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Non-typhoidal *Salmonella* in humans in India, Vietnam, Bangladesh and Sri Lanka: a systematic review

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Objectives: Non-typhoidal *Salmonella* (NTS) commonly causes a self-limiting illness but invasive disease (iNTS) can be life-threatening. Antimicrobial resistance (AMR) increases the risk of mortality. This systematic review aimed to estimate the proportion of NTS isolated in those attending healthcare services, serovar burden, AMR, serovar-specific AMR, and case fatality rate (CFR) in India, Bangladesh, Sri Lanka and Vietnam.

Methods: The review included quantitative studies on NTS and AMR from 1980 to 2020 but excluded studies unrelated to humans or selected countries. Data were extracted from articles identified from Ovid SP, Web of Science, Wiley Cochrane Library, Elsevier Scopus and WHO Global Index Medicus. The Joanna Briggs Institute Critical Appraisal Tools Checklist for Prevalence Studies was used for risk-of-bias assessment. Meta-analyses were performed for the proportion of NTS isolated, the proportion of specific serovars isolated, percentage of AMR and CFR.

Results: Six thousand and twenty-six isolates (79 serovars) were identified from 73 studies, with *Salmonella enterica* serovar Typhimurium being the most common. Of the 73 selected studies, 46% were hospital/laboratory surveillance studies, examining the aetiology of invasive or non-invasive infections. The pooled proportion estimate for non-iNTS was 2.1% (95% CI: 1.2%–3.2%) and for iNTS was 0.3% (95% CI: 0.1%–0.5%). The pooled CFR was 14.9% (95% CI: 4.0%–29.6%). Pooled resistance estimates for ampicillin, ceftriaxone, chloramphenicol, ciprofloxacin, co-trimoxazole, nalidixic acid and azithromycin were calculated. MDR iNTS was less prevalent in India [22.3% (95% CI: 0.0%–66.8%)] than in Vietnam [41.2% (95% CI: 33.6%–49.3%)]. Heterogeneity of studies was high as the majority were observational surveillance studies.

Conclusions: Despite data scarcity in some countries, this review highlights the continued contribution of NTS infection to disease burden, compounded by high AMR rates.

Introduction

Diarrhoeal disease is a significant health burden worldwide, causing approximately 80.9 million disability-adjusted life years (DALYs) and an estimated 1.5 million deaths.[1] The main foodborne aetiological agents of diarrhoeal disease are non-typhoidal *Salmonella* (NTS), *Escherichia coli*, *Campylobacter*, *Staphylococcus*

aureus and norovirus.[2,3] NTS infections usually present as self-limiting diarrhoeal illness, although dehydration in the elderly and children can be life-threatening. In about 5% of cases, NTS can escape the gastrointestinal tract and cases/patients develop bacteraemia or invasive infection.[4,5] Invasive NTS (iNTS) is often associated with severe life-threatening complications such as sepsis, osteomyelitis, pneumonia, encephalopathy and acute kidney injury.[6] Mortality and morbidity rates of iNTS are higher among infants, older adults and immunocompromised individuals.[7] The Institute for Health Metrics and Evaluation (IHME) 2017 study estimated the iNTS case fatality rate (CFR) at 14.5% (95% CI: 9.2%–21.1%), with an age-standardized incidence of 7.5 (95% CI: 5.7–10.0) cases per 100 000 person-years (PY).[8] These 2017 Global Burden of Disease (GBD) estimates are slightly lower than the 2005 estimates of 15.64 (95% CI: 9.9–22.4) CFR and incidence of 10.7 (95% CI: 8.5–13.6) cases per 100 000 PY.[8] The GBD 2017 incidence was estimated at 2.7 (95% CI: 2.0–3.5) per 100 000 PY in South Asia and 1.2 (95% CI: 0.9–1.6) in Southeast Asia, East Asia and Oceania.[8] In South Asia, it was higher in Bangladesh [4.2 (95% CI: 3.0–5.9)] than in India [2.2 (95% CI: 1.7–2.8)] and Sri Lanka [1.4 (95% CI: 1.0–1.8)].[8] iNTS infections are linked to clinical complications and have a high CFR because they are frequently underreported or not surveyed. There is a scarcity of effective surveillance and antimicrobial resistance (AMR) data on NTS from developing countries in Asia, resulting in underreporting of the burden.[8,9]

Salmonellae are Gram-negative bacteria within the family Enterobacteriaceae. The genus has two species: *Salmonella bongori* and *Salmonella enterica*.[7,10–12] Over 2610 different serovars[13] have been identified to date, with *S. enterica* subsp. *enterica* accounting for 99% of serovars responsible for human and animal infections.[14] *S. enterica* serovar Typhi, the aetiological agent of typhoid fever, remains one of the most important serovars, with 26.9 million cases attributed to it in 2010.[15] The most common serovars of NTS isolated from non-invasive and invasive infections in humans are *S. enterica* subsp. *enterica* Typhimurium and *S. enterica* subsp. *enterica* Enteritidis.[11,16] Serovars such as Typhimurium, Dublin and Choleraesuis tend to have more potential to cause extraintestinal infections than others.[5] As the Kaufman-White scheme has not been updated since 2007, traditional serotyping is often replaced by MLST.

Cases of NTS are usually self-limiting; however, invasive disease in elderly and immunocompromised people can be life-threatening and may be treated with antibiotics such as ciprofloxacin, azithromycin and ceftriaxone.[17] Indiscriminate antibiotic use for growth promotion, prophylaxis and metaphylaxis among farm animals has been suggested to play an important role in zoonotic transmission of AMR to humans from animal sources.[18,19] Zoonotic transmission of NTS is associated with consumption of poultry, beef and pork meat, eggs, milk, cheese, fish and shellfish contaminated at various stages of food production.[20,21] Contact with farm animals, pets and reptiles is also associated with human infection.[22,23] AMR is common in iNTS and the resistance pattern varies with different serovars. *S.* Typhimurium isolates have been shown to possess AMR-associated genes linked to ampicillin, chloramphenicol, streptomycin, sulphonamide and tetracycline resistance.[24] MDR *S.* Typhimurium has been associated with a higher risk of invasive infection, higher frequency and longer duration of hospitalization, as well as illness, and increased mortality compared with infections caused by susceptible strains.[25] Increasing resistance to oral antimicrobials such as ciprofloxacin, resulting in treatment failures, also heralds the need to bridge the AMR information gap, especially in Southeast Asia where the disease burden is high.[24]

This study was part of the UKRI Global Challenges Research Fund (GCRF) One Health Poultry Hub, an impact-driven development research programme working in Bangladesh, India, Sri Lanka and Vietnam (www.onehealthpoultry.org/). This systematic review was undertaken to provide an update on information on NTS infections, including AMR, irrespective of age in Bangladesh, India, Sri Lanka and Vietnam. The data will be used to put into context NTS isolated during the surveillance phase of the hub and provide cross-country comparisons. This study also aimed to understand the quantity and quality of studies within the selected countries.

Materials and methods

Protocol and objectives

In the present study we sought to address the following questions: what is the proportion of NTS isolated in humans attending healthcare services for diarrhoea, the proportion of different serovars isolated and mortality associated with NTS serovars in the different populations; and what is the occurrence of MDR serovars of NTS? We developed a protocol *a priori* in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) to document the search process.[26] As this involved analysis of published data, it did not require the approval of the institutional review board.

Search strategy and selection criteria

References for this systematic review were identified through searches of the bibliographic databases Ovid SP MEDLINE ALL, Ovid SP Embase, Ovid SP Global Health, Web of Science Core Collection (SCI-Expanded, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI), Wiley Cochrane Library, Elsevier Scopus and WHO Global Index Medicus (limited to results from WPRIM and IMSEAR). The search was run by one author (J.F.) on 18 December 2020 to identify publications. The search was limited to papers using human subjects and published from 1980 to the date of the search. Complete search strategies for all databases are available (Table S1, available as Supplementary data at *JAC-AMR* Online). The search was narrowed down to the four countries (Bangladesh, India, Sri Lanka and Vietnam) where the GCRF One Health Poultry Hub is conducting research exploring the link between poultry production and disease. Only papers published in English were reviewed.

Study selection

NTS studies that included population-based surveillance, hospital surveillance, laboratory surveillance, sentinel site surveillance, clinical trials, cohort studies, case–control studies, cross-sectional studies, case series and case reports were considered for inclusion. The inclusion criteria were: (i) NTS-related studies ranging from 1980 onwards; (ii) quantitative-based studies; (iii) AMR-related studies; (iv) source-attribution studies; and (v) the source of isolates was within Southeast Asia. The exclusion criteria were: (i) anything related to typhoid fever; (ii) studies with no relation to humans; (iii) studies of infections not linked to Bangladesh, India, Sri Lanka or Vietnam.

Text files for each database search result were downloaded and imported into Endnote. After removing duplicates from the combined reference list, for each reference teams of three authors screened the titles and abstracts first, then the selected full text in parallel for inclusion (L.O'N., B.L., C.K., M.H., T.S., A.C., T.T.M.H., S.S.). Data were then abstracted by two authors (C.K., L.O'N.), compiled into an Excel sheet, checked and

analysed by a third author (R.R.). Co-authors (R.S., P.M., P.N.D.) were consulted to resolve discrepancies through discussion and to review the final dataset for completeness and accuracy. Risk-of-bias (ROB) assessment was performed (C.K., R.R.) for all selected studies except case series and case reports.[27]

Data abstraction and analysis

For estimation of the proportion of NTS isolated and the proportion of specific serovars isolated, the study characteristics extracted included study country, location, study design, year the study was conducted, sampling frame, sample size, age group, male:female ratio, source of biological sample, number of biological samples tested, number of NTS isolated, number of specific serovars isolated, laboratory methods used in the study for identification of NTS, and the standard used for the antibiotic susceptibility test. ST data were extracted whenever they were reported. For the estimation of the percentage of AMR, the number of serovar-specific isolates that were found to be resistant to specific antimicrobial agents (where available) was extracted for each study. The number of deaths reported from each study were also collected for the estimation of CFR. For the proportion of NTS isolated, the proportion of specific serovars isolated, and the percentage of AMR and CFR, meta-analysis was performed where there was a minimum of two studies (case reports and case series were excluded for meta-analysis). Evaluation of the heterogeneity of studies was assessed using the random-effects model in STATA 17.

ROB

All studies, other than case reports and case series, were critically assessed using the Joanna Briggs Institute Critical Appraisal Tools Checklist for Prevalence Studies.[27] The domains assessed included the appropriateness of the sampling frame, appropriateness of sampling of the study participants, adequateness of sample size, description of the study subjects and study setting, coverage of the identified samples during data analysis, validity of the methods used for identification of the condition, reliability of the measurement of the condition, appropriateness of the statistical analysis and adequateness of the response rate.

Results

Study selection

Our search strategy identified 13 936 articles to be screened (Figure 1).[26,28] After removing 6118 duplicates, we screened 7803 titles and abstracts for inclusion. Of these, 6086 were excluded and 1717 were sought for retrieval and assessed for eligibility. We excluded 1644 articles after reviewing the full text; the most common reasons for exclusion were country other than the selected ones (747) and not being about NTS (370). Finally, 73 articles published between 1980 and 2020 from the four countries were eligible for analysis (Figure 1, Table S2).

Study characteristics and quality assessment

Most studies were from India (57/73; 78%) followed by Vietnam (9/73; 12%), Bangladesh (5/73; 7%) and Sri Lanka (2/73; 3%) (Table S2). As only 10 studies were conducted between 1980 and 1999, all of which were from India, only data from 2000–20 were pooled. The most common study type (34/73; 46%) was hospital/laboratory surveillance. These studies either examined the aetiology of diarrheal disease (31 studies), invasive disease (25 studies) or both (17 studies). Whichever studies used both invasive and non-invasive biological samples were considered under invasive disease during analysis. There were 44 prevalence studies (Table S3), 22 case reports and 7 case series. The ROB assessments of the 44 prevalence studies are summarized in Table S4.

Proportion of NTS isolated by culture

The pooled estimate of the proportion[29,30] of non-invasive NTS isolated in those attending healthcare services for diarrhoea in India, Vietnam and Bangladesh combined was 2.1% (95% CI: 1.2%–3.2%) (from 10 studies)[31–40] (Figure 2), whereas for iNTS from invasive infection it was 0.3% (95% CI: 0.1%–0.5%) (5 studies)[41–43] (Figure 2). However, the heterogeneity between studies was very high ($I^2 = 99\%$) (Figure 2). The majority of studies were from India, from which the overall proportion of non-invasive NTS isolated was 1.4% (95% CI: 0.6%–2.6%) (7 studies)[31–34,36,37,40] and the proportion of iNTS was 0.4% (95% CI: 0.0%–1.3%) (3 studies).[30,41,43]

Proportion of specific serovars identified

Fifty-eight studies identified NTS and described serotyping data, from which 79 different serovars were identified from 6026 isolates (Table S5). The majority (1865/2024; 92.1%) of isolates from Bangladesh were only reported to O-antigen group level and the most common were Group C1 (693/2024; 34.24%), Group B (533/2024; 26.33%) and Group C2 (254/2024; 12.55%) (Figure 3, Table S5). Only four serovars were isolated in all four countries: *S. enterica* serovar Enteritidis, *S. enterica* serovar Paratyphi B var Java, *S.* Typhimurium and *S. enterica* serovar Weltevreden (Figure 3, Table S5). The serovar associated with the highest pooled frequency of isolation in non-invasive disease was *S.* Typhimurium in India [26.7% (95% CI: 18.7%–35.5%)][33,34,37,40,44–46] and Vietnam [33.2% (95% CI: 19.5%–48.5%)].[18,38,47] In India the second most common serovar was *S. enterica* serovar Worthington [18.1% (95% CI: 3.5%–40.1%)],[33,36,45] which was rare in Vietnam [0.5% (95% CI: 0.0%–2.0%)]. The second most common serovar in Vietnam was *S.* Weltevreden [11.1% (95% CI: 4.1%–20.6%)],[18,38,47] which was also common in India [5.8% (95% CI: 2.9%–9.5%)].[33,34,36,40,44,45,48] Another frequent NTS serovar in both countries was *S.* Enteritidis [India 5.9% (95% CI: 2.1%–11.1%);[33,34,36,44,45] Vietnam 4.7% (95% CI: 1.8%–8.8%)].[18,38,47] The pooled estimates of the most common invasive disease serovars were only calculable for India with *S.* Typhimurium [52.4% (95% CI: 15.8%–87.8%)][46,48–51] and *S.* Enteritidis [14.9% (95% CI: 7.7%–23.8%)][48–51] being the most prevalent serovars. Only one study reported invasive isolates from Vietnam and hence pooled estimates could not be determined.

MLST data were available for 958 isolates across all studies. Although only two studies from Vietnam included MLST data, these two studies contributed ST data for 809 isolates (Table S6), compared with 101 isolates from India, 40 from Sri Lanka and 8 from Bangladesh.[18,33,38,44] Even though 98 different STs were reported across all studies, only ST11 (linked to *S.* Enteritidis) was present in all four countries (113/958 isolates; 11.8%). Four STs linked to *S.* Typhimurium were identified in the studies: ST19 [60/809 (7.4%) Vietnam; 8/101 (8.0%) India]; ST34 [181/809 (20.3%) Vietnam]; ST313 [1/809 (0.1%) Vietnam; 2/101 (2.0%) India]; and ST36 [32/809 (4.0%) Vietnam; 1/40 (2.5%) Sri Lanka; 22/101 (22%) India]. None of the eight Bangladesh isolates with MLST

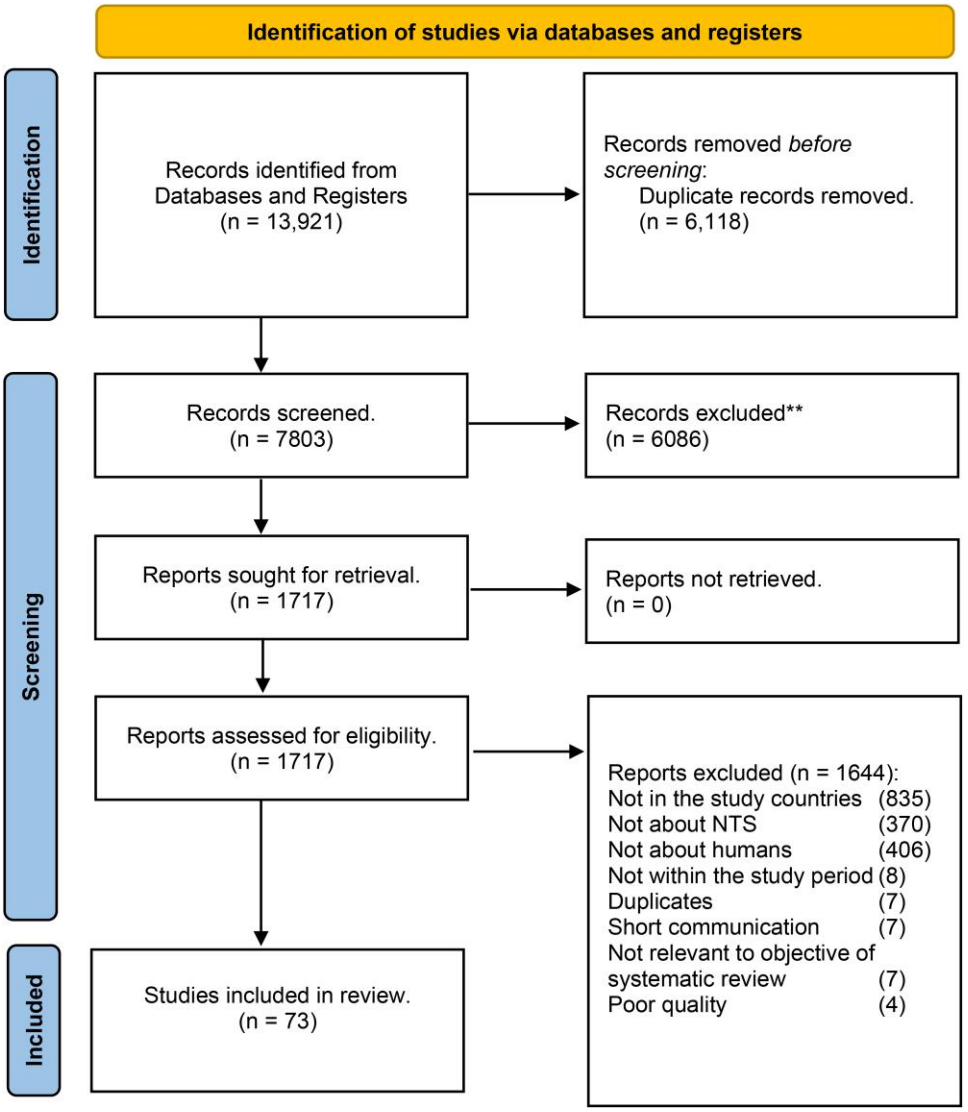

Figure 1. PRISMA 2020 flow diagram.

data had an ST linked to *S.* Typhimurium. The next most common ST was ST365, linked to *S.* Weltevreden [68/809 (8.4%) Vietnam; 1/40 (2.5%) Sri Lanka; 6/101 (6%) India], followed by ST29 linked to *S. enterica* serovar Stanley [73/809 (9.0%) Vietnam; 1/40 (2.5%) Sri Lanka].

AMR

Pooled estimates of resistance for seven antibiotics, including the first-line drugs of choice for iNTS (ciprofloxacin, ceftriaxone and azithromycin), were only possible for India and Vietnam (Table 1). The pooled estimate of the proportion of non-invasive NTS isolates resistant to ciprofloxacin was 9.8% (95% CI: 0.5%–25.0%) (7 studies)[33,34,36,37,40,44,46] in India, which was higher than the 4.1% (95% CI: 2.4%–6.2%) (4 studies) in Vietnam[18,38,52,53] (Figure S1). However, for iNTS infection the pooled estimate of resistance to ciprofloxacin in India was 0.0% (95% CI: 0.0%–1.7%) (4 studies),[30,49,51,54] compared with 41.1% (95% CI: 34.1%–48.3%) in Vietnam (2 studies)[18,53] (Figure S1). The pooled proportion of non-invasive NTS isolates resistant to ceftriaxone in India was 9.9% (95% CI: 0.0%–43.7%) (6 studies),[33,36,40,46,54,55] slightly higher than the 6.6% (95% CI: 1.1%–15.8%) (3 studies) in Vietnam[18,38,53] (Figure S2). For iNTS, it was 0.6% (95% CI: 0.0%–15.9%) (5 studies)[30,46,49,51,54] in India, which was lower than the 2.4% (95% CI: 0.5%–5.4%) (2 studies) in Vietnam[18,53] (Figure S2). The pooled proportion of non-invasive NTS isolates resistant to azithromycin was 16.1% (95% CI: 0.0%–55.6%) (5 studies)[33,34,40,46,55] in India (Figure S3) and 18.0% (95% CI: 14.7%–21.8%) in Vietnam (1 study).[38] Again, the pooled proportion of iNTS isolates resistant to azithromycin was much lower for non-invasive NTS at 0.0% (95% CI: 0.0%–32.4%) in India (1 study).[46] No data were available for Vietnam (Table 1). MDR, as defined by publication-defined criteria, was estimated to be lower in India in non-invasive isolates [30.2% (95% CI: 2.1%–68.2%)

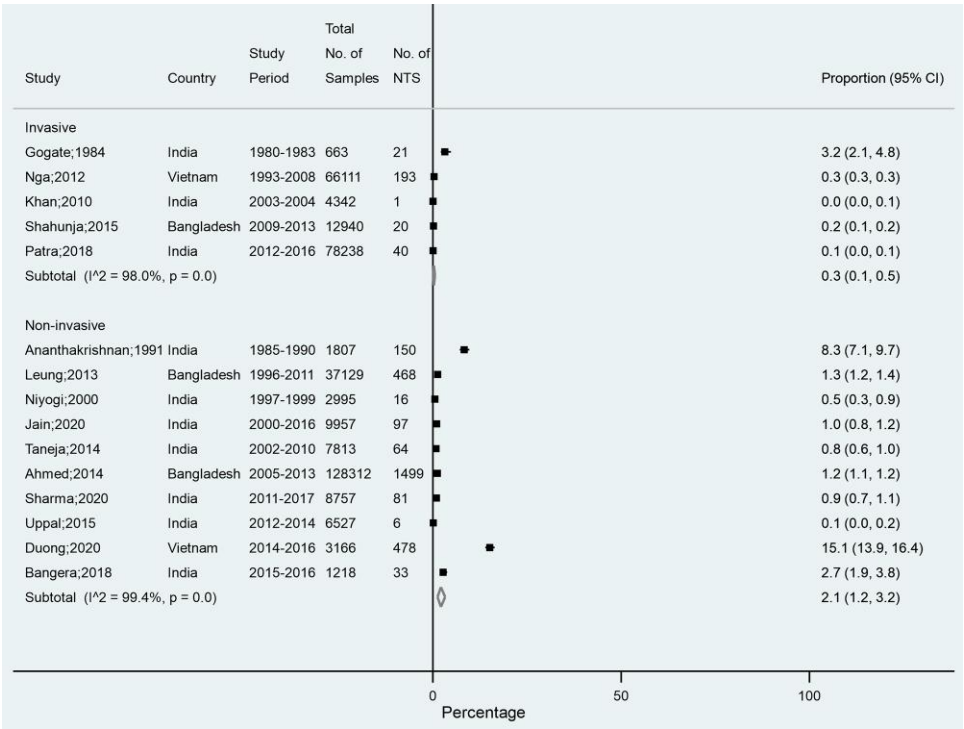

Figure 2. Isolation rate of NTS in India, Vietnam and Bangladesh.

Rank	1	2	3	4	5	6	7	8	9	10
India (3097)	S. Typhimurium (898, 29.0%)	S. Weltevreden (322, 10.4%)	S. Worthington (316, 10.2%)	S. Bareilly (255, 8.2%)	S. Newport (151, 4.9%)	S. Enteritidis (145, 4.7%)	S. Infantis (132, 4.3%)	S. Cholerasuis (61, 2.0%)	S. Kentucky (46, 1.5%)	S. Lidenberg (46, 1.5%)
Vietnam (863)	S. Typhimurium (299, 34.7%)	S. Enteritidis (93, 10.8%)	S. Weltevreden (80, 9.3%)	S. Stanley (75, 8.7%)	S. Newport (42, 4.9%)	S. Rissen (20, 2.3%)	S. Java (16, 1.9%)	S. Cholerasuis (15, 1.7%)	S. Kentucky (12, 1.4%)	S. Derby (11, 1.3%)
Bangladesh (2024)	Group C1 (693, 34.2%)	Group B (533, 26.3%)	Group C2 (254, 12.6%)	Group E (186, 9.2%)	Group D (119, 5.9%)	Group G (79, 3.9%)	S. Typhimurium (21, 1.0%)	S. Java (16, 0.8%)	S. Enteritidis (6, 0.3%)	S. Kentucky (6, 0.3%)
Sri Lanka (42)	S. Enteritidis (21, 50.0%)	S. Java (4, 9.5%)	S. Weltevreden (4, 9.5%)	S. Corvallis (3, 7.1%)	S. Chester (3, 7.1%)	S. Worthington (2, 4.8%)	S. Typhimurium (1, 2.4%)	S. Stanley (1, 2.4%)	S. Mbandaka (1, 2.4%)	S. Mountpleasant (1, 2.4%)

Figure 3. Most frequent serovars isolated by country. Combined invasive and non-invasive NTS isolates. Presented as serovar (number of isolates, percentage of isolates from that country). *S.* Java, *S.* Paratyphi B var Java. Group C1 includes *S. enterica* serovar Rissen, *S. enterica* serovar Mbandaka and others; Group B includes *S.* Typhimurium, *S. enterica* serovar Derby and others; Group C2 includes *S. enterica* serovar Newport, *S. enterica* serovar Manhattan and others), Group E includes *S. enterica* serovar Liverpool, *S. enterica* serovar Senftenberg and others); Group D includes *S.* Enteritidis, *S.* Dublin and others); Group G includes *S.* Worthington, *S. enterica* serovar Agbeni and others.

(5 studies)][33,34,44,46,54] compared with Vietnam [41.9% (95% CI: 21.1%–64.3%) (3 studies)].[18,38,52] In iNTS, the pooled proportion of MDR dropped slightly in India [22.3% (95% CI: 0.0%–66.8%) (3 studies)][46,54,55] but remained high in Vietnam [41.2% (95% CI: 33.6%–49.3%) (1 study)].[18] Analysis of serovar-specific pooled AMR pattern estimation was not possible due to too few isolates for which serovar-specific AMR data were available. However, study data indicated that the reported proportion of resistant isolates was higher than the pooled estimates in *S.* Worthington for ceftriaxone, azithromycin and ampicillin (Figures S2–S4), in *S. enterica* serovar Kentucky for ampicillin, co-trimoxazole and nalidixic acid (Figures S4 and S6–S7), in *S.* Typhimurium for ampicillin (Figure S4) and in *S. enterica* serovar Agona for ceftriaxone, ampicillin and chloramphenicol (Figures S2 and S4–S5).

Table 1. Summary of AMR from the review

Antibiotic	Non-invasive NTS, % (95% CI)		iNTS, % (95% CI)	
	India	Vietnam	India	Vietnam
Ampicillin	26.7 (11.3–44.9)	51.0 (31.8–70.0)	0.6 (0.0–15.9)	70.2 (63.4–76.6)
Ceftriaxone	9.9 (0.0–43.7)	6.6 (1.1–15.8)	0.6 (0.0–15.9)	2.4 (0.5–5.4)
Chloramphenicol	0	33.4 (16.7–52.2)	2.4 (0.0–20.8)	46.0 (38.9–53.2)
Ciprofloxacin	9.8 (0.5–25.0)	4.1 (2.4–6.2)	0.0 (0.0–1.7)	41.1 (34.1–48.3)
Co-trimoxazole	9.2 (3.6–16.2)	34.0 (30.5–37.7)	0.0 (0.0–1.9)	39.2 (31.7–47.2)
Nalidixic acid	73.1 (54.3–89.1)	33.5 (19.4–49.0)	61.0 (38.2–82.2)	51.2 (36.5–65.7)
Azithromycin	16.1 (0.0–55.6)	18.0 (14.7–21.8)	0.0 (0.0–32.4)	—
MDR	30.2 (2.1–68.2)	41.9 (21.1–64.3)	22.3 (0.0–66.8)	41.2 (33.6–49.3)

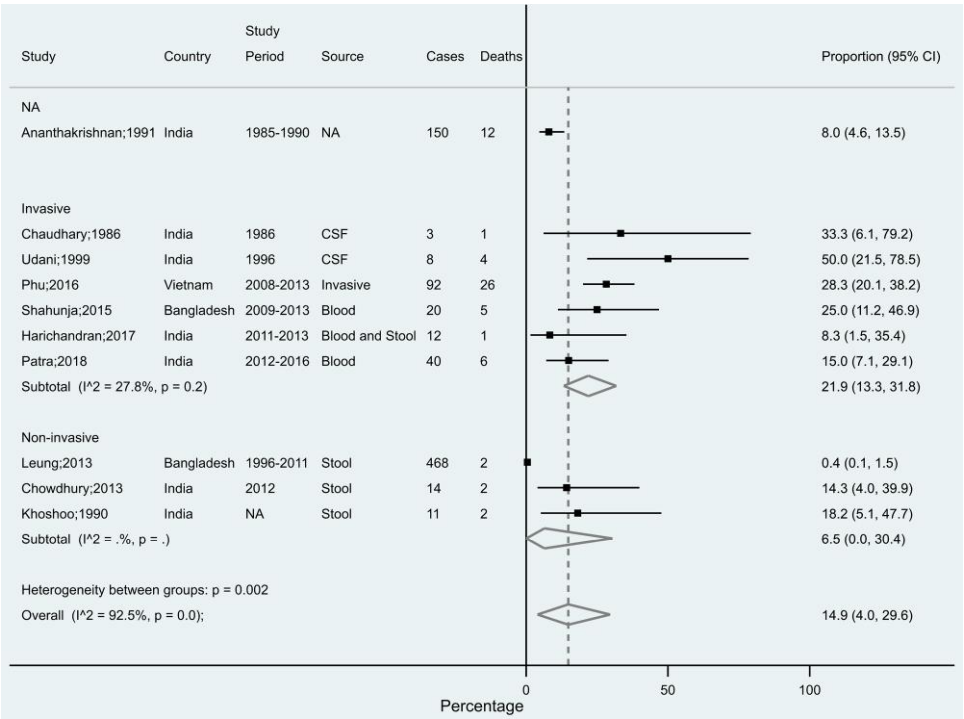

Figure 4. CFR in India, Vietnam and Bangladesh.

CFR

The pooled CFR for invasive and non-invasive NTS from studies in India and Bangladesh was 14.9% (95% CI: 4.0%–29.6%) (10 studies)[29–31,39,46,56–60] (Figure 4). Country-specific pooled CFRs were not computed due to fewer studies reporting mortality from Vietnam, Bangladesh and Sri Lanka. The CFR for invasive disease was 21.9% (95% CI: 13.3%–31.8%) and for non-invasive disease it was 6.5% (95% CI: 0.0%–30.4%) (Figure 4). The details of the studies included in the calculation of CFR are summarized in Table S7.

Discussion

Understanding the burden of NTS infection and AMR-associated patterns within a country, or even smaller geographical regions, is vital in guiding local clinicians to provide rapid and appropriate care to reduce mortality and morbidity. While there are many studies within global North countries, data are scarce in countries with a high burden of disease. In this review we aimed to provide an update on previous studies, including a deep dive into the data available in the four global South countries that are part of the One Health Poultry Hub. The search of the public databases identified 73 articles suitable for analysis, but these were heavily biased towards India. While Vietnam only provided 12% of the studies, these were rich with molecular data. This demonstrates the urgent need for more rigorous studies, particularly in Bangladesh and Sri Lanka, to understand the local disease burden.

Only 14 hospital-based surveillance studies and one community-based surveillance study provided disease burden figures, from which the proportion of NTS isolated was estimated to be 2.1%

(95% CI: 1.2%–3.2%) for non-invasive NTS and 0.3% (95% CI: 0.1%–0.5%) for iNTS; however, high heterogeneity was observed between these studies. Our systematic review found only one community-based surveillance study from these regions and hence we could not estimate the incidence. Hospital-based surveillance provides a higher rate of infection and AMR than would be occurring in the community, underscoring the need to undertake routine community-based surveillance.[61]

Estimates in this review were lower than the proportion of NTS isolated (≤5.3%) in the Global Enteric Multicentre Study (GEMS), which was conducted only among <5-year-old children in Africa and Asia between 2007 and 2010.[16] In low- and middle-income countries (LMICs), the highest burden is among children, with low rates anticipated throughout adulthood.[10] The lack of age-specific data from the studies included in this review meant it was not possible to determine the age-specific pattern in these countries and resulted in a lower overall estimate.

Serotyping has multiple functions, including linkage of pathogen lineages to antibiotic resistance patterns or virulence, which may affect the severity of illness, and can guide healthcare professionals in choosing appropriate therapeutic strategies. The studies identified 79 serovars; however, data from Bangladesh were mainly only reported to O-antigen level, making comparison difficult and demonstrating the usefulness of a globally accepted method[62] that can be used to understand the global context of NTS in a country. *S.* Typhimurium is a leading cause of gastroenteritis in humans worldwide, so it was unsurprising that over 20% of isolates in the study countries belonged to this serovar and that it was the most common serovar in non-invasive NTS. *S.* Weltevreden was the second most common serovar in non-invasive NTS in Vietnam. This serovar is often isolated from fish and aquatic samples[63] and potentially seafood-based pig feed.[64] The predominance of this serovar in Vietnam could be due to differences in diet between the countries. For example, pork consumption in 2021 was estimated at 27.3 kg/capita/year in Vietnam but only 0.23 kg/capita/year in India.[65] Additionally, per capita consumption of crustaceans was higher in Vietnam in 2021 than in India (5.25 versus 0.4 kg/capita/year, respectively).[65] Egg consumption is common in all four countries (in 2021, consumption was estimated at 3.92 kg/capita/year in Bangladesh, 4.11 in India, 4.12 in Sri Lanka and 3.59 in Vietnam)[65] and egg contamination by *S.* Enteritidis is one of the most important causes of foodborne gastroenteritis in humans throughout the world so the detection of this serotype in all study countries was expected.

Molecular data defining NTS are still rare from the study countries. Although India provided most studies and isolates, Vietnam provided the majority of the MLST data. The public MLST database (accessed 28 September 2023; 21226 isolates)[66] is dominated by isolates from the UK (1589 submissions with country data), Australia (1382), China (687), Brazil (353) and the USA (344) and may not be representative of the actual disease burden in the study countries. In the MLST database,[66] *S.* Enteritidis was the most commonly submitted NTS serovar (4049 isolates; 19.1%), followed by *S.* Typhimurium (2300; 10.8%), *S.* Agona (228; 1.4%), *S. enterica* serovar Montevideo (216; 1.0%), *S. enterica* serovar Bareilly (194; 0.9%) and *S. enterica* serovar Heidelburg (150; 0.7%). In our study, the most common STs in Vietnam were STs linked to *S.* Typhimurium (274/809 isolates; 33.9%) followed by *S.* Enteritidis (81/809; 10%). *S.* Agona (ST13) was rarely found (4; 0.5%). The most common *S.* Montevideo STs (ST316, ST138, ST81, ST4, ST195) were absent from all study countries. *S.* Bareilly (primarily ST909 and ST203) was present in 13 isolates (13/958; 1.3%) from all four countries. *S. enterica* serovar Heidelburg (ST15) was absent from all study countries. Instead, the next most common STs were linked to *S.* Stanley (ST29: 74/958; 7.7%) and *S.* Weltevreden (ST365: 75/958; 7.8%), which are present in the MLST database in 0.2% and 0.4% of isolates, respectively. This may suggest that while *S.* Typhimurium and *S.* Enteritidis are prominent globally, the frequency of other NTS in this review may reflect local food consumption patterns, for instance the high pork consumption in Vietnam compared with high levels of vegetarianism in India.[65]

S. Typhimurium in the MLST database represent at least six STs, ST19 being the most common (58.8%) followed by ST34 (14.9%), ST313 (14.5%) and ST36 (2.2%). Across the study countries, ST34 was the most common (181/311; 58.2%) followed by ST19 (68; 21.9%), ST36 (55; 17.7%) and ST313 (3; 1.0%). ST34 is linked to a monophasic clone, which has rapidly disseminated globally and is known to be resistant to many antimicrobials, partly due to carrying the mobile colistin resistance (*mcr*) gene.[67] ST34 variants from Vietnam have been reported to be associated with invasive disease among immunocompromised individuals.[53] The high incidence and spread of this clone may be being facilitated by the overuse of antimicrobials within these countries. A single ST313 from Vietnam and two from India were identified; the low prevalence can be explained as ST313 strains are commonly associated with bloodstream infections in Africa and rarely seen outside that continent.[8,68]

Although non-invasive NTS disease is usually self-limiting and should not be treated with antibiotics, a high level of resistance was detected to all seven antibiotics analysed in non-invasive NTS. High levels of resistance to antibiotics that have been on the market for a long time, such as ampicillin and nalidixic acid, were demonstrated, which restricts the use of these antibiotics. Nalidixic acid is a narrow-spectrum fluoroquinolone antibiotic introduced in 1962 and used against enteric bacteria causing uncomplicated urinary tract infections (UTIs). While the level of nalidixic acid resistance was slightly lower in iNTS compared with non-invasive NTS in India (61% versus 73%), in Vietnam the level of resistance increased from 33% to 51% in iNTS. In this review, ampicillin resistance similarly increased in Vietnam between non-invasive NTS and iNTS but appears to be reduced to low levels in India. The majority of the Indian iNTS data in this review come from three papers. These do, however, indicate that some serovars may have increased resistance.

Third-generation cephalosporins and fluroquinolones are the first-line drugs for treating iNTS, yet non-invasive isolates had high levels of resistance to these antibiotics. High levels of resistance to azithromycin, an antibiotic used to treat many infections from gonorrhoea to mass drug administration (MDA) to children to reduce all-cause childhood mortality,[69–72] were described in India and Vietnam, with roughly one in six NTS isolates being resistant. While many of the articles examined were hospital based, which may be responsible for increasing AMR burden estimates, NTS is not normally considered nosocomial and we presume these are mostly community-acquired infections. However, when considering iNTS, the studies in India reported a low occurrence of resistance to azithromycin in iNTS isolates, suggesting azithromycin could be an

effective alternative to first-line antibiotics. Ciprofloxacin and ceftriaxone resistance rates were slightly lower, with approximately 1 in 10 non-invasive isolates being resistant in India and a lower rate in Vietnam. The proportion of iNTS ciprofloxacin resistance in Vietnam was 10-fold higher when compared with non-invasive isolates but iNTS ceftriaxone resistance was lower than in non-invasive samples. Phu *et al.*[73] reported that the pooled prevalence of resistance to ciprofloxacin, among NTS isolates from humans from two studies in Vietnam, was 8% and was similar to non-invasive NTS from India (9.2%) but twice the estimate in Vietnam (4.1%) in this study.[71] In Thailand, iNTS resistance to ciprofloxacin was previously reported at 41% and this is similar (41.1%) to that reported from Vietnam in this study.[74]

This study estimated non-invasive NTS co-trimoxazole resistance to be 9.2% in India, lower than that reported in Thailand (59%).[74] Phu *et al.*[73] reported co-trimoxazole resistance to be 25% in Vietnam, slightly lower than our pooled estimates from Vietnam (non-invasive: 34%; iNTS: 39.2%). In 2018, the EU reported the proportions of human *Salmonella* isolates resistant to sulphonamides to be 30.5%, to ampicillin 25.9% and to ciprofloxacin 12.5%, which is comparable to our results from India. Overall, the AMR burden associated with NTS isolates is greater in Vietnam than that estimated from India in our review.

In Thailand, a 1 year study involving 10 hospitals and 166 patients identified MDR-NTS in 68.8% of patients, which is higher than our estimates in India (non-invasive: 30.2%; iNTS: 22.3%) and Vietnam (non-invasive: 41.9%; iNTS: 41.2%).[74] Countrywide data in the USA showed MDR was present only in 9.3% of human NTS isolates in 2014, while it was 26% over 10 EU member states, although very high prevalence was present in some countries.[19] Effective national antimicrobial surveillance programmes are essential for halting the risk posed by AMR.[75] Targeted interventions can be planned by tracking AMR in both humans and animals. Denmark has made it mandatory for veterinarians to report the usage of medicines (via VetStat). Even though some countries such as the USA and Japan collect the annual sales data of drugs by class, it is of limited utility and is not a true surrogate for actual antibiotic use in animals.[76,77] Systematic efforts to collect epidemiological data relevant to monitoring AMR in Southeast Asian regions is lacking, and existing data imply that AMR is a burgeoning and often neglected issue.[75]

The pooled CFR for invasive and non-invasive NTS in this review [14.9% (95% CI: 4.0%–29.6%)] is similar to that reported by Marchello *et al.*[6] in 2022 [14.7% (95% CI: 12.2%–17.3%)] and the GBD (2019) estimate [14.5% (95% CI: 9.2%–21.1%)].[8] Given its rapid onset and high CFR, it is likely that some deaths occur before the patients reach any healthcare facility, particularly those from remote regions in Asia.[8]

This study has several limitations. Firstly, resource limitations restricted our ability to widen the search to include non-English language papers. The majority of studies were from India, with very few from Sri Lanka (2) and Bangladesh (5) making comparison across the countries difficult. There was a lack of serovar-specific and molecular data from Sri Lanka and Bangladesh, preventing provision of reliable estimates from these countries. Some of the studies included had a high ROB, which would have affected the results. Even though we sought to find evidence on source attribution to poultry and the link between poultry and humans, few studies addressed this and hence we were not able to fulfil this objective. The scarcity of data did not enable an investigation of how incidence and AMR patterns may have changed over time. Finally, the studies included in the review belonged to different geographical and clinical settings and hence data were heterogeneous. Since the studies were mostly based in hospital settings, were not designed to calculate accurate prevalence and were retrospective, these estimates might not be nationally representative as they would have missed those cases that did not reach the hospital seeking healthcare. In future, burden estimates from the community would prove useful for provision of reliable estimates. For this, in a resource-poor setting, the cost of community-based surveillance could be reduced by conducting hybrid surveillance that combines hospital-based surveillance with a yearly healthcare utilization survey in the community.[78,79]

A 'One Health' approach for the control of NTS should also be implemented in the future, as the organism circulates between humans, animals and the environment. The current lack of reliable surveillance data to determine the true burden and AMR of NTS in South Asian countries, should be tackled through the One Health initiative for sustainable and cost-effective control of the disease.

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Transparency declarations

None to declare.

Author contributions

Conceptualization: R.S., F.T., G.F. Methodology: J.F., P.M. Searching and screening of articles: J.F., L.O'N., B.L., C.K., M.H., T.S., A.C., T.T.M.H., S.S. Data abstraction: C.K., L.O'N., R.R. ROB assessment: R.R., C.K. Formal analysis: R.R. Validation: R.S., P.M., P.N.D. Visualization: R.R., C.K., L.O'N. Manuscript writing: R.R., R.S. Reviewing and editing: R.S., P.M., S.S.R.A., C.K., L.O'N., G.F., B.L., M.H., T.S., S.S., P.N.D.

Supplementary data

Figures S1 to S7 and Tables S1 to S7 are available as Supplementary data at *JAC-AMR* Online.

References

1 Institute for Health Metrics and Evaluation. Diarrheal diseases—Level 3 cause. https://www.healthdata.org/research-analysis/diseases-injuries-risks/factsheets/2021-diarrheal-diseases-level-3-disease.

2 Havelaar AH, Kirk MD, Torgerson PR *et al.* World Health Organization global estimates and regional comparisons of the burden of foodborne disease in 2010. *PLoS Med* 2015; **12**: e1001923. https://doi.org/10.1371/journal.pmed.1001923

3 Abebe E, Gugsa G, Ahmed M. Review on major food-borne zoonotic bacterial pathogens. *J Trop Med* 2020; **2020**: 4674235. https://doi.org/10.1155/2020/4674235

4 de Jong HK, Parry CM, van der Poll T *et al*. Host-pathogen interaction in invasive Salmonellosis. *PLoS Pathog* 2012; **8**: e1002933. https://doi.org/10.1371/journal.ppat.1002933

5 Gal-Mor O, Boyle EC, Grassl GA. Same species, different diseases: how and why typhoidal and non-typhoidal *Salmonella enterica* serovars differ. *Front Microbiol* 2014; **5**: 391. https://doi.org/10.3389/fmicb.2014.00391

6 Marchello CS, Birkhold M, Crump JA *et al*. Complications and mortality of non-typhoidal *Salmonella* invasive disease: a global systematic review and meta-analysis. *Lancet Infect Dis* 2022; **22**: 692–705. https://doi.org/10.1016/S1473-3099(21)00615-0

7 Feasey NA, Dougan G, Kingsley RA *et al*. Invasive non-typhoidal *Salmonella* disease: an emerging and neglected tropical disease in Africa. *Lancet* 2012; **379**: 2489–99. https://doi.org/10.1016/S0140-6736(11)61752-2

8 GBD 2017 Non-Typhoidal Salmonella Invasive Disease Collaborators. The global burden of non-typhoidal *Salmonella* invasive disease: a systematic analysis for the Global Burden of Disease study 2017. *Lancet Infect Dis* 2019; **19**: 1312–24. https://doi.org/10.1016/S1473-3099(19)30418-9

9 Kumar S, Kumar Y, Kumar G *et al*. Non-typhoidal *Salmonella* infections across India: emergence of a neglected group of enteric pathogens. *J Taibah Univ Med Sci* 2022; **17**: 747–54. https://doi.org/10.1016/j.jtumed.2022.02.011

10 Chattaway MA, Langridge GC, Wain J. *Salmonella* nomenclature in the genomic era: a time for change. *Sci Rep* 2021; **11**: 7494. https://doi.org/10.1038/s41598-021-86243-w

11 Crump JA, Sjölund-Karlsson M, Gordon MA *et al*. Epidemiology, clinical presentation, laboratory diagnosis, antimicrobial resistance, and antimicrobial management of invasive salmonella infections. *Clin Microbiol Rev* 2015; **28**: 901–37. https://doi.org/10.1128/CMR.00002-15

12 Zhang J, Peng Z, Chen K *et al*. Genomic characterization of *Salmonella enterica* serovar Weltevreden associated with human diarrhea. *Microbiol Spectr* 2023; **11**: e0354222. https://doi.org/10.1128/spectrum.03542-22

13 Guibourdenche M, Roggentin P, Mikoleit M *et al*. Supplement 2003–2007 (No. 47) to the White-Kauffmann-Le Minor scheme. *Res Microbiol* 2010; **161**: 26–9. https://doi.org/10.1016/j.resmic.2009.10.002

14 Chan K, Baker S, Kim CC *et al*. Genomic comparison of *Salmonella enterica* serovars and *Salmonella bongori* by use of an *S. enterica* serovar typhimurium DNA microarray. *J Bacteriol* 2003; **185**: 553–63. https://doi.org/10.1128/JB.185.2.553-563.2003

15 Buckle GC, Walker CL, Black RE. Typhoid fever and paratyphoid fever: systematic review to estimate global morbidity and mortality for 2010. *J Glob Health* 2012; **2**: 010401. https://doi.org/10.7189/jogh.01.010401

16 Kasumba IN, Pulford CV, Perez-Sepulveda BM *et al*. Characteristics of *Salmonella* recovered from stools of children enrolled in the global enteric multicenter study. *Clin Infect Dis* 2021; **73**: 631–41. https://doi.org/10.1093/cid/ciab051

17 Plumb I, Fields PI, Bruce B. Salmonellosis, Nontyphoidal: CDC Yellow Book 2024. https://wwwnc.cdc.gov/travel/yellowbook/2024/infections-diseases/salmonellosis-nontyphoidal.

18 Parisi A, Phuong TLT, Mather AE *et al*. The role of animals as a source of antimicrobial resistant nontyphoidal *Salmonella* causing invasive and non-invasive human disease in Vietnam. *Infect Genet Evol* 2020; **85**: 104534. https://doi.org/10.1016/j.meegid.2020.104534

19 McDermott PF, Zhao S, Tate H. Antimicrobial resistance in nontyphoidal *Salmonella*. *Microbiol Spectr* 2018; **6:** 10.1128/microbiolspec.ARBA-0014-2017. https://doi.org/10.1128/microbiolspec.ARBA-0014-2017

20 Mazurek J, Salehi E, Propes D *et al*. A multistate outbreak of *Salmonella enterica* serotype Typhimurium infection linked to raw milk consumption —Ohio, 2003. *J Food Prot* 2004; **67**: 2165–70. https://doi.org/10.4315/0362-028X-67.10.2165

21 Espié E, De Valk H, Vaillant V *et al*. An outbreak of multidrug-resistant *Salmonella enterica* serotype Newport infections linked to the consumption of imported horse meat in France. *Epidemiol Infect* 2005; **133**: 373–6. https://doi.org/10.1017/S0950268804003449

22 Kariuki S, Revathi G, Kariuki N *et al*. Invasive multidrug-resistant non-typhoidal *Salmonella* infections in Africa: zoonotic or anthroponotic transmission? *J Med Microbiol* 2006; **55**: 585–91. https://doi.org/10.1099/jmm.0.46375-0

23 CDC. Reptile-associated salmonellosis—selected states, 1996-1998. *MMWR Morb Mortal Wkly Rep* 1999; **48**: 1009–13.

24 WHO. Global antimicrobial resistance and use surveillance system (GLASS) report: 2022. 2022. https://www.who.int/publications/i/item/9789240062702.

25 EFSA Panel on Biological Hazards. Joint opinion on antimicrobial resistance (AMR) focused on zoonotic infections. *EFSA J* 2009; **7**: 1372. https://doi.org/10.2903/j.efsa.2009.1372

26 Moher D, Liberati A, Tetzlaff J *et al*. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *BMJ* 2009; **339**: b2535. https://doi.org/10.1136/bmj.b2535

27 Munn Z, Moola S, Lisy K *et al*. Methodological guidance for systematic reviews of observational epidemiological studies reporting prevalence and cumulative incidence data. *Int J Evid Based Healthc* 2015; **13**: 147–53. https://doi.org/10.1097/XEB.0000000000000054

28 Page MJ, McKenzie JE, Bossuyt PM *et al*. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. *BMJ* 2021; **372**: n71. https://doi.org/10.1136/bmj.n71

29 Shahunja KM, Leung DT, Ahmed T *et al*. Factors associated with non-typhoidal *Salmonella* bacteremia versus typhoidal *Salmonella* bacteremia in patients presenting for care in an urban diarrheal disease hospital in Bangladesh. *PLoS Negl Trop Dis* 2015; **9**: e0004066. https://doi.org/10.1371/journal.pntd.0004066

30 Patra S, Mukim Y, Varma M *et al*. Invasive nontyphoidal *Salmonella* disease in southern India: a 5-year experience from a tertiary care hospital. *Turk J Med Sci* 2018; **48**: 1030–5. https://doi.org/10.3906/sag-1804-90

31 Ananthakrishnan S, Mahadevan S, Srinivasan S. Non-typhoidal salmonellosis infection in persistent childhood diarrhoea from south India. *J Trop Pediatr* 1991; **37**: 84–5. https://doi.org/10.1093/tropej/37.2.84

32 Niyogi SK, Dutta D, Bhattacharya MK *et al*. Multi-drug resistant non-typhoidal *Salmonella* spp. associated with acute diarrhoeal disease. *Indian J Med Res* 1999; **110**: 183–5. https://www.proquest.com/openview/6c39915d3c5f8b08bd6f86d175903eac/1

33 Jain P, Chowdhury G, Samajpati S *et al*. Characterization of non-typhoidal *Salmonella* isolates from children with acute gastroenteritis, Kolkata, India, during 2000–2016. *Braz J Microbiol* 2020; **51**: 613–27. https://doi.org/10.1007/s42770-019-00213-z

34 Taneja N, Appannanavar SB, Kumar A *et al*. Serotype profile and molecular characterization of antimicrobial resistance in non-typhoidal *Salmonella* isolated from gastroenteritis cases over nine years. *J Med Microbiol* 2014; **63**: 66–73. https://doi.org/10.1099/jmm.0.061416-0

35 Ahmed D, Ud-Din AI, Wahid SU *et al*. Emergence of bla_{TEM} type extended-spectrum β-lactamase producing *Salmonella* spp. in the urban area of Bangladesh. *ISRN Microbiol* 2014; **2014**: 715310. https://doi.org/10.1155/2014/715310

36 Sharma NC, Kumar D, Sarkar A *et al*. Prevalence of multidrug resistant salmonellae with increasing frequency of *Salmonella enterica* serovars Kentucky and Virchow among hospitalized diarrheal cases in and around Delhi, India. *Jpn J Infect Dis* 2020; **73**: 119–23. https://doi.org/10.7883/yoken.JJID.2019.063

37 Uppal B, Perween N, Aggarwal P *et al*. A comparative study of bacterial and parasitic intestinal infections in India. *J Clin Diagn Res* 2015; **9**: DC01–4. https://doi.org/10.7860/JCDR/2015/11965.5619

38 Duong VT, The HC, Nhu TDH *et al*. Genomic serotyping, clinical manifestations, and antimicrobial resistance of nontyphoidal *Salmonella* gastroenteritis in hospitalized children in Ho Chi Minh City, Vietnam. *J Clin Microbiol* 2020; **58**: e01465-20. https://doi.org/10.1128/JCM.01465-20

39 Leung DT, Das SK, Malek MA *et al*. Non-typhoidal *Salmonella* gastroenteritis at a diarrheal hospital in Dhaka, Bangladesh, 1996–2011. *Am J Trop Med Hyg* 2013; **88**: 661–9. https://doi.org/10.4269/ajtmh.12-0672

40 Bangera SR, Umakanth S, Mukhopadhyay AK *et al*. Draft genome sequence of *Salmonella enterica* subsp. *enterica* serotype Typhimurium sequence type 313, isolated from India. *Microbiol Resour Announc* 2018; **7**: e00990-18. https://doi.org/10.1128/MRA.00990-18

41 Gogate A, Deodhar L. *Salmonella* meningitis. *Indian J Pediatr* 1984; **51**: 549–51. https://doi.org/10.1007/BF02776620

42 Nga TV, Parry CM, Le T *et al*. 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. *Trans R Soc Trop Med Hyg* 2012; **106**: 26–34. https://doi.org/10.1016/j.trstmh.2011.10.004

43 Khan MI, Ochiai RL, von Seidlein L *et al*. Non-typhoidal *Salmonella* rates in febrile children at sites in five Asian countries. *Trop Med Int Health* 2010; **15**: 960–3. https://doi.org/10.1111/j.1365-3156.2010.02553.x

44 Jacob JJ, Solaimalai D, Muthuirulandi Sethuvel DP *et al*. A nineteen-year report of serotype and antimicrobial susceptibility of enteric non-typhoidal *Salmonella* from humans in Southern India: changing facades of taxonomy and resistance trend. *Gut Pathog* 2020; **12**: 49. https://doi.org/10.1186/s13099-020-00388-z

45 Kumar Y, Sharma A, Sehgal R *et al*. Distribution trends of *Salmonella* serovars in India (2001–2005). *Trans R Soc Trop Med Hyg* 2009; **103**: 390–4. https://doi.org/10.1016/j.trstmh.2008.09.009

46 Harichandran D, Dinesh KR. Antimicrobial susceptibility profile, treatment outcome and serotype distribution of clinical isolates of *Salmonella enterica* subspecies *enterica*: a 2-year study from Kerala, South India. *Infect Drug Resist* 2017; **10**: 97–101. https://doi.org/10.2147/IDR.S126209

47 Vo AT, van Duijkeren E, Fluit AC *et al*. Distribution of *Salmonella enterica* serovars from humans, livestock and meat in Vietnam and the dominance of *Salmonella* Typhimurium phage type 90. *Vet Microbiol* 2006; **113**: 153–8. https://doi.org/10.1016/j.vetmic.2005.10.034

48 Shahane V, Muley V, Kagal A *et al*. Non-typhoid salmonellosis: emerging infection in Pune? *Indian J Med Microbiol* 2007; **25**: 173–4. https://doi.org/10.1016/S0255-0857(21)02186-1

49 Menezes GA, Khan MA, Harish BN *et al*. Molecular characterization of antimicrobial resistance in non-typhoidal salmonellae associated with systemic manifestations from India. *J Med Microbiol* 2010; **59**: 1477–83. https://doi.org/10.1099/jmm.0.022319-0

50 Behl P, Gupta V, Sachdev A *et al*. Patterns in antimicrobial susceptibility of salmonellae isolated at a tertiary care hospital in northern India. *Indian J Med Res* 2017; **145**: 124–8. https://doi.org/10.4103/ijmr.IJMR_862_14

51 Sudhaharan S, Kanne P, Vemu L *et al*. Extraintestinal infections caused by nontyphoidal *Salmonella* from a tertiary care center in India. *J Lab Physicians* 2018; **10**: 401–5. https://doi.org/10.4103/JLP.JLP_79_18

52 Vo AT, van Duijkeren E, Gaastra W *et al*. Antimicrobial resistance, class 1 integrons, and genomic island 1 in *Salmonella* isolates from Vietnam. *PLoS One* 2010; **5**: e9440. https://doi.org/10.1371/journal.pone.0009440

53 Mather AE, Phuong TLT, Gao Y *et al*. New variant of multidrug-resistant *Salmonella enterica* serovar Typhimurium associated with invasive disease in immunocompromised patients in Vietnam. *mBio* 2018; **9**: e01056-18. https://doi.org/10.1128/mBio.01056-18

54 Jain P, Sudhanthirakodi S, Chowdhury G *et al*. Antimicrobial resistance, plasmid, virulence, multilocus sequence typing and pulsed-field gel electrophoresis profiles of *Salmonella enterica* serovar Typhimurium clinical and environmental isolates from India. *PLoS One* 2018; **13**: e0207954. https://doi.org/10.1371/journal.pone.0207954

55 Sinha S, Pazhani GP, Sen B *et al*. Molecular characterization of *Salmonella enterica* serotype Worthington isolated from childhood diarrhea cases in Kolkata, India. *Jpn J Infect Dis* 2006; **59**: 275–6. https://doi.org/10.7883/yoken.JJID.2006.275

56 Khoshoo V, Raj P, Srivastava R *et al*. *Salmonella* Typhimurium-associated severe protracted diarrhea in infants and young children. *J Pediatr Gastroenterol Nutr* 1990; **10**: 33–6. https://doi.org/10.1097/00005176-199001000-00006

57 Chaudhary U, Sabharwal U, Tewari AD. *Salmonella* meningitis: report of five cases. *Indian J Pediatr* 1986; **53**: 419–22. https://doi.org/10.1007/BF02760431

58 Chowdhury G, Sarkar A, Pazhani GP *et al*. An outbreak of foodborne gastroenteritis caused by dual pathogens, *Salmonella enterica* serovar Weltevreden and *Vibrio fluvialis* in Kolkata, India. *Foodborne Pathog Dis* 2013; **10**: 904–6. https://doi.org/10.1089/fpd.2013.1491

59 Udani RH, Kabra NS, Nanavati RN *et al*. Outbreak of *Salmonella* Worthington meningitis in neonatal intensive care unit. *Indian Pediatr* 1999; **36**: 300–3. https://indianpediatrics.net/mar1999/mar-300-303.htm

60 Phu Huong Lan N, Le Thi Phuong T, Nguyen Huu H *et al*. Invasive non-typhoidal *Salmonella* infections in Asia: clinical observations, disease outcome and dominant serovars from an infectious disease hospital in Vietnam. *PLoS Negl Trop Dis* 2016; **10**: e0004857. https://doi.org/10.1371/journal.pntd.0004857

61 Feasey NA, Everett D, Faragher EB *et al*. Modelling the contributions of malaria, HIV, malnutrition and rainfall to the decline in paediatric invasive non-typhoidal *Salmonella* disease in Malawi. *PLoS Negl Trop Dis* 2015; **9**: e0003979. https://doi.org/10.1371/journal.pntd.0003979

62 Grimont PA, Weill FX. Antigenic Formulae of the Salmonella Serovars, 9th edition. 2007. https://www.pasteur.fr/sites/default/files/veng_0.pdf.

63 Hounmanou YMG, Dalsgaard A, Sopacua TF *et al*. Molecular characteristics and zoonotic potential of *Salmonella* Weltevreden from cultured shrimp and tilapia in Vietnam and China. *Front Microbiol* 2020; **11**: 1985. https://doi.org/10.3389/fmicb.2020.01985

64 Minh DK, Hounmanou YMG, Mai HBT *et al*. Prevalence and genomic characterization of *Salmonella* Weltevreden in commercial pig feed. *Vet Microbiol* 2020; **246**: 108725. https://doi.org/10.1016/j.vetmic.2020.108725

65 FAOSTAT. Food Balances (2010-). https://www.fao.org/faostat/en/#data/FBS.

66 Jolley KA, Bray JE, Maiden MCJ. Open-access bacterial population genomics: BIGSdb software, the PubMLST.org website and their applications. *Wellcome Open Res* 2018; **3**: 124. https://doi.org/10.12688/wellcomeopenres.14826.1

67 Biswas S, Li Y, Elbediwi M *et al*. Emergence and dissemination of *mcr*-carrying clinically relevant *Salmonella* Typhimurium monophasic clone ST34. *Microorganisms* 2019; **7**: 298. https://doi.org/10.3390/microorganisms7090298

68 Kingsley RA, Msefula CL, Thomson NR *et al*. Epidemic multiple drug resistant *Salmonella* Typhimurium causing invasive disease in sub-Saharan Africa have a distinct genotype. *Genome Res* 2009; **19**: 2279–87. https://doi.org/10.1101/gr.091017.109

69 Lu Z, Tadi DA, Fu J *et al*. Global status of azithromycin and erythromycin resistance rates in *Neisseria gonorrhoeae*: a systematic review and meta-analysis. *Yale J Biol Med* 2022; **95**: 465–78. https://pmc.ncbi.nlm.nih.gov/articles/PMC9765340/

70 Lin EY, Adamson PC, Klausner JD. Epidemiology, treatments, and vaccine development for antimicrobial-resistant *Neisseria gonorrhoeae*: current strategies and future directions. *Drugs* 2021; **81**: 1153–69. https://doi.org/10.1007/s40265-021-01530-0

71 Kahn R, Eyal N, Sow SO *et al*. Mass drug administration of azithromycin: an analysis. *Clin Microbiol Infect* 2023; **29**: 326–31. https://doi.org/10.1016/j.cmi.2022.10.022

72 Luoma J, Adubra L, Alber D *et al*. Statistical analysis plan for the LAKANA trial: a cluster-randomized, placebo-controlled, double-blinded, parallel group, three-arm clinical trial testing the effects of mass drug administration of azithromycin on mortality and other outcomes among 1–11-month-old infants in Mali. *Trials* 2023; **24**: 733. https://doi.org/10.1186/s13063-023-07771-6

73 Phu DH, Wongtawan T, Truong DB *et al*. A systematic review and meta-analysis of integrated studies on antimicrobial resistance in Vietnam, with a focus on Enterobacteriaceae, from a One Health perspective. *One Health* 2022; **15**: 100465. https://doi.org/10.1016/j.onehlt.2022.100465

74 Hengkrawit K, Tangjade C. Factors associated with multi-drug-resistant non-typhoidal *Salmonella* in the invasive disease, Thailand. *Infect Drug Resist* 2022; **15**: 6563–76. https://doi.org/10.2147/IDR.S387037

75 WHO. Integrated surveillance of antimicrobial resistance in foodborne bacteria: application of a One Health approach: guidance from the WHO Advisory Group on Integrated Surveillanec of Antimicrobial Resistance (AGISAR). 2017. https://www.who.int/publications/i/item/9789241512411.

76 EMA. Sales of veterinary antimicrobial agents in 29 European countries in 2014. 2016. https://www.ema.europa.eu/en/documents/report/sixth-esvac-report-sales-veterinary-antimicrobial-agents-29-european-countries-2014_en.pdf.

77 Bondt N, Jensen VF, Puister-Jansen LF *et al*. Comparing antimicrobial exposure based on sales data. *Prev Vet Med* 2013; **108**: 10–20. https://doi.org/10.1016/j.prevetmed.2012.07.009

78 Raju R, Kezia Angelin J, Karthikeyan AS *et al*. Healthcare utilization survey in the hybrid model of the Surveillance for Enteric Fever in India (SEFI) study: processes, monitoring, results, and challenges. *J Infect Dis* 2021; **224**: S529–39. https://doi.org/10.1093/infdis/jiab371

79 Andrews JR, Barkume C, Yu AT *et al*. Integrating facility-based surveillance with healthcare utilization surveys to estimate enteric fever incidence: methods and challenges. *J Infect Dis* 2018; **218**: S268–76. https://doi.org/10.1093/infdis/jiy494