

An Epidemiologic Study of Vaccination Exemptions and Pertussis Risk

A Dissertation Presented for the

Doctor of Philosophy

Degree

The University of Tennessee, Knoxville

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December 2021

DEDICATION

This dissertation is dedicated to my parents, Kirsten Benson and David Tandy; my siblings, Peter, Gustav, and Aphra Tandy; my partner, Jason Moon; and my best pal, Karmen Stephenson. I would also like to dedicate this work to my late friend and mentor, Dr. Donald Siwek. Your constant support and encouragement have been invaluable throughout my life. I couldn't have done this without you all.

ACKNOWLEDGEMENTS

This dissertation could not have been completed without the support from Dr. Agricola Odoi. I don't have the words to express my gratitude for his unwavering support throughout my doctoral studies—his expertise and support have been invaluable through my doctoral studies and career, and I am forever grateful. I am a better epidemiologist, researcher, and person because of the opportunity to work with him. I would also like to acknowledge the support of my committee: Dr. Jennifer Jabson Tree, Dr. Marcy Souza, and Dr. Kimberly Fortner. They also provided invaluable professional and personal support during my studies. I want to acknowledge my spouse for his continued patience with me being in school for the whole of our relationship and I cannot wait to see what our life together brings moving forward. Finally, I want to acknowledge Dr. Stephen Kania, for his support during my time in the program.

ABSTRACT

The incidence of pertussis, a vaccine-preventable disease that can have severe complications in infants, has been increasing in the United States over the past three decades. Vaccine hesitancy and refusal have also increased and are associated with vaccination exemptions, which in turn are associated with outbreaks of vaccine-preventable diseases, including pertussis. Understanding attitudes towards vaccinations and identifying geographic disparities of vaccination exemptions and pertussis risks is useful for guiding control programs. Therefore, the objectives of this study were to: (i) investigate attitudes towards vaccinations; (ii) identify county-level geographic disparities and sociodemographic predictors of vaccination exemptions in Florida; (iii) investigate county-level geographic disparities, temporal changes, and sociodemographic predictors of pertussis risk in Florida between 2010 and 2018.

Qualitative methods were used to investigate attitudes towards vaccinations in the Knoxville area of Tennessee. Spatial patterns of vaccination exemption and pertussis risks were identified using county-level choropleth maps. Tango's spatial scan statistics were used to identify clusters of pertussis risk, which were displayed in maps. Negative binomial and ordinary least squares regression models were used to investigate predictors of vaccination exemption and pertussis risks, respectively.

Risk perception as well as family and social group attitudes were the primary contributors to vaccination hesitancy. High vaccination exemption risks were observed in Western and

Central Panhandle, Northeastern, Central-eastern, Central-western, and South-western coastal counties of Florida. High risks of total vaccination exemptions were observed in counties with high densities of primary care providers, high median income, high percentage of Hispanic population, and high percentage of population with college education. High risks of non-medical exemptions tended to occur in counties with high percentage of white population. Clusters of high pertussis risks were identified in Western Panhandle, Northeastern coast, and along the Western coast. Significant predictors of high county-level pertussis risks were rurality, high median income, and high percentage of females.

The identified drivers of vaccination hesitancy as well as disparities in and predictors of vaccination exemptions and pertussis risks are invaluable in guiding evidence-based health planning, resource allocation, and policy decisions aimed at reducing the burden and disparities in pertussis risk.

TABLE OF CONTENTS

CHAPTER 1	1
Introduction.....	1
CHAPTER 2	4
Literature Review.....	4
2.1 Etiology	5
2.2 Clinical Signs	5
2.2.1 Clinical Complications	7
2.3 Pathogenesis	7
2.4 Diagnosis and Treatment.....	8
2.4.1 Diagnostic Criteria	10
2.4.2 Treatment	11
2.5 Transmission	12
2.6 Epidemiology	13
2.6.1 Global Burden	13
2.6.2 Burden in North America	15
2.6.2.1 United States.....	16
2.6.2.2 Florida.....	17
2.6.3 Geographic Distribution	18
2.6.4 Temporal Patterns	20
2.6.5 Risk Factors.....	21
2.6.6 Reporting.....	23
2.7 Control and Prevention	25
2.7.1 Pertussis Vaccines	26
2.7.2 Immunity	27
2.7.3 Vaccine Efficacy	28
2.7.4 Pertussis Vaccination for Special Populations	29
2.7.5 Vaccination Coverage in the United States.....	29
2.7.6 Attitudes Towards Vaccinations	31
2.7.7 Vaccination Exemptions in the United States	32
2.8 Conclusions	33
CHAPTER 3	34
Attitudes of East Tennessee Residents Toward General and Pertussis Vaccination: A Qualitative Study	34
3.1 Disclosure.....	35
3.2 Abstract	36
3.3 Background	37
3.3.1 Vaccination Attitudes.....	38
3.3.2 Attitudes towards pertussis-containing vaccines.....	39
3.3.3 Approaches to Understanding Health Behaviors and Vaccine Attitudes	40
3.4 Methods.....	42
3.4.1 Participants and Recruitment	42
3.4.2 Procedures	43

3.4.3 Analysis	45
3.5 Results	49
3.5.1 Participant Demographic Characteristics	49
3.5.2 Theme 1: Attitudes Towards Vaccination.....	49
3.5.3 Theme 2: Reasons for Supporting Vaccination.....	51
3.5.4 Theme 3: Concerns and Reasons for Hesitancy	52
3.5.4.1 Number of Vaccines Administered	52
3.5.4.2 Denial of Efficacy and Safety Concerns	53
3.5.4.3 Concern Regarding Safety, Side Effects, or Negative Consequences of Vaccination	53
3.5.4.4. Risk Perception of Getting Pertussis	54
3.5.5 Theme Four: Knowledge and Information Sources	55
3.6 Discussion	57
3.6.1 Dunning-Kruger, Knowledge, and Vaccine Hesitancy	57
3.6.2 Social and Familial Group Influence	59
3.6.3 Strengths and Limitations.....	61
3.7 Conclusions	61
CHAPTER 4	63
Geographic Disparities and Predictors of Vaccination Exemptions in Florida	63
4.1 Disclosure.....	64
4.2 Abstract	65
4.2 Introduction	67
4.3 Methods.....	69
4.3.1 Study Area.....	69
4.3.2 Data Sources and Cartographic Displays	71
4.3.3 Predictors of Total and Non-Medical County-Level Vaccination Exemption Risks	71
4.3.4 Ethical Statement.....	77
4.4 Results	77
4.4.1 Geographic Patterns of Vaccination Exemptions.....	77
4.4.2 Predictors of Total Vaccination Exemptions	80
4.4.3 Predictors of Non-Medical Vaccination Exemptions.....	80
4.5 Discussion	81
4.5.1 Geographic Disparities in Vaccination Exemptions	81
4.5.1.1 Total Exemptions.....	81
4.5.1.2 Non-Medical Exemptions.....	86
4.5.2 Predictors of Vaccination Exemptions.....	87
4.5.2.1 Total Exemptions.....	87
4.5.2.2 Non-Medical Exemptions.....	88
4.5.3 Strengths and Limitations.....	91
4.6 Conclusions	92

CHAPTER 5	93
Geographic Disparities and Sociodemographic Predictors of Pertussis RISK in Florida.....	93
5.1 Disclosure.....	94
5.2 Abstract	95
5.3 Introduction	96
5.4 Methods.....	100
5.4.1 Study Area.....	100
5.4.2 Data Sources and Variable Selection	101
5.4.3 Investigation of High-Risk Clusters of Pertussis	103
5.4.4 Investigation of Predictors of County-Level Pertussis Risk	103
5.4.5 Cartographic Displays	106
5.4.6 Ethical Statement.....	106
5.5 Results	106
5.5.1 Geographic and Temporal Distribution of Pertussis Risk.....	106
5.5.2 Clusters of High Pertussis Risk	108
5.5.3 Predictors of Pertussis Risk.....	109
5.5.4 Geographic Distribution of Significant Predictors of Pertussis Risk	113
5.6 Discussion	120
5.6.1 Predictors of Pertussis Risk.....	123
5.6.2 Strengths and Limitations.....	125
5.7 Conclusions	126
CHAPTER 6	127
SUMMARY, CONCLUSIONS, AND RECOMMENDATIONS.....	127
REFERENCES	133
APPENDICES	172
Appendix A: Demographic Questionnaire.....	173
Appendix B: Interview Questionnaire	175
VITA	180

LIST OF TABLES

Table 3.1 Deductive and Inductive Codes Utilized in Qualitative Analysis.....	47
Table 3.2 Demographic Characteristics of Participants in Qualitative Study of Vaccination Attitudes in East Tennessee	50
Table 4.1 Summary Statistics of potential predictors of vaccination exemptions in Florida, 2014	74
Table 4.2 Results of univariable associations of potential predictors of total vaccination exemptions in Florida, 2014.....	75
Table 4.3 Results of univariable associations of potential predictors of non-medical vaccination exemptions in Florida, 2014.....	76
Table 4.4 Results of the final Poisson model showing significant predictors of total vaccination exemptions in Florida, 2014.....	82
Table 4.5 Results of the final negative binomial model showing significant predictors of total vaccination exemptions in Florida, 2014.....	83
Table 4.6 Results of the final Poisson model showing significant predictors of non-medical vaccination exemptions in Florida, 2014.....	84
Table 4.7 Results of the final negative binomial model showing significant predictors of non-medical vaccination exemptions in Florida, 2014.....	85
Table 5.1 Variables Considered as potential predictors of county-level pertussis risk in Florida	104
Table 5.2 Significant geographic clusters of pertussis risk in Florida, 2010-2018.....	112
Table 5.3 Significant geographic clusters of pertussis risk in Florida, 2010-2012.....	114
Table 5.4 Significant geographic clusters of pertussis risk in Florida, 2013-2015.....	115
Table 5.5 Significant geographic clusters of pertussis risk in Florida, 2016-2018.....	116
Table 5.6 Summary statistics and results of univariable analysis of potential predictors of pertussis risk in Florida	117
Table 5.7 Significant predictors of county-level pertussis risk in Florida, 2010-2018.....	118

LIST OF FIGURES

Figure 4.1 Geographic distribution of counties and major cities in Florida	70
Figure 4.2 Conceptual model showing sociodemographic variables considered as potential predictors of vaccination exemptions in Florida, 2014.....	73
Figure 4.3 Total and non-medical vaccination exemptions per 10,000 persons in Florida, 2014.....	79
Figure 5.1 Geographic distribution of counties and major cities in Florida	102
Figure 5.2 Choropleth Maps Showing Spatial Distribution of Pertussis Risks in Florida	110
Figure 5.3 High Risk Pertussis Clusters in Florida, 2010-2018	111
Figure 5.4 Choropleth maps of significant predictors of pertussis risk in Florida, 2010-2018.....	119

LIST OF ABBREVIATIONS

ACIP: Advisory Committee on Immunization Practices
ACT: adenylate cyclase toxin
cAMP: cyclic adenosine monophosphate
CDC: Centers for Disease Control and Prevention
CSSS: Circulate Spatial Scan Statistic
CSTE: Council for State and Territorial Epidemiologists
DTP: Diphtheria, tetanus toxoid, whole cell pertussis
IRR: Incidence Risk Ratio
DTaP: Diphtheria-tetanus toxoid-acellular pertussis
DTwP: Diphtheria, tetanus toxoid, whole cell pertussis
ECDC: European Centre for Disease Prevention and Control
EPSS: Enhanced Pertussis Surveillance Program
FDA: Food and Drug Administration
FIM: fimbriae
FHA: Filamentous hemagglutinin adhesin
FSSS: Flexible Spatial Scan Statistic
GIS: Geographic Information Systems
GPI :Global Pertussis Initiative
GVAP: Global Vaccine Action Plan
HepB: Hepatitis B
Hib: *Haemophilus influenzae* type B
HIV: Humane Immunodeficiency Virus
HPV: Human papillomavirus
IHPS: infantile hypertrophic pyloric stenosis
IPV: Inactivated Polio Vaccine
LMIC: Low and Middle Income Countries
LM_{error}: Robust Lefrange Multiple, error
LM_{lag}: Robust Lefrange Multiple, lag
MMR: Measles, mumps, rubella
OR: Odds Ratio
PAHO: Pan American Health Organization
PT: Pertussis toxin
PCR: Polymerase Chain Reaction
PRN: pertactin
RLM: Robust Lagrange Multiplier
RR: Relative Risk
RT-PCR: Real time polymerase chain reaction
Se: Sensitivity
Sp: Specificity
TCT: tracheal cytotoxin
Td: Tetanus and diphtheria
Tdap: Tetanus-diphtheria-acellular pertussis

TMP-SMZ: Trimethoprim-sulfamethoxazole
TTI: Theory of Triadic Influence
VIF: Variance Inflation Factor
WHO: World Health Organization

CHAPTER 1
INTRODUCTION

Pertussis, or whooping cough, is a vaccine-preventable disease that remains a major health concern for infants across the globe. Globally, an estimated 24.1 million people experience pertussis illness and 160,700 children under five years die annually (Centers for Disease Control and Prevention (CDC), 2021; World Health Organization (WHO), 2021). Despite being preventable through vaccination, pertussis remains one of the leading causes of preventable deaths across the globe, as most deaths occur in infants who have not been vaccinated or are under-vaccinated.

The primary risk factor for pertussis is not being vaccinated. Vaccination exemptions, refusals, and hesitancy are critical barriers to improving vaccination coverage and reducing the burden of the disease. Since non-medical exemptions (such as philosophical or religious exemptions) are associated with vaccination hesitancy and refusal, investigation of the factors that contribute to these choices or attitudes is needed to reduce/eliminate local pockets of low vaccination coverage. In addition, investigation of the socioeconomic and demographic predictors of pertussis risk is necessary to help understand the epidemiology of the disease. Utilizing qualitative and quantitative analyses with geographic information system (GIS) technology provides the opportunity to assess attitudes towards vaccination as well as identify geographic disparities and predictors of vaccination exemptions and pertussis risk. The information obtained from such investigations would provide a robust understanding of local pertussis epidemiology that is important in guiding local public health planning and service provision.

The objectives of this project were to: (i) qualitatively investigate general vaccination attitudes and behaviors with specific focus on pertussis vaccination (Chapter 3); (ii) identify geographic disparities in prevalence of vaccination exemptions and socioeconomic and demographic predictors of vaccination exemptions among school-aged children (Chapter 4) (iii) investigate geographic disparities and temporal changes in pertussis risk at the county level (Chapter 5). Qualitative investigation of vaccination attitudes was conducted in East Tennessee and quantitative investigation of disparities and predictors of vaccination exemptions and pertussis risk at the county level were conducted in Florida.

This dissertation is divided into six chapters. The first and second chapters include the introduction and literature review, respectively. Chapters 3, 4, and 5 describe studies addressing the above three objectives. The findings of chapters 3 and 5 have been published in peer reviewed journals while those of chapter 4 have been submitted for publication and are currently under peer review. Finally, Chapter 6 provides a summary of key findings, conclusions and recommendations for future research.

CHAPTER 2

LITERATURE REVIEW

2.1 Etiology

The causative agent for pertussis is *Bordetella pertussis*, an aerobic gram-negative bacteria that produces multiple antigenic products including pertussis toxin (PT), filamentous hemagglutinin (FHA), agglutinogens, adenylate cyclase, pertactin, and tracheal cytotoxin, all of which contribute to the clinical features of pertussis (Centers for Disease Control and Prevention, 2015a). *Bordetella pertussis* is one of ten distinct species belonging to the family *Alcaligenaceae* (Kilgore et al., 2016). However, *B. parapertussis* and *B. holmseii* have been identified as causative agents of similar respiratory infections (Bergfors et al., 1999; Njamkepo et al., 2011; Mooi et al., 2012). An analysis of nasopharyngeal specimens submitted for polymerase chain reaction (PCR) analysis in suspected pertussis cases between 2008 and 2010 from nine US states reported that approximately 14% of the specimens were identified as positive for *B. parapertussis* (Cherry & Seaton, 2012). Although human infections with *B. parapertussis* have been reported, it appears that it produces less severe illness (Heininger et al., 1994) and is more often the causative agent of respiratory illness in domestic farm animals, specifically sheep (Leber, 2014).

2.2 Clinical Signs

The incubation period of pertussis is 7-10 days, with a range of 4-21 days. The clinical course of the disease is characterized by three phases: the catarrhal, paroxysmal, and convalescent (Centers for Disease Control and Prevention, 2015a; Kilgore et al., 2016). The duration of illness varies by the time of each phase of the illness. The catarrhal phase

of the disease lasts 1-2 weeks with patients exhibiting symptoms including runny nose, sneezing, fever, and mild cough that gets progressively severe over the course of the phase. Paroxysmal coughing episodes followed by vomiting and exhaustion are characteristic of the second phase of the disease. The paroxysmal coughing episodes can result in decreased oxygen saturation and cyanosis. Paroxysmal attacks often increase in frequency for 1-2 weeks, stabilize for approximately 2 weeks, and then decrease. Patients have an average of 15 attacks per day. The final phase, the convalescent phase, lasts approximately 2-3 weeks wherein the severe cough gradually resolves (Centers for Disease Control and Prevention, 2015a; Kilgore et al., 2016).

Clinical signs vary by age with the most severe disease occurring in infants (Kilgore et al., 2016). Adolescents and adults usually experience milder disease; pertussis infections in adolescents and adults may be asymptomatic or present as a mild cough or cold-like illness, typically without the characteristic “whooping” cough. Adolescent and adult populations that are considered to be at high risk for severe illness include: women in their third trimester of pregnancy, adults with moderate to severe asthma, and immunocompromised individuals (Centers for Disease Control and Prevention, 2014). Clinical presentation has also been reported to vary by gender, infecting species (*B. pertussis* versus *B. parapertussis*), infectious dose, and time since last vaccination (Cherry, 1999; Mattoo & Cherry, 2005; Cherry & Heininger, 2009; Kilgore et al., 2016; Heininger, 2018).

2.2.1 Clinical Complications

The most common complication of pertussis is secondary bacterial pneumonia which is the cause of most pertussis-related deaths with infants having the highest risk of developing this outcome. Data from 2000 to 2017 show that pneumonia occurred in 13.2% of reported cases, 18.6% of which were in infants less than six months old (Centers for Disease Control and Prevention, 2015a). It has been estimated that, in the United States, approximately half of the infants with pertussis will be hospitalized and 1 in 100 infants will die from the disease. The overall case fatality rate in the United States is 0.8% in infants less than six months old (Hoey, 2003; Kilgore et al., 2016).

Other complications of pertussis include seizures and encephalopathy, likely secondary to hypoxia from the paroxysmal coughing episodes. These neurologic complications are more common in infants. Less serious complications include otitis media, anorexia, and dehydration. The repeated thoracic and abdominal pressure from paroxysmal episodes can also result in pneumothorax, nose bleeds, subdural hematomas, hernias, and rectal prolapse. Adolescent and adult complications include difficulty sleeping, urinary incontinence, pneumonia, rib fracture, syncope, and weight loss (Centers for Disease Control and Prevention, 2015a).

2.3 Pathogenesis

Exposure occurs through aerosol transmission from an infected host to a susceptible one. The attachment phase of pathogenesis begins with the adherence of *B. pertussis* to the

tracheal epithelium and lungs (Kilgore et al., 2016). After initial adherence, the bacteria multiply locally, causing damage to the respiratory tract. As the bacteria colonize lower into the respiratory tract and lungs, they produce necrotizing bronchitis and diffuse alveolar damage (Paddock et al., 2008). In severe cases, these events can lead to pulmonary hypertension, respiratory failure, and death (Paddock et al., 2008; Kilgore et al., 2016).

2.4 Diagnosis and Treatment

Diagnosis of pertussis depends on clinical history and laboratory testing. Laboratory tests include bacterial culture, polymerase chain reaction (PCR), and serological testing.

Bacterial culture is considered the gold standard for diagnosis as it is the most specific (100%) laboratory test for pertussis, although it has lower sensitivity (12-60%) than PCR (93.5% specificity, 97.1% sensitivity) (Loeffelholz et al., 1999; Lee et al., 2018). It is critical that nasopharyngeal specimens are collected as early as possible, as they are more likely to produce accurate test results less than two weeks after the onset of coughing symptoms as viable bacteria are available during this time period, after which the sensitivity decreases and false negative rates increase (Centers for Disease Control and Prevention, 2015a; Centers for Disease Control and Prevention (CDC), 2019a). A study comparing sensitivities (Se) and specificities (Sp) of culture, PCR, and serological tests for pertussis reported that after two weeks of cough onset, both culture and PCR are markedly less sensitive; cultures were reported to have an estimated sensitivity of 9.7%

after two weeks of cough onset compared to 93.2% in the first two weeks after onset of cough while the sensitivity of PCR reduced to 21.4% from 81.7% (Lee et al., 2018).

While bacterial culture is considered the gold standard, PCR is the most commonly used diagnostic test for pertussis as real-time Polymerase Chain Reaction (RT-PCR) allows for rapid diagnosis in less than 24 hours (Tatti et al., 2013; Lee et al., 2018) while bacterial culture requires 7 days. Although PCR is not as specific (93.5%) as culture for pertussis (100%), it does have higher sensitivity (97.1%). An evaluation of the use of PCR for diagnosis of pertussis reported a specificity of 98%, a positive predictive value of 95%, and a negative predictive value of 81% (Lind-brandberg et al., 1998). While limited in their usefulness for prompt diagnosis, serologic assays are routinely used across the globe for surveillance and diagnosis for late stage illness (>4 weeks after onset of cough) when culture and PCR have poor diagnostic utility (May et al., 2012; Vaz-de-Lima et al., 2014; World Health Organization (WHO), 2018). Serologic tests may be used to diagnose late-stage pertussis infections, though there are many barriers to using serology for successful diagnosis. For examples, past infections and recent (within the past year) vaccination against pertussis can be detected by serological testing. Due to the limitations of using serological tests for diagnosis of active pertussis infections, the World Health Organization (WHO) recommends that serological testing be used for diagnosis of pertussis only if it has been more than four weeks since onset of coughing (World Health Organization (WHO), 2018). It also should not be used within a year of pertussis vaccination as IgG antibodies may persist (World Health Organization (WHO), 2018).

There is currently no assay approved by the US Food and Drug Administration (FDA) for use in the United States. Moreover, results of serological testing are not included in the pertussis case definition used by the Council of State and Territorial Epidemiologists (CSTE). However, serological testing may be useful for identification of adolescent and adult cases that may have low clinical suspicion until the cough has persisted for several weeks (World Health Organization (WHO), 2018).

2.4.1 Diagnostic Criteria

The WHO clinical case definition of pertussis is, “a case diagnosed as pertussis by a physician or a person with a cough lasting at least two weeks with one of the following symptoms: paroxysmal cough, inspiratory whooping, or post-tussive vomiting” (Cherry et al., 2012). The definition for a laboratory confirmed case of pertussis, on the other hand, includes isolation of *B. pertussis* through culture, detection by PCR, or positive paired serology (World Health Organization (WHO), 2001).

In the United States, the clinical pertussis case definition by the CSTE is “a cough lasting greater than or equal to two weeks with at least one of the following signs or symptoms (in the absence of a more likely diagnosis): paroxysms of coughing, inspiratory whoop, post-tussive vomiting, or apnea (with or without cyanosis)” (Council of State and Territorial Epidemiologists, 2019). The CSTE laboratory criteria for diagnosis of the disease also includes isolation of *B. pertussis* from a clinical specimen through culture or positive PCR for *B. pertussis*. The CSTE also presents criteria for a probable case, which

include meeting the clinical criteria in absence of a more likely diagnosis or having epidemiologic linkage through known contact with a laboratory confirmed case *and* having a cough of any duration with at least one of the following symptoms: paroxysmal cough, inspiratory whooping, post-tussive vomiting, or apnea (Council of State and Territorial Epidemiologists, 2019).

2.4.2 Treatment

Antimicrobial treatment does not lessen the severity of pertussis illness unless it is started early in the course of infection, specifically prior to the onset of paroxysmal coughing. Three macrolide antibiotics (azithromycin, erythromycin, and clarithromycin) are recommended for treatment of pertussis. The most commonly used antibiotic is azithromycin, because it requires a short (5 day) course of treatment and is preferred amongst the macrolides for infants younger than one month. Caution is indicated for macrolide use in infants less than one month old because of its potential association with infantile hypertrophic pyloric stenosis (IHPS). However, macrolides are still used because the risk of IHPS in infants is lower than the risk of developing severe complications from pertussis infection (Centers for Disease Control and Prevention, 2005). Trimethoprim-sulfamethoxazole (TMP-SMZ) is recommended for infants older than 2 months when macrolides are contraindicated or when antibiotic resistance is suspected. The Centers for Disease Control and Prevention recommend macrolide antibiotic chemoprophylaxis for any high risk contacts and household contacts of a pertussis patient for outbreak control (Sprauer et al., 1992; Centers for Disease Control

and Prevention, 2005). *B. pertussis* resistance to macrolide antibiotics is rare, though some studies have reported that *B. parapertussis* is less susceptible to macrolide antibiotics. Other studies, however, have reported that macrolides (including azithromycin, erythromycin, clarithromycin), TMP-SMZ, and ciprofloxacin are useful when treating *Bordetella parapertussis* infections (Hoppe, Rahimi-Galougahi & Seibert, 1996; Hoppe & Bryskier, 1998; Centers for Disease Control and Prevention, 2005).

2.5 Transmission

Bordetella pertussis has been thought to be transmitted through aerosolized respiratory droplets but it was not until 2012 that this mode of transmission was documented in a controlled study in a baboon challenge trial (Schellekens, Von König & Gardner, 2005; Warfel, Beren & Merkel, 2012). While the mode of transmission has only recently been confirmed through controlled studies, high transmissibility has been consistently documented in epidemiologic studies of outbreaks, in households, and in school settings. Adults and adolescents have been identified as important sources of infection for infants (Wendelboe et al., 2007; Centers for Disease Control and Prevention, 2015b). An international prospective study of laboratory confirmed cases reported that parents accounted for 55% of cases followed by siblings (16%), friends or cousins (10%), and grandparents (6%) (Wendelboe et al., 2007).

Household transmission studies report attack rates ranging from 58% to 100% (Warfel, Beren & Merkel, 2012). The Center for Disease Control and Prevention reports that the

household attack rate is around 80%, though other studies have reported estimates ranging from 64% to 86%, with an average of 76% (Mertsola et al., 1983; Stehr et al., 1998; Warfel, Beren & Merkel, 2012; Centers for Disease Control and Prevention, 2015a). Transmission outside of the household has been reported as lower, though it is more difficult to quantify. Classroom studies from the United States and Canada have reported a range of attack rates from 0% to 36% (de Moissac, Ronald & Pepler, 1994; Brennan et al., 2000; Berger et al., 2010; Warfel, Beren & Merkel, 2012). A similar classroom study from Estonia reported an attack rate of 36% (Torm et al., 2005).

2.6 Epidemiology

2.6.1 Global Burden

Pertussis is endemic worldwide and epidemics typically occur in 3-5 year cycles (Centers for Disease Control and Prevention, 2015b). The global burden of pertussis disease and death is estimated to be upwards of 24 million cases and over 160,000 deaths in children under 5 years old per year (Yeung et al., 2017; Centers for Disease Control and Prevention (CDC), 2021). Pertussis incidence and distribution across the world has significant geographic variability (Gabutti & Rota, 2012; Jackson & Rohani, 2014; Tan et al., 2015). For example, estimates from the WHO report that Africa has the highest case counts of the disease, contributing 33% (7.8 million) of the global cases and 58% (92,500) of global deaths, followed by the southeast Asia which contributes 26% (6.3 million) of the global cases (Yeung et al., 2017). Europe has the lowest estimated cases of disease globally, contributing 1.6 million cases and 900 deaths annually (Yeung et al.,

2017). Pertussis incidence data are more often available in western and developed nations (Crowcroft et al., 2003) and therefore, outbreaks of the disease are frequently reported in North America and Europe. These outbreaks have been reported in Canada, the United States, the Netherlands, Finland, and Germany. Surveillance data from Europe indicate a resurgence of pertussis cases and an increase in the number of outbreaks since the late 1990s (Syed & Bana, 2014).

A review of global pertussis epidemiology between 1990 and 2010 reported that many nations including Japan, Israel, Australia, Belgium, the Czech Republic, Bulgaria, the Netherlands, Hungary, and Poland have had significant increases in disease incidence risks. The range of reported incidence risks in these nations in 2010 was between 0.3 (Hungary) and 153.8 (Australia) cases per 100,000. Other nations have seen significant decreases in incidence risk, including Vietnam, Thailand, China, Ukraine, Denmark, Belarus, Spain, the United Kingdom, Greece, Italy, Saudi Arabia, and Canada. The range of reported incidence in these nations in 2010 was between 0.1 cases per 100,000 in China and 2.3 cases per 100,000 in Ukraine (Jackson & Rohani, 2014).

Data from Low- and Middle-income countries (LMIC) is often sparse. However, a few serologic surveillance studies have been conducted. Pertussis cases have decreased overall in the WHO African region between 2000 and 2013, however, Nigeria reported the second highest number of cases (11,281) worldwide in 2009 (Tan et al., 2015). A recent report of findings and recommendations of the Global Pertussis Initiative (GPI)

highlights the difficulties of understanding the epidemiology of the disease in developing nations (Muloiwa et al., 2018). In South Africa between 2008 and 2011, 67% of laboratory confirmed cases were in children less than three months old and as of 2011 had a reported incidence rate of 5.8 per 1,000 child-months (Nunes et al., 2016; Muloiwa et al., 2018). A hospital study from Niger reported an incidence risk of 8.2 per 1,000 children less than five years old (Jusot et al., 2014). Similar hospital studies have reported incidence risks of 1.3 per 1,000 population in Ethiopia (Alamaw, Kassa & Gelaw, 2017), 114 per 1,000 population over seven years old in Kenya (Muller, Leeuwenburg & Voorhoeve, 1984) , and incidence rate of 2.4 cases per 1,000 infant-months in Zambia (Gill et al., 2016).

A multicenter study in China reported an annual incidence risk of 7,000 per 100,000 population, with age-specific annual incidence risks of 9,100 per 100,000 in children aged 6-8 years and 14,600 per 100,000 in people aged 12-20 years (Wang & Zhu, 2011). This shift in risks to older age groups is consistent with trends identified globally (Mooi et al., 2009; Syed & Bana, 2014). A review of the epidemiology of pertussis in Italy between 1996 and 2009 also reported increases in incidence risk in adolescents (Gabutti & Rota, 2012).

2.6.2 Burden in North America

Pertussis incidence risk in Canada as of 2012 was reported as 13.9 per 100,000 (Smith et al., 2014; Public Health Agency of Canada, 2020). A trend of increasing incidence risk in

older children and adolescent populations has been reported in Canada as well (Smith et al., 2014; Thommes et al., 2020). Pertussis incidence risk varies by province, with the highest risk in 2000 being in British Columbia and Yukon (Smith et al., 2014).

A recent time trend analysis reported that the incidence risk of pertussis in infants less than one year old in Mexico was approximately 12 per 100,000 infants (Guzman-holst et al., 2021). A seroprevalence study conducted in Mexico in 2010 reported that 47.4% of subjects were seropositive for anti-pertussis toxin (anti-PT) antibodies (Conde-Glez et al., 2013). The same study reported that males and children aged one to nine years old had the highest seroprevalence, at 53.4% and 59.3%, respectively (Conde-Glez et al., 2013). Another seroprevalence study of pertussis in adolescents in Mexico City reported the incidence risk to be 5 per 1,000 students (Sandoval et al., 2008).

2.6.2.1 United States

The incidence of pertussis and number of pertussis epidemics have been increasing in the United States for the past thirty years. The cause of the changing epidemiology of pertussis in the US remains unclear, however, it is likely the result of multiple factors, including rising vaccine hesitancy, the change from a whole-cell vaccine to the currently used combination **D**iphtheria and **T**etanus toxoids and **a**cellular **P**ertussis (DTaP) vaccine as well as non-medical or philosophical vaccination exemptions from vaccination requirements for school entry (Clark, 2014).

Infants less than one year old have the highest rates of pertussis in the United States (Wirsing von Konig et al., 2002). Between 2000 and 2006, infants less than one year old accounted for 93% of the pertussis-related mortality and had the highest burden of disease in the country (Tanaka et al., 2003; Vitek et al., 2003; Murphy et al., 2008; Liang et al., 2018). In 2019, the incidence risk of the disease among infants less than 6 months old in the United States was 72.3 per 100,000 and 1.4 per 100,000 in adults over 20 years old (Centers for Disease Control and Prevention (CDC), 2019b). Adolescents accounted for over 30% of cases in epidemics in 2004 and 2005 in the United States (Clark, 2014). A review of pertussis in the United States between 2000 and 2016 reported that cases of pertussis occurred predominantly in white people (88.2%). Ten percent of total cases were hospitalized and 0.1% of total cases lead to death. Infants had the highest incidence (75.3 per 100,000) and accounted for 88.8% of deaths. During the study period, significant increases in risks were reported for all age groups except infants less than one year old and 19-64 years old, consistent with global trends (Skoff, Hadler & Hariri, 2019).

2.6.2.2 Florida

A review of pertussis epidemiology in Florida between 2000 and 2006 reported an increase in incidence risk during the study period from 0.44 to 1.28 per 100,000 population (Schulte et al., 2010). Increases in incidence risk has clearly continued as evidenced by the risk reported in 2019, when the annual incidence risk in children less than one year old was 38.1 per 100,000 and 3.4 per 100,000 in adolescents aged 12-18

years. Higher incidence risk of pertussis was reported in central Florida and in the panhandle. Forty nine percent of cases in 2019 were not fully vaccinated, with 28% never vaccinated, 14% under vaccinated, and 7% too young to be vaccinated (Florida Department of Health, 2019). The trend of increasing incidence risk among adolescent populations was reported during this time as well. Prior to 2001, the most frequently reported cases were in infants less than one year old, but after 2001, adolescents and adults were more frequently affected. The proportion of cases in adolescents and adults increased from 12% to 21% between 2000 and 2006 (Schulte et al., 2010).

2.6.3 Geographic Distribution

Pertussis occurs in all six WHO regions: Africa, the Americas, the Eastern Mediterranean, Europe, Southeast Asia, and the Western Pacific (Tan et al., 2015). Between 2003 and 2007, the European Centre for Disease Prevention and Control (ECDC) reported an overall annual incidence risk of 4.1 per 100,000 population, with the highest incidence risks being reported in Norway, Sweden, and Finland (Gabutti & Rota, 2012; Jackson & Rohani, 2014). The incidence risk of pertussis in central and eastern European nations between 1995 and 2005 was reported to be less than 3 per 100,000 population (Gabutti & Rota, 2012). Another analysis of 54 countries between 1990 and 2010 reported significant geographic variability in incidence risk (Jackson & Rohani, 2014).

Pertussis incidence risk varies greatly at the state or provincial geographic scale, as well. A recent study of the geographic variability within Iran analyzed data from 2009 to 2015 with the intention of modeling future risk. The authors reported significant increases in incidence risks that varied by province and identified several provinces with higher than average risks: Qom, Mazandaran, Tehran, Qazvin, and Zanzan provinces (Moradi & Azim, 2021). Zanzan, Qazvin, and Qom provinces were also identified as provinces with significantly higher pertussis risks in a separate cross-sectional study investigating the spatial and temporal distribution of pertussis in Iran between 2012 and 2018 (Alimohamadi et al., 2020). A recent analysis of the epidemiology of reported pertussis cases in the United States between 2000 and 2016 reported that the West North Central (Iowa, Kansas, Minnesota, Missouri, Nebraska, North Dakota, and South Dakota) and Mountain (Arizona, Colorado, Idaho, Montana, Nevada, New Mexico, Utah, and Wyoming) regions have the highest annual incidence risks at 11.9 and 11.5 per 100,000, respectively. The regions with the lowest annual incidence risks included the South Atlantic (Delaware, Washington, D.C., Florida, Georgia, Maryland, North Carolina, South Carolina, Virginia, and West Virginia) and East South Central (Alabama, Kentucky, Mississippi, and Tennessee), reporting risks of 2.5 and 3.1 per 100,000, respectively (Skoff, Hadler & Hariri, 2019).

Geographic variation at the county level was noted in a review of pertussis cases in Florida between 2000 and 2006, with three counties (Hillsborough, Pinellas, and Duval) around metropolitan areas (Tampa, St. Petersburg, and Jacksonville, respectively)

reporting at least 10% of the total cases each. More than half of total cases were reported in females (53%) and the majority were white non-Hispanic (64%) (Schulte et al., 2010).

2.6.4 Temporal Patterns

Seasonal patterns of pertussis have been inconsistent. A review of worldwide pertussis epidemiology suggests that pertussis has a summer-fall seasonality (Gabutti & Rota, 2012). A hierarchical time-series analysis of pertussis seasonality and periodicity in the Netherlands between 1996 and 2006 showed peak incidence in August each year for all age groups except among adolescents, for whom peaks occurred in November (de Greeff et al., 2009). Seasonality may vary geographically as the peak incidence has been reported to occur in February and September in England and Wales while in Germany the highest incidence was between June and September, similar to Australia (Fine & Clarkson, 1986; Clarke et al., 2013; Hitz, Tewald & Eggers, 2020).

Pertussis incidence risk has been increasing in the United States, as well as globally, over the past three decades. An analysis of the reported cases of pertussis in the United States between 2000 and 2016 revealed a significant increase over time in all age groups except infants less than one year old and adults aged 19-34 years (Skoff, Hadler & Hariri, 2019). The increase in incidence risk over time occurred in adolescents aged 11-18, increasing from 6.1 to 26.1 per 100,000 between 2001 and 2004, and children aged 7-10, increasing from 8.5 to 58.5 per 100,000 (Skoff, Hadler & Hariri, 2019).

A comparative study of 64 countries reported that pertussis epidemics have a cyclic pattern every 2-4.6 years, where the magnitude of the cycles varies geographically (Broutin et al., 2010). An analysis of pertussis transmission dynamics in the United States between 1938 and 2010 identified that pertussis peaks occur in four year cycles (Magpantay & Rohani, 2015). Cyclicity does seem to vary by geographic region. Skoff and colleagues reported that epidemic peak intervals ranged from 2 to 7 years depending on US region (Skoff, Hadler & Hariri, 2019). In the United States, the average national incidence risk in non-peak years from 2000 to 2008 was 3.4 per 100,000 and during peak years between 2009 and 2016 the national average incidence increased to 5.9 per 100,000 (Skoff, Hadler & Hariri, 2019). The overall percent of hospitalizations decreased significantly from 20.6% in 2000 to 6.7% in 2016. However, hospitalizations increased in patients 7-10 years old (6.7%), 30-64 (4.7%), and ≥ 65 year old (2.8%) patients (Skoff, Hadler & Hariri, 2019).

2.6.5 Risk Factors

Lack of vaccination or delayed vaccination is the primary risk factor for pertussis infection (Sealey, Belcher & Preston, 2016). Low birth weight, low gestational age of the infant, and lymphocytosis are risk factors of fatal disease in infants (Wortis et al., 1996; Murray et al., 2013; Winter et al., 2015; Winter, 2016). An analysis of the US Multiple Cause-of-Death and Linked Birth/Infant Death databases between 1999 and 2004 reported that birth weight of less than 2500g, female sex, an Apgar score <8 (assessment of newborn health; score out of possible 10), a mother with <12 years of education, and

Hispanic ethnicity were associated with high risk of pertussis deaths (Haberling et al., 2009). An Australian study reported that predictors of hospitalization with pertussis in infants less than two months old included indigenous ethnicity (RR=1.7, 95% CI=1.03-2.83), and receiving less than two doses of vaccine (RR=4.1, 95% CI=1.37-12.11) (Kolos, Menzies & McIntyre, 2007). A prospective study in Africa reported that HIV exposure or infection, poor nutrition, and maternal *B. pertussis* infection were associated with high risk of pertussis in children (Muloiwa et al., 2020). This study also reported higher risk of pertussis among infants when they had a caregiver with pertussis (Muloiwa et al., 2020).

Risk of fatal disease in infants is reduced through vaccination, early detection and early delivery of treatment (Winter et al., 2015). An analysis of hospitalizations in France reported that having the first dose of vaccine and being seen by a doctor late in the course of the disease were associated with decreased risk of hospitalization in an intensive care unit, assisted ventilation, or death (Briand, Bonmarin & Lévy-Bruhl, 2007). Other studies also report that being under-vaccinated increased risk of hospitalization from pertussis (Clarke et al., 2013). Risk factors for pertussis hospitalization among adults include high body mass index (30+ kg/m²) and asthma (Liu et al., 2012).

Female sex has been reported as a risk factor for pertussis (Jenkinson, 1995; De Serres et al., 2000; Broutin et al., 2004; Paradowska-Stankiewicz & Rudowska, 2015; Huang et al., 2017; Abu-Raya et al., 2020; Alimohamadi et al., 2020). An analysis of an outbreak of

pertussis in Quebec, Canada, reported that the main risk factors for pertussis were being female and working in an educational or healthcare setting (De Serres et al., 2000). The authors proposed that the higher risk may be the result of higher awareness of pertussis among females as well as healthcare workers, which could lead them to seek medical care more readily than men (De Serres et al., 2000). Higher pertussis risk and pertussis complications among females have also been reported in the United Kingdom and Canada (Jenkinson, 1995; Abu-Raya et al., 2020). Lower socio-economic status, particularly living below poverty line, poor access to medical care, no vaccination or under-vaccination, and female sex have been identified as sociodemographic predictors of high pertussis risk (De Serres et al., 2000; Klevens MR, 2001; Paddock et al., 2008; Paradowska-Stankiewicz & Rudowska, 2015). Additionally, higher rates of pertussis cases, hospitalization, and deaths have been reported among infants of Hispanic ethnicity compared to other racial and ethnic groups since 1990 in California (Tanaka et al., 2003; Winter et al., 2012; Winter, 2016).

2.6.6 Reporting

Although pertussis is a reportable disease, it remains markedly under-reported and so the true burden of morbidity and mortality from pertussis is higher than what is reported to public health agencies (Tan et al., 2015). Most studies of pertussis incidence and reemergence are from developed or Western nations and it has been proposed that records from some countries including China, India, Pakistan, Nigeria, South Africa, and Indonesia have greatly under-reported pertussis cases (Mooi et al., 2009; Syed & Bana,

2014; Tan et al., 2015). Differences in health care access, infrastructure, diagnostic tools, case definitions, and clinical training all contribute to under-reporting (Tan et al., 2015).

One source of under-reporting includes clinicians failing to suspect pertussis when presented with non-classical presentation or in age groups where infection is not as severe. For example, a study of under-reporting in the Netherlands reported that 19% of cases are missed if physicians rely on clinical suspicion alone and recommended that routine diagnostics should be considered to address this gap (van den Brink et al., 2014). Cases in adolescent and adult patients may go undetected and unreported as these patients often have milder symptoms. Their diagnosis is often delayed or missed because of low clinical suspicion as well as the lower effectiveness of diagnostic tests in later stages of illness. Culture and PCR tests have lower sensitivity (culture: 9.7%; PCR:21.4%) later in the course of the illness (Syed & Bana, 2014; Centers for Disease Control and Prevention, 2015a). Non-classical clinical presentation as well as asymptomatic infections have been proposed as sources of under-reporting. It has been suggested that asymptomatic infection is approximately five times more common than reported (Ward et al., 2006; Sealey, Belcher & Preston, 2016).

Another source of under-reporting is poor surveillance, although recent collaborations have worked to improve this. The Integrated Disease Surveillance and Response system was created and provided to WHO member states in order to improve surveillance but this point data remains limited in many nations (Lukwago et al., 2013; Tan et al., 2015).

The Latin American Pertussis Project is a collaborative effort between the Sabin Vaccine Institute, the Pan American Health Organization (PAHO), the CDC, and the Latin American Ministries of Health. It has worked to establish access to RT-PCR for case confirmation to improve diagnostic capabilities so that more robust surveillance systems may be developed.

2.7 Control and Prevention

The most critical aspect of control and prevention of pertussis is vaccination. The WHO estimates that approximately 294,000 preventable deaths in children under five occur worldwide as a result of incomplete vaccination (Forsyth et al., 2007). To address global vaccination goals, the Global Vaccine Action Plan (GVAP) set goals for pertussis vaccination coverage during an initiative called “The Decade of Vaccines”. Their goal of 95% global pediatric vaccine series coverage by 2015 was not met and coverage plateaued at 86% globally as of 2018. Interestingly, the global trends in other critical childhood vaccinations increased between 2010 and 2018, with pertussis vaccination being the only one to plateau below the target. The WHO estimates that approximately 20 million infants are not fully immunized. This documented low coverage is worsening in nations impacted by conflict and socioeconomic crises (World Health Organization (WHO), 2020).

Other prevention and control strategies for pertussis include hygienic practices (e.g. hand washing) to prevent the spread through respiratory secretions as well as

chemoprophylaxis with macrolide antibiotics in known exposed cases. A study of the effectiveness of chemoprophylaxis with azithromycin in exposed contacts in Spain between 2012 and 2013 reported that a full course of azithromycin was 43.9% effective (Alvarez et al., 2020). However, a review of the use of erythromycin as chemoprophylaxis in the UK reported that there was no evidence of benefit (Dodhia et al., 2002).

2.7.1 Pertussis Vaccines

There are multiple acellular pertussis vaccines currently available and approved for use in the United States, including **D**iphtheria and **T**etanus toxoids and **a**cellular **P**ertussis (DTaP) vaccine, **T**etanus, **d**iphtheria and **a**cellular **p**ertussis (Tdap) vaccine, DTaP with **H**epatitis **B** and **I**nactivated **P**olio **V**accine (DTaP-HepB-IPV) vaccine, DTaP with **I**nactivated **P**olio **V**accine and ***H**aemophilus **i**nfluenzae type **B*** (DTaP-IPV/Hib) vaccine, and DTaP-IPV-Hib with **H**epatitis **B** (DTaP-IPV-Hib-HepB) vaccine (Centers for Disease Control and Prevention, 2015a). These combination vaccines have been developed with the goal of improving vaccination coverage rates by reducing the number of injections needed per visit and in total. The different versions of these pediatric pertussis vaccines are utilized based on availability, patient preference, and provider assessment (Oliver & Moore, 2020). Acellular pertussis vaccines are the predominant pertussis vaccines used in North America, Europe, Australia, the Middle East, China, Japan, and New Zealand (Chitkara et al., 2020). While whole cell pertussis vaccines are no longer used in the United States due to concerns about adverse side effects,

Diphtheria-**T**etanus-whole cell **P**ertussis (DTwP, DTP) vaccines are still in use in many areas across the globe, including South America, parts of Central America, Russia, Northern Asia, the Middle East, India, South East Asia, Indonesia, and Africa, and are also regularly combined with *Haemophilus influenzae* type B (Hib), Hepatitis B (HepB), and Polio (IPV) (World Health Organization (WHO), 2010; Chitkara et al., 2020).

In the United States, it is recommended that children under the age of seven receive DTaP vaccines and that persons over the age of seven receive **T**etanus-**d**iphtheria (Td) or Tdap vaccines. Pertussis vaccines are administered through intramuscular injection in two series: a childhood and an adult “booster” series. The childhood series (DTaP varieties) are recommended at 2, 4, 6, 15-18 months, and at 4-6 years. Recommendation for timing of doses is dependent on the type of DTaP vaccine used and previous vaccination history. A single dose adult vaccination is recommended at age 11-18 and should continue every ten years unless indicated sooner for tetanus prophylaxis (Centers for Disease Control and Prevention, 2015a; Havers et al., 2020).

2.7.2 Immunity

An immune response to any of the antigenic, biologically active products of *B. pertussis* produces temporary immunity (Centers for Disease Control and Prevention, 2015a; Kilgore et al., 2016). Estimates of period of immunity from natural infection range from 3.5 to 30 years (Wirsing Von König et al., 1995; Versteegh et al., 2002; Wendelboe et al.,

2005; Wearing & Rohani, 2009) and 4-7 years for vaccine-induced immunity (Tindberg, Blennow & Granstrom, 1999; Klein et al., 2012; Kilgore et al., 2016).

Immunity from all pertussis vaccines is provided by a combination of humoral and cellular immunity (Kapil & Merkel, 2019). The pediatric DTaP and adult Tdap vaccines in use seem to provide immunity by inducing a Th-2 CD4-positive cellular immune response, though antibodies are produced through a humoral immune response as well (Higgins et al., 2006; Kilgore et al., 2016).

2.7.3 Vaccine Efficacy

The DTaP vaccine in children who receive all five doses on schedule protects 98% of recipients within a year of the most recent dose and approximately 71% of children five years after their last dose (Centers for Disease Control and Prevention, 2015a). The same levels of protection against pertussis infection is provided by the combination vaccines (DTaP-HepB-IPV, DTaP-IPV/Hib, and DTaP-IPV-Hib-HepB) (Committee on Infectious Diseases, 1999). Tdap has demonstrated 73% protection in adolescents in the first year and 34% of people four years after receiving the vaccine (Centers for Disease Control and Prevention, 2015a).

A systematic review of the safety and efficacy of all pertussis vaccines reported that whole cell vaccines are more effective than two-component acellular vaccines, less effective than three component acellular vaccines, and equally effective as five-

component acellular vaccines against mild pertussis. A comparative efficacy trial in Germany reported that the whole cell DTP provided 93% efficacy compared to the DTaP, which had a reported 83% efficacy (Stehr et al., 1998; Jefferson, Rudin & DiPietrantonj, 2003).

2.7.4 Pertussis Vaccination for Special Populations

Pertussis vaccinations including the childhood series and booster doses are recommended for everyone over the age of 2 months (World Health Organization (WHO), 2021).

Recommendations specific to high-risk or special populations include pregnant women and healthcare workers. The Centers for Disease Control and Prevention (CDC) in conjunction with the Advisory Committee on Immunization Practices (ACIP) recommend that pregnant women receive a dose of the adult booster of Tdap during each pregnancy between gestational weeks 27 and 36. The goal of this recommendation is to provide maternal pertussis antibodies to the newborn as well as to prevent transmission from mother to baby during the birth process (Centers for Disease Control and Prevention (CDC), 2020). It is recommended that healthcare personnel receive a single Tdap dose if they have not received one previously and they have direct patient contact (Centers for Disease Control and Prevention (CDC), 2020).

2.7.5 Vaccination Coverage in the United States

The Advisory Committee on Immunization Practices (ACIP) includes pertussis among the fourteen illnesses they recommend vaccination for by 24 months. There are reports

of increasing percentage of children that are under-vaccinated and pockets of susceptibility occurring where protection is much lower than the national estimates (Hill et al., 2018). Among children born in 2014-2017, 93.3% had received three or more doses of DTaP by 2017 and 80.6% had received four or more doses by age 24 months, a 0.2% decrease from 2016 (Hill et al., 2020). Pertussis vaccination coverage varies across the United States. The states with the lowest coverages (84.0-92.6%) in the 2019-2020 school year include: Oregon, Idaho, Utah, Arizona, Kansas, Minnesota, Indiana, Ohio, New Hampshire, and Alabama (Centers for Disease Control and Prevention, 2020).

While vaccination coverage for pediatric vaccination against pertussis has been declining, receipt of the adult booster (Tdap) has improved, though overall coverage remains low. A recent survey of pertussis vaccination receipt in the United States reported that only 31.2% of adults 19 years and older had received a Tdap vaccine in the ten years prior to 2018 (Lu et al., 2021). White adults had the highest coverage (36.7%), followed by Black adults (20.1%), Hispanic adults (20.5%), and Asian adults (25.6%) (Lu et al., 2021). Between 2010 and 2018, Tdap vaccination coverage increased by 3.2% per year, increasing from 6.9% in 2010 to 31.2% in 2018 (Lu et al., 2021). While these increases are encouraging, they are still well below the levels needed to achieve herd immunity (>95%) necessary to protect vulnerable child and infant populations (Plans-Rubió, 2021).

A separate report on vaccinations in pregnant women reported that Tdap vaccine receipt during pregnancy in 2019-2020 was 56.6%. Tdap vaccination during pregnancy was

lowest in Black women (38.8%) and Hispanic women (35.8%). Tdap receipt is highest among pregnant women in the Midwest (68.8%) and lowest in the South (50.1%) (Razzaghi et al., 2020).

2.7.6 Attitudes Towards Vaccinations

Attitudes towards immunizations are complex and are influenced by social and cultural norms, family and peer attitudes, relationship with the medical community, and personal history of immunization experiences, amongst others (Fiebach & Viscoli, 1991; Weinstein et al., 2007; Kata, 2010; Yaqub et al., 2014). Understanding attitudes towards vaccination and particularly about why people are hesitant or resistant to vaccination is necessary for increasing vaccination coverage, reducing vaccination hesitancy, and ultimately reducing morbidity and mortality from vaccine-preventable diseases such as pertussis. Physician or healthcare professional recommendation of a vaccination has been reported as the most common reason people get vaccinations (Yaqub et al., 2014). However, fear of negative side-effects and vaccine safety have become barriers to vaccine acceptance and adherence to vaccination recommendations (Fredrickson et al., 2004; Kennedy, Basket & Sheedy, 2011; Jana & Osborn, 2013; Yaqub et al., 2014; Saada et al., 2015; Dubé et al., 2015; Hussain et al., 2018). A critical analysis of attitudes towards vaccinations reported that safety concerns were the most frequently cited reasons for hesitancy amongst both the general population as well as healthcare practitioners in the United Kingdom (Yaqub et al., 2014). While concerns about safety and side effects are among the most commonly given reasons for vaccine hesitancy, other factors

including distrust of the medical community (Richmond et al., 2017), governmental vaccination recommendations (Lee et al., 2016), and a growing interest in treating diseases with homeopathic methods contribute to hesitancy towards and rejection of vaccines (Wheelock et al., 2014).

2.7.7 Vaccination Exemptions in the United States

In the United States, state-level policies requiring vaccination of school-going children have been identified as important strategies for improving vaccination coverage (Omer et al., 2009). However, vaccination exemptions can be granted for medical, religious, or philosophical reasons depending on state policy. Currently all states and Washington, D.C. allow exemptions for medical reasons, 48 states allow religious exemptions, and 20 states allow philosophical or personal belief exemptions (National Conference of State Legislatures (NCSL), 2021). Increases in vaccination exemptions have been associated with increased risk of vaccine-preventable diseases like pertussis. Omer et al. (2006) reported that philosophical/personal belief exemptions were associated with increased pertussis incidence (Incidence Risk Ratio [IRR]=1.48) between 2000 and 2004 (Omer et al., 2006). Similarly, Atwell et al.'s geographic analysis of nonmedical exemptions and pertussis risk in California reported that clusters of non-medical exemptions at the census tract level were associated with higher pertussis risk (IRR=1.20) (Atwell et al., 2013).

2.8 Conclusions

Pertussis is a serious disease that has high morbidity and mortality, particularly in infants. As pertussis is preventable through vaccination, strategies to increase vaccination coverage are critical to reducing burden of the disease. Research focusing on barriers to vaccination, including vaccination hesitancy and policies regarding vaccination exemptions is necessary to develop more effective vaccination strategies. Additionally, understanding local socioeconomic and demographic risk factors for pertussis are needed to guide disease control programs.

CHAPTER 3

ATTITUDES OF EAST TENNESSEE RESIDENTS TOWARD GENERAL AND PERTUSSIS VACCINATION: A QUALITATIVE STUDY

3.1 Disclosure

A version of this chapter was published in BMC Public Health. The full citation is:

Corinne B. Tandy, Jennifer M. Jabson Tree. Attitudes of East Tennessee residents towards general and pertussis vaccination: a qualitative study. *BMC Public Health* 21:446 (2021). <https://doi.org/10.1186/s12889-021-10465-w>.

My primary contribution to this paper included data collection, data analysis, interpretation of results, and the preparation of the manuscript. Dr. Jennifer Jabson Tree was involved in the development of study design, research materials, and preparation of the manuscript.

3.2 Abstract

Background. Despite vaccination being one of the safest and most successful public health tools to control infectious diseases, some people still doubt the efficacy and safety of vaccines. In order to address vaccine hesitancy and anti-vaccination sentiments, it is necessary to understand vaccination attitude development and vaccination behaviors. The objective of this project was to qualitatively investigate general vaccination attitudes and behavior with an additional emphasis on pertussis vaccination.

Methods. To identify factors that influence attitudes toward vaccination and behaviors in East Tennessee, eleven one-on-one interviews were conducted with participants recruited through convenience and purposive sampling. Interview protocol and deductive codes were developed using the Triadic Theory of Influence as a theoretical framework. Interview transcripts were analyzed qualitatively and themes were identified through constant comparison of interviews, considering both deductively and inductively coded data.

Results. Most participants (8) held positive attitudes towards vaccination. Participants (8) comfortable with vaccinating themselves or their children said they followed recommendations of doctors. Vaccine hesitant participants' (3) most frequently cited concern was safety concerns about side effects. These participants also reported that they referenced non-academic or professional sources and felt confident about their knowledge of vaccines and diseases. Vaccine hesitant participants had low perception of risk of vaccine-preventable diseases, particularly pertussis. Participants with children

reported that friends and family were influential when deciding to vaccinate their children.

Conclusions. This study identified themes in the attitudes towards vaccination of participants recruited in East Tennessee. We found that risk perception and family and social group attitudes were the primary influences on vaccination decision making. We recommend that future studies include anti-vaccination participants and should further explore the relationship between perception of one's own knowledge and health behaviors.

3.3 Background

The United States and Europe are experiencing a return of vaccine-preventable diseases which has been attributed to anti-vaccine movements (Hotez, 2019). The United States has experienced multiple measles outbreaks among mostly unvaccinated persons. Additionally, in 2018, the United States had one of the worst influenza seasons in decades; it is estimated that 80,000 people died, including many children who were not vaccinated despite ACIP recommendations (Hotez, 2019).

Vaccines are one of the safest and most successful tools to control and prevent infectious diseases (SAGE Working Group, 2015). Despite this public health and medical truth evidenced by extensive empirical literature (Andre et al., 2008), doubt of vaccine efficacy as well as concerns over side effects by the general public has increased and has resulted in considerably lower vaccination coverage (SAGE Working Group, 2015). This rise in

anti-vaccine sentiment has resulted in the World Health Organization (WHO) declaring vaccine hesitancy, defined as “the reluctance or refusal to vaccinate despite the availability of vaccines”, as one of the top ten threats to global health in 2019 (World Health Organization (WHO), 2019). Efforts to understand the contributors to and the context within people make decisions about vaccinations is necessary for understanding how to address vaccine hesitancy.

3.3.1 Vaccination Attitudes

Immunization behavior is complicated and difficult to assess. The most commonly cited reason for receiving vaccines given by those who support vaccination is that they are recommended by healthcare professionals (Yaqub et al., 2014). However, fear of vaccine-induced illness and side-effects has become a major barrier to vaccine acceptance and adherence (Jana & Osborn, 2013; Yaqub et al., 2014; Hussain et al., 2018). There is evidence that safety is a major concern of parents when deciding to vaccinate their children (Fredrickson et al., 2004; Kennedy, Basket & Sheedy, 2011; Saada et al., 2015; Dubé et al., 2015) and has also been identified as the most important consideration when making vaccine decisions (Fredrickson et al., 2004; Kennedy, Basket & Sheedy, 2011; Saada et al., 2015) In fact, according to Yaqub and colleagues’ (2014) critical analysis ‘safety concerns’ were the most frequently cited reason for hesitancy amongst both the general population as well as healthcare practitioners in the United Kingdom.

Recently, public concern regarding adverse outcomes of vaccination such as autism and Guillain-Barré syndrome has risen (Nowak et al., 2013; Hussain et al., 2018; DeStefano, Bodenstein & Offit, 2019). Concern regarding autism as an adverse outcome after vaccination rose after Wakefield et al.'s 1998 study investigating the relationship between the measles, mumps, and rubella (MMR) vaccine and autism and diarrhea (Baker, 2008). Despite a complete lack of confirmation by large epidemiologic studies (Fitzpatrick, 2004), a retraction of the article on the grounds of research misconduct (Eggertson, 2010), and the scientific consensus being that there is no causal relationship between the MMR vaccine and autism, public concern and controversy about the risk for autism after vaccination has persisted. While concerns about safety and side effects, particularly those discussed here, are among the most commonly given reasons for vaccine hesitancy, other factors such as general distrust of the medical community (Richmond et al., 2017), the government agencies recommending the vaccines (Lee et al., 2016), a growing interest in homeopathic treatments and obtaining “natural” immunity through exposure to the disease, contribute to hesitancy towards and rejection of vaccines (Wheelock et al., 2014).

3.3.2 Attitudes towards pertussis-containing vaccines

The majority of literature regarding vaccine hesitancy focuses on **m**easles, **m**umps, and **r**ubella (MMR), **h**uman **p**apillomavirus (HPV), and influenza vaccine attitudes.

However, there are only a few empirical publications that address attitudes and barriers to pertussis vaccination. For example, Miller et al.'s 2011 study investigated the attitudes

about receipt of the pertussis vaccine shortly after the adult booster was introduced and found a general willingness of adults to receive the vaccine but a lack of awareness of its existence or usefulness. Respondents that were not interested in receiving the Tdap vaccine (55%) gave the following reasons for their decisions: low perceived risk of getting the disease, fear of needles, a general distrust of vaccines, and that more information was needed before they could make a decision (Miller et al., 2011). Another study conducted during a large pertussis outbreak in San Diego found that 66% of the unvaccinated respondents cited a lack of awareness of the vaccine or that they didn't know they needed it (McAuliffe et al., 2011).

Lack of awareness or lack of perception of need has been established as a major barrier to pertussis vaccine receipt. We do not know, however, what and if other health behavior, attitudinal, and decision-making factors play a role in people's decision regarding pertussis vaccination. Filling this gap is necessary as the incidence of pertussis is increasing and can cause severe illness in one of our most vulnerable populations—infants.

3.3.3 Approaches to Understanding Health Behaviors and Vaccine Attitudes

Several models of health behavior have at their foundation the assumption that health behavior decisions are made rationally (e.g. Health Belief Model, Theory of Reasoned Behavior). However, we know that people often make health decisions that are not rational or in their best interest. Behavioral economics asserts that people do not act

rationally, make decisions based on, amongst other things, inadequate understanding of possible outcomes, and do not always learn from their mistakes (Rice, 2013). Therefore, it is necessary to consider psychological and sociological influences when seeking to understand health behavior. We sought to explore vaccination attitudes using a theoretical model that does not assume rational decision making in health behavior, specifically the Theory of Triadic Influence (TTI).

Understanding the social and psychological contexts in which people develop their vaccination attitudes and make vaccination decisions is necessary to address vaccine hesitancy (Dubé et al., 2015). The Theory of Triadic Influence (TTI), an integrative, ecological model, assesses the proximal and distal influences on behavior (Flay et al., 2009). Extant literature suggests that individual rights (Kata, 2010), previous medical experiences (Fiebach & Viscoli, 1991), risk assessment (Weinstein et al., 2007), and family and friends' attitudes towards vaccination (Yaqub et al., 2014) influence how people make their vaccine decisions. The TTI includes perceived sense of control, motivation to comply, others' behaviors and attitudes, perceived norms, knowledge, information sources, and institutional interactions as central concepts. We used the TTI as a framework to investigate how these components related to attitudes and behaviors regarding vaccination.

Understanding vaccination attitudes is critical to understanding vaccine hesitancy, which has been identified as a major barrier to vaccination coverage. In fact, a call to action

regarding further understanding of attitudes towards vaccinations and the barriers hesitancy and negative attitudes present has been made by global research and public health communities (Salmon et al., 2015; World Health Organization (WHO), 2019). The objectives of this project were to qualitatively investigate vaccine attitudes and behavior, with emphasis on pertussis vaccination. We sought to explore these phenomena by developing a semi-structured interview protocol based on an integrative, ecological behavioral model.

3.4 Methods

This project was approved by the University of Tennessee Institutional Review Board (UTK IRB-15-02724-XP).

3.4.1 Participants and Recruitment

This study involved two samples. The first sample was drawn from the population of the greater Knoxville, TN area. Participants were recruited using convenience sampling from community events and through distribution of advertisements around the greater metro area. Participants were recruited from sixteen community events that occurred between June 2016 and July 2018. Events included farmer's markets and multicultural events from downtown, northern, and western areas of the greater Knoxville area. Flyers were distributed at these events to recruit people to participate in the study, which led to eleven interviews, all of which took place in-person at a private location of the participants' choosing.

The second sample was purposely recruited using advertisements in a Facebook group for people in the Knoxville area that explicitly identified as anti-vaccination. Between June 2016 and July 2018, a total of ten posts were made in this group to recruit participants. This purposive sampling yielded three responses and zero interviews.

We used snowball sampling with both samples. Participants from both samples and people who expressed interest in the study were asked to aid in recruiting people they knew would be interested in participating. We considered that this approach (Luborsky & Rubinstein, 1995) may increase participant response, particularly from the second, anti-vaccination sample where trust of researchers is already low and positive word-of-mouth amongst the community may increase participation. Physical and/or digital copies of the recruitment flier were offered to all participants or interested persons. Study participation was voluntary. Each participant was assigned a pseudonym to maintain confidentiality. No incentives or remuneration were offered to participants.

3.4.2 Procedures

The participants, prior to the beginning of the interview and after obtaining informed consent, completed a questionnaire developed by the authors for this study to collect demographic information (Appendix A). Demographic variables included: race, age, education level, gender, income, and health insurance status (Abdelal et al., 2009; Brady & Kaplan, 2009).

The questionnaire asked whether or not the participant has ever received any vaccinations, if they have children, if they vaccinate their children, and if they had received a tetanus shot in the last ten years and, if so, what variety it was (e.g. Td (tetanus and diphtheria), Tdap (tetanus, diphtheria, and acellular pertussis), or unknown).

Semi-structured interviews were conducted with participants (n=11). Semi-structured interviews followed a pre-determined interview guide, consisting of questions and topics that would be covered in the interviews but also allow for the interview to cover other topics if and as they arise (Bernard, 2011). Semi-structured interviews provided consistency across interviews while also providing flexibility for unanticipated responses and interviewer follow-up to responses.

Interview topics were developed based on previous literature and theory. Our protocol included questions about past vaccination experiences, vaccine experiences regarding the participants' children (if applicable), comfort level with the medical community, perceived vaccination attitudes of family and social networks, and the participants' knowledge of pertussis (Appendix B). Individual values (Kata, 2010), previous medical experiences (Fiebach & Viscoli, 1991), risk assessment (Weinstein et al., 2007), and family and friends' attitudes towards vaccination (Yaqub et al., 2014) are particularly influential in the development of vaccination attitudes and decisions regarding vaccination.

Our interview guide utilized the Theory of Triadic Influence (TTI) as a framework which includes perceived sense of control, motivation to comply, others' behaviors and attitudes, perceived norms, knowledge, information sources, and institutional interactions as central concepts. Our interview guide was developed to understand the participants' thoughts about these concepts as they relate to vaccination. For example, the TTI suggests that others' attitudes and behaviors influence perceived norms and motivation to comply. Therefore we explicitly asked our participants about their family and friends' attitudes towards vaccination. We also asked follow-up questions regarding concerns expressed by friends or family to understand how participants' attitudes and behaviors were received by family and friends. All interviews were conducted in person and were audio recorded with the consent of the participants. Interviews ranged from 30 to 75 minutes in length. Interviews were transcribed by the first author in word processing software.

3.4.3 Analysis

Qualitative transcripts were entered into NVivo 12 (QSR International, 2018) for data management and analysis. Transcripts were read and reviewed multiple times to achieve immersion. Transcripts were analyzed continuously which allowed for consideration of saturation defined as no new themes emerging from additional transcripts (Fusch & Ness, 2015). Saturation was used as a guide for sample size following the definition by Given (2016)-- that additional data do not lead to any new emergent themes (Given, 2016) . We

knew that saturation had been achieved when, as new data were added, no new themes emerged but instances of existing codes increased instead (Urquhart, 2013).

A hybrid approach of theory-informed and data-driven deductive and inductive coding was used when analyzing interview data. For deductive coding, *a priori* codes were developed based on the Theory of Triadic Influence as well as extant literature (Fereday et al., 2006). The first cycle of coding, deductive coding, included nine codes, seven of which were developed utilizing the Theory of Triadic Influence (Flay, Snyder & Petraitis, 2009) (Table 3.1). These codes were developed to identify anticipated responses based on the Theory of Triadic Influence as well as by prior literature, including academic and media publications about vaccination attitudes and behaviors. Theory driven codes were based on the distal predisposing influences and proximal immediate predictors of the TTI model and indicated with an asterisk in Table 3.1.

Inductive codes (Table 3.1) were identified throughout the coding process as unanticipated themes or responses were observed in the transcripts during reading and coding. Inductive coding was informed by the enumeration of terms and phrases and constant comparison methods (Boyatzis, 1998). These codes described a new theme or expanded on *a priori* deductive codes. A complete list of the codes is presented in Table 3.1.

Table 3.1 Deductive and Inductive Codes Utilized in Qualitative Analysis

Deductive Codes	Comfort with medical community	
	Concerns about vaccines	
	Family beliefs*	
	Social group beliefs*	
	General attitude toward vaccines*	
	Risk perception*	
	Related behaviors*	
	Knowledge of disease*	
	Information sources*	
	Reason for vaccinating children	
	Reason for not vaccinating children	
Inductive Codes	Confidence in Science	
	Comfort	
	Common Sense	
	Evidence	
	Too many vaccines	
	Research	
	Experience resulted in change	
	Making own choices/individual freedoms	
	Trust	
Theme 1 “Attitudes Toward Vaccination” Codes	General Attitude: Evaluation: Positive	“I think that [vaccination] is a good idea”; “I generally think it is a good thing. It is saving lives and protecting people, stopping diseases from being passed around”
	General Attitude: Evaluation: Negative	“The flu shot, that’s just a load of crap”; “I think some vaccines work”
Theme 2: “Reasons for Supporting Vaccination: Codes	Reason for Vaccinating Children	“Because children used to die because we had all these diseases”; “make sure they don’t get these common diseases, protect them in the future”; “everybody gets
Theme 3: “Concerns and Reasons for Vaccine Hesitancy” Codes	Perceived Risk	“I know the flu shot is recommended but I have not caught the flu in a long time”
	Perceived Risk of Getting Pertussis	“now that the kids are older, I don’t see how we could get [pertussis]”

Table 3.2 Continued

	Concerns about Vaccines	“Maybe like allergic reactions”; “I’m more of a skeptic about what the government says is safe”; “The idea that mercury is one of the preservatives”
	Too Many Vaccines	“I think if you pump five vaccines into your child, their poor little bodies can’t deal with it”
Theme 4: “Types of Knowledge and Information Sources” Codes	Knowledge—Information Sources	“Mostly just our doctors”; “Our own research”; “WebMD”
*TTI informed codes		

*Theory of Triadic Influence

Four predominant themes emerged from the data: Attitudes Toward Vaccination, Reasons for Supporting Vaccination, Concerns and Reasons for Vaccine Hesitancy, and Types of Knowledge and Information Sources. These themes were identified through constant comparison of interviews, considering both deductively and inductively coded data.

3.5 Results

3.5.1 Participant Demographic Characteristics

Participant's demographic characteristics are summarized in Table 3.2. The mean age of the participants was 34 years and the majority were female (n=6, 55%). Most participants (n=10, 91%) self-identified as white and non-Hispanic. All participants had completed high school and most had completed college (n=7, 64%). Most of the study participants (n=9, 81%) had health insurance and the majority (n=6, 55%) had children.

3.5.2 Theme 1: Attitudes Towards Vaccination

The majority of respondents (n=8, 73%) held positive attitudes regarding vaccination in general. If participants had had children, they reported that they had their children vaccinated and up-to-date according to current recommendations. Expressions of support ranged from vague positivity to clear and thorough sentiment. For example, Aileen said that they "think [vaccination] is generally a good thing," and Amelia reported that they "think vaccinations are a great thing," and even considered getting vaccinated part of their civil duty.

Table 3.3 Demographic Characteristics of Participants (n=11) in Qualitative Study of Vaccination Attitudes in East Tennessee

Demographic Characteristic	Mean / Percentage
Age (mean)	34
Gender	
Male	45%
Female	55%
Race/Ethnicity	
White	91%
Black	0%
Hispanic	9%
Asian	0%
Education	
High School or Higher	100%
College or Higher	82%
Graduate	
School/Professional	64%
Annual Household Income	
<10,000	9%
10,001-25,000	18%
25,001-40,000	9%
40,001-60,000	27%
60,001-75,000	27%
>75,000	0%
Health Insurance	
Yes	81%
Private	45%
Public	36%
No	9%
Vaccinated?	100%
Tetanus	
Yes	82%
Unsure	18%
Tdap	
Yes	27%
Unsure	73%
Has Children	55%
Children Vaccinated	100%
Children have DTaP	100%

They continued, “I think that in order to keep people healthy that is basically a civil...part of being a citizen is to have your children vaccinated...”

Three (27%) participants had either mixed or negative feelings about at least some aspect of vaccination. Vaguely negative sentiments expressed included Fred indicating that they perceived the necessity of vaccines differently by age group, stating “I think some vaccines work. Obviously, the ones for the polio, the ones you receive as kids. I think those work and flu vaccines are needed maybe for children and the elderly but not as a yearly thing.” Explicitly negative sentiments included participants doubting the efficacy of some vaccine completely; as Fred said, “The flu shot...that’s just a load of crap.”

3.5.3 Theme 2: Reasons for Supporting Vaccination

The most commonly offered explanation when asked why parents chose to vaccinate their children was to prevent their children from getting diseases. “Because we don’t want [them] to get sick,” shared David. Most participants that held positive beliefs about vaccination also cited historical prevalence of many diseases as a contributing factor to their consideration of vaccination. Aileen shared that one of their major considerations when considering vaccination as a general practice was the availability of modern technology and medicine to prevent diseases,

Because children used to die because we had all of these diseases
that killed off I don’t know how many children in their early years

and I think it is incredible that we have these things where you can have one shot and then we don't have to worry that our kids are going to die of all these...I mean it makes me want to cry that I don't have to worry about it. So I just think it is one of those achievements of modern medicine that we can eradicate and prevent some really awful things.

Others shared that they would feel guilty if their child got someone else sick. David expressed concern that they “wouldn't want [their child] to be the vector that got one of [their] immune-suppressed friends sick.”

3.5.4 Theme 3: Concerns and Reasons for Hesitancy

3.5.4.1 Number of Vaccines Administered

Vaccine-hesitant participants cited side effects and the number of vaccines administered at once as the primary reasons for delaying their children's vaccination schedule. Aileen said that they felt like “it's a lot of stuff to put in [their] tiny body in one visit.” Fred and Rosemary also expressed the same concern. “Personally, I think if you pump five vaccines into your child, their poor little bodies can't deal with it,” Rosemary offered. Fred asked “How much can your auto-immune system take? Is that something that you should really be pushing with your children's health?”

3.5.4.2 Denial of Efficacy and Safety Concerns

Some participants reported that a major contributor to their refusal or hesitancy to get vaccines included not trusting vaccine efficacy. “The flu shot...that’s just a load of crap,” shared Fred. “Like, you’re injecting the flu shot into your body. It’s a virus...you can’t kill it. So your chances of getting the flu when you take the shot are higher than when you don’t.” Not only does this reject that the influenza vaccine is effective, it also suggests that the vaccine causes the very illness it is intended to prevent. Fred was the only participant to explicitly state that vaccines were ineffective.

3.5.4.3 Concern Regarding Safety, Side Effects, or Negative Consequences of Vaccination

Most (n=9, 82%) participants expressed minimal concern regarding the safety of vaccines and stated that while they had safety concerns, they were not significant enough to cause them to delay or refuse vaccines for themselves or their children. David reported that when they were getting their first child vaccinated they were concerned that their child would have an allergic reaction or adverse outcome because of the ingredients. “Oh there’s egg albumin, does she have any allergies? Then the idea that mercury is one of the preservatives...,” David recalled from when they had their first child and said that their concern as normal, explaining “Oh, we’re parents! We worry.”

Some participants had major concerns about side effects and other adverse outcomes. When discussing vaccines and particularly the influenza vaccine with Rosemary, they

expressed major concerns about the vaccine's safety and its impact. "The thing that I worry about, really, is these diseases mutating and making a comeback...kind of like how the flu makes a new strand every time they come out with a new vaccine." Fred added,

I don't think [influenza vaccines] are healthy for adults. The RNA mutation is a big concern. And they say that the influenza in the shot is dead but I'm like 'yeah but how do you know that?' That's what I can't seem to get an answer for. A virus can reanimate at any time and you can't guarantee that. Other than that, I think the rest of them are safe.

3.5.4.4. Risk Perception of Getting Pertussis

Most participants conceptualized risk of disease differently for their children than they did for themselves. In fact, many reported that their children were fully vaccinated against pertussis, but they themselves were not sure if they were up to date. Aileen seemed to become aware of this incongruence between their behaviors and self-described attitudes while discussing risk in adult and children. "I feel in some ways that my attitudes are more pro than my actions," they said while discussing them not receiving an influenza vaccine this year while their children did. They went on to say that "maybe I have some kind of division in my mind between children and adults."

All participants perceived themselves at very low risk for contracting pertussis. Fred thought that "now that the kids are older, I don't see how we could get it." Rosemary stated,

“I don’t think we can get it. The doctor says everyone carries it around but from what I’ve been told, the chances of an adult getting it are slimmer than elderly or an infant so we’re not worried.” Other notable responses included “I feel like I’ve heard that it affects a lot of elderly people, maybe? That’s about it,” offered Ted. Nancy thought they didn’t “think [they] could get it, because [they’ve] had the vaccine.” “I hope,” they continued, “And if I did get it, it probably wouldn’t be as serious.”

3.5.5 Theme Four: Knowledge and Information Sources

The majority of participants reported speaking with physicians or another healthcare provider about vaccines when prompted, but otherwise reported either not intentionally seeking information or seeking it on the internet. Participants that reported never having sought information themselves reported that they spoke with their doctor when it was necessary.

Conversations with doctors, pamphlets at physicians’ offices, and internet research were the most cited sources of information about vaccinations. Elizabeth stated that they talked to “my doctor and my kids’ doctors. My husband a little bit. And I’ve heard stories on the news or heard things on the radio, people on TV.” They admitted “Sometimes I google things about ‘what is this...’ but generally I get more information when I go to the doctor and they hand you a sheet that has pros and cons and possible reactions...”.

Amelia reported that they consulted their “primary care physician” and got most of their information at the “the doctor’s office. They give you those pamphlets.” Though the

same participant also said, “I’ll also go online and look up things...I’ll google and then go to maybe Mayo Clinic, or someplace I recognize...Cleveland Clinic, CDC, some place I feel is more credible.”

Participants who perceived their knowledge of pertussis and vaccination as high did not have high knowledge of these topics and referenced popular science writing as their primary information sources. Fred and Rosemary cited vague sources like “medical books from the library” and popular science blogs including “IFL Science” as sources of information.

Many parents that participated in this study (n = 6, 55%) reported that they did not do much research about vaccinations or side effects until faced with the idea of vaccinating their children. Aileen said that they went through “some kind of evolution as far as how I felt about it because I didn’t do a ton of research before I had kids.”

Outside of physicians and the internet, participants reported discussing vaccinations with their family and friends and other social entities. Casey even cited “physicians and coworkers” as the primary two entities with whom they discussed vaccines. David said they talked with their friends and spouse about vaccines. They reported discussing with people in their larger social network that planned to not vaccinate their children. The participant reported that they had conversations about this so that they could try to understand. Fred reported discussing vaccines with their mother who is “a nurse and she

even did a little paper about the chemicals in the vaccines and the things that build up in your system.”

3.6 Discussion

We found that our participants were generally supportive of vaccination, though some expressed hesitation and concerns. Two participants would be best described as “hesitant compliers”, people who have major concerns or objections but ultimately decide to comply with vaccination recommendations. Knowledge about vaccines and disease risk, types of information sources utilized, and the attitudes of friends and family were important considerations in our participants’ vaccine behaviors.

3.6.1 Dunning-Kruger, Knowledge, and Vaccine Hesitancy

An important finding in our study was that participants that perceived their knowledge of pertussis and vaccination as high did not, in fact, have high knowledge of those topics. This cognitive phenomenon is known as the Dunning-Kruger effect (Dunning, 2011). These participants were more likely to cite non-academic, non-peer-reviewed, or vague sources of information when attributing facts. Our participants who demonstrated the most confidence in their knowledge of pertussis and vaccination and their associated risks were also the most likely to be incorrect about pertussis risk factors and vaccination side effects. These participants were also the most vaccine hesitant. Motta and colleagues (2018) propose that vaccine receipt and vaccination policy ideas are influenced by the Dunning-Kruger effect, a cognitive bias that results from an overconfidence and assessment of their

own knowledge regarding a subject as higher than it truly is (Dunning, 2011). Fred is an excellent example of this phenomenon—they offered what they considered factual knowledge about vaccinations and pertussis with confidence (“The flu makes a new strand every time they come out with a new vaccine”), referred to the information sources they utilized and thought them trustworthy (“IFL Science and New Scientist...I try to go with more credible sources.”), and had major concerns about vaccinating their children (“How much can your auto-immune system take? Is that something that you should really be pushing with your children’s health?”). Fred’s overconfidence in their own knowledge of pertussis, vaccination, and biology is not unusual in vaccine-hesitant or vaccine-refusing parents (Motta, Callaghan & Sylvester, 2018).

Participants that shared concerns about side effects or consequences of vaccination but who were not as confident in their knowledge reported following the professional recommendations of the medical community. David admitted that while they “didn’t know much about vaccines,” and “were more on the disbelief side and with the belief that there might be some link to autism,” they ultimately vaccinated their children at their physician’s recommendation. Vaccinating despite being uncertain about health or other outcomes is common in vaccine-hesitant parents (Enkel et al., 2018).

Finally, participants that admitted their lack of knowledge regarding pertussis or vaccination, such as Casey, who at one point in our conversation asked, “is there a vaccine for pertussis?”, were fully vaccinated and did not express any concerns that

would prevent them from getting a vaccine. This spectrum of knowledge confidence and outcomes seen in our participants echoes the hypothesis that overconfidence in one's own knowledge about vaccines is consistent with high hesitancy (Motta, Callaghan & Sylvester, 2018).

3.6.2 Social and Familial Group Influence

Many participants reported that family and friends significantly contributed to their vaccination beliefs and decisions to get a vaccine for themselves, particularly when considering vaccinating their children. Rosemary and Fred mentioned that they got their kids their pertussis vaccine because Fred's mother "encouraged us to do it" and that "some friends that had kids said so." Another participant reported that they had not considered not vaccinating their child until a family member suggested that they should not. At that point, the participant reported becoming concerned about vaccines and their side effects, citing the difficulty of understanding the information about vaccines and deciding what resources could be trusted. Ultimately, they did decide to vaccinate their children, but the participant reported that it caused a great deal of anxiety. These findings are consistent with previous literature that suggests that social networks play a significant role in vaccination decision-making for parents (Brunson, 2013). Acknowledging the impact that family and friends' attitudes have on the development of vaccine attitudes may be useful when developing public health initiatives to address vaccination hesitancy. Unfortunately, we were unable to recruit any participants who reported being wholly anti-vaccination despite purposive recruitment efforts. The purposive methodology used

(posting invitations to participate in an anti-vaccination Facebook group) allowed us to access a large anti-vaccination group in the study area but no members agreed to participate. We expect that this is the result of other cultural and ideological factors shared by this population. It is possible that the anti-vaccination group shares a reluctance to participate with other hard-to-reach populations (Ozawa et al., 2019). Anti-vaccination attitudes are not the mainstream ideology and it is possible that people who hold anti-vaccination beliefs may feel persecuted or unable to safely share their thoughts. Threat of social consequences, specifically concerns over child protective services being called, have been expressed in social media posts as a barrier to participation of anti-vaccine parents.

Our research did not identify any attitudinal barriers to pertussis vaccination specifically. A lack of awareness of the vaccine was common amongst our participants, with 73% of participants unsure if they were vaccinated against pertussis or not. Participants that were aware of their pertussis vaccination status indicated that recent news reports or recently having a baby as the only reason they knew they were vaccinated. Many participants perceived their risk of getting pertussis to be low, assumed they were vaccinated as children and therefore still protected, or assumed that pertussis only made infants sick. These findings are consistent with reports by Miller et al. (2011) and McAuliffe et al. (2011).

3.6.3 Strengths and Limitations

This study has several limitations. We were unable to successfully recruit any explicitly anti-vaccine persons despite purposive recruitment strategies. As a result, those voices are not included in our study. Future research should include the perspective of people who hold anti-vaccination attitudes so that those may be better understood and so that we can develop and test interventions that would assist in improving vaccination rates for these groups. Finally, the study sample for this research was small but saturation was achieved.

Despite this, the authors still feel confident that the major research objective of understanding important factors of vaccine attitudes was addressed. Additionally, the theoretical framework that was utilized to create the interview protocol and initial deductive coding in analysis aided in analyzing interplay of social, cultural and contextual factors of vaccine attitudes and behaviors. To the best of the authors' knowledge, this study is the first to utilize the Theory of Triadic Influence to analyze vaccine attitudes and behavior.

3.7 Conclusions

The results of this study identified themes in the vaccination attitudes of persons in Knoxville, TN. We found that risk perception and family and social group attitudes were the primary influences on vaccination decision making, whether for themselves or on behalf of their children. This is consistent with prior literature that aims at increasing trust

in and improving access to accurate knowledge about vaccination, increasing educational campaigns regarding vaccine-preventable diseases, and highlighting the importance of a physician or medical professional actively addressing vaccine hesitancy in clinical settings. Our results contribute to the knowledge base utilized by public health officials to develop and direct immunization health policies and initiatives, as knowledge of local attitudes and barriers towards vaccination are necessary to guide vaccination coverage improvement and awareness campaigns. We recommend that future studies include anti-vaccination participants and should further explore the relationship between perception of one's own knowledge and health behaviors.

CHAPTER 4

GEOGRAPHIC DISPARITIES AND PREDICTORS OF VACCINATION EXEMPTIONS IN FLORIDA

4.1 Disclosure

A version of this chapter has been submitted for publication in PeerJ. The full citation is:

Corinne B. Tandy, Odoi Agricola. 2021. Geographic Disparities and Predictors of Vaccination Exemptions in Florida. Submitted to *PeerJ*.

My contributions to the paper included study design, data identification, data analysis and interpretation, and preparation of the manuscript. Dr. Agricola Odoi was involved in the development of the research idea, data analysis, interpretation, and preparation of the manuscript.

4.2 Abstract

Background: In the United States, state-level policies requiring vaccination of school-going children constitute a critical strategy for improving vaccination coverage.

However, policies allowing vaccination exemptions have also been implemented and contribute to reductions in vaccination coverage and potential increases in the burden of vaccine-preventable diseases. Understanding the geographic disparities in the distribution of vaccination exemptions and identifying high risk areas is necessary for guiding resource allocation and public health control strategies. This study investigated geographic disparities in vaccination exemptions as well as socioeconomic and demographic predictors of vaccination exemptions in Florida.

Methods: Vaccination exemption data were obtained from the Florida Department of Health's Florida HealthCHARTS web interface. Spatial patterns in geographic distribution of total and non-medical vaccination exemptions were assessed using county-level choropleth maps. Negative binomial models were used to identify significant predictors of county-level risks of both total and non-medical vaccination exemptions.

Results: Total exemptions varied from 0 to 30.2 per 10,000 people. Nine counties had exemption risks in the top two classes (10.4-15.9 and 15.9-30.2 exemptions per 10,000 people). These counties were distributed in five distinct areas: Western Panhandle, central northern area, central, South-eastern coastal area, and the southern coastal border of the state. Non-medical exemptions varied from 0 to 10.4 per 10,000 people. Fifteen counties had exemption risks in the top two classes (3.7-5.6 and 5.6-10.4 exemptions per 10,000 people), and were located in six distinct areas: Western and Central Panhandle,

Northeastern, Central-eastern coastal area, Central-western coastal area, and the South-western coastal border of the state. Predictors of high risk of total vaccination exemptions were high density of primary care providers ($p<0.001$), high median income ($p=0.001$), high percentage of Hispanic population ($p=0.046$), and low percentage of population with a college education ($p=0.013$). A predictor of high risk of non-medical vaccination exemptions was high percentage of White population ($p=0.045$). However, predictors of low risks of non-medical exemptions were high percentages of population: living in rural areas ($p=0.023$), with college education ($p=0.013$), with high school education ($p=0.009$), and with less than high school education ($p<0.001$).

Conclusions: There is evidence of county-level geographic disparities in both total and non-medical vaccination exemption risks in Florida. These disparities are explained by differences in county-level socioeconomic and demographic factors. Study findings are important in guiding resource allocation for health planning aimed at improving vaccination rates and reducing incidence of vaccine-preventable diseases.

4.2 Introduction

The United States and Europe are experiencing an increase in incidence of vaccine-preventable diseases which has been attributed to anti-vaccine movements (Hotez, 2019). As a result, the United States has experienced multiple outbreaks of vaccine-preventable diseases such as measles and pertussis among mostly unvaccinated persons (Sanyaolu et al., 2019). The resurgence of vaccine preventable diseases has been, at least partially, attributed to decreased vaccination coverage.

There is evidence that vaccination coverage varies by geographic region. In the United States, state-level policies requiring vaccination of school-going children have been identified as important strategies for improving vaccination coverage (Omer et al, 2009). On the other hand, policies allowing vaccination exemptions, particularly philosophical and religious exemptions, have been implicated in contributing to reductions in vaccination coverage and potential increases in the burden of vaccine-preventable diseases (Blank, Caplan & Constable, 2013). Unfortunately, vaccination exemption policies are not consistent across the country and vary widely from state to state. Currently, all 50 US states and Washington, DC allow medical exemptions for school-going children while 48 states and Washington, DC allow religious exemptions, and 20 allow philosophical or personal belief exemptions (National Conference of State Legislatures (NCSL), 2021). Across the country, only California, Maine, New York, Mississippi, and West Virginia do not allow these types of non-medical exemptions (Constable, Blank & Caplan, 2014; Williams et al., 2019; National Conference of State

Legislatures (NCSL), 2021). Since states vary widely in the rates of accommodations of religious or philosophical objections to vaccination (Omer et al., 2006, 2008; Atwell et al., 2013; Constable, Blank & Caplan, 2014), the ease of getting vaccination exemptions varies widely. As a result, states having more strict or arduous exemption processes have lower rates of vaccination exemptions (Omer et al., 2006, 2008; Atwell et al., 2013; Constable, Blank & Caplan, 2014). The rigor of the approval process for religious exemptions also varies significantly across the country and often only requires a parent/guardian's signature (Blank, Caplan & Constable, 2013).

The role of vaccine exemptions in the transmission of vaccine-preventable diseases, particularly measles and pertussis, has been of particular interest as incidence rates of vaccine-preventable diseases have increased. Omer et al. (2006) reported that philosophical/personal belief exemptions were associated with increased pertussis incidence (Incidence Risk Ratio [IRR]=1.48) between 2000 and 2004 (Omer et al., 2006). Similarly, Atwell et al.'s geographic analysis of non-medical exemptions and pertussis risk in California reported that clusters of non-medical exemptions at the census tract level were associated with higher pertussis risk (IRR=1.20) (Atwell et al., 2013). An understanding of the predictors of vaccination exemptions may be useful in guiding public health policy decisions and efforts geared towards improving vaccination coverage.

Non-medical reasons for vaccination exemptions may be closely related to population socioeconomic and demographic characteristics that, if identified, would guide efforts to reduce these non-medical exemptions, improve vaccination coverage, and better control vaccine-preventable diseases. Therefore, the objectives of this study were to identify: (a) geographic disparities in prevalence of vaccination exemptions; (b) socioeconomic and demographic predictors of vaccination exemptions among school-going children in Florida.

4.3 Methods

4.3.1 Study Area

This retrospective study was conducted in Florida, which consists of 67 counties, both rural and urban (Figure 4.1). Miami-Dade County is the most urban and most populated with approximately 2.7 million residents while Liberty County is the most rural and least populated county with approximately 8,300 residents (US Census Bureau, 2018). Florida population is comprised of 53.2% non-Hispanic White, 26.4% Hispanic, 3% Asian, and 16.9% Black or African American. The remaining 0.5% of the population are Native Hawaiian or Other Pacific Islander or two or more races (United States Census Bureau). The population is 51.1% female and 48.9% male and has the following age distribution: <5 years (5.3%), 6-18 years (19.7%), 19-64 (54.1%), and 65 years and older (20.9%) (United States Census Bureau).

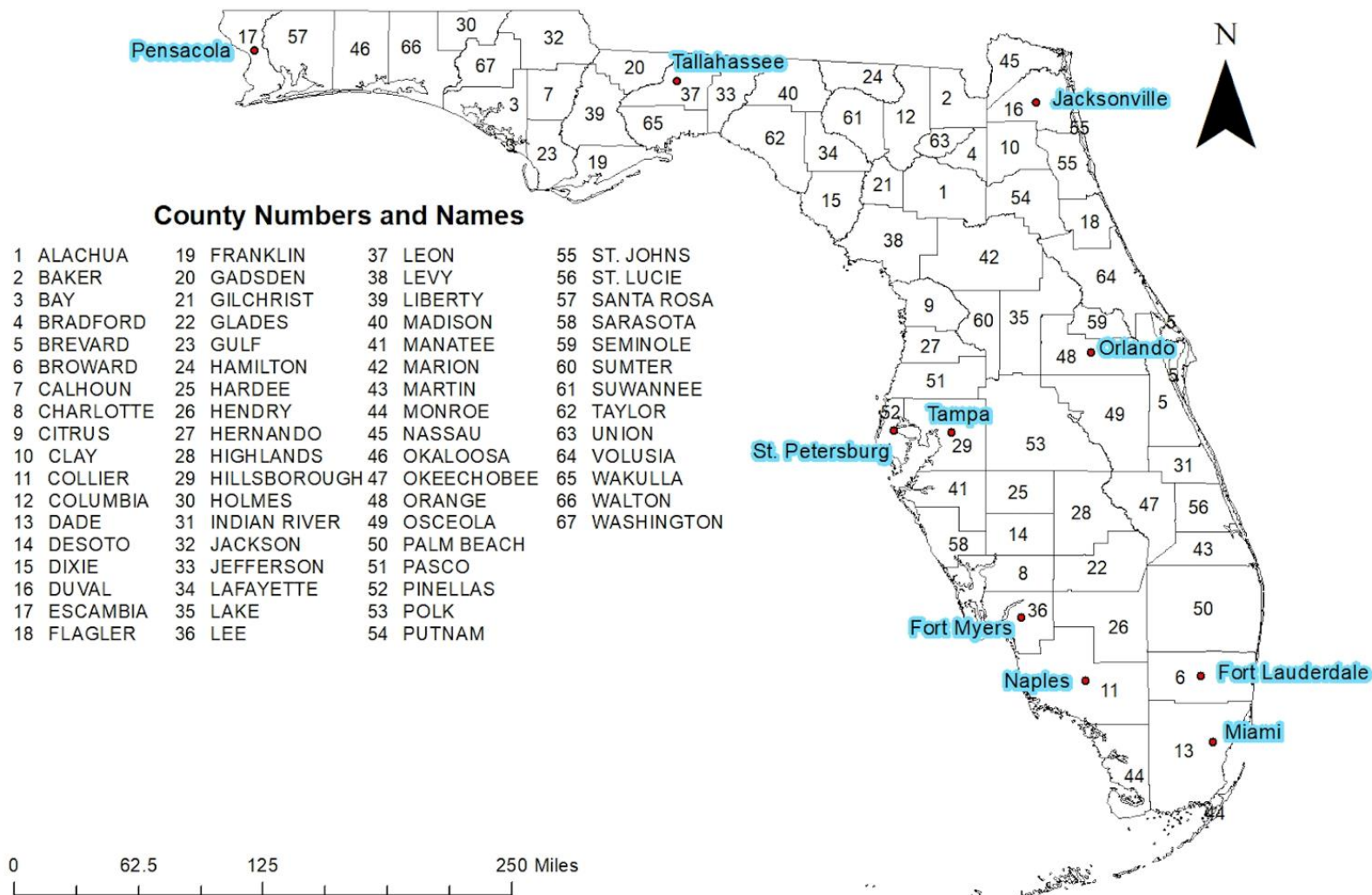


Figure 4.1 Geographic distribution of counties and major cities in Florida

4.3.2 Data Sources and Cartographic Displays

County-level vaccination exemption and population data for 2014 were downloaded from Florida Health CHARTS (Florida Department of Health, 2020). Cartographic boundary files, used for creating maps, were obtained from the United States Census Bureau's TIGER files (United States Census Bureau, 2019) and the State of Florida Geographic Data Portal (Southwest Florida Water Management District, 2019). Vaccination exemptions per 10,000 population at the county level were calculated and displayed in choropleth maps using ArcGIS (ESRI, 2019). Critical intervals of the choropleth maps were determined using Jenk's optimization classification scheme.

4.3.3 Predictors of Total and Non-Medical County-Level Vaccination Exemption Risks

A conceptual model was used to identify potential county-level predictors of vaccination exemption risks (Figure 4.2). Based on the conceptual model, a total of 16 potential predictors were assessed for potential associations with either total and non-medical vaccination exemption risks (Table 4.1). Predictors of total and non-medical county-level vaccine exemption risks were investigated using two sets of Poisson models for the two outcomes, total and non-medical vaccination exemptions. The first step in building the models involved fitting univariable models between each of the potential predictors and each of the outcome variables (number of total and non-medical vaccination exemptions) with population used as the offset (Tables 4.2 and 4.3). Univariable associations were assessed at a liberal p-value of 0.2 and variables with a $p < 0.2$ were considered for further

investigation in step two. To minimize potential multicollinearity, two-way Spearman rank correlation coefficients were computed among variables that had $p < 0.2$. Only one of a pair of highly correlated variables (i.e., with $p > 0.7$) was retained for assessment in step 2 of the modeling process. The decision on the variable to retain was guided by biological and statistical considerations (i.e. biological plausibility as well as strength of association between each of the variables and the outcome). The second step in the modeling process involved fitting multivariable Poisson model using backwards elimination with the predictor variables that had $p < 0.2$ in step 1 but this time using a critical p-value of 0.05. Confounding was assessed by examining whether the removal of a predictor variable resulted in a $>20\%$ change in the coefficients of any other variables in the model (Dohoo, Martin & Stryhn, 2012). Identified confounders were retained in the models regardless of their statistical significance. Overdispersion was assessed by comparing model deviance and degrees of freedom. The Poisson models showed evidence of overdispersion and, therefore, negative binomial regression models were fit to the data using the same process outlined above for the Poisson model. All statistical analyses were performed in STATA version 16.1 (StataCorp, 2019). Overall goodness-of-fit of the final models were assessed using Deviance and Pearson Chi-square goodness-of-fit tests.

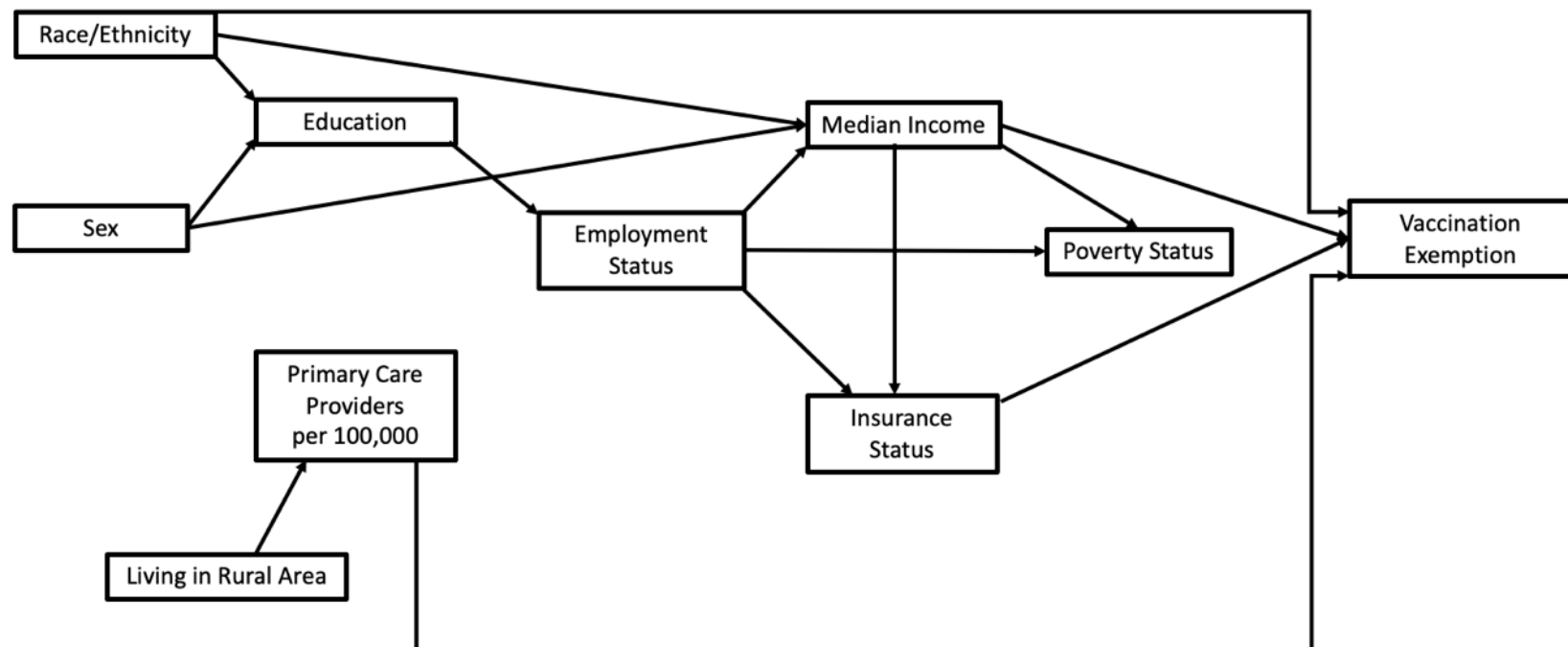


Figure 4.2 Conceptual model showing sociodemographic variables considered as potential predictors of vaccination exemptions in Florida, 2014

Table 4.1 Summary Statistics of potential predictors of vaccination exemptions in Florida, 2014

Variable	Median	1st Quartile	3rd Quartile
Less Than High School Education (%)	14.5	11.5	21.7
High School Education (%)	34.3	28.9	37.5
College Education (%)	18.6	11.4	26.7
White, non-Hispanic (%)	83.0	77.8	87.6
Black, non-Hispanic (%)	13.1	8.6	19.1
Hispanic (%)	8.65	5.29	18.1
Male (%)	49.4	48.6	53.3
Female (%)	50.6	46.7	51.4
Unemployed (%)	6.6	5.8	7.2
Uninsured (%)	18.1	15.6	21.1
Family Below Poverty Line (%)	12.8	10.1	16.9
Individuals Below Poverty Line (%)	17.7	14.3	22.5
Primary Care Providers (per 100,000 pop)	48.0	28.0	68.0
% Living in Rural Area	23.8	8.5	67.5
Rural County (vs Urban)	-	-	-
Scaled Median Income (Divided by \$10,000)	43063	36907	48483

Table 4.2 Results of univariable associations of potential predictors of total vaccination exemptions in Florida, 2014

Variable	Risk Ratio	Lower 95% CI¹	Upper 95% CI¹	p-value
Less Than High School Education (%)	1.036	1.032	1.039	<0.001
High School Education (%)	0.968	0.964	0.972	<0.001
College Education (%)	1.012	1.009	1.015	<0.001
White, non-Hispanic (%)	0.998	0.997	1.000	0.072
Black, non-Hispanic (%)	1.005	1.003	1.007	<0.001
Hispanic (%)	1.014	1.012	1.014	<0.001
Male (%)	0.954	0.941	0.966	<0.001
Female (%)	1.049	1.035	1.062	<0.001
Unemployed (%)	0.958	0.939	0.977	0.282
Uninsured (%)	1.059	1.056	1.062	<0.001
Family Below Poverty Line (%)	1.047	1.042	1.052	<0.001
Individuals Below Poverty Line (%)	1.024	1.019	1.028	<0.001
Primary Care Providers (per 100,000 pop)	1.007	1.006	1.008	<0.001
% Living in Rural Area	0.986	0.984	0.987	<0.001
Rural County (vs Urban)	0.523	0.477	0.573	<0.001
Scaled Median Income (Divided by \$10,000)	1.011	0.983	1.039	0.454

¹95% Confidence Interval

Table 4.3 Results of univariable associations of potential predictors of non-medical vaccination exemptions in Florida, 2014

Variable	Risk Ratio	Lower 95% CI¹	Upper 95% CI¹	p-value
Less Than High School Education (%)	0.956	0.949	0.963	<0.001
High School Education (%)	1.010	1.003	1.017	0.002
College Education (%)	0.994	0.990	0.999	0.007
White, non-Hispanic (%)	1.010	1.007	1.013	<0.001
Black, non-Hispanic (%)	0.986	0.983	0.989	<0.001
Hispanic (%)	0.989	0.988	0.991	<0.001
Male (%)	1.032	1.014	1.049	<0.001
Female (%)	0.969	0.953	0.986	<0.001
Unemployed (%)	0.977	0.945	1.011	0.177
Uninsured (%)	0.969	0.964	0.976	<0.001
Family Below Poverty Line (%)	0.938	0.929	0.947	<0.001
Individuals Below Poverty Line (%)	0.948	0.939	0.955	<0.001
Primary Care Providers (per 100,000 pop)	0.996	0.995	0.998	<0.001
% Living in Rural Area	0.999	0.008	1.001	0.563
Rural County (vs Urban)	0.845	0.745	0.958	0.008
Scaled Median Income (Divided by \$10,000)	1.229	1.173	1.285	<0.001

¹95% Confidence Interval

4.3.4 Ethical Statement

This study was reviewed by the University of Tennessee, Knoxville Institutional Review Board (IRB Number: UTK IRB-20-05957). The board determined that it did not involve human subjects and, therefore, did not require IRB oversight.

4.4 Results

The largest number of exemptions was in Miami-Dade County (4,157) while the lowest was in Lafayette county which had no exemptions during the study period. The highest county-level percentages of exemptions were seen in Seminole (4.8%), Miami-Dade (2.6%), Columbia (2.6%), Palm Beath (2.4%), Sarasota (2.3%) and St. John's (2.0%) counties.

4.4.1 Geographic Patterns of Vaccination Exemptions

Total exemptions varied from 0 to 30.16 per 10,000 persons (Figure 4.3). Nine counties had exemption risks in the top two classes (10.35-15.85 and 15.86-30.16 exemptions per 10,000 persons) (Figure 4.3). These counties were distributed in five distinct areas of the state: Western Panhandle (Santa Rosa County), central northern area (Columbia, Union, and Gilchrist counties, central (Osceola County), South-eastern coastal area (Palm Beach, Martin, and St. Lucie counties), and the southern coastal border of the state (Miami-Dade County) (Figure 4.3). Areas with the lowest exemptions (0-3.48 per 10,000 persons) were primarily seen in the central portion of the state (Hardee, Desoto, Glades, Okeechobee counties), in the central panhandle (Holmes, Washington, Jackson, Gadsden, Liberty, and

Gulf counties), and along north-western coastal and northern body of the state (Jefferson, Taylor, Lafayette, Dixie, Levy, Suwannee, and Hamilton counties). Two other counties in the northern central part of the state also had low risks of total exemptions (Bradford and Sumter counties).

Non-medical exemptions varied from 0 to 10.40 per 10,000 persons (Figure 4.3). Fifteen counties had exemption risks in the top two classes (3.71-5.60 and 5.61-10.40 exemptions per 10,000 persons) (Figure 4.3). These counties were distributed in six distinct areas of the state: Western Panhandle (Santa Rosa and Okaloosa Counties), Central Panhandle (Franklin County), Northeastern (Flagler and Columbia Counties), Central-eastern coastal area (Indian River, Brevard, Martin, and St. Lucie Counties), Central-western coastal area (Pinellas, Hernando, and Citrus Counties), and the South-western coastal border of the state (Monroe, Collier, and Charlotte Counties) (Figure 4.3). Areas with the lowest non-medical exemptions (0-1.20 per 10,000 persons) were primarily seen in the central portion of the state (Hardee, Desoto, Hendry, and Okeechobee Counties), in the central panhandle (Holmes, Washington, Gadsden, Liberty, and Gulf counties), and along the northern gulf and eastern panhandle area (Jefferson, Taylor, Dixie, Levy, Lafayette, Suwannee, and Hamilton counties). One other county in the northern central part of the state also had low medical exemptions (Bradford County).

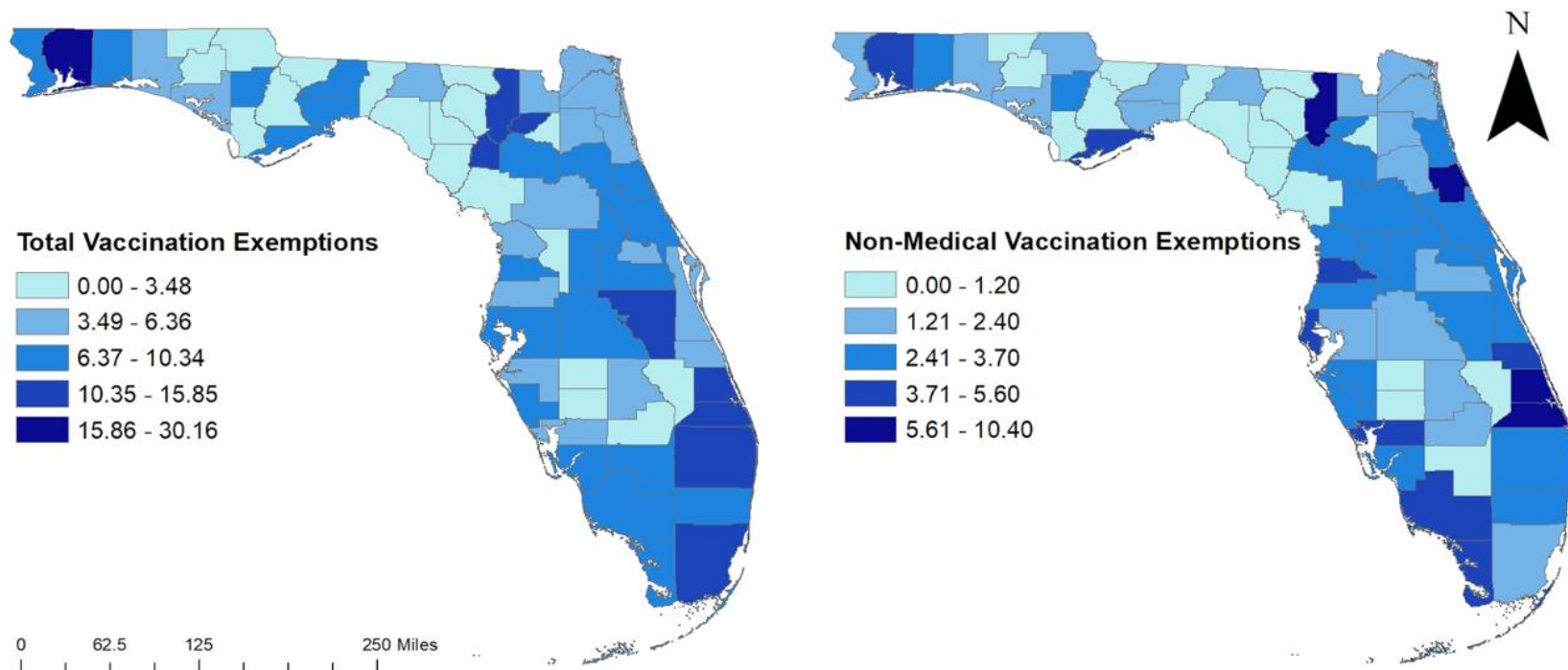


Figure 4.3 Total and non-medical vaccination exemptions per 10,000 persons in Florida, 2014

4.4.2 Predictors of Total Vaccination Exemptions

Since the results of the multivariable Poisson model (Table 4.4) showed evidence of overdispersion (Deviance/df=29.7; Pearson Chi-square/df=34.02; Likelihood Ratio Test of overdispersion parameter=0, $p<0.001$), a negative binomial model was more appropriate for these data and hence the results of investigation of predictors of total vaccination exemptions focuses on the negative binomial model results (Table 4.5).

Based on the results of this model, the risk of total vaccination exemptions tended to be higher in counties with more primary care providers per 10,000 persons, higher median income, higher percentage of Hispanic population, and higher percentage of population with a college education than in counties with lower values of these predictors (Table 4.5). There was no evidence of lack of fit of the total exemptions negative binomial model based on the Deviance goodness-of-fit test ($p=0.169$) although the Pearson goodness-of-fit test indicated that the model may not fit the data very well ($p=0.048$).

4.4.3 Predictors of Non-Medical Vaccination Exemptions

As was the case with the total exemptions model, there was evidence of over-dispersion (Deviance/df=13.98; Pearson Chi-square/df=16.28; Likelihood Ratio Test of over-dispersion parameter=0, $p<0.001$) of the final Poisson model (Table 4.6) used to investigate predictors of non-medical exemptions implying that the Poisson model was not appropriate for the investigation. Therefore, subsequent results presented are based on the final multivariable negative binomial model (Table 4.7). Based on this model, high risks of non-medical exemptions tended to occur in counties with higher percentage of white population. By contrast, lower risks of non-medical exemptions tended to occur in

counties with higher percentages of the population: (a) living in rural areas, (b) with a college education, (b) having high school education, and (c) having less than a high school education. As for the total exemptions model, this model indicated no evidence of lack of fit based on the Deviance goodness-of-fit test ($p=0.153$) although the Pearson goodness-of-fit test indicated that the model did not fit the data well ($p=0.003$).

4.5 Discussion

This study identified county-level geographic disparities and sociodemographic predictors of both total and non-medical vaccination exemptions in Florida in 2014. Study findings provide information that is useful for guiding public health programs and policy.

4.5.1 Geographic Disparities in Vaccination Exemptions

4.5.1.1 Total Exemptions

The identification of county-level geographic disparities of total vaccination exemptions in this study is consistent with findings from other studies that investigated geographic patterns of vaccination exemptions and vaccine-preventable diseases (Omer et al., 2006; Aloe, Kulldorff & Bloom, 2017). An examination of total vaccination exemptions in Florida between 2013 and 2019 reported variations of exemptions at the county level (Muller & Gwynn, 2021). The same study reported that, within Miami-Dade county, vaccination exemptions varied by school during the 2017-2018 school year (Muller & Gwynn, 2021). Another study which investigated clustering of vaccination exemptions by

Table 4.4 Results of the final Poisson model showing significant predictors of total vaccination exemptions in Florida, 2014

Variable	Risk Ratio	Lower 95% CI¹	Upper 95% CI¹	p-value
PCP (per 100,000 pop)	1.002	1.000	1.004	0.046
Rural (%)	0.997	0.995	0.999	0.041
Rural (vs. Urban)	0.421	0.360	0.493	<0.001
White (%)	1.069	1.053	1.084	<0.001
Black (%)	1.063	1.045	1.080	<0.001
Uninsured (%)	1.039	1.032	1.047	<0.001
Male (%)	1.054	1.029	1.080	<0.001
Unemployed (%)	0.873	0.835	0.913	<0.001
Individuals Below Poverty (%)	1.0147	1.003	1.027	0.014
High School Education (%)	0.919	0.901	0.936	<0.001
Scaled Median Income (Divided by \$10,000)	1.101	1.013	1.198	0.023
College Education (%)	0.948	0.937	0.960	<0.001

¹95% Confidence Interval

Table 4.5 Results of the final negative binomial model showing significant predictors of total vaccination exemptions in Florida, 2014

Variable	Risk Ratio	Lower 95% CI¹	Upper 95% CI¹	p-value
PCP (per 100,000 pop) ²	1.017	1.008	1.027	<0.001
Scaled Median Income (Divided by \$10,000)	1.523	1.181	1.964	0.001
Hispanic (%)	1.009	1.00	1.019	0.046
College Education (%)	0.962	0.933	0.992	0.013

¹95% Confidence Interval

²Primary Care Provide

Table 4.6 Results of the final Poisson model showing significant predictors of non-medical vaccination exemptions in Florida, 2014

Variable	Risk Ratio	Lower 95% CI¹	Upper 95% CI¹	p-value
Scaled Median Income (Divided by \$10,000)	1.631	1.444	1.843	<0.001
Rural (%)	0.993	0.989	0.996	<0.001
Rural (vs. Urban)	0.740	0.595	0.920	0.007
White (%)	1.053	1.023	1.084	<0.001
Black (%)	1.050	1.019	1.083	0.002
Hispanic (%)	0.988	0.982	0.993	<0.001
Male (%)	1.082	1.044	1.120	<0.001
Families Below Poverty (%)	0.904	0.861	0.949	<0.001
Individuals Below Poverty (%)	1.119	1.081	1.157	<0.001
Unemployed (%)	1.082	1.018	0.913	0.012
Uninsured (%)	1.082	1.062	1.027	<0.001
Less than High School (%)	0.905	0.885	0.926	<0.001
High School Education (%)	0.918	0.892	0.944	<0.001
College Education (%)	0.897	0.879	0.916	<0.001

¹95% Confidence Interval

Table 4.7 Results of the final negative binomial model showing significant predictors of non-medical vaccination exemptions in Florida, 2014

Variable	Risk Ratio	Lower 95% CI¹	Upper 95% CI¹	p-value
Rural (%)	0 .992	0 .986	0 .999	0.023
White (%)	1.016	1.000	1.032	0.045
College Education (%)	0 .897	0.846	0.951	<0.001
High School Education (%)	0 .898	0 .829	0 .973	0.009
Less than High School (%)	0 .908	0 .874	0 .944	<0.001

¹95% Confidence Interval

exemption type (medical, religious, and philosophical) at the school level in Michigan identified clusters for each exemption type, indicating that geographic differences occur by type of exemption (Mashinini et al., 2020). Medical exemptions clustered in the southeast and northwestern regions of the state, religious exemptions were clustered in the southeastern areas, and philosophical exemptions were clustered in the northeast and southeastern areas. Another analysis of total vaccination exemptions in Ontario reported that total vaccination exemptions varied greatly by geographic area (Wilson et al., 2015). The same study reported that communities with higher vaccination exemption rates tended to report outbreaks of vaccine-preventable diseases in southwestern Ontario, including a 2005 rubella outbreak and a 2011 pertussis outbreak (Wilson et al., 2015). Identifying areas with high exemption rates can not only provide public health professionals with information to guide resource allocation and programming, but can also direct surveillance efforts to known areas of increased risk.

4.5.1.2 Non-Medical Exemptions

The geographic disparities in non-medical vaccination exemptions observed at the county level in this study are consistent with findings from other studies that have reported that non-medical exemptions are often geographically clustered (Omer et al., 2006). This is a cause for concern as clustering of unvaccinated or under-vaccinated individuals increases the risk of outbreaks of vaccine-preventable diseases (Parker et al., 2006). A geospatial study of non-medical vaccine exemptions and pertussis outbreaks in the United States reported that geographic clusters of non-medical exemptions were associated with

pertussis outbreaks in children under five and those aged 10-14 years (Aloe, Kulldorff & Bloom, 2017). Clusters of non-medical exemptions have also been identified in a school-level cluster analysis in Miami-Dade County in the 2017-2018 school year, during which wide variations between schools were reported (Muller & Gwynn, 2021). The study also reported that several schools had less than 90% vaccine compliance (Muller & Gwynn, 2021). As with total vaccination exemptions, identification of geographic clusters of non-medical exemptions can highlight areas for further research, programming, or surveillance.

4.5.2 Predictors of Vaccination Exemptions

4.5.2.1 Total Exemptions

The observed association between higher median income and total vaccination exemptions in this study is inconsistent with reports by Quinn et al. from a study of public attitudes towards vaccination exemptions (Quinn, Jamison & Freimuth, 2020). The authors reported that adults with an annual income greater than \$40,000 favored the idea of required vaccination and had less favorable attitudes towards exemptions (Quinn, Jamison & Freimuth, 2020). However, since Quinn et al.'s study reported individual-level attitudes towards vaccination, direct comparisons cannot be made with the findings of this county-level study and should be interpreted with caution.

The finding that higher percentage of Hispanic population was a predictor of higher risk of total exemptions in this study contrasts reports from an Arizona study which reported

that Hispanic ethnicity was associated with higher vaccination acceptance and coverage (Birnbaum et al., 2013). Although the observed association between density of primary care providers and total vaccination exemptions in this study has not been reported elsewhere, there have been reports of association between density of primary care providers and non-medical exemptions (Walker & Rea, 2016).

4.5.2.2 Non-Medical Exemptions

The association between white race and higher risk of non-medical vaccination exemptions observed in this study is consistent with findings from several other studies that have consistently reported that White race was a predictor of both higher non-medical exemptions and vaccination hesitancy and refusals (Gust et al., 2005, 2008; Kennedy, Brown & Gust, 2005; Kennedy et al., 2011; Birnbaum et al., 2013; Richards et al., 2013; Yang et al., 2016; Morrison, Castro & Meyers, 2020). Yang et al. (2016) explored the relationship between sociodemographic factors and philosophical exemptions in California and reported that personal belief exemptions were higher in areas with higher percentages of white populations (Yang et al., 2016). Similarly, a study of Arizona school systems reported that schools with higher proportions of white students had the highest philosophical/personal belief vaccination exemptions (RR=14.11) (Birnbaum et al., 2013).

Counties with higher percentages of people living in rural areas had lower risk of non-medical vaccination exemptions, a finding that is consistent with those from a study in

California which reported lower exemption rates in rural areas (Yang et al., 2016). However, a longitudinal analysis of community factors associated with non-medical exemptions in California reported that schools in rural areas had higher non-medical exemption rates than those in urban areas (Richards et al., 2013). Since that study investigated exemptions at the census tract level, the differences in findings at different geographic levels implies that future investigations should consider assessing several geographic scales including counties, census tracts or school districts.

The finding that higher percentage of the population having a college degree were associated with lower risk of non-medical vaccination exemptions is consistent with findings from previous studies. For example, Yang et al. reported that higher education level was associated with a lower percentage of exemptions at school and regional geographic levels (Yang et al., 2016). The current study also identified that counties with higher percentage of the population having high school education and less than high school education were associated with lower risk of non-medical vaccination exemptions. These findings highlight the need to investigate the nuances of groups with different education levels, as they may have attitudinal factors including variations in degrees of vaccination hesitancy, support of compulsory vaccination policies, and access. For example, a study by Kennedy and co-workers done at the individual level reported that persons with at least some college education were more likely to be opposed to compulsory vaccination (Kennedy, Brown & Gust, 2005). While Kennedy et al.'s study focused on individual attitudes towards vaccination, it is interesting to see the contrast

between the individual-level findings of their study compared to the county-level associations identified here.

Although this study did not identify higher median income as a predictor of higher non-medical vaccination exemptions, other studies have reported associations between the two. For instance, McNutt et al. reported that affluence was associated with higher rates of non-medical exemptions in California (McNutt et al., 2016). Other studies, including Yang et al.'s analysis of predictors of vaccination exemptions in California, have reported an association between higher median income and higher percentages of students with non-medical exemptions (Yang et al., 2016).

Density of primary care providers was a predictor of higher total vaccination exemptions in this study but was not a significant predictor of non-medical exemptions, which has been reported in other studies. Walker et al.'s study reported that for every 10% increase in density of pediatricians there was an 11% decrease in philosophical/personal belief vaccination exemptions in California (Walker & Rea, 2016). However, they also reported that a 10% increase in the proportion of family medicine practitioners was associated with a 3.5% increase in philosophical/personal belief vaccination exemptions (Walker & Rea, 2016). Future individual-level studies should take these practitioner type differences into consideration in investigations aimed at improving our understanding of the socioeconomic and demographic predictors of vaccination exemptions. Finally, the seemingly counterintuitive observed associations between total/non-medical vaccination

exemptions and both high levels of education and high median income demonstrates the complexity of vaccination attitudes and the different streams of influence that impact them. As mentioned earlier, white race and affluence have been consistently identified as predictors of vaccination hesitancy and vaccination exemptions. These relationships have been explored further in ethnographic work that has identified privileged and powerful identities in society as those that value individual beliefs over guidance offered by scientific and regulatory or other state entities. For example, a qualitative analysis examining privilege and personal belief exemptions examined issues of choice as they relate to concepts of class, gender, and social responsibility (Reich, 2014). The investigators reported that mothers who refused vaccinations for their children for philosophical/ideological reasons related their choice to parenting practices. The authors suggested that members of privileged identities are able to draw upon their access to resources and privilege to make such choices, like adopting parenting practices based in natural living and nutritional regimens for disease prevention (Bryden et al., 2019).

4.5.3 Strengths and Limitations

This study has shown evidence of county-level geographic disparities in vaccination exemptions and that these disparities are influenced, at least in part, by socioeconomic and demographic factors. However, this study is not without limitations. Exemption data did not include students in home-school programs and therefore this study could not account for the home-schooled population. Regardless of this limitation, the findings of

this study are important for guiding and planning public health programs to reduce vaccination exemptions and improve health outcomes for vaccine-preventable diseases.

4.6 Conclusions

There is evidence of county-level geographic disparities in both total and non-medical vaccination exemption risks in Florida. These disparities are explained by differences in county-level socioeconomic and demographic factors. Study findings are important in guiding resource allocation for health planning aimed at improving vaccination rates and reducing incidence of vaccine-preventable diseases.

CHAPTER 5

GEOGRAPHIC DISPARITIES AND SOCIODEMOGRAPHIC PREDICTORS OF PERTUSSIS RISK IN FLORIDA

5.1 Disclosure

A version of this chapter was published in PeerJ. The full citation is:

Tandy CB, Odoi A. 2021. Geographic disparities and socio-demographic predictors of pertussis in Florida. *PeerJ* 9:e11902 <https://doi.org/10.7717/peerj.11902>

My contributions to the paper included study design, data identification, data analysis and interpretation, and preparation of the manuscript. Dr. Agricola Odoi was involved in the development of the research idea, data analysis, interpretation, and preparation of the manuscript.

5.2 Abstract

Background. Pertussis is a toxin-mediated respiratory illness caused by *Bordetella pertussis* that can result in severe complications and death, particularly in infants. Between 2008 and 2011, children less than 3 months old accounted for 83% of the pertussis deaths in the United States. Understanding the geographic disparities in the distribution of pertussis risk and identifying high risk geographic areas is necessary for guiding resource allocation and public health control strategies. Therefore, this study investigated geographic disparities and temporal changes in pertussis risk in Florida from 2010 to 2018. It also investigated socioeconomic and demographic predictors of the identified disparities.

Methods. Pertussis data covering the time period 2010–2018 were obtained from Florida HealthCHARTS web interface. Spatial patterns and temporal changes in geographic distribution of pertussis risk were assessed using county-level choropleth maps for the time periods 2010–2012, 2013–2015, 2016–2018 and 2010–2018. Tango’s flexible spatial scan statistics were used to identify high-risk spatial clusters which were displayed in maps. Ordinary least squares (OLS) regression was used to identify significant predictors of county-level risk. Residuals of the OLS model were assessed for model assumptions including spatial autocorrelation.

Results. County-level pertussis risk varied from 0 to 116.31 cases per 100,000 people during the study period. A total of 11 significant ($p < 0.05$) spatial clusters were identified with risk ratios ranging from 1.5 to 5.8. Geographic distribution remained relatively consistent over time with areas of high risk persisting in the western panhandle,

northeastern coast, and along the western coast. Although county level pertussis risks generally increased from 2010–2012 to 2013–2015, risk tended to be lower during the 2016–2018 time period. Significant predictors of county-level pertussis risk were rurality, percentage of females, and median income. Counties with high pertussis risk tended to be rural ($p = 0.021$), those with high median incomes ($p = 0.039$), and those with high percentages of females ($p < 0.001$).

Conclusion. There is evidence that geographic disparities exist and have persisted over time in Florida. This study highlights the application and importance of Geographic Information Systems (GIS) technology and spatial statistical/epidemiological tools in identifying areas of highest disease risk so as to guide resource allocation to reduce health disparities and improve health for all.

5.3 Introduction

Pertussis is a toxin-mediated respiratory illness caused by *Bordetella pertussis* that can result in severe complications, particularly in infants (<1 year old) (Centers for Disease Control and Prevention (CDC), 2015). Severe complications include pneumonia and neurological complications. Between 2008 and 2011, children less than three months old accounted for 83% of pertussis deaths in the United States. While most of the cases and especially those that are severe occur in infants, people of all ages are susceptible to the disease (Clark, 2014) and adolescents and adults are considered the most important sources of infection for susceptible infants (Centers for Disease Control and Prevention, 2015a; Esposito & Principi, 2016).

Prior to the development of a vaccine, pertussis was a common disease of childhood and infancy. Immunization programs initiated in the 1950s dramatically reduced the incidence of the disease in the United States until the 1980s, when a re-emergence occurred (Chiappini et al., 2013). While the cause(s) of the re-emergence are still unclear (Clark, 2014), the severity of disease in infants makes ensuring high vaccination coverage in all age groups a public health necessity. The rise in cases of the disease among vaccinated adolescents and school-aged (5–9 years) children (Clark, 2014) has resulted in concerns that the efficacy and length of the period of immunity provided by the vaccine may not be as long as initially thought (Jackson & Rohani, 2014; Schwartz et al., 2016; Esposito et al., 2019). Although vaccines have been well-established as one of the safest and most successful tools to control and prevent infectious diseases, doubt of vaccine efficacy as well as concerns over side effects by the general public has increased and has resulted in decreasing vaccination coverage (Hickler et al., 2015). Research indicates that variations in vaccination coverage as well as socioeconomic and demographic factors has contributed to changes in pertussis epidemiology (Omer et al., 2008; Atwell et al., 2013; Clark, 2014). Race and ethnic disparities in vaccination uptake have also been reported with minority populations usually having lower vaccination coverage (Williams et al., 2015). Vaccine hesitancy has been shown to be influenced by demographic, socioeconomic, and attitudinal factors. For instance, socioeconomic status and level of education have been identified as major predictors of vaccination acceptance (Blue & Valley, 2002; Larson et al., 2014). Since pertussis is a vaccine-preventable disease and demographic and socioeconomic factors influence acceptance and uptake of vaccines, it

is important to investigate and identify how these factors impact pertussis vaccination and disease epidemiology.

A number of studies have reported temporal trends in the occurrence of pertussis (Broutin et al., 2010; Bouchez & Guiso, 2015; Cherry, 2015). Epidemics of the disease have been reported to occur approximately every 3-5 years across the globe (Broutin et al., 2010; Clark, 2014; Centers for Disease Control and Prevention, 2015a). This cyclical pattern is seen in the United States as well (Broutin et al., 2010; Bouchez & Guiso, 2015). Bouchez and Guiso have suggested that these cycles result from an increase in susceptible hosts which is influenced by demographic differences and varying vaccine coverage (Bouchez & Guiso, 2015). They also suggest that temporal changes in disease surveillance may play an important role in the observed cyclical nature of pertussis epidemics (Bouchez & Guiso, 2015).

Between 2000 and 2008, the average annual incidence of pertussis in the United States was 3.4 per 100,000 and between 2009 and 2016, the average incidence rose to 5.9 per 100,000 persons (Skoff, Hadler & Hariri, 2019). An investigation of the geographic distribution of pertussis in the United States from 2000 to 2016 (Skoff, Hadler & Hariri, 2019) showed that pertussis incidence was highest in the central mid-west (i.e. Kansas, Nebraska, South Dakota) [11.9 per 100,000 persons] and Rocky Mountain (i.e. Colorado, Montana, Utah) [11.5 per 100,000 persons] areas. Lowest annual average incidence was seen in the south Atlantic (i.e. Delaware, Georgia, North Carolina) [2.5 per 100,000

persons] and southeastern (i.e. Tennessee, Kentucky, Alabama) [3.1 per 100,000 persons] areas.

The state of Florida has seen a rise in pertussis cases and, as of 2010, it was the only vaccine-preventable disease with consistent case increases in that state (Schulte et al., 2010). As of 2019, Florida had a pertussis incidence of 1.85 per 100,000 persons (CDC, 2019). Schulte et al. (2010) reported that the incidence increased from 0.44 to 1.7 per 100,000 persons between 2000 and 2006. (Schulte et al., 2010). This increase in incidence over time mirrors trends reported across the United States. The authors also assessed geographic patterns and identified a cluster of ten counties that reported 66% of the cases seen in the state (Schulte et al., 2010).

Geographic Information System (GIS) technology are increasingly being used in the investigation and control of chronic and infectious diseases. Geographic and spatial epidemiologic methods, ranging from data visualization to sophisticated geographically weighted spatiotemporal models, can be used to understand the degree of geographic variation in the epidemiology of a disease as well as identify areas and populations at high risk of illness. The result of this approach can often lead to more targeted, cost-effective intervention and prevention efforts. Kauh et al. (2017), in their analysis of pertussis testing and incidence in the Netherlands, have suggested that GIS methods and geographically weighted regression be considered for identifying pertussis outbreaks and to better direct disease control strategies. Other studies, such as Aloe et al.'s (Aloe,

Kulldorff & Bloom, 2017) investigation of non-medical vaccination exemptions and pertussis outbreaks in the United States, demonstrate the utility of exploring sociopolitical predictors of disease risk, particularly vaccine-preventable disease, as high rates of exemptions can compromise herd immunity at a small geographic scale that may otherwise go undetected.

Investigating the spatial epidemiology of pertussis is useful in identifying: (a) geographic disparities of the disease and (b) determinants of the identified disparities. Moreover, identification of the predictors of high pertussis risk is important in guiding resource allocation so as to target control programs to reduce disease risk and improve population health (Siegal et al., 1997). Therefore, this study investigated geographic disparities and temporal changes in pertussis risk in Florida from 2010 to 2018. It also investigated and identified socioeconomic and demographic predictors of the identified geographic disparities in pertussis risk in Florida.

5.4 Methods

5.4.1 Study Area

This retrospective study investigated pertussis risk in the state of Florida, which consists of 67 counties, both rural and urban (Figure 5.1). Miami-Dade County is the most urban and most populated with approximately 2.7 million residents, while Liberty County is the most rural and least populated county with approximately 8,300 residents (US Census Bureau, 2018). Florida is 75.4% White, 25% Hispanic, and 16.1% Black or African

American (US Census Bureau, 2018). The state is 51.1% female and 48.9% male and has the following age distribution: <5 years (5.4%), 5-9 years (5.5%), 10-14 years (5.7%), 15-19 years (5.8%), 20-24 years (6.2%), 25-34 years (12.9%), 35-44 years (12.1%), 45-54 years (13.3%), 55-59 years (6.8%), 60-64 years (6.4%), 65-74 years (10.9%), 75-84 years (6.2%), and ≥ 85 years and older (2.6%) (US Census Bureau, 2018).

5.4.2 Data Sources and Variable Selection

Yearly number of cases of pertussis for each county for the time period 2010–2018 were obtained from the Florida Department of Health. Cases were aggregated into three time periods: 2010–2012, 2013–2015, and 2016–2018. The 3-year aggregation was necessary due to the very small numbers of yearly cases observed and the fact that pertussis occurrence has a 3–5 year periodicity (Broutin et al., 2010; Clark, 2014; Bouchez & Guiso, 2015; Centers for Disease Control and Prevention, 2015b). Population data were downloaded from Florida Health CHARTS, a community health assessment tool created by the Florida Department of Health (Florida Department of Health, 2020). Vaccination exemption data were also obtained from the Florida Department of Health. All cartographic boundary files used for creating maps were downloaded from the United States Census Bureau’s TIGER files and the State of Florida Geographic Data Portal (Southwest Florida Water Management District, 2019). County level age-adjusted pertussis risks were computed and presented as number of cases per 100,000 persons. A total of 20 potential predictors of pertussis risk were identified and considered for investigation at the county level: education, sex,

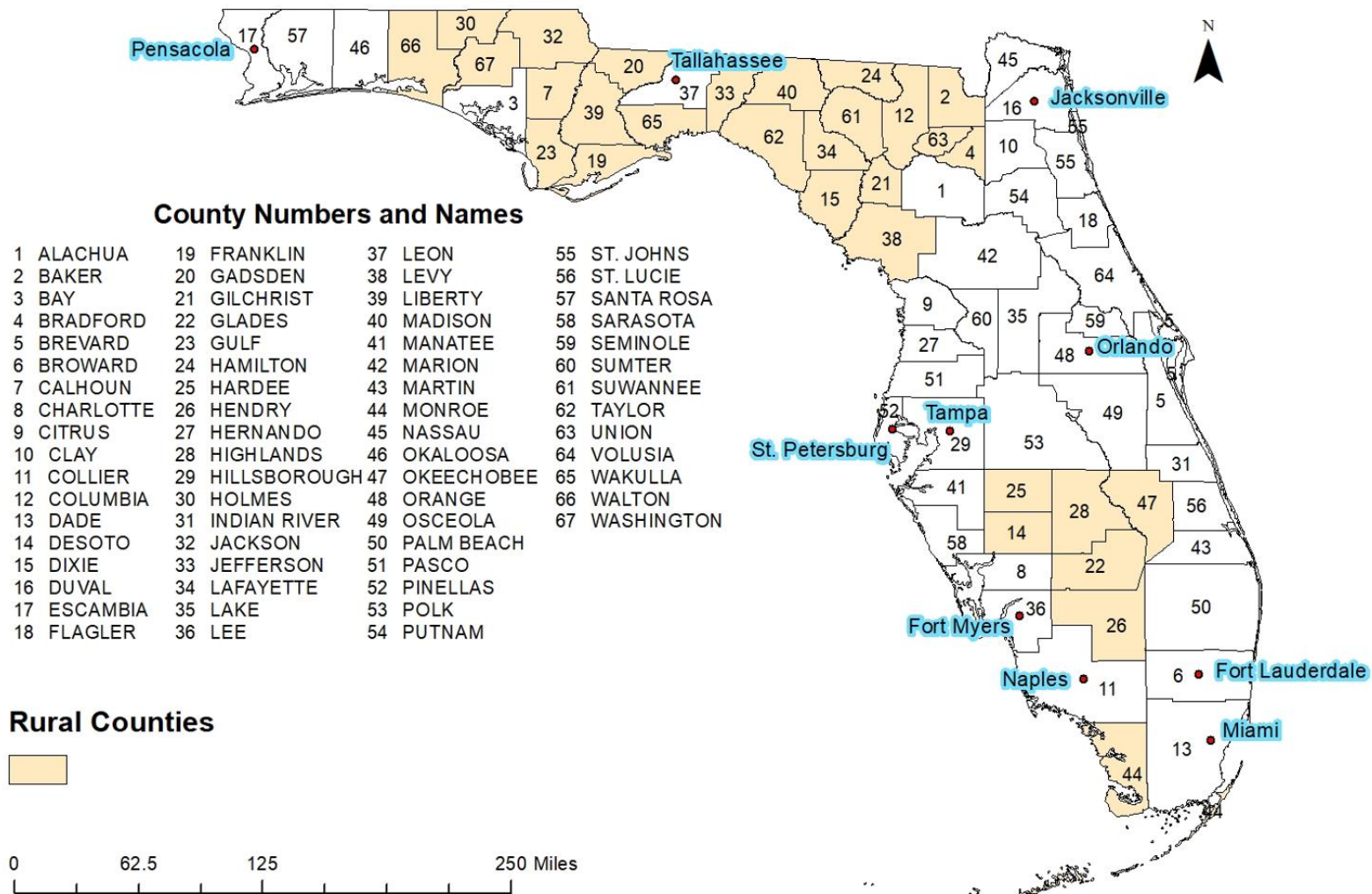


Figure 5.1 Geographic distribution of counties and major cities in Florida

race/ethnicity, income level, employment, health insurance, number of primary care physicians, percentage of population living in rural areas, vaccination coverage, and vaccination exemptions (Table 5.1). Variables were initially identified based on literature as well as biological plausibility of relationships with the outcome.

5.4.3 Investigation of High-Risk Clusters of Pertussis

Tango's flexible spatial scan statistic (FSSS) was used to identify the geographic locations of high-risk clusters of pertussis using FleXScan (Tango & Takahashi, 2013). Since the flexible spatial scanning window detects both circular and irregularly shaped clusters (Jacquez, 2009; Odoi et al., 2019; Lord, Roberson & Odoi, 2021) it is ideal for situations like this one involving investigation of clusters whose shapes are unknown at the outset (Roberson et al., 2019). It has been shown that Tango's flexible scan statistics has good power as well as the ability to detect irregularly shaped clusters more accurately than Kulldorff's spatial scan statistics (Tango & Takahashi, 2005). Poisson probability model was used specifying maximum spatial scanning window size of 15 counties. Clusters were identified based on likelihood ratio tests. For statistical inference, 999 Monte Carlo replications were used, and the null hypothesis of total spatial randomness was rejected if the p-value was ≤ 0.05 .

5.4.4 Investigation of Predictors of County-Level Pertussis Risk

Predictors of county-level pertussis risk were investigated using an ordinary least squares regression model.

Table 5.1 Variables Considered as potential predictors of county-level pertussis risk in Florida

Variable Theme	Specific Variable
Education	% Less than High School
	% Completed High School
	% Completed Bachelor's Degree
Race and Ethnicity	% White, Non-Hispanic
	% Black, Non-Hispanic
	% Hispanic
Sex	% Male
	% Female
Economic	% Unemployed
	% Family Living Below Poverty
	% Individual Living Below Poverty
	Median Income
Vaccination	% Vaccinated in K-12 Population
	% Total Exemptions
	% Temporary Medical Exemptions
	% Permanent Medical Exemptions
	% Religious Exemptions
Healthcare	% Uninsured
	Primary Care Physicians per 100,000 population
Geography	Rural County (Yes or No)
	% Population Living in a Rural Area

The first step in building the model involved fitting univariable models between each of the potential predictors and the outcome variable (log-transformed age-adjusted pertussis risk). Univariable associations were assessed at a liberal p-value of 0.2 and variables with a $p < 0.2$ were considered for further investigation in step two. Two-way correlations were run for variables considered for step 2. Only one of a pair of highly correlated variables (absolute value of $r > 0.7$) were assessed in step two. The decision regarding which of a pair of highly correlated variables to include in step two was based on biological and statistical considerations. The second step involved fitting multivariable ordinary least squares model using manual backwards elimination with the predictor variables identified for inclusion in step one. During this step statistical significance was assessed using $p \leq 0.05$. Confounding was investigated by assessing whether the removal of a variable resulted in a $> 20\%$ change in the coefficients of any other variables in the model (Dohoo, Martin & Stryhn, 2012). If a confounder was identified, it was forced into the model regardless of its statistical relationship with the outcome variable. Robust Lagrange Multiplier (RLM) tests, implemented in GeoDa, were used to assess for spatial autocorrelation in the residuals using queen spatial weight (Anselin, 2019). Multicollinearity was assessed using both Variance Inflation Factor (VIF) in SPSS (IBM, 2017) and the Multicollinearity Condition Number in GeoDa (Anselin, Syabri & Kho, 2006).

5.4.5 Cartographic Displays

All geographic information system (GIS) manipulations and cartographic displays were performed in ArcGIS (Environmental Systems Research Institute, 2019). Statistically significant county-level predictors of pertussis risks, age-adjusted pertussis risks, and significant clusters of pertussis risk were displayed in maps. The choropleth maps of pertussis risk and of high-risk clusters were generated for the full study period and three-year time periods: 2010-2012, 2013-2015, and 2016-2018. Critical intervals in maps of the determinants of pertussis risk as well as maps of pertussis risk were determined using Jenk's optimization classification scheme for the full study period (2010-2018) and were applied to pertussis risk maps of other time periods for consistency.

5.4.6 Ethical Statement

This study was assessed by the University of Tennessee Institutional Review Board (IRB Number: UTK IRB-20-05957) which determined that it did not involve human subjects as defined in 45 CFR 46.102 (e) (1), since it did not involve use of identifiable private information. Thus, the IRB determined that neither IRB review, nor certification of exemption from review, was required.

5.5 Results

5.5.1 Geographic and Temporal Distribution of Pertussis Risk

County-level pertussis risk varied from 0 to 116.31 cases per 100,000 persons during the study period (2010-2018) (Figure 5.2A). Four regions with high risks of pertussis were

evident: the Pensacola metropolitan area in the western panhandle (Escambia, Santa Rosa, and Washington counties), the Tampa Bay area (Hillsborough, Pasco, and Polk counties), Jacksonville metropolitan area (Nassau, Duval, Flagler, Putnam, and St. Johns counties), and the Cape Coral-Fort Meyers-Naples Area (Collier, Hendry, and Lee counties) (Figures 5.1 and 5.2A). High risks were also observed in Columbia and Suwannee counties. Areas of low risk, on the other hand, were evident around Glades, Union, Liberty, and Calhoun Counties (Figures 5.1 and 5.2A).

The pattern of geographic distribution of pertussis risk was slightly different for the time period 2010-2012, compared to the whole time period (2010-2018), with high risks being observed in Santa Rosa county in the western Panhandle, around the northern gulf coast in Taylor, Lafayette, and Levy counties, in the northwestern region around Jacksonville in Nassau, Baker, Duval, and Putnam counties, and around the Tampa Bay area in Pasco, Hillsborough, and Polk counties (Figures 5.1 and 5.2B). Though the general spatial patterns of pertussis risk for the time period 2013-2015 were similar to those of 2010-2012, a number of counties (such as Columbia, Suwannee, Washington, etc.) had higher overall risks in 2013-2015 than 2010-2012 (Figures 5.1 and 5.2B-C). In addition, high risks were identified in Gilchrist County, around the Tampa Bay area in Pasco, Hillsborough, Polk, Highlands, DeSoto, Manatee, and Sarasota counties, and around the Cape Coral area in Lee and Collier counties. Although county level pertussis risks generally increased from 2010-2012 to 2013-2015, risk tended to be lower during the

2016-2018 time period compared to the 2013-2015 period (Figures 5.2C-D). Highest risks were observed in Nassau County followed by Hillsborough and Hendry counties.

5.5.2 Clusters of High Pertussis Risk

A total of 11 clusters were identified for the analysis that included data for the whole study period (2010-2018) (Table 5.2 and Figure 5.3A). The primary cluster during this time period included one county (Hillsborough) and had a risk ratio (RR) of 2.1. The risk of pertussis in this cluster was 43.1 cases per 100,000 and it had a total of 556 observed cases of pertussis when only 264 cases were expected. Based on geographic size, the largest cluster was Cluster 3 which included two counties (Polk and Pasco). The risk of pertussis in this cluster was 1.51 times higher than the risk outside the cluster. A total of 340 pertussis cases were observed in this cluster when only 223 cases were expected. It is worth mentioning that the cluster with the highest RR (Cluster 2) included only one county (Columbia) and had an RR of 5.7, a risk of 116.3 cases per 100,000 persons, 79 observed cases while only 13 were expected. Counties in the Tampa Bay area (Hillsborough, Polk, and Pasco counties) were consistently included in high-risk clusters throughout the study period (Figure 5.3A).

Seven clusters, having RRs ranging from 1.6 (in cluster 7) to 3.4 (in cluster 4), were identified during the time period 2010-2012 (Table 5.3 and Figure 5.3B). The time period 2013-2015, on the other hand, had a total of 11 clusters with RRs ranging from 1.4 (in cluster 9) to 12.4 (in the primary cluster) (Table 5.4 and Figure 5.3C).

The latter was located in Columbia County and had the highest RR across all time periods. Collier county, in the Naples metropolitan area, and Nassau county, in the greater Jacksonville area, were also identified as parts of high-risk clusters during the time periods 2013-2015 (Figure 5.3C) and 2016-2018 (Figure 5.3D). The smallest number of clusters were identified in the 2016-2018 time period (Table 5.5 and Figure 5.3D). This was also the only time period during which a multi-county high pertussis risk cluster (RR=1.9; p=0.002) was identified.

5.5.3 Predictors of Pertussis Risk

Results of descriptive analysis of the potential predictors and assessment of their associations with pertussis risk are presented in Table 5.6. The following variables were assessed in the multivariable model: rural status, education variables, percent female, primary care providers per 100,000 persons, median income, percent vaccinated, percent with medical exemption, and percent with religious exemptions. Only three of these variables were significant in the final model: rurality, county level median income and percentage of females in the county. County level pertussis risks tended to be high in rural counties (p=0.021), those with higher median income (p=0.039), and those with higher percentages of females (p<0.001). It is worth pointing out that % female was a distorter variable for the association between rurality and risk of pertussis with the coefficient of the rural variable switching from a negative association with log-risk of

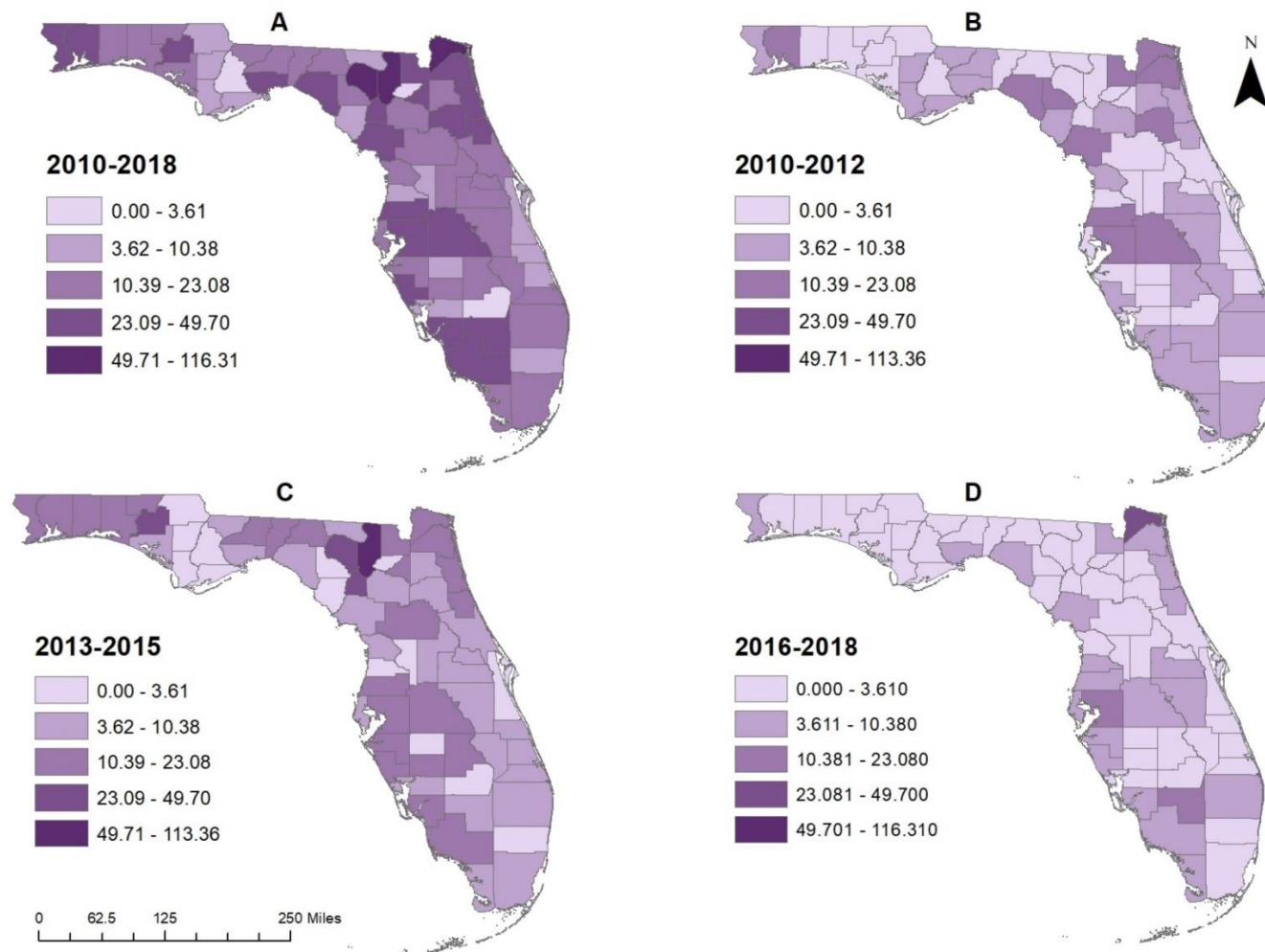


Figure 5.2 Choropleth Maps Showing Spatial Distribution of Pertussis Risks in Florida, 2010-2018

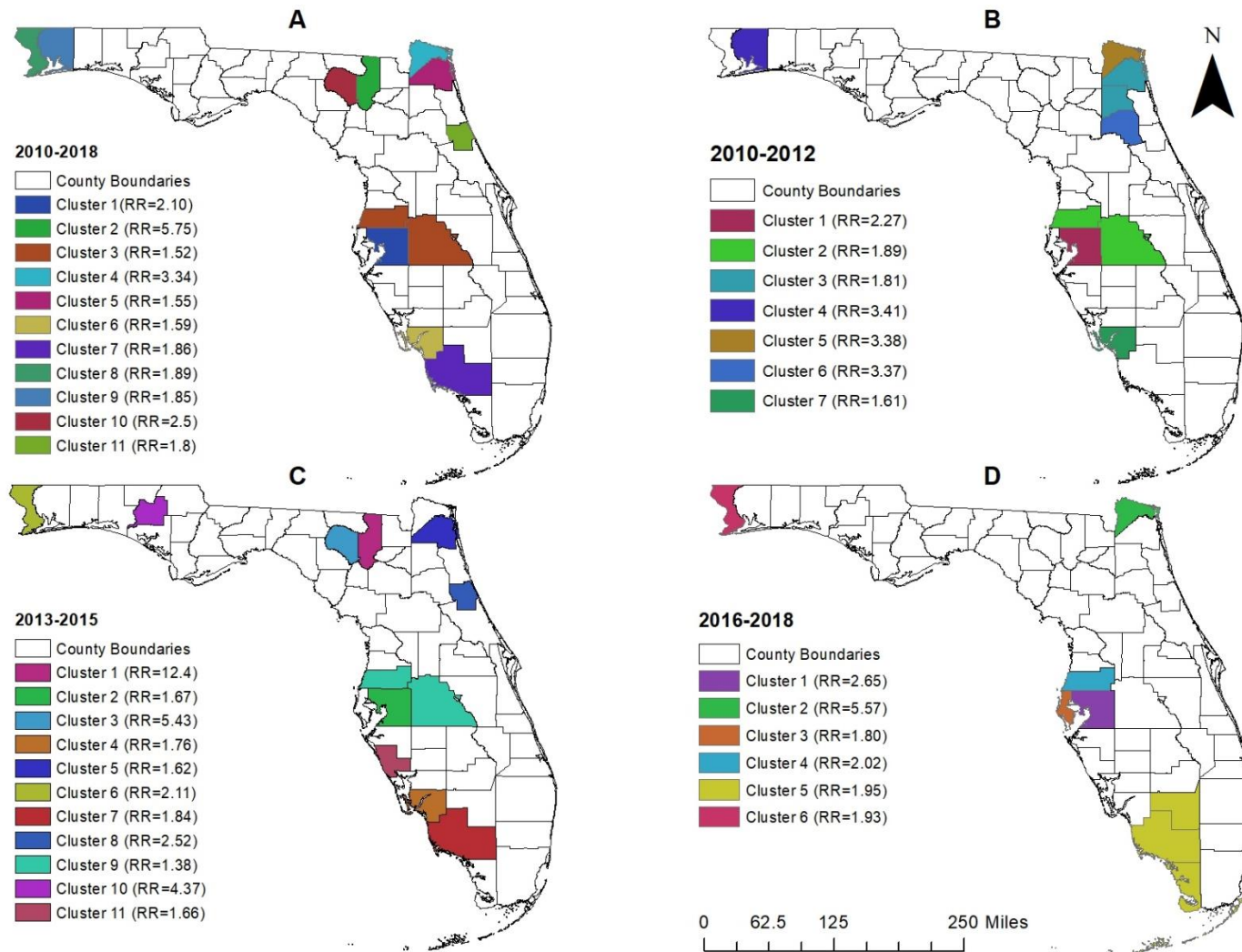


Figure 5.3 High Risk Pertussis Clusters in Florida, 2010-2018

Table 5.2 Significant geographic clusters of pertussis risk in Florida, 2010-2018

Cluster	Population	Observed Number of Cases	Expected Number of Cases	Risk per 100,000 people	Risk Ratio	p-value
1	1,307,906	556	264.45	43.10	2.10	0.001
2	67,924	79	13.7	116.3	5.75	0.001
3	1,106,654	340	223.7	32.28	1.52	0.001
4	75,569	51	15.2	67.48	3.34	0.001
5	893,858	281	180.7	31.88	1.55	0.001
6	656,466	212	132.7	32.44	1.59	0.001
7	338,270	127	68.3	37.54	1.86	0.001
8	304,654	117	61.6	38.40	1.89	0.001
9	160,475	60	32.4	38.01	1.85	0.001
10	44,263	22	8.9	49.70	2.46	0.01
11	99,646	37	20.1	37.13	1.83	0.029

pertussis, in the univariable model, to a positive association in the final model when percent females is added to the model. There was no evidence of multicollinearity as all the VIFs were <4 and the multicollinearity condition number was <20 (Table 5.7). Additionally, there was no evidence of non-normality of the residuals (Jarque-Bera test $p=0.678$). Both the Robust Lagrange Multiplier tests for lag (LM_{lag} $p=0.585$) and error (LM_{error} $p=0.472$) showed no evidence spatial dependence of the residuals.

5.5.4 Geographic Distribution of Significant Predictors of Pertussis Risk

Geographic distributions of the three significant predictors of county-level pertussis risk are shown in Figure 5.4. Unsurprisingly, the general distribution of these predictors is similar to the geographic distribution of pertussis risk in Florida between 2010 and 2018 (Figures 5.2 and 5.4A). Santa Rosa and Okaloosa counties in the western panhandle, Nassau, St. John's, and Clay counties in the Northwestern coastal area, Hillsborough, Manatee, and Sarasota counties in the Tampa Bay area, and Collier and Monroe counties in the Fort Myers area all had relatively high median incomes (Figure 5.4A). These counties were also consistently identified as counties with high pertussis risk and in high risk clusters (Figures 5.2 and 5.3)

Counties with higher female population densities are evident in the central panhandle (Gadsden and Hernando counties) and along the eastern and western coastal borders. Counties with greater than 52% of the population being female include: Gadsden, Leon, Sarasota, Hernando, and Pinellas counties (Figures 5.1 and 5.4B). All of these counties

Table 5.3 Significant geographic clusters of pertussis risk in Florida, 2010-2012

Cluster	Population	Observed Number of Cases	Expected Number of Cases	Risk per 100,000 people	Risk Ratio	p-value
1	1,242,491	181	79.69	14.57	2.27	0.001
2	1,072,014	130	68.76	12.14	1.89	0.001
3	1,056,763	123	67.7	10.97	1.81	0.001
4	155,225	34	9.95	21.9	3.41	0.001
5	73,671	16	4.72	21.72	3.38	0.001
6	73,864	16	4.73	21.66	3.37	0.001
7	628,356	65	40.30	10.34	1.61	0.012

Table 5.4 Significant geographic clusters of pertussis risk in Florida, 2013-2015

Cluster	Population	Observed Number of Cases	Expected Number of Cases	Risk per 100,000 people	Risk Ratio	p-value
1	67,924	77	6.2	113.36	12.4	0.001
2	1,307,906	200	119.5	15.29	1.67	0.001
3	44,263	22	4.04	49.70	5.43	0.001
4	656,466	106	59.9	16.14	1.76	0.001
5	893,858	133	81.6	14.87	1.62	0.001
6	304,654	59	27.8	19.36	2.11	0.001
7	338,270	57	30.9	16.85	1.84	0.002
8	99,646	23	9.1	23.08	2.52	0.005
9	1,106,654	140	101.1	12.68	1.38	0.005
10	24,076	10	2.2	40.01	4.37	0.005
11	388,037	59	35.4	15.20	1.66	0.006

Table 5.5 Significant geographic clusters of pertussis risk in Florida, 2016-2018

Cluster	Population	Observed Number of Cases	Expected Number of Cases	Risk per 100,000 people	Risk Ratio	p-value
1	1,388,111	183	68.8	13.18	2.65	0.001
2	79,592	22	3.94	27.64	5.57	0.001
3	961,253	86	47.6	8.94	1.80	0.001
4	507,081	51	25.1	10.05	2.02	0.001
5	474,481	46	23.5	9.47	1.95	0.002
6	312,811	30	15.5	9.59	1.93	0.034

Table 5.6 Summary statistics and results of univariable analysis of potential predictors of pertussis risk in Florida

Variable	Median	1st Quartile	3rd Quartile	Unadjusted Parameter Estimate	Lower 95% CI	Upper 95% CI	p-value
Less Than High School Education	14.5	11.5	21.7	-0.313	-0.080	-0.011	0.010
High School Education	34.3	28.9	37.5	-0.258	-0.090	-0.003	0.035
College Education	18.6	11.4	26.7	0.269	0.003	0.056	0.028
White, non-Hispanic	83.0	77.8	87.6	0.094	-0.016	0.035	0.449
Black, non-Hispanic	13.1	8.6	19.1	-0.116	-0.038	0.014	0.351
Hispanic	8.65	5.29	18.1	0.040	-0.017	0.023	0.751
Male	49.4	48.6	53.3	-0.494	-0.184	-0.072	0.00
Female	50.6	46.7	51.4	0.494	0.072	0.184	0.00
Unemployed	6.6	5.8	7.2	-0.133	-0.334	0.099	0.282
Uninsured	18.1	15.6	21.1	-0.224	-0.106	0.004	0.069
Family Below Poverty Line	12.8	10.1	16.9	-0.164	-0.087	0.017	0.184
Individuals Below Poverty Line	17.7	14.3	22.5	-0.145	-0.075	0.019	0.24
Primary Care Providers (per 100,000)	48.0	28.0	68.0	0.305	0.003	0.021	0.012
% Living in Rural Area	23.8	8.5	67.5	-0.256	-0.015	-0.001	0.036
Rural County (Yes or No)	-	-	-	-0.254	-0.978	-0.028	0.038
Median Income	43063	36907	48483	0.307	0.095	0.719	0.011
% K-7 th Grade Vaccinated	92.9	89.9	95.1	-0.240	-0.108	0.000	0.051
% K-7 th Grade with Vaccination Exemptions	7.1	4.9	10.1	0.240	0.000	0.108	0.051
% K-7 th Grade with Medical Exemptions	1.7	0.8	2.3	0.138	-0.084	0.300	0.265
% K-7 th Grade with Religious Exemptions	2.4	1.2	3.5	0.178	-0.033	0.214	0.15

Table 5.7 Significant predictors of county-level pertussis risk in Florida, 2010-2018

Variables	Exponentiated Parameter Estimate	Lower CI (95%)	Upper CI (95%)	p-value	VIF
Rural (vs. Urban)	1.511	1.134	4.540	0.021	2.82
Scaled Median Income (\$10,000)	1.317	1.019	2.031	0.039	1.57
Percent Female	1.982	1.102	1.293	0.000	2.17

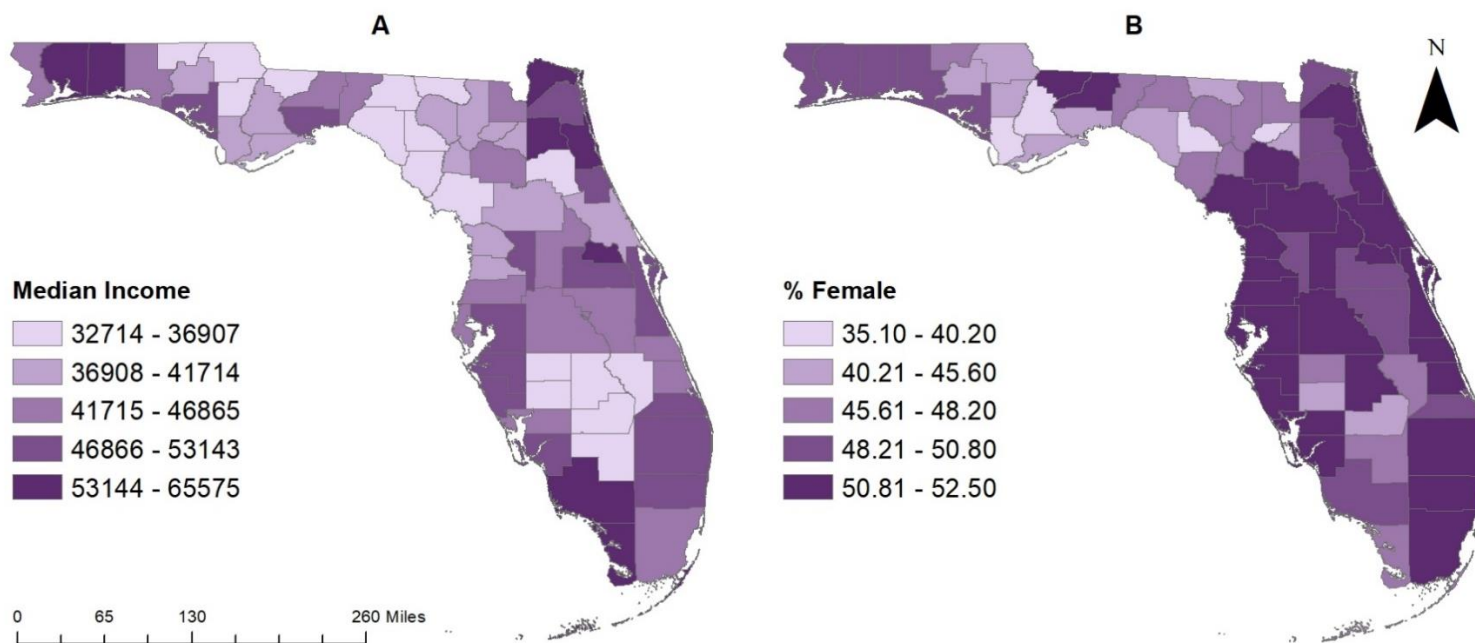


Figure 5.4 Choropleth maps of significant predictors of pertussis risk in Florida, 2010-2018

have high pertussis risk (>8 per 100,000 persons) and many counties with higher female populations were identified in high risk clusters, including Hillsborough, Lee, Escambia, Santa Rosa, Duval, St. John's, Polk, and Pasco counties. Finally, rural counties, were predominately located in the central and eastern panhandle and the central body of the state (Figure 5.1).

5.6 Discussion

This study investigated county-level geographic disparities and temporal changes in, as well as socioeconomic and demographic predictors of, pertussis risk in Florida from 2010 to 2018. Study findings provide information that is useful for guiding resource allocation for disease control programs. There is a dearth of research investigating the geospatial epidemiology of pertussis in the United States and spatial epidemiologic studies of pertussis predominantly explore the uptake of pertussis vaccines. The information obtained from this study is useful in understanding of geographic distribution of pertussis as well as its socioeconomic and demographic predictors. This knowledge is necessary for guiding public health response, as it helps guide health practitioners to prioritize areas to target existing public health campaigns as well as develop new programs to reduce morbidity and mortality. While prevention of pertussis through education campaigns and vaccination efforts is critical, identifying the sociodemographic and economic predictors of pertussis risk cannot be overlooked. Therefore, it is necessary to investigate geographic disparities in risk of the condition and identify socioeconomic and demographic predictors of any identified geographic disparities in pertussis risk.

The results of this study indicate that spatial patterns of high pertussis risk exist at the county level in Florida. This is consistent with findings from other studies that have reported spatial disparities in pertussis risk in the US (Siegal et al., 1997; Iroh Tam et al., 2016) and other countries (Kauhl et al., 2017; Mohammadbeigi et al., 2020). A study in Colorado analyzed data for the time period 1986-1994 and identified consistent clusters of high pertussis risk in the state (Siegal et al., 1997). The authors reported that high rates of pertussis were associated with census tracts with higher proportions of residents living below the poverty line (Siegal et al., 1997). An Iranian study of vaccine-preventable diseases at the district-level using data for the time period 2015-2018, reported that pertussis cases were identified in urban areas exclusively (Mohammadbeigi et al., 2020).

Findings from this study indicate that the risk of pertussis was higher during the time period 2010-2012 than any other time within the study period and a greater number of counties had higher risks during this time period. This is consistent with an increase in pertussis risk reported in the United States during this period (Clark, 2014). Temporal changes and epidemic cycles of pertussis are well documented in the literature (Fine & Clarkson, 1982; Broutin et al., 2010; Bouchez & Guiso, 2015). Broutin *et al.*'s comparative study of 64 countries reported that pertussis epidemics were characterized by a 3-5 year cyclical pattern. They suggested that these temporal variations were due to regional variations of demographics, vaccination coverage, surveillance strategies, and

changes in the circulating bacteria subtypes (Broutin et al., 2010; Bouchez & Guiso, 2015).

The current study also identified high-risk clusters of county-level pertussis risk around some major metropolitan areas in Florida. These findings are consistent with findings from other studies, including an analysis of pertussis in Ohio, which reported geographic clusters of pertussis cases around metropolitan areas (Rowe, 2006). Additionally, a comparative study of two outbreaks in Minnesota reported an association between population density and pertussis case density (Wi et al., 2019) which is consistent with high risk clusters being identified in large metropolitan areas. Similarly, an ecological analysis of pertussis in Minnesota reported that urban counties had 1.79 times higher risk of the disease than rural counties (Iroh Tam et al., 2016). Moreover, population density was also reported as a significant predictive factor, increasing pertussis risk by 6% for every 100 persons/km² increase in population density at the public health unit-level in southern Ontario, Canada (Elghamudi & Berke, 2020). This is expected given that pertussis is transmitted through respiratory droplets, and hence has high transmissibility in crowded environments. Given the relatively high reproductive number of 15-17 of pertussis, it stands to reason that the more densely populated an area is, the more effective transmission will be (European Centre for Disease Prevention and Control, 2012).

5.6.1 Predictors of Pertussis Risk

Significant predictors of county-level pertussis risk identified in the current study were percentage of females, median income, and rurality. Counties with high proportions of females tended to have high pertussis risk. This is consistent with findings from individual level studies that reported higher risks of pertussis among females than males in the United States, Canada, and Poland (De Serres et al., 2000; Paradowska-Stankiewicz & Rudowska, 2015). An analysis of an outbreak of pertussis in Quebec, Canada, reported that the main risk factors for pertussis were being female and working in an educational or healthcare setting. The authors proposed that the higher risk may be attributed to greater awareness of pertussis among females which could lead them to seek medical care more readily than their male counterparts (De Serres et al., 2000). Higher pertussis risk and pertussis complications among females have also been reported in the United Kingdom and Canada (Jenkinson, 1995; Abu-Raya et al., 2020). Since the current study is not an individual-level study, the findings of the above individual-level studies cannot be directly implied to it. However, it is possible that the associations seen at the individual-level may apply at the county-level as well. Suffice it to say that this is the first ecological study that has investigated sex as a potential sociodemographic predictor of pertussis risk despite evidence at the individual level that sex is an important predictor of pertussis risk (Broutin et al., 2004; Huang et al., 2017; Alimohamadi et al., 2020).

The association between higher median income and higher county-level pertussis risk may be related to vaccine refusal since higher median income has been well-documented

as associated with vaccine refusal for ideological reasons (Wei et al., 2009; Remes et al., 2014). However, it is worth noting that vaccination delay has also been identified as a significant contributor to disparities in vaccination coverage and often occurs along socioeconomic and demographic lines. Children from economically disadvantaged families, with poor access to healthcare services, often have delays in their vaccination schedules. This is of particular interest because this delay can increase risk of not only pertussis illness but other vaccine-preventable diseases as well (Luman et al., 2005; Feemster et al., 2009; Schaller, Schulkind & Shapiro, 2019). However, children with vaccine delays are usually fully vaccinated by the time they begin attending school since it is required unless an exemption has been approved (Schaller, Schulkind & Shapiro, 2019). This may explain why the current study did not identify an association between vaccination coverage and county-level pertussis risk, since we could not assess the vaccination coverage of children prior to starting compulsory kindergarten education.

While high-risk clusters were identified around metropolitan areas, the final multivariable model indicated that risk of pertussis was higher in rural counties than urban counties. These contradictory findings may be the result of distortion effects of percent females in the model. However, our finding that rurality is a predictor of higher county-level pertussis risk is consistent with reports of a geospatial analysis of pertussis in Saskatchewan, Canada, that rural areas had higher pertussis risk than non-rural areas (Medu et al., 2018). There is a clear need to explore the relationship between population density, rurality, and risk of pertussis more deeply, as there is conflict not only in this

study but also in the literature. Possible explanations for these findings include lower vaccination rates due to lack of access to healthcare services or geographical differences related to objections to vaccinations.

5.6.2 Strengths and Limitations

To our knowledge, this is the first study to investigate spatial patterns and clusters of pertussis in Florida using rigorous spatial epidemiologic methods. The FSSS has several strengths, over other methods such as the Kulldorff's spatial scan statistics and local indicators of spatial associations (LISA) methods such as Moran's I: (a) it does not have the problem of multiple comparisons associated with LISA; (b) does not have pre-selection bias; (c) it is able to detect irregularly shaped clusters since it identifies all cluster shapes as opposed to Kulldorff's spatial scan statistics which only identifies circular or elliptical clusters (Tango & Takahashi, 2005). Moreover, the Tango's FSSS has been shown to work better than Kulldorff's scan statistic for identifying small clusters (Tango & Takahashi, 2005). County level spatial analysis was necessary to avoid the small number problem associated with analysis at lower geographical scales because of the small numbers of cases of pertussis. The identified spatial clusters and predictors are useful for guiding health planning and policy. In addition to identifying county-level predictors of pertussis risk, this study has demonstrated the usefulness of using spatial scan statistic to identify areas where preventive resources are needed through the identification of high-risk clusters of pertussis. However, this study is not without limitations. Pertussis is an under-reported disease and, therefore, the county-level

pertussis risk reported in this study is likely lower than the true risk. Due to the small number of cases and to protect anonymity and confidentiality of cases, only yearly pertussis data were used. These data were further aggregated into 3-year time periods for descriptive investigation to ensure stable estimates due to the small yearly case counts. Future studies will need to investigate individual level data covering longer study periods. These limitations notwithstanding, the findings of this study are important for guiding and planning public health programs.

5.7 Conclusions

There is evidence that geographic disparities exist and have persisted over time in Florida. This study highlights the importance and application of GIS technology and spatial statistical/epidemiological tools in identifying areas of highest disease risk so as to guide targeting of resource allocation to reduce health disparities and improve health for all.

CHAPTER 6

SUMMARY, CONCLUSIONS, AND RECOMMENDATIONS

The objectives of this project were to: (a) investigate attitudes towards vaccines and vaccinations; (b) identify county-level geographic disparities and socioeconomic and demographic predictors of vaccination exemptions in Florida; and (c) identify geographic and temporal changes as well as county-level socioeconomic and demographic predictors of pertussis risk in Florida.

To my knowledge, this study is the first of its kind to utilize the Theory of Triadic Influence (TTI) to investigate behaviors and attitudes towards vaccines and vaccinations. This theoretical framework considers the interplay of social, cultural, and contextual factors of behaviors and attitudes towards vaccines and vaccinations. Risk perception, safety, and family and social group attitudes were the primary considerations regarding vaccination decision-making for both individuals, regarding their own vaccinations, and for parents when considering vaccinating their children. Increasing trust in and improving access to accurate information about vaccination is critical when making vaccination decisions. The importance of the role played by physicians and other medical professionals in actively addressing vaccine hesitancy in clinical settings is also highlighted by the findings of this study. Knowledge of local attitudes and barriers towards vaccinations are necessary to guide health education programs aimed at increasing awareness of the importance of vaccinations and improving vaccination coverage. Unfortunately, this study covered a predominantly white population with relatively high education. Therefore, future studies will need to include individuals with broader racial, educational as well as economic backgrounds. Additionally, better

understanding of perspectives of individuals who hold explicit anti-vaccination attitudes should be pursued to gather information that can better guide strategies to improve vaccination coverage and curb vaccine-preventable diseases. Finally, it is necessary to bear in mind the political and social contexts of health behaviors, as individuals' perceptions regarding vaccinations and vaccine preventable diseases may be driven by their political and social beliefs. Therefore, political ideologies and how they influence health decisions should be considered. Future studies should consider these issues in both qualitative and quantitative investigations of attitudes towards vaccinations and their impact on vaccine preventable diseases.

This study is also the first of its kind to use rigorous spatial epidemiological techniques to identify geographic disparities of vaccination exemptions in the state of Florida. High total vaccination exemption risks (greater than 10.35 per 10,000 persons) were observed in four distinct areas of the state: the western panhandle, north central, central, and southeastern coast. High non-medical vaccination exemption risks (greater than 3.71 per 10,000 persons) were observed in seven distinct areas of the state: the western and central panhandle, north central, northeastern coast, central eastern and western coasts, and the southwestern coast.

High densities of primary care providers, high median income, and high percentages of Hispanic populations were all associated with high risks of total vaccine exemptions at the county level while high county-level percentages of population with college

education were associated with low risks of total vaccine exemptions. On the other hand, high county-level percentages of white populations were associated with high risks of non-medical exemptions. By contrast, low risks of non-medical exemptions tended to occur in counties with higher percentages of the population living in rural areas and in counties with high percentages of the population with college education, high school education, and less than a high school education. Knowledge of the geographic distribution of high total vaccination exemptions can be used to identify areas that are potentially at high risk of vaccine-preventable diseases. Thus, identifying geographic disparities of both total and non-medical exemptions can provide valuable insight into where risks of vaccine-preventable disease may be higher. These findings can be used to guide disease control initiatives in areas with high exemptions as well as other risk factors. Future studies should investigate geographic disparities and their predictors at finer geographic scales to identify how exemptions and risk factors impact disease risk at the community level for more targeted intervention. Future studies should also consider further examination of the role that educational level and type of primary care provider play in vaccination exemption risk.

This study has shown the strength of using spatial scan statistics and Geographic Information System (GIS) technology for identification of high-risk geographic clusters of pertussis. The geographic distribution of clusters of high pertussis risk remained relatively consistent over time, with areas of high risk persisting in the western panhandle, northeastern coast, and along the western coast. High-risk clusters were also

consistently identified around some major metropolitan areas of the state. These findings show evidence of geographic disparities of pertussis risk in Florida and is useful for guiding resource allocation to control the disease. Future studies should explore not only pertussis risk at finer geographic levels but should also include other vaccine-preventable diseases.

Significant predictors of county-level pertussis risk identified in this study included higher percentage of females, higher median income, and rurality. The association between high median income and high county-level pertussis risk may be related to vaccination refusal, as higher median income has been well-documented as associated with vaccination refusal for ideological reasons. There is a clear need for more detailed investigations to explore the relationship between population density, rurality, and risk of pertussis, as there is conflict not only in this study's findings but also in the literature. It is possible that these findings reflect lower vaccination rates due to lack of access to healthcare services or ideological differences regarding vaccinations. Therefore, better understanding of these issues would be useful for guiding public health interventions.

In conclusion, this project identified important disparities in county-level vaccination exemptions and pertussis risk as well as important contributors to vaccination hesitancy. These findings provide useful information for the identification of avenues for further scientific inquiries on vaccination hesitancy, ways to improve vaccination acceptance and coverage as well as strategies to reduce burden and disparities in risk of pertussis. This

project has demonstrated the value of using geographic epidemiologic methods to identify disparities to guide both public health planning/intervention and future research. It has also demonstrated that a novel application of theoretical frameworks to investigate vaccination attitudes is useful for considering the complexities of influences regarding vaccination hesitancy and vaccination decision-making. Overall, the findings of this project are important for developing evidence-based public health initiatives, prioritizing geographic areas, and focusing efforts to reduce the disparities in and burden of vaccine-preventable diseases at the local level.

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APPENDICES

Appendix A: Demographic Questionnaire

Date: _____

Participant Number _____

Age: _____

Gender (please circle): Male Female Transgender

Another Gender Identity (fill in blank if
desired): _____

Prefer not to answer

Race/Ethnicity (Circle all that apply): White (Non--Hispanic) Hispanic

Black Other: _____

Education (please circle):

Some High School

High School Degree

Some College

College Degree

Graduate/Professional Degree

Average Annual Income (please circle):

<10,000

10,001--25,000

25,001--40,000

40,001--60,000

60,001--75,000

>75,000

Do you have health insurance? (please circle): Yes No

If yes: Private Government

Have you ever received a vaccine? (please circle): Yes No

If yes, Have you gotten a tetanus shot in the last 10 years? **(please circle):** Yes
No

If yes, do you know if it included protection against pertussis/whooping
cough (Tdap)? **(please circle):**

Yes No Don't Know

Do you have children? (please circle): Yes No

If yes, have they ever received a vaccine? Yes No

If yes, have they received their pertussis/whooping cough (DTaP) series?:

Yes No

Appendix B: Interview Questionnaire

I. Vaccine Attitudes and Knowledge

- a. I'd like to hear your thoughts about vaccination in general.
 - i. What positive things come to mind when you think about vaccination?
 - ii. What negative things come to mind when you think about vaccination?
- b. Who do you talk to about vaccines?
 - i. What do you talk about when you talk about vaccines?
 - ii. Who do you feel most comfortable talking to about vaccines?
- c. How would you describe your family's attitudes towards getting vaccines?
 - i. What do they think about getting vaccines?
 - ii. What concerns have they expressed about getting any vaccines?
- d. How would you describe your friends' attitudes towards getting vaccines?
 - i. What do they think about getting vaccines?
 - ii. Have any of them ever expressed concern that you were getting any vaccines?
- e. Where do you get information about vaccines?

II. Vaccination Behavior

[Self]

- a. From your survey it looks like that, at some point in your life, you have received a vaccine. Can you describe one of your experiences when you've received a vaccine?

- b. Tell me about a time that you have purposefully sought out a vaccine(s). For example: making an appointment specifically to get one?
 - i. *Prompts and follow ups:*
 - 1. What were your reasons for getting that vaccine?
 - 2. What made you decide to schedule the appointment?
 - 3. What, if any, other options did you consider instead of vaccination?
- c. Where do you find it easiest to get your vaccines?
 - i. What about this place makes it easier for you?
- d. Is there anything about getting a vaccine that would you change?
- e. What kind of unpleasant experiences have you had getting vaccinated?
 - i. What caused the unpleasantness?
 - ii. How have negative experiences like that one influenced your thoughts about future vaccination?
- f. How do you feel about going to the doctor or talking to doctors?
- g. How has your doctor impacted your vaccine behavior?
 - i. Tell me about your thought process when hearing your physicians' recommendation.

IF "NO" TO HAVING CHILDREN ON QUESTIONNAIRE, SKIP TO III. PERTUSSIS KNOWLEDGE.

IF “YES” TO VACCINATING THEIR CHILDREN ON QUESTIONNAIRE:

[Child]

- h. You filled in on the questionnaire that you have a child(ren). I’d like to hear about your experiences getting your child(ren) vaccinated.
- i. Why did you get your child(ren) vaccinated?
- j. What is it like bringing your child(ren) in to get vaccinated?
 - i. Where do you find it easiest to get your vaccines?
 - ii. What part of the process of getting a vaccine would you change?
- k. How does the experience of getting your child(ren) vaccinated compare to getting vaccines for yourself?
 - i. Did you have any concerns or questions about the vaccine(s) that you didn’t have when you were getting vaccinated?

IF “NO” TO VACCINATING THEIR CHILDREN ‘ON SCHEDULE’ ON QUESTIONNAIRE:

[Child]

- l. You filled in on the questionnaire that you have a child(ren). I’d like to hear about your experiences getting your child(ren) vaccinated.
- m. What made you decide to not vaccinate/vaccinate on an alternative schedule?

[VACCINATED, BUT OFF SCHEDULE]

- n. What is it like bringing your child(ren) in to get vaccinated?
 - i. Where do you find it easiest to get your vaccines?

- ii. What part of the process of getting a vaccine would you change?
- o. How does the experience of getting your child(ren) vaccinated compare to getting vaccines for yourself?
 - i. Did you have any concerns or questions about the vaccine(s) that you didn't have when you were getting vaccinated?

[NOT VACCINATED]

- p. What has been the response from your child's medical caregivers regarding your choice not to vaccinate?
 - i. How do you feel about this feedback?

III. Knowledge of Pertussis

- a. What do you know about whooping cough?
 - i. Is there anything else that you can think of that you know about this illness?
- b. Sometimes doctors tell us things about specific illnesses. What has your doctor told you about whooping cough?

- c. Besides your doctor, where else have you heard about whooping cough?
 - i. Some people tell us that they get information about whooping cough from the internet, friends, and brochures at the health department. Can you think of any places where you have heard about whooping cough?
- d. Can you tell me about any experience you have had with the disease?
 - i. I'd like to know more about anyone you know, in your family or community for example, who has had the disease.
- e. How likely do you think it is that you would get whooping cough?
 - i. What about your children? [if applicable] .

Is there anything else you'd like to share with me about your experiences and ideas about vaccination or whooping cough?

VITA

Corinne Tandy was born in Knoxville, TN. They pursued degrees in Anthropology at the University of Tennessee, Knoxville (BA, 2009) and Forensic Anthropology at the Boston University School of Medicine (MS, 2011) before pursuing their PhD in Comparative and Experimental Medicine with concentrations in infectious diseases and epidemiology at the University of Tennessee, Knoxville.