ACM/1242

ADVISORY COMMITTEE ON THE MICROBIOLOGICAL SAFETY OF FOOD

SYSTEMATIC REVIEW OF AMR BACTERIA IN FOOD AT THE POINT OF RETAIL (FS102127)

1. The aim of this FSA-funded project was to appraise and summarise existing evidence of antimicrobial resistance (AMR) in bacteria from domestically-produced and imported foods at retail level that could result in the exposure of British consumers. A systematic review including scientific and grey literature published between 1999 and the end of May 2016 was conducted. Priority was given to studies focused on British-produced food and food from the main exporting countries trading with the UK. We investigated the prevalence of AMR at phenotype level in *Campylobacter* spp. (poultry meat), *Salmonella* spp. (pork meat) and in indicator commensal bacteria: *Enterococcus faecalis*, *E. faecium* and *Escherichia coli* in poultry and pork meat, dairy, seafood and fresh produce. Resistance to critically important antimicrobials [i.e., β-lactam antimicrobials (including carbapenems), fluoroquinolones, macrolides and polymyxins (i.e., colistin)], and multidrug resistance (MDR) was explored.

2. A total of 304 studies from 58 countries fulfilled the criteria for inclusion. There was a heterogeneity in AMR levels observed across countries. This heterogeneity could be due to differences in antimicrobial usage (AMU) across diverse animal production systems as well as due to diversity of food processing practices. It was difficult to assess AMR and MDR as authors used different antimicrobial susceptibility breakpoints and definitions and therefore results were not often comparable across studies.

3. For the UK, 15 studies were identified; from those, eight were original articles, five were targeted surveys conducted by the Food Standards Agency (FSA) and two were surveillance reports. A paucity of AMR data for domestically-produced food was observed and did not allow the detection of trends in AMR in food in the UK. The targeted FSA retail surveys conducted since 2001 provide “snapshots” of AMR in relevant foodborne pathogens in pork and poultry meat. There is, nevertheless, a lack of AMR data on commensal bacteria in the UK.

4. In other countries, those with most eligible studies were the USA (n= 29) and Denmark (n= 27), and to a lesser extent, China (n= 17), Brazil (n= 16), Spain (n= 14), Poland (n= 14), Turkey (n= 9), the Netherlands (n= 10) and Thailand (n= 8), which are also major food exporters trading with the UK. There were 189 studies that covered AMR and 117 in organisms from poultry and pork meat, respectively. Data were scarce for AMR in dairy (n= 33), seafood (n= 32) and fresh produce (n= 27).

5. Existing evidence from the UK and USA seem to show that prevalence of AMR is higher in bacterial isolates from conventional than in free range and organic

systems, the data are limited; as such it was not possible to assess this in a systematic manner.

6. For European exporting countries, AMR data were of robust quality particularly in Nordic countries and the Netherlands. In the remaining European countries, AMR data was inconsistent up to 2011, when the harmonisation criteria for sampling and antimicrobial susceptibility testing were introduced by EFSA for mandatory surveillance conducted by European Union's (EU) Member States (MSs)[1].

7. There was limited, dated scientific evidence available for British pork or imported pork at retail level in the UK; low prevalence levels of erythromycin resistance in *E. faecalis* and *E. faecium* isolates and absence of vancomycin-resistant Enterococci or VRE were noted in 2002. A very low prevalence (1%) of ESBL (extended-spectrum β-Lactamase)-producers in *E. coli* isolates from British pork was reported.

8. Denmark detected an increase in ampicillin resistance (up to 73%) in salmonella isolates from pork and very low prevalence levels of fluoroquinolone resistance (up to 6%); all isolates were susceptible to colistin in 2013. Ampicillin resistance was up to 33% in *E. coli* isolates from pork meat in 2012. In 2013, low prevalence levels of resistance to third generation cephalosporins (3GCs) and to fluoroquinolones (< 1.5%). In the Netherlands, very low prevalence of resistance to ampicillin (< 2%) was observed in enterococci from pork. Higher resistance levels to erythromycin (15% and 41.4%) in *E. faecalis* and *E. faecium* isolates respectively, were detected in Dutch pork. No VRE isolates were observed. In *E. coli*, a decrease in ampicillin resistance was noted down to 12.7% in 2014 from 34% in 2006; low levels of resistance to 3GCs and no resistance to carbapenems was detected in *E. coli* isolates. Resistance to fluoroquinolones and macrolides remained low.

9. In the USA, ampicillin resistance has increased to 13% but a reduction has been observed in cefotaxime resistance down to 0% in salmonella isolates from pork in 2013 since 2002 (40%) and no resistance to fluoroquinolones. Low prevalence levels of ampicillin resistance (4%) in *E. faecalis* and of penicillin (8%) resistance were stated for both *E. faecalis* and *E. faecium* isolates from pork meat. Erythromycin resistance was low (8%) in *E. faecalis* isolates. In contrast to European countries, MDR prevalence levels in enterococci were observed at 8.2% for *E. faecalis* but were considerably higher for *E. faecium* isolates at 54.6%. In *E. coli* isolates, amoxicillin-clavulanic acid and ampicillin resistance prevalence levels were low (< 12%) in 2013. Resistance to 3GCs and to fluoroquinolones was below 1.5%. Up to 13.9% of *E. coli* isolates were MDR in USA pork.

10. Poultry meat was the food group for which there was most evidence available for the UK. There has been an upwards trend to fluoroquinolones resistance since

[1] Technical specifications for the analysis and reporting of data on antimicrobial resistance (AMR) in the European Union Summary Report, EFSA Journal 2012;10(2):2587 [53 pp.] at: https://www.efsa.europa.eu/en/efsajournal/pub/2587

2001, when resistance levels were at 12.6% and 15.6% in *C. jejuni* isolates from chicken meat from conventional systems. Resistance to ciprofloxacin and nalidixic acid showed an upwards trend from 2005 (15% and 22%, respectively), and at a high to 2014-2015, (50% and 51.5%). Prevalence of MDR has increased from 19.1% in 2008 to 43.4% in 2014-2015 in *C. jejuni* isolates from chicken meat at retail level in the UK; the most common phenotype was ciprofloxacin, nalidixic acid, tetracyclines and trimethoprim (n= 71). Data were scarce and dated for AMR levels in commensal bacteria isolated from British poultry meat.

11. In the Netherlands, high levels of resistance to ciprofloxacin and nalidixic acid (at 63.4% in 2014, a sharp increase from 39% in 2004) were detected in *C. jejuni* isolates from poultry meat; higher levels of resistance to these fluoroquinolones (up to 100%) were observed in isolates from Polish poultry. Argentina, Brazil and Chile, similarly observed high levels of fluoroquinolone resistance. In contrast, the USA reported lower resistance levels to these antimicrobials at 21.3% and at 46.2% in isolates from chicken and turkey meat, respectively. Low erythromycin resistance levels in *C. jejuni* were reported in Netherlands (0.7%) and in the USA (< 10%). Higher levels of resistance were noted in isolates from Argentinian (20%) and Brazilian (68.8%) poultry meat; Chile reported similar levels to those observed in European countries (1.8%). No MDR isolates were detected from Dutch poultry meat up to 2013, whilst in Poland, MDR levels up to 45% were noted in *C. jejuni* isolates from poultry meat.

12. In commensal bacteria, data were limited in exporting countries. Low levels of ampicillin resistance (1.8%) and an increase of erythromycin resistance to 51.8% were reported in *E. faecalis* isolates from Dutch poultry in 2013. In the same country, ampicillin resistance has decreased in *E. faecium* isolates between 2002 (16%) and 2013 (6%). Similar levels to erythromycin resistance to those of the UK were observed in *E. faecium*. In the USA, a downwards trend was observed in recent years in ampicillin resistance (from 44.2% to 9.9%) in *E. faecium* and erythromycin resistance, (from 45.5% to 35.1%) in *E. faecalis* for the same period. High levels of erythromycin resistance were detected in *E. faecalis* isolates from poultry meat in Brazil at 90.2% in 2004 but this evidence is dated. MDR was reported in the USA of up to 69.7% and up to 79.4% in *E. faecalis* and *E. faecium* respectively, from poultry meat. Lower MDR levels (43.9%) were noted in enterococci from Brazilian poultry meat.

13. In the Netherlands, ampicillin resistance was down to 40.7% in in *E. coli* isolates from chicken meat in 2014 with the highest levels of resistance (65.9%) observed in isolates from turkey meat. Cefotaxime resistance has also decreased since 2002, down to 1.9%, according to surveillance data. Colistin resistance was higher in turkey meat (4%) than in chicken meat (1.5%). In *E. coli* isolates from Polish poultry meat, higher levels of resistance were observed to ampicillin (100%), and to cefotaxime (41.7%) compared to the Netherlands and no resistance to carbapenems was detected.

14. In the USA, high resistance to β-lactams, particularly to ampicillin (57.9%), 3GCs (up to 90.1% to cefotaxime and ceftriaxone) and to fluoroquinolones (97.5%) was reported in *E. coli* isolates from poultry meat from conventional systems in 2010.

In in the Netherlands in 2014 on ESBL-producing *E. coli* in poultry meat, colistin resistance was detected in 1.7% of isolates.

15. A lack of AMR data was observed for milk and dairy products, seafood and fresh produce in the UK and major exporting countries trading with the UK. This is particularly worrying as due to evidence of national and multi-national outbreaks of foodborne disease with these foods as the source of human exposure. No surveillance programs, to our knowledge, assess AMR bacteria in dairy or seafood in a systematic manner. Fresh produce is covered by some surveillance systems in European countries (i.e., the Netherlands and by EFSA) but only in recent years.

16. AMR data were only available for *E. coli* isolates from seafood at harvest and retail levels for China, Vietnam and USA. The highest levels of ampicillin resistance (78.9%) were observed in *E. coli* isolates from farmed fish in China, compared to Vietnam (30% in shellfish). In China, resistance to 3CGs and fluoroquinolones was low in *E. coli*. In Vietnam, slightly higher resistance levels were observed to ciprofloxacin (10%) but higher levels of resistance were noted against nalidixic acid (25%) in *E. coli* isolates from farmed seafood at retail level. China noted 1.5% ESBL-producing *E. coli* isolates from farmed fish, whilst studies in Vietnam detected higher prevalence of ESBL-producers of 18.3% in isolates from farmed shrimp.

17. Amongst the main exporting European countries trading with the UK, only the Netherlands assessed AMR in vegetables and fruit as part of the MARAN surveillance program. In the Netherlands, no ampicillin resistance was reported in both *E. faecalis* or *E. faecium* isolates from fresh produce but resistance to erythromycin was at 6.3 and 25.8%, respectively. In 2012, in *E. coli* isolates from fresh produce, low prevalence levels of ampicillin, ciprofloxacin and nalidixic acid resistance (between 1.5 and 2.3%) and no resistance to either cefotaxime or colistin were detected. It was not possible to assess MDR from vegetables across countries due to the paucity of data.

18. The final report of this work can be accessed on the FSA website at https://www.food.gov.uk/science/research/foodborneillness/b14programme/b14projlist/fs102127/a-systematic-review-of-amr-in-pork-and-poultry-dairy-products-seafood-and-fresh-produce

19. Recommendations resulting from this systematic review include (in no particular order of importance):

- Standardization in the selection of antimicrobials for antimicrobial susceptibility testing (AST) panels as recommended by EFSA[2], the use of epidemiological cut-off values (ECOFFs) for surveillance of resistance,

[2] Technical specifications for the analysis and reporting of data on antimicrobial resistance (AMR) in the European Union Summary Report, EFSA Journal 2012;10(2):2587 [53 pp.] at: https://www.efsa.europa.eu/en/efsajournal/pub/2587

adoption of a standardized definition for MDR, the adoption of random sampling and adequate study design for epidemiological studies and when implementing surveillance systems for determination of AMR in the food chain as previously recommended in the Advisory Committee on the Microbiological Safety of Food (ACMSF) report published in 1999[3].

- Surveillance priorities could be set using a risk-based approach, taking into account the importance of antimicrobials used for treatment in both humans and animals, and continued surveillance of the prevalence and emerging resistance (including MDR) in commensal bacteria also important.

- There is scarce evidence of AMR and MDR occurrence in dairy, fresh produce and seafood to several antimicrobials in commensal bacteria. These gaps should be addressed using a risk-based approach taking also into account the extent of expected consumer exposure using consumption and import volumes.

- Efforts should be made to continue to monitor AMR and MDR trends in *Campylobacter* spp. strains and commensal bacteria from both imported and domestically-produced poultry meat in the UK; differentiation should be made for different types of poultry meat sampled (i.e., chicken and turkey meat) due to variations observed in farming management practices across species.

- Research and surveillance are needed to monitor AMR and MDR in pathogenic and commensal bacteria from imported and British pork meat in the UK.

- Data on AMU and type of production systems in food-producing animals should be collected for food samples in order to explain the occurrence and dynamics of AMR, resistance genes and MDR phenotypes in in the UK.

- There is a need for more studies to quantify the contribution of both domestic and imported foods to the occurrence of AMR. Information on country of origin for imported products should be collected.

- Finally, further research and surveillance are needed to establish and quantify the risk of transmission to humans of AMR to critically important antimicrobials (CIAs) in organisms from foods of both animal and non-animal origin.

Action

20. Members are invited to comment on the findings from this study.

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[3] https://acmsf.food.gov.uk/committee/acmsf/acmsfsubgroups/amrwg