Epidemiology and disease burden of typhoid fever and iNTS disease in sub-Saharan Africa

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Coalition against Typhoid meeting
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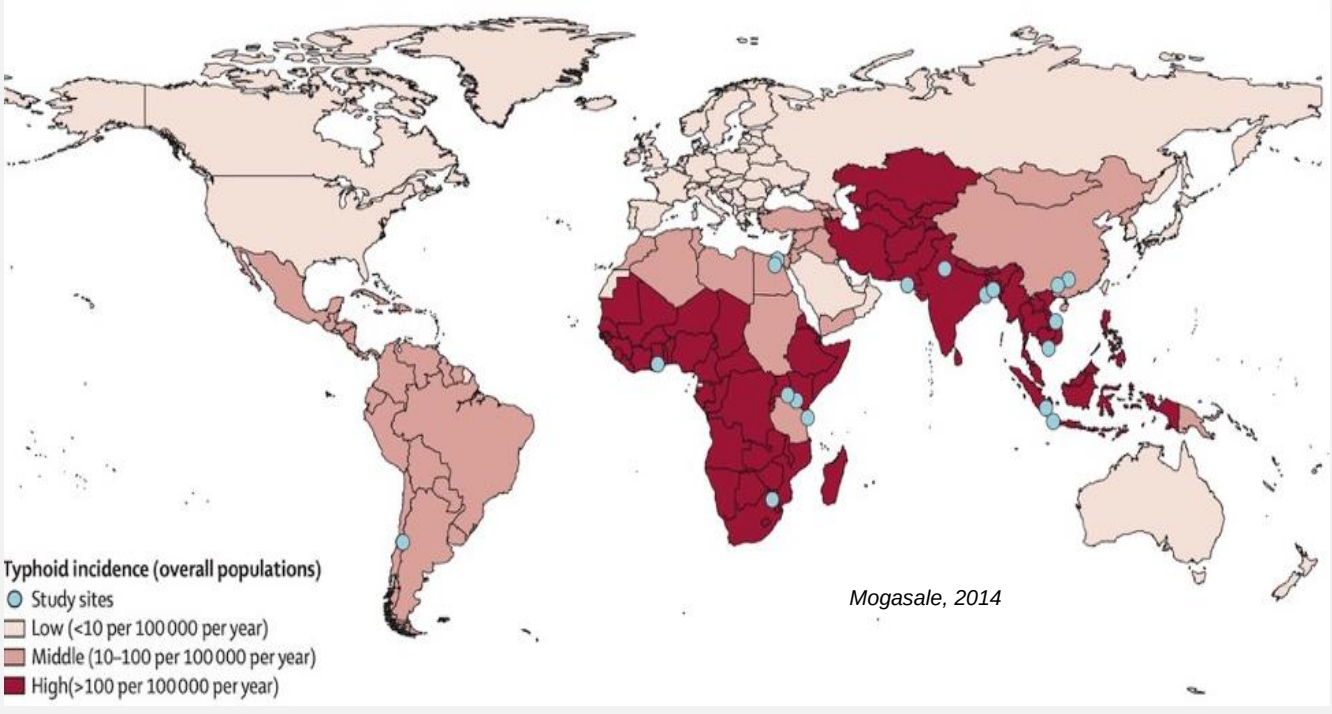
INTERNATIONAL VACCINE INSTITUTE

Context

Salmonella infections – major cause of global morbidity and mortality

Ivanoff (1994)	Crump (2004)	Buckle (2012)	Mogasale (2014)
17 million cases and 600,000 deaths	21.7 million cases and 216,000 deaths	26.9 million cases	20.6 million cases and 222,000 deaths



Mogasale, 2014

2008 - Need for epidemiological information on invasive *Salmonella* disease in sub-Saharan Africa (sSA) expressed by WHO

2009 - Consortium established to investigate invasive *Salmonella* disease burden sSA

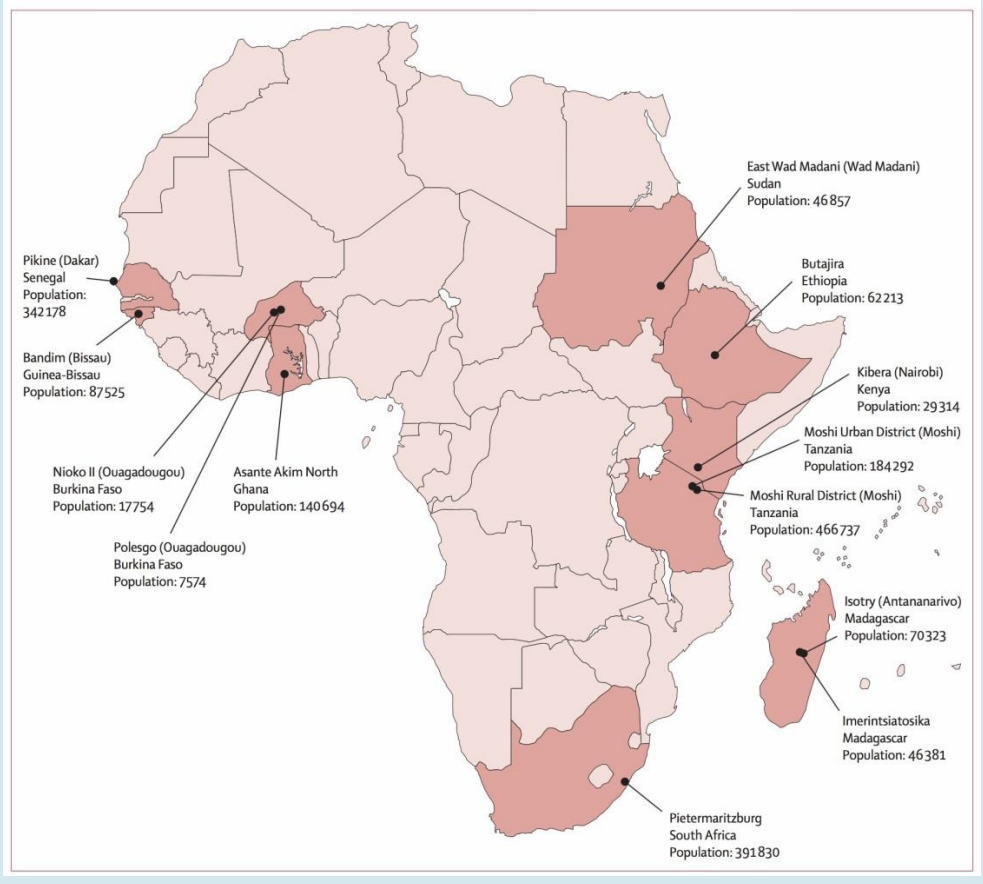
2010 – Surveillance implemented in sSA: The Typhoid Surveillance in Africa Program (TSAP)

Typhoid Fever Surveillance in Africa Program (TSAP) - methods

TSAP methods

- ✓ Mar 2010 to Jan 2014
- ✓ 13 African sites
- ✓ 13,431 febrile patients sampled
- ✓ Standardized procedures
  - inclusion criteria
  - laboratory
  - case definition
  - healthcare utilization
  - database

S. Typhi and iNTS positivity
Blood culture



Typhoid Fever Surveillance in Africa Program (TSAP) – major findings[1]

Typhoid fever disease

- ✓ Overall adjusted incidences – two to three times higher compared to previous estimates (10-100 cases/100,000 people[2]).
- ✓ In some settings – adjusted rates comparable to data from Asia. (Ghana, Burkina Faso, and Kenya).
- ✓ Greatest burden – in children aged 2-14 years.

Age group, years	Burkina Faso, Nioko II	Burkina Faso, Polesgo	Guinea Bissau, Bandim	Ghana, AAN	Tanzania, Moshi rural	Tanzania, Moshi urban	Kenya, Kibera	Madagascar, Imerintsiatosika	Madagasar, Isotry
0 to 1	0 (0 - 0)	0 (0 - 0)	0 (0 - 0)	120 (49 - 290)	0 (0 - 0)	0 (0 - 0)	148 (48 - 458)	0 (0 - 0)	0 (0 - 0)
2 to 4	251 (107 - 590)	1,890 (1,202 – 2,972)	53 (13 - 208)	1,079 (762 – 1,528)	0 (0 - 0)	1,028 (472 – 2,237)	490 (264 - 912)	0 (0 - 0)	0 (0 - 0)
5 to 14	315 (191 - 519)	485 (263 - 896)	18 (5 - 72)	314 (230 - 430)	18 (8 - 44)	103 (54 – 199)	489 (338 - 709)	171 (81 - 360)	62 (11 - 359)
< 15	227 (148 - 350)	719 (500 – 1,035)	20 (8 - 53)	389 (310 - 486)	18 (7 - 42)	155 (94 – 256)	419 (308 - 569)	95 (45 - 201)	42 (7 - 247)
≥15	0 (0 - 0)	107 (46 - 252)	4 (1 - 20)	n.a.	28 (8 - 95)	201 (99 - 408)	141 (82 - 243)	20 (4 - 103)	42 (12 - 151)
All	104 (68 - 161)	383 (274 - 535)	10 (4 - 22)	n.a.	20 (10 - 41)	168 (111 – 253)	284 (217 - 371)	58 (29 - 114)	42 (15 - 119)

[1]Incidence of invasive *Salmonella* disease in sub-Saharan Africa: a multicenter population-based surveillance study. *LANCET Global Health* 2017; 5: e310-23.
[2]Crump JA, Luby SP, Mintz ED. The global burden of typhoid fever. *Bull World Health Organ*. 2004;82:346–53.

Typhoid Fever Surveillance in Africa Program (TSAP) – major findings[1]

iNTS disease

- ✓ Overall adjusted incidences – comparable to previous reports.
- ✓ Greatest burden – in children aged 0-5 years.
- ✓ Most common serovars
  1. *S.* Typhimurium (40%, 38/94)
  2. *S.* Enteriditis (12%, 11/94)
  3. *S.* Dublin (11%, 10/94)

Age group, years	Burkina Faso, Nioko II	Burkina Faso, Polesgo	Guinea Bissau, Bandim	Ghana, AAN	Tanzania, Moshi rural	Tanzania, Moshi urban	Kenya, Kibera	Madagascar, Imerintsiatosika	Madagasar, Isotry
0 to 1	753 (460 – 1,233)	431 (162 - 1147)	291 (176 - 482)	1,733 (1,373 – 2,188)	0 (0 - 0)	427 (125 – 1,461)	49 (7 - 350)	100 (18 – 562)	0 (0 - 0)
2 to 4	753 (460 – 1,233)	630 (288 – 1,380)	53 (13 - 208)	1,908 (1,469 – 2,479)	0 (0 - 0)	0 (0 - 0)	49 (7 - 348)	0 (0 - 0)	0 (0 - 0)
5 to 14	236 (133 - 420)	0 (0 - 0)	53 (14 - 97)	147 (93 - 232)	0 (0 - 0)	0 (0 - 0)	17 (2 - 124)	0 (0 - 0)	0 (0 - 0)
< 15	475 (352 - 640)	255 (138 - 470)	116 (69 - 161)	742 (631 - 873)	0 (0 - 0)	26 (8 - 88)	31 (10 - 95)	18 (3 – 99)	0 (0 - 0)
≥15	35 (13 - 96)	54 (16 - 179)	0 (0 - 0)	n.a.	28 (8 - 95)	0 (0 - 0)	33 (10 - 101)	0 (0 - 0)	0 (0 - 0)
All	237 (178 – 316)	144 (83 - 249)	37 (24 - 57)	n.a.	7 (2 - 23)	19 (5 - 64)	32 (14 - 70)	9 (2 – 50)	0 (0 - 0)

[1]Incidence of invasive *Salmonella* disease in sub-Saharan Africa: a multicenter population-based surveillance study. *LANCET Global Health* 2017; 5: e310-23.

Typhoid Fever Surveillance in Africa Program (TSAP) – major findings[1]

Antimicrobial resistance patterns

- ✓ High number of MDR *S.* Typhi isolates – 47% (64/135)
- ✓ High number of MDR NTS isolates – 48% (45/94)

	Burkina Faso	Guinea-Bissau	Senegal*	Ghana	Ethiopia	Madagascar	South Africa	Tanzania	Kenya	All
Total S Typhi isolates, N	18	3	7	30	3	9	2	9	54	135
Isolate with antimicrobial resistance, n (%)†										
Ampicillin	0	NR	NR	20 (67%)	2 (67%)	NR	0	8 (89%)	41 (76%)	71 (53%)
Amoxicillin-clavulanic acid	0	NR	NR	3 (10%)	0	NR	0	4 (44%)	24 (44%)	31 (23%)
Chloramphenicol	2 (11%)	NR	NR	23 (77%)	0	NR	0	5 (56%)	43 (80%)	73 (54%)
Co-trimoxazole	2 (11%)	NR	NR	24 (80%)	0	NR	0	8 (89%)	43 (80%)	77 (57%)
Ceftriaxone	0	NR	NR	0	0	NR	0	0	0	0
Ciprofloxacin	0	NR	NR	0	0	NR	1 (50%)	0	11 (20%)	12 (9%)
Multidrug resistance‡	0	NR	NR	19 (63%)	0	NR	0	5 (56%)	40 (74%)	64 (47%)
Total iNTS isolates, N	14	8	4	59	0	1	0	2	6	94
Isolate with antimicrobial resistance, n (%)†										
Ampicillin	10 (71%)	1 (13%)	NR	38 (64%)	NR	NR	NR	0	2 (33%)	51 (54%)
Amoxicillin-clavulanic acid	3 (21%)	0	NR	9 (15%)	NR	NR	NR	0	2 (33%)	14 (15%)
Chloramphenicol	12 (86%)	1 (13%)	NR	34 (58%)	NR	NR	NR	0	1 (17%)	48 (51%)
Co-trimoxazole	13 (93%)	1 (13%)	NR	34 (58%)	NR	NR	NR	0	2 (33%)	50 (53%)
Ceftriaxone	0	0	NR	0	NR	NR	NR	0	1 (17%)	1 (1%)
Ciprofloxacin	1 (7%)	0	NR	2 (3%)	NR	NR	NR	0	0	3 (3%)
Multidrug resistance‡	10 (71%)	1 (13%)	NR	33 (56%)	NR	NR	NR	0	1 (17%)	45 (48%)

Resistant isolates are reported per country, rather than per site. No *Salmonella enterica* serotype Typhi (S Typhi) or iNTS isolates were cultured in Sudan. iNTS=invasive non-typhoidal salmonella. NR=no resistant isolates identified. *Seven S Typhi, four iNTS, and three S *enterica* serotype Paratyphi (S Paratyphi) isolates. One of the S Paratyphi isolates was resistant to ciprofloxacin. †Includes isolates fully and intermediately resistant against the respective drug, as defined by the Clinical Laboratory and Standards Institute guidelines 2013.[35] ‡Defined as resistance against ampicillin or amoxicillin AND chloramphenicol AND co-trimoxazole.

Table 3: **Antimicrobial resistance patterns of *Salmonella enterica* serotype Typhi and iNTS isolates across sites**

[1]Incidence of invasive *Salmonella* disease in sub-Saharan Africa: a multicenter population-based surveillance study. *LANCET Global Health* 2017; 5: e310-23.

Manuscripts published

25 manuscripts published and several planned for 2017

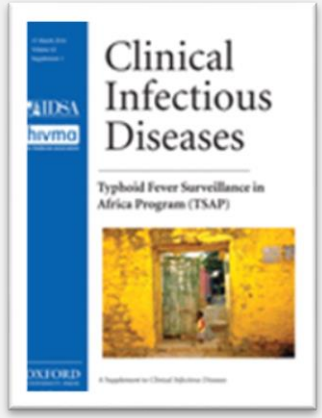
Mar 2017

Articles

Incidence of invasive salmonella disease in sub-Saharan Africa: a multicentre population-based surveillance study

Summary

Introduction



Mar 2016

Clinical Infectious Diseases

TYPHOID FEVER SURVEILLANCE IN AFRICA PROGRAM (TSAP)

Updated disease burden estimates

submitted

Table 1: Typhoid fever burden per 100,000 individuals in Africa

Region	2014 estimate[2]	Updated estimates		
	Base estimates*	Base estimates*		Alternate estimates†
	Risk-factor adjusted‡ (95% CI)	Risk-factor adjusted‡ (95% CI)	Risk-factor un-adjusted (95% CI)	Risk-factor un-adjusted (95% CI)
North Africa	33,807 (25,809 – 44,185)	33,807 (26,213-44,165)	61,971 (50,089-75,713)	76,207 (60,448-94,790)
East Africa	1,749,861 (1,386,537-2,203,996)	1,270,040 (992,192-1,509,643)	1,715,321 (1,353,111-2,013,337)	2,109,357 (1,625,493-2,514,001)
West Africa	489,669 (309,531 – 729,282)	1,259,073 (998,327-1,536,530)	1,672,045 (1,325,851-2,011,005)	2,056,140 (1,582,635-2,530,004)
Middle Africa	713,517 (568,060–887,805)	713,517 (569,039-889,638)	881,368 (704,662-1,091,018)	1,083,833 (846,026-1,371,996)
Southern Africa	103,542 (76,359–140,868)	103,542 (75,835-140,861)	188,529 (143,043-244,423)	231,837 (170,995-304,842)
Africa total	3,090,395 (2,504,427–3,829,277)	3,379,978 (2,796,753-3,949,796)	4,519,234 (3,761,267-5,181,078)	5,557,373 (4,483,729-6,553,323)
Global	**11,883,047 (9,925,551-14,751,214**	**12,172,630 (9,999,237-14,845,639)**	**20,940,154 (17,730,988-24,426,186)**	**25,750,435 (21,203,991-30,637,959)**

* Base estimates assume 61% blood culture sensitivity[2]. †Alternate estimates assume 50% blood culture sensitivity. ‡Risk-factor adjustment extrapolates incidence from longitudinal studies directly to rural population lacking access to improved water and urban population living in slums; and extrapolates corrected incidence to rural population having access to improved water and an urban population not living in slums based on water-related risk correction factor of 2.4 (95% CI 1·7-3·6). Detailed methodology is available elsewhere[2]. CI= confidence interval

Updated estimates mean annual typhoid fever incidence (/100,000)

- decreased from 526 to 376 in East Africa
- increased from 160 to 411 in West Africa

→ average annual incidence of 328/100,000 people in Africa

(an increase of 28/100,000 from the previous estimate)

Mogasale V, Maskery B, Ochiai RL, Lee JS, Mogasale VV, Ramani E, et al. Burden of typhoid fever in low-income and middle-income countries: a systematic, literature-based update with risk-factor adjustment. Lancet Glob Health. 2014; **2**: e570-80.

Typhoid and iNTS disease burden in children and infants

Invasive *Salmonella* infections in young children across TSAP[1] sites

Age Group in years	# of enrolled patients	PYO[2] by age group	S. Typhi			iNTS		
			Crude Cases	Cases adjusted for recruitment[3]	Adjusted incidence per 100,000 PYO (95% CI)	Crude Cases	Cases adjusted for recruitment[3]	Adjusted incidence per 100,000 PYO (95% CI)
0 to 1	1,217	8,658	1	1	4.1 (0.38-43.4)	14 (15)*	33	81.6 (25.5-261.0)
1 to 2	1,057	9,102	4	7	31.4 (7.6-130.5)	27	77	238.3 (77.4-733.8)
2 to 3	818	6,407	7	19	122.9 (34.0-445.0)	13	35	143.0 (45.1-453.4)
3 to 4	685	5,507	13	27	195.3 (55.3-689.6)	15	38	208.9 (66.4-656.7)
4 to 5	575	4,800	12 (16)*	28	245.2 (69.9-860.1)	2	8	47.1 (12.4-179.1)
Total	4,352	34,474	37 (41)*	82		71 (72)*	191	

[1]Ethiopia, South Africa and Senegal are excluded in the analysis because no person time information is available in these sites.
[2]Study population was adjusted for health-seeking behavior.
[3]Crude cases were adjusted for recruitment proportion (number of patients analyzed divided by number of patients with febrile illness from study area who visited a recruitment health facility, multiplied by 100.)
*Crude cases have been adjusted for recruitment pattern unique to the site in Tanzania: before Nov. 11, 2011 every 5th eligible patient was recruited; from Nov. 11, 2011 every 2nd eligible patient was recruited. Adjusted cases (presented inside parenthesis) were used to calculate crude rates.

→ Poster

Higher risk for typhoid fever disease with increasing age

Invasive *Salmonella* infections in young children by TSAP region

Age Group in years	TSAP study sites in West Africa[1]				TSAP study sites in East Africa[2]			
	S. Typhi		iNTS		S. Typhi		iNTS	
	# of adjusted cases	Adjusted incidence per 100,000 PYO (95% CI)	# of adjusted cases	Adjusted incidence per 100,000 PYO (95% CI)	# of adjusted cases	Adjusted incidence per 100,000 PYO (95% CI)	# of adjusted cases	Adjusted incidence per 100,000 PYO (95% CI)
0 to 1	0	0	29	464.5 (314.9-685.3)	1	41.4 (5.5-312.9)	4	165.6 (59.9-457.6)
1 to 2	5	82.5 (33.4-203.7)	76	1,254 (948.1-1658.0)	2	65.8 (15.7-274.8)	1	32.9 (4.3-250.1)
2 to 3	18	427.5 (265.7-687.8)	35	831.2 (578.9-1194.0)	1	45.5 (6.0-344.0)	0	0
3 to 4	22	683.7 (437.6-1068.0)	37	1,205 (845.2-1717.0)	5	205.3 (82.9-508.5)	1	41.1 (5.4-311.5)
4 to 5	18	689 (428.2-1109.0)	8	267.9 (130.1-551.9)	10	457.1 (241.3-865.8)	0	0
Total	63		185		19		6	

NOTE.
[1]TSAP West Region includes Burkina Faso, Ghana and Guinea Bissau.
[2]TSAP Easat Region includes Kenya, Madagascar, Sudan and Tanzania

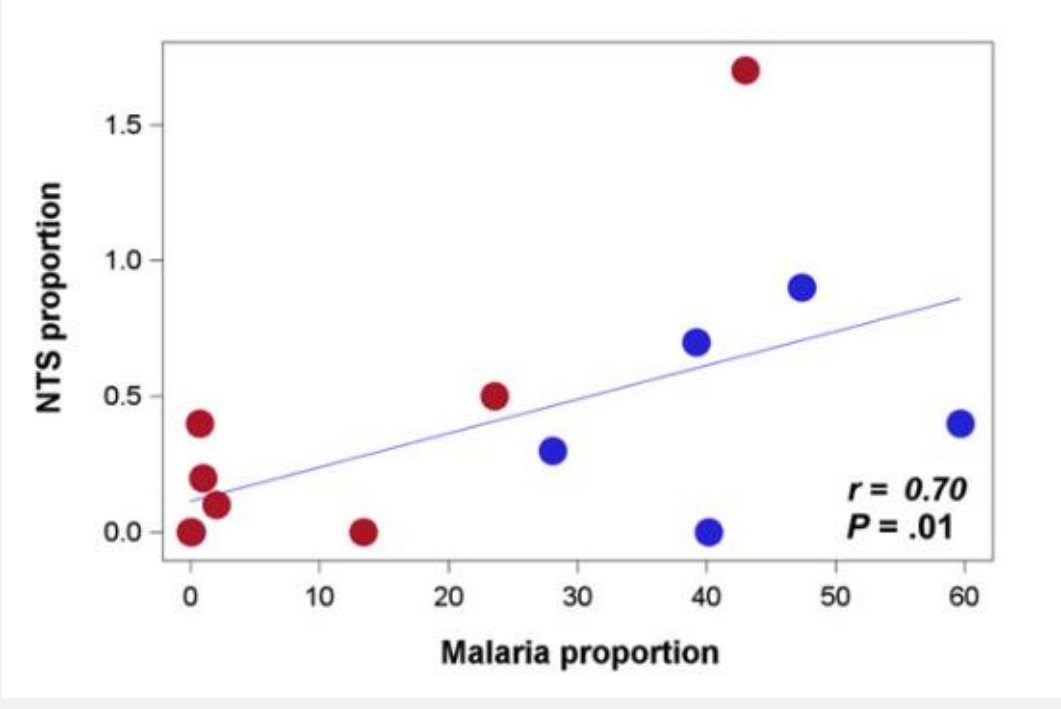
Higher risk of iNTS disease in infants and very young children

Higher risk of both diseases at sites located in West Africa

Typhoid Fever Surveillance in Africa Program (TSAP) – further analysis

iNTS disease and malaria

✓ Positive correlation between frequency proportions of malaria and iNTS disease – observed at the TSAP sites endemic for malaria[1]



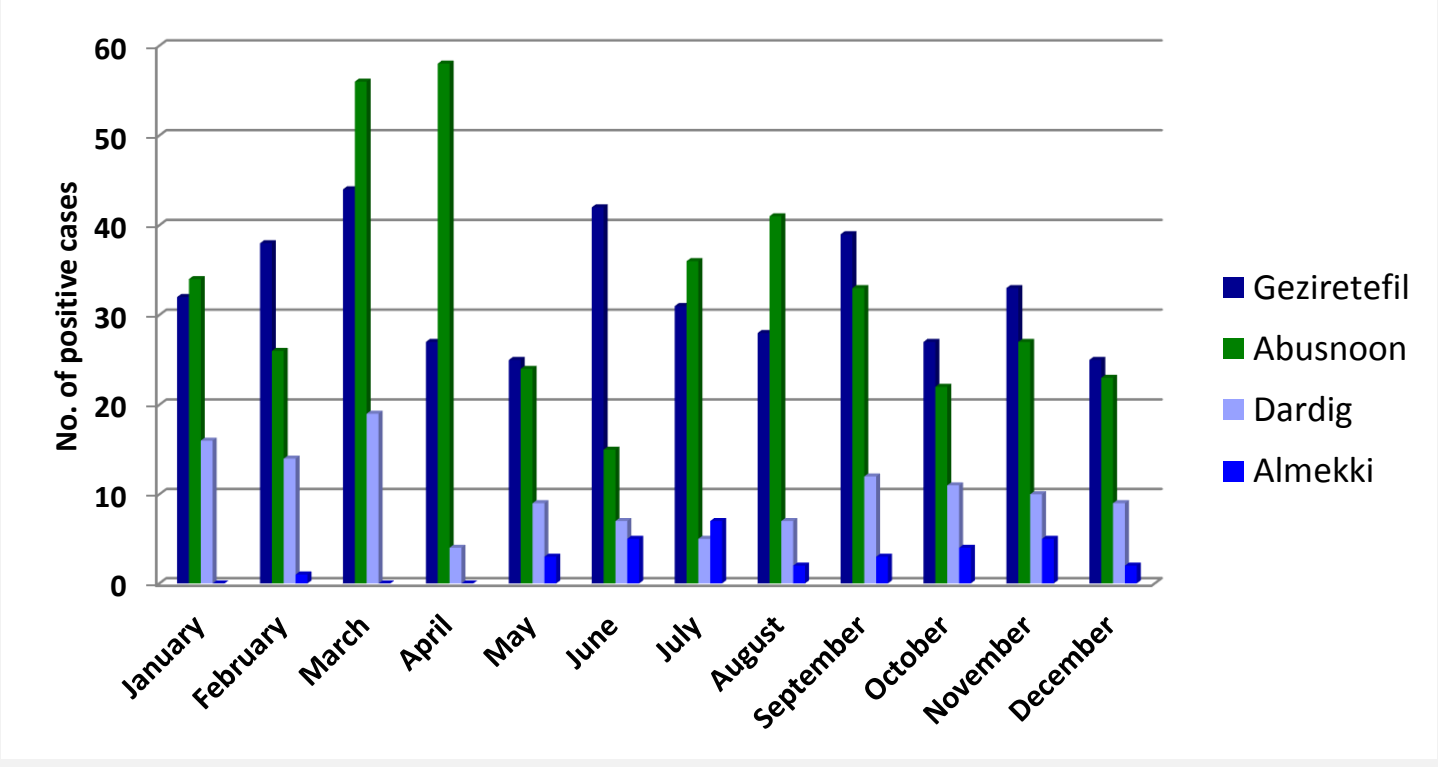
[1] Park SE, Pak GD, Aaby P, et al. *Salmonella* disease, other bloodstream infections, and malaria in sub-Saharan Africa. *Clin Infect Dis*. 2016; 62: S23

Widal test

Widal test – Commonly used in many countries

- ✓ Measures agglutinating antibodies specific to *S.* Typhi
- ✓ Difficult to know if the patient is in the acute phase
- ✓ Patients rarely demonstrate a 4-fold increase
- ✓ Not rapid (takes 14 days)
- ✓ Not standardized
- ✓ Negative in 30% of culture-confirmed cases
- ✓ Often done in a single tube
- ✓ Lacks sensitivity and specificity

Number of TF cases in the study area 2010



Annual reports Ministry of Heath Gezira State, 2010

Sudan, 2010

	Nioko II, Burkina Faso	Polesgo, Burkina Faso	Bandim, Guinea-Bissau	Pikine, Senegal	Asante Akim North, Ghana	East Wad Medani, Sudan	Butajira, Ethiopia	Imerintsiatosika, Madagascar	Isotry, Madagascar	Pietermaritzburg, South Africa	Moshi Urban District, Tanzania	Moshi Rural District, Tanzania	Kibera, Kenya*
(Continued from previous page)													
Laboratory results													
Total blood culture, N	918	756	1021	1058	2651	644	847	976	1501	1128	406	274	1251
Total contaminated blood cultures, n (% of N)	220 (24%)	145 (19)	125 (12%)	96 (9%)	182 (7%)	54 (8%)	90 (11%)	6 (1%)	49 (3%)	192 (17%)	8 (2%)	13 (5%)	16 (1%)
Total positive blood cultures, n (% of N)||||	29 (3%)	31 (4)	30 (3%)	31 (3%)	175 (7%)	16 (2%)	26 (3%)	11 (1%)	30 (2%)	51 (5%)	17 (4%)	11 (4%)	110 (9%)
Positive for malaria, n (% of all patients tested)***	430/908 (47%)	444/744 (60%)	206/525 (39%)	297/1058 (28%)	1139/2651 (43%)	254/632 (40%)	110/822 (13%)	19/955 (2%)	2/274 (1%)	0	4/406 (1%)	2/274 (1%)	226/956 (24%)

UoO=University of Ouagadougou, Ouagadougou. BHP=Bandim Health Project, Bissau. IPD=Institute Pasteur de Dakar, Dakar. KCCR/BNITM=Kumasi Centre for Collaborative Research in Tropical Medicine, Kumasi/Bernhard Nocht Institute for Tropical Medicine, Hamburg, Germany. UoG=University of Gezira, Wad Medani. AHRI=Armauer Hansen Research Institute, Addis Ababa. UoA=University of Antananarivo, Antananarivo. NICD=National Institute for Communicable Diseases, Johannesburg. KCMC/Duke=Kilimanjaro Christian Medical Center, Moshi/Duke University Medical Center, Durham, NC, USA. KEMRI/US-CDC=Kenya Medical Research Institute/US Centers for Disease Control and Prevention, Nairobi. IPD=inpatient department. OPD=outpatient department. HDSS=Health and Demographic Surveillance System. KEMRI=Kenya Medical Research Institute. NA=not available. *In Kibera, active population mobilisation was done in addition to passive surveillance. †Setting reflects the classification commonly used at each site and does not refer to a standard definition. ‡Surveillance activities were scheduled for 12 months in Burkina Faso, Guinea-Bissau, Senegal, Sudan, Ethiopia, and Madagascar and for 24 months in Ghana, Kenya, South Africa, and Tanzania. If funds allowed, the scheduled period was extended. §Population data were provided from the HDSS country office. ¶Population data for Senegal and Madagascar were provided by Ministry of Health. Population data correspond to the 2012 population census and 2010 estimated population for the area, respectively. ||Population data for Ghana were obtained from the Ghana Statistical Service, 2010 population, and housing census. It includes 53 towns distributed in what is now Asante Akim North and Central. **Population data for Sudan were provided by the Statistics Department, Population Center, University of Gezira, Sudan, and correspond to year 2008. ††Population data for South Africa were provided by the Statistics Department in South Africa and corresponds to the 2011 census. ‡‡Population data for Tanzania were provided by the National Bureau of Statistics and correspond to the 2012 population and housing census. §§Patients who met inclusion criteria, consented to take part in the study, and had a blood culture taken and a documented blood culture result. ¶¶Recruitment health-care facility providing outpatient services only. ||||Positive for non-contaminant isolates. ***Denominator differs from all blood cultures analysed because of missing values. Malaria results are based on blood smears, except for the site in Butajira (52% of patients positive for malaria were diagnosed with malaria rapid tests).

Table 1: **Demographics and laboratory results of the sites in the Typhoid Fever Surveillance in Africa Program**

[1]Incidence of invasive *Salmonella* disease in sub-Saharan Africa: a multicenter population-based surveillance study. *LANCET Global Health* 2017; 5: e310-23.

Sudan, 2010

	Proportion of individuals from study population visiting recruitment facility in case of fever (95% CI)	PYO estimation			Recruitment proportion	*Salmonella* Typhi				iNTS			
		Study population	Study population adjusted by health-seeking behaviour	PYO		Crude cases	Crude incidence per 100 000 PYO	Cases adjusted for recruitment	Adjusted incidence per 100 000 PYO (95% CI)	Crude cases	Crude incidence per 100 000 PYO	Cases adjusted for recruitment	Adjusted incidence per 100 000 PYO (95% CI)
(Continued from previous page)													
Asante Akim North, Ghana													
0–1 years	16% (14–18)	11 222	1760	4080	41%*	2	49	4·9	120 (49–290)	29	711	70·7	1733 (1373–2188)
2–4 years	16% (13–18)	8086	1268	2940	41%*	13	442	31·7	1079 (762–1528)	23	782	56·1	1908 (1469–2479)
5–14 years	16% (15–17)	34 439	5415	12 554	623/1657 (38%)	15	119	39·5	314 (230–430)	7	56	18·4	147 (93–232)
<15 years	NA	53 747	8443	19 574	NA	30	153	76·1	389 (310–486)	59	301	145·3	742 (631–873)
≥15 years	NA	NA†	NA	NA	NA	NA†	NA	NA	NA	NA†	NA	NA	NA
All	NA	NA†	NA	NA	NA	NA†	NA	NA	NA	NA†	NA	NA	NA
Pikine, Senegal‡§													
0–1 years	39% (32–46)	20 120	7837	11 194	NA	0	0	NA	NA	0	0	NA	NA
2–4 years	37% (33–41)	30 180	11 097	15 851	NA	0	0	NA	NA	0	0	..	NA
5–14 years	31% (28–34)	96 152	29 807	42 577	NA	3	7	NA	NA	1	5	..	NA
<15 years	NA	146 452	48 741	69 623	NA	3	4	NA	NA	0	0	..	NA
≥15 years	30% (28–31)	195 726	58 718	83 874	NA	4	5	NA	NA	3	6	..	NA
All	NA	342 178	107 459	153 496	NA	7	5	NA	NA	4	5	..	NA
East Wad Medani, Sudan§													
0–1 years	23% (14–32)	2377	537	589	2/85 (2%)	0	0	0·0	0 (0–0)	0	0	0·0	0 (0–0)
2–4 years	22% (15–29)	3566	781	857	29/108 (27%)	0	0	0·0	0 (0–0)	0	0	0·0	0 (0–0)
5–14 years	25% (21–28)	11 071	2735	2999	160/234 (68%)	0	0	0·0	0 (0–0)	0	0	0·0	0 (0–0)
<15 years	NA	17 014	4053	4445	NA	0	0	0·0	0 (0–0)	0	0	0·0	0 (0–0)
≥15 years	29% (27–31)	29 843	8684	9525	131/147 (89%)	0	0	0·0	0 (0–0)	0	0	0·0	0 (0–0)
All	NA	46 857	12 737	13 970	NA	0	0	0·0	0 (0–0)	0	0	0·0	0 (0–0)

[1]Incidence of invasive *Salmonella* disease in sub-Saharan Africa: a multicenter population-based surveillance study. *LANCET Global Health* 2017; 5: e310-23.

Widal test does not reflect bloodculture-based results

Lessons learnt in conducting typhoid surveillance

Site selection

- Selection bias
- Representativeness
- Determining a denominator, catchment area
- Local capacity

Quality of data

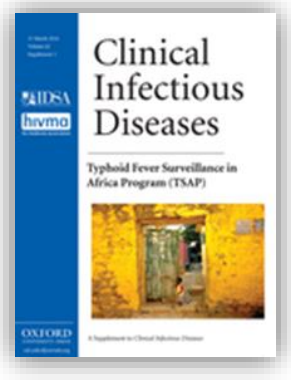
- Protocol adherence
- Difficult to screen all febrile patients
- Period of surveillance: Variable disease burden in adjacent sites/between years
- Severe cases in tertiary care facilities

Case definition/ diagnostics

- Limited resources for blood culture
- Large volume of blood required
- Contamination
- Antibiotic pre-treatment
- Logistics of sample transport

Typhoid Fever Surveillance in Africa Program (TSAP) – Value and implications

TSAP
(2010-2014)



THE LANCET Global Health

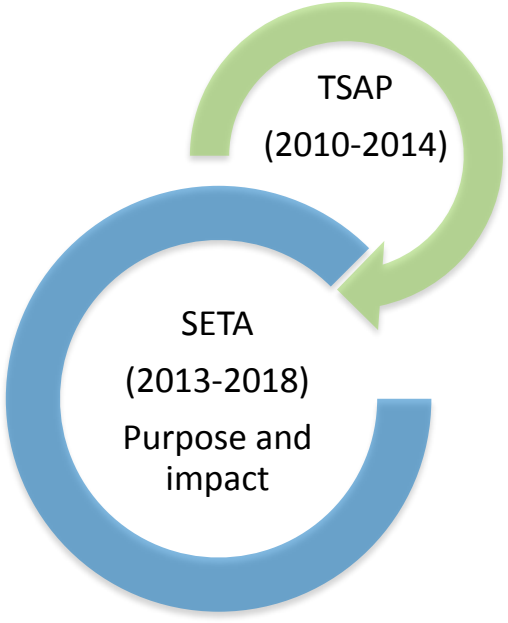
Added value

- ✓ Most comprehensive standardized analysis of the incidence and antimicrobial resistance patterns of invasive *Salmonella* infections in sub-Saharan Africa
- ✓ Results used by key stakeholders to decide on potential subsidies for typhoid fever vaccines

Implications of the evidence

- ✓ Results underscore the need for preventive measures, including vaccines
- ✓ Emphasize the potential increase of drug-resistance *Salmonella* strains in the region
- ✓ Need to further assess the severity and mortality of the disease

Severe Typhoid in Africa Program (SETA) – filling the gaps on severity and mortality



Filling the gaps on severity and mortality

- ✓ Network of surveillance sites across 6 countries in sSA
- ✓ To estimate the severity, immune response, long-term sequelae and the associated costs of invasive *Salmonella* infections in sub-Saharan Africa
- ✓ Further assessment of the incidence in infants
- ✓ Essential evidence for key stakeholders (WHO, GAVI) to develop prevention strategies including a strategy for advent typhoid vaccines.

Summary

Invasive *Salmonella* infections in sub-Saharan Africa

- ✓ TSAP results - invasive *Salmonella* infections are a major cause of invasive bacterial febrile illness in the sampled locations, specially in children, with incidence rates higher than previously estimated.
- ✓ This evidence will be used by key stakeholders to make decisions on introduction of available and advent vaccines against typhoid fever disease.
- ✓ Knowledge gaps on disease severity, mortality and associated costs are being assessed by SETA.

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