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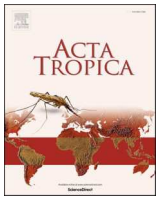

A compartmental model for *Schistosoma japonicum* transmission dynamics in the Philippines

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ABSTRACT

Schistosomiasis is a chronic and debilitating neglected tropical disease (NTD), second only to malaria as one of the most devastating parasitic diseases. Caused by a parasitic flatworm of the genus *Schistosoma*, infection occurs when skin comes in contact with contaminated freshwater that contains schistosome-hosting snails. The disease continues to be endemic in many regions of the Philippines, where it poses a significant public health challenge due to a lack of healthcare resources. In the Philippines, additional mammalian reservoirs for the *S. japonicum* parasite, especially bovines such as carabaos, also facilitate the spread of schistosomiasis. We extend existing compartment models to include human, snail, bovine, and free-living *Schistosoma* for a comprehensive look at the transmission dynamics of the disease. Sensitivity analysis of model parameters shows that the carabaos themselves can sustain the endemicity of schistosomiasis. Thus, we consider the control method of farming mechanization to avoid contaminated freshwater sources. We find that a reduction of contaminated water contacts by at least 77% will break the transmission cycle and eliminate the disease. However, reducing the contact by about 70% will still result in decrease of human schistosomiasis prevalence to under 1% in 15 years or less. Achieving such high reduction of contact rates could be a daunting task, especially in rural areas. Still, the potential to eliminate or at least reduce the schistosomiasis prevalence should be considered an additional benefit of mechanization efforts in the Philippines.

1. Introduction

Schistosomiasis, commonly known as bilharziasis, is a chronic and debilitating neglected tropical disease (NTD), second only to malaria as one of the most devastating parasitic diseases (Siddiqui et al., 2023). The disease is particularly prevalent in regions where access to clean water, proper sanitation, and adequate healthcare is limited. In 2021, it was estimated that 251.4 million individuals required treatment for schistosomiasis (WHO, 2023). Schistosomiasis claims the lives of almost 12,000 individuals each year; however, this is likely an underestimate of the disease's impact (WHO, 2023). Thus, implementing preventive measures is of utmost importance in addressing schistosomiasis.

The disease is caused by a parasitic flatworm belonging to the genus *Schistosoma*. Among the 23 known species of *Schistosoma*, three main species, namely *S. mansoni, S. haematobium*, and *S. japonicum*, primarily infect humans (CDC, 2020) but also other mammals (Chen et al., 2010; Riley et al., 2008). The parasites have a complex life cycle, requiring an intermediate snail host before they can infect humans; see Fig. 1. The exposure occurs when the human or animal skin comes into contact with contaminated freshwater inhabited by specific freshwater snail species carrying schistosomes.

Schistosomiasis remains a significant public health challenge in the endemic regions of the Philippines (Olveda and Gray, 2019). In 2018 alone, around 800,000 individuals were diagnosed with *Schistosoma* infection, and 12 million people remain at risk of contracting the disease. The prevalence of schistosomiasis is widespread across the three

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major island groups of Luzon, Visayas, and Mindanao, spanning 28 provinces, 190 municipalities, and 2230 barangays (Olveda et al., 2014). These regions, characterized by non-dry seasons, are predominantly rice-growing areas that facilitate interactions between humans and freshwater snails, contributing to disease transmission. *S. japonicum* remains the predominant species responsible for human infections (Chan et al., 2021). The transmission dynamics of *S. japonicum* are known to involve additional mammalian hosts (Chen et al., 2010; Riley et al., 2008). The substantial presence of water buffaloes, commonly referred to as carabaos, plays a significant role in the widespread transmission of the disease in the country.

The primary method of treating schistosomiasis in the Philippines is mass drug administration (MDA) of praziquantel (PZQ), with molluscicides serving as a supplementary approach (Leonardo et al., 2016). However, PZQ is most effective against the adult worm and requires the presence of a mature antibody response to the parasite; it is not a preventative treatment and does not affect immature worms (CDC, 2020). Moreover, despite the availability of treatment, many areas in the Philippines face challenges in accessing it. Limited accessibility is compounded by remote locations and inadequate infrastructure, hindering the delivery of treatment and healthcare services (Leonardo et al., 2016). Furthermore, there is a shortage of healthcare professionals and medical equipment, further impeding the effective management of schistosomiasis in the country.

The use of carabaos by rice farmers in the endemic areas is a significant factor in a transmission of the disease (Riñon et al., 2022). The mechanization level of the agriculture sector in the Philippines is 2.679 hp/ha which is classified as a low mechanization level (Cariño, 2023). However, there are government initiatives and programs to encourage the mechanization of farming practices, with a goal of reaching at least 4 hp/ha to match other countries in the Association of Southeast Asian Nations (ASEAN) (Tacio, 2022). The increase of mechanization level will reduce the contact of people and carabaos with the freshwater sources which has a potential to reduce the disease prevalence. Our goal is to create a mathematical model that will quantify this relationship.

Numerous mathematical models have been developed for the dynamics of schistosomiasis. Woolhouse (1991) provides an overview of modeling natural transmissions, Woolhouse (1992) focuses on controls. Recently, Lowe et al. (2023) systematically reviewed modeling efforts since 2000 and identified 19 papers. Only two, Ishikawa et al. (2006) and Riley, Carabin, Bélisle, Joseph, Tallo, Balolong, A. L. W., F., Gonzales, Olveda, McGarvey, 2008 modeled the situation in the Philippines. The remaining 17 papers considered provinces in China.

As nicely illustrated in Lowe et al. (2023), the modeling concepts can

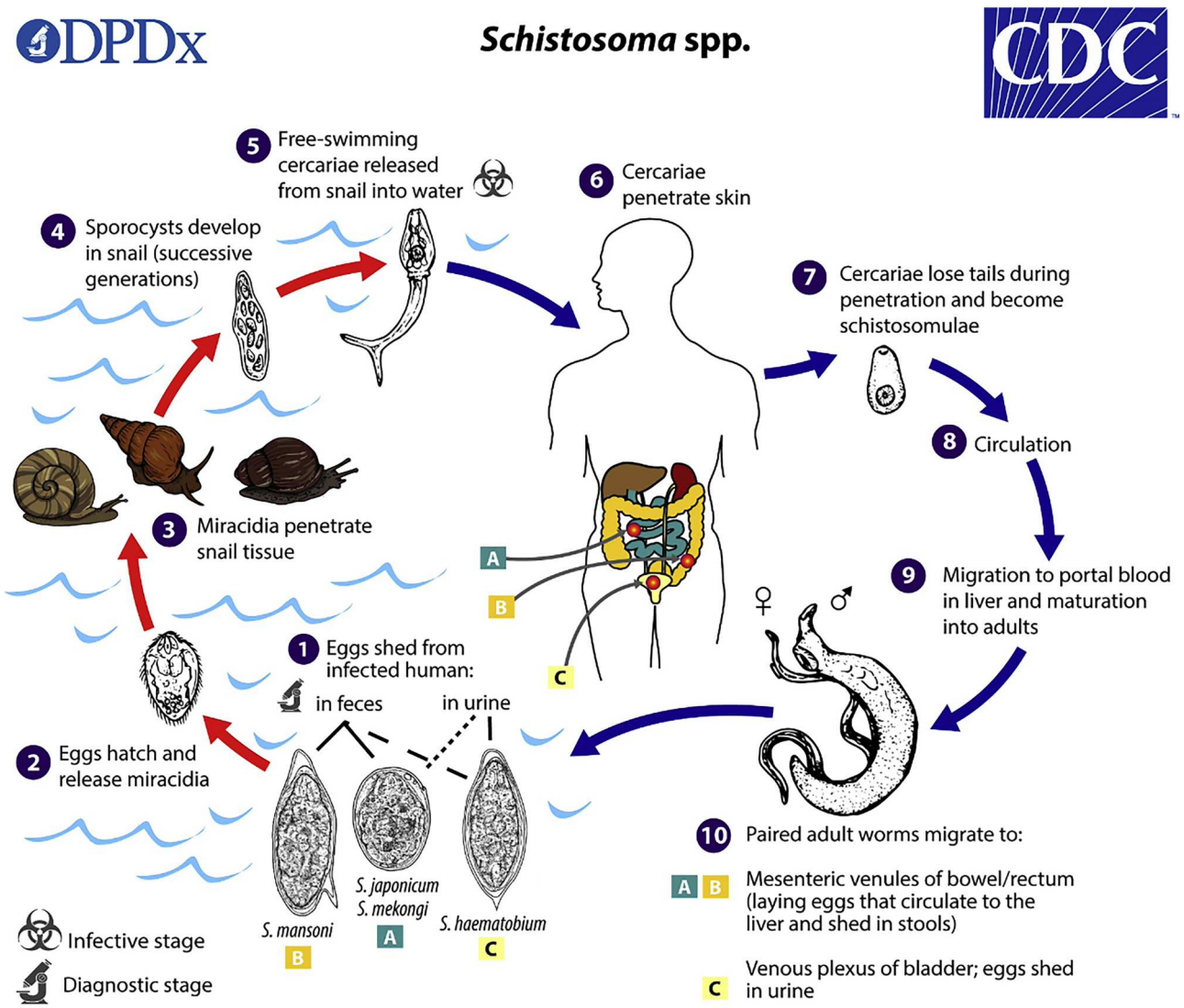

Fig. 1. Life cycle of Schistosoma spp. Only a human definitive host is shown. For *S. japonicum*, bovines and other mammals can serve as definitive hosts as well (Chen et al., 2010; Riley et al., 2008). Image courtesy of Public Health Image Library, Centers for Disease Control and Prevention, CDC (2019).

be traced back to the modeling frameworks of helminth infections in general (Anderson and May, 1985; 1991) and schistosomiasis in particular (Barbour, 1996). Five studies, Gao et al. (2013), Li et al. (2017), Liang et al. (2002), Spear et al. (2002) considered human and snail hosts only. Ten studies, Zou and Ruan (2015), Williams et al. (2002), Da'Dara et al. (2008), Gray et al. (2008), Williams et al. (2019), Gao et al. (2017), Guo et al. (2006), Xiang et al. (2013), Chen et al. (2010), Zhou et al. (2011) included humans, snail and bovine hosts. Finally, the remaining four studies included humans, snails and either (a) rats Ishikawa et al. (2006), (b) two to extra host classes for bovines and other hosts (Zhou et al., 2016), or (c) a multitude of separate classes of hosts like dogs, rats, goats, cats, buffaloes, and pigs (Riley et al., 2008; Rudge et al., 2013).

Finally, Kadaleka et al. (2021a) performed an optimal control analysis for a model with human and bovines, Kadaleka et al. (2021b) created a model with treatment and mullusticides, and Kadaleka et al. (2022) created model that included contaminated environment.

Our objective is to develop a comprehensive mathematical model that effectively captures the dynamics of schistosomiasis in the context of the Philippines. This model will consider the interplay between the human, snail, and bovine (carabao) populations to accurately simulate the transmission of the disease. We will focus on the effects of freshwater contact reduction on the schistosomiasis transmission. We demonstrate that when the contacts are substantially reduced, for example by increasing the mechanization level, the disease can be eliminated.

2. Model

2.1. Compartmental model

Here we describe the compartmental model of schistosomiasis transmission. We consider three host populations: (1) humans (subscript H), (2) bovines, specifically Carabao (subscript B), and (3) snails (class Gastropoda, subscript G). Humans and bovines act as definitive hosts and snails as intermediate hosts. We also consider the following "free-ranging" stages of schistosoma: eggs (E), miracidia (M) and cercariae (C).

The human population is divided into the following compartments: Susceptible (S_H) - no parasite and no immunity, Latent infection (L_H) - infected by schistosoma but not discharging any eggs, Infectious (I_H) - infected and discharging eggs, and Recovered (R_H) - previously infected but now with natural immunity and no longer discharging eggs. Humans are born susceptible at a rate Λ_H. All individuals die at the natural death rate μ_H and we assume no disease-related mortality. The susceptible individuals become latently infected at a rate $\beta_H C$ after coming into contact with cercariae in contaminated freshwater sources (Chiyaka and Garira, 2009; Gao et al., 2011; Madubueze et al., 2022b); here C is the concentration of cercariae and β_H is the transmission rate, i.e., a product of the contact rate and a probability of infection during a contact. To model the effect of freshwater contact avoidance, we assume $\beta_H = (1-r_H)\beta_{H0}$ where $r_H \in [0,1]$ signifies the proportions at which human populations implement the control method of avoiding contaminated freshwater sources and β_{H0} corresponds to the transmission rate at the baseline.

There is no vertical transmission (Chiyaka and Garira, 2009). The worms need time σ_H^{-1} to mature, i.e., the latently infected humans become infectious at a rate σ_H. The infectious humans shed eggs at rate η_H. Infectious humans slowly develop immunity at a rate ρ_H and move to the recovered class. For our model, we assume that the naturally dying worms are the main source of antigens that stimulate a strong immune response (Kura et al., 2021). The natural immunity wanes at rate θ_H. The human population is treated by mass administration of PZQ at a rate ϕ_H. However, the treatment affects only mature worms and does not offer immunity (CDC, 2020; Stylianou et al., 2017; WHO, 2023); thus only individuals in the infectious compartment move to the susceptible compartment.

The bovine population follows a similar progression. Bovines are born susceptible at a rate Λ_B, become latently infected at a rate $\beta_B C$ and then infectious at a rate σ_B. As with the human population, $\beta_B = (1-r_B)\beta_{B0}$ where $r_B \in [0,1]$ is the reduction of the freshwater contacts and β_{B0} is the transmission rate at the baseline. Infectious bovines shed schistosoma eggs at a rate η_B. The bovines live for an average time μ_B^{-1} which is too short to develop an immunity. Thus, we do not consider recovered compartments for the bovines. While PZQ can be used as a treatment, it is uneconomically expensive to do so (Yogeshpriya, 2022) and we thus do not consider it in our model.

The human and bovine populations together release eggs (E) at a rate $\eta_H I_H + \eta_B I_B$. The eggs have a natural mortality rate μ_E and hatch at a rate γ_E. After hatching, they become miracidia (M) which can live for a time μ_E^{-1}.

Snails are born as susceptible at a rate Λ_G. They can become latently infected only through the contact with miracidia (Gao et al., 2011) which happens at a rate $\beta_G M$. Within snails, the larvae develop into sporocysts and asexually reproduce. This takes a time σ_G^{-1}. The snails then become infectious and shed cercariae (C) into the water at a rate δ_G. We assume that the snails cannot be reinfected and cannot recover (Anderson et al., 2021; Chiyaka and Garira, 2009). The snails' mortality rate is μ_G and we assume no additional disease-related mortality.

Cercariae are released from snails at a rate $\delta_G I_G$. The cercariae have a natural mortality rate μ_C and can infect humans and bovines as described above. This concludes the transmission cycle shown as a diagram in Fig. 2.

2.2. System of differential equations

The model described above yields the following system of differential equations:

$$\frac{dS_H}{dt} = \Lambda_H + \theta_H R_H - \beta_H S_H C - \mu_H S_H + \phi_H I_H, \tag{1}$$

$$\frac{dL_H}{dt} = \beta_H S_H C - \sigma_H L_H - \mu_H L_H, \tag{2}$$

$$\frac{dI_H}{dt} = \sigma_H L_H - \phi_H I_H - \rho_H I_H - \mu_H I_H, \tag{3}$$

$$\frac{dR_H}{dt} = \rho_H I_H - (\theta_H + \mu_H) R_H, \tag{4}$$

$$\frac{dE}{dt} = \eta_H I_H + \eta_B I_B - (\gamma_E + \mu_E) E, \tag{5}$$

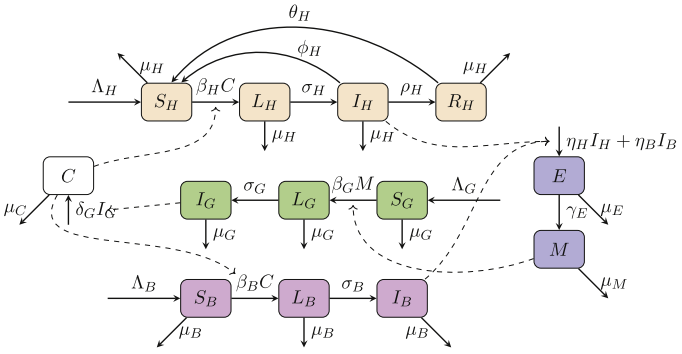

Fig. 2. Model for Humans (orange compartments), Snails (green compartments), Bovine (purple compartments), Miracidia (navy blue compartments), and Cercariae (white compartment). The solid arrows represent transitions between compartments with an appropriate per capita rate. The dashed arrows represent influences on the rates. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

$$\frac{dM}{dt} = \gamma_E E - \mu_M M, \tag{6}$$

$$\frac{dC}{dt} = \delta_G I_G - \mu_C C, \tag{7}$$

$$\frac{dS_G}{dt} = \Lambda_G - \beta_G S_G M - \mu_G S_G, \tag{8}$$

$$\frac{dL_G}{dt} = \beta_G S_G M - \sigma_G L_G - \mu_G L_G, \tag{9}$$

$$\frac{dI_G}{dt} = \sigma_G L_G - \mu_G I_G, \tag{10}$$

$$\frac{dS_B}{dt} = \Lambda_B - \beta_B S_B C - \mu_B S_B, \tag{11}$$

$$\frac{dL_B}{dt} = \beta_B S_B C - \sigma_B L_B - \mu_B L_B, \tag{12}$$

$$\frac{dI_B}{dt} = \sigma_B L_B - \mu_B I_B. \tag{13}$$

We will consider the above system with the initial conditions at the current endemic equilibrium ($I_H/N_H \approx 0.02$, $I_G/N_G \approx 0.007$, $I_B/N_B \approx 0.75$; see the next section).

2.3. Model calibration

The model parameters are summarized in Table 1. Based on the data from the Philippines (The World Bank, 2021a; 2021b) we use a birth rate of 22 births per 1000 people, per year and a death rate of 7 deaths per 1000 people per year.

We will consider the snail *Oncomelania hupensis quadrasi*, a very small tropical freshwater snail, as the snail intermediate host of *S. japonicum* in the Philippines (Leonardo et al., 2020). Their life span ranges from 4 to 6 months in the wild (Australian Government, 2017), we thus use 5 months as an average giving $\mu_G^{-1} = 5/12$ year. The birth rate was estimated as 0.0097 per day from Ishikawa et al. (2006), giving $\Lambda_G = 3.54$ per year.

We consider the bovine host *Bubalus bubalis* (carabao). Their birth rate was estimated by Riñon et al. (2022), which data-fitted this rate using data from the carabao population in Agusan del Sur, Mindanao, Philippines to obtain 0.0046889 per week, i.e., $\Lambda_B = 0.244$ per year. The death rate 0.0049 per week, i.e., $\mu_B = 0.255$ per year was adopted from Mingala and Gundran (2008).

The eggs die within 1–2 weeks after being released by the adult worm (Colley et al., 2015). We thus assume $\mu_E^{-1} = 1.5/52$ years. In sunlit conditions, most eggs hatch within 6 h, i.e., typically within a day of entering fresh water (Wanlop et al., 2022). Since there is typically a period between the egg being released by the worm and the egg entering the fresh water, we assume the total hatching time is 2 days, i.e., $\gamma_E^{-1} = 2/365$ years.

Miracidia are reported to survive on average for 9–10 h, depending on the water temperature; with the optimal time for snail exposure being less than 10 h after hatching (Sun et al., 2000). We thus assume the lifespan of 9 h, i.e., $\mu_M^{-1} \approx 10^{-3}$ years. The parasite requires 4–6 weeks in the snails before infectious cercariae are released (Sun et al., 2000). We thus assume the incubation period is 5 weeks, i.e., $\sigma_G^{-1} = 5/52$ years. The cercaria can survive about 2 days (in 20C water) but the survival decreases sharply for higher temperatures (Jones and Brady, 1947). Furthermore, their energy levels are typically depleted within a few hours (Sun et al., 2000). Thus, we estimate the lifespan as about 1/2 day similar to Lopez et al. (2023). Once cercariae enter the definitive host, they require about 5–7 weeks to mature and start producing eggs (Sun et al., 2000). We thus use 6 weeks as the incubation period for both the humans and bovines, i.e., $\sigma_H^{-1} = \sigma_B^{-1} = 6/52$ years.

Humans acquire natural immunity through the presence of dying worms in their bodies (CDC, 2020; Kura et al., 2021). Since the schistosomas live on average 4 years (Doumenge and Mott, 1984), we use $\rho_H^{-1} = 4$ years. Kura et al. (2021) estimated that the immunity lasts about 5 years, i.e., it is lost at a rate $\theta_H = 0.2$ per year.

The shedding rate of eggs is 84,000 eggs per day from an individual carabao (Tenorio and Molina, 2020), i.e., $\eta_B = 3.07 \times 10^7$ eggs per year. The number of eggs shed by the humans was estimated from a study on mice (Cheever et al., 1994) and other small mammals. The worms produce about 1000 eggs per day, but most get caught in the tissue rather than excreted. Based on Cheever et al. (1994) and references therein, we assume the shedding rate is 300 eggs per day, i.e., $\eta_H = 1.1 \times 10^5$ eggs per year. Qian et al. (1997) observed cercaria shedding in snails; the averages were 13 and 26 cercaria per snail per day (depending on the isolate). We adopt the average of the two, 19.5 cercaria per snail per day, which yields the rate $\delta_G = 7.1 \times 10^3$ eggs per snail per year.

The MDA (PZQ) treatment rate, was adopted from Riñon et al. (2022) as $\phi_H = 0.3242$ per year; it was calculated as a rate of administering MDA (once a year), times the efficacy of the treatment (0.999) times the coverage of the treatment (0.3245).

To find values of the transmission rates, we assumed that the controls (avoidance of freshwater) are initially set as $r_H = r_B = 0$ and the population is in the endemic equilibrium. We matched the model predictions with the reported prevalence of infections in humans, bovines and snails as follows. Magalhães et al. (2014) found 718 infections in 35,754 people, giving the overall prevalence $\frac{I_H}{N_H} = 0.02$. There was a regional variation of the prevalence from 0.006 to 0.041 but we will adopt the overall prevalence of 0.02 for our purposes. Fornillos et al. (2019) found a total of 44 infected snails amongst a total of 6279 snails *Oncomelania hupensis quadrasi* giving a total prevalence $\frac{I_G}{N_G} = 0.007$. Based on the location, the prevalence varied from 0 to 1.51%. Jiz et al. (2021) found an almost universal prevalence, 97% of schistosoma infections in their region. Other studies (Gordon et al., 2015; 2012; Olveda et al., 2014; Wu et al., 2010) found the prevalence between 0.51 and 0.91. We thus adopt $\frac{I_B}{N_B} = 0.75$ for our study. With these data and using formulas (25) and (31)–(42), we obtain a set of three equations for three unknowns, β_{H0},β_B, β_{G0}. We used Matlab to solve those equations and obtained

$$\beta_{H0} = 0.1214, \tag{14}$$

$$\beta_G = 1.1255 \times 10^{-6}, \tag{15}$$

$$\beta_{B0} = 8.596. \tag{16}$$

3. Analysis

3.1. Disease-Free equilibrium

The Disease-Free Equilibrium (DFE) is a 13-tuple of constant solutions to the system (1)–(13) for which there is no parasite in the population. Thus, $L_H = I_H = R_H = E = M = L_G = I_G = C = L_B = I_B = 0$. Consequently, $S_H = \frac{\Lambda_H}{\mu_H}$, $S_G = \frac{\Lambda_G}{\mu_G}$, and $S_B = \frac{\Lambda_B}{\mu_B}$.

3.2. Basic reproduction number

The local stability of the DFE will be determined using the basic reproduction number, R_0. We find R_0 by the next-generation matrix method (van den Driessche and Watmough, 2002) as shown in Appendix A. It follows that

$$R_0 = R_0^{EM} R_0^{MG} R_0^{GC} \left(R_0^{CH} R_0^{HE} + R_0^{CB} R_0^{BE}\right), \tag{17}$$

where

$$R_0^{EM} = \frac{\gamma_E}{\gamma_E + \mu_E}, \tag{18}$$

$$R_0^{MG} = \frac{1}{\mu_M}\beta_G\frac{\Lambda_G}{\mu_G}, \tag{19}$$

$$R_0^{GC} = \frac{\sigma_G}{\sigma_G + \mu_G}\frac{1}{\mu_G}\delta_G, \tag{20}$$

$$R_0^{CH} = (1 - r_H)\beta_{H0}\frac{1}{\mu_C}\frac{\Lambda_H}{\mu_H}, \tag{21}$$

$$R_0^{CB} = (1 - r_B)\beta_{B0}\frac{1}{\mu_C}\frac{\Lambda_B}{\mu_B}, \tag{22}$$

$$R_0^{HE} = \frac{\sigma_H}{\sigma_H + \mu_H}\frac{1}{\phi_H + \rho_H + \mu_H}\eta_H, \tag{23}$$

$$R_0^{BE} = \frac{\sigma_B}{\sigma_B + \mu_B}\frac{1}{\mu_B}\eta_B. \tag{24}$$

Note that R_0^{EM} corresponds to the number of miracidia resulting from a single egg (as the egg hatches with probability $\frac{\gamma_E}{\gamma_E+\mu_E}$). Similarly, R_0^{MG} corresponds to the number of snails a single miracidia can infect on average; $\frac{1}{\mu_M}$ is the expected time the miracidia lives and during that time it infects the snails at rate $\beta_G N_G$. Using analogous reasoning, we see that R_0^{GC} is the expected number of cercaria from a single latently infected snail, R_0^{CH} and R_0^{CB} are the expected numbers of humans and bovines, respectively, infected by a single cercaria. Finally, R_0^{HE} and R_0^{BE} are the expected number of eggs produced from a single latently infected human and bovine, respectively.

It follows that when $R_0 < 1$, then, on average, one egg generates fewer than one new egg in the next generation, preventing schistosomiasis from spreading. Formally, when $R_0 < 1$, then DFE is locally asymptotically stable (van den Driessche and Watmough, 2002). While we do not explicitly investigate the global stability of DFE, we believe that the global stability of DFE for $R_0 < 1$ can be shown by constructing a suitable Lyapunov function as done for a similar model in Kadaleka et al. (2021b).

By plugging our parameter values into (17), we get $R_0 \approx 4.42$ at the baseline.

3.3. Endemic equilibrium

The endemic equilibrium (EE) is an equilibrium where the parasite is still present in the population. The calculations are outlined in Appendix B. It follows that

$$L_G^* = y\frac{\mu_C}{R_0^{GC}(\sigma_G + \mu_G)} \tag{25}$$

where y is a positive roots of a quadratic equation

$$ay^2 + by + c = 0 \tag{26}$$

for

$$a = R_0^{EM}R_0^{MG}R_0^{GC}\left(\frac{R_0^{CH}R_0^{HE}\beta_B}{\mu_B} + \frac{R_0^{CB}R_0^{BE}\beta_H x_H}{\sigma_H + \mu_H}\right)\frac{\mu_C}{N_G^* R_0^{GC}\mu_G} + \frac{\beta_B\beta_H x_H}{(\sigma_H + \mu_H)\mu_B}, \tag{27}$$

$$b = -R_0^{EM}R_0^{MG}R_0^{GC}\left(\frac{R_0^{CH}R_0^{HE}\beta_B}{\mu_B} + \frac{R_0^{CB}R_0^{BE}\beta_H x_H}{\sigma_H + \mu_H} + \frac{(R_0^{CH}R_0^{HE} + R_0^{CB}R_0^{BE})\mu_C}{N_G^* R_0^{GC}\mu_G}\right) - \left(\frac{\beta_B}{\mu_B} + \frac{\beta_H x_H}{\sigma_H + \mu_H}\right), \tag{28}$$

$$c = 1 - R_0, \tag{29}$$

$$x_H = 1 + \frac{\sigma_H}{\phi_H + \rho_H + \mu_H} + \frac{\sigma_H\rho_H}{(\mu_H + \theta_H)(\phi_H + \rho_H + \mu_H)}. \tag{30}$$

Since the constant coefficient of the quadratic equation is $c = 1 - R_0$ and the leading coefficient $a > 0$, it follows that the (26) has a positive root if and only if $R_0 > 1$.

Once L_G^* is given by (25), the other compartments are evaluated by

$$L_H^* = \frac{R_0^{CH}R_0^{GC}L_G^*}{\beta_H x_H\frac{1}{\mu_C}R_0^{GC}L_G^* + \frac{\sigma_H + \mu_H}{\sigma_G + \mu_G}}, \tag{31}$$

$$L_B^* = \frac{R_0^{CB}R_0^{GC}L_G^*}{\beta_B\left(1 + \frac{\sigma_B}{\mu_B}\right)\frac{1}{\mu_C}R_0^{GC}L_G^* + \frac{\sigma_B + \mu_B}{\sigma_G + \mu_G}}, \tag{32}$$

$$I_G^* = \frac{\sigma_G}{\mu_G}L_G^*, \tag{33}$$

$$C^* = \frac{\delta_G}{\mu_C}I_G^* = \frac{\delta_G}{\mu_C}\frac{\sigma_G}{\mu_G}L_G^*, \tag{34}$$

$$I_B^* = \frac{\sigma_B}{\mu_B}L_B^*, \tag{35}$$

$$I_H^* = \frac{\sigma_H}{\phi_H + \rho_H + \mu_H}L_H^*, \tag{36}$$

$$R_H^* = \frac{\rho_H}{\mu_H + \theta_H}I_H^*, \tag{37}$$

$$S_H^* = \frac{\Lambda_H}{\mu_H} - \left(L_H^* + I_H^* + R_H^*\right), \tag{38}$$

Table 1
Parameter notation and values. The times are in years, the rates are per capita per year. The details behind estimating the parameter values are shown in Section 2.3.

Symbol	Description	Value	Reference
Λ_H	Birth rate of humans	0.022	The World Bank (2021a)
Λ_G	Birth rate of snails	3.54	Ishikawa et al. (2006)
Λ_B	Birth rate of carabaos	0.244	Riñon et al. (2022)
μ_H	Natural death rate of humans	0.007	The World Bank (2021b)
μ_G^{-1}	Lifespan of snails	5/12	Australian Government (2017)
μ_B	Natural death rate of carabaos	0.2548	Mingala and Gundran (2008)
μ_E^{-1}	Lifespan of eggs	1.5/52	Colley et al. (2015)
μ_M^{-1}	Lifespan of miracidia	0.001	Sun et al. (2000)
μ_C^{-1}	Lifespan of cercariae	0.5/365	Whitfield et al. (2003)
β_{H0}	Transmission rate in humans at the baseline	0.1214	Fitted
r_H	Control method, proportion of time the human contact with freshwater is avoided (compared to the baseline)	variable	Assumed to be the same as r_B
β_H	Transmission rate in humans (with control)	$(1-r_H)\beta_{H0}$	Assumed
β_G	Transmission rate in snails	1.1255×10^{-6}	Fitted
β_{B0}	Transmission rate in carabaos without control	8.596	Fitted
r_B	Control method, proportion of time the human contact with freshwater is avoided (compared to the baseline)	variable	Assumed 0 at baseline
β_B	Transmission rate in carabaos (with control)	$(1-r_B)\beta_{B0}$	Assumed
ρ_H^{-1}	Schistosoma egg production period	4	Doumenge and Mott (1984)
θ_H	Rate of losing immunity	0.2	Kura et al. (2021)
ϕ_H	MDA (PZQ) treatment rate of humans	0.3242	Olliaro et al. (2020); Riñon et al. (2022)
σ_H^{-1}	Schistosoma latency periods in humans	6/52	Colley et al. (2014)
σ_G^{-1}	Schistosoma latency periods in snails	5/52	Sun et al. (2000)
σ_B^{-1}	Schistosoma latency periods in carabaos	6/52	Yang et al. (2012)
η_H	Shedding rate of eggs for humans	1.1×10^5	Cheever et al. (1994)
η_B	Shedding rate of eggs for carabaos	3.07×10^7	Tenorio and Molina (2020)
γ_E	Hatching rate of miracidia	365/2	Wanlop et al. (2022)
δ_G	Cercariae release rate	7100	Qian et al. (1997)

$$S_B^* = \frac{\Lambda_B}{\mu_B} - \left(L_B^* + I_B^*\right), \tag{39}$$

$$S_G^* = \frac{\Lambda_G}{\mu_G} - \left(L_G^* + I_G^*\right), \tag{40}$$

$$E^* = \frac{\eta_H I_H^* + \eta_B I_B^*}{\gamma_E + \mu_E}, \tag{41}$$

Table 2
Sensitivity index of R_0 for different parameters.

Parameters	Sensitivity indices
Λ_G	1
β_G	1
δ_G	1
Λ_B	0.99993
β_{B0}	0.99993
η_B	0.99993
σ_G	0.1875
γ_E	0.15963
σ_B	0.028564
Λ_H	7.4914e-05
β_{H0}	7.4914e-05
η_H	7.4914e-05
σ_H	6.0458e-08
θ_H	0
r_H	0
r_B	0
ρ_H	− 3.2224e-05
ϕ_H	− 4.1788e-05
μ_H	− 7.5877e-05
μ_E	− 0.15963
μ_M	− 1
μ_C	− 1
μ_B	− 2.0284
μ_G	− 2.1875

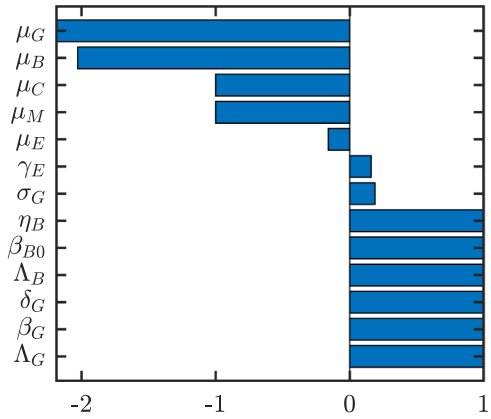

Fig. 3. Sensitivity indices of R_0 on various parameters; only the parameters for which the absolute value of the sensitivity index is larger than 0.05 are shown.

$$M^* = \frac{\gamma_E}{\mu_M} E^*. \tag{42}$$

We did not explicitly consider stability analysis of the endemic equilibrium. However, we believe that the equilibrium is globally asymptotically stable when $R_0 > 1$; this kind of result has been shown, for example, in Diaby (2015). Similarly, Madubueze et al. (2022a) also showed the stability of the endemic equilibrium for a similar system using the center manifold theory by Castillo-Chavez et al. (2002).

4. Results

At the baseline, the reproduction number is $R_0 \approx 4.42$, meaning that in a completely susceptible population, a typical fertile adult worm would on average produce 4.42 female worms during its life.

We conducted sensitivity analysis of R_0 based on Arriola and Hyman (2009); the sensitivity index of R_0 on a parameter p is defined as $\frac{p}{R_0}.\frac{\partial R_0}{\partial p}$. Table 2 shows the numerical values of the sensitivity indices and Fig. 3 shows the indices graphically for all the significant parameters. The actual dependence of R_0 on r_B and r_H is plotted in Fig. 4 and the dependence of R_0 on all other parameters can be seen in Appendix C.

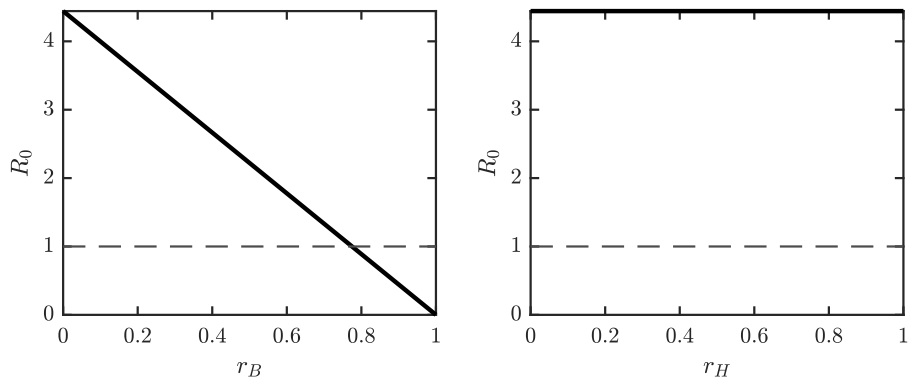

Fig. 4. Dependence of R_0 on r_B (left) and r_H (right). Parameters that are not varied are as specified in Table 1. Left: As r_B increases, R_0 decreases and eventually, for large enough r_B, $R_0 < 1$. This means that schistosimiasis can be eliminated by reducing bovine contact with water. In contrast, R_0 is almost constant in r_H, i.e., schistosomiasis cannot be eliminated by reducing human contact with water.

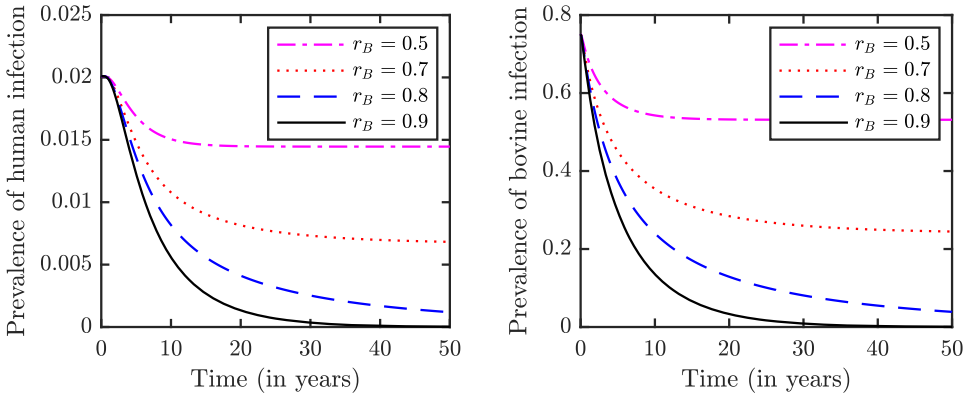

Fig. 5. The evolution of the prevalence of human (left) and bovine (right) infection for different values of r_B based on the numerical simulation of the system (1)–(13) with initial conditions at the current endemic equilibrium ($I_H/N_H \approx 0.02, I_G/N_G \approx 0.007, I_B/N_B \approx 0.75$). The parameter values are as specified in Table 1.

For completeness, we also performed uncertainty and sensitivity indices based on LHS-PRCC sampling scheme based on Blower and Dowlatabadi (1994), similarly to what has been done in Madubueze et al. (2022a). The results are qualitatively similar to the sensitivity analysis by Arriola and Hyman (2009) and are shown in Appendix C in Figs. 6–10.

The effect of snail-related parameters is most profound. Decreasing the number of snails, i.e., Λ_G/μ_G or decreasing the transmission rate β_G would result in significant decrease of R_0. The effect of human related parameters on the reproduction number is negligible. The control strategy of freshwater avoidance by humans has almost no effect on R_0. This is in sharp contrast with the same control strategy for carabaos.

We are primarily interested to see whether it is possible to eliminate schistosomiasis by avoiding contact with fresh water. Since the effects of r_H on R_0 are negligible, we set, for simplicity, $r_H = r_B$. Then, we get, by (17),

$$R_0(r_B) = (1 - r_B)R_0(0). \tag{43}$$

Thus, to eliminate schistosomiasis, we need $r_B > r_B^{EL}$, where

$$r_B^{EL} = 1 - \frac{1}{R_0(0)} \approx 0.77. \tag{44}$$

In other words, at least 77% of the bovine population must avoid contaminated freshwater sources in order to break the schistosomiasis cycle and eliminate the disease.

Fig. 5 demonstrates the time component of the elimination. If the contact between bovines and freshwater is reduced by about 80%, the prevalence of human infection would decrease by over 50% approximately every 10 years. In other words, the current prevalence of 2% could be reduced to under 1% in 10 years and to under 0.5% in 20 years from now. Reducing the contact between bovines and water by 90% would speed up the elimination even more; the prevalence of 0.5% could be reached in about 10 years. Even a contact reduction by 70% still results in disease prevalence under 1% in about 10 years although this reduction would not eliminate schistosomiasis completely. On the other hand, we can see that reducing the contact by 50% will reduce the disease prevalence by about 25%. While this effect could be felt within 10 years, no further significant decrease of prevalence would follow afterwards.

5. Conclusion

We formulated and analyzed a compartmental model depicting schistosomiasis disease dynamics in the Philippines. We expanded on existing schistosomiasis models to consider the different life stages of *S. japonicum*, the human, snail, and bovine populations, latent periods of *S. japonicum* in the three host populations, and recovery and acquired immunity in humans.

We derived the formula for the reproduction number and, based on model calibrations, we estimated the reproduction number to be approximately 4.42. Our strategy for effectively combating disease transmission focuses on reducing infection rates by reducing the contacts with freshwater sources. We have shown that the reduction of bovine contact with water by about 77% can eliminate schistosomiasis. While this reduction seems significant, we argue that it could be achieved by increasing the mechanization level which is already planned in the Philippines.

Our numerical simulations also demonstrate that the effects of the contact reduction could be felt within 10 years. The water contact reduction does not even have to be the full 77% required for the complete elimination. When the water contact reduction is 50%, the disease prevalence in humans will drop from the current 2% to about 1.5% in 10 years (but will not change much afterwards). The water contact reduction by 70% would achieve the disease prevalence under 1% in slightly more than 10 years.

Overall, we argue that the potential elimination of schistosomiasis should be considered as an additional benefit of the mechanization efforts in the Philippines.

Our proposed compartmental model extends previous models of schistosomiasis in the Philippines. Chen et al. (2010) use a conceptually similar model, although they involve only susceptible and infectious compartments for each population and did not explicitly consider miracidia and cercariae. The model in Ishikawa et al. (2006) is similar, but considers rats instead of bovines and does not consider a recovered compartment. On the other hand, their model considers low and high shedding snails.

For simplicity, we considered only human, bovine and snail populations. However, other hosts are involved in the transmission and incorporating those hosts would make the model more precise. At the same time, Rudge et al. (2013) showed that bovine is the most critical to transmission. Thus, incorporating other hosts thus does not substantially alter the qualitative results; it would only result in the necessity for even bigger reduction of bovine contact with water to eliminate the disease. Also, for simplicity we assumed a simple relationship between the density of miracidia, the force of infection in snails as well as between the density of cercaria and the force of infection in humans and bovines. Chiyaka and Garira (2009) considered Holling II type response, Gao et al. (2011) considered Holling III type response. These differences could play a role in the model calibration, but overall should not influence the analysis of the reproduction number at the disease-free equilibrium. Finally, in our model, we assumed that seasonal and weather variations do not affect the snail, miracidia, and cercariae populations. Incorporating seasonality would significantly improve the model realism.

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CRediT authorship contribution statement

Yuan-Jen Kuo: Formal analysis, Investigation, Software, Writing – original draft. **Gian Paras:** Formal analysis, Investigation, Software, Writing – original draft. **Taiyo Tagami:** Formal analysis, Investigation, Software, Writing – original draft. **Claire Yi:** Formal analysis, Investigation, Software, Writing – original draft. **Leslie J Camacho Aquino:** Conceptualization, Formal analysis, Funding acquisition, Methodology, Project administration, Supervision, Writing – original draft, Writing – review & editing. **Hyunju Oh:** Conceptualization, Formal analysis, Funding acquisition, Methodology, Project administration, Supervision, Writing – original draft, Writing – review & editing. **Jan Rychtář:** Conceptualization, Formal analysis, Software, Funding acquisition, Methodology, Supervision, Writing – original draft, Writing – review & editing. **Dewey Taylor:** Conceptualization, Formal analysis, Funding acquisition, Methodology, Supervision, Writing – original draft, Writing – review & editing.

Declaration of Competing Interest

The authors declare no competing interests

Data availability

No data was used for the research described in the article.

Appendix A. Basic reproduction number

We follow the next-generation matrix procedure described in van den Driessche and Watmough (2002). The compartments associated with infection in our model are $\{L_H, I_H, L_G, I_G, L_B, I_B, C, E, M\}$ and we will keep them in this order.

The rate of appearance of new infections are

$$\mathscr{F} = \begin{bmatrix} \beta_H S_H C \\ 0 \\ \beta_G S_G M \\ 0 \\ \beta_B S_B C \\ 0 \\ \delta_G I_G \\ \eta_H I_H + \eta_B I_B \\ 0 \end{bmatrix} \tag{45}$$

and the net outflow (outflow minus inflow) from the compartments carrying the pathogen is

$$\mathscr{V} = \begin{bmatrix} \sigma_H L_H + \mu_H L_H \\ \phi_H I_H + \rho_H I_H + \mu_H I_H - \sigma_H L_H \\ \sigma_G L_G + \mu_G L_G \\ \mu_G I_G - \sigma_G L_G \\ \sigma_B L_B + \mu_B L_B \\ \mu_B I_B - \sigma_B L_B \\ \mu_C C \\ \mu_E E + \gamma_E E \\ \mu_M M - \gamma_E E \end{bmatrix} \tag{46}$$

This gives the Jacobian matrices

$$F = \begin{bmatrix} 0 & 0 & 0 & 0 & 0 & 0 & \frac{\beta_H \Lambda_H}{\mu_H} & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & \frac{\beta_G \Lambda_G}{\mu_G} \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & \frac{\beta_B \Lambda_B}{\mu_B} & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & \delta_G & 0 & 0 & 0 & 0 & 0 \\ 0 & \eta_H & 0 & 0 & 0 & \eta_B & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \end{bmatrix} \tag{47}$$

and

$$V = \begin{bmatrix} \sigma_H + \mu_H & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ -\sigma_H & \phi_H + \rho_H + \mu_H & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & \sigma_G + \mu_G & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & -\sigma_G & \mu_G & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & \sigma_B + \mu_B & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & -\sigma_B & \mu_B & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & \mu_C & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & \mu_E + \gamma_E & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & -\gamma_E & \mu_M \end{bmatrix} \tag{48}$$

Thus,

$$V^{-1} = \begin{bmatrix} \frac{1}{\sigma_H + \mu_H} & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ \frac{\sigma_H}{(\phi_H + \rho_H + \mu_H)(\sigma_H + \mu_H)} & \frac{1}{\phi_H + \rho_H + \mu_H} & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & \frac{1}{\sigma_G + \mu_G} & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & \frac{\sigma_G}{\mu_G(\mu_G + \sigma_G)} & \frac{1}{\mu_G} & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & \frac{1}{\sigma_B + \mu_B} & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & \frac{\sigma_B}{\mu_B(\sigma_B + \mu_B)} & \frac{1}{\mu_B} & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & \frac{1}{\mu_C} & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & \frac{1}{\mu_E + \gamma_E} & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & \frac{\gamma_E}{\mu_M(\mu_E + \gamma_E)} & \frac{1}{\mu_M} \end{bmatrix} \tag{49}$$

and

$$FV^{-1} = \begin{bmatrix} 0 & 0 & 0 & 0 & 0 & 0 & \frac{\beta_H \Lambda_H}{\mu_C \mu_H} & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & \frac{\gamma_E \beta_G \Lambda_G}{\mu_G \mu_M (\mu_E + \gamma_E)} & \frac{\beta_G \Lambda_G}{\mu_M \mu_G} \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & \frac{\beta_B \Lambda_B}{\mu_B \mu_C} & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & \frac{\delta_G \sigma_G}{\mu_G (\sigma_G + \mu_G)} & \frac{\delta_G}{\mu_G} & 0 & 0 & 0 & 0 & 0 \\ \frac{\eta_H \sigma_H}{(\sigma_H + \mu_H)(\phi_H + \rho_H + \mu_H)} & \frac{\eta_H}{\phi_H + \rho_H + \mu_H} & 0 & 0 & \frac{\eta_B \sigma_B}{\mu_B (\sigma_B + \mu_B)} & \frac{\eta_B}{\mu_B} & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \end{bmatrix} \tag{50}$$

The spectral radius of FV^{-1}, is given by

$$\rho\left(FV^{-1}\right) = \sqrt[4]{R_0^{EM} R_0^{MG} R_0^{GC} \left(R_0^{CH} R_0^{HE} + R_0^{CB} R_0^{BE}\right)} \tag{51}$$

where

$$R_0^{EM} = \frac{\gamma_E}{\gamma_E + \mu_E}, \tag{52}$$

$$R_0^{MG} = \frac{1}{\mu_M} \beta_G \frac{\Lambda_G}{\mu_G}, \tag{53}$$

$$R_0^{GC} = \frac{\sigma_G}{\sigma_G + \mu_G} \frac{1}{\mu_G} \delta_G, \tag{54}$$

$$R_0^{CH} = \frac{1}{\mu_C} \beta_H \frac{\Lambda_H}{\mu_H}, \tag{55}$$

$$R_0^{CB} = \frac{1}{\mu_C} \beta_B \frac{\Lambda_B}{\mu_B}, \tag{56}$$

$$R_0^{HE} = \frac{\sigma_H}{\sigma_H + \mu_H} \frac{1}{\phi_H + \rho_H + \mu_H} \eta_H, \tag{57}$$

$$R_0^{BE} = \frac{\sigma_B}{\sigma_B + \mu_B} \frac{1}{\mu_B} \eta_B. \tag{58}$$

Because we model the life-cycle of schistosoma through four stages (eggs/miracidia, snails, cercaria, humans/bovines), this yields

$$R_0 = R_0^{EM} R_0^{MG} R_0^{GC} \left(R_0 C H R_0^{HE} + R_0^{CB} R_0^{BE}\right). \tag{59}$$

Note that R_0^{EM} corresponds to the number of miracidia resulting from a single egg (as the egg hatches with probability $\frac{\gamma_E}{\gamma_E + \mu_E}$. Similarly, R_0^{MG} corresponds to the number of snails a single miracidia can infect on average; $\frac{1}{\mu_M}$ is the expected time the miracidia lives and during that time it infects the snails at rate $\beta_G N_G$. Using analogous reasoning, we see that $R_0 XY$ is the expected number of parasites at stage Y caused by a single parasite at stage X.

Appendix B. Solving for endemic equilibrium

The endemic equilibrium, $E^* = (S_H^*, L_H^*, I_H^*, R_H^*, E^*, M^*, S_G^*, L_G^*, I_G^*, C^*, S_B^*, L_B^*, I_B^*)$ is found by setting the right-hand sides of the equations to 0 and solving the resulting system of algebraic equations.

Separately adding the equations for the humans, snails, and bovines, yields

$$0 = \Lambda_H - \mu_H N_H^*, \tag{60}$$

$$0 = \Lambda_G - \mu_G N_G^*, \tag{61}$$

$$0 = \Lambda_B - \mu_B N_B^*, \tag{62}$$

where

$$N_H = S_H + L_H + I_H + R_H, \tag{63}$$

$$N_G = S_G + L_G + I_G, \text{and} \tag{64}$$

$$N_B = S_B + L_B + I_B \tag{65}$$

are the total population sizes. Thus, at equilibrium,

$$N_H^* = \frac{\Lambda_H}{\mu_H}, \tag{66}$$

$$N_G^* = \frac{\Lambda_G}{\mu_G}, \tag{67}$$

$$N_B^* = \frac{\Lambda_B}{\mu_B}. \tag{68}$$

We also easily find

$$E^* = \frac{\eta_H I_H^* + \eta_B I_B^*}{\gamma_E + \mu_E}, \tag{69}$$

$$M^* = \frac{\gamma_E}{\mu_M} E^* = \frac{\gamma_E \left(\eta_H I_H^* + \eta_B I_B^*\right)}{\mu_M(\gamma_E + \mu_E)}, \tag{70}$$

$$I_G^* = \frac{\sigma_G}{\mu_G} L_G^*, \tag{71}$$

$$C^* = \frac{\delta_G}{\mu_C} I_G^* = \frac{\delta_G}{\mu_C} \frac{\sigma_G}{\mu_G} L_G^*, \tag{72}$$

$$I_B^* = \frac{\sigma_B}{\mu_B} L_B^*, \tag{73}$$

$$I_H^* = \frac{\sigma_H}{\phi_H + \rho_H + \mu_H} L_H^*, \tag{74}$$

$$R_H^* = \frac{\rho_H}{\mu_H + \theta_H} I_H^* = \frac{\sigma_H \rho_H}{(\mu_H + \theta_H)(\phi_H + \rho_H + \mu_H)} L_H^*. \tag{75}$$

Thus,

$$S_H^* = N_H^* - \left(L_H^* + I_H^* + R_H^*\right) \tag{76}$$

$$= N_H^* - L_H^* x_H \tag{77}$$

where

$$x_H = 1 + \frac{\sigma_H}{\phi_H + \rho_H + \mu_H} + \frac{\sigma_H \rho_H}{(\mu_H + \theta_H)(\phi_H + \rho_H + \mu_H)}. \tag{78}$$

Similarly,

$$S_B^* = N_B^* - \left(L_B^* + I_B^*\right) = N_B^* - L_B^* \left(1 + \frac{\sigma_B}{\mu_B}\right), \tag{79}$$

$$S_G^* = N_G^* - \left(L_G^* + I_G^*\right) = N_G^* - L_G^* \left(1 + \frac{\sigma_G}{\mu_G}\right). \tag{80}$$

By (2) and (72),

$$0 = \beta_H S_H^* . \frac{\delta_G \sigma_G}{\mu_C \mu_G} L_G^* - (\sigma_H + \mu_H) L_H^*. \tag{81}$$

By (77), this yields

$$0 = \beta_H \left(N_H^* - L_H^* x_H\right) . \frac{\delta_G \sigma_G}{\mu_C \mu_G} L_G^* - (\sigma_H + \mu_H) L_H^* \tag{82}$$

and thus

$$L_H^* = \frac{\beta_H N_H^* \frac{\delta_G \sigma_G}{\mu_C \mu_G} L_G^*}{\beta_H x_H \frac{\delta_G \sigma_G}{\mu_C \mu_G} L_G^* + \sigma_H + \mu_H} = \frac{R_0^{CH} R_0^{GC} L_G^*}{\beta_H x_H \frac{1}{\mu_C} R_0^{GC} L_G^* + \frac{\sigma_H + \mu_H}{\sigma_G + \mu_G}}. \tag{83}$$

By (12) and (72),

$$0 = \beta_B S_B^* \cdot \frac{\delta_G \sigma_G}{\mu_C \mu_G} L_G^* - (\sigma_B + \mu_B) L_B^*. \tag{84}$$

By (79), this yields

$$0 = \beta_B \left[N_B^* - L_B^* \left(1 + \frac{\sigma_B}{\mu_B} \right) \right] \cdot \frac{\delta_G \sigma_G}{\mu_C \mu_G} L_G^* - (\sigma_B + \mu_B) L_B^* \tag{85}$$

and thus

$$L_B^* = \frac{\beta_B N_B^* \frac{\delta_G \sigma_G}{\mu_C \mu_G} L_G^*}{\beta_B \left(1 + \frac{\sigma_B}{\mu_B} \right) \frac{\delta_G \sigma_G}{\mu_C \mu_G} L_G^* + \sigma_B + \mu_B} = \frac{R_0^{CB} R_0^{GC} L_G^*}{\beta_B \left(1 + \frac{\sigma_B}{\mu_B} \right) \frac{1}{\mu_C} R_0^{GC} L_G^* + \frac{\sigma_B + \mu_B}{\sigma_G + \mu_G}}. \tag{86}$$

By (9),

$$0 = \beta_G S_G^* \frac{\gamma_E}{\mu_M (\gamma_E + \mu_E)} \left(\frac{\eta_H \sigma_H}{\phi_H + \rho_H + \mu_H} L_H^* + \frac{\eta_B \sigma_B}{\mu_B} L_B^* \right) - (\sigma_G + \mu_G) L_G^*. \tag{87}$$

Substituting formulas for S_G^*, L_H^* and L_B^* yields

$$\begin{aligned} 0 = \beta_G \left[N_G^* - L_G^* \left(1 + \frac{\sigma_G}{\mu_G} \right) \right] \frac{\gamma_E}{\mu_M (\gamma_E + \mu_E)} \left(\frac{\eta_H \sigma_H}{\phi_H + \rho_H + \mu_H} \left[\frac{R_0^{CH} R_0^{GC} L_G^*}{\beta_H x_H \frac{1}{\mu_C} R_0^{GC} L_G^* + \frac{\sigma_H + \mu_H}{\sigma_G + \mu_G}} \right] \right. \\ \left. + \frac{\eta_B \sigma_B}{\mu_B} \left[\frac{R_0^{CB} R_0^{GC} L_G^*}{\beta_B \left(1 + \frac{\sigma_B}{\mu_B} \right) \frac{1}{\mu_C} R_0^{GC} L_G^* + \frac{\sigma_B + \mu_B}{\sigma_G + \mu_G}} \right] \right) - (\sigma_G + \mu_G) L_G^*. \end{aligned} \tag{88}$$

This yields either $L_G^* = 0$ or we can substitute for appropriate R_0s and get

$$0 = R_0^{EM} R_0^{MG} R_0^{GC} \left(1 - \frac{L_G^*}{N_G^*} \frac{\sigma_G + \mu_G}{\mu_G} \right) \left(\frac{R_0^{CH} R_0^{HE}}{\frac{\beta_H x_H R_0^{GC} L_G^* (\sigma_G + \mu_G)}{\mu_C (\sigma_H + \mu_H)} + 1} + \frac{R_0^{CB} R_0^{BE}}{\frac{\beta_B R_0^{GC} L_G^* (\sigma_G + \mu_G)}{\mu_B \mu_C} + 1} \right) - 1. \tag{89}$$

Temporarily substitute $y = R_0^{GC} L_G^* (\sigma_G + \mu_G)/\mu_C$ and we get

$$0 = R_0^{EM} R_0^{MG} R_0^{GC} \left(1 - \frac{y}{N_G^* R_0^{GC}} \frac{\mu_C}{\mu_G} \right) \left(\frac{R_0^{CH} R_0^{HE}}{\frac{\beta_H x_H y}{\sigma_H + \mu_H} + 1} + \frac{R_0^{CB} R_0^{BE}}{\frac{\beta_B y}{\mu_B} + 1} \right) - 1. \tag{90}$$

This yields

$$\begin{aligned} 0 = R_0^{EM} R_0^{MG} R_0^{GC} \left(1 - \frac{y}{N_G^* R_0^{GC}} \frac{\mu_C}{\mu_G} \right) \left(R_0^{CH} R_0^{HE} \left(\frac{\beta_B y}{\mu_B} + 1 \right) + R_0^{CB} R_0^{BE} \left(\frac{\beta_H x_H y}{\sigma_H + \mu_H} + 1 \right) \right) \\ - \left(\frac{\beta_H x_H y}{\sigma_H + \mu_H} + 1 \right) \left(\frac{\beta_B y}{\mu_B} + 1 \right) \end{aligned} \tag{91}$$

which becomes a quadratic equation

$$a y^2 + b y + c = 0 \tag{92}$$

where

$$a = R_0^{EM} R_0^{MG} R_0^{GC} \left(\frac{R_0^{CH} R_0^{HE} \beta_B}{\mu_B} + \frac{R_0^{CB} R_0^{BE} \beta_H x_H}{\sigma_H + \mu_H} \right) \frac{\mu_C}{N_G^* R_0^{GC} \mu_G} + \frac{\beta_B \beta_H x_H}{(\sigma_H + \mu_H) \mu_B}, \tag{93}$$

$$b = -R_0^{EM} R_0^{MG} R_0^{GC} \left(\frac{R_0^{CH} R_0^{HE} \beta_B}{\mu_B} + \frac{R_0^{CB} R_0^{BE} \beta_H x_H}{\sigma_H + \mu_H} + \frac{\left(R_0^{CH} R_0^{HE} + R_0^{CB} R_0^{BE}\right) \mu_C}{N_G^* R_0^{GC} \mu_G} \right) - \left(\frac{\beta_B}{\mu_B} + \frac{\beta_H x_H}{\sigma_H + \mu_H} \right), \tag{94}$$

$$c = 1 - R_0. \tag{95}$$

When y is solved from (92), we have

$$L_G^* = \frac{y \mu_C}{R_0^{GC} (\sigma_G + \mu_G)}. \tag{96}$$

Appendix C. Sensitivity Graphs

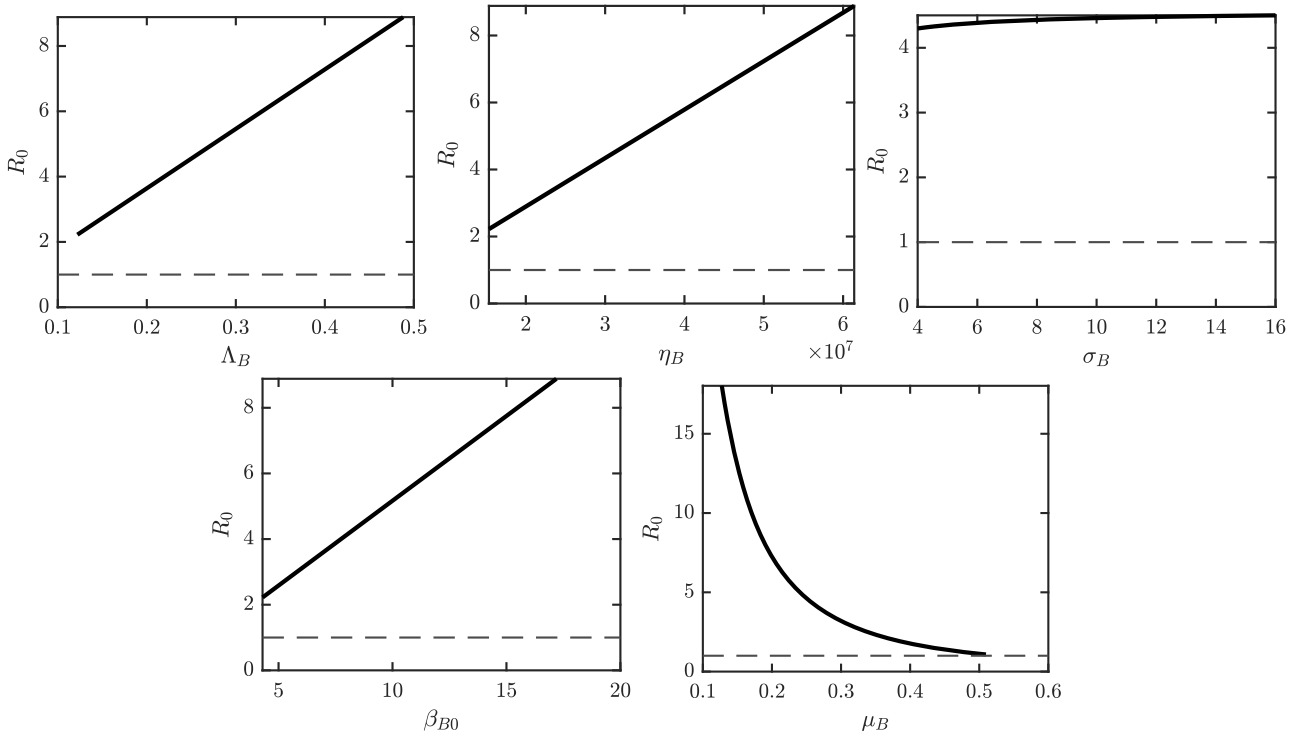

Fig. 6. Dependence of R_0 on parameters related to bovines. Dependence of R_0 on r_B was already shown in Fig. 4. Parameters that are not varied are as in Table 1.

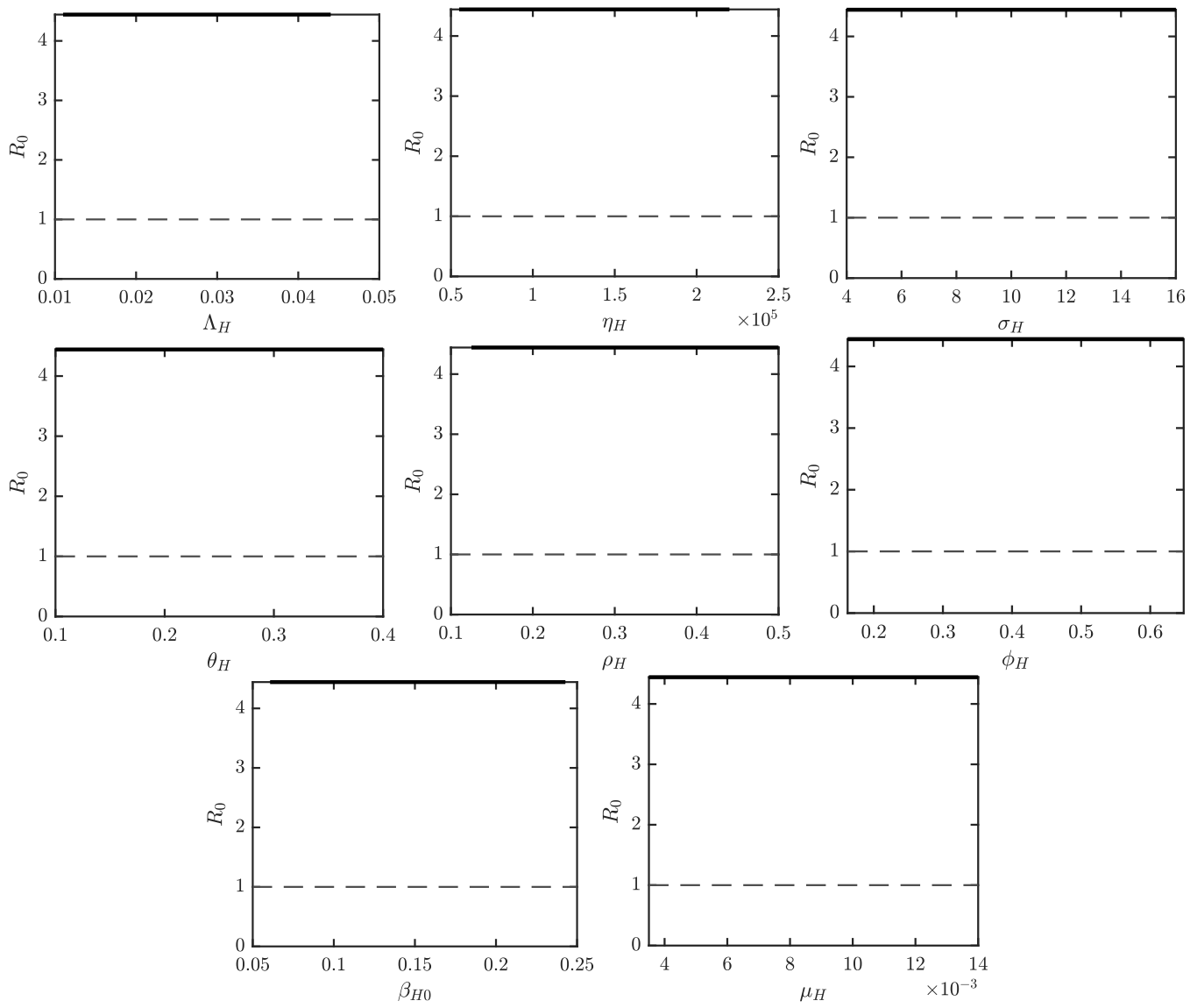

Fig. 7. Dependence of R_0 on parameters related to humans; R_0 is nearly constant with respect to all of them. Dependence of R_0 on r_H was already shown in Fig. 4. Parameters that are not varied are as in Table 1.

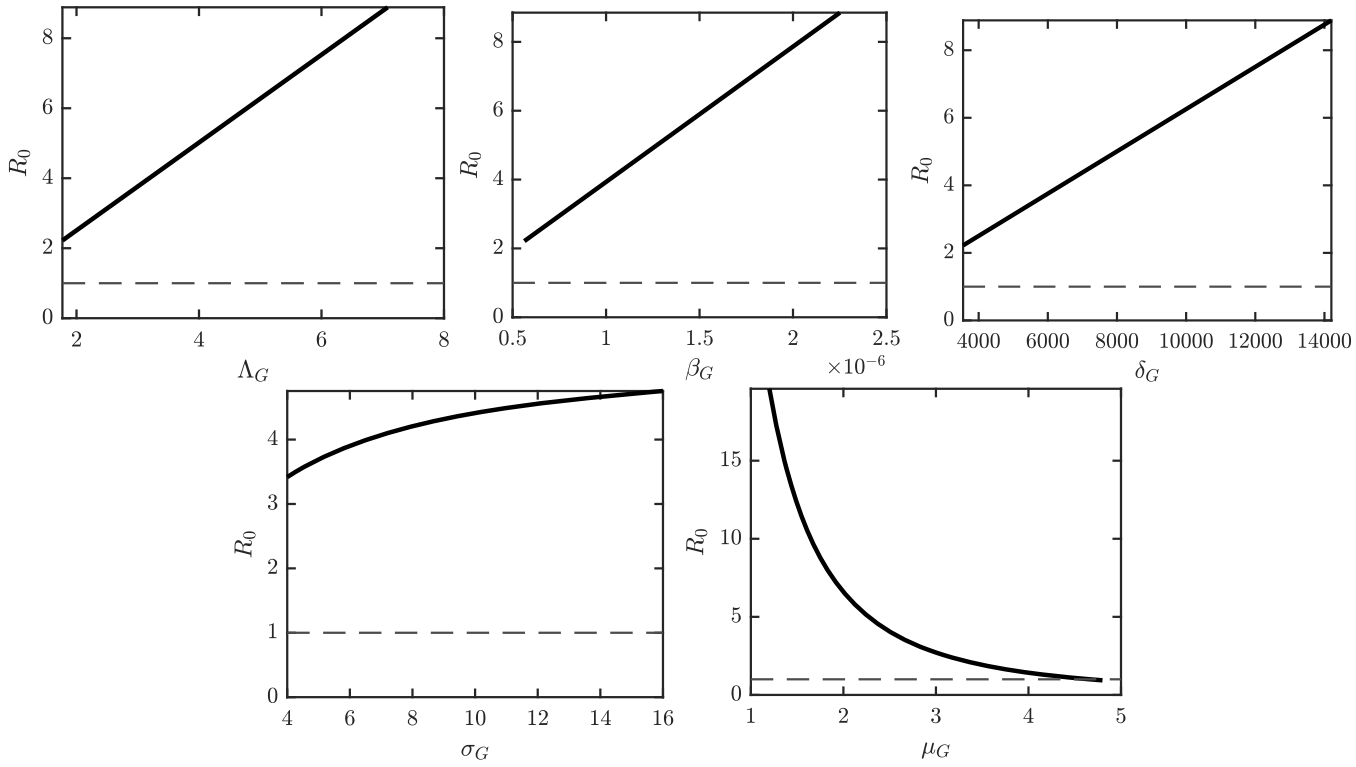

Fig. 8. Dependence of R_0 on parameters related to snails. Parameters that are not varied are as in Table 1.

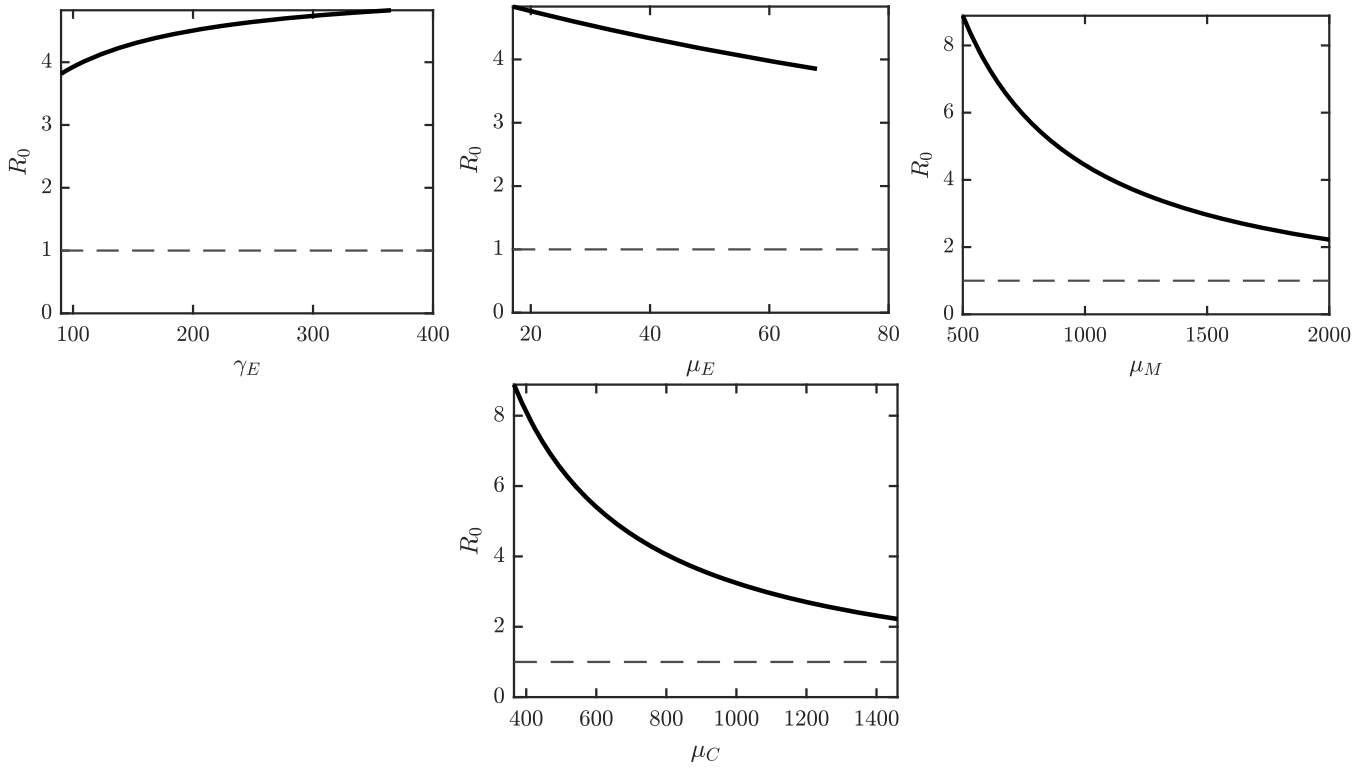

Fig. 9. Dependence of R_0 on parameters related to free ranging stages of the parasite. Parameters that are not varied are as in Table 1.

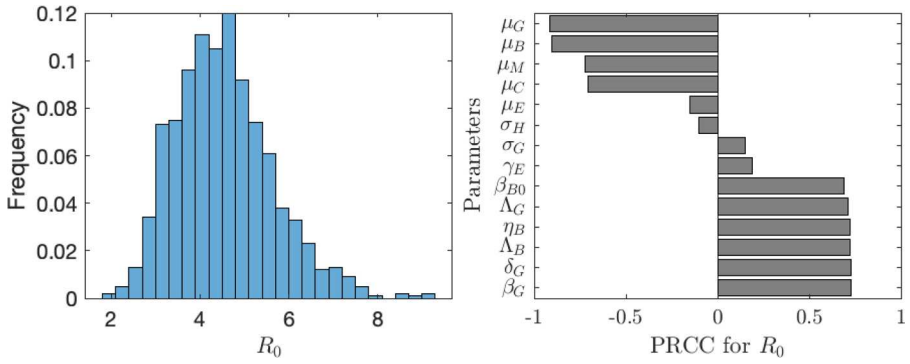

Fig. 10. Uncertainty and sensitivity indices based on LHS-PRCC sampling scheme based on Blower and Dowlatabadi (1994). Only the parameters for which the absolute value of the sensitivity index is larger than 0.05 are shown.

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