Supplemental information

Methods

Participants and Follow-up

A researcher not involved in data collection generated a randomised code list blocks of 9 that allocated women enrolled to the study to either control group or to1 of 2 intervention groups. On the basis of this list, individual code slips containing unique identification number s, but not group allocation, were sealed in individual opaque randomization envelopes. Eligible persons who consented to participate picked 1 envelope that contained an identification number. A research assistant not involved in outcome assessment gave the corresponding prepacked study drugs to the participant under direct observation and monitored her for possible adverse reactions. Research personnel assessing child anthropometrics and development were blinded to the intervention group throughout the follow-up.

All participants were given ferrous sulfate (200 mg/ day) and folic acid (0.25 mg/day) throughout pregnancy. All children received standard Malawian care during follow-up; HIV-positive mothers and their newborns received nevirapine for prevention of mother-to-child transmission of HIV.

None of the deaths were judged to be due to the maternal intervention. Other types of neonatal severe adverse events (SAEs) were evenly distributed between the groups. Most SAEs were not considered related to trial interventions.

The study was performed according to Good Clinical Practice and the ethical standards of the Declaration of Helsinki. The protocol was approved by the College of Medicine Research and Ethics Committee (COMREC), Malawi, and the Ethical Committee of Pirkanmaa Hospital District, Finland.

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Outcomes

At 5 years of age the cognitive development was tested using Griffith's Mental Development Scales, Extended Revised, 2-8 years (GMDS-ER 2-8), which covers 6 domains: locomotor, personal-social, language, eye and hand coordination, performance and practical reasoning.

References

1 De Onis M. WHO Child Growth Standards based on length/height, weight and age. *Acta Paediatr Int J Paediatr* 2006;**95**:76–85. doi:10.1080/08035320500495548

Supplemental table 1. Baseline characteristics of the mothers of included (follow-up) and excluded (lost to follow-up) participants at approximately 13 years of age

Characteristics	Follow-up (n=1002)	Lost to follow-up (n=318)	Difference (95%CI)	P-value
Age, years, mean (SD)	24.9 (6.4)	24.7 (6.4)	-0.13 (-0.94 to 0.68)	0.8
Gestational age at enrollment, weeks, mean (SD)	20.1 (3.1)	20.0 (2.9)	-0.16 (-0.54 to 0.23)	0.4
Proportion of primiparity	24 %	23 %	-0.01 (-0.06 to 0.04)	0.7
Proportion of HIV-positive participants	11 % (N = 908)	22 % (N =291)	0.11 (0.06 to 0.16)	<0.001
Proportion of literate participants (%)	29 %	29 %	-0.01 (-0.06 to 0.05)	0.8
Proportion of moderate or severe anemia, Hb <100g/L (%)	26 %	29 %	0.03 (-0.03 to 0.08)	0.3
Years of schooling completed, mean (SD)	2.2 (2.7)	2.3 (2.7)	0.02 (-0.32 to 0.36)	>0.9

Supplemental table 2. Mean developmental outcome, height, weight, body mass index (BMI), mid-upper arm circumference (MUAC) and head circumference (HC) of boys in preadolescence, by intervention group

Outcome	Control (SP twice) (N=161). Mean (SD)	Monthly SP (N=182). Mean (SD)	AZI-SP (N=161). Mean (SD)	Global p-value	Global p-value, adjusted[b]
Raven's score[a]	14.4 (4.1)	14.6 (4.0)	14.7 (4.2)	>0.9	0.8
Height (cm)	140.3 (7.8)	141.4 (7.9)	140.7 (8.1)	0.4	>0.9
Weight (kg)	31.9 (5.3)	32.5 (5.7)	32.3 (5.3)	0.6	0.9
BMI	16.1 (1.4)	16.2 (1.5)	16.2 (1.2)	0.2	0.8
MUAC (cm)	18.9 (1.6)	19.0 (1.7)	19.3 (1.6)	0.2	0.08
HC (cm)	52.0 (1.5)	52.0 (1.5)	52.0 (1.4)	>0.9	0.6

[a] For the Raven's score N=160, 181 and 160.
[b] Adjusted for child age, socioeconomic status and pubertal stage at the time of developmental assessment and anthropometric measurements.
SP = sulfadoxine-pyrimethamine. AZI-SP = intervention group with monthly SP and two doses of azithromycin.

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Supplemental table 3. Mean developmental outcome, height, weight, body mass index (BMI), mid-upper arm circumference (MUAC) and head circumference (HC) of girls in preadolescence, by intervention group

Outcome	Control (SP twice) (N=172). Mean (SD)	Monthly SP (N=151). Mean (SD)	AZI-SP (N=175). Mean (SD)	Global p-value	Global p-value, adjusted[b]
Raven's score[a]	13.6 (3.1)	14.0 (3.4)	13.8 (3.5)	0.5	0.2
Height (cm)	145.0 (7.8)	143.8 (8.4)	145.3 (8.1)	0.3	0.3
Weight (kg)	35.5 (6.7)	35.3 (8.0)	36.0 (7.0)	0.6	0.9
BMI	16.8 (2.0)	16.9 (2.6)	16.9 (1.9)	0.8	0.6
MUAC (cm)	20.7 (2.1)	20.7 (2.6)	20.8 (2.1)	>0.9	>0.9
HC (cm)	51.2 (1.3)	51.0 (1.5)	51.6 (1.6)	0.006	0.009

[a] For the Raven's score N=171, 151 and 174.
[b] Adjusted for child age, socioeconomic status and pubertal stage at the time of developmental assessment and anthropometric measurements.
SP = sulfadoxine-pyrimethamine. AZI-SP = intervention group with monthly SP and two doses of azithromycin.

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Supplemental table 4. Prevalence of stunting, severe stunting, low BMI and very low BMI in preadolescence, by intervention group

Outcome	Control (SP twice), N=333 (n)	Monthly SP, N=333 (n)	AZI-SP, N=336 (n)	Global p-value	Global p-value, adjusted[a]
Stunting, HAZ <-2SD	36.0 % (120)	39.0 % (130)	36.0 % (121)	0.6	0.9
Severe stunting, HAZ <-3SD	7.5 % (25)	8.7 % (29)	6.0 % (20)	0.4	0.7
Low BMI, (BMIZ<-2)	13.2 % (44)	13.5 % (45)	9.2 % (31)	0.2	0.2
Very low BMI, (BMIZ<-3)	1.5 % (5)	3.0 % (10)	0.3 % (1)	0.06	0.09

[a] Adjusted for child's pubertal stage and socioeconomic status at the time of anthropometric measurements.
SP = sulfadoxine-pyrimethamine. AZI-SP = intervention group with monthly SP and two doses of azithromycin

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