

Severe Anaemia and Invasive Non-Typhoidal *Salmonella* Bacteraemia in Kenyan Children

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The Open
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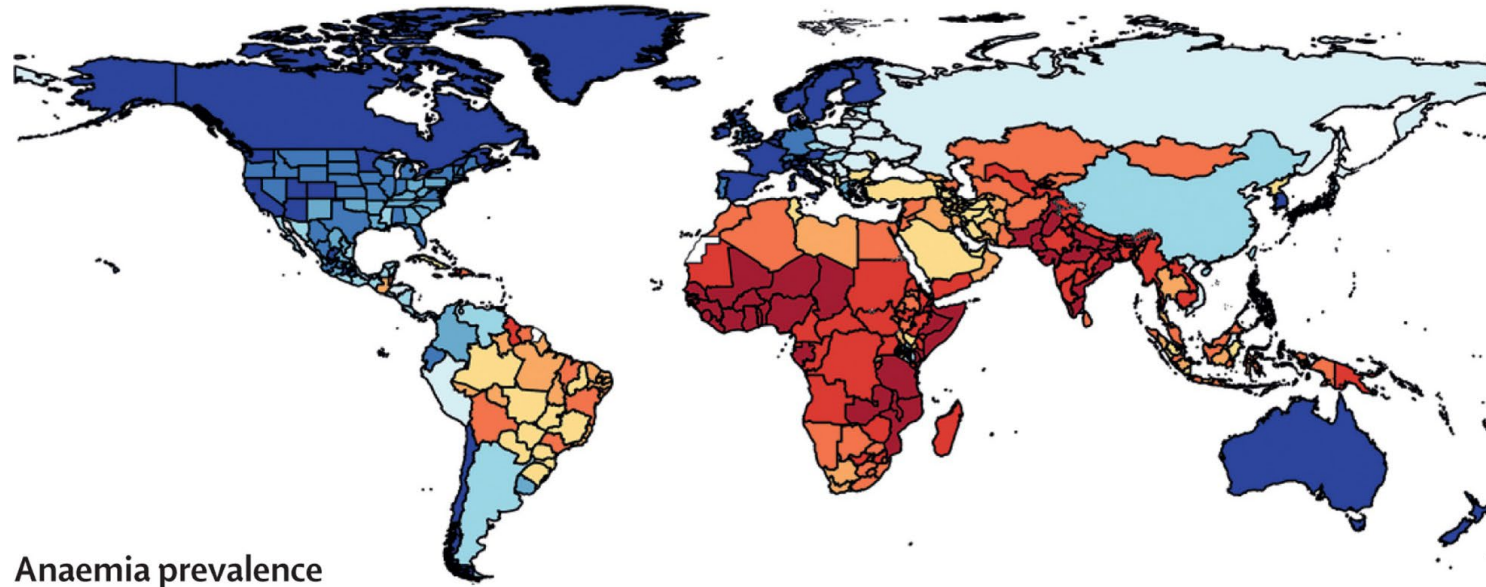


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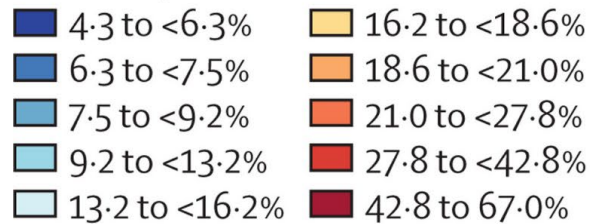
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Anaemia – A global problem



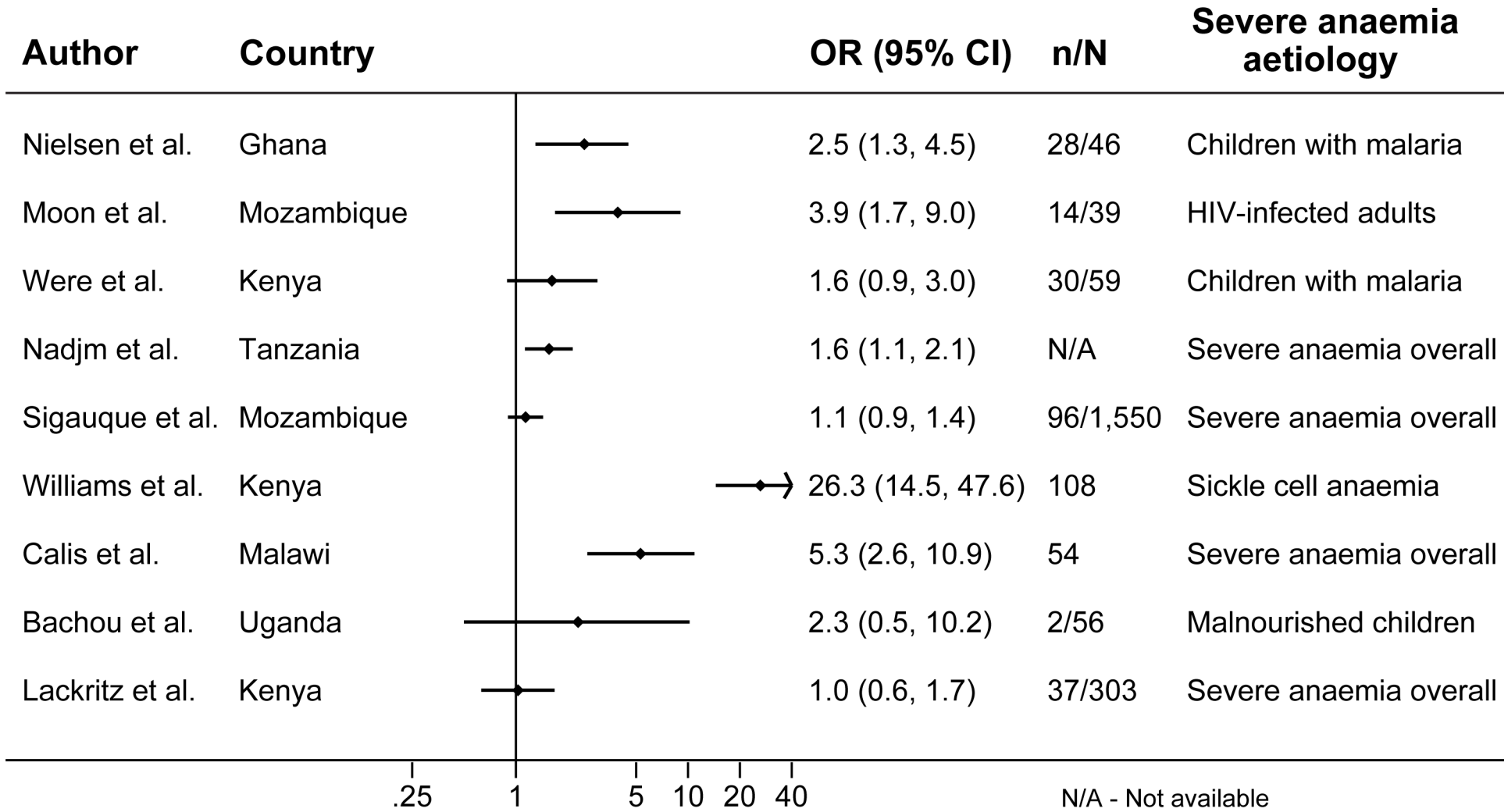
Anaemia prevalence



Source: GBD anaemia collaborators, Lancet Haemat, 2023

	Global	Central Europe, eastern Europe, and central Asia	High income	Latin America and Caribbean	North Africa and Middle East	South Asia	Southeast Asia, east Asia, and Oceania	Sub-Saharan Africa
Dietary iron deficiency	1	1	1	1	1	1	1	1
Haemoglobinopathies and haemolytic anaemias	2	2	2	2	2	2	2	3
Other neglected tropical diseases	3	3	4	3	3	3	3	4
Other unspecified infectious diseases	4	4	5	4	4	4	4	7
Malaria	5	14	15	10	10	8	10	2
Vitamin A deficiency	6	8	10	5	5	6	7	5
Intestinal nematode infections	7	12	14	8	13	5	8	6
Chronic kidney disease	8	5	3	6	7	7	6	9
Endocrine, metabolic, blood, and immune disorders	9	6	6	7	8	9	5	10
Gynaecological diseases	10	7	7	11	6	10	12	13
Schistosomiasis	11	16	16	12	9	16	13	8
Upper digestive system diseases	12	9	8	9	12	11	9	14
Maternal disorders	13	10	11	13	11	12	1	12
HIV/AIDS	14	15	13	14	16	15	16	11
Cirrhosis and other chronic liver diseases	15	13	12	15	14	13	14	15
Inflammatory bowel disease	16	11	9	16	15	14	15	16

Severe anaemia is associated with bacteraemia

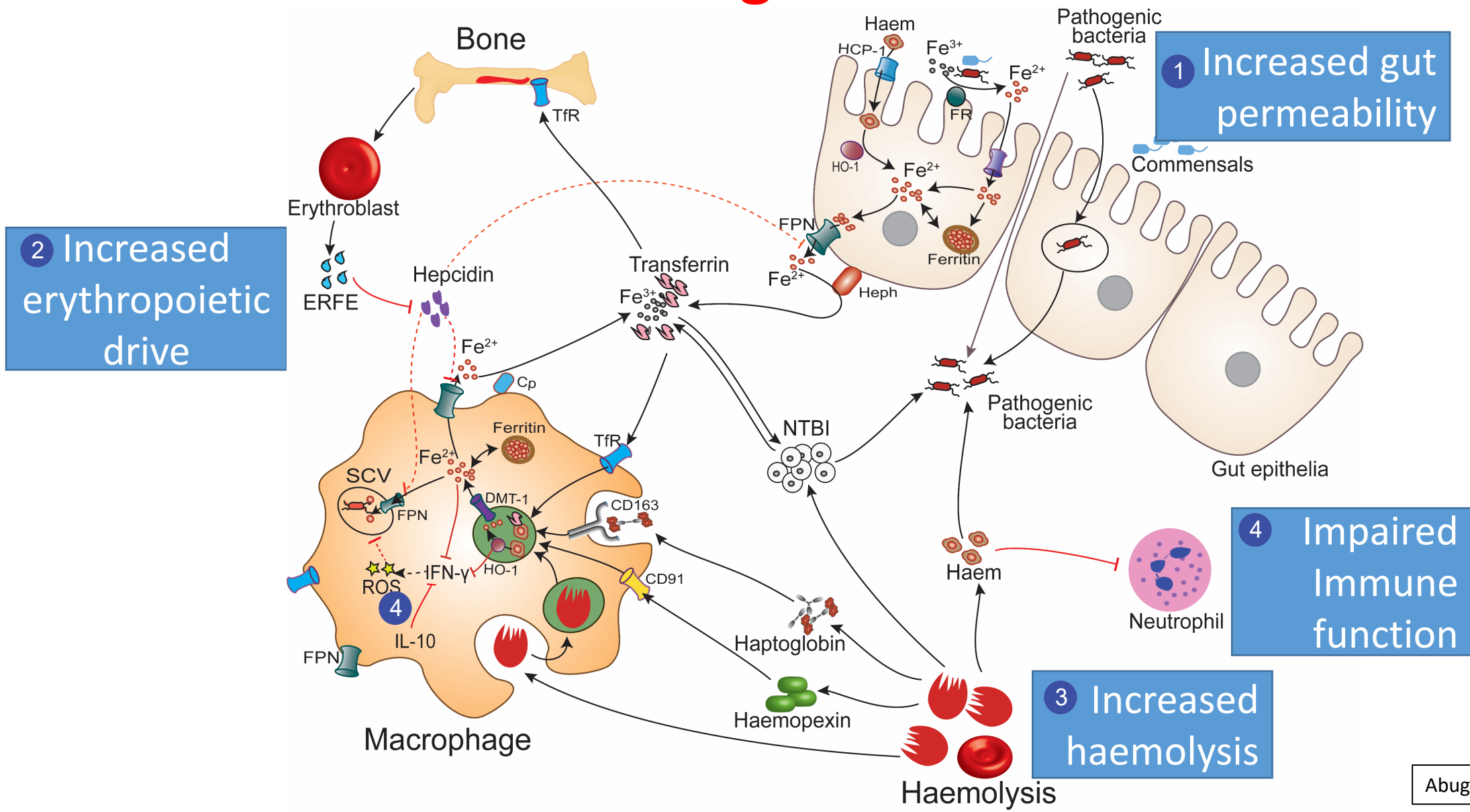


- ✓ Small sample sizes
- ✓ Single causes of severe anaemia
- ✓ Reverse causality?

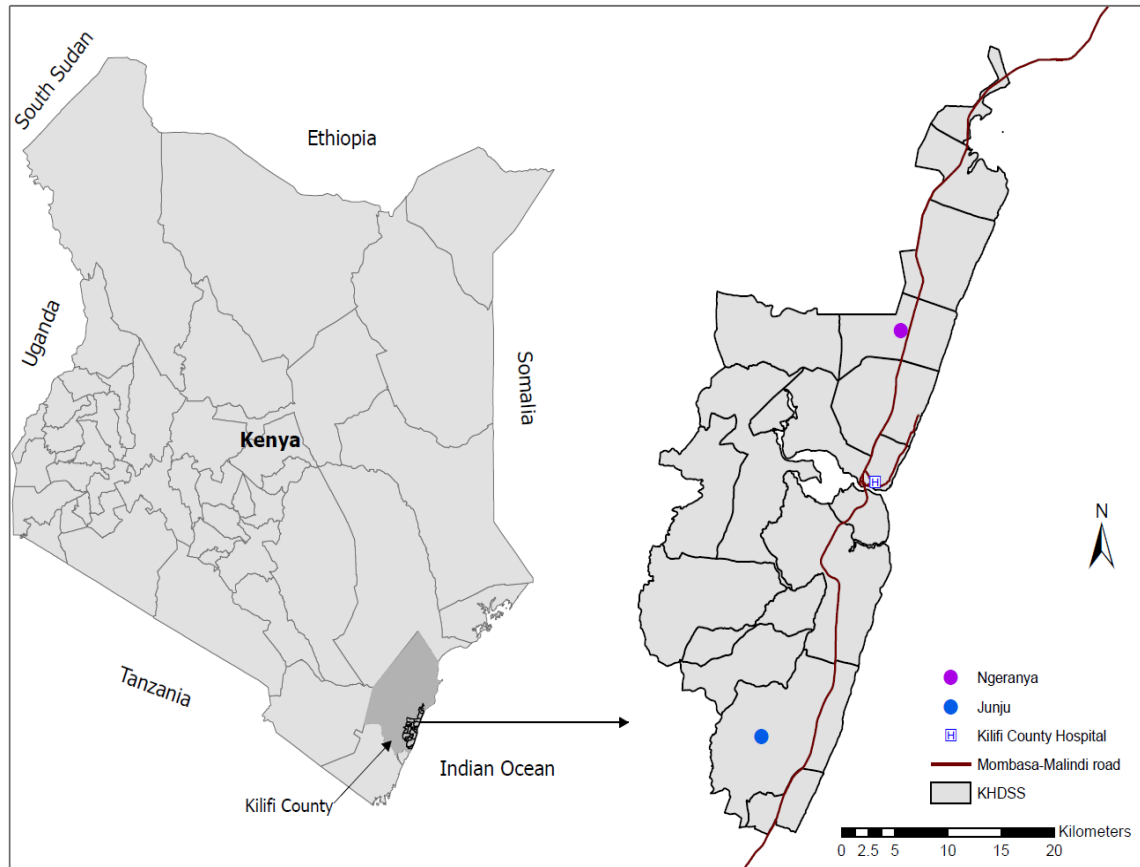
Odds Ratio

n = Severe anaemia with bacteraemia
N = Total bacteraemia

Severe anaemia might increase risk of iNTS



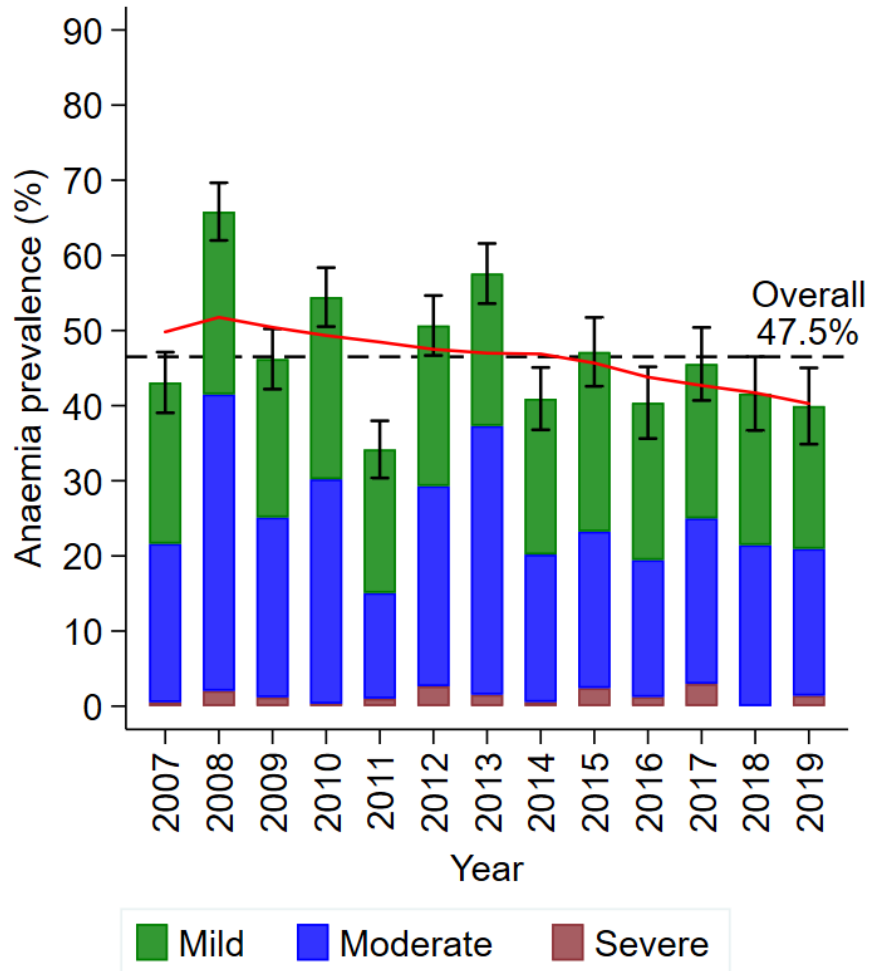
Approaches



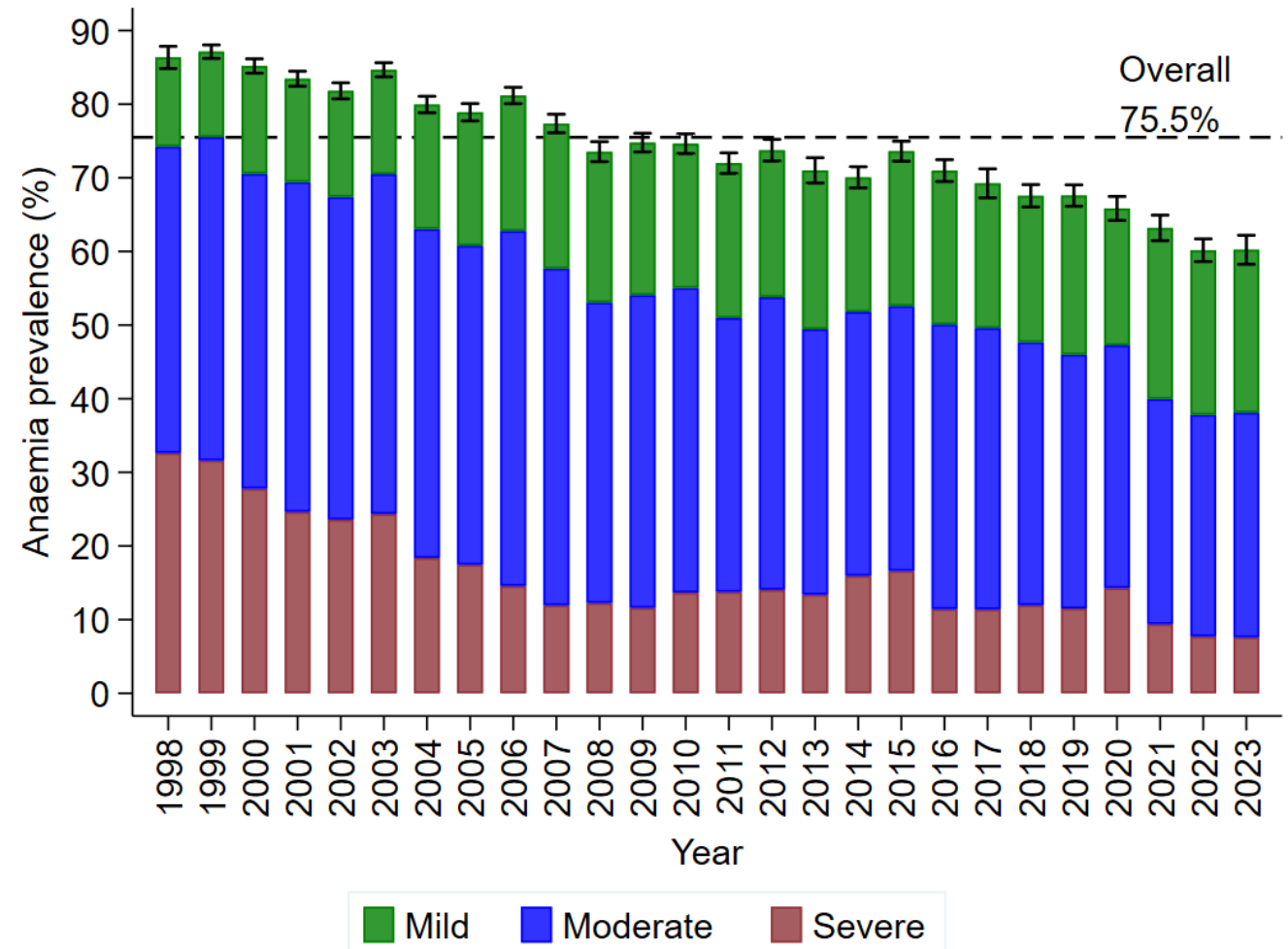
1. Epidemiological associations between severe anaemia and iNTS.
2. Assays of iron and immune-mediated biomarkers.
3. Bacterial growth assays.
4. Effects of anaemia on NTS vaccine responses.

Anaemia is prevalent among children living in Kilifi, Kenya

Community surveys (N=6,717)

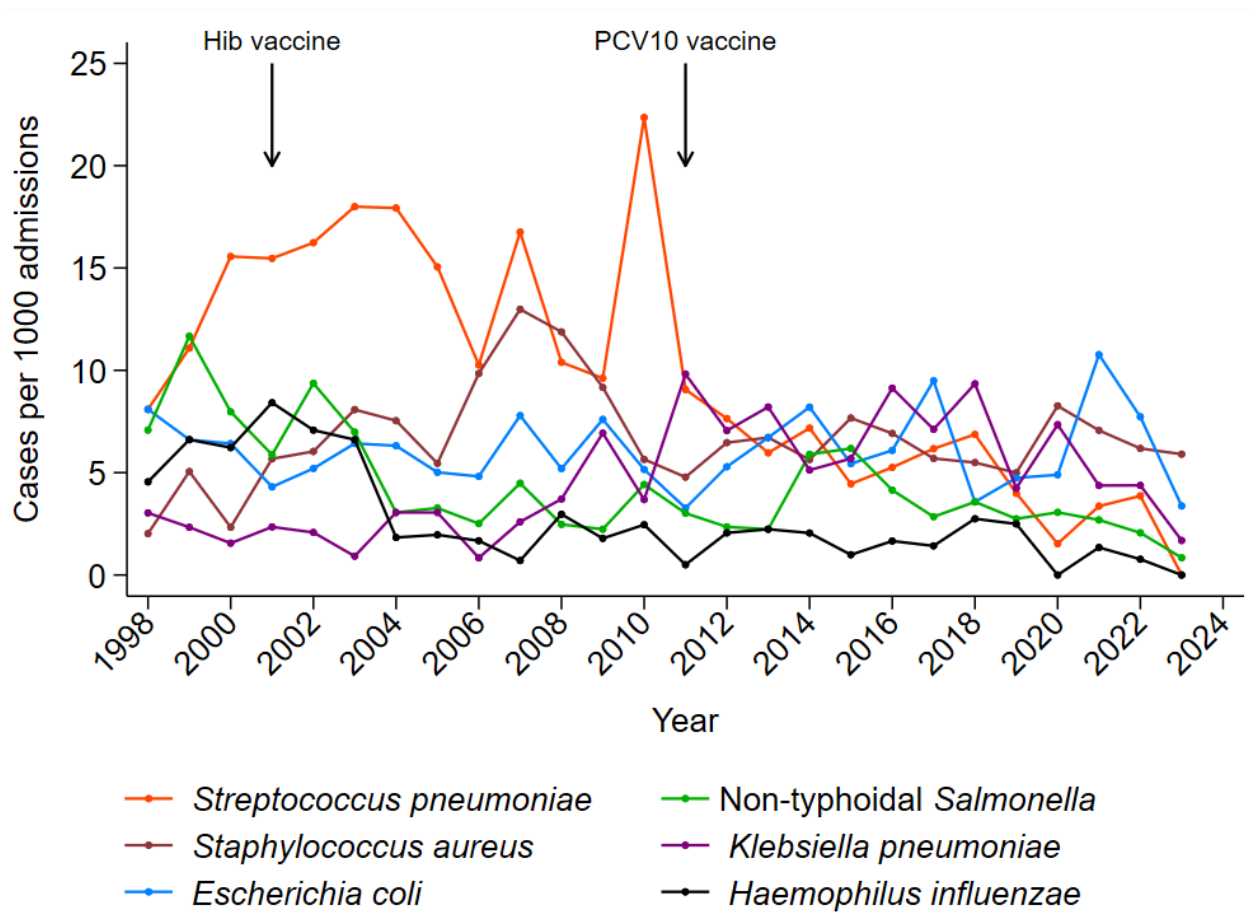


Hospital admissions (N=102,559)



iNTS remains an important cause of paediatric admissions

Bacteraemia, n=5,050 (4.9%)

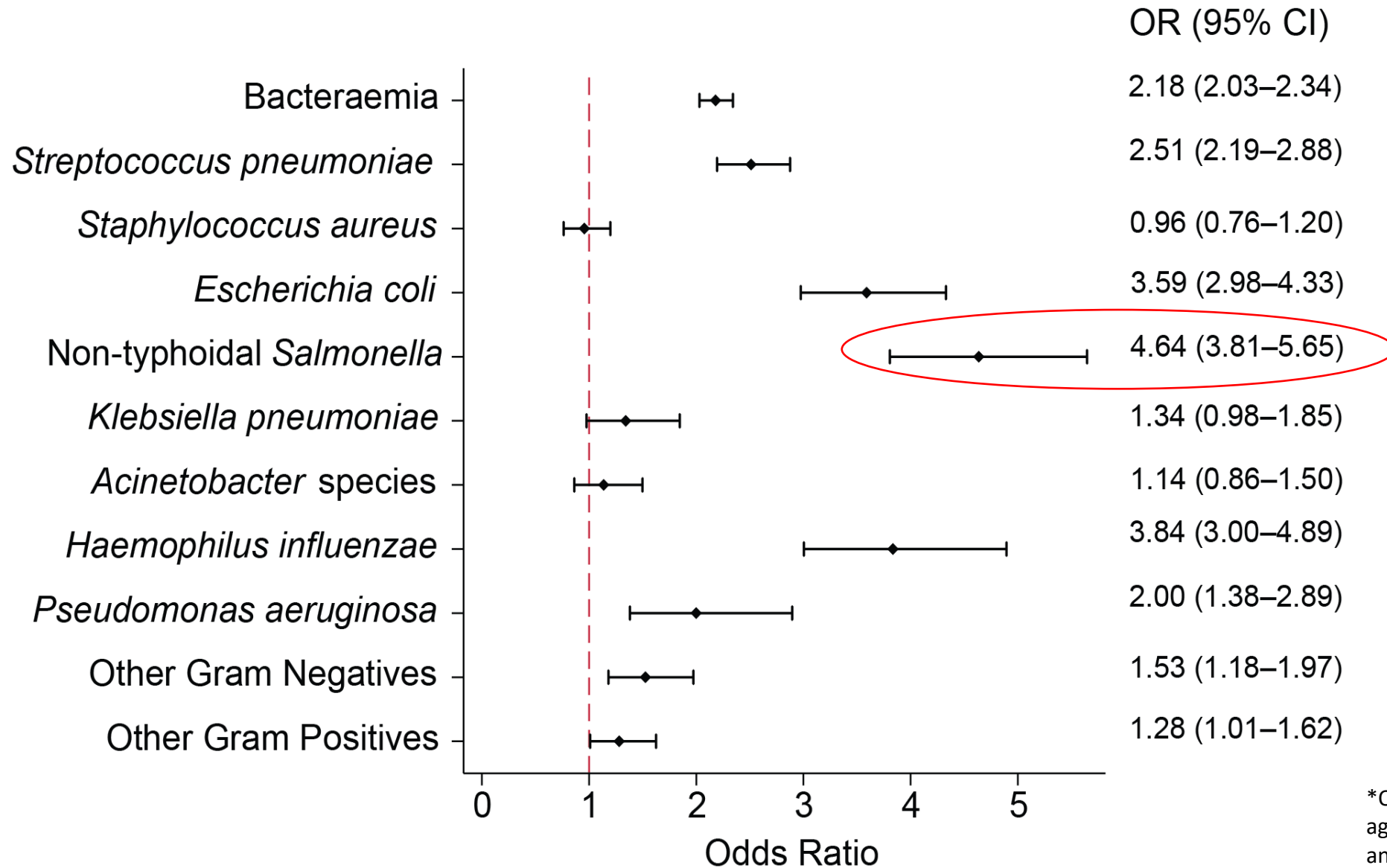


iNTS, n=474 (9.4% of bacteraemia)

- *Salmonella* Enteritidis: 154 (32.5%)
- *Salmonella* Typhimurium: 149 (31.4%)
- Not typeable: 39 (8.2%)
- Not tested: 132 (27.8%)

In-hospital iNTS mortality = **21.4%**
(vs 8.2% overall)

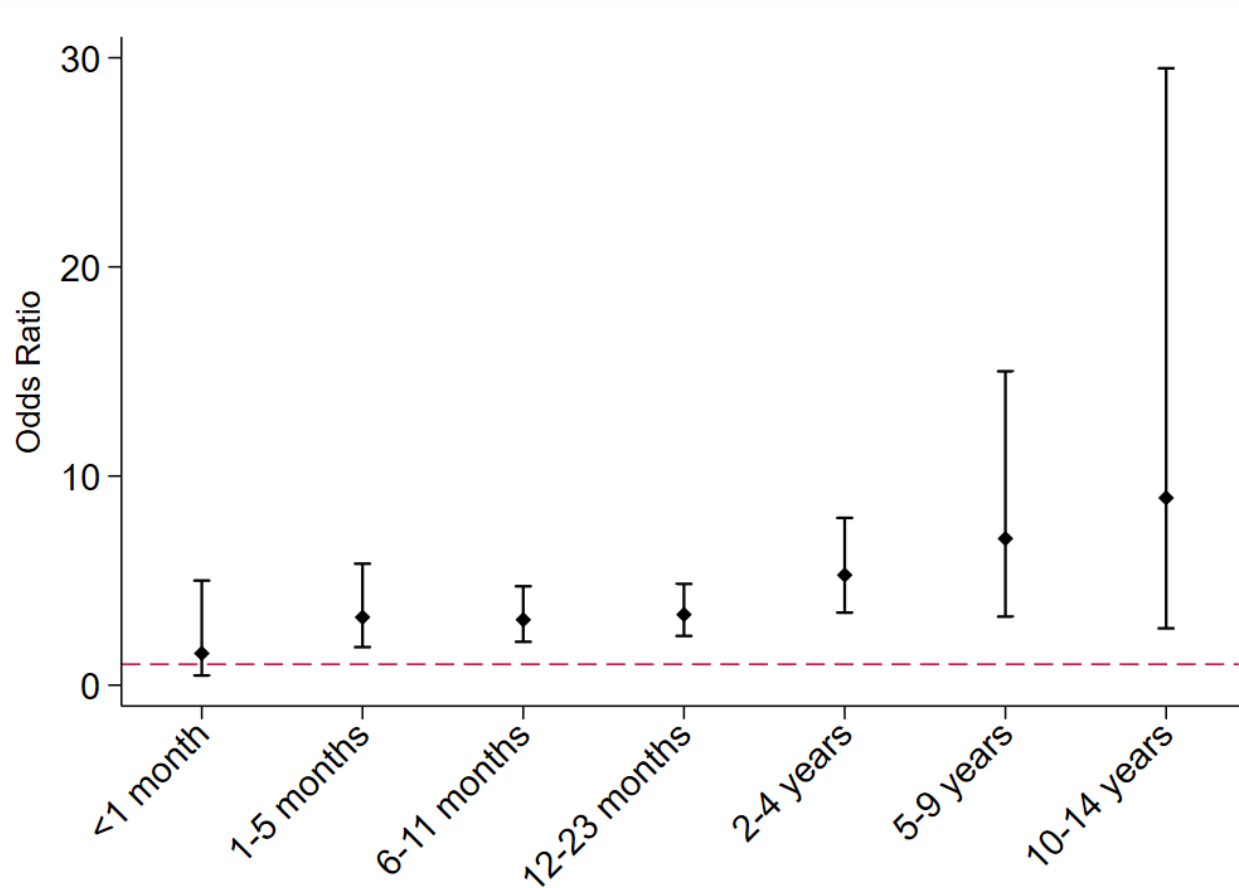
Severe anaemia associated with 4-fold increased risk of iNTS



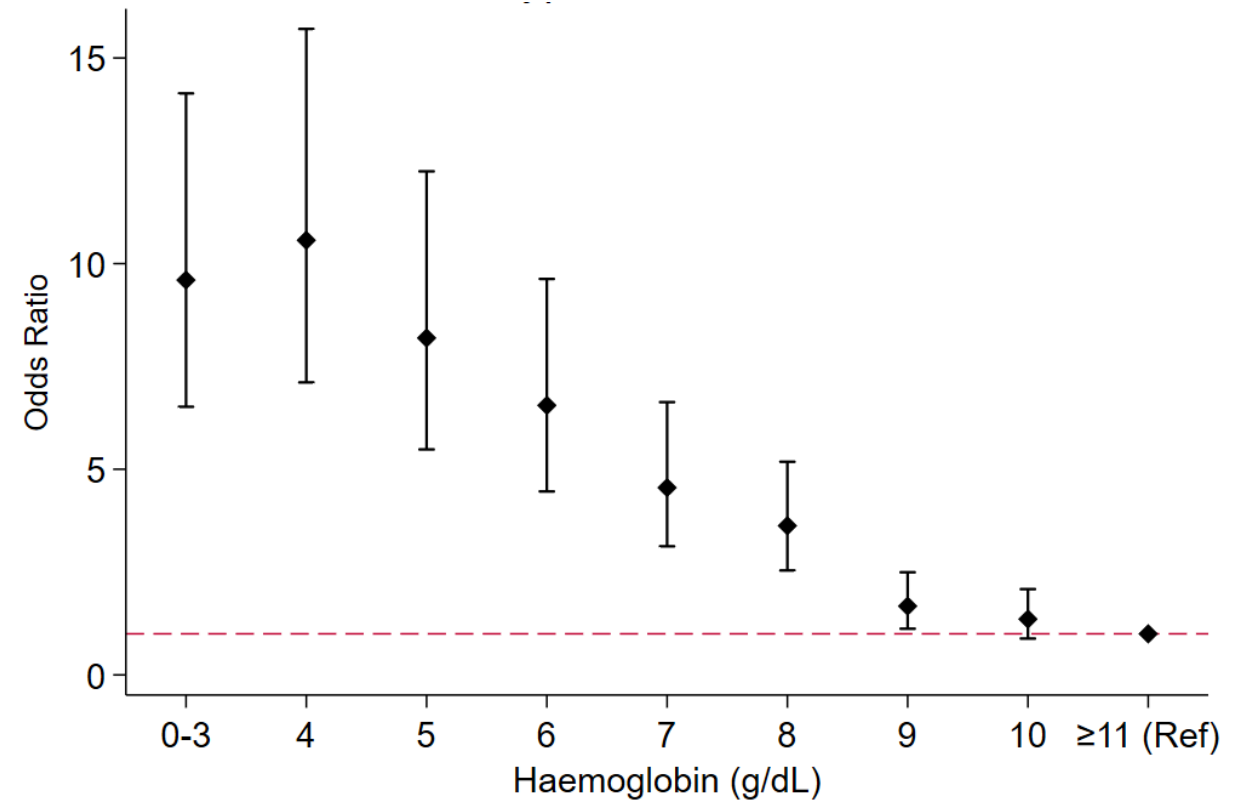
*Odds ratios adjusted for age, sex, year of admission and number of readmissions

Risk of iNTS was not age-dependent, but increased with each 1g/dL decrease in haemoglobin levels

Age

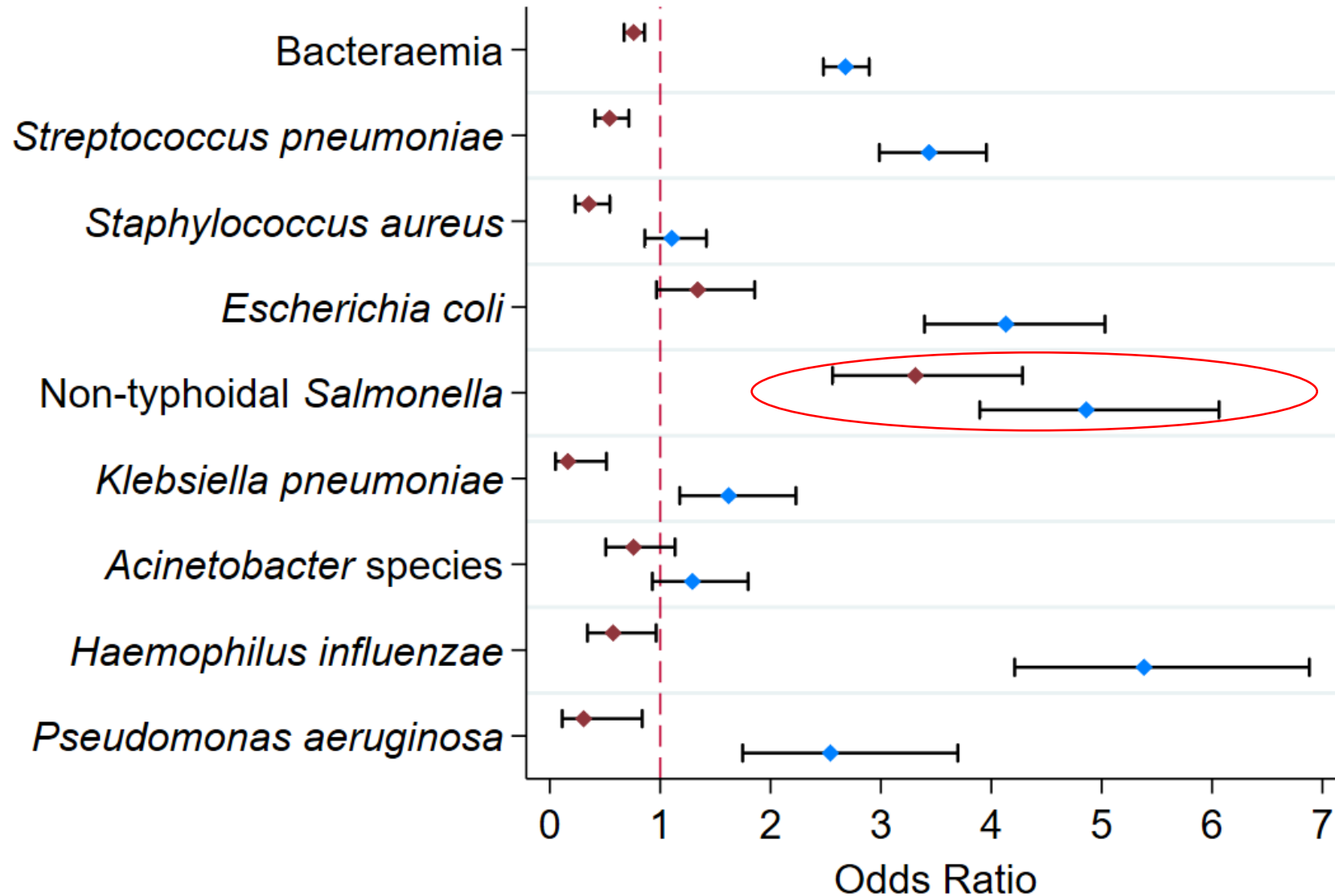


Haemoglobin levels



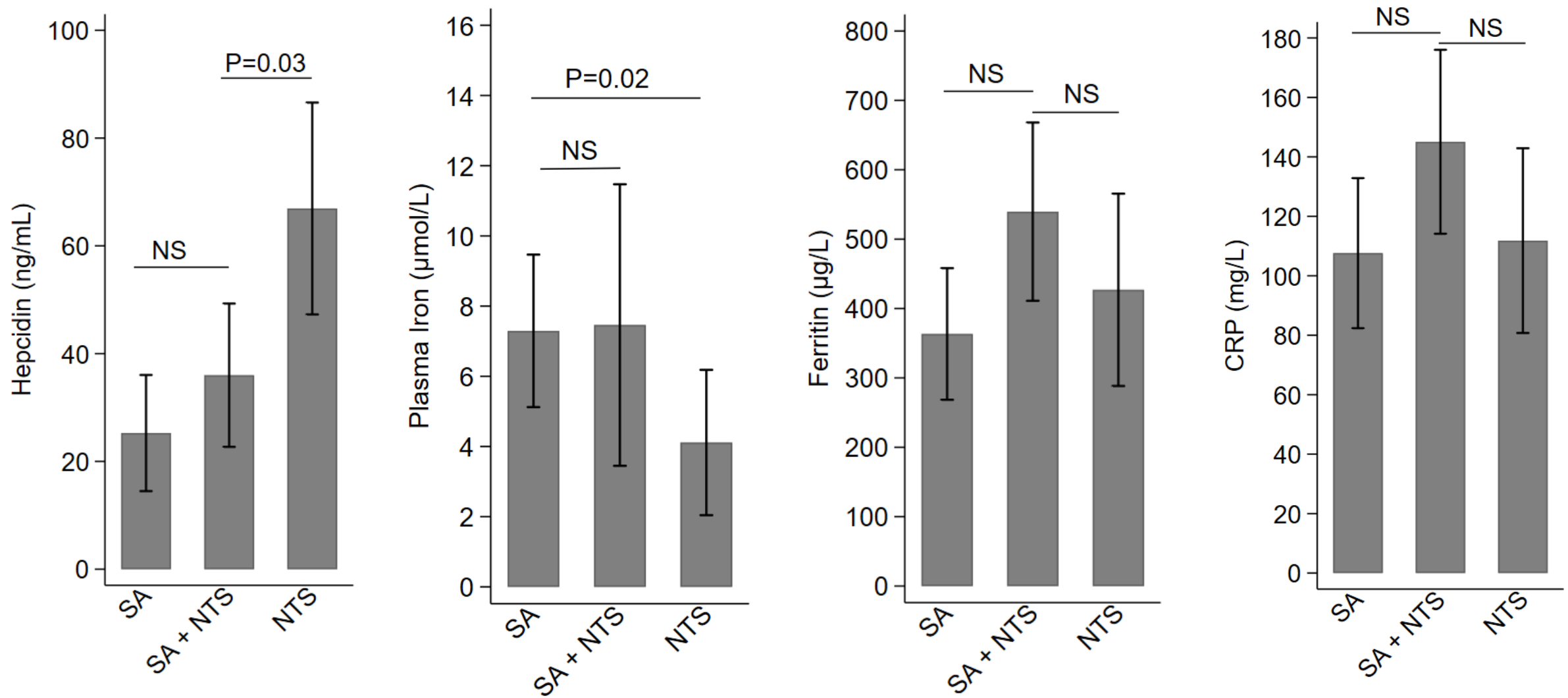
*Odds ratios adjusted for age, sex, year of admission and number of readmissions

iNTS risk in severely anaemic children with and without malaria



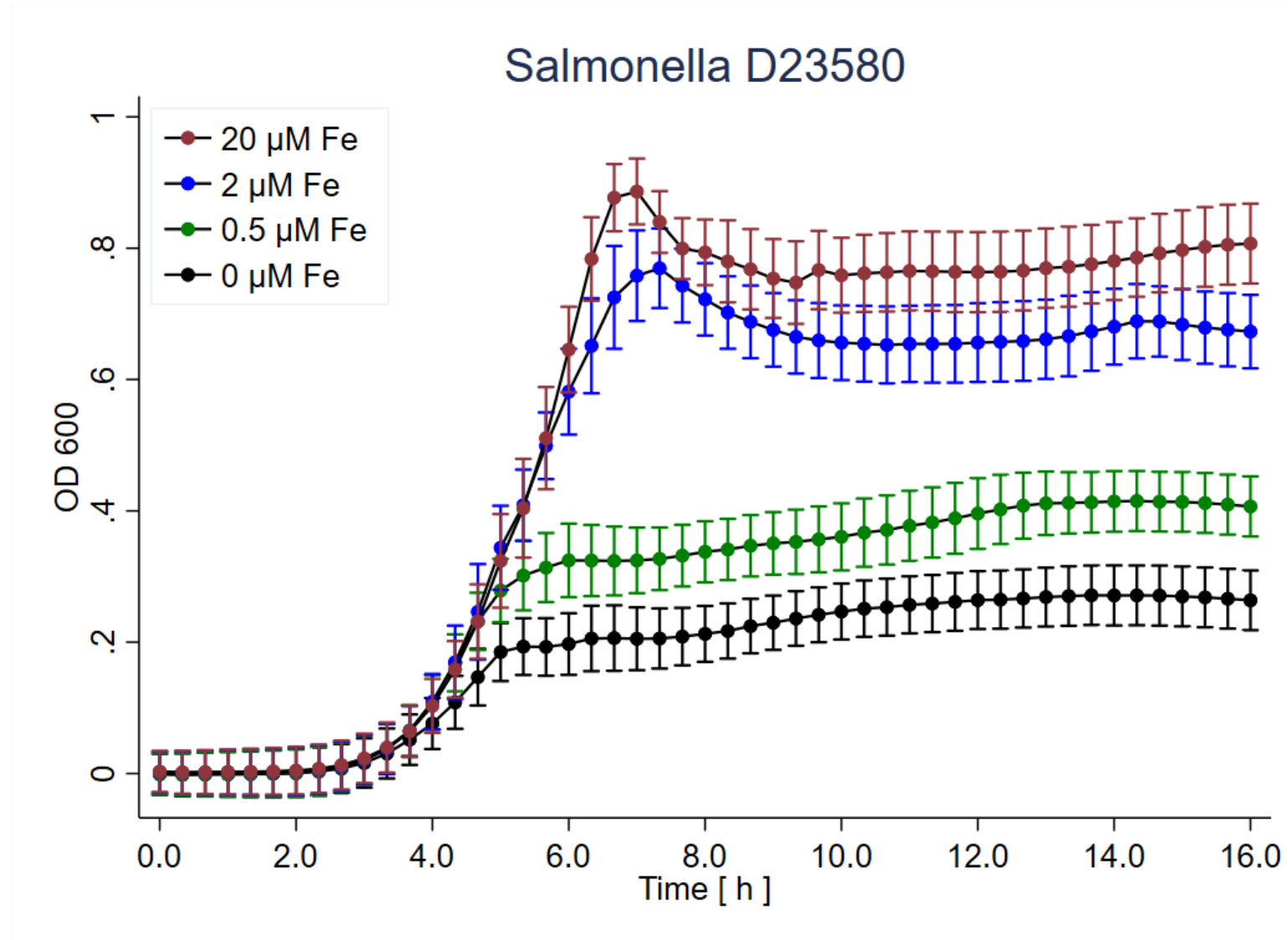
*Odds ratios adjusted for age, sex, year of admission and number of readmissions

Low hepcidin and high plasma iron levels in severe anaemia

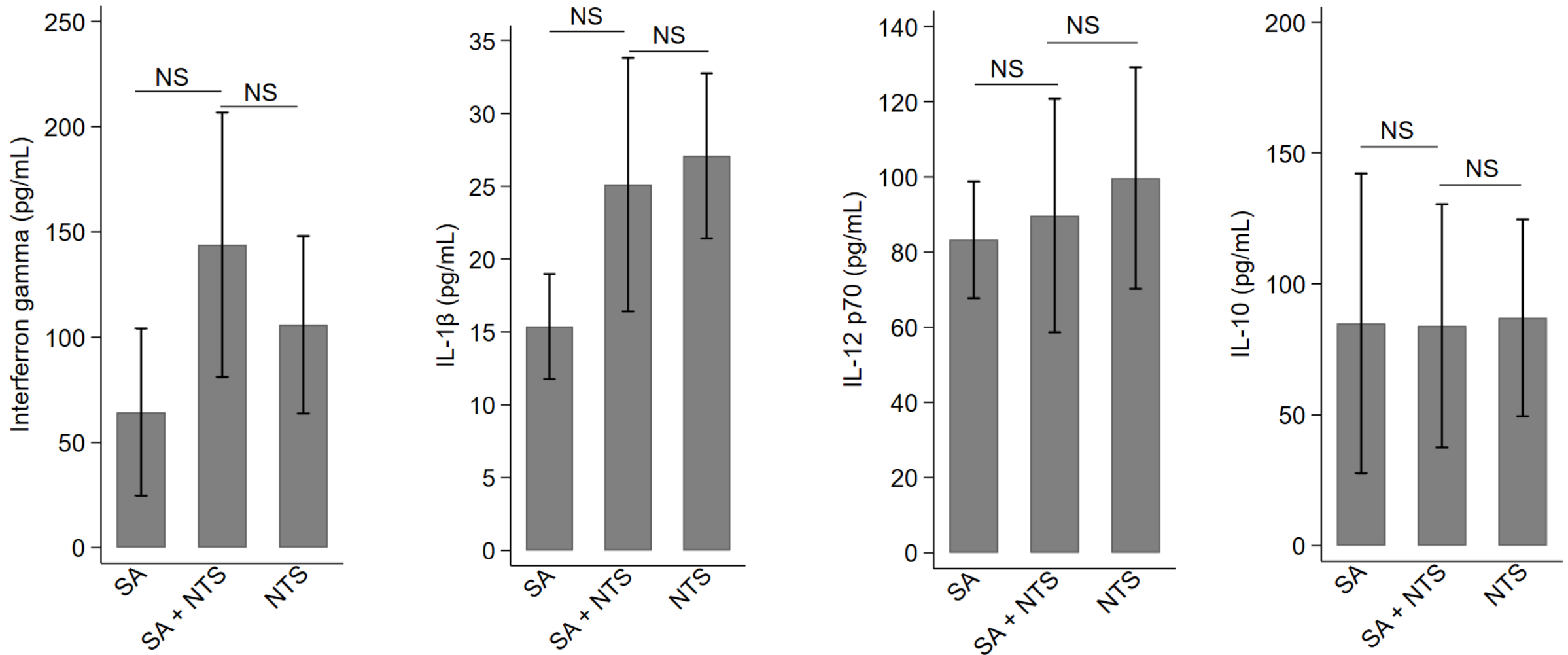


SA – severe anaemia (n=52); NTS – non-typhoidal Salmonella (n=44); SA+NTS (n=29)

High iron levels associated with bacterial growth in-vitro



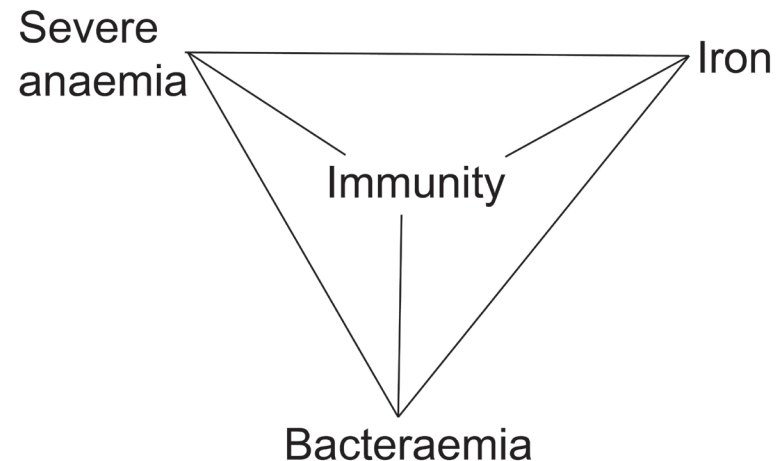
Severe anaemia doesn't impair cytokine production in children with iNTS



SA – severe anaemia (n=52); NTS – non-typhoidal Salmonella (n=44); SA+NTS (n=29)

Why this work is important

- Anaemia and iNTS are important causes of hospitalization and death
- Strategies to manage iNTS remain ineffective.
- Understanding underlying risk factors for iNTS (such as severe anaemia) → better interventions.



Summary

- Anaemia and iNTS are prevalent among Kenyan children.
- Severe anaemia is associated with a four-fold increased risk of iNTS.
- The risk is independent of malaria parasitaemia.
- Severe anaemia may increase iNTS risk through iron-dependent mechanisms.

Acknowledgements



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