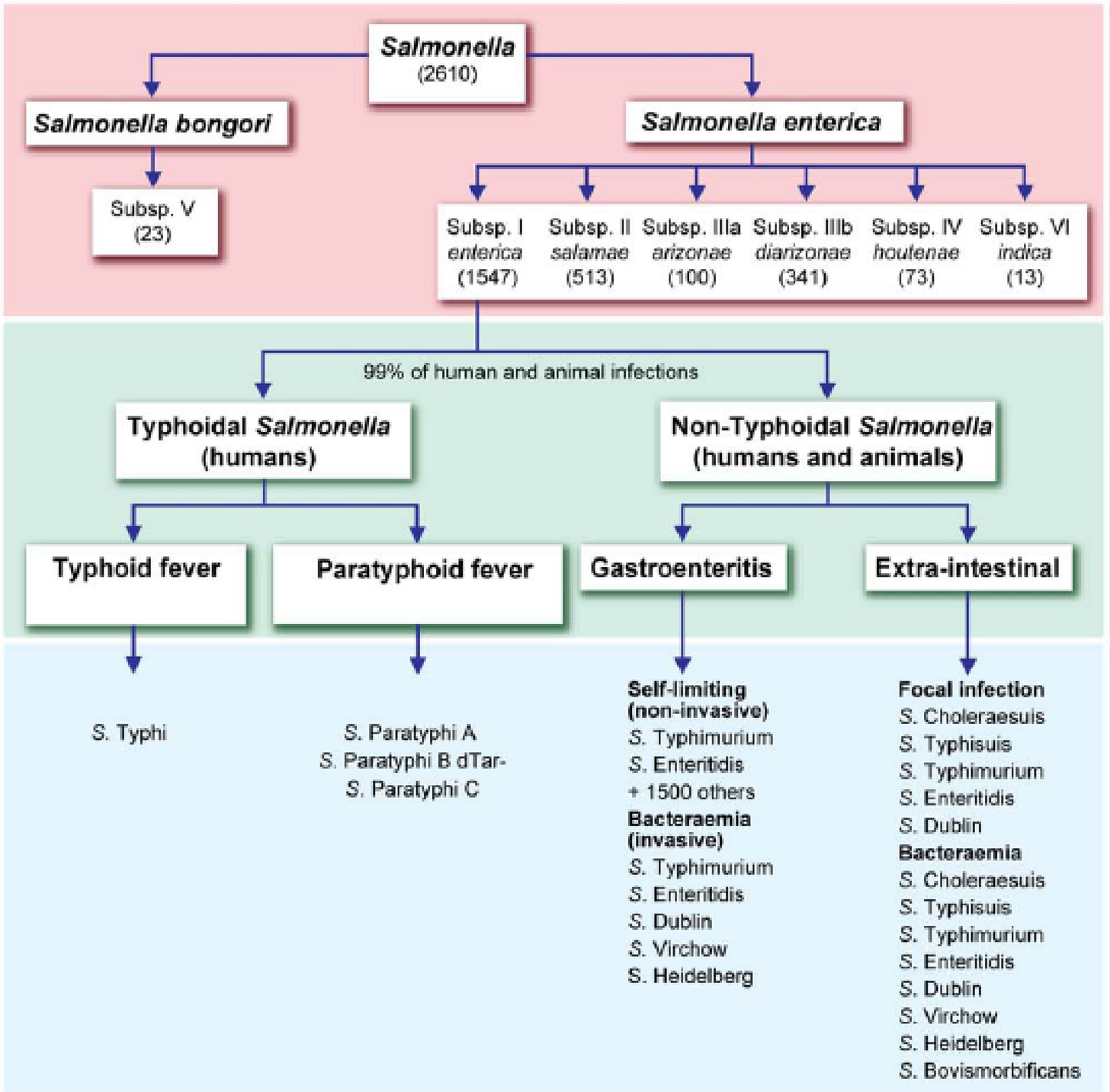
Invasive non-typhoidal *Salmonella* in Asia: An emerging infection?

Stephen Baker 01/02/13

wellcome trust

UNIVERSITY OF OXFORD



Species and subspecies were originally defined by DNA-DNA hybridisation, confirmed by MLEE and MLST and are currently differentiated by biochemistry and serology.

The split in typhoidal and non-typhoidal is based on the disease syndrome. Typhoid and paratyphoid fever is prolonged, whilst extra-intestinal infection is usually acute and metastatic. Gastroenteritis is characterised by diarrhoea.

Differentiation of serovars is by agglutination with specific antisera against LPS (O), two phases of flagella (H1 and H2). There are 46 O, 85 H and 1 capsule (Vi) antigen which have been described in about 1,500 combinations within subspecies I.

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Salmonella Epidemiology

- Estimated 93.8 million cases of gastroenteritis due to *Salmonella spp* with 155,000 deaths occur globally each year (Majowicz et al, CID, 2010).

In developed countries

- Report from US: estimated 1.4 million infections (population 293 million) with 168,000 visits to GP (Mead PS et al, 1999)
- Report from UK: 41.000 cases occur each year (population 60 million, resulting in 1,500 hospitalization and 119 deaths. (McDermott, 2006)

In developing countries

- Report from Africa: NTS is the most common cause of bacteremia in sub Saharan Africa, results in 1million cases/year, case fatality rate around 20% (Crump JA, Lancet Infect. Dis., 2010)

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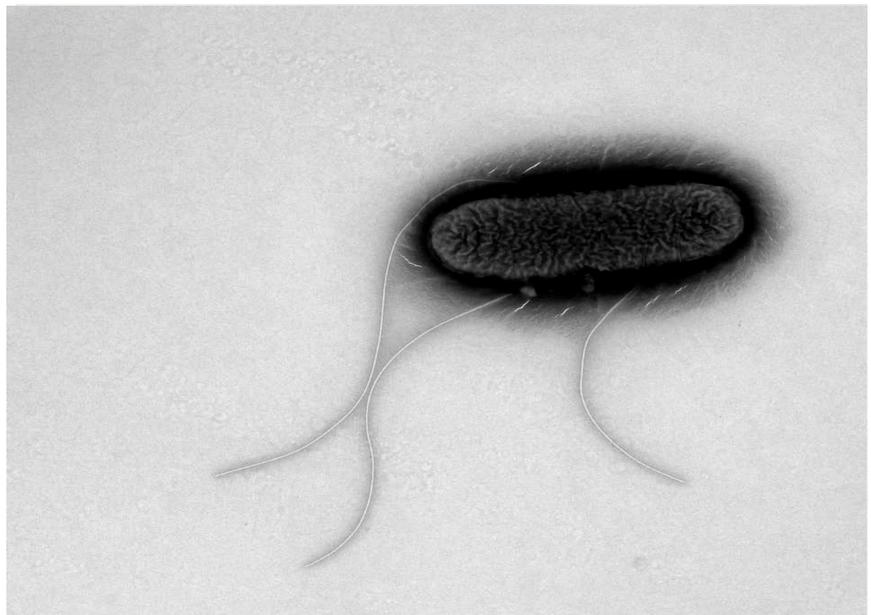
Enteric infections where I am

NT *Salmonella*



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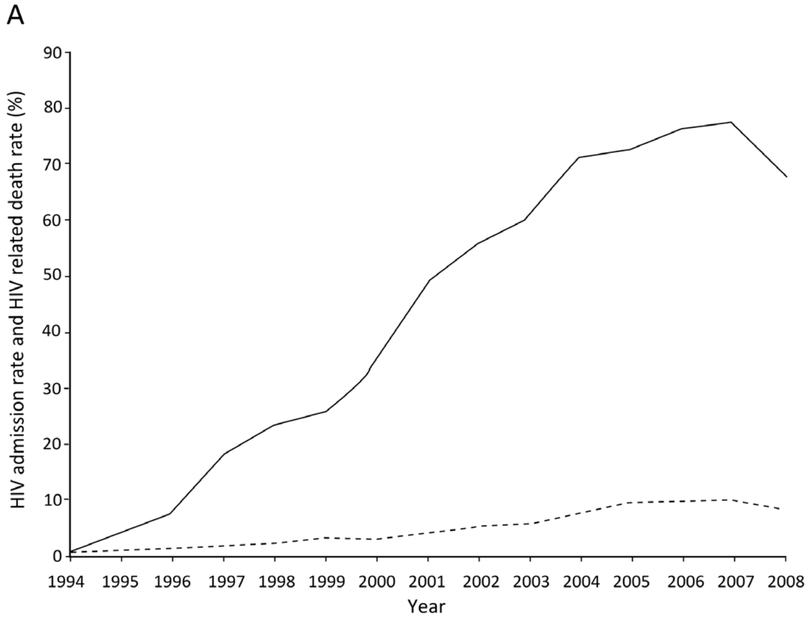
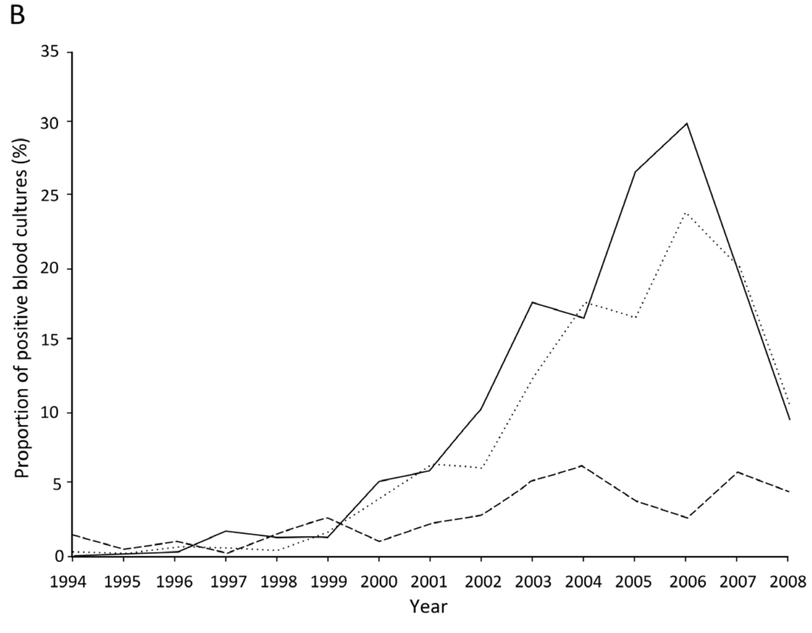
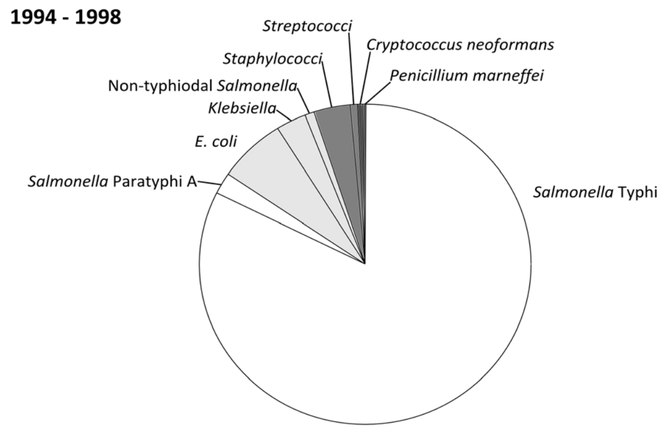
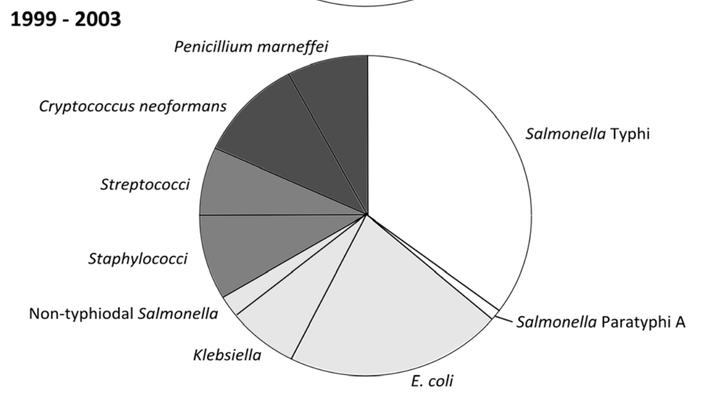
The decline of typhoid and the rise of non-typhoid salmonellae and fungal infections in a changing HIV landscape: bloodstream infection trends over 15 years in southern Vietnam

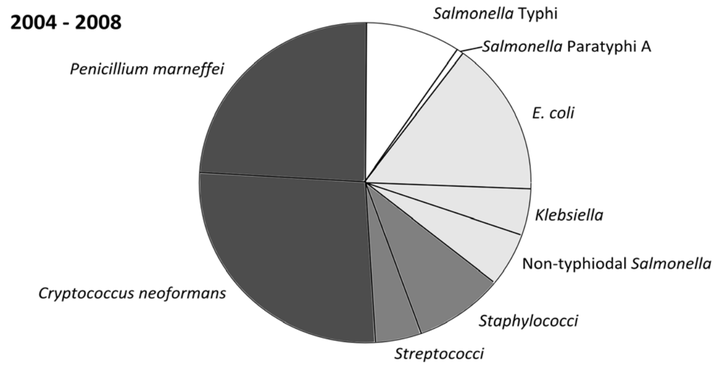
Tran Vu Thieu Nga[a], Christopher M. Parry[a, b], Thuy Le[a, c], Nguyen Phu Huong Lan[d], To Song Diep[d], James I. Campbell[a, e], Nguyen Van Minh Hoang[a], Le Thi Dung[d], John Wain[f], Christiane Dolecek[a, e], Jeremy J. Farrar[a, e], Nguyen Van Vinh Chau[d], Tran Tinh Hien[a, e], Jeremy N. Day[a, e], Stephen Baker[a, e],











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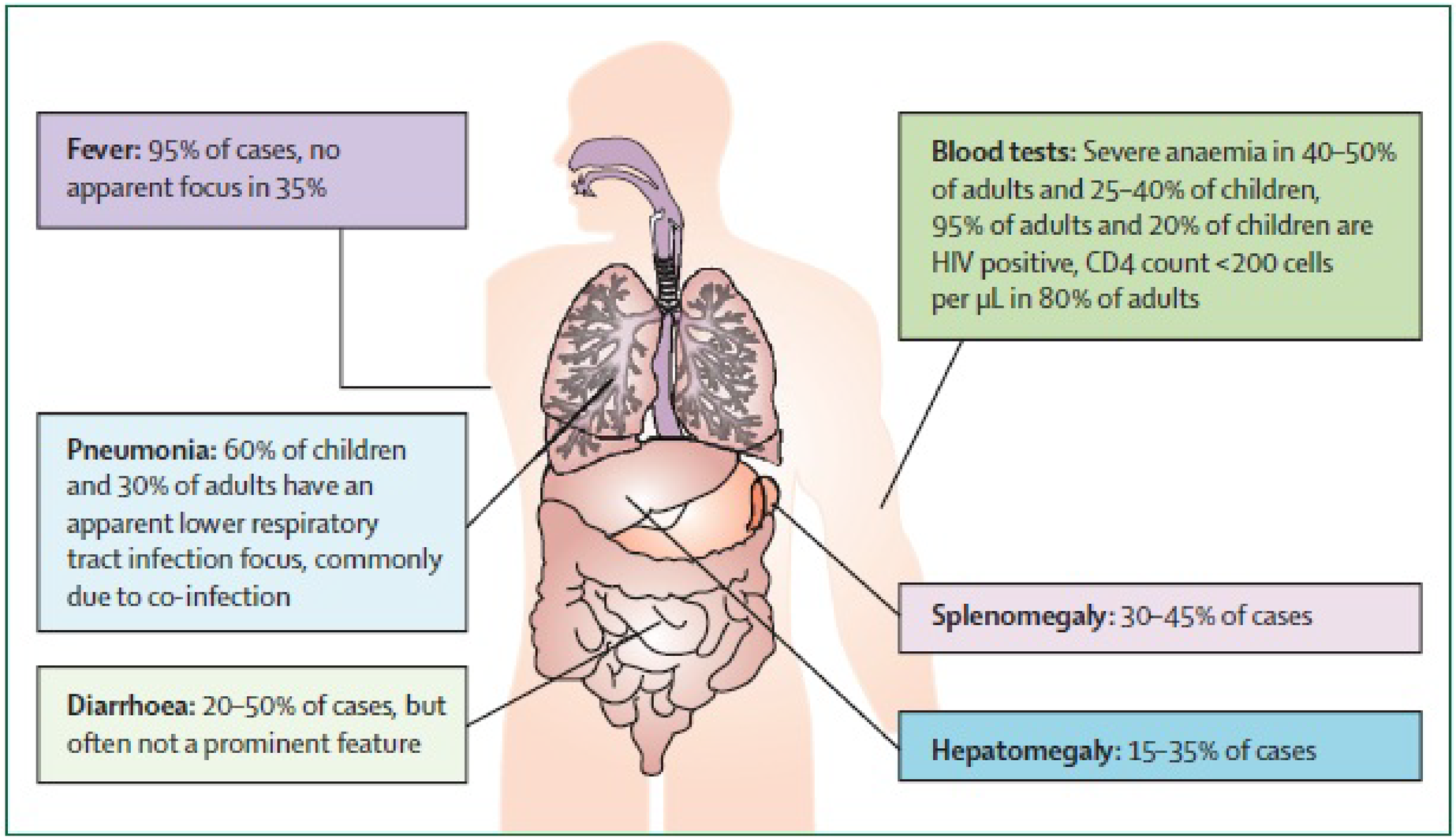
How does our invasive NTS relate to that seen in Africa?



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Case/control for gastrointestinal NTS infections

- May 2009-December 2010
- 1,419 total cases under 5 years of age
- 77 (5.4%) were infected with *Salmonella*
- 609 total controls
- 38 (6.2%) of the controls were infected with *Salmonella* but were asymptomatic

Descriptive characteristics

Characteristic	Salmonella (n=77)	All cases (n=1342)	Controls (n=571)
Male sex, %	63.6	63.8	63.2
Breastfed, %	77.9	71.3	77.6
Median age (IQR)*	10 (6.5-15)	13 (8-20)	12 (8-21)
Median z-score (IQR)	-0.3 (-1 to 0.5)	-0.3 (-0.8 to 0.6)	-0.8 (-1 to -0.2)

* months

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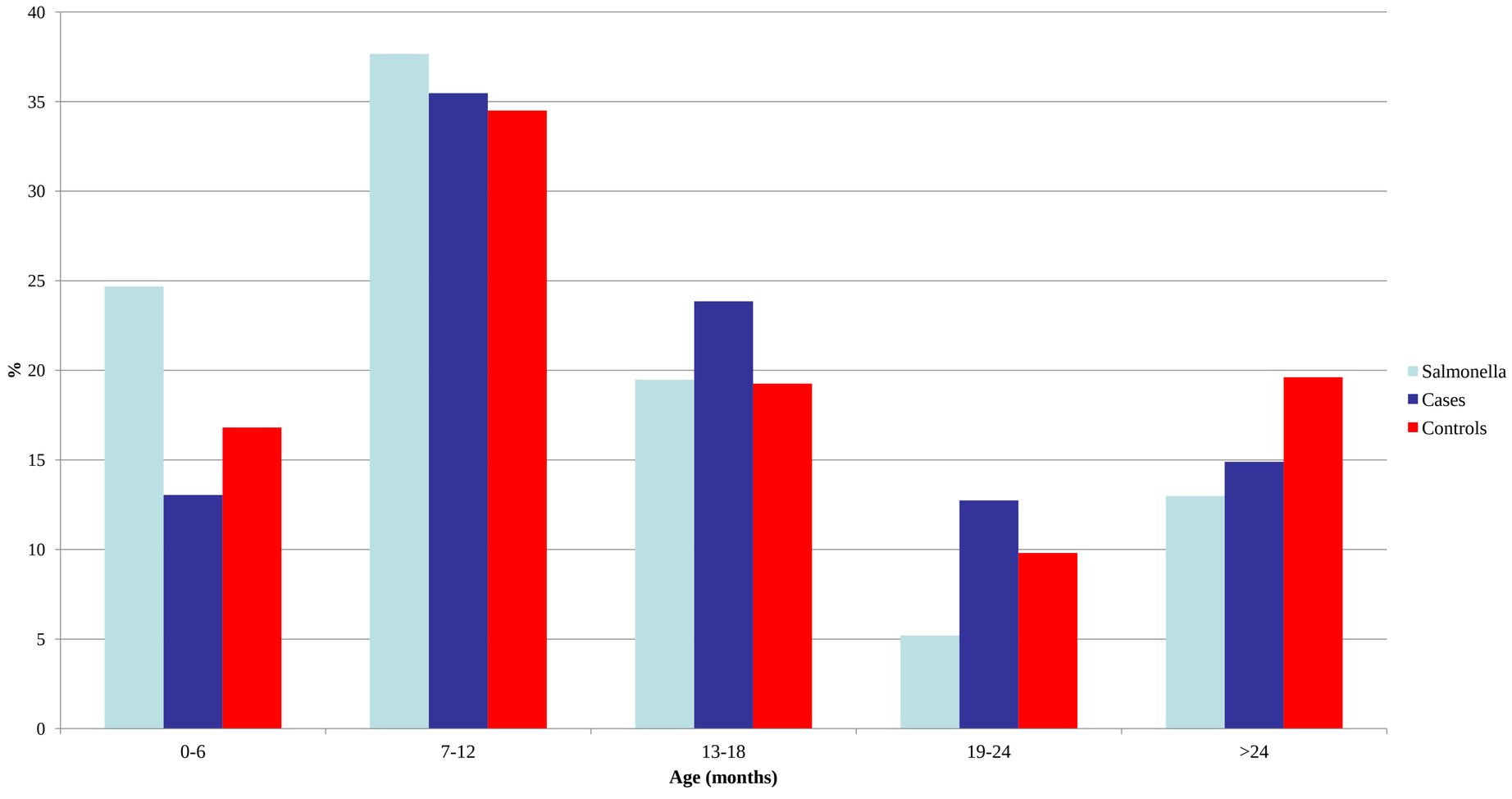
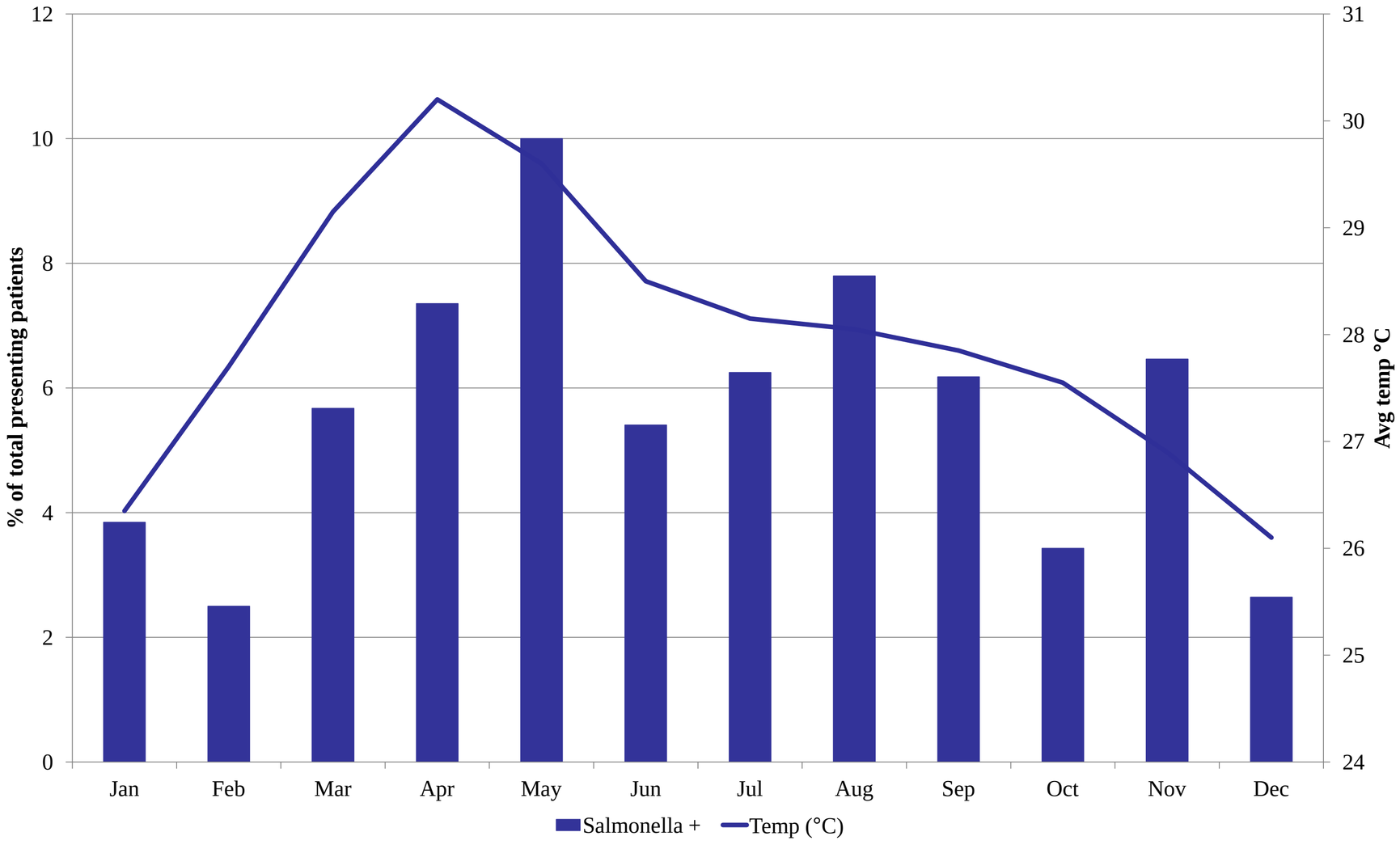
Age


40
35
30
25
20
15
10
5
0
%
0-6
7-12
13-18
19-24
>24
Age (months)
Salmonella
Cases
Controls

Seasonality



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Univariate & multivariate analyses

Risk Factors	OR	95%CI	p	AOR	95%CI	p
Previous illness	2.21	1.08-4.52	0.029*	1.77	0.73-4.26	0.204
Symptomatic contact	3.14	1.12-8.83	0.030*	5.98	1.76-20.36	0.004*
Age	0.98	0.96-1.00	0.036*	0.97	0.94-0.99	0.021*
Hand washing^	2.67	1.29-5.53	0.008*	1.99	0.85-4.63	0.111
Market food	2.22	1.27-3.88	0.005*	2.27	1.22-4.24	0.010*
>2 children in house	2.32	1.26-4.29	0.007*	2.32	1.15-4.67	0.019*
Outside toilet						
Rural	1.67	0.41-6.81	0.475	1.53	0.30-7.86	0.612
Urban	0.27	0.11-0.70	0.007*	0.25	0.09-0.72	0.010*

OR: Odds ratio; CI: Confidence interval; AOR: Adjusted Odds Ratio

*p-value ≤0.05

^Answering “No” or “Don’t Know” to the question “Does the child wash their hands after using the toilet?”

Salmonella serogroups

Serogroup	Cases (N=79)		Asymptomatic (N=95)		Total (N=174)		p
	n	%	n	%	n	%	
Group B	**44**	**55.7**	**21**	**22.1**	**65**	**37.4**	**0.004***
Derby	2	2.5	7	7.4	9	5.2	0.096
Paratyphi B mono	2	2.5	2	2.1	4	2.3	1.000
Stanley	4	5.1	3	3.2	7	4.0	0.706
Typhimurium	34	43.0	8	8.4	42	24.1	<0.001*
Group C	**10**	**12.7**	**13**	**13.7**	**23**	**13.2**	**0.532**
Newport	3	3.8	3	3.2	6	3.4	1.000
Group D	**6**	**7.6**	**4**	**4.2**	**10**	**5.7**	**0.157**
Enteritidis	1	1.3	3	3.2	4	2.3	0.317
No group	**19**	**24.1**	**57**	**60.0**	**76**	**43.7**	**<0.001***
Weltevreden	9	11.4	24	25.3	33	19.0	0.009*

*p≤0.05

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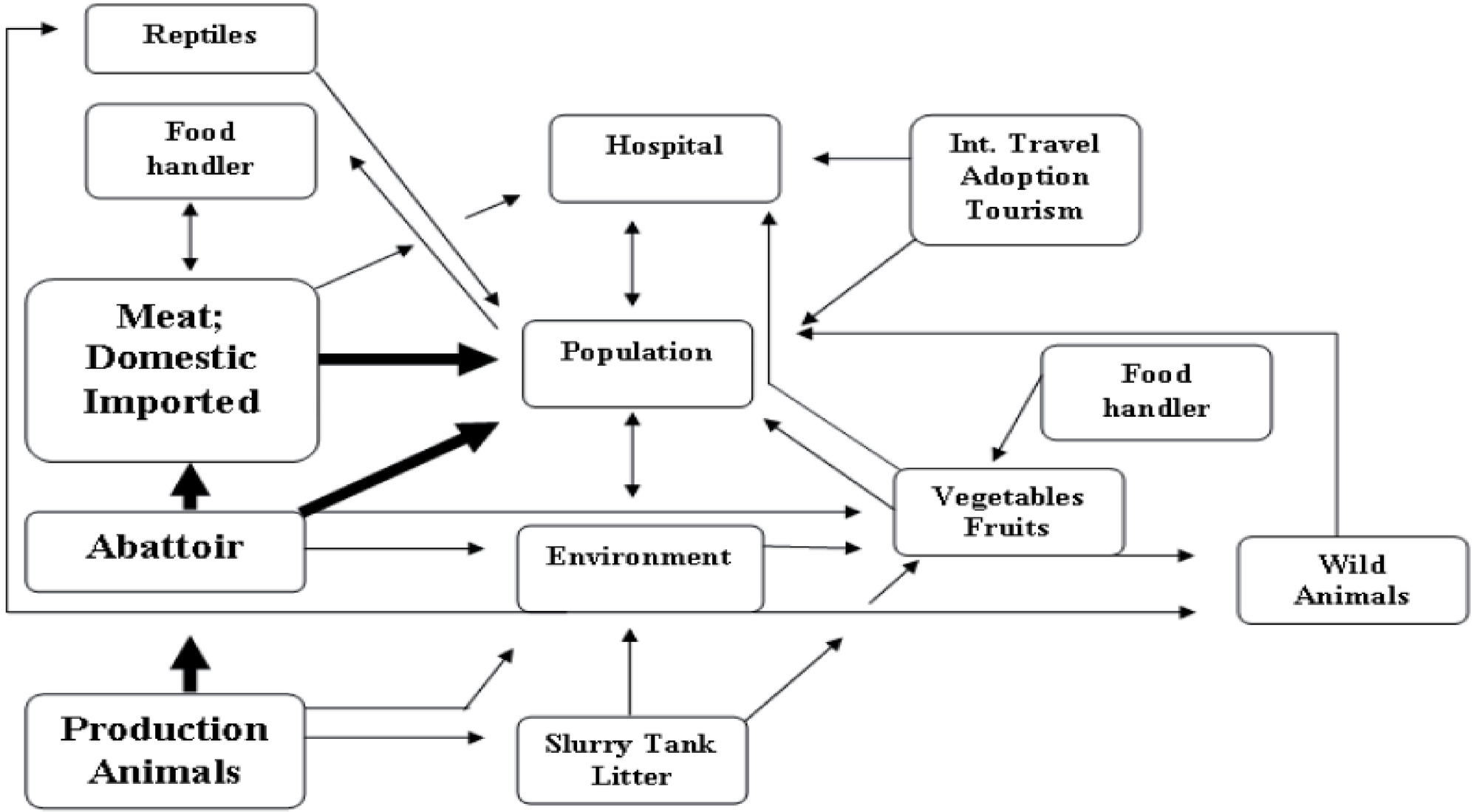
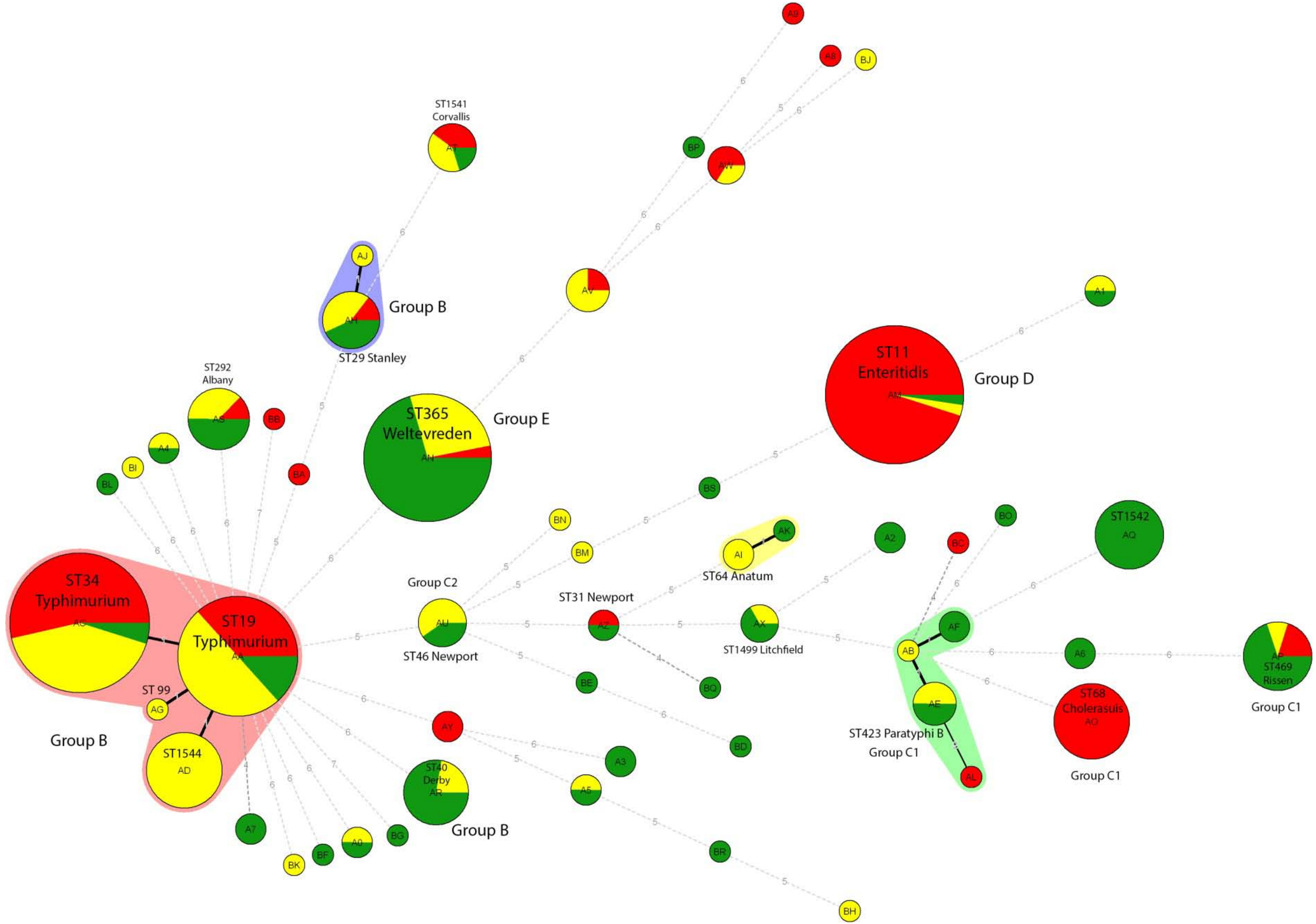
Central dogma of *Salmonella* transmission




A9
A8
BJ
ST1541
Corvallis
AT
BP
AW
AJ
AH
Group B
ST29 Stanley
AV
ST292
Albany
AS
BB
A4
BI
BL
BA
ST365
Weltevreden
AN
Group E
ST11
Enteritidis
AM
Group D
A1
BS
BN
BM
AK
AI
ST64 Anatum
A2
BC
BO
ST1542
AQ
ST34
Typhimurium
AC
ST19
Typhimurium
AA
ST 99
AG
ST1544
AD
Group B
Group C2
AU
ST46 Newport
ST31 Newport
AZ
BE
BQ
AX
ST1499 Litchfield
AF
AB
AE
AL
ST423 Paratyphi B
Group C1
A6
ST68
Cholerasuis
AO
Group C1
ST469
Rissen
Group C1
AY
A3
A5
BD
ST40
Derby
AR
Group B
A7
A0
BK
BF
BG
BR
BH

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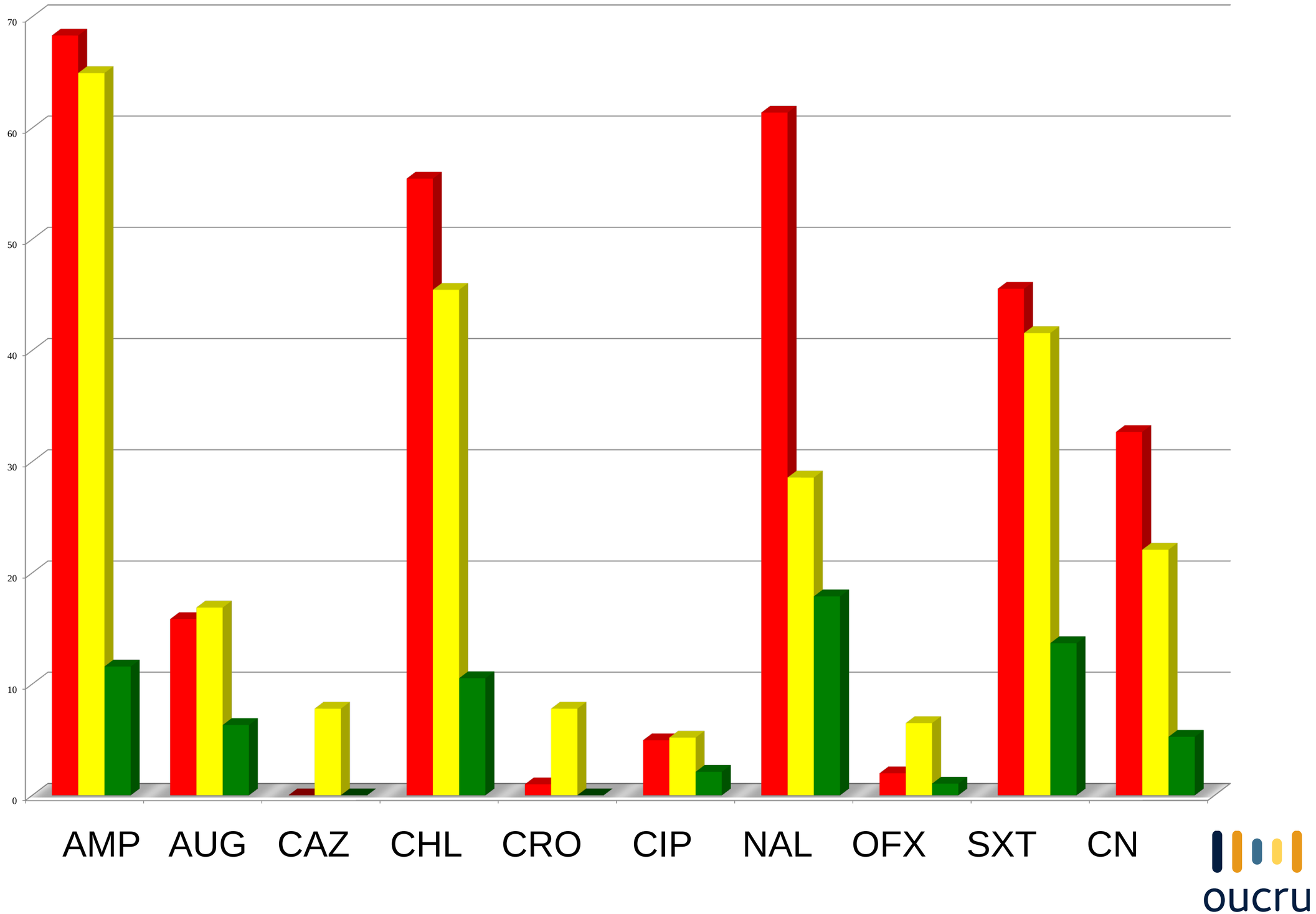
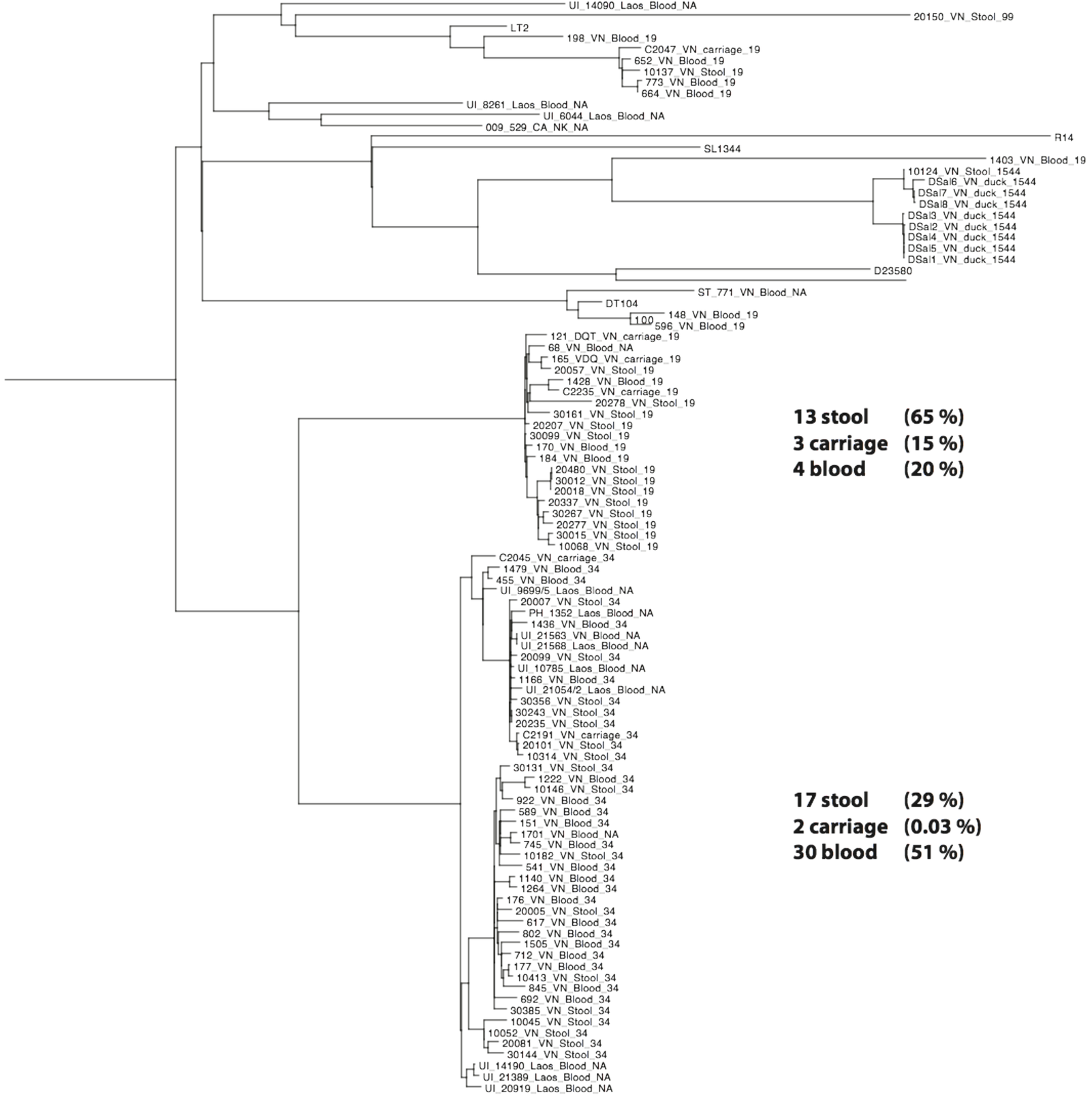

70
60
50
40
30
20
10
0
AMP
AUG
CAZ
CHL
CRO
CIP
NAL
OFX
SXT
CN


UI_14090_Laos_Blood_NA
20150_VN_Stool_99
LT2
198_VN_Blood_19
C2047_VN_carriage_19
652_VN_Blood_19
10137_VN_Stool_19
773_VN_Blood_19
664_VN_Blood_19
UI_8261_Laos_Blood_NA
UI_6044_Laos_Blood_NA
009_529_CA_NK_NA
R14
SL1344
1403_VN_Blood_19
10124_VN_Stool_1544
DSal6_VN_duck_1544
DSal7_VN_duck_1544
DSal8_VN_duck_1544
DSal3_VN_duck_1544
DSal2_VN_duck_1544
DSal4_VN_duck_1544
DSal5_VN_duck_1544
DSal1_VN_duck_1544
D23580
ST_771_VN_Blood_NA
DT104
100
148_VN_Blood_19
596_VN_Blood_19
121_DQT_VN_carriage_19
68_VN_Blood_NA
165_VDQ_VN_carriage_19
20057_VN_Stool_19
1428_VN_Blood_19
C2235_VN_carriage_19
20278_VN_Stool_19
30161_VN_Stool_19
20207_VN_Stool_19
30099_VN_Stool_19
170_VN_Blood_19
184_VN_Blood_19
20480_VN_Stool_19
30012_VN_Stool_19
20018_VN_Stool_19
20337_VN_Stool_19
30267_VN_Stool_19
20277_VN_Stool_19
30015_VN_Stool_19
10068_VN_Stool_19
C2045_VN_carriage_34
1479_VN_Blood_34
455_VN_Blood_34
UI_9699/5_Laos_Blood_NA
20007_VN_Stool_34
PH_1352_Laos_Blood_NA
1436_VN_Blood_34
UI_21563_VN_Blood_NA
UI_21568_Laos_Blood_NA
20099_VN_Stool_34
UI_10785_Laos_Blood_NA
1166_VN_Blood_34
UI_21054/2_Laos_Blood_NA
30356_VN_Stool_34
30243_VN_Stool_34
20235_VN_Stool_34
C2191_VN_carriage_34
20101_VN_Stool_34
10314_VN_Stool_34
30131_VN_Stool_34
1222_VN_Blood_34
10146_VN_Stool_34
922_VN_Blood_34
589_VN_Blood_34
151_VN_Blood_34
1701_VN_Blood_NA
745_VN_Blood_34
10182_VN_Stool_34
541_VN_Blood_34
1140_VN_Blood_34
1264_VN_Blood_34
176_VN_Blood_34
20005_VN_Stool_34
617_VN_Blood_34
802_VN_Blood_34
1505_VN_Blood_34
712_VN_Blood_34
177_VN_Blood_34
10413_VN_Stool_34
845_VN_Blood_34
692_VN_Blood_34
30385_VN_Stool_34
10045_VN_Stool_34
10052_VN_Stool_34
20081_VN_Stool_34
30144_VN_Stool_34
UI_14190_Laos_Blood_NA
UI_21389_Laos_Blood_NA
UI_20919_Laos_Blood_NA
13 stool (65 %)
3 carriage (15 %)
4 blood (20 %)
17 stool (29 %)
2 carriage (0.03 %)
30 blood (51 %)

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Ongoing and future work

Animal sampling for *Salmonella*

- Pigs, chickens, ducks, reptiles, shellfish

MLST

- 500+ isolates from different hosts
- That asymptomatic strains have an animal reservoir
- Invasive strains are transmitted from human to human (or a 2ndary reservoir)

Retrospective analysis of invasive NTS

- Outcome, risk factors for outcome, disease history, HIV rate
- Low morality rate, weak effect of HIV, liver abnormalities are common

Case/control investigation for invasive NTS

- Currently in design

1000 child cohort

- To assess Salmonella incidence in the first 3 years of life
- Assess long term carriage of NTS serotypes

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