Does Malaria in pregnancy affect neurodevelopmental outcomes?

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Background

Approximately 125 million pregnant women are at risk of placental malaria (PM) and ~25% of all pregnancies in sub-Saharan Africa are complicated by placental malaria at delivery.

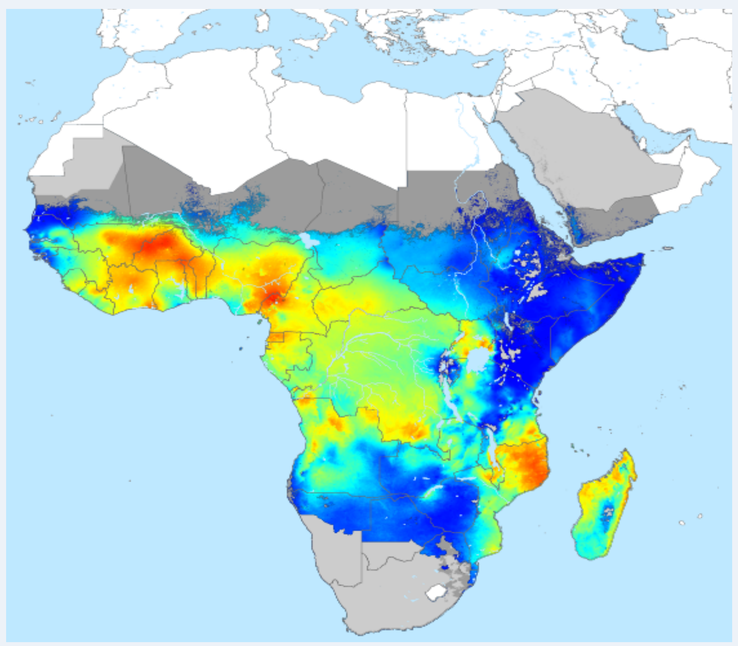

Figure 1: Proposed model of fetal neurocognitive injury.

Research has shown that malaria exposure in utero leads to permanent neurocognitive impairments in offspring in an experimental model of PM. This potentially shifts the focus from measuring neonatal mortality and low birth weight in children born to malaria infected mothers to measuring long-term neurodevelopment.

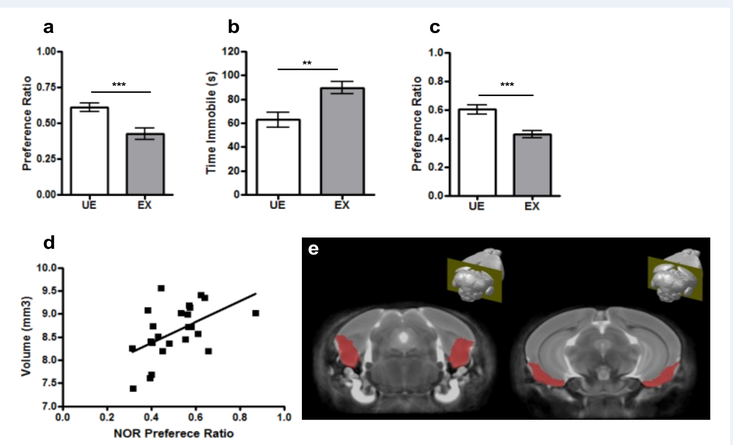

Figure 2: Experimental PM infection induces persistent neurocognitive injury. Compared to unexposed (UE) pups, exposed (EX) offspring have significant deficits in memory (a) and affective disorders (b) that persist to adulthood (c). Lesions are mapped to MRI images.

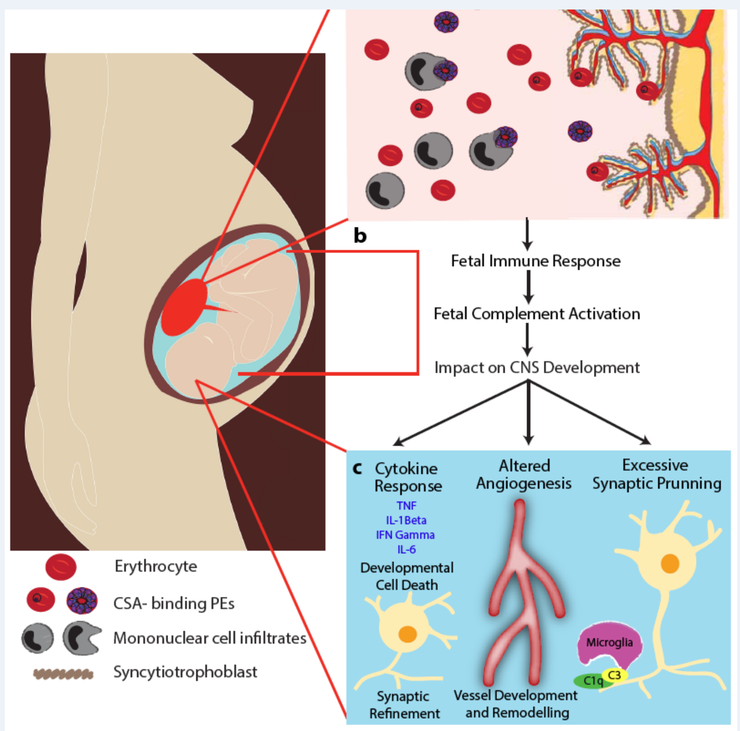

Figure 3: Proposed model of fetal neurocognitive injury.

Aims and objective

- To investigate whether providing intermittent preventative treatment in pregnancy (IPTp) vs intermittent screening and treatment in pregnancy (ISTp) influences development of language (the most sensitive measure of development in children at 18 and 24 months) born to mothers who were part of an original randomised controlled trial to look at birth outcomes
- To investigate the association between low birth weight, socioeconomic status, maternal education, weight, corrected gestational age, mean upper arm circumference (muac), gravida status and gender with neurodevelopmental outcomes

Methods

Design: A randomised control trial conducted in Malawi comparing intermittent preventive treatment (IPTp) in pregnancy versus intermittent screening and treatment (ISTp) in pregnancy for malaria was used as the "parent study" to evaluate the association between malaria in pregnancy and developmental outcomes

Figure 4: Antenatal clinics (Mpemba health centre)

Participants: Infants of women who were recruited in antenatal clinic (HIV negative, gestational age 16 – 28 weeks), in two rural sites – Blantyre and Chikwawa, southern Malawi

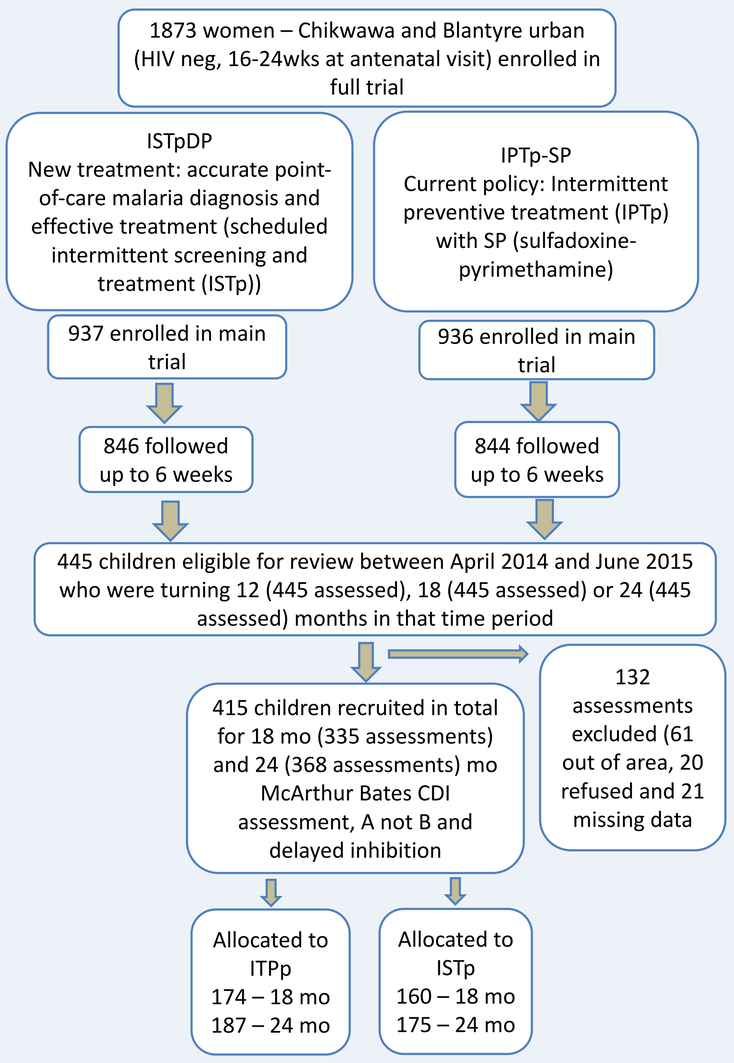

Figure 5: Consort diagram to show flow of participants followed up to assess early child development and language outcomes at 18 and 24 months of age.

Results

Table 1 – Background subset sample characteristics of the two study arms from parent study trial

Characteristic	Level/type	IPTp (n=211, 51.6%)	ISTp (n=198, 48.4%)	p-value
Gender	Male	112 (53.1%)	94 (47.5%)	
	Female	99 (46.9%)	104 (52.5%)	0.28*
Socioeconomic status	Low	61 (28.9%)	64 (32.3%)	
	Medium	78 (37.0%)	60 (30.3%)	
	High	71 (33.6%)	73 (36.9%)	0.00**
Maternal education status	Low	67 (31.8%)	56 (28.3%)	
	Medium	109 (51.7%)	112 (56.6%)	
	High	34 (16.1%)	29 (14.6%)	0.00**
Gravidity	1 to 2	144 (68.2%)	131 (66.2%)	
	3+	67 (31.8%)	67 (33.8%)	0.03*
Low birth weight	No	193 (91.5%)	176 (88.9%)	
	Yes	14 (6.6%)	14 (7.1%)	0.04*
Pre-term birth	No	169 (80.1%)	160 (80.8%)	
	Yes	42 (19.9%)	38 (19.2%)	0.90*
HIV	Negative	174 (82.5%)	164 (82.8%)	
	Not done/known	35 (16.6%)	34 (17.2%)	0.24*
Gestational age	N	211	198	
	Min	30.43	32.29	
	Max	43.14	42.86	
	Mean (sd)	38.69 (1.79)	38.47 (1.71)	0.20***
MUAC	N	176	164	
	Min	20.00	20.60	
	Max	31.50	33.00	
	Mean (sd)	24.21 (1.83)	24.23 (2.15)	0.90***
PCR malaria	Negative	112 (53.1%)	99 (50.0%)	
	Positive	66 (31.3%)	62 (31.3%)	
	Not known	33 (15.6%)	37 (18.7%)	0.36*

IPTp – Intermittent preventative treatment; **ISTp** – Intermittent screening and treatment. *Chi-squared test **One–way ANOVA *** Independent T-test

Table 2 - Table demonstrating the difference in MacArthur Bates CDI language scores, A not B score and Delayed Inhibition score between the study arms

Developmental test	Visit (months)	Study arm	n	Unadjusted Mean (SD)	p-value*	Adjusted Mean (SD)**	P value*
MacArthur Bates CDI	18	ISTp	83	36.20 (21.44)	0.42	35.15 (7.87)	0.34
		IPTp	103	33.34 (26.05)		34.10 (6.83)	
	Mean difference (CI)			- 2.86 (-9.88 – 4.15)		-1.05 (-3.16 – 1.09)	
	24	ISTp	97	77.13 (20.52)	0.27	75.60 (7.27)	0.68
		IPTp	110	73.85 (21.76)		75.17 (7.70)	
	Mean difference (CI)			-3.28 (-9.10 – 2.54)		-0.43 (-2.49 – 1.63)	
A not B	18	ISTp	61	8.57 (1.48)	0.39	8.44 (0.35)	0.96
		IPTp	64	8.33 (1.71)		8.45 (0.31)	
	Mean difference (CI)			-0.24 (-0.81 – 0.32)		0.01 (-0.11 – 0.12)	
	24	ISTp	70	9.40 (0.94)	0.76	9.35 (0.28)	0.47
		IPTp	89	9.35 (1.15)		9.38 (0.27)	
	Mean difference (CI)			0.05 (-0.39 – 0.28)		0.03 (-0.05 – 0.12)	
Delayed inhibition	18	ISTp	81	64.09 (68.07)	0.92	65.71 (15.17)	0.50
		IPTp	100	65.07 (65.78)		64.07 (16.77)	
	Mean difference (CI)			0.98 (-18.72 – 20.69)		-1.64 (-6.38 – 3.10)	
	24	ISTp	93	126.48 (45.62)	0.07	119.47 (8.87)	0.76
		IPTp	107	113.08 (58.06)		119.97 (9.10)	
	Mean difference (CI)			-13.40 (-28.12 – 1.32)		-0.40 (-2.91 – 2.12)	

*Independent T-test; ** Adjust for baseline covariates: gender, socioeconomic status, maternal education, gravida, mean upper arm circumference, corrected age, low birth weight, haemoglobin, PCR malaria

Table 3 - Table demonstrating the interaction between co-variates at baseline and MacArthur Bates language scores (later to be taken into the adjusted model)

Co-variate	Categories	Category	n	Mean (SD)	Unadjusted mean difference	p-value
SES	18 months	Low	100	33.90 (23.52)		
		Medium	117	33.87 (21.81)	- 0.03	
		High	115	37.77 (24.84)	3.90	0.11*
	24 months	Low	109	73.09 (24.45)		
		Medium	124	73.07 (22.62)	- 0.02	
		High	129	80.65 (17.73)	7.58	0.02*
Maternal education	18 months	Low	94	30.28 (24.08)		
		Medium	186	35.18 (22.75)	4.9	
		High	52	42.12 (23.18)	6.94	0.01*
	24 months	Low	116	69.91 (27.14)		
		Medium	190	77.13 (19.00)	7.22	
		High	56	83.38 (14.84)	6.25	0.00*

* One-way ANOVA test performed
** Independent sample t-test performed

Conclusions

It is clear from this study that ISTp is not necessarily to be recommended as a new policy for prevention and management of malaria in pregnancy and improving childhood developmental outcomes. We have shown, however, that there needs to be more emphasis on interventions to improve maternal education, socioeconomic status and other maternal factors

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