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Modeling the Economic and Epidemiologic Impact of Hookworm Vaccine and Mass Drug Administration (MDA) in Brazil, a High Transmission Setting

Sarah M. Bartsch, MPH[a,b], **Peter J. Hotez, MD, PhD**[c,d], **Daniel L. Hertenstein**[a,b], **David J. Diemert, MD**[d,e], **Kristina M. Zapf, MPH**[a,b], **Maria Elena Bottazzi, PhD**[c,d], **Jeffrey M. Bethony, PhD**[d,e], **Shawn T. Brown, PhD**[f], and **Bruce Y. Lee, MD, MBA**[a,b]

[a]Public Health Computational and Operational Research (PHICOR), Johns Hopkins Bloomberg School of Public Health, 615 N Wolfe Street, Baltimore, MD 21205 USA

[b]Global Obesity Prevention Center, Johns Hopkins Bloomberg School of Public Health, 615 N Wolfe Street, Baltimore, MD 21205 USA

[c]National School of Tropical Medicine, and Departments of Pediatrics and Molecular Virology & Microbiology, Baylor College of Medicine, One Baylor Plaza, BCM113, Houston, TX 77030, USA

[d]Sabin Vaccine Institute, 2000 Pennsylvania Avenue NW, Washington, DC 20006, USA

[e]Department of Microbiology, Immunology and Tropical Medicine, The George Washington University Medical Center, Washington, DC 20037, USA

[f]Pittsburgh Supercomputing Center, Carnegie Mellon University, 300 S Craig St, Pittsburgh, PA 15213, USA

Abstract

Background—Although mass drug administration (MDA) has helped reduce morbidity attributed to soil-transmitted helminth infections in children, its limitations for hookworm infection have motivated the development of a human hookworm vaccine to both improve morbidity control and ultimately help block hookworm transmission leading to elimination. However, the potential economic and epidemiologic impact of a preventive vaccine has not been fully evaluated.

Methods—We developed a dynamic compartment model coupled to a clinical and economics outcomes model representing both the human and hookworm populations in a high transmission region of Brazil. Experiments simulated different implementation scenarios of MDA and vaccination under varying circumstances.

Corresponding Author: Bruce Y. Lee, MD MBA, Associate Professor of International Health, Director of the Global Obesity Prevention Center (GOPC), Director of Operations Research, International Vaccine Access Center (IVAC), Johns Hopkins Bloomberg School of Public Health, 615 N. Wolfe Street, Room W3501, Baltimore, MD 21205, brucelee@jhu.edu, Phone: 410-502-6079.

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Results—Considering only intervention costs, both annual MDA and vaccination were highly cost-effective (ICERs ≤$790/DALY averted) compared to no intervention, with vaccination resulting in lower incremental cost-effectiveness ratios (ICERs ≤$444/DALY averted). From the societal perspective, vaccination was economically dominant (i.e., less costly and more effective) than annual MDA in all tested scenarios, except when vaccination was less efficacious (20% efficacy, 5 year duration) and MDA coverage was 75%. Increasing the vaccine's duration of protection and efficacy, and including a booster injection in adulthood all increased the benefits of vaccination (i.e., resulted in lower hookworm prevalence, averted more disability-adjusted life years, and saved more costs). Assuming its target product profile, a pediatric hookworm vaccine drastically decreased hookworm prevalence in children to 14.6% after 20 years, compared to 57.2% with no intervention and 54.1% with MDA. The addition of a booster in adulthood further reduced the overall prevalence from 68.0% to 36.0%, nearly eliminated hookworm infection in children.

Conclusion—Using a human hookworm vaccine would be cost-effective and in many cases economically dominant, providing both health benefits and cost-savings. It could become a key technology in effecting control and elimination efforts for hookworm globally.

Keywords

hookworm; transmission; vaccine; drug treatment; economics; cost

Introduction

Human hookworm infection is a major cause of anemia and malnutrition, affecting almost 500 million people in low- and middle-income countries[1]. Unlike other soil-transmitted helminth (STH) infections (e.g., ascariasis and trichuriasis), high intensity hookworm infection commonly affects both children and adults. Although mass drug administration (MDA) programs have successfully reduced morbidity due to STHs among children, it is not having a similar effect on hookworm. In fact, MDA with mebendazole is not reducing the prevalence of hookworm-related anemia[2], while the impact of MDA with albendazole in children is inconsistent[3, 4]. Moreover, while MDA is having a large impact on reducing the prevalence of ascariasis, the Global Burden of Disease Study 2013 estimates that MDA is not having a significant effect in reducing in the prevalence of hookworm infection[1]. MDA's existing limitations have motivated the search for additional measures to reduce hookworm transmission and prevalence, such as a preventive human hookworm vaccine[5-8]. The World Health Organization (WHO) reports that <35% of school-age children living in areas identified as required for MDA coverage actually received mass chemotherapy in 2013[9]. Even when MDA programs are in place they primarily target pre-school and school-aged children[10, 11], leaving high-burden groups untreated, resulting in a marginal impact on hookworm transmission[8, 12, 13]. In response, some experts have suggested exploring community-wide MDA programs that target both children and adults[14, 15]. However, as highlighted above, existing anti-helminthics exhibit highly variable effectiveness[16], high failure rates[17], diminished efficacy following repeated use[18], provide no protection against reinfection, and require frequent and repeated administration to maintain disease control.

A human hookworm vaccine could potentially overcome some of MDA's limitations by preventing reinfection and interrupting parasite transmission. The recombinant antigens *Na*-GST-1 and *Na*-APR-1 from the adult stage of the human hookworm *Necator americanus* are currently in Phase I clinical testing in the United States, Brazil, and Gabon[19]. The clinical development plan for this vaccine calls for these two antigens to eventually be combined into a single human hookworm vaccine product. To date, these candidate hookworm vaccine antigens have been shown to be safe and immunogenic when administered separately or when co-administered to healthy adults.

In light of this progress in vaccine development, this is an ideal time to characterize and quantify the potential benefit of a human hookworm vaccine. A key component of the human hookworm vaccine global access strategy includes studies to inform immunization program managers and global health policymakers on the potential use and benefits of a hookworm vaccine, including its potential health impact and cost-effectiveness. An individual-based modeling study found vaccination plus MDA to be a more cost-effective control strategy than MDA alone[20]; however, this study did not account for the potential transmission-blocking effects of either control measure. Therefore, there is a need to further explore the economic impact of such effects. We developed a human hookworm transmission model coupled to a clinical and economics outcome model to evaluate the potential economic (e.g., cost-effectiveness) and epidemiologic benefits of a vaccine in a representative endemic setting.

Methods

We developed a compartment model in Python (Python Software Foundation, Wilmington, DE) representing both the human and hookworm populations in Brazil and the resulting transmission dynamics, coupled with a clinical and economic model in Microsoft Excel (Microsoft, Redmond, WA) to translate hookworm infections into health outcomes and corresponding costs and health effects. A number of previous hookworm models [21-28] focused on hookworm populations themselves, simulating changes in the mean worm burden in the human population and changes in the worm populations in the environment, not representing infection in individual persons. Those that evaluate interventions, such as MDA, model them as the proportion of parasites targeted or impacted. Since this study focused on evaluating the impact of MDA and vaccination on individuals and infections within persons, we developed a compartment model that included detailed representations of both the human and hookworm populations. Table 1 presents key parameter values and sources for the models. The appendix provides details of both models.

Dynamic Hookworm and Human Populations Model

Appendix Figure 1 outlines the model structure. This model represents each member of the hookworm and human populations. Each member of the free-living hookworm population fell into one of two mutually exclusive compartments: Dormant Eggs and Larvae (DL, eggs that were excreted into the environment via infected feces) and Infectious (L3) Larvae (IL, third-stage larvae that could infect a human host by skin penetration). The human population (N=30,000) consisted of two age groups, children (0-14 years) and adults (≥15 years). Each

person started in one of four mutually exclusive compartments: Susceptible (S, individuals without hookworm infection); Exposed (E, individuals who are infected but are not yet excreting eggs in their feces); Infectious (I, individuals harboring adult worms and capable of excreting eggs into the environment); and Resistant (R, individuals who do not come into contact with hookworm in the environment[12] or have innate host factors that do not allow for hookworm establishment or are predisposed to have no infection[29]). Thus, hookworm infection refers to those harboring 2 or more adult worms and able to excrete eggs. The model proceeds in one-day time steps for 20 simulated years. Each day, members of both the hookworm and human populations could move between compartments, based on an individual's intensity of infection and the number of eggs excreted into the environment. In the absence of any intervention, the model is at endemic equilibrium (i.e., hookworm prevalence is stable), where prevalence refers to the proportion of the population who harbor enough worms to produce eggs.

Interventions: MDA and Vaccination

We modeled two interventions to control hookworm: annual MDA and vaccination of infants (9-12 months). MDA was administered to school-aged children (5-14 years old) annually, and the cure rate of MDA determined the number of infectious children clearing infection (i.e., moving from the I to S compartment), with no protection provided against reinfection. This represents those children who are completely cured of infection (i.e., no eggs are excreted and considered helminth egg negative). Those children that receive MDA but do not undergo clearance (i.e., those that still excrete eggs, but show a reduction in egg output) experience a reduction in their intensity of infection (which results in egg reduction) as a dynamic result of MDA decreasing prevalence and mean worm burden.

The modeled vaccine resembles the one currently under development[30] and contains antigens that target the mature adult stage of the hookworm's life cycle in the human host. It's presumed mechanism of protection is to induce antibodies that interfere with adult parasite blood feeding within the host intestine, thereby ultimately reducing the average worm burden (by reducing worm survival) and egg excretion in the community[31]. It does not prevent infection altogether, but rather the likelihood that a newly infected individual will become infectious (i.e., that larvae will survive to become mature adult worms). Thus, we modeled the vaccine to decrease the likelihood that invading L3 larvae develop into mature adults (i.e., prevents new worms from establishing in the host) and to increase the likelihood that a proportion of mature worms present at vaccination are killed. Once effectively vaccinated, susceptible and exposed persons moved to the vaccinated compartment (V), where they could encounter worms in the environment, but not develop infection. Vaccinated infected persons could move to the S or V compartment, based on the vaccine efficacy for each effect (i.e., moved to V if all worms were killed and establishment of new patent infections was prevented, or S if the killing effect was higher than the maturity effect).

Clinical and Economic Model

Our clinical and economics model translated hookworm infections from the transmission model into health outcomes (i.e., anemia and cognitive impairment) and corresponding costs

from the societal perspective (intervention plus productivity losses). The number of children and adults with hookworm infections from the transmission model fed into the economic model, as well as the number of children receiving MDA each year and the number of vaccinated persons. Our model measured health effects in disability-adjusted life years (DALYs) and calculated intervention and hookworm-related costs. We considered the direct healthcare costs of hookworm-associated anemia to be negligible and assumed anemia and cognitive impairment only resulted in indirect costs due to reduced productivity. Our model determined the incremental cost-effectiveness ratio (ICER) for each scenario. All costs are presented in 2015 values. Further details are found in the Appendix.

Modeled Scenarios

We modeled scenarios of no intervention, MDA for school-aged children, and vaccination of infants with an available booster in adulthood. Baseline MDA scenarios assumed the use of albendazole (with an economic cost of $0.50 per treated child in school-based programs[14, 32-35]) and a coverage rate of 56.2% of school-aged children, following the current reported rate in Brazil[36]. The baseline vaccination scenario assumed the criteria described in the human hookworm vaccine's target product profile (TPP)[37]. Infants (9-12 months of age) were considered susceptible and were vaccinated at the same time as other EPI vaccines given at this age; we assumed coverage of 97%, the same rate in Brazil as for the measles vaccine administered at this age. The modeled vaccine had an efficacy of 80% in preventing the maturation of L3 larvae and with a 10 year duration of protection. The booster dose administered in adulthood (i.e., 15 years of age), when given, had a 80% efficacy in preventing L3 maturation, 80% killing effect, 10 year duration of action, and 78% coverage rate (infant coverage with 20% loss to follow-up). Thus, the vaccine efficacy of killing worms is not applied in the infant model (as all persons are born susceptible and are assumed to remain as such at the time of vaccination), but applies to scenarios in which a booster is given when entering adulthood. We assumed a baseline vaccination cost of $1 per dose and 100% compliance with a two-dose regimen.

Sensitivity analysis varied key parameters in the model. We varied vaccine efficacy (20% to 80%), duration of protection (5 to 20 years), vaccination coverage of infants (75% to 97%), probability of getting a booster in adulthood (60% to 78%), MDA coverage of school-aged children (56.2% to 75%, following the WHO's 2020 coverage goal[38]), the cost of MDA per child treated ($0.21[34] to $0.79[35]), and the vaccination cost per dose ($0.50 to $2). Additional sensitivity analysis varied the disability weights utilized from the Global Burden of Disease 2004 to 2010 estimates (Table 1). Scenarios were run with and without the administration of the booster dose in adulthood.

Results

Considering only intervention costs, compared to no intervention, both MDA and vaccination were highly cost-effective (ICERs ≤$790/DALY averted) at all costs, coverages rates, vaccine efficacies, and DW estimates tested, with vaccination resulting in lower ICER values (ICERs ≤$444/DALY averted), even at a cost of $2 per dose of vaccine. From the societal perspective, MDA and all vaccination scenarios tested were economically dominant

(i.e., saved costs and averted more DALYs) than the no intervention scenario. Compared to annual MDA, almost all vaccination scenarios were dominant from the societal perspective for all costs per dose tested, regardless of MDA cost, MDA coverage rate, and DW estimate used. Only a vaccine with a 20% efficacy and 5 year duration was dominated (i.e., more costly and less effective) by annual MDA (75% coverage) when MDA cost ≤$0.50 per child treated and vaccination cost $0.50 per dose and when MDA cost ≥$0.21 per child treated and vaccination cost ≥$1 and only when using 2010 DW estimates (these scenarios were cost-effective or dominant when using 2004 DW estimates). Figure 1 plots the costs (y-axis) versus DALYs accrued (x-axis) for all MDA scenarios, vaccination following the vaccine's TPP (with and without an adult booster), and vaccination with a less efficacious vaccine. Increasing the cost of MDA increased the cost-effectiveness of vaccination strategies (i.e., decreased ICER values). The distance between two points on the y-axis is the difference in cost and the difference in the x-axis is the difference in DALYs accrued, thus the slope between them represents the ICER value. Therefore, interventions lower on the y-axis and further to the left on the x-axis are better than the ones to the right and above it. Even a less efficacious vaccine (e.g., 50% efficacy and 5 year duration, 20% efficacy and 10 year duration) was more cost-effective than a robust MDA program (75% coverage). Table 2 shows the economic results for all three modeled strategies.

Vaccination had the largest impact on the prevalence among children. Figure 2 shows the prevalence of hookworm over time in children (2a), adults (2b), and the total population (2c) with no intervention, annual MDA (baseline assumptions), and infant vaccination with a vaccine that meets the current vaccine's TPP (i.e., vaccine efficacy 80%, 10 year protection duration, 97% coverage, and no booster). While the prevalence in children decreased drastically to 16.2% at year 10 and 14.6% at year 20, there was no impact on the prevalence among adults during the 20 simulated years. At year 20, there were 1,097 hookworm infections among 7,500 children (all light intensity infections) with vaccination, compared to 4,060 with annual MDA, and 4,287 with no intervention. Figure 3 shows similar plots, but for a less efficacious (50%), shorter duration of protection (5 year) vaccine. This vaccine resulted in 3,170 hookworm infections in children at year 20 (97% light intensity infections). Appendix Figures 2 and 3 show the corresponding plots for the mean worm burden.

Figure 4 shows the impact of varying various vaccine characteristics on hookworm prevalence under infant vaccination scenarios. Increasing the protection duration resulted in prevalence changes in adults around year 15, when vaccinated children begin to age into adulthood (Figure 4a). Likewise, introducing a booster (78% coverage) led to reductions in adult prevalence (Figure 4b). Figure 4c shows the minimum and maximum value of infant vaccination with a booster in adulthood. Using a vaccine with a higher efficacy and protection duration can achieve more benefits. By year 20, the total population prevalence was reduced to 36.0%; lower than what could be achieved in children alone with a less efficacious vaccine with a shorter duration of action. Moreover, the prevalence among children was reduced to nearly zero.

Discussion

With a human hookworm vaccine currently in clinical trials, the time is right for economic evaluations, which can help guide and refine development, provide support for development, and inform potential plans for implementation, while there is still opportunity to make necessary adjustments. Once a vaccine reaches the market, there is less flexibility in making changes in the vaccine design or the implementation plans[39]. Moreover, economic evaluations during development can also help guide support for development, which ultimately may affect the vaccine's chances of reaching the market[39, 40].

Our study found that a human hookworm vaccine would be highly cost-effective and even economically dominant (saving costs while averting DALYs) compared to no intervention or annual MDA use. Compared to MDA, a vaccine meeting the requirements of the current TPP could save as much as $596,000 (2004 DW estimates) to $1,100,000 (2010 DW estimates) in societal costs among the modeled population of 30,000 persons in Brazil while costing ~$1,700 more for a $1 per dose, two-dose vaccination. For the same population, vaccination resulted in savings up to $18.5 million with a booster administered in adulthood ($0.50 per dose, 20 year duration of protection). Relative reductions in total population prevalence with vaccination ranged from 1.0% to 46.7% at year 20, compared to annual MDA use with 56.2% coverage. A vaccine would potentially be effective in other high prevalence areas (e.g., India[41], Nigeria[42], and Lao People's Democratic Republic[43]).

Our study does not suggest that a vaccine would obviate the need for MDA, which has been a very important intervention for hookworm control. Evidence shows that MDA decreases the intensity of infection and reduces transmission in endemic areas, especially over time in school-aged children receiving MDA[44]. There is also evidence to suggest that these benefits of MDA can subsequently reduce morbidity[44]. Additionally, some studies have shown increases in school attendance with anthelminthic treatment[45, 46] and MDA had been found to be a cost-effective intervention for STH infections[14, 47].

However, as already stated, the impact of MDA on hookworm has been inconsistent[2, 14, 15]. Since 1990, the worldwide prevalence of hookworm infection has been reduced only 5% through MDA[1]. Additionally, as high intensity hookworm infections occur in both children and adults, administering MDA to children, even with a highly effective drug, would not be expected to have an impact on transmission as adults with hookworm release large numbers of eggs into the environment. In effect, increased coverage of children with MDA has not led to elimination of hookworm. A recent modeling study estimates that to eliminate STHs from endemic areas, high levels of coverage will be needed and the target population receiving MDA must be expanded[21].

MDA has limitations that an effective vaccine could overcome. That vaccination could result in comparable or lower prevalence reductions compared to MDA is an important finding, as decreasing the frequency of MDA administration could reduce the need for additional community health workers to deliver MDA on an annual or semi-annual basis, especially in many areas of Africa where hookworm prevalence is much higher than the other STH infections[48]. Moreover, it could alleviate selection pressure on hookworm populations that

may result from repeated drug treatment and thereby reduce the likelihood of emergence of drug resistance. Alarming trends in decreased drug efficacy with repeated use of benzimidazole anthelminthics have been demonstrated in some locations[18], and multi-dose regimens are now often needed in other locations[49]. These suggest that interventions able to reduce MDA frequency while maintaining control of parasite transmission would be quite valuable. It should be noted that the value of vaccination can change with the impact and use of MDA. MDA use in Brazil is highly variable, with national coverage rates of school-aged children of 0.96% in 2009, 0% in 2010 and 2011, 0.24% in 2012, 33.2% in 2013, and 56.22% in 2015[36]. When MDA coverage is low, the value of vaccination will increase.

A recombinant human hookworm vaccine is currently under development and in clinical trials[30]. The development plan is to produce a vaccine product that contains two recombinant antigens known as *Na*-GST-1[50] and *Na*-APR-1[51, 52] formulated on aluminum hydroxide adjuvant. Each antigen is undergoing separate testing in Phase 1 trials prior to combining them and evaluating the vaccine for its efficacy to prevent hookworm infection. The vaccine targets *Necator americanus*, the most common human hookworm worldwide. The vaccine targets the establishment and blood feeding of adult hookworms in the human gastrointestinal tract. The current TPP calls for a vaccine that prevents moderate and heavy hookworm infections in children who are at risk of hookworm anemia and malnutrition. The major strength of such a vaccine is that it would interfere with the major cause of morbidity linked to infection, although it is not expected to necessarily elicit sterilizing immunity.

We attempted to be conservative in estimating the value of vaccination and did not capture some additional potential benefits of vaccination. For example, we did not include potential vaccine effects on reducing egg output of worms that do manage to establish in vaccinated individuals. We calculated annual DALYs (vs. lifetime DALYs, which may be accrued for cognitive impairment); thus, vaccination may avert the loss of additional DALYs by reducing the number of moderate and heavy intensity infections. We also did not consider the potential development of anthelminthic drug resistance over time. Additionally, we only evaluated vaccination of infants with a possible booster in adulthood. Vaccinating other target populations may have additional benefits and further reduce the burden of hookworm. Last, we chose to focus on hookworm in a high transmission setting, whereas vaccination may have a different impact in areas of low transmission. Our future work intends to evaluate vaccination in such areas. Likewise, we were conservative in estimating the value of MDA, as we assumed a constant coverage rate overtime, assumed the impact was immediate, and did not consider drug resistance.

Models are simplified representations of reality and are unable to account for all complexities that exist in nature[53]. Our model assumes that individuals mix homogeneously. Input data for both models come from studies of varying quality and our results can be refined as new data emerges. We divided the population into children and adults, however transmission patterns may be different between younger and older children. We assumed a consistent coverage level for MDA, which may change over time. Additionally, we assumed the impact of vaccination was immediate (e.g., no lag time

between vaccination and its effects taking place) and that vaccine efficacy did not wane over time. We also considered disability from cognitive impairment (when utilizing the 2004 disability weight estimates) and while chronic hookworm infection can lead to cognitive impairment[54-58], there is come controversy and uncertainty regarding the amount of cognitive impairment caused by hookworm.

Conclusion

The use of an effective human hookworm vaccine in endemic areas would be cost-effective and in many cases economically dominant, providing both health benefits and cost-savings, over a wide range of vaccine characteristics. Vaccination provided additional benefits above those that could be garnered with MDA, even with shorter duration vaccine with a lower efficacy. It could also become a key technology in effecting control and elimination efforts for hookworm globally.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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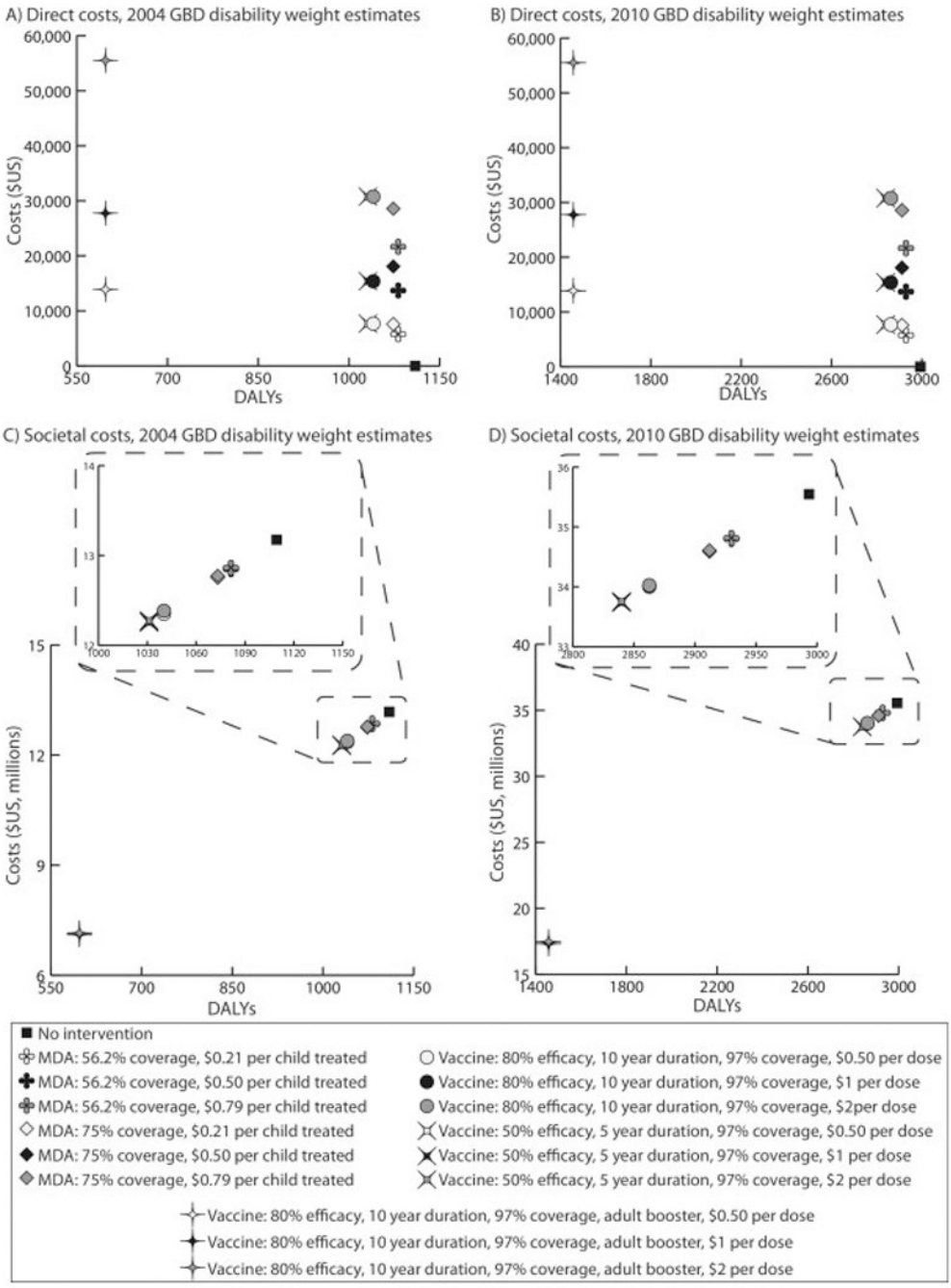

Figure 1.

Cost-effectiveness planes for all MDA scenarios and select vaccination scenarios [infant vaccination with a vaccine having an efficacy of 80%, 10 year duration of protection, 97% coverage rate, and no booster (i.e., the TPP of the vaccine currently in development), the same vaccine with a booster in adulthood; and infant vaccination with a vaccine having an efficacy of 50%, 5 year duration of protection, 97% coverage rate, and no booster] for a) direct costs and 2004 disability weight estimates, b) direct costs and 2010 disability weight estimates, c) societal costs and 2004 disability weight estimates, and d) societal costs and

2010 disability weight estimates. Costs are on the y-axis, DALYs accrued on the x-axis, with the difference between two points on these axes representing the difference in costs and DALYs; the slope represents the incremental cost-effectiveness value.

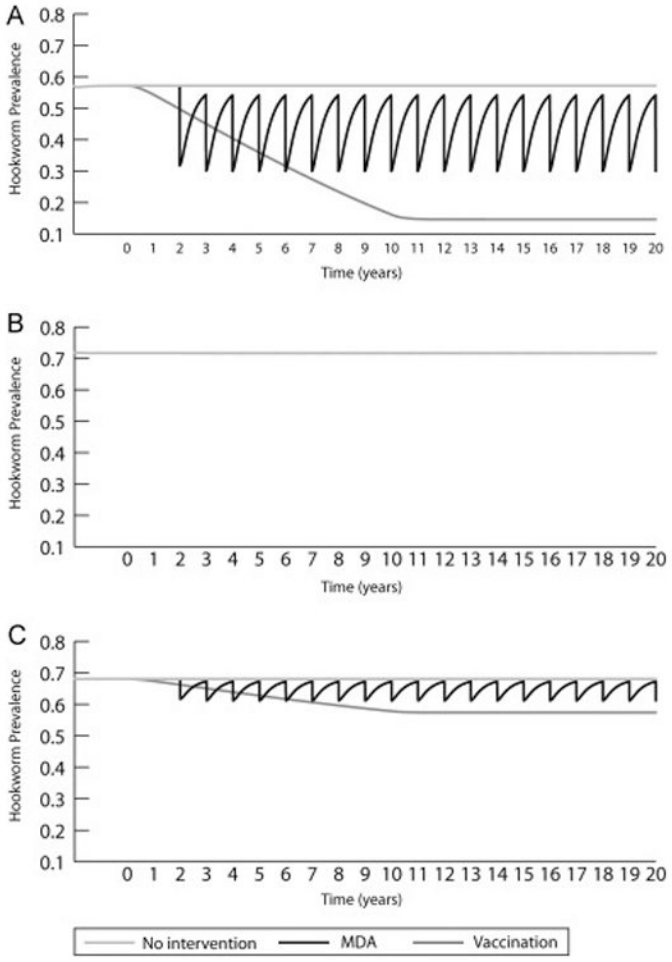

Figure 2.

Hookworm prevalence over 20 simulated years in: a) children, b) adults, and c) the total population with no intervention, annual MDA for school-aged children (56.2% coverage), and infant vaccination with a vaccine having an efficacy of 80%, 10 year duration of protection, 97% coverage rate, and no booster (i.e., the TPP of the vaccine currently in development).

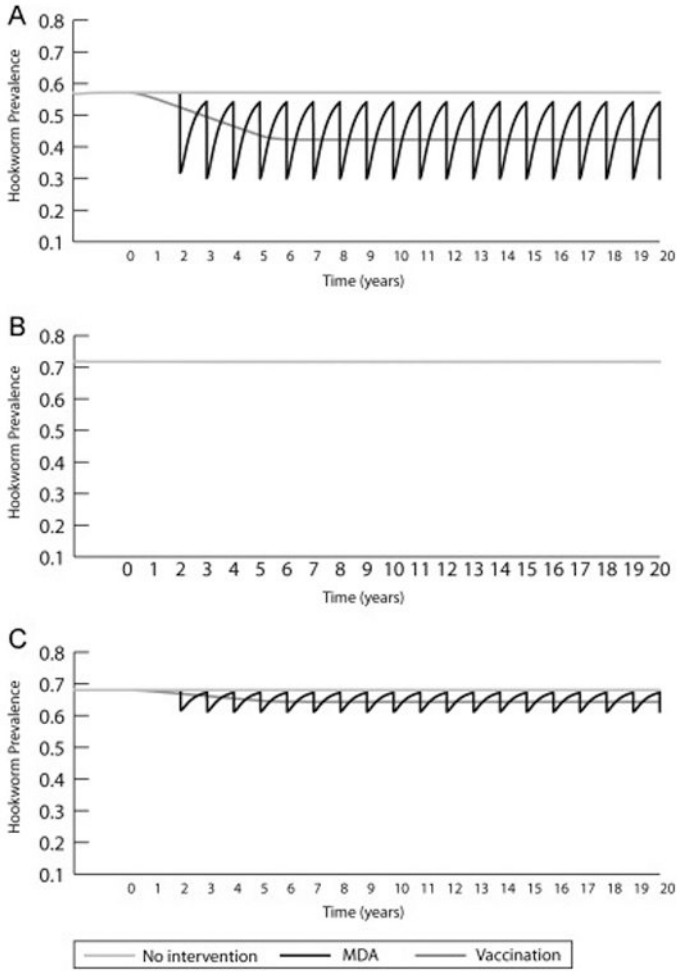

Figure 3.

Hookworm prevalence over 20 simulated years in: a) children, b) adults, and c) the total population with no intervention, annual MDA for school-aged children (56.2% coverage), and infant vaccination with a vaccine having an efficacy of 50%, 5 year duration of protection, 97% coverage rate, and no booster.

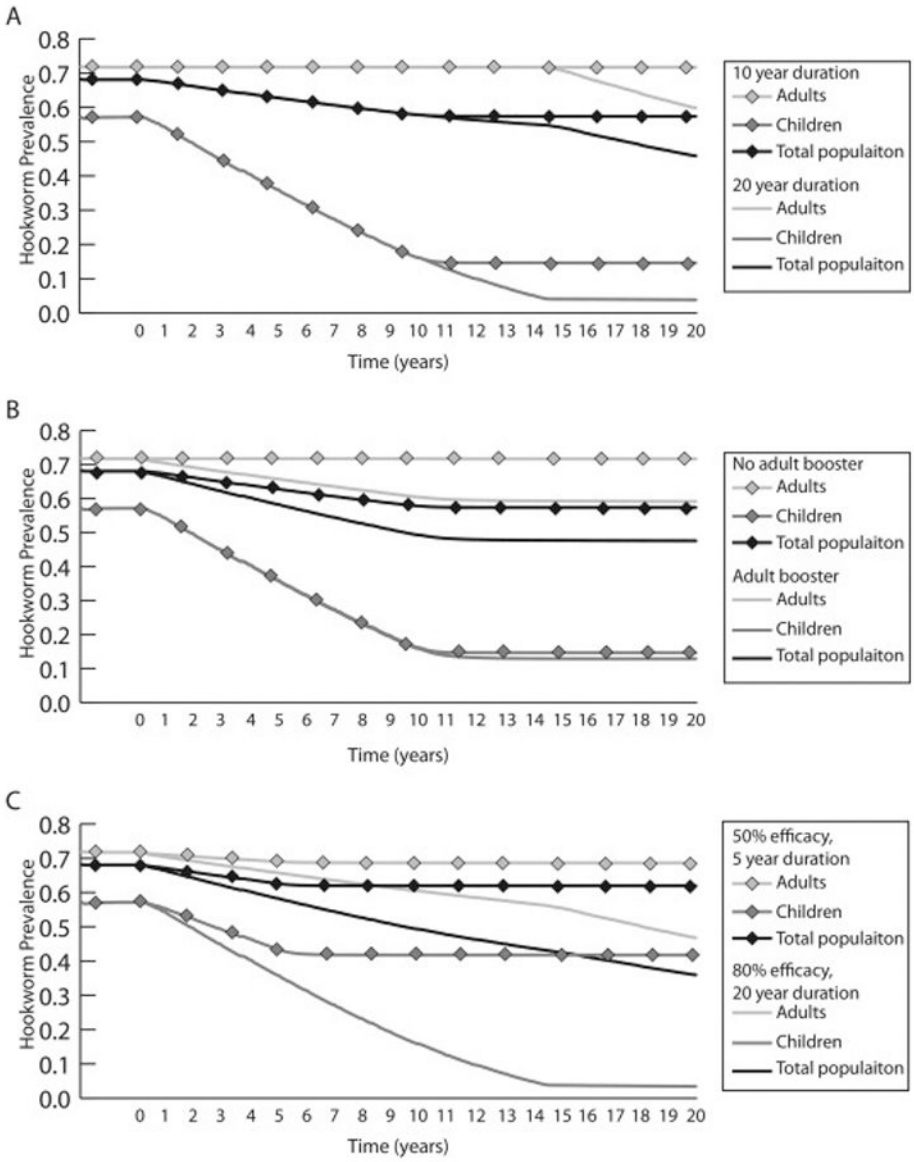

Figure 4.

Hookworm prevalence over 20 simulated years varying key vaccine characteristics while holding all else constant. A) Impact of duration of protection (10 year vs. 20 year) with a vaccine having 80% efficacy, 97% coverage rate, and no booster; b) impact of adding a booster in adulthood for a vaccine having 80% efficacy, 10 year duration of protection, and 97% coverage rate; and c) impact of varying vaccine efficacy and duration together for a vaccine having a booster in adulthood. 577

Table 1
Transmission and economic model input parameter values and sources

Transmission Model Inputs			
Parameters	**Symbol**	**Value**	**Source**
Proportion of population 0-14 years old		25%	[59]
Proportion of child population aging to adulthood (aging out of MDA cohort)		6.9%	[59]
Proportion of child population 5-14 years old (school-aged children)†		69%	[59]
Child hookworm prevalence in the absence of any intervention		57.1%	[60]
Adult hookworm prevalence in the absence of any intervention		71.8%	[60]
Worm mortality rate, daily	$\mu 1$	0.0868%	[61, 62]
Larval mortality rate, daily	$\mu 2$	21.67%	[61, 63]
Human mortality rate, daily	μ	0.003653%	[64]
Rate of human infectiousness, daily	$\gamma 1$	2.25%	[63]
Rate of larvae infectiousness (rate of egg maturation to infectious L3 larvae), daily	$\gamma 2$	25.0%	[63]
Probability larvae mature^	$d1$	50.0%	[63]
Probability eggs mature (live to become infectious L3 larvae)	$d2$	68.75%	[63]
Daily egg output*	λ	4500	[63]
Proportion of total worms that are female	s	50.0%	[63]
Clumping parameter‡	k	0.35	[65-67]
Reproductive rate•	R_0	3	[63, 68]
Cure rate with albendazole, 400mg		78.4%	[69]
MDA coverage rate		56.2%	[36]
Economic Model Inputs			
Parameter		**Value**	**Source**
Cost MDA per child treated		0.50	[14, 32-35]
2004 estimate disability weights			
Anemia		0.024	[70]
Iron deficiency anemia		0.09	[70]
Cognitive impairment		0.024	[70]
Heavy intensity infection		0.006	[70]
2010 estimate disability weights			
Mild anemia		0.005	[71]
Moderate anemia		0.058	[71]
Severe Anemia or iron deficiency anemia		0.164 (0.112-0.228)	[71]
Symptomatic intestinal nematode infections (heavy intensity infection)		0.03 (0.016-0.048)	[71]
Probability of anemia			
Light intensity infection		Children: 8.8% Adults: 4.1%	[72]
Moderate intensity infection		Children: 18.2% Adults: 10.0%	[72]

Transmission Model Inputs			
Parameters	**Symbol**	**Value**	**Source**
Heavy intensity infection		Children: 18.2% Adults: 16.2%	[72]
Probability of iron deficiency anemia			
Light intensity infection		Children: 3.0% Adults: 2.9%	[72]
Moderate intensity infection		Children: 11.0% Adults: 6.3%	[72]
Heavy intensity infection		Children: 17.6% Adults: 7.7%	[72]
PAF anemia		22.0%	[72]
PAF iron deficiency anemia		37.2%	[72]
Probability of mild anemia			
Light intensity infection		Children: 17.4% Adults: 50.2%	[54, 72-76]
Moderate intensity infection		Children: 19.7% Adults: 43.4%	[54, 72-76]
Heavy intensity infection		Children: 24.5% Adults: 36.3%	[54, 72-76]
Probability of moderate anemia			
Light intensity infection		Children: 68.2% Adults: 45.4%	[54, 72-76]
Moderate intensity infection		Children: 67.8% Adults: 46.0%	[54, 72-76]
Heavy intensity infection		Children: 67.6% Adults: 49.8%	[54, 72-76]
Probability of severe anemia			
Light intensity infection		Children: 14.4% Adults: 4.3%	[54, 72-76]
Moderate intensity infection		Children: 12.4% Adults: 10.6%	[54, 72-76]
Heavy intensity infection		Children: 7.9% Adults: 13.9%	[54, 72-76]

† Propor on eligible for MDA

ˆ Probability that larvae will survive to become a sexually mature worms in host; dependent upon free-living larval life expectancy and maturation delay in human host

* Maximum daily egg output per female worm in the absence of crowding or other attenuating factors

‡ Degree or worm aggrega on within the popula on, where the total parasite popula on is concentrated in fewer and fewer people as k approaches 0

• Number of female progeny that survive to become sexually mature adults per female worm assuming no density dependent constraints

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Table 2

Economic Outcomes

Scenario	Number Treated*		Intervention Costs ($)	Productivity Losses due to Hookworm ($)		DALYs Accrued	
	Children	Adults		2004 DW Estimate	2010 DW Estimate	2004 DW Estimate	2010 DW Estimate
$1 per vaccine dose							
No intervention	-	-	-	13,175,573	35,548,601	1,109	2,993
MDA 56.2% coverage, $0.21 per treated child	36,337	-	5,756	12,842,097	34,794,782	1,081	2,930
MDA 56.2% coverage, $0.50 per treated child	36,337	-	13,705	12,842,097	34,794,782	1,081	2,930
MDA 56.2% coverage, $0.79 per treated child	36,337	-	21,653	12,842,097	34,794,782	1,081	2,930
MDA 75% coverage, $0.21 per treated child	47,944	-	7,596	12,745,909	34,581,431	1,073	2,912
MDA 75% coverage, $0.50 per treated child	47,944	-	18,086	12,745,909	34,581,431	1,073	2,912
MDA 75% coverage, $0.79 per treated child	47,944	-	28,576	12,745,909	34,581,431	1,073	2,912
Vaccine 80% efficacy, 10 year duration of protection, 97% coverage	9,538	-	15,387	12,245,979	33,726,708	1,031	2,840
Vaccine 80% efficacy, 20 year duration of protection, 97% coverage	9,538	-	15,387	11,196,399	30,785,229	943	2,592
Vaccine 50% efficacy, 5 year duration of protection, 97% coverage	9,538	-	15,387	12,353,566	33,996,238	1,040	2,863
Vaccine 20% efficacy, 5 year duration of protection, 97% coverage	9,538	-	15,387	12,722,791	34,654,925	1,071	2,918
Vaccine 20% efficacy, 10 year duration of protection, 97% coverage	9,538	-	15,387	12,554,269	34,356,742	1,057	2,893
Vaccine 80% efficacy, 10 year duration of protection, 75% coverage	7,374	-	11,897	12,071,254	33,452,491	1,016	2,817
Vaccine 50% efficacy, 5 year duration of protection, 75% coverage	7,374	-	11,897	12,464,979	34,192,858	1,049	2,879
Vaccine 80% efficacy, 10 year duration of protection, 97% coverage, 78% booster coverage	9,538	7,669	27,760	7,094,695	17,306,121	597	1,457
Vaccine 80% efficacy, 20 year duration of protection, 97% coverage, 78% booster coverage	9,538	7,669	27,760	6,707,298	16,263,820	564	1,369
Vaccine 50% efficacy, 5 year duration of protection, 97% coverage, 78% booster coverage	9,538	7,669	27,760	10,425,152	27,542,128	878	2,319
Vaccine 80% efficacy, 10 year duration of protection, 97% coverage, 60% booster coverage	9,538	5,899	24,905	7,875,815	19,759,765	663	1,664

*with either MDA or vaccination, depending on scenario, over the 20 simulated years