



Translation of risk factor estimates into on-farm interventions and their effect on *Campylobacter* broiler flock prevalence



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ABSTRACT

Before deciding upon interventions to control *Campylobacter* in broiler flocks, it would be useful to estimate the potential effects of different interventions. Certain previously identified risk factors for colonization of broiler flocks with *Campylobacter* may seem to have large impact on the broiler flock prevalence. Nevertheless, interventions related to these risk factors may have only limited effect on the overall prevalence estimate, since in practice only a relatively small fraction of farms are actually amenable for an intervention related to a given risk factor.

We present a novel method for the risk assessor that predicts effects of interventions at the farm, based on results from a risk factor study that included data from six European countries (Denmark, Netherlands, Norway, Poland, Spain and United Kingdom). In the present study, five previously identified risk factors, which had shown to have significant impact on *Campylobacter* flock prevalence, were translated into practical on-farm interventions. Given the implementation of these interventions the population prevalence was predicted by developing and using a statistical method anchored in the ideas behind standardized population estimations using logistic regression. To obtain population estimates per country, the predicted prevalence values were multiplied by the frequencies (no. of farms) in a reference population based on data from the risk factor study and a large questionnaire. The latter was included to improve the representativeness of the reference population. Population prevalence estimates were calculated before and after implementation of a given intervention in the six countries. Results showed that if biosecurity was not accounted for, some individual interventions resulted in a limited reduction of the population prevalence. The reduction differed between countries depending on the current farm management practices and the actual flock prevalence level. In general, the most effective interventions were “building new houses with strict biosecurity for all houses older than 15 years” and “apply drinkers with nipples without cups”. In conclusion, the novel method translates results from risk factor studies into effects of on-farm interventions for the reduction of the prevalence of *Campylobacter* in broiler flocks. The method is very useful for providing the basis for risk management decisions. The usefulness would improve further when the results are integrated with costs of interventions in a cost effectiveness study. The approach was developed for *Campylobacter* in broiler flocks, but it can also be applied to other pathogens and other farm animals, given that the required data are available.

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1. Introduction

Campylobacter is the most commonly reported human gastrointestinal bacterial pathogen in Europe and broiler chickens are identified as its main reservoir (EFSA 2011). Control of *Campylobacter* on broiler chicken farms is therefore considered of utmost importance to reduce the spread of the pathogen and to reduce the human health risk of acquiring campylobacteriosis.

Identification of risk factors for introducing *Campylobacter* into broiler flocks is an important first step to decide upon preventive measures. Consequently, over the last decades, many risk factor studies have been published (Adkin et al., 2006). Recently, within the European seventh framework project CamCon, a large risk factor study was performed that included six European countries (Denmark, Norway, Spain, Netherlands, Poland and the UK) (Sommer et al., 2016). This study identified the following significant risk factors: *Anteroom+barrier*, *Downtime*, *Drinkers*, *Age of house*, *Tools plus Temperature* and *Country* and concluded that interventions successfully addressing these risk factors will have signif-

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icant impact on the prevalence of *Campylobacter* in broiler flocks. However, the significance of an effect is not the same as the size of the effect. In practice, in a specific country, the reduction in flock prevalence will also depend on the current prevalence in that country and on the percentage of farms in which the intervention is already implemented.

For risk management, the reduction of the population prevalence is important information, as quantitative microbiological risk assessment studies show that the public health risk for campylobacteriosis acquired through the consumption of chicken meat, is proportional to the flock prevalence (Rosenquist et al., 2003, Nauta et al., 2009, EFSA 2011). Furthermore, effects and costs of interventions are crucial information for risk managers. The population estimates and the number of involved farms found in this study were therefore used in the study of Van Wagenberg and co-workers to assess the cost-effectiveness of the interventions (Van Wagenberg et al., 2016b).

The translation of *Campylobacter* risk factors into estimated effects of interventions in terms of decrease in prevalence has to our knowledge never been published and no suitable method has been suggested. Development of a model for this translation will therefore be very useful for risk assessment and risk management.

The aim of the present study was therefore firstly to develop a method that allows a translation of a given risk factor obtained in an epidemiological study into a prediction of the reduction in flock prevalence (population prevalence) given implementation of an intervention based on this risk factor; and secondly to apply this method to the risk factors for *Campylobacter* colonization of broilers as identified in the CamCon project (Sommer et al., 2016) and assess the reduction in the population prevalence that might be obtained in the different countries if implementing a given intervention.

The method used to transform risk factor estimates (derived from a logistic regression) into predictions of population prevalences and further on to estimates of population prevalence reductions, is based on ideas behind model-based marginal standardization methods (Beckett et al., 1992, Greenland, 2004, Localio et al., 2006, Muller and MacLehose, 2014).

1.1. Methods

Using a model-based method will smooth the sampling group prevalence estimates. In this study, we standardized the population prevalences according to the margins of the variable *Country* and the standardization of the marginal population prevalences was performed not according to a confounder but according to country specific reference populations. Estimates of the reduction in the marginal population prevalence of 'before' and 'after' applying different interventions were performed.

Furthermore, in the logit scale marginal population prevalences were standardized according to a balanced experimental design. The purpose was to compare effects of categories (within a risk factor) adjusted for confounders, that is, to compare the effect levels conditioned on significant variables (confounders) in the model. This was carried out to define groups of categories within risk factors that could be used in forming interventions that significantly would lower the prevalence levels.

The method here applied includes (1) the definition of a reference population (needed for the marginal population estimate), (2) the definition of practical interventions from significant risk factors, and (3) estimation of the population prevalence values 'before' and 'after' interventions have been applied. All analyses and calculations were performed using the SAS software, version 9.14.

1.2. Data input to this study

Estimates on significant risk factors for colonization of broiler flocks with *Campylobacter* in the EU countries Denmark, Netherlands, Norway, Poland, Spain and United Kingdom were obtained from Sommer et al. (2016). Significant risk factors were identified by using a logistic regression model (Eq. 1):

$$\text{logit}(p) = \log\left(\frac{p}{1-p}\right) = \beta_0 + (\beta_1 + \beta_{2i})T + \sum_{r=3}^{11} \beta_r \quad (1)$$

where we have suppressed the indexes on the p 's and the β 's, which are described in the following. $p = p_{ijklmno}$ is the prevalence of *Campylobacter* defined as the estimate of the fraction of slaughtered flocks that were positive per month per farm, T is a continuous variable for the temperature, $\beta_1 T$ expresses a regression term and β_r expresses a categorical term, where $r = 3, 4, \dots, 11$. The parameters in the model (in the linear predictor) are:

- β_0 = intercept
- β_1 = Temperature (mean outdoor temperature in the month of growth)
- β_{2i} = Temperature \times Group, $i = 1, 2$ (Denmark and Norway had a higher regression coefficient than the rest)
- β_{3j} = Country, $j = 1, 2, 3, 4, 5, 6$ (Denmark, Spain, Netherlands, Norway, Poland, UK)
- β_{4k} = Age of house, $k = 1, 2, 3$ (age of broiler house; 0–5 years, 6–15 years, > 15 years)
- β_{5l} = Anteroom/barrier, $l = 1, 2$ (having anteroom and barrier in all houses at the farm, or not)
- β_{6m} = Tools, $m = 1, 2$ (having designated tools in each broiler house e.g. fork, spade, bucked, etc., or not)
- β_{7n} = Downtime, $n = 0, 1, 2, 3, 4$ (days between flocks in the broiler house; 0, 1–9, 10–19, 20–29, >30 days)
- β_{8o} = Drinkers, $o = 1, 2, 3$ (drinker system; nipples without cups, nipple with cups, bells)
- β_{9jk} = Country*Age of house, interaction term
- β_{10kl} = Age of house*Anteroom/barrier, interaction term
- β_{11km} = Age of house*Tools, interaction term

The data from Denmark and Norway constituted a considerable proportion of the entire farm populations (104/170.173/600, respectively) (Høg et al., 2011), but that was not the case for the other four countries where only about 20 farms participated (dataset A). To achieve a more representative population for each country more farms were included (dataset B) and thereby larger fractions of the populations of broiler farms within countries were achieved. When samples are used to generate estimates of the population prevalences statistical 'weights' may be applied to adjust for non-representativity.

The reference population was thus obtained from two datasets: dataset (A) with response values (*Campylobacter* status) plus information according to all the significant variables in the model (Sommer et al., 2016) and dataset (B) without the response values but with information on the model variables except for the variable 'mean temperature at growth' since no slaughtered flocks linked to these data (Høg et al., 2011). In dataset B information was available from approximately 200 farms in each of the following countries: Netherlands, Poland, Spain and United Kingdom. In order to be able to use dataset B, we needed to combine the frequency of numbers of observations (farms) in the population distribution with predicted prevalence estimates.

By a target population we understand a subset population of the reference population conditioned on a given variable e.g. *Country*. The estimates of uncertainty for the marginal population prevalence values were only based on dataset (A).

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