Title of case study: K: Sustained long-term control of Human African Trypanosomiasis infections in Uganda through economically viable strategies

1. Summary of the impact

Underpinning Research: As reported in REF2014, our research showed that domestic livestock were the main reservoir for the Rhodesian form of Human African Trypanosomiasis (rHAT) in Uganda, and that mass treatment of cattle with trypanocidal drugs could prevent transmission of HAT infection in humans. Since REF2014, we have shown that spraying only 25% cattle with inexpensive insecticide can effectively control transmission of infection.

Significance and Reach of Impact: Emergency intervention through the public-private partnership Stamping Out Sleeping Sickness (SOS), reported in REF2014, virtually eliminated rHAT from Uganda. Since then, the challenge has been to maintain low levels of infection in a sustainable manner. This is now managed through a new national policy based on our novel research, with the Coordinating Office for Control of Trypanosomiasis in Uganda (COCTU) now mandating routine spray of 25% of cattle with insecticide. Delivered through a catalytic model involving local communities, this policy has since 2016 sprayed approximately 1,000,000 cattle every year (5,671,266 in total by 2020). As a result, infection rates have remained low and cattle productivity has increased by USD30 (GBP22; 10-20) per head, adding USD30,000,000 (GBP21,910,443; 10-20) in income to impoverished communities. The catalytic model has contributed to local capacity building, training 453 youths to coordinate spraying activities, adding a further USD98 (GBP72; 10-20) per month to the income of these households.

SOS activities have been cited as one of the most successful examples of One Health in practice in at least 6 World Health Organization (WHO), Food and Agriculture Organization of the United Nations (FAO), and World Organisation for Animal Health (OIE) publications since August 2013.

2. Underpinning research

The Challenge: Sustainable control of sleeping sickness in Uganda

Human African Trypanosomiasis (HAT), or sleeping sickness, is caused by trypanosome parasites that are transmitted by tsetse flies. HAT exists in two forms, of which *Trypanosoma brucei rhodesiense* HAT (rHAT) causes acute disease in East Africa. In Uganda, the different forms of HAT cause a significant disease burden; 10 million people, or 30% of the Ugandan population, were at risk of HAT in 2020. The primary reservoir for rHAT infection is domestic livestock, especially cattle.

For sustainable control, WHO recommends cases be identified and treated, and transmission interrupted by vector control. Given that rHAT is a zoonosis, the source of infection must be eliminated from the animal reservoir. This is critical since cattle in particular are not only reservoirs of human infection but also long-term investments on which livelihoods depend. Importantly, any disease control strategy must be cost-effective to be sustainable in the long term.

Reported in REF2014: rHAT can be controlled by mass-treating cattle with parasite-killing drugs

Key research led by our team identified that up to 18% of cattle in south-eastern Uganda were infected with *T. b. rhodesiense* [3.1]. A case-control study then showed that a major rHAT outbreak in eastern Uganda was seeded by movement of infected cattle from endemic areas, leading to a large expansion of the rHAT focus [3.2]. WHO saw this expansion as a major public health emergency that demanded action. In a seminal paper using mathematical modelling, we demonstrated that treating 86% of cattle with a curative and prophylactic chemotherapeutic (i.e. parasite-killing, or 'trypanocidal') drug would prevent disease transmission [3.3].

Reported in REF2014: SOS activities reduced HAT cases by 90%

Based on our research findings, the Government of Uganda established the Public-Private Partnership "Stamp Out Sleeping Sickness" (SOS) in 2006 to mount an emergency response to

HAT. The main activities of SOS were 1) mass treatment of cattle in 5 districts with trypanocidal drugs to prevent northwards migration of rHAT; 2) establishment of veterinary businesses (3V Vets) to provide veterinary services and support treatments; 3) support Ministry of Health in a coordinated One Health approach for human and animal surveillance and treatments. Between 2006 and 2008, SOS oversaw the treatment of 500,000 cattle with trypanocidal drugs across 7 districts in Northern Uganda, resulting in 75% reduction of trypanosome prevalence and a 90% reduction in HAT cases [3.4]. [The PPP consists of the Government of Uganda, the University of Edinburgh, the University of Makerere, CEVA Sante Animale (a global veterinary health company), IKARE (a UK-based charity) and COCTU.]

While this mass treatment with trypanocidal drugs was highly successful in removing the parasite from the treated animal population, it did not represent a long-term solution, since the animals remained at risk of reinfection from infected tsetse flies. We therefore investigated the feasibility and efficacy of another disease control strategy in sustaining the control reported in REF2014: a restricted application protocol (RAP) of an inexpensive spray containing diluted insecticide, applied to only to the main tsetse predilection sites (the legs and belly) of the animals.

NEW since REF2014: Transmission of HAT to humans from animals can be prevented by treatment of 25% of the animal reservoir with insecticide

Modelling undertaken through the GBP6,500,000 EU-funded project ICONZ, coordinated by Welburn, showed that a simple monthly application of insecticide to cattle would bring the reproduction number R_0 to below 1, and therefore prevent rHAT transmission. We then demonstrated, in 20 village herds in eastern Uganda, that RAP insecticide treatment of only 25% of cattle in each village was sufficient to achieve sustained protection of herds from both animal trypanosomiasis and rHAT. Surprisingly, the level of protection did not increase further if a higher proportion of animals was treated [3.5].

Our research furthermore found that the RAP treatment of 25% of cattle is cost-effective compared to mass treatment with trypanocidal drugs (USD1.72 per head compared to USD6.04 per head) and avoids the risk of developing drug resistance [3.6].

Thus, our research first underpinned a highly effective emergency intervention that virtually eliminated HAT from Uganda, and subsequently identified that an affordable cost-effective insecticide treatment of 25% of cattle was sufficient to sustain low levels of infection.

3. References to the research

[3.1] Welburn SC, Picozzi K, Fèvre EM, Coleman PG, Odiit M, Carrington M, Maudlin I. (2001). Identification of human infective trypanosomes in animal reservoir of sleeping sickness in Uganda by means of serum-resistance-associated (SRA) gene. Lancet 358:2017-19. doi: 10.1016/S0140-6736(01)07096-9

[3.2] Picozzi K, Fèvre EM, Odiit M, Carrington M, Eisler MC, Maudlin I, Welburn SC. (2005). Sleeping sickness in Uganda: a thin line between two fatal diseases. BMJ 331:1238. doi: 10.1136/bmj.331.7527.1238

[3.3] Welburn SC, Coleman PG, Fèvre EM, Odiit M, Maudlin I, Eisler MC. (2006). Crisis, what crisis? Control of Rhodesian sleeping sickness. Trends in Parasitology. 22:123-8 doi: 10.1016/j.pt.2006.01.011

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[3.5] Muhanguzi D, Picozzi K, Hattendorf J, Thrusfield M, Welburn SC, Kabasa JD & Waiswa C. (2014). Improvements on restricted insecticide application protocol for control of human and animal African trypanosomiasis in Eastern Uganda. PLoS Neglected Tropical Diseases, 8: e3284. doi: 10.1371/journal.pntd.0003284

[3.6] Muhanguzi D, Okello WO, Kabasa JD, Waiswa C & Welburn SC. (2015). Cost-analysis of options for management of African Animal Trypanosomiasis using interventions targeted at cattle in Tororo District: south-eastern Uganda. Parasites & Vectors 8:387 doi:10.1186/s13071-015-0998-8

4. Details of the impact

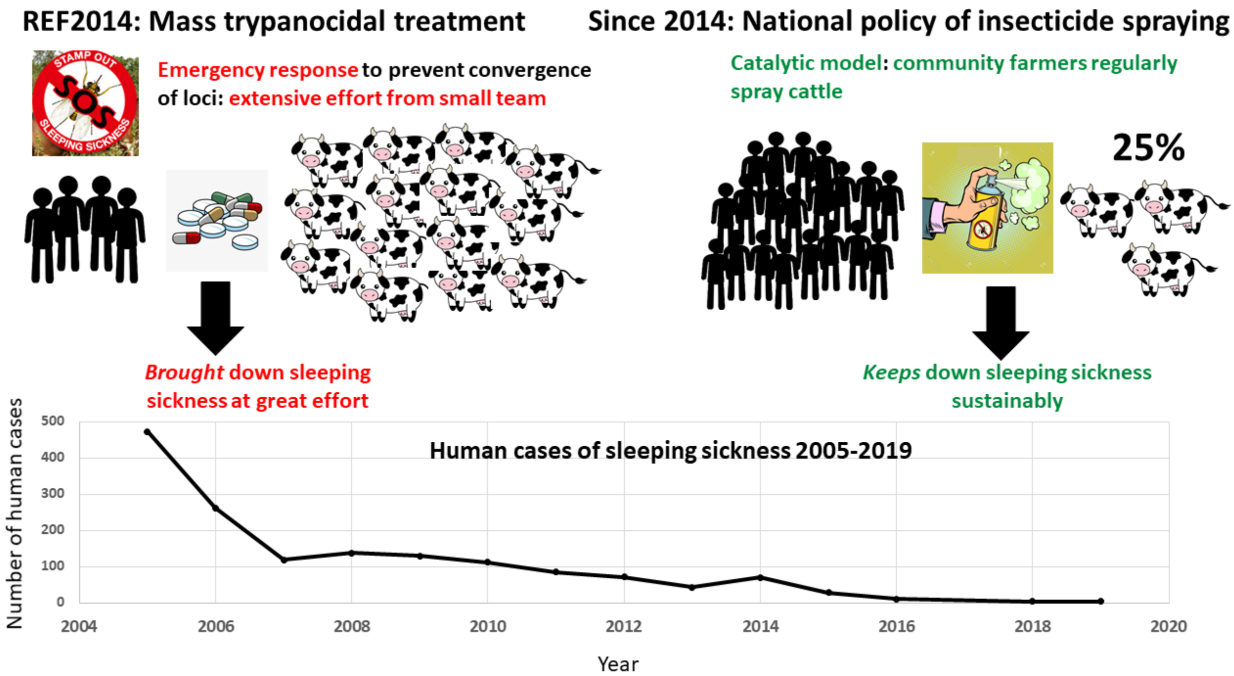

Figure 1. Summary of the impacts described in RF2014 and in this impact case study.

Reported in REF2014: Impact of mass trypanocidal treatment on human cases of HAT
The establishment of the SOS partnership in 2006 led directly to the development of cattle treatment strategies to reduce HAT infections. These strategies all but eliminated rHAT from Uganda. However, this action was always intended to be a one-off intervention for emergency use [5.1]. Deployment of mass drug administration is human resource-intensive, and repeated administration of trypanocidal drugs at scale runs risks of developing drug resistance. Crucially, trypanocidal drugs could not prevent cattle from reinfection by infected tsetse flies.

New since REF2014: Challenge of sustainably maintaining low levels of infection
Since REF2014, the challenge has been to maintain low levels of infection in an economically sustainable fashion. This is now being achieved through changes to Ugandan government policy based on our novel research since REF2014, which identified that RAP spraying only 25% of cattle with insecticide could cost-effectively result in sustainable suppression of the tsetse vector. The Minister of Agriculture, Animal Industry and Fisheries of Uganda states that this research "*directly provided the scientific evidence which underpins our national strategy and policy for sustainable control of sleeping sickness and animal trypanosomiasis in Uganda*" [5.2].

Delivery of this national policy is coordinated through COCTU, which now mandates routine spray of 25% of the cattle population using RAP [5.1]. This activity is scaled up using a catalytic model, working together with local veterinary services, 3V Vets and community farmers. The initial target in 2014 was to spray 25% of cattle (n=412,521) in 23 high-risk districts for rHAT on a regular basis. The costs for this are met by COCTU, and any additional costs by the farmers themselves, who recognise the benefits of vector control in not only suppressing rHAT transmission but also protecting cattle against ticks [5.2].

COCTU confirms that the catalytic model has "*directly supported over 1,000,000 treatments of cattle a year since 2016, introducing farmers to this new approach and supporting the farmers to adopt this cheap and effective technology for healthier animals and to prevent sleeping sickness spreading in the community.*" [5.1].

New since REF2014: Impact of routine cattle spraying on health and welfare
The elimination of HAT from Uganda, achieved through the emergency action described in REF2014, is now being sustainably maintained through the new national policy of routine spraying

with insecticide, informed by our novel research [5.1; 5.2]. The success of the catalytic model is seen in the increasing numbers of cattle sprayed over time: 250,000 cattle (30% of all cattle in the target districts) in 2014, 1,000,000 cattle (50%) in 2016 and 1,500,000 cattle (70%) in 2018. Altogether, since 2014, 5,671,266 RAP treatments have been delivered, with 3,277,173 paid for by COCTU and the remainder paid for by the community [5.3a; 5.4]. The farmers readily exceed the target of spraying 25% of animals, as insecticide treatment has the additional desirable effect of protecting the cattle from tick-borne diseases.

As a result of this routine spray treatment managed sustainably by farmer communities themselves, human cases of HAT in Uganda have remained at negligible levels since 2014; 14 cases recorded by COCTU in 2016 and 5 in 2019 (compared with 473 recorded in 2005 prior to the SOS activities) [5.3b, c; 5.4].

New since REF2014: Impact on the economy

The Ugandan Minister of Agriculture, Animal Industry and Fisheries describes the financial impact of the new policy of routine insecticide spraying as follows: "*One of the most dramatic outcomes of this research is the fiscal benefit to the farmer of this more sustainable approach, which results in increased revenues of USD30 per head of cattle. This financial benefit was the key driver for policy recommendation by COCTU to promote cattle spraying at community level which has directly resulted in over 1,000,000 cattle receiving regular treatment since 2016 across 23 districts of Uganda. An additional benefit of this approach is the wider range of diseases which are prevented by this vector-based control methodology, including disease transmitted by ticks*." [5.2.]

Given that over 1,000,000 cattle are treated annually, the increase of USD30 per head of cattle results in over USD30,000,000 (GBP21,910,000; 10-20) per year of increased productivity in impoverished rural communities in Uganda [5.4]. A recently published cost-benefit analysis indicated that the increased revenue from cattle results in a mean annual income per household of USD125 (GBP91; 10-20) [5.5]. Moreover, since only a proportion of cattle need to be treated, disease control can be undertaken by a limited number of wealthier farmers, as village cattle are co-grazed, and does not represent a financial burden for poorer communities [5.1].

New since 2014: Impact on local capacity building

The catalytic model for delivering the national policy of routine spraying has helped to build local public health expertise and human capital through mobilising and training local vets and farmers.
This is coordinated through the 3V Vets initiative, a delivery network for veterinary products and services established in 2009 as part of the SOS partnership [5.6a]. In 2014, 3 of these vets, now operating financially sustainable businesses, came together to form a joint purchasing company, 3V Vets Franchise, which procures products on a commercial basis from a number of importers and suppliers [5.6b].
Facilitated by COCTU, the 3V Vets have identified and trained individuals in villages to become Animal Resource Key (ARK) persons. ARKs help to deliver the catalytic model for rHAT control through providing link points for cattle owners to access insecticides required for spraying from the local vet [5.4]. Between 2013 and 2017, 453 ARKs were trained to understand the basics of insecticide dilution, proper handling of the chemicals involved, animal spraying techniques, entrepreneurship, as well as the scientific basis for spraying animals [5.4]. The intention was for each ARK to spray a minimum of 50 head of cattle per day for 20 days a month, totalling 1,000 cattle per month. COCTU reimburses each ARK USD0.98 per head of cattle sprayed; thus, this activity represents significant contribution to the ARKs' monthly income, since they typically only use a few hours a day to carry out spraying and can spend the rest of the day engaging in other income-generating activities [5.4].

In this way, the catalytic model has empowered local communities to take charge of disease control in their area and add to their income at the same time, ensuring long-term cost-effectiveness and sustainability of the HAT control strategy. The buy-in from the local communities is illustrated by their investment of over UGX398,000,000 Ugandan shillings (GBP78,400, 08-19) towards the cost of RAP activity between 1 July 2016 and 30 June 2017 [5.4].

New since REF2014: Impact on international guidelines and consensus

Our research and the resulting action through SOS and COCTU has been widely highlighted by WHO (2014, 2016, 2017 [5.7a-c]) and FAO (2017 [5.7d]) as one of the most successful examples of One Health in practice globally. In addition, the academic One Health community has noted the leading role of SOS: for example, an OIE Scientific and Technical Review (2014) highlighted the importance of COCTU's established One Health platform for trypanosome disease management [5.8] and an international review published in PLoS Neglected Tropical Diseases in 2014 concluded that *"This PPP could be a model for other regions and diseases in order to develop a sustainable prevention and control system."* [5.9; p.3].

5. Sources to corroborate the impact

[5.1] Letter of support from COCTU, October 2020
[5.2] Letter of support from Minister of Agriculture, Animal Industry and Fisheries Uganda, August 2020
[5.3] Data from COCTU a. Cattle sprayed 2014-2020 b. HAT cases 2005-2019 c. WHO data on human cases of rHAT, 2003-2020
[5.4] Waiswa C, Wangoola MR (2019) Sustaining Efforts of Controlling Zoonotic Sleeping Sickness in Uganda Using Trypanocidal Treatment and Spray of Cattle with Deltamethrin.
Vector Borne Zoonotic Dis.19:613-618. doi: 10.1089/vbz.2018.2382 (contains numbers of cattle sprayed until 30th June 2017)
[5.5] Okello et al. 2021 Controlling tsetse flies and ticks using insecticide treatment of cattle in Tororo district Uganda: cost benefit analysis. Frontiers in Veterinary Science.

- [5.6] a. Establishing of the 3V vets b. 3V Vets Franchise website

[5.7] International agencies highlighting SOS as an exemplary One Health approach
a. Report of the 1st WHO stakeholders meeting on rHAT, October 2014
b. Report of the 2nd WHO stakeholders meeting on rHAT, April 2017
c. "From advocacy to action": Report of the 4th international WHO meeting, November 2014
d. FAO Technical and Scientific Series report: "Intervening against bovine trypanosomosis in eastern Africa: mapping the costs and benefits", 2017.
[5.8] Vandersmissen, A, and Welburn, SC (2014) Current Initiatives in One Health – Consolidating the One Health Global Network. OIE Scientific and Technical Review, 33(2); p426 doi: 10.20506/rst.33.2.2297
[5.9] Wondwossen A et al. (2014) The Global One Health Paradigm: Challenges and Opportunities for Tackling Infectious Diseases at the Human, Animal, and Environment Interface in Low-Resource Settings doi: 10.1371/journal.pntd.0003257