Antibiotic Resistance and Microbiome in Children Aged 1-59 months in Nouna, Burkina Faso

Manual of Operations and Procedures

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Statistical Analysis Plan, Version 1.0, June 15 2017

Study Overview

We will randomize 120 households containing 2 or more children aged 6-59 months to one of four study arms: 1) azithromycin, 2) amoxicillin, 3) cotrimoxazole, or 4) placebo. All children will receive 5 days of treatment. Full intervention details can be found in the Manual of Operations and Procedures. Rectal and nasopharyngeal swabs will be collected pre-treatment (baseline) and on Day 9 following the 5 days of treatment. Anthropometric indices (weight, height, and mid-upper arm circumference) will be collected at baseline and Day 35 (one month following treatment completion).

Randomization

The 120 households will be randomized in blocks of size 8 to one of the four treatment arms. In households randomized to treatment, all children aged 6-59 months of age will be treated, with the exception of one random child from within the household who will receive placebo. All children aged 6-59 months in households randomized to placebo will receive placebo. A random treated child from antibiotic arm households will be selected as the sentinel child for outcome assessment, and the untreated child from antibiotic arm households will also receive outcome assessment. Two children will be randomly selected from placebo households for outcome assessment.

Primary Outcome

We will compare diversity across arms at Day 9 and between time points. The primary outcome will be Simpson's index of alpha diversity. We will compare the mean Simpson's index between treatment arms with a t-test. All *P*-values will be calculated via permutation test.

Secondary Outcomes

As a secondary outcome, we will compare Shannon's index (L1 norm) between time points using a t-test. To compare if treatment significantly explains difference between the four treatment groups, we will compare Simpson's index (L1-norm) and Shannon's index (L2-norm) distances using PERMANOVA on bacterial reads.

To determine if there are differences in nutritional outcomes across treatment arms one month following treatment, we will calculate weight-for-height (WHZ), weight-for-age (WAZ), and height-for-age (HAZ) Z-scores based on 2006 WHO standards. We will compare mean WHZ, WAZ, HAZ, and mid-upper-arm circumference (MUAC) across treatment arms as continuous variables adjusting for baseline anthropometric values using an ANCOVA. We will also compare

the prevalence of stunting (HAZ <-2 SD) and moderate (WHZ <-2 SD) and severe (WHZ <-3 SD) acute malnutrition across study arms with a logistic regression model.