

**Incidence, presentation and outcomes
of *Salmonella* bacteraemia among
young children in sub-Saharan Africa:
MAL055 RTS,S-AS01 *Salmonella*
Ancillary Study**

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AS01 *Salmonella* Ancillary Study Team

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First Results of Phase 3 Trial of RTS,S/AS01 Malaria Vaccine in African Children

The RTS,S Clinical Trials Partnership*

Table 3. Serious Adverse Events after the First Dose of a Study Vaccine in the Intention-to-Treat Population, According to Age Category.*

Serious Adverse Event	5–17 Mo				6–12 Wk			
	RTS,S/AS01 Vaccine (N = 5949)		Rabies Vaccine (N = 2974)		RTS,S/AS01 Vaccine (N = 4358)		Meningococcal Vaccine (N = 2179)	
	<i>no. of children</i>	<i>% (95% CI)</i>	<i>no. of children</i>	<i>% (95% CI)</i>	<i>no. of children</i>	<i>% (95% CI)</i>	<i>no. of children</i>	<i>% (95% CI)</i>
Salmonella sepsis	41	0.7 (0.5–0.9)	23	0.8 (0.5–1.2)	16	0.4 (0.2–0.6)	10	0.5 (0.2–0.8)
Sepsis	48	0.8 (0.6–1.1)	35	1.2 (0.8–1.6)	23	0.5 (0.3–0.8)	8	0.4 (0.2–0.7)

Average follow-up 18 months and 9 months

Approx. 500 cases of *Salmonella* bacteraemia per 100,000 PYO

11 sites selected to represent diversity of malaria endemicity in sub-Saharan Africa

Children randomised into 3 groups:

- RTS,S-AS01 3 doses + booster
- RTS,S-AS01 3 doses
- Comparator vaccine

Cohorts: 6-12 weeks & 5-17 months

Median follow-up: 38 & 48 months

Duration: 2009 to 2014

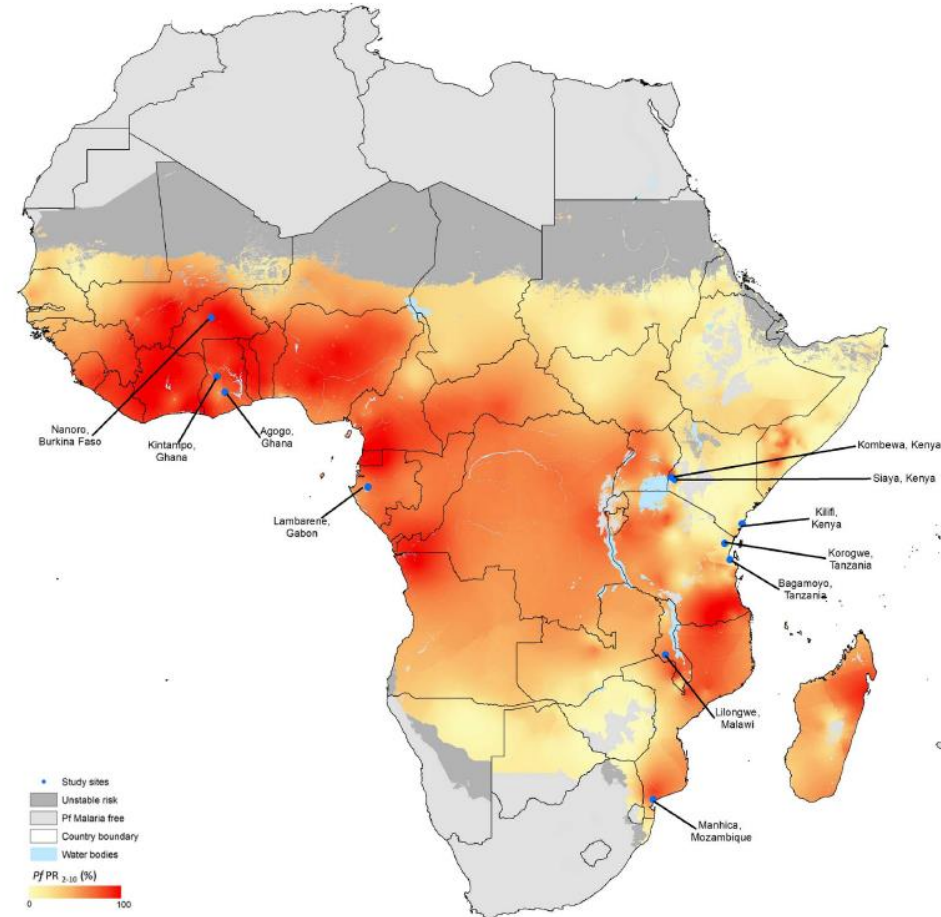
Passive surveillance

Blood cultures for febrile admissions

WGS of isolates (ongoing)

AMR profiling (ongoing)

The RTS,S-AS01 phase 3 trial: MAL055



- Main exclusion criteria included
 - Malnutrition requiring hospitalisation
 - Severe anaemia (<5 g/dL)
- 15,460 children enrolled
- Mean baseline Hb = 10.3 g/dl (IQR 9.3 to 11.2).
- Mean height-for-weight z score = 0.2 (IQR -0.7 to 1.1)
- HIV not systematically tested
- Incidence of clinical malaria
 - (min) Kilifi, Kenya 0.05 cases per person year
 - (max) Siaya, Kenya 4.41 and 5.41 per person year

Our Aim: Use data from MAL055 to determine incidence of *Salmonella* bacteraemia in children under five years across sub-Saharan Africa.

Workshop held in Nairobi, Kenya, September 2016.

Incidence and Prevalence

257 episodes of *Salmonella* bacteraemia.

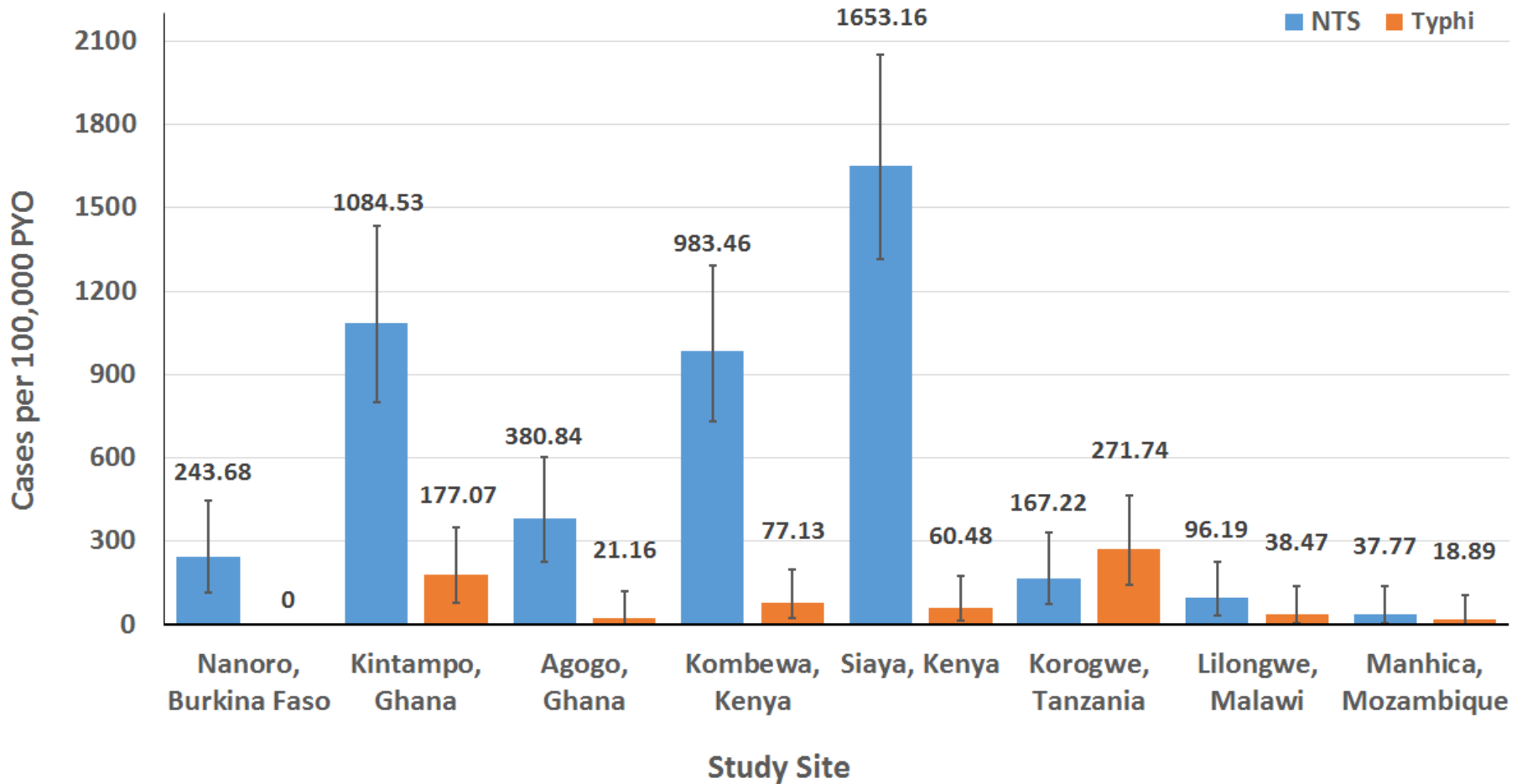
50,280 person years of observation

<u>Incidence*</u> :	per 100,000 PYO (95% CIs)	
All <i>Salmonella</i>	534 (471, 604)	
S. Typhi	66.5 (45.5, 93.9)	n=32
NTS	461 (402, 526)	n=222
S. Typhimurium	283 (237, 334)	n=136
S. Enteritidis	133 (102, 170)	n=64

Prevalence*: approx **60%** of all bacteraemias

*subject to confirmation

Incidence by Study Site

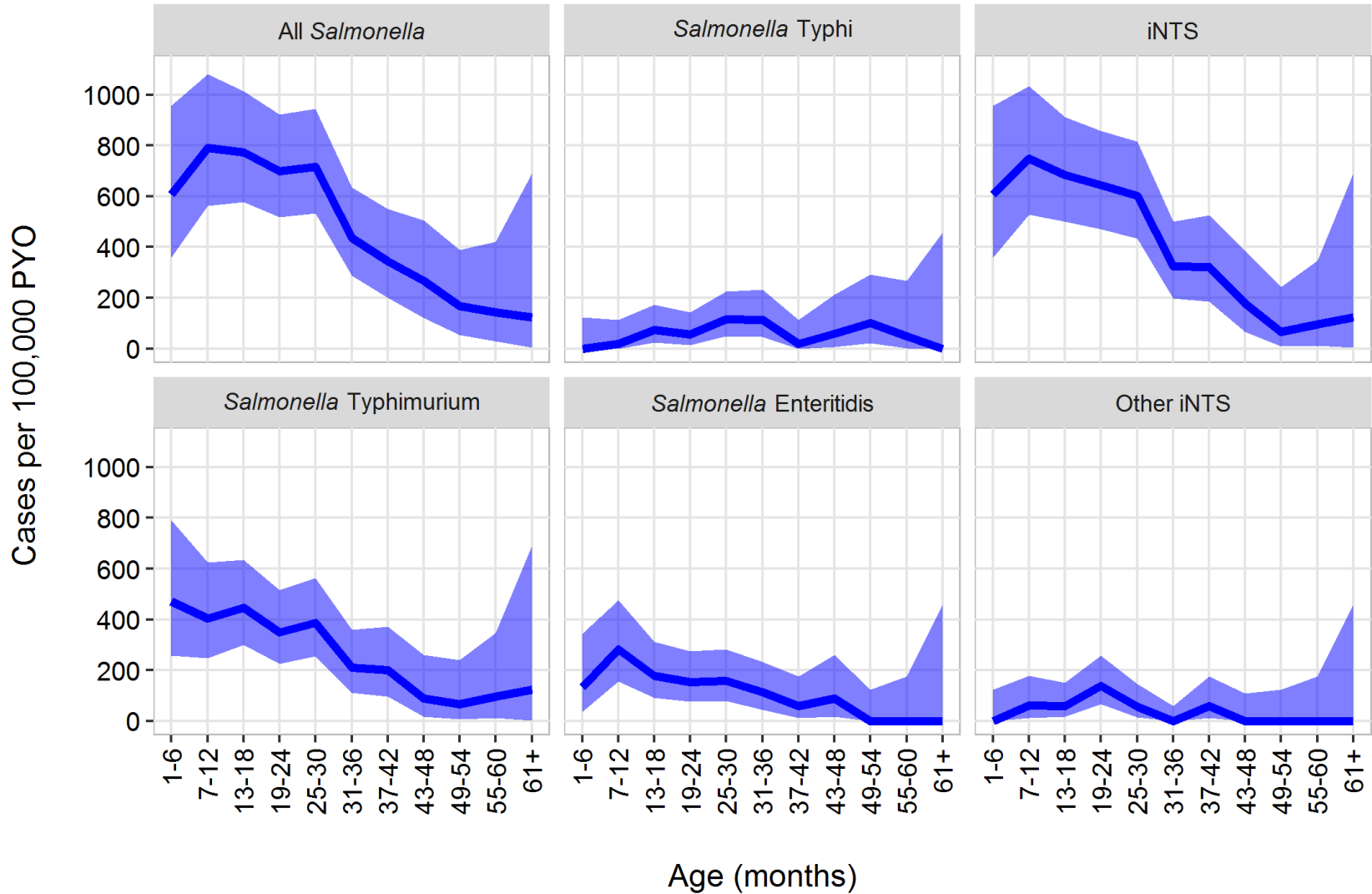


lines = 95%CIs

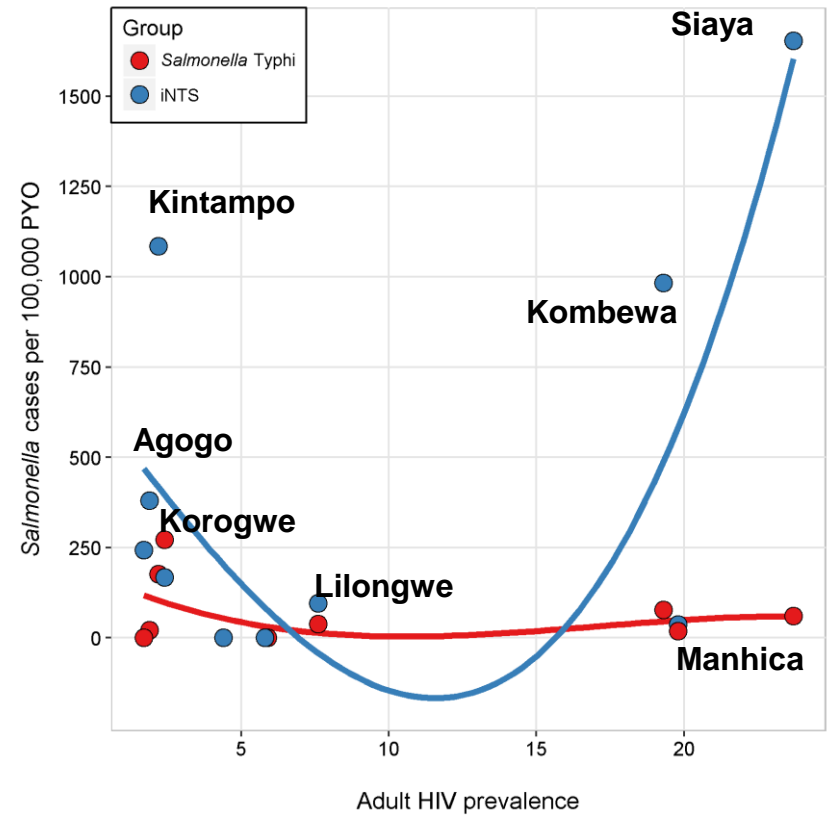
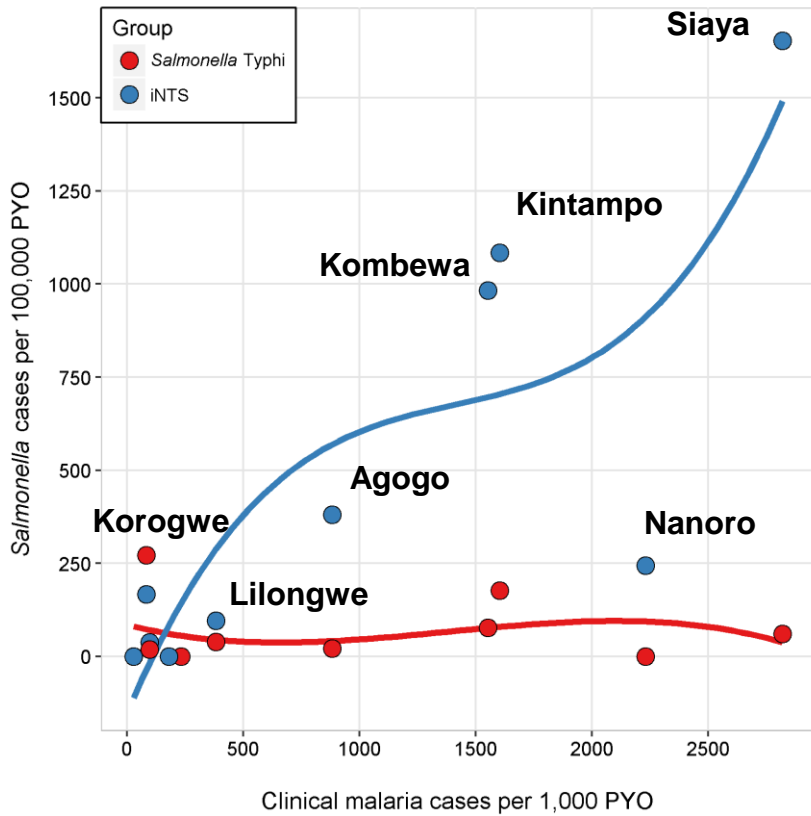
Incidence by Age – cases per 100,000 PYO (95% CIs)

	Typhimurium	Enteritidis	Typhi	Other
0-12 months	517 (362-716)	216 (121-356)	14.4 (0.363-80.1)	43.1 (8.9-126.0)
12-24 months	438 (335-566)	168 (107-253)	80.6 (40.2-144)	95.2 (50.7-162)
24-60 months	236 (183-301)	109 (74-156)	80.0 (50.2-121)	32.7 (15.0-62.2)
Overall	283 (237-334)	133 (102-170)	66.5 (45.5-93.9)	45.7 (28.7-69.3)

Incidence by Age

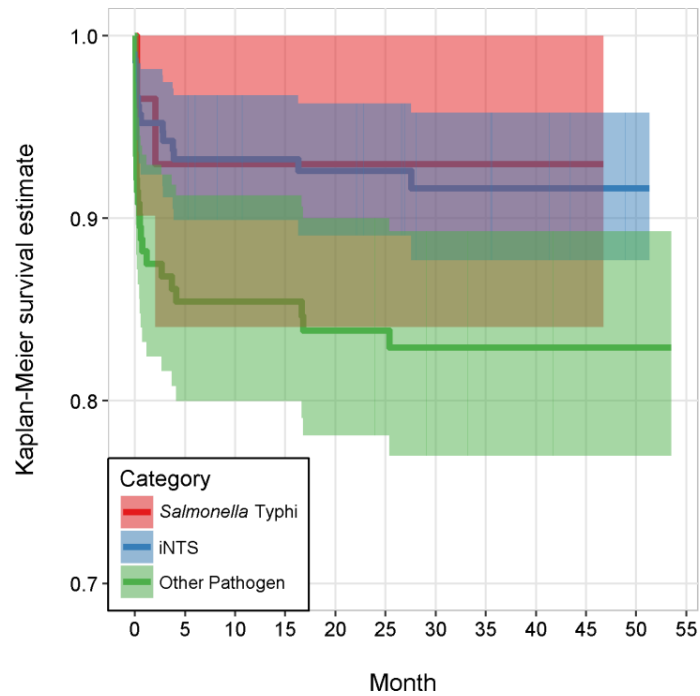


Incidence Association with Malaria and HIV by Site

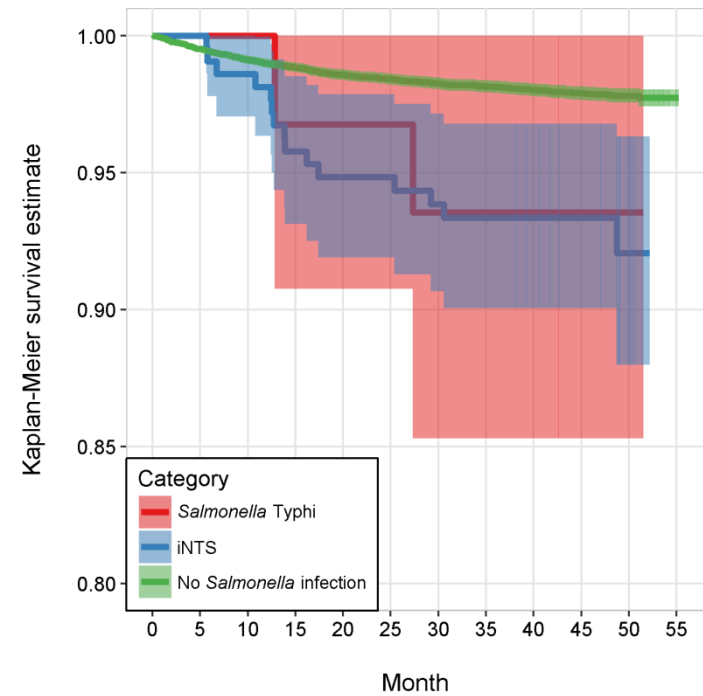


Fatality Outcomes

Following *Salmonella* bacteraemia



Throughout study



Salmonella bacteraemia association with malaria

83.8% cases are aparasitaemic at presentation

Positive association with number of malaria infections/year:

	incidence	incidence ratio	p value
• 0 infections	136	<i>reference</i>	
• 0-1 infections	300	2.09	0.009
• 1-2 infections	774	5.37	<0.001
• >2 infections	1217	8.50	<0.001

Non-significant reduction in bacteremia in RTS,S-AS01 group compared with comparator vaccine

- incidence rate ratio = **0.83** (95%CI **0.63-1.10**)

Conclusions

- *Salmonella* is a major and persistent cause of bacteremia among children under five years across sub-Saharan Africa
- 3 commonest serovars:
 1. *S. Typhimurium*
 2. *S. Enteritidis*
 3. *S. Typhi*
- iNTS disease 7x higher incidence than typhoid fever
- A **monovalent typhoid vaccine** could have prevented **12.5%** of bacteraemias in this study.
- A **trivalent *Salmonella* vaccine** could have prevented **90.3%** of bacteraemias in this study.
- A vaccine able to protect against all three serovars could have a major public health impact



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