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**EFFECT OF REPEATED ANTHELMINTHIC TREATMENT ON
MALARIA IN SCHOOL CHILDREN IN KENYA: A RANDOMIZED,
OPEN LABEL, EQUIVALENCE TRIAL**

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ABSTRACT

Background: In Africa, malaria and soil-transmitted helminths (STHs) occur in the same populations and sometimes in the same individuals, with school-age children being at the greatest risk of coinfection. It has been hypothesized that the immune response evoked by helminth infections may modify immune responses to plasmodia species and consequently alter infection and disease risks. Studies conducted to date have been typically cross-sectional and produced conflicting results. This thesis investigated the epidemiology of STH-*Plasmodium falciparum* coinfection among school children in western Kenya and the impact of deworming on risk of parasitaemia and clinical malaria, using cross-sectional survey and randomized trial data.

Methods: This thesis used data from an open label, equivalence trial among 2,346 school children in 23 schools in western Kenya, a high malaria transmission setting. The objectives of this study were, first to describe the epidemiology of helminth, malaria and the resulting coinfection among school children. Secondly to investigate the effect of repeated deworming on the risk of clinical malaria and malaria parasitaemia to better inform both deworming and malaria control programmes. Eligible children were randomized to receive either four repeated or a single dose of albendazole and followed up during 13 months to assess the incidence of clinical malaria. Secondary outcomes were hookworm, *Ascaris lumbricoides*, *Plasmodium* prevalence and density, assessed by repeated cross-sectional surveys over 15 months. Additional work investigated the impact of deworming on STH and provided a detailed analysis of malaria morbidity.

Results: At baseline 46% of the children had *P. falciparum* infection and one in four was infected with STH. In multivariable analysis, there was an ensuing association between hookworm and *P. falciparum*, adjusting for age and sex. The main trial showed that during 13 months, the incidence rate of malaria was 0.27 episodes/person-year in the repeated treatment group and 0.26 episodes/person-year in the annual treatment group (incidence difference, 0.01; 95% confidence interval, -.03 to .06). The prevalence and density of malaria parasitemia did not differ by treatment group at any of the cross-sectional surveys. At final follow-up, 9.6% of

children in the repeated treatment group were still infected with either hookworm or *A. lumbricoides* infection despite receiving up to four rounds of albendazole treatment. Mixed effects regression models demonstrate that this residual infection was associated with anthropometry, being male, individual- and school-level baseline infection. Analysis of malaria morbidity showed that the incidence of malaria was associated with being female, while *P. falciparum* infection was associated with being male, lower socioeconomic status and stunting.

Conclusion: Together these findings show that although coinfection is common and there is a significant association between *P. falciparum* and hookworm infection, repeated anthelmintic treatment is not associated with an increased or decreased risk of parasitaemia or clinical malaria. In addition to controlling STH by school-based deworming, efforts should be made to address malaria morbidity among school children.