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

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**Key words**

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

**Abstract**

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

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

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

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

Although the number of r-HAT cases reported globally has declined in the last 15 years (Figure 1A), this trend is driven to a great extent by the reduction in cases in south-eastern Uganda, where outbreaks associated with civil unrest and livestock-dominated transmission have gradually been brought under control (Figure 1B). Reported cases in Tanzania have also declined. In contrast, in Malawi and Zambia, reported case numbers have been relatively consistent over the last decade (Figure 1B). In addition, the data illustrated in Figure 1 are likely an underestimate. Many r-HAT foci are in remote areas; a lack of diagnostic facilities and awareness of HAT are frequently reported around foci [8,9] and under-detection of cases is a recognised problem [10]. Small numbers of cases are also regularly diagnosed in non-endemic countries, serving to highlight transmission which may not be reliably detected [11]. Many r-HAT foci have been linked to devastating outbreaks in the past, and more recent outbreaks, although smaller in magnitude, suggest this risk is still present [12–14].

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

Mathematical models can be powerful tools for understanding transmission dynamics and assisting in disentangling such complexity. Recent reviews of the mathematical modelling literature for mosquito and tsetse-borne pathogens have highlighted gaps with respect to incorporating heterogeneity into model structures - variation which is likely to be required to understand and predict invasion and transmission dynamics of such pathogens [17,18]. In this paper we therefore review the current literature concerning the transmission ecology of r-HAT at the wildlife-livestock interface by focusing upon core parameters in mathematical models of trypanosome transmission [18]. These parameters are summarised in Figure 2, alongside potential impacts of increasing human and livestock density and changing land use patterns. It is anticipated that this review will stimulate efforts to integrate empirical and quantitative approaches to better understand the variation in r-HAT transmission observed across ecological contexts. We consider examples from four foci: Serengeti in Tanzania, Luangwa Valley in Zambia, Rumphi in Malawi, and Ugala River/Moyowosi in western Tanzania (Table 1, Figure 3).

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

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

*Host competence*

Host competence reflects a combination of the susceptibility of the host when bitten by an infected vector, the ability of the pathogen to persist in the host, and the likelihood that the host infects a feeding susceptible vector [19]. A large number of wildlife host species are competent for *T. brucei* s.l., and wildlife hosts form a reservoir community that can maintain transmission (discussed in Box 1). Of the few experimental studies available comparing wild and domestic hosts, the proportion of susceptible tsetse that developed a mature *T. brucei* infection after feeding on an infected host was approximately 16% in susceptible cattle breeds, compared to 8% in buffalo, 10% in eland and 12% in waterbuck [20]. Although these figures were based on single host animals, the pattern is consistent with the parasitaemia patterns seen in cattle and wild hosts. After the initial acute phase of infection, cattle infected with *T. brucei* s.l. tend to show low parasitaemia, which is present for extended periods but only intermittently detectable [21,22]. Wild bovids show even fewer patent parasitaemic waves, and lower overall parasitaemia [20,23,24].

T. brucei s.l. *prevalence in hosts*

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

*Abundance, distribution and species composition of animal hosts*

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

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

Countries such as Tanzania, Zambia and Malawi are undergoing rapid human population expansion, and around protected areas increasing human and livestock densities are common [16]. Some boundary areas show disproportionately higher population increases, as illustrated to the west of Serengeti National Park in Tanzania where demand for land for cultivation and grazing is leading to high rates of immigration [16,35]. In this area, the density of cattle around the protected areas is now very high (Fig. 3), having undergone substantial increases in the last two decades (Basic data for Livestock and Fisheries Sectors 2013, United Republic of Tanzania Ministry of Livestock and Fisheries Development www.mifugouvuvi.go.tz/wp-content/uploads/2014/12/DRAFT-ONE-\_Basic-Data-1.pdf) (Table 1). Increasing human and livestock density around protected areas has also been reported in Eastern Province of Zambia where immigration to find more fertile land is common (J. Mubanga, PhD thesis, University of Edinburgh, 2008). Historically, the presence of tsetse-transmitted trypanosomes pathogenic to cattle has acted as a disincentive to grazing in protected areas. However, to the west of Serengeti the availability of trypanocides and insecticides appears to have reduced this barrier; cattle incursions into protected areas are likely to bring both people and livestock in contact with tsetse.

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

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

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

*Vector competence*

Vector competence, the innate ability of a vector to acquire, maintain and transmit a pathogen, varies with tsetse species, as well as other intrinsic (e.g., sex) and extrinsic factors (e.g., environmental temperature and nutritional status) [41]. Low prevalence of mature *T. brucei* s.l. is common in tsetse, reflecting the general refractoriness of tsetse to trypanosome infection and maturation [reviewed by 42]. Experimental infections suggest that *G. morsitans* has higher vector competence than *G. pallidipes* (0 to 2.7% of *G. pallidipes* became infected after feeding on hosts infected with two different strains of *T. brucei brucei*, compared to 9.3 to 18.4% of *G. morsitans centralis*) [43]. Although both *G. pallidipes* and *G. morsitans* *spp*. are found in r-HAT foci, they vary in abundance and their relative importance as vectors is likely to also depend on their host feeding patterns, as well as inherent vector competence.

*Abundance, distribution and mortality*

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

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

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

*Host selection*

In south-eastern Uganda, cattle are the most important host of *G. fuscipes fuscipes* providing ~50% of bloodmeals [54]. The only remaining important wild host of tsetse in the area is the Nile monitor lizard, which rarely carries *T. brucei*. In wilderness areas savannah tsetse have preferred hosts (particularly warthog, buffalo, giraffe and elephant [39]) but they are able to feed on a wide range of wildlife species. Although savannah flies are known to feed on both livestock and wildlife hosts [34,55], few studies have looked specifically at feeding patterns in areas where both are present. At two sites in Kenya where both wildlife and livestock were present, Bett *et al*. reported that 16% of *G. pallidipes* feeds identified at Nguruman and 58% at Nkineji came from livestock, with the rest from wildlife [56] but the absence of data on the relative abundance of wildlife and livestock at these two sites makes it is difficult to draw more general conclusions about tsetse choice. The likelihood that tsetse will feed on a particular species is driven by a number of factors. Experimental studies suggest the numbers of tsetse attracted to and landing on a host are related to mass: larger hosts attract more tsetse [36,57,58].  The probability that tsetse attracted to a host take a meal seems to be largely controlled by host defensive behaviour [59]. Impala and warthog are of comparable size but the high rates of defensive behaviour displayed by the former probably explains why it is rarely identified in bloodmeals [34].  It appears that tsetse rarely feed on impala or other antelope species (gazelle, wildebeest) despite their abundance.  Similarly, amongst domestic livestock species, goats display high rates of defensive behaviour [59] and hence are relatively rare as hosts [34], whilst adult cattle display low rates of defensive behaviour [59,60]. In conclusion, cattle, with their large size and relatively low rates of defensive behaviour, make particularly good hosts.

**Understanding Transmission in a Changing Environment**

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

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

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

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

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

While the elimination of r-HAT seems unlikely, a better understanding of transmission dynamics in specific foci would allow control to be targeted more effectively. Insecticide-treated cattle are the most cost-effective method of vector control where sufficient cattle are present [64] but this approach requires that cattle form at least 10% of the diet of tsetse for transmission of HAT to be interrupted [65]. In practice, a minimum density of around 10 cattle/km2 [66] distributed relatively evenly [67] can provide effective control. In foci where livestock are at a sufficient density, such as Serengeti in Tanzania, insecticide treated cattle could provide a cost-effective means of containing r-HAT, depending on the extent of r-HAT transmission outside the protected areas. Cattle-based interventions to control r-HAT will also impact on diseases of veterinary importance, particularly tsetse and tick-borne diseases affecting livestock in the boundary areas. However, the lack of understanding about transmission in r-HAT foci is currently limiting development of effective control, and it is not feasible to assess the likely effectiveness of potential control options without better data to parameterise models of transmission in these areas.

**Concluding Remarks**

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

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

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

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

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

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

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | **Serengeti, Tanzania** | **Ref.** | **Luangwa Valley, Zambia** | **Ref.** | **Rumphi, Malawi** | **Ref.** | **Ugala RIver/Moyowosi, Tanzania** | **Ref.** |
| **Protected areas** | Serengeti NPa, Ikorongo, Grumeti and Maswa GRsb, wildlife management areas | u | North Luangwa NP, South Luangwa NP, Luambe NP, Lukusuzi NP, game management areas | u | Vwaza Marsh WRc and Nyika NP | u | Moyowosi GR, Kigozi GR, Ugala River GR, wildlife management areas | u |
| **Presence of wildlife** | Very high density and diversity of wildlife within PAd. Low density outside PA, variable by species. | [79]v | High density and diversity of wildlife within PA. | [80,81] | High diversity within PA. | w | High density and diversity of wildlife present within PA Lower densities outside PA, variable by species. | [82,83]. |
| **Trypanosomes in wildlife** | *T. brucei* s.l. and *T. b. rhodesiense* commonly reported. | [14,84]. | *T. brucei* s.l. and *T. b. rhodesiense* commonly reported. | [68,85] | No data. |  | No data. |  |
| **Presence of livestock** | 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. | x | Historically very few livestock within the valley, increasing density towards plateau, high density on plateau (11 cattle/km2). Cattle density currently increasing in mid Luangwa valley. | [80,86] y | 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] |
| **Trypanosomes of *T. brucei* s.l. in cattle** | 29/518 *T. brucei* s.l., 6/518 *T.b. rhodesiense* in cattle around PA by PCR.  *T. brucei* 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] y | *T. brucei* s.l. identified in 1 out of 481 cattle in Rumphi district. | [90] | 134/865 cattle reported positive for *T. brucei* s.l. on ITS PCR from Ugala ecosystem but location details not provided. | z |
| **Tsetse distribution** | Widespread *G. swynnertoni* and *G. pallidipes* in PA, small populations *G. brevipalpis* in PA. Tsetse appears to be low outside PA but little published data. | [91–93]. | *G. pallidipes, G morsitans morsitans, G. brevipalpis* widespread in PA. Increasing fragmentation and decreasing tsetse density towards the plateau. | [48,50] | *G. morsitans, G. pallidipes,* predominantly confined to PA. | [51,90] | Tsetse populations reported close to villages. *G. morsitans* present. | [9,45] |
| **Human cases** | Cases in local population within PA and close to PA boundary. Cases diagnosed in NECe 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] |

a NP, National Park; b GR, game reserve; c WR, wildlife reserve; d PA, protected area; e NEC, non-endemic countries;

u United Nations List of Protected Areas (<http://www.protectedplanet.net/>, accessed 03/05/16); v Goodman, P.S. 2014. Large herbivore population estimates for the Grumeti Reserves – August 2014. Grumeti Fund, Sasakwa, Serengeti District, Tanzania, unpublished report; w <http://www.nyika-vwaza-trust.org/Articles/Mammals.pdf>; x Basic data for Livestock and Fisheries Sectors 2013, United Republic of Tanzania Ministry of Livestock and Fisheries Development [www.mifugouvuvi.go.tz/wp-content/uploads/2014/12/DRAFT-ONE-\_Basic-Data-1.pdf](http://www.mifugouvuvi.go.tz/wp-content/uploads/2014/12/DRAFT-ONE-_Basic-Data-1.pdf), accessed 03/05/16); y J. Mubanga, PhD thesis, University of Edinburgh, 2008; z Malele, I.I. *et al.* (2013), The role of livestock in the epidemiology of sleeping sickness in Tanzania, in 32nd Conference of the AU IBAR ISCTRC Sudan (<http://www.au-ibar.org/isctrc/374-the-32nd-international-scientific-council-for-trypanosomiasis-research-and-control-isctrc-conference>, accessed 03/05/16).

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

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

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

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**References**

1 Holmes, P. (2015) On the Road to Elimination of Rhodesiense Human African Trypanosomiasis: First WHO Meeting of Stakeholders. *PLoS Negl. Trop. Dis.* 9, e0003571

2 Xong, H. V *et al.* (1998) A VSG expression site-associated gene confers resistance to human serum in *Trypanosoma rhodesiense*. *Cell* 95, 839–846

3 Echodu, R. *et al.* (2015) Genetic diversity and population structure of *Trypanosoma brucei* in Uganda: implications for the epidemiology of sleeping sickness and Nagana. *PLoS Negl. Trop. Dis.* 9, e0003353

4 Koffi, M. *et al.* (2009) Population genetics of *Trypanosoma brucei gambiense*, the agent of sleeping sickness in Western Africa. *Proc. Natl. Acad. Sci. U. S. A.* 106, 209–214

5 Morrison, L.J. *et al.* (2008) *Trypanosoma brucei gambiense* Type 1 populations from human patients are clonal and display geographical genetic differentiation. *Infect. Genet. Evol.* 8, 847–54

6 Balmer, O. *et al.* (2011) Phylogeography and taxonomy of *Trypanosoma brucei*. *PLoS Negl. Trop. Dis.* 5, e961

7 Weir, W. *et al.* (2016) Population genomics reveals the origin and asexual evolution of human infective trypanosomes. *Elife* 5, 1–14

8 Mulenga, G.M. *et al.* (2015) Assessing the capacity to diagnose human African trypanosomiasis among health care personnel from Chama and Mambwe districts of eastern Zambia. *BMC Res. Notes* 8, 433

9 Reid, H. *et al.* (2012) Assessment of the burden of human African trypanosomiasis by rapid participatory appraisal in three high-risk villages in Urambo District, Northwest Tanzania. *Afr. Health Sci.* 12, 104–113

10 Odiit, M. *et al.* (2005) Quantifying the level of under-detection of *Trypanosoma brucei rhodesiense* sleeping sickness cases. *Trop. Med. Int. Heal.* 10, 840–849

11 Simarro, P.P. *et al.* (2012) Human African trypanosomiasis in non-endemic countries (2000-2010). *J. Travel Med.* 19, 44–53

12 Ripamonti, D. *et al.* (2002) African sleeping sickness in tourists returning from Tanzania: The first 2 Italian cases from a small outbreak among European travelers. *Clin. Infect. Dis.* 34, E18–E22

13 Jelinek, T. *et al.* (2002) Cluster of African trypanosomiasis in travellers to Tanzanian national parks. *Emerg. Infect. Dis.* 8, 634–635

14 Kaare, M.T. *et al.* (2007) Sleeping sickness - a re-emerging disease in the Serengeti? *Travel Med. Infect. Dis.* 5, 117–124

15 Simarro, P.P. *et al.* (2013) Diversity of human African trypanosomiasis epidemiological settings requires fine-tuning control strategies to facilitate disease elimination. *Res. Rep. Trop. Med.* 4, 1–6

16 Estes, A.B. *et al.* (2012) Land-cover change and human population trends in the greater Serengeti ecosystem from 1984–2003. *Biol. Conserv.* 147, 255–263

17 Reiner, R.C. *et al.* (2013) A systematic review of mathematical models of mosquito-borne pathogen transmission: 1970-2010. *J. R. Soc. Interface* 10, 20120921

18 Rock, K.S. *et al.* (2015) Mathematical Models for Neglected Tropical Diseases: Essential Tools for Control and Elimination, Part A. *Adv. Parasitol.* 87, 53–133

19 LoGiudice, K. *et al.* (2003) The ecology of infectious disease: effects of host diversity and community composition on Lyme disease risk. *Proc. Natl. Acad. Sci. U. S. A.* 100, 567–71

20 Moloo, S.K. *et al.* (1999) Study of the sequential tsetse-transmitted *Trypanosoma congolense, T. brucei brucei* and *T. vivax* infections to African buffalo, eland, waterbuck, N’dama and Boran cattle. *Vet. Parasitol.* 80, 197–213

21 Van den Bossche, P. *et al.* (2005) Transmissibility of *Trypanosoma brucei* during its development in cattle. *Trop. Med. Int. Heal.* 10, 833–839

22 Picozzi, K. *et al.* (2002) The diagnosis of trypanosome infections: Applications of novel technology for reducing disease risk. *African J. Biotechnol.* 1, 39–45

23 Redruth, D. *et al.* (1994) African buffalo serum contains novel trypanocidal protein. *J. Eukaryote Microbiol.* 41, 95–103

24 Rurangirwa, F.R. *et al.* (1986) Immune effector mechanisms involved in the control of parasitemia in *Trypanosoma brucei*-infected wildebeest (*Connochaetes taurinus*). *Immunology* 58, 231–237

25 Muhanguzi, D. *et al.* (2014) Collateral benefits of restricted insecticide application for control of African trypanosomiasis on *Theileria parva* in cattle: a randomized controlled trial. *Parasit. Vectors* 7, 432

26 Selby, R. *et al.* (2013) Cattle movements and trypanosomes: restocking efforts and the spread of *Trypanosoma brucei rhodesiense* sleeping sickness in post-conflict Uganda. *Parasit. Vectors* 6, 281

27 von Wissmann, B. *et al.* (2011) Factors associated with acquisition of human infective and animal infective trypanosome infections in domestic livestock in Western Kenya. *PLoS Negl. Trop. Dis.* 5, e941

28 Laohasinnarong, D. *et al.* (2015) Studies of trypanosomiasis in the Luangwa valley, north-eastern Zambia. *Parasit. Vectors* 8, 497

29 Laohasinnarong, D. *et al.* (2011) Prevalence of *Trypanosoma* sp. in cattle from Tanzania estimated by conventional PCR and loop-mediated isothermal amplification (LAMP). *Parasitol. Res.* 109, 1735–1739

30 Fevre, E.M. *et al.* (2001) The origins of a new *Trypanosoma brucei rhodesiense* sleeping sickness outbreak in eastern Uganda. *Lancet* 358, 625–628

31 Batchelor, N. a *et al.* (2009) Spatial predictions of Rhodesian Human African Trypanosomiasis (sleeping sickness) prevalence in Kaberamaido and Dokolo, two newly affected districts of Uganda. *PLoS Negl. Trop. Dis.* 3, e563

32 Bhola, N. *et al.* (2012) Comparative changes in density and demography of large herbivores in the Masai Mara Reserve and its surrounding human-dominated pastoral ranches in Kenya. *Biodivers. Conserv.* 21, 1509–1530

33 East, R. (1999) *African Antelope Database 1998*, IUCN/SSC Antelope Specialist Group, IUCN. Gland, Switzerland and Cambridge, UK.

34 Clausen, P.-H. *et al.* (1998) Host preferences of tsetse (Diptera:Glossinidae) based on bloodmeal identifications. *Med. Vet. Entomol.* 12, 169–180

35 Kideghesho, J. *et al.* (2013) Emerging issues and challenges in conservation of biodiversity in the rangelands of Tanzania. *Nat. Conserv.* 6, 1–29

36 Vale, G.A. (1974) Responses of tsetse flies (Diptera, Glossinidae) to mobile and stationary baits. *Bull. Entomol. Res.* 64, 545–588

37 Vale, G.A. (1979) Field responses of tsetse (Diptera: Glossinidae) to odours of men, lactic acid and carbon dioxide. *Bull. ent. Res.* 69, 459–467

38 Torr, S.J. *et al.* (2012) Where, when and why do tsetse contact humans? Answers from studies in a national park of Zimbabwe. *PLoS Negl. Trop. Dis.* 6, e1791

39 Clausen, P.-H. *et al.* (1998) Host preferences of tsetse (Diptera : Glossinidae ) based on bloodmeal identifications. *Med. Vet. Entomol.* 12, 169–180

40 Reid, R.S. *et al.* (2000) Human population growth and the extinction of the tsetse fly. *Agric. Ecosyst. Environ.* 77, 227–236

41 Geiger, A. *et al.* (2015) Adult blood-feeding tsetse flies, trypanosomes, microbiota and the fluctuating environment in sub-Saharan Africa. *ISME J.* 9, 1496–1507

42 Welburn, S.C. and Maudlin, I. (1999) Tsetse-typanosome interactions: Rites of passage. *Parasitol. Today* 15, 399–403

43 Moloo, S.K. *et al.* (1992) Vector competence of *Glossina pallidipes* and *Glossina morsitans centralis* for *Trypanosoma vivax, Trypanosoma congolense* and *T. b. brucei*. *Acta Trop.* 51, 271–280

44 Torr, S.J. *et al.* (2005) Towards a rational policy for dealing with tsetse. *Trends Parasitol.* 21, 537–541

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

46 Muriuki, G.W. *et al.* (2005) Tsetse control and land-use change in Lambwe valley, south-western Kenya. *Agric. Ecosyst. Environ.* 106, 99–107

47 Bourn, D. *et al.* (2001) *Environmental Change and the Autonomous Control of Tsetse and Trypanosomosis in Sub-Saharan Africa*, Environmental Research Group Oxford Limited.

48 Ducheyne, E. *et al.* (2009) The impact of habitat fragmentation on tsetse abundance on the plateau of eastern Zambia. *Prev. Vet. Med.* 91, 11–18

49 Gondwe, N. *et al.* (2009) Distribution and density of tsetse flies (glossinidae: Diptera) at the game/people/livestock interface of the nkhotakota game reserve human sleeping sickness focus in malawi. *Ecohealth* 6, 260–265

50 Mweempwa, C. *et al.* (2015) Impact of habitat fragmentation on tsetse populations and trypanosomosis risk in Eastern Zambia. *Parasit. Vectors* 8, 406

51 Van den Bossche, P. *et al.* (2010) A changing environment and the epidemiology of tsetse-transmitted livestock trypanosomiasis. *Trends Parasitol.* 26, 236–43

52 Rogers, D.J. and Randolph, S.E. (1986) Distribution and abundance of Tsetse flies (*Glossina* spp.). *J. Anim. Ecol.* 55, 1007–1025

53 Dale, C. *et al.* (1995) The kinetics of maturation of Trypanosome infections in tsetse. *Parasitology* 111, 187–191

54 Kabbale, F. *et al.* (2010) Feeding preferences and *Trypanosoma brucei* species identified in blood meals of *Glossina fuscipes fuscipes* in Kamuli district, South Eastern Uganda. *Africa J. Anim. Biomed. Sci.* 5, 99–105

55 Muturi, C.N. *et al.* (2011) Tracking the feeding patterns of tsetse flies (*Glossina* genus) by analysis of bloodmeals using mitochondrial cytochromes genes. *PLoS One* 6, e17284

56 Bett, B. *et al.* (2008) Estimation of tsetse challenge and its relationship with trypanosomosis incidence in cattle kept under pastoral production systems in Kenya. *Vet. Parasitol.* 155, 287–98

57 Hargrove, J.W. and Vale, G.A. (1978) The effect of host odour concentration on catches of tsetse flies (Glossinidae) and other Diptera in the field. *Bull. Entomol. Res.* 68, 607–612

58 Hargrove, J.W. *et al.* (1995) Catches of tsetse (*Glossina* spp.) (Diptera: Glossinidae) from traps and targets baited with large doses of natural and synthetic host odour. *Bull. Entomol. Res.* 85, 215

59 Vale, G.A. (1977) Feeding responses of tsetse flies (Diptera: Glossinidae) to stationary hosts. *Bull. Entomol. Res.* 67, 635–649

60 Torr, S.J. and Mangwiro, T.N.C. (2000) Interactions between cattle and biting flies: Effects on the feeding rate of tsetse. *Med. Vet. Entomol.* 14, 400–409

61 Haydon, D.T. *et al.* (2002) Identifying reservoirs of infection: A conceptual and practical challenge. *Emerg. Infect. Dis.* 8, 1468–1473

62 Viana, M. *et al.* (2014) Assembling evidence for identifying reservoirs of infection. *Trends Ecol. Evol.* 29, 270–279

63 Kgori, P.M. *et al.* (2006) The use of aerial spraying to eliminate tsetse from the Okavango Delta of Botswana. *Acta Trop.* 99, 184–199

64 Shaw, a. P.M. *et al.* (2013) Estimating the costs of tsetse control options: An example for Uganda. *Prev. Vet. Med.* 110, 290–303

65 Hargrove, J.W. *et al.* (2012) Modeling the control of trypanosomiasis using trypanocides or insecticide-treated livestock. *PLoS Negl. Trop. Dis.* 6, e1615

66 Vale, G.A. and Torr, S.J. (2005) User-friendly models of the costs and efficacy of tsetse control: application to sterilizing and insecticidal techniques. *Med. Vet. Entomol.* 19, 293–305

67 Torr, S.J. and Vale, G. a (2011) Is the even distribution of insecticide-treated cattle essential for tsetse control? Modelling the impact of baits in heterogeneous environments. *PLoS Negl. Trop. Dis.* 5, e1360

68 Anderson, N.E. *et al.* (2011) Characterisation of the wildlife reservoir community for human and animal trypanosomiasis in the Luangwa Valley, Zambia. *PLoS Negl. Trop. Dis.* 5, e1211

69 Geigy, R. and Kauffman, M. (1973) Sleeping sickness survey in the Serengeti area (Tanzania) 1971: I. Examination of large mammals for trypanosomes. *Acta Trop.* 30, 12–23

70 Geigy, R. *et al.* (1971) Sleeping sickness survey in Musoma District, Tanzania: IV. Examination of wild mammals as a potential reservoir for T. rhodesiense. *Acta Trop.* 28, 211–220

71 Baker, J.R. (1968) Trypanosomes of wild mammals in the neighbourhood of the Serengeti National Park. *Symp. Zool. Soc. London* 24, 147–158

72 Sachs, R. *et al.* (1967) Isolation of trypanosomes of the *T. brucei* group from lion. *Acta Trop.* 14, 109–112

73 Drager, N. and Mehlitz, D. (1978) Investigations on prevalence of Trypanosome carriers and antibody response in wildlife in Northern Botswana. *Tropenmed. Parasitol.* 29, 223–233

74 Welburn, S.C. *et al.* (2008) Patterns in age-seroprevalence consistent with acquired immunity against *Trypanosoma brucei* in Serengeti lions. *PLoS Negl. Trop. Dis.* 2, e347

75 Dillmann, J.S.S. and Townsend, A.J. (1979) Trypanosomiasis survey of wild animals in the Luangwa Valley, Zambia. *Acta Trop.* 36, 349–356

76 Carmichael, I.H. and Hobday, E. (1975) Blood parasites of some wild Bovidae in Botswana. *Onderstepoort J. Vet. Res.* 42, 55–62

77 Corson, J.F. (1939) The infections produced in sheep and antelopes by a strain of *Trypanosoma rhodesiense*. *Trans Roy Soc Trop Med Hyg* 33, 37–46

78 Ashcroft, M.T. *et al.* (1959) The experimental infection of some African wild animals with *Trypanosoma rhodesiense, T. brucei* and *T. congolense*. *Am. J. Trop. Med. Parasitol.* 53, 147–161

79 Sinclair, A.R.E. *et al.* (2008) *Serengeti III: Human impacts on ecosystem dynamics*, University of Chicago Press.

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

95 Madanitsa, M. *et al.* (2009) The epidemiology of trypanosomiasis in Rumphi district, Malawi: A ten year retrospective study. *Malawi Med. J.* 21, 22–27

96 Nicolas, G. *et al.* (2016) Using Random Forest to Improve the Downscaling of Global Livestock Census Data. *PLoS One* 11, e0150424