MATHEMATICAL POPULATION STUDIES
2016, VOL. 23, NO. 2, 95–122
http://dx.doi.org/10.1080/08898480.2013.836427

Routledge
Taylor & Francis Group

# A mathematical model of a theoretical sleeping sickness vaccine

Yasmine Samia[a], Alison Kealey[b], and Robert J. Smith?[c]

[a]Department of Mathematics, The University of Ottawa, ON, Canada; [b]Department of Community Health and Epidemiology, Queen's University, Kingston, ON, Canada; [c]Department of Mathematics and Faculty of Medicine, The University of Ottawa, ON, Canada

**ABSTRACT**

Human African sleeping sickness is found throughout sub-Saharan Africa. It affects up to 70,000 individuals per year, primarily the poor. Existing treatments are limited, costly, and often toxic. Recent evidence suggests that a vaccine may be viable. Potential vaccines against Rhodesian sleeping sickness may be imperfect, may only be delivered to some proportion of the population, may wane over time, and may not always mount an immunogenic response in the individual receiving it. The potential effects of such a vaccine are addressed and compared to vector control. The basic reproductive ratio for both unvaccinated and vaccinated individuals is derived. The fitness ratio is used to show that vaccines that grant longer life must be accompanied by a corresponding reduction in transmissibility. A sensitivity analysis shows that control of tsetse flies through insecticide is superior to an idealized vaccine. Such a vaccine is unlikely to eradicate the disease, even if delivered to 100% of the population. Consequently, efforts to control sleeping sickness that do not incorporate vector control may be flawed.

**KEYWORDS**

insecticide; mathematical model; sleeping sickness; vaccine



## 1. Introduction

Human African sleeping sickness has had, and continues to have, a profound effect on both host and vector demographics throughout the African continent (Knight, 1971). The prevalence and incidence of the disease are determined by its intimate relationship with both environmental and anthropogenic factors (Knight, 1971; Berrang-Ford et al., 2006). Human African sleeping sickness, caused by *Trypanosoma brucei* subspecies and transmitted by the bite of infected *Glossina spp*. (tsetse flies), is fatal without treatment and is responsible for a significant loss in quality of life, as measured by disability-adjusted life years in endemic areas (WHO, 2006; Heymann, 2008).

**CONTACT** Robert J. Smith? rsmith43@uottawa.ca Department of Mathematics and Faculty of Medicine, The University of Ottawa, 585 King Edward Avenue, Ottawa, ON K1N 6N5, Canada.
The question mark in "Smith?" is part of the author's name.

The loss of viable animal livestock and the loss of human agricultural ability through debilitating sickness both incur large economic costs (Hide et al, 1999; Welburn et al., 2006). The distribution of the disease is limited by the distribution of its tsetse fly vectors, which are dispersed throughout sub-Saharan Africa (WHO, 1998; Heymann, 2008). Approximately 50,000–70,000 individuals are infected per year worldwide, with infection levels nearing 300,000 cases; at present, 60 million individuals may be at risk of infection (WHO, 2006; Heymann, 2008). The control and prevention of sleeping sickness has become a pressing public-health issue. Historical evidence suggests that the disease has previously had a wider geographic spread; current evidence indicates that present-day foci are expanding, which some fear may result in a catastrophic merger of *T. brucei* subspecies (Berrang-Ford et al., 2006; Odiit et al., 2006).

The burden of African sleeping sickness weighs heavily on the poor as the innate difficulties associated with the diagnosis and treatment of the disease are frequently exacerbated in rural communities where access to health care may be limited or even impossible due to civil instability (Welburn et al., 2006). Due to its undue effect on the poor, it is known as a neglected tropical disease (Kealey and Smith?, 2010).

Human African sleeping sickness is caused by two *T. brucei* subspecies that differ in terms of their clinical manifestation, epidemiology, ecology, control, and, most importantly, their diagnosis and treatment: *T. b. gambiense*, responsible for Gambian or chronic sleeping sickness, and *T. b. rhodesiense*, responsible for acute or Rhodesian sleeping sickness (Berrang-Ford, 2007; Heymann, 2008). If left untreated, *T. b. gambiense* may take a number of years to overcome the host while *T. b. rhodesiense* is fatal in the majority of human hosts within six months (Welburn et al., 2001).

Existing treatments are limited, costly, and may be toxic to the host and to the parasite (WHO, 1998; Stitch et al., 2002); only one treatment is less than 40 years old (Stitch et al., 2002). International intervention was required when Western pharmaceutical companies slowed drug production due to insufficient profit.

Infectious trypanosomes are transmitted through the bite of an infected tsetse fly; if infected, the flies, which feed on the bloodmeal of their hosts, remain infectious for the duration of their lifespan (WHO, 1998; Heymann, 2008). Not all species of *Glossina* are viable vectors of human or animal disease (WHO, 1998). Vertical transmission has not been documented within *Glossina spp*., although it has been observed in humans (Heymann, 2008). Tsetse flies are capable of traveling vast distances on their own or with the aid of migrating animals (WHO, 1998). The tsetse fly has a relatively low reproductive rate, in contrast to other insects that often have an extremely high reproductive rate (Rogers and Randolph, 1985). The disease is believed

to be maintained at endemic levels around specific foci and may become epidemic given the right circumstance (Hide et al, 1999). Sudden changes in the environment or vector or host populations may initiate sleeping sickness epidemics (WHO, 1998). Large-scale dispersal of human populations driven by conflict and war have long been associated with epidemic cycles (Welburn et al., 2001; WHO, 1998; Berrang-Ford et al., 2006). Epidemics are controlled by a number of host and vectorial factors, including host behavior or vector density in the case of *T. b. rhodesiense* (WHO, 1998). Day-to-day activity associated with the availability of water may increase the probability of exposure to riverine vectors, while a person's occupation might cause them to enter a tsetse-infested thicket or wooded area, increasing their risk of infection (WHO, 1998).

International efforts to control sleeping sickness initiated in the mid-1990s have shown some success in reducing the incidence of new cases; these efforts include improved awareness and surveillance of the disease (Cattand et al., 2001; WHO, 2006). Systematic screening and prompt diagnosis of human populations are of particular importance in controlling *T. b. gambiense*, while a reduction in the parasite burden within cattle reservoirs is necessary for the control of *T. b. rhodesiense* (Heymann, 2008).

Limited diagnostic tools and a lack of health-care infrastructure makes treatment difficult to attain and implement, which in turn increases the probability that an infected individual will continue to be a source of new infection (WHO, 1998). The targeted destruction of tsetse fly habitats or chemical spraying of insecticides based on tsetse fly resting habits may reduce the prevalence of the disease; the indiscriminate use of chemical controls has decreased in recent years and the use of sustainable methods such as trapping have come into favor, particularly in dry riverine environments (Rogers and Randolph, 1985; WHO, 1998; Heymann, 2008). The development of better diagnostic tools, safer pharmaceuticals, treatment networks, and control programs specific to the unique ecological and social constraints of the disease at local, regional, and even national scales will be necessary to reach eradication (Gubler, 1998; Fèvre et al., 2004; Welburn et al., 2006; WHO, 2006). Welburn et al. (2006) suggested that top-down control methods should be limited to large-scale epidemics and that efforts should be focused on providing the tools and infrastructure for affordable community-based programs.

Vaccine development has been impeded by the high amount of antigenic variation found within trypanosome species, and there is no available vaccine (Murray et al., 1984; Barrett et al., 2003). Recent evidence suggests that a multicomponent livestock vaccine may be able to overcome antigenic variation (Kristjanson et al., 1999). Such a vaccine would be of significant economic value; it could improve prevention and control efforts and enable the subsequent development of a human vaccine (Kristjanson et al., 1999). Also

such a vaccine would need to consider geographic changes in both vector and host populations.

Mathematical modeling has been recognized as a very efficient tool for understanding the dynamics of many vector-borne infectious diseases such as malaria (Ross, 1911; MacDonald, 1957; Smith?, 2007; Teboh-Ewungkem et al., 2013). In particular, general mathematical models of African sleeping sickness exist (Rogers, 1988; Artzrouni and Gouteux, 1996a; Welburn et al., 2001). Rogers (1988) proposed a two hosts/one vector model for sleeping sickness, relying on the interactions among human, cattle or domestic animals and tsetse flies. Rogers argued that domestic animals might be essential in the maintenance of *T. b. gambiense*, since $R_0$ in humans alone might fall below unity. This led to suggestions that the existence of a nonhuman animal reservoir in *T. b. gambiense* infections might have contributed to the failure of human population surveillance and treatment campaigns to eradicate sleeping sickness in certain settings. However, the existence of an animal population on which tsetse flies preferentially feed might result in humans receiving infectious bites at a lower rate than when flies feed only on humans. Unlike Rogers (1988), Artzrouni and Gouteux (1996a) assumed that only humans are reservoirs for the parasite and presented a compartmental model for the spread of Gambian sleeping sickness in Central Africa and identified important parameters that determine the equilibrium points of the model.

Cattand et al. (2001), Welburn et al. (2001), Picozzi et al. (2002), and Welburn et al. (2006) have used models of sleeping sickness transmission to examine how the effectiveness of different interventions—early curative treatment of humans, chemoprophylatic treatment of animals, and vector control—will affect the control of the disease. We include vaccination as a potential preventive method for the spread of *T. b. rhodesiense* and investigate its effectiveness.

We propose a compartmental model for the possible control of Rhodesian sleeping sickness through vaccination. We adapt the model proposed by Smith? (2007) on the effect of vaccination on malaria and consider the effect of animal livestock on the spread of the disease. The potential effects of a vaccine for infectious diseases could include the reduction of the infection rate, the reduction of the mortality due to the disease, or the increase of the recovery rate. Possible limitations are that the vaccine may only be delivered to some proportion $p$ of the population, that the vaccine may not always take when administered to individuals, that the vaccine may not always protect against infection, or that the vaccine may wane over time.

## 2. The model

We model a theoretical vaccine that takes in a proportion $\epsilon$ of vaccinated people, reduces the infection rate $\beta$, reduces the disease-specific death rate $\gamma$,

but wanes over time with rate $\xi$. The vaccination process takes place before infection. Humans are born at rate $\pi_H$, a proportion $p$ of whom receive the vaccine. We also assume that tsetse flies can be either susceptible (in number $T_s$) or infected ($T_i$) and have a birth rate $\pi_T$ and a death rate $\omega$ that does not vary significantly if they are infected. Livestock are born susceptible (in number $L_s$) at a rate $\pi_L$, become infected ($L_i$), and die at a rate $\theta$. A susceptible individual—vaccinated (in number $H_{sv}$) or unvaccinated ($H_{su}$)—becomes infected through the bite of an infected tsetse fly ($T_i$), transferring to the class of infected vaccinated people (total number of this class: $H_{iv}$) with rate $\beta$ or to the class of infected unvaccinated people (total number of this class: $H_{iu}$) with rate $(1-\psi)\beta$.

An infected tsetse fly can infect susceptible livestock at rate $\delta$. Conversely, a susceptible tsetse fly $T_s$ becomes infected with rate $\alpha$ when taking a blood meal from an infected individual or infected livestock. Unvaccinated infected individuals may recover at rate $\nu$, while vaccinated infected individuals recover at rate $\nu_v$; vaccinated individuals recover at rates equal to or faster than those unvaccinated because any vaccine that increases the infection period is unlikely to be approved. Infected individuals may also die because of the disease, with corresponding rates $\gamma$ for unvaccinated individuals and $\gamma_v$ for vaccinated individuals $(\gamma_v < \gamma)$.

Under these assumptions, the model is:

$$H'_{su}(t) = (1-\epsilon p)\pi_H - \beta H_{su}(t)T_i(t) - \mu H_{su}(t) + \nu H_{iu}(t) + \xi H_{sv}(t) \quad (1)$$

$$H'_{iu}(t) = \beta H_{su}(t)T_i(t) - (\mu+\gamma+\nu)H_{iu}(t) + \xi H_{iv}(t) \quad (2)$$

$$H'_{sv}(t) = \epsilon p\pi_H - (1-\psi)\beta_v H_{sv}(t)T_i(t) - \mu H_{sv}(t) + \nu_v H_{iv}(t) - \xi H_{sv}(t) \quad (3)$$

$$H'_{iv}(t) = (1-\psi)\beta_v H_{sv}(t)T_i(t) - (\mu+\gamma_v+\nu_v)H_{iv}(t) - \xi H_{iv}(t) \quad (4)$$

$$T'_s(t) = \pi_T - \alpha H_{iu}(t)T_s(t) - (1-\psi)\alpha H_{iv}(t)T_s(t) - \zeta T_s(t)L_i(t) - \omega T_s(t) \quad (5)$$

$$T'_i(t) = \alpha H_{iu}(t)T_s(t) + (1-\psi)\alpha H_{iv}(t)T_s(t) + \zeta T_s(t)L_i(t) - \omega T_i(t) \quad (6)$$

$$L'_s(t) = \pi_L - \delta L_s(t)T_i(t) - \theta L_s(t) \quad (7)$$

$$L'_i(t) = \delta L_s(t)T_i(t) - \theta L_i(t). \quad (8)$$

The model is shown in Figure 1.

## 3. Analysis

The disease-free equilibrium is given by: $\overline{H}_{su} = \left(\frac{1}{\mu} - \frac{\epsilon p}{\mu+\xi}\right)\pi_H$, $\overline{H}_{sv} = \frac{\epsilon p\pi_H}{\mu+\xi}$, $\overline{T}_s = \pi_T/\omega$, $\overline{L}_s = \pi_L/\theta$, and $\overline{H}_{iu} = \overline{H}_{iv} = \overline{T}_i = \overline{L}_i = 0$. When the infection

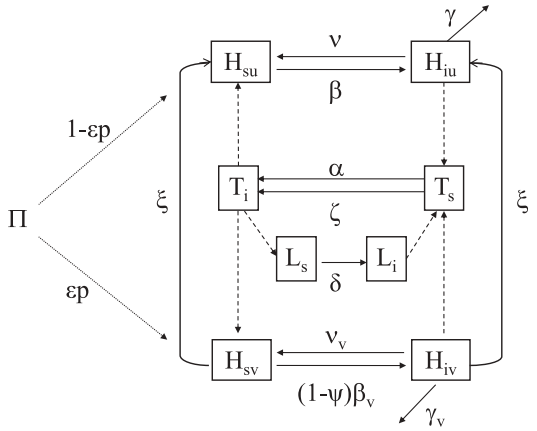


**Figure 1.** The flow chart representing the vaccination model for African trypanosomiasis. *H* refers to humans, *T* to tsetse flies, and *L* to livestock. Compartments with susceptible individuals are designated with index *s*, while those with infected individuals are designated with index *i*. The index *u* refers to unvaccinated individuals and the index *v* to vaccinated individuals. The human birth rate is denoted by $\pi_H$, while *p* represents the proportion of vaccinated humans. Infections among different populations are given by dashed arrows, while transfer from one class to another within the same population is given by solid arrows. All compartments have background death rates (arrows not shown for clarity). An explanation of the transfer and interaction parameters is given in Table 1.



is present in human, livestock, and tsetse populations, the endemic equilibrium in terms of $\tilde{T}_i$ is given by:

$$\tilde{H}_{su} = \frac{1-\epsilon p}{\mu}\pi_H - \frac{\mu+\gamma}{\mu}\left(\frac{\omega^2\tilde{T}_i}{\alpha\left(\pi_T-\omega\tilde{T}_i\right)} - \frac{\zeta\delta\pi_L}{\alpha\theta\left(\theta+\delta\tilde{T}_i\right)}\tilde{T}_i\right) + \frac{1}{\mu}\left(\frac{\xi(1-\psi)\beta_v\tilde{T}_i + (1-\psi)^2(\mu+\gamma)\beta_v\tilde{T}_i + \xi\left(\mu+\gamma_v+\nu_v+\xi\right)}{(\mu+\xi)\left(\mu+\gamma_v+\nu_v+\xi\right)+\left(\mu+\gamma_v+\xi\right)(1-\psi)\beta_v\tilde{T}_i}\right)\epsilon p\pi_H \tag{9}$$

$$\tilde{H}_{sv} = \frac{\epsilon p\pi_H}{\mu+\xi}\left(\frac{(\mu+\xi)\left(\mu+\gamma_v+\nu_v+\xi\right)}{(\mu+\xi)\left(\mu+\gamma_v+\nu_v+\xi\right)+\left(\mu+\gamma_v+\xi\right)(1-\psi)\beta_v\tilde{T}_i}\right) \tag{10}$$

$$\tilde{H}_{iu} = \frac{\omega^2\tilde{T}_i}{\alpha\left(\pi_T-\omega\tilde{T}_i\right)} - \frac{\zeta\delta\pi_L\tilde{T}_i}{\alpha\theta\left(\theta+\delta\tilde{T}_i\right)} - \frac{(1-\psi)^2\beta_v\epsilon p\pi_H\tilde{T}_i}{(\mu+\xi)\left(\mu+\gamma_v+\nu_v+\xi\right)+\left(\mu+\gamma_v+\xi\right)(1-\psi)\beta_v\tilde{T}_i} \tag{11}$$

$$\tilde{H}_{iv} = \frac{(1-\psi)\beta_v\epsilon p\pi_H\tilde{T}_i}{(\mu+\xi)\left(\mu+\gamma_v+\nu_v+\xi\right)+\left(\mu+\gamma_v+\xi\right)(1-\psi)\beta_v\tilde{T}_i} \tag{12}$$

**Table 1.** Parameter values.

| Parameter | Definition | Range | Sample Value | Unit | Comments | Reference |
|---|---|---|---|---|---|---|
| | | Unvaccinated humans | | | | |
| $\pi_H$ | Human birth rate | 0 – 1 | 0.27 | people day$^{-1}$ | - | - |
| $\beta$ | Rate of transmission of infection from infected tsetse fly to humans | 0 – $10^{-6}$ | $9.12 \times 10^{-6}$ | tsetse$^{-1}$ day$^{-1}$ | - | (Rogers, 1988; Leak, 1999) |
| $\mu$ | Human death rate | 1/21900 – 1/14600 | 1/18250 | days$^{-1}$ | Human lifetime of 50 years | (Artzrouni and Gouteux, 1996a) |
| $\gamma$ | Disease-induced death rate | 1/180 – 1/30 | 1/180 | days$^{-1}$ | Death caused by disease occurs between 1 and 6 months following the infection (if the treatment fails) | (Onyango, 1969; Welburn et al., 2001) |
| $\nu$ | Recovery rate | 1/30 – 1/7 | 1/14 | days$^{-1}$ | Infection duration between 7 and 30 days | (Chappuis et al., 2010) |
| | | Vaccinated individuals | | | | |
| $p$ | Proportion of people vaccinated | 0 – 1 | variable | - | - | - |
| $\xi$ | Waning rate of vaccine | 0 – 1/730 | variable | days$^{-1}$ | The vaccine could wane in 2 years or could ensure permanent immunity | - |
| $\epsilon$ | Vaccine immunogenicity in vaccinated people | 75% – 98% | 80% | - | - | (Llamazares and Smith?, 2008) |
| $\psi$ | Vaccine efficacy | 85% – 95% | 95% | - | - | (Llamazares and Smith?, 2008) |
| $\beta_v$ | Rate of transmission of infection from infected tsetse fly to vaccinated humans | 0 – $10^{-6}$ | $5 \times 10^{-6}$ | tsetse$^{-1}$ day$^{-1}$ | - | - |
| $\nu_v$ | Recovery rate | 1/30 – 1/7 | 1/10 | days$^{-1}$ | Infection duration between 7 and 30 days | - |
| $\gamma_v$ | Disease induced death rate | 1/1200 – 1/150 | 1/360 | days$^{-1}$ | Death due to the disease is smaller in vaccinated individuals | - |

(*Continued*)

**Table 1.** (Continued).

| Parameter | Definition | Range | Sample Value | Unit | Comments | Reference |
|---|---|---|---|---|---|---|
| | | Tsetse flies | | | | |
| $\pi_T$ | Tsetse birth rate | 0 – 100 | 20 | tsetse day$^{-1}$ | 20 tsetse flies are born every day in the region | (Jarry et al., 1996; Holmes et al., 2004) |
| $\alpha$ | Rate of transmission of infection from human to tsetse flies | 0 – $10^{-3}$ | $1.5 \times 10^{-5}$ | human$^{-1}$ day$^{-1}$ | - | (Tait et al., 1996; Leak, 1999) |
| $\zeta$ | Rate of transmission of infection from infected livestock to tsetse flies | 0 – $10^{-3}$ | $1.75 \times 10^{-4}$ | infected livestock$^{-1}$ day$^{-1}$ | - | (Rogers, 1988; Welburn et al., 2005) |
| $\omega$ | Tsetse death rate | 1/240 – 1 | 1/40 | day$^{-1}$ | We chose a large range here to reflect the option of insecticide spraying | (Artzrouni and Gouteux, 1996b; Carey, 2001) |
| | | Livestock | | | | |
| $\pi_L$ | Livestock birth rate | 0 – 0.1 | 1/90 | tsetse day$^{-1}$ | - | (Holt et al., 2006) |
| $\delta$ | Rate of transmission of infection from infected tsetse fly to livestock | 0 – $10^{-3}$ | $1.085 \times 10^{-4}$ | tsetse$^{-1}$ day$^{-1}$ | - | (Rogers, 1988) |
| $\theta$ | Livestock death rate | $1.095 \times 10^{-4}$ – 0.06 | 1/365 | day$^{-1}$ | The lifespan of livestock is chosen to be about 1 year, due to harvesting | - |

$$\tilde{T}_s = \frac{\pi_T}{\omega} - \tilde{T}_i \tag{13}$$

$$\tilde{L}_s = \frac{\pi_L}{\theta + \delta\tilde{T}_i} \tag{14}$$

$$\tilde{L}_i = \frac{\delta\pi_L}{\theta\left(\theta + \delta\tilde{T}_i\right)}\tilde{T}_i. \tag{15}$$

We use the next-generation method (van den Driessche and Watmough, 2002; Heffernan et al., 2005) to determine the basic reproduction number $R_0$. Consider only infected compartments $x_i$. $\mathbb{F}$ is the vector of all new infections in each compartment, and $\mathbb{V}$ the vector of transfers between these compartments:

$$\begin{aligned}\mathbb{F} &= \begin{pmatrix} \beta H_{su} T_i \\ (1-\psi)\beta_v H_{sv} T_i \\ \alpha H_{iu} T_s + (1-\psi)\alpha H_{iv} T_s + \zeta T_s L_i \\ \delta L_s T_i \end{pmatrix} \text{ and} \\ \mathbb{V} &= \begin{pmatrix} (\mu+\gamma+\nu)H_{iu} - \xi H_{iv} \\ \left(\mu+\gamma_v+\nu_v\right)H_{iv} + \xi H_{iv} \\ \omega T_i \\ \theta L_i \end{pmatrix}.\end{aligned} \tag{16}$$

Let $F = \left(\frac{\partial \mathbb{F}}{\partial x_i}\right)$ and $V = \left(\frac{\partial \mathbb{V}}{\partial x_i}\right)$. $R_0$ is then given by the spectral radius of $FV^{-1}$ evaluated at the disease-free equilibrium and represents the mean number of new infections per infective in any class, per generation:

$$R_0 = B^{1/2}, \tag{17}$$

where

$$\begin{aligned}B = &\frac{\zeta\delta}{\omega\theta}\overline{T}_s\overline{L}_s + \frac{\alpha\beta}{\omega(\mu+\gamma+\nu)}\overline{H}_{su}\overline{T}_s \\ &+ \frac{\alpha\beta_v(1-\psi)}{\omega\left(\mu+\gamma_v+\nu_v+\xi\right)}\left(\frac{\xi}{\mu+\gamma+\nu}+1-\psi\right)\overline{T}_s\overline{H}_{sv}.\end{aligned} \tag{18}$$

This value represents a mathematical threshold, not necessarily the average number of secondary infections (Li et al., 2011).

We denote the proportion of the population that is successfully vaccinated by $S$, satisfying $S = \frac{\overline{H}_{sv}}{\overline{H}_{sv}+\overline{H}_{su}} = \frac{\epsilon p\mu}{\mu+\xi}$. Because vaccinated individuals can still get infected, they can cause secondary infections. We define $R_V$ as the

reproduction number in a population with vaccination, in contrast to $R_U$, the basic reproduction number in an unvaccinated population.

In the absence of vaccination, $S = 0$, $\overline{H}_{sv} = 0$, $\overline{H}_{su} = \pi_H/\mu$, $\overline{T}_s = \pi_T/\omega$, and $\overline{L}_s = \pi_L/\theta$. From the expression for $R_0$, we derive

$$R_U = \frac{1}{\omega}\left(\frac{\zeta\delta}{\theta^2}\pi_T\pi_L + \frac{\alpha\beta}{\mu(\mu+\gamma+\nu)}\pi_H\pi_T\right)^{1/2}. \tag{19}$$

If the entire population is successfully vaccinated, $S = 1$, $\overline{H}_{sv} = \pi_H/\mu$, $\overline{H}_{su} = 0$, $\overline{T}_s = \pi_T/\omega$, and $\overline{L}_s = \pi_L/\theta$. In this case, the expression for $R_0$ gives

$$R_V = \frac{1}{\omega}\left(\frac{\zeta\delta}{\theta^2}\pi_T\pi_L + \frac{\alpha\beta_v\xi(1-\psi)}{\mu(\mu+\gamma+\nu)(\mu+\gamma_v+\nu_v+\xi)}\pi_H\pi_T + \frac{\alpha\beta_v(1-\psi)^2}{\mu(\mu+\gamma_v+\nu_v+\xi)}\pi_T\pi_H\right)^{1/2}. \tag{20}$$

Using the Jacobian method, we get comparable expressions for both $R_U$ and $R_V$ to the ones we get using the next-generation method. The population reproduction number is

$$R_P = (1 - S)R_U + SR_V. \tag{21}$$

When $R_P = 1$, the minimum vaccinating coverage level $p_c$ can be determined. This represents the minimal proportion of people that should be vaccinated in order to stop the disease from spreading. Rearranging Eq. (21) yields:

$$S = \frac{\epsilon p_c \mu}{\mu + \xi} = \frac{1 - R_U}{R_V - R_U}. \tag{22}$$

Hence $p_c = \frac{(\mu+\xi)(1-R_U)}{\epsilon\mu(R_V-R_U)}$, and eradication is theoretically possible for vaccination programs covering at least a proportion $p_c$ of people, if $p_c < 1$.

## 4. Numerical analysis

### 4.1. *Parameters*

*Initial values.* We consider a sub-Saharan African village with a well-mixed population. We set the initial population to 5,000 individuals. We assume 10 tsetse flies per human, so the initial tsetse population is 50,000. We also assume the cattle in this village initially counts 1,000. The infection rates with Human African trypanosomiasis among human, tsetse, and cattle

populations are 0.6%, 0.26%, and 18% respectively (Welburn et al., 2005). For our initial infected populations, we consider 30 infected humans, 140 infected flies, and 180 infected cattle.

***Human parameters.*** We suppose that the human population is initially at a steady state. The birth rate of humans is 0.27, which is derived from the equilibrium formula for susceptible humans, by multiplying the initial number of individuals by the death rate. Individuals live for an average of 50 years, so the death rate of humans is $\mu = 1/18250$ days$^{-1}$ (Artzrouni and Gouteux, 1996a). The transmission rate from infected tsetste flies to uninfected humans is the product of the daily biting rate of flies from humans times the probability of a fly bite producing an infection in humans, divided by the initial total number of flies present in the population, so $\beta = 9.12 \times 10^{-6}$day$^{-1}$tsetse$^{-1}$ (Rogers, 1988). The typical treatment against Rhodesian sleeping sickness lasts 14 days (Chappuis et al., 2010). If this treatment is successful, the recovery rate is $\nu = 1/14$ days$^{-1}$. If the treatment fails, death can occur 30–270 days after infection (Onyango, 1969). The disease-induced death rate is 1/180 days$^{-1}$ (Welburn et al., 2001). When an individual is vaccinated, the transmission rate of the infection from flies is reduced by a given proportion relative to each vaccine. We denote this parameter $\beta_v$. A competent vaccine that grants high protection usually has relatively high efficacy. A recently developed vaccine is the HPV vaccine, which has an efficacy between 85% and 95% (Llamazares and Smith?, 2008). We choose the same range for the parameter $\psi$, which allows us to test the effect of a theoretically strong vaccine. Recovery occurs faster in vaccinated individuals who are more protected against the disease, so $\nu_v > \nu$. Disease-induced death is less likely for vaccinated individuals so $\gamma_v < \gamma$.

***Tsetse flies parameter values.*** The tsetse fly breeding cycle takes between 7 and 12 days (Holmes et al., 2004). Considering the huge number of tsetse flies in the affected regions, we suppose 20 flies are born each day, giving a tsetse birth rate of $\pi_T = 20$. The rate of transmission of infection from humans to flies is given by the daily biting rate of flies from humans, divided by the total initial human population. So we need a sample value of $\alpha = 1.5 \times 10^{-5}$ day$^{-1}$human$^{-1}$ (Rogers, 1988). The rate of transmission of infection from cattle to flies is given by the daily biting rate of flies from cattle, divided by the total initial cattle population. Our sample value was $\zeta = 1.75 \times 10^{-4}$ day$^{-1}$cattle$^{-1}$ (Rogers, 1988). A tsetse fly can survive several months in some conditions (Gooding and Krasfur, 2005). We set $\omega = 1/40$ days$^{-1}$ so that the endemic equilibrium exists in the absence of vaccination (see Appendix).

***Livestock parameter values.*** Because the gestation period of cows is about 9 months, we suppose that 1 new cow is born every 3 months, so that the cattle birth rate is $\pi_L = 1/90$. The rate of transmission of the infection from infected flies to livestock is the product of the daily biting rate of flies from cattle, times the probability of a fly bite producing an infection in cattle, divided by the initial total number of flies present in the population, giving $\delta = 1.085 \times 10^{-4}$ day$^{-1}$tsetse$^{-1}$ (Rogers, 1988). In normal conditions, the lifespan of cattle can last up to 20 years or more. But cattle are used for their meat, so they do not live longer than one or two years. So the death rate we choose is $\theta = 1/365$ days$^{-1}$, which corresponds to a lifespan of one year.

***Vaccine parameters.*** $p$ is the proportion of people vaccinated, varying from 0 (no vaccination) to 1 (all the population vaccinated). $\epsilon$ is the vaccine take or immunogenicity in vaccinated individuals, which we assume varies between 75% and 98% (Llamazares and Smith?, 2008). $\xi$ represents the waning rate of the vaccine; it depends on the vaccine itself, falling between 0 and 1/365, so that the vaccinated individual is immune from at least one year to a lifetime duration.

### 4.2. *Stability analysis*

We examine the stability of the disease-free equilibrium using numerical simulations. Figure 2 represents a bifurcation diagram of the asymptotic total number of infected tsetse flies; that is, the corresponding population size in the long run, with respect to the population reproduction number $R_p$.

We calculated the value of $\omega$ such that $R_p = 1$ gives a critical value for the death rate of the flies at which $T_i = 0$. Table 2 shows the different situations we considered. In particular, we varied the waning rate of the vaccine and the proportion of people vaccinated. All other parameters were fixed at their sample values in Table 1.

In each of these situations, for any value of $\omega$ higher than $\omega_{R_p=1}$, $R_p$ is smaller than 1, and $T_i$ is still negligible, meaning that the endemic equilibrium does not exist in this case, and the disease-free equilibrium is stable. On the other hand, for values of $\omega$ smaller than $\omega_{R_p=1}$, $R_p$ is higher than 1 and running the time series for sufficiently long produces positive values of $T_i$. This result suggests that stability of disease-free equilibrium is given by the threshold condition $R_p = 1$, and guarantees the existence of the endemic equilibrium when the disease-free equilibrium becomes unstable. Furthermore, this result is independent of initial population size; to generate this graph, we started with more than 50,000 flies and still converged to the disease-free equilibrium.

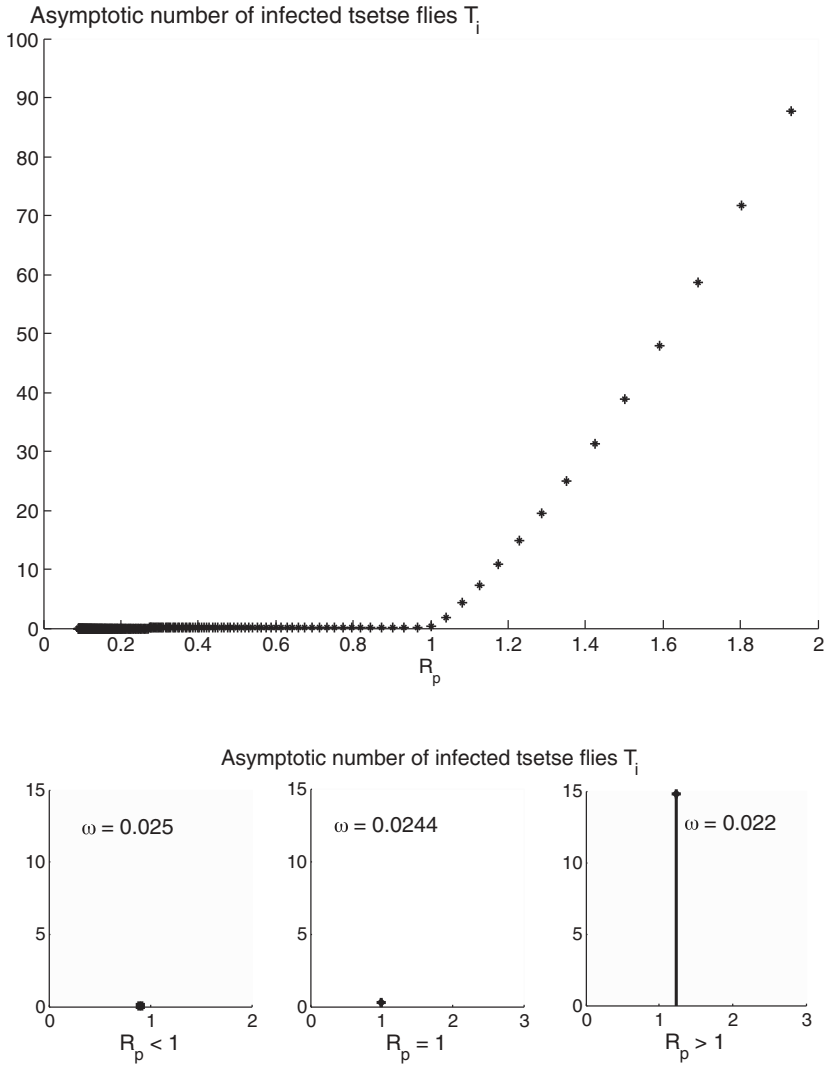


**Figure 2.** The upper graph is a bifurcation diagram of the asymptotic values of infected tsetse flies, $T_i$, as $R_p$ varies. The lower three subgraphs show the values of $T_i$ for three different point values of $R_p$, calculated for corresponding values of $\omega$. The values of $\omega$ are decreasing. These three subplots correspond to $R_p < 1$, $R_p = 1$, and $R_p > 1$. The results are given for the case of $p = 1$ and $\xi = 0$.

In Table 2, we calculated the proportion of the population needing vaccination coverage, the fitness ratio, and the population reproduction number using $\omega = 0.025$. This is lower than the critical value in all cases except the last, when the vaccine was assumed to be given to all individuals, with no waning. This suggests that only extremely effective vaccines will be viable, which are unlikely to occur in reality.

With the parameter values used in our model, eradication of Rhodesian sleeping sickness may not be possible through vaccination, because vaccinating the entire population is not feasible and a vaccine that induces life-long immunity is unlikely. In all situations we considered, a small increase in the

**Table 2.** Numerical values for some critical parameters for six different combinations of $p$ and $\xi$. The point value of the tsetse flies' death rate $\omega$ is 0.025, which lies in the interval of existence of the endemic equilibrium in the absence of vaccination. We calculated values of $\omega_{R_p=1}$ by fixing all other parameters and finding $\omega$ using $R_p = 1$. For values of $\omega > \omega_{R_p=1}$, the disease-free equilibrium is stable $(R_p < 1)$, while for values of $\omega < \omega_{R_p=1}$, $R_p > 1$, and the disease-free equilibrium becomes unstable. For the disease to be eradicated, $p_c$ should be smaller than 1. The fitness ratio $f$ is practically the same in all cases, and the parameters are chosen to have $f < 1$, so that vaccination reduces secondary infections caused by infected individuals. A condition for the disease to be eradicated is that $R_p$ should be smaller than 1, which is only found in the last combination, where $p = 1$ and $\xi = 0$.

| $p$ | $\xi$ | Values of $\omega$ for which the endemic equilibrium exists | $\omega\|_{R_p=1}$ | $p_c$ | f | $R_p$ |
|---|---|---|---|---|---|---|
| 0 | 1/730 | (0.024, 0.027) | 0.0271 | 20.3 | 0.87345 | 1.0860 |
| 0 | 0 | (0.024, 0.027) | 0.0271 | 0.78 | 0.87340 | 1.0860 |
| 0.3 | 1/730 | (0.024, 0.027) | 0.0271 | 20.3 | 0.87345 | 1.0847 |
| 0.3 | 0 | (0.024, 0.026) | 0.0263 | 0.78 | 0.87340 | 1.0530 |
| 1 | 1/730 | (0.024, 0.027) | 0.0271 | 20.3 | 0.87345 | 1.0817 |
| 1 | 0 | 0.024 | 0.0244 | 0.78 | 0.87340 | 0.9760 |



death rate of tsetse flies eliminates the disease. This suggests that efforts should focus on controlling the vector population to achieve eradication of Rhodesian sleeping sickness.

### 4.3. *Fitness ratio and relative infectivity*

Smith? and Blower (2004) define the relationship between $R_U$ and $R_V$ as the fitness ratio $f = \frac{R_V}{R_U}$. When the total number of secondary infections caused by an individual in a vaccinated population is less than the number of secondary infections caused by an individual in an unvaccinated population—that is, when $R_V < R_U$—we have $f < 1$. For $R_V$ to be smaller than $R_U$, we need $\nu_v > \nu$; that is, the recovery rate for vaccinated individuals is higher than for those unvaccinated. In the particular case where $R_V = R_U$—or, equivalently, $f = 1$—the relative infectivity of an individual is given by

$$\frac{\beta_v}{\beta} = \frac{\mu + \gamma_v + \nu_v + \xi}{(1-\psi)(\xi + (1-\psi)(\mu + \gamma + \nu))}. \tag{23}$$

An efficient vaccine needs to lower the infectivity of the infected individual (that is, $\beta_v < \beta$).

The surface in Figure 3 corresponds to $f = 1$, varying with the vaccine efficacy $\psi$, the infection transmission rate for vaccinated individuals $\beta_v$, and the sum of the recovery rate and the disease-induced death rate for vaccinated individuals $\gamma_v + \nu_v$. The region below the surface corresponds to the case where $f > 1$ (that is, $R_V > R_U$), which means the vaccine increases the prevalence of the disease, increasing the transmission and the number of secondary infections. Eradication is impossible in this case. The region above the surface corresponds to the case where $f < 1$ and $R_V < R_U$. If the

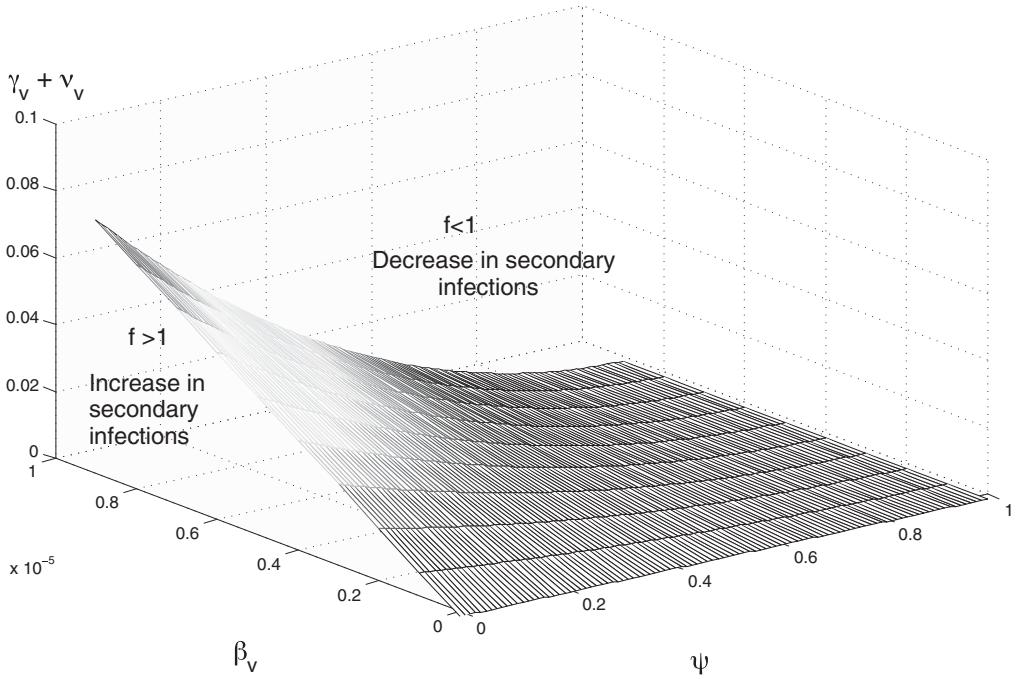


**Figure 3.** The surface corresponding to the fitness ratio value of 1 ($f = 1$) as a function of the vaccine efficacy $\psi$, the infection transmission rate of vaccinated individuals $\beta_v$, and the sum of the recovery rate and the disease-induced death rate for vaccinated individuals $\gamma_v + \nu_v$. The region below the surface corresponds to the case where $f > 1$, resulting in an increase in secondary infections for parameters in this region. The region above the surface corresponds to the case where $f < 1$, resulting in a decrease in secondary infections for parameters in this region. If the vaccine has low efficacy and high transmission, then the disease will persist unless the death rates are sufficiently high.

characteristics of the vaccine correspond to parameter values in this region, the vaccine will reduce secondary infections.

The parameter values used for the numerical analysis are chosen according to the criteria of the region above the surface $f = 1$, so that the vaccine reduces infections in the vaccinated population. Values of $f$ for different situations considered in our analysis are given in Table 2. Of the two parameters we vary in our simulations, $f$ only depends on the waning rate $\xi$ of the vaccine. The values of $f$ for the two different tested values of $\xi$ are very close (both practically equal to 0.8734), because the variation in the $R_v$ values with respect to $\xi$ is of an order of $10^{-5}$.

### 4.4. *Time series*

We use MATLAB to show the effect of the theoretical vaccine on a Rhodesian sleeping sickness outbreak in an African village. For the sake of comparison, we represent the time series of the model in the absence of vaccination first. Figure 4 represents the situation of the village in the

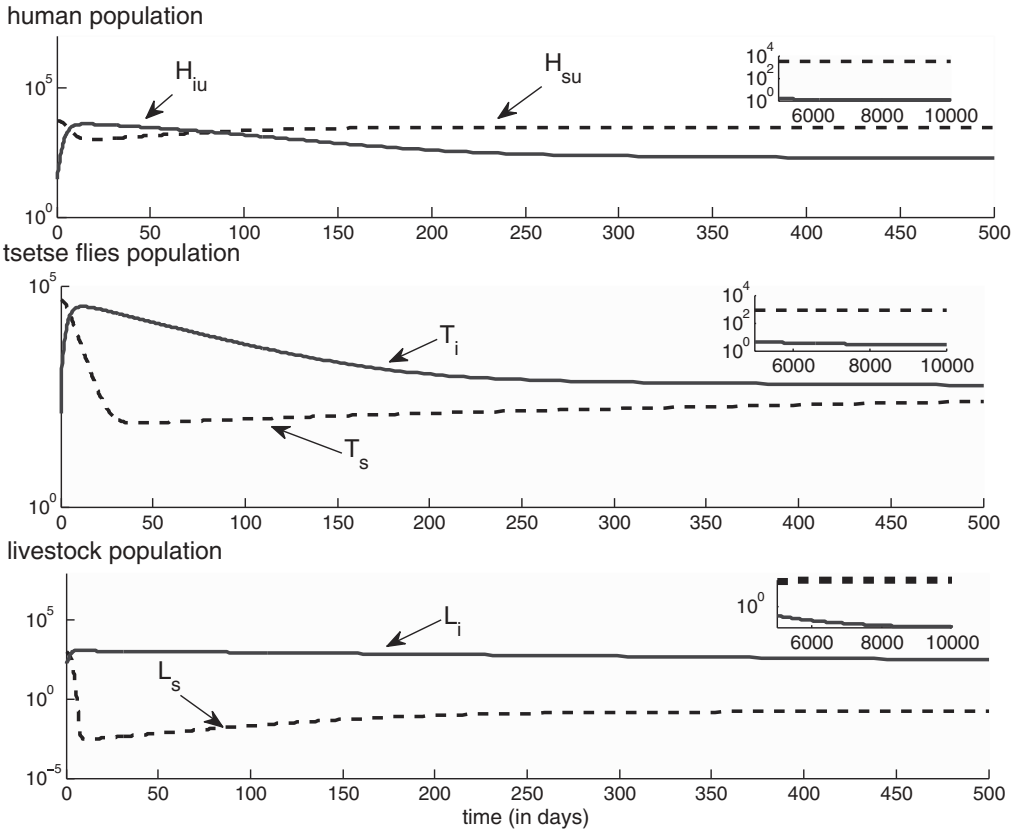


**Figure 4.** Time series of the model in the absence of vaccination.

absence of vaccination ($p = 0$). Starting with 30 infected people, 130 infected flies, and 180 infected livestock, the disease spreads quickly among the population, and infects more than half the village in the first month; however, recovery and the decrease in the fly population cause the human population to rebound. In the long run (up to 27 more years), the population reaches an endemic steady state, where infected and susceptible people coexist. Infections are still present among the tsetse flies, maintaining the disease in a stable situation. The total numbers of infected people and flies remaining in the population are very small. Only the infected livestock population keeps decreasing, and becomes free of infections.

Figure 5 shows the situation when 30% of the village inhabitants are vaccinated with a vaccine that wanes after two years. The uninfected vaccinated population is not affected by the disease; it maintains its size until the vaccine starts to wane after two years. However, once the vaccine wanes, this population decreases, and individuals losing their immunity become unvaccinated, which increases the unvaccinated human population. This situation of partial vaccination is practically similar to the previous one: the disease is still present among the human and the tsetse fly

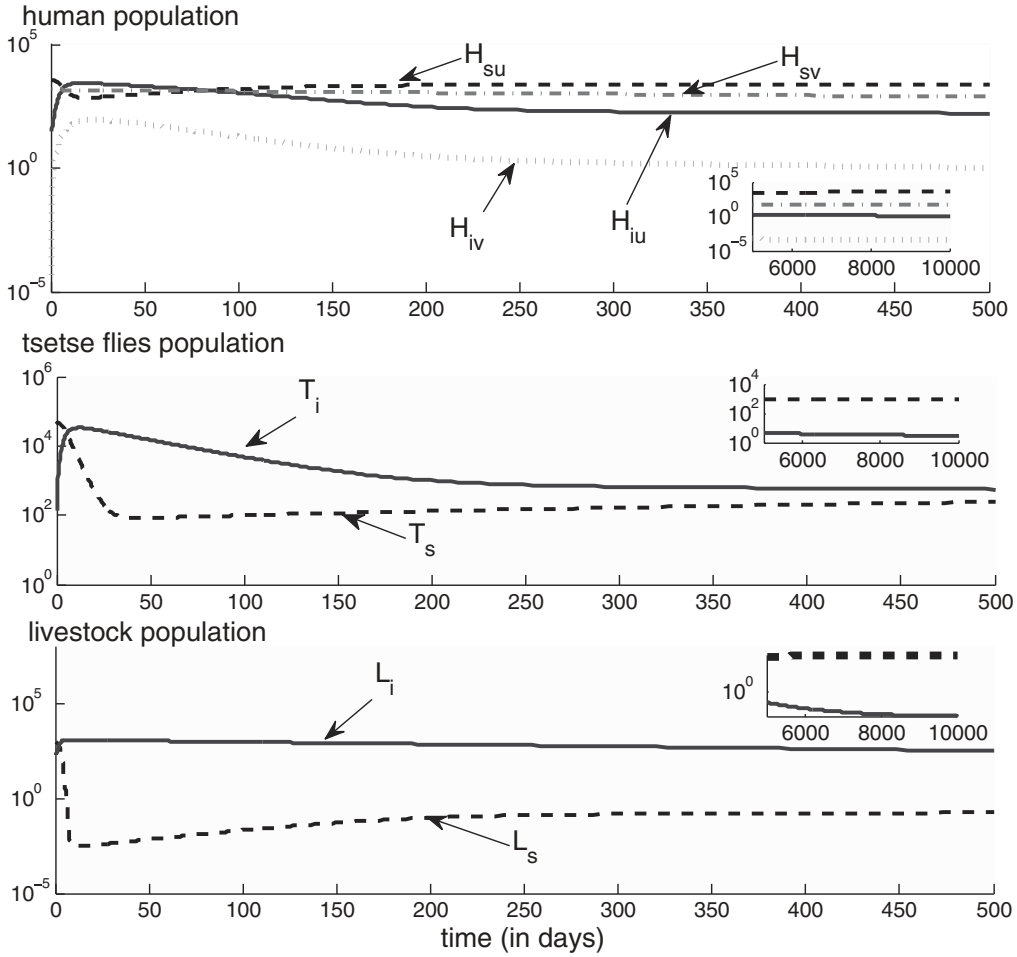


**Figure 5.** Time series of the model with vaccination: 30% of the population is vaccinated, with a vaccine that wanes in 2 years.



populations, but not within the livestock population. Vaccination in this case only protects vaccinated individuals against infection, but has no effect on the long-term results.

Figure 6 represents the ideal situation of a vaccination program, where the entire human population is vaccinated ($p = 1$) and the vaccine provides lifetime immunity ($\xi = 0$). In this case, the outbreak and infections are significantly reduced. Susceptible vaccinated humans maintain their immunity permanently, and the only loss in this class is either through natural background death, or through infection (because the vaccine does not prevent infection), which increases the infected vaccinated population size. Then recovery brings the susceptible population back to its initial number after the outbreak. The outbreak has practically no effect on the total human population; it is "absorbed" by the vaccination. All three population classes (humans, tsetse flies, and livestock) end up

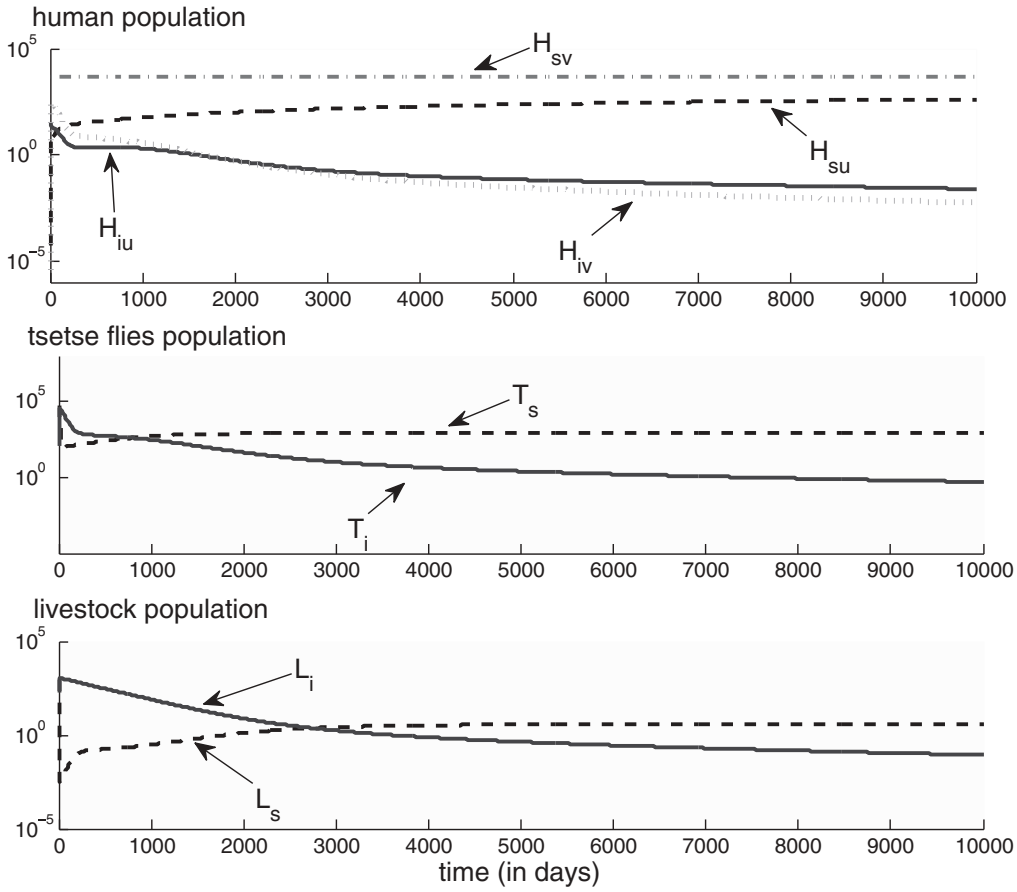


**Figure 6.** Time series of the model with the entire population being vaccinated ($p = 1$) with a vaccine that provides lifelong immunity $(\xi = 0)$. The disease is not eradicated and infection remains in the population.

with a disease-free situation in the long term, with infections below 1 for each class. This is the only situation we came across in which eradication is possible through the depletion of the infected classes in every population. A vaccine that ensures lifetime immunity and a population completely vaccinated theoretically leads to eradication of Rhodesian trypanosomiasis.

These time series, supported by our numerical results given in Table 2, indicate that the proportion of people vaccinated and the duration of immunity that the vaccine provides are two equally important conditions that lead to eradication. Full vaccination coverage of the population, alone, does not result in eradication, nor does a vaccine that never wanes but has less than perfect coverage. For instance, if the total population is vaccinated and the vaccine wanes after two years, the outbreak is very small, leaving some infections in the population and leading to an endemic situation (time series not shown; numerical results are presented in Table 2). We need both conditions to be satisfied simultaneously.

With the parameters used in the model, the minimum vaccinating coverage level required for a vaccine that wanes after two years is $p_c = 20.3 > 1$, while the minimum vaccinating coverage level for a vaccine that provides lifetime immunity is $p_c = 0.78 < 1$. The former value is larger than 1, indicating that it will be impossible to eradicate the disease with human vaccination alone if the vaccine loses its protection capabilities. In this vaccine-waning case, $R_V$ is smaller than $R_U$, but $R_p$ is still larger than 1 (Table 2), indicating that whenever there is an outbreak of Rhodesian trypanosomiasis the disease still spreads among the population. On the other hand, when the waning rate is zero, the value of $p_c$ is smaller than one, which means that vaccinating at least 78% of the human population should result in eradication. However, this minimal proportion alone will not provide eradication; rather, it should be combined with the condition that $R_p < 1$. This is possible when the entire population is successfully vaccinated with a vaccine that induces lifetime immunity (or situations very close to this). A vaccination program that aims to eradicate Rhodesian trypanosomiasis should satisfy these conditions. Otherwise, the disease remains endemic.

However, in practice, a nonwaning vaccine is unlikely to be developed for sleeping sickness. The development of such vaccines is limited by the lack of funding resources available to support this research by the international community and the concerned countries (Hotez, 2011). Furthermore, even if such a vaccine were developed, reaching more than 78% of the target population is not feasible. We should then use alternative efficient methods.

### 4.5. *Sensitivity analysis*

Because vaccination alone cannot lead to disease eradication, we performed a sensitivity analysis to determine which parameters can reduce infections and help eradicate the disease.

Latin Hypercube Sampling and partial rank correlation coefficients are used to explore the sensitivity of the reproductive numbers $R_U$, $R_V$, and $R_P$ to parameter variations. LHS is a statistical sampling method that allows for an efficient analysis of parameter variations across simultaneous uncertainty ranges in each parameter (Blower and Dowlatabadi, 1994; Smith? et al., 2012). We used 1,000 simulations per run. Figures 7, 8, and 9 show the degree of sensitivity of $R_U$, $R_V$, and $R_P$ to each parameter, using ranges in Table 1.

The sign of the partial rank correlation coefficient corresponding to every parameter reflects the correlation between this parameter and $R_U$, $R_V$, or $R_P$. Parameters with strictly positive partial rank correlation coefficients increase $R_U$, $R_V$, and $R_P$ when they are increased, while parameters with strictly

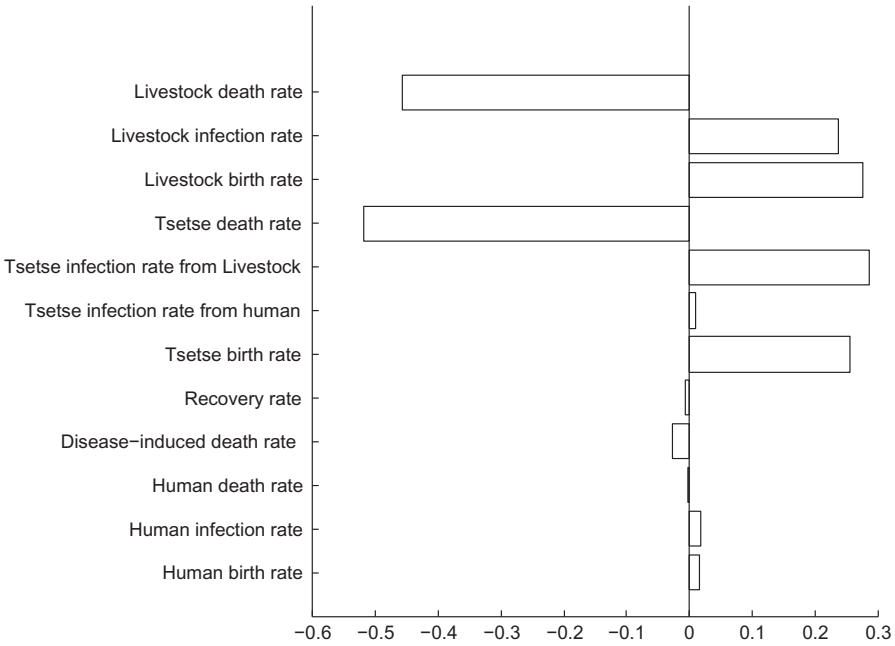


**Figure 7.** Partial rank correlation coefficients for the parameters that affect $R_U$.

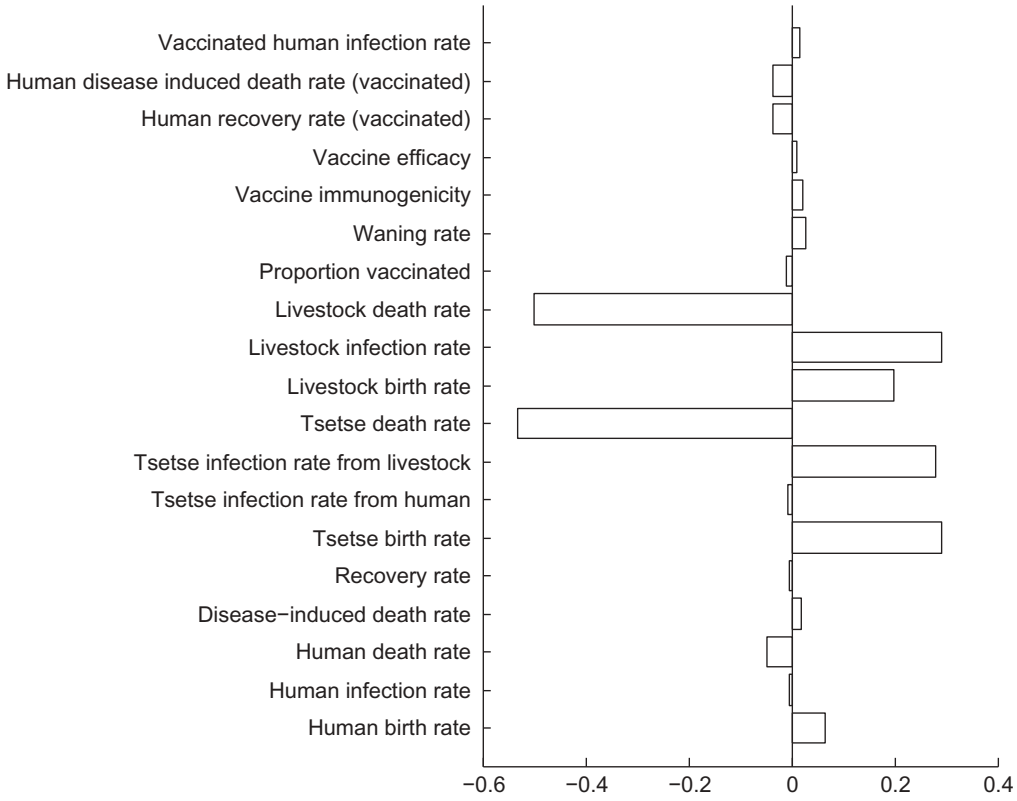


**Figure 8.** Partial rank correlation coefficients for the parameters that affect $R_V$.

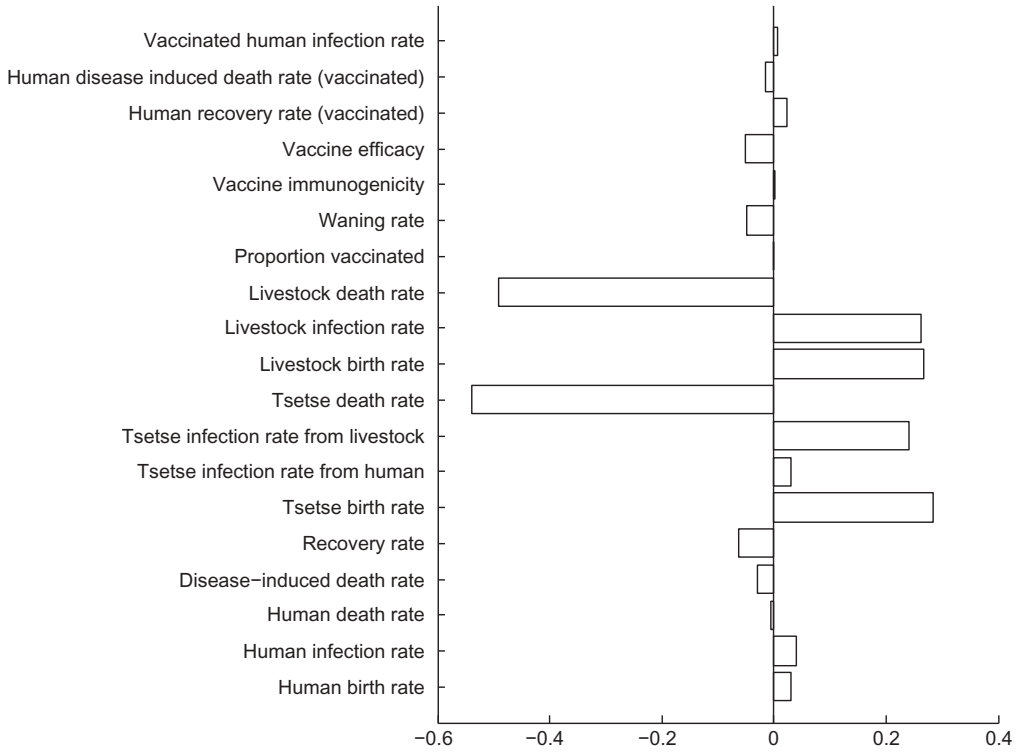


**Figure 9.** Partial rank correlation coefficients for the parameters that affect $R_p$.

negative partial rank correlation coefficients decrease $R_U$, $R_V$, and $R_P$ when they are increased. Six parameters have the most significant effect on $R_U$, $R_V$, and $R_P$: the tsetse flies' birth rate $\pi_T$, the tsetse death rate $\omega$, the tsetse infection rate from livestock $\zeta$, the livestock birth rate $\pi_L$, the livestock death rate $\theta$, and the livestock infection rate from tsetse flies $\delta$.

Figures 10, 11, and 12 show the effect of the parameters that most affect the three reproduction numbers $R_U$, $R_V$, and $R_P$ as all parameters are varied simultaneously. The semi-log plots of $R_U$, $R_V$, and $R_P$ against the model parameters show that all of these reproduction numbers are highly dependent on variations in these six parameters, all of which are unrelated to vaccination. However, they can all lead to eradication, by reducing the reproduction numbers below 1. For instance, decreasing the birth rates and increasing the death rates of both tsetse flies and livestock can help achieve eradication.

Each of these parameters can be controlled in a different manner and can have different ecological, biological, and epidemiological effects. The control of the tsetse flies' birth rate can be achieved through larvacide or genetical control of the species (Leak, 1999). The livestock birth rate might be controlled through sterilization. While controlling the birth rates can be complicated (Welburn et al., 2006), the death rates may be more easily handled. However, controlling the livestock birth or death rates may not be practical, given the lifestyle of populations in sub-Saharan Africa. The infection transmission rates can be

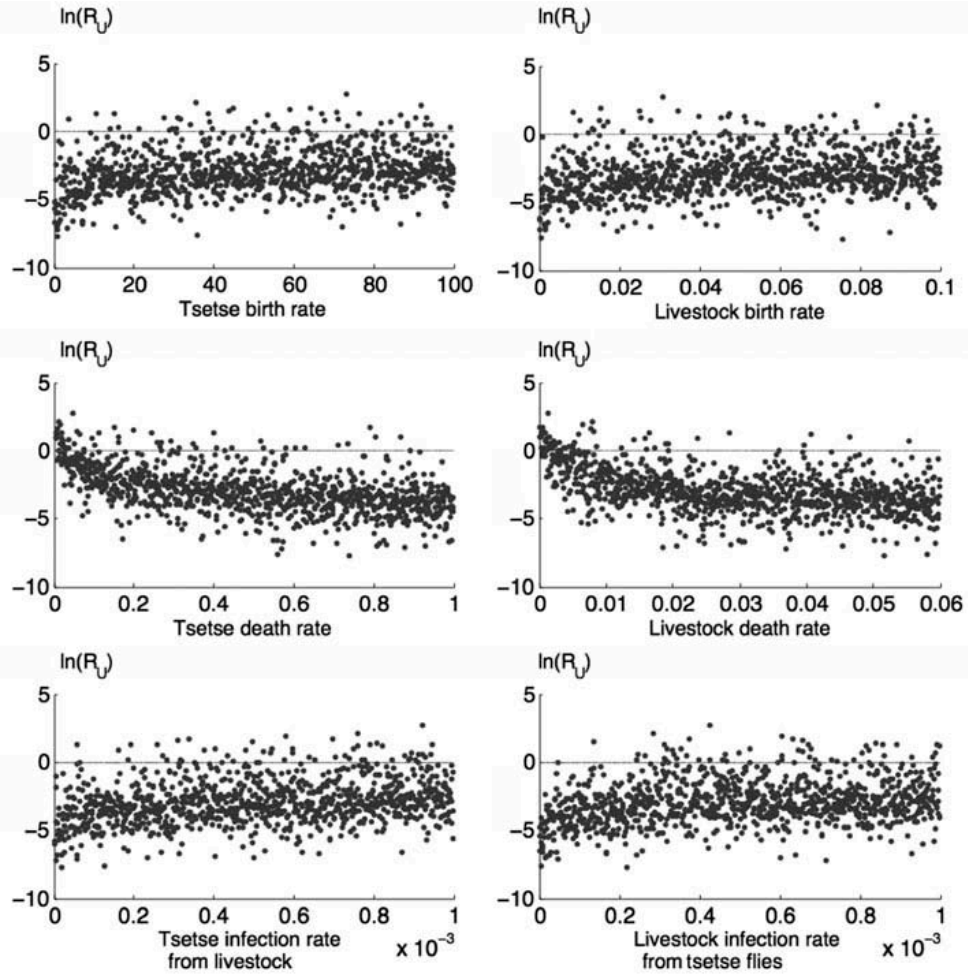


**Figure 10.** Monte Carlo simulations for $R_U$, the basic reproduction number in the absence of vaccination.



controlled by applying insecticides to livestock (Thomson and Wilson, 1992; Kotlyar, 2010) and by designing and developing vaccines specific to livestock to reduce their infectivity (Welburn et al., 2008; Hotez, 2011).

We show that focusing on the control of tsetse flies is of particular interest and induces a tremendous effect in reducing Rhodesian sleeping sickness infections. Although the effects of the death rates of both livestock and tsetse populations are similar, the tsetse death rate is likely to be the more controllable parameter.

## 5. Conclusion

We have explored the effect of a theoretical vaccine on the Rhodesian human African trypanosomiasis in a sub-Saharan African village that can be representative of a wider African area. We have shown that human

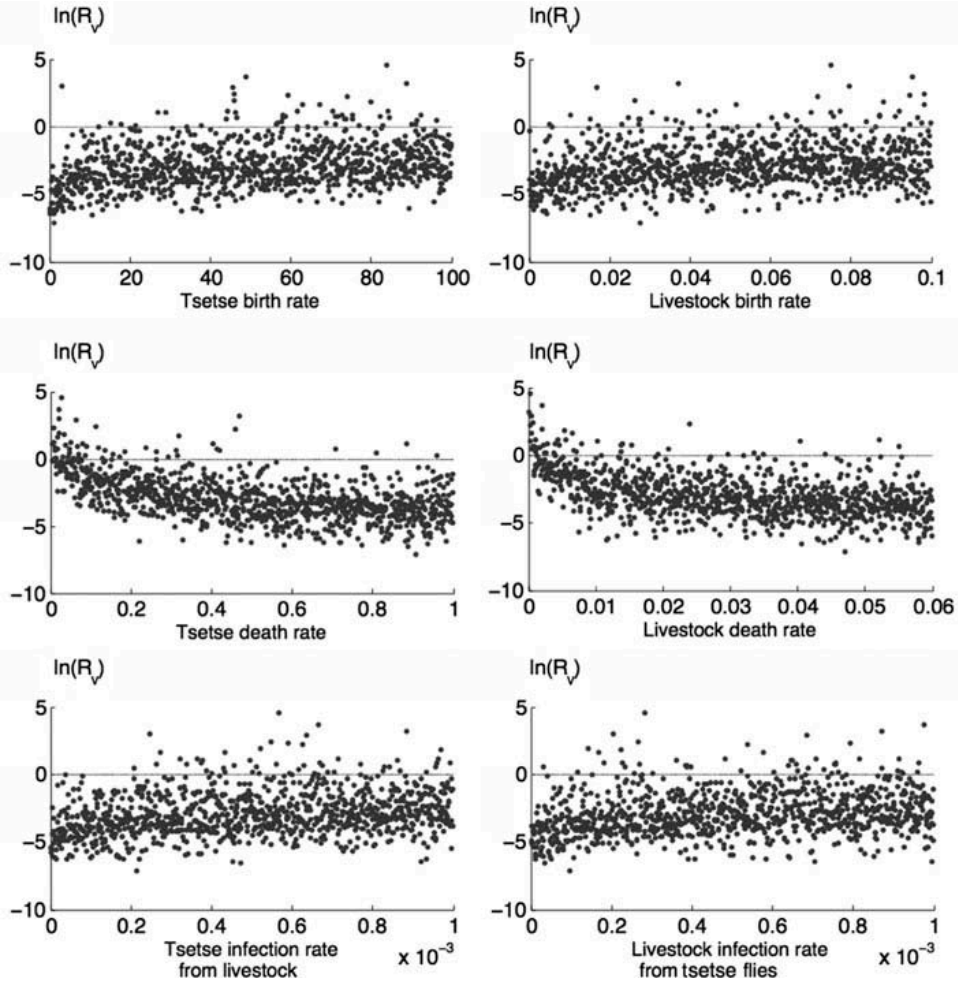


**Figure 11.** Monte Carlo simulations for $R_V$, the basic reproduction number when the entire population is vaccinated.

vaccination helps reduce infection, but can completely eradicate the disease only in the unlikely case that more than 78% of the population is successfully vaccinated with a vaccine whose efficacy does not wane after injection.

Furthermore, screening is inappropriate in the case of Rhodesian sleeping sickness, given its quick proliferation in host and its fatality. Efficient prevention methods of African trypanosomiasis are not available yet. Personal measures to reduce exposure to tsetse flies include wearing protective clothes, using screens or bed nets while sleeping, and checking the inside of the car for tsetse flies before getting in it. Testing and diagnosis facilitate early medical interventions. Improving treatment methods would be of great benefit for patients. Technical expertise for testing and treating patients, which is not available at peripheral health facilities, is also necessary.

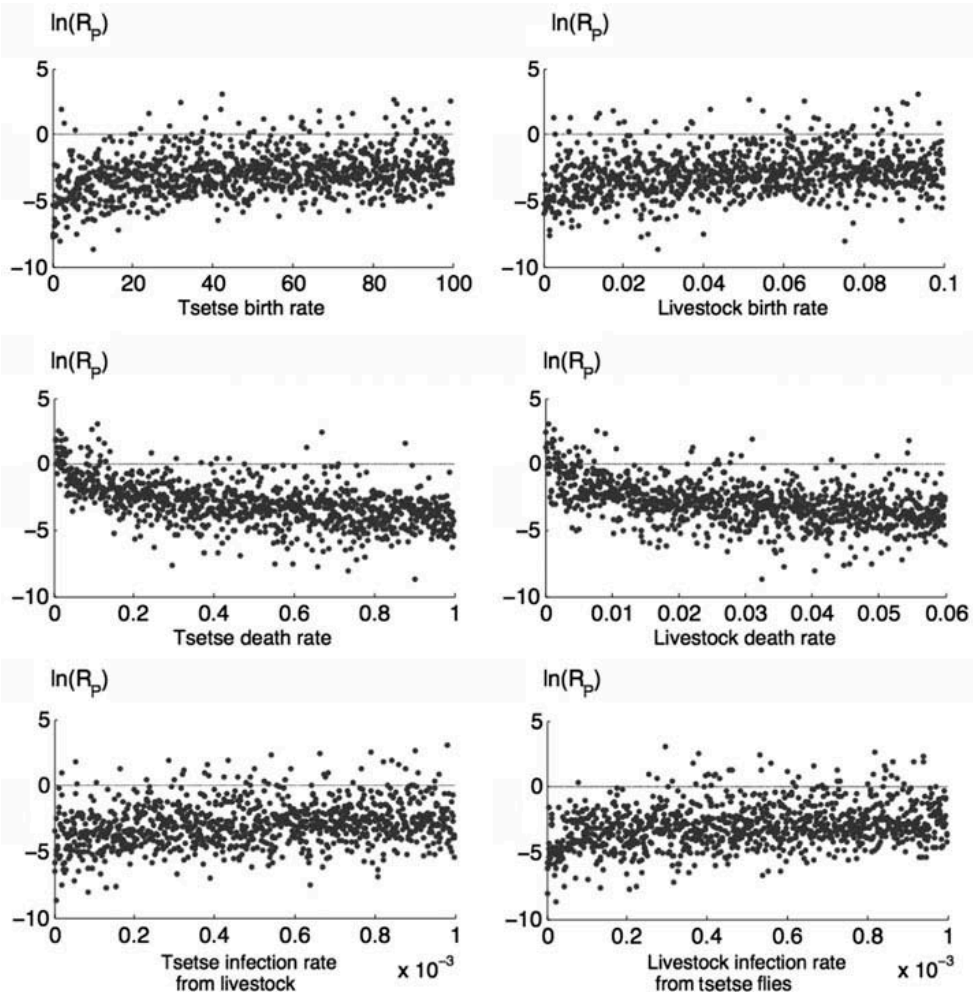


**Figure 12.** Monte Carlo simulations for $R_p$, the population reproduction number when a mixture of vaccinated and unvaccinated individuals are present.

Other aspects of controlling sleeping sickness comprise vector and livestock control. Controlling tsetse populations could be the simplest way of dealing with sleeping sickness. Control methods include targets and traps, chemical control, and sterile insect techniques (Leak, 1999). Artzrouni and Gouteux (1996b) explored control strategies for sleeping sickness using a model of Gambian sleeping sickness. They compared vector control and detection of infected individuals, and concluded that each of these two methods is efficient in different endemic and epidemic situations. Gouteux et al. (1997) and Chalvet-Monfray et al. (1998), based on the same model of Gambian sleeping sickness as in Artzrouni and Gouteux (1996a), demonstrate the importance of vector control in the plantations and in areas where large numbers of flies can be captured. We can expect that the previous results on vector control strategies would be similar in the case of Rhodesian sleeping sickness. More efficient is the simultaneous

control of vector and animal reservoirs to decrease the prevalence of Rhodesian trypanosomiasis (Abenga and Lawal, 2005; Welburn et al., 2006; Kotlyar, 2010).

Despite the attractiveness of developing a vaccine for humans, the control of tsetse flies and livestock can be more efficient than vaccination. Efforts should be increased to develop new control methods of vector and animal reservoir populations. These methods should also be environmentally friendly, to reduce the side effects of chemical control methods. Eradicating African trypanosomiasis is an ecological and economic issue as much as it is a medical one.

## Funding

Robert J. Smith? is supported by an NSERC Discovery Grant, an Early Researcher Award from the Ontario Ministry of Research and Innovation, and funding from MITACS.



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## Appendix

At the endemic equilibrium, $\tilde{T}_i$ satisfies the cubic equation

$$A\tilde{T}_i^3 + B\tilde{T}_i^2 + C\tilde{T}_i + D = 0, \tag{24}$$

where

$$A = (1-\psi)\beta\beta_v\omega\delta\alpha\mu\big(\theta\pi_H\big(\epsilon p\gamma_v - \gamma_v - \xi\big) - \epsilon p\theta\gamma(1-\psi) - (\omega\theta\gamma + \pi_L\gamma)\big(\mu + \gamma_v + \xi\big)\big) \tag{25}$$

$$B = \beta\pi_H\alpha^2\theta\big((\delta\pi_T - \omega\theta)\big(\mu + \gamma_v + \xi\big)(1-\psi)\beta_v - \omega\delta(\mu+\xi)\big(\mu + \gamma_v + \nu_v + \xi\big)\big) + \epsilon p\pi_H\alpha^2\theta\big(\beta\omega\delta\mu\big(\mu + \gamma_v + \nu_v + \xi\big) + \beta\beta_v(\delta\pi_T - \omega\theta)(1-\psi)\big((\mu+\gamma)(1-\psi) - \mu - \gamma_v\big)\big) - \omega^2\alpha\theta\big(\beta\delta(\mu+\gamma)(\mu+\xi)\big(\mu + \gamma_v + \nu_v + \xi\big) + \beta_v\big(\mu + \gamma_v + \xi\big)(1-\psi)(\beta\theta(\mu+\gamma) + \mu\delta(\mu+\gamma+\nu))) + \zeta\delta\pi_L\alpha\big(\beta_v\big(\mu + \gamma_v + \xi\big)((\mu+\gamma)(1-\psi)\beta\pi_T - \mu\omega(\mu+\gamma+\nu)) - \beta\omega(\mu+\gamma)(\mu+\xi)\big(\mu + \gamma_v + \nu_v + \xi\big)\big) \tag{26}$$

$$C = \beta\pi_H\alpha^2\theta\big((\delta\pi_T - \omega\theta)(\mu+\xi)\big(\mu + \gamma_v + \nu_v + \xi\big) + \theta\pi_T\beta_v\big(\mu + \gamma_v + \xi\big)(1-\psi)\big) + \epsilon p\pi_H\alpha^2\theta\big(-\beta\mu(\delta\pi_T - \omega\theta)\big(\mu + \gamma_v + \nu_v + \xi\big) + \beta\beta_v\theta(1-\psi)\big((\mu+\gamma)(1-\psi) - \mu - \gamma_v\big) + \beta_v\mu(1-\psi)(\delta\pi_T - \omega\theta)((\mu+\gamma+\nu)(1-\psi) + \xi)\big) - \omega^2\alpha\theta\big(\beta_v\theta\mu(\mu+\gamma+\nu)\big(\mu + \gamma_v + \xi\big)(1-\psi) + (\mu+\xi)\big(\mu + \gamma_v + \nu_v + \xi\big)(\beta(\mu+\gamma) + \mu\delta(\mu+\gamma+\nu))\big) + \zeta\delta\pi_L\alpha\big((\mu+\xi)\big(\mu + \gamma_v + \nu_v + \xi\big)((\mu+\gamma)\beta\pi_T - (\mu+\gamma+\nu)\mu\omega) + (\mu+\gamma+\nu)\big(\mu + \gamma_v + \xi\big)(1-\psi)\mu\beta_v\pi_T\big) \tag{27}$$

$$D = \beta\pi_H\alpha^2\theta^2\pi_T\big(\mu + \gamma_v + \nu_v + \xi\big)(\mu + \xi - \epsilon p\mu) + \epsilon p\pi_H\beta_v\mu\alpha^2\theta^2\pi_T((\mu+\gamma+\nu)(1-\psi) + \xi) + (\mu+\gamma+\nu)(\mu+\xi)\big(\mu + \gamma_v + \nu_v + \xi\big)\mu\alpha\big(\zeta\delta\pi_L\pi_T - \omega^2\theta^2\big). \tag{28}$$

We cannot solve Eq. (24) analytically. However, numerical simulations showed that the existence of both a unique real positive solution of Eq. (24) ($\tilde{T}_i > 0$) and the endemic equilibrium overall ($\tilde{H}_{iu}$, $\tilde{H}_{iv} > 0$) depends on the chosen value of $\omega$, the death rate of tsetse flies. The range of possible $\omega$ values that satisfy this condition is (0.024, 0.027) (Table 2). We chose the value of $\omega$ to be 0.025 in Eq. (1) and (8), which corresponds to a tsetse lifetime of 40 days. Introducing partial vaccination to the population does not affect the existence of the endemic situation, so infections will still be present. We found the same result if 100% of the population is vaccinated with a vaccine that wanes over time. However, in the particular ideal situation when the total population is vaccinated with a vaccine whose efficacy never wanes after injection, eradication is possible. The endemic equilibrium collapses to zero, and a disease-free situation is recovered.