

# Global Health Impact: Neglected Tropical Disease Model

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## Abstract

Neglected tropical diseases (NTDs) receive relatively little research and development but have a tremendous impact on lifespan and livelihood in endemic regions.<sup>1</sup> Many NTDs cause lifelong disability if the affected persons are not treated.<sup>2</sup> These disabilities often undermine patients' ability to meet their basic needs and, on a macro-scale, NTDs can compromise the social and economic development of affected countries.<sup>2</sup> Here we use existing data on the need for drugs, their efficacy, and their treatment percentages to estimate the impacts of various drug regimens on the global burden of several NTDs: schistosomiasis, onchocerciasis, lymphatic filariasis, and three soil-transmitted helminths over time. For an interactive visualization of our models' results, see: <https://global-health-impact.org/>. We found that a total of 192 million NTD DALYs were alleviated in 2010, 2013, and 2015 together due to pharmaceutical interventions. One third of global estimated NTD DALYs that would have been lost absent treatment are due to schistosomiasis; however, interventions used to treat schistosomiasis only alleviate 2% of this need. Our models highlight the importance of focusing not just on the burden of these diseases, but also their alleviation in the effort to expand access to treatment.

Key words: NTDs; global burden; disease alleviation; Global Health Index; Sustainable Development Goals; Global health.

## Introduction

### The Health Impact of NTD Medicines on the Global Burden these Diseases are Poorly Understood

In order to expand access to treatment for NTDs, it is important to measure the health impact of life-saving drugs on the global burden of these diseases. Worldwide, NTDs cause 534,000 deaths a year.<sup>1</sup> However, this statistic does not take into account the long-term suffering and disability these diseases afflict on over a billion people in poor countries.<sup>2</sup> Policy makers, pharmaceutical companies, and other stakeholders require information about treatment success in addressing NTD epidemics over time to evaluate performance and allocate resources.

Our NTD models include many more treatment interventions than most individual disease-based models. NTD interventions are increasingly integrated, targeting more than one disease or groups of disease at once with multiple medications, which suggests that there is a growing need for a modelling framework that allows for the analysis of multiple diseases and drugs.<sup>3</sup> Most existing models attempt to predict the future course of a single epidemic and treatment efforts' likely consequences in alleviating a single disease, though studies employ a variety of approaches of varying complexity.<sup>4-6</sup> Few models assess the impact of multiple pharmaceutical products on a particular disease, opting instead to focus on the efficacy of a single drug on a single disease.<sup>7,8</sup>

One purported advantage of many existing models is that they are dynamic, but such modelling efforts have several drawbacks. Dynamic models embody a great deal of uncertainty as they require significant assumptions about the likely developments of epidemics over time (transmission dynamics etc.). Moreover, many models developed to simulate the transmission and control of NTDs have a restricted geographical scope, frequently being limited to one country or region. These models' predictions often are not generalizable to other areas.<sup>9</sup> For example, several models for lymphatic filariasis have only had a modest role in the planning and design of control programs.<sup>10</sup> Jambulingam et al. 2016 produced a model to determine the effectiveness of mass drug administration (MDA) in eradicating lymphatic filariasis in Indian settings, finding that MDA must be continued for longer periods of time in high transmission areas in order to be effective.<sup>11</sup> The model's predictions could potentially be valid in other nations within the Indian subcontinent, but cannot be used in other areas with differing vectors due to different transmission dynamics.<sup>12</sup>

While our models emphasize broad epidemiological patterns, they include country-level differences in key parameters such as endemicity and prevalence in order to accurately capture burden of disease alleviation within each affected nation and, so, globally. Moreover, they have low computational complexity, which is important for our global analysis of five interventions on six NTDs. There is also a need for NTD modeling efforts to incorporate comprehensive disability metrics, such as QALYs or DALYs, in order to fully capture the disease burden of NTD infections that often have low mortality rates but high disability burdens. Few models utilize DALYs to estimate the effectiveness of efforts to combat NTDs.<sup>13,14</sup> Instead, many models utilize microfilarial load, average annual number of vector bites received by an adult, or simply disease cases averted.<sup>15-20</sup> Utilizing DALY information allows us to create comparable estimates of the

interventions' impacts on disability as well as death over time and across interventions. Moreover, we examine contributions to drug development across the pharmaceutical industry. In short, our models provide a flexible framework for simulating the impact of NTD treatment efforts that can be easily adjusted to reflect new data and standardizes results so that impact can be compared across diseases.

## Materials and Methods

This paper describes a series of models that evaluate the global health consequences of medicines for six NTDs: schistosomiasis, onchocerciasis, lymphatic filariasis, roundworm, whipworm, and hookworm in 2010, 2013 and 2015.<sup>21,22</sup>

We use existing data on the need for drugs, their efficacy, and their treatment percentages to estimate the impacts of various treatment regimens on the global burden of our target diseases.<sup>23</sup> DALYs remaining, efficacy, treatment coverage, and prevalence. DALY data is gathered from the Global Health Data Exchange.<sup>24</sup> Efficacy data is gathered from a systematic review of the scientific literature.<sup>23</sup> We use country level data whenever possible, but in the case of missing data we resort to regional and then to global estimates. Treatment coverage is calculated by dividing the total population treated by the population requiring preventive chemotherapy. This data was gathered using the World Health Organization (WHO) Preventive Chemotherapy (PCT) databank.<sup>2</sup> Prevalence data was gathered using the Global Health Data Exchange results tool.<sup>24</sup> We gather data on endemicity from the WHO's PCT database; we consider a disease endemic to a country if it has a recorded population requiring treatment.<sup>25</sup>

We estimate the burden of disease that occurs in the absence of treatment, the impact of drugs on this burden over time, and the contribution of firms' interventions to alleviating the burden. The models provide information on the consequences of treatment by company as well as country, drug, and disease.

**Figure 1: Conceptual diagram of impact model**

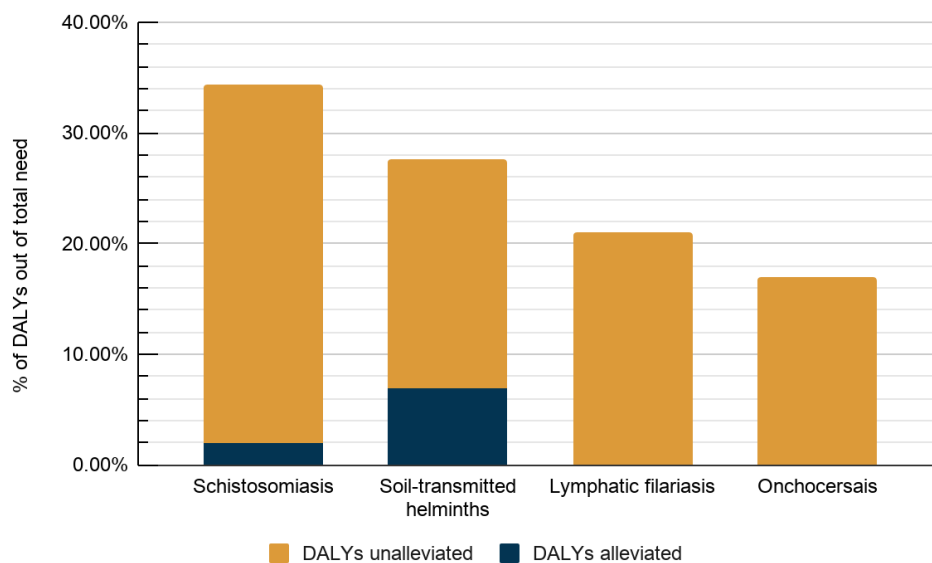


Figure 1 describes our conceptual framework. The framework embodies the critical components and relationships pertinent to estimating the burden of disease alleviated by treatment. Our first goal is to estimate the total morbidity and mortality (in DALYS) that would be lost in the absence of treatment, or the sum of the two boxes. We do this based on estimated death and disability, disease incidence, patient treatment coverage, and treatment effectiveness. We then multiply the population infected by the average impact of an untreated or ineffectively treated case. We assume this average impact is the global burden of disease remaining divided by the sum of the population untreated and/or ineffectively treated. We can estimate the number of people who need a drug who are treated effectively (and the number who are either untreated or ineffectively treated) using data on treatment percentage and effectiveness. We assume the impact of treatment is the average impact of an untreated or ineffectively treated case multiplied by the number of people who need treatment who are treated effectively.

We reduce estimated impact by prevalence to account for the fact that treatment is primarily delivered via mass drug administration (MDA) which is provided to almost all individuals in a given area (as only a percentage of the treated population will be infected with an NTD and we aim to estimate only direct treatment effect).<sup>26</sup> This reduces our final impact score to account for the difference between the population requiring preventive chemotherapy and the actual number of people with the NTD as we intend to measure only the direct impact of treatment.

To determine which MDA was initiated in each country, we applied two decision trees provided by the WHO's guidance for preventive chemotherapy in human helminthiasis (PCHH).<sup>26</sup> The decision trees specify treatments for each possible epidemiological combination of the diseases our NTD models analyze. There are instances in which a targeted treatment is to be administered along with the MDA. The PCHH defines a targeted treatment as the group-level application of drugs irrespective of infection status, barring some exclusion criteria; however, the report does not specify exclusion criteria for targeted treatments, therefore we model these treatments the same as we do MDAs.<sup>26</sup>

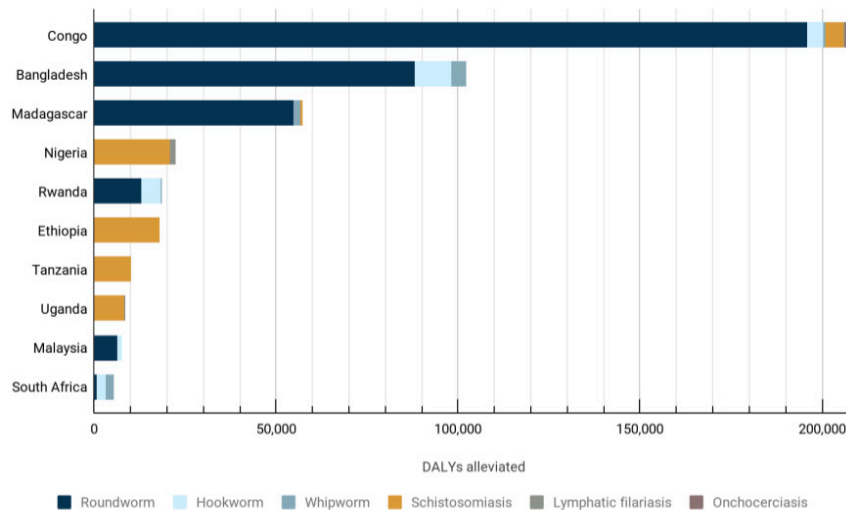
## Results

### The Effects of Interventions on the Burden of Disease Alleviated

Our NTD models estimate the global distribution of DALYs alleviated across countries. Figure 2 suggests that key medicines are having the most impact in Africa and Southeast Asia; need and treatment for soil-transmitted helminths and schistosomiasis are highly concentrated in these regions. The marked change in albendazole impact from 2013 to 2015 comes from roundworm intervention in Cameroon -- the combination of high efficacy and treatment coverage in 2013 increased impact substantially, but roundworm was not considered endemic to Cameroon in 2015 so an impact score was not calculated.<sup>25</sup> Drugs for our target diseases are having the greatest impact in the Democratic Republic of Congo. There is a considerable amount of roundworm infection in the Democratic Republic of Congo receiving highly effective treatment. Globally, there are areas with great need but correspondingly little impact. The most glaring example of this failure can be found in South America: the ratio of impact to need in this region is 5.26%. In other words, out of 218,500 DALYs we estimate would be lost absent treatment, approximately 8,500

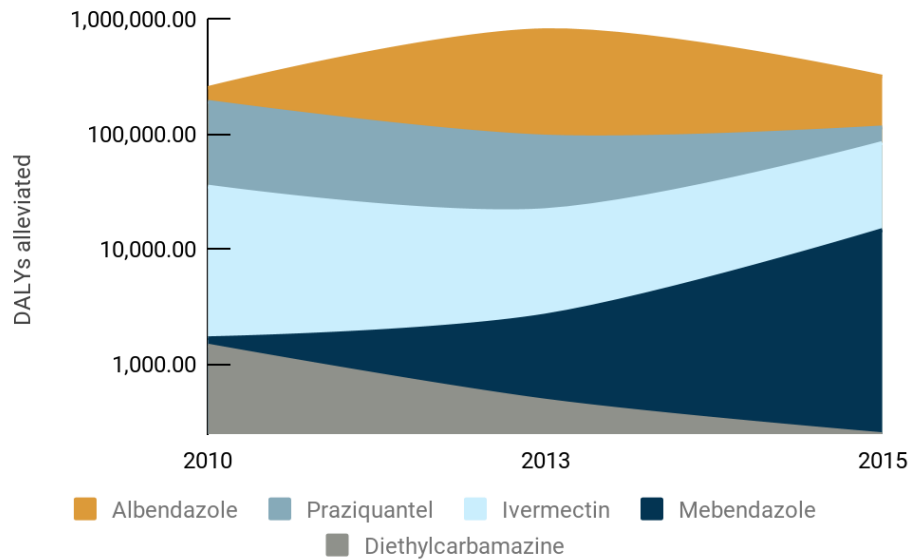
life-years were saved in South America using NTD interventions, leaving 210,000 DALYs lost. Additionally, the models highlight substantial regional disparities in treatment coverage, efficacy, and need. Treatment coverage for schistosomiasis in 2015 is considerably higher in the Western Pacific region than Africa, for instance, even though the majority of schistosomiasis DALYs are located in Africa.

**Figure 2: Top 10 countries by impact in 2015. Impact scores of the top 10 highest impact countries for NTDs in 2015, separated by disease.**



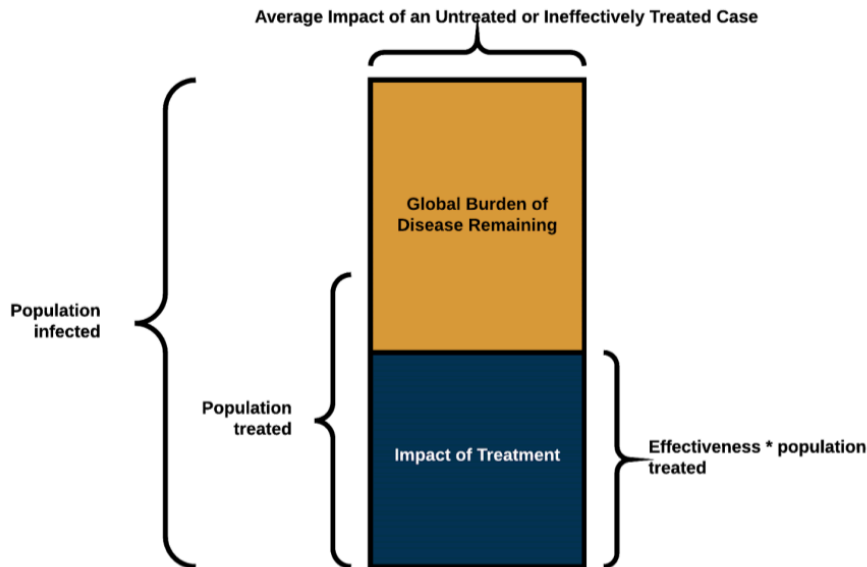
Our models measure the impact of drugs used to treat NTDs. Albendazole, a key drug for soil-transmitted helminths, has the largest impact out of all observed drugs because it is widely recommended and highly effective; albendazole alleviates 60% of the global burden of the NTDs in the models. Praziquantel for schistosomiasis also has a large impact. Figure 3 illustrates the impact of these drugs. Even with many highly effective drugs available, 91% of the burden of these diseases remains unalleviated: in 2015, our NTD models estimate that treatment saved 526,458 life-years, leaving 5,343,366 life-years lost globally.

**Figure 3: Impact score by drug. Logarithmic scale comparative impact of five drugs for the treatment of certain NTDs internationally in 2010, 2013, and 2015.**



Moreover, our models provide an overall picture of treatment impact on the six diseases observed. Together, treatments targeting soil-transmitted helminths together alleviated 77% of the total life-years saved from all NTD treatments, while onchocerciasis, lymphatic filariasis, and schistosomiasis medicines saved .5%, 1%, and 21% respectively. Observing the global estimated need, or burden of disease in the absence of treatment, reveals that resources may not be allocated in the manner most efficient to eradicate these diseases. In fact, Figure 4 shows that one third of total global DALYs originate from schistosomiasis.

Figure 4: Estimated DALYs alleviated and unalleviated out of total need in 2015



Finally, our models evaluate the impact of drugs aggregated by patent holding companies. The 2015 model suggests drugs patented by GlaxoSmithKline and Bayer alleviate more than three quarters of global NTD DALYs that are alleviated due to treatment. GlaxoSmithKline's impact comes from its drug used to treat lymphatic filariasis and soil-transmitted helminths, albendazole.

## Discussion

Our models produce data that can provide states, non-governmental organizations, and companies with the means of promoting new market strategies and innovative health policies to help achieve sustainable development goals that call to eliminate NTDs by 2030. This is the first project of its kind that provides a common framework for evaluating treatment impact across a wide variety of interventions across several NTDs.

Although many existing models try to predict the impact of treatment on the evolution of these diseases in a population, we estimate direct treatment impact in line with the other Global Health Impact models ([global-health-impact.org/new](http://global-health-impact.org/new)). With some modifications, the models can be rendered as part of traditional epidemiological models. Researchers can estimate the proportion of effectively treated individuals susceptible to reinfection, the number not effectively treated who transmit the disease to the larger susceptible population, the chance of transmission before treatment, and so forth. However, we avoid complicated mathematical modeling and do not make significant assumptions about patterns of change over time globally in the face of uncertainty. The advantage of our approach is that our models are simple and transparent and our results are not highly assumption driven.

We can improve estimates of treatment impact at the country level as further sub-national data becomes available. Similarly, treatment effectiveness information can replace country-level drug



efficacy studies that may overestimate drug effectiveness. We utilize cure rates from treatment efficacy trials for onchocerciasis modeling, which does not accurately capture factors like parasite burden and length of infection. Modelling utilizing egg reduction rate data may improve our estimates. Still, we incorporate the best existing data on drug's likely consequences into our models and conduct sensitivity analysis to determine how this affects results (see supplementary information).

Access to a framework that standardizes the health impact of NTDs and their interventions is critical in promoting equitable access to essential health care services by enabling policy makers to better understand, treat, and prevent NTDs. Existing models often try to predict time to eliminate NTDs based on potential policies, but our models provide important information about impact before the diseases are eliminated. WHO-CHOICE, a model provided by the World Health Organization, gives key decision-makers information on cost-effectiveness and strategic planning.<sup>27</sup> Our models provide important information on firms' contributions but also aggregate information on drugs' country and disease level effects essential for health systems planning.

## Conclusion

There are several strategies currently deployed to combat NTDs around the world. National public health institutes and international organizations are contributing to the global control of NTDs through the development of laboratory surveillance tools and epidemiologic methods to monitor program success.<sup>28</sup> Pharmaceutical companies like Pfizer, Merck, Novartis, and GlaxoSmithKline have donated millions of doses of drugs to diminish the effect of NTDs.<sup>29</sup> There are also many public-private initiatives that aim to accelerate research and development of effective health tools like diagnostics and vaccines to combat these diseases.<sup>30</sup> Our results demonstrate that although we are making great strides in alleviating the burden of certain NTDs, pharmaceutical interventions may not be efficiently allocated, for instance you can see this mismatch when comparing need versus treatment for global schistosomiasis cases. Although there are proven approaches to control the spread of NTDs, these diseases continue to cause a disproportionate amount of morbidity. Our models can help policy makers evaluate treatment access, set targets, and reduce the burden of NTD infection around the world.

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## Disclosures

We declare that there are no conflicts of interest in this paper.

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## Figure legends

Figure 1. Conceptual diagram of impact model.

Figure 2. Top 10 countries by impact in 2015. Impact scores of the top 10 highest impact countries for NTDs in 2015, separated by disease.

Figure 3. Impact score by drug. Logarithmic scale comparative impact of five drugs for the treatment of certain NTDs internationally in 2010, 2013, and 2015.

Figure 4. Estimated DALYs alleviated and unalleviated out of total need in 2015.

# Supplementary Materials

## Supplementary Methods

Equation S1 below is the impact formula that is used throughout our models to calculate a drug's lives saved in a single country.

$$I = \frac{D * e * \theta}{1 - e * \theta} * p$$

$D$  represents the DALYs observed within the patient group using data gathered from the Global Health Data Exchange.<sup>1</sup>

$e$  represents the efficacy for a specific drug in its respective country. This data was gathered from systematic review of the scientific literature.<sup>2</sup> We use country level data whenever possible, but in the case of missing data we resort to regional and then to global estimates.

$\theta$  represents the treatment coverage of a specific drug. It is calculated by dividing the total population treated by the population requiring preventative chemotherapy. This data was gathered using the WHO's Preventive Chemotherapy and Transmission Control databank.<sup>3</sup>

$p$  represents the prevalence percentage of a particular disease. This data was again gathered using the Global Health Data Exchange results tool.<sup>1</sup> We multiply our impact score by the percentage prevalence because mass drug administration (MDA) is given to all individuals in a given area and only a percentage of the population will be infected with a given NTD. This reduces our final impact score to account for the difference between the population requiring preventative chemotherapy and the actual number of people with the NTD as we intend to measure only the direct impact of treatment.

To determine which mass drug intervention was initiated in each country we applied two decision trees provided by the WHO's Preventive Chemotherapy in Human Helminthiasis manual.<sup>4</sup> The decision trees effectively suggest the requisite treatments for different combinations of the four parasitic diseases our NTD models analyze. The decision trees are illustrated in Figures 1 and 2. T1, T2, and T3 refer to a unique targeted treatment (T1 = albendazole + praziquantel or mebendazole + praziquantel, T2 = praziquantel, and T3 = albendazole or mebendazole). MDA1, MDA2, and MDA3 refers to a unique mass drug administration (MDA1 = ivermectin + albendazole, MDA2 = diethylcarbamazine + albendazole, and MDA3 = ivermectin). As an example, if lymphatic filariasis, onchocerciasis, and schistosomiasis are endemic in a country, and the endemicity for soil-transmitted helminthiasis is high, we will select MDA1 and T1 as our mass drug administration and targeted treatment respectively. We gather data on endemicity from the WHO's Preventive Chemotherapy and Transmission Control databank and assume that having a population requiring treatment for a disease in a given country makes the disease endemic in that country when endemicity is not listed explicitly.<sup>3</sup>

The information on specific drugs used to address different NTDs is contained in table S1.<sup>4</sup> Information on the dosage for each respective anthelmintic drug along with its frequency of intervention is found in table S2.<sup>4</sup> Information regarding a regimen's targeted disease and its frequency of implementation is found in table S3.<sup>4</sup>

**Table S1. WHO recommended anthelmintic drugs for use in preventive chemotherapy**

Disease	ALB	MBD	DEC	IVM	PZQ
Ascariasis	X	X		X	
Hookworm	X	X			
Lymphatic filariasis	X		X	X	
Onchocerciasis				X	
Schistosomiasis					X
Trichuriasis	X	X		X	

**Table S2. Drugs, doses, implementation thresholds and regimens in preventive chemotherapy**

Disease	Drugs and dosages	Frequency of intervention
Lymphatic filariasis (where onchocerciasis is co-endemic)	IVM (according to height) plus ALB 400 mg	Once a year
Lymphatic filariasis (where onchocerciasis is not co-endemic)	DEC 6 mg (using age as criterion for dose) plus ALB 400 mg	Once a year
Onchocerciasis	IVM (according to height)	Once a year
Schistosomiasis	PZQ 40 mg	According to prevalence of infection
Soil-transmitted helminthiasis	ALB 400 mg or MBD 500mg	According to prevalence of infection

**Table S3. Preventive chemotherapy courses of action**

<b>Intervention</b>	<b>Diseases targeted</b>	<b>Drugs</b>	<b>Frequency of implementation</b>
MDA1	LF or LF and ONCHO or LF and STH or LF and ONCHO and STH	Ivermectin and albendazole, administered together	Repeated at yearly intervals
MDA2	LF or LF and STH	Diethylcarbamazine and albendazole, administered together	Repeated at yearly intervals
MDA3	ONCHO	Ivermectin	Repeated at yearly intervals
T3	SCHIST and STH	Praziquantel and albendazole or mebendazole, administered together	Repeated at yearly intervals
T2	SCHIST	Praziquantel	T2 should take place once a year in high-risk communities, once every 2 years in moderate risk communities, and twice during the period of primary schooling age in low-risk communities
T3	STH	Albendazole or mebendazole	Once or twice per year

The WHO's weekly epidemiological record provides a framework to determine soil-transmitted helminths' level of endemicity for an individual country.<sup>5</sup> According to the WHO, a disease is highly endemic in a country if the proportion of the population requiring preventive chemotherapy is greater than or equal to 2/3 of preschool-aged and school-aged children. The disease is moderately endemic if the proportion of the population requiring preventive chemotherapy is between 1/3 and 2/3 of preschool-aged children and school-aged children. Finally, the disease has low endemicity if the proportion of the population requiring preventive chemotherapy is less than 1/3 of preschool-aged children and school-aged children. We utilize information taken from the WHO's Preventive Chemotherapy and Transmission Control databank to work with this framework: we sum the population requiring preventive chemotherapy for soil-transmitted helminths for preschool-aged children and school-aged children and divide this by population data taken from the World Bank database.<sup>6</sup> Table S4 outlines the categorization of a country's endemicity for soil-transmitted helminth data from the Global Health Data Exchange is used to determine this categorization.<sup>1</sup>



**Table S4. Recommended treatment strategy for STH in preventive chemotherapy**

Category	Prevalence of any STH infection among school-aged children	Action to be taken
High-risk community	≥50%	Treat all school-aged children (enrolled and not enrolled) twice each year
Low-risk community	≥20% and <50%	Treat all school-aged children (enrolled and not enrolled) once each year

Consider how we estimate drugs' impacts for Ethiopia. Schistosomiasis, onchocerciasis, and lymphatic filariasis are endemic in Ethiopia. The population receives MDA1+T2; praziquantel is used to treat schistosomiasis, ivermectin is used to treat onchocerciasis, and ivermectin + albendazole is used to treat lymphatic filariasis.<sup>4</sup> We will first calculate the impact score for praziquantel. 210,340.92 DALYs were lost to schistosomiasis in Ethiopia in 2015.<sup>1</sup>

Estimated praziquantel efficacy in Ethiopia for schistosomiasis in 2015 is 94%.<sup>2</sup> Schistosomiasis treatment coverage was 28%.<sup>3</sup> Finally, estimated prevalence is 23%.<sup>3</sup> We calculate impact for praziquantel on schistosomiasis in Ethiopia in 2015 in Equation S2:

$$I_{PZQ} = \frac{210,340.92 * 94% * 28%}{1 - 94% * 28%} * 23% = 17,958.81$$

We calculate ivermectin's impact on onchocerciasis in the same way. Ivermectin efficacy in Ethiopia was 81%.<sup>2</sup> Onchocerciasis treatment coverage was 64.23%.<sup>3</sup> Estimated prevalence is 0.36%.<sup>3</sup> The CDC states that for treatment to be effective, ivermectin must be administered every 6 months for the life span of the adult worms.<sup>7</sup> The CDC also states that adult worms can live in the nodules for approximately 15 years.<sup>8</sup> The overall impact formula for ivermectin's alleviated onchocerciasis DALYs is derived by Equation S3:

$$I_{IVM} = \frac{25,148.53 * 81% * 64.23%}{1 - 81% * 64.23%} * 0.36% \div 2 \div 15 = 3.27$$

To calculator ivermectin + albendazole's impact on lymphatic filariasis we used estimates of efficacy and treatment coverage from the same WHO region as Ethiopia because country level data was not available in this case.<sup>2</sup> Estimated prevalence is 0.02%.<sup>3</sup> The overall impact formula for ivermectin's alleviated lymphatic filariasis DALYs is Equation S4:

$$I_{IVM + ALB} = \frac{1,168.19 * 29.43% * 29.58%}{1 - 29.43% * 29.58%} * 0.02% = 0.02$$



We employ a similar methodology to derive impact scores for targeted NTD drugs in all endemic countries. We then aggregate all drug scores by country to get country-level impact estimates for all NTDs and by drug to get drug-level estimates for impacts both on individual NTDs and overall. We aggregate drug scores on individual diseases to get disease level impact scores. Finally, we aggregate data on drugs' impacts by originator company to provide company level impact scores. We determine drug accreditation based on Table S5.

**Table S5. Accreditation list**

<b>Drug</b>	<b>Abbreviation</b>	<b>Expired</b>	<b>Originator</b>	<b>Reference</b>
Praziquantel	PZQ	Yes	Bayer	Bayer officially developed the drug and it named Biltricide. <sup>9</sup>
Ivermectin	IVM	Yes	Merck	W. C. Campbell, R. W. Burg, M. H. Fisher, and R. A. Dyba discovered Ivermectin as part of research conducted for Merck Labs. <sup>10</sup>
Albendazole	ALB	Yes	GlaxoSmithKline	SmithKline Corporation originally patented Albendazole in 1975. <sup>11</sup> SmithKline then merged with Beecham in 1989 to form SmithKline Beecham. <sup>12</sup> SmithKline Beecham then merged with Glaxo Wellcome to become GlaxoSmithKline. <sup>13</sup>
Diethylcarbamazine	DEC	Yes	Pfizer	Yellaragada Subb Rao first discovered DEC at Lederle Labs in 1946. <sup>14</sup> Lederle Labs was owned at the time by American Cyanamid. <sup>15</sup> American became a subsidiary of American Home Products Corp. in 1995. <sup>16</sup> American Home Products eventually changed its name to Wyeth, and Wyeth was subsequently acquired by Pfizer. <sup>17,18</sup>
Mebendazole	MBD	Yes	Johnson & Johnson	Janssen Pharmaceuticals originally patented Mebendazole 1969. <sup>19,20</sup> Johnson and Johnson acquired Janssen Pharmaceuticals in 1961.

## Sensitivity analysis

We conducted sensitivity analyses to quantify uncertainty in our models. We ran a monte carlo simulation for 11 variables for 1,000 trials. For each trial, a value was randomly chosen from the assigned distribution. Company, drug, and disease rankings were then recalculated and any changes in rank were noted. In each test, if the parameter has a solution to maximum likelihood estimator (MLE), then we use MLE, otherwise we choose a particular mean based on our assumption with small variance (0.05). We define stability for an individual company or drug as follows: if the main box of the boxplot lies at 1 to -1, we will say the result is relatively stable. If no more than two rankings are unstable we classify our model as stable.

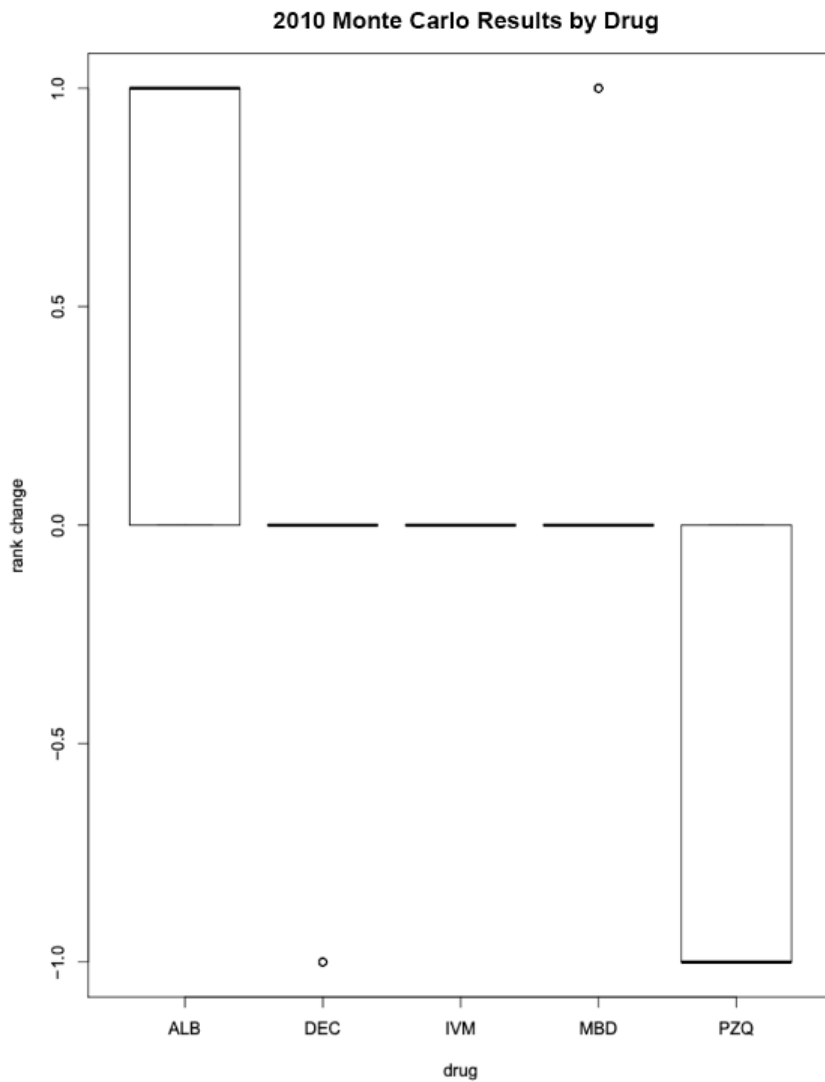
The y-axis indicates changes in company, drug, or disease ranks. Each number on the y-axis indicates the rank change e.g., 1 stands for a rank decrease by 1, -1 stands for rank increase by 1, 0 stands for not changing. The x-axis corresponds to company, drug, or disease for each year. For each company, drug, and disease combining all tests together, we processed the monte carlo test 1,000 times. So there are 1,000 new ranks for each company and drug. For example, Bayer might be ranked as follows in the different iterations: (4, 5, 6, 1, 8, 9, etc.), and then we compare each company's rank to its original rank to see whether its rank increased or decreased.

For each boxplot, the bold line in the middle represents the median, or 2nd quartile, and the box represents the 1st quartile to 3rd quartile. The upper whisker corresponds to the 3rd quartile + 1.5 \* (3rd quartile - 1st quartile). Similarly, the lower whisker corresponds to the 1st quartile - 1.5 \* (3rd quartile - 1st quartile). Any points above or below the whisker are outliers. We consider the upper whisker and lower whisker to be the maximum and minimum changed-rank in the 1,000 trials. The boxplot for each company represents the changed-rank.

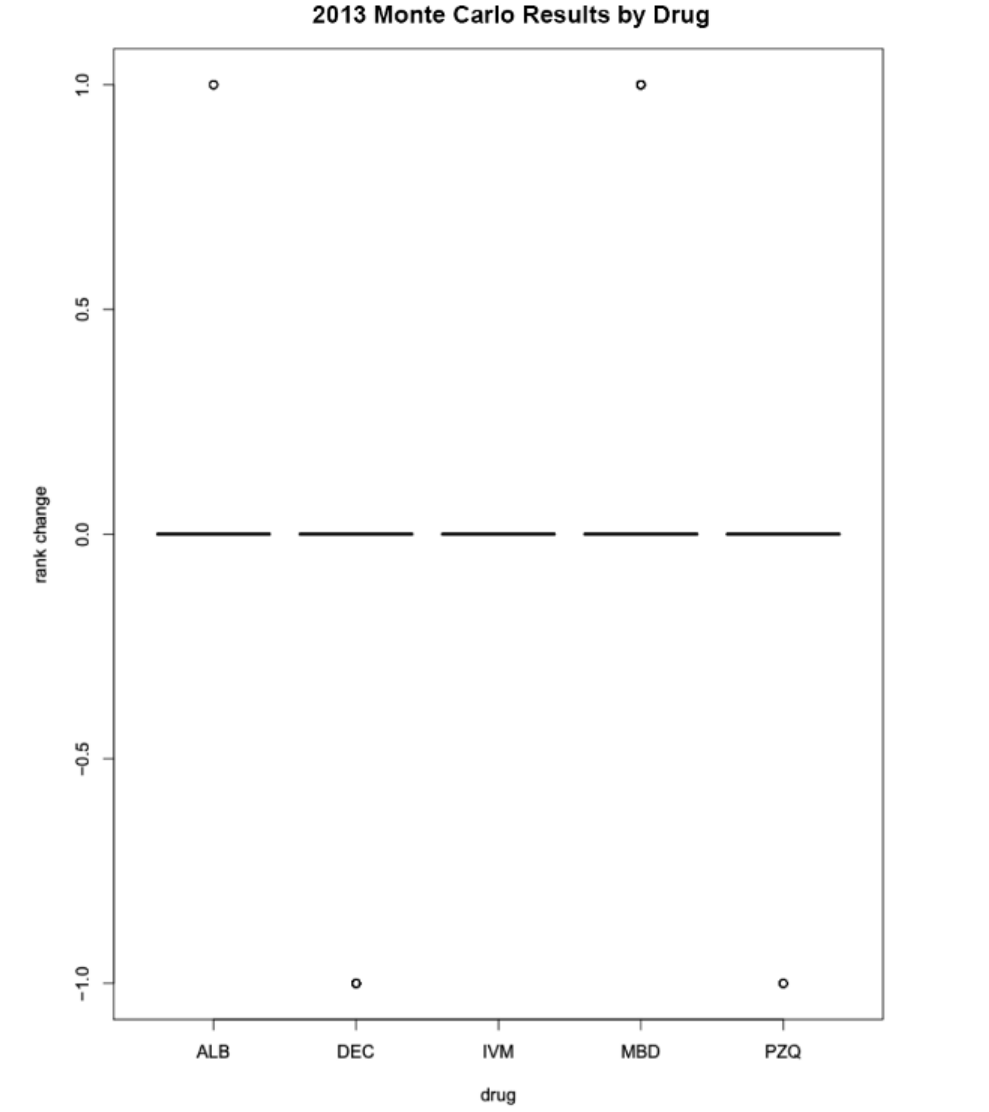
## Sensitivity analysis results

In 2010 most drugs had a stable ranking except for albendazole and praziquantel; albendazole's rank has a tendency to move down in 50% of cases and praziquantel's rank has a tendency to move up in 50% of cases. All companies held a stable ranking except for Bayer and GlaxoSmithKline; GlaxoSmithKline's rank has a tendency to move up in 50% of cases and Bayer's rank has a tendency to move down in 50% of cases. Hookworm, lymphatic filariasis, and whipworm held stable rankings while schistosomiasis' rank tended to move down in 50% of cases. Although roundworm's rank does exceed one positive interval change in the maximum case, the interquartile range remains within our acceptable bounds of stability. This is visualized in Figures S3, S4, and S5.

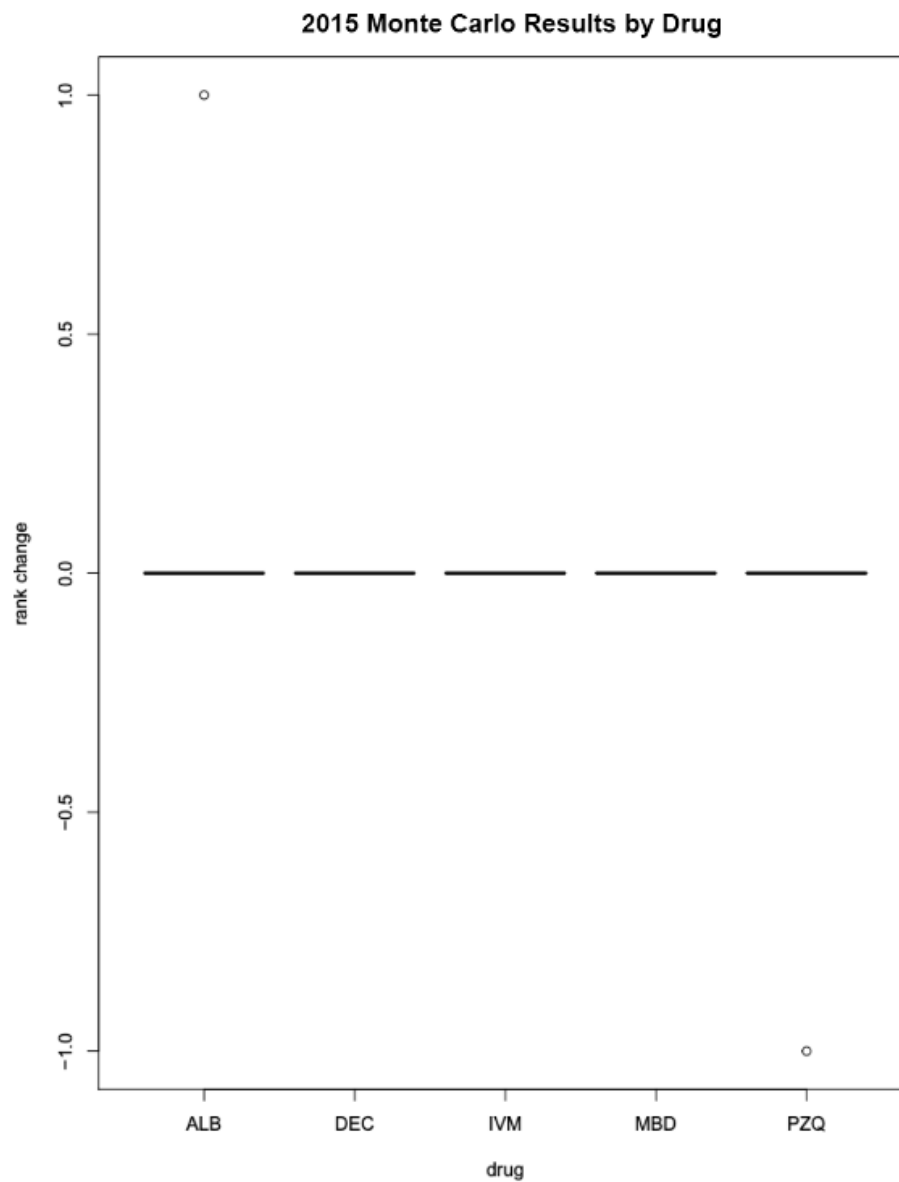
**Figure S3. Monte Carlo results by drug, 2010.** Changes in drug ranking in 2010. Note that albendazole's rank has a tendency to move down in 50% of cases and praziquantel's rank has a tendency to move up in 50% of cases.



**Figure S4. Monte Carlo results by drug, 2013.** Changes in drug ranking in 2013. Note that all drugs held a stable ranking.

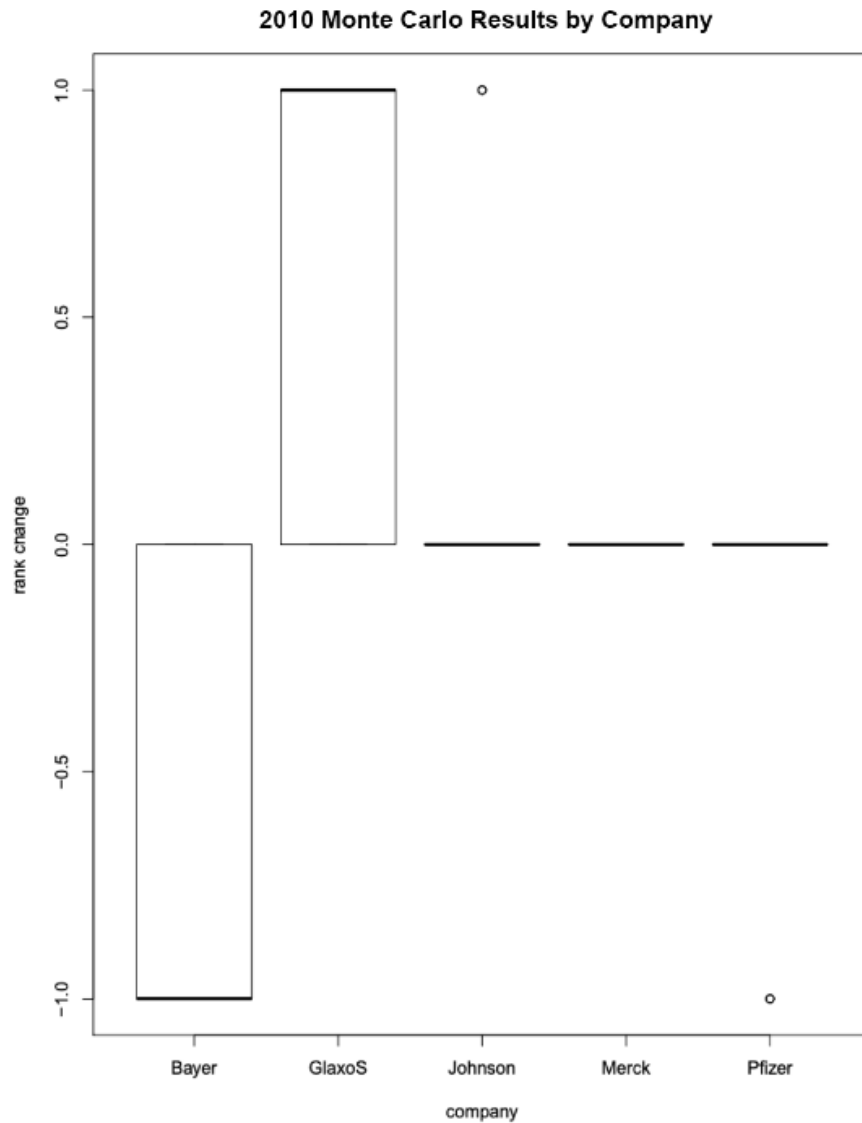


**Figure S5. Monte Carlo results by drug, 2015.** Changes in drug ranking in 2015. Note that all drugs held a stable ranking.

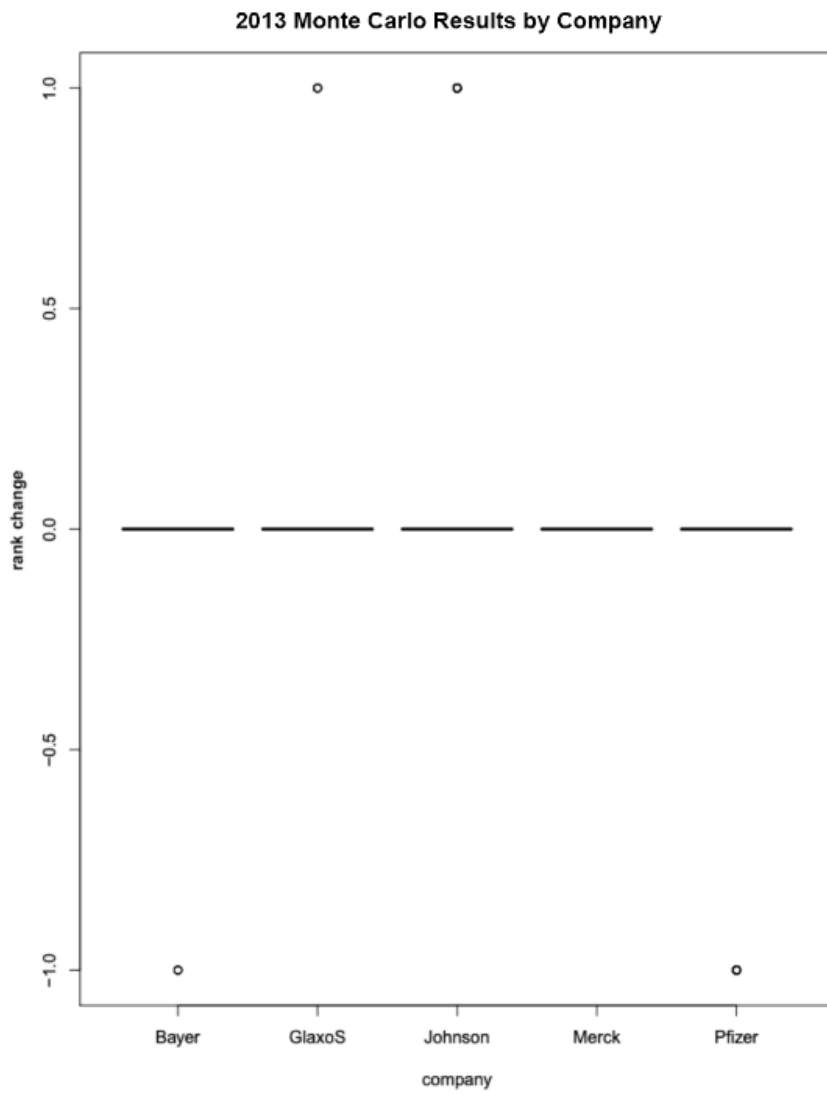


In 2013 all drugs and companies had a stable ranking. Most diseases had a stable ranking except for lymphatic filariasis and onchocerciasis: they changed rank by one negative and positive interval, respectively. See Figures S6, S7, and S8 for an illustration of these results.

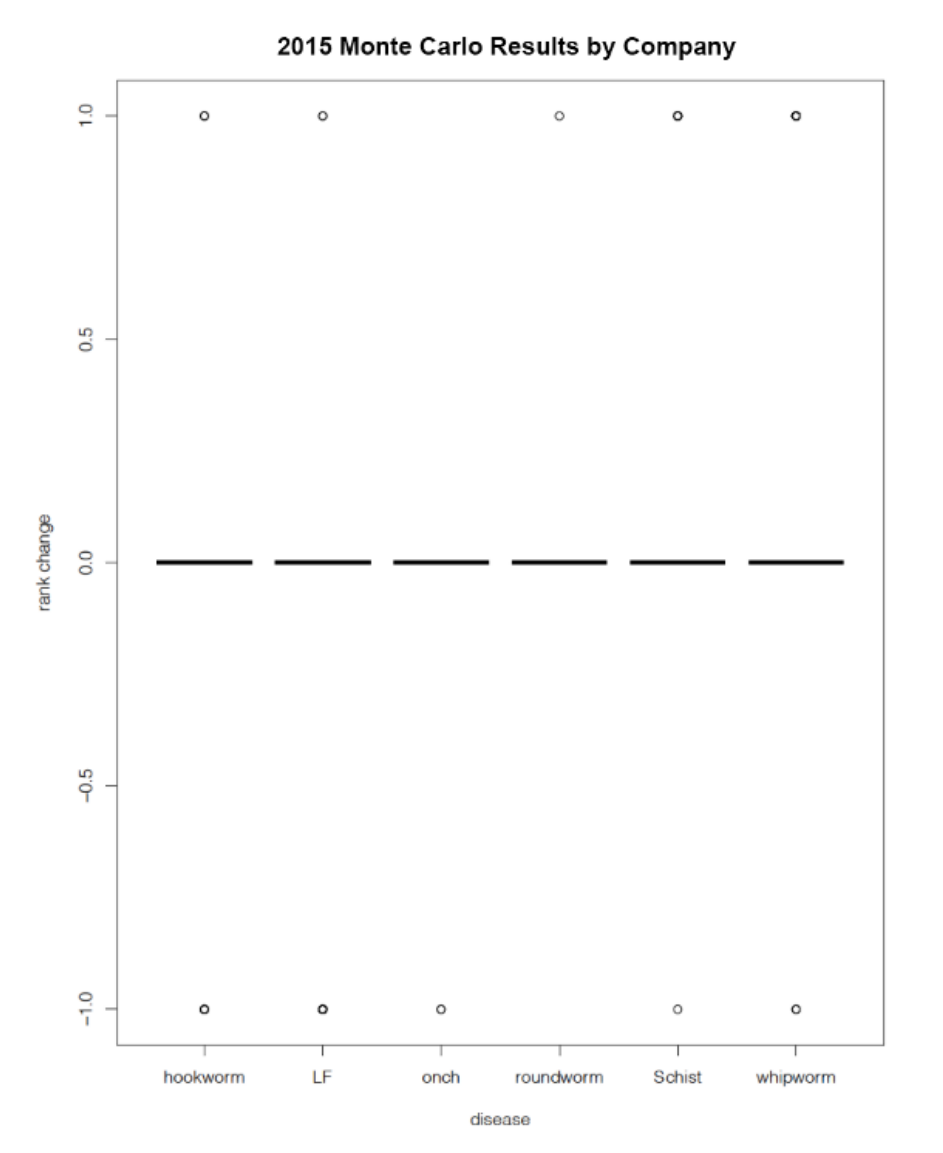
**Figure S6. Monte Carlo results by company, 2010.** Changes in company ranking in 2010. Note that GlaxoSmithKline's rank has a tendency to move up in 50% of cases and Bayer's rank has a tendency to move down in 50% of cases.



**Figure S7. Monte Carlo results by company, 2013.** Changes in company ranking in 2013. All companies held a stable ranking.



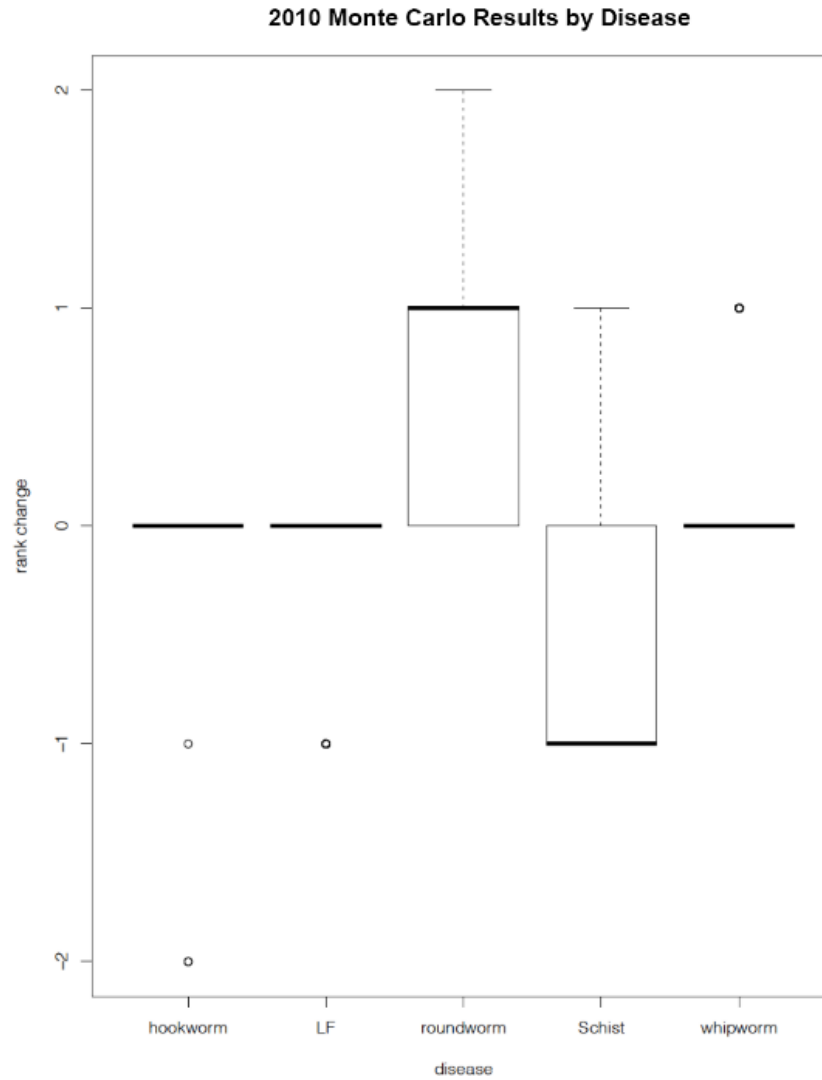
**Figure S8. Monte Carlo results by company, 2015.** Changes in company ranking in 2015. All companies held a stable ranking.



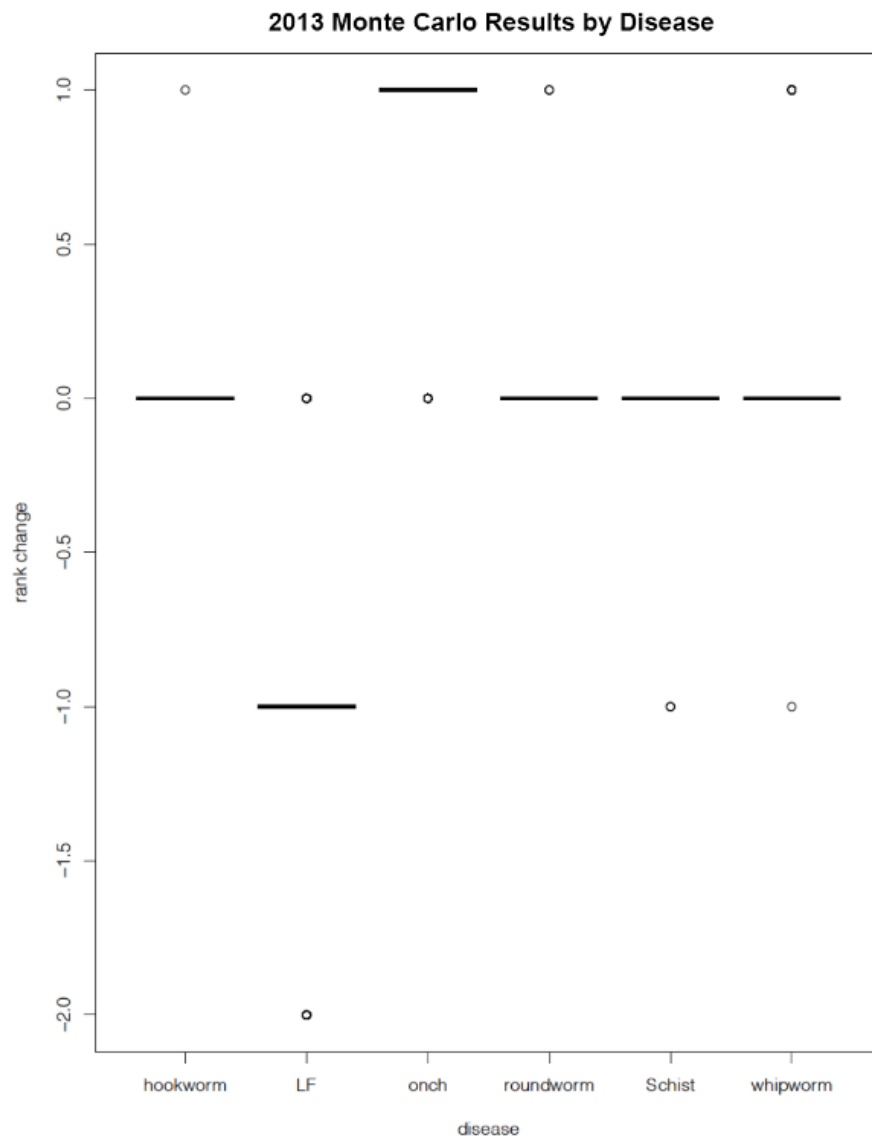


In 2015 all drugs, companies, and diseases had a stable ranking. This is shown in Figures S9, S10, and S11.

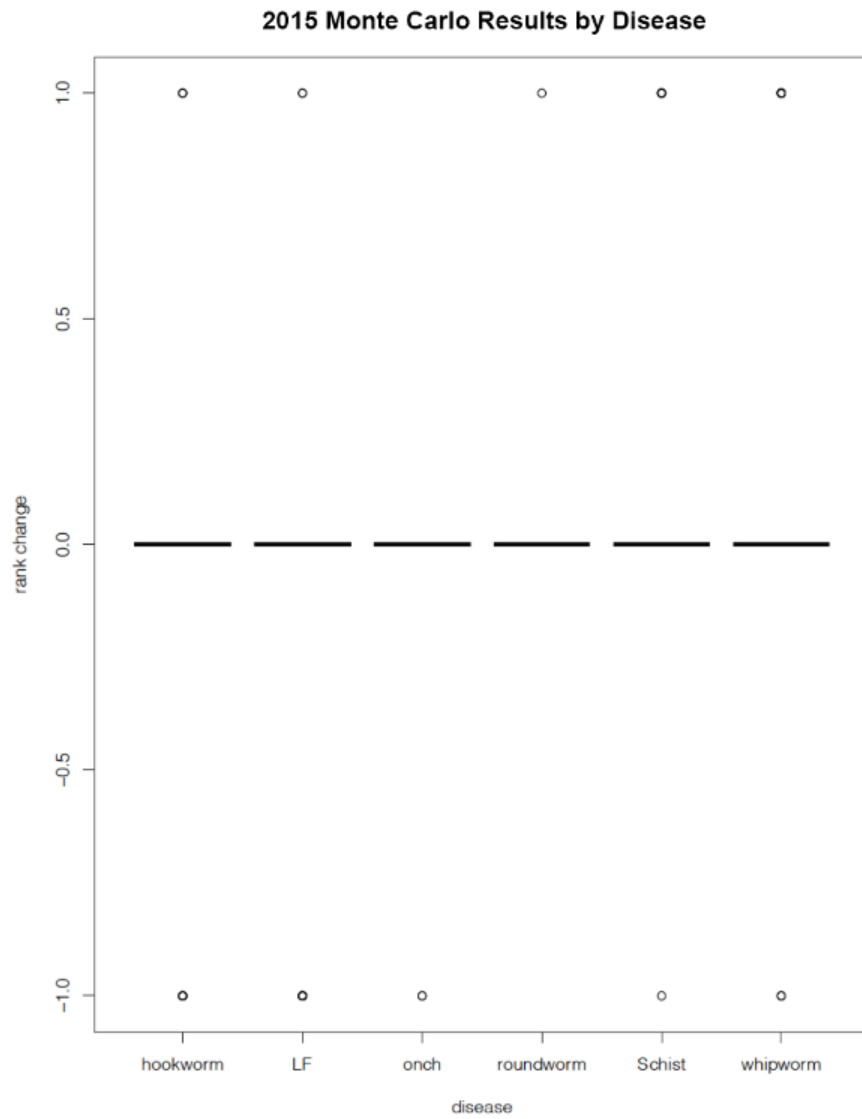
**Figure S9. Monte Carlo results by disease, 2010.** Changes in disease ranking in 2010. Note that schistosomiasis' rank tended to move down in 50% of cases.



**Figure S10. Monte Carlo results by disease, 2013.** Changes in disease ranking in 2013. Note that lymphatic filariasis and onchocerciasis changed rank by one negative and positive interval, respectively.



**Figure S11. Monte Carlo results by disease, 2015.** Changes in disease ranking in 2015. All



diseases held a stable ranking.

**Test #1 assumption tested:** Our model constrains the fallback data used to estimate treatment efficacy for NTDs to studies that took place before or during our model year. We tested different time constraints by removing all time constraints.

**Test #2 assumption tested:** In calculating lymphatic filariasis' impact score, the average regional treatment coverage of a drug is used as fallback data for that drug if treatment coverage data is not available for a country. When treatment coverage is not available for a given country, we assume it follows a beta distribution, with mean equal to global average and 0.05 variation.

**Test #3 assumption tested:** In calculating schistosomiasis's impact score, the average regional treatment coverage of a drug is used as fallback data for that drug if treatment coverage data is not available for a country. When treatment coverage is not available for a given country, we assume it follows a beta distribution, with mean equal to the global average and 0.05 variation.

**Test #4 assumption tested:** In calculating the impact score for soil-transmitted helminths, the average regional treatment coverage of a drug is used as fallback data for that drug if treatment coverage data is not available for a country. When efficacy data is not available for a given country, we assume it follows beta distribution, with mean equal to the regional or global average and 0.05 variation.

**Test #5 assumption tested:** Assumption tested: In calculating lymphatic filariasis impact score, the average regional or global efficacy of a drug is used as fallback data for that drug if efficacy data is not available for a country. When efficacy data is not available for a given country, we assume it follows a beta distribution, with mean equal to regional or global average and 0.05 variation.

**Test #6 assumption tested:** In calculating schistosomiasis's impact score, the average regional or global efficacy of a drug is used as fallback data for that drug if efficacy data is not available for a country. When efficacy data is not available for a given country, we assume it follows a beta distribution, with mean equal to the regional or global average and 0.05 variation.

**Test #7 assumption tested:** In calculating whipworm's impact score, the average regional or global efficacy of a drug is used as fallback data for that drug if efficacy data is not available for a country. When efficacy data is not available for a given country, we assume it follows a beta distribution, with mean equal to the regional or global average and 0.05 variation.

**Test #8 assumption tested:** In calculating hookworm's impact score, the average regional or global efficacy of a drug is used as fallback data for that drug if efficacy data is not available for a country. When efficacy data is not available for a given country, we assume it follows beta distribution, with mean equal to the regional or global average and 0.05 variation.

**Test #9 assumption tested:** In calculating roundworm's impact score, the average regional or global efficacy of a drug is used as fallback data for that drug if efficacy data is not available for a country. When efficacy data is not available for a given country, we assume it follows beta distribution, with mean equal to the regional or global average and 0.05 variation.

**Test #10 assumption tested:** Our model uses the average regional and then global treatment

coverage for an onchocerciasis drug as fallback data if that drug's treatment coverage data is not available for a given country. When treatment coverage is not available for a given country, we assume it follows a beta distribution, with mean equal to regional or global average and 0.05 variation.

**Test #11 assumption tested:** Our model uses the average regional and then global treatment efficacy for an onchocerciasis drug as fallback data if that drug's efficacy data is not available for a given country. When a drug's efficacy is not available for a given country, we assume the drug's efficacy follows a beta distribution, with mean equal to the regional or global average and 0.05 variation.

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## Supplementary figures

Figure S1. Intervention implementation in lymphatic filariasis endemic areas

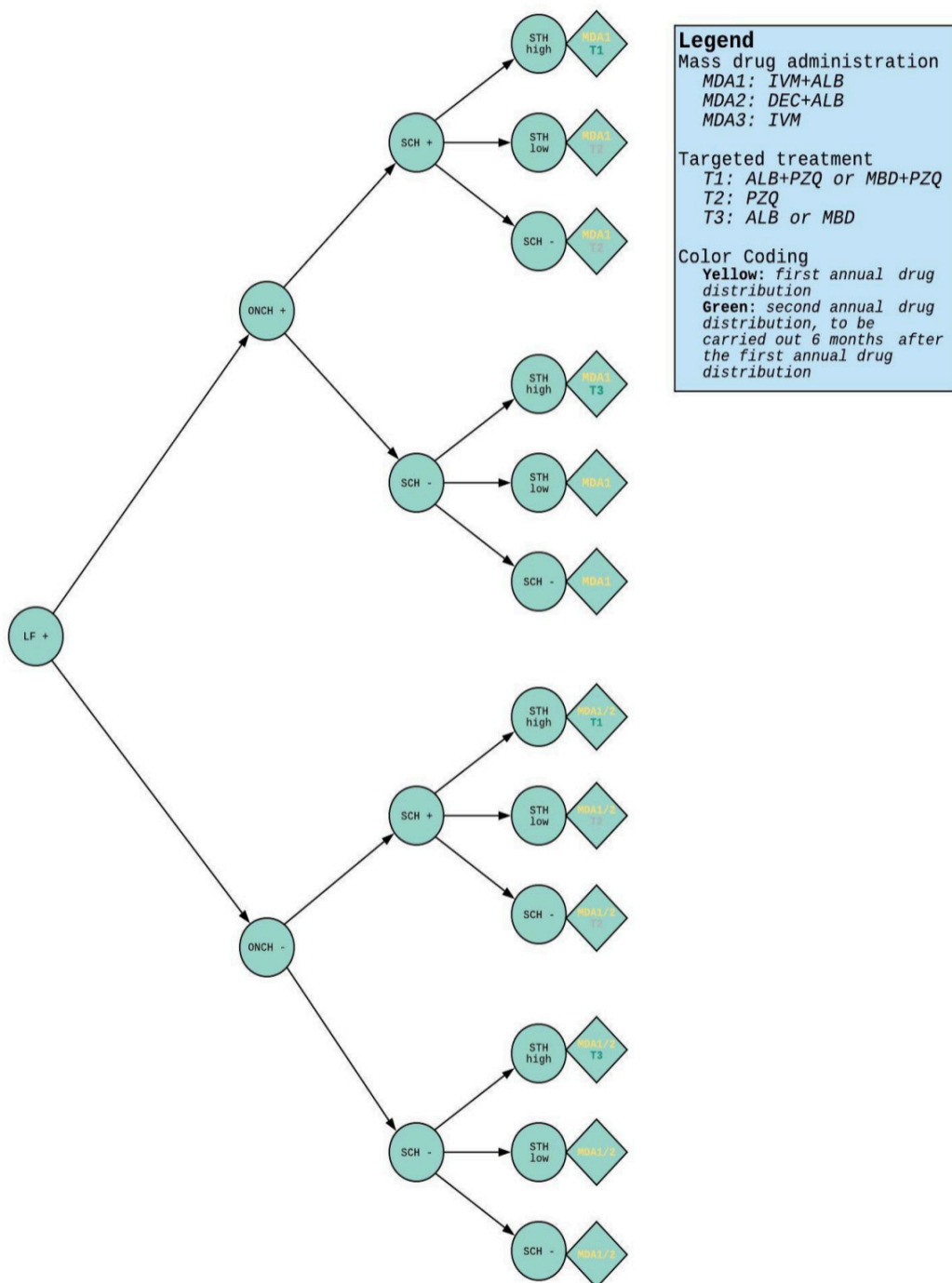


Figure S2. Intervention implementation in areas where lymphatic filariasis is not endemic

