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## A review: Updates on the treatment and integrated control strategies to eliminate *Trichuris trichiura*

**Abstract** – Current treatment of *Trichuris trichiura* infection predominantly relies on benzimidazole derivatives, namely albendazole and mebendazole. However, emerging evidence of suboptimal efficacy and potential drug resistance has prompted the investigation of alternative therapeutic approaches. Recent clinical trials have demonstrated enhanced efficacy through novel drug combinations, including albendazole co-administered with ivermectin or oxantel pamoate. In parallel, integrated control strategies encompassing mass drug administration (MDA), water, sanitation, and hygiene (WASH) interventions, and vaccine development are gaining attention as sustainable solutions to reduce transmission and reinfection rates. This review synthesizes recent advances in pharmacological and public health interventions, highlighting the need for multifaceted approaches to effectively combat *T. trichiura* infections.

**Keywords:** *Trichuris trichiura*, soil-transmitted helminths, treatment, integrated control.

## 1 INTRODUCTION

*Trichuris trichiura*, commonly known as the human whipworm, remains a significant public health concern, particularly in resource-limited settings where sanitation infrastructure is inadequate. As one of the major soil-transmitted helminths (STHs), *T. trichiura* contributes to chronic morbidity, especially among children, manifesting as growth retardation, anemia, and impaired cognitive development. Despite global efforts to reduce the burden of STHs, the treatment and control of *T. trichiura* continue to pose unique challenges.

Therapeutically, albendazole and mebendazole remain the most widely used anthelmintics, but their single-dose cure rates for *T. trichiura* are disappointingly low, frequently falling below 45%. The growing problem of drug resistance, particularly involving  $\beta$ -tubulin gene mutations, further complicates treatment efforts and raises concerns about the long-term viability of benzimidazole monotherapy. In response, combination regimens such as albendazole-ivermectin and albendazole-oxantel pamoate have demonstrated superior efficacy in clinical trials, offering promising alternatives for improved therapeutic outcomes (1,2).

However, pharmacological interventions alone are insufficient to achieve sustained control or elimination. Reinfection in high-transmission settings due to environmental contamination and ongoing exposure. This pattern necessitates a

broader consideration of ecological and behavioral drivers. Community-level sanitation improvements, hygiene promotion, and sustained treatment coverage modify transmission dynamics over time. Additionally, advances in vaccine development and diagnostic technologies offer new avenues for enhancing surveillance and targeting interventions more effectively.

This review synthesizes current evidence on the treatment strategies of *T. trichiura*, evaluates emerging combination therapies, and examines integrated control approaches aligned with global goals for STH elimination. Compared with earlier reviews, this article incorporates key developments from 2021–2025, including recent randomized trials, fixed-dose ivermectin–albendazole formulations, new data on moxidectin combinations, progress in vaccine research, and updated molecular insights into drug resistance.

## 2.0 TREATMENT

### 2.1 First-line Anthelmintics

Anthelmintic treatment is essential for eliminating STH infections, preventing complications, and reducing transmission. The commonly used medications include albendazole and mebendazole, both effective in reducing worm burden (3). Albendazole is typically administered at 400 mg once daily for three days, while mebendazole is given at 100 mg twice daily for three days (4).

A 2014 study previously described albendazole–ivermectin as a potential first-line therapy for *T. trichiura* infections (5). However, this conclusion was based on early clinical evidence and does not reflect current WHO recommendations. Although albendazole–ivermectin combination therapy has demonstrated superior efficacy against *T. trichiura* in recent trials, it is not yet universally adopted as first-line treatment in public-health deworming programs. WHO preventive chemotherapy guidelines continue to recommend single-dose benzimidazoles (albendazole or mebendazole) for large-scale deworming (2017).

Both albendazole and mebendazole inhibit tubulin polymerization, leading to the loss of cytoplasmic microtubules in the parasite (6). While ivermectin (200 mcg/kg daily) can be used as a treatment, it is generally less efficient than albendazole and mebendazole (6). Recent clinical trials, however, indicate that ivermectin becomes substantially more effective when used in combination with albendazole, particularly for *T. trichiura*. (Table 1) Additionally, in cases of severe infections or drug resistance, ivermectin may be used as an alternative (7,8). The appropriate dosage and treatment duration vary depending on the infection's severity and the patient's condition. Although these drugs are effective in reducing parasite load, multiple treatment cycles may be required to fully eliminate the infection, particularly in cases of heavy infestation.

## 2.2 Drug Resistance and Treatment Challenges

In the case of *T. trichiura*, standard single-dose treatments with albendazole or mebendazole have shown low cure rates. A systematic review and network meta-analysis found that mebendazole had a cure rate of 42.1% and an egg reduction rate of 66.0% against *T. trichiura* (9). In comparison, albendazole's efficacy was lower, with cure rates dropping from 38.6% in 1995 to 16.4% in 2015 and egg reduction rates falling from 72.6% to 43.4% (9). In addition, Gebreyesus et al. in southern Ethiopia found that *Trichuris trichiura* had a low cure rate (49.5%) following MDA, and notably, 52.4% of children who were considered cured at week 4 were reinfected by week 8, indicating a high reinfection rate and possible drug resistance (10). These findings highlight the low efficacy of current drugs and the high rate of reinfection after cure, underscoring the need for alternative treatments and integration of additional preventive measures.

The widespread use of anthelmintic drugs has led to concerns about emerging resistance, particularly in regions with high endemicity and mass drug administration programs. In addition, resistance to benzimidazoles (BZs), including albendazole and mebendazole, is primarily linked to mutations in the  $\beta$ -tubulin gene, reducing drug efficacy (11–13). However, Gandasegui et al. found no association between the two  $\beta$ -tubulin genes and benzimidazole resistance in *T. trichiura*, suggesting that other factors may influence treatment response and that genetic markers of resistance might lie outside the  $\beta$ -tubulin genes (14). Prolonged and repeated use of these drugs can further contribute to reduced curative effect, necessitating alternative treatment strategies. (Table 1)

## 2.3 Combination and Alternative Therapies

Conventional anthelmintics such as albendazole have long served as the first-line treatment for *T. trichiura*, but their limited efficacy and the threat of emerging resistance have driven efforts to find more effective alternatives. Among the most promising strategies is combination therapy, which aims to enhance efficacy through synergistic mechanisms and to delay resistance development.

### 2.3.1 Benzimidazole -Based Combination Therapy

Combinations pairing benzimidazoles with complementary agents have demonstrated markedly improved performance compared to monotherapy. Early studies focused on combining albendazole with ivermectin, yielding encouraging results. For example, albendazole combined with ivermectin has demonstrated improved efficacy against *T. trichiura* infections (15). Subsequently, the combination of BZ and IVM has recently demonstrated near-complete cure and egg reduction rates, particularly when IVM is administered at higher doses, such as 600  $\mu$ g/kg (2). A 2024 randomized controlled trial in Uganda demonstrated that co-administration of ivermectin and albendazole resulted in notably higher cure rates (31.3% vs. 12.3%) and egg reduction rates (91.4% vs. 52.7%) compared to albendazole alone, with both treatment regimens exhibiting a strong safety profile and no severe adverse events (16).

In parallel with these drug repurposing efforts, researchers began exploring new anthelmintic candidates. For instance, a study demonstrated that the combination of oxantel pamoate and

albendazole resulted in higher cure and egg reduction rates for *T. trichiura* infection compared to standard therapy (17), underscoring the value of using drugs with complementary mechanisms of action. Together, these results underscore the sustained clinical advantage of combination therapy, particularly in high-burden settings.

### 2.3.2 Novel Anthelmintic Agents

Beyond repurposed combinations, several new anthelmintics have progressed into clinical evaluation. Emodepside has emerged as a promising new anthelmintic candidate. Phase 2a trials conducted in Tanzania demonstrated cure rates exceeding 80% at higher doses, substantially outperforming albendazole monotherapy (18). Reported adverse events were generally mild and transient, supporting its suitability for further evaluation in upcoming phase 3 trials.

Additionally, moxidectin, an anthelmintic approved for human use in 2018, has been evaluated for its efficacy against *T. trichiura* (7). A randomized trial in Tanzania demonstrated that moxidectin-albendazole achieved a geometric mean egg reduction rate of 96.8% against *T. trichiura*, compared to 99.0% with ivermectin-albendazole (1). Despite its slightly lower efficacy, moxidectin remains a viable alternative in settings where ivermectin is unavailable or contraindicated (1), offering a favorable safety profile and extended half-life. These emerging agents expand the therapeutic landscape and provide non-benzimidazole options valuable for resistance mitigation strategies.

### 2.3.3 Fixed-Dose Co-Formulations

The evidence base for ivermectin-albendazole continued to grow. Recent clinical trials have reinforced the efficacy of ivermectin-albendazole combinations. In a large Phase 2/3 multinational trial (ALIVE), Krolewiecki et al. found that the fixed-dose combination (FDC) of albendazole and ivermectin exhibited higher efficacy in treating *T. trichiura* infections while maintaining a safety profile comparable to albendazole alone (19). In response to such evidence, the European Medicines Agency (EMA) approved in 2025 a fixed-dose dispersible tablet combining ivermectin (9 or 18 mg) with albendazole (400 mg) for the treatment of soil-transmitted helminth infections, including *T. trichiura* (20). This new formulation is especially promising for MDA programs, and is expected to improve access to more effective treatment regimens in endemic regions.

## 3.0 INTEGRATED CONTROL STRATEGIES

Effective management of *T. trichiura* infections requires not only therapeutic interventions but also public health strategies such as improved access to safe water, adequate sanitation, and hygiene, along with enhanced health education, and MDA (21).

### 3.1 Mass Drug Administration (MDA)

The WHO recommends MDA as a primary strategy for the prevention and control of neglected tropical diseases (NTDs) (22). STH is one of the major NTDs. A study in Southern Malawi found that while most people knew STH is treatable with medication (97%), only 20% understood its causes (22). In 2018 and 2019, school-based MDA with albendazole achieved high coverage (75–91%) and was well-received by communities (22), highlighting the need to pair high drug coverage with improved community knowledge to ensure long-term effectiveness.

To further interrupt transmission, strategies are evolving towards community-wide coverage. The DeWorm3 project validated this approach in Benin, India, and Malawi, reporting that community-wide MDA (cMDA) consistently met the WHO coverage target of 75%, with actual rates ranging from 78% to 95% across all rounds (23).

### 3.2 WASH and Community Education

Notably, a study by Sahimin et al. found that although Malaysia provides migrant workers with basic facilities such as clean water and toilets, intestinal parasitic infections, particularly *T. trichiura*, remain common (24). Consistently, a meta-analysis conducted by Mohammad et al. reported that among the identified helminth species, *T. trichiura* showed the highest pooled prevalence estimate (PPE), reaching 46% (95% CI: 27–65) (25). These indicate the need to strengthen migrant health policies through mandatory mass drug administration for new workers, continued monitoring of protozoan infections with metronidazole treatment when necessary, and health education programs to improve awareness of hygiene, sanitation, and infection prevention (24). Because WASH improvements require long-term investment and show gradual effects, the rapid reduction in prevalence still relies primarily on anthelmintic treatment (26). At the same time, the WHO advocated regular deworming as a key strategy for controlling and preventing parasitic infections (27).

### 3.3 Vaccine Development

Vaccine for trichuriasis development is being explored as a long-term strategy to reduce infection rates and community transmission, although significant challenges remain (28). A 2022 study showed that a recombinant mucosal vaccine (Tm-WAP49), derived from *Trichuris muris*, significantly reduced worm burden and induced strong systemic and mucosal immune responses in mice, suggesting its potential as a promising strategy for trichuriasis control (29). In 2025, Briggs et al. further reported that Tm-WAP49-specific antibodies can serve as serological markers of exposure to human trichuriasis in endemic populations, suggesting diagnostic and immunological relevance beyond its role as a vaccine antigen (30). Although still in at preclinical stages, such vaccine approaches represent a promising complement to chemotherapy, particularly in high-transmission settings where reinfection is frequent.

### 4.0 RECENT ADVANCES

Recent progress between 2021 and 2025 has substantially refined the therapeutic and regulatory landscape for *T. trichiura*. The ALIVE phase 2/3 trial demonstrated that a fixed-dose ivermectin–albendazole co-formulation, particularly when administered over three days, achieves markedly higher cure and egg-reduction rates than standard albendazole (19,33), and these findings supported the 2025 EMA positive opinion for the orodispersible ivermectin–albendazole tablet. Parallel investigations of moxidectin–albendazole have produced encouraging but context-dependent results, with high efficacy in school-aged children but more variable outcomes in adult community settings, highlighting the importance of epidemiological factors in treatment performance.

At the molecular level, deep-amplicon sequencing studies have challenged long-standing assumptions regarding benzimidazole resistance. Recent analyses detected no canonical  $\beta$ -tubulin mutations after treatment, suggesting that reduced drug efficacy may involve alternative genetic or regulatory pathways (14). Together, these advances underscore a shifting paradigm toward fixed-dose combination therapies, precision in selecting optimal regimens based on local epidemiology, and the need for expanded genomic surveillance to better inform control strategies.

### 5.0 FUTURE PERSPECTIVES AND CONCLUSION

Recent advances have substantially reshaped the therapeutic landscape for *T. trichiura*, and this review highlights several developments that were not available in earlier summaries. Clinical evidence generated between 2021 and 2025 has clarified the superior efficacy of combination therapies, particularly the coadministration of albendazole and ivermectin. These trials also provide new insights into dosing strategies, age-specific responses, and performance across diverse epidemiological settings. In addition, novel agents such as emodepside and moxidectin have entered clinical evaluation, expanding treatment options beyond the traditional benzimidazole class. The recent approval of a fixed-dose albendazole–ivermectin tablet further represents a programmatic advance that was not addressed in previous reviews.

These developments carry important clinical implications. Combination regimens now represent a more reliable therapeutic approach than benzimidazole monotherapy, especially in high-intensity infections where cure rates have historically been low. New anthelmintics broaden the drug portfolio and offer alternatives that may reduce selective pressure on benzimidazole-based treatments. Alongside pharmacological progress, improvements in diagnostic tools and quantitative egg-counting methods provide greater accuracy for detecting low-intensity infections and for monitoring treatment and control programs.

Despite these advances, several gaps remain, where evidence for treatment effectiveness in preschool-aged children, pregnant women, and individuals with coinfections is still insufficient. Resistance mechanisms to benzimidazoles and macrocyclic lactones are better understood than in the past, but surveillance platforms capable of detecting early resistance signals are not yet widely implemented. Research on long-term integrated control strategies, including sanitation improvements, behavior change interventions, and potential vaccine candidates, remains limited and requires sustained evaluation in real-world settings.

Future priorities include broader implementation of newly validated combination regimens, completion of phase 3 trials for emodepside, and expanded molecular surveillance for emerging resistance. Additional work is needed to optimize dose frequency, assess treatment responses across different population groups, and integrate therapeutic interventions with ecological and

behavioral components of transmission control. Continued progress across these areas will be essential for advancing toward durable reduction and eventual elimination of *T. trichiura* transmission.

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#### **AUTHOR CONTRIBUTIONS**

WY: Writing-original draft, formula analysis, writing-review and editing; NO: Writing-Review & Editing, supervision

#### **AUTHORSHIP CLARIFICATION**

All authors have contributed significantly to the work, reviewed the final manuscript, and approved its submission. Each author consents to the publication of this article in the journal.

#### **ETHICS APPROVAL AND CONSENT TO PARTICIPATE**

Not applicable

#### **CONSENT FOR PUBLICATION**

All authors have read and approved the final manuscript and consent to its publication in this journal

#### **CONFLICTS OF INTEREST**

The authors declare that they have no competing interests.

**Table 1** Treatment Regimens and Efficacy against *T. trichiura*

Drugs	Study	Country	Year	Sample Size	Dose Type	Cure Rate (%)	Egg Reduction Rate (%)	Adverse Events (AE)	Reference
Albendazole 400 mg	Randomized controlled trial (RCT)	Honduras	2021	39	Single dose	~4.2	~47.7	Mostly mild	(2)
	Single-blind RCT (Phase 2a)	Tanzania	2023	30	Single dose	~17.0	~76.0		(18)
	Open-label RCT	Uganda	2024	81	Single dose	~12.3	~52.7		(16)
	Phase 2/3 ITT	Ethiopia, Kenya, Mozambique	2025	131	Single dose	~35.9	~83.4		(19)
Albendazole 400 mg x3 day	RCT	Honduras	2021	24	Multi-dose (3 days)	~33.3	~72.1	Mild–moderate	(2)
Mebendazole 500 mg	Double-blind RCT	Tanzania	2017	120	Single dose	~11.8	~75.0	Mainly mild	(17)
Ivermectin 200 µg/kg	Double-blind RCT	Tanzania	2022	19	Single dose	~10.5	~94.2	Mostly mild	(31)
Albendazole 400 mg + Ivermectin 200 µg/kg	Double-blind RCT	Tanzania	2022	211	Single dose	~54.0	~99.0	Mostly mild	(31)
	Open-label RCT	Uganda	2024	80		~31.3	~91.4		(16)
Albendazole 400 mg + Ivermectin 600 µg/kg	RCT	Honduras	2021	57	Single dose	~88.6	~96.7	Mild–moderate, well tolerated	(2)
Albendazole 400 mg + Ivermectin 600 µg/kg x 3 days	RCT	Honduras	2021	57	Multi-dose (3 days)	~100	~100	Mostly mild	(2)
Albendazole 400 mg + Ivermectin (9 mg or 18 mg)	Phase 2/3 ITT	Ethiopia, Kenya, Mozambique	2025	251	Single dose (FDCx1)	~82.9	~99.2	Mostly mild	(19)
				254	Multi-dose (3 days) (FDCx3)	~97.2	~99.9		
Albendazole 400 mg + Oxantel Pamoate 20 mg/kg	Double-blind RCT	Tanzania	2014	119	Multi-dose (2 days)	~31.2	~96.0	Mostly mild	(17)

Albendazole 400 mg + Oxantel Pamoate 25 mg/kg	Single-blind RCT (non-inferiority)	Tanzania	2018	212	Single dose	~83	~99.8	Mostly mild	(32)
Oxantel pamoate 20 mg/kg	Double-blind RCT	Tanzania	2014	121	Single dose	~26.3	~93.2	Mainly mild	(17)
Moxidectin 8 mg	Single-blind RCT (non-inferiority)	Tanzania	2018	124	Single dose	~14.4	~83.2	Mostly mild	(32)
Moxidectin 8 mg + Albendazole 400 mg	Single-blind RCT (non-inferiority)	Tanzania	2018	206	Single dose	~50.8	~98.5	Mostly mild	(32)
	Double-blind RCT		2022	207		~34.3	~96.8		(31)
Moxidectin 8 mg + Tribendimidine 200 mg/400mg	Single-blind RCT (non-inferiority)	Tanzania	2018	121	Single dose	~22.7	~91.6	Mostly mild	(32)
Emodepside	Single-blind RCT (Phase 2a)	Tanzania	2023	171	Single dose (5, 10, 15, 20, 25, 30 mg)	83% (5 mg), 93% (10 mg), 100% (15 mg), 96% (20mg), 97% (25 mg), 89% (30 mg)	~99.6–100% (dose-dependent, plateau at 15 mg)	Mostly mild	(18)

Note: This table summarizes pivotal clinical trials evaluating therapeutic regimens for *T. trichiura* from 2014 to 2025, including trial design, dosing strategy, sample size, and efficacy outcomes.

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