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Re-evaluating Albendazole-Based Preventive Chemotherapy for Soil-Transmitted Helminths in Indonesia: A Narrative Review on Efficacy, Challenges, and Future Strategies

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Abstract: This narrative review seeks to critically analyze the efficacy of albendazole, the cornerstone anthelmintic of the program. Relevant literature (2020-2025) was identified through a systematic search of the ScienceDirect and Google Scholar databases. While evidence confirms albendazole's effectiveness, with cure rates up to 93%, its performance is inconsistent and influenced by a confluence of factors. A critical constraint identified is the absence of robust, large-scale national surveillance data on STH prevalence and drug efficacy, hindering a comprehensive assessment of albendazole's performance within the program. The persistent burden of STH underscores a gap between program implementation and its intended public health impact. While albendazole remains essential, its variable efficacy and operational barriers necessitate a critical reassessment of the current strategy.

Keywords: Albendazole, Efficacy, Soil-Transmitted Helminth, Mass Drug Administration

Introduction

Soil-transmitted helminthiases (STH), caused primarily by *Ascaris lumbricoides*, *Trichuris trichiura*, and hookworms (*Necator americanus* and *Ancylostoma duodenale*), remain a formidable public health challenge in tropical and subtropical regions. The World Health Organization (WHO) estimates that over 1.5 billion people are infected globally, with the highest burden in impoverished communities with inadequate access to clean water and sanitation (World Health Organization, 2023). In Indonesia, STH is endemic, with prevalence historically ranging from 45% to 65% in some areas, predominantly affecting pre-school and school-aged children (Murhandarwati et al, 2024) (Rahayu et al, 2023). Chronic STH infection contributes to malnutrition, iron-deficiency anaemia, stunted growth, and impaired cognitive development, perpetuating cycles of poverty and hindering human capital development (Djuardi et al, 2021) (Fauziah et al, 2022).

The cornerstone of the global STH control strategy is preventive chemotherapy (PC) through periodic mass drug administration (MDA) of safe, single-dose anthelmintics—primarily albendazole (400 mg) or mebendazole (500 mg)—to at-risk populations, especially

children. Indonesia launched its national deworming program, integrating it with filariasis elimination efforts, aiming to reduce microfilaria incidence and STH-associated morbidity (Adrizain et al, 2020). The program has historically utilized albendazole, administered through school-based and, in some areas, community-based platforms.

However, after more than a decade of implementation, the epidemiological landscape is mixed. While successes have been reported in specific districts, such as parts of South Kalimantan where post-MDA STH prevalence fell below 5% (Rahayu et al, 2023), numerous studies from across the archipelago continue to report alarmingly high prevalence rates. For instance, studies reveal prevalence of 58.8% among preschoolers in East Nusa Tenggara (Djuardi et al, 2021), 44.4% among schoolchildren in Pandeglang (Sungkar et al, 2024), and 58.3% among children in Southwest Sumba despite MDA (Ali et al, 2025). This persistent burden raises critical questions about the effectiveness of the current strategy.

A central concern is the efficacy of albendazole itself. While the drug is highly effective against *A. lumbricoides*, its performance against *T. trichiura* is notoriously suboptimal and variable. Meta-analyses confirm this differential efficacy, with cure rates (CR) for trichuriasis often falling below 50% for a single 400mg dose (Bekele et al, 2023) (Gray et al, 2023). In the Indonesian context, direct, large-scale efficacy studies of the albendazole used in national PC programs are conspicuously lacking. Conversely, studies from Malaysia and other Southeast Asian nations report CRs for *T. trichiura* as low as 11.6% to 41% with single-dose albendazole (Khir et al, 2023) (Nisha et al, 2021), prompting the evaluation of multi-day regimens (Gultom et al, 2020) (Tee et al, 2022) and alternative drugs like ivermectin (Djune-Yemeli et al, 2020).

Beyond drug efficacy, programmatic challenges abound. These include logistical hurdles in drug distribution, inconsistent implementation and supervision (Febriyanti & Idris, 2020), low community adherence and misconceptions about MDA (Mitchell et al, 2022) (Sindhu et al, 2023), diagnostic limitations of the widely used Kato-Katz method (Coffeng et al, 2023) (Sukmana et al, 2025), and the ever-present risk of emerging anthelmintic resistance due to sustained drug pressure (Gandasegui et al, 2024) (Grau-Pujol et al, 2022). Furthermore, the exclusion of adults from school-based MDA may preserve transmission reservoirs (delos Trinos et al, 2024) (Gomez et al, 2023).

This narrative review aims to synthesize current evidence to address several pivotal questions for Indonesian STH control: Is the continued reliance on single-dose albendazole justified given its variable efficacy? Is there an urgent need for country-specific efficacy and resistance monitoring studies? Should Indonesia consider alternative drug regimens, including combination therapy or a switch to other anthelmintics like ivermectin? What are the primary systemic and community-level challenges hindering the success of the PC program? Finally, what integrated, evidence-based strategies should be prioritized to accelerate progress towards elimination targets? By examining findings from Indonesia and relevant global studies, this review seeks to inform policy recalibration and future research directions.

Methodology

This narrative review was conducted through a systematic search of the ScienceDirect and Google Scholar databases for relevant literature published between 2020 and 2025, utilizing keywords and combinations thereof including "albendazole," "efficacy," "soil-transmitted helminth," "mass drug administration," and "Indonesia." The identified literature was screened for relevance to the core objective of critically analyzing the efficacy of albendazole within the Indonesian STH control program and the multifactorial challenges influencing its outcomes. Data pertaining to drug performance, program implementation barriers, and alternative strategies were extracted and synthesized thematically to address the central questions regarding the justification of the current monotherapy, surveillance gaps, and potential strategic evolution.

Result and Discussion

1. Pharmacokinetics and Pharmacodynamics of Albendazole as an Antihelmintic

Benzimidazole derivatives are recognized for their efficacy as antihelmintic agents, with studies highlighting their potent activity against various parasitic worms. Their effectiveness is often linked to specific structural features and their interaction with biological targets. **A prime example is albendazole, a key anthelmintic drug whose core structure is the benzimidazole ring system.** The antihelmintic efficacy of benzimidazole derivatives arises from their pharmacodynamic action of selectively binding to parasite beta-tubulin, thereby inhibiting microtubule polymerization and disrupting critical cellular processes such as nutrient uptake and cell division. Pharmacokinetically, strategic structural modifications—exemplified by albendazole's carbamate group at the 1-position and propylthio chain at the 5-position—enhance cellular permeability and target affinity, optimizing drug bioavailability and tissue penetration. Furthermore, specific substituents, including fluoroethyl moieties, can improve membrane permeability, while substitutions at the 2-position of the benzimidazole core are known to amplify anthelmintic potency through refined structure-activity relationships (Alheety et al, 2025).

2. The Variable and Species-Dependent Efficacy of Albendazole

The compiled evidence unequivocally demonstrates that the efficacy of single-dose albendazole (400 mg) is not uniform across all STH species and is subject to significant geographical variation.

a) High Efficacy against *Ascaris lumbricoides*

Consistent with global data, albendazole remains highly effective against *A. lumbricoides*. Studies from Indonesia and the region report cure rates (CR) consistently above 90% and egg reduction rates (ERR) near 99% (Gray et al, 2026) (Gultom et al, 2020) (Nisha et al, 2021). This confirms albendazole's continued value for controlling ascariasis.

b) Suboptimal and Variable Efficacy against *Trichuris trichiura*

This is the most significant pharmacologic challenge. Efficacy against *T. trichiura* is frequently inadequate. In Malaysia, CRs were reported at 41% (Nisha et al, 2021) and as low

as 11.6% (Khir et al, 2023). In Southern Mozambique, CR was only 28% by Kato-Katz and 7.8% by more sensitive qPCR (Grau-Pujol et al, 2022). In China, two rounds of albendazole yielded a CR of just 6.3% for *T. trichiura* (Gray et al, 2026). Indonesian studies, while not always reporting direct CRs, indicate a high and persistent burden of trichuriasis (Ali et al, 2025) (Ipa et al, 2024), indirectly suggesting suboptimal drug performance. This low efficacy necessitates repeated dosing or alternative drugs to achieve a public health impact.

c) Moderate Efficacy against Hookworms

Efficacy against hookworms appears more variable. Studies report CRs ranging from 56.7% (qPCR) in Mozambique (Grau-Pujol et al, 2022) to 64.9% in Vietnam for a local brand (Dyer et al, 2022), and up to 92.2% after a second dose in China (Gray et al, 2026). This variability may relate to drug quality, pharmacokinetics, or initial infection intensity.

d) The Case for Multi-Day Regimens

In response to poor trichuriasis outcomes, trials of multi-day albendazole have been conducted. In North Sumatra, Indonesia, a three-day regimen achieved a CR of 79.5% for *T. trichiura*, compared to 32.2% for a single dose (Gultom et al, 2020). Similarly, a triple-dose regimen in Malaysian indigenous communities showed significantly improved outcomes (Tee et al, 2022). While more effective, these regimens present challenges for MDA in terms of cost, logistics, and potential side effects affecting adherence.

3. Systemic and Community-Level Challenges to PC Success in Indonesia

The persistence of STH cannot be attributed solely to drug efficacy. The review identifies a confluence of implementation barriers.

a) Inconsistent Program Implementation and Coverage

Evaluations of Indonesia's national program reveal critical weaknesses. A study in Palembang found suboptimal albendazole distribution, with some schools not receiving medication, limited staff, and coverage failing to meet targets (Febriyanti & Idris, 2020). Inconsistent deworming practices across districts and difficulties in maintaining a nationwide campaign have been reported, which foster pockets of sustained transmission (Adrizain et al, 2020).

b) Diagnostic Limitations and Surveillance Gaps

The reliance on the Kato-Katz method for prevalence surveys and efficacy monitoring is a significant constraint. Its low sensitivity, particularly for low-intensity infections and *T. trichiura*, leads to underestimation of the true burden. A study in Papua found qPCR increased the detection of *T. trichiura* by 17.7% compared to Kato-Katz (Sukmana et al, 2025). Furthermore, there is a striking lack of systematic, country-wide studies monitoring albendazole efficacy within the PC program—a gap highlighted as critical for detecting resistance (Coffeng et al, 2023) (Vlaminck et al, 2020).

c) Community Perceptions, Knowledge, and Adherence

The success of MDA hinges on community acceptance. Qualitative studies identify key barriers: misconceptions that deworming is only for the visibly ill, fear of side effects, and concerns about drug safety during pregnancy (Mitchell et al, 2022) (Sindhu et al, 2023). In Indonesia, while maternal knowledge about deworming can be high, translating this into consistent preventive behavior remains a challenge (Suryawati et al, 2024). Non-adherence, if systematic, can create untreated reservoirs that sustain transmission (Hardwick et al, 2021).

d) The Sanitation and Poverty Nexus

Drug administration alone cannot break the cycle of transmission without addressing environmental contamination. Numerous studies from Indonesia directly link high STH prevalence to poor sanitation, lack of access to clean water, open defecation, and flooding (Darlan et al, 2025) (Sungkar et al, 2024) (Surja et al, 2021). Albendazole treats the individual but does not prevent rapid reinfection in contaminated environments.

4. The Emerging Concern: Anthelmintic Resistance

The prolonged, large-scale use of a single drug class (benzimidazoles) creates selection pressure for resistant parasites—a well-documented phenomenon in veterinary parasitology. While confirmed resistance in human STH is not yet definitively proven, warning signs are present. Studies have found putative resistance-associated Single Nucleotide Polymorphism in the beta-tubulin gene of *T. trichiura* and *N. americanus* (Grau-Pujol et al, 2022), although their clinical significance remains unclear (Gandasegui et al, 2024). The low efficacy observed against *T. trichiura* in many settings is consistent with a pattern of reduced drug susceptibility. The absence of a formal surveillance system for anthelmintic resistance in Indonesia means the country is "flying blind" to this potential threat.

5. Strategic Alternatives and the Path Forward

Evidence points to several strategic shifts that could enhance STH control in Indonesia.

a) Community-Wide Mass Drug Administration (cMDA)

School-based deworming excludes adults, who can act as infection reservoirs. Trials like DeWorm3 have shown that cMDA (treating all age groups) is feasible, achieves high coverage (>75%), and is more effective in reducing overall community prevalence and potentially interrupting transmission, especially for hookworm (Ajjampur et al, 2025) (delos Trinos et al, 2024) (Means et al, 2018). It also ensures treatment for out-of-school children and those with disabilities (Witek-McManus et al, 2021).

b) Combination Therapy and Alternative Drugs

To improve efficacy against *T. trichiura* and mitigate resistance risk, combination therapy is a promising avenue. Ivermectin, effective against *T. trichiura* and *A. lumbricoides*, has been successfully co-administered with albendazole in integrated NTD programs (Djune-Yemeli et al, 2020) (McPherson et al, 2023). This approach could be piloted in high-

burden Indonesian districts. The safety profile of such combinations has been established in large trials.

The global evidence base for the superior efficacy of ivermectin-albendazole combination therapy against *Trichuris trichiura* is now substantial and compelling, offering a direct pharmacological solution to a key limitation of Indonesia's current monotherapy strategy. A recent open-label randomized controlled trial in Ugandan children demonstrated a definitive superiority of the combination, with cure rates for *T. trichiura* reaching 31.3% compared to only 12.3% for albendazole alone, alongside a dramatic increase in egg reduction rates, about 91.4% vs. 52.7% (Palmeirim et al, 2024). This aligns with findings from Peru, where combination therapy significantly improved cure rates for persistent *T. trichura* infections (Curico et al, 2024). The rationale for this approach is further supported by a systematic review and meta-analysis which concluded that MDA with ivermectin and albendazole combined achieved an 89.4% prevalence reduction for *T. trichiura*, a marked improvement over the 49.9% reduction with ivermectin alone (Le et al, 2024). Beyond trichuriasis, ivermectin has demonstrated a lasting impact on *Strongyloides stercoralis*, a parasite not effectively targeted by benzimidazoles, with significant prevalence reductions observed 21 months post-MDA in the Solomon Islands (Le et al, 2024).

Operational and safety considerations for this shift are increasingly addressed by contemporary research. The development of orodispersible fixed-dose combinations (FDCs) of ivermectin and albendazole is actively pursued to enhance palatability, safety (especially for children by eliminating choking risk), and logistical simplicity for MDA campaigns, as evidenced by ongoing adaptive clinical trials (Algorta et al, 2022) (Krolewiecki et al, 2022). While a specific FDC demonstrated bioequivalence for ivermectin but not albendazole in one pharmacokinetic study, the overall safety profile of ivermectin-albendazole co-administration is well-established, including in settings with co-endemic scabies and soil-transmitted helminths (Hardy et al, 2020). Furthermore, the broader antiparasitic spectrum of ivermectin provides added value for integrated NTD control, as seen in Liberia where annual or semiannual MDA with ivermectin and albendazole effectively reduced lymphatic filariasis, onchocerciasis, and STH concurrently (Eneanya et al, 2022). This positions ivermectin not merely as an alternative but as a cornerstone for future integrated NTD platforms. For Indonesia, piloting ivermectin-albendazole combination therapy in high-burden *T. trichiura* districts, potentially leveraging existing filariasis MDA infrastructure and experience, represents a strategic opportunity to overcome a persistent efficacy gap and accelerate progress toward elimination targets.

c) Investing in Improved Diagnostics and Surveillance

Building capacity for more sensitive diagnostic tools (e.g., qPCR) for periodic surveillance and efficacy monitoring is crucial. Furthermore, innovative tools like smartphone-attached microscopy (SAM) could empower frontline health workers for rapid

screening (Ameen et al, 2023). Establishing a national surveillance system for STH prevalence and drug efficacy, as piloted in the Vlaminck et al. study, is a foundational step for evidence-based decision-making.

d) True Integration with Water, Sanitation, and Hygiene (WASH) and Behavior Change

Sustainable control requires breaking transmission pathways. PC programs must be integrally linked with concerted efforts to improve access to latrines, promote their use, ensure clean water supply, and drive community-led total sanitation (CLTS) initiatives. The effectiveness of combined drug therapy and WASH education has been demonstrated in reducing reinfection rates (Nachaiwieng et al, 2024).

Conclusion

Indonesia's deworming program, while achieving some gains, has proven insufficient to eliminate soil-transmitted helminths (STH) as a public health problem, necessitating a candid reassessment and strategic evolution of current approaches due to pharmacological limitations of single-dose albendazole against Trichuris trichiura and programmatic weaknesses in distribution and coverage. To address these gaps, robust nationwide efficacy studies using sensitive diagnostics like qPCR are urgently needed, alongside pilot programs evaluating alternative regimens such as albendazole-ivermectin combination therapy and multi-day albendazole in high-burden areas, while transitioning from school-based deworming to community-wide mass drug administration (MDA) to target adult reservoirs and reduce transmission. Future research should prioritize species-specific efficacy assessments and drug resistance monitoring to inform evidence-based policy adjustments, with practical recommendations including piloting alternative regimens in diverse settings, strengthening supply chains and implementation frameworks for consistent coverage, and embedding these efforts within a funded, integrated strategy that pairs preventive chemotherapy with sustained WASH infrastructure improvements and community engagement. Only through such comprehensive, data-driven, and adaptive approaches can Indonesia achieve sustainable STH control, alleviate the burden on affected populations, and meet WHO 2030 targets.

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