Phylogeography and incidence of MDR invasive nontyphoidal *Salmonella* in sub-Saharan Africa

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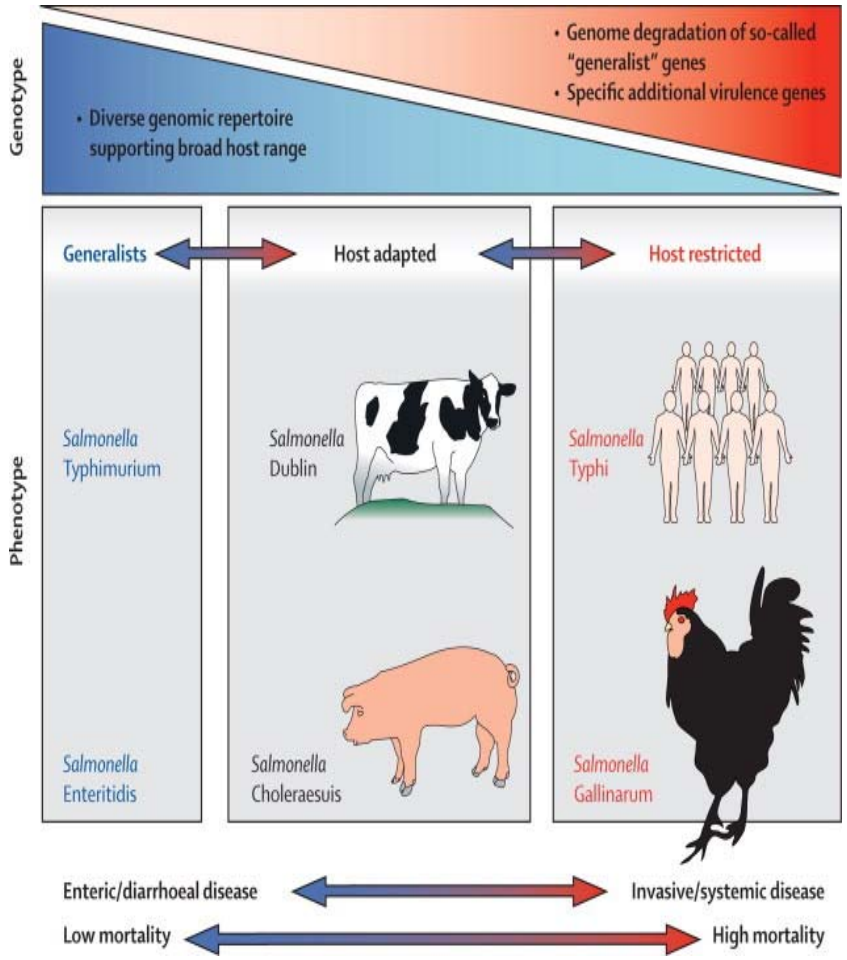
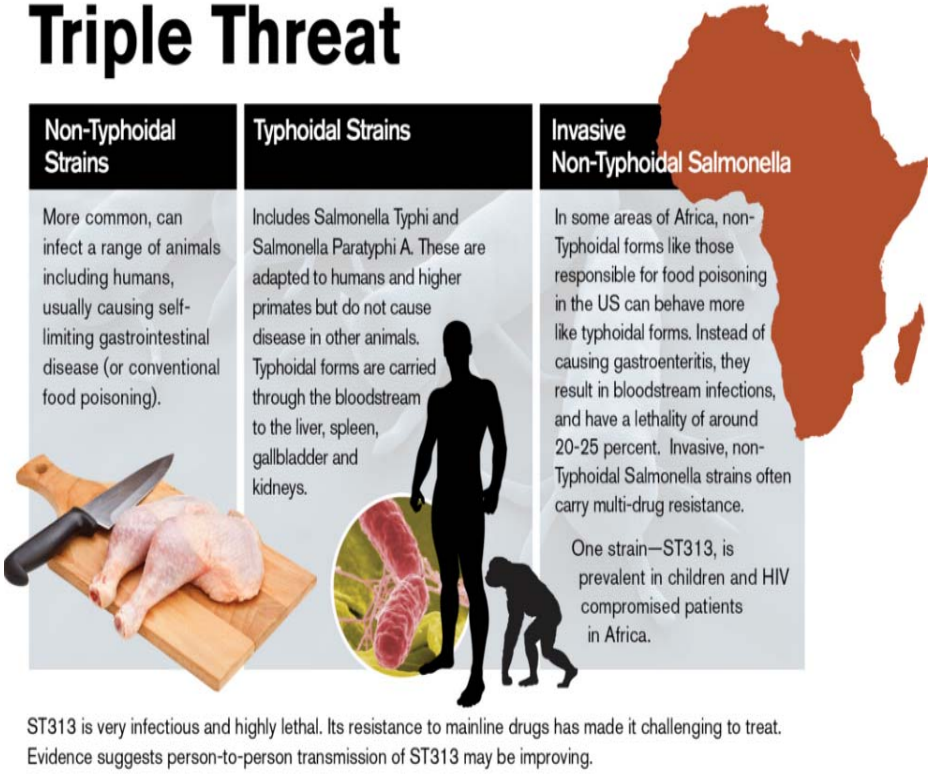
Nontyphoidal *Salmonella*



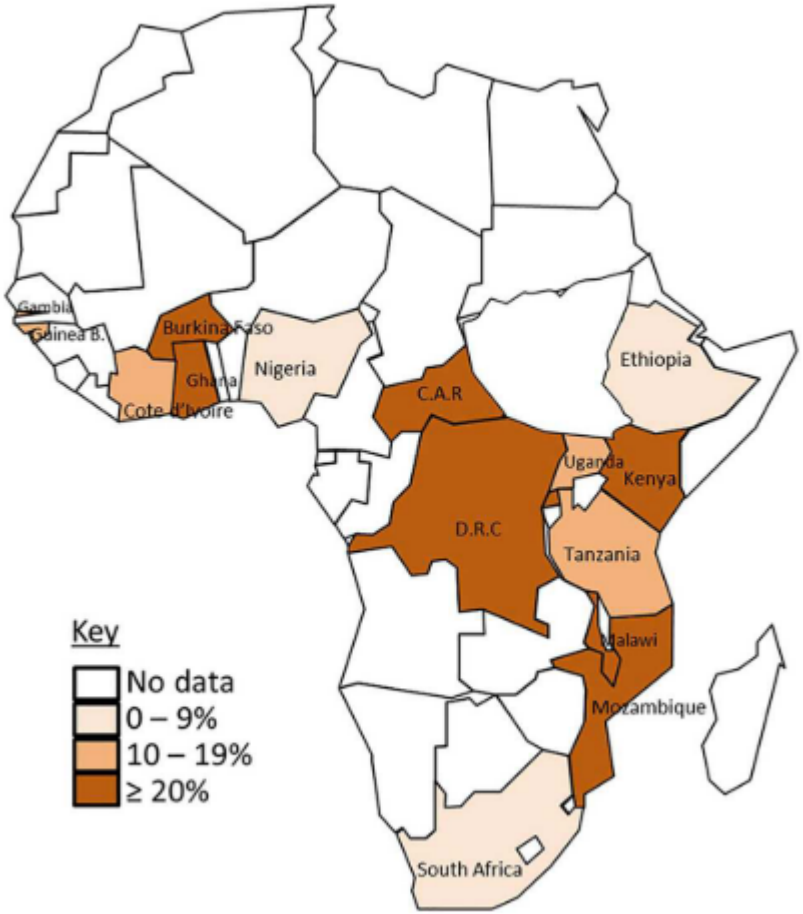
Nicholas A Feasey et al, Lancet 2012; 379(9835): 2489-2499



"In Africa, a deadly salmonella strain takes hold"
Medical Press, Sept 9, 2015 by Richard Harth, Arizona State University
https://medicalxpress.com/news/2015-09-africa-deadly-salmonella-strain.html

Invasive NTS in Africa

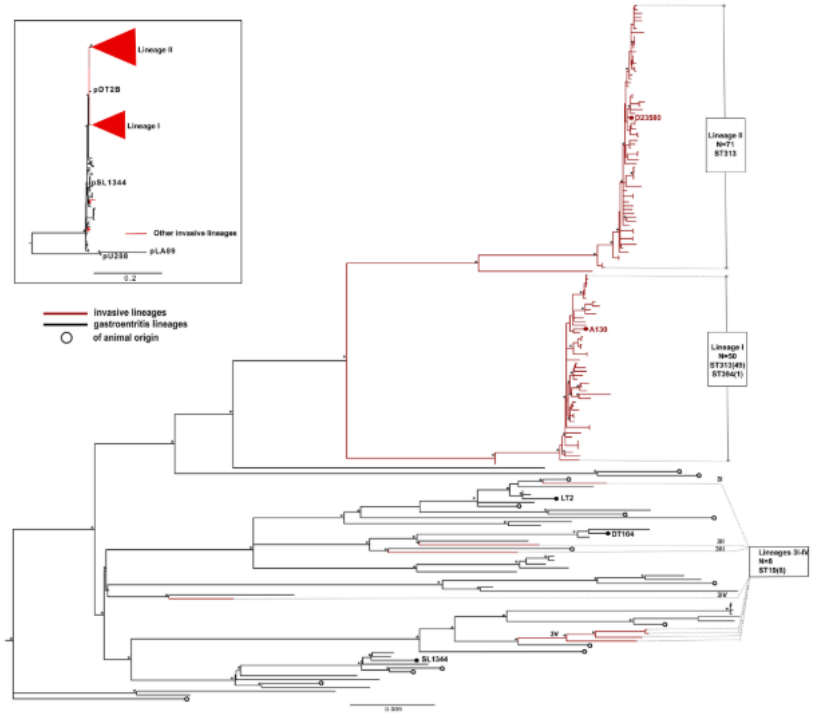
- Main cause of bacteraemia in 33/54 African countries (systematic review 1966-2014)
- Responsible for up to 39% of community acquired blood stream infections in sub-Saharan Africa with an average CFR of 19%
- Salmonella Typhimurium and Enteritidis responsible for 91%% of iNTS disease cases (where serotype was determined)
- More prevalent amongst HIV-infected individuals, infants, and young children with malaria, anaemia and malnutrition



Proportion of Community acquired blood stream infections caused by NTS in African countries (1966 to 2014)

Uche et al, 10.1371/journal.pntd.0005118

iNTS phylogenetics



_S._ Typhimurium ST313

Chinyere Okoro et al, Nat Genet 2012; 44(11)

_S._ Enteritidis

Feasey N et al, Nat Genet 2016; 48(10)

Study aims and methodology

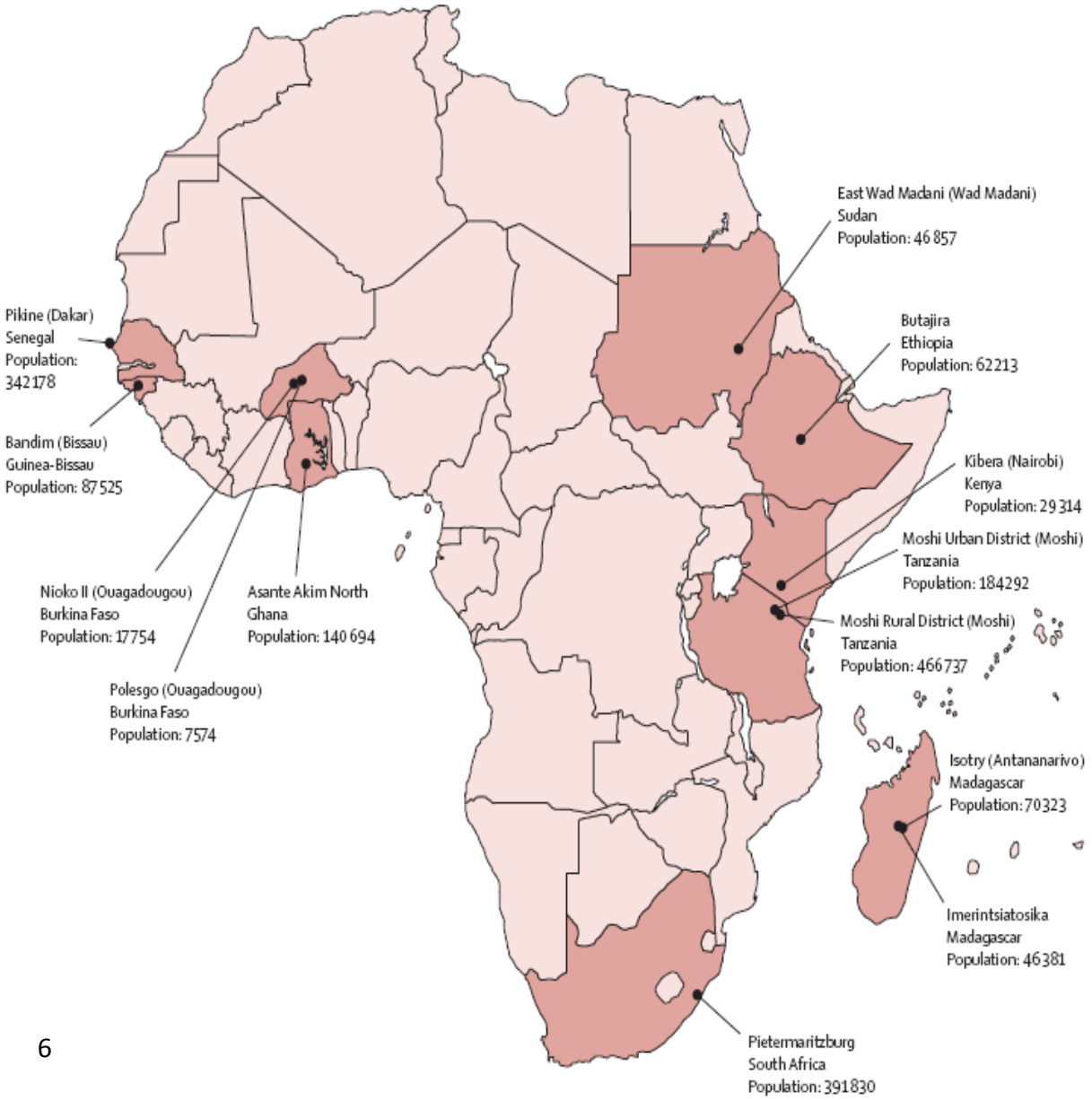
To assess:

- Distribution of iNTS serotypes /genotypes
- MDR determinants
- Phylogeography of dominant iNTS serotypes
- Age-stratified incidence of MDR iNTS in sub-Saharan Africa

Material & Method

- 166 iNTS isolates between 2007-2013 in 8 sub-Saharan African countries (No iNTS yielded in Sudan and Ethiopia during TSAP)
- Genome sequencing: Illumina Hiseq sequencing
- Serotyping: Multi locus sequence typing
- Pan-genome analysis with ROARY
- Phylogenetic analyses: Maximum Likelihood
- Resistant genes & plasmid investigation: SRST2, ACT, BLASTN
- MDR incidence estimation: adjusted incidence estimation based on method described in TSAP manuscript (Marks et al, Lancet Glob Health 2017; 5(3):e310-323)

Research Sites



Location

13 sites, 10 countries

Type of surveillance

population-based, passive[1]

Duration of surveillance

13-27 months

Target age

All ages[2]

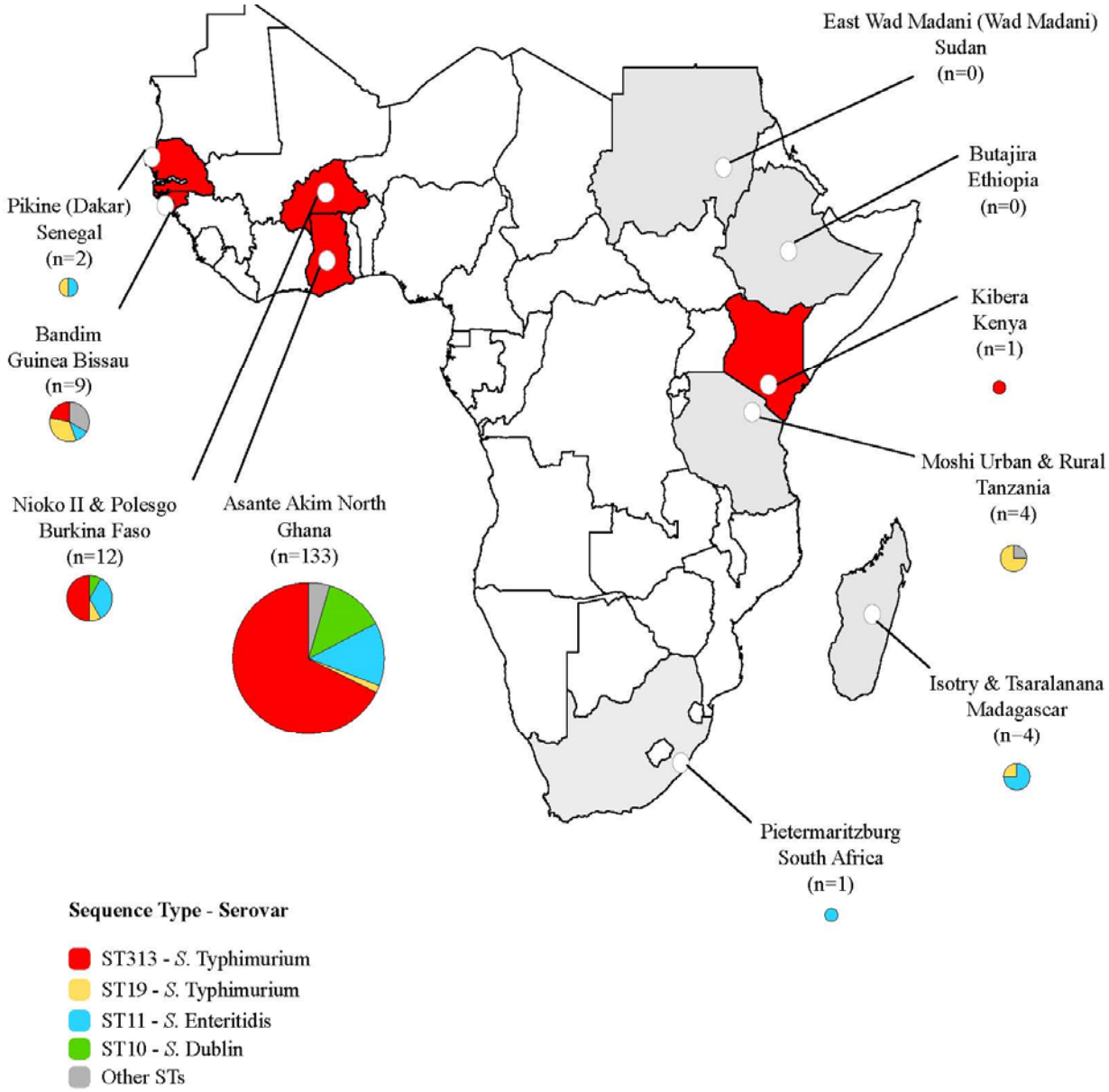
Procedures

Standardized inclusion criteria (fever)
recruitment & lab procedures (blood culture-based)
antimicrobial resistance

[1]except Kenya; active household; [2] except Ghana; < 15 years

Marks et al, Lancet Glob Health 2017; 5(3)

Distribution of iNTS serotypes and sequence types



Distribution of MDR iNTS

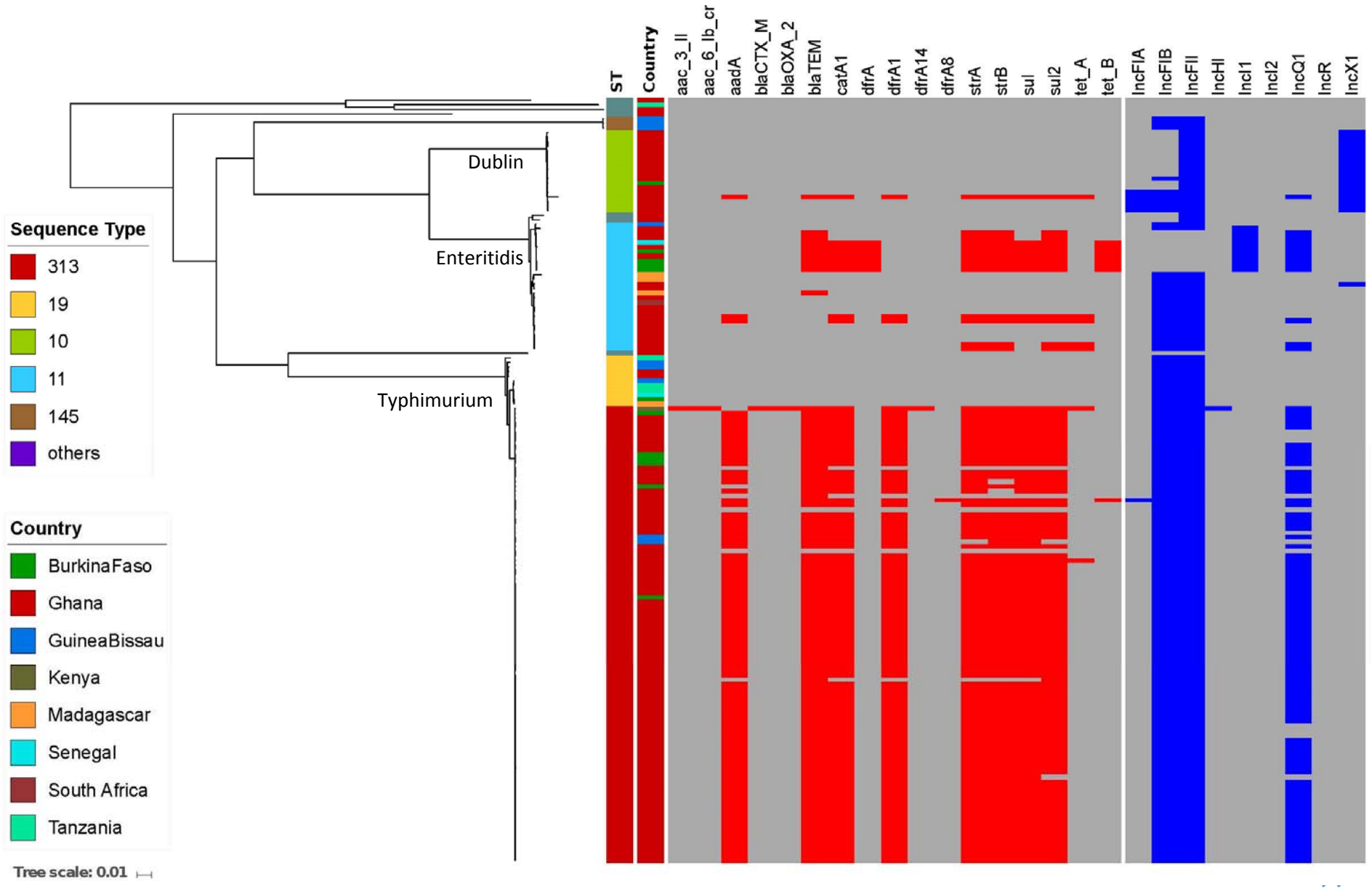
Serotypes (number) N=166	MDR iNTS per serotypes (%, number)	MDR iNTS serotype per country (%, number)	MDR iNTS per genotype (%, number)
Typhimurium (n=110)	85% (94/110)	Burkina Faso (50%, 6/12) Ghana (64%, 85/133) Guinea Bissau (22%, 2/9) Kenya (100%, 1/1)	ST313 (95%, 94/99) ST19 (0%, 0/11)
Enteritidis (n=30)	23% (7/30)	Burkina Faso (33%, 4/12) Ghana (2%, 2/133) Senegal (50%, 1/2)	ST11 (25%, 7/28)
Dublin (n=18)	6% (1/18)	Ghana (1%, 1/133)	ST10 (6%, 1/18)
Others (n=8)	0% (0/8)	n.a.	n.a.

Countries with MDR iNTS and *gyr* mutations

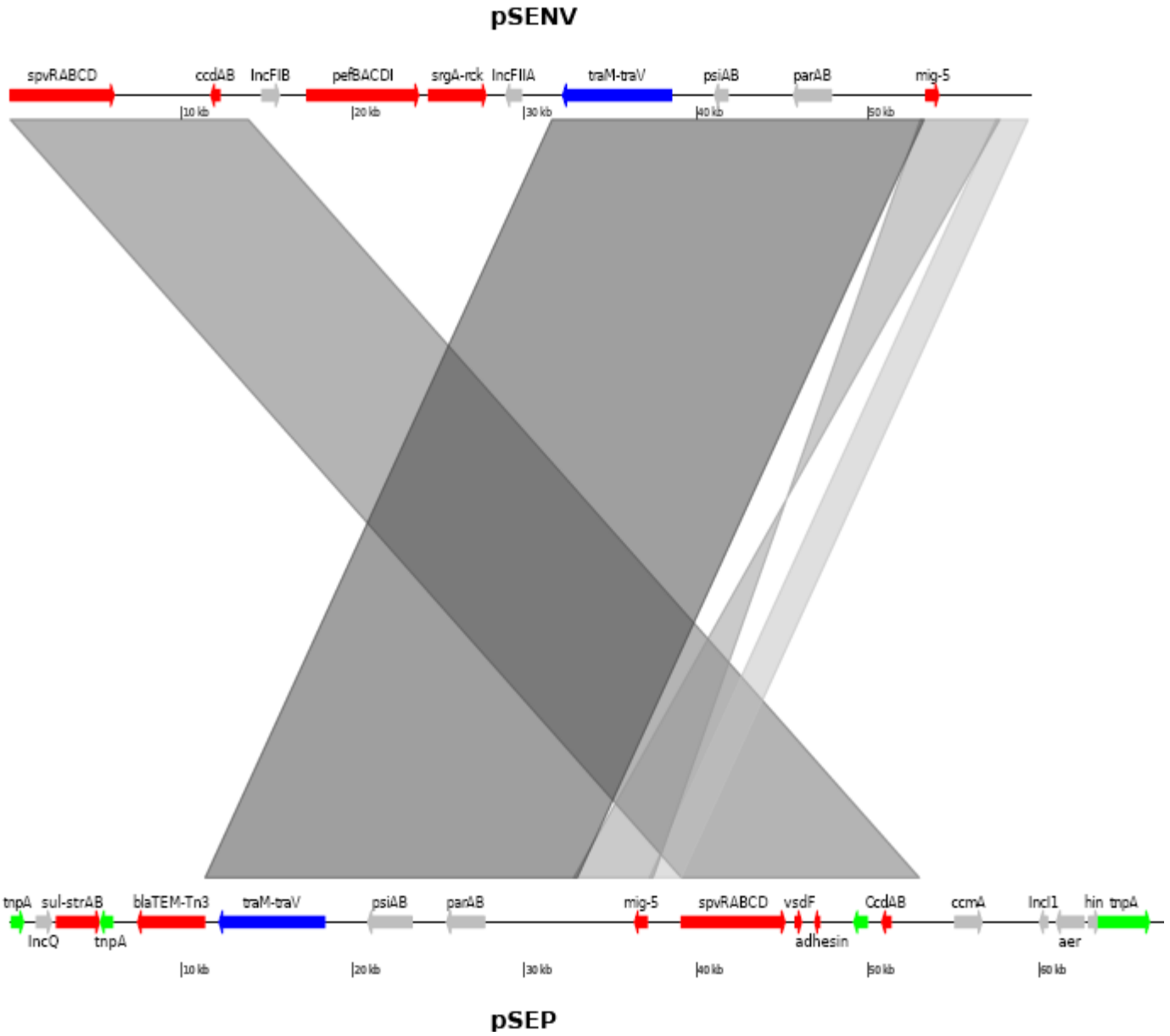
No. of iNTS (n) (N=157)	No. of MDR iNTS (n) (N=102)	% of MDR iNTS	gyrA
Burkina Faso (n=12)	10	10/12 (83%)	0
Ghana (n=133)	88	88/133 (66%)	13
Guinea-Bissau (n=9)	2	2/9 (22%)	0
Kenya (n=1)	1	1/1 (100%)	0
Senegal (n=2)	1	1/2 (50%)	0

Ghana (n=133)	13 iNTS isolates non-susceptible to fluoroquinolones (*gyrA*)
	11 Enteritidis ST11 (all non-MDR)
	6 isolates (D87G)
	3 isolates (D87N)
	2 isolates (D87Y)
	2 Typhimurium ST313 (all MDR) (S83Y)

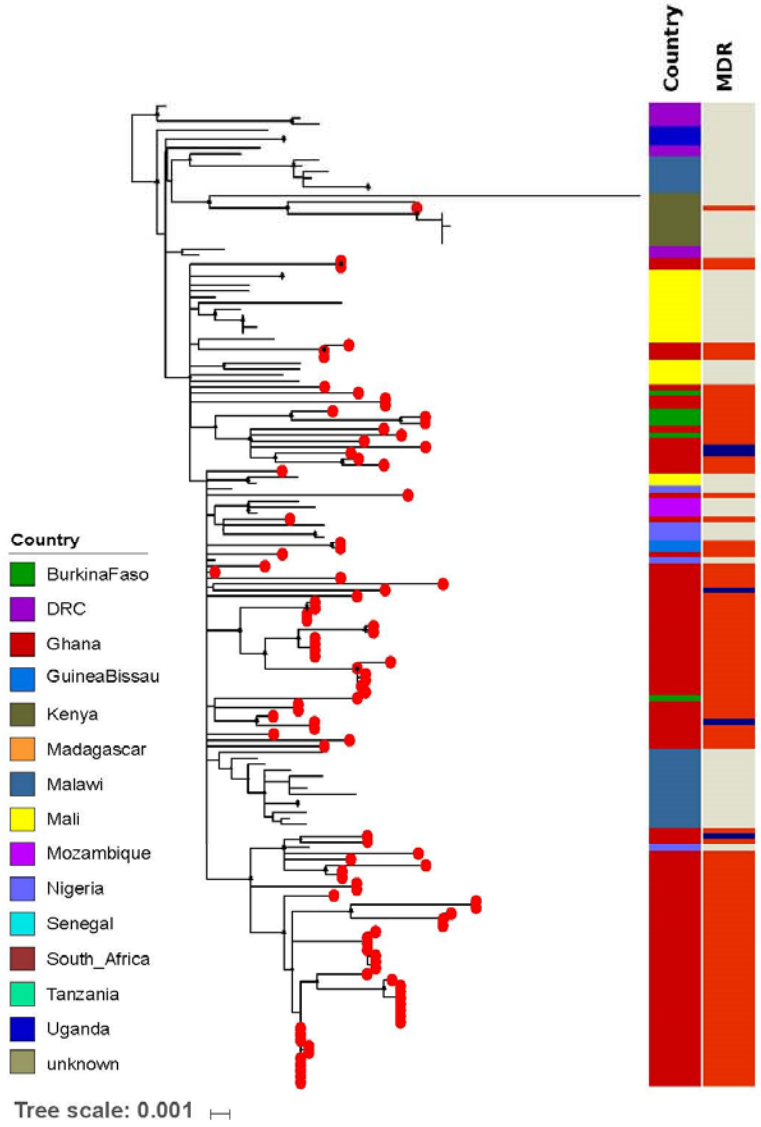
Phylogenetics and AMR determinants of iNTS isolates in Africa

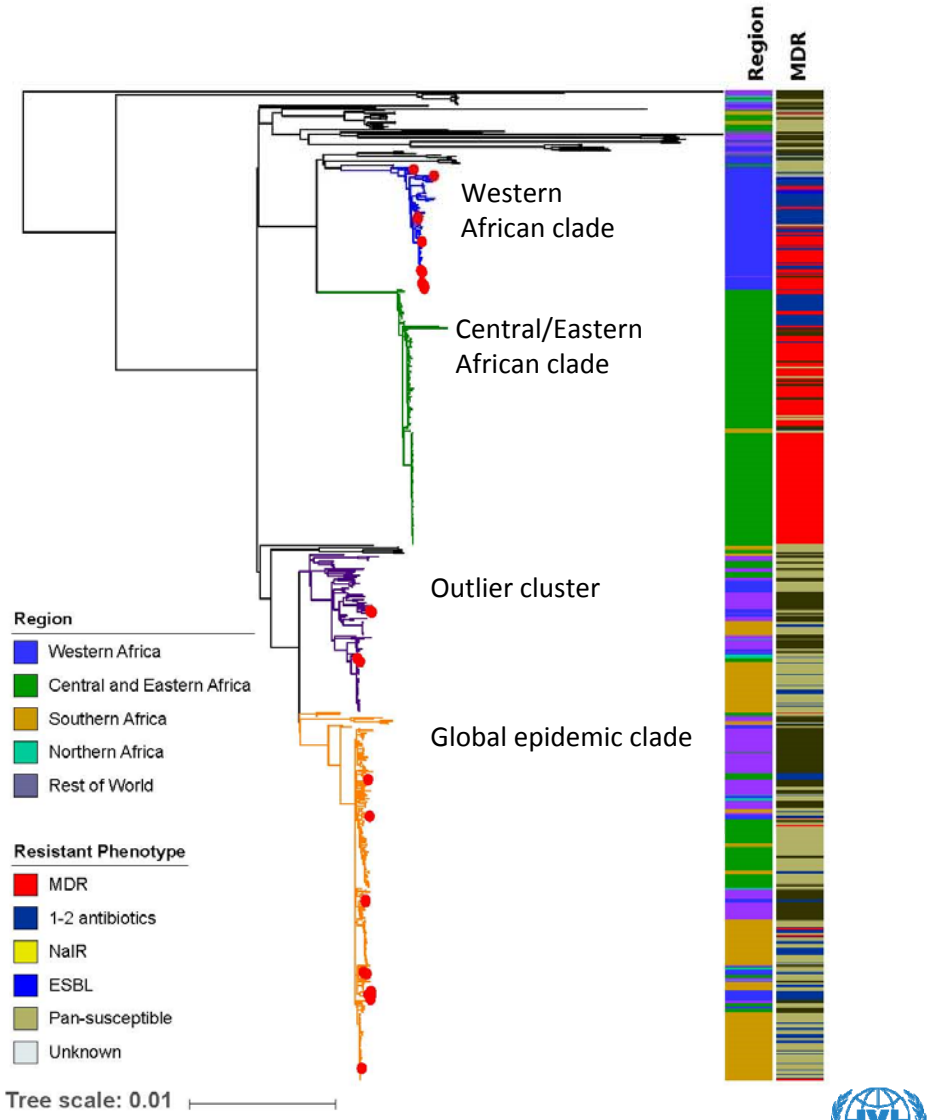


Novel IncI1 plasmid in *S.* Enteritidis isolate



Phylogenetic structure of *S.* Typhimurium ST313 lineage II and *S.* Enteritidis ST11 in the global context





Incidence of MDR iNTS disease

Country		Age group in years	Adjusted MDR iNTS incidence per 100,000 PYO (95% CI)
Burkina Faso			
	Nioko II	0-1	251 (107-590)
		2-4	753 (460-1233)
		5-14	79 (29-214)
		<15	274 (185-406)
		≥15	35 (13-96)
		All	145 (100-209)
	Polesgo	0-1	431 (162-1147)
		2-4	630 (288-1380)
		5-14	0
		<15	255 (138-470)
		≥15	54 (16-179)
		All	144 (83-249)

Incidence of MDR iNTS disease (continued)

Country	Age group in years	Adjusted MDR iNTS incidence per 100,000 PYO (95% CI)
Ghana		
AAN	0-1	1435 (1110-1854)
	2-4	747 (491-1135)
	0-4	n.a.
	5-14	126 (77-206)
	<15	414 (333-515)
	≥15	n.a.
	All_TSAP	n.a.
	Non_TSAP[6]	n.a.
	All	n.a.

Incidence of MDR iNTS disease (continued)

Country	Age group in years	Adjusted MDR iNTS incidence per 100,000 PYO (95% CI)
Guinea Bissau		
Bandim	0-1	291 (176-482)
(Simao Hospital)	2-4	53 (13-208)
	5-14	37 (14-97)
	<15	105 (69-161)
	≥15	0
	All	37 (24-57)
Kenya		
Kibera	0-1	0
	2-4	0
	5-14	0
	<15	0
	≥15	11 (2-77)
	All	5 (1-37)

Summary

- *S.* Typhimurium (ST313 and ST19) was the most dominant serovar of iNTS disease in sub-Saharan Africa, followed by *S.* Enteritidis (ST11) and *S.* Dublin (ST10)
- All our *S.* Typhimurium ST313 belonged to lineage II with some evidences of transmission between Ghana and Burkina Faso/Guinea Bissau
- Three lineages associated with our *S.* Enteritidis ST11 isolates
  - ✓ 40% (11/28; Ghana, Burkina Faso, Senegal, Guinea-Bissau) fell into the West African clade
  - ✓ 46% (13/28; Madagascar, South Africa, Ghana) belonged to the Global Epidemic clade
  - ✓ 14% (4/28; Ghana, Madagascar) belonged to the Outliner cluster
- *S.* Typhimurium ST313 exhibited highest MDR followed by *S.* Enteritidis ST11
- Emergence of a MDR lineage of *S.* Enteritidis associated with IncI1 plasmid
- 1 Kenya *S.* Typhimurium ST313 carried CTX-M-15 (resistant to third generation cephalosporin) on both plasmid and chromosome
- Non-susceptibility to fluoroquinolone detected in iNTS isolates in Ghana
- High incidence of MDR iNTS infection in Burkina Faso, Ghana, and Guinea-Bissau (<5 year olds)

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Thank you












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