Bull Math Biol
DOI 10.1007/s11538-014-9938-6

Society for Mathematical Biology

ORIGINAL ARTICLE

Modelling the Use of Insecticide-Treated Cattle to Control Tsetse and *Trypanosoma brucei rhodesiense* in a Multi-host Population

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Received: 5 August 2013 / Accepted: 30 January 2014

Abstract We present a mathematical model for the transmission of *Trypanosoma brucei rhodesiense* by tsetse vectors to a multi-host population. To control tsetse and *T. b. rhodesiense*, a proportion, ψ, of cattle (one of the hosts considered in the model) is taken to be kept on treatment with insecticides. Analytical expressions are obtained for the basic reproduction number, R_{0n} in the absence, and R_{0n}^T in the presence of insecticide-treated cattle (ITC). Stability analysis of the disease-free equilibrium was carried out for the case when there is one vertebrate host untreated with insecticide. By considering three vertebrate hosts (cattle, humans and wildlife) the sensitivity analysis was carried out on the basic reproduction number (R_{03}^T) in the absence and presence of ITC. The results show that R_{03}^T is more sensitive to changes in the tsetse mortality. The model is then used to study the control of tsetse and *T. b. rhodesiense* in humans through application insecticides to cattle either over the whole-body or to restricted areas of the body known to be favoured tsetse feeding sites. Numerical results show that while both ITC strategies result in decreases in tsetse density and in the incidence of *T. b. rhodesiense* in humans, the restricted application technique results

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Published online: 01 March 2014

in improved cost-effectiveness, providing a cheap, safe, environmentally friendly and farmer based strategy for the control of vectors and *T. b. rhodesiense* in humans.

Keywords Trypanosomiasis · Tsetse · Vector control · Insecticide-treated cattle · ITC

1 Introduction

African human trypanosomiasis or sleeping sickness is caused by the parasite *Trypanosoma brucei* and transmitted by tsetse flies (genus *Glossina* spp.). The acute form of trypanosomiasis is caused by *T. b. rhodesiense* and is restricted to East and Southern Africa. *T. b. gambiense* is a chronic disease form of the disease found in West Africa (Zoller et al. 2008). Human African trypanosomiasis is almost always fatal if left untreated (Coleman and Welburn 2004; Davis et al. 2011), and during the clinical disease, patients suffer a variety of debilitating symptoms and sequelae (Fèvre et al. 2008). Trypanosomes are multi-host parasites capable of infecting a wide range of domestic and wildlife species, which constitute a reservoir for human infections. In domesticated animals clinical cases have been detected in cattle, water buffalo, sheep, goats, camels, horses, donkeys, alpacas, llamas, pigs, dogs, cats and other species. In wild animals clinical cases have been detected in bushbuck, duiker, giraffe, impala, lion, warthog, waterbuck, zebra and other species (Anderson et al. 2011; Waiswa et al. 2006; Welburn et al. 2006). In most parts of Africa, cattle are the main species affected, tsetse preferring to feed on them rather than smaller domesticated animals such as goats and pigs (The Center for Food Security and health 2009).

1.1 Control of Tsetse and Trypanosomiasis

Trypanosomiasis control is based on case finding and treatment, coupled with tsetse control (Magona and Walubengo 2011). Treatment of livestock in sub-Saharan Africa with trypanocidal drugs has been hindered by drug resistance (Bourn et al. 2005; Hargrove et al. 2000) and proves expensive for many farmers. Treatment of human sleeping sickness is also expensive, normally ranging from US $150 to US $800 per patient, depending on the stage of the infection. Due to the toxicity of the drugs used for treating *T. b. rhodesiense*, about 5 % of the patients die from the treatment (WHO 2011). The disease is accordingly controlled by attacking the tsetse vectors (Rowlands et al. 2000). Tsetse control methods include aerial and ground spraying, sterile insect technique, and bait technology, including the use of insecticide-treated cattle (ITC). Bait technology methods cause little damage to the environment and are very effective if applied properly in appropriate circumstances (Hargrove et al. 2000; Vale and Torr 2005).

There has been an increasing emphasis in sub-Saharan Africa on getting farmers to control tsetse and animal trypanosomiasis themselves, instead of relying on governments or donor organisations. The only feasible techniques that can be taken up by farmers as self-help schemes are bait methods, and the most cost-effective of these is the use of ITC in tsetse infested areas where cattle provide a substantial proportion

of tsetse blood-meals. The original protocol for these applications involved the treatment of all the cattle in an area with insecticide applied at intervals of about a month, using the standard "whole-body" dose as recommended for tick control. To be effective, the technique should be applied over an area of at least several hundred square kilometers, necessitating participation by all livestock keepers over relatively large areas. However, this technique is still too costly for ready adoption by poor farmers, especially since they usually have to use expensive pour-on insecticides.

1.2 Tsetse Feeding Preference and ITC

Since its inception, the ITC approach has been refined through the demonstration that it is not necessary to treat every animal in a herd since tsetse feed preferentially on larger animals in a herd. Tsetse find it hard feeding on young cattle due to their higher defensive movements. Moreover, field observations show that tsetse feed preferentially on the legs and belly of these larger, generally older, cattle (Torr et al. 2001). By restricting the application of insecticides to these locations, and to the ears where ticks accumulate, the amount of insecticides required for tsetse and trypanosomiasis can be reduced, and simultaneously provide tick control. This restricted application approach thereby provides financial benefits to the farmers, plays to the farmers' overriding concern with tick control, and helps to allay concerns about the environmental impact of insecticide use (Bourn et al. 2005; Torr et al. 2007; Vale and Torr 2005).

1.3 Studies on ITC

ITC has been used to control tsetse and trypanosomiasis in various sub-Saharan African countries including Zambia (Chizyuka and Liguru 1986), Zimbabwe (Thomson et al. 1991; Torr et al. 2007), Tanzania (Fox et al. 1993; Hargrove et al. 2000), Ethiopia (Bekele et al. 2010; Rowlands et al. 2000), Burkina Faso (Bauer et al. 1992, 1999) and Uganda (Magona and Walubengo 2011; Okello-Onen et al. 1994). Degrees of success differ between control programme, being affected by the size and shape of the control areas, and the number and density of treated cattle (Hargrove et al. 2003). If the area treated is small and is surrounded by a tsetse-infested area, invasion from the untreated area can re-infest much or all of the controlled region (Torr and Vale 2011).

In this paper, we use a mathematical model to study the control of tsetse and *T. b. rhodesiense* infection in humans, using ITC. Two techniques of application of insecticides on cattle, that is, whole-body (WB) and restricted application (RAP) of insecticides, are considered. Note that the proportion of cattle treated with insecticides is generated by the model, instead of being estimated by using a probability function as in a recent study (Hargrove et al. 2012).

2 Multi-host *T. b. rhodesiense* Transmission Model with Time Delay

We present a mathematical model that describes the transmission of *T. brucei* parasites by the tsetse vector species to a population of n different host species. Tsetse

flies feed at a rate a per day so that each fly takes a new blood meal on average every $\frac{1}{a}$ days. Tsetse vectors are assumed to feed from the n hosts at random, but with a fixed preference taking a proportion f_i of its blood meals from each host, where $\sum_i f_i = 1$ and $i = 1, 2, \ldots, n$. Thus, tsetse flies feed from each host at rates $a_i = af_i$ per day, with $a = \sum_i a_i$. Each host population is divided into three classes, susceptible (S_i), infectious (I_i) and recovered (R_i), whereas the tsetse population is divided into two classes, susceptible (S_V) and infectious (I_V). We define time delays T_i and T_V representing the incubation period in the host and tsetse vector populations, respectively.

We assume that vector infection can only occur when the teneral fly takes its first blood meal (Artzrouni and Gouteux 2001; Rogers 1988). We obtain the daily recruitment rate, Λ_V, for susceptible teneral tsetse, composed of flies that survive and have not taken their first feed in one unit of time (that is, between $t-1$ and t) from

$$\Lambda_V = B_V \int_{t-1}^{t} e^{-\int_s^t (a+m_V(p(\xi)))\,d\xi}\,ds = B_V \int_0^1 e^{-\int_{-u}^0 (a+m_V(p(t+x)))\,dx}\,du, \qquad (1)$$

where B_V is the constant birth rate for the tsetse population, a is the tsetse feeding rate, and $m_V(p(t+x))$ is the tsetse mortality, which depends on the proportion of cattle, $p(t+x)$, that is on ITC, and $u \in [0, 1]$. Recruitment of tsetse is said to occur when teneral flies survive to be added to the population which is susceptible to *T. b. rhodesiense* infection. The solution of Eq. (1) is given in the Appendix. Susceptible teneral flies get infected after biting an infectious host with a probability α_i and move to the infectious class, I_V. Tsetse flies are assumed to die at a background rate μ and at an additional rate due to the effects of ITC. An estimated proportion $e^{-m_V(p(t))T_V}$ of infected flies will thus survive the incubation period, T_V (Hargrove et al. 2012; Rogers 1988).

We assume a constant recruitment rate Λ_i for each vertebrate host that arises through birth and immigration. Following the bite of an infectious tsetse fly, the probability of a susceptible host becoming infected is β_i. Infectious vertebrate hosts are assumed to recover at a rate g_i due to treatment. Recovered hosts lose their immunity at a rate ν_i and become susceptible again. A schematic representation of the *T. b. rhodesiense* transmission model in a multi-host population is shown in Fig. 1. Table 1 shows the model parameters and their definitions.

2.1 Including Insecticide-Treated Cattle (ITC) in the Model

To include ITC in the model, we split the cattle population from the rest of the $(n-1)$ host populations as shown in Fig. 1. Cattle are assumed to be treated with insecticides at a rate ψ, thus moving to the treated classes, S_1^T, I_1^T and R_1^T. The insecticide effect is assumed to be maximum on the day of application, and it reduces with time, lasting on average for $\frac{1}{d}$ days. The value of $\frac{1}{d}$ will depend mainly on the type of insecticide formulation used, as well as the method of application. The insecticides applied to cattle are not repellents (Vale et al. 1999) and therefore, do not prevent tsetse from biting cattle. However, each fly that bites or touches an animal that is treated with insecticides is assumed to die within a few hours. We assume that cattle treated with

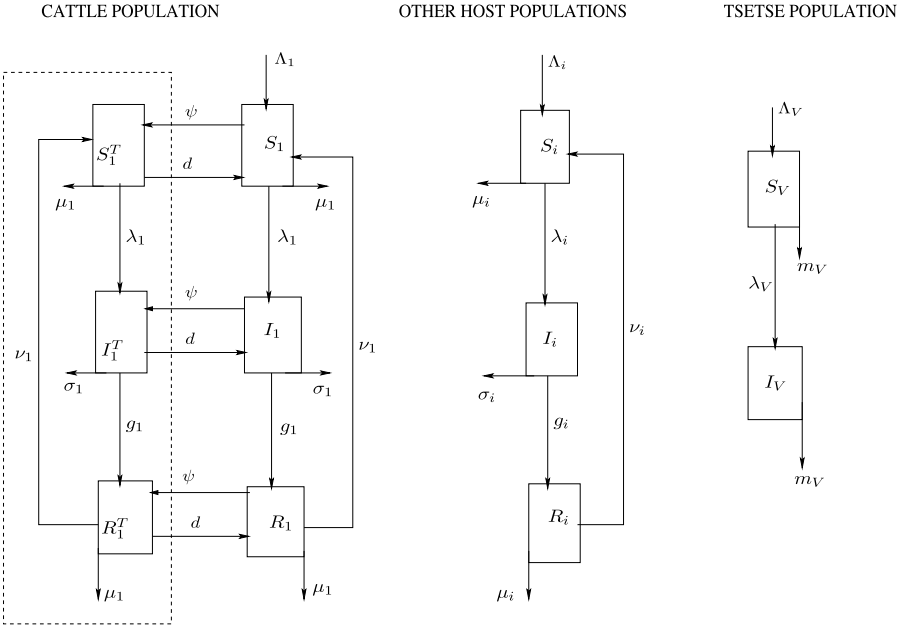

Fig. 1 Flow diagram of the compartmental model of *T. b. rhodesiense* in tsetse and a multi-host population that includes treatment of cattle with insecticides. The cattle population that is treated with insecticides is enclosed in a dotted rectangle. λ_i and λ_V are the forces of infection for the host and tsetse vector populations, respectively

Table 1 Definitions of the parameters used in the model

Parameter	Definition
Λ_i	Recruitment rate for host *i*
Λ_V	Recruitment rate for tsetse flies
μ_V	Tsetse natural mortality
m_V	Tsetse mortality in the presence of ITC
μ_i	Natural mortality for host *i*
a_i	Tsetse-host biting rate
β_i	Probability of infected fly bite producing an infection in host *i*
α_i	Probability of the first infected blood meal from host *i* giving rise to infection in tsetse flies
σ_i	Mortality rate of infected host *i*
g_i	Recovery rate of infected host *i*
ν_i	Rate of loss of immunity in recovered hosts *i*
T_V	Incubation period for tsetse flies
T_i	Incubation period for host *i*
ψ	Proportion of cattle treated with insecticides per day
d	Rate of loss of insecticidal killing effect

insecticide, when bitten by an infectious tsetse fly, get infected with the same probability β_1 as for untreated cattle. After infection, treated susceptible cattle progress to the infectious class, I_1^T, from which they can either die of the disease or recover at a rate g_1 due to treatment. The recovery and loss of immunity rates are taken to be the same for treated and untreated cattle. Each animal in the treated compartments S_1^T, I_1^T and R_1^T return to S_1, I_1 and R_1, respectively, at a rate d after the insecticides have lost their killing effect.

When tsetse flies alight on cattle treated with insecticides, their mortality will be increased by a factor

$$a_1 m \frac{(S_1^T + I_1^T + R_1^T)}{N_1},$$

which is a function of the tsetse-cattle biting rate, a_1, the proportion of cattle treated with insecticides, $\frac{(S_1^T+I_1^T+R_1^T)}{N_1}$, and the additional mortality m in tsetse due to the insecticides. The increased tsetse mortality is assumed to be due to direct insecticidal effect. Thus, the tsetse mortality in the presence of ITC is given by

$$m_V = \mu_V + a_1 m \frac{(S_1^T + I_1^T + R_1^T)}{N_1}, \tag{2}$$

where μ_V is the tsetse natural mortality rate. The value of m is assumed to depend on the area of the animal covered by the insecticides, either whole-body (WB) treatment or restricted application (RAP), the insecticide formulation, and the duration of insecticide efficacy. For the same formulation and duration of insecticide efficacy, m is higher for WB treatment than for RAP (Torr et al. 2007).

The equations for the model are given by

$$\begin{aligned}
\frac{d}{dt}S_1 &= \Lambda_1 + \nu_1 R_1 + d S_1^T - (\psi + \mu_1) S_1 - \lambda_1(t - T_1) S_1(t - T_1),\\
\frac{d}{dt}I_1 &= \lambda_1(t - T_1) S_1(t - T_1) + d I_1^T - (\psi + g_1 + \sigma_1) I_1,\\
\frac{d}{dt}R_1 &= g_1 I_1 + d R_1^T - (\psi + \mu_1 + \nu_1) R_1,\\
\frac{d}{dt}S_1^T &= \psi S_1 + \nu_1 R_1^T - (\mu_1 + d) S_1^T - \lambda_1(t - T_1) S_1^T(t - T_1),\\
\frac{d}{dt}I_1^T &= \psi I_1 + \lambda_1(t - T_1) S_1^T(t - T_1) - (d + g_1 + \sigma_1) I_1^T,\\
\frac{d}{dt}R_1^T &= \psi R_1 + g_1 I_1^T - (d + \mu_1 + \nu_1) R_1^T,\\
\frac{d}{dt}S_i &= \Lambda_i + \nu_i R_i - \mu_i S_i - \lambda_i(t - T_i) S_i(t - T_i),\\
\frac{d}{dt}I_i &= \lambda_i(t - T_i) S_i(t - T_i) - (g_i + \sigma_i) I_i,\\
\frac{d}{dt}R_i &= g_i I_i - (\mu_i + \nu_i) R_i,
\end{aligned} \tag{3}$$

$$\frac{d}{dt}S_V = \Lambda_V - e^{-m_V T_V}\lambda_V(t-T_V)S_V(t-T_V) - m_V S_V,$$
$$\frac{d}{dt}I_V = e^{-m_V T_V}\lambda_V(t-T_V)S_V(t-T_V) - m_V I_V,$$

where $\lambda_1(t) = \frac{a_1\beta_1 I_V(t)}{N_1(t)}$, $\lambda_i(t) = \frac{a_i\beta_i I_V(t)}{N_i(t)}$, $\lambda_V(t) = \alpha_1 a_1 \frac{(I_1(t)+I_1^T(t))}{N_1(t)} + \sum_i \frac{\alpha_i a_i I_i(t)}{N_i(t)}$ and $i = 2, 3, \ldots, n$. The total population sizes N_1 (for cattle hosts), N_i (for non-cattle hosts) and N_V (for tsetse vectors) can be determined by $S_1 + I_1 + R_1 + S_1^T + I_1^T + R_1^T = N_1$, $S_i + I_i + R_i = N_i$ and $S_V + I_V = N_V$, respectively. All variables and parameters in the model (3) are considered to be positive, and the model lies in the region

$$\Gamma^T = \left\{ \left(S_1, I_1, R_1, S_1^T, I_1^T, R_1^T, S_i, I_i, R_i, S_V, I_V\right) \in \mathbb{R}_+^{3n+8} : N_1 \le \frac{\Lambda_1}{\mu_1}, \right.$$
$$\left. N_i \le \frac{\Lambda_i}{\mu_i}, N_V \le \frac{\Lambda_V}{m_V} \right\},$$

where $i = 1, 2, 3, \ldots, n$.

3 Mathematical Analysis

Before carrying out the mathematical analysis of the whole model, it is enlightening to consider its sub-model. We are able to gain insights into the dynamics of the whole model by considering smaller models. We consider, firstly, the multi-host model in the absence of insecticide-treated cattle (ITC), by setting $S_1^T = I_1^T = R_1^T = 0$. Secondly, we consider the whole model. Qualitative analysis of some models is not tractable, and we resort to simulations to obtain insights into the dynamics of the model.

3.1 Analysis of the Multi-host Model in the Absence of ITC

In the absence of treatment of cattle with insecticides, the recruitment rate, Λ_V, reduces to

$$\Lambda_V = B_V \int_0^1 e^{-\int_{-u}^0 (a+\mu_V)\,dx}\,du = \frac{B_V}{(a+\mu_V)}\left(1 - e^{-(a+\mu_V)}\right).$$

Model (3) also reduces to

$$\frac{d}{dt}S_i = \Lambda_i + \nu_i R_i - \mu_i S_i - \lambda_i(t-T_i)S_i(t-T_i), \tag{4}$$
$$\frac{d}{dt}I_i = \lambda_i(t-T_i)S_i(t-T_i) - (g_i+\sigma_i)I_i, \tag{5}$$
$$\frac{d}{dt}R_i = g_i I_i - (\mu_i+\nu_i)R_i, \tag{6}$$
$$\frac{d}{dt}S_V = \Lambda_V - e^{-\mu_V T_V}\lambda_V(t-T_V)S_V(t-T_V) - \mu_V S_V, \tag{7}$$

$$\frac{d}{dt}I_V = e^{-\mu_V T_V}\lambda_V(t-T_V)S_V(t-T_V) - \mu_V I_V, \tag{8}$$

where $\lambda_i(t) = \frac{a_i\beta_i I_V(t)}{N_i(t)}$, $\lambda_V(t) = \sum_i \frac{\alpha_i a_i I_i(t)}{N_i(t)}$ and $i = 1, 2, \ldots, n$. The total population sizes N_i (for each host) and N_V can be determined by $S_i + I_i + R_i = N_i$ and $S_V + I_V = N_V$, respectively, or from the differential equations

$$\frac{d}{dt}N_i = \Lambda_i - \mu_i N_i - (\sigma_i - \mu_i)I_i, \tag{9}$$

$$\frac{d}{dt}N_V = \Lambda_V - \mu_V N_V, \tag{10}$$

that are derived by adding Eqs. (4)–(6) for each host population and (7)–(8) for the tsetse population. All variables and parameters in the model (4)–(8) are considered to be positive, and the model lies in the region

$$\Gamma = \left\{(S_i, I_i, R_i, S_V, I_V) \in \mathbb{R}_+^{3n+2} : N_i \le \frac{\Lambda_i}{\mu_i}, N_V \le \frac{\Lambda_V}{\mu_V}\right\}.$$

3.1.1 Basic Reproduction Number, R_{0n}

The expression of the basic reproduction is derived by using the next generation method developed in Van den Driessche and Watmough (2002). The model system (4)–(8) has a disease-free equilibrium given by

$$E_0 = \left(\frac{\Lambda_1}{\mu_1}, 0, 0, \ldots, \frac{\Lambda_n}{\mu_n}, 0, 0, \frac{\Lambda_V}{\mu_V}, 0\right).$$

Following Van den Driessche and Watmough (2002), we obtain the matrices F (for the new infections) and V (for the transition terms) as

$$F = \begin{pmatrix} 0 & 0 & \ldots & 0 & a_1\beta_1 \\ 0 & 0 & \ldots & 0 & a_2\beta_2 \\ \vdots & \vdots & \ldots & \vdots & \vdots \\ 0 & 0 & \ldots & 0 & a_n\beta_n \\ \frac{e^{-\mu_V T_V}\alpha_1 a_1 \mu_1 \Lambda_V}{\Lambda_1 \mu_V} & \frac{e^{-\mu_V T_V}\alpha_2 a_2 \mu_2 \Lambda_V}{\Lambda_2 \mu_V} & \ldots & \frac{e^{-\mu_V T_V}\alpha_n a_n \mu_n \Lambda_V}{B_n \mu_V} & 0 \end{pmatrix} \quad \text{and}$$

$$V = \begin{pmatrix} g_1 + \sigma_1 & 0 & \ldots & 0 & 0 \\ 0 & g_2 + \sigma_2 & \ldots & 0 & 0 \\ \vdots & \vdots & \ldots & \vdots & \vdots \\ 0 & 0 & \ldots & g_n + \sigma_n & 0 \\ 0 & 0 & \ldots & 0 & \mu_V \end{pmatrix},$$

respectively. To obtain the expression for R_{0n}, we need to find the eigenvalues of the matrix FV^{-1}. First, we observe that V is a diagonal matrix and its inverse is obtained

by replacing each element in the diagonal with its reciprocal. Thus,

$$V^{-1} = \begin{pmatrix} \frac{1}{g_1+\sigma_1} & 0 & \dots & 0 & 0 \\ 0 & \frac{1}{g_2+\sigma_2} & \dots & 0 & 0 \\ \vdots & \vdots & \dots & \vdots & \vdots \\ 0 & 0 & \dots & \frac{1}{g_n+\sigma_n} & 0 \\ 0 & 0 & \dots & 0 & \frac{1}{\mu_V} \end{pmatrix} \quad \text{and}$$

$$FV^{-1} = \begin{pmatrix} 0 & 0 & \dots & 0 & \frac{a_1\beta_1}{\mu_V} \\ 0 & 0 & \dots & 0 & \frac{a_2\beta_2}{\mu_V} \\ \vdots & \vdots & \dots & \vdots & \vdots \\ 0 & 0 & \dots & 0 & \frac{a_n\beta_n}{\mu_V} \\ \frac{e^{-\mu_V T_V}\alpha_1 a_1 \mu_1 \Lambda_V}{\Lambda_1 \mu_V (g_1+\sigma_1)} & \frac{e^{-\mu_V T_V}\alpha_2 a_2 \mu_2 \Lambda_V}{\Lambda_2 \mu_V (g_2+\sigma_2)} & \dots & \frac{e^{-\mu_V T_V}\alpha_n a_n \mu_n \Lambda_V}{B_n \mu_V (g_n+\sigma_n)} & 0 \end{pmatrix}.$$

It can be shown that the eigenvalues, λ, of the matrix FV^{-1} are given by the following characteristic equation:

$$(-\lambda)^{n-1}\left(\lambda^2 - \sum_{i=1}^{n} \frac{e^{-\mu_V T_V}\alpha_i a_i^2 \mu_i \beta_i \Lambda_V}{\Lambda_i \mu_V^2 (g_i+\sigma_i)}\right) = 0, \tag{11}$$

from which the basic reproduction number, R_{0n}, is obtained as the spectral radius of the next generation matrix, FV^{-1}, and is given by

$$R_{0n} = \sqrt{\sum_{i=1}^{n} \frac{e^{-\mu_V T_V}\alpha_i a_i^2 \mu_i \beta_i \Lambda_V}{\Lambda_i \mu_V^2 (g_i+\sigma_i)}}. \tag{12}$$

This is the net number of secondary infections arising from one infectious index case in an otherwise disease-free equilibrium (DFE). The square root arises due to the fact that two generations are required for an infected tsetse fly or host to reproduce itself (Van den Driessche and Watmough 2002). If R_{0n} is greater than 1, the disease-free equilibrium is unstable, and we are in the presence of an endemic equilibrium, where the disease can invade and persist. However, if R_{0n} is smaller than 1, then the disease-free equilibrium is stable, and the disease dies out.

3.1.2 Local Stability of the Disease-Free Equilibrium of the One-Host T. b. rhodesiense *Transmission Model in the Absence of ITC*

In this subsection, we study the local stability of the disease-free equilibrium of the one-host *T. b. rhodesiense* transmission model with time delay in the absence of insecticide-treated cattle. In a case where there is one host population, system (4)–(8)

reduces to

$$\begin{aligned}
\frac{d}{dt}S_1 &= \Lambda_1 + \nu_1 R_1 - \mu_1 S_1 - \lambda_1(t-T_1)S_1(t-T_1),\\
\frac{d}{dt}I_1 &= \lambda_1(t-T_1)S_1(t-T_1) - (g_1+\sigma_1)I_1,\\
\frac{d}{dt}R_1 &= g_1 I_1 - (\mu_1+\nu_1)R_1,\\
\frac{d}{dt}S_V &= \Lambda_V - e^{-\mu_V T_V}\lambda_V(t-T_V)S_V(t-T_V) - \mu_V S_V,\\
\frac{d}{dt}I_V &= e^{-\mu_V T_V}\lambda_V(t-T_V)S_V(t-T_V) - \mu_V I_V,
\end{aligned} \tag{13}$$

where $\lambda_1(t) = \frac{a_1\beta_1 I_V(t)}{N_1(t)}$ and $\lambda_V(t) = \frac{\alpha_1 a_1 I_1(t)}{N_1(t)}$ are the forces of infection for the host and tsetse populations, respectively. System (13) satisfy the initial conditions: $S_1(\theta) = S_1^0, I_1(\theta) = I_1^0, R_1(\theta) = R_1^0, S_V(\theta) = S_V^0, I_V(\theta) = I_V^0$, for $\theta \in [-\tau, 0]$, where $\tau = \max(T_1, T_V)$. The respective total host and tsetse population sizes can be determined by $N_1 = S_1 + I_1 + R_1$ and $N_V = S_V + I_V$ or from the differential equations

$$N_1' = \Lambda_1 - \mu_1 N_1 - (\sigma_1 - \mu_1)I_1 \quad \text{and} \quad N_V' = \Lambda_V - \mu_V N_V,$$

which are derived by adding the equations in system (13). We study system (13) in the region

$$\Gamma_1 = \left\{(S_1, I_1, R_1, S_V, I_V) \in \mathbb{R}_+^5 : 0 \le S_1 + I_1 \le \frac{\Lambda_1}{\mu_1}, 0 \le I_V \le \frac{\Lambda_V}{\mu_V}, S_1 \ge 0, I_1 \ge 0\right\},$$

where $\mathbb{R}_+^5$ denotes the non-negative cone of $\mathbb{R}^5$ including its lower dimensional faces. It can be verified that Γ_1 is positively invariant with respect to system (13). We denote the boundary and interior of Γ_1 by $\partial\Gamma_1$ and $\dot{\Gamma}_1$, respectively. System (13) has a disease-free equilibrium $E_{01} = (\frac{\Lambda_1}{\mu_1}, 0, 0, \frac{\Lambda_V}{\mu_V}, 0)$. An explicit expression for the basic reproduction number of system (13) can be obtained from Eq. (12) for $n = 1$ as $R_{01} = \sqrt{\frac{e^{-\mu_V T_V}\alpha_1 a_1 \mu_1 \beta_1 \Lambda_V}{\Lambda_1 \mu_V^2 (g_1+\sigma_1)}}$.

We consider the local stability of the disease-free equilibrium, E_{01}, in two cases, that is, where $R_{01} < 1$ and where $R_{01} > 1$.

Theorem 3.1 *The disease-free equilibrium, E_{01}, of the one-host* T. b. rhodesiense *transmission model with time delay in the absence of ITC is locally asymptotically stable in Γ_1 if $R_{01} < 1$ and unstable if $R_{01} > 1$.*

Proof Linearising system (13) around the disease-free equilibrium, $E_{01} = (\frac{\Lambda_1}{\mu_1}, 0, 0, \frac{\Lambda_V}{\mu_V}, 0)$, we obtain three negative eigenvalues, $-(\nu_1 + \mu_1)$, $-\mu_1$ and $-\mu_V$, and the

following characteristic equation whose solutions (real or complex) give the remaining eigenvalues:

$$\lambda^2 + (\mu_V + g_1 + \sigma_1)\lambda - \mu_V(g_1 + \sigma_1)\left[(R_{01})^2 e^{-\lambda(T_1+T_V)} - 1\right] = 0. \tag{14}$$

For $T_1 = T_V = 0$, Eq. (14) will have only roots with negative real parts if $R_{01} < 1$, and the disease-free equilibrium will be locally stable, according to the Routh–Hurwitz criterion. Otherwise, Eq. (14) will have one positive root if $R_{01} > 1$ and E_{01} is unstable.

For $T_1 = 0$ and $T_V \neq 0$, we first consider the case where $R_{01} > 1$ and arrange Eq. (14) in the form

$$\lambda^2 + (\mu_V + g_1 + \sigma_1)\lambda = \mu_V(g_1 + \sigma_1)\left[(R_{01})^2 e^{-\lambda T_V} - 1\right]. \tag{15}$$

Let $F(\lambda)$ and $G(\lambda)$ denote the left-hand and right-hand sides of Eq. (15), respectively. It is clear that $F(\lambda)$ is an increasing function of λ for $\lambda \in \mathbb{R}$, with $F(0) = 0$ and $\lim_{\lambda\to\infty} F(\lambda) = \infty$. The function $G(\lambda)$ is a decreasing function of λ, $\lambda \in \mathbb{R}$, and $G(0) = \mu_V(g_1 + \sigma_1)[(R_{01})^2 - 1] > 0$. Thus, the two functions must intersect for some $\lambda^* > 0$. Hence, (15) has a positive real solution for $R_{01} > 1$, and the disease-free equilibrium is unstable.

Moving to the case $R_{01} < 1$, we notice that $F(\lambda)$ is still an increasing function of λ. $G(\lambda)$ is also a decreasing function of λ, with $G(0) = \mu_V(g_1 + \sigma_1)[(R_{01})^2 - 1] < 0$. Thus, Eq. (15) has no positive real roots. If Eq. (15) is to have positive real roots, they must be complex and should have been obtained from a pair of complex conjugate roots that cross the imaginary axis. So, we need to show that these roots do not exist for E_{01} to be stable. Assume that $\lambda = i\omega$ for $\omega > 0$. Substituting for λ in Eq. (15), we obtain

$$-\omega^2 + i(\mu_V + g_1 + \sigma_1)\omega - \mu_V(g_1 + \sigma_1)\left[(R_{01})^2\big(\cos(\omega T_V) - i\sin(\omega T_V)\big) - 1\right] = 0.$$

Separating the real and imaginary parts, we have the following system of equations:

$$\begin{aligned} -\omega^2 + \mu_V(g_1 + \sigma_1) &= \mu_V(g_1 + \sigma_1)(R_{01})^2\cos(\omega T_V), \\ (\mu_V + g_1 + \sigma_1)\omega &= -\mu_V(g_1 + \sigma_1)(R_{01})^2\sin(\omega T_V). \end{aligned}$$

Adding the above equations together and using the trigonometric identity $\cos^2(\omega T_V) + \sin^2(\omega T_V) = 1$, we obtain the following four degree equation in ω:

$$\omega^4 + \big(\mu_V^2 + (g_1 + \sigma_1)^2\big)\omega^2 + \mu_V^2(g_1 + \sigma_1)^2\big(1 - (R_{01})^4\big) = 0. \tag{16}$$

To reduce this fourth-order equation to a quadratic equation, we let $z = \omega^2$, and the resulting equation in terms of z is

$$z^2 + \big(\mu_V^2 + (g_1 + \sigma_1)^2\big)z + \mu_V^2(g_1 + \sigma_1)^2\big(1 - (R_{01})^4\big) = 0. \tag{17}$$

It is clear that for $R_{01} < 1$, Eq. (17) does not have positive real roots, which leads to the conclusion that there is no ω such that $\lambda = i\omega$ is a solution of (15). In a similar way, it can be shown that there are no positive real roots for cases $T_1 \neq 0$ and $T_V = 0$,

and for the general case where $T_1 \neq 0$ and $T_V \neq 0$. Therefore, the real parts of all eigenvalues of the characteristic equation (14) are negative for all values of the time delay $T_1 \geq 0$ and $T_V \geq 0$. Thus, the disease-free equilibrium, E_{01}, is locally asymptotically stable for $R_{01} < 1$ and unstable for $R_{01} > 1$. This completes the proof of the theorem. □

3.1.3 The Endemic Steady States of the Multi-Host T. b. rhodesiense *Transmission Model in the Absence of ITC*

Assuming that $R_{0n} > 1$, we can now put our attention to the existence and uniqueness of an endemic equilibrium. An endemic equilibrium is a time-independent solution of system (4)–(8). Since a time-independent solution has the same values at time t as at time $t - \tau$, where τ is the time delay, the solution of the endemic equilibrium of system (4)–(8) can be obtained by considering the system without time delay. Let

$$\lambda_i^* = \frac{a_i \beta_i I_V^*}{N_i^*} \quad \text{and} \quad \lambda_V^* = \sum_{i=1}^{n} \frac{\alpha_i a_i I_i^*}{N_i^*} \tag{18}$$

be the respective forces of infection for the host and tsetse vector populations. Further, let the endemic steady state of model (4)–(8) be given by $E^* = (S_i^*, I_i^*, R_i^*, S_V^*, I_V^*)$. Solving Eqs. (4)–(8) at the steady state gives

$$\begin{aligned} I_i^* &= \frac{B_i \lambda_i^*}{D_i \lambda_i^* + F_i}, \qquad R_i^* = \frac{g_i I_i^*}{\mu_i + \nu_i}, \qquad S_i^* = \frac{\Lambda_i + \nu_i R_i}{\mu_i + \lambda_i^*}, \qquad N_i^* = \frac{G_i \lambda_i^* + H_i}{D_i \lambda_i^* + F_i}, \\ I_V^* &= \frac{A \Lambda_V \lambda_V^*}{\mu_V (A \lambda_V^* + \mu_V)}, \qquad S_V^* = \frac{\Lambda_V}{A \lambda_V^* + \mu_V}, \qquad N_V^* = \frac{\Lambda_V}{\mu_V}, \end{aligned} \tag{19}$$

where $B_i = \Lambda_i(\mu_i + \nu_i)$, $D_i = g_i \mu_i + \sigma_i(\mu_i + \nu_i)$, $F_i = \mu_i(\nu_i + \mu_i)(g_i + \sigma_i)$, $G_i = \Lambda_i(g_i + \nu_i + \mu_i)$, $H_i = \Lambda_i(\nu_i + \mu_i)(g_i + \sigma_i)$ and $A = e^{-\mu_V T_V}$.

Substituting I_V^*, I_i^* and N_i^* into Eq. (18) and solving, we obtain the endemic equilibrium in terms of λ_i^* as

$$\begin{aligned} &\lambda_i^* \big(G_i \lambda_i^* + H_i\big)\mu_V^2 + A\big(\lambda_i^* \big(G_i \lambda_i^* + H_i\big)\mu_V \\ &\quad - a_i \beta_i \Lambda_V \big(D_i \lambda_i^* + F_i\big)\big) \sum_{i=1}^{n} \left[\frac{\alpha_i a_i B_i \lambda_i^*}{G_i \lambda_i^* + H_i} \right] = 0. \end{aligned} \tag{20}$$

Considering a case where the transmission of *T. b. rhodesiense* is occurring between the tsetse vector species and one host population (that is, $n = 1$), Eq. (20) becomes

$$\begin{aligned} &\lambda_1^* \big(G_1 \lambda_1^* + H_1\big)\mu_V^2 + A\big(\lambda_1^* \big(G_1 \lambda_1^* + H_1\big)\mu_V \\ &\quad - a_1 \beta_1 \Lambda_V \big(D_1 \lambda_1^* + F_1\big)\big) \left(\frac{\alpha_1 a_1 B_1 \lambda_1^*}{G_1 \lambda_1^* + H_1} \right) = 0. \end{aligned} \tag{21}$$

Simplifying Eq. (21), we obtain a non-zero equilibria for model (4)–(8) for a special case where $n = 1$ as

$$\lambda_1^*\left(a_0\left(\lambda_1^*\right)^2 + b_0\lambda_1^* + c_0\right) = 0, \tag{22}$$

where $a_0 = G_1\mu_V(A\alpha_1 a_1 B_1 + G_1\mu_V)$, $b_0 = AH_1\alpha_1 a_1 B_1\mu_V + 2H_1 G_1\mu_V^2 - A\alpha_1 a_1^2 \Lambda_V B_1 D_1\beta_1$ and $c_0 = \Lambda_1\mu_V^2(g_1 + \sigma_1)(1 - (R_{01})^2)$.

Thus, the positive endemic equilibria of model (4)–(8) for the special case where $n = 1$ is obtained by solving Eq. (22) and substituting the results of λ_1^* into expressions (19). It can be seen that a_0 is always positive and c_0 is positive (negative) if R_{01} is less than (greater than) one, respectively. Thus, the following result is obtained.

Theorem 3.2 *The one-host* T. b. rhodesiense *transmission model with time delay in the absence of ITC has*:

(i) *a unique endemic equilibrium if* $c_0 < 0 \Longleftrightarrow R_{01} > 1$;
(ii) *a unique endemic equilibrium if* $b_0 < 0$ *and* $C_0 = 0$ *or* $b_0^2 - 4a_0c_0 = 0$;
(iii) *two endemic equilibrium if* $c_0 > 0$, $b_0 < 0$ *and* $b_0^2 - 4a_0c_0 > 0$;
(iv) *no endemic equilibrium otherwise*.

The computation of the endemic equilibria for the cases where $n > 1$ leads to polynomials whose degree is more than three and are difficult to analyse analytically. We thus resort to numerical results which are given in Sect. 4.

3.2 Mathematical Analysis of the Multi-host Model in the Presence of ITC

After putting insecticide-treated cattle (ITC) into consideration we obtain the new model, which is schematically represented by Fig. 1 and given by system (3). Again using the method in Sect. 3.1 with the disease-free equilibrium

$$E_0^T = \left(\frac{\Lambda_1(1-\pi)}{\mu_1}, 0, 0, \frac{\Lambda_1\pi}{\mu_1}, 0, 0, \frac{\Lambda_2}{\mu_2}, 0, 0, \ldots, \frac{\Lambda_n}{\mu_n}, 0, 0, \frac{\tilde{\Lambda}_V}{\tilde{m}_V}, 0\right),$$

where $\pi = \frac{\psi}{\psi+d+\mu_1}$ and $\tilde{m}_V = \mu_V + a_1 m\pi$. The expression for $\tilde{\Lambda}_V$ is given by Eq. (34) in the Appendix. The basic reproduction number for the multi-host model in the presence of ITC is thus obtained as

$$R_{0n}^T = \sqrt{\frac{e^{-\tilde{m}_V T_V}\tilde{\Lambda}_V}{\tilde{m}_V^2}\sum_{i=1}^{n}\frac{\alpha_i a_i^2\beta_i\mu_i}{\Lambda_i(g_i+\sigma_i)}}. \tag{23}$$

R_{0n}^T gives the expected number of secondary cases produced in a completely susceptible population, by a typical infective host or tsetse fly in the presence of insecticide-treated cattle. If $R_{0n}^T > 1$, then the disease may emerge in one of the populations. However, if $R_{0n} < 1$, then the disease-free equilibrium is locally asymptotically stable (Van den Driessche and Watmough 2002). It can be noticed that when $p = 0$, Eq. (23) reduced to (12).

For our study, we will consider a special case where the host population is limited to three, that is, cattle, humans and wildlife as in Davis et al. (2011). Studies on trypanosomiasis infection in East Africa show that cattle are an important reservoir for *T. b. rhodesiense*. The importance of wildlife in the transmission of trypanosomiasis has also been identified in most parts of sub-Saharan Africa (Coleman and Welburn 2004; Fèvre et al. 2008; Waiswa et al. 2006; Welburn et al. 2006). For this case where $n = 3$, the basic reproduction number can be obtained from Eq. (23) as

$$R_{03}^{T} = \sqrt{\frac{e^{-\tilde{m}_V T_V}\tilde{\Lambda}_V}{\tilde{m}_V^2}\left\{\frac{\alpha_1 a_1^2 \beta_1 \mu_1}{\Lambda_1(g_1+\sigma_1)} + \frac{\alpha_2 a_2^2 \beta_2 \mu_2}{\Lambda_2(g_2+\sigma_2)} + \frac{\alpha_3 a_3^2 \beta_3 \mu_3}{\Lambda_3(g_3+\sigma_3)}\right\}}. \tag{24}$$

3.2.1 *Sensitivity Analysis of R_{03}^{T} to Parameter Valves*

R_{03}^{T} is determined by several parameters, and therefore, it is necessary to investigate the sensitivity of R_{03}^{T} to each parameter. This can be determined by calculating the sensitivity index of R_{03}^{T} with respect to each parameter as in Chitnis et al. (2008). The definition shows that the sensitivity of a variable X with respect to a parameter μ is given by

$$\Upsilon_{\mu}^{X} = \frac{\partial X}{\partial \mu}\frac{\mu}{X}. \tag{25}$$

The definition shows that the sensitivity index measures the relative change in X for a small relative change in the parameter μ. A negative sensitivity index means that an increase in the value of the parameter would lead to a decrease in the variable X. On the other hand, a positive sensitivity index means that an increase in the parameter value would lead to an increase in the variable X. By using this definition, we obtain the sensitivity indices of R_{03}^{T} with respect to all parameters. The results are given in Table 2.

The sensitivity analysis shows that the parameter that has a greater impact on the basic reproduction number in the absence of ITC is the tsetse natural mortality, μ_V. Other important parameters are the tsetse-cattle biting rate, a_1, and the tsetse birth rate, B_V. In the presence of insecticide-treated cattle (ITC), the basic reproduction number, R_{03}^{T}, is most sensitive to the parameter for the additional tsetse mortality, m. Other important parameters are the tsetse natural mortality, μ_V, proportion of cattle with insecticides treated per day, ψ, and the rate of loss of the insecticidal effect, d. It can also be noticed that the sensitivity index for R_{03}^{T} with respect to the tsetse-cattle biting rate, a_1, is positive and negative in the absence and presence of ITC, respectively. This is because, in the absence of ITC, increased tsetse biting on cattle leads to an increase in *T. b. rhodesiense* infection rate and hence an increase in the basic reproduction number. Conversely, in the presence of ITC, increased tsetse biting on cattle leads to the increased tsetse death rate, which results in a decrease in the tsetse density, hence reducing the *T. b. rhodesiense* infection rate and the basic reproduction number.

Table 2 Sensitivity indices of R_{03}^T of the 3-host *T. b. rhodesiense* model with and without insecticide-treated cattle. All parameters were fixed to the values given in Table 3, and p was taken to be 0.2

Without ITC				With ITC (RAP case)			
Parameter	Sensitivity index	Parameter	Sensitivity index	Parameter	Sensitivity index	Parameter	Sensitivity index
μ_V	−1.2772			m	−0.8278	Λ_3	−0.1973
a_1	+0.5626	g_3	−0.1184	μ_V	−0.7537	β_3	+0.1973
B_V	+0.500	σ_1	+0.0906	T_V	−0.5665	μ_3	+0.1973
a_3	+0.3927	σ_3	−0.0789	ψ	−0.5543	g_3	−0.1184
α_1	+0.3022	a_2	−0.0049	d	+0.5468	σ_1	−0.0906
β_1	+0.3022	μ_2	+0.0005	B_V	+0.5000	σ_3	−0.0789
Λ_1	−0.3022	β_2	+0.0005	a_3	+0.3828	a_2	+0.0049
μ_1	+0.3022	α_2	+0.0005	μ_1	+0.3097	β_2	+0.0005
T_V	−0.2700	Λ_2	−0.0005	α_1	+0.3022	α_2	+0.0005
g_1	−0.2115	g_2	−0.0004	β_1	+0.3022	Λ_2	−0.0005
α_3	+0.1973	σ_2	−0.0001	Λ_1	−0.3022	μ_2	+0.0005
β_3	+0.1973			a_1	−0.2649	g_2	−0.0004
Λ_3	−0.1973			g_1	−0.2115	σ_2	−0.0001
μ_3	+0.1973			α_3	+0.1973		

4 Numerical Results

Table 3 gives all the parameter values used in solving the 3-host *T. b. rhodesiense* transmission model with time delay in the absence and presence of ITC.

With all the parameters fixed or estimated (Table 3), we look at the numerical results following from the model (4)–(8) for $n = 3$. In the absence of ITC, the basic reproduction number, R_{03}, for the case when the number of hosts is limited to three, can be obtained from (12). First, the disease-free steady state is given by $\Lambda_1 = 40{,}000$, $\Lambda_2 = 500{,}000$ and $\Lambda_3 = 5{,}000$ for cattle, humans and wildlife populations, respectively. In the absence of ITC , we obtain $R_{03} = 2.5$. This value is close to 2.65 obtained in Rogers (1988) for *T. brucei* species in humans and cattle. Davis et al. (2011) did a global sensitivity analysis for African sleeping sickness by considering three host groups; humans, livestock and wildlife, and they obtained a basic reproduction number that lies in the range 0.097–4.955 for *T. b. rhodesiense*.

4.1 Application of Insecticides to Cattle to Prevent the Transmission

In this subsection, we investigate the impact of ITC on the *T. b. rhodesiense* transmission potential (R_{03}^T) and human incidence for different scenarios of cattle treatment coverage. We estimate the critical proportion ψ of cattle required to be treated with insecticides for R_{03}^T to be less than one, by setting $R_{03}^T = 1$ and solving for ψ.

The results in Fig. 2(b) show that in areas where vectors feed predominantly on cattle, insecticide treatment of about 1.1 % or 1.6 % per day of the cattle population using the WB or RAP approaches, respectively, can potentially reduce $R_{03}^T < 1$ and

Table 3 Numerical values for the parameters of the three-host model

	Host 1 (Cattle)			Host 2 (Humans)			Host 3 (Wildlife)		
Host population parameters									
Recruitment rate	Λ_1	22.0	WHO (2008)	Λ_2	27.5	Uganda Bureau of Statistics (2008)	Λ_3	1.25.0	Davis et al. (2011)
Natural mortality	μ_1	0.00055	WHO (2008)	μ_2	0.000055	WHO (2008)	μ_3	0.00025	Davis et al. (2011)
Proportion of blood tsetse meal	f_1	0.7	Hargrove et al. (2012), Rogers (1988)	f_2	0.10	Davis et al. (2011)	f_3	$(1 - f_1 - f_2)$	–
Biting rate	a_1	af_1	–	a_2	af_2	–	a_3	af_3	–
Probability of infected fly producing infection	β_1	0.62	Rogers (1988)	β_2	0.53	Coleman and Welburn (2004)	β_3	0.62	Rogers (1988)
Incubation period	T_1	7.0	Coleman and Welburn (2004)	T_2	10.0	Coleman and Welburn (2004)	T_3	7.0	Coleman and Welburn (2004)
Mortality of infected hosts	σ_1	0.006	Davis et al. (2011)	σ_2	0.004	Davis et al. (2011)	σ_3	0.008	Davis et al. (2011)
Recovery rate	g_1	0.014	Davis et al. (2011), Rogers (1988)	g_2	0.012	Davis et al. (2011)	g_3	0.002	Davis et al. (2011)
Duration of immunity in recovered hosts	$\frac{1}{\nu_1}$	1.0	Coleman and Welburn (2004)	$\frac{1}{\nu_2}$	1.0	Coleman and Welburn (2004)	$\frac{1}{\nu_3}$	1.0	Coleman and Welburn (2004)
Probability of first blood meal giving rise to infection in tsetse flies	α_1	0.065	Coleman and Welburn (2004), Rogers (1988)	α_2	0.065	Coleman and Welburn, Rogers (2004, 1988)	α_3	0.065	(Rogers 1988)

Table 3 (*Continued*)

	Host 1 (Cattle)		Host 2 (Humans)	Host 3 (Wildlife)
Tsetse population parameters				
Tsetse birth rate	B_V	1,440	Davis et al. (2011)	
Recruitment rate	Λ_V	Varying	–	
Natural mortality	μ_V	0.03	Rogers (1988)	
Feeding cycle	$\frac{1}{a}$	4.0	Coleman and Welburn (2004), Davis et al. (2011)	
Incubation period	T_V	18.0	Coleman and Welburn (2004), Davis et al. (2011)	

	Whole-body (WB)		Restricted application (RAP)	
Insecticide-treated cattle (ITC) parameters				
Proportion of cattle treated with insecticides per day, ψ	Varying	–	Varying	–
Average duration of insecticide efficacy, $\frac{1}{d}$	4 weeks	Torr et al. (2007)	4 weeks	Torr et al. (2007)
Tsetse additional mortality due to insecticides, m	0.78	Torr et al. (2007)	0.57	Torr et al. (2007)

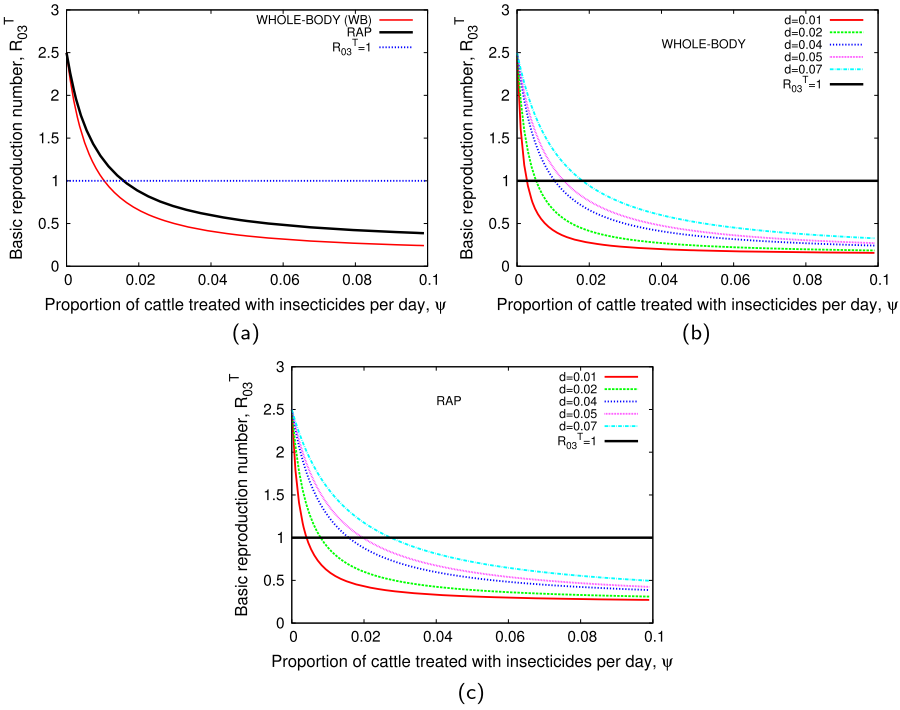

Fig. 2 The effect of treating cattle with insecticides on the basic reproduction number, R_{03}^T: (**a**) shows the plot of the basic reproduction number, R_{03}^T, with respect to the proportion of cattle treated with insecticides, ψ for $d = 0.04$; (**b**) and (**c**) show the critical proportions of cattle needed to be treated with insecticides for different values of d for whole body and restricted application, respectively (Color figure online)

therefore, lead to the control of *T. b. rhodesiense*. The duration of insecticide efficacy was taken to be $\frac{1}{d} = 4$ weeks, which is the same as the duration of the waning of the insecticidal effect. For both treatment strategies, the proportion of animals needing to be treated with insecticide per day decreases with the increase in the duration, $\frac{1}{d}$, of the killing effect of the insecticide. For example, reducing the duration of the killing effect provided by insecticides from 4 weeks to 3 weeks, implies that 1.3 % and 2.0 % of the cattle population need to be treated with insecticides through whole-body or restricted application, respectively, for $R_{03}^T < 1$. Results for the proportion of cattle required to be treated with insecticides for different values of d are shown in Figs. 2(b) and 2(c) for whole-body and restricted application, respectively.

The results for the proportions of cattle kept on insecticides were obtained by running model (3) up to a steady state and are shown in Fig. 3. The results show that the critical proportions of 1.1 % or 1.6 % required to be treated with insecticides per day through whole-body or restricted application for R_{03}^T to be less than one are equivalent to keeping 21.0 % or 27.0 % of the cattle population on insecticides, respectively. Figures 4 and 5 show the impact of ITC on the incidence and prevalence of *T. b. rhodesiense* in humans for both strategies. In both strategies, there is a significant decrease in the prevalence and incidence of *T. b. rhodesiense* in humans. The results are shown for the proportion of cattle treated with insecticides per day, ψ,

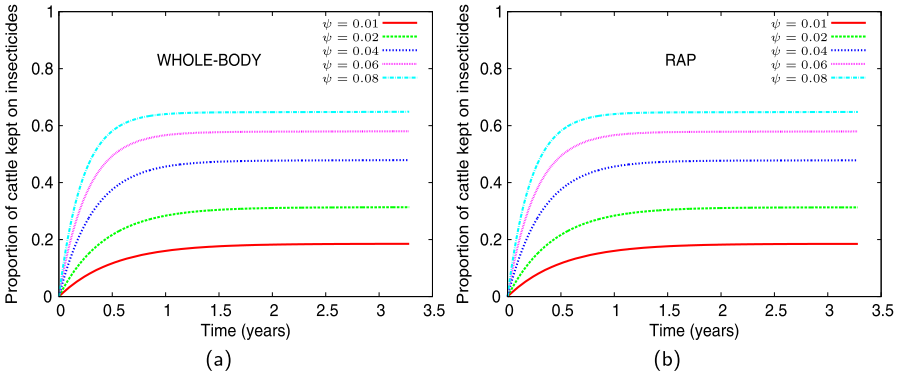

Fig. 3 Proportion of cattle kept on insecticides (Color figure online)

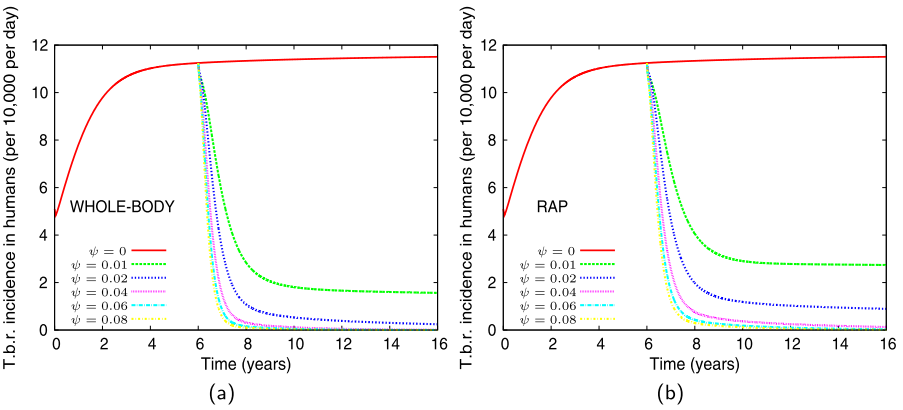

Fig. 4 Increased tsetse mortality through ITC. *T. b. rhodesiense* incidence in humans for both strategies; whole-body treatment (**a**) and restricted application of insecticides to cattle (**b**) (Color figure online)

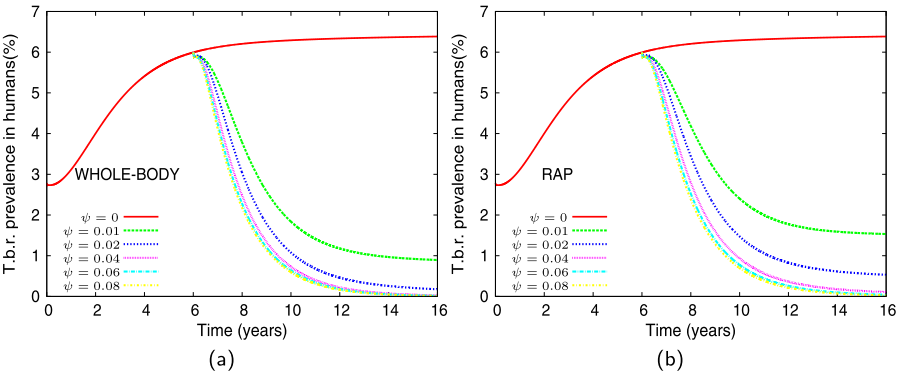

Fig. 5 Increased tsetse mortality through ITC. *T. b. rhodesiense* prevalence in humans for both strategies; whole-body treatment (**a**) and restricted application of insecticides to cattle (**b**) (Color figure online)

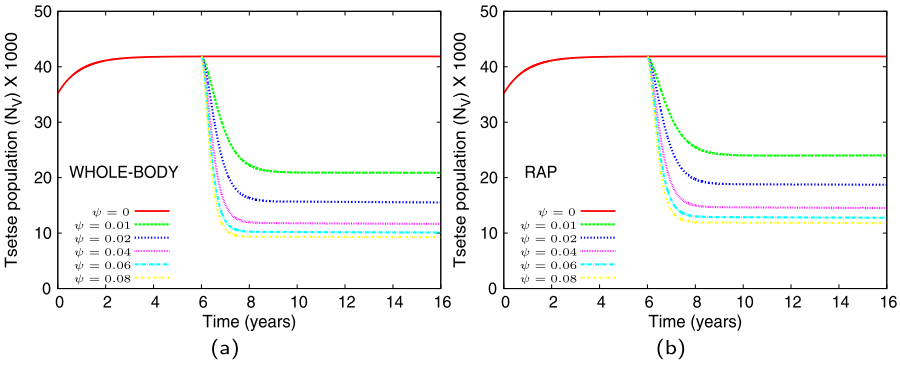

Fig. 6 Effect of increased tsetse mortality through ITC on the tsetse population for both strategies; whole-body treatment (**a**) and restricted application of insecticides to cattle (**b**) (Color figure online)

taken to be 0, 0.01, 0.02, 0.04, 0.06 and 0.08 for both strategies. The results are also shown for the case where different proportions of cattle are treated with insecticides in the presence of wildlife hosts.

4.2 Effect of ITC on the Tsetse Population

For both strategies. there are significant decreases in the tsetse population (Fig. 6), which can only be kept constant in the presence of ITC if the increased mortality is balanced by an increase in birth and/or immigration. The results shown in Fig. 6 reflect the situation where birth is the predominant source of replacements. If immigration is the predominant source, then older flies—which are above the average age of being able to transmit trypanosome infections—are entering the population. In that case the results shown in Fig. 6 under-estimate the level of disease control to be expected from the use of ITC at the stated levels. Generally, where ITC is used, either against closed populations of tsetse or on a sufficiently large scale that the vast majority of the area is uninfected by immigration of tsetse flies across the boundary, the expectation is that the fly population will decrease (Hargrove et al. 2012).

5 Conclusions

This paper provides support for previous theoretical and field experimental studies suggesting that the use of the ITC approach can provide a highly cost-effective approach to tsetse and trypanosomiasis control (Hargrove et al. 2000, 2012; Torr and Vale 2011; Torr et al. 2007; Vale and Torr 2005; Bourn et al. 2005; Vale et al. 1999) and is the method of choice whenever there are appropriate densities of cattle in a tsetse area (Shaw et al. 2013).

5.1 Whole-Body vs. Restricted Application

By limiting the number of host groups to three (i.e. humans, cattle and wildlife) the model was used to study the impact of treating cattle with insecticides on the control of *T. b. rhodesiense* in humans, using either the WB or RAP versions of ITC

approach. In areas where cattle provide the majority of feeds for tsetse both the WB and RAP strategies of insecticidal treatment can be used for the effective control of tsetse and of human trypanosomiasis. As expected, the absolute impact per animal treated was greater when the WB approach was used. But what is encouraging is that the restricted application approach, which uses about 20 % of the insecticide required for the whole-body treatment, is about 21 % less effective per animal treated (Torr et al. 2007). Whereas a strict cost-benefit analysis was beyond the scope of the present paper, it is nonetheless obvious from our theoretical analysis that the RAP approach has strong economic advantages, in accord with findings in the field.

The approach also has a number of other livestock health and productivity benefits. For example, most farmers in Africa have indigenous breeds of cattle, which are resistant to several tick-borne diseases. The resistance depends on young cattle being bitten by infected ticks. With the RAP approach, tsetse and human trypanosomiasis control can be achieved without needing to treat young cattle: these young animals will thus still be bitten by ticks, allowing them to build up immunity to tick-borne diseases (Torr et al. 2007).

Widespread use of pyrethroids can adversely impact invertebrate dung fauna, which play an important role in maintaining soil fertility (Bourn et al. 2005; Torr et al. 2007; Vale and Torr 2005). This adverse effect can be mitigated by using the RAP instead of WB approach, as indicated above. Finally, studies have shown that most cattle-feeding Diptera land on the animals' legs (Torr et al. 2007). This means that the use of RAP on cattle may be an appropriate method for controlling other vector-borne diseases of livestock and humans. Studies on the use of ITC to control malaria transmitted by *Anopheles arabiensis* have been done is Tanzania (Aneth et al. 2007). It was also shown that the cost of treating malaria using ITC in Pakistan is 80 % less than the standard method of indoor spraying (Mark et al. 2001).

5.2 Limitations

Our analysis has been restricted to the situation where the cattle to be treated with insecticide form a stationary population, uniformly distribution over a given area. Where this is the case, and where cattle provide the bulk of tsetse blood-meals, ITC will be most successful as a control technique. The more difficult situation to handle in practical control terms is one where cattle populations are migratory. The potential controlling effect of ITC on the tsetse and trypanosome populations is then much diminished. This problem is particularly severe for groups such as the Maasai peoples of East Africa, who traditionally travel widely with their cattle through tsetse infested country. The associated analytical problem is equally difficult to handle, involving variations in fly, host and parasite levels in both time and space and concomitant increases in mathematical complexity that were beyond the scope of the present study (Torr and Vale 2011).

Acknowledgements This study was supported by the European Union's Seventh Framework Program (FP7/2007–2013) under grant agreement No. 221948 Integrated Control of Neglected Zoonoses (ICONZ) (DK/JH, SCW); the United Kingdom Department for International Development Research into Use Programme (DFID-RIU) (PGC/JH/SCW) and by a European Science Foundation Senior Investigator(s) award Investigating Networks of Zoonosis Innovation INZI (SCW). We would like to thank all of the many research participants that were involved in this study, the numerous government officials and others who contributed.

Appendix

A.1 Derivation of the Tsetse Recruitment Rate, Λ_V

The recruitment rate for the tsetse flies is based on newly emerged flies that are feeding for the first time (Hargrove et al. 2012; Rogers 1988; Welburn et al. 2006). These newly emerged flies have to survive death due to natural mortality and the effects of insecticides, and should not have fed for them to be susceptible to *T. b. rhodesiense* infection. Assuming a constant birth rate, B_V, the number of newly born flies that survive and have not fed in one unit of time (that is, between $t-1$ and 1) is given by

$$\Lambda_V = B_V \int_{t-1}^{t} e^{-\int_s^t (a+m_V(p(\xi)))\,d\xi}\,ds. \tag{26}$$

Changing variables by letting $u = t - s$, Eq. (26) becomes

$$\Lambda_V = B_V \int_0^1 e^{-\int_{t-u}^t (a+m_V(p(\xi)))d\xi}\,du. \tag{27}$$

Changing variables again by letting $x = \xi - t$, Eq. (27) becomes

$$\Lambda_V = B_V \int_0^1 e^{-\int_{-u}^0 (a+m_V(p(t+x)))\,dx}\,du. \tag{28}$$

Equation (28) can be solved by using the the trapezium rule given by,

$$\int_{x_1}^{x_2} f(x)\,dx = \frac{(x_2-x_1)}{2n}\left[f(x_1)+f(x_2)+2\sum_{k=1}^{n-1} f\left(x_1+k\left(\frac{x_2-x_1}{n}\right)\right)\right]. \tag{29}$$

Using Eq. (29), the exponential part of Eq. (28) becomes

$$\frac{-u}{2n_1}\left[2a+m_V\big(p(t-u)\big)+m_V\big(p(t)\big)+2\sum_{k_1=1}^{n_1-1}\left(a+m_V\left(p\left(t+u\left(\frac{k_1}{n_1}-1\right)\right)\right)\right)\right]. \tag{30}$$

Substituting Eq. (30) into (28), we obtain

$$\Lambda_V = B_V \int_0^1 e^{\frac{-u}{2n_1}[2a+m_V(p(t-u))+m_V(p(t))+2\sum_{k_1=1}^{n_1-1}(a+m_V(p(t+u(\frac{k_1}{n_1}-1))))]}\,du. \tag{31}$$

Again, using Eq. (29), (31) becomes

$$\Lambda_V = \frac{B_V}{2n_2}\left(1+e^{\frac{-1}{2n_1}[2a+m_V(p(t-1))+m_V(p(t))+2\sum_{k_1=1}^{n_1-1}(a+m_V(p(t+\frac{k_1}{n_1}-1)))]}\right.$$
$$\left.+2\sum_{k_2=1}^{n_2-1} e^{-\frac{1}{2n_1}(\frac{k_2}{n_2})[2a+m_V(p(t-\frac{k_2}{n_2}))+m_V(p(t))+2\sum_{k_1=1}^{n_1-1}(a+m_V(p(t+\frac{k_2}{n_2}(\frac{k_1}{n_1}-1))))]}\right). \tag{32}$$

Taking $n_1 = n_2 = 2$, Eq. (32) reduces to

$$\Lambda_V = \frac{B_V}{4}\left[1 + 3e^{-\frac{1}{4}(4a + m_V(p(t-1)) + 3m_V(p(t))}\right]. \tag{33}$$

Due to the delay terms in Eq. (32), cases where $n_1 = n_2 > 2$ reduce to a Λ_V that is complex to be solved with system (3) given in Sect. 2.

At the DFE, the proportion of cattle on insecticides is constant and given by $\pi = \frac{\psi}{\psi + d + \mu_1}$. The solution for the tsetse recruitment rate at the DFE can thus be obtained by integrating Eq. (28) and is given by

$$\tilde{\Lambda}_V = \frac{B_V}{(a + \tilde{m}_V(\pi))}\left(1 - e^{-(a + \tilde{m}_V(\pi))}\right). \tag{34}$$

References

Aneth, M. M., Franklin, W. M., Johnson, M. M., & Eliningaya, J. K. (2007). Role of cattle treated with deltamethrine in areas with a high population of *Anopheles arabiensis* in Moshi, Northern Tanzania. *Malar. J.*, *6*, 109.

Artzrouni, M., Gouteux, J. (2001). A model of Gambian sleeping sickness with open vector populations. *IMA J. Math. Appl. Med. Biol.*, *18*, 99–117.

Anderson, N. E., Mubanga, J., Fevre, E. M., Picozzi, K., Eisler, M. C., Thomas, R., & Welburn, S. C. (2011). Characterisation of the wildlife reservoir community for human and animal trypanosomiasis in the Luangwa valley, Zambia. *PLoS Negl. Trop. Dis.*, *5*, e1211.

Bauer, B., Amsler-Delafosse, S., Kabore, I., & Kamuanga, M. (1999). Improvement of cattle productivity through rapid alleviation of African animal trypanosomiasis by integrated disease management practices in the agropastoral zone of Yale, Burkina Faso. *Trop. Anim. Health Prod.*, *31*, 89–102.

Bauer, B., Kabore, I., Liebisch, A., Meyer, F., & Petrich-Bauer, J. (1992). Simultaneous control of ticks and tsetse flies in Satiri, Burkina Faso, by the use of flumethrin pour-on for cattle. *Ann. Trop. Med. Parasitol.*, *42*, 41–46.

Bekele, J., Asmare, K., Abebe, G., Ayelet, G., & Gelaye, E. (2010). Evaluation of deltamethrin applications in the control of tsetse and trypanosomosis in the southern rift valley areas of Ethiopia. *Vet. Parasitol.*, *168*, 177–184.

Bourn, D., Grant, I., Shaw, A., & Torr, S. (2005). Cheap and safe tsetse control for live stock production and mixed farming in Africa. *Asp. Appl. Biol.*, *75*, 1–12.

Chitnis, N., Hyman, J. M., & Cushing, J. M. (2008). Determining important parameters in the spread of malaria through the sensitivity analysis of a mathematical model. *Bull. Math. Biol.*, *70*, 1272–1296.

Chizyuka, H. G. B., & Liguru, S. M. K. (1986). Dipping to control vectors of cattle parasites. *Parasitology*, *2*, 123.

Coleman, P. G., & Welburn, S. C. (2004). Are fitness costs associated with resistance to human serum in *Trypanosoma brucei rhodesiense*? *Trends Parasitol.*, *20*, 311–315.

Davis, S., Aksoy, S., & Galvani, A. (2011). A global sensitivity analysis for African sleeping sickness. *Parasitology*, *138*, 516–526.

Fèvre, E. M., Odiit, M., Coleman, P. G., Woolhouse, M. E. J., & Welburn, S. C. (2008). Estimating the burden of rhodesiense sleeping sickness during an outbreak in Serere, eastern Uganda. *BMC Public Health*, *8*, 96.

Fox, R. G. R., Mmbando, S. O., Fox, M. S., & Wilson, A. (1993). Effect on herd health and productivity of controlling tsetse ad trypanosomiasis by applying deltamethrin to cattle. *Trop. Anim. Health Prod.*, *25*, 203–214.

Hargrove, J. W., Omolo, S., Msalilwa, J. S. I., & Fox, B. (2000). Insecticide-treated cattle for tsetse control: the power and the problems. *Med. Vet. Entomol.*, *14*, 123–130.

Hargrove, J. W., Torr, S. J., & Kindness, H. M. (2003). Insecticide-treated cattle against tsetse (Diptera: *Glossinidae*): what governs success? *Bull. Entomol. Res.*, *93*, 203–217.

Hargrove, J. W., Ouifki, R., Kajunguri, D., Vale, G. A., & Torr, S. J. (2012). Modeling the control of trypanosomiasis using trypanocides or insecticide-treated livestock. *PLoS Negl. Trop. Dis.*, *6*, e1615.

Magona, J. W., & Walubengo, J. (2011). Mass-treatment and insecticide-spraying of animal reservoirs for emergency control of Rhodesiense sleeping sickness in Uganda. *J. Vector Borne Dis.*, *48*, 105–108.

Mark, R., Naeem, D., Mike, K., Nasir, M., Hameed, U., & Sean, H. (2001). Control of malaria in Pakistan by applying deltamethrin insecticide to cattle: a community-randomised trial. *Lancet*, *357*, 1837–1841.

Okello-Onen, J., Heinonen, R., Ssekitto, C. M. B., Mwayi, W. T., Kakaire, D., & Kabarema, M. (1994). Control of tsetse flies in Uganda by dipping cattle in deltamethrin. *Trop. Anim. Health Prod.*, *26*, 21–27.

Rogers, D. J. (1988). A general model for the African trypanosomiases. *Parasitology*, *97*, 193–212.

Rowlands, G. J., Leak, S. G. A., Woudyalew, M., Nagda, S. M., Wilson, A., & d'Ieteren, G. D. M. (2000). Use of deltamethrin 'pour-on' insecticide for the control of cattle trypanosomosis in the presence of high tsetse invasion. *Med. Vet. Entomol.*, *15*, 87–96.

Shaw, A. P. M., Torr, S. J., Waiswa, C., Cecchi, G., Wint, G. R. W., Mattioli, R. C., & Robinson, T. P. (2013). Estimating the costs of tsetse control options: an example for Uganda. *Prev. Vet. Med.*, *110*, 290–303.

The Center for Food Security and Public health (2009). African animal trypanosomiasis. www.cfsph.iastate.edu.

Thomson, J. W., Mitchell, M., Rees, R. B., Shereni, W., Schoenfeld, A. H., & Wilson, A. (1991). Studies on the efficacy of deltamethrin applied to cattle for the control of tsetse flies (*Glossina spp.*) in southern Africa. *Trop. Anim. Health Prod.*, *23*, 221–226.

Torr, S. J., & 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.

Torr, S. J., Maudlin, I., & Vale, G. A. (2007). Less is more: restricted application of insecticide to cattle to improve the cost and efficacy of tsetse control. *Med. Vet. Entomol.*, *21*, 53–64.

Torr, S. J., Wilson, P. J., Schofield, S., Mangwiro, T. N. C., & White, B. N. (2001). Application of DNA markers to identify the individual-specific hosts of tsetse feeding on cattle. *Med. Vet. Entomol.*, *15*, 78–86.

Uganda Bureau of Statistics (UBOS) (2008). *National livestock census*. http://www.ubos.org.

Van den Driessche, P., & Watmough, J. (2002). Reproduction numbers and sub-threshold endemic equilibria for compartmental models of disease transmission. *Math. Biosci.*, *180*, 29–48.

Vale, G. A., & 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.

Vale, G. A., Mutika, G., & Lovemore, D. F. (1999). Insecticide-treated cattle for controlling tsetse flies (Diptera: *Glossinidae*): some questions answered, many posed. *Bull. Entomol. Res.*, *89*, 569–578.

Waiswa, C., Picozzi, K., Katunguka-Rwakishaya, E., Olaho-Mukani, W., Musoke, R. A., & Welburn, S. C. (2006). *Glossina fuscipes fuscipes* in the trypanosomiasis endemic areas of south eastern Uganda: apparent density, trypanosome infection rates and host feeding preferences. *Acta Trop.*, *99*, 23–29.

Welburn, S. C., Coleman, P. G., Maudlin, I., Fèvre, E. M., Odiit, M. O., & Eisler, M. C. (2006). Crisis, what crisis? Control of Rhodesian sleeping sickness. *Trends Parasitol.*, *22*, 123–128.

WHO (2008). Uganda: country health profile. http://www.who.int/countries/uga/en/.

WHO (2011). The control of neglected zoonotic diseases. http://www.who.int/neglected_diseases/zoonoses/en/.

Zoller, T., Fèvre, E. M., Welburn, S. C., Odiit, M., & Coleman, P. G. (2008). Analysis of risk factors for *T. brucei rhodesiense* sleeping sickness within villages in south-east Uganda. *BMC Infect. Dis.*, *8*, 88.