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Modeling The Effects Of Climate Factors On The Incidence Of Future Campylobacter Infections In Connecticut

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**Modeling the Effects of Climate Factors on the Incidence of Future *Campylobacter*
Infections in Connecticut**

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Abstract:

Background & Introduction: Campylobacter is one of the most common foodborne bacteria in the United States, accounting for 48 million infections each year. Campylobacter infections can arise from consuming contaminated food, especially poultry, water, or contact with infected animals. Due to its strong seasonality, cases peaking in the summer and declining in the winter, potential relationships between climate and campylobacter have been analyzed.

Methods: Weekly campylobacter surveillance data was obtained from the Connecticut Department of Public Health for 2000 through 2018. Historical and projected temperature and precipitation data were also gathered from the National Oceanic and Atmospheric Administration. A statistical analysis was conducted examining the relationship between weekly campylobacter cases and climate variables. A hierarchical Autoregressive Integrated Moving Average (ARIMA) model was also estimated using this weekly data and projected climate data to estimate the future burden of campylobacter by county in Connecticut.

Results: The Poisson regression analysis showed a statistically significant relationship between weekly campylobacter cases and temperature at all lags, 0-8, but only a significant relationship with precipitation at lag 5. The optimal ARIMA model determined by lowest AIC score predicted with 87% accuracy future campylobacter infections by county in Connecticut. The model showed no increase in cases projected from 2019 through 2050.

Discussion: Even with a projected increase in temperature and precipitation in the future because of climate change, campylobacter cases were not found to significantly increase. However, this analysis assumes a climate scenario in which the increase in global temperature will remain below 3° C through 2100. This analysis also did not consider probable increases in antimicrobial resistance and the recent decline in poultry consumption in the United States.

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Background & Introduction:

The CDC estimates that approximately 48 million people each year are infected with a foodborne illness in the United States. Campylobacter specifically accounts for 1.5 million of these infections. However, as this estimate accounts for only laboratory-confirmed cases, the actual incidence of campylobacter in the United States is estimated to be as high as 1% of all Americans annually (C.D.C). The underestimate is largely attributed to the low mortality rate and self-limiting nature of the illness (Weisent, et al., 2014). Infection has been shown to stem from exposures such as consuming contaminated meat, particularly poultry, drinking untreated water, or having direct contact with animals who are infected with the pathogen. Symptoms of campylobacter most commonly include diarrhea, vomiting, fever, and stomach cramps (C.D.C). Most of those infected will recover from a campylobacter infection without antibiotics, but antibiotics are prescribed in some situations, particularly for individuals at high risk for severe illness, such as those with underlying medical conditions or compromised immune systems (C.D.C.).

There have been seasonal variations found with respect to campylobacter infections that suggest it may be sensitive to changes in climate. Peaks in cases usually occur in late spring and summer, with cases at their lowest in the winter (Kuhn, et al., 2020). However, the determinants of this seasonal pattern are still unknown (Louis, et al., 2005) (Lake, et al., 2019). While much research has been conducted regarding potential causes of the seasonality, no definitive conclusions have been drawn. Research investigating possible environmental factors such as temperature, precipitation, humidity, and extreme climate events has yielded inconsistent results. In contrast, research of the association between climate factors and other foodborne bacteria,

such as salmonella, has shown stronger relationships (Kuhn, et al., 2020) (McMichael, Woodruff, & Hales, 2006) (Lal, et al., 2013).

Current research studies assessing the relationship between campylobacter infections and climatic factors have not only differed in their conclusions, but also their methods. A study quantifying the link between ambient temperature and campylobacter cases in Germany found a positive association for *Campylobacter jejuni* using a negative binomial regression model (Yun, et al., 2016). However, another study utilizing negative binomial regression in Canada found a small, not statistically significant association (Allard, et al., 1990). Poisson regression models used in Northern European countries also found positive associations between campylobacter cases and temperature, as well as heavy precipitation events (Kuhn, et al., 2020) (Sari Kovats, et al., 2005), while a New Zealand study using a similar Poisson regression model found no link between temperature and the seasonality of campylobacter (Spencer, et al., 2012). Kuhn et al., however suggested that while a Poisson regression model might be valid in some geographic locations, it might not be a valid approach for other locations (Kuhn, et al., 2020). Additional research has been conducted utilizing more advanced models for time series data, such as wavelet analysis and Autoregressive Integrated Moving Average (ARIMA) models. One study, employing the former approach, found changes in temperature predicted one-third of campylobacter cases in England and Wales, with a less pronounced relationship with rainfall (Djennad, et al., 2019). A New Zealand study using an ARIMA model accounting for seasonality found an association with temperature for salmonella infections but failed to find a significant relationship for campylobacter (Lal, et al., 2013).

While most research into campylobacter and climate has looked at European countries, Australia, New Zealand, and Canada, much less research has been conducted on this potential

relationship in the United States. Existing research in the United States has been limited to specific geographies. One study assessed the campylobacter and climate relationship in the state of Georgia, concluding a positive relationship with temperature, but a negative relationship with precipitation, as cases increased in drought circumstances (Weisent, et al., 2014). Another study, in Maryland, only assessed extreme heat and precipitation events. While extreme precipitation was positively associated with campylobacter infections, it was only so for coastal regions of the state. Extreme heat was less associated, only a significant factor during La Niña periods (Soneja, et al., 2016). A comprehensive study of a range of climate factors including temperature, humidity, and surface water variables such as river levels, river temperature, and pH, was conducted solely for Philadelphia County. Campylobacter was associated with increased average temperature, as well as humidity and the temperature of the nearby Delaware River, a source of drinking water for Philadelphia (White, et al., 2009).

Even though current research on the relationship between climate and campylobacter has generated inconsistent results, more research is needed, especially in different geographic regions and utilizing potentially more advanced models, to provide a clearer picture of this relationship. With a documented link between climate change and the potential effects on food- and water-borne diseases (Sterk, et al., 2013), quantifying these effects could aid in mitigating infections in the future. Even though campylobacter infections are typically not deadly, the high incidence and potential increase of infections could have a substantial impact on healthcare systems (Louis, et al., 2005). As surface temperatures around the globe are expected to rise in the coming decades, so is the frequency of severe weather events.

In Connecticut, campylobacter is a reportable illness, requiring both physicians and laboratories to report cases to the Connecticut Department of Public Health (DPH) and the local

health department (LHD). Connecticut currently experiences approximately 700 cases of campylobacter per year, with a total population of roughly 3.5 million. The state of Connecticut experiences a continental climate with an average annual high temperature of 82.55°F in the summer and an average low temperature of 19.9 in the winter (Visit CT). Both averages are higher than the U.S. average overall. Connecticut also experiences higher than average precipitation, totaling approximately 50 inches per year, compared to the U.S. average of 38 inches (CT.gov; NOAA). The objective of this analysis is to create a model for campylobacter infections in Connecticut based on historical temperature and precipitation data and employ this model to project cases of campylobacter in Connecticut using projected climate data.

Methods:

Campylobacter Data

Surveillance of reportable foodborne illnesses, including campylobacter, is conducted in Connecticut through the Foodborne Pathogens Active Surveillance Network (FoodNet), in partnerships with the Yale Emerging Infections Program (EIP), Connecticut Department of Public Health (DPH), and the Centers for Disease Control and Prevention (CDC). Cases are detected by either polymerase chain reaction (PCR) and/or culture diagnostic laboratory testing from stool, urine, or blood samples. All reported cases are entered into the Connecticut Electronic Disease Surveillance System (CTEDSS), which houses laboratory testing information, demographic information, as well as data collected by interview conducted by the Yale EIP or LHDs. Campylobacter case data from 2000-2018 were used for this analysis, excluding those cases who reported international travel, restricting to only domestically acquired cases. An individual's specimen collection date (week number, month, and year) as well as county of

residence were used to link the case to the corresponding temperature and precipitation for that week and county in Connecticut.

Cases over time by county were visualized to examine the geographical burden of disease across the state. The seasonality of campylobacter was also assessed over time by comparing the number of cases by week of the year over the entire time period of the data from 2000-2018, in order to determine whether there have been any shifts and/or expansion of the historical seasonal period of campylobacter cases in Connecticut over time.

Climate Data

Both historical and projected climate data were available publicly from the National Climatic Data Center at the National Oceanic and Atmospheric Administration (NOAA). Historical daily average temperature and daily total precipitation observations were collected for each county in Connecticut and then aggregated to obtain weekly averages. The relationship between campylobacter cases and temperature and precipitation observations at differing lags from 0 weeks through 8 weeks was analyzed by using a Poisson regression model. This preliminary analysis assessed the statistical significance of each lag for both temperature and precipitation to determine the optimal lag of most significance to be used in the model.

Projected weekly average temperature and precipitation was used based on the Representative Concentration Pathway (RCP) 4.5 scenario, which assumes radiative forcing stabilizes at 4.5 watts per meter squared (W/m^2) by the year 2100. This scenario has been thought to be the most likely situation and assumes carbon dioxide (CO_2) emissions will begin to decline by 2045. RCP 4.5 is an intermediate scenario, with more stringent possibilities of RCP 1.9, 2.6 and 3.4 requiring global temperature increases to not exceed $3^\circ C$, and worsening scenarios of RCP 6, 7, and 8.5 accounting for less interventions allowing global temperatures to

rise by more than 3° C. Assuming the most likely scenario of RCP 4.5 allows for the forecasted results to also be those of the most likely scenario. This projected data was sourced for years 2019-2050.

Autoregressive Integrated Moving Average (ARIMA) Model

Autoregressive Integrated Moving Average (ARIMA) models are a type of regression analysis that offer an approach to modeling and forecasting time series data based on historical data. This makes it an optimal choice of model to assess campylobacter time series data by geographical region. There are three approaches for calculating forecasts of hierarchical time series data (1) bottom-up, (2) top-down, (3) middle-out, and (4) optimal reconciliation. For this analysis, we use the optimal reconciliation method as it produces more accurate forecasts, in large part due to its increased complexity. To examine the relationship between climate variables and campylobacter cases in Connecticut, we utilized a seasonal hierarchical ARIMA model, considering the seasonality of campylobacter as well as creating a hierarchical structure to assess the trends of the data by county, with the most aggregated level that of the entire state.

ARIMA terms were estimated using the Box-Jenkins method. The first step was to assess the stationarity of the data, which was done by plotting the mean and range of the data against one another and calculating the Pearson's correlation coefficient. If the mean and range are correlated, the data is not stationary. Using log-transformed data can result in stationarity, however, and the data were log-transformed, with a constant of 1 added to the data prior to log transformation to avoid the undefined result of $\log(0)$. The predicted data was then de-transformed to estimate the raw case numbers. The Pearson's correlation coefficient was then re-calculated showing no correlation and indicating the data were now stationary.

The next step was to determine the (p, d, q) and (P, D, Q) values for the model by plotting the autocorrelation function (ACF) and partial autocorrelation function (PACF). The p, d, q values denote the AR (p), I (d), and MA (q) terms in the ARIMA model. The AR term contains the relationship of one observation to a certain number (p) of previous observations. The I term (d) denotes the amount of differencing to occur to create a stationary dataset. Since, the data was already stationary from the log transformation, we set this value equal to 0. Finally, the MA term (q) represents the relationship between one observation and the residual error. Additionally, the P, D, Q values denote the seasonal ARIMA terms, which can account for consistent seasonality in the data. Because the log-transformed data were stationary, the differencing term (d) was set to 0. Multiple variations of these terms were considered, and the best fit model was selected based on the lowest Akaike Information Criterion (AIC) score.

The historical weekly average temperature and precipitation values were included in the model as external regressors and assessed at different lags. The optimal model was then fitted to the first fourteen years of campylobacter data (the training set) and prediction values for the final five years of data (the testing set) were generated and compared to the observed number of campylobacter cases during these five years, to assess the fit of the model.

Forecasting Hierarchical Time Series

Campylobacter cases per Connecticut county were combined into a hierarchical time series data type, creating a top level that includes the total cases in Connecticut for each week from week 1, 2000 to week 52, 2018. The second level contained each county's case data by week. Historical temperature and precipitation were used again as external regressors for the historical campylobacter data; we incorporated these at the best-fit lag identified by the ARIMA model with the lowest AIC score, as well as from the Poisson regression analysis. Both methods

identified the same optimal lag time. The projected temperature and precipitation were also included in the forecast as the external predictors (at the best-fit lag) for the predicted campylobacter case values. These forecasts were then generated, mapped, and assessed for historical accuracy by examining both the Mean Absolute Percentage Error (MAPE) and the Mean Absolute Scaled Error (MASE).

Results:

The burden of campylobacter infections in Connecticut in the 21st century was concentrated in the most populated counties, as expected, with Fairfield, New Haven, and Hartford counties accounting for more than three-quarters of all cases statewide (Figures 1 & 2). Litchfield, Middlesex, New London, Tolland, and Windham counties, therefore, have historically made up a minority of reported cases. When observing cases across years by week of the year to assess seasonality, the seasonality of the campylobacter data remained strong over time, with a distinct peak in the summer weeks occurring between late May to early September (Figure 3). The average number of cases by week from 2000-2009 and from 2010-2018 is also shown in Figure 3. While the average has not changed during the beginning of the year, there has been an increase at the peak of the season (approximately week 27) in more recent years compared to 2000-2009. From 2010-2018 there was also larger peaks in cases later in the year, showing that any increase in cases is occurring either during the summer season or late in the year during the winter season.

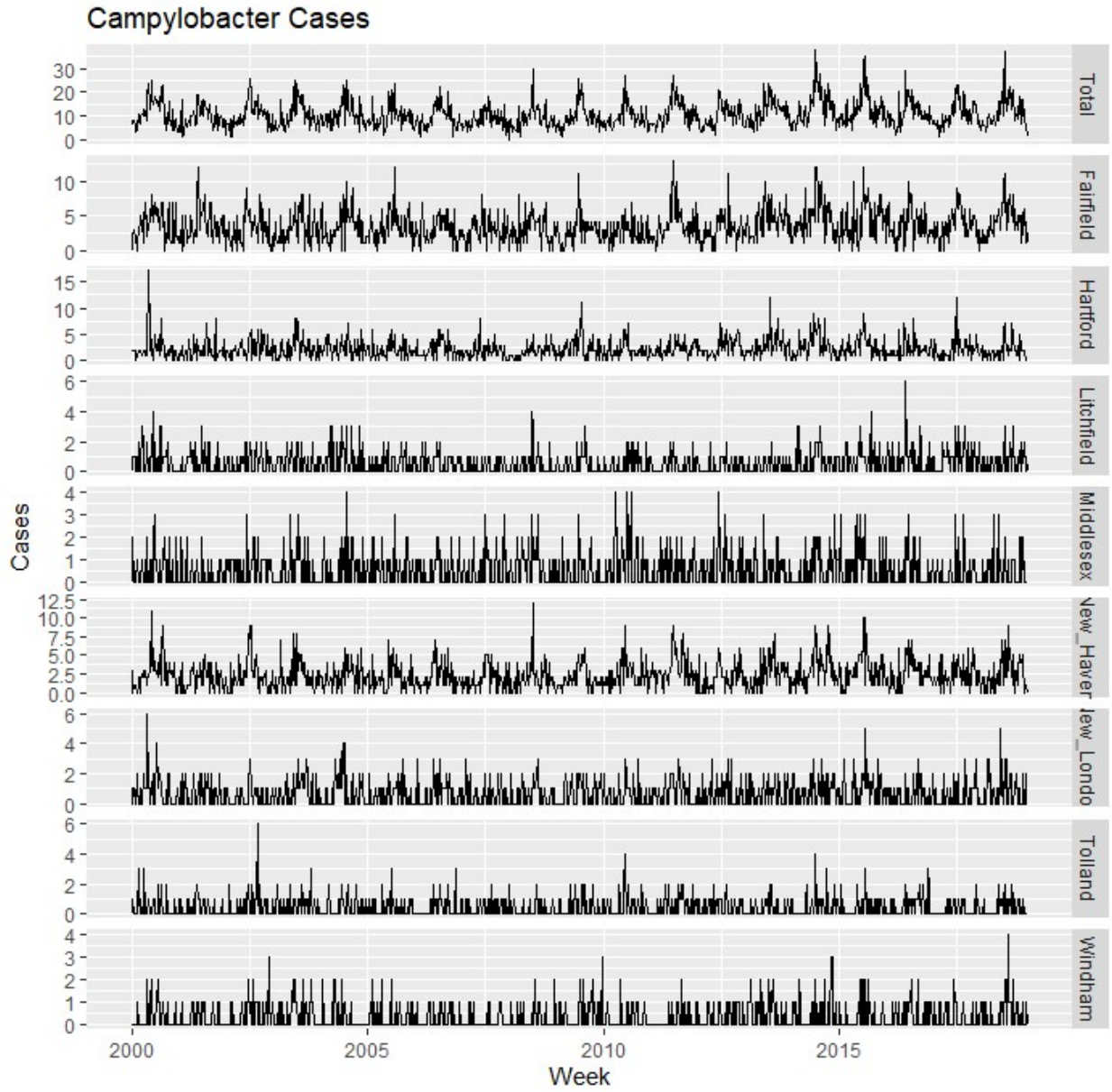


Figure 1. Time Series of Campylobacter Cases in Connecticut, by County (2000-2018)

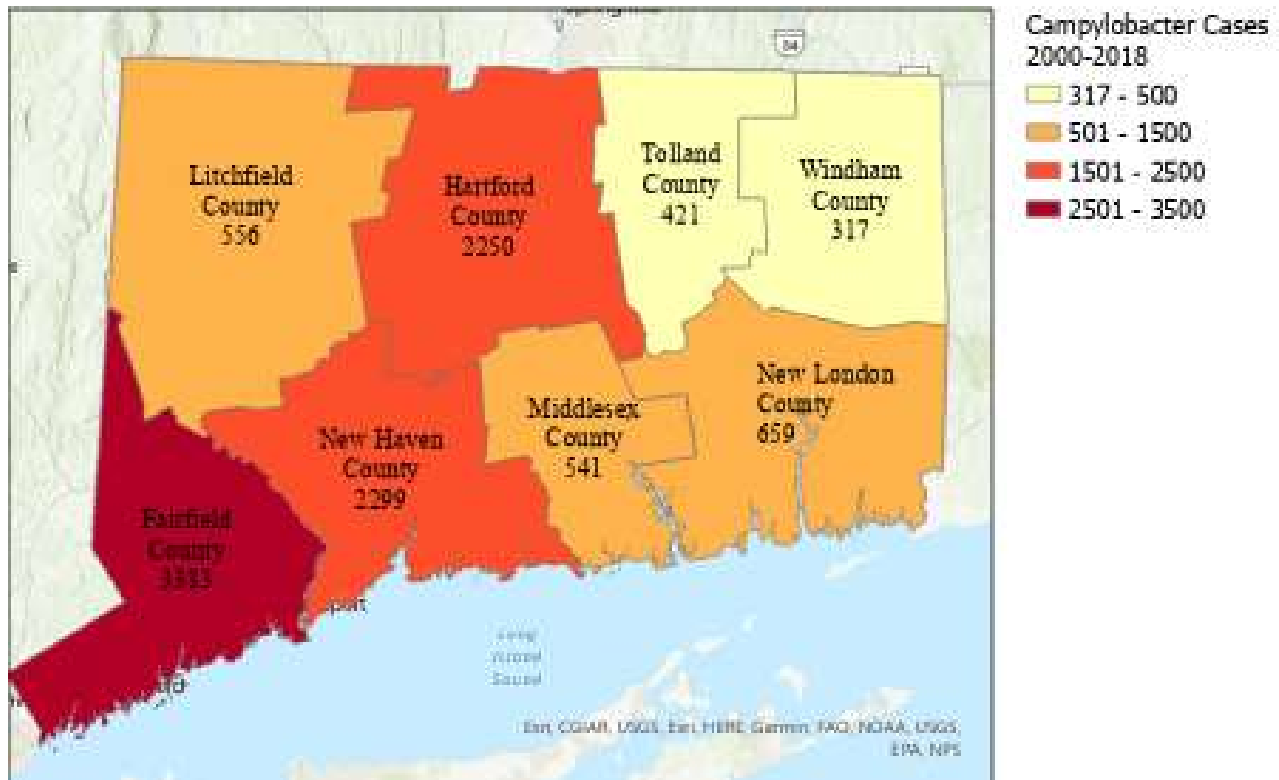


Figure 2. Total Campylobacter Cases by County, 2000-2018

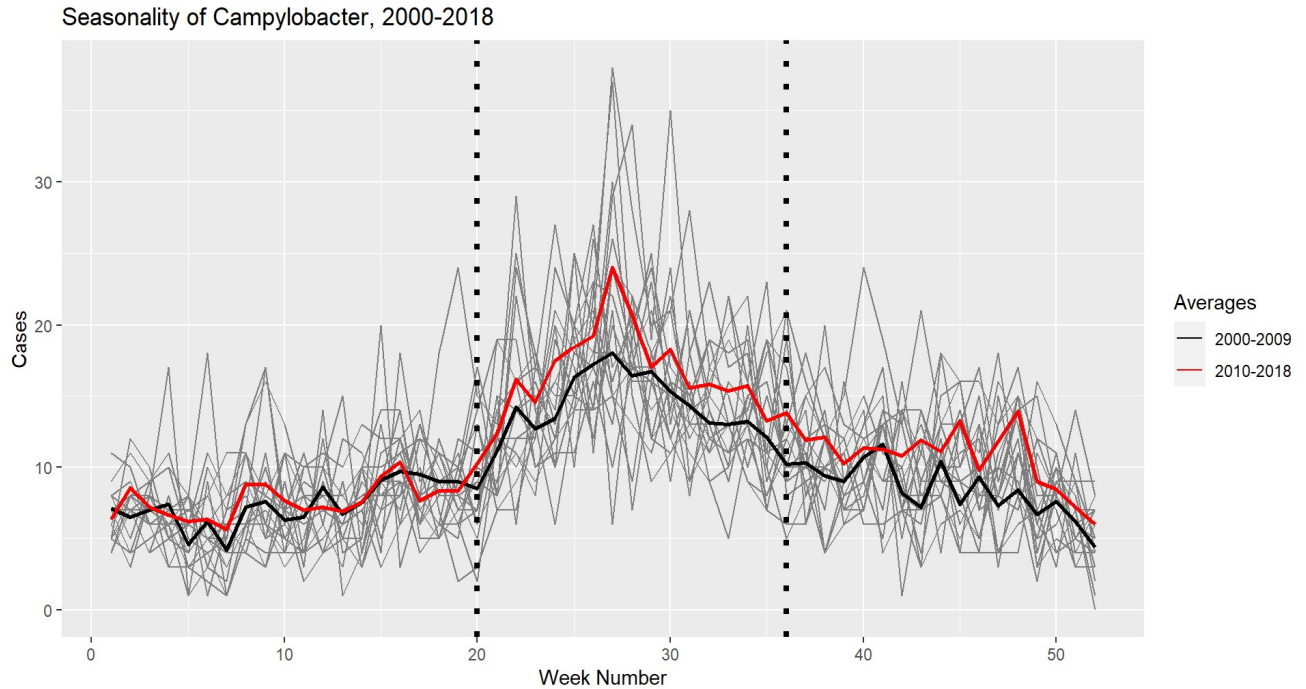


Figure 3. Seasonality of Campylobacter, 2000-2018

The preliminary Poisson regression analysis showed a statistical significance for temperature at every lag, 0-8 weeks. However, precipitation was found to only be statistically significant at a lag of 5 weeks. At a lag of 5 weeks, the incidence rate ratios (IRR) for temperature and precipitation were 1.018 and 1.024, respectively. A 1° increase in temperature was associated with a 1.8% increase in campylobacter cases. Similarly, a 1-inch increase in precipitation was associated with a 2.4% increase in campylobacter cases (Table 1).

Lag (weeks)	Regressor	Coefficient	IRR	95% CI	P-value
0	Temperature	0.021	1.022	(0.020, 0.023)	<2e-16
	Precipitation	0.012	1.012	(-0.008, 0.032)	0.244
1	Temperature	0.021	1.021	(0.020, 0.022)	<2e-16
	Precipitation	0.003	1.003	(-0.017, 0.023)	0.756
2	Temperature	0.021	1.021	(0.020, 0.022)	<2e-16
	Precipitation	0.011	1.011	(-0.009, 0.022)	0.279
3	Temperature	0.020	1.020	(0.019, 0.021)	<2e-16
	Precipitation	0.016	1.016	(-0.005, 0.036)	0.126
4	Temperature	0.019	1.020	(0.018, 0.021)	<2e-16
	Precipitation	0.005	1.005	(-0.015, 0.025)	0.615
5	Temperature	0.018	1.018	(0.017, 0.020)	<2e-16
	Precipitation	0.024	1.024	(0.004, 0.044)	0.019
6	Temperature	0.017	1.017	(0.016, 0.018)	<2e-16
	Precipitation	-0.002	0.998	(-0.022, 0.019)	0.879
7	Temperature	0.016	1.016	(0.014, 0.017)	<2e-16
	Precipitation	-0.008	0.992	(-0.029, 0.012)	0.441
8	Temperature	0.014	1.014	(0.012, 0.015)	<2e-16
	Precipitation	0.016	1.016	(-0.004, 0.036)	0.118

Table 1. Poisson Regression Analysis of Lagged External Regressors

Utilizing the Box-Jenkins approach to assess stationarity of the data, the mean and range of cases was somewhat positively correlated with a correlation coefficient of 0.622. By log-transforming the data, however, this correlation was removed, and the log of cases was then used in the model going forward. In determining the ARIMA terms, the autocorrelation (ACF) and partial autocorrelation (PACF) plots showed the need for both AR and MA terms (Figure 4). Based on the ACF and PACF plots, an AR term was needed at p lags. The p term was estimated from the PACF plot where lags of 1 through 5 were found to be significant. The ACF plot also indicated a potential MA term at q lags. Because these plots also show spikes at annual lags (52 weeks), possible seasonal AR and MA terms were also included in the model. Evaluating several models with differing AR and MA terms, from 1 to 5, and including seasonal AR and MA terms, the best fit seasonal ARIMA model with the lowest AIC score was found to be ARIMA (3,0,3) (1,0,1) [52] (Table 2).

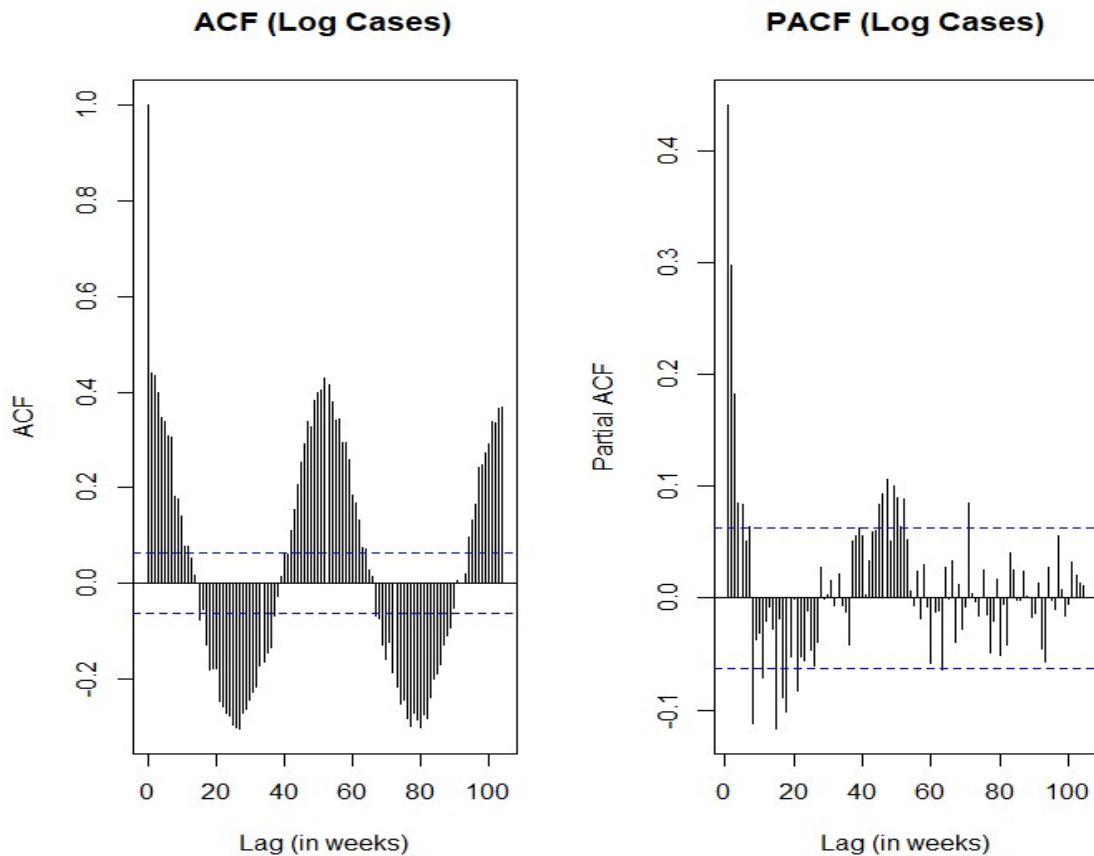


Figure 4. Autocorrelation (ACF) and partial autocorrelation (PACF) plots of log-transformed *Campylobacter* cases.

External regressors of temperature and precipitation for the accompanying week were also evaluated in the model at differing lags, from 0 to 8 weeks. The best-fit model included temperature and precipitation lagged five weeks behind the reporting of campylobacter cases (Table 2), matching the results from the Poisson regression analysis (Table 1). In addition to the AIC score, the model was also evaluated by fitting the chosen ARIMA model to the first fourteen years of cases and then using the fitted model to predict the final five years of the historical data. When compared with the observed data from 2000-2013, the predicted values for 2014-2018 showed the model to be a good fit (Figure 5). The mean absolute percent error

(MAPE) for the model was 13.04, indicating an approximate 13% error between the observed and predicted values, and resulting in the model being 86.96% accurate.

ARIMA Terms	AIC Score
(3,0,3) (1,0,1)	911.86
(4,0,1) (1,0,1)	912.71
(4,0,3) (1,0,1)	913.78
(4,0,4) (1,0,1)	912.05
(5,0,5) (1,0,1)	913.18
(3,0,3) (1,0,1) + external regressor (lag=0)	893.04
(3,0,3) (1,0,1) + external regressor (lag=1)	889.89
(3,0,3) (1,0,1) + external regressor (lag=2)	893.94
(3,0,3) (1,0,1) + external regressor (lag=3)	901.77
(3,0,3) (1,0,1) + external regressor (lag=4)	887.36
(3,0,3) (1,0,1) + external regressor (lag=5)	878.2
(3,0,3) (1,0,1) + external regressor (lag=6)	881.86
(3,0,3) (1,0,1) + external regressor (lag=7)	884.63
(3,0,3) (1,0,1) + external regressor (lag=8)	895.52

Table 2. Potential ARIMA Models

Observed vs. Predicted Number of Cases

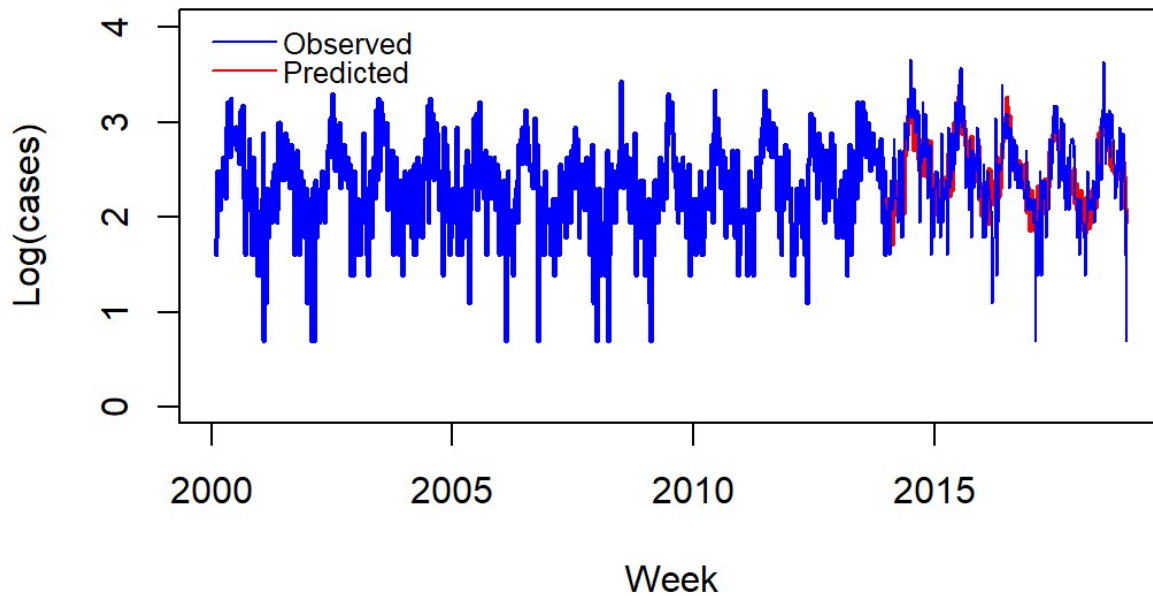


Figure 5. Model Fit, Observed vs. Predicted

Using the forecasted temperature and precipitation for future years 2019 through 2050 as external predictors, the best fit ARIMA model was used to predict cases of campylobacter by each county in the hierarchical time series. The optimal reconciliation (combination) method was

used for the model resulting in estimating cases with both the bottom-up and top-down strategies (Figure 6). Overall, the model predicts 17,352 cases during the forecast period in Connecticut, with Fairfield County having the most cases (Table 3).

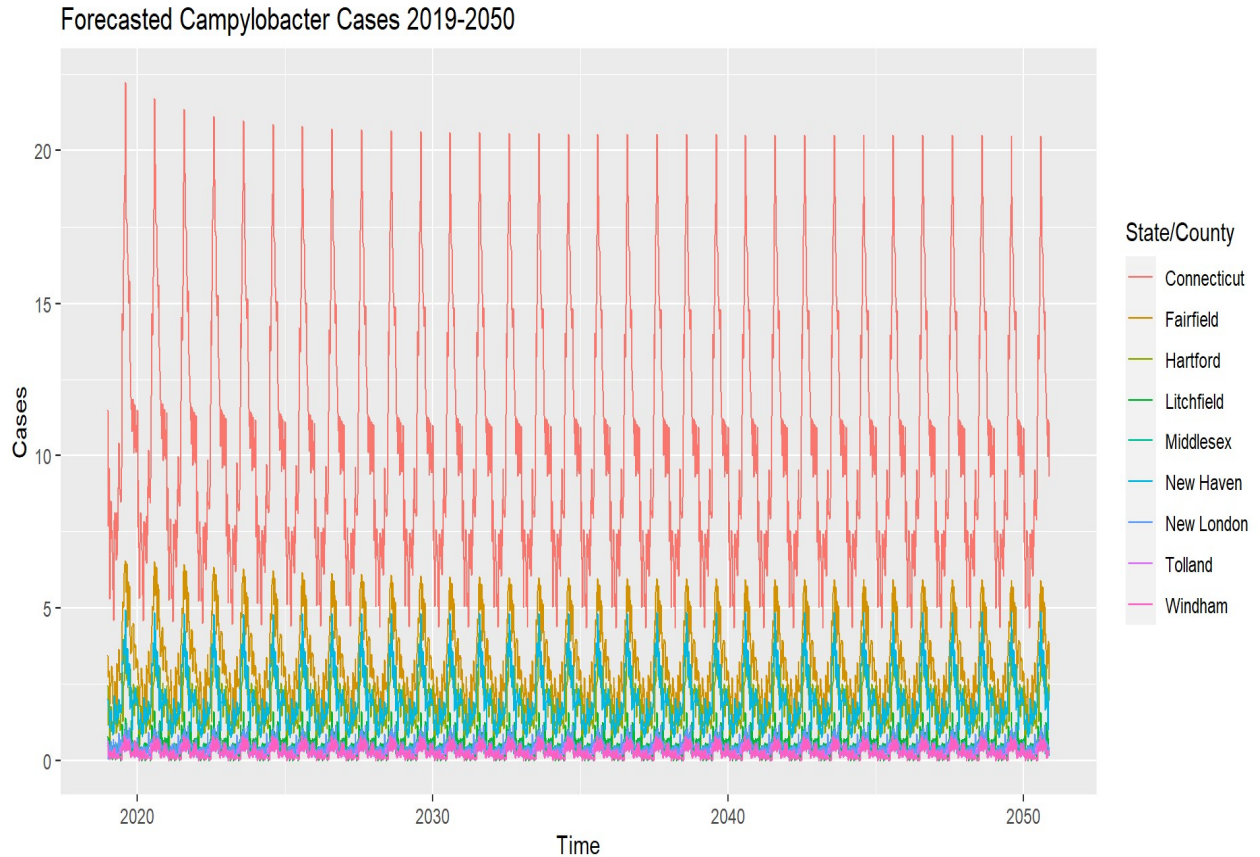


Figure 6. Projected Campylobacter Cases by County, 2019-2050

County	Total Cases (2019-2050)	Average Cases per Year (2019-2050)	Average Cases per Year (2000-2018)
Connecticut	17,352.61	542.79	548.74
Fairfield	5,397.61	168.60	178.05
Hartford	3,239.71	101.56	118.42
Litchfield	879.02	27.54	29.26
Middlesex	678.15	21.25	28.47
New Haven	3,416.31	107.28	121
New London	846.26	26.51	34.68
Tolland	545.51	17.09	22.16
Windham	462.15	14.47	16.68

Table 3. Forecasted Campylobacter Cases, 2019-2050

Discussion/Limitations:

The main objective of this analysis was to determine that, given the overall rise in temperature and precipitation that is likely to occur over the next several decades because of climate change, what impact will this have on the burden of campylobacter in Connecticut. This analysis found that campylobacter cases are highly correlated with the temperature and precipitation five weeks prior to the specimen collection date of a case. However, even with this correlation, cases of campylobacter are not projected to increase, on average, across the state through 2050. Counties that currently have a high burden of illness will continue to experience a similar burden in the coming decades.

Even though it is estimated that the underreporting multiplier for campylobacter in the United States is approximately 30, resulting in hundreds of thousands of cases not reported annually, because this model assumes this underreporting factor remains constant over time, the accuracy of the model is not affected (Wagenaar & Havelaar, 2013) (Scallan, et al., 2011). However, the total number of campylobacter cases both observed historically and in the future in the population can be estimated with this multiplier. In addition, the most significant time lag between temperature and precipitation and the specimen collection of a reported campylobacter case was found to be five weeks. Because specimen collection date is collected for all confirmed campylobacter cases in Connecticut, this measure was used for case identification. Unfortunately, symptom onset date is not collected for all cases, as it relies on either physician reported onset dates or successful contact of the case by either the Yale EIP or the LHD to gather this information. Even when collected from the case, self-reported symptom onset dates can be less accurate and prone to poor recall. If complete symptom onset dates would have existed for

all cases, this would have potentially resulted in different, possibly shorter, time lags between the timing of a case and the climate drivers.

The weekly availability of the campylobacter data was able to produce a more detailed analysis than that of previous analyses relying on monthly or annual data. However, the availability of daily data would have been able to provide a more granular analysis over the time period. Even though this analysis did not find a significant increase in cases over time, the study did not account for antimicrobial resistance changes. With evidence that higher prevalence of antimicrobial resistance is associated with higher temperatures, future campylobacter cases could potentially prove harder to treat (MacFadden, et al., 2018). Even though most cases are not treated with antibiotics, high-risk individuals such as those of older age and/or with compromised immune systems often rely on antibiotics to clear their infection. This could prove more difficult with the increasing surface temperatures over the next few decades, resulting in more prolonged infections and higher hospitalizations.

In addition, one of the largest sources of campylobacter infections stems from consuming undercooked and/or contaminated poultry products. In the United States, consumption of chicken has increased drastically compared to that of other meat such as beef or pork, which have been decreasing over time. Since 1970, consumption per capita of chicken has grown by 160%, while beef and pork have decreased by 31% and 6%, respectively (Tonsor & Lusk, 2021). Because this consumption of chicken is only projected to grow, the risk of contamination may increase as poultry farming attempts to keep up with demand, and environmental policies to ensure safe products could fall behind. This threat, and its impact on the burden of campylobacter infections in the future, warrants further analysis. Climate change does not only directly correlate to disease, but can also impact indirect channels, such as antimicrobial resistance and food supply

safety. To reduce the effect that worsening climate change might have on foodborne illnesses, intervention in multiple sectors is imperative. Further research is needed in better understanding how climate change, and our inability to properly respond and prevent its consequences, can keep foodborne diseases on the rise in the United States.

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