HHS Public Access

Author manuscript

*J Travel Med*. Author manuscript; available in PMC 2025 August 03.

Published in final edited form as:

*J Travel Med*. 2024 August 03; 31(6): . doi:10.1093/jtm/taad054.

# Cost-effectiveness of treatment strategies for populations from strongyloidiasis high-risk areas globally who will initiate corticosteroid treatment in the United States

**Heesoo Joo, PhD**[1,*], **Brian A. Maskery, PhD**[1], **Jonathan D. Alpern, MD**[2,3], **Michelle Weinberg, MD**[1], **William M. Stauffer, MD**[1,3,4]

[1]Division of Global Migration and Quarantine, U.S. Centers for Disease Control and Prevention, Atlanta, GA, USA

[2]Infectious Disease Section, Minneapolis Veterans Affairs Health Care System, Minneapolis, MN, USA

[3]Department of Medicine, Infectious Diseases and International Medicine, University of Minnesota, Minneapolis, MN, USA

[4]Center for Global Health and Social Responsibility, University of Minnesota, Minneapolis, MN, USA

## Abstract

**Background:** The risk of developing strongyloidiasis hyperinfection syndrome appears to be elevated among individuals who initiate corticosteroid treatment. Presumptive treatment or treatment after screening for populations from *Strongyloides stercoralis*-endemic areas has been suggested before initiating corticosteroids. However, potential clinical and economic impacts of preventative strategies have not been evaluated.

**Methods:** Using a decision tree model for a hypothetical cohort of 1,000 individuals from *S. stercoralis*-endemic areas globally initiating corticosteroid treatment, we evaluated clinical and economic impacts of two interventions, “Screen and Treat” (i.e., screening and ivermectin treatment after a positive test), and “Presumptively Treat,” compared to current practice (i.e., “No Intervention”). We evaluated the cost-effectiveness (net cost per death averted) of each strategy using broad ranges of pre-intervention prevalence and hospitalization rates for chronic strongyloidiasis patients initiating corticosteroid treatment.

**Results:** For the baseline parameter estimates, “Presumptively Treat” was cost-effective (i.e., clinically superior with cost per death averted less than a threshold of $10.6 million per life) compared to “No Intervention” ($532,000 per death averted) or “Screen and Treat”

[*]Address: U.S. Centers for Disease Control and Prevention, 1600 Clifton Road NE, MS H16-4, Atlanta, GA 30329, USA; hjoo@cdc.gov.

Conflict of Interest: WS: reported receiving partial chapter royalties from UpToDate and an honorarium from Haymarket Education outside the submitted work and acting as a consultant for BCTPartners. None of these would be considered direct COI to this manuscript.

Disclaimer: The findings and conclusions in this article are those of the authors and do not necessarily represent the official position of the U.S. Centers for Disease Control and Prevention (CDC).

($39,000 per death averted). The two parameters contributing the most uncertainty to the analysis were the hospitalization rate for individuals with chronic strongyloidiasis who initiate corticosteroids (baseline 0.166%) and prevalence of chronic strongyloidiasis (baseline 17.3%) according to a series of one-way sensitivity analyses. For hospitalization rates greater than 0.022%, "Presumptively Treat" would remain cost-effective. Similarly, "Presumptively Treat" remained preferred at prevalence rates of 4% or above; "Screen and Treat" was preferred for prevalence between 2% and 4%, and "No Intervention" was preferred for prevalence less than 2%.

**Conclusions:** The findings support decision-making for interventions for populations from *S. stercoralis* endemic areas before initiating corticosteroid treatment. Although some input parameters are highly uncertain and prevalence varies across endemic countries, "Presumptively Treat" would likely be preferred across a range for many populations given plausible parameters.

### Keywords

cost-effectiveness; strongyloidiasis; corticosteroid; presumptive treat; treatment strategies

## Introduction

Infections caused by the nematode parasite *Strongyloides stercoralis* are rare in the United States, with an estimated prevalence rate of only 0.01%.[1] Most U.S. cases have been reported among refugees and immigrants who migrated from *S. stercoralis* endemic areas, such as Southeast Asia, South America and sub-Saharan Africa.[2, 3] A recent review reported an average strongyloidiasis seroprevalence among migrants of 12.2%.[4] However, the prevalence of strongyloidiasis among specific populations can be much higher. For example, the prevalence of strongyloidiasis among Sudanese refugees resettled in the U.S. was 46%.[5]

Unlike other nematode infections, the eggs of *Strongyloides* may hatch into filariform larvae in the intestines and directly autoinoculate the infected individual, without an environmental stage, allowing a chronic infection that can last decades even outside an endemic area.[6, 7] Most patients with chronic strongyloidiasis are asymptomatic, although they may experience symptoms including skin rash (e.g., cutaneous larva migrans), abdominal (e.g., vomiting, diarrhea, constipation), or respiratory symptoms.[8–10] Although rare, patients may develop disseminated strongyloidiasis or hyperinfection syndrome (or both simultaneously), especially among people with immunodeficiency, which has a high fatality rate, even with treatment.[8, 10–12] Compared to other intestinal parasite infections among immigrant populations in the United States, *S. stercoralis* has been reported to result in the greatest medical costs, morbidity, and loss of life.[13, 14]

Corticosteroid use is the most commonly associated risk factor for developing disseminated strongyloidiasis or hyperinfection syndrome in *Strongyloides*-infected individuals, as it suppresses the immune system.[6, 12] Among patients admitted to the intensive care unit of tertiary hospitals with strongyloidiasis hyperinfection between 2000 and 2013, 83.5% reported oral corticosteroid treatment at a median dose of 40 mg per day.[15] To avoid serious disease and fatal outcomes, presumptive treatment or screening and treatment for populations from *S. stercoralis*-endemic areas prior to initiating immunosuppressant

therapy, particularly corticosteroid treatment, has been suggested in various settings.[6, 16–18] In addition, chronic strongyloidiasis is often misdiagnosed.[19] Some patients with chronic strongyloidiasis have been misdiagnosed with asthma and prescribed corticosteroids, resulting in adverse health outcomes.[20]

The cost-effectiveness (CE) of these strategies for individuals from *S. stercoralis*-endemic areas and initiating corticosteroids in the United States has yet to be evaluated due to the many unknowns and the complexity of modelling. Although several barriers exist, the primary difficulty is that the probability that a patient with chronic strongyloidiasis who initiates corticosteroids will develop disseminated disease or hyperinfection syndrome has not been previously reported and remains uncertain.

This study provides estimates of the potential costs and health impacts of two preventative interventions, “Screen and Treat” (i.e., screening and ivermectin treatment after a positive test), and “Presumptively Treat” with ivermectin, compared to the current practice (i.e., “No Intervention”) for a hypothetical cohort of 1000 individuals being initiated on corticosteroid treatment in the United States. Since the number of chronic strongyloidiasis patients initiating corticosteroids who would develop disseminated strongyloidiasis or hyperinfection syndrome and be hospitalized is unknown, we estimated a baseline hospitalization rate and conducted a sensitivity analysis to examine how the change in that rate would affect the CE of preventative strategies. We also estimated the CE of preventative strategies over a range of pre-intervention prevalence rates. This is a population-based analysis to guide public health policy and is not intended to provide guidance for individual patient-level decision-making, which must consider specific geographic exposures, patient social determinants, and other factors such as previous treatment into consideration when recommending screening and/or presumptive treatment.

## Material and methods

This study’s target population was a hypothetical cohort of 1,000 individuals who have lived in *S. stercoralis*-endemic areas and will initiate corticosteroid treatment. The cost and epidemiological parameters (baseline values, upper and lower bounds) and data sources are presented in Table 1. We used the Merative® MarketScan® Commercial Database (Merative®, Ann Arbor, MI) with an online tool MarketScan® Treatment Pathways to estimate the cost parameters, which were adjusted to 2019 US dollars. More details about the methodology to estimate costs are available in the Appendix 1. Epidemiological parameters were estimated from values reported in the literature. We assumed the individuals in the cohort were either infected with *S. stercoralis* or uninfected depending on the assumed pre-intervention prevalence (baseline: 17.3%, range: 4.1%–32%).[4] The baseline prevalence estimate and uncertainty range were based on reported prevalence estimates among migrants born in east Asia and the Pacific from a recent meta-analysis.[4]

A decision tree model was developed to evaluate three strategies, “No Intervention” and two preventative strategies before initiating corticosteroid treatment, “Screen and Treat” and “Presumptively Treat” (Appendix Figure 1). We assumed that all individuals in the hypothetical cohort would have corticosteroid treatment recommended at an initial

outpatient visit in all three arms of the decision tree (i.e., “Screen and Treat,” “Presumptively Treat,” and “No Intervention”).

“No Intervention” arm is the status quo in which a target cohort would initiate corticosteroid treatment without any preventive strategy. After which, some chronic strongyloidiasis patients would develop severe disease resulting in hospitalization. A previously reported estimate of the annual strongyloidiasis hospitalization rate (0.0029%)[21] was calculated for all chronic strongyloidiasis patients without consideration of corticosteroid treatment. Among the general U.S. population, the proportion of individuals who receive corticosteroid treatment is approximately 1.46% annually.[22] Assuming that 1.46% of individuals with chronic strongyloidiasis would initiate corticosteroid treatment in a given year and that 83.5% of hospitalized patients had recently initiated corticosteroid treatment,[15] we estimated a baseline hospitalization rate of 0.166% for chronic strongyloidiasis patients who initiate corticosteroid treatment. More information is provided in the Appendix 2. The baseline cost of hospitalization associated with severe disease was estimated using inpatient payments associated with primary and non-primary diagnoses of strongyloidiasis $172,084 per patient (range: $20,569-$288,383) from the MarketScan® Commercial Database.[23] The case fatality rate among those with severe disease was estimated at 16.7% (range: 8.5%–64.3%).[12, 14, 24]

The “Screen and Treat” strategy included screening during the initial outpatient visit. The time required for screening would increase the complexity of the initial outpatient visit, and would result in additional costs (baseline:$20, range:$0-$40.25).[25] In addition, costs of strongyloidiasis serologic testing, the method of screening in this analysis, were estimated at $25.79 (range: $10.89-$35).[25] We assumed that 20% (range: 15%–25%) of individuals with positive test results would make a second outpatient visit to follow up the results and receive a prescription, which resulted in an additional cost of $32.97 (range: $19.98-$39).[25]

We assumed that the serologic screening test had a sensitivity of 92.3% (range: 87.7%–96.9%) and specificity of 97.4% (range: 95.5%–99.3%)[26] and that some individuals had false negative or false positive test results. Individuals with false negative test results would undergo the same disease progression route as individuals with chronic strongyloidiasis in the “No Intervention” arm of the decision tree. Patients diagnosed with chronic strongyloidiasis (both true positive and false positive) would be offered treatment with ivermectin before initiating corticosteroid treatment. Some individuals with true positive results would remain infected because of nonadherence to the ivermectin regimen or because they failed ivermectin treatment. We assumed that 90% of those with positive test results (range: 80%–100%) were treated with ivermectin. The baseline cost estimate for ivermectin treatment was $40.66 with a range of $24.69-$52.67 based on reported payments.[23] We used an estimated drug efficacy of ivermectin against strongyloidiasis of 84% (range: 72%–98%)[13], and assumed the treatment would not cure 16% of infected individuals. After initiating corticosteroid treatment, we assumed some uncured chronic strongyloidiasis patients (baseline estimate: 0.166%, range: 0.0029%–2%) would develop severe disease and be hospitalized.

Ivermectin treatment would be offered to all individuals in the cohort before initiating corticosteroid treatment for the “Presumptively Treat” strategy. Ivermectin is considered

safe with a low adverse event profile.[6] A single dose of oral ivermectin treatment for 1–2 days is the recommended first line therapy for strongyloidiasis patients.[27] Consistent with assumptions for the "Screen and Treat" strategy, patients would spend extra time during their initial outpatient visit to receive an explanation of ivermectin treatment. This would result in a charge for a higher-level outpatient visit with additional average costs (baseline:$20, range:$0-$40.25) for some patients.[25] Because we assumed that 10% (range: 0%–20%) of the cohort would choose not to fill the prescription, 90% of the cohort would be treated with ivermectin (baseline ivermectin cost estimate: $40.66, range: $24.69-$52.67).[25] Some individuals in the cohort would remain infected because of nonadherence to ivermectin or treatment failure and could develop severe disease resulting in hospitalization.

The time horizon for this analysis was one year. We assumed that if chronic strongyloidiasis patients developed severe symptoms, all costs associated with hospitalization would occur during the first year after initiation of corticosteroid treatment. The median time from initiation of corticosteroids to the onset of strongyloidiasis hyperinfection syndrome reported in a case series was 42 days.[15] Our analysis used a healthcare provider perspective.

For each strategy, we reported health outcomes including the numbers of chronic strongyloidiasis patients before and after interventions, numbers of deaths associated with strongyloidiasis, and total cost estimates, including intervention and hospitalization costs. For the economic evaluation, comparisons between an intervention and a defined alternative (comparator) were reported as numbers of deaths averted, incremental costs, and incremental cost-effectiveness ratio (ICER). A defined alternative could be either "No Intervention" or the next best strategy. For instance, the next best strategy for "Screen and Treat" is "Presumptively Treat." The ICER was defined as the incremental cost between two strategies divided by the difference in health outcomes (i.e., averted deaths), reported as 2019 U.S. dollars per death averted. We chose the central value of the Value per Statistical Life (VSL) recommended by the Department of Health and Human Services (HHS) in 2019 ($10.6 million) as the willingness to pay (WTP) threshold such that interventions with ICERs less than this VSL estimate were considered cost-effective.[28] Interventions resulting in net cost savings (i.e., negative incremental cost) and improvements in health outcomes were considered dominant relative to comparators.

We conducted one-way sensitivity analyses by adjusting key input parameters one by one according to the reported lower and upper bound values in Table 1 to evaluate the impact of each input parameter on estimated ICERs and to test the robustness of models. The results were presented using tornado diagrams. In addition, we summarized how the changes in strongyloidiasis prevalence rates before intervention and hospitalization rates of strongyloidiasis patients after corticosteroid treatment would affect the CE of preventative strategies. More information about the evaluation methodology is available in the Appendix 3.

## Results

Using baseline parameters, including a prevalence rate of 17.3%, a hospitalization rate of 0.166% for individuals with chronic strongyloidiasis who initiate corticosteroid treatment,

and a case fatality rate of 16.7% among hospitalized patients, a total of 173 individuals in the cohort would be expected to be infected with strongyloidiasis per 1,000 people who have lived in *S. stercoralis*-endemic areas and will initiate corticosteroid treatment. The "No Intervention" strategy would result in 0 cured patients, 173 with chronic strongyloidiasis, and 0.05 deaths (see Table 2). "Screen and Treat" would result in 121 cured individuals, 52 with chronic strongyloidiasis, and 0.014 deaths. "Presumptively Treat" would result in 131 cured individuals, 42 with chronic strongyloidiasis, and 0.012 deaths. "No Intervention" had zero intervention costs and $49,376 in hospitalization costs. "Screen and Treat" had an intervention cost of $53,616 and $14,918 for hospitalization costs. "Presumptively Treat" had an intervention cost of $56,594 and $12,048 for hospitalization.

The estimated numbers of deaths averted, incremental costs, and ICERs with baseline input parameters are shown in Table 3. "Screen and Treat" and "Presumptively Treat" averted 0.033 and 0.036 deaths, respectively, compared to "No intervention." "Presumptively Treat" averted 0.003 deaths compared to "Screen and treat." The incremental costs of "Screen and Treat" and "Presumptively Treat" compared to "No Intervention" were roughly equivalent: $19,158 and $19,266, respectively. The incremental cost of "Presumptively Treat" compared to "Screen and Treat" was $108. The estimated ICERs of "Screen and Treat" and "Presumptively Treat" compared to "No Intervention" were $572,900 per death averted and $531,821 per death averted, respectively. The estimated ICER of "Presumptively Treat" compared to "Screen and Treat" was $38,715 per death averted. These ICER estimates compare favorably to the HHS-recommended WTP of $10.6 million per averted statistical death; "Presumptively Treat" and "Screen and Treat" would both be considered cost-effective compared to "No intervention." "Presumptively Treat" was more cost-effective than "Screen and treat."

The one-way sensitivity analyses (tornado diagrams) showed that hospitalization rate and prevalence of strongyloidiasis were the most important parameters contributing to uncertainty in ICER estimates (Figure 1 and Appendix Figure 2). All negative ICERs reported in Figure 1 and Appendix Figure 2 were associated with a comparison in which cost savings (i.e., negative incremental costs) and positive incremental health outcomes (i.e., averted more deaths) were achieved. Thus, all instances where negative ICER values were reported would correspond to strategy comparisons in which the comparator was dominated. For instance, when we compared "Screen and Treat" to "No Intervention," the ICER varied from $90.7 million per averted death to a negative value when the hospitalization rate among those with strongyloidiasis who initiate corticosteroids was varied from 0.0029% to 2%.

"Presumptively Treat" was consistently the preferred strategy for most of the ranges of plausible values used for each input parameter, except for hospitalization rate and prevalence. We separately estimated cost-effective and dominant threshold values for these two parameters for which our models were most sensitive (Appendix 3, and Appendix Tables 2–3). When holding all other estimates at baseline values, "Presumptively Treat" would be the preferred strategy at hospitalization rates ≥0.022%. Otherwise, "No Intervention" would be preferred. In other words, neither "Screen and Treat" nor "Presumptively Treat" would be cost-effective compared to "No Intervention" for hospitalization rates lower than 0.022%.

Using the baseline hospitalization rate of 0.166%, neither “Screen and Treat” nor “Presumptively Treat” would be considered cost-effective compared to “No Intervention” for populations with pre-intervention prevalence rates below 2.1% (Table 4 and Appendix Tables 2–3). “Screen and Treat” would be the preferred strategy with prevalence between 2.1% and 4.3%. “Presumptively Treat” would be preferred at prevalence rates of 4.3% or above.

## Discussion

In our analyses, we evaluated the implementation of strategies to prevent severe disease in cohorts who have lived in *S. stercoralis*-endemic areas and will initiate corticosteroid treatment in the U.S. compared to no intervention. Using conservative baseline parameters, “Presumptively Treat” would be preferred to either “No Intervention” or “Screen and Treat.” The estimated ICER for “Presumptively Treat” versus “No Intervention” was $0.5 million per death averted. Further, the estimated ICER for “Presumptively Treat” versus “Screen and Treat” was only $38,715 per death averted at the baseline prevalence of 17.3%. These ICER estimates are much less than the lower bound of recommended VSL of $5 million per statistical death averted in 2019.[28]

Given a relative paucity of strongyloidiasis outcome data for the United States, we attempted to use conservative baseline parameter assumptions including relatively low prevalence rates and case fatality rates. In general, CE would be improved by targeting populations from regions where strongyloidiasis prevalence is highest or if the hospitalization rate among individuals with chronic strongyloidiasis who initiate corticosteroids is higher than our relatively conservative estimates.

Since the hospitalization rate is uncertain, the use of prevalence rate for selection of strategy is most useful. A recent review reported average prevalence rates among migrants from South Asia (4.9%), Middle East and North Africa (5.5%), Latin America and the Caribbean (11.4%), sub-Saharan Africa (14.6%), and East Asia and the Pacific (17.3%)[4] were greater than 4% for which the preferred strategy would be “Presumptively Treat.” “Screen and Treat” was only preferred to “Presumptively Treat” for populations with low strongyloidiasis prevalence (2–4%). For populations with prevalence below 2% the ICER would exceed $10.6 million for both intervention strategies and “No Intervention” would be preferred. The average seroprevalence rate among migrants from eastern Europe and central Asia is less than 2%.[4] The heterogeneity of prevalence within these geographic areas may need to be considered.

The aim of this publication is to provide a population-based analysis to guide public health policy and is not intended to inform individual patient-level decision-making. When an approach is being considered for an individual patient, factors such as specific geographic exposure, including migration route, and urban vs. rural living, as well as other social determinants, such as occupation, socio-economic status, and living conditions, must be considered. Additional factors such as availability of serologic testing, access to ivermectin, and time and continuity of care may need to be considered in preventive strategies.[29] For example, “Screen and Treat” takes additional time for follow-up, which may result in delays

in corticosteroid treatment compared to “Presumptively Treat.” Also, certain individuals from *S. stercoralis*-endemic areas such as most refugees arriving through the U.S. Refugee Resettlement Program may have received ivermectin treatment for strongyloidiasis. This program began in 2011 and if an individual arrived through this program, ideally they would have a medical record indicating treatment.[30] In addition, although serious adverse effects are extremely rare for the ivermectin dosage recommended for treating strongyloidiasis, there are no published estimates of how commonly adverse events occur or their associated costs. Presumptive ivermectin should not be used in individuals less than 15 kg, in pregnant or lactating women, or in persons at risk of *Loa loa* infection without ruling out microfilaria (encephalitis has been reported among individuals treated with ivermectin who have a high *Loa loa* microfilarial load).[27]

This study has limitations. First, since we chose a healthcare provider perspective, we did not account for any disutility associated with chronic strongyloidiasis or non-medical costs. Our ICER estimates were conservative because we did not account for the potential benefits of averting less severe symptoms that would not result in hospitalization or the potential reduced risk of hospitalization occurring in subsequent years. Second, because we used payments for commercially-insured patients, the relative CE of interventions for patients with Medicare or Medicaid may be less than for patients with private insurance. Third, the program costs did not include any implementation costs, such as training or development of clinical protocols. Fourth, the benefit of treating other parasitic infections for which ivermectin is effective, such as ascariasis, trichuriasis, or scabies was not considered. In addition, the risk associated with *Loa loa* infection is limited to patients from West or Central Africa and we did not calculate additional costs associated with screening, diagnosis or treatment of patients who may have previous exposure to *Loa loa* in this analysis.[31] Next, although we tested the robustness of our results using one-way sensitivity analyses, we did not consider the combined effect of varying input variables simultaneously in the model. Some assumptions that are far off may also affect the recommended strategies. “Presumptively Treat” would not be a dominant strategy if the hospitalization rate is lower than 0.022% or for populations with prevalence rates lower than 4.3%. The “Screen and Treat” strategy would provide more certainty around prevalence rates within different populations. Last, the hospitalization rate, case fatality rate for hospitalized patients, and prevalence are highly uncertain. We tried to address this limitation by using conservative estimates and wide ranges to assess the robustness of models in sensitivity analyses.

## Conclusions

Our findings provide a benchmark to consider intervention strategies for cohorts from *S. stercoralis*-endemic areas before initiating corticosteroid treatment in the United States. “Presumptively Treat” was identified as a cost-effective strategy compared to “No Intervention” and “Screen and Treat” with the baseline values for pre-intervention prevalence (17.6%), case fatality rate (16.7%), and hospitalization rate for patients with chronic strongyloidiasis who initiate corticosteroid treatment (0.166%). The main determinants of CE were hospitalization rate and pre-intervention prevalence. At the baseline prevalence rate (17.6%), “Presumptively Treat” would be the preferred strategy if more than 22 hospitalizations per 100,000 individuals with chronic strongyloidiasis who

initiate corticosteroid treatment would occur. Using our estimated baseline hospitalization rate (16.6 hospitalizations per 10,000 individuals with chronic strongyloidiasis who initiate corticosteroid treatment), “Presumptively Treat” was the preferred strategy at pre-intervention prevalence rates of 4% or above. Greater prevalence rates have been reported among immigrants from South Asia, Middle East, North Africa, Latin America, the Caribbean, sub-Saharan Africa, East Asia, and the Pacific.

## Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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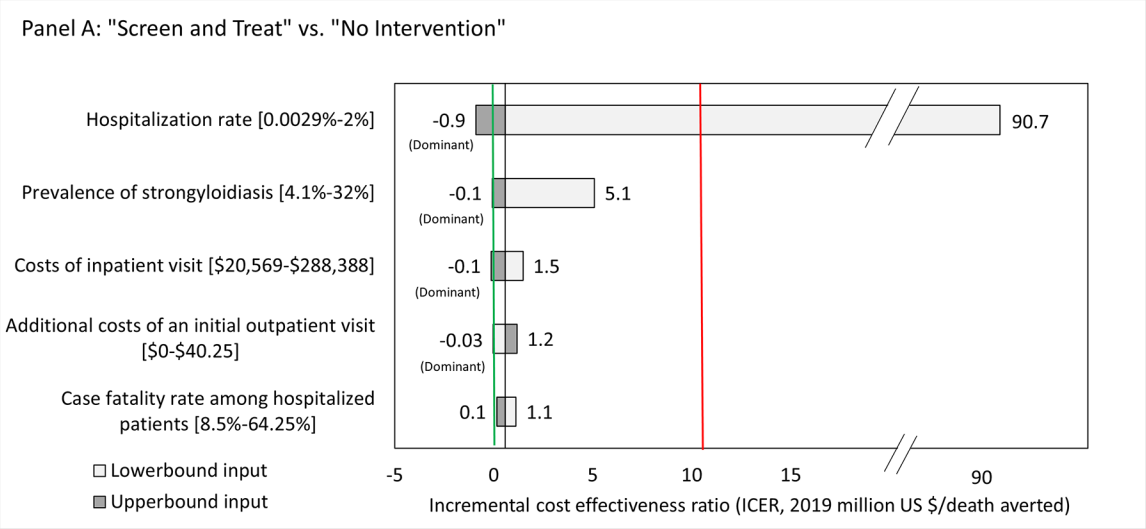


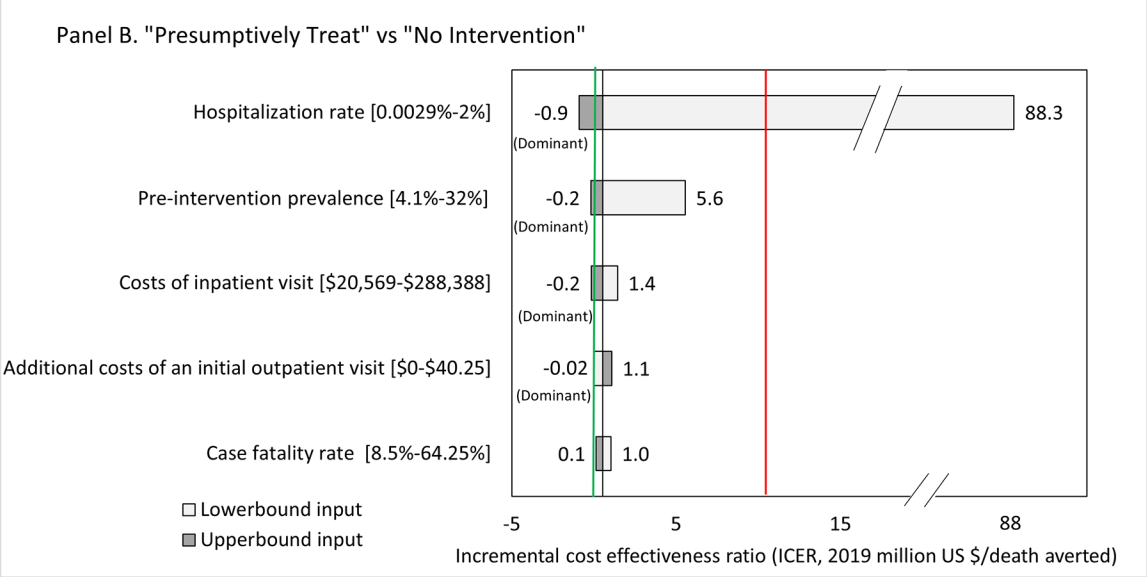

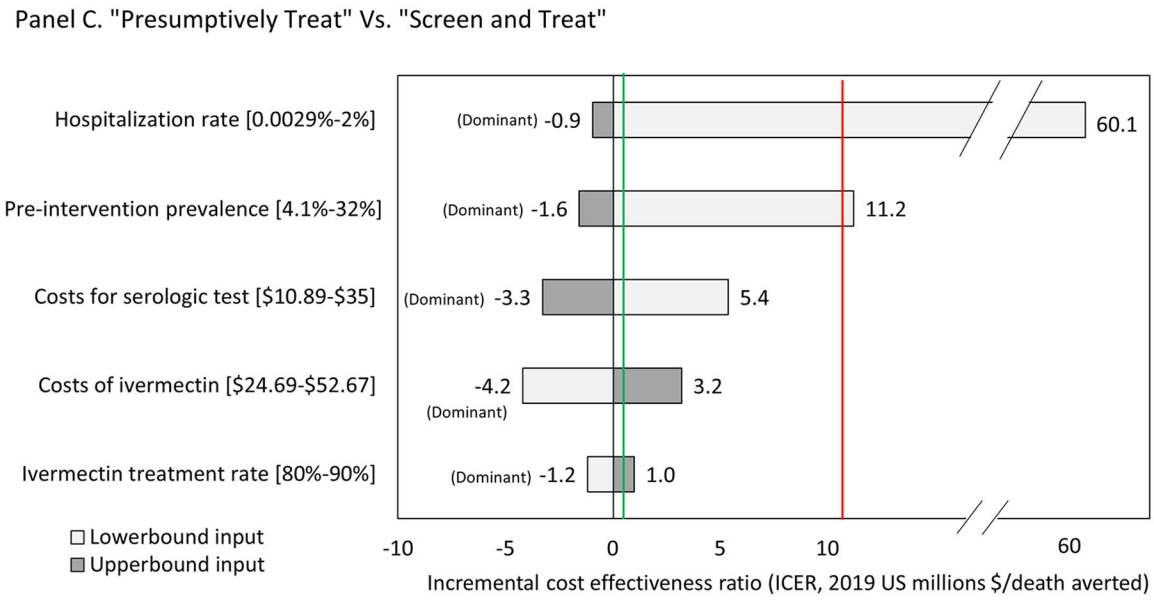


**Figure 1.**

One-way sensitivity analyses for incremental cost-effectiveness ratios (ICERs) (2019 US dollars per death averted).

"Screen and Treat" vs. "No Intervention"

Notes: The black, red, and green vertical lines represent the baseline ICER, the cost-effectiveness threshold (i.e., $10.6 million per statistical life), and the zero ICER, respectively. The width of horizontal bars showed the change in ICER when each input parameter was varied over the lower and upper bound estimates. All negative values (i.e., the portions of horizontal bars on the left side of the green vertical line) indicate that "Screen and Treat" is a dominant strategy (i.e., achieves net cost savings [negative incremental costs] and averts more deaths) compared to "No Intervention." The portions of horizontal bars between the green and red vertical lines indicate that "Screen and Treat" is a cost-effective strategy (i.e., averts more deaths at an incremental cost per statistical death less than the threshold value) compared to "No Intervention." The portions of horizontal bars on the right side of the red vertical line represent that "Screen and Treat" is not a cost-effective strategy (i.e., averts more deaths at an incremental cost per statistical death greater than the threshold value) compared to "No Intervention." The figure focuses on the parameters with the greatest effect on this ICER; the effects of additional parameters is shown in Appendix Figure 2.

"Presumptively Treat" vs. "No Intervention"

Notes: The black, red, and green vertical lines represent the baseline ICER, the cost-effectiveness threshold (i.e., $10.6 million per statistical life), and the zero ICER, respectively. The width of horizontal bars showed the change in ICER when each input parameter was varied over the lower and upper bound estimates. All negative values (i.e., the portions of horizontal bars on the left side of the green vertical line) indicate that "Presumptively Treat" is a dominant strategy (i.e., achieves net cost savings [negative incremental costs] and averts more deaths) compared to "No Intervention." The portions of horizontal bars between the green and red vertical lines indicate that "Presumptively Treat"

is a cost-effective strategy (i.e., averts more deaths at an incremental cost per statistical death less than the threshold value) compared to “No Intervention.” The portions of horizontal bars on the right side of the red vertical line represent that “Presumptively Treat” is not a cost-effective strategy (i.e., averts more deaths at an incremental cost per statistical death greater than the threshold value) compared to “No Intervention.” The figure focuses on the parameters with the greatest effect on this ICER; the effects of additional parameters is shown in Appendix Figure 2.

“Presumptively Treat” vs. “Screen and treat”

Notes: The black, red, and green vertical lines represent the baseline ICER, the cost-effectiveness threshold (i.e., $10.6 million per statistical life), and the zero ICER, respectively. The width of horizontal bars showed the change in ICER when each input parameter was varied over the lower and upper bound estimates. All negative values (i.e., the portions of horizontal bars on the left side of the green vertical line) indicate that “Presumptively Treat” is a dominant strategy (i.e., achieves net cost savings [negative incremental costs] and averts more deaths) compared to “Screen and Treat.” The portions of horizontal bars between the green and red vertical lines indicate that “Presumptively Treat” is a cost-effective strategy (i.e., averts more deaths at an incremental cost per statistical death less than the threshold value) compared to “Screen and Treat.” The portions of horizontal bars on the right side of the red vertical line represent that “Presumptively Treat” is not a cost-effective strategy (i.e., averts more deaths at an incremental cost per statistical death greater than the threshold value) compared to “Screen and Treat.” The figure focuses on the parameters with the greatest effect on this ICER; the effects of additional parameters is shown in Appendix Figure 2.

**Table 1:**

Cost and epidemiological input parameters for evaluating strongyloidiasis treatment strategies in a hypothetical cohort of 1,000 individuals from *Strongyloides stercoralis* endemic areas who initiate corticosteroid treatments

| | Baseline | Range | Data source |
|---|---|---|---|
| **Cost parameters (2019 $)** [1] | | | |
| Marginal increase in cost for an initial outpatient visit to discuss a chronic strongyloidiasis intervention (screen and treat; or ivermectin presumptive treatment) | $20 | [$0–$40.25] | MarketScan Commercial Database 2019 Set B – 10 million subsample[25] |
| Costs for strongyloidiasis serologic tests | $25.79 | [$10.89–$35.00] | MarketScan Commercial Database 2019 Set B[25] |
| Costs of an additional outpatient visit for a patient with positive serologic test results (Screen and treat) | $32.97 | [$19.98–$39.00] | |
| Proportion of patients who require a second outpatient visit due to positive serologic test results | 20% | [15%–25%] | Assumption |
| Costs of ivermectin treatment | $40.66 | [$24.69–$52.67] | MarketScan Commercial 2014–2020 Set B[23] |
| Costs of hospitalization associated with severe disease[2] | $172,084 | [$20,569–$288,383] | |
| **Epidemiological parameters** | | | |
| Baseline infection seroprevalence (before intervention) | 17.3% | [4.1%–32.0%] | Asundi et al. 2019[4] |
| Sensitivity of strongyloidiasis serologic test | 92.31% | [87.73%–96.86%] | Bisoffi et al. 2014[26] |
| Specificity of strongyloidiasis serologic test | 97.40% | [95.50%–99.30%] | Bisoffi et al. 2014[26] |
| Probability of filling ivermectin prescription | 90% | [80%–100%] | Assumption |
| Efficacy of ivermectin against strongyloidiasis | 84% | [72%–98%] | Henriquez-Camacho et al. 2016[32] |
| Hospitalization rates of strongyloidiasis patients after corticosteroid treatment | 0.166% | [0.0029%–2%] | Estimated (See Appendix)<br>Maskery et al. 2016 |
| Case fatality rate of strongyloidiasis among hospitalized patients | 16.7% | [8.5%–64.25%] | NIS 2016–2020[24]<br>Muennig et al. 1999[14]<br>Buonfrate et al. 2013[12] |

Abbreviations: IVD-ELISA, IVD Research Inc. Enzyme-Linked Immunosorbent Assay; NIS, National Inpatient Sample from Healthcare Cost and Utilization Project (HCUP)

[1] All economic parameters are costs per person.

[2] Costs of hospitalization associated with severe disease were estimated by using inpatient payments associated with primary and non-primary diagnosis of strongyloidiasis.

**Table 2:**

Estimated health outcomes and costs of each strategy with a hypothetical cohort of 1,000 individuals from *Strongyloides stercoralis* endemic areas who initiate corticosteroid treatments

| | No Intervention | Screen and Treat | Presumptively Treat |
|---|---|---|---|
| **Health outcomes** | | | |
| Hypothetical target cohort population, (a) | 1,000 | | |
| Number of chronic strongyloidiasis patients before intervention, (b)=(a)× 17.3%[1] | 173 | | |
| Number of patients cured by intervention, (c) | 0 | 121 | 131 |
| Number of patients with chronic strongyloidiasis after intervention, (d)=(b)–(c) | 173 | 52 | 42 |
| Number of patients with chronic strongyloidiasis who develop severe disease requiring hospitalization after initiating corticosteroid treatment, (e)=(d) × 0.166%[2] | 0.287 | 0.087 | 0.070 |
| Number of deaths among patients hospitalized with strongyloidiasis, (f)=(e) ×16.7%[3] | 0.048 | 0.014 | 0.012 |
| **Costs** | | | |
| Cost of intervention, (g) | $0 | $53,616 | $56,594 |
| • Marginal costs during initial outpatient visit | $0 | $45,790 | $20,000 |
| • Costs of follow-up outpatient visits for those with positive serologic test results | $0 | $1,195 | $0 |
| • Ivermectin treatment costs | $0 | $6,631 | $36,594 |
| Cost of treating hospitalized strongyloidiasis patients, (h)= $172,084 × (e) | $49,376 | $14,918 | $12,048 |
| Total cost, (i)=(g)+(h) | $49,376 | $68,534 | $68,642 |

[1]The baseline strongyloidiasis prevalence rate (17.3%) was used to estimate clinical outcomes and costs of each strategy. The lower bound (4.1%) and the upper bound (32%) were evaluated in sensitivity analyses.

[2]The baseline hospitalization rate (0.166%) was used to estimate clinical outcomes and costs of each strategy. The lower bound (0.0029%) and the upper bound (2%) were evaluated in sensitivity analyses.

[3]The baseline case fatality rate of strongyloidiasis patients who were hospitalized (16.7%) was used to estimate numbers of deaths. The lower bound (8.5%) and upper bound (64.25%) were evaluated in sensitivity analyses.

**Table 3:**

Changes in health outcomes, incremental costs, and incremental cost-effectiveness ratios (ICER) for a hypothetical cohort of 1,000 persons from *S. stercoralis*-endemic areas who initiate corticosteroid treatment for chronic strongyloidiasis patients

| | **"Screen and Treat" vs. "No Intervention"** | **"Presumptively Treat" vs. "No Intervention"** | **"Presumptively Treat" vs. "Screen and Treat"** |
|---|---|---|---|
| **Changes in health outcomes** | | | |
| Incremental number of chronic strongyloidiasis patients effectively treated prior to initiating corticosteroid treatment, (a)[1] | 121 | 131 | 10 |
| Incremental number of strongyloidiasis hospitalizations averted, (b) | 0.200 | 0.217 | 0.017 |
| Incremental number of strongyloidiasis deaths averted, (c)[2] | 0.033 | 0.036 | 0.003 |
| **Incremental costs, 2019 US dollar** | | | |
| Incremental cost of intervention, (d) | $53,616 | $56,594 | $2,978 |
| Incremental cost of treating hospitalized strongyloidiasis patients, (e) | −$34,458 | −$37,328 | −$2,871 |
| Incremental cost, (f)=(d)+(e) | $19,158 | $19,266 | $108 |
| **ICER, incremental cost per death averted** | | | |
| ICER, (g)=(f)/(c) | $572,900 | $531,821 | $38,715 |

[1]These estimates are calculated from the difference in numbers of deaths from row (c) in Table 2. Baseline strongyloidiasis prevalence rate (17.3%) was used. The lower bound is 4.1% and the upper bound is 32%.

[2]The baseline hospitalization rate (0.166%) was used to estimate numbers of hospitalizations. The lower bound is 0.0029% and the upper bound was 2%.

[3]The baseline case fatality rate of strongyloidiasis patients who were hospitalized (16.7%) was used to estimate numbers of deaths. The lower bound was 8.5% and the upper bound was 64.25%.

**Table 4:**

Preferred strategies by strongyloidiasis prevalence rate before intervention

| Range of prevalence rates for which each strategy is preferred | Region with reported prevalence rates within each range from Asundi et al. 2019 | Preferred strategy |
|---|---|---|
| <2.1% | Eastern Europe and central Asia (0%) | No Intervention |
| ≥2.1% and <4.3% | N/A | Screen and Treat |
| ≥4.3% | South Asia (4.9%)<br>Middle East and north Africa (5.5%)<br>Latin America and Caribbean (11.4%)<br>Sub-Saharan Africa (14.6%)<br>East Asia and Pacific (17.3%, baseline) | Presumptively Treat |

Notes: All input values except prevalence rate are baseline estimates. The prevalence rate for each region is from Asundi et al. 2019. To identify preferred strategies, each intervention strategy, “Screen and Treat” or “Presumptively Treat”, were compared to “No Intervention” and to each other. If both interventions have ICER estimates of more than $10.6 million per death averted relative to “No Intervention”, then “No Intervention” would be the preferred strategy. Otherwise, the two intervention strategies would be compared against each other, and “Presumptively Treat” would be preferred to “Screen and Treat” if the ICER estimate is less than $10.6 million.