

## Review Article

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# Intervention strategies to reduce the burden of soil-transmitted helminths in India

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**Soil-transmitted helminth (STH) infections continue to be a major global cause of morbidity, with a large proportion of the burden of STH infections occurring in India. In addition to direct health impacts of these infections, including anaemia and nutritional deficiencies in children, these infections also significantly impact economic development, as a result of delays in early childhood cognitive development and future income earning potential. The current World Health Organization strategy for STH is focused on morbidity control through the application of mass drug administration to all pre-school-aged and school-aged children. In India, the control of STH-related morbidity requires mobilization of significant human and financial resources, placing additional burdens on limited public resources. Infected adults and untreated children in the community act as a reservoir of infection by which treated children get rapidly reinfected. As a result, deworming programmes will need to be sustained indefinitely in the absence of other strategies to reduce reinfection, including water, hygiene and sanitation interventions (WASH). However, WASH interventions require sustained effort by the government or other agencies to build infrastructure and to promote healthy behavioural modifications, and their effectiveness is often limited by deeply entrenched cultural norms and behaviours. Novel strategies must be explored to provide a lasting solution to the problem of STH infections in India other than the indefinite provision of deworming for morbidity control.**

**Key words** *Ascaris* - hookworm - India - mass drug administration - soil-transmitted helminths - *Trichuris* - WASH

## Introduction

Soil-transmitted helminth (STH) infections are the most prevalent neglected tropical diseases (NTDs) globally, with 1.22 billion people estimated to be infected<sup>1,2</sup>. The World Health Organization (WHO) recommends a strategy of mass drug administration (MDA) of preventive chemotherapy

to all 875 million children worldwide at risk of STH infection<sup>3</sup>. In India alone, 225 million children are estimated to be at risk of STH<sup>4</sup>. The STH includes human hookworm species (*Ancylostoma duodenale* & *Necator americanus*), roundworms (*Ascaris lumbricoides*) and whipworms (*Trichuris trichiura*). Although *A. lumbricoides* has been reported to be the most prevalent STH infection<sup>5,6</sup>, human hookworm

infections are responsible for the majority of the morbidity, as measured by disability-adjusted life years (DALY's) or years lived with disability<sup>5,7</sup>. In pregnant women, STH infections have been associated with intrauterine growth retardation and low birth weight<sup>8-10</sup>. Morbidity associated with hookworm infections includes iron deficiency anaemia and protein loss and further exacerbation of pre-existing nutritional deficiencies in susceptible populations<sup>11</sup>. Infection with *Ascaris* and *Trichuris* species is also associated with increased risk of stunting, protein-energy malnutrition, decreased physical performance and lower body mass index in children<sup>12,13</sup>. While the impact of hookworm infections appears to disproportionately affect children, women in the reproductive age group and pregnant women in resource-poor settings, the prevalence of hookworm infection is greatest in adults who are not treated under the current morbidity control guidelines<sup>8,14-17</sup>.

#### **Prevalence of soil-transmitted helminths and burden of disease in India**

India has the highest burden of STH infections globally<sup>18</sup>. Studies on the prevalence of STH in the Indian subcontinent have been reviewed recently and suggest that the prevalence of STH infections may exceed 50 per cent in school-aged children (SAC) in six States of India<sup>6,19</sup>. These reviews have demonstrated considerable heterogeneity in the prevalence and burden of STH, likely due to diverse climatic and geographic conditions, socio-demographic status and behavioural and cultural practices of the population<sup>5,19</sup>. Although many studies on the prevalence of STH have been carried out in the country, very few have attempted to estimate the prevalence in age groups other than SAC<sup>20-22</sup>. Differences in study methods, age groups and types of populations studied have also contributed to the wide variation in the reported prevalence and intensity of STH infections in India.

More recent estimates from surveys carried out in the past decade include a study in 20 schools from four districts of Bihar by Greenland *et al*<sup>23</sup>, which demonstrated an overall prevalence of 67.90 per cent in SAC (*Ascaris* 51.90%, hookworm 41.80%, *Trichuris* 4.70% with 26.70% dual infection) and most infections were of light intensity. Ganguly *et al*<sup>24</sup> carried out a study in SAC in 27 districts of Uttar Pradesh in a total of 130 schools and found an overall prevalence of 75.60 per cent (*Ascaris* 69.60%, hookworm 22.60%,

*Trichuris* 4.60%) although most of these infections were of light intensity. Additional school-based surveys in multiple States have been carried out in SAC in Madhya Pradesh (14.76%, *Ascaris* 9.84%, hookworm 4.92%), Rajasthan (21.10%, *Ascaris* 20.20%, hookworm 1.00%, *Trichuris* 0.20%) and Chhattisgarh (74.60%, *Ascaris* 70.40%, hookworm 10.50%, *Trichuris* (0.05%)<sup>25-27</sup>. In the south, studies showed a higher prevalence for hookworm both in SAC (6.30%) and when all age groups were surveyed (38.00%) than *Ascaris* (1.50 and 1.20%)<sup>20,28</sup>. Taken together, there are sufficient data to demonstrate that the current STH prevalence is high and both control of morbidity and strategies to potentially interrupt transmission are of high public health significance in India.

#### **Recommended control strategies**

The WHO strategic plan 2011-2020<sup>29</sup> for the control and eventual elimination of STH infection includes preventive chemotherapy of at-risk populations in endemic areas, health and hygiene education focussing on behavioural modification to reduce transmission and provision of adequate sanitation. The WHO guidelines emphasize targeted deworming programmes aimed at 'at-risk' populations including children (greater than one year of age), non-pregnant adolescent girls (10-19 yr), non-pregnant women of the reproductive age group (15-49 yr) and pregnant women (second and third trimester) to control morbidity associated with these infections<sup>29</sup>. In areas where the baseline prevalence of any STH infection is greater than 20 per cent, the recommendations are an annual single dose of albendazole (400 mg; 200 mg for children 1-2 yr of age) or mebendazole (500 mg). In areas where the baseline prevalence is greater than 50 per cent, the recommendation is biannual deworming. In addition, if the prevalence of anaemia is greater than 40 per cent among pregnant women, deworming is conditionally recommended<sup>29</sup>. In India, deworming is carried out with albendazole, which has been shown to have highly effective cure rates for *Ascaris* and hookworm infection but less so for *Trichuris* infections<sup>30</sup>. The National Deworming Day programme was initiated by the Indian government in February 2015 with the aim of deworming every child between 1 and 19 yr of age biannually and is one of the largest national public health programmes in the world<sup>31</sup>. While there has been considerable debate regarding the effectiveness of mass deworming programmes in the academic community<sup>32-34</sup>, several studies conducted in India have suggested benefit.

The effect of mass treatment for ascariases was recognized in early studies carried out in India by Gupta *et al.*<sup>35</sup> in the 1970s. In this study, where undernourished pre-SAC (PSAC) were randomized to receive either tetramisole every four months or placebo, the prevalence of *Ascaris* decreased in the treatment group (although it was not eliminated) and the nutritional status of the children receiving treatment improved significantly at 8-12 months. In addition, there are several observational studies that have shown improvements in multiple outcomes including weight and haemoglobin levels in children in communities following deworming<sup>14,32,34</sup>. However, treatment of infected individuals and subsequent resolution of infection do not prevent recurrence of infection. STH infections are over-dispersed in populations, with approximately 80 per cent of infections harboured by 20 per cent of the population<sup>1</sup>. As a result, populations in endemic areas have high rates of reinfection following deworming<sup>36</sup>. Surveys in all age groups indicate that adults have high rates of hookworm infections in these communities and likely act as a reservoir of infection<sup>11,37</sup>. Although the drugs used in the MDA programmes are now available off patent and significant drug donation programmes have been put in place following the London Declaration on NTDs<sup>38</sup>, national programmes still require substantial logistical and financial investment by developing countries.

Environmental reservoirs have also been shown to contribute to the high rates of reinfection<sup>39,40</sup>. The lack of access to safe drinking water, open defecation practices, and poor hygiene practices are risk factors for poor gastrointestinal health, including STH infection, in India<sup>41</sup>. Water, hygiene and sanitation (WASH) interventions consist of a multi-pronged approach which includes community management of water resources, empowering local bodies and private agencies to increase capacities for procuring safe drinking water, promotion of hand hygiene and provision of latrines<sup>42</sup>. The 'Swachh Bharat Abhiyan' programme (<http://swachhbharatmission.gov.in/sbmcms/index.htm>) is an example of a large government-led initiative which provides funds for villages to construct toilets and prevent open defecation.

An attempt was made to identify all relevant studies (published and available in full text) conducted in India since 1995 that involved community-based interventions to reduce the prevalence of STH, reduce the burden of disease or potentially interrupt transmission of STH in the community. An online

search was conducted on PubMed, EMBASE and Cochrane library with the following search terms: (soil transmitted helminths) OR *Ascaris*) OR Hookworm) OR Trichuris) AND (intervention OR deworming OR WASH OR health education) AND India. A total of 74 full text articles were assessed for eligibility and only nine were included in this review (Figure).

### Studies on intervention strategies in India

The trials involving community-based interventions to reduce the prevalence of and/or morbidity associated with STH infection in India over the past two decades were reviewed from the currently available literature (Table). Although several studies on the prevalence of STH have been conducted, only five randomized control trials (RCTs) of preventive chemotherapy with MDA of albendazole and four studies on WASH interventions have been carried out in India.

### Mass drug administration (MDA) interventions

Among the studies of MDA<sup>43-48</sup>, all involved biannual treatment of PSAC or SAC under-five years of age and a majority were conducted in Uttar Pradesh. A single MDA RCT was conducted in West Bengal<sup>45</sup>. All studies involved co-administration of a vitamin or other supplement that was also received by the control group. Other than the large DEVTA trial conducted in rural administrative blocks in Uttar Pradesh in about two million children<sup>47</sup>, all the other studies recruited about 1000-4000 children in urban slums followed up for a period of 1-2 years<sup>43-46</sup>. When parasitological outcomes were measured (3 of 5 trials), the prevalence of *Ascaris* was reduced by

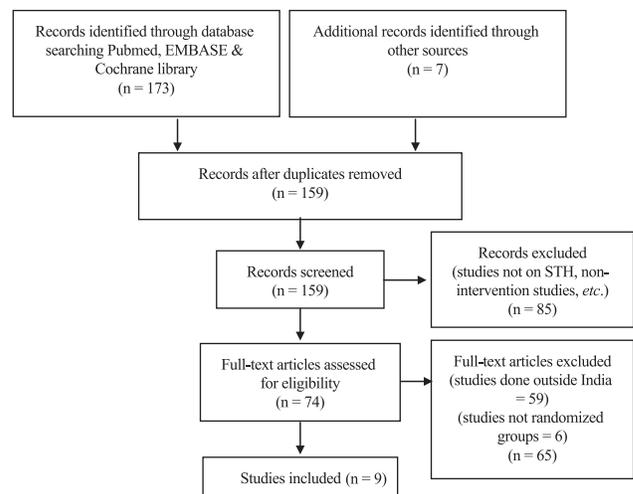


Figure. Flowchart showing selection of studies.

Table. Summary of soil-transmitted helminth intervention studies conducted in India since 1995

Study	Study design	Intervention	Placebo	Setting	Study population	n	Duration (months)	Outcome: STH prevalence	Outcome: Weight	Other outcomes
Preventive chemotherapy interventions										
Awasthi <i>et al</i> , 2000 <sup>43</sup>	Community-based, randomized, single-blind, placebo-controlled trial	Biannual 600 mg ABZ powder	Calcium powder	32 urban slums, Lucknow, Uttar Pradesh	Children 1.5-3.5 yr	1061	24	Increase in <i>Ascaris</i> prevalence of both arms. Post-intervention prevalence of <i>Ascaris</i> in ABZ arm - 41.20%, Control group - 55.30%, $P < 0.001$	Mean difference in prevalence of underweight children: 2.43% (95% CI: 1.90-6.76)	Mean difference in stunting: 9.38% (95% CI: 6.01-12.35); Mean Hb in both arms post-intervention - 9.67 g/dl; NS; Cognitive performance: Risk reduction of questionable R-PDQ -1.03 (95% CI: 0.88-1.21); NS; coverage-95.90-96.90%
Awasthi and Pande 2001 <sup>44</sup>	Cluster-randomized, placebo-controlled trial	Biannual 400 mg ABZ suspension and vitamin A (100,000 U)	Vitamin A (100,000 U)	124 Urban slums, Lucknow, Uttar Pradesh	Children 0.5-1 yr	2010	18	Not measured	Mean difference in weight gain in ABZ arm - 0.13 kg; $P = 0.043$	Proportion of stunting: ABZ arm: 54.70%, control: 52.50%, $P = 0.3$ ; NS
Sur <i>et al</i> , 2005 <sup>45</sup>	Community-based, randomized, double-blind, placebo-controlled trial	Biannual 400 mg ABZ suspension in vitamin B complex base	Vitamin B complex	Tiljala urban slum, Kolkata, West Bengal	Children 2-5 yr	702	14	Prevalence of <i>Ascaris</i> post-intervention in ABZ arm - 24.00%, control arm - 58.60%, $P < 0.01$	Mean difference in weight: 0.54 kg; $P < 0.001$	Diarrhoea incidence 28% lower in intervention group: RR=1.30 (95% CI: 1.07-1.53)
Awasthi <i>et al</i> , 2008 <sup>46</sup>	Cluster-randomized, placebo-controlled trial	Biannual 400 mg ABZ suspension and vitamin A (100,000 U)	Vitamin A (100,000 U)	50 urban slums, Lucknow, Uttar Pradesh	Children 1-5 yr	3935	24	Not measured	Mean difference in weight gain: 1.00 kg (95% CI: 0.6-1.4)	Mean difference in height: 1.20 cm, $P = 0.06$

Contd...

Study	Study design	Intervention	Placebo	Setting	Study population	n	Duration (months)	Outcome: STH prevalence	Outcome: Weight	Other outcomes
DEVTA, 2013 <sup>47,48</sup>	Cluster-randomized, placebo-controlled trial	Biannual 400 mg ABZ tablet/ABZ with vitamin A(200000 IU)	Vitamin A (200,000 IU)	72 administrative blocks (largely rural) of 7 adjacent districts in Uttar Pradesh	Children 1-6 yr	2,000,000	60	Prevalence of <i>Ascaris</i> post-intervention in ABZ arm - 12.90%, Control arm - 28.10%, $P < 0.001$ ; Hookworm in ABZ arm - 8.90%, Control arm - 3.80%, $P < 0.001$ - subset of 5165 participants	Mean difference in weight: 0.04 kg (95% CI: -0.19-0.09)	Mortality rate ratio: 0.95, $P = 0.16$ - NS, Mean difference in Hb: 0.02 g/dl (95% CI: -0.15-0.12)
WASH interventions										
Freeman and Clasen 2011 <sup>49</sup>	School-based randomized controlled trial	Provision of commercial water purifier, hygiene and water treatment information provided to teachers (UNICEF/HUL)	-	72 schools in Krishnagiri District, Tamil Nadu	Schools	72	12	Not measured	Not measured	Household ownership of purifier in intervention arm - 26.00%, Control - 19.00%, $P = 0.53$ ; Boiling of water in intervention arm - 22.00%, Control - 25.00%, $P = 0.6$ ; Purification in intervention arm - 22.00%, Control - 20.00%, $P = 0.33$
Boisson <i>et al</i> , 2013 <sup>50</sup>	Double-blind, randomized controlled trial	Bimonthly distribution of NaDCC tablets for disinfection	Placebo with similar base	11 informal urban settlements in Bhubaneswar, Odisha, and 20 villages in Dhenkanal, Odisha	Households	2163	12	Not measured	Mean WAZ in intervention arm: -1.59, Control: -1.59; NS	Risk ratio of diarrhoea: 1.02 (95% CI: 0.80-1.30) - NS

Contd...

Study	Study design	Intervention	Placebo	Setting	Study population	n	Duration (months)	Outcome: STH prevalence	Outcome: Weight	Other outcomes
Clasen <i>et al</i> , 2014 <sup>51,52</sup>	Cluster-randomized, controlled trial	Rural sanitation campaign under the 'total sanitation campaign', GOI: Construction of pour flush latrines, latrine promotion and community mobilization	-	100 villages in Puri district, Odisha	Households	2902	43	Prevalence of STH in intervention arm: 16.00%, Control: 16.40%; <i>Ascaris</i> in intervention arm: 0.70%, Control: 0.30%; hookworm in intervention arm: 14.10%, Control: 15.60%; <i>Trichuris</i> in intervention arm: 2.60%, Control - 0.60%	Mean WAZ in intervention arm: -1.48, Control: -1.43 NS	Period prevalence ratio for diarrhoea: 0.97 (95% CI: 0.83-1.12); NS
Patil <i>et al</i> , 2014 <sup>53</sup>	Cluster-randomized, controlled trial	'Total Sanitation Campaign', GOI: Provision of subsidies for construction of pour flush latrines and community 'triggering' exercises to affect behavioural change	-	80 villages in 2 districts of Madhya Pradesh	Households	3039	23	Prevalence of <i>Ascaris</i> in intervention arm: 4.30%, Control: 4.40%	Mean WAZ in intervention arm: -1.92, Control: -1.83 NS	Diarrhoea in intervention arm: 7.40%, control arm: 7.70%, <i>P</i> =0.687, Anaemia in intervention arm: 56.20%, control arm: 50.80% - NS

\*Study conducted in 1995 and results published in 2008. ABZ, albendazole; CI, confidence interval; IU, international units; NS, not significant; RR, relative risk; R-PDQ, revised Denver- pre-screening developmental questionnaire; DEVTA, deworming and enhanced vitamin A; WASH, water, sanitation and hygiene; UNICEF, United Nations Children's Fund; HUL, Hindustan Unilever Limited; NaDCC, sodium dichloroisocyanurate; WAZ, weight-for-age Z score; GOI, Government of India; U, units; STH, soil-transmitted helminth

more than half in the treatment arm in the Kolkata trial (53.90-24.00% in the intervention arm) with large effects seen for ascariasis at three months post albendazole administration (*Ascaris* 24.00% in intervention & 58.60% in control,  $P<0.01$ )<sup>45</sup>. The DEVTA trial also demonstrated significant reductions in STH prevalence following MDA (*Ascaris* 12.90% in intervention & 28.10% in control,  $P<0.001$ ; hookworm 3.80% in intervention and 8.90% in control,  $P<0.001$ )<sup>47,48</sup>. At the end of the study period, none of the studies that measured STH prevalence post-intervention demonstrated prevalence less than 15 per cent, despite high reported treatment coverage (96.90%)<sup>43</sup>. Rapid reinfection with STH following deworming is the plausible explanation for the lack of long-term positive outcomes in such interventions. A study in slum children in Vishakhapatnam, Andhra Pradesh, in 1998 showed that the disease prevalence returned to pre-treatment levels within nine months following deworming; however, the intensity was lowered<sup>54</sup>. Jia *et al*<sup>36</sup> also published a meta-analysis that illustrated the rapid rate of reinfection for STH post-deworming. From an analysis of 51 studies, they concluded that *Ascaris* infection reached 68 per cent [95% confidence interval (CI) 60-76] of pre-treatment prevalence six months post-deworming, hookworm 55 per cent (95% CI: 34-87) and *Trichuris* 67 per cent (95% CI: 42-100)<sup>36</sup>.

Since the introduction of government-run MDA for lymphatic filariasis (LF) in endemic areas in 1998 in Tamil Nadu, several observational studies have documented the impact of mass interventions for STH in the community<sup>55-58</sup>. In Villupuram district, Tamil Nadu, community-wide MDA with albendazole and diethylcarbamazine (DEC) resulted in a decrease of STH (measured in a subgroup of children aged 9-10 yr) from 60.40 to 15.60 per cent [percentage reduction of *Ascaris* - 74.30% in intervention arm (albendazole with DEC) and 30.80% in control (DEC alone), hookworm reduction of 89.50% in intervention arm and 25.99% in the control arm, *Trichuris* reduction of 81.58% in intervention arm and 77.25% in the control arm]<sup>55</sup>. There was also a difference in intensity of STH infection (measured as eggs per gram by the Kato-Katz technique) with an egg reduction rate of 97.34 per cent in the intervention arm and 79.02 per cent in the control arm (*Ascaris* - 96.55% in intervention arm and 76.64% in control arm; hookworm - 94.18% in intervention arm and 36.05% in control arm; and *Trichuris* - 83.96% in intervention arm and 85.57% in control arm)<sup>55</sup>. A bounce back in STH infection levels was seen

following treatment, but the difference in prevalence between albendazole and DEC-treated SAC compared to DEC-treated SAC remained significant (34.56% prevalence of STH in the intervention arm and 59.60% in control arm 11 months post-MDA) ( $P<0.005$ )<sup>56</sup>. A subsequent study demonstrated that biannual MDA had greater benefit in keeping the prevalence of STH low following treatment (14.15% in intervention arm and 50.25% in control arm, 11 months post-two rounds of MDA,  $P<0.001$ )<sup>57</sup>. After seven annual rounds of LF MDA from March 2001 to February 2010, STH prevalence was 12.48 per cent in the intervention arm, with hookworm showing the largest reduction with a final prevalence of 1.17 per cent, *Ascaris* 10.92 per cent and *Trichuris* 1.17 per cent ( $P<0.05$ )<sup>58</sup>. Similar findings have also been reported in a meta-analysis of 38 studies by Clarke *et al*<sup>59</sup>, where they observed that mass deworming of entire communities was a superior strategy to targeted deworming for the reduction of STH prevalence in children. The pattern of rapid fall in prevalence and bounce back/reinfection has been included in mathematic modelling studies by Anderson *et al*<sup>60,61</sup> to formulate strategies to break transmission and further demonstrate the advantage of mass deworming of the community at high coverage levels over targeted deworming.

In addition to measuring impacts on STH prevalence, other outcomes evaluated in these studies included effects on malnutrition (anthropometry), anaemia and cognitive function<sup>43,47</sup>. In three studies conducted in India, deworming interventions resulted in a significant mean weight gain in children in the intervention arm<sup>44-46</sup>. These findings were consistent with the results reported elsewhere<sup>62,63</sup>. In addition to these direct effects on treated children, several studies also suggested indirect 'spillover' benefits from deworming programmes that resulted in positive outcomes in siblings of the children who received the drug and positive educational outcomes in untreated children in schools where deworming was done<sup>64,65</sup>. However, the largest clinical trial to date, the DEVTA trial, involving two million children<sup>47,48</sup>, reported negligible weight gain following deworming. In addition, meta-analyses of multiple studies of deworming have failed to demonstrate consistent benefit of deworming on anthropometric and cognitive outcomes<sup>32,34</sup>.

### **Water, hygiene and sanitation (WASH) interventions**

Only four trials involving WASH interventions for STH have been reported from India since 1995. These

studies were carried out in Tamil Nadu, Madhya Pradesh and Orissa. Two of these were based on association with the 'Total Sanitation Campaign' initiated by the Indian government, which included the provision of flush pit latrines and community mobilization in village populations in whom parasitological measures of STH were recorded<sup>51,53</sup>. Clasen *et al*<sup>51</sup> did not observe any difference in the prevalence of STH between the intervention arm (16.00%) and the control arm (16.40%). There were also no significant differences in the prevalence of *Ascaris* (0.70 and 0.30%), hookworm (14.10 and 15.60%) or *Trichuris* (2.60 and 0.60%) between the two arms. Patil *et al*<sup>53</sup> had similar findings with no significant difference in the prevalence of *Ascaris* between the intervention arm (4.30%) and control arm (4.40%). Other outcomes assessed were anaemia and weight gain. None of the studies found a significant difference in the weight-for-age Z scores between the two trial arms<sup>49-53</sup> while one study which measured levels of anaemia did not find a significant difference in anaemia between the two arms post-intervention<sup>53</sup>. All four studies showed benefit in terms of the intervention being adopted in the households<sup>49-53</sup>. One study showed coverage of 60 per cent by residual chlorine in the households of the intervention arm<sup>50</sup> and another study showed increased latrine coverage in the villages of intervention arms, although there was clear resistance to the adoption and usage<sup>51</sup>. Patil *et al*<sup>53</sup> also demonstrated a reduction in open defecation in adult men (9.50%,  $P=0.001$ ), adult women (10.00%,  $P<0.001$ ) and under-five children (5.00%,  $P=0.014$ ). Although there was some evidence of behavioural change following the intervention, no effect on STH and other clinically relevant outcomes was seen. However, studies conducted in other settings have reported benefits. A meta-analysis by Strunz *et al*<sup>66</sup> found a significant decrease in STH infections associated with sanitation and hygiene interventions. They found that access to treated water decreased the odds of infection with *Ascaris* [odds ratio (OR)-0.40, 95% CI: 0.39-0.41] and *Trichuris* (OR 0.57, 95% CI: 0.45-0.72) and similarly so did availability of sanitation facilities. Usage of footwear decreased the risk of hookworm infection (OR 0.29, 95% CI: 0.18-0.47%). Hand hygiene and usage of soap were also associated with lower rates of infection with STH overall (OR 0.47, 95% CI: 0.24-0.90 and 0.53, 0.29-0.98, respectively)<sup>66</sup>.

Recently, two large studies on WASH interventions for the prevention of diarrhoea and stunting, the WASH

Benefits Study (in Kenya and Bangladesh) and the Sanitation, Hygiene, Infant Nutrition Efficacy (SHINE) Study in Zimbabwe have been carried out. The WASH Benefits Study includes two cluster RCTs to assess the impact of WASH interventions to infants in Kenya and Bangladesh which were conducted between 2012 and 2014<sup>67,68</sup>. In both these sites, WASH interventions alone, which included improvement of latrines, provision of handwashing stations and promotion of behavioural change, did not show any significant positive outcomes with relation to decrease in the prevalence of diarrhoea or increase in linear growth<sup>67,68</sup>. The SHINE Study, undertaken in two rural districts of Zimbabwe, was a cluster-randomized community-based study that aimed to determine the combined and independent effects of a WASH intervention and improved nutrition in 18-month old babies as measured by anaemia and linear growth<sup>69</sup>. Findings from this trial (unpublished) also indicate that WASH interventions did not independently improve growth outcomes or reduce the prevalence of diarrhoea<sup>70</sup>. Overall, the 'sanitary awakening'<sup>71</sup>, even if achieved, does not seem to ensure success with regard to positive disease outcomes and mortality in developing nations. However, it is important to note that the outcomes in these studies were not measured uniformly, and a longer follow up period might be required.

## Conclusions

Intervention studies of preventive chemotherapy with albendazole in India have demonstrated significant reductions in STH prevalence following treatment. However, despite reports of high coverage, none of the studies demonstrated a post-intervention prevalence of STH infection less than 15 per cent, suggesting that ongoing transmission is likely to continue to occur. These studies were done largely in SAC and reported secondary outcomes including effects of deworming on weight gain, anaemia, cognition and growth. These studies did not demonstrate consistently significant differences in these outcomes although a few showed a significant weight gain in children following deworming. The inability to sustain very low levels of prevalence, due to rapid reinfection, could explain the lack of appreciable changes in the secondary outcomes in these studies. Some of the impact assessment studies done in India have also observed the pattern of lowering of the prevalence of STH infection followed by reinfection, post-community deworming. The untreated individuals in these communities might be contributing to this rapid reinfection rate.

It appears that the current strategy of reducing morbidity by providing routine MDA to SAC and PSAC will need to continue for the foreseeable future in many areas of India given the inability of the current strategy to interrupt transmission. This strategy may not be sustainable in the long term due to the economic costs involved in running such a large public health programme. In addition to the findings following deworming, WASH interventions did not prove to be effective in reducing STH prevalence or in attenuating other secondary outcomes in most of the reported studies done in India. The lack of consistent and demonstrable benefit with WASH interventions suggests that interventions with much higher coverage, quality and fidelity are needed, in addition to improved WASH behaviour to sustain usage and eventually influence health outcomes.

Given the need for long-term investments in morbidity control programmes and WASH infrastructure, it may be valuable to explore other strategies to interrupt transmission of STH in India. These strategies could include community-wide MDA at increased frequency to attempt to reduce reinfection and reach the elimination threshold within communities. The DeWorm3 project is a large multi-country set of cluster-randomized trials being conducted in Benin, Malawi and India to determine the feasibility of such an approach in interrupting STH transmission<sup>72</sup>. In addition, WASH interventions need further development and evaluation to optimize their impact in the Indian context and programmes aimed at behavioural modification may need to be locally adapted to be acceptable to communities, as a ‘one size fits all’ strategy may not work in a diverse country like India.

Maximizing the value of public resources to improve healthcare in India requires careful consideration of strategies for the control and possible elimination of disease. STH infections are prevalent in India, and alternative approaches to interrupt transmission may be highly cost-effective in many settings.

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## References

- Hotez PJ, Bundy DAP, Beegle K, Brooker S, Drake L, Silva de N, *et al.* *Helminth infections: Soil-transmitted helminth infections and schistosomiasis*. Available from: <https://www.ncbi.nlm.nih.gov/books/NBK11748/>, accessed on March 27, 2018.
- de Silva NR, Brooker S, Hotez PJ, Montresor A, Engels D, Savioli L, *et al.* Soil-transmitted helminth infections: Updating the global picture. *Trends Parasitol* 2003; 19 : 547-51.
- World Health Organization. *Investing to overcome the global impact of neglected tropical diseases: Third WHO report on neglected tropical diseases*. Geneva: WHO; 2015. p. 191.
- World Health Organization. *Neglected tropical diseases: PCT Databank*. Geneva: WHO; 2017. Available from: [http://www.who.int/neglected\\_diseases/preventive\\_chemotherapy/sth/en/](http://www.who.int/neglected_diseases/preventive_chemotherapy/sth/en/), accessed on March 27, 2018.
- Pullan RL, Smith JL, Jasrasaria R, Brooker SJ. Global numbers of infection and disease burden of soil transmitted helminth infections in 2010. *Parasit Vectors* 2014; 7 : 37.
- Silver ZA, Kaliappan SP, Samuel P, Venugopal S, Kang G, Sarkar R, *et al.* Geographical distribution of soil transmitted helminths and the effects of community type in South Asia and South East Asia - A systematic review. *PLoS Negl Trop Dis* 2018; 12 : e0006153.
- Murray CJ, Vos T, Lozano R, Naghavi M, Flaxman AD, Michaud C, *et al.* Disability-adjusted life years (DALYs) for 291 diseases and injuries in 21 regions, 1990-2010: A systematic analysis for the Global Burden of Disease Study 2010. *Lancet* 2012; 380 : 2197-223.
- Christian P, Khatry SK, West KP Jr. Antenatal anthelmintic treatment, birthweight, and infant survival in rural Nepal. *Lancet* 2004; 364 : 981-3.
- Egwunyenga AO, Ajayi JA, Nmorsi OP, Duhlińska-Popova DD. Plasmodium/intestinal helminth co-infections among pregnant Nigerian women. *Mem Inst Oswaldo Cruz* 2001; 96 : 1055-9.
- Bundy DA, Chan MS, Savioli L. Hookworm infection in pregnancy. *Trans R Soc Trop Med Hyg* 1995; 89 : 521-2.
- Brooker S, Bethony J, Hotez PJ. Human hookworm infection in the 21<sup>st</sup> century. *Adv Parasitol* 2004; 58 : 197-288.
- Tshikuka JG, Gray-Donald K, Scott M, Olela KN. Relationship of childhood protein-energy malnutrition and parasite infections in an urban African setting. *Trop Med Int Health* 1997; 2 : 374-82.
- Müller I, Yap P, Steinmann P, Damons BP, Schindler C, Seelig H, *et al.* Intestinal parasites, growth and physical fitness of schoolchildren in poor neighbourhoods of Port Elizabeth, South Africa: A cross-sectional survey. *Parasit Vectors* 2016; 9 : 488.
- Smith JL, Brooker S. Impact of hookworm infection and deworming on anaemia in non-pregnant populations: A systematic review. *Trop Med Int Health* 2010; 15 : 776-95.
- Stephenson LS, Latham MC, Ottesen EA. Malnutrition and parasitic helminth infections. *Parasitology* 2000; 121 : S23-38.
- Hotez PJ, Brooker S, Bethony JM, Bottazzi ME, Loukas A, Xiao S, *et al.* Hookworm infection. *N Engl J Med* 2004; 351 : 799-807.

17. Bethony J, Brooker S, Albonico M, Geiger SM, Loukas A, Diemert D, *et al.* Soil-transmitted helminth infections: Ascariasis, trichuriasis, and hookworm. *Lancet* 2006; *367* : 1521-32.
18. Murray John S. Soil-transmitted Helminthiasis in India. *J Spec Pediatr Nurs* 2016; *21* : 48-53.
19. Salam N, Azam S. Prevalence and distribution of soil-transmitted helminth infections in India. *BMC Public Health* 2017; *17* : 201.
20. Kaliappan SP, George S, Francis MR, Kattula D, Sarkar R, Minz S, *et al.* Prevalence and clustering of soil-transmitted helminth infections in a tribal area in Southern India. *Trop Med Int Health* 2013; *18* : 1452-62.
21. Nitin S, Venkatesh V, Husain N, Masood J, Agarwal GG. Overview of intestinal parasitic prevalence in rural and urban population in Lucknow, North India. *J Commun Dis* 2007; *39* : 217-23.
22. Traub RJ, Robertson ID, Irwin P, Mencke N, Andrew Thompson RC. The prevalence, intensities and risk factors associated with geohelminth infection in tea-growing communities of Assam, India. *Trop Med Int Health* 2004; *9* : 688-701.
23. Greenland K, Dixon R, Khan SA, Gunawardena K, Kihara JH, Smith JL, *et al.* The epidemiology of soil-transmitted helminths in Bihar state, India. *PLoS Negl Trop Dis* 2015; *9* : e0003790.
24. Ganguly S, Barkataki S, Karmakar S, Sanga P, Boopathi K, Kanagasabai K, *et al.* High prevalence of soil-transmitted helminth infections among primary school children, Uttar Pradesh, India, 2015. *Infect Dis Poverty* 2017; *6* : 139.
25. Kiran T, Shashwati N, Vishal B, Kumar D. Intestinal parasitic infections and demographic status of school children in Bhopal region of Central India. *IOSR J Pharm Biol Sci* 2014; *9* : 83-7.
26. GiveWell. Prevalence of Soil Transmitted Helminths in the State of Rajasthan. Summary Report prepared by 'Deworm the World Initiative'; 2013. Available from: <http://files.givewell.org/files/DWDA%202009/DtWI/DtWI%20Rajasthan%202013%20prevalence%20survey%20report.pdf>, accessed on March 30, 2018.
27. GiveWell. Report on Prevalence and Intensity of Soil Transmitted Helminth Infections in Chattisgarh. Available from: [http://files.givewell.org/files/DWDA%202009/DtWI/Deworm\\_the\\_World\\_Chhattisgarh\\_prevalence\\_survey\\_report\\_August\\_2016.pdf](http://files.givewell.org/files/DWDA%202009/DtWI/Deworm_the_World_Chhattisgarh_prevalence_survey_report_August_2016.pdf), accessed on March 30, 2018.
28. Kattula D, Sarkar R, Rao Ajjampur SS, Minz S, Levecke B, Muliyl J, *et al.* Prevalence & risk factors for soil transmitted helminth infection among school children in South India. *Indian J Med Res* 2014; *139* : 76-82.
29. World Health Organization. *Preventive chemotherapy to control soil-transmitted helminth infections in at-risk population groups: Guideline*. Geneva: WHO; 2017. Available from: <http://www.who.int/nutrition/publications/guidelines/deworming/en/>, accessed on March 3, 2018.
30. Vercruyse J, Behnke JM, Albonico M, Ame SM, Angebault C, Bethony JM, *et al.* Assessment of the anthelmintic efficacy of albendazole in school children in seven countries where soil-transmitted helminths are endemic. *PLoS Negl Trop Dis* 2011; *5* : e948.
31. National Deworming Day | National Health Portal of India. Available from: [https://www.nhp.gov.in/National-Deworming-Day\\_pg](https://www.nhp.gov.in/National-Deworming-Day_pg), accessed on April 15, 2018.
32. Taylor-Robinson DC, Maayan N, Soares-Weiser K, Donegan S, Garner P. Deworming drugs for soil-transmitted intestinal worms in children: Effects on nutritional indicators, haemoglobin and school performance. *Cochrane Database Syst Rev* 2012; *11* : CD000371.
33. Croke K, Hicks JH, Hsu E, Kremer M, Miguel E. Does mass deworming affect child nutrition? Meta-analysis, cost-effectiveness, and statistical power. USA. National Bureau of Economic Research. Report No.: 22382; July, 2016. Available from: <http://www.nber.org/papers/w22382>, accessed on April 15, 2018.
34. Welch VA, Ghogomu E, Hossain A, Awasthi S, Bhutta ZA, Cumberbatch C, *et al.* Mass deworming to improve developmental health and wellbeing of children in low-income and middle-income countries: A systematic review and network meta-analysis. *Lancet Glob Health* 2017; *5* : e40-50.
35. Gupta M, Arora KL, Mithal S, Tandon BN. Effect of periodic deworming on nutritional status of ascariis-infested preschool children receiving supplementary food. *Lancet* 1977; *2* : 108-10.
36. Jia TW, Melville S, Utzinger J, King CH, Zhou XN. Soil-transmitted helminth reinfection after drug treatment: A systematic review and meta-analysis. *PLoS Negl Trop Dis* 2012; *6* : e1621.
37. Dunn JC, Turner HC, Tun A, Anderson RM. Epidemiological surveys of, and research on, soil-transmitted helminths in Southeast Asia: A systematic review. *Parasit Vectors* 2016; *9* : 31.
38. London Declaration on Neglected Tropical Diseases. Uniting to Combat NTDs. Available from: <http://www.unitingtocombatntds.org/london-declaration-neglected-tropical-diseases/>, accessed on April 23, 2018.
39. Steinbaum L, Njenga SM, Kihara J, Boehm AB, Davis J, Null C, *et al.* Soil-transmitted helminth eggs are present in soil at multiple locations within households in rural Kenya. *PLoS One* 2016; *11* : e0157780.
40. Steinbaum L, Kwong LH, Ercumen A, Negash MS, Lovely AJ, Njenga SM, *et al.* Detecting and enumerating soil-transmitted helminth eggs in soil: New method development and results from field testing in Kenya and Bangladesh. *PLoS Negl Trop Dis* 2017; *11* : e0005522.
41. Kar S, Samantaray P, Sarma N, Mistry C, Pal R. WASH practices - A determinant of gastrointestinal community health: A community study from rural Odisha, India. *J Gastrointest Dig Syst* 2017; *7* : 490.
42. Kumar GS, Kar SS, Jain A. Health and environmental sanitation in India: Issues for prioritizing control strategies. *Indian J Occup Environ Med* 2011; *15* : 93-6.

43. Awasthi S, Pande VK, Fletcher RH. Effectiveness and cost-effectiveness of albendazole in improving nutritional status of pre-school children in urban slums. *Indian Pediatr* 2000; 37 : 19-29.
44. Awasthi S, Pande VK. Six-monthly de-worming in infants to study effects on growth. *Indian J Pediatr* 2001; 68 : 823-7.
45. Sur D, Saha DR, Manna B, Rajendran K, Bhattacharya SK. Periodic deworming with albendazole and its impact on growth status and diarrhoeal incidence among children in an urban slum of India. *Trans R Soc Trop Med Hyg* 2005; 99 : 261-7.
46. Awasthi S, Peto R, Pande VK, Fletcher RH, Read S, Bundy DA, *et al*. Effects of deworming on malnourished preschool children in India: An open-labelled, cluster-randomized trial. *PLoS Negl Trop Dis* 2008; 2 : e223.
47. Awasthi S, Peto R, Read S, Richards SM, Pande V, Bundy D, *et al*. Population deworming every 6 months with albendazole in 1 million pre-school children in North India: DEVTA, a cluster-randomised trial. *Lancet* 2013; 381 : 1478-86.
48. Garner P, Taylor-Robinson D, Sachdev HS. DEVTA: Results from the biggest clinical trial ever. *Lancet* 2013; 381 : 1439-41.
49. Freeman MC, Clasen T. Assessing the impact of a school-based safe water intervention on household adoption of point-of-use water treatment practices in Southern India. *Am J Trop Med Hyg* 2011; 84 : 370-8.
50. Boisson S, Stevenson M, Shapiro L, Kumar V, Singh LP, Ward D, *et al*. Effect of household-based drinking water chlorination on diarrhoea among children under five in Orissa, India: A double-blind randomised placebo-controlled trial. *PLoS Med* 2013; 10 : e1001497.
51. Clasen T, Boisson S, Routray P, Torondel B, Bell M, Cumming O, *et al*. Effectiveness of a rural sanitation programme on diarrhoea, soil-transmitted helminth infection, and child malnutrition in Odisha, India: A cluster-randomised trial. *Lancet Glob Health* 2014; 2 : e645-53.
52. Clasen T, Boisson S, Routray P, Cumming O, Jenkins M, Ensink JH, *et al*. The effect of improved rural sanitation on diarrhoea and helminth infection: Design of a cluster-randomized trial in Orissa, India. *Emerg Themes Epidemiol* 2012; 9 : 7.
53. Patil SR, Arnold BF, Salvatore AL, Briceno B, Ganguly S, Colford JM Jr., *et al*. The effect of India's total sanitation campaign on defecation behaviors and child health in rural Madhya Pradesh: A cluster randomized controlled trial. *PLoS Med* 2014; 11 : e1001709.
54. Paul I, Gnanamani G. Quantitative assessment of *Ascaris lumbricoides* infection in school children from a slum in Visakhapatnam, South India. *Southeast Asian J Trop Med Public Health* 1999; 30 : 572-5.
55. Mani TR, Rajendran R, Munirathinam A, Sunish IP, Md Abdullah S, Augustin DJ, *et al*. Efficacy of co-administration of albendazole and diethylcarbamazine against geohelminthiasis: A study from South India. *Trop Med Int Health* 2002; 7 : 541-8.
56. Rajendran R, Mani TR, Munirathinam A, Sunish IP, Abdullah SM, Augustin DJ, *et al*. Sustainability of soil-transmitted helminth control following a single-dose co-administration of albendazole and diethylcarbamazine. *Trans R Soc Trop Med Hyg* 2003; 97 : 355-9.
57. Mani TR, Rajendran R, Sunish IP, Munirathinam A, Arunachalam N, Satyanarayana K, *et al*. Effectiveness of two annual, single-dose mass drug administrations of diethylcarbamazine alone or in combination with albendazole on soil-transmitted helminthiasis in filariasis elimination programme. *Trop Med Int Health* 2004; 9 : 1030-5.
58. Sunish IP, Rajendran R, Munirathinam A, Kalimuthu M, Kumar VA, Nagaraj J, *et al*. Impact on prevalence of intestinal helminth infection in school children administered with seven annual rounds of diethyl carbamazine (DEC) with albendazole. *Indian J Med Res* 2015; 141 : 330-9.
59. Clarke NE, Clements AC, Doi SA, Wang D, Campbell SJ, Gray D, *et al*. Differential effect of mass deworming and targeted deworming for soil-transmitted helminth control in children: A systematic review and meta-analysis. *Lancet* 2017; 389 : 287-97.
60. Anderson RM, Turner HC, Truscott JE, Hollingsworth TD, Brooker SJ. Should the goal for the treatment of soil transmitted helminth (STH) infections be changed from morbidity control in children to community-wide transmission elimination? *PLoS Negl Trop Dis* 2015; 9 : e0003897.
61. Anderson R, Farrell S, Turner H, Walson J, Donnelly CA, Truscott J, *et al*. Assessing the interruption of the transmission of human helminths with mass drug administration alone: Optimizing the design of cluster randomized trials. *Parasit Vectors* 2017; 10 : 93.
62. Alderman H, Konde-Lule J, Sebuliba I, Bundy D, Hall A. Effect on weight gain of routinely giving albendazole to preschool children during child health days in Uganda: Cluster randomised controlled trial. *BMJ* 2006; 333 : 122.
63. Sarkar NR, Anwar KS, Biswas KB, Mannan MA. Effect of deworming on nutritional status of ascariis infested slum children of Dhaka, Bangladesh. *Indian Pediatr* 2002; 39 : 1021-6.
64. Ozier O. Exploiting Externalities to Estimate the Long-Term Effects of Early Childhood Deworming. (Policy Research Working Papers 7052). The World Bank; 2014. Available from: <http://www.elibrary.worldbank.org/doi/book/10.1596/1813-9450-7052>, accessed on March 13, 2018.
65. Miguel E, Kremer M. Worms: Identifying impacts on education and health in the presence of treatment externalities. *Econometrica* 2004; 72 : 159-217.
66. Strunz EC, Addiss DG, Stocks ME, Ogden S, Utzinger J, Freeman MC, *et al*. Water, sanitation, hygiene, and soil-transmitted helminth infection: A systematic review and meta-analysis. *PLoS Med* 2014; 11 : e1001620.
67. Null C, Stewart CP, Pickering AJ, Dentz HN, Arnold BF, Arnold CD, *et al*. Effects of water quality, sanitation, handwashing, and nutritional interventions on diarrhoea and child growth in rural Kenya: A cluster-randomised controlled trial. *Lancet Glob Health* 2018; 6 : e316-29.

68. Luby SP, Rahman M, Arnold BF, Unicomb L, Ashraf S, Winch PJ, *et al*. Effects of water quality, sanitation, handwashing, and nutritional interventions on diarrhoea and child growth in rural Bangladesh: A cluster randomised controlled trial. *Lancet Glob Health* 2018; *6* : e302-15.
69. Humphrey JH, Jones AD, Manges A, Mangwadu G, Maluccio JA, Sanitation Hygiene Infant Nutrition Efficacy (SHINE) Trial Team, *et al*. The sanitation hygiene infant nutrition efficacy (SHINE) trial: Rationale, design, and methods. *Clin Infect Dis* 2015; *61* (Suppl 7) : S685-702.
70. Humphrey JH, Null C. WASH and Nutrition Interventions for Child Growth and Development: Results from the WASH-Benefits and SHINE Trials. Webinar Presented at: WASH and Nutrition Interventions for Child Growth and Development: Results from the WASH-Benefits and SHINE Trials; February 14, 2018. Available from: <https://coregroup.org/event/wash-and-nutrition-interventions-for-child-growth-and-development-results-from-the-wash-benefits-and-shine-trials/>, accessed on April 23, 2018.
71. Majra JP, Gur A. India needs a great sanitary awakening. *Indian J Occup Environ Med* 2008; *12* : 143.
72. Ásbjörnsdóttir KH, Ajjampur SSR, Anderson RM, Bailey R, Gardiner I, Halliday KE, *et al*. Assessing the feasibility of interrupting the transmission of soil-transmitted helminths through mass drug administration: The deWorm3 cluster randomized trial protocol. *PLoS Negl Trop Dis* 2018; *12* : e0006166.

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