Longitudinal analysis of antibiotic resistance amongst UK *Campylobacter* isolates from human disease and retail meat.

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Introduction

- *Campylobacter* is regarded as a high priority antibiotic resistant pathogen by the World Health Organisation due to its high levels of fluoroquinolone resistance. The lack of surveillance data in livestock, food and a One Health approach is also noted.

- We present data from two sentinel surveillance sites in the UK; Oxfordshire and Newcastle and North Tyneside (2015-2018), compared with a retail meat survey (2015-2018), and historical human disease isolates from 1997-1998, 2003/4 and 2006/7

Methods

- A total of 4,362 *Campylobacter* isolates from cases of human disease in 2015-2018 were collected from the 2 sentinel surveillance sites.

- The following isolate collections from human disease were also included; 1,245 isolates from 1997/8, archived by the UK Health Security Agency (UK HSA); and 429 (2003/4) and 552 isolates (2006/2007) from Oxfordshire. They were compared with 2,007 isolates from the Food Standards Agency retail meat survey, including ruminant liver, duck, pig and chicken sources.

- *Campylobacter* isolates were whole genome sequenced, and the antibiotic resistance profiles were predicted from nucleotide sequence data using the validated UK HSA pipeline, and additionally by using the BIGSdb software (https://pubMLST.org/organisms/campylobacter-jejunicoli/).

Results

- *C. jejuni:* fluoroquinolone resistance increased 9-fold (5.2 – 45.1%) amongst human disease isolates between 1997 and 2018, and was highest amongst isolates from retail chicken meat (52.4%). **Tetracycline** resistance doubled (21.0% to 42.8%) amongst human disease isolates and was common amongst pig (70%), retail chicken meat (60.6%) and duck (59.1%) sources. **Aminoglycoside** and **macrolide** resistance was low (<1%) amongst human disease isolates. Aminoglycoside resistance was highest amongst pig isolates (10%). No macrolide resistance was recorded amongst retail meat isolates.

- *C. coli*: **fluoroquinolone** resistance increased from ~6-43%, with highest levels seen also in duck (54.5%) and retail chicken meat (48.1%). **Tetracycline** resistance increased from ~6-38% in human disease isolates, with highest levels seen in pig (85.5%), duck (81.8%) and retail chicken meat (60.2%) sources. Resistance to **macrolides** peaked at 10% in human disease isolates in 2006/7 before falling 5% more recently, but **aminoglycoside** resistance has doubled from 6-12% since 1997/8. Resistance to these antibiotic classes was highest in pigs; macrolides (33.7%) and aminoglycosides (59%).

- **Ciprofloxacin** and **tetracycline** resistance were significantly associated with a number of clonal complexes (CCs) (Figure 2). In addition, there was some evidence of clonal expansion of specific alleles associated with Ciprofloxacin and Tetracycline resistance in the ST-354 and ST-464 CCs, and Tetracycline resistance in ST-206 and ST-574 CCs.

Figure 1. Percentage of genetically estimated antimicrobial resistance amongst *C. jejuni* and *C. coli* isolates from human disease and livestock:
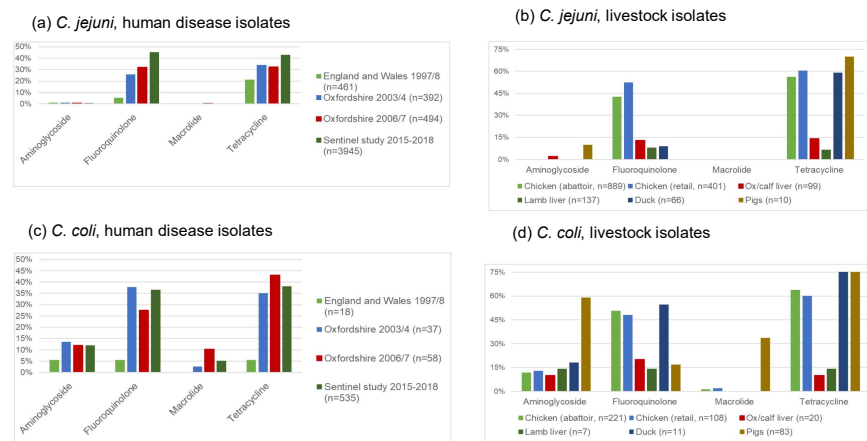
(a) *C. jejuni*, human disease isolates

(b) *C. jejuni*, livestock isolates

(c) *C. coli*, human disease isolates

(d) *C. coli*, livestock isolates

Figure 2. Clonal complexes significantly associated with resistance to:

Tetracycline: ST-206 CC, ST-257 CC, ST-353 CC, ST-354 CC, ST-464 CC, ST-574 CC, ST-607 CC, UA *C. jejuni*

(shared) ST-354 CC, ST-464 CC, UA *C. jejuni*

Ciprofloxacin: ST-353 CC, ST-354 CC, ST-464 CC, ST-607 CC, UA *C. jejuni*
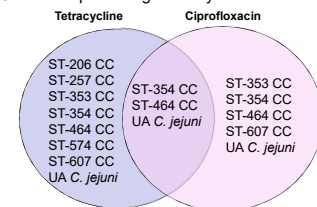
Figure 3. Examples of clonal expansion amongst human disease isolates

tetO allele 7 (84.8%)

tetO allele 7 84.8%

cipR; tetR
cipS; tetR
cipR; tetS
cipS; tetS
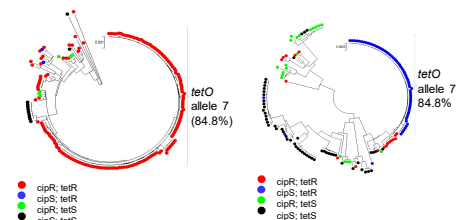
Conclusions

- The results of this study demonstrate the importance of continued surveillance of antibiotic resistance profiles amongst sources of infection as well as human disease, in order to gain greater understanding of the underlying driving forces.

- In contrast to macrolides, resistance levels to Ciprofloxacin and Tetracycline were consistently high in the later years of testing, despite falling sales for use on farms, and more work is needed to understand this apparent paradox.