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The impacts of biosecurity measures on *Campylobacter* contamination in broiler houses and slaughterhouses in the Netherlands: A simulation modelling approach

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ABSTRACT

Intestinal campylobacteriosis, caused by *Campylobacter* ingestion, is the most reported zoonosis in the EU; it is societally costly and can lead to more severe sequelae. To reduce *Campylobacter* infections, biosecurity measures at both farms and slaughterhouses are warranted. However, the potential improvements achieved by these interventions have not been quantified. We used a systems science approach to develop a simulation model, synthesizing information from interviews with stakeholders in the Dutch broiler production industry and the current literature. The model includes both farms and slaughterhouses in a "system of systems," helping to clarify the complexity of interrelated components of these systems and analyse the impact of various interventions. Insects, transportation crates, farm personnel, and catchers were identified as potential *Campylobacter* sources and modelled as elements of feedback loops. Insect control, farm hygiene, visitor control, thinning, and transportation control interventions were analysed. The model was shown to accurately describe the seasonality of *Campylobacter*, which supports its validity. Model simulation revealed that insect control interventions had the strongest impacts, followed by combined farm hygiene and visitor control, and combined thinning and transportation control. Insect control interventions alone reduced the peak percentage of contaminated chickens from 51% to 26% and the peak percentage of highly contaminated (>1000 CFU/g) neck samples of chicken carcasses from 13% to 8%. Implementing all interventions concurrently reduced the peak percentages of contaminated chickens to 5% and highly contaminated chicken neck samples to 2%. These results suggest that multiple biosecurity measures must be implemented to reduce *Campylobacter* contamination.

1. Introduction

Campylobacteriosis is the most reported zoonosis in the European Union (EU). Campylobacteriosis infections made up 69% of confirmed human zoonosis cases in 2018 (EFSA, 2014; EFSA&ECDC, 2019), and there are approximately nine million zoonosis cases among EU residents each year at a cost of around 2.4 billion euros due to public health expenses and loss of productivity (EFSA&ECDC, 2013). In the Netherlands, the number of campylobacteriosis infections rose in both 2018 and 2019, peaking at nearly 73,000 estimated cases (Pijnacker et al., 2019).

Campylobacteriosis cases can be largely ascribed to poultry (EFSA&ECDC, 2021; Wagenaar et al., 2006). Approximately 60–80% of human campylobacteriosis cases in the Netherlands can be attributed to broiler chicken as a reservoir (Mughini-Gras et al., 2016). Chicken intestines provide ideal conditions for *Campylobacter* growth, reaching levels of around 10^9 colony forming units (CFU) per gram in the chicken caeca (Kuana et al., 2007). It is crucial to prevent *Campylobacter* from spreading on farms before it begins spreading throughout the food supply (Lin, 2009; Mbabazi, 2011; Sibanda et al., 2018). Despite substantial efforts from regulatory institutions, national authorities, and the poultry production industry to control the spreading, campylobacteriosis remains the zoonosis with the highest incidence in the EU

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(EFSA&ECDC, 2019).

The difficulty in controlling the spread of *Campylobacter* on chicken farms arises from the bacteria's transmission cycle complexity and a lack of understanding of the underlying mechanisms of *Campylobacter* spread on farms (Rawson et al., 2020; Sibanda et al., 2018; Wagenaar et al., 2006). Typical sources of *Campylobacter* on a conventional chicken farm include the environment (other animals, contaminated farm grounds, insects), humans (farmers and personnel, veterinarians, poultry catch crew, and other visitors), farm utensils and equipment (thinning (i.e., the removal of a proportion of the poultry from the rearing area to decrease crowding) equipment and other farm equipment), water (puddles, ditches, and mud), and other chicken flocks (Agunos et al., 2013; Hald et al., 2008; Hertogs et al., 2021; Sibanda et al., 2018). These sources are not mutually exclusive and differ across farms and seasons (Chowdhury et al., 2012; Djennad et al., 2019). *Campylobacter* infection rates peak during the summer months in Europe (Agunos et al., 2013; Newell et al., 2011; Rawson et al., 2020). Furthermore, *Campylobacter* infections in chickens are typically undetected because chickens do not show symptoms. As a result, it is difficult to predict and prevent *Campylobacter* infection at the animal level (Agunos et al., 2013; Sibanda et al., 2018).

The European Food Safety Authority (EFSA) estimates that the public health risk from the consumption of broiler meat could be reduced by more than 50% if chicken carcasses are limited to containing less than 1000 CFU/g of *Campylobacter* on neck and breast skin samples (EFSA BIOHAZ et al., 2020). Since January 1, 2018, the European Process Hygiene Criterium has been implemented for *Campylobacter*, requiring random testing and issuance of violations if more than 40% of the samples are positive (>1000 CFU/g) (EU Commission, 2005). This criterion is designed to become progressively stricter, reducing the proportion of allowed positive samples; the proportion of positive samples warranting a regulatory violation will drop to 20% by 2025 (Cuperus et al., 2020). Currently, *Campylobacter* concentrations on chicken skin in slaughterhouses are determined by using Part 2 of the ISO's "horizontal method for detection and enumeration of *Campylobacter* spp.," the colony-count technique (ISO, 2017), which takes at least three days to perform.

Various measures to control *Campylobacter* on chicken farms exist or are under development, such as those aiming at reduction of environmental exposure (e.g., biosecurity measures), increasing chickens' resistance to *Campylobacter* (e.g., vaccination), and methods to reduce and eliminate *Campylobacter* from colonized chickens (e.g., feed additives, bacteriophage therapy). However, their impact on transmission factors has not been systematically studied (EFSA BIOHAZ et al., 2020; Lin, 2009; Newell et al., 2011).

Existing research focuses on monitoring strategies and reactive interventions. There are only a few rigorous policy analyses with large sample sizes available for guidance (e.g. (EFSA BIOHAZ et al., 2020),). Additionally, current analyses observe or model the impact of various isolated sources and measures on *Campylobacter* contamination in chickens. However, they do not capture the system-wide issue of chicken contamination by modelling the transmission mechanisms. Examples of such research include measuring the impact of partial depopulation, i.e., flock thinning (Allen et al., 2008), insects' and rodents' impact on disease spread (Allain et al., 2014; Hald et al., 2004), the impact of ventilation systems (Romero-Barrios et al., 2013), presence of a separate anteroom or barrier in broiler houses (Høg et al., 2016), and acidification of drinking water and the use of antibiotics (Allain et al., 2014) on *Campylobacter* spread. Furthermore, current approaches in microbial risk analysis are based on Modular Process Risk Models (MPRM) (Nauta et al., 2012), where each step of the food chain is described using either kinetic or probabilistic models or both. Although useful, MPRM models are static and cannot easily incorporate dynamic characteristics (i.e., factors that change over time) such as seasonality, which is crucial to understand *Campylobacter* transmission (EFSA&ECDC, 2019).

To address this research gap, we use a systems approach to develop a system dynamics simulation model. These methods are commonly used in health policy and public health (e.g., (Jalali et al., 2019; Leerapan et al., 2021), however, there are few examples in food sciences (Horvat et al., 2019, 2020). System dynamics models can illustrate and quantify the complexity of a system of interrelated components, facilitate the communication of such complexity with various stakeholders (Horvat, Rommens, et al., 2021), and analyse the impact of various interventions in a simulation setting (Sterman, 2000). Our model aims to aid in 1) understanding the complex problem of *Campylobacter* prevalence on conventional Dutch broiler chicken farms, and 2) analysing the effects of various interventions to reduce the rates of *Campylobacter*-contaminated chickens.

2. Methods

2.1. Model conceptualization

To conceptualize our system dynamics (SD) model of *Campylobacter* incidence on Dutch poultry farms, semi-structured interviews were performed with different stakeholders in the poultry sector to understand the process of chicken meat production on farms and in slaughterhouses. We interviewed three farmers, two slaughterhouse employees, one poultry catcher, one veterinarian, one veterinary microbiologist performing research on the control of *Campylobacter* in the poultry industry in the Netherlands, one employee of the Dutch Ministry of Agriculture, Nature, and Food Quality, and one employee of the Dutch Ministry of Health, Welfare, and Sports. These initial interviews were summarized, and the information obtained was used to conceptualize the SD model. We report on the interview questions in the supplementary document.

2.2. Model formalisation

The model was formalised to represent conventional Dutch chicken farms and slaughterhouses. A typical flock cycle on a farm starts with each new flock arriving at the farm during the first week and living in a broiler house on the farm for six weeks. Chickens are typically not susceptible to *Campylobacter* colonization during their first two weeks in the broiler house (Battersby et al., 2016; Lin, 2009). By the fifth week, the thinning process takes place, during which a portion of the chickens are captured and transported to the slaughterhouse. The remaining chickens are transported to the slaughterhouse during week six. In week seven, the broiler house is cleaned and prepared for the new flock.

Parameter data for the model were obtained from literature and governmental reports (e.g., maximum development rate of insects (Damos & Savopoulou-Soultani, 2012) and life cycle duration of a conventional broiler flock on Dutch farms (Gibson & Compassion in World Farming., 2020; Neilson, 2016, pp. 2020–2029)), and interviews with five additional farmers. The remaining parameters were calibrated to real historical data obtained from the Nederlandse Pluimveeverwerkende Industrie (NEPLUVI, 2021), i.e., percentage of *Campylobacter*-infected chicken flocks delivered to slaughterhouses and percentage of chicken carcass neck samples with more than 1000 CFU/g of *Campylobacter*. To facilitate transparency and reproducibility of our simulation analysis (Jalali et al., 2021), all data and model files are included in the supplementary material.

2.3. Model testing

Model testing included model verification and validation based on guidelines set by (Barlas, 1996; Sterman, 2000). Model testing included empirical structure verification through expert interviews with five scientists who are experienced on the topic of *Campylobacter* incidence in broiler chicken on farms and in slaughterhouses to validate the structure of the conceptualised model. These interviewees were shown various parts of the model and were asked to state their opinion on

whether the model represents the *Campylobacter* spread on chicken farms and in slaughterhouses well, and if not, to give suggestions for improvement. The model structure was further modified based on their suggestions. Model testing also involved inspecting the variable equations and unit consistency as well as extreme conditions testing. Moreover, sensitivity analysis was conducted by varying the parameters used to test potential interventions by 20% of their baseline value in either direction. Varying these parameters allowed us to assess the sensitivity of parameters for which the literature, empirical data, and interview data were heterogeneous and thus uncertain to our proposed interventions.

2.4. Model analysis

We explored three intervention portfolios of biosecurity measures (see Table 1). The value of each parameter has a range from zero to one, with a baseline value informed by literature or by model calibration, and their intervention values were set at either 0.9 or 0.1 to represent an increase (or decrease) of a given parameter to its highest (or lowest) plausible value. The main model outcomes included the percentages of *Campylobacter*-positive chickens delivered to the slaughterhouse and of *Campylobacter*-positive chicken carcass neck samples. Because the main dynamic behaviours happen in seasonal cycles and as there is a lack of evidence for major long-term trend changes, we considered two years in our projections. Model analysis was performed using Vensim DSS (version 8.2.1). All Vensim files are included in the supplementary document. We also designed an online, interactive platform to run the model without any software requirements. This online model interface is available at: mj-lab.mgh.harvard.edu/campydynamics. An earlier version of this model (Horvat, Rommens, et al., 2021) was presented at a modeling conference for the purpose of collecting feedback on model structure and analysis.

3. Results

3.1. Model conceptualization

In this section, we describe the structure of the model, which was used to study the impact of biosecurity measures on *Campylobacter* contamination in Dutch broiler houses and slaughterhouses. Fig. 1-A shows the overall process flow of the model. The flow (i.e., transition) *chickens arriving at broiler houses* represents the entrance of chickens to the farm and into the stock (i.e., state) of *Campylobacter negative chickens in broiler houses*. Vertical transmission (passage from the hen to her chicks via the egg) is considered to be a rare event (Callicott et al., 2006). However, the chickens in the broiler houses may come into contact with *Campylobacter* in the course of the production cycle and become colonized through a flow of *chickens getting colonized in broiler houses*, leading to a *Campylobacter* positive flock, which is shown in the model as *Campylobacter positive chickens in broiler houses*. The probability that the chickens will be colonized with *Campylobacter* in broiler houses depends on the probability of chickens getting into contact with *Campylobacter*-carrying insects, equipment/utensils, and humans on the farm. An additional flow that may lead to *Campylobacter* positive chickens in broiler houses is *chickens getting colonized after thinning*. These represent only a limited number of factors and other transmission routes can also play a role, such as air, drinking water, and rodents. We prioritized focusing on these factors based on stakeholder interviews, data availability, and other resources.

Next, a percentage of the chicken flock will undergo thinning and be transported to the slaughterhouse in week 5, while the remaining chickens at the farm will continue to grow until they are transported to slaughterhouses in week 6 (i.e., represented with flows *transporting Campylobacter negative chickens* and *transporting Campylobacter positive chickens*). The chickens that arrive at the slaughterhouse, which are either *Campylobacter* negative or positive, are represented with two stocks, i.e., *Campylobacter negative chickens in the slaughterhouse* and *Campylobacter positive chickens in the slaughterhouse*.

Chicken flocks are slaughtered in the order of their arrival at the slaughterhouse. Therefore, when a positive flock arrives at the slaughterhouse, they will be slaughtered first and may contaminate the slaughtering equipment with *Campylobacter*. Consequently, some uninfected chickens can become contaminated through cross-contamination by equipment, represented as *probability of contamination during slaughtering* (see Campynamics model.vmfx in the supplementary material). On the other hand, if the slaughtering process is executed in strict accordance with hygienic slaughtering practices, neck samples of chicken carcasses from *Campylobacter*-positive chickens can be *Campylobacter*-negative after slaughtering.

Fig. 1-B displays four feedback mechanisms that may contribute to *Campylobacter*-colonized chickens—these feedback mechanisms affect the flows between stocks shown in Fig. 1-A. Feedback loop R1 represents the colonization of *Campylobacter* in chickens through bacteria-carrying insects on the farm. *Campylobacter* negative insects can come into contact with *Campylobacter* via chicken faeces and carcasses, from environmental sources or other animals present on or around the farm. Insects that carry *Campylobacter* may enter the broiler house through various openings (e.g., ventilation, cracks in the walls, doors) and may transmit *Campylobacter* either mechanically or by being eaten by the chicken. Because *Campylobacter* multiplies in the chicken intestines to very high amounts, a *Campylobacter* positive flock may lead to contamination of the direct environment, including insects that may spread the bacterial infection to other chicken houses.

Feedback loop R2 shows that farmers and visitors can also transmit *Campylobacter* to chickens, which occurs if they bring the bacteria into the broiler house (e.g., by contaminated shoes or boots by walking through mud and puddles on the farm, by bringing in contaminated tools from outside the broiler house including other broiler houses on the farm) or through contaminated clothes and hands. The more *Campylobacter*-positive chickens present on the farm, the higher the

Table 1
List of analysis portfolios and parameters.

Intervention Portfolios	Interventions	Model parameters[a]	Baseline value (±20%)[b]	Intervention value
Insect control	1. Eliminate insect entry through ventilation when ventilation is on	probability of flies' ability to enter broiler houses when ventilation is working	0.8 (0.64–0.96)	0.1
	2. Eliminate insect entry through other openings	probability of insects entering broiler houses through other openings	0.8 (0.64–0.96)	0.1
Thinning and transportation control	3. Maximum catcher hygiene	probability of catchers to follow hygiene protocols	0.6 (0.48–0.72)	0.9
	4. Maximum crate cleaning	probability of cleaning the crates adequately	0.6 (0.48–0.72)	0.9
Farm hygiene and visitor control	5. Maximize farm hygiene	level of farm environment hygiene	0.7 (0.56–0.84)	0.9
	6. Maximum human awareness of hygiene protocols	human awareness personality traits	0.7 (0.56–0.84)	0.9

[a] All parameters have a range of zero to one.
[b] Each baseline parameter was changed ±20% for sensitivity analysis.

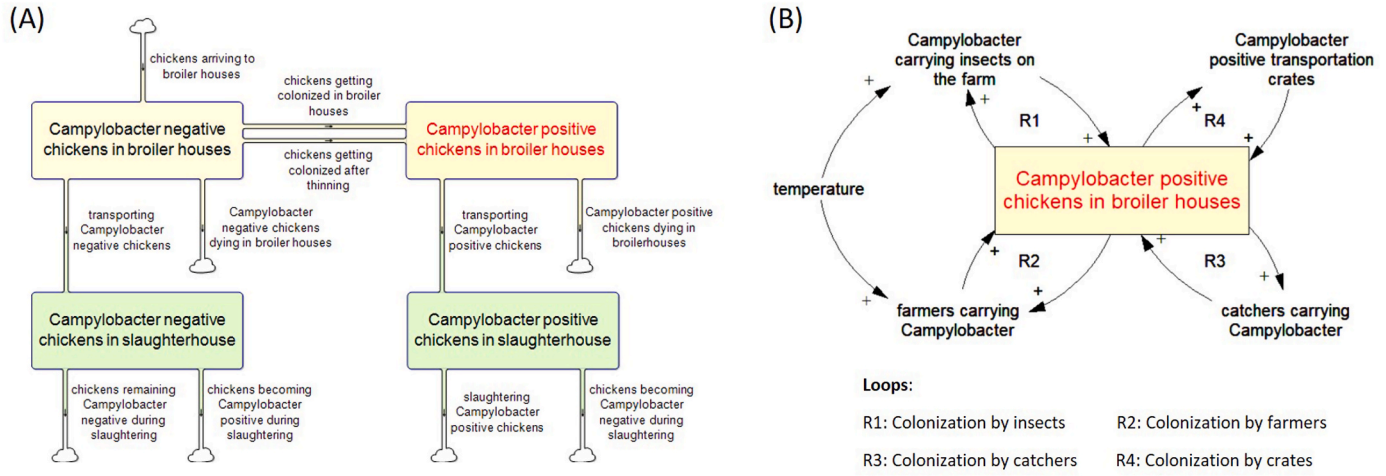

Fig. 1. Simplified presentation of the model, including broiler houses (yellow) and slaughterhouse (green). A) Stock and flow structure of the model. B) Main feedback loops in the model.

probability that the farmer will carry *Campylobacter* to another broiler house if multiple houses exist on the farm.

Feedback loop R3 concerns the thinning process through which poultry catchers can transmit *Campylobacter* from one farm to another. Therefore, the more farms with *Campylobacter*-positive chickens that catchers visit during one working day, the higher the probability that they might contaminate *Campylobacter*-negative chickens on another farm.

Feedback loop R4 shows that transportation crates are also a possible fomite of *Campylobacter* contamination. *Campylobacter*-positive chickens will contaminate crates with *Campylobacter* during transportation from the farm to the slaughterhouse. Since the washing and disinfection process of crates in the slaughterhouse may not be sufficient to eliminate all bacteria, they may become a reservoir of *Campylobacter*.

Finally, the temperature affects both farmers and insects. Higher temperatures in spring and summer lead to a higher development rate of insects, which slows down in the autumn and winter months. Similarly, farmers in the Netherlands generally visit the broiler houses more frequently in warmer months to check for heat stress and adjust the ventilation if needed.

3.2. Model analysis

3.2.1. Baseline scenario

In the baseline historical scenario, which was simulated based on the parameter values listed in Table 1 and the supplementary material, 60% of chickens arriving at the slaughterhouse are *Campylobacter* positive at the peak. At the peak, 15% of chicken carcass neck samples are contaminated with levels >1000 CFU/g. Fig. 2 shows the fit to historical data. In the baseline projected scenario, the peak percentages of chickens arriving that were *Campylobacter* positive and of the contaminated chicken neck samples were 51.1% and 13.4%, respectively.

3.2.2. Intervention analysis

We analysed two outcome measures: the percentage of *Campylobacter*-positive chickens arriving at the slaughterhouse and chicken carcass neck samples with >1000 CFU/g of *Campylobacter*. Fig. 3 presents these simulated outcomes for the various combined intervention portfolios projected over two years. Overall, the insect control portfolio offered the strongest reduction to the peaks of both outcome measures, followed by the farm hygiene and visitor control portfolio. Enacting each of these portfolios in the model reduces the rate of chickens being colonized in broiler houses, which in turn slows the transition of *Campylobacter*-negative chickens becoming *Campylobacter* positive. The thinning and transportation control portfolio offered the lowest reduction in both outcomes; enacting this portfolio reduces the rate of chickens getting colonized after thinning, and only one-sixth of the chickens undergo thinning each cycle. Therefore, the relatively low impact of the thinning and transportation control portfolio may be explained at least in part by the reduced number of chickens affected at once compared to the other two portfolios. Thinning does outperform the farm hygiene portfolio from roughly December to June; while the

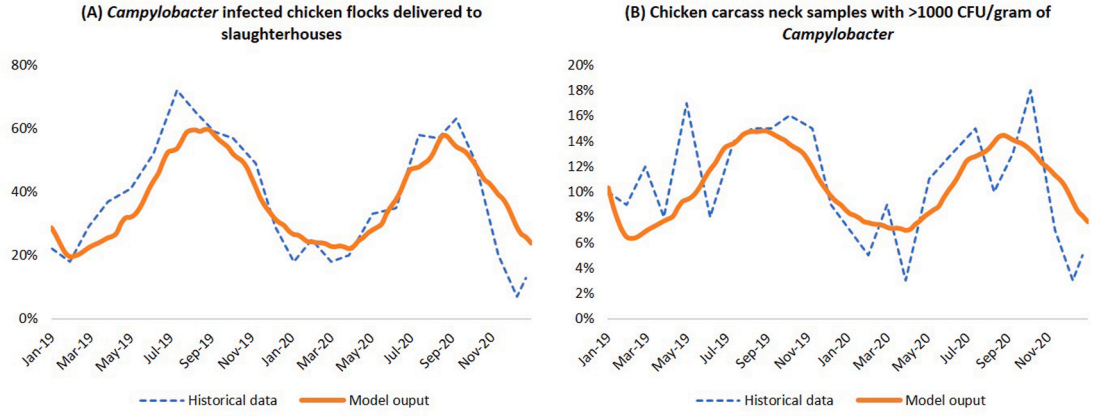

Fig. 2. Model output fit to historical data at baseline of A) *Campylobacter*-infected flocks delivered to slaughterhouses; and B) chicken carcass neck samples with more than 1000 CFU/g of *Campylobacter* in the Netherlands, 2019–2020 (Nederlandse Pluimveeverwerkende Industrie (NEPLUVI), 2021).

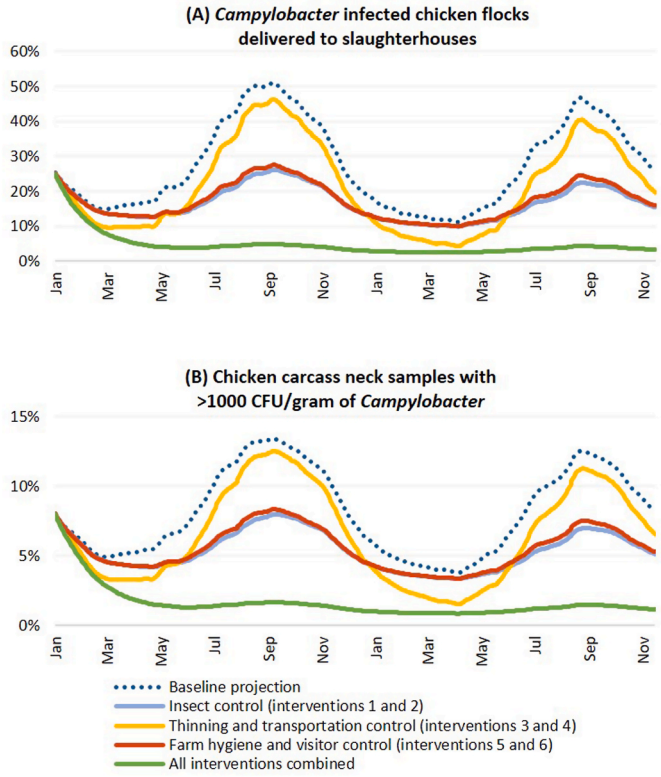

Fig. 3. Modelled projection results of the intervention portfolios analysis showing percentages of (A) Campylobacter positive chickens arriving at the slaughterhouse and (B) Chicken carcass neck samples with >1000 CFU/g of Campylobacter.

other two portfolios are mitigated by the weather (e.g., there are more insects in the summer), the thinning and transportation control processes are independent of the season.

Table 2 presents the minimum, maximum, and average of the two outcome measures. We calculated these values starting at four months after the change in parameter to capture the full effect of the interventions. Given that a high percentage of both outcome measures over the summertime could be concerning, we particularly focused on maximum values.

At maximum, 26.2% of chickens arriving at the slaughterhouse were *Campylobacter*-positive in the insect control portfolio, 27.5% were positive in the farm hygiene and visitor control portfolio, and 46.3% were positive in the thinning and transportation control portfolio. When all portfolios are enacted at once, a maximum of 4.9% of chickens arriving at the slaughterhouse were infected with *Campylobacter*, as compared to 51.1% at baseline.

Similarly, at maximum, 8% of chicken carcass neck samples were contaminated with *Campylobacter* in the insect control portfolio, 8.4% were contaminated in the farm hygiene and visitor control portfolio, and 12.5% were contaminated in the thinning and transportation control portfolio. When all portfolios are enacted, 1.7% of chicken carcass neck samples were contaminated with *Campylobacter*, as compared to 13.4% at baseline.

4. Discussion

The current study aimed at understanding the complex dynamics of *Campylobacter* in chickens and the environment using a simulation model. We found that multiple interventions must be implemented in combination to control the spread of *Campylobacter* and reduce the incidence of *Campylobacter* infection; single interventions do not offer a meaningful reduction in *Campylobacter* levels (see Fig. 3 and Table 2).

We built upon prior work on individual measures of *Campylobacter* reduction in the primary production of broiler chickens, which was predominantly focused on modelling parts of the *Campylobacter* contamination problem in isolation (e.g., (EFSA BIOHAZ et al., 2020; EFSA Panel on Biological Hazards, 2012). In our model, we combined four commonly reported mechanisms, i.e., carryover of *Campylobacter* by insects, farmers, thinning transportation crates, and catchers. The model structure could replicate the historical data on the percentage of infected chickens arriving at slaughterhouses and on the percentage of contaminated neck samples of chicken carcasses (see Fig. 2). We also developed an interactive model interface for readers to simulate and test interventions (https://mj-lab.mgh.harvard.edu/campydynamics).

Employing system dynamics allowed us to engage field experts in model development, represent data trends such as the seasonal oscillation of *Campylobacter* contamination, and explore the impact of measures over time, which is not commonly reported, e.g., (Mughini-Gras et al., 2016; Nauta et al., 2005). Importantly, it allowed us to incorporate feedback mechanisms that are essential to study complex systems (Jalali et al., 2017). We explored various intervention scenarios that, if enacted, could sustain reduced *Campylobacter* contamination over time.

We observed that interventions to prevent insects from entering broiler houses demonstrated the largest relative reduction in the percentage of infected chicken and contaminated neck samples of chicken carcasses (see Fig. 3 and Table 2). Insect control by introducing flyscreens has been previously reported as highly effective in reducing the risk of *Campylobacter* colonization in chickens (Bahrndorff et al., 2013; EFSA BIOHAZ, 2011; Hald et al., 2007).

Interventions to control farm hygiene and visitors from entering the broiler house reduce *Campylobacter* to a similar extent as interventions aimed at insects, according to our model (see Fig. 3 and Table 2). Other work also found that combined farm hygiene measures, such as

Table 2
Simulation results, comparing baseline with six interventions and their combinations.

Scenarios		*Campylobacter* infected chicken flocks delivered to slaughterhouses			Chicken carcass neck samples with >1000 CFU/g of *Campylobacter*		
		minimum	maximum	average	minimum	maximum	average
Baseline		11.2%	51.1%	29.8%	3.8%	13.4%	8.7%
Insect control	1. Eliminate insect entry through ventilation when ventilation is on	10.8%	42.4%	25.3%	3.7%	11.8%	7.7%
	2. Eliminate insect entry through other openings	10.3%	39.3%	22.8%	3.5%	11.1%	7.0%
	Interventions 1 and 2 combined	9.9%	26.2%	16.9%	3.4%	8.0%	5.4%
Thinning and transportation control	3. Maximum catcher hygiene	4.7%	47.5%	24.2%	1.7%	12.8%	7.2%
	4. Maximum crate cleaning	10.6%	50.0%	28.8%	3.6%	13.2%	8.5%
	Interventions 3 and 4 combined	4.3%	46.3%	23.3%	1.5%	12.5%	7.0%
Farm hygiene and visitor control	5. Maximize farm hygiene	10.2%	33.5%	20.3%	3.5%	9.8%	6.4%
	6. Maximum human awareness of hygiene protocols	11.0%	45.9%	27.2%	3.7%	12.5%	8.1%
	Interventions 5 and 6 combined	10.0%	27.5%	17.6%	3.4%	8.4%	5.6%
All interventions combined		2.5%	4.9%	3.6%	0.9%	1.7%	1.2%

personnel hygiene and broiler house disinfection, decreased *Campylobacter* prevalence to below 40% (Gibbens et al., 2001).

Modelled interventions that focused on the strictness of catchers during thinning and hygiene of transportation crates revealed smaller overall reductions in the number of contaminated chickens and the number of contaminated neck samples, compared to the other two interventions (see Fig. 3 and Table 2). It should be noted that these interventions have the greatest relative percentage reduction during the wintertime, but their effects across the rest of the year are small. These small effects may be due to the sub-model structure of the thinning process, which only accounts for risks associated with catchers' hygiene and hygiene of transportation crates and ultimately results in a small probability that chickens will be colonized after the thinning process is complete. During the thinning process, other factors may be relevant, including the possibility of insects and other animals entering through open doors and the size of the crew (Newell et al., 2011). However, these other factors may have varying effects. While some research indicates a relationship between thinning and *Campylobacter* prevalence (e.g. (Hald et al., 2001),), Russa et al. (2005) found no association between thinning and colonization of chickens in the Netherlands.

Finally, the largest reduction was observed when all interventions were simulated at the same time, indicating that one measure alone is not enough to prevent the occurrence of *Campylobacter* contaminated chickens. Given that *Campylobacter* colonization in broiler chickens arises from a combination of multiple behaviours and factors (Newell et al., 2011), multiple measures to address this public health threat are warranted.

This work is subject to several limitations. First, we focused on the Netherlands, and the dynamics of *Campylobacter* colonization may be different in other countries (CORDIS, 2016; EFSA, 2010). Additionally, we only model conventionally raised chickens; other slower-growing breeds and free-range chickens are slaughtered at a higher age and do not have a thinning process (van Horne, 2020). Therefore, the mechanisms in the model structure might have to be adjusted to study other ways of growing chickens. Further, the model parameters are based on limited data. Based on the interviews with different stakeholders, assumptions were made for the values of various model parameters, as documented in the supplementary document. These uncertain data can lead to uncertain results for the percentage of contaminated chickens arriving at slaughterhouses and the levels of *Campylobacter* on neck samples of chicken carcasses, especially in the minimum and maximum values. Therefore, we strongly recommend readers focus on the comparison results and simulated trends rather than focusing on exact numbers. Additionally, the assumption is made that when one chicken is infected, the whole flock will be infected (Lin, 2009). These infection rates pertain to the individual chickens, but the infection probabilities in the broiler house and after thinning are employed as a probability for the entire flock getting infected. Also, a chicken is assumed to be either *Campylobacter* positive or negative. Moreover, amounts of *Campylobacter* on chicken samples are expressed in CFU/gram. According to the Process Hygiene Criterion (EU Commission, 2017), when chicken carcasses are contaminated with less than 1000 CFU/g after chilling, the test results are interpreted as satisfactory. More in-depth details about these numbers were not represented in the model due to reporting practices and the specific concentration of *Campylobacter* per gram of chicken was not estimated.

Given that the current model represents feedback mechanisms of *Campylobacter* occurrence in chickens on Dutch farms and a limited number of measures, more sophisticated models can be developed by including other relevant mechanisms and measures. For example, while we considered the environment on the farm, we did not consider potential environmental factors beyond farm grounds such as the proximity of other farms and surface water (e.g., lakes and rivers), and other animals such as wild birds and rodents. Potential relationships between environmental hygiene, proximity, and corresponding impacts on *Campylobacter* spread on the farm are factors that can be added to the model and could be explored in future research. Moreover, in the current model we represented *Campylobacter* spp. although different strains of *Campylobacter* exist, i.e., *C. jejuni* and *C. coli* (Eberle & Kiess, 2012). Different strains can differ in host specificity and in survival under various circumstances, which can ultimately impact the risk for human infections. To determine their phenotypic characteristics including host specificity and pathogenicity, and transmission routes of different strains, advanced and standardised genotyping methods are required, such as multilocus sequence typing (MLST) and whole genome sequencing (WGS) (Eberle & Kiess, 2012; Llarena et al., 2017). MLST results can be reproduced but the technique is complex and expensive to perform (Eberle & Kiess, 2012). Although WGS for pathogens is becoming more and more common, it is not yet routinely performed (Llarena et al., 2017). In the future, it could be of added value to include genotyping results in the model, however, the requirements to do so (i.e., having sufficient data and knowledge on the different behaviour of various strains) are not yet feasible. Furthermore, other broiler production concepts, such as organic and free-range and other countries could be studied. Additionally, the introduction of new technologies, e.g., on-site biosensors (Givanoudi et al., 2021), to test for *Campylobacter* presence may allow farmers to better monitor the status of their farms and implement additional decontamination measures as needed. Also, since the ultimate goal of *Campylobacter* reduction in chickens is to reduce the incidence of gastrointestinal illness in humans in the Netherlands and other countries, a model that incorporates Campylobacteriosis occurrence in humans could be developed. Finally, given the numerous measures that can be undertaken and resource limitations for intervention implementation, a cost-benefit analysis could be performed to identify particularly effective and efficient measures for farmers and other actors in the chicken production food chain. The system dynamics approach was shown to successfully reproduce actual data (including the seasonality), even with a limited number of portfolios. This model may be developed further to improve its accuracy, and its structure may be applied to analyse contexts outside of the Netherlands with appropriate adjustments to the underlying data to correspond with the country of interest.

5. Conclusions

Campylobacter contamination in broiler chickens does not arise from a single factor, but rather the combination of multiple factors both at farms and in slaughterhouses. This interconnectedness within the system is reflected in the relatively modest reduction in colonized chickens and contaminated chicken carcass neck samples when one biosecurity measure is enacted, in contrast to the reductions achieved by combining measures into more comprehensive portfolios.

The utility of the system dynamics approach to studying *Campylobacter* contamination in chickens lies in its possibility to combine various risk factors and feedback loop structures, and to include both farms and slaughterhouses in a single model. This model will generate insight in the complexity of *Campylobacter* ecology and provide farmers, slaughterhouses and policy makers with educated estimates on the efficiency of various (combinations of) interventions, with the ultimate goal of reducing *Campylobacter* cases in humans.

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CRediT authorship contribution statement

Andrijana Horvat: Conceptualization, Methodology, Validation, Investigation, Writing – original draft, Writing – review & editing, Supervision, Project administration, Funding acquisition. **Pieternel A. Luning:** Conceptualization, Writing – review & editing, Funding

acquisition. **Catherine DiGennaro:** Methodology, Validation, Data curation, Investigation, Visualization, Writing – review & editing. **Edien Rommens:** Conceptualization, Methodology, Investigation. **Els van Daalen:** Methodology, Writing – review & editing, Supervision. **Miriam Koene:** Writing – review & editing, Resources. **Mohammad S. Jalali:** Conceptualization, Methodology, Validation, Investigation, Writing – review & editing, Supervision.

Declaration of competing interest

None.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.foodcont.2022.109151.

References

Agunos, A., Léger, D., Avery, B. P., Parmley, E. J., Deckert, A., Carson, C. A., & Dutil, L. (2013). Ciprofloxacin-resistant *Campylobacter spp*. in retail chicken, Western Canada. *Emerging Infectious Diseases, 19*(7), 1121–1124. https://doi.org/10.3201/eid1907.111417

Allain, V., Chemaly, M., Laisney, M., Rouxel, S., Quesne, S., & Le Bouquin, S. (2014). Prevalence of and risk factors for *Campylobacter* colonisation in broiler flocks at the end of the rearing period in France. *British Poultry Science, 55*(4), 452–459. https://doi.org/10.1080/00071668.2014.941788

Allen, V., Weaver, H., Ridley, A., Harris, J., Sharma, M., Emery, J., Sparks, N., Lewis, M., & Edge, S. (2008). Sources and spread of thermophilic *Campylobacter spp*. during partial depopulation of broiler chicken flocks. *Journal of Food Protection, 71*(2), 264–270. https://doi.org/10.4315/0362-028x-71.2.264

Bahrndorff, S., Rangstrup-Christensen, L., Nordentoft, S., & Hald, B. (2013). Foodborne disease prevention and broiler chickens with reduced *Campylobacter* infection. *Emerging Infectious Diseases, 19*(3), 425. https://doi.org/10.3201/eid1903.111593

Barlas, Y. (1996). Formal aspects of model validity and validation in system dynamics. *System Dynamics Review: The Journal of the System Dynamics Society, 12*(3), 183–210. https://doi.org/10.1002/(SICI)1099-1727(199623)12:3<183::AID-SDR103>3.0.CO;2-4

Battersby, T., Whyte, P., & Bolton, D. (2016). The pattern of *Campylobacter* contamination on broiler farms; external and internal sources. *Journal of Applied Microbiology, 120*(4), 1108–1118. https://doi.org/10.1111/jam.13066

Callicott, K. A., Friðriksdóttir, V., Reiersen, J., Lowman, R., Bisaillon, J.-R., Gunnarsson, E., Berndtson, E., Hiett, K. L., Needleman, D. S., & Stern, N. J. (2006). Lack of evidence for vertical transmission of *Campylobacter spp*. in chickens. *Applied and Environmental Microbiology, 72*(9), 5794–5798. https://doi.org/10.1128/AEM.02991-05

Chowdhury, S., Sandberg, M., Themudo, G., & Ersbøll, A. (2012). Risk factors for *Campylobacter* infection in Danish broiler chickens. *Poultry Science, 91*(10), 2701–2709. https://doi.org/10.3382/ps.2012-02412

CORDIS. (2016). *Final Report Summary - CAMCON (Campylobacter control - novel approaches in primary poultry production)*. https://cordis.europa.eu/project/id/244547/reporting.

Cuperus, T., Opsteegh, M., Wit, B., Gijsbers, E., Dierikx, C., Hengeveld, P., Dam, C., van Hoek, A., & van der Giessen, J. (2020). *Surveillance zoönosen in vleeskuikens 2018-2019*. https://doi.org/10.21945/RIVM-2020-0073

Damos, P., & Savopoulou-Soultani, M. (2012). Temperature-driven models for insect development and vital thermal requirements. *Psyche: Journal of Entomology*. , Article 123405. https://doi.org/10.1155/2012/123405, 2012.

Djennad, A., Iacono, G. L., Sarran, C., Lane, C., Elson, R., Höser, C., Lake, I. R., Colón-González, F. J., Kovats, S., & Semenza, J. C. (2019). Seasonality and the effects of weather on *Campylobacter* infections. *BMC Infectious Diseases, 19*(1), 1–10. https://doi.org/10.1186/s12879-019-3840-7

Eberle, K. N., & Kiess, A. S. (2012). Phenotypic and genotypic methods for typing *Campylobacter jejuni* and *Campylobacter coli* in poultry. *Poultry Science, 91*(1), 255–264. https://doi.org/10.3382/ps.2011-01414

EFSA. (2010). Analysis of the baseline survey on the prevalence of *Campylobacter* in broiler batches and of *Campylobacter* and Salmonella on broiler carcasses, in the EU, 2008-Part A: *Campylobacter* and Salmonella prevalence estimates. *EFSA Journal, 8*(3), 1503. https://doi.org/10.2903/j.efsa.2010.1522

EFSA. (2014). *EFSA explains zoonotic diseases: Campylobacter*. https://www.efsa.europa.eu/sites/default/files/corporate_publications/files/factsheetcampylobacter.pdf.

EFSA BIOHAZ. (2011). Scientific opinion on *Campylobacter* in broiler meat production: Control options and performance objectives and/or targets at different stages of the food chain. *EFSA Journal, 9*(4), 2105. https://doi.org/10.2903/j.efsa.2011.2105

EFSA BIOHAZ, Koutsoumanis, K., Allende, A., Alvarez-Ordóñez, A., Bolton, D., Bover-Cid, S., … Hilbert, F. (2020). Update and review of control options for Campylobacter in broilers at primary production. *EFSA Journal, 18*(4), Article e06090. https://doi.org/10.2903/j.efsa.2020.6090

EFSA Panel on Biological Hazards. (2012). Scientific Opinion on the development of a risk ranking framework on biological hazards. *EFSA Journal, 10*(6), 2724.

EFSA, & ECDC. (2013). The European Union summary report on trends and sources of zoonoses, zoonotic agents and food-borne outbreaks in 2011. *EFSA Journal, 11*(4), 3129. https://doi.org/10.2903/j.efsa.2013.3129

EFSA, & ECDC. (2019). The European union one health 2018 zoonoses report. *EFSA Journal, 17*(12), Article e05926. https://doi.org/10.2903/j.efsa.2019.5926

EFSA, & ECDC. (2021). The European union one health 2019 zoonoses report. *EFSA Journal, 19*(2), Article e06406. https://doi.org/10.2903/j.efsa.2021.6406

EU Commission. (2005). Commission Regulation (EC) No 2073/2005 of 15 November 2005 on microbiological criteria for foodstuffs. *Official Journal of the European Union, 338*, 1–26. https://eur-lex.europa.eu/eli/reg/2005/2073/oj.

EU Commission. (2017). Commission Regulation (EU) 2017/1495 https://eur-lex.europa.eu/legal-content/EN/TXT/HTML/?uri=CELEX:32017R1495&from=EN.

Gibbens, J., Pascoe, S., Evans, S., Davies, R., & Sayers, A. (2001). A trial of biosecurity as a means to control *Campylobacter* infection of broiler chickens. *Preventive Veterinary Medicine, 48*(2), 85–99. https://doi.org/10.1016/s0167-5877(00)00189-6

Gibson, R., & Compassion in World Farming.. (2020). *Dutch slower growing chickens require less antibiotics than fast growing chickens*. https://www.ciwf.org.uk/media/7438137/dutch-slower-growing-broilers-require-less-antibiotics-than-fast-growing-chickens.pdf.

Givanoudi, S., Cornelis, P., Rasschaert, G., Wackers, G., Iken, H., Rolka, D., Yongabi, D., Robbens, J., Schöning, M. J., Heyndrickx, M., & Wagner, P. (2021). Selective *Campylobacter* detection and quantification in poultry: A sensor tool for detecting the cause of a common zoonosis at its source. *Sensors and Actuators B: Chemical, 332*, Article 129484. https://doi.org/10.1016/j.snb.2021.129484

Hald, B., Rattenborg, E., & Madsen, M. (2001). Role of batch depletion of broiler houses on the occurrence of *Campylobacter spp*. in chicken flocks. *Letters in Applied Microbiology, 32*(4), 253–256. https://doi.org/10.1046/j.1472-765X.2001.00896.x

Hald, B., Skovgård, H., Bang, D. D., Pedersen, K., Dybdahl, J., Jespersen, J. B., & Madsen, M. (2004). Flies and *Campylobacter* infection of broiler flocks. *Emerging Infectious Diseases, 10*(8), 1490. https://doi.org/10.3201/eid1008.040129

Hald, B., Skovgård, H., Pedersen, K., & Bunkenborg, H. (2008). Influxed insects as vectors for *Campylobacter jejuni* and *Campylobacter coli* in Danish broiler houses. *Poultry Science, 87*(7), 1428–1434. https://doi.org/10.3382/ps.2007-00301

Hald, B., Sommer, H. M., & Skovgård, H. (2007). Use of fly screens to reduce *Campylobacter spp*. introduction in broiler houses. *Emerging Infectious Diseases, 13*(12), 1951. https://doi.org/10.3201/eid1312.070488

Hertogs, K., Haegeman, A., Schaumont, D., Gelaude, P., De Zutter, L., Dewulf, J., Heyndrickx, M., & Rasschaert, G. (2021). Contamination sources and transmission routes for *Campylobacter* on (mixed) broiler farms in Belgium, and comparison of the gut microbiota of flocks colonized and uncolonized with *Campylobacter*. *Pathogens, 10*(1), 66. https://doi.org/10.3390/pathogens10010066

Høg, B. B., Sommer, H. M., Larsen, L. S., Sørensen, A. I. V., David, B., Hofshagen, M., & Rosenquist, H. (2016). Farm specific risk factors for *Campylobacter* colonisation in Danish and Norwegian broilers. *Preventive Veterinary Medicine, 130*, 137–145. https://doi.org/10.1016/j.prevetmed.2016.04.002

van Horne, P. (2020). *Economics of broiler production systems in The Netherlands: Economic aspects within the Greenwell sustainability assessment model*. Wageningen Economic Research.

Horvat, A., Bartelet, H. A., Andersen, D. F., Behdani, B., & Luning, P. A. (2021). Uncovering causes of stagnating product sales of a healthy snack: A system dynamics group model building project in a food processing company. *Journal of the Operational Research Society*, 1–15. https://doi.org/10.1080/01605682.2021.1924089

Horvat, A., Behdani, B., Fogliano, V., & Luning, P. A. (2019). A systems approach to dynamic performance assessment in new food product development. *Trends in Food Science & Technology, 91*, 330–338. https://doi.org/10.1016/j.tifs.2019.07.036

Horvat, A., Fogliano, V., & Luning, P. A. (2020). Modifying the Bass diffusion model to study adoption of radical new foods-The case of edible insects in The Netherlands. *PLoS One, 15*(6), Article e0234538. https://doi.org/10.1371/journal.pone.0234538

Horvat, A., Rommens, E., DiGennaro, C., C Vandaalen, C., Luning, P. A., & Jalali, M. S. (2021). A model for Campylobacter contamination in chicken meat production systems. In *International system dynamics conference, virtual*.

ISO. (2017). *6579-1: 2017 microbiology of the food chain—horizontal method for the detection, enumeration and serotyping of Salmonella—Part 1: Detection of Salmonella spp*. Geneva, Switzerland: International Organization for Standardization.

Jalali, M. S., DiGennaro, C., Guitar, A., Lew, K., & Rahmandad, H. (2021). Evolution and reproducibility of simulation modeling in epidemiology and health policy over half a century. *Epidemiologic Reviews*. https://doi.org/10.1093/epirev/mxab006

Jalali, M. S., Rahmandad, H., Bullock, S. L., & Ammerman, A. (2017). Dynamics of implementation and maintenance of organizational health interventions. *International Journal of Environmental Research and Public Health, 14*(8). https://doi.org/10.3390/ijerph14080917

Jalali, M. S., Rahmandad, H., Bullock, S. L., Lee-Kwan, S. H., Gittelsohn, J., & Ammerman, A. (2019). Dynamics of intervention adoption, implementation, and maintenance inside organizations: The case of an obesity prevention initiative. *Social Science & Medicine, 224*, 67–76. https://doi.org/10.1016/j.socscimed.2018.12.021

Kuana, S. L., Santos, L., Rodrigues, L., Borsoi, A., Moraes, H. L.d. S., Salle, C. T. P., & Nascimento, V. P.d. (2007). Risk factors and likelihood of *Campylobacter* colonization in broiler flocks. *Brazilian Journal of Poultry Science, 9*(3), 201–204. https://doi.org/10.1590/S1516-635X2007000300010

Leerapan, B., Kaewkamjornchai, P., Atun, R., & Jalali, M. S. (2021). How systems respond to policies: Intended and unintended consequences of COVID-19 lockdown policies in Thailand. *Health Policy and Planning*. https://doi.org/10.1093/heapol/czab103

Lin, J. (2009). Novel approaches for *Campylobacter* control in poultry. *Foodborne Pathogens and Disease, 6*(7), 755–765. https://doi.org/10.1089/fpd.2008.0247

Llarena, A.-K., Taboada, E., Rossi, M., & Kraft, C. S. (2017). Whole-genome sequencing in epidemiology of Campylobacter jejuni infections. *Journal of Clinical Microbiology, 55*(5), 1269–1275. https://doi.org/10.1128/JCM.00017-17

Mbabazi, J. (2011). Principles and methods for the risk assessment of chemicals in food. *International Journal of Environmental Studies*. https://doi.org/10.1080/00207233.2010.549617

Mughini-Gras, L., Penny, C., Ragimbeau, C., Schets, F. M., Blaak, H., Duim, B., Wagenaar, J. A., de Boer, A., Cauchie, H.-M., & Mossong, J. (2016). Quantifying potential sources of surface water contamination with *Campylobacter jejuni* and *Campylobacter coli*. *Water Research, 101*, 36–45. https://doi.org/10.1016/j.watres.2016.05.069

Nauta, M. J., Jacobs-Reitsma, W. F., Evers, E. G., Van Pelt, W., & Havelaar, A. H. (2005). *Risk assessment of Campylobacter in The Netherlands via broiler meat and other routes*. https://www.rivm.nl/bibliotheek/rapporten/250911006.pdf.

Nauta, M. J., Sanaa, M., & Havelaar, A. H. (2012). Risk based microbiological criteria for *Campylobacter* in broiler meat in the European Union. *International Journal of Food Microbiology, 158*(3), 209–217. https://doi.org/10.1016/j.ijfoodmicro.2012.07.018

Nederlandse Pluimveeverwerkende Industrie (NEPLUVI). (2021). *Rapportage Campylobacter monitoring 2020 op Nederlandse vleeskuikenslachterijen*. https://www.nepluvi.nl/dynamic/media/1/documents/Campylobacter/2021-015_eindrapportage_campylobactermonitoring_2020_NL_vleeskuikenslachterijen.pdf.

Neilson, Z. (2016). *The case of the exploded Dutch chickens*. Sustainable Food Trust. https://sustainablefoodtrust.org/articles/exploded-dutch-chickens-plofkip/.

Newell, D., Elvers, K., Dopfer, D., Hansson, I., Jones, P., James, S., Gittins, J., Stern, N., Davies, R., & Connerton, I. (2011). Biosecurity-based interventions and strategies to reduce *Campylobacter spp*. on poultry farms. *Applied and Environmental Microbiology, 77*(24), 8605–8614. https://doi.org/10.1128/AEM.01090-10

Pijnacker, R., Friesema, I., Mughini Gras, L., Lagerweij, G., Van Pelt, W., & Franz, E. (2019). *Disease burden of food-related pathogens in The Netherlands*, 2018 https://www.rivm.nl/bibliotheek/rapporten/2019-0086.pdf.

Rawson, T., Paton, R. S., Colles, F. M., Maiden, M. C., Dawkins, M. S., & Bonsall, M. B. (2020). A mathematical modeling approach to uncover factors influencing the spread of *Campylobacter* in a flock of broiler-breeder chickens. *Frontiers in Microbiology, 11*, 2481. https://doi.org/10.3389/fmicb.2020.576646

Romero-Barrios, P., Hempen, M., Messens, W., Stella, P., & Hugas, M. (2013). Quantitative microbiological risk assessment (QMRA) of food-borne zoonoses at the European level. *Food Control, 29*(2), 343–349.

Russa, A., Bouma, A., Vernooij, J., Jacobs-Reitsma, W., & Stegeman, J. (2005). No association between partial depopulation and *Campylobacter spp*. colonization of Dutch broiler flocks. *Letters in Applied Microbiology, 41*(3), 280–285. https://doi.org/10.1111/j.1472-765X.2005.01751.x

Sibanda, N., McKenna, A., Richmond, A., Ricke, S. C., Callaway, T., Stratakos, A. C., Gundogdu, O., & Corcionivoschi, N. (2018). A review of the effect of management practices on *Campylobacter* prevalence in poultry farms. *Frontiers in Microbiology, 9*. https://doi.org/10.3389/fmicb.2018.02002, 2002.

Sterman, J. (2000). *Business dynamics*. Irwin/McGraw-Hill c2000.

Wagenaar, J., Mevius, D., & Havelaar, A. (2006). *Campylobacter* in primary animal production and control strategies to reduce the burden of human campylobacteriosis. *Scientific and Technical Review, 25*(2), 581–594. https://doi.org/10.20506/rst.25.2.1680