ANIMAL BITE INJURIES IN NORTH CAROLINA: EMERGENCY DEPARTMENT VISITS AND RISK FACTORS FOR HOSPITALIZATION

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ABSTRACT

SARAH KATHLEEN RHEA, DVM, MPH: Animal Bite Injuries in North Carolina: Emergency Department Visits and Risk Factors for Hospitalization
(Under the direction of David J. Weber, MD, MPH)

Animal bites may lead to costly healthcare utilization, such as emergency department (ED) visits, hospitalization, and rabies post-exposure prophylaxis. Directed public health interventions may reduce the animal bite burden but require knowledge of current epidemiology. Within the cohort of North Carolina (NC) residents from 2008-2010, 38,971 incident animal bite-related visits were identified from statewide ED surveillance data. Rates were calculated using census denominators. ED visit and patient characteristics were examined. By age 10, a NC child had a 1 in 50 risk of dog bite injury. Although dog bite incidence among adults declined steeply with age, this trend was reversed for cat bites and scratches, which reached peak incidence among residents age >79 years. For both dog bites and cat bites and scratches, secular incidence trends showed pronounced seasonal patterns which peaked in spring and early summer. Infection was diagnosed in 3% of dog bites and 17% of cat bites or scratches. Hospitalization occurred in 3% of animal bite visits.

Risk factors for hospitalization after dog bite injury have not been examined quantitatively. A case-cohort study of ED patients evaluated for dog bite injury from 2000-2011 was conducted to examine the association between the following risk factors and hospitalization: infection, complicated injury, host defense abnormality, number of previous evaluations, and anatomic location of bite. Cases (n=111) were more likely to be male, white, or insured by Medicaid than subcohort members (n=221). Using logistic regression, all factors evaluated were associated with increased risk of hospitalization. However, infection was associated with the largest relative risk (odds ratio=7.8, 95% confidence interval 3.8, 16.0). Having had ≥1 prior evaluation for the dog bite was associated with a lower risk of hospitalization for females than males and for whites than non-whites.

In NC, dog bite prevention efforts should be directed toward children ≤14 years in early spring. Older adults should be educated on avoidance of cat bites and scratches. The strongest risk for hospitalization was associated with infection at the time of ED visit for dog bite injury, highlighting the importance of proper wound care, patient counseling, and consideration of antibiotic prophylaxis at initial evaluation.

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LIST OF ABBREVIATIONS

CC	Chief Complaint
CDC	Centers for Disease Control and Prevention
CI	Confidence Interval
CLD	Confidence Limit Difference
CLR	Confidence Limit Ratio
E-code	External cause of injury code
ED	Emergency Department
EMM	Effect Measure Modification
EMR	Electronic Medical Record
GEE	Generalized Estimating Equations
HCUP	Health Care Utilization Project
HIPPA	Health Insurance Portability and Accountability Act
HIV	Human Immunodeficiency Virus
IC	Interaction Contrast
ICARIS	Injury Control and Risk Survey
ICD-9-CM	International Classification of Diseases – 9th Revision, Clinical Modification
MRSA	Methicillin-resistant *Staphylococcus aureus*
NC	North Carolina
NC DETECT	North Carolina Disease Event Tracking and Epidemiologic Collection Tool
NC DPH	North Carolina Division of Public Health
NEISS-AIP	National Electronic Injury Surveillance System-All Injury Program

NHAMCS	National Hospital Ambulatory Medical Care Survey
OR	Odds Ratio
PEP	Post-exposure prophylaxis
py	Person-years
RD	Risk Difference
ROR	Ratio of Odds Ratios
RR	Relative Risk
SD	Standard Deviation
spp	Species (plural)
TN	Triage Note
US	United States

CHAPTER I

BACKGROUND

A. Overview

Animal bites continue to be an important public health issue with potentially devastating consequences. Substantial trauma, infection, rabies exposure, hospitalization, psychological effects, and, rarely, death may result from animal bites (1-5). Approximately 45% of children are bitten by a dog before they graduate from high school (6). Nationally, an estimated 0.2% to 1.1% of emergency department (ED) visits are animal bite-related (7).

Animal bite reports have been monitored by local health departments and animal control agencies for decades (1, 8). However, the precise incidence of animal bites is difficult to obtain. Methods for recording and storing animal bite data and the quality of that data vary significantly among municipalities. North Carolina does not have a statewide system for reporting and surveillance of animal bites, and a national system for animal bite reporting does not exist. Additionally, many animal bites are likely not reported to the appropriate agencies. It has been estimated that only about 17% of dog bites are reported to medical or legal authorities (9).

Despite these difficulties, several data sources have been used previously to describe the epidemiology of animal bites and estimate animal bite incidence in cities, states, and the nation. These data sources include local and state health departments, animal control agencies, police departments, hospital discharge records, and emergency department visit records. In most instances, researchers focus on dog bites only. The few studies that have included bites from animal species other than dogs use data that is now nearly 20 years old. No published studies have described the epidemiology of animal bites using ED visit data from a statewide syndromic surveillance system.

There are two likely reasons why the majority of animal bite-related studies include only dog bites. Dog bites constitute the majority of reported bites and bites requiring medical care (10). And, a specific International Classification of Diseases, 9th revision - Clinical Modification (ICD-9-CM) external cause of injury code (E-code) exists for dog bites, making identification of dog bite-related medical visits more straightforward than identification of medical visits for injury caused by other animal species (11). E-codes for other animal species are typically grouped. For example, ICD-9-CM code E906.0 is “Dog bite”. In contrast, ICD-9-CM code E906.3 is “Bite of other animal except arthropod”, including cats, rodents (except rats), moray eel, and shark.

Nationally, approximately 2.5% of dog bite-related ED visits are hospitalized (12). Several authors have described the distribution of patient and ED visit characteristics in populations hospitalized for dog bite-related injury (12-15). However, no previous studies have examined the relationship between patient and injury characteristics and the risk of hospitalization after a dog bite-related ED visit. Findings may assist physicians during patient assessment, impact treatment decisions, and reduce hospitalizations for dog bite injury.

Chapter IV (Manuscript 1) describes the incidence and epidemiology of animal bite-related ED visits in North Carolina from 2008-2010 using North Carolina Disease Event Tracking and Epidemiologic Collection Tool (NC DETECT) ED visit data. ICD-

9-CM E-codes and Chief Compliant and Triage Notes data were used to identify animal bite-related ED visits. For instances when the ICD-9-CM E-code was not specific for an animal species (e.g. E906.3), the Chief Complaint and Triage Notes data was used to identify the biting animal species. Statewide, patient age-specific, patient sex-specific, biting species-specific, and patient residence rural and urban-specific incidences were determined. Patient and ED visit characteristics were described. Benefits of using NC DETECT ED visit data for animal bite research include the ability to conduct a statewide population-based animal bite-related ED visit incidence study and to describe patient and ED visit characteristics across the state using one, comprehensive data source.

Chapter V (Manuscript 2) examines the relationship between risk factors and hospitalization after dog bite-related ED visit. A case-cohort study was conducted using UNC Health Care medical records. The cohort consisted of ED visits to the UNC Health Care ED between January 1, 2000 and December 31, 2011 with an ICD-9-CM E-code for dog bite (E906.1). Cases were defined as cohort ED visits that met the above criteria and resulted in an inpatient admission to UNC Health Care directly from the ED. A simple random sample from the cohort was selected as the subcohort. Logistic regression models were used to describe the relationship between each of the following risk factors and hospitalization: anatomic location of the dog bite, presence of complicated injury, number of previous medical evaluations for the dog bite, presence of host defense abnormality, and presence of infection. Effect measure modification (EMM) was examined by patient sex and race for the relationship between previous evaluation for the dog bite injury and hospitalization.

The following review provides a background and summary of the animal bite literature. A comparison of animal bite incidence studies leads the discussion, followed by an explanation of the descriptive epidemiology of animal bites. Risk factors for hospitalization after dog bite injury are then explored, paying particular attention to those risk factors examined in the case-cohort study. Finally, the public health significance of the dissertation manuscripts is outlined.

B. Animal bite incidence studies conducted in the United States

Animal bite incidence rates differ by the biting animal species and the human population under study. The review that follows includes findings from animal bite studies of multiple species and from dog bite only studies. In the United States (US) and other developed nations, many aspects of animal bite and dog bite epidemiology are similar. However, the focus of this review is on animal bite and dog bite incidence in the US.

B.1 Incidence of reported dog bites in a city or county

Multiple researchers have examined the incidence of reported dog bites in cities or counties in the US. One of the earliest such studies was conducted in New York City from 1965 through 1970 (16). Harris et al. discovered an increasing incidence of reported dog bites, from 353.3 per 100,000 persons in 1965 to 456.6 per 100,000 persons in 1970. From a similar time period, Morton used dog bite report data from the Norfolk, Virginia Rabies Control Program to find 319 dog bites per 100,000 population in a 6 month time period in 1971 (17). Beck et al. examined the dog bite problem in St. Louis, Missouri in 1972-1973 (6). Incidence rates were highest for children 5-9 years of age and increased from 1972 to 1973. In a 1989-1991 Milwaukee, Wisconsin study, Ndon et al. found an incidence of 171 reported dog bites per 100,000 persons per year and a geographic association between reported dog bites and poverty (18). Chang et al. employed a capture-recapture approach to address the known difficulty of gaining accurate dog bite incidence information (19). Using reports from multiple municipal and health providers in Pittsburgh, Pennsylvania in 1993, Chang et al. found a crude incidence of 21.4 dog bites per 10,000 persons and an adjusted 58.9 dog bites per 10,000 persons. Shuler et al. reported an incidence of 93 dog bites per 100,000 persons per year in one Oregon county in 2002-2003 (20). Healthcare provider dog bite reports were used by Borud et al. to calculate an incidence of 0.85 dog bites per 1,000 persons per year in New York City in 1998 (21). In that study, children 7-9 years of age had the highest incidence, and 18% of all reported dog bites were in children under 18 years old. Finally, Tan et al. used capture-recapture methods to estimate the incidence of dog bites in children in three Georgia counties using multiple agency sources (22). They estimated 4.6 dog bites per 1,000 children per year and discovered that local hospital EDs are an especially useful source of dog bite data.

B.2 Incidence of reported animal bites or exposures in a city or state

Although most animal bite incidence studies have included only dog bites, some have examined incidence of all animal bites in a region without regard to biting animal species. One of the first such studies was by R. Moore et al. in 1971-1972 (23). Animal bite records from 12 states, plus Washington D.C., Trenton, New Jersey, and the Manhattan borough of New York City were compiled. Incidence ranged from 20 animal bites per 100,000 persons per year to 927 animal bites per 100,000 persons per year, depending on the region and the year. In a more geographically defined study, Berzon et al. examined the animal bite epidemic in Baltimore, Maryland between 1970 and 1976 and found an incidence of 579 to 791 animal bites per 100,000 persons per year (24).

More recently, the epidemiology of reported animal bites in Indiana from 1990-1992 was described by Sinclair et al (3). Age and sex-specific incidence rates ranged from 38 reported animal bites per 100,000 persons per year for females >60 years of age to 360 reported animal bites per 100,000 persons per year for males aged 5-9 years. D. Moore and colleagues described reported animal exposures in 65 of 67 Pennsylvania counties in 1995 (8). Animal exposures included any potential rabies exposure or animal exposure leading to medical follow-up. The overall incidence of animal exposures was 137.2 exposures per 100,000 persons per year, while dog exposure incidence was 104 per 100,000 persons per year and cat exposure incidence was 23.6 per 100,000 persons per year. Children under 5 years of age had the highest incidence with 324.9 animal bites per 100,000 persons per year.

A 1985 study examining reported cat bites in Dallas, Texas found that the incidence of cat bites was highest in 25-34 year-olds (8.9 cat bites per 10,000 persons per year) and lowest in 18-24 year-olds (4.5 cat bites per 10,000 persons per year) (25). Approximately 60% of the cat bite victims in that study were females.

B.3 Incidence of self-reported dog bites

It is believed that many animal bites are not reported to authorities (9). In an attempt to better quantify the true number of animal bites, some researchers have performed telephone surveys to obtain information about unreported bites. Sacks et al. used the Centers for Disease Control and Prevention's (CDC's) 1994 Injury Control and

Risk Survey (ICARIS) to derive a national 5 month-incidence estimate of 18 dog bites per 1,000 persons and 3 dog bites requiring medical attention per 1,000 persons (26). A follow-up 2001-2003 ICARIS-2 study found an overall incidence of 15.8 dog bites per 1,000 persons and 3.1 dog bites requiring medical attention per 1,000 persons over the 3 year period (27).

B.4 Incidence of animal bites treated in hospitals and emergency departments

The first national study of dog bite-related ED visits was by Weiss and colleagues in 1996 (7). Using 1992-1994 National Hospital Ambulatory Medical Care Survey (NHAMCS) data, the authors estimated that 12.9 dog bite injuries per 10,000 persons per year were treated in United States EDs and that approximately 0.4% of all ED visits were due to dog bite injuries. Using 1994 data from the national Health Care Utilization Project (HCUP) database, Quinlan et al. reported that hospitalizations from dog bites ranged from 1.2 per 100,000 persons for 15-19 year olds and 5 per 100,000 persons for 0-4 year olds (28). More recently, 2008 HCUP data was used to estimate a national incidence of 103.9 ED visits for dog bite injuries per 100,000 persons per year and 3.1 hospitalizations for dog bite injuries per 100,000 persons per year (12). Holmquist et al. showed that, nationally, 2.5% of ED dog bite injury visits were hospitalized. One national study examined nonfatal dog bite-related injuries in EDs in 2001 using the National Electronic Injury Surveillance System-All Injury Program (NEISS-AIP) (29). Gilchrist and CDC colleagues reported an estimated incidence of 129.3 nonfatal, ED-treated dog bite injuries per 100,000 persons per year. Approximately 1.8% of ED visits for non-fatal dog bite-related injuries were hospitalized. The most recent national study examining nonfatal dog bite-related injuries in EDs used NEISS-AIP data for the time period 2005-2009 (30). Quirk reported an average annual rate of 107.2 nonfatal, ED-treated dog bite injuries per 100,000 persons. An estimated 2.0% of such ED visits were hospitalized.

Several statewide studies and one citywide study have utilized hospital discharge data to examine the incidence of dog bite injuries. In their 1998-2005 Minnesota study of hospital discharge data, Day et al. found an incidence of 62.4 dog bite-related ED visits per 100,000 persons per year during that time period (31). Another statewide study of dog bite injuries was performed by Feldman et al. in California using 1991-1998 hospital discharge data (14). In this report, the authors published an incidence of 2.6 dog bite-related hospitalizations per 100,000 persons per year. A 1991-1992 Alaskan study utilized data from the state's trauma registry and found that 3.8 hospitalizations from dog bites occurred per 100,000 population per year (13). A 1998-2002 Kansas City, Missouri study reported an incidence of 157 dog bite-related ED visits per 100,000 persons per year and 4.3 dog bite-related hospitalizations per 100,000 persons per year during that time period (15).

ED surveillance data was used in one study to examine the incidence of dog bites, cat bites, and other animal bites in New York City from 2003-2006 (32). Inclusion criteria for the study included any ED visit record with the word "bite" and a recognizable mammalian animal or the word "animal" in the patient's chief complaint. The average annual rates were 56.2 dog bite-related ED visits per 100,000 persons, 10.2 cat bite-related ED visits per 100,000 persons, and 5.1 rat and mouse bite visits per 100,000 persons. The average annual rates of other animal bite-related ED visits, including unidentified animals, ranged from 2.8 per 100,000 persons for females ≥65 years of age to 7.9 per 100,000 persons for males 2-4 years of age.

C. Descriptive epidemiology of animal bites in the United States

C.1 Biting animal species

Several animal bite studies have discussed the distribution of biting animal species. In a study of animal exposures presenting to 11 university-affiliated urban EDs between 1996 and 1998, 80% of visits were due to dog exposures, 13% were due to cat exposures, and the remaining were due to various small mammals, livestock, and wildlife (10). Similarly, Sinclair et al. found that 78% of reported animal bites in Indiana in 1990-1992 were dog bites, 16% were cat bites, and the remaining 6% were from other species (3). D. Moore's 1995 Pennsylvania study of reported animal exposures found that 75% were due to dogs, 17.2% due to cats, 1.3% due to rodents, 1% due to squirrels and chipmunks, and <1% due to other species (8). A 1989-1991 Milwaukee, Wisconsin study found that 83% of reported animal bites were dog-related, 16% were cat-related, and the remaining 1% were related to other species (18). O'Neil and colleagues' 2001-2004 national study reported the epidemiology of non-canine bite and sting injuries in US EDs (33). Although the majority of these visits were for insect, bee and spider bites, 7.3% of these visits were from cat bites. A 2003-2006 ED surveillance data study in New York City found that of the animal bite-related ED visits included the study, 73.5% were dog bites, 13.3% were cat bites, 6.6% were rat or mouse bites, and 6.6% were other animal bites (32).

C.2 Age and sex of animal bite victim

The incidence of reported animal bites is consistently highest for children ≤14 years of age, especially for those ≤9 years old (3, 8). In Indiana from 1990-1992, 5-9 year olds had a reported animal bite incidence of 613 bites per 100,000 persons per year, more than any other age group in the study (3). Using reported animal exposures in 60 Pennsylvania counties in 1995. D. Moore et al. found that children <5 years of age had the highest incidence of any age group, 324.9 animal exposures per 100,000 persons per year (8). Alternatively, there were 137.2 reported animal exposures per 100,000 persons per year for the overall Pennsylvania population. Similar findings have been described in studies of reported dog bites. Approximately 44% of all reported dog bites in Milwaukee, Wisconsin from 1989-1991 were in children ≤14 years (18).

Emergency department visits for dog bites have a similar distribution among age groups as reported animal bites. A national study of 2008 hospital discharge data found that 5-9 year-olds had an incidence of 199.3 dog bite-related ED visits per 100,000 persons and those <5 years had an incidence of 175.0 dog bite-related ED visits per 100,000 persons (12). Subsequently, children <10 years of age had the highest incidence rates. This is in contrast with the overall national incidence of 103.9 dog bite-related ED visits per 100,000 persons in 2008. Weiss et al., Gilchrist et al, and Quirk found that children 5-9 years old had the highest incidence of dog bite-related ED visits, with Gilchrist et al. reporting 278.2 dog bite-related ED visits per 100,000 persons per year and Quirk reporting 214.5 per 100,000 persons per year (7, 29, 30). Similarly, Bregman et al. found that in New York City children 5-12 years had the highest incidence of dog bite-related ED visits (97.1 per 100,000 persons per year) (32).

Compared to females, males have a higher incidence of reported animal bites, reported dog bites, and dog bite-related ED visits (3, 8, 15, 30, 32). Sinclair et al. found that the overall incidence of reported animal bites in Indiana from 1990-1992 was higher for males than for females, other than the 41-60 year age group which had similar incidence rates for males and females (3). In Shuler et al.'s 2002-2003 study of reported dog bites in one Oregon county, males had a higher incidence than females (20). The incidence of ED visits for dog bite-related injuries was also higher in males than in females in 3 national studies (12, 29, 30) and 1 citywide study (32).

Several studies have examined bites from other specific animal species, finding slightly different epidemiology than that of aggregated animal bites or dog bites only. The occurrence of cat bite or scratch injuries has consistently been highest in adult females (10, 25, 32, 33). Wright's 1985 study of reported cat bites or scratches in Dallas, Texas, found an incidence of 8.9 cat bites per 10,000 persons per year for 25-34 year olds, the age group most affected (25). Fifty-nine percent of reported cat bites or scratches occurred in females. Bregman et al. reported the highest incidence of cat bite-related ED visits in females aged 40-64 years (18.0 per 100,000 persons per year) (32). Females were more likely than males to incur injuries or exposures requiring medical attention from gerbils, hamsters, and rabbits in Steele et al.'s study of 11 urban EDs (10). Approximately 80% of non-dog and non-cat injuries and exposures were in adults. However, children were 3 times more likely than adults to have injury from gerbils, hamsters, and rabbits. In Bregman et al.'s study in New York City, rates of rat and mouse bites were similar in males and females except for the 2-4 year-old age group, in which the rate was twice as high in males as in females (32).

C.3 Anatomic location of animal bite injuries

The types of injuries inflicted by animal bites can vary greatly and depend on the biting species, anatomic location of the bite, and the significance of the bite (1, 34). Wounds may include minor scratches and abrasions, puncture wounds, vascular and nerve damage, limb amputation, and other disfigurement (1). Although rare, death may occur with severe injury (2). Children are especially at risk for severe injury.

The literature describing anatomic location of bites or animal exposure wounds mainly includes dog bites and cat bites or scratches. When considering victims of all ages, 40-47% of dog-inflicted wounds occur to the arm or hand (8, 10, 18, 29); 19-29% are to the head, neck, or face (7, 8, 10, 18, 29); and 24-35% are to the leg or foot (10, 18, 29). The remaining percentage of dog bite injuries occur to other anatomic locations. Bites or scratches occur to the arm and hand in 72-90% of cat-inflicted bite or scratch injuries (8, 10, 25).

Children <10 years old are more likely than other age groups to incur head, neck, or face wounds as a result of bite or exposure from any animal species. This injury pattern reflects the fact that young children are usually at or below face level of an animal and are, therefore, more prone to facial injuries (35). Injuries to the face, neck, and head may also be more serious than injuries to other anatomic locations (36, 37). Dog bites to children <10 years of age occur to the face, neck, or head in 65-73% of cases (7, 29). Injury to the face, neck, or multiple anatomic locations occurs in 33% of cat bite cases in children <5 years of age (25).

C.4 Circumstances of animal bite and relationship of animal to victim

Several dog bite studies have examined the circumstances of the bite and the relationship of the dog to the victim (9, 10, 38, 39). Two manuscripts identified the relationships between cat and human victim for reported cat bites or scratches (8, 25). No studies could be found describing the circumstances of bites from other animal species.

In a Pennsylvania study, owned dogs were responsible for 92.6% of dog exposures reported to animal control authorities and owned cats were responsible for 62% of reported cat exposures (8). A study of reported dog bites in Milwaukee, Wisconsin found that owned dogs were responsible for approximately 50% of reported dog bites (18). The most frequently reported circumstance of animal bite injury in Balsamo et al.'s Louisiana study of reported animal bites was children playing with familiar animals (40). Shuler et al.'s study of an Oregon county found that 36% of victims reporting a dog bite did not know the dog that bit them (20). However, among children <5 years of age who were dog bite victims, 46% were bitten by the family dog. The only study examining cat bites and scratches exclusively showed that 57% of reported cat bites were due to stray cats (25).

Weiss et al. estimated that 58% of dog bite injuries examined in the nation's EDs occurred at the patient's home (7). Research using Minnesota hospital discharge data indicated that 96% of dog bites in children <1 year of age occurred when the child was approaching, provoking, or teasing the dog (31). Using data gathered at animal bite-related ED visits, Steele et al. found that when children were bitten by a dog, it was often while petting, playing with, or feeding the dog (10). This is in contrast to adults, who were more commonly bitten by dogs while breaking up a "dog fight".

C.5 Seasonality of animal bites

Animal bites, specifically dog bites, appear to have seasonality, as multiple studies have found an increased incidence during the summer months (3, 7, 18, 20, 21, 25, 29, 32). This may be attributed to increased outdoor activity of humans, especially children, and animals during warmer weather. Ndon et al. found that 67% of dog bites in Milwaukee, Wisconsin occurred between April and September (18). In New York City and nationally, peaks of dog bite activity were shown to occur in June and July (21, 29). Reported cat bites and scratches were more frequent during summer months in Dallas, Texas in 1985 (25).

C.6 Animal bite wound infections

Due to differences in oral flora and dentition, the potential for infection of an animal bite wound varies between species (34, 41). Infection is typically caused by the biting animal's oral bacteria. However, environmental pathogens, or commensal or pathogenic bacteria on human skin and mucous membranes may also cause animal bite wound infections. Previous reports have indicated that 1%-30% of dog bites and 29%-50% of cat bites become infected (41-44). This differing infection risk is likely related to the deep puncture wounds resulting from most cat bites. Such wounds are difficult to clean and provide a favorable environment for anaerobic bacterial growth. Another factor associated with the differing infection risk between dog and cat bites is the differing oral flora of dogs and cats. Infectious agents most commonly isolated from infected dog bites include *Pasteurella canis*, *Pasteurella multocida, Staphylococcus* species (spp.), *Streptococcus* spp., *Fusobacterium* spp., *Bacteroides* spp., and *Capnocytophaga canimorsus* (5, 41, 44, 45). The most common bacterial pathogen isolated from infected cat bites is *Pasteurella multocida*. Other common pathogens of cat bites include *Staphylococcus* spp., *Streptococcus* spp., *Fusobacterium* spp., *Bacteroides* spp., *Porphyromonas* spp., and *Moraxella* spp. Mixed aerobic and anaerobic infection is found in over 50% of infected dog and cat bite wounds.

C.7 Geography, socioeconomic factors, and animal bites

Several authors have included information about patient residence in studies of reported animal bites and dog bite-related ED visits or hospitalizations. In a study of reported animal bites in Indiana, Sinclair et al. found that residents of urban counties were more likely to have reported an animal bite than residents of less populated metropolitan or rural counties (3). In contrast, a Pennsylvania study showed a higher incidence of reported animal bites or exposures in less populated areas (8). Holmquist's national study of ED discharge data found that there were 4 times as many dog bite-related ED visits in rural areas as in urban areas (12).

Socioeconomic factors may also be associated with the occurrence of animal bites, specifically dog bites. Ndon et al.'s Milwaukee, Wisconsin study of reported dog bites found a positive correlation between the number of dog bites reported and the percentage of households below the poverty level in census tracts (18). In a Minnesota study of hospital discharge records, including ED and inpatient data, authors showed that the rates of hospital-treated dog bites were inversely proportional to the median income of communities where individuals resided (31). An Oregon study found that dogs living in census blocks with incomes below the county median were 50% more likely to be reported as a biting dog (20).

D. Characteristics of patients hospitalized after dog bite injury

Approximately 2.5% of all ED visits for dog bite are admitted to the hospital (7). Characteristics of these hospitalized patients and the potential determinants of their hospitalization have been described. Several authors have hypothesized that children and the elderly may be at increased risk of hospitalization after dog bite (12, 13, 15, 28). Children <5 years of age typically have the highest dog bite-related hospitalization rates of any age group, ranging from 4 hospitalizations per 100,000 persons per year in one national study to 15.1 hospitalizations per 100,000 persons per year in an Alaskan study (13, 28). Children 5-9 years of age usually have the second-highest incidence of hospitalization from dog bite injury. The incidence of dog bite-related hospitalization declines fairly steadily with age until 65 years-of-age, beyond which the incidence increases.

A few studies have examined ED visits and hospitalizations for dog bite injury in children only. In their 1979 review of ED visits for dog bite at one Chicago, Illinois children's hospital, Chun et al. reported that 11 of 199 (6%) dog bite ED patients were admitted to the hospital (46). A similar study in 1997 at a Pittsburgh, Pennsylvania children's ED reported that 188 of 204 (95%) of patients presenting for dog bite were discharged but did not further describe the proportion that were admitted (38). Daniels et al. examined 1999-2006 discharge data from a large health system in Indianapolis, Indiana and found that of 1,347 pediatric dog bite-related injury visits, 66 (5%) were hospitalized as inpatients and 56 (4%) were hospitalized as 23 hour observation (47).

Although males seek ED treatment for dog bite-related injuries with a higher frequency than females, males and females generally have a similar incidence of hospitalization after dog bite (12). In Holmquist el al.'s 2008 national study, there were 3.1 hospitalizations per 100,000 persons for both males and females. A Kansas City, Missouri study found males had 4.4 dog bite-related hospitalizations per 100,000 persons while females had a similar incidence of 4.3 dog bite-related hospitalizations per 100,000 persons per year (15).

Few published reports of dog bite-related hospitalizations include information on race and/or ethnicity. Hoff et al. reported that although the percentages of dog bite-related ED visits were approximately the same for whites and blacks, the incidence of hospital admittance was higher for whites (15). Feldman et al.'s study using statewide hospital discharge data for California found that the incidence of dog bite-related hospitalizations was similar for whites and blacks (3.0 and 3.1 hospitalizations per 100,000 persons per year, respectively) but less for Hispanics (2.3 hospitalizations per 100,000 persons per year) (14).

Several previous studies of hospitalization after dog bite have included information on urban versus rural status of patient residence or median income of patient's community. Holmquist et al. reported that, nationally, patients who lived in rural areas had an incidence of 2.9 dog bite-related hospitalizations per 100,000 persons in 2008 while patients living in urban areas had an incidence of 0.9 dog bite-related hospitalizations per 100,000 persons that same year (12). Day et al.'s study of dog bites in Minnesota found that rates of hospital-treated dog bite injuries were inversely proportional to the median income of the individuals' communities (31). Neither study addressed the distinction between patient residence and the geographic location where the bite occurred.

Few authors have described the medical bill payer of dog bite-related hospitalizations. Holmquist et al. looked at the prevalence of payer options nationally in their 2008 dog bite-related hospitalization study and found that private insurance was the primary payer for 42.9% of dog bite-related hospital stays (12).

E. Potential determinants of hospitalization after dog bite

Potential determinants of hospitalization after dog bite include infection, previous evaluations for the dog bite, anatomic location of the bite, complicated injury, and host defense abnormalities. Some of these potential determinants have been described in populations hospitalized after dog bite injury (12, 14, 15) and in the clinical literature as indicators for hospitalization after dog bite (44, 48). However, quantitative methods have not been used previously to examine the relationships between these determinants and the risk of hospitalization after a dog bite injury. A better understanding of risk factors for hospitalization may reduce dog bite-related hospitalizations and improve patient outcomes.

E.1 Infection and previous treatment for the dog bite injury

Previous reports have indicated that 1%-30% of dog bites become infected (41, 43, 44). A mix of aerobic and anaerobic bacteria both from the patient's skin and the biting dog's mouth can be cultured from most bite infections (41, 44, 45). *Pasteurella* spp. is the most common pathogen isolated from infected dog bites, specifically *Pasteurella canis* (41, 44, 45, 49). Other common dog bite wound pathogens include *Pasteurella multocida, Staphylococcus* spp., *Streptococcus* spp., *Fusobacterium* spp., *Bacteroides* spp., and *Capnocytophaga canimorsus* (5). Methicillin-resistant *Staphylococcus aureus* (MRSA) and other antibiotic resistant bacteria may also be transmitted via dog bite (45, 50).

Most dog bite infections are limited to the soft tissue. The presence of local soft tissue infection was described by principal ICD-9-CM diagnosis codes for hospital stays in several dog bite studies (12, 14, 15). Cellulitis and abscess were the principal diagnoses in the majority of hospitalizations in two studies (12, 15). Hoff et al. reported 57% of primary diagnoses were cellulitis or abscess, while Holmquist et al. indicated that 43.2% of primary diagnoses were skin and subcutaneous tissue infections. Feldman et al. reported 20.1% of primary diagnoses were for cellulitis and abscess.

Dog bite injuries may also result in more complicated infections, such as osteomyelitis, septic arthritis, tenosynovitis, and subcutaneous abscess (45, 51). Depending on microbial and patient characteristics, systemic infection and septicemia can also occur. *Capnocytophaga canimorsus* infection is often associated with severe septicemia, especially in immunocompromised individuals and chronic alcohol users, and has a case fatality rate as high as 28% (5, 34, 44, 45, 52).

Laboratory confirmation of infection includes aerobic and anaerobic wound culture, ideally collected prior to wound manipulation and antibiotic administration (44, 45). Antibiotic susceptibility testing of bacteria grown in culture may assist clinicians in treatment planning. Blood culture may be performed for confirmation of systemic infection.

Certain bite characteristics and patient factors may predispose dog bite injuries to infection. Dire et al. concluded that deep full-thickness wounds, wounds with crushed or devitalized tissue that require debridement, patient age >50 years, and female gender were risk factors for infection (43). Other authors have suggested additional risk factors, including patient age <2 years; presence of immunocompromising and comorbid conditions; contaminated wounds; wounds to the hand, wrist, or foot; complicated injury of bone, joint, tendon, or neurovascular structure; and delayed treatment (>24 hours since injury) (41, 44, 53, 54).

Treatment of a clinically infected dog bite requires administration of appropriate oral and/or intravenous antibiotics chosen empirically or, ideally, with the assistance of culture and susceptibility results. Controversy exists regarding the use of prophylactic antibiotics for uninfected dog bite wounds (44, 45). However, most authors agree that prophylactic oral antibiotic therapy for low risk wounds provides little advantage over thorough wound irrigation (53-57). Low risk wounds include those that are superficial, easily cleansed, and <8 hours old.

Prophylactic antibiotic therapy should be considered for high risk wounds, such as complicated or contaminated wounds and wounds to the extremities, as well as wounds undergoing primary closure (44, 45). Effective empirical therapy should provide microbial coverage against *Pasteurella* spp., *Staphylococcus* spp., *Streptococcus* spp., and *Capnocytophaga canimorsus*. Amoxicillin-clavulanic acid, second-generation cephalosporins with anaerobic activity (e.g. cefoxitin), and third generation cephalosporins (e.g. ceftriaxone) are suitable single agents. For patients with penicillin allergy, clindamycin and a fluoroquinolone (e.g. levofloxacin) or doxycycline alone are acceptable for prophylaxis (44, 45). The typical duration of therapy is from 7 to 14 days but may vary depending on the severity of the bite, complications, and patient comorbidities (44).

Hospitalization for dog bite injury may be related to suboptimal antimicrobial therapy at preceding medical consultations (58). The use of first generation cephalosporins (e.g. cephalexin), erythromycin, or clindamycin alone should be avoided, as these agents provide poor coverage against *Pasteurella* spp. Despite appropriate antimicrobial regimens, some dog bites will become infected and require hospitalization for intravenous antibiotic administration and/or surgical debridement (59).

E.2 Anatomic location of the dog bite and complicated injury

Anatomic location of dog bite injury varies by patient age group. When considering victims of all ages, 40-47% of dog-inflicted wounds occur to the arm or hand (8, 10, 18, 29); 19-29% are to the head, neck, or face (7, 8, 10, 18, 29); and 24-35% are to the leg or foot (10, 18, 29). Alternatively, dog bites to children <10 years occur to the face, neck, or head in 65-73% of cases (7, 29).

In several studies of patients hospitalized for dog bite injury, anatomic location of the bite is described by principal ICD-9-CM diagnosis code. Feldman et al.'s 1991-1998 California study of patients hospitalized from dog bite injury found that 74% of children <10 years of age incurred wounds to the head and face compared with only 10% of those ≥10 years of age (14). However, only 18% of children <10 years of age had documented injury to the forearm, hand, or finger, compared to 71% of patients ≥10 years of age. In a national study of 2008 hospital discharge data, Holmquist et al. reported that, across all age groups, open wounds of the extremities were more frequent than open wounds of the head, neck, or trunk (12).

Injuries to the face, neck, and head may be more severe than injuries to other anatomic locations (36, 37). This is especially true in children. Facial dog bites may result in lacerations or avulsions of ocular adnexa, lips, ears, or nose. Significant vascular, tracheal, esophageal, or spinal cord injury can occur from bites to the neck (36, 60). Dog bite injury to the head may result in skull fractures, blunt head trauma and intracranial pathology. Severe, complicated injuries to the face, neck, or head typically require surgical repair under general anesthesia and may be at increased risk for infection (61).

Extremities, especially the hand, wrist, and forearm, are particularly vulnerable to complicated injury and infection. These anatomic structures consist of multiple small bones, joints, nerves, and enclosed compartments (45). Dog bite injury to the hand, wrist and forearm may result in fractures; nerve, tendon, or vascular damage; or infection, such as septic arthritis, tenosynovitis, compartment syndrome, or osteomyelitis (44, 45). These complicated injuries often require surgical debridement, hospitalization, and significant follow-up care (62).

E.3 Host defense abnormalities and dog bites

Host defense abnormalities are conditions in which the normal immune response is disrupted in some way. Certain comorbid conditions, including diabetes mellitus, human immunodeficiency virus (HIV) infection, liver disease, renal disease, or cancer, may result in host defense abnormalities or immunodeficiencies. Other patient characteristics, such as asplenia or use of immunosuppressive medication(s), may also jeopardize the host immune response.

Comorbid conditions differ in their affect on the host immune system. In both Type I and II diabetics, cell-mediated immunity is most disrupted, with abnormalities to neutrophils, monocytes, and lymphocytes (63). HIV-related immunodeficiency involves a depletion of CD4 T cells and eventual impairment of every arm of the immune system (64). Patients with chronic liver disease, such as cirrhosis, typically have defects to both cell-mediated and humoral immunity and compliment deficiency may be present (65). Chronic renal disease and uremia often result in a state of cellular activation and chronic inflammation with reduced phagocytosis and natural killer cell activity (64, 66). Corticosteroid use inhibits phagocytosis and intracellular killing of bacteria and causes lymphocytopenia and decreased production of inflammatory cytokines (67). Although the method of host defense impairment may differ, each results in a disrupted immune response and increased susceptibility to local and systemic infection.

Some comorbid conditions have been associated with age and race. For example, age ≥45 years and non-white race are risk factors for Type II diabetes. Individuals with a history of diabetes, hypertension, or cardiovascular disease, all conditions associated with advancing age, are at increased risk for chronic renal disease (68). Therefore, these factors should also be considered when evaluating the relationship between host defense abnormalities and hospitalization from dog bite.

F. Summary and Public Health Significance

Animal bite injuries continue to be a major public health concern in the US. However, accurate incidence of animal bites is difficult to determine due to several factors, including the lack of a national reporting system and variations in bite report documentation by municipality. Currently available incidence data includes information on dog bites only or is based on data that is nearly 20 years old.

NC DETECT is a unique public health surveillance system that collects ED visit data from 113 of 114 acute care hospitals in North Carolina (69). The use of this data source to study the incidence of animal bites in North Carolina is novel. No published studies have used a statewide syndromic surveillance system of ED visit data to determine age-specific, sex-specific, biting animal species-specific, and patient residence rural and urban-specific incidence rates. A statewide examination of the animal bite burden in North Carolina has not been previously published. Additionally, NC DETECT ED visit data provide information on patient demographics and ED visit characteristics which have not been explored in previous animal bite studies. In contrast to the existing literature, this dissertation provides current information on animal bite epidemiology by using data from 2008-2010. Current, statewide animal bite incidence data is useful for public health practitioners in North Carolina. Populations with increased incidence of animal bite-related ED visits may be identified, allowing for targeted public health interventions.

Approximately 9,500 dog bite-related hospitalizations occurred nationally in 2008 (12). Descriptive epidemiologic studies of patients with a dog bite-related hospitalization have been published. However, no previous studies have examined risk factors for hospitalization after dog bite injury. A quantitative examination of risk factors for hospitalization after a dog bite injury provides valuable insight for physicians as they assess and treat patients with such injuries.

CHAPTER II

SPECIFIC AIMS

Animals are an integral part of the lives of many Americans. An estimated 39% of US households own at least one dog and 33% own at least one cat (70). As suburban sprawl continues, humans are increasingly placed in contact with wildlife. Many occupations and certain hobbies also put individuals at elevated risk for injury from animals. With numerous potential exposures, animal bites continue to be a major public health concern and a burden on the healthcare system (1).

Consequences of animal bites include trauma, pain, infection, possible rabies exposure, and, rarely, death. Animal bites may lead to costly healthcare utilization, such as ED visits, hospitalization, and rabies post-exposure prophylaxis (PEP) (1, 9, 12). In the US, the cost of care for upper extremity dog and cat bites alone is estimated at >$850 million per year (62). Unintentional dog bite injuries are associated with an estimated average lifetime medical cost, including treatment and rehabilitation, of >$630 for a treat and release ED visit and >$18,000 for hospitalization (12, 71). The aggregated cost of dog bite-related hospitalizations in the US is approximately $53.9 million per year.

Animal bites are largely preventable injuries. Directed public health interventions may reduce the animal bite burden but require knowledge of current animal bite epidemiology. Incidence rates of dog bites are available but not routinely compiled (7, 29, 30). The most recent published rates of all animal bites for a population larger than a single city are from the early to mid-1990s and now outdated (3, 8). These studies examined animal bite and saliva exposures reported to local or state health departments. However, many animal bites are not reported to the appropriate agencies (6, 9). Therefore, ED visit data provide an alternative and, in some ways, superior means of examining the animal bite burden (32, 72).

Previous national estimates indicate that 0.2% to 1.1% of all ED visits are due to animal bites (7). Approximately 80% of bites are from dogs, while about 15% are from cats (10). Bites from other mammals, including rodents, livestock, and wildlife, are reported infrequently in the ED. National incidence rates ranging from 103 ED visits for dog bites per 100,000 persons per year to 129 ED visits for dog bites per 100,000 persons per year have been published (7, 12, 29).

Prior studies have used the ICD-9-CM E-code, E906.0, to identify ED visits for dog bite (7, 12, 15, 29-31). However, no previous studies have used additional E-codes to identify ED visits for other animal bites and a keyword search of ED visit Chief Complaints and Triage Notes to identify additional animal bite-related ED visits not assigned a bite-related E-code. The additional E-codes, Chief Complaints, and Triage Notes provide more accurate incidence rates and, for the first time on a statewide level, biting species-specific ED visit incidence rates. Additionally, this dissertation provides an example of the use of comprehensive, statewide ED syndromic surveillance data for determination of animal bite incidence rates and description of ED visit characteristics and patient attributes.

ED visit data collected through NC DETECT were used to examine and describe the burden of animal bites in North Carolina. NC DETECT is a statewide syndromic surveillance system created in 2004 by the North Carolina Division of Public Health (NC DPH) in collaboration with the Carolina Center for Health Informatics at the University of North Carolina, Department of Emergency Medicine. Currently, more than 99% (113 of 114) of acute care hospitals in North Carolina submit ED visit data daily to NC DETECT, including Chief Complaints, Triage Notes, and up to 11 ICD-9-CM final diagnosis codes or E-codes. In 2008, NC DETECT received data on approximately 4 million patient visits, about 99% of visits made to North Carolina EDs.

Incident animal bite-related visits were identified from statewide ED surveillance data by ICD-9-CM E-codes and Chief Complaint and Triage Note keyword searches for the time period January 1, 2008 through December 31, 2010. Incidence rates of animal bite-related ED visits were calculated using person-time denominators from US Census Bureau North Carolina population estimates (73). A cross-sectional analysis of incident animal bite-related ED visits was performed to examine ED visit and patient characteristics, including mode of transport to the ED, visit month, payment method, administration of rabies PEP, patient sex, patient age, anatomic location of bite(s), ED disposition, biting animal species, and urban versus rural patient residence.

Nationally, approximately 2.5% of all emergency department visits for dog bite are admitted to the hospital (12). The majority of these admitted patients require intravenous antibiotics and/or surgical repair of wounds. Dog bite-related hospitalizations are associated with a greater cost than hospitalizations from other type of injuries. This is despite the fact that dog bite related hospitalizations are typically shorter in duration by 2 days than other injury-related inpatient stays.

Guidelines for hospital admission after dog bite injury typically recommend consideration of the patient's age, as well as other characteristics, including comorbid conditions, systemic or severe local infection, anatomic location of the bite, and presence of complicated or severe injury (44). Comorbid conditions, such as diabetes mellitus or HIV infection, may impair healing or increase the risk for infection (44, 48). Patients with dog bites resulting in severe local infection or in systemic infection are frequently candidates for inpatient intravenous antibiotic administration (41, 44). The most common anatomic locations of dog bite wounds in hospitalized patients include the head and extremities. Complicated wounds that involve injury to bone, joint, or tendon may require surgical intervention and inpatient care.

Risk factors for hospitalization after a dog bite injury have not been examined quantitatively. A comprehensive understanding of patient and injury characteristics that result in an increased risk for hospitalization after a dog bite injury may reduce hospitalizations and improve patient outcomes. Findings may assist physicians during patient assessment and impact treatment decisions.

A case-cohort study was conducted to further explore the relationship between the following risk factors and hospitalization after a dog bite-related ED visit: presence of infection, complicated injury, host defense abnormalities, number of previous evaluations for the injury, and anatomic location of the bite. A medical record review was conducted at UNC Health Care, a large, integrated, teaching hospital (806 licensed beds) in North Carolina (74). The cohort consisted of patients seen at the UNC Health Care ED between January 1, 2000 and December 31, 2011 with ICD-9-CM E-code for dog bite (E906.1).

Cases were defined as cohort members who were admitted to UNC Health Care directly from the ED. From the cohort, a simple random sample was selected as the subcohort.

With this dissertation, the following hypotheses are tested:

Hypotheses for Manuscript 1:

The incidence of dog bite-related ED visits for patients with urban residence is greater than the incidence for patients with rural residence. Children 5-9 years of age have the highest incidence of dog bite-related ED visits. The incidence of cat bite-related ED visits is higher for women than for men.

Hypotheses for Manuscript 2:

Patients with dog bite(s) to the head, neck, or face have an increased risk of being admitted to the hospital after dog bite-related ED visit compared to those with dog bite(s) other anatomic locations. Infection of dog bite wounds will be associated with a greater risk of hospitalization after dog bite-related ED visit than other potential determinants of hospitalization.

With this dissertation, the following aims are addressed:

Specific Aim 1 (Manuscript 1):

Using NC DETECT ED visit data from January 1, 2008 to December 31, 2010, calculate animal bite incidence rates and 95% confidence intervals (CIs) over the 3-year study period and within yearly and monthly intervals for the entire state and by patient sex, age group, rural or urban residence, and biting animal species with age-adjustment to the US Census Bureau 2008 Intercensal Population Estimates for North Carolina by 5-year age groups. Calculate rate differences and 95% CIs.

Specific Aim 2 (Manuscript 1):

Describe incident animal bite-related ED visit and patient characteristics, including mode of transport to the ED, visit month, payment method, administration of rabies PEP, patient sex, patient age, anatomic location of bite(s), ED disposition, biting animal species, and urban versus rural patient residence.

Specific Aim 3 (Manuscript 2):

Using an administrative dataset from the University of North Carolina, Department of Emergency Medicine, identify patients with a dog bite-related ED visit that will be included in the case-cohort study. Create a data collection instrument and data base in preparation for medical record review. Perform a review of UNC Health Care medical records and collect relevant demographic and clinical data on each ED patient included in the study.

Specific Aim 4 (Manuscript 2):

Using logistic regression models, describe the relationship between the following risk factors and the risk of hospitalization after a dog bite-related ED visit: presence of infection, complicated injury, host defense abnormalities, number of previous evaluations for the injury, and anatomic location of the bite. Consider adjustment variables for the relationship between each risk factor and hospitalization based on directed acyclic graphs (DAGs).

Specific Aim 5 (Manuscript 2):

Evaluate effect measure modification by patient sex and race for the relationship between previous evaluation for the dog bite injury and hospitalization.

CHAPTER III

METHODS

A. Overview of study designs

Animal bites may lead to trauma, pain, infection, possible rabies exposure, and, rarely, death. Costly healthcare utilization such as ED visits and hospitalization may follow. Incidence rates of dog bites are available but not routinely compiled (7, 29, 30). The most recent published rates of all animal bites for a population larger than a single city are from the early to mid-1990s and are now outdated (3, 8). Risk factors for hospitalization after a dog bite injury have not been examined quantitatively. A comprehensive understanding of patient and injury characteristics that result in an increased risk for hospitalization after a dog bite injury may reduce hospitalizations and improve patient outcomes.

A cohort study of North Carolina residents from 2008-2010 was conducted to determine the incidence of animal bite-related ED visits. ED visit data from NC DETECT, a statewide syndromic surveillance system, was used for this study. More than 99% of acute care hospitals in North Carolina submit ED data to NC DETECT daily, including Chief Complaints, Triage Notes, and up to 11 ICD-9-CM codes and E-codes (69). Statewide age, gender, rural or urban residence, and biting animal species incidence rates were calculated using US Census denominators (73). A cross-sectional analysis of incident animal bite-related ED visits was performed to examine ED visit and patient characteristics.

A case-cohort study was conducted to examine the association between the following factors and the risk of hospitalization: infection, complicated injury, host defense abnormalities, number of previous evaluations for the injury, and anatomic location of the bite. The cohort consisted of ED patients evaluated for a dog bite injury between January 1, 2000 and December 31, 2011 at UNC Health Care (74). Cases were defined as cohort members who were admitted as inpatients to UNC Health Care directly from the ED. From the cohort, a simple random sample was selected for the subcohort. Logistic regression models were used to describe the relationship between each risk factor and hospitalization. Effect measure modification was examined by patient sex and race for the relationship between previous evaluation for the dog bite injury and hospitalization.

B. Study of animal bite incidence in North Carolina using statewide emergency department visit data

B.1 Population and study design

NC DETECT was the source of ED visit data for this study. NC DETECT is a statewide syndromic surveillance system created by the NC DPH in collaboration with the Carolina Center for Health Informatics in the Department of Emergency Medicine, University of North Carolina at Chapel Hill (69). NC DETECT collects ED visit data as part of a state-mandated bio-surveillance initiative. No recruiting or enrollment procedures are in place, as all ED visits from reporting hospitals are included. From 2008-2010, 108 to 113 of the 114 acute care hospitals in North Carolina submitted ED visit data to NC DETECT. As of 2008, NC DETECT included >99% of ED visits in North Carolina.

Not all animal bite-related injuries are treated at EDs. Animal bite victims may also seek care at private medical practices and urgent care centers, and some may not seek medical care at all. An individual with more severe animal bite wounds may visit an ED rather than a private medical practice or an urgent care center. Uninsured or underinsured individuals may preferentially seek care for animal bite wounds at an ED (75). Despite these limitations, the NC DETECT ED database provides the most comprehensive, complete, and cost-effective source of animal bite data in the state.

This study was a statewide, population-based cohort study including males and females of all ages and races. The incidence of animal bites treated in North Carolina EDs was determined. Animal bite-related ED visits have not previously been quantified in North Carolina. North Carolina is the 10^{th} largest state by population with >9.5 million residents in 2010 and has approximately equal numbers of residents living in urban and rural areas (76). An updated population-based study of the incidence and epidemiology of animal bites in North Carolina may be relevant to similar states and to the nation.

A cross sectional study design was used to examine the prevalence of ED visit characteristics and patient attributes at the time of the ED visit. The NC DETECT ED database contains information on patient age, sex, presenting chief complaint, arrival date and time, ICD-9-CM final diagnosis and injury codes, mode of transport to the ED, ED discharge disposition (e.g. discharged, admitted, transferred), procedure codes (e.g. administration of rabies PEP), and patient county and zip code of residence. Therefore, the cross-sectional dataset contained detailed animal bite-related injury information for a large number of ED visits made in North Carolina.

ED visits made by North Carolina residents from January 1, 2008 through December 31, 2010 and included in NC DETECT data were eligible for inclusion. North Carolina residency was based on the patient's self-reported home county and zip code. ED visits were included in the dataset only once. Eligible visits meeting at least one the following criteria were included.

1) Contained E-code E906.0 (11) (dog bite)
2) Contained E-code E906.1 (rat bite)
3) Contained E-code E906.3 (bite from other animal except arthropod) and was determined to be a mammalian or unidentified animal bite upon review of the CC and TN
4) Contained E-code E906.5 (bite from unspecified animal) and was determined to be a mammalian or unidentified animal bite upon review of the CC and TN
5) The CC or TN indicated a mammalian or unidentified animal bite, cat scratch, or bat scratch, but an animal bite E-code was not present. ED visits with CCs or TNs indicating cat or bat scratches were counted together with bites, as in previous research (25, 42), due to the difficulty in distinguishing bites from scratches by these species.

The following types of visits were not included in the dataset: 1) visits with CCs and TNs indicating bat exposure but no bite or scratch; 2) visits for "cat scratch fever" without mention of a cat scratch or bite in the CC or TN and lacking a bite E-code; 3) visits containing a rabies-related E-code (V01.5, V04.5) but lacking an animal bite E-code, bite-related CC, and bite-related TN; 4) human bite-related visits.

Recheck visit(s) by a patient to the same ED or an ED in the same health system could be identified through a masked identification number, but recheck visit(s) to a different ED or an ED outside the health system could not be identified. Visits to an ED in the same health system were considered the equivalent of visits to the same ED.

Each patient's first animal bite-related ED visit in calendar time was considered an incident visit, with the exception of recheck visits that occurred in January 2008. A recheck was defined as a visit that occurred ≤30 days from an incident visit. The first visit to occur >30 days after the most recent incident visit was considered another incident visit.

The possibility of including a recheck visit for rabies vaccination in the incidence calculations was minimized by defining recheck visits as those that occurred ≤30 days from an incident visit. Traditionally, the rabies PEP schedule included a total of 5 doses of rabies vaccines, the fifth of which was given on day 28 (77). The recommendation for use of a reduced 4-dose vaccine schedule for rabies PEP was released by the Advisory Committee on Immunization Practices on March 19, 2010 and may not have been implemented until near the end of the study period.

Using E-codes, CCs, and TNs, each visit was individually coded by biting animal species. A wildlife bite included a bat bite or scratch or a bite from one of the following animals: raccoon, squirrel or chipmunk, fox, opossum, beaver, groundhog or woodchuck, prairie dog, mole, skunk, bear, coyote, wolf, otter, or hedgehog.

B.2 Analytic approach

Incidence rates of animal bite-related ED visits were estimated with person-time denominators from the US Census Bureau 2008-2010 Intercensal Population Estimates for North Carolina (73). Rates and 95% CIs were calculated over this 3-year period and within yearly and monthly intervals for the entire state and by sex, age group, rural or urban residence, and biting animal species with age-adjustment to the US Census Bureau 2008 Intercensal Population Estimates for North Carolina by 5-year age groups. Rate differences and 95% CIs were calculated using Episheet© (78). Rural versus urban residence, based on self-reported county of residence, was classified as a dichotomous variable in which 85 of the 100 North Carolina counties are rural and 15 are urban (76).

Frequencies and percentages of incident animal bite-related ED visit and patient characteristics were described. Animal bite injuries were examined by ICD-9-CM diagnosis code group (11).

C. Risk factors for hospitalization after a dog bite injury

C.1 Population and study design

A case-cohort study was conducted at UNC Health Care, a large, integrated, teaching hospital (806 licensed beds) in North Carolina (74). The cohort consisted of patients seen at UNC Health Care ED between January 1, 2000 and December 31, 2011 with an ICD-9-CM E-code for dog bite (E906.1) (11). Additional criteria for inclusion into the study were as follows: 1) A physical examination was performed in the ED by a physician or a nurse practitioner. (UNC Health Care ED does not employ physician assistants.) 2) The ED visit chief complaint indicated a dog bite injury or the sequelae from such an injury (e.g. laceration). ED visits for rabies PEP or tetanus vaccination only and without evaluation of or medical care for a dog bite injury were not eligible for inclusion. 3) The ED visit was for injury from one or multiple dogs. Patients with injuries from a dog and another animal species (e.g. cat) were not eligible for inclusion. 4) The ED visit medical record was complete and available for review.

Cases were defined as cohort members who met the above criteria and were admitted as inpatients to UNC Health Care directly from the ED. From the cohort, a simple random sample was selected for the subcohort. Therefore, cases were eligible to be subcohort members. After considering the number of available cases and the approximate time commitment associated with the medical record review, it was my goal to include at least 100 cases and 200 subcohort members in the study. Based on published estimates of infection prevalence in the source population of patients hospitalized for dog bite-related injury, this sample size would have 80% and 90% power to detect odds ratios in the range of 2.6 and 2.9, respectively, at an alpha of 0.05.

It is possible that more severe dog bite-related injuries present to UNC Health Care than to smaller, non-teaching hospitals. Therefore, results of this analysis may not be generalizable to patients treated at smaller, non-teaching hospitals.

C.2 Data collection and quality assurance

Demographic characteristics, clinical data, and medical history for each ED visit included in the study were collected from UNC Health Care medical records. Data on risk factors, the outcome, and covariates were collected from the ED medical record for the specific visit included in the study or from the demographics page of the EMR. Wound microbiologic culture results were collected for descriptive analysis from extended information found in related ED visit medical records and inpatient medical records.

Anatomic location of the dog bite injury was abstracted from the physical examination findings and categorized by major body region: 1) head, neck, or face (including eyes, ears, and oral cavity); 2) upper extremity (including shoulders, arms, wrists and hands); 3) other anatomic location (lower extremity (including hips, legs, ankles and feet) or torso (including thorax, abdomen, genitals, other pelvis, back and buttocks, and other trunk); 4) multiple anatomic locations (a combination of one or more of the above anatomic locations). Presence of a complicated injury was abstracted from physical examination findings and defined as any of the following: 1) injury to tendon or ligament, joint (including dislocation), or nerve; 2) vascular injury requiring specific surgical intervention; 3) piercing injury into the thorax, abdomen, or skull; 4) fracture; 5) compartment syndrome. Presence of host defense abnormality was obtained from the medical history and defined as any of the following: diabetes mellitus, renal disease, hepatic disease, HIV positive, asplenic, or currently taking an immunosuppressive medication. Immunosuppressive medications included alkylating agents, antimetabolites, high-dose oral corticosteroids, immune suppressing antibodies and interferons) (79). Presence of infection was a dichotomous variable abstracted from the ED provider's clinical impression and included any infection related to the dog bite injury. Previous evaluation was defined as a medical evaluation documented in the medical history from any primary care, urgent care, or emergency medicine provider for the same dog bite injury, prior to the study visit at UNC Health Care ED. The number of previous evaluations was categorized as no previous evaluation, 1 previous evaluation, or ≥2 previous evaluations.

Data were entered into a custom, standardized, electronic data abstraction form developed in Epi Info™ (CDC) (Appendix 1) (80). I performed the data abstraction. A random sample of 10 study records was abstracted by a second reviewer, an emergency medicine physician, masked from the data I abstracted. Inter-rater reliability for risk factors, the outcome, and covariates were assessed using intraclass correlation statistics (81). Discrepancies were settled by re-reviewing the medical record.

C.3 Analytic approach

Multivariate logistic regression models were used to describe the relationship between each of the risk factors and the outcome (SAS® 9.2 (Cary, NC)) (82). For each risk factor, a directed acyclic graph (DAG) was used to evaluate potential confounding by covariates, including other risk factors (Appendix 2) (83, 84). DAG analysis indicated that, for each risk factor, the model should be adjusted for all other risk factors and for patient age. Patient age was modeled as a quadratic spline with knots at the 25% and 75% percentiles of the subcohort age distribution. The risk period was the duration of the ED visit for dog bite injury.

Odds ratios (ORs) from logistic regression models directly estimated risk ratios in the cohort, given the case-cohort design (85). The intercept from the model output was corrected by adding the natural log of the sampling fraction, which was 250/1384 (83). In the case-cohort study design, cases may be included in the cohort sample, so standard errors from the logistic regression model output are incorrect (83). Odds ratio 95% CIs were calculated using generalized estimating equation (GEE) robust variance estimates with an independent working covariance matrix and patient medical record number as the clustering variable. (83, 86, 87). Therefore, the GEE robust variance estimates took into account the cases in the cohort sample, as well as the 4 patients in the study with 2 dog bite injury ED visits on different dates.

For risk difference (RD) calculations, cases included in the cohort sample were removed from the cohort sample (83). The adjustment variables were centered by subtracting the mean, and logistic regression was performed. The intercept from the model output was corrected by adding the natural log of the sampling fraction. Coefficients from the logistic regression model output and the corrected intercept were used to create RD point estimates. Bootstrap sampling was used to obtain RD 95% confidence limits by resampling the cases and the non-cases in the cohort sample. A total of 10,000 bootstrap samples were evaluated to obtain stable RD confidence limits.

Odds ratio modification was estimated with product interactions of the risk factor with patient sex and race for the relationship between previous evaluation for the dog bite injury and hospitalization (83). For analysis of modification, the following variables were dichotomized: number of previous evaluations (no previous evaluation, ≥1 previous evaluation) and race (white, non-white). Given the case-cohort study design, the ratios of odds ratios (RORs) in the data estimated the ratios of relative risks (RRRs) in the cohort. Because the sampling fraction was known, the difference of RDs (interaction contrast, IC) could be estimated to assess modification on the additive scale. Bootstrap sampling was used to obtain 95% confidence limits for RORs and ICs. A total of 10,000 bootstrap samples were evaluated to obtain stable confidence limits.

D. Human subjects research

The Institutional Review Boards of the University of North Carolina at Chapel Hill and the NC DPH approved the study, "Animal bite-related emergency department visits: A population-based study of incidence, visit characteristics and patient attributes" (Manuscript 1). The Institutional Review Board of the University of North Carolina at Chapel Hill approved the study, "Risk factors for hospitalization after a dog bite injury: A case-cohort study of emergency department visits" (Manuscript 2) and found that it met criteria for waiver of informed consent for research and waiver of Health Insurance Portability and Accountability Act (HIPPA) authorization.

CHAPTER IV

MANUSCRIPT 1:
ANIMAL BITE-RELATED EMERGENCY DEPARTMENT VISITS: A POPULATION-BASED STUDY OF INCIDENCE, VISIT CHARACTERISTICS AND PATIENT ATTRIBUTES

A. Overview

Consequences of animal bites include trauma, pain, infection, possible rabies exposure, and, rarely, death. Animal bites may lead to costly healthcare utilization, such as emergency department (ED) visits, hospitalization, and rabies post-exposure prophylaxis (PEP). In the United States (US), the cost of care for upper extremity dog and cat bites alone is estimated at >$850 million per year. Directed public health interventions may reduce the animal bite burden but require knowledge of current animal bite epidemiology. Animal bite-related ED visit incidence rates using International Classification of Diseases, 9th Revision, Clinical Modification (ICD-9-CM) external cause of injury codes (E-codes) and Chief Complaint and Triage Note keyword searches have not been previously published. We report the incidence of animal bite-related ED visits in North Carolina and the association with age, sex, urbanicity, and season by biting species. Visit and patient characteristics are described, including use of rabies PEP, anatomic location of injuries, mode of transport to the ED, and ED visit payment method.

Within the cohort of North Carolina residents from 2008-2010, 38,971 incident animal bite-related visits were identified from statewide ED surveillance data by ICD-9-CM E-codes and Chief Complaint and Triage Note keyword searches. Rates were calculated using US Census denominators. A cross-sectional analysis of incident animal bite-related ED visits was performed to examine ED visit and patient characteristics.

Compared with urban North Carolina residents, those who live in rural areas have a substantially higher incidence of animal bite-related ED visits (rate difference 19 visits/10^5 person-years (py), 95% confidence interval 16 to 22 visits/10^5 py). By age 10, a NC child has a 1 in 50 risk of dog bite injury requiring an ED visit. Although dog bite incidence among adults declines steeply with age, this trend is reversed for cat bites and scratches, which reach peak incidence among residents age >79 years. A North Carolinian has a 1 in 60 lifetime risk of cat bit or scratch injury requiring an ED visit. For both dog bites and cat bites and scratches, secular incidence trends show pronounced seasonal patterns, with lows January to February and peaks roughly 50% higher in spring and early summer. Hospitalization occurs in 3% of animal bite visits. Infection is diagnosed in 3% of dog bites and 17% of cat bites or scratches.

Using ED surveillance data to monitor species-specific bite incidence across a state and in various subpopulations provides valuable insight for physicians, public health officials, and veterinarians. Findings may be used to target and renew support for animal bite prevention efforts. In North Carolina, dog bite prevention efforts should be increased and directed toward children ≤14 years-old in the early spring, and older adults should be educated on avoidance of cat bites and scratches.

B. Introduction

Animals are an integral part of the lives of many Americans. An estimated 39% of United States (US) households own at least 1 dog and 33% own at least 1 cat (70). As suburban sprawl continues, humans are increasingly placed in contact with wildlife. Many occupations and certain hobbies also put individuals at elevated risk for injury from animals. With numerous potential exposures, animal bites continue to be a major public health concern and a burden on the healthcare system (1).

Consequences of animal bites include physical and emotional trauma, pain, infection, possible rabies exposure, and, rarely, death (2). Animal bites may also lead to costly healthcare utilization, such as emergency department (ED) visits, hospitalization, and rabies post-exposure prophylaxis (PEP) (4, 9, 12-14, 28-30). Unintentional dog bite injuries are associated with an estimated average lifetime medical cost, including treatment and rehabilitation, of >$630 for a treat and release ED visit and >$18,000 for hospitalization (12, 71). The aggregated cost of dog bite-related hospitalizations in the US is approximately $53.9 million yearly.

Incidence rates of dog bites are available but not routinely compiled (12, 29, 30). The most recent published rates of all animal bites for a population larger than a single city are from the early to mid-1990s and now outdated (3, 8). These studies examined animal bite and saliva exposures reported to local or state health departments. However, many animal bites are not reported to the appropriate agencies (6, 9). Therefore, ED visit data provide an alternative and, in some ways, superior means of examining the animal bite burden (32, 72).

Prior studies have used the International Classification of Diseases, 9th Revision, Clinical Modification (ICD-9-CM) external cause of injury code (E-code) E906.0 to identify ED visits for dog bite (7, 12, 15, 29-31). However, no previous studies have used additional E-codes to identify ED visits for other animal bites and a keyword search of ED visit Chief Complaints (CCs) and Triage Notes (TNs) to identify additional animal bite-related ED visits not assigned a bite-related E-code. The additional E-codes, CCs, and TNs provide more accurate incidence rates and, for the first time on a statewide level, biting species-specific ED visit incidence rates.

North Carolina is the 10th largest state by population with >9.5 million residents in 2010 and has approximately equal numbers of residents living in urban and rural areas (76). An updated population-based study of the incidence and epidemiology of animal bites in North Carolina may be relevant to similar states and the nation. This study demonstrates the analysis of incident animal bites using a statewide, population-based ED visit surveillance system that collects CCs, TNs, and ICD-9-CM codes. Current knowledge of animal bite-related ED visits, including prevalence of infection, return ED visits, and use of rabies PEP, is valuable for physicians, public health officials, and veterinarians.

C. Methods

Dataset background and creation:

The North Carolina Disease Event Tracking and Epidemiologic Collection Tool (NC DETECT) was the source of ED visit data. NC DETECT is a statewide syndromic surveillance system created by the North Carolina Division of Public Health in collaboration with the Carolina Center for Health Informatics in the Department of Emergency Medicine, University of North Carolina at Chapel Hill (69). From 2008-2010, 108 to 113 of the 114 acute care hospitals in North Carolina submitted ED visit data to NC DETECT. As of 2008, NC DETECT included >99% of ED visits in North Carolina.

ED visits made by North Carolina residents from January 1, 2008 through December 31, 2010 and included in NC DETECT data were eligible for inclusion. North Carolina residency was based on the patient's self-reported home county and zip code. ED visits were included in the dataset only once. Eligible visits meeting at least one the following criteria were included.

1) Contained E-code E906.0 (11) (dog bite) (N=26,353)
2) Contained E-code E906.1 (rat bite) (N=213)
3) Contained E-code E906.3 (bite from other animal except arthropod) and was determined to be a mammalian or unidentified animal bite upon review of the CC and TN (N=5,606)
4) Contained E-code E906.5 (bite from unspecified animal) and was determined to be a mammalian or unidentified animal bite upon review of the CC and TN (N=771)
5) The CC or TN indicated a mammalian or unidentified animal bite, cat scratch, or bat scratch, but an animal bite E-code was not present (N=9,671). ED visits with CCs or TNs indicating cat or bat scratches were counted together with bites, as in previous research (25, 42), due to the difficulty in distinguishing bites from scratches by these species.

The following types of visits were not included in the dataset: 1) visits with CCs and TNs indicating bat exposure but no bite or scratch; 2) visits for "cat scratch fever" without mention of a cat scratch or bite in the CC or TN and lacking a bite E-code; 3) visits containing a rabies-related E-code (V01.5, V04.5) but lacking an animal bite E-code, bite-related CC, and bite-related TN; 4) human bite-related visits.

Recheck visit(s) by a patient to the same ED or an ED in the same health system could be identified through a masked identification number, but recheck visit(s) to a different ED or an ED outside the health system could not be identified. Visits to an ED in the same health system were considered the equivalent of visits to the same ED.

Dataset for incident animal bite-related ED visit analysis:

Each patient's first animal bite-related ED visit in calendar time was considered an incident visit, with the exception of recheck visits that occurred in January 2008 (N=11). A recheck was defined as a visit that occurred ≤30 days from an incident visit. The first visit to occur >30 days after the most recent incident visit was considered another incident visit.

Using E-codes, CCs, and TNs, each visit was individually coded by biting animal species. A wildlife bite included a bat bite or scratch or a bite from one of the following animals: raccoon, squirrel or chipmunk, fox, opossum, beaver, groundhog or woodchuck, prairie dog, mole, skunk, bear, coyote, wolf, otter, or hedgehog.

Incidence rates of animal bite-related ED visits:

Incidence rates of animal bite-related ED visits were estimated with person-time denominators from the US Census Bureau 2008-2010 Intercensal Population Estimates for North Carolina (73). Rates and 95% confidence intervals (CIs) were calculated over this 3-year period and within yearly and monthly intervals for the entire state and by sex, age group, rural or urban residence, and biting animal species with age-adjustment to the US Census Bureau 2008 Intercensal Population Estimates for North Carolina by 5-year age groups. Rate differences and 95% CIs were calculated using Episheet© (78). Rural versus urban residence, based on self-reported county of residence, was classified as a dichotomous variable in which 85 of the 100 North Carolina counties are rural and 15 are urban (76).

Cross-sectional analysis of incident animal bite-related ED visits:

Frequencies and percentages of incident animal bite-related ED visit and patient characteristics were described. Animal bite injuries were examined by ICD-9-CM diagnosis code group (11).

The Institutional Review Boards of the University of North Carolina at Chapel Hill and the North Carolina Division of Public Health approved this study.

D. Results

Overview of animal bite-related ED visits:

In North Carolina from 2008-2010, 38,479 patients made 42,614 animal bite-related ED visits, or 0.3% of all ED visits in the state. Nine percent (3,313) of the patients made animal bite-related recheck visits to the same ED. Of these patients, 2,724 (82%) made two, 421 (13%) made three, and 168 (5%) made four or more recheck visits.

Of the 38,971 incident animal bite-related ED visits from 2008-2010, 25,054 (64%) had an E906.0 code (dog bite), 211 (1%) had an E906.1 code (rat bite), 5,129 (13%) had an E906.3 code (bite from other animal except arthropod), 722 (2%) had an

E906.5 code (bite from unspecified animal), and 7,855 (20%) indicated bite in the CC and/or TNs but did not have an animal bite E-code. Of the 7,855 incident ED visits lacking an animal bite E-code, the majority were dog bite (N=4,315), cat bite or scratch (N=1,801), or unidentified animal bite (N=1,381).

Incidence rate of animal bite-related ED visits:

The statewide incidence rate of animal bite-related ED visits remained approximately constant over the study period: $135/10^5$ person-years (py) (95% CI, 132-137) in 2008, $141/10^5$ py (95% CI, 139-144) in 2010. The incidence rate was highest for children under 10 years of age, after which the rate declined fairly steadily with age (Table 1). The overall rates for males and females were quite similar (Table 1).

The rate of dog bite-related ED visits was much higher than for any other mammalian species (Table 1). The age trend in dog bite-related ED visits mirrored that of the overall trend, with the highest incidence in children age 5-9 years (Figure 1). The incidence of dog bite-related ED visits was higher in males ($115/10^5$ py) than in females ($95/10^5$ py), with a rate difference of $20/10^5$ py (95% CI, 17-22).

ED visits related to cat bites and scratches were next most common (Table 1), with highest rates among adults >75 years of age. The incidence of cat bite or scratch-related ED visits was higher in females ($26/10^5$ py) than in males ($12/10^5$ py), with a rate difference of $14/10^5$ py (95% CI, 13-15).

The incidence of visits for dog bites, cat bites or scratches, and other specified animal bites (bites from wildlife, equines, swine, small ruminants, other small animals, and rodents) demonstrated a seasonal pattern, with an increase in the late spring, peak in the summer, and decrease through the fall (Figure 2). This pattern was especially prominent for dog bite visits.

The age-adjusted incidence of animal bite-related ED visits was higher in rural than in urban NC counties (Table 2).

Cross-sectional evaluation of incident animal bite-related ED visits:

Among North Carolina residents with an incident animal bite ED visit from 2008-2010, the mean age was 32 years (range: 0-99; standard deviation: 22). Thirty percent (11,570) of such visits were made by children ≤14 years (Table 3). Similar numbers of incident animal bite-related ED visits were made by males and females. Patients from rural North Carolina counties made 19,555 (50%) of incident animal bite ED visits, while 17,623 (45%) were made by patients from urban North Carolina counties.

In 35,297 (91%) of incident animal bite ED visits the patient was discharged, while in 1,091 (3%) of incident visits the patient was hospitalized (Table 3). Fewer than 10 patients had a discharge disposition indicating death. However, identifying information was not available for death certificate verification. Private insurers paid for 14,139 (36%) of the incident animal bite ED visits (Table 3). Among the 30,865 visits with information regarding mode of transport to the ED, 27,908 (90%) were walk-ins.

Rabies PEP was administered during 1,664 (4%) of the incident animal bite-related visits (Table 3). Among the 698 ED visits for a wildlife bite, rabies PEP was administered at 234 (34%) visits. Rabies PEP was administered at 379 (7%) of cat bite or scratch-related visits and at 839 (3%) of dog bite-related ED visits.

Among those with an incident animal bite ED visit, the highest frequencies of ICD-9-CM diagnosis code(s) for skin or subcutaneous tissue infections were in adults aged 35-69 (Table 4). Skin or subcutaneous tissue infection was diagnosed at 796 (3%) of 29,586 dog bite-related incident visits and 898 (17%) of 5,314 cat bite or scratch-related incident visits, resulting in a prevalence difference of 14% (95% CI, 13-15). Wounds to the head, neck, or face were documented in 6,304 animal bite-related ED visits, 1,931 (31%) of which were made by 0-4 year-olds and 1,456 (23%) of which were made by 5-9 year-olds. Wounds to the upper limbs, including hands, were consistent across age groups, with the exception of lower frequencies in the youngest and oldest age groups. Of 54 incident animal bite-related ED visits with a skull fracture, 19 (35%) were made by 0-4 year-olds.

E. Discussion

Animal bites are an important target for public health interventions. At 0.3%, the percentage of animal bite-related ED visits to all ED visits in North Carolina is greater than the percentage of ED visits for cardiac arrest (69). From 2008-2010, unintentional dog bite injuries were associated with an estimated average lifetime medical cost of >$630 for a treat and release ED visit and >$18,000 for hospitalization (12, 71). Therefore, North Carolina ED-evaluated dog bite injuries alone cost an average of >$9.1 million per year during the study period.

Although animal bites are largely preventable, directed intervention efforts require an understanding of current epidemiology. The incidence of animal bites has been examined previously. However, published estimates included only dog bites (12, 29, 30), were based on data from the early to mid-1990's (3, 8), relied on reported animal bites or exposures (3, 8), or were for a single city (32). Biting species-specific ED visit incidence rates have not been previously published on a statewide level.

This study provides an example of the use of comprehensive, statewide ED syndromic surveillance data for determination of animal bite incidence rates and description of ED visit characteristics and patient attributes. Twenty percent of incident animal bite-related ED visits in this study were identified by keyword search of CCs and TNs and did not contain an animal bite E-code. Therefore, identification of animal bite-related ED visits either by animal bite E-code or by CCs and TNs keyword searches alone may lead to an underestimation of the true animal bite incidence.

Fifteen percent of incident dog bite-related ED visits did not contain an E-code for dog bite and were identified by the CCs and TNs keyword search. However, the incidence of dog bite-related ED visits in North Carolina from 2008-2010 was $105/10^5$ py (95% CI, 103-106), similar to recent national estimates ($103.9/10^5$ py, $107.2/10^5$ py) (12, 30) and slightly less than other older national studies ($12.9/10^4$ py, $129.3/10^5$ py) (7, 29). Each of these previous studies included only ED visits identified by the E-code E906.0. Therefore, previously published national rates may have underestimated the true incidence of dog bite-related ED visits.

Several of this study's findings support previously published work. Greater than 75% of animal bites examined in North Carolina EDs were from dogs, nearly 14% from cats, and the remaining from wildlife, horses, food animals, rodents, and other animals. Males had a higher incidence of dog bites than females, while females had a higher incidence of cat bites or scratches than males.

Children ≤14 years had the highest rates of animal bite-related ED visits, specifically dog bites. By the age of 10, a North Carolina child has a 1 in 50 risk of dog bite injury requiring an ED visit. This finding may be related to the physical stature of children and their behavior around dogs (9), as well as the healthcare-seeking behavior of guardians. Dog bite incidence was highest in the spring and early summer and decreased in late summer and fall. The seasonal variation is likely associated with greater outdoor activity of humans and dogs in the spring and early summer months (9, 21, 32, 88), which in North Carolina are often more temperate than the hotter late summer months (89). Dog bite prevention efforts in North Carolina should be directed at children ≤14 years of age in the early spring. Targeted interventions could be made in schools and daycares (90), with a special focus on educating toddler boys. Dissemination of bite prevention education materials at the point of sale of animals should be encouraged, specifically for animals adopted from shelters and humane societies or purchased from breeders or pet stores (90).

This study is the first to examine the statewide incidence of cat bite or scratch-related ED visits. By age 85, a North Carolinian has a 1 in 60 risk of cat bite or scratch injury requiring an ED visit. Despite the fact that individuals >79 years had the lowest animal bite incidence in this study, the highest incidence of cat bite or scratch-related ED visits was in adults >79 years. This may be related to the population that seeks ED care for cat bites and scratches, ownership of cats in this group, and increased skin fragility and decreased motor skills in the elderly (91). Older adults should be educated on avoidance of cat bites and scratches. Targeted interventions could be made through church groups, senior citizen centers, or meals-on-wheels programs (90).

Previous reports indicated that 1%-30% of dog bites and 29%-50% of cat bites become infected (41-44). Many of these estimates are based on data from a single institution or a small number of institutions. In North Carolina, 3% of incident dog bites and 17% of incident cat bites or scratches examined in EDs were infected.

Previous statewide studies comparing the incidence of animal bites in rural and urban areas have varied by state (3, 8). In North Carolina, urban counties have a lower median age and higher proportion of individuals <45 years than rural counties (76). However, factors other than age may also influence the rate difference, such as differences in the animal density and species distribution in rural and urban counties.

This study has several limitations. Only 3 years of ED visit data were evaluated, making it difficult to assess trends over time. Medical record review was not performed to verify E-coding, CCs, or TNs. This study is based on data from North Carolina only. However, North Carolina is the 10th largest state by population and contains an approximate equal distribution of rural and urban populations. Therefore, these findings may be applicable to other similar states and to the nation. Additionally, the rates presented are population-based and did not rely on complex sampling methods for estimation.

Animal bites, specifically dog and cat bites, are typically monitored and prevention efforts undertaken at state and local levels. This study demonstrates the use of statewide ED syndromic surveillance data for other public health initiatives without additional burden on data providers. Monitoring species-specific bite incidence across the state and in various subpopulations provides valuable insight for state and local public health officials, physicians, and veterinarians. Findings may be used to renew support and target efforts for animal bite prevention.

Table 1. Animal bite-related ED[a] visit incidence rates by patient age group, patient sex, and biting animal species, NC DETECT[b], 2008-2010.

Patient Age Group (years)	ED[a] visits for Animal bite	Person-years	Incidence Rate per 100,000 person-years (95% CI[c])
0-4	3,827	1,897,515	201.7 (195.3, 208.1)
5-9	4,405	1,888,142	233.3 (226.4, 240.2)
10-14	3,338	1,873,179	178.2 (172.2, 184.2)
15-19	2,504	1,977,678	126.6 (121.7, 131.6)
20-24	2,849	1,956,315	145.6 (140.3, 151.0)
25-29	2,776	1,859,107	149.3 (143.8, 154.9)
30-34	2,442	1,853,649	131.7 (126.5, 137.0)
35-39	2,411	2,004,414	120.3 (115.5, 125.1)
40-44	2,470	2,002,900	123.3 (118.5, 128.2)
45-49	2,700	2,083,789	129.6 (124.7, 134.5)
50-54	2,387	1,979,368	120.6 (115.8, 125.4)
55-59	1,915	1,773,231	108.0 (103.2, 112.8)
60-64	1,503	1,553,499	96.8 (91.9, 101.6)
65-69	1,143	1,166,162	98.0 (92.3, 103.7)
70-74	812	867,916	93.6 (87.1, 100.0)
75-79	642	663,229	96.8 (89.3, 104.3)
>79	842	920,480	91.5 (85.3, 97.7)
missing	5	-	-
total	38,971		
Patient Sex			
Male	19,382	13,802,570	140.4 (138.4, 142.4)
Female	19,583	14,518,003	134.9 (133.0, 136.8)
missing	6	-	-

total	38,971		
Biting Animal			
Dog	29,586	28,320,573	104.5 (103.3, 105.7)
Cat (bite or scratch)	5,314	28,320,573	18.8 (18.3, 19.3)
Wildlife		28,320,573	
Bat (bite or scratch)	266	28,320,573	0.94 (0.83, 1.05)
Raccoon	149	28,320,573	0.53 (0.44, 0.61)
Squirrel or chipmunk	126	28,320,573	0.44 (0.37, 0.52)
Fox	88	28,320,573	0.31(0.25, 0.38)
Opossum	30	28,320,573	0.11 (0.07, 0.14)
Other wildlife	39	28,320,573	0.14 (0.09, 0.18)
Equine, swine, & small ruminants		28,320,573	
Horse, donkey, or mule	110	28,320,573	0.39 (0.32, 0.46)
Swine or Small ruminant (sheep or goat)	32	28,320,573	0.11 (0.07, 0.15)
Other small animals & rodents		28,320,573	
Rat	232	28,320,573	0.82 (0.71, 0.92)
Mouse	102	28,320,573	0.36 (0.29, 0.43)
Rabbit	40	28,320,573	0.14 (0.10, 0.19)
Hamster, guinea pig, or gerbil	40	28,320,573	0.14 (0.10, 0.19)
Other rodent (including ferret)	19	28,320,573	0.07 (0.04, 0.10)
Other animals		28,320,573	
Unidentified animal	2,781	28,320,573	9.8 (9.5, 10.2)

Non-human primate	13	28,320,573	0.05 (0.02,0.07)
Other animal	11	28,320,573	0.04 (0.02, 0.06)
total	38,978[d]		

[a]Emergency Department
[b]North Carolina Disease Event Tracking and Epidemiologic Collection Tool
[c]Confidence interval
[d]Total is >38,971, as some patients were evaluated for animal bites from multiple species.

Table 2. Animal bite-related ED[a] visit age-adjusted incidence rates and rate differences by rural versus urban county of residence, NC DETECT[b], 2008-2010.

Patient Residence	**ED[a] visits for Animal bite by Age group**	**Person-years**	**Age-adjusted Incidence Rate[c]** per 100,000 person-years (95% CI[d])	**Age-adjusted Rate Difference** per 100,000 person-years (95% CI[d])
Urban	17,620	14,268,735	122.4 (120.6, 124.2)	0
Rural	19,553	14,051,838	141.2 (139.2, 143.1)	18.8 (16.1, 21.5)

[a]Emergency Department

[b]North Carolina Disease Event Tracking and Epidemiologic Collection Tool

[c]Age-adjusted Incidence Rate, standardized to the 2008 United States Census Intercensal Population Estimate for North Carolina by the following age groups (in years): 0-4, 5-9, 10-14, 15-19, 20-24, 25-29, 30-34, 35-39, 40-44, 45-49, 50-54, 55-59, 60-64, 65-70, 70-74, 75-79, >79.

[d]Confidence Interval

Table 3. Patient attributes and ED[a] visit characteristics for incident animal bite-related ED[a] visits, NC DETECT[b], 2008-2010.

Patient Age Group (years)	**ED[a] visits for Animal bite, No. (%)**
0-4	3,827 (9.8)
5-9	4,405 (11.3)
10-14	3,338 (8.6)
15-19	2,504 (6.4)
20-24	2,849 (7.3)
25-29	2,776 (7.1)
30-34	2,442 (6.3)
35-39	2,411 (6.2)
40-44	2,470 (6.3)
45-49	2,700 (6.9)
50-54	2,387 (6.1)
55-59	1,915 (4.9)
60-64	1,503 (3.9)
65-69	1,143 (2.9)
70-74	812 (2.1)
75-79	642 (1.7)
>79	842 (2.2)
missing	5 (0.01)
Patient Sex	
Male	19,382 (49.7)
Female	19,583 (50.3)
missing	6 (0.02)
Patient Residence	
Urban county	17,623 (45.2)
Rural county	19,555 (50.2)
missing	1,793 (4.6)
ED[a] Disposition	
Discharged	35,297 (90.6)
Admitted	1,091 (2.8)
Left Against or Without Medical Advice	882 (2.3)
Transferred	293 (0.8)
Unknown	124 (0.3)
Other or died	102 (0.3)

Observation	25 (0.1)
missing	1,157 (3.0)
Method of Payment	
Private Insurance	14,139 (36.3)
Self-pay	8,907 (22.9)
Medicaid	7,880 (20.2)
Medicare	3,979 (10.2)
Other	2,339 (6.0)
Worker's compensation	974 (2.5)
Unknown or No charge	179 (0.5)
Missing	574 (1.5)
Mode of Transport	
Walk-in	27,908 (71.6)
Ambulance or air transport	1,790 (4.6)
Other	1,167 (3.0)
Unknown	869 (2.2)
Missing	7,237 (18.6)
Year of Visit	
2008	12,534 (32.2)
2009	12,934 (33.2)
2010	13,503 (34.7)
Missing	0 (0)
Month of Visit	
January	2,423 (6.2)
February	2,454 (6.3)
March	3,116 (8.0)
April	3,544 (9.1)
May	3,907 (10.0)
June	3,853 (9.9)
July	3,964 (10.2)
August	3,648 (9.4)
September	3,207 (8.2)
October	3,081 (7.9)
November	3,005 (7.7)
December	2,769 (7.1)
Missing	0 (0)
Administration of Rabies PEP[c]	
No	37,307 (95.7)

Yes	1,664 (4.3)

[a]Emergency department
[b]North Carolina Disease Event Tracking and Epidemiologic Collection Tool
[c]Rabies Post-exposure Prophylaxis

Table 4. International Classification of Diseases, 9th revision - Clinical Modification (ICD-9-CM) diagnosis code groupings of animal bite injury from incident animal bite-related ED[a] visits, NC DETECT[b], 2008-2010.

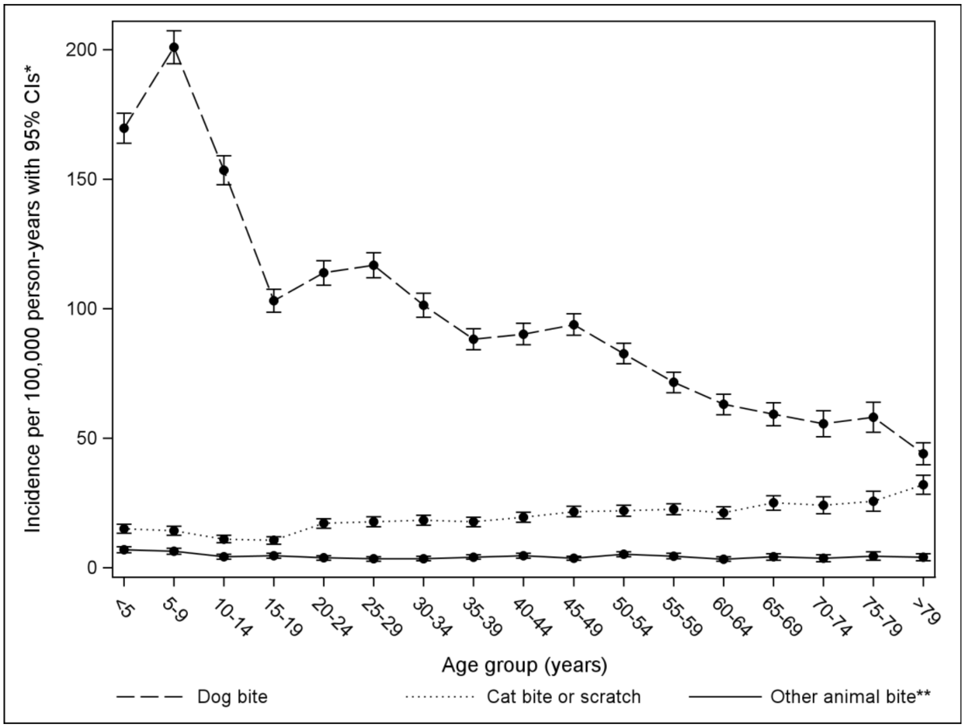
Patient Age Group (years)	Infection of skin and/or subcutaneous tissue[c], No. (%)	Wound(s) to head, face, and/or neck[d], No. (%)	Wound(s) to upper limb(s)[e], No. (%)	Wound(s) to hand(s)[f], No. (%)	Wound(s) to lower limb(s)[g], No. (%)	Skull fracture[h], No. (%)
0-4	73 (3.6)	1,931 (30.6)	588 (4.1)	357 (3.7)	171 (2.8)	19 (35.2)
5-9	55 (2.7)	1,456 (23.1)	1016 (7.1)	472 (4.9)	612 (10.1)	<10[i] (<18.5)
10-14	56 (2.7)	675 (10.7)	917 (6.4)	498 (5.1)	732 (12.1)	<10[i] (<18.5)
15-19	53 (2.6)	318 (5.0)	848 (5.9)	548 (5.7)	495 (8.2)	<10[i] (<18.5)
20-24	117 (5.7)	307 (4.9)	1,175 (8.2)	817 (8.4)	488 (8.1)	<10[i] (<18.5)
25-29	105 (5.1)	282 (4.5)	1,119 (7.8)	802 (8.3)	495 (8.2)	<10[i] (<18.5)
30-34	116 (5.7)	193 (3.1)	1,079 (7.5)	722 (7.5)	416 (6.9)	<10[i] (<18.5)
35-39	162 (7.9)	204 (3.2)	1,038 (7.2)	699 (7.2)	410 (6.8)	<10[i] (<18.5)
40-44	158 (7.7)	211 (3.4)	1,086 (7.5)	752 (7.8)	430 (7.1)	<10[i] (<18.5)
45-49	215 (10.5)	237 (3.8)	1,183 (8.2)	830 (8.6)	442 (7.3)	<10[i] (<18.5)
50-54	186 (9.1)	166 (2.6)	1,039 (7.2)	738 (7.6)	395 (6.5)	<10[i] (<18.5)
55-59	161 (7.9)	127 (2.0)	920 (6.4)	676 (7.0)	284 (4.7)	<10[i] (<18.5)
60-64	145 (7.1)	73 (1.2)	723 (5.0)	536 (5.5)	230 (3.8)	0 (0)
65-69	141 (6.9)	53 (0.8)	555 (3.9)	415 (4.3)	145 (2.4)	<10[i] (<18.5)
70-74	95 (4.6)	40 (0.6)	395 (2.7)	303 (3.1)	112 (1.9)	0 (0)
75-79	74 (3.6)	14 (0.2)	344 (2.4)	248 (2.6)	78 (1.3)	0 (0)
>79	136 (6.6)	17 (0.3)	379 (2.6)	282 (2.9)	123 (2.0)	0 (0)
total	2,048	6,304	14,404	9,695	6,058	54

[a]Emergency department

[b] North Carolina Disease Event Tracking and Epidemiologic Collection Tool

[c]681-Cellulitis and abscess of finger and toe; 682-Other cellulitis and abscess; 684-Impetigo; 686-Other local infections of skin and subcutaneous tissue
[d]870-874-Open wound of ocular adnexa(870), eyeball(871), ear(872), head(873), neck(874)
[e]880-887-Open wound of upper limb
[f]882-Open wound of hand except finger(s) alone; 883-Open wound of finger(s); 885-Traumatic amputation of thumb; 886-Traumatic amputation of other finger(s)
[g]890-897-Open wound of lower limb
[h]800-804-Skull fracture
[i]To maintain confidentiality, cells with values >0 and <10 are not enumerated.

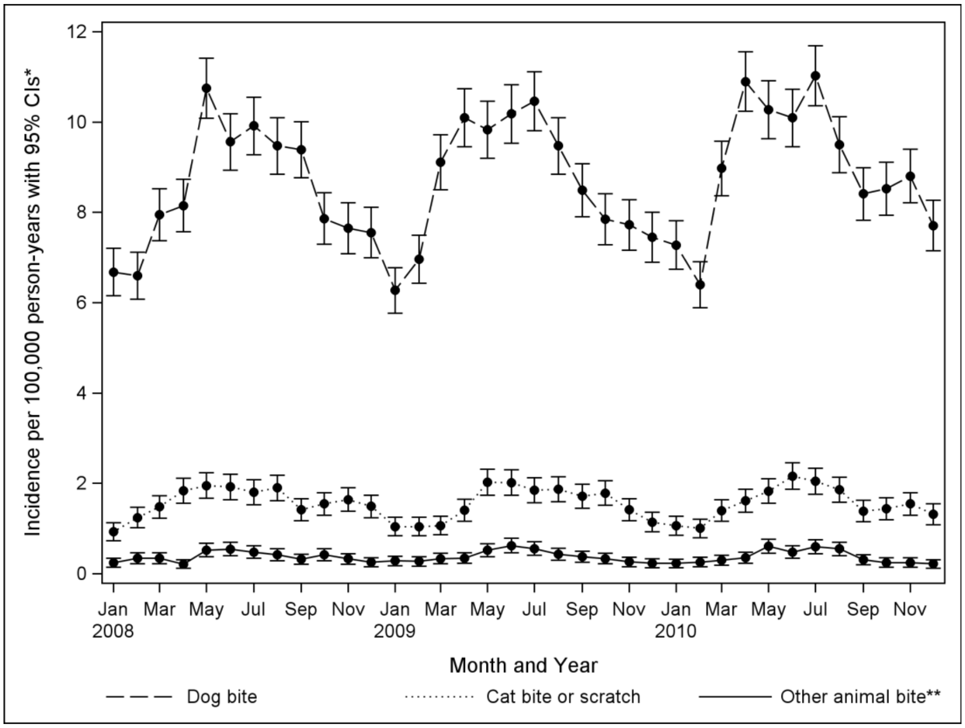
Figure 1. Animal bite-related emergency department (ED) visit incidence rates by patient age group and biting animal species, North Carolina Disease Event Tracking and Epidemiologic Collection Tool (NC DETECT), 2008-2010.



*Confidence interval

** Bites from wildlife, equine, swine, small ruminant, other small animals, and rodents

Figure 2. Animal bite-related emergency department (ED) visit incidence rates by month and year and biting animal species, North Carolina Disease Event Tracking and Epidemiologic Collection Tool (NC DETECT), 2008-2010.



*Confidence interval

** Bites from wildlife, equine, swine, small ruminant, other small animals, and rodents

CHAPTER V

MANUSCRIPT 2: RISK FACTORS FOR HOSPITALIZATION AFTER DOG BITE INJURY: A CASE-COHORT STUDY OF EMERGENCY DEPARTMENT VISITS

A. Overview

Dog bite injuries may result in trauma, pain, and infection and lead to costly healthcare utilization such as emergency department (ED) visits and hospitalizations. Although clinical guidelines exist, risk factors for hospitalization after a dog bite injury have not been examined quantitatively. A comprehensive understanding of patient and injury characteristics that result in an increased risk for hospitalization after dog bite injury may reduce hospitalizations and improve patient outcomes.

A case-cohort study was conducted to examine the association between the following risk factors and hospitalization: infection, complicated injury, host defense abnormality, number of previous evaluations for the injury, and anatomic location of the bite. The cohort consisted of ED patients evaluated for a dog bite injury between January 1, 2000 and December 31, 2011 at a large North Carolina teaching hospital. Cases were cohort members who were admitted as inpatients directly from the ED. From the cohort, a simple random sample was selected for the subcohort. Data on risk factors, the outcome and covariates were collected from ED medical records. Logistic regression models, informed by directed acyclic graphs (DAGs), were used to describe the relationship between each risk factor and hospitalization. Effect measure modification was examined by patient sex and race for the relationship between previous evaluation for the dog bite injury and hospitalization.

Cases (n=111) were more likely to be male, white, or insured by Medicaid than were members of the subcohort (n=221). The most common type of complicated injury was tendon or ligament injury for cases and fracture for the subcohort. All factors evaluated were associated with increased risk of hospitalization after dog bite injury. However, infection at the time of ED visit (odds ratio (OR) = 7.8, 95% confidence interval (CI) 3.8, 16.0) and injury to multiple anatomic locations (OR = 6.0, 95% CI 1.2, 30.9) were associated with the largest relative risks of hospitalization. For every 3 ED visits for an infected dog bite, 1 resulted in hospitalization. Having had ≥1 prior evaluation for the dog bite injury was associated with a lower risk of hospitalization for females than males and for whites than non-whites.

This study provides a unique, quantitative examination of risk factors for hospitalization after dog bite injury. The relative risk of hospitalization associated with each factor was substantial. However, the strongest relative and absolute associations were for infection and hospitalization. This intuitive relationship highlights the importance of wound care, patient counseling, and consideration of antibiotic prophylaxis at the initial patient evaluation.

B. Introduction

Human injuries from dog bites have long been recognized as a public health concern. These injuries may result in physical and emotional trauma, pain, infection, rabies exposure, and, rarely, death (2, 9). Dog bites may also lead to costly healthcare utilization, such as rabies post-exposure prophylaxis (PEP), emergency department (ED) visits, and hospitalization (4, 8, 12-14, 28-30). The aggregated cost of dog bite-related hospitalizations in the United States (US) is approximately $53.9 million yearly (12). The average cost of a dog bite-related hospitalization is $18,200, substantially more than the average injury-related hospitalization of $12,100.

Guidelines for hospital admission after dog bite injury typically recommend consideration of the patient's age, as well as other characteristics, including comorbid conditions, systemic or severe local infection, anatomic location of the bite, and presence of complicated or severe injury (44). Host-defense abnormalities, such as diabetes mellitus or human immunodeficiency virus (HIV) infection, may impair healing or increase infection risk (44, 48). Patients with dog bites resulting in severe local or systemic infection are candidates for inpatient intravenous (IV) antibiotic administration (41, 44). The most common anatomic locations of dog bite wounds in hospitalized patients include wounds to the head and extremities (12, 48). Complicated wounds that involve injury to bone, joint, or tendon may require surgical intervention and inpatient care (44).

Risk factors for hospitalization after a dog bite injury have not been examined quantitatively. The purpose of this study was to examine and quantify the relationship between patient and injury characteristics and the risk of hospitalization after dog bite injury. Specifically, the association between each risk factor, or exposure, and hospitalization, the outcome, were evaluated. The following risk factors were examined: presence of infection, complicated injury, host defense abnormality, number of previous evaluations for the injury, and anatomic location of the bite.

Effect measure modification of the association between previous evaluations and hospitalization was examined by patient sex and race. Having a previous evaluation for the dog bite injury by a medical professional suggests a patient received some amount of consultation and treatment for the injury prior to the ED visit. This study examined whether having at least one previous evaluation for the dog bite was associated with a different risk of hospitalization for females versus males and for white versus non-white individuals.

A comprehensive understanding of patient and injury characteristics that result in an increased risk for hospitalization after a dog bite injury may reduce hospitalization and improve patient outcomes. Results from this study may assist emergency medicine physicians during patient assessment and inform treatment decisions.

C. Methods

Case-cohort design and study population:

A case-cohort study was conducted at UNC Health Care, a large, integrated, nonprofit teaching hospital (806 licensed beds) in North Carolina (74). The cohort consisted of patients seen at UNC Health Care ED between January 1, 2000 and December 31, 2011 with an International Classification of Diseases, 9th Revision, Clinical Modification (ICD-9-CM) external cause of injury code for dog bite (E906.1) (11). Additional criteria for inclusion into the study were as follows: 1) A physical examination was performed in the ED by a physician or nurse practitioner. 2) The ED visit chief complaint indicated a dog bite injury or the sequelae from such an injury (e.g. laceration). ED visits for rabies PEP or tetanus vaccination only and without evaluation of or medical care for a dog bite injury were not eligible for inclusion. 3) The ED visit was for injury from one or multiple dogs. Patients with injuries from a dog and another animal species (e.g. cat) were not eligible for inclusion. 4) The ED visit medical record was complete and available for review. Cases were defined as cohort members who met the above criteria and were admitted as inpatients to UNC Health Care directly from the ED. From the cohort, a simple random sample of 250 was selected for the subcohort. Cases were eligible to be subcohort members.

The Institutional Review Board of the University of North Carolina at Chapel Hill approved this study and found that it met criteria for waiver of informed consent for research and waiver of Health Insurance Portability and Accountability Act (HIPPA) authorization.

Data collection:

Demographic characteristics, clinical data, and medical history for each ED visit included in the study were collected from UNC Health Care medical records. Data on risk factors, the outcome, and covariates were collected from the ED medical record for the specific visit included in the study or from the demographics page of the electronic medical record (EMR). Wound microbiologic culture results were collected for descriptive analysis from extended information found in related ED visit medical records and inpatient medical records.

Anatomic location of the dog bite injury was abstracted from the physical examination findings and categorized by major body region: 1) head, neck or face (including eyes, ears, and oral cavity); 2) upper extremity (including shoulders, arms, wrists and hands); 3) other anatomic location (lower extremity (including hips, legs, ankles and feet) or torso (including thorax, abdomen, genitals, other pelvis, back and buttocks, and other trunk)); and 4) multiple anatomic locations (a combination of one or more of the above anatomic locations). Presence of a complicated injury was abstracted from physical examination findings and defined as any of the following: 1) injury to tendon or ligament, joint (including dislocation) or nerve; 2) vascular injury requiring specific surgical intervention; 3) piercing injury into the thorax, abdomen, or skull; 4) fracture; and 5) compartment syndrome. Presence of a host defense abnormality was obtained from the medical history and defined as any of the following: diabetes mellitus, renal disease, hepatic disease, human immunodeficiency virus (HIV) infection, asplenic, or currently taking an immunosuppressive medication (included alkylating agents, antimetabolites, high-dose oral corticosteroids, immune suppressing antibodies and interferons) (79). Presence of infection was a dichotomous variable abstracted from the ED provider's clinical impression and included any infection related to the dog bite injury. Previous evaluation was defined as a medical evaluation documented in the medical history from any primary care, urgent care, or emergency medicine provider for the same dog bite injury, prior to the study visit at UNC Health Care ED. The number of previous evaluations was categorized as no previous evaluation, 1 previous evaluation, or ≥2 previous evaluations.

Data were entered into a custom, standardized, electronic data abstraction form developed in Epi Info™ (Centers for Disease Control and Prevention (CDC)) (Appendix 1) (80). Data abstraction was performed by the first author. A random sample of study records was abstracted by a second reviewer (C. Cairns), an emergency medicine physician who was masked from the data abstracted by the first author. Inter-rater reliability for risk factors, the outcome, and covariates was assessed using intraclass correlation statistics (81). Discrepancies between the raters were settled by re-reviewing the medical record.

Data analysis:

Multivariate logistic regression models were used to describe the relationship between each of the risk factors and the outcome (SAS® 9.2 (Cary, NC)) (82). For each risk factor, a directed acyclic graph (DAG) was used to evaluate potential confounding by covariates, including other risk factors (Appendix 2) (83, 84). DAG analysis indicated that, for each risk factor, the model should be adjusted for all other risk factors and for patient age. Patient age was modeled as a quadratic spline with knots at the 25% and 75% percentiles of the subcohort age distribution. The risk period was the duration of the ED visit for dog bite injury.

Odds ratios (ORs) from logistic regression models directly estimated risk ratios in the cohort, given the case-cohort design (85). Odds ratio 95% confidence intervals (CIs) were calculated using generalized estimating equation (GEE) robust variance estimates (86, 87). Risk differences (RDs) were calculated using the sampling fraction and coefficients from logistic regression models with centered adjustment variables (83). Risk difference 95% CIs were estimated using bootstrap sampling.

Odds ratio modification was estimated with product interactions of risk factors with patient sex and race for the relationship between previous evaluation for the dog bite injury and hospitalization. For analysis of modification, the following variables were dichotomized: number of previous evaluations (no previous evaluation, ≥1 previous evaluation) and race (white, non-white). Given the case-cohort study design, the ratios of odds ratios (RORs) in the data estimated the ratios of relative risks (RRRs) in the cohort. Because the sampling fraction was known, the difference of RDs (interaction contrast, IC) could be estimated to assess modification on the additive scale (83). Bootstrap sampling was used to estimate 95% CIs for RORs and ICs.

D. Results

Between January 1, 2000 and December 31, 2011, there were 1,384 visits to UNC Health Care ED with an ICD-9-CM E-code for dog bite (E906.1). Of the 125 ED visits for dog bite resulting in admission to UNC Health Care (cases), 12 (10%) were excluded because they did not meet one or more of criteria 1-3 described in the methods, 1 (1%) was excluded because the medical record was incomplete or not available, and 1 (1%) was excluded because the patient declined hospitalization against medical advice (Figure 3a). The remaining 111 cases were included in this analysis.

Of the 250 ED visits randomly sampled from the cohort for the subcohort, 19 (8%) were excluded because they did not meet one or more of criteria 1-3 described in the methods, and 10 (4%) were excluded because the medical record was incomplete or not available (Figure 3a). The remaining 221 in the subcohort were included in this analysis. Twenty-one (10%) visits in the subcohort were also cases (Figure 3b). Four patients in the dataset had 2 dog bite injury ED visits on different dates. ED visits made from 2000 to mid-2004 were documented in paper medical records, while ED visits made from mid-2004 through 2011 were documented in the electronic medical record (EMR). EMR was used to collect information for 79 (71%) cases and 151 (68%) subcohort members.

Inter-rater agreement for a 10 record sample was 100% for all but one variable within a single ED visit record. The discrepancy between raters was on the coding of complicated injury, resulting in an intraclass coefficient of 0.64 for the variable. The medical record was re-reviewed to assess the discrepancy, and coding was adjusted appropriately in preparation for the analysis.

The distribution of select characteristics for cases and the subcohort is presented in Table 5. Cases were more likely to be male, white, or insured by Medicaid than were members of the subcohort. The mean age of cases was 28.4 years (standard deviation (SD) 21.7; range 0 to 80), slightly less than the mean age of the subcohort at 30.4 years (SD 21.2; range 1 to 91). The most common type of complicated injury was tendon or ligament injury for cases and fracture for the subcohort. The biting dog was known to the patient in 82 (74%) of cases and 168 (76%) of the subcohort.

An infectious diagnosis was provided for 57 (51%) of cases and 22 (10%) of the subcohort. The most common infectious diagnosis was cellulitis for both the cases and the subcohort. For those cases in which wound culture resulted in microbial growth, the most common pathogen isolated was *Pasteurella multocida*. *Pasteurella canis* was isolated from the dog bite of one case. Prescriptions for antibiotics were provided to 175 (87%) of the 201 subcohort members who were not hospitalized. Of those 175, 138 (79%) were prescribed amoxicillin/clavulanate.

Estimates of relative and absolute effect measures for risk of hospitalization are presented in Table 6. Point estimates for all factors were elevated above the null. Compared to all other risk factors, infection at the time of ED visit had the largest relative risk (RR) and RD point estimates. With the second highest RR point estimate, the association between injury to multiple anatomic locations and hospitalization had a confidence limit ratio (CLR) of 26 and was the least precise estimate (92). Using a model adjusted for all risk factors and patient age, the risk of hospitalization for multiple dog bite injuries to the same or multiple anatomic locations was 40% greater than that for a single injury (OR=1.4, 95% CI 0.8-2.6). As the number of previous evaluations increased from 1 to ≥2, there was a monotonic decrease in relative and absolute effect measures for risk of hospitalization.

Stratified associations between prior evaluations and hospitalization are presented in Table 7. The relative and absolute effect measure point estimates differed by sex and race. Females and white individuals with ≥1 prior evaluation had lower relative risks of hospitalization than males and non-white individuals with ≥1 prior evaluation, respectively. Point estimates were least precise for the analysis by race.

E. Discussion

Nationally, approximately 2.5% of all ED visits for dog bite are admitted to the hospital (12). The majority of these admitted patients require intravenous antibiotics and/or surgical repair of wounds. The aggregated yearly cost of dog bite-related hospitalizations in the US is approximately $53.9 million. Dog bite-related hospitalizations are associated with a greater cost than hospitalizations from other type of injuries. This is despite the fact that dog bite related hospitalizations are typically shorter in duration by 2 days than other injury-related inpatient stays.

Previous reports indicate that the rate of hospitalization from dog bite injury is highest for children <5 years of age and adults >65 years of age (12). Significant physical trauma may result from dog bite injuries to small children. Older adults may have complicating comorbid conditions and increased risk of infection. Guidelines suggest providers consider anatomic location of the bite, presence of complicated or severe injury, and failure of outpatient therapy, in addition to age and presence of infection, when determining whether to admit a patient with dog bite injury (44). However, a quantitative evaluation of the associations between hospitalization after dog bite injury and potential risk factors has not yet been published. A comprehensive understanding of patient and injury characteristics that result in an increased risk for hospitalization after a dog bite injury may reduce hospitalizations for dog bite injury, improve patient outcomes, and inform future research.

For all factors evaluated in this study, point estimates for the risk of hospitalization after dog bite injury were above the null. The largest relative and absolute effect measure point estimates in the study were for the association between infection and hospitalization. This association, although intuitive, is substantial. For every 3 ED visits for an infected dog bite, 1 resulted in hospitalization. Therefore, upon initial evaluation of a dog bite injury, complete assessment, proper wound care, and patient education are crucial. Depending on the nature and location of the wound, timely reevaluations may be prudent and the use of antibiotic prophylaxis should be considered.

The RR point estimate for injury to multiple anatomic locations was also relatively strong but the least precise, due in part to the small number of such injuries. Compared to patients with a single dog bite injury, patients with multiple injuries were at increased risk for hospitalization. Presence of multiple injuries may be related to bite severity and the nature and circumstances of the injury, including the size and number of dogs involved.

Injuries to single anatomic locations were also risk factors for hospitalization in this study. Head, neck and face injuries can be severe and traumatic and occur most commonly in children <10 years of age. Such injuries often require hospitalization, reconstructive procedures, and frequent medical evaluations, especially in young children. Clinical guidelines suggest that animal bite wounds to the hands and wrist may be at increased risk of infection compared to other anatomic locations (44). *Pasteurella* species and anaerobic bacteria are more commonly isolated from wounds of the upper extremities than from lower extremity wounds and from puncture wounds than lacerations (93). This may be related to the nature of such wounds and possible increased efficiency in transfer of the dog's oral flora. Additionally, fractures, joint penetration, and tendon, ligament, or neurovascular injuries should be considered as possible complications, especially for dog bite wounds of the hand and forearm (44).

The monotonic decrease in relative and absolute effect measure point estimates as the number of previous evaluations increased from 1 to ≥ 2 may be related to local and regional referral patterns. As a tertiary medical center and 1 of 6 designated Level I Trauma Centers in North Carolina, UNC Health Care provides emergency treatment for severe dog bite injuries and related complications through direct access and referral by local and regional providers. Patients with complicated dog bite injuries or infections may be referred to UNC Health Care ED after initial evaluation by an outside provider. Such patients could have become cases in this study if they were hospitalized directly from the ED for inpatient surgery and/or intravenous antibiotic therapy. Alternatively, patients with multiple previous evaluations for their dog bit injury may have more minor injuries or fewer complications that are amenable to outpatient therapy, including wound management and intravenous antibiotic administration in the ED.

Effect measure modification was difficult to assess due to the small study size. However, on both the multiplicative and additive scales the impact of prior evaluations on the risk of hospitalization differed by sex and by race. Findings suggest that having ≥1 prior evaluation for the dog bite injury was associated with a lower risk of hospitalization for females and white individuals. This may be related to the type and severity of the injury, the medical care accessed by the patient, and patient education and understanding of wound care and medication compliance.

Future studies of dog bite injury-related hospitalizations could include a larger number of patients to allow for investigation of additional risk factors and effect measure modifiers, including the size and type of medical facility. A prospective study of dog bite injury patients could assess the impact of situational factors and previous treatment on hospitalization. Finally, a large clinical trial may help clarify the role of prophylactic antibiotics in reducing hospitalizations from dog bite injury.

There were several limitations inherent in this study. Generalizability may be limited, as the study cohort originated from ED visits made to a single, large academic medical center. Results may not be applicable to smaller, non-teaching, hospitals or to primary or urgent care facilities. The study sample was not large, leading to dichotomization of most exposure variables, wide confidence intervals, and reduced power to study effect measure modification. To obtain enough cases, the study spanned an 11-year period. Patient care plans and treatment protocols may have changed over that time. Additionally, data abstraction from both paper medical records and EMR was required. Analysis was limited to data documented in the medical record. Although DAGs were used to assess confounding, unknown or unmeasured confounders may exist.

F. Conclusions

Dog bite injuries may result in trauma, pain, and infection and lead to costly healthcare utilization, such as ED visits and hospitalization (9, 12-14, 28-31). The average cost for a dog bite-related treat and release ED visit is >$630 and for a dog bite-related hospitalization is $18,200 (12, 71). This case-cohort study provides a unique, quantitative examination of risk factors for hospitalization after dog bite injury. Point estimates for each factor evaluated (infection; complicated injury; injury to the head, upper extremities, or multiple anatomic locations; ≥1 previous evaluation for the injury; and presence of host defense abnormalities) were above the null. The strongest relative and absolute effect measures in this analysis were for infection and hospitalization. This intuitive association highlights the importance of proper wound care, patient counseling, and consideration of antibiotic prophylaxis at the initial patient evaluation after a dog bite injury.

Table 5. Characteristics of case and subcohort emergency department (ED) visits for dog bite injury, UNC Health Care, 2000-2011.

	Case ED visits (n=111)		Subcohort ED visits (n=221)	
Characteristics	N	%	N	%
Patient sex				
Female	51	46.0	126	57.0
Male	60	54.1	95	43.0
Patient race				
White	93	83.8	160	72.4
Black	11	9.9	31	14.0
All other races	4	3.6	30	13.6
missing	3	2.7	0	.
Payment method on record				
Private or commercial	37	33.3	98	44.3
Medicaid	26	23.4	31	14.0
Medicare	9	8.1	19	8.6
Self-pay	24	21.6	45	20.4
Worker's compensation	1	0.9	5	2.3
Other	6	5.4	10	4.5
missing	8	7.2	13	5.9
Infectious diagnosis[a]				
No infectious diagnosis	54	45.8	199	89.6
Cellulitis	38	32.2	12	5.4
Abscess	2	1.7	1	0.5
Tenosynovitis	9	7.6	1	0.5
Osteomyelitis	0	0	1	0.5
Intra-abdominal infection	1	0.8	0	0
Renal abscess/infected hematoma	1	0.8	0	0
Infection not otherwise specified	13	11.0	8	3.6
Wound microbiology culture results[a]				
No culture submitted or no growth	92	80.0	218	98.2

Pasteurella multocida	10	8.7	0	0
Pasteurella species (unspecified)	2	1.7	1	0.5
Pasteurella canis	1	0.9	0	0
Coagulase negative *Staphylococcus* species	2	1.7	1	0.5
Staphylococcus aureus	1	0.9	1	0.5
Streptococcus viridians group	2	1.7	0	0
Mixed gram positive/gram negative unspecified	2	1.7	0	0
Mycobacterium abscessus	1	0.9	0	0
Neisseria weaver	1	0.9	0	0
Candida species	1	0.9	1	0.5
Host defense abnormality type[a]				
No host defense abnormality	100	87.7	206	93.2
Diabetes mellitus	4	3.5	7	3.2
Hepatic disease	4	3.5	3	1.4
Renal disease	1	0.9	1	0.5
HIV positive	1	0.9	1	0.5
Asplenic	2	1.8	0	0
Use of immunosuppressive medication(s)	2	1.8	3	1.4
Complicated injury type[a]				
No complicated injury	92	79.3	214	95.5
Fracture	8	6.9	6	2.7
Joint involvement	2	1.7	1	0.4
Tendon or ligament involvement	9	7.8	0	0
Vascular injury	1	0.9	1	0.4
Nerve injury	0	0.0	1	0.4
Internal injury	3	2.6	1	0.4
Compartment syndrome	1	0.9	0	0
Owner of biting dog				
Patient or patient's relative	53	47.7	100	45.2
Friend, neighbor, or other individual known to the patient	29	26.1	68	30.8

Police dog	2	1.8	2	0.9
Unknown or stray	10	9.0	26	11.8
Missing	17	15.3	25	11.3

[a]For each clinical characteristic above, a patient could be included in >1categories.

Table 6. Odds ratios and risk differences for hospitalization by risk factor among emergency (ED) visits for dog bite injury, UNC Health Care, 2000-2011.

Risk factor	No. exposed: Case visits (n=111)	No. exposed: Subcohort visits (n=221)	Adjusted[a] odds ratio (95% CI[b])	Adjusted[a] risk difference[c] (95% CI[b])
Host-defense abnormality				
Present	11	15	1.6 (0.5, 4.6)	0.02 (-0.03, 0.1)
Absent	100	206	1	0
Anatomic location				
Multiple locations	11	7	6.0 (1.2, 30.9)	0.06 (-0.0006, 0.4)
Upper extremity only	65	112	3.0 (1.0, 8.9)	0.02 (0.004, 0.04)
Head only	28	66	1.4 (0.4, 4.9)	0.006 (-0.008, 0.03)
Other location[d]	7	36	1	0
Infection				
Present	57	22	7.8 (3.8, 16.0)	0.3 (0.1, 0.6)
Absent	54	199	1	0
Number of previous evaluations				
≥2	17	6	4.2 (1.3, 13.7)	0.1 (0.006, 0.9)
1	55	31	5.7 (3.1, 10.4)	0.2 (0.07, 0.4)
0	39	184	1	0
Complicated injury				
Present	19	7	3.2 (1.1, 9.4)	0.1 (0.006, 1.0)
Absent	92	214	1	0

[a]Analysis of directed acyclic graphs (DAGs) indicated the association of each risk factor and hospitalization should be adjusted for age and all other risk factors.
[b]Confidence interval

[c]Using centered adjustment variables
[d]Torso only or lower extremity only

Table 7. Analysis of prior evaluations and the risk of hospitalization after dog bite injury by patient sex and race, emergency department (ED) visits for dog bite injury, UNC Health Care, 2000-2011.

	Prior evaluations					
	≥1 prior evaluation(s)		No prior evaluation			
Sex	**Cases (n)**	**Subcohort (n)**	**Cases (n)**	**Subcohort (n)**	**Odds ratio[a] (95% CI[b])**	**Risk difference[a] (95% CI[b])**
Male	39	14	21	81	10.7 (5.2, 22.2)	0.4 (0.2, 0.6)
Female	33	23	18	103	8.2 (4.2, 15.9)	0.3 (0.2, 0.4)
					ROR[c] (95% CI[b]) = 1.3 (0.4, 4.0)	**IC[d] (95% CI[b])=** 0.1 (-0.1, 0.4)
Race[e]						
Non-white	8	4	7	56	16.0 (3.9, 66.2)	0.2 (0.1, 0.6)
White	62	33	31	128	7.8 (4.6, 13.1)	0.3 (0.2, 0.4)
					ROR[c] (95% CI[b]) = 2.1 (0.5, 19.8)	**IC[d] (95% CI[b])=** -0.1 (-0.3, 0.4)

[a]Reference is no prior evaluations.
[b]Confidence interval
[c]Ratio of odds ratios
[d]Interaction contrast
[e]Race is missing for 3 individuals.

Figure 3. Design for case-cohort study of risk factors for hospitalization after dog bite injury, UNC Health Care, 2000-2011; (a) case-cohort profile (b) conceptual illustration.

Figure 3a

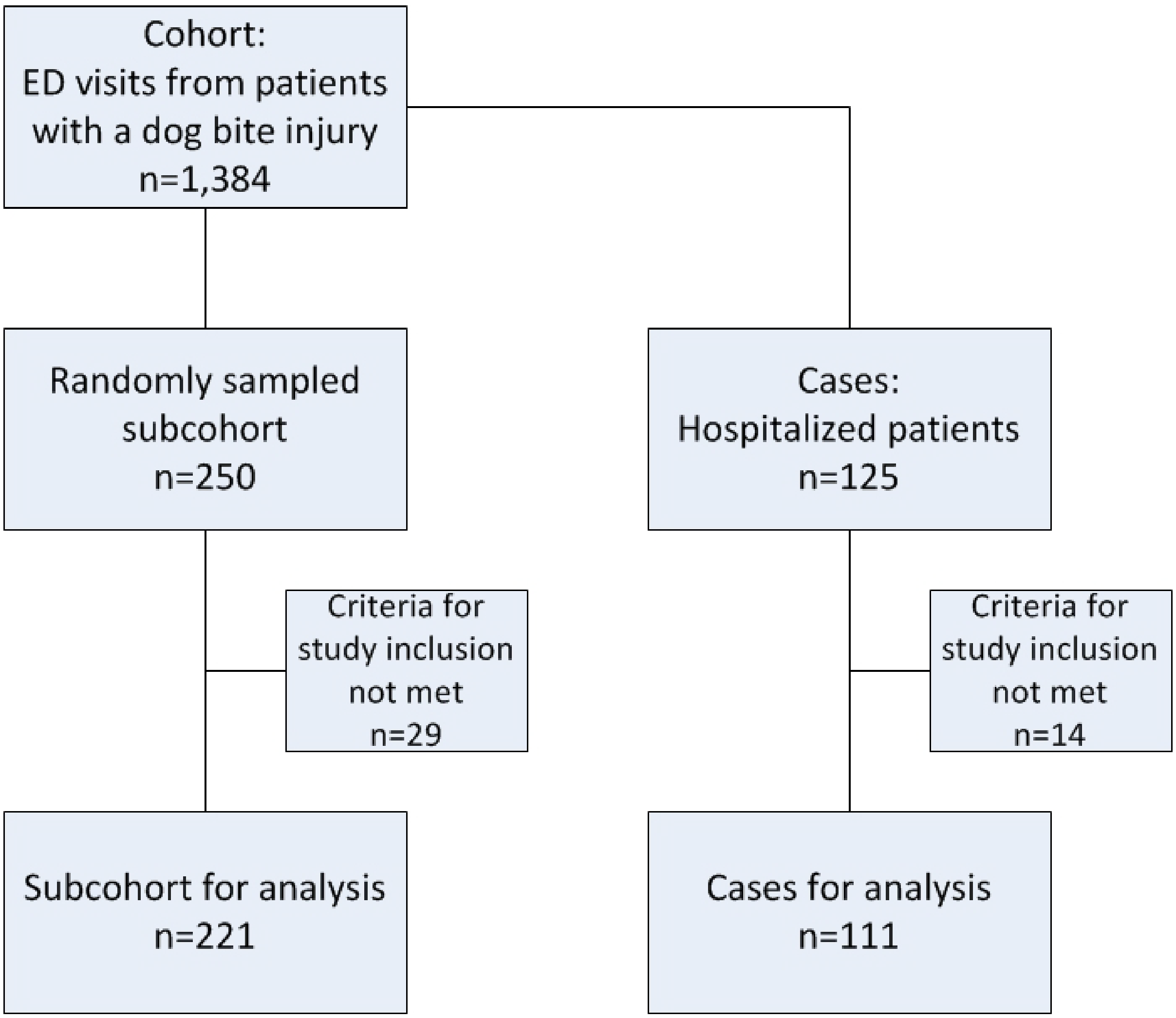
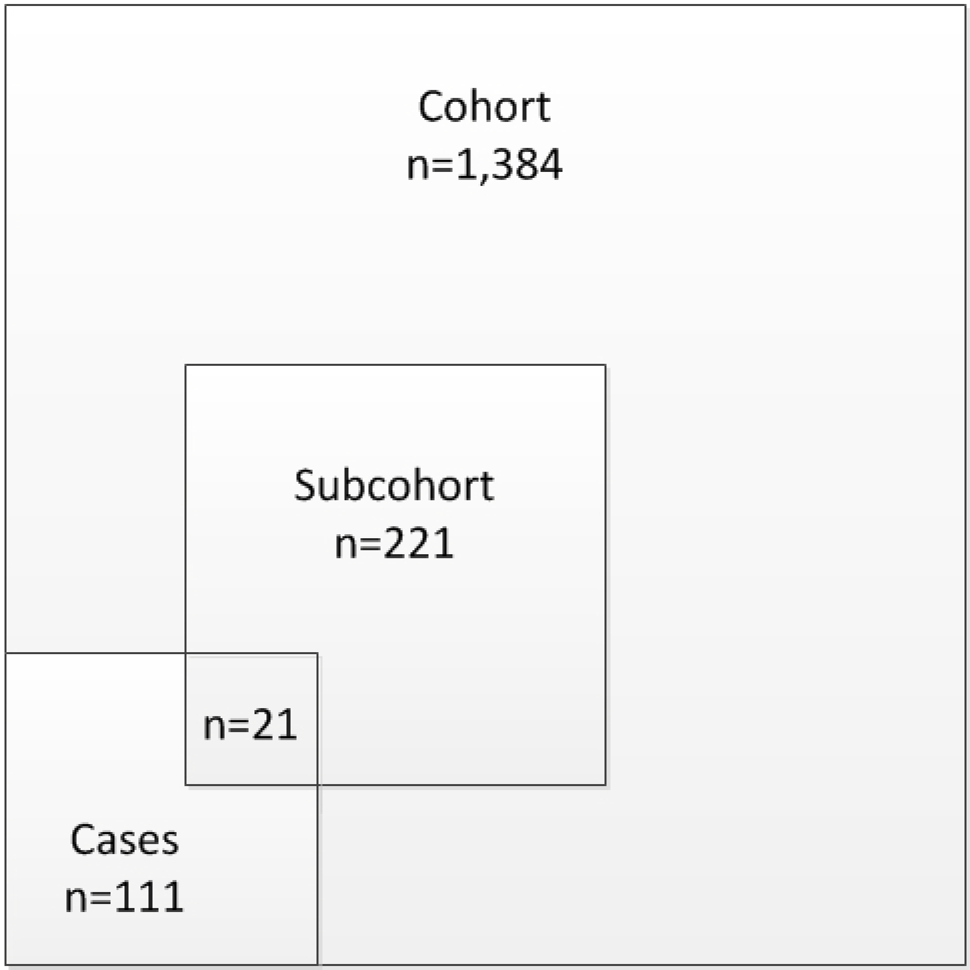


Figure 3b



CHAPTER VI

CONCLUSIONS

A. Recapitulation of Specific Aims

Aim 1 (Manuscript 1):

Using NC DETECT ED visit data from January 1, 2008 to December 31, 2010, calculate animal bite incidence rates and 95% CIs over the 3-year study period and within yearly and monthly intervals for the entire state and by patient sex, age group, rural or urban residence, and biting animal species with age-adjustment to the US Census Bureau 2008 Intercensal Population Estimates for North Carolina by 5-year age groups. Calculate rate differences and 95% CIs.

Conclusions:

The statewide incidence rate of animal bite-related ED visits remained approximately constant over the study period: $135/10^5$ py (95% CI, 132-137) in 2008, $141/10^5$ py (95% CI, 139-144) in 2010. The incidence rate was highest for children under 10 years of age, after which the rate declined fairly steadily with age. The overall rates for males and females were quite similar.

The rate of dog bite-related ED visits was much higher than for any other mammalian species. The incidence of dog bite-related ED visits was higher in males ($115/10^5$ py) than in females ($95/10^5$ py), with a rate difference of $20/10^5$ py

(95% CI, 17-22). ED visits related to cat bites and scratches were next most common, with highest rates among adults >75 years of age. The incidence of cat bite or scratch-related ED visits was higher in females ($26/10^5$ py) than in males ($12/10^5$ py), with a rate difference of $14/10^5$ py (95% CI, 13-15).

The incidence of visits for dog bites, cat bites or scratches, and other specified animal bites (bites from wildlife, equines, swine, small ruminants, other small animals, and rodents) demonstrated a seasonal pattern, with an increase in the late spring, peak in the summer, and decrease through the fall. The age-adjusted incidence of animal bite-related ED visits was higher in rural than in urban North Carolina counties.

Aim 2 (Manuscript 1):

Describe the incident animal bite-related ED visit and patient characteristics, including mode of transport to the ED, visit month, payment method, administration of rabies PEP, patient sex, patient age, anatomic location of bite(s), ED disposition, biting animal species, and urban versus rural patient residence.

Conclusions:

Among North Carolina residents with an incident animal bite ED visit from 2008-2010 (38,479), the mean age was 32 years (range: 0-99; standard deviation: 22). Thirty percent (11,570) of such visits were made by children ≤14 years. Similar numbers of incident animal bite-related ED visits were made by males and females. Patients from rural North Carolina counties made 19,555 (50%) of incident animal bite ED visits, while 17,623 (45%) were made by patients from urban North Carolina counties.

In 35,297 (91%) of incident animal bite ED visits the patient was discharged, while in 1,091 (3%) of incident visits the patient was hospitalized. Private insurers paid for 14,139 (36%) of the incident animal bite ED visits. Among the 30,865 visits with information regarding mode of transport to the ED, 27,908 (90%) were walk-ins. Rabies PEP was administered during 1,664 (4%) of the incident animal bite-related visits.

Among those with an incident animal bite ED visit, the highest frequencies of ICD-9-CM diagnosis code(s) for skin or subcutaneous tissue infections were in adults aged 35-69. Skin or subcutaneous tissue infection was diagnosed at 796 (3%) of 29,586 dog bite-related incident visits and 898 (17%) of 5,314 cat bite or scratch-related incident visits. Wounds to the head, neck, or face were documented in 6,304 animal bite-related ED visits, 1,931 (31%) of which were made by 0-4 year-olds and 1,456 (23%) of which were made by 5-9 year-olds.

Aim 3 (Manuscript 2):

Using an administrative dataset from the University of North Carolina, Department of Emergency Medicine, identify the dog bite-related ED visits that will be included in the case-cohort study. Create a data collection instrument and data base in preparation for medical record review. Perform a review of UNC Health Care medical records and collect relevant demographic and clinical data on each ED patient included in the study.

Conclusions:

Between January 1, 2000 and December 31, 2011, there were 1,384 visits to UNC Health Care ED with an ICD-9-CM E-code for dog bite (E906.1). Of the 125 ED visits for dog bite that resulted in hospitalization (cases), 14 (11%) did not meet eligibility criteria and were excluded. The remaining 111 cases were included in the analysis. Of the 250 visits randomly sampled for the subcohort, 29 (12%) did not meet eligibility criteria and were excluded. The remaining 221 in the subcohort were included in the analysis. Twenty-one (10%) patients in the subcohort were also cases. Four patients in the dataset had 2 dog bite injury ED visits on different dates. ED visits made from 2000 to mid-2004 were documented in paper medical records, while ED visits made from mid-2004 through 2011 were documented in the EMR. EMR was used to collect information for 79 (71%) cases and 151 (68%) subcohort members.

Aim 4 (Manuscript 2):

Using logistic regression models, describe the relationship between the following risk factors and the risk of hospitalization after a dog bite-related ED visit: presence of infection, complicated injury, host defense abnormalities, the number of previous evaluations for the injury, and anatomic location of the bite. Consider adjustment variables for the relationship between each risk factor and hospitalization based on DAGs.

Conclusions:

Point estimates for all risk factors were elevated above the null. Compared to all other risk factors, infection at the time of ED visit had the largest relative risk (OR=7.8, 95% CI 3.8-16.0) and RD (0.3, 95% CI 0.1-0.6) point estimates. With the second highest relative risk point estimate, the association between injury to multiple anatomic locations and hospitalization (OR=6.0, 95% CI 1.2-30.9) had a CLR of 26 and was the least precise estimate. As the number of previous evaluations increased from 1 to ≥2, there was a monotonic decrease in relative and absolute effect measures for risk of hospitalization.

Aim 5 (Manuscript 2):

Evaluate EMM by patient sex and race for the relationship between previous evaluation for the dog bite injury and hospitalization.

Conclusions:

Females and white individuals with ≥1 prior evaluation had lower relative risks of hospitalization than males and non-white individuals with ≥1 prior evaluation, respectively. Point estimates were least precise for the analysis by race.

B. Summary

Animal bites are an important target for public health interventions. From 2008-2010, unintentional dog bite injuries were associated with an estimated average lifetime medical cost of >$630 for a treat and release ED visit. In North Carolina ED-evaluated dog bite injuries alone cost an average of >$9.1 million per year. Nationally, approximately 2.5% of all ED visits for dog bite are admitted to the hospital (12). The majority of these admitted patients require intravenous antibiotics and/or surgical repair of wounds. The aggregated yearly cost of dog bite-related hospitalizations in the US is approximately $53.9 million.

Although animal bites are largely preventable, directed intervention efforts require an understanding of current epidemiology. The incidence of animal bites has been examined previously. However, published estimates included only dog bites (12, 29, 30) were based on data from the early to mid-1990's (3, 8), relied on reported animal bites or exposures (3, 8), or were for a single city (32). Biting species-specific ED visit incidence rates described in this dissertation have not been previously published on a statewide level.

This dissertation provides an example of the use of comprehensive, statewide ED syndromic surveillance data for determination of animal bite incidence rates and description of ED visit characteristics and patient attributes. Greater than 75% of animal bites examined in North Carolina EDs were from dogs, nearly 14% from cats, and the remaining from wildlife, horses, food animals, rodents, and other animals. Children ≤14 years had the highest rates of animal bite-related ED visits, specifically dog bites. By the age of 10, a North Carolina child has a 1 in 50 risk of dog bite injury requiring an ED visit. Dog bite prevention efforts in North Carolina should be increased and directed at children ≤14 in the early spring. Despite the fact that those >79 years had the lowest animal bite incidence, the highest incidence of cat bite or scratch-related ED visits was in adults >79 years. A North Carolinian has a 1 in 60 lifetime risk of cat bite or scratch injury requiring an ED visit. Older adults should be educated on avoidance of cat bites and scratches.

Previous reports indicate that the rate of hospitalization from dog bite injury is highest for children <5 years of age and adults >65 years of age (12). Significant physical trauma may result from dog bite injuries to small children. Older adults may have complicating comorbid conditions and increased risk of infection. Guidelines suggest providers consider anatomic location of the bite, presence of complicated or severe injury, and failure of outpatient therapy, in addition to age and presence of infection, when determining whether to admit a patient with dog bite injury (44). However, a quantitative evaluation of the associations between hospitalization after dog bite injury and potential risk factors has not yet been published.

This dissertation describes a case-cohort study of risk factors for hospitalization after a dog bite injury, including presence of infection, complicated injury, host defense abnormalities, number of previous evaluations for the injury, and anatomic location of the bite. For all factors evaluated, point estimates for the risk of hospitalization after dog bite injury were above the null. The largest relative and absolute effect measure point estimates in the study were for the association between infection and hospitalization. This intuitive association highlights the importance of proper wound care, patient counseling, and consideration of antibiotic prophylaxis at the initial patient evaluation. Compared to patients with a single dog bite injury, patients with multiple injuries were at increased risk for hospitalization. Presence of multiple injuries may be related to bite severity and the nature and circumstances of the injury, including the size and number of dogs involved.

Animal bites, specifically dog and cat bites, are typically monitored and prevention efforts undertaken at state and local levels. Monitoring species-specific bite incidence across the state and in various subpopulations provides valuable insight for state and local public health officials, physicians, and veterinarians. The quantitative examination of risk factors for hospitalization after dog bite injury informs clinical guidelines and may reduce dog bite related-hospitalizations.

APPENDIX A. DATA COLLECTION FORM FOR CASE-COHORT STUDY:
Data collection form (Epi Info (80)) for medical record review (Manuscript 2).

Risk factors for Hospitalization from a Dog Bite Injury

Date of data abstraction

Initials of abstractor

Study ID Number

Medical Record Number

ED Visit Number

Case or Control?

NOTES: Case or Control

Demographics

Date of Birth

Gender

Insurance on record

NOTES: Demographics

Race

Preferred Language

Ethnicity

Registration, Arrival, Attending

ED Registration Date

ED Registration Time (military)

Chief Complaint

Mode of Transport

Resident or NP

Attending Physician

MRN2

USE ONLY THE INFO AVAILABLE IN THIS VISIT REPORT
(If available, greater detail from a previous ED report for this injury may be entered in the NOTES sections. Indicate ED report date(s) that provided the additional info.)

History of the Injury

Date of injury

Time of injury (military)

Place of injury occurrance

NOTES: Place of occurrence

What were the circumstances of the injury?

Was animal control notified?

Who owns the dog?

Was the dog up-to-date on rabies vaccination?

NOTES: Other info about circumstances (If from another ED report, state this and include date of that report.)

Treatment and Evaluation History

Does the patient report a history of fever?

NOTES: History of Fever

Patient previously evaluated by a medical professional for this injury?

NOTES: Previous evaluation

If previously evaluated by a medical professional, how many times?

Date(s) of previous evaluation(s) for this injury(MM/DD/YYYY)

Previous wound treatment for this injury. (If from another WebCIS ED report include date of that report.)

Previous ABX for this injury (administered and RX). (If from another WebCIS ED report include date of that report.)

Patient previously admitted for this injury? (according to this ED report)

NOTES: Previous admission

MRN3

Past History

COMORBIDITIES

Comorbidity 1

Comorbidity 2

Comorbidity 3

Comorbidity 4

Comorbidity 5

NOTES: Comorbidities

MEDICATIONS and VACCINATION STATUS

Current Medication 1

Current Medication 2

Current Medication 3

Current Medication 4

Current Medication 5

Current Medication 6

Allergies to antibiotics

Tetanus immunization status

Social History

Smoker?

Alcohol use

Drug use

NOTES: Social history

MRN4

Physical Examination - Bite(s)

Number of bite wounds (text)

NOTES: Number of bite wounds

Anatomic location of bite 1

Type of bite injury 1

Type of bite injury 1b

Anatomic location of bite 2

Type of bite injury 2

Type of bite injury 2b

Anatomic location of bite 3

Type of bite injury 3

Type of bite injury 3b

Anatomic location of bite 4

Type of bite injury 4

Type of bite injury 4b

Anatomic location of bite 5

Type of bite injury 5

Type of bite injury 5b

Anatomic location of bite 6

Type of bite injury 6

Type of bite injury 6b

NOTES: Anatomic location of bite(s)

NOTES: Type of bite injury

MRN5

Infection

Signs of infection 1

Signs of infection 4

NOTES: Signs of infection

Signs of infection 2

Signs of infection 5

NOTES: LN enlargement

Signs of infection 3

Signs of infection 6

Complicated Injury

Complicated injury 1

Complicated injury 3

NOTES: Complicated injury

Complicated injury 2

Complicated injury 4

Concurrent Injury

Concurrent injury

Other Findings

Other relevant PE findings

MRN6

Acuity level

Vital Signs

Vitals from Initial Triage

Systolic BP 1

Diastolic BP 1

NOTES: BP

HR 1

NOTES: HR

RR 1

NOTES: RR

Temp 1 (degrees Celsius)

Temp location 1

NOTES: Temp

HIGHEST Vitals while in ED (If highest are same as initial, please note that.)

Systolic BP HIGH

associated Diastolic BP HIGH

NOTES: HIGH Vitals

HR HIGH

RR HIGH

Temp HIGH

Temp location HIGH

LOWEST Vitals while in ED (If lowest are same as initial, please note that.)

Systolic BP LOW

associated Diastolic LOW

NOTES: LOW Vitals

HR LOW

RR LOW

Temp LOW

Temp location LOW

MRN7

ED Procedures 1

WOUND CARE

Wound treatment performed in the ED 1

Wound treatment performed in the ED 2

Wound treatment performed in the ED 3

Wound treatment performed in the ED 4

NOTES: Wound treatment in ED

ANTIBIOTICS

Antibiotic administered in ED 1

Antibiotic administered in ED 2

Antibiotic administered in ED 3

Antibiotic administered in ED 4

Route antibiotic in ED 1

Route antibiotic in ED 2

Route antibiotic in ED 3

Route antibiotic in ED 4

NOTES: Abx in ED

CONSULTS IN THE ED

Consult in the ED 1

Consult in the ED 2

Consult in the ED 3

NOTES: Consult

MRN8

ED Procedures 2

VACCINATIONS

Tetanus

Was tetanus immunization administered at this ED visit?

NOTES: Tetanus

Rabies

Had the patient received Rabies Pre-exposure Prophylaxis before this bite?

NOTES: Rabies Pre-exposure Prophy

Was Rabies Ig administered at this ED visit?

NOTES: Rabies Ig

Was rabies vaccine administered at this ED visit?

NOTES: Rabies Vax

Which number in the rabies vaccine series was administered?

OTHER ED PROCEDURES

Other treatment in the ED?

MRN9

Imaging **PRINT REPORT(S)**

Were X-rays taken while the individual was an ED patient?

What abnormalities were noted on the X-rays?

NOTES: X-Rays

Was a CT scan performed while the individual was an ED patient?

NOTES: CT scan

Was a MRI performed while the individual was an ED patient?

NOTES: MRI

Other imaging performed while individual was an ED patient?

MRN10

Microbiology **PRINT REPORT(S)**

Were microbiology samples submitted?

NOTES: Micro in ED

Was the patient on antibiotics prior to micro sample(s) being obtained?

NOTES: Patient on abx prior to sample

RESULTS

Microbiology 1

Results Microbiology 1

NOTES: Microbiology

Microbiology 2

Results Microbiology 2

Microbiology 3

Results Microbiology 3

MRN11

Hematology **PRINT REPORT**

Was hematology performed and results retunred while the patient was in the ED?

NOTES: Hematology

WBC (x10 9th/L)

Abs Neuts (x10 9th/L)

Neut left shift (+)

Chemistry **PRINT REPORT**

Was a chemistry ordered and results returned while the patient was in the ED?

NOTES: Chemistry

MRN12

Final Diagnosis(es)

Infection-related diagnosis 1

Infection-related diagnosis 3

Infection-related diagnosis 5

Infection-related diagnosis 2

Infection-related diagnosis 4

NOTES: Infection dx

Where was/were infection-related diagnosis/es found?

Other diagnosis 1

Other diagnosis 3

Other diagnosis 5

Other diagnosis 2

Other diagnosis 4

NOTES: Other diagnosis

Where was/were other diagnosis/es found?

Disposition/Discharge

Discharged or admitted on this visit?

NOTES: ED Discharge Dispo

Written RX 1

Written RX 2

Written RX 3

MRN13

Cases only

Was surgery performed on the patient while admitted? If so, explain briefly.

PRINT REPORT

List the antibiotic(s) administered to the patient while admitted.

List antibiotic(s) patient was discharged on.

Date of Admission

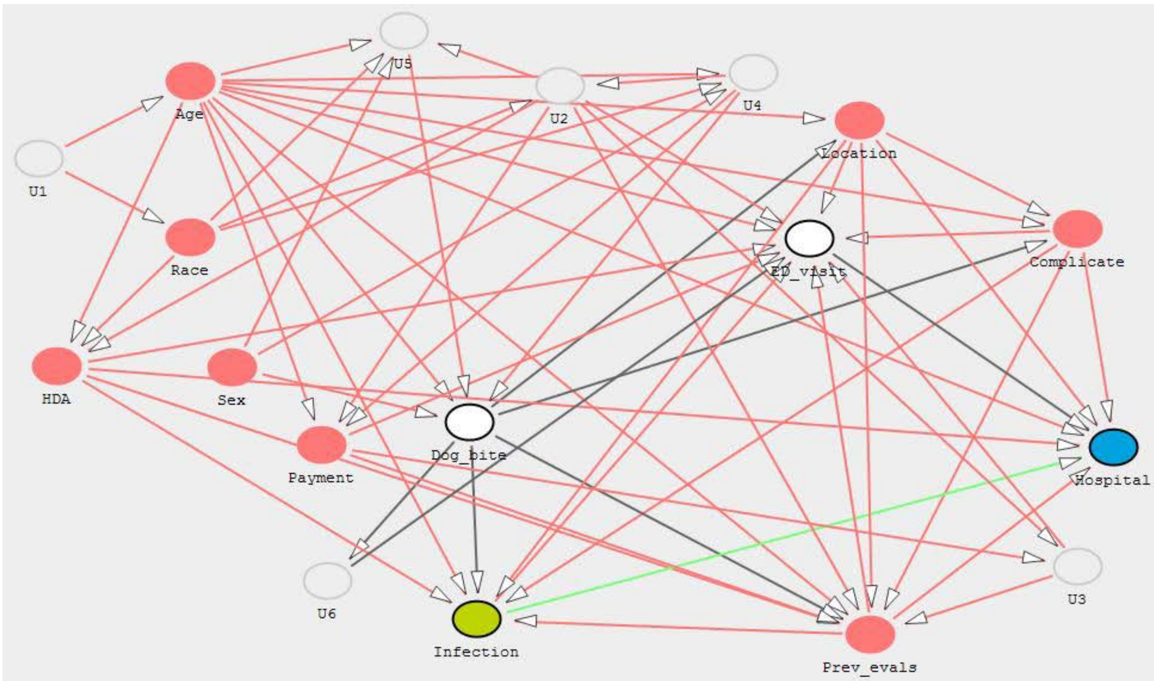
Date of Discharge

Was imaging performed while an inpatient? If so, explain briefly.

PRINT REPORT

NOTES: Case ONLY

APPENDIX B. DIRECTED ACYCLIC GRAPH (DAG) FOR CASE-COHORT STUDY: DAG for the relationship between the exposure, infection, and the outcome, hospitalization after dog bite injury (Manuscript 2) (83, 84). DAGs for the relationship between each of the other risk factors and hospitalization were based on this model.



Complicated injury=Complicate; Previous evaluation=Prev_evals; Payment method=Payment; Host defense abnormality=HDA; Hospitalization=Hospital; Relationship between Age and Race in North Carolina (unmeasured)=U1; Socioeconomic status (unmeasured)=U2; Ease of access to a medical provider (unmeasured)=U3; Occupation (unmeasured)=U4; Dog ownership (unmeasured)=U5; Other unmeasured=U6

Model Text Data for DAGitty (84):
Age 1 @0.137,-0.065
Complicate 1 @0.926,-0.005
Dog_bite A @0.392,0.056
ED_visit A @0.702,-0.011
HDA 1 @0.070,0.067
Hospital O @0.981,0.075
Infection E @0.394,0.116
Location 1 @0.734,-0.042
Payment 1 @0.251,0.059
Prev_evals 1 @0.759,0.123
Race 1 @0.139,-0.005
Sex 1 @0.156,0.027
U1 U @-0.010,-0.038
U2 U @0.449,-0.053
U3 U @0.951,0.100
U4 U @0.630,-0.058
U5 U @0.327,-0.081
U6 U @0.257,0.105

Age Location Infection Prev_evals Hospital HDA Dog_bite ED_visit Payment U4 U5 Complicate
Complicate Infection Prev_evals ED_visit Hospital
Dog_bite Infection Prev_evals Location Complicate U6
ED_visit Hospital
HDA Prev_evals Infection ED_visit Hospital
Infection ED_visit Hospital
Location ED_visit Infection Prev_evals Complicate Hospital
Payment Prev_evals U3 ED_visit
Prev_evals Infection ED_visit Hospital
Race HDA U2 U4 U5
Sex Dog_bite U4 U5
U1 Age Race
U2 Prev_evals ED_visit U5 U3 Payment HDA
U3 Prev_evals ED_visit
U4 U2 Dog_bite Payment
U5 Dog_bite
U6 ED_visit

REFERENCES

1. Patronek GJ, Slavinski SA. Animal bites. J Am Vet Med Assoc. 2009 Feb 1;234(3):336-45.

2. Langley RL. Human fatalities resulting from dog attacks in the United States, 1979-2005. Wilderness Environ Med. 2009 Spring;20(1):19-25.

3. Sinclair CL, Zhou C. Descriptive epidemiology of animal bites in Indiana, 1990-92--A rationale for intervention. Public Health Rep. 1995 Jan-Feb;110(1):64-7.

4. Christian KA, Blanton JD, Auslander M, Rupprecht CE. Epidemiology of rabies post-exposure prophylaxis--United States of America, 2006-2008. Vaccine. 2009 Nov 27;27(51):7156-61.

5. Abrahamian FM, Goldstein EJ. Microbiology of animal bite wound infections. Clin Microbiol Rev. 2011 Apr;24(2):231-46.

6. Beck AM, Jones BA. Unreported dog bites in children. Public Health Rep. 1985 May-Jun;100(3):315-21.

7. Weiss HB, Friedman DI, Coben JH. Incidence of dog bite injuries treated in emergency departments. JAMA. 1998 Jan 7;279(1):51-3.

8. Moore DA, Sischo WM, Hunter A, Miles T. Animal bite epidemiology and surveillance for rabies postexposure prophylaxis. J Am Vet Med Assoc. 2000 Jul 15;217(2):190-4.

9. Overall KL, Love M. Dog bites to humans--Demography, epidemiology, injury, and risk. J Am Vet Med Assoc. 2001 Jun 15;218(12):1923-34.

10. Steele MT, Ma OJ, Nakase J, Moran GJ, Mower WR, Ong S, et al. Epidemiology of animal exposures presenting to emergency departments. Acad Emerg Med. 2007 May;14(5):398-403.

11. ICD-9-CM: International Classification of Diseases 9th Revision Clinical Modification Sixth Edition, Color Coded 2010 Hospital Edition, Volumes 1, 2, &3. 6th ed. Los Angeles, California: Practice Management Information Corporation (PMIC); 2009.

12. Emergency department visits and inpatient stays involving dog bites, 2008 [Internet]. Rockville, MD: Agency for Healthcare Research and Quality; cited 3/18/2011]. Available from: http://www.hcup-us.ahrq.gov/reports/statbriefs/sb101.pdf.

13. Castrodale L. Hospitalizations resulting from dog bite injuries -- Alaska, 1991-2002. Int J Circumpolar Health. 2007 Sep;66(4):320-7.

14. Feldman KA, Trent R, Jay MT. Epidemiology of hospitalizations resulting from dog bites in California, 1991-1998. Am J Public Health. 2004 Nov;94(11):1940-1.

15. Hoff GL, Cai J, Kendrick R, Archer R. Emergency department visits and hospitalizations resulting from dog bites, Kansas City, MO, 1998-2002. Mo Med. 2005 Nov-Dec;102(6):565-8.

16. Harris D, Imperato PJ, Oken B. Dog bites--An unrecognized epidemic. Bull N Y Acad Med. 1974 Oct;50(9):981-1000.

17. Morton C. Dog bites in Norfolk, Va. Health Serv Rep. 1973 Jan;88(1):59-64.

18. Ndon JA, Jach GJ, Wehrenberg WB. Incidence of dog bites in Milwaukee, Wis. Wis Med J. 1996 Apr;95(4):237-41.

19. Chang YF, McMahon JE, Hennon DL, LaPorte RE, Coben JH. Dog bite incidence in the city of Pittsburgh: A capture-recapture approach. Am J Public Health. 1997 Oct;87(10):1703-5.

20. Shuler CM, DeBess EE, Lapidus JA, Hedberg K. Canine and human factors related to dog bite injuries. J Am Vet Med Assoc. 2008 Feb 15;232(4):542-6.

21. Borud LJ, Friedman DW. Dog bites in New York City. Plast Reconstr Surg. 2000 Oct;106(5):987-90.

22. Tan RL, Powell KE, Lindemer KM, Clay MM, Davidson SC. Sensitivities of three county health department surveillance systems for child-related dog bites: 261 cases (2000). J Am Vet Med Assoc. 2004 Dec 1;225(11):1680-3.

23. Moore RM, Jr, Zehmer RB, Moulthrop JI, Parker RL. Surveillance of animal-bite cases in the United States, 1971-1972. Arch Environ Health. 1977 Nov-Dec;32(6):267-70.

24. Berzon DR, Farber RE, Gordon J, Kelley EB. Animal bites in a large city--A report on Baltimore, Maryland. Am J Public Health. 1972 Mar;62(3):422-6.

25. Wright JC. Reported cat bites in Dallas: Characteristics of the cats, the victims, and the attack events. Public Health Rep. 1990 Jul-Aug;105(4):420-4.

26. Sacks JJ, Kresnow M, Houston B. Dog bites: How big a problem? Inj Prev. 1996 Mar;2(1):52-4.

27. Gilchrist J, Sacks JJ, White D, Kresnow MJ. Dog bites: Still a problem? Inj Prev. 2008 Oct;14(5):296-301.

28. Quinlan KP, Sacks JJ. Hospitalizations for dog bite injuries. JAMA. 1999 Jan 20;281(3):232-3.

29. Centers for Disease Control and Prevention (CDC). Nonfatal dog bite-related injuries treated in hospital emergency departments--United States, 2001. MMWR Morb Mortal Wkly Rep. 2003 Jul 4;52(26):605-10.

30. Quirk JT. Non-fatal dog bite injuries in the U.S.A., 2005-2009. Public Health. 2012 Apr;126(4):300-2.

31. Day H, Roesler JS, Kinde M. Hospital-treated dog bites in Minnesota, 1998-2005. Minn Med. 2007 Jul;90(7):43,5, 47.

32. Bregman B, Slavinski S. Using emergency department data to conduct dog and animal bite surveillance in New York City, 2003-2006. Public Health Rep. 2012 Mar-Apr;127(2):195-201.

33. O'Neil ME, Mack KA, Gilchrist J. Epidemiology of non-canine bite and sting injuries treated in U.S. emergency departments, 2001-2004. Public Health Rep. 2007 Nov-Dec;122(6):764-75.

34. Dendle C, Looke D. Review article: Animal bites: An update for management with a focus on infections. Emerg Med Australas. 2008 Dec;20(6):458-67.

35. Kaye AE, Belz JM, Kirschner RE. Pediatric dog bite injuries: A 5-year review of the experience at The Children's Hospital of Philadelphia. Plast Reconstr Surg. 2009 Aug;124(2):551-8.

36. Calkins CM, Bensard DD, Partrick DA, Karrer FM. Life-threatening dog attacks: A devastating combination of penetrating and blunt injuries. J Pediatr Surg. 2001 Aug;36(8):1115-7.

37. Mcheik JN, Vergnes P, Bondonny JM. Treatment of facial dog bite injuries in children: A retrospective study. J Pediatr Surg. 2000 Apr;35(4):580-3.

38. Bernardo LM, Gardner MJ, O'Connor J, Amon N. Dog bites in children treated in a pediatric emergency department. J Soc Pediatr Nurs. 2000 Apr-Jun;5(2):87-95.

39. Reisner IR, Nance ML, Zeller JS, Houseknecht EM, Kassam-Adams N, Wiebe DJ. Behavioural characteristics associated with dog bites to children presenting to an urban trauma centre. Inj Prev. 2011 Mar 28.

40. Balsamo GA, Ratard R, Claudet A. The epidemiology of animal bite, scratch, and other potential rabies exposures, Louisiana. J La State Med Soc. 2009 Sep-Oct;161(5):260-5.

41. Weber DJ, Hansen AR. Infections resulting from animal bites. Infect Dis Clin North Am. 1991 Sep;5(3):663-80.

42. Dire DJ. Cat bite wounds: Risk factors for infection. Ann Emerg Med. 1991 Sep;20(9):973-9.

43. Dire DJ, Hogan DE, Riggs MW. A prospective evaluation of risk factors for infections from dog-bite wounds. Acad Emerg Med. 1994 May-Jun;1(3):258-66.

44. Abrahamian FM. Dog bites: Bacteriology, management, and prevention. Curr Infect Dis Rep. 2000 Oct;2(5):446-53.

45. Oehler RL, Velez AP, Mizrachi M, Lamarche J, Gompf S. Bite-related and septic syndromes caused by cats and dogs. Lancet Infect Dis. 2009 Jul;9(7):439-47.

46. Chun YT, Berkelhamer JE, Herold TE. Dog bites in children less than 4 years old. Pediatrics. 1982 Jan;69(1):119-20.

47. Daniels DM, Ritzi RB, O'Neil J, Scherer LR. Analysis of nonfatal dog bites in children. J Trauma. 2009 Mar;66(3 Suppl):S17-22.

48. Morgan M, Palmer J. Dog bites. BMJ. 2007 Feb 24;334(7590):413-7.

49. Weber DJ, Wolfson JS, Swartz MN, Hooper DC. *Pasteurella multocida* infections: Report of 34 cases and review of the literature. Medicine (Baltimore). 1984 May;63(3):133-54.

50. Johnson JK, Perencevich EN, Lincalis DP, Venezia RA. Dog bite transmission of antibiotic-resistant bacteria to a human. Infect Control Hosp Epidemiol. 2006 Jul;27(7):762-3.

51. Stevens DL, Bisno AL, Chambers HF, Everett ED, Dellinger P, Goldstein EJ, et al. Practice guidelines for the diagnosis and management of skin and soft-tissue infections. Clin Infect Dis. 2005 Nov 15;41(10):1373-406.

52. Kullberg BJ, Westendorp RG, van't Wout JW, Meinders AE. Purpura fulminans and symmetrical peripheral gangrene caused by *Capnocytophaga canimorsus* (formerly DF-2) septicemia--A complication of dog bite. Medicine (Baltimore). 1991 Sep;70(5):287-92.

53. Dire DJ, Hogan DE, Walker JS. Prophylactic oral antibiotics for low-risk dog bite wounds. Pediatr Emerg Care. 1992 Aug;8(4):194-9.

54. Callaham M. Prophylactic antibiotics in common dog bite wounds: A controlled study. Ann Emerg Med. 1980 Aug;9(8):410-4.

55. Quinn JV, McDermott D, Rossi J, Stein J, Kramer N. Randomized controlled trial of prophylactic antibiotics for dog bites with refined cost model. West J Emerg Med. 2010 Dec;11(5):435-41.

56. Cummings P. Antibiotics to prevent infection in patients with dog bite wounds: A meta-analysis of randomized trials. Ann Emerg Med. 1994 Mar;23(3):535-40.

57. Rosen RA. The use of antibiotics in the initial management of recent dog-bite wounds. Am J Emerg Med. 1985 Jan;3(1):19-23.

58. Holm M, Tarnvik A. Hospitalization due to *Pasteurella multocida*-infected animal bite wounds: Correlation with inadequate primary antibiotic medication. Scand J Infect Dis. 2000;32(2):181-3.

59. Feder HM, Jr, Shanley JD, Barbera JA. Review of 59 patients hospitalized with animal bites. Pediatr Infect Dis J. 1987 Jan;6(1):24-8.

60. Benfield R, Plurad DS, Lam L, Talving P, Green DJ, Putty B, et al. The epidemiology of dog attacks in an urban environment and the risk of vascular injury. Am Surg. 2010 Feb;76(2):203-5.

61. Wu PS, Beres A, Tashjian DB, Moriarty KP. Primary repair of facial dog bite injuries in children. Pediatr Emerg Care. 2011 Sep;27(9):801-3.

62. Benson LS, Edwards SL, Schiff AP, Williams CS, Visotsky JL. Dog and cat bites to the hand: Treatment and cost assessment. J Hand Surg Am. 2006 Mar;31(3):468-73.

63. Calvet HM, Yoshikawa TT. Infections in diabetes. Infect Dis Clin North Am. 2001 Jun;15(2):407,21, viii.

64. Clinical immunology: Principles and practice (eBook). 4th ed. Rich RR, Fleisher TA, Shearer WT, Schroeder Jr HW, Frew AJ, Weyand CM, editors. Elseiver Saunders; 2013.

65. Johnson DH, Cunha BA. Infections in cirrhosis. Infect Dis Clin North Am. 2001 Jun;15(2):363,71, vii.

66. Minnaganti VR, Cunha BA. Infections associated with uremia and dialysis. Infect Dis Clin North Am. 2001 Jun;15(2):385,406, viii.

67. Klein NC, Go CH, Cunha BA. Infections associated with steroid use. Infect Dis Clin North Am. 2001 Jun;15(2):423,32, viii.

68. Levey AS, Atkins R, Coresh J, Cohen EP, Collins AJ, Eckardt KU, et al. Chronic kidney disease as a global public health problem: Approaches and initiatives - a position statement from Kidney Disease Improving Global Outcomes. Kidney Int. 2007 Aug;72(3):247-59.

69. The UNC Department of Emergency Medicine Carolina Center for Health Informatics Report, Overview and Analysis of NC DETECT Emergency Department Data: 2009. [Internet].: Carolina Center for Health Informatics, Department of Emergency Medicine, University of North Carolina at Chapel Hill; 2011; cited February 15, 2012]. Available from: http://www.ncdetect.org/Final_2009NCDETECT_ANNUALREPORT_Color.pdf.

70. 2009-2010 APPA National Pet Owners Survey. Greenwich, Connecticut: American Pet Products Association, Incorporated; 2009-2010.

71. Centers for Disease Control and Prevention. Web-Based Injury Statistics Query And Reporting System (WISQARS) [Internet].: Centers for Disease Control and Prevention, National Center for Injury Prevention and Control [updated May 2, 2012; cited June 25, 2012]. Available from: http://wisqars.cdc.gov:8080/costT/.

72. Rhea S, Ising A, Waller A, Haskell MG, Weber DJ. Using ICD-9-CM E-codes in addition to chief complaint keyword searches for identification of animal bite-related emergency department visits. Public Health Rep. 2012 Nov-Dec;127(6):561-2.

73. Intercensal estimates of the resident population by sex and age for North Carolina: April 1, 2000 to July 1, 2010 (ST-EST00INT-02-37) [Internet].: U.S. Census Bureau, Population Division [updated September 2011; cited November 1, 2011]. Available from: http://www.census.gov/popest/intercensal/state/ST-EST00INT-02.html.

74. UNC Health Care: About us [Internet].: UNC Health Care; 2013; cited December 15, 2012]. Available from: http://www.unchealthcare.org/site/aboutus.

75. Carlson JN, Menegazzi JJ, Callaway CW. Magnitude of national ED visits and resource utilization by the uninsured. Am J Emerg Med. 2013 Jan 30.

76. Rural/urban counties in North Carolina [Internet].: North Carolina Rural Economic Development Center, Incorporated; 2012; cited December 1, 2011]. Available from: http://www.ncruralcenter.org./index.php?option=com_content&view=article&id=75&Itemid=126.

77. Centers for Disease Control and Prevention. Use of a reduced (4-dose) vaccine schedule for postexposure prophylaxis to prevent human rabies-recommendations of the Advisory Committee on Immunization Practice. Ann Emerg Med. 2010 Jul;56(1):64-7.

78. Rothman KJ. EpiSheet: Spreadsheets for the analysis of epidemiologic data.;June 11, 2008.

79. List of medications contraindicating receipt of smallpox vaccine [Internet].: Centers for Disease Control and Prevention [updated February 7, 2007; cited March 15, 2012]. Available from: http://www.bt.cdc.gov/agent/smallpox/vaccination/immuno_suppress_meds.asp.

80. Centers for Disease Control and Prevention, Atlanta, GA. Epi Info. 2012;Verson 7.

81. Gilbert EH, Lowenstein SR, Koziol-McLain J, Barta DC, Steiner J. Chart reviews in emergency medicine research: Where are the methods? Ann Emerg Med. 1996 Mar;27(3):305-8.

82. SAS, Cary, NC. SAS. 2010;9.2.

83. Rothman KJ, Greenland S, Lash TL. Modern Epidemiology. Third ed. Philadelphia, Pennsylvania: Lippincott Williams & Wilkins; 2008.

84. Textor J, Hardt J, Knuppel S. DAGitty: A graphical tool for analyzing causal diagrams. Epidemiology. 2011 Sep;22(5):745.

85. Pearce N. What does the odds ratio estimate in a case-control study? Int J Epidemiol. 1993 Dec;22(6):1189-92.

86. Schouten EG, Dekker JM, Kok FJ, Le Cessie S, Van Houwelingen HC, Pool J, et al. Risk ratio and rate ratio estimation in case-cohort designs: Hypertension and cardiovascular mortality. Stat Med. 1993 Sep 30;12(18):1733-45.

87. Zeger SL, Liang KY. Longitudinal data analysis for discrete and continuous outcomes. Biometrics. 1986 Mar;42(1):121-30.

88. Beck AM, Loring H, Lockwood R. The ecology of dog bite injury in St. Louis, Missouri. Public Health Rep. 1975 May-Jun;90(3):262-7.

89. Monthly and seasonal climate information [Internet].: Southeast Regional Climate Center [updated February 2013; cited March 15, 2013]. Available from: http://www.sercc.com/climateinfo/monthly_seasonal.html.

90. American Veterinary Medical Association Task Force on Canine Aggression and Human-Canine Interactions. A community approach to dog bite prevention. J Am Vet Med Assoc. 2001 Jun 1;218(11):1732-49.

91. Moragas A, Castells C, Sans M. Mathematical morphologic analysis of aging-related epidermal changes. Anal Quant Cytol Histol. 1993 Apr;15(2):75-82.

92. Poole C. Low P-values or narrow confidence intervals: Which are more durable? Epidemiology. 2001 May;12(3):291-4.

93. Talan DA, Citron DM, Abrahamian FM, Moran GJ, Goldstein EJ. Bacteriologic analysis of infected dog and cat bites. Emergency Medicine Animal Bite Infection Study Group. N Engl J Med. 1999 Jan 14;340(2):85-92.