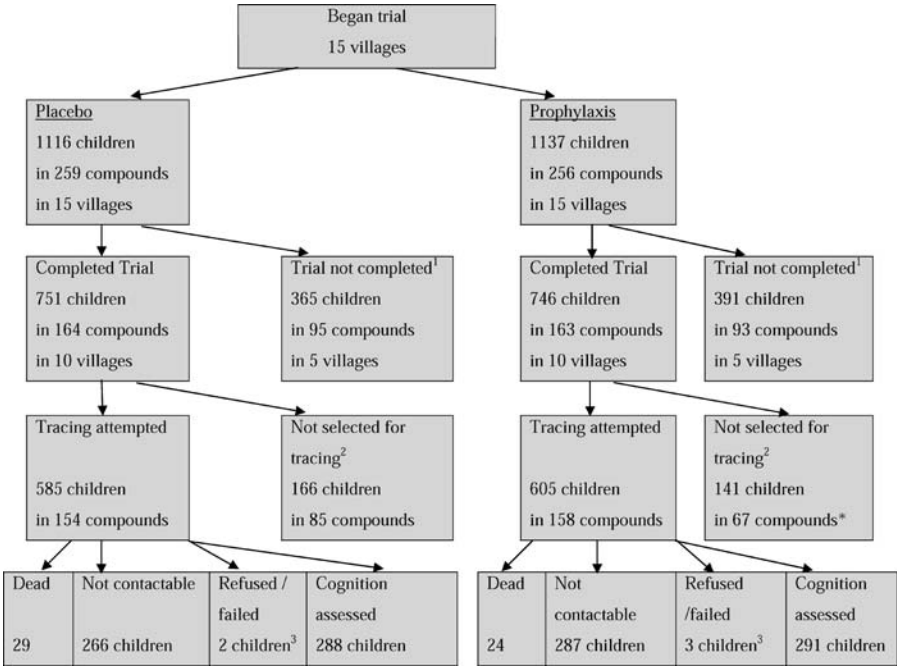

Figure 1. Participant Flow in Follow-Up to Chemoprophylaxis Cluster-Controlled Trial

Participant flow in the malaria chemoprophylaxis trial and follow-up 11 y later. Fifteen villages took part in the trial, with treatment allocated systematically by compound. Follow-up was conducted in the ten villages that completed the trial. Children who completed a whole year of the trial were selected to take part in the follow-up.

[1]The village health worker died in one village and was dismissed in another. Drugs were insufficient in three villages.

[2]Only children participating in at least one complete transmission season were selected for tracing. Some compounds contained both children selected and children not selected.

[3]One child refused and one child failed to understand cognitive test instructions in the placebo group. One child refused and two failed to understand instructions in the prophylaxis group.

*Intervention group allocation was by compound, trial completion was on a village basis, and selection for tracing was conducted for individual children.

DOI: 10.1371/journal.pctr.0010019.g001

However, they were less advantaged in that fewer of them had a radio in their compounds.

Outcomes and Estimation

There were no significant differences in the cognitive function scores between the two arms, with or without adjustment for covariates (adjusted estimates in Table 2; $p > 0.10$ for all; the intracluster correlation coefficient for the cognitive function score was 0.212). The two groups were very similar in the proportion enrolled in school (unadjusted odds ratio = 1.020, 95% confidence interval [CI] 0.658 to 1.583; $p = 0.928$; logistic regression), and adjustment for covariates was without effect (adjusted estimates in Table 2). However, there was a significant ($p = 0.013$) interaction between school enrolment and female gender. In an adjusted model that included this interaction term, the odds ratios (95% CI) on the intervention (control = 0 and prophylaxis = 1), gender (male = 0 and female = 1), and the interaction were 0.674 (0.383 to 1.184), 0.154 (0.087 to 0.272), and 2.773 (1.243 to 6.193). Hence the intervention effect in boys was 0.674 (0.383 to 1.184; $p = 0.170$) and in girls was $0.674 \times 2.773 = 1.869$ (0.943 to 3.702; $p = 0.073$). The prophylaxis appeared to increase the odds that the girls attended school and decrease the odds that the boys attended school, though these effects did not reach statistical significance.

The prophylaxis group's mean educational attainment was 4.47 grades at school compared to the placebo group's 3.81. Unadjusted regression analysis gave a mean attainment 0.65 grades higher in the intervention arm (0.023 to 1.276; $p = 0.042$). This estimate was reduced slightly to 0.52 ($p = 0.069$; Table 2) when covariates were included in the analysis. Estimates were similar using ordinal logistic regression (Table S2).

Ancillary Analyses

Supplementary analyses were conducted, stratified by number of years children were eligible for post-trial prophylaxis. For the cognitive function score, there was a significant interaction between the four sub-groups and the trial intervention ($p = 0.034$), with larger treatment effects for the two groups that spent the longest on trial and received the least post-trial prophylaxis (Table 3). There was a small effect (0.264, or, in units of SD, approximately 0.24 SD, 95% CI –0.03 to 0.51) in the group of individuals that were not eligible for post-trial prophylaxis and spent 3 y in the trial, and a somewhat larger effect (0.43 SD, 95% CI 0.10 to 0.77) among those eligible for less than 1 y of post-trial prophylaxis and who were in the trial for all 4 y. There was no effect among those eligible for more than 1 y of post-trial prophylaxis. For both educational measures, there was no significant interaction between years of post-trial prophylaxis and treatment, but the pattern of results for the highest grade reached (Table 3) was similar to that found for cognitive function, with the largest effects for sub-groups receiving less than 1 y of post-trial prophylaxis.