

# The Causal Effect of Malaria on Stunting: A Mendelian Randomization and Matching Approach,

Hyunseung Kang<sup>1\*</sup>, Benno Kreuels<sup>2,3\*</sup>, Ohene Adjei<sup>4</sup>, Ralf Krumkamp<sup>3</sup>,  
Jürgen May<sup>3</sup>, Dylan S. Small<sup>1\$</sup>

<sup>1</sup>Department of Statistics, The Wharton School, University of Pennsylvania, Philadelphia, PA, USA; <sup>2</sup> Section for Tropical Medicine, I. Medical Department, University Medical Center Eppendorf, Hamburg, Germany; <sup>3</sup> Infectious Disease Epidemiology, Bernhard Nocht Institute for Tropical Medicine, Hamburg, Germany; <sup>4</sup> Kumasi Center for Collaborative Research in Tropical Medicine, Kumasi, Ghana

\*These authors contributed equally to this work.

<sup>\$</sup>Corresponding author: Dylan S. Small, Department of Statistics, The Wharton School, University of Pennsylvania, 3730 Walnut Street, Philadelphia, PA, USA 19104. Phone: 215.898.8222. Fax: 215.898.1280. E-mail: dsmall@wharton.upenn.edu

## Summary

**Background:** Previous studies on the association of malaria and stunted growth delivered inconsistent results. These conflicting results may be due to different levels of confounding and due to considerable difficulties in elucidating a causal relationship. Randomized experiments are impractical and previous observational studies have not fully controlled for potential confounding including nutritional deficiencies, breast-feeding habits, other infectious diseases and socioeconomic status.

**Methods:** This study aims to estimate the causal effect between malaria episodes and stunted growth by applying a combination of Mendelian randomization, using the sickle cell trait, and matching. We demonstrate the method on a cohort of children in the Ashanti Region, Ghana.

**Results:** We found that the risk of stunting increases by 0.32 (p-value: 0.004, 95% CI: (0.09,1.0)) for every malaria episode. The risk estimate based on Mendelian randomization substantially differs from the multiple regression estimate of 0.02 (p-value: 0.02, 95% CI: (0.003,0.03)). In addition, based on the sensitivity analysis, our results were reasonably insensitive to unmeasured confounders.

**Conclusions:** The method applied in this study indicates a causal relationship between malaria and stunting in young children in an area of high endemicity and demonstrates the usefulness of

sickle cell trait as an instrument for the analysis of conditions that might be causally related to malaria.

**Keywords:** malaria, stunting, children, Mendelian randomization, matching

**MeSH Terms:** Mendelian Randomization Analysis, Sickle Cell Trait, Malaria, Infants, Growth Disorders, Ghana