SEROEPIDEMIOLOGY IN AFRICA OF INTS (SAINTS)

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Coalition Against Typhoid Conference

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Vacc iNTS

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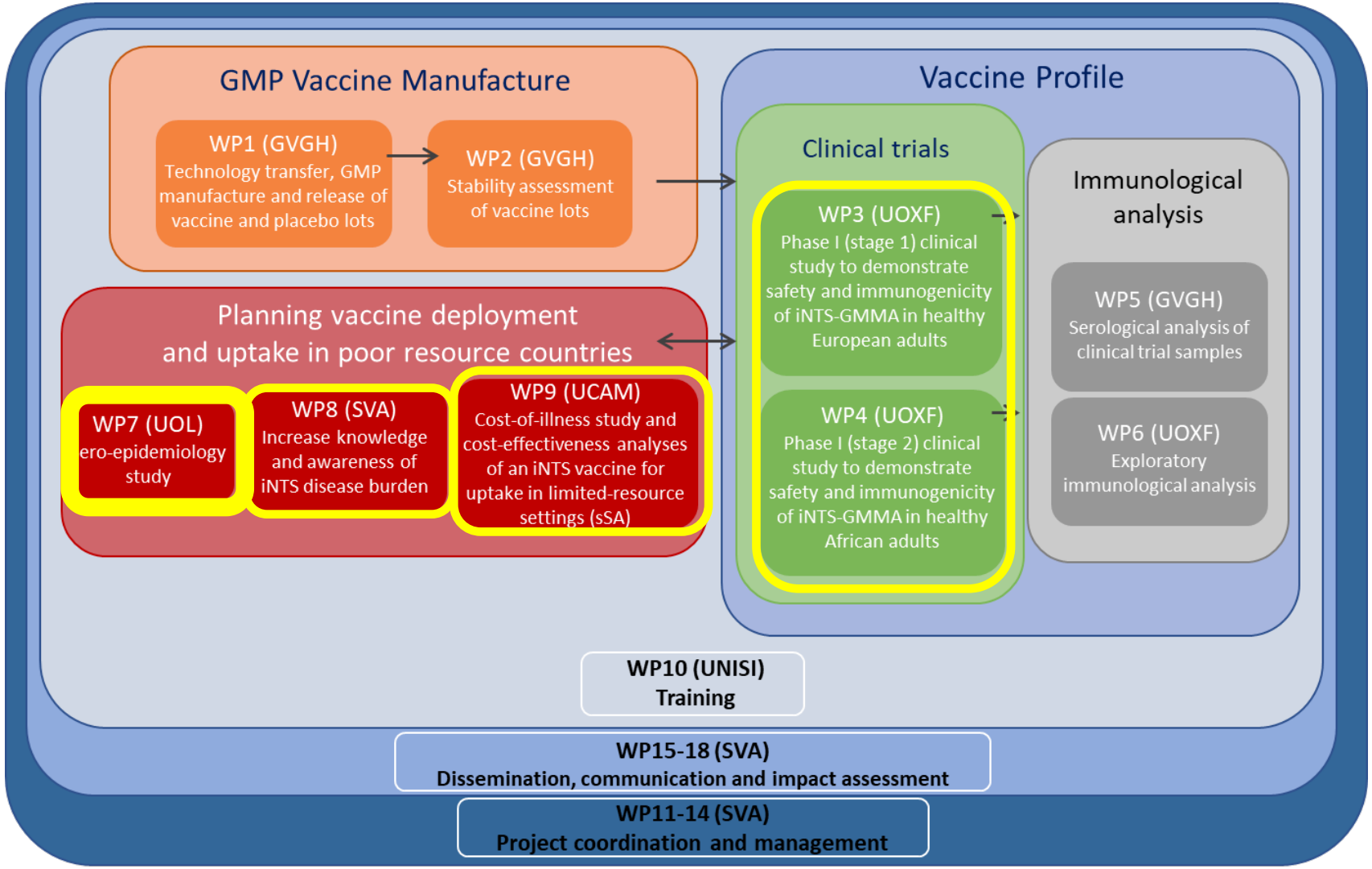
Accelerating iNTS vaccines - VacciNTS consortium, EU H2020

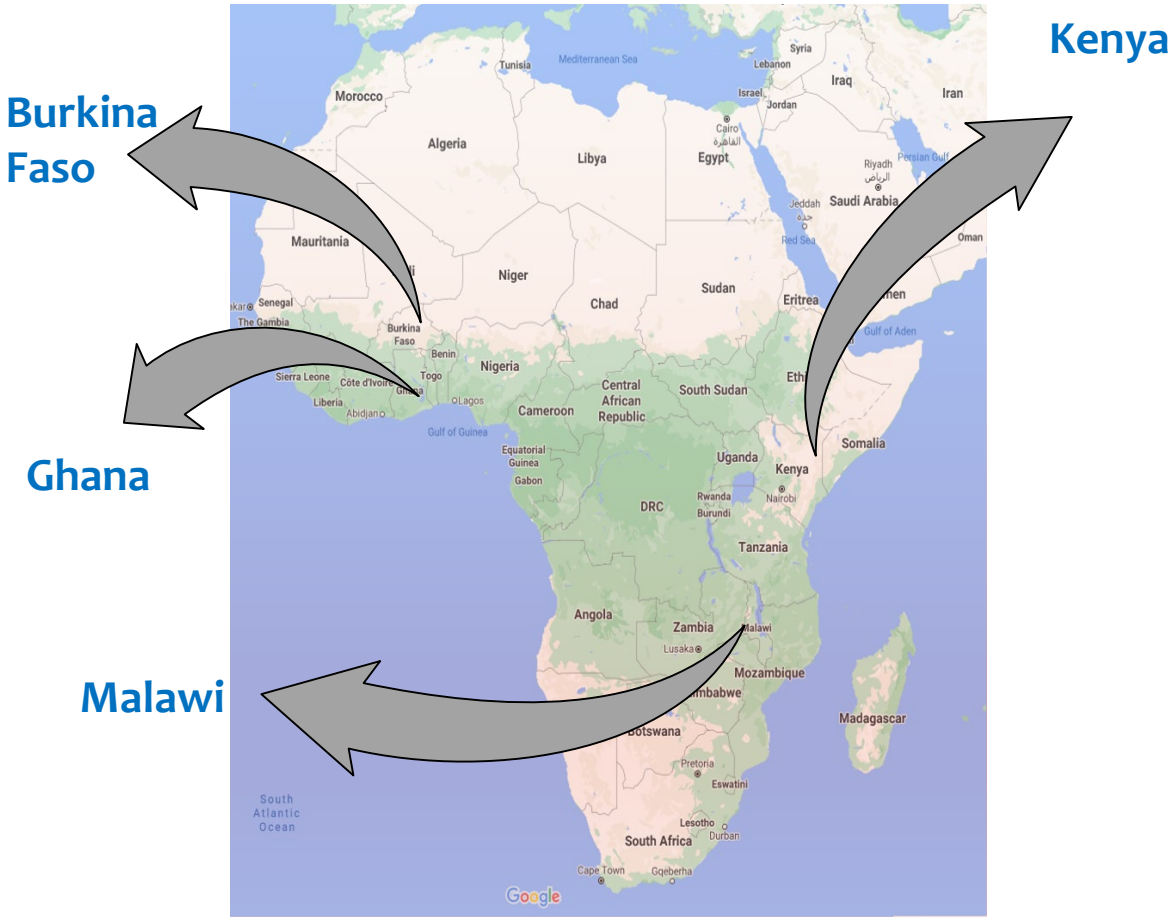


EU Horizon

Study Aims

- To understand across different sub-Saharan African sites:
  - Age of acquisition of humoral immunity to non-typhoidal salmonella (NTS)
    - Children 0-5 years
    - Common iNTS serovars: Typhmurium & Enteritidis
    - O-Ag IgG
    - Serum bactericidal activity

Seroepidemiology in **A**frica of **iNTS** (SAiNTS)



VacciNTS consortium

4 African countries

- 1000 samples aged 0-5 years per site
- 200 per annual age-stratum
- Children randomly selected from mapped and censused study areas

- 2 commonest serovars causing invasive disease (Typhimurium , Enteritidis)
  - ELISA (OAg IgG)
  - Serum Bactericidal Activity

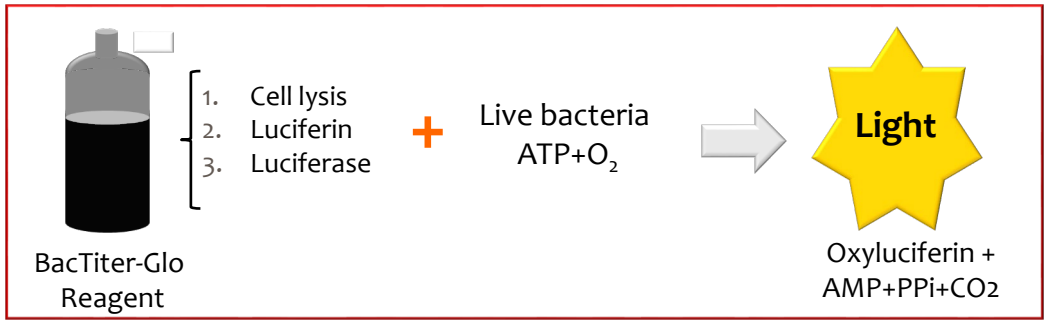
Recruitment by site

- **Burkina Faso:**
  - 21st February – 28th March 2022 (1 month)
    - 1008 serum samples
- **Ghana:**
  - 12th August 2021 - 24th May 2022 (8 months)
    - 1032 serum samples
- **Kenya:**
  - 26th April – 29th July 2021 (3 months)
    - Rainy season
    - 1346 serum samples
- **Malawi:**
  - 13th January – 30th March 2022 (14 months)
    - Across seasons and geographic regions
    - 2412 serum samples

Laboratory assays

Assays developed by GSK Vaccines Institute for Global Health (GVGH)

- ELISA[1]: IgG to O antigen: *S.* Tm/ *S.* En
- High-throughput Serum Bactericidal Activity (SBA) assay: *S.* Tm/ *S.* En
  - New technology platform for African sites
  - Samples processed at Kamuzu University of Health Sciences (KUHES), Malawi and Kwame Nkrumha University of Science and Technology (KNUST), Ghana

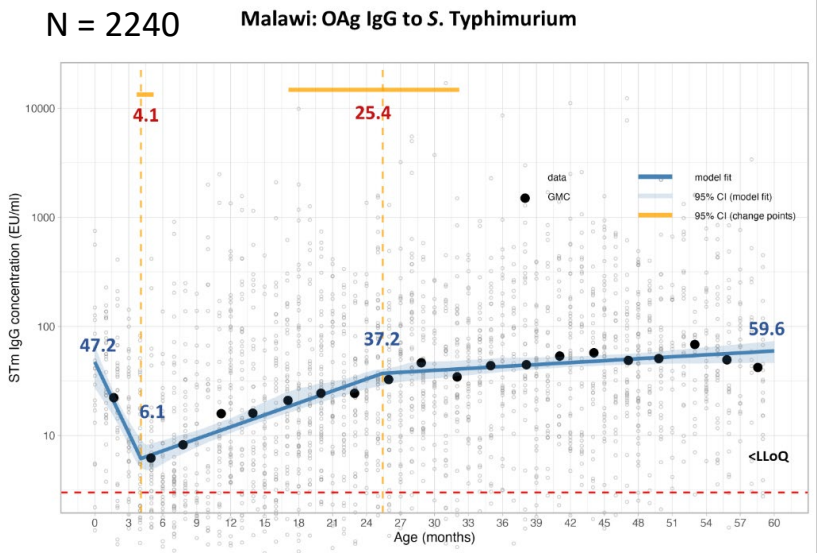


- Serum standard for assays across VacciNTS sites
- Assays to reflect those used in assessment of immunogenicity from phase 1 trials

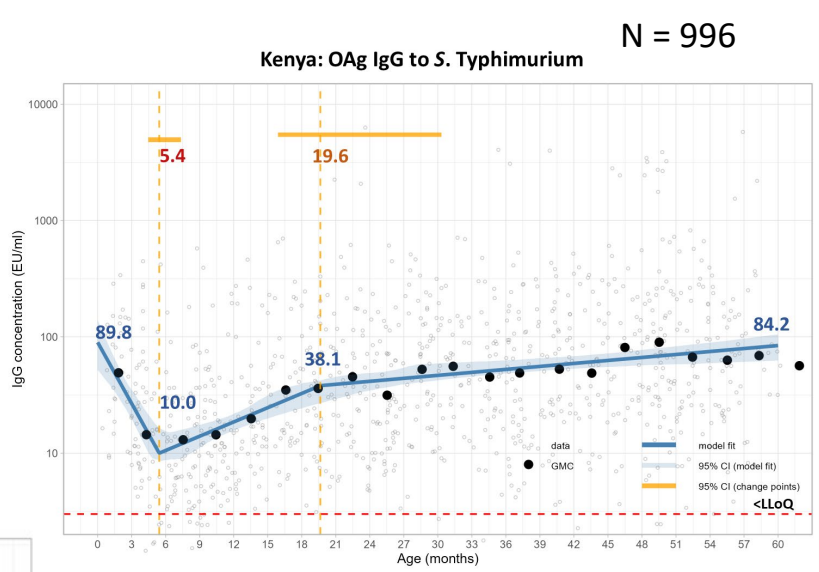
1. Aruta MG, et al. BioTech. 2023, 2. Aruta MG, et al. Methods, 2022

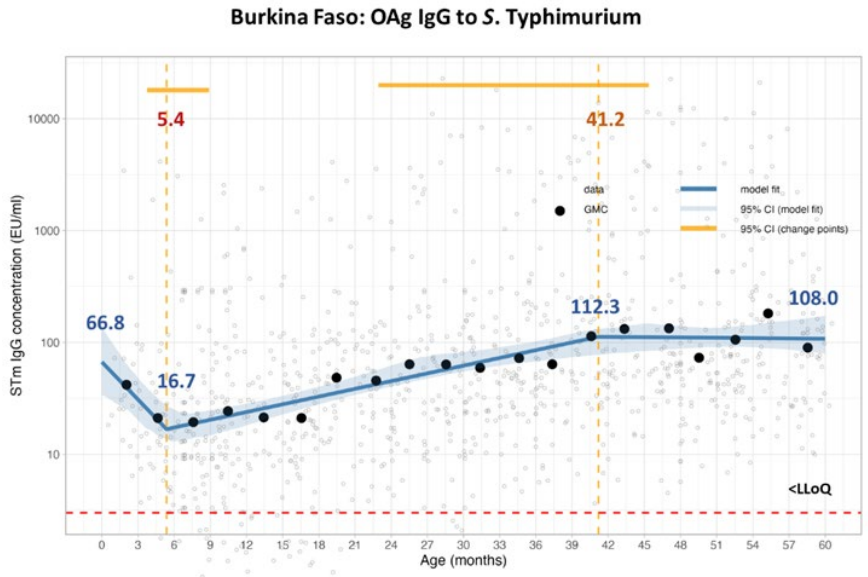
Salmonella Typhimurium O-Antigen IgG

N = 2240



N = 996

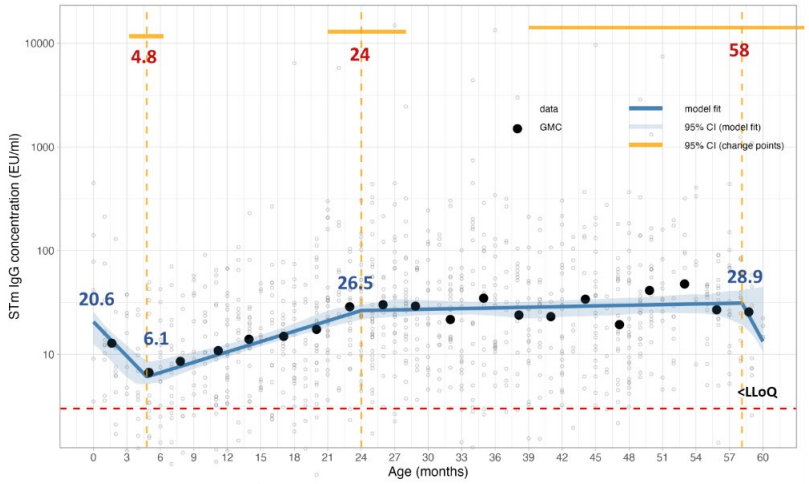


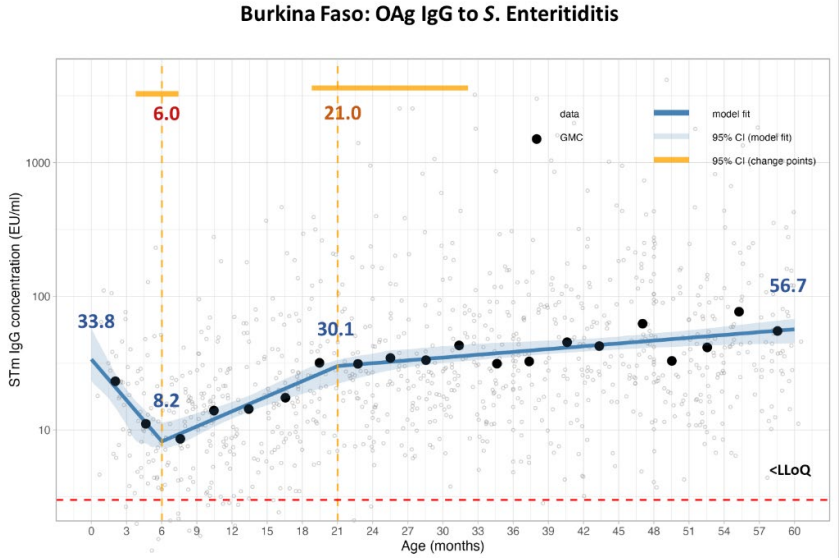


N = 1004

Salmonella Enteritidis O-Antigen IgG

N = 999





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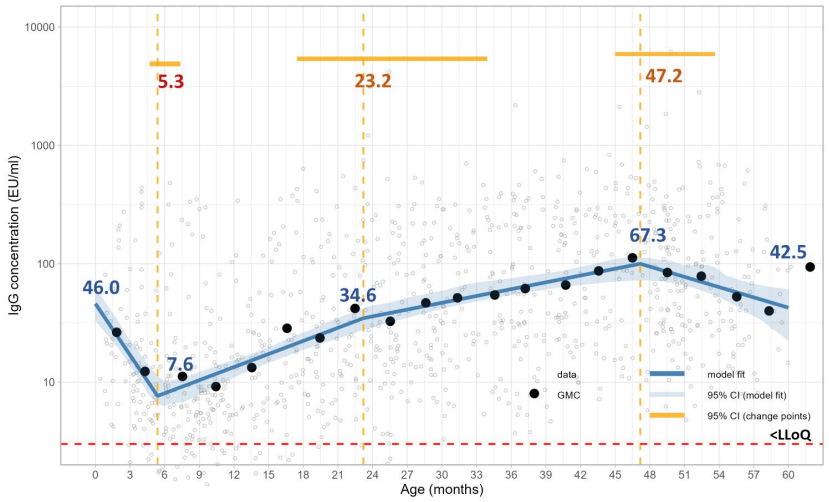
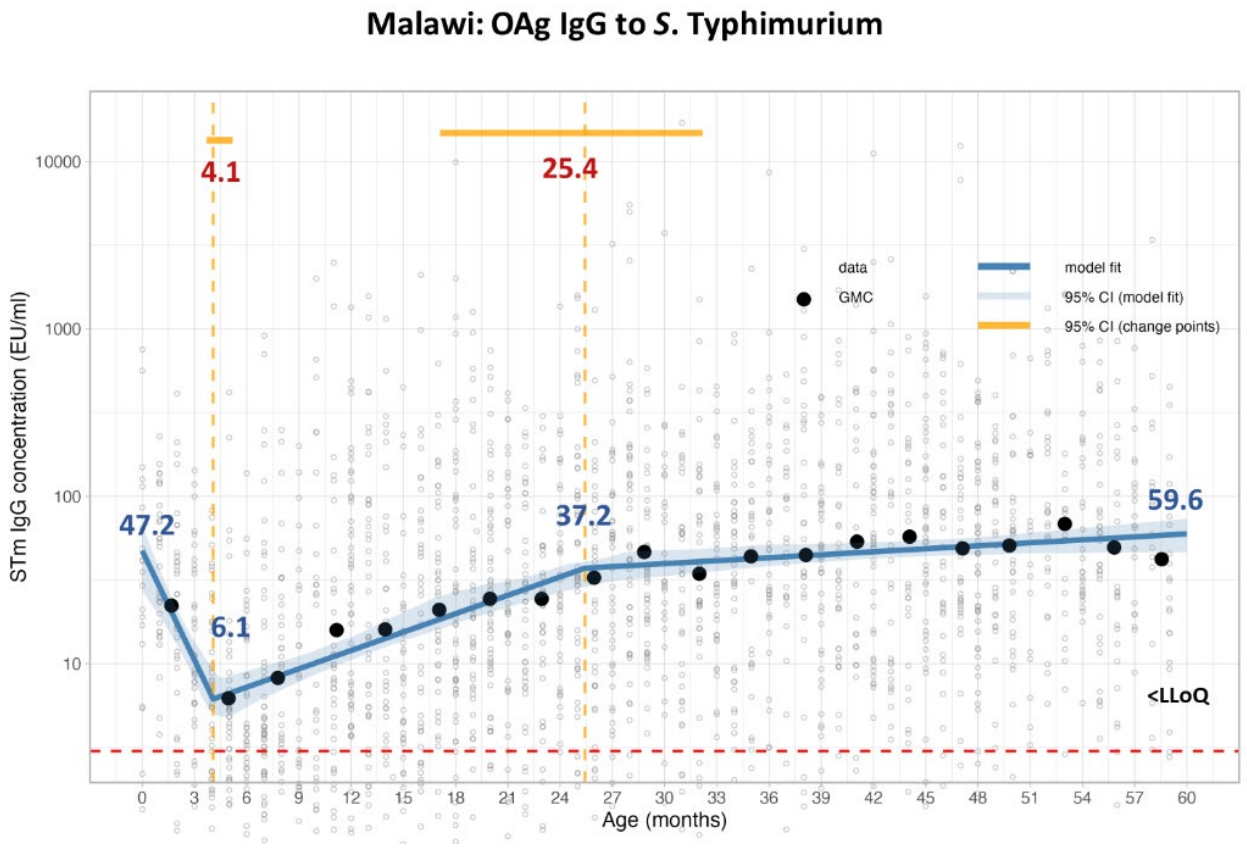


N = 999

O-Antigen IgG vs Serum Bactericidal Activity



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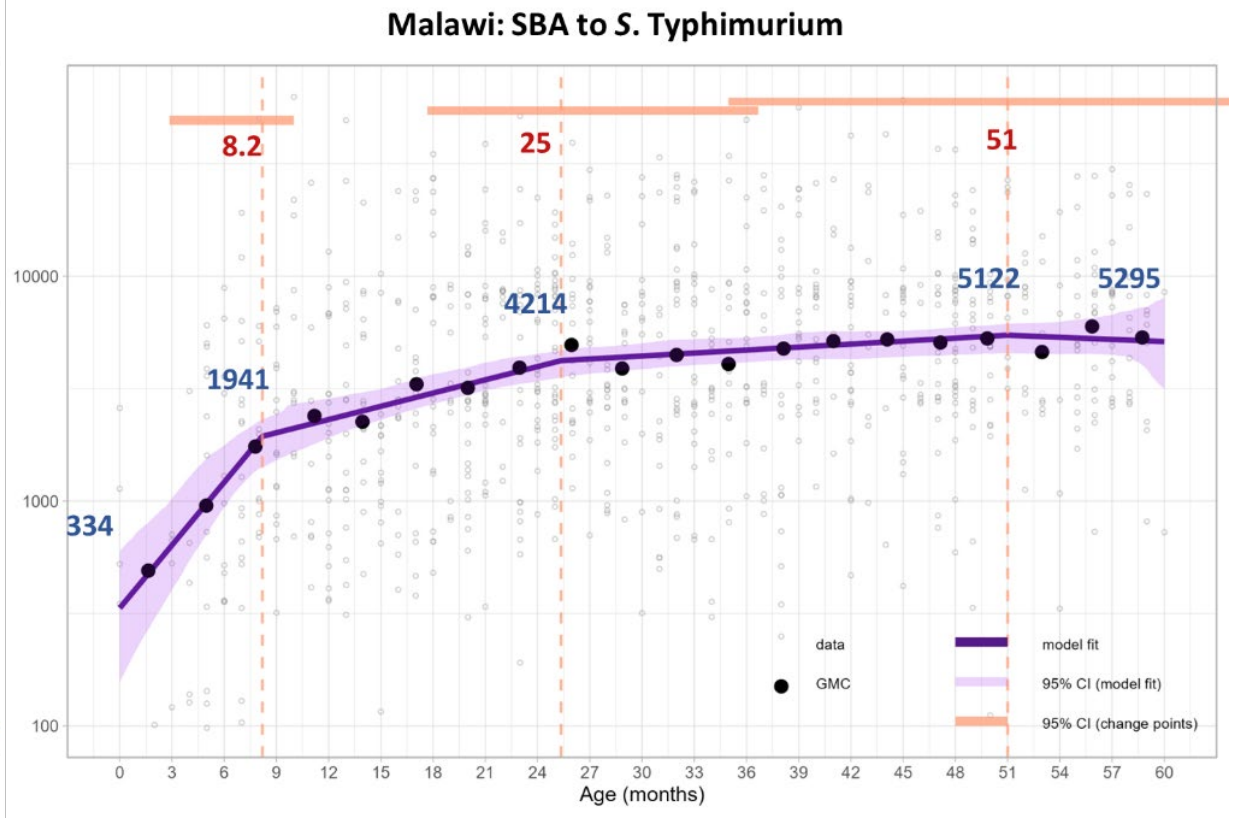
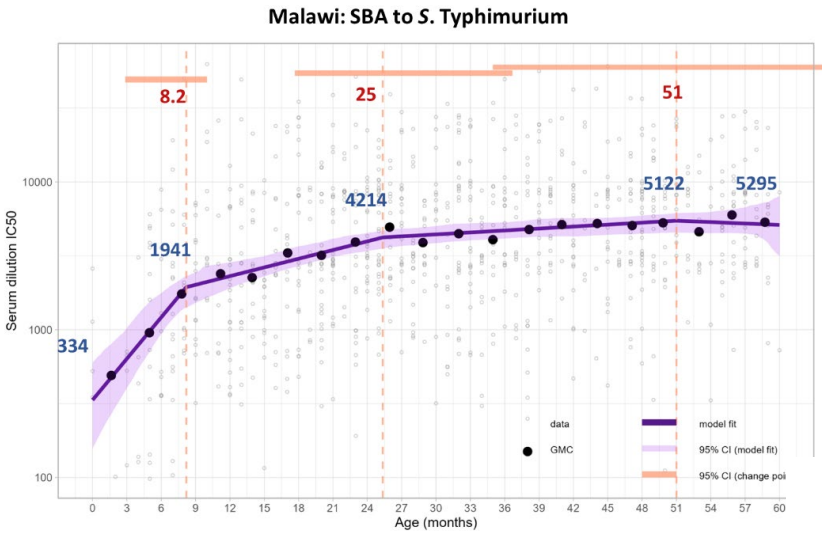


N = 993

Salmonella Typhimurium: Serum Bactericidal Activity

N = 993



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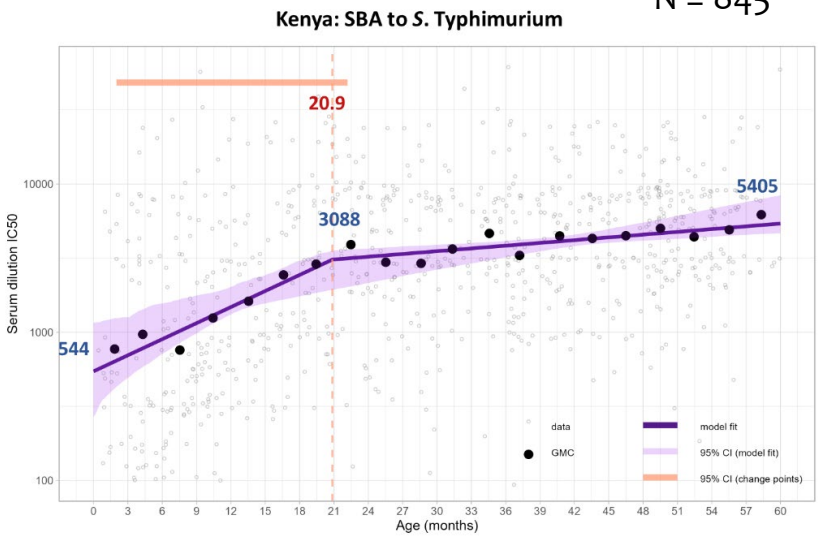
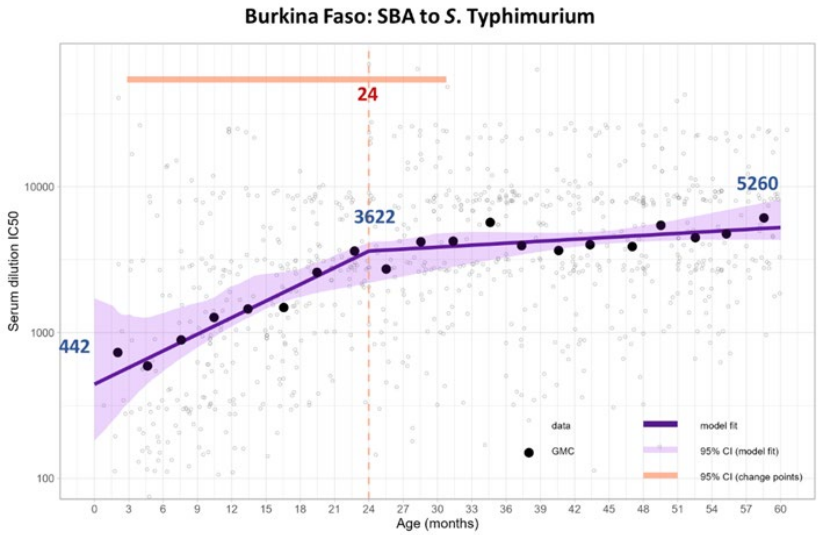
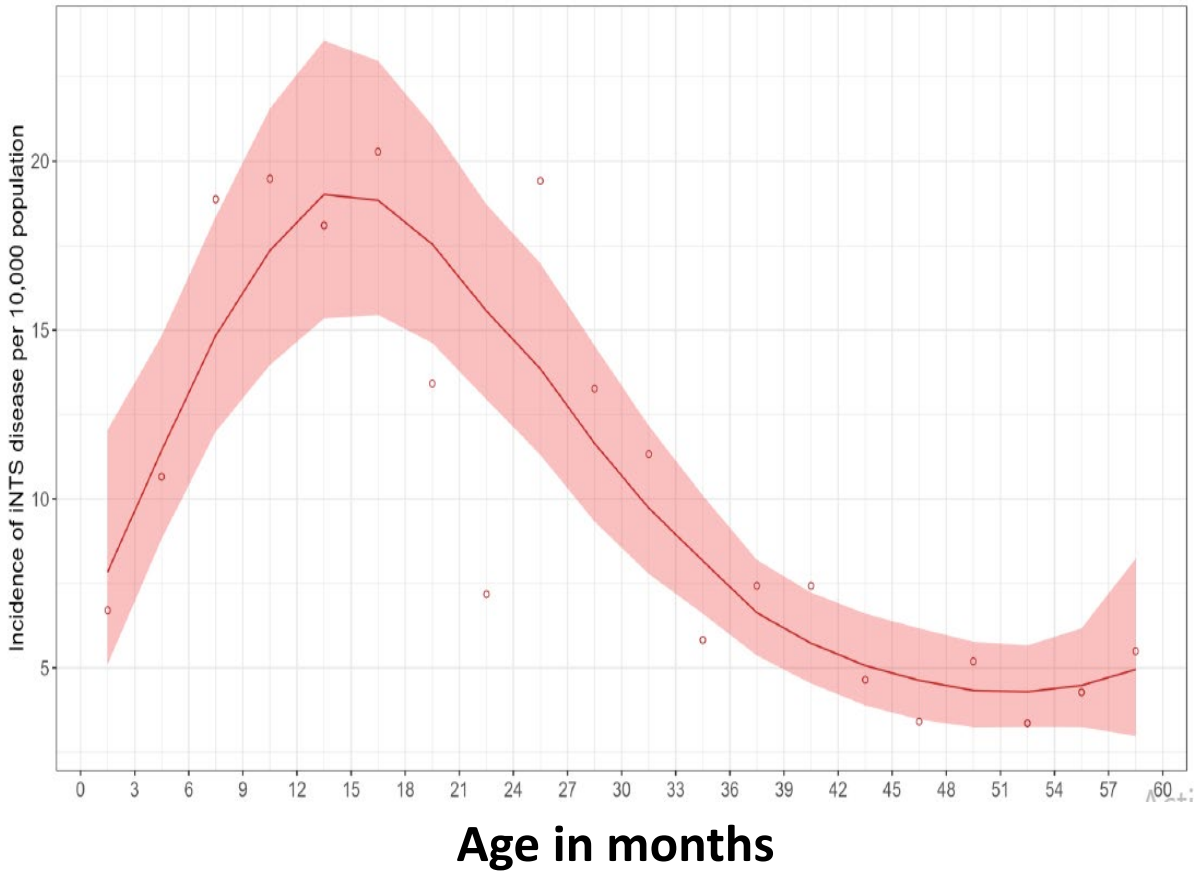




N = 934

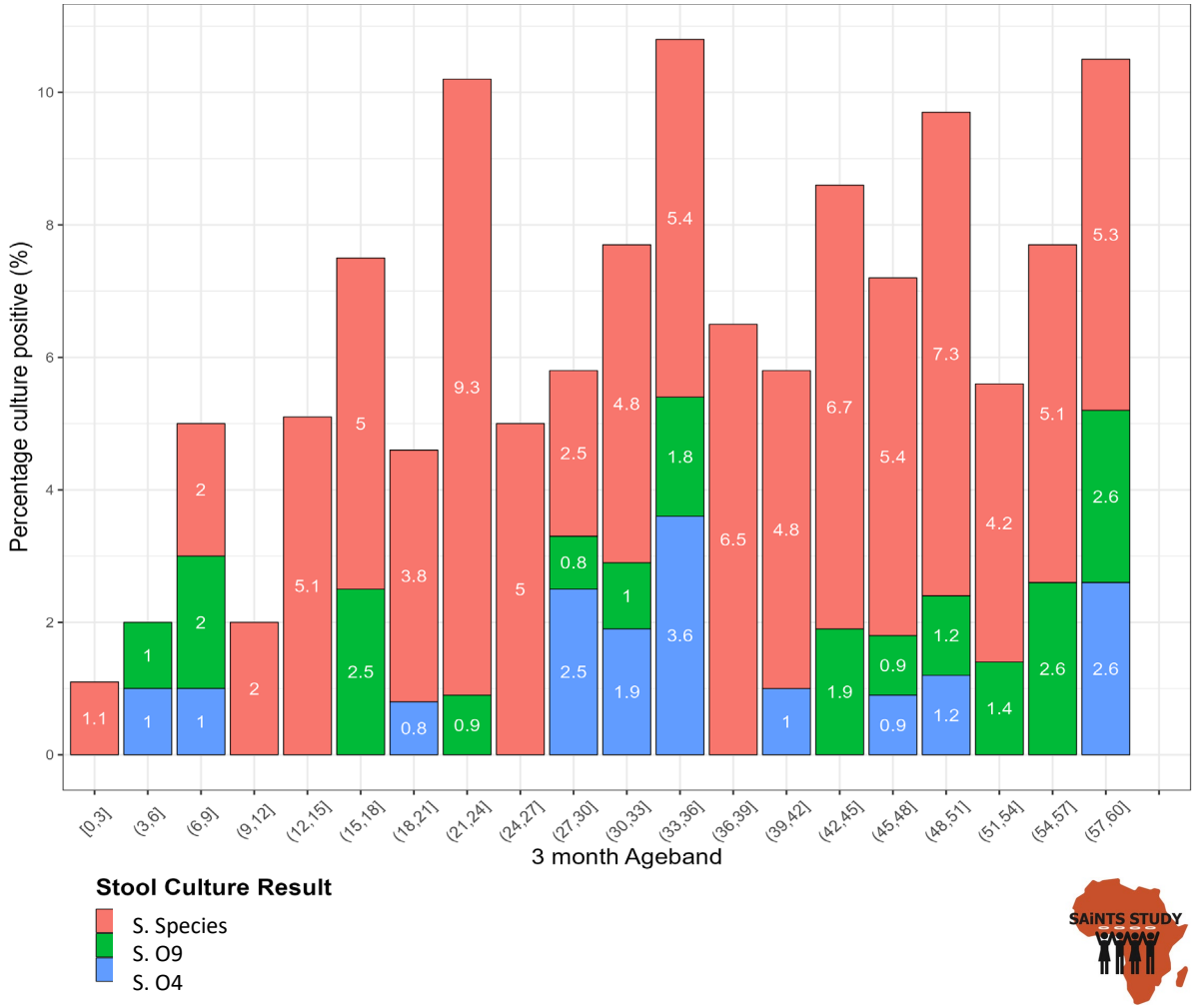
Low early-life incidence may be caused by low stool exposure in first 6 months

iNTS disease incidence in children 0-60 months



Age in months

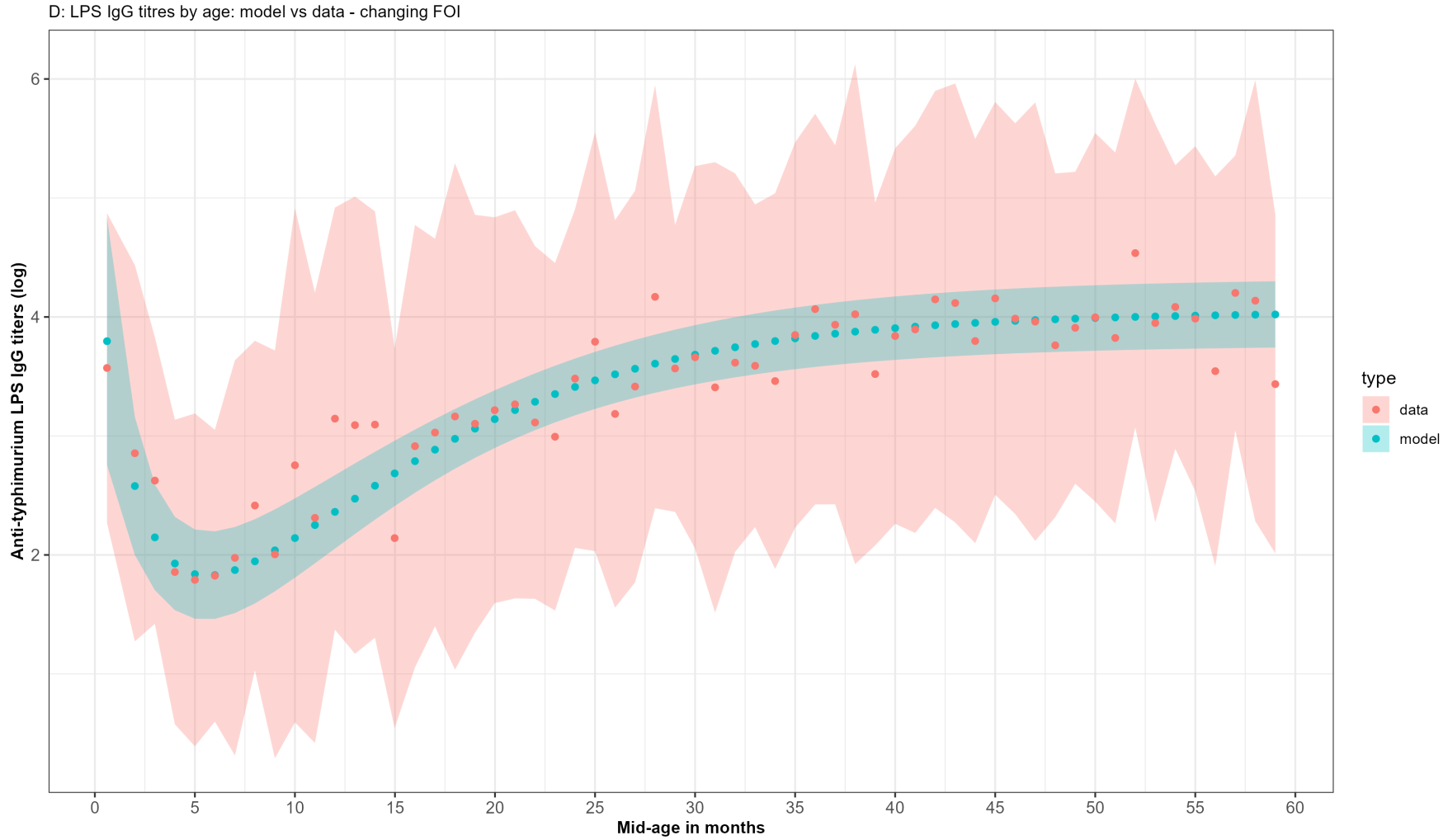
Salmonella stool detection children 0-60 months



H Dale, unpublished data

O-Antigen S. typhimurium IgG in Malawian Children 0-5 years

Serocatalytic Model



Conclusions

- Maternal antibodies offer less bactericidal function than naturally acquired immunity (IgG & IgM)
- Age-pattern of iNTS disease likely due to faeco-oral exposure patterns after weaning
- Variation in nadirs, peaks and plateaus indicate a variable force of e-NTS infection.
- Levels of natural protection likely to be different at different sites

Next steps

- Additional testing of samples for IgA and IgM
- Systems serology/ functional assays – **OptiVaNTS**
- Parameters estimates from these models to develop mechanistic and dynamic modelling to understand relationships in age-distribution of:
  - Invasive disease
  - Enteric NTS
  - Serological correlates of protection
- Cross-validate models across multiple epidemiological/ geographical settings; additional data collection from multiple high burden sites
- Possible tool to monitor WASH interventions

Participating organizations

1. University of Liverpool – lead participant (Prof. Gordon)
2. l'Institut Supérieur des Sciences de la Population (ISSP), Burkina Faso (Prof. Soura)
3. Kwame Nkrumha University of Science and Technology (KNUST), Ghana (Prof. Owusu-Dabo)
4. Centre for Microbiology Research Kenyan Medical Research Institute (KEMRI), Kenya (Prof. Kariuki)
5. GSK Vaccines Institute for Global Health, Italy
6. University of Cambridge (Prof. Marks)
7. International Vaccine Institute (IVI), South Korea