In March, Côte d'Ivoire became the second country in the world, after Togo in 2020[1], to be validated by the World Health Organization as having eliminated human African trypanosomiasis as a public health problem. Benin, also in West Africa, and Equatorial Guinea, in Central Africa, have submitted data to the WHO seeking similar validation. The designation demonstrates that a country has achieved a reduction in incidence of the illness, also known as sleeping sickness, to a single case per 10,000 inhabitants in all districts of a country over a five-year period.[2]

"Sustained control measures over the past two decades have brought a significant decline in cases – a positive sign that many countries will soon be crossing this landmark," said Dr Matshidiso Moeti, WHO Regional Director for Africa, in a press release.

The milestone in Côte d'Ivoire is the culmination of years of work to screen populations for sleeping sickness and treat those who contract it with recently-developed new drugs. Innovation in vector control solutions, like Vestergaard's Tiny Targets, have contributed significantly to this achievement. Alongside control measures, WHO has determined that prevention of "neglected tropical diseases" such as Human African trypanosomiasis (HAT) is one of the "best buys in global public health,"[3].

To that end, scientific, funding, and organisational partners at the Liverpool School for Tropical Medicine, the Foundation for Innovative New Diagnostics (FIND) in Kenya, the French National Research Institute for Sustainable Development (IRD), the Institute for Tropical Medicine (ITM) in Belgium, the Bill and Melinda Gates Foundation[4], government ministries in Africa, and local health workers have spent more than a decade testing, training, and deploying a vector control solution known as Tiny Targets that Vestergaard helped to design and now manufactures free of charge[5].

A brief history of Human African trypanosomiasis (g-HAT) or sleeping sickness

HAT is caused by parasites which infected tsetse flies carry to a mammalian host through their bite. The disease brings flu-like symptoms in its initial stage, and, if left untreated, progresses to the central nervous system, causing behavioural change and disturbances in

sleep patterns. Eventually, almost all people infected with either form of sleeping sickness, Gambiense Human African trypanosomiasis (g-HAT) or Rhodesiense Human African trypanosomiasis (r-HAT), fall into a coma and die. It occurs only in sub-Saharan Africa, often in remote rural areas with little or no access to health care. In 2012, more than 70 million people were at risk[6].

A graphic of sleeping sickness cases over time looks like a roller coaster. Areas of what is now Uganda, and parts of the Congo River basin, saw significant epidemics around the turn of the 20th Century. Another occurred in a number of African countries in 1920.[7] Beginning in the 1930s, British colonial powers took an environmental approach to tackling sleeping sickness, moving Africans to fly-free areas, while French and Belgians focused on reducing disease incidence in humans, mainly through medical intervention and screening.[8] In the transition to independence, with the disease largely in retreat, new governments on the continent turned their attention to more pressing plagues, such as malaria and maternal mortality.[9] By the 1970s, the roller coaster was climbing again, pushed up the slope by civil war and social instability from what is now South Sudan through neighbouring Uganda, and south to the Democratic Republic of Congo and Angola. “That really disrupted monitoring and control campaigns and depleted resources,” said Prof. Stephen Torr, chair in neglected tropical diseases at LTSM. By 1990 the region was in the grips of another major epidemic. The WHO estimated incidence at around 350,000 cases per year in the middle[10] and late years[11] of that decade. That’s around 350,000 people dying—far more than Covid-19 has killed in all but three countries[12]—every year.

Treatment options over these years improved from nonexistent to potentially fatal, then merely difficult to implement. The first drugs were effective only in the first stage of the disease, when it presents with symptoms similar to common illnesses such as malaria.[13] Side effects were non-negligible, so it was of questionable benefit to dose patients with a potentially dangerous drug when they might not even have the targeted disease. An arsenic derivative was found effective against HAT’s second stage but, like arsenic, it’s highly toxic. Only in 2009 did a safe drug emerge, but it could only be delivered intravenously over 10 days, involving dozens of bags and bottles of medicine[14]. In difficult to access areas with sparse healthcare facilities, this was often as useful as no drug at all.

Sending the rollercoaster back down the slope—and, perhaps, to the end of the track—has been a combination of factors. Researchers pursued an effective treatment, and in 2018 the European Medicines Agency approved a pill, fexinidazole, that can be administered safely at

both stages of disease.[15] But with drugs relatively expensive and not always available to everyone, prevention remains an essential strategy. So the Liverpool School of Tropical Medicine and partners in Africa and Europe researched ways to keep people from getting infected in the first place.

Tiny Targets: the vibrant blue tool controlling the spread of sleeping sickness

The strategy is to control the disease's vector—the means by which the parasite that causes it is transmitted. It was assumed that odours attracted the insects. If a "target" could be developed that attracts the tsetse, and dipped in insecticide, perhaps its placement at the right density in areas where the flies were infecting people could wipe out sleeping sickness locally. Then, by testing people's blood for the presence of the parasite, areas where illness popped up could be prioritised for intervention.

Earlier research suggested that tsetse flies were attracted to the colour blue. Researchers experimented instead with a target consisting of a piece of blue cloth placed beside a black netting coated in insecticide. "Their visual acuity is inadequate to detect that it's a net, and not empty space," Prof. Torr said of the tsetse. "Then they collide with that netting and picks up a lethal dose of insecticide.

"Working with Vestergaard, we said we want netting the flies can't see, that lasts a long time, and releases insecticide easily to a tsetse that contacts it," said Prof. Torr. "We defined the colour we needed, and then worked with the manufacturer to determine what's the nearest they could get to that colour that would last a long time and won't fade." Vestergaard was able to bring its experience with insecticide-treated nets that are used to fight malaria to the development of Tiny Targets.


Tiny Target deployed on a river in DRC. Photo: Sophie Dunkley

“It’s really a collaboration between industry that can provide materials that fit the product profile, with the basic underlying knowledge about tsetse behaviour,” he continued.

High impact, low cost

Early prototypes consisted of around one meter square each of blue target cloth and netting tied to tall stakes. But these proved unwieldy for deployment. “Each team could carry maybe a few of them,” says Allan Mortensen, now Vestergaard’s Managing Director for Food Security, who led the company’s work on the tsetse targets from 2017 until 2020. “It’s just a much bigger logistical operation.”

A quick look at this video provides understanding of the challenges of bringing health care solutions to some of the areas where tsetse flies live and breed:

> A snapshot of some of the #challenges of bringing #vector #control to #remote areas of #DRCongo where #SleepingSickness #transmission occurs.
>
> This is part of the journey of 3,207 #TinyTargets to Bulungu for #tsetse control.
>
> Video credit @SteveBlackBox1 #RDCongo #RDC #PNLTHA pic.twitter.com/I4bbXGqBln
>
> — tsetse.org (@tsetse_org) May 19, 2021

An international team that included researchers at the health ministries of Guinea and Burkina Faso working alongside Torr and colleagues at LSTM conducted experiments to see how small they could get the targets and maintain effectiveness. In 2009, research was published showing that a cloth and net of just 25 square centimetres each were just as adept at attracting and killing the flies as the large targets—and 10 times more cost-effective[16]. Two years after that, it was demonstrated that the smaller size works on four subspecies that carry the parasite. A year later, they established the shade of blue with the particular reflectance of ultraviolet light, which is visible to tsetses, that attracts them best.[17] The next year they showed these targets reduced tsetse density by nearly 80%, driving down new cases to almost zero[18], and that a single year of vector control to completely stop transmission in an area could be done for under $43,000.[19] (Just 900 people can be treated with the latest drug at that cost.) By the time fexinidazole was approved, the team nailed down the density at which the targets needed to be spaced—20 per linear kilometre in a riverine basin. Just 2,600 targets costing less than a dollar apiece, when produced at scale, reduced tsetse density by 99.99% and were responsible for 70% of the decline of cases[20]. Even when Ebola disrupted screening activities in West Africa, areas with vector control were able to sustain protection and keep HAT cases subdued.[21]

“You have to kill about 4% or more of the female tsetse fly population every day, and you will drive it to extinction” in the selected area, said Prof. Torr.

Vestergaard & LTSM's: the academia-industry commitment to eliminating sleeping sickness

At the end of 2016, dozens of NGOs, countries, academic institutions, and private sector partners declared support for WHO targets to reduce the number of cases of HAT globally to under 2,000 by 2020[22]. In 2018, 977 cases were reported and have continued to decline since[23]. The goal to eliminate transmission entirely and reach the WHO NTD 2030 targets appears within reach.

Vestergaard was one of the signatories of the declaration and moved from a for-profit model to a donation model in its continuing involvement with the elimination of sleeping sickness.

The company's commitment to donate enough Tiny Targets for each country currently implementing vector control "is a huge contribution that solved an important part of the sustainability of the programmes," said Dr. Andrew Hope, LTSM's programme manager tsetse fly control in Uganda and DRC. In DRC, the largest remaining contributor to cases of sleeping sickness, LSTM and ITM are supporting the largest gHAT control programme in existence, with Vestergaard donating 90,000 Tiny Targets in 2021 alone.

"Sleeping sickness may become one of the neglected tropical diseases we actually succeed in eliminating from this planet," Mortensen said. "There aren't a lot of diseases we've been able to reduce so dramatically that elimination seems possible."

To go from 70 million people at risk and hundreds of thousands dying needlessly to a few thousand cases of sleeping sickness in just two decades is a tremendous achievement for science and public health.

Vestergaard remains committed to our role as a donating partner until this disease is eliminated. The company strongly believes in achieving zero transmissions worldwide by 2030 as major programmes now suppress the tsetse fly in the last pockets of the DRC, where 70% of the transmissions still occur today.

[1] https://news.un.org/en/story/2020/08/1071122

[2]https://www.who.int/news/item/25-03-2021-who-validates-cote-d-ivoire-for-eliminating-sleeping-sickness-as-a-public-health-problem

[3] https://www.who.int/neglected_diseases/Revised-Draft-NTD-Roadmap-23Apr2020.pdf?ua=1

[4] https://www.lstmed.ac.uk/projects/trypa-no

[5] Personal communication with S. Torr and A. Mortensen

[6] https://journals.plos.org/plosntds/article?id=10.1371/journal.pntd.0001859

[7]https://www.who.int/news-room/fact-sheets/detail/trypanosomiasis-human-african-%28sleeping-sickness%29

[8] https://journals.plos.org/plosntds/article?id=10.1371/journal.pntd.0002772#s6~~S.Torr~~

[9] S. Torr, A. Mortensen

[10] https://www.who.int/health-topics/human-african-trypanosomiasis#tab=tab_1

[11]https://www.who.int/news-room/fact-sheets/detail/trypanosomiasis-human-african-%28sleeping-sickness%29

[12] https://coronavirus.jhu.edu/map.html

[13]https://www.who.int/news-room/fact-sheets/detail/trypanosomiasis-human-african-%28sleeping-sickness%29

[14] YouTube video

[15] https://www.sanofi.com/en/media-room/press-releases/2019/2019-01-30-15-00-00

[16]https://journals.plos.org/plosntds/article?id=10.1371/journal.pntd.0000474

[17] https://journals.plos.org/plosntds/article?id=10.1371/journal.pntd.0001661

[18] https://journals.plos.org/plosntds/article?id=10.1371/journal.pntd.0003727

[19] https://journals.plos.org/plosntds/article?id=10.1371/journal.pntd.0003822

[20] https://journals.plos.org/plosntds/article?id=10.1371/journal.pntd.0003822

[21] https://www.biorxiv.org/content/10.1101/202762v1

[22] https://www.finddx.org/newsroom/trypa-no-partnership-will-accelerate-elimination-of-sleeping-sickness-in-africa/

[23] https://www.finddx.org/newsroom/pr-04dec19/#_ftn2