

TULAREMIA ANALYSIS-KANSAS, 2012-2015

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SUBMITTED IN PARTIAL FULFILLMENT OF THE REQUIREMENTS FOR THE DEGREE
MASTER OF PUBLIC HEALTH

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June 2016-August 2016

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2016

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ABSTRACT

Tularemia is a zoonotic disease caused by the bacteria *Francisella tularensis* that is endemic in the United States. With the potential to cause severe illness and even death as well as concern for its use as a biological weapon of warfare, tularemia is a mandated reportable disease. Tularemia can be transmitted to humans through exposure to other infected small mammals, ticks, deerflies, or contaminated soil or water. Although tularemia is a relatively rare disease investigation into the incidence rate and causes are important for identifying changes in the typical disease trend of tularemia.

The goal of this field experience and project with the Kansas Department of Health and Environment (KDHE) was to perform quality assessment and analysis of data regarding tularemia infections in Kansas between the years 2012 to 2015. Data was assessed for commonalities among cases that would provide the KDHE with an in-depth understanding of tularemia in Kansas. The data analyzed in this report was compared to a report done by the Centers for Disease Control and Prevention (CDC) regarding tularemia in the United States from 2001 to 2010. Overall, the 2012-2015 Kansas tularemia analysis was comparable to the CDC analysis in 2010, with the exception of a 345 percent increase in tularemia incidence in Kansas.

The findings from this report may be used to enhance the KDHE's knowledge of tularemia in Kansas. As well as provide a background for healthcare providers to improve awareness and prevention methods across Kansas.

SUBJECT KEYWORDS: TULAREMIA, KANSAS, KDHE, ZOOONOTIC, REPORTABLE

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Definitions and Abbreviations

KDHE: Kansas Department of Health and Environment

BEPHI: Bureau of Epidemiology and Public Health Informatics

CDC: Centers for Disease Control and Prevention

FDA: Food and Drug Administration

SAS: Statistical Analysis Software

MMWR: Morbidity and Mortality Weekly Report

CSTE- Council of State and Territorial Epidemiologists

LHD: Local Health Department

Bioterrorism Agent Categories: Agents are separated into 3 categories (A, B, and C) depending on how easily they are transmitted and the severity of the associated illness. Category A are the highest risk while Category C are emerging threats.

CHAPTER 1- Introduction

Field Experience Overview

I began my field experience on June 1st, 2016 at the Kansas Department of Health and Environment (KDHE) in Topeka, Kansas. My time at the KDHE was facilitated by Daniel Neises, Senior Epidemiologist in the Bureau of Epidemiology and Public Health Informatics (BEPHI). The Kansas State University Graduate School requires a minimum of 240 contact hours for completion of the MPH 830 Field Experience credit. At the end of my time at the KDHE I had accumulated a total of over 400 hours.

The Bureau of Epidemiology and Public Health Informatics (BEPHI) is directed by Charlie Hunt. The purpose of this department is to collect, analyze, and interpret human health data on a variety of conditions of public health importance and the health status of the populations (1). My experiences at the KDHE began with completing introductory courses; HIPAA Awareness (1047429) and KALHD-KDHE: Epidemiology Training for Local Health Departments (1031281) via KS-Train. I also attended training on "The Do's and Don'ts of Outbreak Interviewing" sourced from the Oregon Health Authority. Additionally, I completed the Learn SAS training offered through KDHE.

Throughout my time at the KDHE I got the opportunity to experience the daily routine for infectious disease epidemiologists at the state level. This included conference calls, presentations, and meetings. Conference calls covered topics such as H3N2 (Swine Influenza A), disease investigation relating to salmonellosis, shigella, and Zika virus, MRSA outbreaks, and pathogens acquired through raw milk or algal exposure. Presentations given by KDHE staff members included topics regarding epidemiological investigations, the opium overdose epidemic, and the ArcMap Program. I also participated in a salmonella investigation interview and the questions directed to the on call epidemiologist. Daily I attended the 4:00 pm meeting where the on call epidemiologist reviewed the calls and events that they handled that day. Additionally, we toured the Kansas Health and Environment Laboratory facilities where we learned about their daily routines and procedures.

Outside of the KDHE office, I along with other KDHE staff assisted the Centers for Disease Control and Prevention Arbovirus Disease Branch field researchers from Fort Collins with tick collection in the field. We collected from KS-Site 12 near Fort Scott. Collection procedures included dragging a felted flag along grassy areas, using forceps to remove the ticks from the flag and placing them into a prepared glass vial. Tick vials were then collected, safely packaged, and taken back to CDC for testing.

This project was completed in partial fulfillment of the Masters of Public Health program at Kansas State University. The overall objective of the program is to prepare individuals to better address health issues on local, state, national, and international levels. Completion of the program requires the individual to complete 42 credit hours of class work covering five core competencies as well as fulfilling 240 contact hours at an external public health site. The competencies are as follows; epidemiology, environmental health sciences,

biostatistics, health service administration, and social and behavioral sciences. This course work aided in preparing me for this field experience. I was able to apply the skills I learned in the biostatistics and epidemiology courses to the data analysis and outbreak investigations during my time at the KDHE. Similarly, knowledge from my health administration and behavioral science was applied when observing interactions between KDHE epidemiologist and citizens or other health care professionals.

Within the program my emphasis was infectious disease and zoonosis. This emphasis, as defined by Kansas State University, prepares graduates to become leaders in zoonoses protection programs, investigation of new and emerging disease, strengthening the public's ability to respond to bioterrorism and biosecurity emergencies, and conducting rapid response activities among various government, agricultural, and academic entities. It was through this coursework that I became interested in vector borne diseases which affect both animals and humans.

Background

Between the years 2001-2010, Kansas, along with 6 other states in the US, reported 59 percent of the total 1,208 reported cases of tularemia (2). Tularemia is a zoonotic disease that results from a bacterial infection with *Francisella tularensis*. Morphologically, *F. tularensis* presents as a gram-negative coccobacillus organism. The bacterium is non-motile and nonsporulating but can be easily aerosolized, and therefore is classified as a potential bioterrorism agent (3). While many aspects of the mechanism of infection by *F. tularensis* are unknown, in order to survive and produce clinical infection the bacteria must replicate intracellularly in the host cells. Due to a relatively low average number of cases per year, 126.5 for 2001-2010 for the U.S., and lack of extensive epidemiological investigation information about disease trends of tularemia are limited (2, 4).

Since the formal discovery of *F. tularensis* in 1912 by George W. McCoy and Charles W. Chapin, four subspecies have been identified (5, 6). Human infection of *F. tularensis* is commonly due to two of the four subspecies. The more virulent Type A (*F. tularensis* subsp. *tularensis*) and the less virulent Type B (*F. tularensis* subsp. *holarctica*). Type A is found almost exclusively in North America and associated with rabbits, ticks, and sheep (4). Type B is found in North America and Europe and is associated most frequently with hares and rodents, as well as bodies of water and aquatic dwelling species like muskrats, beavers, and ground voles. (4). Type A is estimated to be the cause of 70 percent of human tularemia cases in North America. However, the data obtained for this report did not include subspecies, so difference in subspecies incidence could not be determined (3, 4).

The incidence rate of tularemia has remained relatively constant in the United States in the last two decades, and reports suggest that modern medications may have successfully reduced the mortality to less than 2 percent (2, 4). However, continued surveillance is needed to recognize national or state-level changes in incidence that may indicate an outbreak or bioterrorism event. Since there is no licensed vaccination available in the U.S., it is pertinent that health care professionals have a thorough understanding of

the disease in order to reduce the 60 percent mortality risk associated with untreated cases (7).

Vectors and Transmission

Soon after serious epidemiological tracking of tularemia began around the 1940s, approximately two-thirds of cases were related to interactions with cottontail rabbits (*Sylvilagus sp.*) (4). Thus, the disease began to be associated with occupational and environment-related sources; this association also led to the common name “rabbit fever” for tularemia (6). Today, it is understood that over 200 species can be affected by infections with *F. tularensis*. Including but not limited to; rabbits, hares, voles, muskrats, beavers, domestic cats and dogs, ticks, and biting insects (5). In North America, the most common arthropod vector that result in human infection are the ticks; specifically, the American dog tick (*Dermacentor variabilis*), the Lone Star tick (*Amblyomma americanum*), and the Rocky Mountain wood tick (*Dermacentor andersoni*) (4).

Tick species *D. variabilis* and *A. americanum* are widely prevalent in Kansas. Preferring meadow habitats with little tree cover, *D. variabilis* is found across much of the state, according to geographic distribution from the Centers for Disease Control and Prevention (CDC) (8, 9). Peak activity level for an adult *D. variabilis* typically runs from April to August (13). They are known vectors of tularemia and other tick-borne illnesses such as Rocky Mountain spotted fever (8). Additionally, the *A. americanum* species is found primarily in the Eastern half of the state, in woody areas or environments with dense undergrowth, and a recent study suggests that the spatial distribution of these ticks may cover a larger area than originally considered (19). The *A. americanum* ticks are known vectors for ehrlichiosis, Southern Tick-Associated Rash Illness (STARI), and tularemia (8, 9). They are active between late April and August. The nymph and adult stages of both *D. variabilis* and *A. americanum* are capable of transmitting tularemia (9).

Transmission to humans can occur via bites by infected ticks and or exposure of the skin, eyes, or mucous membranes to the bacteria from other sources such as contaminated water. Potential exposures to the bacteria may occur through activities such as handling infected carcasses, consuming improperly cooked infected meat, ingesting contaminated soil or water, or inhalation of aerosolized bacteria (11). While it has not been confirmed, it is thought that contamination of water sources may result from the presence of larval stages of infected flies or mosquitos (4). Accidental laboratory-related exposures may also occur; therefore, it is necessary that the proper precautionary measures be taken when working with suspect tularemia cases and specimens (11).

Classified as a Category A bioterrorism agent by the CDC, tularemia is known to be extremely infectious (4). A dose of only 10 organisms is enough to cause subcutaneous disease and 25 aerosolized organisms is enough to cause severe respiratory disease in humans (4). An outbreak of tularemia has the potential to cause mortality and create widespread panic, which makes tularemia a concern for use as a biological weapon of warfare (10).

Clinical Presentation and Case Definition

General case presentation may include any combination of nonspecific symptoms, such as fever, malaise, chills, headache, weakness, cough, chest pain, and muscle or joint pain (4, 12). However, based on the original site of infection, clinical presentation of tularemia may differ from case to case. There are seven recognized forms of tularemia which are accompanied by distinctive symptoms (11). The seven major forms of tularemia, their associated clinical presentations, and common methods of acquisition are shown below (Table 1) (11, 12). The typical incubation period can range from one to 14 days with an average of 3 to 5 days. Infective period of vectors can vary depending on the species. While human to human infection is not recognized, drainage from ulcers or infected wounds are potentially infective. It is assumed that long-term immunity is acquired post infection, although re-infections have been documented (11).

Table 1. Definition of clinical forms of tularemia—Kansas, 2012-2015

Clinical Form	Definition	Common Method of Acquisition
Ulceroglandular	<ul style="list-style-type: none"> • Ulcers on cutaneous layer of the skin • Regional lymphadenopathy 	<ul style="list-style-type: none"> • Insect bite • Handling infected animal
Glandular	<ul style="list-style-type: none"> • Regional lymphadenopathy 	<ul style="list-style-type: none"> • Insect bite • Handling infected animal
Oculoglandular	<ul style="list-style-type: none"> • Conjunctivitis • Preauricular lymphadenopathy 	<ul style="list-style-type: none"> • Handling infected animal
Oropharyngeal	<ul style="list-style-type: none"> • Stomatitis, pharyngitis, tonsillitis • Cervical lymphadenopathy 	<ul style="list-style-type: none"> • Ingesting contaminated food, water, or soil
Intestinal	<ul style="list-style-type: none"> • Intestinal pain • Vomiting • Diarrhea 	<ul style="list-style-type: none"> • Ingesting contaminated food, water or soil
Pneumonic	<ul style="list-style-type: none"> • Primary pleuropulmonary disease 	<ul style="list-style-type: none"> • Inhaling aerosolized bacteria • Progression of untreated tularemia
Typhoidal	<ul style="list-style-type: none"> • Fever • Lack of other identifying symptoms 	<ul style="list-style-type: none"> • Unknown

In the U.S., cases of tularemia are classified as confirmed or probable by the Council of State and Territorial Epidemiologists (CSTE) and CDC. Cases of tularemia are classified as confirmed through clinical observations matching one of the forms listed in Table 1 and the isolation of *F. tularensis* from a clinical specimen or a four-fold or greater increase in serum antibody titer. Probable cases are defined by elevated serum antibody titers or detection of the bacteria by fluorescent assay (11).

Reporting

The CDC has documented cases of endemic or travel-related tularemia in every U.S. state with the exception of Hawaii (12). Due to the infectiousness of the bacteria as well as

its potential for use as a biological weapon, suspect cases are reportable to State and National Health Departments within 7 days for naturally-occurring or occupational related events. Unusual or suspected intentional release cases must be reported immediately and state epidemiologists must report to the CDC within 4 hours following notification (11).

Treatment and Control

The CDC recommends streptomycin as the primary drug of choice for severe cases, if streptomycin is not available or cannot be used, gentamicin is also a recognized effective treatment; these treatments should be continued for a period of 10 days. Doxycycline is recommended for those with less severe forms of tularemia and should be continued for a period of 14 days. Any contaminated objects should be properly disinfected following the standard hospital procedure. Bodies of deceased infected individuals should be handled under standard precautions with special emphasis on avoiding contact with aerosolized droplets (11).

Project Objectives

The objectives of this project were to organize and gain more insight from data regarding cases of tularemia in Kansas from 2012 to 2015. Specifically, Daniel Neises, my project supervisor from the KDHE, outlined tasks as follows;

- Perform data quality assessment regarding *Francisella tularensis* infection reported to KDHE between the years 2012-2015 in the state of Kansas;
- Perform descriptive analysis of tularemia infection data;
- Summarize the data into a written report and PowerPoint presentation;
- Assist with outbreak investigations should they arise in which possible tasks included; telephone interviews, data entry, data quality assessment, or observing epidemiological analysis by KDHE staff.

The expected learning objectives of the field experience were to have a thorough understanding of the processes surrounding descriptive analysis and disease investigation at the state level, as well as learning proper methods to organize and carry out an outbreak investigation and data analysis. The results from this project will give KDHE a more thorough understanding of tularemia in Kansas. The information detailed in this report may also aid in the development of methods that could be used to educate health care professionals and the general public about the best practices to prevent infections of *F. tularensis*.

CHAPTER 2 – Methods

Data Acquisition

Kansas Administrative Regulation (28-1-2) requires medical laboratories and health care workers who suspect a case of tularemia to report to the state or local health department within seven days. The KDHE provides local health departments with investigation guidelines and forms for all of the recognized reportable conditions. These forms are unique for each disease or condition. The local health departments are then responsible for carrying out the disease investigation and recording case information in the EpiTrax system (11).

The data and case information used for this project were acquired from the EpiTrax system. EpiTrax is the online disease surveillance system used by KDHE to organize and track patient information related to infectious diseases. It allows information to be securely stored and shared between various health organizations. All cases of confirmed or probable tularemia between the years 2012 to 2015 and relevant information obtained from public health investigations for each case were exported into two Microsoft Excel (2013) spreadsheets. The specific information pulled for each EpiTrax case were; record number, specimen collection date(s), specimen type collected, test type(s), test result(s), lab(s), year, case state, date reported to public health department, date disease onset, location 1st seen, date diagnosed, date seen by medical professional, date reported to local health department (LHD), primary/secondary clinical syndrome, date LHD investigation started, date LHD investigation completed, county, zip code, sex, birthdate, age at onset, died, hospitalized, imported from, treatment, ethnicity, race, occupation, primary work environment, follow up status, underlying conditions, travel, and associated potential exposures.

The Statistical Analysis Software (SAS) Studio 3.5 (Enterprise Edition) was used to assess data quality and process the data from the previously mentioned Excel spreadsheets. Missing or inaccurate information found in the spreadsheets was cross referenced with patient data in EpiTrax. Frequencies and percentages of specified variables were computed using the PROC FREQ statement in SAS. Incidence rates were computed in SAS using population data from 2014 available from the KDHE Office of Vital Statistics with information sourced from the National Center for Health Statistics vintage post-censal estimates of the resident population of the United States. (13). Microsoft Excel (2013) was used to create tables and figures based on the analyzed data.

Data Quality Assessment and Analysis

Data was imported into SAS and both files (tularemia data-1 and tularemia data-2 spreadsheets) were merged by an identifying unique record number. In the original data files, patient record numbers with multiple laboratory results appeared as duplicate rows for a total of 330 observations and 87 variables. The data was rearranged in order to create one row per each individual case for the following variables; Specimen Collection Date,

Specimen Source, Test Type, Test Result, Result Value, and Lab Name. Output was merged resulting in one row per record number for a total of 114 observations and 129 variables.

Additional variables for age group, region, and peer group were created in the SAS program according to KDHE guidelines. Age group categories were created based on the variable "Age at Onset", which recorded the age of the individual at the time they were infected with *F. tularensis*. Age groups were categorized as follows; 0-4 years of age, 5-14 years of age, 15-24 years of age, 25-34 years of age, 35-44 years of age, 45-54 years of age, 55-64 years of age, and 65 years of age or older. Counties were grouped by region and peer group. Based on predetermined boundaries acquired from the KDHE, counties were divided into five regions; North Central (NC), North East (NE), North West (NW), South Central (SC), and South East (SE) (14). Tularemia data was mapped according to county of residence rather than county of exposure to avoid recall bias. The variable 'peer group' grouped counties with similar populations. The KDHE typically lists five peer groups (frontier, rural, densely-settled rural, semi-urban, and urban). For the purposes of this report three peer groups, previously established by the KDHE for describing other diseases, were used. Rural was classified as those counties with 0 to 19.9 persons per square mile. Densely-settled rural was a combination of the 'rural' and 'densely-settled rural' peer groups. It was defined as counties with 20.0-39.9 persons per sq. mi. Urban was a combination of peer groups 'semi-urban' and 'urban'. Counties with between 40.0-150 or more persons per sq. mi. were considered urban.

Cases in EpiTrax were also distinguished by the specific syndrome of tularemia experienced under the variable 'Primary Clinical Syndrome'. For cases in which a primary clinical syndrome was not listed the variable 'Secondary Clinical Syndrome' was used. If no clinical type was identified, the clinical syndrome was classified as 'unknown'. Of the seven recognized forms only six were diagnosed in Kansas between the years 2012-2015. The six forms included; glandular, intestinal, oculoglandular, pneumonic, typhoidal, and ulceroglandular. Investigations for potential tularemia cases include questions regarding 12 behaviors of potential exposure to the bacteria that are commonly associated with tularemia. Patients were asked to respond to these questions with specific reference to 10 days prior to onset of illness (15). The 12 potential exposures and their response formats as defined by the EpiTrax case investigation form used by the KDHE are shown below (Table 2) (15). Because patients could respond 'yes' or 'no' to multiple exposures there was a total of 325 total responses regarding potential exposures for the 114 cases.

Table 2. Potential exposures to tularemia from the KDHE disease investigation form—Kansas, 2012-2015

Potential Exposures	Response Format
Pets in home	Dog/Puppy, Cat/Kitten, Other
Any pets been ill /died	Yes/No
Pets brought home dead animal	Yes/No
Other Pets	Open text response
Tick, deerfly, or other biting fly bite	Yes/No
Lawn mowing or landscaping	Yes/No
Contact with sick/dead animal	Yes/No
Contact/ingest water or soil	Yes/No
Hunting	Yes/No
Contact/ingest uncooked meat	Yes/No
Laboratory worker	Yes/No
Association with other human tularemia case	Yes/No
Other Exposure	Open text response

In order to get a better understanding of the potential risks associated with owning specific pets, variables 'Pet Dog' and 'Pet Cat' were created in excel from the original variable 'Pet(s) in Home'. Making a total of 14 potential exposures considered in this report. Due to the variations in the open text responses for interview questions regarding 'other exposures' and 'occupation', answers were used to supplement missing information for other variables, if applicable. Specifically, individuals were questioned about their occupations at the time of infection. In addition, a separate question was asked regarding whether their work was primarily, indoors, outdoors, or both indoors and outdoors. If 'works primarily' information for a patient was not listed, it was filled using information reported in the 'occupation' field. If both 'works primarily' and 'occupation' information for a case were missing it was excluded from the analysis. The variable 'other exposure' was also reviewed for any information that may have contributed to contracting tularemia.

The ArcMap software was used to create a detailed map of Kansas counties. The ArcGIS program is a mapping and visualization software that allows the user to create spatially accurate maps. This project used a base-map of Kansas provided by the KDHE. County incidence rates of tularemia were imported into ArcMap and graduated colors that corresponded to one of six categories of incidence rates. Incidence rates were found using county population information from 2014 and calculated per 100,000 persons.

CHAPTER 3 – Results

Data Background

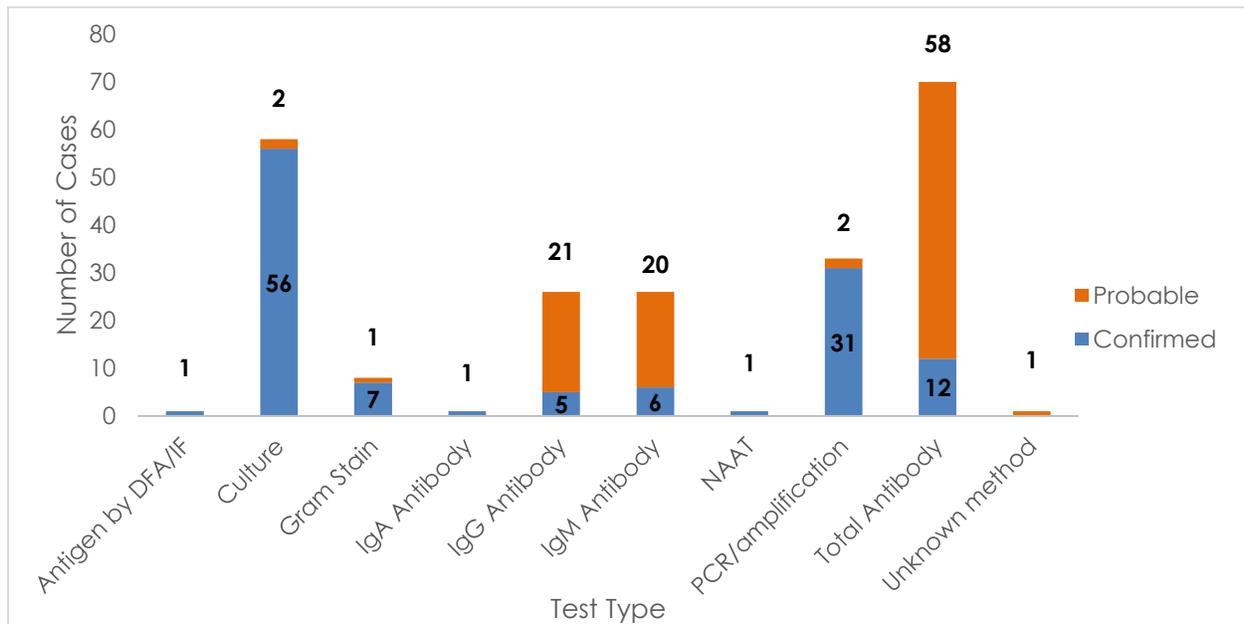
Between the years 2012 to 2015 there were a total of 114 (46 confirmed and 68 probable) cases of tularemia recorded in the EpiTrax system. Of the 114 cases, 77 were male and 37 were female. The median age was 42 years. The youngest individual infected was one year of age, while the oldest was eighty-nine years of age.

Laboratory Tests Incidence

Diagnosis of tularemia can be achieved through a number of different laboratory tests. In Kansas between the years 2012-2015 there were a total of nine different tests used to identify tularemia. They included; antigen detection by direct fluorescent assay or immunofluorescent assay, culture, gram stain, IgA antibody, IgG antibody, IgM antibody, nucleic acid amplification test (NAAT), polymerase chain reaction (PCR) or amplification, and total antibody tests. According to KDHE disease investigation guidelines, a confirmed case must exhibit clinical symptom(s) matching one of the seven defined forms of tularemia as well as isolation of the bacteria from a clinical specimen or a four-fold or greater increase in serum antibody titer. Probable cases must also match a defined clinical form but require isolation of the bacteria by fluorescent assay or an increase in serum antibody. In order to reach a confirmed or probable diagnosis most individuals were tested multiple times using a variety of methods (the most being six tests for one case). Therefore, there was a total of 225 tests run for the 114 cases. Both confirmed and probable cases were considered in the total number of cases for this analysis.

The frequency of the test types used for confirmatory and presumptive diagnosis of tularemia between the years 2012-2015 is illustrated below (Figure 1). The majority of probable cases were identified using total antibody test (55 percent), IgG antibody test (20 percent), and IgM antibody test (19 percent). Culture (47 percent) and PCR/amplification (26 percent), were the primary tests types used in confirmed cases.

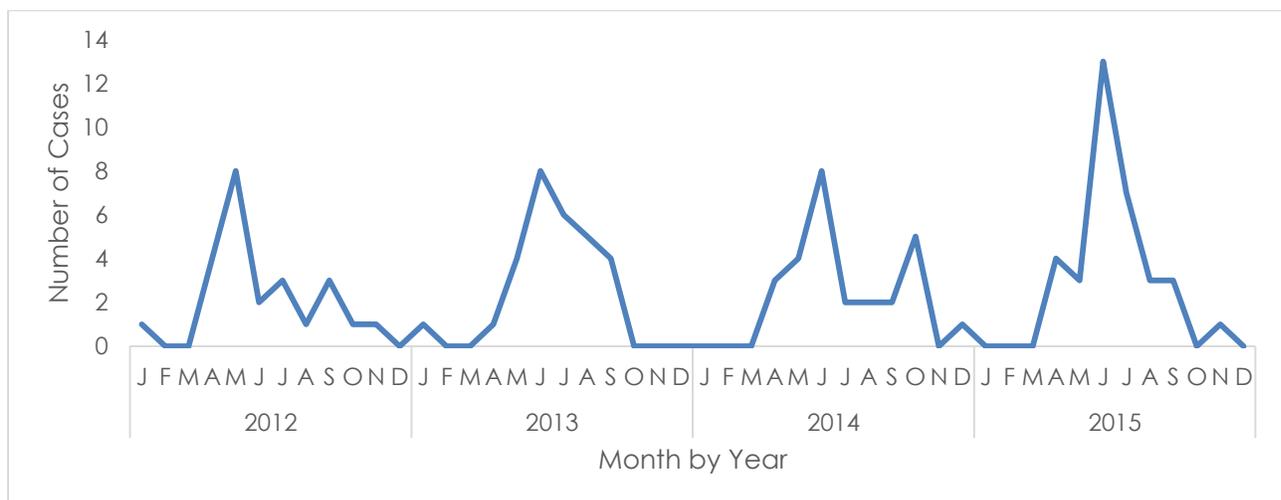
Figure 1. Comparison of diagnostic tests performed on confirmed and probable tularemia cases—Kansas, 2012-2015



Yearly Incidence and Seasonality

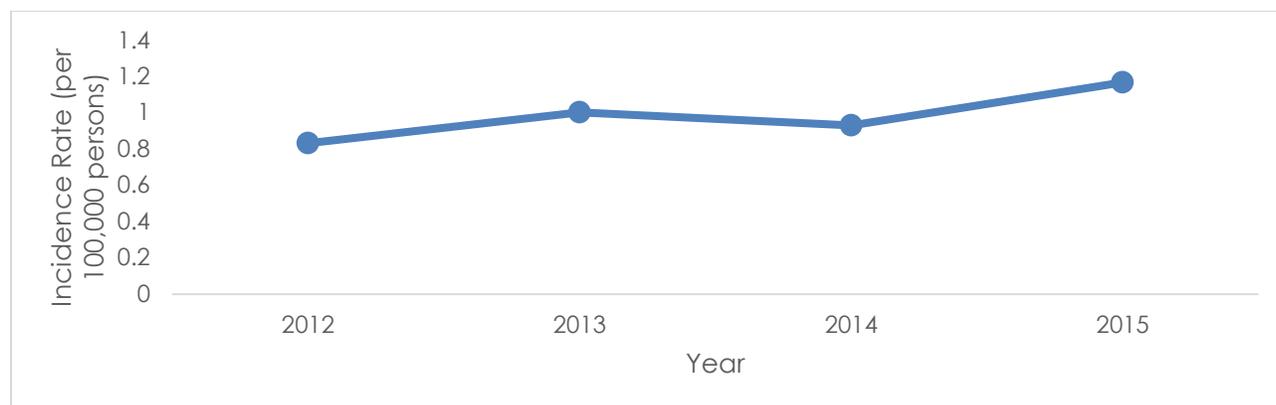
A peak in disease occurrence appeared every year, with incidence increasing during spring (months), peaking in late spring (months), and returning to low levels in the fall (months) and winter (months) (Figure 2). In 2012, 12 of the 24 total cases occurred in April and May. During 2013, eight of the 29 cases occurred during the month of June. In 2014 there was a peak of 12 cases between May and June, followed by a secondary peak of seven cases between September and October. In 2015, 20 of the 34 occurred between the months of June and July.

Figure 2. Number of tularemia cases by month—Kansas, 2012-2015



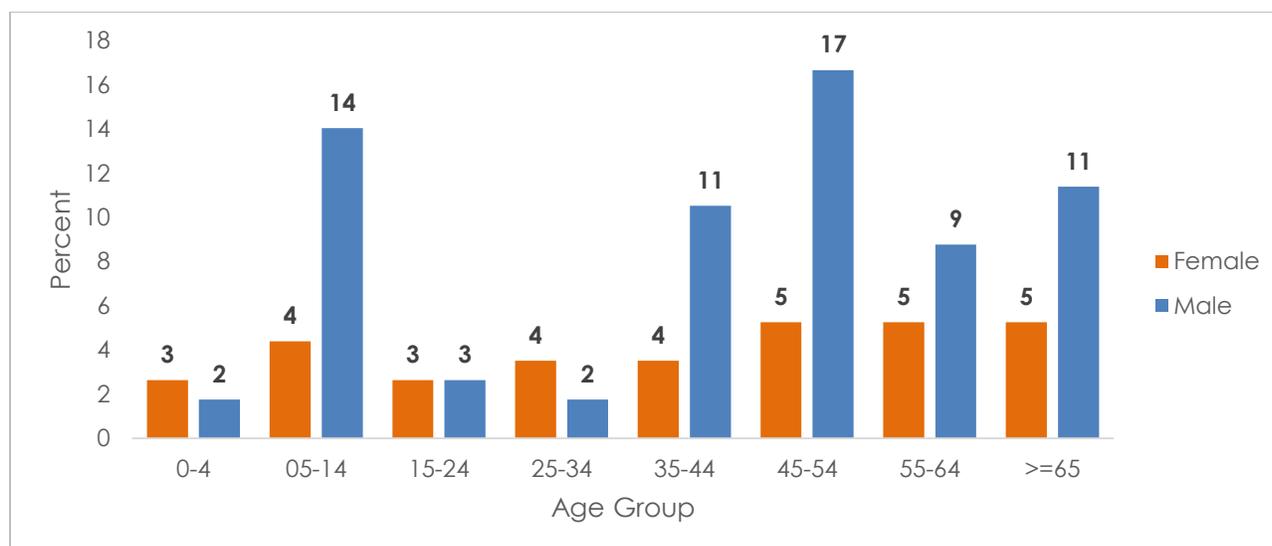
Over the four-year period for which the data was collected there were no large increases or decreases in annual disease incidence. Disease incidence was the highest (1.16 per 100,000 persons-year) in 2015, accounting for 30 percent of the total 114 cases, between the years 2012-2015 (Figure 3). The second highest annual incidence (1.00 per 100,000 persons-year) was in the year 2013, making up 25 percent of the total cases. Followed by an incidence rate of (0.92 per 100,000 persons-year) in the year 2014, for 24 percent of total. The lowest incidence rate (0.83 per 100,000 persons-year) was seen in the year 2012, at 21 percent of the total 114 cases.

Figure 3. Incidence rate of tularemia per 100,000 persons—Kansas, 2012-2015



Age and Demographic Factors

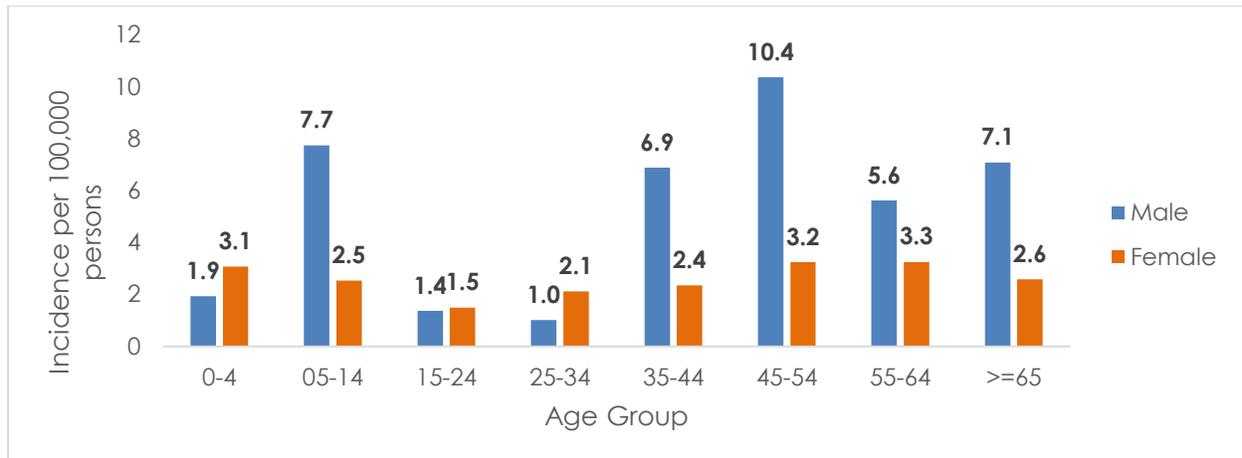
As mentioned in the data background section of this report, the median age of infection was 42 years, with one year of age being the youngest and 89 years of age the oldest. The frequency of disease by age group and sex from 2012 to 2015 is shown below (Figure 4). The age groups with the highest incidence of tularemia in Kansas were; 45-54 years of age (6.77 per 100,000 persons) accounting for 25 of the 114 total cases, 5-14 years of age (5.20 per 100,000) accounting for 21 of the total cases, and 65 years of age or older (4.57 per 100,000) accounting for 19 of the total cases. Age groups 35-44 (4.64 per 100,000) and 55-64 (4.41 per 100,000) each accounted for 16 of the total cases. Persons 0-4 years of age (2.49 per 100,000) accounted for five of the total cases. The age groups with the lowest incidence of tularemia were; 15-24 years of age (1.42 per 100,000) and 25-34 years of age (1.03 per 100,000) each accounting for six of the total 114 cases.

Figure 4. Percentage of tularemia by age group and sex—Kansas, 2012-2015

Of the 114 total tularemia cases 68 percent were male, and 32 percent were female. The annual incidence rates of tularemia by age group and sex in Kansas between the years 2012-2015 are illustrated below (Figure 5). Tularemia incidence was highest in males (5.32 per 100,000), compared to females (2.54 per 100,000). Males had a higher incidence in all but three of the age groups. Female incidence of tularemia was higher than male incidence for age groups 0-4 years of age (male; 1.9 per 100,000) (female; 3.1 per 100,000), 15-24 years of age (male; 1.4 per 100,000) (female; 1.5 per 100,000), and 25-34 years of age (male; 1.0 per 100,000) (female; 2.1 per 100,000).

Similar to Figure 2, the overall incidence rates, incidence rates for males were highest in persons 45-54 years of age (10.4 per 100,000), 5-14 years of age (7.7 per 100,000), and 65 years of age or older (7.1 per 100,000). Males in the age groups 35-44 years of age (6.9 per 100,000) and 55-64 years of age (5.6 per 100,000) were the next highest. The lowest incidence for males was seen in age groups 0-4 years of age (1.9 per 100,000), 15-24 years of age (1.4 per 100,000), and 25-34 years of age (1.0 per 100,000).

Incidence for females was highest in age groups 55-64 years of age (3.3 per 100,000), 45-54 years of age (3.2 per 100,000), and 0-4 years of age (3.1 per 100,000). The next highest were persons aged 65 or older (2.6 per 100,000), 5-14 years of age (2.5 per 100,000), and 35 to 44 years of age (2.4 per 100,000). The lowest incidence of disease in females was seen in groups 25-34 years of age (2.1 per 100,000) and 15-24 years of age (1.5 per 100,000).

Figure 5. Average annual incidence of tularemia, by age group and sex—Kansas, 2012-2015

Race information was available for 110 (96 percent) of the 114 total tularemia cases. The only races recorded in this data set were white and black. The remaining cases had race listed as unknown. Statewide proportion for these races were 88 percent and seven percent accordingly in 2014. Race was recorded as White for 98 percent of the cases (4.2 per 100,000). Race was recorded as Black for two percent of the cases (0.96 per 100,000).

Ethnicity information was available for 103 (90 percent) of the total 114 cases. The ethnicities recorded in this data set were Hispanic and Non-Hispanic. Statewide ethnicity proportions in 2014 were; 89 percent Non-Hispanic and 11 percent Hispanic. Non-Hispanic (3.84 per 100,000) was recorded for 96 percent of the cases while Hispanic (1.2 per 100,000) was recorded for four percent of cases.

Clinical Syndrome Incidence

The frequencies of the six forms of tularemia reported from 2012-2015 are illustrated in Figure 6a. Ulceroglandular and glandular forms of the disease were the most commonly reported at 39 and 30 percent respectively. Less commonly reported were pneumonic (five percent), intestinal (three percent), typhoidal (two percent), and oculoglandular (one percent). The remaining 20 percent of cases were reported as unknown. The count of clinical syndrome according to sex and age group is illustrated below (Figure 6b). Overall, males were diagnosed equally and/or more than females for every form of the disease with the exception of oculoglandular (0 male, and 1 female). Ulceroglandular was the most commonly reported at 39 percent of male cases, glandular was reported in 30 percent of cases, and the remaining 31 percent were distributed among the remaining syndromes. Ulceroglandular was reported most frequently within all age groups, with the exception of groups 15-24 years of age and 25-34 years of age, in which the glandular clinical syndrome was reported more often than ulceroglandular. Similarly, Ulceroglandular was the most commonly reported at 41 percent of female cases, glandular was reported at 30 percent, and the remaining 30 percent was comprised of the remaining syndromes. Ulceroglandular was the most frequently reported syndrome for age groups 0-4 years of age (three cases), 5-14 years of age (four cases), and 35-44 years of age (three cases). Glandular was the

most frequently reported syndrome for age groups 15-24 years of age (two cases), 25-34 years of age (two cases), and 55-64 years of age (three cases). Other syndromes were most commonly reported for females aged 45-54 (three cases) and 65 years or greater (three cases).

Figure 6 a. Tularemia clinical syndrome—Kansas 2012-2015

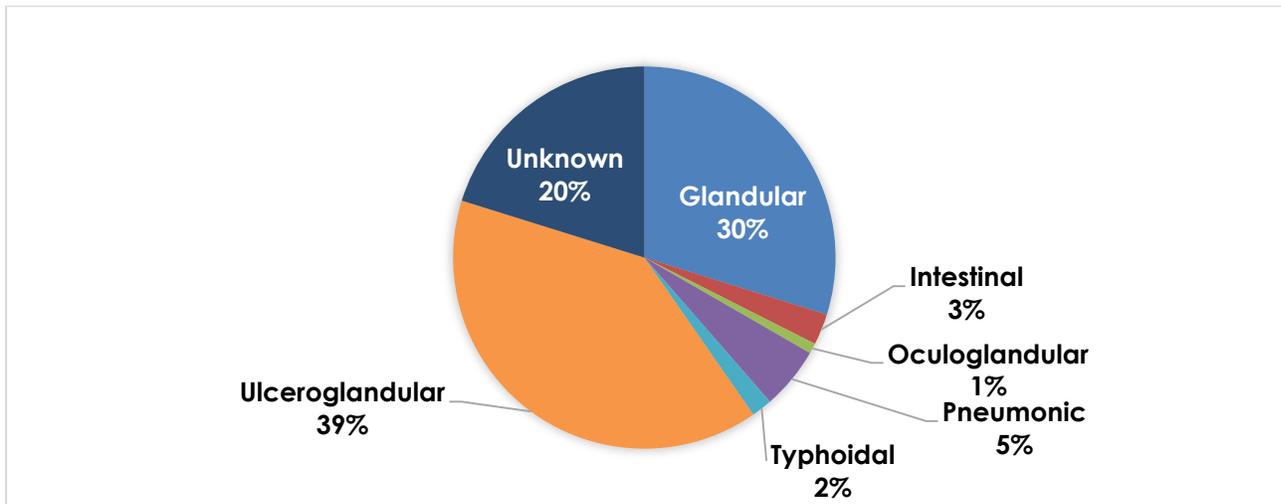
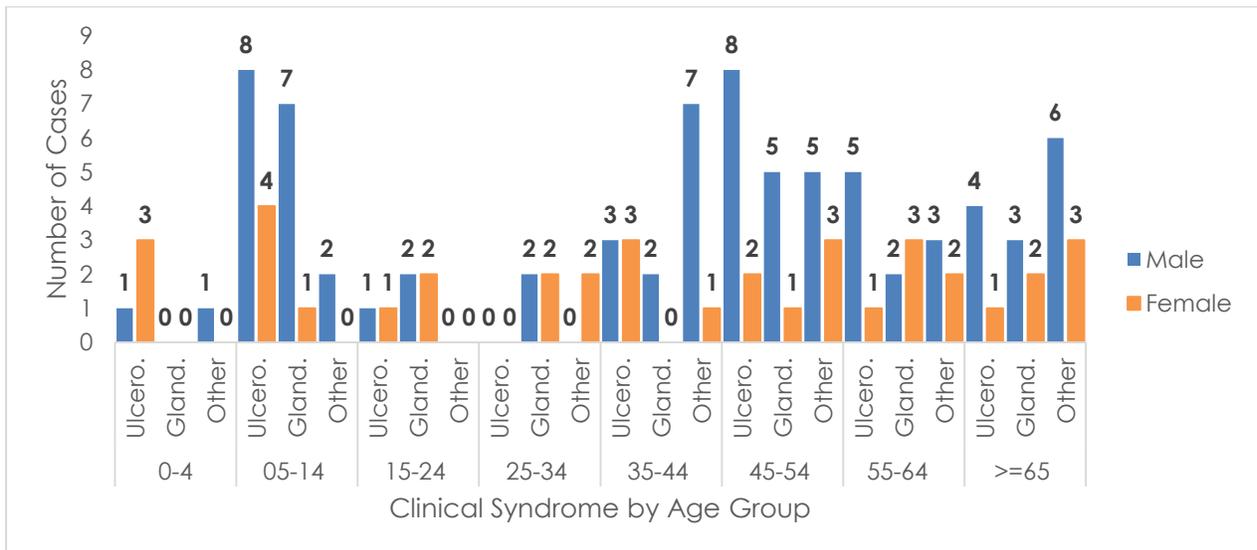


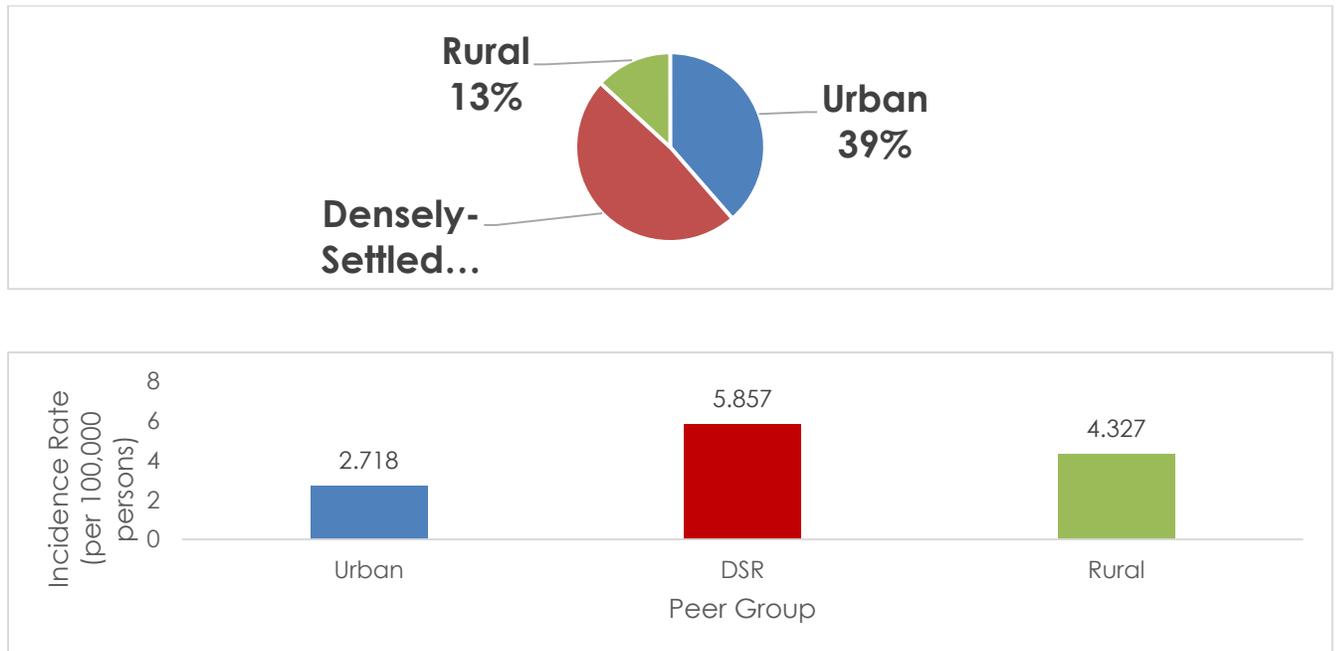
Figure 6b. Clinical syndrome by age group and sex-Kansas, 2012-2015



State and County Incidence

Over the four-year period from 2012-2015, residents of the North East region of Kansas comprised almost half of the reported cases of tularemia at 46 percent. The map below demonstrates tularemia incidence rate according to the county of residence of the cases in Kansas from the years 2012 to 2015 (Figure 7). It is noted that the county of residence may not necessarily be the county of acquisition of the bacteria. Of the 105 Kansas counties only 33 reported a case of human tularemia from 2012 to 2015. Incidence of tularemia is primarily concentrated in the Eastern portion of the state, with the exception

Figure 8 a-b. Tularemia case count and incidence by population based peer group - Kansas, 2012-2015



Potential Exposure Incidence

The behaviors of potential exposure to tularemia and their corresponding frequencies are shown below (Table 3). Overall Pet(s) in the home was the most commonly reported exposure with a total of 69 positive responses (62 percent). Tick, deerfly, or other biting fly bite was the second most common with 65 positive responses (59 percent). Pet dog had 58 positive responses (85 percent), Lawn mowing or landscaping had 44 positive responses (40 percent), and pet cat had 30 positive responses (44 percent). The remaining exposures each had less than 20 positive responses.

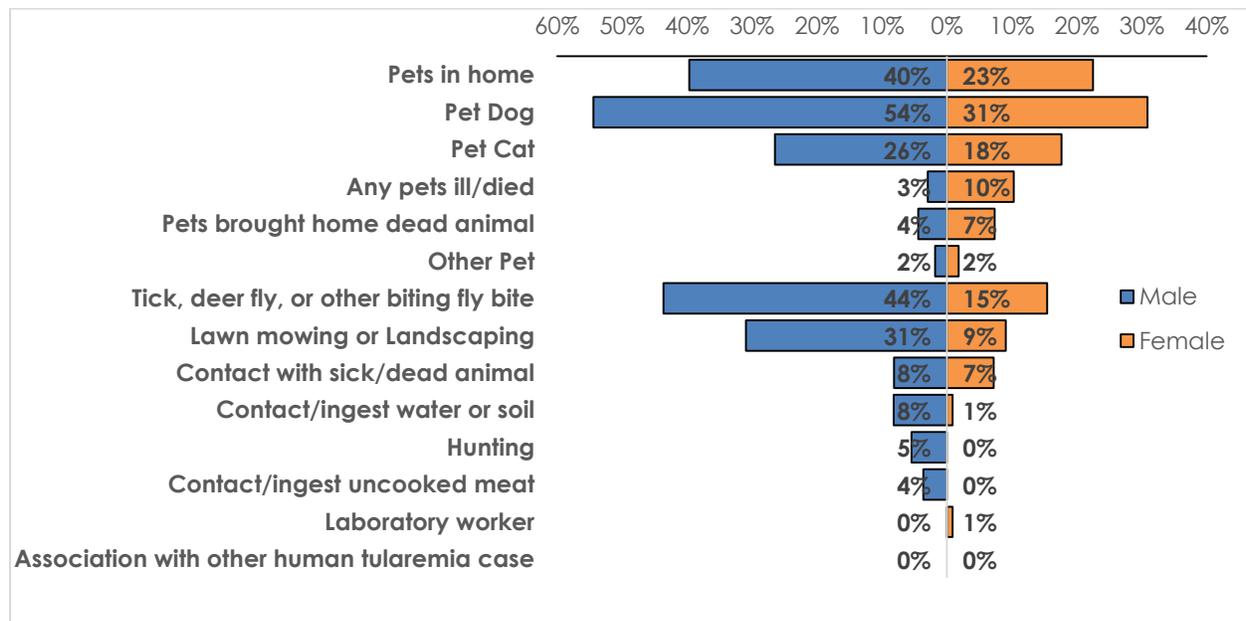
Table 3. Frequency and percentage of reported behaviors of potential exposure to tularemia—Kansas, 2012-2015

Potential Exposures	Frequency	Percent	n
Pets in home	69	62%	111
Pet Dog	58	85%	68
Pet Cat	30	44%	68
Any pets ill/died	9	13%	68
Pets brought home dead animal	8	12%	68
Other Pet	4	4%	110
Tick, deer fly, or other biting fly bite	65	59%	110
Lawn mowing or Landscaping	44	40%	110
Contact with sick/dead animal	17	15%	111
Contact/ingest water or soil	10	9%	110
Hunting	6	5%	111
Contact/ingest uncooked meat	4	4%	111
Laboratory worker	1	1%	110

Association with other human tularemia case	0	0%	106
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As noted in the sub-section 'Age and Gender' above, this data showed that males contracted tularemia more often than females from 2012-2015. Similarly, it was found that males reported more positive exposures than females. Differences in reported exposures between males and females from 2012 to 2015 is illustrated below (Figure 9). Pet associated exposures were the most commonly reported for both males and females. Potential exposure 'pet dog' was reported for 54 percent of male cases and 31 percent of female cases. Potential exposure 'pet cat' was reported for 26 percent of males and 18 percent of females. Less frequently reported by both genders were factors; 'any pets ill/died' (male; three percent, female; ten percent), 'pet brought home dead animal' (male; four percent, female; seven percent), and 'other pet' (male and female; two percent). Male cases reported exposure to tick or biting fly bite at 44 percent, compared to females at only 15 percent. Males also reported lawn mowing and landscaping at 31 percent, compared to females who reported only 9 percent. The remaining exposures were not as frequently reported or did not show notable discrepancies between males or females.

Figure 9. Comparison of reported potential exposures by sex - Kansas, 2012-2015



The potential exposures were also analyzed by age group. The percent frequency of reported potential exposure by age group is listed below (Table 4). Age group 0-4 showed an equal frequency for 'pet dog' and 'tick, deerfly, or other biting fly bite' at four percent. The most reported exposure for cases aged 5-14 was 'pet dog' at 18 percent. Age group 15-24 also reported 'pet dog' as the most common potential exposure at four percent. Age group 25-34 had an equal frequency for 'pet(s) in home' and 'pet dog' at four percent. Age groups 35-44 and 45-54 reported 'pet dog' at 12 percent and 19 percent, respectively. Age group 55-64 reported exposure to 'pet dog' and 'tick, deerfly, or other biting fly bite' equally at 9 percent. The most commonly reported potential exposure for cases 65 years of age or greater was 'pet dog' at 15 percent.

Table 4. Percentage of cases reporting potential exposure to tularemia by age group--Kansas, 2012-2015

Potential exposure	0-4	05-14	15-24	25-34	35-44	45-54	55-64	>=65	n
Pets in home	3%	13%	3%	4%	7%	14%	8%	11%	111
Pet Dog	4%	18%	4%	4%	12%	19%	9%	15%	68
Pet Cat	1%	9%	1%	1%	4%	10%	7%	9%	68
Any pets ill/died	0%	1%	0%	1%	1%	3%	3%	3%	68
Pets brought home dead animal	0%	3%	1%	0%	3%	1%	1%	1%	68
Other Pet	0%	0%	0%	0%	1%	2%	1%	0%	110
Tick, deer fly, or other biting fly bite	4%	16%	2%	2%	7%	11%	9%	8%	110
Lawn mowing or Landscaping	0%	0%	3%	2%	9%	12%	6%	8%	110
Contact with sick/dead animal	0%	2%	1%	2%	3%	4%	2%	3%	111
Contact/ingest water or soil	1%	2%	1%	0%	0%	3%	0%	3%	110
Hunting	0%	0%	1%	0%	2%	2%	1%	0%	111
Contact/ingest uncooked meat	0%	0%	1%	0%	1%	2%	0%	0%	111
Laboratory worker	0%	0%	0%	1%	0%	0%	0%	0%	110
Association with other human tularemia case	0%	0%	0%	0%	0%	0%	0%	0%	106

Lastly, the potential exposures were analyzed according to the reported clinical syndrome. Percent frequency of each potential exposure according to the reported clinical syndromes is listed below (Table 5). Ulceroglandular was the most commonly reported clinical syndrome overall. The most commonly reported potential exposure noted for ulceroglandular cases were; 'pet dog' (44 percent), 'pet cat' (35 percent), 'pets in home' (25 percent), 'any pets ill/died' (24 percent), and 'pets brought home dead animal' (24 percent). The second most common clinical syndrome was glandular. The most commonly reported potential exposure for glandular cases were; 'pet dog' (31 percent), 'pet cat' (25 percent), 'pets in home' (20 percent), 'any pets ill/died' (15 percent), and 'pets brought home dead animal' (12 percent). Few potential exposures were reported for the clinical syndromes; pneumonic, intestinal, oculoglandular, and typhoidal.

Table 5. Percentage of cases reporting potential exposure to tularemia by the primary clinical syndrome- Kansas 2012-2015

Potential Exposure	Ulceroglandular	Glandular	Pneumonic	Intestinal	Typhoidal	Oculoglandular	Unknown	n
Pets in home	25%	20%	5%	2%	0%	1%	10%	111
Pet Dog	44%	31%	3%	1%	3%	0%	13%	68
Pet Cat	35%	25%	4%	3%	0%	1%	16%	68
Any pets ill/died	24%	15%	6%	3%	1%	0%	16%	68
Pets brought home dead animal	24%	12%	3%	1%	0%	1%	3%	68
Other Pet	4%	5%	2%	0%	0%	0%	5%	110
Tick, deer fly, or other biting fly bite	2%	3%	1%	2%	0%	0%	2%	110
Lawn mowing or Landscaping	2%	4%	1%	2%	0%	0%	0%	110
Contact with sick/dead animal	1%	4%	0%	0%	0%	0%	3%	111
Contact/ingest water or soil	1%	4%	1%	0%	0%	0%	0%	110
Hunting	1%	3%	0%	0%	0%	0%	0%	111
Contact/ingest uncooked meat	1%	0%	1%	0%	0%	1%	1%	111
Laboratory worker	0%	0%	0%	0%	0%	0%	1%	110
Association with other human tularemia case	0%	0%	0%	0%	0%	0%	0%	106

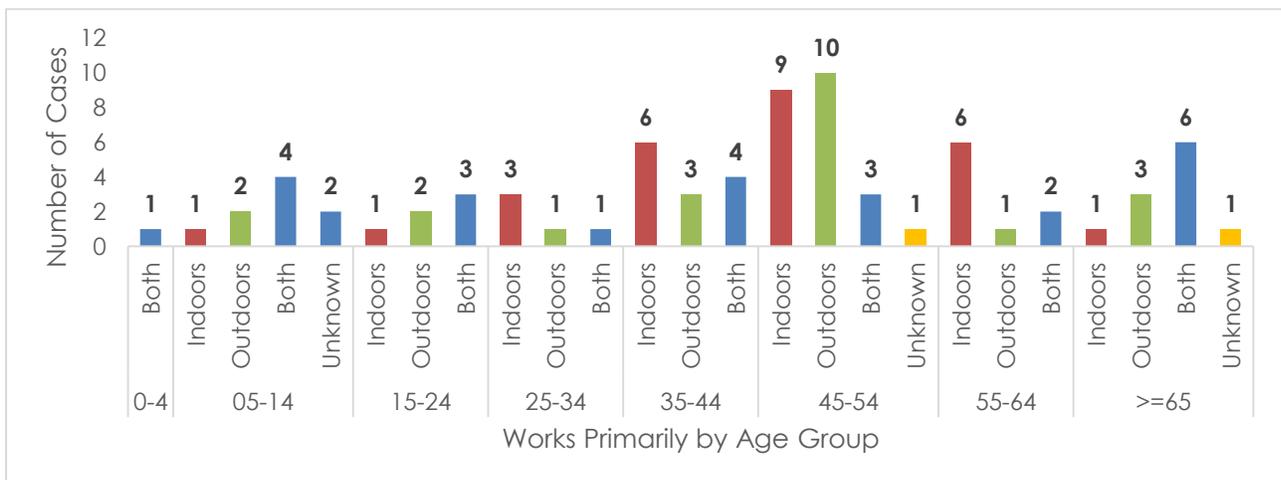
Primary work environment according to the overall count of reported occupations by sex is illustrated below (Figure 10). Of the 100 cases that reported an occupation only 77 reported information regarding their primary work environment, of which 23 were female and 54 were male. An outdoor work environment was reported for 22 (29 percent) of the 77 cases, in which male cases accounted for 21 of the 22 responses. Work environments consisting of both indoor and outdoor exposure were reported for 24 (31 percent) of the 77 cases, with 16 male cases reported compared to eight female cases. An indoor work environment was reported for 27 (35 percent) of the 77 cases, with 14 male cases and 13 female cases.

Figure 10. Primary work environment by sex - Kansas, 2012-2015



The primary work environment was further broken down by individual age groups. The number of cases that reported working primarily indoors, outdoors, or both and the corresponding age group is illustrated below (Figure 11). Due to limited data for persons under the age of 18 conclusive analysis of the primary work environment could not be interpreted statistically. However, all the data that was reported is shown in Figure 11 below. Starting with age group 15-24 years of age (eight percent of the total cases) reported both an outdoor and indoor work environment, with four cases and three cases respectively. Age groups 25-34 (5 cases) and 35-44 (13 cases) both reported working primarily indoors, at three and six cases respectively. Cases aged 45-54 (30 percent of the total cases) reported the greatest amount of cases who worked primarily outdoors, at ten of the 23 cases in that age group. An indoor work environment was reported in six of the nine cases 55-64 year of age (12 percent of the total cases). Six of the 11 cases 65 years of age or greater (14 percent of the total cases) reported working in both indoor and outdoor environments as well.

Figure 11. Primary work environment by age group - Kansas, 2012-2015



CHAPTER 4 – Discussion

Conclusion

From 2012 to 2015 there was a total of 114 confirmed or probable cases of tularemia reported in Kansas. The average number of cases per year was 28.5. The average annual cases for the U.S. was 126.5 from 2001-2010, with Kansas accounting for 59 of the total 1,208 cases reported in that ten-year period (2). The median age of tularemia cases in Kansas was 41.9, was similar to the median age of tularemia in the U.S. of 39 years of age. The overall incidence in Kansas between the years 2001-2010 according to the CDC was 0.22 per 100,000 persons per year (2). The data in this reports shows that overall incidence in Kansas from 2012-2015 was 0.98 per 100,000. This suggests a 345 percent increase in the overall incidence of tularemia since 2010. This data set did not allow us to determine the cause of the increase, however it is not linked to changes in case definitions. The case definition of tularemia used by both the CDC and KDHE have not changed since 1999 which was prior to both studies.

Confirmatory laboratory tests for tularemia include isolation by culture and or an increase of fourfold or greater change in serum antibody to the *F. tularensis* antigen. The confirmatory uses of the culture and total antibody tests may account for the prevalence of their use when testing for tularemia. Total antibody accounted for 31 percent of the total tests used, with culture accounting for 26 percent. The remaining 43 percent included the other seven testing methods. It is expected that both total antibody and culture will remain the primary methods of diagnostic testing for tularemia as they are the most reliable and cost effective at the present time.

Males accounted for 68% of reported cases of tularemia in Kansas from the years 2012-2015, and the United States from 2001-2010 (2). The increased probability of infection in men may be attributed to the tendency of males to participate in activities or occupations that are linked to a higher potential risk of exposure to *F. tularensis*. The CDC reported that in the U.S. children aged 5-9 years of age and men 65-69 years of age had the highest incidence of tularemia (2). In Kansas from 2012-2015, cases 5-14 years of age and 45-54 years of age had the highest incidence (5.20 and 6.77 per 100,000 persons respectively). Further research through a case-control study would be needed to determine activities that result in an actual increase in risk. However, differences in behavior or activities of individuals may result in possible exposure to the bacteria. Those age groups with a higher incidence of tularemia may contain a large percentage of individuals who are involved in activities (i.e. hunting, hiking, landscaping, etc....) that could be a potential source of acquiring the disease.

Demographic factors such as race and ethnicity were also considered in this data analysis. Similar to the CDC's U.S. statistics on tularemia, White Americans made up the greatest percentage of those infected, 86 percent in the U.S. and 98 percent in Kansas (2). The major ethnicity reported was non-Hispanic, accounting for 96 percent of the Kansas cases. This discrepancy in Kansas cases may be attributed to the fact that the primary race

and ethnicity reported by Kansas residents was White, non-Hispanic according to data available from the KDHE office of vital statistics (13). Kansas individuals who reported their race as Black made up two percent of the total cases. Similarly, Hispanic individuals made up four percent of tularemia cases in Kansas and five percent in the United States. The race and ethnicity of the remaining patients was listed as missing or unknown. Overall, the race and ethnicity incidence in Kansas was similar to those recorded by the CDC between the years 2001-2010.

The form of tularemia acquired depends on the method of entry into the host by the bacteria. Due to this, it is important to consider the form of disease as it compares to the associated potential exposures. Ulceroglandular and glandular were the primary diagnoses, at 39 percent and 30 percent respectively. Both forms are commonly associated with tick or insect bites and or contact with infected animals or carcasses. The ulceroglandular form manifests as an infected ulcer or wound typically considered the initial site of bacterial entry. The glandular form presents with infection of regional lymph nodes, but without presence of an ulcer at the site of infection. As the two most commonly reported potential exposures in Kansas were; pet(s) in the home and tick or other biting fly bite. It appears as if pet related factors were responsible for the majority of the ulceroglandular and glandular diagnoses. The other four forms of tularemia diagnosed in Kansas during the study period accounted for remaining 11 percent of the diagnoses. These forms required infection to occur in specific parts of the body (e.g. ocular or oropharyngeal systems) or through specific exposures (e.g. ingestion or inhalation). This correlates with the CDC report that these forms of the disease are less common (12). The most severe form, pneumonic, accounted for five percent of Kansas cases. Overall mortality from tularemia in the United States is less than two percent due to effective treatment methods (2). During the entire study period, there was one reported death related to tularemia infection in Kansas. However, it was noted that the deceased patient had comorbidities that could have contributed to the death. However, even one death related to tularemia is too many and something communities can work toward preventing.

The association of tularemia with outdoor occupations and activities can be illustrated by higher incidences of disease in densely-settled or rural counties. In the United States 53 percent of cases were considered to be in rural counties (2). According to the 2010 U.S. census 19.3 percent of the U.S. counties were classified as rural (20). In Kansas the population percent in rural counties was 25.8 in 2010. Using the adjusted peer group categorization, 15 percent of Kansas cases were linked to rural counties with between 0 to 19.9 persons per sq. mi. The county with the highest average incidence (five cases, 35.91 per 100,000 persons per year) was Chautauqua County in South East Kansas with a population of 3,481 in 2014. Comparatively, the county with the lowest incidence was Johnson county (ten cases, 0.44 per 100,000 persons per year), an urban area with a population of 574,272 in 2014 located in the North East region of Kansas. Over half of Kansas counties did not report any incidence of tularemia between the years 2012-2015. The majority of reported cases occurred in counties located in the Eastern portion of the state. This division correlates with the preferred habitats of both the brown dog tick (*D. variabilis*)

and the Lone Star tick (*A. americanum*). It may also be related to differences in human population between the Eastern and Western halves of the state. Due to recent studies regarding the increases habitat range of the Lone Star tick, it is important that surveillance is continued and any changes in incidence of tularemia recorded.

Diagnosis of tularemia in Kansas peaked annually starting around May and continuing through August or September. Over the four-year period, 80 percent of the total cases were diagnosed between May and September. This is consistent with the CDC findings that 77 percent of cases occurred from May to September across the United States from 2001 to 2010 (2). These peaks may be attributed to an increase in human outdoor activities paralleled with prime tick and insect season. This increase may also overlap with variations in hunting seasons across the U.S. In Kansas increases in tularemia could be due to increases in outdoor activities during the spring and summer months. While there were significant changes in the number of cases of tularemia diagnosed between the months, over the entire four-year period there was no significant change in overall tularemia incidence.

Perhaps the most important information with regards to tularemia infection in humans is the associated potential exposures. Of the 14 potential exposures specifically looked at in this report, the top five reported and their percent frequencies were as follows; pet(s) in the home (61 percent), tick or biting fly bite (57 percent), pet dog (51 percent), lawn mowing and landscaping (39 percent), and pet cat (26 percent). With the exception of the pet exposures, which may occur constantly throughout the year, the frequency of the other exposures correlates with the annual peaks in disease. What was most surprising from this information was the relatively low association with hunting. Historically, tularemia was largely attributed to contact with infected animals, especially the cottontail rabbit, which occur in high number across the state. Other species of wild rabbits (jack rabbits, snowshoe hares, etc....) are also susceptible to tularemia but are less commonly associated with human cases of the disease (17). In Kansas hunting both cottontail and jack rabbits is permitted year-round with a daily bag limit of 10 and a possession limit of 30 (18). Hunting was only reported in 5 percent of the 114 cases studied in this report.

Of the 14 potential exposures examined in this report eight were reported in less than 15 percent of the cases. Those eight factors were; 'any pets ill/died' (13 percent), 'pets brought home dead animal' (12 percent), 'other pet' (four percent), 'contact/ingest water or soil' (nine percent), 'hunting' (five percent), 'contact/ingest uncooked meat' (four percent), 'laboratory worker' (one percent), and 'association with other human tularemia case' (zero percent). Because there were no control cases available to compare, we were unable to determine if any of the potential exposures statistically increase one's risk of contracting tularemia. These potential exposures were taken from documents used by the KDHE in the tularemia disease investigation form in order to obtain a general knowledge of activities that an infected individual may have participated in.

Of the total 114 cases 70 percent of both male and female patients reported more than one potential exposure. This was surprising because it was assumed males would show

a higher frequency of multiple potential exposures based on the idea that males are more commonly affected than females. The top five reported exposures for male patients were; pet dog (54 percent), tick or biting fly bite (44 percent), pet(s) in the home (40 percent), lawn mowing or landscaping (31 percent), and pet cat (26 percent). Female patients reported; pet dog (31 percent), pet(s) in home (23 percent), pet cat (18 percent), tick or other biting fly bite (15 percent), any pets ill/died (10 percent). These discrepancies in the most common potential exposures could be due to differences in occupation or activities that lead to different exposures.

It was important to look at differences between reported exposures by age group, in order to gain better insight into activities that may be common among specific groups. Pet(s) in the home and tick or biting fly bite, were the most common exposures for persons 5-14 years of age and 45-54 years of age (the age groups with the highest incidence of tularemia). For all clinical syndromes the overall top five exposures reported were; pet(s) in the home, tick or biting fly bite, pet dog, lawn mowing or landscaping, and pet cat. Potential exposures; pet(s) in home and tick and biting fly bite were associated most frequently with the ulceroglandular and glandular syndromes. The most severe pneumonic form was associated most often with pet(s) in the home and lawn mowing or landscaping. These findings correlate with the common methods of acquisition listed in Table 1, sourced from the CDC resources on tularemia (12).

As pet(s) in the home and tick or biting fly bites were the primary potential exposure reported, action to reduce the risk from these type of exposures should be taken. Personal protective clothing (i.e. long pants, long sleeves, and long socks) should be worn when individuals are in environments where ticks or other biting insects may be present. The CDC also recommends the use of insect repellents with 20-30 percent DEET, picaridin, or IR3535 (16). Similarly, pet owners should be taking precautions to ensure that their pets do not bring ticks or carcasses of infected animals into areas where humans contact is possible. While these actions cannot guarantee that an individual will not become infected with *F. tularensis* they may however significantly reduce the risk of a potential exposure.

One of the most significant findings from this report was the fact that tularemia incidence in Kansas has increase from 0.22 per 100,000 persons in the 2010 CDC study to 0.98 per 100,000 persons determined in this analysis. While we were unable confidently determine the cause of this increase there are a number of scenarios that could have contributed to the increase. One thought is that this might be due to under-reporting or under-testing of tularemia during CDC study period. On the other side of the spectrum increase in tularemia could be linked to increases in disease awareness which may lead to more extensive testing of clinical specimens that may not have been tested otherwise. It may also be an actual increase in incidence, the cause of which would require further investigation. It is noted that the increase in incidence is not linked to any changes in case definition as the definition used by both the CDC and KDHE has not changed since 1999, prior to both studies.

In conclusion, while tularemia remains a fairly uncommon disease, it does have the potential to cause severe symptoms and even death. Thus, prevention should be the major focus of health care facilities in regards to tularemia. This report could be used to prepare a Kansas tularemia risk flow chart that would enable individuals or health care personnel to ascertain the risk based on lifestyle. Health officials should warn patients of the increased risk of tularemia during the peak months of May through September, or when the patients may be participating in activities that put them at higher risk. Since the bacterium is endemic in Kansas it is important that we continue to monitor the annual incidence in order to track changes in the disease trend that might indicate a severe outbreak or intentional release.

Limitations

This report attempts to provide a statistical analysis regarding tularemia in Kansas. Thus the above discussion seeks to provide the most educated explanation for the findings based on the data obtained from 2012 to 2015. However, it is noted that conclusive answers may not be limited due to the small number of cases available for study affecting the overall statistical analysis. Differences in incidence rates and population estimates may also change depending on the source used in the calculation. Incomplete or missing information regarding tularemia cases may also influence the conclusions drawn in this report. There was also a significant amount of bias that limited the results of this analysis. This bias may result from the lack of control cases available for comparison. Because this was a retrospective analysis we were unable to make appropriate case-control matches. Another source of bias was the differences county classification based on population. These biases may also explain the drastic increases in tularemia incidence in Kansas since 2010.

Suggestions for Improvement

Throughout my research I came across limitations in the data that if remedied would aid in simplifying future tularemia data analysis. The first suggestion would be to separate questions regarding pet(s) in the home based on the species of animal. While having pets in the home is a known potential exposures, having separate variables would enable health officials to determine if a particular species harbors a greater association with tularemia. Secondly, the variable 'Works Primarily' was vague and may have unintentionally limited the responses received. My recommendation is to rephrase the question, or create a new question, that includes activities outside of the patient's reported occupation. Such as; outside of your job do you primarily spend time indoors or outdoors? Or would you say that a typical day for you is spent primarily indoors, outdoors, or an equal combination of both? This would also make this question applicable to children and unemployed individuals. Lastly, many individuals in this data set were exposed to multiple potential exposures prior to their onset of illness. Due to this it is difficult to accurately determine which exposures were the most likely cause of tularemia. While this may not be possible in all cases regardless of more in-depth information, it would be useful to have supplementary questions that could be used in cases with exposure to more than one potential exposure. Such as; of the previously mentioned exposures which would you say fall outside of your normal routine?

This would allow for more accurate causation data, which may be useful in developing prevention methods.

Future Research

While the dataset on tularemia from 2012-2015 is relatively small compared to other more prevalent diseases, there are still opportunities for expansion that could not be included in this report. One consideration for future research may be to focus on the most likely route of exposure as it relates to the primary clinical syndrome. Specifically, looking into how often pet(s) in the home is the actual cause of infection. This would allow health officials the ability to give more precise recommendations on ways to reduce the risk of contracting tularemia. Another consideration may be to look deeper into how vector habitat expansion affects incidence of *F. tularensis* infection across the state. For record and reporting purposes it would be beneficial to continue collecting yearly incidences in order to better monitor for significant increases or decreases across the state.

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APPENDIX

U.S. DEPARTMENT OF
HEALTH AND HUMAN SERVICES
CENTERS FOR DISEASE CONTROL
AND PREVENTION
ATLANTA, GA 30329-4027

Tularemia Case Investigation Report



OMB No. 0920-0728

Case ID #: _____

Patient History

Age: _____	Sex: <input type="checkbox"/> Female <input type="checkbox"/> Male <input type="checkbox"/> Unknown	Patient Ethnicity: <input type="checkbox"/> Hispanic or Latino <input type="checkbox"/> Not Hispanic or Latino <input type="checkbox"/> Unknown	Patient race: (select all that apply) <input type="checkbox"/> American Indian/Alaska Native <input type="checkbox"/> Asian <input type="checkbox"/> Black or African American <input type="checkbox"/> Native Hawaiian or Pacific Islander <input type="checkbox"/> White <input type="checkbox"/> Unknown/other
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Residence: State: _____ County: _____	Concurrent conditions: <input type="checkbox"/> Pregnant <input type="checkbox"/> Immunocompromised (please specify): _____
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Course of Current Illness

Date of initial symptom onset: _____ mm/dd/yyyy	Was the patient hospitalized? <input type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> Unknown
Date first seen by a medical person: _____ mm/dd/yyyy	Admit date: _____ Discharge date: _____ mm/dd/yyyy mm/dd/yyyy

Symptoms at presentation:	<input type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> Unknown	<input type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> Unknown
Fever/sweats/chills	<input type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> Unknown	Cough
Confusion/delirium	<input type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> Unknown	Chest Pain
Vomiting/diarrhea/abdominal pain	<input type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> Unknown	Shortness of breath
Sore throat	<input type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> Unknown	Other: _____

Localized signs:	<input type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> Unknown	<input type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> Unknown
Lymphadenopathy Location/description: _____	<input type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> Unknown	Conjunctivitis
Skin lesions (e.g., ulcer, papules) Location/description: _____	<input type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> Unknown	Pharyngitis/tonsillitis
Chest X-ray: <input type="checkbox"/> Not Done <input type="checkbox"/> Unknown <input type="checkbox"/> Infiltrates or nodules <input type="checkbox"/> Pleural effusion <input type="checkbox"/> Clear/normal		

Treatment:	Illness outcome:
Receipt of effective antibiotics (check all that were administered):	<input type="checkbox"/> Recovered, no complications
<input type="checkbox"/> Aminoglycosides (e.g., streptomycin, gentamicin) start date: _____ mm/dd/yyyy	<input type="checkbox"/> Recovered, complications (please specify): _____
<input type="checkbox"/> Tetracyclines (e.g., doxycycline) start date: _____ mm/dd/yyyy	<input type="checkbox"/> Recovered, unknown complications
<input type="checkbox"/> Fluoroquinolones (e.g., ciprofloxacin, levofloxacin) start date: _____ mm/dd/yyyy	<input type="checkbox"/> Died (please specify cause and date of death): _____
	<input type="checkbox"/> Unknown

Primary clinical syndrome:	<input type="checkbox"/> Ulceroglandular <input type="checkbox"/> Oculoglandular <input type="checkbox"/> Typhoidal <input type="checkbox"/> Meningitic
	<input type="checkbox"/> Glandular <input type="checkbox"/> Oropharyngeal <input type="checkbox"/> Pneumonic <input type="checkbox"/> Unknown

CDC 56.50 (E), Revised May 2016, CDC Adobe Acrobat 10.1, S508 Electronic Version, May 2016
Public reporting burden of this collection of information is estimated to average 20 minutes per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing the collection of information. An agency may not conduct or sponsor, and a person is not required to respond to a collection of information unless it displays a currently valid OMB control number. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden to CDC/ATSDR Reports Clearance Officer; 1600 Clifton Road NE, MS D-74, Atlanta, Georgia 30329-4027; ATTN: PRA (0920-0728).

ACKNOWLEDGMENTS

I would like to offer my sincerest thanks to all of those involved throughout the process of pursuing my MPH degree.

- Dr. Ram Raghavan for serving as my major professor and mentor in finding a project and continuing to help me take it to the next level.
- Dr. Michael Sanderson and Dr. Douglas Goodin for serving on my MPH committee and lending their support and advice throughout my project.
- Daniel Neises for agreeing to take me on as a student intern at the KDHE and showing me the ropes of life in a state health department.
- My family and friends for their constant love and support through my entire educational pursuits.
- Dr. Elyn Mulcahy for her kindness and interest in my future plans and the future of the KSU MPH program.
- Mrs. Barta Stevenson for always being an email away and keeping us all organized and on track.