Summary:
A modelling assessment of short- and medium-term risks of programme interruptions for *gambiense* human African trypanosomiasis in the DRC

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Abstract

Gambiense human African trypanosomiasis (gHAT) is a deadly vector-borne, neglected tropical disease found in West and Central Africa which is targeted for elimination of transmission (EoT) by 2030. In light of the recent global pandemic, it is important to quantify the impact that unplanned disruption to programme activities may have in achieving EoT. We used a previously developed model of gHAT fitted to data from the Democratic Republic of the Congo (DRC), a country with the highest global case burden, to explore how interruptions to intervention activities, due to e.g. COVID-19, Ebola or political instability, could impact progress towards EoT. We simulated transmission and reporting dynamics in 38 health zones of the former Bandundu province under six interruption scenarios lasting for nine or twenty-one months. Interruption scenarios all include the cessation of active screening, and some also include reduction in passive detection rates, and a delay or suspension of vector control deployments. Our results indicate that, even under the most extreme 21-month interruption scenario, EoT is not predicted to be delayed by more than one additional year compared to the length of the interruption. If existing vector control deployments continue, we predict a marginal impact on the year of EoT even when both active and passive screening activities are interrupted. If passive screening remains fully functional, we expect the EoT delay to be shorter, however this depends on the strength of passive screening in each health zone. We predict a pronounced increase in additional gHAT disease burden (morbidity and mortality) in many health zones when active and passive screening are interrupted compared to the interruption of active screening alone. The ability to continue existing vector control during medical activity interruption is also predicted to avert a moderate proportion of disease burden.

Introduction

Whilst the COVID-19 pandemic has produced wide-spread disruption for many disease programmes there are also a range of other factors that continue to risk programme interruptions including other disease outbreaks (e.g. Ebola, cholera, yellow fever and measles) and the potential for political instability. In this study we examine the impact of interruptions by external factors to the *gambiense* human African trypanosomiasis (gHAT, sleeping sickness) elimination programme of the Democratic Republic of the Congo (DRC), a country which has the highest global case burden. We use our previously fitted gHAT model to simulate how transmission dynamics might be impacted by disruption to medical interventions and (where relevant) vector control (VC) activities in 38 health zones of the former Bandundu province. For each of the six interruption scenarios we use the model to forecast case numbers and disability-adjusted life years (DALYs, a measure of disease burden) as well as estimating the expected years and probabilities of elimination of transmission (EoT). This analysis provides invaluable insight into the impact that interruptions of any persuasion could have on the burden, case reporting and EoT of gHAT in the DRC.

Methods

Model

We used our mechanistic, deterministic gHAT model, previously fitted at the health zone level [1], to perform projections under six interruption scenarios, which were compared to a baseline scenario in 38 health zones in the former Bandundu province. Outputs from the model include expected annual active and passive case reporting, numbers of new infections each year, and annual DALYs which is a measure of disease burden.

Baseline Scenario (No interruption)

The Baseline scenario represents the intervention plans for the health zone in the absence of interruptions. For those health zones without previous VC or future plans, the baseline strategy used was *MeanAS* representing a mean coverage of active screening (AS) with the mean number of people screened in each health zone begin calculated based on the 2014–2016 HAT Atlas and the 2017–2018 PNLTHA-DRC active screening data. For those health zones with previous VC or future VC plans, the baseline strategy is *MeanAS+VC*. All health zones were assumed to have passive screening (PS) in fixed health facilities with detection rates inferred through fitting to the historical data (2000–2016).

Interruption Scenarios

We considered two different durations of interruption to gHAT activities in the DRC based on the recent COVID-19 pandemic (see Figure 1 for details). The scenarios begin from April 2020, coinciding with the government national lockdown and travel ban announcement made on 28 March 2020, until either the end of 2020 (9-month) or 2021 (21-month). We accounted for three categories of restrictions with different levels of impact on current interventions:

1. *No AS* - AS suspension
2. *No AS and reduced PS* - AS suspension and a reduction in the passive detection rate due to limited health facility capacity or reduced levels of gHAT patients self-presenting at facilities
3. *No AS or VC, and reduced PS* - AS suspension, reduced PS detection rate, and no VC deployment (if on-going or planned)

We assumed that AS continued as planned between January to March 2020 and therefore AS coverage in 2020 is a quarter of the baseline strategy. Interruption to PS is assumed to be partial and we therefore reduced PS detection rates to the post-1998 level for scenarios in which PS is interrupted. For health zones that had VC prior to the interruption period, we assume deployments planned for July 2020 are suspended in the 9-month scenario with no VC, and deployments planned for July 2020, January 2021 and July 2021 are suspended in the 21-month scenario with no VC. In regions with planned roll out of VC in 2020 or 2021, we assumed deployments would be suspended until July 2021 and July 2022, for the 9- and 21-month scenarios, respectively.

Results

Health zone with no previous or planned VC: Mosango

We selected Mosango, as a health zone with no previous or planned VC, to illustrate the impact of the 9- and 21-month interruption scenarios on active and passive case numbers, DALYs, probability of EoT by 2030 (PEoT) and the expected year of EoT (YEoT). We have highlighted our main findings for Mosango below:

1. ***No AS* interruption scenario:** Numbers of passive cases and new infections increase marginally during and after the interruption period and the model predicts an average of 35.2 and 76.3 extra DALYs accrued over the next ten years in the 9- and 21-month interruption scenarios (Figure 2). The estimated median YEoT remains the same between *No AS* and baseline scenarios but the PEoT by 2030 is predicted to be lowered by 2.7 and 5.9% when AS is interrupted by 9 and 21 months, respectively.
2. ***No AS and reduced PS* interruption scenario:** The model predicts more post-interruption active and passive cases and new infections compared to those in the *No AS scenario*. This scenario could also result in increasing DALYs accrued by around 2-fold compared to interruption of AS alone (61.4 and 152.7 DALYs, 9- and 21-months, respectively). This highlights the importance of PS in managing disease burden in the absence of VC. Delay in the median YEoT only occurs in the 21-month interruption scenario for Mosango (delay of one year). The model predicts a 4.6 and 11.2% reduction in the PEoT by 2030 for the 9- and 21-month interruptions, respectively.

Health zone with existing VC: Kwamouth

We selected Kwamouth, as a health zone with existing VC, to illustrate the impact of the 9- and 21-month interruption scenarios on active and passive case numbers, DALYs, PEoT and YEoT. We have highlighted our main findings for Kwamouth below:

1. ***No AS* interruption scenario:** The model predicts that if AS is interrupted there are very few extra new infections (< 1) and limited impact on the PEoT. Additional DALYs accrued in the next ten years are 160.4 and 268.8, for 9- and 21-month interruption periods, respectively, which is greater compared to 35.2 and 76.3 additional DALYs accrued (9- and 21-months, respectively) in Mosango. However, the increment, as a percentage of the total DALYs under the baseline, are lower in Kwamouth compared to Mosango because of the existing and continuing VC (Figure 3).
2. ***No AS and reduced PS* interruption scenario:** As in the scenario above, reductions in medical interventions cause very few extra new infections (< 1) and limited impact on PEoT (lowered by up to 20.4% in 2021 only). The *no AS and reduced PS* scenarios is predicted to accrue 365.9 and 727.5 additional DALYs during 2020–2030, for 9- and 21-month interruption periods, respectively, which is greater compared to 61.4 and 152.7 additional DALYs accrued (9- and 21-months, respectively) in Mosango. However, the increment, as a percentage of the total DALYs under the baseline, are lower in Kwamouth compared to Mosango because of the existing and continuing VC.

3. ***No AS or VC, and reduced PS*** **interruption scenario:** New infections do not fall as rapidly in this scenario compared to the baseline or other interruption scenarios where VC continues. The model also predicts a substantial increase in new infections (11.4 and 36.2 accumulated over 2020–2025). This is explained by there being only two rounds of VC deployments in Kwamouth prior to the start of the interruptions. Consequently a small, but non-zero, remaining tsetse population can bounce back, causing more new infections in humans while VC deployments are interrupted. The shifted PEoT curves show that Kwamouth health zone is expected to be able to reach EoT within two years after VC resumes and the average estimated delays to YEoT are equal to the length of interruptions (i.e. one year for a 9-month interruption and two years for a 21-month interruption).

Across the 38 health zones in the former Bandundu province we show the predicted impact of the three interruption types of either 9- or 21-month duration to the expected year of EoT (Figure 4). There are several low-incidence health zones where there might be no delay to YEoT (on average) even for 21-month interruptions, and for the "worst-case" health zones we predict a delay to EoT would be two years (similar to the interruption timescale).

Conclusion

In this study we simulated six interruption scenarios to the gHAT elimination programme in the DRC to predict the impact on case reporting, burden and EoT for the health zones in the former Bandundu province. We predicted that EoT could be delayed by a maximum of the length of interruptions in the worst case scenarios considered (i.e. No AS and reduced detection rate in PS for the interruption period, and, if a health zone had had previous or planned VC, an interruption to VC deployments). However, the additional DALYs accrued due to interruptions varies from < 0.1 to 1069.3 compared to the baseline (no interruption) depending on the endemicity, strength and coverage of medical interventions, and the VC history of the health zone.

This analysis also identified that the interruption of VC has a direct short-term impact on EoT as implementation of VC is expected to reduce the population of tsetse and therefore substantially decrease the transmission of gHAT from tsetse to humans. We also found that a reduction in the PS detection rate (scenarios including "reduced PS") generally introduced more DALYs (disease burden) compared to the interruption of VC for those health zones where VC had previously been deployed. In summary, this modelling study indicates that the gHAT elimination programme is fairly robust to short shocks if activities can be resumed again afterwards. We believe this to be largely due to the slow-progressing nature of the gHAT infection, however, additional disease burden is predicted with interruptions and the longer the interruption and the fewer interventions that occur during the interruption, the more DALYs are expected to be accrued.

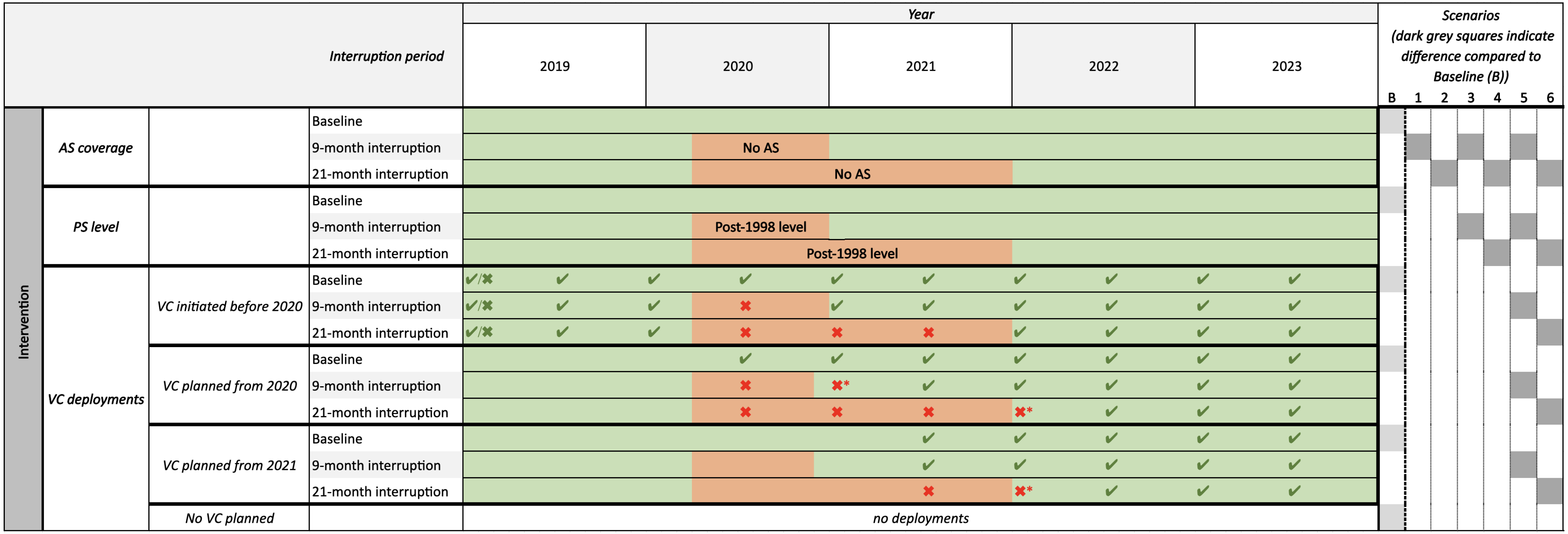

Figure 1: **Gantt chart showing simulated baseline (no interruption) and interruption scenarios.** Each section shows the model assumptions for the timing of interruptions to different strategy components (interventions). Green background indicate the intervention is running as normal. Orange background indicates the intervention has been suspended (in the case of AS or VC) or reduced (in the case of PS). *E.g.* a 9-month interruption to AS is assumed to last from April 2020 to December 2020 and so has and orange background for this time period. The right hand side of the diagram shows how the different types of interruptions are combined together to make up the baseline and six interruption scenarios. Each health zone falls into one of four categories, (i) there was existing VC prior to 2020, (ii/iii) VC was planned to be started in 2020/21 or (iv) no VC was planned. For health zones with existing or planned VC, interruption is indicated by crosses for no deployment when there was one expected in the baseline. In these health zones there may or may not have been deployments at the beginning of 2019 – we simulate the deployments that occurred in specific health zones. In regions with existing VC deployments, only the deployments during the interruption period are impacted. However, for health zones planning to start new VC intervention, we assume initial deployment of VC to a new health zone was pushed back by a one or two full years and so deployment does not take place immediately; these additional missed deployments are denoted by crosses with stars.
AS: active screening; PS: passive screening; VC: vector control

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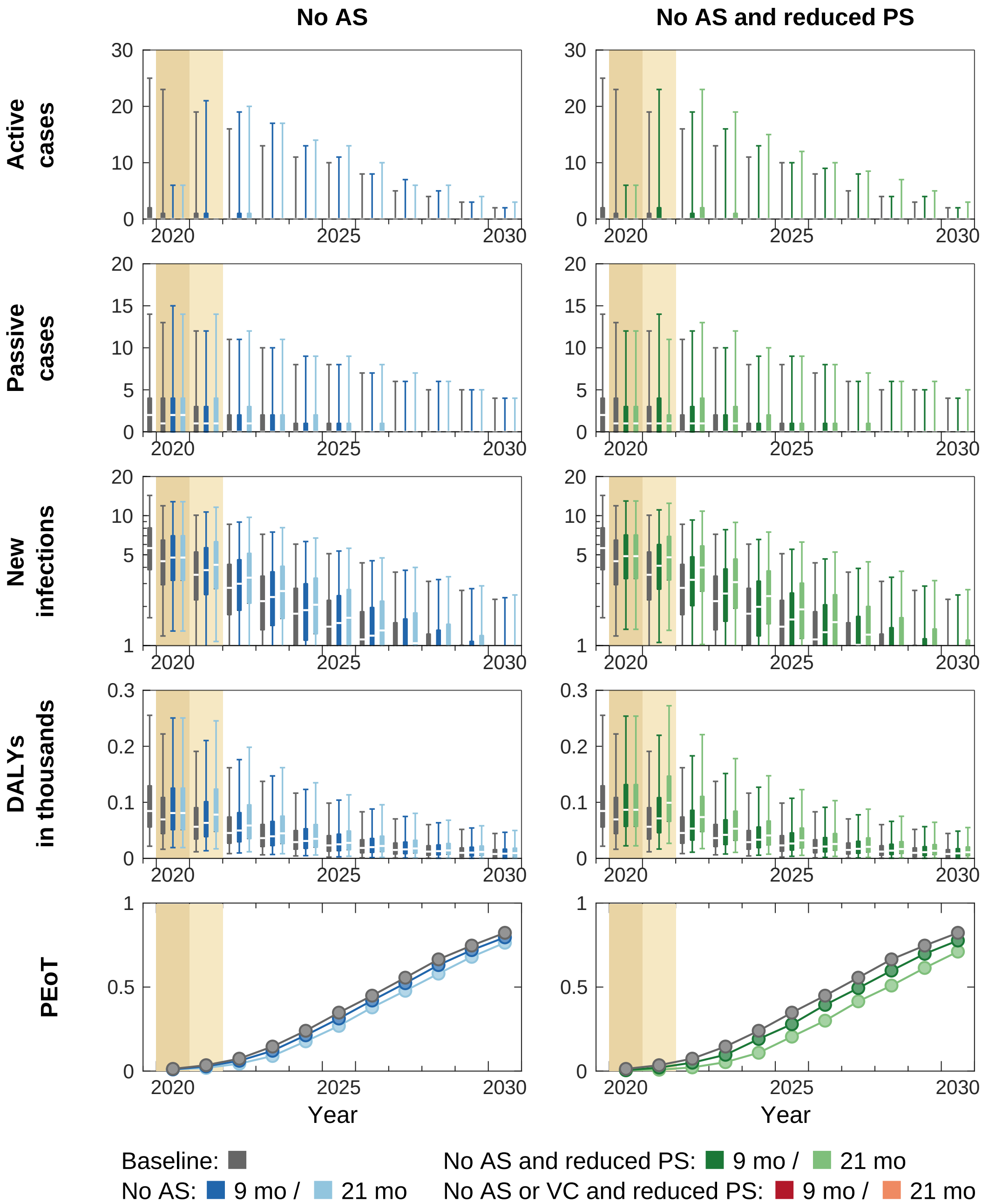

Figure 2: **Time series of model outputs in Mosango health zone (no on-going or planned vector control) under the baseline and six interruption scenarios.** One year (2019) of fitted results and the projected baseline are shown in gray. Interruptions, indicated by coloured background, are assumed to take place in April 2020 and last until the end of 2020 (darker tan) or 2021 (lighter tan) in our simulations. Thus, the projections of the baseline (gray) and interruption scenarios (coloured) starts from 2020. Note that the results of the *No AS or VC, and reduced PS* scenarios are identical to *No AS and reduced PS* because there was no on-going or planned vector control (VC) in Mosango and so is not shown. There are n = 10,000 independent samples, 10 from each of 1,000 independent samples from the joint posterior distributions of the fitted model parameters. Box plots summarise parameter and observational uncertainty. The lines in the boxes represent the medians of predicted results. The lower and upper bounds of the boxes indicate 25th and 75th percentiles. The minimum and maximum values are 2.5th and 97.5th percentiles and therefore whiskers cover 95% prediction intervals.

AS: active screening; PS: passive screening; VC: vector control; DALYs: disability-adjusted life years; PEoT: probability of elimination of transmission

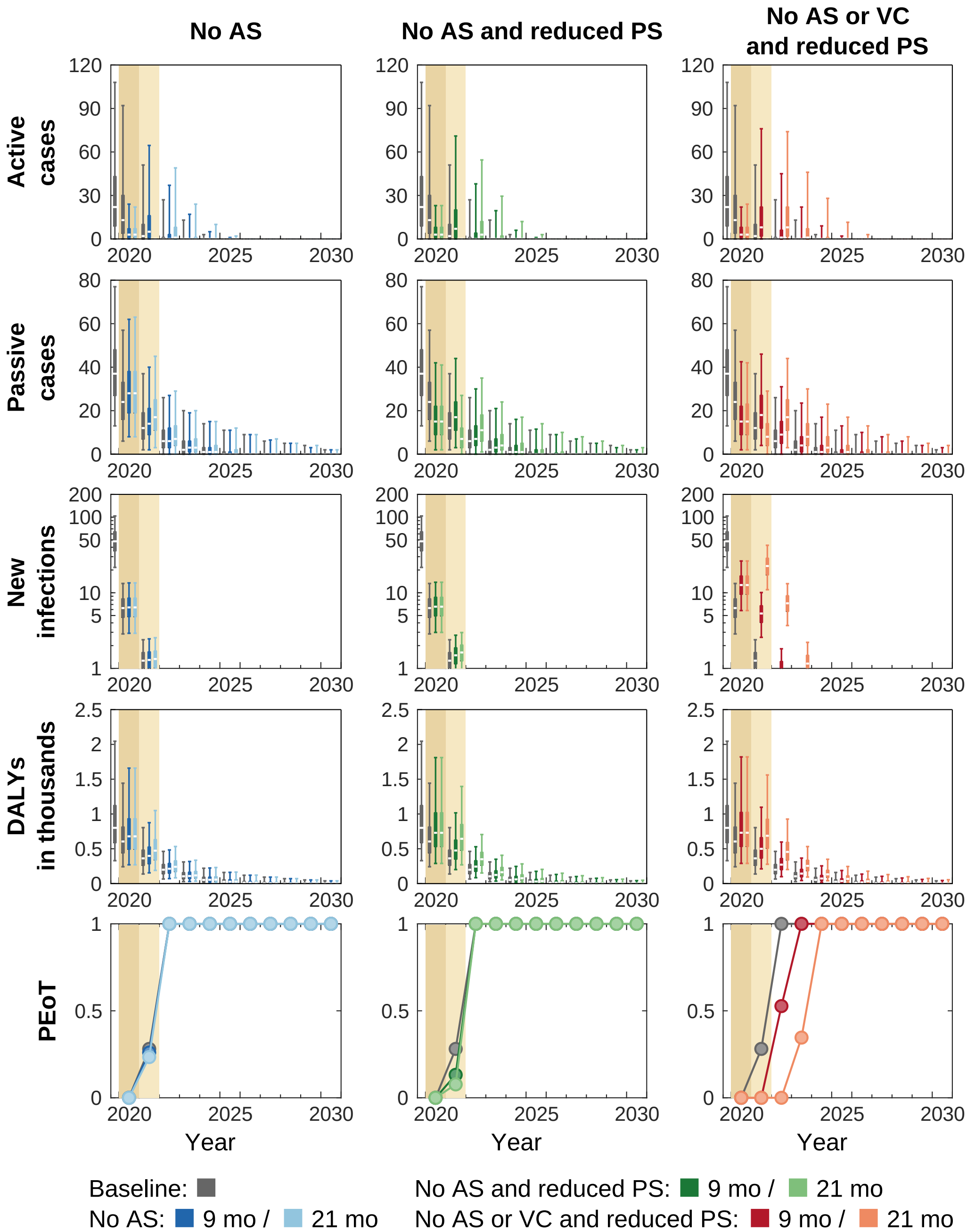

Figure 3: **Time series of model outputs in Kwamouth health zone (on-going vector control since 2019) under the baseline and six interruption scenarios.** One year (2019) of fitted results and the projected baseline are shown in gray. Interruptions, indicated by coloured background) are assumed to take place in April 2020 and last until the end of 2020 (darker tan) or 2021 (lighter tan) in our simulations. Thus, the projections of the baseline (light gray) and interruption scenarios (coloured) starts from 2020. There are n = 10,000 independent samples, 10 from each of 1,000 independent samples from the joint posterior distributions of the fitted model parameters. Box plots summarise parameter and observational uncertainty. The lines in the boxes represent the medians of predicted results. The lower and upper bounds of the boxes indicate 25th and 75th percentiles. The minimum and maximum values are 2.5th and 97.5th percentiles and therefore whiskers cover 95% prediction intervals.

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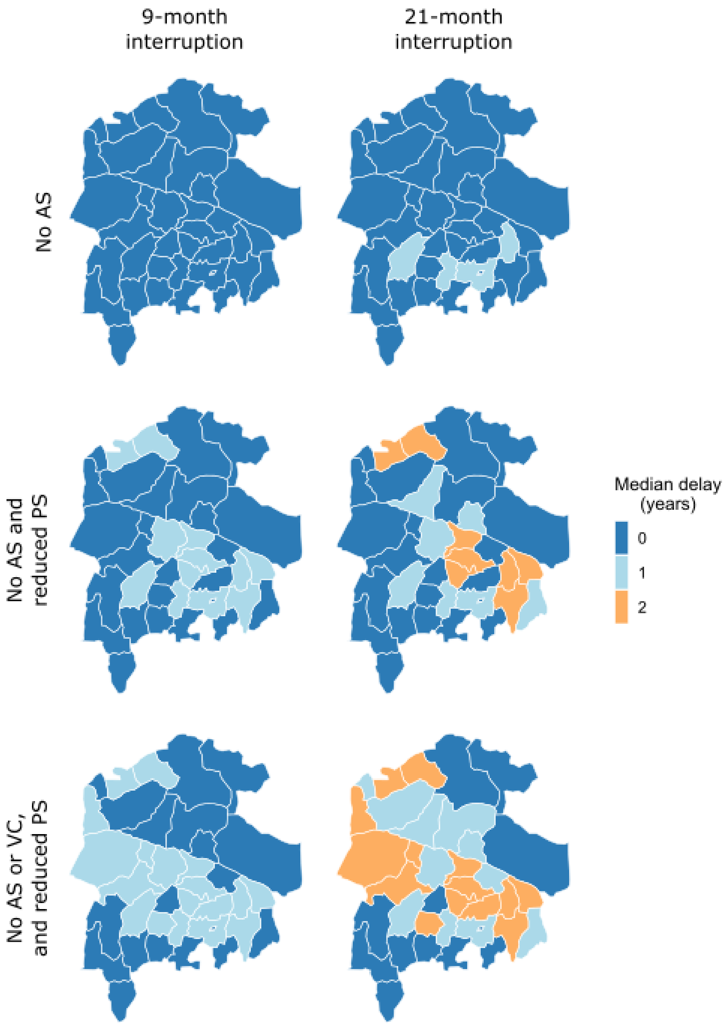

Figure 4: **Median delay in EoT in the former Bandundu province under six interruption scenarios.**