Our analysis is consistent with previous findings (Sutherland and colleagues, 2017, [3]) that VC would be both an expedited method of EOT and cost-effective in one moderate-incidence health zone (Mosango) and one high-incidence

health zone (Kwamouth). To be transparent we have shown cost-effectiveness results in a three-way sensitivity analysis in places where VC might be warranted and it is not currently in place.

In our lower-incidence health zones (Boma Bungu and Budjala) our analysis showed that strategies without VC are very likely to reach EOT under current strategy (Table-E4), unlike the previous analyses.

E4.2 Limitations and future directions

- Any expansions to the publicly available cost estimates would allow analysis to have more confident insights to support policy-making, especially for AS and VC.
- We have not accounted for personnel resource constraints which could play an important factor in whether or not large-scale VC is practical in multiple locations. Although it appears cost-effective to deploy VC in Mosango, there may be competing priorities with other higher-risk health zones for trained VC deployment teams. For example, many more DALYs are averted by deploying in Kwamouth compared to Mosango.
- Potential economies of scale achieved by resource-sharing between neighbouring regions would be pivotal in an expanded, nation-wide analysis of gHAT activities in DRC.
- Although this is the first analysis where fexinidazole was the default treatment, WHO guidelines propose caution in its use, and therefore almost of 65% of patients have to be treated with NECT or on an in-patient basis due to late-stage detection, low body weight, or early age of the patient. The extent of the impact on transmission of a single-dose drug that overcomes the limitations of the current treatment arsenal is beyond the scope of this analysis, and careful treatment of the matter ought to be pursued [4].
- Our findings took into account historical improvements in passive surveillance, but the impact of strengthening PS across DRC ought to be evaluated.
- The prospect of a one-dose acoziborole treatment for gHAT.
- The potential impact of disruption of gHAT activities (e.g. Ebola, COVID-19) on elimination was not assessed here but a related study found that the EOT goal could still be within reach as long as disruptions remain short [5].

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E5 Glossary of epidemiologic and health economic terms

Box 1: Glossary

Epidemiology Terms

Intervention Interventions are separate activities to address a health need (e.g. active screening (AS) or vector control (VC)).

Strategy A strategy is a combination of interventions, carried out with a specific coverage, and in parallel. In this paper, we simulate strategies with and without an improvement in AS and with and without VC (e.g. strategy 1 is passive surveillance (PS) and mean AS, and strategy 4 is PS, maximum AS and VC).

Elimination of transmission (EOT) Globally this is the 2030 goal for gHAT; here we also consider local EOT for health zones. The feasibility of EOT is expressed as a probability equal to the proportion of our simulations in which new infections is zero before a given year (usually 2030).

Disability-adjusted life-year (DALY) In order to present the burden of disease in one common metric across diseases, DALYs are calculated in cost-effectiveness analyses. This is the sum of the years lived with disability due to the disease and the years of life lost by fatal cases. See section A.3.

Health Economics Terms

Parameter uncertainty Uncertainty in the level of transmission or in the costs of interventions and treatment due to unknown underlying parameters (see supplementary section G for an explanation of our parameterization of the health outcomes and cost model).

Willingness-to-pay (WTP) or cost-effectiveness threshold The amount of money that payers would pay to avert one DALY arising from the disease in the analysis (gHAT). No specific threshold is recommended, but a recent analysis shows that the WTP in DRC is between 5 - 230 USD per DALY averted [6–8].

Incremental cost-effectiveness ratio A ratio of marginal cost for a marginal benefit, calculated as follows:

$$\text{ICER} = \frac{\Delta\text{Costs}}{\Delta\text{DALYs}} = \frac{\text{Costs}_{\text{strategy}} - \text{Costs}_{\text{next best}}}{\text{Effects}_{\text{strategy}} - \text{Effects}_{\text{next best}}}$$

For an example on how interventions are ranked and ICERs are calculated, see Section C.1.

Cost-effective strategy The strategy where the ICER is less than the WTP (or cost-effectiveness threshold). We say that the cost-effective strategy is “conditional" on the WTP.

Dominated strategy A strategy that costs more than the minimum cost intervention while reducing the burden by a smaller degree. This strategy ought not be implemented.

Weakly dominated strategy (or strategies under extended dominance) A strategy in which the ICER is higher that the next more expensive strategy. See section C.1 for a discussion on this matter with respect to the strategies presented in this analysis.

Net monetary benefit The net benefits (NMB) framework is derived from ICERs, but also takes uncertainty into account.

$$\text{NMB|WTP} : \text{WTP} \times \Delta\text{DALYs} - \Delta\text{Costs}$$

The optimal strategy at a given WTP is the strategy with the highest mean NMB at that value of WTP.

Optimal strategy Analogous to the cost-effective strategy when no uncertainty is assumed, this is the strategy that is recommended by the NMB framework.

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 (km^2)	2,606	2,673	14,589	2,866	4,397
Active screening as a percent of 2016 population (mean, max)	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

Table E1: 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.

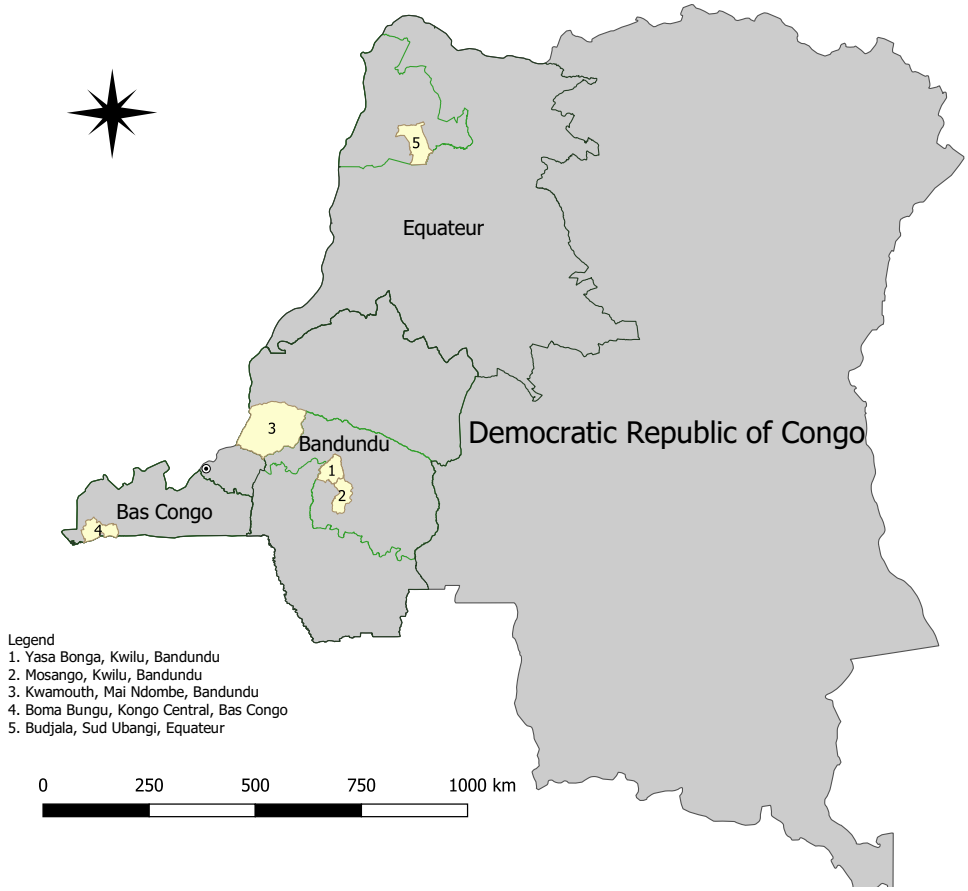

Figure E1: Locations of the specific health zones considered in this study are shown in yellow. New provincial boundaries are denoted in green, and former provincial designations are denoted in black.

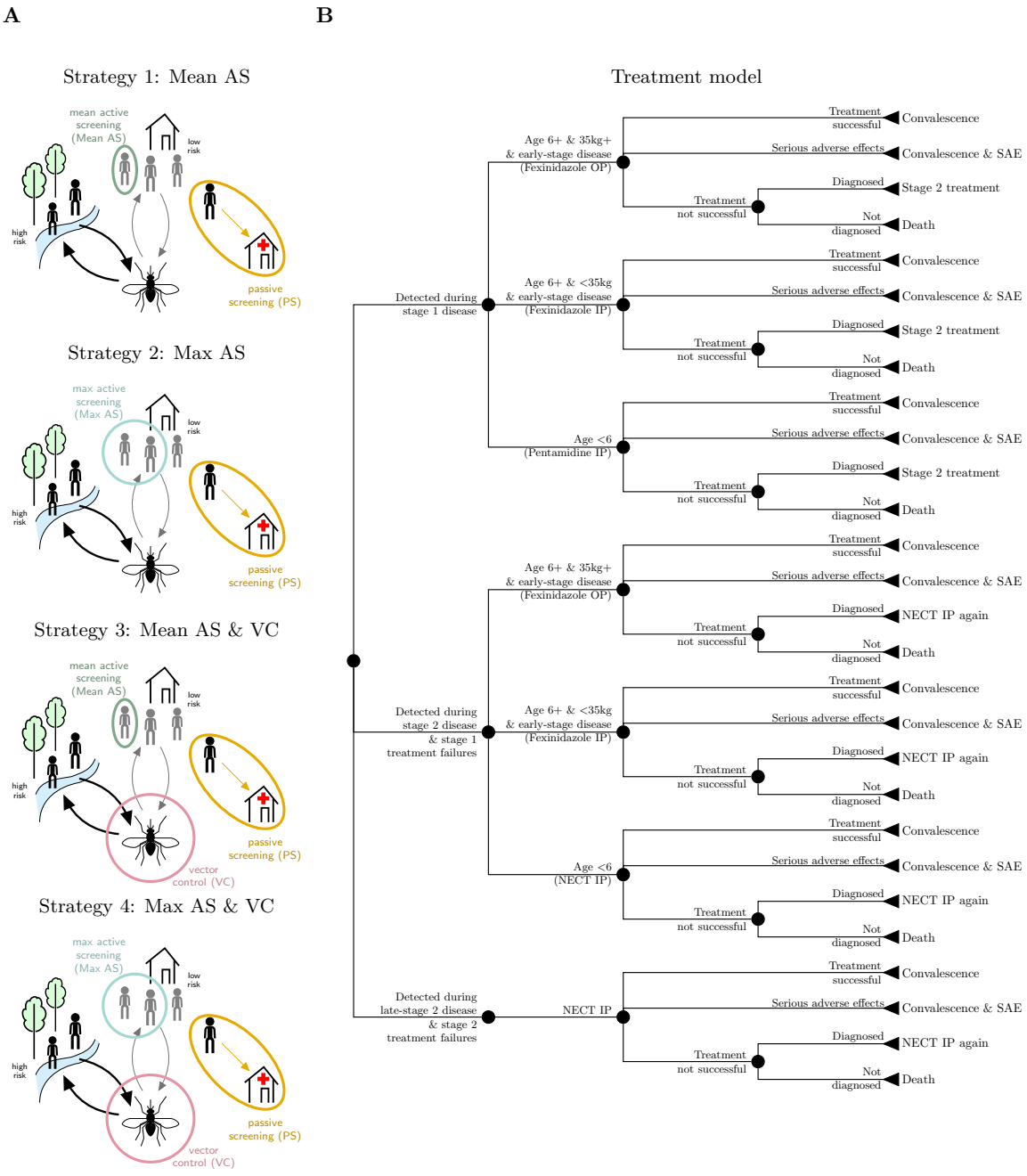

Figure E2: Model of strategies and treatment against gHAT in DRC. A) Strategies against gHAT, including active screening (AS) by mobile teams, passive surveillance (PS) in fixed health facilities, and vector control (VC). In two strategies ('Mean AS' and 'Mean AS & VC') the proportion screened equalled 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. B) Treatment for diagnosed gHAT patients is modeled as a branching tree process of possible health outcomes including eligibility for novel fexinidazole. Abbreviations: SAE: Serious adverse events, IP: inpatient care, OP: outpatient care.

	Year of EOT (95% PI)	Prob. EOT by 2030	Prob. EOT by 2040	Year AS ends (95% PI)	Prob. RS
Yasa Bonga					
Mean AS & VC	2017 (2016, 2017)	>0.99	>0.99	2024 (2021, 2028)	0.11
Max AS & VC	2017 (2016, 2017)	>0.99	>0.99	2024 (2021, 2028)	0.12
Mosango					
Mean AS	2028 (2021, 2037)	0.79	0.99	2028 (2022, 2036)	0.39
Max AS	2026 (2021, 2033)	0.92	>0.99	2027 (2022, 2033)	0.33
Mean AS & VC	2021 (2020, 2021)	>0.99	>0.99	2025 (2022, 2028)	0.09
Max AS & VC	2021 (2020, 2021)	>0.99	>0.99	2025 (2022, 2028)	0.07
Kwamouth					
Mean AS	2048 (2036, Post-2050)	<0.01	0.11	2043 (2034, Post-2050)	0.58
Max AS	2047 (2036, Post-2050)	<0.01	0.13	2043 (2033, Post-2050)	0.62
Mean AS & VC	2022 (2022, 2023)	>0.99	>0.99	2029 (2026, 2035)	0.12
Max AS & VC	2022 (2022, 2023)	>0.99	>0.99	2029 (2026, 2035)	0.13
Boma Bungu					
Mean AS	2019 (2017, 2022)	>0.99	>0.99	2023 (2021, 2027)	0.02
Max AS	2019 (2017, 2022)	>0.99	>0.99	2023 (2021, 2026)	0.02
Mean AS & VC	2018 (2017, 2020)	>0.99	>0.99	2022 (2021, 2026)	0.02
Max AS & VC	2018 (2017, 2020)	>0.99	>0.99	2022 (2021, 2025)	0.01
Budjala					
Mean AS	2023 (2017, 2031)	0.97	>0.99	2023 (2020, 2030)	0.36
Max AS	2021 (2017, 2024)	>0.99	>0.99	2023 (2020, 2027)	0.22
Mean AS & VC	2020 (2017, 2024)	>0.99	>0.99	2023 (2020, 2026)	0.19
Max AS & VC	2020 (2017, 2023)	>0.99	>0.99	2023 (2020, 2026)	0.15

Table E2: Feasibility of elimination (additional scenarios are shown in the supplement). Estimates shown are means and their 95% prediction intervals (PI). Color scheme for years: earlier years are in blue tones and later years are in red tones. Prob. EOT (elimination of transmission) is calculated as a proportion of the iterations of the dynamic transmission model for which transmission has reached <1 person by the designated year (2030 or 2040). Prob. RS (reactive screening) is calculated as a proportion of the iterations of the dynamic transmission model for which active screening must be re-activated after it has ceased.

	Cases detected (95% PI)	Deaths (95% PI)	DALYs (95% PI)	Total costs ($ millions) (95% PI)	Yearly costs ($) per capita (95% PI)
Yasa Bonga					
Mean AS & VC	5 (0, 23)	2 (0, 7)	62 (1, 240)	3.11 (1.63, 5.27)	0.67 (0.35, 1.13)
Max AS & VC	4 (0, 23)	2 (0, 7)	62 (1, 242)	3.84 (1.83, 6.80)	0.82 (0.39, 1.46)
Mosango					
Mean AS	23 (1, 79)	12 (1, 42)	426 (32, 1,418)	1.27 (0.62, 2.33)	0.48 (0.23, 0.89)
Max AS	22 (0, 92)	8 (0, 28)	282 (2, 987)	1.69 (0.75, 3.25)	0.64 (0.29, 1.24)
Mean AS & VC	9 (0, 41)	5 (0, 15)	169 (2, 510)	1.15 (0.63, 1.85)	0.44 (0.24, 0.70)
Max AS & VC	10 (0, 54)	4 (0, 12)	131 (1, 421)	1.46 (0.74, 2.46)	0.56 (0.28, 0.94)
Kwamouth					
Mean AS	477 (144, 1,081)	207 (41, 614)	7,229 (1,496, 21,131)	4.19 (2.88, 6.42)	1.52 (1.05, 2.33)
Max AS	463 (136, 1,047)	174 (36, 499)	6,067 (1,304, 17,296)	5.43 (3.64, 8.54)	1.97 (1.32, 3.10)
Mean AS & VC	116 (41, 235)	54 (18, 116)	1,890 (628, 4,025)	3.78 (2.49, 5.92)	1.37 (0.91, 2.15)
Max AS & VC	120 (38, 270)	49 (16, 105)	1,718 (562, 3,656)	4.33 (2.77, 7.03)	1.57 (1.01, 2.55)
Boma Bungu					
Mean AS	1 (0, 10)	0 (0, 4)	17 (0, 149)	0.49 (0.32, 0.71)	0.27 (0.18, 0.39)
Max AS	1 (0, 10)	0 (0, 3)	13 (0, 109)	0.60 (0.37, 0.92)	0.33 (0.21, 0.51)
Mean AS & VC	1 (0, 7)	0 (0, 3)	13 (0, 107)	0.62 (0.39, 0.95)	0.35 (0.21, 0.53)
Max AS & VC	1 (0, 8)	0 (0, 3)	11 (0, 97)	0.73 (0.43, 1.16)	0.40 (0.24, 0.64)
Budjala					
Mean AS	4 (0, 22)	5 (0, 18)	163 (0, 601)	0.55 (0.36, 0.80)	0.20 (0.13, 0.29)
Max AS	4 (0, 24)	2 (0, 8)	80 (0, 277)	0.92 (0.45, 1.55)	0.33 (0.16, 0.55)
Mean AS & VC	2 (0, 12)	2 (0, 8)	83 (0, 274)	0.69 (0.41, 1.06)	0.25 (0.15, 0.38)
Max AS & VC	3 (0, 19)	2 (0, 6)	56 (0, 208)	1.01 (0.46, 1.68)	0.36 (0.17, 0.60)

Table E3: Summary of effects and costs 2020-2040. Two differences should be noted between these estimates and those used for decision analysis shown in Table 4. 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 95% prediction intervals (PI) of the cases, deaths, disability-adjusted life-years (DALYs), and costs across iterations of the dynamic transmission model.

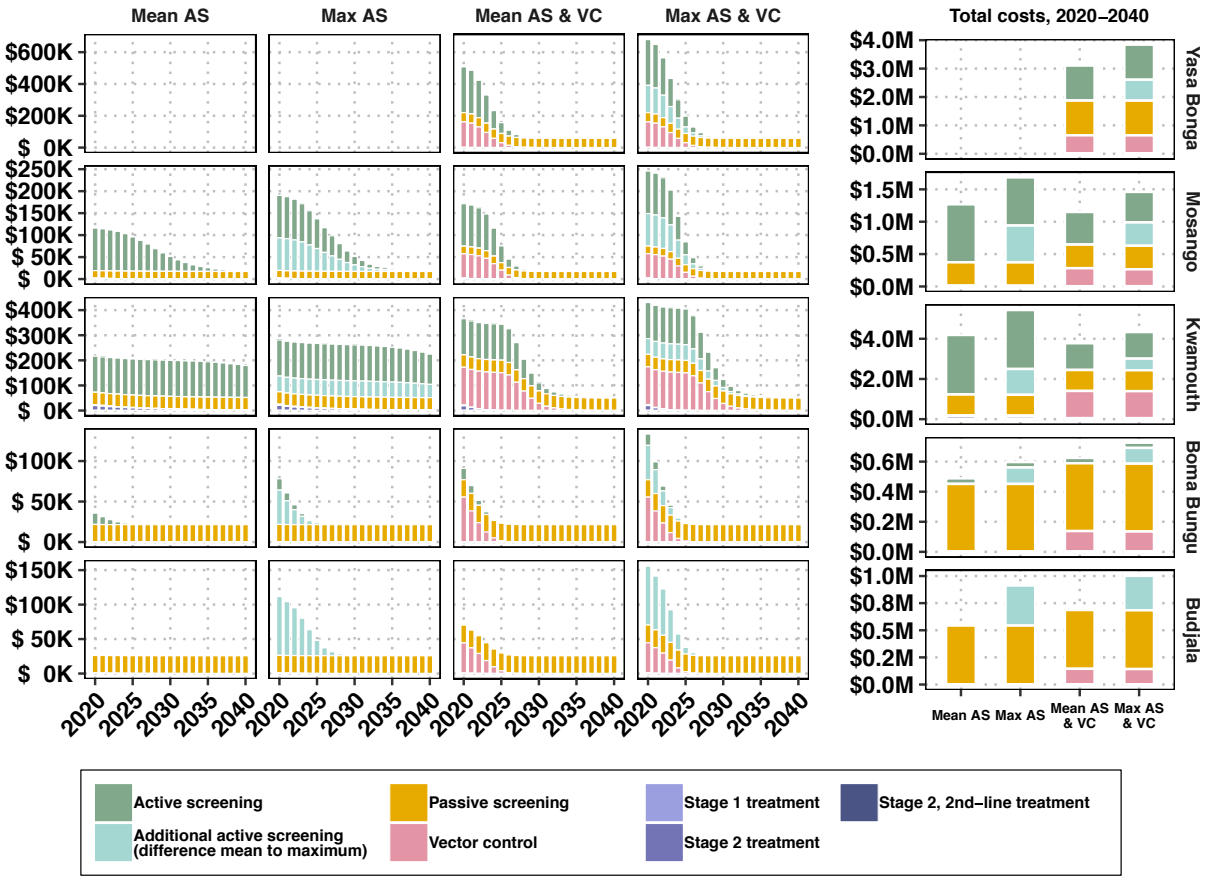

Figure E3: Displayed costs are not discounted. Treatment costs, indicated in purple, are expressed here although relatively small.

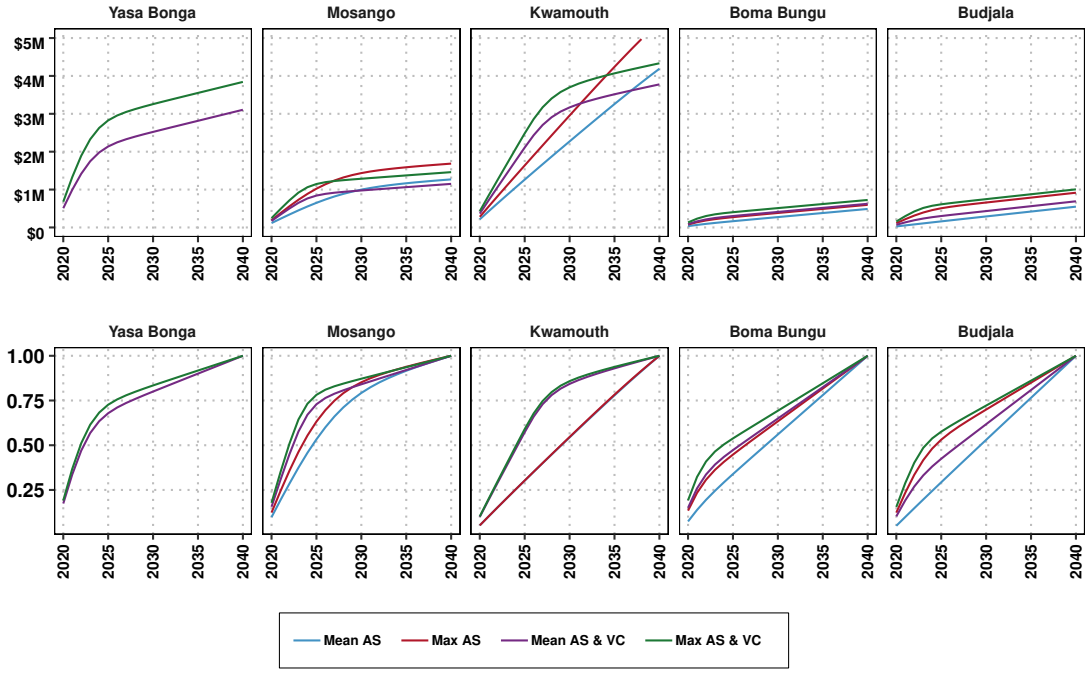

Figure E4: Cumulative costs for each strategy through time, by health zone (top row) and the percent of the total cost spent by each year (bottom). Costs are not discounted.

	Cost-effectiveness analysis without uncertainty			Net benefit (uncertainty) analysis: Prob. that a strategy is optimal, (conditional on willingness-to-pay)				
	Cost difference vs comparator	DALYs averted vs comparator	ICER	$0 per DALY averted	$250 per DALY averted	$500 per DALY averted	$1,000 per DALY averted	Prob. EOT by 2030
Yasa Bonga								
Mean AS & VC	0	0	Min Cost	0.78	0.78	0.78	0.78	>0.99
Max AS & VC	671,462	0	2,209,891	0.22	0.22	0.22	0.22	>0.99
Mosango								
Mean AS	0	0	Dominated	0.38	0.33	0.29	0.24	0.79
Max AS	377,463	80	Dominated	0.04	0.04	0.04	0.05	0.92
Mean AS & VC	-48,090	142	Min Cost	0.49	0.53	0.56	0.59	>0.99
Max AS & VC	237,522	165	12,215	0.08	0.09	0.1	0.13	>0.99
Kwamouth								
Mean AS	0	0	Min Cost	0.44	0.21	0.14	0.07	<0.01
Max AS	921,216	602	Dominated	0	0	0	0	<0.01
Mean AS & VC	11,632	2,753	4	0.49	0.65	0.68	0.69	>0.99
Max AS & VC	489,117	2,861	4,421	0.07	0.14	0.18	0.24	>0.99
Boma Bungu								
Mean AS	0	0	Min Cost	1	0.99	0.99	0.99	>0.99
Max AS	101,606	3	40,288	0	0	0	0.01	>0.99
Mean AS & VC	127,894	2	Dominated	0	0	0	0.01	>0.99
Max AS & VC	223,232	4	93,060	0	0	0	0	>0.99
Budjala								
Mean AS	0	0	Min Cost	0.91	0.87	0.85	0.76	0.97
Max AS	335,786	47	Weakly Dominated	0.04	0.03	0.03	0.03	>0.99
Mean AS & VC	131,747	45	2,922	0.04	0.07	0.1	0.18	>0.99
Max AS & VC	423,280	62	17,515	0.01	0.02	0.02	0.03	>0.99

Table E4: Summary of cost-effectiveness, assuming a time horizon of 2020-2040. Cost differences and differences in disability-adjusted life-years (DALYs) averted are relative to the comparator–first strategy listed for each location. Mean DALYs averted and mean cost differences are shown; these estimates are discounted at 3 percent per year in accordance with guidelines. The uncertainty analysis (columns 5-8) shows the probability that a strategy is cost-effective. Strategies highlighted in pink are optimal strategies: the strategies for which the mean net monetary benefit (NMB) is highest, equivalent to the information found in cost-effectiveness acceptability frontiers (CEAFs), which are shown Supplementary Figures 7- 8. ICER: incremental cost-effectiveness ratio. For an extended discussion of these terms, see the Supplementary Note 1: Glossary of Technical Terms. For a full explanation of the concept of strong and weak dominance, see the Supplementary Discussion.

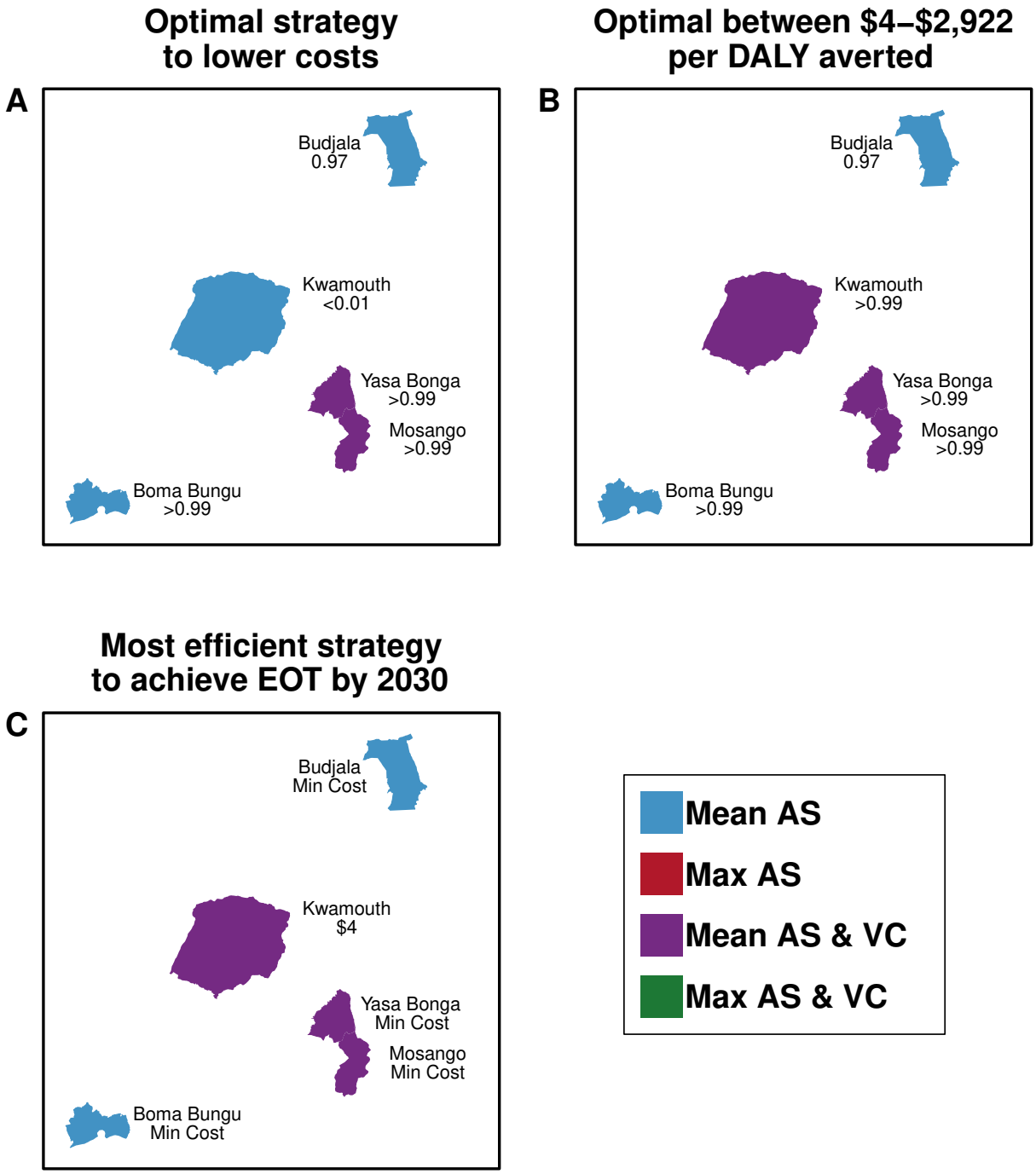

Figure E5: Maps of preferred strategies according to economic or budgetary goals for 2020–2040. Maps A & B show the optimal strategies depending on WTP. The text indicates the probability that the optimal strategy will lead to EOT by 2030. Map C shows the most efficient strategy that has >90% probability 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 shown in Supplementary Figures 9 and 10.