Institution: Liverpool School of Tropical Medicine (LSTM)

Unit of Assessment: UOA1

Title of case study: Working towards the elimination of sleeping sickness through vector control

Period when the underpinning research was undertaken: 2007 – 2020

Details of staff conducting the underpinning research from the submitting unit:

Name(s):	Role(s) (e.g. job title):	Period(s) employed by submitting HEI:
Steve Torr	Professor, Entomology	2013 –
Alvaro Acosta-Serrano	Senior Lecturer, Parasitology	2008 –
Martin Donnelly	Professor, Evolutionary Genetics	1999 –
Ian Hastings	Senior Lecturer, Medical Statistics	1999 –
Mike Lehane	Professor, Medical Entomology	2004 – 2015
David Molyneux	Professor, NTDs	2008 – 2018
Michelle Stanton	Lecturer, Spatial Epidemiology	2012 – 2017; 2020 –

Period when the claimed impact occurred: 2013 – 2020

Is this case study continued from a case study submitted in 2014? Y/**N NO**

1. Summary of the impact (indicative maximum 100 words)

Gambian Human African trypanosomiasis (g-HAT), commonly called sleeping sickness, is a fatal disease caused by trypanosomes transmitted by tsetse flies.
World Health Organization (WHO) leads a global programme to eliminate g-HAT as a public health problem by 2020. International research led by the Liverpool School of Tropical Medicine (LSTM) produced 'Tiny Targets', a simple method of tsetse control. By 2020, Tiny Targets protected approximately 1,800,000 people in the 5 countries where most (90%) cases of g-HAT occur. Vector control has contributed to WHO achieving its goal of reducing the number of cases of gHAT reported globally to less than 2,000 cases/year by 2020; between 2017 and 2019, the number of new cases reported annually ranged between 1,409 and 864 compared to 10,466 and 2,110 for the previous decade (between 2007 and 2016).

2. Underpinning research (indicative maximum 500 words)

Most (more than 95%) cases of Human African Trypanosomiasis (HAT) occur in Central and West Africa and are caused by *Trypanosoma brucei gambiense* (Gambian HAT, g-HAT) transmitted by riverine species of tsetse. There are no vaccines or prophylactic drugs effective against g-HAT and disease management has relied almost exclusively on case detection and treatment. Achieving high coverage (more than 70% cases detected) of the population is difficult in the remote settings where g-HAT occurs. Between 30% and 90% of cases are never detected, and without treatment, patients inevitably die. In addition, the standard treatment for advanced (second-stage) disease, nifurtimox-eflornithine combination therapy (NECT), is complex to administer (e.g. 14 intravenous infusions over a fortnight) in the remote settings where g-HAT commonly occurs. Vector control offers the only means of protecting people from infection, but the standard methods of control were not cost-effective for the vectors of *T. b. gambiense*. Accordingly, Lehane initiated an international programme to develop new, low-cost methods of tsetse control, as part of a global effort, led by WHO, to eliminate g-HAT as a public health problem by 2020 and achieve complete interruption of transmission by 2030.

Six academic staff from LSTM led a multinational team of vector biologists (LSTM, University of Greenwich, Institut de Recherche pour le Développement (IRD), France) and chemical ecologists (Rothamsted Research). The team worked in partnership with scientists from some of the most affected countries (Burkina Faso (Centre international de recherche-développement sur l'elevage en zone subhumide (CIRDES)), Cote d'Ivoire (Institut Pierre Richer(IPR)), Kenya (International Centre of Insect Physiology and Ecology (ICIPE)) and Democratic Republic of

Congo (Labovet)), to develop cost-effective methods of controlling tsetse vectors of pathogenic trypanosomes in sub-Saharan Africa. We first carried out field-based analyses of the behavioural responses of riverine tsetse to the visual and olfactory cues produced by hosts (between 2007 and 2011). LSTM led the research programme (PI= Lehane) and LSTM vector biologists worked in Africa with national researchers from each country.

Our work led to the discovery that riverine tsetse are highly responsive to small (25cm^2) blue-coloured targets. These initial findings applied to all the most important vectors of *T. b. gambiense* [1], suggesting that deploying small insecticide-treated targets in the riverine habitats where tsetse concentrate could provide a cost-effective means of vector control. Working with an industrial partner (Vestergaard), we developed 'Tiny Targets', small (25cm x 25cm) panels of blue polyester flanked by a panel of insecticide-impregnated netting. Results from field trials of Tiny Targets conducted in Kenya, Uganda and Guinea between 2012 and 2015 showed that the targets dramatically reduced densities of tsetse by 70% to more than 90% [2,3,4], and the incidence of g-HAT by more than 90% [3, 4] For example, in the Mandoul focus of Chad, Tiny Targets were estimated to have contributed 70.4% (95% CI: 51–95%) of the reduction in reported cases between 2014 (90 cases) and 2015 (47 cases) [4]. Economic analyses of the trials conducted in Uganda [5] and Chad [6] showed that the cost of tsetse control was reduced to less than USD100/km^2, representing a more than 80% reduction in costs compared to standard methods of tsetse control. More than 80% of g-HAT cases occur in Democratic Republic of Congo (DRC), and epidemiological models of g-HAT in high-endemicity foci suggested that the existing strategy of detecting and treating cases only would delay achieving the 2030 goal by 91- 206 years (2121 and 2236) compared to the year 2024 if Tiny Targets were also used [7]. The development of a cost-effective and logistically simple method of tsetse control led to a shift in the strategies of national programmes and the WHO for eliminating g-HAT, with vector control becoming a named tool that should be combined with case detection and treatment.

3. References to the research (indicative maximum of six references)

1. Esterhuizen J, Rayaisse JB, Tirados I, Mpiana S, Solano P, Vale GA**, Lehane MJ**, **Torr SJ**. Improving the cost-effectiveness of visual devices for the control of riverine tsetse flies, the major vectors of human African trypanosomiasis. PLoS Negl Trop Dis. 2011. DOI: 10.1371/journal.pntd.0001257
2. Tirados I, Esterhuizen J, Kovacic V, Mangwiro TN, Vale GA, Hastings I, Solano P, **Lehane MJ**, **Torr SJ**. Tsetse Control and Gambian Sleeping Sickness; Implications for Control Strategy. PLoS Negl Trop Dis. 2015. DOI: 10.1371/journal.pntd.0003822
3. Courtin F, Camara M, Rayaisse JB, Kagbadouno M, Dama E, Camara O, Traoré IS, Rouamba J, Peylhard M, Somda MB, Leno M, **Lehane MJ**, **Torr SJ**, Solano P, Jamonneau V, Bucheton B. Reducing Human-Tsetse Contact Significantly Enhances the Efficacy of Sleeping Sickness Active Screening Campaigns: A Promising Result in the Context of Elimination. PLoS Negl Trop Dis. 2015. DOI: 10.1371/journal.pntd.0003727
4. Mahamat MH, Peka M, Rayaisse JB, Rock KS, Toko MA, Darnas J, Brahim GM, Alkatib AB, Yoni W, Tirados I, Courtin F, Brand SPC, Nersy C, Alfaroukh IO, **Torr SJ**, **Lehane MJ**, Solano P. Adding tsetse control to medical activities contributes to decreasing transmission of sleeping sickness in the Mandoul focus (Chad). PLoS Negl Trop Dis. 2017. DOI: 10.1371/journal.pntd.0005792
5. Shaw AP, Tirados I, Mangwiro CT, Esterhuizen J, **Lehane MJ**, **Torr SJ**, Kovacic V. Costs of using "tiny targets" to control Glossina fuscipes fuscipes, a vector of *gambiense* sleeping sickness in Arua District of Uganda. PLoS Negl Trop Dis. 2015. DOI: 10.1371/journal.pntd.0003624
6. Rayaisse JB, Courtin F, Mahamat MH, Chérif M, Yoni W, Gadjibet NMO, Peka M, Solano P, **Torr SJ**, Shaw APM. Delivering 'tiny targets' in a remote region of southern Chad: a cost analysis of tsetse control in the Mandoul sleeping sickness focus. Parasit Vectors. 2020. DOI: 10.1186/s13071-020-04286-w

7. Rock KS, **Torr SJ**, Lumbala C, Keeling MJ. Predicting the Impact of Intervention Strategies for Sleeping Sickness in Two High-Endemicity Health Zones of the Democratic Republic of Congo. PLoS Negl Trop Dis. 2017. DOI: 10.1371/journal.pntd.0005162

4. Details of the impact (indicative maximum 750 words)

Tiny Targets protected approximately 1,800,000 people in the 5 countries where 89.6% (34653 of the total 38668 cases) of all g-HAT cases were reported in the last decade (between 2010 and 2019) [1]. Evidence of the impact of Tiny Targets on g-HAT across a range of epidemiological settings led to tsetse control being included in national and global strategies to eliminate g-HAT as a public health problem.

Impact on populations at risk of g-HAT

Following successful trials conducted between 2011 and 2013 (reference 3 & 4 in Section 3), use of Tiny Targets was scaled up in in Uganda and Guinea to cover all g-HAT foci by 2020. Tiny Targets were also adopted by national HAT control programmes in Chad (2014), DRC (2015) and Côte d'Ivoire (2016). The largest deployment was in DRC where the Tryp-Elim programme, funded by the Bill & Melinda Gates Foundation (BMGF) supported the annual deployment of 43,000 Tiny Targets and by 2019 approximately 300,000 people across 5,300km^2 were protected from g-HAT. A second BMGF-funded programme ("Trypa-NO!") has supported the scale-up of Tiny Targets in additional countries and, since 2017, a total of approximately 1,500,000 people have been protected in Guinea (1,900km^2, 200,000 people protected), Chad (960km^2, 80,000 people), Uganda (3,900km^2, 1,139,000 people) and Ivory Coast (250km^2, 170,000 people) [2].

The scale-up of Tiny Targets has had a dramatic impact on disease incidence. In addition to our own data from Chad (reference 4 in Section 2), others have shown that targets reduced the annual incidence of g-HAT in the Boffa focus in Guinea by over 90% (14/1279=1.09% without vector control *vs* 2/2777=0.07% with vector control) [3]. Continued deployment of Tiny Targets in the Mandoul and Maro foci of Chad has contributed to a decrease from 95 (2014) to 16 (2019) in the total number of cases reported nationally. The development of a tsetse control method that is affordable and practicable for local communities (Tiny Targets can be distributed using bikes and dugout canoes rather than lorries) has strengthened the resilience of control programmes. In Guinea, the Ebola crisis interrupted programmes to screen-and-treat populations for g-HAT and in the Boffa focus, prevalence of g-HAT increased in areas where Tiny Targets were absent but remained low in areas where the local community deployed Tiny Targets [3]. Similarly, deployment of Tiny Targets continued in all countries during the Covid-19 pandemic.

Impact on national g-HAT strategies

Economic [4] and epidemiological models [5] indicated that the addition of tsetse control using Tiny Targets to the standard screen-and-treat strategies accelerates progress towards the WHO elimination goals. For instance, analyses of progress towards elimination goals in DRC suggested that 37 of 43 Health Zones in DRC health zones will require vector control to meet the 2030 elimination goal [5]. Since starting with a pilot project in 2015, deploying Tiny Targets in Yasa Bonga Health Zone, which demonstrated >85% reduction in tsetse numbers [6], activities have now expanded to six further Health Zones (Masi Manimba, Kikongo, Bandundu, Kwamouth, Bulungu and Bolobo) as part of the national strategy to meet the 2030 elimination goal. Theoretical and empirical evidence of the impact of Tiny Targets led the national programmes of Chad (PNLTHA), Cote d'Ivoire (IPR), DRC (PNLTHA), Guinea (PNLTHA) and Uganda (COCTU) to adopt Tiny Targets as part of their national strategies to control g-HAT. Consequently, use of Tiny Targets has increased from 10,000 deployed in 2013 to 100,000 deployed annually in 2020. Over the same period, the aggregate area over which Tiny Targets were deployed increased from approximately 750km^2 to 13,000km^2 to protect approximately 1,800,000

people. Recognising its philanthropic and ethical responsibilities, Vestergaard, the manufacturer of Tiny Targets, announced that they will donate all Tiny Targets free from 2020 onwards [7].

Global policy

Our empirical and theoretical evidence combined with outreach and engagement activities with normative bodies led to a 2014 WHO recommendation that tsetse control should be an integral part of the global programme to eliminate g-HAT [8]. Policy makers were engaged through regular visits by LSTM researchers to the headquarters of WHO (Geneva), African Union (Addis Ababa) and national ministries of health, as well as presentations at international meetings organised by WHO [7], the AU's Pan-African Tsetse and Trypanosomiasis Eradication Campaign (PATTEC) and International Scientific Council for Trypanosomiasis Research and Control (ISCTRC), meetings with the leaders of national programmes [9] and engagement with print and broadcast media [10].

the inclusion of vector control tools has ensured that the WHO's program to eliminate g-HAT as a public health problem by 2020 is on track with, for example, the specific goal of less than 2,000 new cases reported annually being achieved from 2017 (1,409 cases) onwards (2018, 953 cases; 2019, 864 cases). These low numbers contrast with the decade between 2005 and 2014, prior to the inclusion of vector control, when the number of new cases reported globally ranged between 3,679 (2014) and 15,624 (2005) annually [1].

5. Sources to corroborate the impact (indicative maximum of 10 references)

1. **WHO data showing decline in reported cases of HAT and relative importance of DRC, Chad and Guinea for global burden**. http://apps.who.int/neglected_diseases/ntddata/hat/hat.html
2. **Manuscript describing scale up of Tiny Targets** Ndung'u JM, Boulangé A, Picado A, Mugenyi A, Mortensen A, Hope A, Mollo BG, Bucheton B, Wamboga C, Waiswa C, Kaba D, Matovu E, Courtin F, Garrod G, Gimonneau G, Bingham GV, Hassane HM, Tirados I, Saldanha I, Kabore J, Rayaisse JB, Bart JM, Lingley J, Esterhuizen J, Longbottom J, Pulford J, Kouakou L, Sanogo L, Cunningham L, Camara M, Koffi M, Stanton M, Lehane M, Kagbadouno MS, Camara O, Bessell P, Mallaye P, Solano P, Selby R, Dunkley S, Torr S, Biéler S, Lejon V, Jamonneau V, Yoni W, Katz Z. Trypa-NO! contributes to the elimination of *gambiense* human African trypanosomiasis by combining tsetse control with "screen, diagnose and treat" using innovative tools and strategies. PLoS Negl Trop Dis. 2020. DOI: 10.1371/journal.pntd.0008738
3. **Tiny Targets controlling HAT during the Ebola crisis in Guinea**. Kagbadouno, M.S., Camara, O., Camara, M., Ilboudo, H., Camara, M.L., Rayaisse, J.-B., Diaby, A., Taore, B., Leno, M., Courtin, F., Jamonneau, V., Solano, P., Bucheton, B., 2018. Ebola outbreak brings to light an unforeseen impact of tsetse control on sleeping sickness transmission in Guinea. bioRxiv, 202762. https://www.biorxiv.org/content/10.1101/202762v1.full.pdf
4. **Economics models showing the cost-effectiveness of tsetse control using Tiny Targets**. Sutherland CS, Stone CM, Steinmann P, Tanner M, Tediosi F. Seeing beyond 2020: an economic evaluation of contemporary and emerging strategies for elimination of *Trypanosoma brucei gambiense*. Lancet Glob Health. 2017. DOI: 10.1016/S2214-109X(16)30237-6
5. **Epidemiological models showing predicted contribution of vector control to efforts against HAT in DRC**. Huang C-I, Crump RE, Brown P, Spencer SEF, Mwamba Miaka E, Shampa C, et al. Shrinking the gHAT map: identifying target regions for enhanced control of *gambiense* human African trypanosomiasis in the Democratic Republic of Congo. medRxiv. https://www.medrxiv.org/content/10.1101/2020.07.03.20145847v1
6. **Reduction in testse fly numbers following implementation of Tiny Targets.** Tirados I, Hope A, Selby R, Mpembele F, Miaka EM, Boelaert M, Lehane MJ, Torr SJ, Stanton MC. Impact of tiny targets on Glossina fuscipes quanzensis, the primary vector of human African trypanosomiasis in the Democratic Republic of the Congo. PLoS Negl Trop Dis. 2020. DOI: 10.1371/journal.pntd.0008270

7. **WHO website reporting donation of Tiny Targets by Vestergaard** https://www.who.int/neglected_diseases/news/Global_resolve_to_end_NTDs_amid_unprecedented_progress/en/ and **Letter from Vestergaard**
8. **WHO meeting showing support for vector control as part of elimination programme and specific mention of Tiny Targets**. Barrett MP. The elimination of human African trypanosomiasis is in sight: Report from the third WHO stakeholders meeting on elimination of *gambiense* human African trypanosomiasis. PLoS Negl Trop Dis. 2018. https://doi.org/10.1371/journal.pntd.0006925
9. **Government document reporting national strategy to control HAT in DRC using screen-and-treat integrated with use of Tiny Targets to control tsetse.** HAT Republique Democratique du Congo, Ministere de la Sante Programme National de Lutte contre la Trypanosomiase Humaine Africaine (PNLTHA-RDC). Declaration de la Politique de Lutte Contre la Trypanosomiases Humaine Africaines en Republique Democratique du Congo (December 2015)
10. **BBC website reporting use of Tiny Targets in Uganda** Tangled up in blue: A sticky end to sleeping sickness. BBC reports use of Tiny Targets in Uganda. Broadcast 28/6/2015. https://www.bbc.co.uk/news/av/health-33274658/tangled-up-in-blue-a-sticky-end-to-sleeping-sickness