One Health perspective on *Clostridioides difficile* infection

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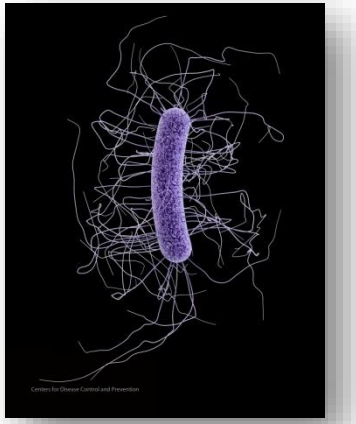
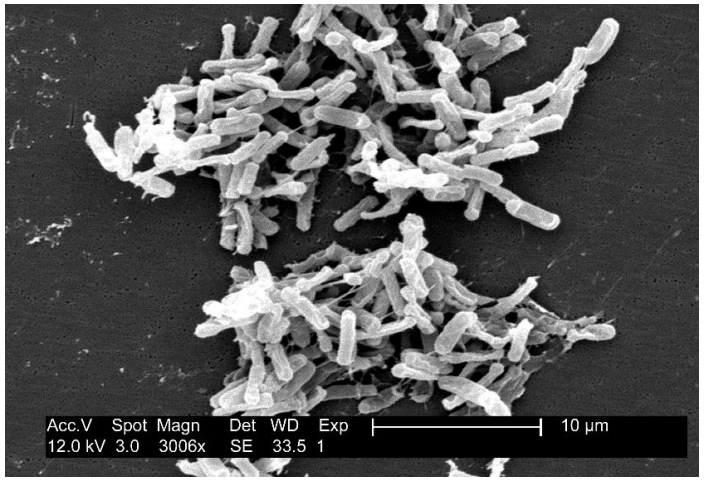
Outline

- Background on *Clostridioides difficile*
- *C. difficile* infection in human in China
- *C. difficile* in animals, food, and environment and clonal transmission
- *C. difficile* in animals in China
- Take home message

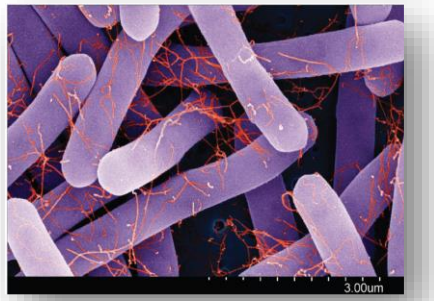


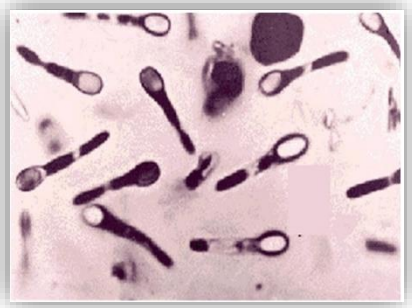
Clostridioides difficile

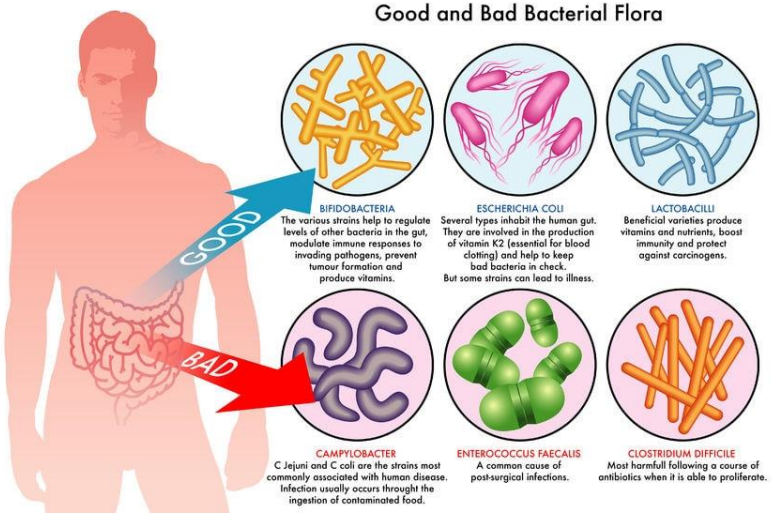
- Firstly found in 1935, called as *Bacillus difficilis*
- G-positive, spore forming obligate anaerobe
- Widely found in environment, animal and human as a zoonotic pathogen
- Colonization resistance: 4-15% health people, 21% inpatients, 15-30% long-term inpatients



CDC/ Lois S. Wiggs (PHIL #6260), 2004



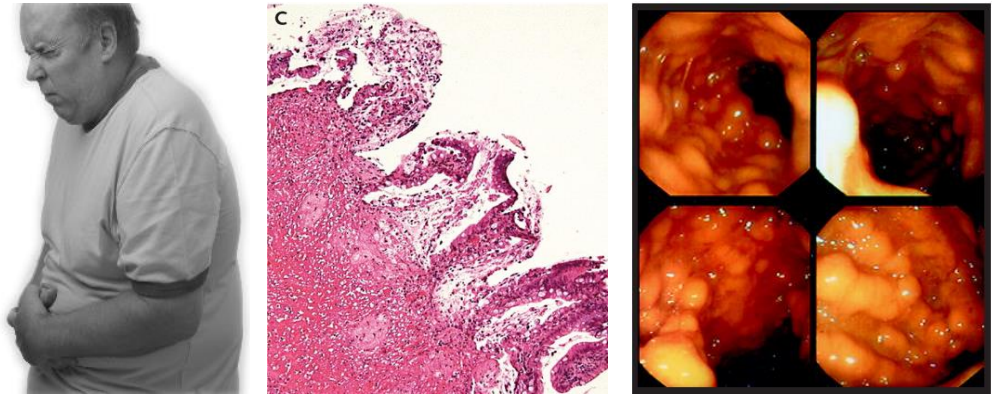




Clostridioides difficile infection, CDI

- Diarrhea
- Belly tenderness or pain
- Fever
- Nausea

- Kidney failure
- Toxic megacolon
- Bowel perforation ➡ peritonitis
- Sepsis



Kawamoto S, et al. Radiographics, 1999, 19(4): 887-897.

CDI is 12–14 times more common than Methicillin-resistant *Staphylococcus aureus* (MRSA) bacteraemia*

*Jones, A.M. et al. (2012) *Clostridium difficile*: a European perspective. J. Infect. 66, 115–128

The importance of CDI

C. difficile is considered as an **immediate** public health threat that required urgent and aggressive action.

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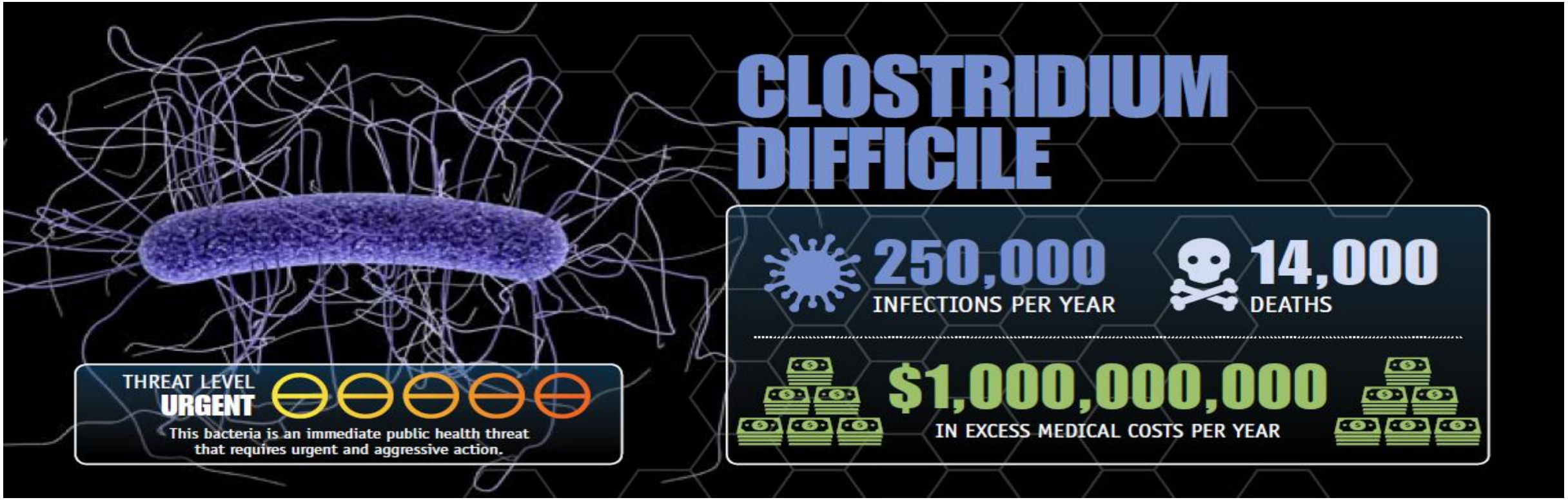


The importance of CDI

ANTIBIOTIC RESISTANCE THREATS in the United States, 2013

Urgent Threats

- *Clostridium difficile*
- Carbapenem-resistant Enterobacteriaceae (CRE)
- Drug-resistant *Neisseria gonorrhoeae*

Serious Threats

- Multidrug-resistant *Acinetobacter*
- Drug-resistant *Campylobacter*
- Fluconazole-resistant *Candida* (a fungus)
- Extended spectrum β-lactamase producing Enterobacteriaceae (ESBLs)
- Vancomycin-resistant *Enterococcus* (VRE)
- Multidrug-resistant *Pseudomonas aeruginosa*
- Drug-resistant Non-typhoidal *Salmonella*
- Drug-resistant *Salmonella* Typhi
- Drug-resistant *Shigella*
- Methicillin-resistant *Staphylococcus aureus* (MRSA)
- Drug-resistant *Streptococcus pneumoniae*
- Drug-resistant tuberculosis

Concerning Threats

- Vancomycin-resistant *Staphylococcus aureus* (VRSA)
- Erythromycin-resistant Group A *Streptococcus*
- Clindamycin-resistant Group B *Streptococcus*

ANTIBIOTIC RESISTANCE THREATS in the United States, 2019

DRUG-RESISTANT
MYCOPLASMA GENITALIUM

Urgent Threats

- Carbapenem-resistant *Acinetobacter*
- *Candida auris*
- *Clostridioides difficile*
- Carbapenem-resistant Enterobacteriaceae
- Drug-resistant *Neisseria gonorrhoeae*

Serious Threats

- Drug-resistant *Campylobacter*
- Drug-resistant *Candida*
- ESBL-producing Enterobacteriaceae
- Vancomycin-resistant *Enterococci*
- Multidrug-resistant *Pseudomonas aeruginosa*
- Drug-resistant nontyphoidal *Salmonella*
- Drug-resistant *Salmonella* serotype Typhi
- Drug-resistant *Shigella*
- Methicillin-resistant *Staphylococcus aureus*
- Drug-resistant *Streptococcus pneumoniae*
- Drug-resistant Tuberculosis

Concerning Threats

- Erythromycin-resistant group A *Streptococcus*
- Clindamycin-resistant group B *Streptococcus*

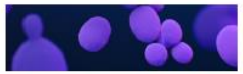
Watch List

- Azole-resistant *Aspergillus fumigatus*
- Drug-resistant *Mycoplasma genitalium*
- Drug-resistant *Bordetella pertussis*

Urgent Threats

These germs are public health threats that require urgent and aggressive action

CARBAPENEM-RESISTANT
ACINETOBACTER



CANDIDA AURIS

CLOSTRIDIOIDES DIFFICILE

CARBAPENEM-RESISTANT
ENTEROBACTERIACEAE

DRUG-RESISTANT
NEISSERIA GONORRHOEAE

The importance of CDI

WHAT YOU NEED TO KNOW

- While healthcare-associated *C. difficile* cases are decreasing, community-associated cases are not.
- Strategies to reduce *C. difficile* infections include improving antibiotic use, infection control, and healthcare facility cleaning and disinfection.
- *C. difficile* infections are more common and tend to be more severe in older patients.

Previously *Clostridium difficile*. Also called *C. diff*. Cost includes hospital-onset cases only.

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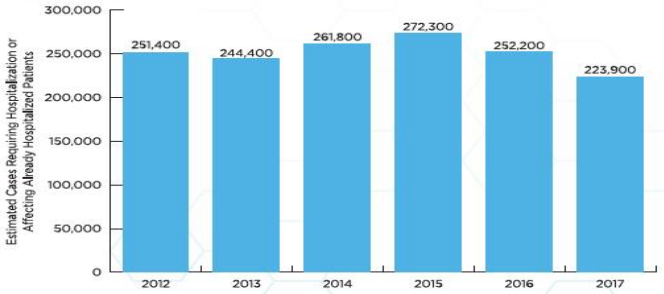
CASES OVER TIME

Continued appropriate infection control, antibiotic use, and diagnostic testing are important to maintain decreases in *C. difficile* cases.



The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Trends in U.S. Burden of *Clostridioides difficile* Infection and Outcomes

A.Y. Guh, Y. Mu, L.G. Winston, H. Johnston, D. Olson, M.M. Farley, L.E. Wilson, S.M. Holzbauer, E.C. Phipps, G.K. Dumyati, Z.G. Beldavs, M.A. Kainer, M. Karlsson, D.N. Gerding, and L.C. McDonald, for the Emerging Infections Program *Clostridioides difficile* Infection Working Group*

Table 1. Reported Cases of *Clostridioides difficile* Infection (CDI) and Crude Incidence, According to Epidemiologic Class, at 10 U.S. Emerging Infections Program Sites, 2011–2017.*

Surveillance Year	Population ≥1 Yr of Age	Community-Associated CDI		Health Care–Associated CDI		All CDI	
		No. of Cases	Incidence per 100,000 Persons	No. of Cases	Incidence per 100,000 Persons	No. of Cases	Incidence per 100,000 Persons
	no.						
2011	10,971,319	5284	48.16	10,177	92.76	15,461	140.92
2012†	11,283,326	5967	52.88	10,482	92.90	16,449	145.78
2013	11,552,955	6441	55.75	9,938	86.02	16,379	141.77
2014	11,533,856	6669	57.82	9,662	83.77	16,331	141.59
2015	11,682,427	7697	65.89	9,655	82.65	17,352	148.53
2016	11,777,482	7915	67.20	8,881	75.41	16,796	142.61
2017	11,906,512	7539	63.32	7,973	66.96	15,512	130.28

Molecular epidemiology of *Clostridioides difficile* infection has been changing.....

CDI in human in China

SCIENTIFIC REPORTS

OPEN

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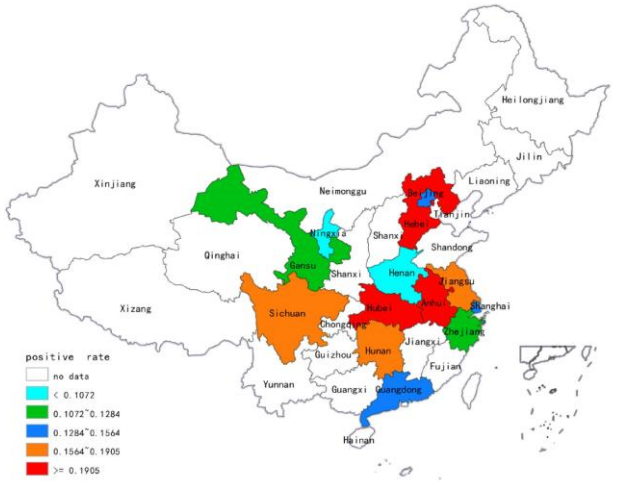
The incidence and drug resistance of *Clostridium difficile* infection in Mainland China: a systematic review and meta-analysis

Chenjie Tang[1,*], Lunbiao Cui[2,*], Yuqiao Xu[1], Le Xie[1], Pengfei Sun[1], Chengcheng Liu[1], Wenying Xia[1] & Genyan Liu[1]



Antimicrobial agents	Drug resistance (95%CI) (%)	Chi-squared	P	I-squared	Model	n/N	References
Metronidazole	0	—	—	—	—	0/960	23–29, 40, 54, 94
Vancomycin	0	—	—	—	—	0/960	23–29, 40, 54, 94
Tigecycline	0	—	—	—	—	0/41	27, 94
Piperacillin/Tazobactam	0	—	—	—	—	0/288	24, 40, 54
Erythromycin	80.2(73.5–86.9)	8.26	0.041	63.70%	REM	340/433	25, 26, 40, 54, 94
Clindamycin	81.7(76.1–87.3)	13.08	0.023	61.80%	REM	476/581	24–27, 29, 40, 54, 94
Tetracycline	46.8(36.7–56.9)	15.9	0.001	81.10%	REM	231/498	26, 29, 40, 54
Moxifloxacin	39.0(27.9–50.1)	38.79	0	84.50%	REM	247/549	24–26, 29, 40, 54, 94
Ciprofloxacin	98.3(96.9–99.7)	0	—	—	FEM	688/694	28, 29, 40, 54
Fusidic acid	16.8(5.4–28.2)	21.06	0	90.50%	REM	72/404	26, 40, 54
Rifampicin	18.3(7.2–29.4)	59.61	0	93.30%	REM	89/527	25, 26, 29, 40, 54, 94
Rifaximin	22.1(17.1–27.0)	2.48	0.115	59.70%	FEM	60/600	28, 40, 54
Meropenem	8.8(−8–25.6)	6.25	0.012	84.00%	REM	11/388	24, 27, 28
Levofloxacin	60.2(44.4–75.9)	97.42	0	94.9%	REM	436/779	26–28, 40, 54, 94

MLST	Molecular epidemiology of *C. difficile* (95% CI) (%)	Chi-squared	P	Model	n/N	References
ST-1	0	—	—	—	0/407	19, 23, 24, 27, 82, 87
ST-2	0.086(0.05–0.118)	1.41	0.494	FEM	26/288	24, 38, 78
ST-3	0.181(0.083–0.278)	8.36	0.039	REM	67/295	24, 38, 78, 92
ST-11	0	—	—	—	0/280	24, 27, 82, 87
ST-26	0.123(0.042–0.204)	0.5	0.479	FEM	8/62	24, 78
ST-35	0.136(0.063–0.210)	16.00	0.003	REM	64/455	36, 38, 78, 87, 92
ST-37	0.172(0.122–0.221)	43.77	0	REM	152/913	19, 24, 36–38, 42, 77–78, 82, 87, 92–94
ST-39	0.159(0.068–0.250)	0.17	0.68	FEM	10/62	24, 78
ST-54	0.167(0.098–0.237)	50.99	0	REM	146/711	24, 36, 38, 42, 77–78, 82, 87, 93

CDI in human in China

Update

Contents lists available at ScienceDirect

International Journal of Infectious Diseases

journal homepage: www.elsevier.com/locate/ijid

Prevalence and molecular characterization of *Clostridioides difficile* infection in China over the past 5 years: a systematic review and meta-analysis

Bao-Jiang Wen[1,2,†], Ning Dong[1,2,†], Zi-Rou Ouyang[1,2,†], Pu Qin[1,2], Jing Yang[1,2], Wei-Gang Wang[1,2], Cui-Xin Qiang[1,2], Zhi-Rong Li[1,2], Ya-Nan Niu[1,2], Jian-Hong Zhao[1,2,*]

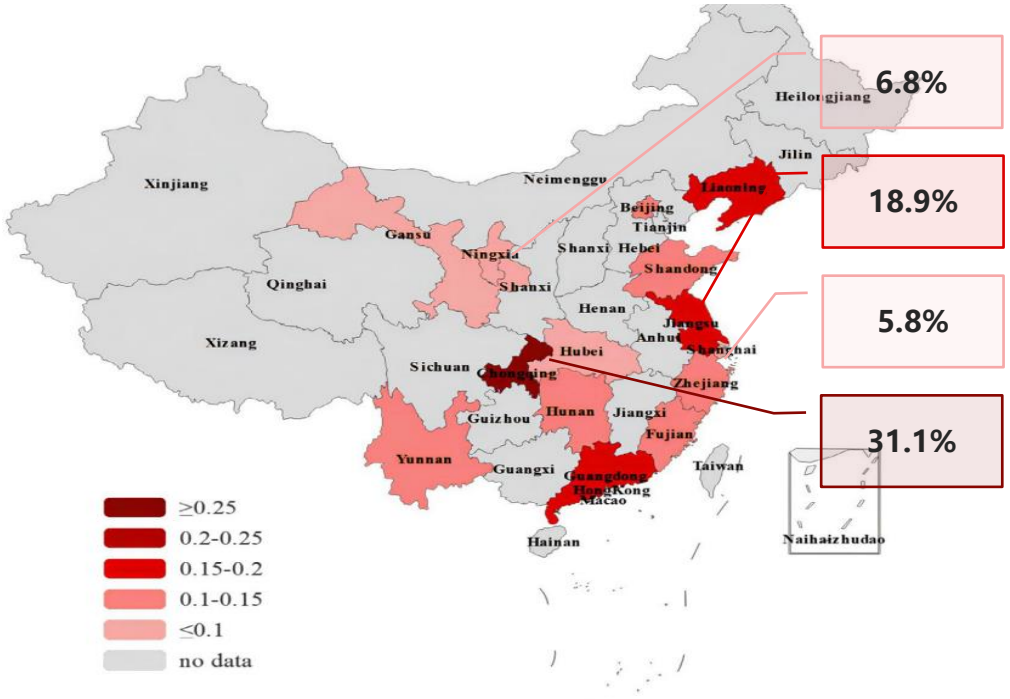


Table 2
Pooled prevalence of *C. difficile* infection in China.

	No. studies	n/N	Prevalence of CDI (95% confidence interval) (%)
Region			
Southern	27	2423/24786	11.0 (8.4-13.8)
Northern	6	273/2066	13.6 (9.4-18.5)
Population			
Inpatients	26	1627/16974	11.5 (8.6-14.7)
Outpatients	1	115/804	14.3 (12.0-16.9)
Community individuals	3	370/2874	11.7 (6.7-17.8)
Route of acquisition			
Community-acquired CDI	5	500/4517	9.5 (4.4-16.2)
Hospital-acquired-CDI	10	702/8024	13.3 (8.0-19.8)
Overall	38	3006/29284	12.7 (10.3-15.1)

11.0%
13.6%

9.5%
13.3%

Table 3
The main *C. difficile* genotypes reported in China.

	n/N	Molecular epidemiology of *C. difficile* (95% confidence interval) (%)
China		
ST54/RT012	784/5627	14.0 (12.1-15.9)
ST3	627/4867	12.9 (11.2-14.6)
ST37/RT017	531/4384	10.1 (8.0-12.4)
ST2	452/4394	9.7 (8.8-10.6)
ST35/RT046	407/4145	9.3 (7.4-11.3)
ST81	444/3374	6.9 (3.4-11.5)
RT027	10/1186	0.7 (0.2-1.3)
RT078	12/2153	0.0 (0.0-0.4)
Southern China		
ST54/RT012	612/3971	16.0 (13.6-18.5)
ST3	449/3349	13.6 (11.7-15.8)
ST37/RT017	374/2765	11.6 (8.6-14.9)
ST2	270/2988	8.4 (7.4-9.5)
ST35/RT046	311/2776	11.1 (9.0-13.3)
ST81	270/2143	5.9 (1.8-11.9)
RT027	2/339	0.4 (0.0-1.5)
RT078	1/784	0.0 (0.0-0.2)
Northern China		
ST54/RT012	140/1319	10.1 (8.5-11.9)
ST3	148/1319	11.0 (8.1-14.4)
ST37/RT017	114/1282	7.1 (4.4-10.3)
ST2	153/1069	13.9 (11.8-16.1)
ST35/RT046	80/1032	5.6 (3.2-8.5)
ST81	170/1032	9.5 (3.2-18.4)
RT027	6/510	0.6 (0.0-1.8)
RT078	2/1032	0.0 (0.0-0.1)

ST2: 8.4%

ST2 : 13.9%

Molecular characteristics of CDI epidemiology have been more clarified, but community-acquired CDI should be further studied.

CDI in human in China

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EPIDEMIOLOGY

Molecular Epidemiology of *Clostridium difficile* Infection in Hospitalized Patients in Eastern China

Dazhi Jin,[a,e] Yun Luo,[a] Chen Huang,[a] Jian Cai,[b] Julian Ye,[a] Yi Zheng,[c] Liqian Wang,[d] Peng Zhao,[c] Anbing Liu,[d] Weijia Fang,[c] Xianjun Wang,[d] Shichang Xia,[a,b] Jianmin Jiang,[a,b] Yi-Wei Tang[e,f]

Departments of Microbiology[a] and Disease Control and Prevention,[b] Zhejiang Provincial Center for Disease Control and Prevention, Hangzhou, Zhejiang, China; Biotherapy Center for Medical Oncology, the First Affiliated Hospital, Zhejiang University, Hangzhou, Zhejiang, China[c]; and Department of Laboratory Medicine, Hangzhou First People's Hospital, Hangzhou, Zhejiang, China[d]; Department of Laboratory Medicine, Memorial Sloan Kettering Cancer Center,[e] and Department of Pathology and Laboratory Medicine,[f] Weill Medical College of Cornell University, New York, New York, USA

- **Eight medical centers** belonging to two hospital alliances
- A cross-sectional study was conducted
- From June 2012 to September 2015 with two gaps
- All patients involved and identified
  - Hangzhou and nearby cities
  - 2010 SHEA/IDSA definition
- Clinical data
  - Six CDI severities graded
- Stool samples collected and shipped to ZJCDC's lab
  - Toxigenic *C. difficile* culture
  - Detection of toxin genes
  - PCR ribotyping
  - Multilocus sequence typing
  - Antimicrobial susceptibility testing

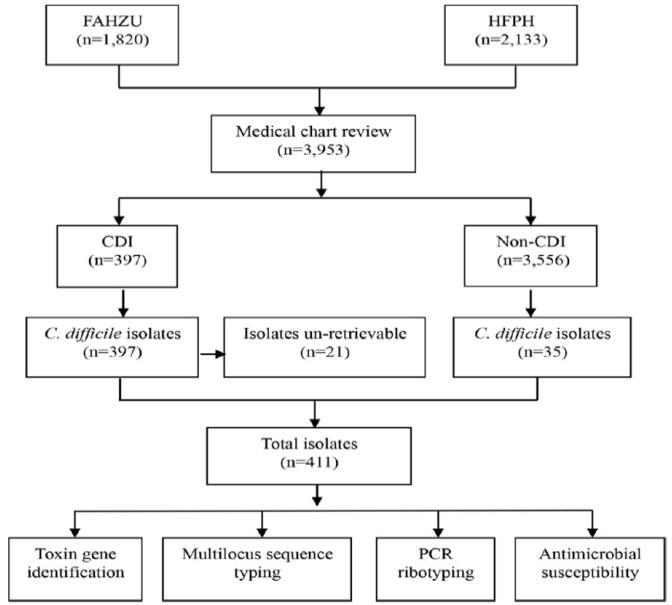
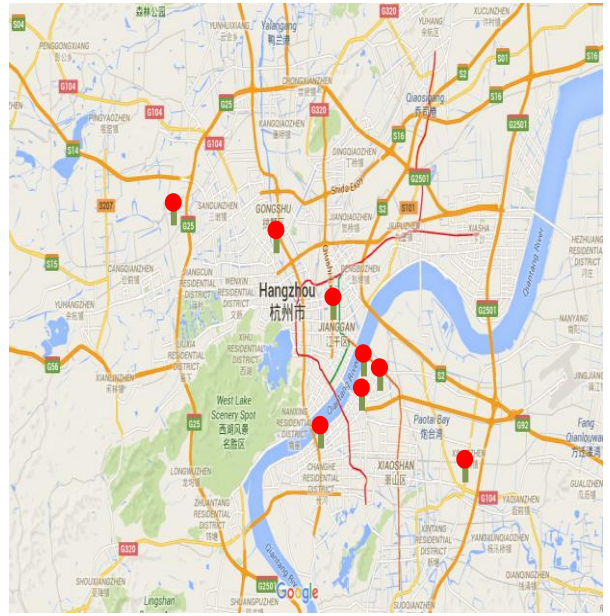
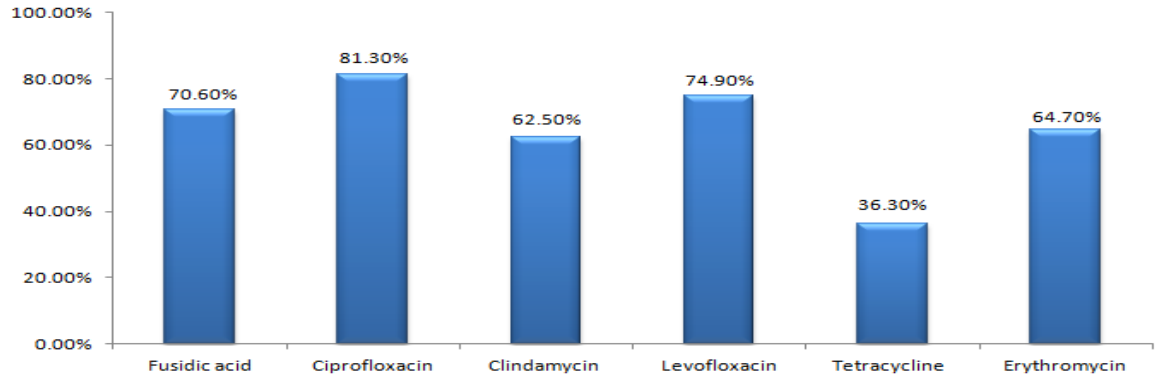


FIG 1 Flow diagram of data collected during the cross-sectional study (1 June 2012 to 30 September 2015).

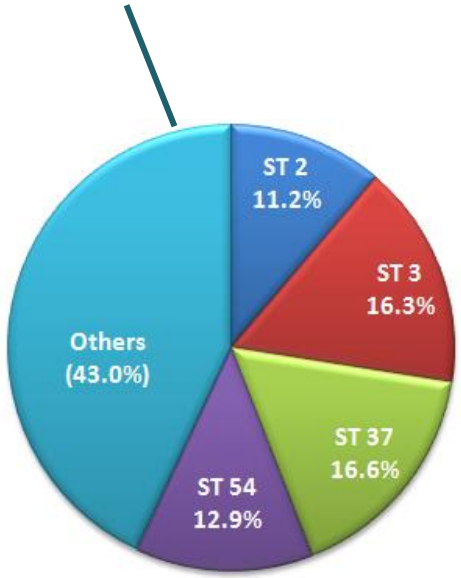


CDI in human in China

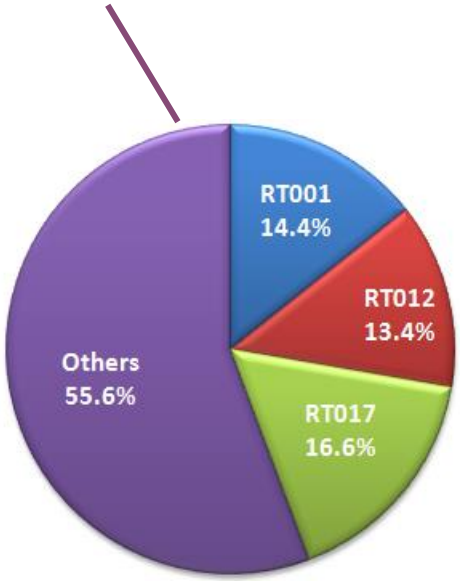
- 282 (68.6%): A^+B^+ 94 (22.9%): A^-B^+ 35 (8.5%): A^-B^-
- No ribotype 027 with 18-bp deletion in tcdC



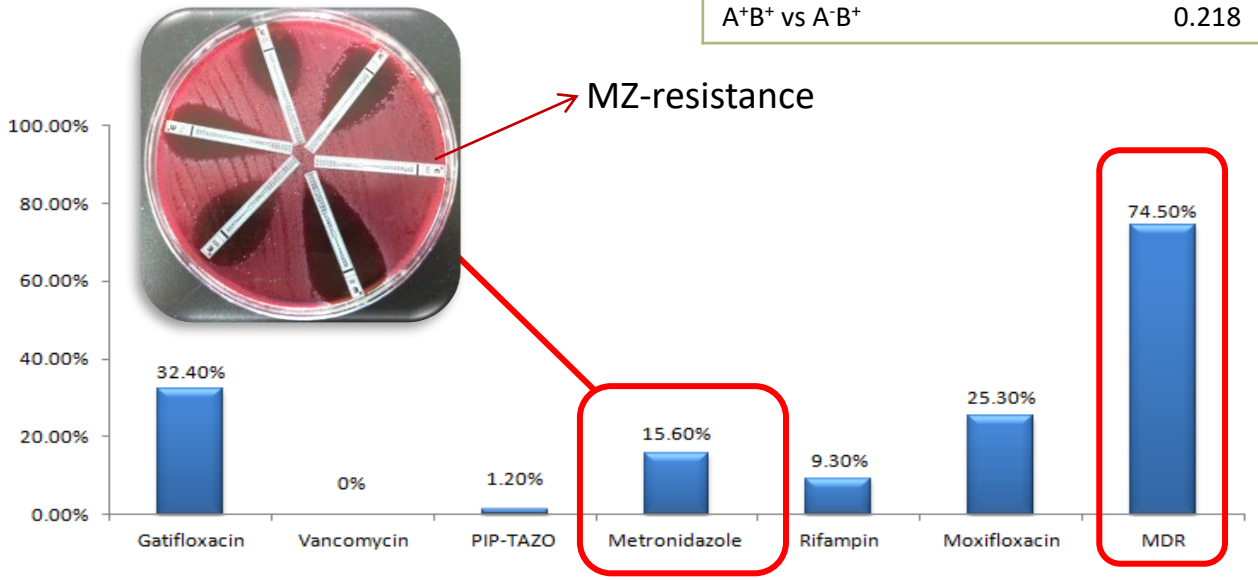
27 STs revealed



53 ribotypes revealed



MDR	*P*
Toxigenic vs Non-toxigenic isolate	<0.001
A^+B^+ vs A^-B^+	0.218



CDI in human in China

Assessment of Risk Factors for CDI

Parameters	No. (%) of clinical samples with *C. difficile* isolated		Multivariant logistic
	Toxigenic *C. difficile* (n=397)	No toxigenic *C. difficile* (n=3,556)	*P* value
Years of age, >55	333 (83.9%)	1248 (35.1%)	< 0.001
Previous hospitalization, yes	300 (75.6%)	1613 (45.4%)	< 0.001
Previous antibiotics treatment within 8 weeks, yes	388 (97.7%)	2052 (57.7%)	< 0.001
Hospitalized stay over three days before sampling, yes	132 (33.3%)	663 (18.6%)	< 0.001
Chemotherapy, yes	101 (25.4%)	432 (12.2%)	< 0.001
Abdominal surgery, yes	208 (52.4%)	993 (27.9%)	< 0.001

CDI in human in China

Conclusions

- *C. difficile* is circulating in hospitalized patients with diarrhea in eastern China
  - A CDI prevalence of 10.0% was found
- The age threshold could be much younger in eastern China compared to those of developed countries
  - The age of >55 years was a risk factor for inpatients in eastern China
  - Different from the age of >64 years in the U.S and other developed regions
- The antimicrobial susceptibility profiles have changed dramatically
  - The resistance rate for fusidic acid (66.7%) was markedly higher than previously reported
  - Metronidazole resistances (15.6%) was reported
- The risk factors were identified in eastern China
  - Including advanced age, previous hospitalization, antibiotic administration, chemotherapy, abdominal surgery, and extended hospitalization
- The ST37/ribotype 017 strain is likely to be an emergent epidemic clone in China
  - Even though CDI severity is generally mild to moderate (2.61±1.01)
  - Severe cases were associated with ST37/RT017 genotypes

CDI in human in China

Shuai *et al. BMC Infectious Diseases* _####################_
https://doi.org/10.1186/s12879-020-05030-6

BMC Infectious Diseases

RESEARCH ARTICLE Open Access

Molecular characteristics of *Clostridium difficile* in children with acute gastroenteritis from Zhejiang

Huiqun Shuai[1†], Qiao Bian[2†], Yun Luo[3,4], Xiaohong Zhou[1], Xiaojun Song[5], Julian Ye[3], Qinghong Huang[1], Zhaoyang Peng[6,7], Jun Wu[8], Jianmin Jiang[9*] and Dazhi Jin[10*]

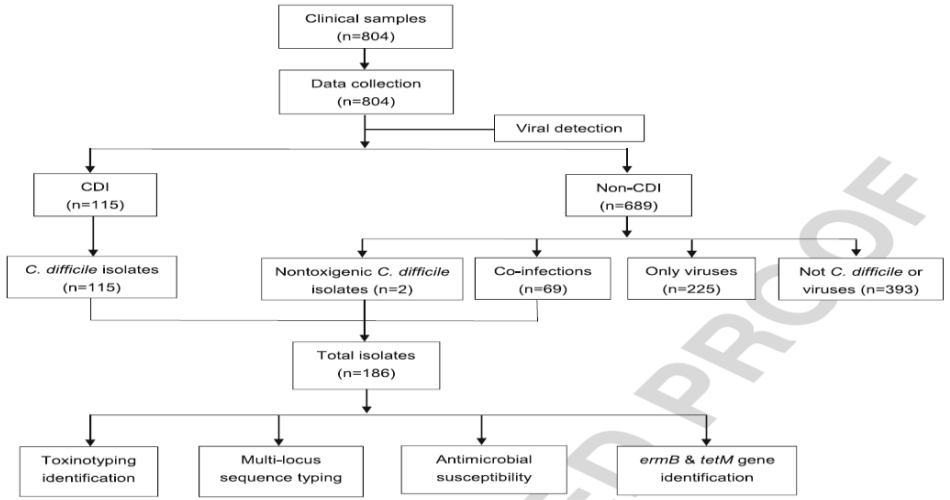


Table 1 Clinical information of outpatients participated in this study

Characteristics	2013 (*n* = 84)	2014 (*n* = 102)	2015 (*n* = 223)	2016 (*n* = 203)	2017 (*n* = 192)	Total (*n* = 804)
Gender, male n, (%)	55 (65.5)	70 (68.6)	128 (57.4)	129 (63.5)	119 (62.0)	501 (62.3)
Age (yr), *Median*, (*IQR*)	0.50 (0.25, 0.73)	0.50 (0.25, 1.00)	0.75 (0.42, 1.25)	0.75 (0.33, 1.25)	0.79 (0.47, 1.00)	0.67 (0.38, 1.00)
Age (yr) n, (%)						
< 6 months (ms)	40 (47.6)	36 (35.3)	70 (31.4)	65 (32.0)	48 (25.0)	259 (32.2)
6 ms~	32 (38.1)	40 (39.2)	67 (30.0)	67 (33.0)	60 (31.3)	266 (33.1)
1 yr~	6 (7.1)	16 (15.7)	43 (19.3)	42 (20.7)	55 (28.6)	162 (20.1)
2 yr~	6 (7.1)	10 (9.8)	43 (19.3)	29 (14.3)	29 (15.1)	117 (14.6)
Occupation, Scattered children	81 (96.4)	101 (99.0)	216 (96.9)	193 (95.1)	186 (96.9)	777 (96.6)
Fever, > 38.5 °C	17 (20.2)	24 (23.5)	66 (29.6)	44 (21.7)	65 (33.9)	216 (26.9)
C. difficile isolates n, (%)	11 (13.1)	35 (34.3)	60 (26.9)	36 (17.7)	44 (22.9)	186 (23.1)
Only toxigenic *C. difficile*, CA-CDI	10 (11.9)	23 (22.5)	40 (17.9)	26 (12.8)	16 (8.3)	115 (14.3)
Co-infections	1 (1.2)	11 (10.8)	19 (8.5)	10 (4.9)	28 (14.6)	69 (8.6)
Total viral infections	4 (4.8)	23 (22.5)	88 (39.5)	63 (31.0)	116 (60.4)	294 (36.6)
Rotavirus group A[a]	2 (2.4)	0	44 (19.7)	30 (14.8)	47 (24.5)	123 (15.3)
Norovirus GI & GII[b]	1 (1.2)	20 (19.6)	19 (8.5)	26 (12.8)	32 (16.7)	98 (12.2)
Astrovirus	1 (1.2)	0	3 (1.3)	0	3 (1.6)	7 (0.9)
Sapovirus	0	1 (1.0)	9 (4.0)	3 (1.5)	3 (1.6)	16 (2.0)
Adenovirus	0	2 (2.0)	4 (1.8)	3 (1.5)	1 (0.5)	10 (1.2)
Multiple viruses	0	0	9 (4.0)	1 (0.5)	30 (15.6)	40 (5.0)

Table 2 Correlations among MLST types, toxin genotypes, and antimicrobial susceptibility patterns of the 186 *C. difficile* isolates

Antimicrobial agent	Total no. (%) of all the isolates (*n* = 186)	MLST types (no. [%] of non-susceptible isolates)						Analysis results[b]		Toxinotypes[c] (no. [%] of non-susceptible isolates)		Analysis results	
		ST26 (*n* = 33)	ST35 (*n* = 21)	ST39 (*n* = 23)	ST54 (*n* = 31)	ST152 (*n* = 21)	Other STs[a] (*n* = 57)	χ^2	*P* value	A^+B^+ (*n* = 145)	A^-B^+ (*n* = 39)	χ^2	*P* value
Clindamycin	159 (85.5)	33 (100.0)	21 (100.0)	18 (78.3)	30 (96.8)	13 (61.9)	44 (77.2)	F	< 0.001	125 (86.2)	34 (87.2)	0.02	0.875
Erythromycin	160 (86.0)	33 (100.0)	21 (100.0)	23 (100.0)	30 (96.8)	7 (33.3)	46 (80.7)	F	< 0.001	120 (82.8)	39 (100.0)	7.78	0.005
Fusidic acid	129 (69.4)	12 (36.4)	15 (71.4)	15 (65.2)	28 (90.3)	20 (95.2)	39 (68.4)	30.18	< 0.001	102 (70.3)	27 (69.2)	0.02	0.893
Rifampin	7 (3.8)	0	0	5 (21.7)	0	1 (4.8)	1 (1.8)	F	0.001	2 (1.4)	5 (12.8)	8.09	0.004
Levofloxacin	148 (79.6)	19 (57.6)	21 (100.0)	16 (69.6)	24 (77.4)	21 (100.0)	47 (82.5)	F	< 0.001	117 (80.7)	30 (76.9)	0.27	0.602
Moxifloxacin	14 (7.5)	0	0	6 (26.1)	0	1 (4.8)	7 (12.3)	F	0.001	3 (2.1)	11 (28.2)	29.26	< 0.001
Gatifloxacin	14 (7.5)	0	0	6 (26.1)	0	1 (4.8)	7 (12.3)	F	0.001	3 (2.1)	11 (28.2)	29.26	< 0.001
Tetracycline	17 (9.1)	0	11 (52.4)	0	1 (3.2)	0	5 (8.8)	F	< 0.001	13 (9.0)	4 (10.3)	0.06	0.805
Metronidazole	0	0	0	0	0	0	0	N/A	N/A	0	0	N/A	N/A
Vancomycin	0	0	0	0	0	0	0	N/A	N/A	0	0	N/A	N/A
PIP-TAZ	0	0	0	0	0	0	0	N/A	N/A	0	0	N/A	N/A
Ciprofloxacin	184 (100.0)	33 (100.0)	21 (100.0)	23 (100.0)	31 (100.0)	21 (100.0)	57 (100.0)	N/A	N/A	145 (100.0)	39 (100.0)	N/A	N/A
MDR	166 (89.2)	33 (100.0)	21 (100.0)	21 (91.3)	30 (96.8)	15 (71.4)	46 (80.7)	F	0.001	129 (89.0)	37 (94.9)	0.64	0.425

CDI in human in China

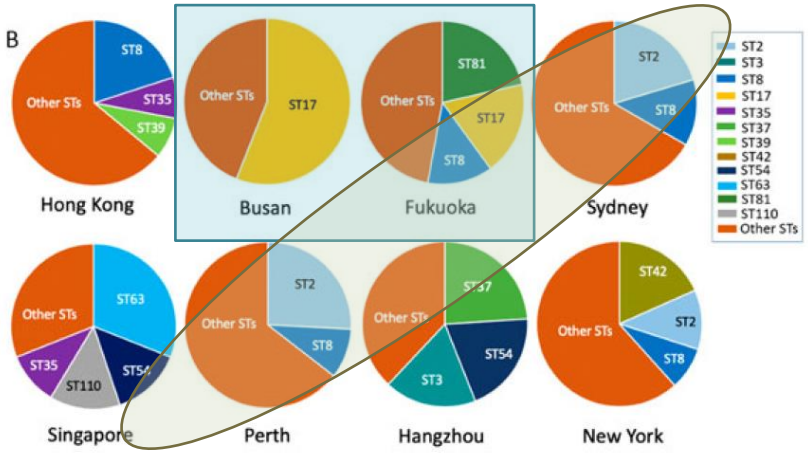
Emerging Microbes & Infections
https://doi.org/10.1080/22221751.2019.1682472

Different molecular characteristics and antimicrobial resistance profiles of *Clostridium difficile* in the Asia-Pacific region*

Yun Luo[a,b], Elaine Cheong[c,d], Qiao Bian[e], Deirdre A. Collins[f], Julian Ye[a], Jeong Hwan Shin[g,h], Wing Cheong Yam[i], Tohru Takata[j,k], Xiaojun Song[l], Xianjun Wang[m], Mini Kamboj[n,o], Thomas Gottlieb[c,d], Jianmin Jiang[a,p], Thomas V. Riley[q,r], Yi-Wei Tang[n,o] and Dazhi Jin[l,s,a]

- **The dominant STs varied in different regions**

ST8 in Hongkong (20.0%)
ST17 in Busan (56.0%), Fukuoka (18.6%)
ST2 in Sydney (20.4%), Perth (25.8%)
ST63 in Singapore (31.0%)
ST3 (20%), ST37 (26.0%) and ST54 (20.0%) in Hangzhou
ST42 in New York (18.3%)
★ ST35 and ST2 widespread presence

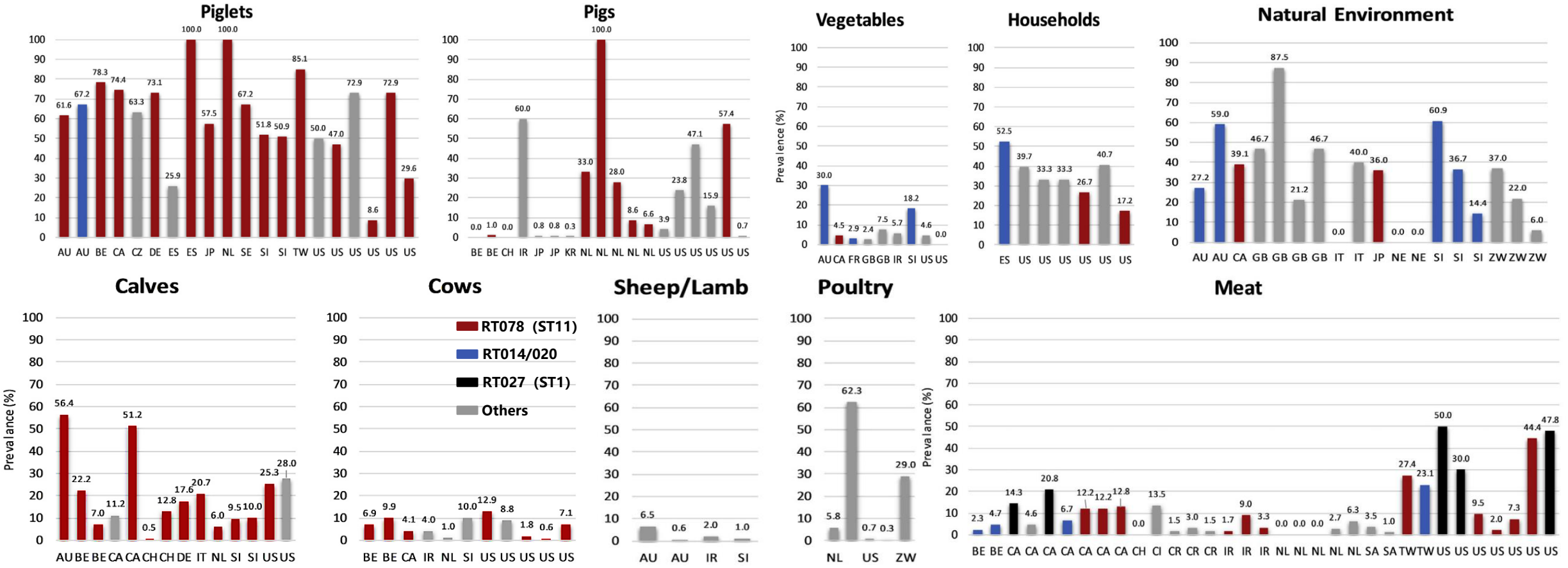


- **AMR profiles varied in different regions** (All susceptible to vancomycin and metronidazole)

In New York, Sydney and Perth, higher fusidic acid resistance, but lower moxifloxacin, tetracycline, and erythromycin resistance
Lower gatifloxacin resistance in Sydney and Perth

C. difficile in animals, food, and environment

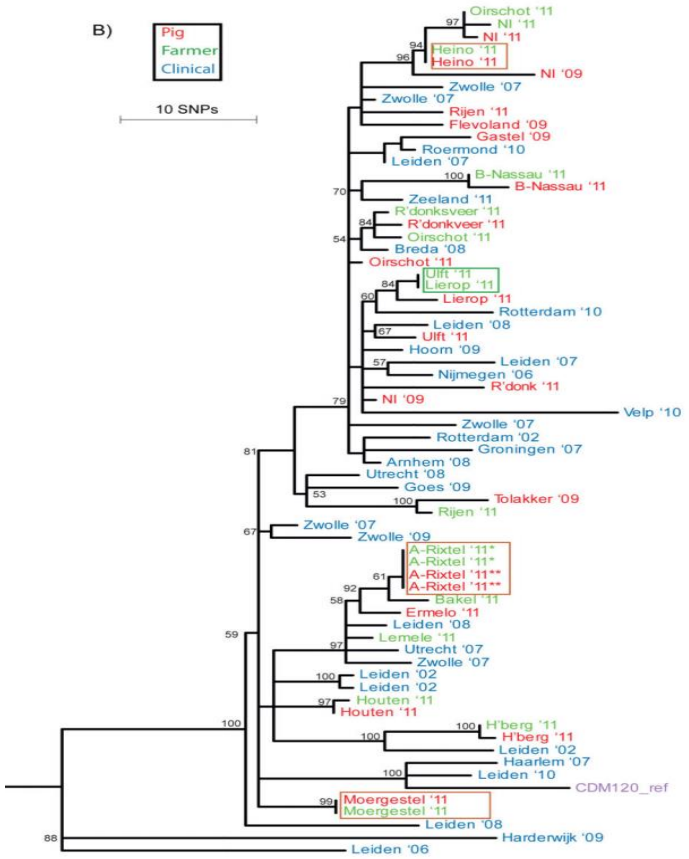
- Food animals, retail food, and the environment are important reservoirs of *C. difficile*.
- This further demonstrates the relevance of *C. difficile* to the One Health concept.

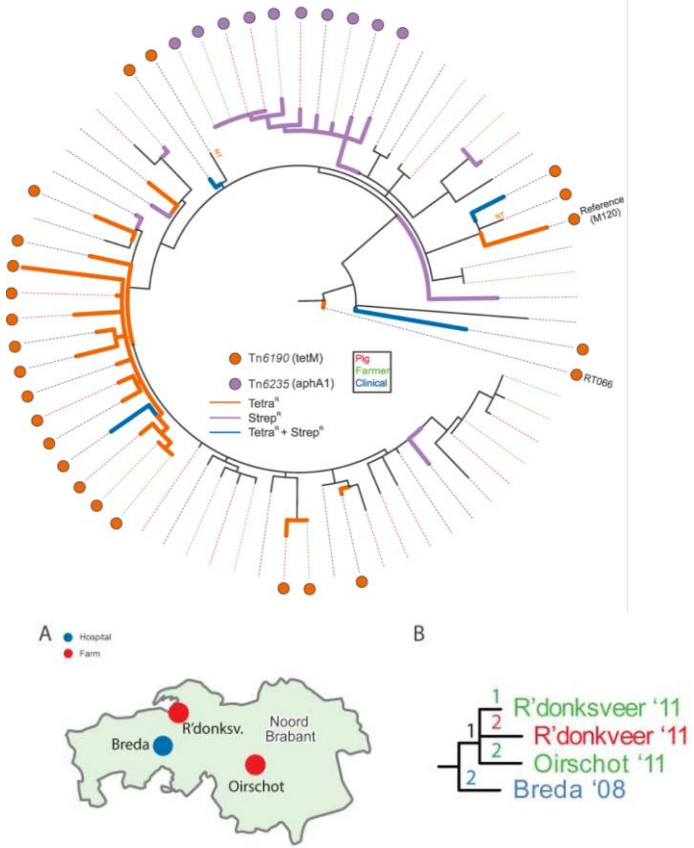


Lim SC, et al. *Clostridium difficile* and One Health. Clin Microbiol Infect. 2020;26(7):857-63.

C. difficile interspecies transmission

- It is the first time to use whole genome SNP typing to study the relevance of *C. difficile* isolates.
- The 65 *C. difficile* RT078 isolates were sequenced and analyzed by core genome SNPs.
- Clonal transmission of *C. difficile* RT078 has been found from pigs to farmers in Netherlands.

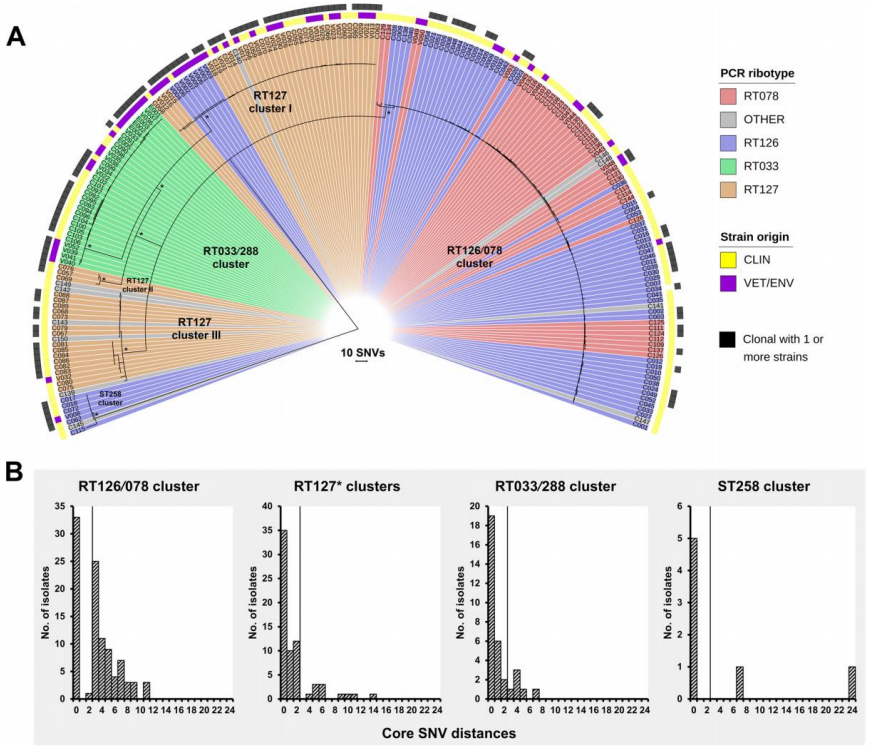


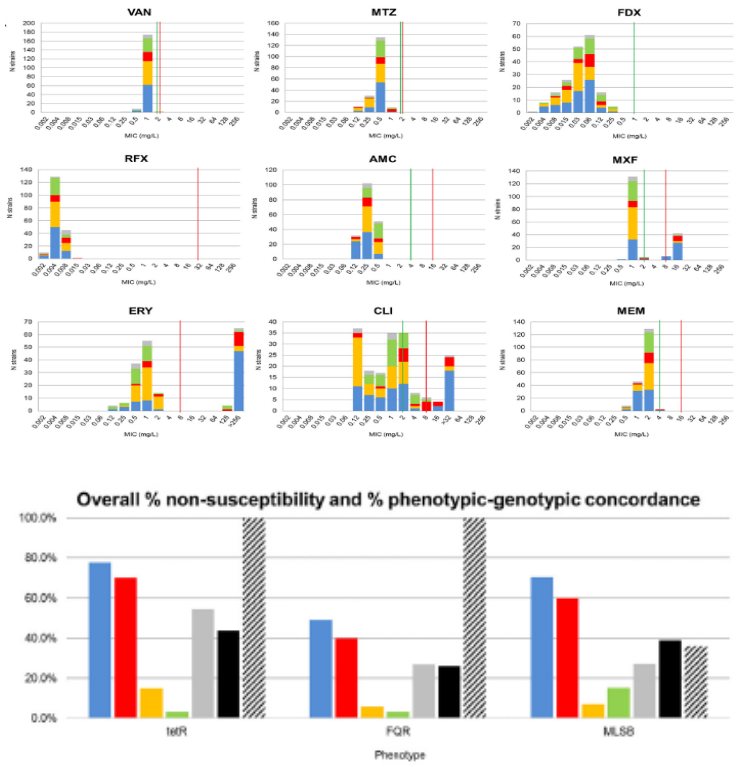


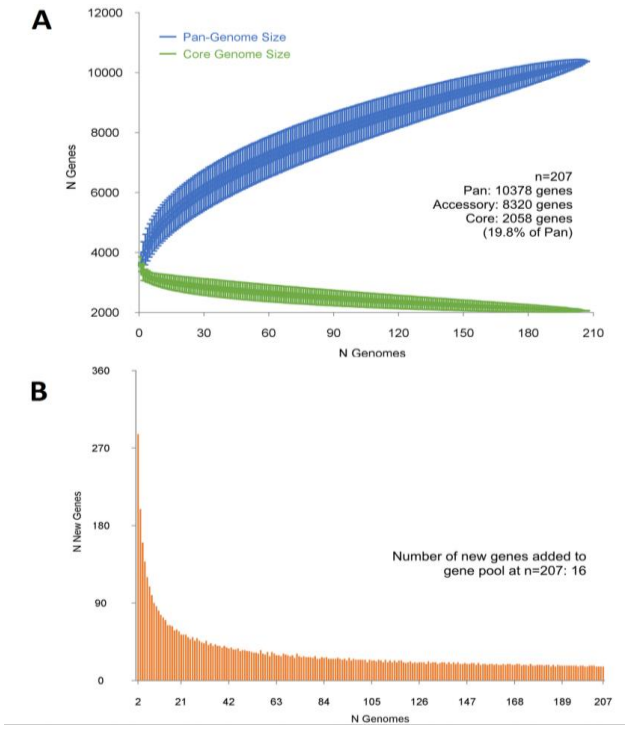
Knetsch CW et al. Euro Surveill 2014 Nov 13;19(45):20954

C. difficile interspecies transmission

- The 200 ST11 and 7 ST258 isolates from human and animal/environmental source worldwide were sequenced.
- Antibiotic resistance geno- and phenotypes varied across host species, geographic regions in *C. difficile* ST11.
- The core genome accounted for just 19.8% of the pan-genome in *C. difficile* ST11.
- This study provided novel insights into genetic relationship of ST11, a lineage of global One Health importance.



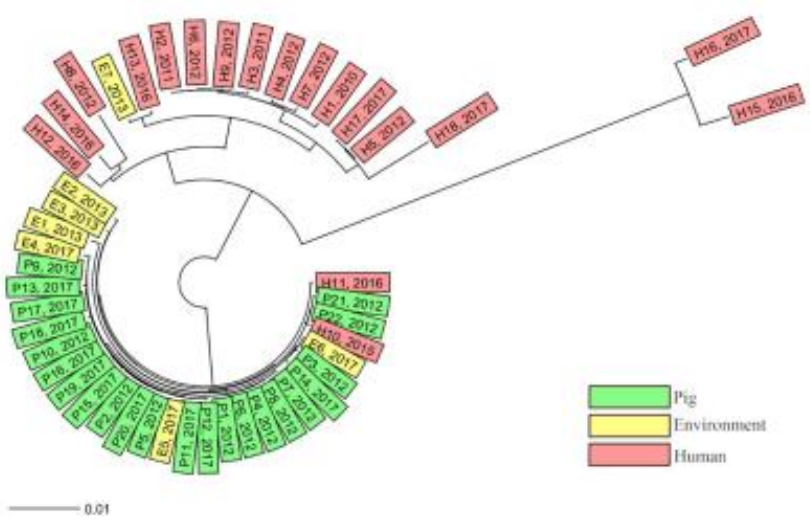




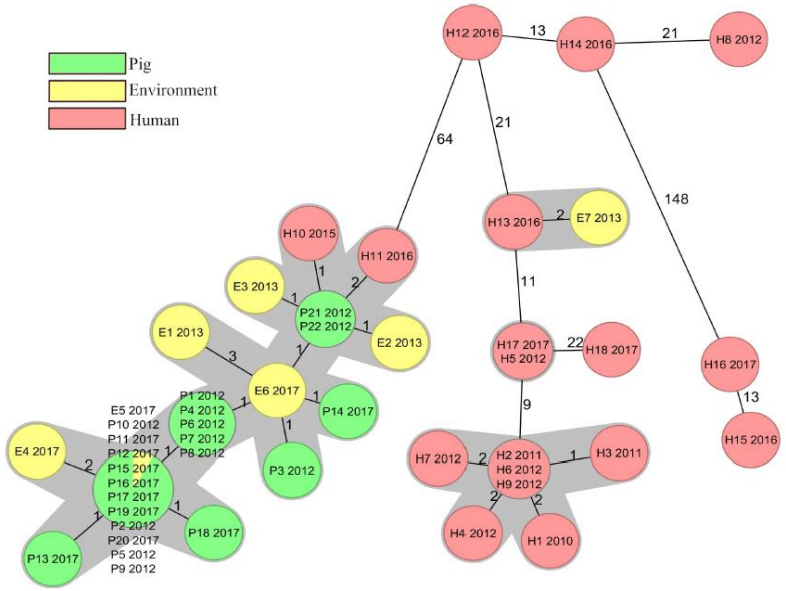
Knight DR et al. mBio 201910: e00446-19

C. difficile interspecies transmission

- WGS was performed on 47 *C. difficile* RT046 isolates from pigs, environment and human cases of CDI in Sweden.
- Genetic relationship among them was analyzed by SNPs and core genome MLST.
- Whole genome sequencing of *C. difficile* PCR ribotype 046 suggests transmission between pigs and humans.



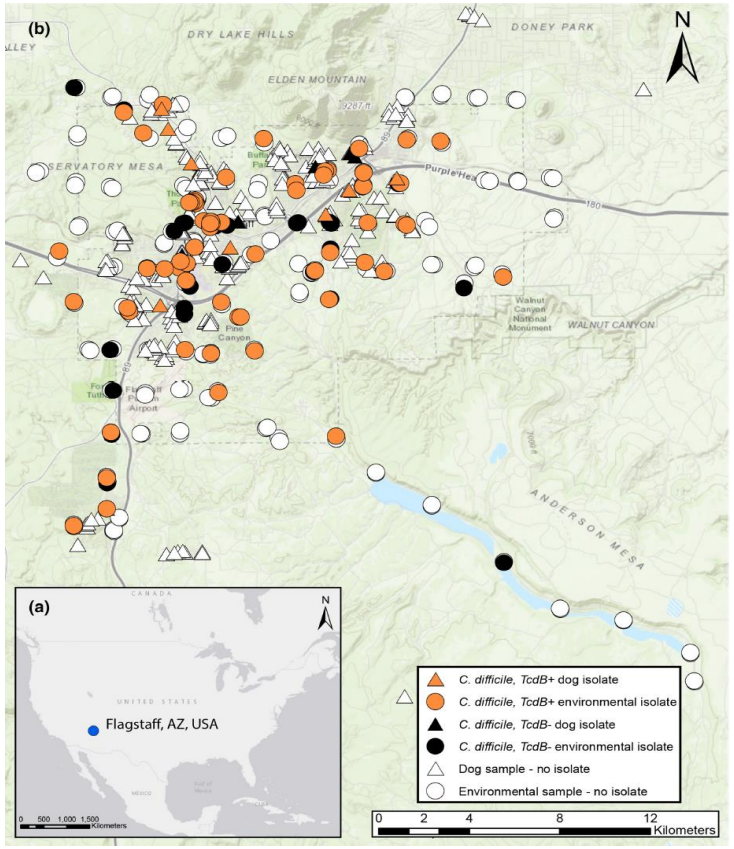
NGS+cgMLST

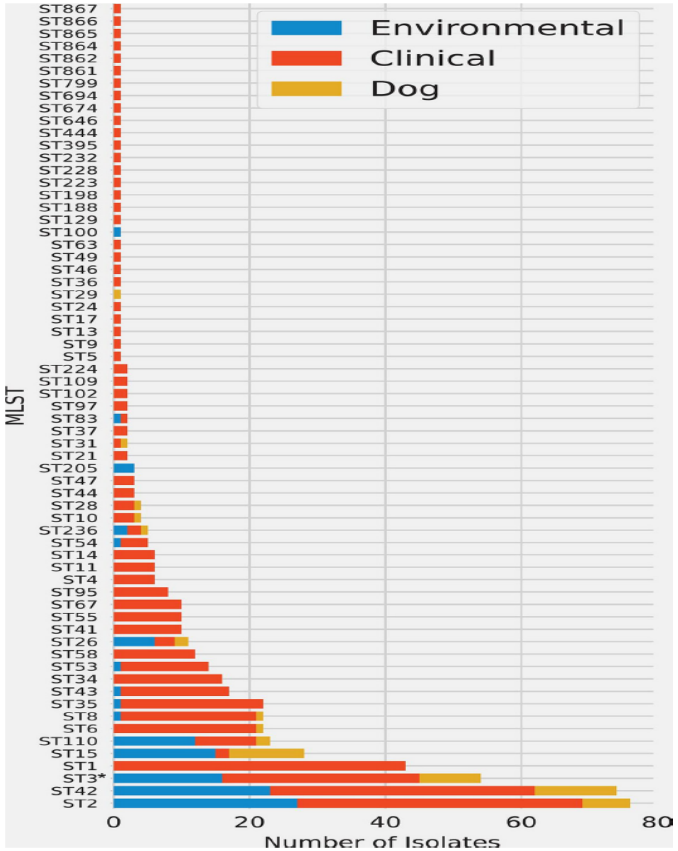


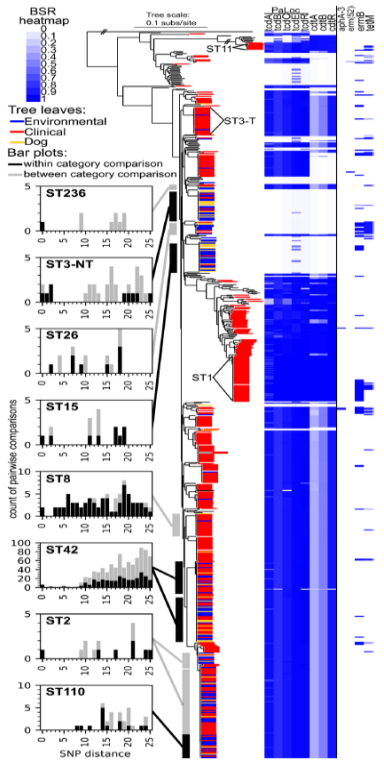
Werner A et al. PLoS One. 2020 Dec 21;15(12):e0244227

C. difficile interspecies transmission

- WGS was performed on 562 *C. difficile* isolates from clinical, environmental and dog in Flagstaff, AZ, in USA.
- Eight STs were found across all three reservoirs, nine STs were shared across clinical and environmental reservoirs.
- This study provides a One Health framework for comprehensive surveillance of *C. difficile* in a single community.







Williamson CHD et al. Microbial Genomics. 2023;9:001046

C. difficile in animals in China

- There were just two studies focusing on *C. difficile* from animals in China.
- ST11/RT078 from pigs was firstly reported in 2019 in China.
- ST35/RT046 from pigs was also reported with the gyrA mutation in China.

PLOS ONE

RESEARCH ARTICLE

The first isolation of *Clostridium difficile* RT078/ ST11 from pigs in China

Toxin profile	Total No. of Strains	Multidrug-Resistant Patterns			Amino acid substitutions		ST≠	RT §	Animal source
		Quadruple Drug Resistance	Quintuple Drug Resistance	Sextuple Drug Resistance	*GyrA*	*GyrB*			
A^-, B^-,	5	CIP/CXT/TET/CTX	CIP/CXT/TET/CTX/ERY	CIP/CXT/TET/CTX/ERY/MXF	Thr87-Ile	Ser366-Ala	1		
	1			CIP/CXT/TET/CTX/ERY/MXF			2		
A^-, B^+,		CXT/CLI/CTX/ERY		CIP/CXT/TET/CTX/ERY/CLI			4		
	7	CIP/CXT/TET/CTX					2		
	4		CIP/CXT/TET/CTX/MXF			Ser366-Ala	1		
A^+, B^+,	4	CIP/CXT/TET/CTX			Thr82-Ile		3		
	9	CIP/CXT/TET/CTX	CIP/CXT/TET/CTX/IPM	CIP/CXT/TET/CTX/IPM/ERY	Thr82-Ile		35	GZ3	Pig
A^+,B^+, CDT^+	14	CIP/CXT/TET/CTX	CIP/CXT/TET/CTX/IPM			Ser366-Val Ser416-Ala	11	GZ2 (RT078)	Pig

SCIENTIFIC REPORTS

OPEN

The incidence and drug resistance of *Clostridium difficile* infection in Mainland China: a systematic review and meta-analysis

Chenjie Tang[1,*], Lunbiao Cui[2,*], Yuqiao Xu[1], Le Xia[1], Pengfei Sun[1], Chengcheng Liu[1], Wenying Xia[1] & Genyan Liu[1]

MLST	Molecular epidemiology of *C. difficile* (95% CI) (%)	Chi-squared	P	Model	n/N	References
ST-1	0	—	—	—	0/407	19, 23, 24, 27, 82, 87
ST-2	0.086(0.05–0.118)	1.41	0.494	FEM	26/288	24, 38, 78
ST-3	0.181(0.083–0.278)	8.36	0.039	REM	67/295	24, 38, 78, 92
ST-11	0	—	—	—	0/280	24, 27, 82, 87
ST-26	0.123(0.042–0.204)	0.5	0.479	FEM	8/62	24, 78
ST-35	0.136(0.063–0.210)	16.00	0.003	REM	64/455	36, 38, 78, 87, 92
ST-37	0.172(0.122–0.221)	43.77	0	REM	152/913	19, 24, 36–38, 42, 77–78, 82, 87, 92–94
ST-39	0.159(0.068–0.250)	0.17	0.68	FEM	10/62	24, 78
ST-54	0.167(0.098–0.237)	50.99	0	REM	146/711	24, 36, 38, 42, 77–78, 82, 87, 93

C. difficile in animals in China

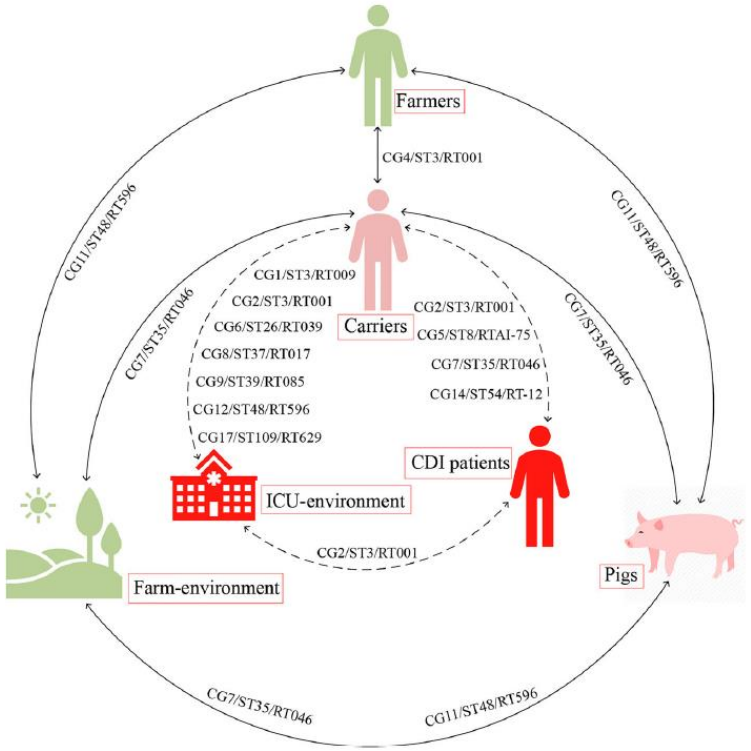
- ST11 was the predominant genotype in animals in China.
- The 15 isolates resistant to ciprofloxacin.
- All isolates were susceptible to tetracycline.

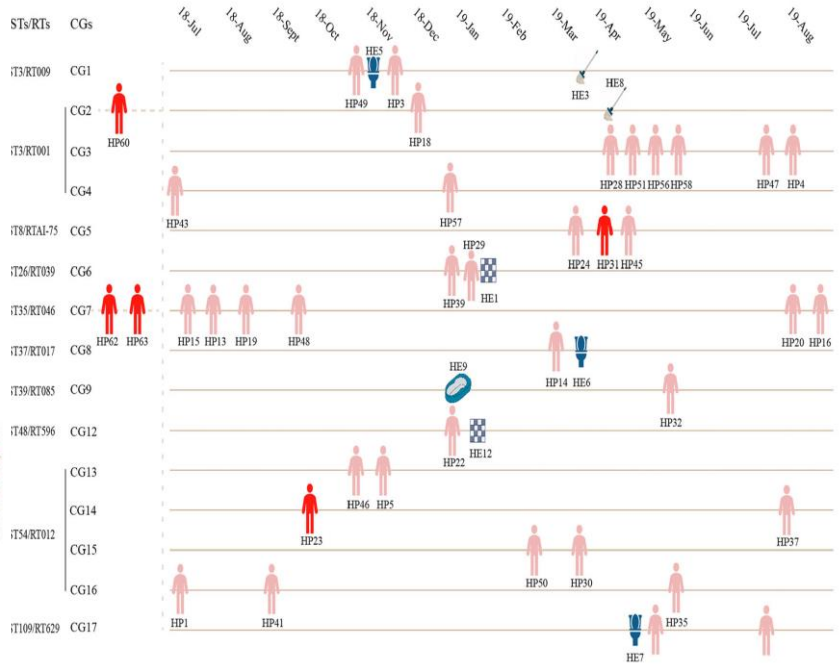
Source	NO.	STs	RTs	Toxin				No. of resistant isolates / Clinical breakpoints									
				tcdA	*tcdB*	*cdtA*	*cdtB*	MXF ≥8	CLI ≥8	TET ≥16	ERY ≥8	LVX ≥8	CIP ≥8	CHL ≥32	MEM ≥16	VAN ≥4	MTZ ≥32	RIF ≥4
SN	1	11	ICDC028 (RT078)	+	+	+	+	0	0	0	1	0	1	0	0	0	0	0
SN	21	11	ICDC035 (RT126)	+	+	+	+	0	14	0	21	0	2	0	0	0	0	0
SN	7	11	ICDC050	+	+	+	+	0	4	0	7	0	1	0	0	0	0	0
SN	6	11	ICDC052	+	+	+	+	0	1	0	6	0	2	0	0	0	0	0
N	4	11	ICDC035 (RT126)	+	+	+	+	0	3	0	4	0	2	0	0	0	0	0
YCVTN	1	11	ICDC028 (RT078)	+	+	+	+	0	0	0	1	0	1	0	1	0	0	0
YCVTN	9	11	ICDC035 (RT126)	+	+	+	+	0	6	0	9	0	3	0	0	0	0	0
YCVTN	1	11	ICDC050	+	+	+	+	0	0	0	1	0	0	0	0	0	0	0
YNY	1	11	ICDC035 (RT126)	+	+	+	+	0	1	0	0	0	0	0	0	0	0	0
ND	1	3	ICDC039 (RT220)	+	+	–	–	0	1	0	1	0	1	1	0	0	0	0
YNY	3	468	ICDC094	+	+	–	–	0	1	0	0	0	2	0	0	0	0	0
Total	55							0	31	0	51	0	15	1	1	0	0	0

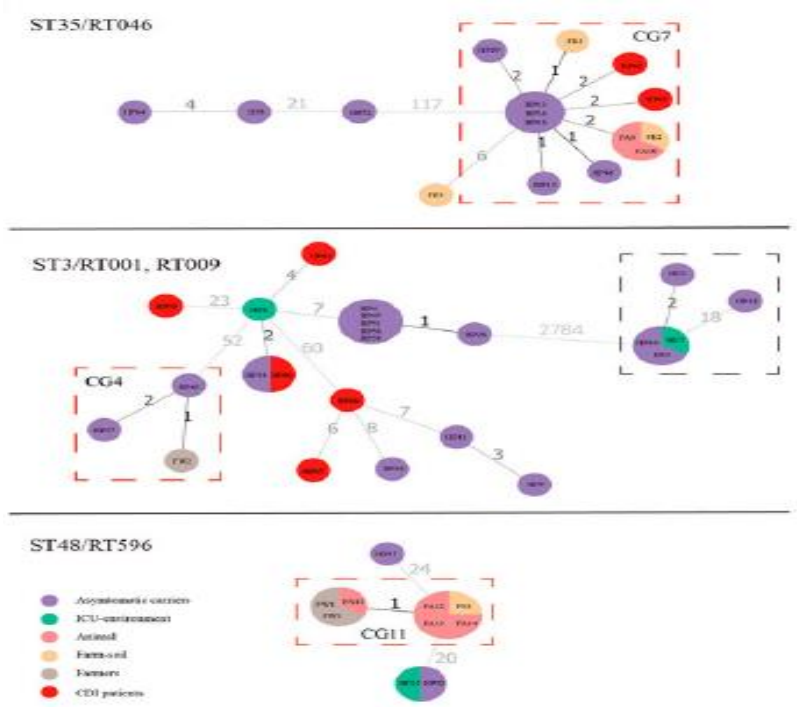
The characteristics of *C. difficile* molecular epidemiology in animals are still unclear in China

C. difficile interspecies transmission in China

- WGS was performed on 98 *C. difficile* isolates from hospitals, environment, animals, soil, and farmers in Zhejiang.
- Three clonal groups (CG4, CG7, and CG11) shared across hospital and farm strains by SNP analysis.
- Interspecies and cross-regional transmission of *C. difficile* happened among different sources.

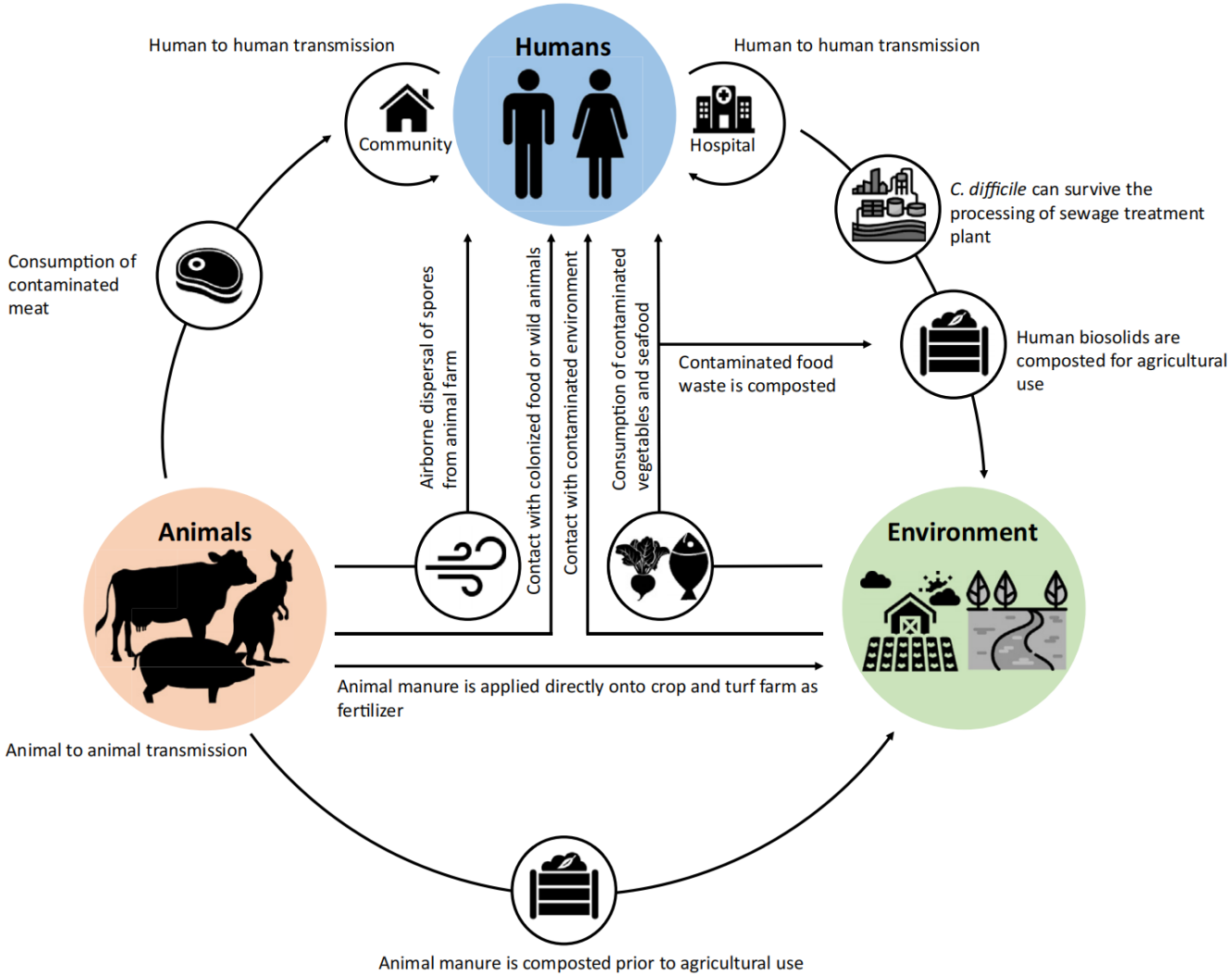






Zhou Y et al. Emerging Microbes & Infections. 2021;2005453

One Health on *C. difficile* transmission



Lim SC,et al. *Clostridium difficile* and One Health. Clin Microbiol Infect. 2020;26(7):857-863.

Take home message

- *C. difficile* is a spore forming obligate anaerobe, leading to not only hospital-acquired infection, but also community-acquired infection.
- Molecular characteristics of CDI epidemiology in China are different from those in other regions.
- Studies on *C. difficile* in animals has demonstrated that this is a zoonotic pathogen, leading to interspecies clonal transmission.
- Molecular characteristics of *C. difficile* in animals in China should be further studied in the futre.
- It is essential that One Health perspective on CDI needs multi-disciplinary, multi-field cooperation.
- More multi-center prospective or retrospective studies on *C. difficile* from different sources should be performed in order to better understand CDI and conduct control and prevention of CDI in the future.

Thank you for your attention