# Protocol

# A systematic literature review to assess the significance of the food chain in the context of antimicrobial resistance

A project commissioned by the Food Standards Agency

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# Background

Antimicrobial resistance (AMR) is currently a major public health issue. It leads to antibiotic therapeutic failure and to increased morbidity and mortality of those affected with infections caused by resistant pathogens. Resistant pathogens are responsible for 25,000 deaths every year in Europe (ECDC and EMEA, 2009); it is estimated that these numbers will rise up to 390,000 by 2050 (Anon., 2014). Resistant infections have also a negative economic impact in healthcare with a cost up to €1.5 Billion annually (ECDC and EMEA, 2009).

Antimicrobial usage is one of the major factors associated with the emergence and spread of AMR (ECDC and EMEA, 2009). Antimicrobials are widely used in agriculture to prevent and treat infectious diseases and, in some countries they are also used as growth promoters in food-producing animals (McEwen, 2006, Rushton et al., 2014). The epidemiology of AMR is complex; humans can become exposed through varied pathways such as; hospitals (i.e. nosocomial infections), environmental, through direct contact with pets, wildlife, food-producing animals or humans in the community, but also through water and food.

Resistant foodborne pathogens such as fluoroquinolone-resistant Campylobacter spp. or Extended-Spectrum Beta-Lactamase (ESBLs) bacteria have been isolated in food, food-producing animals and humans (EFSA, 2015). There is currently the perception that the food chain is an important pathway for transmission of resistant pathogens to humans (WHO, 2015); however, it is not certain if this is the current trend for AMR transmission or if it is due to the selective reporting of foodborne outbreaks and target surveillance.

Phylogenetic and whole genome sequence analysis of Salmonella enterica serovar Typhimurium DT104 in human and livestock populations in Scotland has shown a greater diversity of AMR genes in human S. Typhimurium DT104, by comparison to isolates found in local livestock populations. This suggests that there were contributing sources other than food-producing animals or foods derived from those observed in human isolates (Mather et al., 2011, Mather et al., 2013).

The aim of our study will be to assess the frequency of antimicrobial resistance observed in foodborne pathogens and commensal bacteria transmitted via the food chain (i.e. from farm to fork) that could pose a risk to UK consumers. For this purpose we will conduct a systematic review through which current existing evidence will be collected and assessed. This is a change from our previous scope that was to assess transmission of AMR at different steps of the food chain and the impact of this on public health. The scope of the review was redefined after expert consultation and preliminary scope searches (described below).

The protocol here presented will be registered and made available through the International Prospective Register of Systematic Reviews, also known as PROSPERO. The upload of the protocol will take place before the literature search strategy is executed. The protocol may be subjected to further modifications if

deemed necessary; updated versions of the protocol will be uploaded accordingly on PROSPERO (CRD, 2009).

# Scope search

A scope search was conducted to explore extent and range of studies published between 1999 and 2015 using PubMed. For this purpose wide search terms covering the theme of interest were used (e.g. antimicrobial resistance, by food item and livestock species of interest) to ascertain the volume of scientific publications available for the period of interest (Appendix 1). These scans of the literature were conducted as part of a decision tree exercise to refine the scope of the systematic review.

Current evidence from integrated surveillance reports at European level (EFSA, 2015) was taken into consideration for identifying relevant food and bacterial combinations in the context of antimicrobial resistance and food safety. The scope search covered scientific studies published on antimicrobial resistance in food of animal origin including meat, fresh produce (e.g. vegetables, salads, fruits and nuts), minimally processed foods (e.g., milk), fish and shellfish at retail level and food handlers (as a potential source of cross-contamination). The latter were dropped from the scope of the systematic review due to the lack of relevance and reduced number of studies identified.

An assessment of the number of studies for each of the nodes ("categories") identified was conducted. The findings were then used to refine the focus of the systematic review, together with the findings of the expert elicitations conducted (see below "Expert elicitation") and the current evidence from international surveillance reports (e.g., EFSA, MARAN, SWARM).

# Expert elicitation

Experts in antimicrobial resistance were approached for external review of the research questions and eligibility criteria taking into account the scope of the systematic review in two separate exercises. Furthermore, the experts were also be requested to provide a list of grey literature and/or scientific studies that they deemed relevant for inclusion in the review.

A provisional list of antimicrobial resistant experts that were contacted for the purpose of this systematic review and agreed to participate is provided below:

- Katherine Grace, Veterinary Medicines Directorate (UK): k.grace@vmd.defra.gsi.gov.uk
- Professor Christina Greko, Swedish National Veterinary Institute (Sweden): christina.greko@sva.se
- Dr Engeline van Duijkeren, RIVM National Institute for Public Health and the Environment (Netherlands): engeline.van.duijkeren@rivm.nl

- Professor John Threlfall, retired but previously worked for Public Health England (UK): e.j.threlfall@btinternet.com
- Dr Muna Anjum, Animal and Plant Health Agency (UK): muna.anjum@apha.gsi.gov.uk

Our aim is to investigate the frequency of antimicrobial resistance in known foodborne pathogens and commensal bacteria to specific critically important antimicrobials in food at retail level that could pose a risk to British consumers. We will conduct an assessment of the evidence presented in scientific studies and grey literature as part of a systematic review. Research questions were developed taking into consideration current evidence for relevant resistant foodborne pathogens and commensal bacteria observed in animals, food and humans in European countries published by EFSA (European Food Safety Authority)(EFSA, 2015), feedback provided by experts and findings from scope searches of the literature (i.e. PubMed):

## Antimicrobial resistance in pork, poultry meat and fresh produce

a) What is the frequency of resistance (i.e., phenotype) observed in selected foodborne pathogens in the following meats of animal origin at retail:
   i. *Salmonella* spp in pork
   ii. *Campylobacter* spp in poultry meat
   iii. For i) to ii) for the selected critically important antimicrobial groups (i.e., beta-lactams [including carbapenems], fluoroquinolones, macrolides and polymyxin E [colistin][1]) and multidrug-resistance?

b) What is the frequency of resistance (i.e., phenotype) observed in selected commensal bacteria for the following food items at retail level:
   i. *Enterococcus* spp (*Enterococcus faecalis*, *Enterococcus faecium*) in poultry and pork meat, fruit and vegetables?
   ii. *Escherichia coli* in poultry and pork meat, fruit and vegetables?
   **iii.** **For i) to ii)** for the selected critically important antimicrobial groups (i.e., beta-lactams [including carbapenems], fluoroquinolones, macrolides and polymyxin E [colistin]) and multi-drug resistance?

## Antimicrobial resistance in milk, fish and shellfish (deadline: 31st March 2016)

c) Resistance to beta-lactams, fluoroquinolones, macrolides, carbapenems, colistin and multidrug-resistance in commensal bacteria (i.e., *Enterococcus* spp and *Escherichia coli*) in milk, fish and shellfish at retail level

[1] Colistin was added to the list of antimicrobials of interest in May 2016; as the searches of the literature had already been performed, a separated search was conducted separately for colistin.

**Note$_1$:** Food handlers and nuts were removed from the scope of the search due to the limited available number of studies identified and relevance.

**Note$_2$:** Focus was given to assessing resistance at retail level, as it was perceived to be the point at which consumers were more likely to be exposed thereof.

# Eligibility criteria

## Inclusion criteria

- Food items such as foods of animal origin (e.g., fresh meat, meat preparations - which include fresh and minced meat, milk) and fresh produce (e.g., fruit and vegetables);
- Domestically produced (UK) and imported foods (non-UK);
- Studies considering resistance in following foodborne pathogens will be considered; *Salmonella* spp. (pork meat and derived meat preparations), *Campylobacter* spp. (poultry meat and derived meat preparations), - these combinations were selected based on current surveillance evidence published by EFSA
- Studies considering the following indicator bacteria in pork meat, poultry meat, vegetables and fruit will be considered; *Enterococcus faecium*, *Enterococcus faecalis* and commensal *Escherichia coli*. These were selected on the current recommendations by EFSA
- Studies from countries with similar food chain systems to those observed in the UK (i.e., European countries with similar legislation framework and trade arrangements) will be considered. Countries that are currently exporters of foods of animal origin and fresh producer to the UK will be identified through Eurostat and a weight (for relevance) will be attributed accordingly;
- Studies conducted in countries outside Europe will be included as potential exporters to the UK (e.g., Third countries). Countries that are currently exporters of foods of animal origin and fresh producer to the UK will be identified through Eurostat and a weight (for relevance) will be attributed accordingly;
- Reports, reviews, systematic reviews, meta-analyses, risk analysis and mathematical modelling studies published since 1999 until the end of September 2015;
- Scientific expert opinion reports (e.g. EFSA, EMA) deemed relevant to the research questions will be considered published between 1999 and the end of September 2015;
- Observational (e.g. case-control, prospective and retrospective cohort, cross-sectional studies) and experimental studies published since 1999 until the end of September 2015;
- Full text manuscripts of papers that are published in English be included. At a preliminary stage, only abstracts available in English will be considered. If studies reported in other languages are found to be relevant after careful evaluation of

the abstract, these will be considered after selection of a colleague from that "mother tongue" is identified through RVC, SAFOSO or FSA.

## Exclusion criteria

- Highly processed foods (i.e., any food that has been altered from its natural state in some way, either for safety reasons or convenience) will not be considered for the purpose of this systematic review. Processed foods include; breakfast cereals, tinned vegetables, bread, savory snacks, "convenience foods" (e.g., microwave meals or ready meals), drinks (e.g., soft and carbonated drinks). Also, meat products (e.g., products that have been processed so that they do not look like fresh meat, for example bacon, ham or salami) and canned foods will not be considered;
- Pathogenic *Escherichia coli* strains will not be included;
- Any type of study (or part of a study) that assessed frequency of resistance, transmission of resistant bacteria or resistance determinants to humans in/from the following sources:
    - companion animals (including horses) or exotic pets;
    - direct contact with wildlife;
    - healthcare settings (nosocomial infections) unless primary cause was a foodborne pathogen of animal origin (i.e., pork or poultry meat) or from fresh produce (i.e., fruit or vegetables, including fresh salad);
    - occupational settings in veterinary practice;
    - humans, when humans are deemed to be the source of primary infection (e.g., MRSA human clones at community level);
- Any studies considering horse meat will not be included as in the UK horses are deemed as companion animals and horse meat consumption in this country is negligible;
- Studies that were considered to be methodologically poor or otherwise not within the scope.

## Definitions used

Foodborne pathogens (adapted from EFSA definition) [2]

"These are pathogenic (disease-causing) micro-organisms such as bacteria (…). Humans get foodborne infections usually through the consumption of food or drinking water contaminated by these bacteria. Infection can also occur through direct contact with food-producing animals or contaminated environment. Human-to-human transmission through faecal-oral route can also occur (e.g., secondary transmission from primary cases). They enter the body through the gastrointestinal tract where the first symptoms often occur. Many of these micro-organisms are commonly found in the intestines of healthy food-producing animals. The risks of

[2] Foodborne pathogens

contamination are present from farm to fork and require prevention and control throughout the food chain".

Please note that for the purpose of this systematic review, we will focused on specific foodborne pathogenic bacteria (i.e., *Salmonella* spp. and *Campylobacter* spp.).

**Commensal bacteria (EFSA definition) (EFSA, 2011)**

"Are those bacteria that live in or upon the (human or the animal) host without causing disease. Mostly, this co-existence is of mutual benefit. However, many commensals can cause disease if they enter body sites that are normally sterile or when the host's immune defence is impaired".

**Indicator bacteria (EFSA definition) (EFSA, 2011)**

Those micro-organisms that are used to represent Gram-positive and Gram-negative bacteria present in the gut flora of humans and animals. EFSA recommends the use of *Escherichia coli* (Gram-negative) and Enterococci (i.e., *Enterococcus faecium* and *Enterococcus faecalis*) as indicators for Gram-negative and Gram-positive bacteria, respectively. The reasoning provided for the selection of these bacteria as indicators is that most resistance phenotypes present in the animal populations are usually also present in these species; these bacteria are deemed to suffer similar selective pressure and exposure to resistance determinants that other micro-organisms present in the gut flora. According to EFSA indicator bacteria are more suitable for the assessment of selective pressure caused by antimicrobial therapy than foodborne pathogens in livestock species due to being ubiquitous in the gut flora.

For the interpretation of antimicrobial resistance in the selected studies, we will be using the WHO's definition of resistance:

"Antimicrobial resistance is resistance of a microorganism to an antimicrobial drug that was originally effective for treatment of infections caused by it. Resistant microorganisms (including bacteria, fungi, viruses and parasites) are able to withstand attack by antimicrobial drugs, such as antibacterial drugs (e.g. antibiotics), antifungals, antivirals, and antimalarials, so that standard treatments become ineffective and infections persist, increasing the risk of spread to others".

This systematic review will focus on resistance to naturally produced, semi-synthetic and synthetic antibacterial drugs. Antivirals, antifungals and antimalarial drugs as well as biocides and heavy metals will not be considered for the purpose of this systematic review.

Resistance of microorganisms will be assessed at phenotype level for specified groups of antimicrobials deemed as critically important for human medicine (i.e., beta-lactams [including carbapenems], fluoroquinolones, macrolides and polymyxin E [colistin]); loss of efficacy of these antimicrobials to treat severe, life-threatening bacterial infections in humans is a major public health issue (WHO, 2011). For the purpose of interpretation of resistance patterns, we propose using the following

definitions created by EUCAST (European Committee on Antimicrobial Susceptibility Testing):

## Clinical resistance and clinical breakpoints

### Clinically Susceptible (S)

- A micro-organism is defined as susceptible by a level of antimicrobial activity associated with a high likelihood of therapeutic success
- A micro-organism is categorized as susceptible (S) by applying the appropriate breakpoint in a defined phenotypic test system
- This breakpoint may be altered with legitimate changes in circumstances

### Clinically Intermediate (I)

- A micro-organism is defined as intermediate by a level of antimicrobial agent activity associated with uncertain therapeutic effect. It implies that an infection due to the isolate may be appropriately treated in body sites where the drugs are physically concentrated or when a high dosage of drug can be used; it also indicates a buffer zone that should prevent small, uncontrolled, technical factors from causing major discrepancies in interpretations.
- A micro-organism is categorized as intermediate (I) by applying the appropriate breakpoints in a defined phenotypic test system
- These breakpoints may be altered with legitimate changes in circumstances

### Clinically Resistant (R)

- A micro-organism is defined as resistant by a level of antimicrobial activity associated with a high likelihood of therapeutic failure.
- A micro-organism is categorized as resistant (R) by applying the appropriate breakpoint in a defined phenotypic test system
- This breakpoint may be altered with legitimate changes in circumstances

Note: Clinical breakpoints are presented as S≤x mg/L; I>x, ≤y mg/L; R>y mg/L where “x” and “y” are pre-defined breakpoints by EUCAST for each combination of organism and antimicrobial substance

## Microbiological resistance and epidemiological cut-off values (ECOFF)

### Wild type (WT)

- A micro-organism is defined as wild type (WT) for a species by the absence of acquired and mutational resistance mechanisms to the drug in question
- A micro-organism is categorized as wild type (WT) for a species by applying the appropriate cut-off value in a defined phenotypic test system.
- This cut-off value will not be altered by changing circumstances

- Wild type micro-organisms may or may not respond clinically to antimicrobial treatment

**Microbiological resistance - Non-Wild Type (NWT)**

- A micro-organism is defined as non-wild type (NWT) for a species by the presence of an acquired or mutational resistance mechanism to the drug in question.
- A micro-organism is categorized as non-wild type (NWT) for a species by applying the appropriate cut-off value in a defined phenotypic test system.
- This cut-off value will not be altered by changing circumstances
- Non-wild type micro-organisms may or may not respond clinically to antimicrobial treatment.

Note: The wild type is presented as WT≤z mg/L and non-wild type as NWT >z mg/L, where “z” is a pre-defined breakpoint by EUCAST for each combination of organism and antimicrobial substance

It is likely that due to different ways in which antimicrobial resistance is assessed in interpreted (e.g., epidemiological versus ECOFFs) and the variability of tests used to assess and reporting of antimicrobial susceptibility it may not be possible to directly compare findings across studies, within and between countries, due to lack of harmonisation of laboratory methodologies and interpretation criteria used. This has been previously reported in EFSA’s European Report on Antimicrobial Resistance in Zoonotic and Indicator Bacteria from Humans, Animals and Food (EFSA, 2015). In these situations, data will be assessed separately and discussion of limitations and gaps of knowledge will be acknowledged.

For both foodborne and commensal bacteria, epidemiological cut-off breakpoints (based on phenotype) will be used to identify susceptible and resistant strains, according to EFSA recommendations (EFSA, 2008).

## Multidrug resistance (MDR)

Furthermore, occurrence of multidrug antimicrobial resistance (MDR) in commensal and pathogenic bacteria in the food chain will also be assessed at a later stage. For this purpose, the definition developed by Magiorakos et al. (2012) will be applied:

Multidrug resistant bacteria (MRD) “a bacteria that has acquired non-susceptibility to at least one agent in three or more antimicrobial categories”. This definition only applies to acquired resistance.

This definition was elaborated by a group of international experts from the European Centre for Disease Prevention and Control (ECDC) and the Centers for Disease Control and Prevention (CDC) and it is currently used by EFSA and ECDC.

# PICO and search strategy

The research questions were used to define the PICO (Population, Intervention or Exposure, Comparator and Outcome) (Table 1). The PICO guided the definition of the search terms of interest that will be used to identify potential eligible studies for the purpose of the systematic review.

**Table 1- PICO strategy that will be followed for the purpose of the systematic review. Please note that this includes both stages of the systematic review process.**

| PICO | Description |
|---|---|
| Population | Specified foodborne pathogens will be considered: *Salmonella* spp. in pork and *Campylobacter* spp. in poultry meat. For pork and poultry meat, fresh produce (i.e., fruits, vegetables and fresh salads), milk, fish and shellfish, commensal bacteria (*Enterococcus faecium*, *Enterococcus faecalis* and *Escherichia coli*) will be assessed. |
| Intervention, exposure | In this particular review, we will not be looking at the impact of intervention measures on antimicrobial resistance as this is not our aim; our study will focus primarily on the assessment of frequency of resistance at retail level that could pose a risk for the final consumer.<br>• Meat at retail levels<br>• Milk at retail level<br>• Fish and shellfish at retail level<br>• Fresh produce at retail level<br>Resistance to the following critically important antimicrobials groups will be assessed for the bacteria of interest:<br>• Beta-Lactams (including carbapenems)<br>• Fluoroquinolones<br>• Macrolides<br>• Polymyxin E (colistin) |
| Comparator(s) | Studies without comparators will be included.<br>The comparator used will be:<br>• Domestic (“UK”) versus imported (“non-UK”) meat, meat preparations (of swine and poultry origin) and fresh produce |
| Outcome(s) | Assessment of frequency and resistance patterns (phenotype) in bacterial populations of interest (see above “Population”). For the purpose of this systematic review, we will be assessing outcomes, such as the ones defined below:<br>• Counts (e.g., numbers, proportions) |

| PICO | Description |
|---|---|
| | • Prevalence<br>• Incidence<br>Note: when there is lack of quantifiable outcomes, expert opinions will be considered if available (e.g., EFSA expert opinion reports). |

The search strategy will use science database search engines, grey literature websites (e.g., national and international surveillance reports), citation tracking and experts in the domain area to identify potential relevant studies (Table 2). The search criteria were piloted by a single researcher to generate the final search strategy (Appendix 2).

Any searches of the literature and criteria used must be documented at all times to allow replication of the methodology used. Free text searches shall cover both title and abstract, when the latter is available. Searches will include MeSH thesaurus headings and free text terms that cover PIO criteria (e.g. population, interventions and outcomes). The free terms and MeSH headings shall be combined with the Boolean operator OR and/or can be combined with AND, at a later stage of the search process, following these 2 steps; (1) population AND intervention AND outcomes (PIO) AND antimicrobial resistance AND critically important antimicrobial group terms.

The combinations of search terms across the PIO groups will be extracted separately to produce the final list of search hits from each database. Search terms for comparators were not defined, as studies with and without comparator will be included in the study. MeSH thesaurus headings and free text terms may be amended in order to make these compatible with databases which do not use MeSH or cover mainly non-English language literature. As such, for those equivalent and/or translated terms will be used where deemed necessary.

Search interfaces with limited functionality (e.g. those which support single line searches only, limited number of search terms, etc) may be initially searched using broad “antimicrobial resistance” terms followed by longer search strings or by using “advanced search” modalities if these are available in the interfaces used.

# Study screening

All search hits will be imported into reference management software (i.e., Endnote) to collate the identified literature. All duplicates will be removed prior to the 1st stage sifting process electronically via the reference software. Duplicates will be removed by other means (e.g., manually by the reviewer), if importing of the search hits into the reference management software is not viable.

All identified studies and other relevant literature will be screened by a team of researchers for eligibility using a three-stage sifting approach to review the title, abstract and full text adopting a single reviewer approach for each study. This team will work under the supervision of the Principal Investigator (Ana Mateus). A random check of excluded studies will be conducted by a second reviewer and any discrepancies observed will be discussed amongst reviewers.

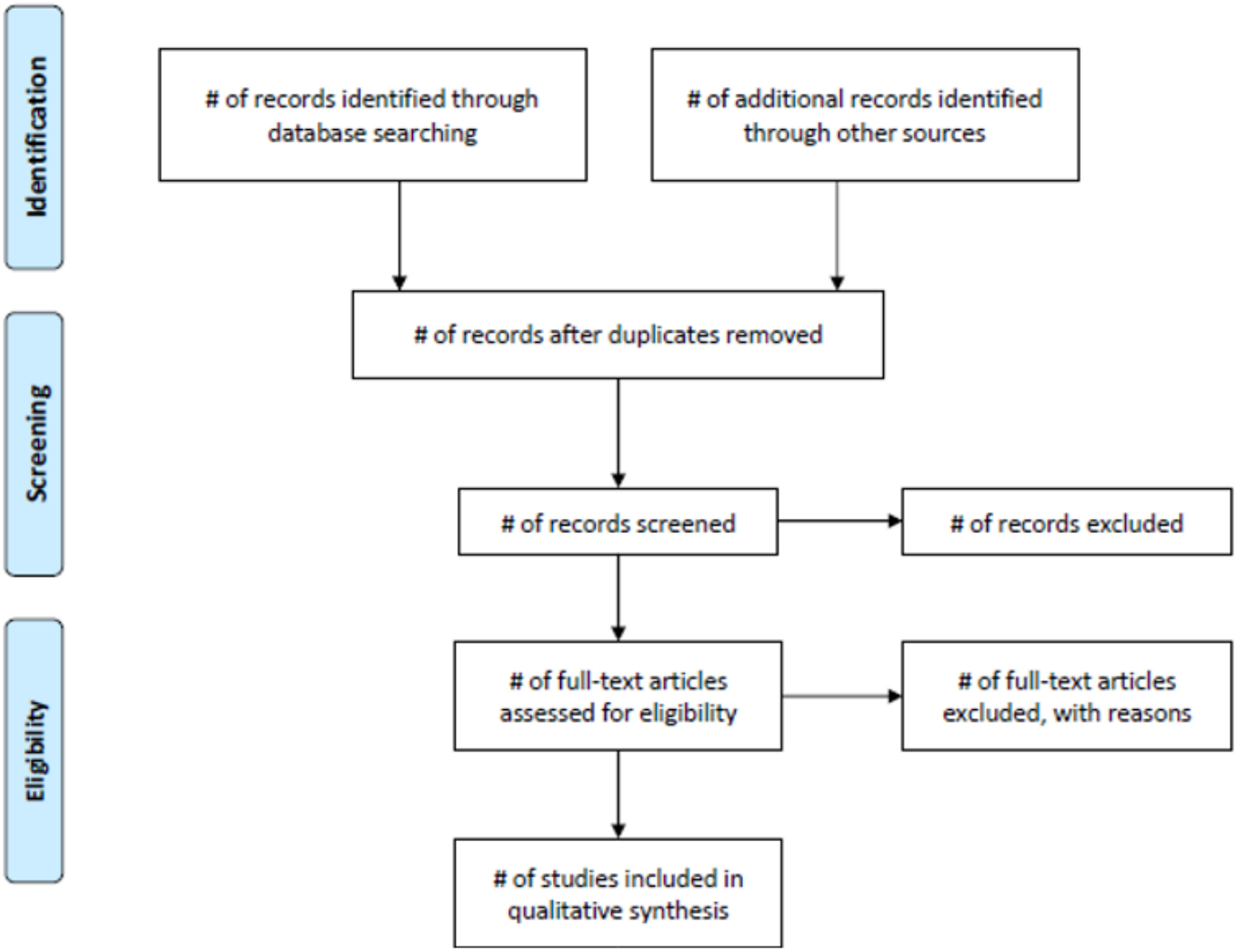
The number of documents identified and screened out will be recorded at each stage and presented accordingly in a PRISMA diagram (Fig. 1). Reasons for exclusion will be disclosed during the process. Any disagreements will be resolved by discussion or by involvement of a third reviewer, if deemed necessary. Furthermore, a random sample of data extracted will be validated by the Principal Investigator.

**Table 2- Study search strategy.**

| Category | Sources |
|---|---|
| Scientific databases | Science Direct<br>Web of Science<br>PubMed |
| Reference tracking | Reference lists of all studies selected for inclusion will be searched to identify further relevant studies |
| Grey literature | World Health Organisation<br>Centre for Diseases Control and Prevention, USA<br>European Centre for Diseases Prevention and Control<br>Public Health England, UK<br>European Food Safety Authority<br>European Medicines Agency<br>Food and Agriculture Organisation of the United Nations<br>Food Standards Agency, UK<br>Veterinary Medicines Directorate, UK<br>DANMAP, DTU, Denmark |

| Category | Sources |
|---|---|
| | NORM-VET, Norwegian Veterinary Institute, Norway<br>MARAN, RIVM, The Netherlands<br>SVARM, SVA, Sweden<br>NARMS, FDA/CDC, USDA, USA<br>CIPARS, Public Health Agency of Canada, Canada<br>Consultation with AMR experts |

**Figure 1- Strategy for screening of studies to be included in the systematic review - adapted from Liberati et al. (2009).**



# Assessment of risk of bias

The risk of bias assessment will be conducted only for studies where probabilistic sampling (e.g., randomised clinical control trials, longitudinal cohort, case-control studies or cross-sectional) has been performed. For studies where convenience sampling was applied (e.g., surveys, pilot studies) where results cannot be extrapolated to the overall population, an assumption will be made of low quality and high risk of bias of the referred study.

Findings of these studies will be described accordingly. Expert opinions and literature reviews will be not be assessed for bias; nevertheless, findings of these studies will also be reported as part of the systematic review.

Risk of bias assessment will be conducted in parallel with the data extraction process. For this purpose, templates will be created in Word document for the assessment of risk of bias according to study design. Criteria used to assess quality of studies will include:

a) Adequacy of study design selected
b) Appropriateness of analysis or review conducted
c) Presence of selective reporting of outcomes of interest
d) Appropriateness of interpretation of findings and recommendations made

Bias will be assessed following the criteria stipulated by the PRISMA statement (Liberati et al., 2009). For this effect, bias in individual studies will be assessed at a) study (i.e. large reporting of small against large scale studies), and b) outcome (i.e. selective reporting).

The Cochrane Collaboration tool (Higgins et al., 2011) will be used to assess risk of bias at study and outcome levels in experimental and prospective cohort studies. In observational studies, the Newcastle-Ottawa Scale (NOS) will be used instead (Wells et al., 2014).

Potential bias in the reporting of outcomes will be assessed in all studies using the quality assessment tools mentioned above. Furthermore, any confounding derived from the risk of selection bias will be assessed in non-randomised studies as per recommendations of the Cochrane Collaboration. Bias in non-randomised studies may contribute to the occurrence of heterogeneity between studies. Reviewers will be required to describe characteristics of study design and statistical analysis used by researchers to control selection bias in each study.

Literature regarding mathematical models used to evaluate antimicrobial resistance will be described in a separate section and will not be assessed for the risk of bias. There is currently a lack of validated instruments to assess quality of evidence presented in mathematical models.

# Data extraction

A template for data extraction will be prepared by the research team based on the PIO (Population, Intervention and Outcome(s)), previously defined in the Protocol document as an Excel document (Microsoft Office, Microsoft Corp). This template will be tested prior to implementation. Once implemented, the template will be used by the independent reviewers to collect the data that will be used for the preparation of the review. This will enable the assessment of accuracy and consistency of data extracted by the reviewers.

# Data synthesis

Study characteristics (e.g. study design, interventions evaluated, sample size, sampling methods amongst others) and outcome(s) of interest will be described and summarised in tables accordingly. To synthesise the data extracted and evaluate its quality a narrative approach will be used according to the framework described by the Economic and Social Research Council and recommended by the University of York Centre for Reviews and Dissemination (CRD, 2009).

This will be used to; a) develop a preliminary synthesis of findings of the integrated studies, b) investigate relationships within and between studies (e.g., frequency of resistance and resistance in the UK and other countries) and c), evaluate the degree of robustness of the synthesis.

# Dissemination of findings

The findings will be included in a draft technical report to be submitted to FSA and peer-reviewers for comments; the list of eligible studies and grey literature included in the systematic review will be delivered as an Excel spreadsheet. The technical report will include an executive summary, background, materials and methods section (based on the protocol), results and discussion sections; the protocol and other supplementary data will be included as appendixes to the report.

The final report will be submitted, after revision, taking into consideration the FSA and peer-reviewers comments received. Regular update meetings will be held with the FSA throughput the duration of this study (e.g. every month, with email exchange when deemed necessary for clarification of queries and discussion of any issues that may occur during the review process). A stakeholder workshop will be organised by FSA where RVC officials will present the main findings of the systematic review.

The findings will also be submitted for publication in a peer-reviewed scientific journal, upon discussion with FSA and interested stakeholders. The findings of this study will be used to inform interested stakeholders and policy makers. Gaps in knowledge identified through this review will help to guide research in the domain of interest.

# Resources implications

The RVC project leads will work closely with the FSA coordinators to define the scope and methods of the systematic review as a dynamic process. The FSA coordinators will aid in the identification of individuals with scientific background that can act as experts as specified in the section “Expert elicitation” in this protocol. Timescales and key milestones will be agreed between the RVC and the FSA coordinators. These will be adjusted and/or modified as deemed necessary based on the data availability, data quality and resources available.

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# Appendix 1- Scope search findings for antimicrobial resistance in the food chain- Broad search terms were used; results for each search term and combination of search terms are presented in the blue boxes.

## a) Scope search- FSA tender antimicrobial resistance (AMR) in the food chain

**AMR in the food industry, imported into and exported food from the UK, in ready to eat foods (sandwiches) and food handlers.**

| Food settings | Number of studies | Geographical distribution | Number of studies | Imported food | Number of studies | Exported food | Number of studies |
|---|---|---|---|---|---|---|---|
| Food industry & Food | 8,030 | & UK (total) | 288 | UK & import | 13 | UK & export | 1 |
| | | & Europe | 834 | Europe & import | 3 | Europe & export | 2 |
| | | & Third countries | 21 | Third countries & import | 0 | Third countries & export | 1 |
| Food handlers | 9 | | | | | | |
| Food sandwich | 5 | | | | | | |

**AMR in livestock species**

| Livestock species | Number of studies | Livestock species/ food chain stage | Number of studies |
|---|---|---|---|
| Cattle (all) | 2,140 | Beef cattle | 263 |
| | | Dairy | 468 |
| | | calves | 240 |
| | | Cattle at slaughter | 71 |
| Pigs (all) | 1,935 | At farm | 249 |
| | | At slaughter | 115 |
| Poultry (all) | 2,003 | At farm | 198 |
| | | At slaughter | 115 |

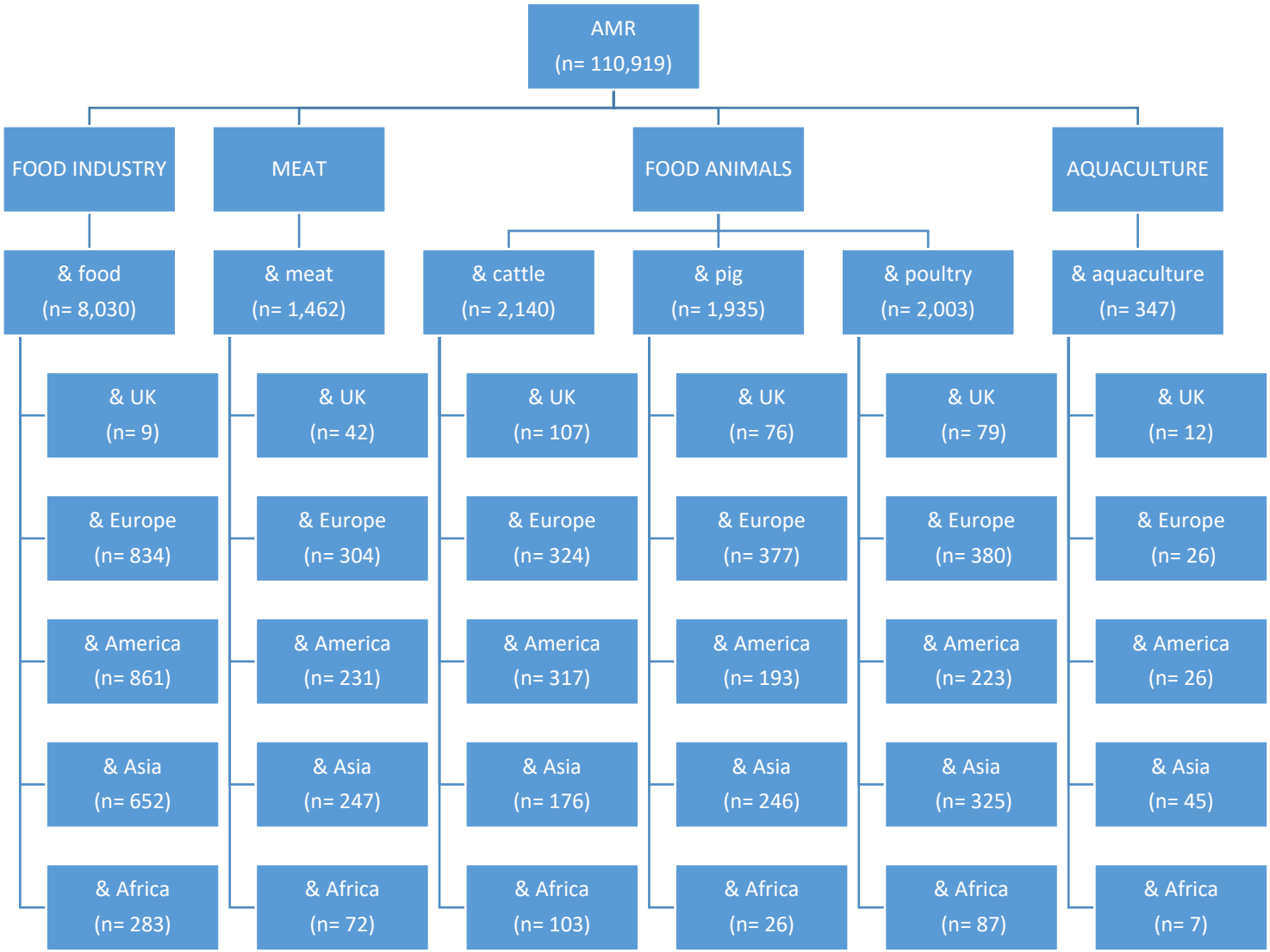
| | | | |
|---|---|---|---|
| Meat (all) | 1,462 | Poultry meat | 791 |
| | | Pork meat | 174 |
| | | Beef meat | 194 |
| | | Sheep meat | 51 |
| | | Sausages | 22 |
| | | Retail level (all) | 283 |

**AMR in food items (meat, dairy, fresh produce and seafood products)**

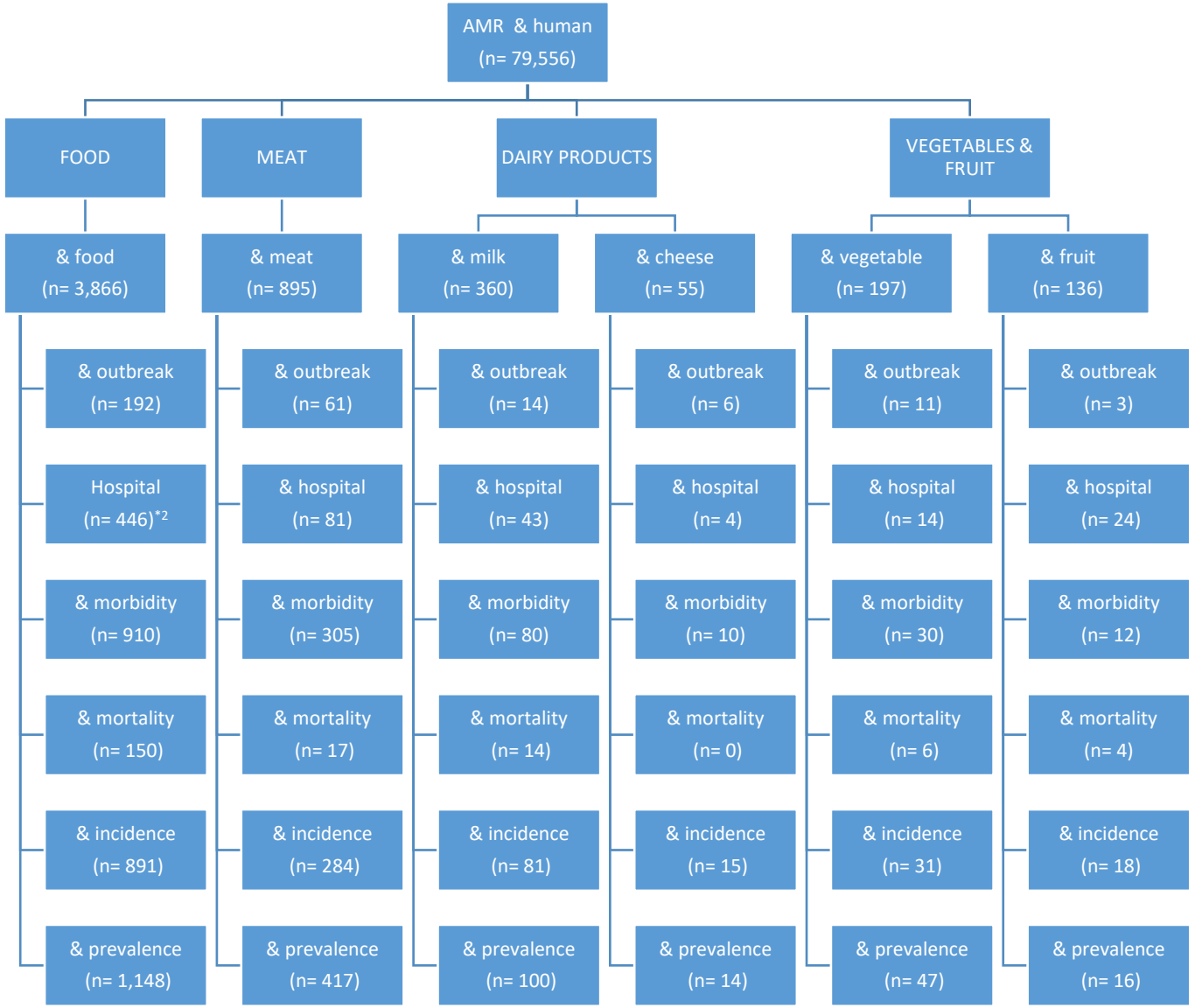
| Food item | Number of studies | Food product/ food chain stage | Number of studies |
|---|---|---|---|
| Meat (all) | 1,462 | Poultry meat | 791 |
| | | Pork meat | 174 |
| | | Beef meat | 194 |
| | | Sheep meat | 51 |
| | | Sausages | 22 |
| | | Retail level (all) | 283 |
| Milk | 758 | At retail | 19 |
| Cheese | 136 | At retail | 12 |
| Fruit | 517 | At retail | 7 |
| Salads | 517 | At retail | 22 |
| Vegetable | 804 | Vegetable salad | 17 |
| | | At retail (all vegetables) | 2 |
| Fresh produce | 45 | At retail | 7 |
| Nut* | 8 | At retail | 0 |
| Fish | 899 | At retail | 22 |
| Aquaculture (all) | 347 | Fish | 253 |
| | | Shellfish | 71 |
| | | Prawn | 7 |
| | | Shrimp | 32 |
| | | Retail | 6 |

*- none of the studies in the search were deemed relevant based on title.

## a) AMR per UK & per continent



## b) AMR burden human cases UK



# Appendix 2- Literature search strategy

Listing of search terms based on the Medical Subject Headings (MeSH) and associated free text that will be used for the purpose of the systematic review.

**Table 1a - Literature search strategy (MeSH and search terms for PIO).**

| **Area** | **MeSH thesaurus headings** | **Free text** |
|---|---|---|
| Population(s) | Meat | Pork, swine, poultry, fowl, domestic |
| | Vegetable(s) | |
| | fruit | |
| | Salmonella | |
| | Campylobacter | |
| | Enterococcus faecium | |
| | Enterococcus faecalis | |
| | Escherichia coli | E. coli |
| Intervention(s) and exposure(s) | (no MeSH term found) | Retail |
| Outcome(s) | Bacterial load | Bacterial count* OR Counts, Bacteria* |
| | Prevalence | |

**Table 1b - Literature search strategy (MeSH and search terms for PIO)- antimicrobial resistance and substance terms.**

**Antimicrobial resistance terms**

| **MeSH thesaurus headings** | **Free text** |
|---|---|
| Drug resistance, Microbial | Antibiotic resistance OR antimicrobial drug resistance OR antimicrobial resistance |
| Beta-lactams | Benzylpenicillin OR (penicillin G) OR Procaine penicillin<br><br>OR Phenoxymethyl penicillin OR (penicillin V) OR Cloxacillin OR Dicloxacillin OR Flucloxacillin OR Methicillin OR Nafcillin OR Oxacillin<br><br>OR Amoxicillin OR Ampicillin OR Hetacillin OR Pivampicillin OR Mecillian OR Temocillin OR Azlocillin OR Mezlocillin OR Piperacillin OR Carbenicillin OR Ticarcillin OR Cephacetrile OR Cephaloridine OR Cephalothin OR Cephapirin OR Cephazolin OR Cefadroxil OR Cephadrine OR Cephalexin OR Cefaclor OR Cefotetan OR Cefoxitin OR Cefuroxime OR Cefamandole OR Cefotaxime OR Ceftiofur OR Ceftriaxone OR Latamoxef OR Cefetamet OR Cefixime OR Cefpodoxime OR Cefoperazone OR Cefovecin OR Cefsulodin OR Ceftazidime OR Cefepime OR cefquinome OR cefpirome |
| Carbapenems | Carbapenem* OR Imipenen OR Meropenem OR Biapenem |
| Fluoroquinolones | Enrofloxacin OR Ciprofloxacin OR Danofloxacin OR Difloxacin OR Ibafloxacin OR Marbofloxacin OR Pradofloxacin OR Orbifloxacin |
| Macrolides | Tulathromycin OR Erythromycin OR Oleandomycin OR Clarytromycin OR Roxithromycin OR Dirithromycin OR Fluorithromycin OR Azithromycin OR Gamithromycin OR Spiramycin OR Tylosin OR Josamycin OR Midecamycin OR Tilmicosin OR Tildipirosin OR Tylvasolin OR Miokamycin OR Rokitamycin |
| Polymyxin E (colistin) | Polymyxyn E OR colistin |
| Drug resistance, multiple | MDR OR Multi-drug resistance OR multidrug resistance |

**Table 2a - Search findings for the research question assessing antimicrobial resistance in salmonella found in pork meat at retail level (PubMed, publication date between 01/01/1999 and 30/09/2015).**

| Number | Search terms | Hits |
|---|---|---|
| 1 | Meat | 44,040 |
| 2 | Pork | 4,865 |
| 3 | Swine | 92,619 |
| 4 | Meat OR pork OR swine | 131,444 |
| 5 | Salmonella | 39,697 |
| 6 | Abattoir | 3,768 |
| 7 | Slaughter* | 11,591 |
| 8 | Retail* | 5,948 |
| 9 | Abattoir OR slaughter* OR retail* | 18,828 |
| 10 | Bacterial load | 7,600 |
| 11 | Bacterial count* OR Counts, Bacteria* | 3,285 |
| 12 | Prevalence | 1,394,638 |
| 13 | Bacterial load OR Bacterial count* OR Counts, Bacteria* OR Prevalence | 1,404,022 |
| 14 | 4 AND 5 AND 9 AND 13 | 492 |
| 15 | Drug resistance, Microbial | 84,766 |
| 16 | Antibiotic resistance OR antimicrobial drug resistance OR antimicrobial resistance | 135,025 |
| 17 | 15 OR 16 | 84,766 |
| 18 | Beta-lactams | 36,282 |
| 19 | Beta-lactam* OR Benzylpenicillin OR (penicillin G) OR Procaine penicillin OR Phenoxymethyl penicillin OR (penicillin V) OR Cloxacillin OR Dicloxacillin OR Flucloxacillin OR Methicillin OR Nafcillin OR Oxacillin OR Amoxicillin OR Ampicillin OR Hetacillin OR Pivampicillin OR Mecillian OR Temocillin OR Azlocillin OR Mezlocillin OR Piperacillin OR Carbenicillin OR Ticarcillin OR Cephacetrile OR Cephaloridine OR Cephalothin OR Cephapirin OR Cephazolin OR Cefadroxil OR Cephadrine OR Cephalexin OR Cefaclor OR Cefotetan OR Cefoxitin OR Cefuroxime OR Cefamandole OR Cefotaxime OR Ceftiofur OR | 76,150 |

| Number | Search terms | Hits |
|---|---|---|
| | Ceftriaxone OR Latamoxef OR Cefetamet OR Cefixime OR Cefpodoxime OR Cefoperazone OR Cefovecin OR Cefsulodin OR Ceftazidime OR Cefepime OR cefquinome OR cefpirome | |
| 20 | 18 OR 19 | 82,207 |
| 21 | 14 AND 17 AND 20 | 73 |
| 22 | 4 AND 5 AND 9 AND 20 | 121 |
| 22 | Fluoroquinolones | 20,191 |
| 23 | Enrofloxacin OR Ciprofloxacin OR Danofloxacin OR Difloxacin OR Ibafloxacin OR Marbofloxacin OR Pradofloxacin OR Orbifloxacin | 16,467 |
| 24 | 22 OR 23 | 27,629 |
| 25 | 4 &5 & 9 AND 24 | 51 |
| 26 | Macrolides | 55,910 |
| 27 | Tulathromycin OR Erythromycin OR Oleandomycin OR Clarytromycin OR Roxithromycin OR Dirithromycin OR Fluorithromycin OR Azithromycin OR Gamithromycin OR Spiramycin OR Tylosin OR Josamycin OR Midecamycin OR Tilmicosin OR Tildipirosin OR Tylvasolin OR Miokamycin OR Rokitamycin | 19,405 |
| 28 | 26 AND 27 | 62,646 |
| 29 | 4 AND 5 AND 9 AND 28 | 15 |
| 30 | Carbapenems | 7,053 |
| 31 | Carbapenem* OR Imipenen OR Meropenem OR Biapenem | 9,707 |
| 32 | 30 OR 31 | 10,795 |
| 33 | 4 AND 5 AND 8 AND 17 AND 32 | 3 |
| 34 | Drug resistance, multiple | 35,880 |
| 35 | MDR OR Multi-drug resistance OR multidrug resistance | 59,221 |
| 36 | 34 OR 35 | 59,221 |
| 37 | 4 AND 5 AND 8 AND 36 | 84 |

**Table 2b- Search findings for the research question assessing antimicrobial resistance on campylobacter found in poultry meat at retail level (PubMed, publication date between 01/01/1999 and 30/09/2015).**

| Number | Search terms | Hits |
|---|---|---|
| 1 | Meat | 44,040 |
| 2 | poultry | 53,518 |
| 3 | Fowls, domestic | 53,548 |
| 4 | Meat OR Poultry OR (fowls, domestic) | 87,904 |
| 5 | Campylobacter | 8,022 |
| 6 | Abattoir | 3,768 |
| 7 | Slaughter* | 11,591 |
| 8 | Retail* | 5,948 |
| 9 | Abattoir OR slaughter* OR retail* | 18,828 |
| 10 | Bacterial load | 7,600 |
| 11 | Bacterial count* OR Counts, Bacteria* | 3,285 |
| 12 | Prevalence | 1,394,638 |
| 13 | Bacterial load OR Bacterial count* OR Counts, Bacteria* OR Prevalence | 1,404,022 |
| 14 | 4 AND 5 AND 9 AND 13 | 346 |
| 15 | Drug resistance, Microbial | 84,766 |
| 16 | Antibiotic resistance OR antimicrobial drug resistance OR antimicrobial resistance | 135,025 |
| 17 | 15 OR 16 | 84,766 |
| 18 | Beta-lactams | 36,282 |
| 19 | Beta-lactam* OR Benzylpenicillin OR (penicillin G) OR Procaine penicillin OR Phenoxymethyl penicillin OR (penicillin V) OR Cloxacillin OR Dicloxacillin OR Flucloxacillin OR Methicillin OR Nafcillin OR Oxacillin OR Amoxicillin OR Ampicillin OR Hetacillin OR Pivampicillin OR Mecillian OR Temocillin OR Azlocillin OR Mezlocillin OR Piperacillin OR Carbenicillin OR Ticarcillin OR Cephacetrile OR Cephaloridine OR Cephalothin OR Cephapirin OR Cephazolin OR Cefadroxil OR Cephadrine OR Cephalexin OR Cefaclor OR Cefotetan OR Cefoxitin OR Cefuroxime OR Cefamandole OR Cefotaxime OR Ceftiofur OR | 76,150 |

| Number | Search terms | Hits |
|---|---|---|
| | Ceftriaxone OR Latamoxef OR Cefetamet OR Cefixime OR Cefpodoxime OR Cefoperazone OR Cefovecin OR Cefsulodin OR Ceftazidime OR Cefepime OR cefquinome OR cefpirome | |
| 20 | 18 OR 19 | 82,207 |
| 21 | 14 AND 17 AND 20 | 24 |
| 22 | 4 AND 5 AND 9 AND 20 | 38 |
| 22 | Fluoroquinolones | 20,191 |
| 23 | Enrofloxacin OR Ciprofloxacin OR Danofloxacin OR Difloxacin OR Ibafloxacin OR Marbofloxacin OR Pradofloxacin OR Orbifloxacin | 16,467 |
| 24 | 22 OR 23 | 27,629 |
| 25 | 4 &5 & 9 AND 24 | 144 |
| 26 | Macrolides | 55,910 |
| 27 | Tulathromycin OR Erythromycin OR Oleandomycin OR Clarytromycin OR Roxithromycin OR Dirithromycin OR Fluorithromycin OR Azithromycin OR Gamithromycin OR Spiramycin OR Tylosin OR Josamycin OR Midecamycin OR Tilmicosin OR Tildipirosin OR Tylvasolin OR Miokamycin OR Rokitamycin | 19,405 |
| 28 | 26 AND 27 | 62,646 |
| 29 | 4 AND 5 AND 9 AND 28 | 246 |
| 30 | Carbapenems | 7,053 |
| 31 | Carbapenem* OR Imipenen OR Meropenem OR Biapenem | 9,707 |
| 32 | 30 OR 31 | 10,795 |
| 33 | 4 AND 5 AND 8 AND 17 AND 32 | 0 |
| 34 | Drug resistance, multiple | 35,880 |
| 35 | MDR OR Multi-drug resistance OR multidrug resistance | 59,221 |
| 36 | 34 OR 35 | 59,221 |
| 37 | 4 AND 5 AND 8 AND 36 | 37 |

**Table 2c- Search findings for the research question assessing antimicrobial resistance on *Enterococcus faecium* and *Enterococcus faecalis* found in vegetables and fruits (PubMed, publication date between 01/01/1999 and 30/09/2015).**

| Number | Search terms | Hits |
|---|---|---|
| 1 | Vegetables | 72,700 |
| 2 | Fruit | 73,915 |
| 3 | Vegetables OR fruit | 130,294 |
| 4 | Enterococcus faecium | 4,190 |
| 5 | Enterococcus faecalis | 7,289 |
| 6 | 4 AND 5 | 9,818 |
| 7 | Retail* | 5,948 |
| 8 | 3 AND 6 AND 7 | 7 |
| 9 | 3 AND 6 | 144 |
| 9 | Bacterial load | 7,600 |
| 10 | Bacterial count* OR Counts, Bacteria* | 3,285 |
| 11 | Prevalence | 1,394,638 |
| 12 | Bacterial load OR Bacterial count* OR Counts, Bacteria* OR Prevalence | 1,404,022 |
| 13 | Bacterial load OR Bacterial count* OR Counts, Bacteria* OR Prevalence | 1,404,022 |
| 14 | Drug resistance, Microbial | 84,766 |
| 15 | Antibiotic resistance OR antimicrobial drug resistance OR antimicrobial resistance | 135025 |
| 16 | 14 OR 15 | 84,766 |
| 17 | Beta-lactams | 36,282 |
| 18 | Beta-lactam* OR Benzylpenicillin OR (penicillin G) OR Procaine penicillin OR Phenoxymethyl penicillin OR (penicillin V) OR Cloxacillin OR Dicloxacillin OR Flucloxacillin OR Methicillin OR Nafcillin OR Oxacillin OR Amoxicillin OR Ampicillin OR Hetacillin OR Pivampicillin OR Mecillian OR Temocillin OR Azlocillin OR Mezlocillin OR Piperacillin OR Carbenicillin OR Ticarcillin OR Cephacetrile OR Cephaloridine OR Cephalothin OR Cephapirin OR Cephazolin OR Cefadroxil OR Cephadrine OR Cephalexin | 76,150 |

| Number | Search terms | Hits |
|---|---|---|
| | OR Cefaclor OR Cefotetan OR Cefoxitin OR Cefuroxime OR Cefamandole OR Cefotaxime OR Ceftiofur OR Ceftriaxone OR Latamoxef OR Cefetamet OR Cefixime OR Cefpodoxime OR Cefoperazone OR Cefovecin OR Cefsulodin OR Ceftazidime OR Cefepime OR cefquinome OR cefpirome | |
| 19 | 17 OR 18 | 82,207 |
| 20 | 8 AND 16 AND 19 | 8 |
| 21 | 8 AND 13 AND16 AND 19 | 2 |
| 22 | Fluoroquinolones | 20,191 |
| 23 | Enrofloxacin OR Ciprofloxacin OR Danofloxacin OR Difloxacin OR Ibafloxacin OR Marbofloxacin OR Pradofloxacin OR Orbifloxacin | 16,467 |
| 24 | 22 OR 23 | 27,629 |
| 25 | 3 AND 6 AND 16 AND 24 | 5 |
| 26 | Macrolides | 55,910 |
| 27 | Tulathromycin OR Erythromycin OR Oleandomycin OR Clarytromycin OR Roxithromycin OR Dirithromycin OR Fluorithromycin OR Azithromycin OR Gamithromycin OR Spiramycin OR Tylosin OR Josamycin OR Midecamycin OR Tilmicosin OR Tildipirosin OR Tylvasolin OR Miokamycin OR Rokitamycin | 19,405 |
| 28 | 26 AND 27 | 62,646 |
| 29 | 3 AND 6 AND 16 AND 28 | 5 |
| 30 | Carbapenems | 7,053 |
| 31 | Carbapenem* OR Imipenen OR Meropenem OR Biapenem | 9,707 |
| 32 | 30 OR 31 | 10,795 |
| 33 | 4 AND 5 AND 8 AND 17 AND 32 | 1 |
| 34 | Drug resistance, multiple | 35,880 |
| 35 | MDR OR Multi-drug resistance OR multidrug resistance | 59,221 |
| 36 | 34 OR 35 | 59,221 |
| 37 | 4 AND 5 AND 8 AND 36 | 10 |

**Table 2c - Search findings for the research question assessing antimicrobial resistance on *Escherichia coli* found in vegetables and fruits (PubMed, publication date between 01/01/1999 and 30/09/2015).**

| Number | Search terms | Hits |
|---|---|---|
| 1 | Vegetables | 72,700 |
| 2 | Fruit | 73,915 |
| 3 | Vegetables OR fruit | 130,294 |
| 4 | Escherichia coli | 157,493 |
| 5 | E coli | 167,393 |
| 6 | 4 AND 5 | 157,493 |
| 7 | Retail* | 5,948 |
| 8 | 3 AND 6 AND 7 | 74 |
| 9 | 3 AND 6 | 3,284 |
| 9 | Bacterial load | 7,600 |
| 10 | Bacterial count* OR Counts, Bacteria* | 3,285 |
| 11 | Prevalence | 1,394,638 |
| 12 | Bacterial load OR Bacterial count* OR Counts, Bacteria* OR Prevalence | 1,404,022 |
| 13 | 3 AND 6 AND 12 | 304 |
| 14 | Drug resistance, Microbial | 84,766 |
| 15 | Antibiotic resistance OR antimicrobial drug resistance OR antimicrobial resistance | 135025 |
| 16 | 14 OR 15 | 84,766 |
| 17 | Beta-lactams | 36,282 |
| 18 | Beta-lactam* OR Benzylpenicillin OR (penicillin G) OR Procaine penicillin OR Phenoxymethyl penicillin OR (penicillin V) OR Cloxacillin OR Dicloxacillin OR Flucloxacillin OR Methicillin OR Nafcillin OR Oxacillin OR Amoxicillin OR Ampicillin OR Hetacillin OR Pivampicillin OR Mecillian OR Temocillin OR Azlocillin OR Mezlocillin OR Piperacillin OR Carbenicillin OR Ticarcillin OR Cephacetrile OR Cephaloridine OR Cephalothin OR Cephapirin OR Cephazolin OR Cefadroxil OR Cephadrine OR Cephalexin OR Cefaclor OR Cefotetan OR Cefoxitin OR Cefuroxime OR Cefamandole OR Cefotaxime OR Ceftiofur OR Ceftriaxone OR Latamoxef OR | 76,150 |

| Number | Search terms | Hits |
|---|---|---|
| | Cefetamet OR Cefixime OR Cefpodoxime OR Cefoperazone OR Cefovecin OR Cefsulodin OR Ceftazidime OR Cefepime OR cefquinome OR cefpirome | |
| 19 | 17 OR 18 | 82,207 |
| 20 | 3 AND 6 AND 16 AND 19 | 26 |
| 21 | 3 AND 6 AND 13 AND 16 AND 19 | 11 |
| 22 | Fluoroquinolones | 20,191 |
| 23 | Enrofloxacin OR Ciprofloxacin OR Danofloxacin OR Difloxacin OR Ibafloxacin OR Marbofloxacin OR Pradofloxacin OR Orbifloxacin | 16,467 |
| 24 | 22 OR 23 | 27,629 |
| 25 | 3 AND 6 and 16 AND 24 | 27 |
| 26 | Macrolides | 55,910 |
| 27 | Tulathromycin OR Erythromycin OR Oleandomycin OR Clarytromycin OR Roxithromycin OR Dirithromycin OR Fluorithromycin OR Azithromycin OR Gamithromycin OR Spiramycin OR Tylosin OR Josamycin OR Midecamycin OR Tilmicosin OR Tildipirosin OR Tylvasolin OR Miokamycin OR Rokitamycin | 19,405 |
| 28 | 26 AND 27 | 62,646 |
| 29 | 3 AND 6 AND 16 AND 28 | 7 |
| 30 | Carbapenems | 7,053 |
| 31 | Carbapenem* OR Imipenen OR Meropenem OR Biapenem | 9,707 |
| 32 | 30 OR 31 | 10,795 |
| 33 | 4 AND 5 AND 8 AND 17 AND 32 | 1 |
| 34 | Drug resistance, multiple | 35,880 |
| 35 | MDR OR Multi-drug resistance OR multidrug resistance | 59,221 |
| 36 | 34 OR 35 | 59,221 |
| 37 | 4 AND 5 AND 8 AND 36 | 29 |

**Table 2d- Search findings for the research question assessing colistin resistance for all pathogens and food combinations considered in the research questions (PubMed, publication date between 01/01/1999 and 16/05/2016).**

| Number | Search terms | Hits |
|---|---|---|
| 1 | (Meat OR pork OR swine) AND (Salmonella OR Escherichia coli OR E. coli OR Enterococcus faecium OR Enterococcus faecalis) AND (retail*) AND (Antibiotic resistance OR antimicrobial drug resistance OR antimicrobial resistance) AND (colistin OR Polymyxin E) | 89 |
| 2 | Meat OR Poultry OR (fowls, domestic) AND (Campylobacter OR Escherichia coli OR E. coli OR Enterococcus faecium OR Enterococcus faecalis) AND (Retail*) AND (Antibiotic resistance OR antimicrobial drug resistance OR antimicrobial resistance) AND (colistin OR Polymyxin E) | 96 |
| 3 | Seafood AND (Escherichia coli OR E. coli OR Enterococcus faecium OR Enterococcus faecalis) AND (Retail*) AND (Antibiotic resistance OR antimicrobial drug resistance OR antimicrobial resistance) AND (colistin OR Polymyxin E) | 148 |
| 4 | (Vegetables OR fruit) AND (Escherichia coli OR E. coli OR Enterococcus faecium OR Enterococcus faecalis) AND (Retail*) AND (Antibiotic resistance OR antimicrobial drug resistance OR antimicrobial resistance) AND (colistin OR Polymyxin E) | 80 |
| 5 | Dairy AND (Escherichia coli OR E. coli OR Enterococcus faecium OR Enterococcus faecalis) AND (Retail*) AND (Antibiotic resistance OR antimicrobial drug resistance OR antimicrobial resistance) AND (colistin OR Polymyxin E) | 235 |