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Prevalence-based modeling approach of schistosomiasis: global stability analysis and integrated control assessment

M. A. Aziz-Alaoui[1] · Jean M.-S. Lubuma[2] · Berge Tsanou[2,3,4,5]

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Abstract
A system of nonlinear differential equations is proposed to assess the effects of prevalence-dependent disease contact rate, pathogen's shedding rates, and treatment rate on the dynamics of schistosomiasis in a general setting. The decomposition techniques by Vidyasagar and the theory of monotone systems are the main ingredients to deal completely with the global asymptotic analysis of the system. Precisely, a threshold quantity for the analysis is derived and the existence of a unique endemic equilibrium is shown. Irrespective of the initial conditions, we prove that the solutions converge either to the disease-free equilibrium or to the endemic equilibrium, depending on whether the derived threshold quantity is less or greater than one. We assess the role of an integrated control strategy driven by human behavior changes through the incorporation of prevalence-dependent increasing the prophylactic treatment and decreasing the contact rate functions, as well as the mechanical water sanitation and the biological elimination of snails. Because schistosomiasis is endemic, the aim is to mitigate the endemic level of the disease. In this regard, we show both theoretically and numerically that: the reduction of contact rate through avoidance of contaminated water, the enhancement of prophylactic treatment, the water sanitation, and the removal of snails can reduce the endemic level and, to an ideal extent, drive schistosomiasis to elimination.

Keywords Schistosomiasis · Human behavior · Prevalence-based modeling · Integrated control · Monotone system · Global stability · Numerical simulation

Mathematics Subject Classification 92B05 · 37N25 · 34D30 · 65L03

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✉ Berge Tsanou
bergetsanou@yahoo.fr; berge.tsanou@up.ac.za

1 Normandie University, UNIHAVRE, LMAH FR-CNRS-3335, ISCN, 76600 Le Havre, France

2 Present Address: Department of Mathematics and Applied Mathematics, University of Pretoria, Pretoria 0002, South Africa

3 Department of Mathematics and Computer Science, University of Dschang, P.O. Box 67, Dschang, Cameroon

4 IRD UMI 209 UMMISCO, University of Yaounde I, P.O. Box 337, Yaounde, Cameroon

5 LIRIMA-EPITAG Team Project, University of Yaounde I, P.O. Box 812, Yaounde, Cameroon

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1 Introduction

Schistosomiasis is one of the most popular parasitic waterborne diseases worldwide. It is also known as bilharzia or bilharziosis. It is caused by blood flukes (trematode worms) of the genus Schistosoma. There are two major forms of schistosomiasis: intestinal and urogenital caused by two main species of schistosomes out of the five well-known species (*Schistosoma haematobium*, *Schistosoma japonicum*, *Schistosoma mansoni*, *Schistosoma mekongi*, and *Schistosoma intercalatum*). However, only three of them (*Schistosoma haematobium*, *Schistosoma japonicum*, and *Schistosoma mansoni*) are especially harmful to humans. In 2016, an estimate of at least 206.4 million people was infected from which more than 89 million were reported to have received successful prophylactic treatment from 78 countries mostly in Sub-Saharan Africa (Musuva et al. 2014; Inobaya et al. 2014; World Health Organization 2018).

The transmission cycle of schistosomiasis is very complex and can be simplified as follows: schistosomes, the causal agents of the disease, lay eggs from the human body through urine (for urinary schistosomiasis) or feces (for intestinal schistosomiasis), which hatch in water and liberate larvae called miracidia that penetrate freshwater snail hosts. After several weeks of growth and multiplication, cercariae emerge from the snails and penetrate human skin during contaminative water contact (e.g., wading, swimming, and washing). Cercariae transform and subsequently migrate through the lungs to the liver where they mature into adult worms. These adult worms move to either the veins of the abdominal cavity and lead to *intestinal schistosomiasis*, or to the urinary tract and give rise to *urinary schistosomiasis*. Most of the eggs produced are trapped in the tissues but a proportion escape through the bowel or urinary bladder and are release into water, and the transmission cycle restarts (Steinmann et al. 2006; World Health Organization 2018; Okosun and Smith 2017). This complicated transmission process and life cycle of schistosomiasis are simplified and captured in Figs. 1 and 2, from which the time evolution mathematical model of the disease will be devised and insightfully investigated.

Like many other neglected tropical diseases (NTD) of poverty, the endemicity of schistosomiasis is largely amplified by human behavior. It is primarily a behavioral disease in relation to water associated with human practices urinating and defecating in water ponds, dams, and canals (Zeng et al. 2011). Although schistosomiasis is prevalent and endemic in most regions in Africa, the majority of people in the community at risk have low awareness (World Health Organization 1990, 2018). In communities with low-to-medium prevalence and good health services, prophylactic treatment with Praziquantel may be the most cost-effective approach to control the disease. On the other hand, in highly endemic places, the combination of prophylactic treatment, snail control measures, water sanitation, and human behavioral changes might be the cost-effective control measure. Above all, long-term sustainable measures have to be based on safe water supply, improvements in sanitation and hygiene, and mass treatment with Praziquantel (Zeng et al. 2011; Steinmann et al. 2006; Musuva et al. 2014; Odhiambo et al. 2014). In line with the WHO NTD Roadmap and the WHO-AFRO 2014–2020 Regional Strategy on NTDs (World Health Organization 2013), an integrated strategy for possible mitigation of schistosomiasis includes: preventive chemotherapy, health education, access to clean water, sanitation improvement, and environmental snail control and focal molluscicidding. More importantly, human behavioral changes through health education are essential for community understanding and participation in the proper use and continuous maintenance of sanitary and water supply facilities, as well as avoiding contacts with contaminated water (Kloos 1995; Watts et al. 1998; World Health Organization 2013). It is therefore vital to

stress the need for health education to raise community's awareness on schistosomiasis in such regions to augment prevention, control, and elimination efforts. Designing of appropriate education messages targeted at raising community awareness on schistosomiasis and driving human behavioral change are therefore required for a success of any control program. An attempt to address these issues requires collaboration between researchers in the fields of Medicine, Biology, Parasitology, Engineering, and Applied Mathematics (Watts et al. 1998). It is therefore clear enough that the integrated control strategy mentioned above can only be efficient and long-lasting if the population at risk adopt favorable behavior changes toward the disease. We do believe that mathematical models that incorporate the previous feature are of paramount importance to provide insights into the understanding and prevention of the schistosomiasis dynamics.

As far as Applied Mathematics is concerned, mathematical modeling had been participating in the struggle since the seminal contribution by Barbour (1978), who elaborated on Macdonald's basic model (Macdonald 1965) and extended it to account for individual variations in water contact patterns. However, being ranked just behind malaria as the second world threat (Okosun and Smith 2017), it is surprising that schistosomiasis has been so neglected by Mathematicians modelers. On the other hand, the interplay between the spread of an infectious disease and the human behavior toward it is well documented (Manfredi and D'Onofrio 2013). A large majority of such models represents the disease transmission rates as decreasing functions of the number of awareness programs (Al et al. 2018; Cai and Wang 2017; Greenhalgh et al. 2015; Li et al. 2014; Lu et al. 2017; Sun et al. 2011; Yang et al. 2017), whereas the lesser part divides the susceptible individuals into two distinct classes depending on their awareness/unawareness of the risk of infection (Njankou and Nyabadza 2017; Kiss 2013; Sahu and Dhar 2015; Wang et al. 2015). All these models are subject to a number of dynamic feedbacks and mathematical models provide an invaluable tools to study such feedbacks. Moreover, it is worth noticeable that there are several ways of interpreting the same influence; in the case of disease prevalence, for example, people could respond to current, recent, or historical prevalences.

Technically, there are two main modeling approaches to incorporate human behavior influences into epidemiological modeling: belief-based and prevalence-based approaches and all the above-mentioned models fall onto the latter approach. Because prevalence-based modeling is objective and the belief-based is subjective, we follow the latter to incorporate for the first time, prevalence-dependent contact, treatment, and shedding rates in a more general schistosomiasis epidemiological model. In this work, the prevalence-based approach accounts for:

- 1—the reduction of contacts with contaminated water;
- 2—an increase in treatment rate of humans;
- 3—the reduction of eggs' sheddings (i.e., the increase in sanitation).

Even though human behavior impacts have been neglected (if not completely ignored so far) since the works by Barbour (1978) and Macdonald (1965), there have been many studies published to help understanding the transmission processes and the control measures of schistosomiasis, which cover almost all types of modeling frameworks. One could mention few of them. Models with general incidence rate were published in Yan-Fang et al. (2016) and Guiro et al. (2017). Some within hosts and/or multi-hosts models could be found in Chiyaka and Garira (2009), Nelson et al. (2009), Diaby et al. (2014), Long-xing and Jing-an (2012), Ding et al. (2015), Shan et al. (2011), Chiyaka et al. (2010) and Zhang et al. (2017). As far as models of co-infection are concerned, we found only two studies (Okosun and Smith 2017; Mushayabasa and Bhunu 2011). While a couple of people devoted their works

on mathematical models with delays or with periodic environment (Yingke et al. 2017; Lin and Zhicheng 2014; Zhang et al. 2014; Guiro et al. 2013; Shan et al. 2011; Long-xing and Jing-An 2012; Yun and Yuanguo 2016; Wu and Feng 2002; Castillo-Chavez et al. 2008), very few researchers investigated the spatial dynamics of schistosomiasis (Long-xing and Jing-an 2012; Milner and Zhao 2008; Mari et al. 2017; Shan et al. 2014), and optimal control models (Ding et al. 2015; Shan et al. 2011; Ding et al. 2017). Since none of these above-mentioned existing works have taken into account the role of human behavior on schistosomiasis, we spare the reader of their respective findings, because we want to remain focus on that newly incorporated transmission feature of the disease.

Surprisingly, despite the call by the WHO (1990) and the emphasis on the WHO NTD Roadmap and the WHO-AFRO 2014–2020 Regional Strategy on NTD (World Health Organization 2013), that human behavior changes is the sustainable control measure to eliminate schistosomiasis, no work, to the best of our knowledge, has addressed this from the mathematical modeling point of view, even though there is a vibrant research activity from the biological perspective (Kloos 1995; Zeng et al. 2011; Inobaya et al. 2014; Musuva et al. 2014; Odhiambo et al. 2014; Watts et al. 1998). Note that human behavior changes are commonly incorporated implicitly by being connected to individual's behavior changes which are expressed in term of (1) the reduction in human contacts and pathogens sheddings; (2) the increase of disease treatment for environmental transmitted diseases when the number of infectious individuals increases (see, for example, Wang et al. (2015), Long-xing and Jing-an (2013) and the references therein). Therefore, as mentioned earlier, we follow this prevalence-based approach and choose the contact rate, the shedding rates, and the treatment rate functions that encompass many prevalence-dependent functions in the form of a convex (or concave up) functions (to emphasize on the saturating behavior of these rates). For instance, if I_h denotes the number of infected humans, β_0 the maximal contact rate between susceptible humans and cercariae in the absence of human behavior, β_M the maximal reduced effective contact rate due to human behavior change in the presence of infectives, assuming that $\beta_0 \geq \beta_M$, without lost of generality, we model the contact rate $\beta_h(I_h)$ as follows:

$$\begin{aligned} &\beta_h(I_h) = \beta_0 - \beta_M \widetilde{\beta}_h(I_h), \quad \text{with} \quad \widetilde{\beta}_h(0) = 0, \quad 0 \leq \widetilde{\beta}_h(I_h) \leq 1, \\ &\lim_{I_h \to \infty} \widetilde{\beta}_h(I_h) = 1, \ \widetilde{\beta}_h'(I_h) \geq 0, \ \widetilde{\beta}_h''(I_h) < 0. \end{aligned} \tag{1}$$

The treatment and shedding rates functions will be chosen similarly and accordingly later.

The remainder of this manuscript is organized as follows. In Sect. 2, we formulate in a more general manner, a model for schistosomiasis dynamics that incorporates human behavior acting specifically on human contacts with water, human shedding rate, and disease treatment. After establishing the basic properties, the model is further reduced thanks to Vidyasagar decomposition technique (Vidyasagar 1980) in Sect. 3. The monotonicity (Smith 1988; Manyombe et al. 2017; Iggidr et al. 2012; Auger et al. 2008) of the reduced system allows us to establish the complete asymptotic analysis of the model, both locally and globally in Sect. 4. Section 5 is devoted to an integrated control strategy investigation both theoretically and numerically by assessing: the avoidance of water contact; the reduction of shedding; the improvement of treatment; and the biological control of snails on schistosomiasis endemicity. The paper is concluded and discussed in Sect. 6.

2 Model framework

Before we proceed to derive the model equations, we give some main modeling assumptions.

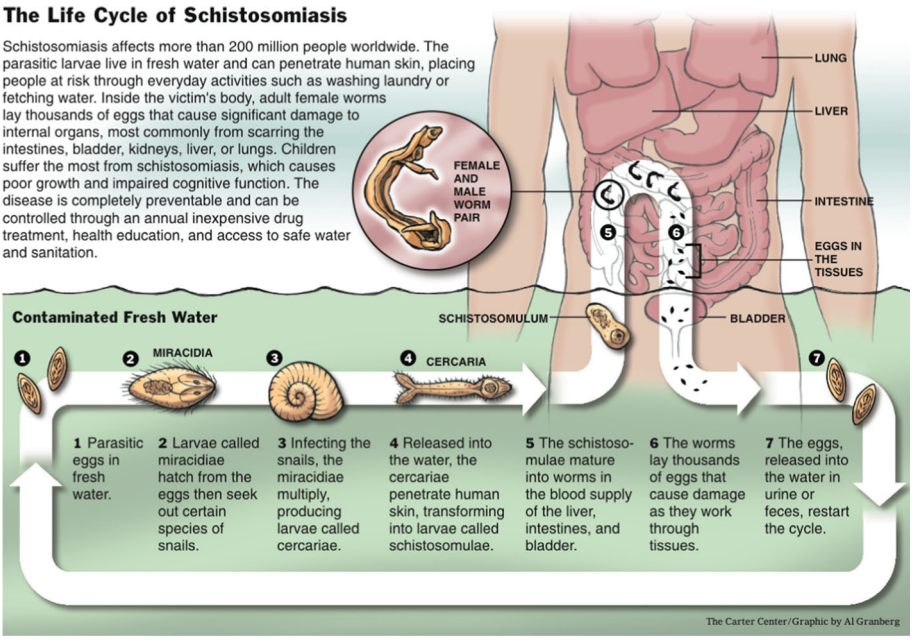

Fig. 1 Simplified life cycle of schistosomiasis

(H1) Susceptible humans S_h become infected through effective contact $\beta_h(I_h)$ with the free-living cercariae C in water. $\beta_h(I_h)$ depends on the number of infected humans I_h as a response to human behavior toward disease knowledge. Actually, the past history of a disease and its current trend force people to adjust their behavior. For instance, when people have in their mind the number of cases for the past outbreak, or when they are informed from time to time on the current outbreak of a disease, they will tend to limit their contacts with infected or suspected individuals. We denote by $\sigma_c = \sigma_c(S_h)$ the consumption rate of cercariae by susceptible human hosts.

(H2) Susceptible snails S_s become infected through effective contact with the free-living miracidia M in water. Contrary to β_h, the contact rate β_s does not depend on the number of infected humans, since human behavior does not directly impact the interactions between snails and miracidia. $\sigma_m = \sigma_m(S_s)$ denotes the consumption rate of miracidia by susceptible snail hosts.

(H3) We assume numerous biological control measures among which many are disease-prevalent dependent:
(i)—Treatment with Praziquantel which is modeled by a positive, increasing, and saturated rate $\gamma(I_h)$. Similar to $\beta_h(I_h)$, one can conduct analogous interpretations and without loss of generality, expresses $\gamma(I_h)$ in the following form:

$$\begin{aligned} &\gamma(I_h) = \gamma_0 + \gamma^m \widetilde{\gamma}(I_h), \quad \text{with} \quad \widetilde{\gamma}(0) = 0, \quad 0 \le \widetilde{\gamma}(I_h) \le 1, \\ &\lim_{I_h \to \infty} \widetilde{\gamma}(I_h) = 1, \ \widetilde{\gamma}'(I_h) \ge 0, \ \widetilde{\gamma}''(I_h) \le 0. \end{aligned} \tag{2}$$

(ii)—Manual or mechanical removal of snails into water at rate θ. Though the latter rate may depend on the human behavior through the number of infected humans, we ignore it in this work for the sake of simplicity and for mathematical tractability.

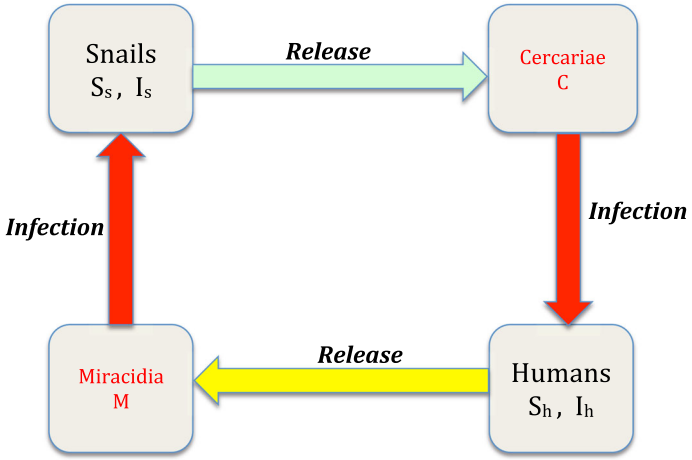

Fig. 2 Simplified schistosomiasis transmission diagram

(iii)—Removal of cercariae from water (e.g., sanitizing water resource using harmless chemicals) at a constant rate η.

(H4) To accentuate to role of human behavior, we denote by a_h the "disease awareness rate" or "health education uptake rate" and explicitly model the deposition rates f and g as a function of (I_h, a_h) and (I_s, a_s), respectively. We assume that infected snails shed cercariae into water at a general rate $g(I_s, a_s)$, where a_s can be referred to as the "indirect disease awareness rate" whose increase acts detrimentally on the ceracariae shedding. Actually, one should look at a_s as a modification of (if not the same as) a_h. Similarly, infected humans deposit fresh miracidia into water at a general rate $f(I_h, a_h)$. The shedding rates $f(I_h, a_h)$ and $g(I_s, a_s)$ are saturated and concave down-functions of the disease prevalence I_h, and they are increasing (resp. decreasing) with respect to I_h and I_s (resp. with respect to a_h and a_s). Further properties of these functions will be specified in the sequel [see assumption (A1) below].

(H5) We assume that susceptible snails are replenished at a constant rate b_s (though a logistic growth is more realistic, it will not change qualitatively the model dynamics).

(H6) Since schistosomiasis is a parasitic endemic disease which mainly cause disability and rarely death, we do not consider any death related to the infection.

In many places of the paper, where necessary, we shall simply denote $f(I_h)$ and $g(I_s)$ instead of $f(I_h, a_h)$ and $g(I_s, a_s)$. Their typical examples will be specified later in Sect. 5.

The population of human hosts is then divided into susceptible (S_h), infected (I_h) individuals. Similarly, the population of snails is split into susceptible (S_s) and infected (I_s) individuals. M and C represent the number of miracidia and cercariae in water, respectively. If b_h, d_h, d_c, d_s, and d_m denote the replenishment rate of humans individuals, the death rates for humans, ceracariae, snails, and miracidia, respectively; then, based on the simplified disease transmission diagram in Fig. 2, we devise the following system of nonlinear differential equations for the temporal evolution of schistosomiasis:

$$\begin{cases} \dfrac{\mathrm{d}S_\mathrm{h}}{\mathrm{d}t} = b_\mathrm{h} - \beta_\mathrm{h}(I_\mathrm{h})S_\mathrm{h}C - d_\mathrm{h}S_\mathrm{h} + \gamma(I_\mathrm{h})I_\mathrm{h}, \\ \dfrac{\mathrm{d}I_\mathrm{h}}{\mathrm{d}t} = \beta_\mathrm{h}(I_\mathrm{h})S_\mathrm{h}C - (d_\mathrm{h} + \gamma(I_\mathrm{h}))I_\mathrm{h}, \\ \dfrac{\mathrm{d}C}{\mathrm{d}t} = g(I_\mathrm{s}) - \sigma_\mathrm{c}\beta_\mathrm{h}(I_\mathrm{h})S_\mathrm{h}C - (d_\mathrm{c} + \eta)C, \\ \dfrac{\mathrm{d}S_\mathrm{s}}{\mathrm{d}t} = b_\mathrm{s} - \beta_\mathrm{s}S_\mathrm{s}M - (d_\mathrm{s} + \theta)S_\mathrm{s}, \\ \dfrac{\mathrm{d}I_\mathrm{s}}{\mathrm{d}t} = \beta_\mathrm{s}S_\mathrm{s}M - (d_\mathrm{s} + \theta)I_\mathrm{s}, \\ \dfrac{\mathrm{d}M}{\mathrm{d}t} = f(I_\mathrm{h}) - \sigma_\mathrm{m}\beta_\mathrm{s}S_\mathrm{s}M - d_\mathrm{m}M. \end{cases} \tag{3}$$

Note that model (4) is general in the following sense:

(a) the behavioral contact rate $\beta_\mathrm{h}(I_\mathrm{h})$ depends monotonically on the number of infected humans I_h;
(b) the replenishment rate of cercariae $g(I_\mathrm{s})$ depends monotonically on the number of infected snails I_s;
(c) the deposit rate $f(I_\mathrm{h})$ of miracidia depends monotonically on the number of infected humans I_h.
(d) the treatment rate $\gamma(I_\mathrm{h})$ depends monotonically on the number of infected humans I_h.

As it is the case for most epidemic models with free-living pathogens (Bani-Yaghoub et al. 2012; Caraco and Wang 2008; Nelson et al. 2009; Wang et al. 2015; Wang and Wang 2015), we assume that the diminution of cercariae and miracidia in the water component do not influence the dynamics of these pathogens. Thus, the depletion terms $(-\sigma_\mathrm{c}\beta_\mathrm{h}(I_\mathrm{h})S_\mathrm{h}C)$ for the cercariae and $(-\sigma_\mathrm{m}\beta_\mathrm{s}S_\mathrm{s}M)$ for miracidia have been removed form the corresponding equations. We shall therefore focus on the simplified model (4):

$$\begin{cases} \dfrac{\mathrm{d}S_\mathrm{h}}{\mathrm{d}t} = b_\mathrm{h} - \beta_\mathrm{h}(I_\mathrm{h})S_\mathrm{h}C - d_\mathrm{h}S_\mathrm{h} + \gamma(I_\mathrm{h})I_\mathrm{h}, \\ \dfrac{\mathrm{d}I_\mathrm{h}}{\mathrm{d}t} = \beta_\mathrm{h}(I_\mathrm{h})S_\mathrm{h}C - (d_\mathrm{h} + \gamma(I_\mathrm{h}))I_\mathrm{h}, \\ \dfrac{\mathrm{d}C}{\mathrm{d}t} = g(I_\mathrm{s}) - (d_\mathrm{c} + \eta)C, \\ \dfrac{\mathrm{d}S_\mathrm{s}}{\mathrm{d}t} = b_\mathrm{s} - \beta_\mathrm{s}S_\mathrm{s}M - (d_\mathrm{s} + \theta)S_\mathrm{s}, \\ \dfrac{\mathrm{d}I_\mathrm{s}}{\mathrm{d}t} = \beta_\mathrm{s}S_\mathrm{s}M - (d_\mathrm{s} + \theta)I_\mathrm{s}, \\ \dfrac{\mathrm{d}M}{\mathrm{d}t} = f(I_\mathrm{h}) - d_\mathrm{m}M. \end{cases} \tag{4}$$

To be complete, system (4) is appended by the following nonnegative initial conditions:

$$S_\mathrm{h}(0) > 0, \quad I_\mathrm{h}(0) \geq 0, \quad S_\mathrm{s}(0) > 0, \quad I_\mathrm{s}(0) \geq 0, \quad M(0) \geq 0, \quad C(0) \geq 0. \tag{5}$$

Moreover, the following biological meaningful assumptions are either natural or direct consequences of the hypotheses (H4), (H5) on the functions $f(I_\mathrm{h})$ and $g(I_\mathrm{s})$, and of the forms of $\beta_\mathrm{h}(I_\mathrm{h})$ and $\gamma(I_\mathrm{h})$ in (1) and (2):

(A1) $\beta_\mathrm{h}(I_\mathrm{h}) > 0, \gamma(I_\mathrm{h}) > 0, f(I_\mathrm{h}, a_\mathrm{h}) \geq 0, g(I_\mathrm{s}, a_\mathrm{s}) \geq 0$. One might reasonably assume that $f(I_\mathrm{h}, a_\mathrm{h})$ vanishes whenever the disease awareness/health education uptake rate a_h goes to infinity. The supposition $f(0, a_\mathrm{h}) = g(0, a_\mathrm{s}) = 0$ is a shortcoming in the sense that, by so doing, we are saying that only infected humans can deposit cercariae into the water environment, which is not always true, because other mammalians (sheep,

cow, etc.) are potential schistosomiasis hosts, and can therefore contribute to shed cercariae. This, together with the drawbacks mentioned in the hypotheses (H3)–(H5), will be addressed in a different work.

(A2) $\beta_h'(I_h) \leq 0, \gamma'(I_h) \geq 0, f'(I_h, a_h) < 0, g'(I_s, a_s) < 0$. Except $\beta_h(I_h)$ which is bounded from below and convex, all the remaining functions are bounded from above (saturated).

(A3) $\gamma'(0) \geq 0, f'(0), g'(0) > 0$. Moreover, $f(I_h)$ and $g(I_s)$ are concave. This implies that $f(I_h) \leq f(0)'I_h$, $g(I_s) \leq g(0)'I_s$, so that the functions f, g cannot grow exponentially. The superscript " ' " in (A2) and (A3) denotes the partial derivatives of f and g with respect to I_h and I_s, respectively.

Specific examples of the functions $\beta_h(I_h)$, $\gamma(I_h)$, $f(I_h)$ and $g(I_s)$ will be provided in Sect. 6 for application purposes. The reader should note that, for the assumptions on the functions $\beta_h(I_h)$, $\gamma(I_h)$, we could give only the conditions (A1)–(A3) which are more mathematically tractable in the sequel, but we prefer to keep also their original forms in (1) and (2) as they permit easy construction of simple examples. Moreover, it should be noted that a_h and a_s are constant parameters used purely for modeling purposes and because they are very difficult to estimate (if not completely unknown), one can vary them without considering them as "pure" model variables.

3 Basic mathematical properties of the system

The aim of this section is threefold: (1) to prove that every Cauchy problem associated with system (4) has a unique global (in time) solution which is nonnegative and bounded; (2) to derive a threshold quantity that will be used later for the investigation of the long run behavior of system (4); (3) to reduce the study of model (4) to that of a small/lower dimensional system.

3.1 Mathematical and epidemiological well-posedness

Clearly, from assumption (A2) above, the vector field defined by the right-hand side of system (4) is continuously differentiable. Thus, the classical Cauchy–Lipschitz theorem applies for the existence and uniqueness of the (local) solution for a initial problem associated with system (4). Since we are dealing with population sizes, it is necessary to prove that the sizes will remain nonnegative for nonnegative initial populations.

Proposition 1 *The positive cone $\mathbb{R}^6_+$ of $\mathbb{R}^6$ is positively invariant under the flow of system* (4)*. That is, for nonnegative initial conditions giving in Eq.* (5)*, the corresponding solution for system* (4) *is nonnegative.*

Proof Denote $\Psi(t) = \beta_s M(t) + d_s + \theta$. Since $b_s > 0$, from the fourth equation of system (4), one has:

$$\frac{dS_s(t)}{dt} > -\Psi(t)S_s(t).$$

Thus:

$$S_s(t) > S_s(0)e^{-\int_0^t \Psi(u)du} > 0, \quad \forall t \geq 0. \tag{6}$$

Using the positivity of $S_s(t)$ given by (6) in the sixth equation of model (4) and the fact that $f(I_h) \geq 0$, we prove similarly that $M(t) \geq 0, \ \forall t \geq 0$. This process can be performed

to prove recursively that $I_s(t) \geq 0$ and $C(t) \geq 0$, $\forall t \geq 0$. It remains to show that $S_h(t)$ and $I_h(t)$ are nonnegative. This is done by observing that, since $C(t)$, $\beta_h(I_h(t))$, $\gamma(I_h)$ are all nonnegative, the first two equations of system (4) define a monotone (cooperative) dynamical system. In fact, if $Y(t) = (S_h(t), I_h(t))^T$, then:

$$\dot{Y}(t) = \Phi(Y)Y(t) + B,$$

where:

$$\Phi(Y) = \begin{bmatrix} -\beta_h(I_h)C - d_h\gamma(I_h) & \\ \\ \beta_h(I_h)C - d_h - \gamma(I_h) & \end{bmatrix} \quad \text{and} \quad B = (b_h, 0)^T.$$

The conclusion follows, because $\Phi(Y)$ is a Metzler matrix and $B \geq 0$ (Berman and Plemmons 1979).

Thanks to assumption A_3, we set:

$$f^M = \max_{I_h \geq 0}\{f(I_h)\}, \quad g^M = \max_{I_s \geq 0}\{g(I_s)\}.$$

After establishment of the positivity, the following result guaranties the global existence of the solutions and of a positively invariant set (i.e., a biological feasible domain).

Proposition 2 *The solutions of system (4) are bounded. Precisely, let*

$$N_h(t) = S_h(t) + I_h(t), \quad N_s(t) = S_s(t) + I_s(t)$$

denote the total number of humans and snails, respectively; g^M and f^M be the upper bounds of g and f, respectively. Then, the set

$$\Omega = \left\{(S_h, I_h, S_s, I_s, C, M) \in \mathbb{R}^6_+ \ / \ N_h \leq \frac{b_h}{d_h}, \ N_s \leq \frac{b_s}{d_s}, \ C \leq \frac{g^M}{d_c + \eta}, \ M \leq \frac{f^M}{d_m}\right\}$$

is positively invariant and absorbing with respect to the flow of system (4).

Proof This follows from the positivity of the solutions shown in Proposition 1; the fact that

$$\frac{dN_h}{dt} = b_h - d_h N_h, \quad \frac{dN_s}{dt} = b_s - d_s N_s, \quad \frac{dC}{dt} \leq g^M - (d_c + \eta)\, C, \quad \frac{dM}{dt} \leq f^M - d_m M;$$

and the application of the Gronwall Lemma.

3.2 Disease-free solution and threshold quantity

The objective of this paragraph is to derive a threshold quantity called *basic reproduction number* and denoted by $\mathcal{R}_0$ that will be used to analyze the asymptotic behavior of system (4). There is a trivial constant solution for system (4) for which the infected components $I_h(t) = I_s(t) = C(t) = M(t) = 0$ called the disease-free equilibrium. We order the component of every solution $X(t)$ as follows: $X(t) = (S_h(t), S_s(t), I_h(t), I_s(t), C(t), M(t))^T$. Denote $X_0(t) = (S_h^0(t), S_s^0(t), 0, 0, 0, 0)^T$ the disease-free solution. Then:

$$S_h^0(t) = \frac{b_h}{d_h}, \quad S_s^0(t) = \frac{b_s}{d_s + \theta}, \quad \forall\, t \geq 0.$$

To compute the threshold quantity $\mathcal{R}_0$, we follow the next-generation approach in Diekmann et al. (1990, 2010) and van den Driessche and Watmough (2002). The components of

the solution corresponding to disease states are $I_h(t)$, $I_s(t)$, $C(t)$, $M(t)$. Following (van den Driessche and Watmough 2002), the vector corresponding to new infections is:

$$[\beta_h(I_h)S_hC,\ \beta_sS_sM,\ 0,\ 0]^T,$$

whereas the remaining transfer terms are gathered in the vector:

$$\mathcal{V} = \left[-(d_h+\gamma(I_h))\,I_h,\ -(d_s+\theta)\,I_s,\ g(I_s)-(d_c+\eta)\,C,\ f(I_h)-d_mM\right]^T.$$

Let F and V be the Jacobian matrices of $\mathcal{F}$ and $\mathcal{V}$ evaluated at X_0, $\rho(A)$ be the spectral radius of the matrix A, then $-FV^{-1}$ defines the so-called next-generation matrix (Diekmann et al. 2010), and the threshold $\mathcal{R}_0$ is the spectral radius of $-FV^{-1}$. Simple calculations give:

$$F = \begin{pmatrix} 0 & 0 & \beta_0S_h^0 & 0 \\ 0 & 0 & 0 & \beta_sS_s^0 \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \end{pmatrix} \quad \text{and} \quad -V = \begin{pmatrix} v_{11} & 0 & 0 & 0 \\ 0 & v_{22} & 0 & 0 \\ 0 & -g'(0) & v_{33} & 0 \\ -f'(0) & 0 & 0 & v_{44} \end{pmatrix},$$

where, $v_{11} = d_h + \gamma(0)$, $v_{22} = d_s + \theta$, $v_{33} = d_c + \eta$, $v_{44} = d_m$. Note that one has:

$$-V^{-1} = \begin{pmatrix} \frac{1}{v_{11}} & 0 & 0 & 0 \\ 0 & \frac{1}{v_{22}} & 0 & 0 \\ 0 & \frac{g'(0)}{v_{22}v_{33}} & \frac{1}{v_{33}} & 0 \\ \frac{f'(0)}{v_{11}v_{44}} & 0 & 0 & \frac{1}{v_{44}} \end{pmatrix},$$

$$-FV^{-1} = \begin{pmatrix} 0 & \frac{\beta_0S_h^0g'(0)}{v_{22}v_{33}} & \frac{\beta_h(0)S_h^0}{v_{33}} & 0 \\ \frac{\beta_sS_s^0f'(0)}{v_{11}v_{44}} & 0 & 0 & \frac{\beta_sS_s^0}{v_{44}} \\ 0 & 0 & 0 & \\ 0 & 0 & 0 & 0 \end{pmatrix}.$$

Since $\mathcal{R}_0 = \rho(-FV^{-1})$, we have:

$$\begin{aligned} \mathcal{R}_0 &= \rho\left(\begin{pmatrix} 0 & \frac{\beta_0S_h^0g'(0)}{v_{22}v_{33}} \\ \frac{\beta_sS_s^0f'(0)}{v_{11}v_{44}} & 0 \end{pmatrix}\right), \\ &= \sqrt{\frac{\beta_0S_h^0f'(0)\beta_sS_s^0g'(0)}{d_m(d_h+\gamma(0))\,(d_c+\eta)\,(d_s+\theta)}}, \\ &= \frac{1}{(d_s+\theta)}\sqrt{\frac{\beta_0b_hf'(0)\beta_sb_sg'(0)}{d_md_h(d_h+\gamma(0))\,(d_c+\eta)}}. \end{aligned} \tag{7}$$

3.3 Equivalent and reduced system

We use the following change of variables to obtain an equivalent system to model (4). Let:

$$S_h = N_h - I_h, \quad S_s = N_s - I_s.$$

Then, the model (4) is equivalent to:

$$\begin{cases} \dfrac{\mathrm{d}N_\mathrm{h}}{\mathrm{d}t} = b_\mathrm{h} - d_\mathrm{h} N_\mathrm{h}, \\ \dfrac{\mathrm{d}N_\mathrm{s}}{\mathrm{d}t} = b_\mathrm{s} - (d_\mathrm{s} + \theta) N_\mathrm{s}, \\ \dfrac{\mathrm{d}I_\mathrm{h}}{\mathrm{d}t} = \beta_\mathrm{h}(I_\mathrm{h})(N_\mathrm{h} - I_\mathrm{h})C - (d_\mathrm{h} + \gamma(I_\mathrm{h}))I_\mathrm{h}, \\ \dfrac{\mathrm{d}C}{\mathrm{d}t} = g(I_\mathrm{s}) - (d_\mathrm{c} + \eta)C, \\ \dfrac{\mathrm{d}I_\mathrm{s}}{\mathrm{d}t} = \beta_\mathrm{s}(N_\mathrm{s} - I_\mathrm{s})M - (d_\mathrm{s} + \theta)I_\mathrm{s}, \\ \dfrac{\mathrm{d}M}{\mathrm{d}t} = f(I_\mathrm{h}) - d_\mathrm{m} M. \end{cases} \tag{8}$$

We reduce the stability analysis of system (8) (or equivalently of system (4)), to the study of a smaller (in dimension) and simpler (cooperative) system. The following theorem by Vidyasagar (1980) serves the purpose and will permit us to reduce the stability analysis to that of a smaller (in dimension) system.

Theorem 1 *Consider the following C^1 system:*

$$\begin{cases} \dfrac{\mathrm{d}x}{\mathrm{d}t} = p(x), \quad x \in \mathbb{R}^n, \quad y \in \mathbb{R}^m, \quad (n, m) \in \mathbb{N}^2, \\ \dfrac{\mathrm{d}y}{\mathrm{d}t} = q(x, y), \\ \text{with an equilibrium point } (x^*, y^*) \text{ i.e.,} \\ p(x^*) = q(x^*, y^*) = 0. \end{cases} \tag{9}$$

If x^* is globally asymptotically stable (GAS) in $\mathbb{R}^n$ for the subsystem $\dfrac{\mathrm{d}x}{\mathrm{d}t} = p(x)$, and if y^* is GAS for $\dfrac{\mathrm{d}y}{\mathrm{d}t} = q(x^*, y)$, then (x^*, y^*) is (locally) asymptotically stable for system (9).

Moreover, if all the trajectories of system (9) are forward bounded, then (x^*, y^*) is GAS for (9).

Denote:

$$x = (N_\mathrm{h}, N_\mathrm{s})^\mathrm{T}, \quad y = (I_\mathrm{h}, I_\mathrm{s}, C, M)^\mathrm{T}.$$

Then, it is straightforward that system (8) is in the form of system (9), because the first two equations do not depend on $y = (I_\mathrm{h}, I_\mathrm{s}, C, M)^\mathrm{T}$. Moreover, let us define the subsystem consisted of the first two equations of model (8) by:

$$\frac{\mathrm{d}x}{\mathrm{d}t} = p(x). \tag{10}$$

Or equivalently:

$$\begin{cases} \dfrac{\mathrm{d}N_\mathrm{h}}{\mathrm{d}t} = b_\mathrm{h} - d_\mathrm{h} N_\mathrm{h}, \\ \dfrac{\mathrm{d}N_\mathrm{s}}{\mathrm{d}t} = b_\mathrm{s} - (d_\mathrm{s} + \theta) N_\mathrm{s}. \end{cases} \tag{11}$$

System (10) or (11) solves explicitly as:

$$\begin{cases} N_\mathrm{h}(t) = \dfrac{b_\mathrm{h}}{d_\mathrm{h}} + \left(N_\mathrm{h}(0) - \dfrac{b_\mathrm{h}}{d_\mathrm{h}} \right) \mathrm{e}^{-t d_\mathrm{h}}, \\ N_\mathrm{s}(t) = \dfrac{b_\mathrm{s}}{d_\mathrm{s} + \theta} + \left(N_\mathrm{s}(0) - \dfrac{b_\mathrm{s}}{d_\mathrm{s} + \theta} \right) \mathrm{e}^{-t(d_\mathrm{s} + \theta)}. \end{cases} \tag{12}$$

Denote:

$$N_{\mathrm{h}}^{*}=S_{\mathrm{h}}^{0}=\frac{b_{\mathrm{h}}}{d_{\mathrm{h}}},\quad N_{\mathrm{s}}^{*}=S_{\mathrm{s}}^{0}=\frac{b_{\mathrm{s}}}{d_{\mathrm{s}}+\theta}.$$

Clearly, $x^{*}=(N_{\mathrm{h}}^{*},N_{\mathrm{s}}^{*})^{\mathrm{T}}$ is the unique equilibrium for the subsystem (10). Furthermore, from (12), one can see that, regardless of the initial condition $x(0)=(N_{\mathrm{h}}(0),N_{\mathrm{s}}(0))^{\mathrm{T}}\in\mathbb{R}_{+}^{2}$, the corresponding solution $x(t)=(N_{\mathrm{h}}(t),N_{\mathrm{s}}(t))^{\mathrm{T}}$ of the system (10) converges to x^{*}. Therefore, x^{*} is GAS in $\mathbb{R}_{+}^{2}$ for the system (10). Hence, Theorem 9 applies to reduce the study of system (8) to that of the following subsystem:

$$\frac{\mathrm{d}y}{\mathrm{d}t}=q(x^{*},y),\tag{13}$$

which is explicitly given by:

$$\begin{cases}\dfrac{\mathrm{d}I_{\mathrm{h}}}{\mathrm{d}t}=\beta_{\mathrm{h}}(I_{\mathrm{h}})(N_{\mathrm{h}}^{*}-I_{\mathrm{h}})C-(d_{\mathrm{h}}+\gamma(I_{\mathrm{h}}))I_{\mathrm{h}},\\ \dfrac{\mathrm{d}I_{\mathrm{s}}}{\mathrm{d}t}=\beta_{\mathrm{s}}(N_{\mathrm{s}}^{*}-I_{\mathrm{s}})M-(d_{\mathrm{s}}+\theta)I_{\mathrm{s}},\\ \dfrac{\mathrm{d}C}{\mathrm{d}t}=g(I_{\mathrm{s}})-(d_{\mathrm{c}}+\eta)C,\\ \dfrac{\mathrm{d}M}{\mathrm{d}t}=f(I_{\mathrm{h}})-d_{\mathrm{m}}M.\end{cases}\tag{14}$$

Therefore, using Theorem 1, the stability properties of system (8) on the set Ω are the same as those of the reduced system (14), defined by:

$$\Omega_{1}=\left\{(I_{\mathrm{h}},I_{\mathrm{s}},C,M)\in\mathbb{R}_{+}^{4}\ /\ I_{\mathrm{h}}\leq N_{\mathrm{h}}^{*}\ ,\ I_{\mathrm{s}}\leq N_{\mathrm{s}}^{*}\ ,\ C\leq\frac{g^{M}}{d_{\mathrm{c}}+\eta}\ ,\ M\leq\frac{f^{M}}{d_{\mathrm{m}}}\right\}.$$

Moreover, it is straightforward that Ω_{1} is a compact, positively invariant and absorbing set for system (14).

4 Global asymptotic analysis

In this section, based on the value of $\mathcal{R}_{0}$, we study the asymptotic behavior of the solutions of (14).

4.1 $\mathcal{R}_{0}\leq 1$-convergence to the disease-free equilibrium: Lyapunov–LaSalle's approach

The disease-free equilibrium for the reduced system (14) is $E_{0}=(0,0,0,0)$. In what follows, we prove that when $\mathcal{R}_{0}\leq 1$, E_{0} is globally asymptotically stable.

Theorem 2 *If $\mathcal{R}_{0}\leq 1$, the disease-free equilibrium E_{0} is GAS in $\mathbb{R}_{+}^{4}$.*

Proof Since Ω_{1} is positively invariant and absorbing, it suffices to prove Theorem 2 in Ω_{1}. To that end, we use the Lyapunov–LaSalle techniques by considering the candidate Lyapunov function:

$$L=I_{\mathrm{h}}+\frac{d_{\mathrm{m}}(d_{\mathrm{h}}+\gamma(0))}{f'(0)\beta_{\mathrm{s}}N_{\mathrm{s}}^{*}}I_{\mathrm{s}}+\frac{\beta_{\mathrm{h}}(0)N_{\mathrm{h}}^{*}}{d_{\mathrm{c}}+\eta}C+\frac{(d_{\mathrm{h}}+\gamma(0))}{f'(0)}M.$$

The derivative of L along the solutions of (14) is:

$$\dot{L} = \frac{\mathrm{d}L}{\mathrm{d}t} = \frac{\mathrm{d}I_\mathrm{h}}{\mathrm{d}t} + \frac{d_\mathrm{m}(d_\mathrm{h}+\gamma(0))}{f'(0)\beta_\mathrm{s}N_\mathrm{s}^*}\frac{\mathrm{d}I_\mathrm{s}}{\mathrm{d}t} + \frac{\beta_\mathrm{h}(0)N_\mathrm{h}^*}{d_\mathrm{c}+\eta}\frac{\mathrm{d}C}{\mathrm{d}t} + \frac{(d_\mathrm{h}+\gamma(0))}{f'(0)}\frac{\mathrm{d}M}{\mathrm{d}t},$$

$$= \beta_\mathrm{h}(I_\mathrm{h})(N_\mathrm{h}^* - I_\mathrm{h})C - (d_\mathrm{h}+\gamma(I_\mathrm{h}))I_\mathrm{h} + \frac{d_\mathrm{m}(d_\mathrm{h}+\gamma(0))}{f'(0)\beta_\mathrm{s}N_\mathrm{s}^*}\left[\beta_\mathrm{s}(N_\mathrm{s}^* - I_\mathrm{s})M - (d_\mathrm{s}+\theta)I_\mathrm{s}\right]$$

$$+\frac{\beta_\mathrm{h}(0)N_\mathrm{h}^*}{d_\mathrm{c}+\eta}\left[g(I_\mathrm{s}) - (d_\mathrm{c}+\eta)C\right] + \frac{(d_\mathrm{h}+\gamma(0))}{f'(0)}\left[f(I_\mathrm{h}) - d_\mathrm{m}M\right].$$

Using assumptions (A1)–(A3), the expansion and simplification of $\dot{L}$ yield:

$$\dot{L} \le -\left[\beta_\mathrm{h}(0) - \beta_\mathrm{h}(I_\mathrm{h})\right]N_\mathrm{h}^*C - \left[\gamma(I_\mathrm{h}) - \gamma(0)\right]I_\mathrm{h} - \frac{d_\mathrm{m}(d_\mathrm{h}+\gamma(0))}{f'(0)N_\mathrm{s}^*}I_\mathrm{s}M - \beta_\mathrm{h}(I_\mathrm{h})I_\mathrm{h}C$$

$$-\left[1 - \frac{\beta_\mathrm{h}(0)N_\mathrm{h}^*N_\mathrm{h}^*f'(0)\beta_\mathrm{s}N_\mathrm{s}^*N_\mathrm{s}^*g'(0)}{d_\mathrm{m}(d_\mathrm{s}+\theta)(d_\mathrm{h}+\gamma(0))(d_\mathrm{c}+\eta)}\right]\frac{d_\mathrm{m}(d_\mathrm{h}+\gamma(0))(d_\mathrm{s}+\theta)}{f'(0)\beta_\mathrm{s}N_\mathrm{s}^*}I_\mathrm{s},$$

$$= -\left[\beta_\mathrm{h}(0) - \beta_\mathrm{h}(I_\mathrm{h})\right]N_\mathrm{h}^*C - \left[\gamma(I_\mathrm{h}) - \gamma(0)\right]I_\mathrm{h} - \frac{d_\mathrm{m}(d_\mathrm{h}+\gamma(0))}{f'(0)N_\mathrm{s}^*}I_\mathrm{s}M - \beta_\mathrm{h}(I_\mathrm{h})I_\mathrm{h}C$$

$$-\frac{d_\mathrm{m}(d_\mathrm{h}+\gamma(0))(d_\mathrm{s}+\theta)\left(1-\mathcal{R}_0^2\right)}{f'(0)\beta_\mathrm{s}N_\mathrm{s}^*}I_\mathrm{s} \le 0.$$

Since $\dot{L} \le 0$, it shows that L is indeed a Lyapunov function. Hence, E_0 is stable. To prove the global attractiveness of E_0, we distinguish two cases:
Case 1: If $\mathcal{R}_0 < 1$, then $\dot{L} < 0$, for all $(I_\mathrm{h}, I_\mathrm{s}, C, M) \neq E_0$. Hence, L is a strict Lyapunov function, and thus, E_0 is GAS.
Case 2: If $\mathcal{R}_0 = 1$, then $\dot{L} = 0$ implies that ($I_\mathrm{h} = C = 0$ and $I_\mathrm{s} = 0$) or ($I_\mathrm{h} = C = 0$ and $M = 0$). Now, let K be an invariant set contained in $\left\{(I_\mathrm{h}, I_\mathrm{s}, C, M) \in \mathbb{R}_+^4,\ \dot{L} = 0\right\}$, and let $w_0 = (I_{h0}, I_{s0}, C_0, M_0)$ be a point in K. Then, ($I_{h0} = C_0 = 0$ and $I_{s0} = 0$) or ($I_{h0} = C_0 = 0$ and $M_0 = 0$). Thus, by the invariance of K, the solution $w(t) = (I_\mathrm{h}(t), I_\mathrm{s}(t), C(t), M(t))$ of system (14) corresponding to the initial condition w_0 satisfies ($I_\mathrm{h}(t) = C(t) = 0$ and $I_\mathrm{s}(t) = 0$) or ($I_\mathrm{h}(t) = C(t) = 0$ and $M(t) = 0$). In either of the previous situations, replacing $C(t) = 0$ in third equation of (14) gives $I_\mathrm{s}(t) = 0$, which in turn is replaced in the second equation of (14) to obtain $M(t) = 0$. Hence, by the positively invariance of K reduces to E_0. That is, the largest invariant set contained in $\left\{(I_\mathrm{h}, I_\mathrm{s}, C, M) \in \mathbb{R}_+^4,\ \dot{L} = 0\right\}$ is the disease-free equilibrium E_0. Thus, by LaSalle's Invariance Principle (LaSalle 1976), E_0 is GAS in Ω_1 whenever $\mathcal{R}_0 = 1$. This achieves the proof. We further illustrate Theorem 2 in Fig. 3.

4.2 $\mathcal{R}_0 > 1$-convergence to the endemic equilibrium: monotone dynamical system approach

Our aim is to prove that, when $\mathcal{R}_0 > 1$, E_0 is unstable, and there exists a unique endemic equilibrium which is GAS for system (14).

Proposition 3 *If $\mathcal{R}_0 > 1$, the disease-free equilibrium E_0 is unstable.*

Proof It is a direct consequence of Theorem 2 in van den Driessche and Watmough (2002).

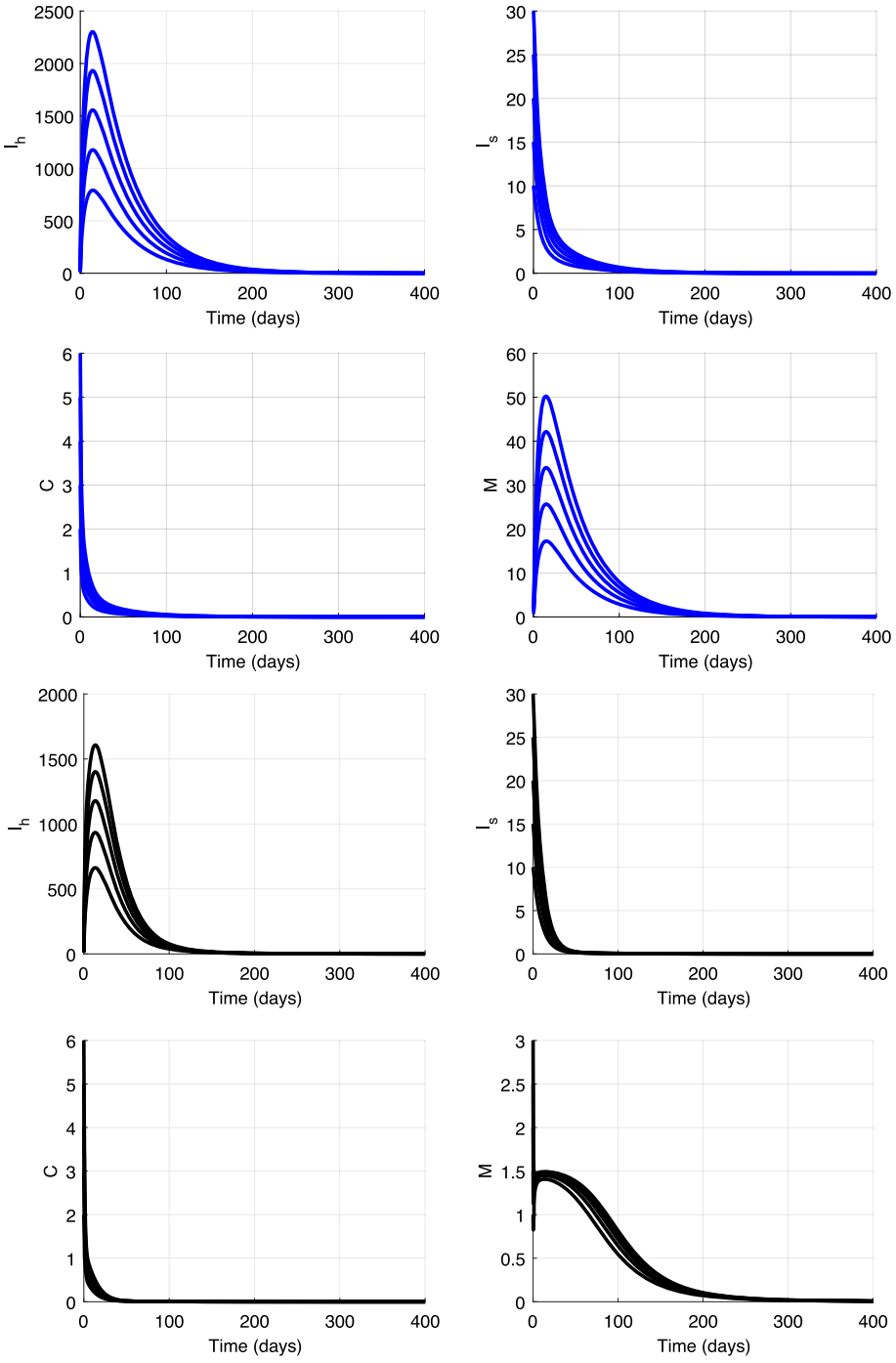

Fig. 3 GAS of the disease-free equilibrium E_0. Blue panel: without human behavior ($a_h = a_s = 0$). Black panel: with human behavior ($a_h = 0.014$, $a_s = 0.033$). All the parameters are as in Table 1 except that the contact rate between snails and miracidia has been reduced to $\beta_s = 8 \times 10^{-5}$, given $\mathcal{R}_0 = 0.9261 < 1$

4.2.1 Existence and uniqueness of the endemic equilibrium

We first give some useful definitions. Let X be a non-empty open set in a real Banach space V. We assume that V has a (partial) ordering defined by a closed convex cone $V_+ \subset V$, and we write $y \geq x$ if $y - x \in V_+$, and $y > x$ if $y \geq x$, but $y \neq x$. We assume that V_+ has non-empty interior. In this case, we say V is strongly ordered and we write $y \gg x$ if $y - x \in \text{Int}(V_+)$. In what follows, we shall take $V = \mathbb{R}^n$ and $V_+ = \mathbb{R}^n_+$ for $n = 3; 4$.

We have shown in Proposition 3 that the disease-free equilibrium is unstable when $\mathcal{R}_0 > 1$. In what follows, we prove that system (14) has a unique endemic equilibrium whenever $\mathcal{R}_0 > 1$. To achieve this, we formulate the problem of the existence as a fixed point, and then afterward, use the fixed point theorem due to Hethcote and Thieme (1985) below to conclude.

Theorem 3 *Let $F(U)$ be a continuous, monotone non-decreasing, strictly sub-linear, bounded function which maps the nonnegative orthant $\mathbb{R}^n_+$ into itself. Let $F(0) = 0$ and suppose the Jacobian matrix $J_F(0)$ exists and is irreducible. Then, $F(U)$ does not have a non-trivial fixed point on the boundary of $\mathbb{R}^n_+$. Moreover, $F(U)$ has a positive fixed point if and only if $\rho(J_F(0)) > 1$. If there is a positive fixed point, then it is unique.*

Note that $F'(U)$ in Theorem 3 denotes the Jacobian matrix $J_F(U)$ of the vector-value function F. An equilibrium point $E^* = \left(I_h^*, I_s^*, C^*, M^*\right)$ for system (14) satisfies:

$$\begin{cases} \beta_h(I_h^*)(N_h^* - I_h^*)C^* - (d_h + \gamma(I_h^*))I_h^* = 0, \\ \beta_s(N_s^* - I_s^*)M^* - (d_s + \theta)I_s^* = 0, \\ g(I_s^*) - (d_c + \eta)C^* = 0, \\ f(I_h^*) - d_m M^* = 0. \end{cases} \tag{15}$$

The system (15) can be easily transformed to:

$$\begin{cases} I_h^* = \dfrac{\beta_h(I_h^*)N_h^* C^*}{d_h + \gamma(I_h^*) + \beta_h(I_h^*)C^*}, \\ I_s^* = \dfrac{\beta_s N_s^* f(I_h^*)}{d_m(d_s + \theta) + \beta_s f(I_h^*)}, \\ C^* = \dfrac{g(I_s^*)}{(d_c + \eta)}. \end{cases} \tag{16}$$

We rewrite Eq. (16) into a fix point problem of the vector function F as follows:

$$U^* = F(U^*), \tag{17}$$

where:

$$U^* = \begin{pmatrix} I_h^* \\ I_s^* \\ C^* \end{pmatrix} \quad \text{and} \quad F(U^*) = \begin{pmatrix} F_1(U^*) \\ F_2(U^*) \\ F_3(U^*) \end{pmatrix} = \begin{pmatrix} \dfrac{\beta_h(I_h^*)N_h^* C^*}{d_h + \gamma(I_h^*) + \beta_h(I_h^*)C^*} \\ \dfrac{\beta_s N_s^* f(I_h^*)}{d_m(d_s + \theta) + \beta_s f(I_h^*)} \\ \dfrac{g(I_s^*)}{(d_c + \eta)} \end{pmatrix}.$$

It is easy to see that $F(U^*)$ is continuous and maps $\mathbb{R}^3_+$ into itself. The equilibrium points satisfy the fixed point problem $U^* = F(U^*)$. We use this formulation to prove existence

and uniqueness of an endemic equilibrium. Moreover, $F(0) = 0$ and it is straightforward that, for $U^* \in \mathbb{R}^3_+$, one has:

$$F_1(U^*) \leq N_{\rm h}^*, \quad F_2(U^*) \leq N_{\rm s}^*, \quad F_3(U^*) \leq \frac{g^M}{d_{\rm c}+\eta}.$$

Thus, one deduces that $F(U^*)$ is a bounded function. More precisely, let:

$$\mathcal{D} = \left\{ \left(I_{\rm h}^*, I_{\rm s}^*, C^*\right) : 0 \leq I_{\rm h}^* \leq N_{\rm h}^*,\ 0 \leq I_{\rm s}^* \leq N_{\rm s}^*,\ 0 \leq C^* \leq \frac{g^M}{d_{\rm c}+\eta} \right\},$$

the function F is a continuous bounded function that maps $\mathcal{D}$ into itself. Next, we prove that $F(U^*)$ is monotone non-decreasing, $J_F(0)$ is irreducible, and $\rho(J_F(0)) > 1$ whenever $\mathcal{R}_0 > 1$. To that end, notice that the Jacobian matrix of $F(U^*)$ is:

$$J_F(U^*) = \begin{pmatrix} J_{11} & 0 & J_{13} \\ J_{21} & 0 & 0 \\ 0 & J_{32} & 0 \end{pmatrix},$$

where:

$$J_{11} = \frac{N_{\rm h}^* C^* [\beta_{\rm h}'(I_{\rm h}^*)(d_{\rm h}+\gamma(I_{\rm h}^*)) - \gamma'(I_{\rm h}^*)\beta_{\rm h}(I_{\rm h}^*)]}{[d_{\rm h}+\gamma(I_{\rm h}^*) + C^*\beta_{\rm h}(I_{\rm h}^*)]^2} \leq 0,$$
$$J_{13} = \frac{\beta_{\rm h}(I_{\rm h}^*) N_{\rm h}^* (d_{\rm h}+\gamma(I_{\rm h}^*))}{[d_{\rm h}+\gamma(I_{\rm h}^*) + C^*\beta_{\rm h}(I_{\rm h}^*)]^2} > 0,$$

$$J_{21} = \frac{d_{\rm m}(d_{\rm s}+\theta)\beta_{\rm s} N_{\rm s}^* f'(I_{\rm h}^*)}{[d_{\rm m}(d_{\rm s}+\theta) + \beta_{\rm s} f(I_{\rm h}^*)]^2} > 0, \quad J_{32} = \frac{g'(I_{\rm s}^*)}{d_{\rm c}+\eta} > 0.$$

Since, from the assumptions (A1)–(A3), the entries J_{13}, J_{21}, and J_{32} are positive, the Jacobian matrix $J_F(U^*)$ is a Metzler matrix. Thus, thanks to Theorem B4 in the Appendix B, $F(U^*)$ is a monotone function. In addition, it is non-decreasing, because $\partial F_i(U^*)/\partial U_j^* \geq 0$ for all $i \neq j$. Moreover, the associated directed graph of the matrix $J_F(0)$ is a cycle. In fact, the directed graph of $J_F(0)$ is such that: edge 1 is connected to edge 3 which in turn is connected to edge 2, which finally connects back to edge 1, giving rise to a cycle. Hence, thanks to the graph theory, this graph is strongly connected, and consequently, $J_F(0)$ is irreducible (see Theorem B1 in the Appendix B). Furthermore:

$$J_F(0) = \begin{pmatrix} 0 & 0 & \dfrac{\beta_0 N_{\rm h}^*}{d_{\rm h}+\gamma(0)} \\ \dfrac{\beta_{\rm s} N_{\rm s}^* f'(0)}{d_{\rm m}(d_{\rm s}+\theta)} & 0 & 0 \\ 0 & \dfrac{g'(0)}{d_{\rm c}+\eta} & 0 \end{pmatrix}.$$

The characteristic polynomial of $J_F(0)$ is:

$$P(x) = -x^3 + \frac{\beta_0 S_{\rm h}^0 f'(0)\beta_{\rm s} S_{\rm s}^0 g'(0)}{d_{\rm m}(d_{\rm h}+\gamma(0))\,(d_{\rm c}+\eta)\,(d_{\rm s}+\theta)} = -x^3 + \mathcal{R}_0^2,$$

from which one deduces easily that the spectral radius of $J_F(0)$ is (since $\mathcal{R}_0 > 1$):

$$\rho(J_F(0)) = \mathcal{R}_0^{2/3} > 1.$$

It remains to prove that $F(U^*)$ is strictly sub-linear, i.e.,

$$\forall\, U^* \gg 0, \quad \forall\, \lambda \in (0,1), \quad \lambda F(U^*) < F(\lambda U^*).$$

Using the fact that $\gamma(I_h^*)$ is increasing, some simple calculations yield:

$$\frac{\lambda F_1(U^*)}{F_1(\lambda U^*)} - 1 < \frac{\lambda N_h^* C^* \left[(d_h + \gamma(I_h^*))(\beta_h(I_h^*) - \beta_h(\lambda I_h^*) + C^* \beta_h(I_h^*)\beta_h(\lambda I_h^*)(\lambda - 1)\right]}{F_1(\lambda U^*)\left[d_h + \gamma(I_h^*) + \beta_h(I_h^*)C^*\right]\left[d_h + \gamma(\lambda I_h^*) + \lambda\beta_h(\lambda I_h^*)C^*\right]}.$$

Since $\lambda \in (0,1)$, we have $I_h^* > \lambda I_h^*$. Thus, using the assumption (A2), one has $(\beta_h(I_h^*) - \beta_h(\lambda I_h^*)) < 0$. Thus:

$$\frac{\lambda F_1(U^*)}{F_1(\lambda U^*)} - 1 < 0.$$

One can also get easily that:

$$\frac{\lambda F_2(U^*)}{F_2(\lambda U^*)} - 1 = \frac{\beta_s N_s^* \left[d_m(d_s + \theta)\left(\lambda f(I_h^*) - f(\lambda I_h^*)\right) + \beta_s f(I_h^*) f(\lambda I_h^*)(\lambda - 1)\right]}{F_2(\lambda U^*)\left[d_m(d_s + \theta) + \beta_s f(I_h^*)\right]\left[d_m(d_s + \theta) + \beta_s f(\lambda I_h^*)\right]}.$$

Since, from the assumption (A3), the function f is concave down, we deduce that $\lambda f(I_h^*) - f(\lambda I_h^*) < 0$ and:

$$\frac{\lambda F_2(U^*)}{F_2(\lambda U^*)} - 1 < 0.$$

A similar proof using the concavity of g shows that:

$$\frac{\lambda F_3(U^*)}{F_3(\lambda U^*)} - 1 < 0.$$

Hence, $F(U^*)$ is strictly sub-linear. Applying Theorem 3, we have established the following result.

Theorem 4 *$\mathcal{R}_0 > 1$, and then, system (14) has a unique endemic equilibrium in the interior of Ω_1 denoted by $E^* = \left(I_h^*, I_s^*, C^*, M^*\right)$, such that $I_h^* > 0$, $I_s^* > 0$, $C^* > 0$, $M^* > 0$.*

4.2.2 Global stability of the endemic equilibrium

Theorem 5 *If $\mathcal{R}_0 > 1$, the endemic equilibrium E^* of Eq. (14) is GAS in $\mathbb{R}^4_+ \setminus \{E_0\}$.*

The proof of Theorem 5 hinges on the monotonicity property of model (14) and on the result below whose proof can be found in Zhao (2003); Zhao and Jing (1996):

Theorem 6 *Let $h : \mathbb{R}^n_+ \to \mathbb{R}^n$, $n \in \mathbb{N} \setminus \{0\}$ be a continuously differentiable map. Assume that:*

(1) *h is cooperative on $\mathbb{R}^n_+$ and the Jacobian matrix $(\partial h_i / \partial y_j)_{1 \le i,j \le n}$ is irreducible for every $y \in \mathbb{R}^n_+$;*
(2) *$h(0) = 0$ and $h_i(y) \ge 0$ for all $y \in \mathbb{R}^n_+$ with $y_i = 0$, $i = 1, 2, ..., n$;*
(3) *h is strictly sub-linear on $\mathbb{R}^n_+$. Then:*

(a) if the stability modulus $s(J_h(0))$ of $J_h(0)$ is nonpositive, then $y = 0$ is GAS in $\mathbb{R}^n_+$;
(b) if $s(J_h(0)) > 0$ and $\varphi(t, y_0)$ is the solution for $\dot{y} = h(y)$ initiate at y_0, then either:
(i) *for any $y \in \mathbb{R}^4_+ \setminus \{E_0\}$, $\lim_{t \to \infty} \| \varphi(t, y) \| = +\infty$, or alternatively,*

(ii) system $\dot{y} = h(y)$ *admits a unique positive steady state* $y^* \gg 0$ *which is GAS in* $\mathbb{R}^4_+ \setminus \{E_0\}$.

Proof of Theorem 5: We write model (14) in the form:

$$\dot{y} = h(y),$$

where:

$$y = \begin{pmatrix} I_h \\ I_s \\ C \\ M \end{pmatrix}, \quad h(y) = \begin{pmatrix} \beta_h(I_h)(N_h^* - I_h)C - (d_h + \gamma(I_h))I_h \\ \beta_s(N_s^* - I_s)M - (d_s + \theta)I_s \\ g(I_s) - (d_c + \eta)C \\ f(I_h) - d_m M. \end{pmatrix}.$$

Clearly h is continuously differentiable from $\mathbb{R}^4_+$ to $\mathbb{R}^4$. The Jacobian matrix of h at $y \in \mathbb{R}^4_+$ is:

$$J_h(y) = \begin{pmatrix} -h_{11} & 0 & h_{13} & 0 \\ 0 & -h_{22} & 0 & h_{24} \\ 0 & g'(I_s) & -h_{33} & 0 \\ f'(I_h) & 0 & 0 & -d_m \end{pmatrix}, \tag{18}$$

with

$$\begin{aligned} h_{11} &= [-\beta_h'(I_h)(N_h^* - I_h) + \beta_h(I_h)]C + (d_h + \gamma(I_h)) + \gamma'(I_h)I_h, \\ h_{13} &= \beta_h(I_h)(N_h^* - I_h), \\ h_{22} &= \beta_s M + d_s + \theta, \\ h_{24} &= \beta_s(N_s^* - I_s), \\ h_{33} &= d_c + \eta. \end{aligned}$$

$J_h(y)$ is a Metzler matrix and h is cooperative (Smith 1988). Moreover, using the graph theory (Hethcote and Thieme 1985), one can easily see that $J_h(y)$ is irreducible, since $h_{13}, h_{24}, f'(I_h), g'(I_s)$ are positive. Thus, condition (1) in Theorem 6 is fulfilled for $n = 4$. Condition (2) of Theorem 6 is straightforward for $n = 4$.

To show that h is strictly sub-linear, observe that for every $y \gg 0$ and $\alpha \in (0, 1)$, if $h_1(y) = \beta_h(I_h)(N_h^* - I_h)C - (d_h + \gamma(I_h))I_h$, then, since $\beta_h(\alpha I_h) > \beta_h(I_h)$, $N_h^* - \alpha I_h > N_h^* - I_h$ and $\gamma(\alpha I_h) < \gamma(I_h)$, we have:

$$\begin{aligned} h_1(\alpha y) &= \alpha\beta_h(\alpha I_h)(N_h^* - \alpha I_h)C - \alpha(d_h + \gamma(\alpha I_h))I_h \\ &> \alpha\left[\beta_h(I_h)(N_h^* - I_h)C - (d_h + \gamma(I_h))I_h\right] \\ &= \alpha h_1(y). \end{aligned}$$

On the other hand, since $g(I_s)$ is concave with $g(0) = 0$, we have:

$$g(\alpha I_s) = g(\alpha I_s + (1 - \alpha)0) > \alpha g(I_s) + (1 - \alpha)g(0) = \alpha g(I_s).$$

Thus:

$$\begin{aligned} h_3(\alpha y) &= g(\alpha I_s) - (d_c + \eta)\alpha C \\ &> \alpha\left[g(I_s) - (d_c + \eta)C\right] \\ &= \alpha h_3(y). \end{aligned}$$

Similarly, since $f(I_h)$ is concave and $f(0) = 0$, one has:

$$f(\alpha I_h) = f(\alpha I_h + (1 - \alpha)0) > \alpha f(I_h) + (1 - \alpha)f(0) = \alpha f(I_h),$$

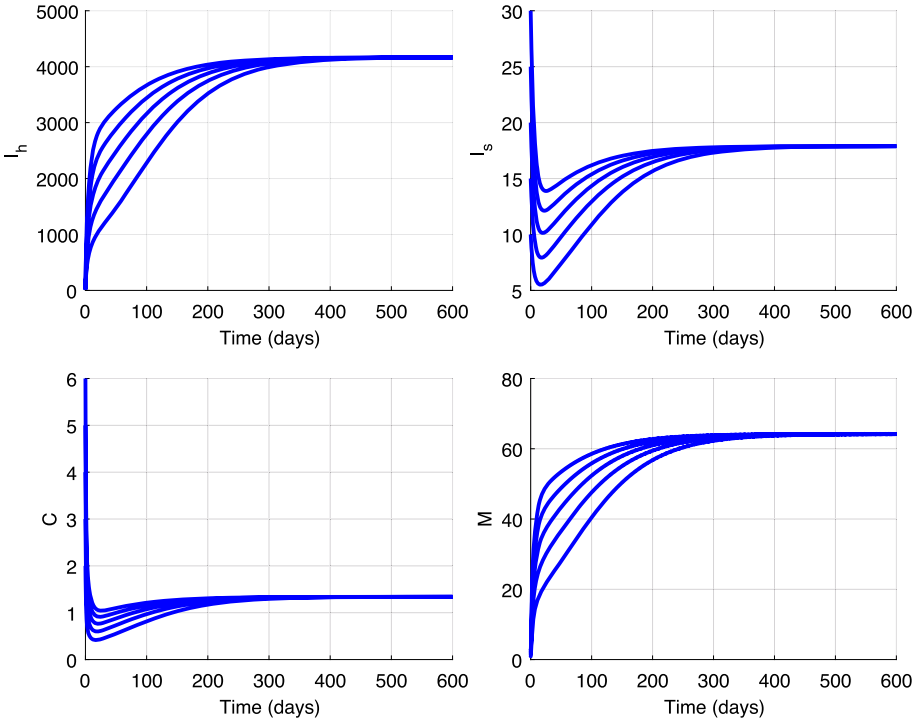

Fig. 4 GAS of the disease-persistent equilibrium E^*. All the parameters are as in Table 1 except that the contact rate between snails and miracidia has been increased to $\beta_s = 3.5 \times 10^{-4}$, leading to $\mathcal{R}_0 = 1.937 > 1$

and therefore:

$$\begin{aligned} h_4(\alpha y) &= f(\alpha I_h) - d_m \alpha M \\ &> \alpha \left[f(I_h) - d_m M \right] \\ &= \alpha h_4(y). \end{aligned}$$

Finally, since $N_s^* - \alpha I_s > N_s^* - I_s$, it is obvious that:

$$\begin{aligned} h_2(\alpha y) &= \beta_s (N_s^* - \alpha I_s) \alpha M - (d_s + \theta) \alpha I_s \\ &> \alpha \left[\beta_s (N_s^* - I_s) M - (d_s + \theta) I_s \right] \\ &= \alpha h_2(y). \end{aligned}$$

Hence, h is strictly sub-linear and condition (3) of Theorem 6 is satisfied for $n = 4$. It remains to verify that $s\left(J_h(0)\right) > 1$. This is straightforward, because $J_h(0) = F + V = F - (-V)$ is a regular decomposition/splitting, and according to (Berman and Plemmons 1979, page 138), one has:

$$s\left(J_h(0)\right) > 1 \iff \mathcal{R}_0 > 1.$$

Since the conditions for Theorem 6 are fulfilled for $n = 4$, its application proves that E^* is GAS in $\mathbb{R}_+^4 \setminus \{E_0\}$. Theorem 5 is further illustrated by Fig. 4.

Remark 1 It is worth noticing that, thanks to Theorem 1, the GAS of the unique endemic equilibrium of the reduced system (14) established in Theorem 5 translates back to the GAS of the unique endemic equilibrium of system (8), which in turn translates back to the GAS of the unique endemic equilibrium of system (4), since the latter system is equivalent to the former one. This, together with the GAS of the disease-free equilibrium established in Theorem 2, completely solves the asymptotic behavior of our original model (4) which, despite its general form, exhibits the classical threshold dynamics similar to most epidemic models.

5 Application: control measures and sensitivity analysis

Since the most important feature of our model is the incorporation of human behavior through the use of the disease prevalence dependent contact rate $\beta_h(I_h)$, the human shedding rate function $f(I_h)$, $g(I_s)$, and the treatment rate function $\gamma(I_h)$, without loss of generality, we reformulate these functions to allow an easy-to-do assessment of their impacts on the disease dynamics.

We study model (14) by choosing simple "human behavior" functions $\beta_h(I_h), \gamma(I_h), f(I_h)$, $g(I_s)$ which satisfy the assumptions $(\mathbf{A_1}) - (\mathbf{A_3})$ as follows:

$$\beta_h(I_h) = \beta_0 - \beta_M \frac{I_h}{1+I_h}, \quad \gamma(I_h) = \gamma_0 + \gamma^m \frac{I_h}{1+I_h}, \quad f(I_h) = \delta_h \frac{I_h}{1+a_h I_h},$$
$$g(I_s) = \xi_s \frac{I_s}{1+a_s I_s}, \tag{19}$$

where β_0, β_M, γ_0, γ^m, a_h, a_s, δ_h, and ξ_s are defined in Table 1. Precisely, δ_h (resp. ξ_s) is the maximal shedding rate of infected humans (resp. snails). The parameter a_h (resp. a_s) models the positive effect of human behavior and represents the "shrinking" rate for the deposition of miracidia (resp. cercariae) by infected humans (resp. by snails) due to human behavior. Clearly, in the absence of human behavior (i.e $a_h = 0$), the cercariae are shed linearly, and a_h can be thought of as *awareness rate* of the disease by humans. Similar remarks apply for the role of a_s on the shedding of cercariae, where a_s could be thought of as *indirect awareness rate* of the disease.

With the "toy functions" given in Eq. (19), we shall revisit, the corresponding expression of the basic reproduction number, the theorem on the existence and uniqueness of the corresponding endemic equilibrium E^*, and further provide insights into the role of human behavior on the endemicity level of the disease. Note that with the choice of the functions above in (19), the basic reproduction number reads:

$$\mathcal{R}_0 = \frac{1}{(d_s+\theta)} \sqrt{\frac{\beta_0 b_h \delta_h \beta_s b_s \xi_s}{d_m d_h (d_h+\gamma_0)(d_c+\eta)}}.$$

Moreover, it is easy to show that the I_h^*-component of the endemic equilibrium E^* of Eq. (14) satisfies the quadratic equation:

$$P(I_h^*) = A_2 I_h^{*2} + A_1 I_h^* + A_0 = 0, \tag{20}$$

Table 1 Parameters description of model (4)

	Description	Values	Ranges	Sources
Transmission param.				
b_h	Human replenishment rate	8000	[6000, 10000]	Chiyaka et al. (2010)
b_s	Snail replenishment rate	200	[150, 3000]	Chiyaka et al. (2010)
$\beta_h(I_h)$	Behavioral contact rate for humans			
β_s	Contact rate for snail	9.1×10^{-5}	[0.00006, 0.0009]	Mangal et al. (2008)
d_h	Human natural death rate	0.014	[0, 0.5]	Feng et al. (2004)
d_c	Cercaria natural death rate	1	[1, 5]	Mangal et al. (2008) and Ngarakana-Gwasira et al. (2016)
d_s	Snail natural death rate	0.004	[0.001, 0.04]	Mangal et al. (2008)
d_m	Miracidium natural death rate	2.52	[2, 10]	Mangal et al. (2008)
$\gamma(I_h)$	Behavioral treatment rate			
θ	Snail removal rate	0.1	[0.01, 0.5]	Variable
η	Cercaria removal rate	0.05	[0.01, 0.5]	Variable
$f(I_h)$	Behavioral human shedding rate			
$g(I_s)$	Behavioral snail shedding rate			
Behavior param.				
β_0	Behavioral contact rate for humans	0.059	[0.05, 0.1]	Mangal et al. (2008)
β_M	Maximal reduced contact rate	0.032	[0.01, 0.04]	Mangal et al. (2008)
γ_0	Constant treatment rate	0.03	[0.01, 0.05]	Feng et al. (2004)
γ^m	Maximum increase treatment rate	0.002	[0.001, 0.02]	Variable
δ_h	Maximum deposit rate of miracidia	500	[300, 800]	Mangal et al. (2008)
ξ_s	Maximum deposit rate of cercariae	0.08	[0.03, 0.1]	Mangal et al. (2008)
a_h	Direct effect of human behavior	[0, 0.05]	[0, ∞]	Variable
a_s	Indirect effect of human behavior	[0, 0.033]	[0, ∞]	Variable

where:

$$
\begin{aligned}
A_2 &= \xi_s\delta_h\beta_s N_s^*(\beta_0-\beta_M) + (d_c+\eta)(d_h+\gamma_0+\gamma^m)\left[\delta_h\beta_s + a_h d_m(d_s+\theta) + a_s\delta_h\beta_s N_s^*\right],\\
A_1 &= d_m(d_s+\theta)(d_c+\eta)(d_h+\gamma_0)\left(1-\mathcal{R}_0^2\right) + \gamma^m d_m(d_s+\theta)(d_c+\eta)\\
&\quad +\xi_s\delta_h\beta_s N_s^*(\beta_0+\beta_M N_h^*) + (d_s+\theta)(d_c+\eta)(d_h+\gamma_0)\left[\delta_h\beta_s + a_h d_m(d_s+\theta) + a_s\delta_h\beta_s N_s^*\right],\\
A_0 &= d_m(d_s+\theta)(d_c+\eta)(d_h+\gamma_0)\left(1-\mathcal{R}_0^2\right).
\end{aligned}
$$

If $\mathcal{R}_0 \leq 1$, then $A_2, A_1, A_0 > 0$, such that Eq. (20) do not have any positive root. Hence, there is no endemic equilibrium in this case.

If $\mathcal{R}_0 > 1$, then $A_0 < 0$, $P(0) = A_0 < 0$. Since $A_2 > 0$, we have $P(+\infty) = +\infty$, so that, applying the intermediate value theorem, there exists a positive root for Eq. (20). Furthermore, by Descartes's rule of signs, the positive root is unique. Therefore, the discriminant $\Delta = A_1^2 - 4A_0A_2$ is positive. Thus, the unique positive solution of Eq. (20) is given by:

$$
I_h^* = \frac{-A_1 + \sqrt{A_1^2 - 4A_0A_2}}{2A_2}. \tag{21}
$$

From Eq. (21) and using the explicit expressions for $\beta_h(I_h)$, $\gamma(I_h)$, $f(I_h)$ in Eq. (19), we recover the remaining positive components of E^* as follows:

$$I_s^* = \frac{\beta_s N_s^* f(I_h^*)}{d_m(d_s+\theta)+\beta_s f(I_h^*)},$$
$$C^* = \frac{\left(d_h+\gamma(I_h^*)\right) I_h^*}{(N_h^*-I_h^*)\beta_h(I_h^*)} = \frac{g(I_s^*)}{d_c+\eta},$$
$$M^* = \frac{f(I_h^*)}{d_m}. \tag{22}$$

5.1 Impact of human behavior: reduction of contacts with contaminated water by cercariae

To assess the positive impact of reducing the contact between cercariae and susceptible humans due to behavior changes, we recall that $\beta_h(I_h)$ is reformulated in Eq. (19) to satisfy Eq. (1), such that $\beta_0 = \beta_h(0) > \beta_M > 0$, β_0 is the usual contact rate in the absence of human behavior, and β_M is the maximal reduced contact rate due to positive behavior change.

Analytically, the positive impact of minimizing $\beta_h(I_h)$ is acknowledged by decreasing the disease endemic level and is summarized in the following theorem.

Theorem 7 *If $\mathcal{R}_0 > 1$, the disease component I_h^* of the unique endemic equilibrium E^* of system (14) is strictly decreasing in the maximal reduced contact rate β_M.*

Proof It suffices to show that $\dfrac{\partial I_h^*}{\partial \beta_M} \leq 0$. To that end, we stress that the direct differentiation of the explicit expression of I_h^* in Eq. (21) with respect to β_M leads to mathematical difficulties hard to overcome. Alternatively, we shall differentiate Eq. (20). Since A_0 in Eq. (20) does not depend on β_M, we have:

$$2A_2 I_h^* \frac{\partial I_h^*}{\partial \beta_M} + I_h^{*2}\frac{\partial A_2}{\partial \beta_M} + A_1 \frac{\partial I_h^*}{\partial \beta_M} + I_h^* \frac{\partial A_1}{\partial \beta_M} = \frac{\partial I_h^*}{\partial \beta_M}\left(2A_2 I_h^* + A_1\right)$$
$$+ I_h^*\left(\frac{\partial A_1}{\partial \beta_M} + I_h^* \frac{\partial A_2}{\partial \beta_M}\right) = 0.$$

From the latter relation, using Eq. (22), we obtain:

$$\frac{\partial I_h^*}{\partial \beta_M} = -\frac{I_h^*\left(\dfrac{\partial A_1}{\partial \beta_M} + I_h^* \dfrac{\partial A_2}{\partial \beta_M}\right)}{2A_2 I_h^* + A_1} = -\frac{I_h^* \xi_s \delta_h \beta_h N_s^* \left(N_h^* - I_h^*\right)}{2A_2 I_h^* + A_1}. \tag{23}$$

Clearly, the numerator of Eq. (23) is positive. Since A_1 can be negative or positive, it remains to prove the positivity of its denominator. This is done by observing that, thanks to Eq. (21), the quantity $2A_2 I_h^* + A_1 = \sqrt{\Delta} > 0$. This achieved the proof.

Corollary 1 *The result in Theorem 7 holds in the generic setting where the functions β_h, γ, f, g are not explicitly specified but satisfy the assumptions (A1)–(A3).*

The proof of this corollary is provided in the Appendix A.

Remark 2 The following observations are in order:

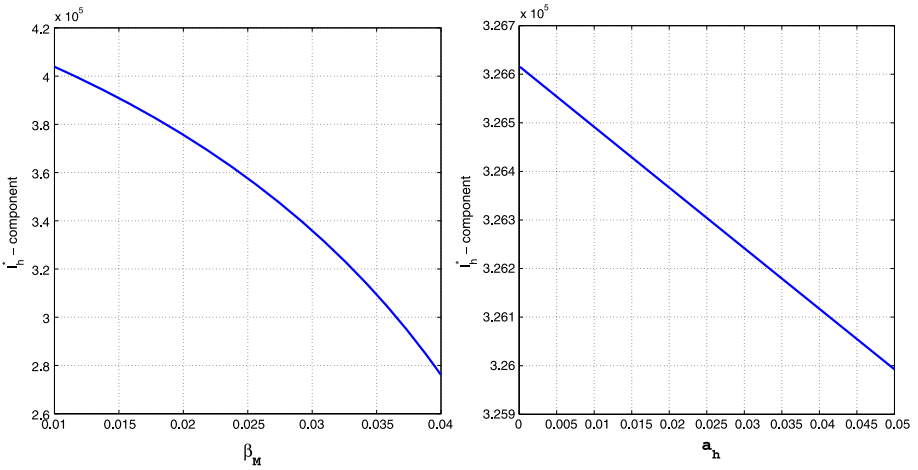

Fig. 5 Effects of sole human behavior change on the endemic level of the disease

(1) The favorable impact of reducing/avoiding contacts with cercariae cannot act on the reduction of $\mathcal{R}_0$ through minimization of β_{M}. This is because human behavior change only starts when the disease outbreak has established itself and $\mathcal{R}_0$ is calculated at the disease-free equilibrium when no behavioral change has already been triggered by the disease burden.
(2) The decrease in I_{h}^* with respect to the increase in β_{M} also leads to the decrease in I_s^*, C^* and M^* (this can be seen analytically on Eq. (22), since the functions f, γ, g are increasing), so that a significant reduction of β_{M} can mitigate the disease. This is further illustrated in Figs. 5 and 10.

5.2 Impact of human behavior: case management/prophylactic treatment

As expected, the positive impact of treating infected humans is first acknowledged right at the beginning of disease through the reduction of the threshold quantity $\mathcal{R}_0$, because $\mathcal{R}_0$ given in Eq. (7) is a decreasing function of γ_0. Unfortunately, the human behavior change through the increase of the treatment rate does not occur at the onset of the disease; it happens rather later. Hence, to assess the impact of increasing the treatment rate on the disease dynamics due to human behavior change, we recall the form of $\gamma(I_{\mathrm{h}})$ in (2): $\gamma(I_{\mathrm{h}}) = \gamma_0 + \gamma^m \tilde{\gamma}(I_{\mathrm{h}})$. Let us recall that γ_0 is the constant treatment rate in the absence of human behavior, while γ^m is the maximum increase treatment rate due to behavior change. The desirable impact of decreasing the endemic level of the disease by increasing human propensity to undergo treatment is theoretically assessed in the following result.

Theorem 8 *If $\mathcal{R}_0 > 1$, the disease component I_{h}^* of the unique endemic equilibrium E^* of (14) is strictly decreasing in the maximum increase treatment rate γ^m due to human behavior change.*

The proof of Theorem 8 is similar to that of Theorem 7 and is skipped. Moreover, the following remark is an analog of Remark 2, item (2).

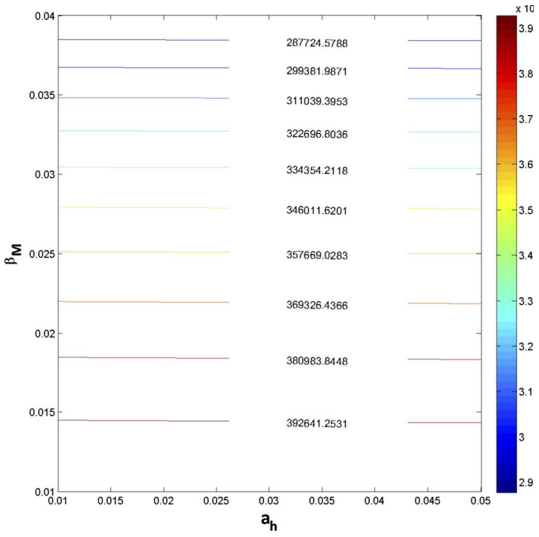

Fig. 6 Effects of combined human behavior changes on the endemic level of the disease

Remark 3 The decrease in I_h^* with respect to the increase in γ^m also leads to the decrease in I_s^*, C^* and M^*, so that by reducing significantly γ^m, the disease can be eradicated or sufficiently mitigated. This is further illustrated in Fig. 11.

5.3 Impact of human behavior: water sanitation enhancement

To capture the influence of positive human behavior change on schistosomiasis evolution via the shedding of miracidia into water, we model in the next section the shedding function $f(I_h, a_h)$, such that, in addition to satisfy the conditions (H4), (A2), and (A3), it vanishes when the disease awareness/health education uptake rate a_h goes to infinity. A typical example for $f(I_h, a_h)$ is proposed in Eq. (19). Since $f(I_h, a_h)$ is a decreasing function of a_h, we intend to show that the endemic level of the disease decreases with the increase of a_h (awareness/health education uptake rate) and eventually approaches zero when a_h becomes large enough. Precisely, the following result is established.

Theorem 9 *If $\mathcal{R}_0 > 1$, the disease component I_h^* of the unique endemic equilibrium E^* of Eq. (14) decreases with the awareness rate a_h. Moreover, $\lim_{a_h \to \infty} I_h^*(a_h) = 0$.*

Proof The first statement is readily shown as in Theorem 7. As for the second statement, it follows by taking the limit of the explicit expression of I_h^* as $a_h \to \infty$, or alternatively in the generic case, one notices that as a_h tends to infinity, the shedding function $f(I_h, a_h)$ goes to zero. Thus, system (14) transforms to the system (i.e when $f(I_h) = 0$) in which the miracidia population $M(t)$ decreases exponentially to zero. Consequently, either component $I_s(t)$, $C(t)$, and $I_h(t)$ decreases exponentially to zero, as well. That is, the disease-free equilibrium is the unique GAS equilibrium of model (14). This proves the theorem. To prove numerically Theorem 9 and emphasize the importance of human behavior on the reduction of the endemic level, we first plot I_h^* versus the maximal reduced contact rate β_M and second plot I_h^* versus the disease awareness rate a_h in Fig. 5, as well as the contour plot of I_h^* in the plane (a_h, β_M) in Fig. 6. On the other hand, the effects of human behavior on the reduction of time series solutions are displayed in Figs. 10, 11, and 12.

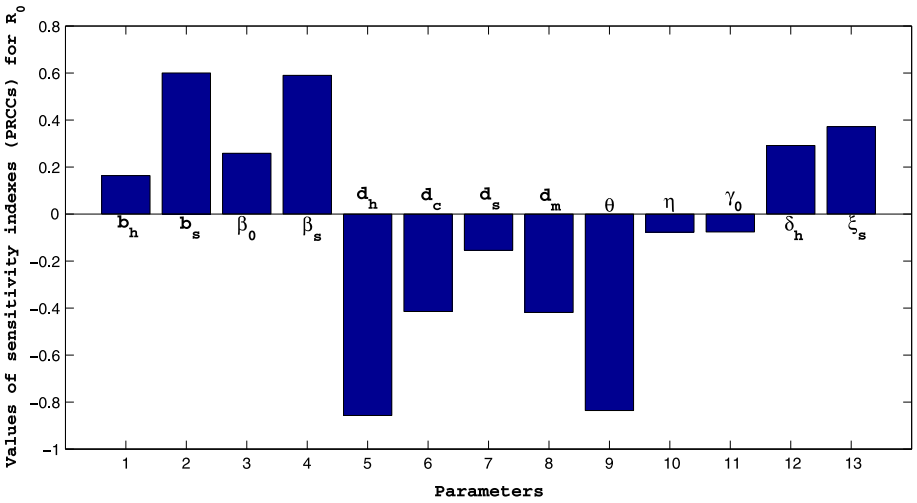

Fig. 7 Partial rank correlation coefficients (PRCCs) for the global sensitivity analysis of $\mathcal{R}_0$ with respect to each model parameter

5.4 Biological control: removal of snails and/or cercariae

The positive impact of providing safe and clean water is first seen right at the beginning of disease through the reduction of $\mathcal{R}_0$, which, according to Eq. (7), is readily a decreasing function of θ and η.

Theorem 10 *If $\mathcal{R}_0 > 1$, the disease component I_h^* of the unique endemic equilibrium E^* for model (14) is strictly decreasing with respect to either the removal rate of snails θ, or of cercariae η.*

This proof is similar to Theorem 7. It suffices to differentiate Eq. (28) with respect to θ for the first case and to η for the second case. We skip the proof and illustrate it numerically in Fig. 13.

The impacts of biological control strategies on schistosomiasis may also be addressed by assessing the effects of the corresponding control on the basic reproduction number $\mathcal{R}_0$. Simultaneous influences of model parameters on $\mathcal{R}_0$ can provide insights into the most effective factors in mitigating $\mathcal{R}_0$. Some of these investigations are shown in Fig. 7, from which the sensitivity analysis via the computation of Partial Rank Correlation Coefficients (PRRCs) of $\mathcal{R}_0$ with respect to involved parameters shows the positive effect of increasing θ on the huge reduction of $\mathcal{R}_0$. Moreover, in Fig. 8, one could realize that, when the contact rate in the absence of human behavior is very large, say for instance $\beta_0 = 0.1$, the removal of snails must be increased to at least $\theta = 0.025$ to bring $\mathcal{R}_0$ below one. Similarly, when the treatment rate in the absence of human behavior is very small, say for instance $\gamma_0 = 0.02$, the removal of snails must be increased to at least $\theta = 0.028$ to bring $\mathcal{R}_0$ below one.

5.5 Biological control: blocking cercariae shedding by snails

One possible way to mitigate schistosomiasis is by controlling the transmission of parasite larvae from the snails that carry them. Snail inhibition is a biological process by which

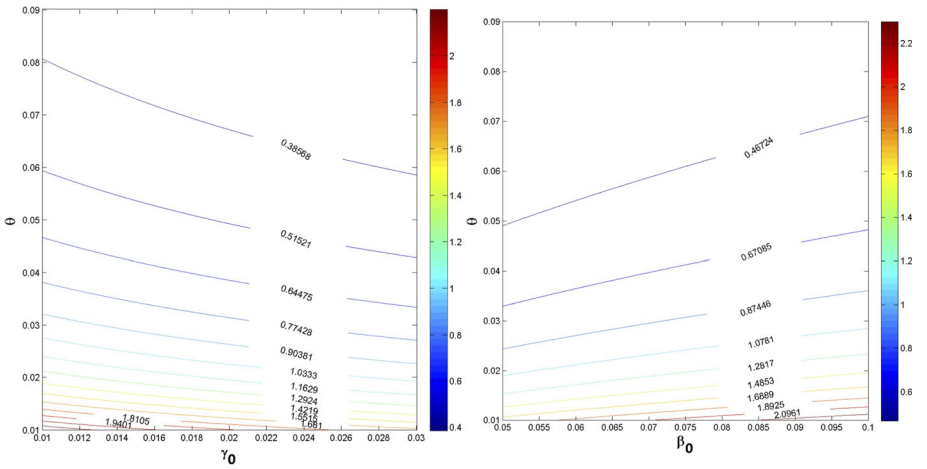

Fig. 8 Effects of the combination of the constant transmission rates and one biological control on $\mathcal{R}_0$. Left panel: constant treatment rate (γ_0) and removal rate of infected snails (θ). Right panel: constant contact rate (β_0) and removal rate of infected snails (θ)

the snails are prevented from shedding cercariae (Allan et al. 2017; Ittiprasert and Knight 2012). We model this by a shedding $g(I_s, a_h)$, such that apart from satisfying the conditions (H4), (A2) and (A3), it increases with the maximum shedding rate ξ_s. A typical and simple example for $g(I_s, a_h)$ is given in Eq. (19). We intend to show that the endemic level of the disease decreases with the decrease in the maximum shedding rate ξ_s of infected snails and eventually approaches zero as ξ_s reaches its minimal value 0. Precisely, the following result is established.

Theorem 11 *If $\mathcal{R}_0 > 1$, the disease component I_h^* of the unique endemic equilibrium E^* of system (14) decreases with the maximum shedding rate ξ_s. Moreover, $\lim_{\xi_s \to 0} I_h^*(\xi_s) = 0$.*

Proof While the proof of the first statement is similar to that of Theorem 7, that of the second statement follows from Theorem 9.

5.6 Global sensitivity analysis

Traditionally, in mathematical epidemiology, sensitivity analysis tells us how important each parameter is to the disease transmission process. It is commonly used to determine the robustness of model predictions to parameter values. Such information can first be drawn from the analysis of the basic reproduction number $\mathcal{R}_0$, to evaluate the strength of involved parameters in triggering or mitigating the disease outbreak. Its ultimate aim being to discover parameters with high influence on $\mathcal{R}_0$, and on which intervention/control strategies should be targeted. To achieve that, the sets of input parameter values sampled using the Latin hypercube sampling (LHS) method is used to run 1000 simulations. We compute the Partial Rank Correlation Coefficients between $\mathcal{R}_0$ and each parameter, and display the results in Fig. 7. Because the parameters of interest to us are those related to human behavior (which unfortunately do not appear in $\mathcal{R}_0$) and those related to biological control, from Fig. 7, one can notice that $\mathcal{R}_0$ is highly sensitive to θ and less sensitive to η. Since θ accounts for the

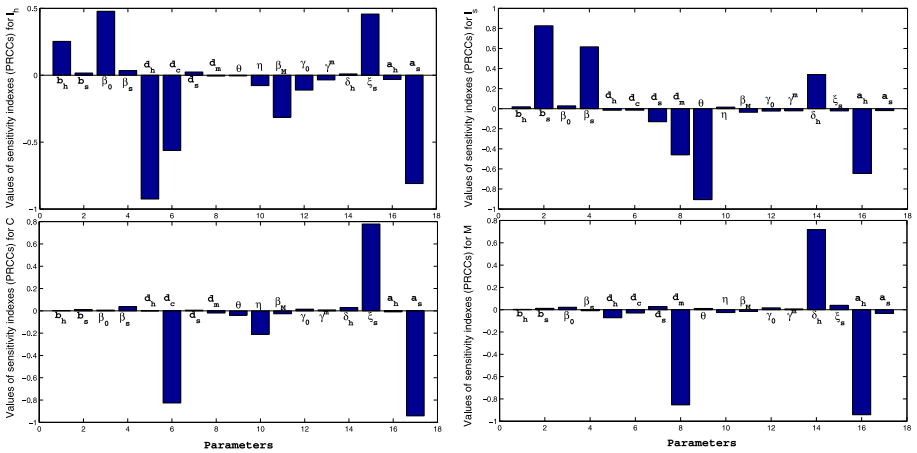

Fig. 9 Partial rank correlation coefficients (PRCCs) for the global sensitivity analysis of I_h^*, I_s^*, C^*, and M^* with respect to each model parameter. Or equivalently, it gives the global influence of model's parameters on the solution $(I_h(t), I_s(t), C(t), M(t))$ of model (14) for large enough values of the time t and is consistent with the results for local sensitivity analyses in Theorems 7–11 in the sense that control measures have positive impacts by decreasing the number of infected humans $I_h(t)$

reduction of snails, whereas η deals with the removal of cercariae, we conclude that an increase in θ will be the best biological control measure to implement to significantly reduce $\mathcal{R}_0$ and consequently minimizes the disease outbreak risk.

On the other hand, the global sensitivity analysis of model variables in Fig. 9 shows that the human and snail infected classes are highly influenced by the increase in the maximum reduced human contact β_M and disease awareness parameters a_h and a_s, respectively; thus, highlighting the role of positive human behavior changes in reducing the severity of schistosomiasis and/or in controlling the disease. Furthermore, infected snails and miracidia are more sensitive the removal rate θ than infected humans and cercariae do. More importantly, Fig. 9 further illustrates the robustness of Theorems 7–11 with respect to the changes on model's parameters, by showing that the latter results remain valid when all the parameters vary simultaneously. Thus, an integrated control strategy will always be beneficial to the reduction of the severity of schistosomiasis.

5.7 Numerical study

Finally, to verify our theoretical findings, we simulate model (8) using the simple "human behavior" functions $\beta_h(I_h)$, $\gamma(I_h)$, $f(I_h)$, $g(I_s)$ formulated in Eq. (19) above. The transmission-related parameters are mostly taken from Feng et al. (2004), Mangal et al. (2008) and Ngarakana-Gwasira et al. (2016), while, due to the lack of data about human behavior toward schistosomiasis, corresponding parameters values mimic those in Mangal et al. (2008), as shown in Table 1. In fact, in Mangal et al. (2008), parameters for schistosomiasis are given for different temperature values. One could observe that the higher the temperature, the higher the tendency of people to have contacts with water to cool themselves. Therefore, since for most tropical regions, the average temperature is 25 °C and the highest is 30 °C, we use the parameter values for these two temperatures to estimate the maximum increase in contact (β_M) with cercariae into water .

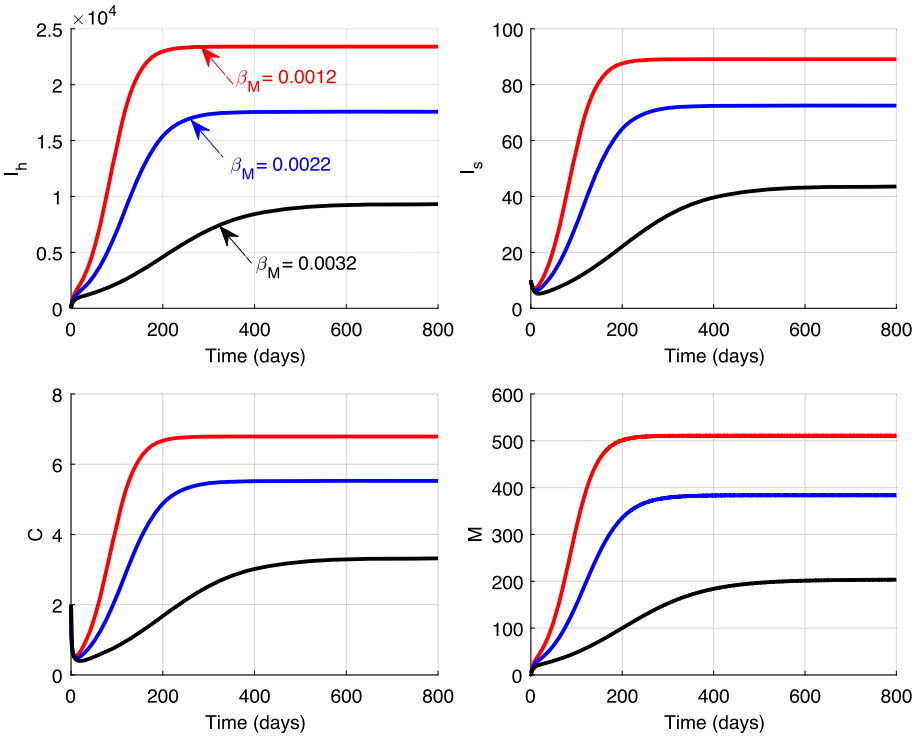

Fig. 10 Illustration of Theorem 7 and Remark 2: positive effect of the maximum reduced contact rate β_{M} in reducing the epidemic/endemic level of the disease. All parameters are as in Table 1. $\mathcal{R}_0 = 1.7933 > 1$. Red curve: $\beta_{\mathrm{M}} = 0.00120$. Blue curve: $\beta_{\mathrm{M}} = 0.0022$. Black curve: $\beta_{\mathrm{M}} = 0.0032$)

The theoretical results are illustrated numerically in the pictures of Fig. 3 for the GAS of the disease-free equilibrium, regardless of the values of a_{h} and a_{s}. The GAS of the endemic equilibrium is shown in Fig. 4 for $\mathcal{R}_0 > 1$ and small value of a_{h}, whereas, when a_{h} is sufficiently high, Fig. 12 highlights the fact the endemic equilibrium becomes sufficiently small (approaches zero), even though $\mathcal{R}_0$ (which is independent of a_{h}) is still greater than one. The latter observation suggests that human behavior only can reduce the endemic level of the disease and can possibly drives it to extinction. The same conclusion is drawn, when in Figs. 10 and 11, one observes that, reducing the maximum contact rate β_{M} of human with cercariae, or increasing the likelihood/propensity γ^m of people to seek for treatment during disease outbreak decreases the endemic level of the disease and possibly help to mitigate/eradicate it. Similarly, Fig. 13 depicts the fact that a biological control consisting of the increase in the removal rate of snails θ (for example, through fish predation) is another efficient strategy to mitigate the infection. Of course, the same result holds if the removal rate of cercariae η (for instance, through the use of safe chemicals) is implemented instead.

6 Conclusion and discussion

6.1 Conclusion

A nonlinear system of ordinary differential equations has been constructed to describe the dynamics of schistosomiasis. The novelty from the modeling perspective lies in the incor-

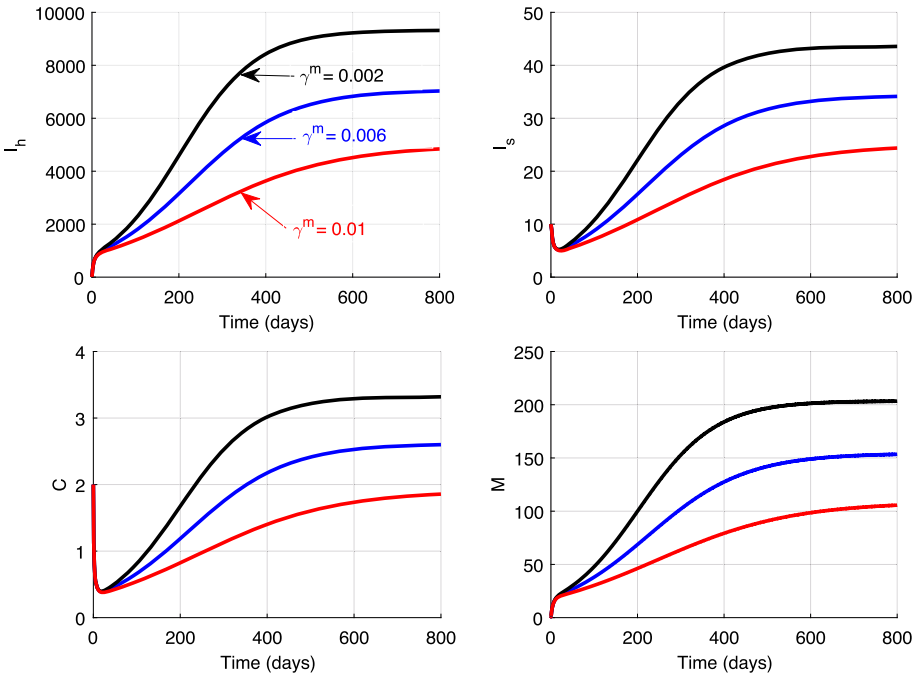

Fig. 11 Illustration of Theorem 8 and Remark 3: positive effect of the minimum reduced contact rate γ^m in reducing the epidemic/endemic level of the disease. All parameters are as in Table 1. $\mathcal{R}_0 = 1.7933 > 1$. Red curve: $\gamma^m = 0.002$. Blue curve: $\gamma^m = 0.006$. Black curve: $\gamma^m = 0.01$)

poration of human behavior through the use of a general prevalence-dependent contact rate $\beta_h(I_h)$, as well as the treatment rate $\gamma(I_h)$ and the shedding rates of miracidia $f(I_h)$ and cercariae $g(I_s)$. The contact rate $\beta_h(I_h)$ is assumed to be a decreasing but with nonzero minimum function of the number of infected human individuals I_h. Its role is to reduce the contact between human beings and cercariae. The shedding rates $f(I_h)$ and $g(I_s)$ are increasing, but saturating functions of the number of infected human beings and snails, respectively. Their respective relevance lies in the fact that we have assumed that the more infected humans are recorded, the more the infected snails and the more the shedding of cercariae and miracidia by humans and snails. As a response to the increase of infected humans (and, of course, the increase in the shedding of infectives agents: cercariae and miracidia), a control measure is launched by assuming an increasing, but saturated treatment rate function $\gamma(I_h)$. Note that the consideration of $\beta_h(I_h)$, $\gamma(I_h)$, $f(I_h)$, and $g(I_s)$ represents four different human behavior-driven control strategies in this work.

The global asymptotic stability analysis of the resulted model has been completely carried out, with the model exhibiting a threshold dynamics: we have shown that the disease dies out when the basic reproduction number $\mathcal{R}_0$ (i.e., the threshold parameter) is less than or equal to one, and persists globally whenever $\mathcal{R}_0$ is greater than one. This threshold dynamics was translated back to the original model via the facilitation of two main ingredients: (1) the decomposition technique by Vidyasagar (1980) which helped to reduce the dimension of the original model and obtain an asymptotically equivalent and more mathematically tractable reduced model; (2) the fact the reduced model was a monotone (cooperative) system with

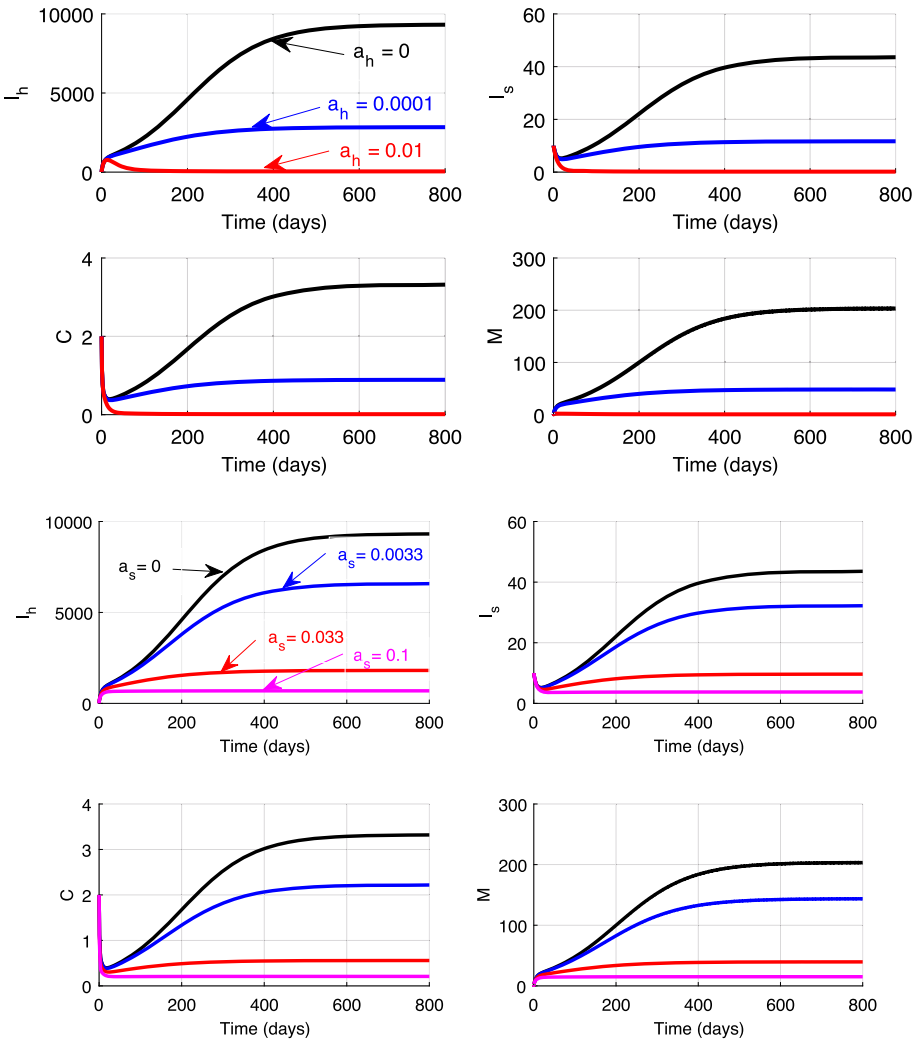

Fig. 12 Positive impact of human behavior in reducing the shedding rate of cercariae and miracidia. One could see that even though the parameters from Table 1 are such that $\mathcal{R}_0 = 1.7933 > 1$, by increasing a_h, while $a_s = 0$, it is possible to bring the disease to extinction (top 2 panels). This progression to the elimination is much more faster than do the increasing of a_s, while $a_h = 0$ (bottom 2 panels)

a nice property of being strictly sub-linear (Smith 1988; Zhao 2003; Zhao and Jing 1996; Anguelov et al. 2012).

Because human behavior change in our modeling framework had no influence the dynamics in the absence of disease, and since the basic reproduction number $\mathcal{R}_0$ is estimated at the disease-free population, human behavior did not alter the value of $\mathcal{R}_0$ (Lu et al. 2017; Manfredi and D'Onofrio 2013; Sahu and Dhar 2015; Wang et al. 2015). Therefore, favorable human behavior changes will not help to bring back larger value of $\mathcal{R}_0$ under unity. Nonetheless, intensifying favorable human behavior changes greatly helped to reduce the number infected humans at the endemic level (i.e., if $\mathcal{R}_0 > 1$). This was illustrated in Figs. 10, 11

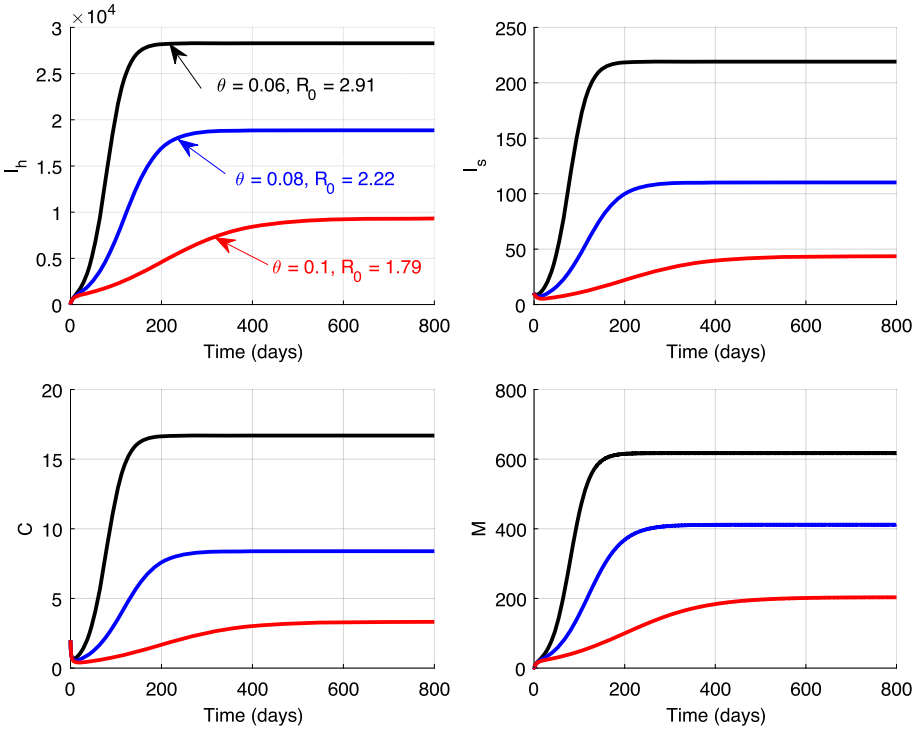

Fig. 13 Illustration of Theorem 10: positive impact of biological control in removing (predation for instance) infected snails. Red curve: $\theta = 0.06$. Blue curve: $\theta = 0.08$. Back curve: $\theta = 0.1$)

and 12. Moreover, if by other (biological) control means such as: removal of snails and cercariae, treatment of infected humans, the basic reproduction number $\mathcal{R}_0$ can be brought to a value less than 1 (see Fig. 8), then positive human behavior change can help to accelerate the extension of the epidemic (see Fig. 3), where the use of $a_{\mathrm{h}} > 0$ halves the elimination time, precisely from 200 to 100 days. Hence, our theoretical and numerical analyses were centered on the implementation of an integrated control strategy, with the main focus on the impacts of human behavior on schistosomiasis dynamics and the quantification of the expectation of positive human behavior changes in mitigating the epidemic and endemic levels of the disease. Complementary to the theoretical analysis above, the global sensitivity analysis (see Fig. 7) of the basic reproduction number has been performed and has shown that it is highly sensitive to the biological control parameter θ accounting for the removal of the snails from the water. The assessment of the effects of model's parameters on the solutions (see Figs. 10, 11, 12, 13) further highlighted the fact that infected humans and snails are highly sensitive to human behavior parameter β_{M} and disease awareness parameter a_{h}, respectively. In addition to the latter, Fig. 9 shows that the combination of all the control strategies will always be beneficial to the reduction of the severity of the endemic level of schistosomiasis.

Specifically, to deepen the assessment of the impacts of human behavior and biological control on the transmission dynamics of schistosomiasis, many control strategies have been investigated both theoretically and numerically, including a biological control in removing the snails and cercariae in water. Our main results with respect to the implementation of this integrated control measure showed that:

(i) minimizing the human contact rate with cercariae, by increasing the maximum reduced contact rate β_M due to human behavior, reduces the endemic level of the disease (see Theorem 7, and Figs. 9, 10).
(ii) increasing the treatment rate of humans by increasing the maximum reduced treatment rate γ^m due human behavior is beneficial (see Theorem 8, and Figs. 9, 11).
(iii) minimizing the shedding rate of cercariae, by increasing the awareness of disease rates a_h and/or a_s is favorable in mitigating the disease (see Theorem 9, and Figs. 9, 12).
(iv) implementing biological control, by increasing the removal rate of snails θ or of cercariae η; each may help to reduce the infection risk, mitigate the disease burden, minimize the epidemic/endemic level, and eventually drive it to the lowest endemic level (see Theorem 10, and Figs. 9, 13).

All these investigations have demonstrated the importance of human behavior and biological control in reducing and/or controlling the schistosomiasis transmission risk and its epidemic/endemic level.

6.2 Discussion

Having realized that amongst all the biological control strategies, the one that mostly minimizes $\mathcal{R}_0$ in a robust sense is the removal/elimination rate θ of snails, we believe and suggest that the reduction of infected snails could be the cost-effective biological control measure for the mitigation of schistosomiasis. This can be simply implemented by introducing into water ponds the predator fishes (pawns, crayfishes, etc.) that prey on snails (Bernot 1999). This latter control strategy was implemented recently in Senegal and has given promising outcomes (Sokolowa et al. 2015). It is worth noticeable that the removal rate of cercariae η has a mild effect on $\mathcal{R}_0$ (very small PRCC coefficient) compared to θ. Moreover, knowing that the removal of cercariae can only be efficiently performed by the utilization of chemicals, which, in fact, is not recommended due to water pollution threat, one can conclude that the best biological measure to lower the basic reproduction number $\mathcal{R}_0$ is the implementation of snails elimination by introducing the snail's predator fishes.

The assessment of the impacts of model's parameters on the solution $(I_h(t), I_s(t), C(t), M(t))$ done through Figs. 10, 11 and 12 showed that, in addition to depict the fact these variables decrease when the favorable human behavior increases, they highlight the fact that the human infected population always decreases, while the snails, the cercaria, and miracidia populations decrease in the beginning of the disease and later increase to reach an equilibrium state in approximately 1 year (400 days). This suggests that human behavior (through the parameters a_h, γ^m, β_M) first acts directly and detrimentally on the populations of snails, cercariae, and miracidia, and do not affect the infected human population (since it is increasing) at the onset of the disease. The same feature cannot be observed in Fig. 13, because the basic reproduction number $\mathcal{R}_0$ does depend on the parameter θ. One should acknowledge, on one hand, that it is very difficult (if not impossible) to practically quantify human behavior parameters $(a_h, \gamma^m, \beta_M, a_s)$ (Funk et al. 2015) to test our results in this work against the reality at hand, and on the other hand that, the intriguing question is more about what type of behavior change is possible, how to measure it, and how to implement in a model? Furthermore, other human behavior modeling approaches might lead to different conclusions, and it is very difficult to say which approach is more relevant or which conclusion is more suitable. Therefore, to dodge the latter difficulty, one should alternatively focus on biological control measures that can be easily implemented. In this regard, among many possibilities, the following extensions of our model are possible alternatives:

(1) Diverting the cercariae to nonsensitive snails (to minimize the population of cercaria producing snails) by the incorporation in our model of a competitor nonsensitive snail population (Diaby et al. 2014).
(2) The introduction of the population of predator fishes that prey on sensitive snails (Sokolowa et al. 2015).

In a more complicated setting, the consideration of:

(a) The inclusion of other and more elaborated behavioral contact and/or shedding rate functions instead of simple prevalence-dependent functions.
(b) The spatial dynamics (reaction–convection–diffusion model) of snails and/or cercariae will be worth investigating.

Besides the above-mentioned possible extensions which will involve additional variables, one should actually note that, in the current work, the dependence of g on a_h indirectly describes the influence of the number of infected human individuals I_h on the shedding of miracidia. In fact, as I_h increases, human hosts get informed/educated, then revised their shedding habit of miracidia, which leads to less infection of snails and latter to less shedding of cercariae by snail hosts. However, if contrary to hypothesis (H4), human behavior change is broadened to educate people to not urinate or defecate in water ponds, it is more reasonable to assume that g depends directly on I_h and that $f(I_h, a_h)$ and $g(I_h, a_h)$ are, respectively, replaced by $f_1(I_h, a_h)I_h$ and $g_1(I_h, a_h)I_s$, where f_1 and g_1 are decreasing convex functions of I_h with nonzero lower bounds. The latter features can be understood by noticing that, the greater the infected humans, the lesser the cercariae are shed (human behavior change), the lesser the snails are infected, and the lesser the miracidia are generated. The current assumptions on f, g have been adopted in this work for simplicity, as well as for mathematical technicalities and for the monotonicity property of the reduced system.

Finally, we draw the attention of the reader that, in this work, we have assumed that human behavior changes are always beneficial in curtailing the spread of disease. However, it is possible that human behavior becomes counterproductive (e.g., the wrong quarantine practices; the release of messages inciting fears over vaccine safety, as it was the case in during West Africa Ebola outbreak, etc.). Thus, more elaborated forms of human behavior contact, treatment function rates (not necessary monotone) should be considered. A more realistic model accounting for the drawbacks mentioned in (H3)–(H5) is been taking care of in a different study, in which, unfortunately, the nice mathematical properties which we have here will be lost, unless one further assumes that the derivative of $(f_1(I_h, a_h)I_h)$ is positive, to recover the monotonicity of the corresponding reduced model. If the latter assumption is relaxed, a different analytical approach should be adopted to deal with the asymptotic dynamics of the model. Nonetheless, philosophically, we believe that the conclusions will be similar as far as the influence of human behavior on the disease control is concerned.

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Appendixes

Appendix A: Proof of Corollary 1

Proof We are going to prove that $\dfrac{\partial I_{\mathrm{h}}^*}{\partial \beta_{\mathrm{M}}} \leq 0$. Recall the equilibrium equations:

$$\begin{cases} \beta_{\mathrm{h}}(I_{\mathrm{h}}^*)(N_{\mathrm{h}}^* - I_{\mathrm{h}}^*)C^* - (d_{\mathrm{h}} + \gamma(I_{\mathrm{h}}^*))I_{\mathrm{h}}^* = 0, \\ \beta_{\mathrm{s}}(N_{\mathrm{s}}^* - I_{\mathrm{s}}^*)M^* - (d_{\mathrm{s}} + \theta)I_{\mathrm{s}}^* = 0, \\ g(I_{\mathrm{s}}^*) - (d_{\mathrm{c}} + \eta)C^* = 0, \\ f(I_{\mathrm{h}}^*) - d_{\mathrm{m}}M^* = 0. \end{cases} \tag{24}$$

In system (24), the fourth equation gives $M^* = \dfrac{f(I_{\mathrm{h}}^*)}{d_{\mathrm{m}}}$, from which the first and second equations yield:

$$C^* = v(I_{\mathrm{h}}^*) = \frac{(d_{\mathrm{h}} + \gamma(I_{\mathrm{h}}^*))I_{\mathrm{h}}^*}{\beta_{\mathrm{h}}(I_{\mathrm{h}}^*)(N_{\mathrm{h}}^* - I_{\mathrm{h}}^*)}, \tag{25}$$

and

$$I_{\mathrm{s}}^* = u(I_{\mathrm{h}}^*) = \frac{\beta_{\mathrm{s}}N_{\mathrm{s}}^* f(I_{\mathrm{h}}^*)}{\beta_{\mathrm{s}} f(I_{\mathrm{h}}^*) + d_{\mathrm{m}}(d_{\mathrm{s}} + \theta)}. \tag{26}$$

Putting the two expressions above into the third equation of (24), yields another expression of $v(I_{\mathrm{h}}^*)$ in the form, one has:

$$v(I_{\mathrm{h}}^*) = \frac{d_{\mathrm{c}} + \eta}{g(u(I_{\mathrm{h}}^*))}. \tag{27}$$

Recalling from (1) that $\beta_{\mathrm{h}}(I_{\mathrm{h}}^*) = \beta_0 - \beta_{\mathrm{M}}\widetilde{\beta}_{\mathrm{h}}(I_{\mathrm{h}}^*)$, $v(I_{\mathrm{h}}^*)$ in (25) becomes:

$$v(I_{\mathrm{h}}^*) = \frac{(d_{\mathrm{h}} + \gamma(I_{\mathrm{h}}^*))I_{\mathrm{h}}^*}{(N_{\mathrm{h}}^* - I_{\mathrm{h}}^*)\left[\beta_0 - \beta_{\mathrm{M}}\widetilde{\beta}_{\mathrm{h}}(I_{\mathrm{h}}^*)\right]}.$$

Thus, the I_{h}^*-component of the endemic equilibrium E^* is the solution of:

$$\frac{(d_{\mathrm{h}} + \gamma(I_{\mathrm{h}}^*))I_{\mathrm{h}}^*}{(N_{\mathrm{h}}^* - I_{\mathrm{h}}^*)\left[\beta_0 - \beta_{\mathrm{M}}\widetilde{\beta}_{\mathrm{h}}(I_{\mathrm{h}}^*)\right]} = \frac{d_{\mathrm{c}} + \eta}{g(u(I_{\mathrm{h}}^*))}. \tag{28}$$

After differentiating both sides of (28) with respect to β_{M} using the chain rule, follow by some rearrangements, one has:

$$\begin{aligned} &\frac{\partial I_{\mathrm{h}}^*}{\partial \beta_{\mathrm{M}}}\left\{\frac{W(I_{\mathrm{h}}^*)}{\left[\beta_0 - \beta_{\mathrm{M}}\widetilde{\beta}_{\mathrm{h}}(I_{\mathrm{h}}^*)\right]^2 (N_{\mathrm{h}}^* - I_{\mathrm{h}}^*)^2} + \frac{(d_{\mathrm{c}} + \eta)g'(u(I_{\mathrm{h}}^*))u'(I_{\mathrm{h}}^*)}{g^2(u(I_{\mathrm{h}}^*))}\right\} \\ &\quad = -\frac{I_{\mathrm{h}}^*\left[d_{\mathrm{h}} + \gamma(I_{\mathrm{h}}^*)\right]\widetilde{\beta}_{\mathrm{h}}(I_{\mathrm{h}}^*)}{\left[\beta_0 - \beta_{\mathrm{M}}\widetilde{\beta}_{\mathrm{h}}(I_{\mathrm{h}}^*)\right]^2 (N_{\mathrm{h}}^* - I_{\mathrm{h}}^*)}, \end{aligned} \tag{29}$$

where:

$$\begin{aligned} W(I_{\mathrm{h}}^*) = &\left[d_{\mathrm{h}} + \gamma(I_{\mathrm{h}}^*)\right]\left[(N_{\mathrm{h}}^* - I_{\mathrm{h}}^*)\beta_{\mathrm{h}}(I_{\mathrm{h}}^*) + I_{\mathrm{h}}^*\beta_{\mathrm{h}}(I_{\mathrm{h}}^*) + \beta_{\mathrm{M}}I_{\mathrm{h}}^*(N_{\mathrm{h}}^* - I_{\mathrm{h}}^*)\widetilde{\beta}_{\mathrm{h}}'(I_{\mathrm{h}})\right] \\ &+ I_{\mathrm{h}}^*(N_{\mathrm{h}}^* - I_{\mathrm{h}}^*)\beta_{\mathrm{h}}(I_{\mathrm{h}}^*)\gamma'(I_{\mathrm{h}}^*). \end{aligned}$$

Have in mind that, from (26), one has:

$$u'(I_{\mathrm{h}}^*) = \frac{\mathrm{d}u(I_{\mathrm{h}}^*)}{\mathrm{d}I_{\mathrm{h}}^*} = \frac{\beta_{\mathrm{s}}N_{\mathrm{s}}^* d_{\mathrm{m}} f'(I_{\mathrm{h}}^*)(d_{\mathrm{s}} + \theta)}{\left[\beta_{\mathrm{s}} f(I_{\mathrm{h}}^*) + d_{\mathrm{m}}(d_{\mathrm{s}} + \theta)\right]^2}.$$

Since f, g and $\widetilde{\beta}_{\mathrm{h}}(I_{\mathrm{h}}^*)$ are increasing, we have $u'(I_{\mathrm{h}}^*)$, $W(I_{\mathrm{h}}^*) \geq 0$, so that the right-hand side of (29) is negative and the expression into the big brackets on the left-hand side of (29) is positive. Hence, the proof is achieved.

Appendix B: A primer on graph theory and monotone dynamical systems

A primer on graph theory

Definition B1 (Berman and Plemmons 1979, page 29) For a $n \times n$ matrix $A = \left(a_{ij}\right)_{1 \leq i,j \leq n}$, the directed graph $G(A)$ consists of P_1, P_2, ..., P_n vertices where an edge leads from P_i, to P_j if and only if $a_{ij} \neq 0$.
Definition B2 (Berman and Plemmons 1979, page 30) A directed graph $G(A)$ is strongly connected if, for any ordered pair (P_i, P_j), $i \neq j$ of vertices of $G(A)$, there exists a sequence of edges (a path) which leads from P_i to P_j.
Theorem B1 (Berman and Plemmons 1979, Theorem (2.7), page 31) *A matrix A is irreducible if and only if $G(A)$ is strongly connected.*

A primer on monotone dynamical systems

Consider an ordinary differential equation (ODE):

$$\frac{\mathrm{d}x}{\mathrm{d}t} = f(x), \tag{30}$$

defined on a positively invariant set U. We denote by $\Phi_t(x)$ the flow of (30). We assume, to avoid complications, that this is defined for any $t \geq 0$ (this will be the case our system). We consider the standard partial order on $\mathbb{R}^n$ and recall the following corresponding notations:

$$\begin{aligned} &x \leq y \Longleftrightarrow \text{for all } i \ x_i \leq y_i; \\ &x < y \text{ if } x \leq y \text{ and } x \neq y; \\ &x \ll y \Longleftrightarrow \text{for all } i \ x_i \leq y_i. \end{aligned}$$

Definition B3 (Hirsch 1988; Iggidr et al. 2012) System (1) is called monotone if $x \leq y$ implies $\Phi_t(x) \leq \Phi_t(y)$.
Definition B4 (Hirsch 1985; Iggidr et al. 2012) System (2) is called strongly monotone if $x < y$ implies $\Phi_t(x) \ll \Phi_t(y)$ for any $t > 0$.
Theorem B4 ((Smith 1988; Sokolowa et al. 2015), **Lemma 2.1**) *If f is C^1, then System* (1) *is monotone if and only if the Jacobian of f is a Metzler matrix. Note that a Metzler matrix is a matrix whose off-diagonal terms are nonnegative.*
Theorem B5 (Hirsch 1988; Iggidr et al. 2012) *System* (2) *is strongly monotone if its Jacobian matrix is irreducible.*
Definition B5 (Berman and Plemmons 1979, page 138) A matrix A has a regular splitting/decomposition if A has a representation $A = M - N$, where $M^{-1} \geq 0$, $N \geq 0$.

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