NTD MODELLING CONSORTIUM

Impact of COVID-19 on NTD programmes progress

4th May 2020

Impact of 1 year interruption on 2030 goals

Disease (Goal)	Minimum average delay to achieving the 2030 goal and type of setting where this would be seen	Maximum average delay in time to achieve the 2030 goals and type of setting where this would be seen	Minimum catch up strategy	Notes
Soil-transmitted helminthiasis (EPHP)	No impact (hookworm, 20-50% prevalence)	< 1 year (hookworm and *A. lumbricoides,* 20-50% prevalence)	Additional round of community wide treatment (hookworm) or semi-annual treatment (*A. lumbricoides*)	High prevalence settings unlikely to reach 2030 target regardless of interruption unless adults are treated (hookworm) or dual treatment with ivermectin is implemented (*T. trichiura*)
Schistosoma mansoni (EPHP)	No impact (<10% prevalence)	< 2 years (>50% prevalence)	Additional treatment round in moderate and high prevalence settings	High prevalence settings may not be on track for EPHP by 2030 unless adults are also being treated
Lymphatic filariasis (EPHP)	No impact (<10% current prevalence)	1 year (15-20% current prevalence)	1 year biannual OR 3 years enhanced (80%) coverage OR 1 year of IDA	Most settings will see a one-year delay in reaching EPHP, but should still achieve the target by 2030. Settings with high baseline prevalence (>25%) and start of MDA after 2017 are at increased risk of not achieving the goal by 2030
Onchocerciasis (EOT)	≤40% baseline prevalence, or/and long treatment duration, then no impact	>40% baseline prevalence and shorter treatment duration, then modest impact	1 year biannual treatment in the subsequent year (2021) helps the programme to get back on track (65% coverage; 5% non-adherence)	Two years of MDA interruption (2020 and 2021) has a larger impact for higher prevalence settings and shorter treatment histories; biannual treatment in 2022 and 2023, or increased coverage mitigates the impact of interruption

Impact of 1 year interruption on 2030 goals

Disease (Goal)	Minimum average delay to achieving the 2030 goal and type of setting where this would be seen	Maximum average delay in time to achieve the 2030 goals and type of setting where this would be seen	Minimum catch up strategy	Notes
Trachoma (EPHP)	<1 year (mean 20% TF prevalence)	>2 years (mean 40% prevalence TF)	Additional treatment round in high prevalence settings	Opportunity to not just catch up, but accelerate in trouble areas
Visceral Leishmaniasis in the Indian sub-continent (EPHP)	0 years (Moderately endemic settings that are already below the EPHP target will remain under the target at sub-district level, also after two years of programme interruption.)	7.5 years (In highly endemic settings that are in the consolidation phase with two years of programme interruption)	Extending or re-implementing the attack phase could reduce the delay to EPHP in highly endemic settings.	In previously highly endemic settings that have already achieved EPHP, VL incidences can increase to above the target due to interruption of the programmes.
Gambiense Human African Trypanosomiasis (EOT)	No difference to EOT year (but some increase in deaths)	3 years (2 year interruption)	None	High-transmission settings may not reach 2030 target regardless of interruption

Soil-transmitted helminthiasis

Individual-based, stochastic models developed by ICL and EMC for STH (*A.lumbricoides, T. trichiura*, hookworm)

- **Demography:** Age-structured host population with birth and death rates typical for LMICs
- **Transmission**:
  - Exposure and contribution to the environmental reservoir are age-specific, parameterisation varies between worm species
  - Infection and worm death are stochastic processes, probability of death depends on mean worm lifespan
- **Control:** different treatment strategies varying treatment efficacy, target population, coverage and access to treatment (random or systematic)
- **Diagnostics:** single slide Kato-Katz

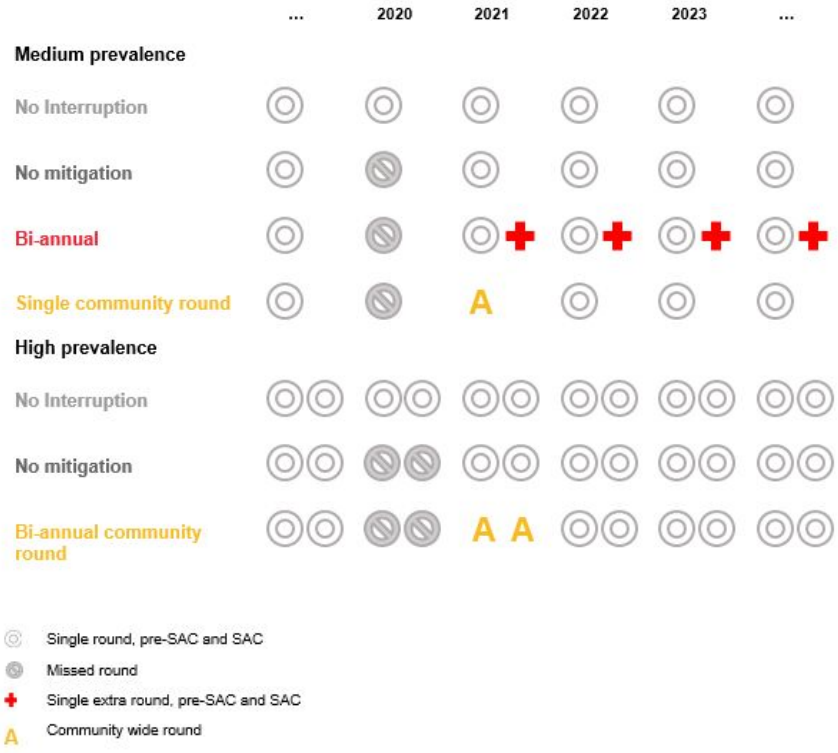
Assumptions:

- Population size of 500 (rural village)
- non-access to treatment is random
- human movement not included

Model details can be found in Truscott *et al.* (2016), Coffeng *et al.* (2015), Coffeng *et al.* (2017)

Soil-transmitted helminthiasis

Scenarios and mitigations strategies modelled



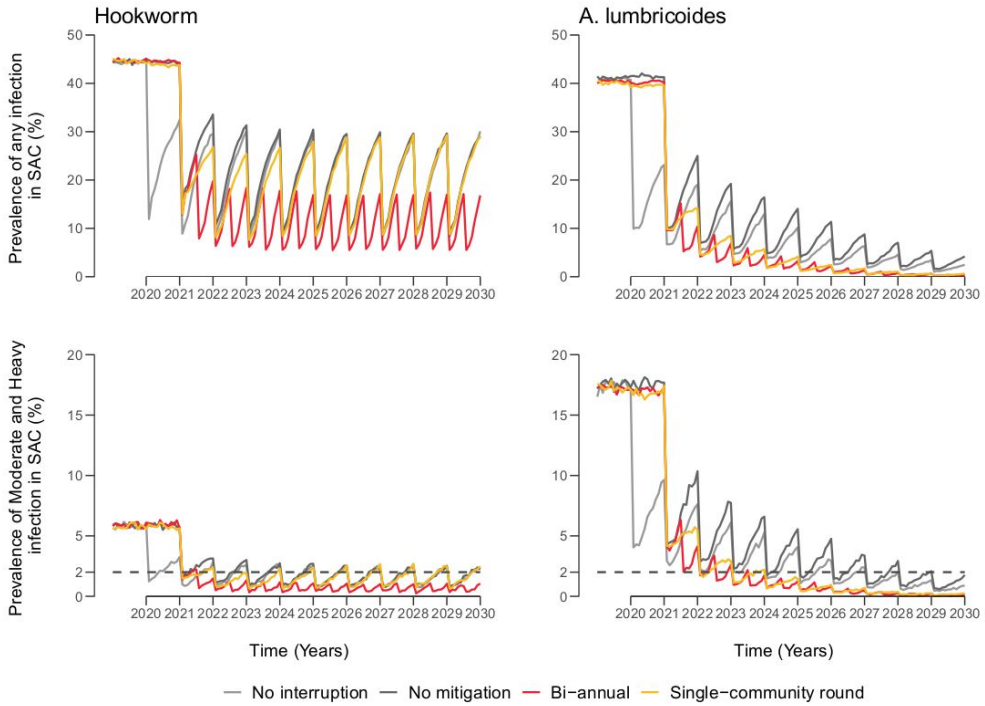
Delays to reach same prevalence in SAC: No mitigation

Prevalence setting (2020)	Moderate (20-50%)	High (>50%)
A.lumbricoides	1.49 years (1 - 3) 1.69 years (1 - 4)	1.66 years (1 - 3.5) 1.49 years (1 - 2)
Hookworm	1.23 years (1 - 2) 1.41 years (1 - 2)	1.23 years (1 - 1.5) 1.30 years (1 - 2)
T. trichiura	1.77 years (1 - 7) 2.00 years (1 - 7)	1.92 years (1 - 6.5) 2.40 years (1 - 6)

Delay to reach the same moderate-heavy prevalence in SAC (progress towards EPHP) if a year of MDA is missed and no mitigation strategy is implemented. ICL results (first line) and EMC results (second line).

Soil-transmitted helminthiasis

Moderate setting (20-50% baseline prevalence)



Mean prevalence dynamics in SAC (single-slide Kato-Katz). The dashed line represents the goal of EPHP. (Only EMC model results are shown).

- A round of community-wide MDA when programmes resume is sufficient to compensate for the year missed for hookworm and *A. lumbricoides*.
- Semi-annual PC further reduces the time to EPHP by 1.5 years on average.
- High prevalence settings are unlikely to meet the EPHP target by 2030 but mitigation strategies to make up for the skipped MDA round(s) will still be beneficial.
- If no mitigation strategy is adopted, programmes will catch up their progress toward meeting the goal in less than two years for *A. lumbricoides* and hookworm. *T. trichiura* may take longer to catch-up.
- Similar dynamics is observed with the ICL model (only results by EMC model are shown).

Schistosomiasis (*Schistosoma mansoni*)

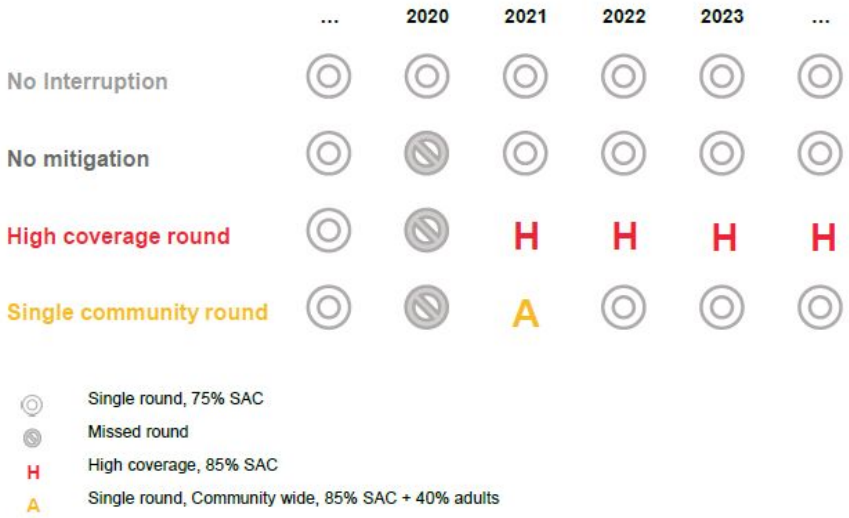
- Fully age-structured deterministic and stochastic individual-based models monitoring parasite transmission and control by MDA
  - Monitor the rate of infection and amount of infectious material within the environment over time
  - MDA benefits individuals treated and reduces the risk of infection to others
  - Single reservoir of infectious material (infected snails-short lived)
    - Egg contribution to the reservoir depends on the age-specific contact rates
  - Vary intrinsic intensity of transmission (R_0) and age-specific contact rates to correspond to different settings

- Model assumptions:
  - Coverage at random at each round of MDA i.e. no systematic non-adherers/non-access individuals
  - No acquired immunity
  - Negative binomial distribution of parasites per host with a fixed aggregation parameter
  - Density dependent fecundity and monogamous sexual reproduction among worms
  - Population size set at 1000, with no effect of migration

- Model description: A comparison of two mathematical models of the impact of mass drug administration on the transmission and control of schistosomiasis. Truscott et al. (2017). *Epidemics*. https://doi.org/10.1016/j.epidem.2017.02.003

Schistosomiasis (*Schistosoma mansoni*)

Scenarios and mitigations strategies modelled



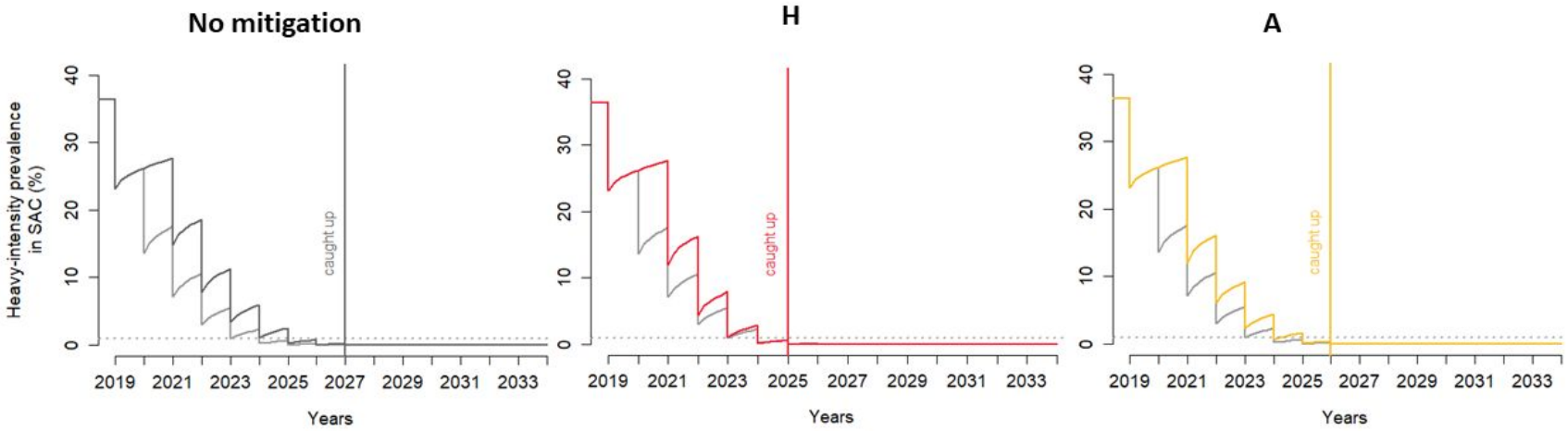
Delays to reach EPHP

Prevalence in SAC	**Moderate** (30%)	**High** (70%)
Years to achieve the goal without interruption	Low-high adult burden: 2 - 3 years	Low-high adult burden: 7 - 16 years
Delay to achievement of the goal with no mitigation	Low-high adult burden: 1 year	Low-high adult burden: 2 - 0 years
Delay with high coverage rounds	Low-high adult burden: 1 - 0 years	Low-high adult burden: 0 years
Delay with single community round followed by 75% SAC	Low-high adult burden: 1 - 0 years	Low-high adult burden: 1 - 0 years

Delays to reach EPHP (≤1% heavy-intensity prevalence in SAC) for S. mansoni when the second MDA is missed. Results are shown for low and high adult burden of infection settings using the ICL deterministic model.

- Postponing MDA results in EPHP goal delayed by up to 2 years
- High prevalence settings: EPHP may not be reached by 2030 regardless of a postponement→ adult treatment is needed
- Postponement has a lower impact in high adult burden settings (here MDA targeting SAC-only is having a small impact on reducing transmission)

Schistosomiasis (*Schistosoma mansoni*)

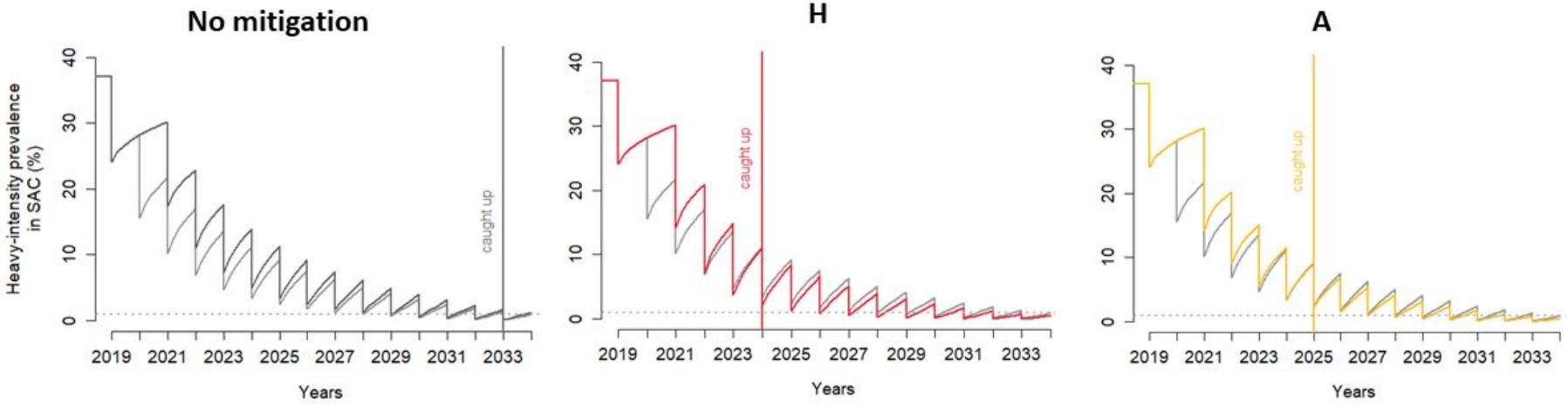


The dashed horizonal line represents the EPHP goal

Heavy-intensity prevalence in SAC in high transmission settings with a low adult burden of infection. The second round of MDA is missed:

- If the programme is reintroduced at the previous 75% SAC-only coverage, then we expect 2 years of delay in reaching EPHP.
- Increasing the coverage level to 85% of SAC, does not require the additional 2 years.

Schistosomiasis (*Schistosoma mansoni*)



The dashed line represents the EPHP goal

Heavy-intensity prevalence in SAC in high transmission settings with a high adult burden of infection. The second round of MDA is missed.

- EPHP is not achieved by 2030, regardless of the mitigation strategy.
- To achieve EPHP within a shorter time frame, higher coverage of SAC and adults would be needed for this setting.

Lymphatic filariasis

Models used: TRANSFIL, EPIFIL, LYMFASIM

(analysis presented here done primarily with TRANSFIL)

✔ Results were qualitatively similar across models and settings/scenarios chosen.

General:

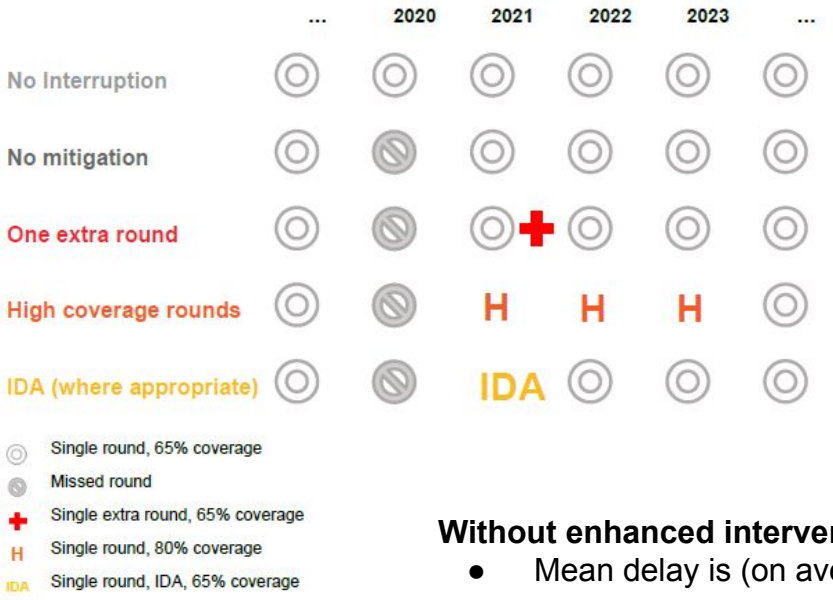
- 30% bednet coverage
- Anopheles vectors
- Small importation rate
- Fixed level of systematic non-adherence (Griffin *et al.* 2010)
- Example scenarios: 15% baseline prevalence, program begun in 2018

Treatment efficacy:

- DA: microfilariae clearance 95%, macrofilariae clearance 55%, 6 months fecundity reduction
- IA: microfilariae clearance 99%, macrofilariae clearance 35%, 9 months fecundity reduction
- IDA: microfilariae clearance 100%, same macrofilaricidal properties as DA (55%), but remaining worms are sterilised permanently (Thomsen *et al.* 2016)

Lymphatic filariasis

Scenarios and mitigations strategies modelled



Delay in achieving EPHP

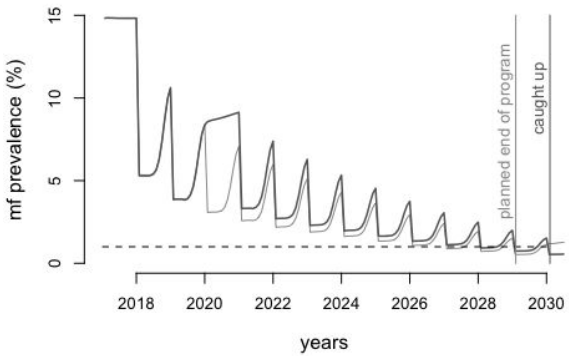
Prevalence setting (2018)	Low (5-10%)	Medium (15-20%)	High (25-30%)
Time to goal if no interruption	7.38 (5-11)	10.25 (7-16)	12.03 (9-16)
Delay to goal if 1 MDA missed	0.65 (0-2)	0.61 (0-3)	0.61 (0-3)
Delay if 2 MDAs missed	1.31 (0-3)	1.24 (0-3)	1.15 (0-4)

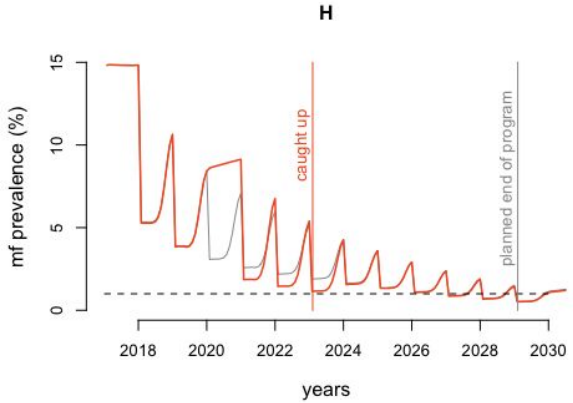
Delay to achieving 1% mf prevalence goal, years (95%CI), if one or two MDAs are missed, plus expected time to goal (from 2018) if no interruption. Timeframes >12 years would not reach the goal by 2030. (IA settings)

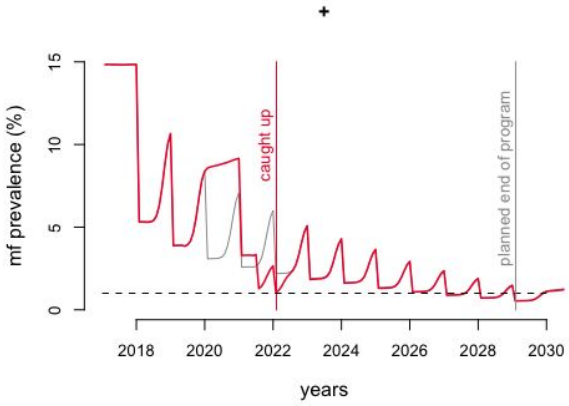
Without enhanced interventions:

- Mean delay is (on average) less than number of missed rounds
- Programs with higher prevalence may see less delay
  - Due to more rounds still to complete
  - BUT variation around this delay may be larger (some delays could be up to 3 years)
- Interruption is most important in places expected to reach the goal in exactly 2030

Lymphatic filariasis







Example IA setting

For this high (15%) prevalence setting

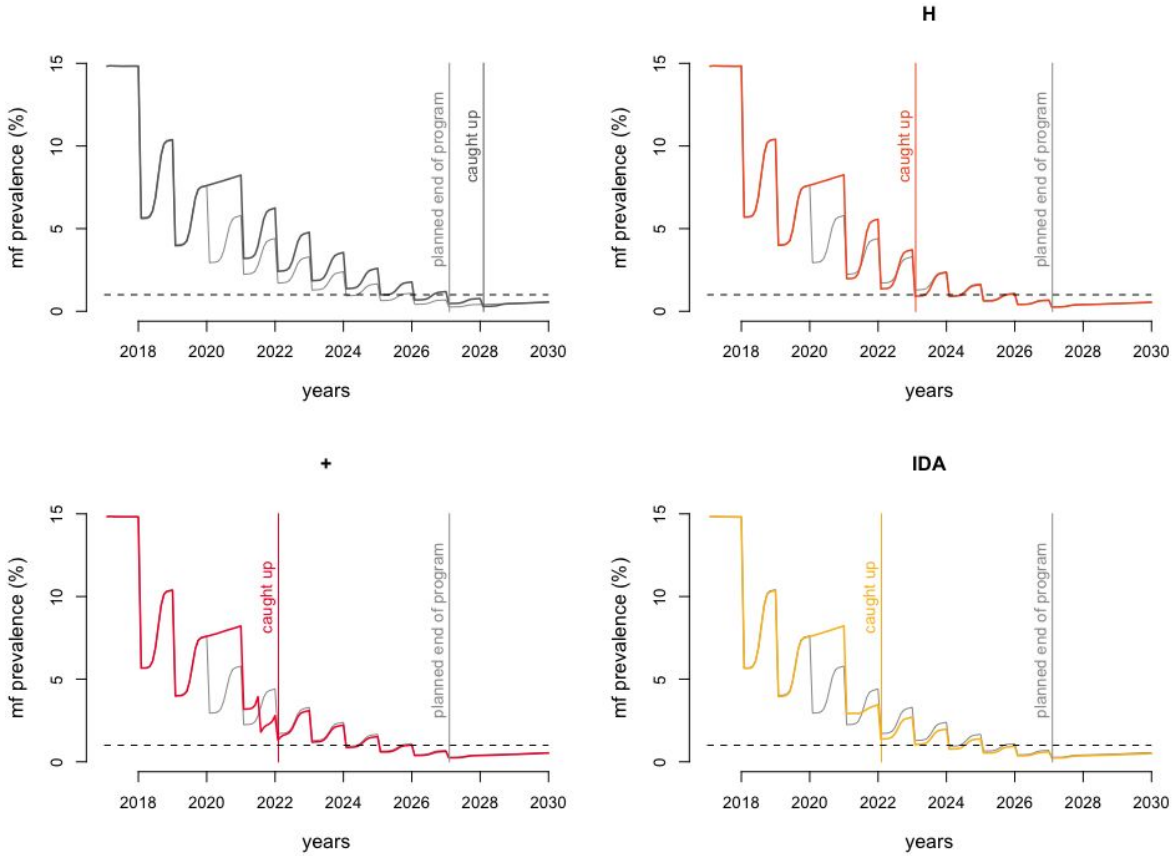
Mitigation(minimum):

- 3 years of 80% coverage
- 1 year of biannual MDA (bMDA)

Acceleration option (not shown):

- 80% coverage: finish 1 year early
- bMDA: finish 3 years early

Lymphatic filariasis



Example DA setting

Mitigation (minimum):

- 3 years of 80% coverage
- 1 year of biannual MDA (bMDA)
- 1 year of IDA

Acceleration option:

- 80% coverage: finish 1 year earlier
- bMDA: finish 2.5 years earlier
- IDA: finish 3 years earlier

Onchocerciasis

EPIONCHO-IBM
Stochastic individual-based model (tracks the number of adult worms (of both sexes) and microfilariae in individual people) Hamley et al. 2019. PLoS Negl Trop Dis

Demography:
- Population size of 440 individuals (rural village)
- Age-structured human, adult worms, microfilariae populations

Transmission:
- Parasite dynamics within a population of blackfly vectors (*Simulium damnosum s.s.*) is modelled deterministically
- Age-and sex-dependent exposure as well as individual variation exposure to vector bites
- Proportion of parasites establishing in people decreases with increasing transmission intensity (no. of L3 larvae potentially received per person per year). Strength of decrease important for elimination prospects (**not assumed in ONCHOSIM**)

ONCHOSIM
Stochastic individual-based model (Stolk et al. 2015 P&V)

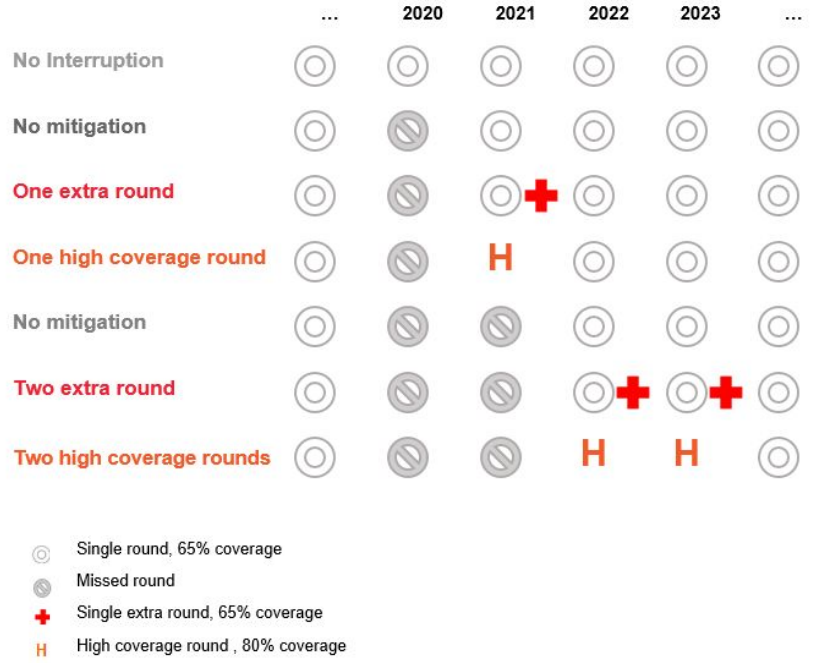
Demography:
- Population size of 440 individuals (rural village)
- Age-structured human and worm populations

Transmission:
- Parasite dynamics within a population of blackfly vectors (*Simulium damnosum s.s.*) is modelled deterministically
- Seasonal variation in transmission defined by monthly biting rates
- Age-and sex-dependent exposure as well as individual variation exposure to vector bites
- Incoming infections from neighbouring villages defined by an external force of infection, which decreases over time (**not assumed in EPIONCHO-IBM**)

Scenarios:
- Simulated pre-control microfilarial prevalence: 20-85% (varying biting rate, exposure and external force of infection)
- Annual ivermectin MDA with 65% coverage and 5% systematic non-participation

Onchocerciasis

Scenarios and mitigations strategies modelled

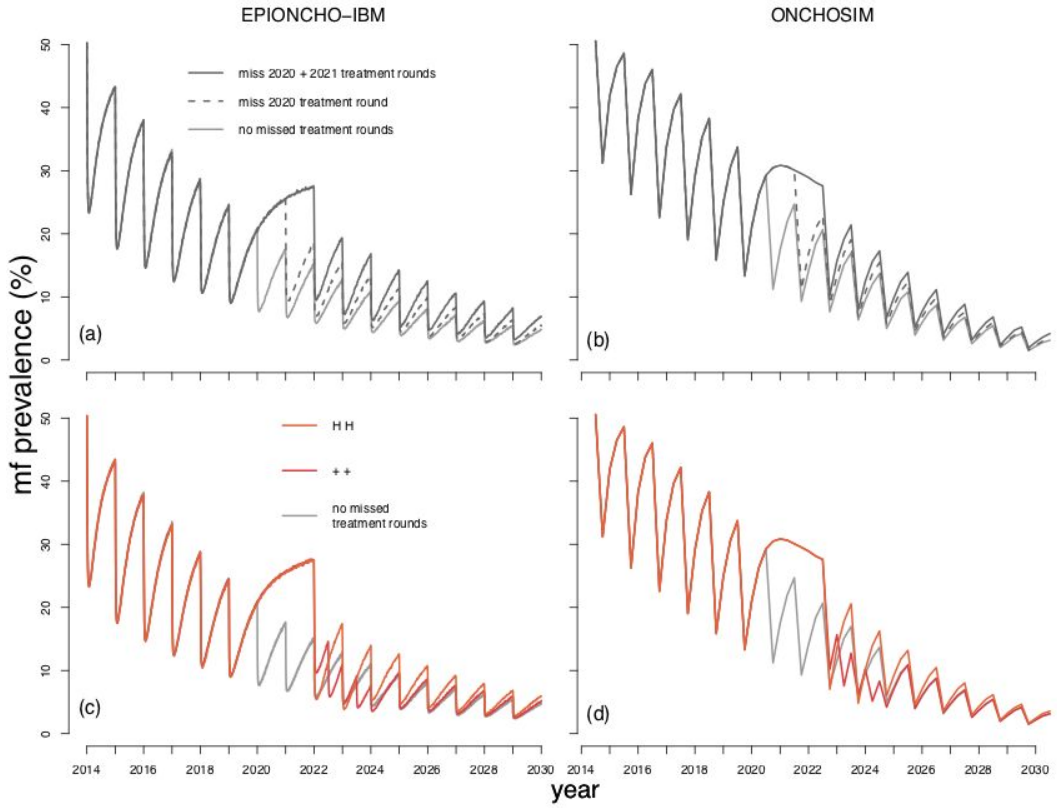


Proportional reduction in probability of elimination (2 years MDA interruption)

Baseline mf prevalence (%)		20-39 (hypoendemic)	40-59 (mesoendemic)	60-80 (hyperendemic)
No mitigation	**EPIONCHO-IBM**	Decreases by 1%	Decreases by 26%	Not achieved
	ONCHOSIM	No change	No change	Decreases by 8%
One extra round	**EPIONCHO-IBM**	No change	Decreases by 9%	Not achieved
	ONCHOSIM	no change	No change	Decreases by 4%
High coverage	**EPIONCHO-IBM**	No change	Decreases by 15%	Not achieved
	ONCHOSIM	No change	No change	Decreases by 3%

The reduction in elimination probability relative to that when there is no interruption in treatment (ivermectin MDA 2006-2030, 65% coverage, 5% non-participation)

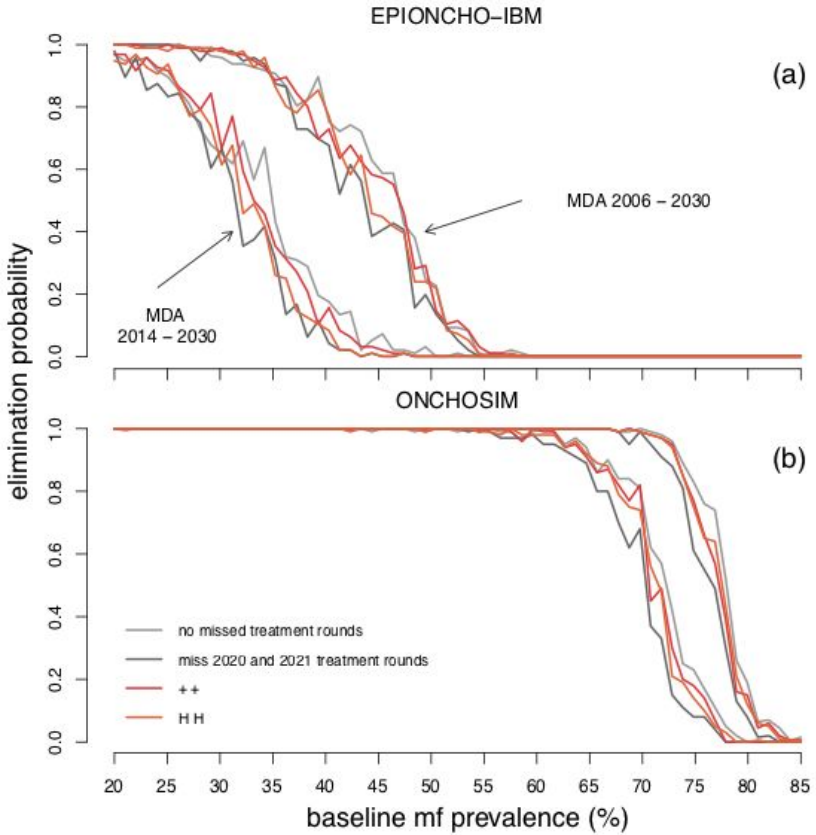
Onchocerciasis



- Missing one round is more tolerable than missing two rounds in the absence of a remedial strategy, in both models
- Prevalence dynamics nearly return to reference trajectory (no MDA interruption) after one year (not shown) or two years (bottom panel) of biannual treatment if, respectively, one or two rounds of MDA were missed
- Annual treatment at high coverage is less effective than biannual treatment at standard coverage as a mitigation strategy

note MDA is assumed to occur at different times of the year in the two models

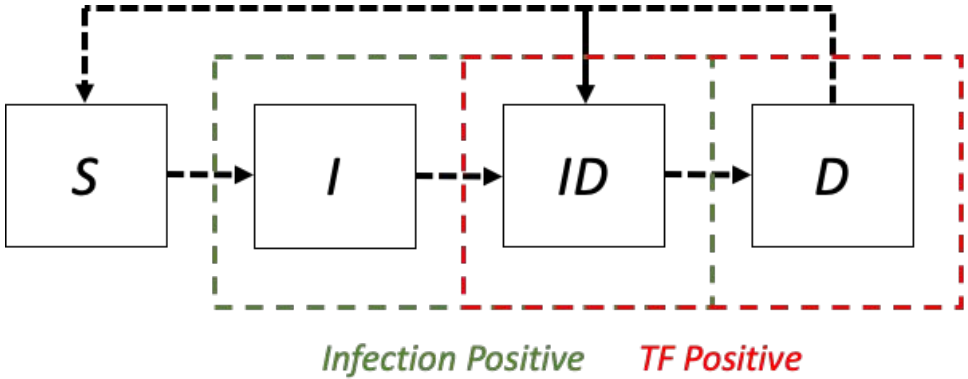
Onchocerciasis



- Models differ in the probability of elimination for a given scenario but the qualitative impact of missed rounds and mitigation on the program between the scenarios are similar.
- Missing two years of treatment noticeably influences elimination when compared with no interruption in both models.
- Interruption can be mitigated by implementing two years of biannual treatment when MDA resumes.
- Mitigation is less effective when simply increasing annual coverage for two years when MDA resumes

Trachoma

Model structure:



S=Susceptible
I=Latent period
ID=Infected and diseased (Infection positive and TF positive)
D=Cleared infection, disease persisting (TF positive)

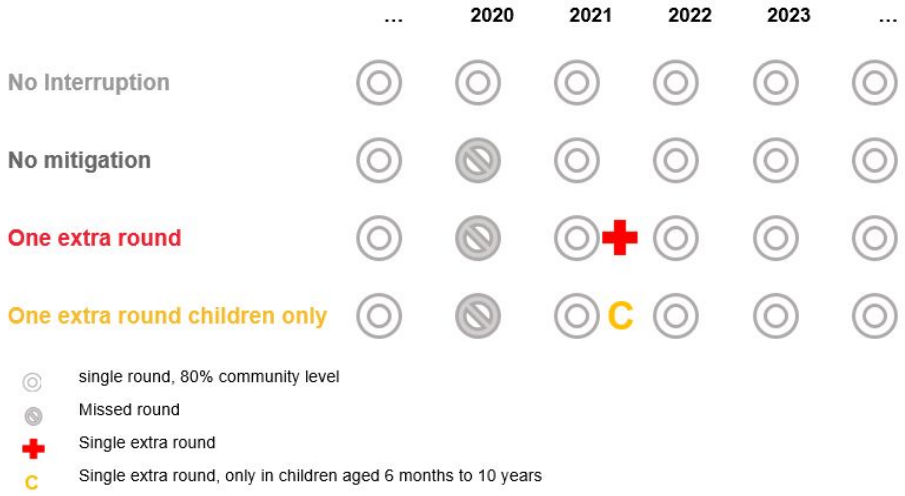
Key model assumptions:

- Model is an individual-based stochastic adaptation of the model described in Pinsent et al, 2018.
- Treatment is applied randomly at each MDA round with 80% coverage and 85% clearance rate assumed.
- Children are effectively core group (longer duration of infection and higher bacterial load).
- The potential additional reduction in transmission afforded by WASH/F&E interventions is not currently incorporated due to uncertainty about the the impact of these strategies.

Pinsent A & Hollingsworth TD (2018)

Trachoma

Scenarios and mitigations strategies modelled



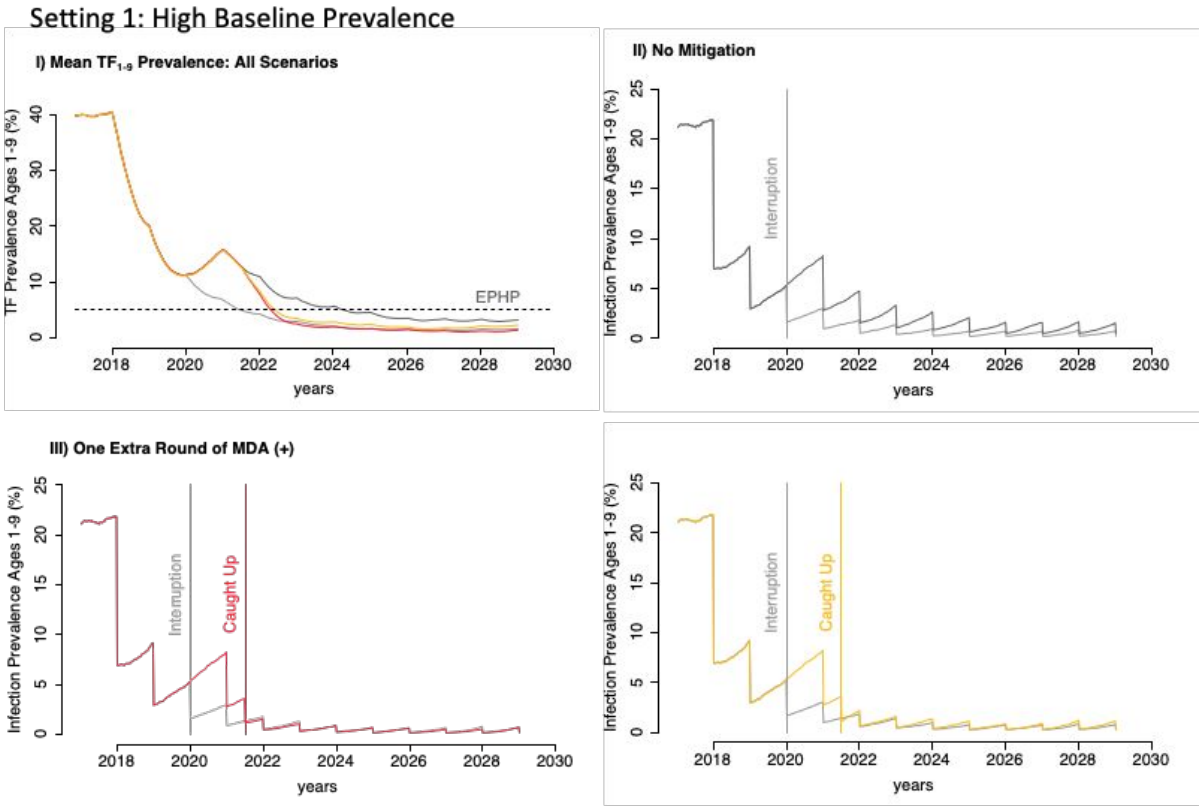
Delays until reaching EHPH for all settings and scenarios

Scenarios	High prevalence setting: Mean years to achieve TF <5% in ages 1-9 (80% CI)	Medium prevalence setting: Mean years to achieve TF <5% in ages 1-9 (95% CI)
No interruption	4.5 (3.1, 8.4)	2.69 (0.29, 5.12)
No mitigation	7.3 (3.1, >12 years)	2.69 (0.29,6.15)
Extra round, (community)	5.3 (3.1, 7.7)	2.69 (0.29, 5.32)
Extra round (children)	5.4 (3.1, 9.4)	2.69 (0.29, 5.42)

Two Settings are considered:

- **Setting 1:** High prevalence, mean 40% prevalence of TF in children aged 1-9 at baseline
- **Setting 2:** Medium prevalence, mean 20% prevalence of TF in children aged 1-9 at baseline

Trachoma



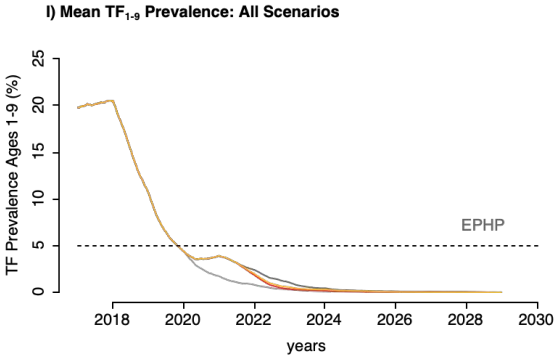
1. In high baseline prevalence settings, missing a single round of treatment will on average lead to an increase in the number of MDA rounds needed to reach elimination targets.

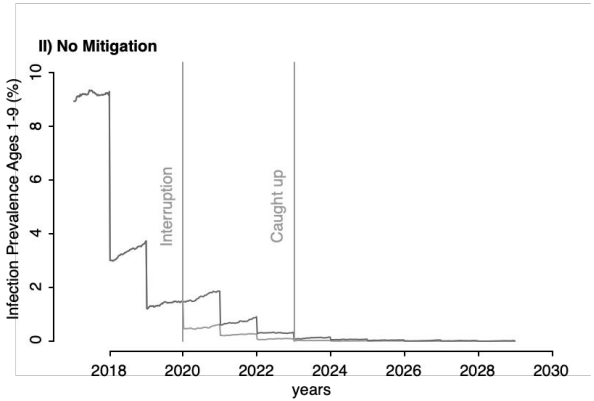
2. On average, without mitigation, it will take 2.8 years to catch-up.

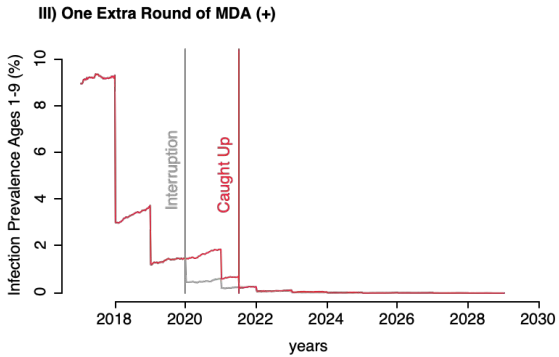
3. An additional round of MDA in the year after programmes are resumed will accelerate catch-up, and progress towards elimination targets will only be delayed by approximately 1 year.

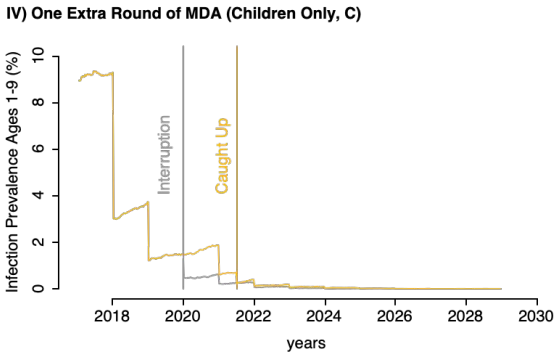
Trachoma

Setting 2: Medium Baseline Prevalence







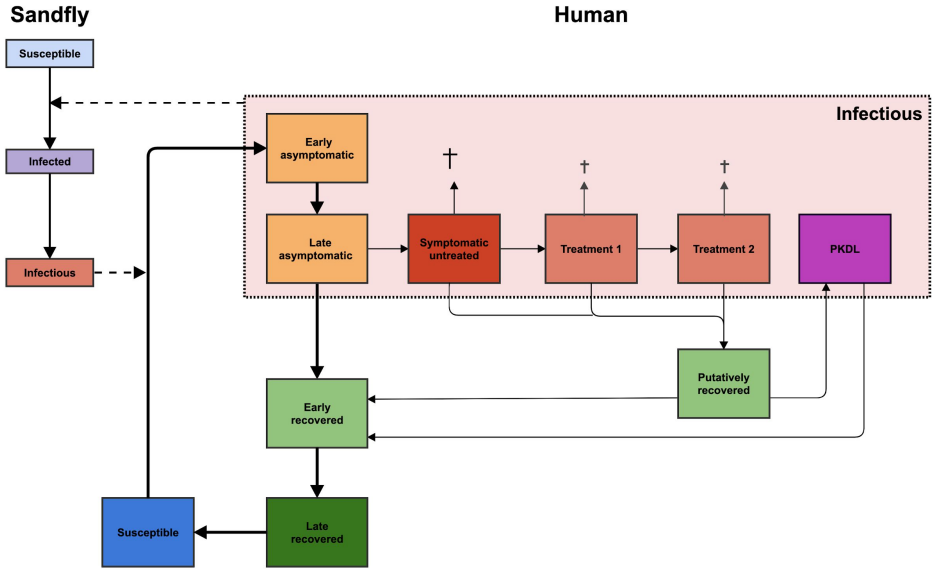


1. In medium baseline prevalence settings, which are already on track for EPHP, the impact of missed MDA will be less profound.

2. In most cases, EPHP targets will still be reached after the same number of treatment rounds.

3. Additional rounds of MDA after programmes are resumed will however accelerate progress towards elimination.

Visceral Leishmaniasis



Schematic presentation of the structure of the VL transmission model.

Interventions

- Indoor residual spraying of insecticide is implemented through a reduction in the sandfly biting rate.
- Active case detection leads to a shorter duration of the symptomatic untreated state.

Model description and key assumptions

- Simulations are performed with a stochastic individual based transmission model based on the age-structured deterministic transmission model of Erasmus MC 'Model E1'. (Le Rutte *et al.*, Clin Infect Dis, 2018).
- The model was fitted to the KalaNet dataset (Le Rutte *et al.*, Parasit Vectors, 2016) and then further validated using geographical cross-validation against the CARE India data (Le Rutte, Chapman *et al.*, Epidemics 2017).
- The infectiousness of asymptomatics remains debated, in this model variant they are ~0.02 times as infectious compared to those with VL symptoms.
- PKDL infectivity is considered 90% of those with VL (Le Rutte *et al.*, Trends Parasitol, 2019).
- The simulated population consists of ~350,000 people, reflecting population sizes of sub-districts in Bihar, India.

Visceral Leishmaniasis

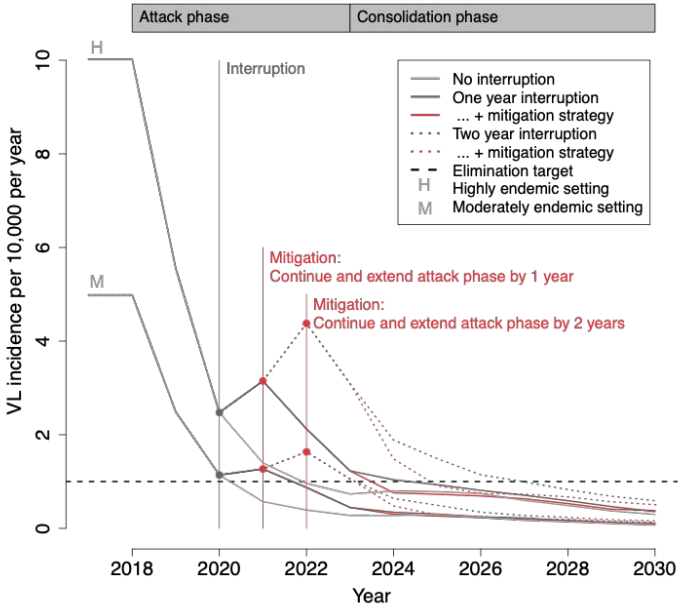
Scenarios and mitigations strategies modelled

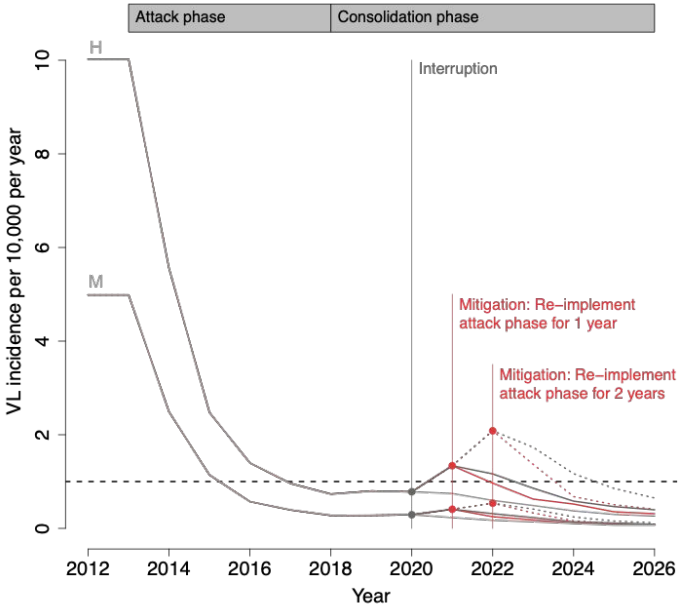
Pre-control: no IRS, no active case detection (time until treatment 60 days)
Interruption
A Attack phase: Intense IRS, active case detection (time until treatment 45 days)
C Consolidation phase: Limited IRS, Increased active case detection (time until treatment 30 days)
A Mitigation strategy: extension or reinintiation of the attack phase

Delays until reaching EHPH for all settings and scenarios

	Time to EPHP	Delay to EPHP			
Timing of interruption *Setting*	**No interruption**	**1 year of interruption**	**1 year of interruption + mitigation** *(reduction)*	**2 years of interruption**	**2 years of interruption + mitigation** *(reduction)*
Attack phase *Moderate*	6 months	1.5 years	1.5 years *(none)*	3 years	3 years *(none)*
Attack phase *High*	2 years	2 years	1.5 years *(6 months)*	5 years	3 years *(2 years)*
Consol phase *Moderate*	*Already below target*	*Remain below target*	*Remain below target*	*Remain below target*	*Remain below target*
Consol phase *High*	*Already below target*	5.5 years	5 years *(6 months)*	7.5 years	6.5 years *(1 year)*

Visceral Leishmaniasis





Interruption during the **attack phase**:

- **H**: The delay to reaching EPHP ranges between 2 and 5 years (after 1 or 2 years of programme interruption).
- **H**: A mitigation strategy that extends the duration of the attack phase can reduce this delay with 6 months to 2 years (after 1 or 2 years of extended attack phase).
- **M**: Delays to reaching EPHP range between 1.5 and 3 years.
- **M**: An extended attack phase will not reduce this delay.

Interruption during the **consolidation phase**:

- **H**: Incidences can increase to >1 VL case per 10,000 per year in sub-districts that had already reached EPHP years earlier.
- **H**: Reimplementing the attack phase can decrease the delay to EPHP.
- **M**: Even after 2 years of program interruption, sub-districts are likely to remain under the EPHP-target. However, (for all settings) outbreaks are likely to occur at a smaller geographical scale (Bulstra *et al.*, 2018).

Gambiense Human African Trypanosomiasis (gHAT)

Models description and key assumptions

Two models were used here, Model W and Model S, to represent moderate- and high-risk settings respectively. These models share the following aspects:

- Deterministic compartmental models, with a high/low-risk structure of exposure to tsetse, and low-risk only participation in active screening (Stone and Chitnis, PLoS Comput Biol, 2015; Rock *et al*, P&V, 2015).
- There are no animal reservoirs, asymptomatic infections or importations.
- Models assume passive detection has improved since 2000, and fitted the improved rate (in both stage 1 and 2).
- Models assume either implicit (Model S) or explicit (Model W) underreporting (level inferred from data), and assume that these individuals die without treatment.

Fitting

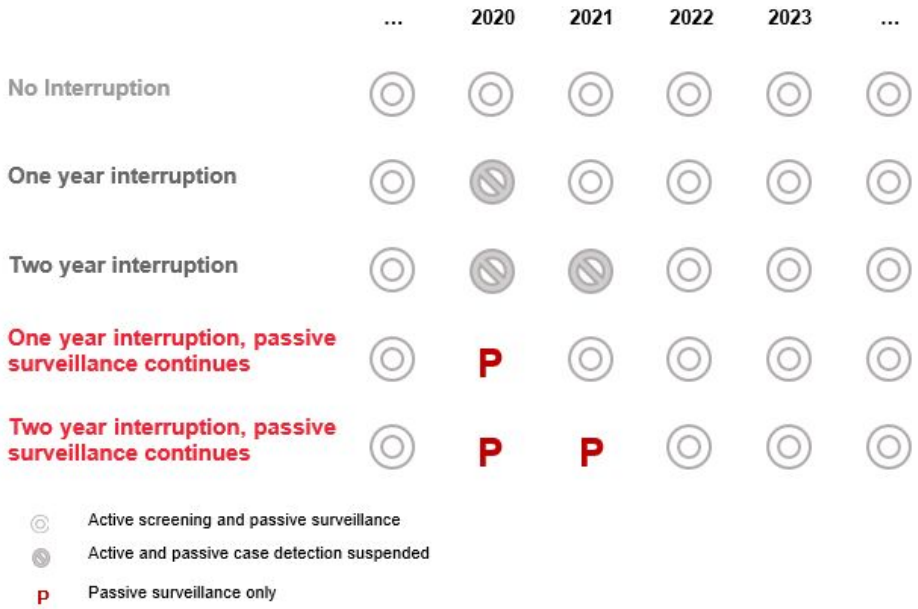
- These models have been published numerous times, and Model W has been fitted to several different data sets (Rock *et al*, P&V, 2015; Rock *et al*, PLoS NTD, 2017; Mahamat *et al*, PLoS NTD, 2017; Rock *et al*, Epidemics, 2018; Rock et al, CID, 2018; Castaño *et al*, PLoS NTD, 2020).
- The fit utilised here uses Bandundu province data (2000-2012) for Model S (Castaño *et al*, PLoS NTD, 2020), and WHO HAT Atlas data (2000-2016), aggregated to the health zone level for DRC, for Model W (Crump et. al in prep).

Projections

- For missing screening data (2017 onwards in Model W; 2013 onwards in Model S) we assume that mean levels of active screening (AS) from 2012-2016 (Model W) and 2008-2012 (Model S) were continued.
- Since we used a deterministic model for estimating EOT, we use a proxy threshold of <1 new infection per year per health zone as the EOT criterion. We believe the median EOT delays will be in line with those generated in an analogous stochastic framework.

Gambiense Human African Trypanosomiasis (gHAT)

Scenarios and mitigations strategies modelled

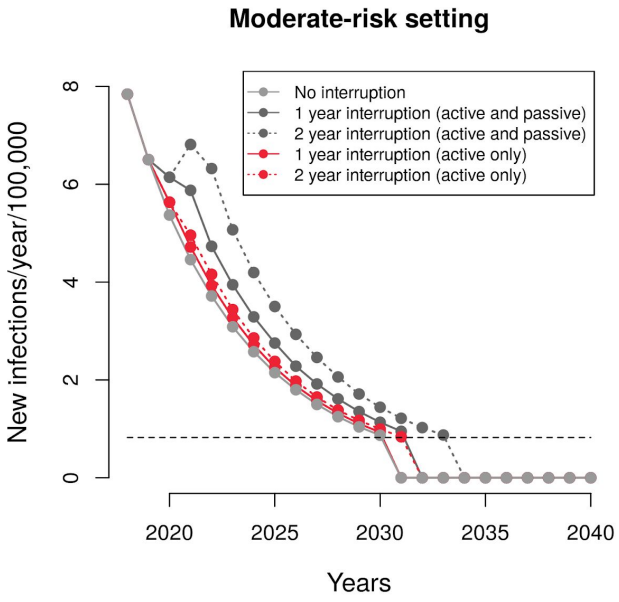


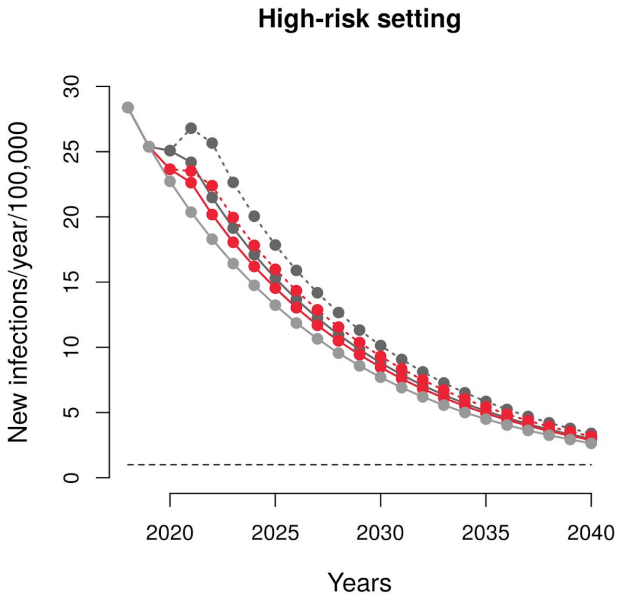
Delays in achieving EOT for all scenarios

Risk setting	Moderate	High
Time to goal if no interruption	13 years (5-29)	30 years (24-41)
Delay to goal in scenario 1 (no AS or PS, 1 year interruption)	1 year (1, 2)	1 year (1, 2)
Delay to goal in scenario 2 (no AS or PS, 2 years interruption)	3 years (2, 4)	3 years (2, 4)
Delay to goal in scenario 3 (no AS, 1 year interruption)	0 years (0, 1)	1 year (1, 2)
Delay to goal in scenario 4 (no AS, 2 years interruption)	1 year (0, 2)	2 years (1, 3)

Delay to achieving EOT goal, years (median and 95% prediction intervals) as the impact of interrupting screening activities in high- and moderate-risk settings, plus expected time to goal (from 2018) if no interruption. Timeframes >12 years would not reach EOT by 2030

Gambiense Human African Trypanosomiasis (gHAT)





Models use proxy EOT threshold marked in horizontal black dashed line

- Delays incurred with interruption of active screening (AS) only (red lines) will be small in both moderate- and high-risk settings
- There could be recrudescence of infection in the second year of interruption if both AS and passive surveillance (PS) are stopped (dark grey dashed)
- High-risk settings may have already required intensified interventions to meet EOT by 2030
- Retaining PS can help prevent substantial (temporary) increases in mortality