iNTS burden in sub-Saharan African children: an African view

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Background

- Invasive nontyphoidal Salmonella disease is a leading cause of bloodstream infection in sub-Saharan Africa
- Associated with high case-fatality rate – 20-25%
- Due to challenges in diagnosis and widespread antibiotic resistance there is need for new interventions e.g. vaccines
- However, there is paucity of data on incidence and public health impact of iNTS disease in sub-Saharan Africa
- Systematically microbiology data collected during the multi-site RTS,S/AS01 malaria vaccine 3 trial presents an excellent opportunity to describe the burden of iNTS disease in Africa

Objectives of the analysis

- Describe the incidence of nontyphoidal Salmonella disease and typhoid fever in children in sub-Saharan Africa
- Genetically characterize the Salmonella isolates associated with iNTS

RTS,S malaria vaccine trial

- Randomized, controlled, double-blind trial
- 11 sites in 7 African countries with different malaria transmission intensities
- From July 2009 to December 2013 infants aged 6-12 weeks and children 5-17 months were randomized to receive RTS,S/AS01 or a comparator vaccine
- Infants followed up for a median of 38 months
- Children followed up for a median of 48 months

Methods

- All hospitalized children were evaluated using a standardized algorithm that included;
  - Blood-culture
  - Blood smear for malaria diagnosis by microscopy

- Microbiology methods
  - Standard microbiology methods for blood and CSF culture using automated BactecTM incubators and pediatric bottles
  - Positive cultures were sub-cultured using standard methods
  - A culture was considered positive if a definite pathogen was isolated or if a bacterium that could be either a pathogen or a contaminant was isolated within 48 hours of incubation
  - Salmonella species were confirmed serologically by slide and tube agglutination tests using specific O and H antisera

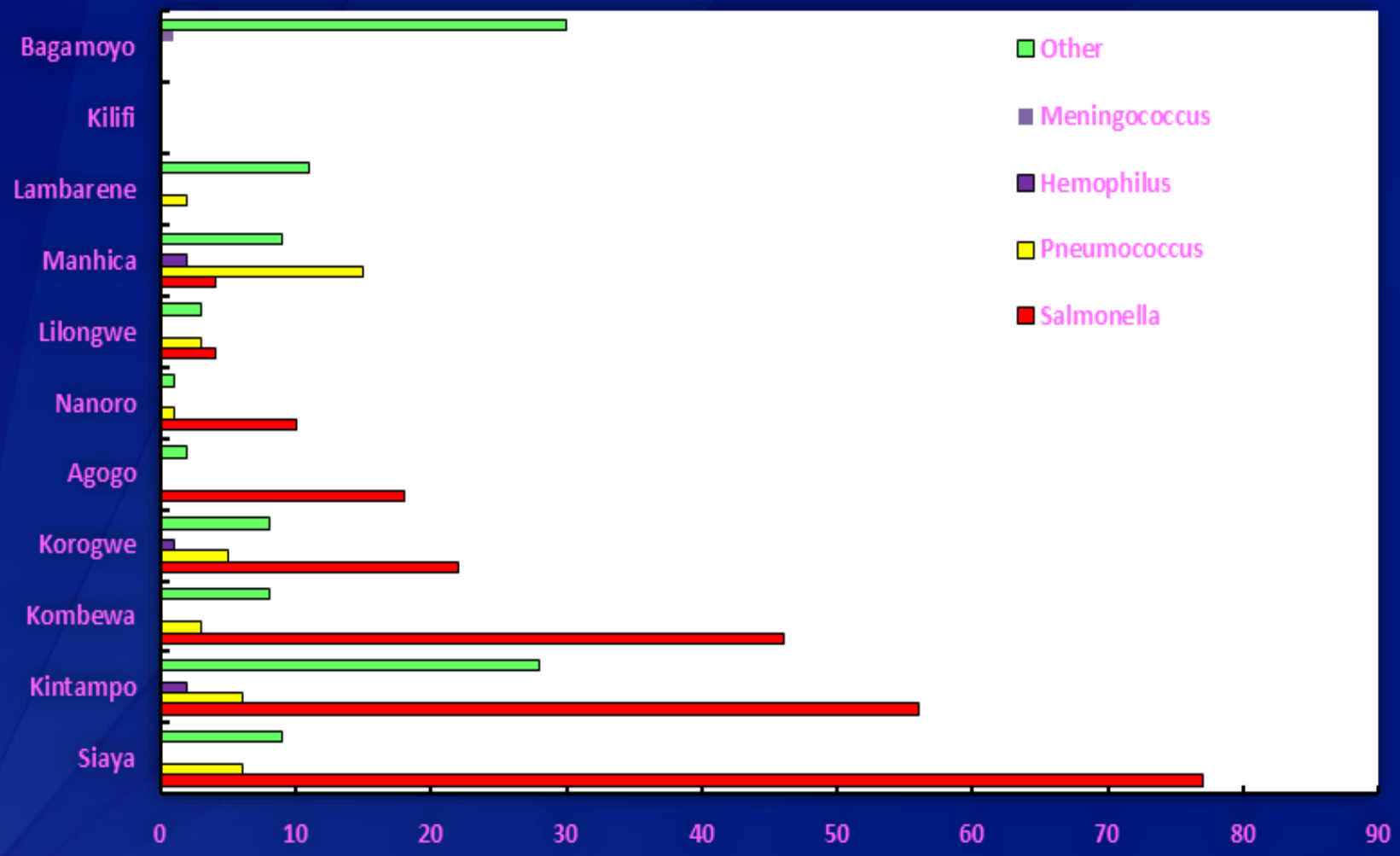
Results – Study population

- From July 2009 through December 2013, a total of 15,459 children were enrolled in the trial (8922 in the older and 6537 in the younger age category)
- Baseline characteristics were similar in the two study groups but differed by site (IPTi, IRS coverage and moderate anemia)

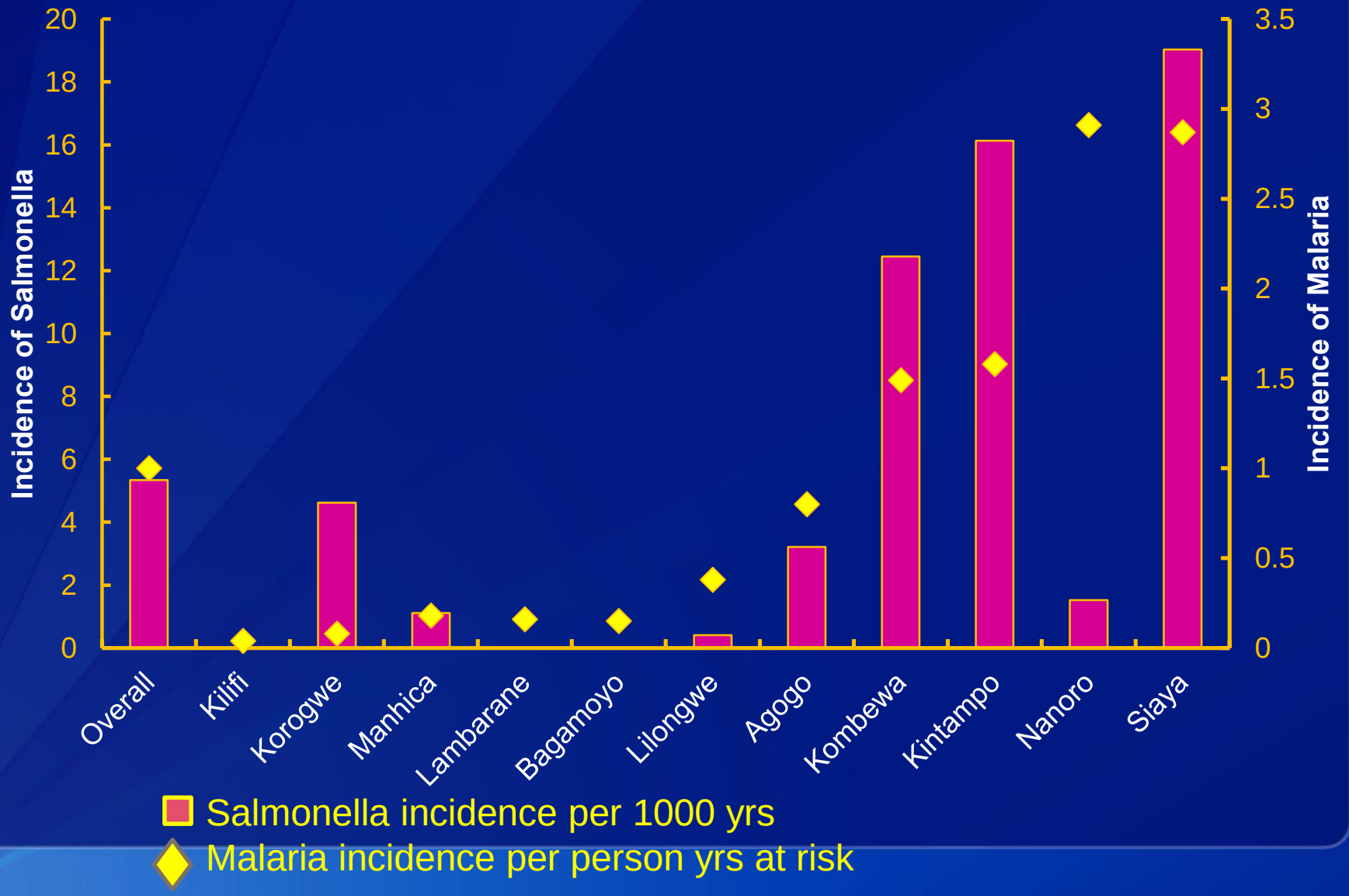
IPTi- Intermittent Protective Therapy-infants

IRS- Indoor residual spray

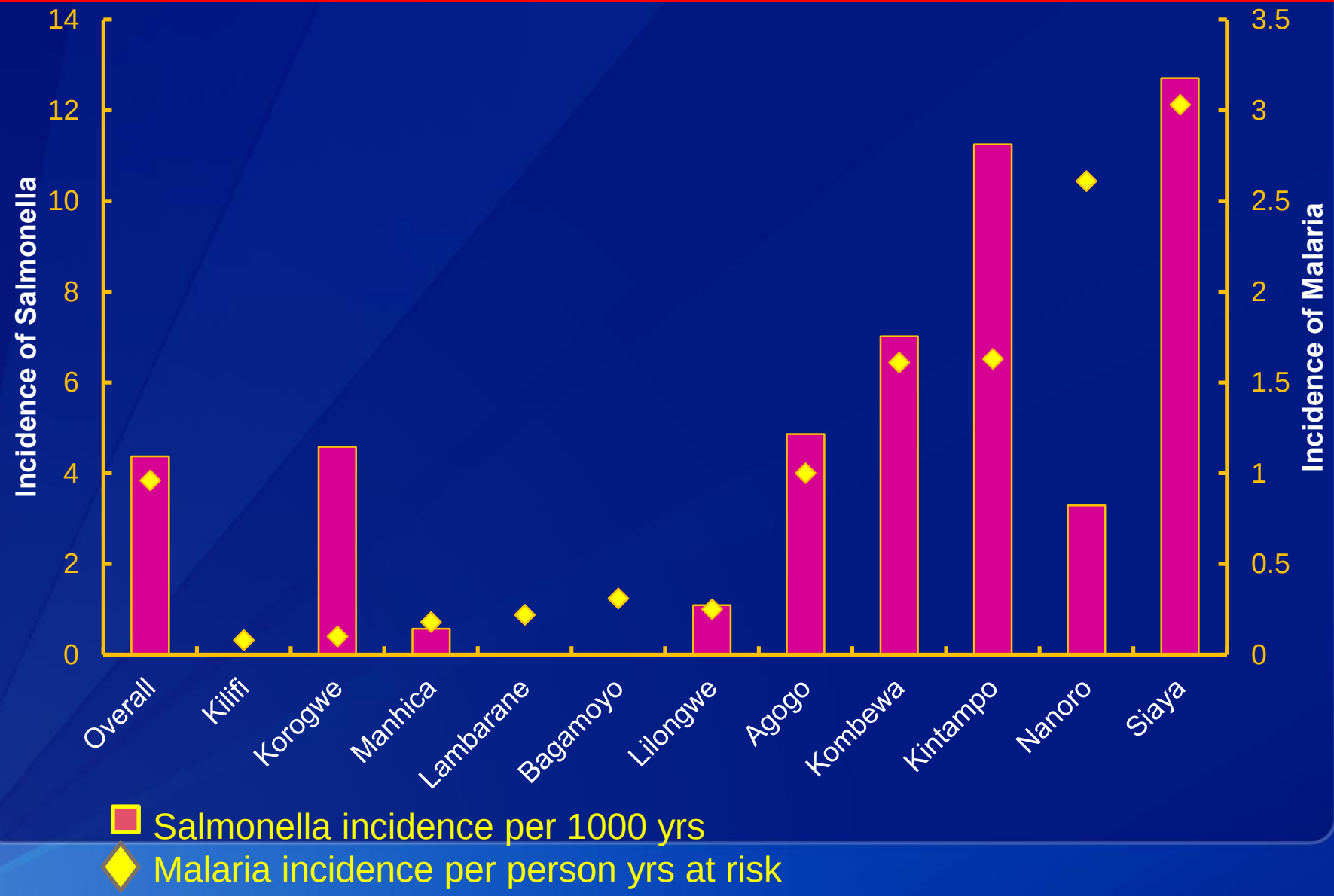
Isolated organisms per site



Salmonella and malaria incidence in infants



Salmonella and malaria incidence in children



Summary

- There is high incidence of iNTS disease in sub-Saharan Africa
- There is an association between iNTS disease and malaria transmission
- These data provide estimates of iNTS bacteremia incidence in children across different sites in Africa
- The data will be useful in guiding evaluation and implementation of interventions to reduce the high burden of iNTS disease in Africa

Next steps

- Define incidence of Salmonella bacteremia according to age, demographics and clinical outcome
- Determine the case fatality rate, among children with iNTS and typhoid fever
- Investigate risk factors for resistant and severe forms of iNTS
- Characterize the isolated Salmonellae at the serovar level and genetic level by whole genome sequencing

Investigators by study site

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- **PATH Malaria Vaccine Initiative, Washington, D.C.:**
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