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Globalization and the

Resurgence of Pertussis in the United States

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List of Abbreviations

CDC	Centers for Disease Control and Preventions
CDPH	California Department of Public Health
CGD	Center for Global Development
CSIS	Center for Strategic and International Studies
DTaP	Diphtheria, Tetanus, acellular Pertussis
DTP	Diphtheria, Tetanus, Pertussis
GAVI	Global Alliance for Vaccines and Immunisations
GDP	Gross Domestic Product
GHSi	Global Health Strategies Initiatives
IDRC	International Development Research Centre
IHME	Institute for Health Metrics and Evaluation
IMF	International Monetary Fund
MERS	Middle East Respiratory Syndrome
NFID	National Foundation for Infectious Diseases
ODI	Overseas Development Institute
PCR	Polymerase Chain Reaction
SARS	Severe Acute Respiratory Syndrome
SD	Standard Deviation
Tdap	Tetanus, Diphtheria, and Pertussis
UNAIDS	Joint United Nations Programme on HIV/AIDS
UNICEF	United Nations International Children's Emergency Fund
UNFPA	United Nations Population Fund
USAID	United States Agency for International Development
WHO	World Health Organization
WTO	World Tourism Organization

Abstract

Globalization is a key challenge to health around the world, but establishing quantifiable linkages between globalization and health is extremely complex. Although a growing amount of literature has appeared in recent years, none seem to focus their efforts on a particular process of globalization, a specific facet of health, or the results of those interactions in a specific country. There is still much to be understood about the direct and indirect relationships between a process of globalization known as “population mobility” and the health outcomes at the destination of a population. This paper reviews the scholarly literature that describes a connection between globalization and health, and then analyzes, both qualitatively and quantitatively, the links between population mobility and the increasing levels of pertussis (whooping cough) in the United States. An exhaustive review of the literature reveals an undeniable connection between population mobility and increases in infectious diseases. Additionally, quantitative analyses also supports the notion that population mobility has a similar effect on pertussis cases in the United States, in particular.

Key words: globalization, population mobility, infectious diseases, pertussis.

Globalization and the Resurgence of Pertussis in the United States

Infectious disease threats know no borders, especially in a world where a potentially deadly infectious disease is only one day's plane travel from anywhere in the world. Thus, it is not surprising that nations are increasingly recognizing the need for global health security, by strengthening local capacity to prevent, detect, and respond to public health threats that indeed could have global implications. Currently, world health officials are keeping an eye on dozens of potentially dangerous pathogens, from H7N9 bird flu in China, to the MERS (Middle East respiratory virus) in the Middle East, and Ebola in Africa.

With this in mind, it is essential for the United States to recognize a more specific and stubborn foe. Despite pertussis (whooping cough) being a vaccine preventable disease, infection rates around the world are steadily on the rise. Altogether, the World Health Organization (2008) states that there were 18.4 million new cases of pertussis worldwide in 2004 (p. 28) and the Centers for Disease Control and Prevention (2013a) reports a 158% increase of pertussis cases in the United States in 2012 compared to 2011.[1] Though pertussis is endemic throughout the United States, recently, multiple factors may have led to the considerable increase in the incidence of pertussis; lower vaccination rates,

[1] 2011: 18,719 cases; 2012: 48,276 cases

waning immunity of the vaccinated population, and increased circulation of the bacteria, worldwide, have all played a role.

My fundamental research question is, *Why are pertussis infections on the rise in the United States, despite it being a vaccine preventable disease?* Combining global health and health policy disciplines, in addition to globalization studies, is critical to systematically examining the problem.

Interdisciplinary Rationale

My question as to why incidence of pertussis, a vaccine-preventable disease, is on the rise in the United States and what public health professionals and other medical providers can do to alleviate the burden of this disease cannot be answered through the limited focus of one discipline. Therefore, I apply ideas and concepts from multiple disciplines to this project.

I bring together health policy, global health, and globalization, which in themselves are informed or employ principles and findings from other disciplines: political science, global affairs, international relations, medicine, ethics, economics, and public administration. Each discipline has a different focus, plays a different role in understanding the complex nature of the transmission of pertussis around the world, and therefore provides a different lens through which to investigate this problem further. More specifically, I know that only the combination of the myriad perspectives mentioned provide the comprehensive

approach to understand the rise in pertussis rates in the U.S. The perceived relationship between such varied disciplines can be seen in ***Figure 1***.

Scholars have consistently argued for or against the utility of an interdisciplinary approach in research over the past few decades. Some academics posit the use of an interdisciplinary approach as merely a scratch in the surface of multiple ideas and subsequently only offers a superficial understanding of the disciplines within. On the contrary, Boix Mansilla and Dawes Duraising (2007) argue that to "thrive in contemporary knowledge societies, young people need not only develop insights and modes of thinking that are informed by a variety of disciplines but also to integrate these forms of knowledge effectively" (p. 215). I maintain that the use of interdisciplinarity in research is the new standard and is the best approach to advancing our understanding of such complex issues.

To begin, I utilize global health theories and data as a means to investigate the burden of pertussis on populations throughout the world. Ilona Kickbush (2006), the director of the Global Health Programme at the Graduate Institute of International and Development Studies in Geneva, Switzerland, refers to global health as the "health issues that transcend national boundaries and governments and call for actions on the global forces that determine the health of people" (p. 561). So, in addition to the burden of pertussis in specific countries, I

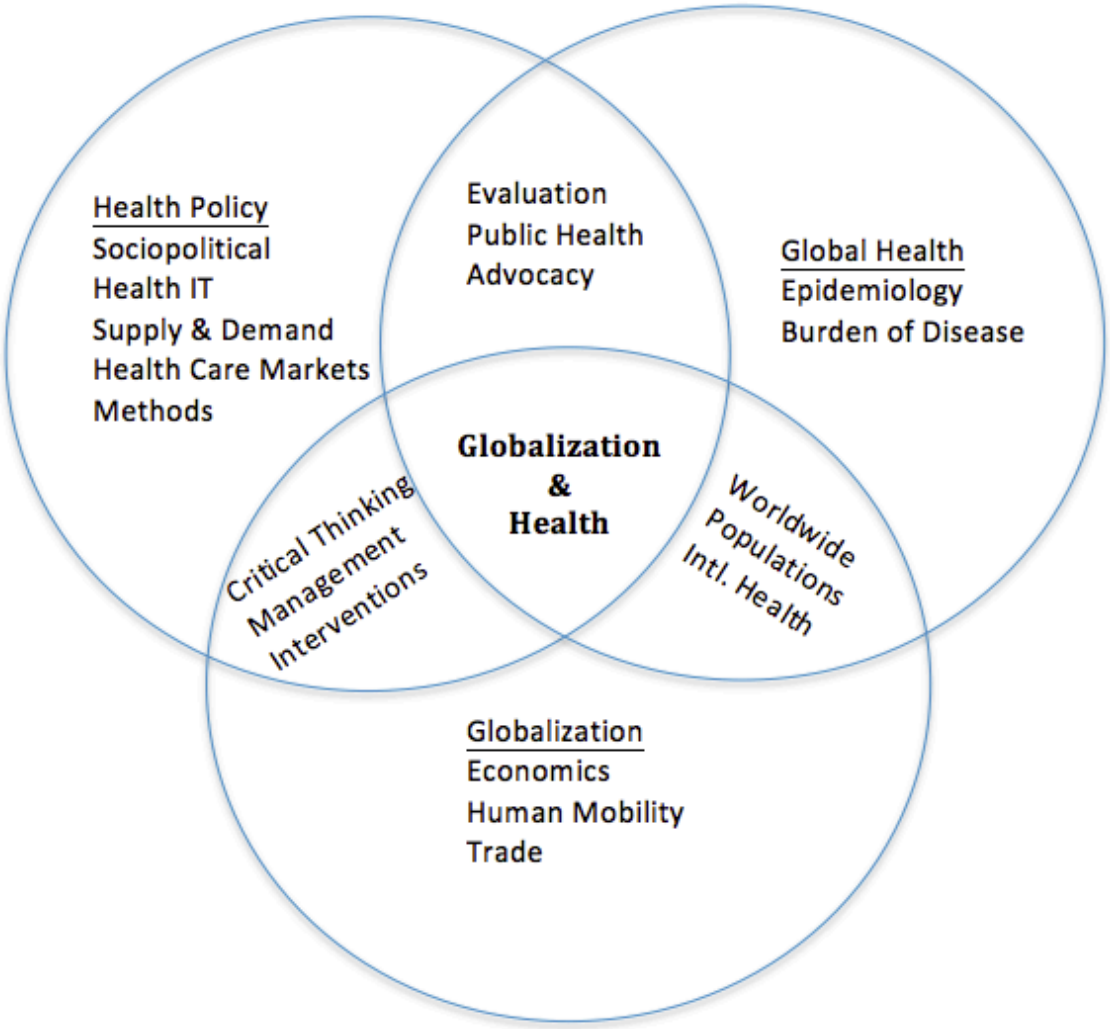

Figure 1. Venn Diagram. The perceived relationship between Global Health, Globalization and Health Policy

explore the effects of that burden outside the boundaries of those countries. This trans-boundary view allows me to study disease trends around the world.

Together with global health and disease, I am particularly interested in the intersection of globalization and the role it plays in health. By itself, globalization is a loaded term, with multiple processes and theories at its foundation. Therefore I focus on the potential effects of population mobility or the movement of people across national and international borders on pertussis rates. Population mobility is also known as geographic mobility or human mobility and can be categorized globally as a form of migration. This migration of people from inside to outside their birth countries serves as a possible mechanism of international disease transmission. Equally important to population mobility is considering why people choose to move from one country to another, not to mention the health threats those people bring to their new region. Do undocumented migrants and/or refugees (e.g. those without health screenings) pose a more serious threat to public health than do documented international travelers or military personnel?

Not only are perspectives from global health and globalization required to understand these interactions, health policy is also necessary to fully comprehend the intricacies set forth in my research. It is a required discipline for a number of reasons; most importantly, it influences health law around the world. Some countries have excellent policies in place to protect their citizens from both

internal and external threats to public health. Other countries, predominantly in the developing world, may lack robust health policies, or may not have them at all. Moreover, developing countries may not have the infrastructure in place or be able to further invest their infrastructure, to implement and enforce the policies that do exist, resulting in epidemics and the potential for resurgence of diseases thought to be eradicated. I use existing health policy theories to develop a conceptual framework with which to study the effects of worldwide infectious disease rates on the health of the United States.

To conclude, my project provides a practical application of an interdisciplinary approach. More precisely, I integrate ideas and theories from multiple disciplines including global health, globalization, and health policy to develop a conceptual framework. I believe that in the intersection of global health, globalization, and health policy lay ideas and explanations that indeed circumvent political barriers and national borders. Infectious diseases do not restrict themselves within the confines of one region or country; why should we limit our approach as such? An integrative approach to answering such a complex problem using the multiple disciplines I have outlined is not only useful, but also essential to identify practical and feasible solutions to why pertussis cases are on the rise in the United States.

Review of the Literature

Pertussis, or whooping cough, is a highly contagious, cyclically recurring disease caused by the bacterium *Bordetella pertussis*. Despite concerted and widespread immunization efforts, pertussis is once again contributing to morbidity and mortality in both developing and developed countries around the world. The theories behind this resurgence are vast and include "causes rooted in biology, including loss of infection and vaccine-derived immunity, vaccine efficacy, and pathogen evolution" (Rohani & Drake, 2011). In addition, other researchers have explored an alternative theory that there is no actual resurgence, per se, but increased awareness and more advanced testing methodologies that have resulted in a more accurate picture of *B. pertussis* infections (Cherry, 2003; Cherry, 2005). Furthermore, there is another possibility that has led to the increase in pertussis infections, namely, globalization. In today's globalized world, the extent of integration in our world means that no country can be isolated from risks that emerge from elsewhere.

This review of the literature consists of four sections. First, I set the stage by laying the groundwork of what *B. pertussis* is and explain its transmission. The second section of the review showcases the varied theories that explain an increase in pertussis infections over the past three decades in the United States. The third section explores the concept of globalization including its defined processes, namely the expansion of economics, technology, and the movement

of people. This section concludes with an overview of the perceived relationship between globalization, specifically population mobility, to the increase in pertussis incidence in the United States.

Bordetella pertussis

To better understand why infection by *Bordetella pertussis* bacterium (also known as whooping cough) is such a significant issue, it is crucial to understand the magnitude of consequences evoked by this bacterium. Pertussis is a notifiable disease in every state of the United States, for good reason. The infection causes coughing spells that are so severe it can be hard to breathe, eat, or sleep. The National Foundation for Infectious Diseases (2014) even attributes cracked ribs and pneumonia to pertussis infections. Moreover, whooping cough can be extremely difficult to accurately diagnose. Early symptoms may appear as the common cold and the classic symptom of a 'whoop' is not found in all cases. This can lead to under- and mis-diagnoses across all age groups.

According to the Centers for Disease Control and Prevention (CDC, 2013b), pertussis is a very contagious disease found only in humans and is spread from person to person; usually by one person coughing or sneezing while in close contact with others, who then breathe in the pertussis bacteria. The *B. pertussis* bacteria attach to the cilia of the upper respiratory system, release toxins, and subsequently damage the cilia and cause inflammation. Pertussis

can lead to violent and rapid coughing until the air is completely expelled from the lungs to the point of forced inhalation - the classic loud 'whooping' sound.

While everyone is susceptible to falling ill, infants are the most vulnerable population. Tan et al. (2005) submit that this is because infants have yet to receive any or only a few of the recommended vaccinations and have not reached full immunity against the disease (p. S83). Therefore, pertussis is still widely considered an infant disease. Tan and colleagues (2005) maintain that because practitioners do not generally consider pertussis when diagnosing adolescents or adults, significant underreporting of the disease can occur (p. S84). Moreover, some experts argue that older siblings, parents, and caregivers, who may not even know they have the disease, infect a large majority of infants (Bisgard et al., 2004; Schellekens, Wirsing von Konig, & Gardner, 2005). Schellekens et al. (2005) add that the main sources of infection for adolescents are friends and schoolmates, whereas in adults, it is their children or work colleagues.

Theories for Increased Incidence of *B. pertussis* in US

The United States is currently in the midst of what may turn out to be the largest outbreak of reported pertussis in 60 years (Rohani & Drake, 2011; Cherry, 2012). In fact, in 2012, 48,277 cases of pertussis were reported in the US, the most since 1955 – 62,786 (CDC, 2013c). Although the United States saw a significant drop in overall cases in 2013, as of June 10, 2014, there have been

3,458 cases in California alone; prompting Dr. Ron Chapman, director of the California Department of Public Health (CDPH) to declare a pertussis epidemic in that state (CDPH, 2014). All told, including domestic pertussis incidence, there are an average of 16 million cases of pertussis and 200,000 deaths in children caused by pertussis worldwide, each year (CDC, 2013c).

Nicole Guiso (2013), of the Pasteur Institute and the National Center for Scientific Research in France, claims the main reason for the marked increase in pertussis is that "individuals are vaccinated when they are young, but their immunity subsequently wanes…." In North America, children commonly receive 5 doses of a combined diphtheria-tetanus-acellular pertussis (DTaP) vaccine; one dose at each of the following ages: 2 months, 4 months, 6 months, between 15-18 months, and between 4-6 years (CDC, 2007). This particular vaccination is not licensed for adolescents, adults, or children 7 years of age or older. A vaccine called Tetanus-diphtheria-acellular pertussis (Tdap) is available, but not as frequently administered, in this older population. Guiso maintains that this modern vaccination strategy is no longer suitable. The duration of protection post-vaccination is 3-5 years (He et al., 1994), and the waning of immunity leaves adolescents and adults vulnerable to infection, making them a source of infection for young infants, other adolescents and adults. Mooi, Van Der Maas, and De Melker (2013) add to this argument, even naming this reason as the "exclusive" cause for the resurgence of pertussis.

Although consensus exists that waning immunity plays an important part in the resurgence, few agree on the exact reason why this occurs. Experts argue the "[quality] of the vaccine"(Mooi et al., 2013), "lack of natural boosters" (Tan et al., 2005), and "adaptation of the pathogen" (Mooi et al., 2013) are all significant players. Camille Sabella (2005) and Tan et al. (2005) separately observed that there is also a large percentage of mild disease that goes undiagnosed or unreported, which leads to a growing reservoir of *B. pertussis*. This growing reservoir can then lead to increased incidence in those individuals who are not immunized or under-immunized. Further, Winter et al. (2012) analyzed the California pertussis epidemic of 2010 and identified other potential causes for the increased incidence in pertussis, including large birth cohorts as well as increased awareness and detection. Forsyth (2007) suggests that increases use of real-time polymerase chain reaction (PCR) testing in laboratories around the world is key to better and more accurate diagnoses.

Globalization

Martens, Akin, Maud, and Mohsin (2010) define contemporary globalization as "the intensification of cross-national interactions that promote the establishment of cultural, economic, ecological, political, technological, and social process on global, supra-national, national, regional, and local levels." This definition, coupled with this addition from Yach and Bettcher (1998) that globalization is a process of increasing "…global integration that takes place as

capital, traded goods, persons, concepts, images, ideas, and values diffuse across state boundaries," truly expresses the complexity that encompasses globalization.

Even with such comprehensive definitions, some scholars feel that globalization is a purely economic concept. Schrecker, Labonte, and DeVogli (2008) advance this discourse defining globalization as the "incorporations of national economies and societies into a world system, through movements of goods and services." Though they do concede that contemporary globalization is multi-faceted and thus more complex than earlier periods of globalization, such as colonization, they remain steadfast that "this incorporation results [solely] in the exposure of economies…outside their borders." In addition, Labonte, Mohindra, and Schrecker (2011) discuss myriad of global flows directly related to globalization; they assert the movement of trade, finances, information, pathogens, and people all play a major role defining what globalization truly exemplifies.

Together, the aforementioned research elucidates key factors that may influence myriad social and economic factors (in the U.S. and globally). While some identify a rise in globalization through an economic lens, others consider technological innovation, social and cultural integration, and political diplomacy as main influences of globalization.

Likewise, the movement of people, is as, or perhaps even more influential in producing economic and social effects for globalization. Human mobility, also known as population mobility, occurs for a variety of reasons. Since ancient times, there have been relentless movements of people in search of new sources of food, water, and security. Additionally, as Saker, Lee, Cannito, Gilmore, and Campell-Lendrum (2004) explain, “mass migrations, both voluntary and forced, have also followed economic hardship, conflict, and environmental disasters.” Globally, all regions have seen increasing numbers of people on the move, albeit driven by widely varying forces.

According to the United Nations Population Fund (UNFPA, 2014), in 2010, approximately 214 million people, or 3 percent of the world’s population, lived outside of their country of origin. The UNFPA (2014) also estimates a rather small portion of migrants, about 10.5 million in 2011, are refugees fleeing armed conflict, natural disaster, famine or persecution. More specifically, asylum seekers or refugees may be fleeing their previous residence out of fear of persecution, due to race, religion, nationality, membership in a particular social group, or due to a certain political opinion (Labonte et al., 2011). Whereas, a person who is recruited, transported, or harbored by means of any sort of coercion for the purpose of exploitation, is considered a trafficked person (Labonte et al., 2011). In addition, there exist undocumented migrants, those without the legal means and paperwork, usually relocating for work.

Unfortunately, this list is not limited with what is documented here. Short-term movement of people for leisure purposes is significantly on the rise. In fact, according to the World Tourism Organization (WTO, 2014), international tourist arrivals grew by 5% in 2013, reaching a record, 1.087 billion arrivals around the world, 48 million of which were in the United States. Moreover, Peter Stalker (2000), in his impeccably applicable book *Workers Without Frontiers*, makes note that "migration to new lands has become easier, less permanent, and less daunting and traumatic." Whether it is a permanent or temporary change, the seemingly porous borders around the world are making it easier for individuals and families alike to pick up and move.

Unarguably, the links between globalization and health are complex; globalization is a multifaceted phenomenon that can affect health in myriad ways. Still, the more specific association between globalization and the spread of infectious diseases, in particular, is possibly best explained through the influence of population mobility (Frenk et al., 2011; Huynen et al., 2005; Martens et al., 2010).

Population Mobility and Infectious Disease

Population mobility and health have a storied history. Despite earlier cross-border interactions, the globalization of disease is typically said to have begun in 1492 when the Europeans discovered the Americas, bringing with them smallpox, measles, and yellow fever. From the age of exploration to the era of

industrialization, and more recently, the advent of air travel, communicable diseases have had ample opportunity to spread more widely and frequently (Lee, 1999). The renowned global health scholar, Kelley Lee (1999), explores the current stage of the relationship between globalization and infectious disease, most important of which is, "the geographical breadth it encompasses [and] the frequency and intensity of human interactions that are taking place." Essentially, the world we inhabit today is a global village in which ideas, goods, and people can travel long distances in a matter of hours (Markel & Stern, 2002). More compelling, Pang and Guindon (2004) posit that it is "entirely possible that a person in the early stages of an infectious disease could be halfway around the world in 12-15 hours…aiding its spread" (p. S13). Indeed, "globalization is evolving at such speed and with such complexity that it challenges our ability to grasp its full extent" (Frenk, Gomez-Dantes, & Knaul, 2011). Along these same lines, Azevedo and Johnson (2011), add that "no matter how [globalization] is defined, it is here to stay, and is causing major changes on the globe."

Without minimizing the intricate relationship between population mobility and infectious disease, modern examples present a more tangible association. The outbreak of Severe Acute Respiratory Syndrome (SARS) in 2003 demonstrated the potential of infectious diseases spreading rapidly throughout the world, increasing the chances for a global pandemic. SARS was first recognized in February 2003 in Vietnam where cases of atypical pneumonia with

an unknown cause began to appear. By the first week of May 2003, 30 countries on six continents had reported a total of more than 7,000 probably cases with more than 500 deaths (WHO, 2003). More recently - May 2014 - we saw the introduction of the Middle East Respiratory Syndrome (MERS) to the United States. According to the CDC (2014), MERS is a severe viral respiratory illness first reported in Saudi Arabia in 2012 with a death rate of approximately 30%. Though MERS is spread from person to person, we have not yet seen continuous transmission in the US.

To summarize this review, the perceived relationship between globalization and health is invariably multifaceted; this paper focuses solely on a single process of globalization – population mobility – and its potential effects on pertussis incidence in the United States.

The distinct emphases presented in this review highlight a clear relationship between population mobility and infectious disease rates around the world. Numerous studies have highlighted this association (Frank et al., 2011; Huynen et al., 2005; Lee, 1999; Markel & Stern, 2002; Martens et al., 2010; Pang & Guindon, 2004). Similarly, understanding the processes of population mobility is imperative to understanding the epidemiology and trends of disease experiences around the globe. Perhaps, it is even expected to see a rise in disease with an influx of people into a country (i.e. immigrants, refugees, travelers). Although the broad relationship between globalization and infectious

diseases exists, the more specific association between population mobility and pertussis infection, specifically, is not well known or documented.

Pertussis is known to have 3-5 year cyclical peaks in which the disease declines and reemerges in a population. Researchers are unsure as to why this ebb and flow occurs. Further research on this topic will surely be necessary but is not in the purview of this paper. Regardless of the underlying stimulus, pertussis infections have been steadily on the rise in the U.S. over the past three decades. Many scholars unfailingly propose consistent and intersecting reasons for this, including decreased vaccine efficacy, lower vaccination rates, and greater awareness of the disease, all of which may influence the increase incidence. However, research has yet to examine the specific relationship between population mobility and pertussis incidence in the U.S. The thesis of the research presented herein submits that one key aspect of globalization, specifically population mobility, explains the rise in pertussis experienced in the U.S. today.

Research Focus

This paper describes my work to better understand the relationship between globalization and pertussis rates in the United States. Today, more people are traveling, especially internationally; there are more migrants leaving their home countries and crossing international borders in search of a different life; and there are an increasing number of conflicts and natural disasters around the world resulting in a growing number of refugees and asylees. Additionally, pertussis, a typical vaccine-preventable disease, is on an increasing ascent, and has reached epidemic levels throughout the world. I study globalization via population mobility, as my primary independent variable, because of its important role in the emerging landscape of a "globalized world," to include international travelers, immigrants, refugees, and asylees. I study pertussis rates as my dependent variable.

In the past 30-40 years, the Unites States has experienced a rapid increase in the number of immigrants and international travelers. For instance, in 1970, there were approximately 9.6 million immigrants living in the United States, while in 2012 that number peaked at nearly 40.8 million, increasing by 447,000 individuals from the year before (Nwosu, Batalova, & Auclair, 2014). As a result, Unites States policy on immigration regulation is in constant transformation. Concomitantly, pertussis incidence in the US has also climbed consistently since the 1970s. Specifically, in 1976, there were only 1,010 cases of pertussis across

the country (the lowest number in recorded history); in 2012, there were 48,277, the highest number since 1955 (CDC, 2014). Examples such as this have prompted various changes to vaccination and infectious disease programs and policies in this country.

Though I acknowledge the policies that are presently in place regarding immigration and infectious diseases, I am ultimately interested in reducing the burden of disease (pertussis) in the United States by uncovering an association between that burden and population mobility.

Methods

I used a mixed methods approach to this research. First, between January and June 2014 I performed a systematic review of the literature related to globalization and human mobility, as well as population health, infectious disease, and pertussis. The literature review included a scan of peer-reviewed and grey literature documenting the associations between globalization and health.

Second, I conducted a search of relevant websites, including: international organizations (i.e WHO, UNICEF, UNAIDS, IMF, CDC, and the World Bank), public-private partnerships (i.e GAVI Alliance), independent research institutions (i.e. CGD, IHME, ODI, CSIS, IDRC, and GHSi), international aid agencies (i.e. USAID), and private philanthropy organizations (i.e. Bill & Melinda Gates Foundation and The Clinton Global Initiative).

In all, I reviewed 127 articles, briefs, reports, and news media pieces. Sources were only retained if they contained substantive qualitative and/or quantitative analysis of the global burden of disease (pertussis), infectious diseases in general, globalization, and an association between globalization and health. Furthermore, my quantitative exploration surveyed databases (secondary data) from the U.S. Census Bureau, U.S. Department of Commerce, CDC, United Nations and the World Health Organization. I analyzed these data using Stata and applied multiple regressions with pertussis cases as my dependent variable, non-immigration (international travel), immigration (documented), refugees, and asylees as my primary independent variables, and I controlled for state population, state median household income, state GDP, state unemployment, state uninsured rate, and state health ranking as secondary independent variables.

Overall, my research was supported by three major studies; one that helped me better define globalization, and two others, which showcase and rationalize the relationship between globalization and health (Martens et al., 2010; Huyun et al., 2005; & Woodward et al., 2001). I combined their models to produce an overarching framework that I used to structure my own investigation (***Figure 2***).

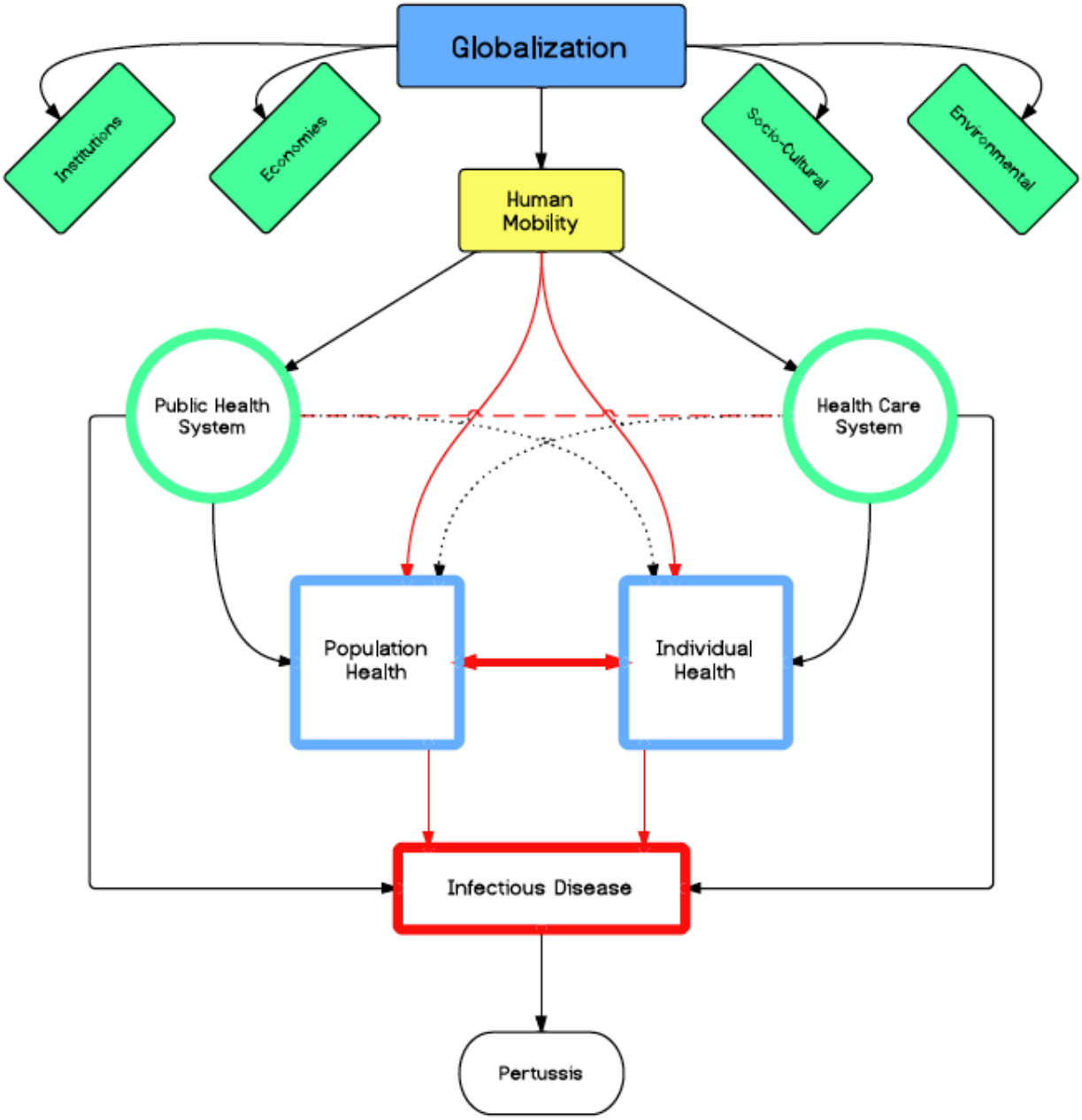

Figure 2. Conceptual Framework: Relationship Between Globalization and Health. Adapted from Huyun et al. (2005) and Woodward et al. (2001).

Analysis

Global Burden of Disease for Pertussis

In the middle of the twentieth century, the predictions for control – and even eradication – of pertussis seemed encouraging. As a result of widespread immunization programs in the 1940s and 1950s, the global prevalence of pertussis was reduced substantially. As a typical example, mean incidence rates in the United States were brought down from an average of about 143 cases/100,000 people in 1922-1931 to roughly 1 case/100,000 people by 1972-1981 (CDC, 2014; U.S. Census Bureau, 2014). Prior to these new immunization practices, pertussis was devastating causing about 71,000 deaths from 1922 to 1931 in the United States; in contrast, the death toll was reduced to 56 deaths between 1982 and 1991in the U.S. (Vital Statistics of the United States, 2013a/b/c).

Despite widespread success of vaccination programs that contributed to drastic reductions in morbidity and mortality related to pertussis infections around the world, there continue to be concerns. First, despite being a vaccine-preventable disease, the annual burden of pertussis morbidity and mortality remains staggering; currently, there are an estimated 16 million cases of pertussis and about 195,000 deaths, globally, per year (CDC, 2014a). Second, pertussis seems to be resurgent in countries that claim high immunization coverage, specifically in developed countries such as the United States and

Australia, both of which claim >95% coverage for children over 24 months (CDC, 2013; Department of Human Services, 2014).[2]

Despite a decrease in worldwide rates of pertussis over the past 20 years, 2012 experienced the worst rates in recent history, with a total of 249,746 cases reported from the 194 member countries of the World Health Organization. More than one fourth of those countries reported zero pertussis cases that year while the top ten reported 177,914 cases, more than 71% of the global burden that year.[3] Interestingly, those same 10 countries have consistently had more than 55% of worldwide cases each year since 1998.[4] This is a significant change from the 1980s when these same 10 countries only accounted for approximately 20-25% of total cases of pertussis worldwide. The epidemiology of the disease is clearly changing.

(***Figure 3.***)

The data highlighted above hold true, in spite of the fact that pertussis incidence decreased worldwide over the past 20 years. Although data show that resurgence in developed countries is not universal, I must emphasize the consistent increase in certain countries is a cause for trepidation.

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[2] United States (children between 19-35 months); Australia (children 24-27 months)
[3] United States, India, Australia, the Netherlands, the United Kingdom, Nigeria, the Russian Federation, Papua New Guinea, Chile, and New Zealand
[4] Exception: 2004, 43%; 1999, 52%

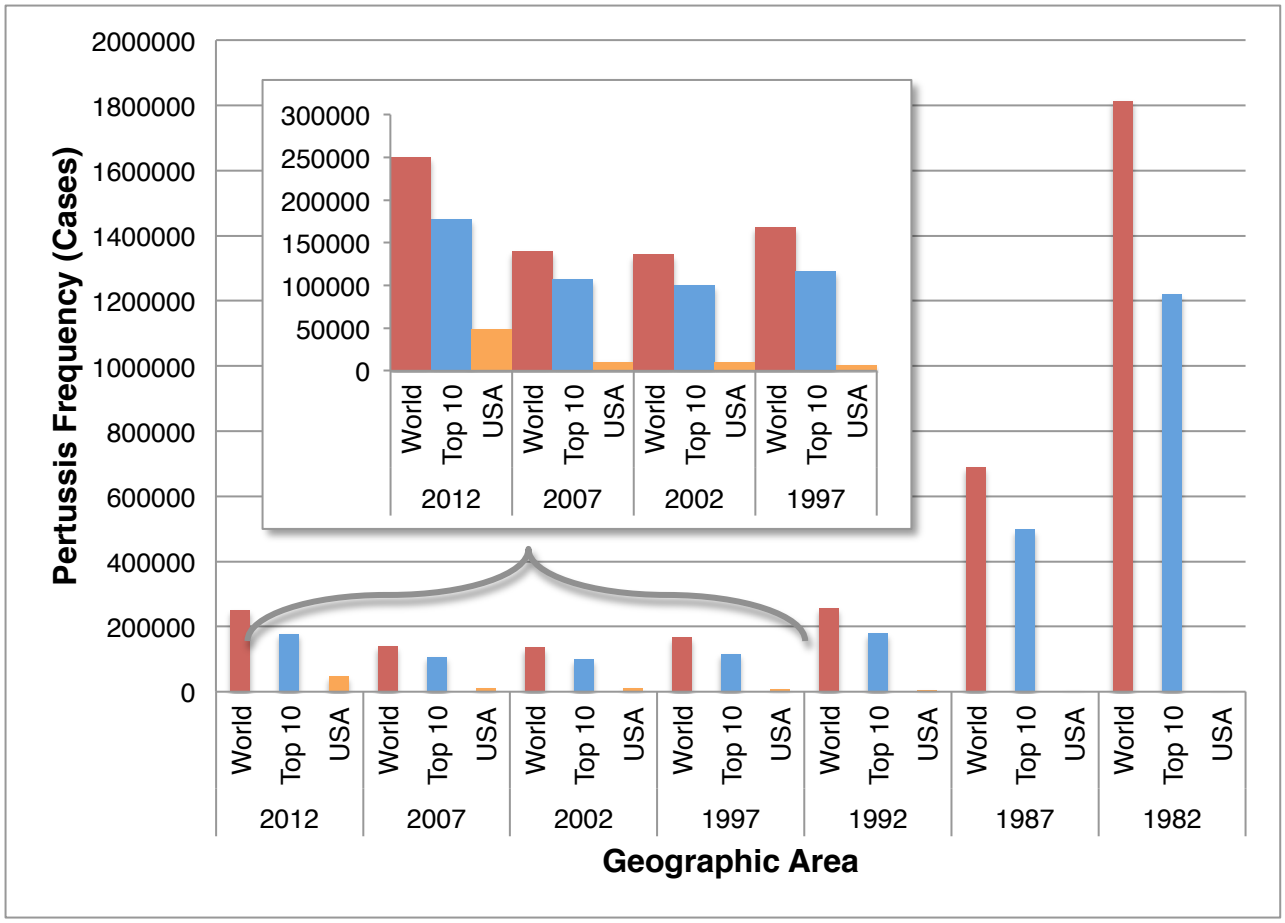

Figure 3. Pertussis frequency in selected years, by geographic area**.** This chart shows the relationship between certain geographic areas (worldwide in selected years, top 10 countries in selected years, and the Unites States in selected years) and pertussis frequency.

Here I have briefly described changes in global pertussis burdens over the past century. Using a combination of pertussis case data compiled by the CDC and WHO along with population data gathered by the United Nations, I calculated absolute incidence rates ([annual cases/population]*100,000 individuals), and used those rates to detect global trends in pertussis burden. Though I concede that incidence data are known to be incomplete and subject to deviation between countries, these data allowed me a first pass at characterizing the magnitude and extent of pertussis burden around the world. Specifically, when viewed from a global perspective, the history of pertussis in the recent past is marked by substantial heterogeneity.

History of Pertussis in the United States

The United States has been hit particularly hard with a reemergence of pertussis over the past decade, and has seen a consistent climb in incidence since the record low of 1,010 cases in 1976. Conversely, the highest recorded number of annual cases was in 1934, with more than 260,000 nationally.

After being isolated in 1906 (The College of Physicians of Philadelphia [TCPP], 2014), *Bordetella pertussis* ravaged the United States causing nearly 7,000 deaths per year in the 1920s (Vital Statistics of the United States, 2013a). As the 1920s and 1930s progressed, multiple vaccines for pertussis were introduced but proved to be unsuccessful. But in 1939, scientists Pearl Kendrick and Grace Elderling from the Michigan Department of Public Health published a

research report that showed the annual attack-rates per 100 children were 2.3 in a vaccinated group versus 15.1 in the control group (Kendrick & Elderling, 1939). In addition, they found that if someone who was vaccinated did indeed get the disease, its health effects were substantially milder than someone who did not get the vaccine (TCPP, 2014). This propelled the vaccination era against *B. pertussis* and other vaccine-preventable diseases around the world, particularly in the United States.

By 1948, the vaccination for pertussis was combined with those for diphtheria and tetanus, creating the first DTP (diphtheria, tetanus, and pertussis) immunization. DTP was extremely successful for decades and led to an incredible decrease in pertussis incidence.

Through time, the public became increasingly worried about the adverse reactions DTP vaccines were causing, such as rash, fever and vomiting, despite its genuine success in reducing morbidity and mortality related to pertussis. Consequently, in 1999 the DTaP (diphtheria, tetanus, and acellular pertussis) vaccine was introduced. Because the DTaP vaccine used only certain parts of the pertussis bacteria and not attenuated whole-cell bacteria, it resulted in fewer side effects than the whole-cell components used in DTP.

As we moved into the 21st century, pertussis incidence seemed to remain consistent, with cyclical peaks every 2-5 years. In 2005, the United States saw approximately 28,000 reported cases. Then, in 2010, California reported the

worst outbreak in that state in 35 years; between January 1 and June 30, the California Department of Public Health reported 1,337 cases in that state alone, a 418% increase from the same period the year before, with 5 attributable deaths (CDPH, 2014). What is more worrisome, between January 1 and June 24, 2014, the CDPH reported 4,558 cases of pertussis, more than 3 times the amount reported over the same period in 2010; and the CDC has reported almost 10,000 cases across the country, representing a 24% increase nationally compared with the same time period in 2013 (CDC, 2014).

The recent on-going pertussis epidemic in the United States reflects an evolving epidemiology of pertussis. Although acellular pertussis vaccinations provide excellent, short-term protection, early waning of immunity might be contributing to increasing population level susceptibility. As Cherry (2012) asserts, “we should maintain some historical perspective on the renewed occurrences of epidemic pertussis and the fact that our current DTaP vaccines are not as good as the previous DTP vaccines.” Nevertheless, vaccination continues to be the single most effective strategy to reduce morbidity and mortality caused by pertussis. Although some U.S. states have noted an incidence similar today to that of the 1940s and 1950s, today’s national incidence is about one twenty-third of what it was during an epidemic year in the 1930s.

What is Globalization?

My understanding of globalization is supported by Martens et al. (2010), where globalization refers to, "the intensification of cross-national interactions that promote the establishment of trans-national structures and the global integration of cultural, economic, ecological, political, technological, and social processes on global, supra-national, national, regional, and local levels." I believe globalization is truly a historical process that has recently been rebranded; it started with the first movement of people out of Africa into other parts of the world but today has become nothing short of the status quo. Traveling short, then longer distances – migrants, merchants, and others have always taken their ideas, customs, and products into new lands. In fact, the commingling, borrowing, and acclimatization of outside influences can be found in many areas of human life today.

History of Globalization

Historically there were four main intentions that drove people to leave the sanctuary of their family and village: conquest (the desire to ensure security and extend political power), prosperity (the search for a better life), evangelizing (spreading the word of their God and converting others to their faith), and a more mundane but still powerful force, curiosity and wanderlust that seem basic to human nature (Chanda, 2002). Therefore, the principal agents of globalization were soldiers (and sailors), traders, vicars and explorers.

The cast of characters whose drive and determination have established associations of both control and cooperation has changed with times. Small bands of traders carrying their commodities on their backs or in boats have been replaced by giant enterprises. In place of solitary pilgrims and priests have come vast religious organizations that spread their beliefs, along with their languages, literatures and architecture. The few intrepid adventurers and travelers of past centuries who brought distant societies together have given way to thousands and even millions of refugees, asylees, and immigrants fleeing across borders, as well as hundreds of millions of tourists roaming the world. All these comings and goings deepen and broaden the connections among far parts of the world and facilitate the transmission of goods, ideas and cultures.

Today's Globalized World

Today, airplanes, cheap telephone service, email, computers, huge oceangoing vessels and instant capital flows have all made the world more inter-connected than ever. Multinational corporations manufacture products in many countries and sell to consumers around the world, often far away from the site of the factory. Money, technology, and raw materials move ever more effortlessly across national borders. Along with products and finances, ideas and cultures circulate more freely as well. As a result, laws, economies, and social movements are forming at the international level. Many politicians, academics, and journalists treat these trends as both inevitable and, most often, welcome.

But for billions of the world's people, business-driven globalization means uprooting old ways of life and threatening livelihoods and cultures.

The most influential force for diffusing ideas across borders is the revolution of information technology in recent decades. The telephone, television and the Internet have been the key tools. Today, vast amounts of information in multiple formats are transmitted at the speed of light. Moreover, a three-minute call from New York to London costs less than a dime, instead of the $300 it cost in 1930. This dramatic drop in the price of telecommunications has made the benefits of the information explosion available to much of humanity.

The term globalization encompasses a range of social, political, and economic changes. Some disciplines including anthropology or sociology focus on cultural changes of growing interconnectedness, such as the expansion of brands and the increasing ease of travel. Other disciplines such as economics track the exchange of finances, goods and services through expanding global markets. Still other disciplines such as political science examine the role of international political institutions like the United Nations and the increasing power of transnational corporations. While one can try to dissect each of these topics to measure the changes of globalization, they are woven together in a complex manner, making it difficult to summarize positive or negative effects. Given these points, it is safe to say that globalization creates new markets and wealth, even

as it causes widespread suffering, disorder, and unrest. It is both a source of repression and a catalyst for global movements.

Globalization's Effect on Health

Although globalization is not new, interest in its potential health effects is relatively recent. Surely, understanding how globalization affects health is not easy; the concept itself is multifaceted and complex, almost to the extent that it defies study for causal relationships. The minimal evidence that does exist is piece-meal and as a researcher, I was forced to build something new; the problem is mainly one of organization and developing a coherent story and outcome.

The consequences of the collateral movement of infectious disease pathogens with mobile segments of human society have had profound effects on the course of human history. Epidemics of infectious disease have influenced the outcome of exploration, military adventures, and colonization, as well as industrial development and the arts. Before the acceptance of Germ Theory in the mid-1800s, the epidemics, and the fear they generated, lead to futile efforts to limit or prevent the importation of infectious diseases in the Western world. In spite of the fact that the actual nature of contagion was undefined, even then, the association between the arrival of individuals and goods and subsequent epidemics was clearly recognized.

Generally, I found the impacts of globalization on health, as whole entities, cannot be inferred from one or two independent variables. Moreover, the task of identifying specific health impacts that are a direct consequence of globalization processes is extremely complicated; some consequences of globalization increase human contact, while others may decrease human contact. Thus, I decided to focus my efforts particularly on human mobility and infectious diseases, particularly pertussis.

Today, while the social and economic impacts of globalization are contentious, the effects on health are clearer. The breakdown of barriers of human movement has enhanced the spread of infectious pathogens to susceptible populations across the planet. Recent examples include West Nile Virus in the late 1990s, SARS in 2004, and MERS this year.

Our Mobile World

Currently, travelers and other mobile populations, such as migrants and asylum seekers are an expanding group of global interest. Concerning this group, health issues often exist between their place of origin and their possible destination. The effects of those health outcomes can be observed at both the individual and population levels. Association among these health and disease patterns influences the epidemiology of certain diseases globally and particularly, in nations receiving these individuals. While specific disease-based outcomes vary between population and location, general epidemiological principles can and

should be applied to any situation where numbers of individuals move between differences in disease frequency.

Most importantly, increased international travel has been an integral component of the growing mobility process of globalization. In much of the developed world, infections that were historically significant causes of illness and death have decreased in both incidence and prevalence or been eliminated. This was accomplished through sanitation, immunization, antibiotic therapy, and improved health care. This creates enormous differences in the prevalence of certain conditions between locations. In a mobile world, travellers and migrants crossing through these gaps can become the source for outbreaks of a disease.

Moreover, the speed of travel today has rendered most existing medical assessments irrelevant in identifying travelers and migrants who may be ill with communicable infectious diseases. High-speed air travel allows the international movement of individuals within the incubation period of virtually all of the contagious infections, including pertussis.

Managing the population-based risk due to the classical infectious diseases in mobile populations has historically been accomplished through combined attempts at screening for the disease and providing treatment or reducing the likelihood of outbreak by immunization, preventative therapy, or isolation and restricted movement. An underlying requirement for each of those practices was the access to the population at risk in addition to early identification

of a disease in an individual. Some travelers and mobile populations are required to present documentation for medical reasons (e.g., verification of certificate for yellow fever vaccination or immigration medical screening). Yet for most international travelers and mobile populations, there are no mandatory or required medical procedures related to their journey. The captains of aircraft and oceangoing vessels are required to report the presence of ill passengers on arrival at an international port. However, as noted above, if the infected person travels within the incubation period of the disease, they may be clinically healthy despite being infected and potentially contagious.

As population-based prevention and control programs become more successful, the incidence of many infectious diseases has decreased or in some cases, such as polio in North America, almost disappeared. Consequently, the arriving population cohorts from areas of the world where these diseases still occur may be the origin of outbreaks. Although the size of outbreaks of this type has been small, they do pose significant public health challenges. First, their relative rarity may hinder recognition and diagnosis. Primary health care providers, relying on their own experience and public health surveillance information, may not be aware that many diseases eliminated or controlled in their local environment continue to circulate in mobile populations. Second, as the perceived risks of some controlled infectious diseases diminish, there may be resistance to preventive interventions such as immunization. This practice may

leave groups of individuals with limited protection should virulent disease be introduced by mobile populations or travelers, as exemplified by the measles outbreaks now occurring throughout the United States.

The etiology of the current pertussis outbreak in California, though technically unknown, may also be a great case study for this. Though there has been no confirmation that a traveler or migrant has brought the disease into the United States, California is home to some of the largest subsets of families who are refusing to vaccinate their children in addition to having one of the busiest airports in the world (Los Angeles) and most utilized borders crossings as well (with Mexico). The association has yet to be proven empirically, but it is easy to speculate that some relationship does indeed exist.

Quantitative Procedures

Numerically, I compare state level data, including the population mobility rate,[5] median household income, unemployment rate, uninsured rate, and state health ranking, over a number of years, to the pertussis rates in those years. I found that an association does exist between population mobility rates and pertussis rates, at the state level.

I estimated my regression equation with my dependent variable and independent variables in log-log functional form; the only exception was state health ranking which was kept in natural units. The logarithmic form for the variables allows a unit-free interpretation and comparison of their estimated coefficients. For the log-log functional form, the estimated coefficient *x* for an independent variable can be interpreted as a 1% increase in the independent variable, other things being equal, leading to a *x*% change in the sum of the percentage increase in the level of the dependent variable. For the log-level functional form in state health ranking, the estimated coefficient *x* for the independent variable can be interpreted as a 1 unit increase in the state health ranking, other things being equal, leading to a *x*% change in the sum of the percentage increase in the level of the dependent variable.

[5] I calculated population mobility rates as the sum of international travelers, documented immigrants, refugees and asylees, divided by the population of each state, each year.

I report one regression with number of pertussis cases as the dependent variable. I regressed aggregate population mobility rates (international travel, migration, refugees, and asylees) on the number of pertussis cases, while controlling for median household income, uninsured rate, unemployment rate, and state health ranking. All analyses were conducted using Stata version 13.1.

Quantitative Results

Table 1. shows the mean and SD of the dependent and all independent variables in natural units. ***Table 2.*** presents the results of the regression equation. All of the significant coefficients in the regression equation had the expected signs in terms of the relationship between the independent and dependent variables. The explained variation, or coefficient of determination R^2, ranged from 13.1% (adjusted) to 13.6% (not adjusted). The independent variables varied in both size of coefficient and level of significance or *p* value.

The aggregate mobility was found to be positively and significantly associated with pertussis cases ($p = 0.000$) after controlling for other variables. When international travel and combined migration, refugees, and asylees were entered separately in the regression (not pictured), I found that both international travel and combined migration were not significantly associated with pertussis cases. The rate of uninsured people per state was found to be an insignificant ($p = 0.651$) predictor of pertussis cases. The coefficient of aggregate population mobility was 0.159. The coefficients of state unemployment rate (0.566,

p=0.000), state median income per household (-1.505, *p*=0.000), and state health ranking (-0.037, *p*=0.000) were also found to be significant predictors of pertussis cases per state.

Table 1.

Summary Statistics[a] Including Mean and Standard Deviation of All Variables

Variable	N	Mean	SD
Pertussis Cases	1047	295	560
International Travelers[b]	850	581	1,313
Immigrants (documented)[b]	1000	18	39
Refugees[c]	206	18	20
Asylees[c]	668	15	38
State Median Household Income[c]	1050	53	81
State Uninsured Rate	1050	13.1	4.9
State Unemployment Rate	1100	5.7	1.9
State Health Ranking	1050	25.5	14.4

Note. [a] Summary statistics are reported in natural units. [b] Reported in 1000s. [c] Reported in 100s. [d] Reported in 10000s. Sources of variable data are listed in the **Appendix**.

Table 2.

Results of Multiple Regression Analysis of Select Factors That Influence the Number of Pertussis Cases in the United States

	Regression		
Variable	*Coef.*	*SE*	*p*
Constant	12.836	4.077	0.002
Aggregate Population Mobility Rate[a]	0.159	0.030	0.000
State Median Household Income[a]	-1.505	0.378	0.000
State Uninsured Rate[a]	-0.077	0.171	0.651
State Unemployment Rate[a]	0.566	0.131	0.000
State Health Ranking[b]	-0.037	0.004	0.000
R^2/*Adj.* R^2		.14/.13	
F Statistic (Overall)	31.10		0.000

Note. [a] Logarithm, [b] Natural unit.

So what does this mean? Quantitatively, the statistical analysis presented supports my hypothesis that population mobility is significantly associated with pertussis cases in the United States. Additionally, ample qualitative evidence supports an association between the two. With the movement of people, there is undoubtedly a risk for individuals or families to carry disease from one place to another. Borders around the world remain open to allow the brightest and best to enjoy international travel. With that comes the risk of lower-class families looking for a better life; a current outbreak of pertussis in migrant farm workers in rural Washington support this point (Crescent Bar Chronicle, 2014).

Discussion

Limitations and Further Research

Throughout my research, I encountered several limitations. Foremost, the global scale of this project lends to incomplete or inaccurate data. It may be argued, for example, that pertussis cases are underreported globally. This very well may be true, but should not cause major bias in my research, because other researchers would be using the same data. Nevertheless, I recognize that future contributions of data to global repositories may indeed change the results found here. Second, due to the sizeable scale of the overall project, I feel this report should be categorized as a first step, rather than a detailed analysis of a particular issue, that can stand as the foundation for future studies. I further recognize that each subset of my analysis could indeed foster its own exploration. Lastly, I dealt with time constraints. I feel if I narrowed this research further, I may have had more success within the time allotted.

Further research on the subject of globalization and health is necessary. Globalization, especially population mobility, is increasingly in the news and scholarly literature. There ought to be analyses done focusing on subsets of mobile populations, such as migrant farm workers or international travelers, and their direct effect on the health outcomes of their destination. Additionally, pertussis is indeed on the rise in the United States. There need to be more detailed investigations as to why this is occurring. Although multiple theories

currently exist, a consensus has yet to be reached. This will be necessary to help prevent further infection.

Conclusion

Herein I considered the impact of a specific process of globalization known as population mobility on the increase in pertussis infections in the United States. Looking at the results, the association between population mobility and infectious disease rates can be seen as more complex than originally thought. I have highlighted that pertussis is still a cause for morbidity and mortality around the world, including highly developed nations such as the United States. Additionally, I have shown the epidemiology of pertussis is ever changing. Globally, the top ten countries reporting pertussis cases are different than they were thirty years ago. Moreover, population mobility has increased exponentially. International travelers have exceeded one billion, and conflicts and natural disasters have pushed entire populations out of their homes and into neighboring countries, if not to other parts of the world.

My findings offer a unique opportunity to prepare for the future. The current lack of research on specific associations between globalization and infectious diseases in the United States does not mean they do not exist. On the contrary, I believe these associations are strong, and therefore should be studied further. The next step should be to focus on specific associations that have the greatest threat for epidemic and pandemic results in the population of the United

States. Achieving this will require immediate action and support by the public, global health professionals, medical providers, and health policy-makers alike. An interdisciplinary approach between these often-separated groups is key to success.

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Appendix

List of sources for all data utilized in statistical analyses, listed by variable.

1. *Pertussis Cases*

World Health Organization. (2014, May 24). Data, statistics and graphics: Disease incidence. *Pertussis Reported Cases.* Retrieved from http://apps.who.int/immunization_monitoring/globalsummary/timeseries/tsincidencediphtheria.html

2. *International Travelers*

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