Background: Lymphatic filariasis (LF) is a neglected tropical disease targeted for elimination as a public health problem by 2020, with the main strategy being the treatment of entire endemic communities. Since the inception of the Global Programme for the Elimination of LF in 2000, tremendous progress has been made in many endemic countries. However, current observations point to the need for improved treatment regimen, frequency of treatment or drug delivery strategies in order to achieve the elimination goals in some endemic areas. In this randomized trial we evaluate the use of twice-yearly treatment with Ivermectin and Albendazole in 18 LF endemic communities in Ghana, where despite 15 years of yearly treatment the disease is still above the elimination thresholds.

Methods: Following demographic data collection, *Wuchereria bancrofti* antigen, microfilaria and antibody prevalence was assessed in study participants using the Alere FTS kit, nucleopore filtration and Wb123 ELISA respectively. The study assessed the communities’ perspectives on persistent transmission of LF towards implementing effective treatment uptake strategies.

Results: The baseline assessments revealed antigen prevalence of 8.2% (95% CI=6.8-9.8), with overall microfilaria prevalence of 1.2%. Infections were higher in males and in individuals who spend significant amount of time outdoors for commercial activities. Medication, Personal, Health system, Disease and Social structure related barriers, were observed to affect MDA compliance. Community members perceived that they were not susceptible to infection and this together with drug adverse effects grossly affect the ingestion of the drugs.

Conclusions: While this trial is still in the early phase, the baseline assessments reveal programmatic challenges to the implementation of a twice-yearly treatment strategy for the control of LF, which must be addressed to enhance implementation success.