



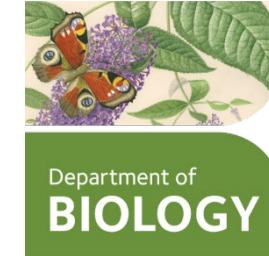
PATH-SAFE work stream 2d

Genomics of antimicrobial resistant *Campylobacter* transmission through UK Agri-Food systems.

Dr Frances Colles

frances.colles@biology.ox.ac.uk

WS2d – Oxford University antimicrobial resistant *Campylobacter* genomics



Isolates to be sequenced

- 2,500 Human disease isolates (Oxfordshire and Wales)
- 1,000 Agri-food isolates (cattle, sheep, deer, duck, turkey, free-range poultry)

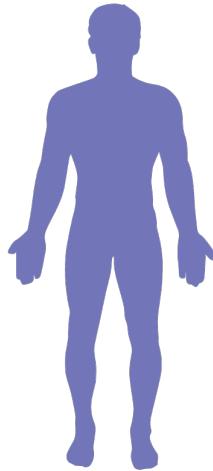
Intended outcomes

- Build a well-defined, representative culture collection for *Campylobacter*, enabling analyses such as source attribution and Genome Wide Association Studies (GWAS)
- Determine the genomic predictive mechanisms of antimicrobial resistance amongst the isolate collection
- Assess longitudinal trends and current risk to human health through AMR *Campylobacter*
- Assess the impact of eating out and foreign travel on cases of human disease
- Integration of PubMLST (<https://pubMLST.org>) with PATH-SAFE resources

Introduction

- Why *Campylobacter*?
- Previous study (2015-2018): ‘ Enhanced molecular-based surveillance and source attribution of *Campylobacter* infections in the UK’
- Overview of current study (preliminary results):
 - Oxfordshire human disease
 - Source attribution
 - Antimicrobial resistance
- Ongoing work and future directions

The problem(s) with *Campylobacter*



In humans:

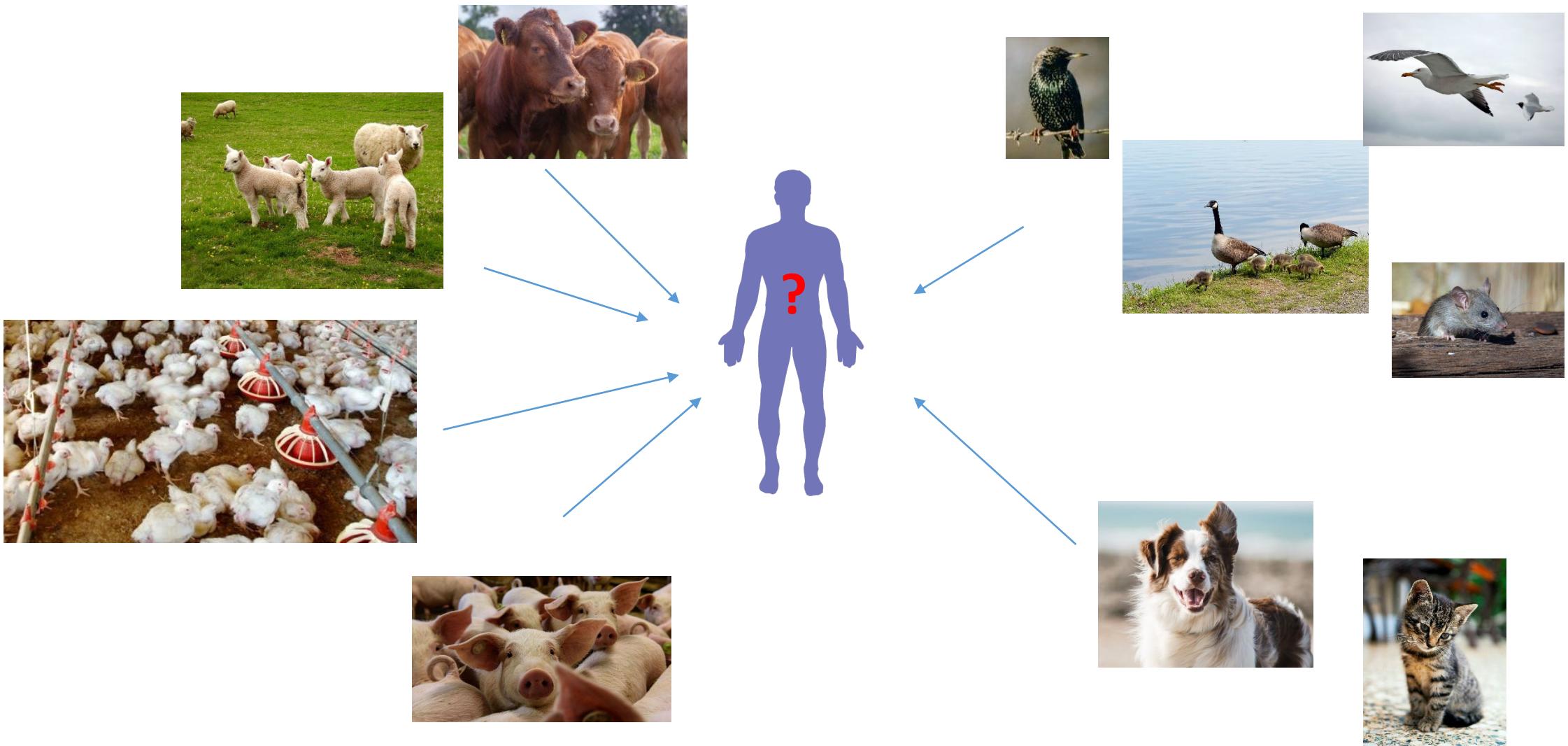
- Severe bloody diarrhoea
- 5-600,000 cases/yr in the UK
- GBS, Reactive arthritis, IBS
- £700 million year cost to economy



WHO watch list for antimicrobial resistance

Campylobacter

The problem(s) with *Campylobacter*



Previous source attribution study (2015-2018)

RESEARCH PROJECT

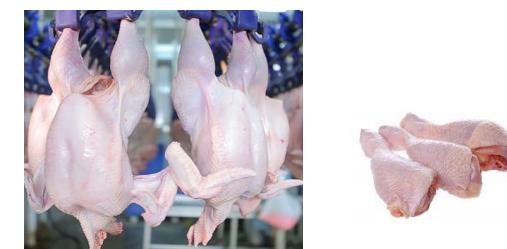
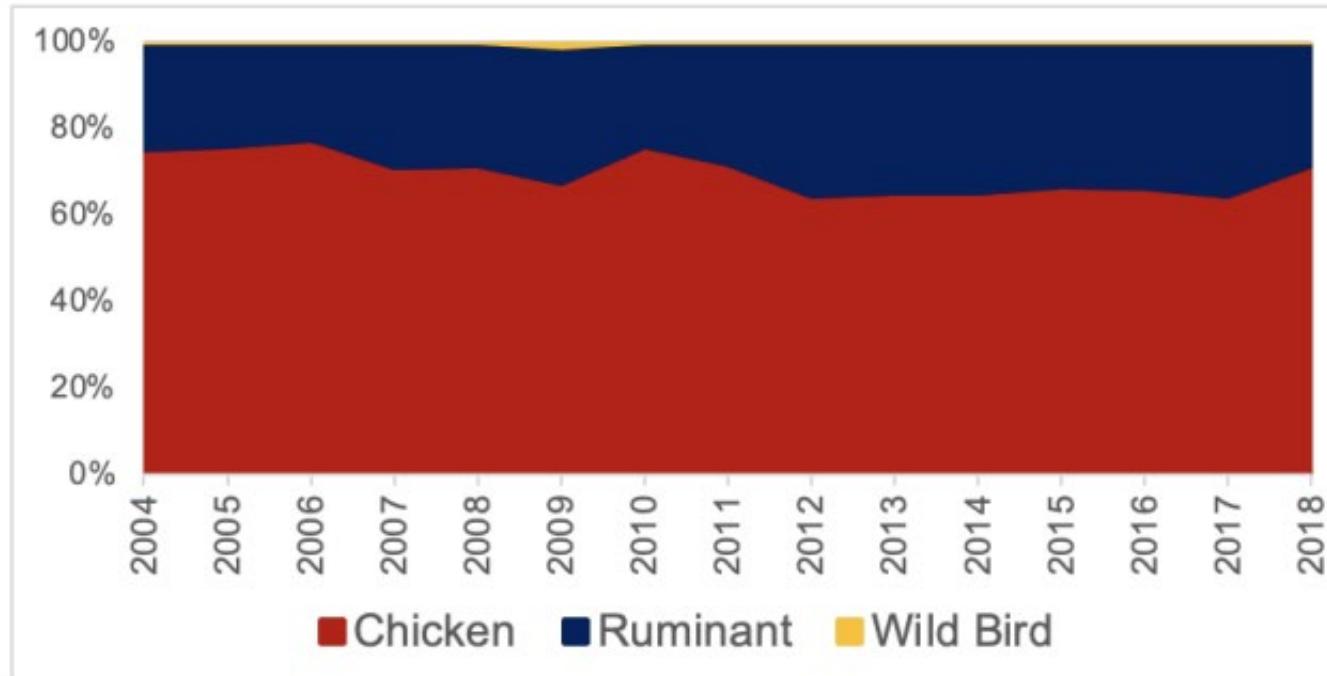
Enhanced molecular-based surveillance and source attribution of campylobacter infections in the UK

This survey estimates the contributions of the main sources of human campylobacter infection and seeks to identify any changes over time.

- Human Disease isolates (Oxfordshire and North East England) in years 2015-18, n= 5,3325,
- Abattoir and retail meat from duck, sheep, cattle, pig, turkey and chicken, n= 3,883

<https://doi.org/10.46756/sci.fsa.ksj135>

Contaminated chicken meat is the predominant source of human disease



Chicken meat:
Source of 60-80% human disease

High levels of antimicrobial resistance in human disease: *C. jejuni*

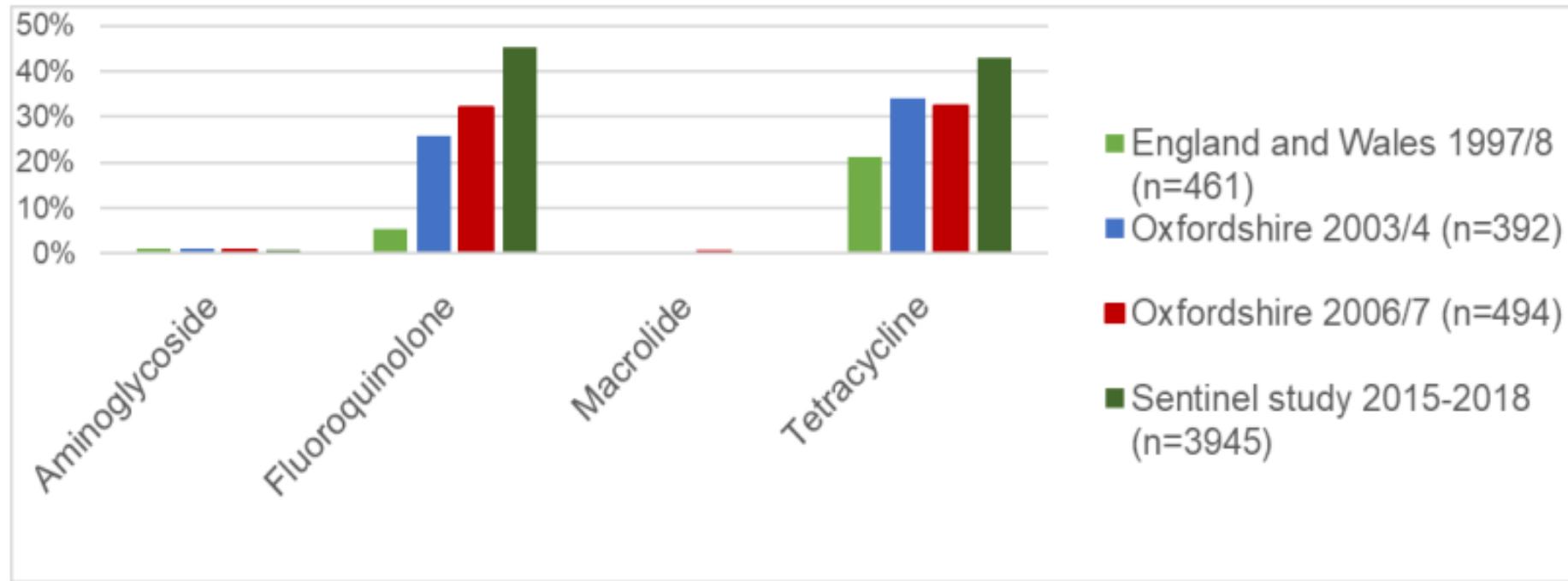


Figure 31: Percentage genetically estimated antimicrobial resistance in isolates of *Campylobacter jejuni* from human cases in datasets spanning 1997 to 2018 in England and Wales.

High levels of antimicrobial resistance in animal sources: *C. jejuni*

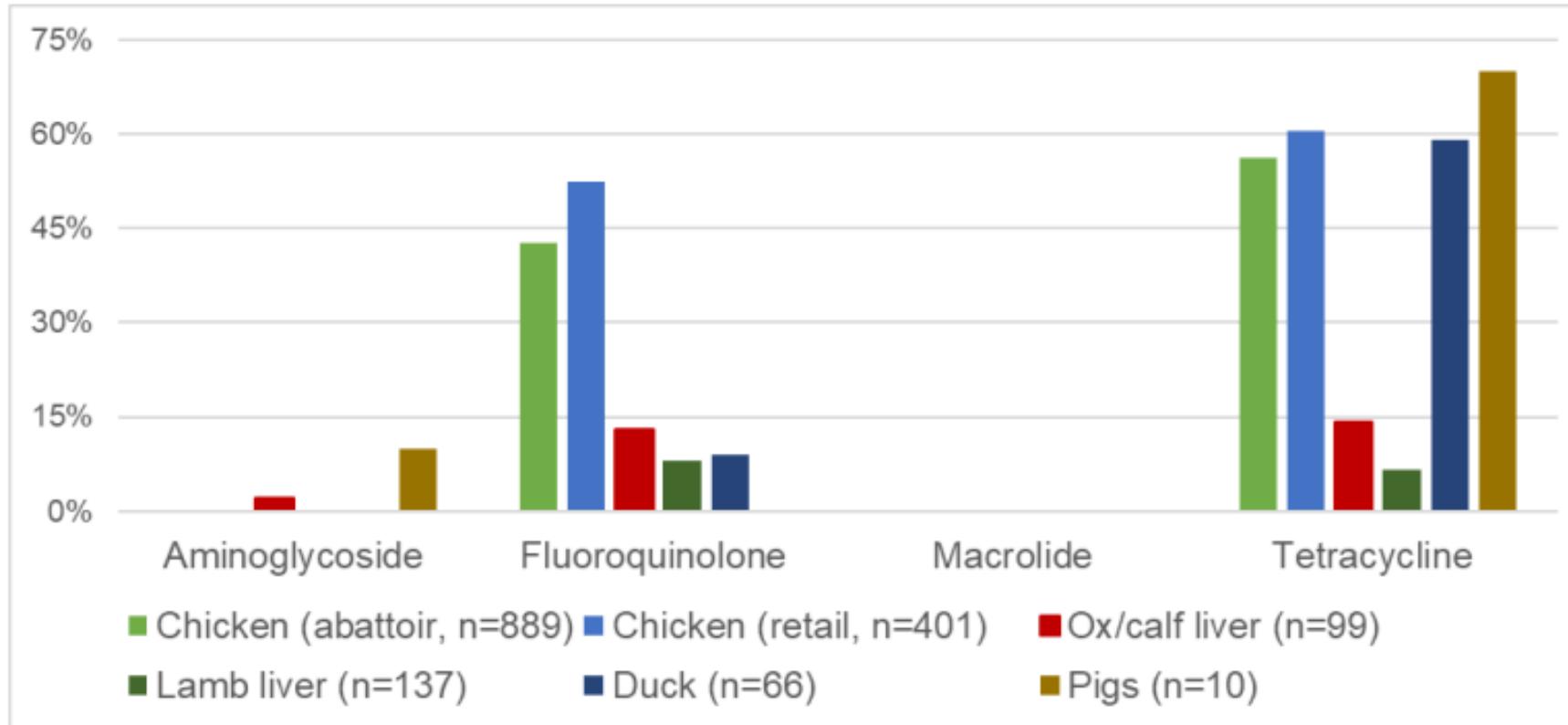


Figure 32: Percentage genetically estimated antimicrobial resistance among isolates of *Campylobacter jejuni* from food animals.

High levels of antimicrobial resistance in human disease: *C. coli*

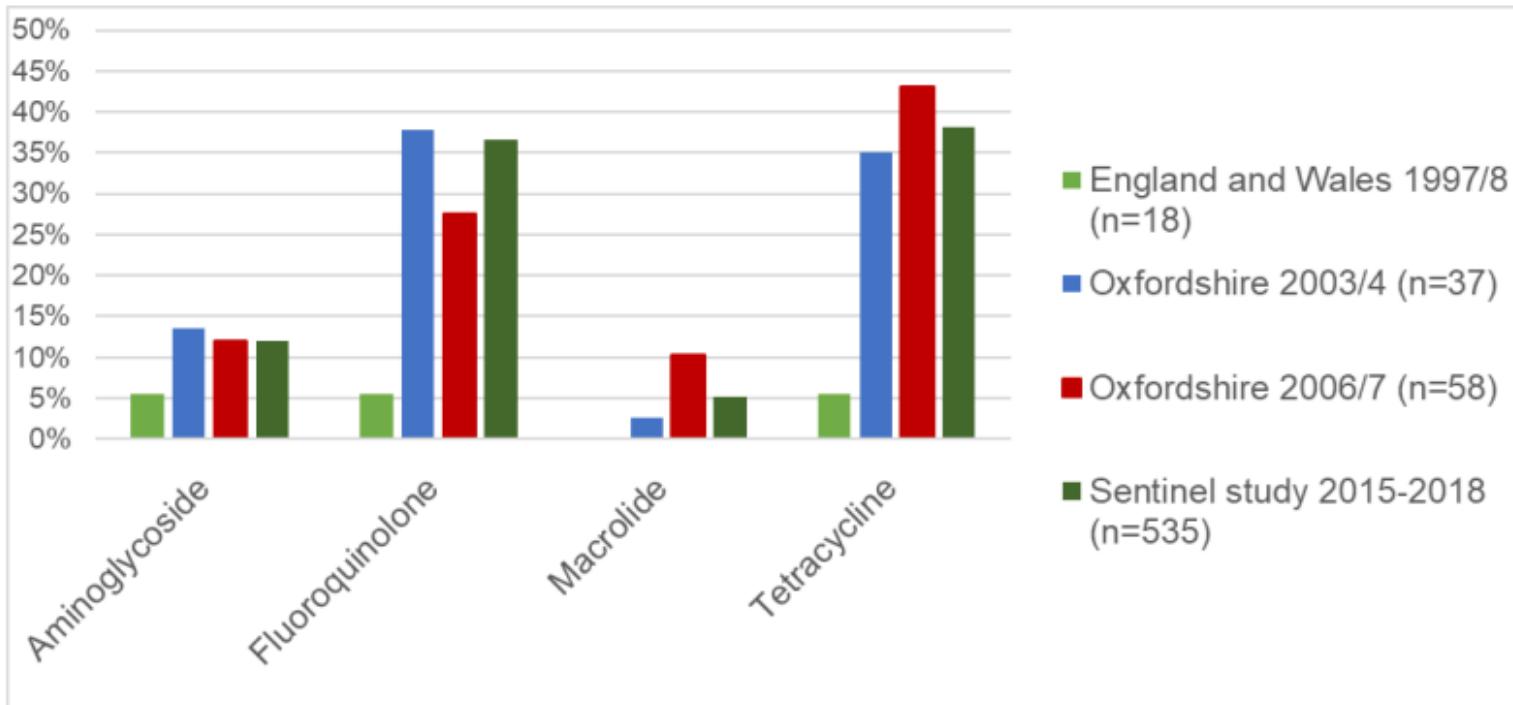


Figure 33: Percentage genetically estimated antimicrobial resistance among isolates of *Campylobacter coli* from human cases in datasets spanning 1997 to 2018 in England and Wales.

Enhanced molecular based surveillance and source attribution of *Campylobacter* infections in the UK
<https://doi.org/10.46756/sci.fsa.ksj135>

High levels of antimicrobial resistance in animal sources: *C. coli*

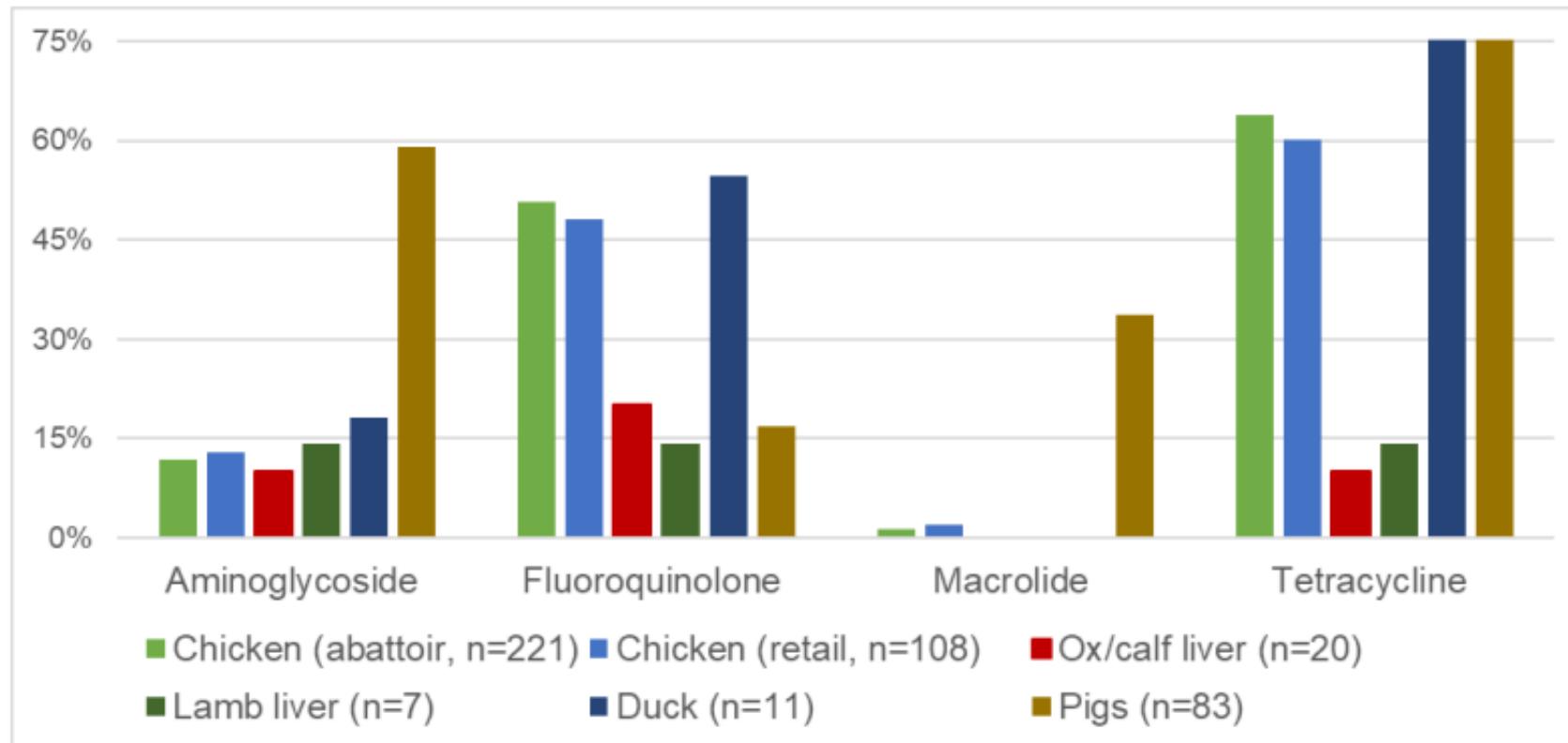
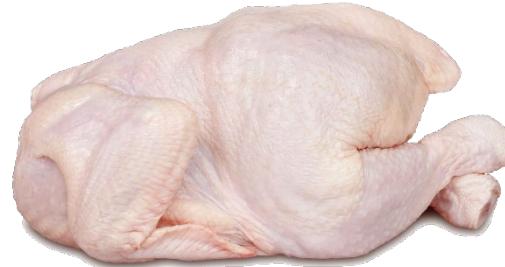


Figure 34: Percentage genetically estimated antimicrobial resistance among isolates of *Campylobacter coli* from food animals.

The percentage of heavily contaminated chicken meat is falling



Chicken meat:

2014/15

73.3% neck skin samples *Campylobacter* positive
19.4% neck skin samples >1,000 CFU/g

2017

56% neck skin samples *Campylobacter* positive
7% neck skin samples >1,000 CFU/g

Higher rates and greater variation amongst smaller retail shops

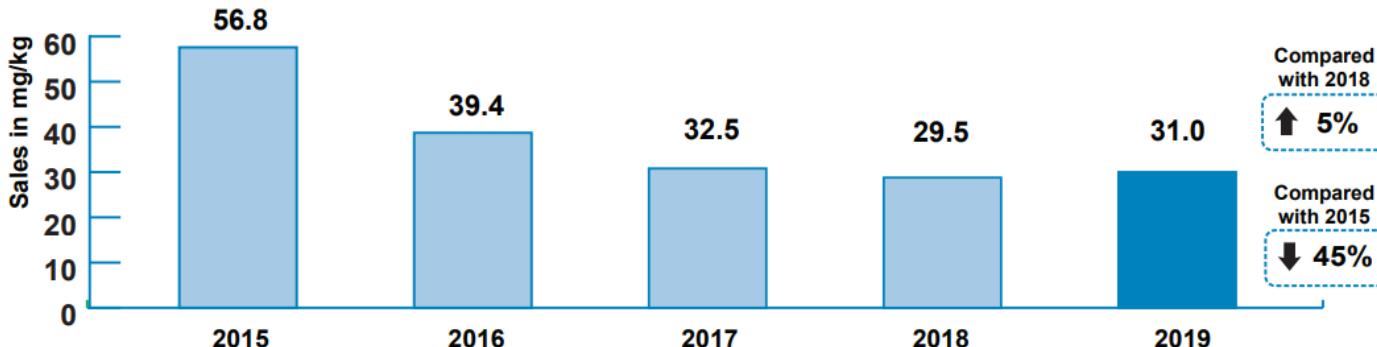
Antibiotic use on farms is falling

Antibiotic Sales

Veterinary medicines directorate UK (VMD)

Sales for food-producing animals (mg/kg)

Sales of veterinary antibiotics for use in food-producing animals, adjusted for animal population, were 31.0 mg/kg; a 1.5 mg/kg (5%) increase since 2018, however there was an overall 25.8 mg/kg (45%) decrease since 2015.



Sales of Highest Priority Critically Important Antibiotics (HP-CIAs) in food-producing animals dropped from 0.21 mg/kg in 2018 to 0.17 mg/kg (21%) in 2019.

	2015	2016	2017	2018	2019	Compared with 2015
Fluoroquinolones (mg/kg)	0.35	0.23	0.16	0.15	0.13	↓ 61%
3rd/4th generation cephalosporins (mg/kg)	0.17	0.14	0.11	0.06	0.03	↓ 82%
Colistin (mg/kg)	0.12	0.02	0.0006	0.0007	0.0002	↓ 99.9%
Total HP-CIAs (mg/kg)	0.64	0.38	0.26	0.21	0.17	↓ 74%

British poultry council

ANTIBIOTICS USED BY THE UK POULTRY MEAT SECTOR
IN THE LAST 7 YEARS 2012-19

76% REDUCTION IN THE TOTAL USE OF ANTIBIOTICS
97.3% REDUCTION IN THE USE OF CRITICALLY IMPORTANT ANTIBIOTICS

IN 2019 WE USED 19.7 TONNES OF ANTIBIOTICS, WHICH ACCOUNTS FOR 9.33%* OF THE TOTAL ANTIBIOTICS LICENSED FOR FOOD PRODUCING ANIMALS *SOURCE: VMD, 2018

Whilst we saw an increase in usage in 2019 due to disease challenges, the sector remains well below Government approved, industry-led specific targets.

Genomics of antimicrobial resistant *Campylobacter* transmission through UK Agri-Food systems.

Preliminary results from the current study

PubMLST: Germs, Genes and Genomes

PubMLST Public databases for molecular typing and microbial genome diversity

Home > Organisms > *Campylobacter jejuni/coli*

Campylobacter jejuni/coli

Source of isolates submitted to the *Campylobacter jejuni/coli* database

The MLST scheme hosted in this database is described in Dingle et al. 2001 *J Clin Microbiol* 39:14-23st. The cgMLST scheme is described in Cody et al. 2017 *J Clin Microbiol* 55:2086-2097st.

Database curated by Frances Colles.

- Primers and conditions
 - MLST
 - MOMP
- *Campylobacteriosis sentinel surveillance in Oxfordshire, UK*

The preferred citation for this website is:

Jolley et al. *Wellcome Open Res* 2018, 3:124 [version 1; referee: 2 approved].

Typing The typing database contains nomenclature - allele definitions that provide an identifier for every unique allele sequence, and MLST profiles that index each unique combination of alleles with a sequence type (ST). Allele sequences: 2,335,864 Last updated: 2024-01-09

Isolate collection The Isolate database consists of Isolate records containing provenance and phenotype information linked to molecular typing information. These records may also include genome assemblies. Isolates: 134,050 Last updated: 2024-01-09

Genome collection A subset of records within the Isolate database may contain genome assemblies. You can access these from the Isolate database by filtering on sequence bin size in a query. Genomes: 83,508 Last updated: 2024-01-04

Updates

PubMLST: Germs, Genes and Genomes

PubMLST Public databases for molecular typing and microbial genome diversity

HOME ORGANISMS SPECIES ID ABOUT US UPDATES

Home > Organisms > *Campylobacter jejuni/coli*

Campylobacter jejuni/coli

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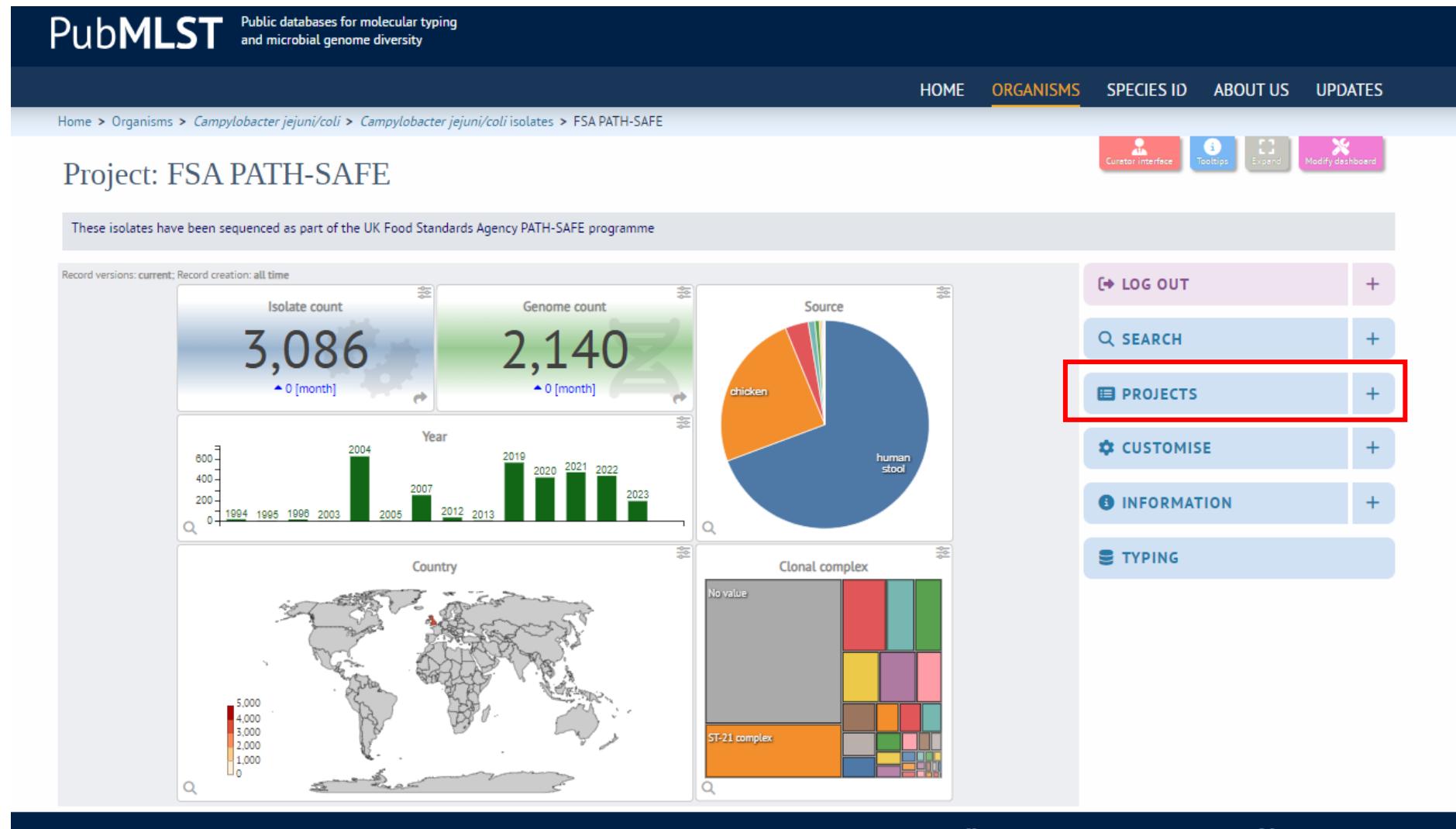
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Updates

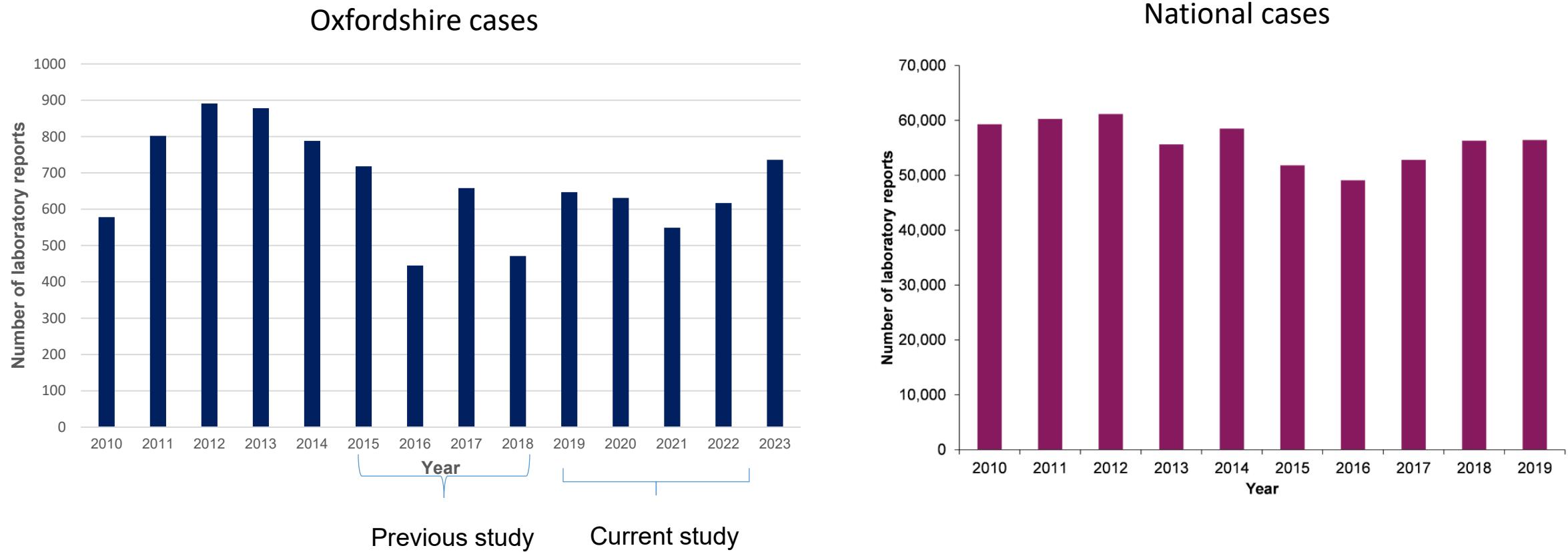
FSA PATH-SAFE project



<https://pubMLST.org>

<https://pubmlst.org/organisms/campylobacter-jejunicoli/>

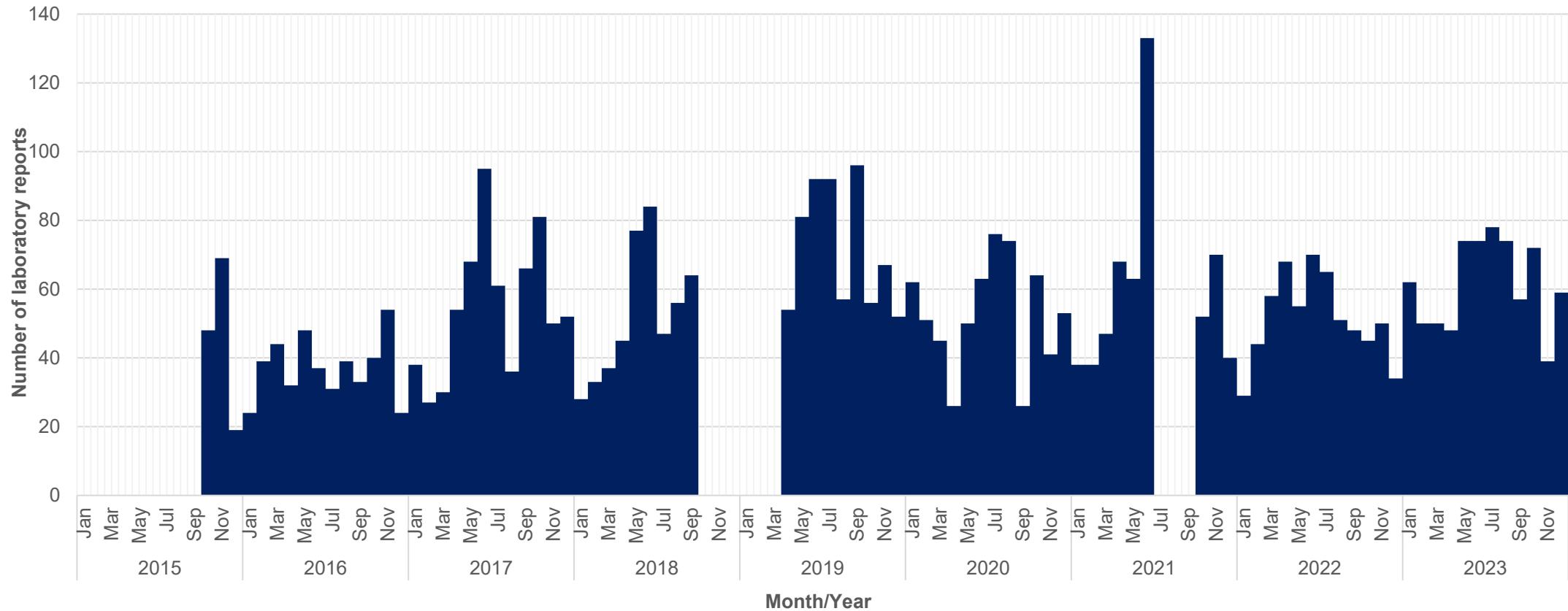
Number of *Campylobacter* case reports per year



Oxford Report: Enhanced molecular-based surveillance and source attribution of *Campylobacter* infections in the UK;
<https://doi.org/10.46756/sci.fsa.ksj135>

National data: <https://www.gov.uk/government/publications/campylobacter-infection-annual-data/campylobacter-data-2010-to-2019>

The number of cases varies seasonally: Oxfordshire data



Nomenclature to describe *Campylobacter* genetic diversity

Sequence query

Please paste in your sequence to query against the database. Query sequences will be checked first identified if an exact match is not found. You can query using either DNA or peptide sequences. ⓘ

Please select locus/scheme Order results by

All loci locus

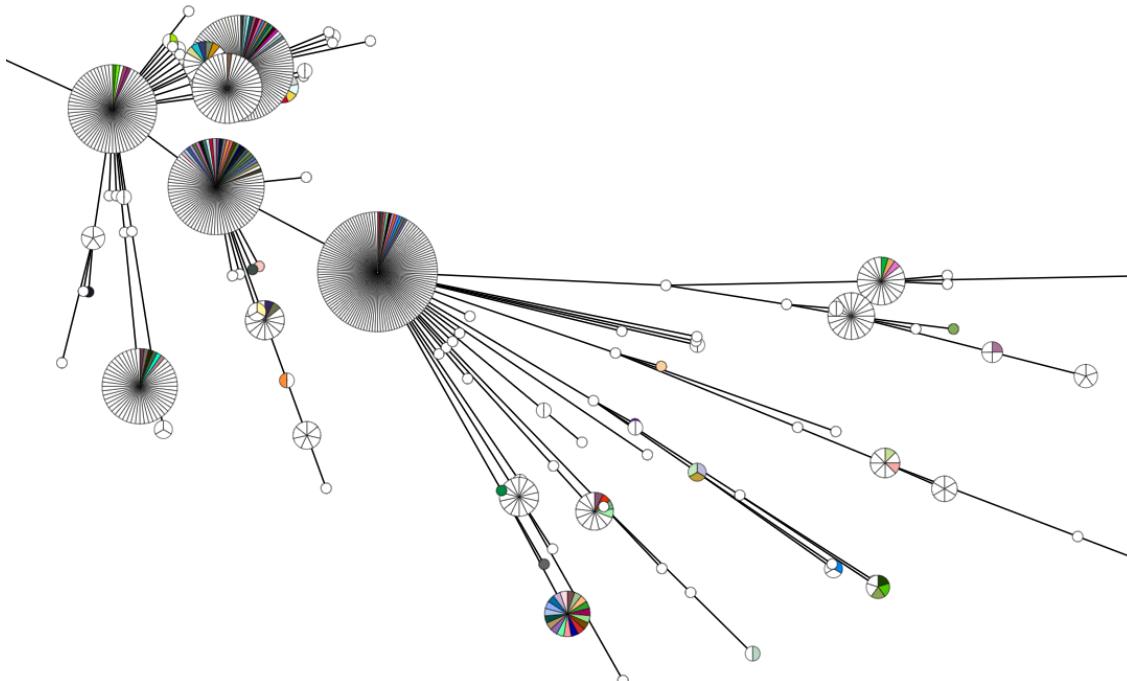
Enter query sequence (single or multiple contigs up to whole genome in size)

```
ATGATAGGCAGAGATATAACAAAGAGTATTAGAAGCTAGAAAATTAAATTAGAGATCAAT  
TTGGGTGGAACGTCTATTGGAACCGGAATTAACTCTCATCCTGATTATCCGAAGGTTGTA  
GAAAGAAAAATAAGAGAAAGTGACAGGTTTGAAATACTGTGCTGAGGATTGATCGAG  
GCGACTCAAGATACGGGAGCTTATGTACAATTTCAGGTGTTAAACGTGTTGCAACA  
AAACTTCTAAAGTATGTAATGACTTAAGACTTTAACGAGTGGTCAAATGTGGCTT  
AATGAGATTAATCTTCAAAAATGCAACCAGGTAGTTCTATTGCCAGGTAAGGTAAT
```



7 locus multilocus sequence typing (MLST)

aspA	glnA	gltA	glyA	pgm	tkt	uncA	Sequence type	Clonal complex
4	7	10	4	1	7	1	ST-45	ST-45 complex
4	7	10	4	42	7	1	ST-137	ST-45 complex
2	61	4	64	74	25	23	ST-1034	ST-1034 complex

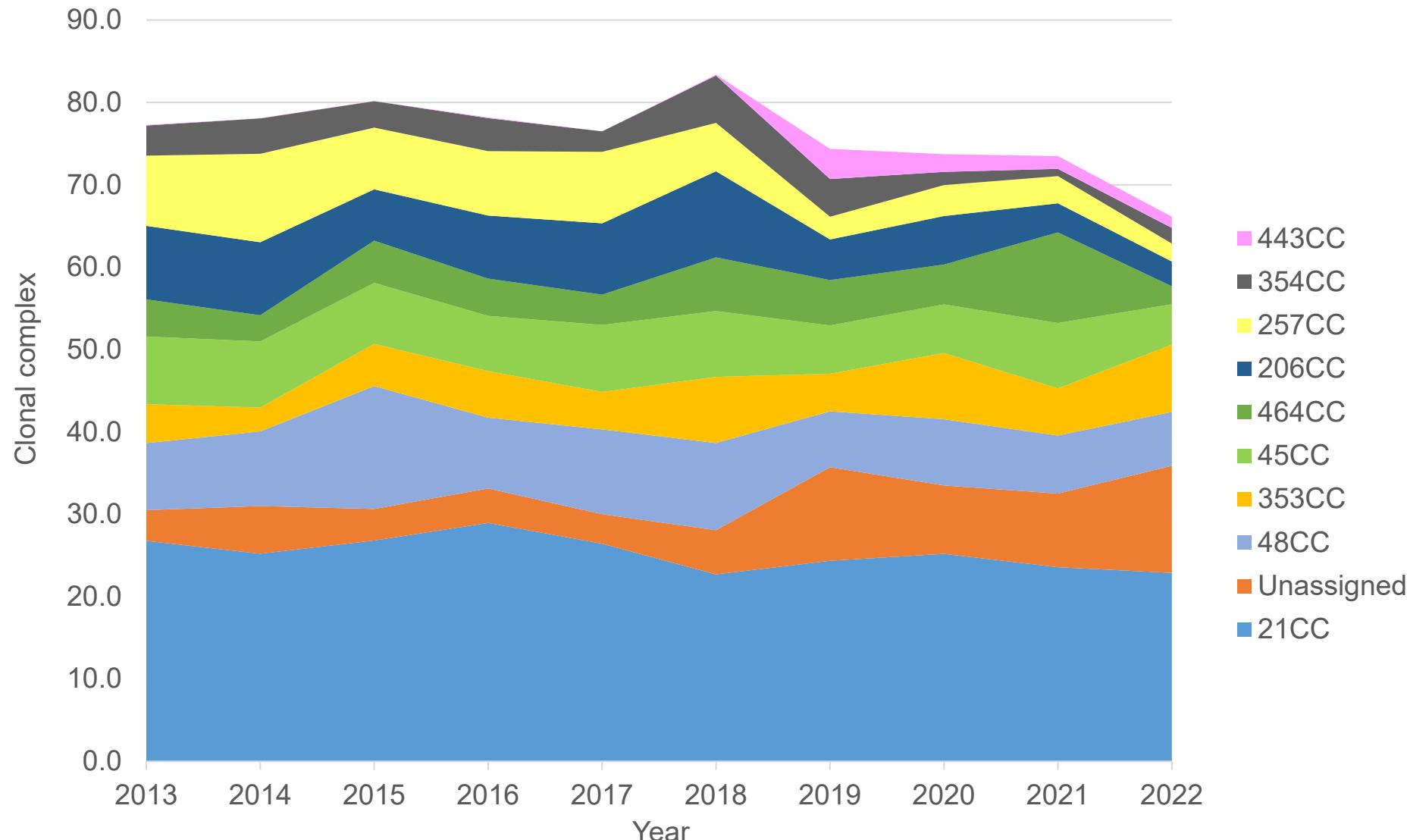


Core genome multilocus sequence typing (cgMLST)

C. jejuni/C. coli v2: 1142 loci

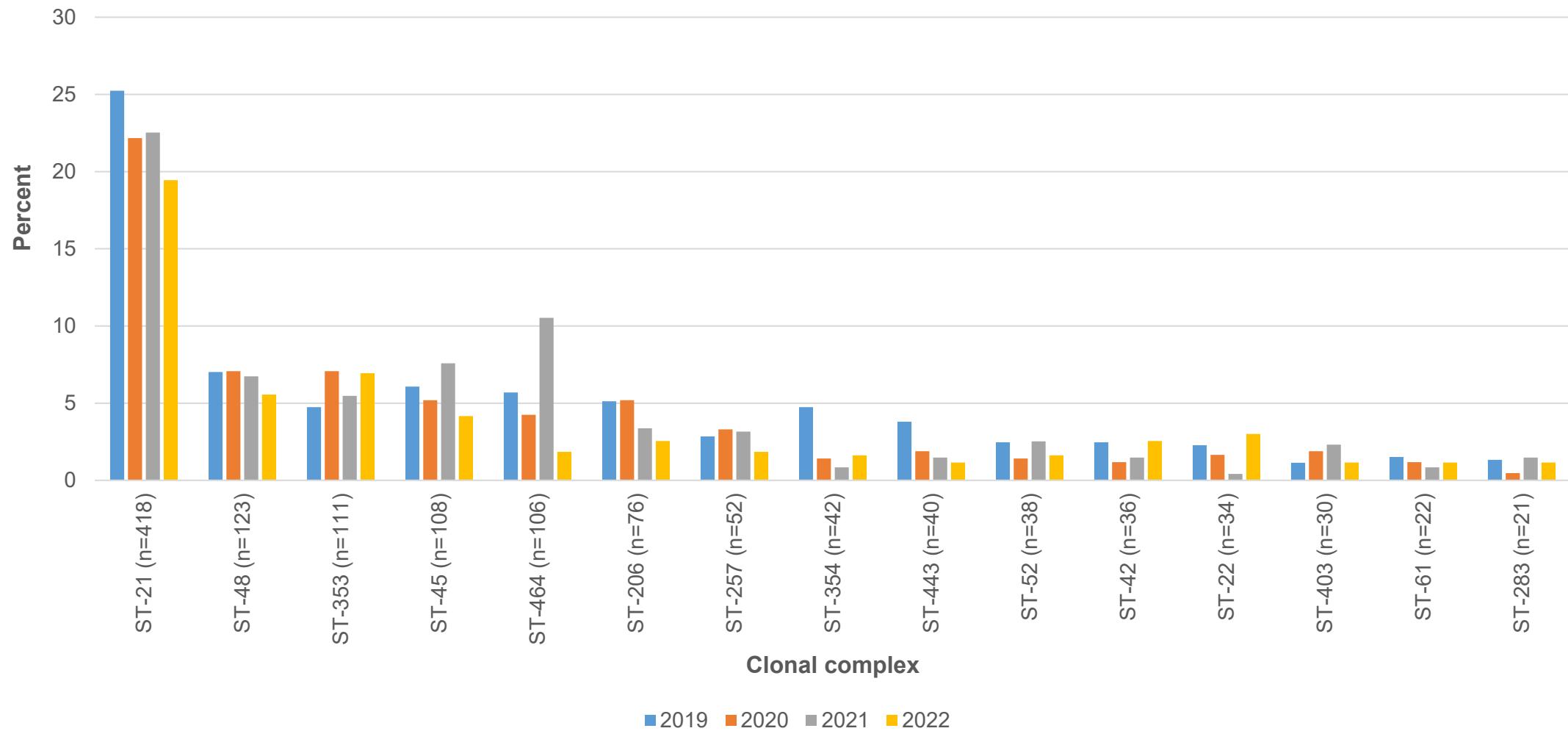
Antimicrobial resistance determinants

The same clonal complexes predominate over time

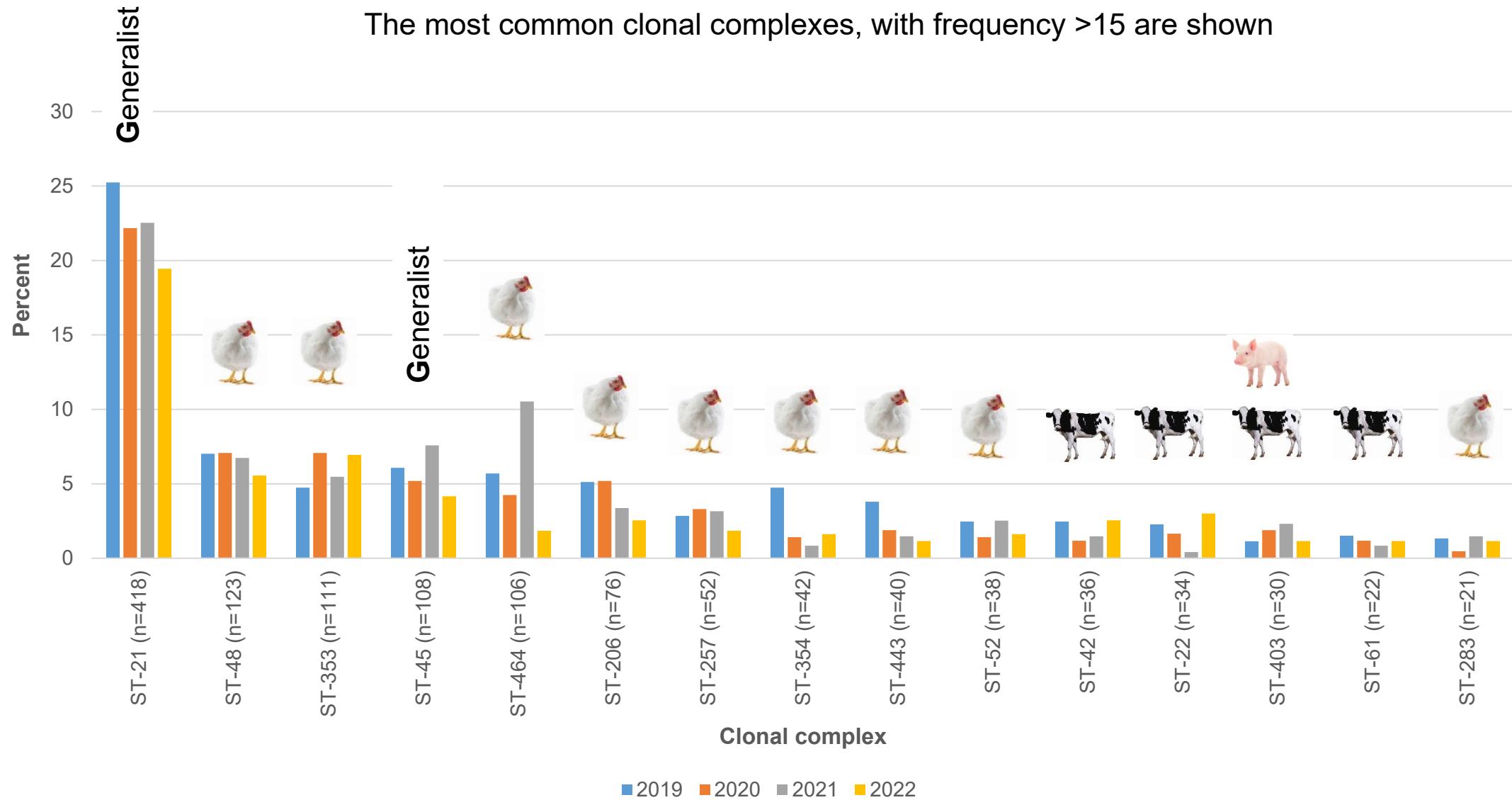


Oxfordshire human disease isolates: source attribution

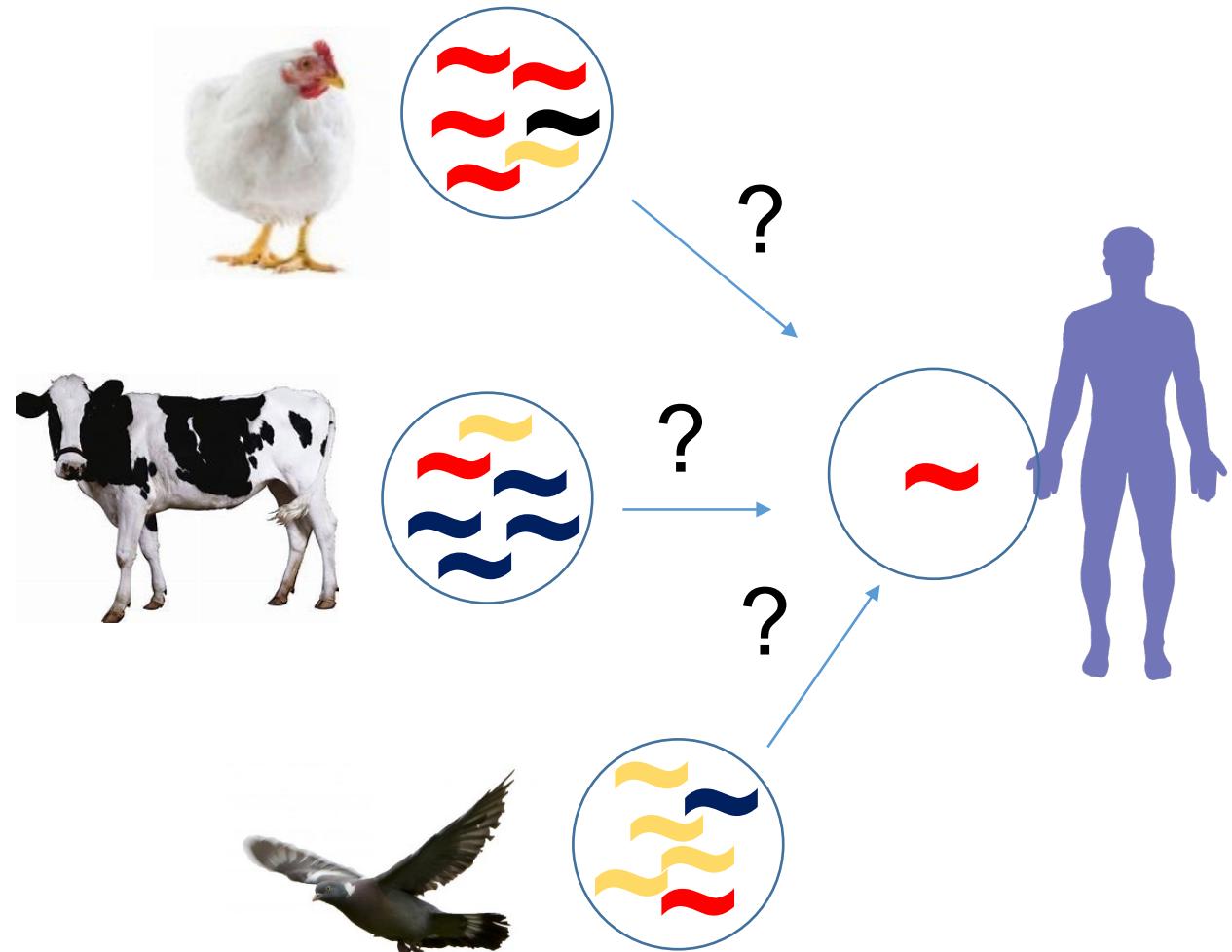
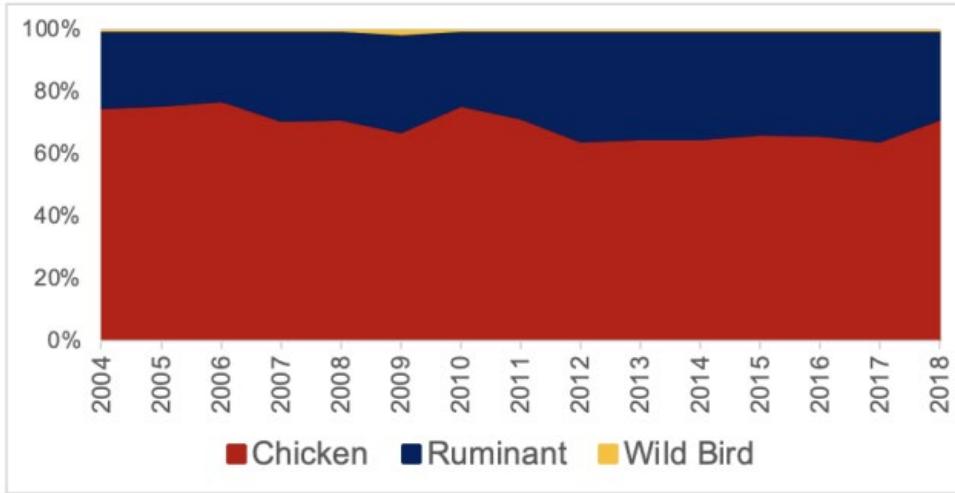
The most common clonal complexes, with frequency >15 are shown



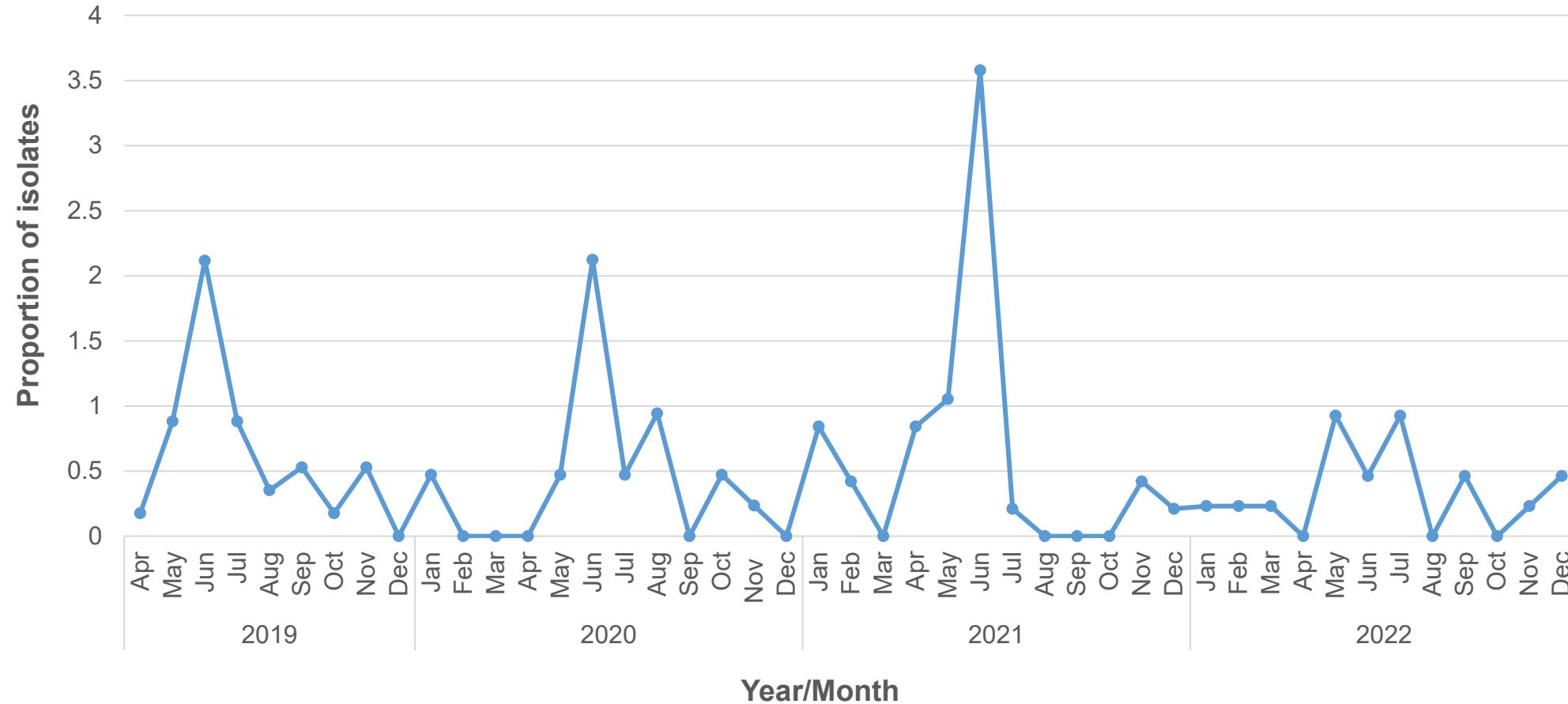
Oxfordshire human disease isolates: source attribution



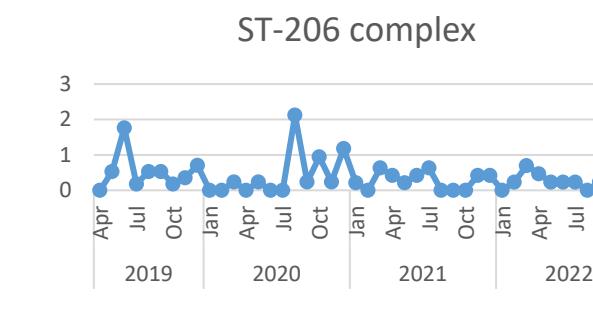
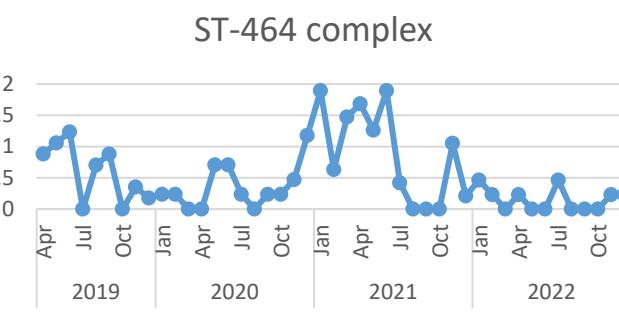
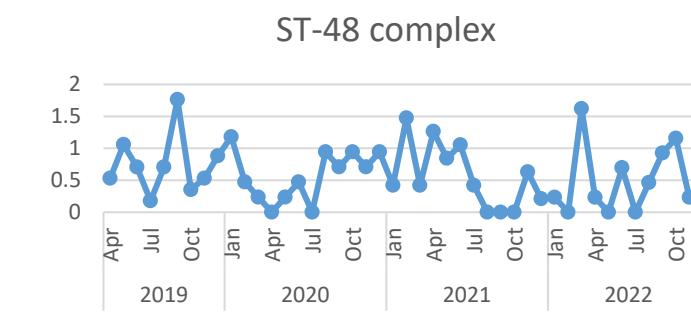
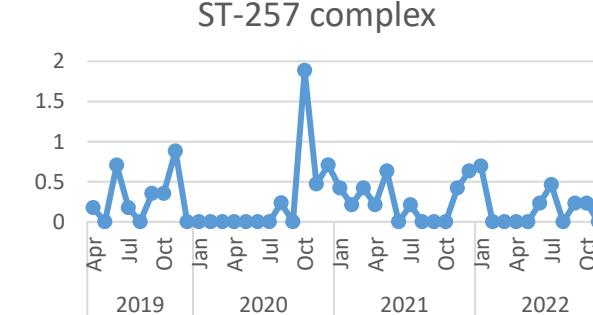
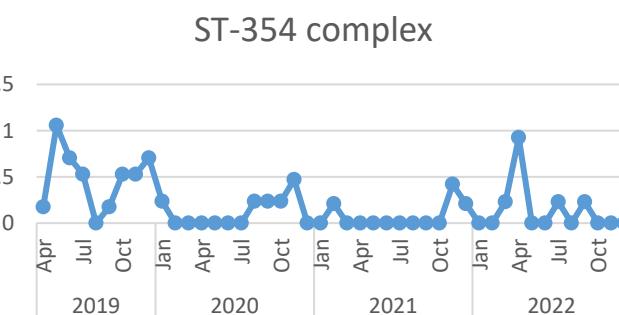
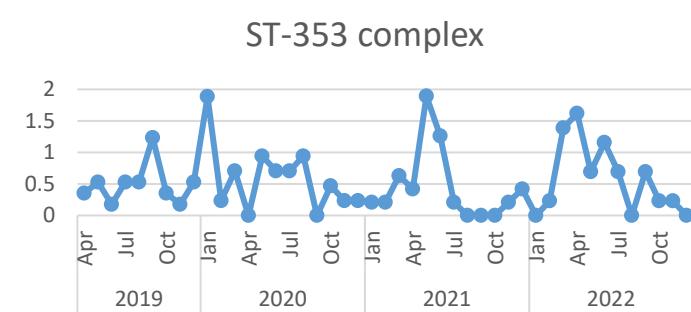
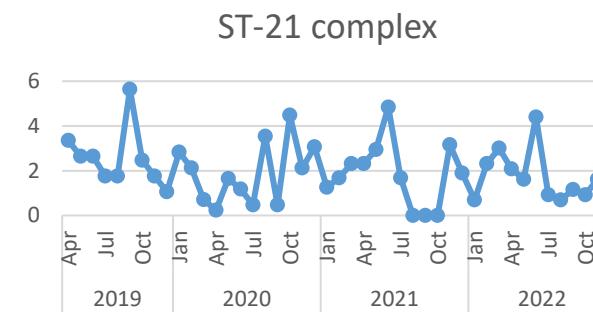
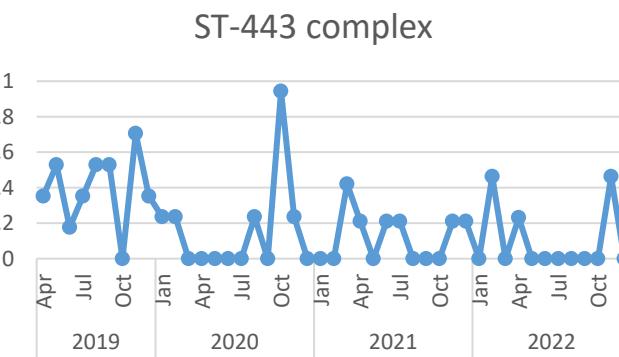
Source attribution models will be used to test results



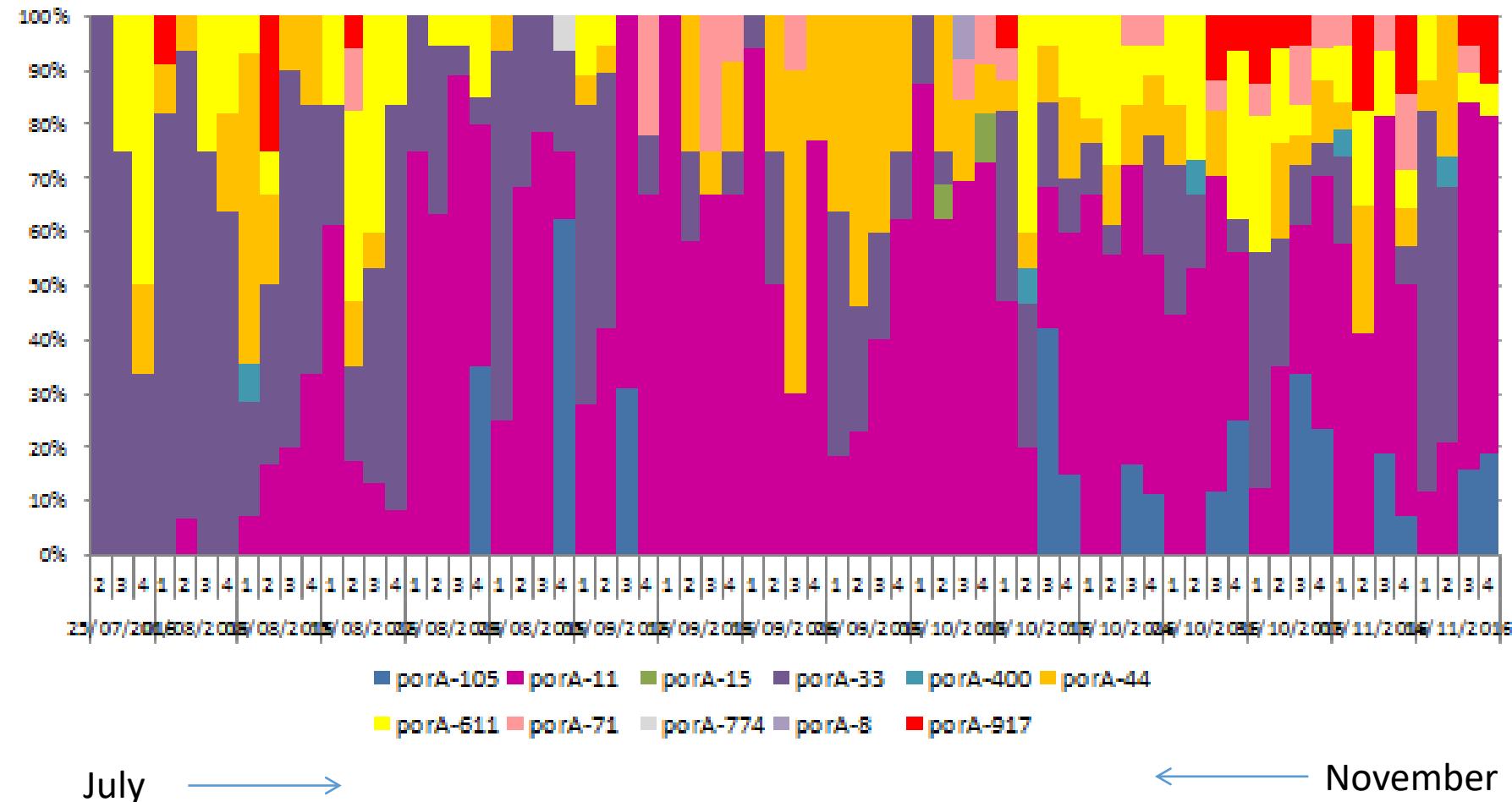
ST-45 complex has a summer peak of infection



Most clonal complexes show no correlation with season



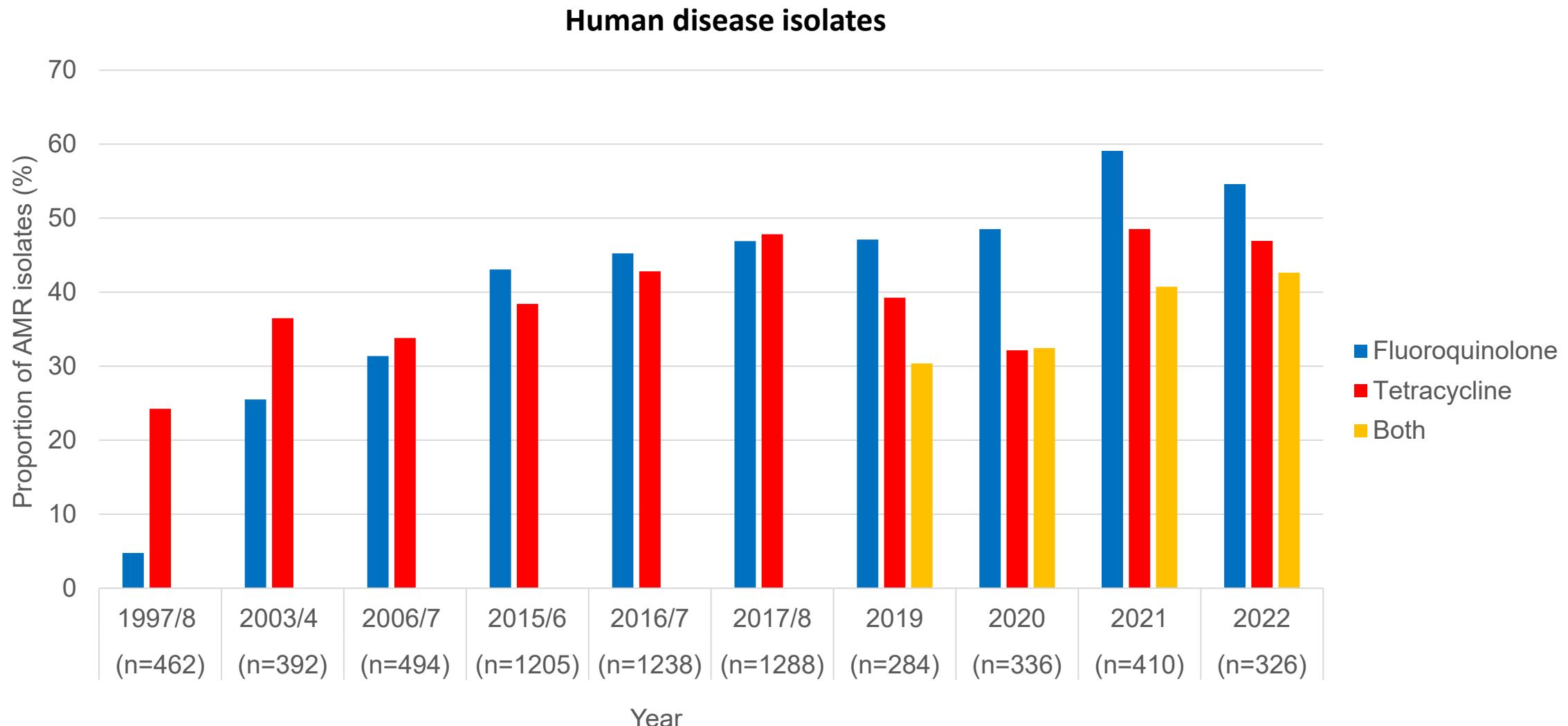
Campylobacter variants in chicken flocks change over time



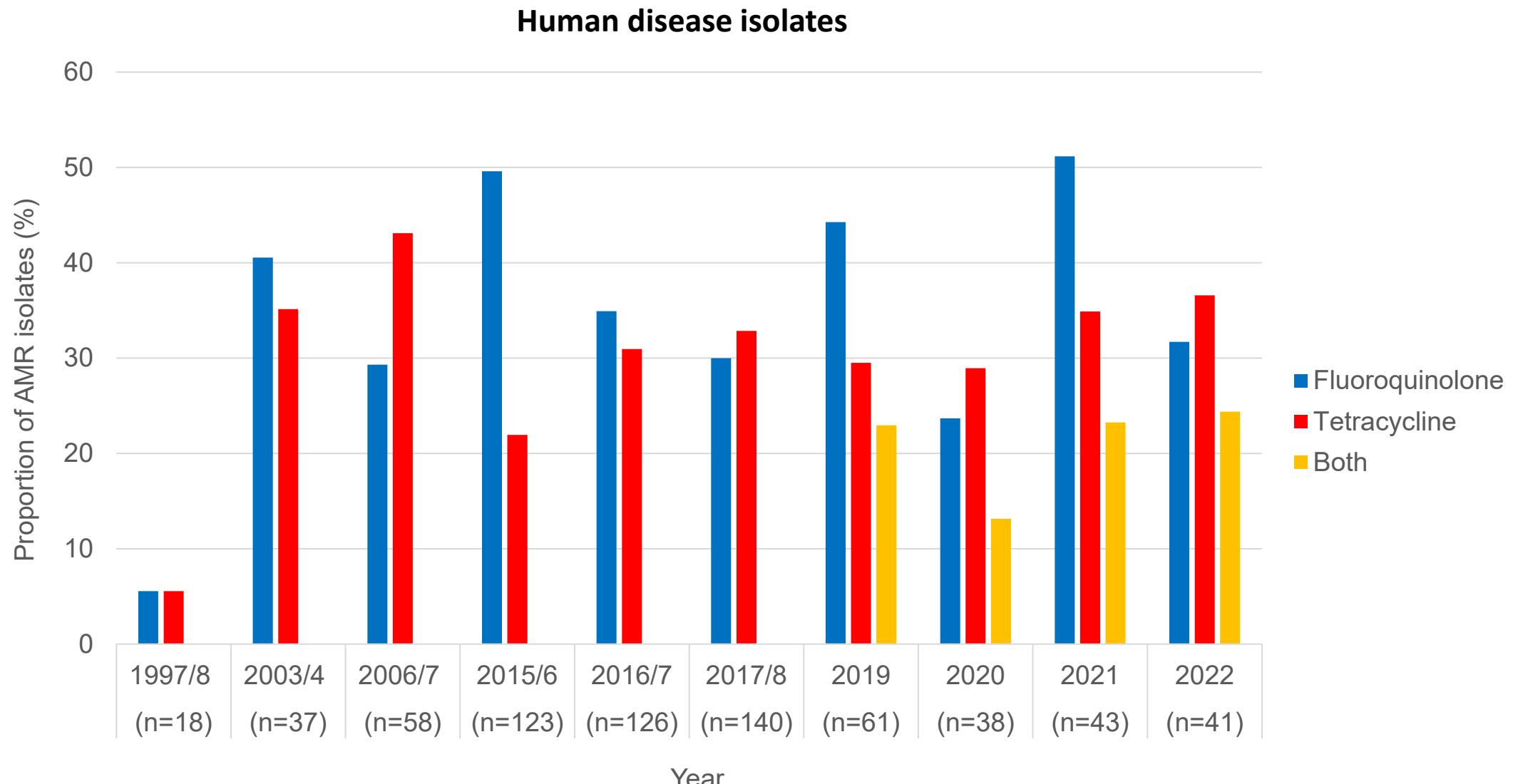
Genomics of antimicrobial resistant *Campylobacter*.

Preliminary results

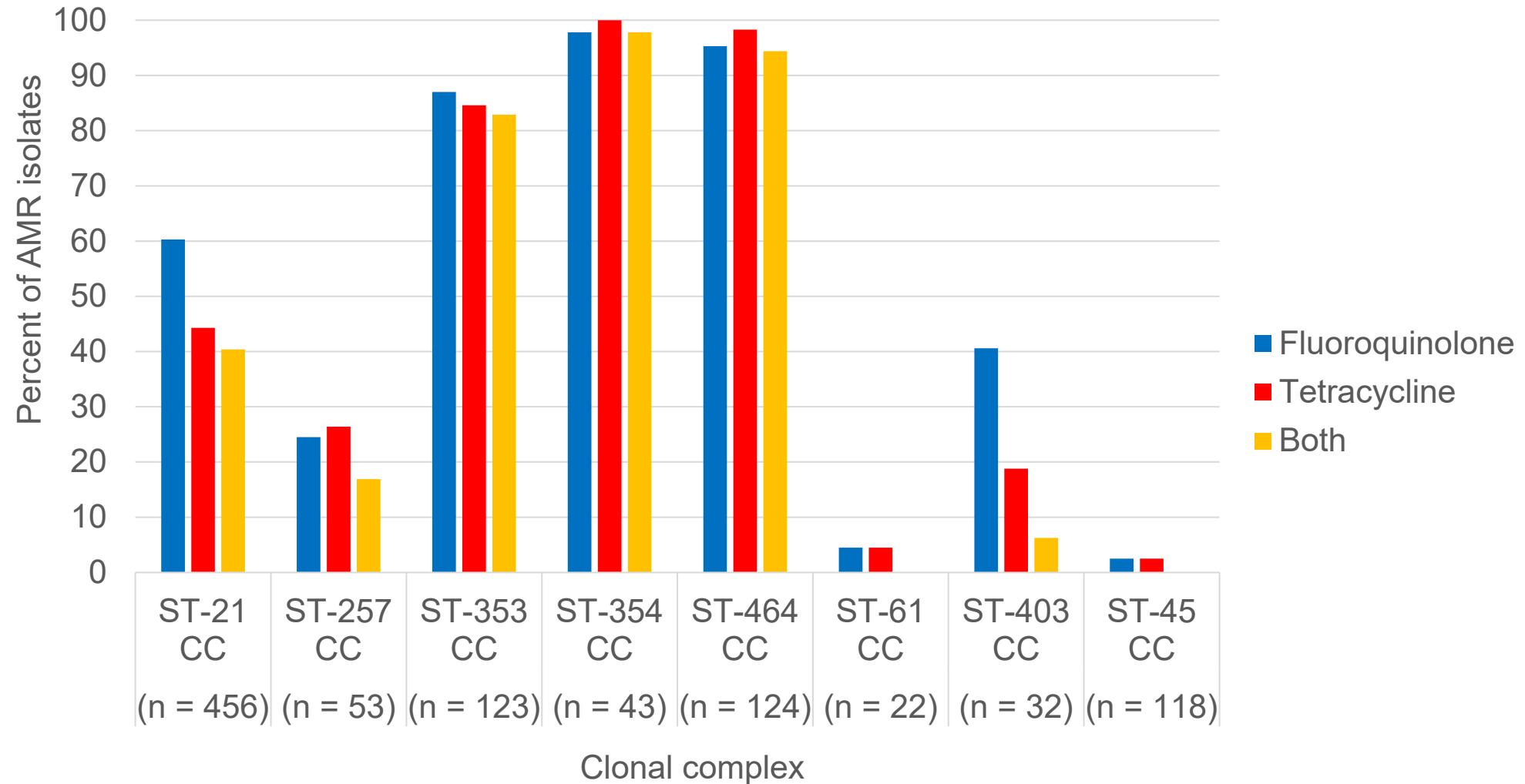
Antimicrobial resistance: *Campylobacter jejuni*



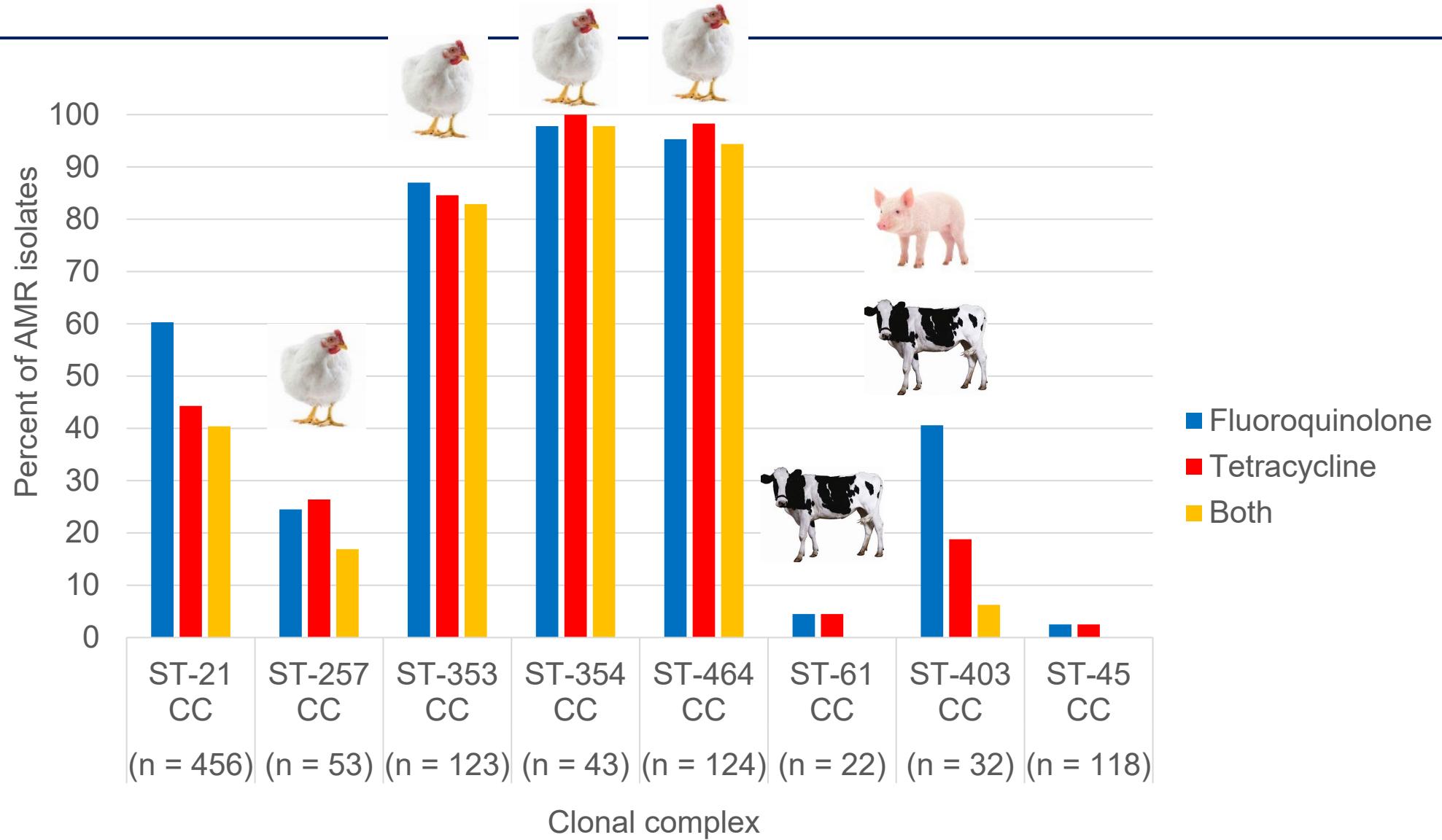
Antimicrobial resistance: *Campylobacter coli*



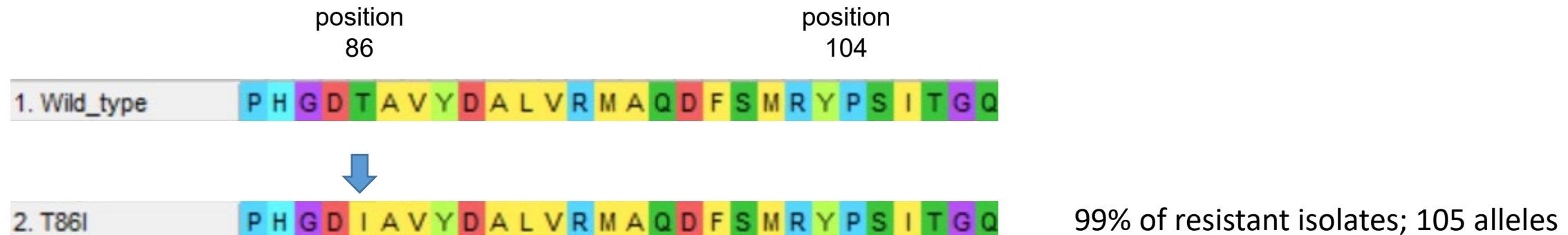
Antimicrobial resistance varies by clonal complex



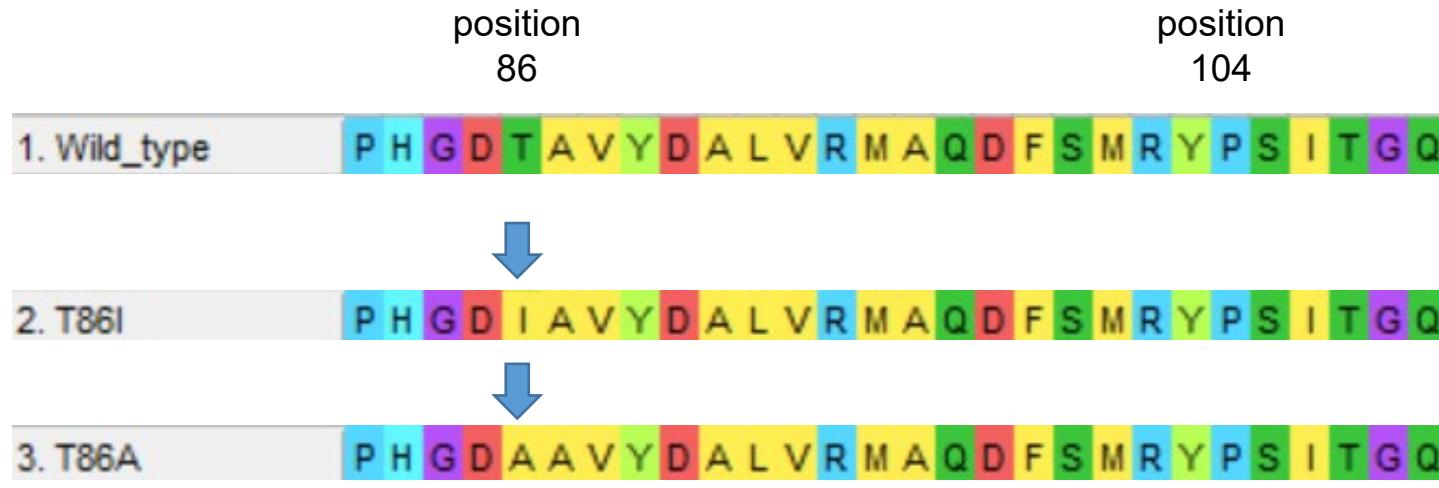
Antimicrobial resistance varies by clonal complex



Fluoroquinolone resistance



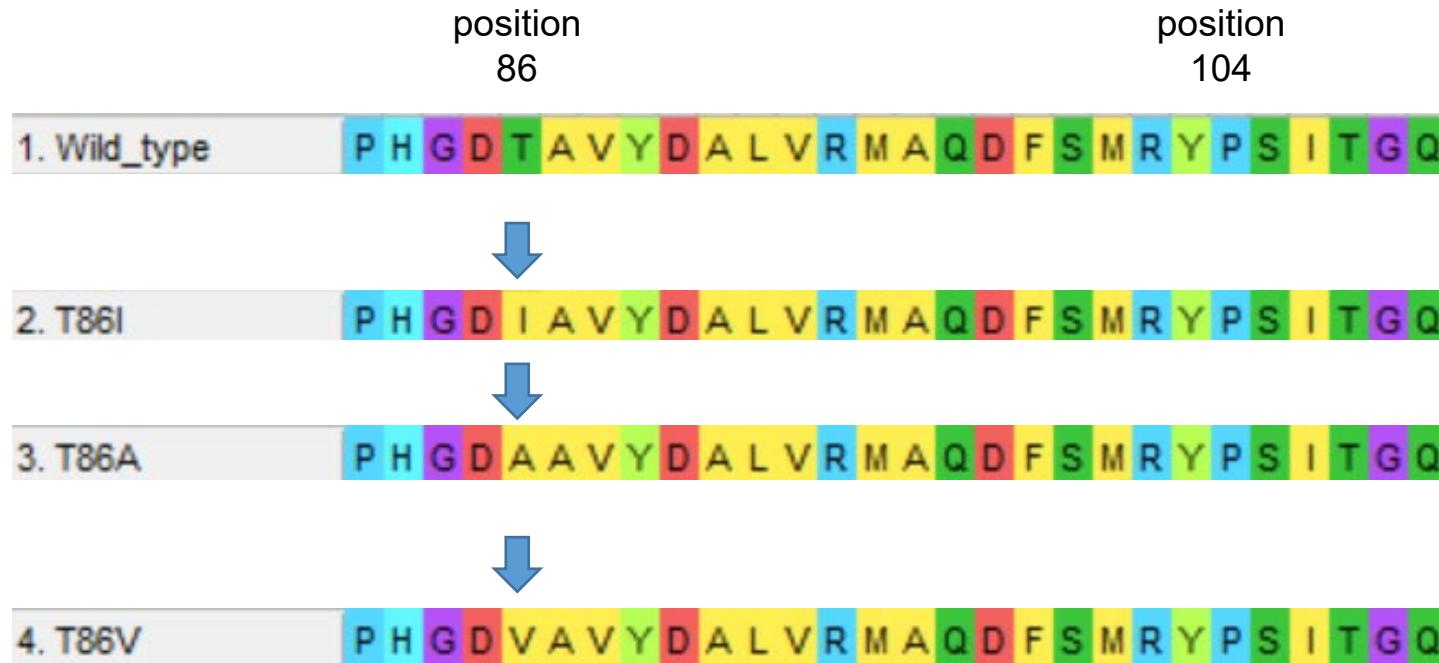
Fluoroquinolone resistance



99% of resistant isolates; 105 alleles

1 isolate, ST-230 (ST-45CC), allele 661
Finland, Scotland, England (2012-18)

Fluoroquinolone resistance

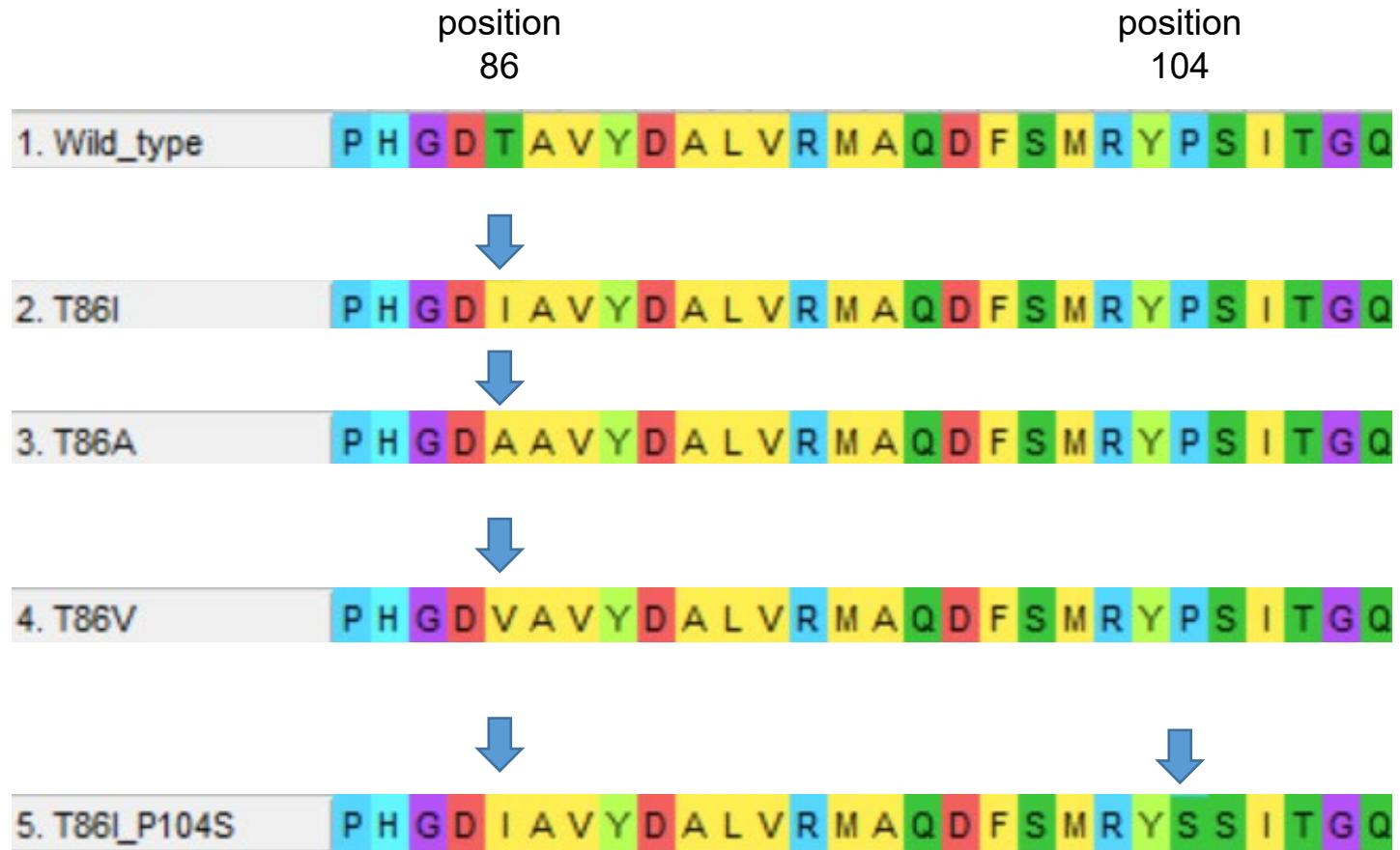


99% of resistant isolates; 105 alleles

1 isolate, ST-230 (ST-45CC), allele 661
Finland, Scotland, England (2012-18)

2 isolates, allele 1510: USA 2018, Italy 2023. **Allele 2298, unique**
T86V: n=257 on PubMLST, 93% *C. lari*

Fluoroquinolone resistance



99% of resistant isolates; 105 alleles

1 isolate, ST-230 (ST-45CC), allele 661

Finland, Scotland, England (2012-18)

2 isolates, allele 1510: USA 2018, Italy 2023. 1 isolate allele 2298, unique T86V: n=257 on PubMLST, 93% *C. lari*

47 isolates, ST-441 (U/A), allele 45 (98%)
UK, France 2006-23
1 isolate, ST-6175 (21CC), allele 176
England, France, Luxembourg 2016-23

PubMLST: AMR genetic determinants

Isolate fields 🔍													MLST									
id	isolate	aliases	country	year	month	isolation date	received date	disease	source	epidemiology	species	penner	aspA	glnA	gltA	glyA	pgm	tkt	uncA	ST	clonal complex	
116665	OXC12152		UK	2019	6				human stool		Campylobacter jejuni	6	4	5	2	2	1	5	122	ST-206 complex		

Analysis tools

Breakdown: [Fields](#) [Two Field](#) [Combinations](#) [Polymorphic sites](#) [Publications](#) [Sequence bin](#)

Analysis: [Codons](#) [Gene Presence](#) [Genome Comparator](#) [BLAST](#) [rMLST species id](#) [PCR](#)

Export: [Dataset](#) [Contigs](#) [Sequences](#)



Secondary metadata

fluoroquinolone genotype... gyrA_CJ[86:T-I]

fluoroquinolone genotype... T86I

tetracycline genotypes 1: tet(O)

tetracycline genotypes 2: tetO

PubMLST: searchable AMR variant

PubMLST Public databases for molecular typing and microbial genome diversity MY ACCOUNT

HOME ORGANISMS SPECIES ID ABOUT US UPDATES

Home > Organisms > *Campylobacter jejuni/coli* > *Campylobacter jejuni/coli* isolates > Search or browse database

Curator interface Help Tooltips Expand Modify form

Search or browse database

Enter search criteria or leave blank to browse all records. Modify form parameters to filter or enter a list of values.

Isolate provenance/primary metadata fields

Action

RESET SEARCH

Sequence variation

Display/sort options

Order by: id ascending
Display: 25 records per page

CAMP0950 T86 wild-type
CAMP0950 T86 variant
CAMP0950 T86I
CAMP0950 T86V
CAMP0950 T86A
CAMP0950 T86K
CAMP0950 D90 wild-type
CAMP0950 D90 variant
CAMP0950 D90N
CAMP0950 D90V
CAMP0950 D90Y
CAMP0950 D98 wild-type
CAMP0950 D98E
CAMP0950 P104 wild-type
CAMP0950 P104 variant
CAMP0950 P104T
CAMP0950 P104S

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Summary

- 80% of human disease in Oxfordshire is coming from 10 clonal complexes which are stable over time.
- There is no apparent effect in clonal complex distribution related to COVID-19 lockdowns.
- Highest levels of AMR are found in chicken associated lineages that are stable over time and globally distributed.

Ongoing and future work

- Finalise the Oxfordshire disease dataset (2019-2022), together with sequencing of Agri-Food isolates.
- Source attribution analysis using machine-learning approaches.
- Genome-wide association studies comparing lineages with high *vs* low AMR.
- Further development of PubMLST to predict AMR from genotypic data.

Acknowledgements

Oxford University

- Martin Maiden
- Sam Sheppard
- Keith Jolley
- James Bray
- Ben Pascoe

Samples

- Clinical Microbiology Staff
- Poultry Industry
- Pet owners

Funding

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The Quadram Institute

- David Baker
- Cara-Jane Moss