

## Policy Brief

# Moving Forward in Eliminating Soil-Transmitted Helminths as a Public Health Problem

### Communication materials

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**EDCTP**

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## Moving Forward in Eliminating Soil-Transmitted Helminths as a Public Health Problem

### Summary

Soil-transmitted helminths (STH) represent a significant public health threat in endemic countries. The current recommended strategy for the treatment and control of these infections faces several challenges, including limited efficacy against certain STH species. A clinical trial conducted by the STOP consortium demonstrated that a single tablet with a fixed dose coformulation (FDC) of ivermectin and albendazole is safe and more effective in treating *T. trichiura* and hookworms in children. Modelling studies suggest that shifting to the FDC and extending treatment to adults could reduce the time and cost required to eliminate STH as a public health problem and ultimately interrupt their transmission.

### Background

A poverty-related disease affecting one of four people in the world

Soil-transmitted helminths (STH) are among the most common infections worldwide, affecting an estimated 1.5 billion people. Most of these people live in tropical and subtropical regions, and in disadvantaged communities with poor access to clean water, sanitation and hygiene. STH are included in the list of Neglected Tropical Diseases (NTDs).

STH infections are caused by different species of parasitic worms present in human faeces, which can infect the human body by contact with soil and water or by larvae that can penetrate the skin. The main STH species are roundworm (*Ascaris lumbricoides*), whipworm (*Trichuris trichiura*), hookworms (*Necator americanus* and *Ancylostoma duodenale*) and *Strongyloides stercoralis*. Depending on the number of infecting worms, a person may experience a range of symptoms including diarrhoea and abdominal pain, malnutrition, weakness, and impaired growth and physical development in children.

260 million preschool-age children  
654 million school-age children  
108 million adolescent girls  
138 million pregnant and lactating women  
live in areas where STH are intensively transmitted  
and need treatment and preventive interventions

(WHO)

STH infections represent a significant public health threat in endemic countries. Every year, they lead to the loss of up to 5 million disability-adjusted life years (DALYs) and result in an estimated 12,000 to 135,000 deaths.

### The challenge of eliminating STH as a public health emergency

In 2001, the World Health Assembly endorsed a resolution (WHA54.19) urging endemic countries to eliminate STH infections as a public health problem by intensifying the control of STH in high-transmission areas, and sustaining control activities in low-transmission areas.

The current strategy recommended by the WHO to reduce and control STH infections is the periodic treatment with albendazole (or mebendazole) to all at-risk people<sup>1</sup> living in endemic areas (particularly pre-school and school-aged children), without previous individual diagnosis<sup>2</sup>.

Albendazole is safe, inexpensive and easy to administer by non-medical personnel. But there are some concerns regarding the success of this monotherapy strategy. First, although the drug remains effective against *Ascaris* and hookworm, its efficacy against *T. trichiura* is low and decreasing, and it is not effective against *S. stercoralis*. Second, the risk of emergence and spread of drug-resistant parasites is always greater when using one single drug.

It is therefore likely that STH will continue to have a large public health impact if the current control strategy including monotherapy with albendazole remains unchanged.

### Adding ivermectin to overcome the problem

Ivermectin has shown an enhanced activity against *T. trichiura* when combined with albendazole, and is considered the drug of choice against strongyloidiasis and other parasitic infections.

This is why the STOP consortium<sup>3</sup> evaluated a new, single pill combining a fixed dose of albendazole and ivermectin. This fixed dose coformulation (FDC) has the advantage of being easy to administer since it involves one single pill and does not require adapting the dose according to the child's weight.



<sup>1</sup> At-risk people include preschool and school-age children, women of reproductive age and adults in high-risk jobs such as miners and tea-pickers.

<sup>2</sup> Preventive chemotherapy should be accompanied by health and hygiene education, and provision of adequate sanitation

<sup>3</sup> The STOP consortium was funded by the EDCTP, grant number RIA2017NCT-1845 and PSIA2020-3072 – STOP-2. [www.stopheworm.org](http://www.stopheworm.org)

## Results

### Clinical trial

The safety and efficacy of the FDC was tested in a **Phase II/III randomised clinical trial** involving a total of **1,001 school age children** in Ethiopia, Kenya and Mozambique. Children infected *with T. trichiura*, hookworms or *S. stercoralis* were randomly assigned to one of three possible treatment arms: albendazole, one single dose of FDC, or three FDC doses in three consecutive days.

The results show that:

1. **The FDC is safe.** No serious adverse events were reported in either treatment arm and the frequency of AEs was similar between the three treatment arms. The most common adverse events were mild gastrointestinal disorders.
2. **The FDC is much more effective against *T. trichiura* than albendazole.** The cure rate and egg reduction rates<sup>4</sup> were significantly higher in participants infected with *T. trichiura* treated with FDC compared to those treated with albendazole. A difference of 47 percentage points was observed between the cure rates of FDC in a single dose and albendazole. Moreover, a difference of 61 percentage points was observed between the cure rates of FDC in three doses and albendazole.
3. **The one-dose FDC regimen showed similar efficacy against hookworms, while the three-dose regimen was more effective than albendazole,** with cure rates 14 and 29 percentage points higher, respectively. The efficacy of the FDC against *Ascaris* was not tested, since albendazole is already highly effective against this STH.

### Modelling predictions

Based on the efficacy data observed in the clinical trial, the STOP consortium conducted a series of modelling studies to predict the effect of introducing the FDC in the deworming program on the time and likelihood of eliminating STH as a public health problem<sup>5</sup> and of interrupting their transmission<sup>6</sup>, as well as the cost implications.

**Time.** The analyses show that **adding ivermectin will shorten the times for eliminating *T. trichiura* as a public health problem.** This is particularly true for moderate prevalence settings. If only school-aged children are targeted with the FDC, elimination as a public health problem could take more than 10 years (and even more than 20 years if coverage is below 80%). But if **all the community (children and adults) are targeted** (covering 80% of school children and 60% of adults), the time to elimination could be shortened to five years (versus 10 years or more with albendazole). Increasing FDC coverage to 80% of schoolchildren and 60% of adults will also increase the chances of **interrupting transmission** of *T. trichiura*. In low prevalence settings, expanding the program to include adults leads to the greatest gains, although the added value of the FDC over albendazole is less substantial (4 years for the FDC, 6-7 years for albendazole).

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<sup>4</sup> Cure rate means absence of eggs in stool after treatment, while egg reduction rates refer to the relative reduction in egg counts compared to pre-treatment levels.

<sup>5</sup> Elimination as a public health problem = <1% moderate and high infection prevalence

<sup>6</sup> Elimination of transmission = no egg-positive individuals in the community



**For hookworms**, treatment of both adults and children is essential to achieve elimination as a public health problem in areas of moderate prevalence of infection. Models suggests this could be achieved within five years if treatment coverage is at least 80% in children and 60% in adults.

**Costs.** While FDC may have a higher cost than albendazole, its superior efficacy allows for reduced time to elimination as a public health problem. This translates into a **substantial reduction in overall total costs**. The total cost to reach elimination as a public health problem through school-based deworming is reduced by 20% when delivery costs are lower (\$39,975 FDC vs \$51,000 albendazole) and by 39% when delivery costs are assumed to be higher (\$96,850 FDC vs \$160,375 albendazole). These results are even more pronounced if a community-wide strategy is applied, with savings of up to 44% if delivery costs are assumed to be high (\$129,678 FDC vs \$229,724 albendazole).

The results emphasise that the timespan to achieve elimination of STH as a public health problem will vary depending on treatment reach and uptake, as well as the baseline transmission setting. This means that **each community will have different trajectories**, even when targeted by the same intervention. However, while elimination as a public health problem may take many years, we predict that a new 'settled' low burden of infection can be reached far before if the FDC is implemented.

## Main conclusions

1. Under the current regimen of preventive chemotherapy with albendazole, *T. trichiura* may persist as a public health problem despite many years of school-based deworming.
2. Introducing ivermectin in combination with albendazole (FDC) AND expanding the treatment programmes to include adults can substantially reduce the number of years required to achieve STH elimination targets (both elimination as a public health problem and elimination of transmission).
3. The FDC is predicted to have a lower cost to reach elimination of *T. trichiura* as a public health problem, compared to albendazole.
4. The safety and efficacy of the FDC against all STH species (including *S. stercoralis*) and other parasitic infections such as scabies should be further explored in larger clinical trials, such as the ongoing STOP2030.
5. STH treatment approaches should be tailored to the type and prevalence of STH species in the community.