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Adapting Strategies for Effective Schistosomiasis Prevention: A Mathematical Modeling Approach

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Abstract: One of the most deadly neglected tropical diseases known to man is schistosomiasis. Understanding how the disease spreads and evaluating the relevant control strategies are key steps in predicting its spread. We propose a mathematical model to evaluate the potential impact of four strategies: chemotherapy, awareness programs, the mechanical removal of snails and molluscicides, and the impact of a change in temperature on different molluscicide performances based on their half-lives and the length of time they persist in contact with target species. The results show that the recruitment rate of humans and the presence of cercaria and miracidia parasites are crucial factors in disease transmission. However, schistosomiasis can be entirely eradicated by combining all of the four strategies. In the face of climate change and molluscicide degradation, the results show that increasing the temperatures and the number of days a molluscicide persists in the environment before it completely degrades decreases the chemically induced mortality rate of snails while increasing the half-life of different molluscicides increases the death rate of snails. Therefore, eradicating schistosomiasis effectively necessitates a comprehensive integration of all preventative measures. Moreover, regions with different weather patterns and seasonal climates need strategies that have been adapted in terms of the appropriate molluscicide and time intervals for reapplication and effective schistosomiasis control.

Keywords: chemotherapy; public literacy; mechanical removal of snails; molluscicide performance; temperature; molluscicide degradation; half-life

MSC: 92B05

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1. Introduction

Schistosomiasis is the second-most significant neglected tropical disease (NTD), a physically debilitating and persistent disease [1,2] that leads to severe morbidity and almost 12,000 deaths globally, of which at least 90% are from sub-Saharan Africa [2]. Human schistosomiasis infection caused by Trematoda worms depends on the availability of suitable freshwater intermediate host snails (IHs) and the final human host to be transmitted [3]. The main symptoms of infection include skin rash and itching, fever, cough, muscle pain, bloody urine, and growth retardation in children [2], while severe cases can lead to damage and failure of the liver, bladder, lungs, and intestines [1,2]. Unfortunately, unlike most NTDs, including lymphatic filariasis, leprosy, and leishmaniasis, there are currently no recommendations for intensive disease management for schistosomiasis [4], and current

disease control strategies rely on mass drug administration (MDA) chemotherapy, which, at times, is combined with health education [5,6]. Although there has been a success in the implementation of chemotherapy, especially in Africa [7,8], this may have limited the implementation of new methods to interrupt parasite transmission through snail control, leading to a resurgence of the disease following drug treatment and education efforts [6,9,10]. Therefore, there is a need to recast the current and future schistosomiasis control strategies to focus on integrated measures and enhanced surveillance response to both changes in infection and snail abundance.

Various methods have been employed in the control of schistosomiasis. For instance, intermediate hosts (IHs) can be controlled through biological, chemical/molluscicides, or environmental/ecological methods [11–13]. Biological measures include the use of predators and competitor snails [12], while chemical control measures consider the use of molluscicides to reduce IH density and abundance [14,15]. The use of molluscicides and their effectiveness has been observed to depend on their proper concentration, half-life, technique and timing of application, and length of contact time with target species, as well as the temperature of the environment where the chemical is released [16]. In addition, environmental/ecological strategies are used to lower the density and abundance of IHs and the risks of snail-to-human transmission (referred to as the mechanical control approach in this study). The approach includes excavating deep channels that act as dry buriers for snails to spread to other water outlets, increasing the flow velocity in irrigation canals, and picking IHs out of the system. Other ways include adopting appropriate cultivation methods, such as shorter fallow times, modifying irrigation techniques, and regulating flooding [11,17].

With the predicted change in global temperature due to climate change, mathematical models have become valuable tools for exploring various infection and control scenarios as they provide both theoretical and practical insights into the epidemiology of infectious diseases. In understanding the transmission and control dynamics of schistosomiasis, different models have been used to create a range of transmission and control outcomes. These models explore dynamics, including free-living parasites, miracidia, and cercariae [18], chemotherapy treatment using praziquantel drugs and the removal of snails and cercariae [19], the impact of public literacy and snail control parameters [20], as well as health education and molluscicides [21].

Our study examines whether molluscicides and/or mechanical control for snail management, combined with mass drug administration and/or health education, can eliminate schistosomiasis. In addition, we postulate that the temperature rise, as predicted by climate change models [22–24], will strongly influence the use of chemicals/molluscicides, and their performance against the target species [25,26] and the general transmission dynamics of the disease. As such, it is important to understand how temperature affects molluscicide usage for the control of schistosomiasis. This can help in the identification and control of chemical-induced environmental hazards that could be harmful to even nontarget species and human health under various environmental conditions [27–30]. The current study will evaluate four controls: mass drug administration/chemotherapy, public literacy, mechanical measures, and chemicals/molluscicides to find the most effective way to eradicate schistosomiasis. In addition, the evaluation includes the effects of temperature rise on various molluscicide performances based on half-lives and contact durations with the targeted species.

2. Materials and Methods

2.1. Schistosomiasis Model Formulation

The dynamics of schistosomiasis [2,3] and stages of intervention strategies are the basis for model formulation (Figure 1). The deterministic model formulated and represented by ordinary differential equations (ODEs) (Equations (1)–(7)) is a modification of those presented by Abokwara and Madubueze [20] and Nur et al. [21], and it is based on the compartment diagram (Figure 1). A population is represented by state time variables that

are associated with the various compartment models and change over time according to the interaction rules. t: the time variable for the sizes of susceptible humans; $S_h(t)$: infected human; $I_h(t)$: eggs released from infected humans; $E_h(t)$: free-living miracidia; $M_f(t)$: susceptible snail vector; $S_v(t)$: infected snail vector; $I_v(t)$: free-living cercariae $C_f(t)$ (Figure 1). The parameters of the model are based on the abiotic and biotic aspects of the *Schistosoma* cycle and transmission, namely the contact rates between the hosts and the free-living cercaria/miracidia population in water and the effective mortality rates.

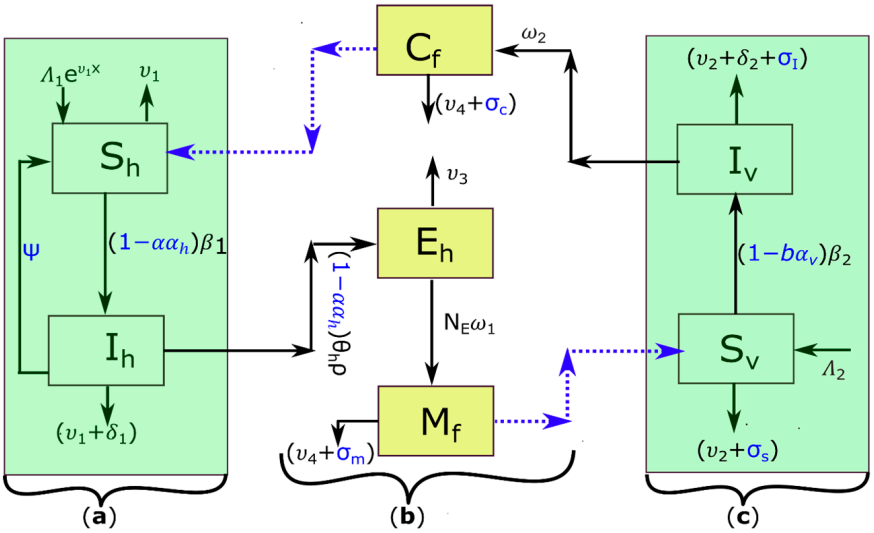

Figure 1. Transmission dynamics of schistosomiasis in (**a**) human definitive hosts (susceptible human S_h; infected human I_h), (**b**) schistosomiasis parasite forms (cercariae C_f; parasite eggs E_h; miracidia M_f), and (**c**) intermediate host snails (susceptible snail S_v; and infected snail I_v). The blue dotted arrows represent the interaction between free-living schistosomiasis parasites and the respective hosts. All parameters are as defined in Section 2.1, and the control parameters are shown in blue.

The population of susceptible human hosts S_h in the model system, Equation (1), increases by an exponential recruitment rate of $\Lambda_1 e^{-\upsilon_1 x}$, where Λ_1 is the maximum per capita birth rate/immigration rate (recruitment rate) of human individuals, υ_1 is the natural mortality rate of humans, and x is the initial age of infection in children. Susceptible human hosts, S_h, are infected only by contact with cercariae in an infested freshwater environment at a rate β_1 per contact. The saturation incidence is a Holling-type II function, which relates the rate of infection transmission and the inhibitory effect, where C_o is the saturation coefficient that represents the transmissibility of infection due to the crowding effect of the cercariae, and ε is the limitation of the growth velocity (density) of the cercaria in contaminated freshwater. Thus, model system, Equation (2) represents the infected humans, I_h. Moreover, due to schistosomiasis infection, infected people die at a rate of δ_1. Thus, our model incorporates chemotherapy treatment for deworming schistosome worms in the infected human body and to stop or limit the release of parasite eggs through urine and feces. We assume that treated infected individuals recover at a rate of ψ and return to the susceptible class because there is no lasting immunity to schistosomiasis, and reinfection is inevitable [9,31]. In addition, public literacy strategy is considered and represented by the parameters $\alpha, \alpha_h \epsilon [0, 1]$, where α is the proportion of people with knowledge/awareness about schistosomiasis, and α_h is the effectiveness of acquired knowledge. This control method focuses on managing the human population by providing access to clean water and improving sanitation and hygiene (WASH) to lower the number of humans being infected [32].

When infected humans I_h indiscriminately release parasite eggs through urine/feces into the environment, their population size increases logistically, as shown in Equation (3).

Where ρ (in grams) is the portion of stool/urine per infected person due to open defecation or urination. θ_h is the number of parasite eggs per gram of stool and/or urine, and K is the carrying capacity of the parasite eggs in the environment. The term $(1 - \alpha\alpha_h)$ represents the public literacy impact in reducing the portion of urine/feces ρ. It describes the impact of public literacy on the density of parasite eggs directly or indirectly deposited in freshwater and lowers the likelihood of human-to-snail transmission. The indirectly deposited parasite eggs find their way into a freshwater source. Each parasite egg E_h hatches, releasing N_E miracidia per parasite egg at a rate ω_1 under suitable conditions, or dies naturally at a rate v_3 when there is no IHs to penetrate, as represented in miracidia population dynamics in Equation (4).

In the model system, Equation (5), the snail host population S_v is recruited at a rate Λ_2 and is infected due to contact with miracidia at a saturation incidence given the saturation coefficient for miracidia infectivity M_o and ε the limitation of the growth velocity of the miracidia. β_2 is the rate of miracidia-to-snail transmission per contact. Both susceptible S_v and infected IH snails I_v die naturally at a rate v_2, but the infected snail (in Equation (6) may also die at a rate of δ_2 due to infection host. Infected snails I_v that survive release infectious cercariae C_f at a rate of ω_2, capable of invading and infecting humans, or dying naturally at a rate of u_5 in the absence of a human host, see Equation (7). Thus, we incorporated a snail management strategy through the mechanical measure, represented by parameter $b, \alpha_v \in [0, 1]$, where b is the proportion of snail density removed and eliminated from the system, and α_v is the effectiveness of such snail management practice. Thus, the impact of a mechanical measure $(1 - b\alpha_v)$ reduces β_2 [20,21].

In addition, we assume that the application of molluscicides into the environment causes susceptible and infected IHs to die at a chemical-induced death rate of $\sigma_s \in [0, 1]$ and $\sigma_I \epsilon [0, 1]$, respectively. Furthermore, molluscicides also reduce viability and cause the deaths of infective cercaria and miracidia at a rate of $\sigma_m \in [0, 1]$ and $\sigma_c \in [0, 1]$, respectively.

Thus, the model equations incorporating terms for control strategies highlighted in blue are given as follows:

$$\dot{S_h}(t) = \Lambda_1 e^{-v_1 x} + \psi I_h - \frac{(1 - \alpha\alpha_h)\beta_1 S_h C_f}{C_o + \varepsilon C_f} - v_1 S_h, \tag{1}$$

$$\dot{I_h}(t) = \frac{(1 - \alpha\alpha_h)\beta_1 S_h C_f}{C_o + \varepsilon C_f} - (v_1 + \delta_1 + \psi) I_h, \tag{2}$$

$$\dot{E_h}(t) = \rho\theta_h(1 - \alpha\alpha_h) I_h \left(1 - \frac{E_h}{K}\right) - (\omega_1 + v_3) E_h, \tag{3}$$

$$\dot{M_f}(t) = N_E \omega_1 E_h - (v_4 + \sigma_m) M_f, \tag{4}$$

$$\dot{S_v}(t) = \Lambda_2 - \frac{(1 - b\alpha_v)\beta_2 M_f S_v}{M_o + \varepsilon M_f} - (v_2 + \sigma_s) S_v, \tag{5}$$

$$\dot{I_v}(t) = \frac{(1 - b\alpha_v)\beta_2 M_f S_v}{M_o + \varepsilon M_f} - (v_2 + \delta_2 + \sigma_I) I_v, \tag{6}$$

$$\dot{C_f}(t) = \omega_2 I_v - (v_5 + \sigma_c) C_f. \tag{7}$$

2.2. Temperature Control

Temperature is a crucial factor for the timing of molluscicide application [16] because molluscicide efficacy is temperature-dependent [33]. The temperature has a significant effect on how quickly the half-lives of molluscicide decrease in water [27]. This has a great influence on the chemical-induced death rates σ_s, σ_I, σ_m, and σ_c and can determine the rate of transmission of the disease. We examine and evaluate the effectiveness of

temperature-dependent molluscicides on the death rates of targeted species. We derive the environmentally dependent chemical-induced deaths of species, where the effect of temperature can be reliably predicted using an Arrhenius equation [27,28,34]. The Arrhenius equation proposed and updated by the European Chemicals Agency, ECHA [29,30] to modify the half-life $t_{1/2}(T)$ at any temperature T of the environment is given as

$$t_{1/2}(T) = t_{1/2}(T_o)e^{0.08[T_o - T]} \tag{8}$$

where $t_{1/2}(T_o)$ is the factory-predetermined half-life of the chemical at the experimental temperature T_o. The preferred experimental temperature in most of the chemicals is $T_o = 20^{\circ}$C [27,35]. Furthermore, we assume that chemically induced mortalities ($\sigma_s, \sigma_I, \sigma_m, \sigma_c$) decrease exponentially with time t according to the following expressions:

$$\sigma_{s,I,m,c} = \sigma'_{s,I,m,c}e^{-kt} \tag{9}$$

where σ'_s, σ'_I, σ'_m, and σ'_c are the maximum mortality rates on the first day ($t = 0$) when the molluscicide is applied in the water. k, is the exponential decay constant of the mortality rate at degradation time t. The terms σ'_s, σ'_I, σ'_m and σ'_c were determined from the withdrawal terms $(d_v + \sigma_s)$, $(d_v + \delta_2 + \sigma_I)$, $(v_3 + \sigma_m)$, and $(v_4 + \sigma_c)$ present in the dynamics of IHs and parasite populations in the absence of humans (Equations (4)–(7)). A maximum value of one (1) is assumed for each term, the same approach as in Carvalho et al. [36]. Furthermore, we link k to the half-life ($t_{1/2}$) of the chemical released by using the following equation:

$$t_{1/2} = In2/k \tag{10}$$

where $1/k$ is the typical time the chemical persists in the environment and is, therefore, in contact with the HIs, the *Schistosoma* parasites, and other nontarget species. The results of substituting σ'_s, σ'_I, and k and substituting Equations (8) and (10) into Equation (9) are shown in Table 1.

Table 1. The continuously exponentially decreasing mortality rates for intermediate hosts and *Schistosoma* parasite forms, as functions of the half-life of the chemical $t_{1/2}$, the temperature T of the environment in which the chemical is released, and the duration t for which the targeted species are exposed to the chemicals.

Intermediate Hosts	***Schistosoma* Parasite Forms**
Susceptible snails	Free-living miracidia
$\sigma_S = (1 - d_v)e^{-\frac{\ln 2}{t_{1/2}\cdot e^{0.08[20-T]}}t}$	$\sigma_M = (1 - v_3)e^{-\frac{\ln 2}{t_{1/2}e^{0.08[20-T]}}t}$
Infected snails	Free-living cercaria
$\sigma_I = (1 - d_v - \delta_2)e^{-\frac{\ln 2}{t_{1/2}e^{0.08[20-T]}}t}$	$\sigma_C = (1 - v_4)e^{-\frac{\ln 2}{t_{1/2}e^{0.08[20-T]}}t}$

Thus, chemical control guarantees the elimination of all three water-dwelling schistosomiasis agents [16]. Furthermore, based on Matthies and Beulke [27] and the European Commission [37], the chemical is nonpersistent (NP) in the environment when $t_{1/2} = 3.1 - 40$, persistent (P) when $t_{1/2} = 41 - 60$, and very persistent (VP) when $t_{1/2} = 61 - 232$. Based on this information, we discriminate the effects of different chemical performances based on their different half-lives $t_{1/2}$, degradation k, and length of chemical exposure $1/k$ on the death rate of the targeted species.

It is worth noting that in our model, we assume that chemotherapy treatment reduces disease morbidity among humans while molluscicide increases the mortality of IHs. Public literacy and mechanical control are management strategies for humans and snails, respectively, that directly and extrinsically prevent the likelihood of parasite-host contact for the transmission of schistosomiasis. Furthermore, there is no vertical transmission of the

disease to humans nor immigration to the infected individuals. Infected snails are unable to reproduce as a side effect of infection and may die more frequently than susceptible snails.

This paper presents the model analysis first, showing that the model is epidemiologically meaningful, realistic, and of interest in a certain invariant region Ω (Appendix A). We then derive the reproduction number (Section 2.3) and show the steady states (Section 2.4).

2.3. Reproduction Number

In epidemiology, one of the most reliable indicators of infection risk is the basic reproduction number R_0, which is the average number of new cases of infection caused by an infectious individual in a fully susceptible population [38]. We derived R_0 by rewriting the model system (Equations (1)–(7)), following Chavez et al. [39], into three components: the number of susceptible individuals (U), the infected schistosomiasis agents that cannot transmit the infection (V), and the infected schistosomiasis agents that transmit the disease (W), as follows:

$$\begin{cases} \frac{dU}{dt} = f(U,V,W) \\ \frac{dV}{dt} = g(U,V,W) \\ \frac{dW}{dt} = H(U,V,W) \end{cases}$$

where $U = (S_h, S_v)$, $V = (E_h, I_h, I_V)$, and $W = \left(M_f, C_f\right)$. We let $U_0 = (U^*, 0, 0)$ represent disease-free at U_0 such that, $\widetilde{g}(U^*, Z) = (\widetilde{g}_1(U^*, W), \widetilde{g}_2(U^*, W))$, where $\widetilde{g}_1(U^*, W) = \frac{\rho\theta_h\beta_1\Lambda_1(1-\alpha\alpha_h)^2e^{-v_1x}C_f}{v_1C_o(\omega_1+v_3)(v_1+\delta_1+\psi)+(1-\alpha\alpha_h)\beta_1\{v_1(v_1+\delta_1+\psi)(\omega_1+v_3)+\rho\theta_h(1-\alpha\alpha_h)\Lambda_2\}C_f}$, and $\widetilde{g}_2(U^*, W) = \frac{(1-b\alpha_v)\beta_2\Lambda_2M_f}{v_2(v_2+\delta_2+\sigma_I)\left(M_o+\varepsilon M_f\right)}$. Suppose, $A = D_Vh(U^*, \widetilde{g}(U^*, 0))$, then A is given by

$$A = \begin{bmatrix} -(v_4+\sigma_m) & \frac{\rho\theta_hN_E\omega_1\beta_1\Lambda_1(1-\alpha\alpha_h)^2e^{-v_1x}}{v_1C_o(\omega_1+v_3)(v_1+\delta_1+\psi)} \\ \frac{(1-b\alpha_v)\omega_2\beta_2\Lambda_2}{v_2M_o(v_2+\delta_2+\sigma_I)} & -(v_5+\sigma_c) \end{bmatrix}$$

Following the next-generation matrix, an approach used by van den Driessche and Watmough [40], and the concept of reproduction numbers by Diekmann et al. [38], the matrix A can be rewritten as $A = F - V$, with $F \geq 0$ (i.e., $f_{ij} \geq 0$) and $V > 0$, a diagonal matrix, where

$$F = \begin{bmatrix} 0 & \frac{\rho\theta_hN_E\omega_1\beta_1\Lambda_1(1-\alpha\alpha_h)^2e^{-v_1x}}{v_1C_o(\omega_1+v_3)(v_1+\delta_1+\psi)} \\ \frac{(1-b\alpha_v)\omega_2\beta_2\Lambda_2}{v_2M_o(v_2+\delta_2+\sigma_I)} & 0 \end{bmatrix}, V = \begin{bmatrix} (v_4+\sigma_m) & 0 \\ 0 & \left(v_5+\sigma_p\right) \end{bmatrix}$$

The basic reproduction number is the spectral radius (dominant eigenvalue) of the matrix FV^{-1} given by

$$R_0 = \rho\left(FV^{-1}\right) = \sqrt{\left(\frac{\rho\theta_hN_E\omega_1\omega_2\beta_1\beta_2\Lambda_1\Lambda_2(1-b\alpha_v)(1-\alpha\alpha_h)^2e^{-v_1x}}{v_1v_2M_oC_o(v_1+\delta_1+\psi)(v_2+\delta_2+\sigma_I)(\omega_1+v_3)(v_4+\sigma_m)(v_5+\sigma_c)}\right)}$$

2.4. Steady State

We show that the model system, Equations (1)–(7) have a disease-free state (E_0) and an endemic steady state E_1, where

$$E_0 = \left(S_h^*, I_h^*, E_h^*, M_f^*S_v^*, I_v^*, C_f^*\right) = \left(\frac{\Lambda_1e^{-v_1x}}{v_1}, 0, 0, 0, \frac{\Lambda_2}{v_2}, 0, 0\right)$$

It always exists in $\mathcal{R}_{+0}^7$ provided $R_0 < 1$.

$E_1 = \left(S_h^1, I_h^1, E_h^1, M_f^1 S_v^1, I_v^1, C_f^1\right)$ is expressed in terms of I_v^1 and E_h^1 by

$$S_h^1\left(I_v^1\right) = \frac{(v_1+\delta_1+\psi)\Lambda_1\left[(v_5+\sigma_c)C_o+\omega_2\varepsilon I_v^1\right]}{(v_1+\delta_1+\psi)(v_5+\sigma_c)C_o+\omega_2[(v_1+\delta_1+\psi)((1-\alpha\alpha_h)\beta_1+\varepsilon)-\psi(1-\alpha\alpha_h)\beta_1]I_v^1},$$

$$I_h^1\left(I_v^1\right) = \frac{\beta_1\omega_2(1-\alpha\alpha_h)(v_1+\delta_1+\psi)\Lambda_1\left[(v_5+\sigma_c)C_o+\omega_2\varepsilon I_v^1\right]I_v^1}{(v_1+\delta_1+\psi)\left((v_5+\sigma_c)C_o+\omega_2 I_v^1\right)\left\{(v_1+\delta_1+\psi)(v_5+\sigma_c)C_o+\omega_2[(v_1+\delta_1+\psi)((1-\alpha\alpha_h)\beta_1+\varepsilon)-\psi(1-\alpha\alpha_h)\beta_1]I_v^1\right\}}$$

$$E_h^1\left(I_v^1\right) = \frac{\beta_1\omega_2\rho\theta_h K(1-\alpha\alpha_h)(v_1+\delta_1+\psi)\Lambda_1\left[(v_5+\sigma_c)C_o+\omega_2\varepsilon I_v^1\right]I_v^1}{(v_1+\delta_1+\psi)\left(\begin{matrix}(v_5+\sigma_c)(\omega_1+v_3)KC_o+\\((\omega_1+v_3)K\omega_2+\rho\theta_h(1-\alpha\alpha_h)\omega_2)I_v^1\end{matrix}\right)\left\{\begin{matrix}(v_1+\delta_1+\psi)(v_5+\sigma_c)C_o+\\\omega_2[(v_1+\delta_1+\psi)((1-\alpha\alpha_h)\beta_1+\varepsilon)-\psi(1-\alpha\alpha_h)\beta_1]I_v^1\end{matrix}\right\}}$$

$$M_f^1\left(I_v^1\right) = \frac{\beta_1\omega_2\rho\theta_h K N_E\omega_1(1-\alpha\alpha_h)(v_1+\delta_1+\psi)\Lambda_1\left[(v_5+\sigma_c)C_o+\omega_2\varepsilon I_v^1\right]I_v^1}{(v_1+\delta_1+\psi)(v_4+\sigma_m)\left(\begin{matrix}(v_5+\sigma_c)(\omega_1+v_3)KC_o+\\((\omega_1+v_3)K\omega_2+\rho\theta_h(1-\alpha\alpha_h)\omega_2)I_v^1\end{matrix}\right)\left\{\begin{matrix}(v_1+\delta_1+\psi)(v_5+\sigma_c)C_o+\\\omega_2[(v_1+\delta_1+\psi)((1-\alpha\alpha_h)\beta_1+\varepsilon)-\psi(1-\alpha\alpha_h)\beta_1]I_v^1\end{matrix}\right\}}$$

$$S_v^1\left(E_h^1\left(I_v^1\right)\right) = \frac{\Lambda_2 M_o+\Lambda_2\varepsilon E_h^1\left(I_v^1\right)}{(v_2+\sigma_s)M_o+((v_2+\sigma_s)\varepsilon+(1-b\alpha_v)\beta_2)E_h^1\left(I_v^1\right)}$$

$$C_f^1\left(I_v^1\right) = \frac{\omega_2 I_v^1}{(v_5+\sigma_c)}$$

when $\dot{I}_v(t)$= 0, we solved I_v^1 using Equation (6) of the model Equations (1)–(7), and this leads to the substitution of $S_v^1\left(E_h^1\left(I_v^1\right)\right)$ and $M_f^1\left(I_v^1\right)$, which yields Equation (11) below.

$$\left(\mathrm{a}_4 I_v^{1^4} + \mathrm{a}_3 I_v^{1^3} + \mathrm{a}_2 I_v^{1^2} + \mathrm{a}_1 I_v^1 + \mathrm{a}_0\right) I_v^1 = 0 \tag{11}$$

where

$$\begin{aligned}
\mathrm{a}_0 &= d_1d_2d_3d_4\mathrm{d}_5d_6C_0M_0K\Lambda_1 - Kk_1k_2k_3k_4\omega_2d_1d_6M_0\Lambda_1\cdot Kd_1d_2d_3\omega_2d_6\varepsilon C_0M_0\Lambda_1\Lambda_2\\
\mathrm{a}_1 &= \mathrm{d}_5(d_1d_2d_3d_4\mathrm{d}_5d_6C_0M_0K\Lambda_1 + M_0C_0d_3d_4d_6\Lambda_1(Kd_1d_2\omega_2+k_1k_2\omega_2)+\varepsilon\omega_2M_0C_0d_6d_4d_3d_1K\Lambda_1\\
&\quad+\varepsilon\Lambda_2Kk_1k_2k_3\omega_2C_0d_1d_6\Lambda_1) - Kk_1k_2k_3k_4\omega_2d_1d_6M_0\Lambda_1\\
&\quad-Kk_1k_2k_3k_4\omega_2d_1\varepsilon C_0\Lambda_1\cdot Kd_1d_2d_3\omega_2d_6\varepsilon C_0M_0\Lambda_1\Lambda_2\\
\mathrm{a}_2 &= \mathrm{d}_5(d_1d_2d_3d_4\mathrm{d}_5d_6C_0M_0K\Lambda_1 + M_0C_0d_3d_4d_6\Lambda_1(Kd_1d_2\omega_2+k_1k_2\omega_2)+\varepsilon\omega_2M_0C_0d_6d_4d_3d_1K\Lambda_1\\
&\quad+\varepsilon\Lambda_2Kk_1k_2k_3\omega_2C_0d_1d_6\Lambda_1 + M_0C_0d_3d_4d_6\Lambda_1(Kd_1d_2\omega_2+k_1k_2\omega_2)+\varepsilon Kk_1k_2k_3\omega_2C_0d_1d_6\Lambda_1)\\
&\quad-\varepsilon M_0C_0d_1d_6\Lambda_1\Lambda_2(Kd_1d_2\omega_2+k_1k_2\omega_2)+M_0C_0d_1d_2^2d_3^2K\Lambda_2\\
&\quad+\varepsilon\Lambda_2Kk_1k_2k_3\omega_2C_0d_1d_6\Lambda_1(Kk_1k_2k_3k_4\omega_2d_1d_6M_0\Lambda_1+Kk_1k_2k_3k_4\omega_2d_1\varepsilon C_0\Lambda_1)\\
\mathrm{a}_3 &= \mathrm{d}_5(M_0C_0d_3d_4d_6\Lambda_1(Kd_1d_2\omega_2+k_1k_2\omega_2)+\varepsilon\omega_2M_0C_0d_6d_4d_3d_1K\Lambda_1+\varepsilon\Lambda_2Kk_1k_2k_3\omega_2C_0d_1d_6\Lambda_1\\
&\quad+M_0C_0d_3d_4d_6\Lambda_1(Kd_1d_2\omega_2+k_1k_2\omega_2)+\varepsilon Kk_1k_2k_3\omega_2C_0d_1d_6\Lambda_1)\\
&\quad-Kk_1k_2k_3k_4\omega_2d_1\varepsilon C_0\Lambda_1\cdot(M_0d_1d_3\varepsilon\omega_2\Lambda_1\Lambda_2(Kd_1d_2\omega_2+k_1k_2\omega_2)+\varepsilon Kk_1k_2k_3\omega_2C_0d_1d_6\Lambda_1)\\
\mathrm{a}_4 &= \mathrm{d}_5(M_0C_0d_3d_4d_6\Lambda_1(Kd_1d_2\omega_2+k_1k_2\omega_2)+\varepsilon Kk_1k_2k_3\omega_2C_0d_1d_6\Lambda_1)(M_0C_0d_3d_4d_6\Lambda_1(Kd_1d_2\omega_2+k_1k_2\omega_2)\\
&\quad+\varepsilon\omega_2M_0C_0d_6d_4d_3d_1K\Lambda_1)\\
k_1 &= (1-\alpha\alpha_h)\beta_1, k_2 = \rho\theta_h(1-\alpha\alpha_h), k_3 = N_E\omega_1, k_4 = (1-b\alpha_v)\beta_2, d_1 = (v_1+\delta_1+\psi),
\end{aligned}$$

$d_2 = (\omega_1+v_3), d_3 = (v_4+\sigma_m), d_4 = (v_2+\sigma_s), \mathrm{d}_5 = (v_2+\delta_2+\sigma_I), \mathrm{d}_6 = (v_5+\sigma_c)$. Equation (11) has one of the solutions $I_v^1 = 0$, which corresponds to a disease-free equilibrium. Other solutions can be determined according to the sign rule of Descartes [41], which states that depending on the change in the sign of the coefficients, a_0, a_1, a_2, and a_3, 3, 2, or 1 positive solutions exist; thus, the proof for existing conditions for E_1 for the model Equations (1)–(7) is complete.

In addition, the stability of the model system depends on the parameters used to build the model and the changes in these parameters affect R_0, with numerous scientific and biological implications for the transmission and control of the disease. For instance, if we use $\beta_1 = \beta^*$ as the bifurcation parameter for model Equations (1)–(7), then $R_0 = 1$ and

$$\beta^* = \frac{\upsilon_1\upsilon_2 M_o C_o(\upsilon_1+\delta_1+\psi)(\upsilon_2+\delta_2+\sigma_I)(\omega_1+\upsilon_3)(\upsilon_4+\sigma_m)(\upsilon_5+\sigma_c)}{\rho\theta_h N_E\omega_1\omega_2\beta_2\Lambda_1\Lambda_2(1-b\alpha_v)(1-\alpha\alpha_h)^2 e^{-\upsilon_1 x}}$$

is the crucial bifurcation value for cercaria-to-human transmission. When $R_0 < 1$ and $\beta_1 < \beta^*$, for instance, only the asymptotically stable disease-free equilibrium point (E_0) can exist, and R_0 provides conditions for disease extinction. The disease-free equilibrium is unstable, whereas the endemic equilibrium (E_1) is asymptotically stable, and both equilibrium points exist when $R_0 > 1$ and $\beta_1 > \beta^*$ [40], and in this case, R_0 provides the conditions for the disease to persist. Thus, the asymptotic dynamic behavior of the infectious disease, which determines whether it will vanish or persist in the future, can be inferred from the steady states. Although we do not provide a stability analysis of the equilibrium points, we acknowledge that control strategies have a role to play in reducing R_0 and possibly eliminating schistosomiasis.

2.5. Parameter Data

For our study, we use data collected in the literature related to *Bulinus* and *Biomphalaria* (Table 2). In the absence of published data, parameter values are assumed or estimated based on expert knowledge using what is commonly known about vector and disease dynamics, as follows. The life expectancy of an adult *Schistosoma* worm within a human host is 3–10.5 years [42–44]; thus, δ_1 vary from $1/(10.5\times 365) \approx 0.000268$ to $1/(3\times 365) \approx 0.000913$. In addition, Dabo et al. [45] establish schistosomiasis infection in preschool children aged 1–4 years through both passive and active exposure to infected water bodies. On average, a child's initial infection age is 2 years [43]; thus, $x = 2\times 365 = 730$ days. Gryseels et al. [46] reported 2–10 weeks as the period a schistosomiasis patient takes to recover after chemotherapy treatment. Thus, we assume that the recovery period for a schistosomiasis patient varies between 14 and 70 days, which sets ψ between $\psi = 1/14 \approx 0.0714$ and $\psi = 1/70 \approx 0.0143$ individuals per day. The *Schistosoma* parasite egg can stay for 7 days, with a 0.14286 per egg death rate, and miracidia survive 12 days in freshwater ($\upsilon_3 = 1/12 \approx 0.0833$) [46,47]. Cercaria can only spend 10–40 h in freshwater [48], which sets υ_4 between $\upsilon_4 = 1/(10\times 24) \approx 0.00417$ and $\upsilon_4 = 1/(40\times 24) \approx 0.00104$. Table 2 shows the numerical values (and potential ranges) of parameters set for the model system Equations (1)–(7) from the literature and estimations.

Table 2. Model parameters, their definition, baseline values, potential ranges, and sources.

Parameter	Definition	Baseline Value	Values Range/Day	References
Λ_1	Human recruitment rate	4127	254–8000	[18,49]
Λ_2	Snail recruitment rate	200	200	[18]
x	Initial age of infection in children	730 d	730 d	[33,46]
δ_1	The human death rate due to infection	0.0039	0.0039	[50]
υ_1	Natural death rate of human	0.00004025	0.0000384–0.0000421	[18,41]
ρ	Proportion of stool/urine per person	115 g	70–160 g	[51]
θ_h	Number of egg parasites in stool/urine	262 g^{-1}	10–513 g^{-1}	[51]
ω_1	Miracidia emergence rate	0.00232	0.00232	[52]
υ_2	Natural death rate of IHs	0.01110	0.004–0.0182	[52]
υ_3	Natural death rate of parasite eggs	0.07193	0.001–0.14286	[44,46,49]
υ_4	Natural death rate of miracidia	0.49165	0.0833–0.9	[46,49]
υ_5	Nautral death rate of cercaria	0.002605	0.00104–0.00417	[52]

Table 2. *Cont.*

Parameter	Definition	Baseline Value	Values Range/Day	References
N_E	Number of miracidia released per egg	500	500	[52]
β_1	Cercaria-human infection rate	0.0750	0.028–0.122	[52]
β_2	Miracidia-snail infection rate	0.001235	0.000127–0.615	[52]
ω_2	Cercaria shedding rate	2.6	2.6	[19,49]
δ_2	Snail death rate due to infection	0.026	0.002–0.05	[52]
K	Parasite egg carrying capacity	100,000	100,000	Estimated
C_o	Saturation coefficient for miracidia infectivity	1,000,000		Estimated
M_o	Saturation coefficient for cercaria infectivity	1,000,000		[19]
ε	limitation of miracidia the growth velocity	0.25	0.2–0.3	[18,19]
$\psi, \alpha, \alpha_h, b, \alpha_v$	Effective rates of control strategies	0.5	0–1	Varied
$\sigma_s, \sigma_I, \sigma_m, \sigma_c$	Chemical-induced death rates	0.5	0–1	Varied

We performed a numerical simulation using the main R package ODE solver Version 1.10-4 for solving ordinary differential equations [53] in the R statistical environment version 4.0.3 [54]. The baseline values in Table 2 were used for all simulations and predictions. We conducted a sensitivity analysis of R_0 with respect to the baseline value using the Partial Rank Correlation Coefficients (PRCC) test to determine how robust our predictions are to changes in parameter values. In this way, we can determine quantitatively which key parameters can be targeted by control measures to reduce disease the most. For instance, R_0 increases when parameters with positive PRCC values are increased, increasing the likelihood of infection.

3. Results

The results show that the key parameters (bold in Table 3) that have the greatest influence on the transmission of the disease include the recruitment rate of human individuals Λ_1, a portion of stool/urine per infected person ρ, number of miracidia per parasite egg N_E, cercaria-to-human transmission per contact β_1, rate of miracidia-to-snail transmission per contact β_2, and rate of cercaria emergence from infected snails ω_2.

Table 3. The partial rank correlation coefficients for the baseline parameter values for R_0 (without control) as a response function, with the most significant parameters that influence the dynamics of the model highlighted in bold.

Parameter	$\mathbf{\Lambda_1}$	Λ_2	x	δ_1	υ_1	$\boldsymbol{\rho}$	θ_h	ω_1	υ_2	υ_3
R_0	**+0.8338**	+0.0451	+0.0195	−0.0089	−0.7899	**+0.7725**	+0.7545	+0.5504	−0.8636	−0.7537
Parameter	υ_5	N_E	$\boldsymbol{\beta_1}$	$\boldsymbol{\beta_2}$	$\boldsymbol{\omega_2}$	δ_2	C_o	M_o	ε	υ_4
R_0	−0.5777	**+0.8186**	**+0.7607**	**+0.7928**	**+0.8005**	−0.6731	−0.7799	−0.8032	−0.0481	−0.8303

The model system Equations (1)–(7) is solved numerically using the initial conditions $S_h(0) = 100,000$, $S_h(0) = 100,000$, $I_h(0) = 1$, $E_h(0) = 0$, $M_f(0) = 0$, $S_v(0) = 100,000$, $I_v(0) = 1$, and $C_f(0) = 0$, and the effects of different control strategies on the targetted human and snail populations are shown graphically in Figure 2. When a chemotherapy treatment of the infected humans is integrated with public literacy (two-tiered approach), the strategy is more successful in managing and reducing disease morbidity in the human population than when each strategy is carried out separately, i.e., the number of infected humans who recover, reduce, and join the susceptible humans, who grow in number

(Figure 2a,b). Chemical/molluscicide control significantly increases IHs mortality, and when paired with a mechanical technique, this effect is essentially identical (Figure 2c,d).

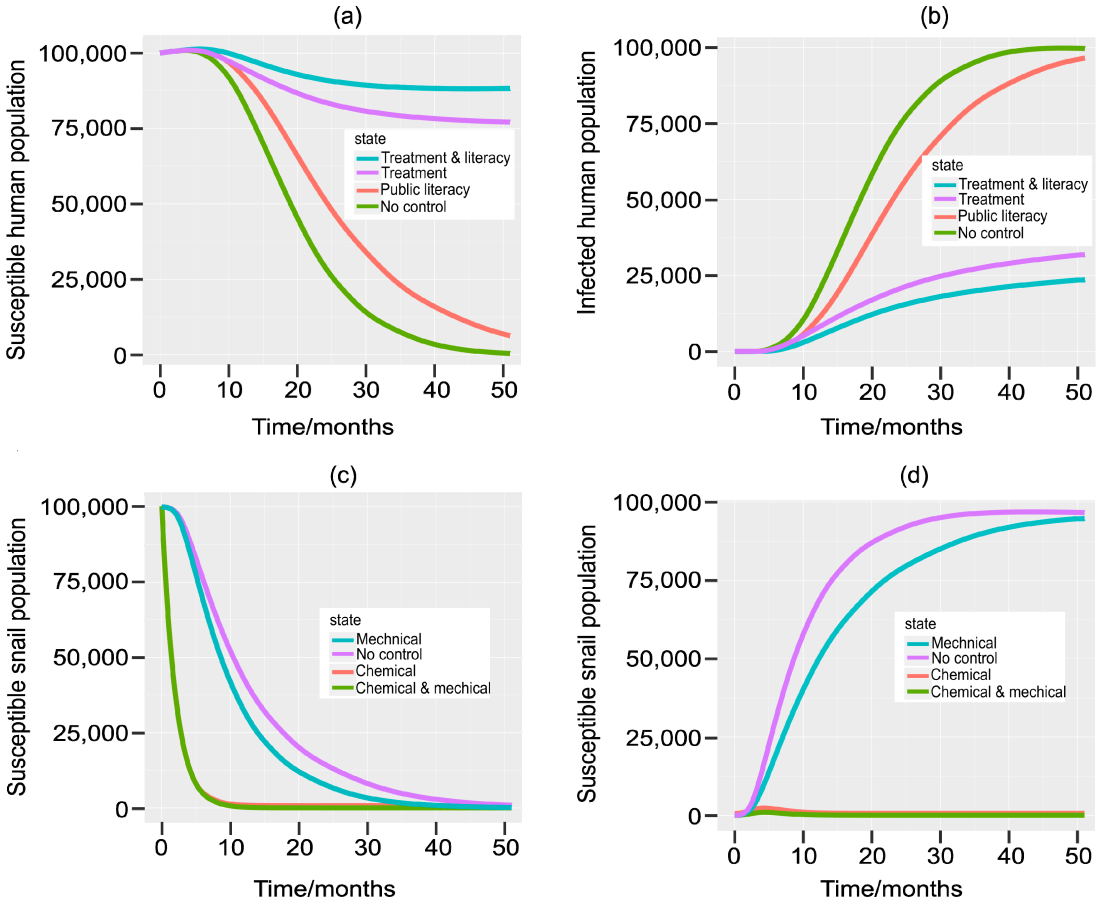

Figure 2. Comparisons between treatment and public literacy targeting the populations of (**a**) susceptible humans, (**b**) infected humans, and molluscicide (chemical) and the mechanical strategies targeting (**c**) susceptible snails and (**d**) infected snails of schistosomiasis in contrast with no control measures.

The impact of individual control measures and various combinations of all control measures on disease transmission is determined by the value of R_0, as shown in Table 4. The more successful a certain level of control is, the smaller the value of R_0. We show that when a single control strategy is used, the chemical/molluscicides strategy ($\sigma_{I,M,C}$) has a greater impact on reducing the value of R_0 followed by the chemotherapy treatment strategy (ψ), public literacy ($\alpha\alpha_h$), and finally mechanical control ($b\alpha_v$). However, a single intervention cannot eradicate the disease, $R_0 \not< 1$: see Table 4. The results of integrating the various strategies show that a combination of two-tiered control measures, treatment strategies (ψ), and molluscicides ($\sigma_{I,M,C}$) have the greatest impact compared to any other pair of strategies (Table 4). Moreover, a combination of a three-tiered approach: treatment (ψ), molluscicides ($\sigma_{I,M,C}$), and mechanical ($b\alpha_v$), as well as another three-tiered approach: public literacy ($\alpha\alpha_h$), molluscicides ($\sigma_{I,M,C}$), and mechanical ($b\alpha_v$) have the potential to lower R_0 below 1, but only if the effectiveness of each separate control is greater than 90% (Table 4). However, schistosomiasis can be eradicated, $R_0 < 1$, if a four-tiered approach (treatment, public literacy, molluscicides, and mechanical) is applied, with each method being more than 70% effective when combined (Table 4).

Table 4. The variability of R_0 across rows for a single or different combination of control strategies, $\psi, \alpha, \alpha_h, \sigma_I, \sigma_M, \sigma_C, b, \alpha_v \in [0,1]$. The lower the R_0, the more successful the strategy(s) are in controlling schistosomiasis.

Control strategies as Functions of R_0	**Effectiveness of Control Strategies; ψ, α, α_h, σ_I, σ_M, σ_C, b, and α_v**										
	0	**0.1**	**0.2**	**0.3**	**0.4**	**0.5**	**0.6**	**0.7**	**0.8**	**0.9**	**1**
$R_0(\psi)$	10,000	1947	1390	1139	988	884	808	748	700	660	643
$R_0(\alpha\alpha_h)$	10,000	9900	9600	9100	8400	7500	6400	5100	3600	1900	975
$R_0(b\alpha_v)$	10,000	9950	9798	9539	9165	8660	8000	7141	6000	4359	3122
$R_0(\sigma_{I,M,C})$	10,000	295	138	86.9	61.6	46.8	37.2	30.6	25.7	22.0	20.5
$R_0(\psi, \alpha\alpha_h)$	10,000	1928	1334	1036	830	663	517	382	252	125	62.7
$R_0(b\alpha_v, \sigma_{I,M,C})$	10,000	294	136	82.9	56.5	40.5	29.8	21.8	15.4	9.6	6.401
$R_0(\psi, \sigma_{I,M,C})$	10,000	57.4	19.3	9.9	6.1	4.1	3.0	2.3	1.8	1.5	1.3
$R_0(\psi, b\alpha_v)$	10,000	1937	1362	1086	905	766	646	534	420	288	201
$R_0(\alpha\alpha_h, \sigma_{I,M,C})$	10,000	292	133	79.1	51.7	35.1	23.8	15.6	9.3	4.2	1.9
$R_0(\alpha\alpha_h, b\alpha_v)$	10,000	9850	9406	8681	7699	6495	5120	3642	2160	828	304
$R_0(\psi, \alpha\alpha_h, \sigma_{I,M,C})$	10,000	292	133	79.1	51.7	35.1	23.8	15.6	9.3	4.2	1.9
$R_0(\psi, \alpha\alpha_h, b\alpha_v)$	10,000	9850	9406	8681	7699	6495	5120	3642	2160	828	304
$R_0(\psi, \sigma_{I,M,C}, b\alpha_v)$	10,000	57.1	18.8	9.4	5.6	3.6	2.4	1.6	1.1	0.63	0.41
$R_0(\alpha\alpha_h, \sigma_{I,M,C}, b\alpha_v)$	10,000	291	130	75.5	47.4	30.4	19.1	11.1	5.5	1.8	0.62
$R_0(\psi, \alpha\alpha_h, \sigma_{I,M,C}, b\alpha_v)$	10,000	56.6	18.1	8.6	4.7	2.7	1.5	0.83	0.39	0.12	0.04

When considering mortality rate functions (Table 1), we show that temperature, the length of chemical exposure, and the chemical's half-life affect the molluscicide performance on the death rates of targeted species. In general, chemical-induced mortality rates for targeted species (host snails and free-living *Schistosoma* cercaria and miracidia) decline as the temperature increases. However, the decline is more rapid when the half-life of molluscicides decreases, i.e., shorter half-lived molluscicides (e.g., non-persistent and persistent molluscicides) lose their toxicity sooner, leading to lower mortality rates. For instance, Figure 3a shows how temperature control impacts the half-life of molluscicides and the consequent mortality rate of susceptible snails. In the same context, chemical-induced mortality rates decrease with an increase in the duration of molluscicide exposure. Molluscicides with a longer half-life (very persistent molluscicides) remain in the environment longer, resulting in a higher mortality rate compared to molluscicides with a shorter half-life (Figure 3b). Thus, increasing the half-life of molluscicides increases the chemically induced mortality rates, especially for cercariae σ_c, and infected snails σ_I (Figure 3c). As a result, increasing the temperature and days of chemical exposure decreases the mortality rate of snails (Figure 3d) associated with higher risks of disease transmission, thus increasing the R_0 value (Figure 3e).

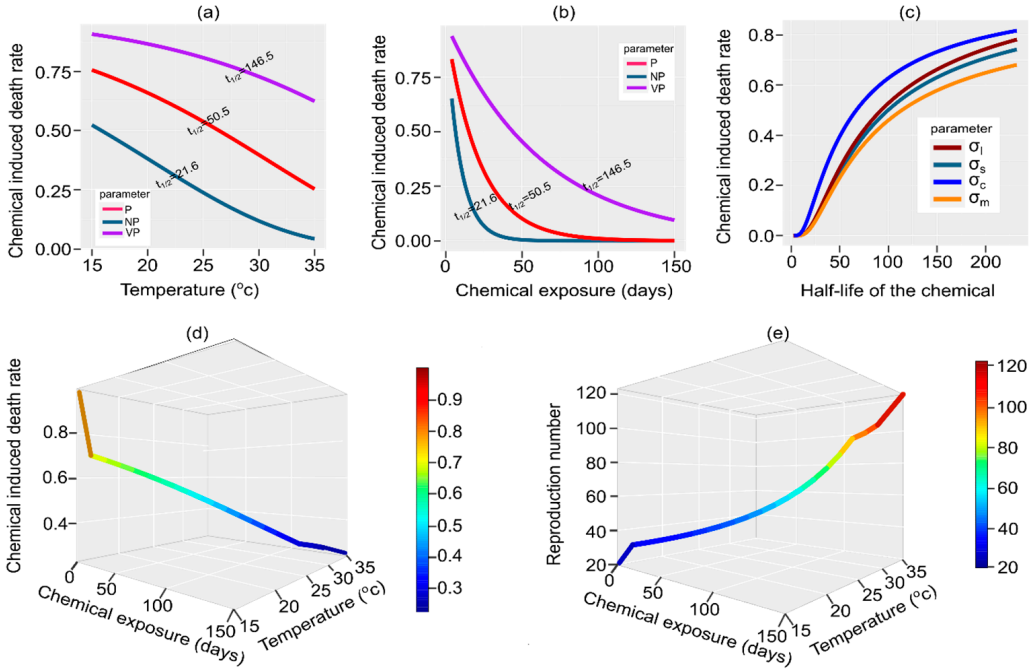

Figure 3. Various molluscicides are regulated by temperature according to their half-lives and durations of chemical exposure to snails. A molluscicide is classified as a non-permanent molluscicide (NP) with a half-life of $t_{1/2} = 21.6$, a persistent molluscicide (P) with a half-life of $t_{1/2} = 50.5$, or a very-permanent molluscicide (VP) with a half-life of $t_{1/2} = 146.5$. (**a**) Shows variations in the temperature of the environment and the duration of chemical exposure (**b**) for different chemicals affecting the death rate of targeted host snails. (**c**) Shows the effect of chemicals with different half-lives on the death rate of different target species (susceptible snails σ_s, infected snails σ_I, cercaria σ_c, and miracidia σ_m). At the same time, the effect of combined chemical exposure and temperature on the death rate of host snails and the subsequent reproduction number is shown in (**d**,**e**).

4. Discussion

We formulate a mathematical model to assess the effectiveness of methods that target humans and those targeting IHs in the control of schistosomiasis. The results of the PRCC test suggest that control strategies focusing on the key parameters N_E, β_1, β_2, and ω_2 in the transmission dynamics may be more effective in reducing R_0 and may result in disease-free conditions of $R_0 < 1$, indicating disease control. Our results show that the chemotherapy treatment strategy (reducing N_E) and application of molluscicides (reducing β_1, β_2, and ω_2) are the most successful methods for reducing R_0 and disease morbidity among the human population and increasing snail mortality, respectively, when applied independently and compared to mechanical control (reducing ω_2) and public literacy (reducing β_1 and β_2) with limited impact. But each strategy cannot eradicate schistosomiasis individually, which complements the finding by Mangal et al. [52], King and Bertsch [9], and Zacharia et al. [10]. Thus, a single approach may reduce morbidity [2,55] but often without reducing the local and environmental transmission of parasites [6], which contributes to the development of the disease. In addition, chemotherapy has shown ineffectiveness against juvenile worms within the body. This is the reason why worms inside infected and treated children can continue to release eggs, observed in their feces three weeks after the drug has been administered [56–58]. This thus perpetuates local transmission, and residents who stay in endemic areas run the risk of re-infection [6,59]. The fragility of drug control alone is demonstrated by this.

On the other hand, mechanical control practices like the physical picking of snails are considered old-fashioned but prove to be a good complementary strategy to drugs, molluscicides, and public literacy [17]. However, its use may be limited, especially in large water bodies, such as lakes, rivers, and streams, or where a larger number of aquatic

inhabitants must be controlled. In addition, public literacy advocates for significant behavior change in water use and contact. However, this ultimately requires the provision of safe and hygienic alternative water supplies, latrines, and washing facilities. When compared to using individual control strategies, integrated strategies are far more effective. Our study further shows that when a four-tiered control strategy is used, the results are much better than using one-, two- or three-tiered controls. Although a three-tiered strategy would be effective as well, it is practically difficult to achieve 90% effectiveness from each method. These findings support, to a certain extent, the findings of Mangal et al. [52], Thétiot-Laurent et al. [56], Lo et al. [58], and Zheng et al. [13], which suggest that the integrated intervention of chemotherapy and snail management has a greater impact on schistosomiasis control than a single method like chemotherapy treatment alone.

However, in such integrated efforts to control schistosomiasis, the time and season of application of molluscicides are crucial. This is relevant in providing a realistic assessment of the spread of schistosomiasis under the current and projected temperature increases in areas like sub-Saharan Africa, where the disease is most prevalent. Our results corroborate with the reports by Feng et al. [60], Fishel [25], Ziska [26], and Zheng et al. [13] that the temperature of the environment, chemical degradation, and half-life of the chemical are important factors in the chemical control of snails. Regardless of the chemical type used, non-persistent (NP), persistent (P), or very persistent (VP), the results show that the chemical strategy may be more effective in areas with low temperatures (15–25 °C). In the first two weeks (14 days) of application, the chemically induced mortality rate of snails is significantly higher, especially for cercariae and infected snails, and consequently, R_0 is less than at unity, indicating disease control. This corroborates the finding by Montanari et al. [33] that, at a standard temperature of 25 °C, molluscicides proved to be effective against adult snails; the snails reduced their food intake and stopped eating, whereas the same effects were significantly stronger at 18 °C. No effects on survival or feeding rate have been recorded at incubations of 30 °C. In regions with higher temperatures, an even longer treatment period using NP chemicals is associated with low rates of induced mortality and is, therefore, less effective in reducing snails, free-living parasite populations, and R_0. The results also show that the molluscicides NP, P, and VP with increasing half-lives reduce species mortality by more than 50% only up to 2 weeks, 3 weeks, and 6 weeks, respectively, suggesting that the chemical should be reapplied regularly thereafter. Thus, the half-life of the molluscicide is directly proportional to the active length of the molluscicides in the water. This result supports the finding of Seligman et al. [61], who observed that the half-lives/chemical degradation of different chemicals ranges from 4 to 19 days and up to several months under specific conditions. For efficient snail management, integration efforts, and schistosomiasis control, different areas with varying weather patterns and seasonal variations may require different molluscicide-type and variable time intervals of reapplication.

Therefore, it is critical to quantify the use of chemical control agents in response to climatic conditions to determine alternative changes in the target intermediate host population and the best season (temperature) for control. This result complements the efforts to investigate molluscicidal action, the structure-activity relationship, and the potential mechanisms of several molluscicides [13,14,62] toward developing suitable chemicals.

Our findings, thus, demonstrate that effective schistosomiasis control programs necessitate a co-ordinated effort and comprehensive integration of preventative treatment, public literacy, and mechanical and molluscicide controls. Despite the promising results, we believe that controlling schistosomiasis with fewer than three different combinations of control strategies will be challenging and may not be worth the effort to eradicate schistosomiasis compared to when the four strategies are integrated and carried out simultaneously. However, achieving the schistosomiasis eradication goal may require a large investment of resources (high cost, which severely limits the use of the molluscicide on a big scale), time, and commitment, and also has associated ecological risks. For instance, chemical management has several negative effects, including the destruction of aquatic biodiversity due to toxicity [63] and the emergence of snail resistance to the chemicals are very likely.

If chemicals are released into the environment, local people will not be able to use the water [13,64]. Several molluscicides have a half-life that ranges from 3.17 to 223 days [65], while others have a half-life of up to 2 years. This means that the presence of molluscicides in water would continue to pose a health risk to people for more than 30 years before it decays completely [61].

Furthermore, the development and use of molluscicide need to be blended with an increase in health education and an assessment of their levels of toxicity when ingested by humans and domestic animals through agricultural products and their effect on non-target aquatic fauna and flora [13]. However, our results suggest that chemicals with shorter half-lives, such as an extract from *C. viminalis* fruits, or natural insecticides, such as *Nereistoxin,* are effective in killing snails at low concentrations in a shorter amount of time [13,66]. They could provide an alternative to long-term exposures to common molluscicides with less effects on biodiversity. Furthermore, specific molluscicides, such as nicotinanilide molluscicides and silver (Ag) nanopowder (Ag-NPs) molluscicides [13], have been shown to exhibit strong molluscicidal effects with less toxicity to humans, animals, fish, and plants, can be applied in small waterbodies to manage snail populations despite their high cost and strong human skin irritant effects. The effect of change in temperature on the environment on molluscicide performance greatly affects the mortality rate of the targeted organism (IHs, cercariae, and miracidia) and general disease transmission. Therefore, better molluscicide performance should be achieved by developing harmless, low-toxicity, and temperature-dependent molluscicides, with low environmental impact to control the targeted species holistically.

Our study has some limitations given that the parameters that best reflect the biological representation and real-life situations of schistosomiasis disease and transmission had to be used based on the published record. Since neither the *Biomphalaria-S. mansoni* nor the *Bulinus-S. haematobium* infection system had a complete list of genus-specific model parameters, we used published parameter values for both infection systems. Due to the absence of specifically published data relating to the two systems, two parameter values were estimated, and two others were assumed based on expert knowledge. Furthermore, the literature data are not always consistent and are collected under different conditions. Nonetheless, the baseline values of such parameters provide a good first approximation of the parameter values, and the model can be used generally to develop a better understanding of the effects of interventions. This model can be improved to incorporate more features, such as the effect of temperature and molluscicides on the development of eggs into miracidia, snail recruitment, and biodiversity of nontarget species.

5. Conclusions

We conclude that the proposed model provides valuable mechanistic insights into how the impact of schistosomiasis and future control programs will depend on the integration of chemotherapy, public literacy, and mechanical and molluscicide types in different endemic regions. In addition, molluscicide performances in different regions with changing temperatures will vary depending on their type and half-life, degradation rate, and reapplication frequency.

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Appendix A

Invariant region

In model system Equations (1)–(7), we prove that non-negative and bounded solutions exist in Ω, as follows:

Let $\mathcal{L}(t) = \Big[S_h(t), I_h(t), E_h(t), M_f(t), S_v(t), I_v(t), C_f(t)\Big]^T \subset \mathbb{R}^7_+$ be the solution set of the model equations Equations (1)–(7) from which $\mathcal{L}(0) \geq 0$ are the non-negative initial conditions.

Lemma A1. *$\mathcal{L}(t)$is non-negative in $\Omega \subset \mathbb{R}^7_+$ with $\mathcal{L}(0) \geq 0$ for $\forall t \geq 0$.*

Proof. It is evident from model equation Equation (1) that

$\dot{S_h}(t) \geq -\Big(\frac{(1-\alpha\alpha_h)\beta_1 C_f}{C_o+\varepsilon C_f} + v_1\Big)S_h$, where $S_h(t) \geq S_h(0)e^{\big(\frac{(1-\alpha\alpha_h)\beta_1 C_f}{C_o+\varepsilon C_f}+v_1\big)t}$, $\forall t \geq 0$.

Thus, $S_h(t) \geq 0$ is non-negative and, in the same way, it can be shown that $I_h(t) \geq 0$, $E_h(t) \geq 0, M_f(t) \geq 0, S_v(t) \geq 0, I_v(t) \geq 0$, and $C_f(t) \geq 0$. Therefore, $\mathcal{L}(t)$ in the region $\Omega \subset \mathbb{R}^7_+$ is positively invariant. □

Lemma A2. *$\mathcal{L}(t)$ remains bounded in $\Omega \subset \mathbb{R}^7_+$.*

Proof. Let the total human population $S_h(t) + I_h(t) = N_h(t)$, and the total snail population $S_v(t) + I_v(t) = N_v(t)$, such that $\dot{N_h}(t) \leqslant \Lambda_1 e^{-v_1 x} - v_1 N_h(t)$ and $\dot{N_v}(t) \leqslant \Lambda_2 - v_2 N_v(t)$ and $\mathcal{L}(t) = \Big[N_h(t), E_h(t), M_f(t), N_v(t), C_f(t)\Big]^T$. Thus, $\mathcal{L}(t)$ can be expressed analytically as follows:

$$\mathcal{L}(t) = \begin{cases} N_h(t) \leqslant \frac{\Lambda_1 e^{-v_1 x}}{v_1} - \Big(\frac{\Lambda_1 e^{-v_1 x}}{v_1} - N_h(0)\Big)e^{-v_1 t} \\ E_h(t) \leqslant K - (K - E_h(0))e^{\rho\theta_h(1-\alpha\alpha_h)I_h t} \\ M_f(t) \leqslant \frac{N_E\omega_1 E_h}{(v_4+\sigma_m)} - \Big(\frac{N_E\omega_1 E_h}{(v_4+\sigma_m)} - M_f(0)\Big)e^{-(v_4+\sigma_m)t} \\ N_v(t) \leqslant \frac{\Lambda_2}{v_2} - \Big(\frac{\Lambda_2}{v_2} - N_v(0)\Big)e^{-v_2 t} \\ C_f(t) \leqslant \frac{\omega_2 I_v}{(v_5+\sigma_c)} - \Big(\frac{\omega_2 I_v}{(v_5+\sigma_c)} - C_f(0)\Big)e^{-(v_5+\sigma_c)t} \end{cases}$$

Assuming $N_h(0) \leqslant \frac{\Lambda_1 e^{-v_1 x}}{v_1}$, and $N_v(0) \leqslant \frac{\Lambda_2}{v_2}$, we conclude that $\lim\limits_{t\to\infty} Sup N_h(t) = \frac{\Lambda_1 e^{-v_1 x}}{v_1}$, and $\lim\limits_{t\to\infty} Sup N_v(t) = \frac{\Lambda_2}{v_2}$, and therefore, both human ($S_h(t), I_h(t)$) and snail ($S_v(t)$, $I_v(t)$) populations are biologically feasible. Similarly $\lim\limits_{t\to\infty} Sup\Big[E_h(t), M_f(t), C_f(t)\Big]^T = \Big[K, \frac{N_E\omega_1 E_h}{(v_4+\sigma_m)}, \frac{\omega_2 I_v}{(v_5+\sigma_c)}\Big]^T$, shows that the egg, miracidia, and cercaria populations are biologically feasible. Thus, $\mathcal{L}(t)$ with initial conditions remains bounded for all $t \geq 0$. □

As a result of Lemmas A1 and A2, our model is epidemiologically and mathematically well-posed.

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