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# Cost-effectiveness of combining drug and environmental treatments for environmentally transmitted diseases

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Control of neglected tropical diseases (NTDs) via mass drug administration (MDA) has increased considerably over the past decade, but strategies focused exclusively on human treatment show limited efficacy. This paper investigated trade-offs between drug and environmental treatments in the fight against NTDs by using schistosomiasis as a case study. We use optimal control techniques where the planner's objective is to treat the disease over a time horizon at the lowest possible total cost, where the total costs include treatment, transportation and damages (reduction in human health). We show that combining environmental treatments and drug treatments reduces the dependency on MDAs and that this reduction increases when the planners take a longer-run perspective on the fight to reduce NTDs. Our results suggest that NTDs with environmental reservoirs require moving away from a reliance solely on MDA to integrated treatment involving investment in both drug and environmental controls.

## 1. Introduction

Neglected tropical diseases (NTDs) affect approximately one in six people, mainly in the poorest rural and remote areas, urban slums, and conflict zones. The loss of disability-adjusted life years (DALYs) due to NTDs (48 million) is as high as tuberculosis (49 million), and more than half of malaria (83 million) and HIV/AIDS (82 million) [1]. NTDs also increase the risk of coinfection; they are responsible for one-half and one-third of sub-Saharan Africa's malaria and HIV/AIDS disease burden, respectively [2]. Despite major donations from pharmaceutical companies, private foundations (e.g. Bill and Melinda Gates) and foreign governments (e.g. UK and US), the World Health Organization (WHO) estimated that an additional 2 billion US dollars was needed to administer preventive chemotherapy to all individuals who were at risk of contracting an NTD between 2012 and 2015 [3].

A subset of NTDs are environmentally transmitted diseases (ETDs) where pathogens rely partially, or entirely, on non-human hosts, reservoirs or vectors. ETDs with focal transmission exhibit a direct link between the infection rate in the hosts and the level of the pathogen in an environmental reservoir [4]. The link can create an inherent cycle between the population's infection rate and the environmental degradation of contaminated reservoirs.

Schistosomiasis, which is a focus of this paper, is an example of an ETD with focal transmission [4]. The global disease burden of schistosomiasis has remained relatively stable despite the development almost a half century ago of an anthelmintic drug, praziquantel, that promised widespread control. In the last two decades,

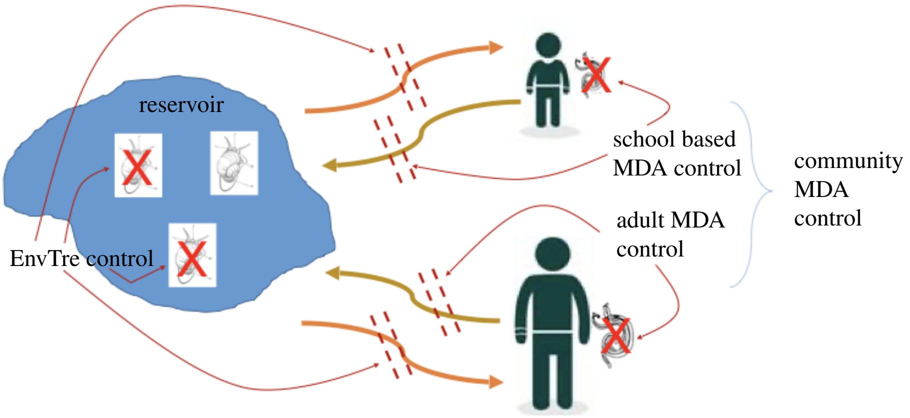

**Figure 1.** Modeled treatment options and transmission pathways for schistosomiasis. (Online version in colour.)

over 1.4 billion US dollars was spent on a mass drug administration (MDA) treatment protocol for schistosomiasis [5].

Completely eliminating schistosomiasis's pathogen transmission seems difficult, if not impossible, to achieve. The WHO's guidelines [6] recommend to target school-age children, given the facility to deliver treatment in schools (see e.g. [7–10]), with community-wide treatment (i.e. including adults) being recommended in high-prevalence communities (see e.g. [11,12]). Elimination is very challenging, because targeting children reduces, but does not eliminate the shedding of pathogens into the reservoir (see figure 1 for different treatment alternatives and how they interrupt the life cycle of the pathogen). Even if the whole community could be treated, shedding of pathogen into the environment remains due to noncompliance to drug treatment [13–15] and limited effectiveness of drug controls [16,17]. Furthermore, the fact that individuals treated via MDA often have no other alternative but to return to parasite-contaminated waters [4] means that reinfection is likely to occur.

Although most treatment of NTDs consists of implementing MDAs [6], there is increasing evidence for focally-transmitted ETDs that water quality, sanitation and hygiene (WASH) measures and environmental treatments (EnvTre) can have significant positive impacts on health outcomes by reducing contamination (e.g. via sanitation measures) and exposure to pathogens (e.g. by providing safe water; see Andres *et al.* [18] for a meta-analysis of WASH impact evaluations). Environmental treatments act in a similar manner to WASH by reducing the transmission pathways between the disease reservoir and human contact but focus more directly on reducing pathogen abundance in the reservoir or preventing transmission from the reservoir to humans (figure 1). For example, an EnvTre can reduce reservoir, vector or intermediate host populations (e.g. chemical molluscicides or insecticides) or reduce the pathogens directly via targeting their free-living stages in water or soil (e.g. chlorination).

The combination of multiple types of treatment for schistosomiasis and other ETDs can potentially reduce the overall cost associated with treating the disease and reduce the disease burden [5,12,19,20]. For example, Lo *et al.* [12] demonstrate a cost-effective combination of controls that reduce the prevalence of the schistosomiasis pathogen in the environment with school-based MDA treatment. Most of the current literature considers combinations of controls using simulation (scenario) analysis under the assumption of a fixed level of MDA treatment occurring on a pre-determined set interval (e.g. every other year) and a fixed level of a WASH or environmental treatment on a similarly fixed interval (not necessarily the same as the MDA treatment interval). In these analyses, understanding the when, where and how much to combine to achieve the most cost-effective combination is challenging due to potential direct and indirect effects of one type of treatment on another and all of the possible combinations of multiple treatments available over time.

Our paper makes a number of important contributions to the literature on treatment for ETDs and specifically schistosomiasis control. First, we consider multiple combinations of treatments that include MDA and environmental controls in an optimal control framework that solves for the optimal cost-effective solution (for other applications of optimal control to schistosomiasis, see [21–24]). We use optimal control to examine the use of both MDA and environmental treatments, and to understand under what conditions both approaches should be used in combination or in series. Our methodological advance enables us to examine optimal trade-offs across time and interventions that are more human targeted (i.e. school-based MDA) versus more environmentally oriented (i.e. EnvTre) when used in isolation and in combination with each other. Investigating these trade-offs using simulation analysis would be a monumental task as the combinatorial nature of the possibilities are significant. Second, we show how the implementation of an optimal environmental treatment reduces the dependency on mass drug administration and that this reduction increases when the planner considers a longer planning period. This latter result highlights potential biases in treatment protocols that are based on simulation analysis using short planning horizons.

## 2. Material and methods

Our economic–epidemiological model of schistosomiasis captures the realistic situation where a central planning agency needs to decide when, what type, and how much treatment to provide to a remote village where the disease is currently endemic. The objective of the central planning agency is to treat the disease at the lowest possible total cost, where the costs include treatment, transportation and damages (reduction in human health). The epidemiological model describes the dynamics of infected intermediate hosts living in the environmental reservoir, the population dynamics of the intermediate host themselves, and the dynamics of the infectious human populations.

The structure of our model incorporates both economic and disease ecological factors that vary based on the nature of the treatments. The model structure and parameters represent schistosomiasis but it is not meant to be a tactical tool. Rather our results are indicative and qualitative. More tactical tools could adopt our optimal control framework but would require adaptations to the particular setting and better data for parametrization.

## (a) Model of disease transmission

The disease model predicts the dynamics of infection of adult and children in a closed population, and the number of intermediate hosts in the environmental reservoir. Adult and children contract the parasite through contact with the environmental reservoir, which here is a body of water next to the village where the disease is endemic, and contribute parasites in the environment via shedding. We assume that part of the population receives MDA (i.e. the children), meaning that it is impossible to completely interrupt the transmission of pathogens into the environment. The number of infected children and adults can go down over time from natural recovery.

In epidemiology, the basic reproduction ratio $R_0$ is defined as being the expected number of secondary infections, at a disease-free equilibrium, caused by a typical infected individual over its entire infectious period [25]. In our model, $R_0$ is a function of relative shedding rates of adult and children, natural recovery rates, and contact rates with the environmental reservoir. New infections of the intermediate hosts depend on the relative shedding rates of adults and children, while the loss of infectious hosts is due to natural mortality and the application of a non-selective environmental treatment that kills both susceptible and infected intermediate hosts. Following Lo *et al.* [12], intermediate infected hosts cannot reproduce. We model a chemical treatment to reduce the freshwater snails, which are the intermediate hosts of schistosomiasis. Disease model parameters are derived from the literature on schistosomiasis [6,7,9,11,12,16,17,20,26–34]. See the electronic supplementary material for details of the disease transmission model and the parameter levels.

## (b) Model of economic costs

Economic components of the model include treatment costs, damages, and transportation and management costs. We assume damages are additively separable across children and adults. Treatment of children via MDA often occurs in a school setting [6,9], which reduces the treatment costs associated with administering the drug to children in the village. Based on this approach, we model the treatment cost of children as the level of MDA treatment times the cost of a dose of praziquantel. The cost of the environmental treatment is linear in the amount of chemical treatment, which assumes realistically that increasing the application either through more chemical per unit area or larger area of application increases the cost in a linear manner. To calibrate the cost, we specify a certain size of environmental reservoir and use estimates for variable costs of snail control (e.g. chemical, labour) from the literature [7,12,33].

Damages derive from disability and reduced intellectual function [35] causing lower school participation for children [36] and lower worker productivity for adults [37–40]. For simplicity, we assume that the per unit damage costs are identical across adults and children for a given infection prevalence, but the cost parameters—representing damages on the whole subpopulation and not just one individual—differ due to the proportions of adults and children in the village. We utilize data from Senegal, a country with a gross domestic product (GDP) *per capita* close to Africa's median, to calibrate the proportions of children and adults in our population; this gives us a population composed of 40% children (0–14 years) and 60% adults (15 years and over) [31]. The level of damages are set such that in the absence of treatment, there is a prevalence of 38% in a community of 5000 people and this yields losses of 550 DALYs [12]. The value of a DALY was set to be approximately the median value of the GDP *per capita* of an African country (approximately 3000 USD).

We model transportation and management costs as a fixed cost in each period during the planning period regardless of whether treatment is being undertaken. We account for potential economies of scale across the different treatment options with a single fixed cost incurred regardless of whether children or environmental treatments are applied. We parametrize the fixed cost from the literature (see, for example, [6,7,9,11,12,32,33]). See the electronic supplementary material for details of the cost functions and the calibration of the parameter levels.

## (c) Planners' decision

Compared to scenario analysis, optimal control techniques require an assumption about the objective of the planning agency. In scenario analysis, one usually computes, for instance, the average cost of an averted DALY to determine the best policy among the simulated ones; highly cost-effective treatments occur when this average cost is below some threshold (e.g. the *per capita* GDP) [11]. With optimal control, we solve for the best (i.e. optimal) policy, conditional on the objective of the planner. In our case, we assume that the objective of the planning agency is to minimize the damages and treatment costs of the disease in a remote village where the disease is currently endemic. The objective function is the net present value of the treatment, damages, and transportation and management costs over a period of years, where we assume a 4% discount rate in the base case.

The main analysis considers a 10-year horizon following the prior literature investigating the cost-effectiveness of schistosomiasis treatment options [4,12,41,42]. We consider longer time horizons in the sensitivity analysis. We also assume that the planning agency does not set any target level in year 10 for the level of infection prevalence in humans, the level of infected hosts, and the host population size (specifically, we are allowing free endpoint conditions, which implies a set of transversality conditions in the optimal control problem). This allows us to investigate whether eradication is the cost-minimizing outcome at the end of the horizon rather than imposing it as the solution of the planning agency.

Given the cost functions of MDA treatment for children and of the environmental treatment, the controls appear linearly in the formulation. Solutions to linear optimal control models often have a bang-bang nature. That is, the optimal level of the control resides at one limit (e.g. the maximum) for a period of time then switches off to a singular (i.e. intermediate) level or another limit (e.g. the minimum) in another phase of the solution [43]. In these problems, the optimal solution of the control over time consists of discrete switch times. For example, we might expect that the optimal treatment of children to be at the maximum possible level for a certain period of time and then drop to zero, after the infection level in children drops below some endogenous threshold. Given the literature on the non-compliance with MDA treatments [13–15], the maximum treatment at any instant is equal to 90% of the population of school-age children. The limited effectiveness and compliance of MDA treatment [16,17] further reduces the extent of successful treatment and transmission reduction.

## (d) Analysis

To examine the optimal set of MDA and environmental treatment, we numerically solve the optimal control problem across four different scenarios: no controls, school-based MDA, environmental treatment (i.e. snail control), and school-based MDA and environmental treatment.

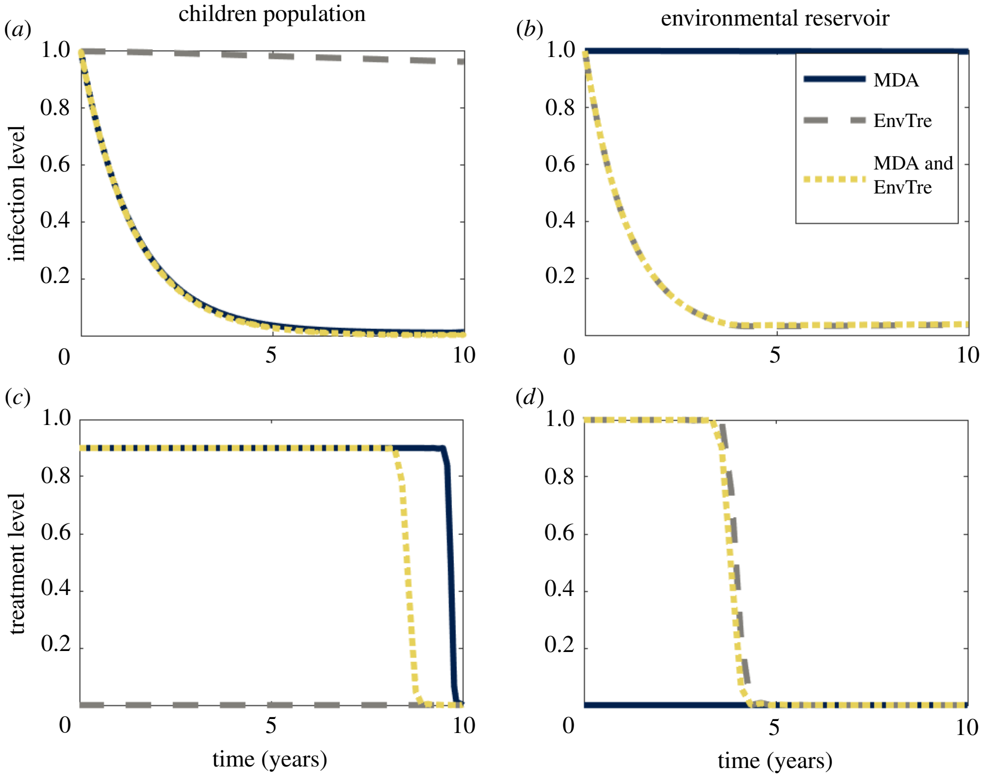

**Figure 2.** Optimal solutions at base case. This figure shows the change over time of the infection level of the child population (*a*), the infection level of the intermediate host population (*b*), the optimal path of drug treatment (*c*) and the optimal path of environmental treatment (*d*). Infection levels are expressed as a proportion of their respective steady-state value. (Online version in colour.)

We use pseudospectral collocation to solve for the optimal dynamics of treatment and infection over time (see [44–46] for applications of this technique and see the electronic supplementary material for more details). We present results from a numerical simulation where initially all state variables are at their no-treatment steady-state levels (sensitivity analyses of initial conditions are presented in the electronic supplementary material; see figure S5). The chosen parameter values imply that without any treatment, the infection prevalence for both the children and adult populations will converge to approximately 38% (consistent with the findings of Lo *et al.* [12]). The steady-state snail population size will converge to the carrying capacity, while the number of infected snails will converge to 54% of total population.

We investigate the impacts of environmental treatments on school-based MDAs by mapping out how the cost of environmental treatments impact the switch time or time at which the planner stops treating school-aged children. Switching off of MDA earlier represents a reduction in treatments and generally a lower reliance on drug treatment as the primary means to address the disease. We also compare the net present value and its components across the different treatment scenarios, and we normalize to one the value of the no treatment case to make comparison easier between cases.

## 3. Results

At our preferred specification of the parameters, we find that the terminal infection levels of the children population are less than 1% when continuously treated with MDA (figure 2*a*). This continuous treatment differs from a pulse treatment, which occurs on a pre-determined fixed interval. Instead of treating the village, e.g. every year, our control mimics a case where the population is being continuously given MDA. The optimal drug treatment (figure 2*c*) is consistent with previous literature on optimal control of epidemics: the disease needs to be hit as hard as possible and as soon as possible [47]. Environmental treatments alone barely reduce the infection level in the children population (figure 2*a*), while driving the infection prevalence in intermediate hosts to about 2% of total intermediate host population (4% of steady-state infection level; figure 2*b*). Unlike the human infection levels that are driven almost to eradication, there are no damages associated with the infected intermediate host, and the incentive to eliminate the disease in the infected intermediate hosts comes exclusively from its effect in the disease's life cycle and its indirect impact on human populations.

Under the optimal scenario, combining environmental treatments with MDA affects the optimal level of drug administrated to children by reducing the switch time (figure 2*c*). Since an EnvTre reduces the level of contaminated intermediate hosts in the environmental reservoir, the transmission of the disease from the intermediate hosts to human populations is reduced, everything else being equal. As a result, less MDA is needed to fight the NTD. The optimal solution suggests that the level of environmental treatment is only slightly impacted (reduced time spent at maximum control) with the addition of MDA treatments (figure 2*d*)

Table 1 summarizes the results in terms of the net present value (NPV, which includes damages and treatment costs), damages (for both the child and adult populations), child MDA costs, costs related to the environmental treatment, and total expenditures (including transportation and management costs) across the different optimal scenarios. By definition, when adding an additional control variable in an optimal control problem, the planner cannot do worse because it could always choose not to utilize this new control

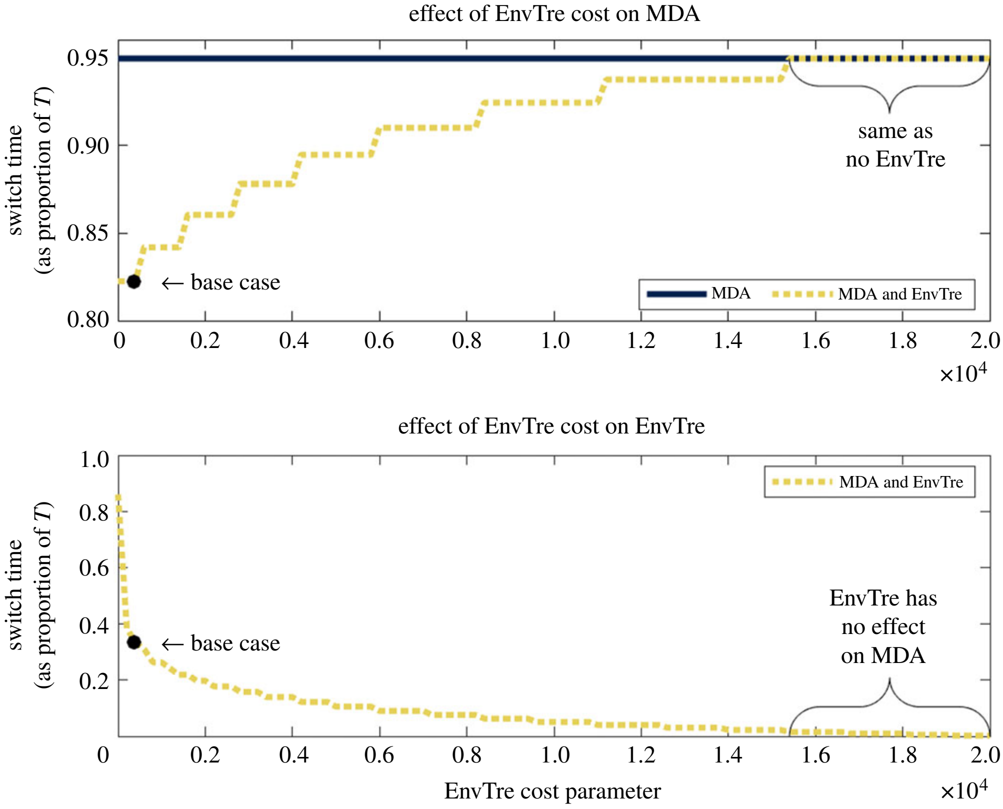

**Figure 3.** Proportion of total treatment time spent at the maximum level of control (MDA or environmental treatment) as a function of the cost parameter associated with the environmental treatment (EnvTre). The point given by 'Base Case' represents the switch time and environmental treatment cost parameter of figure 2 and table 1. (Online version in colour.)

**Table 1.** Normalized values of net present value (NPV), damages (reduction in human health) and treatment costs (child, EnvTre and total, which includes transportation and management costs) for when the planning horizon considered by the social planner is $T = 10$ yr.

| | | | damages | | expenditures | | |
|---|---|---|---|---|---|---|---|
| **EnvTre** | **MDA** | **NPV** | **child** | **adult** | **child** | **EnvTre** | **total** |
| no | none | 1 | 1 | 1 | — | — | — |
| | SBDT | 0.67 | 0.17 | 1.00 | 1 | — | 1 |
| yes | none | 0.99 | 0.98 | 0.98 | — | 1 | 0.99 |
| | SBDT | 0.66 | 0.16 | 0.98 | 0.90 | 0.97 | 1.08 |

variable. To make comparison easier between scenarios, we normalize the measures against the appropriate base (damages are normalized against the no-treatment case).

At these parameter levels, school-based drug treatment (SBDT) reduces NPV by 33%. Consistent with figure 2, environmental treatments only barely impact the level of infected children and therefore reduce damages by 1% after 10 years of optimal chemical snail control. Across both cases, environmental treatments do not contribute to a significant reduction in damages. On the other hand, we find that implementing an environmental treatment reduces the amount of time spent at maximum treatment of MDA by more than 1 year out of the 10 year time horizon, resulting in about a 10% reduction in MDA expenditures. This cost reduction in MDA could be offset by the increase in costs due to environmental treatments. We find that implementing an optimal environmental treatment requires a slight increase in expenditures, implying that funds are redistributed from MDA to environmental treatments (table 1; total expenditures are slightly increased when SBDT is combined with environmental treatments). Even though total expenditures are increased, this situation is still preferable given the lower net present value.

Our results highlight important trade-offs between direct (e.g. treatment of school-aged children) and indirect (e.g. treatment of intermediate hosts) treatments and suggest that the optimal amount of MDA is reduced when the policy is combined with an environmental treatment policy. However, the magnitude of the reduction in MDA due to the implementation of an environmental treatment inherently depends on (i) the costs associated with the environmental treatment (here, the marginal cost of snail control), and (ii) the basic reproduction ratio of the disease, $R_0$. We find not surprisingly that as the cost of the environmental treatment goes up, the planner reduces the time during which the maximum control is applied (figure 3, bottom panel).

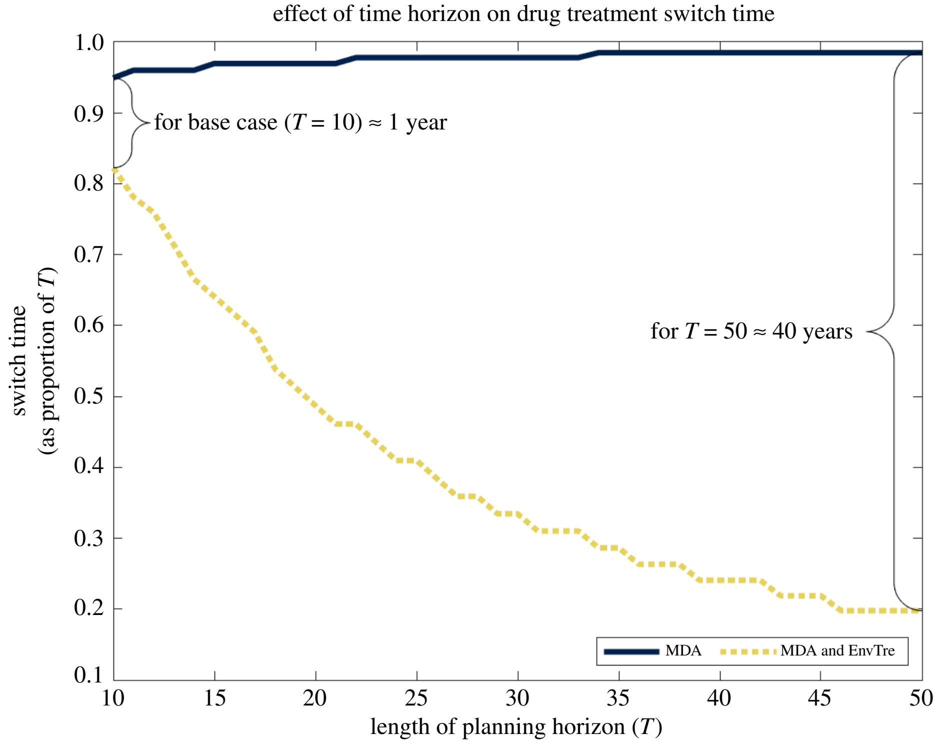

**Figure 4.** Proportion of total treatment time spent at the maximum level of MDA as a function of the time horizon, *T*, considered in our analysis. We show the result for the MDA alone case, and for the MDA & EnvTre case. (Online version in colour.)

Consistent with our base case, we find that as the cost of environmental treatment goes down, the planner utilizes less MDA, as measured by the shorter proportion of the time spent at the maximum treatment level (figure 3, top panel). As the cost increases, we converge to the solution where no environmental treatments is the optimal solution. While we are agnostic on the source of this cost increase, one potential source could stem from the damages of these environmental treatments on other species in the ecosystem (for environmental damages associated with snail control to fight schistosomiasis, see [35,48–50]).

According to Sokolow *et al.* [20], the expected range of $R_0$ for schistosomiasis ranges from 1 to 7. While our base case is 3.5, we investigate the range given in Sokolow *et al.* [20]. There are multiple parameters that affect $R_0$ (see electronic supplementary material for derivation) and the ones for which we have less information are the contact rates and the shedding rates. By varying these parameters to vary the $R_0$, we find that for the majority of the range of $R_0$, our finding on the optimal substitution away from MDA to environmental treatment holds qualitatively (electronic supplementary material, figure S2, top two panels); the impact seems relatively constant at least between 2 and 7. With a $R_0$ higher than in our base case, the amount time spent at the maximum level of environmental treatment will be slightly higher, everything else equal, and more so if this higher $R_0$ is due to higher contact rates, and vice versa (electronic supplementary material, figure S2, bottom panel). Only when the $R_0$ approaches one do we find significant changes to the switch times for MDA and environmental treatment.

Our parametrization of the contact rates (1 infection per 200 water contacts) and shedding rates (1 intermediate host infection per 555 sheds) are consistent with the literature [20,26], but there are multiple different combinations of these parameters that could yield the same basic reproduction ratio. We investigate potential impacts of these combinations by keeping our base case value of 3.5 constant and varying the level of contact rate relative to the shedding rate. We find that (i) the substitution away from MDA due to the environmental treatment remains approximately the same regardless of the relative levels of the contact rate and shedding rate, and (ii) both MDA and the environmental treatment increase as the contact rate becomes relatively higher in magnitude relative to the shedding rate (electronic supplementary material, figure S3).

Following the previous literature [4,12,41,42], we use a 10-year planning period. In our optimal control framework, the implications of a 10-year horizon either imply that costs are no longer incurred after year 10, or that the central planning agency does not consider costs incurred after year 10; both interpretations seem unrealistic. In our model, this implicit assumption explains why, even in a 10-year planning horizon, the optimal solution requires an abandonment of MDA. In the prior literature using scenario analysis, the implicit assumption is that treatment will continue indefinitely in the same *ad hoc* pattern. Considering only shorter planning horizons, however, could bias treatment prescriptions to those that work immediately, which might be a good strategy during an outbreak but not necessarily for an area with endemic disease.

To investigate the interaction between optimal treatment prescriptions and planning horizons, we solve the optimal control model over longer time horizons. We do not impose that either treatment must occur after year 10. That is, we could find that the optimal solution is to abandon the village at some point in the future (i.e. both treatments are optimally set to zero). Our results suggest that as the planning horizon increases, the optimal solution is to substitute away from MDA to environmental treatment. For example, while in our base case the environmental treatment reduced MDA switch time by a little over 1 year, when the planning horizon is 50 years, this reduction is approximately 40 years (figure 4).

This reduction in MDA treatment translates into a more than 50% reduction in MDA expenditures over the entire

**Table 2.** Normalized values of net present value (NPV), damages (reduction in human health), treatment costs (child, EnvTre and total, which includes transportation and management costs) for when the planning horizon considered by the social planner is $T = 50$ yr.

| | | | damages | | expenditures | | |
|---|---|---|---|---|---|---|---|
| **EnvTre** | **MDA** | **NPV** | **child** | **adult** | **child** | **EnvTre** | **total** |
| no | none | 1 | 1 | 1 | — | — | — |
| | SBDT | 0.64 | 0.07 | 1.00 | 1 | — | 1 |
| yes | none | 0.94 | 0.94 | 0.94 | — | 1 | 0.97 |
| | SBDT | 0.59 | 0.06 | 0.94 | 0.47 | 0.90 | 1.01 |

planning horizon. As such, implementing optimal environmental treatment does not require significantly more expenditures (table 2).

With a 10 year planning period, the optimal treatment went from the maximum to zero, and remained there for the rest of the planning period (see bottom panels of figure 2). While the same holds for slightly longer planning periods (see for instance electronic supplementary material, figure S11 for when $T = 15$ yr), we find that this is not necessarily always true. When the planning period is relatively longer, the switch time more often represents the time where treatment goes from the maximum possible level to a non-zero level that varies over time (see electronic supplementary material, figure S12 for when $T = 30$ yr and electronic supplementary material, figure S13 for when $T = 50$ yr).

The qualitative nature of our results are robust to several modelling assumptions. If children represent a greater proportion of the total population, everything else equal, the total amount of time spent treating children does not change (electronic supplementary material, figure S4). As long as initial levels of infection are at least 20% of the no treatment steady-state values, the qualitative nature of the result remains the same; only when initial infection levels approach 10% of the no treatment steady-state values do we find a significant reduction in the substitution away from MDA due to the environmental treatment (electronic supplementary material, figure S5). For the levels of discounting we considered (0–20%), the MDA switch times remain the same (electronic supplementary material, figure S6). Because damages are much larger than treatment costs, the discount rate needs to be very high before it has an impact on the MDA switch times. The amount of time spent on the environmental treatment decreases with higher discount rates, because the long-term benefits to environmental treatment are less important to the optimal solution when the discount rate is high (electronic supplementary material, figure S6). This latter result is consistent with the findings under longer planning horizons. The MDA switch times are invariant to the variations in the effectiveness of the environmental treatment (0.6–1, base case 0.88; electronic supplementary material, figure S9) and to variations of ±50% in the snails' population growth rate (electronic supplementary material, figure S10). Only when the population growth rate of snails approaches its death rate that the amount of time spent at maximum treatment reduces.

Our sensitivity analyses reveal that the reduction in switch time of MDA due to the environmental treatment is mainly affected by (i) the value of a DALY (electronic supplementary material, figure S7) and (ii) the effectiveness of MDA control (electronic supplementary material, figure S8). As the value of a DALY increases, everything else equal, damages due to disease burden become relatively more important than treatment and transportation costs; to compensate for the relative increase in damages, optimal MDA treatment needs to last for a longer period of time. Hence, with a higher value of a DALY, the substitution away from MDA to the environmental treatment reduces (electronic supplementary material, figure S7) because higher MDA effort is preferable, everything else equal. We assumed in our main analysis that treatment was effective 80% of the time. Our sensitivity analyses reveal that by improving the effectiveness of drug treatment, the substitution away from MDA to the environmental treatment could be significantly more important (electronic supplementary material, figure S8). Higher MDA effectiveness reduces the amount of time spent on MDA treatment, and even more so when combined with an environmental treatment due to reduced reinfection.

## 4. Conclusion

We show the potential value of using integrated treatment guidelines. We find that combining environmental controls and MDAs can significantly reduce the time span over which one has to administer drug treatment, especially when considering a long-term planning horizon. Although WHO recognizes both the advantages [51] and the cost-effectiveness [52] of environmental treatments (in particular snail control), its priority is on MDAs since the development of an anthelmintic drug, praziquantel. School-based deliveries in particular are now the main focus of WHO [6] given the facility to deliver treatment in schools and that children are usually associated with higher disease burden [53].

However, few studies have demonstrated the optimal distribution of integrated approaches and under what conditions different treatments should be used in combination or in series. Specifically, we show that, to achieve an optimal outcome in terms of minimized costs and damages, MDA usage rates can be reduced when used in combination with environmental controls. Similarly, using guidelines that are independently optimal but jointly non-optimal for MDA and environmental controls might lead to inefficiencies: excessive usage of public funds and over-utilization of drug and environmental treatments. In our analysis, we assume unlimited public funds and perfect flexibility of these funds across time, relevant future work could investigate the role of budget constraints and lack of flexibility of rolling funds over from year to year or from one type of treatment to another.

We also show that when transportation and management costs of different types of treatment can be combined in one coordinated programme, utilizing both types of controls, instead of only using one control strategy (MDA or environmental control), does not significantly increase total expenditure over 10–50-year time horizons. If these costs were only present during the treatment period, then the reduction in time spent treating due to using the combination of multiple types of treatment could lead to further reduction in costs. These additional savings would reinforce the importance of considering an integrated approach to using both drug and environmental treatments.

The environmental treatment we consider in this paper consists of a chemical treatment of the environment. Such a treatment may have a declining efficacy over time. For instance, chemical pesticides used against mosquitoes in malaria-endemic areas have faced limitations due to resistance evolution, non-target effects and environmental damage [54]. For schistosomiasis, it is well documented that molluscicide niclosamide (the chemical compound used in snail control) can be toxic to other species [35,48–50]. Future work could include both the potential ecosystem damages from environmental treatment and potential reductions in efficacy over time. Another possible path is to investigate the feasibility of interventions that focus on reducing pathogen prevalence in the environment that might not have these additional damages or issues with declining efficacy.

For schistosomiasis, there is recent evidence in support of an ecological intervention where snail predator populations are restored [20]. Biological controls using snail predators (e.g. fish, prawns, ducks, crayfish) aid in schistosomiasis control as they reduce snail-to-man transmission by feeding off of the intermediate host population [20]. A potential ancillary benefit of introducing this treatment is the support of fisheries and aquaculture revenue, since many of the candidate natural enemies of snails are also seafood commodities. In fact, this might be a case where treatment does not only improve health outcomes directly but indirectly offers a source of sustainable development that could address food insecurity [42]. However, aligning the incentives of those who indirectly benefit from aquaculture or fisheries restoration with the public health costs associated with schistosomiasis could be challenging [55]. Optimal control methodologies, like the one applied here, are a fruitful approach to understanding the potential benefits and costs of aquatic snail predator restoration or aquaculture for reductions in disease burden and sustainable development.

Building on our results that redistributing funds across controls (e.g. from MDA to an environmental treatment) can be cost-effective, another important area for future research is also considering the optimal gains from redistributing funds across diseases (e.g. from HIV to NTDs; see [56]).

Data accessibility. This article has no additional data.

Authors' contributions. F.M.C., S.H.S., G.A.D.L. and J.N.S. designed the research. F.M.C. and J.N.S. performed research, conceived and developed the model, and F.M.C. ran the numerical simulations. F.M.C. and J.N.S. wrote the first draft of the paper, and all worked on the revisions.

Competing interests. We declare we have no competing interest.

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