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RAFA 2019

Emergence of Antibiotic-Resistant *Salmonella* in China

2019-11-06

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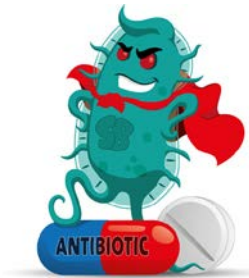
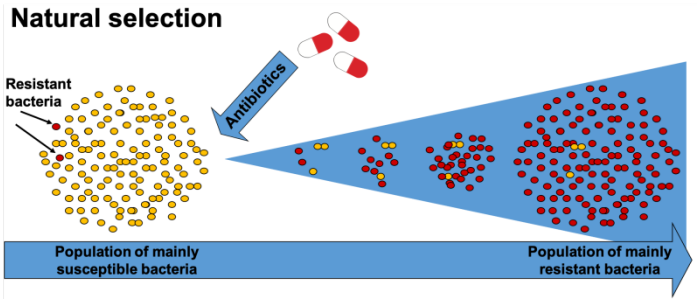
China National Centre For Food Safety Risk Assessment

Prague, Czech Republic

Contents

- ✓ Brief overview of the antibiotic usage in livestock industry
- ✓ Emergence of Antibiotic-Resistant *Salmonella* in China
- ✓ Better tackling AMR in one-health way





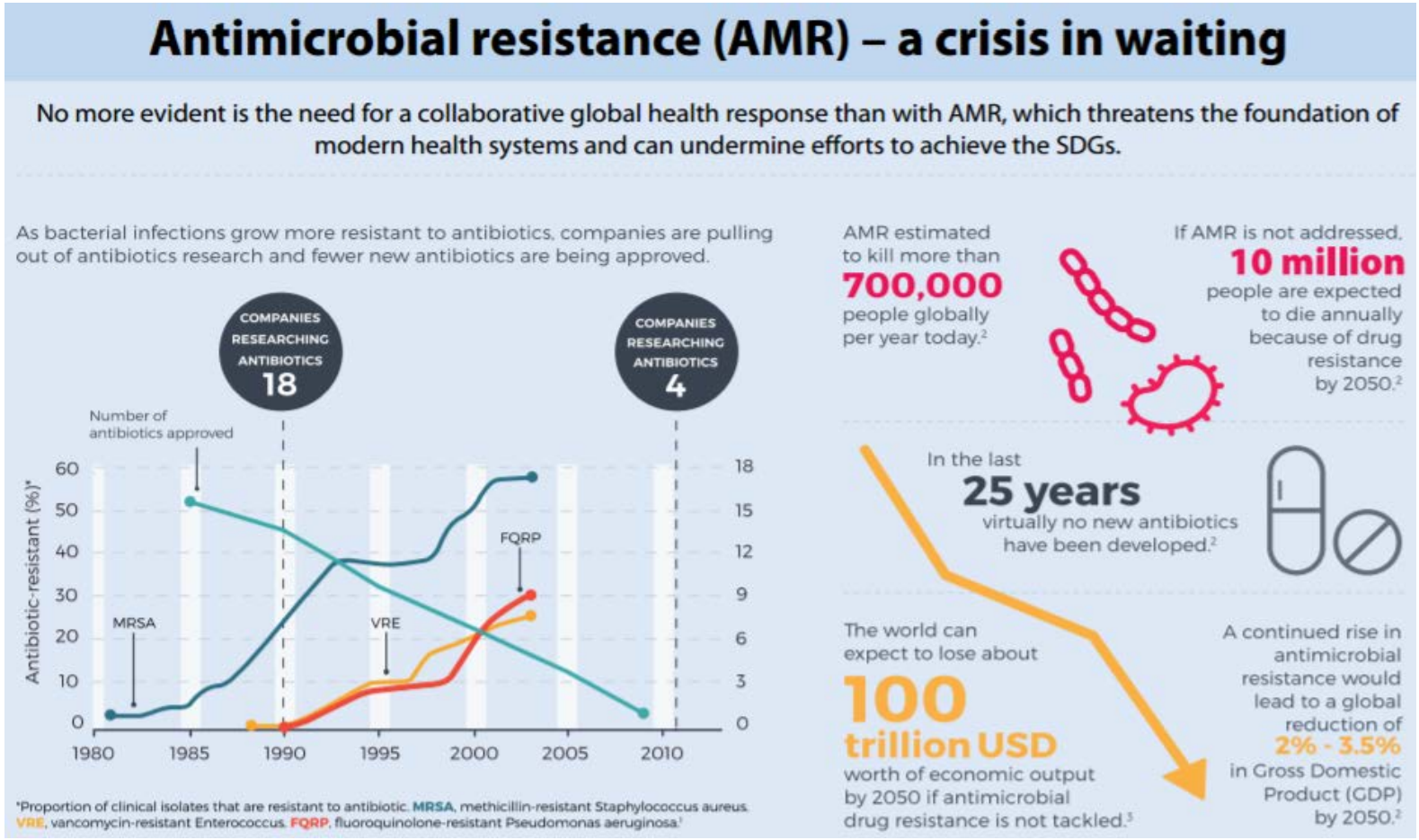
AMR had been listed as a serious threat of global public health by WHO

Antimicrobial resistance (AMR)

a declining effectiveness of medicines to treat bacterial infections

Serious threats

Global health development and food security



Data from：O' Neill, J, 2016; WHO, 2016

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a declining effectiveness of medicines to treat bacterial infections

Serious threats

Global health development and food security

Data from：O' Neill, J, 2016; WHO, 2016

The usage of antibiotics in farm animals

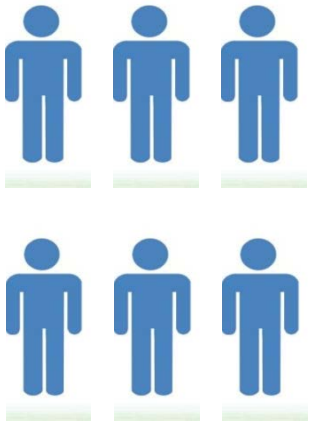
An important and irreplaceable **role** in animal production
Over **70%** of antibiotics used in food-producing animal

therapeutic

Antibiotics

productive

Antimicrobial residues



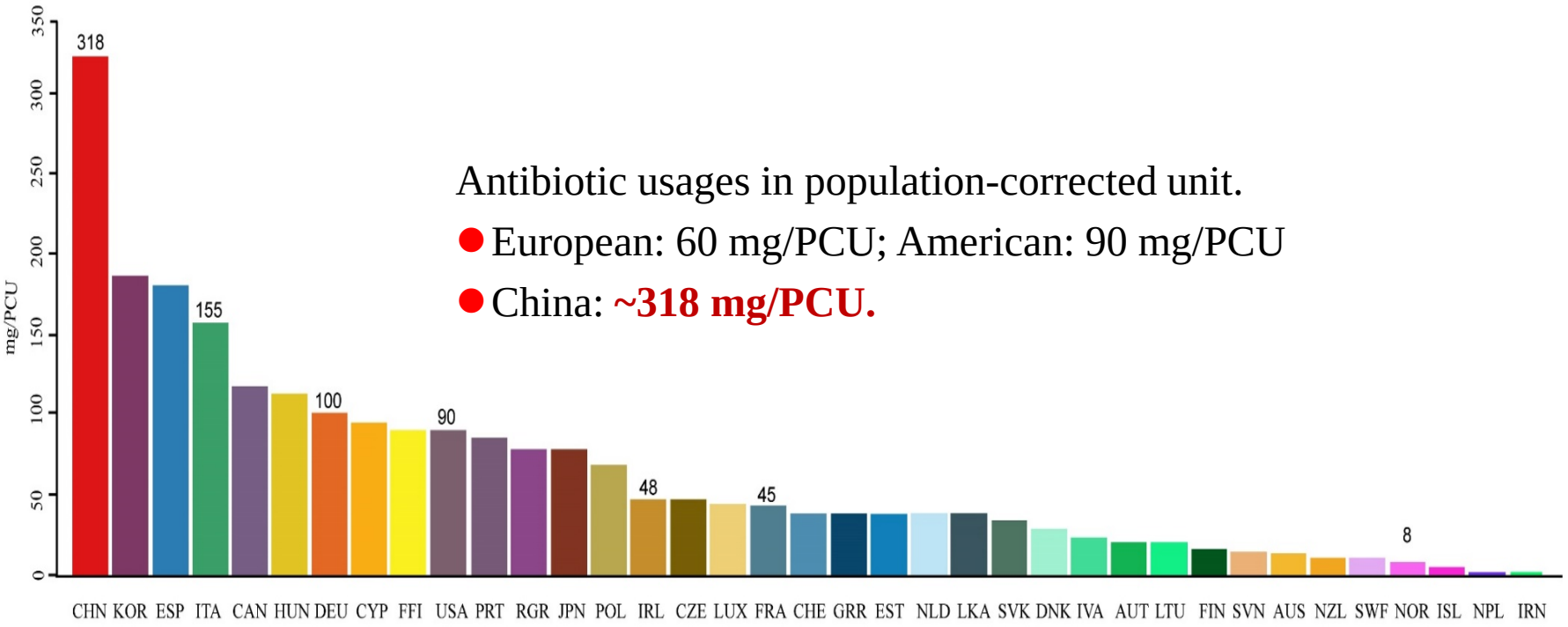
Antimicrobial resistance

Spread from farm to the table

The usage of antibiotics in farm animals in China ranks the top of the world

At least **80,000 tons** of antibacterial drugs were used in animals per year

60% of the antibacterial drugs were used as feed additive（**growth promotion**）



Antibiotic usages in population-corrected unit.

- European: 60 mg/PCU; American: 90 mg/PCU
- China: **~318 mg/PCU.**

Consumption levels varied considerably between countries

Science 357, 1350 (2017)

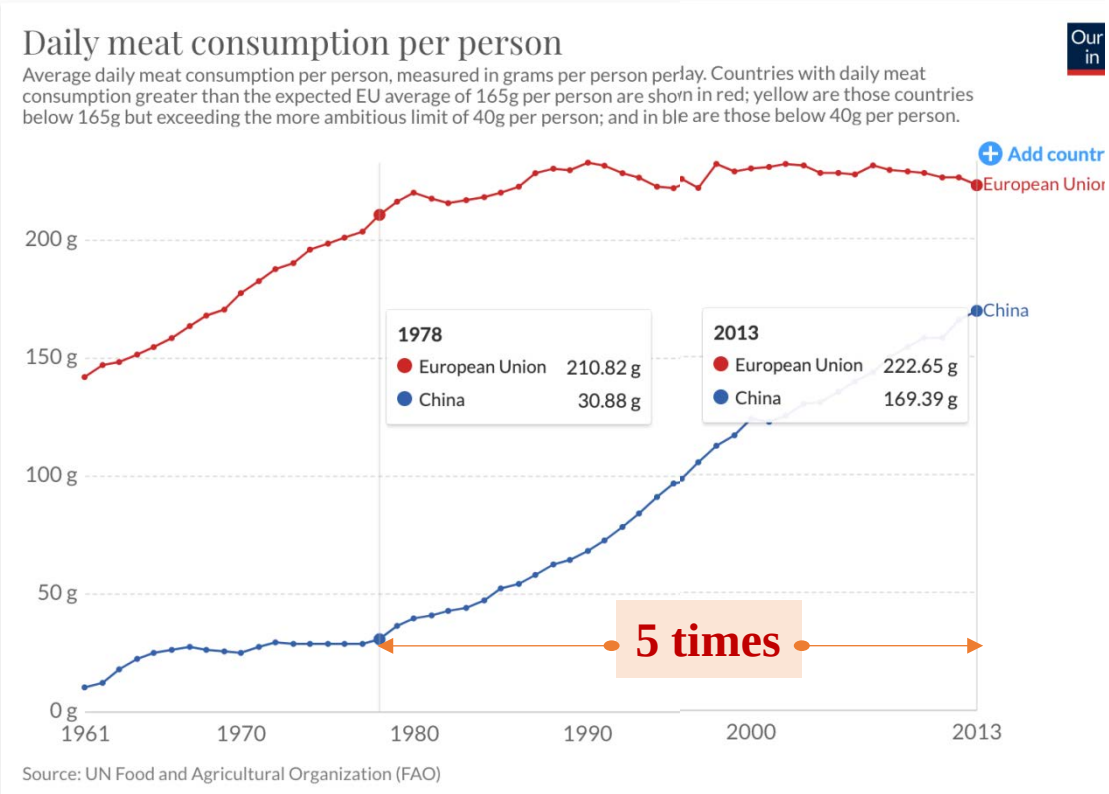
Daily meat consumption per person

EU

CHINA

meat

antibiotics



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- ✓ Emergence of Antibiotic-Resistant *Salmonella* in China
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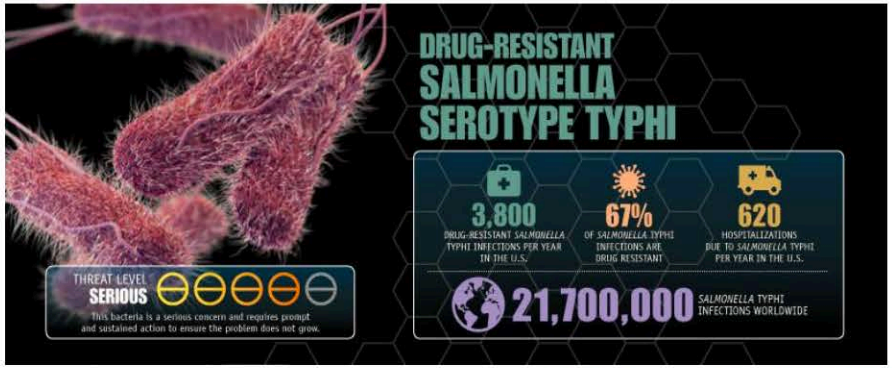
Salmonella

Salmonella enterica remains an important foodborne pathogen in all regions of the world

Mortality and morbidity caused by *Salmonella* infection represent a considerable burden in both developing and developed countries

In 2013, among the 18 kinds of **drug-resistant bacteria** threatened by CDC in the United States, salmonellosis with drug resistance was rated as **"serious"**



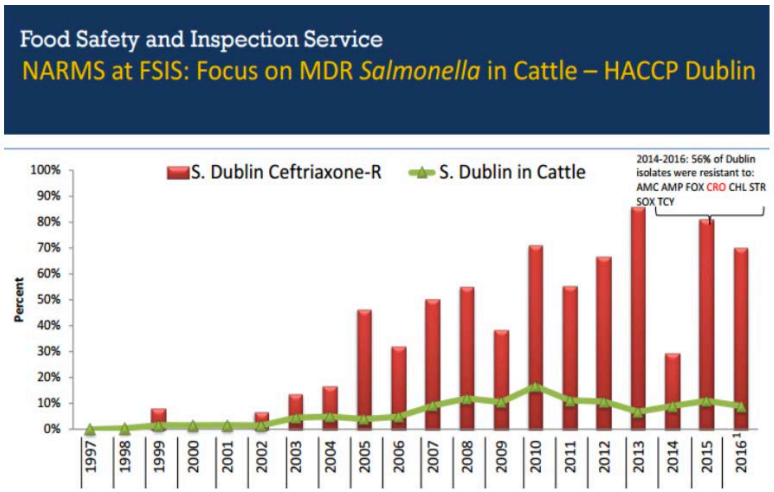
Data from: the US CDC

Salmonella

The resistance level of *Salmonella* in livestock in Europe and America is increasing year by year

Data from： EFSA，2019

MDR Multi-drug resistant



Data from： NARMS report，2015

Centers for Disease Control and Prevention
CDC 24/7: Saving Lives, Protecting People™

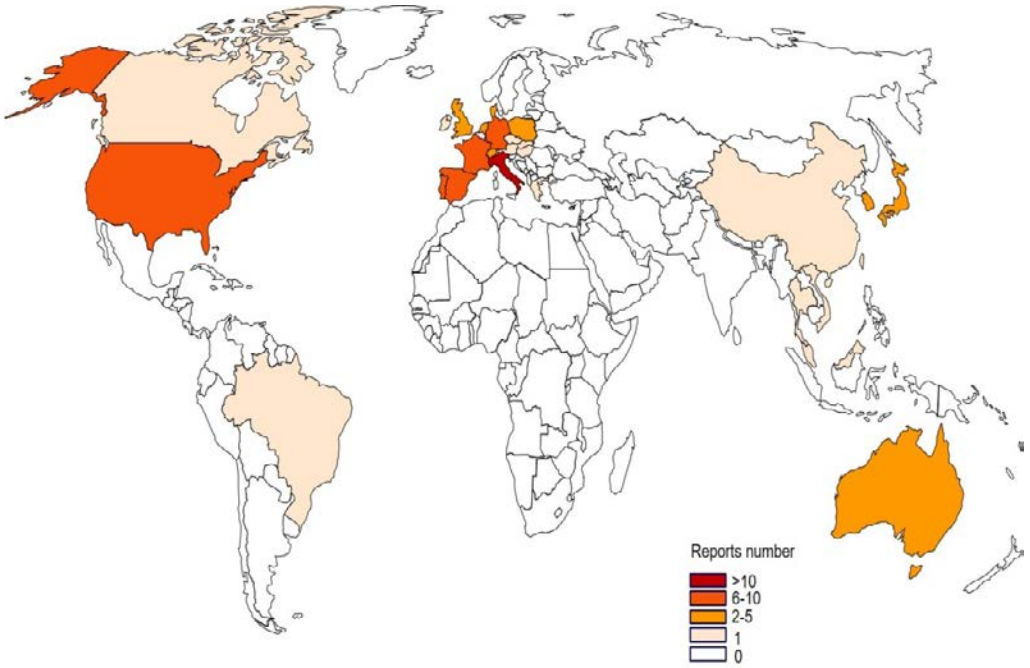
CDC Current Outbreak List

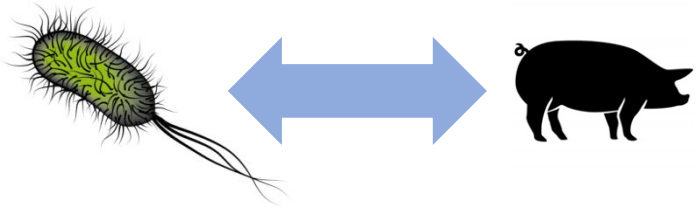
- **MDR** *Salmonella* Infections 2018
- **MDR** *Salmonella* Infections 2017
- **MDR** *Salmonella* Infections 2017

https://www.cdc.gov/outbreaks/

Global hazard of MDR monophasic *Salmonella* Typhimurium

Monophasic Variant of *S.* Typhimurium
lack of expression of the flagellar phase（***fliB***）
Animal and human infections





Two dominant clones

Spanish clone ST19
MDR-ACSuGSTSxT
plasmid/*spv*
Heavy mental
U302 1997

European clone ST34
MDR-ASSuT
Chromosome
Heavy mental
DT193 DT120 2005

Clinical Infectious Diseases, 2018,.66 (6)
Emerging Infectious Diseases, 2017,23(2):204-11
Emerging Infectious Diseases, 2018,40(4):751-753

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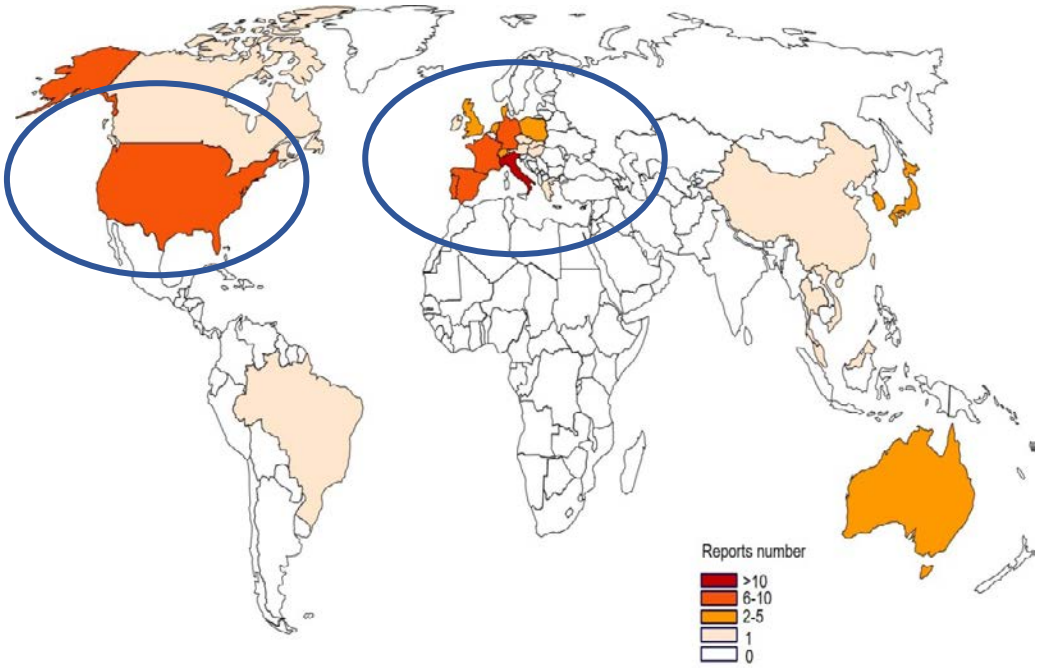

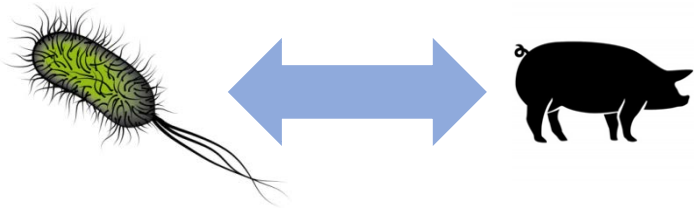

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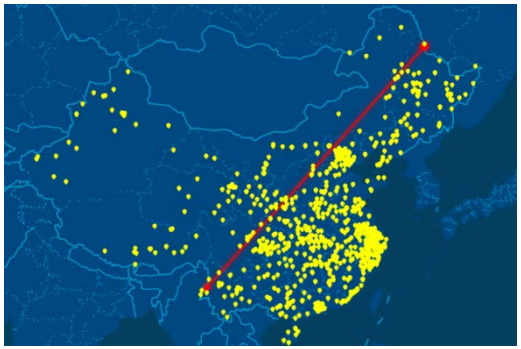
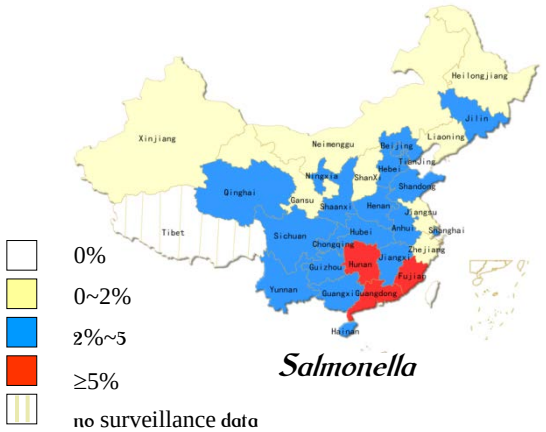
TraNet in China

Active-surveillance based on the lab

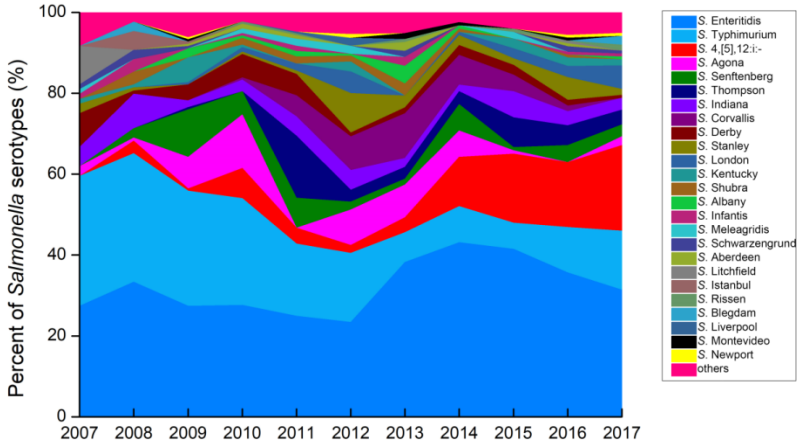
703 sentinel hospital

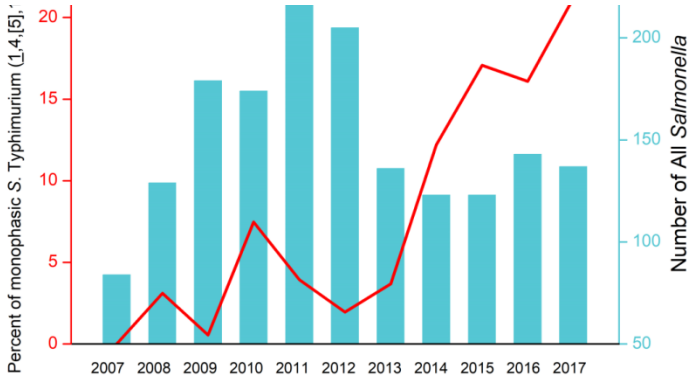


National molecular tracing network for foodborne disease surveillance



Monophysic *Salmonella* Typhimurium





Frontiers of Medicine, 2018 , 12 (1) :48-57

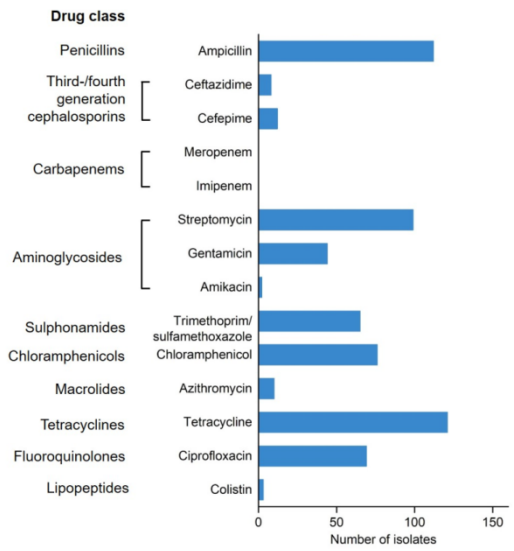
Objectives-

- Whether the Monophasic *S.* Typhimurium isolates in China are part of **a single epidemic**
- How they are **related** to previously Monophasic *S.* Typhimurium strains
- Genetic **diversity** of strains circulating in **humans**

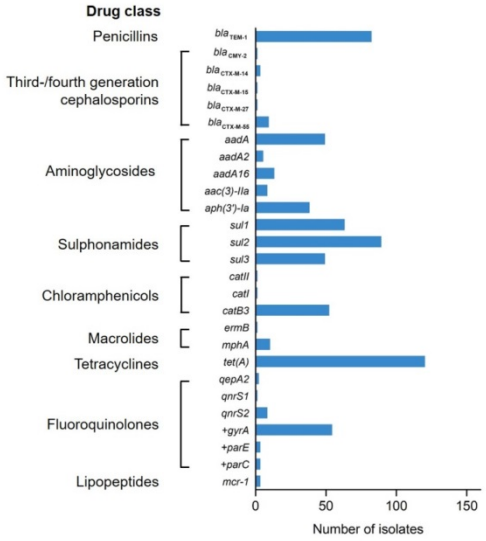
Phenotypic and genotypic characteristics of AMR

105 monophasic isolates from TraNet

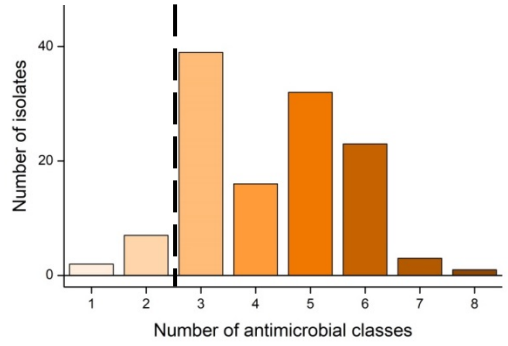
Sequence type: ST34



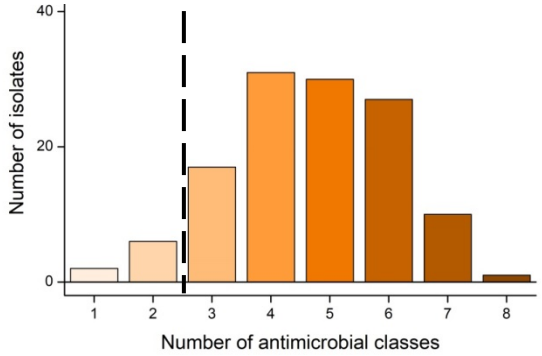
ASSuT

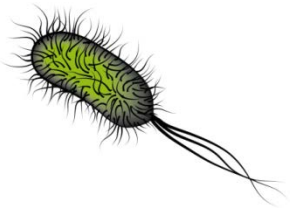


ASSuT



>90% MDR





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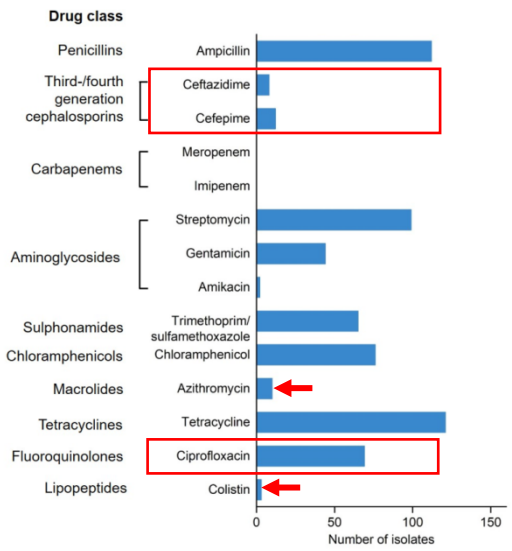

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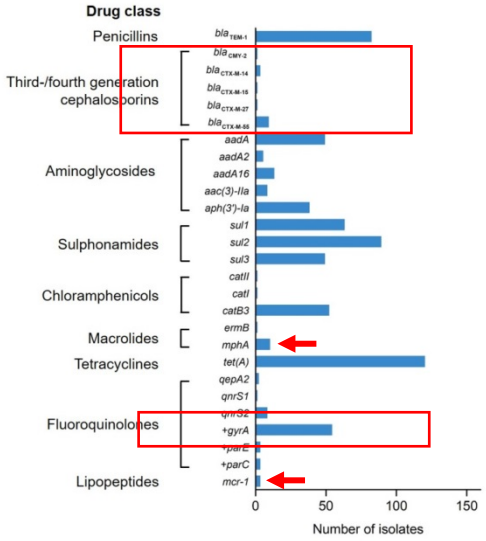

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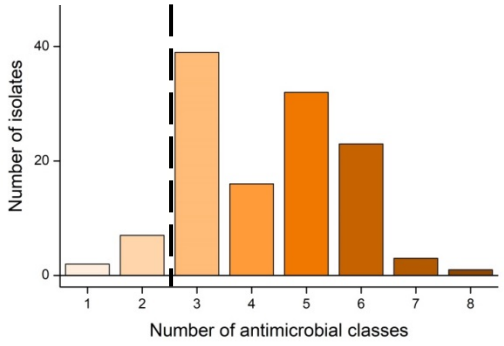

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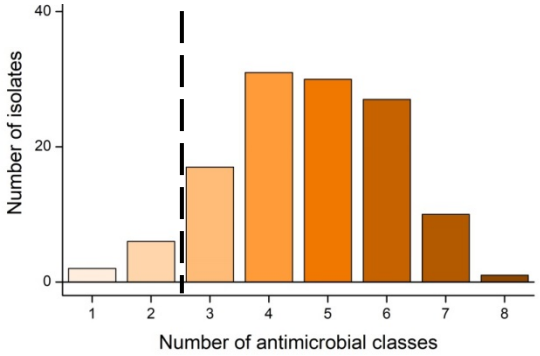
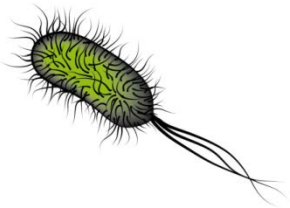
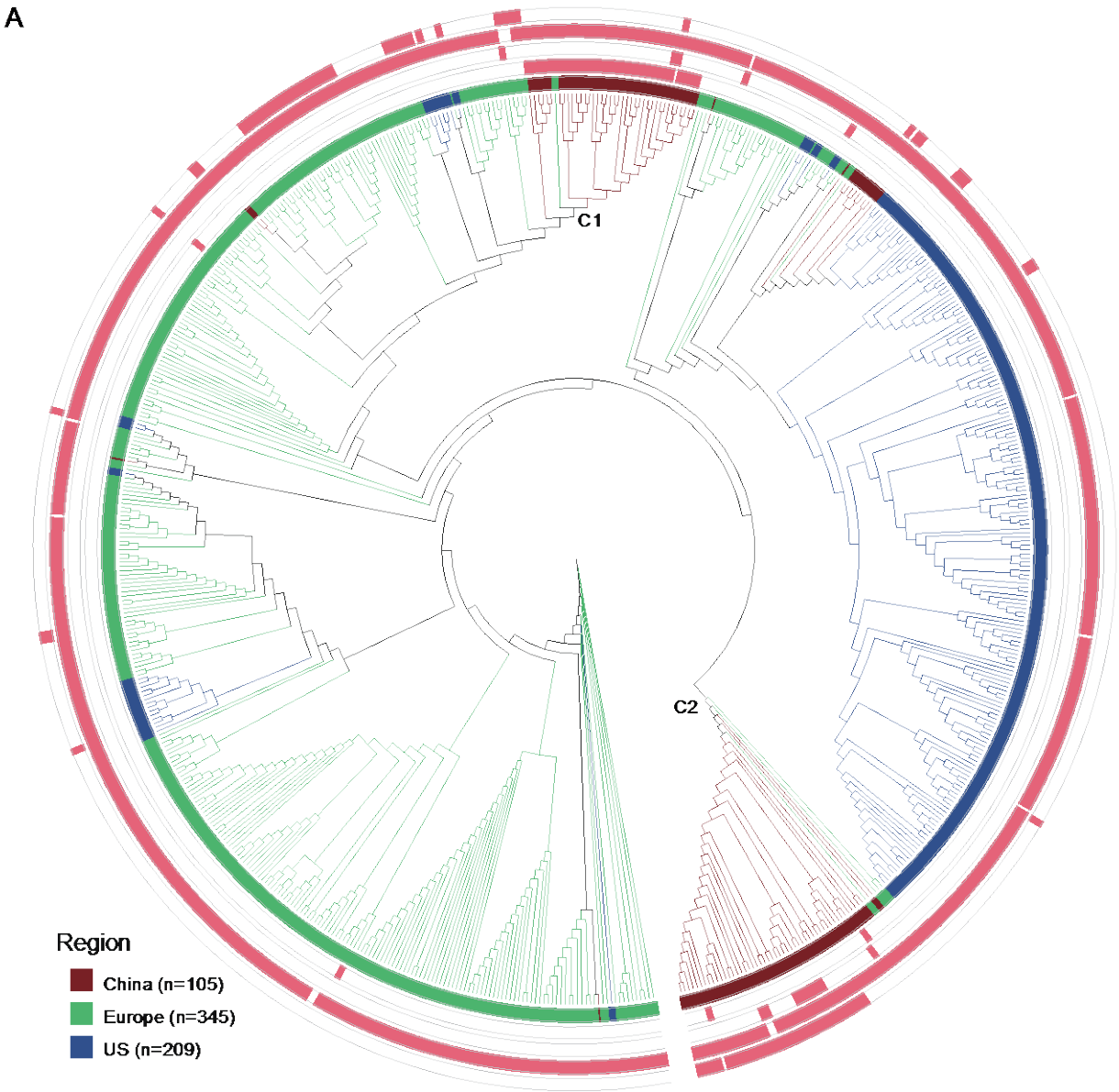




Origin of the Monophysic *S.* Typhimurium ST34 in China



Region	Number
China	105
Europe	345
USA	209

China

Europe

USA

A maximum likelihood phylogenetic tree

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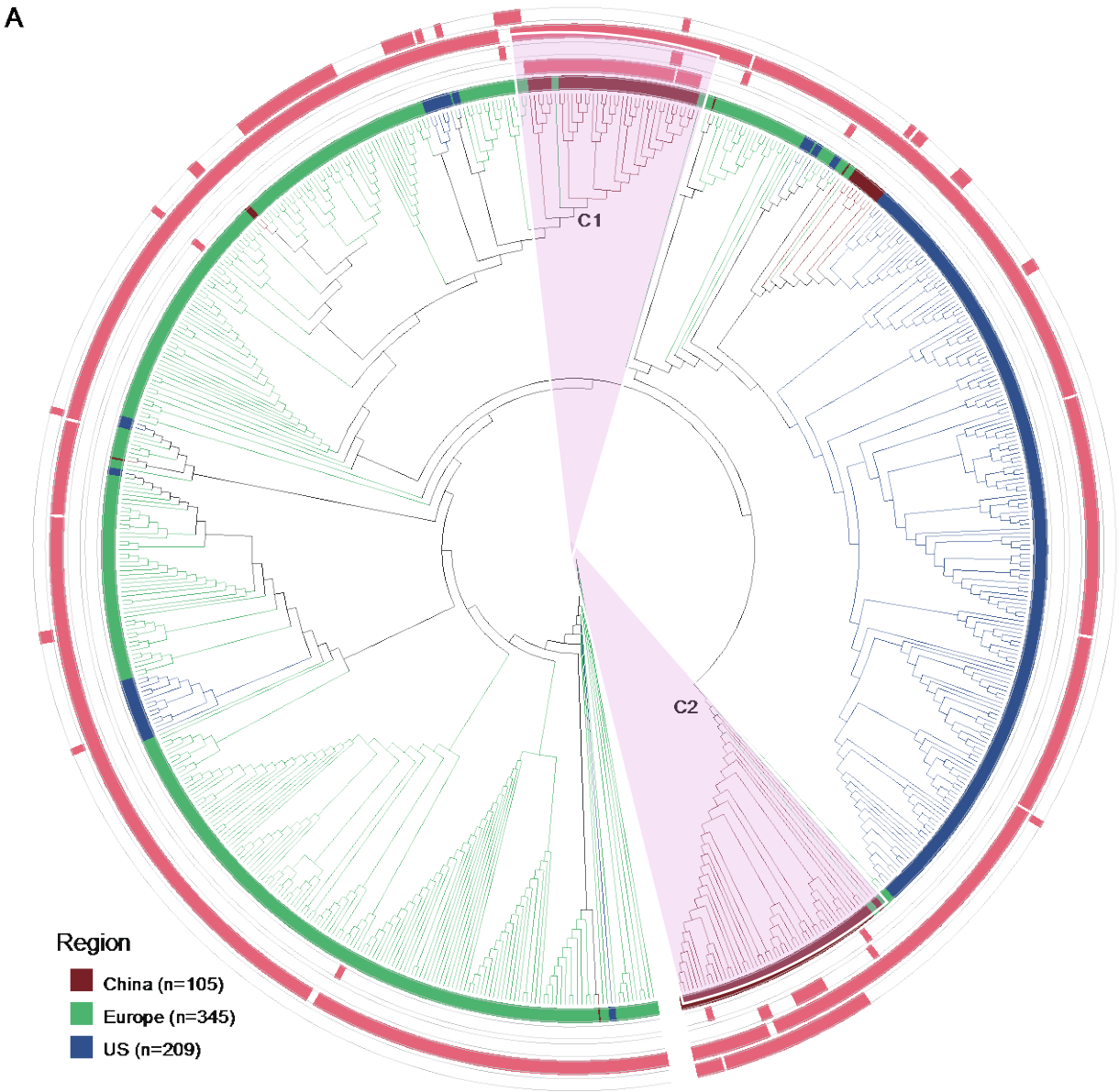

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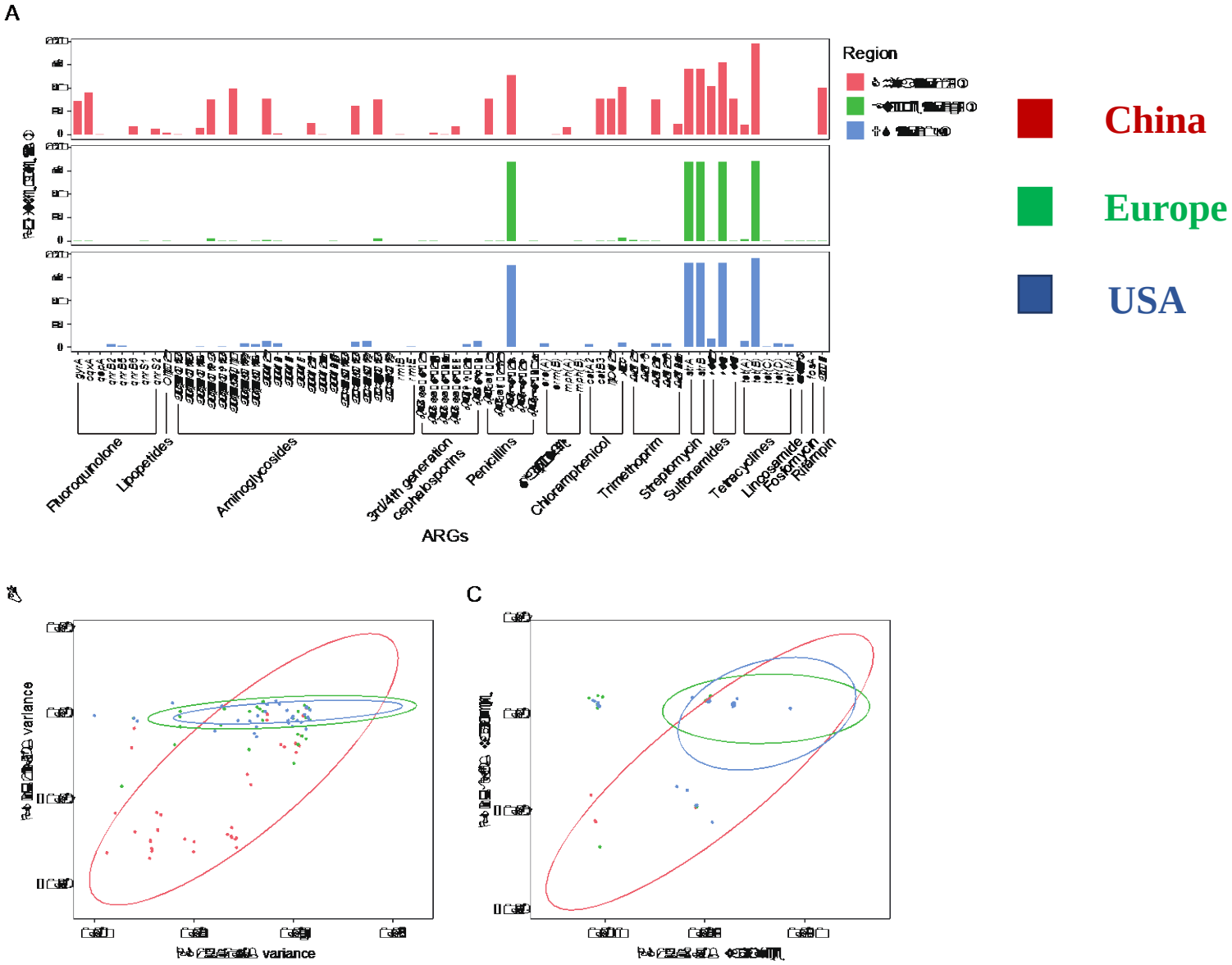
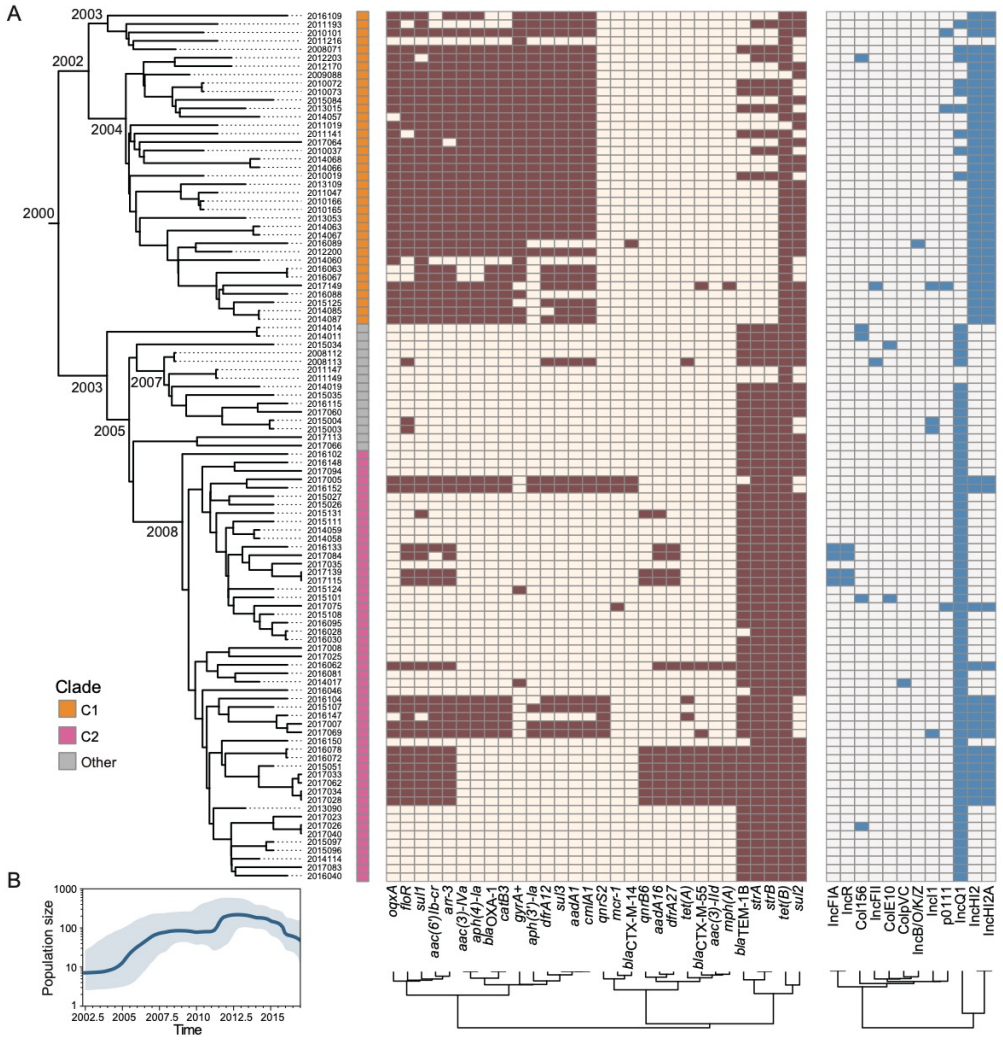
USA

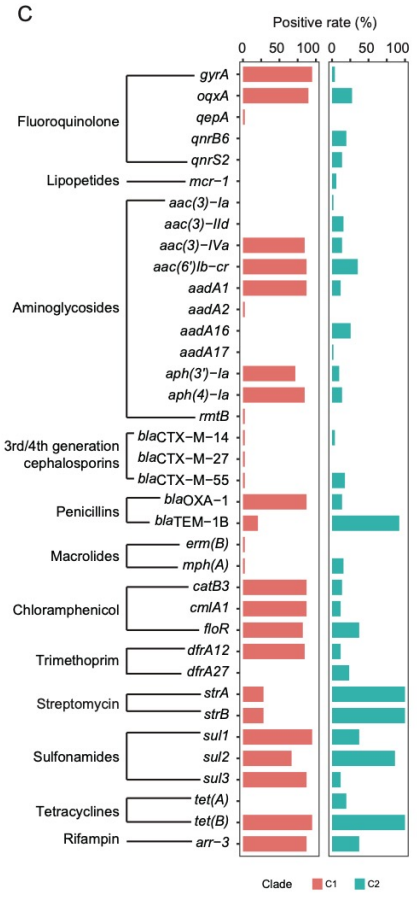
A maximum likelihood phylogenetic tree

High carriage rate of resistance genes



Two distinct clades with different features of resistances





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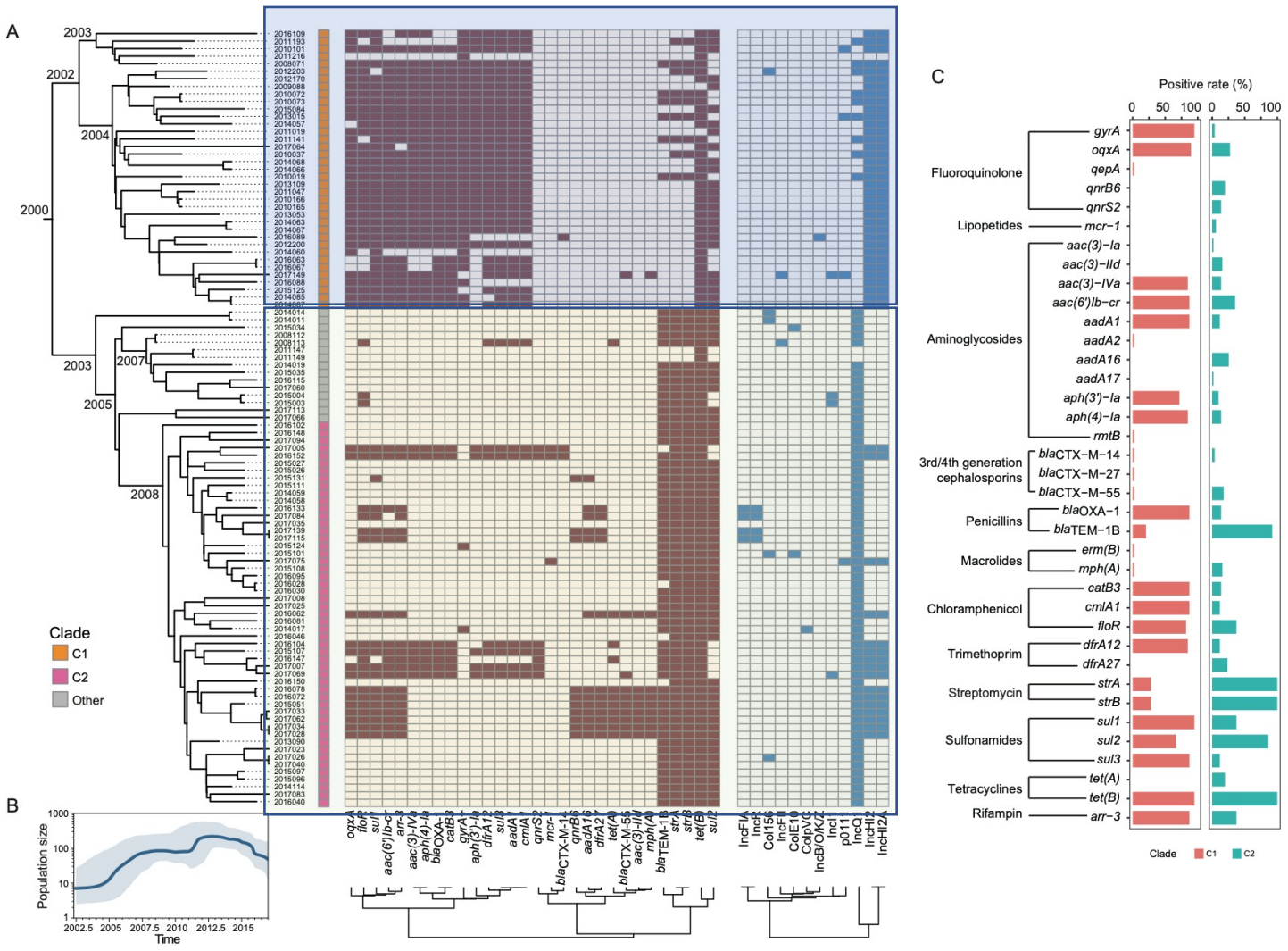

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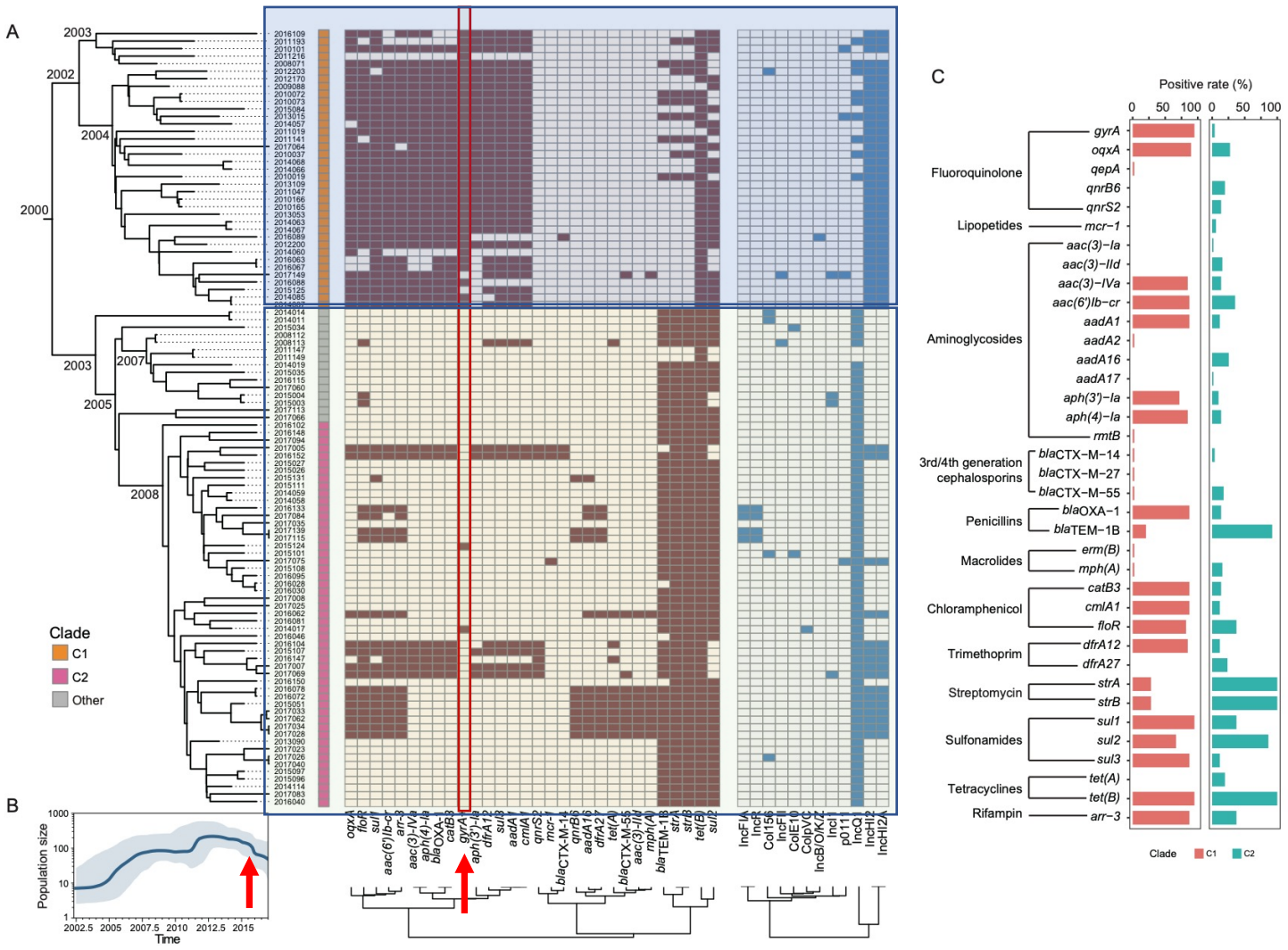

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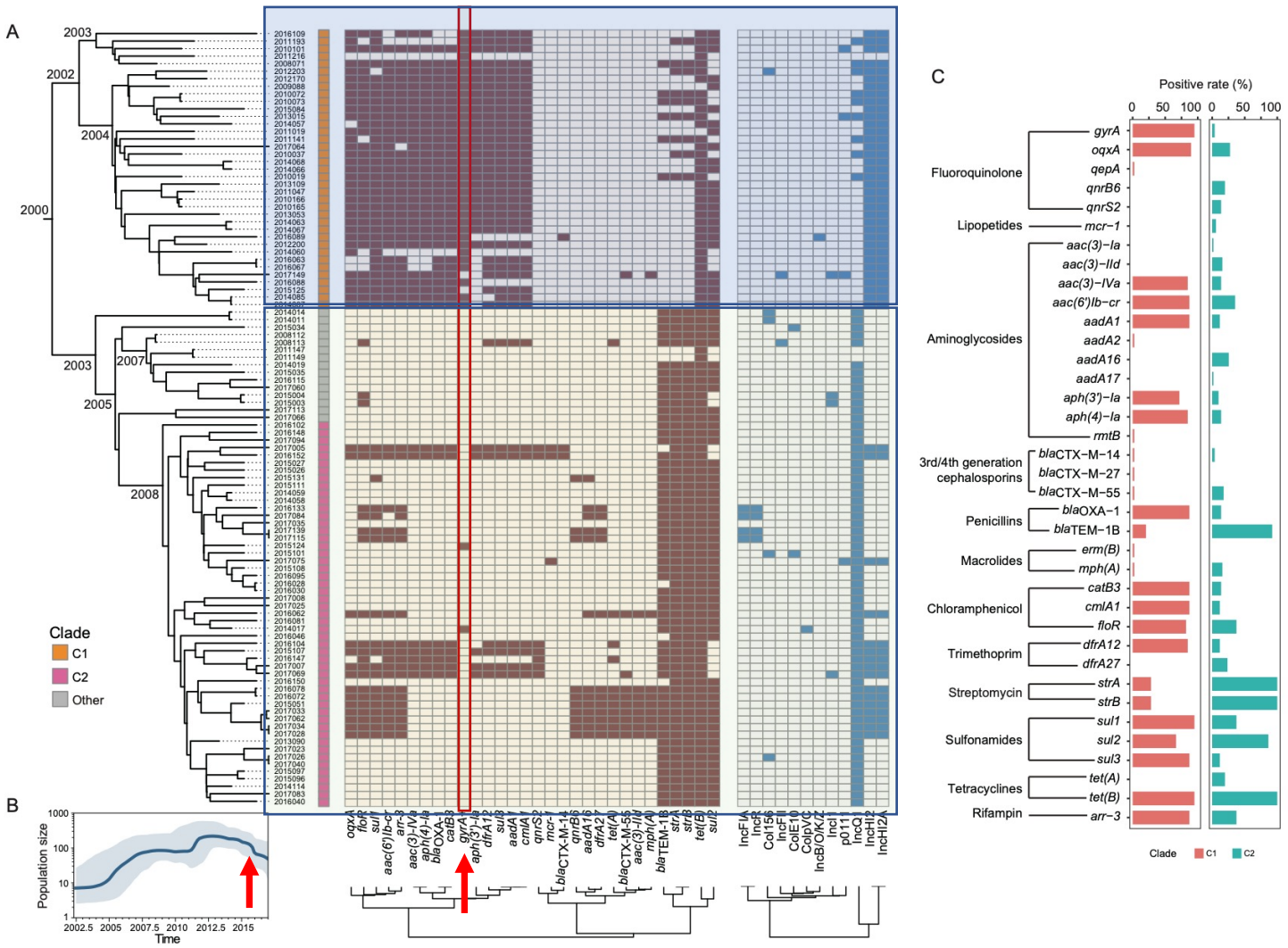
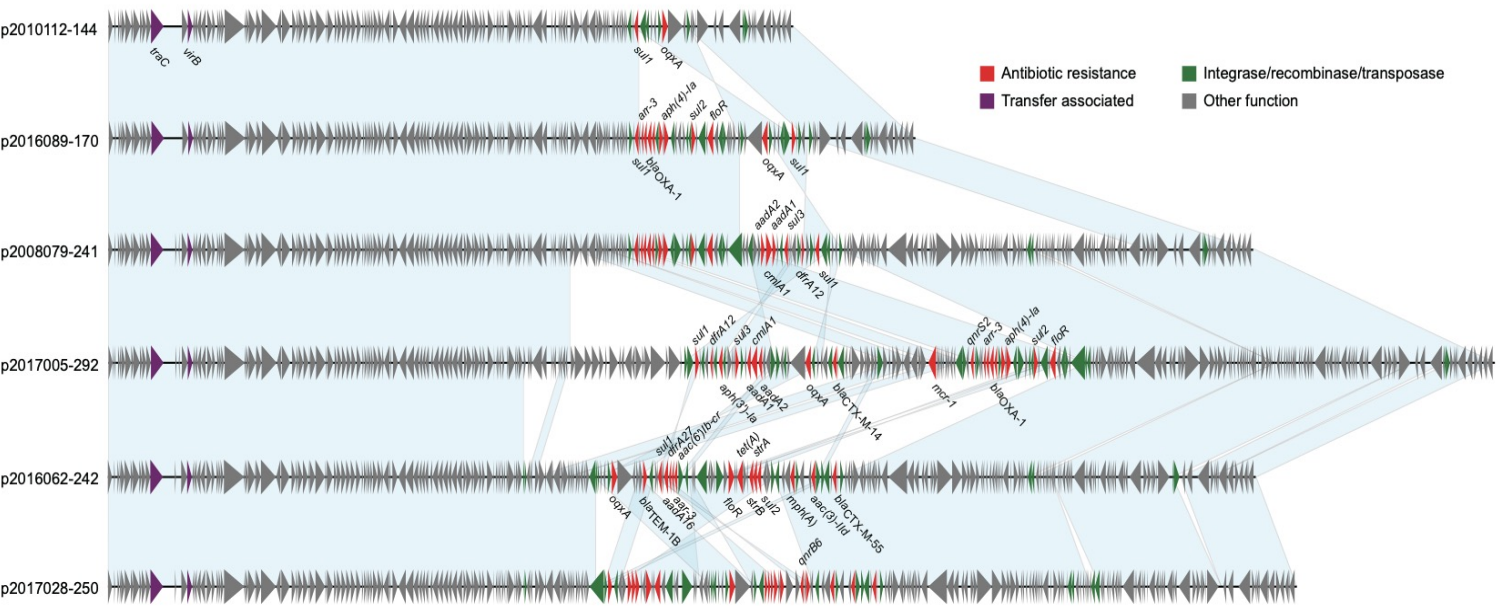
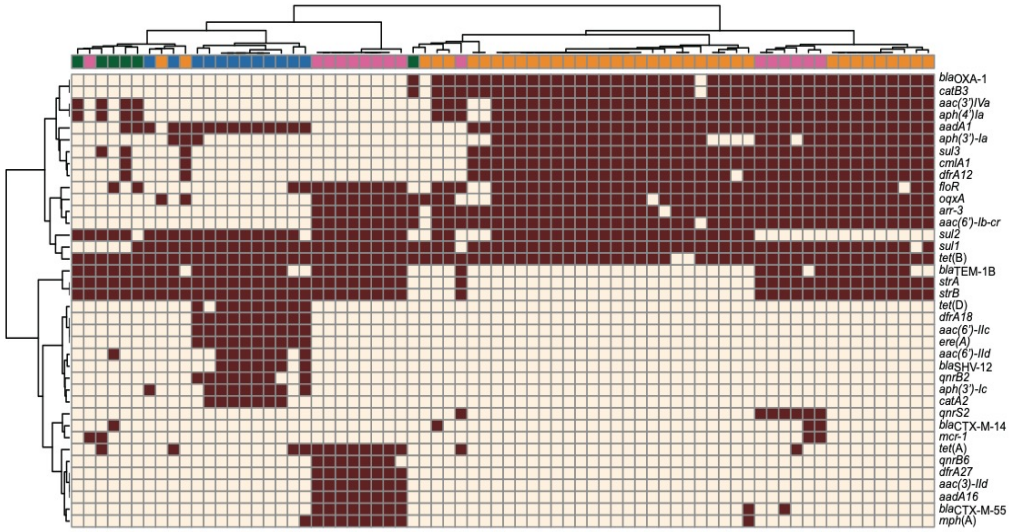


Policy is really important

Plasmids IncHI2/IncHI2A





Clade
- China C1
- China C2
- Europe
- US

IncHI2/IncHI2A

Region	Number	HI2
EU （1.7%）	345	6
USA （5.7%）	209	12
China （**51.4%**）	105	54

Summery

- Monophysic *S.* Typhimurium ST34 prevalent in China was likely emerged from European clone
- Two distinct clades imported into China at different times
- The clade imported earlier has accumulated more ARGs
- The ARGs were mainly harbored by a IncHI2A type MDR plasmid
- Multiple variations demonstrate local acquisition and fitness

Contents

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Better tackling AMR in one-health way

- Reinforce the management of registration, production, distribution, and use of veterinary antibiotics.
- Improve the management of food animal production and reduce the antibiotic use
- Promote the diagnosis of animal diseases and precision medicine
- Develop new antimicrobial agents and antimicrobial substitutes
- Monitor the antibiotic use, residues and antimicrobial resistance in bacteria
- Initiate the risk assessment of both antibiotic residues and the emerging of novel antimicrobial resistance in bacteria
- Educate the public about the awareness of the hazard of antibiotic overuse
- Promote the international cooperation for prevention and control of antimicrobial resistance
- "One Health" approach should be better implemented in national and international level

Acknowledgements

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Center for Disease Control and Prevention, China

Prof. Juan Li

Provincial Center for Disease Control and Prevention, China

Prof. Shengli Xia

Prof. Xiuli Zhang

Prof. Xiaorong Yang

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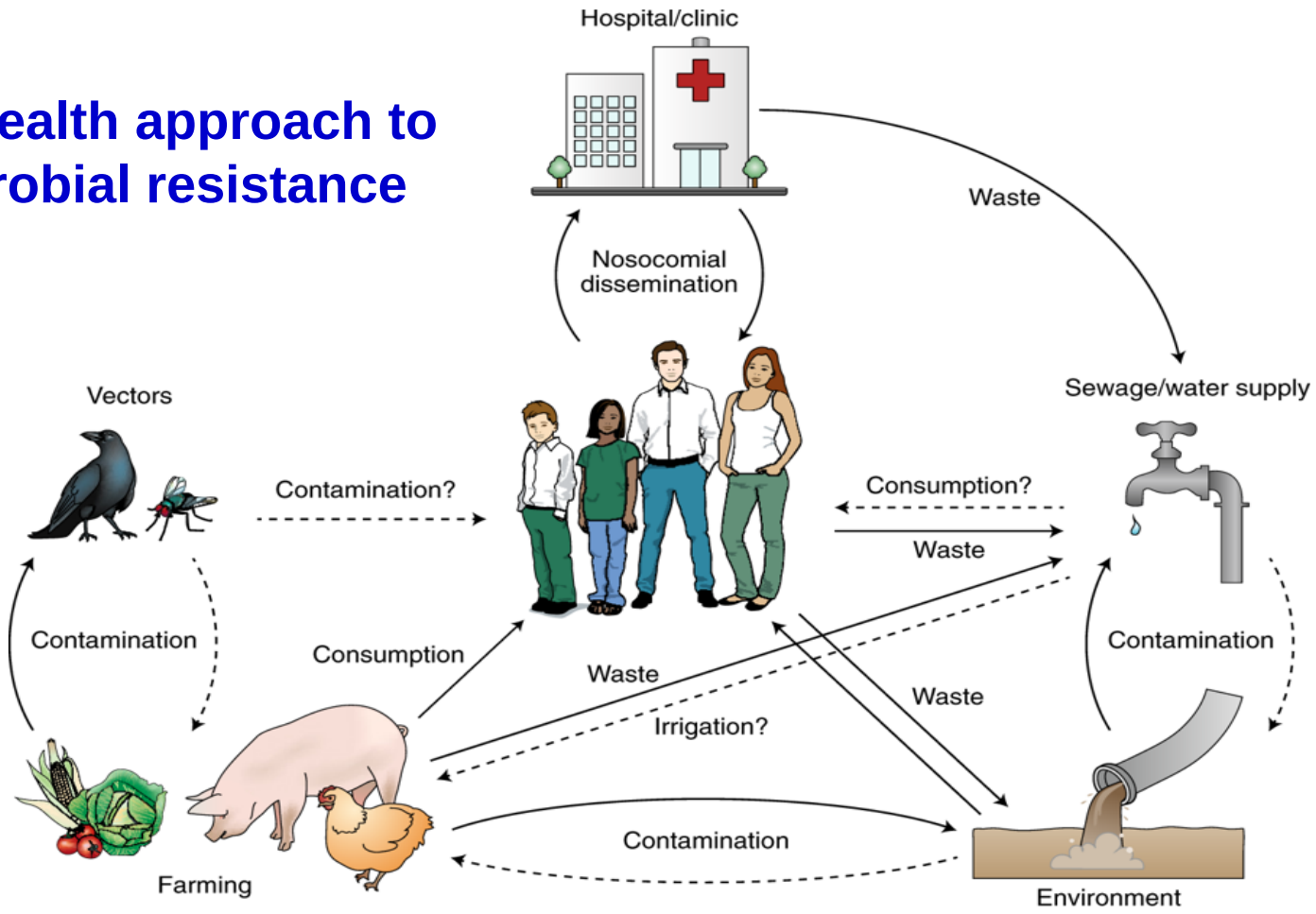
Dr. Pengcheng Du **Beijing ditan hospital capital medical univeristy**

Dr. Ruichao Li **Yangzhou University**

Dr. Pei Zhang **Sun Yat-sen University, SYSU**

A one-health approach to antimicrobial resistance



Walsh TR. *Nat Microbiol*, 2018.

Critical important antimicrobials for human medicine by WHO

WHO Critically Important Antimicrobials for Human Medicine 6th revision

Advisory Group on Integrated Surveillance of Antimicrobial Resistance (AGISAR)
November 2018

Summary of categorization and prioritization of antimicrobials categorized as Critically Important, Highly Important and Important

Critically Important

Antimicrobial class		Criterion / Prioritization factor (Yes = ●)				
CRITICALLY IMPORTANT ANTIMICROBIALS		C1	C2	P1	P2	P3
HIGHEST PRIORITY						
Highest Priority	*Cephalosporins (3rd, 4th and 5th generation)*	●	●	●	●	●
	Glycopeptides	●	●	●	●	●
	Macrolides and ketolides	●	●	●	●	●
	Polymyxins	●	●	●	●	●
	Quinolones	●	●	●	●	●
HIGH PRIORITY						
	Aminoglycosides	●	●		●	●
	Ansamycins	●	●	●	●	
	Carbapenems and other penems	●	●	●	●	
	Glycylcyclines	●	●	●		
	Lipopeptides	●	●	●		
	Monobactams	●	●	●		
	Oxazolidinones	●	●	●		

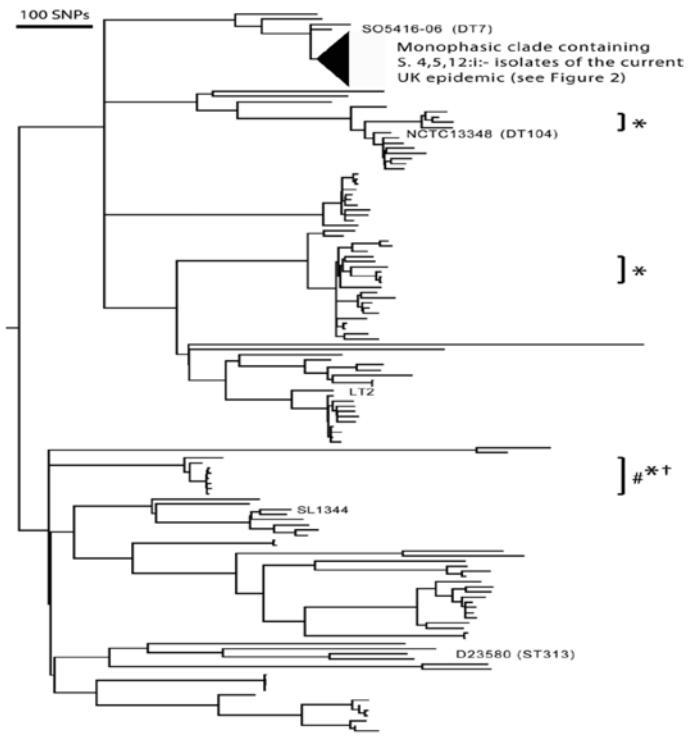
C1 Criterion 1

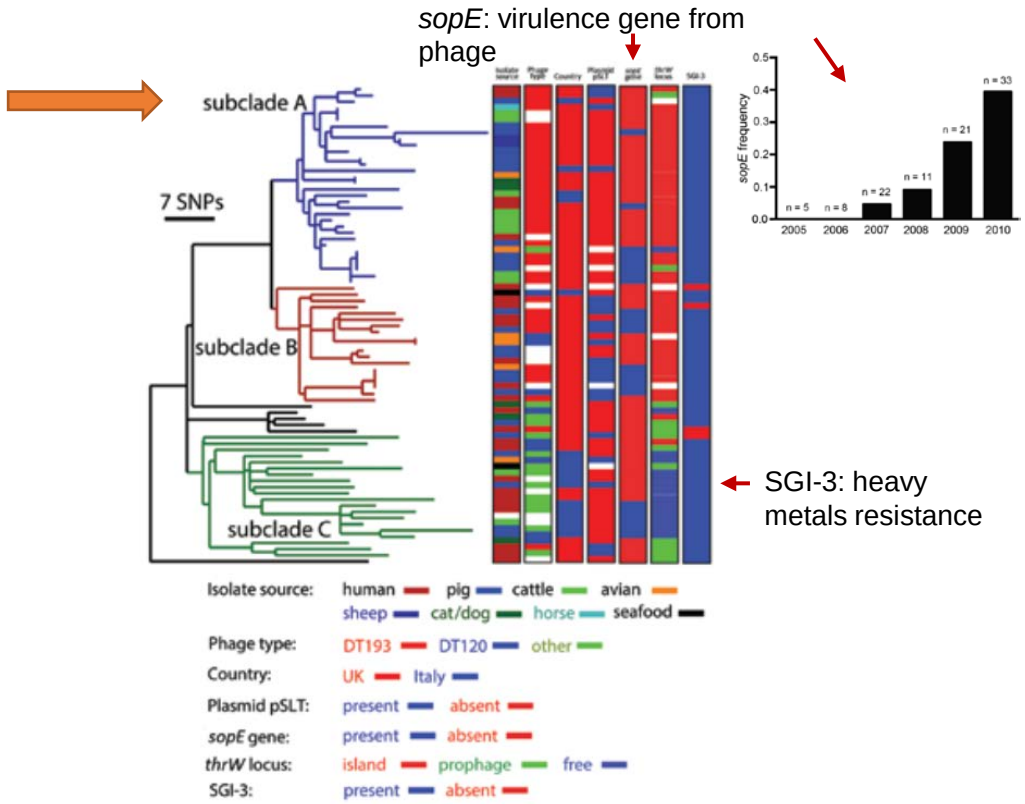
The antimicrobial class is the sole, or one of limited available therapies, to treat serious bacterial infections in people.

C2 Criterion 2

The antimicrobial class is used to treat infections in people caused by either: (1) bacteria that may be transmitted to humans from nonhuman sources, or (2) bacteria that may acquire resistance genes from nonhuman sources.

United Kingdom, 2005–2010

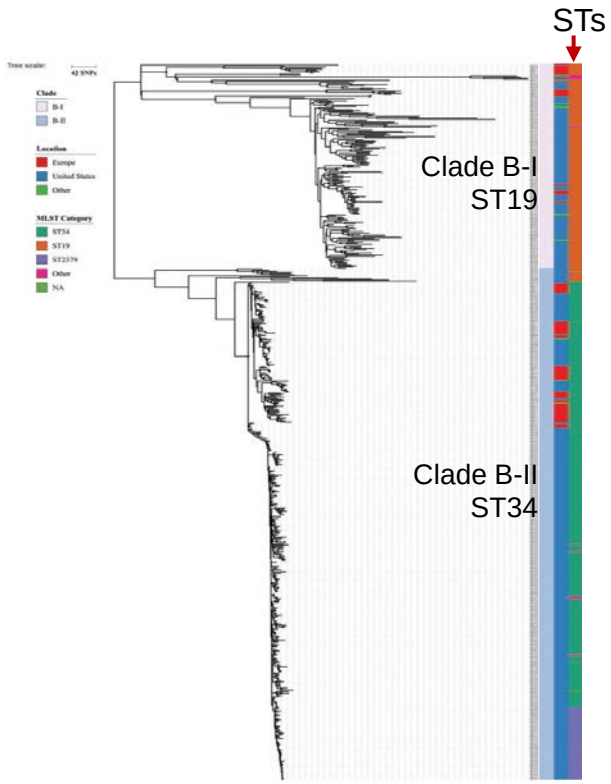




Isolates from UK: 97 *S*. 4,[5],12:i:- and 142 *S*. Typhimurium

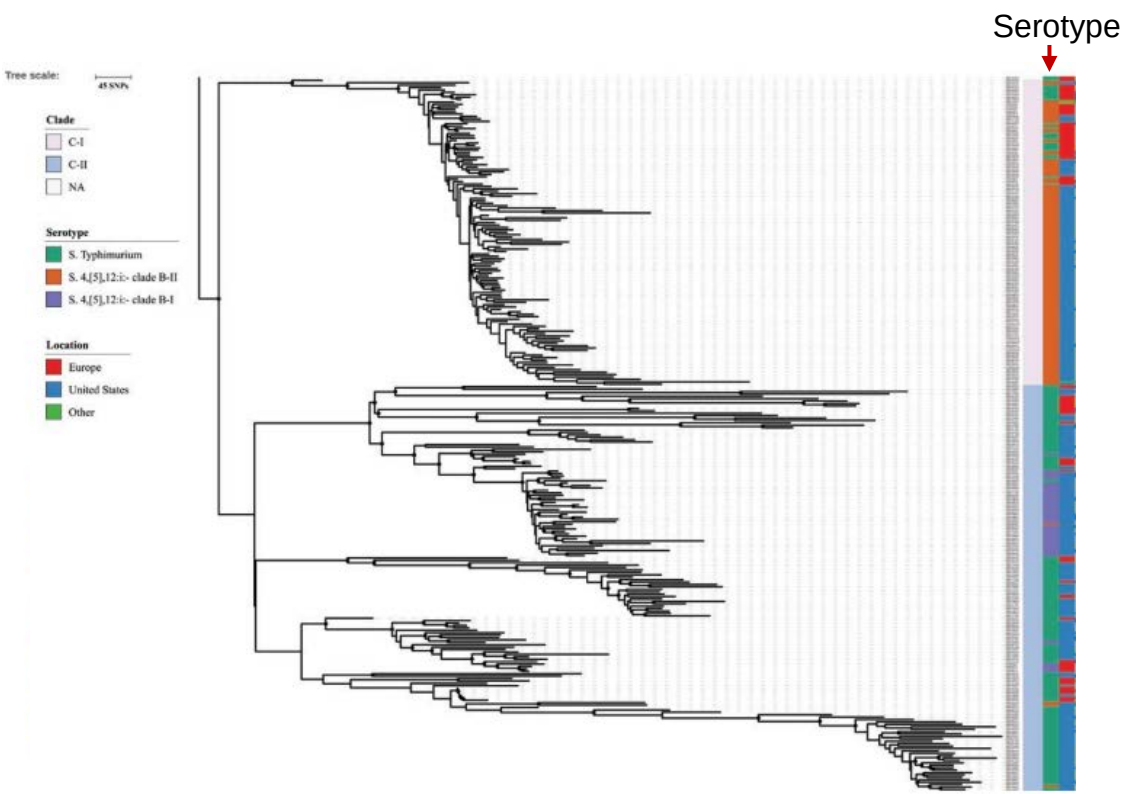
Petrovska L, et al, EID, 2016

United States Midwest, 2014–2016



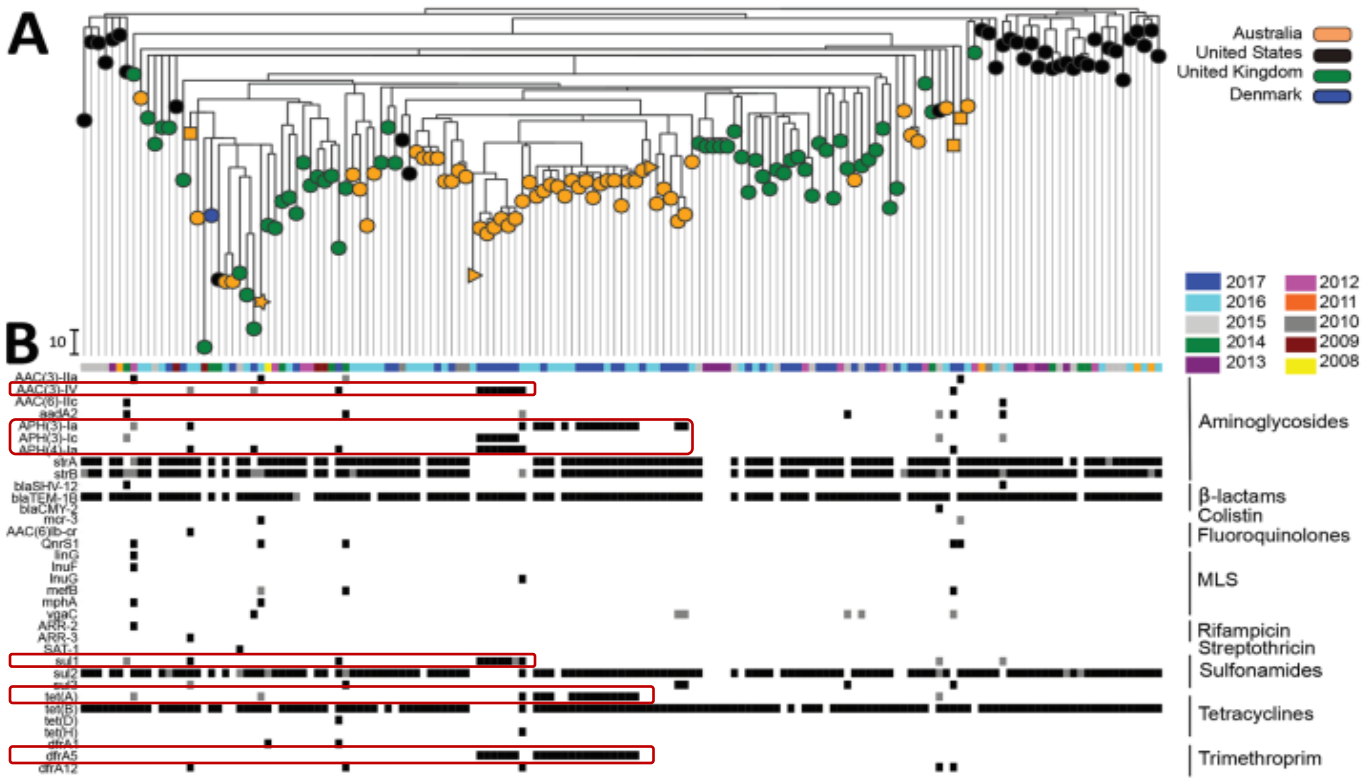
659 *S*. 4,[5],12:i:- isolates from US and Europe

Elnekave E, et al, CID, 2017



S. Typhimurium from US (97) and Europe (49), *S*. 4,[5],12:i:- from B-I (40) and B-II (110)

Australia, 2016–2017



Arnott A, et al. EID, 2018