CAMPYLOBACTERIOSIS ANALYSIS FOR JOHNSON COUNTY, KANSAS

BY

REBECCA MEGEE

B.S. Animal Sciences, Kansas State University, 2014

A FIELD EXPERIENCE REPORT

submitted in partial fulfillment of the requirements for the degree

MASTER OF PUBLIC HEALTH

Master of Public Health Program Department of Diagnostic Medicine/Pathobiology College of Veterinary Medicine

KANSAS STATE UNIVERSITY

Manhattan, KS

2016

© Copyright

REBECCA MEGEE

2016

ABSTRACT

Johnson County is the most populated county in Kansas, with 575,000 residents. Campylobacteriosis is one of the most common enteric diseases reported in Johnson County. Its occurrence is reportable by law to the Kansas Department of Health and Environment. The purpose of this Campylobacteriosis Analysis is to look further into the burden of campylobacteriosis in Johnson County as well as compare current testing methods.

The two most common testing methods for campylobacteriosis are stool culture and the stool antigen test. The stool antigen test can provide same day results but it has a variable positive predicted value ranging from 36.6% to 75.9% (Fitzgerald et al., 2016). Five hospitals in Johnson County were assessed, and it was found that the stool antigen test was the most common test in use to diagnose campylobacteriosis. Two out of the five hospitals assessed also have a protocol in place to perform stool culture confirmations on the samples, which tested positive by the stool antigen test. The culture confirmations are not required to be reported to the Johnson County Department of Health and Environment.

If stool culture results were reported after the respective positive stool antigen tests, then Johnson County might see a change in the apparent prevalence of this disease. If the Johnson County Department of Health and Environment were to follow up with the hospitals' labs to obtain the results of the culture, or the hospitals began reporting the culture results to the Health Department, then apparent campylobacteriosis numbers might decrease. Johnson County can then have a more accurate representation of campylobacteriosis cases.

TABLE OF CONTENTS

List of Figuresvi
List of Tablesvii
Acknowledgements viii
Chapter 1 - Background
1.1 Johnson County Department of Health and Environment
1.2 Objectives of the Campylobacteriosis Analysis1
1.3 Campylobacteriosis and Other Enteric Diseases in Johnson County
1.4 An Overview of Campylobacteriosis
1.5 Comparison of Campylobacteriosis Testing Methods
Chapter 2 - Methods and Results
2.1 Limitations of Data
2.2 Pre/Post Stool Antigen Test Summary
2.3 Hospital Breakdown of Campylobacteriosis Cases
2.4 Follow up on EIA tests for Culture
Chapter 3- Discussion and Conclusion
3.1 Discussion of Data15
3.2 Conclusion and Limtations
Chapter 5- Field Experience and Core Competencies
5.1 Other Duties at JCDHE
5.2 MPH Core Competencies
References

LIST OF FIGURES

Figure 1. Positive Reported Campylobacteriosis Test Counts by
Test Method in Johnson County from 2007-2015
Figure 2. The Incidence Rates of Reported Positive
rigure 2. The merdence Rates of Reported Positive

LIST OF TABLES

Table 1. Campylobacteriosis Cases in Johnson County
and its Sister Counties per 100,000
Table 2. Enteric Disease Counts in Johnson
County in the Last Five years
Table 3. A Comparison of the Sensitivity, Specificity, Positive
Predicted Value, and Negative Predicted Value of Stool Antigen
Tests from Three Different Studies
Table 4. Analysis of increase in Antigen testing by year
Table 5. Summary table of test type and increase rate
11
Table 6. Breakdown of Initial Testing Method used by Hospitals
in Johnson County

ACKNOWLEDGEMENTS

I would like to thank everyone at the Johnson County Department of Health and Environment. It was a great experience to see public health in a real world setting. I would especially like to thank my preceptor, Caitlin Walls, for giving me guidance on this project and teaching me how to navigate the EpiTrax and AVR systems.

I thank my major professor, Dr. Nguyen, for answering all my questions and concerns throughout the year. She gave me support while I was trying to finish the Master's degree program. I thank my Master's committee members, Dr. Davis and Dr. Sanderson, for their responsiveness and discussions about my future in public health.

I also thank Mrs. Barta Stevenson for always being there to answer all my questions, even though some of them might have seemed silly. She was the first person I consulted with when I was thinking about starting the program, and she gave me great advice. I would also like to thank Dr. Mulcahy for taking the time to help me practice my presentation.

Lastly, I would like to thank my family because without them none of this would have been possible. They have stuck by my side and supported me along the way. They have made my future bright and I will forever be grateful.

CHAPTER 1 Background

1.1 Johnson County Department of Health and Environment

This field experience took place at the Johnson County Department of Health and Environment (JCDHE). Caitlin Walls, an MPH Epidemiologist, was the preceptor and provided guidance through the details of this project as well as provided instruction on various internal programs, information on gathering techniques and analysis of the data. The JCDHE has two locations: the Olathe office, 11875 S. Sunset Dr, Suite #300, and an office in Mission, 6000 Lamar Ave, Suite #140. The majority of my field experience was conducted at the Mission location.

Prior to 2012, the JCDHE was divided into two separate entities. The JCDHE now functions as one entity with health and environment divisions. The environment division programs include air quality, hazardous materials, on-site sewage treatment, rabies testing, recycling and waste reduction, solid waste management, and swimming pool and spa inspection. The JCDHE health division includes programs such as prenatal care, women's and men's health, laboratory services, immunizations, disease containment, public health emergency, and customer service specialists. The project for this field experience is under the disease containment sector of the health division.

Johnson County is the most populous county in Kansas with a population of approximately 575,000. It occupies 473 square miles of the south-west quadrant of the Kansas City metropolitan area. Within this area, there are 20 different cities including 3 colleges, 6 hospitals, 66 nursing homes, 6 school districts, and 1,522 restaurants. Johnson County is 59% urban and 41% rural. There are 340 parks spanning 16,000 acres. The median age is 36.5 years and the median income is \$74,761.

1.2 Objectives of the Campylobacteriosis Analysis

The first objective of the campylobacteriosis analysis was to examine the testing methods used by the hospital laboratories of Johnson County. Other objectives of this study were: 1) to conduct background research on campylobacteriosis stool antigen test and its validity, 2) to review reported positive cases of campylobacteriosis and their test methods, 3) to provide a hospital breakdown of reported positive cases when available and finally to provide results to the JCDHE. Due to the likelyhood of stool antigen test to give

false positive results, the number of reported campylobacteriosis cases in Johnson County would decrease if stool antigen tests were confirmed by stool culture tests.

1.3 Campylobacteriosis and other Enteric Diseases in Johnson County

Table 1 shows the positive campylobacteriosis cases reported in Johnson County compared to its sister counties. The sister counties are the Kansas counties that are closest in population. According to the 2014 census, the populations of these counties were as follows: Douglas 116,585, Leavenworth 78,797, Shawnee 178,406, Sedgwick 508,803, and Wyandotte 161,636.

Table 1. Reported Campylobacteriosis Cases in Johnson County and its Sister Counties per 100,000

 persons. This data was obtained through EpiTrax.

County of Residence	Campylobacteriosis Cases per 100,000 persons Year reported to Public Health							
Kesidence								
	2011	2011 2012 2013 2014 2015						
Douglas	10	10	15	21	15			
Johnson	22	20	20	21	26			
Leavenworth	20	9	13	20	24			
Sedgwick	13	15	15	15	11			
Shawnee	62	42	26	36	34			
Wyandotte	15	12	15	16	17			

According to the Centers for Disease Control and Prevention (CDC), campylobacteriosis is one of the most common enteric diseases associated with foodborne illness (2014). Table 2 shows the number of reported campylobacteriosis cases compared to the other enteric diseases in Johnson County from 2011-2015. The staff of JCDHE must review every reported case.

Year Reported to	Disease							
Public Health	Campylobacteriosis	Listeriosis Salmonellosis		Shiga toxin- producing Escherichia coli	Shigellosis			
2011	128	3	67	20	8			
2012	117	2	71	19	14			
2013	116	1	52	21	6			
2014	123	0	58	30	6			
2015	149	1	89	24	40			
Average	126.6	1.4	67.4	22.8	14.8			

Table 2. Enteric Disease Cases in Johnson County 2011-2015. This data was obtained through EpiTrax.

1.4 An Overview of Campylobacteriosis

The CDC estimates campylobacteriosis affects 1.3 million people and causes 76 deaths per year (2014). Campylobacteriosis is caused by gram-negative, rod-shaped bacteria in the genus Campylobacter. There are several Campylobacter species, but two are known to cause the majority of human disease, *Campylobacter jejuni*, and *Campylobacter coli*. Animals such as chickens, cattle, pigs, sheep, ostriches, and shellfish are the main reservoirs for Campylobacter (CDC 2014).

Campylobacter is both waterborne and foodborne. Modes of transmission include fecal-oral, person-toperson, and animal-to-person (CDC 2014). Most cases of infection in the United States are associated with consumption or handling raw poultry. The organism must be swallowed in order to cause disease. Person-to-person transmission is rare but can occur with caretakers of infected persons, employees of day care facilities, and nursing homes. Symptoms of the disease present within 2-5 days of exposure and include diarrhea, cramps, abdominal pain, and fever. Antibiotics may be used for treatment, but most people recover without treatment (CDC 2014). The illness typically lasts 1 week, but patients are infectious as long as they are excreting Campylobacter in their stools, which may occur for several weeks after clinical recovery. On occasion, Campylobacter causes reactive arthritis or Guillain-Barre syndrome where the immune system attacks the nerves (Nachamkin *et al.*, 1998). Rarely bacteremia is primarily seen in immunocompromised patients.

Many campylobacteriosis cases are isolated incidents and go undiagnosed. However, campylobacteriosis is a reportable disease, and when the symptoms are present in a patient, a healthcare provider should send a stool sample to a diagnostic lab for analysis. Campylobacteriosis can also be associated with larger outbreaks as seen with consumption of unpasteurized milk or contaminated water (CDC 2014). Prevention practices such as cooking meat thoroughly, washing hands, avoiding cross contamination, steering clear of unpasteurized products and untreated water decrease Campylobacter infections.

The JCDHE abides by the case classification of the National Notifiable Disease Surveillance System (NNDSS), which requires isolation of Campylobacter spp. from a clinical specimen for confirmation. The only way to isolate the bacterium is through stool cultures, so unless a culture is completed, a campylobacteriosis case remains a suspect case. The staff at the JCDHE are required to investigate any confirmed or suspect case. The Kansas Department of Health and Environment's (KDHE) Campylobacteriosis Investigation Guidelines warn against use of non-culture methods as standalone tests for the detection of Campylobacter in stool specimens. The warning also states that, based on the data available, the performance characteristics of the non-culture stool antigen tests are highly variable with their sensitivity ranging from 78.8%-86.3%, specificity ranging from 95.9%-97.3% and positive predictive value (PPV) ranging from 36.6%-75.9% (Fitzgerald *et al.*, 2016). The KDHE urges culture confirmation of non-culture positive results. Despite these warnings and recommendations, it is unclear if hospitals in Johnson County are following up positive stool antigen tests with culture methods.

1.5 Comparison of Campylobacteriosis Testing Methods

Historically, culture has been the primary method used for recovery of Campylobacter from stool samples and is considered to be the gold standard, with a sensitivity of 93% and specificity of 99% (Hindiyeh *et al.*, 2000; M'ikanatha *et al.*, 2012). Culture methods include using selective media, such as Skirrow's medium, charcoal cefoperazone deoxycholate agar, or Campy-Cefoperazone, Vancomycin, and Amphotericin medium, placed in a microaerophilic growth environment and incubated at 42 ° C (Granato *et al.*, 2010). After 72 hours, the media can be checked for Campylobacter growth. The growth is then identified by Gram's staining and oxidase test (Granato *et al.*, 2010).

Nonculture tests, such as stool antigen tests, allow for direct detection of Campylobacter antigens in stool specimens (Granato *et al.*, 2010; Giltner *et al.*, 2012). These tests detect an antigen called Campylobacter-specific antigen which is shared by both C. *jejuni* and C. *coli*; therefore, these tests are unable to differentiate between serotypes (Granato *et al.*, 2010).

There have been concerns regarding the validity of the antigen tests. The validity of a test depends on its ability to distinguish between those who have a disease and those who do not. This is broken down into two components; sensitivity and specificity. Sensitivity is the ability of the test to correctly identify those who have the disease while specificity is the ability of the test to correctly identify those who do not have the disease. To calculate test's sensitivity and specificity, a reliable gold standard test method is needed or the application of no gold standard Bayesian methods.

Another factor to consider regarding the validity of a testing method is the positive predictive value (PPV), the proportion of cases identified by a test that are true cases. The PPV is affected by the prevalence of the disease, and by the sensitivity and specificity of the test. The prevalence is the number of affected persons present in a population divided by the total population at risk during a specific time. A higher prevalence leads to an increase in PPV for a given sensitivity and specificity. The specificity of the test is particularly influential on the PPV if the prevalence of the disease is low.

A study conducted by Granato *et al.* (2010) compared three stool antigen tests to the traditional culture method, using real-time polymerase chain reaction (PCR) for validation. This study had a prevalence of 26% (Granato *et al.*, 2010). The three tests that were used were 1) the Premier CAMPY enzyme immunoassay (Meridian Biosciences, Cincinnati OH), 2) the ProSpect Campylobacter enzyme immunoassay (Remel, Lexena KS), and 3) the ImmunoCard STAT! CAMPY test (Meridian Biosciences, Cincinnati OH). Both enzyme immunoassay (EIA) tests are microplate assays while the STAT! test is a lateral flow immunochromatographic assay (Granato *et al.*, 2010). The sensitivity and specificity ranged from 98.4%-99.2% and 94.2%-96.1% respectively. The negative predicted value (NPV), the probability the case will test negative given they do not have the disease, ranged from 98.8%-99.7% (Granato *et al.*, 2010). The authors also reported that the culture method had a sensitivity of 94.1%, but the authors did not report the specificity (Granato *et al.*, 2010). The Granato *et al.* (2010) study was conducted in a lab controlled environment.

Another study, by Fitzgerald *et al.* (2016), was conducted in a field setting, using results from hospitals and public health labs. They tested four stool antigen tests, the same three as the previous study and also

the Xpect Campy (Fitzgerald *et al.*, 2016). The Fitzgerald *et al.* study (2016) found that the stool antigen tests had a sensitivity of 78.8%-86.3%, specificity of 95.9%-99.2%, NPV of 99.4%-99.6% and PPV of 36.6%-75.9% across labs with varying testing protocols. The study, which used stool culture as the reference method, found that stool culture had a sensitivity of 89.9%; however, the authors did not report its specificity, PPV or NPV (Fitzgerald *et al.*, 2016). Reasons for the discrepancies between the two studies could be due to prevalence. The Fitzgerald *et al.* study came from an unselected population which represents a more realistic field prevalence, 3.1%, as compared to the Granato studies causing a lower PPV. The Fitzgerald study also mentioned that the detection of other Campylobacter species in the stool antigen tests may account for discordant results in their study (Fitzgerald *et al.*, 2016). It is also a possibility that positive Campylobacter-antigens are seen in combination with positive results for other pathogens, such as Shiga-toxin-producing *E. coli* (Fitzgerald *et al.*, 2016).

The Food and Drug Administration (FDA)'s performance claims on all stool antigen tests were based on outpatient specimens (Giltner *et al.*, 2012). One study, conducted to examine the verification and implementation of the Premier CAMPY EIA test, used specimens from both outpatients and inpatients with complicated medical histories (Giltner *et al.*, 2012). It found that the Premier CAMPY EIA stool antigen test had a sensitivity of 75%, a specificity of 96.5%, a PPV of 42.9%, and an NPV of 99% (Giltner *et al.*, 2012). The prevalence of disease in this study was 1.71% (Giltner *et al.*, 2012). Giltner and colleagues (2012) stated that more verification is needed regarding the stool antigen tests from inpatients. A summary of these studies is provided in Table 3. These study results indicate that none of the tested stool antigen tests provide a high enough PPV, sensitivity and specificity to function as a stand-alone diagnostic test for Campylobacter (Fitzgerald *et al.*, 2016; Giltner *et al.*, 2012).

Table 3. Sensitivity, Specificity, Positive Predictive Value, and NegativePredictive Value of Stool Antigen Tests From Three Different Studies.

Study	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Observed Prevalence
Granato <i>et al</i> . 2010	98.4-99.2	94.2-96.1	90.0-92.6	98.8-99.7	26%
Fitzgerald <i>et al</i> . 2016	78.8-86.3	95.9-99.2	36.6-99.2	99.4-99.6	3.1%
Giltner et al. 2013	75	96.5	42.9	99	1.71%

As mentioned above, a wide variety of laboratory practices for handling and processing specimens can affect the recovery and detection of Campylobacter. A study conducted by M'ikanatha *et al.* (2012) reviewed 176 labs in Pennsylvania to assess their culture methods. While the study did not assess the amount of time from sample collection to delivery to the clinical lab, it did find that 75.7% of labs were processing samples within four hours of them arriving at the lab (M'ikanatha *et al.*, 2012). The labs were finalizing cultures between 24-72 hours and were using different methods of identification (M'ikanatha *et al.*, 2012). A total of 158 labs used the culture method while 17 labs used stool antigen tests instead of culture. One lab used both methods in combination. A study by Hurd et al. (2012), which assessed 411 clinical laboratories from across the United States, found similar results and urged standardization and provided best practice recommendations.

In 2009, the CDC provided testing guidelines for *E. coli* 0157 and other Shiga toxin producing *E. coli* pathogens. They recommended both stool antigen and culture testing of *E. coli* positive stool antigen samples. Since this recommendation, improved surveillance and outbreak investigations of those pathogens has been noted (CDC 2014). Thus, standardized guidelines for Campylobacter testing would likely provide more accurate surveillance of this pathogen as well.

In summary, stool antigen tests have become a popular testing method for diagnosing campylobacteriosis, but the validity of the stool antigen test results is uncertain. More research is needed to test the cross reactions with antigens from other bacteria and how this cross-reactivity may affect the stool antigen test results. There also needs to be a standardization of the laboratory protocol for campylobacteriosis testing.

CHAPTER 2 Methods and Results

2.1 Limitations in Data

There are several factors that affect the data collected by the health department. The health department gets data from physicians' offices and laboratories across the county. In the case of campylobacteriosis, they receive data on those who test positive for the disease. There is no protocol in place to report follow up test results. The health department remains unware of negative follow up test results.

For a person to test positive for the disease, they must have symptoms present and seek medical attention. Their doctor must request a test for campylobacteriosis, a sample must be collected and submitted to the lab, and the lab must identify *Campylobacter* in the sample. The final step is reporting the positive test to the health department. Due to non-compliance, however, there is a possibility that a positive case may not be reported. It is also a possibility that a person with symptoms of the disease may never seek medical attention. Moreover, there are several unknowns. Because some people do not seek medical attention for Campylobacter infection, it is unknown how many people in the county actually have campylobacteriosis. In addition, negative tests are not reported; thus, the number of people who were tested for campylobacteriosis but tested negative is also unknown. This data, including the testing method, is needed to understand the epidemiology of campylobacteriosis in Johnson County.

2.2 Pre/Post Stool Antigen Testing Summary

In 2007, there was no single most popular testing method used to test for campylobacteriosis. As seen in Figure 1, most of the positive reported cases diagnosed fell into the "other" category, which included core antibody testing, microscopy, and PCR assays. In 2008, the culture method was used to diagnose all but four of the reported campylobacteriosis cases. In 2009, two antigen-based tests were approved by the FDA, and use of stool antigen testing started to increase. As shown in Table 4, there has been an 50.8% increase in the use of antigen testing since 2007.

Figure 1. Positive Reported Campylobacteriosis Test Counts by Testing Method in Johnson County from 2007 to 2015. The data from this figure came from EpiTrax.

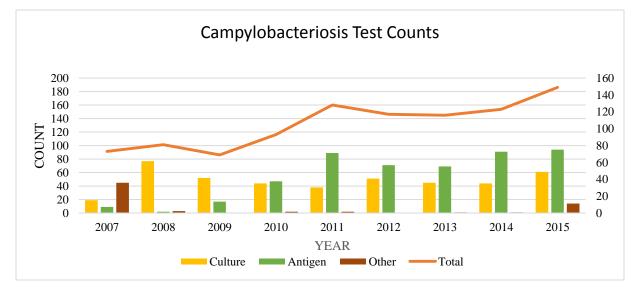


Table 4. Analysis of increase in Antigen testing by year. The data in this table was obtained in Epitrax.

YEAR	Total positive tests reported	Positive tests analyzed by Antigen test	Percent analyzed by Antigen test
2007	73	9	12.3%
2008	81	2	2.5%
2009	69	17	24.6%
2010	93	47	50.5%
2011	128	89	69.5%
2012	117	71	60.7%
2013	116	69	59.5%
2014	123	91	74.0%
2015	149	94	63.1%

The incidence has also increased as shown in Figure 2. However, this is likely not a true incidence rate because not every case of campylobacteriosis gets reported to the health department. The incidence rate is calculated by dividing the number of new cases of disease by the population at risk during a given time period. In this case, the number of new cases of campylobacteriosis reported to the health department in a given year was divided by the population of Johnson County in that same year. A summary of the test type and the incidence rate per 10,000 can be found in Table 5.

Figure 2. The Incidence Rates of Reported Positive Campylobacteriosis Cases in Johnson County from 2007-2015. The data from this figure came from EpiTrax.

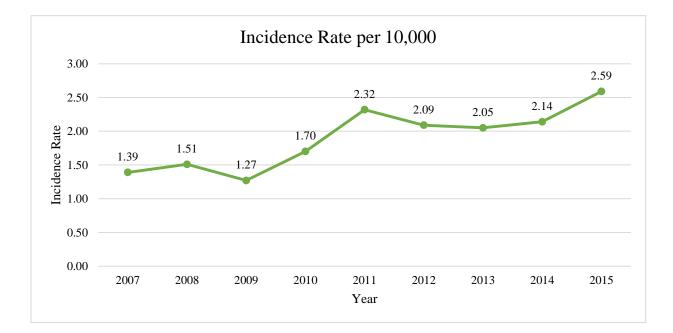


Table 5. Summary table of test type and incidence rate. The data from this table was obtained from EpiTrax.

YEAR	Total positive tests reported	Positive tests analyzed by Antigen test	Percent analyzed by Antigen test	Incidence rate per 10,000
2007	73	9	12.3%	1.39
2008	81	2	2.5%	1.51
2009	69	17	24.6%	1.27
2010	93	47	50.5%	1.7
2011	128	89	69.5%	2.32
2012	117	71	60.7%	2.09
2013	116	69	59.5%	2.05
2014	123	91	74.0%	2.14
2015	149	94	63.1%	2.59

2.3 Hospital Breakdown of Campylobacteriosis Cases

The positive campylobacteriosis cases from 2012-2015 reported to the JCDHE were analyzed using the Analysis, Visualization, and Reporting (AVR) system. Positive campylobacteriosis cases from the hospitals were selected and assessed individually. These hospitals included Menorah Medical Center, Olathe Medical Center, Overland Park Regional Medical Center, St. Luke's South Hospital, and Shawnee Mission Medical Center. There are six hospitals in Johnson County. The one absent from this report is Children's Mercy South. It is not included in this analysis because their protocol is to perform PCR testing for campylobacteriosis, rather than antigen testing or culture, which is the focus of the current study. Each case of reported positive campylobacteriosis was reviewed in EpiTrax to check the AVR's accuracy.AVR data was filtered by the location of diagnosis, year of diagnosis, Epitrax record number,

diagnostic test type and result, and underlying conditions. The data was further analyzed in Microsoft Excel.

Menorah Medical Center reported 16 cases positive by stool antigen test only. The stool antigen was used as the sole test for the reported cases. Olathe Medical Center used both stool antigen and culture tests. They reported 73 positive cases total; 65 cases were reported as tested by a stool antigen test and 8 tests were by culture as the sole testing method. Out of the 65 cases tested by the stool antigen method at Olathe Medical Center, 7 cases did report culture confirmations. The culture test was negative for 2 of the antigen test positives, suggesting two possible false positives.

Overland Park Regional Medical Center reported 19 positive cases. Reported cases were tested by the stool antigen tests, and one case had a confirmation test by PCR, which came back negative. Thus, the stool antigen test result was a possible false positive. Saint Luke's South reported 3 positive cases of campylobacteriosis in the years 2013 and 2015. Two of the reported cases from Saint Luke's South were tested by PCR and one case was tested by a stool antigen test. Shawnee Mission Medical Center, reported 47 cases of campylobacteriosis from 2013-2015. There was no data for 2012. Thirty-seven of these were diagnosed by stool antigen test and the remaining 10 by stool culture. There were 2 reported culture confirmations of stool antigen tests, which came back positive. There was no reason given as to why 2 out of the 37 cases were confirmed by culture.

Based on the data from the cases tested by the antigen method followed by culture confirmation (10 total), there were 3 possible false positives. This is a rate of 30%. However, due to lack of testing on all positive cases, and lack of information on the true negative cases, the false positive rate with antigen testing alone cannot be calculated. Table 6 provides a summary of the hospital breakdown of the initial testing method.

Table 6. Breakdown of Initial Testing Method used by Hospitals in Johnson County. This data was obtained from AVR.

		Breakdown of initial testing method			Antigen test-culture
Hospital	# of cases 2012 - 2015	culture	antigen	other	confirmation: # of possible false positives
Menorah	16	0	16	0	N/A
Olathe	73	8	65 ^b	0	2/7 (28.6%)
Overland Park	19	0	19 ^c	0	1/1 (100%)
St. Luke's South	3	0	1	2^d	N/A
Shawnee Mission	47 ^a	10	37	0	0/2 (0%)

^aOnly data from 2013-2015 was available.

^bSeven cases tested initially by antigen method were subsequently confirmed by culture; 2/7 cases were negative by culture.

^cOnly 1 of 19 cases had confirmatory test, in this case, by PCR analysis; 1/1 cases were negative by PCR ^dTwo cases tested by PCR

2.4 Follow Up on Stool Antigen Tests for Stool Culture Confirmations

Two hospitals, Menorah Medical Center and Olathe Medical Center, were chosen for an in-depth analysis for their follow-up testing. These two hospitals were specifically chosen because their current hospital protocol is to perform culture confirmations. There were 18 cases of campylobacteriosis at Olathe Medical Center in 2015 and 5 cases at Menorah Medical Center in 2015, for a total of 23 cases. All of the cases had culture follow-ups. Surprisingly, all cultures were negative for campylobacteriosis. This could be due to a very high false positive rate for the antigen test, a high false negative rate for the stool culture test, or a combination of both.

The Kansas state statutes, as listed on the KDHE website, require physicians and hospitals to report only the first positive campylobacteriosis test. The JCDHE were never made aware of the negative culture confirmations from Menorah Medical Center or Olathe Medical Center. These probable false positive cases of campylobacteriosis still remain in the count of total positive reported cases of campylobacteriosis in 2015.

CHAPTER 3 Discussion and Conclusion

3.1 Discussion of Data

Campylobacteriosis is the most commonly reported enteric disease in Johnson County. Most of the positive reported cases are diagnosed by either stool culture or stool antigen test. Several studies have reported variability in the specificity, sensitivity, PPV, and NPV for the stool antigen test (Granato *et al.*, 2010; Giltner *et al.*, 2013; Fitzgerald *et al.*, 2016). The current study collected and analyzed campylobacteriosis positive cases reported in Johnson County from 2008-2015. Despite the variability in the stool antigen assays, the present study reveals that, since 2010, the stool antigen test was the most popular method for diagnoses of campylobacteriosis. More research needs to be conducted regarding the accuracy of the stool antigen tests, and how cross reactions with antigens from other bacteria affects the reliability of these tests.

The campylobacteriosis diagnosis puts a strain on health department employees who have to conduct disease investigations on reporteded cases. Based on studies reported, while the antigen testing methods may increase positive reported cases, there is an issue with follow-up communication. The communication after an initial positive antigen test reports, between health care providers and the health department when a confirmatory stool culture is negative.

The use of the stool antigens tests increased in 2009 after two such tests gained FDA clearance that year. By 2010, antigen testing was as common as culture testing and in subsequent years it surpassed culture testing (Figure 2). Reported campylobacteriosis cases were evaluated from five hospitals in Johnson County. These hospitals included Menorah Medical Center, Olathe Medical Center, Overland Park Regional Hospital, St. Luke's South Hospital, and Shawnee Mission Medical Center. The stool antigen test was the most common testing method used in all hospitals except St. Luke's South, where PCR testing was used for 2/3 reported cases and one case used antigen testing.

The hospital breakdown of reported positive cases revealed that, the stool antigen test is the most common test. The breakdown showed some hospitals are using culture to confirm their stool antigen tests. The stool culture is still used as a standalone test in 2 out of 5 hospitals; however, the hospitals' rationale for maintaining this method is unknown. It would be interesting to compare how each hospital has chosen their standard test for this disease.

Two hospitals, Menorah Medical Center and Olathe Medical Center, were chosen for a follow-up analysis due to their standard protocol of performing culture confirmation on positive antigen tests. Data from

15

cases in the year 2015 was collected and revealed that of the positive cases reported to the health department, all 23 were subsequently found to be negative by the culture method. This study revealed that there was a complete discrepancy between the antigen and culture tests in these hospitals. Moreover, these discrepant results were not reported to the health department. Currently, hospitals and physicians' offices are not required to report confirmatory culture results; they are only required to report the initial positive result that came from the stool antigen tests.

3.2 Conclusion and Limitations

It is recommended that hospitals and physician's offices are made aware of the burden that positive campylobacteriosis tests has on the JCDHE. They should be advised on the variation in the validity of the stool antigen tests. Hospitals and physician's offices should be encouraged to incorporate a culture confirmation on stool antigen tests into their standard protocol, if not already in place. Since campylobacteriosis is a reportable disease, cases should still be reported promptly to facilitate detection of an outbreak. However, a procedure needs to be in place for the health department to be made aware of the negative culture results for all antigen tests initially reported as positive. This would enable the JCDHE to maintain a more accurate account of campylobacteriosis infection in the county and the economic burden of case investigations would also be reduced.

One possible method for this follow-up communication would be for the health department to initiate follow-up with the hospitals and physicians' offices to obtain the results of the culture tests. By reducing false positive test cases the number of required disease investigations conducted by the JCDHE would decrease. Preferably, however, hospitals and physicians' offices should be required to report the confirmatory culture results as this affects focus and effort of the health department. Reporting of negative confirmatory culture results would help reduce the workload of investigating reported cases of campylobacteriosis and would, enable more accurate infection burden analysis.

There were several limitations in the current study. First, there was a poor carryover of information from the AVR system to EpiTrax causing missing data. Also, the study was limited by the fact that only information regarding the positive reported cases of campylobacteriosis were included in the database, so it is unknown how many patients total were tested for campylobacteriosis. In addition, access to positive reported campylobacteriosis cases from other counties including Douglas, Leavenworth, Sedgwick, Shawnee, and Wyandotte was denied, so a comparison of testing methods between separate counties could not be conducted.

Lastly, due to the six-week timeframe of this study, only two of the five hospitals were contacted to obtain any culture confirmation data. It is unknown if the other three hospitals have a standard protocol in place to perform confirmatory culture testing. In future studies, data from additional hospitals and physician offices in Johnson County should be analyzed. In addition, the data obtained could be used to calculate the economic cost, in a number of man hours required to investigate cases that were subsequently found to be negative by stool culture test. In addition, a future focus on hospital requirement in reporting confirmatory tests would likely decrease the number of reported positive tests, together with the economic burden of investigating false positive cases.

CHAPTER 5

Field Experience and the MPH Core Competencies

5.1 Other Duties at JCDHE

My time at the JCDHE allowed me to gain real-world experience in the field of public health. While not working on my analysis, I assisted with disease investigations for campylobacteriosis, salmonellosis, and Shiga-toxin-producing E. coli. There was an outbreak of salmonellosis during my time at the JCDHE, and I was able to study the response to the outbreak and help with the investigations. I also had the opportunity to analyze the 2015-2016 influenza data and compile the data into an infographic. In addition, I attended geographic information system (GIS) meetings and participated in staff meetings.

5.2 MPH Core Competencies

Throughout the field experience, I gained knowledge in all five of the core competencies of the Masters of Public Health programs: epidemiology, biostatistics, social and behavioral sciences, environmental health, and health care administration. Epidemiology was the most beneficial to the Campylobacteriosis Analysis. Epidemiology helped me to analyze the data about campylobacteriosis and biostatistics helped me to calculate my own statistical data as well as interpret those I read in the journal articles.

I utilized what I learned in Health Services Administration class to recognize the impact that stakeholders have on the health care system. I learned about the environmental department at the JCDHE and its programs, like the wastewater treatment program and the water quality lab, to reinforce environmental health. I had the opportunity to interact with the social workers and outreach nurses at JCDHE, and learned about some of the services the health department offers, such as coordinating Meals on Wheels for the elderly and providing low-cost health services for those in need. In summary, I feel that my experience has prepared me for a career in public health.

REFERENCES

- Allos, B. M. (2001). Campylobacter jejuni Infections: Update on Emerging Issues and Trends. Clinical Infectious Diseases, 2001; 32, 1201-1206. http://cid.oxfordjournals.org
- Arora, Z., Mukewar, S., Wu, X., & Shen, B. (2015). Risk factors and clinical implication of superimposed *Campylobacter jejuni* infection in patients with underlying ulcerative colitis. *Gastroenterology Reports*, 1-6. doi: 10.1093/gastro/gov029
- Bessede, E., Delcamp, A., Elodie, S., Buissonniere, A., Megraud, F. (2011). New Methods for Detection of Campylobacters in Stool Samples in Comparison to Culture. *Journal of Clinical Microbiology*, 49, 941-944. doi: 10.1128/JCM.01489-10
- Centers for Disease Control and Prevention. (2014). http://www.cdc.gov/foodsafety/diseases/campylobacter/index.html
- Denis, M., Soumet, C., Rivoal, K., Ermel, G., Blivet, D., Salvat, G., & Colin, P. (1999).
 Development of a m-PCR assay for simultaneous identification of *Campylobacter jejuni* and C. coli. *Letters in Applied Microbiology 1998, 29, 406-410*. doi: 10.1046/j. 1472-765X. 1999.00658.x
- Fitzgerald, C., Patrick, M., Gonzalez, A., Akin, J., Polage, C.R., Wymore, K., ... Nachamkin, I. (2016). Multicenter Evaluation of Clinical Diagnostic Methods for Detection and Isolation of *Campylobacter* spp. From Stool. *Journal of Clinical Microbiology*, *54*, *1209-1215*. doi: 10.1128/JCM.01925-15
- Giltner, C.L., Saeki, S., Bobenchik, A. M., & Humphries, R. M. (2013). Rapid Detection of *Campylobacter* Antigen by Enzyme Immunoassay Leads to Increased Positivity Rates. *Journal of Clinical Microbiology*, *51*, 618-620.doi: 10.1128/JCM02565-12
- Granato, P. A., Chen, L., Holiday, I., Rawling, R. A., Novak-Weekley, S.M., Quinlan, T., & Musser, K.A. (2010). Comparison of Premier CAMPY Enzyme Immunoassay (EIA), ProSpecT Campylobacter EIA, and ImmunoCard STAT! CAMPY Tests with Culture for Laboratory
- Diagnosis of *Campylobacter* Enteric Infections. *Journal of Clinical Microbiology*, 48, 4022-4027. doi: 10.1128/JCM.00486-10

- Hindiyeh, M., Jense, S., Hohnmann, S., Benett, H., Edwards, C., Aldeen, W., ... Carroll, K.C. (2000). Rapid Detection of *Campylobacter jejuni* Stool Specimens by an Enzyme Immunoassay and Surveillance for *Campylobacter upsaliensis* in the Greater Salt Lake City Area. *Journal of Clinical Microbiology*, *38*, 3076-3079.
- Hurd, S., Patrick, M., Hatch, J., Clogher, P., Wymore, K., Cronquist, A. B., ... Fitzgerald, C. (2012). Clinical Laboratory Practices for the Isolation and Identification of Campylobacter in FoodBorne Diseases Active Surveillance Network (FoodNet) Sites: Baseline Information for Understanding Changes in Surveillance Data. *Clinical Infectious Diseases, 2012;54 (S5), S440-S445.* doi: 10.1093/cid/cis245

Johnson County Kansas. (2016). http://www.jocogov.org/

- Kansas Department of Health and Environment. (2012). http://www.kdheks.gov/epi/Investigation_Guidelines/Campylobacter_Investigation_Guid eline.pdf
- M'ikanatha, N.M., Dettinger, L.A., Perry, A., Rogers, P., Reynolds, S. M., & Nachamkin, I. (2012). Culturing Stool Specimens for *Campylobacter* spp., Pennsylvania, USA. *Emerging Infectious Diseases, 18, 484-487.* doi: http://dx.doi.org/10.3201/eid1803.111266
- Nachamkin, I., Mishu Allos, B., & Ho, T. (1998). *Campylobacter* Species and Guillain-Barre Syndrome. *Clinical Microbiology Reviews*, *11(3)*, *555-567*.
- Regnath, T., & Ignatius, R. (2014). Accurate Detection of *Campylobacter* Spp. Antigens by Immunochromatography and Enzyme Immunoassay in Routine Microbiological Laboratory. *European Journal of Microbiology and Immunology 4, 156-158*. doi: 10.1556/EUJMI-D-14-00018
- World Health Organization. (2012). The Global View of Campylobacteriosis. www.who.int/iris/bitstream/10665/80751/1/9789241564601_eng.pdf