

Preplanned Studies

Genomic Surveillance of *Salmonella* London and Rissen Reveals International Transmission Patterns and Expanding Antimicrobial Resistance — Shanghai Municipality, China, 2020–2024

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Summary

What is already known about this topic?

Non-typhoidal *Salmonella* (NTS) represents a leading cause of foodborne gastroenteritis worldwide. The epidemiological landscape of NTS continues to evolve, with specific serotypes emerging as significant human pathogens through contaminated food products. This evolution occurs particularly within the context of globalized food supply chains and widespread antimicrobial use in agricultural settings.

What is added by this report?

This study integrated local isolates from Shanghai with global genomic data to reveal distinct international transmission patterns for *Salmonella* London and Rissen. *S. London* disseminated through historical, geographically segregated clades, whereas *S. Rissen* demonstrated recent intercontinental mixing, with Thailand identified as the primary global source. Our analysis identified high-risk plasmids harboring up to 15 resistance genes and demonstrated that Chinese isolates carried the highest antimicrobial resistance burden globally.

What are the implications for public health practice?

The global dissemination of these pathogens is directly linked to international food trade networks. Our findings necessitate a paradigm shift toward integrated global One Health surveillance that bridges human, animal, and food sectors. Implementing harmonized international policies, rigorous trade monitoring, and enhanced antimicrobial stewardship programs is essential to contain the transnational threat posed by resistant foodborne pathogens.

The emergence and worldwide dissemination of specific serotypes, including *Salmonella* London and Rissen, constitute a significant public health threat due to their escalating association with antimicrobial resistance (AMR), which compromises the effectiveness of first-line antibiotic therapies.

Methods: We performed a comprehensive genomic analysis integrating 200 local isolates collected between 2020 and 2024 from Shanghai, China, with a global dataset comprising 1,353 *S. London* and 882 *S. Rissen* genomes retrieved from Enterobase. Through whole-genome sequencing, phylogenetic reconstruction, and AMR gene profiling, we systematically characterized the population structure, transmission dynamics, and resistance profiles of these serotypes.

Results: Phylogeographic analysis revealed contrasting dissemination patterns: *S. London* spread predominantly through historical, geographically segregated clades, whereas *S. Rissen* demonstrated recent intercontinental mixing, with Thailand identified as a primary global source. We detected high-risk plasmids harboring up to 15 resistance genes that drove elevated multidrug resistance rates in 64% of *S. London* and 59% of *S. Rissen* isolates. Notably, Chinese isolates exhibited the highest AMR burden, with clinical environments identified as critical hotspots for resistance amplification.

Conclusion: The global dissemination of *S. London* and Rissen is directly linked to international food trade networks, and their evolving AMR landscape represents a critical public health concern. These findings underscore the urgent need for integrated One Health surveillance strategies to effectively control the spread of resistant foodborne pathogens.

ABSTRACT

Introduction: Non-typhoidal *Salmonella* (NTS) represents a major global cause of foodborne illness.

Non-typhoidal *Salmonella* (NTS), a leading cause of foodborne illness responsible for an estimated 90

million annual cases of acute gastroenteritis worldwide, has undergone significant epidemiological shifts in recent decades (1–2). Globalized food supply chains and extensive antimicrobial use in agriculture have driven the emergence of host-restricted serotypes such as *Salmonella* Rissen and *Salmonella* London. These serotypes have accelerated the dissemination of antimicrobial resistance (AMR) through plasmid-mediated transfer of critical resistance genes (e.g., *bla*_{CTX-M}, *mcr*-1), compromising the efficacy of first-line treatments including extended-spectrum β -lactams and fluoroquinolones (3–4).

In China, the increasing detection of *S. London* and *S. Rissen* represents a notable shift in the epidemiological landscape of foodborne illness. *S. Rissen* has gained clinical prominence in regions such as Jiangsu Province (5), while *S. London* has expanded beyond dairy products to diverse food and clinical sources worldwide (6–7). Despite their growing public health significance, comprehensive molecular epidemiological characterization of these serotypes remains limited.

Understanding the genomic architecture underlying the success of these emerging serotypes is crucial for informing public health interventions and antimicrobial stewardship strategies. We employed whole-genome sequencing (WGS) to systematically characterize the population genomics, virulence repertoire, and antimicrobial resistance profiles of *S. London* and *S. Rissen*. Our approach integrated local isolates from Shanghai's Pudong District with global genomic surveillance data to elucidate transmission patterns and resistance mechanisms.

We sequenced 200 *Salmonella* isolates (*S. London* and *S. Rissen*) collected in Pudong, Shanghai, between 2020 and 2024. These local isolates were integrated with publicly available genomic data retrieved from Enterobase (version November 2023) to construct a comprehensive global dataset comprising 1,353 *S. London* genomes (spanning 24 countries, 1971–2023) and 882 *S. Rissen* genomes (spanning 27 countries, 2001–2023). Genome assembly was performed using EToKi/SPAdes (8), followed by gene annotation with PROKKA (9) and functional characterization using eggNOG-mapper. AMR genes were identified using AMRfinder, and core genome clustering data were obtained from the HierCC database. For phylogenetic reconstruction, we constructed maximum likelihood trees using IQ-TREE (10) after removing recombinant regions from the alignment. Temporal signal analysis using TempEst revealed a weak but significant root-to-

tip correlation ($R^2=0.14$), which exceeded that of date-randomized controls; BactDating further confirmed the presence of a temporal signal in the dataset. Time-calibrated phylogenies were then generated using TreeTime to infer host-switching events and reconstruct geographic transmission pathways. Host-switching and transmission inferences were restricted to phylogenetic nodes supported by bootstrap values exceeding 70%.

Our genomic surveillance of 200 isolates from Pudong, Shanghai, revealed a diverse serotype distribution: *S. Enteritidis* (26.5%, $n=53$), *S. Typhimurium* (16.5%, $n=33$), *S. London* (10.5%, $n=21$), and *S. Rissen* (6.5%, $n=13$). Core genome multi-locus sequence typing (cgMLST) at the HC900 resolution (≤ 900 allelic distances) demonstrated distinct clustering patterns that correlated with both serotype identity and source characteristics. Typing analysis revealed distinct host associations: all *S. London* isolates belonged to ST155 and were predominantly linked to pork products (81.0%), whereas the primary food-derived serovar, *S. Rissen* (ST469), was largely isolated from pig viscera (84.6%, Figure 1A).

To contextualize our local findings, we constructed global datasets comprising 1,353 *S. London* and 882 *S. Rissen* genomes. High-resolution typing delineated two distinct global transmission paradigms and elucidated specific host adaptation patterns. The lineage HC50_37, specific to *S. London*, demonstrated clear evidence of cross-host transmission, directly linking pork products (81.0%) to clinical cases (14.3%). In parallel, HC50_142 encompassed all *S. Rissen* isolates from pig liver (46.2%) and kidney (15.4%), indicating persistent circulation within specific organ systems (Figure 1B).

Core-genome SNP phylogenies revealed distinct population structures. *S. London* stratified into four clades: a China-dominated lineage ($n=212$), a US-dominated clade ($n=778$), and two additional global lineages (Figure 2A). In contrast, *S. Rissen* exhibited significant intercontinental mixing across three primary lineages, characterized by US-mixing ($n=366$), Europe-mixing ($n=255$), and Asia-mixing clades ($n=215$, Figure 3A).

Phylogenetic analysis revealed contrasting transmission dynamics between the two serotypes. *S. London* emerged circa 1905 (HPD: 1889–1914), with subsequent divergence aligning with World War I and trade expansion; a distinct US clade formed between 1951 and 1964 (HPD: 1951–1964), coinciding with

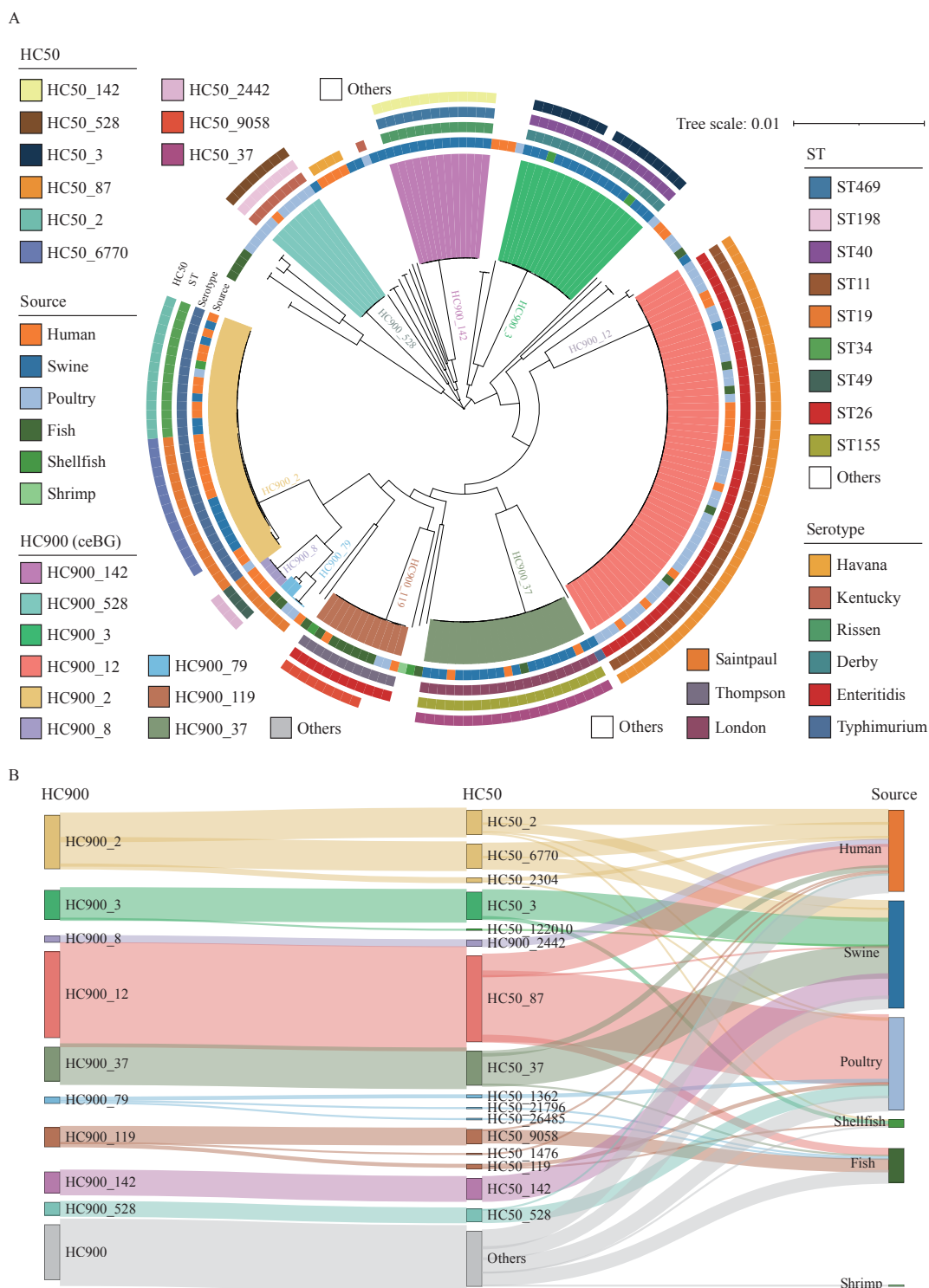


FIGURE 1. Genomic epidemiology of 200 *Salmonella* isolates from Pudong, Shanghai. (A) Maximum-likelihood phylogenetic tree of 200 *Salmonella* isolates, comprising 21 *S. London* and 13 *S. Rissen* strains, constructed through core genome multilocus sequence typing (cgMLST). (B) Sankey diagram depicting the hierarchical relationships between HC900 and HC50 clusters and their corresponding isolation sources among 200 *Salmonella* isolates from Pudong, Shanghai.

Note: For (A), the tree was visualized and annotated using the iTOL platform (<https://itol.embl.de>). Branch colors correspond to serotype classifications. Concentric rings (from inner to outer) represent: 1) isolation source, 2) serotype, 3) sequence type (ST), and 4) HC900 (ceBG) lineage designation. The scale bar indicates single nucleotide polymorphism (SNP) distance. For (B), flow paths connect HC900 clusters (left panel) to their constituent HC50 subclusters (middle panel) and ultimately to their respective isolation sources (right panel), emphasizing predominant epidemiological associations.

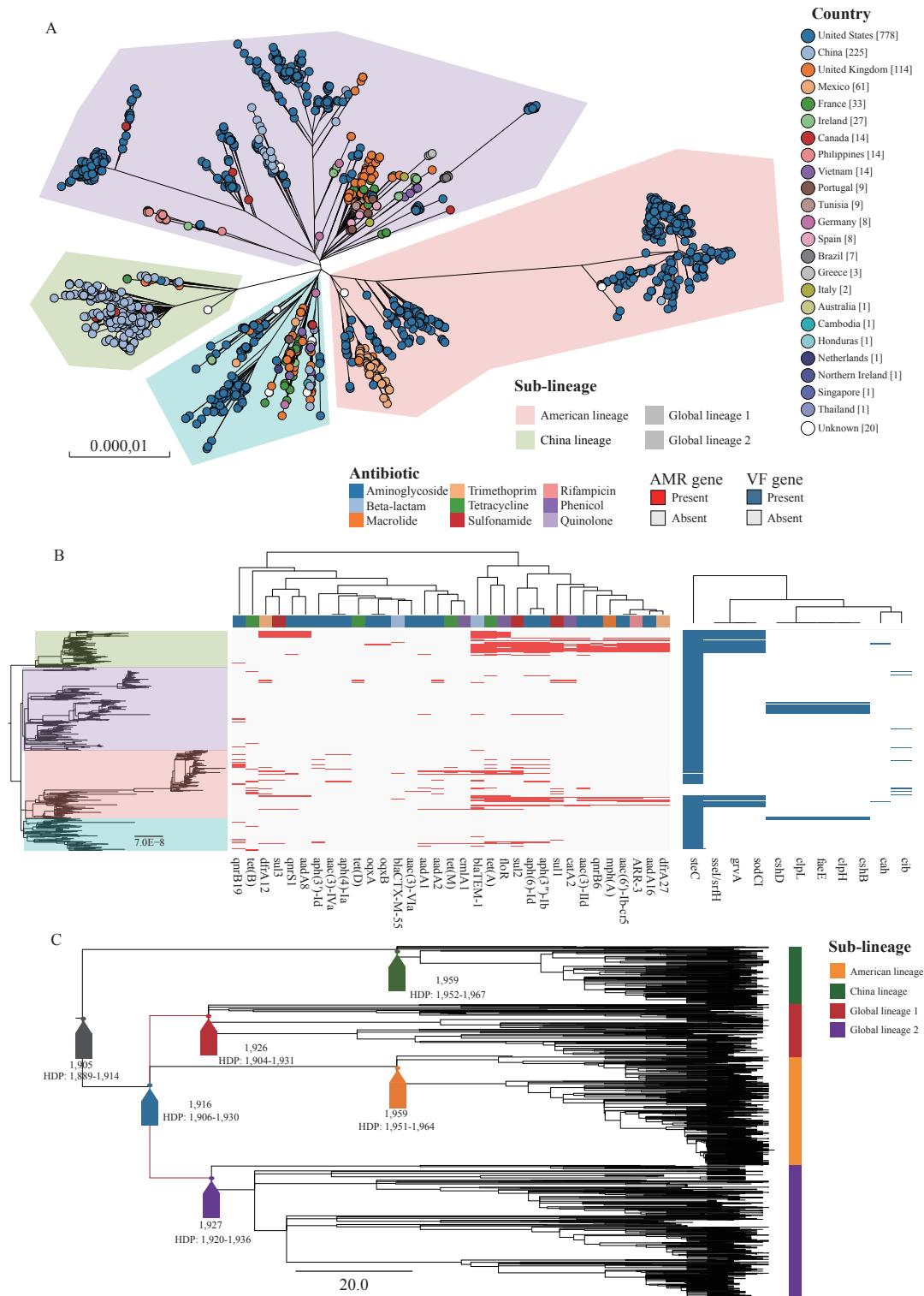


FIGURE 2. Population structure, virulence gene profiles, and antimicrobial resistance in *S. London*. (A) Minimum spanning tree derived from core genome SNP analysis of 1,353 *S. London* isolates, delineating four major phylogenetic clusters. (B) Heatmap displaying the distribution of key virulence genes across the global *S. London* collection. Blue shading indicates gene presence, while white denotes absence. (C) Chronograph depicting the estimated timing of most recent common ancestors (MRCAs) for *S. London* clades.

Note: For (C), arrows denote the MRCA for each clade, with the estimated age (in years) and 95% HPD interval displayed as text.

Abbreviation: HPD=highest posterior density; MRCA=most recent common ancestor.

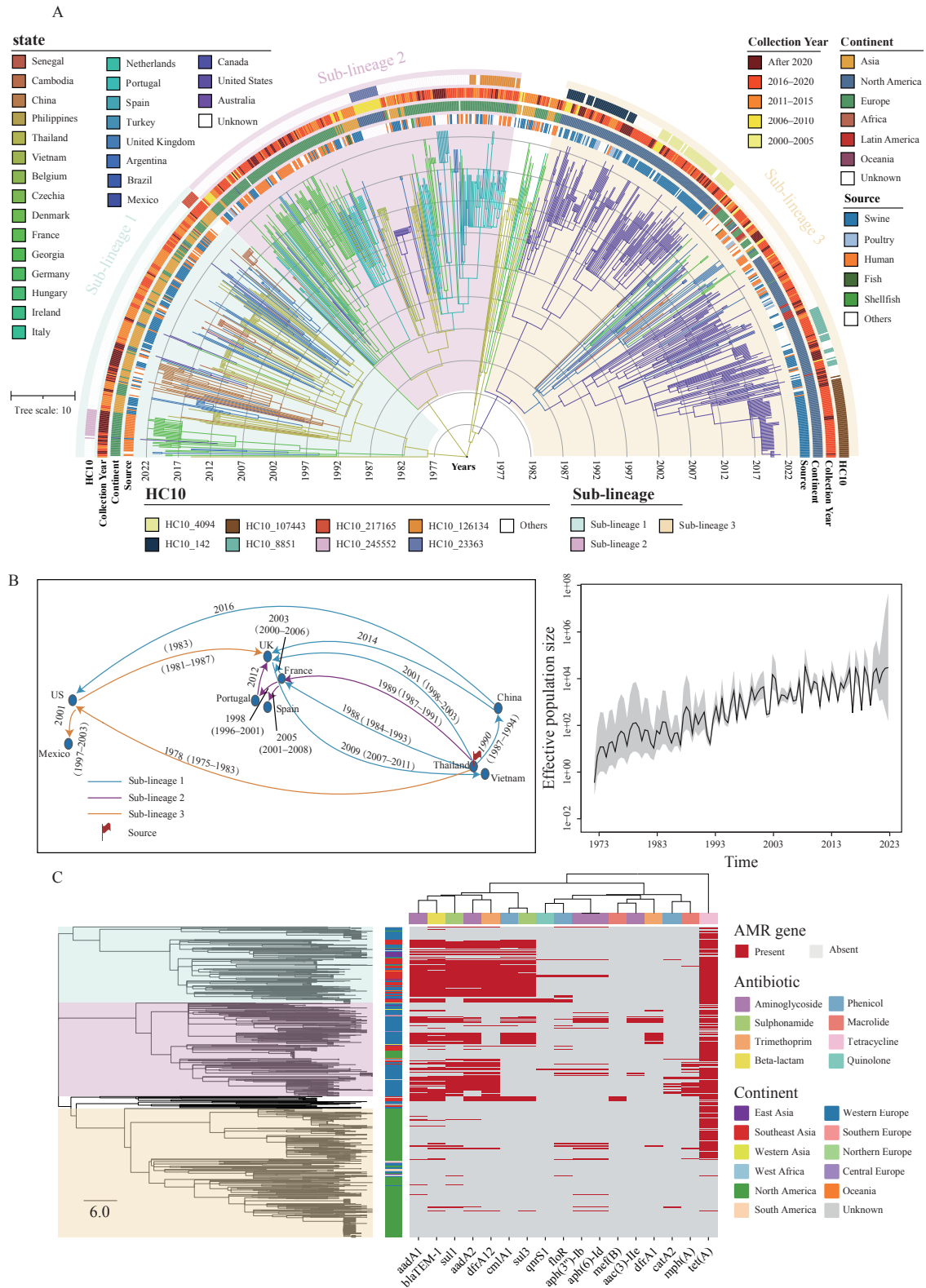


FIGURE 3. Global transmission dynamics and geographically structured antimicrobial resistance (AMR) in *S. Rissen*. (A) Phylogenetic reconstruction of 882 global *S. Rissen* isolates, annotated by continent, country, collection year, isolation source, sub-lineage, and HC10 type. (B) Reconstructed international transmission routes, illustrating inferred directionality, transmission frequency, and estimated years of cross-border dissemination events. (C) Geographic distribution of antimicrobial resistance genes throughout the global *S. Rissen* collection.

agricultural industrialization (Figure 2C). For *S. Rissen*, Thailand was identified as the predominant global source. Between 1983 and 1994, phylogenetic data indicate that Thailand exported over 200 strains, including a single event involving 117 strains to France. Europe and the United States acted as secondary hubs, with France functioning as a key redistribution center (Figure 3B). Evidence of strains being detected in the United Kingdom a decade after their inferred export illustrates the delayed and complex nature of transmission through global food chains. These transmission pathways correlate strongly with international trade in pork products.

AMR profiling revealed striking geographic disparities in resistance gene distribution. Among *S. London* isolates, we identified 75 distinct resistance genes, with 64% (308/480) exhibiting multidrug-resistance (MDR) to three or more antimicrobial categories. Chinese isolates demonstrated the highest resistance burden, with notably elevated prevalence of *tet(A)* (68.0%, 153/225), *bla*_{TEM-1} (62.7%, 141/225), and *floR* (62.2%, 140/225) (Figure 2B). Similarly, *S. Rissen* displayed a comparable global pattern, with 59% (377/635) of isolates exhibiting MDR. Southeast Asian strains harbored the most extensive resistance gene repertoires, including the world's highest documented rates of *tet(A)* (92.4%, 134/145), *sulI* (83.4%, 121/145), and *qnrS1* (83.4%, 121/145). Notably, 18 *S. Rissen* isolates (2.0%) carried *mcr* genes, with eight originating from the United States. Although *bla*_{CTX-M-55} and *mcr-1* were detected in genomes from the global database, both genes were absent from isolates collected in Pudong, Shanghai, China (Figure 3C).

Two high-risk plasmids were identified as key vectors facilitating the rapid dissemination of multidrug resistance. A large conjugative plasmid detected in Chinese *S. London* isolates harbored 15 resistance genes, conferring resistance to nearly all major antibiotic classes (Supplementary Figure S1A, available at <https://weekly.chinacdc.cn/>). More critically, a broad-host-range plasmid (GenBank: CP051314.1) was identified across multiple *Salmonella* serotypes from Shanghai, carrying essential resistance determinants including *bla*_{CTX-M-55}, *qnrS1*, and *tet(M)* (Supplementary Figure S2B). This plasmid demonstrated the highest prevalence in Chinese ($n=24$) and American ($n=93$) isolates; however, the average resistance gene load was greatest in Chinese and Mexican strains, at 8.0 and 5.8 genes per plasmid, respectively (Supplementary Figure S1C). Further

investigation is required to elucidate the precise evolutionary mechanisms underlying plasmid diversification and to experimentally validate conjugation efficiency and horizontal transfer dynamics, as current findings are derived exclusively from genomic inference.

Virulence profiling revealed divergent evolutionary trajectories for *S. London* and *S. Rissen* that reflect their distinct host ranges and ecological adaptations. We identified 294 putative virulence factors in *S. London*, with the effector gene *steC* present in nearly all isolates (93.8%). Other virulence genes demonstrated marked geographic clustering patterns. The gene combination *ssell/srfH*, *grvA*, and *sodCI* was highly prevalent in Chinese mainland strains (87.3%) yet completely absent from Taiwanese isolates. Additionally, *clpH* predominated in UK strains (61.7%), while *cib* was enriched in US isolates (75.0%), indicating region-specific adaptive evolution (Figure 2B). A fundamental genomic distinction emerged in motility and niche adaptation capabilities. *S. Rissen* possesses a complete flagellar system, whereas *S. London* harbors a defective one due to the absence of key genes (*fliC*, *fliB*). This impaired motility likely facilitated *S. London*'s adaptation to a more restricted host range, such as poultry, by favoring persistent colonization over active dissemination. In contrast, the near-universal presence of *ssek2* in *S. Rissen* (99.9%) compared to its rarity in *S. London* suggests this gene plays a critical role in survival across the diverse environmental niches and broader host range characteristic of *S. Rissen* (Figure 3C).

This study integrates genomic surveillance of *Salmonella* in Shanghai with global comparative analysis to reveal local serotype distribution and resistance profiles while elucidating the distinct transmission patterns and adaptive evolution of *S. London* and *S. Rissen*. These findings underscore the essential role of combined local-and-global perspectives in understanding bacterial pathogen dissemination.

DISCUSSION

Our study demonstrates that foodborne pathogens such as *Salmonella* *London* and *Rissen* pose significant transnational threats through their dissemination along global trade routes. The reconstruction of their intercontinental transmission networks over six decades provides conclusive genomic evidence that their spread follows patterns established by modern international trade systems. These findings underscore the need to

transition from reactive, nation-based outbreak responses to proactive, internationally coordinated genomic surveillance strategies.

The two serotypes exhibit divergent global dissemination patterns. *S. London* demonstrates a pattern of geographically isolated clades, suggesting historical introductions followed by regional establishment. In contrast, *S. Rissen* exhibits ongoing intercontinental gene flow, consistent with persistent trade-linked transmission. These distinct dispersal dynamics require tailored surveillance protocols that account for serotype-specific transmission patterns.

Phylogeographic reconstruction identifies Thailand as the primary global source for *S. Rissen*, with its decades-long intercontinental spread directly corresponding to its role as a major pork exporter. The identification of secondary transmission hubs in key European food processing centers, including France and Portugal, demonstrates that effective surveillance systems must integrate trade network data to predict and prevent cross-border transmission. Our phylogeographic analysis further revealed that the global spread of these pathogens is primarily driven by contaminated pork products, with pig viscera representing a particularly high-risk commodity. This direct association between pathogen transmission and specific trade flows emphasizes the critical need for enhanced border surveillance and harmonized international safety standards for meat products.

The identification of broad-host-range conjugative plasmids carrying up to 15 resistance genes substantially expands our understanding of antimicrobial resistance dissemination mechanisms. The co-occurrence of carbapenemase and colistin resistance genes in globally circulating strains represents a critical development in the evolution of pan-drug-resistance. The elevated resistance burden observed in human-derived isolates further indicates that clinical environments serve as evolutionary accelerators for resistance acquisition, underscoring the urgent need for enhanced antimicrobial stewardship and stringent infection control measures in healthcare settings.

Our findings underscore the need for a comprehensive global One Health surveillance framework that integrates harmonized international policies, systematic trade monitoring, and interoperable data-sharing platforms to effectively track and contain the worldwide dissemination of antimicrobial resistance and foodborne pathogens. The high prevalence of resistance to ampicillin and

tetracyclines substantially undermines the effectiveness of standard empirical therapies. Notably, the potential establishment of *bla*_{CTX-M-55} and *mcr-1* in *S. Rissen* populations threatens to generate pan-drug-resistant clones that simultaneously compromise last-resort antibiotics (3–4). These findings support a transition toward treatment strategies guided by rapid molecular diagnostics or whole-genome sequencing to ensure timely administration of effective antimicrobial agents. Implementation of integrated, real-time genomic surveillance platforms that connect human health, veterinary medicine, and food safety sectors would enable more proactive pathogen tracking and containment strategies.

This study has several limitations that warrant consideration. The absence of clinical outcome data limits our capacity to directly correlate genomic characteristics with public health consequences. Sampling biases inherent in global genome databases may result in underrepresentation of certain geographical regions or ecological niches. Furthermore, our transmission analysis relied predominantly on human and food isolates; the scarcity of comprehensive animal and environmental genomic data constrains our ability to fully reconstruct transmission pathways and identify all potential reservoirs. Future investigations should integrate clinical metadata, expand sampling efforts in underrepresented regions, and incorporate multi-sector genomic surveillance to comprehensively elucidate transmission dynamics and optimal intervention strategies.

Ethical statement: The Ethics Review Committee of the Pudong New Area Center for Disease Control and Prevention, Shanghai, reviewed and approved this study protocol. The same committee waived the requirement for informed consent.

Conflict of interest: No conflicts of interest.

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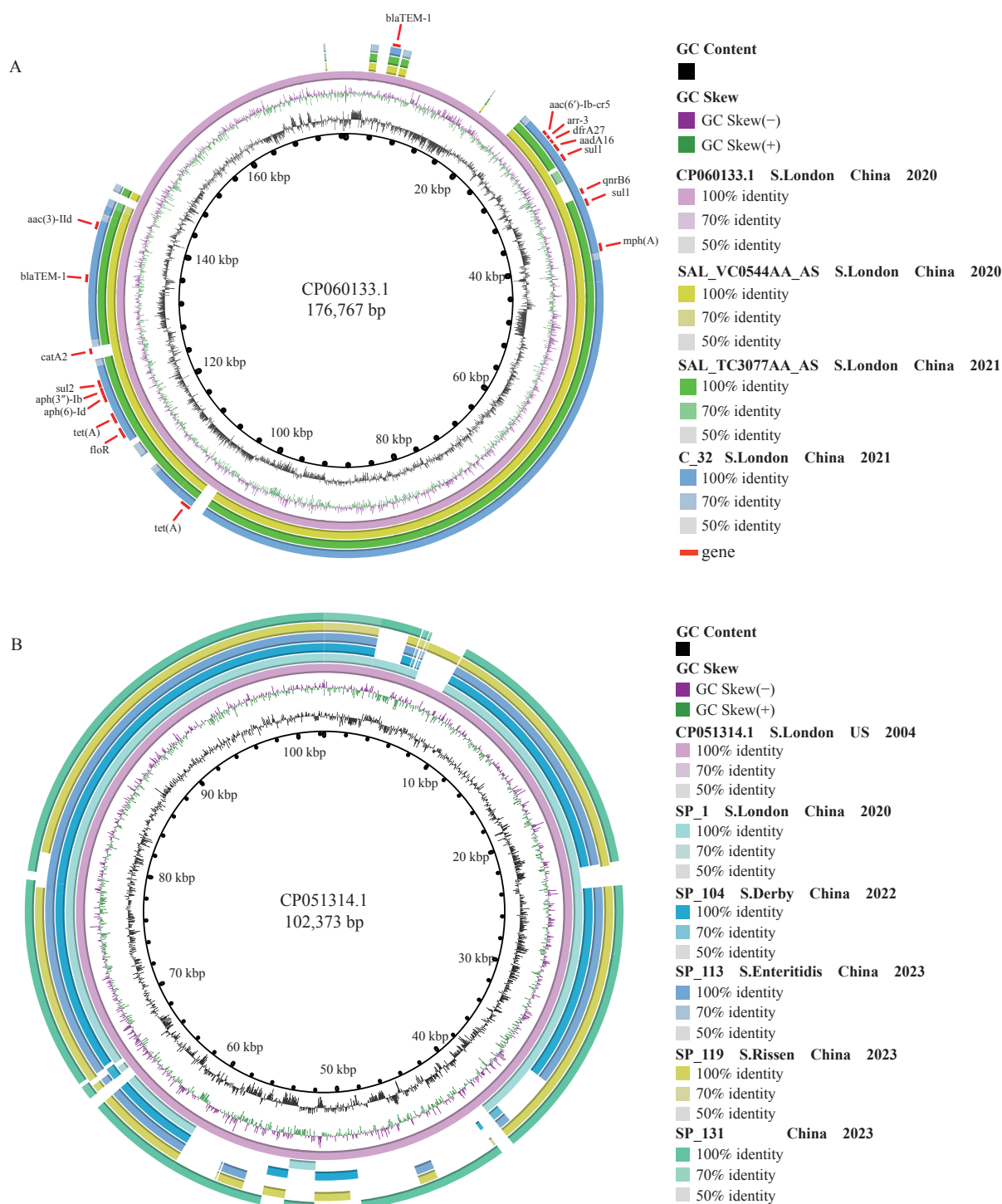
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SUPPLEMENTARY MATERIAL



SUPPLEMENTARY FIGURE S1. Characterization of a Prominent Multidrug-Resistance Plasmid. (A) Circular map of the 176,767 bp MDR plasmid CP060133.1, displaying (from inner to outer rings): GC content, GC skew, reference sequence, and comparative alignment with related plasmids. (B) Circular map of the 102,373 bp MDR plasmid CP051314.1, displaying (from inner to outer rings): GC content, GC skew, reference sequence, and comparative alignment with related plasmids. (C) Mean number of resistance genes harbored by plasmid CP051314.1 per isolate, stratified by country of origin.

Note: For (A), Antimicrobial resistance genes are indicated by red arrows.

Abbreviation: MDR=multidrug-resistance.