

One Health meta-analysis of pooled prevalence of *Salmonella* Typhi and high-priority strains in Nigeria and systematic review of alternative therapeutics

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Abstract

Background:

Salmonella enterica serovar Typhi (S. Typhi) infection has profound clinical and public health consequences, especially the WHO high-priority strains resistant to fluoroquinolones (FLQ) and third-generation cephalosporins (3GC). This study used meta-analysis to understand two decades of One Health epidemiology of S. Typhi in Nigeria.

Methods:

All 91 eligible original research articles published between 2005 and 2024 were scrutinised, data extracted and analysed using random-effects models and bivariate regressions following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.

Results:

The overall pooled prevalences (PPs) of culture-confirmed S. Typhi in humans, food, environmental samples and livestock in Nigeria were 6.2%, 6.1%, 12.1%, and 0.2%, respectively. The PP of S. Typhi varied significantly by geopolitical zone in Nigeria, with the highest in the southeastern zone (16.3%). The PP of FLQ and 3GC resistance among all non-duplicated S. Typhi isolates ranged from 25%–64% and 35.9%–58.4%, respectively. Subgroup analyses showed that the PP of culture-confirmed S. Typhi in healthy or asymptomatic humans (4.6%) was significantly lower (OR = 0.54, $p < 0.001$) than in sick or symptomatic humans (6.1%). We observed significant temporal variation ($p < 0.0001$) in S. Typhi PPs in humans, with the highest PPs in 2015–2019 (11.5%). Plant-based food had a significantly higher PP of S. Typhi contamination than animal-based food (15.8% versus 3%, OR = 7.78, 95% CI: 5.39–11.24, $p < 0.0001$). Among environmental samples, non-drinking water from tap, well, river and pond had the highest PP of S. Typhi contamination (39.3%) with no significant heterogeneity ($p > 0.001$).

Conclusion:

Data from this study indicate widespread persistence of S. Typhi in One Health niches in Nigeria, with environmental samples being its major reservoir. Given the high frequency of FLQ and 3GC resistance in S. Typhi isolates, we recommend developing, re-evaluating, and potentially adopting non-antibiotic therapeutic approaches against S. Typhi.

1.0 INTRODUCTION

Typhoid fever, clinically termed enteric fever, is an invasive systemic infection caused by the motile, Gram-negative bacillus *Salmonella enterica* serovar Typhi [1]. The bacterium belongs to the order Enterobacterales and the genus *Salmonella*, which contains more than 2,600 serovars; *Salmonella enterica* subspecies *enterica* causes over 90% of human and animal infections [2]. S. Typhi is conventionally viewed as a human-restricted pathogen [3], but modern studies show it can persist and spread via indirect environmental and water-associated One Health pathways [4–6]. Moreover, it can cross the placental barrier from an infected mother to the foetus, leading to severe complications like miscarriage, stillbirth, or neonatal sepsis [7–9].

Globally, enteric fever is most common in densely populated, underprivileged regions with inadequate sanitation facilities. Currently, the regions with the highest rates of typhoidal *Salmonella* infection are South-Central Asia, Southeast Asia, and Southern Africa [10]. Typhoid fever is a major driver of mortality in developing nations, though the true epidemiological burden of this classification depends heavily on the diagnostic and empirical methods used across clinical settings [11].

An estimated 12.5 to 16.3 million cases of typhoid fever occur worldwide each year, resulting in approximately 140,000 fatalities [12]. Nigeria is classified as hyperendemic, with an average general incidence rate of roughly 100 cases per 100,000 population [13]. Population-adjusted modelling data from specific urban regions, like Ibadan, show an incidence

rate of 42 per 100,000 [14]. However, documented prevalence varies widely by location and studies [1]. These indices are highly unlikely to reflect the actual *S. Typhi* burden, as definitive diagnostic gold standards remain largely unavailable across the country's rural and peri-urban communities [13, 14].

S. Typhi infection burden is structurally sustained by critical deficits in domestic water, sanitation, and hygiene (WASH) programs, along with inadequate public awareness and fragmented disease surveillance systems [15, 16]. Comprehensive laboratory investigation of enteric fever requires collecting high-quality clinical specimens, including blood, stool, urine, and bone marrow aspirates, for definitive microbiological culture and antimicrobial susceptibility testing [12]. In resource-limited endemic regions like Nigeria, the lack of definitive diagnostic methods forces healthcare facilities to rely heavily on clinical symptoms [17]. Consequently, patients are frequently misdiagnosed due to the profound symptomatic overlap between typhoid and other prevalent febrile pathologies, most notably acute malaria [5]. Although laboratory confirmation relies on isolating *S. Typhi* via blood culture or identifying its specific DNA through molecular techniques like Polymerase Chain Reaction (PCR), routine use of these tools remains severely limited [18].

Because of these infrastructure gaps, the continued use of the serological Widal test across Nigeria has institutionalized a cycle of patient misdiagnosis [19]. This systemic diagnostic inaccuracy directly correlates with an escalating risk of regional antimicrobial resistance (AMR), as broad-spectrum antibiotics are routinely prescribed based on false-positive serological profiles [17, 20].

AMR in typhoid fever causes treatment failure, severe complications, and higher medical costs because standard, affordable drugs no longer kill *S. Typhi*. Multidrug-resistant *S. Typhi* (resistance to first-line antimicrobials: chloramphenicol, trimethoprim-sulfamethoxazole, and ampicillin) was first identified in the 1970s [21]. Lower efficacy of first-line antimicrobials led to the increased use of fluoroquinolones, but decreased susceptibility to fluoroquinolones in *S. Typhi* due to chromosomal mutations, widespread drug use, and clonal expansion has largely replaced older multidrug-resistant strains globally [22]. As treatment options have become limited, third-generation cephalosporins and azithromycin have been used more widely to treat typhoid fever. However, newly circulating extensively drug-resistant (XDR; MDR plus resistance to fluoroquinolones and third-generation cephalosporins) variants of *S. Typhi* have left azithromycin as the only feasible oral antimicrobial for treating typhoid fever across many developing countries [21, 23].

In response to this global threat, the World Health Organization has designated fluoroquinolone (FLQ) and third-generation cephalosporin (3GC) resistance in *S. Typhi* as a high and critical priority within global antimicrobial resistance frameworks [24]. Understanding the extent of FLQ and 3GC resistance is key to classifying *S. Typhi* as a major threat to national and global health. Widespread reliance on suboptimal diagnostic assays obscures whether current epidemiological metrics reflect genuine hyperendemicity or a statistical artifact of clinical overdiagnosis [1, 17]. This study used the Preferred Reporting Items for Systematic Reviews and Meta-Analyses to determine the pooled prevalence of *S. Typhi* infection in humans and contamination in food, livestock, and environmental samples in Nigeria. It examines how well documented *S. Typhi* endemicity in Nigeria reflects the true burden. Moreover, it estimates the pooled prevalence of FLQ and 3GC resistance in non-duplicated *S. Typhi* isolates while systematically evaluating its downstream relationship with regional antibiotic overuse.

2.0 METHODOLOGY

This study has two parts: a systematic review and meta-analysis of pooled prevalence data for *S. Typhi* from culture-confirmed analyses in Nigeria and the corresponding 3GC- and FLQ-resistant strains. Data from studies on the Widal test as a means of determining *S. Typhi* were excluded from the meta-analysis. The second part was a systematic literature review on the ecological epidemiology, drivers, and contemporary non-antibiotic therapeutics currently applied against *S. Typhi* and their potential in Nigeria.

This systematic review and meta-analysis included original research and brief communication articles reporting the investigation and/or detection of *S. Typhi* in Nigeria, regardless of host or sample type, and the frequency of FLQ and 3GC resistance in *S. Typhi*. Samples from ill (febrile and/or diarrhoeal) people living with HIV and AIDS, and healthy humans, including food handlers and abattoir workers, were included. Concerning animals, studies included those that analysed poultry faeces, droppings, and cloacal samples, as well as pigs' and cattle's faeces. Food materials included poultry meat, vegetables, soy milk, smoked fish, animal feed, milk and milk products.

The entire process, including the literature search strategy, selection of appropriate published articles, data extraction, and presentation of results, adhered to the guidelines outlined in the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) (<http://prisma-statement.org/PRISMAstatement/checklist.aspx>), accessed on 20th January 2025. Relevant studies published from 2005–2024, encompassing *Salmonella enterica* serovar Typhi (*S. Typhi*) and its FLQ- and 3GC-resistant strains, were searched and scrutinised in the Scopus, Web of Science, Google Scholar, and PubMed databases. The following word combinations were used: “*S. Typhi* faecal, cloacal, caecal carriage in animal Nigeria”, “ciprofloxacin-resistant Typhi Nigeria”, “ofloxacin-resistant Typhi Nigeria”, “levofloxacin-resistant Typhi Nigeria”, “pefloxacin-resistant Typhi Nigeria”, “ceftriaxone-resistant Typhi Nigeria”, “cefotaxime-resistant Typhi Nigeria”, “ceftazidime-resistant Typhi Nigeria”, “cefixime-resistant Typhi Nigeria”, “Typhi Nigeria”, “Typhoid fever Nigeria”, Typhoid septicaemia Nigeria”, diarrhoea typhoid Nigeria”, “Water Typhoid contamination Nigeria”, “*S. Typhi* wastewater Nigeria”.

Of the initial 934 hits, we eliminated 852 articles because they did not pertain to *S. Typhi* in Nigeria or had inadequate methodology (Figure S1). After this screening process, 91 studies (42 on humans, 12 on livestock, 19 on foods, 18 on water and environmental samples, and 1 on pets) met the selection criteria and were included for the meta-analyses (Table 1a-e). Remarkably, data from five studies (in asterisks) involved two or more ecological niches, such as human and livestock, human and food, or environmental and food samples (Table 1a-e). Moreover, we found 17 articles eligible for the systematic review of non-antibiotic approaches against *S. Typhi*. For articles utilized for meta-analyses, we assessed the eligible studies using a point-scoring system with eight items, with a total score ranging from 0–8, as previously described by Yang *et al.* [25]. Based on this, we graded each study as low- or high-risk of bias (quality). The total score ranges from 0–8 points, and the higher the score, the higher the quality and the lower the risk of bias. Studies with a total score of < 4 points were considered high risk (low quality), while those with a score of ≥ 4 points were considered high quality (low risk).

Data from these studies were used to compute the pooled prevalence (PP) of *S. Typhi* from the four host groups (humans, food, environmental samples, and livestock), ciprofloxacin-resistant *S. Typhi*, ofloxacin-resistant *S. Typhi*, pefloxacin-resistant *S. Typhi*, ceftriaxone-resistant *S. Typhi*, cefixime-resistant *S. Typhi*, ceftazidime-resistant *S. Typhi*, and by geopolitical zones and temporal trends in Nigeria from 2005 to 2024. In eligible studies, the disc diffusion method was used to determine zones of inhibition for the AMR profile.

We used Comprehensive Meta-Analysis (CMA) version 4 (NJ 07631 USA) and MedCalc version 23.0.2 (Ostend, Belgium) for all statistical analyses. Every statistical test used two-tailed testing. $P < 0.05$ was regarded as statistically significant unless otherwise indicated. We used random-effects models to estimate pooled prevalences (PPs) and 95% confidence intervals (CIs). A non-duplicated sample refers to a single sample collected from an individual host. We excluded studies that analysed duplicated samples from this meta-analysis. We conducted a subgroup analysis across study categories with significant heterogeneity. To assess publication bias, we used Egger's test on the funnel plot.

Table 1

Description of eligible studies showing the number of hosts with *S. Typhi* and fluoroquinolone- and third-generation-resistant strains Humans

Reference	Geopolitical zone	Study type	Host type/ sample type	No. of subjects tested	Laboratory methods	No. (%) of non- duplicate <i>S. Typhi</i>	Risk of bias	
[26]	NC/ Ilorin	Cross-sectional	Sick / blood	400	C, B, DD	8	3 (high)	CXM (1), OFL (2)
[27]	NW/ Kano	Cross-sectional	Food handlers/ hand swab	200	C, B	60	2 (high)	NT
[28]	NC/ Nasarawa	Cross-sectional	Febrile patients	400	C, DD, PCR	2	6 (low)	NC
[29]	SW/ Osun	Cross-sectional	diarrhoeal patients	187	C, DD, PCR	7	2 (low)	CXN (5), PEF (4), CIP (2), OFL (4)
[30]	SS/ Rivers	Cross-sectional	Food handlers	480	C, B	30	4 (high)	NT
[31]	SE/ Enugu	Prospective	Asymptomatic	60	C, B	10	4 (high)	NT
[32]	SW/ Lagos	Prospective	Asymptomatic	30	PCR	0	5 (low)	NT
[33]	NW/ Katsina	Cross-sectional	Febrile	300	C, B, PCR, DD	9	3 (low)	OFL (9)
[34]	NW/ Kaduna	Cross-sectional	Febrile	220	C, B, PCR, DD	16	2 (low)	CXN (7), CXM (9), OFL (2), CIP (2)
[35]	NC (Abuja) and NW (Kano)	Cohort	Febrile children	10133	C, S, DD	280	1 (low)	NC
[36]	NC/ Jos	Prospective	Febrile	60	C, B, DD	12	3 (high)	OFL (9), CIP (8), CXM (7), CFD (3)
[37]	SW/ Ibadan	Prospective	Diarrhoeal patients and healthy population	394	C, B, DD, PCR	0	1 (low)	NT

Reference	Geopolitical zone	Study type	Host type/ sample type	No. of subjects tested	Laboratory methods	No. (%) of non- duplicate S. Typhi	Risk of bias	
[12]	SE/ Enugu	Cohort	Febrile patients and healthy population	1098	C, B, DD	42	2 (low)	CXN 81), CXM (23), CFD (9), CIP (0), OFL (6), LEV (0)
[38]	NC/ Nasarawa	Prospective	Asymptomatic	125	C, B	94	2 (high)	NT
[39]	SW/ Ekiti	Cohort	Asymptomatic	510	C, B, DD	195	2 (high)	CFD (118), CIP (26), OFL (32), CXM (68)
[40]	NC/ Benue	Cohort	Sick	1022	C, B	583	3 (high)	NT
[41]	NE/ Bauchi	Cross- sectional	Febrile	150	C, B	7	3 (high)	NT
[42]	NC/ Plateau	Cross- sectional	Febrile	300	C, B	9	3 (high)	NT
[43]	NW/ Kano	Prospective	Febrile children	37	C, B, DD	22	3 (high)	NC
[44]	NW/ Kaduna	Cross- sectional	250 febrile patients and 50 asymptomatic individuals	300	C, B	25	3 (high)	NT
*[45]	NC/ Abuja, SW/ Lagos	Prospective	Abattoir workers	118	C, S, PCR	0	1 (low)	NT
[46]	NW/ Kaduna	Cohort	Sick individuals	420	C, B, PCR	5	1 (low)	NT
[47]	SW/ Lagos	Cross- sectional	Asymptomatic food handlers	358	C, B, PCR	0	1 (low)	NT
[48]	NC/ Plateau	Prospective	Sick individuals	91	C, B, DD	21	3 (high)	CIP (5), OFL (5), CXN (6), CFD (16), CXM (9)
[49]	SW/ Lagos	Prospective	Febrile patients	125	C, B, PCR	0	2 (low)	NT

Reference	Geopolitical zone	Study type	Host type/ sample type	No. of subjects tested	Laboratory methods	No. (%) of non- duplicate S. Typhi	Risk of bias	
[50]	SW/ Osun	Cross-sectional	PLWHA diarrhoea	390	C, B, DD	3	5 (low)	CXN (0), CIP (0), OFL (0)
[51]	SS/ Akwa Ibom	Prospective	Abattoir workers	90	C, B, PCR, DD	4	2 (low)	CIP (0), CXN (0), CFD (0)
[52]	NC/ Nasarawa	Cohort	Febrile patients	400	C, B, PCR	2	3 (low)	NT
[53]	SW/ Osun	Cross-sectional	Healthy school children	120	C, B, PCR	0	1 (low)	NT
[54]	SW/ Lagos	Cohort	Sick individuals	1042	C, B, PCR	0	1 (low)	NT
[55]	NE/ Bauchi	Prospective	Sick individuals	135	C, B	14	3 (high)	NT
[56]	NE/ Yobe	Prospective	Sick individuals	233	C, B, DD, PCR	35	2 (low)	CFD (15), CXM (18), CIP (16), PEF (10), CXN (13)
[57]	NW/ Kano	Prospective	Febrile patients	125	C, B	17	3 (high)	NT
[58]	SS/ Cross River	Cohort	Food handlers	1500	C, B	30	3 (high)	NT
[59]	NC/ Nasarawa	Cross-sectional	Sick patients	252	C, B	158	3 (high)	NT
[60]	SW/ Oyo	Cohort	Febrile patients	682	C, B, DD	27	5 (low)	CXM (4), CIP (19)
[61]	SE/ Abia	Cross-sectional	Febrile patients	135	C, B, DD	72	3 (high)	CIP (30), OFL (25), CXN (49), CXM (51), CFD (47)
[62]	SE/ Imo	Cross-sectional	Febrile patients	150	C, B, DD	27	3 (high)	OFL (3)

Reference	Geopolitical zone	Study type	Host type/ sample type	No. of subjects tested	Laboratory methods	No. (%) of non- duplicate S. Typhi	Risk of bias	
[63]	NC/ Niger	Cros- sectional	Febrile patients	100	C, B, DD	45	3 (high)	NC
[64]	SW/ Lagos	Cohort	Sick patients	3000	C, B, DD	233	3 (high)	NC
[65]	SW/ Lagos	Cohort	Sick patients (febrile and gastroenteritis)	441	C, B, DD	19	5 (low)	CIP (3), OFL (3), CXM (12)
[66]	SW/ Lagos	Cohort	Febrile children	420	C, B, DD	56	5 (low)	NC
[67]	SE/ Ebonyi	Cohort	Febrile children	782	C, B, DD	98	3 (high)	CFD (89), CXM (69), OFL (1), CIP (10)
[68]	NC/ Plateau	Cohort	Sick patients	8935	C, B, DD	7	3 (high)	CXN (7), CIP (7)

1. Food

Reference	Geopolitical zone	Study type	Host type/ sample type	No. of subjects tested	Laboratory methods	No. (%) of non-duplicate S. Typhi	Risk of bias	FLQ and 3GC resistance in S. Typhi (number of isolates)
[69]	SS/ Benin city	Cross-sectional	Poultry meat	250	C, B, PCR, DD	0	5 (low)	NT
[70]	NW/ Kano	Surveillance	Vegetables	238	C, B, PCR, DD	22	6 (low)	NC
[71]	SW/ Ondo	Surveillance	Soy milk	5	C, B	2	3 (high)	OFL (1), CIP (0), CFD (2), CXN (0)
[72]	NW/ Katsina	Prospective	Smoked fish and meat	20	C, DD	0	3 (high)	NT
[73]	SW/ logos	Prospective	Animal feed	8	C, B	2	3 (high)	NT
[74]	SW/ Osun	Prospective	Milk and milk products	30	C, B, PCR, DD	4	2 (low)	
[75]	SW/ Osun	Cross-sectional	Eggs	500	C, B	0	3 (low)	NT
[76]	NE/ Adamawa	Cross-sectional	Milk	122	C, PCR	3	2 (low)	NT
[77]	SW/ Lagos	Prospective	Raw meat	128	C, PCR	0	2 (low)	NT
[78]	NW/ Maiduguri	Cross-sectional	Fish/flesh	200	C, MIC	0	5 (Low)	NT
[79]	SE/ Anambra	Prospective	Fish/ flesh	24	C, B	0	2 (high)	NT
[80]	SE/ Anambra	Prospective	Fish/ flesh	120	C, B	0	2 (high)	NT
[81]		Prospective	Fish/ intestine	60	C, B	7	3 (high)	NT
[82]	NE/ Yobe	Prospective	Vegetable leaves and tomatoes, peppers and carrots	360	C, B, PCR, DD	67	6 (low)	CIP (15) OFL (3)
[83]	NC/ Kwara	Prospective	Ready-to-eat Chicken and gizzard	500	C, B, PCR, DD	0	6 (low)	NT
[84]	NE/ Bauchi	Prospective	Cow milk	50	C, B	23	3 (high)	NT
[85]	SW/ Ogun	Prospective	Fresh fish	45	C, B	3	3 (high)	NT

Reference	Geopolitical zone	Study type	Host type/ sample type	No. of subjects tested	Laboratory methods	No. (%) of non-duplicate S. Typhi	Risk of bias	FLQ and 3GC resistance in S. Typhi (number of isolates)
[86]	SW/ Ekiti	Prospective	Fermented milk	5	C, B	0	3 (high)	NT
[87]	SW/ Oyo	Prospective	Fish	6	C, B	6	3 (high)	NT

1. Environmental samples

Reference	Geopolitical zone	Study type	Host type/ sample type	No. of subjects tested	Laboratory methods	No. (%) of non- duplicate S. Typhi	Risk of bias	FLQ and 3GC resistance in S. Typhi (number of isolates)
[70]	NW/ Kano	Surveillance	Irrigation water, Manure soil	202	C, PCR, DD	12	6 (low)	NC
[88]	NW/ Zaria	Surveillance	Water	5	C, B	3	2 (high)	NT
[89]	NW/ Zaria	Surveillance	Water	5	C, B	1	2 (high)	NT
[90]	NW/ Sokoto	Surveillance	Meat contact surfaces and processing water	260	C, B	12	Low (5)	NT
[91]	NC/ Benue	Prospective	Hostel tap water	20	C, B	18	2 (high)	OFX (4), CIP (7), SPR (7), PEF (18)
[92]	NW/ Kaduna	Prospective	Drinking water	87	P	1	8 (low)	NT
[93]	NW/ kano	Prospective	Household drinking water	212	C, B	9	2 (high)	NT
[94]	SE/ Anambra	Prospective	Water	220	C, B	5	5 (low)	NT
[95]	NW/ Zamfara	Prospective	Sachet water	16	C, B	3	2 (high)	NT
[96]	NC/ Abuja	Prospective	River water	1	C, B	1	2 (high)	NT
*[45]	NC/ Abuja, SW/ Lagos	Prospective	Abattoir environment	58	C, B, PCR	0	7 (low)	NT
[97]	SS/ Bayelsa	Prospective	River and borehole water	7	C, B	4	2 (high)	Cip (0), CXM (2)
[98]	NW/ Kaduna	Prospective	Well water	10	C, B	0	2 (high)	NT
[99]	NC/ Kwara, Benue, Plateau	Cohort	Poultry drinking water	100	C, B, PCR	0	1 (low)	NT
[100]	NC/ Benue	Prospective	Surface swabs of eateries and restaurants	225	C, B	52	2 (high)	NT
[54]	SW/ Lagos	Prospective	Effluent	100	C, P	0	1 (low)	NT

Reference	Geopolitical zone	Study type	Host type/ sample type	No. of subjects tested	Laboratory methods	No. (%) of non- duplicate S. Typhi	Risk of bias	FLQ and 3GC resistance in S. Typhi (number of isolates)
[87]	SW/ Oyo	Prospective	Pond	4	C, B	1	3 (high)	NT
[101]	SE/ Ebonyi	Prospective	Well water	10	C, B, PCR, DD	10	5 (low)	CFD (7), CIP (1), CXM (10)

1. Livestock

Reference	Geopolitical zone	Study type	Host type/ sample type	No. of subjects tested	Laboratory methods	No. (%) of non- duplicate S. Typhi	Risk of bias	FLQ and 3GC resistance in S. Typhi (number of isolates)
[102]	NC/ Kwara	Cross-sectional	Poultry cloacal sample	900	C, B, DD	0	5 (low)	NT
[103]	SW / Ogun	Cross-sectional	Poultry faeces	200	C, B, DD	0	5 (low)	NT
[104]	NC/ Kwara	Cross-sectional	Poultry and pigs faeces	1500	C, B, DD, PCR	0	6 (low)	NT
[105]	NW/ Kebbi, Zamfara and Sokoto	Cross-sectional	Poultry faeces	558	C, B, DD, PCR	0	6 (low)	NT
*[37]	SW/ Ibadan	Prospective	Cattle faeces	422	C, B, DD, PCR	0	5 (low)	NT
[106]	NC/ Plateau	Cross-sectional	Poultry droppings	150	C, B	0	3 (high)	NT
[107]	SW/ Ogun	Cross-sectional	Poultry droppings	100	C, B, DD, PCR	9	6 (low)	CIP (2)
*[45]	NC/ Abuja, SW/ Lagos	Prospective	Cattle	272	C, B, PCR	0	1 (low)	NT
[47]	SW/ Lagos	Cross-sectional	Livestock	306	C, B, PCR	0	1 (low)	NT
[99]	NC/ Kwara, Benue, Plateau	Cohort	Poultry	1108	C, B, PCR	0	1 (low)	NT
[54]	SW/ Lagos	Prospective	Cattle Poultry	270	C, B, PCR	0	1 (low)	NT
[108]	SE/ Enugu	Prospective	Poultry droppings	80	C, B, DD	0	3 (high)	NT

1. Pets

Reference	Geopolitical zone	Study type	Host type/ sample type	No. of subjects tested	Laboratory methods	No. (%) of non-duplicate <i>S. Typhi</i>	Risk of bias	FLQ and 3GC resistance in <i>S. Typhi</i> (number of isolates)
[109]	SW/ Oyo	Prospective	Dogs	458	C, B, PCR, DD	0	3 (high)	NT

Key:

NT: Not tested

NC: Not clearly described

SW: Southwest

SS: Southeast

SS: South-south

NC: Northcentral

NE: Northeast

NW: Northwest

C: Culture

B: Biochemistry

D: Disk diffusion

SPR: Sparfloxacin

CIP: Ciprofloxacin

OFL: Ofloxacin

PEF: Pefloxacin

Lev: levofloxacin

CXN: Ceftriaxone

CXM: Cefixime

CFD: ceftazidime

RESULTS

The prevalence of culture-confirmed *S. Typhi* in humans in Nigeria from eligible studies ranged from 0%–75.2% (95% CI: 66.9–82), with significant heterogeneity among the studies (Cochrane $Q = 3854.4$, $P < 0.001$) (Fig. 1a). The overall pooled prevalence (PP) of culture-confirmed *S. Typhi* in humans in Nigeria was 6.2% (95% CI: 3.8–9.9) among 44 eligible studies (Fig. 1a). The PP of culture-confirmed *S. Typhi* in food samples was 6.1% (95% CI: 3.2–11.5), while it was 12.1% (CI: 5.8–

23.5) in environmental samples. However, it was 0.2% (95% CI: 0–1) in livestock (Fig. 1b-d), all with significant heterogeneity ($p < 0.001$ for corresponding Cochrane Q values) (Supplementary Figures S2a-d).

The PPs of *S. Typhi* across the six geopolitical zones in Nigeria were 2.6%, 3.5%, 9.3%, 9.7%, 10.5%, and 16.3% in the southwest, south-south, north-central, north-east, northwest, and south-east, respectively (Fig. 2 and Supplementary Figures S3a-f).

The PP of ciprofloxacin, ofloxacin and pefloxacin resistance among all the non-duplicated *S. Typhi* isolates were 25%, 21% and 64%, respectively (Fig. 3a-c). PPs were 35.9%, 48.2%, and 58.4% for ceftriaxone, cefixime, and ceftazidime resistance, respectively, among all eligible non-duplicated *S. Typhi* isolates in Nigeria (Fig. 3d-f).

Subgroup analyses showed that the PP of culture-confirmed *S. Typhi* in healthy or asymptomatic humans (4.6%, 95% CI: 1.7–11.4) was significantly lower (OR = 0.54, 95% CI: 0.48–0.59, $p < 0.0001$) than in sick or symptomatic humans (6.1%, 95% CI: 3.5–10.5) (Table 2, supplementary figures S4a and b). A significant temporal variation ($p < 0.0001$) in the PPs of *S. Typhi* in humans was obtained of which the highest PP occurred from 2015–2019 (11.5%, 95% CI: 5–24.4) and lowest from 2020–2024 (4.5%, 95% CI: 2.9–7) compared to the PP of *S. Typhi* earlier than 2015 (4.9, 95% CI: 1.4–16.3) (Table 2, Supplementary Figs. 5a-c).

Plant-based food had a significantly higher PP of *S. Typhi* contamination than animal-based food (15.8% *versus* 3%, OR = 7.78, 95% CI: 5.39–11.24, $p < 0.0001$). Among environmental samples, non-drinking water from tap, well, river, and pond had the highest PP of *S. Typhi* contamination (39.3%) compared to drinking water (13.6%) and Surface swab, soil, effluent, and sewage (5.1%). Remarkably, the PP of *S. Typhi* in non-drinking water from tap, well, river, and ponds had a lower Cochran Q value (10.9) with no significant heterogeneity ($p > 0.001$) (Table 2, Supplementary Figs. 6a-c).

Table 2
Variability of pooled prevalences of *S. Typhi* by epidemiological variables in Nigeria

Category	Variables	No. of studies pooled	Pooled prevalence (%), 95% CI	Q value	P value of I^2	N°. without <i>S. Typhi</i>	N°. with <i>S. Typhi</i>	OR (95% CI)	P value of OR
Health status of human	Healthy or asymptomatic	14	4.6 (1.7–11.4)	526.6	< 0.0001	3670	417	1	1
	Sick or symptomatic	33	6.1 (3.5–10.5)	3176.8	< 0.0001	30503	1858	0.54 (0.48–0.59)	< 0.0001
Study Period of human studies	< 2015	8	4.9 (1.4–16.3)	406.3	< 0.0001	11539	165	1	1
	2015 to 2019	18	11.5 (5–24.4)	2930.2	< 0.0001	15182	1631	7.51 (6.38–8.83)	< 0.0001
	2020 to 2024	18	4.5 (2.9–7)	226.9	< 0.0001	7445	488	4.6 (3.83–5.48)	< 0.0001
Type of food	Animal-based food	15	3 (1–9.1)	117.1	< 0.0001	2014	46	1	1
	Plant-based food	3	15.8 (8.1–28.5)	11.5	0.003	512	91	7.78 (5.39–11.24)	< 0.0001
Environmental sample type	Drinking water	6	13.6 (2–54.4)	61.2	< 0.0001	406	34	1	
	Surface swab, soil, effluent and sewage	5	5.1 (1.6–15.3)	52.2	< 0.0001	769	76	1.18 (0.77–1.79)	0.4416
	Non-drinking water (tap, well, river and pond)	5	39.3 (10.9–77.3)	10.9	0.025	20	17	10.15 (4.87–21.17)	< 0.0001

DISCUSSION

4.1 Overview of Typhoid Fever in Nigeria

Typhoidal salmonellosis remains an enduring public health threat in Nigeria, operating as one of the most frequently diagnosed infectious causes of acute febrile illness across the country [1]. While *S. Typhi* infection occurs across all demographic groups, children, adolescents, and young adults carry a disproportionate share of the clinical burden [14].

The true epidemiological scale of *S. Typhi* varies significantly by geography (2.6 to 16.3%) across Nigeria's six geopolitical zones, with periodic localized outbreaks and predictable seasonal surges during the rainy months that peak in school-aged children in major urban settings [110]. Beyond acute morbidity, typhoid fever imposes a severe structural burden on the healthcare system due to high rates of severe complications, such as ileal perforation due to complications from XDR-*S. Typhi* [111]. Treating these conditions requires prolonged hospital stays and emergency surgery. This care creates catastrophic out-of-pocket costs and lost income for families, worsening poverty in endemic regions [110].

4.2 Socio-environmental factors sustaining *S. Typhi* endemicity

The most critical driver of transmission is the widespread deficit in water, sanitation, and hygiene (WASH) infrastructure. Many households depend entirely on untreated shallow wells, rivers, or boreholes that are highly susceptible to faecal contamination from unlined pit latrines, poor municipal sewage systems, and open defecation practices [112]. In this regard, our meta-analysis found that non-drinking water from tap, well, river, and pond had the highest PP of *S. Typhi* contamination. One possible reason is that old pipes mix sewage into public lines, and heavy rain washes surface waste into the ground [113]. Moreover, shallow wells catch farm runoff and animal faeces; flowing water carries waste from many upstream towns; heavy floods mix dirt and sewage straight into the current; still water traps germs and lets them grow; and cattle and wildlife drink and pollute the edges [114].

Rapid, uncontrolled urban expansion has outpaced municipal engineering, creating an imbalance that results in overcrowded, high-density peri-urban settlements where basic environmental sanitation facilities are insufficient to manage waste disposal for the growing population [14]. This may be linked to the exceedingly high pooled prevalence of *S. Typhi* in some geopolitical zones. Widespread consumption of street-vended foods, coupled with poor food hygiene and limited regulatory oversight of commercial food handlers, creates ongoing opportunities for foodborne contamination networks, with poor handwashing and unimproved water sources remaining major mathematical drivers of endemicity [15].

Individuals who recover from acute infection but continue to asymptotically harbour and shed *S. Typhi* in their stool serve as silent biological reservoirs, unknowingly maintaining transmission chains within their households and broader communities [15]. Given that the pooled prevalence of *S. Typhi* in healthy or asymptomatic individuals was 4.6% (95% CI: 1.7–11.4), a notable reservoir of hidden carriers exists in the community. These carriers sustain *S. Typhi* transmission, risk contaminating local food and water supplies, and complicate public health control efforts in endemic regions [115].

4.3. *S. Typhi* contamination of food compromises safety

Findings from this meta-analysis indicated that plant-based food had significantly higher *S. Typhi* contamination than animal-based food. While animal products are the primary natural reservoirs for non-typhoidal *Salmonella*, plant-based foods, especially raw produce irrigated or washed with tainted water, frequently show high rates of bacterial contamination [116]. However, *S. Typhi* is unique because it infects only humans, so plant and animal foods are usually contaminated through human faecal waste or polluted irrigation water rather than animal hosts. *S. Typhi* contamination in animal-based foods has been reported exclusively in fish, with some studies reporting 11.7% and 100% contamination rates [81, 87]. High *S. Typhi* contamination in fish stems primarily from exposure to polluted aquatic environments and poor post-harvest handling [117]. Consuming these contaminated fish poses severe public health risks and can lead to foodborne *S. Typhi* infections [118].

S. Typhi contamination in food compromises safety and is spread via contaminated water, unwashed raw produce, or infected food handlers with poor hygiene, posing major public health risks globally [119]. Investing in water infrastructure in rural Africa and tightening regulations on street food in urban centres can greatly reduce risk [120]. For long-term typhoid control, schools and high-risk populations must prioritize these tactics.

4.4 Geographic distribution

Typhoid fever is endemic throughout Nigeria, although this meta-analysis reports substantial geographic variation in endemicity, with the highest burden in the southeastern geopolitical zone and the lowest in the southwestern zone. The presence of *S. Typhi* across all geopolitical zones reflects the widespread distribution of environmental and socioeconomic conditions that favour transmission.

Available evidence suggests Nigeria may experience a high burden of *S. Typhi* because of rapid population growth, water scarcity, inadequate sanitation infrastructure, and limited access to healthcare [121]. Studies conducted in Kano State have identified local government areas with persistently high reported prevalence rates, suggesting localized transmission hotspots. Spatial analyses have linked these patterns to population density, socioeconomic deprivation, inadequate water infrastructure, and environmental conditions conducive to *S. Typhi* persistence [122, 123]. Reliable nationwide estimates of

typhoid incidence remain difficult to obtain because diagnostic practices vary considerably across healthcare facilities. Many healthcare institutions continue to rely heavily on serological methods such as the Widal test, while access to blood culture facilities (the diagnostic gold standard) remains limited. This diagnostic heterogeneity may contribute simultaneously to underestimation in some locations and overestimation in others, complicating efforts to accurately characterize the geographic burden of *S. Typhi* [120].

The epidemiology of typhoid fever differs considerably between rural and urban settings in Nigeria [124]. Urban areas, particularly informal settlements and densely populated slums, often experience elevated transmission risks because of overcrowding, inadequate sewage systems, poor drainage infrastructure, and contamination of communal water sources in Nigeria [125]. Rapid urbanization has outpaced sanitation infrastructure expansion in many Nigerian cities, creating conditions that facilitate sustained transmission of enteric pathogens [126].

In urban environments, high population density increases opportunities for human-to-human transmission through shared water sources, food vending activities, and inadequate waste disposal systems. Concentrating large populations in limited geographic areas may amplify outbreaks when water or food supplies become contaminated [120]. Rural communities face different but equally important challenges. Many rural populations depend on rivers, ponds, streams, rainwater collection systems, and shallow wells for domestic water needs [127]. These water sources are often vulnerable to *S. Typhi* contamination from human and animal activities [128].

Although urban centres frequently report more diagnosed cases, the true burden of *S. Typhi* in rural communities may be underestimated because surveillance systems are generally weaker and access to laboratory confirmation is often limited [129]. Consequently, typhoid fever remains an important public health problem across both rural and urban populations in Nigeria.

4.5. Diagnostic challenges and misdiagnosis cascade in Nigeria

The initial clinical manifestations of typhoidal salmonellosis, such as high-grade fever, headache, abdominal pain, and malaise, are highly nonspecific and overlap considerably with other endemic febrile illnesses, most notably acute malaria. This symptomatic similarity poses a significant diagnostic challenge in regions where both infections are endemic.

Several studies highlight this overlap and its clinical implications. For instance, studies of invasive salmonellosis in children in rural Nigerian hospitals [35, 43, 66, 67] found fever to be the predominant symptom, but presentations often overlapped with malaria in this endemic setting. Typhoid fever's clinical presentation was difficult to distinguish from malaria due to overlapping signs and symptoms, leading to empirical simultaneous treatment for both infections. However, diagnostic studies showed that typhoid fever, confirmed by culture or serology, was less prevalent than malaria among febrile patients, suggesting that many febrile illnesses clinically compatible with typhoid were actually malaria or other infections. The high coinfection rates of malaria and typhoid fever further compound clinical differentiation, as both infections may coexist and exacerbate symptom overlap.

From a diagnostic standpoint, this clinical overlap requires improved, rapid diagnostic tools to differentiate these infections. Novel platforms that enable simultaneous detection of malaria and typhoid antigens have been developed, offering rapid (approximately 15 minutes), cost-effective, and resource-appropriate solutions to distinguish these pathogens at the point of care and aid differential diagnosis in settings burdened by both malaria and typhoid [130].

Because of its low cost and rapid turnaround time, routine healthcare facilities heavily over-rely on the Widal agglutination test. This practice has institutionalized a cycle of clinical overdiagnosis; the assay lacks specificity and often yields high seropositivity rates that do not correlate with definitive microbiological confirmation. While blood and bone marrow cultures remain the diagnostic gold standard for *S. Typhi*, their utility is severely constrained by inadequate laboratory infrastructure, high costs, and widespread pre-hospital self-medication with over-the-counter antibiotics, which actively suppresses bacterial recovery *in vitro*, even as multidrug-resistant strains continue to evade detection [131].

4.6. High priority resistance in *S. Typhi* and contemporary non-antibiotic therapeutic

Fluoroquinolone and third-generation cephalosporin resistance in non-duplicated *S. Typhi* isolates reveals how regional antibiotic overuse drives selective pressure. High consumption rates of these critical drugs strongly correlate with the rapid emergence of non-susceptible strains and treatment failures in Nigeria. Widespread, empirical use of ciprofloxacin accelerated target-site mutations (such as in *gyrA*), leading to over 90% non-susceptibility across many African settings [132]. Resistance remains low globally but escalates where cephalosporins replace fluoroquinolones, creating XDR phenotypes [133]. Regional dispensing patterns and lack of diagnostic testing drive high resistance rates in clinical *S. Typhi*. In Nigeria, regional over-the-counter medicine sales and a heavy reliance on unconfirmed rapid tests instead of blood cultures drive the emergence of MDR- and XDR-*S. Typhi* strains [134].

Based on our meta-analysis, the pooled prevalence of FLQ and 3GC resistance in *S. Typhi* is very high, underscoring the need to explore non-antibiotic therapeutic interventions such as quorum sensing inhibitors, probiotics, antimicrobial peptides (bacteriocins), essential oils, organic acids, bacteriophages, and vaccines.

Essential oils disrupt quorum sensing by downregulating key genes such as *luxS*, *sdiA*, *qseB*, and *pfs*, which are essential for biofilm formation and virulence expression in *Salmonella* [135]. Rosemary essential oil reduces movement and communication in *S. Typhi*. It alters proteins involved in energy production, signal transmission, and flagellar assembly. With an IC₅₀ of 2 µg/mL, rosemary essential oil from Ghana demonstrated a distinct dose-response relationship against *S. Typhi* [136].

Subinhibitory concentrations of thymol and carvacrol reduced *Salmonella* counts on polypropylene surfaces by 1–2 log, with 1–5 log reductions at MIC or higher against established biofilms [137]. Essential oil-antibiotic combinations restore drug susceptibility; tetracycline MICs against MDR *S. enterica* dropped from 256 to 4 mg/mL when combined with *C. capitatus*, *E. caryophyllata*, or *T. vulgaris* essential oils, likely through efflux pump inhibition [138].

Most evidence on the use of bacteriocins against *S. Typhi* is limited to *in vitro* or animal models. Gold nanoparticles showed *in vitro* inhibitory effects against *S. Typhi*, and garlic-onion chitosan nanoparticles minimized colonization, but these nanoscale approaches remain preliminary [139]. Several licensed vaccines protect against *S. Typhi*; the WHO officially recommends three types of typhoid vaccines [140]: Typhoid conjugate injectable vaccines that combine the Vi polysaccharide with a carrier protein. They are licensed for infants starting at 6 months of age and provide long-lasting protection. The second is the Vi polysaccharide vaccine for individuals aged 2 years and older, requiring a booster every few years. Moreover, the live attenuated oral vaccine capsules (such as Ty21a) are taken by mouth over several days. They are licensed for adults and older children, usually starting at age 6 [141]. Other non-antibiotic therapeutic approaches target *S. Typhi* virulence, motility, and survival, as shown in Table 3.

Table 3
Contemporary non-antibiotic therapeutics against *Salmonella enterica* serovar Typhi

Intervention category	Agent / Compound	Primary Effect & Mechanism	References
Quorum Sensing Inhibitors (QSIs)	a. Furanone derivatives / Baicalein b. <i>Psidium guajava</i> phytocompounds	a. Blocks LuxS/AI-2 mediated signaling, repressing biofilm and toxin expression. Disrupts cell-to-cell communication by targeting Autoinducer-2 (AI-2) signaling systems	[142–144]
Probiotics	a. <i>Bifidobacterium longum</i> / <i>Lactobacillus acidophilus</i> b. <i>Weissella confusa</i> CFCS (lactic/acetic acid, 2,4-DTBP)	a. Helpful gut bacteria that fight <i>S. Typhi</i> by making the gut acidic, blocking the germ from sticking to cells, and boosting your immune system. b. They make lactic acid and short-chain fatty acids that lower the pH in the gut, thereby making <i>S. Typhi</i> unable to survive well in a high-acid environment. c. Efficacy of > 99.99% population reduction; 100% motility inhibition has been demonstrated against <i>S. Typhi</i> .	[145]
Bacteriophage	Specific virulent lytic phages (Phage STWB21)	a. Specific lysis of bacterial cell walls; frequently combined with essential oils for enhanced disruption of <i>S. Typhi</i> growth b. Improved survival; reduced liver/spleen invasion; effective prophylactically and therapeutically	[146]
Antimicrobial Peptides (Bacteriocins)	Enterocin LD3, Plantaricin LP 21 – 2, and bacteriocins from <i>Lactobacillus acidophilus</i>	a. Inhibit or kill <i>Salmonella typhi</i> by disrupting cell membranes and forming pores.	[147–149]
Vaccines	Vi polysaccharide vaccine / Ty21a	a. Stimulates systemic IgG and mucosal IgA immune protection against invasive typhoid fever.	[150]
Essential Oils (EOs)	Cumin from <i>Cuminum cyminum</i> L	a. Downregulates quorum sensing genes (<i>luxS</i> , <i>qseB</i>) and ruptures cell membrane integrity.	[138, 151]

CONCLUSION

Data from this study indicate widespread transmission and persistence of *S. Typhi* in One Health ecology in Nigeria, with environmental samples being its major reservoir, pointing to compromised sanitation and failing public water infrastructure. Widespread circulation increases the likelihood of encountering XDR-*S. Typhi* complicates antibiotic therapies. Given the high frequency of FLQ and 3GC resistance in *S. Typhi* isolates, we recommend developing, evaluating, and potentially adopting non-antibiotic therapeutic approaches against *S. Typhi*. Positive livestock or environmental samples usually reflect heavy human sewage or waste crossover into soil, feed, or water sources rather than animals acting as true biological reservoirs.

Abbreviations

Acquired Immunodeficiency Syndrome
AIDS
Antimicrobial resistance
AMR

Biochemistry
B
Cefixime
CXM
Ceftazidime
CFD
Ceftriaxone
CXN
Ciprofloxacin
CIP
Confidence Interval
CI
Culture
C
Deoxyribonucleic acid
DNA
Disk diffusion
DD
Extensively drug-resistant
XDR
Fluoroquinolones
FLQ
Half-maximal inhibitory concentration
IC50
Human immunodeficiency virus
HIV
Levofloxacin
LEV
Minimum Inhibitory Concentration
MIC
Multidrug-resistant
MDR
Northcentral
NC
Northeast
NE
Northwest
NW
Not clearly described
NC
Not tested
NT
Odds ratio
OR
Ofloxacin
OFL
Pefloxacin

PEF
Polymerase Chain Reaction
PCR
Pooled prevalence
PP
Preferred Reporting Items for Systematic Reviews and Meta-Analyses
PRISMA
Salmonella enterica serovar Typhi
S. Typhi
Southeast
SS
South-south
SS
Southwest
SW
Sparfloxacin
SPR
Third-generation cephalosporins
3GC
Water, sanitation, and hygiene
WASH

Declarations

Conflict of Interest

None declared by the authors

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Author Contribution

Idris Nasir Abdullahi and Islem Trabelsi: conceptualization, methodology, validation, software, formal analysis, data curation, visualization, writing – original draft, writing – review and editing. Both authors contributed equally. Joseph Momoh Vandy, Fatima Hassan, Muhammad Maimadu Barma, Saifullahi Abusufyan, Aisha Rufai Ahmad, Abbas Salis, Hajjahafsah Kabir Muhammad, Amina Chubado Aminu, Safinat Kure Shuaibu, Muhammad Sagir Shehu, Aminu Sulieman,

Data availability

All data generated from this study are presented in the tables, figures, and supplementary materials. However, further requests could be made through the corresponding authors (Idris Nasir Abdullahi and Islem Trabelsi).

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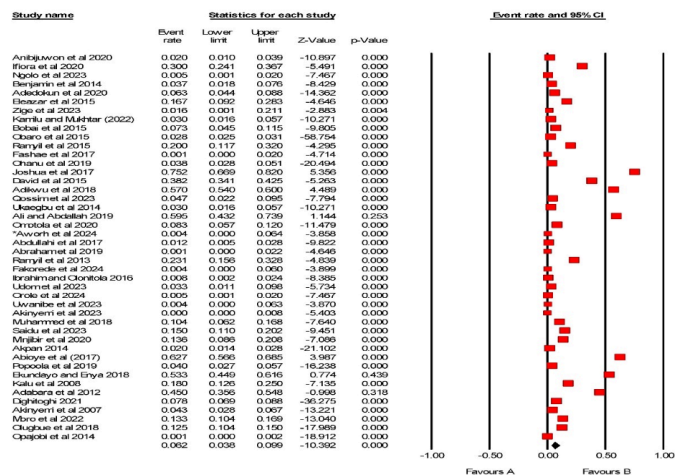
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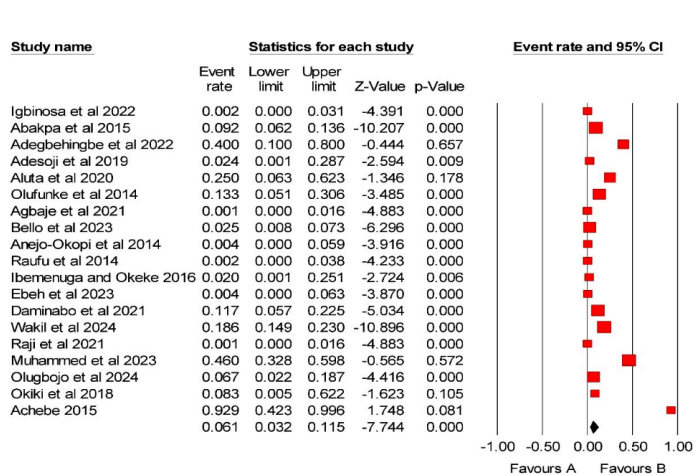
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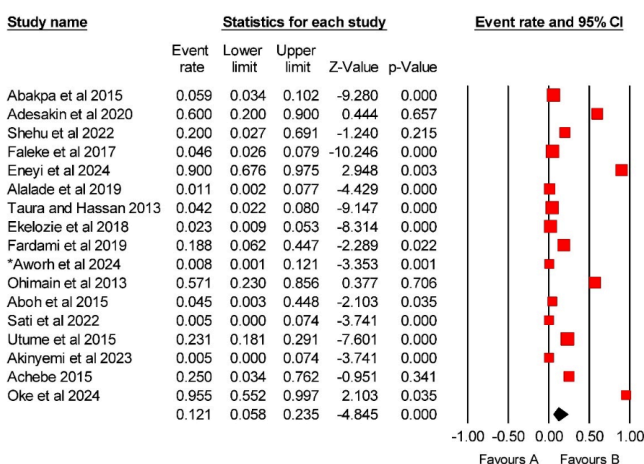
Figures



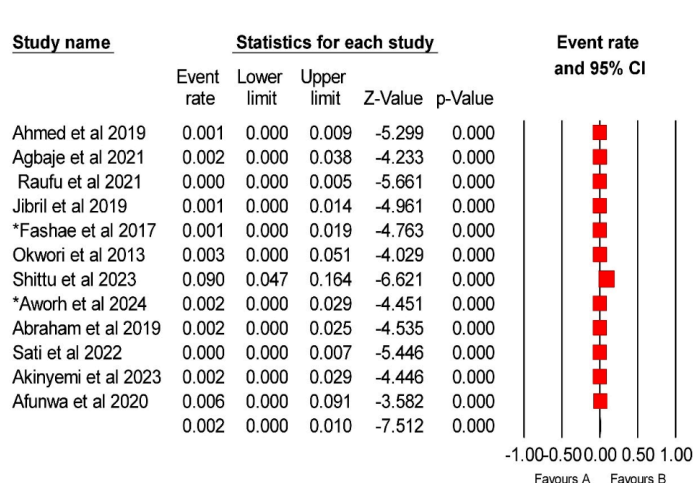
(a) The PP was 6.2% (95% CI: 3.8-9.9) in humans



(b) The PP was 6.1% (95% CI: 3.2-11.5) in Food



(c) The PP was 12.1% (95% CI: 5.8-23.5) in Environment



(d) The PP was 0.2% (95% CI: 0-1) in livestock

Figure 1

Pooled prevalence of *S. Typhi* across One Health niches in Nigeria (2004 to 2024)

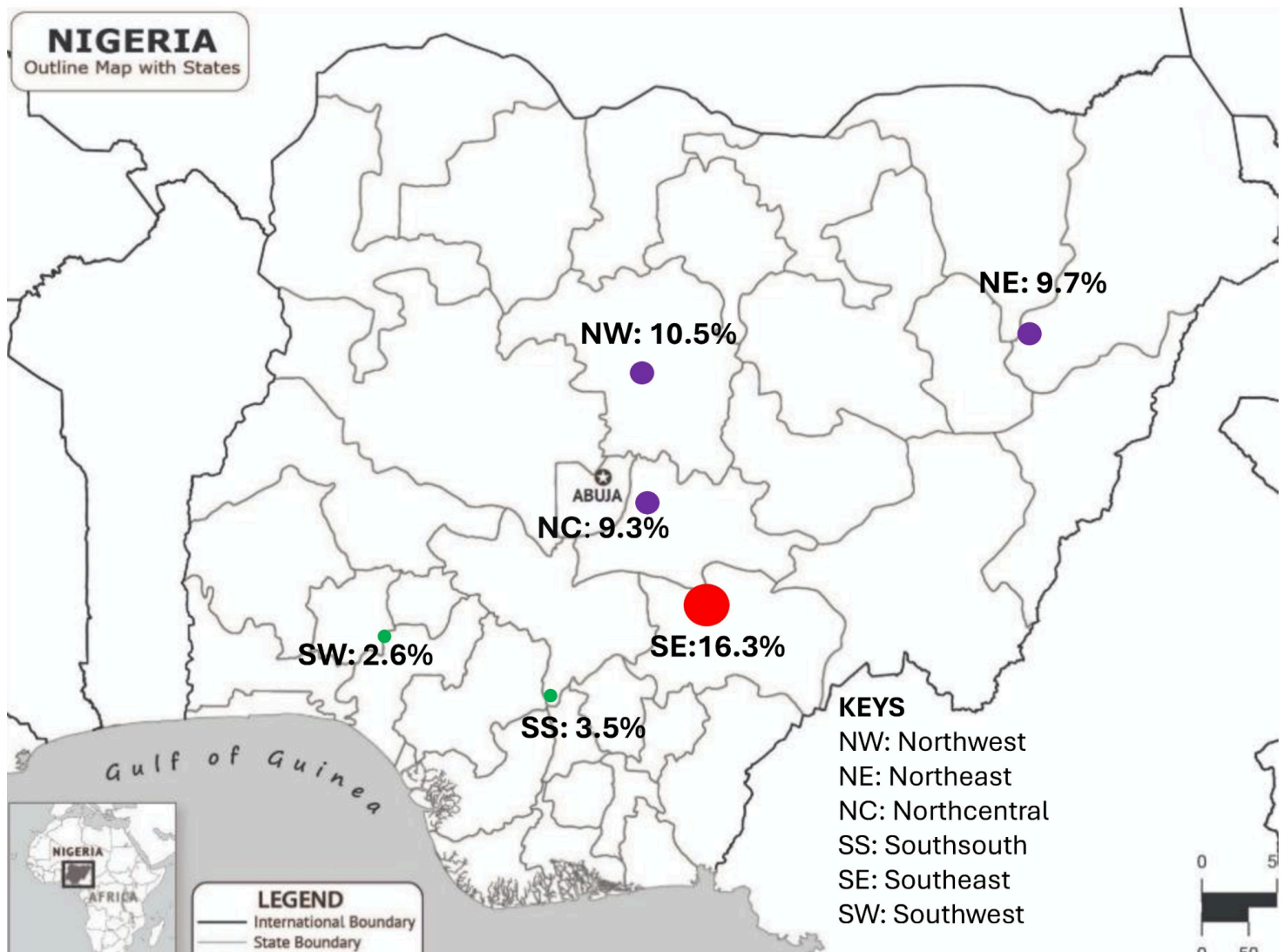
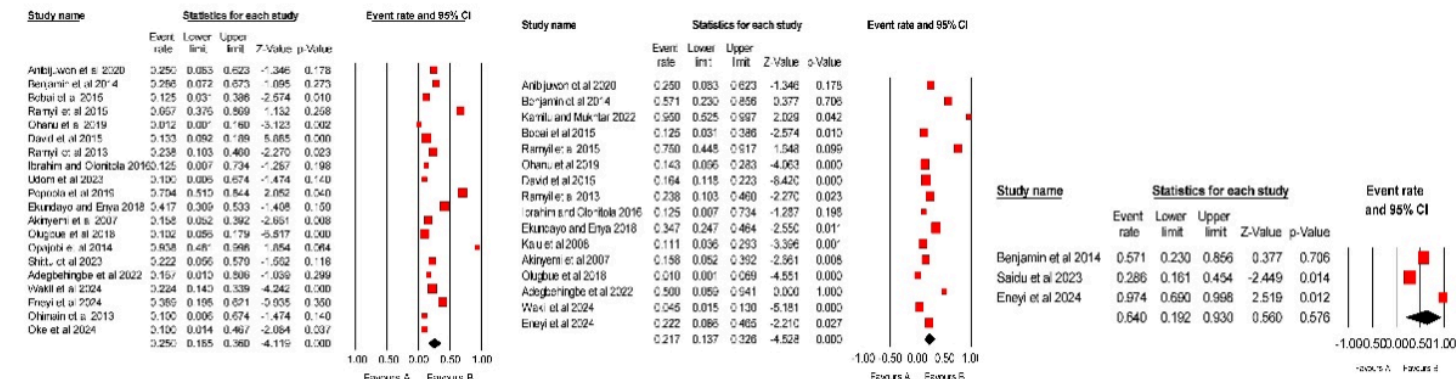
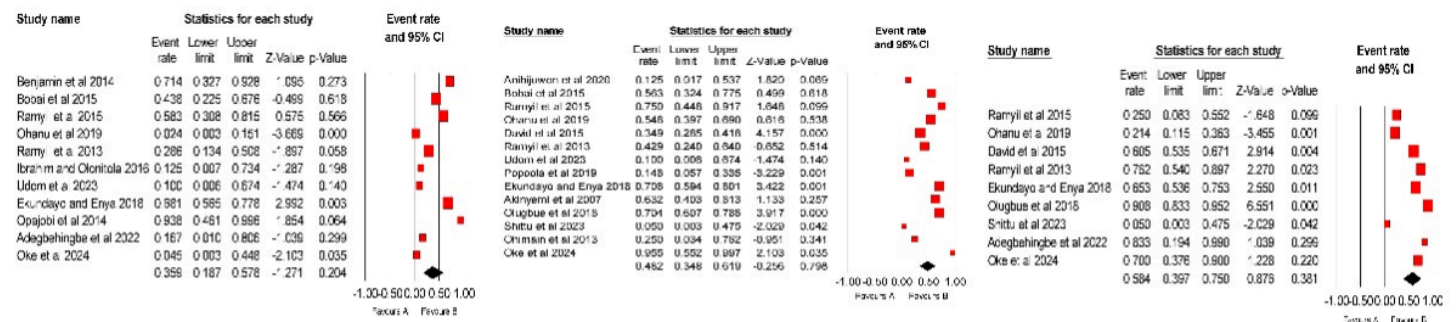


Figure 2

Pooled prevalence of *S. Typhi* across One Health niches by geopolitical zones of Nigeria



(a) The PP was 25% for Ciprofloxacin resistance in S. Typhi (b) The PP was 21.7% for Ofloxacin resistance in S. Typhi (c) The PP was 64% for Pefloxacin resistance in S. Typhi



(d) The PP was 35.9% for Ceftriaxone resistance in S. Typhi (e) The PP was 48.2% for Cefixime resistance in S. Typhi (f) The PP was 58.4% for Ceftazidime resistance in S. Typhi

Figure 3

Pooled prevalence of fluoroquinolone and third-generation cephalosporin resistance among S. Typhi isolates

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