中国疾病预防控制中心
CHINESE CENTER FOR DISEASE CONTROL AND PREVENTION

中国科学院微生物研究所
INSTITUTE OF MICROBIOLOGY
CHINESE ACADEMY OF SCIENCES

AMR in China

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2023.02.17

Threat of AMR

	Associated with resistance				Attributable to resistance			
	Deaths	YLLs	DALYs	YLDs	Deaths	YLLs	DALYs	YLDs
Counts, thousands								
Global	4950 (3620–6570)	189 000 (145 000–245 000)	192 000 (146 000–248 000)	2290 (1520–3450)	1270 (911–1710)	47 600 (35 000–63 400)	47 900 (35 300–63 700)	275 (161–439)
Central Europe, eastern Europe, and central Asia	283 (190–403)	7530 (5240–10 500)	7630 (5320–10 600)	102 (69–140)	73·7 (48·7–105)	1980 (1350–2790)	1990 (1360–2800)	9·95 (4·79–16·8)
High income	604 (434–824)	10 100 (6960–14 200)	10 300 (7040–14 400)	123 (79·7–183)	141 (98·6–197)	2390 (1620–3400)	2410 (1640–3420)	20·2 (12·7–31·2)
Latin America and Caribbean	338 (243–453)	9550 (6770–12 900)	9640 (6830–13 100)	97·2 (63·2–146)	84·3 (60·3–117)	2370 (1660–3310)	2380 (1680–3330)	16 (9·79–24·9)
North Africa and Middle East	256 (174–362)	9970 (6880–13 900)	10 100 (6970–14 000)	116 (73·4–176)	68·3 (45·6–99)	2590 (1770–3700)	2610 (1790–3720)	20·7 (12–33·5)
South Asia	1390 (1030–1830)	58 900 (44 800–76 300)	59 900 (45 700–77 500)	1000 (638–1550)	389 (273–538)	16 000 (11 500–21 600)	16 100 (11 600–21 700)	111 (58·5–188)
Southeast Asia, east Asia, and Oceania	1020 (678–1460)	27 500 (18 700–38 600)	27 900 (19 100–39 100)	437 (256–776)	254 (167–369)	6830 (4620–9840)	6870 (4670–9890)	45·6 (25–80·1)
Sub-Saharan Africa	1070 (847–1340)	65 800 (51 400–83 600)	66 200 (51 800–84 000)	416 (270–599)	255 (196–331)	15 400 (11 700–19 900)	15 500 (11 800–20 000)	51·1 (30·2–81·8)
Rates, per 100 000								
Global	64·0 (46·8–84·9)	2448·1 (1868·9–3170·3)	2477·7 (1889·9–3199·1)	29·6 (19·7–44·5)	16·4 (11·8–22·0)	615·1 (452·4–819·1)	618·7 (455·7–823·2)	3·6 (2·1–5·7)
Central Europe, eastern Europe, and central Asia	67·7 (45·4–96·6)	1802·5 (1253·9–2515·1)	1826·9 (1274·5–2545·4)	24·4 (16·5–33·6)	17·6 (11·7–25·3)	474·3 (323·0–667·3)	476·7 (325·2–671·0)	2·4 (1·1–4·0)
High income	55·7 (40·1–76·0)	935·3 (641·9–1310·1)	946·7 (649·8–1327·2)	11·3 (7·3–16·9)	13·0 (9·1–18·2)	220·4 (149·9–314·0)	222·3 (151·5–315·9)	1·9 (1·2–2·9)
Latin America and Caribbean	57·9 (41·6–77·6)	1633·8 (1158·7–2215·9)	1650·5 (1169·0–2236·6)	16·6 (10·8–25·0)	14·4 (10·3–20·0)	405·3 (284·8–566·6)	408·1 (286·9–570·0)	2·7 (1·7–4·3)
North Africa and Middle East	42·0 (28·7–59·5)	1637·5 (1130·4–2283·2)	1656·6 (1145·2–2300·9)	19·1 (12·1–28·9)	11·2 (7·5–16·3)	425·6 (291·2–608·4)	429·0 (293·7–611·5)	3·4 (2·0–5·5)
South Asia	76·8 (57·2–101·2)	3262·6 (2482·4–4228·2)	3318·1 (2532·9–4291·7)	55·4 (35·4–86·0)	21·5 (15·1–29·8)	885·8 (636·3–1194·6)	892·0 (643·1–1200·2)	6·2 (3·2–10·4)
Southeast Asia, east Asia, and Oceania	47·1 (31·4–67·7)	1272·6 (866·8–1789·0)	1292·8 (884·7–1811·4)	20·2 (11·8–35·9)	11·7 (7·8–17·1)	316·1 (213·9–455·7)	318·2 (216·1–458·0)	2·1 (1·2–3·7)
Sub-Saharan Africa	98·9 (78·6–124·2)	6105·3 (4770·2–7749·1)	6143·9 (4802·8–7792·2)	38·6 (25·1–55·6)	23·7 (18·2–30·7)	1432·0 (1084·6–1848·1)	1436·7 (1090·0–1853·5)	4·7 (2·8–7·6)

DALYs=disability-adjusted life-years. GBD=Global Burden of Diseases, Injuries, and Risk Factors Study. YLDs=years lived with disability. YLLs=years of life lost.

Table 2: **Deaths, YLLs, YLDs, and DALYs (in counts and all-age rates) associated with and attributable to bacterial antimicrobial resistance, globally and by GBD super-region, 2019**

- **In 2019, there were an estimated 4·95 million deaths associated with bacterial AMR, including 1·27 million deaths attributable to bacterial AMR.**
- **This is significantly higher than the previous estimate of 700,000 deaths per year.**

AMR Collaborators. Lancet. (2022).

Threat of AMR

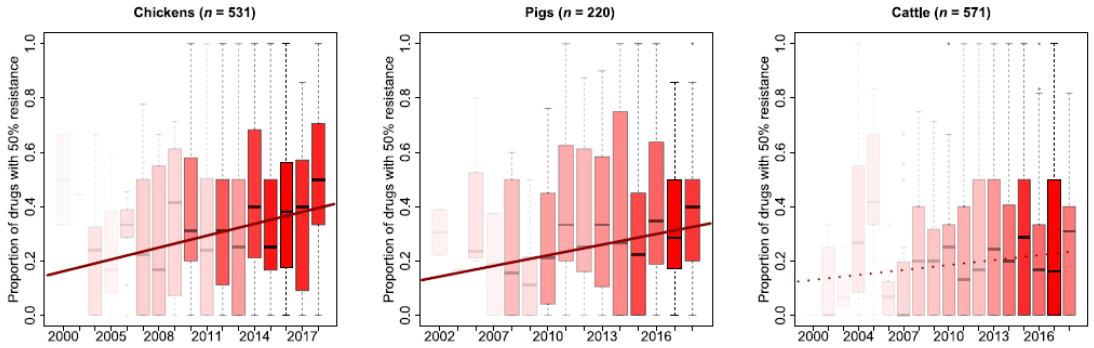


Fig. 2. Increase in antimicrobial resistance in LMICs. Proportion of antimicrobial compounds with resistance higher than 50% (P50) is shown. Solid lines indicate statistically significant (5% level) increases of P50 over time; shading indicates the number of surveys per year relative to total number of surveys per species.

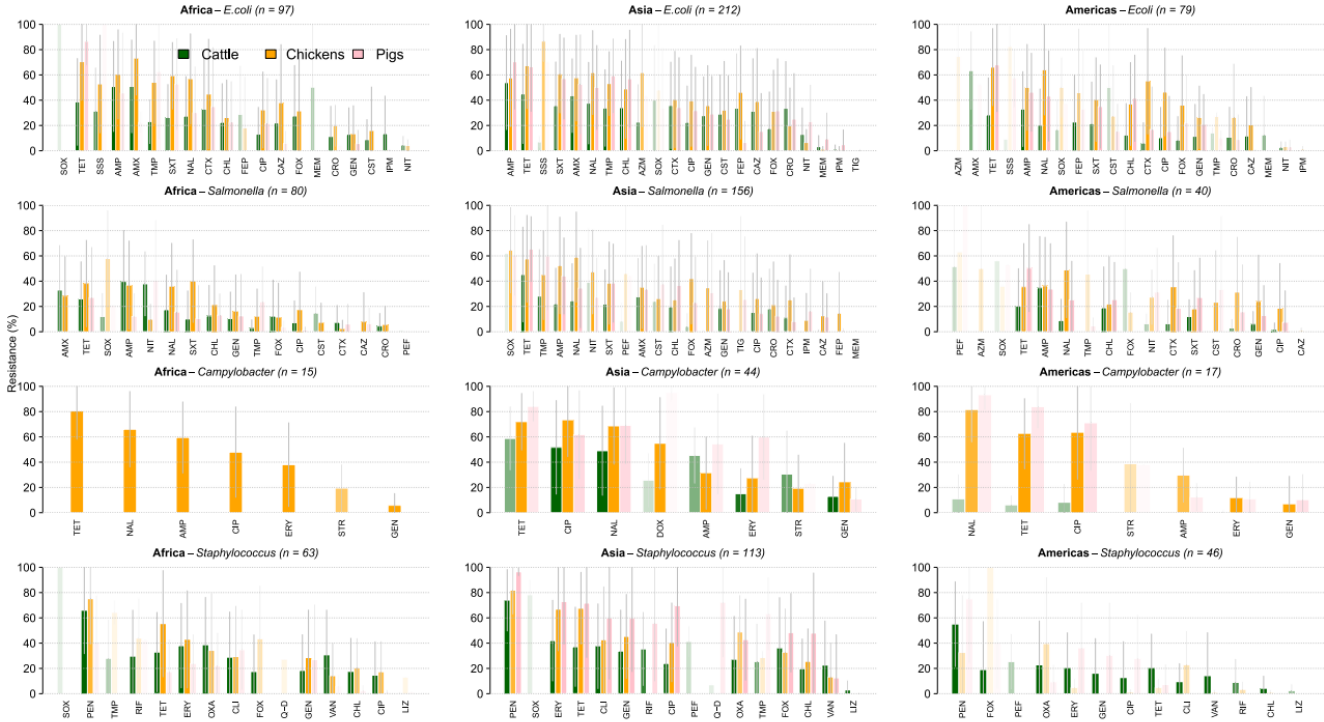
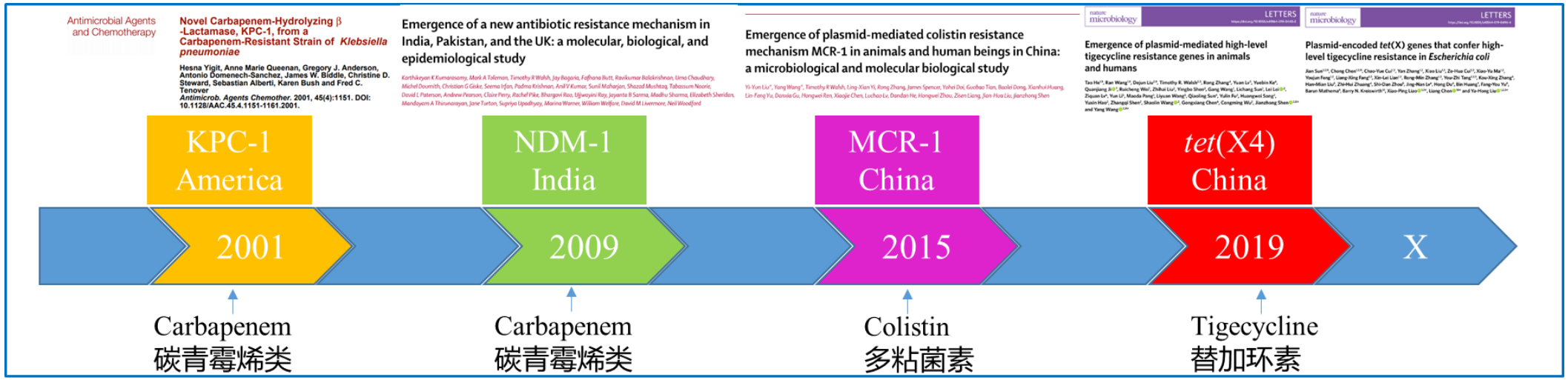


Fig. 4. Resistance in foodborne pathogens recommended for susceptibility testing by the WHO. Shown are resistance rates and number of surveys (*n*) by region. Transparency levels reflect sample sizes for each animal-pathogen combination (for drug acronyms, see supplementary text, protocol S1).

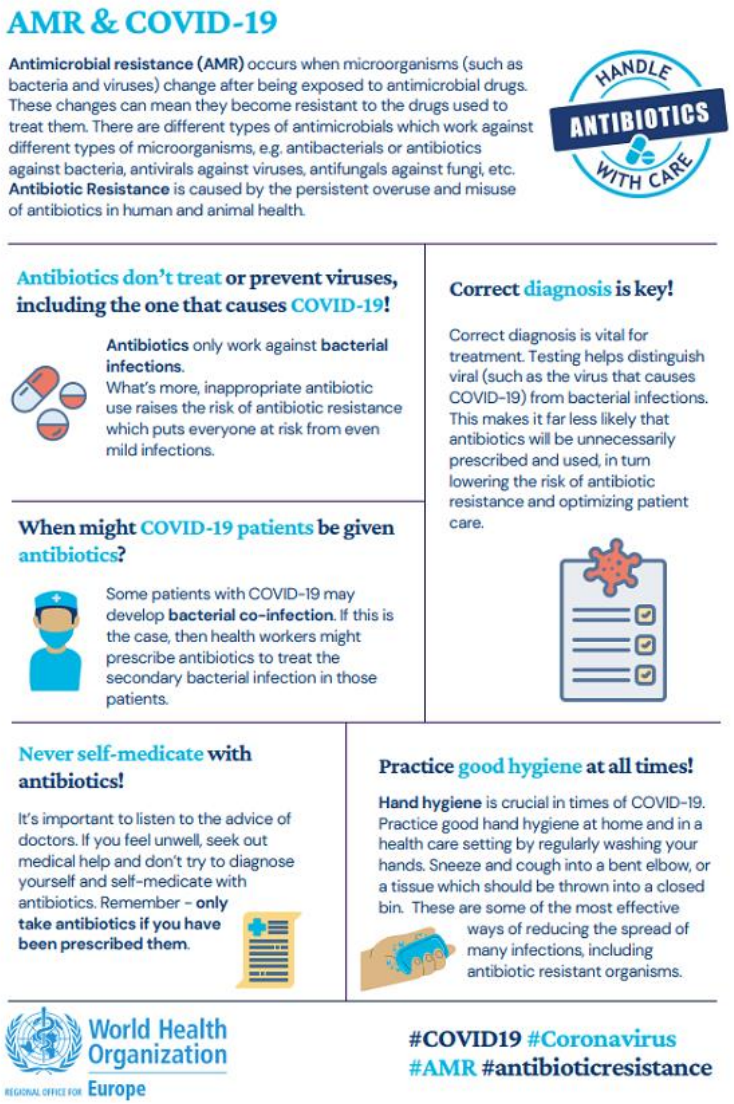
- From 2000 to 2018, the proportion of antimicrobials showing resistance above 50% increased from 0.15 to 0.41 in chickens and from 0.13 to 0.34 in pigs.
- **China** and India represented the largest hotspots of resistance.

Van Boeckel TP, et al. Science. (2019).

Emergence of superbugs



COVID-19 & Antimicrobial Resistance



https://www.who.int/europe/multi-media/item/amr-and-covid-19

Lu J, et al. Science. (2021).

COVID-19 Impacts on 18 Antimicrobial-Resistant Bacteria and Fungi

Threat Estimates

The following table summarizes the latest national death and infection estimates for 18 antimicrobial-resistant bacteria and fungi. The pathogens are listed in three categories—urgent, serious, and concerning—based on level of concern to human health identified in 2019.

	Resistant Pathogen	2017 Threat Estimate	2018 Threat Estimate	2019 Threat Estimate	2017-2019 Change	2020 Threat Estimate and 2019-2020 Change
URGENT	Carbapenem-resistant *Acinetobacter*	8,500 cases 700 deaths	6,300 cases 500 deaths	6,000 cases 500 deaths	Stable*	7,500 cases 700 deaths **Overall: 35% increase*** **Hospital-onset: 78% increase***
URGENT	Antifungal-resistant *Candida auris*	171 clinical cases†	329 clinical cases	466 clinical cases	▲ Increase	754 cases **Overall: 60% increase**
URGENT	*Clostridioides difficile*	223,900 infections 12,800 deaths	221,200 infections 12,600 deaths	202,600 infections 11,500 deaths	▼ Decrease	Data delayed due to COVID-19 pandemic
URGENT	Carbapenem-resistant Enterobacterales	13,100 cases 1,100 deaths	10,300 cases 900 deaths	11,900 cases 1,000 deaths	▼ Decrease*	12,700 cases 1,100 deaths Overall: Stable* **Hospital-onset: 35% increase***
URGENT	Drug-resistant *Neisseria gonorrhoeae*	550,000 infections	804,000 infections	942,000 infections	▲ Increase	Data unavailable due to COVID-19 pandemic
SERIOUS	Drug-resistant *Campylobacter*	448,400 infections 70 deaths	630,810 infections	725,210 infections	▲ Increase	Data delayed due to COVID-19 pandemic‡ 26% of infections were resistant, a 10% decrease
SERIOUS	Antifungal-resistant *Candida*	34,800 cases 1,700 deaths	27,000 cases 1,300 deaths	26,600 cases 1,300 deaths	▼ Decrease*	28,100 cases 1,400 deaths **Overall: 12% increase*** **Hospital-onset: 26% increase***
SERIOUS	ESBL-producing Enterobacterales	197,400 cases 9,100 deaths	174,100 cases 8,100 deaths	194,400 cases 9,000 deaths	▲ Increase*	197,500 cases 9,300 deaths **Overall: 10% increase*** **Hospital-onset: 32% increase***
SERIOUS	Vancomycin-resistant Enterococcus	54,500 cases 5,400 deaths	46,800 cases 4,700 deaths	47,000 cases 4,700 deaths	Stable*	50,300 cases 5,000 deaths **Overall: 16% increase*** **Hospital-onset: 14% increase***

	Resistant Pathogen	2017 Threat Estimate	2018 Threat Estimate	2019 Threat Estimate	2017-2019 Change	2020 Threat Estimate and 2019-2020 Change
SERIOUS	Multidrug-resistant *Pseudomonas aeruginosa*	32,600 cases 2,700 deaths	29,500 cases 2,500 deaths	28,200 cases 2,400 deaths	▼ Decrease*	28,800 cases 2,500 deaths Overall: Stable* **Hospital-onset: 32% increase***
SERIOUS	Drug-resistant nontyphoidal *Salmonella*	212,500 infections 70 deaths	228,290 infections	254,810 infections	▲ Increase	Data delayed due to COVID-19 pandemic‡ 14% of infections were resistant, a 3% decrease
SERIOUS	Drug-resistant *Salmonella* serotype Typhi	4,100 infections <5 deaths	4,640 infections	6,130 infections	▲ Increase	Data delayed due to COVID-19 pandemic‡ 85% of infections were resistant, a 10% increase
SERIOUS	Drug-resistant *Shigella*	77,000 infections <5 deaths	215,850 infections	242,020 infections	▲ Increase	Data delayed due to COVID-19 pandemic‡ 46% of infections were resistant, a 2% increase
SERIOUS	Methicillin-resistant *Staphylococcus aureus*	323,700 cases 10,600 deaths	298,700 cases 10,000 deaths	306,600 cases 10,200 deaths	Stable*	279,300 cases 9,800 deaths Overall: Stable* **Hospital-onset: 13% increase***
SERIOUS	Drug-resistant *Streptococcus pneumoniae*	12,100 invasive infections 1,500 deaths†	See pathogen page if comparing data over time	12,000 invasive infections 1,200 deaths	Stable	Data delayed due to COVID-19 pandemic
SERIOUS	Drug-resistant Tuberculosis (TB)	888 cases 73 deaths†	962 cases 102 deaths	919 cases	Stable	661 cases Decrease‡
CONCERNING	Erythromycin-resistant group A *Streptococcus*	5,400 infections 450 deaths†	See pathogen page if comparing data over time	6,200 infections 560 deaths	▲ Increase	Data delayed due to COVID-19 pandemic
CONCERNING	Clindamycin-resistant group B *Streptococcus*	13,000 infections 720 deaths†	See pathogen page if comparing data over time	15,300 cases 940 deaths	▲ Increase	Data delayed due to COVID-19 pandemic

The CDC COVID-19: USA Impact on Antimicrobial Resistance, Special Report 2022, **concluded that the threat of antimicrobial-resistant infections is not only still present but has gotten worse**.

COVID-19: U.S. Impact on AMR, Special Report 2022

Resistance reported from China antimicrobial surveillance network (CHINET)

	Blood		Urine		Lower respiratory tract		Cerebrospinal fluid	
	n	%	*n*	%	*n*	%	*n*	%
Number of isolates	36,359	100.0	46,081	100.0	97,297	100.0	3157	100.0
Escherichia coli	8381	23.1	21,489	46.6	4553	4.7	122	3.9
Klebsiella pneumoniae	5616	15.4	4592	10.0	18,891	19.4	264	8.4
Pseudomonas aeruginosa	1054	2.9	1710	3.7	15,705	16.1	65	2.1
Acinetobacter baumannii	1164	3.2	728	1.6	16,566	17.0	394	12.5
Staphylococcus aureus	2801	7.7	514	1.1	8000	8.2	110	3.5

Table 1 Percentage of five major species isolated from four specimens

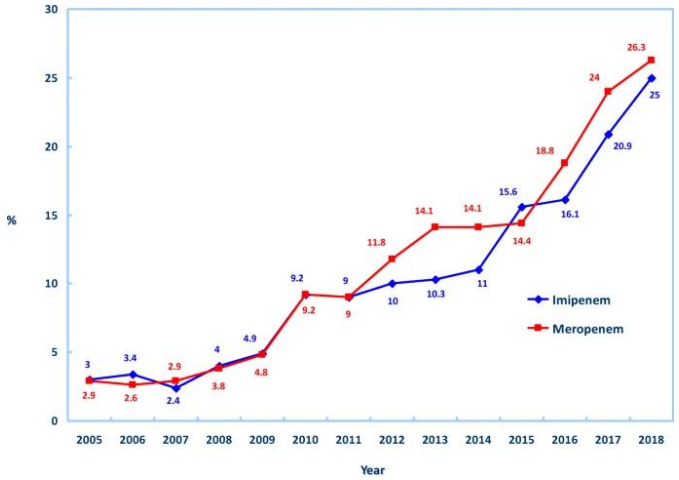


Fig.1. Resistance Change of *Klebsiella pneumoniae* to Imipenem and Meropenem between 2005 and 2018.

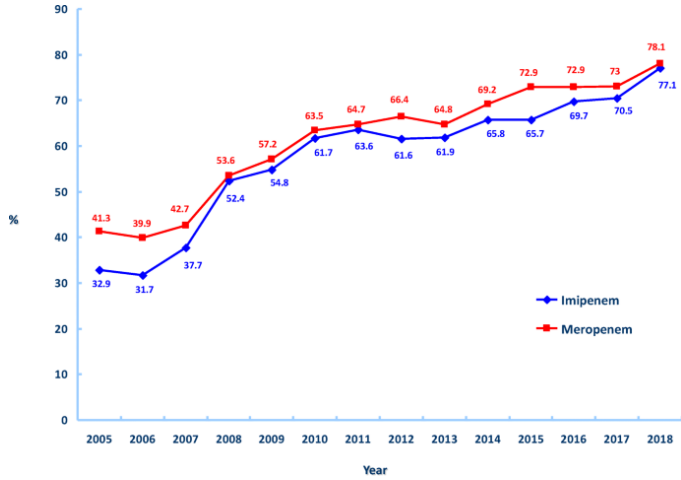


Fig.2. Resistance Change of *Acinetobacter baumannii* to Imipenem and Meropenem between 2005 and 2018.

- **A total of 44 teaching hospitals were involved**. Totally **244,843 strains** were isolated in 2018, of which gram-negative *bacilli* and gram-positive *cocci* were accounting for 71.8% and 28.2%, respectively.
- 39.7% of isolates were cultured from lower respiratory tract, 18.8% from urine, 14.8% from blood, 1.3% from cerebrospinal fluid, respectively.
- The resistance rate of MRSA to most antimicrobial agents was significantly higher than that of MSSA strains, except for to trimethoprim-sulfamethoxazole in urine specimen.
- *E. coli* was still highly susceptible to carbapenem antibiotics, and the resistance rate was less than 5%.
- Carbapenem resistance among *Klebsiella pneumoniae*, especially cultured from cerebrospinal fluid, increased significance from 18.6 to 64.1%.
- **About 80% of *Acinetobacter baumannii* strains was resistant to imipenem and meropenem, respectively.**

Hu F, et al. Eur J Clin Microbiol Infect Dis 2019, 38(12): 2275-2281.

In Vitro Activity of Imipenem/Relebactam Against *Enterobacteriaceae* Isolates Obtained from Intra-abdominal, Respiratory Tract, and Urinary Tract Infections in China: Study for Monitoring Antimicrobial Resistance Trends (SMART), 2015–2018

Pathogen	Total, No. (%)	IAI, No. (%)	RTI, No. (%)	UTI, No. (%)
Enterobacteriaceae	8781 (100.0)	3758 (42.8)	1920 (21.9)	3103 (35.3)
Escherichia coli	4676 (53.3)	2053 (43.9)	325 (7.0)	2298 (49.1)
Klebsiella pneumoniae	2949 (33.6)	1111 (37.7)	1272 (43.1)	566 (19.2)
Enterobacter cloacae	542 (6.2)	310 (57.2)	136 (25.1)	96 (17.7)

Abbreviations: IAI, intra-abdominal infection; RTI, respiratory tract infection; UTI, urinary tract infection.

Table 1.Number of Isolates and Percentages of Most Frequently Collected *Enterobacteriaceae* Pathogens From Patients With Intra-abdominal Infections, Urinary Tract Infections, and Lower Respiratory Tract Infections, 2015–2018.

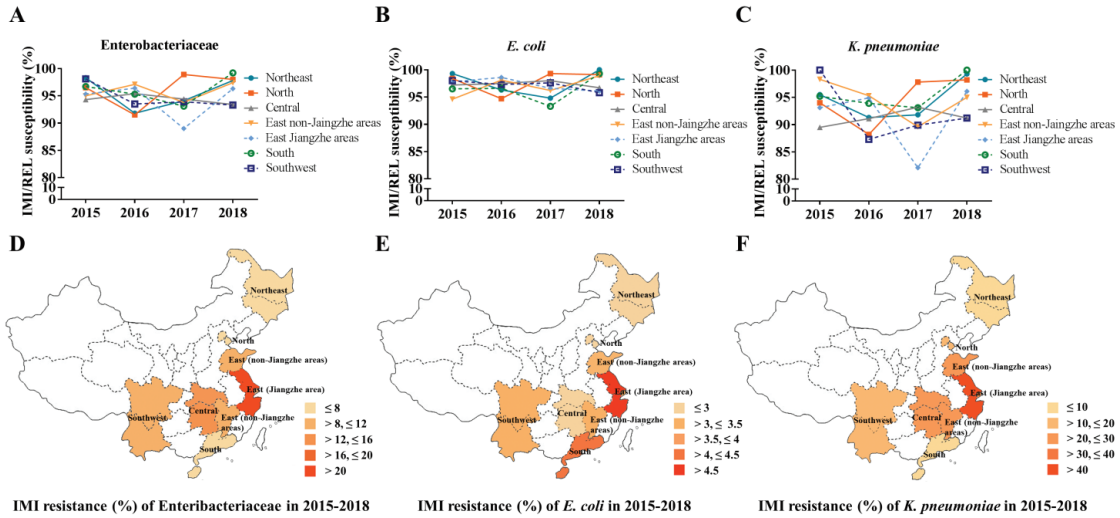


Fig.1. Regional differences in *Enterobacteriaceae* susceptibilities.

- In 2015–2018, the most frequently identified *Enterobacteriaceae* species was *Escherichia coli* (n = 4676 [53.3%]), followed by *Klebsiella pneumoniae* (n = 2949 [33.6%]) and *Enterobacter cloacae* (n = 542 [6.2%]).
- The *Enterobacteriaceae* isolates showed 95.2% overall susceptibility to IMI/REL, of which the susceptibility rates in isolates from IAI, RTI, and UTI were 95.8%, 91.4%, and 96.6%, respectively.
- **For all *Enterobacteriaceae*, IMI/REL susceptibilities were similar across 7 geographic regions of China (94.0%–96.1%), despite significant geographic variation in IMI susceptibility rates** (ranging from 76.4% in the East Jiangzhe area to 92.9% in the South).

Yang Q, et al. Clin Infect Dis 2020, 71(Suppl 4): S427-S435.

Antimicrobial Resistance Trends of the Most Common Causative Pathogens Associated with Community-acquired Respiratory Infections in China

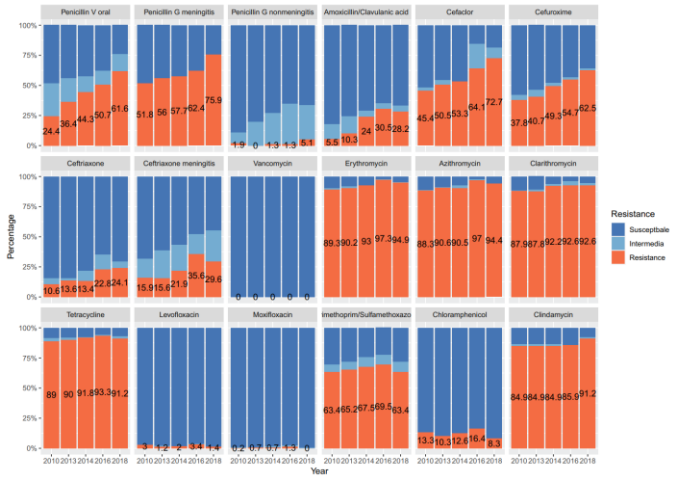


Fig. 1. Resistance of *S. pneumoniae* to routine antibiotics in different years

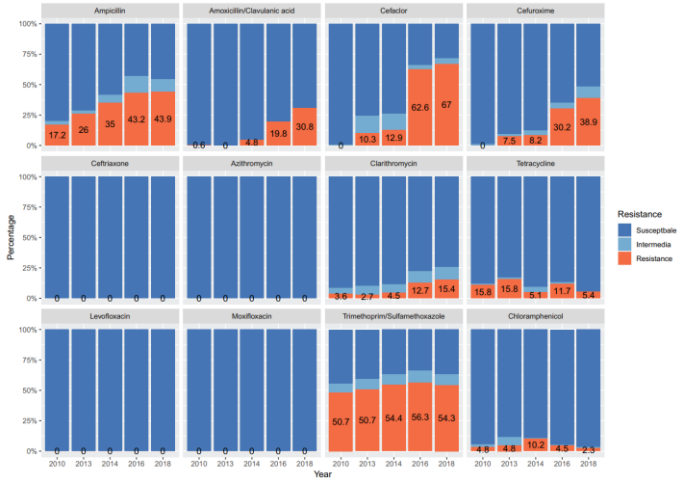


Fig. 2. Resistance of *H. influenzae* to routine antibiotics in different years.

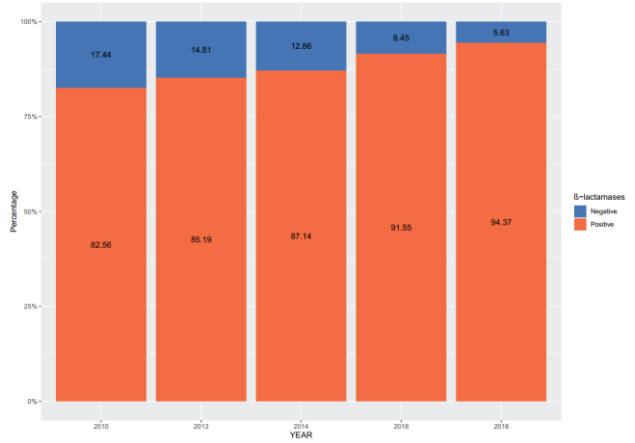


Fig. 3. The prevalence of β-lactamase positive *M. catarrhalis* in different years.

- **From 2009–2018 a total of 3750 isolates were collected from 22 cities located across different regions of China**. Among these the most common bacterial isolates include *S. pneumoniae* (53.7%) followed by *H. influenza* (32.4%), *M. catarrhalis* (13.9%).
- *S. pneumoniae* exhibited reduction in susceptibility and increase in resistance to penicillin, cephalosporins during the surveillance period. Invasive and noninvasive *S. pneumoniae* showed similar resistance.
- In the case of *H. influenzae* susceptibility to β-lactam and β-lactamase inhibitors (ampicillin, amoxicillin and AMC), SXT, clarithromycin and cephalosporins was reduced over the past 10 years with an exception of ceftriaxone.
- Overall, moxifloxacin and levofloxacin have the highest susceptibility rates against *S. pneumoniae* (> 95%) and *H. influenza* (> 90%). *M. catarrhalis* exhibited susceptibility to almost all the tested antimicrobials.
- **In China the 10-year trends showed a substantial increase in resistance to β-lactam drugs and reduction in sensitivity.**

Zhao C, et al. Infect Drug Resist 2022, 15: 5069-5083.

Bacterial Epidemiology and Antimicrobial Resistance Profiles in Children Reported by the ISPED Program in China, 2016 to 2020

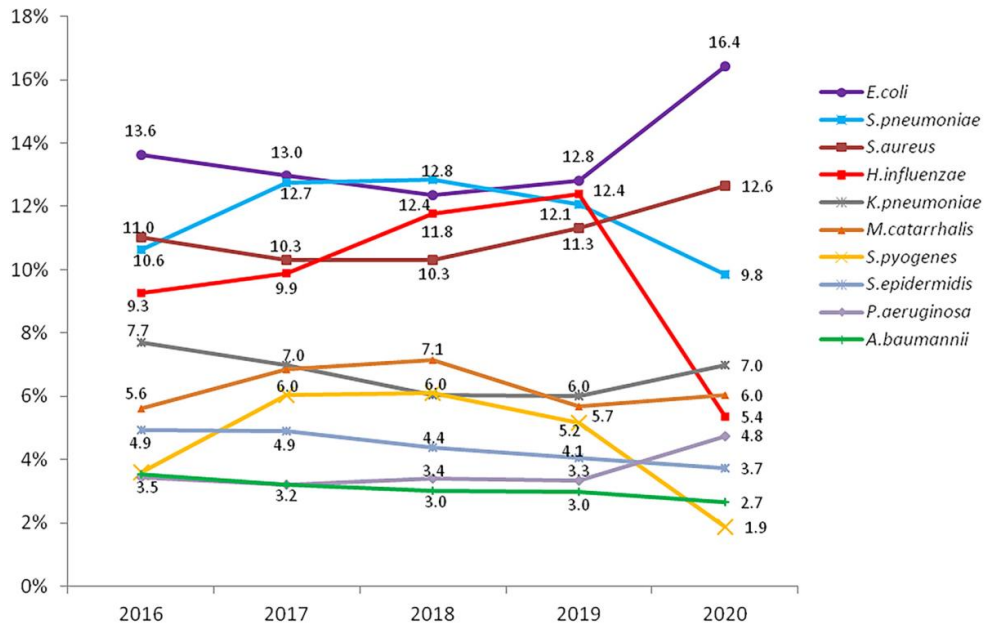


Fig. 1. Distribution trends of main pathogens reported by the ISPED program in 2016 to 2020.

Fig.2. Distribution trends of MDROs in different age groups, as reported by the ISPED program

- A total of 288,377 isolates were collected, and the top 10 predominant bacteria were *Escherichia coli*, *Streptococcus pneumoniae*, *Staphylococcus aureus*, *Haemophilus influenzae*, *Klebsiella pneumoniae*, *Moraxella catarrhalis*, *Streptococcus pyogenes*, *Staphylococcus epidermidis*, *Pseudomonas aeruginosa*, and *Acinetobacter baumannii*.
- In 2020, the coronavirus disease 2019 (COVID-19) pandemic year, we observed a significant reduction in the proportion of respiratory tract samples (from 56.9% to 44.0%).
- The proportions of CRKP, CRAB, and CRPA strains all showed decreasing trends between 2015 and 2020.
- **Carbapenem-resistant Enterobacteriaceae (CRE) and CRPA gradually decreased with age, while CRAB showed the opposite trend with age.**

The Infectious Disease Surveillance of Pediatrics (ISPED)
Multidrug-resistant organisms (MDROs)

Fu P, et al. Microbiol Spectr 2021, 9(3): e0028321.

Penicillin and Cefotaxime Resistance of Quinolone-Resistant *Neisseria meningitidis* Clonal Complex 4821, Shanghai, China, 1965–2020

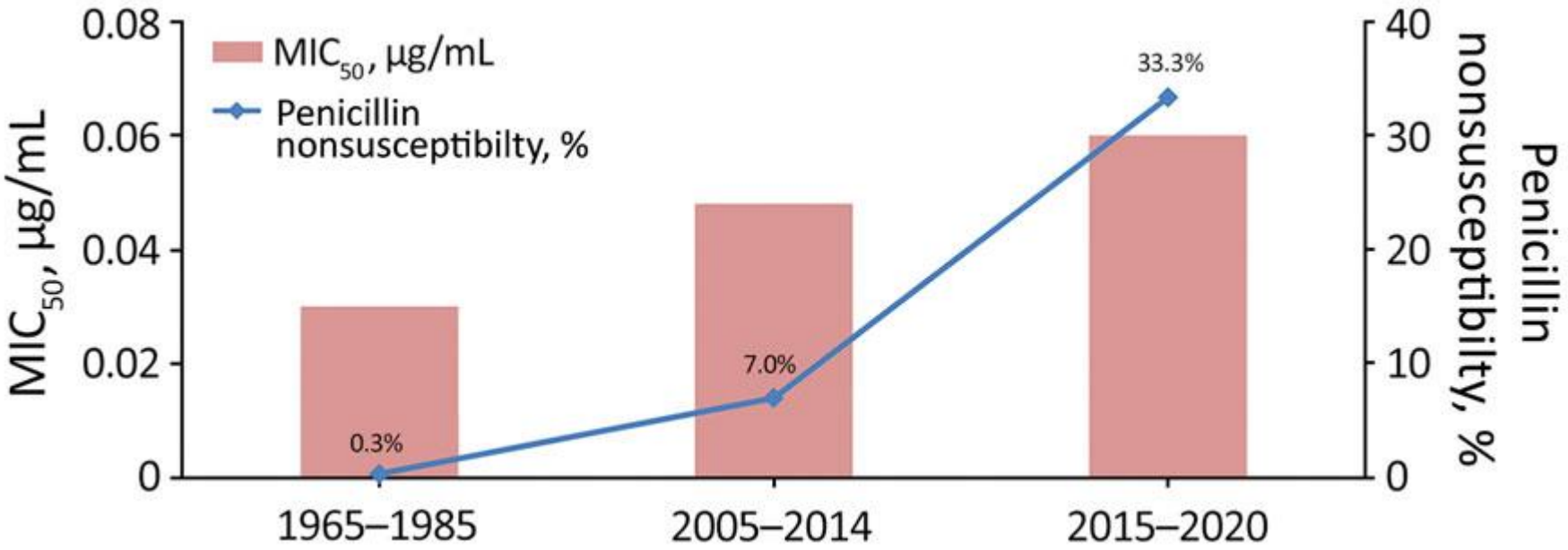


Figure 1. Percentage of meningococcal isolates with penicillin nonsusceptibility and MIC50 values, Shanghai, China, 1965–2020. MIC50, minimum inhibitory concentrations at which 50% of the tested isolates are inhibited.

- To characterize the penicillin-nonsusceptible (Pen^{NS}) meningococci, we analyzed 491 meningococci and 724 commensal *Neisseria* isolates in Shanghai, China, during 1965–2020.
- The Pen^{NS} proportion increased from 0.3% in 1965–1985 to 7.0% in 2005–2014 and to 33.3% in 2015–2020.

Chen M, et al. Emerg Infect Dis 2023, 29(2): 341-350.

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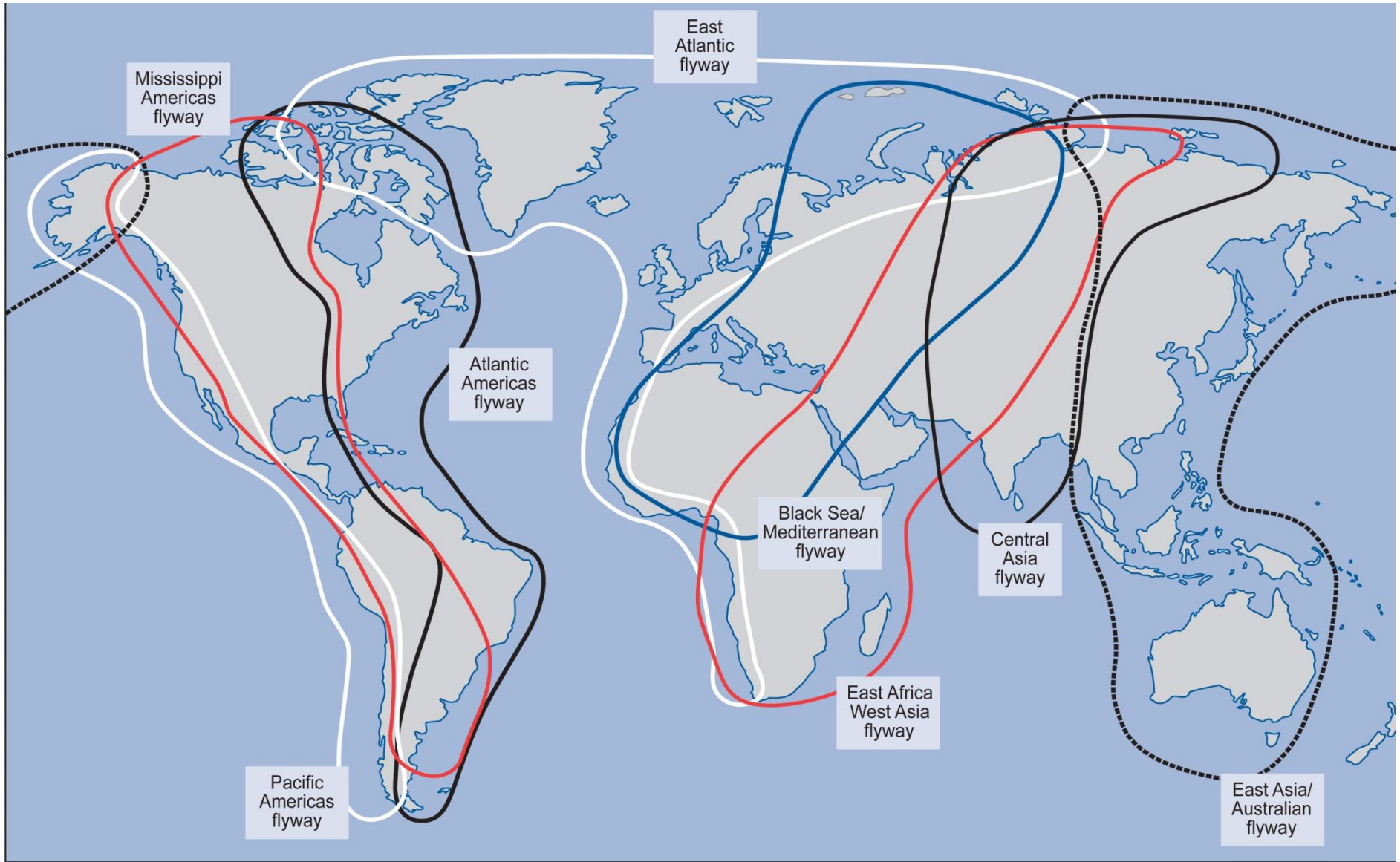
Abundance and diversity of antibiotic resistome in migratory birds

PART 01

Antibiotic resistance spreads easily across the globe

Resistant bacteria and fungi can spread across countries and continents through people, animals, and goods.

Global movement of wild birds



The Map of sampling sites in China

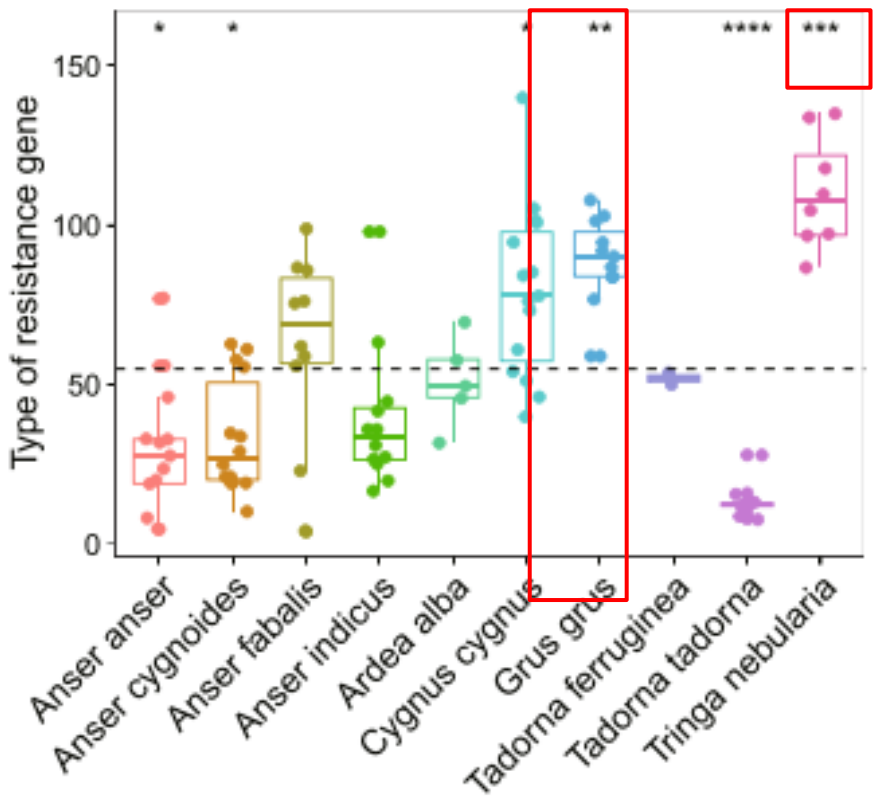
- **Fecal samples**
  - 8 sites
  - 10 species
  - 100 samples for mNGS

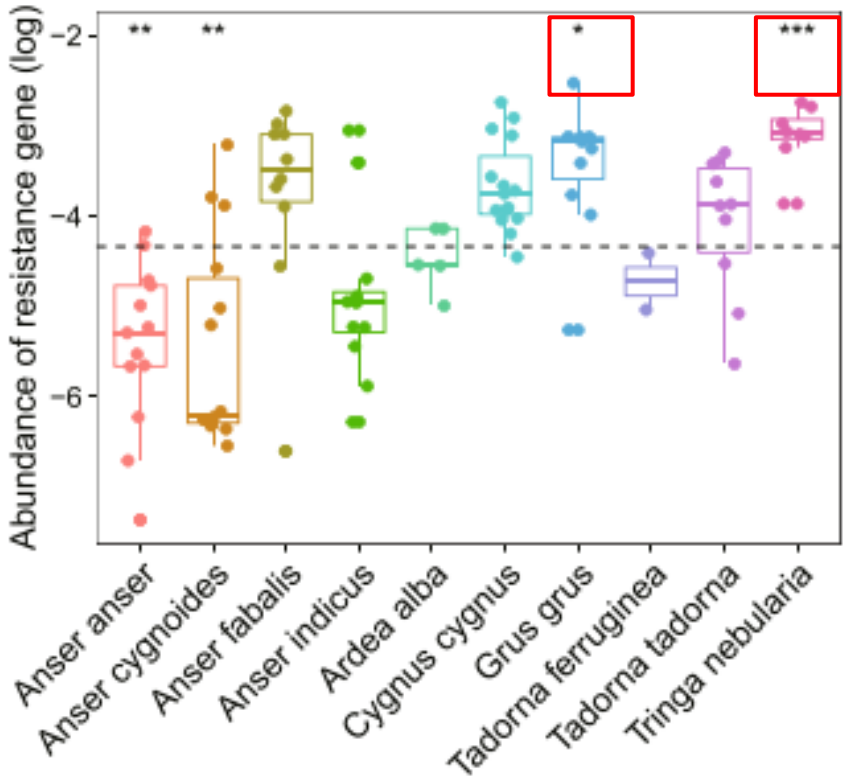
- **Qinghai Lake**
  - 11 bird feces
  - 10 human feces
  - 12 livestock feces
  - 11 soil samples
  - 11 water samples

- **Poyang Lake**
  - 11 bird feces
  - 11 human feces
  - 11 water samples in fishing grounds
  - 15 sewage wastewater samples

Cao et al, Microbiome, 2020

Abundant ARGs in the gut bacteria of migratory birds





- 202 ARG types were identified
- More ARG types existed in *Cygnus cygnus*, *Grus grus* and *Tringa nebularia*

- Based on the abundance of ARGs in different bird species, *Grus grus* and *Tringa nebularia* had the most abundant ARGs;

Cao et al, Microbiome, 2020

21 ARG types shared among different bird populations

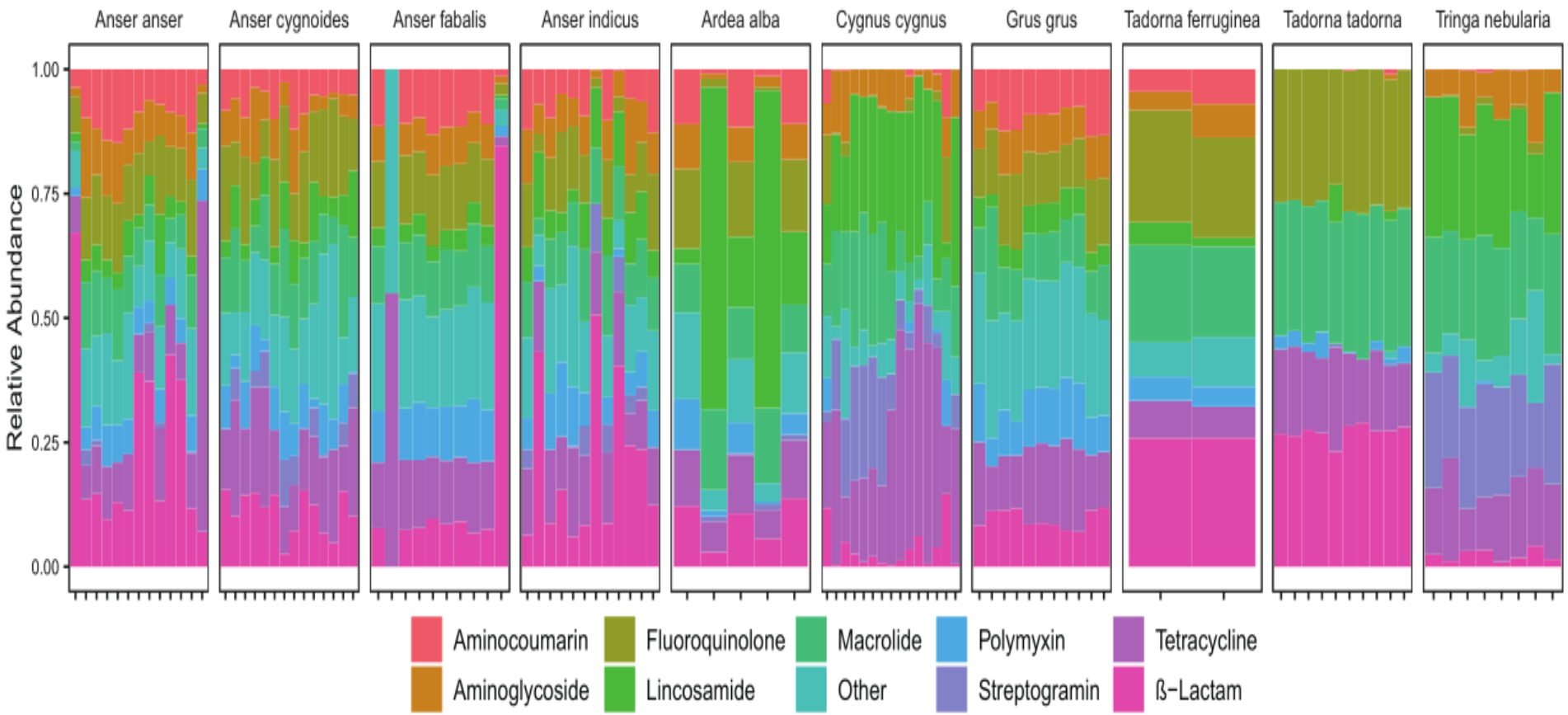
Type Name	Classification	Mechanism
acrF	Multidrug	Efflux pump
arnA	Polymyxin	Altering cell wall charge
baeR	Multidrug	Efflux pump
baeS	Multidrug	Efflux pump
cpxR	Multidrug	Efflux pump
CRP	Multidrug	Efflux pump
emrA	Multidrug	Efflux pump
emrK	Tetracycline	Efflux pump
emrY	Multidrug	Efflux pump
evgS	Multidrug	Efflux pump

Type Name	Classification	Mechanism
lnuC	Lincosamide	Antibiotic inactivation
mdtO	Multidrug	Efflux pump
mexD	Multidrug	Efflux pump
mexN	Aminocoumarin	Efflux pump
mefA	Macrolide	Efflux pump
msrE	Macrolide	Efflux pump
PmrB	Polymyxin	Altering cell wall charge
PmrE	Polymyxin	Altering cell wall charge
TEM-1	Beta-lactam	Antibiotic inactivation
tet32	Tetracycline	Target protection
tolC	Multidrug	Efflux pump

- **A total of 21 ARG types were shared among different bird populations. Among these shared ARG types, the *Tet32* and TEM-1 pose the highest risks to human health.**

Cao et al, Microbiome, 2020

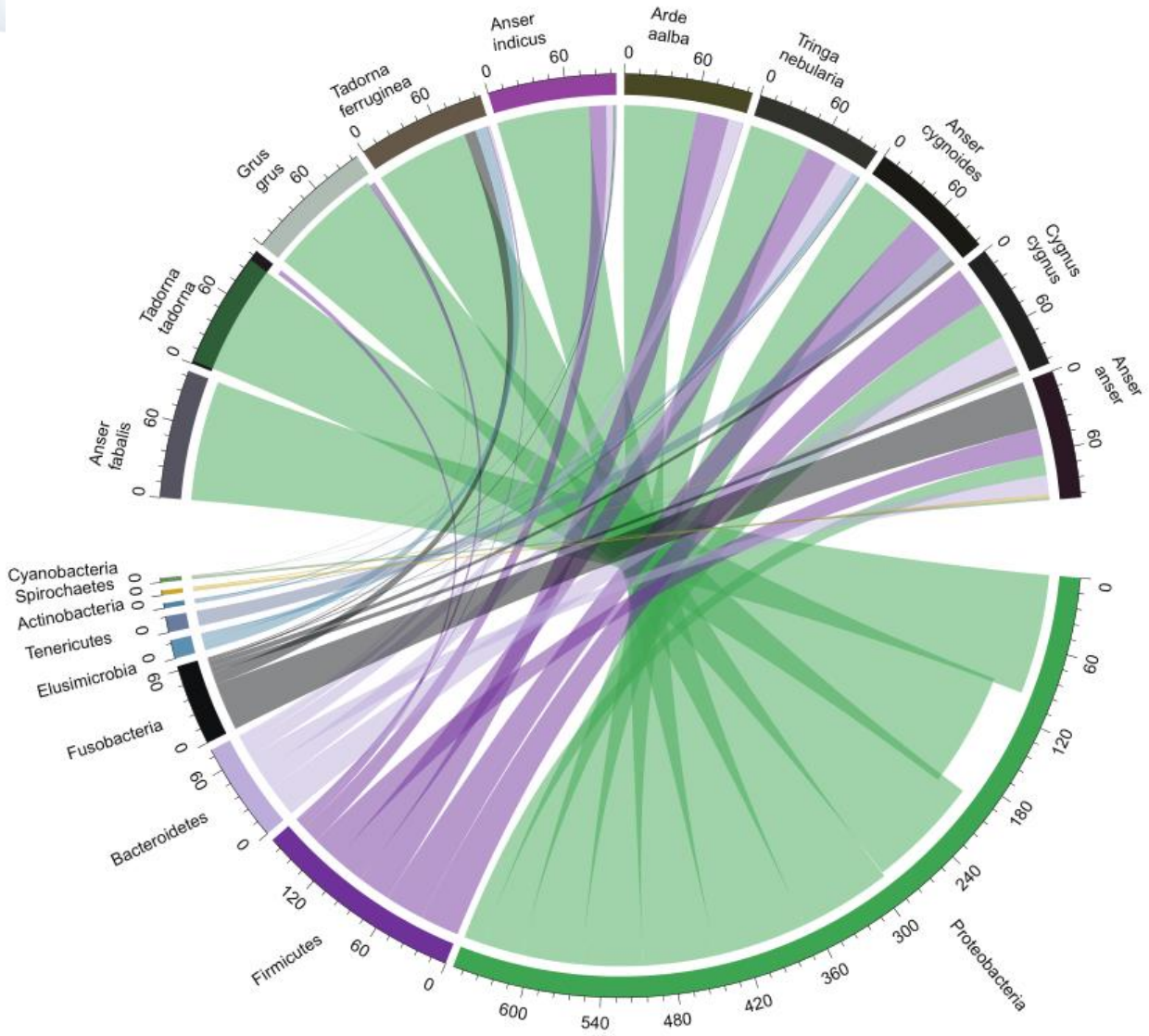
ARG types conferred resistance to major antibiotic classes



- **The resistant gene types in the bird gut microbiota conferred resistance to almost all major antibiotic classes. Among these antibiotics, tetracyclines, macrolide-lincosamide-streptogramin (MLS), and Beta-lactams contributed to most of the percentage of total resistance genes, and tetracycline resistance (TcR) genes were the most prevalent genes in all bird species.**

Cao et al, Microbiome, 2020

The microbial origin of ARG types



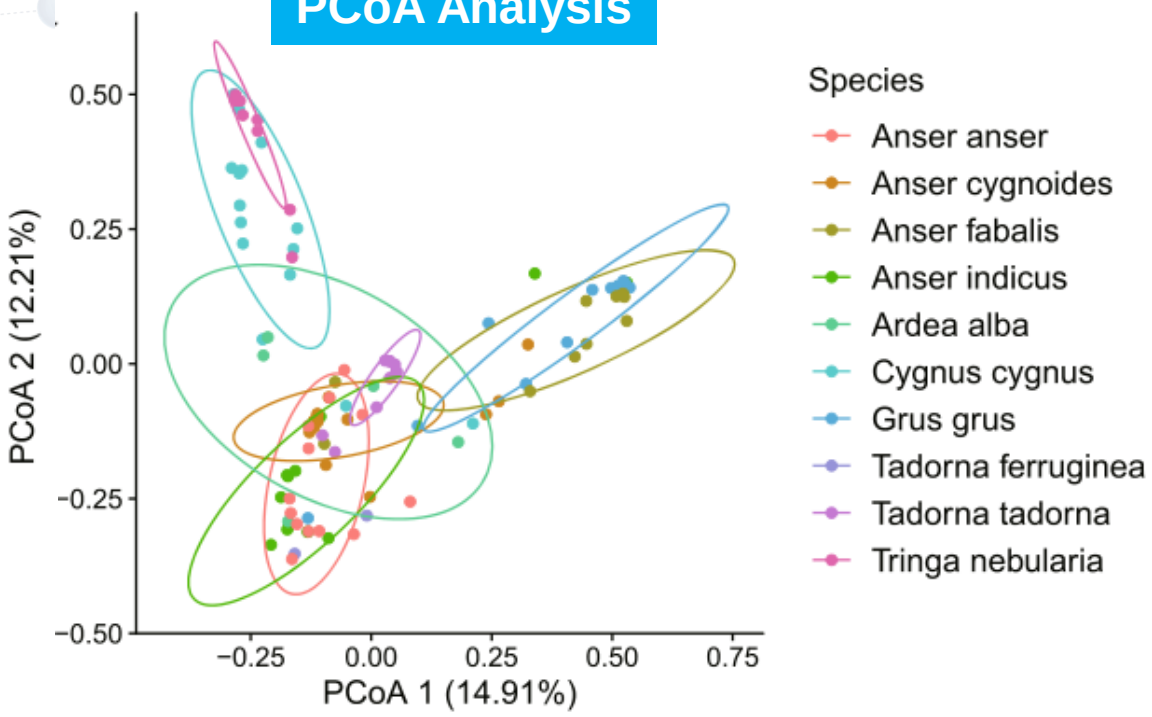
- ***Proteobacteria***, ***Firmicutes***, ***Bacteroidetes***, **and** ***Fusobacteria*** **accounted for most of the phyla inferred from the resistance-conferring contigs;**

- ***Proteobacteria*** **was the dominant phylum in all species except for Anser anser;**

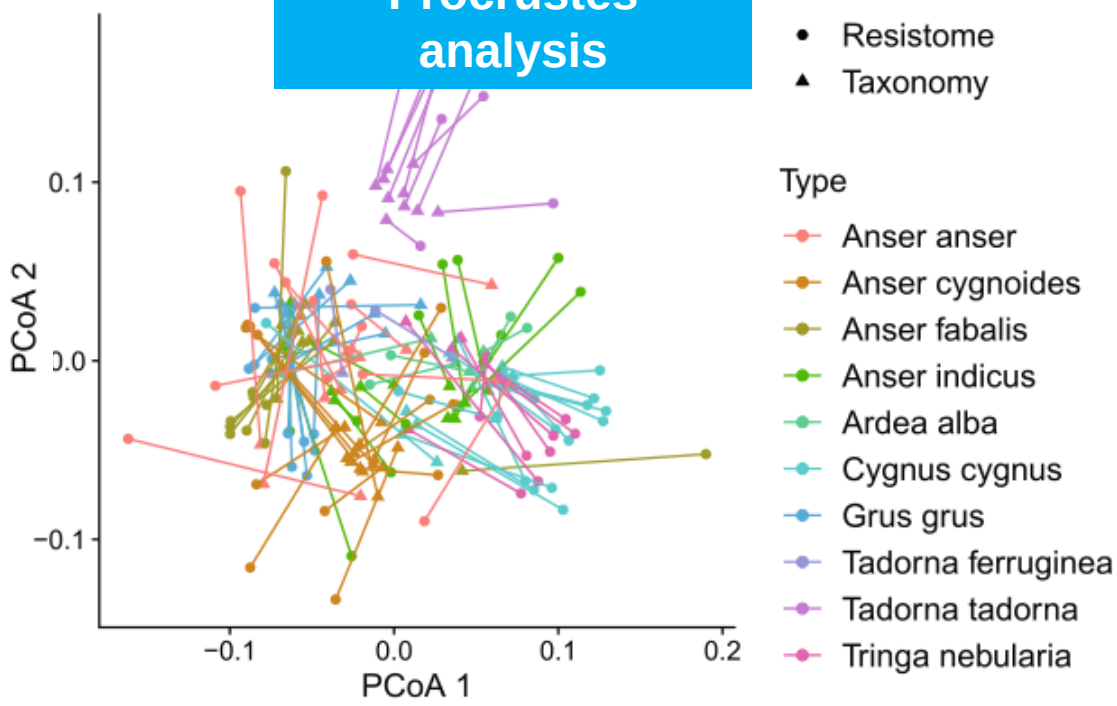
Cao et al, Microbiome, 2020

Bird species differed from each other in ARG composition

PCoA Analysis



Procrustes analysis

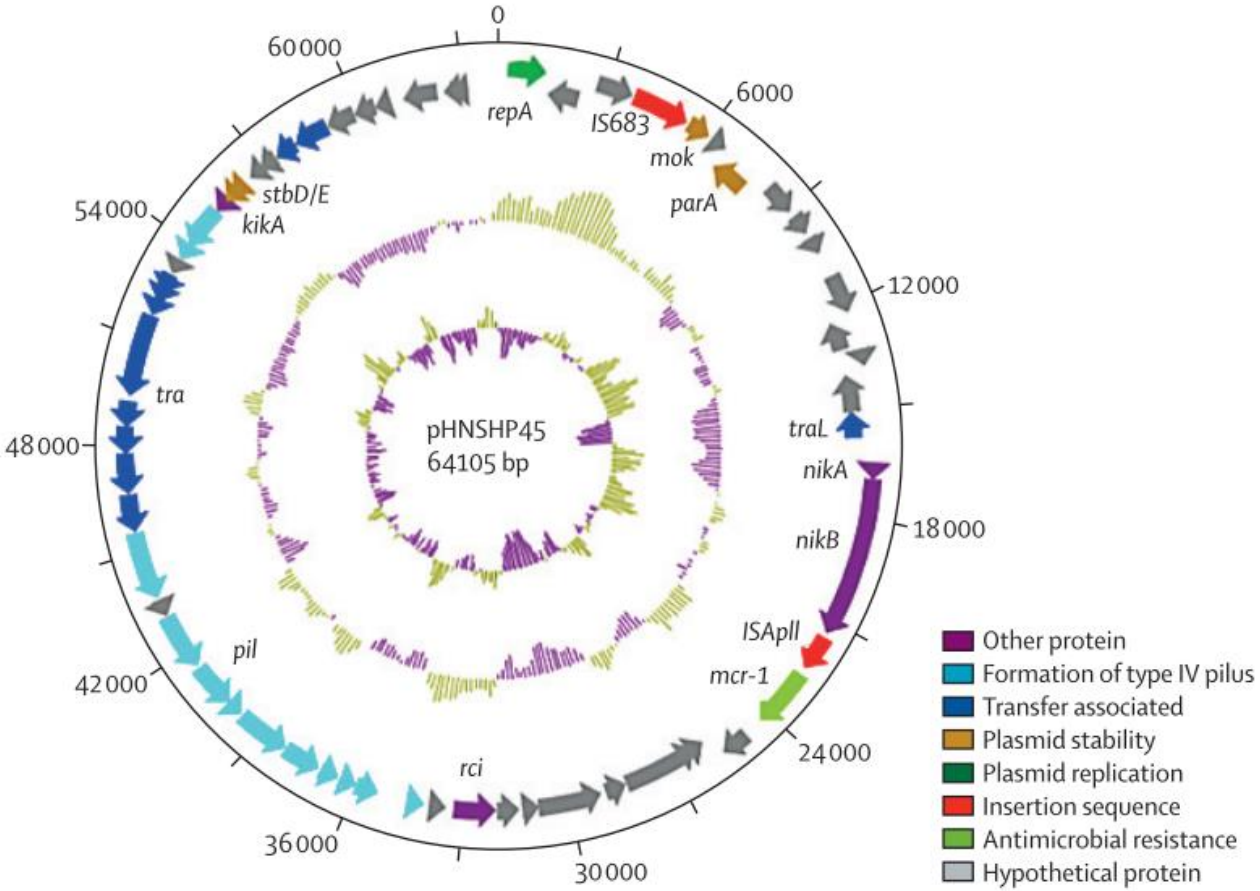


- **Based on PCoA analysis, bird species differed from each other in ARG composition;**

- **Procrustes analysis revealed microbial composition was not correlated with resistance types composition among individuals;**
- **A wide range of MGE sequences in bird metagenomic libraries, including phage-related integrases, putative transposases, type IV secretion systems, and reverse transcriptases.**

Cao et al, Microbiome, 2020

The high prevalence of the *mcr-1* gene at the population



Species	Positive
Grus grus (n=53)	33%
Cygnus cygnus (n=40)	55%
Tringa nebularia (n=22)	60%
Anser indicus (n=55)	35%
Anser fabalis (n=50)	37%
Anser cygnoides (n=38)	35%
Ardea alba (n=36)	85%
Anser anser (n=38)	41%
Tadorna ferruginea (n=8)	100%
Tadorna tadorna (n=32)	65%

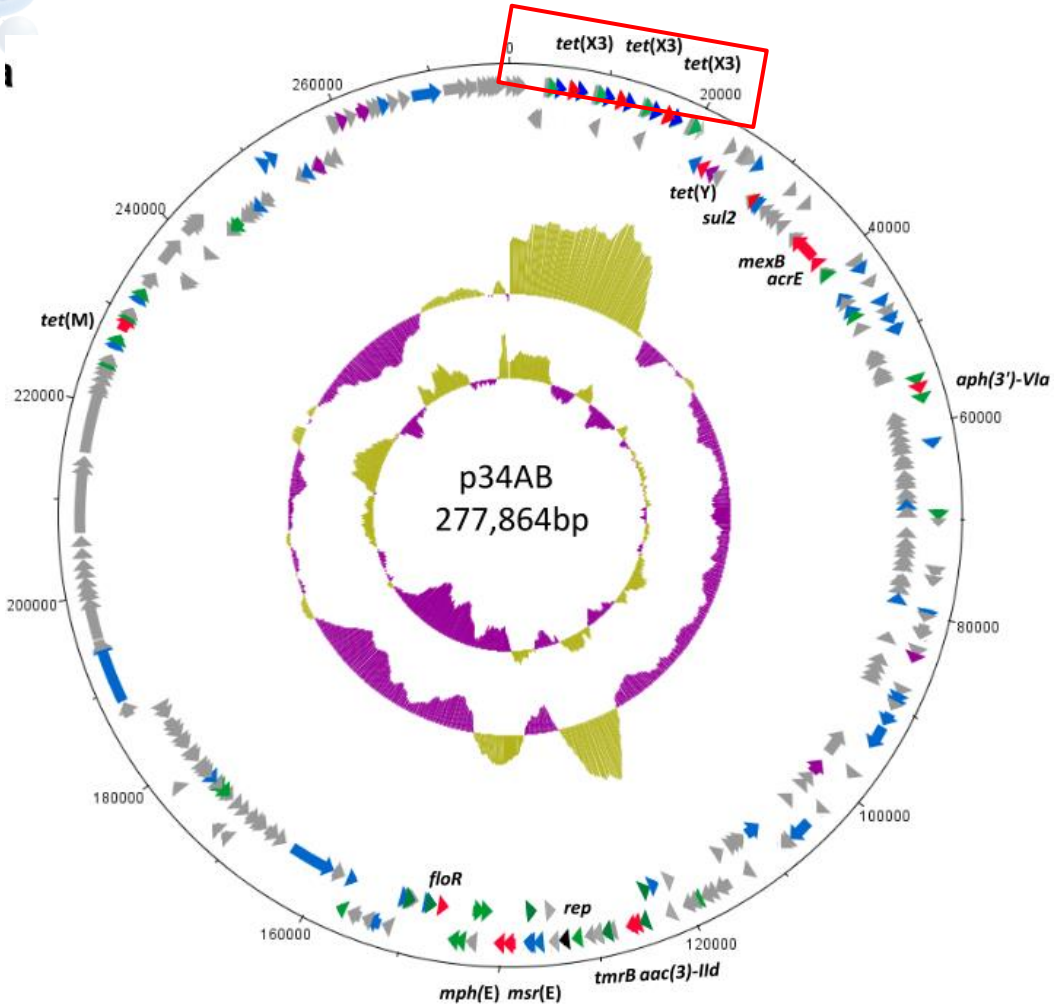
- **The *mcr*-1 gene within plasmid**

Liu et al, The Lancet Infectious Diseases, 2016.

- **The prevalence of *mcr*-1 gene in bird species**

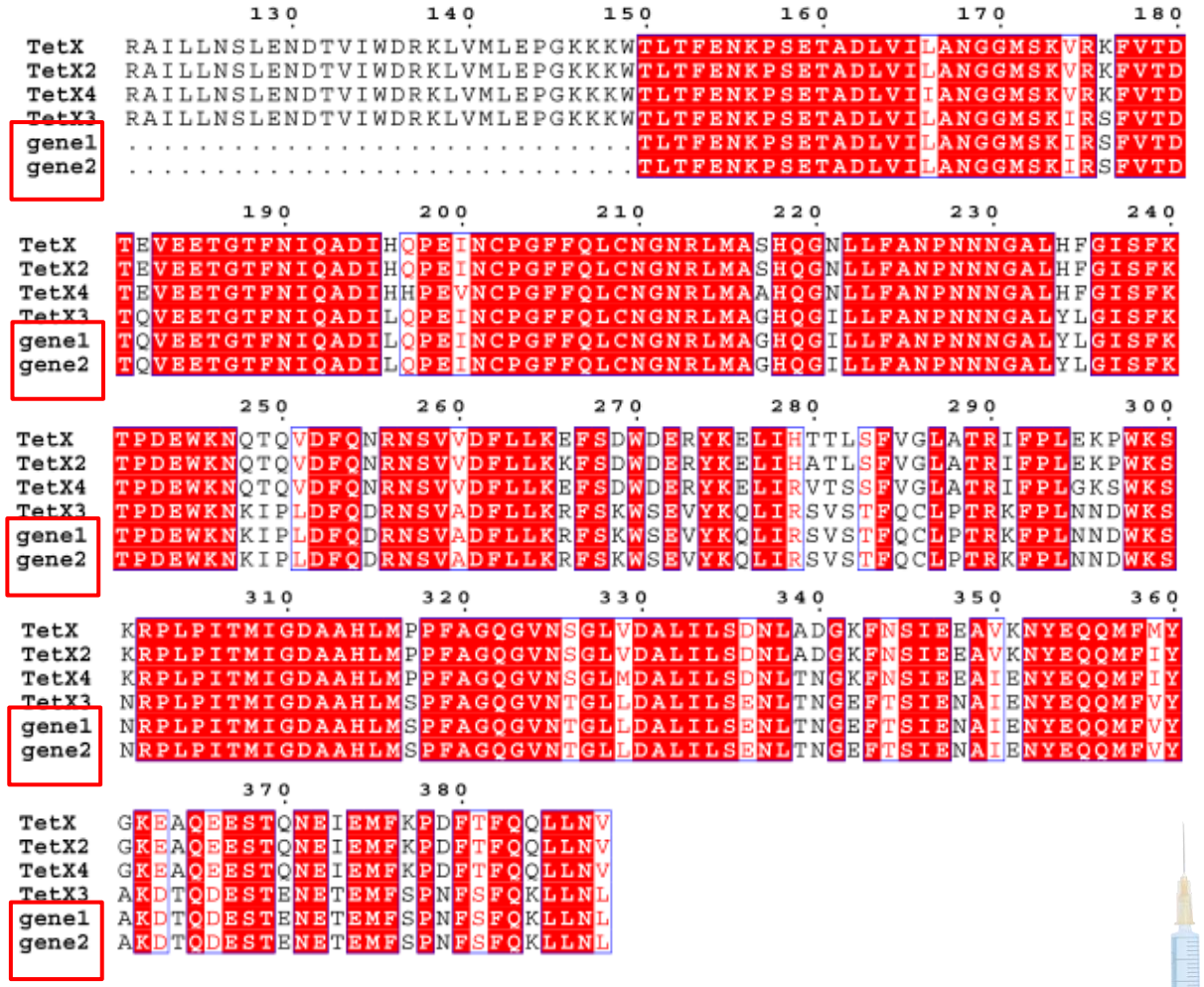
Cao et al, Microbiome, 2020

Tigecycline resistance *tet*(X3) gene is going wild



➢ ***Tet*(X3) within plasmid.**

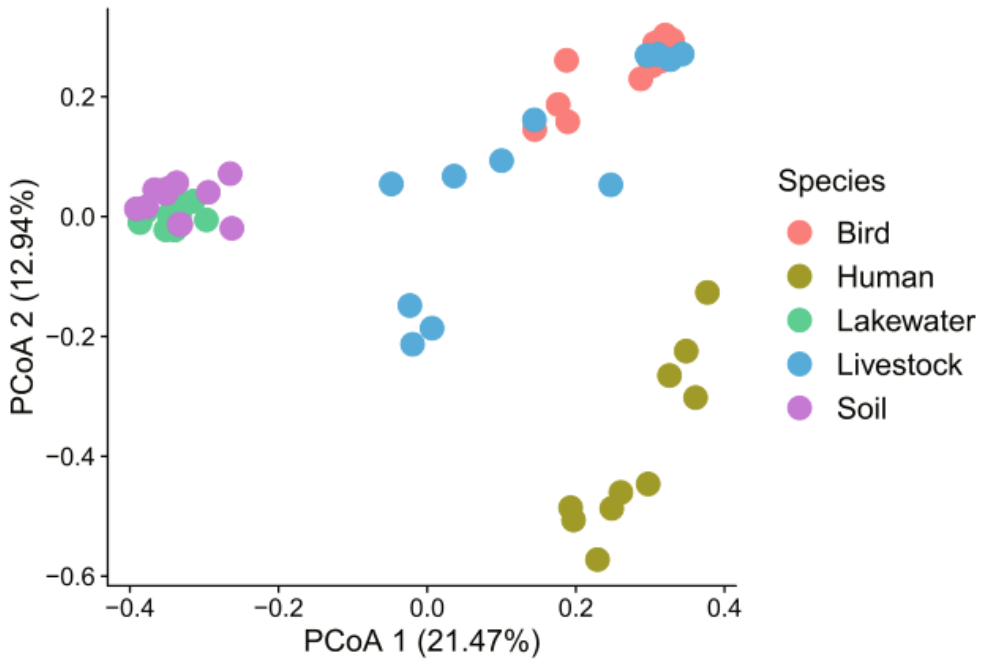
He et al, Nature Microbiology, 2019

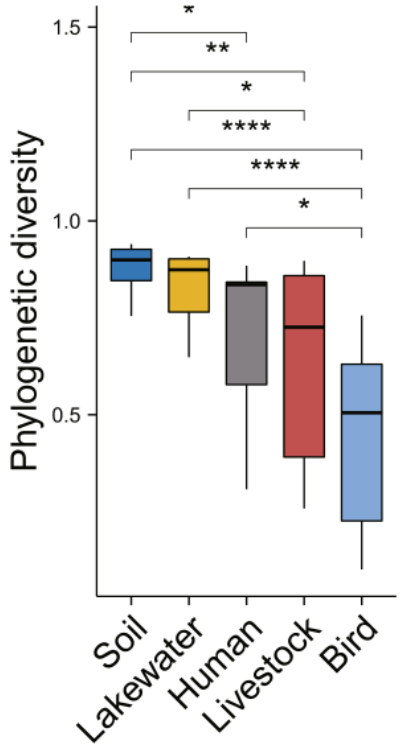


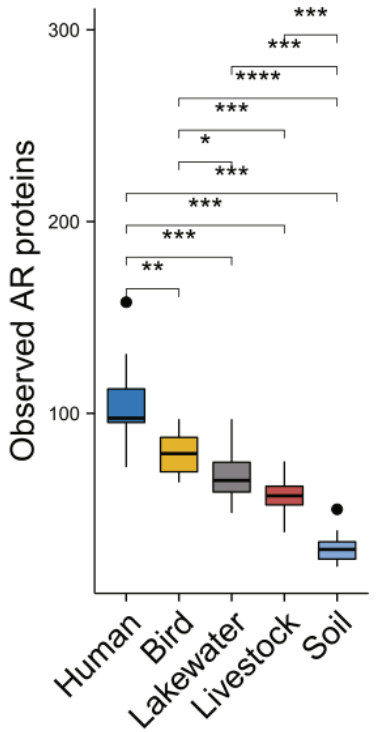
➢ ***tet*(X3) was found in two gut microbiomes of bird fecal samples, with 100% amino acid identity of sites 150–387.**

Cao et al, Biosafety and Health, 2020.

Qinghai Lake-The difference between bird and its environmental microbiomes and resistomes

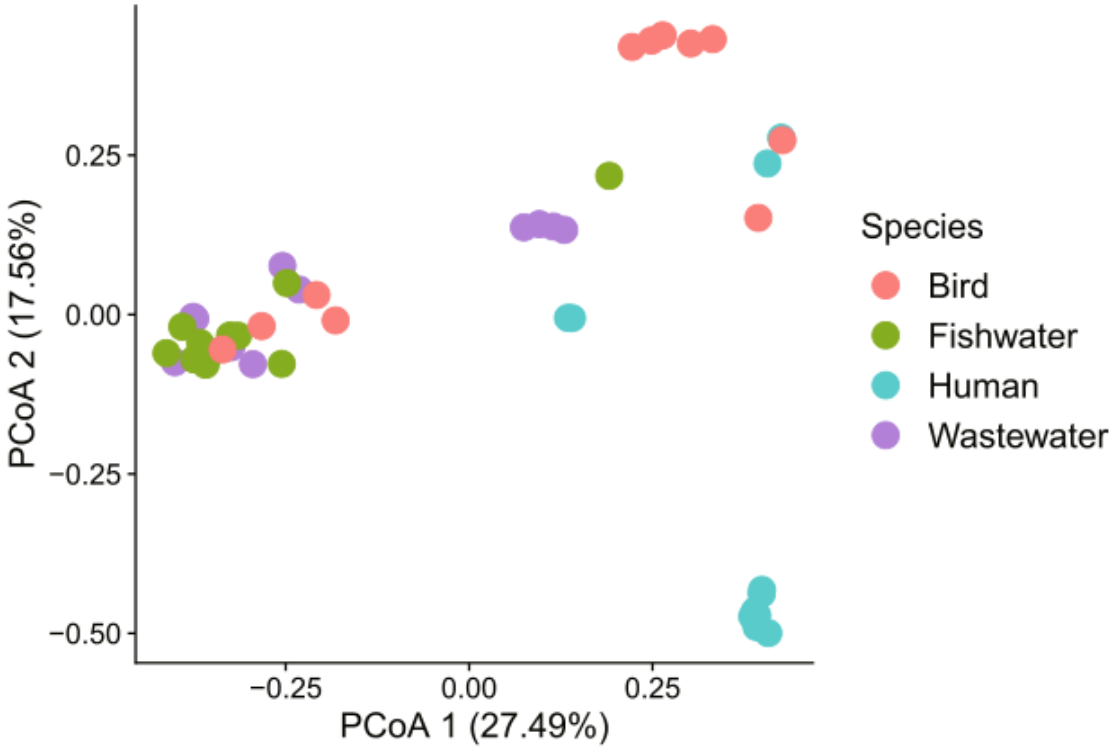


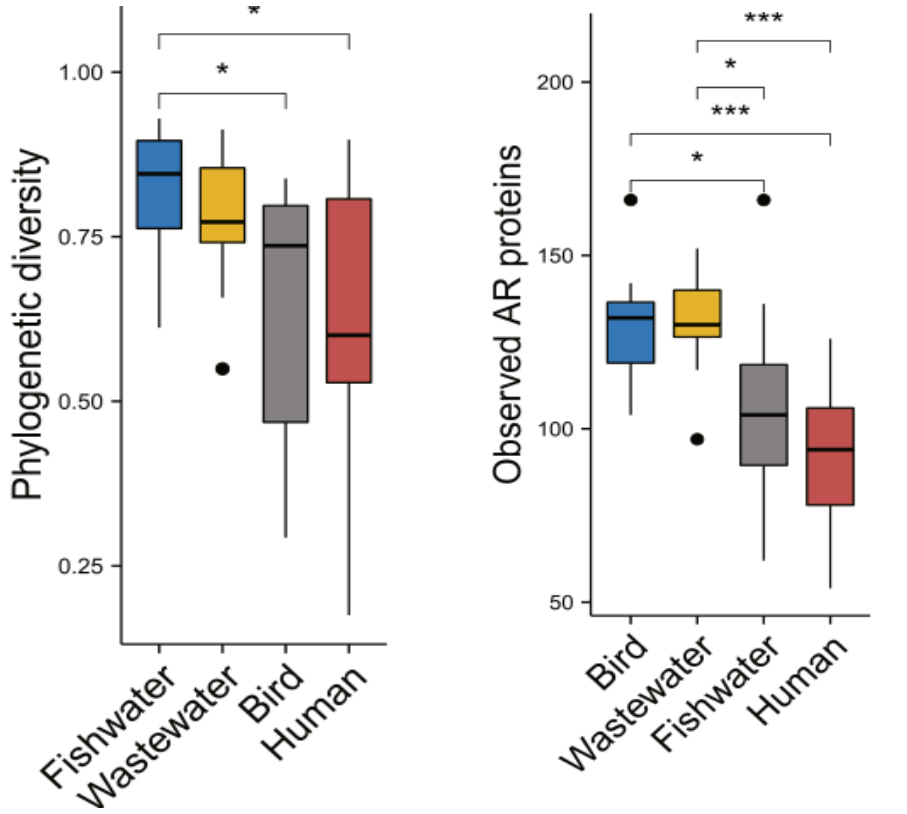




- **The resistomes of samples differed from each. Birds were closer to livestock in ARG composition;**
- **Soil had the highest phylogenetic diversity, but harbored fewer ARGs per sample than other samples;**
- **Bird fecal microbiota contained the lowest phylogenetic diversity but had more ARGs per sample than both soil and water;**

Poyang Lake-The difference between bird and its environmental microbiomes and resistomes





- **Wastewater and fishwater had similar resistomes. Some birds carried similar ARGs compared with wastewater and fishwater;**
- **Human feces harbored both the lowest phylogenetic diversity and ARGs per sample;**
- **birds contained lower phylogenetic diversity, but had the highest ARGs per sample;**

Cao et al, Microbiome, 2020

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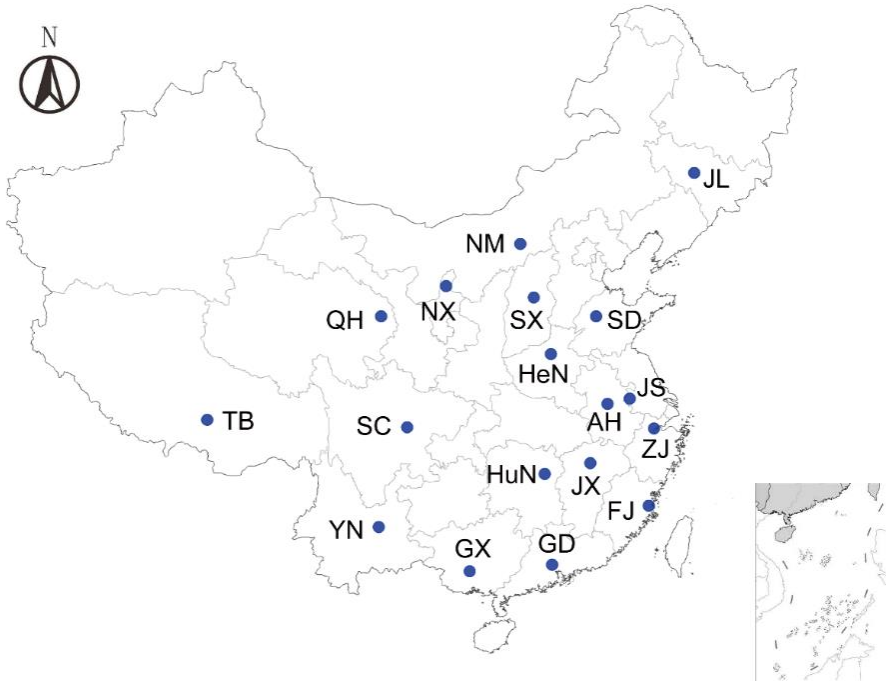
Live poultry market is a huge reservoir of antibiotic resistance genes

PART 02

Map of sampling sites in China

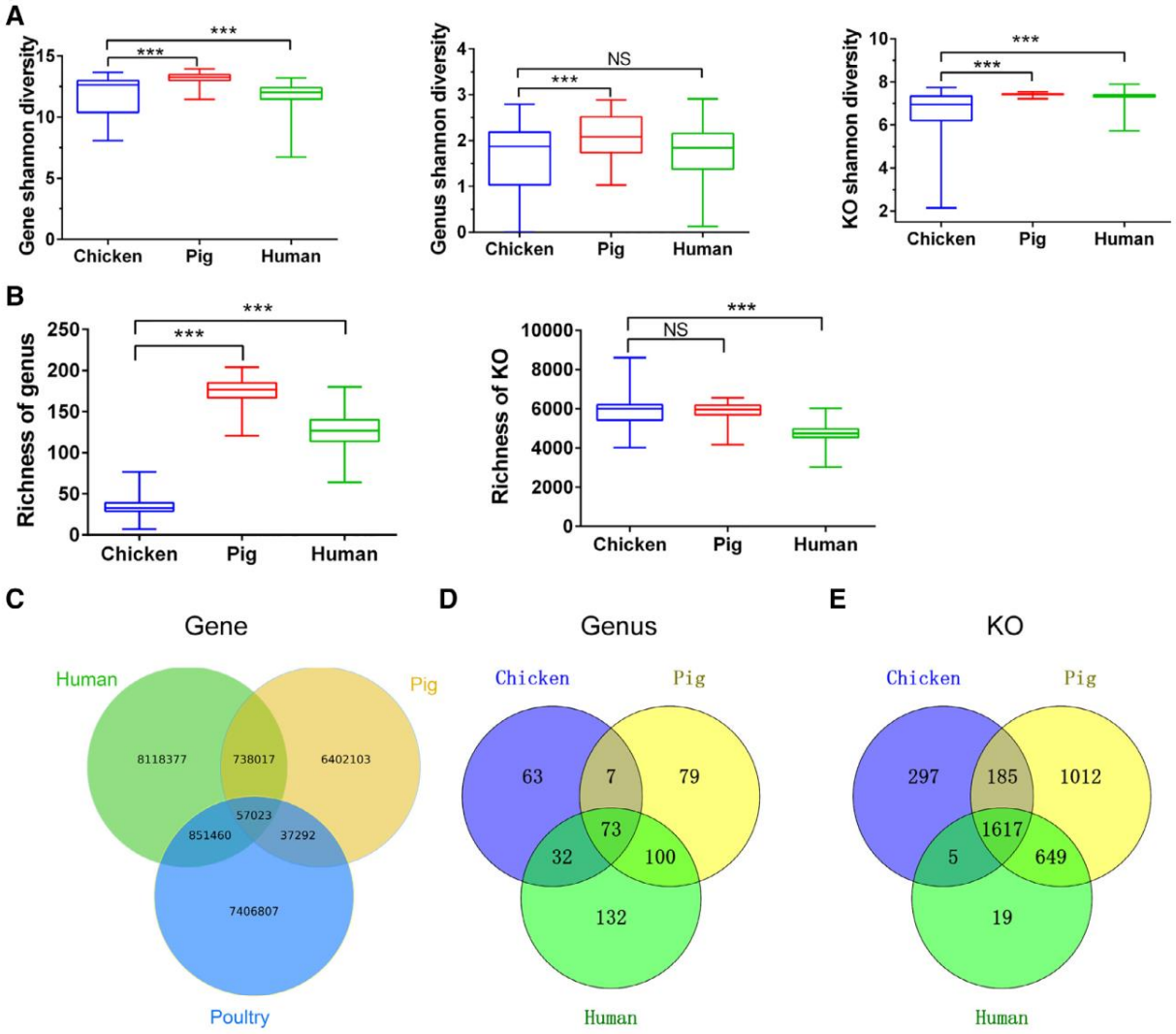


Map of sampling sites (18 provinces) in China

- **The first large-scale study to reveal the overview of ARGs in Chinese LPMs.**
- **We collected 753 poultry fecal samples from LPMs in 18 provinces and municipalities in China between 2016.09-2017.03 and sequenced the metagenomes of 130 samples.**

Wang YN, et al. J Infect. 2019.

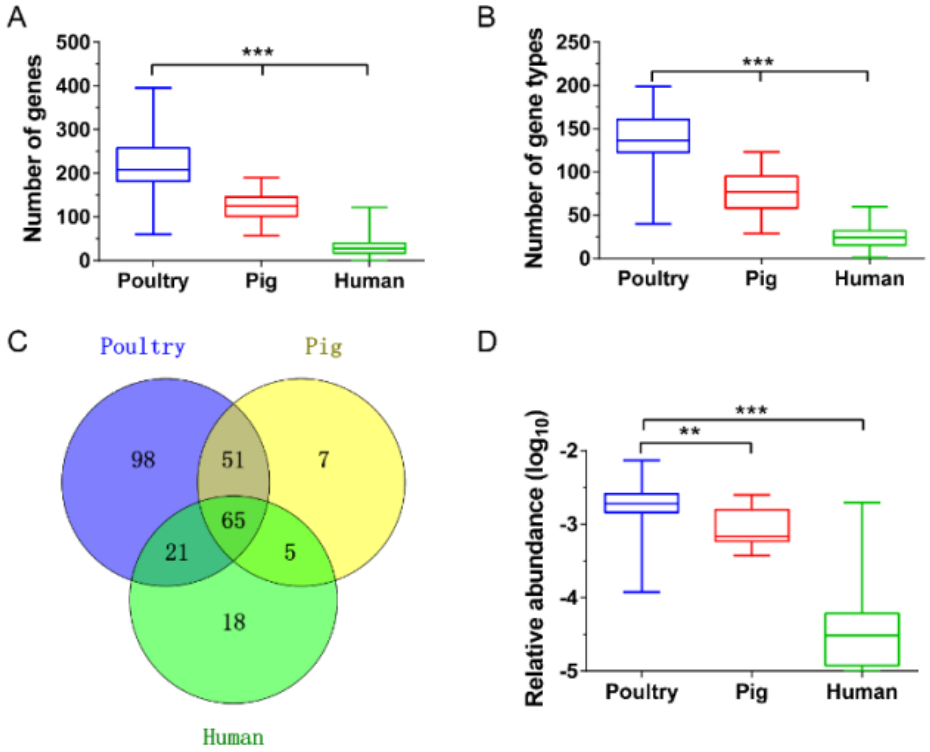
Construction and assessment of poultry gut catalog



- We build a non-redundant gene catalog containing 8,485,510 poultry gut microbial genes, which represents the first gene set generated from poultry and provides a comprehensive reference resource for metagenomics-based research.
- Comparison of the gut microbiome gene catalog of humans, pigs, and poultry.

Wang YN, et al. J Infect. 2019.

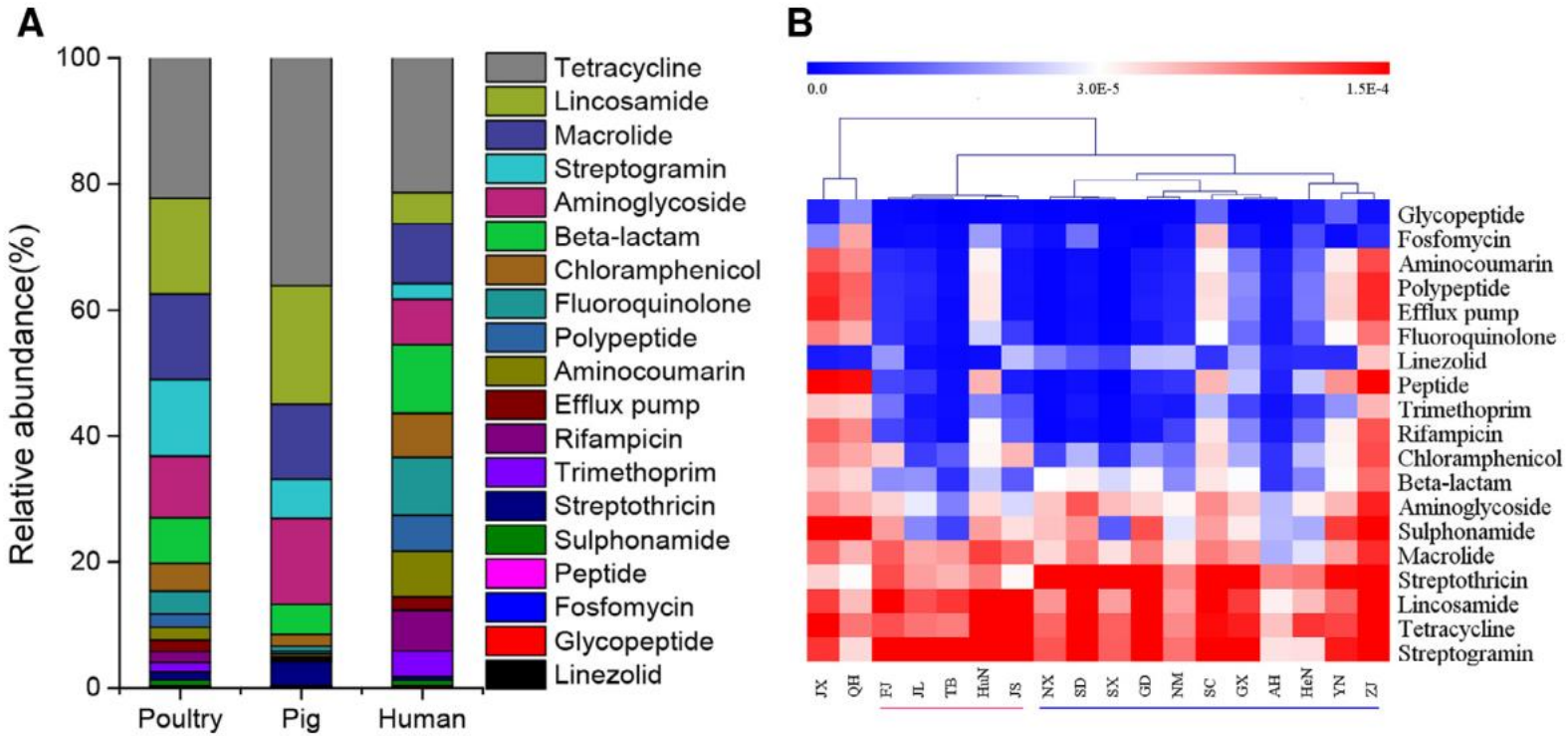
High diversity of ARGs in live poultry gut microbiomes



- We collected 753 poultry fecal samples from LPMs in 18 provinces and municipalities in China between 2016.09--2017.03 and sequenced the metagenomes of 130 samples.
- A total of 539 ARGs classified into 235 types were identified.

Wang YN, et al. J Infect. 2019.

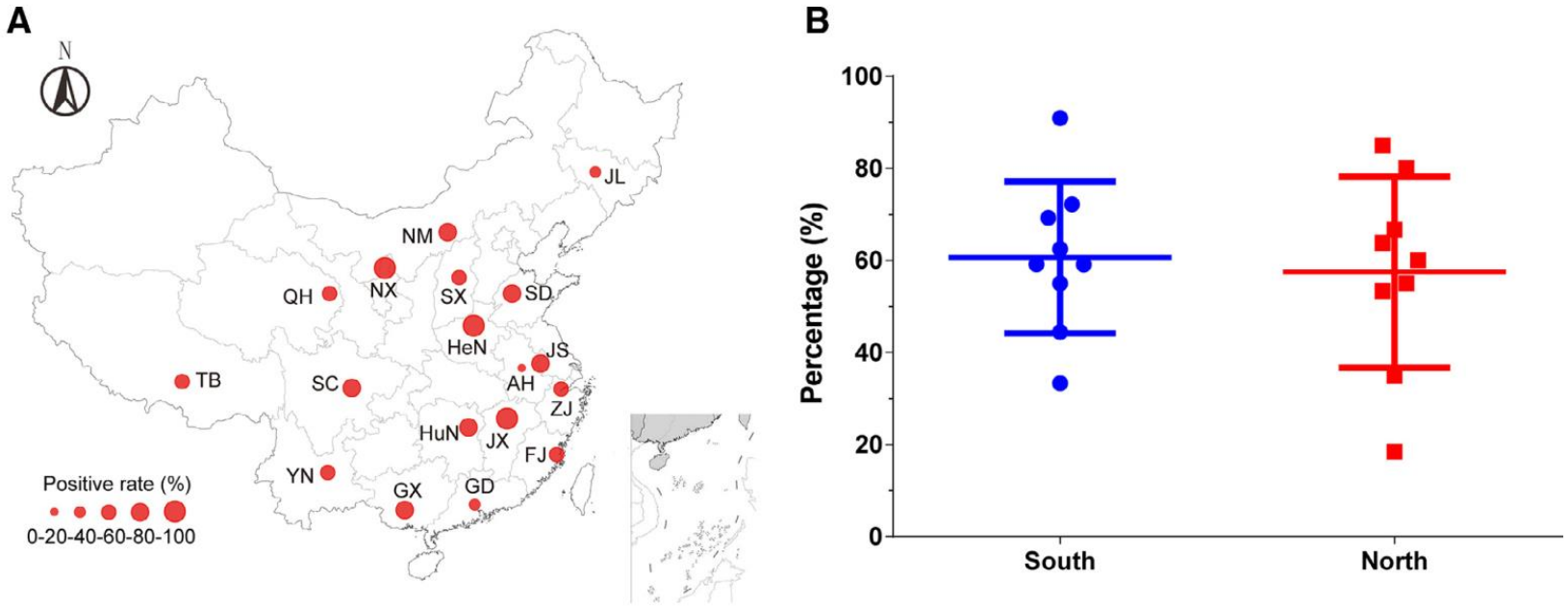
TcR genes are the most abundant ARGs in food animals and humans



- **Tetracycline resistance (TcR) genes are the most abundant ARGs in food animals and humans.**
- **Correlation analyses based on mean relative abundances indicated that the resistance profiles in 18 provinces were clustered into three groups.**

Wang YN, et al. J Infect. 2019.

Prevalence of the *mcr-1* gene in Chinese LPMs



➢ **59.63% LPM samples harbored the colistin resistance gene *mcr-1*.**

Wang YN, et al. J Infect. 2019.

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More diversified antibiotic resistance genes in chickens and workers of the live poultry markets

PART 03

Higher diversity of ARGs in the LPMs than in farms

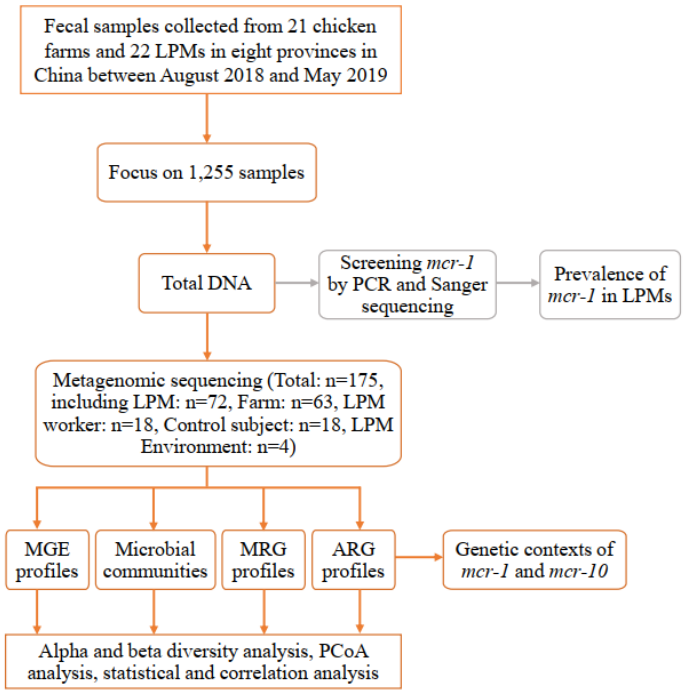
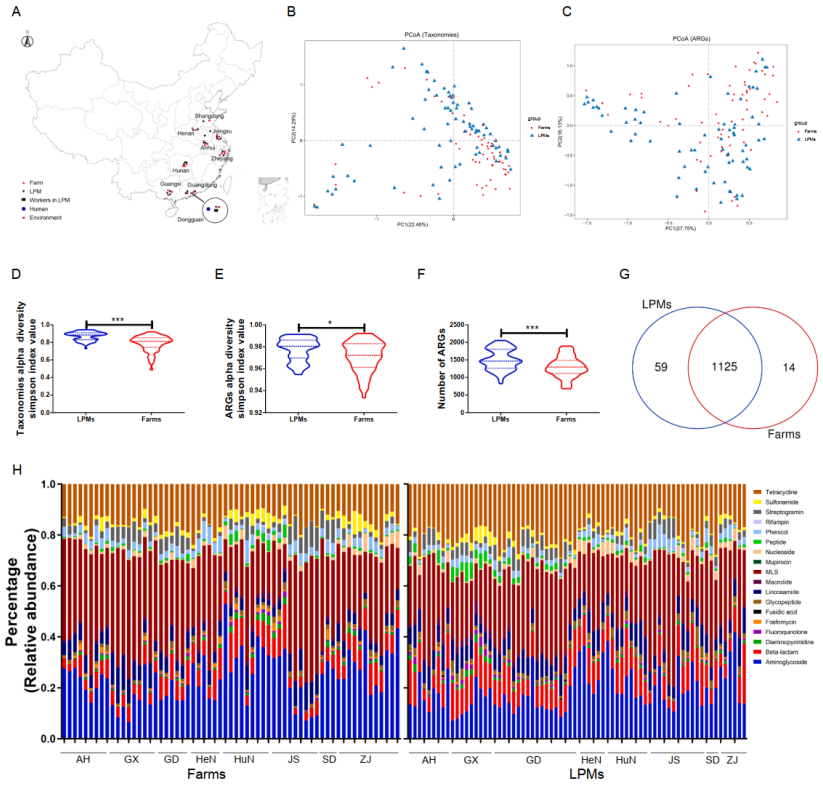


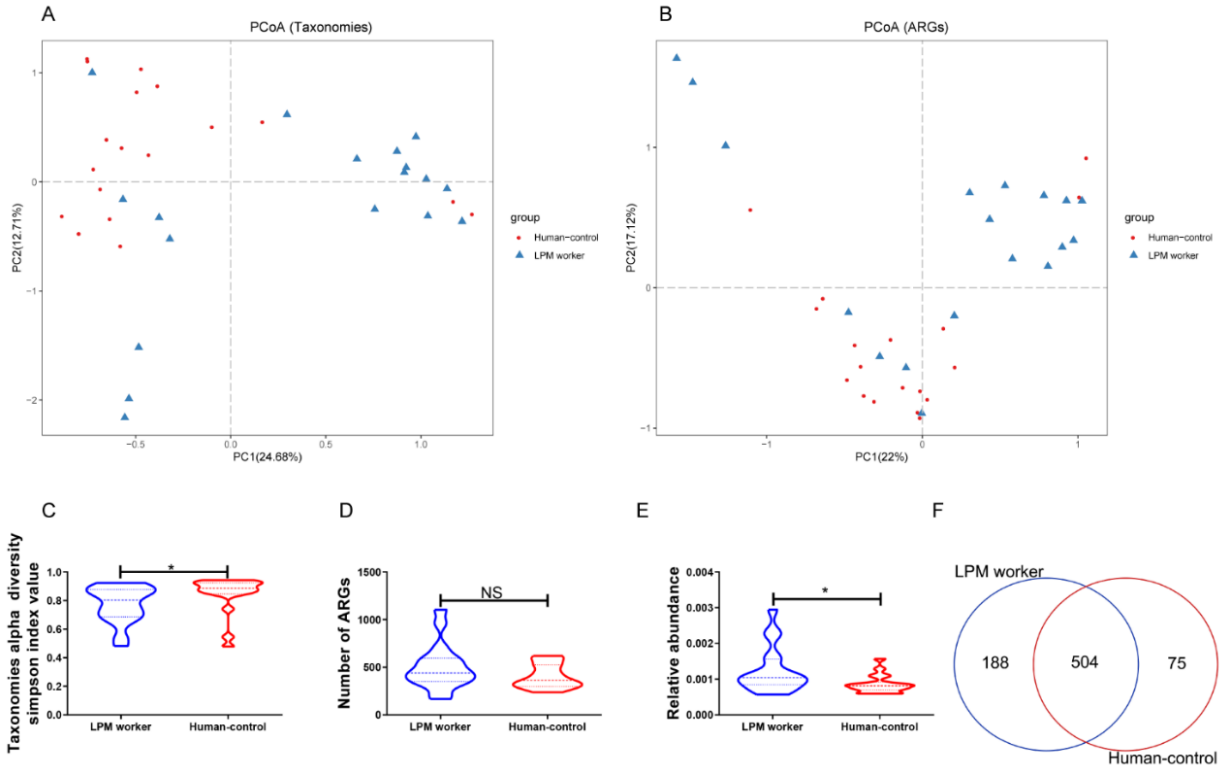
Fig. 1. Flow diagram of study design.



- PCoA of the community composition and resistomes showed that the farm and LPM samples clustered differently, but with some overlap.
- The number of ARGs observed in the LPMs was significantly higher than that in farms.

Wang YN, et al. Environ Int. 2021.

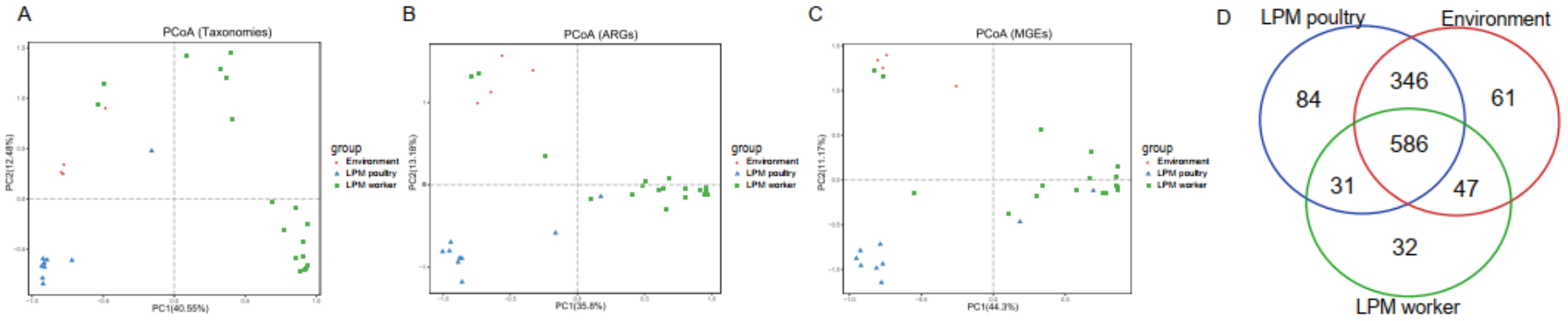
More abundant ARGs in LPM workers gut microbiomes



- Although geographically close to the LPM environment (about 5 km), the control group had a different microbial composition from the LPM workers.
- Although the LPM workers had a lower phylogenetic diversity, both the number and relative abundance of ARGs was higher than those in the control group.

Wang YN, et al. Environ Int. 2021.

Shared and unique ARGs between poultry, human and environment

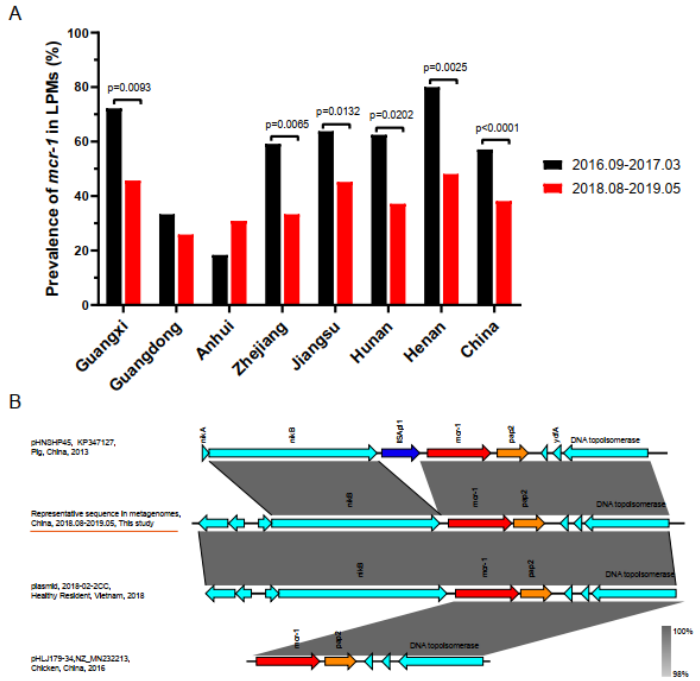


- LPM worker fecal samples separated from LPM chicken and LPM environmental samples in their phylogenetic, resistome, and MGE compositions.
- The majority of ARGs (586 genes) detected in the Dongguan LPM were shared among LPM workers, chicken, and LPM environments, suggested that chicken feces is an important input of environmental resistome in LPMs.
- The *tet*(X3) and *mcr-1* genes were also detected in the farms, LPM chickens, workers, and LPM environments, suggesting the transmission of tigecycline and colistin resistance from the farm chickens to the LPMs, including the LPM environment and the LPM workers, via the live poultry trade.

Wang YN, et al. Environ Int. 2021.

Chicken gut microbiome as reservoirs of MCR-family genes

Origin	Country/Region	Positive samples (%)/ total samples						
		mcr-1	*mcr-3**	*mcr-4**	*mcr-5**	*mcr-8**	*mcr-9*	*mcr-10*
Human (IGC)	China	27 (7.3%)/368	-	-	-	-	9 (2.4%)/368	66 (17.9%)/368
	America	-	-	-	-	-	1 (0.7%)/139	2 (1.4%)/139
	Europe	-	-	-	-	-	12 (1.6%)/760	5 (0.7%)/760
Human	UK	-	-	-	-	-	2 (0.8%)/250	-
Human	India	-	-	-	-	-	2 (1.8%)/110	11 (10.0%)/110
Human	Sweden	-	-	-	-	-	2 (1.0%)/196	1 (0.5%)/196
Human	China	3 (8.3%)/36	2 (5.6%)/36	-	2 (5.6%)/36	-	2 (5.6%)/36*	11 (30.6%)/36
Chicken (September 2016-March 2017)	China	56 (54.9%)/102	1 (1.0%)/102	-	1 (1.0%)/102	-	-	-
Chicken (August 2018-May 2019)	China	102 (75.6%)/135	12 (8.9%)/135	2 (1.5%)/135	1 (0.7%)/135	6 (4.4%)/135	3 (2.2%)/135*	14 (10.4%)/135
Chicken	China	71 (14.3%)/495	-	-	-	-	-	-
Chicken	Germany	1 (5.3%)/19	-	-	-	-	-	-
Chicken	the Netherlands	2 (10%)/20	-	-	-	-	-	-
Chicken	Denmark	3 (15%)/20	-	-	-	-	-	-
Chicken	France	6 (30%)/20	-	-	-	-	-	-
Chicken	Belgium	6 (30%)/20	-	-	-	-	-	-
Chicken	Poland	7 (35%)/20	-	-	-	-	-	-
Chicken	Spain	13 (65%)/20	-	-	-	-	-	-
Chicken	Italy	13 (65%)/20	-	-	-	-	-	-
Chicken	Bulgaria	13 (68.4%)/19	-	-	-	-	-	-
Humans (total)	-	30 (1.6%)/1859	2 (0.1%)/1859	-	2 (0.1%)/1859	-	30 (1.6%)/1859	96 (5.2%)/1859
Chicken (total)	-	293 (32.2%)/910	13 (1.4%)/910	2 (0.2%)/910	2 (0.2%)/910	6 (0.7%)/910	3 (0.3%)910*	14 (1.5%)/910



- Multiple *mcr*-family genes were identified in chicken gut metagenomes, including *mcr-1*, *mcr-3*, *mcr-4*, *mcr-5*, *mcr-8*, *mcr-9*, and *mcr-10*.
- The number of *mcr-10*-carrying fecal samples was higher in Asia than in Europe or America.
- The *mcr-1* gene prevalence decreased significantly in the LPMs across seven provinces in China, from 190/333 (57.1%) samples in 2016.09--2017.03 to 208/544 (38.2%) samples in 2018.08--2019.05.

Wang YN, et al. Environ Int. 2021.

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The temporal and spatial dynamics of antimicrobial-resistant-*Salmonella enterica* and predominant serovars in China

PART 04

Threat of foodborne *Salmonella*

The global burden of non-typhoidal salmonella invasive disease: a systematic analysis for the Global Burden of Disease Study 2017

GBD 2017 Non-Typhoidal Salmonella Invasive Disease Collaborators*

Summary

Background Non-typhoidal salmonella invasive disease is a major cause of global morbidity and mortality. Malnourished children, those with recent malaria or sickle-cell anaemia, and adults with HIV infection are at particularly high risk of disease. We sought to estimate the burden of disease attributable to non-typhoidal salmonella invasive disease for the Global Burden of Diseases, Injuries, and Risk Factors Study (GBD) 2017.

Methods We did a systematic review of scientific databases and grey literature, and estimated non-typhoidal salmonella invasive disease incidence and mortality for the years 1990 to 2017, by age, sex, and geographical location using DisMod-MR, a Bayesian meta-regression tool. We estimated case fatality by age, HIV status, and sociodemographic development. We also calculated the HIV-attributable fraction and estimated health gap metrics, including disability-adjusted life-years (DALYs).

Findings We estimated that 535 000 (95% uncertainty interval 409 000–705 000) cases of non-typhoidal salmonella invasive disease occurred in 2017, with the highest incidence in sub-Saharan Africa (34·5 [26·6–45·0] cases per 100 000 person-years) and in children younger than 5 years (34·3 [23·2–54·7] cases per 100 000 person-years). 77 500 (46 400–123 000) deaths were estimated in 2017, of which 19 400 (12 000–27 700) were attributable to HIV. The remaining 59 100 (33 300–98 100) deaths not attributable to HIV accounted for 4·26 million (2·38–7·38) DALYs in 2017. Mean all-age case fatality was 14·5% (9·2–21·1), with higher estimates among children younger than 5 years (13·5% [8·4–19·8]) and elderly people (51·2% [30·2–72·9] among those aged ≥70 years), people with HIV infection (41·8% [30·0–54·0]), and in areas of low sociodemographic development (eg, 15·8% [10·0–22·9] in sub-Saharan Africa).

Interpretation We present the first global estimates of non-typhoidal salmonella invasive disease that have been produced as part of GBD 2017. Given the high disease burden, particularly in children, elderly people, and people with HIV infection, investigating the sources and transmission pathways of non-typhoidal salmonella invasive disease is crucial to implement effective preventive and control measures.

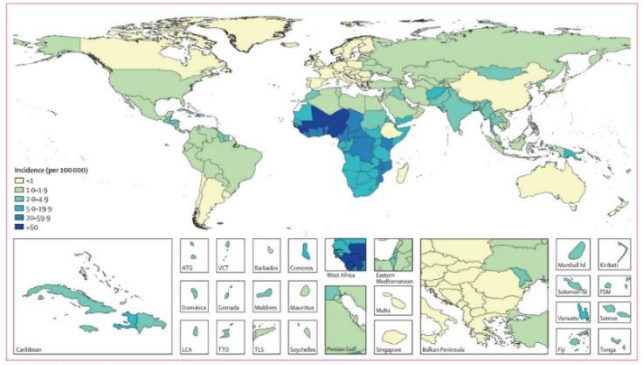


Figure 1: Non-typhoidal salmonella invasive disease incidence rates (per 100 000), by country, in 2017
Locations filled in white are those for which the Global Burden of Disease Study (GBD) does not produce estimates. The inset maps detail smaller locations. ATG=Antigua and Barbuda. VCT=Saint Vincent and the Grenadines. Isl=Islands. FSM=Federated States of Micronesia. LCA=Saint Lucia. TTO=Trinidad and Tobago. TLS=Timor-Leste.

The global burden of typhoid and paratyphoid fevers: a systematic analysis for the Global Burden of Disease Study 2017

GBD 2017 Typhoid and Paratyphoid Collaborators*

Summary

Background Efforts to quantify the global burden of enteric fever are valuable for understanding the health lost and the large-scale spatial distribution of the disease. We present the estimates of typhoid and paratyphoid fever burden from the Global Burden of Diseases, Injuries, and Risk Factors Study (GBD) 2017, and the approach taken to produce them.

Methods For this systematic analysis we broke down the relative contributions of typhoid and paratyphoid fevers by country, year, and age, and analysed trends in incidence and mortality. We modelled the combined incidence of typhoid and paratyphoid fevers and split these total cases proportionally between typhoid and paratyphoid fevers using aetiological proportion models. We estimated deaths using vital registration data for countries with sufficiently high data completeness and using a natural history approach for other locations. We also estimated disability-adjusted life-years (DALYs) for typhoid and paratyphoid fevers.

Findings Globally, 14·3 million (95% uncertainty interval [UI] 12·5–16·3) cases of typhoid and paratyphoid fevers occurred in 2017, a 44·6% (42·2–47·0) decline from 25·9 million (22·0–29·9) in 1990. Age-standardised incidence rates declined by 54·9% (53·4–56·5), from 439·2 (376·7–507·7) per 100 000 person-years in 1990, to 197·8 (172·0–226·2) per 100 000 person-years in 2017. In 2017, *Salmonella enterica* serotype Typhi caused 76·3% (71·8–80·5) of cases of enteric fever. We estimated a global case fatality of 0·95% (0·54–1·53) in 2017, with higher case fatality estimates among children and older adults, and among those living in lower-income countries. We therefore estimated 135·9 thousand (76·9–218·9) deaths from typhoid and paratyphoid fever globally in 2017, a 41·0% (33·6–48·3) decline from 230·5 thousand (131·2–372·6) in 1990. Overall, typhoid and paratyphoid fevers were responsible for 9·8 million (5·6–15·8) DALYs in 2017, down 43·0% (35·5–50·6) from 17·2 million (9·9–27·8) DALYs in 1990.

Interpretation Despite notable progress, typhoid and paratyphoid fevers remain major causes of disability and death, with billions of people likely to be exposed to the pathogens. Although improvements in water and sanitation remain essential, increased vaccine use (including with typhoid conjugate vaccines that are effective in infants and young children and protective for longer periods) and improved data and surveillance to inform vaccine rollout are likely to drive the greatest improvements in the global burden of the disease.

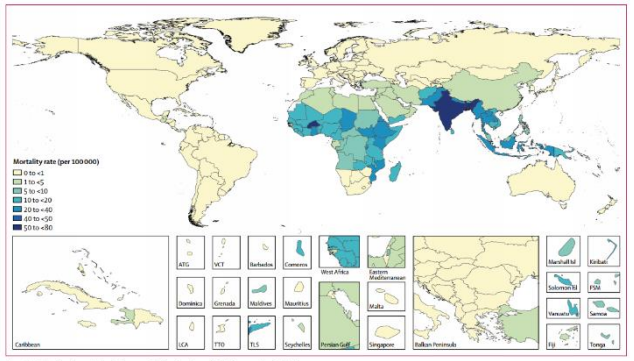


Figure 3: Typhoid and paratyphoid fever mortality rates (per million), by country, in 2017
Unfilled locations are those for which GBD does not produce estimates. The inset maps detail smaller locations. ATG=Antigua and Barbuda. FSM=Federated States of Micronesia. GBD=Global Burden of Diseases, Injuries, and Risk Factors Study. Isl=Islands. LCA=Saint Lucia. TLS=Timor-Leste. TTO=Trinidad and Tobago. VCT=Saint Vincent and the Grenadines.

***Panel:* WHO priority list for research and development of new antibiotics for antibiotic-resistant bacteria**

Multidrug-resistant and extensively-resistant *Mycobacterium tuberculosis*[25]

Other priority bacteria

Priority 1: critical
- *Acinetobacter baumannii*, carbapenem resistant
- *Pseudomonas aeruginosa*, carbapenem resistant
- Enterobacteriaceae, carbapenem resistant, third-generation cephalosporin resistant

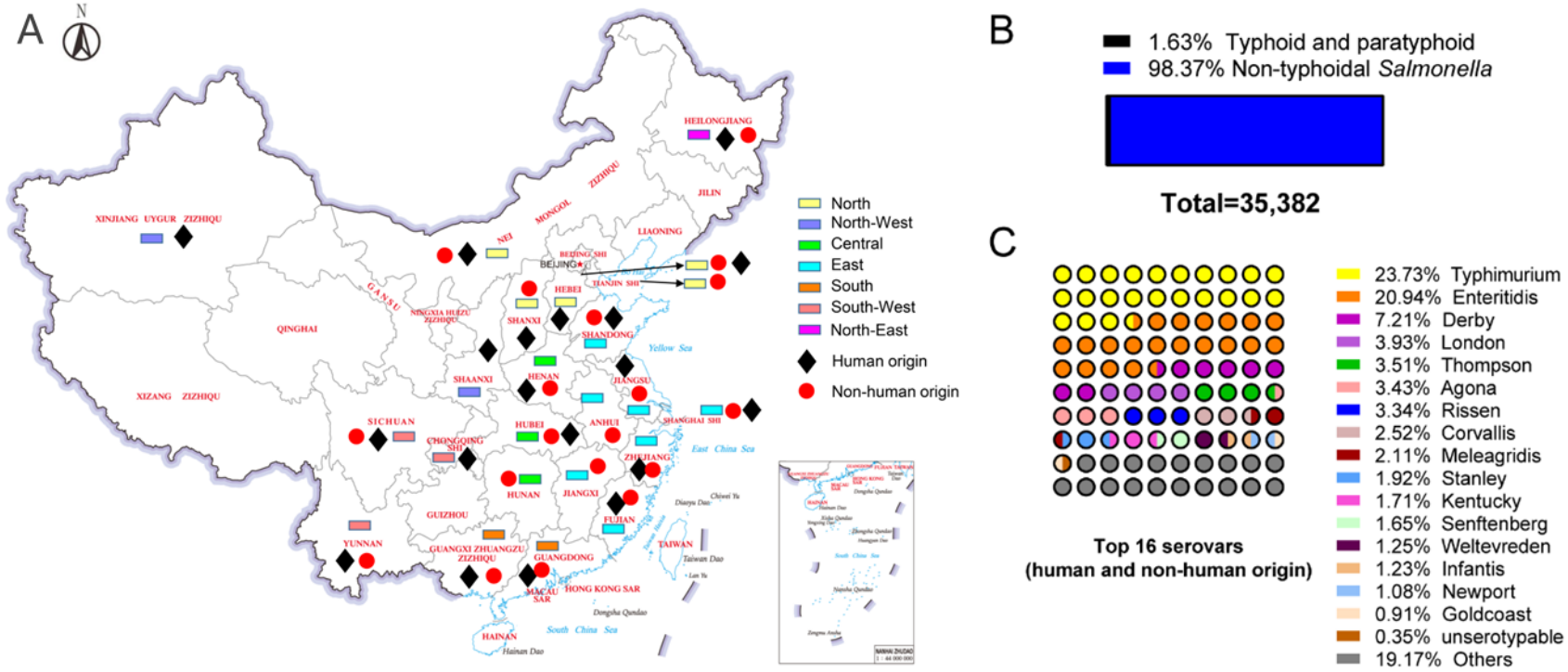
Priority 2: high
- *Enterococcus faecium*, vancomycin resistant
- *Staphylococcus aureus*, methicillin resistant, vancomycin resistant
- *Helicobacter pylori*, clarithromycin resistant
- *Campylobacter* spp, fluoroquinolone resistant
- *Salmonella* spp fluoroquinolone resistant
- *Neisseria gonorrhoeae*, third-generation cephalosporin resistant, fluoroquinolone resistant

Priority 3: medium
- *Streptococcus pneumoniae*, penicillin non-susceptible
- *Haemophilus influenzae*, ampicillin resistant
- *Shigella* spp, fluoroquinolone resistant

- A total of **535 000 cases** of non-typhoidal *Salmonella* invasive disease occurred and **77 500 deaths** were estimated in 2017.
- A total of **14·3 million cases** of typhoid and paratyphoid fevers occurred and **135·9 thousand deaths** in 2017.

- **Systematic studies on the trends and geographical distribution of antimicrobial-resistant *Salmonella* and dominant serovars have been well studied in European and American countries while not in China.**

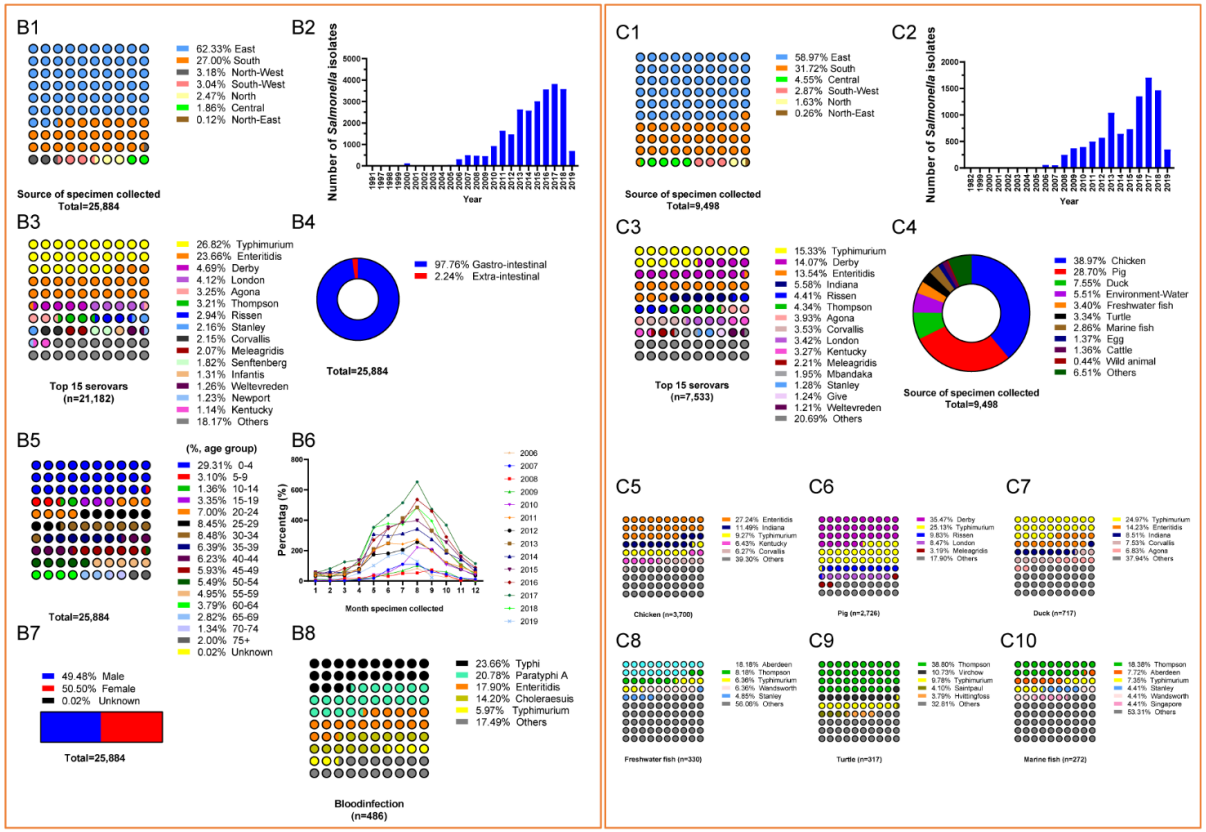
Geographical distribution of 35,382 *Salmonella* isolates in China



- A total of 35,107 isolates were obtained through passive surveillance from public health laboratories in the CDC, sentinel clinical laboratories from general hospitals, and sentinel laboratories from universities participated in 23 Chinese provinces.
- 98.37% of the 35328 isolates were non-typhoidal *Salmonella*.
- *S*. Typhimurium, *S*. Enteritidis, and *S*. Derby were the most three dominant serovars.

Wang YN, et al. Natl Sci Rev. 2022.

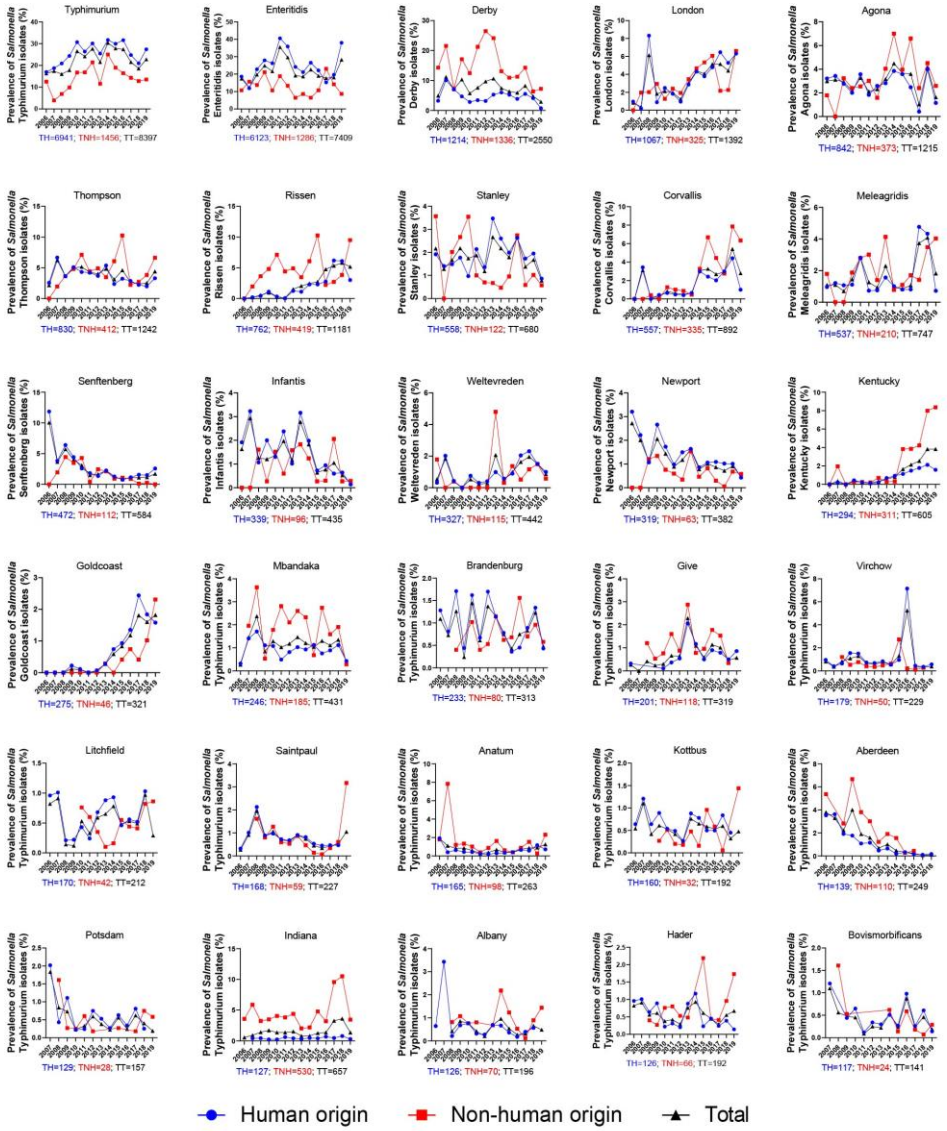
Summary of these strains isolated from human and non-human origins



- A total of 25884 strains classified into 144 serovars isolated from human origin.
- A total of 9498 strains classified into 120 serovars isolated from non-human origin.

Wang YN, et al. Natl Sci Rev. 2022.

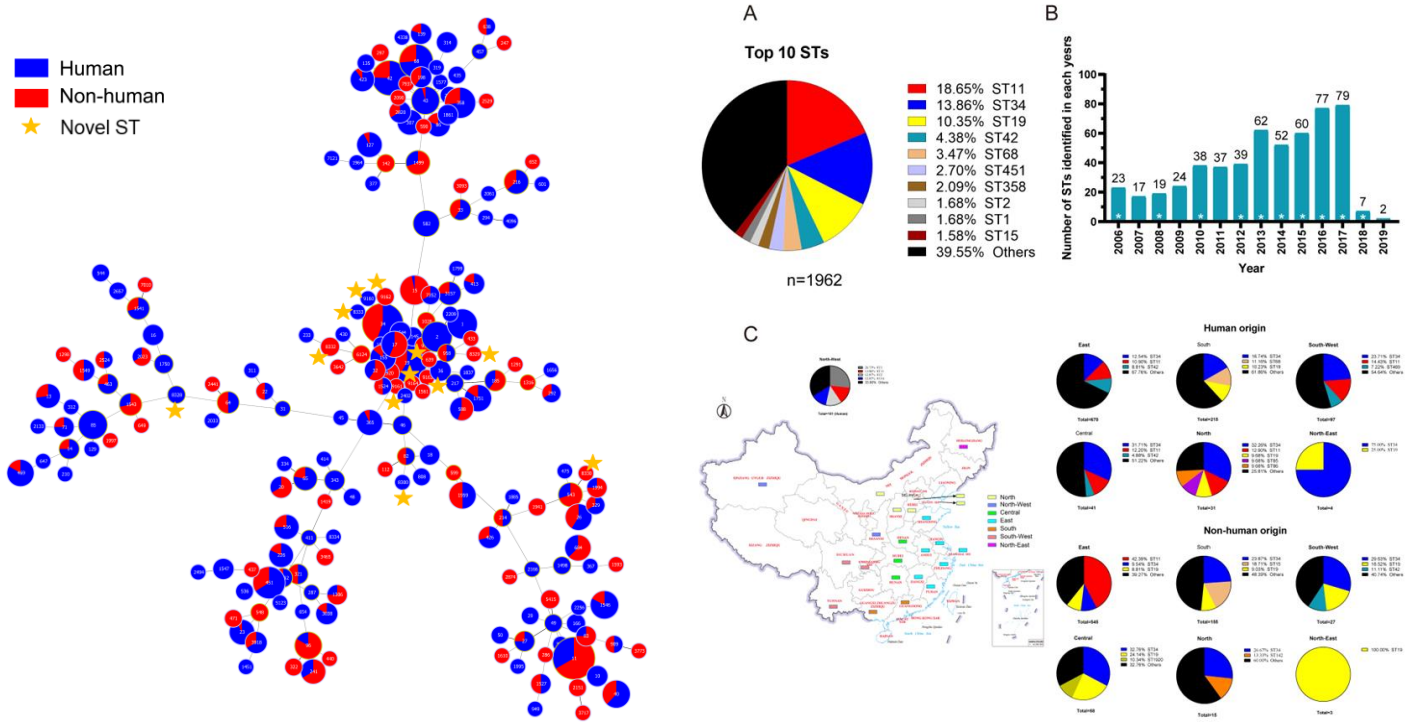
Dominant subtype switch in *Salmonella* serovars during 2006-2019



- The proportion of *Salmonella* serovar Typhimurium, London, Rissen, Corvallis, Meleagridis, Kentucky, and Goldcoast showed an increasing trend in China.
- The proportion of *Salmonella* serovar Derby, Senftenberg, Infantis, Newport, Aberdeen, Potsdam, Bovismorbificans, showing a downward trend in China.

Wang YN, et al. Natl Sci Rev. 2022.

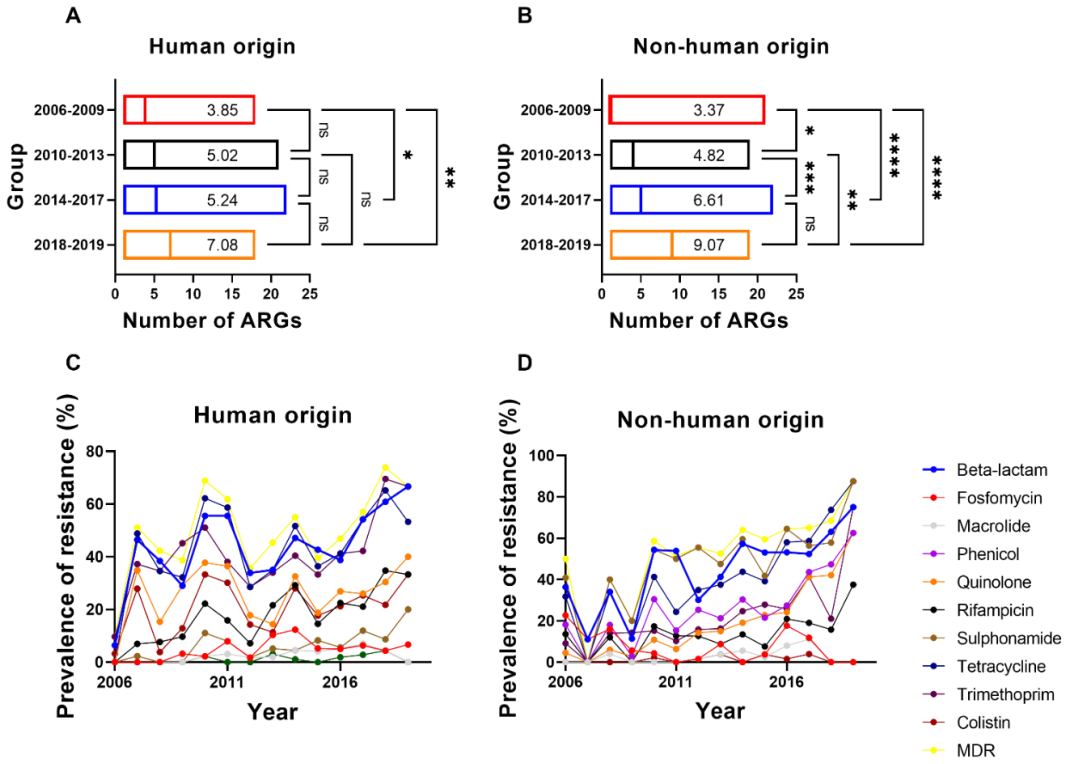
Temporal trends of sequence types (STs) during 2006-2019



- We found that 200 different STs among the 1,962 isolates and twelve novel STs were assigned in seven serovars (16 isolates).
- The ST11 was the dominant ST in the 1,962 genomes, followed by ST34 and ST19 that accounted for 18.65% (366/1,962), 13.86% (272/1,962), and 10.35% (203/1,962) respectively.
- The diversity of STs has had an increasing trend over time in recent years.

Wang YN, et al. Natl Sci Rev. 2022.

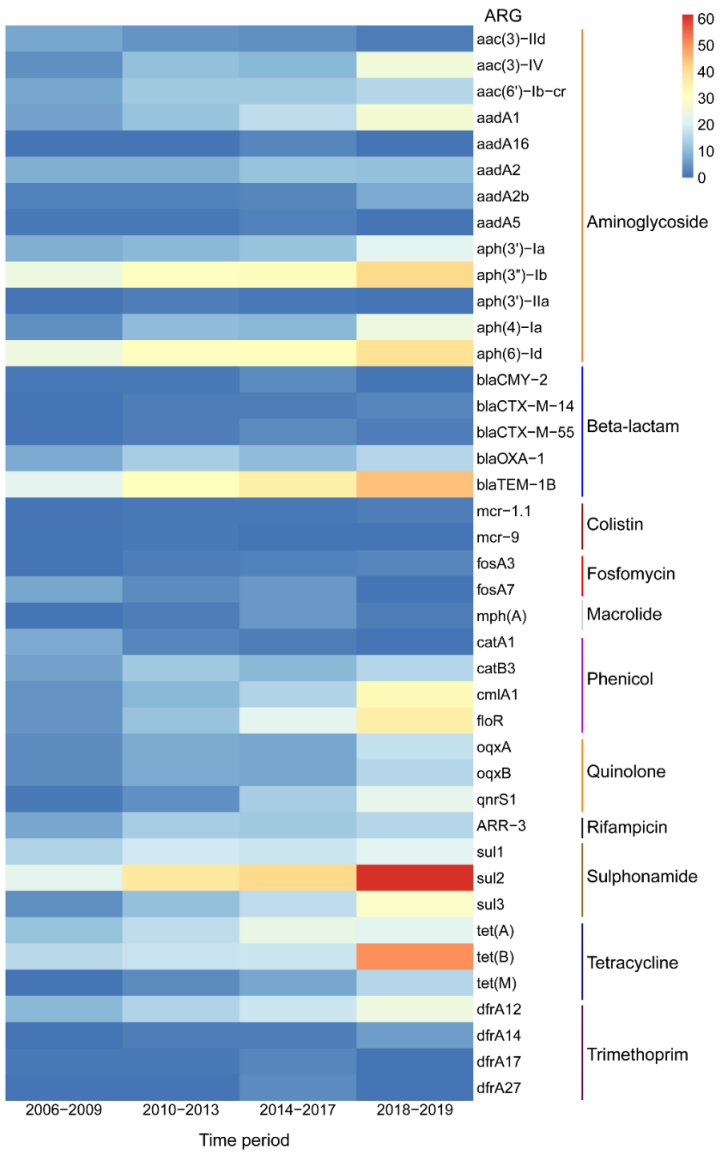
Temporal changes of AMR and ARGs



- The number of ARGs per isolate increased 1.8 and 2.7 times of human and non-human origins respectively, spanning 14 years (2006-2019).
- The proportion of antimicrobial resistance isolates had an increasing trend over time, especially the beta-lactam, quinolone, tetracycline, and rifampicin.

Wang YN, et al. Natl Sci Rev. 2022.

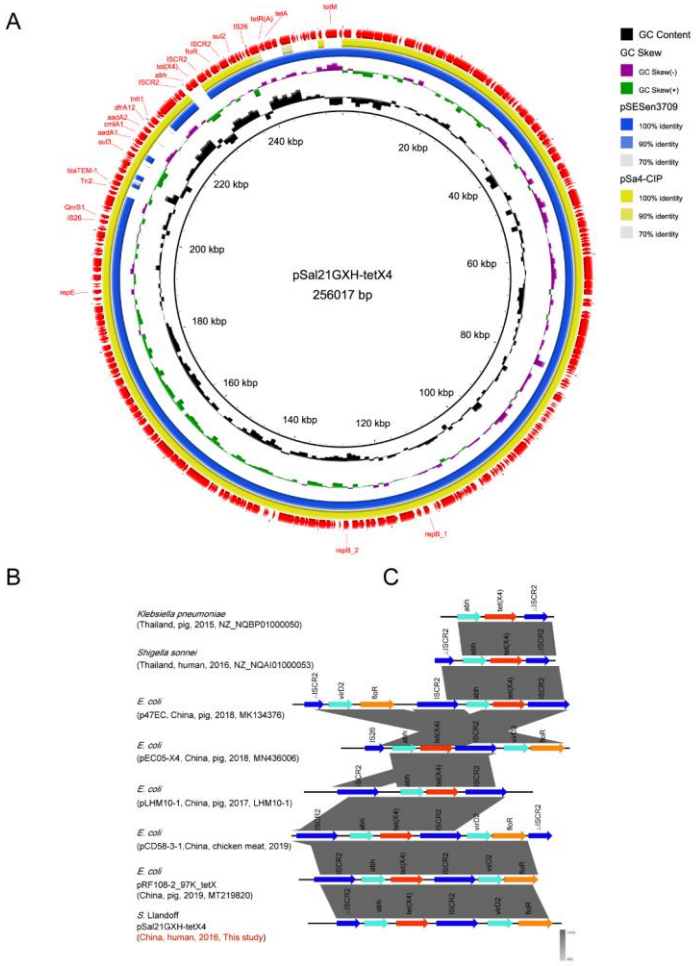
Dynamics in the prevalence of ARGs among NTS isolates



- The increasing dynamics were observed in beta-lactam ARGs *bla*TEM-1B, *bla*OXA-1, and *bla*CTX-M-14, aminoglycoside ARGs *aac(3)-IV*, *aac(6')-Ib-cr*, *aadA1*, *aph(3')-Ia*, *aph(3")-Ib*, *aph(4)-Ia*, and *aph(6)-Id*, fosfomycin ARG, *fosA3*, phenicol ARGs *catB3*, *cmlA1*, and *floR*, rifampicin ARG *ARR-3*, sulphonamide ARGs *sul2* and *sul3*, tetracycline ARGs *tet*(B) and *tet*(M), and Trimethoprim ARGs *dfrA12* and *dfrA14*.
- However, decreasing dynamics were observed in several ARGs, for example, *aac(3)-IId* and *catA1*.

Wang YN, et al. Natl Sci Rev. 2022.

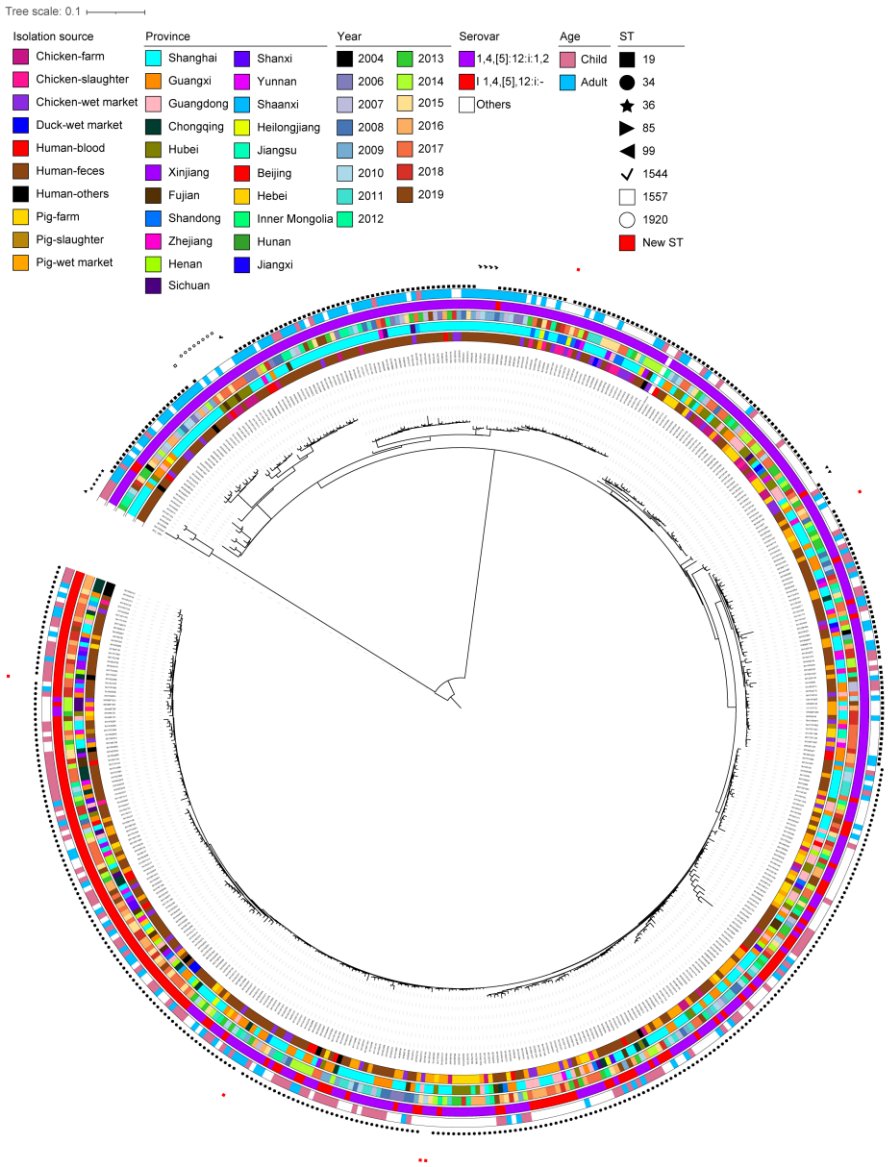
Emergence of the *tet*(X4) gene in *Salmonella* Llandoff isolate



- New tigecycline resistance determinant: *tet*(X4).
- The *Salmonella* Llandoff strain was isolated and identified for the first time in China.
- New sequence type ST8300.
- Genetic environment: IS*CR2*-abh-*tet*(X4)-IS*CR2*.

Wang YN, et al. Natl Sci Rev. 2022.
Wang YN, et al. IMD. 2021.

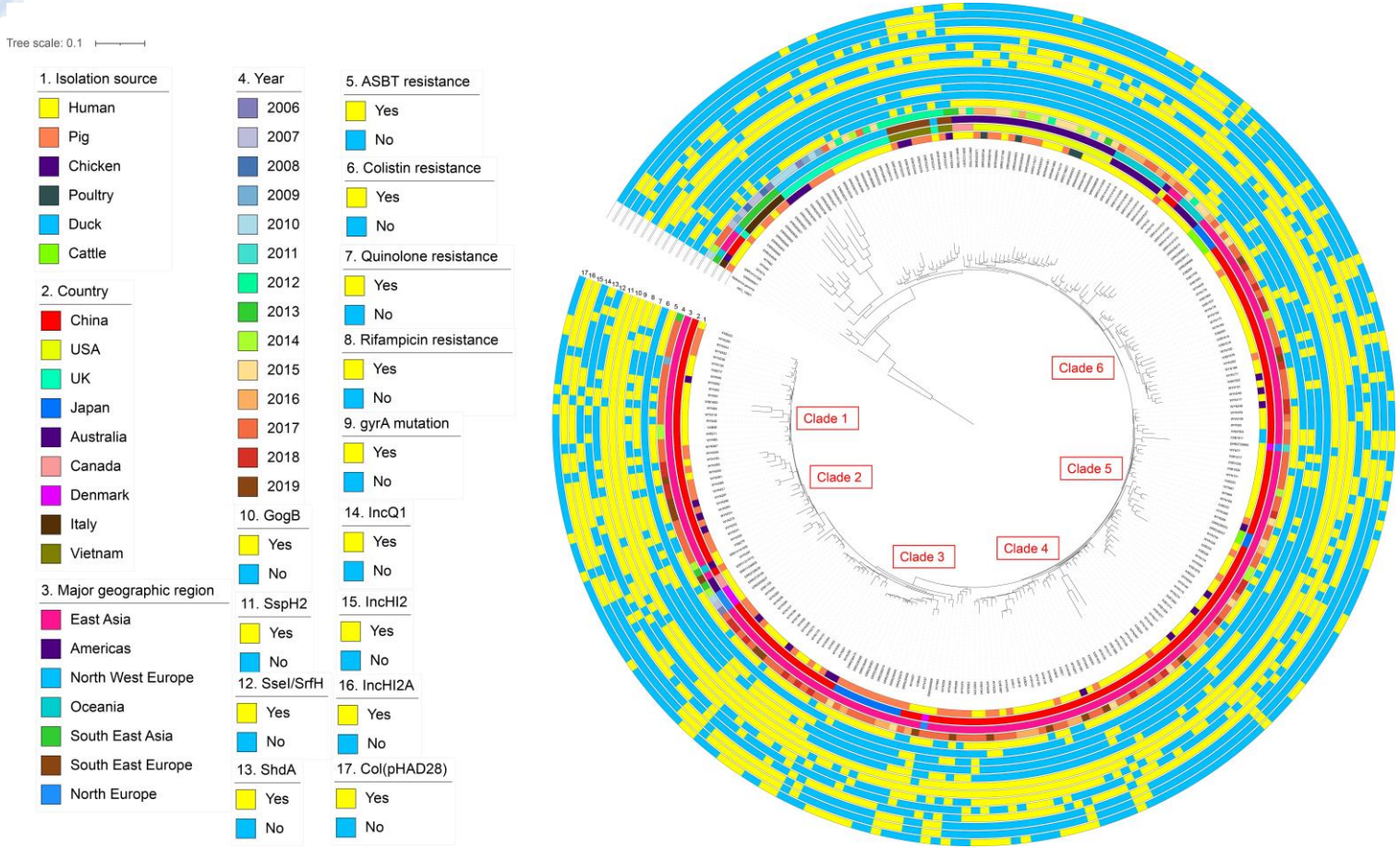
Phylogenetic analysis of *S.* Typhimurium and its variants



- We found that higher diversity of STs in *S.* Typhimurium than in other serovars.
- ST34 from pig and ST19 from chicken origin were mainly associated with isolates caused children and adult gastroinfection respectively.

Wang YN, et al. Natl Sci Rev. 2022.

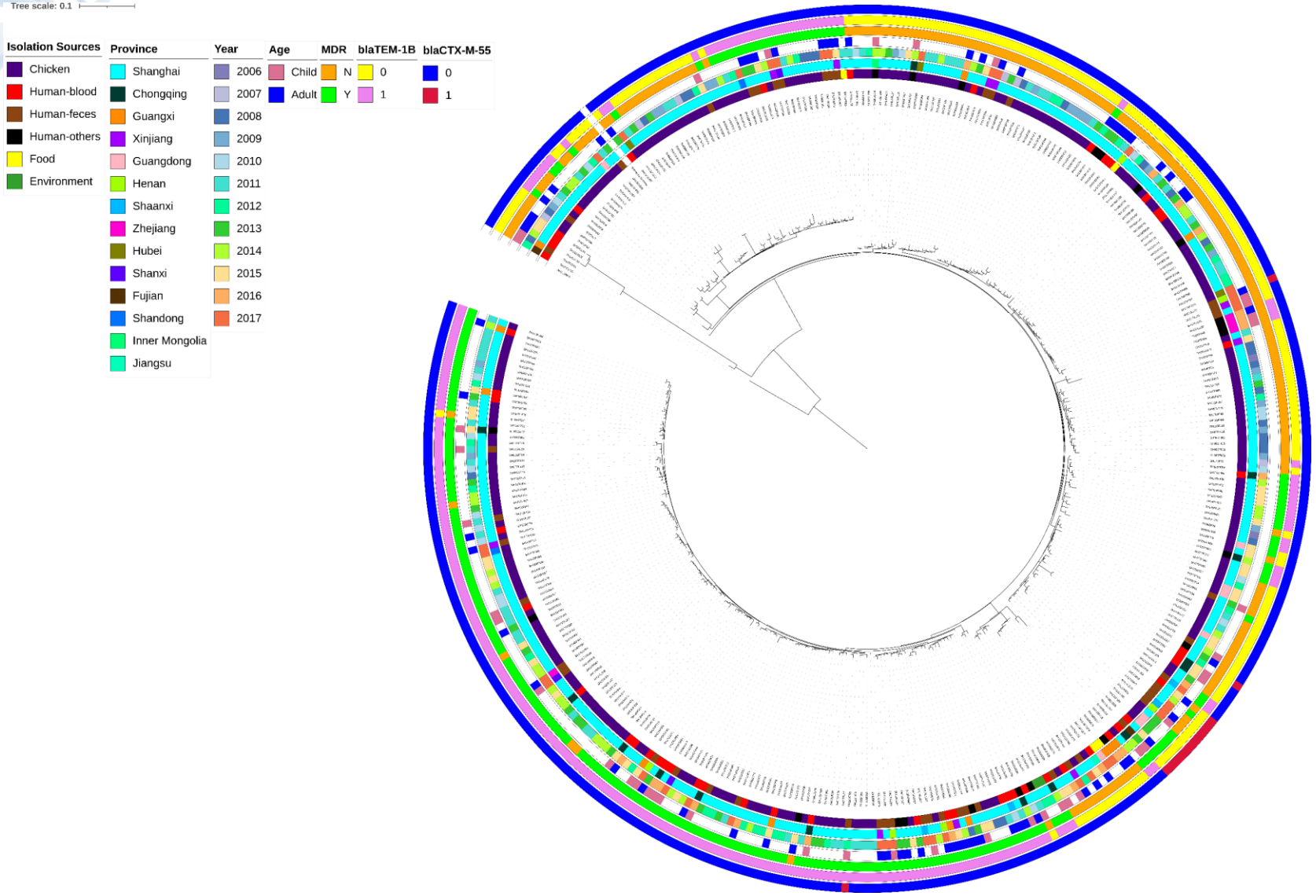
Phylogenetic analysis of global *S.* I 1,4,[5],12:i:- ST34



- These results suggested that Chinese isolates were different from those in Southeast Asia, Northwest Europe, Southeast Europe and America, and with a local evolution.
- We found that 1) the clade 1 and 4 only included Chinese strains; 2) the clade 2 mainly included Chinese strains and one Australian strain which were closely related to 2 and 3 strains from Canada and Denmark, respectively; 3) the clade 3 was Chinese isolates were clustered with those isolated from pigs in Japan; 4) the clade 5 and 6 included Chinese strains and strains isolated from cattle from Japan. In addition, two Chinese isolates from humans clustered with one American isolate from pig and Australian strains from the human.

Wang YN, et al. Natl Sci Rev. 2022.

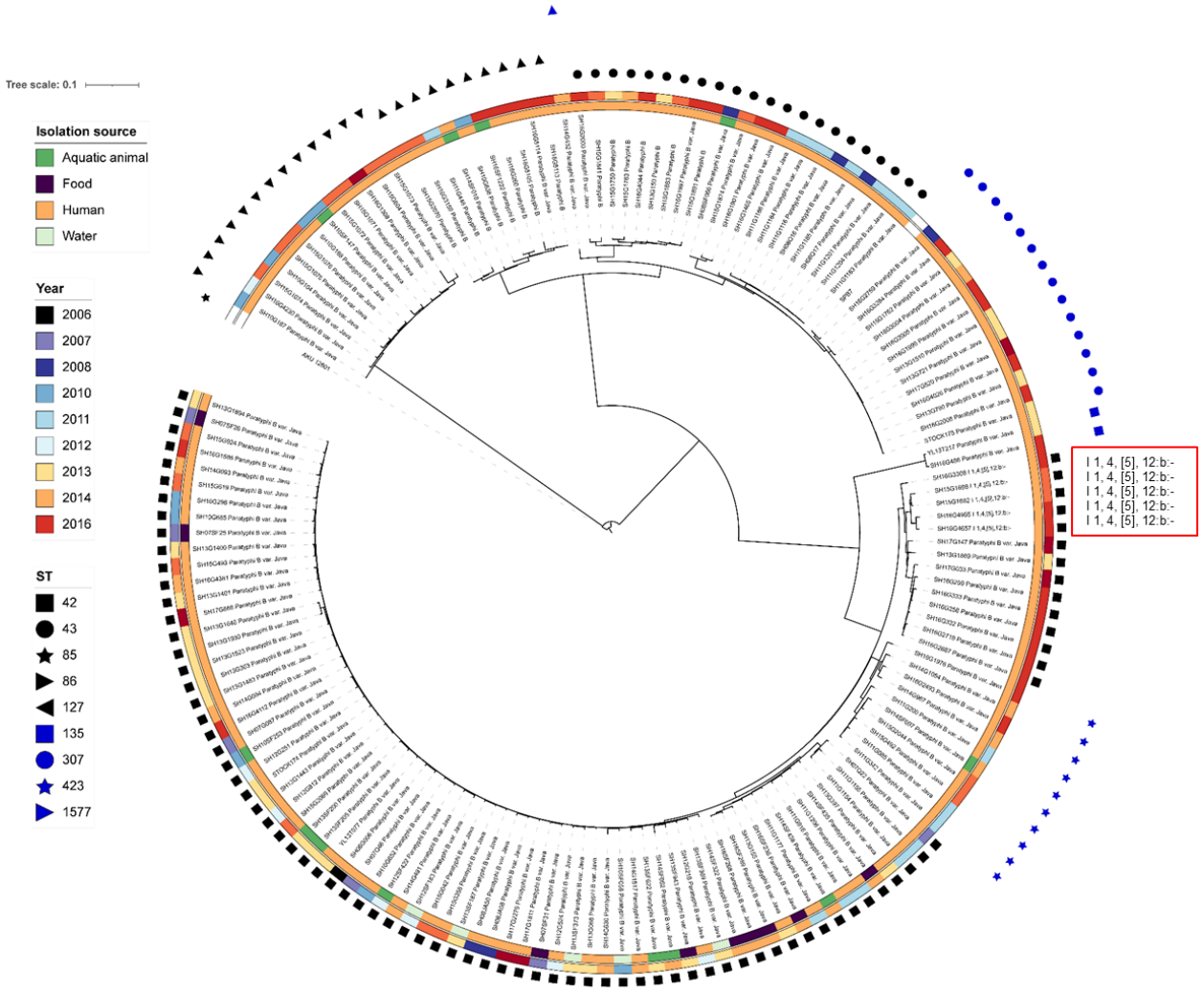
Phylogenetic analysis of *S.* Enteritidis



- We found that *S.* Enteritidis genomes caused human infections mainly associated with chicken.
- The majority of *S.* Enteritidis carrying the blaTEM-1B gene also showed the MDR pattern.

Wang YN, et al. Natl Sci Rev. 2022.

Phylogenetic analysis of *S.* Paratyphi B and its variants



- **Phylogenetic analysis of Paratyphi B and its variants revealed that I 1, 4, [5], 12:b:- and S. Paratyphi B var. Java ST42 genomes recovered from humans clustered together.**
- **S. Paratyphi B ST86 and Paratyphi B var. Java ST42, ST43, ST423 from aquatic animals were clustered with humans, respectively.**
- **These results indicated that aquatic animals are potential host and transmission vectors of Paratyphi B ST86 and its variants.**

Wang YN, et al. Natl Sci Rev. 2022.

中国疾病预防控制中心
CHINESE CENTER FOR DISEASE CONTROL AND PREVENTION

中国科学院微生物研究所
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Drivers and landscape of antibiotic resistome, virulome and mobilome in the *Salmonella* genome database of over 8,000 isolates in China

PART 05

Wang YN, et al. Unpublished data

Drivers and landscape of AMR in China

Monitoring longitudinal AMR data is essential not only for analyzing dynamic trends but also for the early identification of emerging resistance superbugs. However, most AMR surveillance studies on *Salmonella* from animals, humans, or the environment are limited in their spatial or temporal sampling and mostly focus solely on phenotypic or genomic data. Moreover, the association between AMR and climate, social and economic factors in China has rarely been investigated.

More importantly, a high-quality **C**hinese **L**ocal *Salmonella* **G**enome **D**ata**B**ase (CLSGDB) integrating human, animal (especially livestock, food animal, and aquatic products) and environmental sources based on the "One Health" strategy is lacking.

Wang YN, et al. Unpublished data

COVID-19 Impacts on *Salmonella* in the USA

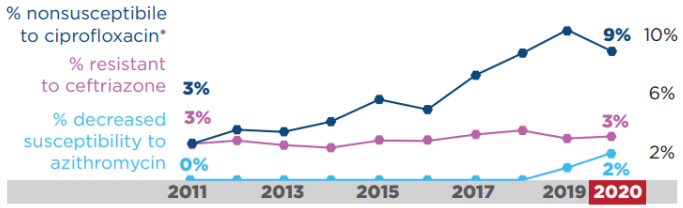
Drug-resistant nontyphoidal *Salmonella*

Spreads through contaminated food and water, or through contact with animals, their feces, and their environment

There were 22% fewer overall *Salmonella* infections (susceptible and resistant) reported during 2020 compared to the average annual incidence from 2017 through 2019. Some of the decrease could be attributed to pandemic behaviors, such as fewer restaurant meals, fewer emergency department visits for abdominal symptoms, and increased telehealth visits that may have reduced stool sample collection.

Understanding the full impact of the COVID-19 pandemic will require continued monitoring of data.

Resistance to ciprofloxacin continued to rise from 2016 through 2019, limiting treatment options.



Data from 2018–2020 are preliminary. Excludes *Salmonella* Typhi and Paratyphi. *Fully or partially resistant to ciprofloxacin.

In 2020, 14% of *Salmonella* infections were resistant to at least one antibiotic used to treat severe infection. This was a 3% decrease from 2019. There were also fewer overall *Salmonella* infections reported in 2020, likely because of factors related to the COVID-19 pandemic.

What's Next

- Prior to the pandemic, resistant *Salmonella* infections were on the rise, making it more difficult to treat the most severe of these infections.
- Continued prevention efforts are needed as the world moves beyond COVID-19, including reducing contamination along the food chain, especially for chicken and other meats and vegetables.
- People can protect themselves by washing hands and following food safety practices.

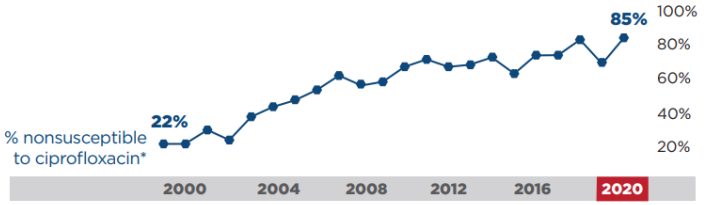
Drug-resistant *Salmonella* serotype Typhi

Spreads through contaminated water, food washed with contaminated water, and person-to-person contact

The number of reported overall Typhi infections (susceptible and resistant) in 2020 was less than half the average annual incidence from 2017 through 2019. Most typhoid cases in the U.S. are acquired during international travel. The decrease is potentially attributed to decreased exposure due to limited travel in 2020.

Although the number of cases and international travel declined in 2020, cases did continue occurring in international travelers, especially to Pakistan. Since 2018, cases of extensively drug-resistant (XDR) Typhi have been on the rise, including among people who traveled to Pakistan and those who did not.

Salmonella Typhi infections require antibiotic treatment to recover from illness. Ciprofloxacin resistance has been increasing since 2002.



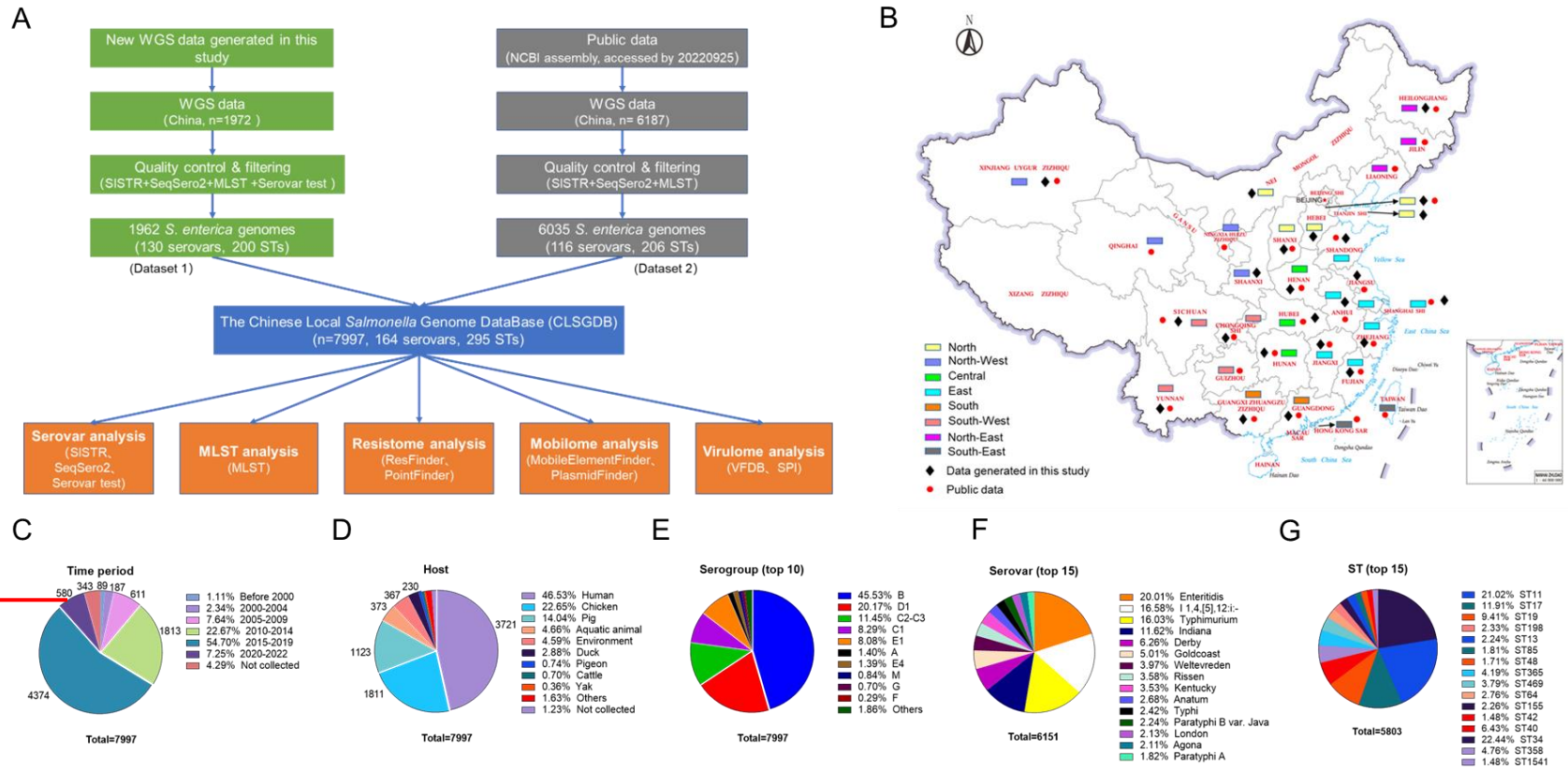
Data from 2018–2020 are preliminary. *Fully or partially resistant to ciprofloxacin.

In 2020, 85% of *Salmonella* Typhi infections were resistant (fully or partially) to ciprofloxacin, severely limiting treatment options.

What's Next

- Increasing resistance indicates a need for increased awareness of prevention measures during travel, such as vaccination and safe eating and drinking practices. Understanding the full impact of COVID-19 will require continued monitoring of data.
- Data also highlight the critical need for continued close monitoring, because infections will increase when international travel increases post-pandemic and may continue to drive resistance levels even higher.
- Further studies are needed to understand the sources of XDR Typhi infections among U.S. residents without international travel.

Construction of the Chinese local *Salmonella* genome database

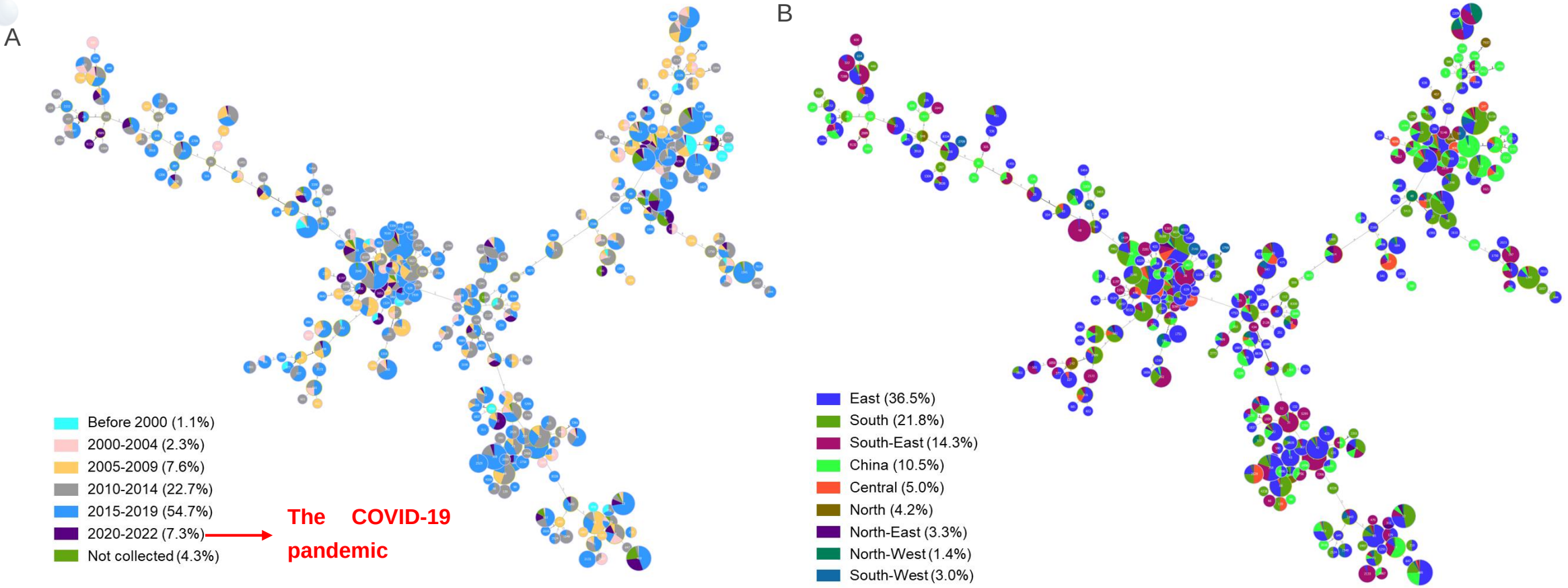


The COVID-19 pandemic

- **To our knowledge, we build the largest Chinese local *Salmonella* genome database (CLSGDB) using 8159 *Salmonella* assembly genomes (1972 from our laboratory and 6187 from the public database) from human, animal and environments in 30 Chinese provinces between 1905 and 2022.**

Wang YN, et al. Unpublished data

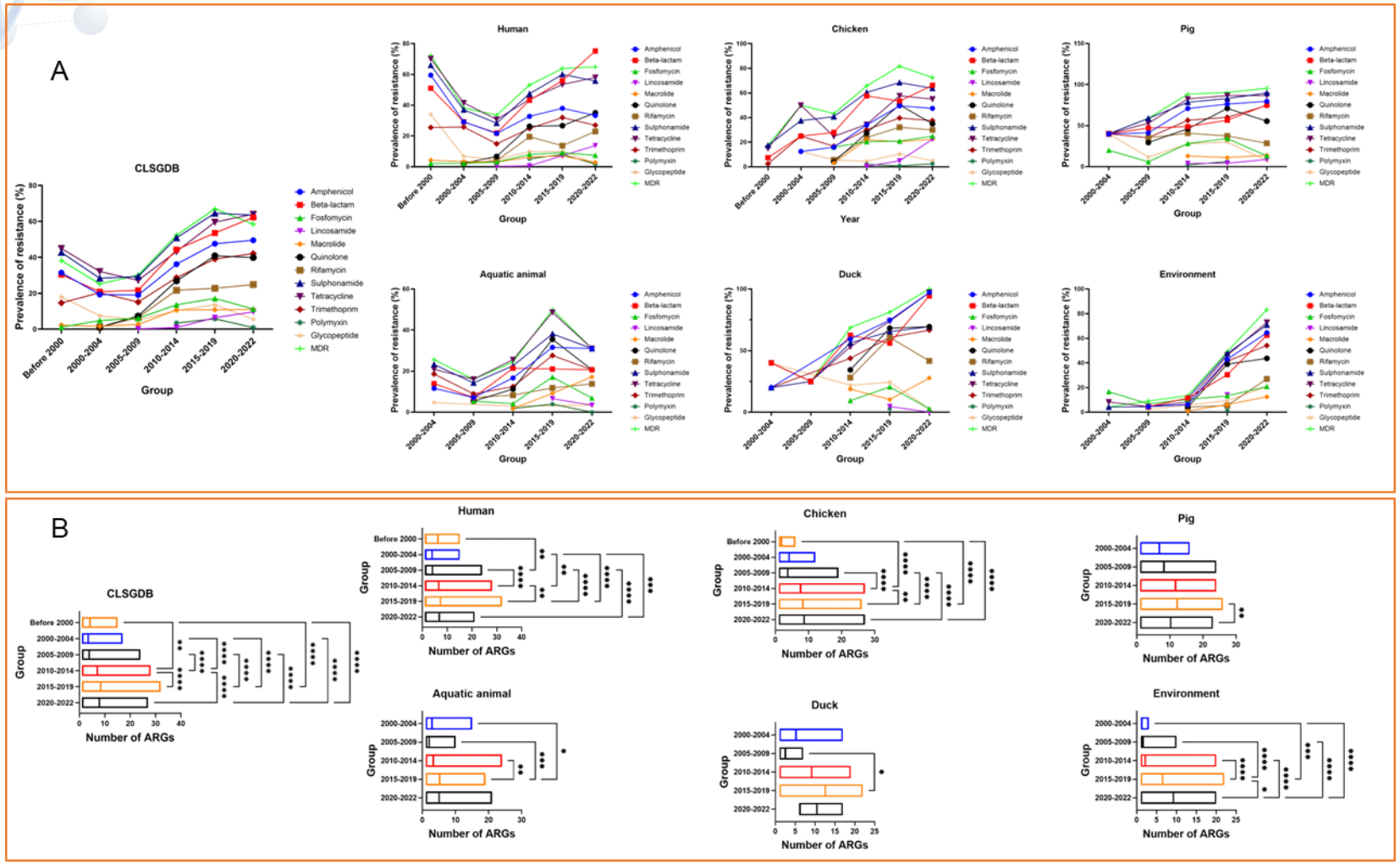
Multi-locus sequence type diversity and patterns



- A total of 295 STs were identified, 33.90% of the STs (100/295) were represented by a single isolate.
- ST34 was the most frequently identified and encompassed 1302 isolates across six chronological datasets.

Wang YN, et al. Unpublished data

Temporal changes of AMR and ARGs



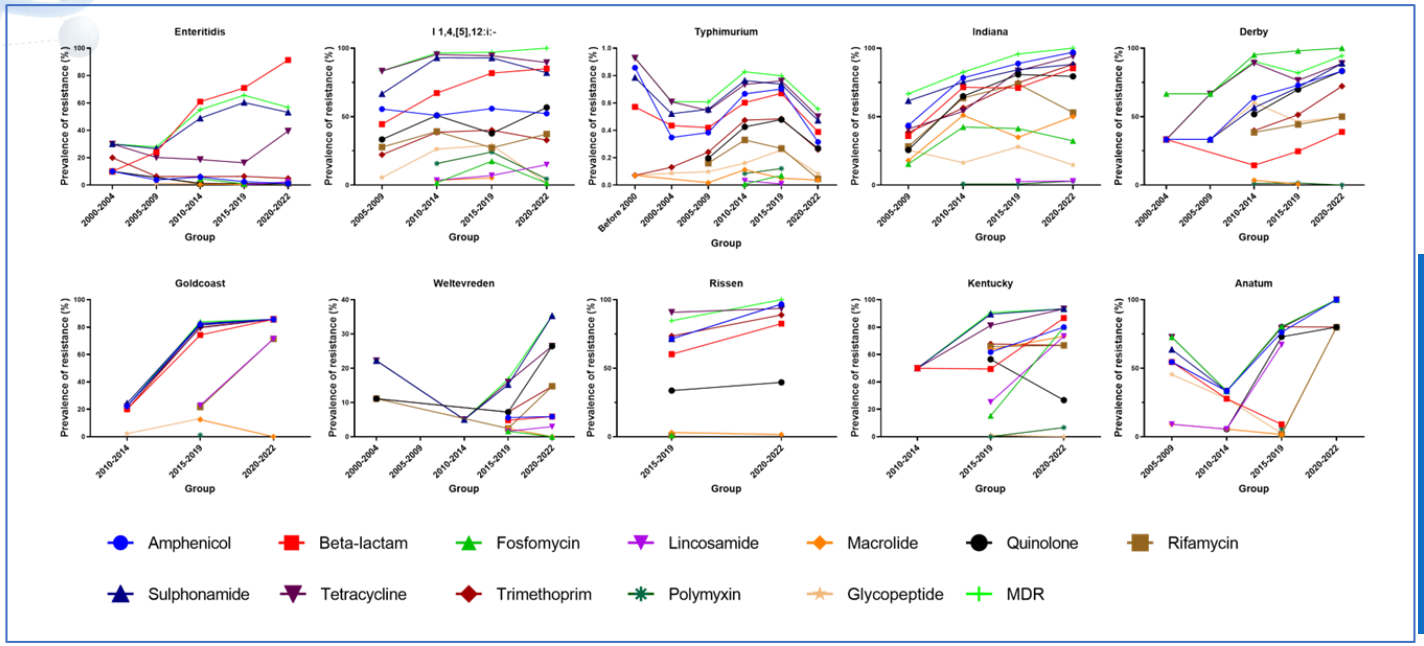
2020-2022 ⟶ The COVID-19 pandemic

- We observed an increasing trend in AMR during the recent 22-year time span.
- Notably, the trend of AMR *Salmonella* from environment has shown an alarming rise since 2010.

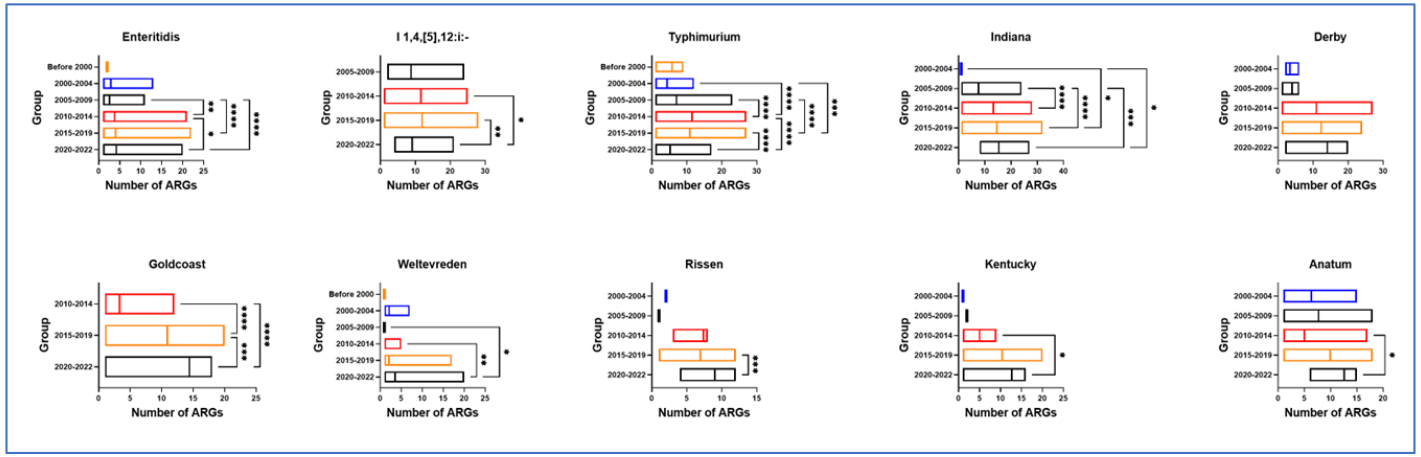
Wang YN, et al. Unpublished data

Temporal changes of AMR and ARGs

A



B

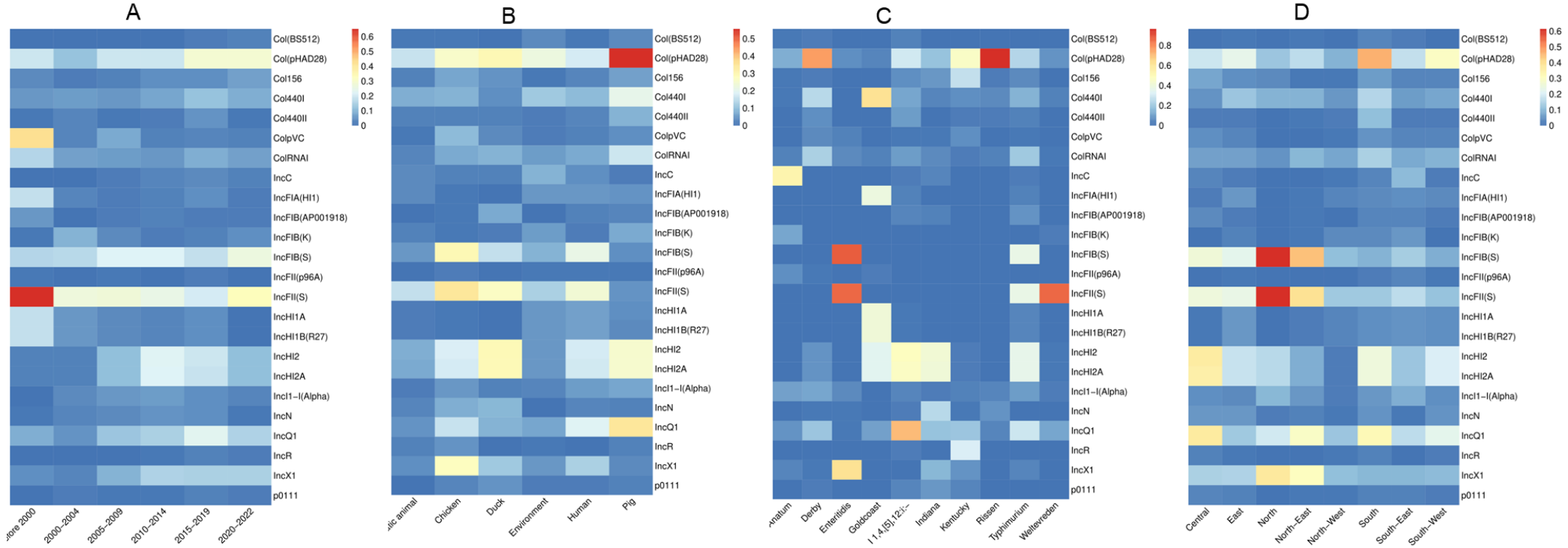


2020-2022 ⟶ The COVID-19 pandemic

- The rates of resistance to β-lactam rose rapidly since 2005-2009 in *S.* Enteritidis, *S.* I 1,4,[5],12:i:-, *S.* Indiana, but decreased in *S.* Anatum.
- The number of ARGs per genome in 2020-2022 showed a significant downward trend than 2015-2019 in *S.* Typhimurium and *S.* I 1,4,[5],12:i:-.

Wang YN, et al. Unpublished data

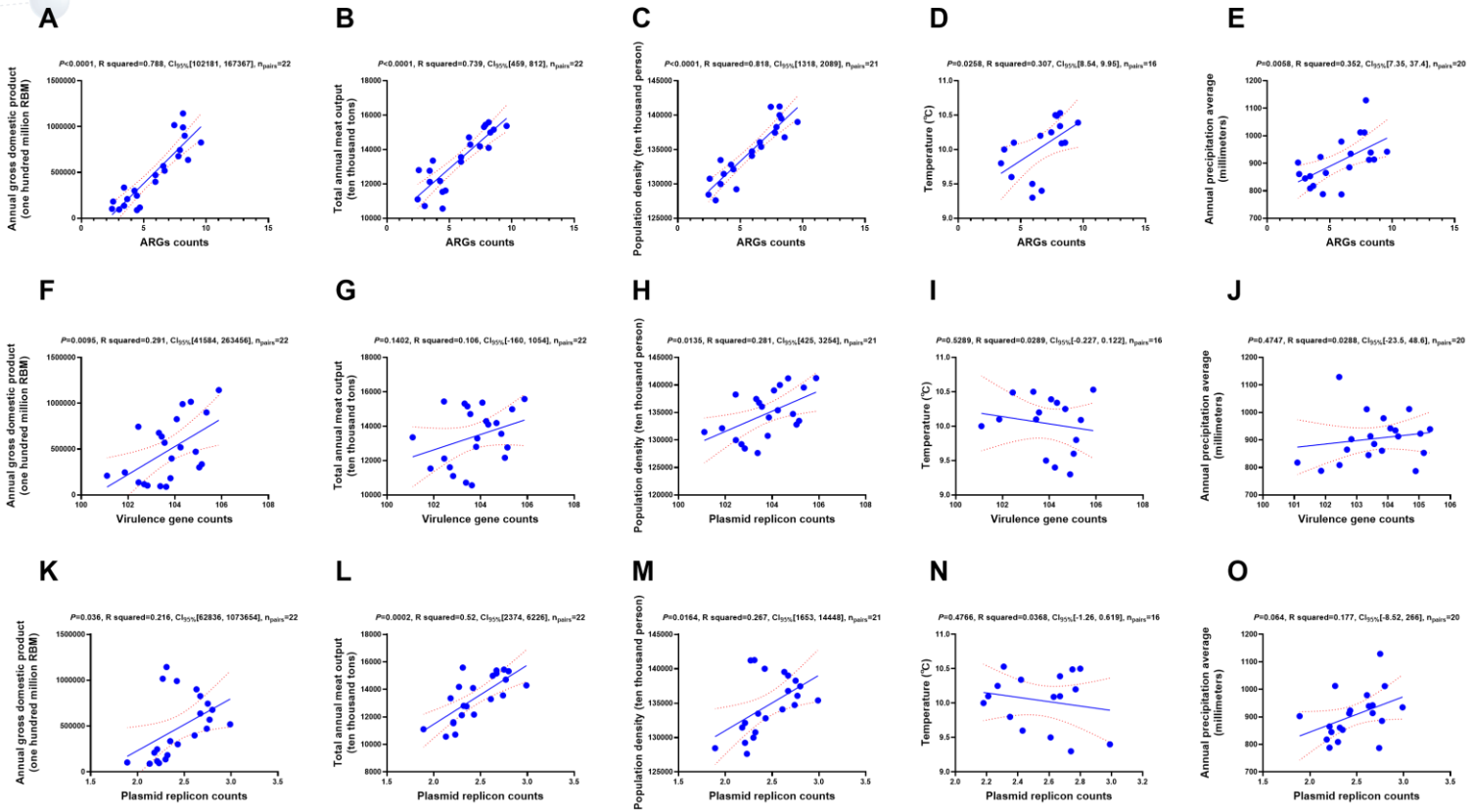
Temporal changes of plasmid-associated replicons



- A total of 16923 plasmid replicons classified into 86 types were identified in the CLSGDB, replicons that were detected at >1% prevalence in *Salmonella* genomes in the CLSGDB are shown.
- The prevalence of several ARG-associated plasmids, such as IncHI2, IncHI2A, IncQ1, and IncX1were significantly higher in 2005-2009 than in before 2000.
- Significant differences were observed among isolates from different serovars and geographic regions.

Wang YN, et al. Unpublished data

Correlation analysis of the climate, social and economic factors with ARGs, VGs and MGEs

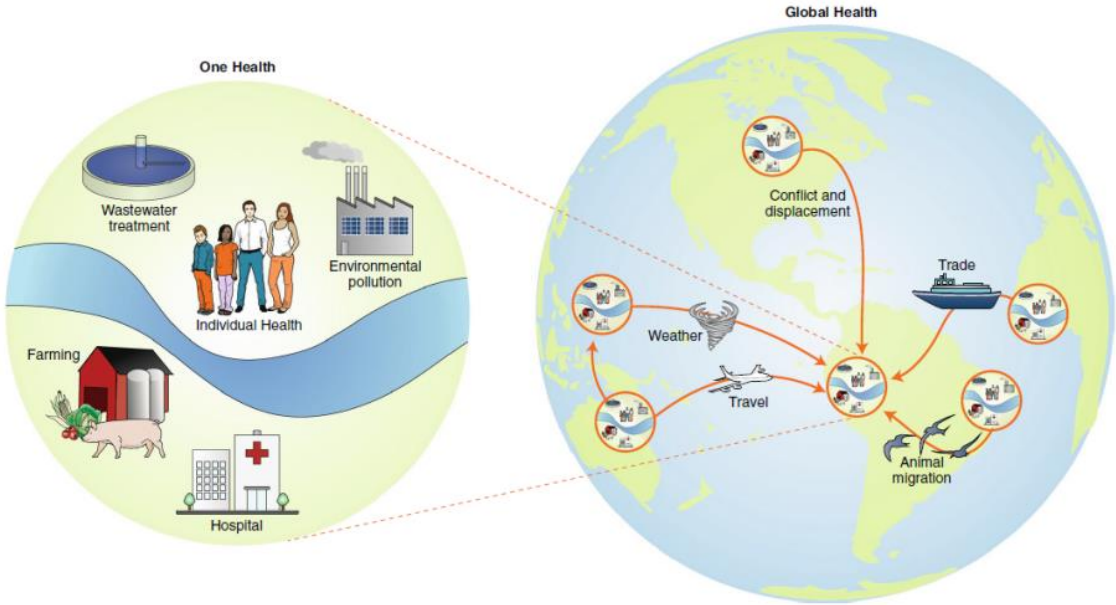


- The gross domestic product (GDP) value, gross output of meat, population density, annual mean temperature and annual mean precipitation were positively correlated with the detected average ARG counts.
- The GDP and population density were positively correlated with the detected average VG counts.
- The GDP, gross output of meat and population density were positively correlated with the average plasmid-associated replicon counts.

N pairs = 22 including 2000-2021; N pairs = 21 including 2001-2021

Wang YN, et al. Unpublished data

Future and outlook



One World, One Health

Metagenomics + Culturomics + Next-generation sequencing

Hernando-Amado S, et al. Nat Microbiol, 2019.

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CHINESE ACADEMY OF SCIENCES

谢谢！

George F. Gao