
Three epidemics of multidrug resistant invasive Salmonella disease in Blantyre, Malawi

Nick Feasey, Gordon Dougan, Melita Gordon, Robert Heyderman

3rd May 2105

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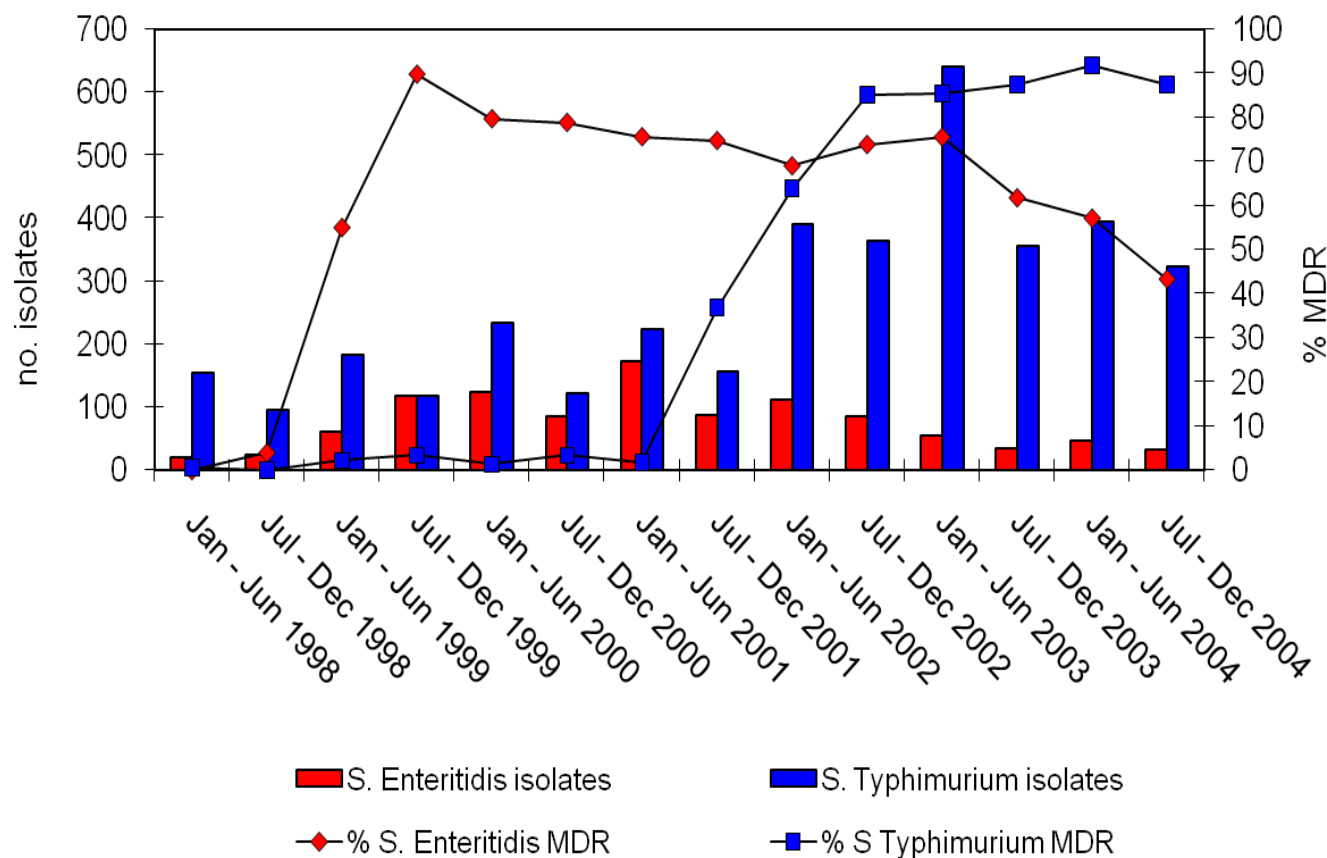
Malawi Liverpool Wellcome Trust Clinical Research Programme at Queen Elizabeth Central Hospital



Longitudinal bacteraemia surveillance since 1998

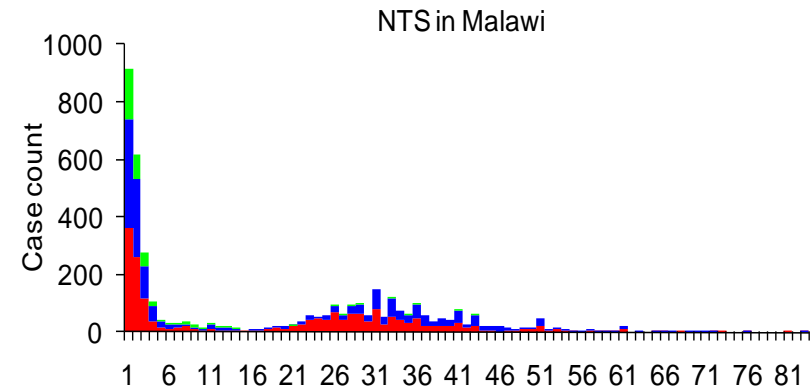
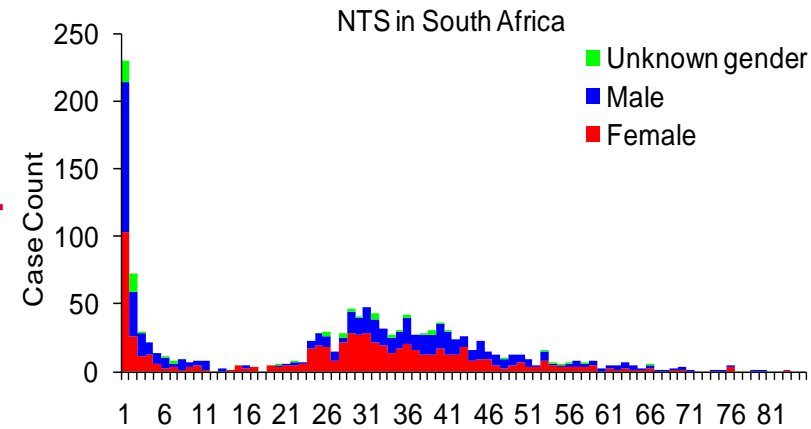


Relationship between MDR and incidence of NTS serovars

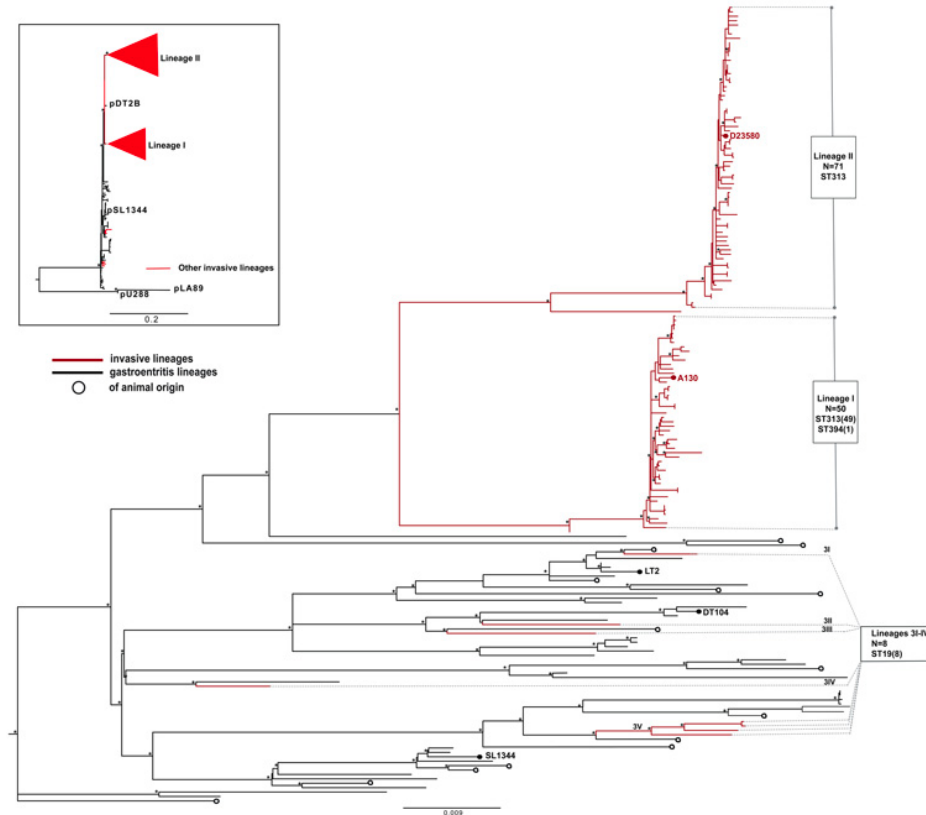
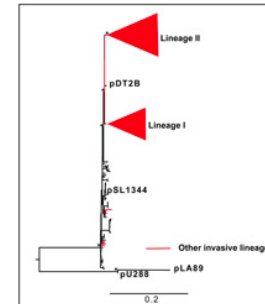
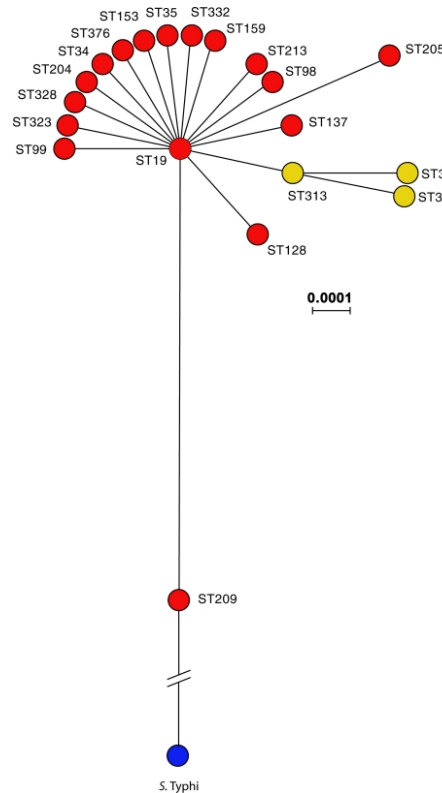


Risk factors for iNTS disease

- Bimodal age distribution
- Adults with severe HIV
- Children with
 - HIV
 - Malaria
 - Malnutrition



Susceptible host or novel pathogen?

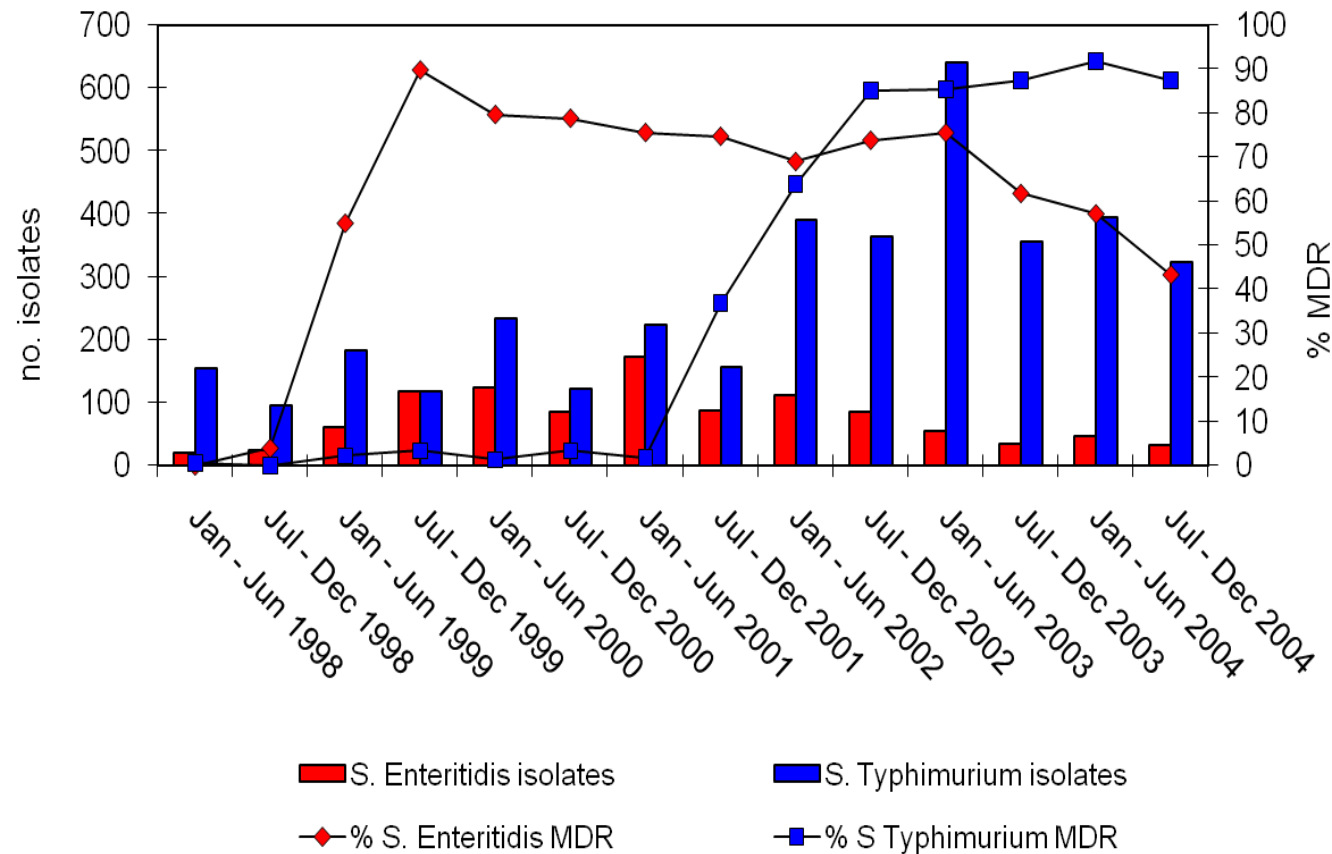


Msefula, Kingsley Gen Res 2009

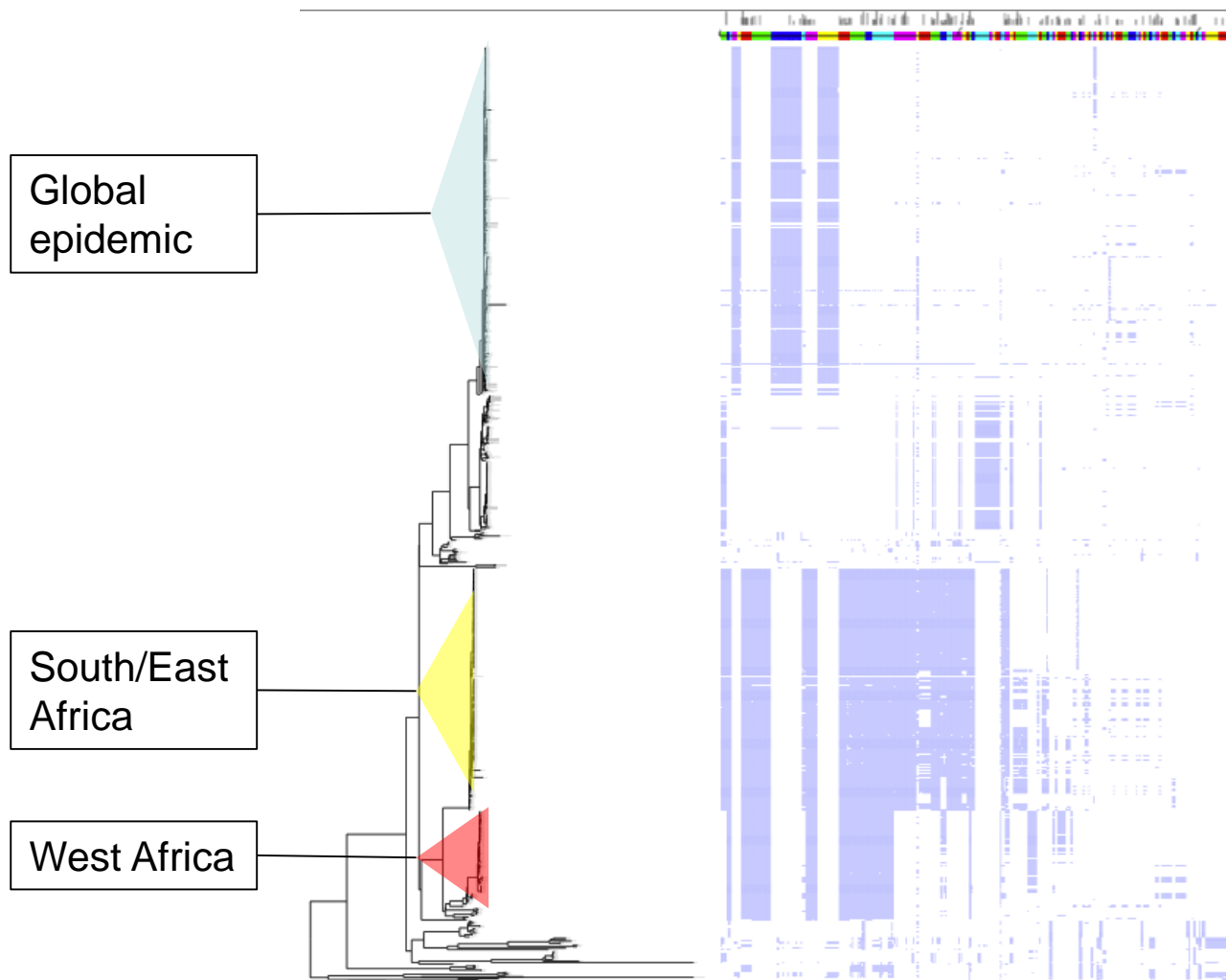
Okoro et al Nat Gen 2012



Prior to the epidemic of *S. Typhimurium* ST313, there was an epidemic of *S. Enteritidis*



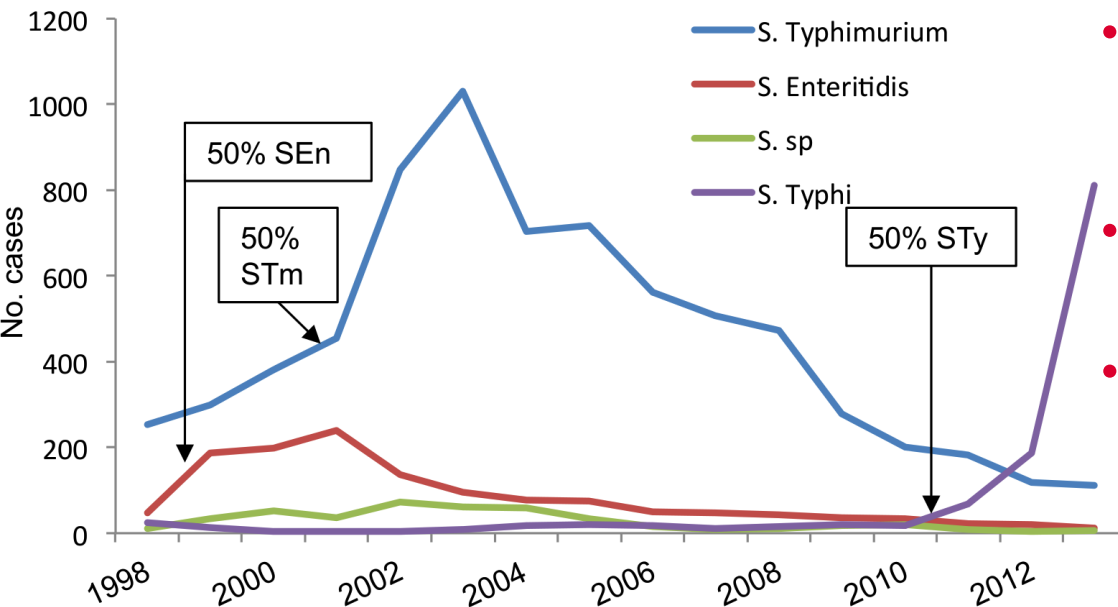
Novel clades of *S. Enteritidis* restricted to sub-Saharan Africa with MDR-plasmids



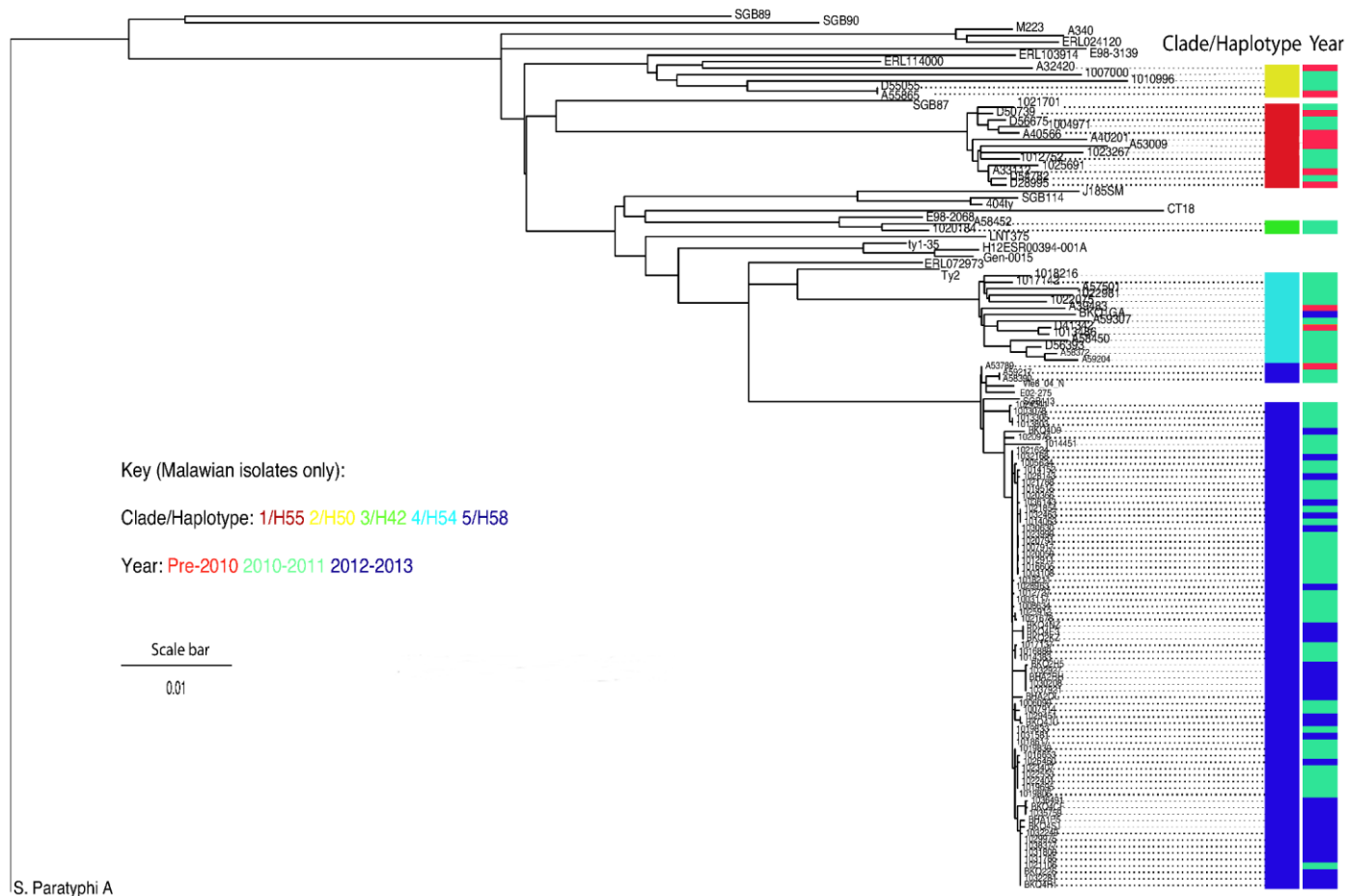
NTS remains a prominent pathogen, but MDR *S. Typhi* has now emerged

- All 3 epidemics preceded by the emergence of MDR
- Reports of ESBL STm and SEn
- FQR STm
- 1 phenotypic DCS & no ESBL amongst *S. Typhi*

Total number of cases of each serotype/year



H58-S. Typhi, but with chromosomal MDR locus



Clinical features and complications of iNTS disease

	2001	2009-11
Recruited	100	63
Inpatient mortality	47%	11%
1 year mortality	77%	38%
HIV positive	99%	98%
Recurrence	43% (19/44)	5%(3/56)
Multiple recurrences	11% (5/44)	2%(1/56)

Clinical features and complications of *S. Typhi*

Adults (n= 77)

- 16% HIV infected
- 5% severe/complicated
- 1% perforation
- 4% mortality

Children (n=330)

- HIV data pending
- 21% complicated
- 2% perforation
- 2% mortality

Does iNTS disease still matter?

- **Decline has leveled off**
- **Still a major pathogen**
- **iNTS disease likely to be responsible for approximately double the number of deaths caused by Typhoid fever in Blantyre, 2014**

- **3 epidemics of Salmonella bloodstream infection since 1999**
- **Epidemics of iNTS disease associated with novel clades**
- **Recent emergence of H58-S. Typhi**

- **Risk factors for iNTS disease and Typhoid fever differ**
- **BUT all 3 epidemics associated with emergence of MDR**
- **In-turn driving increased use of cephalosporins and fluoroquinolones**

- **Reservoirs of pathovars associated with iNTS disease unknown**

Acknowledgements



Sam Kariuki
Calman MacLennan
Robert Onsare
Franscois X Weill
Simon Le Hello
Karen Keddy
Anthony Smith
Michael McClelland
Prereak Desai
Xiangyu Deng
Christopher Parry
John Cheesbrough
Neil French
Jan Jacobs
Josephina Campos
Jose A Chabalgoity
Katie Hopkins
Tom J Humphrey
Tristan Cogan
Sharon Tennant
Kristen Bornstein
Myron Levine
Lizeth Lacharme-Lora



Theresa Feltwell
Simon Harris
Rob Kingsley
Del Pickard
Nick Thomson

