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1 **Transmission Dynamics of Rhodesian Sleeping Sickness at the Interface of Wildlife and**  
2 **Livestock Areas**

3  
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10  
11 **Key words**

12 Rhodesian human African trypanosomiasis, wildlife/livestock interface, wilderness areas,  
13 animal reservoirs, tsetse, mathematical models

14  
15 **Abstract**

16 Many wilderness areas of east and southern Africa are foci for Rhodesian sleeping sickness,  
17 a fatal zoonotic disease caused by trypanosomes transmitted by tsetse flies. Although  
18 transmission in these foci is traditionally driven by wildlife reservoirs, rising human and  
19 livestock populations may increase the role of livestock in transmission cycles. Deciphering  
20 transmission dynamics at wildlife and livestock interface areas is key to developing  
21 appropriate control. Data are lacking for key parameters, including host distributions, tsetse  
22 density and mortality rates, and the relative roles of livestock and wildlife as hosts in  
23 fragmented habitats, limiting the development of meaningful models to assist in the  
24 assessment and implementation of control strategies.

## 1 **Rhodesian Sleeping Sickness: A Disease in Decline?**

2 Human African trypanosomiasis (HAT or sleeping sickness) caused by trypanosomes  
3 transmitted by tsetse flies, is targeted by the World Health Organisation (WHO) for  
4 elimination by 2020  
5 ([http://www.who.int/neglected\\_diseases/NTD\\_RoadMap\\_2012\\_Fullversion.pdf](http://www.who.int/neglected_diseases/NTD_RoadMap_2012_Fullversion.pdf)). This goal  
6 is qualified as 'elimination as a public health problem', defined as an annual incidence of  
7 less than 1 case per 10 000 population, and less than 2000 cases reported globally each year  
8 [1]. Two forms of HAT, Gambian HAT (g-HAT) found in west and central Africa and  
9 Rhodesian HAT (r-HAT) found in east and southern Africa, differ in epidemiology and  
10 control. Although good progress is being made in controlling g-HAT through mass screening  
11 and treatment of affected people with trypanocidal drugs, long term elimination of r-HAT is  
12 considered to be unfeasible due to the existence of animal reservoirs.

13  
14 HAT is caused by subspecies of *Trypanosoma brucei*. The pathogen for g-HAT, *T. b.*  
15 *gambiense*, is transmitted by 'riverine' species of tsetse such as *Glossina palpalis* and *G.*  
16 *fuscipes*. The disease is generally considered to be an anthroponosis with no important  
17 non-human hosts. r-HAT is caused by *T. b. rhodesiense* transmitted largely – but not  
18 exclusively - by 'savannah' species of tsetse such as *G. morsitans* and *G. pallidipes*. r-HAT is  
19 a zoonosis, with livestock and wild mammals such as warthog, buffalo and bushbuck acting  
20 as reservoir hosts. A third subspecies, *T. b. brucei*, is morphologically identical but does not  
21 cause disease in man. The different epidemiology of the two human pathogens reflects their  
22 genetics. *T. b. rhodesiense* is essentially a variant of *T. b. brucei*, but carries a single gene  
23 (Serum Resistance Associated; SRA) [2] that confers the ability to infect humans [3]. In  
24 contrast, *T. b. gambiense* is genetically distinct from both *T. b. brucei* and *T. b. rhodesiense*,  
25 is clonal and evidence suggests it to be reproductively isolated [4–7]. A key feature of HAT is  
26 its focal nature. It tends to be reported in specific areas which appear to remain consistent  
27 over time.

28  
29 Although the number of r-HAT cases reported globally has declined in the last 15 years  
30 (Figure 1A), this trend is driven to a great extent by the reduction in cases in south-eastern  
31 Uganda, where outbreaks associated with civil unrest and livestock-dominated transmission  
32 have gradually been brought under control (Figure 1B). Reported cases in Tanzania have

1 also declined. In contrast, in Malawi and Zambia, reported case numbers have been  
2 relatively consistent over the last decade (Figure 1B). In addition, the data illustrated in  
3 Figure 1 are likely an underestimate. Many r-HAT foci are in remote areas; a lack of  
4 diagnostic facilities and awareness of HAT are frequently reported around foci [8,9] and  
5 under-detection of cases is a recognised problem [10]. Small numbers of cases are also  
6 regularly diagnosed in non-endemic countries, serving to highlight transmission which may  
7 not be reliably detected [11]. Many r-HAT foci have been linked to devastating outbreaks in  
8 the past, and more recent outbreaks, although smaller in magnitude, suggest this risk is still  
9 present [12–14].

10

11 Three types of r-HAT focus have been characterised according to the dominant reservoir  
12 host species: wilderness foci where wildlife-dominated transmission is associated with  
13 natural protected areas; livestock-dominated foci where cattle have replaced wild species as  
14 the non-human reservoir; and foci where both wildlife and livestock are present [15].  
15 However, many of the foci regarded as wilderness foci are also inhabited by increasing  
16 densities of people and livestock (for example in Serengeti, Tanzania, and Luangwa, Zambia  
17 [16; Basic data for Livestock and Fisheries Sectors 2013, United Republic of Tanzania  
18 Ministry of Livestock and Fisheries Development [www.mifugouvuvu.go.tz/wp-](http://www.mifugouvuvu.go.tz/wp-content/uploads/2014/12/DRAFT-ONE-_Basic-Data-1.pdf)  
19 [content/uploads/2014/12/DRAFT-ONE-\\_Basic-Data-1.pdf](http://www.mifugouvuvu.go.tz/wp-content/uploads/2014/12/DRAFT-ONE-_Basic-Data-1.pdf); J. Mubanga, PhD thesis,  
20 University of Edinburgh, 2008]) and transmission associated with both wildlife and livestock  
21 hosts is arguably more common than is widely recognised. r-HAT transmission – particularly  
22 in wildlife/livestock foci - is complex due to the involvement of multiple host and vector  
23 species within heterogeneous and often fragmented landscapes.

24

25 Mathematical models can be powerful tools for understanding transmission dynamics and  
26 assisting in disentangling such complexity. Recent reviews of the mathematical modelling  
27 literature for mosquito and tsetse-borne pathogens have highlighted gaps with respect to  
28 incorporating heterogeneity into model structures - variation which is likely to be required  
29 to understand and predict invasion and transmission dynamics of such pathogens [17,18]. In  
30 this paper we therefore review the current literature concerning the transmission ecology of  
31 r-HAT at the wildlife-livestock interface by focusing upon core parameters in mathematical  
32 models of trypanosome transmission [18]. These parameters are summarised in Figure 2,

1 alongside potential impacts of increasing human and livestock density and changing land  
2 use patterns. It is anticipated that this review will stimulate efforts to integrate empirical  
3 and quantitative approaches to better understand the variation in r-HAT transmission  
4 observed across ecological contexts. We consider examples from four foci: Serengeti in  
5 Tanzania, Luangwa Valley in Zambia, Rumphi in Malawi, and Ugala River/Moyowosi in  
6 western Tanzania (Table 1, Figure 3).

7

### 8 **Host Factors that Affect the Transmission of *T. b. rhodesiense***

9 The abundance and distribution of animal host species, and their respective competence as  
10 hosts for trypanosomes, are key factors affecting transmission of *T. b. rhodesiense*.

11 Serengeti in Tanzania, Luangwa Valley in Zambia, and Rumphi in Malawi are all examples of  
12 foci where wildlife populations within protected areas maintain infection (Table 1). At the  
13 other end of the spectrum, in south-east and central Uganda and western Kenya, cattle  
14 have replaced wild species as the non-human reservoir of *T. b. rhodesiense*. Transmission in  
15 areas where both wild hosts and livestock are present is less well understood. Although  
16 Western Tanzania is often described as a focus where transmission is maintained by both  
17 wildlife and livestock [15] (Table 1), the presence of increasing livestock populations in so-  
18 called ‘wilderness foci’ suggests that livestock are also likely to be important in transmission  
19 in these areas.

20

#### 21 *Host competence*

22 Host competence reflects a combination of the susceptibility of the host when bitten by an  
23 infected vector, the ability of the pathogen to persist in the host, and the likelihood that the  
24 host infects a feeding susceptible vector [19]. A large number of wildlife host species are  
25 competent for *T. brucei* s.l., and wildlife hosts form a reservoir community that can maintain  
26 transmission (discussed in Box 1). Of the few experimental studies available comparing wild  
27 and domestic hosts, the proportion of susceptible tsetse that developed a mature *T. brucei*  
28 infection after feeding on an infected host was approximately 16% in susceptible cattle  
29 breeds, compared to 8% in buffalo, 10% in eland and 12% in waterbuck [20]. Although these  
30 figures were based on single host animals, the pattern is consistent with the parasitaemia  
31 patterns seen in cattle and wild hosts. After the initial acute phase of infection, cattle  
32 infected with *T. brucei* s.l. tend to show low parasitaemia, which is present for extended

1 periods but only intermittently detectable [21,22]. Wild bovids show even fewer patent  
2 parasitaemic waves, and lower overall parasitaemia [20,23,24].

#### 3 4 *T. brucei* s.l. prevalence in hosts

5 Prevalence in host species is influenced by host competence, but also depends on the  
6 exposure of hosts to infected tsetse. As such, prevalence alone cannot indicate the  
7 importance of a species as a reservoir host. However, it is often the only measure that is  
8 available to provide some information about the roles of different host species. *T. brucei* s.l.  
9 is observed in many wildlife species, with prevalence variable by species (Box 1). In Uganda,  
10 where cattle transmission predominates, cattle show a prevalence of *T. brucei* s.l. of 20-27%  
11 in high prevalence villages [25] and up to 17.5% at markets by PCR [26]. Although small  
12 ruminants can also be infected with *T. brucei* s.l., the very low prevalence found in sheep  
13 and goats suggest they are less important than cattle in maintaining transmission [27].  
14 Cattle living in and around wilderness areas are also frequently infected with *T. brucei* s.l.,  
15 although the data available are insufficient to explore differences between foci. Around  
16 Serengeti National Park, 6% of cattle carried *T. brucei* s.l. by PCR, and 30% by loop-mediated  
17 isothermal amplification (LAMP), and around Luangwa Valley in Zambia 1% by PCR and 25%  
18 by LAMP were reported [14,28,29; J. Mubanga, PhD thesis, University of Edinburgh, 2008]  
19 (Table 1). Combined with higher host competence in cattle compared to wild bovids, this  
20 suggests that cattle may be important in r-HAT transmission around wilderness areas.

#### 21 22 *Abundance, distribution and species composition of animal hosts*

23 Given the variability in competence between host species, r-HAT risk is influenced by the  
24 species present. In south-eastern Uganda, where livestock transmission dominates, a large  
25 cattle population combines with a low density of wildlife. Since *T. brucei* s.l. is usually  
26 asymptomatic or causes only mild clinical signs in cattle [27], movements of apparently  
27 healthy cattle have been responsible for introducing disease into new areas in Uganda  
28 [30,31]. At the other extreme, many r-HAT foci are located in protected wilderness areas  
29 where the density and diversity of wildlife species are high, and often well characterised  
30 (Table 1).

1 There are fewer data available on the abundance and species composition of hosts in  
2 wildlife/livestock interface areas. Wildlife populations are less well monitored outside  
3 protected areas and the degree to which wildlife species are found in more fragmented  
4 areas varies by location and wildlife species [32]. For instance, to the west of the Serengeti  
5 National Park, elephant and impala are more common within farming areas than other  
6 species such as buffalo (Goodman, P.S. 2014. Large herbivore population estimates for the  
7 Grumeti Reserves – August 2014, Grumeti Fund, Sasakwa, Serengeti District, Tanzania,  
8 unpublished report). Bushbuck also survive well in human-dominated landscapes [33] and  
9 are competent hosts for *T. brucei* s.l. (Box 1). The presence of bushbuck and other  
10 competent species in farming areas may serve to bring trypanosomes into regions where  
11 cattle and human densities are high and thus contribute to linking wildlife-livestock  
12 transmission cycles. Although savannah tsetse inside protected areas do not frequently  
13 feed on bushbuck [34], the absence of preferred hosts such as buffalo in farming areas  
14 might increase the proportion of bloodmeals taken from bushbuck and therefore disease  
15 risk. Currently not enough is known about the competence of other wild host species to  
16 accurately identify how host distributions in fragmented areas might affect risk.

17

18 Countries such as Tanzania, Zambia and Malawi are undergoing rapid human population  
19 expansion, and around protected areas increasing human and livestock densities are  
20 common [16]. Some boundary areas show disproportionately higher population increases,  
21 as illustrated to the west of Serengeti National Park in Tanzania where demand for land for  
22 cultivation and grazing is leading to high rates of immigration [16,35]. In this area, the  
23 density of cattle around the protected areas is now very high (Fig. 3), having undergone  
24 substantial increases in the last two decades (Basic data for Livestock and Fisheries Sectors  
25 2013, United Republic of Tanzania Ministry of Livestock and Fisheries Development  
26 [www.mifugouvuvu.go.tz/wp-content/uploads/2014/12/DRAFT-ONE-\\_Basic-Data-1.pdf](http://www.mifugouvuvu.go.tz/wp-content/uploads/2014/12/DRAFT-ONE-_Basic-Data-1.pdf))  
27 (Table 1). Increasing human and livestock density around protected areas has also been  
28 reported in Eastern Province of Zambia where immigration to find more fertile land is  
29 common (J. Mubanga, PhD thesis, University of Edinburgh, 2008). Historically, the presence  
30 of tsetse-transmitted trypanosomes pathogenic to cattle has acted as a disincentive to  
31 grazing in protected areas. However, to the west of Serengeti the availability of

1 trypanocides and insecticides appears to have reduced this barrier; cattle incursions into  
2 protected areas are likely to bring both people and livestock in contact with tsetse.

3

4 Changes in the relative densities of cattle may have different impacts on transmission to  
5 humans, depending upon context. The proximity of cattle to their owners, especially in  
6 traditional livestock production systems, may act as a bridge to human infection – this  
7 seems to be the case with r-HAT in Uganda where recent epidemics have been strongly  
8 linked with livestock and riverine tsetse. However, livestock might have a zooprophyllactic  
9 effect protecting people from being bitten. There is some evidence that livestock protect  
10 their owners from infection. A combination of the upright shape [36] and natural odours  
11 [37] of humans repels savannah species of tsetse. On the other hand, the size, shape and  
12 odour of livestock, particularly cattle, are attractive to tsetse [36]. Hence even in areas  
13 where tsetse are abundant, few humans are bitten by tsetse if they are close to livestock: a  
14 study in a national park in Zimbabwe found that the catch of tsetse landing on a human  
15 walking through tsetse-infested woodland was reduced by >95% if he was accompanied by  
16 an ox [38].

17

### 18 **Vector factors that affect transmission of r-HAT**

19 In south-eastern Uganda, *G. fuscipes fuscipes*, a riverine species of tsetse, is responsible for  
20 transmission of *T. b. rhodesiense*. Riverine tsetse such as *G. f. fuscipes* feed on a wide range  
21 of hosts, including humans and cattle [39], and can persist in areas with high densities of  
22 people [40]. However, in most other r-HAT foci, *T. b. rhodesiense* is vectored by savannah  
23 species, such as *G. morsitans spp.*, *G. swynnertoni* and *G. pallidipes*.

24

### 25 *Vector competence*

26 Vector competence, the innate ability of a vector to acquire, maintain and transmit a  
27 pathogen, varies with tsetse species, as well as other intrinsic (e.g., sex) and extrinsic factors  
28 (e.g., environmental temperature and nutritional status) [41]. Low prevalence of mature *T.*  
29 *brucei* s.l. is common in tsetse, reflecting the general refractoriness of tsetse to  
30 trypanosome infection and maturation [reviewed by 42]. Experimental infections suggest  
31 that *G. morsitans* has higher vector competence than *G. pallidipes* (0 to 2.7% of *G. pallidipes*  
32 became infected after feeding on hosts infected with two different strains of *T. brucei*



1 *brucei*, compared to 9.3 to 18.4% of *G. morsitans centralis*) [43]. Although both *G. pallidipes*  
2 and *G. morsitans spp.* are found in r-HAT foci, they vary in abundance and their relative  
3 importance as vectors is likely to also depend on their host feeding patterns, as well as  
4 inherent vector competence.

5

#### 6 *Abundance, distribution and mortality*

7 On a regional scale, a general reduction in investment in large scale tsetse control since the  
8 1980s [44] has been balanced against loss of tsetse habitat for agricultural expansion [45–  
9 48]. This has led to an overall decline in habitat suitable for tsetse. However, protected  
10 areas and their surroundings form islands that can sustain populations of savannah tsetse–  
11 *G. morsitans*, *G. swynnertoni* and *G. pallidipes* [45,49]. These areas are often surrounded by  
12 significant land use change [16], and fragmented tsetse habitat [48,50], but habitat  
13 distribution varies from hard borders where land use changes quickly (for example in  
14 Rumphi, Malawi [51] and Western Serengeti, Tanzania) to more gradual gradients in land  
15 use and tsetse habitat (as seen in Luangwa Valley, Zambia [48,50]).

16

17 Although there are limited data, savannah tsetse do not appear to survive well outside  
18 protected areas. In Malawi, 15 times more *G. m. morsitans* were caught inside the  
19 Nkhotakota Game Reserve than in suitable habitat – predicted from satellite imagery –  
20 outside the reserve (when numbers caught were adjusted by trapping effort). This  
21 difference was attributed to human activity, destruction of tsetse habitat and low density of  
22 hosts [49]. In Zambia, fly-round catches of *G. m. morsitans* were from four to 280 times  
23 higher in natural habitats compared with natural habitats fragmented by agriculture [48,50].  
24 Catches of tsetse from traps and fly-rounds will be affected by sampling biases and may not  
25 reflect the true population densities [36]. Nonetheless, the consistent finding that apparent  
26 numbers of tsetse outside protected areas are much reduced suggests that savannah tsetse  
27 are largely restricted to relatively undisturbed habitat. Savannah tsetse are intolerant of  
28 high temperatures and low humidity [52]. The reduced numbers of trees and bushes in  
29 farming areas that provide the necessary shade and high humidity for tsetse seems an  
30 obvious explanation why they do not persist outside protected areas. However, farming  
31 areas often comprise a mosaic of crop field, pastures and relic savannah and woodland and  
32 hence the essential microclimates are likely to be present. A better understanding of the

1 habitat requirements of savannah tsetse would assist in predicting areas where populations  
2 may be sustained outside protected areas.

3

4 Disease risk is not only influenced by tsetse abundance. Mweempwa [50] reported that  
5 although apparent abundance decreased in more fragmented habitats in Zambia, the flies  
6 present were more likely to be older. Tsetse age is important in HAT risk because flies take  
7 around 18 days to develop a mature transmissible *T. b. rhodesiense* infection [53]; older fly  
8 populations therefore present a higher risk of transmitting HAT to people. Mweempwa *et al.*  
9 found that the most fragmented site showed the highest mature infection rate, although  
10 the entomological inoculation rate (an estimate of disease risk which takes into account fly  
11 abundance as well as infection rates) was highest in the least fragmented site [50].

12

### 13 *Host selection*

14 In south-eastern Uganda, cattle are the most important host of *G. fuscipes fuscipes*  
15 providing ~50% of bloodmeals [54]. The only remaining important wild host of tsetse in the  
16 area is the Nile monitor lizard, which rarely carries *T. brucei*. In wilderness areas savannah  
17 tsetse have preferred hosts (particularly warthog, buffalo, giraffe and elephant [39]) but  
18 they are able to feed on a wide range of wildlife species. Although savannah flies are known  
19 to feed on both livestock and wildlife hosts [34,55], few studies have looked specifically at  
20 feeding patterns in areas where both are present. At two sites in Kenya where both wildlife  
21 and livestock were present, Bett *et al.* reported that 16% of *G. pallidipes* feeds identified at  
22 Nguruman and 58% at Nkineji came from livestock, with the rest from wildlife [56] but the  
23 absence of data on the relative abundance of wildlife and livestock at these two sites makes  
24 it difficult to draw more general conclusions about tsetse choice. The likelihood that  
25 tsetse will feed on a particular species is driven by a number of factors. Experimental studies  
26 suggest the numbers of tsetse attracted to and landing on a host are related to mass: larger  
27 hosts attract more tsetse [36,57,58]. The probability that tsetse attracted to a host take a  
28 meal seems to be largely controlled by host defensive behaviour [59]. Impala and warthog  
29 are of comparable size but the high rates of defensive behaviour displayed by the former  
30 probably explains why it is rarely identified in bloodmeals [34]. It appears that tsetse rarely  
31 feed on impala or other antelope species (gazelle, wildebeest) despite their  
32 abundance. Similarly, amongst domestic livestock species, goats display high rates of

1 defensive behaviour [59] and hence are relatively rare as hosts [34], whilst adult cattle  
2 display low rates of defensive behaviour [59,60]. In conclusion, cattle, with their large size  
3 and relatively low rates of defensive behaviour, make particularly good hosts.

#### 4 5 **Understanding Transmission in a Changing Environment**

6 Reviewing the data available on r-HAT at wildlife/livestock interface areas highlights several  
7 key aspects where a lack of data prevents a full understanding of the transmission  
8 dynamics. In particular, host distributions, vector abundance and mortality around  
9 protected areas and the role of livestock as hosts in savannah tsetse systems, are all key  
10 aspects that are currently lacking in data. The land use change associated with increasing  
11 human and livestock densities may lead to declining tsetse populations outside protected  
12 areas, but there is a risk that this fragmented habitat may actually increase r-HAT risk, at  
13 least in the shorter term, through altered dynamics of tsetse and host populations. Although  
14 the paucity of comparable data limits detailed comparisons, there is considerable  
15 heterogeneity in some parameters between foci. For example the density of cattle around  
16 Serengeti in Tanzania is considerably higher than in foci in Zambia and Malawi, and may  
17 indicate that there is a spectrum of livestock involvement. The lack of published data on  
18 some foci, for example Ugala River/Moyowosi in western Tanzania (Table 1), identifies the  
19 need to focus research not only on well-known protected areas.

20  
21 Of particular concern is that a shift from wildlife- to cattle-dominated transmission may  
22 increase the overall reservoir potential and potentially increase HAT risk: cattle are known  
23 to carry human pathogenic trypanosomes, there is some evidence that they have higher  
24 host competence than wild bovids, and they are particularly good hosts for tsetse. Since the  
25 drivers for epidemic spread are complex, it is not clear whether increasing involvement of  
26 cattle in r-HAT cycles could also increase the risk of epidemic spread, or movement of  
27 disease to new areas as has happened in south-eastern Uganda, although the role of  
28 riverine tsetse in Uganda undoubtedly plays a role in the spread of r-HAT in farming areas in  
29 this focus.

30  
31 Quantifying the relative contribution of livestock and wildlife species in mixed-transmission  
32 settings is not easy. The gold standard of reservoir identification is observation of

1 decreasing disease in the target population following either (i) the control of infection in the  
2 putative reservoir species, or (ii) prevention of contact between the reservoir species and  
3 the target population [61], but realistically in foci with low r-HAT incidence it is not feasible  
4 to assess interventions in this way. As recently highlighted by Viana et al., [62], integration  
5 of multiple methodologies and data sources, for example using mathematic models, are  
6 likely to be needed to improve understanding of the reservoir dynamics. Even when the  
7 current limitations of significant data gaps are overcome, the complexity of these disease  
8 systems mean that model outputs require careful interpretation in order to develop  
9 meaningful control strategies. This emphasizes the need to understand transmission better  
10 at a scale relevant to control at the wildlife-livestock interface; although control measures  
11 aimed at wildlife are not feasible, interventions aimed at cattle could provide an effective  
12 option for control in areas where both wildlife and cattle are present.

13

#### 14 **R-HAT control in wildlife/livestock interface areas**

15 Since humans are not part of the reservoir of r-HAT except perhaps in an epidemic situation,  
16 the mass screening programs that have been effective against g-HAT are not appropriate for  
17 r-HAT. Control of r-HAT in protected areas has been achieved through various methods of  
18 vector control, for example a combination of aerial spraying and odour-baited targets was  
19 used to eliminate tsetse and trypanosomiasis from the Okavango Delta of Botswana [63],  
20 but the costs of control on this scale are usually prohibitive.

21

22 While the elimination of r-HAT seems unlikely, a better understanding of transmission  
23 dynamics in specific foci would allow control to be targeted more effectively. Insecticide-  
24 treated cattle are the most cost-effective method of vector control where sufficient cattle  
25 are present [64] but this approach requires that cattle form at least 10% of the diet of tsetse  
26 for transmission of HAT to be interrupted [65]. In practice, a minimum density of around 10  
27 cattle/km<sup>2</sup> [66] distributed relatively evenly [67] can provide effective control. In foci where  
28 livestock are at a sufficient density, such as Serengeti in Tanzania, insecticide treated cattle  
29 could provide a cost-effective means of containing r-HAT, depending on the extent of r-HAT  
30 transmission outside the protected areas. Cattle-based interventions to control r-HAT will  
31 also impact on diseases of veterinary importance, particularly tsetse and tick-borne diseases  
32 affecting livestock in the boundary areas. However, the lack of understanding about

1 transmission in r-HAT foci is currently limiting development of effective control, and it is not  
2 feasible to assess the likely effectiveness of potential control options without better data to  
3 parameterise models of transmission in these areas.

4

#### 5 **Concluding Remarks**

6 Rhodesian HAT is unlikely to be eliminated completely from wilderness areas due to the role  
7 of animal hosts. Although there is a perception that r-HAT transmission in wilderness foci is  
8 decreasing, there is little evidence to support this. In fact, a number of features of r-HAT in  
9 interface areas could actually lead to an increase in disease risk. The potential involvement  
10 of livestock, the effect of habitat fragmentation on tsetse and host population dynamics,  
11 and the risk of increasing tsetse-human-livestock contact suggest an ongoing risk for r-HAT  
12 transmission. This review highlights substantial gaps in our understanding of transmission in  
13 wilderness areas (see Outstanding Questions box). Improved prediction and more targeted  
14 control of Rhodesian HAT outbreaks will not be possible unless these gaps are addressed.

15

16

17

1 **Box 1- Understanding transmission of *T. b. rhodesiense* in wildlife hosts**

2 In sylvatic transmission cycles, a large number of wildlife species form a reservoir  
3 community. Both *T. brucei* s.l. and *T. b. rhodesiense* have been identified in a wide range of  
4 species, [for example 14,68–73]. The prevalence varies greatly between species. Species  
5 such as bushbuck and reedbuck are consistently reported to show high prevalence with *T.*  
6 *brucei* s.l. (18% to 100% [14,68]), and carnivore species such as lions and hyaena are also  
7 frequently infected (16-64% [14,69,71,72,74]). In contrast, many species, including warthog,  
8 buffalo, and many antelope, have been identified to carry *T. brucei* s.l. but with low  
9 prevalence [68,70,71,73,75,76].

10  
11 The importance of different species in *T. brucei* s.l. transmission depends on a host's  
12 competence, and the likelihood that the host will be fed on by a tsetse. Generally, wildlife  
13 species are considered to control trypanosome infections well, suggesting competence  
14 should be low, but this may not be true for all species: in historic experimental infection  
15 studies, warthog and buffalo generally showed low parasitaemia for a few weeks, but  
16 species such as reedbuck, bushbuck and Thomson's gazelle were reported to be easy to  
17 infect, to show high parasitaemia for several months, and to infect feeding tsetse regularly  
18 [23,77,78].

19  
20 *G. morsitans* spp. and *G. swynnertoni* feed particularly on warthog [34], leading to  
21 speculation that warthog might be particularly important in transmission. In contrast,  
22 bushbuck, reedbuck and other antelope species are rarely fed on [39]. However, it is  
23 possible that the role of species such as reedbuck and bushbuck has been underestimated,  
24 with their high prevalence and high infectivity potentially driving transmission. These  
25 relationships are unlikely to be quantified without developing transmission models, but this  
26 is limited by a lack of robust data. The dynamics of transmission in wildlife are undoubtedly  
27 important in the persistence of r-HAT foci. Without understanding the relative role of  
28 different wildlife species, and their relationship to environmental factors, it is unlikely it will  
29 be possible to understand how foci are maintained within wilderness area, and in particular  
30 identify the drivers that might lead to r-HAT outbreaks.

31 **Table 1. Summary of Key Parameters for Four Exemplar Foci of Rhodesian Human African Trypanosomiasis**

	<b>Serengeti, Tanzania</b>	<b>Ref.</b>	<b>Luangwa Valley, Zambia</b>	<b>Ref.</b>	<b>Rumphi, Malawi</b>	<b>Ref.</b>	<b>Ugala River/Moyowosi, Tanzania</b>	<b>Ref.</b>
<b>Protected areas</b>	Serengeti NP <sup>a</sup> , Ikorongo, Grumeti and Maswa GRs <sup>b</sup> , wildlife management areas	<sup>u</sup>	North Luangwa NP, South Luangwa NP, Luambe NP, Lukusuzi NP, game management areas	<sup>u</sup>	Vwaza Marsh WR <sup>c</sup> and Nyika NP	<sup>u</sup>	Moyowosi GR, Kigozi GR, Ugala River GR, wildlife management areas	<sup>u</sup>
<b>Presence of wildlife</b>	Very high density and diversity of wildlife within PA <sup>d</sup> . Low density outside PA, variable by species.	[79] <sup>v</sup>	High density and diversity of wildlife within PA.	[80, 81]	High diversity within PA.	<sup>w</sup>	High density and diversity of wildlife present within PA. Lower densities outside PA, variable by species.	[82,83].
<b>Trypanosomes in wildlife</b>	<i>T. brucei</i> s.l. and <i>T. b. rhodesiense</i> commonly reported.	[14, 84].	<i>T. brucei</i> s.l. and <i>T. b. rhodesiense</i> commonly reported.	[68, 85]	No data.		No data.	
<b>Presence of livestock</b>	Increasing cattle density, cattle population in Mara region estimated at 1.1 million in 2002/2003 and 1.7 million in 2007/2008. Livestock present close to PA at increasing density.	<sup>x</sup>	Historically very few livestock within the valley, increasing density towards plateau, high density on plateau (11 cattle/km <sup>2</sup> ). Cattle density currently increasing in mid Luangwa valley.	[80, 86] <sup>y</sup>	Cattle density generally low in Malawi (Figure 3). Distribution relative to PA unknown.	[87]	Livestock present around PA (Figure 3). High livestock numbers, agricultural expansion and overgrazing reported in the wider ecosystem.	[87–89]
<b>Trypanosomes of <i>T. brucei</i> s.l. in cattle</b>	29/518 <i>T. brucei</i> s.l., 6/518 <i>T. b. rhodesiense</i> in cattle around PA by PCR. <i>T. brucei</i> s.l. reported in 1/148 and 45/148 in cattle around PA by PCR and LAMP respectively.	[14, 29]	6/649 by PCR towards plateau. 2/241 and 48/195 reported by PCR and LAMP respectively in cattle.	[28] <sup>y</sup>	<i>T. brucei</i> s.l. identified in 1 out of 481 cattle in Rumphi district.	[90]	134/865 cattle reported positive for <i>T. brucei</i> s.l. on ITS PCR from Ugala ecosystem but location details not provided.	<sup>z</sup>
<b>Tsetse distribution</b>	Widespread <i>G. swynnertoni</i> and <i>G. pallidipes</i> in PA, small populations <i>G. brevipalpis</i> in PA. Tsetse appears to be low outside PA but little published data.	[91–93].	<i>G. pallidipes</i> , <i>G. morsitans morsitans</i> , <i>G. brevipalpis</i> widespread in PA. Increasing fragmentation and decreasing tsetse density towards the plateau.	[48, 50]  14	<i>G. morsitans</i> , <i>G. pallidipes</i> , predominantly confined to PA.	[51, 90]	Tsetse populations reported close to villages. <i>G. morsitans</i> present.	[9,45]

<b>Human cases</b>	Cases in local population within PA and close to PA boundary. Cases diagnosed in NEC <sup>e</sup> from within PA (30 cases 2000-2010).	[11, 94]	HAT cases reported from this area (2000-2009). Seven cases reported in NEC from South Luangwa (2000-2010).	[11]	163 cases in Rumphi district 2000-2006; 97% of these from within 5km of Vwaza GR boundary. Two cases reported in NEC from Vwaza (2000-2010).	[11, 95]	Numerous HAT cases reported in this area (2000-2009). Two cases reported in NEC from Moyowosi GR (2000-2010).	[11, 94]
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33 <sup>a</sup> NP, National Park; <sup>b</sup> GR, game reserve; <sup>c</sup> WR, wildlife reserve; <sup>d</sup> PA, protected area; <sup>e</sup> NEC, non-endemic countries;

34 <sup>u</sup> United Nations List of Protected Areas (<http://www.protectedplanet.net/>, accessed 03/05/16); <sup>v</sup> Goodman, P.S. 2014. Large herbivore  
35 population estimates for the Grumeti Reserves – August 2014. Grumeti Fund, Sasakwa, Serengeti District, Tanzania, unpublished report; <sup>w</sup>

36 <http://www.nyika-vwaza-trust.org/Articles/Mammals.pdf>; <sup>x</sup> Basic data for Livestock and Fisheries Sectors 2013, United Republic of Tanzania

37 Ministry of Livestock and Fisheries Development [www.mifugouvuvu.go.tz/wp-content/uploads/2014/12/DRAFT-ONE- Basic-Data-1.pdf](http://www.mifugouvuvu.go.tz/wp-content/uploads/2014/12/DRAFT-ONE-Basic-Data-1.pdf),

38 accessed 03/05/16); <sup>y</sup> J. Mubanga, PhD thesis, University of Edinburgh, 2008; <sup>z</sup> Malele, I.I. *et al.* (2013), The role of livestock in the

39 epidemiology of sleeping sickness in Tanzania, in 32nd Conference of the AU IBAR ISCTRC Sudan ([http://www.au-ibar.org/isctrc/374-the-32nd-](http://www.au-ibar.org/isctrc/374-the-32nd-international-scientific-council-for-trypanosomiasis-research-and-control-isctrc-conference)  
40 [international-scientific-council-for-trypanosomiasis-research-and-control-isctrc-conference](http://www.au-ibar.org/isctrc/374-the-32nd-international-scientific-council-for-trypanosomiasis-research-and-control-isctrc-conference), accessed 03/05/16).

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42



43 **Figure 1. Rhodesian Human African Trypanosomiasis Cases Reported Between 1990 and**  
44 **2014.** The number of Rhodesian human African trypanosomiasis (r-HAT) cases reported is  
45 shown for A) all countries, and B) Malawi, Tanzania, Uganda and Zambia. Data from the  
46 World Health Organisation (WHO)  
47 ([http://www.who.int/gho/neglected\\_diseases/human\\_african\\_trypanosomiasis/en/](http://www.who.int/gho/neglected_diseases/human_african_trypanosomiasis/en/)). Note  
48 different scale for individual country graphs.

49

50 **Figure 2. Factors Influencing Transmission of Rhodesian Human African Trypanosomiasis.**  
51 Key parameters describing hosts, vectors and human risk are listed in grey boxes, alongside  
52 potential effects of increasing human and livestock density and changing land use patterns.

53

54 **Figure 3. Distribution of Cases, Cattle and Protected Areas in Rhodesian Human African**  
55 **Trypanosomiasis Foci.** A) Cases of human African trypanosomiasis in eastern and  
56 southeastern Africa. Boxes (solid line) show four exemplar foci of Rhodesian human African  
57 trypanosomiasis. In addition, a dashed line box indicates livestock-dominated transmission  
58 focus in south-eastern and central Uganda. Reproduced from [94]. B) Detailed maps of the  
59 four exemplar foci highlighted in A, illustrating the density of cattle in 2010 (data from the  
60 Gridded Livestock of the World [96]), and protected areas boundaries (from United Nations  
61 List of Protected Areas <http://www.protectedplanet.net/>). Protected areas shown include  
62 national parks (NP), game reserves (GR), wildlife reserves (WR), game management areas  
63 (GMA), wildlife management areas (WMA) and Ngorongoro Conservation Area (NCA).

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81 **References**

- 82 1 Holmes, P. (2015) On the Road to Elimination of Rhodesiense Human African  
83 Trypanosomiasis: First WHO Meeting of Stakeholders. *PLoS Negl. Trop. Dis.* 9,  
84 e0003571
- 85 2 Xong, H. V *et al.* (1998) A VSG expression site-associated gene confers resistance to  
86 human serum in *Trypanosoma rhodesiense*. *Cell* 95, 839–846
- 87 3 Echodu, R. *et al.* (2015) Genetic diversity and population structure of *Trypanosoma*  
88 *brucei* in Uganda: implications for the epidemiology of sleeping sickness and Nagana.  
89 *PLoS Negl. Trop. Dis.* 9, e0003353
- 90 4 Koffi, M. *et al.* (2009) Population genetics of *Trypanosoma brucei gambiense*, the  
91 agent of sleeping sickness in Western Africa. *Proc. Natl. Acad. Sci. U. S. A.* 106, 209–  
92 214
- 93 5 Morrison, L.J. *et al.* (2008) *Trypanosoma brucei gambiense* Type 1 populations from  
94 human patients are clonal and display geographical genetic differentiation. *Infect.*  
95 *Genet. Evol.* 8, 847–54
- 96 6 Balmer, O. *et al.* (2011) Phylogeography and taxonomy of *Trypanosoma brucei*. *PLoS*  
97 *Negl. Trop. Dis.* 5, e961
- 98 7 Weir, W. *et al.* (2016) Population genomics reveals the origin and asexual evolution of  
99 human infective trypanosomes. *Elife* 5, 1–14
- 100 8 Mulenga, G.M. *et al.* (2015) Assessing the capacity to diagnose human African  
101 trypanosomiasis among health care personnel from Chama and Mambwe districts of  
102 eastern Zambia. *BMC Res. Notes* 8, 433
- 103 9 Reid, H. *et al.* (2012) Assessment of the burden of human African trypanosomiasis by  
104 rapid participatory appraisal in three high-risk villages in Urambo District, Northwest  
105 Tanzania. *Afr. Health Sci.* 12, 104–113
- 106 10 Odiit, M. *et al.* (2005) Quantifying the level of under-detection of *Trypanosoma brucei*  
107 *rhodesiense* sleeping sickness cases. *Trop. Med. Int. Heal.* 10, 840–849
- 108 11 Simarro, P.P. *et al.* (2012) Human African trypanosomiasis in non-endemic countries  
109 (2000-2010). *J. Travel Med.* 19, 44–53
- 110 12 Ripamonti, D. *et al.* (2002) African sleeping sickness in tourists returning from  
111 Tanzania: The first 2 Italian cases from a small outbreak among European travelers.  
112 *Clin. Infect. Dis.* 34, E18–E22

- 113 13 Jelinek, T. *et al.* (2002) Cluster of African trypanosomiasis in travellers to Tanzanian  
114 national parks. *Emerg. Infect. Dis.* 8, 634–635
- 115 14 Kaare, M.T. *et al.* (2007) Sleeping sickness - a re-emerging disease in the Serengeti?  
116 *Travel Med. Infect. Dis.* 5, 117–124
- 117 15 Simarro, P.P. *et al.* (2013) Diversity of human African trypanosomiasis epidemiological  
118 settings requires fine-tuning control strategies to facilitate disease elimination. *Res.*  
119 *Rep. Trop. Med.* 4, 1–6
- 120 16 Estes, A.B. *et al.* (2012) Land-cover change and human population trends in the  
121 greater Serengeti ecosystem from 1984–2003. *Biol. Conserv.* 147, 255–263
- 122 17 Reiner, R.C. *et al.* (2013) A systematic review of mathematical models of mosquito-  
123 borne pathogen transmission: 1970–2010. *J. R. Soc. Interface* 10, 20120921
- 124 18 Rock, K.S. *et al.* (2015) Mathematical Models for Neglected Tropical Diseases:  
125 Essential Tools for Control and Elimination, Part A. *Adv. Parasitol.* 87, 53–133
- 126 19 LoGiudice, K. *et al.* (2003) The ecology of infectious disease: effects of host diversity  
127 and community composition on Lyme disease risk. *Proc. Natl. Acad. Sci. U. S. A.* 100,  
128 567–71
- 129 20 Moloo, S.K. *et al.* (1999) Study of the sequential tsetse-transmitted *Trypanosoma*  
130 *congolense*, *T. brucei brucei* and *T. vivax* infections to African buffalo, eland,  
131 waterbuck, N'dama and Boran cattle. *Vet. Parasitol.* 80, 197–213
- 132 21 Van den Bossche, P. *et al.* (2005) Transmissibility of *Trypanosoma brucei* during its  
133 development in cattle. *Trop. Med. Int. Heal.* 10, 833–839
- 134 22 Picozzi, K. *et al.* (2002) The diagnosis of trypanosome infections: Applications of novel  
135 technology for reducing disease risk. *African J. Biotechnol.* 1, 39–45
- 136 23 Redruth, D. *et al.* (1994) African buffalo serum contains novel trypanocidal protein. *J.*  
137 *Eukaryote Microbiol.* 41, 95–103
- 138 24 Rurangirwa, F.R. *et al.* (1986) Immune effector mechanisms involved in the control of  
139 parasitemia in *Trypanosoma brucei*-infected wildebeest (*Connochaetes taurinus*).  
140 *Immunology* 58, 231–237
- 141 25 Muhanguzi, D. *et al.* (2014) Collateral benefits of restricted insecticide application for  
142 control of African trypanosomiasis on *Theileria parva* in cattle: a randomized  
143 controlled trial. *Parasit. Vectors* 7, 432
- 144 26 Selby, R. *et al.* (2013) Cattle movements and trypanosomes: restocking efforts and

- 145 the spread of *Trypanosoma brucei rhodesiense* sleeping sickness in post-conflict  
 146 Uganda. *Parasit. Vectors* 6, 281
- 147 27 von Wissmann, B. *et al.* (2011) Factors associated with acquisition of human infective  
 148 and animal infective trypanosome infections in domestic livestock in Western Kenya.  
 149 *PLoS Negl. Trop. Dis.* 5, e941
- 150 28 Laohasinnarong, D. *et al.* (2015) Studies of trypanosomiasis in the Luangwa valley,  
 151 north-eastern Zambia. *Parasit. Vectors* 8, 497
- 152 29 Laohasinnarong, D. *et al.* (2011) Prevalence of *Trypanosoma* sp. in cattle from  
 153 Tanzania estimated by conventional PCR and loop-mediated isothermal amplification  
 154 (LAMP). *Parasitol. Res.* 109, 1735–1739
- 155 30 Fevre, E.M. *et al.* (2001) The origins of a new *Trypanosoma brucei rhodesiense*  
 156 sleeping sickness outbreak in eastern Uganda. *Lancet* 358, 625–628
- 157 31 Batchelor, N. a *et al.* (2009) Spatial predictions of Rhodesian Human African  
 158 Trypanosomiasis (sleeping sickness) prevalence in Kaberamaido and Dokolo, two  
 159 newly affected districts of Uganda. *PLoS Negl. Trop. Dis.* 3, e563
- 160 32 Bhola, N. *et al.* (2012) Comparative changes in density and demography of large  
 161 herbivores in the Masai Mara Reserve and its surrounding human-dominated pastoral  
 162 ranches in Kenya. *Biodivers. Conserv.* 21, 1509–1530
- 163 33 East, R. (1999) *African Antelope Database 1998*, IUCN/SSC Antelope Specialist Group,  
 164 IUCN. Gland, Switzerland and Cambridge, UK.
- 165 34 Clausen, P.-H. *et al.* (1998) Host preferences of tsetse (Diptera:Glossinidae) based on  
 166 bloodmeal identifications. *Med. Vet. Entomol.* 12, 169–180
- 167 35 Kideghesho, J. *et al.* (2013) Emerging issues and challenges in conservation of  
 168 biodiversity in the rangelands of Tanzania. *Nat. Conserv.* 6, 1–29
- 169 36 Vale, G.A. (1974) Responses of tsetse flies (Diptera, Glossinidae) to mobile and  
 170 stationary baits. *Bull. Entomol. Res.* 64, 545–588
- 171 37 Vale, G.A. (1979) Field responses of tsetse (Diptera: Glossinidae) to odours of men,  
 172 lactic acid and carbon dioxide. *Bull. ent. Res.* 69, 459–467
- 173 38 Torr, S.J. *et al.* (2012) Where, when and why do tsetse contact humans? Answers  
 174 from studies in a national park of Zimbabwe. *PLoS Negl. Trop. Dis.* 6, e1791
- 175 39 Clausen, P.-H. *et al.* (1998) Host preferences of tsetse (Diptera : Glossinidae ) based  
 176 on bloodmeal identifications. *Med. Vet. Entomol.* 12, 169–180

- 177 40 Reid, R.S. *et al.* (2000) Human population growth and the extinction of the tsetse fly.  
178 *Agric. Ecosyst. Environ.* 77, 227–236
- 179 41 Geiger, A. *et al.* (2015) Adult blood-feeding tsetse flies, trypanosomes, microbiota and  
180 the fluctuating environment in sub-Saharan Africa. *ISME J.* 9, 1496–1507
- 181 42 Welburn, S.C. and Maudlin, I. (1999) Tsetse-trypanosome interactions: Rites of  
182 passage. *Parasitol. Today* 15, 399–403
- 183 43 Moloo, S.K. *et al.* (1992) Vector competence of *Glossina pallidipes* and *Glossina*  
184 *morsitans centralis* for *Trypanosoma vivax*, *Trypanosoma congolense* and *T. b. brucei*.  
185 *Acta Trop.* 51, 271–280
- 186 44 Torr, S.J. *et al.* (2005) Towards a rational policy for dealing with tsetse. *Trends*  
187 *Parasitol.* 21, 537–541
- 188 45 Malele, I.I. *et al.* (2011) Factors defining the distribution limit of tsetse infestation and  
189 the implication for the livestock sector in Tanzania. *African J. Agric. Res.* 6, 2341–  
190 2347
- 191 46 Muriuki, G.W. *et al.* (2005) Tsetse control and land-use change in Lambwe valley,  
192 south-western Kenya. *Agric. Ecosyst. Environ.* 106, 99–107
- 193 47 Bourn, D. *et al.* (2001) *Environmental Change and the Autonomous Control of Tsetse*  
194 *and Trypanosomosis in Sub-Saharan Africa*, Environmental Research Group Oxford  
195 Limited.
- 196 48 Ducheyne, E. *et al.* (2009) The impact of habitat fragmentation on tsetse abundance  
197 on the plateau of eastern Zambia. *Prev. Vet. Med.* 91, 11–18
- 198 49 Gondwe, N. *et al.* (2009) Distribution and density of tsetse flies (glossinidae: Diptera)  
199 at the game/people/livestock interface of the nkhotakota game reserve human  
200 sleeping sickness focus in malawi. *Ecohealth* 6, 260–265
- 201 50 Mweempwa, C. *et al.* (2015) Impact of habitat fragmentation on tsetse populations  
202 and trypanosomosis risk in Eastern Zambia. *Parasit. Vectors* 8, 406
- 203 51 Van den Bossche, P. *et al.* (2010) A changing environment and the epidemiology of  
204 tsetse-transmitted livestock trypanosomiasis. *Trends Parasitol.* 26, 236–43
- 205 52 Rogers, D.J. and Randolph, S.E. (1986) Distribution and abundance of Tsetse flies  
206 (*Glossina* spp.). *J. Anim. Ecol.* 55, 1007–1025
- 207 53 Dale, C. *et al.* (1995) The kinetics of maturation of Trypanosome infections in tsetse.  
208 *Parasitology* 111, 187–191

- 209 54 Kabbale, F. *et al.* (2010) Feeding preferences and *Trypanosoma brucei* species  
210 identified in blood meals of *Glossina fuscipes fuscipes* in Kamuli district, South Eastern  
211 Uganda. *Africa J. Anim. Biomed. Sci.* 5, 99–105
- 212 55 Muturi, C.N. *et al.* (2011) Tracking the feeding patterns of tsetse flies (*Glossina* genus)  
213 by analysis of bloodmeals using mitochondrial cytochromes genes. *PLoS One* 6,  
214 e17284
- 215 56 Bett, B. *et al.* (2008) Estimation of tsetse challenge and its relationship with  
216 trypanosomiasis incidence in cattle kept under pastoral production systems in Kenya.  
217 *Vet. Parasitol.* 155, 287–98
- 218 57 Hargrove, J.W. and Vale, G.A. (1978) The effect of host odour concentration on  
219 catches of tsetse flies (Glossinidae) and other Diptera in the field. *Bull. Entomol. Res.*  
220 68, 607–612
- 221 58 Hargrove, J.W. *et al.* (1995) Catches of tsetse (*Glossina* spp.) (Diptera: Glossinidae)  
222 from traps and targets baited with large doses of natural and synthetic host odour.  
223 *Bull. Entomol. Res.* 85, 215
- 224 59 Vale, G.A. (1977) Feeding responses of tsetse flies (Diptera: Glossinidae) to stationary  
225 hosts. *Bull. Entomol. Res.* 67, 635–649
- 226 60 Torr, S.J. and Mangwiro, T.N.C. (2000) Interactions between cattle and biting flies:  
227 Effects on the feeding rate of tsetse. *Med. Vet. Entomol.* 14, 400–409
- 228 61 Haydon, D.T. *et al.* (2002) Identifying reservoirs of infection: A conceptual and  
229 practical challenge. *Emerg. Infect. Dis.* 8, 1468–1473
- 230 62 Viana, M. *et al.* (2014) Assembling evidence for identifying reservoirs of infection.  
231 *Trends Ecol. Evol.* 29, 270–279
- 232 63 Kgori, P.M. *et al.* (2006) The use of aerial spraying to eliminate tsetse from the  
233 Okavango Delta of Botswana. *Acta Trop.* 99, 184–199
- 234 64 Shaw, a. P.M. *et al.* (2013) Estimating the costs of tsetse control options: An example  
235 for Uganda. *Prev. Vet. Med.* 110, 290–303
- 236 65 Hargrove, J.W. *et al.* (2012) Modeling the control of trypanosomiasis using  
237 trypanocides or insecticide-treated livestock. *PLoS Negl. Trop. Dis.* 6, e1615
- 238 66 Vale, G.A. and Torr, S.J. (2005) User-friendly models of the costs and efficacy of tsetse  
239 control: application to sterilizing and insecticidal techniques. *Med. Vet. Entomol.* 19,  
240 293–305

- 241 67 Torr, S.J. and Vale, G. a (2011) Is the even distribution of insecticide-treated cattle  
242 essential for tsetse control? Modelling the impact of baits in heterogeneous  
243 environments. *PLoS Negl. Trop. Dis.* 5, e1360
- 244 68 Anderson, N.E. *et al.* (2011) Characterisation of the wildlife reservoir community for  
245 human and animal trypanosomiasis in the Luangwa Valley, Zambia. *PLoS Negl. Trop.*  
246 *Dis.* 5, e1211
- 247 69 Geigy, R. and Kauffman, M. (1973) Sleeping sickness survey in the Serengeti area  
248 (Tanzania) 1971: I. Examination of large mammals for trypanosomes. *Acta Trop.* 30,  
249 12–23
- 250 70 Geigy, R. *et al.* (1971) Sleeping sickness survey in Musoma District, Tanzania: IV.  
251 Examination of wild mammals as a potential reservoir for *T. rhodesiense*. *Acta Trop.*  
252 28, 211–220
- 253 71 Baker, J.R. (1968) Trypanosomes of wild mammals in the neighbourhood of the  
254 Serengeti National Park. *Symp. Zool. Soc. London* 24, 147–158
- 255 72 Sachs, R. *et al.* (1967) Isolation of trypanosomes of the *T. brucei* group from lion. *Acta*  
256 *Trop.* 14, 109–112
- 257 73 Drager, N. and Mehltitz, D. (1978) Investigations on prevalence of Trypanosome  
258 carriers and antibody response in wildlife in Northern Botswana. *Tropenmed.*  
259 *Parasitol.* 29, 223–233
- 260 74 Welburn, S.C. *et al.* (2008) Patterns in age-seroprevalence consistent with acquired  
261 immunity against *Trypanosoma brucei* in Serengeti lions. *PLoS Negl. Trop. Dis.* 2, e347
- 262 75 Dillmann, J.S.S. and Townsend, A.J. (1979) Trypanosomiasis survey of wild animals in  
263 the Luangwa Valley, Zambia. *Acta Trop.* 36, 349–356
- 264 76 Carmichael, I.H. and Hobday, E. (1975) Blood parasites of some wild Bovidae in  
265 Botswana. *Onderstepoort J. Vet. Res.* 42, 55–62
- 266 77 Corson, J.F. (1939) The infections produced in sheep and antelopes by a strain of  
267 *Trypanosoma rhodesiense*. *Trans Roy Soc Trop Med Hyg* 33, 37–46
- 268 78 Ashcroft, M.T. *et al.* (1959) The experimental infection of some African wild animals  
269 with *Trypanosoma rhodesiense*, *T. brucei* and *T. congolense*. *Am. J. Trop. Med.*  
270 *Parasitol.* 53, 147–161
- 271 79 Sinclair, A.R.E. *et al.* (2008) *Serengeti III: Human impacts on ecosystem dynamics*,  
272 University of Chicago Press.



273 80 Anderson, N.E. *et al.* (2015) Sleeping sickness and its relationship with development  
274 and biodiversity conservation in the Luangwa Valley, Zambia. *Parasit. Vectors* 8, 1–14

275 81 Ndhlovu, D.E. and Balakrishnan, M. (1991) Large herbivores in Upper Lupande Game  
276 Management Area, Luangwa Valley, Zambia. *Afr. J. Ecol.* 29, 93–104

277 82 Stoner, C. *et al.* (2007) Changes in large herbivore populations across large areas of  
278 Tanzania. *Afr. J. Ecol.* 45, 202–215

279 83 Wilfred, P. and MacColl, A. (2014) Legal subsistence hunting trends in the Ugalla  
280 ecosystem of western Tanzania. *Eur. J. Wildl. Res.* 60, 371–376

281 84 Geigy, R. *et al.* (1973) Wild mammals as reservoirs for Rhodesian sleeping sickness in  
282 the Serengeti. *Trans. R. Soc. Trop. Med. Hyg.* 67, 284–286

283 85 Rickman, L.R. *et al.* (1991) Human serum sensitivities of Trypanozoon isolates from  
284 naturally infected hosts in the Luangwa Valley, Zambia. *East Afr. Med. J.* 68, 880–892

285 86 Simukoko, H. *et al.* (2011) Bovine trypanosomiasis risk in an endemic area on the  
286 eastern plateau of Zambia. *Res. Vet. Sci.* 90, 51–54

287 87 Robinson, T.P. *et al.* (2014) Mapping the global distribution of livestock. *PLoS One* 9, 5

288 88 Masanja, G. (2014) Human Population Growth and Wildlife Extinction in Ugalla  
289 Ecosystem, Western Tanzania. *J. Sustain. Dev. Stud.* 5, 192–217

290 89 Kashaigili, J.J. and Majaliwa, A.M. (2010) Integrated assessment of land use and cover  
291 changes in the Malagarasi river catchment in Tanzania. *Phys. Chem. Earth* 35, 730–  
292 741

293 90 Van Den Bossche, P. *et al.* (2000) The distribution and epidemiology of bovine  
294 trypanosomosis in Malawi. *Vet. Parasitol.* 88, 163–176

295 91 Malele, I.I. *et al.* (2011) Factors defining the distribution limit of tsetse infestation and  
296 the implication for livestock sector in Tanzania. *African J. Agric. Res.* 6, 2341–2347

297 92 Malele, I.I. *et al.* (2007) *Glossina* dynamics in and around the sleeping sickness  
298 endemic Serengeti ecosystem of northwestern Tanzania. *J. Vector Ecol.* 32, 263–268

299 93 Auty, H.K. *et al.* (2012) Using molecular data for epidemiological inference: assessing  
300 the prevalence of *Trypanosoma brucei rhodesiense* in tsetse in Serengeti, Tanzania.  
301 *PLoS Negl. Trop. Dis.* 6, e1501

302 94 Simarro, P.P. *et al.* (2010) The Atlas of human African trypanosomiasis: a contribution  
303 to global mapping of neglected tropical diseases. *Int. J. Health Geogr.* 9, 57

304 95 Madanitsa, M. *et al.* (2009) The epidemiology of trypanosomiasis in Rumphidistrict,

305 Malawi: A ten year retrospective study. *Malawi Med. J.* 21, 22–27  
306 96 Nicolas, G. *et al.* (2016) Using Random Forest to Improve the Downscaling of Global  
307 Livestock Census Data. *PLoS One* 11, e0150424  
308