Transmission of invasive non-Typhoidal *Salmonella*:

Household study from Burkina Faso supports human-to-human transmission

Annelies Post
MD, MSc Global Health, PhD candidate

Institute of Tropical Medicine (Antwerp)
RadboudUMC (Nijmegen)

iNTS in Burkina Faso – previous studies

iNTS primary cause of childhood bacteremia in Nanoro

- 10% of cultures positive, around 30% of positive blood cultures iNTS[1]
- Population based incidence: 4,138 (95%CI: 3,740-4,572) per 100.000 per PYO[2]
- Serotype distribution: Typhimurium 70%, Enteritidis 30%, others sporadically

Nanoro demographic health surveillance (DHS)

- Nanoro DHS catchment area spans 594.3 km^2 with a population density of 125/km^2
- Holoendemic for *Plasmodium falciparum*, seasonal peak
- HIV prevalence 0.9% in 2013
- Population lives in close proximity to livestock

Zoonotic verus human-to-human reservoir and transmission?

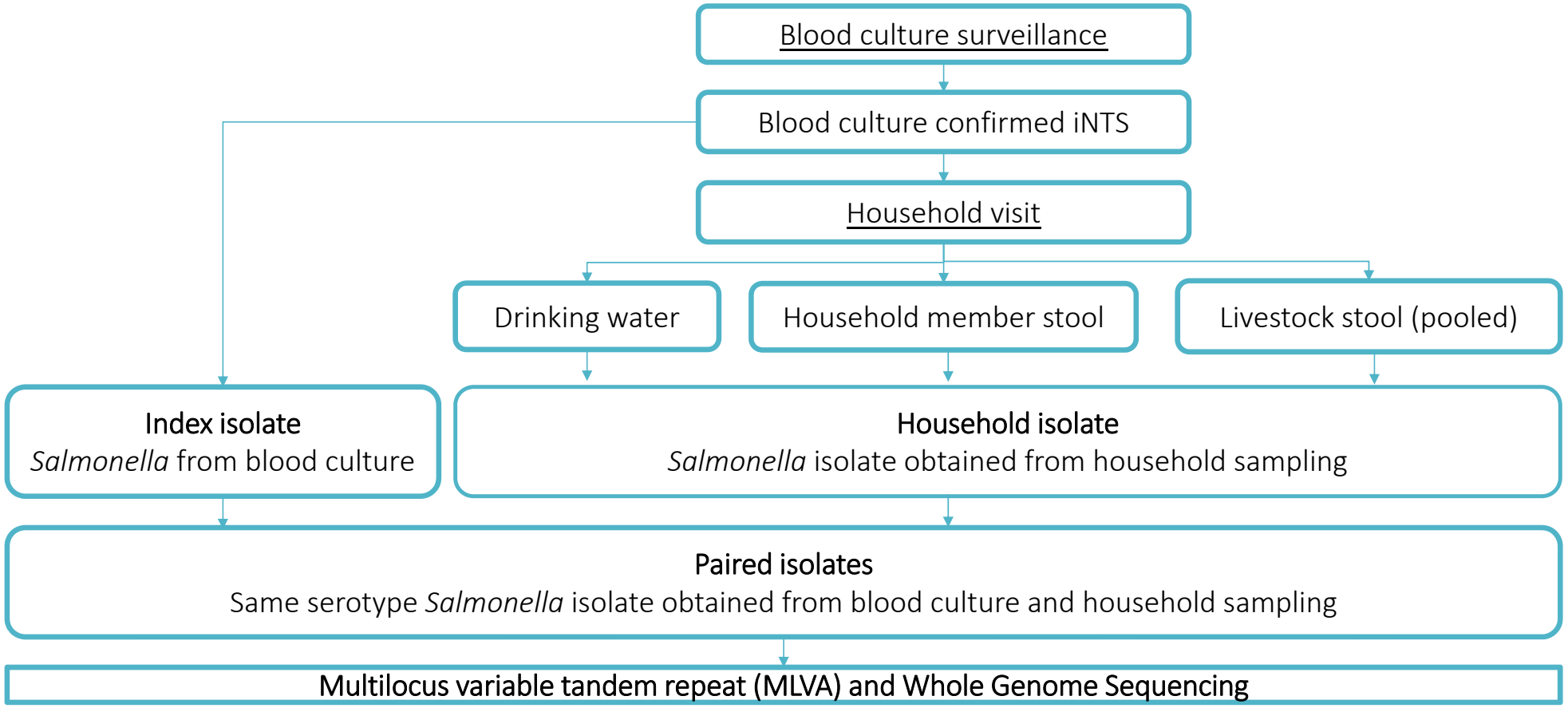
Kariuki (2006): genetic relatedness iNTS isolates to isolates from livestock, soil, water and human stool (PGFE)

Dione (2007): genetic relatedness *Salmonella* gastroenteritis isolates to isolates from livestock

1. Maltha, J., et al. (2014). "Frequency of severe malaria and invasive bacterial infections among children admitted to a rural hospital in Burkina Faso." PLoS ONE
2. Guiraud, I., et al. (2017). "Population-based incidence, seasonality and serotype distribution of invasive salmonellosis among children in Nanoro, rural Burkina Faso." PLoS ONE

Study design

Clinical Research Unit of Nanoro (CRUN): Research institute with Health and Demographic Surveillance System (HDSS) in Rural African area.



Study Results

Household visits

- 29 household visits representing 32/42 (76.2%) eligible index patients
  - 2 households had two index patients, one household had a patient with recurrent infection

	Total obtained	Nrs. of *Salmonella*	Different serotypes
Householdmembers stool samples	290	18 (6.2%)	9 serotypes
Livestock pooled samples	186	16 (8.6%)	13 serotypes
Water samples	30	-	-

Pairs and clusters

- 3 households (4 index patients; 3 household members): all *Salmonella* Typhimurium

- Clusters among household members
  - Drac 1 household 2 human stool samples
  - Derby 2 households 7 human stool samples

- Three serotypes (Brancaster, Tennessee, Muenster) were found in both human stool samples and livestock, but not in the same household.

Study results

May 2013 to August 2014	Serotypes of index patients	Serotypes in stool samples	
	Blood sample	Household members	Livestock
Salmonella Typhimurium	26	3	-
Salmonella Enteritidis	5	0	0
All other serotypes	1	15	16
Salmonella Binningen	-	-	1
Salmonella Brancaster	-	-	1
Salmonella Give	-	-	1
Salmonella Llandorff	-	-	1
Salmonella Poona	-	-	2
Salmonella Schwarzengrund	-	-	1
Salmonella Vilvorde	-	-	1
Salmonella non-typeable	-	-	1
Salmonella I 3,19:z:-	-	-	1
Salmonella I 4:b:-	-	-	1

Paired *Salmonella* Typhimurium isolates obtained from index patients and corresponding household members

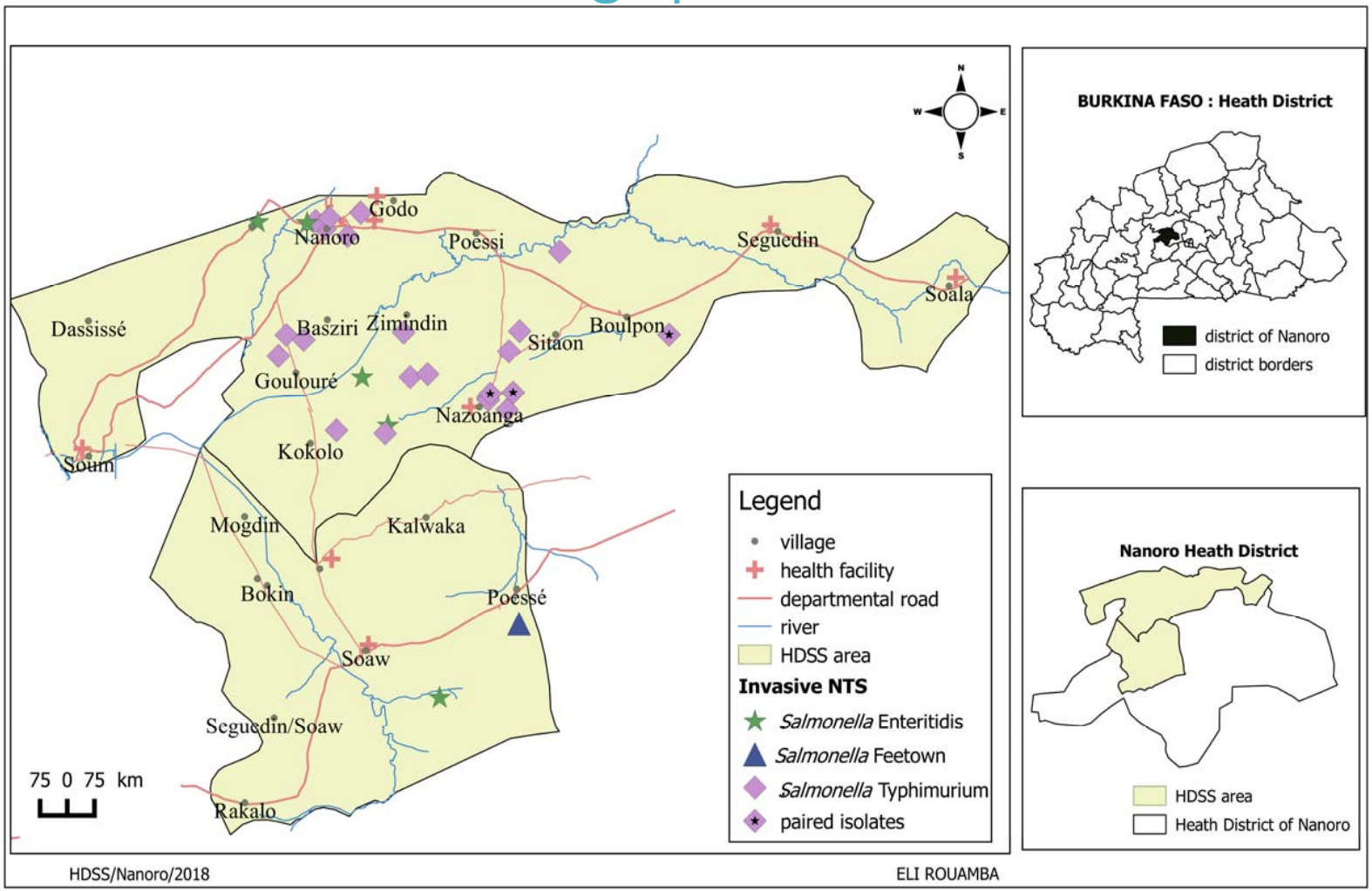
Household visit	* Days between sampling	Village	Index patient				Household member		
			Age (months)	Sex	Malaria diagnosis	MLVA type	Age (years)	Sex	MLVA type
17	10	Boulpon	46	M	negative	2-8-7-9-0210	44	M	2-8-7-9-0210
24	8	Nazoanga	13	M	positive	2-7-10-8-0210	10	F	2-7-10-8-0210
28**	11	Nazoanga	42	F	negative	2-7-12-NA-0210	1	M	2-7-17-8-0210
	7	Nazoanga	11	M	negative	2-7-10-8-0210			

MLVA: multilocus variable number tandem-repeat analysis

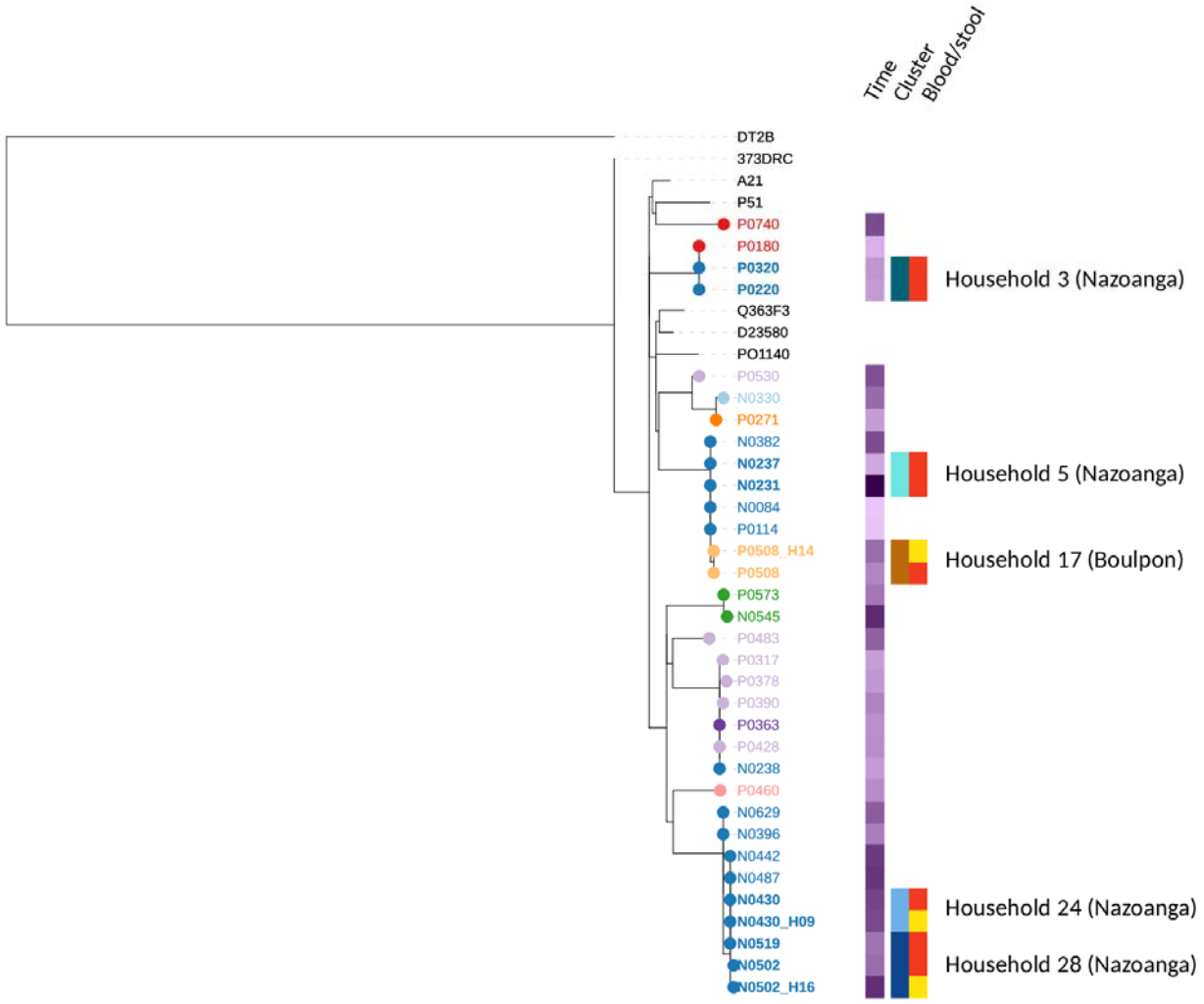
* Number of days between inclusion of the index patient and the household visit.

** Two index patients from the same family, presenting with a 4-day delay.

Geographic distribution of isolates



Phylogenetic tree of *Salmonella* Typhimurium



- Each index/household pair genetically strongly related
- Isolates from the same village often closely related
- Close clonal relation to isolates from DRC;
- All Sequence Type (ST) 313 – Lineage II

Strengths and Limitations

Limitations

- Time between presentation index patient / household sampling
- Limited number of paired cases
- No food sampling
- No follow-up stool samples
- Water culture techniques; notoriously difficult to culture *Salmonella* from water

Strengths

- Despite logistic restrains 32 households sampled
- Good coverage
- Area of high co-habitation;
- Whole Genome Sequencing

In conclusion

- Limited overlap between serotypes obtained from human and livestock sources (in contrast to western countries)
- Strong genetic association between *Salmonella* Typhimurium isolates obtained from blood culture and stool samples from household members of the patient.
- Strong genetic association between *Salmonella* Typhimurium isolates obtained from human sources living within the same village around the same time.
- Incremental arguments for role of humans in transmission of pediatric iNTS.

Dione et al (2007): Overlapping serotypes but wide genetic variation between isolates from human gastroenteritis cases and livestock

Kariuki et al (2006): No evident genetic relatedness (PFGE) between isolates from iNTS cases and livestock living in the same compound in Kenya

- Vessle for transmission still uncertain: further research into day-to-day water and prepared food could provide insight.

Please feel free to ask your questions