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Appl. Environ. Microbiol. 2004, 70(12):7474. DOI:
10.1128/AEM.70.12.7474-7480.2004.

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Effects of Climate on Incidence of *Campylobacter* spp. in Humans and Prevalence in Broiler Flocks in Denmark

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Received 6 April 2004/Accepted 6 August 2004

***Campylobacter* infections are increasing and pose a serious public health problem in Denmark. Infections in humans and broiler flocks show similar seasonality, suggesting that climate may play a role in infection. We examined the effects of temperature, precipitation, relative humidity, and hours of sunlight on *Campylobacter* incidence in humans and broiler flocks by using lag dependence functions, locally fitted linear models, and cross validation methods. For humans, the best model included average temperature and sunlight 4 weeks prior to infection; the maximum temperature lagged at 4 weeks was the best single predictor. For broilers, the average and maximum temperatures 3 weeks prior to slaughter gave the best estimate; the average temperature lagged at 3 weeks was the best single predictor. The combined effects of temperature and sunlight or the combined effects of temperature and relative humidity predicted the incidence in humans equally well. For broiler flock incidence these factors explained considerably less. Future research should focus on elements within the broiler environment that may be affected by climate, as well as the interaction of microclimatic factors on and around broiler farms. There is a need to quantify the contribution of broilers as a source of campylobacteriosis in humans and to further examine the effect of temperature on human incidence after this contribution is accounted for. Investigations should be conducted into food consumption and preparation practices and poultry sales that may vary by season.**

Campylobacter has become the leading cause of enteric zoonotic infections in most developed and developing countries, and the incidence appears to be increasing (1). The typical symptoms include diarrhea, which can be bloody, abdominal pain, fever, nausea, headache, and vomiting. The illness is typically self-limiting and usually resolves in about 1 week; however, severe illness and long-term complications, such as arthritis, septicemia, and Guillain-Barre syndrome, sometimes occur. The incidence of human campylobacteriosis in Denmark has risen steadily since 1992, reaching 4,620 cases (86 cases per 100,000 people) in 2001 (2). The majority of cases occur sporadically, and outbreaks are rare. It is estimated that approximately 80% of cases are domestically acquired (2). *Campylobacter* is commonly found in domesticated animals, including poultry, cattle, pigs, sheep, cats, and dogs (14), and in migratory birds, such as ducks (5, 23) and seagulls (13). *Campylobacter* has also been isolated from rodents (5), beetles (18), houseflies (34), and surface water sources (4, 8).

Many risk factors for *Campylobacter* infection have been identified, including consumption of raw or undercooked poultry (10, 20, 27, 37), handling of raw poultry (17, 26), contact with chickens or hens (37), consumption of unpasteurized or contaminated milk (12, 37) or untreated or contaminated drinking water (11, 25), barbecuing (27, 37), contact with pets

(10, 20, 38), and international travel (10, 33). In Denmark, consumption of poultry is thought to be the major risk factor for *Campylobacter* infections (27). A national monitoring program estimated the average prevalence of *Campylobacter* in Danish broiler flocks to be 42% in 2001 (2).

In Denmark, human *Campylobacter* infections and the percentage of infected broiler flocks show similar seasonal trends, with peak infections occurring in July and August (weeks 27 to 35) (Fig. 1). Seasonal trends in human infection have also been observed in several other countries (30, 32). In Norway, cases show an increased summer peak corresponding to increased latitude (22). Seasonal variations in *Campylobacter* infection in broilers (3, 19, 21, 40) and cattle (36) have been reported for several countries.

These seasonal trends suggest that climatic factors may play a role in infection. Studies have documented an effect of climate, particularly temperature, on human disease (7, 35, 39). Other studies have suggested associations between environmental factors, such as temperature, humidity, and sunlight, and *Campylobacter* carriage in broilers (9, 40). In this study we further examined the role of climate on *Campylobacter* infections by comparing the effects of temperature, precipitation, relative humidity, and sunlight on the human incidence in Denmark and on the prevalence of *Campylobacter* in Danish broiler flocks at slaughter.

MATERIALS AND METHODS

Data collection. Human *Campylobacter* cases reported to the Statens Serum Institute between 1998 and 2001 were summarized by week based on the date that the specimen was received in the laboratory. Our analysis was based on the counties Århus, Bornholm, Frederiksborg, Fyn, Nordjylland, Ribe, Roskilde, Storstrøms, Sønderjylland, Vejle, Vestsjælland, and Viborg and the municipalities Copenhagen and Frederiksberg, which consistently reported incidence by

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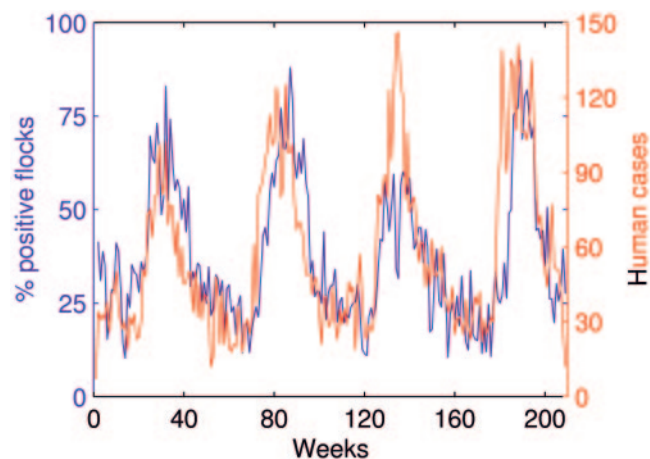


FIG. 1. Seasonality of campylobacteriosis in humans and *Campylobacter* infections in broiler flocks in Denmark from 1998 to 2001.

week between 1998 and 2001. Copenhagen county and Ringkøbing county were excluded from the analysis because of missing weekly information during 1998. This excluded 0.9 million people out of a population of 5.3 million people. Greenland and the Faroe Islands were also excluded from the analysis. Cases in which the subjects reported international travel in the week preceding *Campylobacter* infection were also excluded from the analysis, as were cases for which the county name within Denmark was missing. It was assumed that the remaining cases were due to exposure within Denmark.

Under a national monitoring program for Danish broiler flocks, 10 birds from each flock or batch (one flock may be slaughtered in up to six different batches) are examined for *Campylobacter* by cloacal swabbing at slaughter (41). The percentage of flocks that tested positive by week between 1998 and 2001 were summarized. Only results from the first batch were included in our analysis because slaughtering a flock in several batches may increase the risk of contamination (e.g., by introduction from the machine used to depopulate the house) and because of the dependence between batches from the same flock. If the house on a farm from which the slaughtered flock came was unknown, the sample was excluded from the analysis to ensure the validity of the data.

Between 1998 and 2001, a total of 16,305 human campylobacteriosis cases were reported in Denmark; 94% of these cases were due to *Campylobacter jejuni*. Of these, 2,658 were excluded because they were reported from Copenhagen or Ringkøbing county, 1,554 cases were excluded because there was a known history of international travel, and 85 cases were excluded because the county name was not reported. During this same time, 23,279 broiler samples were collected; 5,338 were excluded from the analysis either because they were not from the first batch slaughtered or because they were from an unknown house. Of the remaining

17,941 samples, 6,860 (38%) tested positive for *Campylobacter* spp.; 85% of these samples contained *C. jejuni*.

Climate data were provided by the Danish Meteorological Institute. The average temperature, maximum temperature, relative humidity, precipitation (in millimeters), and amount of sunlight were averaged for the entire country by week between 1998 and 2001. Some of the climatic factors were found to be highly correlated. For example, relative humidity was negatively correlated with hours of sunlight, and the average temperature was generally 5°C lower than the maximum temperature.

Data analysis. Weekly measurements of the human incidence and the percentage of infected broiler flocks were fitted by using univariate and bivariate models with climate variables as the regressors. Locally fitted linear models (24, 28) (the S-plus library LFLM can be downloaded from www.imm.dtu.dk/~han/software.html) with nearest-neighbor bandwidths were used with zero-, first-, and second-order polynomials. Each of the regressors was lagged 0 to 6 weeks. For each climatic variable a four-fold cross validation (16, 24) was used to select the optimal lag, the degree of the fitting polynomial, and the bandwidth. The bivariate models were estimated independent of the univariate models. The four-fold cross validation was done by using all combinations of 3 years of data to estimate a model used to predict the fourth year; the reported cross validation error is the sum of the squared prediction errors for the 4 years. The model with the lowest cross validation error was determined to be the best model. The squared multiple correlation coefficient (R^2) for each model was also included; however, a higher R^2 did not necessarily correspond to the best model. The human count data were transformed by the logarithm prior to analysis, and the proportion of infected broiler flocks was untransformed in the analysis.

RESULTS

Humans and climate. The maximum temperature 4 weeks prior to the reported infection was the best single predictor of campylobacteriosis incidence, explaining 68% of the variation (Table 1). Maximum temperatures between 13 and 20°C corresponded to the steepest increase in incidence, while a smaller increase was seen at temperatures above 20°C (Fig. 2B). The average temperature 3 weeks prior to reported infections was nearly as good a predictor as the maximum temperature (Table 1). The steepest increase in human incidence occurred at average temperatures between 8 and 13°C, with a smaller increase at temperatures above 13°C (Fig. 2A). Hours of sunlight lagged at 5 weeks explained slightly more than one-half of the variation, while relative humidity also lagged at 5 weeks explained 44% of the variation. Precipitation was not at all important in predicting human incidence, as it explained only 6% of the variation.

TABLE 1. Climatic factors used to predict human *Campylobacter* incidence

Factor(s)	Lag (weeks)	Bandwidth	Order	Cross validation error	R^{2a}
One predictor					
Avg temp	3	0.40	0	22.441	0.6662
Maximum temp	4	0.50	1	21.746	0.6776
Hours of sunlight	5	0.50	2	29.860	0.5748
Relative humidity	5	0.60	1	38.067	0.4398
Precipitation	3	0.20	1	62.758	0.0632
Two predictors					
Avg temp and maximum temp	4	0.45	1	21.549	0.7062
Avg temp and hours of sunlight	4	0.40	1	20.585	0.7159
Avg temp and relative humidity	3	0.55	1	21.838	0.6907
Avg temp and precipitation	1	0.50	1	22.811	0.6687
Maximum temp and hours of sunlight	4	0.45	1	21.967	0.6955
Maximum temp and rel. humidity	4	0.40	1	22.730	0.6948
Maximum temp and precipitation	4	0.25	1	22.343	0.7044

^a Explanation of variation.

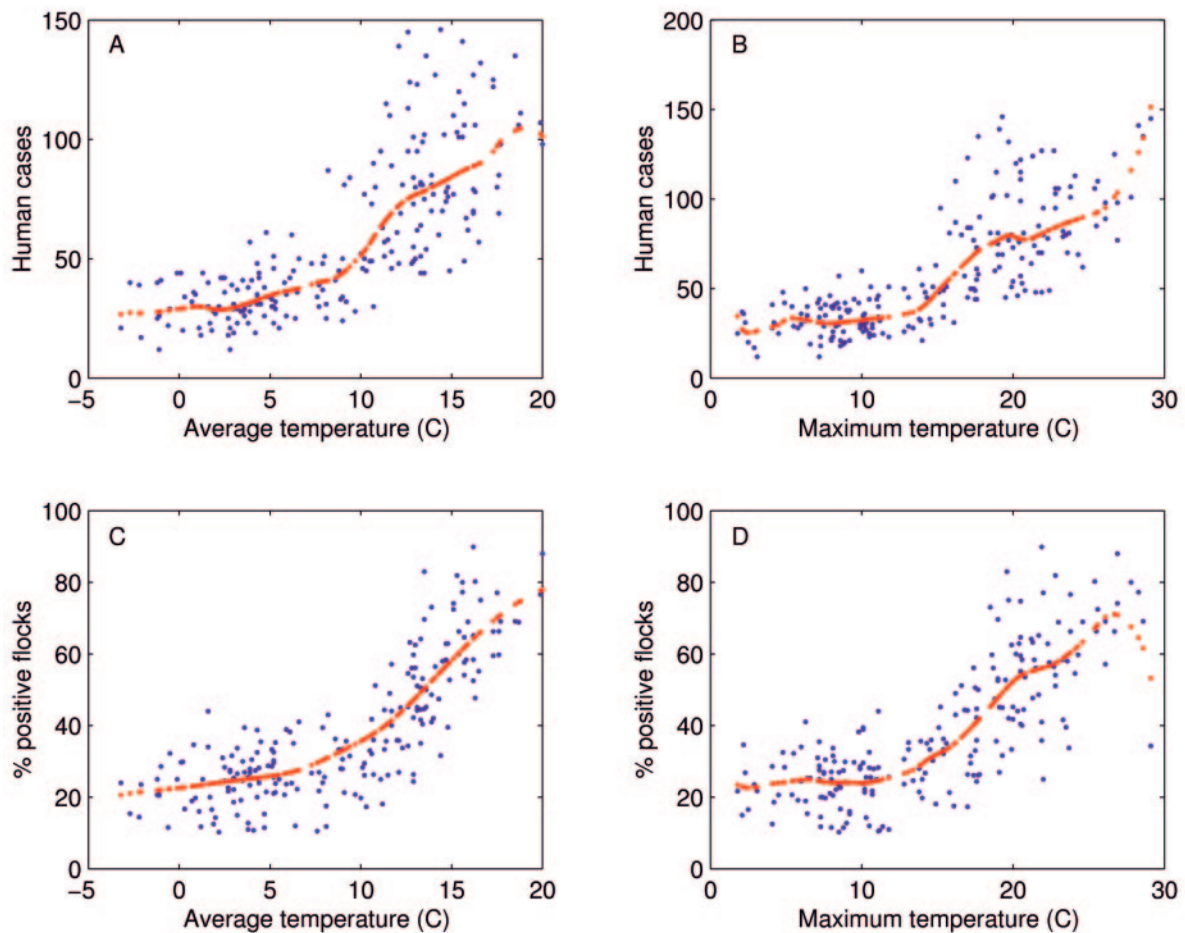


FIG. 2. Impact of temperature on human campylobacteriosis incidence and the percentage of *Campylobacter*-infected broiler flocks at slaughter. The blue dots indicate observations, and the red dots indicate estimates.

When multiple climatic factors were used, the best model for predicting human campylobacteriosis incidence (i.e., the model with the lowest cross validation error) included average temperature and hours of sunlight 4 weeks prior to the reported infection (Table 1). The combination of high average temperatures and many hours of sunlight resulted in the greatest incidence of human campylobacteriosis (Fig. 3B). For temperatures below 17°C, lower average temperatures and more hours of sunlight predicted an incidence similar to the incidence predicted with higher average temperatures with fewer hours of sunlight. For example, at 10°C and 60 h of sunlight the predicted human incidence was approximately the same as that at 15°C and 30 h of sunlight. The combination of average temperature and maximum temperature lagged at 4 weeks was the next best model for predicting human incidence. When the maximum temperature was above 15°C, increases in the maximum temperature resulted in a larger change in incidence than corresponding increases in the average temperature (Fig. 3A). Overall, these models explained 72 and 71% of the variation, respectively, and were each better predictors than using either maximum or average temperature alone.

Using the average temperature and relative humidity 3 weeks prior to the reported infection also provided an important predictor of human incidence (Table 1). The greatest

effect occurred at high temperatures and relatively low humidity. A slight gradient was seen, with low average temperatures and low humidity having an effect on the incidence similar to that of higher temperatures with high humidity (Fig. 4). For example, the estimated incidence at 10°C and 60% relative humidity was similar to that at 13°C and 85% relative humidity. This was not unexpected as relative humidity is inversely correlated with hours of sunlight.

Models that included average temperature and precipitation or models that included maximum temperature and either hours of sunlight, relative humidity, or precipitation did not predict any better than models in which maximum temperature alone was used.

Broilers and climate. The average temperature 3 weeks prior to slaughter explained 74% of the variation and was the single best predictor of broiler flock prevalence (Table 2). Lags of 2 and 4 weeks produced similar cross validation error values. At average temperatures above 8°C, there was a large increase in broiler flock prevalence with increasing temperature (Fig. 2C). Maximum temperature lagged at 4 weeks was the next best single predictor of broiler flock prevalence, explaining 66% of the variation (Fig. 2D). Similar to what was observed with human incidence, a large increase in incidence was seen at temperatures between 13 and 20°C, followed by a smaller in-

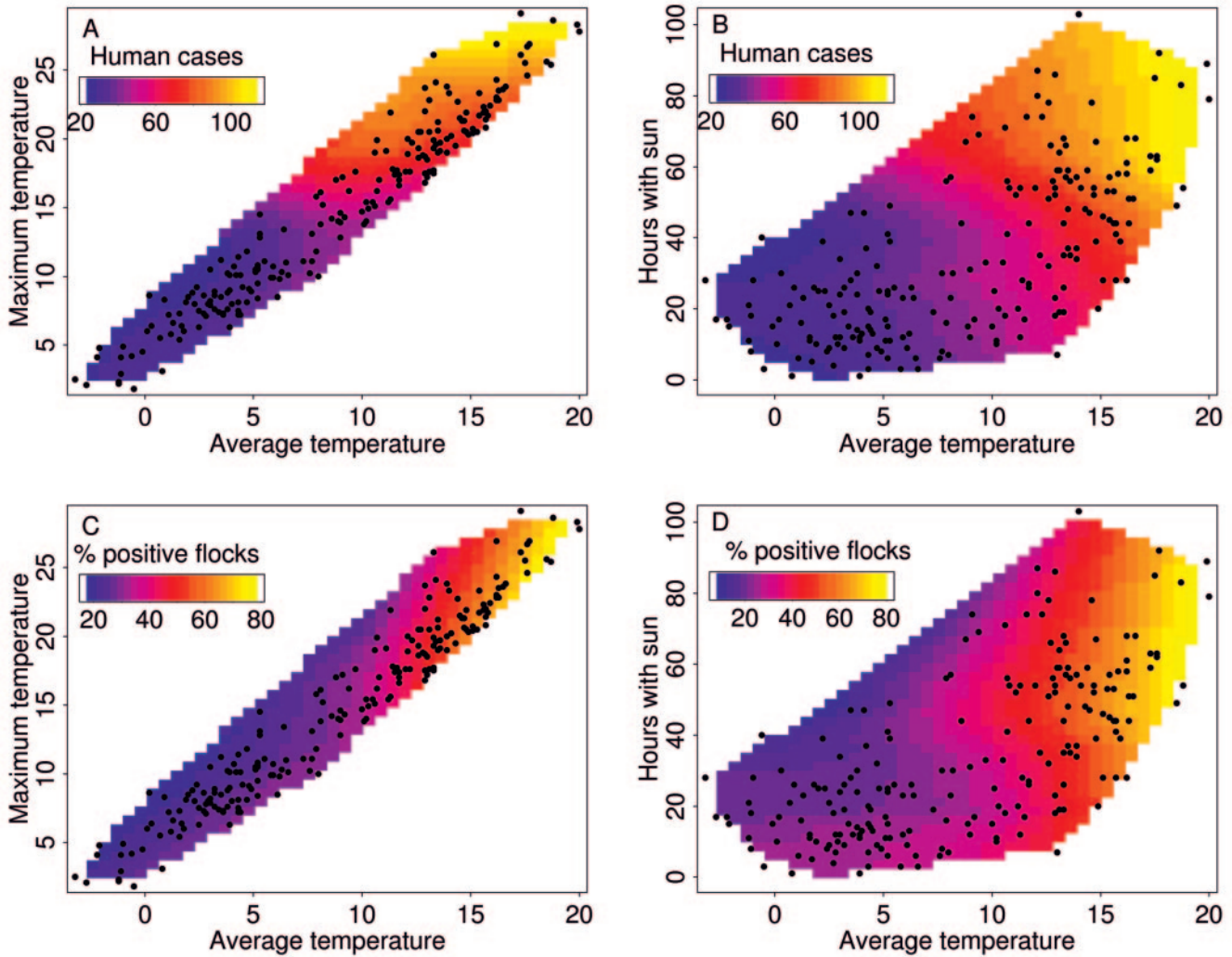


FIG. 3. Effects of temperature and hours of sunlight on the incidence of campylobacteriosis in humans and the percentage of *Campylobacter*-infected broiler flocks at slaughter. The dots indicate observations.

crease at higher temperatures. Although the temperatures were similar during autumn and spring, a higher percentage of broilers was positive for *Campylobacter* in the autumn (Fig. 5). During the fall, the average temperature and the percentage of positive broilers decreased at similar rates; however, in the spring, temperatures began to increase before the percentage of infected broiler flocks began to increase. There appeared to be a threshold at the end of spring after which the broiler flock prevalence increased dramatically. This effect was still visible even after a temperature lag of 3 weeks was accounted for. As single predictors, hours of sunlight and relative humidity lagged at 5 weeks explained 50 and 38% of the variation, respectively, while precipitation lagged at 1 week explained only 17% of the variation.

When multiple climatic factors were used, the combination of average temperature and maximum temperature 3 weeks prior to slaughter provided the best estimate (i.e., the lowest cross validation error) of broiler flock prevalence, explaining 76% of the variation, and was better than any of the single predictors alone (Table 2). In contrast to humans, the greatest prevalence occurred when there was a small difference be-

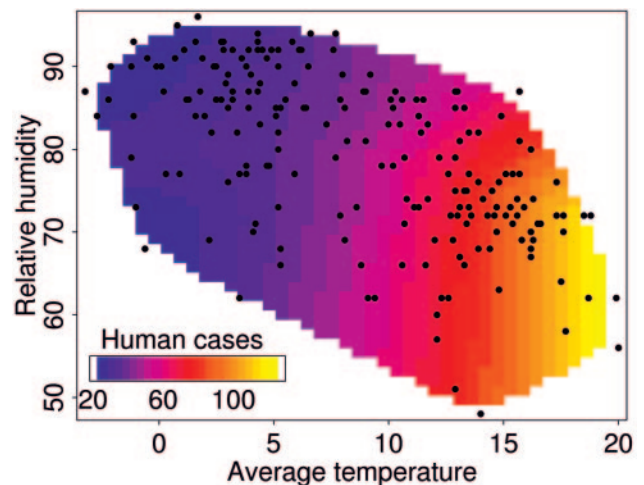


FIG. 4. Effect of average temperature and relative humidity on the incidence of human campylobacteriosis. The dots indicate observations.

TABLE 2. Climatic factors used to predict *Campylobacter* prevalence in broiler flocks

Factor(s)	Lag (weeks)	Bandwidth	Order	Cross validation error	R ^{2a}
One predictor					
Avg temp	3	0.50	1	2.0958	0.7439
Maximum temp	4	0.30	0	2.8193	0.6637
Hours of sunlight	5	0.45	1	3.7508	0.5035
Relative humidity	5	0.40	0	4.7387	0.3770
Precipitation	1	0.50	0	7.1459	0.1706
Two predictors					
Avg temp and maximum temp	3	0.50	1	1.9973	0.7623
Avg temp and hours of sunlight	3	0.50	2	2.0824	0.7702
Avg temp and relative humidity	2	0.50	2	2.1220	0.7616
Avg temp and precipitation	3	0.30	1	2.1064	0.7601
Maximum temp and hours of sunlight	4	0.50	2	2.7474	0.7066
Maximum temp and relative humidity	4	0.50	2	2.7228	0.7245
Maximum temp and precipitation	3	0.50	2	2.7458	0.7027

^a Explanation of variation.

tween the average and maximum temperatures (i.e., high average temperature and relatively low maximum temperature) (Fig. 3C). A model that included average temperature and hours of sunlight was the next best predictor, explaining 77% of the variation, and was better than a model with average temperature alone (Table 2). Interestingly, hours of sunlight had a more pronounced effect at temperatures below 8°C, with fewer hours of sunlight corresponding to a higher prevalence (Fig. 3D). At temperatures above 13°C, the effect was less apparent, with the highest prevalence corresponding to 50 to 60 h of sunlight. However, the overall contribution of hours of sunlight to increased prevalence at these temperatures was not as important. Models that included either relative humidity or precipitation with average temperature were not any better than a model that included average temperature alone.

DISCUSSION

Our study showed that as the temperature increases, there is a corresponding increase in the incidence of human campylobacteriosis and the percentage of infected broiler flocks at slaughter. A threshold average temperature above 8°C and a maximum temperature above 13°C were observed; the largest increase in incidence occurred at temperatures up to 20°C, and a smaller increase occurred at temperatures above 20°C. Temperature had its greatest impact 3 to 4 weeks before reported infections for both broilers and humans. The combination of high average temperature and relatively low maximum temperature (i.e., little variation in temperature within 1 week) corresponded to the second highest human incidence and the highest percentage of infected broiler flocks, indicating that it may be the effect of sustained high temperatures rather than intermittent high temperatures that is the key factor in predicting infection. Climatic factors explained a larger proportion of the variance in *Campylobacter* prevalence in broiler flocks than in humans.

For humans, models that included average temperature and either maximum temperature or hours of sunlight provided the best estimates of *Campylobacter* incidence. At a lag of 4 weeks, a model that included average and maximum temperatures was nearly consistent with a recent study of *Salmonella enterica*

serovar Typhimurium infections that revealed a positive association with air temperature 2 to 3 weeks before notification (15). In a recent case-control study of sporadic *Campylobacter* cases in Denmark, the average time between onset of illness, visiting a healthcare facility, providing a culture, and receiving a diagnosis was 21 days (J. Neimann, personal communication). Thus, sustained high temperatures 4 weeks prior to reported infections roughly correspond to the time of exposure. This could mean either that temperature plays a direct role in exposure or, more likely, that temperature is a marker for behavioral factors, which tend to occur more often in the summer months. At a lag of 4 weeks, a model that included average temperature and hours of sunlight also was consistent with a hypothesis of behavioral factors. In Denmark, as in other northern countries, the amount of sunlight coupled with warmer temperatures during the summer months greatly affects human behavior and may encourage outdoor activities, such as barbecuing, that increase the risk of *Campylobacter*

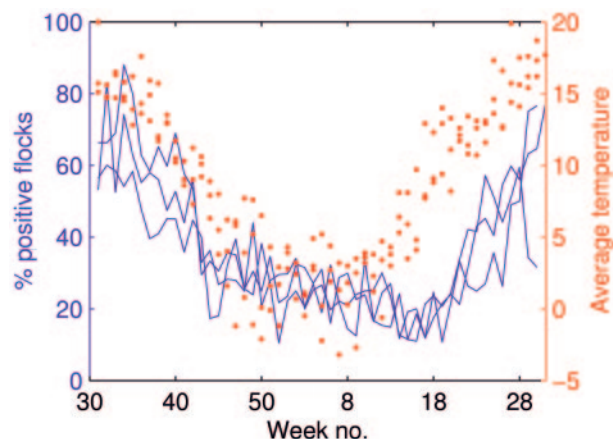


FIG. 5. Effects of cold season on the percentage of *Campylobacter*-infected broiler flocks at slaughter. The blue lines indicate the percentages of positive broiler flocks. Each line represents 1 year from one summer to the next summer (e.g., summer 1998 to summer 1999). The dots indicate average temperatures. The week numbers on the x axis are calendar week numbers.

infection. Other outdoor activities, such as picnicking, camping, or swimming, may increase exposure to *Campylobacter* from the environment and natural water sources, such as lakes and rivers. Additionally, some studies have suggested that exposure to UV radiation (sunlight) may result in increased susceptibility to infectious diseases (29). Although the mechanisms involved are highly complex and have not been fully investigated, this could provide a possible partial explanation for our findings.

Our study also showed that there was an association between average temperature and relative humidity lagged at 3 weeks. This is consistent with a study in Peru in which the workers found that the number of hospital admissions for diarrheal illness was related to increased ambient temperature and decreased humidity during an El Niño year (7). However, the mechanisms behind this association remain uncertain, and more work is needed to support these findings.

The degree to which temperature and sunlight influence *Campylobacter* incidence in humans should be balanced with the contribution to campylobacteriosis that is attributed to consumption of broiler meat. In Denmark, consumption of poultry is a major risk factor for campylobacteriosis. While it is possible that consumption patterns vary by season, this variation is not enough on its own to explain the seasonal trend.

For broilers, use of the average and maximum temperatures 3 weeks prior to slaughter resulted in the most accurate estimate of prevalence, while a model that included average temperature and hours of sunlight was better than any single predictor. This is consistent with another study, which found that there was a positive correlation among minimum temperature, hours of sunshine, and *Campylobacter* carriage in poultry (40). As suggested by Jacobs-Reitsma et al., it may be that temperature has a direct role in *Campylobacter* carriage and/or that sources of contamination within the farm environment, such as migratory birds, beetles, or rodents, are temperature dependent (19). Interestingly, temperature did not seem to have as great an effect on prevalence during colder months as during warmer months, indicating that factors other than temperature play a role during this time or that a threshold temperature is needed. The fact that the incidence was higher during the autumn could mean that the higher temperatures or increased prevalence in reservoirs in the summer affects the prevalence in the fall. The higher prevalence observed with lower temperatures and few hours of sunlight is consistent with the biology of *Campylobacter*, which is known to tolerate cold (6) and to exhibit sensitivity to light (31).

As *Campylobacter* is sensitive to dry conditions, high relative humidity and/or precipitation contributes to the survival of *Campylobacter* in the environment. Although it was observed that elevated temperature and high humidity coincided with increased *Campylobacter* carriage in poultry in one study (9), relative humidity and precipitation were not important predictors of broiler flock prevalence in our study. This lack of an association may have been due to the fact that measurements were taken and summarized nationally and did not account for regional variations. Temperature and humidity levels measured within broiler houses may provide a more accurate assessment of their true impact.

There are complex interactions among climatic factors, making elucidation of the effects of a single factor extremely diffi-

cult to describe, and this should be kept in mind when our results are interpreted. Data describing human incidence, broiler flock prevalence, and climate were analyzed nationally, and the effects of regional climate variation were not examined. Our analysis did not account for factors other than climate that may influence *Campylobacter* prevalence. Although our study excluded persons with a known history of international travel, not all individuals were interviewed about travel history, which may have biased our results.

The model which we used is a static time series model. This model was chosen to investigate the direct effects of the climatic factors and rapid secondary dynamics. The observed difference between spring and autumn could not be described by the model used, and this indicates that there most likely are some dynamics involved in the infection of broiler flocks that have time constants greater than a few weeks. The next step is to construct a dynamic model, but the choice of model structure will affect the results, so some knowledge or assumption about the route of infection is needed to ensure that the results are useful.

Conclusions. We found a strong relationship between temperature and *Campylobacter* infections in both broilers and humans, and the greatest effects were observed at maximum weekly temperatures above 13°C. The combined effect of temperature with hours of sunlight, and to a lesser extent relative humidity, seemed to predict infection in humans, but the role of these parameters in predicting broiler flock prevalence was less apparent and more work is needed to support these findings. Future research should focus on elements in the broiler environment that may be susceptible to climate, as well as the interaction of microclimatic factors on and around broiler farms. There is a need to quantify the contribution of broilers as a source of *Campylobacter* in human infections and to further examine the effect of temperature on human incidence after this contribution is accounted for. Investigations of food consumption, preparation practices, and poultry sales that may vary by season should be conducted. Finally, the role of climatic factors on *Campylobacter* incidence in other countries should be explored.

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