

1 **Supporting Materials**

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5 Natl Acad Sci USA (2017).

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93 **Technical appendix**

94 In this supplement, we describe the data and methodology used to estimate the cost-effectiveness  
95 of mass drug administration (MDA), snail control, and combined public health strategies against  
96 schistosomiasis.

97  
98 Search strategy for review of snail control costing literature

99 We searched PubMed for relevant articles published in English up to February 2017, using the  
100 search term “molluscicide” or “snail control” and “cost\*” (using wildcard) restricted to the  
101 title/abstract field. This identified 53 articles. All studies were screened, and we identified only  
102 one study in the past 15 years that reported costing of snail control against schistosomiasis. The  
103 majority of the literature with costing data was published between 1970 and 1985. These older  
104 studies were used to guide the costing structure.

105  
106 Snail control costing

107 The estimated cost of snail control was informed by data from the recent SCORE trial that  
108 implemented chemical-based mollusciding, historical literature, and online product costs.<sup>1-6</sup> We  
109 used historical literature, mainly from the St. Lucia studies published in the 1980s, to develop a  
110 cost structure: equipment (capital costs), personnel, transportation, and chemical molluscicide.<sup>1-3</sup>  
111 We estimated personal and transportation requirements and costs for Kenya based on historical  
112 literature and the SCORE trial costing experience.<sup>1-3,7</sup> We determined the necessary equipment  
113 based on the SCORE trial and historical literature, which included spraying units, protective  
114 clothing, GPS, and a pH monitor. We surveyed the price and product description (to estimate  
115 lifetime of product) for equipment online.<sup>8</sup> We annualized the capital cost over the estimated  
116 lifetime of the product. The final costing structure is presented in the main text. We used  
117 historical literature on cost of focal chemical mollusciding (adjusted to 2016 US\$ and a 5000-  
118 person community) to provide a check of validity with our estimates.<sup>1-3</sup>

119 Transmission model: snail population biology and infection

120 The snail population model employed in this analysis was developed in earlier papers.<sup>9-11</sup> Total  
121 snail population density  $N = x + y + z$  is partitioned into standard S-E-I (susceptible- “x”,  
122 exposed-“y”, infected-“z”) compartments (Figure A1).



124 *Figure A1: Mathematical schematic of the snail model*

125 In the system,  $\beta$  is snail population growth,  $\Lambda$  is snail force of infection (FOI) as determined by  
126 human infectivity/egg release,  $r$  is patency conversion rate ( $1/r$  - prepatency period), and  $\nu$ ,  $\nu_1$

127 are natural mortality of healthy/prepatent and of patent snails. The resulting system of coupled  
 128 differential equations is:

$$\begin{aligned}
 \frac{dx}{dt} &= \beta - \Lambda x - \nu x \\
 \frac{dy}{dt} &= \Lambda x - (r + \nu) y \\
 \frac{dz}{dt} &= r y - \nu_1 z
 \end{aligned} \tag{1}$$

130 We use logistic-type reproduction term,  $\beta = \beta_0 (1 - N / K)(x + y)$ , with maximal reproduction  
 131 rate  $\beta_0$  and carrying capacity  $K$ . Only susceptible and prepatent snails ( $x + y$ ) can contribute to  
 132 reproduction.

133 In our model, snail FOI ( $\Lambda$ ) is a nonlinear (saturated) function of human infectivity  $E$  (mean egg  
 134 release by host population).<sup>9</sup>

$$\Lambda = \Lambda_0 \left( 1 - \exp \left[ -b \omega \frac{H E}{N} \right] \right) \tag{2}$$

136 Coefficient  $\Lambda_0$  is maximal invasion rate. Paper <sup>9</sup> provides justification for saturated FOI. For  
 137 mixed human population groups (e.g. pre-school aged children, school aged children (SAC),  
 138 adults),  $E$  is the sum of group-infectivity ( $E_C; E_S; E_A$ ) weighted by their population fractions (H),  
 139 and relative exposure/contamination rates ( $\omega$ ).<sup>9,11</sup>

140  
 141 Snail control (mollusciciding) is implemented via instantaneous reduction in snail densities  
 142  $\{x(t), y(t), z(t)\}$  to their fraction  $\{\varepsilon x(t), \varepsilon y(t), \varepsilon z(t)\}$ , where  $\varepsilon$  is the fraction of surviving  
 143 snails (molluscicide efficacy).

144  
 145 As in our previous work,<sup>9</sup> the snail environment is assumed to be stationary, i.e. we take a  
 146 ‘seasonal mean’ carrying capacity  $K(t) = K_0$ , fixed reproduction rate  $\beta_0$ , and human-snail  
 147 contacts. For fixed  $K$ , variables  $(x, y, z)$ , we can rescale over  $K$ , so  $K = 1$ , and total population  
 148  $N < 1$ .

149  
 150 Equilibrium solutions of system (1) along with snail infection data (seasonal mean) are used to  
 151 estimate model parameters (see calibration section below).<sup>9</sup>

152  
 153 Equations (1)-(2) describe an isolated snail habitat. To explore possible external inputs (snail  
 154 migration), we augment system (1) with additional transport terms.

155

$$\begin{aligned} \frac{dx}{dt} &= \dots + r_M (x_M - x) \\ \frac{dy}{dt} &= \dots + r_M (y_M - y) \\ \frac{dz}{dt} &= \dots + r_M (z_M - z) \end{aligned} \quad (3)$$

156 This represents an exchange with an external snail pool having prescribed densities  
 157  $(x_M, y_M, z_M)$ , and transport rate  $r_M$  (a fraction of maximal growth rate  $\beta$ ), that would maintain  
 158 its baseline endemic levels  $(X, Y, Z)$ .

159  
 160 Another modification of system (1)-(2) comes from external human sources of infection. Here  
 161 snail FOI  $\Lambda$  is partitioned into its “local component” (described below) and an external source  
 162 taken as a fraction of maximal FOI  $\Lambda_0$ . This can help simulate “hot spot” environments.

163 Transmission model: human infection in the Stratified Worm Burden (SWB) model

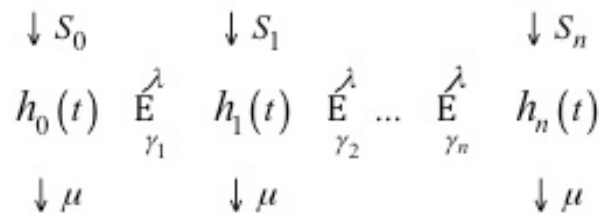
164 The SWB approach used in this model was developed and refined in previous work.<sup>9,11-13</sup> In the  
 165 SWB, the human host population is subdivided into worm burden strata  $\{h_m\}$  ( $\sum_m h_m = 1$ ),  
 166 determined by worm-step  $5 < \Delta w \leq 10$ , so that each  $h_m$  is made up of all local human hosts  
 167 carrying  $m \Delta w \leq w < (m+1) \Delta w$  worms. The worm-step  $\Delta w$  serves as low-density *mating*  
 168 *threshold*, so  $h_0$  are assumed infection-free (no mated couples), while each stratum  $\{h_m : m \geq 1\}$   
 169 carries  $\phi_m$  mated couples.<sup>14,15</sup>

170

$$\phi_m = \frac{m}{2} \left[ 1 - 2^{-m} \binom{m}{m/2} \right] \quad (4)$$

171 The transitions among strata are determined by human FOI  $\lambda$  (rate of worm accumulation/ $\Delta w$ ),  
 172 worm resolution rates  $\gamma_m = \gamma m$  ( $\gamma$  - mean worm mortality), and population turnover rate  $\mu$   
 173 (mortality, maturation, migration, etc.) (Figure A2)

174



175

176

Figure A2: SWB strata and transitions

177 Source terms  $\dot{S} = (S_k)$  in Figure A2 represent demographic inputs from younger to older age  
 178 groups. For the youngest child group, its source  $\dot{S} = (\mu, 0, 0, \dots)$  comes into the zero-infection  
 179 stratum only, as all newborns are infection-free.

180  
 181 In demographically structured communities, each population sub-group is represented by its own  
 182 SWB coupled via demographic transitions (birth, maturation, death). We use three age groups,  
 183 pre-school children (1-5 years), SAC (6-14 years), adults (15+ years), designated by  $\{h_m^i(t)\}$ ,  
 184  $i = (C, S, A)$ . Each SWB -group is described by its transition matrix  $M(\lambda, \mu, \gamma)$ - a function  
 185 with age-specific human FOI  $\lambda = \lambda_i$ , population turnover -  $\mu_i$ , and worm mortalities -  $\gamma_i$ . The  
 186 younger ages enter older SWB as sources. The coupled system of differential equations for  
 187 vector-functions,  $\dot{h}^C = \{h_m^C(t)\}$ ,  $\dot{h}^S$ ,  $\dot{h}^A$  is given by:

$$\begin{aligned}
 \frac{d\bar{h}^C}{dt} &= M(\lambda_C, \mu_C, \gamma_C) \cdot \bar{h}^C + \bar{S}_C + \mu_C \delta_0 \\
 \frac{d\bar{h}^S}{dt} &= M(\lambda_S, \mu_S, \gamma_S) \cdot \bar{h}^S + \mu_S \bar{h}^C \\
 \frac{d\bar{h}^A}{dt} &= M(\lambda_A, \mu_A, \gamma_A) \cdot \bar{h}^A + \mu_A \bar{h}^S
 \end{aligned} \tag{5}$$

189 Egg release by mated females and individual hosts depends on age-specific worm fecundity  $\rho$ ,  
 190 and the mated-couple count  $\phi_m$  (for the  $h_m$  - stratum). A host in  $m$ -th stratum is assumed to  
 191 release random egg-counts determined by negative binomial (NB)-distribution with mean  
 192  $E_m = \rho \phi_m$ , and aggregation parameter  $k_m = k \phi_m$ .<sup>16,9,11,17</sup> So any test pool of an SWB  
 193 community with population strata  $\{h_m\}$  is viewed as random draw of the NB-mixture  
 194 distribution (with weights  $h_m$ ), illustrated in the schematic plot Figure A3.

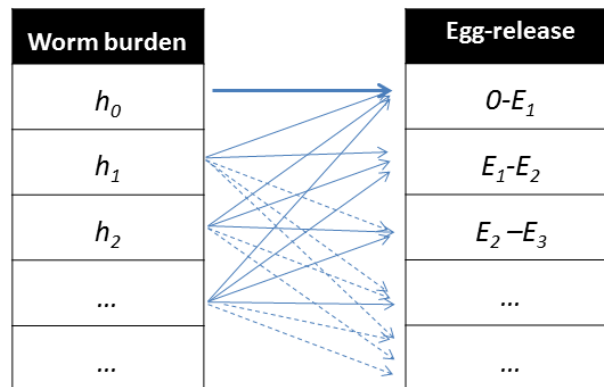


Figure A3: Distributed egg release by SWB strata

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198

$$\mathcal{E} = \sum_m h_m NB(\rho \phi_m | k \phi_m) \quad (6)$$

199 While egg-release by individual hosts is random, their cumulative effect on snail FOI is given by  
200 mean human infectivity.

201

$$E(\lambda) = \rho \sum_m \phi_m h_m(\lambda) = \rho \Phi(\lambda). \quad (7)$$

202  $\Phi(\lambda)$  is mean mated count of SWB group  $\{h_m(\lambda)\}$ .

203 In structured communities, group infectivities (7) are combined into a single human “mean  
204 infectivity”, determined by group population fractions ( $\sum_i H_i = 1$ ), and their exposure rates,  
205  $\omega_C; \omega_S; \omega_A$  “child/SAC/adult”,

206

$$E = H_C \omega_C E_C + H_S \omega_S E_S + H_A \omega_A E_A \quad (8)$$

207 Human infectivity (8) enters the snail FOI (2) of the coupled human-snail model system. Egg-  
208 test results are used for diagnostic purposes to assess low and high infection prevalence at a  
209 particular time (simulated EPG test). Such prevalences depend on human inputs: SWB-state  
210  $\frac{1}{h} = (h_m)$ , worm fecundity ( $\rho$ ), and aggregation parameter  $k$ . For instance, positive prevalence  
211 ( $E > 0$ ), assuming the SWB-NB mixture hypothesis (6), is given by

212

$$P = 1 - \sum h_m \left( \frac{k}{k + \rho} \right)^{k \phi_m}$$

213 Coupled human-snail system and model calibration

214 Human and snail equations (1) - (5) are coupled via two transmission coefficients  $A$  (snail-to-  
215 human) and  $B$  (human-to-snail). The  $A$  -coefficient is included in the human FOI expression  
216  $\lambda = Az$  (patent snail prevalence), and coefficient  $B$  is included in the exponent of the saturated  
217 snail FOI,  $\Lambda$ .

218  
219 The details of model calibration and estimated parameter values are explained in previously  
220 published papers.<sup>9,11</sup> The estimated model parameters include age-specific human FOI  $\lambda_i$ , worm  
221 fecundity  $\rho_i$ , aggregation  $k_i$ , and the resulting transmission rates  $A_i$ ,  $B$ , as summarized in Table  
222 A1. Specifically, A-coefficients are estimated from calibrated human FOI  $\lambda_i$  and (known or  
223 hypothesized) patent snail density  $z$

224

$$A_i = \frac{\lambda_i}{z}, \quad i = (C, S, A)$$

225 The B-coefficient (of reference SAC group) enters in snail FOI  $\Lambda$  (2) along with maximal  
 226 invasion parameter  $\Lambda_0$ , and  $\Lambda$  is expressed through the basic snail inputs (below).

227 There are 3 types of model inputs in our setup.

228 (i) **Human parameters** are made of age-specific triplets  $(\lambda_i, k_i, \rho_i)$ ,  $i = \{C, S, A\}$ ; they  
 229 enter in the human infectivity function  $E_i = \rho_i \Phi(\lambda_i)$ , equation (8)

230 (ii) **Snail inputs** include total (equilibrium) population  $N < 1$ , endemic prepatent and patent  
 231 prevalence  $(Y, Z) = (y, z) / N$ ; natural mortalities  $\nu < \nu_1$ . The remaining parameters of  
 232 snail model (1) are estimated from  $(N, Y, Z)$

$$\begin{aligned} \beta_0 &= \frac{\nu + (\nu_1 - \nu)Z}{(1 - N)(1 - Z)} \\ r &= \frac{\nu_1 Z}{Y} \\ \Lambda_0 &= \frac{\nu Y + \nu_1 Z}{1 - Y - Z} \end{aligned} \quad (9)$$

234 The latter (FOI  $\Lambda$ ) along with estimated human infectivity  $E$ , give an algebraic relation between  
 235  $\Lambda_0$  and transmission coefficient  $B$

$$\Lambda = \Lambda_0 N \left(1 - e^{-B E H / N}\right) \quad (10)$$

237 Combined human infectivity  $E$  in (10) is contributed by all age-groups via

$$E = H_S \Phi_S + H_C \frac{\rho_C}{\rho_S} \Omega_C \Phi_C + H_A \frac{\rho_A}{\rho_S} \Omega_A \Phi_A \quad (11)$$

239 Here  $\{H_i\}$  are known population fractions,  $\{\rho_i\}$  - estimated worm fecundity,  $\Phi_i$  - mean mated

240 count for each age-group. Three addition inputs are uncertain relative exposures:  $\Omega_C = \frac{\omega_C}{\omega_S}$

241 (child/SAC),  $\Omega_A = \frac{\omega_A}{\omega_S}$  (adult/SAC), and transmission coefficient  $B$  in the exponent (10) (for

242 SAC reference group)

$$B = b_S \rho_S \omega_S \quad (12)$$

244 Human calibration in the present study, was obtained from test data on *S. haematobium* collected  
 245 in coastal Kenya.<sup>18,19</sup> A Bayesian-type calibration procedure provides a range of likely parameter  
 246 choices - posterior distribution in 9D space  $\{(\lambda_i, k_i, \rho_i)\}$ .

247 Additional uncertainties include snail inputs  $(N, Y, Z)$  and environmental conditions  $(b, \Omega_C, \Omega_A)$ .



248 We sample model uncertainties to provide variability and generate a 95% uncertainty interval  
 249 (UI) in the transmission projection for control interventions.

250

251 **Table A1: Summary of model parameters**

	Known, fixed			Calibrated	
Human	Demographic inputs			Posterior distributions of $\{\lambda^i, \rho^i, k^i\}$ , for 3 age-group $i = \{C, S, A\}$ , estimated from community test data <sup>(18,19)</sup>	
	Population fractions	C	S		A
	Host turnover/year	0.18	0.28		0.54
	Worm mortality/year	0.21	0.1		0.02
		0.2	0.2	0.25	
Snail	Mortality: (susceptible/prepatent) $\nu = 4$ /year, (patent) $\nu_1 = 12$ /year <sup>20,21</sup> Baseline equilibrium values <sup>1</sup> : $.6 < N < .95$ $.15 < Y < .45$ $.05 < Z < .15$			Estimated Max reproduction rate: $\beta_0$ <sup>2)</sup> Max invasion (FOI) rate: $\Lambda_0$	
Environment/ transmission	Basic (SAC) transmission rate: $.5 < B < 3$ Relative exposure/contamination rates (“child/SAC, adult/SAC): $.5 < \Omega_{C/A} < 1.5$			Transmission coefficients $A_i = \lambda^i / Z$	

252 <sup>1)</sup> These ranges are broadly consistent with published data <sup>21,20,18</sup>

253 <sup>2)</sup> Consistent with observed snail growth/rebound rates <sup>21</sup>

254 Simulation of snail control and human prevalence and incidence

255 The coupled SWB-snail model is used to simulate the effect of focal chemical-based  
 256 mollusciciding programs on human prevalence and infection incidence. The latter (incidence) is  
 257 commonly used in long-term snail control studies. In the SWB setup, the instantaneous incidence  
 258 function can be defined as human FOI times uninfected stratum, i.e. the rate of transition from  
 259 “uninfected to infected”:

260 
$$F(t) = \lambda(t)h_0(t) = Az(t)h_0(t) \quad (13)$$

261 Here  $A$  is snail-to-human transmission coefficient,  $z(t)$  – patent snail density. For mixed  
 262 communities (C-S-A), functions (13) are weighted by population fractions of each group to  
 263 generate a combined population incidence. The incidence function can undergo wide changes  
 264 during molluscicide and frequently rebounds, so the effect on transmission is often temporary.

265 The mean incidence is computed  $F(t)$  over the inter-molluscicide period ( $\tau = 1/2$ -1 years),

266 
$$\bar{F}_j = \frac{1}{\tau} \int_0^\tau F(j\tau + t) dt, \quad (14)$$

267 for  $j$ -th control period ( $j = 0, 1, 2, \dots$ ). The terminal relative incidence,  $\bar{F}_n / \bar{F}_0$  is reported as the  
 268 program outcome (effectiveness).

269  
 270 Each simulated community had biological/transmission parameters and control inputs that affect  
 271 snail control effectiveness. The biological/transmission parameters include,  $A$  – snail-to-human,  
 272  $B$  – human-to-snail,  $\Lambda$  - maximal miracidia invasion,  $\beta$  - max snail reproduction/growth. The  
 273 control inputs are  $\epsilon < 1$  - molluscicide efficacy (fraction of snail removed),  $\tau$  - inter-  
 274 molluscicide interval,  $T$  - program duration. We provide hypothetical simulations below (Figure  
 275 A4).

276  
 277 Mollusciciding removes a fraction of normal snail density,  $N \rightarrow \epsilon N$  ( $\delta = 1$ ) along with infected  
 278 and patent snails, after which the population may return to precontrol snail levels driven by the  
 279 snail population's logistic growth term. We implemented each mollusciciding as an  
 280 instantaneous event (due to short duration of chemical in the environment). Typical long-term  
 281 molluscicide histories (human/snail prevalence and incidence functions) are illustrated below  
 282 with three hypothetical examples using a range of different input parameters (table below) to  
 283 illustrate the effect on snail control dynamics.

	<b>A</b>	<b>B</b>	<b><math>\Lambda</math></b>	<b><math>\beta</math></b>	<b><math>\epsilon</math></b>	<b><math>\tau</math></b>
<b>1</b>	<b>32.</b>	<b>1.54</b>	<b>14.8</b>	<b>12.</b>	<b>0.05</b>	<b>0.33</b>
<b>2</b>	<b>40.2</b>	<b>2.07</b>	<b>13.5</b>	<b>12.1</b>	<b>0.15</b>	<b>0.5</b>
<b>3</b>	<b>37.</b>	<b>1.6</b>	<b>13.5</b>	<b>13.2</b>	<b>0.15</b>	<b>1</b>

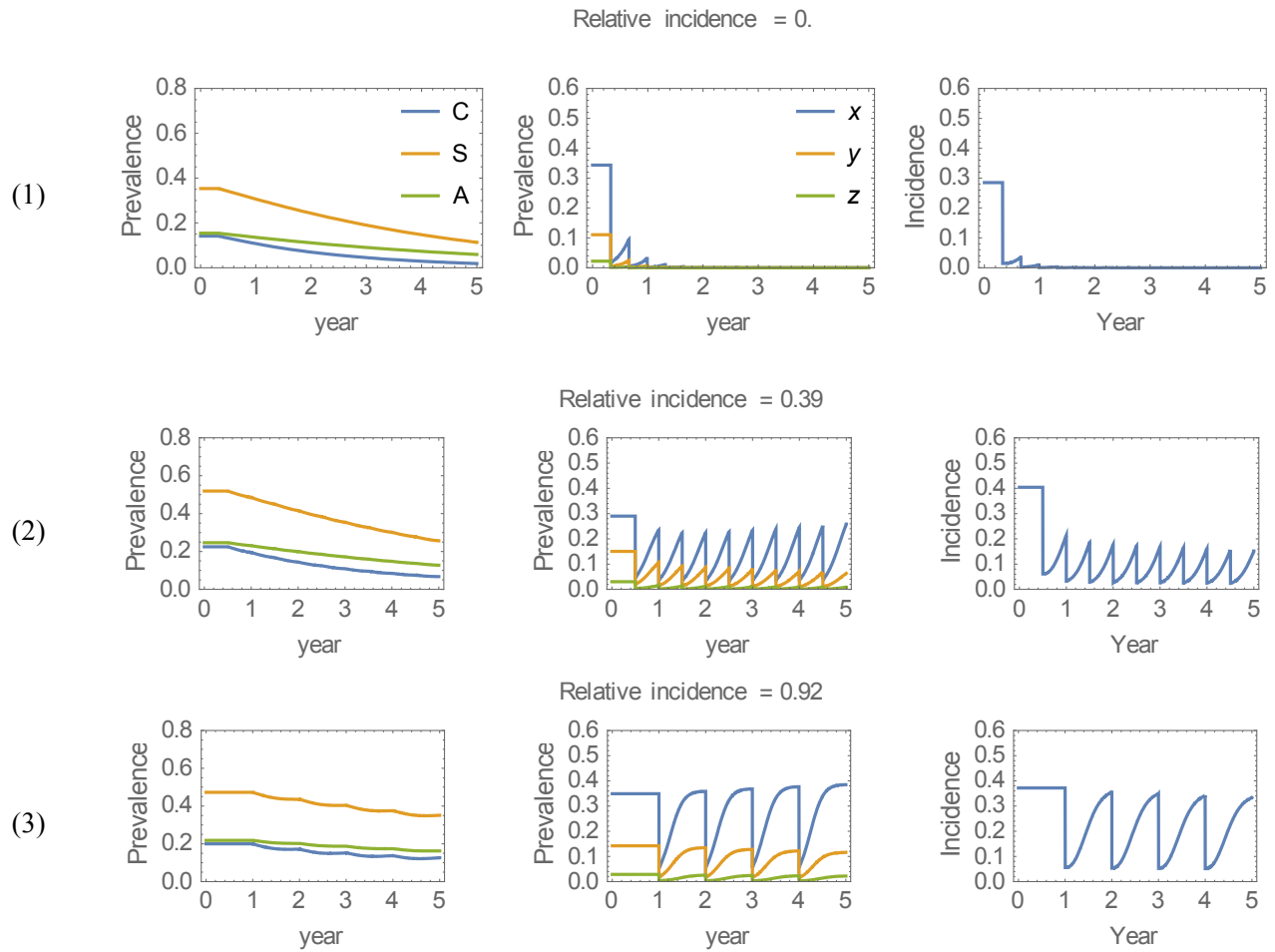
284  
 285 In case (1), shown in Figure A4 (high frequency  $\tau = 1/3$  year, i.e. 3x per year, and high efficacy  
 286  $\epsilon = .05$ ), the snail population is driven to extinction, hence human incidence drops to zero and  
 287 infection prevalence gradually relaxes to zero due to natural worm mortality. This is a  
 288 hypothetical example of a program with perfect effectiveness.

289 In case (2) (frequency  $\tau = 1/2$  year, efficacy  $\epsilon = .15$ ), the system settles in a limit-cycle pattern  
 290 with lower mean snail density and mean incidence (14); the effectiveness = 0.39 is temporary  
 291 and defined over the time period between molluscicide applications.

292 In case (3) (frequency  $\tau = 1$  year, efficacy  $\epsilon = .15$ ), the snail population rebounds to precontrol  
 293 levels and the resulting terminal mean incidence (effectiveness) is limited (effectiveness=0.92),  
 294 so there is only minor reductions in incidence for a short period of time between applications of  
 295 molluscicide.

296 In all cases, reduced incidence combined with natural worm mortality reduces infection  
 297 prevalence between Y1 and Y5. Specifically, SAC prevalence drop: 35% to 12% (case 1), 52%  
 298 to 26% (case 2), and 48% to 35% (case 3).

299



300 *Figure A4: Three hypothetical histories of 5-year molluscicide programs with different choices*  
 301 *of transmission parameters and control inputs to simulate variability of snail control*  
 302 *effectiveness, we simulate: (A) perfect effectiveness; (B) moderate effectiveness; (C) limited*  
 303 *effectiveness for snail control.*

304 Operationally, snail control effectiveness is a function of multiple calibrated parameters that  
 305 produce a wide range of possible values. This distribution (in terms of relative incidence  
 306 reduction) was estimated and calibrated to broadly align with data from a recent meta-analysis of  
 307 observational studies (Figure A5).<sup>22</sup>

308

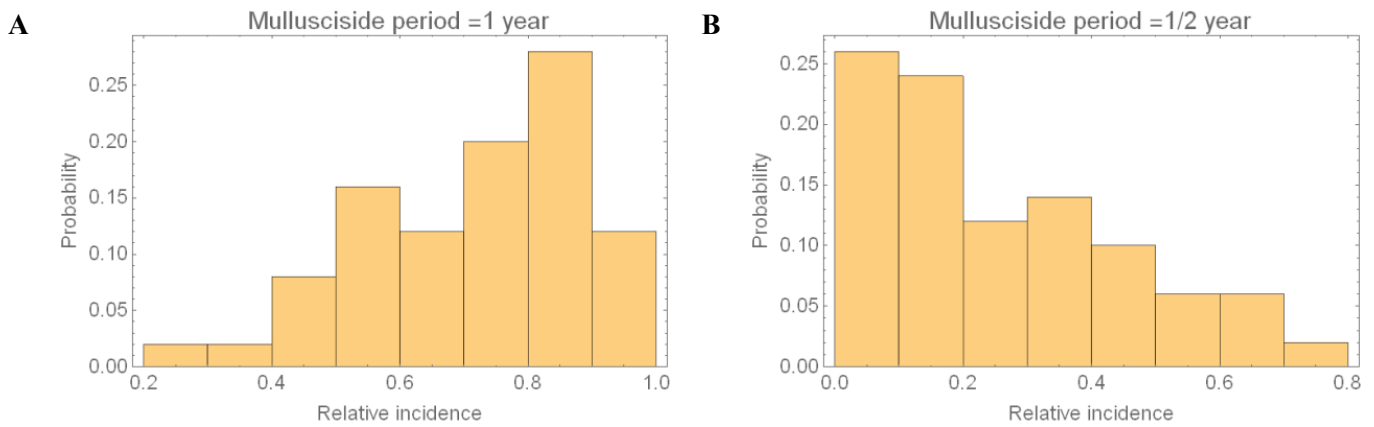
309 In the study, we modeled two frequencies, semiannual ( $\tau = 1/2$  years, twice a year) and annual ( $\tau$   
 310  $= 1$  year). For each  $\tau$ , we simulated an ensemble of 50 virtual communities by random sampling  
 311 from the five fitted parameter ranges (ranges below), which provided a distribution of effect  
 312 sizes for snail control.

313

A	B	$\Lambda$	$\beta$	$\varepsilon$
30-45	1.5-2.5	10-15	10-15	0.05-0.15

314

315 The resulting molluscicide histories differed widely (Fig. A4-5). Semiannual snail control was  
316 more broadly distributed (50% +), while low-frequency (once per year) snail control  
317 demonstrated moderate reduction (30% or less) over this time period. The predicted molluscicide  
318 effectiveness, defined as mean-incidence reduction over a five-year period (Year 5 relative to  
319 Year 1) is provided in Figure A5. These data were calibrated to broadly align with meta-analysis  
320 data from observational studies (Figure A4-5).<sup>22</sup>  
321



322 *Figure A5: Histogram of relative incidence reductions (snail control effectiveness) for annual*  
323 *and semiannual frequency of snail control over a five-year simulation*  
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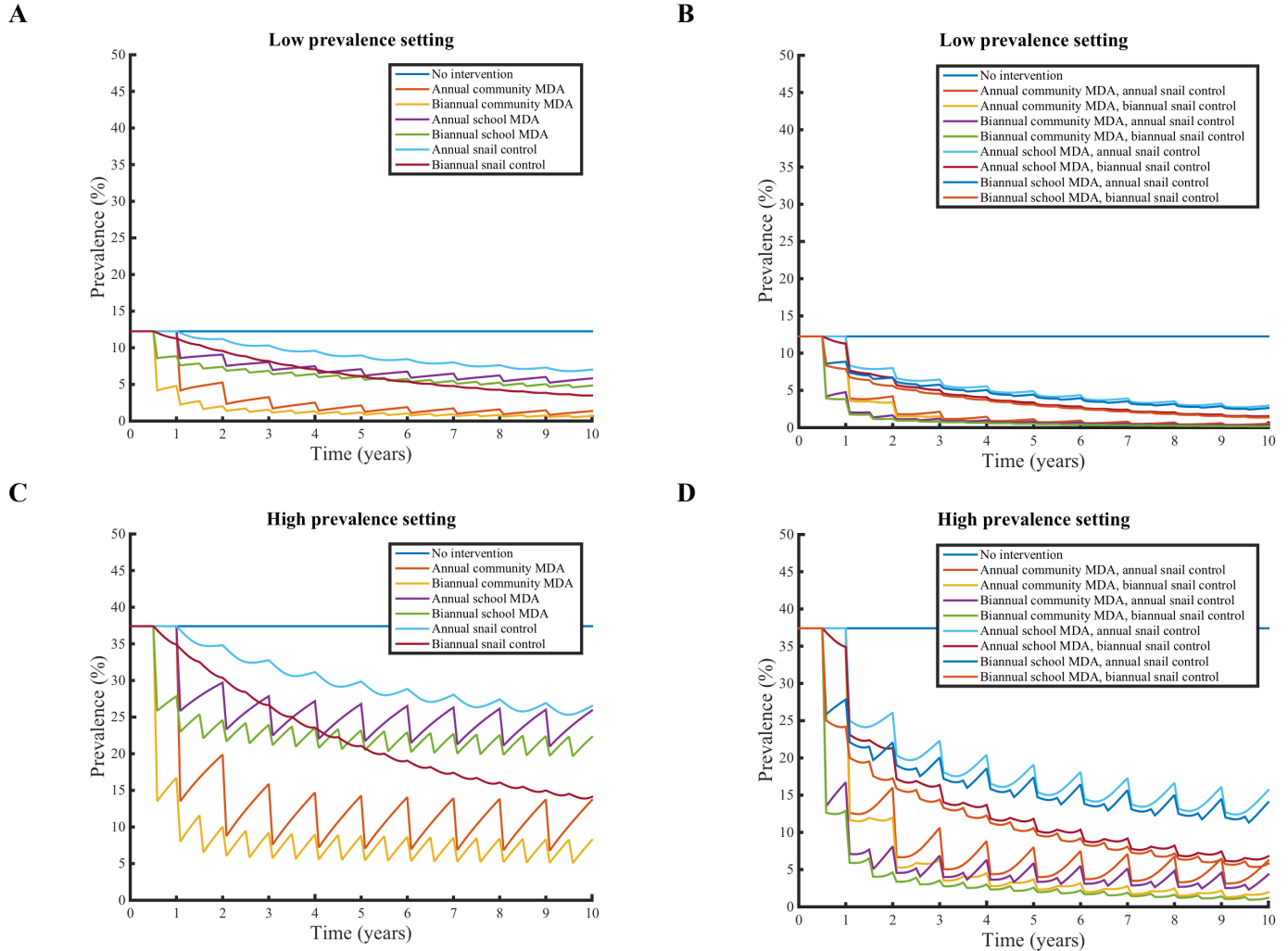
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419 **Supplemental figures and tables**

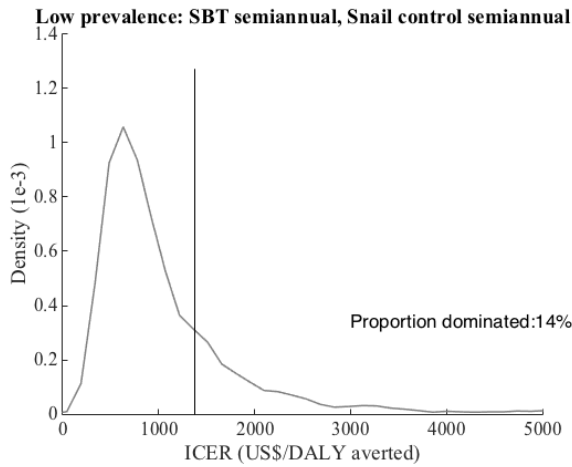
420 Figure S1: Effectiveness of all MDA, snail control, and combined interventions for  
421 schistosomiasis in low and high burden Kenyan communities  
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423 Figure S2: Kernel density plot for the uncertainty analysis with key model parameters  
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425 Figure S3: Cost-effectiveness acceptability curves, plotting proportion of simulations  
426 below a corresponding incremental cost-effectiveness ratio  
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428 Table S1: Costs, disability, and incremental cost-effectiveness of MDA, snail control, and  
429 combined interventions for schistosomiasis in low and high burden Kenyan communities  
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431 Table S2: Scenario analysis for snail and human population density, MDA coverage, and  
432 systematic non-compliance in low prevalence settings  
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434 Table S3: Scenario analysis for snail and human population density, MDA coverage, and  
435 systematic non-compliance in high prevalence settings  
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437 Table S4: Parameter specifications for uncertainty analysis and generation of uncertainty  
438 intervals  
439  
440 Table S5: Undiscounted costs, disability, and incremental cost-effectiveness of MDA,  
441 snail control, and combined interventions for schistosomiasis in low and high burden  
442 Kenyan communities  
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444 Table S6: One-way sensitivity analysis varying cost estimates until key strategies are no  
445 longer highly cost-effective  
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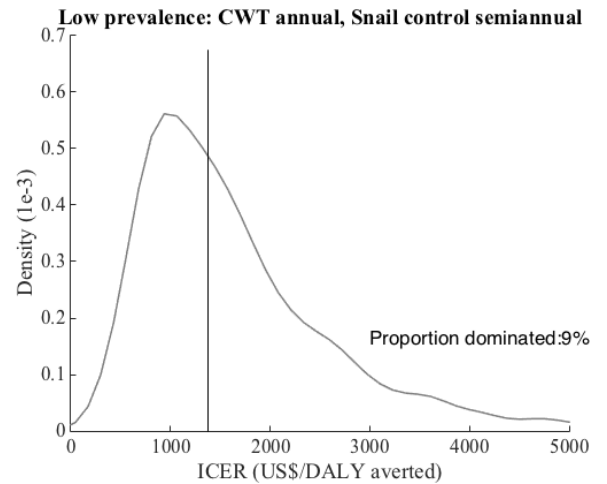
456 **Figure S1: Effectiveness of all MDA, snail control, and combined interventions for**  
 457 **schistosomiasis in low and high burden Kenyan communities.** We simulated interventions of  
 458 MDA, snail control, and combined approaches in an age-stratified population of pre-SAC, SAC,  
 459 and adults in a: (a-b) low prevalence Kenyan community; and (c-d) high prevalence Kenyan  
 460 community with 75% coverage for MDA. We displayed MDA or snail control alone in panel A  
 461 and C and combined strategies in panel B and D for improved visualization.  
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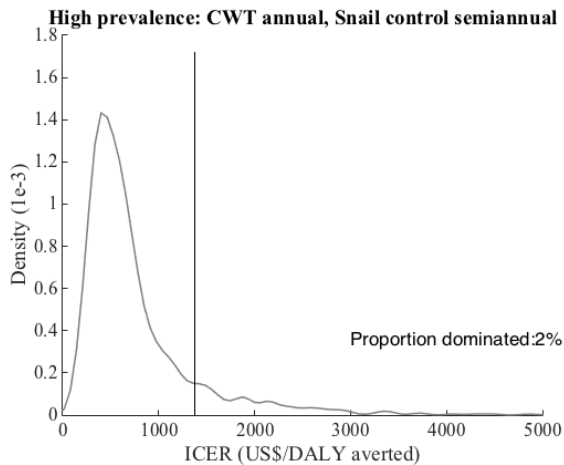
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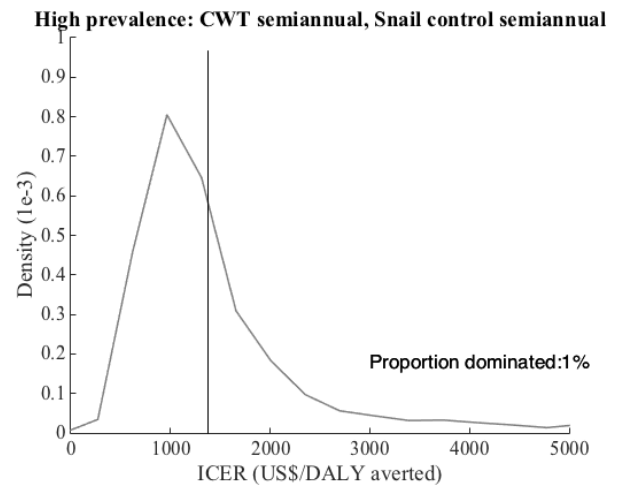
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464 **Figure S2: Kernel density plot for the uncertainty analysis with key model parameters.** This  
 465 uncertainty analysis (probabilistic sensitivity analysis) tested the effect of changing multiple  
 466 model inputs simultaneously on the incremental cost-effectiveness ratio (ICER) of the highly  
 467 cost-effective interventions from the primary analysis: (a) semiannual school-based MDA (SBT)  
 468 with semiannual snail control in low burden settings; (b) annual community-wide MDA (CWT)  
 469 with semiannual snail control in low burden settings; (c) annual community-wide MDA with  
 470 semiannual snail control in high burden settings; and (d) semiannual community-wide MDA  
 471 with semiannual snail control in high burden settings. The distribution left of the vertical line  
 472 (ICER of US\$1,377/DALY) represents a highly cost-effective intervention. The proportion of  
 473 simulations where each strategy is dominated is reported in the figure.

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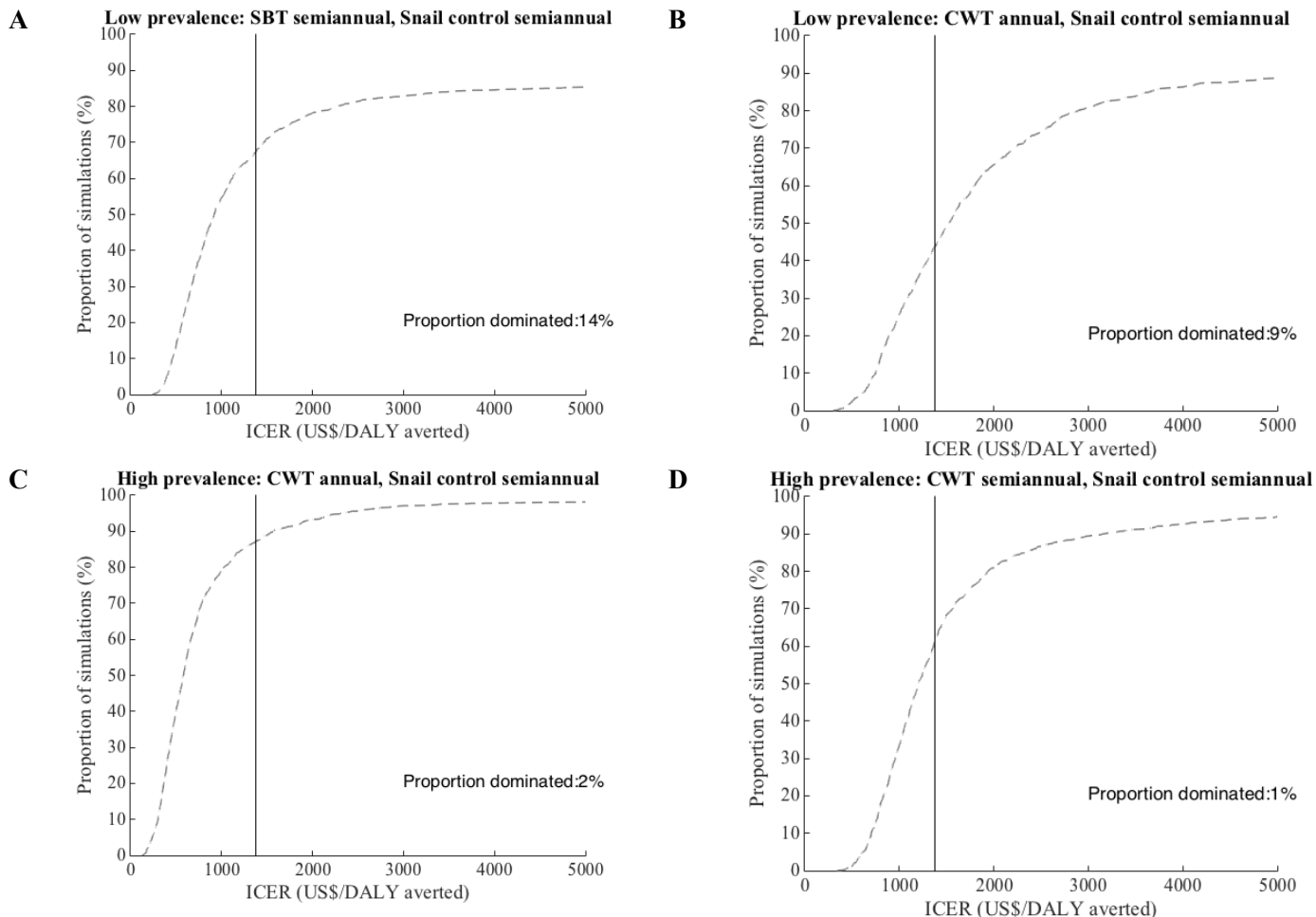
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480 **Figure S3: Cost-effectiveness acceptability curves, plotting proportion of simulations below**  
 481 **a corresponding incremental cost-effectiveness ratio.** This uncertainty analysis (probabilistic  
 482 sensitivity analysis) tested the effect of changing multiple model inputs simultaneously on the  
 483 incremental cost-effectiveness ratio (ICER) of the highly cost-effective intervention from the  
 484 primary analysis, compared with the next most effective, non-dominated strategy. We plotted the  
 485 cumulative proportion of simulations below a corresponding ICER. The proportion of  
 486 simulations where each strategy is dominated by another strategy is reported in the figure, and  
 487 provided a ceiling for maximum proportion of simulations. These results are for: (a) semiannual  
 488 school-based MDA (SBT) with semiannual snail control in low burden settings; (b) annual  
 489 community-wide MDA (CWT) with semiannual snail control in low burden settings; (c) annual  
 490 community-wide MDA with semiannual snail control in high burden settings; and (d)  
 491 semiannual community-wide MDA with semiannual snail control in high burden settings. The  
 492 vertical line (ICER of US\$1,377/DALY) represents one interpretation of a highly cost-effective  
 493 intervention.

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498 **Table S1: Costs, disability, and incremental cost-effectiveness of MDA, snail control, and**  
 499 **combined interventions for schistosomiasis in low and high burden Kenyan communities**

<b>Low prevalence</b>	<b>MDA</b>	<b>Snail control</b>	<b>Total cost (US\$)</b>	<b>Total disability (DALYs)</b>	<b>ICER (US\$/DALY)</b>
	None	None	0	171.6	--
	None	Annual	3,334	127.5	76
	SBT annual	None	6,550	98.5	dominated <sup>b</sup>
	None	Semiannual	6,667	96.2	107
	SBT semiannual	None	13,100	84.3	dominated <sup>a</sup>
	SBT annual	Annual	9,884	74.6	149
	SBT semiannual	Annual	16,434	65.9	dominated <sup>a</sup>
	SBT annual	Semiannual	13,217	60.2	232
	SBT semiannual	Semiannual	19,768	53	904
	CWT, annual	None	47,116	44.6	dominated <sup>b</sup>
	CWT annual	Annual	50,449	35.2	dominated <sup>b</sup>
	CWT annual	Semiannual	53,783	30.7	1,531
	CWT semiannual	None	94,231	26.8	dominated <sup>b</sup>
	CWT semiannual	Annual	97,565	22.7	dominated <sup>b</sup>
	CWT semiannual	Semiannual	100,900	19.9	4,353
<b>High prevalence</b>	<b>MDA</b>	<b>Snail control</b>	<b>Total cost (US\$)</b>	<b>Total disability (DALYs)</b>	<b>ICER (US\$/DALY)</b>
	None	None	0	550	--
	None	Annual	3,334	435.4	29
	SBT annual	None	6,550	352.4	dominated <sup>b</sup>
	None	Semiannual	6,667	326.6	31
	SBT semiannual	None	13,100	304.7	dominated <sup>a</sup>
	SBT annual	Annual	9,884	260.3	49
	SBT semiannual	Annual	16,434	228.8	dominated <sup>a</sup>
	CWT, annual	None	47,116	204.6	dominated <sup>a</sup>
	SBT annual	Semiannual	13,217	194.9	51
	SBT semiannual	Semiannual	19,768	167.4	238
	CWT annual	Annual	50,449	140.1	dominated <sup>b</sup>
	CWT semiannual	None	94,231	132	dominated <sup>a</sup>
	CWT annual	Semiannual	53,783	109.6	588
	CWT semiannual	Annual	97,565	94.2	dominated <sup>b</sup>
	CWT semiannual	Semiannual	100,900	70.7	1,213

500 Base case analysis assumed 10% systematic non-compliance and 3% discounting. For interpretation, a lower ICER  
 501 is a more cost-effective strategy relative to another intervention. An ICER below 1,377 US\$/DALY is highly cost-  
 502 effective in Kenya, although ICERs are provided to relax reliance on a single threshold. SBT, school-based  
 503 treatment with MDA; CWT, community-wide treatment with MDA

504 <sup>a-b</sup> 'dominated' strategy were (a) strictly dominated when they had a lower effectiveness and higher cost than  
 505 another choice; or (b) dominated by extension when the strategy was less effective and had a higher ICER relative to  
 506 another choice.  
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508 **Table S2: Scenario analysis for snail and human population density, MDA coverage, and**  
 509 **systematic non-compliance in low prevalence settings.**

Strategy	Snail/human density	MDA community coverage	Systematic non-compliance	Cost (US\$)	DALYs averted	ICER (US\$/DALY)
SBT semiannual MDA, semiannual snail control	Low	Low, 50%	--	19768	34.2	1327
	High	Low, 50%	--	19768	80.6	400
	Low	High, 85%	--	19768	25.8	1872
	High	High, 85%	--	19768	69.5	577
	Low	--	None, 0%	19768	27.0	1455
	High	--	None, 0%	19768	58.3	569
	Low	--	High, 10%	19768	30.2	1684
	High	--	High, 10%	19768	70.8	579
CWT annual MDA, semiannual snail control	Low	Low, 50%	--	53783	25.6	3961
	High	Low, 50%	--	53783	58.1	1513
	Low	High, 85%	--	53783	16.2	3532
	High	High, 85%	--	53783	38.7	1104
	Low	--	None, 0%	53783	15.6	2965
	High	--	None, 0%	53783	27.8	2988
	Low	--	High, 10%	53783	21.1	3766
	High	--	High, 10%	53783	45.5	1347

The ICER is computed in reference to the next most effective, non-dominated strategy.

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519 **Table S3: Scenario analysis for snail and human population density, MDA coverage, and**  
 520 **systematic non-compliance in high prevalence settings.**

Strategy	Snail/human density	MDA community coverage	Systematic non-compliance	Cost (US\$)	DALYs averted	ICER (US\$/DALY)
CWT annual MDA, semiannual snail control	Low	Low, 50%	--	53783	123.5	948
	High	Low, 50%	--	53783	236.8	491
	Low	High, 85%	--	53783	86.9	688
	High	High, 85%	--	53783	160.4	308
	Low	--	None, 0%	53783	76.8	65
	High	--	None, 0%	53783	105.9	237
	Low	--	High, 10%	53783	124.5	967
	High	--	High, 10%	53783	235.9	532
CWT semiannual MDA, semiannual snail control	Low	Low, 50%	--	100900	82.3	1143
	High	Low, 50%	--	100900	153.6	566
	Low	High, 85%	--	100900	57.5	1601
	High	High, 85%	--	100900	102.7	816
	Low	--	None, 0%	100900	41.5	1336
	High	--	None, 0%	100900	48.1	814
	Low	--	High, 10%	100900	82.5	1120
	High	--	High, 10%	100900	153.5	572

The ICER is computed in reference to the next most effective, non-dominated strategy.

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531 **Table S4: Parameter specifications for uncertainty analysis and generation of uncertainty**  
 532 **intervals**

<b>Model parameter</b>	<b>Uncertainty analysis</b>		
	<b>Base case</b>	<b>Lower limit</b>	<b>Upper limit</b>
Transmission model <sup>a</sup>	Mean	Lower 2.5%	Upper 97.5%
School-based delivery cost (per person)	US\$ 0.50	US\$ 0.25	US\$ 0.75
Community-wide delivery cost (per person)	US\$ 1.50	US\$ 0.50	US\$ 2.50
Snail control cost (per community)	US\$ 379.43	US\$ 285	US\$ 475
Systematic non-compliance	10%	0%	10%
Schistosomiasis disability weight (light, heavy)	(0.014, 0.05)	(0.01, 0.02)	(0.02, 0.1)

533 <sup>a</sup>Sampled posterior distribution from Bayesian model fits.  
 534 We used a normal distribution to sample transmission trajectories, triangle distribution across all cost and disability  
 535 parameters, and simulated 10% of cases with perfect mixing (no systematic non-compliance).  
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560 **Table S5: Undiscounted costs, disability, and incremental cost-effectiveness of MDA, snail**  
 561 **control, and combined interventions for schistosomiasis in low and high burden Kenyan**  
 562 **communities**

<b>Low prevalence communities</b>	<b>MDA</b>	<b>Snail control</b>	<b>Total cost (US\$)</b>	<b>Total disability (DALYs)</b>	<b>ICER (US\$/DALY)</b>
	None	None	0	203.1	--
	None	Annual	3794	148.4	69
	SBT annual	None	7455	113.6	dominated <sup>a</sup>
	None	Semiannual	7589	110.2	99
	SBT semiannual	None	14910	97.2	dominated <sup>a</sup>
	SBT annual	Annual	11249	84.4	142
	SBT semiannual	Annual	18704	74.6	dominated <sup>a</sup>
	SBT annual	Semiannual	15044	67.1	220
	SBT semiannual	Semiannual	22499	59.1	929
	CWT, annual	None	53625	49.4	dominated <sup>a</sup>
	CWT annual	Annual	57419	38.2	dominated <sup>a</sup>
	CWT annual	Semiannual	61214	33	1484
	CWT semiannual	None	107250	29.5	dominated <sup>a</sup>
	CWT semiannual	Annual	111040	24.6	dominated <sup>a</sup>
	CWT semiannual	Semiannual	114840	21.4	4621
<b>High prevalence communities</b>	<b>MDA</b>	<b>Snail control</b>	<b>Total cost (US\$)</b>	<b>Total disability (DALYs)</b>	<b>ICER (US\$/DALY)</b>
	None	None	0	651.2	--
	None	Annual	3794	509.9	27
	SBT annual	None	7455	411.6	dominated <sup>a</sup>
	None	Semiannual	7589	376.2	28
	SBT semiannual	None	14910	355.9	dominated <sup>a</sup>
	SBT annual	Annual	11249	298.5	47
	SBT semiannual	Annual	18704	262.8	dominated <sup>a</sup>
	CWT, annual	None	53625	235	dominated <sup>a</sup>
	SBT annual	Semiannual	15044	218.7	48
	SBT semiannual	Semiannual	22499	188	243
	CWT annual	Annual	57419	156	dominated <sup>a</sup>
	CWT semiannual	None	107250	151.3	dominated <sup>a</sup>
	CWT annual	Semiannual	61214	119.2	562
	CWT semiannual	Annual	111040	105.1	dominated <sup>a</sup>
	CWT semiannual	Semiannual	114840	76.9	1269

563 This analysis assumed 10% systematic non-compliance without discounting. SBT, school-based treatment with  
 564 MDA; CWT, community-wide treatment with MDA.

565 <sup>a</sup>'dominated' strategy were (a) strictly dominated when they had a lower effectiveness and higher cost than another  
 566 choice; (b) dominated by extension when the strategy was less effective and had a higher ICER relative to another.

567 **Table S6: One-way sensitivity analysis varying cost estimates until key strategies are no**  
 568 **longer highly cost-effective.**

		<b>Strategy</b>		<b>Model parameter</b>	
<b>Setting</b>	<b>MDA</b>	<b>Snail control</b>	<b>School-based delivery cost</b>	<b>Community-wide delivery cost</b>	
Base case			\$0.50	\$1.50	
Low prevalence	SBT semiannual	Semiannual	\$0.85	--	
High prevalence	CWT annual	Semiannual	--	\$3.50	
High prevalence	CWT semiannual	Semiannual	--	\$1.75	

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