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Source, spread and control of Campylobacter

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A restatement of the natural science evidence base regarding the source, spread and control of Campylobacter species causing human disease

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This paper was published in June 2022 in the Proceedings of the Royal Society B. It deals with the source and spread of Campylobacter in the food chain and how it might be controlled.

Food poisoning caused by Campylobacter (campylobacteriosis) is the most prevalent bacterial disease associated with the consumption of poultry, beef, lamb and pork meat and unpasteurised dairy products. This Restatement summarises the natural science evidence base relevant to campylobacteriosis control in as policy-neutral terms as possible. A series of evidence statements are listed and categorised according to the nature of the underlying information. It is intended to be accessible to informed, but not expert, policymakers and stakeholders.

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Evidence synthesis

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A restatement of the natural science evidence base regarding the source, spread and control of *Campylobacter* species causing human disease

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Food poisoning caused by *Campylobacter* (campylobacteriosis) is the most prevalent bacterial disease associated with the consumption of poultry, beef, lamb and pork meat and unpasteurized dairy products. A variety of livestock industry, food chain and public health interventions have been implemented or proposed to reduce disease prevalence, some of which entail costs for producers and retailers. This paper describes a project that set out to summarize the natural science evidence base relevant to campylobacteriosis control in as policy-neutral terms as possible. A series of evidence statements are listed and categorized according to the nature of the underlying information. The evidence summary forms the appendix to this paper and an annotated bibliography is provided in the electronic supplementary material.

1. Introduction

The consumption of food and drink contaminated with *Campylobacter* bacteria can cause campylobacteriosis in humans. While food may be made safe with adequate cooking, and by avoiding cross-contamination during food preparation, *Campylobacter* is the most common cause of acute bacterial gastroenteritis both in the UK and globally [1]. Campylobacteriosis is chiefly a sporadic disease with many isolated cases that usually peak in early summer in the UK, though there are occasional larger outbreaks [2]. Most people who become infected with *Campylobacter* suffer from illness and discomfort and require time to convalesce, but severe disease and death can occur. The use of antibiotics is only recommended for those at greatest risk of severe disease or death from campylobacteriosis (chiefly the young, old and immune compromised). In other patients, antibiotics only shorten the disease by a few days and their prescription may accelerate the evolution of antibiotic resistance, which has already been observed in *Campylobacter*. The total cost to society of foodborne campylobacteriosis is estimated at over £700 million per annum in the UK alone [3].

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A suite of producer, food-chain and public health measures have been implemented to attempt to reduce the levels of campylobacteriosis in the UK, particularly targeting poultry, which has been identified as the main source of human infection. Surveys indicate that levels of *Campylobacter* in fresh poultry at retail outlets in the UK have decreased in recent years, but reported human *Campylobacter* infections have remained relatively constant [4]. Further interventions are needed to limit the individual and economic impacts of campylobacteriosis, though each imposes different levels of costs on livestock production, processing and retail sectors. Designing better control measures without unnecessary costs requires a better understanding of the origin and transmission dynamics of the *Campylobacter* species causing human disease.

The aim of this 'Restatement' is to present a clear and succinct summary of the evidence for the source and spread of *Campylobacter* in the food chain and how it might be controlled. We focus on the UK although the evidence base is relevant to many other countries, particularly those in temperate regions. The Restatement is written for an informed but not expert audience, for example, senior policy-makers with food safety in their brief. We also highlight areas where the evidence base is poorly developed to assist policy makers. In a policy area that can be contentious, we aim to be as policy-neutral as possible in the compilation and presentation of evidence.

2. Material and methods

The relevant literature on *Campylobacter* was reviewed with particular focus on studies in the UK and a first draft evidence summary was produced by a subset of the authors. At a workshop, all authors met to discuss the different evidence statements and to assign a description of the nature of the evidence to each statement using a restricted set of terms. The statements and their assessments were subsequently debated via correspondence until a consensus was achieved. We use the following restricted terms to describe the evidence, indicated by abbreviated codes, which are similar to those used in previous Restatements.

[S_{trong}]: A **strong** evidence base likely involving multiple experimental studies or field data collections, with appropriate detailed statistical or other quantitative analysis.

[L_{imited}]: Limited evidence from perhaps only one or few studies, with further studies needed to strengthen the evidence base.

[$E_{xp}O_p$]: A consensus of **expert opinion** extrapolating results from related systems and well-established epidemiological and pathological principles.

[P_{roj}]: **Projections** based on the available evidence for which substantial uncertainty often exists.

3. Results

The summary of the natural science evidence base relevant to *Campylobacter* control policy-making in the UK is given in the appendix, with an extensive annotated bibliography provided as electronic supplementary material.

4. Discussion

The most important source of *Campylobacter* that cause human disease is meat from farmed animals such as cattle, pigs and particularly broiler chickens. *Campylobacter* infect the intestines of most farmed animals and are regularly found on fresh carcasses, particularly the carcasses of broiler chickens, and it is likely that bacteria in digestive tracts are spread to carcasses during slaughter and factory processing. Live bacteria on meat and carcasses may be ingested by humans via cross-contamination to other foods and items if food preparation hygiene is poor prior to cooking, or if meat is not cooked sufficiently.

Poultry is the most consumed meat in the UK and a major source of *Campylobacter*. *Campylobacter* from non-poultry livestock, particularly ruminants, are also a significant cause of human disease, as is increasingly shown by genetic source-attribution studies including recent studies using whole-genome sequencing [5]. The evidence base for *Campylobacter* levels on retail beef, lamb and pork, and the effect of food-chain interventions designed to reduce these, is less well developed than for poultry. The Restatement highlights gaps in our knowledge on the efficacy of on-farm and factory processing food-chain interventions aimed at reducing rates of contamination on cattle, pigs and particularly broiler chickens, where further research would be helpful. There has been a decrease in *Campylobacter* levels on poultry over the last 5 years in the UK but levels of human campylobacteriosis cases have remained static. It is not yet known whether this is due to *Campylobacter* levels on poultry being a poor measure of risk from consuming poultry meat, an increase in the consumption of chicken, an increase in the number of people over 60 years of age who are more susceptible to *Campylobacter*, or whether the risks from consuming other meats or becoming infected from non-food sources has increased [4,6].

The Advisory Committee on the Microbiological Safety of Food recommends a multi-prong approach to tackling disease from *Campylobacter* combining interventions across the entire food system including non-poultry livestock [1]. Our survey of the evidence supports this recommendation as there is no evidence that any single intervention has a major effect, whereas concerted multiple-intervention campaigns in Iceland and New Zealand have had some effect. Nevertheless, to implement more effectively such a 'multiple-hurdle' strategy, it would be helpful to conduct more whole food-chain studies that robustly quantify the likely main environmental sources of *Campylobacter* and then go on to analyse the effect of specific on-farm and in-factory interventions on changing the numbers and types of *Campylobacter* on final food products. Experimental and modelling work that evaluates how different interventions interact and combine across the food-chain to reduce levels on retail products would be particularly valuable [7]. The increasing availability of whole-genome DNA sequencing approaches combined with epidemiological and classic microbiological methods offers new tools to understand *Campylobacter* origins, transmission and disease (e.g. [7]). Lastly, we need to better understand the behavioural science of how people assess and understand the risks of food poisoning from *Campylobacter* (and of course other agents), and how they can be empowered to protect themselves and other people.

Data accessibility. The data are provided in electronic supplementary material [8].

Authors' contributions. M.R.G.: data curation, investigation, methodology, writing—original draft, writing—review and editing; S.O.: investigation, writing—review and editing; N.W.: investigation, writing—

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review and editing; J.G.: investigation, writing—review and editing; A.G.: investigation, writing—review and editing; A.C.: investigation, writing—review and editing; F.C.: investigation, writing—review and editing; J.-C.B.: project administration, writing—review and editing; E.A. and A.S.: data curation, investigation, project administration, writing—original draft; H.C.J.G.: conceptualization, investigation, writing—original draft, writing—review and editing; M.C.J.M.: investigation, writing—original draft, writing—review and editing.

All authors gave final approval for publication and agreed to be held accountable for the work performed therein.

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Appendix

(a) Aims and scope

1. *Campylobacter* bacteria are a major cause of acute gastroenteritis, affecting around 600 000 people a year in the UK and over 150 million people a year globally. The economic burden of identified *Campylobacter* cases in the UK, in terms of costs to the healthcare system and the patient, is estimated to be £50 million per annum. The total UK societal cost from just foodborne *Campylobacter*, based on 299 000 cases, is estimated at over £700 million per annum.
2. The aim of this Restatement is to summarize succinctly the natural science evidence base concerning the origin and transmission dynamics of *Campylobacter* species causing human disease to assist policy making. The Restatement also summarizes evidence for the efficacy of different interventions intended to control *Campylobacter*. The focus is on evidence of greatest applicability to the UK. It also provides a consensus judgement by the authors on the nature of the different evidence components, and a consensus was arrived at using the studies listed in the annotated bibliography. We use the following descriptions, which explicitly are not a ranking, indicated by abbreviated codes. Statements are considered to be supported by **[S$_{trong}$]**, **[L$_{imited}$]**, **[E$_{xp}$O$_{p}$]** and **[P$_{roj}$]** codes, which are defined in the Materials and methods section. Codes at the end of sections and sub-sections after full-stops indicate they apply to the whole previous section; codes preceding full-stops or within sentences apply to that sentence or clause only. Throughout the restatement, we use the terms 'infection' and 'infected' to mean the presence of *Campylobacter* bacteria in animals (humans and farmed animals) regardless of whether they cause disease. World Bank country classifications are used throughout. The abbreviation '95% UI' denotes the 95% uncertainty interval.

(b) *Campylobacter* disease in humans

3. *Campylobacter* can cause acute diarrhoea and gastroenteritis in humans when ingested. *Campylobacter* may derive from food or non-food sources (such as lakes when swimming). Symptoms of campylobacteriosis range from mild to severe, and usually resolve by themselves in around a week. Frail and immunocompromised individuals have greater susceptibility to campylobacteriosis **[S$_{trong}$]**. Only a few studies exist that monitor the effects of deliberate exposure of humans to *Campylobacter*, for understandable ethical reasons, and one shows illness can be caused by the ingestion of as little as a few hundred bacterial cells, but not all humans infected with *Campylobacter* showed signs of disease **[L$_{imited}$]**.
4. The species *Campylobacter jejuni* and *Campylobacter coli* are the major causes of campylobacteriosis globally. In the UK, *C. jejuni* is responsible for approximately 10 times more cases of human disease than *C. coli* **[S$_{trong}$]**.
5. In high income countries, analyses conducted under the assumption that all ages are equally as likely to present to GPs show cases of laboratory confirmed campylobacteriosis are most frequent in children under 5, young adults (aged 20–30), and in those aged over 60 **[S$_{trong}$]**. In low and lower- and upper-middle income countries, illness from *Campylobacter* infection occurs most frequently in children under 2, with severity of symptoms inversely related to age in older individuals **[L$_{imited}$]**.
6. Comparing the incidence of campylobacteriosis across continents and analysing global trends is hard due to differing sampling and reporting conventions, frequent under-reporting (particularly in countries where many uninsured people have to pay for healthcare), and very low surveillance levels in low income and lower- and upper-middle income countries. The WHO estimates 166 million cases of campylobacteriosis occurred worldwide in 2010 (95% UI: 92–301 million) causing 37 600 deaths (95% UI: 27 700–55 100). In 2018, the Centres for Disease Control and Prevention in the USA reported that 20 campylobacteriosis cases were diagnosed for every 100 000 people but that many more cases went undiagnosed or unreported, and they estimated *Campylobacter* infection affects 1.5 million US residents every year. In low income countries, high burdens of *Campylobacter* in children under two are correlated with stunting **[L$_{imited}$]**.
7. There is greater consistency of reporting methods among European countries making these more comparable but difference in access to and costs of healthcare across Europe may skew this. *Campylobacter* was the most commonly reported gastrointestinal bacterial pathogen in humans in the EU in 2019 with over 220 000 confirmed cases, and an average reported incidence of 60 per 100 000 population. European campylobacteriosis rates have remained stable between 2015 and 2019, and are more than twice that of salmonellosis which is caused by the next most prevalent gastrointestinal bacterial pathogen (*Salmonella*). A decrease of 100 000 campylobacteriosis cases was reported in Europe in 2020 (120 000 cases) compared to 2019: it is likely this drop was due to various effects of the COVID-19 pandemic and corresponding social lock-downs making it hard to compare to preceding years. UK campylobacteriosis rates have fluctuated between 86 and 114 reported cases per 100 000 between 2006 and 2017 with no overall trend. In 2019, the UK reported a campylobacteriosis rate of 88 cases per 100 000 population. Rates in the UK have thus consistently exceeded the EU average since 2015. Studies in England and Wales between 1989 and 2011 show campylobacteriosis cases are increasing in those aged over 50 **[S$_{trong}$]**.

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a. For every case recorded by UK national surveillance centres, around 8–9 are estimated to occur in the community without being reported, so calculations of the economic costs of campylobacteriosis based solely on reported cases are an underestimate. Extrapolations from reported data estimated *Campylobacter* to be the largest cause of bacterial food poisoning cases in the UK underlying 299 392 (95% CI 127 128–571 332) or 33% (95% CI 18%-47%) of food-related infections resulting in the greatest number of GP consultations (42 506; 95% CI 18 683–75 857) for foodborne illness in 2018. After correcting for under-reporting, the rate of campylobacteriosis in the England and Wales population is estimated to have remained roughly stable at approximately 1000 cases per 100 000 since 2009 **[P_{roj}]**.

b. Modelling of clinical data indicate *Campylobacter* caused the greatest number of hospitalizations of foodborne diseases in 2018, and approximately 1% of UK all foodborne campylobacteriosis cases led to hospitalization (median 3505 per year, 95% CI 1352–7641). Estimates of deaths due to campylobacteriosis are around 45 people per year in the UK (95% UI: 24–84) **[P_{roj}]**, and foodborne *Campylobacter* was involved in 21 UK deaths in 2019 **[P_{roj}]**. For comparison, influenza was involved in 1213 deaths in England and Wales in 2019 **[S_{trong}]**. Estimating rates of death due to *Campylobacter* is difficult because the impact of campylobacteriosis may be masked or exacerbated by other health problems or by not being properly recorded **[$E_{xp}O_p$]**.

c. Modelling analysis indicates that 70 000 quality-adjusted life years (QALYs) are lost per year in the UK due to just foodborne *Campylobacter*, but with considerable uncertainty (95% UI: 40 000–108 000). Norovirus imposes the largest burden among foodborne diseases and is responsible for 3.5 times more lost QALYs than *Campylobacter*, which imposes the next greatest burden. For comparison, influenza is estimated to be responsible for a loss of around 30 000 QALYs with standard vaccination rates **[P_{roj}]**.

8. The majority (99%) of campylobacteriosis cases represent isolated infections of individuals, although single-source outbreaks can occur. The number of reported outbreaks in the UK ranged from 5 to 22 per year between 2006 and 2016, with the numbers of people affected per outbreak between 2 and 167. The largest recorded outbreak of campylobacteriosis globally occurred in Havelock North, New Zealand in 2016 when over 5000 people were infected by *C. jejuni* from contaminated untreated drinking-water boreholes **[S_{trong}]**.
9. Campylobacteriosis incidence in some high income countries shows marked seasonality. In the UK, the total number of campylobacteriosis cases is greatest in early summer, peaking during May and June **[S_{trong}]**. There is some evidence that the seasonal variation is more marked in rural than in urban areas and in infants under five **[L_{imited}]**. No factor has been proven to drive these seasonal patterns although a number of hypotheses, for example higher temperatures, increased barbeques, prevalence of flies attracted to food, have been suggested **[$E_{xp}O_p$]**.
10. A fraction of campylobacteriosis cases leads to longer-term health conditions such as Guillain–Barré syndrome (between 1 per 1000 and 1 per 5000 cases), reactive arthritis (9 per 1000 cases) and post-infectious irritable bowel syndrome (up to 33 per 1000 cases) **[S_{trong}]**. The role of *Campylobacter* in the development of these clinical conditions is imperfectly understood and these conditions may also be caused by other infections.
11. **Summary:** *Campylobacter* is the major cause of bacterial gastroenteritis in the UK and around the world. *Campylobacter* infections usually cause short illness but because *Campylobacter* prevalence is relatively high this translates into a significant socioeconomic burden. Infrequently, *Campylobacter* infections lead to more serious outcomes, including death, with the young, elderly and infirm at greatest risk. In low income and lower- and upper-middle income countries, *Campylobacter* is endemic and a major cause of childhood diarrhoeal illness.

(c) How humans become infected with *Campylobacter*

12. *Campylobacter jejuni* and *C. coli* are bacteria commonly found in the intestines of domesticated and wild animals, especially birds. *Campylobacter jejuni* tends to be the dominant species in cattle, sheep, broiler chickens and turkeys, and *C. coli* tends to be the dominant species in pigs **[S_{trong}]**.
13. *Campylobacter* has also been isolated from several different environmental sources, including soil, water and sewage. The most likely explanation for the presence of *Campylobacter* in water and soils is shedding by animals **[$E_{xp}O_p$]**. Survival of *Campylobacter* outside the gut is poor relative to many other species of pathogenic bacteria, with the bacteria demonstrating relatively high sensitivity to oxygen, drying, freezing and low pH **[S_{trong}]**.
14. *Campylobacter* can persist outside of animal guts in the environment for short periods; for instance, for several weeks in groundwater **[S_{trong}]**. Animal guts have stable temperatures and very low levels of oxygen and so it is of note that some strains display greater tolerance to elevated oxygen levels or extremes in temperature **[S_{trong}]**, which may aid survival outside of animal guts **[$E_{xp}O_p$]**. Persistence in the environment has also sometimes been associated with the presence of certain protozoa (some bacteria persist in the environment in the bodies of other organisms) **[L_{imited}]**. Some but not all *Campylobacter* variants may form their own biofilms (a community of cells adhering to each other and to a surface). It is possible that survival in the environment may be enhanced by attachment to existing biofilms of other species **[$E_{xp}O_p$]**.
15. Under laboratory exposure to adverse environmental conditions such as prolonged immersion in water or successive freezing-and-thawing, some *C. jejuni* may form viable but non-culturable cells (VBNC) which have low metabolic activity, do not divide, and cannot be resuscitated by conventional culturing techniques. The conditions that promote recovery from a VBNC state, and whether VBNC *Campylobacter* can cause campylobacteriosis, are not understood, and so the biological and epidemiological importance of VBNC *Campylobacter* is uncertain **[L_{imited}]**.

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16. *Campylobacter* species are genetically diverse, with new genotypes continually being identified. Genetic variation among *Campylobacter* is not continuous but tends to cluster into various distinct groups (clonal complexes) which can be identified using DNA sequencing. These clonal complexes appear stable over time and space, and some, but not all, are tightly associated with particular types of host animal **[S$_{trong}$]**.
    a. Several *Campylobacter* clonal complexes are predominantly (but not exclusively) associated with a particular host species, such as ST-257 (ST stands for sequence-type) in chickens or ST-61 in cows, but some, known as 'multi-host complexes' or 'generalist lineages', such as the ST-21 complex, are found across multiple animal host species **[S$_{trong}$]**. There is a suggestion that the intensification of beef production may have provided opportunities for the specialization of some *C. jejuni* sequence types **[L$_{imited}$]**.
    b. In general, wild bird species have their own *Campylobacter* types, and these are distinct from those found in domestic birds such as chickens and farmed ducks; however, some multi-host sequence-types are found in both poultry and wild birds **[S$_{trong}$]**.
17. Genetic attribution studies use knowledge of *Campylobacter* sequence-types that are closely associated with particular types of animals to identify the likely source of *Campylobacter* isolated from human disease cases (see box 1 in the annotated appendix). In the UK, as in other high income countries, host-associated genotyping using genetic markers has shown that the large majority (greater than 95%) of campylobacteriosis cases match *Campylobacter* genotypes that are associated with agricultural livestock. Recent attribution studies in the Netherlands and France using whole genome sequences from hundreds of isolates concluded the main sources of campylobacteriosis were from livestock (78% of cases) but that non-food sources (such as pets and water) were also a significant cause of campylobacteriosis (22% of cases). Two in three livestock cases derived from poultry and the rest from ruminants in studies from France and the Netherlands. Attribution studies using *C. jejuni* isolated from human disease cases in the UK show these predominantly involve genotypes associated with commercial poultry (average 47%, range 19–68%) and then sheep and cattle (average 38%, range 28–54%). *Campylobacter coli* causes one-tenth of human campylobacteriosis cases, but genetic attribution studies indicate these are more likely to derive from ruminants (54%), than poultry (40%) or pigs (6%) **[S$_{trong}$]**.
    a. Some chicken-related clonal complexes (such as ST-661) appear relatively abundant but cause disproportionately fewer cases of human disease than would be predicted given their prevalence. Other types (ST-21) have been reported to increase in relative abundance from farm to clinical cases **[L$_{imited}$]**. It is not yet clear if different *Campylobacter* genotypes differ in their ability to cause human disease **[E$_{xp}$O$_{p}$]**.
18. Genetic attribution studies have shown that non-agricultural animal-associated *Campylobacter* types, for example types found in wild birds, can cause human disease but at substantially lower levels (under 5% of cases) than those associated with livestock **[S$_{trong}$]**.
19. Epidemiological studies correlating disease incidence with risk factors in Europe, Australasia and the USA show both sporadic infections and outbreaks of campylobacteriosis are correlated with the consumption of poultry products such as chicken meat and chicken liver (see box 1 in the annotated appendix). Other risk factors that have frequently been identified include: contact with poultry; handling and eating raw or undercooked meat and seafood; consumption of raw milk; contact with farm animals; contact with companion animals, especially dogs; exposure to environmental water bodies (e.g. lakes); and the consumption of untreated water. The reservoir of *Campylobacter* in poultry is estimated to be responsible for between 50 and 80% of human campylobacteriosis cases **[S$_{trong}$]**.
20. International travel has also been identified as a risk factor for campylobacteriosis **[S$_{trong}$]**. One study suggested that 17–18% of recorded cases in the UK are associated with travel outside the country of residence **[L$_{imited}$]**.
21. Risk factors identified in epidemiological studies can change in importance over time and new risk factors can emerge, for instance, contact with garden soil has only recently been identified as a risk factor. There is an increasing incidence of sporadic cases of campylobacteriosis related to the consumption of unpasteurized milk in the UK and USA **[S$_{trong}$]**.
22. Epidemiological and genetic analyses of campylobacteriosis outbreaks demonstrate these mostly derive from single point sources that directly contaminate many people; human to human transmission is rare (around 3%) in outbreaks. The major risk factors associated with outbreaks are contaminated drinking water and the consumption of raw milk and chicken-liver pâté **[S$_{trong}$]**.
23. Some outbreaks of campylobacteriosis are diffuse, having a common source but not necessarily clustered geographically **[S$_{trong}$]**.
24. In surveys of fresh UK-produced whole chicken at retail outlets by the UK's Food Standards Agency (FSA), the proportion that tested positive for *Campylobacter* using standard microbiological methods dropped from 73 to 40% between 2014 and 2018 **[S$_{trong}$]**. A recent Scottish study reported an incidence of 0.1% (95% UI: 0–0.7%) on retail fresh beef mince sampled in 2019. There are no comparable recent surveys for other food products in the UK. Limited sampling of beef, pork and sheep between 2003 and 2007 in the UK found mean *Campylobacter* prevalence in the range of 0.3–16% **[L$_{imited}$]**.
25. *Campylobacter* prevalence derived from surveys of UK poultry in shops in 2017 and 2018 by the FSA (see paragraph 24) allows the prediction that exposure to as little as 10 g of even the lowest contaminated UK retail poultry samples may be sufficient to cause campylobacteriosis, if food is not cooked sufficiently or if food preparation hygiene is poor, as this represents a few hundred *Campylobacter* cells (see paragraph 3) **[L$_{imited}$]**.
26. Retail surveys in the USA indicate that around 20% of poultry breast meat was positive for *Campylobacter* in 2018, but differences in sampling methods mean this cannot be meaningfully compared the UK retail survey data.

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27. **Summary:** attribution studies, together with risk exposure information based on food surveys, consistently identify meat products as substantial risks for campylobacteriosis. The majority of human *Campylobacter* infections are *C. jejuni* and result from contact with livestock or consumption of meat, with poultry being the most important source followed by ruminant meat. Cases of campylobacteriosis in the UK remain constant despite a decreasing prevalence of *Campylobacter* on poultry in retail outlets.

(d) How *Campylobacter* is transmitted between animals in agriculture

Commercial poultry

28. In domesticated poultry, *Campylobacter* is commonly considered a commensal (i.e. it causes no harm to the host), but in some circumstances, it may act as an opportunistic pathogen **[L_{imited}]**.
    a. In commercial rearing facilities, most infections with *Campylobacter* result in no obvious signs of disease in chickens. Statistically significant relationships between *Campylobacter* infection of broiler flocks and broiler health and welfare markers such as the presence of digital dermatitis and body weight have been recorded in a limited number of commercial operations in the UK **[L_{imited}]**. The direction of causality these limited studies is unclear: birds with poor health and welfare may be more susceptible to *Campylobacter* infections, but generally, flocks with both poor and good welfare are infected with *Campylobacter* **[$E_{xp}O_p$]**.
    b. Stress and immunosuppression in chickens may increase the capacity of *Campylobacter* to move beyond the gut and invade tissues such as muscle and liver **[L_{imited}]**.
29. Once introduced into a population of chickens in a broiler unit, *Campylobacter* spreads rapidly via the faecal–oral route and virtually all animals become infected within a week **[S_{trong}]**.
30. Broiler poultry do not have contact with their parents after hatching. Vertical transmission from breeder to broiler chickens via eggs both internally and from external contamination has been excluded as a major transmission route because live *Campylobacter* has not been detected in eggs or in chicks under 1 week old. However, the increasing sensitivity of sampling and detection methods, including genetic approaches, suggests vertical transmission may occur rarely (at less than 1 in 60 000 chicks) **[L_{imited}]**.
31. Epidemiological investigations have attempted to identify risk factors correlated with the infection of flocks in poultry units. This is difficult due to problems with identifying causality, correlation of risk factors, and considerable farm to farm variability **[$E_{xp}O_p$].** The most implicated risk factors are:
    a. Poor biosecurity (procedures designed to prevent the introduction and spread of disease-causing organisms), including close proximity of other animals (livestock, pets and rodents), partial depopulation (thinning), and poor poultry welfare correlate with *Campylobacter* infections. However, the presence of *Campylobacter per se* is not an indicator of poor welfare **[S_{trong}]**.
    b. There is some evidence that the use of untreated drinking water for poultry is a risk factor **[L_{imited}]**.
    c. Flies and other insects are able to vector *Campylobacter* **[S_{trong}]**. The presence of insects is identified as a risk factor in some, but not all, surveys **[L_{imited}]**.
32. *Campylobacter* can be found in the environment around poultry houses, both before and after a cohort of birds is introduced. The genetic types of *Campylobacter* isolated from the environment surrounding houses are often identical to those found in infected flocks. Similarly, *Campylobacter* types in feed distribution and storage systems, litter, transport crates and external or internal drinking water sources are often the same as those in infected chickens **[S_{trong}]**. The epidemiological interpretation of these observations is difficult as the direction of transfer (flock to environment or environment to flock) is typically not known **[$E_{xp}O_p$]**.
33. Several studies have shown that inadequate cleaning and disinfection between successive flocks in a poultry house is correlated with subsequent *Campylobacter* infection. These studies are unable to show directly if previous flocks or the house/farm generally were the original source of infection **[L_{imited}]**.
34. There is evidence that employees entering and moving between different poultry sheds (for example to remove particular birds) is correlated with higher levels of *Campylobacter* infection **[S_{trong}]**.
35. The preparation and transport of flocks to slaughterhouses increases the risk of *Campylobacter* transmission from catching crews, and between farms via transportation equipment such as crates, in some but not all studies **[L_{imited}]**.
36. Organic and free-range systems where birds have outdoor access are at a greater risk of *Campylobacter* infection than intensively reared flocks (permanently in sheds), and molecular typing studies suggest contamination was from wild birds and other livestock **[S_{trong}]**. However, there is no clear evidence as to whether this translates to differences in contamination levels on retail poultry products **[L_{imited}]**. Slower growing free-range or organic flocks are usually slaughtered when 63–81 days old versus 35–42 days for conventionally reared flocks. Age of birds at slaughter in short-lived broilers is a frequently identified risk factor for flock contamination **[S_{trong}]**, presumably because living longer increases the chances of infection.

Commercial pigs and cattle

37. Evidence for the origin and transmission of *Campylobacter* in pigs and cattle is limited.
38. Pigs are infected with *Campylobacter*, especially *C. coli*, from other herd members less than a week after birth, and prevalence increases through the production cycle from 0% at birth, 33 to 48% 1-week post-birth and 67–96% in finishing pigs around six months old **[S_{trong}]**.
39. Pigs are typically asymptomatic *Campylobacter* carriers but there is some evidence of an association of infection with post-weaning diarrhoea and lower back-fat and weight gain **[L_{imited}]**.
40. *Campylobacter*, especially *C. jejuni*, are found in healthy ruminants, and are easily passed between herd members

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via the faecal–oral route. The *Campylobacter* prevalence in sheep and cattle in the UK is poorly characterized **[L$_{imited}$]**.

41. *Campylobacter* infection in ruminants is associated with higher incidence of abortions **[S$_{trong}$]**.
42. **Summary:** *Campylobacter* is found in a range of livestock species and their associated habitats. Pigs and ruminants are likely infected with bacteria from herd members. Broiler poultry chicks are unlikely infected by bacteria from their parents and there is very limited evidence to understand the sources of poultry infection. In broiler poultry, poor flock health and poor house biosecurity are correlated with increased *Campylobacter* infection making it hard to disentangle the cause of infections. Records of *Campylobacter* prevalence in livestock other than poultry are poor.

(e) Food chain interventions to control levels of *Campylobacter* on retail produce

On-farm interventions

43. In a typical broiler chicken operation, some birds are harvested at around 35 days (partial depopulation) and then the majority of birds harvested at 42 days. In a large field trial in the UK, flocks with enhanced biosecurity interventions were 25 and 50% less likely to be infected with *Campylobacter* at partial and final depopulation, respectively **[S$_{trong}$]**.
    a. Chlorination and/or the acidification of drinking water may reduce *Campylobacter* levels in poultry digestive tracts on farms, but the effect is inconsistent across studies **[L$_{imited}$]**. No consistently positive effects have been found on *Campylobacter* levels from the provision of chicken feed additives, including microbial probiotics, organic and fatty acids, and essential oils. How *Campylobacter* behaves in the gut and its interaction with the rest of the gut microbiome is not well understood **[L$_{imited}$]**.
44. No commercial vaccine currently exists for the prevention of enteric *Campylobacter* infection in animals. There is not a good understanding of the antigens that confer immunity to *Campylobacter* in chickens but these appear strain-specific **[L$_{imited}$]** which makes the production of a general vaccine challenging though this is an area of active research.
45. There are no studies that have systematically evaluated the effect of interventions relating to transport and holding practices of livestock, including poultry, on the public health risk of *Campylobacter* **[E$_{xp}$O$_p$]**.
46. There are no studies that have systematically evaluated the effect of on-farm interventions on *Campylobacter* prevalence in ruminants or pigs **[E$_{xp}$O$_p$]**.

Processing interventions

47. *Campylobacter* resides in the intestines of live animals and can be spread to carcasses during post-slaughter evisceration. The majority of available data on the effects of processing on *Campylobacter* contamination are derived from poultry, and there is little information for other livestock species.
48. A number of analyses show a positive flock-level association between the prevalence of *Campylobacter* in broiler chicken intestines (particularly caeca) and the frequency of *Campylobacter*-contaminated carcasses post-slaughter **[S$_{trong}$]**.
49. For poultry, carcass contamination is primarily found on the neck skin as evisceration occurs through the neck and carcasses are subsequently hung upside down. *Campylobacter* is found at the same rates in chicken livers as on neck skins. Where *Campylobacter* is present in a flock, contamination may be found in breast meat in around 5–10% of *Campylobacter* positive carcasses. There is less evidence about the distribution of *Campylobacter* prevalence on other animal carcasses, but meat from larger ruminants is usually sold pre-portioned or processed and infrequently includes skin tissue **[L$_{imited}$]**.
50. The nature of poultry carcass processing procedures can affect the extent of *Campylobacter* spread over carcasses. For example, there is some evidence that visceral rupture can increase *Campylobacter* contamination across the whole carcasses by up to 10-fold **[L$_{imited}$]**. Attention to processing details, such as ensuring the correct settings on machines for the size of the bird, has the potential to reduce the spread of contamination **[E$_{xp}$O$_p$]**.
51. Methods where the carcass outer surface is frozen without freezing muscle may reduce *Campylobacter* levels with reductions by forced air chilling of one-half and crust freezing up to 30-fold **[L$_{imited}$]**.
52. Heat treatment of poultry carcasses by steam or water-dipping can reduce *Campylobacter* loads by 10- to 100-fold; but hot water baths may serve as a reservoir for contamination if the temperature is not maintained or hygiene is otherwise poor. Combined steam and ultrasound treatments can reduce *Campylobacter* carcass loads by 300-fold **[L$_{imited}$]**. Heat treatments need to be very carefully monitored to avoid part-cooking **[E$_{xp}$O$_p$]**.
53. The application of chlorine and other chemical rinses such as peracetic acid can achieve 10- to 100-fold reductions in levels of *Campylobacter* on poultry carcasses **[S$_{trong}$]**. However, there is no clear evidence that extensive and long-term use of chlorine rinses in other countries (such as the USA) has resulted in lower levels of *Campylobacter* prevalence on raw poultry or rates of campylobacteriosis compared to European countries where the use of chlorine is banned **[P$_{roj}$]**. Concerns have been raised about the introduction of chemicals to the food-chain, and that the use of rinses may lead to a false sense of security and the relaxation of biosecurity on farms **[E$_{xp}$O$_p$]**.
54. Irradiation and UV-light exposure can reduce poultry *Campylobacter* loads by 5- to 10-fold **[S$_{trong}$]**. These treatments are demanding of space, time and energy and require workers to be protected from accidental exposure **[E$_{xp}$O$_p$]**.
55. Processing interventions focusing on the external surface of carcasses (chemical rinses, crust freezing or chilling, heat treatment and irradiation) address risks associated with carcass surface contamination, but not internal contamination such as of viscera. Such treatments may also affect customers' perception of the freshness of the product and hence sales **[E$_{xp}$O$_p$]**.
56. Freezing the entire carcass can reduce *Campylobacter* levels on poultry by approximately 30-fold and the

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freezing of livers can lead to a 100-fold drop **[L_{imited}]**. Implementation of a carcass freezing policy together with a national surveillance programme was considered a critical part of the control of epidemic campylobacteriosis in Iceland **[$E_{xp}O_p$]**.

57. Levels of *Campylobacter* on chicken products decrease after packing and during chilled shelf life **[S_{trong}]**.
    a. Experimental studies show packaging chicken under controlled atmospheres (particularly high levels of O_2 with mixes of N_2 and CO_2), especially in conjunction with reduced temperatures, can reduce *Campylobacter* loads by 100- to 10 000-fold **[L_{imited}]**.
    b. Roast-in-the bag packaging was introduced in the UK to reduce the risk of cross-contamination in the household. Packing interventions were part of the combination of interventions which contributed to the reduction of epidemic disease in Iceland **[P_{roj}]**.
58. Some evidence shows *Campylobacter* may be reduced to undetectable levels on the surfaces of pork carcasses with the use of blast-chilling **[L_{imited}]**. Specific interventions to control *Campylobacter* on beef are not implemented due to the assumption that measures targeted at other microbiological hazards will also control *Campylobacter*, though this has not been tested **[$E_{xp}O_p$]**.
59. Milk pasteurization is effective at controlling *Campylobacter*, which can be inferred by the association of campylobacteriosis only with the consumption of unpasteurized raw milk (or when pasteurization fails) **[P_{roj}]**.

Interventions aimed at consumers

60. Surveys indicate that consumers believe risks in domestic environments are small and awareness of *Campylobacter* risks is low relative to other foodborne diseases **[L_{imited}]**; however, the majority of sporadic cases of campylobacteriosis are associated with food prepared and consumed at home **[L_{imited}]**. Cross-contamination from fresh chicken meat to other foods via hands and food preparation equipment is the main route of human exposure **[L_{imited}]**. Washing raw chicken, a common practice among older consumers, is thought to be a risk factor for cross-contamination **[$E_{xp}O_p$]**. The consumption of raw milk and undercooked chicken livers is also a known risk factor for illness and is implicated in outbreaks **[S_{trong}]** but it is not clear the degree to which this is understood by the general public in the UK **[$E_{xp}O_p$]**.
61. Research into human vaccines, particularly for overseas travellers and the military, is underway. Several candidates have been tested on humans but none have to date conferred sufficient protection **[L_{imited}]**.

Coordinated interventions

62. Coordinated national campaigns in the UK, Iceland and New Zealand, implementing a range of voluntary and regulatory interventions across the production chain from farm to consumer education, have resulted in reductions in rates of *Campylobacter* on poultry and/or campylobacteriosis. The precise drivers for decreases are not easy to disentangle as many changes were applied together.
63. Following a spike in campylobacteriosis in the late 1990s, peaking at 118.2 laboratory reported incidences per 100 000 in 1999, Iceland implemented a series of control measures including enhanced surveillance, increased biosecurity, changes in poultry processing and consumer education. Rates of campylobacteriosis fell to an average of 20.5 incidences per 100 000 in the period 2002–2007 **[S_{trong}]**. While it is not possible precisely to identify the most effective intervention, freezing meat from *Campylobacter*-positive flocks prior to sale was thought to be the most important **[$E_{xp}O_p$]**.
64. Before 2006, New Zealand had high rates of campylobacteriosis compared with other high income countries, peaking at 396 reported cases per 100 000 population in 2003. In 2006, a range of voluntary and regulatory interventions targeted at all levels from the farm to consumer education were implemented and levels of campylobacteriosis dropped 54% by 2008 **[S_{trong}]**. Monitoring and reporting of *Campylobacter* levels on chicken carcasses, and the setting of mandatory performance targets, were considered to be the most important interventions **[$E_{xp}O_p$]**.
65. **Summary**: On-farm enhanced biosecurity interventions can correlate with lower levels of *Campylobacter* on poultry. There is no single poultry processing intervention that provides perfect control of *Campylobacter*, but a combination of the use of cold or heat carcass treatments, and better packaging may reduce overall *Campylobacter* levels on retail poultry, although the evidence base on the efficacy of particular treatments is limited. There is a lack of evidence for how multiple on-farm and processing interventions may interact in terms of *Campylobacter* control. There is a lack of evidence for the value of on-farm and processing interventions for non-poultry livestock.

(f) Antimicrobial resistance

66. *Campylobacter* can acquire antimicrobial resistance through a number of mechanisms, including novel mutations and the acquisition of resistance genes via horizontal gene transfer from other bacteria **[S_{trong}]**.
67. Antimicrobial drugs are used in poultry production to prevent and treat a wide range of bacterial diseases. Poultry are not treated for *Campylobacter* directly, but *Campylobacter* in the poultry caeca and gut will be exposed to any antimicrobials administered. Poultry medications, including antimicrobials, are usually given at the flock level via feed or drinking water **[S_{trong}]**.
68. The most commonly used antimicrobials to treat disease in UK poultry production are fluoroquinolones, followed by penicillin. As a response to concerns over antimicrobial resistance, and a halt in the use of antibiotics as growth promoters in 2006, overall antimicrobial use in the UK poultry industry declined 80% from 2013 to 2017 **[S_{trong}]**.
69. Globally, antimicrobial resistance in *C. jejuni* and *C. coli* has increased in recent years in both human and animal isolates, with high levels of resistance to fluoroquinolones and macrolides and emerging resistance to aminoglycosides. There is increasing evidence for resistance to other antimicrobials and the emergence of multidrug resistant strains **[S_{trong}]**.

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70. Over time, antimicrobial use in the poultry industry is correlated with antimicrobial-resistant *Campylobacter* in humans. There has been a steep and sustained rise in the incidence of disease caused by fluoroquinolone-resistant *Campylobacter* in the UK from 1997 onwards **[S_{trong}]**. The proportion of *Campylobacter* resistant to antimicrobials is greater on farms which use antimicrobials than those which do not **[S_{trong}]**.
71. *Campylobacter* readily acquires resistance to fluoroquinolones via simple genetic mutations, and resistance is not lost even if fluoroquinolones are withdrawn as resistant types have an advantage over non-resistance types **[S_{trong}]**.
72. Resistant infections are disproportionally associated with international travel **[S_{trong}]**, presumably to areas where antibiotics are more commonly used in livestock and humans **[$E_{xp}O_p$]**.
73. Routine antimicrobial treatment of individuals with campylobacteriosis is not usually recommended, as antibiotics only shorten the duration of disease by an average of 1.3 days **[S_{trong}]**. Antimicrobials are recommended in severe cases, typically immunocompromised patients or young children.
    a. People infected with resistant *Campylobacter* may experience illness that is prolonged and more severe than those infected with sensitive strains **[L_{imited}]**. It is not clear whether resistant strains tend to possess additional virulence factors.
    b. Fluoroquinolone-resistant *Campylobacter* is designated by the WHO as a 'high priority' pathogen for new antibiotic research and development.
    c. In the USA, one quarter (23%) of *Campylobacter* isolates were reported to be resistant to fluoroquinolones, and these were associated with approximately half of the 65 deaths per year involving *Campylobacter* in 2013.
74. There is no current evidence that antimicrobial-resistant strains of *Campylobacter* behave differently in the food chain relative to non-resistant strains in terms of their sensitivity to control interventions **[$E_{xp}O_p$]**.
75. **Summary:** the use of fluoroquinolones in poultry production has been consistently associated with the level of resistance in *Campylobacter* isolates from poultry and human cases, and the prevalence of fluoroquinolone resistance in poultry and human derived isolates are both increasing despite the reduction in use of antibiotics for livestock in the UK.

References

1. Advisory Committee on the Microbiological Safety of Food. 2019 *Third report on campylobacter*. London, UK: Food Standards Agency.
2. EFSA Panel on Biological Hazards. 2011 Scientific Opinion on *Campylobacter* in broiler meat production: control options and performance objectives and/or targets at different stages of the food chain. *EFSA J.* **9**, 2105. (doi:10.2903/j.efsa.2011.2105)
3. Daniel N, Casadevall N, Sun P, Sugden D, Aldin V. 2020 *The burden of foodborne disease in the UK 2018*. London, UK: Analytics Unit, Food Standards Agency and London School of Hygiene and Tropical Medicine.
4. Jorgensen F, Charlett A, Arnold E, Swift C, Corcionivoschi N. 2019 Year 4 Report. A microbiological survey of *Campylobacter* contamination in fresh whole UK-produced chilled chickens at retail sale. (Public Health England).
5. University of Oxford. 2021 *Enhanced molecular-based surveillance and source attribution of campylobacter infections in the UK*. London, UK: Food Standards Agency.
6. DEFRA. 2021 Poultry and poultry meat statistics. See https://www.gov.uk/government/collections/poultry-and-poultry-meat-statistics.
7. Mughini-Gras L *et al.* 2021 Sources and transmission routes of campylobacteriosis: a combined analysis of genome and exposure data. *J. Infect.* **82**, 216–226. (doi:10.1016/j.jinf.2020.09.039)
8. Goddard MR *et al.* 2022 A restatement of the natural science evidence base regarding the source, spread and control of *Campylobacter* species causing human disease. Figshare. (doi:10.6084/m9.figshare.c.6011721)

A restatement of the natural science evidence base regarding the source, spread and control of *Campylobacter* species causing human disease

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Annotated Bibliography

(A) Aims and scope

AB1. WHO (2013), Kirk *et al.* (2015). The incidence figure is from Tam *et al.* (2012a), Tam *et al.* (2012b). The estimate for financial burden on the UK economy is from Tam and O'Brien (2016), who calculate annual median costs to patients and the health service of £50 millions (95% CI: £33 to £75 millions), with costs per case of approximately £85. Also see O'Brien (2017). The UK Food Standards Agency (FSA) estimate of the full social cost of *Campylobacter*, which includes both financial (medical and personal costs) and monetary estimates of its non-financial impacts (pain, grief and suffering) at £712.6 millions (median; 95% CI £298.5 to £1,355.8 millions) in 2018 (Daniel *et al.* 2020).

AB2. Codes used in previous Restatements provided in McLean *et al.* (2017), Dadson *et al.* (2017), Godfray *et al.* (2015), Godfray *et al.* (2014), Godfray *et al.* (2013), Godfray *et al.* (2019). We use the World Bank countries classification categories which are based on quantitative measures: low income; lower-middle income; upper-middle income and high income (https://blogs.worldbank.org/opendata/new-world-bank-country-classifications-income-level-2021-2022).

(B) *Campylobacter* disease in humans

AB3. See Man (2011). There is abundant correlational data showing the presence of *Campylobacter jejuni* and *Campylobacter coli* in faeces of patients presenting with diarrhoea and gastroenteritis globally, e.g. Oberhelman *et al.* (2003), Tam *et al.* (2012b), Lajhar *et al.* (2015), Friedrich *et al.* (2016), Kovanen *et al.* (2016), Ohishi *et al.* (2017) with the absence of other known pathogens. The deliberate ingestion of between 10^2 and 10^9 *C. jejuni* cells by 111 young adults shows a relationship between intestinal infection and diarrhoea, abdominal cramps, anorexia and fever (Black *et al.* 1988). Also see Robinson (1981).

Dose response models and self-feeding trials have suggested that the infective dose for *Campylobacter* is very low, with the ID_{50} (the dose at which 50% of exposed individuals become infected) estimated at 900 cells (Medema *et al.* 1996; Teunis *et al.* 2005). An association between dose and occurrence of disease has been observed by Tribble *et al.* (2010). Dose-response relationships between risk of disease and quantity of food product consumed may exist (Edwards *et al.* 2014).

Individuals with pre-existing conditions or who are immunocompromised have greater susceptibility to disease and also tend to suffer prolonged and more severe clinical symptoms, which may be recurrent (van der Meer *et al.* 1986; Helms *et al.* 2003; Janssen *et al.* 2008; Bloomfield *et al.* 2017).

AB4. The genus *Campylobacter* is estimated to comprise up to 56 species and 16 subspecies according to The List of Prokaryotic names with Standing in Nomenclature (https://lpsn.dsmz.de), with this number likely to grow with increasing amounts of genomic data, but unless otherwise stated, we use '*Campylobacter*' to refer to *C. jejuni* and *C. coli* only as these are the major causes of human campylobacteriosis (gastroenteritis caused by *Campylobacter*; Sheppard *et al.* 2009b; Gillespie *et al.* 2002; Mossong *et al.* 2016). A 2005 – 2006 study in Scotland reported that approximately 10% of *Campylobacter* isolates from human stool samples were *C. coli*, with the remaining 90% being *C. jejuni* (Sheppard *et al.* 2009b); surveillance in England and Wales reported that *C. jejuni* was associated with 93% campylobacteriosis cases compared to 7% for *C. coli* (Gillespie *et al.* 2002); and a similar proportion was reported from Luxembourg (Mossong *et al.* 2016).

AB5. Nichols *et al.* (2012) analysed over a million *Campylobacter* cases from England and Wales between 1989 and 2011, which showed spikes in incidence in sub-five year olds and in those aged 20-30, and that cases in over 50 year olds were rising, and there were elevated death rates in those over 60. Also see Gillespie *et al.* (2009), Gillespie *et al.* (2008), Ang *et al.* (2011), Moffatt *et al.* (2017). Epidemiological data from low income and lower- and upper-middle income countries (LMIC) are relatively scarce, but *Campylobacter* is considered to be endemic in these countries. *Campylobacter* is one of the most common pathogens found in children with diarrhoea in low income and LMIC (Coker *et al.* 2002). A large longitudinal birth cohort study covering eight low-resource settings demonstrated that 85% of children (n=1606) tested positive for *Campylobacter* by age 1 (Amour *et al.* 2016). Symptoms of campylobacteriosis are inversely related to age in LMIC (Rao *et al.* 2001; Coker *et al.* 2002), and other studies provide some evidence of acquired immunity against *Campylobacter* in older age-groups from regions with LMIC (Havelaar *et al.* 2009).

AB6. Kaakoush *et al.* (2015). See Wagenaar *et al.* (2013) on global under-reporting issues. Trend analyses for *Campylobacter* are problematic due to low volumes of food and animal monitoring data, costs of seeking medical advice in countries with no state funded medical care, and unharmonised sampling and reporting rules between countries (EFSA and ECDC (2018)). The incidence of campylobacteriosis in low income countries is particularly hard to ascertain WHO (2013). Based on WHO 2010 figures, worldwide there were approximately 166 million (95% uncertainty interval (UI) 95-300 million) cases of *Campylobacter* infections causing 37,600 (27,700-55,000) deaths, with 58% of these (96 million cases and 21,374 deaths) allocated (via a process of structured expert elicitation) to foodborne transmission routes (Hald *et al.* 2016; Havelaar *et al.* 2015; Kirk *et al.* 2015). 2018 USA data from Tack *et al.* (2019). In a large longitudinal study of *Campylobacter* infection in the first two years of life in eight low-resource settings, a high *Campylobacter* burden was associated with a lower length-for-age Z score at 24 months (-1.82; 95% confidence interval, -1.94 to -1.70) compared with a low burden (-1.49; -1.60 to -1.38) (Amour *et al.* 2016).

AB7. For European data see The European Union One Health 2019 and 2020 Zoonoses Report. The UK has among the greatest rates of campylobacteriosis, ranked 4th or 5th highest, in Europe between 2015-2019 (Figure 1). UK rates of campylobacteriosis show no clear trend for change from 2006 to 2017 (FSA Project FS102121 4th year report) and have a mean of 101 (standard deviation ± 9.4) cases per 100,000. No range was given for these data.

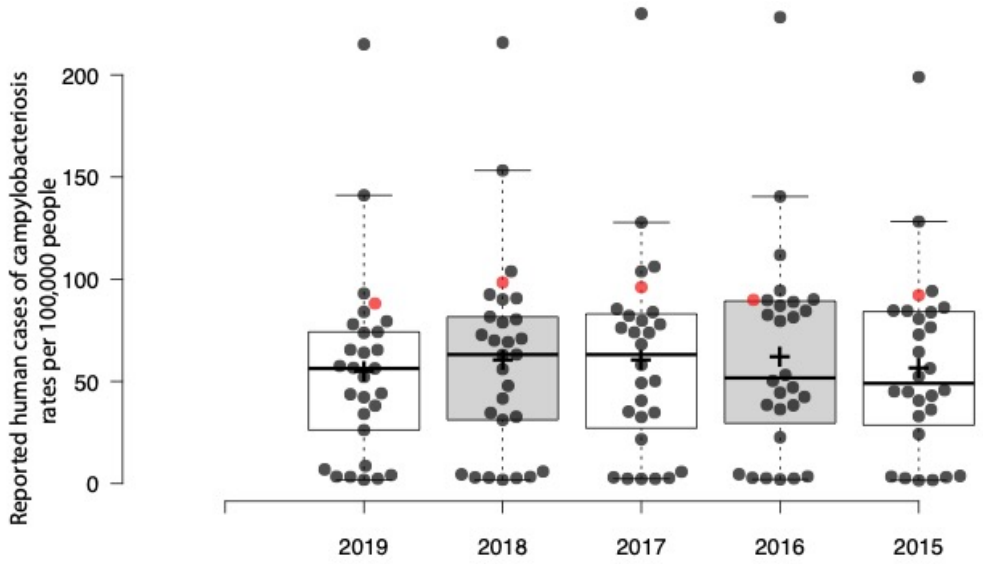

Figure 1 Box and whisker plots showing the rates of reported campylobacteriosis per 100,000 people across 29 countries in Europe from 2015 to 2019. A data point is shown for each country with the UK shown as a red data point. Crosses show the mean of rates for each year, solid lines the median, box limits indicate the 25th and 75th percentiles, and whiskers extend 1.5 times the interquartile range from the 25th and 75th percentiles. Data are from Table 4 in The European Union One Health 2019 Zoonoses Report and can be obtained from https://zenodo.org/record/4298993#.YZTE6S-l1qs. One 2018 estimate from the USA is a campylobacteriosis incidence of 20 per 100,000, but this is likely an underestimate due to people not presenting to healthcare professional due to cost implications Tack *et al.* (2019).

a. A population-based prospective cohort study and a prospective study of presentations to primary care estimated the amount of un-reported cases in the UK to be around 9 times those of reported (Tam *et al.* 2012a; Tam *et al.* 2012b) (9.3, 95% CI, 6 – 14.3). There are various estimates that extrapolate from reported cases for the extent of disease burden caused by *Campylobacter* in the UK. O'Brien *et al.* (2016) estimated *Campylobacter* to be the largest cause of food poisoning cases in the UK, underlying 36%-85% of cases, resulting in 38,860 (95% CI 27,160 – 55,610) GP consultations and 562 (189-1330) hospital admissions in 2009. The figures quoted in the main appendix are from updated estimates from the UK in 2018 (Holland and Mahmoudzadeh, 2020). Another study, based on reported cases of returning Swedish travellers, estimated the UK underreporting factor for campylobacteriosis to be 4.4 (95% CI 1.3 to 11), with a EU-wide underreporting factor of 46.7 (95% 14.1 to 117) (Havelaar *et al.* 2013).

b. Estimates of hospitalisation are from the IID2 updated reported estimates from the UK in 2018 (Holland and Mahmoudzadeh, 2020) and death rates are from an FSA and FSS report by Rigby *et al.* (2017), and Nichols *et al.* (2012) estimated that 82 deaths were attributed to *Campylobacter* between 1989 and 2009 in the UK, and Holland *et al.* (2020) estimate that foodborne *Campylobacter* was involved in 21 UK deaths in 2019 (95% confidence limits of 8 to 47). Deaths due to Influenza estimates are from the UK Office for National Statistics (https://www.ons.gov.uk/aboutus/transparencyandgovernance/freedomofinformationfoi/influenzadeathsin20182019and2020). The precise number of UK deaths due to *Campylobacter* is uncertain due to under-reporting and misdiagnosis.

c. The QALY estimate comes from an FSA and FSS report by Rigby *et al.* and the 95% confidence limits around the mean probabilistic burden of 69,108 QALYs are from 39,284 to 108,238. Influenza QALYs losses are from https://yhec.co.uk/wp-content/uploads/2020/12/economic-modelling-report-pdf-6532084909.pdf. Norovirus estimate are from a FSA Report by Daniel *et al.* (2020).

AB8. The majority of clinical *Campylobacter* cases are thought to be sporadic, and outbreaks from a single source are considered rare (Wilson *et al.* 2008; Tam *et al.* 2012b; EFSA and ECDC 2018; Rotariu *et al.* 2010). Household outbreaks where infection is caused by a single genotype do occur, accounting for between 3-5% of infections in Denmark, Wales and Scotland (Ribeiro and Frost 2000; Ethelberg *et al.* 2004; Rotariu *et al.* 2010). Since co-infection with more than one *Campylobacter* strain has been identified in 5-10% of apparently sporadic cases, estimates of household outbreaks may be conservative (Richardson *et al.* 2001; Frost *et al.* 2002). The number of reported outbreaks in the UK between 2006 and 2016 has ranged between 5 and 22 per year (Advisory Committee on the Microbiological Safety of Food, 2019). Over 4% of all foodborne outbreaks between 1992 and 1998 were due to *Campylobacter* (Gormley *et al.* 2011). Under the national food distribution system, some outbreaks may be recorded erroneously as a series of single source cases (Colles and Maiden 2012). On the Havelock North outbreak see Gilpin (2016).

AB9. In temperate or high income countries, there is a strong seasonal signal for *Campylobacter* incidence (Nylen *et al.* 2002; Kovats *et al.* 2005; Lal *et al.* 2012). In the UK, there is an increased rate of human disease between May and June (Nichols *et al.* 2012) and a linear relationship between ambient temperature and the number of reported *Campylobacter* infections, with a 1 °C rise corresponding to a 5% increase in reports, up to a threshold of 14 °C (Tam *et al.* 2006b). In the UK, seasonal variation appears to be more marked in rural than urban areas (particularly in London), and more marked in children less than five years old than adults (Nichols *et al.* 2012; Louis *et al.* 2005). Kovats *et al.* (2005) reported a correlation between both mean winter and mean spring temperature with peak *Campylobacter* cases across 15 countries. However, an Australian study (Bi *et al.* 2008) investigating seasonality of *Campylobacter* infections found temperature (and humidity) was differentially correlated between two cities and thus showed no trend. Comparisons of genotypes in the United Kingdom (McCarthy *et al.* 2012) and in New Zealand (Hudson *et al.* 199;, Friedrich *et al.* 2016) found that ST-45 complex isolates from both geographical regions increased as a cause of human disease during summer months. Other clonal complexes also appear to be prevalent at different times of year (Colles and Maiden 2012).

No one factor has been identified as driving this seasonal pattern but multiple, often confounding, hypotheses have been put forward, including: changes in human behaviour (Studahl and Andersson 2000); outdoor activity and barbequing (Kovats *et al.* 2005); presence of disease vectors (*e.g.* flies (Nichols 2005); changes in animal behaviour (*e.g.* foraging (Kovats *et al.* 2005); livestock pathogen loads (*Campylobacter* infections in chicken flocks are more common in summer (Jorgensen *et al.* 2011); and, warmer summer temperatures facilitating bacterial population growth. All such hypotheses will have varying relevance for different countries.

AB10. Long-term sequelae of *Campylobacter* infection (e.g. Guillain-Barré syndrome (GBS) http://www.nhs.uk/conditions/Guillain-Barre-syndrome/Pages/Introduction.aspx, reactive arthritis (RA) http://www.nhs.uk/conditions/Reactive-arthritis/Pages/Introduction.aspx, and post-infectious irritable bowel syndrome (IBS) https://aboutibs.org/what-is-ibs-sidenav/post-infectious-ibs.html) contribute considerably to disease burden, reviewed by O'Brien (2017). The incidence of GBS in a large cohort of patients with *Campylobacter* has been estimated at 1.17 per 1000 person-years, a rate 77 times greater than that in the general population (Tam *et al.* 2006a). A meta-analysis of studies published before July 2011 (Keithlin *et al.* 2014) reported that 0.07% (95% CI 0.03-0.15%) of *Campylobacter* cases develop GBS compared with 2.86% (95% CI 1.40-5.61%) and 4.01% (95% CI 1.41-10.88%) for RA and IBS. There was a high degree of heterogeneity among studies meaning that caution with interpretation is needed. A similar meta-analysis stated that the level of heterogeneity across studies was too high to determine a pooled figure (Esan *et al.* 2017). A high proportion of patients with the above conditions are seropositive for *Campylobacter* (Zautner *et al.* 2014) (IBS 23-40%; RA 44-62% and GBS 34-49%). In data derived from Swedish reporting systems from 1987-1995 the incidence of GBS following *C. jejuni* infection was 30.4 cases per 100,000 cases of infection (McCarthy and Giesecke 2001). A systematic review on *Campylobacter*-associated RA suggested that the incidence of RA after *Campylobacter* is 4.3 per 100,000 population (Pope *et al.* 2007). A US matched cohort study (2010-2014) found an incidence rate of IBS in people diagnosed with a *Campylobacter* infection of 33.1 per 1,000 versus 5.9 per 1,000 for non-cases, with an unadjusted risk ratio of 5.6 (95% CI: 4.3-7.3) (Scallan Walter *et al.* 2019). A meta-analysis of IBS pooled prevalence following

Campylobacter infection calculated an incidence of 12% (CI 10-15%). Peters *et al.* (2021) shows particular C. jejuni genotypes are associated with IBS.

AB11. Author's summary.

(C) How humans become infected with *Campylobacter*

AB12. *Campylobacter* have been isolated widely from the intestines and faeces of wild birds and animals across the globe (Benskin *et al.* 2009), livestock (cattle, sheep, poultry, and pigs) (Milnes *et al.* 2008; Wilson *et al.* 2008) and pets (Ramonaite *et al.* 2014). In chickens, *C jejuni* primarily colonises the caeca at the distal end of the gastro-intestinal tract (Sakaridis *et al.* 2018). The optimal limited oxygen and temperature conditions for *Campylobacter* growth in the laboratory are similar to the avian intestine (Young *et al.* 2007). Various studies examining livestock species in different places with varying culture methods report that between 20 and 90% of pigs, cattle, sheep and poultry harbour *Campylobacter* (Stanley and Jones 2003; Milnes *et al.* 2008; Baer *et al.* 2013; Ellis-Iversen *et al.* 2009; Rushton *et al.* 2009; Georgiev *et al.* 2017). Similarly, the prevalence of *Campylobacter* in wild birds varies greatly according to species and geographic regions (Hughes *et al.* 2009). Up to 50% of European and US wild birds harbour *Campylobacter*, predominantly *C. jejuni* (Ramonaite *et al.* 2014; Taff *et al.* 2016). The pubmlst.org/campylobacter database (accessed September 2021) had combined 2,543 wild bird isolate records of which only 126 belonged to *C. coli*.

AB13. A majority of isolates from environmental sources are attributable to animal sources (Ogden *et al.* 2009), and environmental isolates of *Campylobacter* (from water, soil, etc.) may represent bacteria shed from animals that survive for some unknown period of time.

AB14. Survival outside the host has been reported (Park 2002), with survival supported by lower temperatures (4-10 °C), darkness, and a moist atmosphere (Smith *et al.* 2016a; Smith *et al.* 2016b). *C. jejuni* strains can survive in chicken faeces for up to 6 days after excretion (Ahmed *et al.* 2013). *Campylobacter* can survive for several weeks in groundwater (Buswell *et al.* 1998) and for several months in slurries and dirty water (Nicholson *et al.* 2005). Recent data show some *Campylobacter* appear to have greater tolerance to higher levels of oxygen than others. Oxygen tolerant strains of *C. jejuni* are reported as highly prevalent in retail poultry meat, and survive longer than 24 hours (Oh *et al.* 2015; Oh *et al.* 2017). Oh *et al.* (2017) reported hyper-aerotolerant *C. jejuni* strains showing five-fold reduction times in raw poultry of over two weeks compared to 3 days for aero-sensitive strains. There is a potential association between hyper-aerotolerance and other characteristics such as invasion capability (Mihaljevic *et al.* 2007) or association with human disease (Oh *et al.* 2017). *C. jejuni* may survive for up to three days outside an animal digestive tract housed within larger microbes such as protozoa (Hilbert *et al.* 2010; Vieira *et al.* 2015) or for over a week in biofilms (Trachoo *et al.* 2002; Hanning *et al.* 2009; Teh *et al.* 2014). Biofilm formation has been observed for some *C. jejuni* sequence types, but not all (Garcia-Sanchez *et al.* 2019).

AB15. For a discussion of the current understanding of VNC conditions see section 1.27 of Advisory Committee on the Microbiological Safety of Food 3rd report on *Campylobacter* (2019).

AB16. Genetic sequencing studies have shown that *Campylobacter* are very diverse throughout their genomes, with an ever-increasing number of genotypes described, but that variation of *Campylobacter* genotypes is not continuous and clusters can be identified as clonal complexes with distinct genetic characteristics. Techniques such as multi-locus sequence-typing (MLST) (Dingle *et al.* 2001; Dingle *et al.* 2002) and, latterly, whole genome sequencing (WGS) (Cody *et al.* 2013) allow for the characterisation of populations of *Campylobacter* based on genetic sequence data. These data show that the genetic diversity of both *C. jejuni* and *C. coli* is large (*e.g.* Sheppard *et al.* 2009a) and that clusters of genetic types are found among both *C. jejuni* and *C. coli* isolates, although this clustering differs in the two species (Sheppard *et al.* 2010). The stability over time is on the order of decades (Calland *et al.* 2021). *C. jejuni* has a weakly clonal population structure with the majority of currently known isolates belonging to one of forty-two clonal complexes (Dingle *et al.* 2002; Maiden and Dingle 2008). The relative abundance of *C. jejuni* clonal complexes causing human disease in hight income countries is similar, but they differ from the predominant genotypes of isolates from LMIC such as the Caribbean island of Curacao (Dingle *et al.* 2008). *C. coli* either belong to one of two clonal complexes or are unassigned to a clonal complex with the population forming three clonal groups or clades. Most *C. coli* human disease and agricultural isolates belong to clade 1, whereas environmental isolates usually belong to clade 2 or 3, and are rarely associated with human disease (Sheppard *et al.* 2009a).

a. The clonal complex identified by ST-257 is over-represented in isolates from chicken sources, as are clonal complexes identified by ST-353, ST-354, ST-443, ST-574, ST-464, and ST-607 (Sheppard *et al.* 2014). ST-61 is over-represented in isolates from bovine sources. The strength of host association is illustrated by the fact that *C. jejuni* genotypes from starlings and blackbirds in Europe are more similar to those in Australia, than they are to chicken genotypes from the same geographical region (Griekspoor *et al.* 2013; Griekspoor *et al.* 2015). The ST-21 clonal complex is a 'multi-host' complex regularly isolated from a range of hosts (Colles and Maiden 2012). Generalist host lineages are discussed by (Sheppard *et al.* 2014). Rapid host-switching mechanisms were identified by Dearlove *et al.* (2015). Recent work infers the intensification of beef production provided an opportunity for the emergence of a cattle specialist lineage of *C. jejuni* (Mourkas *et al.* 2020).
b. Griekspoor *et al.* (2013).

Box 1
Two main techniques have been used to understand how humans become infected with *Campylobacter*: 1) epidemiological studies correlating disease incidence with risk factors; and 2) genetic studies comparing DNA sequences of bacteria isolated from humans to those isolated from different habitats. Some studies combine both approaches. Epidemiological studies have the benefit of analysing large medical datasets but with the drawback of not being able experimentally to control factors that correlate with campylobacteriosis, resulting in being unable to show directly which factors affect rates of campylobacteriosis. Epidemiological studies usually asses 'risk factors' which are analysed with measures of strength of association such as the odds-ratio (OR) that represents the odds that an outcome will occur given a particular exposure. While the technology to analyse *Campylobacter* DNA is improving, including whole genome sequencing, the existence of multi-host genotypes leads to limitations in accuracy and there is potential for biased attribution from sampling bias towards chicken farm, abattoir and retail isolates. Furthermore, finding the same genetic variant in humans and an environmental habitat does not mean the infection derived from that source: the variant may have originated from a third common unidentified source for both. Epidemiological models are most effective in characterising transmission close to the infected person, whilst genetic models better inform likely animal reservoir sources (Advisory Committee on the Microbiological Safety of Food 2019; Franz *et al.* 2016). Risk factor approaches are reviewed in Humphrey *et al.* (2007); genetic approaches in Mughini Gras *et al.* (2012), Mossong *et al.* (2016), Franz *et al.* (2016); and combined approaches in Mughini-Gras *et al.* (2012), Mossong *et al.* (2016).

AB17. Mughini-Gras *et al.* (2021) concluded that the main livestock sources were poultry (48% of campylobacteriosis cases) followed by cattle (12%) but that non-food sources (pets 18% and water 8.5%) are also major sources for campylobacteriosis using whole genome attributions in the Netherlands. Berthenet *et al.* (2019) genome sequenced 200 isolates and concluded important role for ruminant reservoirs in non-invasive infection (58% of cases, with 39% attributed to poultry sources) and a potentially increased contribution of chicken as a source of invasive isolates (60% and 21% ruminants). Thépault *et al.* (2018) also estimated source attributions from whole genome sequencing using several methods with 156 French clinical isolates and concluded isolates originating from chicken (63%), ruminants (24%), pets (12%) and the environment (7%) sources of human infection in the analysis. Examples of genetic attribution studies using UK samples include Sheppard *et al.* (2009b), Cody *et al.* (2015), Wilson *et al.* (2008), Sheppard *et al.* (2009a), Thepault *et al.* (2017), Bessell *et al.* (2012), Strachan *et al.* (2009) and these show that over 95% of human-derived strains have a high probability of coming from livestock sources. Both poultry and ruminants are inferred as significant *Campylobacter* sources; across these studies, poultry accounts for between 50%-70% and ruminants accounts for an average of 40% of human *C. jejuni* cases. Genetic attribution data infers ruminants as the dominant source of *C. coli* (54%), followed by poultry (40%) and then pigs (6%) in the UK (Roux *et al.* 2013; Sheppard *et al.* 2009a). UK and worldwide studies combining case-controls with source attribution analyses (Mughini Gras *et al.* 2012; Levesque *et al.* 2013; Mossong *et al.* 2016; Rosner *et al.* 2017; Roux *et al.* 2013) show contact with and eating of livestock (poultry is a main focus of most studies) to be the greatest risk factors for campylobacteriosis, followed by contact with pets, water, or soil.

a. Some chicken-related clonal complexes such as ST-661 appear to cause disproportionately few cases of human disease (Sheppard *et al.* 2014). Yahara *et al.* (2017) used genome-wide association methods to infer that isolates belonging to the ST-21 complex increase in relative prevalence from farm to retail meat to clinical cases, but these were pooled samples and this cannot discount the possibility of secondary contamination in the factory or that human cases were non-poultry derived. Intriguingly some genetic signatures were associated with genes involved in oxygen tolerance, but altered tolerance of poultry and food related strains was not shown directly. Studies of virulence factors or virulence-associated genes have not yielded conclusive results on genes associated with human disease (Ellstrom *et al.* 2013).

AB18. Strachan *et al.* (2009), Advisory Committee on the Microbiological Safety of Food (2019). 'Environmental' or 'wild bird' sources account for no more than 3.5% of human disease cases caused by *C. jejuni* in the UK (Cody *et al.* 2015).

AB19. Scientific opinion from the EFSA concluded that the chicken reservoir was responsible for between 50 and 80% of human campylobacteriosis cases (EFSA Panel on Biological Hazards 2011). In outbreaks of *Campylobacter* between 2007 and 2016 in the EU (n=125), 29% of cases that were able to be attributed to a particular source were attributed to poultry. The majority of cases could not be attributed to a source (Pires *et al.* 2010). A case-control study from Norway showed that exposures resulting in significant increases in the odds of *Campylobacter* infection in multivariable analysis included drinking untreated water (OR: 2.96), drinking purchased bottled water (OR: 1.78), eating chicken (1.69), eating undercooked meat (OR: 1.77), eating food cooked on a barbeque (OR: 1.55), living on a farm with livestock (OR: 1.74), having a dog in the household (OR: 1.39) and having household water supply serving fewer than 20 houses (OR 1.92) (MacDonald *et al.* 2015). A combined case-control and attribution analysis based in Luxembourg showed significant associations between *C. jejuni* infection and consuming chicken outside the home (OR: 2.05), and both at home and outside (OR: 4.52), consuming poultry other than chicken outside the home (OR: 2.01), and contact with garden soil (3.03). For analysis of multiple risk factors see MacRitchie *et al.* (2013) and Neal and Slack (1995). On *Campylobacter* in bottled water and salad vegetables see Evans *et al.* (2003).

AB20. International travel is an important risk factor for campylobacteriosis, for instance, a 2012 meta-analysis found OR 4.9; 95% CI 2.9 to 8.2 (Domingues *et al.* 2012). In a combined attribution and epidemiological study (Strachan *et al.* 2013) travel abroad and UK mainland travel were associated with up to 17 and 18% of cases of campylobacteriosis in Scotland.

AB21. For examples of new risk factors see Mossong *et al.* (2016) and Pogreba-Brown *et al.* (2016). On unpasteurised milk, see Fernandes *et al.* (2015) and Mungai *et al.* (2015).

AB22. In outbreaks, Olsen *et al.* (2001), Little *et al.* (2010), Gilpin *et al.* (2013), and Trienekens *et al.* (2014) showed only ~3% of cases are due to human to human transmission. Kuhn *et al*. (2021) showed *Campylobacter* may be sexually transmitted between people. On water borne outbreaks see Taylor *et al.* (1982), Rogol *et al.* (1983). On drinking water as a risk factor see Kapperud *et al.* (2003). Poultry also predominates the food vehicles implicated in single-source outbreaks:

see Table 3.3 in Advisory Committee on the Microbiological Safety of Food (2019). WGS was used in the retrospective investigation of milk- and water-borne outbreaks in Finland (Revez *et al.* 2014a; Revez *et al.* 2014b), a milk-borne outbreak in UK (Fernandes *et al.* 2015), a water-borne outbreak in Canada (Clark *et al.* 2016), and chicken-liver pâté associated outbreaks in Australia (Moffatt *et al.* 2016) and Sweden (Lahti *et al.* 2017).

AB23. WGS is not currently routinely used for the surveillance for *Campylobacter*. The 'Campylobacteriosis in Oxfordshire' project has used near-real-time WGS surveillance since 2011, analysing 379 isolates up to 2021. It has identified clusters of highly similar temporally-associated isolates that were not otherwise epidemiologically linked (Cody *et al.* 2013). Also see Kovanen *et al.* (2014) for a Finnish study identifying clusters of similar isolates from different districts.

AB24. In 2014, the *Campylobacter* prevalence in UK slaughtered batches of chickens of 78% (from a sample of 426 slaughter batches) is amongst the highest in the EU, which averaged 31% (Advisory Committee on the Microbiological Safety of Food, 2019). The FSA carried out a survey of the prevalence and levels of *Campylobacter* on raw whole fresh chickens at retail from neck flap samples from 2014 to 2018, suggesting prevalence dropped from 73 to 55%, but changes in sample methods make it hard to compare the data. The FSA subsequently reported results from a method of analysis that was adjusted to avoid becoming distorted by variations in sample numbers submitted by retailers, and the data are reported in the table below, see Table 1 (FSA Project FS102121). The report of a *Campylobacter* incidence of 0.1% (95% UI 0 – 0.7%) on fresh beef mince is from a 2021 Food Standard Scotland report. There are no data for the incidence of *Campylobacter* associated with other food at retail in the UK other than a brief FSA report from a March 2006-June 2007, a survey of fresh red meats from 1,583 retail premises. *Campylobacter* was detected on the surface of 0.36% of samples (21 of the 5,998 tested). The predominant *Campylobacter* species was *C. jejuni*, which was detected in 20 of the 21 positive samples, *C. coli* being detected in the other. Little *et al.* (2008) reported Lamb and other meats (e.g. mutton, rabbit) exhibited the highest contamination from *Campylobacter* (12.6% and 19.8%, respectively), compared with pork (6.3%) and beef (4.9%) from a 2003-2005 survey of 3,959 raw red meats in the UK.

AB25. FSA retail survey data. The abbreviation 'cfu' stands for 'colony forming units' – each colony counted on an agar plate likely derives from a single *Campylobacter* cell and thus cfu approximate the number of viable cells in a sample. Point 3 in the restatement provides evidence that ingestion of a few hundred *Campylobacter* cells is sufficient to cause disease and thus 10 grammes or more of even the lowest contaminated samples (that have an average of 25 cfu per gram from Table 1) may be sufficient to cause campylobacteriosis if meat is not cooked sufficiently or if food preparation hygiene is poor.

AB26. Retail samples from chicken breasts in the united states report levels of *Campylobacter* positive samples dropped from around 50% to 18% between 2007 and 2018 (Williams et al. 2021). UK retail surveys sampled neck skins and this is a crucial difference as levels of contamination are usually much greater on neck skin than breast meat (see point 34) meaning the UK and USA retail data for the prevalence of *Campylobacter* on poultry cannot be directly compared.

	% cfu of *Campylobacter* spp. per g chicken skin sample				
Year	Negative <10	Positive >10	10-99	100-1000	>1000
July-Sept 2017	48.7	51.3	28.3	18.4	4.6
Oct-Dec 2017	57.7	42.3	22.0	16.7	3.6
Jan-Mar 2018	59.1	40.9	23.9	13.2	3.8

Table 1. Data from the UK FSA survey of retail poultry showing the average percentage levels of *Campylobacter* per gram of chicken skin.

AB27. Authors' summary.

(D) How *Campylobacter* is transmitted between animals in agriculture

Commercial poultry

AB28. *Campylobacter* can be isolated from animals that are not overtly sick (Rossler *et al.* 2019). While *Campylobacter* has commonly been considered a commensal inhabiting the intestines of chickens (Evans 2002), there is evidence that it may be pathogenic in chickens under some circumstances (Humphrey 2006; Bull *et al.* 2008; Humphrey *et al.* 2014; Williams *et al.* 2016). Pathogenicity in chickens may be strain-specific (Stewart-Tull *et al.* 2009).

a. Laboratory studies using artificial infections indicate *Campylobacter* has negative effects on broiler gut health and body weight (Ruiz-Palacios *et al.* 1981; Sanyal *et al.* 1984; Awad *et al.* 2014; Humphrey *et al.* 2014) but broiler breed has little impact on *C. jejuni* colonisation of the caeca following experimental infection (Humphrey *et al.* 2014). Field studies based in commercial systems in the UK found statistically significant relationships between *Campylobacter* infection of broiler flocks and broiler health and welfare markers such as digital dermatitis (odds ratio 2.08; 95% CI 1.20 to 3.61) (Bull *et al.* 2008; Rushton *et al.* 2009). Broiler breeds reared in conventional stocking systems tend to reach slaughter weight (2.2 kg) at around 36 days of age and are grown to a final stocking density of 38 kg/m^2. Slower-growing breeds reared in 'high welfare' systems and stocked at a lower final density of around 30 kg/m^2, reach slaughter weight at around 50 days of age. Artificial infection studies on the effects of *Campylobacter* on 'fast' growth broilers versus 'slow' growth broilers demonstrated that post-infection 'fast' growth chickens had severe diarrhoea and damaged gut mucosa (Williams *et al.* 2013; Humphrey *et al.* 2014).

b. Exposure to noradrenaline increases the virulence-associated properties of *Campylobacter* in *in vitro* experiments, and immune-suppressed chickens challenged with *C. jejuni* display more rapid dissemination of the bacteria to the liver (Cogan *et al.* 2007; Vaezirad *et al.* 2017). Normal levels of *Campylobacter* in the liver of healthy broilers are not known. *Campylobacter* species such as *Campylobacter hepaticus* can cause liver disease in chickens (Crawshaw 2019). Damage to gut mucosa associated with *Campylobacter* presence has been reported in some studies (Ruiz-Palacios *et al.*

1981; Sanyal *et al.* 1984), but not all (Dhillon *et al.* 2006; Larson *et al.* 2008). Awad *et al.* (2015) found that infections compromised gut barrier function and performance and host nutrient uptake.

AB29. Most conventionally reared flocks are *Campylobacter*-negative for the first three weeks of life (Messens *et al.* 2009; O'Mahony *et al.* 2011; Ridley *et al.* 2011). Thereafter, the prevalence of colonised flocks increases. There is a consensus that once some members of a poultry flock become infected *Campylobacter* spreads rapidly and virtually all chickens are infected within a few days (Newell and Fearnley 2003; Wagenaar *et al.* 2013; Koolman *et al.* 2014; Ijaz *et al.* 2018), due to faecal shedding of the bacterium and the coprophagic behaviour of chickens (Line *et al.* 2008). Flocks may become colonised by a succession of different *Campylobacter* genotypes over time (Colles and Maiden 2012).

AB30. Some studies report an absence of evidence for vertical transmission (Callicott *et al.* 2006; Battersby *et al.* 2016; Tangkham *et al.* 2016). Others report that vertical transmission of *Campylobacter* is a possibility (Agunos *et al.* 2014). The extent to which vertical transmission contributes to flock contamination is not clear (Cox *et al.* 2012). Studies have reported the presence of *Campylobacter* DNA in one week old chicks (Chuma *et al.* 1994; Chuma *et al.* 1994), and *Campylobacter* DNA via PCR in day-old chicks before food or water consumption (Idris *et al.* 2006). The presence of DNA does not allow differentiation between live *Campylobacter* cells capable of infection or dead cells. Other studies show no *Campylobacter* present in quarantine-reared chicks; when subsequent *Campylobacter* infection occurred out of quarantine, there was no overlap of *Campylobacter* genes with those of the parent flock (Callicott *et al.* 2006). This study concluded a vertical transmission rate of less than 1 in 60,000. Other reviews assert that vertical transmission is extremely unlikely (Wagenaar *et al.* 2013). There is some evidence that *Campylobacter* can penetrate and colonise eggs from *Campylobacter*-free hens (pseudo-vertical transmission; Fonseca *et al.* 2011).

AB31. Various sources of flock *Campylobacter* contamination are implicated but poorly described (*e.g.* Bull *et al.* 2006; Rushton *et al.* 2009; Battersby *et al.* 2016). The relative importance of risk factors will vary across farm settings and is hampered by a lack of consistent study designs and analyses.

a. Inadequate broiler house operations such as poor biosecurity, decreased animal welfare, and contamination of transport crates are variously correlated with *Campylobacter* contamination (Bull *et al.* 2006; Georgiev *et al.* 2017). The presence of other livestock and/or pets (cats/dogs) on farms is associated with increased risks of broiler flocks becoming *Campylobacter* positive (e.g. Ellis-Iversen *et al.* 2009; Agunos *et al.* 2014). It is unclear whether such animals are a source of poultry acquiring *Campylobacter* or vice-versa.

b. Newell *et al.* (2011), Agunos *et al.* (2014) cite water as a significant potential risk, but note that underlying studies are largely circumstantial or underpowered, with future studies likely to change the conclusions. Water and feeding equipment fouled by birds are significant potential vehicles for transmission (Tangkham *et al.* 2016). Correlation studies for *Campylobacter* presence weakly implicate unchlorinated drinking water as

a risk factor (Ellis-Iversen *et al.* 2009), and bacteria have been isolated from water lines and reservoirs in broiler houses (Pearson *et al.* 1993). The same strains have been isolated from water, feed and infected flocks (Bull *et al.* 2006). Water contamination usually follows rather than precedes flock contamination (Newell and Fearnley 2003; Bull *et al.* 2006), suggesting this may be a consequence not a cause of infection.

c. See Hald *et al.* (2007) and Royden *et al.* (2016) on *Campylobacter* associated with flies. Flies may vector *Campylobacter* into poultry houses (Nichols 2005) and to people (Ekdahl *et al.* 2005); flies are a vector rather than a source of *Campylobacter* (Gill *et al.* 2016). The presence of insects, including darkling beetles, or the use of insecticide were not significant factors in risk factor surveys in Sweden (Berndtson *et al.* 1996) or France (Refregier-Petton *et al.* 2001). In a Danish study (Hald *et al.* 2004), 8.2% of 49 flies captured from around a poultry house were culture-positive for *Campylobacter* while 70.2% of 47 flies were PCR positive. In other on-farm studies, *Campylobacter* was either not cultured from insects (Neubauer and Hess 2006) or was only recovered after the flock became positive (Jacobs-Reitsma *et al.* 1995; Bates *et al.* 2004). The presence of rodents (or lack of rodent control) was significantly correlated with an increase in the percentage of flocks testing positive for *Campylobacter* in Huneau-Salaun *et al.* (2007), McDowell *et al.* (2008), Allain *et al.* (2014) and Arsenault *et al.* (2007). For a review see Meerburg and Kijlstra (2007).

AB32. The presence of *Campylobacter* in poultry is associated with the presence of the same strains of *Campylobacter* in surrounding water, feed and other environmental habitats but attributing the direction of transmission in such studies can be problematic. The same strains have been found in infected flocks, from puddles outside sheds (Hiett *et al.* 2002; Rivoal *et al.* 2005; Hansson *et al.* 2007; Messens *et al.* 2009) and in air sampled 30 m downwind of broiler houses (Bull *et al.* 2006). It is not clear if chickens are infected from such environmental sources, or if *Campylobacter* around broiler sheds are derived from chickens. On feed systems, see Tangkham *et al.* (2016), Alves *et al.* (2017), Battersby *et al.* (2017). On litter, see Line and Bailey (2006), whereby acidification treatments to litter in commercial broiler houses in Georgia (US) saw a slight delay in the onset of *Campylobacter* colonisation but no difference in contamination levels of carcasses at the end of the broiler cycle. Transport crate evidence is supplied by Hastings *et al* (2011).

AB33. Carry over from previous flocks. Inadequate between-flock cleaning is a risk factor for *Campylobacter* infection (Ellis-Iversen *et al.* 2009). Studies of newly constructed poultry houses show that *Campylobacter* can be isolated from chickens by week 2-3 and the flocks fully colonised by 42 days (Gregory *et al.* 1997). A study of sequential broiler flocks of 60 houses suggested that 21% of the 60 houses with *Campylobacter* positive sequential flocks had identical genotypes, suggesting that carryover is a relatively infrequent event (Shreeve *et al.* 2002). In an 80 flock study, 4 of 15 farms appeared to have persistent types in successive flocks (Zweifel *et al.* 2008). Other systematic reviews have not concluded that carryover due to inadequate cleaning was a significant risk factor (Newell *et al.* 2011). In a study of 388 farms in Northern Ireland no significant evidence for carryover was found (McDowell *et al.* 2008). For a review see Newell and Fearnley (2003).

AB34. Thinning of the flock (usually around 30% of birds) is done to allow increased weight gain in the remaining birds whilst adhering to maximum stocking density regulations, and can also sometimes be carried out as part of a phased depopulation process to optimise slaughter operations. The partial de-population of flocks is correlated with an increase in *Campylobacter* in the birds that remain in some (Koolman *et al.* 2014; Smith *et al.* 2016a; Allen *et al.* 2008) but not all studies (including a survey of 1,737 flocks in the Netherlands) show this (Russa *et al.* 2005; Havelaar *et al.* 2007). Partial depopulation or thinning of flocks by catching gangs has been identified as a risk factor for flock infection (Katsma *et al.* 2007; Newell *et al.* 2011; Smith *et al.* 2016a). Surveys have found a statistically significant risk associated with thinning (Refrégier-Petton *et al.* 2001; Bouwknegt *et al.* 2004; Allen *et al.* 2008). Risk appears to be higher when thinning crews are large, visit more than one farm, or are poorly educated
EFSA Panel on Biological Hazards (2011).

AB35. Catching and transportation is recognised as being a significant potential pathway for the introduction of *Campylobacter* into the house and flock (Advisory Committee on the Microbiological Safety of Food 2019), including the crates themselves (Slader *et al.* 2002; Hansson *et al.* 2005). Transport and holding prior to processing contributes to the levels of *Campylobacter* found on processed poultry carcasses (Stern *et al.* 1995). The stress response to depopulation and transport may include the release of noradrenaline into the gut lumen, and this may facilitate *Campylobacter* colonisation (Line *et al.* 1997). Changes in gut colonisation patterns can occur after feed withdrawal, with *Campylobacter* found the length of the intestinal tract rather than in the caecum and colon (Byrd *et al.* 1998; Hinton *et al.* 2002).

AB36. Outdoor access (a feature of both organic and/or free-range systems) is a risk factor for the presence of *Campylobacter* (Ring *et al.* 2005; McCrea *et al.* 2006). Organic farms often have highly individualised production systems, making systematic comparisons challenging. Another study (Bailey *et al.* 2019) showed no significant difference in *Campylobacter* between organic and conventional broilers at the post-chill stage in the slaughter house but lower initial levels in organic birds. In a Danish study, organic carcasses translated to a 1.7 times greater risk of becoming ill per serving compared to conventional meat (Rosenquist *et al.* 2013) but Young *et al.* (2009) found no differences in *Campylobacter* levels between organic and conventionally reared poultry at retail but organic birds had higher levels at slaughter. One study suggests that *Campylobacter* may be more diverse under free-range systems, but this study did not evaluate differences in *Campylobacter* prevalence due to rearing-systems (Colles *et al.* 2008). Multiple sources and routes of transmission are likely for extensively reared birds (Huneau-Salaun *et al.* 2007), including (but not limited to) wild birds or other livestock. Age has previously been identified as a risk factor for *Campylobacter* colonisation in broilers at slaughter (Evans and Sayers 2000; Bouwknegt *et al.* 2004). Extensively reared birds are typically older at slaughter than conventionally reared birds.

Commercial Pigs and Cattle

AB37. Summary of evidence from livestock other than poultry includes:

AB38. Milnes *et al.* (2008), Baer *et al.* (2013).

AB39. Tan *et al.* (2018), Adhikari *et al.* (2019), Shange *et al.* (2019).

AB40. Shange *et al.* (2019). *Campylobacter*, especially *C. jejuni*, are frequently isolated in the intestinal tract and gallbladder of healthy sheep without causing clinical disease (Sahin *et al.* 2017).

AB41. Historically sheep abortions are associated with *Campylobacter fetus* subsp *venerealis* and *C. jejuni* to a lesser extent, although a hypervirulent tetracycline-resistant *C. jejuni* clone is now the predominant cause of sheep abortion in the US (Sahin *et al.* 2017; Sanad *et al.* 2014; Wu *et al.* 2014).

AB42. Authors' summary.

(E) Food chain interventions to control *Campylobacter* and rate of campylobacteriosis

On farm interventions

AB43. Biosecurity and disease prevention measures are designed to reduce the introduction and spread of *Campylobacter* in the poultry house (Newell *et al.* 2011). A meta-analysis (Agunos *et al.* 2014) determined that on-farm sources of *Campylobacter* included workers' boots, crates and equipment for catching and transport; thus, improving biosecurity measures and hygiene should reduce the prevalence of these as sources. Sommer *et al.* (2016) assessed the risk factors associated with *Campylobacter* using data from 6,000 flocks across six European countries (Denmark, the Netherlands, Norway Poland, Spain, and the UK). Factors associated with increased rates of *Campylobacter* presence were: increased temperature; country; houses ≥ 15 years old; absence of anterooms and barriers in each house; shared tools between houses; long downtime and drinking water systems with bells or cups. Between September 2011 and August 2013, the UK poultry industry enhanced biosecurity measures on 16 model farms. *Campylobacter* rates on these farms were compared with rates on farms with standard biosecurity (Georgiev *et al.* 2017). Standard biosecurity farms were chosen to match enhanced biosecurity farms in all measures other than biosecurity. The enhanced biosecurity measures significantly reduced the colonisation rate of *Campylobacter* prior to partial depopulation (thinning) (OR 0.25, 95% CI 0.14 to 0.47), and to a lesser extent at final depopulation (OR 0.47, 95% CI 0.25 to 0.89). All intervention studies include hygiene barriers (van de Giessen *et al.* 1992; Gibbens *et al.* 2001). The use of house-specific boots and clothes and effective use of boot dips are all associated with a reduced risk of flock infection (van de Giessen *et al.* 1992; Evans and Sayers 2000; Bouwknegt *et al.* 2004; Hald *et al.* 2001; Gibbens *et al.* 2001; McDowell *et al.* 2008).

a. See Guyard-Nicodeme *et al.* (2016). Acidification of poultry drinking water may partly reduce caecal load on-farm, but has no clear effect on *Campylobacter* prevalence on carcasses post-slaughter (Jansen *et al.* 2014). Acidified water treatment (PWT) reduced *Campylobacter* concentration in water by more than 7 $\log_{10}$ CFU/mL after 24 hours of exposure *in vitro*, but not on farms prior to thinning (Haughton *et al.* 2013). Adding chlorine to drinking water significantly (P=0.029) reduced the risk of flock colonisation

(OR 0.5, 95% CI 2.1 to 4.9), but 'other' types of disinfection did not (other was not defined) in one UK study (Ellis-Iversen *et al.* 2009). The review by Newell *et al.* (2011) found both studies showing a statistically significant reduction in flock colonisation following chlorination of drinking water, and others that showed no statistical reduction. Klein *et al.* (2015) found favourable effects from using disinfectants in drinking water on the reduction of caecal contamination but variable results in industrial-scale application. For biological feed interventions see Johnson *et al.* (2017). There have been a handful of studies testing the efficacy of probiotics in the form of a range of bacteria and yeasts, but there is no clear consensus that these are effective against *Campylobacter* but these studies are sparse and often low powered (Saint-Cyr *et al.* 2016). Nutritional strategies consist of administering feed or water that is supplemented with various products assumed to have an anti-*Campylobacter* activity. A wide range of organic and fatty acids, essential oils and other plant derived compounds has been tested for effectiveness against *Campylobacter* (Meunier *et al.* 2016), and the efficacy of the various nutritional strategies are mixed at best, and usually rest on small scale underpowered pilot studies. Recent reviews (Johnson *et al.* 2017; Saint-Cyr *et al.* 2016) have concluded that while probiotics, bacteriocins and bacteriophages may have potential, more research on efficacy and safety is needed. Also see Zhang *et al.* (2007) and Manes-Lazaro *et al.* (2017) on lactobacillus. Han *et al.* (2016), Ijaz *et al.* (2018) and Schofield *et al*. (2022) evaluate poultry gut microbiomes.

AB44. The lack of infections in flocks under 2-3 weeks of age (Messens *et al.* (2009); O'Mahony *et al.* 2011; Ridley *et al.* 2011) and high titres of antibodies to *C jejuni* in sera from 1-day and 7-day old chicks (Sahin *et al.* 2001) suggests that broilers may have maternally derived immunity. In birds and mammals this may be strain-specific (Sahin *et al.* 2003). Antigens conferring potential immunity in young chickens are poorly understood. See the review by Johnson *et al.* (2017) for a summary of different antigens under research.

AB45. For instance, no transport and holding interventions are detailed in the 2019 FSA report.

AB46. For a review on common interventions for non-poultry livestock see Adam and Brulisauer (2010).

Processing interventions

AB47. Levels of *Campylobacter* contamination on retail chicken are measured in colony-forming units per gram of tissue (cfu/g). Concentrations are expressed using the base 10 logarithm of the concentration. This allows the assessment of any decontamination process to be calculated in terms of a simple subtraction: one $\log_{10}$ difference thus equates to a ten-fold difference, and a two $\log_{10}$ difference to a hundred-fold and so on, in *Campylobacter* numbers.

AB48. Based on surveys that culture *Campylobacter* using standard methods from fresh poultry samples. Seliwiorstow *et al.* (2016) found the most relevant risk factors for presence of *Campylobacter* within the abattoir to be the levels of incoming contamination, with initial caecal *Campylobacter* counts of 7 log cfu/g resulting in <2.5 cfu/g *Campylobacter* count on chilled

carcasses, and initial caecal *Campylobacter* counts of 9.5 log cfu/g resulting in >3 log cfu/g. Rosenquist *et al.* (2006) sampled six broiler flocks at four different stages of processing and the main finding was a correlation between *Campylobacter* concentration in intestinal contents and on chicken carcasses after defeathering. Allen *et al.* (2007) sampled 22 flocks at 4 UK processing plants, with the main finding that contamination related to within flock prevalence of *Campylobacter*. Also see EFSA Panel on Biological Hazards (2011)

AB49. Hansson *et al.* (2015) recovered *Campylobacter* from 68% of 194 skin samples and 5% of muscle samples from 41 flocks that tested positive for *Campylobacter* in caeca in Sweden. All positive muscle samples had a corresponding positive skin sample and skin samples had 1 log cfu/g greater *Campylobacter* numbers and there was a significant association ($P<0.05$) between findings of *Campylobacter* on carcass skin (logcfu/g) and the proportion of *Campylobacter* positive breast muscle samples. Luber and Bartelt (2007) found a *Campylobacter* prevalence of 87% on the surface of 100 samples and 20% in the deep tissue of 55 samples of fresh chicken retail breasts in Germany. Di Giannatale *et al.* (2019) recovered *Campylobacter* from 17% of 1,243 chicken meat (breast and thigh) and 0.58% of bovine samples (hamburger and knife-cut meat) in Italy in 2015-2016; poultry samples with skin has greater prevalence of *Campylobacter*. Firlieyanti *et al.* (2016) reported *Campylobacter* on the surface of 87% of 109 samples of chicken liver and in deeper tissues in 83% of the chicken liver samples. Levels found in liver can be high as reported by Whyte *et al.* (2006).

AB50. Visceral rupture during slaughter processes increases contamination of carcasses by 0.9 log10 cfu per carcass ($P=0.05$) (Boysen and Rosenquist 2009). Also see EFSA Panel on Biological Hazards (2011). Seliwiorstow *et al.* (2016) also found key risk factors for presence of *Campylobacter* within the abattoir to be lower scald temperature and incorrect settings on machines for plucking, vent cutting and evisceration.

AB51. Forced air chilling and surface freezing may halve numbers, and crust freezing can reduce numbers by 0.4 and 1.5 $\log_{10}$ cfu/g (Haughton *et al.* 2012; Boysen and Rosenquist 2009). For the experience of Iceland see Tustin *et al.* (2011) and Stern *et al.* (2003) on crust-freezing. Crust-freezing is the process of taking a food product to a temperature where a substantial amount of the water in the product is in the form of ice but not all the water has turned to ice.

AB52. The decimal reduction time (D-value, the time required to achieve a log reduction (90%) of the bacteria present) of *Campylobacter* has been reported to be between 1 and 6.6 minutes at 55 °C (Park *et al.* 1991; Nguyen *et al.* 2006). Some studies have reported unusually large D values for *Campylobacter* (Bergsma *et al.* 2007; de Jong *et al.* 2012), but subsequent studies (Sampers *et al.* 2010; Al-Sakkaf 2015) have not supported these measurements. *Campylobacter* attached to chicken flesh appear to be more heat-resistant than cells free in broth (Blankenship and Craven 1982). The scalding of carcasses by dipping in water between 50 and 68 °C has been shown to reduce *Campylobacter* loads by 10 to 100 fold (Yang *et al.* 2001; Lehner *et al.* 2014), but scalding water may also serve as a reservoir for contamination if hygiene and temperature are not adhered to (Shane 1992). Significant reductions using hot water immersion were reported by Purnell *et al.* (2004) and Corry *et al.* (2007). In a study using a sample of 44 carcasses, steam combined with ultrasound significantly ($P<0.001$) reduced *Campylobacter* by ~10 fold (Boysen and Rosenquist 2009; Musavian *et al.* 2014).

AB53. Chlorine rinses (~0.1mg/L) have been experimentally demonstrated to inactivate 99% of bacteria in 5 minutes (Blaser *et al.* 1986). Recent USA studies conclude that peracetic acid may be more effective (Wideman *et al.* 2016; Bucher *et al.* 2015). For studies showing the efficacy of different chemical treatments see (Zakariene *et al.* 2015; Burfoot *et al.* 2015). Chlorine rinses have been used extensively in the USA poultry industry for 30 years. Difference in the methods for surveying retail poultry and levels of campylobacteriosis differ between the USA and the UK (and the EU) making direct comparisons of rates hard. A 2012 US Department of Agriculture survey reported the presence of *Campylobacter* on 62.8% from 5,000 samples of raw chicken compared to a prevalence of 40% from UK retail surveys in 2019. In 2015 rates of *Campylobacter* infection were elevated in the USA (1.39%, CI 0.49-3.2%) compared to the EU (0.52%, CI 0.36-0.69%) (Kirk *et al.* 2015) where chlorine rinses are banned.

AB54. Poultry associated *Campylobacter* have been shown to be reduced by 10-fold after 10 minutes' exposure to 0.12 to 0.25 kGy irradiation (Patterson 1995). Exposure to 405 nm wavelength light has been reported to reduce *C. jejuni* by up to 5 logs (Gunther *et al.* 2016).

AB55. Expert Opinion.

AB56. Several studies (*e.g*. Georgsson *et al.* 2006) report 2-3 $\log_{10}$ (10-100 fold) decreases in levels of *Campylobacter* on broilers after freezing. Complete freezing may reduce *Campylobacter* by 1.44 $\log_{10}$ cfu/g or 27-fold (Boysen and Rosenquist (2009). The freezing of chicken livers may reduce the numbers of *Campylobacter* bacteria by up to 100-fold Harrison *et al.* (2013). However *C. jejuni* may remain viable after being held at both -20 and -70 °C, and is able to survive up to eight freeze-thaw cycles (Lee *et al.* 1998).

AB57. Investigations of the factors dictating *Campylobacter* reductions during shelf life may result in further opportunities for control Advisory Committee on the Microbiological Safety of Food (2019).

a. High oxygen (80% O_2:20% N_2) modified atmosphere packing can reduce *Campylobacter* levels by 10 fold (Rajkovic *et al.* 2010. Lee *et al.* (1998) show chicken packed under vacuum and CO_2 at -20 °C for 56 days may reduce or eliminate *Campylobacter*, but this effect was not present at 14 days. Packing under N_2 or in low oxygen conditions at -20 °C had no effect up to 14 days, albeit these effects were not statistically analysed. Packing under N_2 and CO_2 at 4 °C has been shown to result in a 4 log reduction in cultured numbers of aero-sensitive strains of *C. jejuni*, a three log reduction in aerotolerant strains and a two log reduction for hyper-aerotolerant strains of *C. jejuni* (Oh *et al.* 2017). One study determined an optimum packing gas mix of 40:30:30 CO_2:O_2:N_2, and this was able to achieve a shelf-life in excess of 14 days at 2 °C (Meredith *et al.* 2014).

b. 'Roast in the bag' packaging has been employed commercially and was developed by UK companies, *e.g.*: https://www.thepoultrysite.com/news/2015/04/uks-first-roastinthebag-chicken-ready-to-launch; https://www.thegrocer.co.uk/buying-and-supplying/co-op-to-make-all-its-whole-chickens-roast-in-bag/373711.article and

http://www.dailymail.co.uk/news/article-2826830/Food-stores-flock-stock-roast-bag-chickens-don-t-trust-wash-hands.html For Iceland commentary see Tustin *et al.* (2011).

AB58. For pork, chilling and blast-chilling reduced loads from 3 $logs_{10}$ cfu/cm^2 to 0% (Chang *et al.* 2003; Baer *et al.* 2013). The pasteurisation of milk effectively destroys *Campylobacter*, as demonstrated when there are faults with the process (Fernandes *et al.* 2015). The European Food Standards Agency concluded in a recent review of public health hazards relevant to inspection of meat for bovine animals, sheep, goats and pigs that *Campylobacter* was a low risk organism in terms of transmission via red meat (Hazards 2013). The UK Advisory Committee on the Microbiological Safety of Food (2019) view is that legislated existing procedures for red meat at processing, aimed at the control of *Salmonella* and *E. coli*, are also effective at controlling *Campylobacter*.

AB59. Authors' projections.

Interventions aimed at consumers

AB60. On consumer beliefs on food safety in home environment, see Redmond and Griffith (2003), Redmond and Griffith (2004). A 2014 FSA survey recorded that 28% of respondents had heard of *Campylobacter* compared with 90% who had heard of *Escherichia coli* and *Salmonella* and within the UK, 80% of *Campylobacter* infections in England and Wales are acquired at home (UK Advisory Committee on the Microbiological Safety of Food 2019). In a large combined case-control and source attribution study in Germany, the preparation of poultry meat in the household was a key risk factor (Rosner *et al.* 2017). Evidence from modelling comparing transfer from hands with cross contamination of chopping boards suggests hands were the dominant route of human exposure (Mylius *et al.* 2007). Most sporadic cases of foodborne illness are associated with food prepared and consumed at home (Keegan *et al.* 2009; Vrbova *et al.* 2012), with cross-contamination being more important than undercooking (Nauta *et al.* 2009). Undercooked or lightly cooked chicken liver is an established threat to human health (Moffatt *et al.* 2016; Lahti *et al.* 2017; Edwards *et al.* 2014).

AB61. *Campylobacter* vaccine development is hindered by a lack of understanding of protective epitopes, antigenic diversity, pathogenesis, and association with post-infectious syndromes. Trials of a human vaccine for *C. jejuni* have commenced (Riddle and Guerry 2016). See Johnson *et al.* (2017) for a summary.

Co-ordinated interventions

AB62. Drawing reliable conclusions from cross-country comparisons are problematic due to differences in agricultural systems, climate, and socio-economic structures, as well as different sampling protocols.

AB63. Iceland. See reviews by Tustin *et al.* (2011). Stern *et al.* (2003) concluded one of the main factors in the reduction of chicken-associated campylobacteriosis in Iceland was the programme of freezing carcasses of *Campylobacter*-positive flocks.

AB64. New Zealand. See reviews by Sears *et al.* (2011).

AB65. Authors' summary.

(F) Antimicrobial resistance

AB66. See Dingle *et al.* (2005) and Cody *et al.* (2010). For reviews on mechanisms of AMR acquisition see Blair *et al.* (2015), Luangtongkum *et al.* (2009) and Iovine (2013). *Campylobacter* has a rapid mutation rate compared to other pathogenic bacteria (Eldholm and Balloux 2016); resistance to both fluoroquinolones (Luo *et al.* 2003; Delsol *et al.* 2004) and macrolides (Ladely *et al.* 2007; Lin *et al.* 2007; Logue *et al.* 2010) has been shown to evolve in experimental studies. Horizontal gene transfer (HGT): tetracycline resistance genes have been shown to have been transferred via HGT between strains of *C. jejuni* (Avrain *et al.* 2004), between *C. jejuni* and *C. coli* (Batchelor *et al.* 2004) and into *Campylobacter* spp. from either *Streptococcus* and *Enterococcus* (Zilhao *et al.* 1988). *C. coli* has been the recipient of genes via HGT from *C. jejuni:* the *C. coli* lineage that has colonised agricultural landscapes has 10-11% DNA that has introgressed while non-agricultural *C. coli* and *C. jejuni* has 2% (Sheppard *et al.* 2013).

AB67. Poultry diseases are reviewed in Chapters 5 and 7 to 17 of Jordan *et al.* (2002). Use of antibiotics in agriculture generally is reviewed by Page and Gautier (2012). In some countries, most notably the USA, low-doses of antibiotics are used to improve efficiency of feed conversion i.e. growth promotion (Allen and Stanton 2014; Teillant *et al.* 2015). This is banned under European Union regulations. On the use of poultry medication see British Poultry Council (2016).

AB68. In 2017, 773 tonnes of antibiotics were used in the UK, of which 64% were used in people and 26% in food-producing animals. The poultry industry used 14 tonnes of antibiotics in 2017, the active ingredient comparison giving a 42% drop compared to 2016 figures and an 80% drop compared to 2013 meat poultry figures Veterinary Medicines Directorate (2019) and see Sproston *et al.* (2018).

Annual antibiotic use in poultry, UK, tonnes	2013	2017
Penicillin	31	8.2
Tetracyclines	48	3.3
Macrolides	5	0.6
Fluoroquinolones	741	38

AB69. See Geenen (2011). The CDC reported an increase in ciprofloxacin resistance in *Campylobacter* from 13 to 25% between 1997 and 2011 (Hampton 2013). Some European Union member states report up to a 91.5% incidence of quinolone resistant *Campylobacter*. Ciprofloxacin resistance in *Campylobacter* isolates from raw chicken in South Korea was 92% (Han *et al.* 2007), and 100% in clinical isolates from children in Thailand (Serichantalergs *et al.* 2007). Mourkas *et al.* (2019) analysed 168 *C. jejuni* and 92 *C. coli* strains from Spain and reported that 39% and 88% of *C. jejuni* strains and 100% and 55% of *C. coli* trains from animals and humans respectively were multidrug resistant.

AB70. See Silva *et al.* (2011). Increases in resistance to fluoroquinolones in human cases of *Campylobacter* the Netherlands 1982-1989 was found to mirror increases of resistance in *Campylobacter* from poultry (Endtz *et al.* 1991). Over this time period resistance increased from 0-14% of isolates in poultry and from 0-11% in humans.

Comparisons of rates of AMR *Campylobacter* in livestock on farms which do and do not use antibiotics, include comparisons for poultry (Luangtongkum *et al.* 2006; Price *et al.* 2007), pigs (Thakur and Gebreyes 2005; Rollo *et al.* 2010), and dairy cattle (Halbert *et al.* 2006). For fluoroquinolone resistance <2% resistance was seen amongst organic turkey flocks versus 46-67% resistance in conventional flocks, in the US across 2000-2002 (Luangtongkum *et al.* 2006). 0-15% resistance was seen in organic chicken flocks versus 37.1-42.9% resistance in conventional flocks in the US in 2006 (Price *et al.* 2007). Rollo *et al.* (2010) observed that rates of resistance declined as the number of years a farm had been antibiotic free increased.

AB71. *Campylobacter* can evolve resistance to fluoroquinolone by a single point mutation to the *gyrA* gene, reviewed by Luangtongkum *et al.* (2009) and Payot *et al.* (2006). In a clinical trial of people with diarrhoeal disease, 28% of *Campylobacter* isolates developed resistance to lomefloxacin, a fluoroquinolone, during treatment (Ellis-Pegler *et al.* 1995). Luo *et al.* (2003) experimentally showed that fluoroquinolone resistance of *Campylobacter* in chickens increased following fluoroquinolone treatment. Prior to treatment resistance was not detected, following treatment it was as high as 100% of isolates. Resistance was attributed to single point mutations in the *gyrA* gene and in the function of the CmeABC efflux pump. Spontaneous point mutations conferring fluoroquinolone resistance occur in *gyrA* of *Campylobacter* at a frequency of $\approx 5 \times 10^{-8}$ when cultured in conventional media, reported by Luo *et al.* (2005). *Campylobacter* has a fast mutation rate compared to other pathogenic bacteria (Eldholm and Balloux 2016). Fluoroquinolone-resistant *Campylobacter* may have an advantage over wild type Fluoroquinolone-sensitive strains in the absence of fluoroquinolones, meaning resistance will not easily be lost in the absence of fluoroquinolones; Price *et al.* (2007) found that up to 43% of isolates were resistant to fluoroquinolone four years after last use. Luo *et al.* (2005) showed using pair-wise competition experiments that fluoroquinolone-resistant *C. jejuni* (with *gyrA* mutation) are able to outcompete fluoroquinolone-sensitive in the chicken gut in the absence of antibiotic selection pressure. For a comparison with macrolides see Luangtongkum *et al.* (2009).

AB72. Resistant infections are associated with international travel: in a US study, international travel associated infections had quinolone-resistance rates of 60% compared with 13% of non-travel related cases (Ricotta *et al.* 2014). In countries where fluoroquinolones have not been licenced for use in poultry (*e.g.* Australia), fluoroquinolone-resistance occurs primarily in returning travellers (Rautelin *et al.* 2003; Cheng *et al.* 2012).

AB73. See Johnson *et al.* (2017). A meta-analysis by Ternhag *et al.* (2007) demonstrated that antibiotics shortens the duration of disease caused by *Campylobacter* in patients by 1.32 days.

a. Gibreel and Taylor (2006), Moore *et al.* (2006), Alfredson and Korolik (2007).

b. Fluoroquinolone-resistant *Campylobacter* is listed as a high priority on the WHO priority list for the research and development of new antibiotics WHO (2017). The CDC considers

resistance of *C. jejuni* and *C. coli* to macrolides and ciprofloxacin (a fluoroquinolone) a "serious threat". The WHO (2016) and the OIE (2015) classify antibiotics by degree of importance for human and veterinary medicine respectively. Tetracyclines are classified as "highly important" for human medicine and as a "Veterinary Critically Important Antimicrobial Agent". All fluoroquinolones are considered as "critically important" for human medicine. Ciprofloxacin is critically important and nalidixic acid is highly important for veterinary medicine. Macrolides are classed as "critically important" for both human and veterinary medicine.

c. CDC (2013).

AB74. Geenen (2011).

AB75. Authors' summary.

References

1. Adam K., Brulisauer F. 2010 The application of food safety interventions in primary production of beef and lamb: a review. *International Journal of Food Microbiology* **141 Suppl 1**, S43-52. (doi:10.1016/j.ijfoodmicro.2009.12.020).
2. Adhikari B., Kim S.W., Kwon Y.M. 2019 Characterization of Microbiota Associated with Digesta and Mucosa in Different Regions of Gastrointestinal Tract of Nursery Pigs. *Int J Mol Sci* **20**. (doi:10.3390/ijms20071630).
3. Advisory Committee on the Microbiological Safety of Food. 2010 UK-Wide Survey of Microbiological Contamination of Raw Red Meat on Retail Sale. http://www.food.gov.uk/science/surveillance/fsisbranch2010/fsis0210
4. Advisory Committee on the Microbiological Safety of Food. 2019 Third Report on Campylobacter. Food Standards Agency. https://acmsf.food.gov.uk/sites/default/files/acmsf_campy_sept_2019.pdf
5. Agunos A., Waddell L., Leger D., Taboada E. 2014 A systematic review characterizing on-farm sources of *Campylobacter* spp. for broiler chickens. *PLoS One* **9**, e104905. (doi:10.1371/journal.pone.0104905).
6. Ahmed M.F., Schulz J., Hartung J. 2013 Survival of *Campylobacter jejuni* in naturally and artificially contaminated laying hen feces. *Poult Sci* **92**, 364-369. (doi:10.3382/ps.2012-02496).
7. Al-Sakkaf A. 2015 *Campylobacter* heat resistance - past, current status and future prospect for New Zealand and beyond. *World's Poultry Science Journal* **71**, 111-124. (doi:10.1017/S0043933915000100).
8. Alfredson D.A., Korolik V. 2007 Antibiotic resistance and resistance mechanisms in *Campylobacter jejuni* and *Campylobacter coli* . *FEMS Microbiol Lett* **277**, 123-132. (doi:10.1111/j.1574-6968.2007.00935.x).
9. Allain V., Chemaly M., Laisney M.J., Rouxel S., Quesne S., Le Bouquin S. 2014 Prevalence of and risk factors for *Campylobacter* colonisation in broiler flocks at the end of the rearing period in France. *Br Poult Sci* **55**, 452-459. (doi:10.1080/00071668.2014.941788).
10. Allen H.K., Stanton T.B. 2014 Altered egos: antibiotic effects on food animal microbiomes. *Annu Rev Microbiol* **68**, 297-315. (doi:10.1146/annurev-micro-091213-113052).
11. Allen V.M., Bull S.A., Corry J.E., Domingue G., Jorgensen F., Frost J.A., Whyte R., Gonzalez A., Elviss N., Humphrey T.J. 2007 *Campylobacter* spp. contamination of chicken carcasses during processing in relation to flock colonisation. *International Journal of Food Microbiology* **113**, 54-61. (doi:10.1016/j.ijfoodmicro.2006.07.011).
12. Allen V.M., Weaver H., Ridley A.M., Harris J.A., Sharma M., Emery J., Sparks N., Lewis M., Edge S. 2008 Sources and Spread of Thermophilic *Campylobacter* spp. during Partial Depopulation of Broiler Chicken Flocks. *Journal of Food Protection* **71**, 264-270. (doi:10.4315/0362-028x-71.2.264).
13. Alves M.B., Fonseca B.B., Melo R.T., Mendonca E.P., Nalevaiko P.C., Girao L.C., Monteiro G.P., Silva P.L., Rossi D.A. 2017 Feed can be a source of *Campylobacter jejuni* infection in broilers. *Br Poult Sci* **58**, 46-49. (doi:10.1080/00071668.2016.1258691).
14. Amour, C et al 2016 Epidemiology and Impact of *Campylobacter* Infection in Children in 8 Low-Resource Settings: Results From the MAL-ED Study. *Clinical Infectious Diseases*, **63** (9), 1171–1179, (doi.org/10.1093/cid/ciw542).

15. Ang C.W., Teunis P.F., Herbrink P., Keijser J., Van Duynhoven Y.H., Visser C.E., Van Pelt W. 2011 Seroepidemiological studies indicate frequent and repeated exposure to *Campylobacter* spp. during childhood. *Epidemiol Infect* **139**, 1361-1368. (doi:10.1017/S0950268810002359).
16. Arsenault J., Letellier A., Quessy S., Boulianne M. 2007 Prevalence and risk factors for Salmonella and *Campylobacter* spp. carcass contamination in broiler chickens slaughtered in Quebec, Canada. *J Food Prot* **70**, 1820-1828. (doi:10.4315/0362-028x-70.8.1820).
17. Avrain L., Vernozy-Rozand C., Kempf I. 2004 Evidence for natural horizontal transfer of tetO gene between *Campylobacter jejuni* strains in chickens. *J Appl Microbiol* **97**, 134-140. (doi:10.1111/j.1365-2672.2004.02306.x).
18. Awad W.A., Aschenbach J.R., Ghareeb K., Khayal B., Hess C., Hess M. 2014 *Campylobacter jejuni* influences the expression of nutrient transporter genes in the intestine of chickens. *Vet Microbiol* **172**, 195-201. (doi:10.1016/j.vetmic.2014.04.001).
19. Awad W.A., Molnar A., Aschenbach J.R., Ghareeb K., Khayal B., Hess C., Liebhart D., Dublecz K., Hess M. 2015 *Campylobacter* infection in chickens modulates the intestinal epithelial barrier function. *Innate Immun* **21**, 151-160. (doi:10.1177/1753425914521648).
20. Baer A.A., Miller M.J., Dilger A.C. 2013 Pathogens of Interest to the Pork Industry: A Review of Research on Interventions to Assure Food Safety. *Comprehensive Reviews in Food Science and Food Safety* **12**, 183-217. (doi:10.1111/1541-4337.12001).
21. Bailey M.A., Taylor R.M., Brar J.S., Corkran S.C., Velasquez C., Novoa Rama E., Oliver H.F., Singh M. 2019 Prevalence and antimicrobial resistance of *Campylobacter* from antibiotic-free broilers during organic and conventional processing. *Poult Sci* **98**, 1447-1454. (doi:10.3382/ps/pey486).
22. Batchelor R.A., Pearson B.M., Friis L.M., Guerry P., Wells J.M. 2004 Nucleotide sequences and comparison of two large conjugative plasmids from different *Campylobacter* species. *Microbiology* **150**, 3507-3517. (doi:10.1099/mic.0.27112-0).
23. Bates C., Hiett K.L., Stern N.J. 2004 Relationship of *Campylobacter* isolated from poultry and from darkling beetles in New Zealand. *Avian Dis* **48**, 138-147. (doi:10.1637/7082).
24. Battersby T., Whyte P., Bolton D.J. 2016 The pattern of *Campylobacter* contamination on broiler farms; external and internal sources. *J Appl Microbiol* **120**, 1108-1118. (doi:10.1111/jam.13066).
25. Battersby T., Walsh D., Whyte P., Bolton D. 2017 Evaluating and improving terminal hygiene practices on broiler farms to prevent *Campylobacter* cross-contamination between flocks. *Food Microbiol* **64**, 1-6. (doi:10.1016/j.fm.2016.11.018).
26. Benskin C.M., Wilson K., Jones K., Hartley I.R. 2009 Bacterial pathogens in wild birds: a review of the frequency and effects of infection. *Biol Rev Camb Philos Soc* **84**, 349-373. (doi:10.1111/j.1469-185X.2008.00076.x).
27. Bergsma N.J., Fischer A.R.H., Van Asselt E.D., Zwietering M.H., De Jong A.E.I. 2007 Consumer food preparation and its implication for survival of *Campylobacter jejuni* on chicken. **109**, 548-561. (doi:doi:10.1108/00070700710761536).
28. Berndtson E., Danielsson-Tham M.L., Engvall A. 1996 *Campylobacter* incidence on a chicken farm and the spread of *Campylobacter* during the slaughter process. *International Journal of Food Microbiology* **32**, 35-47. (doi:10.1016/0168-1605(96)01102-6).

29. Berthenet, E., Thépault, A., Chemaly, M. *et al.* 2019 Source attribution of *Campylobacter jejuni* shows variable importance of chicken and ruminants reservoirs in non-invasive and invasive French clinical isolates. *Sci Rep* **9,** 8098. (doi:10.1038/s41598-019-44454-2).
30. Bessell P.R., Rotariu O., Innocent G.T., Smith-Palmer A., Strachan N.J.C., Forbes K.J., Cowden J.M., Reid S.W.J., Matthews L. 2012 Using sequence data to identify alternative routes and risk of infection: a case-study of *Campylobacter* in Scotland. *BMC Infectious Diseases* **12**. (doi:10.1186/1471-2334-12-80).
31. Bi P., Cameron A.S., Zhang Y., Parton K.A. 2008 Weather and notified *Campylobacter* infections in temperate and sub-tropical regions of Australia: an ecological study. *J Infect* **57**, 317-323. (doi:10.1016/j.jinf.2008.08.004).
32. Black R.E., Levine M.M., Clements M.L., Hughes T.P., Blaser M.J. 1988 Experimental *Campylobacter jejuni* infection in humans. *Journal of Infectious Diseases* **157**, 472-479. (doi: 10.1093/infdis/157.3.472)
33. Blair J.M., Webber M.A., Baylay A.J., Ogbolu D.O., Piddock L.J. 2015 Molecular mechanisms of antibiotic resistance. *Nat Rev Microbiol* **13**, 42-51. (doi:10.1038/nrmicro3380).
34. Blankenship L.C., Craven S.E. 1982 *Campylobacter jejuni* survival in chicken meat as a function of temperature. *Appl Environ Microbiol* **44**, 88-92. (doi: 10.1128/aem.44.1.88-92.1982)
35. Blaser M.J., Smith P.F., Wang W.L., Hoff J.C. 1986 Inactivation of *Campylobacter jejuni* by chlorine and monochloramine. *Appl Environ Microbiol* **51**, 307-311. (doi: 10.1128/aem.51.2.307-311.1986)
36. Bloomfield S.J., Midwinter A.C., Biggs P.J., French N.P., Marshall J.C., Hayman D.T.S., Carter P.E., Thornley C., Yap R., Benschop J. 2017 Long-term Colonization by *Campylobacter jejuni* Within a Human Host: Evolution, Antimicrobial Resistance, and Adaptation. *Journal of Infectious Diseases* **217**, 103-111. (doi:10.1093/infdis/jix561).
37. Bouwknegt M., van de Giessen A.W., Dam-Deisz W.D., Havelaar A.H., Nagelkerke N.J., Henken A.M. 2004 Risk factors for the presence of *Campylobacter* spp. in Dutch broiler flocks. *Prev Vet Med* **62**, 35-49. (doi:10.1016/j.prevetmed.2003.09.003).
38. Boysen L., Rosenquist H. 2009 Reduction of thermotolerant *Campylobacter* species on broiler carcasses following physical decontamination at slaughter. *J Food Prot* **72**, 497-502. (doi: 10.4315/0362-028x-72.3.497)
39. British Poultry Council. 2016 The BPC antibiotic stewardship scheme: leading the way in the responsible use of antibiotics. (ed. British Poultry Council).
40. Bucher O., Waddell L., Greig J., Smith B.A. 2015 Systematic review-meta-analysis of the effect of chilling on *Campylobacter* spp. during primary processing of broilers. *Food Control* **56**, 211-217. (doi:10.1016/j.foodcont.2015.03.032).
41. Bull S.A., Allen V.M., Domingue G., Jorgensen F., Frost J.A., Ure R., Whyte R., Tinker D., Corry J.E.L., Gillard-King J., et al. 2006 Sources of *Campylobacter* spp. colonizing housed broiler flocks during rearing. *Applied and Environmental Microbiology* **72**, 645-652. (doi:10.1128/Aem.72.1.645-652.2006).
42. Bull S.A., Thomas A., Humphrey T., Ellis-Iversen J., Cook A.J., Lovell R., Jorgensen F. 2008 Flock health indicators and *Campylobacter* spp. in commercial housed broilers reared in Great Britain. *Appl Environ Microbiol* **74**, 5408-5413. (doi:10.1128/AEM.00462-08).

43. Burfoot D., Allen V., Mulvey E., Jewell K., Harrison D., Morris V. 2015 ReducingCampylobacternumbers on chicken carcasses using lactic acid in processing plants. *International Journal of Food Science & Technology* **50**, 2451-2457. (doi:10.1111/ijfs.12912).
44. Buswell C.M., Herlihy Y.M., Lawrence L.M., McGuiggan J.T., Marsh P.D., Keevil C.W., Leach S.A. 1998 Extended survival and persistence of *Campylobacter* spp. in water and aquatic biofilms and their detection by immunofluorescent-antibody and -rRNA staining. *Appl Environ Microbiol* **64**, 733-741. (doi: 10.1128/AEM.64.2.733-741.1998)
45. Byrd J.A., Corrier D.E., Hume M.E., Bailey R.H., Stanker L.H., Hargis B.M. 1998 Effect of feed withdrawal on *Campylobacter* in the crops of market-age broiler chickens. *Avian Dis* **42**, 802-806.
46. Calland J.K., Pascoe B., Bayliss S.C., Mourkas E., Berthenet E., et al. 2021 Quantifying bacterial evolution in the wild: A birthday problem for *Campylobacter* lineages. *PLOS Genetics* **17**, e1009829. (doi:10.1371/journal.pgen.1009829).
47. Callicott K.A., Friethriksdottir V., Reiersen J., Lowman R., Bisaillon J.R., Gunnarsson E., Berndtson E., Hiett K.L., Needleman D.S., Stern N.J. 2006 Lack of evidence for vertical transmission of *Campylobacter* spp. in chickens. *Appl Environ Microbiol* **72**, 5794-5798. (doi:10.1128/aem.02991-05).
48. *Campylobacter* Joint Working Group, 2014, https://www.food.gov.uk/sites/default/files/media/document/campylobacter-contamination-uk-chickens-year-4-report.pdf
49. CDC. 2013 Antibiotic resistance threats in the United States, 2013. https://www.cdc.gov/drugresistance/pdf/ar-threats-2013-508.pdf
50. Chan K.F., Le Tran H., Kanenaka R.Y., Kathariou S. 2001 Survival of clinical and poultry-derived isolates of *Campylobacter jejuni* at a low temperature (4 degrees C). *Appl Environ Microbiol* **67**, 4186-4191. (doi:10.1128/aem.67.9.4186-4191.2001).
51. Chang V.P., Mills E.W., Cutter C.N. 2003 Reduction of bacteria on Pork carcasses associated with chilling method. *J. Food Prot.* **66**, 1019-1024. (doi: 10.4315/0362-028X-66.6.1019).
52. Cheng A.C., Turnidge J., Collignon P., Looke D., Barton M., Gottlieb T. 2012 Control of Fluoroquinolone Resistance through Successful Regulation, Australia. *Emerging Infectious Diseases* **18**, 1453-1460. (doi:10.3201/eid1809.111515).
53. Chuma T., Yamada T., Yano K., Okamoto K., Yugi H. 1994 A Survey of Campylobacter-*Jejuni* in Broilers from Assignment to Slaughter Using DNA-DNA Hybridization. *Journal of Veterinary Medical Science* **56**, 697-700. (doi:10.1292/jvms.56.697)
54. Clark C.G., Berry C., Walker M., Petkau A., Barker D.O., Guan C., Reimer A., Taboada E.N. 2016 Genomic insights from whole genome sequencing of four clonal outbreak *Campylobacter jejuni* assessed within the global C. *jejuni* population. *Bmc Genomics* **17**, 990. (doi:10.1186/s12864-016-3340-8).
55. Cody A.J., Clarke L., Bowler I.C.J.W., Dingle K.E. 2010 Ciprofloxacin-resistant campylobacteriosis in the UK. *The Lancet* **376**. (doi:10.1016/s0140-6736(10)62261-1).
56. Cody A.J., McCarthy N.D., Jansen van Rensburg M., Isinkaye T., Bentley S.D., Parkhill J., Dingle K.E., Bowler I.C., Jolley K.A., Maiden M.C. 2013 Real-time genomic epidemiological evaluation of human *Campylobacter* isolates by use of whole-genome multilocus sequence typing. *J Clin Microbiol* **51**, 2526-2534. (doi:10.1128/jcm.00066-13).

57. Cody A.J., McCarthy N.D., Bray J.E., Wimalarathna H.M., Colles F.M., Jansen van Rensburg M.J., Dingle K.E., Waldenstrom J., Maiden M.C. 2015 Wild bird-associated *Campylobacter jejuni* isolates are a consistent source of human disease, in Oxfordshire, United Kingdom. *Environ Microbiol Rep* **7**, 782-788. (doi:10.1111/1758-2229.12314).
58. Cody A.J., Maiden M.C., Strachan N.J., McCarthy N.D. 2019 A systematic review of source attribution of human campylobacteriosis using multilocus sequence typing. *Euro Surveill* **24**. (doi:10.2807/1560-7917.Es.2019.24.43.1800696).
59. Cogan T.A., Thomas A.O., Rees L.E., Taylor A.H., Jepson M.A., Williams P.H., Ketley J., Humphrey T.J. 2007 Norepinephrine increases the pathogenic potential of *Campylobacter jejuni* . *Gut* **56**, 1060-1065. (doi:10.1136/gut.2006.114926).
60. Coker A.O., Isokpehi R.D., Thomas B.N., Amisu K.O., Obi C.L. 2002 Human campylobacteriosis in developing countries. *Emerging Infectious Diseases* **8**, 237-244. (doi:10.3201/eid0803.010233).
61. Colles F.M., Jones T.A., McCarthy N.D., Sheppard S.K., Cody A.J., Dingle K.E., Dawkins M.S., Maiden M.C. 2008 *Campylobacter* infection of broiler chickens in a free-range environment. *Environ Microbiol* **10**, 2042-2050. (doi:10.1111/j.1462-2920.2008.01623.x).
62. Colles F.M., Maiden M.C. 2012 *Campylobacter* sequence typing databases: applications and future prospects. *Microbiology* **158**, 2695-2709. (doi:10.1099/mic.0.062000-0).
63. Connerton P.L., Richards P.J., Lafontaine G.M., O'Kane P.M., Ghaffar N., Cummings N.J., Smith D.L., Fish N.M., Connerton I.F. 2018 The effect of the timing of exposure to *Campylobacter jejuni* on the gut microbiome and inflammatory responses of broiler chickens. *Microbiome* **6**, 88. (doi:10.1186/s40168-018-0477-5).
64. Corry J.E.L., James S.J., Purnell G., Barbedo-Pinto C.S., Chochois Y., Howell M., James C. 2007 Surface pasteurisation of chicken carcasses using hot water. *Journal of Food Engineering* **79**, 913-919. (doi:https://doi.org/10.1016/j.jfoodeng.2006.03.018).
65. Cox N.A., Richardson L.J., Maurer J.J., Berrang M.E., Fedorka-Cray P.J., Buhr R.J., Byrd J.A., Lee M.D., Hofacre C.L., O'Kane P.M., et al. 2012 Evidence for horizontal and vertical transmission in *Campylobacter* passage from hen to her progeny. *J Food Prot* **75**, 1896-1902. (doi:10.4315/0362-028.JFP-11-322).
66. Crawshaw T. 2019 A review of the novel thermophilic *Campylobacter*, *Campylobacter hepaticus*, a pathogen of poultry. *Transbound Emerg Dis* **66**, 1481-1492. (doi:10.1111/tbed.13229).
67. Dadson S.J., Hall J.W., Murgatroyd A., Acreman M., Bates P., Beven K., Heathwaite L., Holden J., Holman I.P., Lane S.N., et al. 2017 A restatement of the natural science evidence concerning catchment-based 'natural' flood management in the UK. *Proc Math Phys Eng Sci* **473**, 20160706. (doi:10.1098/rspa.2016.0706).
68. Daniel N., Casadevall N., Sun P., Sugden D., Aldin V. 2020 The Burden of Foodborne Disease in the UK 2018. Analytics Unit, Food Standards Agency and London School of Hygiene and Tropical Medicine. https://www.food.gov.uk/sites/default/files/media/document/the-burden-of-foodborne-disease-in-the-uk_0.pdf
69. de Jong A.E., van Asselt E.D., Zwietering M.H., Nauta M.J., de Jonge R. 2012 Extreme Heat Resistance of Food Borne Pathogens *Campylobacter jejuni* , *Escherichia coli* , and

Salmonella typhimurium on Chicken Breast Fillet during Cooking. *Int J Microbiol* **2012**, 196841. (doi:10.1155/2012/196841).

70. Dearlove B.L., Cody A.J., Pascoe B., Méric G., Wilson D.J., Sheppard S.K. 2015 Rapid host switching in generalist *Campylobacter* strains erodes the signal for tracing human infections. *The ISME Journal* **10**, 721. (doi:10.1038/ismej.2015.149).
71. Delsol A.A., Sunderland J., Woodward M.J., Pumbwe L., Piddock L.J., Roe J.M. 2004 Emergence of fluoroquinolone resistance in the native *Campylobacter coli* population of pigs exposed to enrofloxacin. *J Antimicrob Chemother* **53**, 872-874. (doi:10.1093/jac/dkh150).
72. Dhillon A.S., Shivaprasad H.L., Schaberg D., Wier F., Weber S., Bandli D. 2006 *Campylobacter jejuni* infection in broiler chickens. *Avian Dis* **50**, 55-58. (doi:10.1637/7411-071405r.1).
73. Di Giannatale E., Calistri P., Di Donato G., Decastelli L., Goffredo E., *et al.* 2019 Thermotolerant *Campylobacter* spp. in chicken and bovine meat in Italy: Prevalence, level of contamination and molecular characterization of isolates. *PLOS ONE,* **14**, e0225957. (doi: 10.1371/journal.pone.0225957).
74. Dingle K.E., Colles F.M., Wareing D.R., Ure R., Fox A.J., Bolton F.E., Bootsma H.J., Willems R.J., Urwin R., Maiden M.C. 2001 Multilocus sequence typing system for *Campylobacter jejuni* . *J Clin Microbiol* **39**, 14-23. (doi:10.1128/jcm.39.1.14-23.2001).
75. Dingle K.E., Colles F.M., Ure R., Wagenaar J.A., Duim B., Bolton F.J., Fox A.J., Wareing D.R., Maiden M.C. 2002 Molecular characterization of *Campylobacter jejuni* clones: a basis for epidemiologic investigation. *Emerging Infectious Diseases* **8**, 949-955. (doi:10.3201/eid0809.020122).
76. Dingle K.E., Clarke L., Bowler I.C. 2005 Ciprofloxacin resistance among human *Campylobacter* isolates 1991-2004: an update. *J Antimicrob Chemother* **56**, 435-437. (doi:10.1093/jac/dki192).
77. Dingle K.E., McCarthy N.D., Cody A.J., Peto T.E., Maiden M.C. 2008 Extended sequence typing of *Campylobacter* spp., United Kingdom. *Emerging Infectious Diseases* **14**, 1620-1622. (doi:10.3201/eid1410.071109).
78. Domingues A.R., Pires S.M., Halasa T., Hald T. 2012 Source attribution of human campylobacteriosis using a meta-analysis of case-control studies of sporadic infections. *Epidemiol Infect* **140**, 970-981. (doi:10.1017/s0950268811002676).
79. Edwards D.S., Milne L.M., Morrow K., Sheridan P., Verlander N.Q., Mulla R., Richardson J.F., Pender A., Lilley M., Reacher M. 2014 Campylobacteriosis outbreak associated with consumption of undercooked chicken liver pate in the East of England, September 2011: identification of a dose-response risk. *Epidemiol Infect* **142**, 352-357. (doi:10.1017/s0950268813001222).
80. EFSA and ECDC. 2018 The European Union summary report on trends and sources of zoonoses, zoonotic agents and food-borne outbreaks in 2017. *EFSA Journal* **16**, 5500. (doi:10.2903/j.efsa.2018.5500).
81. EFSA Panel on Biological Hazards. 2011 Scientific Opinion on *Campylobacter* in broiler meat production: control options and performance objectives and/or targets at different stages of the food chain. *EFSA Journal* **9**, 2105. (doi:doi:10.2903/j.efsa.2011.2105).
82. Ekdahl K., Normann B., Andersson Y. 2005 Could flies explain the elusive epidemiology of campylobacteriosis? *BMC Infect Dis* **5**, 11. (doi:10.1186/1471-2334-5-11).

83. Eldholm V., Balloux F. 2016 Antimicrobial Resistance in Mycobacterium tuberculosis: The Odd One Out. *Trends Microbiol* **24**, 637-648. (doi:10.1016/j.tim.2016.03.007).
84. Ellis-Iversen J., Jorgensen F., Bull S., Powell L., Cook A.J., Humphrey T.J. 2009 Risk factors for *Campylobacter* colonisation during rearing of broiler flocks in Great Britain. *Prev Vet Med* **89**, 178-184. (doi:10.1016/j.prevetmed.2009.02.004).
85. Ellis-Pegler R.B., Hyman L.K., Ingram R.J., McCarthy M. 1995 A placebo controlled evaluation of lomefloxacin in the treatment of bacterial diarrhoea in the community. *J Antimicrob Chemother* **36**, 259-263.
86. Ellstrom P., Feodoroff B., Hanninen M.L., Rautelin H. 2013 Characterization of clinical *Campylobacter jejuni* isolates with special emphasis on lipooligosaccharide locus class, putative virulence factors and host response. *Int J Med Microbiol* **303**, 134-139. (doi:10.1016/j.ijmm.2013.01.005).
87. Endtz H.P., Ruijs G.J., van Klingeren B., Jansen W.H., van der Reyden T., Mouton R.P. 1991 Quinolone resistance in *Campylobacter* isolated from man and poultry following the introduction of fluoroquinolones in veterinary medicine. *J Antimicrob Chemother* **27**, 199-208.
88. Esan O.B., Pearce M., van Hecke O., Roberts N., Collins D.R., Violato M., McCarthy N., Perera R., Fanshawe T.R. 2017 Factors Associated with Sequelae of *Campylobacter* and Non-typhoidal *Salmonella* Infections: A Systematic Review. *EBioMedicine* **15**, 100-111. (doi:10.1016/j.ebiom.2016.12.006).
89. Ethelberg S., Olsen K.E., Gerner-Smidt P., Molbak K. 2004 Household outbreaks among culture-confirmed cases of bacterial gastrointestinal disease. *Am J Epidemiol* **159**, 406-412. (doi:10.1093/aje/kwh049).
90. Evans M.R., Ribeiro C.D., Salmon R.L. 2003 Hazards of healthy living: bottled water and salad vegetables as risk factors for *Campylobacter* infection. *Emerging Infectious Diseases* **9**, 1219-1225. (doi:10.3201/eid0910.020823).
91. Evans S. 2002 *Campylobacter*. In *Poultry Diseases* (eds. Jordan F., Pattison M., Alexander D., Faragher T.). London, W. B. Saunders.
92. Evans S.J., Sayers A.R. 2000 A longitudinal study of *Campylobacter* infection of broiler flocks in Great Britain. *Prev Vet Med* **46**, 209-223.
93. Fernandes A.M., Balasegaram S., Willis C., Wimalarathna H.M., Maiden M.C., McCarthy N.D. 2015 Partial Failure of Milk Pasteurization as a Risk for the Transmission of *Campylobacter* From Cattle to Humans. *Clin Infect Dis* **61**, 903-909. (doi:10.1093/cid/civ431).
94. Food Standards Agency (FSA) and Food Standards Scotland (FSS), Final Report. Rigby D., Burton M., Payne K., Wright S., O'Brien S., Harstaff J., Ozdemiroglu E., Gianferrera E., Mistry R. 2017 Estimating Quality Adjusted Life years and willingness to pay values for microbiological foodborne disease (phase 2). https://www.food.gov.uk/research/foodborne-disease/estimating-quality-adjusted-life-years-and-willingness-to-pay-values-for-microbiological-foodborne-disease-phase-2
95. Food Standards Scotland (FSS). A Microbiological Survey of Minced Beef at Retail in Scotland 2021. https://www.foodstandards.gov.scot/downloads/FSS_Report_Retail_Mince_FINAL.pdf

96. Firlieyanti A.S., Connerton P.L., Connerton I.F. 2016 Campylobacters and their bacteriophages from chicken liver: The prospect for phage biocontrol. *International Journal of Food Microbiology* **237**, 121-127. (doi:10.1016/j.ijfoodmicro.2016.08.026).
97. Fonseca B.B., Beletti M.E., Melo R.T., Mendonca E.P., Vieira C.U., Levenhagen M.A., Rossi D.A. 2011 Transfer, viability and colonisation of *Campylobacter jejuni* in the chicken vitellus and in embryos. *Br Poult Sci* **52**, 279-286. (doi:10.1080/00071668.2011.577056).
98. Franz E., Gras L.M., Dallman T. 2016 Significance of whole genome sequencing for surveillance, source attribution and microbial risk assessment of foodborne pathogens. *Current Opinion in Food Science* **8**, 74-79. (doi:10.1016/j.cofs.2016.04.004).
99. Friedrich A., Marshall J.C., Biggs P.J., Midwinter A.C., French N.P. 2016 Seasonality of *Campylobacter jejuni* isolates associated with human campylobacteriosis in the Manawatu region, New Zealand. *Epidemiol Infect* **144**, 820-828. (doi:10.1017/S0950268815002009).
100. Frost J.A., Gillespie I.A., O'Brien S.J. 2002 Public health implications of *Campylobacter* outbreaks in England and Wales, 1995-9: epidemiological and microbiological investigations. *Epidemiol Infect* **128**, 111-118. (doi:10.1017/s0950268802006799).
101. Garcia-Sanchez L., Melero B., Jaime I., Rossi M., Ortega I., Rovira J. 2019 Biofilm formation, virulence and antimicrobial resistance of different *Campylobacter jejuni* isolates from a poultry slaughterhouse. *Food Microbiol* **83**, 193-199. (doi:10.1016/j.fm.2019.05.016).
102. Geenen P.L., Koene, H., Blaak, A.H., van de Giessen, A.W. 2011 Risk profile on antimicrobial resistance transmissable from food animals to humans. National Institute of Public Health and the Environment (RIVM). https://www.rivm.nl/bibliotheek/rapporten/330334001.pdf
103. Georgiev M., Beauvais W., Guitian J. 2017 Effect of enhanced biosecurity and selected on-farm factors on *Campylobacter* colonization of chicken broilers. *Epidemiol Infect* **145**, 553-567. (doi:10.1017/S095026881600251X).
104. Georgsson F., Thornorkelsson A.E., Geirsdottir M., Reiersen J., Stern N.J. 2006 The influence of freezing and duration of storage on *Campylobacter* and indicator bacteria in broiler carcasses. *Food Microbiol* **23**, 677-683. (doi:10.1016/j.fm.2005.10.003).
105. Gibbens J.C., Pascoe S.J.S., Evans S.J., Davies R.H., Sayers A.R. 2001 A trial of biosecurity as a means to control *Campylobacter* infection of broiler chickens. *Preventive Veterinary Medicine* **48**, 85-99. (doi:10.1016/s0167-5877(00)00189-6).
106. Gibreel A., Taylor D.E. 2006 Macrolide resistance in *Campylobacter jejuni* and *Campylobacter coli* . *J Antimicrob Chemother* **58**, 243-255. (doi:10.1093/jac/dkl210).
107. Gill C., Bahrndorff S., Lowenberger C. 2016 *Campylobacter jejuni* in Musca domestica: An examination of survival and transmission potential in light of the innate immune responses of the house flies. *Insect Sci*. (doi:10.1111/1744-7917.12353).
108. Gillespie I.A., O'Brien S.J., Frost J.A., Adak G.K., Horby P., Swan A.V., Painter M.J., Neal K.R., Surveillanc C.S. 2002 A case-case comparison of *Campylobacter coli* and *Campylobacter jejuni* infection: A tool for generating hypotheses. *Emerging Infectious Diseases* **8**, 937-942. (doi: 10.3201/eid0809.10.3201/eid0809.010187)
109. Gillespie I.A., O'Brien S.J., Penman C., Tompkins D., Cowden J., Humphrey T.J. 2008 Demographic determinants for *Campylobacter* infection in England and Wales: implications for future epidemiological studies. *Epidemiol Infect* **136**, 1717-1725. (doi:10.1017/s0950268808000319).

110. Gillespie I.A., O'Brien S.J., Bolton F.J. 2009 Age patterns of persons with campylobacteriosis, England and Wales, 1990-2007. *Emerging Infectious Diseases* **15**, 2046-2048. (doi:10.3201/eid1512.090280).
111. Gilpin B, Walker, T, Paine, S, et al. 2020 A large scale waterborne Campylobacteriosis outbreak, Havelock North, New Zealand. *Journal of Infection* **81**(3), 390-395. (doi: 10.1016/j.jinf.2020.06.065)
112. Gilpin B.J., Walshe G., On S.L., Smith D., Marshall J.C., French N.P. 2013 Application of molecular epidemiology to understanding campylobacteriosis in the Canterbury region of New Zealand. *Epidemiol Infect* **141**, 1253-1266. (doi:10.1017/s0950268812001719).
113. Gittins J., Canning P. 2006 A review of the poultry catching industry in England and Wales. *Report prepared for DEFRA and FSA, October 2006*.
114. Godfray H.C., Donnelly C.A., Kao R.R., Macdonald D.W., McDonald R.A., Petrokofsky G., Wood J.L., Woodroffe R., Young D.B., McLean A.R. 2013 A restatement of the natural science evidence base relevant to the control of bovine tuberculosis in Great Britain. *Proc Biol Sci* **280**, 20131634. (doi:10.1098/rspb.2013.1634).
115. Godfray H.C., Blacquiere T., Field L.M., Hails R.S., Petrokofsky G., Potts S.G., Raine N.E., Vanbergen A.J., McLean A.R. 2014 A restatement of the natural science evidence base concerning neonicotinoid insecticides and insect pollinators. *Proc Biol Sci* **281**. (doi:10.1098/rspb.2014.0558).
116. Godfray H.C., Blacquiere T., Field L.M., Hails R.S., Potts S.G., Raine N.E., Vanbergen A.J., McLean A.R. 2015 A restatement of recent advances in the natural science evidence base concerning neonicotinoid insecticides and insect pollinators. *Proc Biol Sci* **282**, 20151821. (doi:10.1098/rspb.2015.1821).
117. Godfray H.C.J., Stephens A.E.A., Jepson P.D., Jobling S., Johnson A.C., Matthiessen P., Sumpter J.P., Tyler C.R., McLean A.R. 2019 A restatement of the natural science evidence base on the effects of endocrine disrupting chemicals on wildlife. *Proc Biol Sci* **286**, 20182416. (doi:10.1098/rspb.2018.2416).
118. Gormley F.J., Little C.L., Rawal N., Gillespie I.A., Lebaigue S., Adak G.K. 2011 A 17-year review of foodborne outbreaks: describing the continuing decline in England and Wales (1992-2008). *Epidemiol Infect* **139**, 688-699. (doi:10.1017/s0950268810001858).
119. Gregory E., Barnhart H., Dreesen D.W., Stern N.J., Corn J.L. 1997 Epidemiological study of *Campylobacter* spp. in broilers: Source, time of colonization, and prevalence. *Avian Diseases* **41**, 890-898. (doi:Doi 10.2307/1592343).
120. Griekspoor P., Colles F.M., McCarthy N.D., Hansbro P.M., Ashhurst-Smith C., Olsen B., Hasselquist D., Maiden M.C., Waldenstrom J. 2013 Marked host specificity and lack of phylogeographic population structure of *Campylobacter jejuni* in wild birds. *Mol Ecol* **22**, 1463-1472. (doi:10.1111/mec.12144).
121. Griekspoor P., Hansbro P.M., Waldenstrom J., Olsen B. 2015 *Campylobacter jejuni* sequence types show remarkable spatial and temporal stability in Blackbirds. *Infect Ecol Epidemiol* **5**, 28383. (doi:10.3402/iee.v5.28383).
122. Gunther N.W.t., Phillips J.G., Sommers C. 2016 The Effects of 405-nm Visible Light on the Survival of *Campylobacter* on Chicken Skin and Stainless Steel. *Foodborne Pathog Dis* **13**, 245-250. (doi:10.1089/fpd.2015.2084).
123. Guyard-Nicodeme M., Keita A., Quesne S., Amelot M., Poezevara T., Le Berre B., Sanchez J., Vesseur P., Martin A., Medel P., et al. 2016 Efficacy of feed additives

against *Campylobacter* in live broilers during the entire rearing period. *Poult Sci* **95**, 298-305. (doi:10.3382/ps/pev303).

124. Halbert L.W., Kaneene J.B., Ruegg P.L., Warnick L.D., Wells S.J., Mansfield L.S., Fossler C.P., Campbell A.M., Geiger-Zwald A.M. 2006 Evaluation of antimicrobial susceptibility patterns in *Campylobacter* spp isolated from dairy cattle and farms managed organically and conventionally in the midwestern and northeastern United States. *J Am Vet Med Assoc* **228**, 1074-1081. (doi:10.2460/javma.228.7.1074).
125. Hald B., Rattenborg E., Madsen M. 2001 Role of batch depletion of broiler houses on the occurrence of *Campylobacter* spp. in chicken flocks. *Lett Appl Microbiol* **32**, 253-256. (doi:10.1046/j.1472-765x.2001.00896.x).
126. Hald B., Skovgard H., Bang D.D., Pedersen K., Dybdahl J., Jespersen J.B., Madsen M. 2004 Flies and *Campylobacter* infection of broiler flocks. *Emerging Infectious Diseases* **10**, 1490-1492. (doi:10.3201/eid1008.040129).
127. Hald B., Sommer H.M., Skovgard H. 2007 Use of fly screens to reduce *Campylobacter* spp, introduction in broiler houses. *Emerging Infectious Diseases* **13**, 1951-1953.
128. Hald T., Aspinall W., Devleesschauwer B., Cooke R., Corrigan T., Havelaar A.H., Gibb H.J., Torgerson P.R., Kirk M.D., Angulo F.J., et al. 2016 World Health Organization Estimates of the Relative Contributions of Food to the Burden of Disease Due to Selected Foodborne Hazards: A Structured Expert Elicitation. *PLoS One* **11**, e0145839. (doi:10.1371/journal.pone.0145839).
129. Hampton T. 2013 Report reveals scope of US antibiotic resistance threat. *JAMA* **310**, 1661-1663. (doi:10.1001/jama.2013.280695).
130. Han K., Jang S.S., Choo E., Heu S., Ryu S. 2007 Prevalence, genetic diversity, and antibiotic resistance patterns of *Campylobacter jejuni* from retail raw chickens in Korea. *International Journal of Food Microbiology* **114**, 50-59. (doi:10.1016/j.ijfoodmicro.2006.10.042).
131. Han Z., Willer T., Pielsticker C., Gerzova L., Rychlik I., Rautenschlein S. 2016 Differences in host breed and diet influence colonization by *Campylobacter jejuni* and induction of local immune responses in chicken. *Gut Pathog* **8**, 56. (doi:10.1186/s13099-016-0133-1).
132. Hanning I., Donoghue D.J., Jarquin R., Kumar G.S., Aguiar V.F., Metcalf J.H., Reyes-Herrera I., Slavik M. 2009 *Campylobacter* biofilm phenotype exhibits reduced colonization potential in young chickens and altered in vitro virulence. *Poult Sci* **88**, 1102-1107. (doi:10.3382/ps.2008-00307).
133. Hansson I., Ederoth M., Andersson L., Vagsholm I., Olsson Engvall E. 2005 Transmission of *Campylobacter* spp. to chickens during transport to slaughter. *J Appl Microbiol* **99**, 1149-1157. (doi:10.1111/j.1365-2672.2005.02689.x).
134. Hansson I., Vagsholm I., Svensson L., Olsson Engvall E. 2007 Correlations between *Campylobacter* spp. prevalence in the environment and broiler flocks. *J Appl Microbiol* **103**, 640-649. (doi:10.1111/j.1365-2672.2007.03291.x).
135. Hansson I., Nyman A., Lahti E., Gustafsson P., Olsson Engvall E.. 2015 Associations between *Campylobacter* levels on chicken skin, underlying muscle, caecum and packaged fillets. *Food Microbiol*. **48**, 178-181. (doi: 10.1016/j.fm.2014.12.013).
136. Harrison D., Corry J.E.L., Tchorzewska M.A., Morris V.K., Hutchison M.L. 2013 Freezing as an intervention to reduce the numbers of campylobacters isolated from chicken livers. *Letters in Applied Microbiology* **57**, 206-213. (doi:10.1111/lam.12098).

137. Hastings R., Colles F.M., McCarthy N.D., Maiden M.C.J., Sheppard S.K. 2010 *Campylobacter* genotypes from poultry transportation crates indicate source of contamination and transmission. *J. Appl. Microbiol.* **110**, 266-276. (doi: 10.1111/j.1365.2010.04883.z).
138. Haughton P.N., Lyng J., Fanning S., Whyte P. 2013 Potential of a commercially available water acidification product for reducing *Campylobacter* in broilers prior to slaughter. *Br Poult Sci* **54**, 319-324. (doi:10.1080/00071668.2013.786806).
139. Haughton P.N., Lyng J., Cronin D., Fanning S., Whyte P. 2012. Effect of crust freezing applied alone and in combination with ultraviolet light on the survival of *Campylobacter* on raw chicken. *Food. Microbiol*. **32**, 147-151. (doi: 10.1016/j.fn.2012.05.004).
140. Havelaar A.H., Mangen M.J., de Koeijer A.A., Bogaardt M.J., Evers E.G., Jacobs-Reitsma W.F., van Pelt W., Wagenaar J.A., de Wit G.A., van der Zee H., et al. 2007 Effectiveness and efficiency of controlling *Campylobacter* on broiler chicken meat. *Risk Anal* **27**, 831-844. (doi:10.1111/j.1539-6924.2007.00926.x).
141. Havelaar A.H., van Pelt W., Ang C.W., Wagenaar J.A., van Putten J.P.M., Gross U., Newell D.G. 2009 Immunity to *Campylobacter*: its role in risk assessment and epidemiology. *Critical Reviews in Microbiology* **35**, 1-22. (doi:10.1080/10408410802636017).
142. Havelaar A.H., Ivarsson S., Lofdahl M., Nauta M.J. 2013 Estimating the true incidence of campylobacteriosis and salmonellosis in the European Union, 2009. *Epidemiol Infect* **141**, 293-302. (doi:10.1017/s0950268812000568).
143. Havelaar A.H., Kirk M.D., Torgerson P.R., Gibb H.J., Hald T., Lake R.J., Praet N., Bellinger D.C., de Silva N.R., Gargouri N., et al. 2015 World Health Organization Global Estimates and Regional Comparisons of the Burden of Foodborne Disease in 2010. *PLoS Med* **12**, e1001923. (doi:10.1371/journal.pmed.1001923).
144. Hazards E.P.o.B. 2013 Scientific Opinion on the public health hazards to be covered by inspection of meat from sheep and goats. *EFSA Journal* **11**, 3265.
145. Helms M., Vastrup P., Gerner-Smidt P., Molbak K. 2003 Short and long term mortality associated with foodborne bacterial gastrointestinal infections: registry based study. *BMJ* **326**, 357.
146. Hiett K.L., Stern N.J., Fedorka-Cray P., Cox N.A., Musgrove M.T., Ladely S. 2002 Molecular subtype analyses of *Campylobacter* spp. from Arkansas and California poultry operations. *Appl Environ Microbiol* **68**, 6220-6236. (doi:10.1128/aem.68.12.6220-6236.2002).
147. Hilbert F., Scherwitzel M., Paulsen P., Szostak M.P. 2010 Survival of *Campylobacter jejuni* under conditions of atmospheric oxygen tension with the support of Pseudomonas spp. *Appl Environ Microbiol* **76**, 5911-5917. (doi:10.1128/aem.01532-10).
148. Hinton A., Jr., Buhr R.J., Ingram K.D. 2002 Carbohydrate-based cocktails that decrease the population of Salmonella and *Campylobacter* in the crop of broiler chickens subjected to feed withdrawal. *Poult Sci* **81**, 780-784. (doi:10.1093/ps/81.6.780).
149. Holland D. and Mahmoudzadeh N. 2020 Foodborne Disease Estimates for the United Kingdom in 2018. UK Food Standards Agency. https://www.food.gov.uk/sites/default/files/media/document/foodborne-disease-estimates-for-the-united-kingdom-in-2018_0.pdf

150. Holland D., Thomson L., Mahmoudzadeh N., Khaled A. 2020 Estimating deaths from foodborne disease in the UK for the 11 key pathogens. *BMJ Open Gastroenterol*. **7**, e000377. (doi:10.1136/bmjgast-2020-000377).
151. Hudson J.A., Nicol C., Wright J., Whyte R., Hasell S.K. 1999 Seasonal variation of *Campylobacter* types from human cases, veterinary cases, raw chicken, milk and water. *Journal of Applied Microbiology* **87**, 115-124. (doi:10.1046/j.1365-2672.1999.00806.x).
152. Hughes L.A., Bennett M., Coffey P., Elliott J., Jones T.R., Jones R.C., Lahuerta-Marin A., Leatherbarrow A.H., McNiffe K., Norman D., et al. 2009 Molecular Epidemiology and Characterization of *Campylobacter* spp. Isolated from Wild Bird Populations in Northern England. *Applied and Environmental Microbiology* **75**, 3007-3015. (doi:10.1128/AEM.02458-08).
153. Humphrey S., Chaloner G., Kemmett K., Davidson N., Williams N., Kipar A., Humphrey T., Wigley P. 2014 *Campylobacter jejuni* is not merely a commensal in commercial broiler chickens and affects bird welfare. *MBio* **5**, e01364-01314. (doi:10.1128/mBio.01364-14).
154. Humphrey T. 2006 Are happy chickens safer chickens? Poultry welfare and disease susceptibility. *Br Poult Sci* **47**, 379-391. (doi:10.1080/00071660600829084).
155. Humphrey T., O'Brien S., Madsen M. 2007 Campylobacters as zoonotic pathogens: a food production perspective. *International Journal of Food Microbiology* **117**, 237-257. (doi:10.1016/j.ijfoodmicro.2007.01.006).
156. Huneau-Salaun A., Denis M., Balaine L., Salvat G. 2007 Risk factors for *Campylobacter* spp. colonization in French free-range broiler-chicken flocks at the end of the indoor rearing period. *Prev Vet Med* **80**, 34-48. (doi:10.1016/j.prevetmed.2007.02.001).
157. Idris U., Lu J.R., Maier M., Sanchez S., Hofacre C.L., Harmon B.G., Maurer J.J., Lee M.D. 2006 Dissemination of fluoroquinolone-resistant *Campylobacter* spp. within an integrated commercial poultry production system. *Applied and Environmental Microbiology* **72**, 3441-3447. (doi:10.1128/Aem.72.5.3441-3447.2006).
158. Ijaz U.Z., Sivaloganathan L., McKenna A., Richmond A., Kelly C., Linton M., Stratakos A.C., Lavery U., Elmi A., Wren B.W., et al. 2018 Comprehensive Longitudinal Microbiome Analysis of the Chicken Cecum Reveals a Shift From Competitive to Environmental Drivers and a Window of Opportunity for *Campylobacter*. *Front Microbiol* **9**, 2452. (doi:10.3389/fmicb.2018.02452).
159. Iovine N.M. 2013 Resistance mechanisms in *Campylobacter jejuni* . *Virulence* **4**, 230-240. (doi:10.4161/viru.23753).
160. Jacobs-Reitsma W.F., van de Giessen A.W., Bolder N.M., Mulder R.W. 1995 Epidemiology of *Campylobacter* spp. at two Dutch broiler farms. *Epidemiol Infect* **114**, 413-421. (doi:10.1017/s0950268800052122).
161. Jansen W., Reich F., Klein G. 2014 Large-scale feasibility of organic acids as a permanent preharvest intervention in drinking water of broilers and their effect on foodborne *Campylobacter* spp. before processing. *Journal of Applied Microbiology* **116**, 1676-1687. (doi:10.1111/jam.12490).
162. Janssen R., Krogfelt K.A., Cawthraw S.A., van Pelt W., Wagenaar J.A., Owen R.J. 2008 Host-pathogen interactions in *Campylobacter* infections: the host perspective. *Clin Microbiol Rev* **21**, 505-518. (doi:10.1128/CMR.00055-07).

163. Johnson T.J., Shank J.M., Johnson J.G. 2017 Current and Potential Treatments for Reducing *Campylobacter* Colonization in Animal Hosts and Disease in Humans. *Front Microbiol* **8**, 487. (doi:10.3389/fmicb.2017.00487).
164. Jordan F., Pattison M., Alexander D., Faragher T. 2002 Poultry Diseases, 5th Edition. London, WB Saunders, Harcourt Publishers Ltd.
165. Jorgensen F., Ellis-Iversen J., Rushton S., Bull S.A., Harris S.A., Bryan S.J., Gonzalez A., Humphrey T.J. 2011 Influence of season and geography on *Campylobacter jejuni* and C. *coli* subtypes in housed broiler flocks reared in Great Britain. *Appl Environ Microbiol* **77**, 3741-3748. (doi:10.1128/aem.02444-10).
166. Jorgensen G., Charlett A., Swift C., Corcionivoschi N., Elviss N.C. 2019, A microbiological survey of *Campylobacter* contamination in fresh whole UK-produces chilled chickens at retail sale, FSA Project FS102121, Year 4 Report. https://www.food.gov.uk/research/foodborne-disease/a-microbiological-survey-of-campylobacter-contamination-in-fresh-whole-uk-produced-chilled-chickens-at-retail-sale-y234
167. Kaakoush N.O., Castaño-Rodríguez N., Mitchell H.M., Man S.M. 2015 Global Epidemiology of *Campylobacter* Infection. *Clinical Microbiology Reviews* **28**, 687-720. (doi:10.1128/CMR.00006-15).
168. Kaiser P., Howell M.M., Fife M., Sadeyen J.R., Salmon N., Rothwell L., Young J., Poh T.Y., Stevens M., Smith J., et al. 2009 Towards the selection of chickens resistant to *Salmonella* and *Campylobacter* infections. *Bull Mem Acad R Med Belg* **164**, 17-25; discussion 25-16.
169. Kapperud G., Espeland G., Wahl E., Walde A., Herikstad H., Gustavsen S., Tveit I., Natas O., Bevanger L., Digranes A. 2003 Factors associated with increased and decreased risk of *Campylobacter* infection: a prospective case-control study in Norway. *Am J Epidemiol* **158**, 234-242. (DOI:10.1093/AJE/KWG139)
170. Katsma W.E., De Koeijer A.A., Jacobs-Reitsma W.F., Mangen M.J., Wagenaar J.A. 2007 Assessing interventions to reduce the risk of *Campylobacter* prevalence in broilers. *Risk Anal* **27**, 863-876. (doi:10.1111/j.1539-6924.2007.00928.x).
171. Keegan V.A., Majowicz S.E., Pearl D.L., Marshall B.J., Sittler N., Knowles L., Wilson J.B. 2009 Epidemiology of enteric disease in C-EnterNet's pilot site - Waterloo region, Ontario, 1990 to 2004. *Can J Infect Dis Med Microbiol* **20**, 79-87. (doi: 10.1155/2009/978784)
172. Keithlin J., Sargeant J., Thomas M.K., Fazil A. 2014 Systematic review and meta-analysis of the proportion of *Campylobacter* cases that develop chronic sequelae. *BMC Public Health* **14**, 1203. (doi:10.1186/1471-2458-14-1203).
173. Kirk M.D., Pires S.M., Black R.E., Caipo M., Crump J.A., Devleesschauwer B., Dopfer D., Fazil A., Fischer-Walker C.L., Hald T., et al. 2015 World Health Organization Estimates of the Global and Regional Disease Burden of 22 Foodborne Bacterial, Protozoal, and Viral Diseases, 2010: A Data Synthesis. *PLoS Med* **12**, e1001921. (doi:10.1371/journal.pmed.1001921).
174. Klein G., Jansen W., Kittler S., Reich F. 2015 Mitigation strategies for *Campylobacter* spp. in broiler at pre-harvest and harvest level. *Berl Munch Tierarztl Wochenschr* **128**, 132-140.
175. Koolman L., Whyte P., Bolton D.J. 2014 An investigation of broiler caecal *Campylobacter* counts at first and second thinning. *Journal of Applied Microbiology* **117**, 876-881. (doi:10.1111/jam.12580).

176. Kovanen S., Kivisto R., Llarena A.K., Zhang J., Karkkainen U.M., Tuuminen T., Uksila J., Hakkinen M., Rossi M., Hanninen M.L. 2016 Tracing isolates from domestic human *Campylobacter jejuni* infections to chicken slaughter batches and swimming water using whole-genome multilocus sequence typing. *International Journal of Food Microbiology* **226**, 53-60. (doi:10.1016/j.ijfoodmicro.2016.03.009).
177. Kovanen S.M., Kivisto R.I., Rossi M., Schott T., Karkkainen U.M., Tuuminen T., Uksila J., Rautelin H., Hanninen M.L. 2014 Multilocus sequence typing (MLST) and whole-genome MLST of *Campylobacter jejuni* isolates from human infections in three districts during a seasonal peak in Finland. *J Clin Microbiol* **52**, 4147-4154. (doi:10.1128/jcm.01959-14).
178. Kovats R.S., Edwards S.J., Charron D., Cowden J., D'Souza R.M., Ebi K.L., Gauci C., Gerner-Smidt P., Hajat S., Hales S., et al. 2005 Climate variability and *Campylobacter* infection: an international study. *Int J Biometeorol* **49**, 207-214. (doi:10.1007/s00484-004-0241-3).
179. Kuhn K, Hvass A, Christiansen A, Ethelberg S, Cowan S. 2021 Sexual Contact as Risk Factor for *Campylobacter* Infection, Denmark. Emerg Infect Dis. **27**(4):1133-1140. (doi:10.3201/eid2704.202337)
180. Ladely S.R., Harrison M.A., Fedorka-Cray P.J., Berrang M.E., Englen M.D., Meinersmann R.J. 2007 Development of Macrolide-Resistant *Campylobacter* in Broilers Administered Subtherapeutic or Therapeutic Concentrations of Tylosin. *Journal of Food Protection* **70**, 1945-1951. (doi:http://dx.doi.org/10.4315/0362-028X-70.8.1945).
181. Lahti E., Lofdahl M., Agren J., Hansson I., Olsson Engvall E. 2017 Confirmation of a Campylobacteriosis Outbreak Associated with Chicken Liver Pate Using PFGE and WGS. *Zoonoses Public Health* **64**, 14-20. (doi:10.1111/zph.12272).
182. Lajhar S.A., Jennison A.V., Patel B., Duffy L.L. 2015 Comparison of epidemiologically linked *Campylobacter jejuni* isolated from human and poultry sources. *Epidemiol Infect* **143**, 3498-3509. (doi:10.1017/S0950268815000886).
183. Lal A., Hales S., French N., Baker M.G. 2012 Seasonality in human zoonotic enteric diseases: a systematic review. *PLoS One* **7**, e31883. (doi:10.1371/journal.pone.0031883).
184. Larson C.L., Shah D.H., Dhillon A.S., Call D.R., Ahn S., Haldorson G.J., Davitt C., Konkel M.E. 2008 *Campylobacter jejuni* invade chicken LMH cells inefficiently and stimulate differential expression of the chicken CXCLi1 and CXCLi2 cytokines. *Microbiology* **154**, 3835-3847. (doi:10.1099/mic.0.2008/021279-0).
185. Lee A., Smith S.C., Coloe P.J. 1998 Survival and growth of *Campylobacter jejuni* after artificial inoculation onto chicken skin as a function of temperature and packaging conditions. *Journal of Food Protection* **61**, 1609-1614. (10.4315/0362-028X-61.12.1609)
186. Lehner Y., Reich F., Klein G. 2014 Influence of process parameter on *Campylobacter* spp. counts on poultry meat in a slaughterhouse environment. *Curr Microbiol* **69**, 240-244. (doi:10.1007/s00284-014-0575-y).
187. Levesque S., Fournier E., Carrier N., Frost E., Arbeit R.D., Michaud S. 2013 Campylobacteriosis in urban versus rural areas: a case-case study integrated with molecular typing to validate risk factors and to attribute sources of infection. *PLoS One* **8**, e83731. (doi:10.1371/journal.pone.0083731).

188. Lin J., Yan M., Sahin O., Pereira S., Chang Y.J., Zhang Q. 2007 Effect of macrolide usage on emergence of erythromycin-resistant *Campylobacter* isolates in chickens. *Antimicrob Agents Chemother* **51**, 1678-1686. (doi:10.1128/AAC.01411-06).
189. Line J., Hiett K., Conlan A. 2008 Comparison of challenge models for determining the colonization dose of *Campylobacter jejuni* in broiler chicks. *Poult Sci* **87**, 1700-1706. (doi:10.3382/ps.2008-00027).
190. Line J.E., Bailey J.S., Cox N.A., Stern N.J. 1997 Yeast treatment to reduce *Salmonella* and *Campylobacter* populations associated with broiler chickens subjected to transport stress. *Poult Sci* **76**, 1227-1231. (doi:10.1093/ps/76.9.1227).
191. Line J.E., Bailey J.S. 2006 Effect of on-farm litter acidification treatments on *Campylobacter* and *Salmonella* populations in commercial broiler houses in northeast Georgia. *Poult Sci* **85**, 1529-1534. (doi:10.1093/ps/85.9.1529).
192. Little C.L., Gormley F.J., Rawal N., Richardson J.F. 2010 A recipe for disaster: outbreaks of campylobacteriosis associated with poultry liver pate in England and Wales. *Epidemiology and Infection* **138**, 1691-1694. (doi:10.1017/S0950268810001974).
193. Little C.L., Richardson J.F., Owen R.J., de Pinna E., Threlfall E.J. 2008 *Campylobacter* and *Salmonella* in raw red meats in the United Kingdom: prevalence, characterization and antimicrobial resistance pattern, 2003-2005. *Food Microbiol.* **25**, 538-543. (doi: 10.1016/j.fm.2008.01.001).
194. Logue C.M., Danzeisen G.T., Sherwood J.S., Thorsness J.L., Mercier B.M., Axtman J.E. 2010 Repeated therapeutic dosing selects macrolide-resistant *Campylobacter* spp. in a turkey facility. *J Appl Microbiol* **109**, 1379-1388. (doi:10.1111/j.1365-2672.2010.04765.x).
195. Louis V.R., Gillespie I.A., O'Brien S.J., Russek-Cohen E., Pearson A.D., Colwell R.R. 2005 Temperature-driven *Campylobacter* seasonality in England and Wales. *Appl Environ Microbiol* **71**, 85-92. (doi:10.1128/aem.71.1.85-92.2005).
196. Luangtongkum T., Morishita T.Y., Ison A.J., Huang S., McDermott P.F., Zhang Q. 2006 Effect of conventional and organic production practices on the prevalence and antimicrobial resistance of *Campylobacter* spp. in poultry. *Appl Environ Microbiol* **72**, 3600-3607. (doi:10.1128/AEM.72.5.3600-3607.2006).
197. Luangtongkum T., Jeon B., Han J., Plummer P., Logue C.M., Zhang Q. 2009 Antibiotic resistance in *Campylobacter*: emergence, transmission and persistence. *Future Microbiol* **4**, 189-200. (doi:10.2217/17460913.4.2.189).
198. Luber P., Bartelt E. 2007 Enumeration of *Campylobacter* spp. on the surface and within chicken breast fillets. *J Appl Microbiol* **102**, 313-318. (doi:10.1111/j.1365-2672.2006.03105.x).
199. Luo N., Sahin O., Lin J., Michel L.O., Zhang Q. 2003 In vivo selection of *Campylobacter* isolates with high levels of fluoroquinolone resistance associated with gyrA mutations and the function of the CmeABC efflux pump. *Antimicrob Agents Chemother* **47**, 390-394. (doi:10.1128/AAC.47.1.390-394.2003).
200. Luo N., Pereira S., Sahin O., Lin J., Huang S., Michel L., Zhang Q. 2005 Enhanced in vivo fitness of fluoroquinolone-resistant *Campylobacter jejuni* in the absence of antibiotic selection pressure. *Proc Natl Acad Sci U S A* **102**, 541-546. (doi:10.1073/pnas.0408966102).
201. MacDonald E., White R., Mexia R., Bruun T., Kapperud G., Lange H., Nygard K., Vold L. 2015 Risk Factors for Sporadic Domestically Acquired *Campylobacter* Infections in

Norway 2010-2011: A National Prospective Case-Control Study. *PLoS One* **10**, e0139636. (doi:10.1371/journal.pone.0139636).

202. MacRitchie L.A., Hunter C.J., Strachan N.J. 2013 A population-based exposure assessment of risk factors associated with gastrointestinal pathogens: a *Campylobacter* study. *Epidemiol Infect* **141**, 976-986. (doi:10.1017/s0950268812001641).
203. Maiden M., Dingle K.E. 2008 Population biology of *Campylobacter jejuni* and related organisms. In *Campylobacter, Third Edition* (eds. Nachamkin I., Szymanski C., Blaser M.J.), pp. 27-40. Washington, DC, ASM Science.
204. Man S.M. 2011 The clinical importance of emerging *Campylobacter* species. *Nat Rev Gastroenterol Hepatol* **8**, 669-685. (doi:10.1038/nrgastro.2011.191).
205. Manes-Lazaro R., Van Diemen P.M., Pin C., Mayer M.J., Stevens M.P., Narbad A. 2017 Administration of *Lactobacillus johnsonii* FI9785 to chickens affects colonisation by *Campylobacter jejuni* and the intestinal microbiota. *Br Poult Sci* **58**, 373-381. (doi:10.1080/00071668.2017.1307322).
206. McCarthy N., Giesecke J. 2001 Incidence of Guillain-Barre syndrome following infection with *Campylobacter jejuni* . *Am J Epidemiol* **153**, 610-614. (doi:10.1093/aje/153.6.610).
207. McCarthy N.D., Gillespie I.A., Lawson A.J., Richardson J., Neal K.R., Hawtin P.R., Maiden M.C., O'Brien S.J. 2012 Molecular epidemiology of human *Campylobacter jejuni* shows association between seasonal and international patterns of disease. *Epidemiol Infect* **140**, 2247-2255. (doi:10.1017/S0950268812000192).
208. McCrea B.A., Tonooka K.H., VanWorth C., Boggs C.L., Atwill E.R., Schrader J.S. 2006 Prevalence of *Campylobacter* and *Salmonella* species on farm, after transport, and at processing in specialty market poultry. *Poult Sci* **85**, 136-143. (doi:10.1093/ps/85.1.136).
209. McDowell S.W., Menzies F.D., McBride S.H., Oza A.N., McKenna J.P., Gordon A.W., Neill S.D. 2008 *Campylobacter* spp. in conventional broiler flocks in Northern Ireland: epidemiology and risk factors. *Prev Vet Med* **84**, 261-276. (doi:10.1016/j.prevetmed.2007.12.010).
210. McLean A.R., Adlen E.K., Cardis E., Elliott A., Goodhead D.T., Harms-Ringdahl M., Hendry J.H., Hoskin P., Jeggo P.A., Mackay D.J.C., et al. 2017 A restatement of the natural science evidence base concerning the health effects of low-level ionizing radiation. *Proc Biol Sci* **284**. (doi:10.1098/rspb.2017.1070).
211. Medema G.J., Teunis P.F., Havelaar A.H., Haas C.N. 1996 Assessment of the dose-response relationship of *Campylobacter jejuni*. *International Journal of Food Microbiology* **30**, 101-111.
212. Meerburg B.G., Kijlstra A. 2007 Role of rodents in transmission of *Salmonella* and *Campylobacter*. **87**, 2774-2781. (doi:10.1002/jsfa.3004).
213. Meredith H., Valdramidis V., Rotabakk B.T., Sivertsvik M., McDowell D., Bolton D.J. 2014 Effect of different modified atmospheric packaging (MAP) gaseous combinations on *Campylobacter* and the shelf-life of chilled poultry fillets. *Food Microbiol* **44**, 196-203. (doi:10.1016/j.fm.2014.06.005).
214. Messens W., Herman L., De Zutter L., Heyndrickx M. 2009 Multiple typing for the epidemiological study of contamination of broilers with thermotolerant *Campylobacter*. *Veterinary Microbiology* **138**, 120-131. (doi:https://doi.org/10.1016/j.vetmic.2009.02.012).

215. Meunier M., Guyard-Nicodeme M., Dory D., Chemaly M. 2016 Control strategies against *Campylobacter* at the poultry production level: biosecurity measures, feed additives and vaccination. *Journal of Applied Microbiology* **120**, 1139-1173. (doi:10.1111/jam.12986).
216. Mihaljevic R.R., Sikic M., Klancnik A., Brumini G., Mozina S.S., Abram M. 2007 Environmental stress factors affecting survival and virulence of *Campylobacter jejuni* . *Microb Pathog* **43**, 120-125. (doi:10.1016/j.micpath.2007.03.004).
217. Milnes A.S., Stewart I., Clifton-Hadley F.A., Davies R.H., Newell D.G., Sayers A.R., Cheasty T., Cassar C., Ridley A., Cook A.J.C., et al. 2008 Intestinal carriage of verocytotoxigenic *Escherichia coli* O157, *Salmonella*, thermophilic *Campylobacter* and *Yersinia enterocolitica*, in cattle, sheep and pigs at slaughter in Great Britain during 2003. *Epidemiology and Infection* **136**, 739-751. (doi:10.1017/S0950268807009223).
218. Moffatt C.R., Greig A., Valcanis M., Gao W., Seemann T., Howden B.P., Kirk M.D. 2016 A large outbreak of *Campylobacter jejuni* infection in a university college caused by chicken liver pate, Australia, 2013. *Epidemiol Infect* **144**, 2971-2978. (doi:10.1017/s0950268816001187).
219. Moffatt C.R., Glass K., Stafford R., D'Este C., Kirk M.D. 2017 The campylobacteriosis conundrum - examining the incidence of infection with *Campylobacter* sp. in Australia, 1998-2013. *Epidemiol Infect* **145**, 839-847. (doi:10.1017/S0950268816002909).
220. Moore J.E., Barton M.D., Blair I.S., Corcoran D., Dooley J.S., Fanning S., Kempf I., Lastovica A.J., Lowery C.J., Matsuda M., et al. 2006 The epidemiology of antibiotic resistance in *Campylobacter*. *Microbes Infect* **8**, 1955-1966. (doi:10.1016/j.micinf.2005.12.030).
221. Mourkas E., Florez-Cuadrado D., Pascoe B., Calland J.K., Bayliss, S.C., Mageiros L., Méric, G., Hitchings M.D., Quesada A., Porrero C., Ugarte-Ruiz M., Gutiérrez-Fernández J., Domínguez L., Sheppard, S.K. 2019 Gene pool transmission of multidrug resistance among *Campylobacter* from livestock, sewage and human disease. *Environ. Microbiol.*, **21**, 4597-4613. (doi: 10.1111/1462-2920.14760)
222. Mourkas E., Taylor A.J., Meric G., Bayliss S.C., Pascoe B., Mageiros L., Calland J.K., Hitchings M.D., Ridley A., Vidal A., Forbes K.J., Strachan N.J.C., Parker C.T., Parkhill J., Jolley K. A., Cody A.J., Maiden M.C.J., Kelly D.J., Sheppard S.K. 2020 Agricultural intensification and the evolution of host specialism in the enteric *Campylobacter jejuni* . *PNAS*, **117**, 11018-11028. (doi: 10.1073/pnas.1917168117).
223. Mossong J., Mughini-Gras L., Penny C., Devaux A., Olinger C., Losch S., Cauchie H.M., van Pelt W., Ragimbeau C. 2016 Human Campylobacteriosis in Luxembourg, 2010-2013: A Case-Control Study Combined with Multilocus Sequence Typing for Source Attribution and Risk Factor Analysis. *Sci Rep* **6**, 20939. (doi:10.1038/srep20939).
224. Mughini Gras L., Smid J.H., Wagenaar J.A., de Boer A.G., Havelaar A.H., Friesema I.H., French N.P., Busani L., van Pelt W. 2012 Risk factors for campylobacteriosis of chicken, ruminant, and environmental origin: a combined case-control and source attribution analysis. *PLoS One* **7**, e42599. (doi:10.1371/journal.pone.0042599).
225. Mughini-Gras L., Pijnacker R., Coipan C., Mulder A. C. *et al*. 2021 Sources and transmission routes of campylobacteriosis: a combine analysis of genome and exposure data. *J. Infect.* **82**, 216-226. (doi: 10.1016/j.jinf.2020.09.039).
226. Mungai E.A., Behravesh C.B., Gould L.H. 2015 Increased outbreaks associated with nonpasteurized milk, United States, 2007-2012. *Emerging Infectious Diseases* **21**, 119-122. (doi:10.3201/eid2101.140447).

227. Musavian H.S., Krebs N.H., Nonboe U., Corry J.E., Purnell G. 2014 Combined steam and ultrasound treatment of broilers at slaughter: a promising intervention to significantly reduce numbers of naturally occurring campylobacters on carcasses. *International Journal of Food Microbiology* **176**, 23-28. (doi:10.1016/j.ijfoodmicro.2014.02.001).
228. Mylius S.D., Nauta M.J., Havelaar A.H. 2007 Cross-contamination during food preparation: a mechanistic model applied to chicken-borne *Campylobacter*. *Risk Anal* **27**, 803-813. (doi:10.1111/j.1539-6924.2006.00872.x).
229. Nauta M., Hill A., Rosenquist H., Brynestad S., Fetsch A., van der Logt P., Fazil A., Christensen B., Katsma E., Borck B., et al. 2009 A comparison of risk assessments on *Campylobacter* in broiler meat. *International Journal of Food Microbiology* **129**, 107-123. (doi:10.1016/j.ijfoodmicro.2008.12.001).
230. Neal K.R., Slack R.C. 1995 The autumn peak in *Campylobacter* gastro-enteritis. Are the risk factors the same for travel- and UK-acquired *Campylobacter* infections? *J Public Health Med* **17**, 98-102. (http://www.jstor.org/stable/45160592)
231. Neubauer C., Hess M. 2006 Detection and identification of food-borne pathogens of the genera *Campylobacter, Arcobacter* and *Helicobacter* by multiplex PCR in poultry and poultry products. *J Vet Med B Infect Dis Vet Public Health* **53**, 376-381. (doi:10.1111/j.1439-0450.2006.00991.x).
232. Newell D.G., Fearnley C. 2003 Sources of *Campylobacter* Colonization in Broiler Chickens. *Appl Environ Microbiol* **69**, 4343-4351. (doi: 10.1128/AEM.69.8.4343-4351.2003)
233. Newell D.G., Elvers K.T., Dopfer D., Hansson I., Jones P., James S., Gittins J., Stern N.J., Davies R., Connerton I., et al. 2011 Biosecurity-based interventions and strategies to reduce *Campylobacter* spp. on poultry farms. *Appl Environ Microbiol* **77**, 8605-8614. (doi:10.1128/AEM.01090-10).
234. Nguyen H.T., Corry J.E., Miles C.A. 2006 Heat resistance and mechanism of heat inactivation in thermophilic campylobacters. *Appl Environ Microbiol* **72**, 908-913. (doi:10.1128/aem.72.1.908-913.2006).
235. Nichols G.L. 2005 Fly transmission of *Campylobacter*. *Emerging Infectious Diseases* **11**, 361-364. (doi:10.3201/eid1103.040460).
236. Nichols G.L., Richardson J.F., Sheppard S.K., Lane C., Sarran C. 2012 *Campylobacter* epidemiology: a descriptive study reviewing 1 million cases in England and Wales between 1989 and 2011. *BMJ Open* **2**. (doi:10.1136/bmjopen-2012-001179).
237. Nicholson F.A., Groves S.J., Chambers B.J. 2005 Pathogen survival during livestock manure storage and following land application. *Bioresour Technol* **96**, 135-143. (doi:10.1016/j.biortech.2004.02.030).
238. Nylen G., Dunstan F., Palmer S.R., Andersson Y., Bager F., Cowden J., Feierl G., Galloway Y., Kapperud G., Megraud F., et al. 2002 The seasonal distribution of *Campylobacter* infection in nine European countries and New Zealand. *Epidemiol Infect* **128**, 383-390. (doi:DOI: 10.1017}S0950268802006830).
239. O'Brien S.J., Larose T.L., Adak G.K., Evans M.R., Tam C.C., Foodborne Disease Attribution Study G. 2016 Modelling study to estimate the health burden of foodborne diseases: cases, general practice consultations and hospitalisations in the UK, 2009. *BMJ Open* **6**, e011119. (doi:10.1136/bmjopen-2016-011119).
240. O'Brien S.J. 2017 The consequences of *Campylobacter* infection. *Curr Opin Gastroenterol* **33**, 14-20. (doi:10.1097/MOG.0000000000000329).

241. O'Mahony E., Buckley J.F., Bolton D., Whyte P., Fanning S. 2011 Molecular epidemiology of *Campylobacter* isolates from poultry production units in southern Ireland. *PLoS One* **6**, e28490. (doi:10.1371/journal.pone.0028490).
242. Oakley B.B., Vasconcelos E.J.R., Diniz P., Calloway K.N., Richardson E., Meinersmann R.J., Cox N.A., Berrang M.E. 2018 The cecal microbiome of commercial broiler chickens varies significantly by season. *Poult Sci* **97**, 3635-3644. (doi:10.3382/ps/pey214).
243. Oberhelman R.A., Gilman R.H., Sheen P., Cordova J., Taylor D.N., Zimic M., Meza R., Perez J., LeBron C., Cabrera L., et al. 2003 *Campylobacter* transmission in a Peruvian shantytown: A longitudinal study using strain typing of *Campylobacter* isolates from chickens and humans in household clusters. *Journal of Infectious Diseases* **187**, 260-269. (doi:Doi 10.1086/367676).
244. Ogden I.D., Dallas J.F., MacRae M., Rotariu O., Reay K.W., Leitch M., Thomson A.P., Sheppard S.K., Maiden M., Forbes K.J., et al. 2009 *Campylobacter* excreted into the environment by animal sources: prevalence, concentration shed, and host association. *Foodborne Pathog Dis* **6**, 1161-1170. (doi:10.1089/fpd.2009.0327).
245. Oh E., McMullen L., Jeon B. 2015 High Prevalence of Hyper-Aerotolerant *Campylobacter jejuni* in Retail Poultry with Potential Implication in Human Infection. *Front Microbiol* **6**, 1263. (doi:10.3389/fmicb.2015.01263).
246. Oh E., McMullen L.M., Chui L., Jeon B. 2017 Differential Survival of Hyper-Aerotolerant *Campylobacter jejuni* under Different Gas Conditions. *Front Microbiol* **8**, 954. (doi:10.3389/fmicb.2017.00954).
247. Ohishi T., Aoki K., Ishii Y., Usui M., Tamura Y., Kawanishi M., Ohnishi K., Tateda K. 2017 Molecular epidemiological analysis of human- and chicken-derived isolates of *Campylobacter jejuni* in Japan using next-generation sequencing. *Journal of Infection and Chemotherapy* **23**, 165-172. (doi:10.1016/j.jiac.2016.11.011).
248. OIE. 2015 OIE list of antimicrobial agents of veterinary importance. https://www.oie.int/app/uploads/2021/03/a-oie-list-antimicrobials-may2018.pdf
249. Olsen S.J., Hansen G.R., Bartlett L., Fitzgerald C., Sonder A., Manjrekar R., Riggs T., Kim J., Flahart R., Pezzino G., et al. 2001 An outbreak of *Campylobacter jejuni* infections associated with food handler contamination: The use of pulsed-field gel electrophoresis. *Journal of Infectious Diseases* **183**, 164-167. (doi:Doi 10.1086/317657).
250. Pacholewicz E., Swart A., Wagenaar J.A., Lipman L.J., Havelaar A.H. 2016 Explanatory Variables Associated with *Campylobacter* and *Escherichia coli* Concentrations on Broiler Chicken Carcasses during Processing in Two Slaughterhouses. *J Food Prot* **79**, 2038-2047. (doi:10.4315/0362-028x.Jfp-16-064).
251. Page S.W., Gautier P. 2012 Use of antimicrobial agents in livestock. *Rev sci tech* **31**, 145-188. (doi: 10.20506/rst.31.1.2106)
252. Park R.W., Griffiths P.L., Moreno G.S. 1991 Sources and survival of campylobacters: relevance to enteritis and the food industry. *Soc Appl Bacteriol Symp Ser* **20**, 97s-106s.
253. Park S.F. 2002 The physiology of *Campylobacter* species and its relevance to their role as foodborne pathogens. *International Journal of Food Microbiology* **74**, 177-188. (doi:10.1016/s0168-1605(01)00678-x).
254. Patterson M.F. 1995 Sensitivity of *Campylobacter* spp. to irradiation in poultry meat. *Lett Appl Microbiol* **20**, 338-340.

255. Payot S., Bolla J.M., Corcoran D., Fanning S., Megraud F., Zhang Q. 2006 Mechanisms of fluoroquinolone and macrolide resistance in *Campylobacter* spp. *Microbes Infect* **8**, 1967-1971. (doi:10.1016/j.micinf.2005.12.032).
256. Pearson A.D., Greenwood M., Healing T.D., Rollins D., Shahamat M., Donaldson J., Colwell R.R. 1993 Colonization of broiler chickens by waterborne *Campylobacter jejuni* . *Appl Environ Microbiol* **59**, 987-996. (doi: 10.1128/aem.59.4.987-996.1993)
257. Peters S., Pascoe B., Wu Z. *et al.* 2021 *Campylobacter jejuni* genotypes are associated with post-infection irritable bowel syndrome in humans. *Commun. Biol.* **4**, 1015. (doi: 10.1038/s42003-021-02554-8)
258. Pires S.M., Vigre H., Makela P., Hald T. 2010 Using Outbreak Data for Source Attribution of Human Salmonellosis and Campylobacteriosis in Europe. *Foodborne Pathogens and Disease* **7**, 1351-1361. (doi:10.1089/fpd.2010.0564).
259. Pogreba-Brown K., Baker A., Ernst K., Stewart J., Harris R.B., Weiss J. 2016 Assessing risk factors of sporadic *Campylobacter* infection: a case-control study in Arizona. *Epidemiol Infect* **144**, 829-839. (doi:10.1017/s0950268815002162).
260. Pope J.E., Krizova A., Garg A.X., Thiessen-Philbrook H., Ouimet J.M. 2007 *Campylobacter* reactive arthritis: a systematic review. *Semin Arthritis Rheum* **37**, 48-55. (doi:10.1016/j.semarthrit.2006.12.006).
261. Price L.B., Lackey L.G., Vailes R., Silbergeld E. 2007 The persistence of fluoroquinolone-resistant *Campylobacter* in poultry production. *Environ Health Perspect* **115**, 1035-1039. (doi:10.1289/ehp.10050).
262. Purnell G., Mattick K., Humphrey T. 2004 The use of 'hot wash' treatments to reduce the number of pathogenic and spoilage bacteria on raw retail poultry. *Journal of Food Engineering* **62**, 29-36. (doi:https://doi.org/10.1016/S0260-8774(03)00168-7).
263. Rajkovic A., Tomic N., Smigic N., Uyttendaele M., Ragaert P., Devlieghere F. 2010. Survival of *Campylobacter jejuni* on raw chicken legs packed in high-oxygen or high-carbon dioxide atmosphere after the decontamination with lactic acid/sodium lactate buffer. *Int. J. Food. Microbiol*., **140**, 201-206. (doi: 10.1016/j.ijfoodmicro.2010.03.034).
264. Ramonaite S., Kudirkiene E., Tamuleviciene E., Leviniene G., Malakauskas A., Golz G., Alter T., Malakauskas M. 2014 Prevalence and genotypes of *Campylobacter jejuni* from urban environmental sources in comparison with clinical isolates from children. *J Med Microbiol* **63**, 1205-1213. (doi:10.1099/jmm.0.072892-0).
265. Rao M.R., Naficy A.B., Savarino S.J., Abu-Elyazeed R., Wierzba T.F., Peruski L.F., Abdel-Messih I., Frenck R., Clemens J.D. 2001 Pathogenicity and Convalescent Excretion of *Campylobacter* in Rural Egyptian Children. *Am J Epidemiol* **154**, 166-173. (doi:10.1093/aje/154.2.166 %J American Journal of Epidemiology).
266. Rautelin H., Vierikko A., Hanninen M.L., Vaara M. 2003 Antimicrobial Susceptibilities of *Campylobacter* Strains Isolated from Finnish Subjects Infected Domestically or from Those Infected Abroad. *Antimicrobial Agents and Chemotherapy* **47**, 102-105. (doi:10.1128/aac.47.1.102-105.2003).
267. Redmond E.C., Griffith C.J. 2003 Consumer food handling in the home: a review of food safety studies. *J Food Prot* **66**, 130-161. (doi: 10.4315/0362-028x-66.1.130)
268. Redmond E.C., Griffith C.J. 2004 Consumer perceptions of food safety risk, control and responsibility. *Appetite* **43**, 309-313. (doi:10.1016/j.appet.2004.05.003).
269. Refregier-Petton J., Rose N., Denis M., Salvat G. 2001 Risk factors for *Campylobacter* spp. contamination in French broiler-chicken flocks at the end of the rearing period. *Prev Vet Med* **50**, 89-100. (doi:10.1016/s0167-5877(01)00220-3).

270. Refrégier-Petton J., Rose N., Denis M., Salvat G. 2001 Risk factors for *Campylobacter* spp. contamination in French broiler-chicken flocks at the end of the rearing period. *Preventive Veterinary Medicine* **50**, 89-100. (doi:10.1016/s0167-5877(01)00220-3).
271. Revez J., Llarena A.K., Schott T., Kuusi M., Hakkinen M., Kivisto R., Hanninen M.L., Rossi M. 2014a Genome analysis of *Campylobacter jejuni* strains isolated from a waterborne outbreak. *Bmc Genomics* **15**, 768. (doi:10.1186/1471-2164-15-768).
272. Revez J., Zhang J., Schott T., Kivisto R., Rossi M., Hanninen M.L. 2014b Genomic variation between *Campylobacter jejuni* isolates associated with milk-borne-disease outbreaks. *J Clin Microbiol* **52**, 2782-2786. (doi:10.1128/jcm.00931-14).
273. Ribeiro C.D., Frost J.A. 2000 Family clusters of *Campylobacter* infection. *Commun Dis Public Health* **3**, 274-276.
274. Richardson J.F., Frost J.A., Kramer J.M., Thwaites R.T., Bolton F.J., Wareing D.R., Gordon J.A. 2001 Coinfection with *Campylobacter* species: an epidemiological problem? *J Appl Microbiol* **91**, 206-211. (doi:10.1046/j.1365-2672.2001.01377.x).
275. Ricotta E.E., Palmer A., Wymore K., Clogher P., Oosmanally N., Robinson T., Lathrop S., Karr J., Hatch J., Dunn J., et al. 2014 Epidemiology and antimicrobial resistance of international travel-associated *Campylobacter* infections in the United States, 2005-2011. *Am J Public Health* **104**, e108-114. (doi:10.2105/ajph.2013.301867).
276. Riddle M.S., Guerry P. 2016 Status of vaccine research and development for *Campylobacter jejuni* . *Vaccine* **34**, 2903-2906. (doi:10.1016/j.vaccine.2016.02.080).
277. Ridley A.M., Morris V.K., Cawthraw S.A., Ellis-Iversen J., Harris J.A., Kennedy E.M., Newell D.G., Allen V.M. 2011 Longitudinal molecular epidemiological study of thermophilic campylobacters on one conventional broiler chicken farm. *Appl Environ Microbiol* **77**, 98-107. (doi:10.1128/aem.01388-10).
278. Ring M., Zychowska M.A., Stephan R. 2005 Dynamics of *Campylobacter* spp. spread investigated in 14 broiler flocks in Switzerland. *Avian Dis* **49**, 390-396. (doi:10.1637/7319-010305r1.1).
279. Rivoal K., Ragimbeau C., Salvat G., *Coli* n P., Ermel G. 2005 Genomic diversity of *Campylobacter coli* and *Campylobacter jejuni* isolates recovered from free-range broiler farms and comparison with isolates of various origins. *Appl Environ Microbiol* **71**, 6216-6227. (doi:10.1128/aem.71.10.6216-6227.2005).
280. Robinson D.A. 1981 Infective dose of *Campylobacter jejuni* in milk. *Br Med J (Clin Res Ed)* **282**, 1584. (doi:10.1136/bmj.282.6276.1584).
281. Rogol M., Sechter I., Falk H., Shtark Y., Alfi S., Greenberg Z., Mizrachi R. 1983 Waterborne outbreak of *Campylobacter enteritis*. *Eur J Clin Microbiol* **2**, 588-590. (doi: 10.1007/BF02016571)
282. Rollo S.N., Norby B., Bartlett P.C., Scott H.M., Wilson D.L., Fajt V.R., Linz J.E., Bunner C.E., Kaneene J.B., Huber J.C., Jr. 2010 Prevalence and patterns of antimicrobial resistance in *Campylobacter* spp isolated from pigs reared under antimicrobial-free and conventional production methods in eight states in the Midwestern United States. *J Am Vet Med Assoc* **236**, 201-210. (doi:10.2460/javma.236.2.201).
283. Rosenquist H., Sommer H.M., Nielsen N.L., Christensen B.B. 2006 The effect of slaughter operations on the contamination of chicken carcasses with thermotolerant *Campylobacter*. *International Journal of Food Microbiology* **108**, 226-232. (doi:10.1016/j.ijfoodmicro.2005.12.007).
284. Rosenquist H., Boysen L., Krogh A.L., Jensen A.N., Nauta M. 2013 *Campylobacter* contamination and the relative risk of illness from organic broiler meat in comparison

with conventional broiler meat. *International Journal of Food Microbiology* **162**, 226-230. (doi:10.1016/j.ijfoodmicro.2013.01.022).

285. Rosner B.M., Schielke A., Didelot X., Kops F., Breidenbach J., Willrich N., Golz G., Alter T., Stingl K., Josenhans C., et al. 2017 A combined case-control and molecular source attribution study of human *Campylobacter* infections in Germany, 2011-2014. *Sci Rep* **7**, 5139. (doi:10.1038/s41598-017-05227-x).
286. Rossler E., Signorini M.L., Romero-Scharpen A., Soto L.P., Berisvil A., Zimmermann J.A., Fusari M.L., Olivero C., Zbrun M.V., Frizzo L.S. 2019 Meta-analysis of the prevalence of thermotolerant *Campylobacter* in food-producing animals worldwide. *Zoonoses Public Health* **66**, 359-369. (doi:10.1111/zph.12558).
287. Rotariu O., Smith-Palmer A., Cowden J., Bessell P.R., Innocent G.T., Reid S.W., Matthews L., Dallas J., Ogden I.D., Forbes K.J., et al. 2010 Putative household outbreaks of campylobacteriosis typically comprise single MLST genotypes. *Epidemiol Infect* **138**, 1744-1747. (doi:10.1017/s0950268810001457).
288. Rothrock M.J., Jr., Locatelli A., Feye K.M., Caudill A.J., Guard J., Hiett K., Ricke S.C. 2019 A Microbiomic Analysis of a Pasture-Raised Broiler Flock Elucidates Foodborne Pathogen Ecology Along the Farm-To-Fork Continuum. *Front Vet Sci* **6**, 260. (doi:10.3389/fvets.2019.00260).
289. Roux F., Sproston E., Rotariu O., Macrae M., Sheppard S.K., Bessell P., Smith-Palmer A., Cowden J., Maiden M.C., Forbes K.J., et al. 2013 Elucidating the aetiology of human *Campylobacter coli* infections. *PLoS One* **8**, e64504. (doi:10.1371/journal.pone.0064504).
290. Royden A., Wedley A., Merga J.Y., Rushton S., Hald B., Humphrey T., Williams N.J. 2016 A role for flies (Diptera) in the transmission of *Campylobacter* to broilers? *Epidemiol Infect* **144**, 3326-3334. (doi:10.1017/S0950268816001539).
291. Ruiz-Palacios G.M., Escamilla E., Torres N. 1981 Experimental *Campylobacter* diarrhea in chickens. *Infect Immun* **34**, 250-255.
292. Rushton S.P., Humphrey T.J., Shirley M.D., Bull S., Jorgensen F. 2009 *Campylobacter* in housed broiler chickens: a longitudinal study of risk factors. *Epidemiol Infect* **137**, 1099-1110. (doi:10.1017/s095026880800188x).
293. Russa A.D., Bouma A., Vernooij J.C., Jacobs-Reitsma W., Stegeman J.A. 2005 No association between partial depopulation and *Campylobacter* spp. colonization of Dutch broiler flocks. *Lett Appl Microbiol* **41**, 280-285. (doi:10.1111/j.1472-765X.2005.01751.x).
294. Sahin O., Zhang Q., Meitzler J.C., Harr B.S., Morishita T.Y., Mohan R. 2001 Prevalence, antigenic specificity, and bactericidal activity of poultry anti-*Campylobacter* maternal antibodies. *Appl Environ Microbiol* **67**, 3951-3957. (doi:10.1128/aem.67.9.3951-3957.2001).
295. Sahin O., Luo N., Huang S., Zhang Q. 2003 Effect of *Campylobacter*-specific maternal antibodies on *Campylobacter jejuni* colonization in young chickens. *Appl Environ Microbiol* **69**, 5372-5379. (doi:10.1128/aem.69.9.5372-5379.2003).
296. Sahin O., Yaeger M., Wu Z., Zhang Q. 2017 *Campylobacter*-Associated Diseases in Animals. *Annu Rev Anim Biosci* **5**, 21-42. (doi:10.1146/annurev-animal-022516-022826).
297. Saint-Cyr M.J., Guyard-Nicodeme M., Messaoudi S., Chemaly M., Cappelier J.M., Dousset X., Haddad N. 2016 Recent Advances in Screening of Anti-*Campylobacter*

Activity in Probiotics for Use in Poultry. *Frontiers in Microbiology* **7**. (doi:w10.3389/fmicb.2016.00553).

298. Sakaridis I., Ellis R.J., Cawthraw S.A., van Vliet A.H.M., Stekel D.J., Penell J., Chambers M., La Ragione R.M., Cook A.J. 2018 Investigating the Association Between the Caecal Microbiomes of Broilers and *Campylobacter* Burden. **9**. (doi:10.3389/fmicb.2018.00927).
299. Sampers I., Habib I., De Zutter L., Dumoulin A., Uyttendaele M. 2010 Survival of *Campylobacter* spp. in poultry meat preparations subjected to freezing, refrigeration, minor salt concentration, and heat treatment. *International Journal of Food Microbiology* **137**, 147-153. (doi:10.1016/j.ijfoodmicro.2009.11.013).
300. Sanad Y.M., Jung K., Kashoma I., Zhang X., Kassem, II, Saif Y.M., Rajashekara G. 2014 Insights into potential pathogenesis mechanisms associated with *Campylobacter jejuni* -induced abortion in ewes. *BMC Vet Res* **10**, 274. (doi:10.1186/s12917-014-0274-8).
301. Sanyal S.C., Islam K.M., Neogy P.K., Islam M., Speelman P., Huq M.I. 1984 *Campylobacter jejuni* diarrhea model in infant chickens. *Infect Immun* **43**, 931-936.
302. Scallan Walter E.J., Crim S.M., Bruce B.B., Griffin P.M. 2019 Postinfectious Irritable Bowel Syndrome After *Campylobacter* Infection. *Am J Gastroenterol* **114**, 1649-1656. (doi:10.14309/ajg.0000000000000408).
303. Schofield BJ., Andreani NA, Günther CS, Law GR, McMahon G., Swainson M., Goddard MR. 2022 Livestock microbial landscape patterns: Retail poultry microbiomes significantly vary by region and season. *Food Microbiology* **101**, 103878 (doi:10.1016/j.fm.2021.103878).
304. Sears A., Baker M.G., Wilson N., Marshall J., Muellner P., Campbell D.M., Lake R.J., French N.P. 2011 Marked Campylobacteriosis Decline after Interventions Aimed at Poultry, New Zealand. *Emerging Infectious Diseases* **17**, 1007-1015. (doi:10.3201/eid1706.101272).
305. Seliwiorstow T., Baré J., Berkvens D., Van Damme I., Uyttendaele M., De Zutter L. 2016 Identification of risk factors for *Campylobacter* contamination levels on broiler carcasses during the slaughter process. *International Journal of Food Microbiology* **226**, 26-32. (doi:https://doi.org/10.1016/j.ijfoodmicro.2016.03.010).
306. Serichantalergs O., Dalsgaard A., Bodhidatta L., Krasaesub S., Pitarangsi C., Srijan A., Mason C.J. 2007 Emerging fluoroquinolone and macrolide resistance of *Campylobacter jejuni* and *Campylobacter coli* isolates and their serotypes in Thai children from 1991 to 2000. *Epidemiol Infect* **135**, 1299-1306. (doi:10.1017/s0950268807008096).
307. Shane S.M. 1992 The significance of *Campylobacter jejuni* infection in poultry: a review. *Avian Pathol* **21**, 189-213. (doi:10.1080/03079459208418836).
308. Shange N., Gouws P., Hoffman L.C. 2019 *Campylobacter* and Arcobacter species in food-producing animals: prevalence at primary production and during slaughter. *World J Microbiol Biotechnol* **35**, 146. (doi:10.1007/s11274-019-2722-x).
309. Sheppard S.K., Dallas J.F., MacRae M., McCarthy N.D., Sproston E.L., Gormley F.J., Strachan N.J., Ogden I.D., Maiden M.C., Forbes K.J. 2009a *Campylobacter* genotypes from food animals, environmental sources and clinical disease in Scotland 2005/6. *International Journal of Food Microbiology* **134**, 96-103. (doi:10.1016/j.ijfoodmicro.2009.02.010).

310. Sheppard S.K., Dallas J.F., Strachan N.J., MacRae M., McCarthy N.D., Wilson D.J., Gormley F.J., Falush D., Ogden I.D., Maiden M.C., et al. 2009b *Campylobacter* genotyping to determine the source of human infection. *Clin Infect Dis* **48**, 1072-1078. (doi:10.1086/597402).
311. Sheppard S.K., Colles F., Richardson J., Cody A.J., Elson R., Lawson A., Brick G., Meldrum R., Little C.L., Owen R.J., et al. 2010 Host association of *Campylobacter* genotypes transcends geographic variation. *Appl Environ Microbiol* **76**, 5269-5277. (doi:10.1128/AEM.00124-10).
312. Sheppard S.K., Didelot X., Jolley K.A., Darling A.E., Pascoe B., Meric G., Kelly D.J., Cody A., Colles F.M., Strachan N.J., et al. 2013 Progressive genome-wide introgression in agricultural *Campylobacter coli* . *Mol Ecol* **22**, 1051-1064. (doi:10.1111/mec.12162).
313. Sheppard S.K., Cheng L., Meric G., de Haan C.P., Llarena A.K., Marttinen P., Vidal A., Ridley A., Clifton-Hadley F., Connor T.R., et al. 2014 Cryptic ecology among host generalist *Campylobacter jejuni* in domestic animals. *Mol Ecol* **23**, 2442-2451. (doi:10.1111/mec.12742).
314. Shreeve J.E., Toszeghy M., Ridley A., Newell D.G. 2002 The carry-over of *Campylobacter* isolates between sequential poultry flocks. *Avian Dis* **46**, 378-385. (doi:10.1637/0005-2086(2002)046[0378:Tcooci]2.0.Co;2).
315. Silva J., Leite D., Fernandes M., Mena C., Gibbs P.A., Teixeira P. 2011 *Campylobacter* spp. as a Foodborne Pathogen: A Review. *Front Microbiol* **2**, 200. (doi:10.3389/fmicb.2011.00200).
316. Slader J., Domingue G., Jorgensen F., McAlpine K., Owen R.J., Bolton F.J., Humphrey T.J. 2002 Impact of transport crate reuse and of catching and processing on *Campylobacter* and Salmonella contamination of broiler chickens. *Appl Environ Microbiol* **68**, 713-719. (doi:10.1128/aem.68.2.713-719.2002).
317. Smith S., Messam L.L., Meade J., Gibbons J., McGill K., Bolton D., Whyte P. 2016a The impact of biosecurity and partial depopulation on *Campylobacter* prevalence in Irish broiler flocks with differing levels of hygiene and economic performance. *Infect Ecol Epidemiol* **6**, 31454. (doi:10.3402/iee.v6.31454).
318. Smith S., Meade J., Gibbons J., McGill K., Bolton D., Whyte P. 2016b The impact of environmental conditions on *Campylobacter jejuni* survival in broiler faeces and litter. *Infection ecology & epidemiology* **6**, 31685-31685. (doi:10.3402/iee.v6.31685).
319. Sommer H.M., Høg B.B., Larsen L.S., Sørensen A.I.V., Williams N., Merga J.Y., Cerdà-Cuéllar M., Urdaneta S., Dolz R., Wieczorek K., et al. 2016 Analysis of farm specific risk factors for *Campylobacter* colonization of broilers in six European countries. *Microbial Risk Analysis* **2-3**, 16-26. (doi:10.1016/j.mran.2016.06.002).
320. Sproston E.L., Wimalarathna H.M.L., Sheppard S.K. 2018 Trends in fluoroquinolone resistance in *Campylobacter*. *Microbiol. Genom.* **4**. (doi: 10.1099/mgen.0.000198).
321. Stanley K., Jones K. 2003 Cattle and sheep farms as reservoirs of *Campylobacter*. *Journal of Applied Microbiology* **94**, 104S-113S. (doi:DOI: 10.1046/j.1365-2672.94.s1.12.x).
322. Stern N.J., Clavero M.R., Bailey J.S., Cox N.A., Robach M.C. 1995 *Campylobacter* spp. in broilers on the farm and after transport. *Poult Sci* **74**, 937-941. (doi:10.3382/ps.0740937).
323. Stern N.J., Hiett K.L., Alfredsson G.A., Kristinsson K.G., Reiersen J., Hardardottir H., Briem H., Gunnarsson E., Georgsson F., Lowman R., et al. 2003 *Campylobacter* spp. in Icelandic poultry operations and human disease. *Epidemiol Infect* **130**, 23-32.

324. Stewart-Tull D.E., Coote J.G., Thompson D.H., Candlish D., Wardlaw A.C., Candlish A. 2009 Virulence spectra of typed strains of *Campylobacter jejuni* from different sources: a blinded in vivo study. *J Med Microbiol* **58**, 546-553. (doi:10.1099/jmm.0.005611-0).
325. Strachan N.J., Gormley F.J., Rotariu O., Ogden I.D., Miller G., Dunn G.M., Sheppard S.K., Dallas J.F., Reid T.M., Howie H., et al. 2009 Attribution of *Campylobacter* infections in northeast Scotland to specific sources by use of multilocus sequence typing. *Journal of Infectious Diseases* **199**, 1205-1208. (doi:10.1086/597417).
326. Strachan N.J., Rotariu O., Smith-Palmer A., Cowden J., Sheppard S.K., O'Brien S.J., Maiden M.C., Macrae M., Bessell P.R., Matthews L., et al. 2013 Identifying the seasonal origins of human campylobacteriosis. *Epidemiol Infect* **141**, 1267-1275. (doi:10.1017/s0950268812002063).
327. Studahl A., Andersson Y. 2000 Risk factors for indigenous *Campylobacter* infection: a Swedish case-control study. *Epidemiol Infect* **125**, 269-275.
328. Tack D.M., Marder E.P., Griffin P.M., et al. 2019 Preliminary Incidence and Trends of Infections with Pathogens Transmitted Commonly Through Food — Foodborne Diseases Active Surveillance Network, 10 U.S. Sites, 2015–2018. *MMWR Morb Mortal Wkly Rep* **68**, 369–373. (doi:10.15585/mmwr.mm6816a2).
329. Taff C.C., Weis A.M., Wheeler S., Hinton M.G., Weimer B.C., Barker C.M., Jones M., Logsdon R., Smith W.A., Boyce W.M., et al. 2016 Influence of Host Ecology and Behavior on *Campylobacter jejuni* Prevalence and Environmental Contamination Risk in a Synanthropic Wild Bird Species. *Appl Environ Microbiol* **82**, 4811-4820. (doi:10.1128/AEM.01456-16).
330. Tam C.C., Rodrigues L.C., Petersen I., Islam A., Hayward A., O'Brien S.J. 2006a Incidence of Guillain-Barre syndrome among patients with *Campylobacter* infection: a general practice research database study. *Journal of Infectious Diseases* **194**, 95-97. (doi:10.1086/504294).
331. Tam C.C., Rodrigues L.C., O'Brien S.J., Hajat S. 2006b Temperature dependence of reported *Campylobacter* infection in England, 1989-1999. *Epidemiol Infect* **134**, 119-125. (doi:10.1017/s0950268805004899).
332. Tam C.C., O'Brien S.J., Tompkins D.S., Bolton F.J., Berry L., Dodds J., Choudhury D., Halstead F., Iturriza-Gomara M., Mather K., et al. 2012a Changes in causes of acute gastroenteritis in the United Kingdom over 15 years: microbiologic findings from 2 prospective, population-based studies of infectious intestinal disease. *Clin Infect Dis* **54**, 1275-1286. (doi:10.1093/cid/cis028).
333. Tam C.C., Rodrigues L.C., Viviani L., Dodds J.P., Evans M.R., Hunter P.R., Gray J.J., Letley L.H., Rait G., Tompkins D.S., et al. 2012b Longitudinal study of infectious intestinal disease in the UK (IID2 study): incidence in the community and presenting to general practice. *Gut* **61**, 69-77. (doi:10.1136/gut.2011.238386).
334. Tam C.C., O'Brien S.J. 2016 Economic Cost of *Campylobacter*, Norovirus and Rotavirus Disease in the United Kingdom. *PLoS One* **11**, e0138526. (doi:10.1371/journal.pone.0138526).
335. Tan Z., Wang Y., Yang T., Ao H., Chen S., Xing K., Zhang F., Zhao X., Liu J., Wang C. 2018 Differences in gut microbiota composition in finishing Landrace pigs with low and high feed conversion ratios. *Antonie Van Leeuwenhoek* **111**, 1673-1685. (doi:10.1007/s10482-018-1057-1).

336. Tangkham W., Janes M., LeMieux F. 2016 Prevalence and Distribution of *Campylobacter jejuni* in Small-Scale Broiler Operations. *J Food Prot* **79**, 75-81. (doi:10.4315/0362-028x.Jfp-15-331).
337. Taylor D.N., Brown M., McDermott K.T. 1982 Waterborne transmission of *Campylobacter enteritis*. *Microb Ecol* **8**, 347-354. (doi:10.1007/bf02010674).
338. Teh K.H., Flint S., Palmer J., Andrewes P., Bremer P., Lindsay D. 2014 Biofilm – An unrecognised source of spoilage enzymes in dairy products? *International Dairy Journal* **34**, 32-40. (doi:https://doi.org/10.1016/j.idairyj.2013.07.002).
339. Teillant A., Brower C.H., Laxminarayan R. 2015 Economics of Antibiotic Growth Promoters in Livestock. *Annual Review of Resource Economics* **7**, 349-374. (doi:10.1146/annurev-resource-100814-125015).
340. Ternhag A., Asikainen T., Giesecke J., Ekdahl K. 2007 A meta-analysis on the effects of antibiotic treatment on duration of symptoms caused by infection with *Campylobacter* species. *Clin Infect Dis* **44**, 696-700. (doi:10.1086/509924).
341. Teunis P., Van den Brandhof W., Nauta M., Wagenaar J., Van den Kerkhof H., Van Pelt W. 2005 A reconsideration of the *Campylobacter* dose-response relation. *Epidemiol Infect* **133**, 583-592. (doi: 10.1017/s0950268805003912)
342. Thakur S., Gebreyes W.A. 2005 Prevalence and antimicrobial resistance of *Campylobacter* in antimicrobial-free and conventional pig production systems. *J Food Prot* **68**, 2402-2410. (doi: 10.4315/0362-028x-68.11.2402).
343. The European Union One Health 2019 Zoonoses Report. (doi: 102903/j/efsa.2021.6406).
344. The European Union One Health 2020 Zoonoses Report. (doi: https://doi.org/10.2903/j.efsa.2021.6971).
345. Thépault A., Meric G., Rivoal K., Pascoe B., Mageiros L., Touzain F., Rose V., Beven V., Chemaly M., Sheppard S.K. 2017 Genome-Wide Identification of Host-Segregating Epidemiological Markers for Source Attribution in *Campylobacter jejuni* . *Appl Environ Microbiol* **83**. (doi:10.1128/AEM.03085-16).
346. Thépault, A., Rose, V., Quesne, S. *et al.* 2018 Ruminant and chicken: important sources of campylobacteriosis in France despite a variation of source attribution in 2009 and 2015. *Sci Rep* **8,** 9305. (doi:10.1038/s41598-018-27558-z).
347. Trachoo N., Frank J.F., Stern N.J. 2002 Survival of *Campylobacter jejuni* in biofilms isolated from chicken houses. *J Food Prot* **65**, 1110-1116.
348. Tribble D.R., Baqar S., Scott D.A., Oplinger M.L., Trespalacios F., Rollins D., Walker R.I., Clements J.D., Walz S., Gibbs P., et al. 2010 Assessment of the duration of protection in *Campylobacter jejuni* experimental infection in humans. *Infect Immun* **78**, 1750-1759. (doi:10.1128/iai.01021-09).
349. Trienekens S., Anderson C., Duffy J., Gill R., Harvey-Vince L., Jones H., Mook P., Ihekweazu C., Kar-Purkayastha I. 2014 Don't Count Your Chicken Livers: an Outbreak of *Campylobacter* sp. Not Associated with Chicken Liver Parfait, England, November 2013. *PLOS Currents Outbreaks*. (doi:10.1371/currents.outbreaks.c1b19bae7bac20dccf00ef18b19d8d2a).
350. Tustin J., Laberge K., Michel P., Reiersen J., Dadadottir S., Briem H., Hardardottir H., Kristinsson K., Gunnarsson E., Fridriksdottir V., et al. 2011 A national epidemic of campylobacteriosis in Iceland, lessons learned. *Zoonoses Public Health* **58**, 440-447. (doi:10.1111/j.1863-2378.2010.01387.x).

351. United States Department of Agriculture. 2012 The Nationwide Microbiological Baseline Data Collection Program: Raw Chicken Parts Survey.
352. Vaezirad M.M., Keestra-Gounder A.M., de Zoete M.R., Koene M.G., Wagenaar J.A., van Putten J.P.M. 2017 Invasive behavior of *Campylobacter jejuni* in immunosuppressed chicken. *Virulence* **8**, 248-260. (doi:10.1080/21505594.2016.1221559).
353. van de Giessen A., Mazurier S.I., Jacobs-Reitsma W., Jansen W., Berkers P., Ritmeester W., Wernars K. 1992 Study on the epidemiology and control of *Campylobacter jejuni* in poultry broiler flocks. *Appl Environ Microbiol* **58**, 1913-1917. (10.1128/aem.58.6.1913-1917.1992)
354. van der Meer J.W., Mouton R.P., Daha M.R., Schuurman R.K. 1986 *Campylobacter jejuni* bacteraemia as a cause of recurrent fever in a patient with hypogammaglobulinaemia. *J Infect* **12**, 235-239. (doi:10.1016/s0163-4453(86)94190-3).
355. Veterinary Medicines Directorate. 2019 Joint report on antibiotic use and antibiotic resistance, 2013-2017.
356. Vieira A., Seddon A.M., Karlyshev A.V. 2015 *Campylobacter-Acanthamoeba* interactions. *Microbiology* **161**, 933-947. (doi:10.1099/mic.0.000075).
357. Vrbova L., Johnson K., Whitfield Y., Middleton D. 2012 A descriptive study of reportable gastrointestinal illnesses in Ontario, Canada, from 2007 to 2009. *BMC Public Health* **12**, 970. (doi:10.1186/1471-2458-12-970).
358. Wagenaar J.A., French N.P., Havelaar A.H. 2013 Preventing *Campylobacter* at the source: why is it so difficult? *Clin Infect Dis* **57**, 1600-1606. (doi:10.1093/cid/cit555).
359. WHO. 2013 The global view of Campylobacteriosis.
360. WHO. 2016 Critically Important Antimicrobials for Human Medicine, 4th Revision 2013.
361. WHO. 2017 Global priority list of antibiotic-resistant bacteria to guide research, discovery, and development of new antibiotics.
362. Whyte R., Hudson J.A., Graham C. 2006 *Campylobacter* in chicken livers and their destruction by pan frying. *Lett Appl Microbiol* **43**, 591-595. (doi:10.1111/j.1472-765X.2006.02020.x).
363. Wideman N., Bailey M., Bilgili S.F., Thippareddi H., Wang L., Bratcher C., Sanchez-Plata M., Singh M. 2016 Evaluating best practices for *Campylobacter* and *Salmonella* reduction in poultry processing plants. *Poult Sci* **95**, 306-315. (doi:10.3382/ps/pev328).
364. Williams L.K., Sait L.C., Trantham E.K., Cogan T.A., Humphrey T.J. 2013 *Campylobacter* Infection Has Different Outcomes in Fast- and Slow-Growing Broiler Chickens. *Avian Diseases* **57**, 238-241. (doi: 10.1637/10442-110212-Reg.1)
365. Williams L.K., Fonseca B.B., Humphrey T.J. 2016 *Campylobacter jejuni* in Poultry: A Commensal or a Pathogen? In Campylobacter spp. and Related Organisms in Poultry pp 75–87, 75-87. (doi:10.1007/978-3-319-29907-5_5).
366. Wilson D.J., Gabriel E., Leatherbarrow A.J., Cheesbrough J., Gee S., Bolton E., Fox A., Fearnhead P., Hart C.A., Diggle P.J. 2008 Tracing the source of campylobacteriosis. *PLoS Genet* **4**, e1000203. (doi:10.1371/journal.pgen.1000203).
367. Wu Z., Sahin O., Wang F., Zhang Q. 2014 Proteomic identification of immunodominant membrane-related antigens in *Campylobacter jejuni* associated with sheep abortion. *J Proteomics* **99**, 111-122. (doi:10.1016/j.jprot.2014.01.018).
368. Yahara K., Méric G., Taylor A.J., de Vries S.P.W., Murray S., Pascoe B., Mageiros L., Torralbo A., Vidal A., Ridley A., Komukai S., Wimalarathna H., Cody A.J., Colles F.M.,

McCarthy N., Harris D., Bray J.E., Jolley K.A., Maiden M.C.J., Bentley S.D., Parkhill J., Bayliss C.D., Grant A., Maskell D., Didelot X., Kelly D.J., Sheppard, S.K. 2017, Genome-wide association of functional traits linked with *Campylobacter jejuni* survival from farm to fork. *Environ. Microbiol.*, **19,** 361-380. (doi: 10.1111/1462-2920.13628).

369. Yang H., Li Y., Johnson M.G. 2001 Survival and death of *Salmonella typhimurium* and *Campylobacter jejuni* in processing water and on chicken skin during poultry scalding and chilling. *J Food Prot* **64**, 770-776. (doi: 10.4315/0362-028x-64.6.770)
370. Young I., Rajic A., Wilhelm B.J., Waddell L., Parker S., McEwen S.A. 2009 Comparison of the prevalence of bacterial enteropathogens, potentially zoonotic bacteria and bacterial resistance to antimicrobials in organic and conventional poultry, swine and beef production: a systematic review and meta-analysis. *Epidemiol Infect* **137**, 1217-1232. (doi:10.1017/S0950268809002635).
371. Young K.T., Davis L.M., Dirita V.J. 2007 *Campylobacter jejuni*: molecular biology and pathogenesis. *Nat Rev Microbiol* **5**, 665-679. (doi:10.1038/nrmicro1718).
372. Zakariene G., Serniene L., Malakauskas M. 2015 Effects of lactic acid, linalool and cinnamaldehyde against *Campylobacter jejuni* in vitro and on broiler breast fillets. *Vet Ir Zootechnika **72**,* 45-52.
373. Zautner A.E., Johann C., Strubel A., Busse C., Tareen A.M., Masanta W.O., Lugert R., Schmidt-Ott R., Gross U. 2014 Seroprevalence of campylobacteriosis and relevant post-infectious sequelae. *Eur J Clin Microbiol Infect Dis* **33**, 1019-1027. (doi:10.1007/s10096-013-2040-4).
374. Zhang G., Ma L., Doyle M.P. 2007 Potential competitive exclusion bacteria from poultry inhibitory to *Campylobacter jejuni* and *Salmonella*. *J Food Prot* **70**, 867-873. (doi:10.4315/0362-028x-70.4.867).
375. Zilhao R., Papadopoulou B., Courvalin P. 1988 Occurrence of the *Campylobacter* resistance gene tetO in *Enterococcus* and *Streptococcus* spp. *Antimicrob Agents Chemother* **32**, 1793-1796. (doi: 10.1128/AAC.32.12.1793)
376. Zweifel C., Scheu K.D., Keel M., Renggli F., Stephan R. 2008 Occurrence and genotypes of *Campylobacter* in broiler flocks, other farm animals, and the environment during several rearing periods on selected poultry farms. *International Journal of Food Microbiology* **125**, 182-187. (doi:10.1016/j.ijfoodmicro.2008.03.038).

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