Summary: Economic evaluation of disease elimination: an extension to the net-benefit framework and application to human African trypanosomiasis

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The global health community has earmarked a number of diseases for elimination or eradication, and these goals have often been praised on the premise of long-run cost-savings. However, decision-makers must contend with a multitude of demands on health budgets in the short- or medium-term, and costs-per-case often rise as the burden of a disease falls, rendering such efforts beyond the cost-effective use of scarce resources. In addition, these decisions must be made in the presence of substantial uncertainty regarding the feasibility and costs of elimination or eradication efforts. Therefore, analytical frameworks are necessary to consider the additional effort for reaching global goals, like elimination or eradication, that are beyond the cost-effective use of country resources. We propose a modification to the net-benefit framework to consider the implications of switching from an optimal strategy, in terms of cost-per-burden-averted, to a strategy with a higher likelihood of meeting the global target of elimination of transmission by a specified date. We illustrate the properties of our framework by considering the economic case of efforts to eliminate transmission of *gambiense* human African trypanosomiasis (gHAT), a vector-borne parasitic disease in West and Central Africa, by 2030.

eradication | elimination | economic evaluation | mathematical modeling

Various diseases are now earmarked for elimination by the global health community. While the health economic implications of elimination have been discussed before, the combination of uncertainty, cost-effectiveness in terms of cases averted, and elimination in the face of rising per-case costs has not been tackled before. The absence of probabilistic thinking in previous literature fails to capture a key component of the decision-making process.

We propose an approach that considers the tension between the dual objectives of cost-effectiveness and elimination while incorporating uncertainty in these objectives. Specifically, we extend the net-benefits framework, useful for decision-analysis in the presence of uncertainty, in order to simultaneously evaluate cost-effectiveness of public health strategies while explicitly outlining the 'premium' of elimination, or the additional resources that are necessary to bring a country activities in line with global goals. We then apply our new framework to the analysis of campaigns against *gambiense* human African trypanosomiasis (gHAT) in three distinct regions of the Democratic Republic of Congo (DRC).

Economic framework

The metric of efficiency within the net benefits framework is the net monetary benefit (NMB):

$$\mathrm{NMB}(\lambda^{\mathrm{WTP}}) = \lambda^{\mathrm{WTP}} \times \Delta E - \Delta C$$

The NMB captures the justifiable cost of a strategy minus the actual cost of the strategy. The justifiable cost is the product of the disease burden averted, denominated as Disability-Adjusted Life-Years (DALYs), and the willingness-to-pay (WTP)* for a marginal gain in a unit of health. The strategy whose justifiable cost surpasses the actual cost by the largest margin is the strategy that yields the largest net monetary cost, and hence, the most efficient strategy.

We propose the following adjustment for the NMB, which we term the net monetary elimination benefit (NMEB), which distinguishes between the cost of an intervention justifiable by disease averted (e.g. DALYs) the cost justifiable by an objective of elimination of transmission (EOT), above and beyond the disease objective.

$$\mathrm{NMEB}(\lambda^{\mathrm{WTP}}_{\mathrm{DALY}}, \lambda^{\mathrm{WTP}}_{\mathrm{EOT}}) = \lambda^{\mathrm{WTP}}_{\mathrm{DALY}} \times \Delta\mathrm{DALYs} + \lambda^{\mathrm{WTP}}_{\mathrm{EOT}} \times \Delta\mathbb{I}_{\mathrm{EOT}} - \Delta C$$

We used disease model projections and cost model from previous studies (1–3) to apply our framework to the analysis of end-game interventions in three illustrative settings in the Democratic Republic of Congo (DRC). The strategies analyzed are in table 1.

For the purpose of this summary, we present Region 1 (Kwamouth) and Region 3 (Sia), further described in Table S1.

Table 1. Strategies for control and elimination of gHAT in a typical endemic health district.

Component Interventions	Strategy: Mean AS‡	Max AS	Mean AS & VC	Max AS & VC
Mean active screening	✓	✓	✓	✓
Additional active screening		✓		✓
Passive surveillance	✓	✓	✓	✓
Vector control			✓	✓
Treatment of cases	✓	✓	✓	✓

‡ Status quo strategy.

*Note on willingness-to-pay (WTP) values The WTP is not a metric equivalent to the total cost of the program, it is a metric of comparative efficiency, considering incremental costs and incremental effects between two or more strategies. In general, it is difficult to take the previous policy behaviour as a guide of what current WTP might be, unless similar cost-effectiveness analyses were done at the time. Moreover, incremental costs are expected to rise when there are other efforts in place to address the burden of that disease. Because we aim to provide guidance rather than prescription, we adhere to recent WHO recommendations to show a variety of WTP values in cost-effectiveness analyses. There are no recommendations for the WTP values for elimination, $\lambda^{\mathrm{WTP}}_{\mathrm{EOT}}$.

M.A. performed the formal analysis, created visualizations. M.A., K.S.R. and F.T. conceptualized the study and wrote the original draft. K.S.R. and F.T. acquired funding and supervised the study. C.H. performed simulations. All authors reviewed and edited the final draft.

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Results

Net Monetary Elimination Benefits: Region 1, where success and failure of EOT by 2030 are certain. For Region 1, where success and failure of EOT by 2030 is certain, the probability of EOT is shown in 1A and the results of our decision analysis under the traditional net benefits framework are shown in Figure 1B. At the low $\lambda^{\mathrm{WTP}}_{\mathrm{DALY}}$=\$0, our analysis shows that Mean AS has an 80% probability of being the only cost-neutral or cost-saving strategy. The expected $\mathrm{Premium}_{\mathrm{EOT}}$, is shown in 1C. In a policy environment of low $\lambda^{\mathrm{WTP}}_{\mathrm{DALY}}$, any health planner must be able to justify the entire \$709,800 in additional economic resource on the basis of EOT alone.

We show the optimal choice of strategy for a range of $\lambda^{\mathrm{WTP}}_{\mathrm{DALY}}$ and $\lambda^{\mathrm{WTP}}_{\mathrm{EOT}}$ values in Figure 1D. In a policy environment where $\lambda^{\mathrm{WTP}}_{\mathrm{DALY}}$=0 and $\lambda^{\mathrm{WTP}}_{\mathrm{EOT}}$>7,100, the optimal strategy guarantees elimination, as that is the $\lambda^{\mathrm{WTP}}_{\mathrm{EOT}}$ that justifies the \$709,800 premium of elimination.

However, as the policy environment becomes more generous, for instance if $\lambda^{\mathrm{WTP}}_{\mathrm{DALY}}$=\$300, the strategy Mean AS & VC has between a 47%-55% probability of being optimal, which is the strategy that reaches EOT. Therefore, EOT is entirely justifiable on the health gains achieved (DALYs averted), and the $\mathrm{Premium}_{\mathrm{EOT}}$ is therefore \$0.

Net Monetary Elimination Benefits: Region 3, where success and failure is uncertain. Our most complex setting, Region 3, is shown in Figure 2. Under the traditional net benefits framework, either the Mean AS or Max AS strategy are cost-effective at $\lambda^{\mathrm{WTP}}_{\mathrm{DALY}}$ values consistent with historical investment levels in low-income countries (Fig 2C), but these strategies have only a 42% and 54% probability of EOT respectively (inset Fig 2B). Without an investment justifiably by an EOT objective, EOT will remain uncertain.

At $\lambda^{\mathrm{WTP}}_{\mathrm{DALY}}$=0, then a decision-maker must have a $\lambda^{\mathrm{WTP}}_{\mathrm{EOT}} \geq$ \$15,747 and incur a $\mathrm{Premium}_{\mathrm{EOT}}$=\$194,000 to bolster the chances of elimination from 42% to 54% or $\lambda^{\mathrm{WTP}}_{\mathrm{EOT}} \geq$ \$11,210 and incur a $\mathrm{Premium}_{\mathrm{EOT}}$=\$651,000 to bolster the probability of elimination from 42% to >99%. Therefore, as long as one does not value DALYs averted, the switch from Mean AS to Max AS would incur a lower premium, but switching to Mean AS & VC would be more efficient on the basis of per-point probability of reaching EOT (Fig 3 and Table S4).

Discussion

We have extended the net benefits framework to inform decisions that contain an elimination objective that may stand at odds with concerns about efficient resource allocation. The illustrative analysis shows that in Region 1 elimination is nearly impossible with the comparator strategy, but elimination is cost-effective at a relatively low $\lambda^{\mathrm{WTP}}_{\mathrm{DALY}}$>260. The other region presents a more complicated policy prescription: elimination is likely in Region 3 (42%) even with the comparator strategy (Mean AS), but the value-for-money in terms of EOT objectives is lower. However, raising the probability of EOT to >99% has a lower Premium of Elimination but is less efficient in Region 3 than in Region 1.

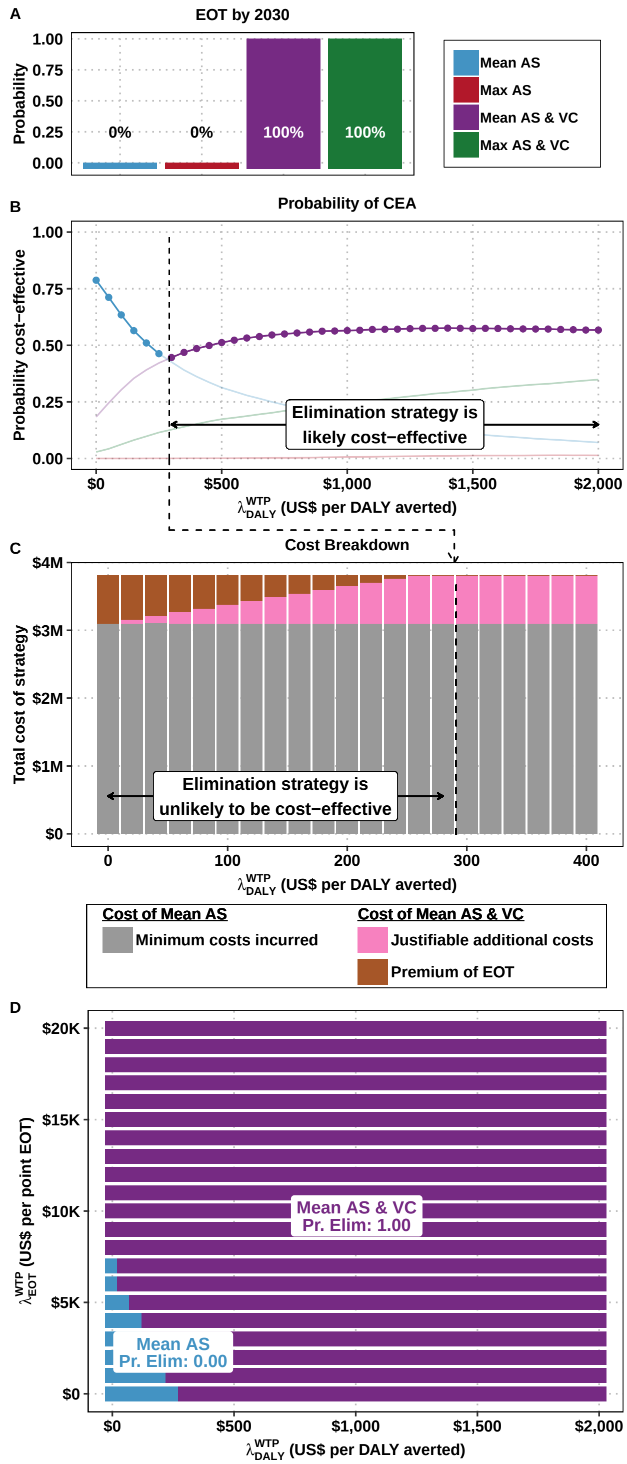

Fig. 1. A) Probability of elimination for each strategy, B) cost-effectiveness acceptability curves, C) cost breakdown, and D) Cost-effectiveness acceptability heatmap (CEAH) for Region 1. On (D) along the x-axis is the willingness-to-pay (WTP) for control (to avert disability-adjusted life-years (DALYs), and along y-axis are the WTP for elimination of transmission (EOT); the resources available above and beyond those dedicated to averting DALYs.

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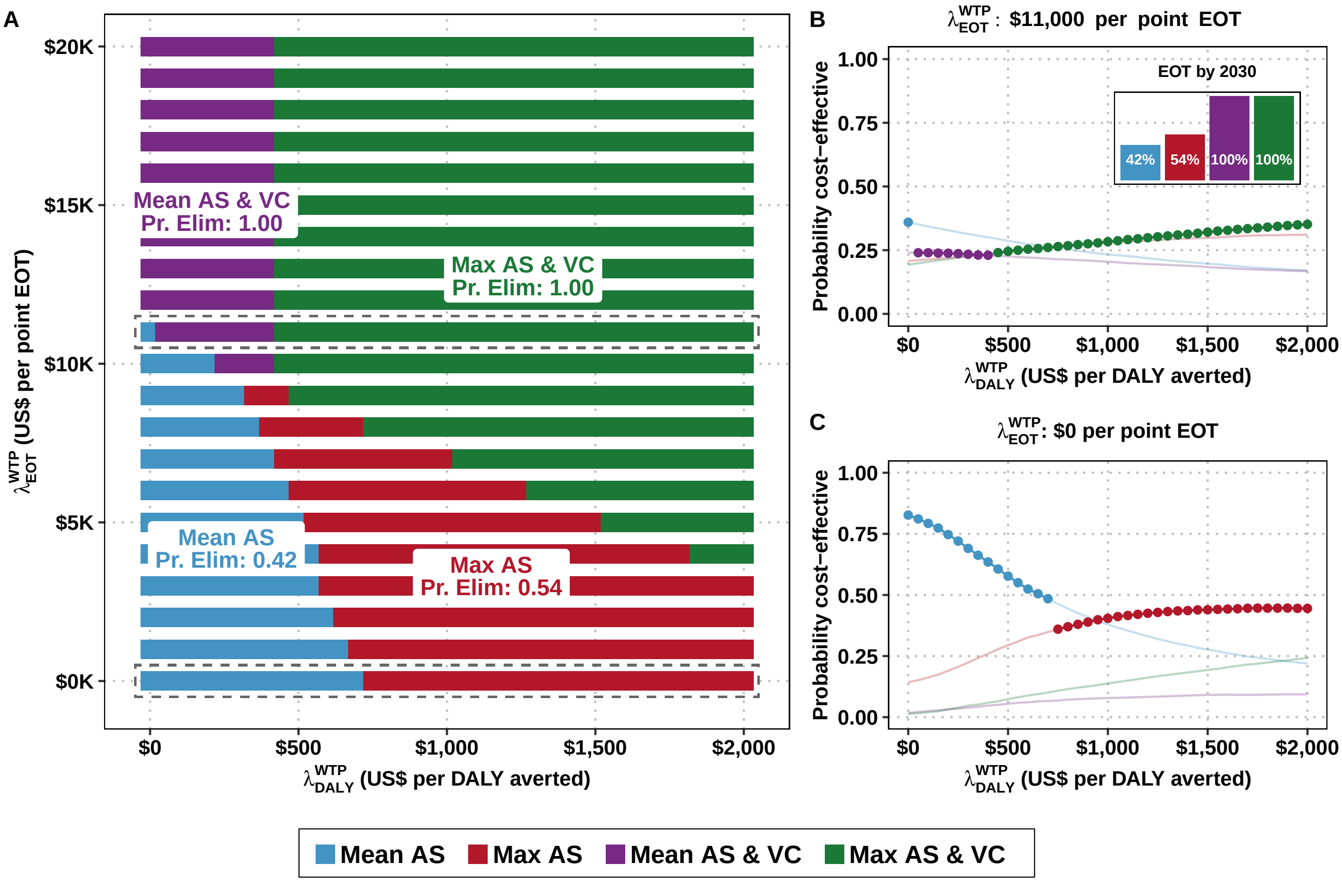

Fig. 2. Cost-effectiveness acceptability heatmaps for Region 3. A) Cost-effectiveness acceptability heatmap (CEAH). Along the x-axis is the willingness-to-pay (WTP) for control (to avert disability-adjusted life-years (DALYs), and along y-axis are the WTP for elimination of transmission (EOT); the resources available above and beyond those dedicated to averting DALYs. B-C) traditional cost-effectiveness acceptability frontiers (CEAFs). The inset in (B) is the probability of each strategy's EOT by 2030.

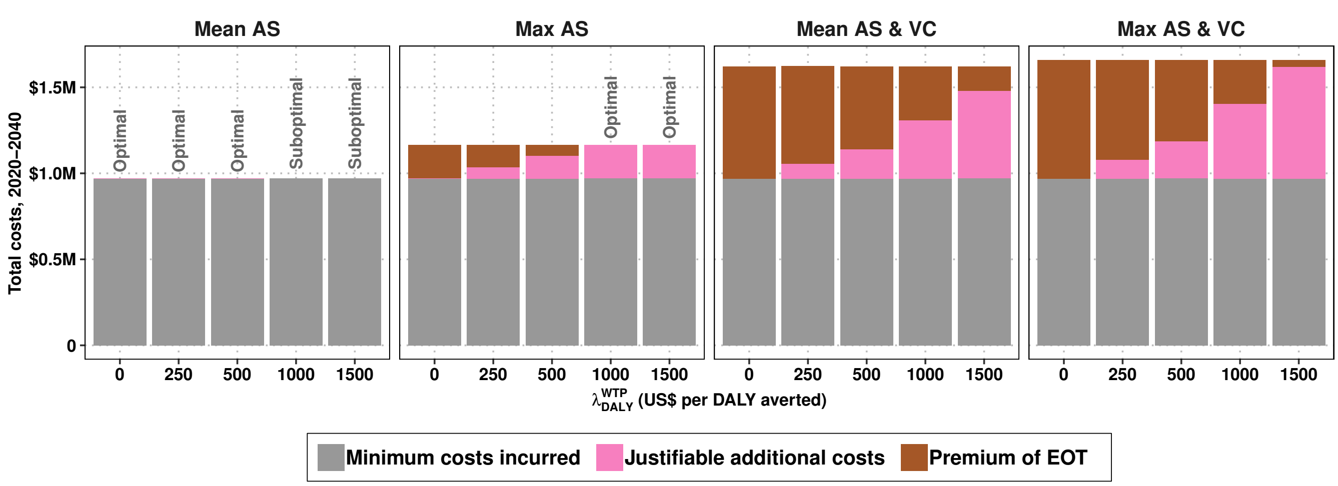

Fig. 3. Premium of elimination in Region 3, across different values of λ_{DALY}^{WTP}, contextualized in table 1.