

Review Article

Asian Pacific Journal of Tropical Medicine

doi: 10.4103/apjtm.apjtm_288_26

Soil-transmitted helminths and childhood development: Nutrition, anemia, cognitive outcomes, and school-based deworming

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ABSTRACT

Infections with soil-transmitted helminths (STHs) are one of the most common neglected tropical diseases globally and drive poor childhood development, which is a cycle within low and middle-income countries (LMICs). The infection is caused by *Ascaris lumbricoides*, *Trichuris trichiura*, and the hookworms (*Necator americanus*, *Ancylostoma duodenale*) and disproportionately affects school-age children and adolescents in the impoverished areas where water, sanitation, and hygiene are inadequate. This review is an integration to understand the association between STH infection and 4 key domains of childhood development: nutrition status, anemia, cognitive function and effect of school-based deworming, a public health intervention. At the global level, 37.16% of school-age children in LMICs are infected with STH, and the highest prevalence can be found in the Western Pacific (50.41%) and in Africa (37.10%). Chronic STH infection causes damage to nutritional status by inducing intestinal blood loss, malabsorption of nutrients and anorexia, directly contributing to stunting and underweight. In addition, hookworm infection worsens iron deficiency anemia, which is closely associated with cognitive development problems and lower academic attainment. Preventive chemotherapy, which is deworming for STH at school, is the main method for controlling STH at the global level and the World Health Organization recommends that children be dewormed annually or biannually depending on endemicity. Recent programmatic evaluations indicate that school-based deworming can decrease STH prevalence, improve nutritional markers, and can have long-term cognitive and economic impacts. Despite this, there are still barriers to be addressed: suboptimal deworming coverage in many areas, high risk of reinfection following deworming, low efficacy against *Trichuris* and

Strongyloides, and a limited number of large-scale RCTs that provide evidence of benefit with regards to hemoglobin concentrations and cognitive function. The current review summarizes epidemiological data from the different regions, explains how STH is related to poor developmental outcomes, and summarizes the effectiveness of school-based deworming. It also identifies key areas of uncertainty that require research such as long-term cohort studies, identifiable and standardized integrated deworming protocols, and scalable protocols to help ensure the sustainability of deworming benefits.

KEYWORDS: Anemia; Cognitive development; Deworming; Nutrition; Soil-transmitted helminths

1. Introduction

The soil-transmitted helminth (STH) infections are the most prevalent neglected tropical diseases (NTDs) globally and are a huge, preventable burden for children in resource-limited areas. The World Health Organization (WHO) estimates that some 1.5 billion people (24% of the world's population) suffer from STH infections,

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How to cite this article: Ahmed B, Ahmed AS, Tanveer R. Soil-transmitted helminths and childhood development: Nutrition, anemia, cognitive outcomes, and school-based deworming. Asian Pac J Trop Med 2026; 19(11): 473–485.

Article history: Received 5 June 2026 Revision 27 July 2026
Accepted 20 September 2026 Available online 16 October 2026

mainly in sub-Saharan Africa, China, South America and Southeast Asia[1]. The estimated Disability Adjusted Life Years attributable to STH worldwide were reported as high as 1.5 million in the Global Burden of Disease (GBD) in 2019[2]. School-age children (SAC) (5-18 years) are the highest risk population with an estimated 654 million living in high intensity STH transmission zones and needing timely and regular STH prevention interventions to prevent lifelong morbidity[1].

The major STH species that infect humans are the roundworm [*Ascaris (A.) lumbricoides*], the whipworm [*Trichuris (T.) trichiura*], and the hookworms (*Necator americanus*, *Ancylostoma duodenale*)[3]. The fifth species, *Strongyloides stercoralis*, is a neglected form of strongyloidiasis, not sensitive to common anthelmintic drugs and possesses a peculiar life cycle, necessitating consideration of it separately from the other species[4]. All STH species are transmitted from fecally contaminated soil, food or water and infection is achieved by ingesting infective eggs or by active penetration of the skin by hookworm larvae. A notable exception is hookworm *Ancylostoma duodenale*, which can also be transmitted by the ingestion of the infective larva (L3) through the mouth[5]. In areas where sanitation and hygiene levels are low, children are constantly exposed to these parasites throughout their lives, and there is no natural elimination unless public health measures are taken[4].

STH infection is frequently referred to as a "neglected" as they generally affect poorer populations often living in remote rural or peri-urban areas in developing countries without adequate sanitation, in poor housing conditions and with little access to health services, and as most are focal in nature and occur in remote areas, they are rarely given high priority by decision makers in endemic countries. However, the indirect and long-term morbidity due to these infections is immense: chronically infected children have reduced cognitive function and academic achievement, iron deficiency anemia, and impaired economic productivity in adulthood[6]. These adverse outcomes are not merely correlated with STH infection but are causally driven by it, triggering long-term cascading health burdens that persist in the absence of targeted deworming treatment.

The WHO has promoted school-based deworming (SBD) [preventive chemotherapy (PC)] as the most economical approach to reducing the morbidity of STH in SAC for over two decades[7]. The school can serve as a platform for the distribution of anthelmintic drugs to a large number of children including remote and poor areas. This review aims to summarize the current global epidemiological evidence, mechanistic studies and program evaluation data over the last 5 years (2020-2024) to better understand the links between STH infection and nutritional status in children, anemia, cognitive function, and the impact of school-based deworming as a public health intervention. It also explores the geographic differences in the burden of disease, identifies challenges in implementation and

gaps in research needed to eradicate STH morbidity by 2030, and discusses the key research priorities[8].

2. Methodology

This review employed a systematic literature search of PubMed, Web of Science, Scopus, WHO IRIS, and Google Scholar for peer-reviewed articles, programmatic evaluations, and WHO guidelines published from January till December 2025, using search terms related to STH infections, *A. lumbricoides*, *T. trichiura*, hookworm, school-based deworming, preventive chemotherapy, nutrition, anemia, and cognitive function in low and middle-income countries (LMICs). We included English-language studies involving school-age children that reported outcomes relevant to any of the four domains of interest. Data were extracted and study quality was assessed using the Cochrane RoB 2 tool for RCTs and the Newcastle-Ottawa Scale for observational studies.

3. Soil-transmitted helminthes and global childhood disease burden

The global epidemiological burden of STH must first be understood to appreciate the population-level impacts of these infections on childhood development. Agral *et al.* carried out an extensive literature search using PubMed, Embase, CINAHL, and PsycINFO for studies published between 1999 and 2022 reporting rates of STH infection in school-going children aged 5-18 years. A total of 19 725 of the 49 630 children examined were infected with STH, yielding an overall pooled prevalence of 37.16% (95% CI 29.74-44.89). This analysis found that there was significant variation in the level of burden by region, with 50.41% in the Western Pacific region, 37.10% in Africa, 39.60% in Southeast Asia and 19.86% in the Eastern Mediterranean region. The most common species was *A. lumbricoides* (24.07%) followed by *T. trichiura* (16.04%) and hookworms (10.73%), which showed great variation in the geographic distribution of the species[2].

The differences between the regions are not arbitrary, but are related to environmental, socioeconomic, and programmatic influences. The warm and moist soil conditions required for the development of STH eggs and larvae into infective stages are the reason for their high burden in tropical and subtropical climate. High risk areas are also areas of poverty, poor access to clean water and basic sanitation and poor hygiene education, all of which are associated with frequent, repeated exposure of children to infective STH stages[9].

Since 2010, the number of countries using mass drug administration (MDA) has increased, but as expected, the reduction in STH prevalence has been slow[10]. The temporal trend analysis from 1999

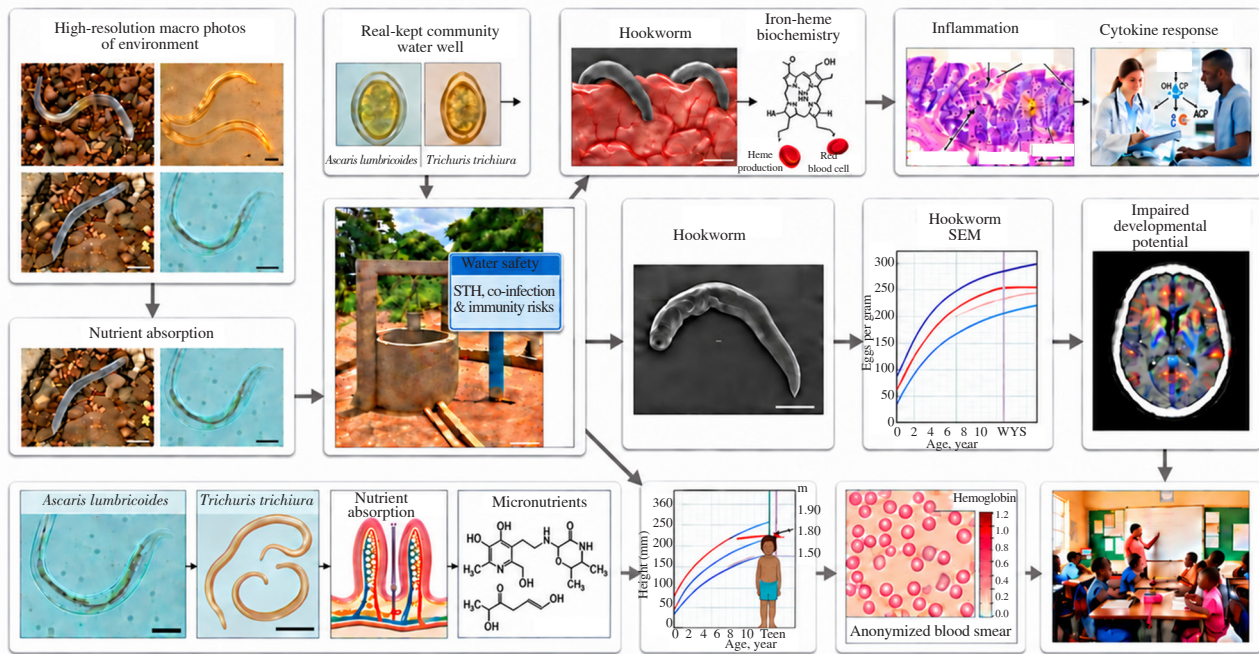


Figure 1. Soil-transmitted helminths infections and its effects on child nutrition and development. The schematic illustrates the route of environmental exposure for *Ascaris lumbricoides*, *Trichuris trichiura* and Hookworm, which are all transmitted through contaminated soil, water and sanitation. Intestinal infection impairs nutrient and micronutrient uptake and hookworm blood loss is a cause of iron deficiency and anemia. Persistent infection can also drive inflammatory and cytokine responses, yielding suboptimal growth, anemia, suboptimal school performance, and altered neurodevelopmental outcomes. Diagnostic panels consist of parasite microscopy, growth assessment, blood smear analysis, neuroimaging, and scanning electron microscopy imaging.

to 2022 revealed limited reduction in prevalence in STH (12%)[2], which is not sufficient to meet the WHO elimination targets[11,12]. This slow progress has been multifactorial, including poor coverage of deworming programmes particularly in remote and conflict-affected areas, ongoing environmental contamination leading to high reinfection rates after deworming and suboptimal efficacy of the drugs against certain species of STH (particularly *T. trichiura* and *S. stercoralis*). These results were also further hampered by the COVID-19 pandemic: School-based deworming programs and water, sanitation, and hygiene (WASH) interventions were suspended in many countries for up to 18 months due to national lockdowns, and STH re-emerged in previously controlled areas worldwide[13,14].

Epidemiological information clearly indicates a higher prevalence of STH in rural areas, in families with low socio-economic status and in communities that have poor access to formal health care[15]. Children in informal settlements, rural areas and high open defecation prevalence areas are at the greatest risk of infection, and have the least access to supportive nutrition programs and deworming services. The resulting inequity in distribution translates to a disproportionate burden of STH on children who already

have the most structural barriers to healthy development, and thus exacerbates existing health and socioeconomic inequities[16].

4. STH infection and nutrition status

STH infection and poor nutrition are interdependent and synergistic. Children's vulnerability to STH infection and its downstream morbidity is further exacerbated by the negative effects that STH parasites have on their nutrition through several parallel biological mechanisms, which are exacerbated by pre-existing malnutrition in children (Figure 1). In high-burden areas of sub-Saharan Africa and South Asia, STH infections and child malnutrition share the same vulnerable groups, and this cycle is most pronounced[17].

4.1. Causal mechanisms

The nutritional depletion associated with STH parasites works through four well-documented pathways that lead to nutritional deficits and progressive, chronic depletion of STH-infected

children[18]. Hookworms are attached to the mucosa of the small intestine (duodenum and jejunum), sucking host blood and leading to chronic low volume gastrointestinal blood loss. Small amounts of blood loss from individuals over short periods of time do not cause a lot of concern, but over time, the bodies of individuals with a persistent hookworm infection can be depleted of iron, an essential nutrient for proper growth and cognitive function. This is the primary mechanism of iron deficiency anemia in children with high hookworm infections[19]. The primary mechanism of anemia due to *T. trichiura* is chronic intestinal blood loss caused by the adult worms attaching to and feeding on the colonic mucosa. This leads to iron deficiency anemia, particularly in heavy infections[20].

All STH species are associated with varying degrees of inflammation of the intestinal mucosa and damage to the brush border of the small intestine that leads to decreased surface area for nutrient absorption, known as nutrient malabsorption. This inflammation hinders the uptake of essential micronutrients such as iron, zinc, vitamin A and B vitamins, and macronutrients such as proteins and carbohydrates. This malabsorption is a cause of growth faltering and micronutrient deficiencies even if children have access to nutrient-rich foods[21]. STH infection alters the host's enteric nervous system and inflammatory response, which suppresses appetite and lowers total food intake, according to experimental and clinical research. This effect is most likely to be seen in children with moderate to heavy infection intensity, who may eat substantially less than uninfected children. The decreases in dietary intake compound the nutrient depletion associated with blood loss and malabsorption, resulting in a vicious cycle of worsening nutrient depletion[22]. There is some evidence that STH worms in their adult stages in the intestinal lumen compete directly with the host for ingested nutrients. In particular, *A. lumbricoides* can sequester vitamin A and other micronutrients essential for the growth of children and their immune system. This mechanism is not as great as the blood loss or the malabsorption, but this can add up and exacerbate the problem in children with poor nutrition intake[23].

4.2. Epidemiological evidence linking the STH to childhood stunting and micronutrient deficiencies

Many cross-sectional studies have reported a consistent relationship between impaired growth and STH infection, but this correlation has been stronger in some areas than others, and is different for different STH species and infection intensities. Soil-transmitted helminths deplete nutrients by feeding on host tissues and blood, with hookworms causing iron loss and anemia. They also reduce nutrient absorption, may compete for vitamin A, and suppress appetite, leading to lower food intake. Additionally, *T. trichiura* triggers

diarrhoea and dysentery, further worsening nutritional loss[1].

Regionally, the burden is highest in areas where there is high STH transmission. STH infection intensity was found to be significantly associated with underweight status among schoolchildren in Banda District, Ghana in 2024 where 13.1% of the population was underweight[24]. The dynamics of STH within Asia and the Americas are of greater complexity. The prevalence of STH in children under 7 years of age was 32.5%. Malnutrition, indicated by stunted and severely stunted children with a range of cases from 5% to 37%, was strongly linked with *A. lumbricoides* infection (*OR* 3.45, 95% *CI* 1.70-7.02, *P*<0.001)[25]. Similar associations to those found above have been reported in other STH endemic areas, such as Central and South America, where infections are 15%-30% and where stunted children are significantly more likely to be infected than uninfected children, especially in rural areas and in the presence of poor sanitation[26].

In particular, the association of poor nutritional outcomes with each STH species is not equal, with hookworm and *Trichuris* infection being most consistently linked to poor nutrition outcomes; this is probably because hookworm and *Trichuris* cause chronic intestinal blood loss and directly damage the intestinal mucosa, whereas *Ascaris* infection does not[27].

4.3. Effect of deworming on nutritional status

There is strong evidence from observational studies that there is a relationship between STH and malnutrition among children. Data from 67 RCTs from around the world involving more than 50 000 children were combined in a 2015 Cochrane Review (2023 update) that was the most robust analysis performed to date. In most study settings, deworming did not have a statistically significant effect on children's benefits such as weight gain in the review. But when children were found to be moderately-to-heavily infected with STH at baseline, or when deworming coverage was maintained over several years, the effects of deworming on weight gain and another important indicator of nutritional status, the mid-upper arm circumference, were small but significant[28].

There are two main reasons for these diverse results. Many deworming trials are done under conditions of high reinfection rates: children who are dewormed with anthelmintic are often re-infected within months after deworming, negating any possible nutritional benefit. Second, children in high-burden areas may already have a high prevalence of enteric illnesses, numerous micronutrient deficiencies, and restricted access to nutrient-rich foods, so STH is not usually the main cause of malnutrition. However, in these settings, deworming alone is not enough to address malnutrition; it requires a combination of other measures, including complementary

feeding, micronutrient supplementation, or school feeding programs, and/or WASH interventions. While a deworming-only intervention did not show significant differences, a deworming plus school-based nutrition supplementation intervention was shown to significantly improve weight-for-age Z-scores in children in Ethiopia in 2024[29].

5. STH infection and anemia

Anemia is the most reported and clinically meaningful haematozoological effect of STH infection in school-age children and adolescent girls[30]. The STH and anemia relationship is largely represented by iron deficiency resulting from chronic intestinal blood loss, as well as by decreased micronutrient absorption and anemia of chronic inflammation, which is linked to helminth infection, and can lead to rapid reinfection[31]. The biological links of STH to iron deficiency anemia (IDA) are threefold: (1) chronic intestinal bleeding, *Ancylostoma duodenale* worm taking up to 0.3 mL and *Necator americanus* up to 0.04 mL of blood every day[32]; (2) reduction in absorption of dietary iron and micronutrients such as vitamin B12 and folate due to damage to brush borders[33]; (3) hepcidin induction by inflammation, which binds iron in the reticuloendothelial stores, aggravating IDA[34]. The STH egg burden is associated with the prevalence of anemia, in an epidemiologically consistent dose-response relationship, especially in school-age children and adolescent girls[35]. Meta-analyses of the literature around the world suggest that 12%-15% of the anemia cases in endemic areas are due to STH, of which 14.40% occur in sub-Saharan Africa and 15.8% in South Asia[36]. Based on field data from Ethiopia, Ghana and India, moderate to heavy infections increase the risk of anemia with adolescent girls being compounded by menstrual losses, thus increasing their risk by 2.3 to 3.2 fold compared with uninfected girls[37,38].

However, there is no consistent evidence to suggest that deworming is enough to decrease the prevalence of anemia. A cochrane synthesis of 14 RCTs found no significant differences in hemoglobin levels or the rates of anemia between deworming and placebo[39]. However, subgroup analyses suggest that deworming alone may be beneficial in specific contexts: in high prevalence areas of moderate to heavy baseline infections, deworming alone is associated with an increase in hemoglobin and reduction in anemia prevalence; and in areas where deworming is combined with iron and folic acid[39,40]. Based on these results, deworming is a key but not sufficient intervention, and should be combined with micronutrient supplementation, dietary diversification, and WASH interventions to achieve sustainable impacts on reducing anemia in STH endemic regions to prevent rapid reinfection and sustain hematologic benefits.

6. STH infection and cognitive development

The studies showed that STH infections have consistently been linked to lower IQ, memory, attention, and school performance. The deficits in attention, memory, processing speed, and executive function in each region (Ghana, Ethiopia, and South Africa) are consistently reported[41–44]. These impairments have been observed in IQ testing (using the WISC and RPM) as well as in academic performance and absenteeism in the school setting. A study carried out in Jamaica also showed that the academic performance, as evaluated by school records and teacher reports, was significantly impaired by concurrent infections with the two species *T. trichiura* and *A. lumbricoides*.

While Africa suffers the highest burden of STH infection, there are important comparative lessons to be learned from Asia and Latin America. Studies in Indonesia and Malaysia indicated that *A. lumbricoides*, *T. trichiura* and hookworm infected children exhibited a reduction in working memory and an increase in school absenteeism[45,46]. Across China, moderate to heavy STH infections were significantly related to verbal comprehension, working memory, and processing speed deficits[47]. Results from Cambodia and Vietnam also showed that the level of infection and nutrition influenced cognition, with deficits noted in reasoning and working memory tasks[48,49]. Coinciding with this, a study conducted in the Philippines revealed that helminth infection was a risk factor for poor learning and memory, independent of socioeconomic and nutritional factors[50].

In the context of the mechanism, STH infections lead to impaired cognitive development by causing nutritional deficiency due to infections and chronic inflammation[51]. Hookworm causes iron deficiency anemia through chronic gastrointestinal bleeding that limits the supply of oxygen to the brain and disrupts some cognitive functions that require adequate iron[52]. *A. lumbricoides* and *T. trichiura* infections compound the effects of malnutrition and energy deficits important for brain growth and function[53]. Like schistosomiasis, STH infections cause chronic low-level inflammation, which can deplete resources for neurodevelopmental processes and lead to neuroinflammation[54]. Children's concentration and participation in school activities are further affected by clinical symptoms like lethargy, abdominal discomfort, diarrhea, and general ill health, which lead to poorer school attendance and thereby to poorer performance.

Although there are documented cases of helminth-induced cognitive deficits in certain environments, several studies found no or inconclusive relationships. In one study, no differences were observed in IQ scores between infected and uninfected pupils from Nigeria. According to the Newcastle-Ottawa Scale, the study was rated at a high quality (score 7), suggesting that methodologically

the null findings are strong. The authors hypothesized that the lack of measurable effects could be due to low infection levels and/or the potential protective effects of hygiene measures, with regular handwashing being found to be significantly protective[55]. Likewise, another study found no significant relationship was observed between light intensity STH infections and working memory, processing speed, or children's school scores, which were recorded by children, in Zambian children[56]. The methodological limitations may explain this lack of association, and the authors highlight the need for larger, carefully designed studies on the cognitive and educational impacts of STH infection.

7. Global strategy, effectiveness and implementation

Preventing morbidity due to STH in school-age children is at the centre of the WHO global strategy which is known as school-based deworming, or school-based preventive chemotherapy. WHO's approach to controlling soil-transmitted helminth infections is based on prevention of morbidity by targeting at-risk groups in endemic regions for helminths with periodic deworming. In contrast to individual diagnosis, the WHO is calling for MDA to everyone who is at risk, with administration once a year if the prevalence of infection in the community is above 20%, and twice a year if above 50%. The method helps decrease not only the total worm burden but also the associated health problems in the affected communities[57].

WHO's current STH control guidelines (2023) suggest a preventive chemotherapy strategy of treating all preschool and school-age children in endemic areas. The goal of morbidity elimination for STH in 100% of endemic countries, outlined in the 2030 NTD road map, is dependent on maintaining at least 75% coverage of the target population of STH-prone children. The roadmap also underscores the importance of ensuring that SBD is combined with other school-based health interventions like WASH education, micronutrient supplementation, and malaria control to achieve greater impact and minimize the risk of reinfection after treatment[58].

The main objective of SBD is to minimize the prevalence and severity of moderate to heavy STH infections and thereby decrease the subsequent nutritional, hematological and cognitive morbidities of chronic disease. Recent program assessments throughout Africa and Asia have confirmed that SBD can accomplish this fundamental public health objective, but the impact is widely different in various regions and program designs[59]. A reduction in the frequency and severity of STH is the most consistent and noticeable consequence of SBD, particularly in regions with a high baseline transmission rate. In Nigeria, the long-term effectiveness of an MDA program for the school was assessed in 2024, where children were administered five successive doses of biannual albendazole over 6 years. The

prevalence of any STH infection was significantly reduced after 5 rounds of STH treatment with a relative reduction of 34% in Ese-Odo LGA ($P<0.001$). When analyzed at program level, across the three implementation units, STH prevalence decreased to 9.7%, which is close to the WHO threshold for considering STH prevalence $<2\%$ and possibly for suspension of treatment. The greatest reductions in infection prevalence were observed for *A. lumbricoides* and hookworms, whereas the programme is known to be less effective against *T. trichiura* when using single-dose albendazole[60,61]. In a similar study published in *PLoS Neglected Tropical Diseases* in 2023, researchers assessed a 6-year programme of preventive chemotherapy using annual or biannual albendazole (depending on prevalence) for children in the Republic of Angola. The analysis indicated that the program was effective in the targeted districts, the overall prevalence of STH was reduced by 68%, with the greatest reductions in hookworm and *Ascaris* infections. The number of children who had moderate-to-heavy intensity infections dropped by over 80% during the 6-year period; these children are most likely to have morbidity. A decrease in the intensity of infection will directly lead to a decrease in STH-related morbidity such as anemia and stunting. If deworming coverage were above 85% throughout the program, as was seen in both Nigeria and Angola, then high quality and continuous MDA delivery is essential for successful STH control[62].

Although the clinical effect on morbidity outcomes is mixed, SBD is one of the most effective public health interventions in LMICs. The most important contributing factor to this cost-effectiveness is the low cost of the drugs: albendazole and mebendazole, the two most widely used anthelmintic drugs, are donated for free by the pharmaceutical industries in the endemic countries, so that the cost of the program is only that of personnel, drug distribution and social mobilization. The 2025 *PLoS Neglected Tropical Diseases* cost-effectiveness analysis estimated a viable school-based MDA using albendazole alone and school-based MDA using the combination of albendazole plus ivermectin (for enhanced *Trichuris* control) to be delivered in Uganda[61]. The study determined that both programs were very cost effective with the cost per DALY (disability adjusted life year) averted of USD 125 for the albendazole-only program. This makes SBD one of the most cost-effective child health interventions in LMICs, significantly more cost effective than most other public health treatment or prevention programs. The analysis also showed that adding ivermectin to the standard albendazole regimen would be a cost-effective addition that would yield an additional 24% reduction in STH-related morbidity, thereby helping to meet program elimination goals, with only a 15% increase to program costs[63]. Given their low mortality, the best epidemiological measure to show the impact of STHs is disability adjusted life years. The DALY is an internationally agreed indicator that fully reflects

the burden, combining premature death (years of life lost) with the more substantial health losses from disability (years lived with disability)[64].

Not having adequate coverage of school-age children is the biggest threat to the effectiveness of SBD. Coverage of at least 75% are recommended to stop transmission of the STH, but most endemic countries have been unable to achieve these levels, especially in rural areas where the logistical challenges to program delivery are the most significant. In the Philippines, for instance, deworming coverage among school-age children decreased continuously from 58.55% in 2019 to 41.56% in 2022[65]. This reduction stemmed from multiple factors: school closures during the COVID-19 pandemic, insufficient funding for social mobilization activities, shortages of health workers responsible for drug administration, and parental refusal driven by misinformation regarding the safety of anthelmintic drugs. There are also gaps in the coverage between and within countries: in a 2024 WHO case study in Kenya, for instance, deworming coverage in remote, arid counties was below 30%, while it was more than 80% in urban and peri-urban counties. This patchy coverage allows for STH transmission to continue in low coverage areas, despite high coverage in neighbouring districts[66].

One of the other significant issues is that of re-infection after deworming. However, when no other WASH intervention is provided, endemic children are often re-infected with STH within months of treatment. This is supported by the results of field studies conducted all over Africa and Asia: A systematic review and meta-analysis was used to assess the relationships between increased WASH and infection with STH (*A. lumbricoides*, *T. trichiura*) and *Strongyloides stercoralis*. In general, the likelihood of contracting STH increases with decreasing access to WASH and hygiene practices. Most poolings of the individual estimates from the meta-analyses showed an odds reduction of at least 33% for each individual WASH practice or access[67]. The pattern of treatment and rapid reinfection reiterates the need for an ongoing deworming program in order to keep infection prevalence low, unless other WASH interventions are used to help reduce environmental contamination and transmission[68].

In most MDA programs, both albendazole and mebendazole, the two drugs used, are effective against only two of the five major species of STH. Single dose treatment with albendazole is generally less than 30% effective for *Trichuris* infections, resulting in the majority of children with an infection retaining the worm burden after treatment. The situation is even more complicated with *Strongyloides stercoralis* which possesses a unique autoinfective life cycle that allows ongoing endogenous reinfection within the host, unlike classical STHs which require exogenous environmental maturation for transmission[69]. WHO defines *Strongyloides stercoralis* as an intestinal helminth with peculiar characteristics: the parasite requires different diagnostic methods than other soil-

transmitted helminthiases, and for this reason is frequently not identified. In addition, the parasite is not sensitive to albendazole or mebendazole and therefore not impacted by large-scale preventive treatment campaigns targeting other soil-transmitted helminthiases[5]. This is an important public health knowledge deficit because disseminated infection with *Strongyloides* can be fatal in immunocompromised children, particularly in malnourished and HIV infected children. This has been acknowledged by WHO, and in 2021, the Organization integrated *Strongyloides* control into their 2030 STH elimination plan. However, scaling up treatment for this species will only be achieved if ivermectin is used more extensively, but it is not currently available in most deworming programs in the endemic countries and is not widely available[70,71].

Lastly, there is a proven disconnect between deworming treatment and ongoing morbidity reduction: deworming cannot reverse the malnutrition, anemia and cognitive impairment resulting from chronic STH infections. The morbidity outcomes require a complementary intervention for the underlying risk factors and for the multifactorial causes of the morbidity, in addition to deworming. These interventions are most critical[72].

8. Synthesizing the interrelationships: STH, nutrition, anemia, and cognition

The four areas of interest for this review (STH infection, nutritional status, anemia, and cognitive function) are not independent variables. Rather, they are part of a synergistic, self-reinforcing vicious cycle of poor child development, with STH infection as the key trigger and the cycle can be divided into four feedback loops that strengthen each other shown in Figure 2[73]. Due to chronic STH infection, iron, zinc, vitamin A and other micronutrients are depleted because of blood loss from the gut, malabsorbed nutrients, and decreased appetite. This results in stunting, underweight and generalized malnutrition[74]. Micronutrient deficiencies, especially IDA are a significant contributor to anemia in children. These deficiencies are compounded by the blood loss and malabsorption caused by STH and the synergistic effects of moderate-to-severe anemia[75].

Iron deficiency anemia, directly, affects children's neurodevelopment, impacting memory, executive function and attention span. These learning impairments add up and result in substandard school performance and other learning difficulties[76]. Children with untreated cognitive and academic impairments are less likely to be provided with good hygiene *e.g.*, wash hands or wearing shoes which will protect them from exposure to hookworm larvae. Additionally, they could be more likely to engage in play activities that expose them to contaminated water or dirt. They are more vulnerable to STH reinfection as a result of this increased exposure, creating a

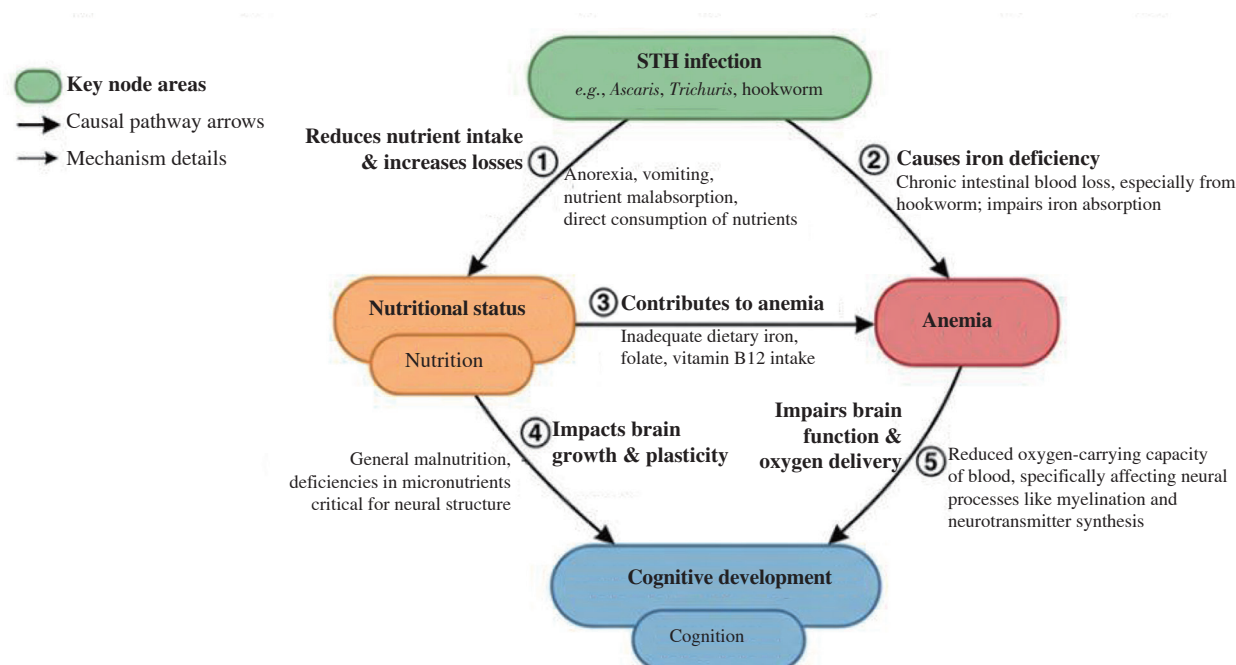


Figure 2. Conceptual framework illustrating the interrelationships between soil-transmitted helminth (STH) infection, nutritional status, anemia, and cognitive development.

perpetual cycle that persists through childhood into adolescence and adulthood[77].

The cycle is further compounded by the underlying socio-economic inequalities: children living in poverty, the rural population and informal settlements are at the highest risk of STH infection, and the least likely to have access to deworming services, nutritious food and quality education. In such settings, STH infection may reflect existing disadvantages and contribute directly to additional developmental delays.

What is important about this vicious cycle is that interventions which only focus on deworming, nutrition, or WASH alone will not break the vicious cycle. In order to lower STH-related morbidity and promote healthy childhood development, public health programs must provide a full range of interventions. It is this fundamental principle that lies at the heart of the recent campaign by WHO for integrating deworming, micronutrient supplementation, school feeding programs and WASH education into a single school-based health service delivery model[78].

9. Discussion and future perspective

There is a vicious cycle of STH infection leading to malnutrition, anemia and cognitive impairment, which create a synergy that reinforces developmental inequalities in low and middle income

countries[30]. From a biological perspective, the consequences of hookworm induced blood loss, malabsorption, and sequestration of iron in hepcidin are responsible for the development of iron deficiency anemia, and chronic inflammation and micronutrient depletion lead to developmental and cognitive impairment independent of anemia[79]. However, linking this pathophysiology to the public health impact is limited by the lack of evidence and implementation problems. Lack of a hemoglobin or cognitive benefits from deworming does not challenge the biological significance of STH control, but rather highlights the need for deworming as a building block that needs to be paired with other interventions. Synergies are observed when using integrated approaches and a combination of deworming and iron and folic acid can reduce anemia by up to 41%. The prevalence of STH in the global population has only decreased by 12% over 20 years, and this is not enough; without environmental interventions, mass drug administration alone will not bring a decrease. However, if reinfection occurs within the few months of partial recovery, potential gains are obviated, resulting in a "reinfection trap". Community-wide MDA, in addition to sanitation, hygiene, and safe water, results-based financing (provision of disbursement based on prevalence reduction); and combination anthelmintics (*e.g.*, albendazole plus ivermectin) to increase efficacy against *Trichuris* and *Strongyloides* are examples of solutions that have been proposed,

though procurement, training, and regulatory barriers remain.

Digital health has a transformative role in precision targeting, with the ability to use geospatial mapping, machine learning and mobile surveillance to adaptively allocate resources to infection hotspots and maximise cost-effectiveness. Deworming can be integrated with childhood vaccination, growth monitoring and school health service delivery to reach out-of-school children, and mobile apps by community health workers can improve coverage and surveillance. There is a critical need for longitudinal cohorts to provide the cumulative effect of deworming on cognition, education and productivity, thus bolstering the economic arguments and cost-effectiveness studies. To bridge context-specific barriers, financial, logistical, cultural, and political barriers and to engage in testing solutions that are tailored, implementation science must identify such barriers. Notably, the added benefit of WASH interventions was not found after 12 months, indicating a longer timeframe for evaluation is needed. Behavioural innovations (school competitions, CLTS, latrine incentives) should be tested thoroughly.

Success measures need to move beyond parasitological outcomes and into child development outcomes (height-for-age, hemoglobin, cognition testing); this will also need to involve cross-sectoral governance and accountability. Although *Strongyloides stercoralis* is a neglected microfilariæ producer, it requires species-specific attention because of its potential for fatal disseminated disease. To be resilient after COVID-19, program supply chains need to be decentralized, distribution needs to be community based, and funding needs to be diversified. Innovation, integration, and equity can help to reframe incremental steps and make a difference in the health, cognition, and life possibilities for millions of children.

10. Conclusions

STH infections continue to be a worldwide public health issue, with a long-term impact on nutritional outcomes, hemoglobin, cognitive function, and future economic productivity, and as a result of the poor childhood development they cause. In order to demonstrate that STH infection is a direct and avoidable cause of stunting, IDA, and reduced cognitive function in school-aged children in LMICs, this review aims to compile the most recent epidemiological, clinical, and programmatic evidence. The impact of these infections is not equal; the poorest, and most marginalized, children in the Western Pacific, sub-Saharan Africa and Southeast Asia are at greatest risk of infection and its downstream effects[80].

Developing and implementing school-based deworming is the cornerstone of global activities to control STH-related morbidity, and it has been shown to be highly effective in decreasing the prevalence

and intensity of STH infection in endemic areas. But deworming is not enough. Unless combined with complementary interventions (micronutrient supplementation, school feeding, and ongoing WASH improvements, which help to tackle the underlying risk factors of STH infection and STH-related morbidity), the nutritional, anemia, and cognitive benefits of deworming are frequently limited and transient to halt the cycle of poor child health. To improve children's health and development in a meaningful and lasting way, integrated, multi-sectoral programs are needed to address STH transmission, nutrient deficits, and healthy neurodevelopment[81].

The WHO 2030 roadmap for neglected tropical diseases seeks to eradicate morbidity attributable to STH globally. Expanding deworming coverage to at-risk children, including those who are not in school, funding synergies between deworming and WASH and nutrition programs, conducting high-quality research to close important evidence gaps, and enhancing national surveillance to monitor deworming prevalence and long-term health outcomes are all necessary to meet this goal. It will also need to have continued political will, funding from international health donors, and inter-sectoral coordination between the health, education, and water sectors in individual countries[82].

All of the data in this review are consistent with the idea that STH control isn't only about decreasing parasitic infection; it's about making an investment in child health and human development around the world. By ending the vicious cycle of STH-related morbidity, millions of children in the poorest communities in the world will have better nutritional status, school attendance and economic productivity for the rest of their lives. Moving forward to eliminate NTD related morbidity and progress towards improving child health equity globally, scaling up effective, integrated, and sustained school-based deworming programs should continue to be a key priority for organizations in the global health community, as well as national governments and the public health sector[83].

Conflict of interest statement

The authors declared no conflict of interest

Data availability statement

The manuscript does not contain any new or generated data. All the data obtained from other work are properly cited and obtained permission where required.

Funding

The authors received no extramural funding for the study.

Authors' contributions

B.A. conceptualized and designed the study project, developed theoretical formalism, and drafted the manuscript. A.S.A. contributed to the data collection, analysis, and interpretation, and critically revised the manuscript for important intellectual content. R.T. assisted with data analysis and interpretation and reviewed and edited the manuscript. All authors contributed to the final version of the manuscript. B.A. supervised the project and approved the final submission.

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Edited by Pan Y, Lei Y, Zhang Q