SCIENTIFIC OPINION

Update and review of control options for Campylobacter in broilers at primary production

EFSA Panel on Biological Hazards (BIOHAZ),
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Abstract

The 2011 EFSA opinion on *Campylobacter* was updated using more recent scientific data. The relative risk reduction in EU human campylobacteriosis attributable to broiler meat was estimated for on-farm control options using Population Attributable Fractions (PAF) for interventions that reduce *Campylobacter* flock prevalence, updating the modelling approach for interventions that reduce caecal concentrations and reviewing scientific literature. According to the PAF analyses calculated for six control options, the mean relative risk reductions that could be achieved by adoption of each of these six control options individually are estimated to be substantial but the width of the confidence intervals of all control options indicates a high degree of uncertainty in the specific risk reduction potentials. The updated model resulted in lower estimates of impact than the model used in the previous opinion. A 3-$\log_{10}$ reduction in broiler caecal concentrations was estimated to reduce the relative EU risk of human campylobacteriosis attributable to broiler meat by 58% compared to an estimate larger than 90% in the previous opinion. Expert Knowledge Elicitation was used to rank control options, for weighting and integrating different evidence streams and assess uncertainties. Medians of the relative risk reductions of selected control options had largely overlapping probability intervals, so the rank order was uncertain: vaccination 27% (90% probability interval (PI) 4–74%); feed and water additives 24% (90% PI 4–60%); discontinued thinning 18% (90% PI 5–65%); employing few and well-trained staff 16% (90% PI 5–45%); avoiding drinkers that allow standing water 15% (90% PI 4–53%); addition of disinfectants to drinking water 14% (90% PI 3–36%); hygienic anterooms 12% (90% PI 3–50%); designated tools per broiler house 7% (90% PI 1–18%). It is not possible to quantify the effects of combined control activities because the evidence-derived estimates are inter-dependent and there is a high level of uncertainty associated with each.

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Summary

In 2011, EFSA published an opinion on 'Campylobacter in broiler meat production: Control options and performance objectives and/or targets at different stages of the food chain'. In 2018, the European Commission requested the Panel on Biological Hazards to deliver a scientific opinion updating and reviewing control options for Campylobacter in broilers, focussing on primary production. In particular, the Panel was requested to review, identify and rank the possible control options at the primary production level, considering and, if possible, quantifying the expected efficiency in reducing human campylobacteriosis cases. Advantages and disadvantages of different options at primary production should be assessed, as well as the possible synergic effect of combined control options.

The update of the previous opinion was carried out by reviewing the scientific literature published since then and by estimating the relative risk reduction, expressed as the percentage reduction in human campylobacteriosis in the EU associated with the consumption of broiler meat that could be achieved by implementing control options at primary production of broilers. The relative risk was estimated for on-farm control options using population attributable fractions (PAF) for interventions that reduce Campylobacter flock prevalence, updating the modelling approach for interventions that reduce caecal concentrations and reviewing the scientific literature. The effect of control options that reduce the prevalence of Campylobacter spp. in broilers was estimated by calculating PAF, derived from epidemiological risk factors studies, and assuming a proportionate relation between flock prevalence prior to slaughter and the associated public health risk. The effect of control options that reduce Campylobacter spp. concentration in broilers was estimated by using a regression model, associating concentrations in the caeca and on skin samples, combined with a consumer phase and a dose response model. For some control options, the relative risk reduction could not be calculated by these methods and their effect was estimated using evidence from the scientific literature.

The PAF were calculated for six control options from several studies and included hygienic anteroom; effective rodent control; having no animals in close proximity to the broiler house; addition of disinfectant to drinking water; employing few and well-trained staff and avoiding drinkers that allow standing water. The variation was greater between the different control options than for the same control options in different studies, which increased the confidence in the extrapolation potential of the results to the European Union (EU).

According to the PAF analyses, the mean relative risk reductions that could be achieved by adoption of each of these six control options individually are estimated to be substantial but the width of the confidence intervals of all control options indicates a high degree of uncertainty in the specific risk reduction potentials. For example, the mean estimate of the relative risk reduction for the control option 'Addition of disinfectants to drinking water' was between 5 (95% CI 0.6–8.2) and 32% (95% CI 6.0–54.9) based on three available studies.

The modelling approach for relative risk reductions achieved by a reduction of Campylobacter concentrations in the caeca, previously used in the 2011 opinion, was updated. A wider variety of consumer phase models and a newly published dose response model were also included. Furthermore, newly and more extensive published data on the relationship between Campylobacter concentrations in the caeca and corresponding broiler carcass skin samples were used. The updated model resulted in lower estimates of the slope of the linear regression line describing the relation between concentrations in caecal contents and on skin. As a result of the decrease of this slope, lower estimates were obtained for the effectiveness of control options directed at a reduction in the caecal concentrations. For example, for a 2-$\log_{10}$ reduction in caecal concentrations, the median estimate was now a relative risk reduction of campylobacteriosis attributable to the consumption of broiler meat produced in the EU of 42% (95% CI 11–75%), whereas in the previous opinion, this relative risk reduction was 76–98% based on data from four Member States (MSs). Similarly, a 3-$\log_{10}$ reduction in broiler caecal concentrations was estimated to reduce the relative EU risk of human campylobacteriosis attributable to broiler meat by 58% (95% CI 16–89%), compared to a relative risk reduction estimate of more than 90% in four MSs, which was found previously.

Overall, the ranking of control options was informed by three different evidence streams: effect of control options to reduce flock prevalence (supported by PAF calculations based on literature data), effect of control options to reduce the concentrations in broiler caeca (supported by estimates obtained by a combination of models) and effect of control options directly obtained from literature (not supported by either PAF or modelling). Also, the evidence from regional studies and laboratory experiments had to be translated into EU wide effects in field conditions, and the current application of control measures, as well as the modelling assumptions, had to be taken into account when assessing

the effectiveness of the control options. Therefore, expert judgement was required for ranking the control options considering the associated uncertainties. The Panel agreed on the use of a structured approach, based on EFSA's (2014) guidance on expert knowledge elicitation (EKE), to ensure that all the identified evidence and uncertainties were considered in a balanced way and to improve the rigour and reliability of the judgements involved.

The effectiveness of 20 control options if implemented by all broiler farms in the EU, taking into account the current level of implementation, was estimated using a two-step EKE process informed by the results from modelling of the updated scientific evidence, literature review (including the previous EFSA opinion) and also the experts' knowledge and experience. Within the time frame of this opinion, experts made selections through the first step where all the options were considered and for the second step where eight control options were prioritised for further assessment of the magnitude of their effects.

In the first step of the EKE, for each of the control options, experts (i.e. working group members and selected EFSA staff) individually estimated the probability that the relative risk reduction would be larger than 10%. This 10% was chosen for its discriminative power in differentiating between the effectiveness of control options. The relative risk reduction was judged to have a higher probability to be larger than 10% for 12 control options: hygienic anterooms at broiler house entrance; no animals in close proximity of the broiler houses; employing few and well-trained staff; addition of disinfectants to drinking water; avoiding drinkers that allow standing water; effective cleaning and disinfection between flocks; reduced slaughter age; discontinued thinning; designated tools for each broiler house; feed and water additives; bacteriophages and vaccination. The remaining eight control options, which were judged to have a lower probability to give more than 10% relative risk reduction included: effective rodent control; adjusting downtime between flocks; fly screens and keeping insects out of the broiler house; clean or amended litter; stocking density and flock size; the number of houses on site; selective breeding and feed structure.

From the 12 selected control options, eight options were selected for risk prioritisation based on the quality of evidence available and practical feasibility in the implementation of the control option.

The median values of the relative risk reduction of the eight prioritised control options were judged to be as follows; vaccination 27% (90% probability interval (PI) 4–74%); feed and water additives 24% (90% PI 4–60%); discontinued thinning 18% (90% PI 5–65%); employing few and well-trained staff 16% (90% PI 5–45%); avoiding drinkers that allow standing water 15% (90% PI 4–53%); addition of disinfectants to drinking water 14% (90% PI 3–36%); hygienic anterooms at broiler house entrance 12% (90% PI 3–50%); designated tools per broiler house 7% (90% PI 1–18%). It was not possible to rank the selected control options according to effectiveness based on the EKE judgements because there is a substantial overlap of the probability intervals, due to the large uncertainties involved.

There are advantages and disadvantages associated with each control option. The advantages include ease of application (e.g. hygiene barrier, adding additives to feed), improved bird health (e.g. biosecurity actions), better broiler welfare (e.g. discontinued thinning), cross-protection against other pathogens (e.g. drinking water treatments, feed additives). The disadvantages for a given control option may include a requirement for investment (e.g. if structural changes are required to install an anteroom), lack of control (e.g. the farmer may not own the fields adjacent to the broiler house and therefore cannot prevent other animals being close by), reduced broiler growth due to decreased consumption of feed and/or water (e.g. if an additive affected the sensory (odour, taste or appearance) properties making the feed or water less palatable).

Multiple control activities are expected to have a higher effect preventing Campylobacter spp. from entering the broiler house and infecting the birds. To minimise the risk of Campylobacter colonisation, all control activities relating to biosecurity would have to be implemented in full. It is not possible to reliably assess the effect of combined control activities because they are inter-dependent and there is a high level of uncertainty associated with each. Some control options enhance while others reduce the effect of others. Combining two control measures targeting prevalence and concentration, respectively, may result in an additive effect, if their specific targets are unrelated.

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1. Introduction

1.1. Background and Terms of Reference as provided by the requestor

The 2012 EFSA opinion on the public health hazards to be covered by inspection of poultry meat[1] identified the need to address *Campylobacter* spp. as a high priority. Since 2005, *Campylobacter* spp. was the most frequently reported food-borne pathogen in the EU (more than 200,000 confirmed cases per year). The reported number of confirmed cases of campylobacteriosis represented almost 70% of the 13 reported confirmed human zoonoses in the EU in 2016. Most patients are young children and elderly people. Its occurrence was high in broiler flocks (27.3%) and in fresh meat from broilers (36.7%) in Europe. In 2010, EFSA published an opinion on 'Quantification of the risk posed by broiler meat to human campylobacteriosis in the EU'[2] and estimated that broiler meat may account for 20–30% of campylobacteriosis cases in humans, while 50–80% of these may be attributed to the chicken reservoir as a whole.

In April 2011, EFSA published an opinion on '*Campylobacter* in broiler meat production: control options and performance objectives and/or targets at different stages of the food chain'.[3] Taking into account EFSA's recommendations on poultry meat inspection, the Commission proposed the introduction of a process hygiene criterion for *Campylobacter* spp. on poultry carcases to be respected in slaughterhouses. If not respected, the criterion leads to corrective measures taken to improve both slaughter hygiene and farm biosecurity.

Secondly, the revision of poultry meat inspection includes enhanced control of *Campylobacter* spp. (and *Salmonella* spp.), in line with the high priority set by the EFSA opinion on poultry meat inspection. Competent authorities must sample themselves for these pathogens or carefully verify the implementation of the process hygiene criterion by the operator.

According to the 2011 EFSA opinion, the public health benefits of controlling *Campylobacter* spp. in primary broiler production are expected to be greater than control later in the chain as the bacteria may also spread from farms to humans by other pathways than broiler meat. Nevertheless, limited information was available about such pathways, and quantification of the impact of interventions at farm level was done only for broiler meat-related cases.

Since 2011, new scientific information is available on this matter (e.g. CAMCON, CAMPYBRO, CAMPYSAFE, CAMPYLOW projects). Thus, the time is right to request an update of the assessment of the impact of interventions at farm level and identify effective control options at primary production.

Examples of some relevant projects are provided below:

— **CAMCON project** (https://cordis.europa.eu/project/rcn/95053 en.html), looking at *Campylobacter* control at primary production level (2010–2015), with participants from different countries. Publications derived from this project are available at https://www.vetinst.no/camcon-eu;
— **CAMPYBRO project** (http://campybro.eu), looking at *Campylobacter* control at primary production through nutrition and vaccination, with several partners including producers.
— **CAMCHAIN project** (http://gtr.rcuk.ac.uk/projects?ref=BB%2FK004514%2F1) looking at transmission of *Campylobacter* at primary production level;
— **CAMPYSAFE** and **CAMPYLOW projects** looking at the use of probiotics to control *Campylobacter* populations;
— Other scientific papers are also reported in the literature since 2011.

Terms of Reference (ToR)

To further support food business operators in the fight against *Campylobacter* at farm level, in accordance with Article 29(1) (a) of Regulation (EC) No 178/2002, the Commission requests EFSA to provide an update of the scientific opinion on '*Campylobacter* in broiler meat production: control options and performance objectives and/or targets at different stages of the food chain', more in particular to review, identify and rank the possible control options at primary production level, taking into account, and if possible quantifying, the expected efficiency in reducing human campylobacteriosis cases. Advantages and disadvantages of different options at primary production should be assessed, as well as the possible synergic effect of combined control options.

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[1] EFSA Journal 2012;10(6):2741.
[2] EFSA Journal 2010; 8(1):1437.
[3] EFSA Journal 2011;9(4):2105, 141 pp. https://doi.org/10.2903/j.efsa.2011.2105

1.2. Interpretation of the Terms of Reference

In 2011, EFSA published a scientific opinion on 'Campylobacter in broiler meat production: control options and performance objectives and/or targets at different stages of the food chain'. The aim of this mandate was interpreted to be to review and update the 2011 opinion but focussing on control options at primary production of broiler chickens in the EU/EEA.

Moreover, it was considered that the mandate included a quantitative assessment of the effectiveness of control options at primary production using risk assessment models and expressing the relative risk reduction in terms of the number of cases of human campylobacteriosis attributable to the consumption of broiler meat from the EU that could be avoided if a specific control option is implemented in all farms across Member States in EU. While the cost of implementation or feasibility of control options was outside of this remit, the advantages and disadvantages of each were discussed. Throughout the opinion, control options were assessed in terms of effectiveness. The efficiency was considered in the section discussing advantages and disadvantages of control options. 'Biosecurity' was defined as in the previous opinion to be, 'a set of preventative measures implemented to reduce the risk of transmission of infectious disease from reservoirs of the infectious agent to the target host'.

To address the different parts of the ToR, assessment questions (AQ) have been formulated as:

1) AQ: What new scientific evidence about control options has become available since the previous opinion of 2011 and what is their relative risk reduction on campylobacteriosis?
2) AQ: What is the ranking in terms of effectiveness of the selected control options in reducing human campylobacteriosis cases at the primary production level?
3) AQ: What are the advantages and disadvantages of the selected control options?
4) AQ: What would be the effect of combining control options?

1.3. Additional information

1.3.1. Previous scientific opinions of the BIOHAZ Panel

In 2008, the European Commission requested EFSA to deliver a scientific opinion on the quantification of the risk posed by broiler meat to human campylobacteriosis in the EU, which was expressed as a percentage of the total number of human campylobacteriosis cases. It was concluded that handling, preparation and consumption of broiler meat may account for 20% to 30% of human cases of campylobacteriosis, while 50% to 80% may be attributed to the chicken reservoir as a whole. However, the conclusions of this scientific opinion had to be interpreted with caution because, as stated in that opinion, data for source attribution in the EU were limited and unavailable for the majority of Member States (MS) and there were indications that the epidemiology of human campylobacteriosis differed between regions. Among several recommendations, the BIOHAZ Panel recommended the establishment of active surveillance of campylobacteriosis in all MS and also to quantify the level of under-ascertainment and underreporting of the disease, in order to more precisely estimate the burden of the disease and facilitate evaluation of the human health effects of any interventions (EFSA BIOHAZ Panel, 2010).

In 2011, EFSA delivered a scientific opinion on Campylobacter in broiler meat production: control options and performance objectives and/or targets at different stages of the food chain. A quantitative microbiological risk assessment (QMRA) model was used to estimate the impact on human campylobacteriosis arising from the presence of Campylobacter spp. in the broiler meat chain. The model also used available quantitative data to rank/categorise selected intervention strategies in the farm to fork continuum. At the primary production level, the quantitative risk assessment concluded that there was a proportionate relationship between the prevalence of Campylobacter spp. in broiler flocks and public health risk from broiler meat. The opinion described how reducing either the level of Campylobacter spp. in chicken caeca or the prevalence of positive flocks could reduce the risk to humans. The risk reduction associated with interventions in primary production was expected to vary considerably between MS. Reducing the numbers of Campylobacter spp. in the caeca at slaughter by 3 $\log_{10}$ units was estimated to result in a reduction of the public health risk by at least 90%. However, no feasible intervention that would achieve a reduction in the level of Campylobacter spp. in chicken caeca was identified. The models calculated that in one MS (among four MS used in the model), a 50–90% risk reduction could be achieved using fly screens in conjunction with other strict biosecurity measures. Primary production interventions assessed included fly screens (in one MS), biosecurity (in one MS), earlier slaughter and discontinued thinning. Their impact was estimated as a reduced

incidence of campylobacteriosis in humans attributable to the consumption of broiler meat. However, data were sparse, introducing uncertainty in the estimates and the applicability for all EU MS was also uncertain. Thus, it was recommended that individual MS pilot any control measure before full implementation to assess the efficiency in that specific environment (EFSA BIOHAZ Panel, 2011).

Following the previous opinions, a request from the European Commission in 2010 asked EFSA to deliver a scientific opinion on the public health hazards (biological and chemical, respectively) to be covered by inspection of poultry meat and to consider any implications for animal health and animal welfare of any changes proposed to current meat inspection methods. For biological hazards, a decision tree was developed and used for risk ranking poultry meat-borne hazards. The ranking was based on the magnitude of the human health impact, the severity of the disease in humans, the proportion of human cases that can be attributed to the handling, preparation and consumption of poultry meat and the occurrence of the hazards in poultry flocks and carcasses. *Campylobacter* spp. and *Salmonella* spp. were considered to have high public health relevance for poultry meat inspection. As none of the main biological hazards of public health relevance and associated with poultry meat can be detected by traditional visual meat inspection methods, the BIOHAZ Panel proposed the establishment of an integrated food safety assurance system including improved food chain information (FCI) and risk-based interventions (EFSA BIOHAZ Panel, 2012). A series of recommendations were made regarding biological hazards in relation to data collection, interpretation of monitoring results, future evaluations of the meat inspection system and hazard identification/ranking, training of all parties involved in the poultry carcass safety assurance system and needs for research on optimal ways to use FCI and approaches for assessing the public health benefits.

1.3.2. Legal background

A Process Hygiene Criterion (PHC) (Commission Regulation (EU) 2017/1495 of 23 August 2017 amending Regulation (EC) No 2073/2005) for *Campylobacter* spp. came into effect in January 2018. The objective of the PHC is to control contamination of carcases during the slaughtering process through monitoring and taking corrective actions when the mandated targets are breached. These actions include, in the case of unsatisfactory results (from 1.1.2020, if 15 out of 50 samples of carcasses after chilling have counts $> 1,000$ CFU/g) improvements in the slaughter hygiene, the review of process controls and improvement in the biosecurity measures in the farms of origin.

1.3.3. Approach to answer the term of reference

A literature search focussing on the time period after the previous scientific opinion (i.e. between 2011 and 2019) was carried out to update the scientific opinion on 'Campylobacter in broiler meat production: control options and performance objectives and/or targets at different stages of the food chain.'

The effectiveness of control options was estimated using two different modelling approaches for (a) control options reducing the *Campylobacter* spp. prevalence in broiler flocks sent to slaughter and (b) control options reducing the *Campylobacter* spp. concentration in their caecal content. The modelling steps used to estimate the effect on public health by reducing *Campylobacter* spp. flock prevalence (1–2) and concentrations in caecal content (3–5) are illustrated in Figure 1.
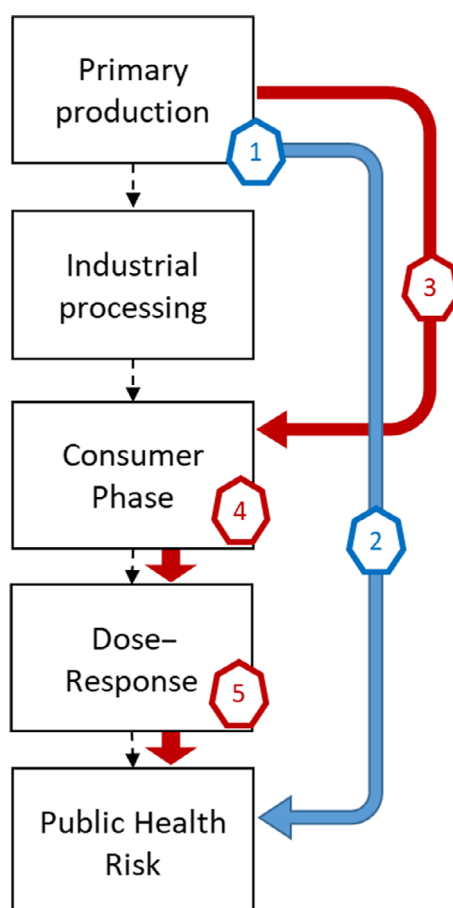
Figure 1: Modelling steps used to estimate the effect on public health by reducing Campylobacter spp. flock prevalence (blue arrow) and concentrations in caecal content (red arrows) in broilers. The numbers show the steps used in the two models, respectively

The reduction of flock prevalence was estimated by using (1) population attributable fractions (PAF)[4] derived from epidemiological risk factors studies and (2) assuming a proportionate relationship between flock prevalence and public health risk (see Section 2.2 for details).

The effect of reduced *Campylobacter* spp. concentrations was modelled by (3) a regression model relating the concentration in the caeca with the concentration on the broiler meat, (4) a consumer phase model describing the effect of food preparation and (5) a dose response (DR) model (see Section 2.3 for details). In both approaches, the effectiveness of the control options is expressed as the relative risk reduction, that is the relative reduction in the incidence of human campylobacteriosis caused by the consumption of broiler meat, if the control option is implemented at all farms in the EU:

$$RRR = 1 - Inc_{int}/Inc_{curr}$$

where

- – RRR is the relative risk reduction,
- – Inc_{curr} is the current incidence of human campylobacteriosis attributable to broiler meat in the EU,
- – Inc_{int} is the new estimated incidence of human campylobacteriosis attributable to the consumption of broiler meat after implementation of the control option at all farms in the EU.

The ranking of control options is based on the assessment of their potential effectiveness, using Expert Knowledge Elicitation (EKE) to combine the different streams of evidence and consider their associated uncertainties.

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[4] https://www.who.int/healthinfo/global_burden_disease/metrics_paf/en/

Advantages and disadvantages of selected control options were assessed using literature search and expert judgement.

The impact of combinations of two or more selected control options, including the potential for synergism, was assessed based on the literature search and expert judgement.

2. Data and methodologies

2.1. Literature search

A literature search was undertaken, focusing on papers published between 2011 and 2019 (inclusive) on *Campylobacter*, risk factors and control options on broiler farms. In addition, manual searching of the reference list of these documents was performed to identify additional relevant information. This was supplemented by relevant published studies identified by the members of the Working Group (WG) and EFSA Biological Hazards (BIOHAZ) Panel throughout the term of the mandate until the WG members were satisfied that a thorough coverage of the subject had been achieved.

2.2. Modelling the effect of control options to reduce the prevalence of *Campylobacter* spp. in broilers

2.2.1. Literature search to inform calculation of population-attributable fractions (PAF)

For the analysis of the PAF, the timeframe searched was expanded to 2004–2019 (inclusive) because epidemiological risk factor studies are limited and PAF analyses had not been carried out in the previous opinion. Only those studies that contained all of the following were included: [1] presentation of multi-variable model outputs including estimates to calculate adjusted odds ratio (OR) and confidence intervals; [2] descriptive data showing the proportion of farms/flocks in the different categories, [3] data on biosecurity/on-farm practices and [4] the sample size was ≥ 35 study units.

The search string used was: ((campylobacter AND (risk AND factor*) AND (farm* OR husbandry* OR (primary AND production*)) AND (chicken* OR broiler* OR poultry OR Gallus gallus)) and yielded 245 studies.

Abstracts of these papers were screened and, if no multivariable analysis was reported, the studies were excluded because, if the model does not adjust for confounding effects, where farming practices interact and are associated with each other (Stafford et al., 2008), the risk factor specific estimates are likely to be highly distorted. Overall, 31 studies were retained.

Full papers of these 31 studies were assessed and excluded if they did not contain all of the following: [1] presentation of multi-variable model outputs including estimates to calculate adjusted OR and confidence intervals; [2] descriptive data showing the proportion of farms/flocks in the different categories and [3] data on biosecurity/on-farm practices. Studies were also excluded if the sample size was less than 35 study units. This resulted in 17 studies in 15 articles for inclusion in the PAF analysis (see Table 6 in chapter 3.3.1).

2.2.2. Calculation of population attributable fractions (PAF)

Control measures to reduce the prevalence in broilers are aimed at preventing the introduction of *Campylobacter* spp. into the broiler house and the subsequent colonisation of the birds. A wide variety of measures and practices improve hygiene and biosecurity and are described in the literature review (Section 3.3). To assess the magnitude of control obtained by an intervention, studies that measure the prevalence with and without a control option are required. Intervention studies on the effect of improving biosecurity and changing farmer behaviour are limited. Assessing the effect of changes to multiple practices, with large variability in behaviours before and after interventions, varying compliance levels and interaction between practices, requires a very large sample size and repeated sampling to identify even large effects of interventions (Ellis-Iversen et al., 2008). Therefore, most studies on biosecurity practises and their association with *Campylobacter* status are designed as risk factor studies providing a cross-sectional picture of what happens more often during rearing of positive flocks than during rearing of negative flocks. Such epidemiological risk factor studies allow for multivariate modelling and the possibility to adjust for confounding factors and thereby provide an estimate of risk of a specific behaviour or practice.

Epidemiological risk factor studies are by their nature field studies. The data include the heterogeneity, diversity and variability in human and animal populations, e.g. different genetics or behavioural differences, differences in biosecurity practices, etc., reflecting real life. This contrasts with the standardisation used for experimental studies, where the study design usually removes diversity and minimises variability.

The strength of association derived from epidemiological risk factor studies is often much smaller than the measure of the effect of the same control option in an experimental study, due to the variability and heterogeneity of the population in the epidemiological study. Epidemiological risk factor studies are not able to detect small associations, which fully controlled experimental studies may be able to identify with statistical significance. On the other hand, the effects measured in the epidemiological risk factor studies include the heterogeneity of the farm environment, human factors and variety in practices and the results can be extrapolated to 'real life' situations with higher certainty than experimental studies in a small designed setting.

To interpret the effect of changing farm management practices on the risk of colonisation of broiler flocks with *Campylobacter* spp., the ORs can be transformed into PAF. This provides a measure of the proportion of cases (positive flocks) estimated to be linked to a specific risk factor. The World Health Organisation defines PAF as 'the proportional reduction in population disease or mortality that would occur if exposure to a risk factor were reduced to an alternative ideal exposure'. It is assumed that the interventions are applied on the new farms to a similar degree as on farms that already applied the intervention at the time of the risk factor study. PAF is also applied to food-borne zoonotic diseases in public health and has been calculated in at least two published studies on *Campylobacter* spp. in chicken (Georgiev et al., 2017; Rosner et al., 2017). For the scope of this opinion, population disease or mortality is interpreted as colonised broiler flocks, and only modifiable risk factors, for which control options within the farmer's control exist, were considered for the PAF analysis. Non-modifiable risk factors such as the season or factors related to the geographical location of the farm were excluded. Only control options identified in at least two MS were included.

In epidemiological studies exploring associations with risk factors, there is a marked heterogeneity not only in the risk factors included in the analysis but also in the definition or wording of the risk factors related to the explanatory variables. As an example, a French study (Allain et al., 2014) found '*No rodent control outside the house*' to be significantly associated with the occurrence of *Campylobacter* spp. in the broiler flocks while '*presence of rodents in the poultry house*' was identified as a risk factor in a Spanish study (Torralbo et al., 2014).

Although these definitions relate to two different aspects, they are assessing the presence of the same underlying risk (i.e. presence of rodents); hence, 'Having an effective rodent control program in place' is the control practice reducing the risk recommended in both studies. Widening the wording of the control option to address several narrowly defined risk factors may also help account for variability in farming systems within and between MS.

PAF estimates need to be as precise as possible for the control option, despite farming practices which often interact or are associated with each other (confounding) (Stafford et al., 2008). In epidemiological risk factor studies, confounding is adjusted for by statistical modelling, usually by regression analysis, providing adjusted ORs to reduce this bias. In this opinion, we have only used adjusted OR.

From the selected studies, we extracted the following variables: (1) country, (2) number of units in study, (3) year of data collection. We also extracted the following parameters for each modifiable risk factor:

- Wording of risk practice
- Baseline practice (comparison)
- Adjusted OR + confidence intervals
- % positive in exposed group
- % positive in non-exposed group
- % in study carrying out risk practice

If any of the above estimates were not directly available in the publication, they were calculated by inversing 'protective ORs' into 'risk ORs' including their confidence intervals or estimated from other model outputs, e.g. the standard error (SE).

After the extraction, adjusted OR and their confidence intervals were transformed to adjusted Relative Risk with confidence intervals using the formula (Equation 1) from Zhang and Kai (1998).

$$RR_{adj} = OR_{adj}/(1 - P_0 + P_0 OR_{adj}) \qquad (1)$$

with P_0 the *Campylobacter* spp. prevalence in the group without implementation of the control option and ORadj the adjusted OR.

If a risk factor was identified as significant and data needed in the equation were available from the literature, the PAF was estimated using Levin's formula (Equation 2, Levin, 1953):

$$PAF = p_{exp}(RR_{adj} - 1)/[1 + p_{exp}(RR_{adj} - 1)] \qquad (2)$$

where p_{exp} is the proportion of the population exposed to the risk factor and RR_{adj} is the calculated adjusted relative risk between colonised and non-colonised flocks as described above (Equation 1).

Risk factors from all studies were then grouped by the practice or action needed to control the risk. For each control measure the representativeness was considered and factors were only included in the final modelling if PAF estimates were available from at least two MS.

2.2.3. The proportionate relationship between flock prevalence and public health risk

The model assumes that the relative reduction in flock prevalence caused by an intervention at primary production translates directly into a relative reduction in risk from the broiler meat to humans. Hence, with Inc_{curr} and Inc_{int} as defined in Section 1.3.3; and FP_{curr} being the current flock prevalence and FP_{int} being the flock prevalence after implementation of a control option, it is assumed that $Inc_{int}/Inc_{curr} = FP_{int}/FP_{curr}$.

This assumption is also made in several previous published risk assessment models and in the previous EFSA opinion (Nauta et al., 2009; EFSA BIOHAZ Panel, 2011). The underlying argument is that analyses performed by these risk assessment models suggest that meat from flocks that are not colonised does not add significantly to the public health risk. Even though cross-contamination between carcases of birds from flocks is known to occur during slaughter, it is assumed to only have a small effect on the public health risk, because *Campylobacter* spp. concentrations on meat from cross-contaminated flocks will be several orders of magnitude lower than those from flocks colonised at primary production (Havelaar et al., 2007; Nauta et al., 2009; EFSA BIOHAZ Panel, 2011).

In this opinion, the PAF values were interpreted as the proportional reduction in flock prevalence that would occur if exposure to a risk factor was eliminated (i.e. the associated control option was applied throughout the EU). This means that the PAF is equivalent to: $1 - FP_{int}/FP_{curr}$ and also to the estimated RRR defined in Section 1.3.3.

2.3. Modelling the effect of control options to reduce the concentration of *Campylobacter* spp. in broilers

The modelling approach applied for the effect of control options to reduce the concentration of *Campylobacter* spp. is explained below; details are given in Appendix A.

2.3.1. Literature search

A generic literature search has been carried out to identify studies that analysed the association between concentrations in the caeca of broilers and broiler meat products after industrial processing (see Appendix B).

2.3.2. Linear regression for concentration in caecal content and on skin of broiler meat

A model for the effect of control options that reduce the caecal concentration of *Campylobacter* spp. in broilers at primary production should describe how the caecal concentrations relate to concentrations on the meat. Two approaches have been used to describe this relationship: (i) the use of QMRA models that describe the dynamics of transfer and survival of *Campylobacter* spp. through the broiler meat production chain after primary production (Nauta et al., 2009; Chapman et al., 2016); (ii) the study of the association between concentrations of *Campylobacter* spp. found in the caecal content (usually called 'caecal samples') and on the end products (whole carcass, skin or meat samples) after the industrial processing, by means of linear regression. When the two approaches

(QMRA and regression models) were compared, the results were similar, even though the QMRA models predicted the relation between the two concentrations as not linear, but J-shaped (Nauta et al., 2016).

As in the previous opinion (EFSA BIOHAZ Panel, 2011), a linear regression approach was applied using a regression model to translate a change in bacterial concentration in the chicken caeca into a change in concentration on broiler skin, which assumes to represent a change in concentration on the meat. The approach allows the use of observational data from different European studies and does not require assumptions and data interpretation on the complex dynamics of transfer and survival of *Campylobacter* spp. during industrial processing. As explained in Appendix A, the slope of the regression line is needed to estimate the change in concentrations on broiler skin after industrial processing, given that the mean effect of an intervention (in terms of log reduction) and its standard deviation (expressing the variability in effect) are known. Data on *Campylobacter* spp. concentration on broiler skin were obtained from the EU baseline survey from 2008 (EFSA, 2010). Although these data are more than 10 years old and do not take into account the improvements in *Campylobacter* control arising from the measures implemented in MSs since then, they are, none-the-less, the only data available for all MSs, obtained using a harmonised sampling strategy.

The results of the literature review for the association between concentrations in the caeca and on skin samples or broiler meat after industrial processing are summarised in Appendix B and Table 1. In total, 15 studies were retrieved, that used different analytical methods for enumeration. Six of those studies reported no significant correlation and nine found values of the slope of the regression line between 0.21 and 1.15. In one of the six largest studies, with more than 50 batches analysed, Reich et al., 2018, found no positive correlation; the four studies publishing a regression line found slopes varying between 0.21 and 0.32. In this assessment, the uncertainty of the slope was expressed as a BetaPert distribution with minimum of 0, maximum of 0.7 and a most likely value of 0.27. This last value corresponds to the slope value obtained by linear regression on the largest data set, from the APHA/FSA monitoring programme for *Campylobacter* spp. in broiler flocks and broiler carcasses in the UK (2012–2017) (FS241051, FS101126). The data set included paired caeca–skin microbiological data (enumeration according to ISO 10272-2) for 1752 batches slaughtered in different abattoirs in UK.

Table 1: Summary table of regression lines found in the literature

Reference	Significant correlation?[a]	Slope	r or r^{2}[a]	Number of batches	Number of slaughter plants
Allen et al. (2007)	No	–	–	26	4
Boysen et al. (2016)	Yes	0.70	$r^2 = 0.72$	15	3
Brena et al. (2013)	Yes	0.21	$r^2 = 0.23$	76	3
Duffy et al. (2014)	No	–	–	4	2
Elvers et al. (2011)	No	–	–	5	–
Hue et al. (2011)	Yes	0.32	r = 0.33	425 (297 pos.)	58
Laureano et al. (2013)	Yes	0.28	$r^2 = 0.26$	80	10
Malher et al. (2011)	Yes	ND	r = 0.28	140 (91 pos.)	3
Nauta et al. (2009)	No	–	–	22	–
Reich et al. (2008)	Yes	ND	r = 0.64	40	1
Reich et al. (2018)	No	–	–	365	3
Rodgers (2020)	Yes	0.27	$r^2 = 0.48$	1,146	19
Rosenquist et al. (2006)	Yes	1.15	–	6	2
Stern and Robach (2003)	No	–	–	20	1
Vinueza-Burgos et al. (2018)	Yes	0.50	$r^2 = 0.57$	15	3

An extended version of this table is given in Appendix B.
(a): As reported in the given reference.
r = linear correlation coefficient; r^2 = coefficient of determination.
– = not determined or no value given.

2.3.3. Consumer Phase model (CPM)

The consumer phase is the last part in the food chain, where exposure to *Campylobacter* spp. occurs. As explained in more detail in Appendix A, it describes how the concentration on the skin or on the meat is linked to the dose ingested by the consumer. Food preparation and associated cross-contamination of other foods have an important effect on the exposure. Modelling the consumer phase is challenging because data are scarce and difficult to obtain, the variability in food handling practices between (groups of) consumers is large and the effect on transfer and survival of *Campylobacter* spp. is not easily described.

As reviewed by Chapman et al. (2016), a large variety of CPMs are available that may include different routes of *Campylobacter* spp. transfer (cross-contamination) and undercooking. Recently, another model estimating the effects of consumer habits during preparation of chicken meat has been proposed (Poisson et al., 2015; ANSES, 2018). From an initial level of contamination of 1.4 $\log_{10}$ CFU/g, the authors estimated a risk reduction of 50% if 100% of consumers adopted best practice during preparation or the initial load is reduced to 0.4 $\log_{10}$ CFU/g. A comparative analysis, Nauta and Christensen (2011) studied eight different CPMs and compared their performance in terms of the predicted effect of intervention measures before the consumer phase on the risk estimates. It was found that the difference between the relative risk estimates of the different models is often small. A CPM that performs intermediately (i.e. providing results falling in the range of the others) is based on the observational data described by Nauta et al. (2008) and has been applied in the previous EFSA opinion as the 'classic +' DR model (EFSA BIOHAZ Panel, 2011; Nauta et al., 2012).

In this opinion, the eight available CPMs (Christensen et al., 2001; Mylius et al., 2007; van Asselt et al., 2008; Brynestad et al., 2008; Calistri and Giovannini, 2008; Lindqvist and Lindblad, 2008; Nauta et al., 2008; WHO, 2009) that were compared by Nauta and Christensen (2011) were used to evaluate the uncertainty due to the choice of the CPMs. These CPMs apply a broad range of different cross-contamination scenarios and use different data on food handling practices, routes of cross-contamination, transfer rates and meat product and/or cross contaminated food product. None of the models specifically addresses undercooking, although it is implicitly included in the Nauta et al. (2008) model, which is solely based on observational data. No additional CPMs were included as the selected eight already represent a large variety of models and it appeared that the choice of the CPM had only limited impact on the uncertainty of the results (Nauta and Christensen (2011); see also the tornado plots for correlation coefficients in Appendix C).

2.3.4. Dose response model

A dose response model describes how an ingested dose relates to the probability of infection and/ or the probability of illness in humans. Until now, the majority of *Campylobacter* QMRA studies, including the previous EFSA opinion (EFSA BIOHAZ Panel, 2011), have applied the 'classic' dose response model published by Teunis and Havelaar (2000), based on a human challenge study (Black et al., 1988) in which the strain A3249 was used. After an analysis of several additional data sets from both human and primate challenge studies, as well as a set of outbreak studies, the choice of this model was recently criticised by Teunis et al. (2018) as 'an unfortunate choice' as the default model for many risk assessments for *Campylobacter* spp., because A3249 seems to be of low virulence and is therefore a non-representative strain. Therefore, next to the classic dose response model, two additional dose response models were used that were considered representative for the challenge studies and the outbreak studies reported by Teunis et al. (2018), as explained in Appendix A.

2.3.5. Selection of control options

A set of control options affecting the concentrations in the caecal content was selected, based on the literature study as described in Section 2.1.

Control options to reduce *Campylobacter* spp. concentration in the caeca were primarily selected based on new information that became available since the EFSA 2011 Opinion was published. From these, several control interventions (vaccines, prebiotic/other feed additives and bacteriophages) were selected for inclusion in model analysis based on: [1] evidence that the control activity had a reductive effect on the *Campylobacter* spp. concentrations in the caeca and/or faeces; [2] type of study (experimental and field trials using broilers); [3] inclusion of control (untreated) birds in the study; [4] sufficient data including mean log reduction and standard error (or equivalent); [5] number of birds included in the trial and frequency of sampling (statistically- based experimental design), [6] samples

tested (at least caecal content samples); and [7] the length of the trial including the period of sampling (close to field practices, 35–42 days).

From the selected studies, the most and least effective values of different control options found (i.e. for vaccines and feed additives) were selected for modelling. The values were used to indicate the range of potential beneficial effects found in the literature, but references to specific vaccines or feed additives are not made, as the reproducibility of the quantitative results obtained by simulations in the present opinion, if applied in field conditions, remains unknown.

2.3.6. Model description and implementation

Appendix A provides a more detailed description of the modelling approach for the effect of control options to reduce the concentration of *Campylobacter* spp. in broilers. The linear regression model, consumer phase model and DR model are combined and implemented in an Excel spreadsheet (Nauta, 2020), using the model implementation approach described by Nauta and Christensen (2011).

The model allows an estimation of the RRR to be made based on a mean and standard deviation of the effect of the intervention in terms of log reduction in caecal concentration (d and s_d); the regression line slope (a); the choice of an EU MS or the EU average (for current concentrations of broiler skin after processing (m_{skin} and s_{skin})); a value of the log difference between skin samples and meat (τ); the choice of a CPM; the choice of a DR model. A version of the model implemented in @Risk version 7.6 allows analysis of the uncertainty by providing the uncertainty of the input parameters a, d, and τ, as well as the uncertainty in the choice of the MS (m_{skin} and s_{skin}), the choice of the CPM and the choice of the DR. Variability is included into the model analytically, uncertainty is modelled by Monte Carlo simulation, using 250.000 iterations per simulation.

Table 2 shows the options included in this model. For the uncertainty analysis of the model that informed the EKE, the difference between skin concentrations found in different MSs was not included, as the effect of control options is expressed at EU level.

Table 2: Overview of the default model values chosen, if uncertainty is not included, and the way the uncertainty about the choice of the model or model parameter is described, if uncertainty is included. The options given in bold are used for the uncertainty analysis that informed the Expert Knowledge Elicitation (the reference model)

	Default values	Reference	Uncertainty	Reference
Slope of regression line caeca – skin samples	a = 0.27	Rodgers (2020)	**BetaPert (0, 0.27, 0.7)**	This opinion
Log difference between concentration on skin and meat	$\tau = 1$	EFSA BIOHAZ Panel (2011)	**Uniform (0,3)**	Nauta et al. (2012)
Member States (skin concentrations measured in EU baseline 2008)	**EU-weighted mean**	Nauta et al. (2012) (derived from EU baseline study 2008)	Randomly select 1 Member State	Nauta et al. (2012) (derived from EU baseline study 2008)
Consumer phase model	Nauta et al. (2008)	EFSA BIOHAZ Panel (2011)	**Randomly select one of eight models**	Nauta and Christensen (2011)
Dose response model	Classic model	EFSA BIOHAZ Panel (2011)	**Randomly select 'classic' or 'median challenge' model**	This opinion

A sensitivity analysis was performed to evaluate the effect of different modelling choices on the estimated effects of the selected control options.

2.4. Ranking and Uncertainty assessment

The ToR required a ranking of the possible control options at primary production level, and, if possible, quantifying the expected effectiveness of control actions on the broiler farm in terms of reducing human campylobacteriosis cases. Uncertainties affecting both the effectiveness estimates and

the ranking of the different control options were considered by application of the framework provided by EFSA's uncertainty guidance (EFSA Scientific Committee, 2018).

For some control options, the expected reduction in campylobacteriosis cases could be estimated in one of two ways: calculate the PAF for control options that reduce the prevalence of *Campylobacter* spp. in broilers (Section 2.2); or by means of quantitative probabilistic modelling for control options aimed at reducing the level of intestinal *Campylobacter* spp. concentrations in broilers (Section 2.3). Statistical uncertainty affecting these estimates was described and quantified by confidence intervals for the PAF and sensitivity analysis for the stochastic model (See Appendix C). Other uncertainties are addressed as described below.

The expected effect of the control options in reducing the incidence of human campylobacteriosis in EU by all MS was made by means of expert judgement; thus taking into account sources of systematic uncertainty arising when trying to infer the analytical evidence from the PAF analysis and simulation model at EU level. Expert judgement was also used to take additional evidence on these control options from the 2011 Opinion and subsequent publications (for which PAF could not be calculated or quantitative effects could not be simulated) into account.

Ranking of control options was therefore informed by three different evidence streams: effect of control options to reduce prevalence (supported by PAF and literature), effect of control options to reduce the level of contamination in broilers (supported by probabilistic modelling) and the effect of control options from the scientific literature (not supported by either PAF or probabilistic modelling). Expert judgement was therefore essential for ranking the control options, both for weighing and integrating the different streams of evidence and for considering their associated uncertainties. The BIOHAZ Panel agreed on the use of a structured approach, based on EFSA's (2014) guidance on expert knowledge elicitation (EKE), to ensure that all the identified evidence and uncertainties were considered in a balanced way and to improve the rigour and reliability of the judgements involved.

Due to the large number of control options to be considered within the time available, the EKE was conducted in two steps to allow for greater focus on the control options that were more likely to be effective. In the first step, experts assessed the probability that each control option would, if implemented by all EU broiler producers, reduce the incidence of campylobacteriosis in the EU by at least 10%. This step provided an initial ranking that was used to identify a subset of control options for more detailed assessment in the second step.

In the second step, experts assessed the magnitude of reduction in campylobacteriosis in the EU that each of the prioritised control options would achieve, if implemented by all EU broiler producers. In both steps, each control option was assessed separately, assuming all other control options remained at their present level of implementation. The detailed process is described in Section 3.5, together with the results and in Appendix D.

In both steps, the expert judgements were made by members of the EFSA Working Group and EFSA staff that were involved in the drafting of this Opinion. When assessing the effects of control options, all the relevant evidence available to the Working Group was considered. This included evidence from the 2011 Opinion, evidence from scientific literature published since 2011 and results from both the modelling approaches. The sources of systemic uncertainty identified by the Working Group as relevant to the assessment of the control options were also considered. To help experts take all the relevant evidence and uncertainties into account in a balanced way, the Working Group prepared two tables summarising key aspects of the evidence on control options affecting concentrations and prevalence, and a third table summarising the identified sources of uncertainty (Appendix D).

2.4.1. Step 1. Screening of all control options

A list of 21 control options was agreed to be considered for ranking. This list resulted from the review of the 2011 opinion and updating the information provided (Section 2.1), the PAF analysis (Section 2.2) and modelling (Section 2.3):

- Reduced slaughter age
- Discontinued thinning
- Employing few and well-trained staff
- Vaccination
- No animals in close proximity to the broiler houses
- Feed and water additives
- Avoiding drinkers that allow standing water
- Bacteriophage

- Addition of disinfectants to drinking water
- Designated tools per broiler house
- Effective cleaning and disinfection
- Hygienic anterooms at broiler house entrance
- Selective breeding
- Effective rodent control
- Fly screens and keeping insects out of the broiler house
- Stocking density and flock size
- Downtime between flocks
- Feed structure
- The number of houses on site
- Clean litter
- Litter amendments

In the first step of EKE, for each control option, each expert assessed the probability that it would reduce the campylobacteriosis incidence in humans in the EU associated with the preparation and consumption of broiler meat by 10% or more, if implemented by all broiler farmers in the EU. The threshold was set at 10% to obtain sufficient discriminatory power in the EKE. If a lower threshold was used (i.e. 5%), most of the control options would have been considered as potentially effective, undermining the identification of the most promising control options that would be subject to detailed assessment in step 2. Note that the 10% was not meant to indicate a threshold level in terms of effectiveness and does not imply that 10% would be a sufficient reduction or not. To ensure that questions for eliciting probability judgements were well defined (EFSA, 2014), it was agreed to define the question for step 1 in more detail as follows:

What is the probability that, if the specified control option was implemented by all broiler producers in the EU that are not currently using it, the average annual incidence of campylobacteriosis cases in the whole EU population caused by *Campylobacter* spp. in broiler meat produced from chickens raised in the EU would reduce by more than 10% (compared to the current level), all other things being equal?

The following subsidiary definitions were used:

- The meaning of 'campylobacteriosis cases' was clear for the experts and does not require further definition.
- 'Other things being equal' includes other control options remaining at the current level of implementation, production and processing practices remain unaltered and no change in the consumption in the EU of meat from broilers raised in the EU.
- If a control option acts on both prevalence and concentration, both should be considered when answering the question.
- For each control option, the experts answered the question assuming that, of the specific practices for this control option which are referred to in this Opinion (e.g. different vaccines, or different methods of rodent control), the practice that would, on its own, achieve the largest reduction in campylobacteriosis would be implemented by all EU broiler producers.

Experts expressing their judgement as precise or ranges of probabilities (see Table 3) (EFSA Scientific Committee, 2018).

Table 3: Approximate probability scale adopted for harmonised use in EFSA (EFSA Scientific Committee, 2018)

Probability term	Subjective probability range	Additional options	
Almost certain	99–100%	More likely than not: > 50%	Unable to give any probability: range is 0–100%
Extremely likely	95–99%		
Very likely	90–95%		
Likely	66–90%		
About as likely as not	33–66%		Report as 'inconclusive', 'cannot conclude' or 'unknown'
Unlikely	10–33%		
Extremely unlikely	1–5%		
Almost impossible	0–1%		

2.4.2. Step 2. Detailed assessment of selected control options

The subset of the control options to be prioritised for detailed assessment in step 2 was informed by experts' discussion upon results of step 1, the quality of evidence available, practical feasibility in the implementation of the control option and unequivocal definition of the control measure.

Selection resulted in eight control options (i.e. discontinued thinning, employing few and well-trained staff, vaccination, feed and water additives, avoiding drinkers that allow standing water, addition of disinfectants to drinking water, designated tools per broiler house, hygienic anterooms at broiler house entrance) for which it was considered that the second step of EKE process could be done within the time frame of this opinion.

The question for the experts to consider in the second step was:

If the specified control option is implemented by all broiler producers in the EU that are not currently using it, what will be the resulting percentage reduction (compared to the current level of implementation) in average annual incidence of campylobacteriosis cases in the whole EU population caused by Campylobacter spp. *in broiler meat produced from chickens raised in the EU, other things being equal?*

The individual experts were asked to quantify their uncertainty about the percentage reduction in the form of a probability distribution, elicited by a version of the Sheffield or SHELF protocol (EFSA, 2014; Oakley and O'Hagan, 2019) adapted to the needs of the current assessment. Each probability distribution was assessed by estimating by a median, lower bound and upper bound, and the two remaining quartiles.

Thereafter, the judgements of the different experts were aggregated for each control option by calculating the equal-weighted linear pool of the distributions providing the best fits to the individual judgements, using the SHELF software app for multiple experts.[5] The linear pool distributions were plotted together with the individual expert distributions (See Appendix D) and discussed in the expert group. Following the discussions, the group of experts decided on a consensus distribution for the effect of each of the eight control options considered.

Finally, the resulting consensus distributions reflecting the uncertainty of the estimated effectiveness of each of the prioritised control options were presented in figures and tables that included uncertainty around each estimate (See Section 3.5).

3. Assessment

3.1. Update on broiler production

The EFSA BIOHAZ Panel (2011) describes the broiler meat production chain in the EU in detail.

Production of poultry meat in the EU increased from ~ 12 million tons in 2008 to ~ 15 million tonnes in 2018, comprising largely broilers (75% in 2008 and 83% in 2018), followed by turkeys (16% in 2008 and 13% in 2018) and ducks (~ 3%). Based on FAO and OECD data from 2017, the EU is the third largest poultry meat producer in the world (US 21.3 million tonnes, followed by China 17.0 million tonnes and EU 15.9 million tonnes, at an estimated world production of 118.1 million tonnes) (Damme et al., 2017).

Export of poultry meat increased from 1.3 million tonnes in 2014 to 1.5 million tonnes in 2017 (Table 4). The level of imported poultry meat remained the same during this time period (0.82 million tonnes in 2014 and 0.83 million tonnes in 2017). The rate of self-sufficiency was estimated at 104.7% (2017) (AVEC, 2018).[6]

Poultry meat consumption per capita in the EU was 24.1 kg in 2017 (22.1 kg in 2014) with large differences between Member States (e.g. 36.2 kg in Portugal vs. 20.8 kg in Italy). Broiler meat consumption dominated (19.4 kg per head), followed by turkey meat (4.0 kg per head) (Damme et al., 2017).

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[5] https://jeremy-oakley.shinyapps.io/SHELF-multiple/
[6] http://www.avec-poultry.eu/wp-content/uploads/2018/10/8.-WF-28-09-2018-AVEC-annual-report-2018.pdf

Table 4: EU data on poultry meat (1,000 tonnes carcass weight) (AVEC, 2018; Eurostat, 2020)[7]

	2012	2013	2014	2015	2016	2017	2018	2019
Gross production in the EU	12,716	12,805	13,263	13,788	14,495	14,570	15,248	15,557f
Export	1,324	1,311	1,361	1,508	1,679	1,671	1,780	n.a.
Import	841	791	821	875	902	807	813	n.a.
Consumption	12,233	12,285	12,719	13,254	13,831	13,827	14,457	14,761[b]
Consumption per head, kg	21.3	21.3	22.1	22.9	23.9	24.1	25.0[a]	25.5[a]

n.a.: data not available.
(a): Estimated.
(b): Forecast.

Six Member States account for 71% of the total EU poultry meat production (PL-16%, UK 13%, FR 11%, ES 11%, DE 10%, IT 9%) (Figure 2) (Eurostat, 2018).[8]
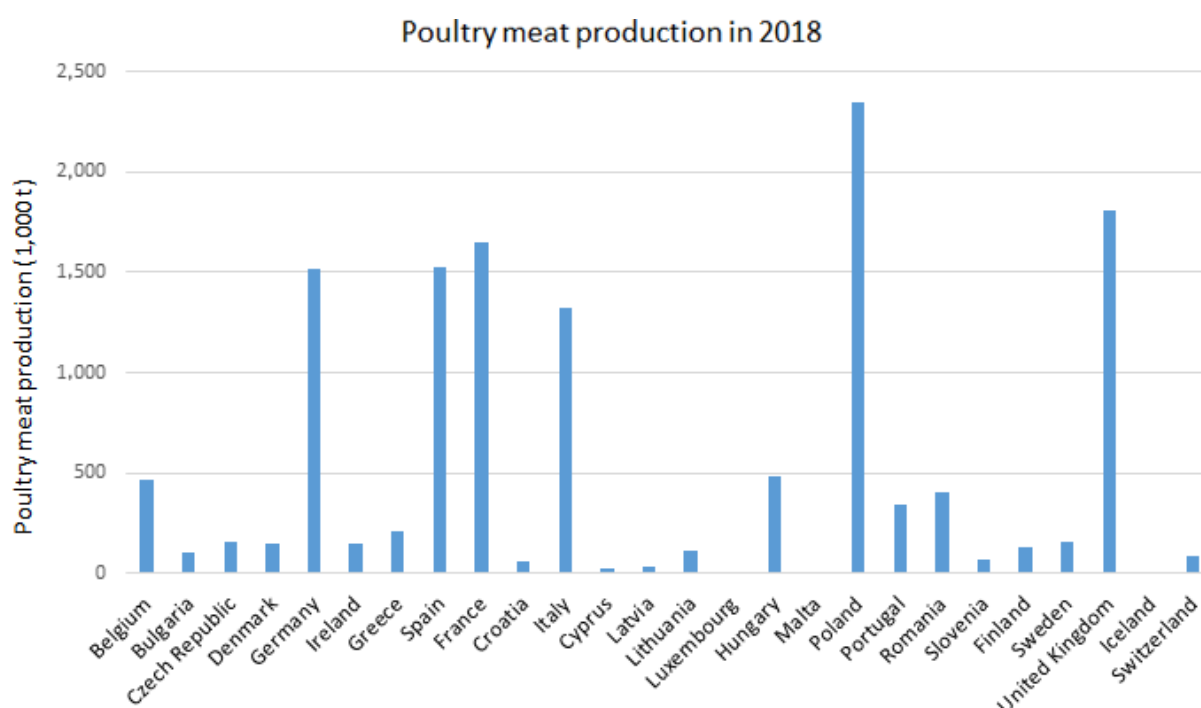
Figure 2: Poultry meat production in 2018 (source: Eurostat)[5] (Estimated: Croatia; Provisional: Spain, France; Confidential: Estonia, The Netherlands, Austria, Slovakia; Not available: Liechtenstein, Norway)

The EU statistics showed a 14% yearly increase in the overall organic poultry production between 2005 and 2015 (European Commission, 2016).[9] An EU-wide baseline survey on *Campylobacter* spp. in broiler batches and on broiler carcasses was carried out in 2008 (results are given and analysed in EFSA BIOHAZ Panel, 2010). Although these data are out of date and pre-date major *Campylobacter* control initiatives in many MSs, it is nonetheless the most recent EU-wide study. The prevalence of *Campylobacter* spp. colonisation in broiler batches was 71% (determined from caecal contents) and the prevalence of *Campylobacter*-contaminated broiler carcasses was 75.8% (based on neck and breast skin samples).

In general, large differences were seen among MSs, with prevalence in broiler batches ranging from 2.0% to 100.0%, and prevalence on broiler carcasses ranging from a 4.9% to 100.0%.

Table 5 shows the prevalence of *Campylobacter* spp. in broiler meat and broilers based on data reported in the annual European Union summary reports on trends and sources of zoonoses, zoonotic agents and food-borne outbreaks. It appears that the *Campylobacter* spp. prevalence in broilers and on broiler meat has remained quite constant over the years. However, since the number of countries reporting prevalence data changed over the years, the data are not directly comparable.

Table 5: *Campylobacter* spp. prevalence (% positive (total tested)) in the EU, 2010–2018

Year	*Campylobacter* spp. prevalence % (n)			
	Fresh broiler meat at retail	Fresh broiler meat at processing plant	Broilers (flock based)	Reference
2018	37.5 (7,441)*		26.0 (13,636)	EFSA and ECDC (2019)
2017	37.4 (13,445)*		12.3 (10,077)	EFSA and ECDC (2018)
2016	36.7 (11,495)*		27.3 (13,558)	EFSA and ECDC (2017)
2015	59 (3,652)	37.7 (297)	15.3 (7,033)	EFSA and ECDC (2016)
2014	36.4 (1,570)	9.9 (1,248)	27.2 (9,907)	EFSA and ECDC (2015a)
2013	25.2 (3,102)	12.0 (1,904)	15.1 (n. n.)	EFSA and ECDC (2015b)
2012	24.9 (3,495)	15.8 (2,049)	13.2 (6,001)	EFSA and ECDC (2014)
2011	34 (5,059)	29.3 (1,260)	17.8 (6,656)	EFSA and ECDC (2013)
2010	22.9 (3,508)	44.65 (1,010)	18.2 (9,212)	EFSA and ECDC (2012)

*: Not specified in the corresponding report.

3.2. Update on risk factors for *Campylobacter* spp. in broiler production

There are multiple sources and dissemination routes for *Campylobacter* spp. on broiler farms. The EFSA '*Campylobacter* in broiler meat' Opinion (EFSA BIOHAZ Panel, 2011) identified several risk factors for *Campylobacter* spp. in primary production. All those risk factors were reviewed and, when there was new information (since 2011), updated. Factors for which there was more recent information included vertical transmission, slaughter age, season, thinning, *Campylobacter*-contaminated drinking water, a previous *Campylobacter*-positive flock in the house (carry-over) and the use of therapeutic antimicrobials for treatment. The remaining risk factors either did not have new information or were discussed in terms of control options (Section 3.3).

3.2.1. Vertical transmission

Vertical transmission is the internal contamination of the egg within the genital tract and before intact shell deposition. As stated in the last EFSA opinion (EFSA BIOHAZ Panel, 2011), vertical transmission does not appear to be an important risk factor for broiler colonisation with *Campylobacter* spp. Recent articles reported no evidence of vertical transmission of *Campylobacter* spp. from hatching eggs to commercial flocks (Battersby et al., 2016b; Tangkham et al., 2016; Colles et al., 2019).

3.2.2. Slaughter age

Most conventionally housed broilers test *Campylobacter*-negative for the first 21 days of rearing (EFSA BIOHAZ Panel, 2011). This may be due to maternal antibodies and/or the inability of current testing methods to detect low concentrations of the organism in a small subset of the flock population. Slaughter age is still found among the risk factors identified in epidemiological investigations with conventionally produced birds almost always having higher prevalence and caecal concentration towards the end of the production cycle (Sommer et al., 2013; Legaudaite-Lydekaitiene et al., 2017; Higham et al., 2018). Higham et al. (2018) showed that age was significantly positively associated with *Campylobacter* spp.

3.2.3. Season

It is still generally agreed that season is a risk factor with increased prevalence in broilers in the summer months. This was reflected in the EU baseline survey which suggested an increased risk in the period of July–September as compared to January–March (EFSA BIOHAZ Panel, 2011). Based on data collected in six EU MSs, the CAMCON project (Sommer et al., 2016a) found that seasonality affected

prevalence values and so did the monthly mean temperatures reported in the study. Although the reason for this observation is not clear, and different studies report conflicting findings, enhanced survival of *Campylobacter* spp. in the farm environment during the warmer months, more water consumption by the birds, heat stress of the birds and/or increased numbers of insects and dust from the neighbouring environment entering the broiler house (facilitated by increased additional ventilation), may be some of the factors contributing to the increased prevalence of *Campylobacter* spp. in broilers during the warmer months.

3.2.4. Thinning

Thinning or partial depopulation is a practice where a subset of the birds is removed for slaughter and processing, leaving the remaining birds to grow to the required size (Allen et al., 2008). Sometimes several rounds of thinning are performed in a flock (Millman et al., 2017). The 2011 EFSA Opinion highlighted thinning as a major risk factor and this is supported by research since then. Lawes et al. (2012) and Millman et al. (2017) reported thinning as a risk factor for *Campylobacter* spp. infection as it breaches the biosecurity barrier and catching crews, cages, modules and trucks visit multiple farms. Catching crews bring *Campylobacter* spp. into the house on their boots, forklift trucks or broiler harvester machines, trolley wheels, crates etc. (Ellis-Iversen et al., 2012; Smith et al., 2016; Georgiev et al., 2017). In addition to breaching biosecurity, thinning also stresses the birds and the presence of stress hormones in the gastrointestinal tract may promote the growth, proliferation and virulence of *Campylobacter* spp. (Aroori et al., 2014). Thus, *Campylobacter* spp. introduced at thinning, spread rapidly throughout the flock reaching levels in the birds of up to 10^8 cells per gram of caecal matter within 4–5 days after thinning (Koolman et al., 2014). In a recent investigation, Higham et al. (2018) confirmed previous findings and showed that thinned houses had a 309% increase in the odds of being highly contaminated and concluded that further investigations are required to elucidate farm and individual factors related to thinning (Higham et al., 2018).

3.2.5. *Campylobacter* spp. contaminated drinking water

Contaminated water was previously considered an important source of *Campylobacter* spp. on farms (EFSA BIOHAZ Panel, 2011). *Campylobacter* spp. are commonly found in surface water on farms (Mughini-Gras et al., 2016) and, if used without proper treatment, water may serve as a vehicle of transmission (Jonsson et al., 2012; Agunos et al., 2014; Allain et al., 2014; Torralbo et al., 2014; Borck Høg et al., 2016).

3.2.6. A previous *Campylobacter*-positive flock in the house (carry-over)

When a flock is *Campylobacter*-positive the broiler house and surrounding environment is often heavily contaminated and, if not cleaned and disinfected properly between flocks, a previous positive flock will become an important source of *Campylobacter* spp. for the new flock (EFSA BIOHAZ Panel, 2011). More recent studies also support this conclusion. Damjanova et al. (2011) and Battersby et al. (2017) both demonstrated that inadequate cleaning and disinfection was a risk factor in the spread of *Campylobacter* spp. from one flock to the next. Other studies detected the same genotypes of *Campylobacter* spp. in broiler house samples before or during flock placement (Allen et al., 2011; Damjanova et al., 2011). Broiler house surroundings such as the tarmac apron, anteroom, house door, feeders, drinkers, walls, columns, barriers and bird scales may act as a source of direct or indirect infection resulting in carryover of persistent genotypes through several rearing cycles (Battersby et al., 2016b). The failure to eliminate *Campylobacter* spp. at these sites between flocks has been attributed to a range of factors including the design of feeders and drinkers, insufficient down time, a lack of knowledge or utilisation of proper cleaning methods and bacterial resistance to the disinfectants used (Agunos et al., 2014).

3.2.7. The use of therapeutic antimicrobials

The EFSA 2011 Opinion reported conflicting results on the effect of antibiotics on *Campylobacter* spp. carriage and shedding, with Herman et al. (2003) observing no effect while Refregier-Petton et al. (2001) concluded that administering antibiotics to the birds decreased the risk of colonisation with this organism. Similar results were reported by Allain et al. (2014). These conflicting results may be due to the resistance of *Campylobacter* spp. to the antimicrobial administered or that *Campylobacter* spp. was introduced after the treatment. More recent research examining the effect of antibiotic treatments on

the microbiome of the broiler gastrointestinal tract is similarly inconclusive (Allen and Stanton, 2014; Mancabelli et al., 2016). The use of antimicrobials to reduce *Campylobacter* spp. carriage and shedding may induce resistance in bacteria colonising the birds and is contrary to current EU policy to reduce antibiotic usage in animal husbandry. Therefore, it is not be considered further in this opinion.

3.2.8. Concluding remarks

New information was published since the EFSA 2011 Opinion that provides additional evidence indicating slaughter age, season, thinning, contaminated drinking water and carry-over from a previous flock are still important risk factors for *Campylobacter spp.* colonisation of a broiler flock. Vertical transmission does not seem to be a relevant risk factor and the results on the use of antimicrobials are still inconclusive.

3.3. Control options to reduce the prevalence of *Campylobacter* spp. in broilers

In the following section, the updated knowledge on the expected effect of the individual biosecurity options that can be implemented at primary production level to control for the identified risk factor is summarised. In Section 3.3.1, the results of the control options associated with the risk factors for which PAF could be calculated are presented. In Section 3.3.2, the observed effects of the control options associated with the risk factors for which PAF could not be calculated are provided.

3.3.1. Calculation of population attributable fraction for control options

The systematic literature search resulted in 17 eligible studies published in 15 articles, as one of the articles (Borck Høg et al., 2016) presented two studies: one carried out in Norway and one in Denmark and another article presented both a summer and a winter study in Germany (Näther et al., 2009). Two studies were further excluded, because they investigated fewer than 10 farming practices resulting in difficulties excluding confounding or interaction with other known risk practices on the farms (Lawes et al., 2012; Sandberg et al., 2015). The remaining studies had examined multiple risk factors on more than 2,400 farms, calculated adjusted ORs and presented descriptive results to provide estimates for the PAF analyses. The 15 studies are described in Table 6.

Table 6: Overview of the selected studies for calculation of the population attributable fraction for control options to reduce the prevalence of *Campylobacter* spp. in the primary production of broilers

Reference	Country	Year of study	Number of flocks/farms	*Campylobacter* spp. prevalence
Allain et al. (2014)	France	2008	121/121*	71.9
Barrios et al. (2006)	Iceland	2001–2003	1091/36	15.4
Borck Høg et al. (2016)	Denmark	2010–2012	3328/104	9.5
Borck Høg et al. (2016)	Norway	2010–2012	1381/173	3.5
Bouwknegt et al. (2004)	Netherlands	1997–2000	495/461*	26.3
Chowdhury et al. (2012)	Denmark	2009–2010	2835/187	14
Ellis-Iversen et al. (2009)	United Kingdom	2003–2006	603/137	34.2
Hansson et al. (2010)	Sweden	2005	37/37	56.8
Jonsson et al. (2012)	Norway	2002–2007	18488/623	4.7
Lyngstad et al. (2008)	Norway	2005	131/131	n.a.
McDowell et al. (2008)	Northern Ireland	2001–2002	388/88	42
Näther et al. (2009) Summer	Germany	2004–2005	146/146	53
Näther et al. (2009) Winter	Germany	2004–2005	146/146	34
Refregier-Petton et al. (2001)	France	2001	75/75	42.7
Torralbo et al. (2014)	Spain	2010–2012	291/134	62.5

*: Estimated from information provided in the articles.

Of the six main poultry producing MS, four were represented in the study data (FR, UK, ES, DE). Half of the studies were conducted in the Nordic countries, over-representing this region of the EU

that had a lower prevalence of *Campylobacter* spp. than the rest of the MS in the 2008 baseline survey (Table 5).

Modifiable risk factors from all studies were grouped by the practice or action needed to control the risk and for which PAF was calculated. Control options were only included in the final modelling if the risk factor had been identified in at least two MS.

The PAF analysis identified six control practices with sufficient evidence including [1] Hygienic anteroom at broiler house entrance; [2] effective rodent control; [3] no animals in close proximity of the poultry houses; [4] having few and well-trained staff; [5] adding disinfectants to drinking water and [6] avoiding drinkers that allow standing water.

The PAF was calculated for each risk factor for each study and interpreted as the reduction factor, i.e. the level of reduction in prevalence, if all broiler farms in the EU implemented the control practice effectively. The results are presented in Figure 3 and discussed below.
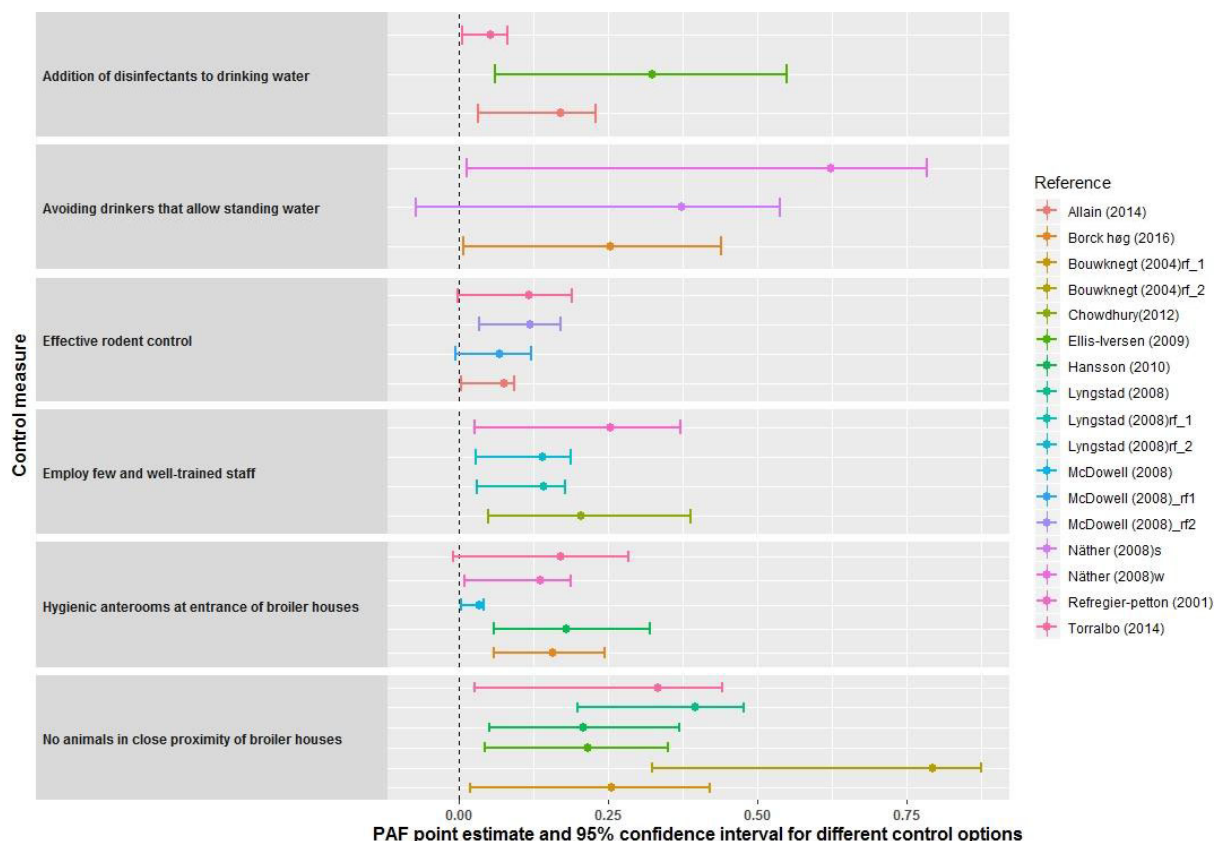
Figure 3: Population Attributable Fractions (PAF) point estimate values and 95% confidence intervals for six control measures with evidence for PAF calculation from the risk factor studies carried out in EU MSs

3.3.1.1. Addition of disinfectants to drinking water

Contaminated water was previously considered an important source of *Campylobacter* spp. on farms in contrast, to feed, where the lack of moisture creates a hostile environment for *Campylobacter* spp. (EFSA BIOHAZ Panel, 2011). *Campylobacter* spp. are commonly found in surface water on farms (Mughini-Gras et al., 2016) and, if used without proper treatment, water may serve as a vehicle of transmission (Jonsson et al., 2012; Agunos et al., 2014; Allain et al., 2014; Torralbo et al., 2014; Borck Høg et al., 2016).

The PAF analysis suggested that adding organic acids, chlorine-based biocides or hydrogen peroxide to the drinking water could reduce the risk of *Campylobacter*-positive flocks up to 55% (Table 7). Mainly chlorination (UK, ES) and acidification (FR) were found to reduce the risk, but in Spain, hydrogen peroxide added to drinking water was also reported as common and effective. Other studies did not identify a significant effect and, again, this is probably due to the variation in practices such as concentration and type of additive, baseline cleanliness of water, temperature and many other

factors. In addition, one French study (Refregier-Petton et al., 2001) found that acidification of drinking water was a risk factor for the presence of *Campylobacter* spp., but this was most likely due to poor hygiene.

Table 7: The effect of implementing the control option 'Addition of disinfectants to drinking water' on the *Campylobacter* spp. prevalence of broilers

Estimated reduction in prevalence (PAF)	95% confidence interval of PAF	Risk factors identified in studies in the EU	Study location	References
32.4%	6.0–54.9	Non-chlorinated water	United Kingdom	Ellis-Iversen et al. (2009)
5.3%	0.6; 8.2	Untreated water	Spain	Torralbo et al. (2014)
17.1%	3.3; 23.0	No acid in drinking water	France	Allain et al. (2014)

PAF: population attributable fraction.

3.3.1.2. Avoiding drinkers that allow standing water

Drinker types have been associated with a risk of positive poultry flocks, and studies suggest that removing cups, trays and other parts that allow standing water that may enhance the transmission, could reduce the risk up to 79% in Denmark and Germany (Table 8). PAFs could not be calculated for the recent multicountry (ES/UK/DK/NL/PL/NO) study (Sommer et al., 2016b); however, the authors identified drinkers with cups as significantly associated with increased risk. This finding is supported by Borck Høg et al. (2016) who also found that drinker nipples with cups were a risk factor, when compared to nipples without cups. Sommer et al. (2016a,b) estimated a reduction of up to 24% in human *campylobacter*iosis, if the broiler industry used drinking nipples without cups.

Table 8: The effect of implementing the control option 'Avoid drinkers that allow standing water' on the *Campylobacter* spp. prevalence of broilers

Estimated reduction in prevalence (PAF)	95% confidence interval of PAF	Risk factors identified in studies in the EU	Study location	References
37.2%	0; 53.9	Nipple drinker with tray	Germany	Näther et al. (2009) Summer
62.4%	1.2; 78.5	Nipple drinker with tray	Germany	Näther et al. (2009) Winter
25.4%	0.8; 44.0	Drinker with cups	Denmark	Borck Høg et al. (2016)

PAF: population attributable fraction.

3.3.1.3. Effective rodent control

If effective rodent control was achieved on all broiler farms in the EU, the overall prevalence of *Campylobacter* spp. in EU flocks could decrease by up to 19% according to the studies in Table 9. The risk factors that were identified in Spain and Northern Ireland were farmers reporting the presence of rodents during the production cycle and/or rodent droppings were observed at a sampling visit. The French study measured whether rodent control was applied outside the house and found that lack of control was a risk factor.

In a French study of outdoor reared birds (Huneau-Salaun et al., 2007), rodent control carried out by contractors instead of farmers was found to be a risk factor, possibly due to the infrequent bait changes by the contractor. Since the study was for outdoor flocks, it was not included in the PAF analysis. In the CAMCON study, rodent control was not included in the final analyses due to too many missing values (Sommer et al., 2016a).

Table 9: The effect of implementing the control option 'Effective Rodent Control' on the *Campylobacter* spp. prevalence of broilers

Estimated reduction in prevalence (PAF)	95% confidence interval of PAF	Risk factors identified in studies in the EU	Study location	References
7.5%	0.4; 9.3	No Rodent control outside house	France	Allain et al. (2014)
11.8%	3.4; 17.1	Rodents seen by sampler	Northern Ireland	McDowell et al. (2008)
6.7%	0.0; 12.1	Farmer reported rodents	Northern Ireland	McDowell et al. (2008)
11.7%	0.0; 18.9	Presence of rodents in shed	Spain	Torralbo et al. (2014)

PAF: population attributable fraction.

3.3.1.4. Employing few and well-trained staff

Farm workers, maintenance personnel and catching crews who move between and within farms are a source of *Campylobacter* spp. dissemination via contaminated boots and poor hygiene practices. Thus, farm staff are often the vehicle of *Campylobacter* spp. carriage into the broiler house (Battersby et al., 2016a). In the study by Van Limbergen et al. (2018), the parameter 'visitors and staff' scored the lowest, suggesting that better education of the staff may help to improve the overall biosecurity on broiler farms in Europe. Similar research by Ansari-Lari et al. (2011) using 100 flocks on 100 commercial broiler farms reported that the odds of flock infection decreased when the level of education of the farmers increased.

The PAF analysis suggested that restricting the number of employees and only using permanently or long-term employed staff may reduce the prevalence by up to 40% (Table 10). Researchers in both France and Denmark found that having more than one person managing a flock increased the risk of *Campylobacter* spp. infection in the broilers. In Norway, the risk increased if the farmer hired staff and/or allowed external staff in the shed at bird delivery.

Table 10: The effect of implementing the control option 'Employing few and well-trained staff' on the *Campylobacter* spp. prevalence of broilers

Estimated reduction in prevalence (PAF)	95% confidence interval of PAF	Risk factors identified in studies in the EU	Study location	References
14.2%	2.9; 17.7	Personnel in house at delivery	Norway	Lyngstad et al. (2008)
13.9%	2.7; 18.6	Hired caretaker staff	Norway	Lyngstad et al. (2008)
25.3%	2.7; 37.1	≥ 2 persons taking care of broilers	France	Refregier-Petton et al. (2001)
20.5%	5.0; 38.8	≥ 2 persons entering houses	Denmark	Chowdury et al. (2012)

PAF: population attributable fraction.

3.3.1.5. Hygienic anterooms at broiler house entrance

Pre-2011 research demonstrated the importance of anterooms. This describes a room between the outside door and the entry to the production area where the birds are housed. The anteroom may be separated into a 'dirty' zone (area closest to the outside door) and a clean zone (area closest to the door to the broiler production area) where the farmer changes footwear and puts on clean house-specific overalls and washes hands before accessing the production area. Ensuring that anterooms are clean and function as an effective division, may result in between 5% and 13% reduction in the *Campylobacter* spp. flock prevalence.

The PAF analysis highlighted differences in the use and effectiveness of anterooms in different MS (Table 11). In Spain, for example, the absence of an anteroom in some broiler houses was identified as a risk factor. The studies from Denmark and Northern Ireland rated the anterooms and divided them into categories and in both countries; untidy and low-quality anterooms were risk factors. In France, litter beetles in the changing room were associated with a higher risk of *Campylobacter*-positive flocks. This observation was probably primarily a proxy for insect infestation within the broiler houses, but also a sign of unclean changing/anterooms. PAFs could not be calculated for all countries

in the recent multi-country (ES/UK/DK/NL/PL/NO) study (Sommer et al., 2016b), but the absence of an anteroom plus barrier (no effective biosecurity at the entrance of the houses) was identified as significantly associated with increased risk.

Table 11: The effect of implementing the control option 'Hygienic anterooms at shed entrance' on the *Campylobacter* spp. prevalence of broilers

Estimated reduction in prevalence (PAF)	95% confidence interval of PAF	Risk factors identified in studies in the EU	Study location	References
17.0%	0.0; 28.4	No anteroom in poultry house	Spain	Torralbo et al. (2014)
3.3%	0.4; 4.2	Tidiness and cleanliness could be improved	Northern Ireland	McDowell et al. (2008)
13.6%	0.9; 18.8	Presence of litter-beetles in anterooms	France	Refregier-Petton et al. (2001)
15.6%	5.9; 24.4	Low quality anteroom	Denmark	Borck Høg et al. (2016)
18%	5.9;31.9	General tidiness score reflecting a combination of a number of hygiene parameters	Sweden	Hansson et al. (2010)

3.3.1.6. No animals in close proximity of the broiler houses

Animals in adjacent fields may be a source of *Campylobacter* spp. in broilers. Several studies have applied typing methods to test for the presence of the same clones, sequence types, etc. in broilers and other animals in the immediate vicinity of the poultry farm (Ellis-Iversen et al., 2012; Mughini Gras et al., 2012; Sheppard and Maiden, 2015; Weis et al., 2016). In general, relatively small numbers of isolates are tested and even when the same strain is detected, the results are inconclusive as the direction of spread is unknown. Some *Campylobacter* strains are capable of colonising several different farm animal species (Ellis-Iversen et al., 2012; Mughini Gras et al., 2012; Sheppard and Maiden, 2015; Weis et al., 2016) although not all studies find direct matches (Agunos et al., 2014).

While this might suggest that other livestock on the farm rarely act as a source of *Campylobacter* spp. in broilers, the inability to match strains between farm animal species could also be due to one flock, herd or even one animal carrying several genotypes of *Campylobacter* spp. at once and most studies normally look at only one isolate (Grove-White et al., 2011; Sheppard and Maiden, 2015). In contrast, Ridley et al. (2011) used molecular typing to demonstrate similar *Campylobacter* strains in the broilers and in the cattle around the farm and, as these were first detected in the dairy herd, concluded that horizontal transmission from the cattle to the birds was a risk factor for colonisation of the broilers.

Nonetheless, epidemiological studies repeatedly identify other animals on or next to the farm as significant risk factors. It is likely that they play a role in maintaining the *Campylobacter* spp. between flocks. If other animals are kept away from broiler houses or surrounding areas, the risk of *Campylobacter*-positive flocks can be reduced by up to 88%, but most likely up to 45%. This is a broad category as it includes both pets (Spain), pigs (NL), cattle (UK) or just a broad category of other livestock (NL; SE) on same or adjacent premises (Table 12). The PAF could not be calculated for the Norwegian study (Jonsson et al., 2012) investigating the presence of livestock farms within 2 km from poultry farms, but the variable was identified as a risk factor in the multivariate model.

Table 12: The effect of implementing the control option 'No animals in close proximity of broiler houses' on the *Campylobacter* spp. prevalence of broilers

Estimated reduction in prevalence (PAF)	95% confidence interval of PAF	Risk factors identified in studies in the EU	Study location	References
25.5%	1.8; 42.1	Other animal species on farm	Netherlands	Bouwknegt et al. (2004)
79.3%	32.3; 87.5	Other animals within 1 km radius	Netherlands	Bouwknegt et al. (2004)

Estimated reduction in prevalence (PAF)	95% confidence interval of PAF	Risk factors identified in studies in the EU	Study location	References
21.5%	4.4; 35.0	Cattle adjacent	United Kingdom	Ellis-Iversen et al. (2009)
39.5%	19.8; 47.8	Pigs closer than 2 km	Norway	Lyngstad et al. (2008)
33.4%	2.6; 44.1	Presence of dogs/cats at farm	Spain	Torralbo et al. (2014)
20.9%	5.0;37.0	Other livestock on farm	Sweden	Hansson et al. (2010)

3.3.2. Control options for which the population attributable fraction cannot be calculated

The PAF can only be estimated from studies that provide an adjusted risk estimate from a properly designed epidemiological risk factor. However, some other types of studies also identify 10 other risk factors that are summarised below.

3.3.2.1. Effective cleaning and disinfection

As described in Section 3.2.6, cleaning a broiler house after the flock has been harvested requires the removal of the waste materials, which are often heavily contaminated with *Campylobacter* spp. from the bird faeces. During this operation, the external area immediately adjacent to the main doors is often heavily contaminated. Effective cleaning and disinfection therefore require that the inside of the broiler house (including feeders and drinkers which are not designed to facilitate cleaning) and the concrete apron outside the main door to be effectively disinfected. This is often not done properly, resulting in a risk of carry-over between flocks (EFSA BIOHAZ Panel, 2011; Damjanova et al., 2011; Battersby et al., 2016b).

There is a wide range of different cleaning agents and biocides commercially available for eliminating *Campylobacter* spp. in the broiler house between flocks. However, these vary in their effectiveness. Battersby et al. (2017) examined six different treatment combinations, applied as per manufacturer's instructions, and found that thermal fogging with the combination of potassium peroxymonosulfate, sulfamic acid and sodium chloride (5% v/v) or a glutaraldehyde and quaternary ammonium complex (0.3%, v/v) were effective treatments.

3.3.2.2. Downtime between flocks

The downtime between flocks is an important consideration linked to biosecurity. Pre-2011, research data were contradictory on whether longer or shorter periods of time between cleaning and disinfection of the house and restocking reduced the risk of *Campylobacter* spp. infection in the subsequent flock (Hald et al., 2000; Lyngstad et al., 2008). In theory, longer periods should result in greater reduction of any *Campylobacter* spp. present as this organism is a poor competitor in the environment and sensitive to desiccation. However, longer periods also increase the chances of *Campylobacter* spp. ingress into the house, if strict biosecurity is not maintained. Based on the data reported by Borck Høg et al. (2016) and Georgiev et al. (2017), a downtime of more than 2 weeks would increase the risk of the next flock becoming infected with *Campylobacter* spp. Similarly, Sommer et al. (2016b) suggested a downtime of less than 10 days was best and would translate into a 2–8% reduction in the human incidence of campylobacteriosis if this was applied across the whole of the poultry industry.

3.3.2.3. Fly screens and keeping insects out of the broiler house

In previous studies, insects, especially flies, were considered as potential carriers of *Campylobacter* spp. into the broiler house (EFSA BIOHAZ Panel, 2011). Since then, there have been few, if any, new studies to either confirm or contradict this conclusion. The long-term effect of fly screens in Denmark was studied by Bahrndorff et al. (2013) in a 4-year intervention study with 10 fly-screened and 10 control farms. They found that there was no effect of applying fly screens in winter but that, in fly screen houses, *Campylobacter* spp. prevalence did not peak during the summer. Royden et al. (2016) investigated the role of flies in the *transmission* of *Campylobacter* spp. to broilers and found that despite the low prevalence of *Campylobacter* spp. cultured from flies, the risk of transmission could be high, especially during summer when fly populations are greatest.

3.3.2.4. Clean litter and litter amendments

Dry clean litter was not considered to be a source of *Campylobacter* spp. although these organisms could survive in contaminated litter especially if it became wet (EFSA BIOHAZ Panel, 2011). Recent research supports this finding and fresh or dry litter is still not considered to be a source of *Campylobacter* spp. introduction into the broiler house, but wet litter may play a role in the survival and spread of these bacteria (Robyn et al., 2015).

Zhang et al. (2016) added sodium bisulfate to litter in order to reduce ammonia concentration and emissions. While multiple litter amendment applications significantly reduced ammonia emissions, there was no effect on *Campylobacter* spp. concentration. Similarly, applying a mixture of microorganisms (EM), Nuengjamnong and Luangtongkum (2014)reported that a product containing lactic acid bacteria, yeasts, Bacillus spp. and Actinomycetes was beneficial in terms of reducing ammonia in poultry houses, but there was no reduction in Campylobacter spp.

3.3.2.5. Stocking density and flock size

There is little new research on the association between flock *Campylobacter* positivity and stocking density or flock size that would contradict evidence previously reported (EFSA BIOHAZ Panel, 2011). Stocking density can influence the levels of stress experienced by the birds. Borck Høg et al. (2016) reported a reduced risk associated with a high stocking density in Denmark, but not in Norway, probably due to farms applying stricter management routines and a higher level of biosecurity.

3.3.2.6. The number of broiler houses on site

The 2011 EFSA Opinion reported that the risk of *Campylobacter* spp. colonisation increased with the number of broiler houses on site but the association between the degree of risk and the number of houses was unclear. Interestingly, adjacent flocks are still considered to be a risk for *Campylobacter* spp. transmission to new flocks (Newell et al., 2011; Agunos et al., 2014) and the range of influence was reported to range from 9 to 14 km between positive farms in Denmark (Chowdhury et al., 2013).

3.3.2.7. Reduced slaughter age

The prevalence of flock positivity is directly related to slaughter age and reducing the slaughter age could be an effective action to reduce *Campylobacter* spp. prevalence in flocks (EFSA BIOHAZ Panel, 2011). This conclusion was based on the analysis of the EU baseline data (EFSA, 2010) and suggested that the overall incidence of campylobacteriosis in the human population would be reduced by 21% to 43% if the slaughter age was reduced to 28 days. Berndtson et al. (1996) reported a twofold increase in flock positivity after 42–44 days and a fourfold increase after 48–61 days. Kalupahana et al. (2013) demonstrated that it is at least 14 to 21 days before *Campylobacter* spp. are detected even on broiler farms with poor biosecurity. The EFSA BIOHAZ Panel (2011) found that reducing the slaughter age to 35 days would not have any effect in one MS, where the current average slaughter age was 32 days, but in three other MSs, this was estimated to result in a relative risk reduction of 9–18%. Using a similar approach, in the CAMCON project, van Wagenberg et al. (2016) estimated that if all flocks were slaughtered by 35 days or less, there would be a reduction in human campylobacteriosis of 10–18%.

3.3.2.8. Discontinued thinning

Thinning presents a high risk of introducing *Campylobacter* spp. into the broiler house and stopping thinning would reduce this risk (EFSA BIOHAZ Panel, 2011). This is supported by Georgiev et al. (2017), who demonstrated that discontinuing thinning would reduce the number of contaminated broiler flocks by at least one-third.

The EFSA BIOHAZ Panel (2011) estimated the effect of a ban on thinning in four MSs and found relative risk reductions between 2% and 25%. The effect of thinning could not be analysed using the data collected in the CAMCON project due to there being too many missing values (Sommer et al., 2016b), but using the approach applied by the EFSA BIOHAZ Panel (2011), the estimated relative risk reduction in the six countries involved varied between 3% and 13% (van Wagenberg et al., 2016).

3.3.2.9. Selective breeding

Selective breeding of *Campylobacter*-resistant chickens was suggested by Kaiser et al. (2009) but given the prioritisation of high meat or egg production, it is considered a long-term goal (EFSA BIOHAZ Panel, 2011). However, findings from a recent paper concluded that *Campylobacter* spp. load in broilers could have a low but significant heritability estimate (0.095 +/− 0.037), which indicated a

limited genetic basis and that non-genetic factors have a greater influence on the level of *Campylobacter* spp. found in the broiler chicken (Bailey et al., 2018). In another paper comparing *Campylobacter* spp. colonisation between four breeds (two broilers and two layers), it has been found lower prevalence and count of *Campylobacter* spp. and a quicker decrease in the shedding by the layer breeds than in broiler lines (Hankel et al., 2018).

3.3.2.10. Designated tools per broiler house

The presence and use of designated tools per broiler house, meaning that tools commonly used in broiler houses are applied in one broiler house only, were found to be an efficient control option in the CAMCON project (Sommer et al., 2016b). The estimated relative risk reduction of the application of designated tools in the six countries involved in this project varied between 1% and 16% (van Wagenberg et al., 2016). It was the most cost-effective control option analysed in their study.

3.3.3. Concluding remarks

- Compared to the 2011 opinion, the PAF approach was applied to convert results of epidemiological studies into quantitative control option effect estimates. European epidemiological risk factor studies on *Campylobacter* spp. in broilers were identified and when data were available, PAF was calculated for risk factors that could be associated with specific control options. This improved the interpretation of the available evidence basis and added new and more precise estimates of the effect of individual biosecurity practices to control *Campylobacter* spp.
- PAF were calculated for six control options from several studies: hygienic anteroom, effective rodent control, having no animals in close proximity to the broiler houses, addition of disinfectant to drinking water, employing few and well-trained staff and avoiding drinkers that allow standing water. The variation was greater between the different control options than for the same control options in different studies, which increased the confidence in the extrapolation potential of the results to the EU.
- When PAF was calculated for independent studies across several locations in Europe, the majority of the point estimate values were of similar magnitude for control options such as rodent control, hygienic anterooms, employing few and trained staff and no animals in close proximity to the broiler houses in all broiler farms in the EU. This adds confidence to the validity of the associations and the potential of the control options to reduce *Campylobacter* spp. prevalence in the EU.
- According to the PAF analyses, the mean relative risk reductions that could be achieved by adoption of each of these six control options individually are estimated to be substantial but the width of the confidence intervals of all control options indicates a high degree of uncertainty in the specific risk reduction potentials. For example, the mean estimate of the relative risk reduction for the control option 'Addition of disinfectants to drinking water' was between 5 (95% CI 0.6–8.2) and 32% (95% CI 6.0–54.9) based on three available studies.

3.4. Control options to reduce the concentration of *Campylobacter* spp. in broiler caeca

3.4.1. Literature update and selection of control options for model analysis

There are several papers reviewing potential *Campylobacter* control interventions on broiler farms to reduce the concentration of *Campylobacter* spp. in the birds. Several of these were described in the EFSA 2011 Opinion and new information when available is provided in this section including feed and water additives, bacteriophages, vaccination and feed structure. Information from relevant papers (Appendix E) was used for a final selection of studies to be included in the quantitative analyses.

3.4.1.1. Feed and water additives

A range of different feed and water additives, including biological cultures (probiotics/competitive exclusion), short chain fatty acids, organic acids, potassium sorbate, monocaprin (for water only) and chlorination (also water only) individually and in various combinations, were previously reviewed. They were not included in the quantitative models in the EFSA 2011 Opinion as the evidence behind the reductions achieved in *Campylobacter* spp. was too inconsistent to warrant consideration. Since then,

several papers have been published on feed and water additives. Aguiar et al. (2013) concluded that probiotics may reduce the levels of *Campylobacter* spp. in broilers but only when administered early in the production period before exposure to *Campylobacter* spp. Other *in vivo* challenge studies have also observed reduced *Campylobacter* spp. caecal counts using probiotic cultures, including *Bacillus* spp. and *Lactobacillus* spp. although it was difficult to obtain consistent results (Ghareeb et al., 2013; Guyard-Nicodème et al., 2016; Schneitz and Hakkinen, 2016; Manes-Lazaro et al., 2017; Saint-Cyr et al., 2017; Shrestha et al., 2017). Similar research has been undertaken using bacterial cultures that produce bacteriocins, a heterogenous group of mainly cationic, hydrophobic or amphiphilic peptides produced by a range of bacteria. These molecules cause pore formation in the bacterial cell membrane which usually results in cell lysis (Jozefiak and Sip, 2013). Umaraw et al. (2017) used bacteriocins in drinking water to combat *Campylobacter* spp. colonisation in broilers, while Messaoudi et al. (2011) reported that bacteriocin production by 3 different strains of *Lactobacillus salivarius isolated* from chicken caeca were active against both *C. jejuni* and *C. coli.* Other researchers had previously used *L. salivarius* strains in feed or drinking water to reduce the gut concentration of *C. jejuni* (Stern et al., 2006). *Enterococcus durans* and *Enterococcus hirae* also produce bacteriocins that may have potential application in broilers, but to date, no commercial bacteriocin products are available for controlling *Campylobacter* spp. in poultry (Svetoch et al., 2011) and it is difficult to extrapolate the results of small-scale laboratory-based studies to field conditions.

More recent research has also been reported on the potential application of organic and medium chain fatty acids. Haughton et al. (2013) reported reduced *Campylobacter* spp. concentrations in water treated with a commercial acidification product, but caecal counts were unchanged. In contrast, Jansen et al. (2014) achieved reduced caecal counts when organic acids were added to the drinking water but the *Campylobacter* spp. concentrations on the broiler carcasses obtained from these birds were unchanged. Other studies have also failed to observe a consistent positive effect (van Bunnik et al., 2012a,b). Hermans et al. (2012) added a mixture of medium chain fatty acids (caproic, caprylic, capric and lauric acid) to the drinking water in pilot studies. After 24 h, none of the 10 test birds that received a dose of 2×10^3 CFU *C. jejuni* were positive while 60% of the control birds were colonised. After 5 days, *Campylobacter* spp. colonisation or transmission was not reduced as all the birds were colonised with similar concentrations of *Campylobacter* spp. in the caeca. Thibodeau et al. (2015) developed and tested a feed additive based on a mixture of essential oils and organic acids which achieved a 0.7 log reduction in the caecal concentration of *Campylobacter* spp. without impacting on the gut microbiome. Robyn et al. (2013) reported that allicin (a compound produced when garlic is crushed or chopped) in drinking water eliminated *Campylobacter* spp. *in vitro* (laboratory studies), but did not have a similar impact *in vivo* (experimental trials) and attributed this to the presence of mucin-containing mucus in the caecum. Within the 'Campybro' project, 24 different additives belonging to either organic acids, plant extracts or pre- and probiotics have been tested in experimental husbandries (Gracia et al., 2016a; Guyard-Nicodème et al., 2016). Whilst no additive was able to prevent broiler colonisation by *Campylobacter* spp., some of them showed significant reductions reaching 3 $\log_{10}$ in one experimental trial. However, the main drawbacks found were the non-reproducibility between trials and the high level of within-batch variability (Gracia et al., 2016a,b; Guyard-Nicodème et al., 2016). The same conclusions were reached after field trials using organic acids and a cation exchange clay-based product in feed (Guyard-Nicodème et al., 2016; Huneau-Salaun et al., 2018). Other additives including ferric tyrosine (Skoufos et al., 2019) and a phytophenolic compound b-resorcylic acid (Wagle et al., 2017) were found to reduce *C. jejuni* concentrations in the caeca. In the study of Wagle et al., 2017, 2.5 log10 and 1.7 log10 reductions in birds were observed, 14 days after treatment, when the feed additive was applied at 0.5% and 1%, respectively (Wagle et al., 2017). In the study reported by Skoufos et al. (2019), the authors showed a significant 2 $\log_{10}$ reduction in the treated group of broilers.

Considering the criteria reported in Section 2.3.5 on selection of control options, two studies were included in the model analysis. The one from 'Campybro project' (Guyard-Nicodème et al., 2016) from which the least effective (referred to here as FA1, an organic acid) and most effective feed additive (FA2, a prebiotic) were selected, and the study reported by Skoufos et al. (2019) (FA3, an amino acid with iron) (Table 13). Raw data from Guyard-Nicodème et al. (2016) were reanalysed by a maximum likelihood estimation method that allows distribution fitting in the presence of censored data (Lorimer and Kiermeier, 2007), to obtain estimates for the mean log reduction (d) and the variability therein between applications, as well as the uncertainty of the mean estimate. The result d = 2 found by Skoufos et al. (2019) can be used to compare the results obtained by the model applied here with the results that were obtained by the model that was applied in the previous opinion (EFSA BIOHAZ Panel, 2011).

Table 13: Effect of three selected feed additives in terms of mean $\log_{10}$ reduction (d) of caecal concentration of *Campylobacter* spp. and the variability (standard deviation) in the $\log_{10}$ reduction (s_d). The standard error of the mean (S.E.M) is used to express the uncertainty about the mean and is used in the uncertainty analysis. NA = Not Available

Feed additive	d	s_d	S.E.M.	Number of birds tested	Reference
FA1	1.23	0	0.66	15	Guyard-Nicodème et al. (2016)
FA2	3.25	2.2	0.64	15	Guyard-Nicodème et al. (2016)
FA3	2	NA	NA	36 (3 replicates of 12)	Skoufos et al. (2019)

NA: Not Available.

3.4.1.2. Bacteriophages

Bacteriophages, also referred to as phages, are viruses that infect bacteria. Several pre-2011 studies indicated that bacteriophages have potential use as a therapeutic rather than a preventive treatment to reduce the concentration of *Campylobacter* spp. carriage in caecal contents and faeces immediately before slaughter (Loc Carrillo et al., 2005; Wagenaar et al., 2005; Carvalho et al., 2010; Hermans et al., 2011). Robyn et al. (2015) describe the minimum requirements for a phage treatment to be effective including [1] having a broad spectrum host capable of killing multiple strains of *C. jejuni* and *C. coli*; [2] having an obligate lytic cycle; [3] being safe and cost-effective and [4] being able to overcome host resistance. However, most phages are highly specific in the strains they can infect and as broiler flocks are infected with multiple strains of *C. jejuni* the results achieved are inconsistent. Kittler et al. (2013) applied a phage cocktail via drinking water. While a 3.2 $\log_{10}$ CFU of caecal contents reduction was achieved in one treatment group, the results were inconsistent and significant reductions were not obtained in other trials. More recent work by Richards et al. (2019) developed a phage cocktail that could achieve a *Campylobacter* spp. reduction of up to 2.4 $\log_{10}$ CFU of caecal material as compared to the untreated control birds. However, this reduction, achieved 2 days post treatment, was not maintained and the difference between the treated and control birds was reduced to 1.3 $\log_{10}$ CFU/g by 5 days post treatment (no data is provided beyond that time point). Although the authors reported a stable phage titre over time, approximately 10% of the *C. jejuni* population showed resistance. Sorensen et al. (2015) highlighted the fact that many phages rely on the highly diverse capsular polysaccharide (CPS) for infection that may be different in different *Campylobacter* spp. species and strains thus limiting the effectiveness of any phage-based intervention if not developed using multiple phage isolation strains known to carry different CPS variants. In addition to the requirement for multiple phage populations, there are other limitations in phage application including safety (from the human and veterinary health perspective) and practical (effective administration) aspects, logistic problems associated with treatment immediately before harvest and the development of resistant strains. It was therefore concluded that this technology is in the early stages of development and requires more research, including field trials, before it can be considered a viable option for *Campylobacter* control in broilers. This control option was not included in the model analysis due to the non-compliance with the selection criteria defined in Section 2.3.4.

3.4.1.3. Vaccination

Pre-2011, the proof of principle that *Campylobacter* antibodies (induced by vaccination in chickens), has protective properties, had been demonstrated (Stern et al., 1990) and several vaccination regimes and strategies have previously been tested but without success (EFSA BIOHAZ Panel, 2011). More recently, a range of candidate vaccines have been developed and tested. using as antigens; whole cells, live-attenuated strains, flagellin, an ATP-binding cassette (ABC) transporter protein, an outer membrane protein, an aspartate/glutamate-binding ABC transporter protein, a glutamine-binding ABC transporter protein, a hemin-uptake outer membrane protein, an outer membrane component of the CmeABC multidrug efflux pump and a periplasmic protein (Robyn et al., 2015). Although the majority of these achieved partial protection at best, there is no vaccine commercially available yet. However, work is ongoing, and several candidate molecules have shown promise. Okamura et al. (2012) immunised two groups of Jidori chicks subcutaneously with a formalin-killed *C. jejuni* with two different adjuvants. Both vaccines induced high levels of anti-*Campylobacter* IgG, but in challenge studies, the concentration of the organism in the caeca and faeces remained the same. Annamalai et al. (2013) used poly (lactide-co-glycolide) nanoparticle (NP) encapsulated outer membrane proteins (OMP) of *C. jejuni* that was administered subcutaneously. Seven days after vaccination, *Campylobacter* were not

detected in any of the test groups of broilers. Neal-McKinney et al. (2014) achieved a 2 log$_{10}$ reduction in *C. jejuni* colonisation in specific pathogen-free (SPF) chickens, using a vaccine based on recombinant surface-exposed proteins involved in broiler gut colonisation, but field trial validation has yet to be undertaken. Riazi et al. (2013) found that orally administered *C. jejuni* specific single domain antibodies were effective in preventing *C. jejuni* colonisation of day-old SPF broilers but future studies are required over the entirety of the growth cycle. Recently, Meunier et al. (2016) using reverse vaccinology identified 14 new antigens based on their subcellular localization, immunogenicity, B-cell epitopes density and their sequence conservation among *C. jejuni* and *C. coli* strains. Six of them were tested on broilers in experimental husbandries and four candidates showed *Campylobacter* load decreases in caeca by 2–4 logs CFU/g correlated with the induction of specific humoral responses (Meunier et al., 2017). Liu et al. (2019) used a native protein microarray approach and identified 30 new immunogenic *C. jejuni* proteins but no information was provided about *in vivo* testing. Vandeputte et al. (2019) reported that in ovo-vaccinated birds using vaccines based on maternal antibodies were not protected with the treated birds showing similar caecal *C. Jejuni* concentrations to the control birds. Adams et al. (2019) developed and tested live-attenuated *Salmonella*-vectored vaccines but found that oral vaccination of the broilers failed to trigger significant systemic and intestinal mucosal immune responses and hence did not confer protection against *C. jejuni*.

Considering the criteria reported in Section 2.3.4, only one study was included in the model analysis. From the 'Campybro' project (Meunier et al., 2017), the most effective (referred to here as VA2, YP9817 protein) and least effective vaccine (VA1, YP562 protein) in terms of caecal log reduction when birds were 42 days of age were selected (Table 14). Raw data from Meunier et al. (2017) were reanalysed by a maximum likelihood estimation method that allows distribution fitting in the presence of censored data (Lorimer and Kiermeier, 2007), to obtain estimates for the mean log reduction (d) and the variability therein between applications, as well as the uncertainty of the mean estimate.

Table 14: Effect of two selected vaccines in terms of mean log reduction (d) of caecal concentration of *Campylobacter* spp. and the variability in the log reduction (s$_d$). The standard error of the mean (S.E.M) is used to express the uncertainty about the mean, and is used in the uncertainty analysis

Vaccination	d	s$_d$	S.E.M.	Number of birds tested	Reference
VA1	2.03	1.83	0.49	15 birds for each vaccine test	Meunier et al. (2017)
VA2	4.15	1.63	0.51	15 birds for each vaccine test	Meunier et al. (2017)

3.4.1.4. Feed structure

Coarse feed materials are retained in the gizzard where they are ground down and exposed to hydrochloric acid. Thus, any feeds that delay the passage of materials through the gizzard may reduce the passage of *Campylobacter* spp. further along the gastrointestinal tract. This was demonstrated by Moen et al. (2012) who reported that a diet supplemented with 15% oat/barley hulls increased gizzard weight and delayed the spread of *Campylobacter* spp. within the birds. They concluded that stimulating the bird's natural barriers was an effective means of reducing the spread of *Campylobacter* spp. in broiler flocks. However, within the Campybro EU project, it was concluded that, feed structure had no significant effect on *Campylobacter* colonisation (Gracia et al., 2016a,b) and most commercial broiler flocks are already fed a proportion of whole grain within the ration.

This control option was not included in the model analysis due to the lack of evidence on the effect and/or missing quantitative data.

3.4.2. Results of model analysis

The selected control options (feed additives and vaccination) affecting the concentration in the caecal content were analysed and results are shown in Figure 4.
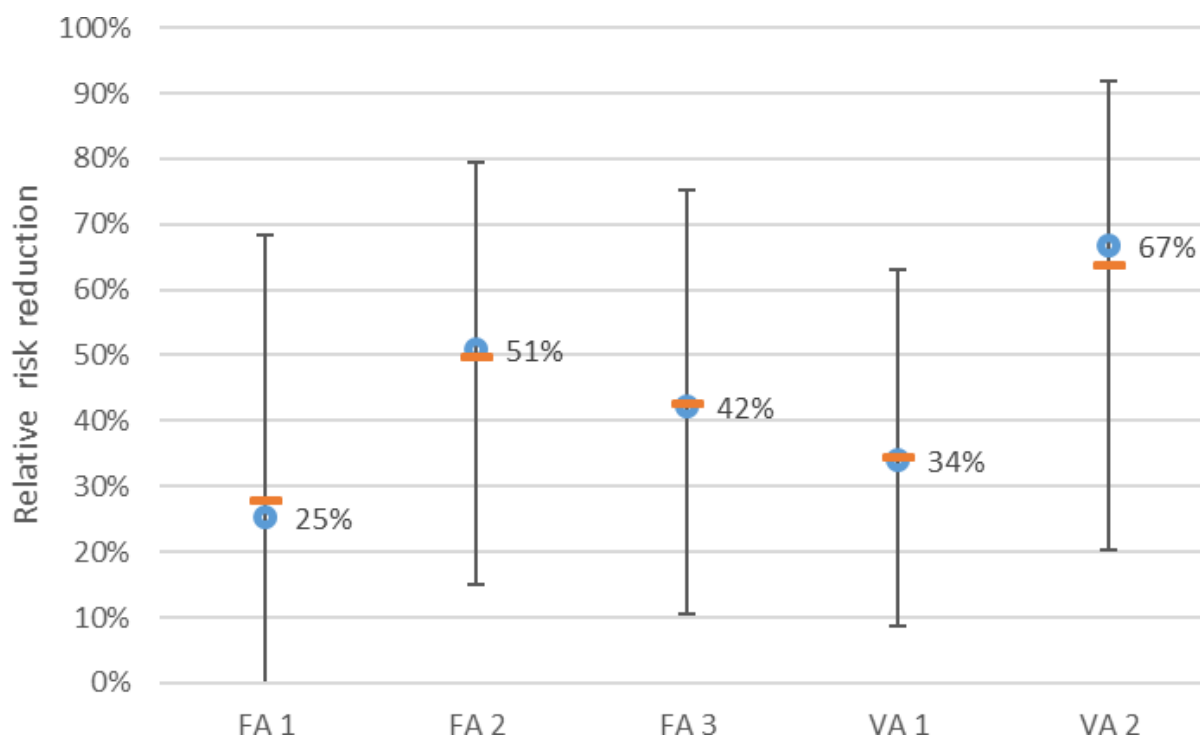
Figure 4: Estimated relative risk reductions achieved by *Campylobacter* control options 'feed additives' and 'vaccination', for the selected feed additives (FA) and vaccines (VA) (see Tables 13 and 14). Blue circle: median effect (numeric result given); orange line: mean effect; error bar: 95% confidence interval

According to the model, the most effective feed additive analysed (FA2) gave a median 51% risk reduction (95% CI 15–79%; mean 50%), FA3 gave a median 42% risk reduction (CI 11%–75%; mean 42%) and the low effective feed additive (FA1) gave median 25% risk reduction (CI 0%–68%; mean 28%). For the two vaccines studied, the most effective one studied (VA2) gave median 67% risk reduction (CI 20%–92%; mean 64%), whereas the less effective one (VA1) gave a median 34% risk reduction (CI 9%–63%; mean 34%).

Note that the effects of these interventions are less than estimated in the previous opinion (EFSA BIOHAZ Panel, 2011), where a 3 $\log_{10}$ reduction of the concentration of *Campylobacter* spp. in the caecal content was found to reduce the public health risk of campylobacteriosis associated with the consumption of broiler meat by at least 90%. With the model used in this opinion, the same hypothetical intervention would give a median 58% risk reduction at EU level (PI 16–89%; mean 56%). A 2 $\log_{10}$ reduction reduced the risk by 76–98% in four MSs in the 2011 opinion, which contrasts with the relative risk reduction estimated for FA3 that gave 2 log reductions. This decreased effect is mainly due to the update of the value of the slope of the regression line, based on an update of the literature (Table 2 and Appendix B), and a large unpublished data set (Rodgers, 2020).

3.4.3. Concluding remarks

- The modelling approach used in the 2011 opinion was updated using newly published data on the relationship between *Campylobacter* spp. concentrations in caecal contents and on broiler carcass skin samples, a larger variety of consumer phase models and a newly published dose response model.
- In a review of information available since 2011, new experimental *in vivo* studies were identified that reported estimates of the log reduction (and variation therein) that may be obtained by providing feed or water additives or through application of vaccination. However, no new information was available from field studies, which adds uncertainty to the actual log reductions that can be achieved in practice.
- The updated model resulted in lower estimates of the slope of the linear regression line describing the relation between concentrations in caecal contents and on skin samples.

Consequential to the decrease of this slope, lower estimates of the relative risk reduction were obtained for the effectiveness of control options directed at a reduction in the caecal concentrations. For example, for a 2-$\log_{10}$ reduction in caecal concentrations, the median estimate of the relative risk reduction of campylobacteriosis attributable to the consumption of broiler meat produced in the EU is now 42% (95% CI 11–75%), whereas in the previous opinion, this relative risk reduction was 76–98% based on data from four MSs; similarly, a 3-$\log_{10}$ reduction is now estimated to reduce this risk in the EU by 58% (95% CI 16–89%), compared to a relative risk reduction larger than 90% in four MSs, as found previously.

3.5. Ranking of control options

Within the time frame of this opinion, experts had to conduct a first-stage selection (step 1), where all the 21 control options were considered, leading to the second step where eight selected control options were prioritised for further assessment of the magnitude of their effect. The 21 control options included in the screening step 1 of the EKE were collated and plotted in descending order of probability of controlling *Campylobacter* spp. with more than 10% in the EU from top to bottom, sorted by the mean of the midpoints of the experts' ranges (Figure 5).
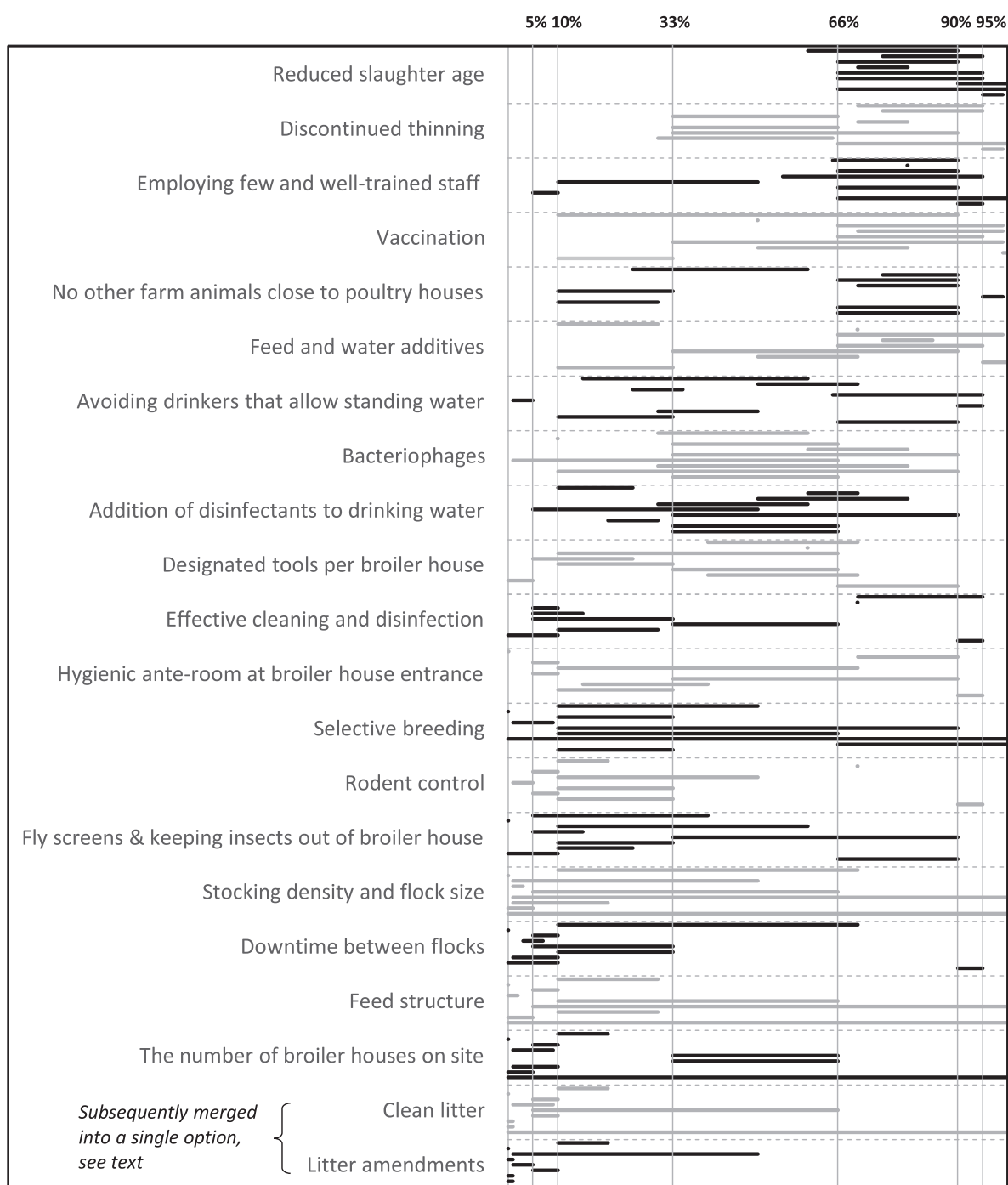
Figure 5: Results of step 1 of the ranking and uncertainty analysis. The horizontal axis is the probability, that, if the specified control option was implemented by all broiler producers in the EU, the average annual incidence of campylobacteriosis cases in the whole EU population caused by *Campylobacter* spp. in broiler meat produced from chickens raised in the EU would reduce by more than 10% (compared to the current level), assessed by expert judgement. For each control option, the set of horizontal bars shows the probability ranges given by the participating experts. Where a precise probability was given, the bar appears as a black dot. Dotted lines separate the control options. Black and grey bars are alternated to distinguish the different control options

Results of step 1, as shown in Figure 5, were collectively discussed until consensus was reached on which control options to take forward to Step 2.

The control options 'clean litter' and 'litter amendments' were combined into one 'clean litter and litter amendments' resulting in a final list of 20 possible control options.

After the first screening, the experts (i.e. the working group members and selected EFSA staff) agreed to exclude the eight control options in the lower part of Figure 5, up to and including 'selective breeding'. Based on visual inspection of Figure 5, and further discussion of the rationales behind individual experts' estimates, these eight control options were overall judged to have a rather low probability (less than about 30–40% as shown in Figure 5) to result in a relative risk reduction higher than 10%. In the remainder of this opinion, these eight options are identified as having a 'lower probability to have more than 10% effect'. The other 12 control options are identified as having a 'higher probability to have more than 10% effect'.

Of these 12 top ranked control options based on the probability of causing more than 10% risk reduction, four (4) were excluded from EKE step 2 for the following reasons:

- No other farm animals in close proximity to the broiler houses: lack of feasibility of implementation of this control option (the adjacent fields may belong to a different farmer) and doubts about the evidence of direction of transfer of *Campylobacter* spp.
- Effective cleaning and disinfection: The definition of 'cleaning and disinfection' was not precise enough for the experts to enable judgements, i.e. it combines a group of activities and evidence of effectiveness is based on a variety of different activities;
- Reduced slaughter age: current practices vary largely between EU countries and welfare issues relating to fast-growing birds might prevent application;
- Bacteriophages: lack of convincing evidence of effectiveness in the field due to shortage of field studies.

Hence, the following eight control options were selected for further consideration:

- Discontinued thinning
- Employing few and well-trained staff
- Vaccination
- Feed and water additives
- Avoiding drinkers that allow standing water
- Addition of disinfectants to drinking water
- Designated tools per broiler house
- Hygienic anterooms at broiler house entrance

The outcomes of step 2 of the EKE for the eight prioritised control options are sorted by the medians and presented in a boxplot (Figure 6). As the uncertainty around the effectiveness of each control option largely overlapped with the effectiveness of all other control options, a meaningful ranking of these eight control options was not considered possible. More detailed results are available in Appendix D.
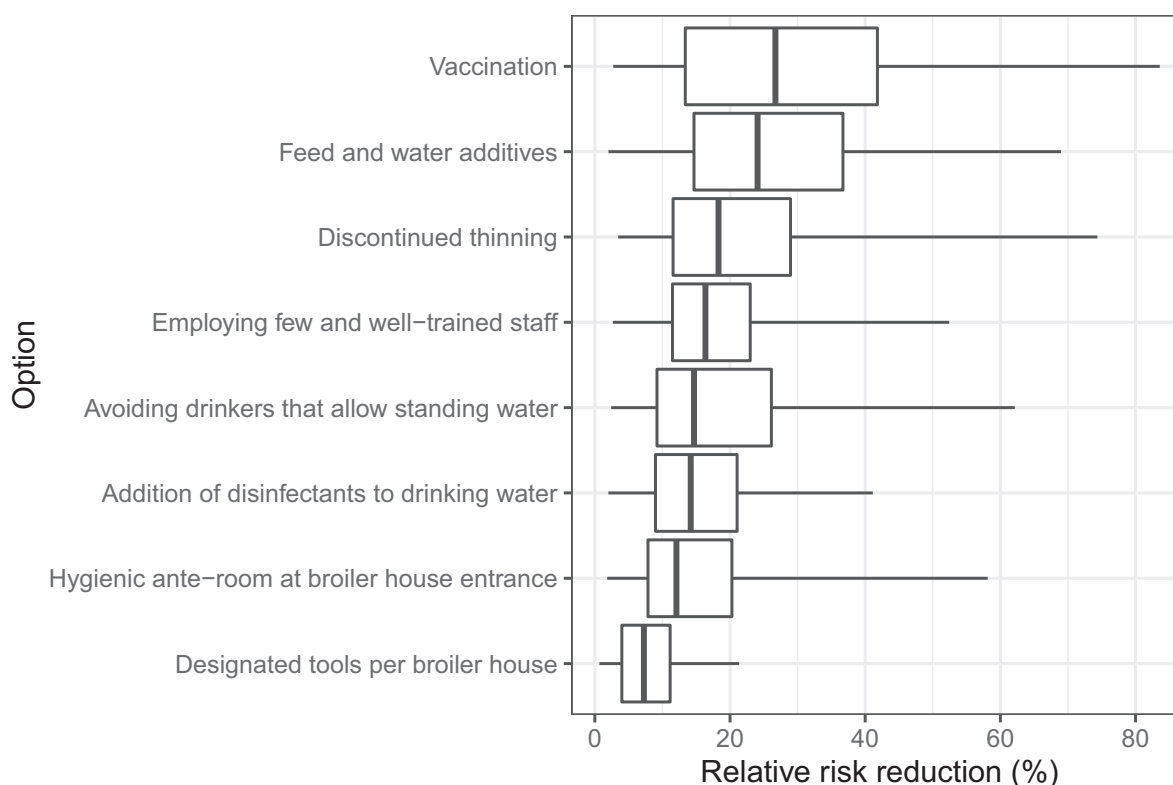
Figure 6: Results of step 2 of the ranking and uncertainty analysis. The horizontal axis is the relative risk reduction for each control option, assessed by expert judgement and expressed as % relative risk reduction in EU campylobacteriosis cases if the control option was implemented by all EU broiler producers. For each control option, the horizontal line shows the 95% probability interval for the estimated risk reduction (P2.5 and P97.5), the box shows the interquartile range (P25 and P75) and the vertical line shows the median (P50). The control options are ordered by the medians, but this should not be interpreted as a ranking due to the large degree of overlap between options

The consensus distributions obtained were based on discussions between the experts and the available evidence from the three evidence streams (effect of control options to reduce flock prevalence (supported by PAF calculations based on literature data), effect of control options to reduce the concentrations in broiler caeca (supported by estimates obtained by a combination of models) and effect of control options directly obtained from literature (not supported by either PAF or modelling). Table 15 summarises the main arguments.

Table 15: Overview of arguments leading to the consensus distributions for the eight selected control options. Next to the arguments for low and high effectiveness and some general comments, the table shows the largest range of quantitative estimates as given in this opinion, the source of these estimates (i.e. the PAF analysis, the concentration model or literature data), and the relative risk reduction estimates obtained by EKE

Control option	Arguments for low effectiveness	Arguments for high effectiveness	General comment	Largest range of quantitative estimates (%)*	Source of quantitative estimates	Median consensus (90% Probability interval) (%)
Vaccination	Doubts about inconsistencies in field conditions after upscaling Despite many efforts, there is no vaccine (proven to be effective in practice) currently available	Model results confirm large potential of vaccination The results are more consistent than for feed or water additives	It is generally agreed that the wide distribution reflects existing uncertainty and differences in judgement between experts	9–92	Concentration model	27 (4–74)
Feed and water additives	Doubts about inconsistencies under field conditions; very little evidence of reproducibility Publication bias: negative results are not published	Some additives show a large effect When effective, the risk reduction achieved is large	Unclear which specific additive is chosen Large variability between additives and studies	0–80	Concentration model	24 (4–60)
Discontinued thinning	Discontinued thinning will not reduce prevalence under poor biosecurity conditions	Data suggest that flocks are rarely *Campylobacter* negative after thinning (Koolman et al., 2014) It is very difficult to maintain high biosecurity during thinning; undermines the motivation to, and effect of, carrying out good biosecurity	Different experiences in different countries Differences between countries will be large Unclear how often thinning is currently applied in EU MSs; CAMCON project found that majority of flocks (> 80%) were thinned in large producer countries: ES, UK and PL	2–25	EFSA Opinion 2011; van Wagenberg et al. (2016)	18 (5–65)
Employing few and well-trained staff	Training and/or certification alone does not mean that good biosecurity is consistently implemented	Key for good overall biosecurity Good biosecurity and husbandry are reliant on people knowing what they are doing and why	Main peak reflects PAF results	2.7–38.8	PAF analysis	16 (5–45)

Control option	Arguments for low effectiveness	Arguments for high effectiveness	General comment	Largest range of quantitative estimates (%)*	Source of quantitative estimates	Median consensus (90% Probability interval) (%)
Avoiding drinkers that allow standing water	Not clear why nipple drinkers are associated with lower prevalence of Campylobacter in the flock	Standing water may facilitate cross-infection between birds using the same drinker. Drinker cups are quickly contaminated with bedding materials and possibly feed providing a niche in which Campylobacter may survive and cross-infect other birds Cups on drinkers may allow spillage onto the bedding resulting in a higher moisture content that supports *Campylobacter* survival	Experts agreed on average (linear pool) of distributions based on individual judgements, without detailed discussion	0–78.5	PAF analysis	15 (4–53)
Addition of disinfectants to drinking water	The birds may dislike the odour or taste of the water resulting in lower effectiveness	Prevents water acting as a source of *Campylobacter* Effective way of administering anti-*Campylobacter* agents ensuring all birds are treated	Experts agreed on average (linear pool) of distributions based on individual judgements, without detailed discussion	0.6–54.9	PAF analysis	14 (3–36)
Hygienic anterooms at broiler house entrance	Requires motivation on the part of the farmers	A key part of any biosecurity system ensuring *Campylobacter* are not transmitted form a contaminated farmyard into the broiler house Easy to implement	Experts agreed on average (linear pool) of distributions based on individual judgements, without detailed discussion	0–31.9	PAF analysis	12 (3–50)
Designated tools per broiler house	Will not be effective as stand-alone measure Sharing tools indicates poor overall biosecurity	There is evidence that it is effective, although the effect is small		1–16	CAMCON project	7 (1–18)

*: As presented in the opinion.

Apart from information on mean and percentiles of the consensus distribution, the probability distribution obtained in step 2 of the EKE also contains an estimate of the probability that the relative risk reduction is more than 10% (i.e. the percentile where the relative risk reduction as illustrated in Figure 6 is 10%). This estimate, which was implicitly agreed on after the discussions between the experts, can be compared with the estimates obtained in step 1 of the EKE, where individual experts were asked to assess the likelihood that the relative risk reduction would be more than 10% (Figure 5). Table 16 compares these estimates, where the ranges shown in Figure 5 are summarised by the mean of the midpoint estimates for each of the individual experts.

The comparison shows that the estimated probability of more than 10% relative risk reduction is considerably higher for all control options after step 2 of the EKE, except the designated tools per broiler house. It should be stressed that step 1 was an approximate screening step, while step 2 was more refined. It is therefore expected that the results differ to some degree, and more weight should be given to the step 2 results, as they followed more detailed consideration and thorough discussions between the experts. Other reasons for the differences between the estimated likelihoods might be the difference in the EKE questions at step 1 and step 2, where experts were asked to estimate the probability that the relative risk reduction is more than 10% (step 1) or to assess the relative risk reduction itself (step 2), and the choice of the mean of the midpoints (i.e. ignoring the uncertainty which was an explicit part of the question and may give a bias towards values for the midpoint closer to 50%).

Table 16: The estimated probability that the relative risk reduction is more than 10%, as obtained from the mean of the midpoints of the individual experts in step 1 of the EKE (Figure 5); and as derived from the probability distributions obtained in step 2 of the EKE, after discussion between the experts (Figure 6)

Control options	Mean of midpoints of EKE step 1	Estimate derived from probability distribution of EKE step 2
Vaccination	67%	83%
Feed and water additives	64%	86%
Discontinued thinning	70%	81%
Employing few and well-trained staff	67%	81%
Avoiding drinkers that allow standing water	49%	71%
Addition of disinfectants to drinking water	45%	70%
Hygienic anterooms at broiler house entrance	38%	62%
Designated tools per broiler house	42%	31%

EKE: expert knowledge elicitation.

3.5.1. Concluding remarks

- The effectiveness of 20 control options if implemented by all broiler farms in the EU, taking into account the current level of implementation, was estimated by means of a two-step expert knowledge elicitation (EKE) process that was informed by results from modelling of the updated scientific evidence and literature review (including previous opinion).
- Eight control options, when considered separately, were judged to have a lower probability of achieving a reduction of at least 10% in the incidence of campylobacteriosis, as follows; effective rodent control, extended downtime between flocks, fly screens and keeping insects out of the broiler house, clean or amended litter, stocking density and flock size, the number of houses on site, selective breeding and feed structure.
- The 12 other control options were judged as having a higher probability of achieving a reduction of at least 10% in the incidence of campylobacteriosis in humans: hygienic anteroom at broiler house entrance, no animals in close proximity to the broiler houses, employing few and well-trained staff, addition of disinfectants to drinking water, avoiding drinkers that allow standing water, effective cleaning and disinfection, reduced slaughter age, discontinued thinning, designated tools per broiler house, feed and water additives, bacteriophages and vaccination.

- From the 12 selected control options, eight options were selected for ranking their risk reduction efficiency, based on the quality of evidence available, practical feasibility in the implementation of the control option.
- The median values of the relative risk reduction of eight control options were judged using EKE to be as follows: for vaccination 27% (90% Probability interval (PI) 4–74%); for feed and water additives 24% (90% PI 4–60%); for discontinued thinning 18% (90% PI 5–65%); for employing few and well-trained staff 16% (90% PI 5–45%); for avoiding drinkers that allow standing water 15% (90% PI 4–53%); for addition of disinfectants to drinking water 14% (90% PI 3–36%); for hygienic anterooms at broiler house entrance 12% (90% PI 3–50%); for designated tools per broiler house 7% (90% PI 1–18%).
- It was not possible to rank the selected control options according to effectiveness based on the EKE judgements because there is a large overlap between the probability intervals, due to the large uncertainties involved.

3.6. Advantages, disadvantages and availability of control options

After the first EKE step, the first 12 control options judged as having a higher probability of achieving a reduction of at least 10% in the incidence of campylobacteriosis are listed in Table 17 to consider further their advantages and disadvantages (apart from the effect on campylobacteriosis), if they are to be applied.

Table 17: Advantages and disadvantages of the first 12 control options judged as having a higher probability of achieving a reduction of at least 10% in the incidence of campylobacteriosis

Control option	Advantages	Disadvantages
Vaccination	Systems of multiple vaccines applied at the same time and mass vaccinations are available to which an anti-*Campylobacter* vaccine could be added	The effective vaccine does not yet exist and testing is still at experimental level No vaccines available that work consistently in field trials Unavailability of vaccines at commercial scale Consumers may prefer meat from birds that have not been vaccinated If there are side effects, there could be broiler welfare issues
Feed and water additives	Feed and water additives are relatively easy to administer to the birds These could improve the birds gut microbiota resulting in healthier broilers and better welfare Relatively easy application	At experimental level, there is still a lack of reproducibility among tests and large variability in effect between treated birds The effects observed at experimental level are lower or non-existent at field level and there are not yet results reproducing the effect at the field level If the additive changes the odour or taste of the water, the birds may not drink
Discontinued thinning	Avoiding stress at thinning is likely to increase flock welfare	This may cause problems with birds in different sizes at slaughter increasing the risk of broken intestines and faecal contamination during evisceration in the processing plant
Employing few and well-trained staff	Permanency and higher skill levels will benefit the industry generally and may have positive impacts on broiler welfare, health, etc Well-trained staff are more likely to dedicate sufficient time to hygiene and biosecurity in general and may improve the effectiveness of other control measures The lower the number and the higher the competency of staff the more likely biosecurity measures will be understood and consistently implemented	Initially, there may be a lack of trained staff and the workload may be an issue During specific times (e.g. when bringing a new batch of birds into the broiler house), relatively high numbers of staff are required (which are not needed thereafter). At those times, a few well trained staff may not be sufficient
Avoiding drinkers that allow standing water	Easy application and a relatively limited resource-demanding intervention Easier to clean and disinfect between flocks	Requires modifications in broiler houses May result in a higher moisture content in the litter and therefore an increased occurrence and severity of contact dermatitis
Addition of disinfectants to drinking water	Easy application May have protective effect against other pathogens and increase health and welfare and reduce the need for antimicrobials	Low pH of water and palatability for birds could lead to issues for animal growth and welfare Varying effect depending on organic material and solubility in water Some treatments may dislodge biofilm within water lines which can block nipple drinkers The *Campylobacter* spp. may develop resistance May adversely affect the gut microbiota resulting in poorer broiler performance May be used to cover up poor operator performance in terms of biosecurity and hygiene

Control option	Advantages	Disadvantages
Hygienic anterooms at broiler house entrance	Easy to use and serves as a reminder to practice biosecurity Facilitates other activities as the anteroom accommodates the temperature monitoring equipment, bird weight recording, feed and water supply monitoring equipment, etc May include a glass panel that allows inspection of the flock without always entering the production area	May require structural changes to broiler houses and staff training Double barrier systems installed in small anterooms can lead to cramped conditions and increased risk of poor usage May promote a false sense of biosecurity resulting in other essential hygienic activities, such as disinfectant boot dips, being ignored Many are poorly designed and are ineffective
Designated tools per broiler house	Easy and rapid implementation Relatively cheap to implement Does not require any specific training	The farmer will have to purchase multiple sets of tools
Reduced slaughter age	Reduced probability of biosecurity breaches resulting in less opportunity to contract avian diseases	The large heterogeneity in the industry complicates implementation. Some companies use slower growing breeds and consumer demands drive specific bird sizes. By slaughtering earlier, the industry may have to introduce faster growing birds and breeds, which may introduce welfare problems Smaller birds may lead to more carcass contamination due to gut rupture at slaughter if automated evisceration equipment is designed for larger birds
No animals in close proximity of the broiler houses	Efforts and resources are focused on broiler houses Reducing the *Campylobacter* spp. load in the environment	Farmers can restrict access of some animals (dogs and cats) to the broiler houses and choose not to have other animals close by but may have little control over animals on neighbouring farms or fields Even within a given farm, it may not be possible to place a 'buffer biosecurity zone' around the broiler houses unless the farmer has other land not currently in use
Bacteriophage	Relatively easy to administer to the birds	Bacteriophages are specific of strains of *Campylobacter* spp., their use would not cover the diversity of strains prevalent in birds unless a comprehensive cocktail of phage is used Their effects are transient and do not last until the end of rearing *Campylobacter* spp. can develop a resistance to bacteriophages
Effective cleaning and disinfection	Allows the elimination of contamination between successive flocks	Some disinfectants may need to be changed to avoid appearance of resistance to those used for a certain time Nearly impossible to clean everywhere for example feeders and drinkers are not designed to facilitate cleaning as there are parts that cannot be reached

3.6.1. Concluding remarks

- There are advantages and disadvantages associated with each control option.
- The advantages include ease of application (e.g. hygiene barrier, adding additives to feed), improved bird health (e.g. biosecurity actions), better broiler welfare (e.g. discontinued thinning), cross-protection against other pathogens (e.g. drinking water treatments, feed additives).
- The disadvantages for a given control option may include a requirement for investment (e.g. if structural changes are required to install an anteroom), lack of control (e.g. the farmer may not own the fields adjacent to the broiler house and therefore cannot prevent other animals being close by), reduced broiler growth due to decreased consumption of feed and/or water (e.g. if an additive affects the sensory (odour, taste or appearance) properties making the feed or water unpalatable).

3.7. Combinations of control options

It is difficult to assess the effects of combined control options, as studies that systematically assess such effects (experimentally or by observation) are not available; the number of possible combinations is large and the dependence on effective performance of control options could not be included in the modelling approaches used, and poor application of one control measure may undermine the effectiveness of another. Inclusion of interaction in the epidemiological models would provide an estimate of the combined effects, but interaction is rarely examined, probably due to lack of statistical power in studies due to inadequate numbers of flocks being included. However, the epidemiological risk factor studies do attempt to adjust for confounding factors, or the risk posed by the other risk factors included in the same multi-variable model (Pourhoseingholi et al., 2012). These models and studies provide relatively specific risk estimates and can be converted to specific risk reduction estimates. Nonetheless, applying control to one farming practice is likely to affect other practices and the relative reduction potential of each factor will change. In general, every control option applied correctly on a farm will further decrease the probability of colonisation of the broiler flock. For biosecurity control options, interaction is evident, as explained in the previous opinion (EFSA BIOHAZ Panel, 2011), because biosecurity depends on many interrelated local factors. In some cases, the interaction may be synergistic increasing the effects beyond the added effect of the individual measures. As an example, training staff in the importance of biosecurity is very likely to increase the effect of all other biosecurity measures, as the level of implementation of these in their daily routines should also improve. Using an anteroom correctly with good division between sections and corresponding biosecurity actions such as putting on house-dedicated overalls, boots, using a boot dip, washing hands etc., reduces the risk more than just having, but not properly operating, an anteroom.

Another case illustrating synergistic effect is where control options prevent colonisation of the birds before thinning. If thinning is then also abolished, the opportunity for introduction of infection of the broilers is removed allowing continuation of the benefits of disease control activities.

In other situations, applying multiple control measures may result in less than the additive effect. For example, it is expected that if disinfectant was added to drinking water, the risk of standing water in drinkers would decrease thus and there would be no additional benefit to using nipple only drinkers.

Combining two control measures targeting prevalence and concentration, respectively, may result in a cumulative effect. Combining biosecurity measures with a future effective vaccine would for example provide a cumulative effect. Furthermore, a transient effect (e.g. a few days after treatment only) from a feed additive administered just before slaughter, combined with discontinued thinning, may also have a cumulative effect.

3.7.1. Concluding remarks

- Multiple control activities are expected to have a higher effect preventing *Campylobacter* spp. from entering the broiler house and infecting the birds. To minimise the risk of *Campylobacter* colonisation, all control activities relating to biosecurity would have to be implemented in full.
- It is not possible to estimate the effect of combined control options because the current estimates are inter-dependent and there is a high level of uncertainty of their effect in the EU as a whole.
- Combining two control options targeting prevalence and concentration, respectively, may result in a cumulative effect.

3.8.　Comparison to the 2011 Opinion

As explained above, the 2011 EFSA opinion on 'Campylobacter in broiler meat production: control options and performance objectives and/or targets at different stages of the food chain' was updated for control options at primary production, by a review of new evidence and, when possible, incorporating this evidence in a novel modelling approach applying the PAF or a new version of the model to assess the effectiveness of control options reducing the concentrations in caecal contents.

As in the 2011 opinion, biosecurity measures are considered essential to prevent flock colonisation with Campylobacter spp. However, the previous opinion did not assess the effectiveness of individual control options related to biosecurity, as it was argued that they depend on many interrelated local factors. Although interrelating factors are still complicated, the current opinion includes such an assessment. This was possible by consideration of the PAF as reported in various European studies, and by the application of the EKE where all available evidence was evaluated. By means of the EKE, the effect of application of the control options could be assessed for the whole EU, instead of only four MSs as in the previous opinion, and the uncertainty attending the effect estimates was quantified. Table 18 provides a comparative overview of the effects of individual interventions as described in the previous and the current opinion. It includes the control options with higher probability of producing more than 10% effect (First step of EKE; including all those for which the concentration model was applied), those for which a PAF analysis was performed (Section 3.3.1) and those specifically referred to in the 2011 opinion. When possible, quantitative estimates from the 2011 opinion are presented, otherwise quotes are given from the conclusions or descriptions of the control measures. Overall, the descriptive conclusions from the 2011 opinion are still considered appropriate.

Table 18:　Control options with higher probability to have more than 10% effect (1st step EKE), those for which a PAF analysis was performed (Section 3.3.1) and those specifically referred to in the 2011 opinion. Quotes from the 2011 opinion are given in italics

Control option	Conclusion EFSA BIOHAZ Panel (2011)	Conclusions in this opinion	
		Analysed by	Judged risk reduction effect[a]
Vaccination	*Vaccination could reduce flock prevalence as well as numbers of Campylobacter* spp. *in the intestines. However, vaccination is still being developed and no evidence of effective vaccines was found*	Concentration model; 2nd step EKE	27 (4–74)
Feed and water additives	*Inclusion of additives to feed or drinking water could reduce flock prevalence as well as numbers of Campylobacter* spp. *in the intestines. However, there is conflicting evidence regarding the effectiveness of additives.*	Concentration model; 2nd step EKE	24 (4–60)
Discontinued thinning	*Thinning (partial depopulation) is a risk factor for flock colonisation. The public health impact of stopping this practice as estimated in four countries is expected to reduce the risk by up to 25%*	EFSA Opinion 2011; 2nd step EKE	18 (5–65)
Employing few and well-trained staff	Not considered (part of biosecurity)	PAF analysis; 2nd step EKE	16 (5–45)
Avoiding drinkers that allow standing water	Not considered	PAF analysis; 2nd step EKE	15 (4–53)
Addition of disinfectants to drinking water	*The effectiveness of drinking water decontamination as an individual biosecurity measure is unclear*	PAF analysis; 2nd step EKE	14 (3–36)

Control option	Conclusion EFSA BIOHAZ Panel (2011)	Conclusions in this opinion	
		Analysed by	Judged risk reduction effect[a]
Hygienic anterooms at broiler house entrance	*The strict use of a hygiene barrier about 50% and seems especially important when there are other livestock on the farm* Not considered as a separate control option (part of biosecurity)	PAF analysis; 2nd step EKE	12 (3–50)
Designated tools per broiler house	Not considered (part of biosecurity)	CAMCON Project; 2nd step EKE	7 (1–18)
Reduced slaughter age	*Restricting the broiler slaughter age of indoor flocks to 35 or 28 days, as estimated from four countries, would reduce the public health risk by 10–20% or up to 50%, respectively*	EFSA Opinion 2011; 1st step EKE	Higher probability (mm = 83%) to have more than 10% effect
No animals in close proximity of the broiler houses	Recognised as a risk factor but not considered as a control option	PAF analysis; 1st step EKE	Higher probability (mm = 64%) to have more than 10% effect
Bacteriophages	*The use of bacteriophages as currently envisaged has limited practicality*	1st step EKE	Higher probability (mm = 47%) to have more than 10% effect
Effective cleaning and disinfection	Not considered (part of biosecurity)	1st step EKE	Higher probability (mm = 40%) to have more than 10% effect
Selective breeding	*Selective breeding programmes, especially in poultry previously selected for high meat or egg production, must be considered as a very long term goal. Therefore, this potential intervention was not modelled*	1st step EKE	Lower probability (mm = 33%) to have more than 10% effect
Rodent control	Not considered (part of biosecurity)	PAF analysis; 1st step EKE	Lower probability (mm = 30%) to have more than 10% effect
Fly nets and keeping insects out	*Where strict biosecurity measures are applied in indoor production, the use of fly screens effectively reduces flock colonisation in summer and thereby reduces public health risk by 50–90% as estimated in one MS*	1st step EKE	Lower probability (mm = 28%) to have more than 10% effect

EKE: expert knowledge elicitation; PAF: population attributable fractions.
(a): Numeric results indicate the median relative risk reductions (and 90% probability interval) as obtained in the 2nd step EKE; otherwise the result of the 1st step EKE is given, in terms of the probability to have achieve more than 10% relative risk reduction ('lower' and 'higher' probability are explained in Section 3.5; mm refers to the mean of the midpoint estimates for the probability to have more than 10% relative risk reduction, obtained from the individual experts).

3.8.1. Concluding remarks

In comparison with the previous opinion, new data and novel analyses allowed for a more informative estimate of the effectiveness of individual control options.

The effect estimates of vaccination and application of feed and/or water additives still rank high, but are less pronounced, due to the use of newly published data on the relationship between

Campylobacter spp. concentrations in caecal contents and on skin samples, a larger variety of consumer phase models and a newly published dose response model, as well as inclusion of uncertainty when extrapolating from experimental data to field conditions.

The updated model resulted in lower effect estimates than the model used in the 2011 opinion. For a 2-log_{10} reduction in caecal concentrations, the median estimate of relative risk reduction is 42% (95% CI 11–75%), compared to the previous opinion, where this relative risk reduction was 76–98% in four MSs. A 3-log_{10} reduction is estimated to reduce the risk in the EU by 58% (95% CI 16–89%), compared to a relative risk reduction larger than 90% in four MS in the previous opinion.

For several control options related to biosecurity (i.e. employing few and well-trained staff, hygienic anterooms at broiler house entrance, designated tools per broiler house), numerical estimates of the effectiveness were obtained after consideration of evidence obtained after the 2011 opinion was published.

4.   Conclusions

To address the different parts of the ToR, the conclusions have been reformulated as answers to the following assessment questions:

Assessment question 1: What new scientific evidence about control options has become available since the previous opinion of 2011 and what is their relative risk reduction on campylobacteriosis?

- New information was published since the EFSA 2011 Opinion that provides additional evidence that slaughter age, season, thinning, contaminated drinking water and carry-over from a previous flock are important risk factors for *Campylobacter spp.* colonisation of a broiler flock.
- New epidemiological evidence was analysed by the use of PAFs to obtain estimates of the effectiveness of several control options at primary production that reduce the flock prevalence.
- PAFs were calculated for six control options from available studies including; hygienic anteroom, effective rodent control, having no animals in close proximity to the broiler house, addition of disinfectant to drinking water, employing few and well-trained staff and avoiding drinkers that allow standing water.
- According to the PAF analyses, the mean relative risk reductions that could be achieved by adoption of each of these six control options individually are estimated to be substantial but the width of the confidence intervals of all control options indicates a high degree of uncertainty in the specific risk reduction potentials. For example, the mean estimate of the relative risk reduction for the control option 'Addition of disinfectants to drinking water' was between 5 (95% CI 0.6–8.2) and 32% (95% CI 6.0–54.9) based on three available studies.
- In a review of information available since 2011, new experimental studies were identified that reported estimates of the log reduction in caeca (and variation therein) that may be obtained by providing feed or water additives or through application of vaccination. However, no new information was available from field studies.
- Newly published data on the relationship between *Campylobacter* spp. concentrations in caecal contents and on skin samples, a larger variety of consumer phase models and a newly published dose response model allowed an update of the modelling approach for interventions that reduce the *Campylobacter* spp. concentrations in broiler caeca. This led to lower effect estimates than with the model used in the 2011 opinion. For a 2-log_{10} reduction in caecal concentrations, the median estimate of relative risk reduction is 42% (95% CI 11–75%), compared to the previous opinion, where this relative risk reduction was 76–98% in four MSs. A 3-log_{10} reduction is estimated to reduce the risk in the EU by 58% (95% CI 16–89%), compared to a relative risk reduction larger than 90% in four MS in the previous opinion.

Assessment question 2: What is the ranking in terms of effectiveness of the selected control options in reducing human campylobacteriosis cases at the primary production level?

- The effectiveness of 20 control options if implemented by all broiler farms in EU, taking into account the current level of implementation, was estimated by means of a two-step expert knowledge elicitation (EKE) process informed by results from modelling of the updated scientific evidence, literature review (including the 2011 EFSA opinion) and experts' experience.
- The following eight control options were judged to have lower probability of achieving a reduction of at least 10% in the incidence of campylobacteriosis: effective rodent control, downtime between flocks, fly screens and keeping insects out of the broiler house, clean or

amended litter, stocking density and flock size, the number of houses on site, selective breeding and feed structure.

- The other 12 control options were judged as having a higher probability of achieving a reduction of at least 10% in the incidence of campylobacteriosis: hygienic anterooms at broiler house entrance, no animals in close proximity of the broiler houses, employing few and well-trained staff, addition of disinfectants to drinking water, avoiding drinkers that allow standing water, effective cleaning and disinfection, reduced slaughter age, discontinued thinning, designated tools per broiler house, feed and water additives, bacteriophages and vaccination.
- From the 12 selected control options, eight options were selected for further evaluation based on the quality of evidence available and practical feasibility in the implementation of the control option.
- The median relative risk reduction for those eight control options was judged in the EKE process to be as follows; vaccination 27% (90% Probability interval (PI) 4–74%); feed and water additives 24% (90% PI 4–60%); discontinued thinning 18% (90% PI 5–65%); employing few and well-trained staff 16% (90% PI 5–45%); avoiding drinkers that allow standing water 15% (90% PI 4–53%); addition of disinfectants to drinking water 14% (90% PI 3–36%); hygienic anterooms at broiler house entrance 12% (90% PI 3–50%); designated tools per broiler house 7% (90% PI 1–18%).
- It was not possible to rank the selected control options according to their effectiveness based on the EKE judgements because there was a large overlap between the probability intervals, due to the large uncertainties involved.

Assessment question 3: What are the advantages and disadvantages of the selected control options?

- The advantages include ease of application for some measures (e.g. hygiene barrier, adding additives to feed), improved bird health (e.g. biosecurity actions), better broiler welfare (e.g. discontinued thinning) or cross-protection against other pathogens (e.g. drinking water treatments, feed additives).
- The disadvantages for a given control option may include a requirement for investment (e.g. if structural changes are required to install an anteroom), lack of control (e.g. the farmer may not own the fields adjacent to the broiler house and therefore cannot prevent other animals being close by) or reduced broiler growth due to decreased consumption of feed and/or water (e.g. if an additive affected the sensory (odour, taste or appearance) properties making the feed or water unpalatable).

Assessment question 4: What would be the effect of combining control options?

- Multiple control activities are expected to have a higher effect preventing *Campylobacter* spp. from entering the broiler house and infecting the birds. To minimise the risk of *Campylobacter* colonisation, all control activities relating to biosecurity would have to be implemented in full.
- It is not possible to quantify the effects of combined control activities because the evidence-derived estimates are inter-dependent and there is a high level of uncertainty associated with each. Some control options enhance the effect of others and some could reduce the effect of other control options.
- Combining two control options targeting prevalence and concentration, respectively, may result in a cumulative effect, if their targets are unrelated.

5. Recommendations

- It is recommended to collect new data (new baseline study) for an update of the current *Campylobacter* spp. prevalence in the EU, including the quantification of *Campylobacter* spp. in caeca and on carcass skin samples of the same flocks, for a better estimation of the correlation between *Campylobacter* concentrations at caeca and carcases.
- More field studies of sufficient scale and consistency to provide definitive findings at EU level should be encouraged, especially on the effect of vaccination, probiotics, water and feed additives and pre-slaughter phage treatment on *Campylobacter* spp. in broilers because of the large uncertainty related to the extrapolation from experimental studies. Moreover, field studies should also be undertaken on different combinations of control options.
- It is recommended to extend this update of the 2011 opinion to include control options throughout the whole broiler chain.

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Abbreviations

ABC	ATP-binding cassettes
AQ	Assessment question
CFU	Colony-forming units
CI	Confidence Interval
CPM	Consumer Phase model
DR	Dose response

EKE   Expert Knowledge Elicitation
FA   Feed Additive
FCI   Food chain intervention
FP   Flock Prevalence
Inc   Incidence
MS   Member State
NP   Nanoparticle
OMP   Outer membrane proteins
OR   Odds ratio
PAF   Population attributable fractions
PHC   Process Hygiene Criterion
PI   Probability Interval
QMRA   Quantitative microbiological risk assessment
RR   Risk Reduction
RRR   Relative risk reduction
SD   Standard Deviation
SE   Standard Error
S.E.M.   Standard error of the mean
SPF   Specific pathogen free
ToR   Terms of Reference
VA   Vaccine
WG   Working Group

Appendix A – Modelling approach for control options affecting the concentration in the caecal content of broilers

Control options affecting the concentration in the caecal content are assessed by in three steps using following models:

- A **regression model** to describe the relation between a change in the *Campylobacter* concentration in the caecal content of broilers and a change in the *Campylobacter* concentration on the meat at the end of the slaughterhouse (i.e. the concentration on neck or breast skin, whole carcass rinses or otherwise, for carcasses after the industrial chilling process or chicken meat products);
- A **consumer phase model** describing the effect of storage and food preparation (inactivation and cross contamination);
- A **dose response model**.

First, an explanation is given of the regression model approach (See also Nauta et al. (2016)). The approaches for the consumer phase model and dose response model are explained next.

A.1. Regression model for the relation between caecal samples and skin samples

The regression model translates a change in *Campylobacter* concentration in the chicken caeca in batches of broiler chicken into a change in *Campylobacter* concentration in batches of broiler meat, in terms of change in distributions on skins of carcasses after chilling or whatever is measured as 'contamination of the meat' in the regression model.

Based on published data, different regression models were explored describing a linear relation between the log concentration on broiler skin (or meat) samples taken at the end of processing (log C_{skin}) and the log concentration found in the caeca (log C_{cec}).

$$\text{Log10 } C_{skin} = a \log10 C_{cec} + b. \tag{A1}$$

In this equation, a indicates the slope of the regression line and b is the intercept. It is assumed that caecal samples and skin samples are taken from the same slaughter batch. The possible pooling of samples is not considered in this analysis.

The regression model is applied to estimate the effect of reducing the concentration C_{cec} (by Δ log C_{cec}) on the concentration C_{skin}.

If the concentration on the skin after reduction of C_{cec} (due to intervention) is represented by C_{skin}' and Equation (A1) is rewritten to $\Delta \log10 C_{skin} = - a \Delta \log10 C_{cec}$, then

$$\text{Log10 } C_{skin}' = \log10 C_{skin} - a \Delta\log10 C_{cec}. \tag{A2}$$

The EU baseline data from 2008 are used to describe initial concentration on broiler skin (log10 C_{skin}), being described by a normal distribution with mean m_{skin} and standard deviation s_{skin}. Nauta et al. (2012) describe the values for m_{skin} and s_{skin} in positive batches for each Member State (MS), along with the mean batch prevalence and the contribution to the EU production of the MS at the time of the baseline survey. These data are used in the analysis. From the data, it is derived that, for the EU including Norway and Switzerland, the weighted mean m_{skin} = 2.44 log CFU/g skin; s_{skin} = 1.24; the weighted flock prevalence for the whole EU is 67%.

The effect of the intervention, Δ log C_{cec} is implemented by a Normal distribution with mean d and standard deviation s_d. Distributions for log C_{skin}' can then be obtained analytically. The mean and sd after intervention are:

$$m_{skin\ after} = m_{skin} - a \times d \tag{A3}$$

$$s_{skin\ after} = \sqrt{(s_{skin}^2 + a^2 s_d^2)}.$$

With this model, the distribution of concentrations after implementation of an intervention is characterised by a mean log reduction d with standard deviation s_d can be derived based on the slope of the regression line a.

The default value for a is set at a = 0.27, based on the largest data set, Rodgers (2020). In the uncertainty analysis, a BetaPert distribution with minimum 0, most likely 0.27 and maximum 0.7 is used, based on the results of the literature search (Section 2.3.1). This distribution is illustrated in Figure A.1.
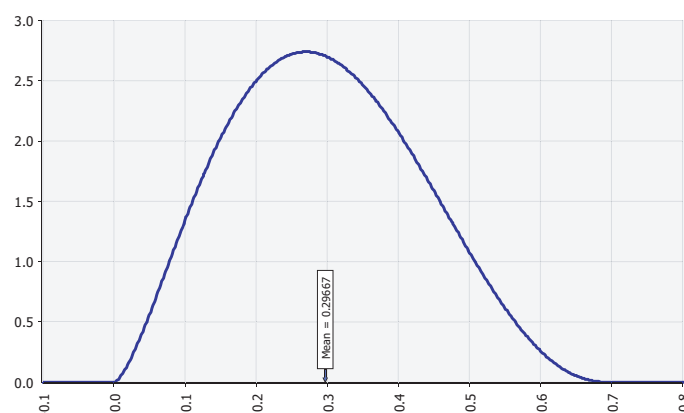
Figure A.1: The BetaPert (0, 0.27, 0.7) distribution used to describe the uncertainty about a, the slope of the regression line

A.2.   Consumer phase models (CPM)

The eight CPMs described and analysed by Nauta and Christensen (2011) (Nauta and Christensen, 2011) are used (see Section 2.3.2). As in the previous opinion (EFSA BIOHAZ Panel, 2011), the model presented by Nauta et al. (2008), who collected observational data from Dutch consumers preparing a chicken salad, is used as the default CPM in simulations where the uncertainty about the choice of the CPM is not included (see Table 3; results not shown). Also an assumption made by all CPMs is the following relation between the concentration per gram of skin and the concentration per gram of meat

$$\log C_{meat} = \log C_{skin} - \tau.$$

Based on expert opinion in EFSA Biohaz Panel (2011) (EFSA 2011), the default assumption is $\tau = 1$. In the uncertainty analysis, a Uniform distribution of τ between 0 and 3 is used, as in Nauta et al. (2012).

All CPMs translate the distribution of concentrations of *Campylobacter* on the meat (C_{meat}) in a distribution of ingested dose, by models that describe the transfer and survival of *Campylobacter*, and the variation therein, during the preparation of a meal including chicken meat, based on observational and/or experimental data obtained in different countries. Details of the models (as also implemented in this opinion) are presented in Nauta and Christensen (2011). All models apply the same serving sizes, based on observational data from Christensen et al. (2001) (a lognormal distribution with mean 189 g and standard deviation 127, with a maximum portion size of 1 kg).

A.3.   Dose response models

Teunis et al. (2018) presented new dose response models for *Campylobacter*, which differ substantially from the one used in the previous opinion (the 'classic' DR model). Their paper presents an elaborated quantitative analysis of the uncertainty associated with the data and provides a variety of outbreaks and challenge studies. The outbreaks are four raw milk outbreak studies. The challenge studies include human and primate challenge studies for specific Campylobacter jejuni strains, and include the challenge study (Black et al., 1988) that is used for the classic model.

In this opinion, two alternative DR models derived from the Teunis et al. (2018) paper are compared to the classic DR model, by a comparative analysis of relative risk reduction estimates of interventions affecting the concentrations on the meat (similar to what Nauta and Christensen (2011) (Nauta and Christensen, 2011) did for CPMs).

The alternative DR models are those defined by the median estimates of the model parameters provided by Teunis et al. (2018) for the challenge studies and the outbreak studies. These median

parameter values do not necessarily give a median DR relation, but some unreported trials suggested that they get close.

A comparison of the dose response curves for illness, using the median estimates of the model parameters, is given in the graph below.

Table A.1: The model parameter values for the models used are given below. For details, see Teunis et al. (2018)

	P_{inf}		$P_{ill\|inf}$		
	α	ß	r	η	Constant
Classic model	0.145	7.59			0.33
Median Challenge model	0.44	0.51	0.06	0.88	
Median Outbreak model	0.38	0.51	0.76	0.0092	

For this opinion, the default choice for the DR model remains the 'classic model', for best comparison with the 2011 opinion. In the uncertainty analysis, a random choice is made between the

Campy DRs
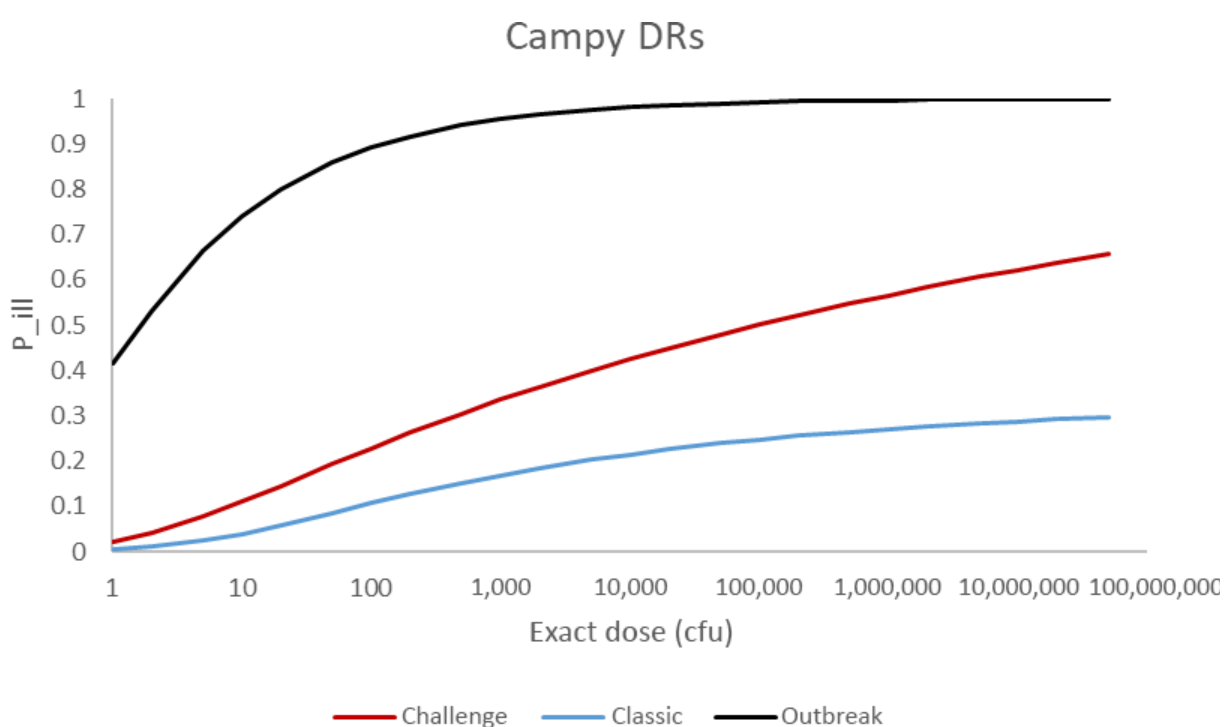
'classic model' and the 'median challenge model'. The 'median outbreak model' is based on (potentially non representative) raw milk outbreaks and gives very high estimates of the probability of illness. It is therefore not included.

Appendix B – Studies on the association between caecal content samples and skin or meat samples

No	Reference	Study content	Tested matrices (caecal content)	Tested matrices (skin or meat)	Samples	Results
01	Allen et al. (2007)	Relation: contamination of carcasses during processing – degree of flock colonisation	Caeca after evisceration (caecal content)	Neck skin	26 slaughter groups, originating from 22 single-house flocks	**No correlation** was found overall between the numbers of campylobacters detected in caeca and on carcasses All carcasses from high prevalence flocks were contaminated with campylobacters After chilling, they carried significantly ($p < 0.001$) higher numbers than carcasses originating from low prevalence flocks
02	Boysen et al. (2016)	*Campylobacter* spp. and Escherichia coli contamination of broiler carcasses across the slaughter line	24 individual caeca per flock	24 thigh skins per flock	15 broiler flocks (from 3 slaughterhouses)	**A significant positive correlation** was found, $r^2 = 0.72$, $p < 0.0001$, regression line $y = 0.692 \times - 2.45$. This relationship was not dependent on slaughterhouse
03	Brena (2013) (PhD thesis Liverpool)	PhD thesis on *Campylobacter* in broiler slaughter plants	10 caeca per flock	10 neck skins per flock	76 batches of broiler chickens (from 46 different farms); 3 slaughterhouses	**Significant correlation** $r^2 = 0.23$. $y = 0.21 \times + 1.13$ $p < 0.005$
04	Duffy et al. (2014)	Effect of processing practices on prevalence/concentration of *Campylobacter* correlation concentration of *E. coli* and *Campylobacter*	Caeca after evisceration (caecal content)	whole bird rinse technique	n = 240	**Prevalence** in caeca **has influence** on prevalence on carcasses (3/4 flocks) 'Control of processing parameters may play more important role in reducing concentration on whole chickens than the initial concentration in caeca

No	Reference	Study content	Tested matrices (caecal content)	Tested matrices (skin or meat)	Samples	Results
05	Elvers et al. (2011)	Molecular tracking through processing	Caeca	Neck and breast skin	5 Campylobacter-positive flocks	'no obvious correlation …between the number of campylobacters in the ceca and those on the carcasses… ' There was also a significant association between flock bacterial load and sampling point (p =0.033). This suggests that *Campylobacter* numbers on the flock and at the point at which they were sampled combine to influence the overall numbers on the carcass
06	Hue et al. (2011)	*Campylobacter* and *Salmonella* contamination	Caeca from 10 birds per batch	1 carcass per batch	425 batches	**A positive correlation** (r = 0.59) between average number of *Campylobacter* in caeca and on carcasses (p < 0.001) (n = 425). Considering only positive batches (n = 297), correlation was significant (p < 0.001) and Spearman coefficient was lower (r = 0.33). Slope of the regression line shown in figure is 0.3243
07	Laureano, Corujo and Van Gerwe (2013)	Correlation of different matrices with *Campylobacter* counts in neck skin of broiler carcasses	Two pooled samples of 5 caeca per flock	Two pooled samples of 5 neck skins	80 flocks (from 10 slaughter plants)	**A significant positive correlation**. $r^2 = 0.26$; $y = 0.276 \times + 1.276$ The introduction of the variable slaughterhouse as a random effect had no effect in the model

No	Reference	Study content	Tested matrices (caecal content)	Tested matrices (skin or meat)	Samples	Results
08	Malher et al. (2011)	Factors associated with carcass contamination	Pooled caeca (1 pooled sample per batch)	Pooled neck skin samples (1 pooled sample per batch)	140 batches	When a carcass was contaminated . . ., the level of skin contamination appeared to be **poorly correlated** (r = 0.28) to the level of caecal contamination in the batches where the skin test was positive. No slope of regression line published
09	Nauta et al. (2009)	'testing and scheduling' strategy	10 caecal samples per flock	5 (skinned) breast fillet samples	62 flocks	Numbers of *Campylobacter* on breast fillets **do not correlate** with those of caecal contents
10	Reich et al. (2008)	Correlation caeca-carcasses	10 caeca per flock	5 carcasses per flock (breast caps)	40 flocks caeca/18 flocks carcasses	**Positive correlations** between numbers in caeca and on carcasses and breast caps **Positive correlation** between mean numbers of Campylobacter in caecal contents and mean count on carcasses at various processing steps (correlation coefficients and corresponding p-values were: 0.56 p = 0.058 for carcasses after scalding/ defeathering, 0.81 p = 0.0013 for carcasses after evisceration and 0.64 p = 0.0196 for carcasses after chilling, 0.72 p = 0.0057 for breast caps). No slope of regression line for carcass after chilling of breast caps published
11	Reich et al. (2018)	Contamination in broilers and microbiological criteria	10 caecal samples per batch (pooled)	50 neck skin samples per batch (pooled into 5 neck skin samples)	365 batches	Counts on neck skin were **not predictable** (from counts in caecal content) by linear regression due to the low r^2-values found (slaughterhouse A: 0.083; slaughterhouse B: 0.274; slaughterhouse C: 0.134, respectively)

No	Reference	Study content	Tested matrices (caecal content)	Tested matrices (skin or meat)	Samples	Results
12	Rodgers (2020)	Carcass-caeca	10 caecal samples per batch	Neck skin from 1 carcass per batch	1,146 slaughter batches	Contamination of carcasses **correlated** to caecal colonisation
13	Rosenquist et al. (2006)	Influence of slaughter operation on contamination level	Caecal content (30 per flock) after evisceration	Neck skin samples (30 per flock)	900 samples from 6 broiler flocks	Regression analysis of concentrations in caecal material and on neck skin of carcasses after defeathering showed a **correlation** ($\alpha = 1.15$; $\beta = -5.29$) between these two variables. Mean concentrations in neck skin samples after defeathering can be explained by the mean concentration in the caecal samples
14	Stern and Robach. 2003	Enumeration in faeces and corresponding carcasses	Faecal droppings (day before slaughter)	Carcass rinses	20 broiler flocks	**No significant correlation** between Campylobacter spp. levels recorded for the faecal samples and those recorded for the prechill carcasses No correlation ($p > 0.05$) between levels of Campylobacter spp. in faeces and those on fully processed carcasses was observed
15	Vinueza-Burgos et al. (2018)	Contamination of broilers along the slaughter line	One pooled sample of 25 caeca per flock	5 breast skin samples per flock	15 batches (from 3 slaughterhouses)	Data published in supplementary material, no correlation study performed. Analysis of the published data gives a slope 0.498, $r^2 = 0.57$, $p = 0.001$

Appendix C − Sensitivity analyses of the model for the effect of control options affecting the concentration in the caecal content of broilers

The performance of the model to estimate the effect of control options to reduce the *Campylobacter* concentration in the caecal content of broilers was analysed by a sensitivity analysis to investigate the sources of the uncertainty in the estimated relative risk reduction.

The model was run for the reference model (as detailed in Table 3), and results obtained for the effects of five selected control options (three feed additives and two vaccines). Additionally, the model was run with additional uncertainty by including (1) a random choice of MSs instead of using the EU mean and (2) randomly selecting the median outbreak DR model, the classic DR model or the median challenge DR model, instead of only the last two, for the least effect vaccine (VA1).

The uncertainty distributions for the relative risk reductions obtained are presented in Figure C.1. It shows that the uncertainty is large in all cases, the added uncertainty for VA1 does not add much to it. The distributions are obtained from Monte Carlo simulations with 250.000 iterations.

Figure C.2 presents the correlation of the uncertainty in the input distributions and the uncertainty in the relative risk reductions. It shows that in most cases the uncertainty in the slope is the main source of uncertainty, except in one case where the uncertainty of the effect of the control option (Δ log C_{cec}) dominates (FA1). An obvious explanation is that the impact of the uncertainty in the effect of the control option varies between the scenarios, and not only depends on this uncertainty itself, but also on the mean size and the variability of this effect. The results also show that the uncertainty about the choice of the CPM, the DR and the MS (i.e. the concentrations on the skin after processing) has a smaller impact on the total final.

After these several alternative scenarios were run where some of the uncertainties or variabilities in the model were modified, to explore their effect on the relative risk reduction estimates. Results are shown graphically in Figure C.3. for (1) the reference scenario, and scenarios where (2) the uncertainty about the choice of the MS was added; (3) the slope was not uncertain, fixed at 0.27; (4)) the slope was not uncertain, fixed at 1 (as in EFSA Biohaz Panel, 2011) (EFSA 2011); (5) only the median outbreak DR model was used; (6) only the classic DR model was used; (7) only the median challenge DR model was used; (8) one of the three DR model was randomly selected; (9) all uncertainties (S.E.M.) in the effects of control options were set at zero; (10) all variabilities (s_d) in the effects of control options were set at zero. These analyses confirm the importance of the lower values for the slope as obtained and applied in this opinion, compared to the previous one. They also show that the impact of other sources of uncertainty is less pronounced.

This information was made available to inform the EKE and taken into account by the experts in their judgements.
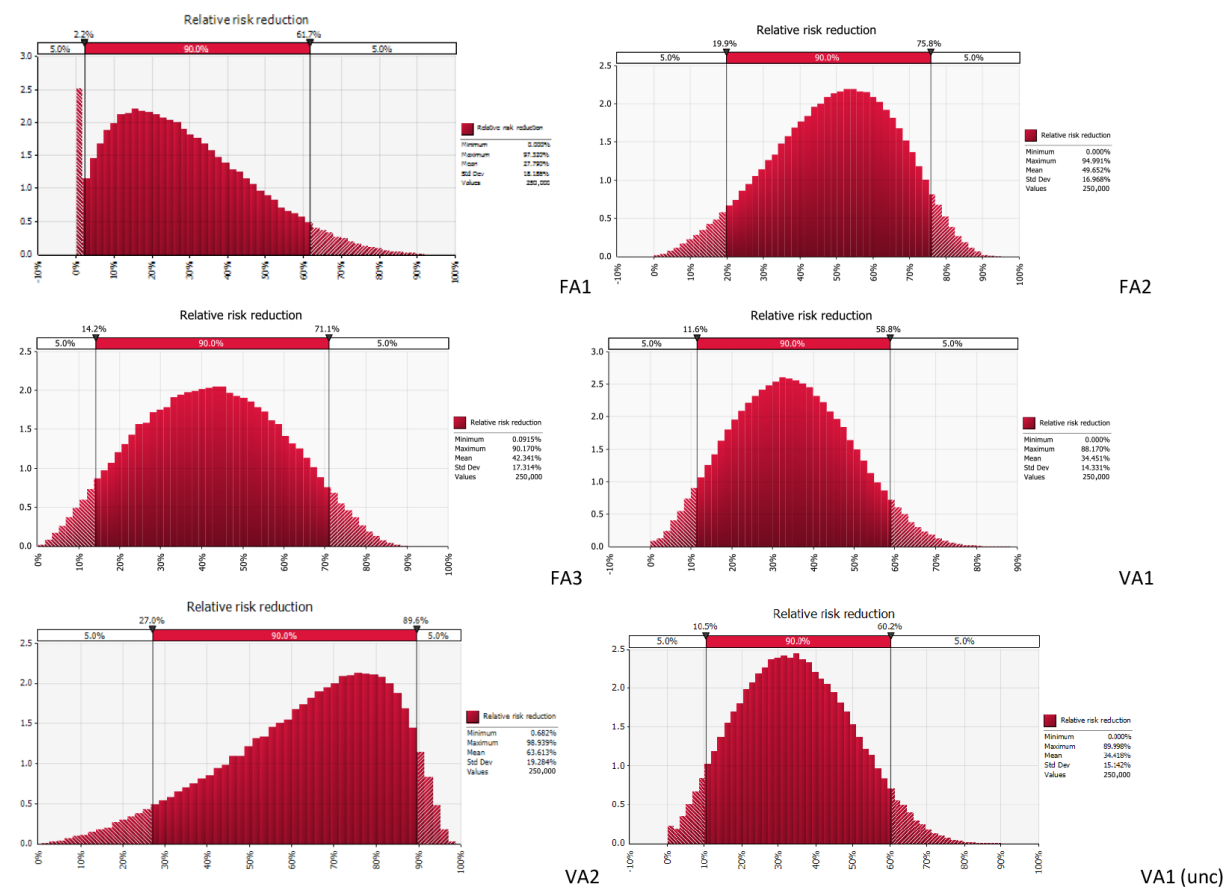
Figure C.1: Uncertainty distributions for the relative risk reductions for the three feed additives (FA1, FA2 and FA3) and the two vaccines (VA1 and VA2) as well as VA1 with additional uncertainty, respectively
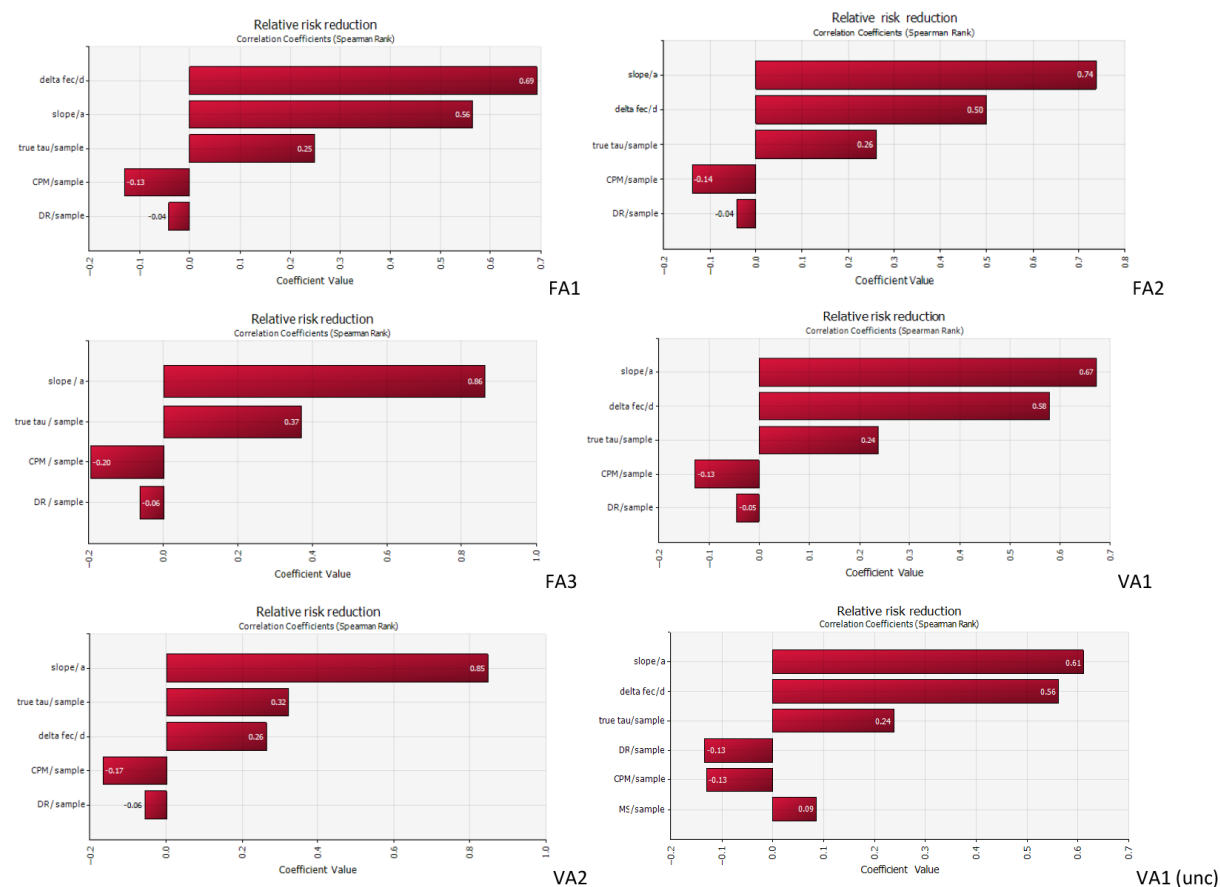
Figure C.2: Tornado graphs showing the correlation of the uncertainty in the input distributions with the uncertainty in the relative risk reductions for the three feed additives (FA1, FA2 and FA3), the two vaccines (VA1 and VA2) and VA1 with additional uncertainty. A larger correlation coefficient indicates that the uncertainty in the input parameter has a larger impact on the uncertainty in the relative risk reductions found (and illustrated in Figure A
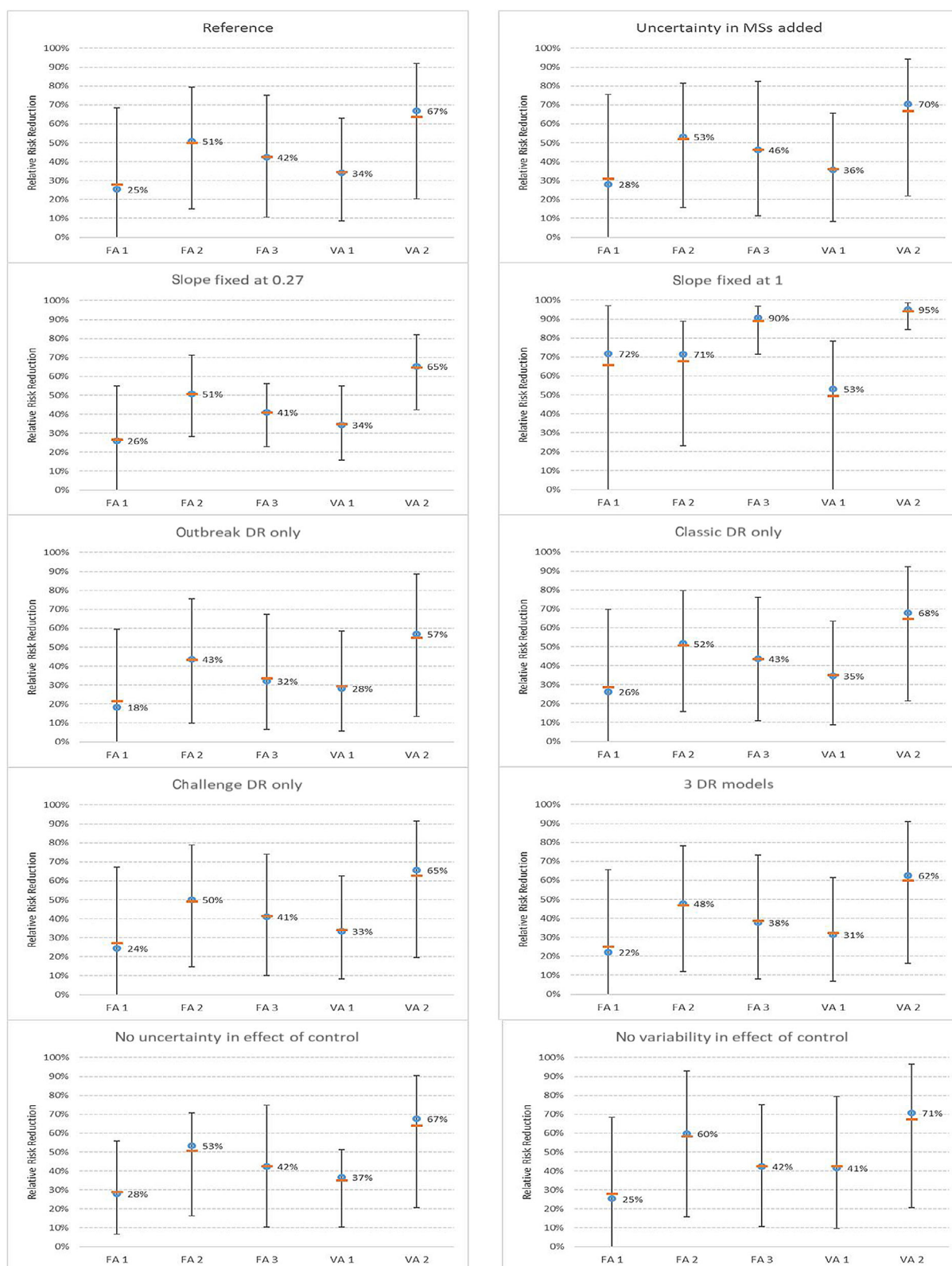
Figure C.3: Relative risk reductions found in the reference scenario (as in Figure 4) and nine other scenarios. Blue circle: median effect (numeric result given); orange line: mean effect; error bar: 95% credible interval

Appendix D – Uncertainty analysis

D.1. Evidence table for control options affecting prevalence

Specific factor studied	Estimated measure	Result (CI)	MS	Year (data)	Stud	Year (pub)	Specific strengths	Specific uncertainties	Uptake 2016 %
Hygienic anterooms at entrance of broiler houses							– Five different epidemiological studies from different countries identified this as a risk. – repeatability is evidenced, 'control' always included, field studies, – includes two newer study incl. CAMCON – magnitude of PAF fairly similar – Two of the large producer countries are included – Effects are fairly similar across populations		69–94%* CAMCON REPORT

51–73% Van Wagenberg et al. |
no anteroom in poultry house	PAF %	17.1 (0*–28.4)	ES	2010–2012	Torralbo	2014		only carried out in Andalusia	
Could be improved	PAF %	3.3 (0.4–4.2)	NI	2001–2002	McDowell	2008			
Litter-beetles in anterooms	PAF %	13.6 (0.9–18.8)	FR	2001	Refregier-petton	2001		Only representative of 60% of French broilers	
Low quality anteroom	PAF %	15.6 (5.9–24.4)	DK/NO?	2010–2012	Borck høg	2016			
General tidiness score reflecting a combination of a number of hygiene parameters	PAF %	18 (5.9–31.9)	SW	2005	Hansson	2010			

Specific factor studied	Estimated measure	Result (CI)	MS	Year (data)	Stud	Year (pub)	Specific strengths	Specific uncertainties	Uptake 2016 %
Non-significant (i.e. explored in univariate analysis but not retained for the multivariate model) studies	PAF %	–	–	2004–2005 1997–2000 2001–2004 2003–2004 2003–2006 2008 1999–2000 2005	Näther Bouwknegt Guerin Huneau-salun Ellis-Iversen Allain Sommer Lyngstad	2008 2004 2007 2007 2009 2014 2013 2008	(Mention here if any of these studies are strong negatives)		
* = Non-significant in multivariate model									
No 'anteroom and hygiene barrier in houses < 15 years old'	RRR	3 4 6 13 9 12	PL ES UK NL DK NO	2012	CAMCON Sommer Van Wagenberg	2016 2016	EU study	No PAF calculated, as another type of data analysis was performed Based on only few (20) farms in ES, NL, PL and EK, 100 and 160 farms in DK and NO Data are imputed based on assumptions to provide significance and allow modelling Two risk factors in one	
ADD ROWS FOR LIT STUDIES									
Effective rodent control							– Three epidemiological studies finds similar results = repeatability – Similar PAFS – includes a newer study Includes large producer countries		> 95% (professional 8–74%) CAMCON report

Specific factor studied	Estimated measure	Result (CI)	MS	Year (data)	Stud	Year (pub)	Specific strengths	Specific uncertainties	Uptake 2016 %
No Rodent control outside house	PAF %	7.5 (0.4–9.3)	FR	2008	Allain	2014		Only carried out in Brittany	
Rodents seen by sampler	PAF %	11.8 (3.3, 17.1)	NI	2001–2002	McDowell_rf1	2008			
Farmer reported rodents	PAF %	6.7(0*–12)	NI	2001–2002	McDowell_rf2	2008			
presence of rodents in shed	PAF %	11.7 (0*–18.9)	ES	2010–2012	Torralbo	2014		Only carried out in Andalusia	
Non-significant (i.e. explored in univariate analysis but not retained for the multivariate model)	PAF %	–	–	2005 1997–2000 2001 2001–2004 2004–2005	Lyngstad Bouwknegt Refregier-petton Guerin Näther	2008 2004 2001 2007 2008	Huneau-Salun (2007) reported the presence of control measures against rodents as significantly associated with risk increase		
* = Non-significant in multivariate model									
ADD ROWS FOR LIT STUDIES									
No animals in close proximity of broiler houses							– Repeatability from five countries – PAFs (but one) fairly similar magnitude – Includes newer study – Supported by Jonsson et al. (2012), PAF for this study not calculated due to lack of information	– Large variation in the risk factor measurements in individual studies	Low (< 10%?) CAMCON REPORT
Other animal species on farm	PAF %	25.5 (1.8–42.1)	NL	1997–2000	Bouwknegt rf_1	2004			
Other animals within 1 km radius	PAF %	79.3 (32.3–87.5)	NL	1997–2000	Bouwknegt rf_2	2004		Only 27 flocks (out of 457) did not have a farm within 1 km, lack of statistical power cannot be ruled out	

Specific factor studied	Estimated measure	Result (CI)	MS	Year (data)	Stud	Year (pub)	Specific strengths	Specific uncertainties	Uptake 2016 %
Other livestock on farm	PAF %	20.9 (5–37)	SE	2005	Hansson	2010			
Cattle adjacent	PAF %	21.5 (4.4–35)	UK	2003–2006	Ellis-Iversen	2009			
Pigs closer than 2 km	PAF %	39.5 (19.8–47.8)	NO	2005	Lyngstad	2008			
Presence of dogs/cats at farm	PAF %	33.4 (2.6–44.1)	ES	2010–2012	Torralbo	2014		Only carried out in Andalusia	
Non-significant (i.e. explored in univariate analysis but not retained for the multivariate model)	PAF %	–	–	1999–2000 2004–2005 2001 2008 2009–2010 2001–2002	Sommer Näther Refregier-petton Allain Chowdhury McDowell	2013 2008 2001 2014 2012 2008			
ADD ROWS FOR LIT STUDIES									
Employing few and well-trained staff							– repeatability from four countries – fairly similar PAFs – supported by other study types	– Nordic countries are over-represented – newest data from 2009–2010	
Personnel in house at delivery	PAF %	14.2 (2.9–17.7)	NO	2005	Lyngstad rf_1	2008			
Hired caretaker staff	PAF %	13.9 (2.7–18.6)	NO	2005	Lyngstad rf_2	2008			
≥ 2 persons taking care of birds	PAF %	25.3 (2.7–37.1)	FR	2001	Refregier-petton	2001			
≥ 2 persons entering houses	PAF %	20.5 (5–38.85)	DK	2009–2010	Chowdhury	2012			

Specific factor studied	Estimated measure	Result (CI)	MS	Year (data)	Stud	Year (pub)	Specific strengths	Specific uncertainties	Uptake 2016 %
Non-significant (i.e. explored in univariate analysis but not retained for the multivariate model)	PAF %	–	–	2004–2005 1999–2000	Näther Sommer	2008			
ADD ROWS FOR LIT STUDIES									
Addition of disinfectants to drinking water							Repeatability in three countries Newer data included		50–90% (CAMCON report)
Non-chlorinated water	PAF %	32.5 (6–54.9)	UK	2003–2006	Ellis-Iversen	2009			
Water not treated	PAF %	5.3 (0.6–8.2)	ES	2010–2012	Torralbo	2014		Only carried out in Andalusia	
No Acid in drinking water	PAF %	17.1 (3.3–23)	FR	2008	Allain	2014		Only carried out in Brittany	
Non-significant (i.e. explored in univariate analysis but not retained for the multivariate model) studies	PAF %	–	–	2003–2004	Huneau-salun	2007	Refregier-Petton et al. (2001) found treating drinking water as significantly associated with risk increase		
ADD ROWS FOR LIT STUDIES									
Avoid drinkers that allow standing water							Supported by Sommer et al. (CAMCON) Newer data included	– Only from DK and DE Two studies – same study	15–49% (Van Wagenberg)

Specific factor studied	Estimated measure	Result (CI)	MS	Year (data)	Stud	Year (pub)	Specific strengths	Specific uncertainties	Uptake 2016 %
Nipple drinker with tray	PAF %	37.2 (0*–53.9)	DE	2004–2005	Näther s	2008		These studies were convenience samples of farms: may not represent all of Germany and may be less variable than a representative sample	
Nipple drinker with tray	PAF %	62.4 (1.2–78.5)	DE	2004–2005	Näther w	2008			
Drinker with cups	PAF %	25.4 (0.8-44)	DK/NO?	2010–2012	Borck høg	2016			
Non-significant studies (i.e. explored in univariate analysis but not retained for the multivariate model)	PAF %	–	–	2001–2004 2001 2003–2006 1999–2000 2010–2012	Guerin Refregier-petton Ellis-Iversen Sommer Torralbo	2007 2001 2009 2013 2014			
* = Non-significant in multivariate model									
No' drinkers with drink nipples without cups in farmhouses < 15 years old'	RRR	5 8 12 14 24 24	PL ES UK NL DK NO	2012	CAMCON Sommer Van Wagenberg	2016 2016	EU study RR reduction DK estimate is similar to PAF for DK study (same data)	No PAF calculated, as another type of data analysis is performed Based on only few (20) farms in ES, NL, PL and EK, 100 and 160 farms in DK and NO Data are imputed based on assumptions to provide significance and allow modelling No CI given	
ADD ROWS FOR LIT STUDIES									

Specific factor studied	Estimated measure	Result (CI)	MS	Year (data)	Stud	Year (pub)	Specific strengths	Specific uncertainties	Uptake 2016 %
EXTRA OPTIONS FROM LIT REVIEW									
No 'designated tools for each house in farmhouses < 15 years old'	RRR	1 6 11 16 2 6	PL ES UK NL DK NO	2012	CAMCON Sommer Van Wagenberg	2016 2016	EU study	No PAF calculated, as another type of data analysis is performed Based on only few (20) farms in ES, NL, PL and EK, 100 and 160 farms in DK and NO Data are imputed based on assumptions to provide significance and allow modelling No CI given Not found in other studies	23–93% (report) 63–98 (Van Wagenb.)
No 'establishing a maximum downtime of 10 days between flocks including rodent control more than 6 times per year and clean- ing and disinfection between flocks'	RRR	8 10 2 7 7 42	PL ES UK NL DK NO	2012	CAMCON Sommer Van Wagenberg	2016 2016	EU study	No PAF calculated, as another type of data analysis is performed Based on only few (20) farms in ES, NL, PL and EK, 100 and 160 farms in DK and NO Data are imputed based on assumptions to provide significance and allow modelling No CI given Not reported in other RF studies included	

Specific factor studied	Estimated measure	Result (CI)	MS	Year (data)	Stud	Year (pub)	Specific strengths	Specific uncertainties	Uptake 2016 %
Farmhouses > 15 years old	RRR	4 57 27 26 22 27	PL ES UK NL DK NO	2012	CAMCON Sommer Van Wagenberg	2016 2016	EU study	No PAF calculated, as another type of data analysis is performed Based on only few (20) farms in ES, NL, PL and EK, 100 and 160 farms in DK and NO Data are imputed based on assumptions to provide significance and allow modelling No CI given Not reported in other RF studies	
Stop thinning	RRR	2 13 25 23		2011	EFSA		Previous opinion		37–97% (Van Wagenberg ea)
Reduced slaughter age 35 days 28 days	RRR	0–18 22–43		2011	EFSA		Previous opinion		

Table column	Explanation
Control options	General name for class of control practices
Specific factor studied	The specific practice or risk factor studied
Measure	The measure of effect on risk we use from that study, plus units (if multiple measures available from same study, take the most relevant or add multiple measures as separate rows in table). Key: RRR = Relative risk reduction
Result (CI)	The result from the study (and 95% confidence interval (CI) where available). If the result cannot be given as a number, describe it verbally but as concisely as possible. (To make more space for this, you could merge this cell with the 'measure' cell just for this study, if that helps)
MS	Member State(s) study was conducted in
Year	Year(s) study was conducted in (not year of publication)
Study	First author name (only include year if more than one study for same first author)
Strengths	Brief summary of notable strengths of this study. Exclude strengths that affect all studies using the same measure (e.g. PAF)
Specific uncertainties	Brief summary of notable uncertainties affecting this study. Exclude uncertainties that affect control options, as these will be listed in the general uncertainty table
Uptake 2016 %	Uptake of the control practice (i.e. the % of farms that do already apply the control option) in 2016; data from the CAMCON project (van Wagenberg et al., 2016)

D.2.   Evidence table for control options affecting concentration

Control practice	Specific factor studied	Measure	Result (CI)	MS	Year	Study/model	Specific strengths	Specific uncertainties
Vaccination	4 antigens	log reduction	1.96 – 3.54 – 4.2 – 2.01 (ND)	France	2015–2016	Meunier et al. (2017)	New antigens found by the reverse vaccinology and tested on animals with a promising result of log reduction	Lack of reproducibility between trials Experimental level, not tested on field
Feed additive	Probiotic	log reduction	1.79 (1.18)	France	2014–2015	Guyard-Nicodème et. al	Reduction measured at the end of the rearing of standard broilers (42 day), close to the field conditions	Lack of reproducibility between trials
Feed additive	Probiotic	Log reduction	1.67 (1.2)	France	2014–2015	Guyard-Nicodème et. al		Lack of reproducibility between trials
Feed additive*	Prebiotic	Log reduction	3.25 (2.2)	France	2014–2015	Guyard-Nicodème et. al		Lack of reproducibility between trials

Control practice	Specific factor studied	Measure	Result (CI)	MS	Year	Study/model	Specific strengths	Specific uncertainties
Feed additive*	Organic acid	log reduction	1.23 (0)	France	2014–2015	Guyard-Nicodème et. al		Lack of reproducibility between trials
Feed additive	Organic acid	log reduction	0.9	Spain	2014–2015			Lack of reproducibility between trials
Feed additive	Mixture of ion-exchanged clay in feed and organic acid in water	log reduction	0.82	France	2014–2015		Reduction measured at the end of the rearing of free range broilers (78 day), close to the field conditions	
Feed additive*	Amino acid with iron	log reduction	2	Greece		Skoufos et al.	Reduction measured at the end of the rearing of standard broilers (42 day) based on 3 replicates	

Table column	Explanation
Control practices	General name for class of control practices
Specific factor studied	The specific practice or risk factor studied or modelled
Measure	The measure of effect on risk we use from that study/model, plus units (if multiple measures available from same study/model, take the most relevant or add multiple measures as separate rows in table)
Result (CI)	The result from the study/model (and 95% confidence interval where available). If the result cannot be given as a number, describe it verbally but as concisely as possible. (To make more space for this, you could merge this cell with the 'measure' cell just for this study, if that helps)
MS	Member State(s) study was conducted in, or model refers to. If EU model, enter 'EU'
Year	Year(s) study was conducted in (not year of publication). For models, enter year of publication
Study/model	First author name (only include year if more than one study/model for same first author)
Strengths	Brief summary of notable strengths of this study/model. Exclude strengths that affect all studies using the same measure or model
Specific uncertainties	Brief summary of notable uncertainties affecting this study/model result. Exclude uncertainties that affect all control options, or all results from same model, as these will be listed in the general uncertainty table
Uptake 2016 %	% uptake of the control practice in 2016 from countries studied in CAMCON project. Can we list all the countries and values in the space available in this column? If not, would it be sufficient to show the range?
*	Analysed by the C-model

D.3. Uncertainty table

Risk factor, parameter or model feature affected by the uncertainty	One sentence description of the cause of uncertainty affecting this risk factor, parameter or model feature (one row per cause of uncertainty)	One sentence description of how this source of uncertainty might lead to incorrect ranking of control options, or why that might be possible	Which types of model or study does this uncertainty affect? (e.g. PAFs, C model, etc.)
Risk factors for broiler infection with *Campylobacter* spp.	Small numbers of broiler farms are a cause of uncertainty in many studies	Sources of *Campylobacter* on broiler farms are many and varied and may depend on the farms studied. Thus, the findings of a given study, which often includes small numbers of farms, may not be applicable on other farms and the ranking will reflect the choice of farms in published studies and might be different if the observations were made using a larger number of farms	PAFs
Risk factors for broiler infection with Campylobacter spp.	The difference in key climate, broiler husbandry practices etc. in different countries is a cause of uncertainty	Many studies on the risk factors for Campylobacter in broilers are undertaken in a single country or a few countries and the data generated and conclusions may not be applicable to other countries in the EU, where, for example, the climate and broiler farm practices may be different	PAFs – representativeness of all of the EU is uncertain
Risk factors for broiler infection with Campylobacter spp.	Sample size is a cause of uncertainty	Sample size may also be an issue with many studies using 1 g or 10 g samples, which may or may not be representative of the flock or broiler house. For example, a 10 g sample of broiler faeces or 10 cloacal swabs from a flock of 30,000 may or may not be representative of the flock as a whole The result may be false-negative flocks	PAFs
Risk factors for broiler infection with Campylobacter spp.	Seasonal effects are a cause of uncertainty	Seasonality greatly affects *Campylobacter* survival in the environment, sources and dissemination routes and data from studies that do not include a seasonal consideration may not be applicable throughout the year	PAFs
Risk factors for broiler infection with Campylobacter spp.	Assumptions about the direction of Campylobacter spread is a cause on uncertainty	Contrary to the conclusion in some papers, the detection of similar *Campylobacter* genotypes in farm animals adjacent to the broiler house before they appear in the birds should not be indicative of horizontal transmission form these animals to the birds. It is equally possible that these animals were infected by *Campylobacter* from previous broiler flocks and/or the levels in the birds were below the level of detection if tested at the same time as the farm animals	PAFs
Risk factor and control options	No/little adjustment for confounding or interaction of all other factors	Measured effects or risks may actually be caused by other factors, unless these are deliberately adjusted for – either by exclusion (laboratory trials) or statistically (epidemiological studies)	All -except for epistudies and carefully designed experimental studies

Risk factor, parameter or model feature affected by the uncertainty	One sentence description of the cause of uncertainty affecting this risk factor, parameter or model feature (one row per cause of uncertainty)	One sentence description of how this source of uncertainty might lead to incorrect ranking of control options, or why that might be possible	Which types of model or study does this uncertainty affect? (e.g. PAFs, C model, etc.)
Control options for preventing broiler infection with Campylobacter spp.	Unrepresentative laboratory studies are a cause of uncertainty	Laboratory studies may not accurately reflect the conditions encountered in the broiler house and there is considerable uncertainty in laboratory data with respect to its application on commercial broiler farms	The model including the impact of interventions on Campylobacter count reduction?
Control options for preventing broiler infection with Campylobacter spp.	Unrepresentative field trials are a cause of uncertainty	Field trials may not reliably predict the impact of specific interventions under real-world conditions where there may be up to 30,000 birds in a shed with a stocking density of 20 birds per m^2	The model including the impact of interventions on Campylobacter count reduction?
Control options for preventing broiler infection with Campylobacter spp.	Human behaviour is a cause of uncertainty	In biosecurity studies, the participants are often volunteers who are aware they are being assessed and may behave differently to their normal practices	Minor for PAFs as variability – incl. Compliance is included and thus accounted for in epi-studies
Control options for preventing broiler infection with Campylobacter spp.	Broiler farm selection is a cause of uncertainty	Many studies are undertaken on a relatively low number of broiler farms that may not be representative of broiler farms in general. Moreover, their selection is often agreed with their contract processor, who is more likely to suggest farms that have a good Campylobacter performance record	?
Control options for preventing broiler infection with Campylobacter spp.	The specificity of bacteriophage is a cause of uncertainty	The high specificity of phage in terms of the Campylobacter strains they can infect introduces great uncertainty in phage research especially when extrapolating to a real-world situation where there may be multiple Campylobacter strains within a given bird or flock	?
Control options for preventing broiler infection with Campylobacter spp.	The age and lineage of the test birds is a source of uncertainty	When evaluating probiotic bacteria as a feed additive, a range of factors including the age and lineage of the birds and the mode of administration greatly influence the outcome of the experiments. Moreover, if the birds are exposed to Campylobacter first, the probiotic strain is considerably less likely to have a positive effect	?
Control options for preventing broiler infection with Campylobacter spp.	Lack of reproducibility between trials Experimental level, not tested on field	In one trial, the product can have a very significant effect in terms of reduction but when repeating the same conditions in a second trial, no significant effect can be obtained. This loss of significance between two trials is often (but not the only reason) the variability of Campylobacter counts between (control) animals	C-model

Risk factor, parameter or model feature affected by the uncertainty	One sentence description of the **cause** of uncertainty affecting this risk factor, parameter or model feature (one row per cause of uncertainty)	One sentence description of **how** this source of uncertainty might lead to incorrect ranking of control options, or why that might be possible	Which types of model or study does this uncertainty affect? (e.g. PAFs, C model, etc.)
Risk factors for broiler infection with Campylobacter spp. Control options for preventing broiler infection with Campylobacter spp.	The ability of *Campylobacter* to enter the viable but not culturable (VBNC) state is a cause of uncertainty	Campylobacter can enter a viable but not culturable (VBNC) state which may greatly affect the data obtained, especially in studies designed to reduce or eliminate these pathogens. An alternative is to use PCR-based methods, but the presence of *Campylobacter* DNA does not indicate the presence of viable cells	?
C-model: Use of caecal concentration	It is not necessarily the caeca that contaminate the carcass, it may also be leaking faeces, which has a lower concentration	This increases the variability in the data and the uncertainty about the regression line and the uncertainty of the ranking. *(In general: The ranking between measures within the C-model is not altered, only the ranking compared to the P-model measures)*	C-model
C-smodel: Use of caecal concentration	It need not be the caecal count that is used to measure the impact of the intervention	The regression line is not representative for the evaluated intervention if no caecal counts are used, it increases the overall uncertainty of the ranking	C-model
C-model: In reality, the relation between caecal concentration and carcass concentration is probably not linear	If the slope at high caecal concentrations is larger than the slope at low values (i.e. there is not really a linear relation, it is j-shaped), the regression line may overestimate the effect of the intervention at low concentrations	The effect of the intervention may be slightly overestimated if the regression is based on high concentrations	C-model
C-model: Censored data on caeca and/or skins	Concentration data usually suffer from the presence of data below (or above) a limit of quantification, so-called censored data. The way these are traditionally dealt with (taking a fixed value, the lower limit or so; or simply omitting the data) may have high large impact on the regression line obtained. Methods for regression with censored data may help (Tobit regression), but there is no established method to deal with regression and censored data in both the dependent and independent variable	This impacts the uncertainty of the slope obtained	C-model

Risk factor, parameter or model feature affected by the uncertainty	One sentence description of the cause of uncertainty affecting this risk factor, parameter or model feature (one row per cause of uncertainty)	One sentence description of how this source of uncertainty might lead to incorrect ranking of control options, or why that might be possible	Which types of model or study does this uncertainty affect? (e.g. PAFs, C model, etc.)
C-model: assumption that $\tau = 1$: the contamination of the meat is always 1 log less than the skin	Lack of data led to an expert estimate of the *Campylobacter* WG in 2010	This impacts the effect estimate (in terms of relative risk reduction), it is included in the model	C-model
C-model: CPM used (with assumptions on cross contamination) is representative for all prepared chicken meals	Consumer food preparation is highly variable, not under control and hard to measure or influence	Increases the overall uncertainty; this is studied by comparing different CPMs	C-model
C-model: DR model used: actual dose response for Campylobacter on chicken is highly uncertain	The DR relations are based on one or a few strains; not from chicken meat; are for healthy adults or primates that are not immune	Increases the overall uncertainty; this is studied by comparing different DRs	C-model
C-model: use of 2008 baseline data on skin samples	These are old data, but collected all over Europe in a harmonised way. In the meantime, action may have been taken to reduce these concentrations	Not really sure how this impacts the results; we may overestimate the (relative) risks. The high incidence of human infection suggests that *Campylobacter* prevalence at farm and slaughter at has not improved since 2008	C-model
C-model: implementation effect of control options	The variation between log reductions as observed in the (raw) data is interpreted both as variability (the st. dev in the data) and the uncertainty (the s.e.m.), whilst it actually is a combination of both	Both variability and uncertainty are overestimated, which leads to underestimation of the effect and overestimation of the uncertainty. The impact of this phenomenon can be assessed by considering the scenarios where either the variability or uncertainty are omitted, in the sensitivity analysis	C-model
Risk factors (all) for PAF calculation	PAFs are calculated from adjusted Relative Risks, different studies adjust for different confounders in the final multivariate model	Impact on the estimates of the multivariate model and thus on the size of PAFs	PAF
Risk factors (all) for PAF calculation	Few studies considered the effect of including non-significant (but potentially confounding) factors in the final multivariate model	Impact on the estimates of the multivariate model and thus on the size of PAFs	PAF

Risk factor, parameter or model feature affected by the uncertainty	One sentence description of the cause of uncertainty affecting this risk factor, parameter or model feature (one row per cause of uncertainty)	One sentence description of how this source of uncertainty might lead to incorrect ranking of control options, or why that might be possible	Which types of model or study does this uncertainty affect? (e.g. PAFs, C model, etc.)
Risk factors (all) for PAF calculation	Heterogeneity in the biological samples that are collected on farm/slaughter (Pool of different number of caeca samples, cloacal swabs, sock samples) and analysed to define a flock as 'positive'. Possible differences in sensitivity between methods	Probably little impact under the assumption that within-flock-prevalence is typically considered to by high in infected flocks	PAF
All risk factors	Underreporting of non-significant effects	If no significant effect is found for a risk factor or control option, it may not be published. This means the 'mean published' effect size of a potential control option may be larger than it actually is	All
Control measure: 'Avoid presence of standing water in drinkers'	Two of the studies were convenience samples of farms and may not represent all of Germany. Furthermore, a convenience sample may have less variability than a representative sample	Introduces more uncertainty about the effect in all of EU and the altered variance may have over- or underestimated the PAF	PAF
Effective hygiene barrier at broiler house entrance	One of the studies was only representative of 60% of French broilers and the Spanish study was only carried out in Andalusia	This introduces more uncertainty about the control effect of all of EU and the biased variability may over- or underestimate the PAF	PAF
Effective rodent control	Two of the studies were carried out in regions (Brittany and Andalusia) and are unlikely to be nationally representative	This introduces uncertainty about the control effect of all of EU and the biased variability may over- or underestimate the PAF	PAF
No animals in close proximity	This control estimate was derived from a broad range of risk factors	This adds uncertainty around the precision of the PAF estimate	PAF
Have few and permanent staff			PAF
Additives to drinking water	One of the studies was carried out using a convenience sample and another was from Brittany	This introduces uncertainty about the control effect in all of EU and a biased variability may over- or underestimate the PAF	PAF

D.4.   Report on expert knowledge elicitation, 19–20 November 2019

The ranking and quantification of control options reported in the Opinion was conducted in two steps:

- Step 1: Experts assessed the probability that each of 22 (later reduced to 20) control options would, if implemented by all EU broiler producers, reduce the incidence of campylobacteriosis in the EU by at least 10%.
- Step 2: Experts assessed the magnitude of reduction in incidence of campylobacteriosis in the EU that each of the prioritised control options would achieve, if implemented by all EU broiler producers.

The methods and results for the first step are reported in the opinion and were used to prioritise eight control options to be considered in step 2. Methods and results for step 2 are summarised in the opinion and documented in more detail in this appendix.

Note: the names used for control options in this appendix are those used during the elicitation workshop.

Methods for step 2 of elicitation process

The precise question to be addressed in step 2 was specified as follows: *If the specified control option is implemented by all broiler producers in the EU that are not currently using it, what will be the resulting % reduction (compared to the current level of implementation) in average annual incidence of campylobacteriosis cases in the whole EU population caused by campylobacter in broiler meat produced from chickens raised in the EU, other things being equal?*

When addressing this question, the following definitions were applied:

- The meaning of 'campylobacteriosis cases' was clear for the experts and did not require further definition.
- 'Other things being equal' includes other control options remaining at the current level of implementation, production and processing practices remain unaltered and no change in the consumption in the EU of meat from broilers raised in the EU.
- If a control option acts on both prevalence and concentration, both should be taken into account when answering the question.
- For each control option, the experts will answer the question assuming that, of the specific practices for this control option which are referred to in this Opinion (e.g. different vaccines, or different methods of rodent control), the practice that would, on its own, achieve the largest reduction in campylobacteriosis will be implemented by all EU broiler producers.

The experts comprised all members of the Working Group developing the Opinion, plus three EFSA scientists who were supporting the WG.

Expert judgements on the question were elicited in the course of a one day (midday to midday) expert knowledge elicitation (EKE) workshop. The elicitation method was based on the Sheffield or SHELF protocol (EFSA 2014, Oakley and O'Hagan, 2019), which first elicits judgements from each expert individually and then seeks to elicit a consensus judgement from the group, integrating their individual judgements by a process of discussion (behavioural aggregation, EFSA 2014) rather than calculation. The elicitation was conducted by a facilitator and rapporteur who are experienced in use of the Sheffield method. The experts were trained on the approach to making both the individual and consensus judgements using an example question unrelated to the Opinion.

Two modifications were made to the normal Sheffield protocol (EFSA, 2014) in order to complete the exercise within the time allocated. First, experts made individual judgements on all eight of the selected control options during a single session, before proceeding to the consensus process. Second, the unweighted linear pool of the individual judgements was used as a starting point to be discussed by the group and modified as necessary to reflect their consensus judgement, rather than eliciting consensus quantiles and fitting a distribution.

Evidence and sources of uncertainty relevant to answering the question had been collated and summarised in the course of the work on the Opinion, as described in the main text. The experts were familiar this information, having used it for their judgements on the question for Step 1 during the preceding 2 weeks.

The experts completed their individual judgements in a period of 40 min at the end of the first half of the workshop. Overnight, the facilitator and rapporteur collected and processed the individual judgements, using a downloaded copy of the SHELF app for multiple experts (http://www.jeremy-oakley. staff.shef.ac.uk/project/elicitation/). For each control option considered in step 2, the app was used to plot, on a single graph, a separate distribution fitted to the judgements of each expert (selecting the option 'best-fitting' in the app) plus an additional distribution representing the unweighted linear pool of the individual expert distributions, together with the median and 95% probability interval for the linear pool. An example of this for one control option is shown in Figure D.1.
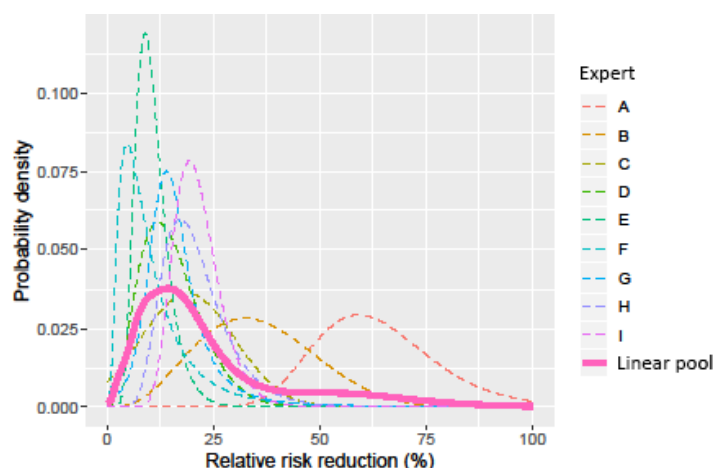

Figure D.1: Example of the initial results of the elicitation for the control option 'discontinued thinning', prior to the consensus process. The dashed curves represent the best-fitting distributions for the individual experts and the solid line represents the unweighted linear pool (average) of those distributions

A boxplot was produced, comparing the linear pool distributions for all eight control options. The first version of this, depicting the results prior to the consensus process, is shown in Figure D.2.
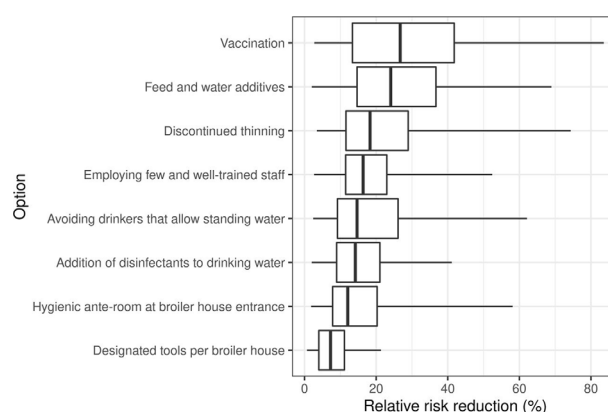

Figure D.2: Boxplots comparing the initial unweighted linear pool distributions for all eight control options considered in step 2, prior to the consensus process. For each control option, the horizontal line represents the 95% probability interval of the linear pool distribution, the box represents the interquartile range (covering 50% probability) and the vertical bar within the box is the median

At the beginning of the second half-day of the workshop, the initial results (Figure D.2 plus a version of Figure D.1 for each control option) were displayed and discussed by the group. In view of the limited time, the group prioritised five options (designated tools; additives; discontinued thinning; few and well-trained staff; and vaccination) to discuss in detail for developing consensus distributions. For each of these options in turn, the facilitator asked experts with contrasting individual distributions to summarise the reasoning behind their judgements. For three control options (designated tools; discontinued

thinning; few and well-trained staff), this led to agreement by the group to accept the unweighted linear pool as representing their consensus judgement. For additives, the discussion led one expert to suggest reducing the weight given to this expert's distribution. A linear pool giving zero weight to this expert was displayed and the group unanimously agreed to accept this as their consensus judgement for additives. For vaccination, the discussion led three experts to revise their individual judgements, after which the group agreed to accept the revised linear pool as their consensus.

After agreeing the consensus for each of the five options that were discussed in detail, the group briefly summarised the principal evidence and reasoning behind it, as shown in Table D.1.

Table D.1: Rapporteur's notes summarising the expert group's collective rationale for the consensus distributions for the five control options that were discussed in detail

Control option	Summary of rationale as recorded by rapporteur
Designated tools per broiler house	Reason why it is unlikely that designated tools would have more than 10% effect: very little evidence that the tools are the main risk; sharing tools is such a bad biosecurity sign that unlikely to be more than 10% effect just by changing this practice; available evidence points to less than 10% effect
Feed and water additives	Consensus distribution represents experts' judgement of difference from model estimates due to likelihood of unreported negative studies, expectation of less effects in field, expectation that effect will not happen always
Discontinued thinning	Start from old opinion (4 Member States between 2% and 25%, CANCOM between 3% and 13%, but various biases), but long tail due to uncertainty about differences between countries and differing experiences in different countries)
Employing few and well-trained staff	Main peak reflects the PAF results, but the tail reflects variation of judgement about how large the bonus biosecurity effect would be
Vaccination	Diversity of views about role of strain specificity and about transfer to the field is key to the wide distribution of uncertainty with some experts close to the model results and others much lower

Finally, the experts reviewed a revised set of boxplots, which had been updated with the modified consensus distributions for additives and vaccination. The group accepted this plot as representing its consensus judgement about all eight control options considered in step 2, including the three which it had not been possible to discuss in detail (hygienic anterooms; avoiding drinkers that allow standing water; and disinfectants added to drinking water). This final set of boxplots representing the group's consensus judgements are shown in Figure 6 in the main text of the opinion. Selected quantiles for the consensus distributions (including those shown in the boxplots) are shown in Table D.2.

Table D.2: Selected quantiles of the consensus distribution for each of the control options considered in step 2. The P2.5 and P97.5 provide the 95% probability interval for each option, while the P16.7 and P83.3 provide a 66.6% probability interval (corresponding to the category 'Likely' in EFSA's approximate probability scale, (EFSA Scientific Committee, 2018)

Control options	P2.5	P5	P16.7	P25	P50	P75	P83.3	P95	P97.5
Vaccination	3	4	10	13	27	42	50	74	84
Feed and water additives	2	4	11	15	24	37	43	60	69
Discontinued thinning	3	5	9	12	18	29	39	65	74
Few and well-trained staff	3	5	9	11	16	23	28	45	52
Avoiding drinkers that allow standing water	2	4	7	9	15	26	34	53	62
Addition of disinfectants to drinking water	2	3	7	9	14	21	25	36	41
Hygienic anterooms at broiler house entrance	2	3	6	8	12	20	26	50	58
Designated tools per broiler house	1	1	3	4	7	11	13	18	21

Appendix E – Studies on effects of control options on broiler farms to reduce the concentration of *Campylobacter* in the birds

Numbers in bold are obtained after re-analysing the raw data with a method that allows inclusion of censored data (Lorimer and Kiermeier, 2007).

Intervention	Specification	Type of study	Mean log reduction	SD log reduction	S.E. of mean	Sample size	Reference
Vaccination	Recombinant (DNA + protein) new antigen 1	Experimental on broilers	1.96 **2.03**	**1.83**	**0.49**	15 birds for each vaccine test	Meunier et al. (2017)
	Recombinant (DNA + protein) new antigen 2	Experimental on broilers	3.54 **3.47**	**2.14**	**0.63**	15 birds for each vaccine test	Meunier et al. (2017)
	Recombinant (DNA + protein) new antigen 3	Experimental on broilers	4.2 **4.15**	**1.63**	**0.51**	15 birds for each vaccine test	Meunier et al. (2017)
	Recombinant (DNA + protein) new antigen 4	Experimental on broilers	2.01 **2.09**	**1.82**	**0.5**	15 birds for each vaccine test	Meunier et al. (2017)
Feed additive	Probiotic	Experimental on broilers (45–49 birds)	1.88 (at 35 day) 1.79 1.88	**1.18**	**0.42**	15 birds	Guyard-Nicodème et al. (2016)
	Probiotic	Experimental on broilers (45–49 birds)	1.70 (at 42 day) **1.68**	**1.2**	**0.65**	15 birds	Guyard-Nicodème et al. (2016)
	prebiotic	Experimental on broilers (45–49 birds)	3.17 (at 42 day) **3.25**	**2.2**	**0.64**	15 birds	Guyard-Nicodème et al. (2016)
	Organic acid	Experimental on broilers	2.13 (at 42 day) **1.23**	**0**	**0.66**	15 birds	Guyard-Nicodème et al. (2016)
	Organic acid	Experimental on broilers (45–49 birds)	0.9 (at 42 day)		0.206	10 birds	Gracia et al. (2016a, b)
	Microencapsulated mixture of short chain fatty acids and phenolic essential oils, 2,000 ppm	Chickens inoculated with a mixture of 2 strains of C, jejuni (10,000 CFU)	0.7 log reduction in treated birds (after 35 days)	Not given	Not given	Not given	Thibodeau et al. (2015)
	Ferric tyrosine	Experimental on broilers	2 (at 42 day)			36 birds (3 replicates of 12)	Skoufos et al. (2019)
	Mixture of ion-exchanged clay in feed and organic acid in water	Experimental on free range broilers (78 day)	0.82	0.25		15 birds	Guyard-Nicodème et al. (2017)

Intervention	Specification	Type of study	Mean log reduction	SD log reduction	S.E. of mean	Sample size	Reference
Bacteriophage	4 phage cocktail applied via drinking water, 5.8–7.5 log pfu dose per bird, 6–7 days before slaughter	3 field trials using broilers under commercial conditions. Data (control and trial groups) have been provided for the 3 field trials	Trials 1, 2 & 2 Treatment groups (trial number, days after application, mean faecal count t plus SD in brackets) 1, 0, 2.4 (0.6) 1, 1, < 1.8 (0) 1, 6, 3.8 (0.5) 2, 0, 3.1 (0.8) 2, 1, 4.6 (0.4) 2, 6, 5.9 (0.2) 3, 0, 0.5 (0.7) 3, 1, 4.6 (1.0) 3,7, 0, 6.7 (0.2)	Corresponding data for control groups 1, 0, 1.2 (0.6) 1, 1, 2.6 (0.7) 1, 6, 7.0 (0.2) 2, 0, 4.6 (0.7) 2, 1, 4.7 (0.6) 2, 6, 4.4 (1.0) 3, 0, 2.7 (0.9) 3, 1, 5.6 (0.6) 3,7, 0, 4.5 (0.4)		9 birds per each of the 3 trials	Kittler et al. (2013)
Water additive	Commercial additive composed of short chain organic acids and medium chain fatty acids	Commercial flocks. broilers-3 consecutive rearing cycles. Caecal reductions did not result in lower carcass counts	Treated birds 35 days mean count (SD) 5.67 (1.28) 0.85 (0) 0.85 (0) Treated birds (42 days 4.19 (1.59) 0.85 (0) 0.85 (0)	Control birds 35 days) 2.95 (3.39) 7.72 (0.92) 0.85 (0) 6.26 (1.19) 5.09 (2.14) 7.36 (0.92)			Jansen et al. (2014)
Thinning	Naturally contaminated broilers before and after thinning	Commercial flocks – Data provided for prevalence and caecal counts for 14 commercial flocks	Mean counts and SD provided	Too much data to be included here but well presented in Table 1 (page 878) of the paper			Koolman et al. (2014) (incl. Bolton)

Intervention	Specification	Type of study	Mean log reduction	SD log reduction	S.E. of mean	Sample size	Reference
Vaccination	2 vaccines both formalin killed C. jejuni but in 2 different adjuvants (oil and aluminium hydroxide gel)	Field-based trial using Jidori chicks	26 days post challenge: oil: 7.0 (1.2) Aluminium: 7.5 (0.7) Control: 7.0 (1.1) 56 days post challenge: Oil: 6.8 (1.2) Aluminium: 6.6 (2.2) Control: 7.2 (1.1)			17	Okamura et al. (2012)
Feed additive	MCFA	Applied test conditions. Birds experimentally infected with *C. jejuni* at 15 days old and tested at 27 days old	Control: 7.0 (0.8) Tylosin 2.8 (1.5) Caproic acid 7.3 (0.8) Caprylic acid 7.8 (0.7)			10	Hermans et al. (2010)
Bacteriophage	Ross 308 broilers were given 7 log CFU C. jejuni after 20 days rearing	Birds were housed in a commercial environment in individual pens	The control was birds treated with a placebo or carrier alone	1 log reduction after 1 day, 2.4 log reduction after 2 days, 1.9 log reduction after 3 days, 1.4 log reduction after 4 days & 1.6 reduction after 6 days	Provided, see Figure 1	5 birds tested per sampling time	Richards et al. (2019)
	At 24 days, the birds were given a 2 phage mixture, & log PFU						
	5 chickens were tested on each day from 25 to 29 days and *C. jejuni* enumerated in ceca						