Article

# A global atlas and drivers of antimicrobial resistance in *Salmonella* during 1900-2023

Yanan Wang [1,2,3,4,12] ✉, Xuebin Xu [5,12], Shulei Jia [6,12], Mengqi Qu[1,12], Yuhang Pei[1], Shaofu Qiu [7], Jianmin Zhang[8], Yue Liu[5], Sufang Ma[2], Na Lyu[2], Yongfei Hu[9], Jianli Li[1], Erqin Zhang[1], Bo Wan[1], Baoli Zhu [2,10,11] & George F. Gao [2,10,11] ✉

Although previous studies using phenotypic or/and genomic approaches monitoring have revealed the spatiotemporal distribution of antimicrobial resistance (AMR) in *Salmonella* in local areas, their geographical patterns and driving factors remain largely unknown at a global scale. Here, we performed an analysis of publicly available data of 208,233 *Salmonella* genomes in 148 countries/regions between 1900 and 2023 and explored driving indicators of AMR. Overall, we found that the geographic distribution of AMR varied depending on the location, source, and serovar. The proportion of AMR levels increased across six continents, especially in serovars Agona, Dublin, I 1,4,[5],12:i:-, Muenchen, Senftenberg, Mbandaka mainly from chickens, food, wild animals, and the environment, while decreased in Schwarzengrund and Saintpaul mainly from cattle, pigs, and turkeys. We also found that *S.* Typhimurium exhibiting macro, red, dry, and rough was detected as early as 1992 in the USA, earlier than in China. Moreover, we identified that antibiotic consumption, agriculture, climate, urban, health, and socioeconomic factors contribute to the development of AMR in *Salmonella*. We present a globally high-resolution genetic atlas of *Salmonella* and also identify some factors driving the rise of AMR, which can provide valuable information for understanding the transmission dynamics and evolutionary trajectories of *Salmonella*.

*Salmonella enterica* (*S. enterica*) is one of the leading causes of foodborne disease around the world. In 2019, non-typhoidal *Salmonella* (NTS), *Salmonella* Typhi (*S.* Typhi), and *Salmonella* Paratyphi caused 215,000, 182,000, and 23,300 deaths worldwide, respectively,

according to the estimates of the Global Burden of Disease (GBD) Study[1]. The emergence and spread of antimicrobial-resistant *S. enterica* have increased the GBD posed by *S. enterica*, especially to critically important antimicrobials such as fluoroquinolones and broad-

[1]International Joint Research Center of National Animal Immunology, College of Veterinary Medicine, Henan Agricultural University, Zhengzhou, Henan, China. [2]CAS Key Laboratory of Pathogen Microbiology and Immunology, Institute of Microbiology, Chinese Academy of Sciences (CAS), Beijing, China. [3]Longhu Laboratory, Zhengzhou, Henan, China. [4]Henan Academy of Innovations in Medical Science, Zhengzhou, Henan, China. [5]Department of Microbiology, Shanghai Municipal Center for Disease Control and Prevention, Shanghai, China. [6]School of Basic Medical Sciences, Tianjin Medical University, Tianjin, China. [7]Center for Disease Control and Prevention of Chinese PLA, Beijing, China. [8]Center of Emerging and Zoonotic Diseases, National and Regional Joint Engineering Laboratory for Medicament of Zoonoses Prevention and Control, Key Laboratory of Zoonoses, Ministry of Agriculture, Key Laboratory of Zoonoses Prevention and Control of Guangdong Province, Guangdong Laboratory for Lingnan Modern Agriculture, College of Veterinary Medicine, South China Agricultural University, Guangzhou, China. [9]State Key Laboratory of Animal Nutrition and Feeding, College of Animal Science and Technology, China Agricultural University, Beijing, China. [10]University of Chinese Academy of Sciences, Beijing, China. [11]Beijing Key Laboratory of Microbial Drug Resistance and Resistome, Institute of Microbiology, Chinese Academy of Sciences, Beijing, China. [12]These authors contributed equally: Yanan Wang, Xuebin Xu, Shulei Jia, Mengqi Qu. ✉e-mail: wangyanan1001@henau.edu.cn; gaof@im.ac.cn

spectrum β-lactam antimicrobial agents (including third- and fourth-generation cephalosporins, 3GCs and 4GCs), which are the first choice for combating the severe *Salmonella* infection[2,3]. Fluoroquinolone-resistant *S*. Typhi and NTS, carbapenem-resistant and 3GCs-resistant *Enterobacterales* were categorized as high-priority and critical-priority pathogens, respectively, in the 2024 World Health Organization Bacterial Priority Pathogens List (WHO BPPL)[3–5]. The antimicrobial-resistant *S. enterica* poses a serious threat to global public health and biosecurity, which needs the development of new antimicrobial agents.

Previous studies have revealed the spatiotemporal distribution of antimicrobial resistance (AMR) in *Salmonella* in local regions/countries using phenotypic or/and genomic approaches, such as the European Union countries (https://www.efsa.europa.eu/en/topics/topic/antimicrobial-resistance)[6,7], the United States of America (USA) (https://www.fda.gov/animal-veterinary/antimicrobial-resistance/national-antimicrobial-resistance-monitoring-system)[8,9], Canada (https://www.canada.ca/en/public-health/services/surveillance/canadian-integrated-program-antimicrobial-resistance-surveillance-cipars.html)[10], Australia[11], China[12,13], Chile[14], and African countries[15]. Although effective phenotypic AMR monitoring remains crucial and phenotypic resistance detection can guide antibiotic treatment options in clinical and veterinary settings, genomic technologies provide a powerful tool for the timely understanding of the mobilization, persistence, diversity, and abundance of AMR genes (ARGs) and chromosomal gene mutations within and between microbial populations, as well as in strain typing, phylogenetic analysis, and the investigation of outbreaks[16,17]. Data on point prevalence surveys were also used to document AMR trends and maps in AMR bacteria from animals in low- and middle-income countries in recent reports[18–20]. Despite recent significant advances that have been made in AMR surveillance studies in the One Health strategy[12,13,17,21,22], the biogeographical patterns of ARGs in antimicrobial-resistant *Salmonella* remain largely unknown at a global scale.

AMR presents a continually evolving threat. With the emergence and spread of multidrug-resistant and extensively drug-resistant gram-negative pathogens worldwide, fosfomycin has been moved up to the highest priority critically important antimicrobials on the 2024 WHO list of medically important antimicrobials, because of evidence of the emergence and dissemination of plasmid-mediated fosfomycin resistance genes (FRGs) in food-producing animals, and limited therapies for treating carbapenem-resistant *Enterobacteriaceae* infections[23,24]. The emergence and global dissemination of fosfomycin-resistant *Salmonella* poses a serious threat to public health[25,26]. Monte et al. identified 4.75% (26,165) of 550,780 *Salmonella* genomes carried FRGs and were distributed in 73 distinct serovars[25]. The recent discovery of *Salmonella* Typhimurium (*S*. Typhimurium) with a distinct rough colony morphology in China (showed macro, red, dry, and rough, MRDR) with severe multidrug resistance (MDR) pattern and localized clonal expansion[27], raising public health concerns. However, genomic data from China and other countries did not include those of animal origin, such as chicken, pig, cattle, etc. Furthermore, the spatiotemporal patterns in the prevalence of fosfomycin-resistant MRDR *S*. Typhimurium (MRDRST) at a global scale have not yet been fully revealed.

Driven by rising demand, global animal protein is experiencing rapid growth, leading to the increase in global usage of antimicrobials in the animal husbandry sector by nearly 70%, while the majority of global antimicrobial consumption was used in the production of animal products[28,29]. However, massive use or exposure of antimicrobials in health care, agriculture, and the environment facilitated the rapid emergence of multidrug-resistant bacteria[20,30,31]. In addition to the bidirectional significant associations of antimicrobial consumption and AMR between humans and animals, several socioeconomic factors, environmental indicators, health-related indicators, and cattle density had positive associations with AMR on a global scale specifically in WHO critical priority (carbapenem-resistant *Acinetobacter baumanii*, 3GCs-resistant *Escherichia coli*, 3GCs-resistant *Klebsiella pneumoniae*, carbapenem-resistant *Pseudomonas aeruginosa*) and high priority (oxacillin-resistant *Staphylococcus aureus*, vancomycin-resistant *Enterococcus faecium*) pathogens, while better infrastructure and better governance indicators were associated with lower AMR[31,32]. The growing population and climate change (temperature) were positive to the increase of the AMR rate of *Klebsiella pneumoniae*, *Staphylococcus aureus*, and *Escherichia coli* were observed in 28 European countries[33] and the USA[34]. Metagenomic analysis revealed that the abundance of ARGs in sewage was not significantly associated with antimicrobial consumption[35,36], while it was positively associated with the prevalence of clinical phenotypic resistance, *pondus hydrogenii* (pH) of the sample, and season[35]. In addition, our previous study showed that the gross domestic product (GDP) value, the gross output of meat, population, temperature, and precipitation had positive associations with AMR in China[13]. However, the associations between socio-economic, climate, environmental, financial sector, infrastructure, health, poverty, trade, and anthropogenic indicators and country-level AMR in global *Salmonella* have not been assessed on a global scale.

In this study, we used genomic and evolutionary approaches with a curated data set and a global collection of 208,233 *Salmonella* genomes (from 1900 to 2023) to explore the dynamics and evolution of AMR patterns over time in different ecological niches (continent, country, and source), serovars, sequence types (STs) and identify potential drivers contributing to the spread and persistence of antimicrobial-resistant *Salmonella*. We sought to analyze the associations between different socioeconomic, climate, environmental, health, urban development, and anthropogenic indicators and country-level AMR in *Salmonella*. In addition, we explored the distribution characteristics of MRDRST and FRGs in China and other countries by analyzing 35,767 publicly available *S*. Typhimurium genomes with year, source, and location of collection information.

## Results
### Construction of a global *Salmonella* genome dataset
To our knowledge, the current work is a global-level analysis of genetic atlas and AMR patterns in *Salmonella* to date, with 471,617 publicly available genomes worldwide. After screening by using STSTR, SeqSero2, and MLST, as well as clear metadata information, a total of 208,233 high-quality genomes were used in the following analysis (Fig. 1A and Supplementary Data 1). From this data set, 99.12% were belonging to subspecies I (*enterica*) (Fig. 1B). These genomes were collected from six continents, and 51.80% of them were isolated from North America, followed by Europe (31.46%), and Asia (7.25%) (Fig. 1C). These genomes were collected from different time periods and were chronologically divided into 1900–1950 ($n = 51$), 1951–1960 ($n = 59$), 1961–1970 ($n = 74$), 1971–1980 ($n = 106$), 1981–1990 ($n = 506$), 1991–2000 ($n = 1739$), 2001–2010 ($n = 19,579$), 2011–2020 ($n = 158,449$), and 2021–2023 ($n = 27,670$) (Fig. 1D and Supplementary Fig. S1A).

Overall, the majority of genomes were from human (43.77%), chicken (15.30%), environment (8.16%), pig (7.55%), cattle (7.28%), food (4.22%), turkey (3.71%), wild animal (1.83%), and aquatic animal (1.25%) (Fig. 1E). These genomes were classified into 40 serogroups, and serogroup B was the most dominant, accounting for 30.77% (Fig. 1F). These genomes were classified into 708 serovars and 3006 STs (Fig. 1G, H and Supplementary Figs. S1C–S3). These genomes were collected from 148 countries/regions, with the top five being the USA, the United Kingdom, Canada, China, and Australia (Fig. 1I and Supplementary Fig. S4).
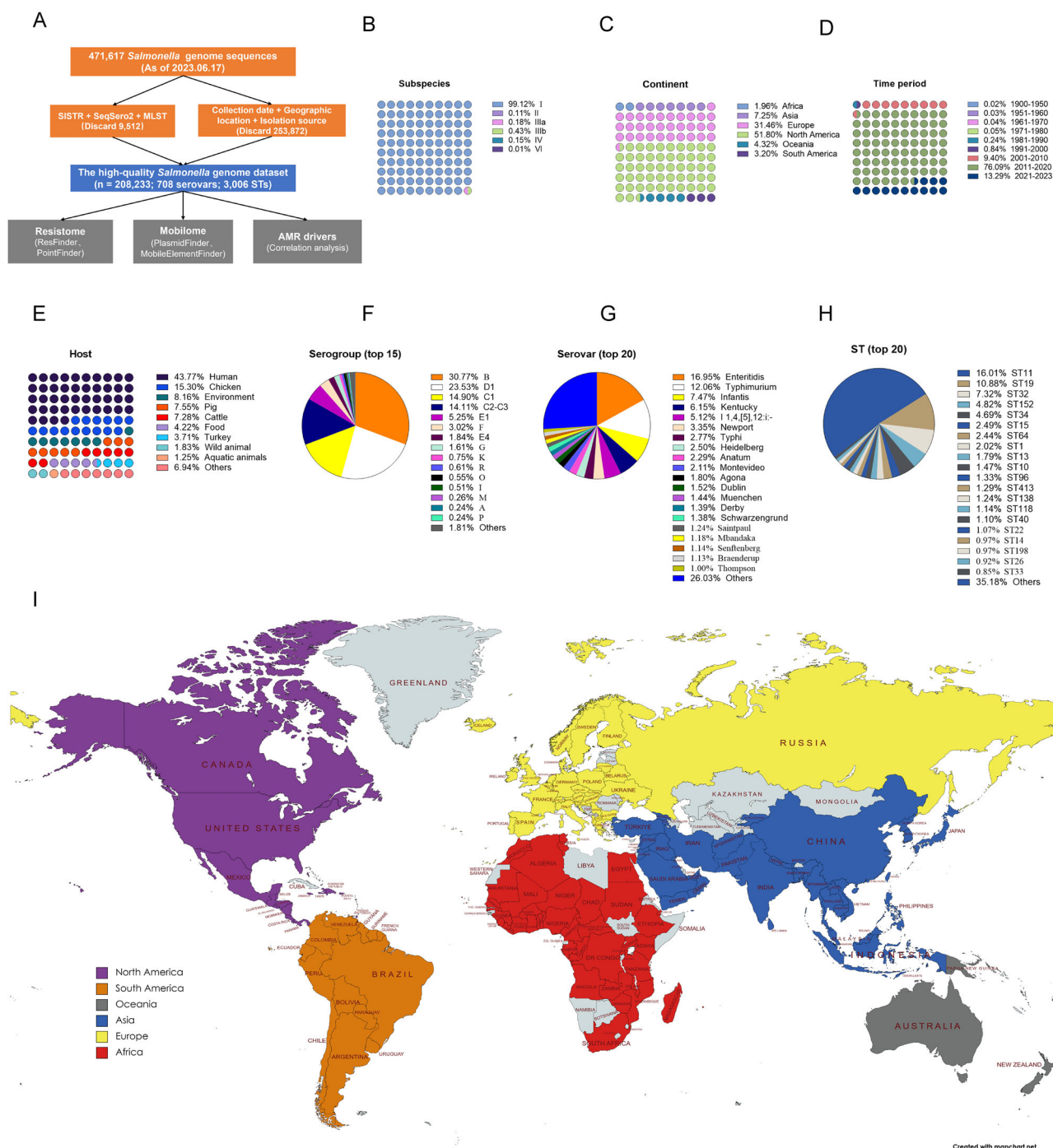
**Fig. 1 | Study design and overview of the global high-quality *Salmonella* genome catalog. A** Flowchart of the global atlas of AMR in *Salmonella* analysis pipeline. A total of 471,617 publicly available *Salmonella* genomes were downloaded (as of June 17, 2023), after screening by both bioinformatic software (including STSTR, SeqSero2, and MLST) and clear metadata, a total of 208,233 genomes were obtained. A total of 708 serovars and 3006 sequence types (STs) were detected. **B** Distribution of *S. enterica* genomes in six subspecies. **C** Distribution of *S. enterica* genomes in six continents. **D** Distribution of *S. enterica* genomes in different periods. **E** Overview of *S. enterica* genomes from different sources. **F** Overview of *S. enterica* genomes from different serogroups. **G** Top 20 serovars among the global *Salmonella* genome catalog. **H** Top 20 STs among the global *Salmonella* genome catalog. **I** A global map showing the geographic distribution of the 208,233 *Salmonella* genomes from 148 countries or regions across six continents. The map was generated using the MapChart (https://www.mapchart.net). Source data are provided as a Source Data file.

## Differences in AMR levels across geographic locations, sources, and serovars

For each drug, we estimated the prevalence of resistance (R%) for all antimicrobial classes based on whole-genome sequencing (WGS) prediction. We identified large variations in the AMR rates of antimicrobial classes. The prevalence of tetracyclines resistance and fluoroquinolones non-susceptible were high (R% >25%) across all tested *Salmonella* genomes at the global scale. In comparison, the prevalence of resistance has remained at low levels in polymyxins, macrolides, rifamycin, lincosamide, and disinfectants (R% <2.5%). Globally, resistance levels represented considerable geographic variations (Table 1).

**Table 1 | Differences in AMR rates in *Salmonella* across geographic locations, sources, and serovars**

| Antimicrobial class | | Disinfectant | Amphenicol | Beta-lactam | Fosfomycin | Lincosamide | Rifamycin | Sulfonamide | Tetracycline | Trimethoprim | Fluoroquinolone | Polymyxin | Macrolide | MDR |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Global (*n* = 208,233)** | | 2.44% | 9.48% | 18.27% | 7.67% | 0.42% | 1.05% | 21.84% | 27.68% | 7.43% | 65.50% | 0.65% | 1.11% | 34.05% |
| **Continent** | Africa (*n* = 4088) | 1.32% | 19.91% | 23.65% | 3.47% | 0.00% | 0.10% | 28.69% | 23.85% | 20.87% | 56.51% | 0.02% | 0.7% | 35.10% |
| | Asia (*n* = 15,103) | 5.86% | 28.42% | 41.31% | 10.47% | 3.32% | 12.49% | 41.73% | 40.77% | 25.54% | 77.29% | 1.32% | 6.79% | 50.96% |
| | Europe (*n* = 65,500) | 0.24% | 6.54% | 18.67% | 4.70% | 0.28% | 0.30% | 19.48% | 21.31% | 7.17% | 52.89% | 0.23% | 0.98% | 26.54% |
| | North America (*n* = 107,870) | 3.65% | 8.39% | 14.68% | 9.09% | 0.13% | 0.08% | 20.72% | 30.97% | 4.16% | 74.46% | 0.88% | 0.49% | 37.62% |
| | Oceania (*n* = 9001) | 0.09% | 3.01% | 12.81% | 3.11% | 0.34% | 0.22% | 10.37% | 11.53% | 4.88% | 28.17% | 0.47% | 0.69% | 15.70% |
| | South America (*n* = 6671) | 0.61% | 15.32% | 24.46% | 16.26% | 0.36% | 0.01% | 29.19% | 31.67% | 17.21% | 73.72% | 0.16% | 0.45% | 35.99% |
| **Country** | China (*n* = 8378) | 10.41% | 40.49% | 57.30% | 15.19% | 5.55% | 21.60% | 58.46% | 54.62% | 35.44% | 83.39% | 2.22% | 10.91% | 69.37% |
| | India (*n* = 1494) | 0.00% | 3.48% | 5.49% | 3.68% | 0.00% | 0.00% | 5.69% | 3.28% | 4.55% | 88.35% | 0.13% | 0.87% | 11.11% |
| | United Kingdom (*n* = 58,971) | 0.23% | 6.50% | 17.86% | 4.46% | 0.26% | 0.31% | 18.27% | 20.43% | 7.10% | 53.89% | 0.16% | 0.90% | 25.20% |
| | Germany (*n* = 1959) | 0.36% | 6.89% | 22.56% | 10.57% | 0.51% | 0.10% | 23.69% | 21.18% | 8.78% | 47.88% | 1.74% | 1.84% | 34.86% |
| | Australia (*n* = 8207) | 0.10% | 3.18% | 13.94% | 3.40% | 0.38% | 0.24% | 11.23% | 12.65% | 5.23% | 30.45% | 0.51% | 0.74% | 17.07% |
| | Chile (*n* = 2456) | 0.00% | 12.21% | 15.68% | 12.17% | 0.53% | 0.00% | 21.62% | 22.31% | 13.27% | 73.78% | 0.08% | 0.45% | 27.69% |
| | Nigeria (*n* = 694) | 0.58% | 13.54% | 13.40% | 5.62% | 0.00% | 0.00% | 23.20% | 24.06% | 14.99% | 74.93% | 0.00% | 0.29% | 29.68% |
| | South Africa (*n* = 755) | 6.49% | 6.89% | 3.18% | 0.53% | 0.00% | 0.00% | 8.61% | 7.81% | 3.18% | 64.24% | 0.00% | 0.66% | 10.46% |
| | Brazil (*n* = 2555) | 1.17% | 5.91% | 22.62% | 15.46% | 0.20% | 0.04% | 22.78% | 27.55% | 6.81% | 75.34% | 0.23% | 0.31% | 31.12% |
| | USA (*n* = 91,748) | 4.10% | 8.78% | 14.94% | 8.53% | 0.08% | 0.03% | 22.13% | 33.80% | 4.19% | 76.83% | 0.98% | 0.37% | 39.70% |
| | Canada (*n* = 12,763) | 0.68% | 5.27% | 14.53% | 13.11% | 0.31% | 0.41% | 12.80% | 14.57% | 3.11% | 53.00% | 0.27% | 0.85% | 26.50% |
| **Source** | Aquatic animals (*n* = 2610) | 0.50% | 7.13% | 9.28% | 4.60% | 0.61% | 3.56% | 11.58% | 12.65% | 7.55% | 79.00% | 0.15% | 1.76% | 17.17% |
| | Cattle (*n* = 15,153) | 0.40% | 19.63% | 22.57% | 6.41% | 0.13% | 0.14% | 25.88% | 29.74% | 3.13% | 74.24% | 0.33% | 0.64% | 33.72% |
| | Chicken (*n* = 31,852) | 9.81% | 11.23% | 17.91% | 10.54% | 0.47% | 1.78% | 32.21% | 48.39% | 9.27% | 73.91% | 0.38% | 1.35% | 56.59% |
| | Environment (*n* = 16,987) | 0.47% | 4.82% | 6.45% | 6.78% | 0.37% | 0.16% | 9.46% | 12.52% | 4.15% | 82.99% | 0.22% | 0.82% | 17.38% |
| | Food (*n* = 8780) | 0.68% | 2.84% | 12.49% | 11.66% | 0.42% | 0.16% | 15.74% | 17.15% | 3.36% | 79.86% | 0.42% | 0.82% | 24.01% |
| | Human (*n* = 91,141) | 0.58% | 8.46% | 19.15% | 4.54% | 0.49% | 0.97% | 18.80% | 20.04% | 8.59% | 50.77% | 0.36% | 1.11% | 25.77% |
| | Pig (*n* = 15,721) | 2.37% | 13.65% | 26.04% | 15.60% | 0.63% | 2.52% | 31.73% | 42.97% | 9.66% | 79.14% | 1.21% | 2.22% | 48.37% |
| | Turkey (*n* = 7731) | 1.40% | 4.40% | 28.53% | 15.53% | 0.00% | 0.00% | 25.93% | 47.02% | 3.52% | 84.65% | 5.87% | 0.17% | 63.64% |
| | Wild animal (*n* = 3810) | 0.71% | 9.29% | 15.80% | 5.33% | 0.03% | 0.52% | 18.64% | 19.08% | 5.04% | 66.25% | 1.29% | 1.13% | 24.49% |
| **Serovar** | Agona (*n* = 3747) | 0.03% | 15.56% | 18.98% | 99.87% | 0.83% | 3.28% | 26.47% | 34.21% | 16.87% | 99.92% | 0.91% | 1.23% | 99.76% |
| | Anatum (*n* = 4775) | 0.21% | 6.37% | 8.84% | 0.02% | 1.86% | 0.06% | 8.90% | 21.28% | 3.41% | 99.96% | 0.21% | 0.34% | 23.12% |
| | Braenderup (*n* = 2346) | 0.04% | 0.85% | 2.34% | 0.00% | 0.04% | 0.04% | 2.39% | 3.15% | 1.53% | 99.83% | 0.13% | 0.21% | 5.92% |
| | Derby (*n* = 2894) | 6.60% | 11.85% | 17.45% | 83.17% | 0.76% | 5.04% | 41.19% | 62.58% | 10.06% | 95.44% | 0.07% | 0.86% | 88.87% |
| | Dublin (*n* = 3157) | 0.22% | 49.64% | 50.87% | 0.00% | 0.03% | 0.03% | 54.74% | 55.02% | 0.35% | 18.31% | 0.03% | 0.70% | 55.81% |
| | Enteritidis (*n* = 35,290) | 0.05% | 1.18% | 8.25% | 0.07% | 0.02% | 0.10% | 4.52% | 6.57% | 1.50% | 26.28% | 0.00% | 0.24% | 8.31% |
| | Heidelberg (*n* = 5196) | 0.56% | 4.00% | 35.55% | 99.08% | 0.06% | 0.00% | 33.87% | 35.01% | 4.27% | 99.98% | 3.29% | 1.14% | 99.94% |
| | I 1,4,[5],12:i:- (*n* = 10,658) | 2.94% | 15.35% | 73.60% | 2.07% | 2.01% | 4.33% | 73.67% | 80.84% | 14.34% | 15.09% | 2.72% | 2.73% | 76.46% |
| | Infantis (*n* = 15,555) | 0.07% | 28.82% | 28.73% | 11.16% | 0.08% | 0.00% | 59.34% | 60.64% | 26.83% | 99.97% | 0.21% | 0.23% | 65.17% |
| | Kentucky (*n* = 12,803) | 17.29% | 2.41% | 13.91% | 0.84% | 0.87% | 1.22% | 12.06% | 59.74% | 2.80% | 99.98% | 0.10% | 1.68% | 63.31% |

**Table 1 (continued) | Differences in AMR rates in Salmonella across geographic locations, sources, and serovars**

| Antimicrobial class | Disinfectant | Amphenicol | Beta-lactam | Fosfomycin | Lincosamide | Rifamycin | Sulfonamide | Tetracycline | Trimethoprim | Fluoroquinolone | Polymyxin | Macrolide | MDR |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Mbandaka (n = 2458) | 0.33% | 1.10% | 1.79% | 0.04% | 0.33% | 0.37% | 7.40% | 11.43% | 4.19% | 99.92% | 0.94% | 0.73% | 13.79% |
| Montevideo (n = 4401) | 0.32% | 1.64% | 1.25% | 0.02% | 0.00% | 0.02% | 2.70% | 7.02% | 0.80% | 99.93% | 0.16% | 0.18% | 8.07% |
| Muenchen (n = 2989) | 0.50% | 1.57% | 2.44% | 0.00% | 0.47% | 0.00% | 12.95% | 13.32% | 1.67% | 99.67% | 0.23% | 0.17% | 14.99% |
| Newport (n = 6983) | 0.19% | 12.60% | 14.11% | 0.00% | 0.13% | 0.13% | 15.31% | 16.23% | 4.48% | 92.71% | 0.10% | 2.79% | 17.26% |
| Saintpaul (n = 2578) | 0.81% | 5.78% | 27.66% | 1.40% | 1.12% | 2.02% | 11.87% | 27.97% | 5.55% | 22.65% | 9.81% | 1.75% | 28.94% |
| Schwarzengrund (n = 2868) | 47.66% | 1.95% | 6.59% | 0.10% | 0.84% | 0.45% | 11.85% | 14.26% | 4.67% | 100.00% | 1.43% | 0.98% | 17.68% |
| Senftenberg (n = 2377) | 0.88% | 5.30% | 9.05% | 0.08% | 0.08% | 0.34% | 11.02% | 10.90% | 5.43% | 100.00% | 2.10% | 2.23% | 17.37% |
| Thompson (n = 2076) | 0.19% | 2.84% | 5.20% | 0.14% | 0.39% | 2.26% | 5.64% | 5.01% | 4.09% | 99.95% | 0.24% | 3.08% | 6.50% |
| Typhi (n = 5775) | 0.00% | 26.20% | 27.27% | 0.02% | 0.00% | 0.00% | 28.29% | 11.84% | 27.69% | 58.15% | 0.02% | 0.62% | 29.21% |
| Typhimurium (n = 25,109) | 1.59% | 16.74% | 28.03% | 0.31% | 0.25% | 0.84% | 38.02% | 38.06% | 8.27% | 8.53% | 0.60% | 0.90% | 40.02% |

Comparative analysis of AMR rates in *Salmonella* across different countries, continents, sources, and serovars. Note: 1, Geographic distribution of AMR levels across six continents. 2, Differences in AMR rates among different sources. 4, Differences in AMR rates among the top twenty serovars.

Regional hotspots (R% > 60%) of fluoroquinolone non-susceptible were predicted in India, China, the USA, Brazil, Nigeria, Chile, and South Africa (Table 1 and Supplementary Data 2–7). A low fluoroquinolone non-susceptible rate was predicted in the Oceania continent (28.17%). The prevalence of fosfomycin resistance was higher in South America (16.26%), Asia (10.47%), and North America (9.09%) than in other continents (R% < 5%). Regional hotspots (R% > 10%) of fosfomycin resistance were predicted in Brazil, China, Canada, Chile, and Germany (Table 1 and Supplementary Data 2–7). The prevalences of beta-lactam and amphenicol resistance were higher in Asia, South America, and Africa than in other continents. High beta-lactam (57.30%) and amphenicol (40.49%) resistance rates were observed in China, Asia. MDR rates vary across continents, the highest MDR rate was found in Asia (50.96%), followed by North America, South America, and Africa, both of them above the global average (34.05%) (Table 1).

The prevalences of resistance rates for individual antimicrobial classes differed among different sources (Table 1 and Supplementary Data 2–7). As for amphenicol resistance, higher prevalences of resistance rates were observed in cattle (19.63%), pigs (13.65%), and chickens (11.23%), when compared with turkey (4.40%) and food (2.84%). The rates of resistance to beta-lactam were the highest in turkey (28.53%), followed by pig (26.04%), cattle (22.57%), and human (19.15%), both of which were above the global average (18.27%). The prevalence of fosfomycin resistance rates was higher in pigs (15.60%), turkeys (15.53%), chickens (10.54%), and food (11.66%) than that in humans (4.54%) and the global average (7.67%). Host hotspots (R% > 40%) of MDR were predicted in turkeys, chickens, and pigs (Table 1). High fluoroquinolone non-susceptible rates were observed in both animals, food, and the environment. The prevalence of resistance to polymyxin was above 0.65% (global average) in turkeys (5.87%), wild animals (1.29%), and pigs (1.21%). The prevalence of resistance to macrolide was above 1.11% (global average) in pigs (2.22%), aquatic animals (1.76%), chickens (1.35%), and wild animals (1.13%). These results may be influenced by the prevalence of *Salmonella* serovars in different hosts/sources. Therefore, it is particularly important to investigate the prevalence of resistance by serovars.

Then, we estimated the prevalences of resistance in different continents for the twenty dominant serovars. Some serovars had positive correlations with resistance to critically important antimicrobials were observed. For example, positive correlations were observed for fosfomycin resistance in *S.* Agona, *S.* Derby, *S.* Heidelberg, *S.* Indiana, and *S.* Kentucky (Table 1 and Supplementary Data 2 and 6), polymyxin resistance in *S.* Saintpaul, *S.* I 1,4,[5],12:i:-, *S.* Heidelberg, (Table 1 and Supplementary Data 2 and 5), and macrolide resistance in *S.* Kentucky, *S.* Indiana, *S.* Newport, *S.* I 1,4,[5],12:i:-, and *S.* Saintpaul (Supplementary Data 2–7). Notably, fluoroquinolone non-susceptible rates positive correlations in *S.* Agona, *S.* Anatum, *S.* Braenderup, *S.* Derby, *S.* Heidelberg, *S.* Infantis, *S.* Kentucky, *S.* Mbandaka, *S.* Montevideo, *S.* Muenchen, *S.* Newport, *S.* Schwarzengrund, *S.* Senftenberg, *S.* Thompson were observed, while lower fluoroquinolone non-susceptible rates were identified in *S.* Typhimurium, *S.* I 1,4,[5],12:i:-, and *S.* Enteritidis (Table 1), both of three serovars were frequently isolated from humans.

### Longitudinal AMR trends of *S. enterica* worldwide

At the global level, AMR patterns showed an increasing trend of diverse wave shapes (Fig. 2). It was worth noting that an alarming increase in the proportion of fluoroquinolone non-susceptible *Salmonella* genomes worldwide, particularly in Asia, Oceania, and South America (Fig. 2A, B). Results showed high spatial variability in our estimates of AMR patterns, both between and within continents/countries. Despite regional differences and regional specificity, the overall trend is worrying.
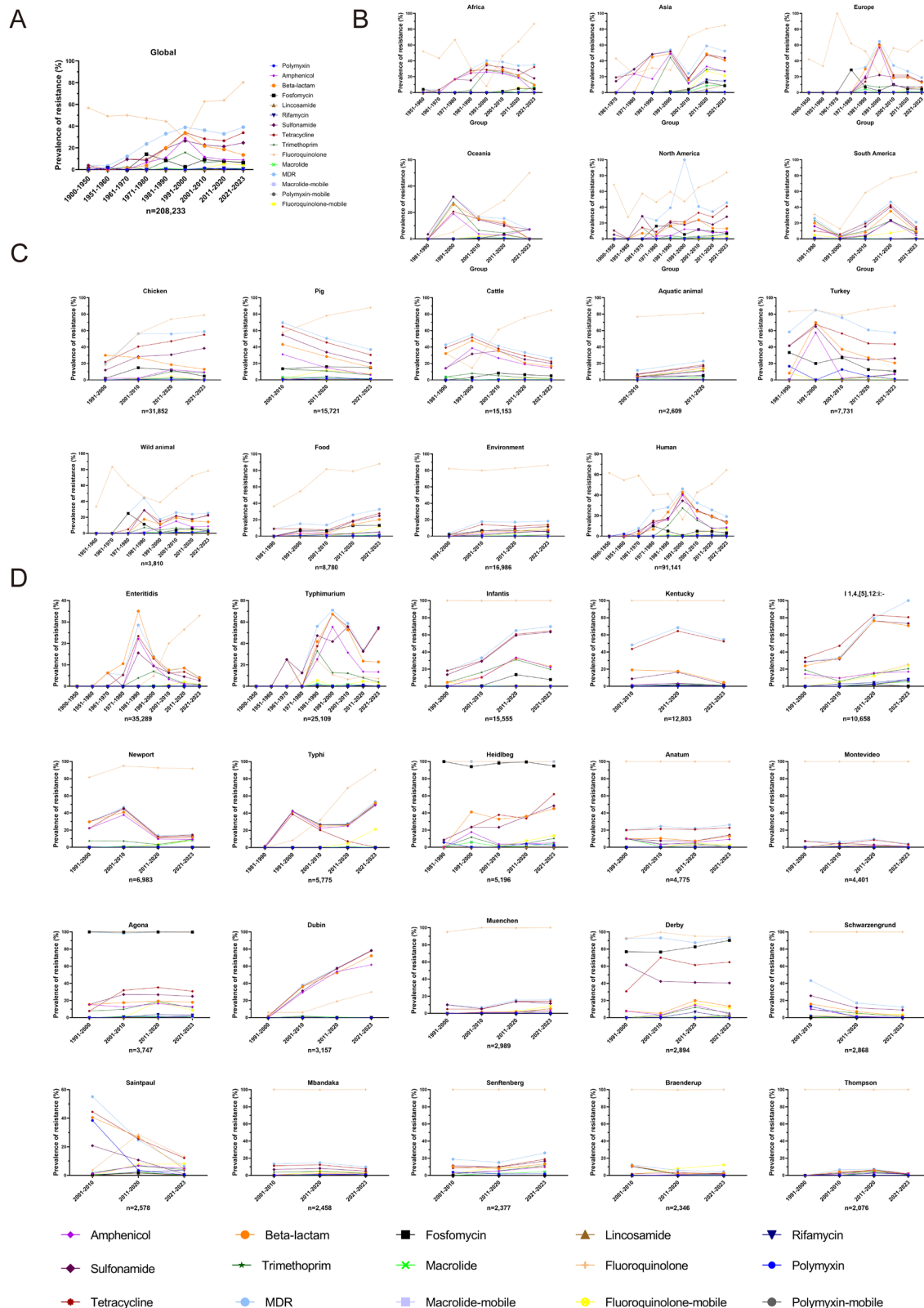
**Fig. 2 | Temporal changes of AMR in *Salmonella enterica*. A** Temporal trends of AMR rates at the global scale. **B** Temporal trends of AMR phenotypes across six continents. **C** Temporal trends of AMR rates among nine sources. **D** Temporal trends of AMR rates among the twenty predominant *Salmonella* serovars.

Then, we analyzed AMR trends in nine sources separately. For all antimicrobial classes, the prevalence of resistance in *Salmonella* in food increased after 2000, except for polymyxin and lincosamide (Fig. 2C). For example, plasmid-mediated fluoroquinolone resistance in food-derived *Salmonella* increased from 0.18% to 12.11%. In chickens,

between 1991 and 2023, prevalence increases were observed in fluoroquinolones, tetracyclines, and amphenicol resistance (Fig. 2C). In cattle, between 1991 and 2023, prevalence increases significantly in fluoroquinolone non-susceptible and decreases in amphenicols, beta-lactams, trimethoprim, and tetracyclines. In contrast, in pigs, between

2001 and 2023, the prevalence increased significantly in fluoroquinolone non-susceptible, while decreasing in amphenicols, beta-lactams, sulfonamides, and tetracyclines (Fig. 2C). In turkeys, between 2001 and 2023, prevalence increases were observed in fluoroquinolones, amphenicols, trimethoprim, and macrolides resistance, and decreases in polymyxin and beta-lactams resistance (Fig. 2C). In aquatic animals, between 2001 and 2020, increased trends were observed in amphenicols, beta-lactams, fosfomycin, rifamycin, tetracyclines, trimethoprim, fluoroquinolones, and macrolides resistance, a slight decrease after 2020 (Fig. 2C). This may be due to the lack of enough genomes. In humans, an increase in the prevalence of resistance after 1991 was observed in fluoroquinolones and macrolides resistance, while decreases in amphenicols, sulfonamide, beta-lactams, trimethoprim, and tetracyclines resistance. In the environment, between 1991 and 2023, significant prevalence increases were observed in macrolides, trimethoprim, sulfonamides, amphenicols, and beta-lactam resistance, as well as fluoroquinolone non-susceptible. In wild animals, between 1991 and 2023, prevalence increases were observed in fluoroquinolones and polymyxin resistance (Fig. 2C). The increasing resistance of *Salmonella* in animals, food, and the environment, especially for antibiotics that have been listed by WHO as critically important to human medicine, is very worrying.

In addition, AMR rate increases were also observed for some dominant serovars, for example, *S.* I 1,4,[5],12:i:-, *S.* Infantis, *S.* Heidelberg, *S.* Typhi, *S.* Dubin, *S.* Derby, *S.* Muenchen, *S.* Thompson, and *S.* Senftenberg (Fig. 2D). An increase in the prevalence of fluoroquinolone non-susceptible was observed in *S.* Typhi, *S.* Enteritidis, *S.* I 1,4,[5],12:i:-, and *S.* Dubin, while stable high resistance rates in other serovars, such as *S.* Infantis, *S.* Kentucky, *S.* Heidelberg, *S.* Anatum, *S.* Montevideo, *S.* Muenchen, *S.* Derby, *S.* Mbandaka, *S.* Senftenberg, *S.* Thompson, *S.* Braenderup, *S.* Schwarzegrund, and *S.* Newport (Fig. 2D). In serovars showing trends of increasing prevalence in the top twenty serovars, only *S.* Infantis, *S.* I 1,4,[5],12:i:-, *S.* Typhi, and *S.* Dubin presented higher MDR rates in the 2020s than in the 2000s (Fig. 2D).

To investigate the longitudinal profiles of ARGs in the *S. enterica* genomes, the ARGs were analyzed. A total of 363 types of acquired ARGs and 35 chromosomal gene mutations were detected in all of the *S. enterica* genomes. We found that ARGs in *S. enterica* showed a significant upward trend over time at the global scale (Supplementary Fig. S5A), especially in Asia and North America (Supplementary Fig. S5B). Globally, the acquired ARGs increased from 1.16 per genome in 1900–1950 to 2.87 per genome after 2020. From the genomic analysis, the number of ARGs per genome increased sharply with increasing years observed in chickens, food, wild animals, and the environment (Supplementary Fig. S5C). The results were similar to the AMR trends in the corresponding sources. Between 1991 and 2023, the average number of ARGs carried by genomes decreased in humans, cattle, turkeys, and pigs (Supplementary Fig. S5C).

Similar to AMR rates increases in some dominant serovars, we found that the numbers of ARGs carried by genomes increased in *S.* Agona, *S.* Anatum, *S.* Derby, *S.* Dubin, *S.* Heidelberg, *S.* I 1,4,[5],12:i:-, *S.* Infantis, *S.* Kentucky, *S.* Mbandaka, *S.* Muenchen, *S.* Senftenberg, and *S.* Typhi in recent 30 years (Fig. 3A). From 2001 to 2023, the average number of ARGs carried by genomes decreased in *S.* Montevideo, *S.* Saintpaul, and *S.* Schwarzegrund (Fig. 3A).

### Temporal dynamics of ARGs
Then, we analyzed the dynamic trends of individual ARGs and chromosomal gene mutations mediating AMR carried by *Salmonella* genomes at the global scale. The prevalence of ARGs conferring resistance to critically important antimicrobials increased from 1981 to 2023, for example, $bla_{CTX-M-65}$ and $bla_{TEM-206}$, and $bla_{TEM-214}$, *fosA3*, *qnrB19*, *gyrA* p.D87Y, and *parC* p.T57S (Fig. 3B and Supplementary Data 8).

The number of ARGs per genome was the highest in Asia, followed by Africa and South America (Supplementary Fig. S6A). In Asia, the prevalence of ARGs increased in $bla_{CTX-M-55}$, $bla_{LAP-2}$, $bla_{OXA-10}$, *mph(A)*, and *qnrS1*, decreased in *catA1* and $bla_{CARB-2}$ (Supplementary Data 9). Chromosomal gene mutations, *gyrA* p.D87N, *gyrA* p.S83Y, and *parC* p.S80I, were also showing an increased trend in Asia. In Africa, the prevalence of ARGs increased observed in *fosA7*, *qnrB19*, and decreased in $bla_{OXA-1}$ and $bla_{TEM-1B}$ (Supplementary Data 10). Moreover, the prevalence of gene mutations increased were observed in *gyrA* p.D87N, *gyrA* p.D87Y, *gyrA* p.S83F, *gyrA* p.S83Y, *parC* p.S80I, and *parC* p.T57S. In Europe, the prevalence of ARGs increased observed in $bla_{CMY-2}$, $bla_{TEM-106}$, $bla_{TEM-135}$, *fosA4*, *mph(A)*, and *qnrB19*, while decreased in *mcr-1.1* (Supplementary Data 11). However, it was worth noting that, unlike in Asia and Africa, *gyrA* p.D87N, and *parC* p.S80I showed a declining trend in Europe. In North America, the prevalence of ARGs increased were observed in $bla_{CTX-M-65}$, *aph(4)-Ia*, *aac(3)-IV*, *fosA3*, and *qnrB19*, decreased in *tet(G)* and *cmlA1* (Supplementary Data 12). In South America, the prevalence of ARGs increased were observed in $bla_{CTX-M-65}$, *mph(A)*, and *qnrB19*, and decreased in *catA1*, $bla_{OXA-2}$, and *aac(6′)-Ib-cr* (Supplementary Data 13). We found an increased trend in *parC* p.T57S and a decrease in *gyrA* p.D87N. In Oceania, the prevalence of ARGs increased were observed in *qnrS1*, *fosA7*, *sul3*, *cmlA1*, $bla_{CTX-M-55}$, *mph(A)*, $bla_{CTX-M-9}$, and *mcr-3.1*, decreased in $bla_{TEM-1B}$, $bla_{CTX-M-14}$, *catA1*, *sul1*, and *sul2* (Supplementary Data 14). In addition, we also observed that gene mutations, *parC* p.T57S, and *gyrA* p.D87N, *gyrA* p.D87Y increased while *acrB* p.R717Q decreased in Oceania.

### Differences in ARGs among different geographic locations, sources, and serovars
We observed region-specific associations with the prevalence of ARGs carried by *Salmonella* (Fig. 3C). For example, $bla_{VIM-1}$ was detected in Europe, $bla_{VIM-2}$ in Oceania, $bla_{KPC-2}$ in Asia and South America, *cfr* in Asia and Europe, and *sul4* in Asia (Supplementary Data 15). We then investigated the characteristics of ARGs in different hosts. Although most acquired ARGs are shared among different hosts, some ARGs are host-specific (Fig. 3D). For example, *tet*(X6) in pigs, *sul4* in chickens, pigs, and humans, *rmtC* in humans, *cfr* in aquatic animals and pigs, $bla_{NDM-9}$ in chickens, and $bla_{VIM-2}$ in humans (Supplementary Data 16). The number of acquired ARGs per genome was the highest in chickens, followed by pigs and turkeys (Supplementary Fig. S6B). The emergence and spread of $bla_{NDM-5}$, $bla_{VIM-1}$, *cfr*, *tet*(X4), *tet*(X6), and *sul4* in *Salmonella* of human and pig origin are of particular concern.

Positive correlations with ARG resistance to critically important antimicrobials were also observed with some serovars (Fig. 3E and Supplementary Data 17). For example, *fosA7* was mainly detected in *S.* Agona, *S.* Heidelberg, and *S.* Derby, *fosA3* in *S.* Infantis, *mcr-1.1* in *S.* I 1,4,[5],12:i:- and *S.* Typhimurium, $bla_{CTX-M-65}$ in *S.* Infantis, $bla_{TEM-206}$ in *S.* Dublin. The *tet*(X4) was mainly detected in *S.* Kentucky and *S.* Typhimurium. The $bla_{VIM-1}$ was mainly identified in *S.* Infantis and *S.* Typhimurium. The *tet*(C) and *tet*(G) were mainly identified in *S.* Anatum and *S.* Typhimurium, respectively.

### Differences in plasmid replicons across sampling periods, serovars, locations, and sources
Plasmid replicon analysis also indicated an increasing trend in the number of replicons over time in some serovars, for example, *S.* Kentucky, *S.* Thompson, *S.* Mbandaka, *S.* Montevideo, *S.* Muenchen, *S.* Sainpaul, *S.* Heidelberg, and *S.* Dublin, while a downward trend was observed in *S.* Typhimurium, *S.* Typhi, *S.* Schwarzengrund, *S.* Derby, and *S.* Senftenberg (Fig. 4A). For different geographical and host sources, different dynamic trends were observed (Supplementary Fig. S7). The number of plasmid replicons per genome over time was observed only in Oceania, food, and aquatic animals. The prevalences of several ARG-associated replicons, such as IncFIB, IncFII, and IncHI2A, were significantly higher in the 2020s than before 2000 (Fig. 4B). Significant differences were observed among genomes from
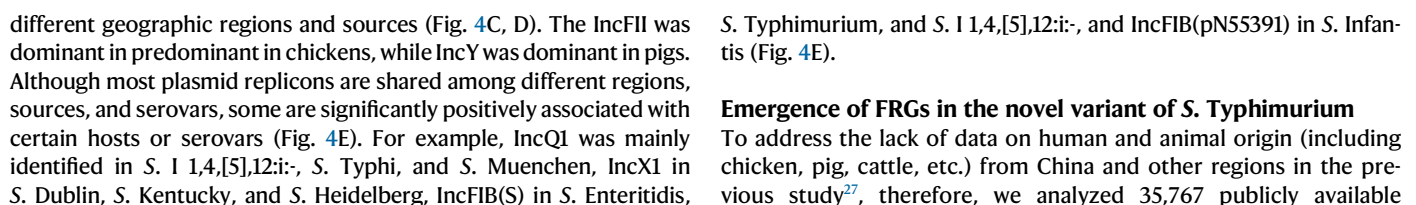
different geographic regions and sources (Fig. 4C, D). The IncFII was dominant in predominant in chickens, while IncY was dominant in pigs. Although most plasmid replicons are shared among different regions, sources, and serovars, some are significantly positively associated with certain hosts or serovars (Fig. 4E). For example, IncQ1 was mainly identified in *S.* I 1,4,[5],12:i:-, *S.* Typhi, and *S.* Muenchen, IncX1 in *S.* Dublin, *S.* Kentucky, and *S.* Heidelberg, IncFIB(S) in *S.* Enteritidis,

*S.* Typhimurium, and *S.* I 1,4,[5],12:i:-, and IncFIB(pN55391) in *S.* Infantis (Fig. 4E).

## Emergence of FRGs in the novel variant of *S.* Typhimurium

To address the lack of data on human and animal origin (including chicken, pig, cattle, etc.) from China and other regions in the previous study[27], therefore, we analyzed 35,767 publicly available

*S.* Typhimurium genomes from 1938 to 2023. We were surprised to find that the point mutation (−44G > T) in the promoter of the *csgD* gene was present (100% nucleotide identity) in 616 (1.72%) of 35,767 *S.* Typhimurium genomes, which is much lower than that in the previous reported (29.57%)[27]. These MRDRST strains were isolated from humans, pigs, chickens, ducks, cattle, wildlife, aquatic animals, and other sources between 1992 and 2022 (Supplementary Fig. S8 and S9). Notably, the earliest strain was isolated from Equus caballus in the USA in October 1992, followed by frozen squid in India on July 26, 2001, and frozen eel fish in Vietnam on Jun 4, 2007. These results suggest that MRDRST strains might have been in the USA and India for a long time, and already spread internationally and to China, where represented hotspots of resistance worldwide.

Of these genomes, 1.15% and 3.07% were identified in *S.* Typhimurium and monophasic *S.* Typhimurium (*S.* I 1,4,[5],12:i:-), respectively. Notably, the majority of MRDRST clones were found in Asia (19.76% [584] of 2955), followed by Europe (0.15% [20] of 13,258), South America (0.10% [1] of 966), Oceania (0.06% [3] of 4901), and North America (0.06% [8] of 13,206). These MRDRST genomes are distributed across 12 countries, most of them in China (93.99% [579] of 616) (Fig. 5A).

Then, we focused on 4524 Chinese *S.* Typhimurium strains to better uncover the distribution characteristics of MRDRST and FRGs in China. A total of 1233 MRDRST genomes were identified, mainly distributed in humans (*n* = 706), pigs (*n* = 295), chickens (*n* = 120), and ducks (*n* = 32) (Supplementary Fig. S10). The emergence of MRDRST in China was in 2006, later than that in the United States (1992) and India (2001). Subsequently, local adaptive clones of MRDRST appeared and rapidly expanded (Fig. 5B). In brief, the prevalence of MRDR in different sources was different in different regions of China, the prevalence of MRDR was higher in Southern and Eastern than in Northern China (Supplementary Fig. S11).

We identified the presence of FRGs in 76 MRDRST genomes, including seventy-five *fosA3* and one *fosA7*. Among these FRGs positive strains, sixty-six, two, and seventy genomes coexisted with *mcr-1*, *mph(A)*, and *bla*$_{\text{CTX-M}}$ genes (Fig. 5B, C), which were resistant to polymyxin, azithromycin, and 3GCs, respectively. Moreover, six MRDRST genomes were found to carry *bla*$_{\text{NDM}}$ genes. All these antibiotics have been listed as critical antibiotics for the treatment of salmonellosis (especially invasive diseases) by the WHO.

## Association between AMR and several driving indicators

To explore the relationships between the level of agriculture & rural development, socioeconomic, climate change, environment, health, and the AMR of *S. enterica* genomes, data on the indicators of each country or region in each year (from 1990 to 2023) were collected. The correlations between the 115 indicators and the number of ARGs in the top twelve countries across six continents, with the number of genomes collected, were analyzed. Using data published between 2000 and 2018, we found a significant association between human antimicrobial consumption and the number of ARGs in China, India, and Brazil (Supplementary Data 18). Similarly, the usage of animal antimicrobial and AMR levels in food animals was positively associated in Germany and the United Kingdom (Supplementary Data 18).

Consumption of total antibiotics was significantly associated with increased AMR in the USA and Brazil.

In agriculture & rural development, agriculture, forestry, and fishing value added, livestock production index, cereal yield, cereal production, crop production index, and food production index were significantly associated with an increase in AMR in both China and Brazil (Supplementary Data 18). The rural population was significantly associated with an increase in AMR in the United Kingdom, while negatively associated with an increase in AMR in China, Germany, and Brazil. Agricultural methane emissions (thousand metric tons of $CO_2$ equivalent) were significantly associated with an increase in AMR in the USA, Fiji, Brazil, and South Africa.

In climate change, $CO_2$ emissions, total greenhouse gas emissions, and population were significantly associated with an increase in AMR in China, Brazil, and the USA (Supplementary Data 18). In the environment, aquaculture production was significantly associated with an increase in AMR in China, Germany, the USA, and Brazil, and capture fisheries production was significantly associated with an increase in AMR in Fiji. Methane emissions, methane emissions in the energy sector, and $CO_2$ emissions were significantly associated with an increase in AMR in China, Brazil, and the USA (Supplementary Data 18).

In economy & growth, manufacturing, value added, gross national expenditure, Households, and NPISHs Final consumption expenditure, R&D expenditure, Services, value added, Industry (including construction), value added, GDP, GDP per capita, GNI, GNI per capita, households and NPISHs final consumption expenditure, current health expenditure per capita, imports of goods and services, goods exports, service exports were significantly associated with an increase in AMR in both China and Brazil, while negatively associated with an increase in AMR in both Fiji and the United Kingdom (Supplementary Data 18). In trade, travel services were significantly associated with an increase in AMR in Nigeria, China, the United Kingdom, the USA, and Australia, food imports were significantly associated with an increase in AMR in China and Germany, goods imports were significantly associated with an increase in AMR in China and Brazil (Supplementary Data 18). In the financial sector, the consumer price index was significantly associated with an increase in AMR in both China and Germany (Supplementary Data 18).

In health, domestic private health expenditure per capita and current health expenditure per capita were significantly associated with an increase in AMR in China, Germany, and Brazil (Supplementary Data 18). In aid effectiveness, the incidence of tuberculosis was significantly associated with an increase in AMR in the USA, while negatively associated with an increase in AMR in China and Brazil (Supplementary Data 18).

In urban development, both pump prices for diesel fuel and pump prices for gasoline were significantly associated with an increase in AMR in China and Germany, while negatively associated with an increase in AMR in South America and the USA (Supplementary Data 18). In energy & mining, nitrous oxide emissions in the energy sector were significantly associated with an increase in AMR in both China and Brazil (Supplementary Data 18). In infrastructure, both air transport and railway ability were significantly associated with an increase in AMR were observed (Supplementary Data 18).
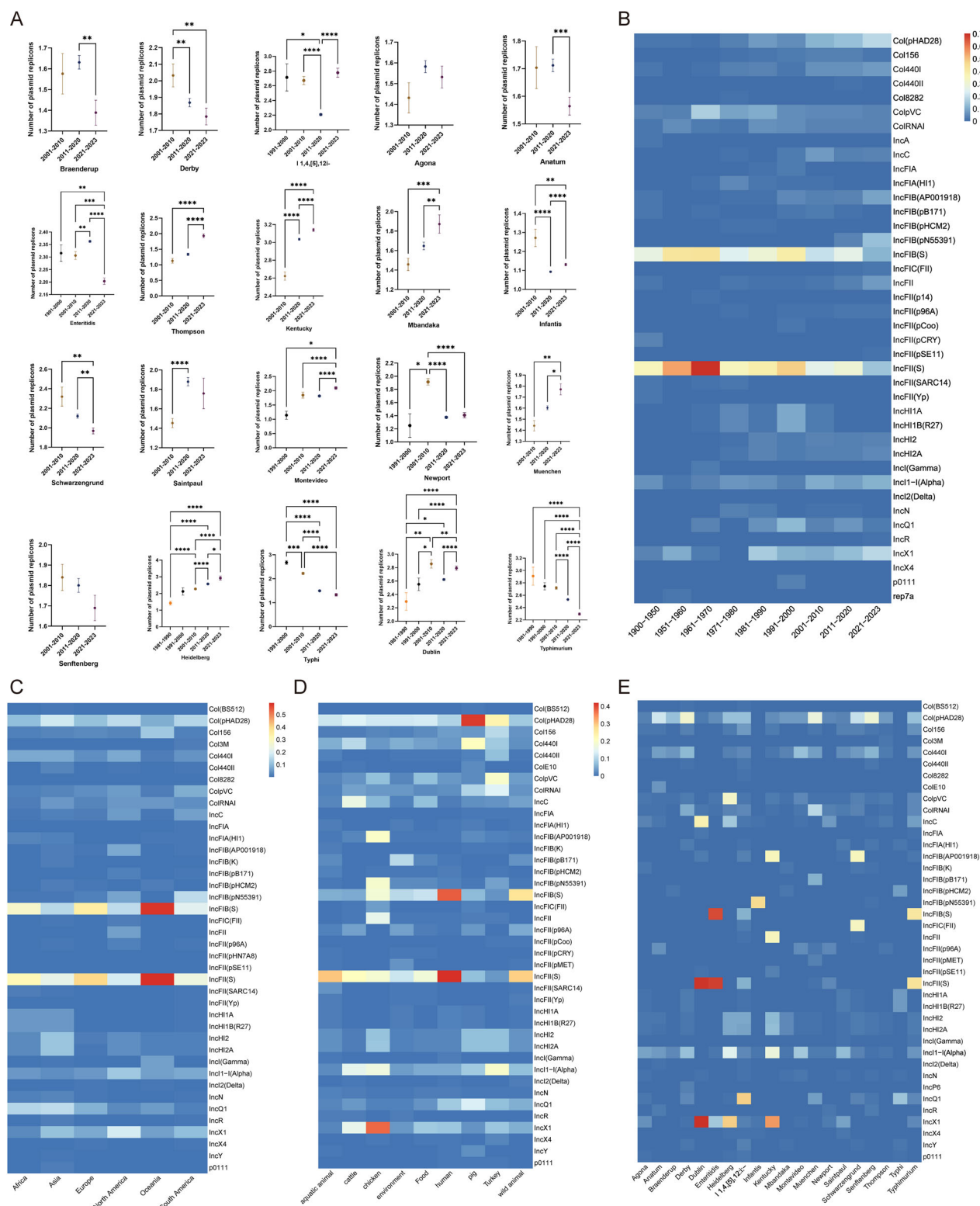
**Fig. 4 | Temporal dynamics and differences in plasmid replicons across sampling periods, serovars, locations, and sources. A** The distribution of numbers of plasmid replicons per genome among the top 20 serovars. A total of 316,327 plasmid replicons classified into 120 types were identified in the global *Salmonella* catalog. A total of 40 dominant plasmid replicons are shown. Kruskal-Wallis tests were used to compare differences among different groups. The "*" on the right represents *P*-values. *: *P* < 0.05; **: *P* < 0.01; ***: *P* < 0.001; ****: *P* < 0.0001. No significant differences were not shown. Data are presented as mean values with SEM. Braenderup: *n* = 114, 1858, 366. Derby: *n* = 260, 2136, 477. I 1,4,5,12:i-: *n* = 21, 591, 9576, 468. Agona: *n* = 347, 2912, 461. Anatum: *n* = 385, 3314, 1052. Enteritidis:

*n* = 317, 1911, 30,577, 2349. Thompson: *n* = 138, 1668, 258. Kentucky: *n* = 761, 8409, 3623. Mbandaka: *n* = 568, 1525, 358. Infantis: *n* = 634, 9885, 5011. Schwarzengrund: *n* = 176, 2049, 636. Saintpaul: *n* = 481, 1867, 221. Montevideo: 14, 509, 3045, 831. Newport: *n* = 27, 738, 5220, 987. Muenchen: *n* = 202, 2292, 466. Senftenberg: *n* = 454, 1590, 324. Heidelberg: *n* = 35, 17, 925, 4059, 155. Typhi: *n* = 364, 1229, 3897, 206. Dublin: *n* = 35, 98, 374, 2238, 407. Typhimurium: *n* = 91, 498, 3165, 18,757, 2569. **B** Differences in plasmid replicons across different periods. **C** Differences in plasmid replicons across different geographic regions. **D** Differences in plasmid replicons across different isolation sources. **E** Differences in plasmid replicons across different serovars.
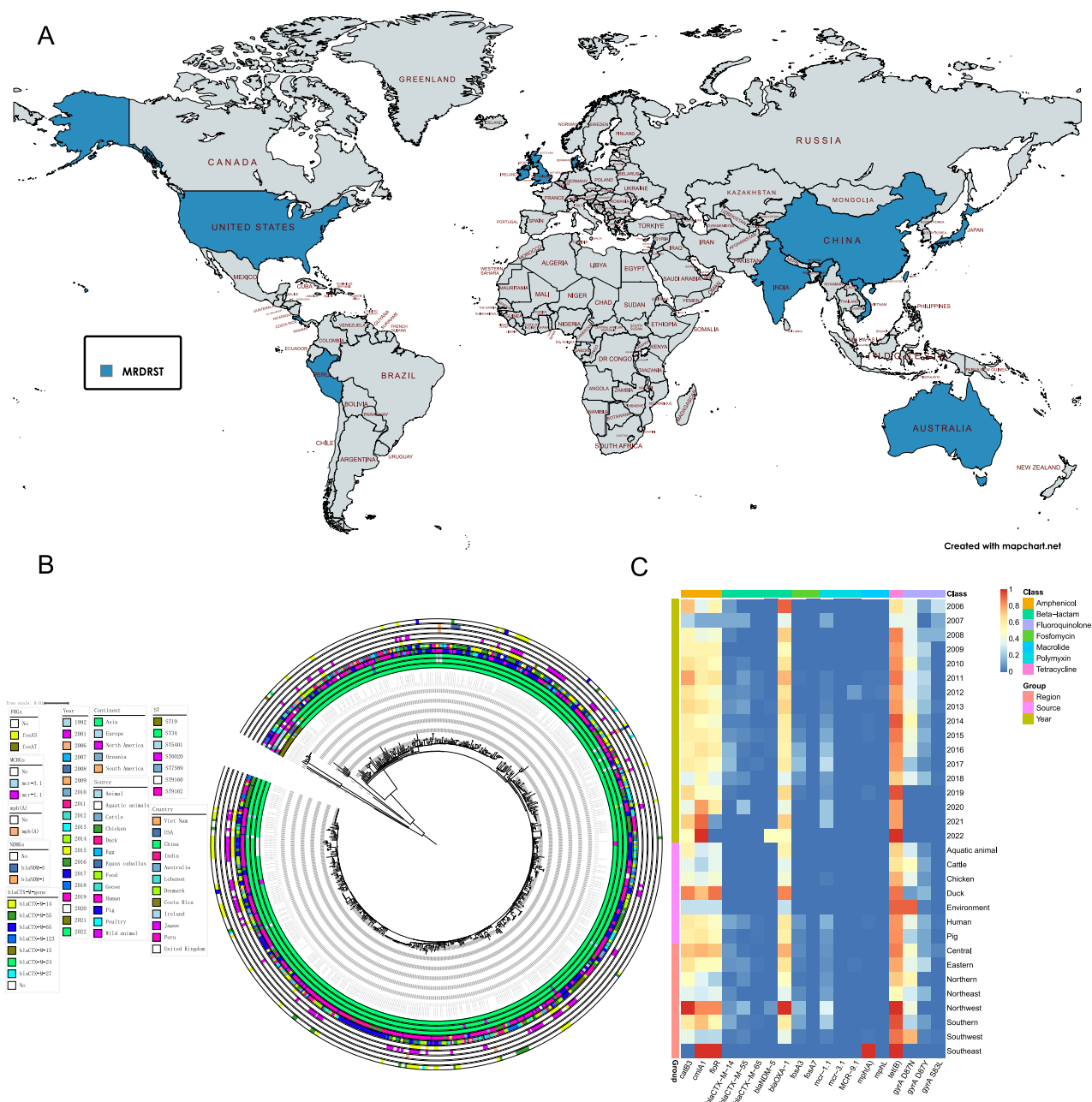
**Fig. 5 | Genetic characterization and phylogeny of the global MRDRST genomes. A** A global map showing the geographic distribution of these MRDRST strains. The map was generated using the MapChart (https://www.mapchart.net). Source data are provided as a Source Data file. **B** Phylogenetic analysis and functional annotations of 616 global MRDRST strains. From the inner to outer circles are ST, Country, Continent, Source, Year, FRGs, MCRs, *mph(A)*, NDMGs, and *bla*CTX-M genes. **C** A heatmap showing the differences of AMR in MRDRST strains. Temporal, regional, and host distribution of genes that are resistant to fosfomycin and other important antibiotics (including amphenicol, polymyxin, azithromycin, fluoroquinolone, carbapenem, and 3GCs).

In the private sector, agricultural raw materials imports were significantly associated with an increase in AMR in South Africa and the United Kingdom (Supplementary Data 18). In international tourism, the number of arrivals was significantly associated with an increase in AMR in Germany, Canada, and Brazil. Merchandise imports from high-income economies were significantly associated with an increase in AMR in Canada, Fiji, and the United Kingdom. Merchandise imports from low- and middle-income economies in Europe & Central Asia, merchandise imports from low- and middle-income economies in Sub-Saharan Africa, and the import volume index, were significantly associated with an increase in AMR in China, Germany, and Brazil. Fuel imports were significantly associated with an increase in AMR in China, Germany, and Australia. Merchandise imports were significantly associated with an increase in AMR in China, Germany, and Brazil, while negatively associated with an increase in AMR in South America, Fiji, and the United Kingdom (Supplementary Data 18).

## Discussion

Despite concerted global and regional efforts, myriad gaps remain in our understanding of the geographic heterogeneity and temporal trends of drug-resistant *Salmonella* at the global scale. In this study, we provide the first global AMR surveillance report for *Salmonella* from 148 countries/regions encompassing 208,233 genomes from different food-producing animals, food, humans, wild animals, and

the environment, mainly from after the 1950s, the time when antimicrobial agents were rarely used in veterinary and human medicines. Our results highlight vital spatial disparities in AMR in *Salmonella* and provide estimates for countries/regions lacking genomic surveillance data.

The previous study provided a preliminary ARG profile of *Salmonella* using 47,452 genomes classified into 11 sources and 22 serovars from 116 countries/regions between 1900 and 2020 and did not explore the spatiotemporal characteristics of the AMR and their driving factors[37]. In our analysis, a total of 208,233 genomes classified into 708 serovars were used for bioinformatic analysis, which is much larger than in the previous study[37]. As genome sequencing becomes cheaper, more genomic data will be uploaded to public databases in the future and could help shed light on the global atlas and drivers of AMR.

The predicted atlas of AMR was based on WGS, which has been used for addressing the public health concern and routine surveillance of AMR in *Salmonella* and outbreak investigation[12,13,22,38–40]. In this analysis, China, India, Brazil, Nigeria, Slovenia, Spain, Ecuador, Mexico, and the USA were identified as hotspots of AMR, which were similar to previous global estimates on AMR in food animals[20,22]. However, previous studies predicted AMR trends for two and four pathogens, respectively, and not disaggregated for individual serovars. Our analysis was conducted for globally available *Salmonella* genomes with year, source, and location of collection information, and ensured comparability for monitoring AMR trends by focusing on six continents, major countries, nine sources, and twenty dominant serovars. Our choice of notable community pathogen was also in line with other global/regional surveillance actions, such as the European Union surveillance that uses different *Salmonella* serovars as the proxy[41].

In this work, we showed that the geographic pattern of AMR varied depending on the host/source considered. For example, Asia and Europe were resistance hotspots of beta-lactam resistance in pigs, and Asia was resistance hotspots of beta-lactam resistance in cattle. A higher prevalence of fosfomycin resistance was observed in chickens from South America (33.45%), Asia (23.61%), and Africa (14.71%), pigs from Asia (24.68%), North America (15.15%), and Europe (13.94%), food from Europe (21.13%), the environment (43.53%) from Oceania, and turkeys (15.58%) from North America. Our findings also indicated that the geographic pattern of AMR varied depending on the classes of antimicrobials considered. For example, Asia, North America, and South America were identified as resistance hotspots for fluoroquinolone. For the eleven countries on six continents, China was identified as a resistance hotspot for all antimicrobials except fosfomycin and fluoroquinolone. In addition, Oceania had relatively lower AMR prevalence in, for example, amphenicol, beta-lactam, fosfomycin, and tetracycline compared to other continents.

Between 1991 and 2023, the prevalence increased significantly in fluoroquinolone non-susceptible was observed across six continents, especially in chickens, pigs, cattle, food, wild animals, and humans, which is in line with those from surveillance in the GLASS and has been listed as an urgent threat[42]. Globally, 73% of antimicrobials sold are used in food animals for animal protein production[29]. The rapid global expansion of intensive animal production has made a great contribution to the scale-up in demand for animal protein, in the same way that antimicrobials help maintain health and productivity (https://www.fao.org/faostat/en/#home). Notably, significant associations between the increase of ARGs and veterinary antimicrobials consumption were observed[43]. Excessive use of fluoroquinolones (for example, norfloxacin, ofloxacin, lomefloxacin, and pefloxacin) in animals may have caused much higher resistance rates of these in animals[21]. Similar to the previous report[43], chromosomal mutations in *gyrA*, *gyrB*, *parC*, or *parE* were frequently identified in fluoroquinolone resistance isolates. In this work, we found that fluoroquinolone non-susceptible rates were much higher in turkeys, pigs, aquatic animals, chickens, cattle, food,

environment, and wild animals than in humans. Previous studies also reported that centralized industrialization for chickens and pigs and global trade for poultry and pork products contribute to the global spread of antimicrobial-resistant *Salmonella*[38,39].

Similar to the fluoroquinolone resistance profile, excessive use of cephalosporins (for example, ceftriaxone) and fosfomycin in animals may result in novel resistance genes and beta-lactam-resistant and fosfomycin-resistant *Enterobacterales* from non-human sources (food animals) to the human-associated environment[24]. The previous study reported higher fosfomycin resistance rates in humans than in non-human origins in China[12], here we identified higher fosfomycin resistance rates in chickens, pigs, turkeys, and food than in humans at the global level. The absurd increase in fluoroquinolones, beta-lactam, and fosfomycin resistance may be mainly caused by the excessive use of antimicrobials in veterinary medicine and then spread to food, the environment, and humans[44,45].

In addition to antibiotics, bacteria exposure to non-antibiotic drugs (for example, metals and antibacterial biocides) and plant protection products (such as herbicides) can induce or select for bacteria survival adaptations that result in decreased susceptibility to one or more antibiotics[46,47]. Stricter use of antibiotics in human and veterinary medicine is starting to be a global trend. In order to deal with increasing AMR, many countries/regions and organizations have made efforts and actions. For example, since 2006, antibiotic growth promoters have been banned in animals by the European Union (Regulation (EC) No. 1831/2003), and recently, the Ministry of Agriculture and Rural Affairs of the People's Republic of China has launched a regulation (No. 194) to prohibit growth-promoting drugs as feed additives after 1 July 2020. To address AMR threats to humans, animals, plants and environment, a One Health Joint Plan of Action was launched by the Quadripartite – the WHO, the World Organization for Animal Health (WOAH, founded as OIE), the Food and Agriculture Organization of the United Nations (FAO), and the United Nations Environment Program (UNEP) in 2022.

Our data suggest that for cattle, pigs, and turkey, the decreases in *Salmonella* resistance were concomitant with a decline in the numbers of ARGs per genome, especially in *S.* Schwarzengrund and *S.* Saintpaul, which has also been observed in the USA[48]. However, our data suggest that for chickens, food, wild animals, and the environment, the increases in *Salmonella* resistance were concomitant with rises in the numbers of ARGs per genome, especially in *S.* Agona, *S.* Dublin, *S.* I 1,4,[5],12:i:-, *S.* Muenchen, *S.* Senftenberg, *S.* Mbandaka. For these acquired ARGs, we observed serovar-specific (top 20 serovars) and significant correlation with regions or hosts, for example, *fosA7* was frequently identified in *S.* Derby, *S.* Heidelberg, and *S.* Agona, *fosA3* was frequently identified in *S.* Infantis, which has been observed in the previous study[13]. Notably, our data suggest that there is a clear spillover effect of *fosA* family genes from these four serovars spreading to more serovars, especially MDR strains, which was similar to previous reports[12,13,25].

In this work, we found, for example, the *fosA7*-positive *Salmonella* genomes were mainly ST13 (*S.* Agona), ST15 (*S.* Heidelberg), ST40 (*S.* Derby), *S.* Heidelberg ST15 and *S.* Derby ST40 were mainly isolated from chickens, and pigs, respectively, while *fosA7*-producing *S.* Agona ST13 was isolated from multiple sources, for example, human, pig, chicken, and turkey, etc (Supplementary Data 19). The majority of *fosA3*-positive genomes were ST34 (*S.* I 1,4,[5],12:i:-), ST32 (*S.* Infantis), and ST198 (*S.* Kentucky), which were mainly isolated from humans, chickens, and chickens, respectively. The mobile colistin resistance gene *mcr-1.1* was frequently identified in ST34 (*S.* I 1,4,[5],12:i:- and *S.* Typhimurium) in Asia, which usually exhibited an MDR phenotype[12,27,40]. MCR-1-producing *Salmonella* ST34 links animal foods (for example, pork) to children's community infections[49–51]. The third-generation cephalosporin resistance gene *bla*$_{CTX-M-65}$-producing *S.* Infantis ST32 mainly originated from chickens and turkeys in North

America and South America. Chromosomal gene mutation *parC* p.S80I mediating fluoroquinolone resistance was mainly identified in ST198 (*S.* Kentucky), ST1 (*S.* Typhi), and ST13 (*S.* Agona) originated from humans.

In agreement with previous studies[31,32,35], we found that the available antimicrobial usage data in humans and animals explain only a small fraction of the variation in the global AMR levels in *Salmonella*. Due to economic factors, significant differences in the usage and growth rate of consumption of antibiotics between high-income and low-income regions were observed[52], and the use and overuse of antibiotics are high in South and Southeast Asia[20,53]. In our previous study, we found that higher temperature, precipitation, GDP, gross output of meat, and population can indirectly promote the AMR levels in *Salmonella* in China[13], and had not been extrapolated to a global scale. Moreover, human development index, temperature, the ratio of private to public health expenditure, nutrition, environment, and several socioeconomic factors in the World Bank were positively correlated with the AMR levels in some pathogens, for example, *Escherichia coli*, *Acinetobacter baumanii*, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa*, *Staphylococcus aureus*, *Shigella flexneri*[31–35]. Here, using data on twelve representative countries across six continents, for the first time, we found that the World Bank's agriculture & rural development, climate change, the environment, economy & growth, trade, the financial sector, private sector, urban development, energy & mining, and infrastructure indicator variables explained a large amount of variation in animal and human AMR levels in *Salmonella*. We found that higher AMR levels in aquatic animals were positive with warmer temperatures, which is the relationship that has also been observed in aquaculture and clinical bacteria worldwide[34,54]. Merchandise imports from low- and middle-income economies in Latin America & the Caribbean were high-risk points for AMR levels in China and the USA. Merchandise imports from low- and middle-income economies in South Asia were high-risk points for AMR levels in Germany and Brazil. Merchandise imports from low- and middle-income economies in Europe, Central Asia, and Sub-Saharan Africa were high-risk points for AMR levels in both China and Germany. Importantly, the amount of variation explained by these indicators varied between the different countries/regions.

The emergence and global spread of critical antibiotic-resistant MRDRST strains pose an important threat, as they limit treatment options for this common infection. Our genomic analysis of the global distribution of MRDRST strains revealed their presence in at least twelve countries across five continents, except for Africa. The global distribution of MRDRST underscores the need for international collaborations and monitoring to track and prevent the spread of antimicrobial-resistant *Salmonella* effectively. The phylogenetic tree showed that MRDRST forms adaptive and localized transmission clones in China, which was consistent with the previous report by Xiang and colleagues[27]. Our findings provide evidence to guide future fosfomycin-resistant MRDRST epidemic prevention and treatment in Asia. A total of 1233 MRDRST genomes were identified from the global dataset of *S.* Typhimurium, seventy-six of them were positive for FRGs, including seventy-five *fosA3* and one *fosA7* from 2011 to 2019. Of note, invasive cases and food-borne outbreaks were not analyzed in this study, which needs further monitoring of prevalence and AMR trends of MRDRST in invasive and food-borne outbreak cases[55]. Taken together, our data provide more insight into the global trends in the increasing co-existing prevalence of the FRGs and *mcr-1*, *bla*CTX-M, *bla*NDM, or *mph(A)* in novel variants of *S.* Typhimurium and suggest that prevalence varies widely between different regions, animals, and countries, which needs immediate worldwide attention and to be investigated, especially through enhanced genomic surveillance.

Our study and our analytical component have several limitations. First, many countries/regions still lack sufficient data on both *Salmonella* genomes and antibiotic consumption in animals or humans,

which limits the number of countries/regions included in variable analyses. Although we used the best available data, there remained inconsistencies in the number of genomes in different serovars, sources, collection years, and countries/regions, which is not systematic surveillance and may represent a potential sampling bias. Second, even though 471,617 publicly available *Salmonella* genomes were downloaded from NCBI and analyzed (as of June 17, 2023), 263,384 genomes were discarded due to a lack of detailed background information or quality control issues. We discarded genomes without serovar and ST results using SISTR, SeqSero2, and MLST tools. Without detailed information on collection time, location, and source, it could not be used for the spatiotemporal and traceable analysis and outbreak investigation, which needs to be improved in the quality of uploaded data in the future. Third, the data used in this study were mainly derived from nine sources, including humans, chickens, pigs, cattle, turkeys, aquatic animals, food, wild animals, and the environment. The number of genomes from other sources was too small, and this needs to be improved in the future. However, to our knowledge, an up-to-date global *Salmonella* genome database on AMR surveillance has not been conducted. Fourth, our data did not capture the phenotype of antimicrobial susceptibility testing for *Salmonella*. Fifth, we used the regression correlation analysis between the total amount of antibiotic consumption in humans and animals and the number of ARGs carried by *Salmonella*, respectively, while no correlation analysis was performed for antibiotic consumption in each class. In addition, antibiotic consumption data are not equivalent to antibiotic exposure, however, they were representative of the best data available. Sixth, we did not obtain comprehensive data on antibiotic consumption in both humans and animals worldwide, antibiotic consumption was obtained in two previous reports[52,56]. Seventh, a total of 708 serovars were identified, and only twenty predominant serovars were selected for AMR trends analysis. Eighth, we only analyzed the spatiotemporal patterns of AMR and mobile genetic elements, and their correlation with serovars and hosts, but did not analyze the genetic environments of acquired ARGs. Therefore, long-read sequencing sequences were needed to determine the precise location of mobile ARGs. Ninth, only assembly genomes were used for ARG prediction in this analysis, which has been recommended in AMR in pathogen surveillance systems[13,57,58]. Tenth, there is latency in the genomic data we use. Therefore, we call for the establishment of an up-to-date open-source *Salmonella* genome database (for example, CLSGDB v2, https://nmdc.cn/clsgdbv2) for accurately monitoring specific hosts or serovars, and the establishment of a data-sharing consortium. Finally, we also did not explicitly investigate the indirect effects of driving factors on AMR in *Salmonella*. Because this was an association study at the global level, any interpretation should be taken with caution, as the results may be influenced by multiple variations. Future studies should consider comparing the evolutionary trajectory of AMR in *Salmonella* due to the influence of a single variable.

In summary, this study presents a valuable to-date genetic atlas of antimicrobial-resistant *Salmonella* in the concept of "One Health" including humans, animals, food, and the environment across the world. To our knowledge, our study provides a valuable collection and systematical study reporting the temporal and spatial dynamics of AMR in *S. enterica*, including multiple serovars from diverse sources in 148 countries/regions across six continents. Our work suggests that the proportion of AMR levels increased across six continents in chickens, food, wild animals, and the environment (especially in serovars Agona, Dublin, I 1,4,[5],12:i:-, Muenchen, Senftenberg, Mbandaka). Our study enhances our understanding of the dynamic trends, evolution, and transmission of AMR in *Salmonella* over the past 100 years. We used the best available *S. enterica* genomic data, analyzed the correlation between AMR levels and agriculture & rural development, climate change, the environment, urban development, infrastructure, and socioeconomic factors, and antibiotic consumption in

both humans and animals. Merchandise imports from low- and middle-income countries were high-risk points for AMR levels in some countries/regions, for example, China, Brazil, Germany, and the USA. This was the first study to investigate how several factors influence AMR in *S. enterica* at the global level. Our findings suggest that these driving factors play an underappreciated role in the spread of AMR in *Salmonella* and have critical implications for public health policy. Therefore, further strengthening and refining of genomic monitoring for AMR in zoonotic pathogens is vital to maintain global health and planet health. For future directions, it is vital to build an up-to-date and globally high-quality *Salmonella* genome database, which will enhance surveillance for transmission dynamics, evolutionary trajectories, outbreak tracing, and early warning of antimicrobial-resistant *Salmonella* using artificial intelligence, as well as for predicting minimal inhibit concentrations, novel ARGs, and antimicrobial peptides.

## Methods

### Study design and data collection
This study aimed to map the global atlas of AMR in *Salmonella* in humans, animals (food-producing animals and wildlife), food, and the environment, as well as to identify the major determinants of AMR *Salmonella*. To ensure the comprehensiveness of the analyzed genomes, a total of 471,617 publicly available *Salmonella* genomes on the National Center of Biotechnology Information (NCBI, https://www.ncbi.nlm.nih.gov/) were collected and utilized in this study (downloaded on June 17, 2023).

First, we screened and summarized the metadata of publicly available *Salmonella* genomes from the NCBI BioSample (https://www.ncbi.nlm.nih.gov/biosample/, as of June 17, 2023), and genomes with information on the collection time, isolation source, and sampling sites are used for next step analysis. A total of 253,872 genomes were discarded because no background information on the collection time, isolation source, and sampling sites was simultaneously recorded.

Second, in silico serotyping was carried out by both the *Salmonella* in silico typing resource (SISTR v1.1.2, https://github.com/phac-nml/sistr_cmd)[59] and *Salmonella* Serotyping by whole genome sequencing (SeqSero2 v1.3.1, https://github.com/denglab/SeqSero2)[60]. Only the prediction result matching between the SeqSero2 and SISTR is used for downstream analysis.

Third, multilocus sequence typing (MLST v2.0, https://github.com/tseemann/mlst)[61] was used to assign STs to these genomes based on seven housekeeping genes for examining bacterial relatedness. A total of 9512 genomes were discarded because no serotype or sequence typing information was predicted. Then, we summarized and re-recorded background information for each isolate, including sampling time, isolation source (host), geographic location (country and continent), serovar, and ST.

As a result, we obtained a high-quality *Salmonella* genome dataset containing 208,233 genomes divided into 708 serovars and 3006 STs. Metadata and accession numbers are available in Supplementary Data 1. The frequency and distribution of strains were analyzed by period, continent, country (two major from each continent), source (i.e., host species), STs, and serovar.

### In silico analysis of AMR markers and plasmid replicons
ResFinder 4.1 (https://bitbucket.org/genomicepidemiology/resfinder/src/master/) was used to identify acquired AMR genes and (*Salmonella*-specific) chromosomal gene mutations mediating AMR with the ResFinder database (https://bitbucket.org/genomicepidemiology/resfinder_db/src), PointFinder database (https://bitbucket.org/genomicepidemiology/pointfinder_db/src/master/), and DisinFinder database (https://bitbucket.org/genomicepidemiology/disinfinder_db/src/master/), respectively[62,63]. The thresholds of AMR genes are consistent with our previous studies[12,13]. Also, the phenotypes of strains were predicted based on genotypes. PlasmidFinder v2.1

(https://bitbucket.org/genomicepidemiology/plasmidfinder.git/src)[64] was used to identify plasmid replicons with the PlasmidFinder database (https://bitbucket.org/genomicepidemiology/plasmidfinder_db/src/master/). The results were transformed into a presence-absence matrix in which "1" represented the presence of an ARG and "0" was the absence. The frequency and distribution of AMR determinants to antimicrobial classes were analyzed by period, continent, country, source (i.e., host species), and serovar. For AMR levels in different sources, we mainly focused on the following categories: chicken, pigs, cattle, turkey, aquatic animals, food, wild animals, humans, and the environment. The numbers of AMR genes for each isolate were compiled and compared by analyzing the distribution of their frequencies among periods for each source and continent. A similar method was used for phenotypes and mobile genetic elements. In addition, the reference sequence (a point mutation ($-44\,G > T$) in the *csgD* gene promoter, upregulation of the *csgDEFG* operons) for MRDRST was obtained from the previous study[27].

### Data collection on agriculture, antimicrobial, climate, environment, and socioeconomic indicators
To examine the association between antimicrobials, agriculture, climate, environment, socioeconomic, trade indicators, and AMR, a total of 115 indicators were collected and analyzed. The relevant data of indicators including Agriculture & Rural Development ($n = 9$; Agriculture, forestry, and fishing, value added; Agricultural methane emissions; Livestock Production Index; Cereal yield; Cereal production; Crop Production Index; rural population; Employment in agriculture; Food Production Index; Agricultural methane emissions (thousand metric tons of $CO_2$ equivalent)), Economy & Growth ($n = 28$; GDP; GDP per capita (current US\$); GDP per capita (current LCU); GNI; GNI per capita growth; GNI per capita; Households and NPISHs Final consumption expenditure (current LCU); Households and NPISHs Final consumption expenditure, PPP; Households and NPISHs Final consumption expenditure per capita growth; Current health expenditure per capita, PPP; Imports of goods and services; Gross national expenditure; R&D expenditure; Services, value added; Industry (including construction), value added; Food, beverages and tobacco; Manufacturing, value added; GDP growth rate (annual %); Goods exports (BoP, current US\$); Service exports (BoP, current US\$); Services, value added (annual % growth); GNI (current LCU); Households and NPISHs Final consumption expenditure (constant LCU); Transport services (% of service exports, BoP); Imports of goods and services (% of GDP); Imports of goods and services (annual % growth); GDP per capita (constant LCU); per capita GDP growth rate (annual growth rate)), Aid Effectiveness ($n = 1$; Incidence of tuberculosis), Climate Change ($n = 6$; $CO_2$ emissions; HFC gas emissions; PFC gas emissions; Community health workers; Total greenhouse gas emissions; Population, total), Environment ($n = 13$; Capture fisheries production; Aquaculture production; Total fisheries production; PM2.5 air pollution, mean annual exposure; PM2.5 pollution, population exposed to levels exceeding WHO Interim Target-1 value (% of total); Methane emissions; Methane emissions in energy sector; Renewable inland freshwater resources per capita; People practicing open defecation; People practicing open defecation, urban; People practicing open defecation, rural; $CO_2$ emissions (kt); $CO_2$ emissions from the transport sector), Energy & Mining ($n = 1$; Nitrous oxide emissions in energy sector), Financial Sector ($n = 2$; Consumer price index and Wholesale price index), Health ($n = 5$; Domestic private health expenditure per capita; Population growth; People using safely managed drinking water services, urban; People using safely managed drinking water services, rural; People using safely managed drinking water services), Infrastructure ($n = 5$; air transport, passenger traffic; Railways; Railway freight volume; Railway passenger traffic; Air transport, cargo volume), Poverty ($n = 3$; Gini index; Proportion of people living below 50 percent of median income (%); Population living in slums (% of urban

population)), Private Sector (n = 18; Agricultural raw materials imports; Fuel imports; Merchandise imports from low- and middle-income economies in Latin America & the Caribbean; Merchandise imports from low- and middle-income economies in South Asia; Merchandise imports from low- and middle-income economies in Europe & Central Asia; Merchandise imports from low- and middle-income economies in Sub-Saharan Africa; Merchandise imports from low- and middle-income economies in Middle East & North Africa; Import volume index; Merchandise imports from high-income economies; Merchandise imports; International tourism, number of arrivals; International tourism, number of departures; Fuel exports (% of merchandise exports); Food exports (% of merchandise exports); Agricultural raw materials exports (% of merchandise exports); Transport services (% of commercial service imports); Trade (% of GDP); International tourism, receipts (% of total exports)), Public Sector (n = 1; Human Capital Index), Trade (n = 11; Merchandise trade; Goods imports; Food imports; Manufactures imports; Travel services, % of service import; Travel services, % of commercial service imports; International tourism, receipts; Exports of goods and services (annual % growth); Exports of goods and services (current US$); International tourism, expenditures; Travel services (% of service exports, BoP)), and Urban Development (n = 3; Population density; Pump price for diesel fuel; Pump price for gasoline) were downloaded from the World Bank open database (https://data.worldbank.org). Indicators were collected for 12 countries, including China, India, Nigeria, South Africa, Germany, the United Kingdom, Canada, the USA, Australia, Fiji, Brazil, and Chile, across six continents for which we computed. These countries are composed of developed and developing countries.

In addition, to analyze the relationships between the number of ARGs in the *Salmonella* genomes and the consumption of antibiotics, we collected available data on human antibiotic consumption in different countries from 2000 to 2018 in a previous study[52], data on the usage of antibiotics in animals from 2006 to 2020 were collected from a previous study[56]. Regression correlation analysis between Agriculture & Rural Development, Economy & Growth, Aid Effectiveness, Climate Change, Environment, Energy & Mining, Financial Sector, Health, Poverty, Private Sector, Public Sector, Infrastructure, Trade, Urban Development indicators, and AMR (the mean of ARGs in each isolate) was performed to investigate sources that might affect AMR. The simple linear regression models (Pearson analysis) were used to measure the association between indicators and AMR genes per genome over time, adjusting for 12 representative country-level data available across six continents, ranging from 2000 to 2023. Pairs of data in each country from year to year are available in Supplementary Data 20. Source data are provided as a Source Data file.

## Phylogenetic and statistical analyses and visualization

The map of the *Salmonella* genome collection location was visualized on MapChart (https://www.mapchart.net/). The phylogenetic analysis for the novel variant of *S*. Typhimurium was based on the core genome was conducted by Parsnp v2.0.5 (https://github.com/marbl/parsnp)[65], *S*. Typhimurium str. LT2 (GenBank: AE006468) was used as the reference genome. The phylogenetic tree was annotated and visualized using the interactive tree of life (iTOL version 6.9, https://itol.embl.de/)[66]. Differences between numbers of ARGs and plasmid replicons per genome in different decade-specific datasets (1900–1950, 1951–1960, 1961–1970, 1971–1980, 1981–1990, 1991–2000, 2001–2010, 2011–2020, and 2021–2023) were compared by the Kruskal-Wallis test using GraphPad Prism v9.0. Heatmaps were generated using the ImageGP platform (http://www.ehbio.com/ImageGP/)[67]. Regression correlation analysis was performed using GraphPad Prism version 9.0. Only *P* < 0.05 was considered statistically significant, Pearson's r in 0.4–0.6 was a moderate correlation, and 0.7–0.9 was a high correlation.

## Reporting summary

Further information on research design is available in the Nature Portfolio Reporting Summary linked to this article.

## Data availability

The publicly available genomes were downloaded from the NCBI assembly (https://www.ncbi.nlm.nih.gov/assembly), and accession numbers are listed in Supplementary Data 1. Indicators were downloaded from the World Bank open database (https://data.worldbank.org). The data on antibiotic consumption were obtained from previous studies[52,56]. Source data are provided in this paper.

## References

1.  Ikuta, K. S. et al. Global mortality associated with 33 bacterial pathogens in 2019: a systematic analysis for the Global Burden of Disease Study 2019. *Lancet* **400**, 2221–2248 (2022).
2.  Murray, C. J. L. et al. Global burden of bacterial antimicrobial resistance in 2019: a systematic analysis. *Lancet* **399**, 629–655 (2022).
3.  World Health Organization. WHO bacterial priority pathogens list, 2024: Bacterial pathogens of public health importance to guide research, development and strategies to prevent and control antimicrobial resistance. https://www.who.int/publications/i/item/9789240093461/ (2024).
4.  Ma, Y. et al. WHO revised bacterial priority pathogens list to encourage global actions to combat AMR. *hLife* **2**, 607–610 (2024).
5.  Xiao, Y. & Nishijima, T. Status and challenges of global antimicrobial resistance control: A dialogue between Professors Yonghong Xiao and Takeshi Nishijima. *hLife* **2**, 47–49 (2024).
6.  EFSA, E. C. D. C. The European Union summary report on antimicrobial resistance in zoonotic and indicator bacteria from humans, animals and food in 2021-2022. *E.F.S.A. J.* **22**, e8583 (2024).
7.  Waterlow, N. R., Cooper, B. S., Robotham, J. V. & Knight, G. M. Antimicrobial resistance prevalence in bloodstream infection in 29 European countries by age and sex: An observational study. *PLoS Med.* **21**, e1004301 (2024).
8.  Medalla, F. et al. Increased incidence of antimicrobial-resistant nontyphoidal *Salmonella* infections, United States, 2004-2016. *Emerg. Infect. Dis.* **27**, 1662–1672 (2021).
9.  Plumb, I. D. et al. Increased multidrug-resistant *Salmonella* enterica I serotype 4,[5],12:i:- infections associated with pork, United States, 2009-2018. *Emerg. Infect. Dis.* **29**, 314–322 (2023).
10. Cox, G. W. et al. A one health genomic investigation of gentamicin resistance in *Salmonella* from human and chicken sources in Canada, 2014-2017. *Antimicrob. Agents Chemother.* **65**, e0096621 (2021).
11. Williamson, D. A. et al. Increasing antimicrobial resistance in nontyphoidal *Salmonella* isolates in Australia from 1979 to 2015. *Antimicrob. Agents Chemother.* **62**, e02012-17 (2018).
12. Wang, Y. N. et al. The temporal dynamics of antimicrobial-resistant *Salmonella* enterica and predominant serovars in China. *Natl. Sci. Rev.* **10**, nwac269 (2023).
13. Wang, Y. N. et al. Genomic analysis of almost 8000 *Salmonella* genomes reveals drivers and landscape of antimicrobial resistance in China. *Microbiol. Spectr.* **11**, e0208023 (2023).
14. Pina-Iturbe, A. et al. Genomic characterisation of the population structure and antibiotic resistance of *Salmonella* enterica serovar Infantis in Chile, 2009-2022. *Lancet Reg. Health Am.* **32**, 100711 (2024).
15. Pulford, C. V. et al. Stepwise evolution of *Salmonella* Typhimurium ST313 causing bloodstream infection in Africa. *Nat. Microbiol.* **6**, 327–338 (2020).

16. Baker, S., Thomson, N., Weill, F. X. & Holt, K. E. Genomic insights into the emergence and spread of antimicrobial-resistant bacterial pathogens. *Science* **360**, 733–738 (2018).

17. Djordjevic, S. P. et al. Genomic surveillance for antimicrobial resistance — a one health perspective. *Nat. Rev. Genet.* **25**, 142–157 (2024).

18. Van Boeckel, T. P. et al. Global trends in antimicrobial resistance in animals in low- and middle-income countries. *Science* **365**, eaaw1944 (2019).

19. Zhao, C. et al. Geographically targeted surveillance of livestock could help prioritize intervention against antimicrobial resistance in China. *Nat. Food* **2**, 596–602 (2021).

20. Zhao, C., Wang, Y., Mulchandani, R. & Van, B. T. P. Global surveillance of antimicrobial resistance in food animals using priority drugs maps. *Nat. Commun.* **15**, 763 (2024).

21. Wang, Y. et al. Detection of plasmid-mediated tigecycline resistance gene *tet*(X4) in a *Salmonella enterica* serovar Llandoff isolate. *Infect. Microbes Dis.* **3**, 198–204 (2021).

22. Wang, Y. et al. Comparative genomic analysis of mobile colistin resistance gene *mcr-9* in *Salmonella enterica*. *J. Infect.* **82**, e15–e17 (2021).

23. Falagas, M. E., Vouloumanou, E. K., Samonis, G. & Vardakas, K. Z. Fosfomycin. *Clin. Microbiol. Rev.* **29**, 321–347 (2016).

24. World Health Organization. WHO's list of medically important antimicrobials: a risk management tool for mitigating antimicrobial resistance due to non-human use (2024).

25. Monte, D. F. M., Doi, Y. & Lincopan, N. High prevalence and global distribution of fosfomycin resistance genes in *Salmonella* serovars. *Lancet Microbe* **4**, e968 (2023).

26. Wang, J., Li, Q. C., Jiang, Y., Wang, Z. Y. & Jiao, X. FosA7: a silent fosfomycin resistance gene in *Salmonella*? *Lancet Microbe* **5**, e211 (2023).

27. Xiang, Y. et al. Characterization of a *Salmonella enterica* serovar Typhimurium lineage with rough colony morphology and multidrug resistance. *Nat. Commun.* **15**, 6123 (2024).

28. Van, B. T. P. et al. Global trends in antimicrobial use in food animals. *Proc. Natl. Acad. Sci. USA* **112**, 5649–5654 (2015).

29. Van, B. T. P. et al. Reducing antimicrobial use in food animals. *Science* **357**, 1350–1352 (2017).

30. Holmes, A. H. et al. Understanding the mechanisms and drivers of antimicrobial resistance. *Lancet* **387**, 176–187 (2016).

31. Allel, K. et al. Global antimicrobial-resistance drivers: an ecological country-level study at the human-animal interface. *Lancet Planet. Health* **7**, e291–e303 (2023).

32. Collignon, P., Beggs, J. J., Walsh, T. R., Gandra, S. & Laxminarayan, R. Anthropological and socioeconomic factors contributing to global antimicrobial resistance: a univariate and multivariable analysis. *Lancet Planet. Health* **2**, e398–e405 (2018).

33. McGough, S. F., MacFadden, D. R., Hattab, M. W., Molbak, K. & Santillana, M. Rates of increase of antibiotic resistance and ambient temperature in Europe: a cross-national analysis of 28 countries between 2000 and 2016. *Euro. Surveill.* **25**, 1900414 (2020).

34. MacFadden, D. R., McGough, S. F., Fisman, D., Santillana, M. & Brownstein, J. S. Antibiotic resistance increases with local temperature. *Nat. Clim. Chang.* **8**, 510–514 (2018).

35. Njage, P. M. K., van, B. B., Munk, P., Marques, A. R. P. & Aarestrup, F. M. Association of health, nutrition, and socioeconomic variables with global antimicrobial resistance: a modelling study. *Lancet Planet. Health* **7**, e888–e899 (2023).

36. Hendriksen, R. S. et al. Global monitoring of antimicrobial resistance based on metagenomics analyses of urban sewage. *Nat. Commun.* **10**, 1124 (2019).

37. Nuanmuang, N., Leekitcharoenphon, P., Njage, P. M. K., Gmeiner, A. & Aarestrup, F. M. An overview of antimicrobial resistance profiles of publicly available *Salmonella* genomes with sufficient quality and metadata. *Foodborne Pathog. Dis.* **20**, 405–413 (2023).

38. Li, S. T., He, Y. S., Mann, D. A. & Deng, X. Y. Global spread of *Salmonella* Enteritidis via centralized sourcing and international trade of poultry breeding stocks. *Nat. Commun.* **12**, 5109 (2021).

39. Li, H. et al. Centralized industrialization of pork in Europe and America contributes to the global spread of *Salmonella enterica*. *Nat. Food* **5**, 413–422 (2024).

40. Ingle, D. J. et al. Evolutionary dynamics of multidrug resistant *Salmonella enterica* serovar 4,[5],12:i:- in Australia. *Nat. Commun.* **12**, 4786 (2021).

41. EFSA, E. C. D. C. The European Union summary report on antimicrobial resistance in zoonotic and indicator bacteria from humans, animals and food in 2018/2019. *EFSA J.* **19**, e06490 (2021).

42. WHO. Global Antimicrobial resistance and use surveillance system (GLASS) report (2022).

43. Yang, Y. et al. Distinct increase in antimicrobial resistance genes among *Escherichia coli* during 50 years of antimicrobial use in livestock production in China. *Nat. Food* **3**, 197–205 (2022).

44. Klein, E. Y. et al. Global trends in antibiotic consumption during 2016-2023 and future projections through 2030. *Proc. Natl. Acad. Sci. USA* **121**, e2411919121 (2024).

45. Klein, E. Y. et al. Global increase and geographic convergence in antibiotic consumption between 2000 and 2015. *Proc. Natl. Acad. Sci. USA* **115**, E3463–E3470 (2018).

46. Wales, A. & Davies, R. Co-selection of resistance to antibiotics, biocides and heavy metals, and its relevance to foodborne pathogens. *Antibiotics* **4**, 567–604 (2015).

47. Blair, J. et al. Molecular mechanisms of antibiotic resistance. *Nat. Rev. Microbiol.* **13**, 42–51 (2015).

48. Pires, J., Huisman, J. S., Bonhoeffer, S. & Van, B. T. P. Multidrug resistance dynamics in *Salmonella* in food animals in the United States: an analysis of genomes from public databases. *Microbiol. Spectr.* **9**, e0049521 (2021).

49. Zheng, B. & Feng, Y. MCR-1-producing *Salmonella* Typhimurium ST34 links animal foods to human community infections. *EBioMedicine* **42**, 10–11 (2019).

50. Lu, X. et al. Epidemiologic and genomic insights on *mcr-1*-harbouring *Salmonella* from diarrhoeal outpatients in Shanghai, China, 2006-2016. *EBioMedicine* **42**, 133–144 (2019).

51. Luo, Q. et al. MDR *Salmonella enterica* serovar Typhimurium ST34 carrying *mcr-1* isolated from cases of bloodstream and intestinal infection in children in China. *J. Antimicrob. Chemother.* **5**, 92–95 (2020).

52. Browne, A. J. et al. Global antibiotic consumption and usage in humans, 2000-18: a spatial modelling study. *Lancet Planet. Health* **5**, e893–e904 (2021).

53. Fink, G., D'Acremont, V., Leslie, H. H. & Cohen, J. Antibiotic exposure among children younger than 5 years in low-income and middle-income countries: a cross-sectional study of nationally representative facility-based and household-based surveys. *Lancet Infect. Dis.* **20**, 179–187 (2020).

54. Reverter, M. et al. Aquaculture at the crossroads of global warming and antimicrobial resistance. *Nat. Commun.* **11**, 1870 (2020).

55. Lv, P. et al. Genomic insights into antimicrobial-resistant non-typhoidal *Salmonella* isolates from outpatients in Minhang District in Shanghai. *Commun. Med.* Accepted (2025).

56. Mulchandani, R., Wang, Y., Gilbert, M. & Van, B. T. P. Global trends in antimicrobial use in food-producing animals: 2020 to 2030. *PLOS Glob. Public Health* **3**, e0001305 (2023).

57. Black, A., MacCannell, D. R., Sibley, T. R. & Bedford, T. Ten recommendations for supporting open pathogen genomic analysis in public health. *Nat. Med.* **26**, 832–841 (2020).

58. Carey, M. E. et al. Global diversity and antimicrobial resistance of typhoid fever pathogens: insights from a meta-analysis of 13,000 *Salmonella* Typhi genomes. *eLife* **12**, e85867 (2023).

59. Yoshida, C. E. et al. The *Salmonella* in silico typing resource (SISTR): an open web-accessible tool for rapidly typing and subtyping draft *Salmonella* genome assemblies. *PLoS ONE* **11**, e0147101 (2016).

60. Zhang, S. et al. SeqSero2: rapid and improved *Salmonella* serotype determination using whole-genome sequencing data. *Appl. Environ. Microbiol.* **85**, e01746–19 (2019).

61. Larsen, M. V. et al. Multilocus sequence typing of total-genome-sequenced bacteria. *J. Clin. Microbiol.* **50**, 1355–1361 (2012).

62. Bortolaia, V. et al. ResFinder 4.0 for predictions of phenotypes from genotypes. *J. Antimicrob. Chemother.* **75**, 3491–3500 (2020).

63. Zankari, E. et al. F.M. PointFinder: a novel web tool for WGS-based detection of antimicrobial resistance associated with chromosomal point mutations in bacterial pathogens. *J. Antimicrob. Chemother.* **72**, 2764–2768 (2017).

64. Carattoli, A. et al. In silico detection and typing of plasmids using PlasmidFinder and plasmid multilocus sequence typing. *Antimicrob. Agents Chemother.* **58**, 3895–3903 (2014).

65. Kille, B. et al. Parsnp 2.0: scalable core-genome alignment for massive microbial datasets. *Bioinformatics* **40**, btae311 (2024).

66. Letunic, I. & Bork, P. Interactive tree of life (iTOL) v6: recent updates to the phylogenetic tree display and annotation tool. *Nucleic Acids Res.* **52**, W78–W82 (2024).

67. Chen, T., Liu, Y. X. & Huang, L. Q. ImageGP: An easy-to-use data visualization web server for scientific researchers. *iMeta* **1**, e5 (2022).

## Author contributions

G.F.G. and Y.N.W. conceived and designed the project. S.L.J., X.B.X., and Y.N.W. collected the genomic data and epidemiological data. Y.N.W. and S.L.J. performed bioinformatics analysis. M.Q.Q. and Y.H.P. performed statistical analysis. S.F.Q., J.M.Z., Y.L., S.F.M., N.L., Y.F.H., J.L.L., E.Q.Z., B.W., and B.L.Z. provided invaluable insights into the analysis. Y.N.W. created the figures and tables and drafted the original manuscript. W.Y.N., X.B.X., S.L.J., M.Q.Q., and G.F.G. revised the manuscript. All authors read and approved the submitted version.

## Competing interests

The authors declare that there are no competing interests.

## Additional information

**Supplementary information** The online version contains supplementary material available at https://doi.org/10.1038/s41467-025-59758-3.

**Correspondence** and requests for materials should be addressed to Yanan Wang or George F. Gao.

**Peer review information** *Nature Communications* thanks Rafaela Gomes Ferrari, Junia Jean-Gilles Beaubrun, and the other anonymous reviewer(s) for their contribution to the peer review of this work. A peer review file is available.

**Reprints and permissions information** is available at http://www.nature.com/reprints

**Publisher's note** Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.