HAT MEPP Newsletter

Issue 1 (Aug 2021 – Aug 2022)

NEWS IN BRIEF

We would like to thank all our partners and colleagues who participated in the Direction Setting Meeting last summer, from which we have used the feedback to lay the foundation for the next phase of HAT MEPP's research. This includes a strong focus on modelling new and novel strategies, working at smaller spatial scales and completing or updating fits for Chad, Guinea, Côte d'Ivoire and Uganda. Please contact us if you would like a copy of the meeting outcomes.

OUR WORK

This year has seen the publication of a range of our work including papers on updating the Mandoul transmission model, the role of animals in transmission and elimination of gHAT, a health economics evaluation of disease elimination as well as the future strategy projections and cost-effectiveness analysis of five health zones in the DRC. Watch this space for upcoming modelling and health economic results for other countries and visit our website for an overview of our past and current work.

VISITING OUR COLLABORATORS

Regular meetings with collaborators have continued to take place virtually throughout the year and have been critical to the project's progress. Alongside this and with the lifting of restrictions we have started making our first in-country visits. Early February saw Kat meet with PNETHA and IRD colleagues in Côte d'Ivoire. The teams discussed how modelling can be used to estimate transmission reductions, quantify the strength of passive screening and understand the risks of animal reservoirs. This was swiftly followed by the TrypElim meeting, hosted by ITM and LSTM in Belgium which provided a great opportunity to reconnect in person with many of our partners.

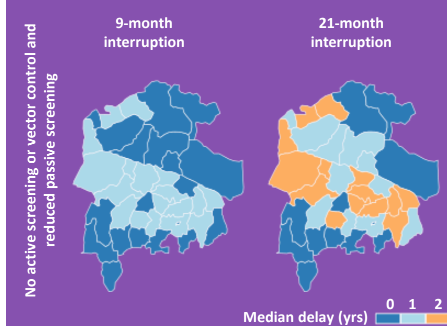
WORK IN THE PIPELINE

Work on the modelling code which now allows new and novel strategies to be considered in our analyses including "screen and treat" with acoziborole and screening of targeted high-risk populations will be used for future analysis by the team. Work is also underway to finalise the modelling and health economic analyses for Uganda, Guinea and Côte d'Ivoire alongside the refinement of the graphical user interface (GUI). Finally, the team have been making progress in the much-anticipated objective to perform modelling at smaller spatial scales (e.g. health area or village scale).

Dr Ching-I Huang
HAT MEPP Modeller

INTERRUPTIONS IMPACT

Motivated by the widespread disruption to health systems caused by the COVID-19 pandemic, Ching-I's recent research has sought to understand the impact that unplanned disruptions to the gHAT control programme could have on disease burden and time to achieve the elimination of transmission (EoT).



Delay in EoT in the former Bandundu province under interruption scenarios

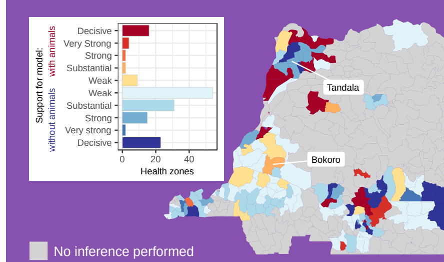
Ching-I's results suggest that gHAT programmes appear robust to short shocks if activities can be resumed again post-interruption with EoT not predicted to be delayed by more than the length of interruption plus one additional year under the most extreme interruption scenario.

+ Read more

Dr Ron Crump
HAT MEPP Modeller

ANIMAL RESERVOIRS

Questions remain around the existence and impact of gHAT infections in animals, whether animal infections can be transmitted via the tsetse vector to humans slowing, or preventing progress towards EoT.



Support for the model with or without animals contributing to the transmission of gHAT

With a focus on the DRC, Ron used mathematical modelling to assess whether animals are likely to contribute to the transmission cycle and, if so, how their presence may impact the achievability and timing of EoT.

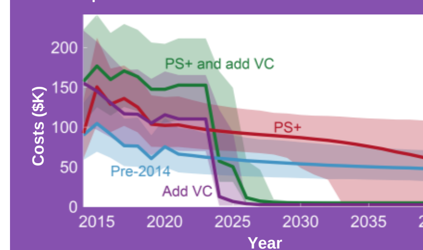
His research found that 24 out of 158 health zones included in the analysis had "substantial to decisive" statistical support for some contribution of animals to the transmission cycle. Despite these findings he estimates that animals, in the presence of the vector, are extremely unlikely to maintain transmission alone.

+ Read more

Dr Marina Antillon
HAT MEPP Health Economist

HEALTH ECONOMICS IN MANDOUL

PNLTHA-Chad and their partners made substantial changes to their gHAT interventions in Mandoul from 2014 including improved screening in health facilities and the use of vector control. In Marina's most recent paper she explores whether these past interventions were an effective use of resources and what the health economic implications would have been had less ambitious strategies been performed.

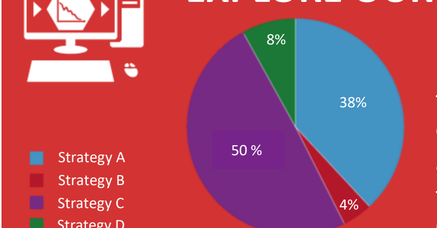


Cost per year for strategies carried out from 2014 onwards (retrospective analysis)

Her paper also considers future strategies concluding that the scaleback of vertical interventions appears cost-effective if passive screening remains robust in Mandoul. This could enable the shifting of resources to tackle other extant foci in Chad.

+ Read more

EXPLORE OUR INTERACTIVE RESULTS



Probability a strategy is cost-effective

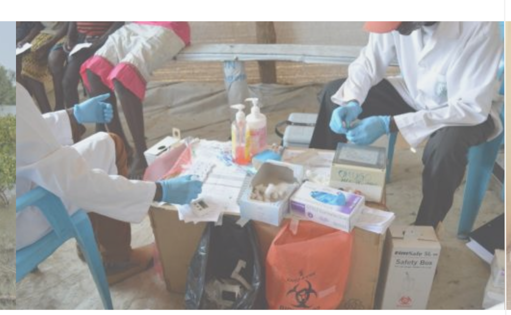
HAT MEPP's software developer, Paul, has been working alongside the modellers and health economists to integrate the results generated by our models into a user-friendly platform: our HAT MEPP graphical user-interface (GUI). Our publicly available GUIs, that accompany several of our papers, allow an exploration of our transmission and health economic results for both the DRC and Chad as well as model fitting with the inclusion of animals in the transmission cycle. GUIs for Uganda, Côte d'Ivoire and Guinea are in development and will be available soon.

Dr Paul Brown, HAT MEPP Software Developer

OTHER NEWS

- This year we welcomed Sam Sutherland into the HAT MEPP team who, amongst other things, will be working on the health economics analysis for the Côte d'Ivoire. We also welcomed back to the group Dr Chris Davis who will be working alongside Ron to adapt the model for analyses at smaller spatial scales. Click here to view members of the HAT MEPP team.
- Greater accessibility for our Francophone colleagues will be on the agenda for the coming months with the addition of bilingual content to the HAT MEPP website.



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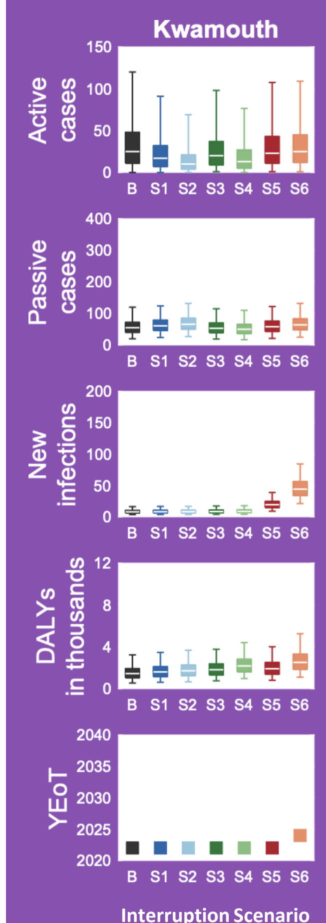
INTERRUPTIONS IMPACT

Analysis of interruption scenarios was performed on 38 health zones from the former Bandundu province of the DRC. Dates and durations of interruptions were loosely based on the recent COVID-19 pandemic and we considered how interruptions to different programme components would impact transmission dynamics, disease burden and the probability and year of EoT. Below we show an example of how the health zone Kwamouth, in which vector control has been deployed since 2019, was predicted to be impacted in response to a 9 and 21 month interruption to active screening, passive screening and vector control under these different scenarios (S1 – S6, see paper for details) :



Model outputs for Kwamouth health zone under the baseline and six interruption scenarios (S1-S6) from 2020–2030

SCENARIO WITH NO ACTIVE SCREENING

The model predicts that if active screening is interrupted there are very few extra new infections and limited impact on the probability of EoT. Although there is an increase in disease burden ten years post-interruption the proportional increase is lower compared to health zones which have no plans for vector control, such as Mosango, because of the on-going vector control in Kwamouth.

SCENARIO WITH NO ACTIVE SCREENING AND REDUCED PASSIVE SCREENING

Very few additional infections are caused by the further reduction in medical interventions as well as having limited impact on the probability of EoT. As in the "no active screening" scenario the proportional increase in disease burden is lower compared to a health zones without vector control.

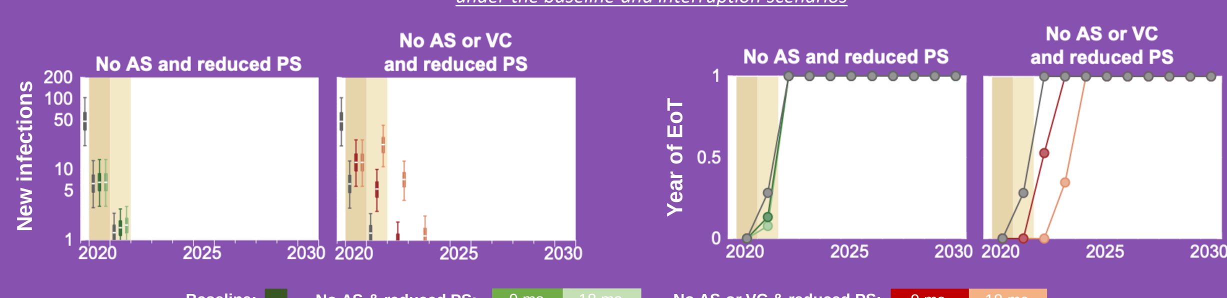
SCENARIO WITH NO ACTIVE SCREENING OR VECTOR CONTROL AND REDUCED PASSIVE SCREENING

What is notable about this scenario is that new infections do not fall as rapidly compared to scenarios without interruption or where vector control continues, and a substantial increase in new infections accumulate between 2020–2024. It is likely that this is a consequence of there being only two rounds of vector control deployments in Kwamouth prior to the start of the interruptions meaning the remaining low numbers of tsetse carry on passing the parasite to humans. This can result in more new infections in humans during the vector control deployment interruption period. Despite the shift in the year of EoT, in this scenario Kwamouth would be expected to reach EoT within two years after vector control resumes and the average estimated delays to the year of EoT are equal to the length of interruptions (i.e. one year for a 9-month interruption and two years for a 21-month interruption).

This important piece of research demonstrates that disruptions to gHAT control programmes can impact the level of disease burden and the probability and year of EoT. However, they are believed to be fairly resilient to short-term shocks if activities are resumed post-interruption. This is likely to be a consequence of the slow-progressing nature of the gHAT infection.

To find out more about this research click here.

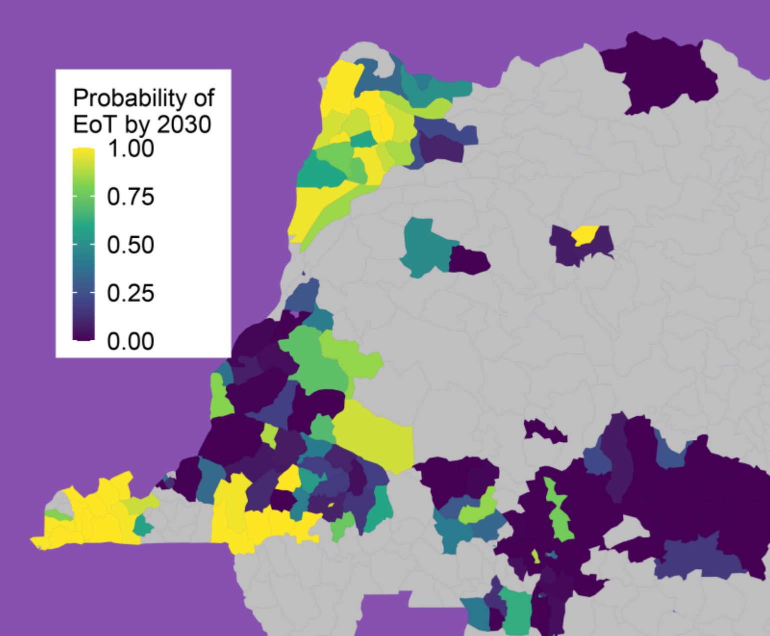
Time series of new infections and the probability of elimination of transmimssion in Kwamouth health zone under the baseline and interruption scenarios



ANIMAL RESERVOIRS

Despite evidence that the sleeping sickness parasite, *Trypanosoma brucei gambiense*, can be found in both wildlife and domestic livestock, it is uncertain if and to what extent non-human animals contribute to the transmission cycle. Mathematical modelling can, however, be applied to this particular problem in unpicking the quantitative contribution of animals and whether they can maintain transmission cycles in the absence of humans. In Ron's study, he used two different model variants, with and without animals, to better understand the transmission of gHAT, fitting them to longitudinal data (2000–2016) across 158 endemic health zones of the DRC and assessed whether there is more support for a model with animal transmission or for one without. The model was also used to assess whether animals are able to maintain transmission on their own and to predict how the time to reach EoT might change if animals contribute to onward infections.

In the health zones that have the best statistical support for the model with animal transmission, case reports have been low but persistent for several years. Despite this, the modelling indicates that the EoT should be achievable over time, although progress is slower. The map on the right shows the model-estimated probability of EoT occurring by 2030 for all health zones based on an Ensemble model, weighted by the statistical support of models with or without animal transmission.



Probability EoT to humans is achieved by 2030 using model weightings based on statistical evidence

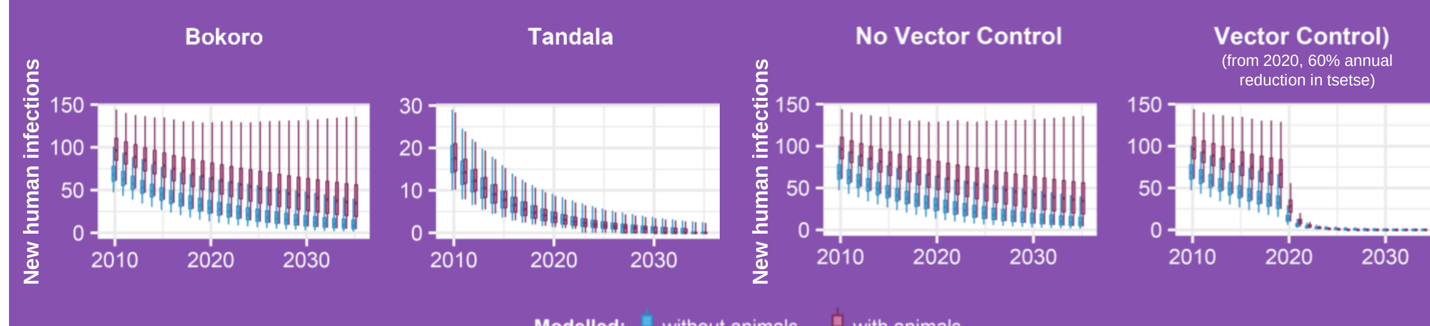
Two example health zones – Bokoro (in Bandundu) and Tandala (in Equateur) - are displayed in the figures below which show the contrasting impact of animal transmission on the number of new human infections as predicted by the model. Whilst Tandala has similar results between the model variants with and without animal transmission, Bokoro has substantially more estimated underlying new human infections each year if animal transmission is possible (see Figure below left). Inclusion of vector control in Bokoro (see Figure below right) is predicted to result in a rapid decline in new infections whether there is animal transmission or not.

Explore the results from all 158 health zone level fits with and without animal transmission and projections in the GUI.

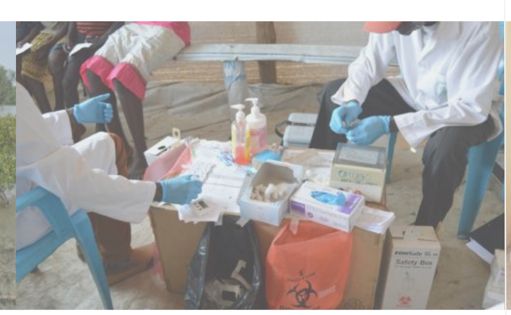
To find out more about this research click here.

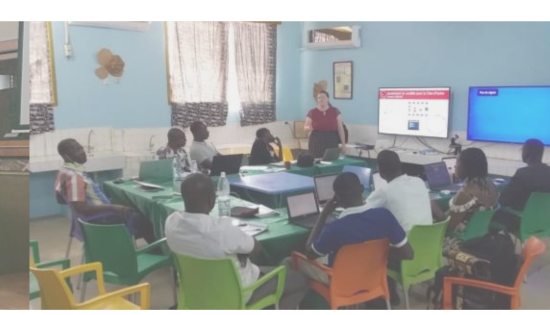
New human infections predicted for Bokoro and Tandala health zones for models with and without animals contributing to gHAT transmission

The impact of vector control on new human infections in Bokoro for models with and without animals contributing to gHAT transmission







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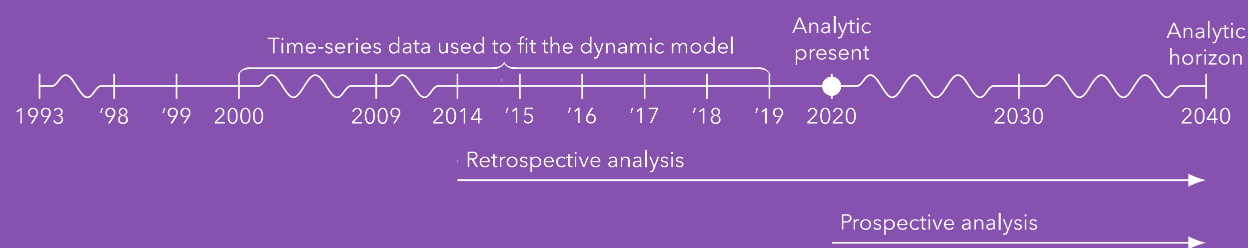
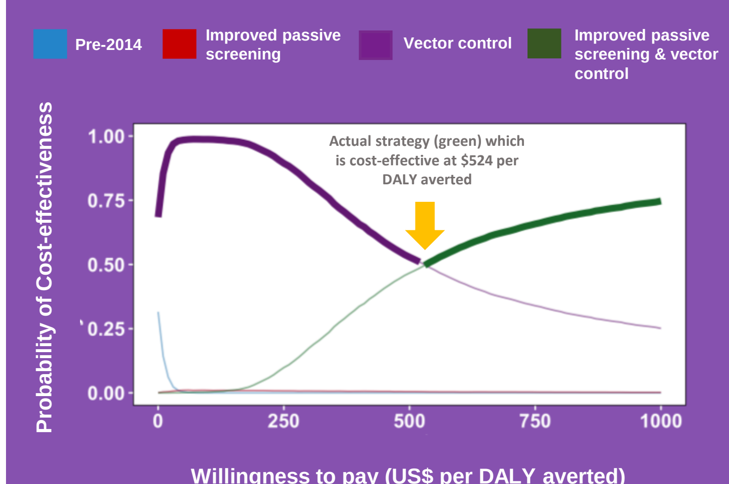
HEALTH ECONOMICS IN MANDOUL



RETROSPECTIVE ANALYSIS

Improvements rolled out for active and passive screening from 2015 have paved the way for more rapid diagnosis and accessible treatment. However, including vector control as part of the strategy from 2014 has been shown to be good value-for-money and substantially increased the probability of reaching the target of EoT in Mandoul. The strategy that was implemented in Mandoul (*Improved passive screening & vector control)* cost an additional $500,996 (with 3% yearly discounting), for an additional 957 Disability adjusted life years (DALYs) averted compared to what would have been expected with continuation of the previous strategy (*Pre-2014*). While investment in vector control was computed to be cost-saving, the investment in improved passive screening was cost-effective at a willingness-to-pay (WTP) of $524/DALY averted. At $500/DALY averted, there is 47% probability that the implemented strategy (*Improved passive screening & vector control)* was optimal, while at a WTP of $1000/DALY averted, the probability that the implemented strategy was optimal is 75% (see figure below).

Uncertainty in cost-effectiveness for the retrospective analysis. Cost-effectiveness acceptability frontier marked in bold.

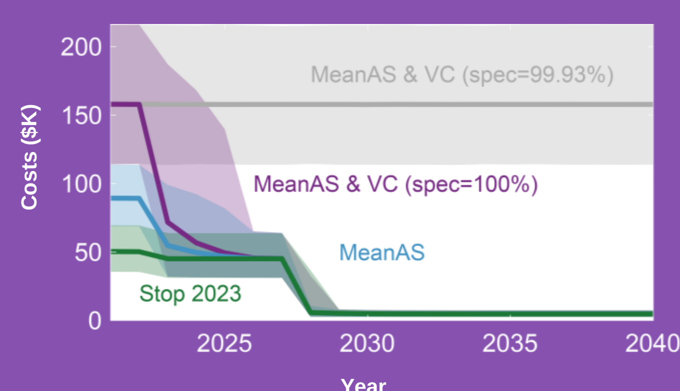


PROSPECTIVE ANALYSIS

The prospective analysis predicts that any strategies with interventions other than basic continuation of passive screening are not cost-effective. The model indicates that halting active screening and vector control in Mandoul is cost-effective provided passive screening remains robust. Resources towards gHAT prevention and treatment in Mandoul could therefore be diverted to address the existing gHAT burden in Moissala and Maro. The analysis also showed that imperfect test specificity in active screening (see scenario *MeanAS & VC (spec = 99.93%)*) is very likely to incur some direct costs in over-treatment, but that these costs would be overshadowed by the inability to confidently stop vertical activities. If vector control and active screening continue until no more parasitologically positive cases are detected, costs are predicted to be at most $650,000 for the period of 2021–2040.

Explore the results from the Mandoul cost-effectiveness analysis in the GUI.

Cost per year for strategies carried out from 2021 onwards (prospective analysis)



THE HAT MEPP TEAM

Dr Kat Rock
Team Leader and Modeller
"A mathematician by training, I guide our team from big research questions through to technical implementation and dissemination"

Dr Ron Crump
Modeller
"My primary focus is on fitting gHAT models to historical case data and understanding epidemiological drivers of transmission"

Dr Emily Crowley
Scientific Project Manager
"I manage many of the external and internal components of the project as well as taking charge of the groups dissemination activities"

Dr Ching-I Huang
Modeller
"I customise the model to capture location-specific historical interventions and tailor future strategies based the national programme and partners plans"

Dr Paul Brown
Software Developer
"My role involves the development of a user-friendly interface allowing users to explore visually the results of our simulations in detail"

Dr Christopher Davis
Modeller
"I develop gHAT models at different spatial scales, from villages to larger regions, with a focus on stochastic modelling"

Dr Marina Antillon
Health Economist
"I specialise in decision analysis, which considers optimal allocation of resources in the face of scarce resources"

Dr Simon Spencer
Statistician
"I specialise in fitting transmission models for infectious diseases to data, especially for neglected tropical diseases"

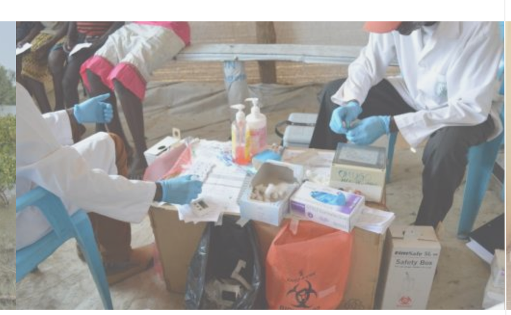
Samuel Sutherland
Health Economist
"My role involves projection of resource use and health burden to enable comparison of alternative interventions"

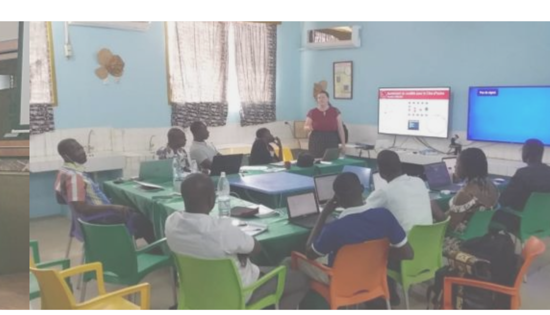
Dr Louise Dyson
Modeller
"My primary focus on the HAT-MEPP project is developing methods to monitor gHAT elimination progress and robustness of local elimination"

Prof Fabrizio Tediosi
Health Economist
"I specialise in economic evaluations in the context of elimination, drawing on my experiences from other NTDs and LMIC health systems"

Prof Matt Keeling
Modeller
"I support methodological modelling aspects of the project, using my experience analysing many other infections of humans and animals"

Dr Jason Madan
Health Economist
"I provide guidance on health economic methods, drawing on my research interests in Global Health Economics and Health Economic Modelling"





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This research was funded by the Bill & Melinda Gates Foundation

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