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Appendix

Details of statistical models: design of survey illustrating nested structure

Level 3: District (k) (constant artemisinin-based combination therapy [ACT] policy and hence duration within each district)	1				2					3				4				5					6			7	
Level 2: Site within district (j) (constant mutation and parasite prevalence within each site)	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26
Level 1: Parasitemic children within sentinel sites (i)	$N = 53$	$N = 52$	$N = 90$	$N = 168$	$N = 100$	$N = 100$	$N = 241$	$N = 94$	$N = 38$	$N = 90$	$N = 143$	$N = 21$	$N = 235$	$N = 40$	$N = 30$	$N = 14$	$N = 18$	$N = 18$	$N = 18$	$N = 23$	$N = 70$	$N = 141$	$N = 50$	$N = 55$	$N = 19$	$N = 14$

Logistic model for log (odds of quintuple mutation) as a function of parasite prevalence and duration of ACT policy:

$\text{logit}(p_{ijk}) = -2.464 - 0.019 \times \text{paraprev} + 0.112 \times \text{ACTmonths} + a_{jk}^{(2)} + a_{k}^{(3)} + e_{ijk}$

where p_{ijk} = probability of a quintuple mutation for subject i in sentinel site j in district k

$a_{jk}^{(2)} \sim N\left(0; \sigma^2_{a_{jk}}\right)$ = random effect for second level nesting factor, sentinel sites ($\sigma^2_{a_{jk}}$ measures between site variability)

$a_{k}^{(3)} \sim N\left(0; \sigma^2_{a_{jk}}\right)$ = random effect for third level nesting factor, districts ($\sigma^2_{a_{k}}$ measures between district variability)

$a_{ijk}^{(3)} \sim N\left(0; \sigma^2_{e}\right)$ = random effect for first level factor, subjects (σ^2_{e} measures between subject variability)

All random effects are independent of one another.