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In Search of Better Health

PRIMARY RESEARCH EVIDENCE BRIEF

Soil-Transmitted Helminths Elimination in Kenya: Using Mathematical Modelling to Guide Policy

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Key Messages

[1.] Reduction of STH burden and elimination period heavily depended on four parameter groups; drug efficacy, treatment rounds, proportion of individuals treated, and WASH coverage.

[2.] Control programmes implementing annual MDA alone, would take very long, about 15 years, to achieve STH elimination.

[3.] However, if the annual MDA is complemented with WASH (at high coverage of 95%), elimination would be reached within a shorter period of below 5 years.

[4.] Drug efficacy assessment for each STH species indicated that for *Trichuris trichiura* to be effectively eliminated, a highly efficacious drug (or drug combination) needs to be considered.

[5.] For STH control programme in Kenya to effectively eliminate STH, annual community-based treatment strategy coupled with prioritized, high coverage, WASH interventions need to be considered.

Context

Soil-transmitted helminths (STH) are part of a group of diseases categorized by the World Health Organization (WHO) as neglected tropical diseases (NTDs). The three main types of STH are *Ascaris lumbricoides* (roundworm), *Trichuris trichiura* (whipworm), and hookworms (*Necator americanus* and *Ancylostoma duodenale*) (WHO, 2012). STH are estimated to be endemic in about 166 countries, including Kenya, and affect more than 1.5 billion people globally (Pullan et al., 2014). In Kenya, over five million individuals, especially school going children, across over66 sub-counties are at-risk of STH (Okoyo et al., 2020). STH can be effectively controlled through mass drug administration (MDA) using any of the four WHO-recommended drugs; albendazole, mebendazole, levamisole, or pyrantel to all at-risk individuals either through school-based deworming (SBD) or community- based deworming (CBD) programmes. Additionally, improvements in water, sanitation and hygiene (WASH)related interventions are strongly recommended to accelerate the infection interruption and safely stop MDA without the risk of infection rebound (Okoyo et al., 2021).

Since the year 2012, Kenya has been implementing an annual MDA programme through the SBD platform targeting all school going children in 66 sub-counties identified as STH endemic. The aim of the programme was to reduce the national STH infection levels to where the infections are no longer a public health problem (defined by a prevalence of below 1% (Giardina et al., 2019)). After five years (2012-2017) of implementation, the programme has not achieved the target of reducing the infection levels to below 1%, mainly attributable to the following four key challenges: (i) Which age group(s) should be targeted for treatment? pre-school aged children (PSAC), school aged children (SAC), or adults, (ii) How often should treatment be delivered in each age group?, (iii) Can infection be eliminated using repeated treatment alone?, and (iv) Can elimination be achieved faster when contemporary interventions like WASH are incorporated?

In this evidence brief, we highlight the key outcomes of a robust mathematical modelling study conducted between 2019 and 2021 to help answer the above questions and inform on the right mix of strategies for the control of STH infections in Kenya. Specifically, the mathematical model was used to; (i) determine the single and combined impacts of MDA and WASH interventions on worm burden and elimination period, (ii) compare the impacts of the two interventions under various delivery plans and coverage, and (iii) predict the STH elimination period in Kenya. The results from this model are important since STH control programmes globally are targeting to eliminate the infection by the year 2030 (WHO, 2020).

Approach

The study formulated a three age-structured mathematical model for STH transmission specific to Kenyan context. The model fully incorporated the following; (i) categorization of the population into three complete age groups, (ii) comparison of the effects of two interventions (i.e., MDA and WASH), and (iii) dynamics of the infectious materials in the environment (i.e., STH egg or larvae). Modelling approach followed a four-dimensional system of ordinary differential equations (ODEs). The study developed three model scenarios; (i) no intervention assumed (model 1), (ii) only MDA intervention assumed (model 2), and (iii) both MDA and

WASH interventions assumed (model 3). The study calculated the infection equilibria and basic reproduction number from each of the three model scenarios. Additionally, the study determined the most sensitive (influential) parameters to the model outcomes (worm burden and elimination period) using the robust *extended Fourier Amplitude Sensitivity Test (eFAST)*, which is an efficient sensitivity analysis technique. The study model was validated using field research data collected by the Kenya National School-Based Deworming (KNSBD) programme and from community-based studies conducted by individual researchers.

Results

Ascaris lumbricoides

The model results indicated that elimination of *Ascaris lumbricoides* is possible at various MDA plans (Figure 1). With annual plan (panel A), elimination would be reached after a long period of about 15 years. With 6-monthly plan (panel B), elimination period would be reduced to eight years and endemic worm burden shortened by a third. With 3-monthly plan (panel C), elimination period would be shortened further to six years and endemic worm burden reduced by half. Therefore, if MDA alone is used as the mainstay elimination strategy for *Ascaris lumbricoides*, then a 3-monthly plan would be desirable to achieve a faster infection elimination.

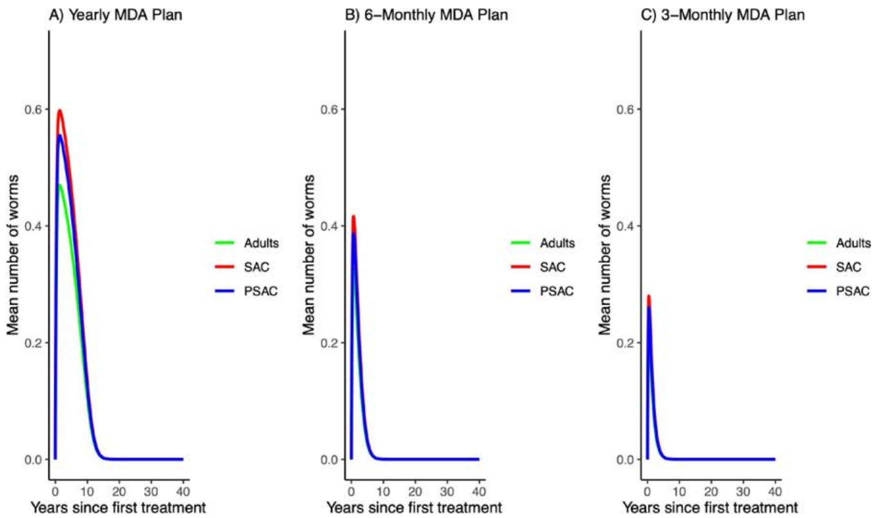

Figure 1: Model solution for Ascaris lumbricoides when various MDA plans are assumed as indicated in panels (A) to (C) i.e., tau = 1.0 for yearly plan, tau = 0.5 for 6-monthly plan and tau = 0.25 for 3-monthly plan. We assumed treatment coverage (g) of 75% for each host group and drug efficacy (h) of 80%. These assumptions followed the current WHO and NSBD guidelines (WHO, 2011)

Further, elimination of *Ascaris lumbricoides* would even be much faster if WASH intervention is implemented together with MDA (Figure 2). For instance, the impact of implementing an annual MDA complemented with WASH at various coverage levels is demonstrated in panels (A) to (E). From the figure, for STH control programme in Kenya to achieve a near-complete elimination of *Ascaris lumbricoides* within five years, an annual MDA plan complemented with 95% WASH coverage in the entire community would be most effective.

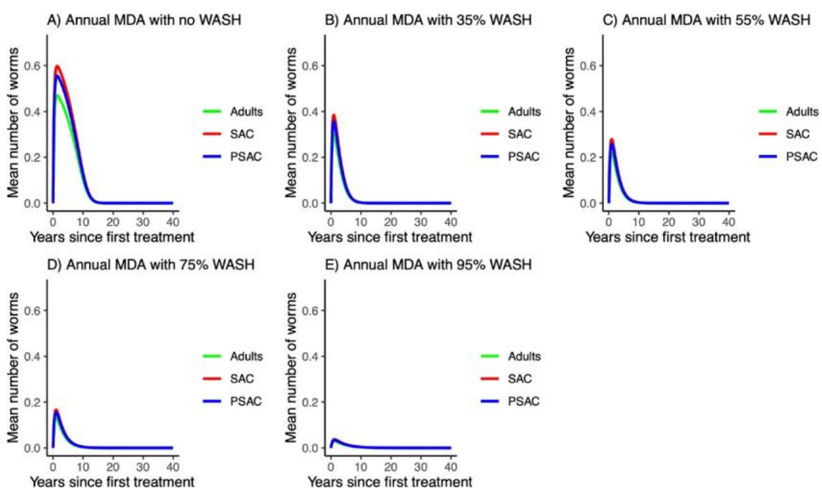

Figure 2: Model solution for Ascaris lumbricoides when annual MDA plan is complemented with WASH at various levels as indicated in panels (A) to (E) i.e., phi =0 for no WASH, phi = 0.35 for 35% WASH, phi = 0.55 for 55% WASH, phi = 0.75 for 75% WASH and phi = 0.95 for 95% WASH coverage. We assumed treatment coverage (g) of 75% for each host group and drug efficacy (h) of 80%. These assumptions followed the current WHO and NSBD guidelines (WHO, 2011)

Additionally, the model assessed all the parameters and determined those that were significantly influencing the elimination of *Ascaris lumbricoides*. From the analysis (Figure 3), WASH coverage (phi), worm mortality rate (mu), drug efficacy (h), environmental contamination rate by adults (lambdaa), proportion of adults reached with MDA (ga), strength of density dependence of worm egg production (gma), and the number of MDA rounds offered (tau) were found to be significantly influential in determining the elimination of *Ascaris lumbricoides*.

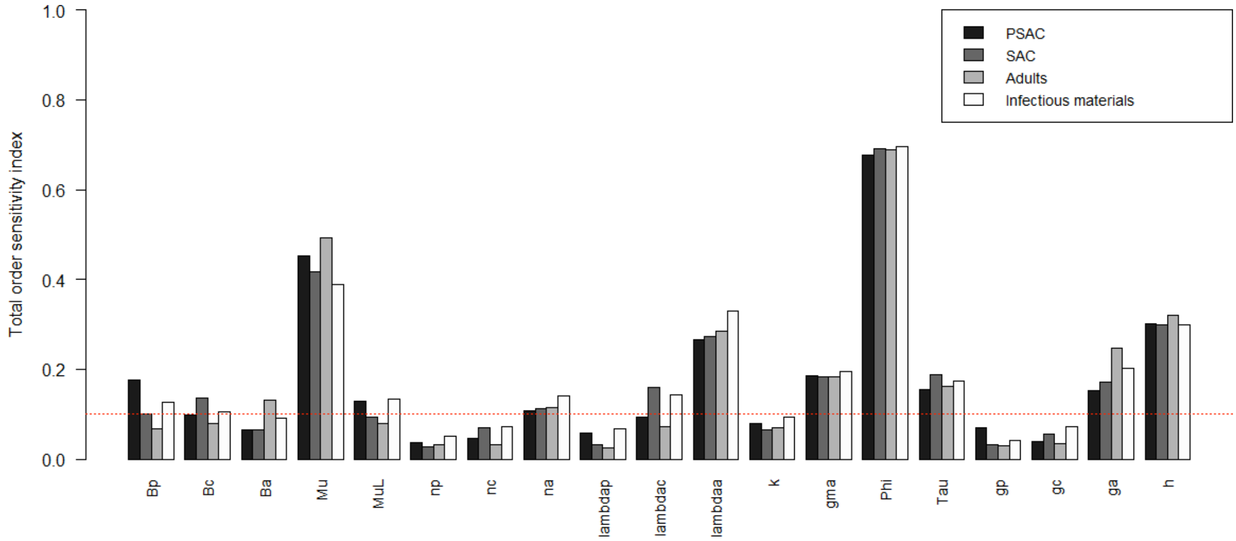

Figure 3: Comparison of the total-order sensitivity index of the parameters among the hosts using the eFAST method of sensitivity analysis for the case of Ascaris lumbricoides. The greater the sensitivity index, the more critical the parameter is to the model. The red dotted line indicated the cut-off sensitivity index value (SI=0.1) above which a parameter was deemed significantly influential to the model outcome. Bp: PSAC infection transmission rate, Bc: SAC infection transmission rate, Ba: adults infection transmission rate, Mu: mature worm mortality rate, MuL: infectious materials mortality rate, np: PSAC population proportion, nc: SAC population proportion, na: adults population proportion, lambdap: relative contributions by PSAC, lambdac: relative contributions by SAC, lambdaa: relative contributions by adults, k: over-dispersion parameter, gma: strength of density dependence of worm egg production, phi: WASH effect, Tau: interval between treatment rounds per year, gp: proportion of PSAC treated, gc: proportion of SAC treated, ga: proportion of adults treated, and h: drug efficacy

Hookworm

Similarly, the model analysis indicated that hookworm elimination was possible at various MDA plans (Figure 4). With annual plan (panel A), elimination would be reached within a short period of under five years. With 6-monthly and 3-monthly plans (panels B and C), elimination period as well as the endemic worm burden would be further reduced. Therefore, MDA alone (regardless of the three plans) was observed to be effective in eliminating hookworm within less than five years.

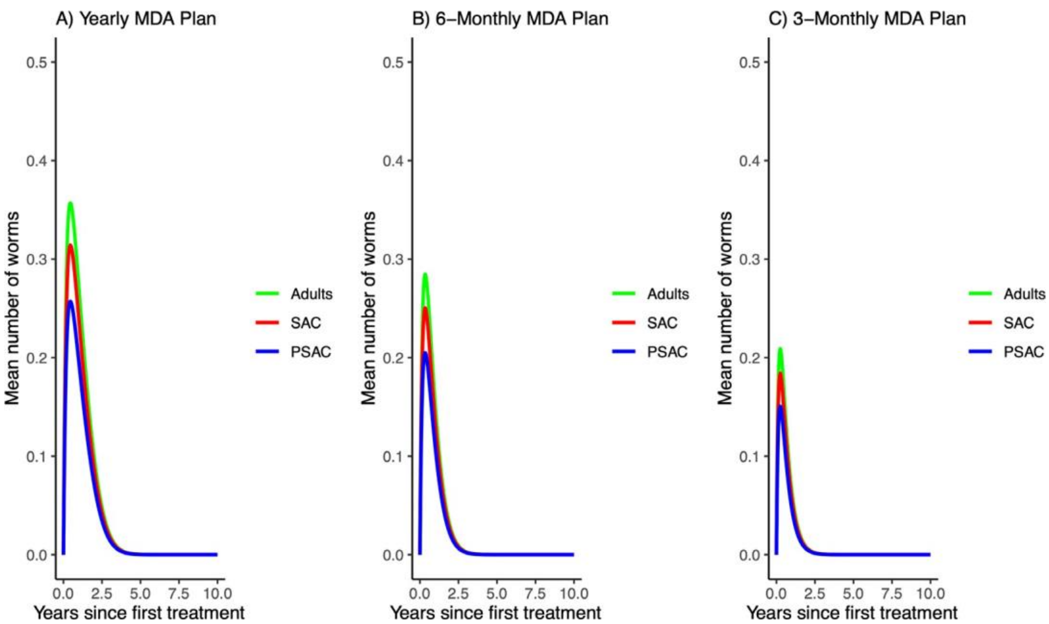

Figure 4: Model solution for hookworm when various MDA plans are assumed as indicated in panels (A) to (C) i.e., tau = 1.0 for yearly plan, tau = 0.5 for 6-monthly plan and tau = 0.25 for 3-monthly plan. We assumed treatment coverage (g) of 75% for each host group and drug efficacy (h) of 95%. These assumptions followed the current WHO and NSBD guidelines (WHO, 2011)

Further, elimination of hookworm would even be much faster if WASH intervention is implemented together with MDA (Figure 5). For instance, the impact of implementing an annual MDA plan when complemented with WASH at various coverage levels is demonstrated in panels (A) to (E). From the figure, for the STH control programme in Kenya to achieve a near-complete elimination of hookworm in under five years, an annual MDA plan complemented with 95% WASH coverage in the entire community would be most effective.

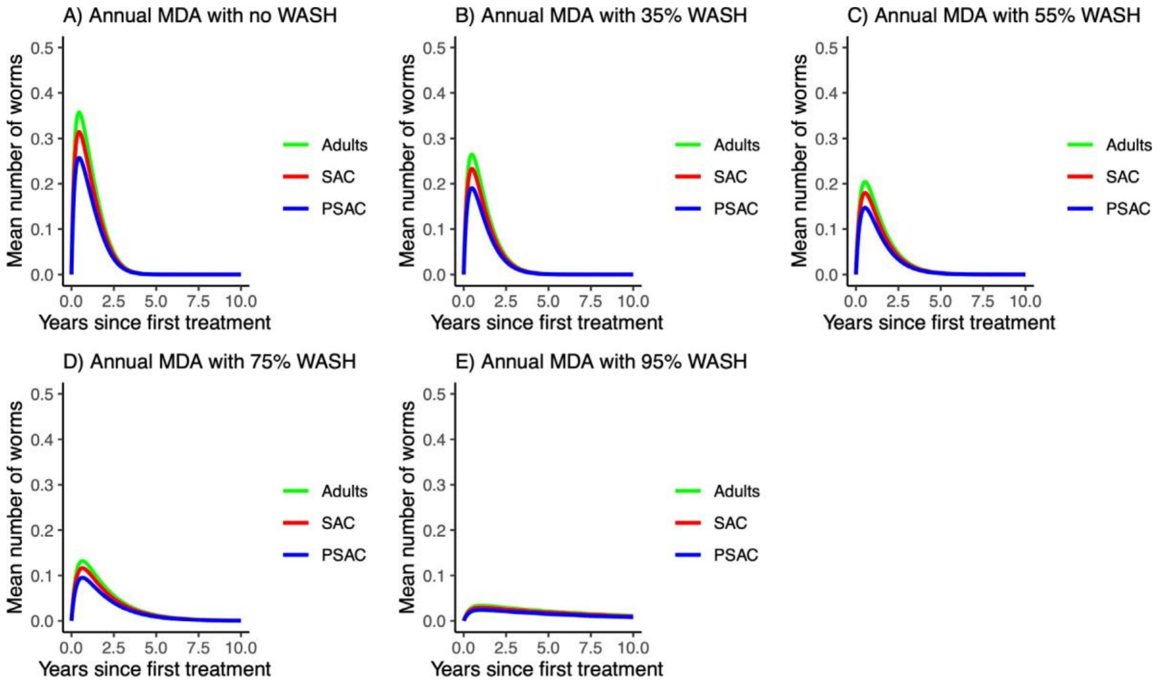

Figure 5: Model solution for hookworm when annual MDA plan is complemented with WASH at various levels as indicated in panels (A) to (E) i.e., phi = 0 for no WASH, phi = 0.35 for 35% WASH, phi = 0.55 for 55% WASH, phi = 0.75 for 75% WASH and phi = 0.95 for 95% WASH coverage. We assumed treatment coverage (g) of 75% for each host group and drug efficacy (h) of 95%. These assumptions followed the current WHO and NSBD guidelines (WHO, 2011)

Additionally, the model assessed all the parameters and determined those that were significantly influencing the elimination of hookworm. From the analysis (Figure 6), worm mortality rate (mu), WASH coverage (phi), environmental contamination rate by adults (lambdaa), drug efficacy (h), infection transmission rate by PSAC (Bp), strength of density dependence of worm egg production (gma), proportion of adults reached with MDA (ga), and the number of MDA rounds offered (tau) were found to be significantly influential in determining the elimination of hookworm.

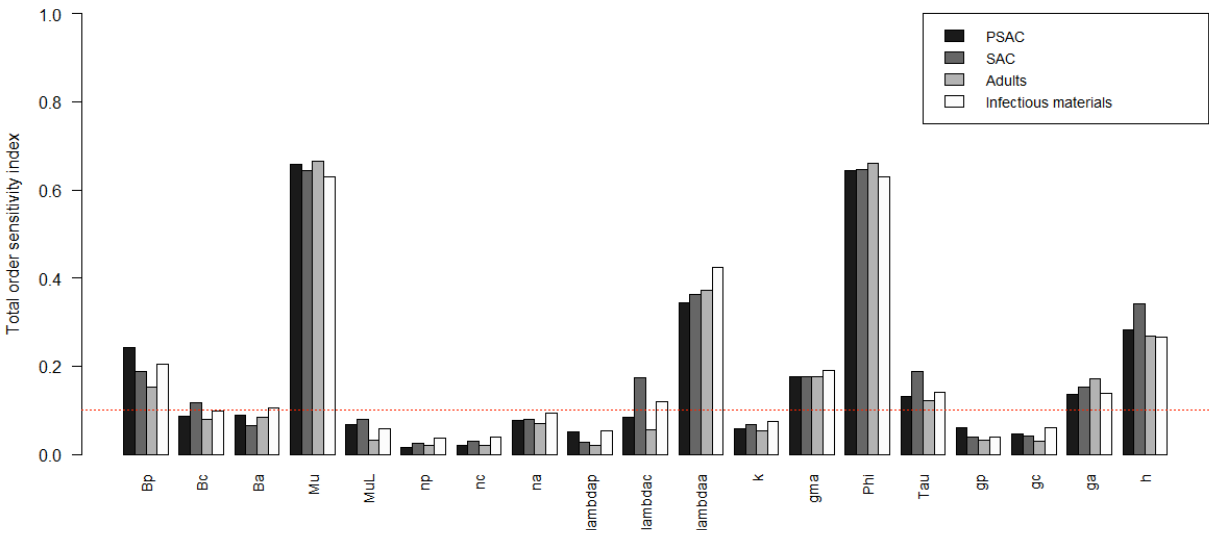

Figure 6: Comparison of the total-order sensitivity index of the parameters among the hosts using the eFAST method of sensitivity analysis for the case of hookworm. The greater the sensitivity index, the more critical the parameter is to the model. The red dotted line indicated the cut-off sensitivity index value (SI=0.1) above which a parameter was deemed significantly influential to the model outcome. Bp: PSAC infection transmission rate, Bc: SAC infection transmission rate, Ba: adults infection transmission rate, Mu: mature worm mortalityrate, MuL: infectious materials mortality rate, np: PSAC population proportion, nc: SAC population proportion, na: adults population proportion, lambdap: relative contributions by PSAC, lambdac: relative contributions by SAC, lambdaa: relative contributions by adults, k: over-dispersion parameter, gma: strength of density dependence of worm egg production, phi: WASH effect, Tau: interval between treatment rounds per year, gp: proportion of PSAC treated, gc: proportion of SAC treated, ga: proportion of adults treated, and h: drug efficacy

Trichuris trichiura

The impact of various MDA plans with varying drug efficacy on *Trichuris trichiura* is demonstrated using (Figure 7). Clearly, it can be seen that it will take longer than 10 years to eliminate *Trichuris trichiura* under any of the MDA plans compared to the other species. Specifically, the variation of the drug efficacy indicated that the higher the drug efficacy level the shorter the elimination period. Unlike the other species, we noted that MDA alone will note eliminate *Trichuris trichiura* in the short period (though it will suppress the worm burden), hence a higher efficacious drug or rather drug combination should be considered (Vercruysse et al., 2011).

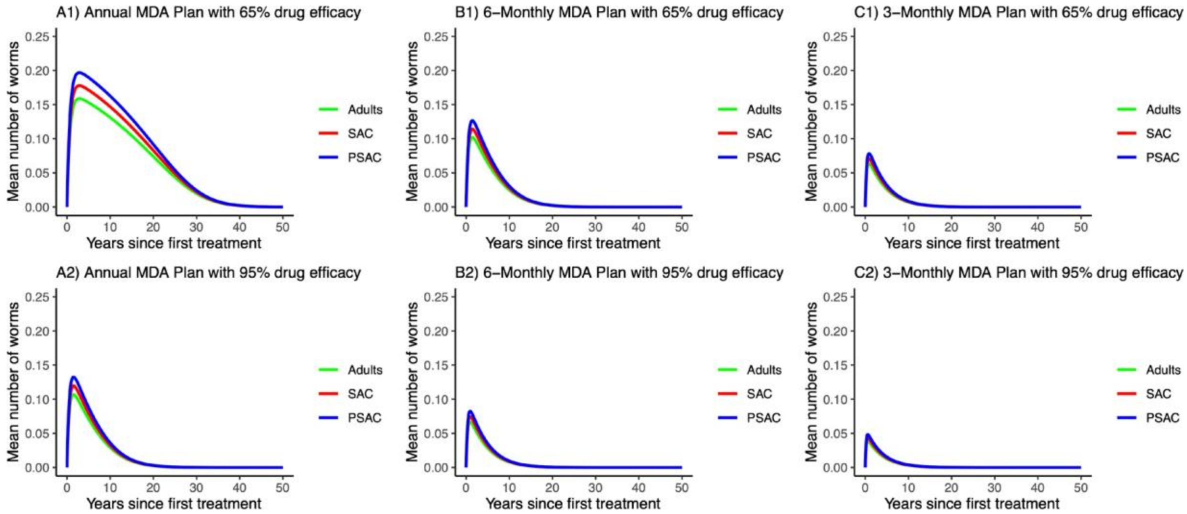

Figure 7: Model solution for Trichuris trichiura when various MDA plans are assumed as indicated in panels (A) to (C) i.e., tau = 1.0 for yearly plan, tau = 0.5 for 6-monthly plan and tau = 0.25 for 3-monthly plan. Additionally, for each MDA plan we varied the drug efficacy (h) as either 65% or 95%. We assumed treatment coverage (g) of 75% for each host group. These assumptions followed the current WHO and NSBD guidelines (WHO, 2011)

Similarly, the impact of complementing WASH with MDA on *Trichuris trichiura* is well illustrated in (Figure 8), panels (A) to (E). Just like with the other species, WASH at various coverage levels was shown to be very effective in reducing the elimination period and worm burden. WASH was observed to be most effective when administered at a high coverage level of 95%.

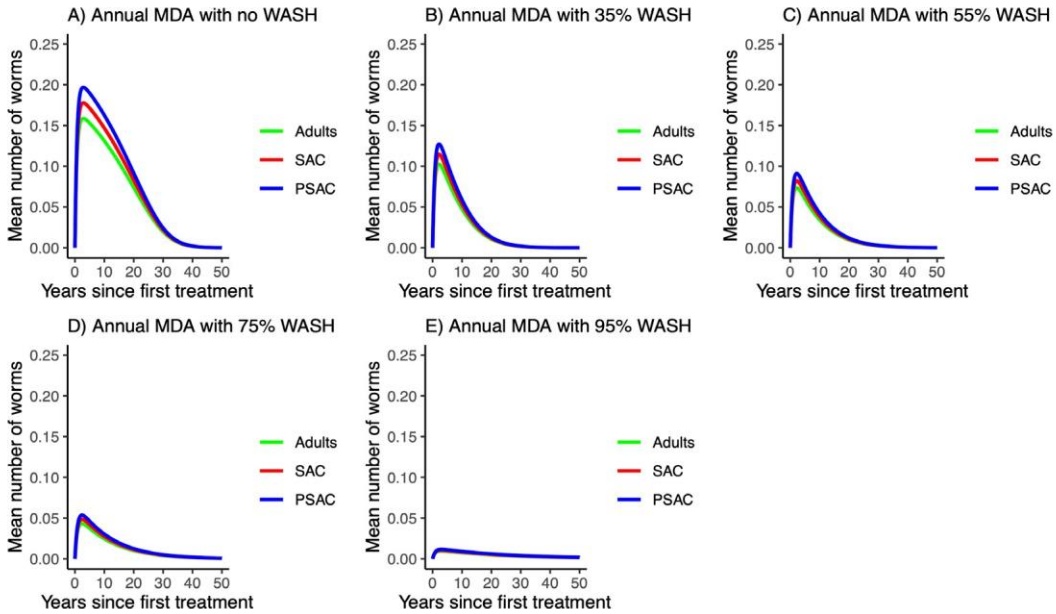

Figure 8: Model solution for Trichuris trichiura when annual MDA plan is complemented with WASH at various levels as indicated in panels (A) to (E) i.e., phi = 0 for no WASH, phi = 0.35 for 35% WASH, phi = 0.55 for 55% WASH, phi = 0.75 for 75% WASH and phi = 0.95 for 95% WASH coverage. Further, we assumed treatment coverage (g) of 75% for each host group and drug efficacy (h) of 65%. These assumptions followed the current WHO and NSBD guidelines (WHO, 2011)

Additionally, the model assessed all the parameters and determined those that were significantly influencing the elimination of *Trichuris trichiura*. From the analysis (Figure 9), WASH coverage (phi), drug efficacy (h), worm mortality rate (mu), environmental contamination rate by adults (lambdaa), proportion of adults reached with MDA (ga),the number of MDA rounds offered (tau), strength of density dependence of worm egg production (gma), and the adults population proportion (na) were found to be significantly influential in determining the elimination of *Trichuris trichiura*.

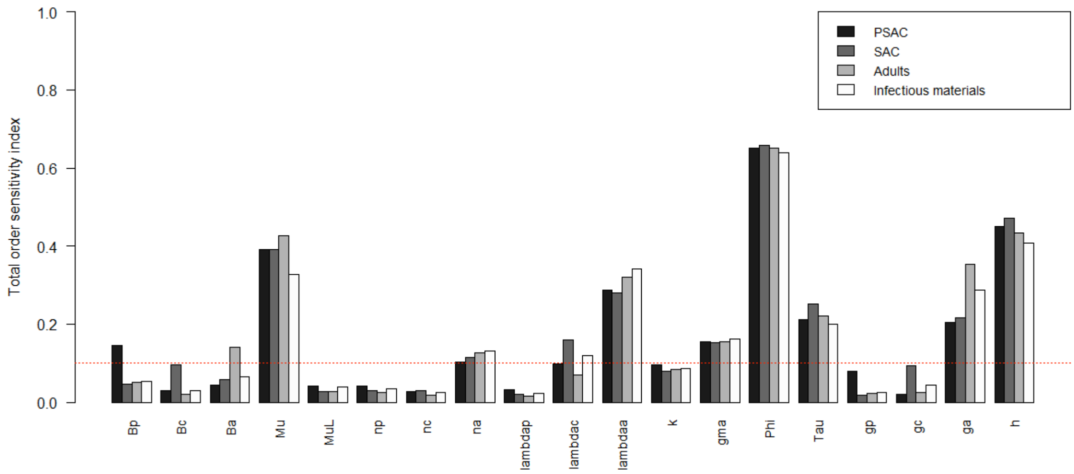

Figure 9: Comparison of the total-order sensitivity index of the parameters among the hosts using the eFAST method of sensitivity analysis for the case of Trichuris trichiura. The greater the sensitivity index, the more critical the parameter is to the model. The red dotted line indicated the cut-off sensitivity index value (SI=0.1) above which a parameter was deemed significantly influential to the model outcome. Bp: PSAC infection transmission rate, Bc: SAC infection transmission rate, Ba: adults infection transmission rate, Mu: mature worm mortalityrate, MuL: infectious materials mortality rate, np: PSAC population proportion, nc: SAC population proportion, na: adults population proportion, lambdap: relative contributions by PSAC, lambdac: relative contributions by SAC, lambdaa: relative contributions by adults, k: over-dispersion parameter, gma: strength of density dependence of worm egg production, phi: WASH effect, Tau: interval between treatment rounds per year, gp: proportion of PSAC treated, gc: proportion of SAC treated, ga: proportion of adults treated, and h: drug efficacy

Policy Recommendations

Short-term:

[1.] Shift from annual school-based to annual community-based deworming strategy.

[2.] Ensure the drug efficacy is at least 80% or consider using drug combination, this will enable the programme address the issue of *Trichuris trichiura*.

[3.] Ensure treatment coverage among all the community members is at least 80%.

Long-term:

[1.] Complement the annual community-based deworming with revamped WASH interventions at household and school levels.

[2.] Ensure the WASH coverage is at least 95% at both household and school levels.

Acknowledgments

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1) Modelling the interruption of the transmission of soil-transmitted helminths infections in Kenya: Modelling deworming, water, and sanitation impacts (https://doi.org/10.3389/fpubh.2021.637866),
2) Statistical regression model of water, sanitation, and hygiene; treatment coverage; and environmental influences on school-level soil-transmitted helminths and schistosome prevalence in Kenya: Secondary analysis of the national deworming program data (https://doi.org/10.4269/ajtmh.20-1189),
3) Prevalence and correlation analysis of soil-transmitted helminths infections and treatment coverage for preschool and schoolaged children in Kenya: Secondary analysis of the national school-based deworming program data (https://doi.org/10.3389/fpubh.2021.645522), and
4) Sensitivity analysis of a transmission interruption model for the soil-transmitted helminth infections in Kenya (https://doi.org/10.3389/fpubh.2022.841883).

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