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BETTER UNDERSTANDING INFLUENZA VACCINATION IN U.S. CHILDREN: DETERMINANTS, FAMILY IMPACT, AND POLICY

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ABSTRACT

Child influenza vaccine uptake in the United States is substantially lower than that of other child vaccines and has plateaued despite high risk of complications in young children and affordable, safe, effective vaccines. This dissertation sought to better understand determinants, family impact, and policies for influenza vaccine uptake in US children. Chapter One outlines literature on influenza, its vaccines and why children under 5 (especially under 2) years are a high priority. Chapter Two presents analysis of provider-verified data nationally-representative of children under 2, focusing on those up-to-date on a large vaccine series except influenza. Major findings are that parental compliance with child vaccine recommendations and lack of vaccine hesitancy may not necessarily predict child influenza vaccination and maternal college education may not confer improved influenza vaccine behavior for Black and Hispanic children though it does for White children. Chapter Three presents analysis nationally-representative of working US adults on reduced illness-related work loss associated with household child influenza vaccination. Adults with sick leave and a vaccinated (versus not) household child may miss one less work day annually, an association five times larger than those without sick leave. Sick leave is distributed inequitably, suggesting those with lower pay or education bring influenza to work and are less able to care for themselves or their children with influenza. Chapter Four is an analysis of system-level policy alternatives states can use to improve influenza vaccination uptake of young children. The final recommendation is enactment of mandatory annual influenza vaccine requirements for children 6-59 months old for childcare and pre-school entry, allowing sufficiently rigorous-to-obtain religious exemptions. Lessons learned, best practices and mechanisms to incentivize states to enact such policy are discussed. Chapter Five ends with remarks on the overall contribution of the dissertation to better understanding influenza vaccination of US children, as well as on future research directions and a call-to-action for the Health in All Policies approach.

TABLE OF CONTENTS

List of Figures vi

List of Tables vii

Acknowledgements viii

Chapter 1 Introduction 1

Influenza 2
Influenza vaccination: the best measure preventing influenza 4
Influenza vaccine types 4
Influenza vaccine effectiveness 6
Influenza vaccine safety 7
Influenza vaccine supply and availability 10
Young children: high-risk for influenza, high-priority for vaccination 12

Chapter 2 A hidden vulnerable population: determinants of young children up-to-date on vaccine series recommendations but not those for influenza vaccines 16

Abstract 16
Introduction 18
Background 18
Statement of research aims 19
Literature review 20
Methods 25
Data source 25
Dependent variable 27
Determinants of influenza vaccination 28
Study population 30
Analysis 31
Results 33
Bivariate (unadjusted) results 36
Multivariate (fully-adjusted) results 39
Intersectional (fully-adjusted) results 43
Discussion 49

Chapter 3 The association of child influenza vaccination status with household adult work loss due to illness 56

Abstract 56
Introduction 58
Background 58
Statement of research aims 59
Literature Review 59
Methods 61
Data source 61
Dependent variable 63

Independent variables of interest....63
Covariates....64
Study population....65
Analysis....66
Results....67
Bivariate (unadjusted) results....69
Multivariate (adjusted) results....71
Discussion....76

Chapter 4 System-level policy alternatives for improving influenza vaccine uptake in young U.S. children....80

Abstract....80
Introduction....82
Background....82
Statement of research aims....87
Methods....88
Policy alternatives....89
Definitions of relevant terms....89
Policy Alternative 1 – a mandatory approach: influenza vaccine requirements for preschool and childcare....94
Policy Alternative 2 – a voluntary approach: on-site influenza vaccination in preschool and licensed organized childcare facilities....95
Projected impact....96
Assumptions....96
Reduced influenza cases (illness)....99
Reduced influenza-related healthcare visits....100
Reduced influenza-related hospitalizations....101
Reduced influenza-related mortality....101
Reduced influenza-related economic burden....102
Feasibility....103
Stakeholder reception....106
Recommendation and discussion....109

Chapter 5 Concluding remarks....116

References....122

LIST OF FIGURES

Figure 2-1. Model-predicted probability (with 95% confidence intervals) of "series but not flu" outcome among main coefficients from Table 2-5. 43

Figure 2-2. Model-predicted probability (with 95% confidence intervals) of "series but not flu" outcome among two-way interaction term subgroups: child's race/ethnicity*mother's education From Table 2-5. 46

Figure 2-3. Model-predicted probability (with 95% confidence intervals) of "series but not flu" outcome among three-way interaction term subgroups: child's race/ethnicity*mother's education, stratified by mother's marital status from Table 2-5. 48

LIST OF TABLES

Table 2-1. Summary of published literature on factors associated with higher influenza vaccination uptake in US children. 20

Table 2-2. Descriptive statistics of study population, U.S children aged 6-23 months old (N=7,246), 2011 NIS. 34

Table 2-3. Correlates of vaccination up-to-date variables, U.S children aged 6-23 months old (N=7,246), 2011 NIS. 37

Table 2-4. Change in predicted probabilities of up-to-date vaccine status, multivariate linear probability model regression, U.S children aged 6-23 months old (N=7,246), 2011 NIS. 41

Table 2-5. Predicted probabilities of up-to-date vaccine outcomes among intersectional interaction term subgroups, multivariate linear probability model regression, U.S children aged 6-23 months old (N=7,246), 2011 NIS. 44

Table 3-1. Descriptive statistics of study population, working US adults with children in the household (N=7,938), 2014 NHIS 68

Table 3-2. Bivariate statistics of work loss days stratified by covariates, working US adults with children in the household (N=7,938), 2014 NHIS..70

Table 3-3. Incident Rate Ratios of work loss days from multivariate zero-inflated negative binomial regression, working US adults with children in the household (N=7,938), 2014 NHIS...73

Table 3-4. Predicted work loss days due to illness or injury (previous 12 months) among interaction term subgroups from Table 3 (Model 4), working US adults with children in the household (N=7,938), 2014 NHIS 76

Table 4-1. High-level summary of projected national impact, feasibility, and stakeholder reception of proposed policy alternatives relative to status quo (70% national uptake)..109

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Chapter 1

Introduction

Vaccination is one of the greatest preventive health achievements in human history - other than improvements in water sanitation, no other public health intervention has had a greater effect on population growth and mortality reduction (Plotkin, Orenstein, & Offit, 2008). It is estimated that, since routine mass immunization began in the United States in 1924, vaccines have conservatively prevented at least 103 million cases of communicable diseases (van Panhuis et al., 2013). A vaccine-preventable disease of importance is influenza, and young children are arguably the most important population group as it relates to influenza. Not only are young children at increased risk group for severe influenza complications simply due to their age (Neuzil, Zhu, et al., 2002), but young children play a large role in the transmission of influenza to family members/caregivers (Teo, Nguyen-Van-Tam, & Booy, 2005), and to the community (Jordan et al., 2006). Moreover, prevention of disease in young children is crucial given that early childhood health is a “critical period” which can have lasting, lifelong effects on health (Ben-Shlomo & Kuh, 2002) and optimal childhood health and development are widely recognized as key determinants of health and well-being throughout the life course (National Research Council & Institute of Medicine, 2004). Yet, influenza vaccination uptake in children in the US is sub-optimal (Lu et al., 2013) and lower than uptake of other recommended childhood vaccines. Below, characteristics of influenza disease and of influenza vaccines in the United States are detailed, leading to a summary of the context of influenza and influenza vaccination in US children. Then, three chapters follow describing empirical analyses to better understand the determinants of, family impacts of, and policy solutions to influenza vaccination in young US children. The last chapter ends with remarks on the overall contribution of the dissertation to these aims, future research directions, and a call-to-action for the Health in All Policies approach.

Influenza

Influenza refers to a variety of viruses from the family *Orthomyxoviridae*, which includes influenza types A, B, and C. Influenza types A is associated with moderate to severe illness in humans, affects all age groups, and also affects animals, whereas influenza Type B causes milder disease and only affects humans (primarily children). Influenza type C is rarely reported in humans and has not been associated with epidemics. The influenza virus mutates at a rapid pace. Typically, these mutations are minor changes that do not prevent most humans from having some degree of immune protection but do often result in epidemics (i.e., "seasonal influenza," which, in the United States, usually occurs from late fall through early spring). However, the virus occasionally undergoes major changes such that most adults have no immune protection and global pandemics can occur; pandemics have occurred five times in the last 100 years and most pandemics results in moderate to severe mortality and morbidity. The virus is primarily spread through respiratory secretions. Roughly 50% of persons infected with influenza will develop "classic" influenza, which entails abrupt onset of fever, muscle pain, weakness/exhaustion, sore throat, a dry cough, and headache lasting up to 5 days (typically 2-3). Other infected persons experience complications, the most common of which is pneumonia – typically a secondary bacterial pneumonia, but rarely influenza can cause primary influenza viral pneumonia which has a high fatality rate. Other than pneumonia, less common complications from influenza include heart inflammation, chronic bronchitis, and other chronic diseases of the lungs. (Centers for Disease Control and Prevention, 2015a).

Data from 1976 through 2001 estimate that, each year in the United States, influenza results in anywhere from 18,908 to 193,561 hospitalizations (Thompson et al., 2004), and data from 1976-2007 estimates 3,349 to 48,614 deaths (Centers for Disease Control and Prevention, 2010a). The mortality burden is mainly among those aged 65 years or older, though the hospitalization burden is comparatively high in young children (Centers for Disease Control and Prevention, 2010a; Thompson et al., 2004). The burden varies from year to year due to the genetic makeup of the particular viruses in circulation, the susceptibility of the population to circulating viruses, and even weather conditions (Fraaij & Heikkinen, 2011), though the true burden may be underestimated given the difficulties of directly attributing mortality to influenza (Centers for Disease Control and Prevention, 2011; Curwen, Dunnell, & Ashley, 1990). Additionally, influenza puts a tremendous burden on the U.S. economy – influenza-like illness is estimated to cause nearly half of lost workdays during the influenza season (Nichol, D'Heilly, Greenberg, & Ehlinger, 2009), equating to an estimated annual cost of $87 billion (2003 dollars) due to influenza related illness, lost work time, and loss of life (Molinari et al., 2007). These burdens are higher among certain populations considered to be "high risk" for influenza complications resulting in hospitalization or death. Namely, this includes five population groups – (1) children younger than 5 years but especially younger than 2 years; (2) adults 65 years and older; (3) women who are pregnant (or up to two weeks post-partum); (4) residents of nursing homes and other long-term care facilities; and (5) American Indians and Alaskan Natives – though it also broadly includes individuals with certain medical conditions, including asthma, neurological/neurodevelopmental conditions, chronic lung disease, heart disease, blood disorders, endocrine disorders (such as diabetes), kidney disorders, liver disorders, metabolic disorders, immunocompromised persons, children receiving long-term aspirin therapy, and persons with a Body Mass Index of 40 or greater (Centers for Disease Control and Prevention, 2015b).

Influenza vaccination: the best measure preventing influenza

A measure exists to prevent loss of life and burden associated with influenza – influenza vaccination. There are other methods for preventing influenza, such as avoiding close contact with sick persons, frequent hand washing with soap and water, avoiding touching one's eyes, nose, and mouth, cleaning and disinfecting surfaces and objects that may be contaminated, and even use of antiviral preventive prescription drugs for people who are caring for someone with influenza (Centers for Disease Control and Prevention, 2014e), though influenza vaccination is the most effective method (Cox & Subbarao, 1999). Prior to 2010, influenza vaccination was recommended annually to high-risk populations, but in 2010 the CDC updated their recommendation to include all persons 6 months or older annually given improvements in cost and supply of the vaccines and their continued safety and effectiveness (Fiore et al., 2010).

Influenza vaccine types

There are three categories of recommended vaccines available. The first category of influenza vaccines are inactivated influenza vaccines (IIVs) which refers to influenza vaccines that contain influenza virus grown in culture media which is then inactivated (killed) through the use of heat and/or chemicals (Centers for Disease Control and Prevention, 2015b). There are multiple different IIVs which are approved for people of different ages, though together they cover the entire recommended population group of all persons 6 months and older. The most common is the trivalent inactivated influenza vaccine (TIV, also sometimes referred to as the IIV3), which contains three inactivated strains of influenza virus: two Type A viruses and a Type B virus. The TIV is most commonly administered via intrasmuscular injection, though there are also jet injection TIVs and intradermal TIVs approved for working age adults only. There is also a high-dose TIV shot licensed for persons 65 or older to specifically overcome lowered vaccine response observed in this population. Most TIVs are grown in fertilized chicken eggs with the exception of one that is grown in a cell line of canine kidney cells. Recently, the United States Food and Drug Administration licensed a quadrivalent IIV shot which contains an additional influenza B virus. Children 6 months through 8 years of age who are receiving their first ever TIV should receive two doses of the vaccine at least 1 month apart to boost immune response (Centers for Disease Control and Prevention, 2014, 2015a).

The second category of influenza vaccines are live, attenuated influenza vaccines (LAIVs). These vaccines contain influenza viruses that are alive and can thus reproduce in the body and induce immunity more closely mimicking the body's natural immune response, but are attenuated (weakened) so they only cause mild "disease" (Centers for Disease Control and Prevention, 2015b). The LAIV has been offered in both trivalent and quadrivalent formulations, is licensed for persons 2 through 49 years of age, and in the past has been preferentially recommended for healthy children ages 2 through 8 years due to a potential higher efficacy in this age group (Centers for Disease Control and Prevention, 2014, 2015a).

The last category of influenza vaccine is comprised by one vaccine – the recombinant influenza vaccine. Recombinant vaccines refer to those that contain antigen produced by genetic engineering technology (Centers for Disease Control and Prevention, 2015b). The recombinant influenza vaccine is licensed for adults only; it contains an isolated protein from naturally-occurring vaccine virus that is combined with portions of another virus that replicates well in insect cells, the product of which is then injected and grown in an insect cell line. This replicated influenza protein is then extracted and purified, and packaged for injection (Centers for Disease Control and Prevention, 2014, 2015a).

Influenza vaccine effectiveness

One challenge related to influenza vaccination and communication surrounding influenza vaccination is that the effectiveness of seasonal vaccines can vary widely from season to season. There are two primary factors influencing this: the first pertains to characteristics of the person being vaccinated (particularly their age and health), since these factors determine which vaccines are available for that individual to use as well as the immune response that will be elicited; and the second pertains to how well the strains included in the vaccine match the actual circulating wild-type strains, since each year researchers must predict which strains they think will be circulating ahead of time so that sufficient production can occur in time for the influenza season (Centers for Disease Control and Prevention, 2015c). If there is a very poor match, it is possible that the vaccines may provide no benefit. However, it has been demonstrated that influenza vaccines can still provide protection even in years when the strains included in the vaccine are poorly matched with naturally circulating strains (Xie et al., 2011). Fortunately, over the last three decades, a very low match between vaccine and circulating strains has rarely occurred (Centers for Disease Control and Prevention, 2008). Another set of challenges relates to the numerous methodological complications to studying and surveilling of influenza morbidity and mortality in humans, namely that laboratory confirmation is required to distinguish influenza as the true cause of outcomes that also have other causes, and that outcomes often vary between studies (Monto, 2008; National Vaccine Advisory Committee, 2013).

Given these limitations and challenges, there is naturally some debate about the efficacy and effectiveness of influenza vaccines. A recent meta-analysis concluded that the TIV has a pooled efficacy of 59% in adults 18-65 years old, the LAIV has a pooled efficacy of 83% in children aged 6 months to 7 years, and that the vaccines significantly protected against influenza in the outpatient or inpatient setting, but that data was limited in older adults and children over the age of 7, and that effectiveness varied from season to season (Osterholm, Kelley, Sommer, & Belongia, 2012). In this meta-analysis, "efficacy" was defined as the relative reduction in influenza risk after vaccination as established by randomized placebo-controlled clinical trials. In addition to this meta-analysis, the CDC's review of the literature (Centers for Disease Control and Prevention, 2014a) reveals estimates of influenza vaccine effectiveness for additional populations and outcomes: 92% reduction in hospitalizations of infants for 6 months after birth when women were vaccinated during pregnancy (Benowitz, Esposito, Gracey, Shapiro, & Vázquez, 2010); 93% reduction of culture-confirmed influenza and significantly fewer febrile illnesses in children who received the LAIV (Belshe et al., 1998); 74% reduction in children's risk of influenza-related pediatric intensive care unit admissions (Ferdinands et al., 2014); 52%, 71%, 61-77%, and 79% reduction in influenza-related hospitalization among, respectively, adults with chronic lung disease (Nichol, Baken, & Nelson, 1999), all adults (Talbot et al., 2013), adults 50 years and older (Talbot et al., 2011, 2013), and diabetic adults (Colquhoun, Nicholson, Botha, & Raymond, 1997); and a 3 and 10% reduction in the risk of major cardiovascular events, respectively, in adults with coronary artery disease broadly (Ciszewski et al., 2008) or more specifically acute coronary syndrome (Phrommintikul et al., 2011), the effect of the latter being larger among persons with an event in the previous year (Udell et al., 2013). From a population perspective, CDC estimates that influenza vaccination reduces the risk of doctor visits due to influenza by 60% in the overall US population (Centers for Disease Control and Prevention, 2014a).

Influenza vaccine safety

The US federal government has a comprehensive, multi-agency system for monitoring the safety of vaccines in the pre-licensure, licensure, and post-licensure phases that re-evaluates and improves upon itself and has successfully identified and addressed unexpected, emerging vaccine safety issues (Centers for Disease Control and Prevention, 2015c; Jacobson, 2003; National Vaccine Advisory Committee, 2011; Salmon et al., 2011). Though post-licensure surveillance specifically for adverse events following vaccination did not begin in the United States until 1990 with the establishment of the Vaccine Adverse Event Reporting System, the Institute of Medicine conducted its first report on vaccine safety in 1977 (Salmon et al., 2011), and the federal government reports that they have monitored influenza vaccines for over half a century and continually find them to be very safe (Centers for Disease Control and Prevention, 2013a).

Still, like any pharmaceutical product or health intervention, routine influenza vaccination carries some known risks. About 15-20% of persons administered IIVs experience minor, local reactions (such as soreness, erythema, and induration at the site of injection), fewer than 1% experience nonspecific systemic symptoms (such as fever, chills, malaise, and myalgia), and rarely persons experience immediate allergic hypersensitivity (such as hives, angioedema, allergic asthma, or systemic anaphylaxis) (Centers for Disease Control and Prevention, 2015a). Persons who received the 1976 pandemic influenza vaccine or the 2009 H1N1 pandemic influenza vaccine experienced a small increased risk of the very rare but serious neurological disorder, Guillain-Barré syndrome (on the order of about 10 and 1.6 additional cases per million vaccinations for the 1976 and 2009 pandemic influenza vaccines, respectively: Salmon et al., 2013). There is no clear association of this small increased risk in those receiving the seasonal vaccine (Centers for Disease Control and Prevention, 2015a). The LAIVs have a similar safety profile, though there are few safety data available for LAIV given their relatively recent licensure. The most common adverse reactions to LAIVs are runny nose, headache, cough, nasal congestion, sore throat, wheezing, and chills, and no serious adverse reactions have been identified (Centers for Disease Control and Prevention, 2015a). It is important to distinguish these known risks as true, "adverse reactions," which are distinct from "adverse events." Adverse reactions are *true* reactions caused by the vaccine which can only be determined via close monitoring and timely assessment, whereas adverse events following immunization ("AEFIs") are *all* events following vaccination in time, many of which are coincidental and unrelated to vaccination (Centers for Disease Control and Prevention, 2015c).

In addition to known safety risks, there are known medical contraindications. Though all persons 6 months or older are recommended to receive annual influenza vaccination, persons with the following valid medical contraindications should not receive any influenza vaccine: a history of a severe (anaphylactic) allergic reaction to an influenza vaccine component; a history of Guillain-Barré syndrome within 6 weeks following a vaccine dose; and currently having moderate or severe acute illness (Centers for Disease Control and Prevention, 2015a). There are additional contraindications pertaining only to the LAIV, including children younger than the age of 2 years, children younger than 5 years with recurrent wheezing, adults 50 years or older, persons with chronic medical conditions, children and adolescents receiving long-term aspirin therapy, persons immunosuppressed from any cause, and pregnant women (Centers for Disease Control and Prevention, 2015a).

One last influenza vaccine safety topic to address is the use of thimerosal, a mercury-containing antibacterial vaccine preservative used in multi-dose vials of TIV. Thimerosal has received attention in the public eye as a potential vaccine safety controversy connected to autism (Chatterjee & O'Keefe, 2010). However, an extensive amount of research has revealed no support for any link between thimerosal and autism and the only adverse reaction it is known to cause is local redness and swelling at the site of injection (Centers for Disease Control and Prevention, 2015d; Fiore et al., 2010; Institute of Medicine, 2012).

Influenza vaccine supply and availability

The ideal influenza vaccine would not need to be given annually and would confer long-lasting protection to the general population. There has been a focus for some time now on developing such a “universal” influenza vaccine that elicits an immune response to a protein conserved across all virus subtypes, and though progress has been made, numerous challenges remain and no universal influenza vaccines have made it through clinical trials to licensure (Pica & Palese, 2013). Until then, the best preventive options against influenza are seasonal influenza vaccines, the generation of which requires production and distribution of large quantities of the vaccines annually.

There are multiple challenges to this process, however, that affect the balance between influenza vaccine supply and demand (Orenstein & Schaffner, 2008). On the supply side, the largest factor is that once researchers have selected the strains to be included in the vaccines, there is a very tight timeline during which manufacturers must produce, test, release, and distribute them. Thus, any problems encountered during this process can cause shortages or delays in the US vaccine supply (Centers for Disease Control and Prevention, 2014d), which not only results in lower vaccination uptake but in increased racial/ethnic disparities in influenza vaccination (Yoo et al., 2011). Generally, the first lots of influenza vaccines become available at the beginning of the influenza season (August), with production and availability peaking in October or November and rapidly declining thereafter, though vaccines continue to be available later in the influenza season (Centers for Disease Control and Prevention, 2014d). In the past, when seasonal influenza vaccine manufacturing was more limited, the CDC recommended the vaccine to a list of high-risk populations that steadily expanded over the years to the point where it contained nearly 85% of the US population. In 2010, however, the CDC determined that supply-side capacity was sufficient to extend the recommendation to *all* persons 6 months and older, prioritizing high-risk groups in the event of future vaccine supply issues (Fiore et al., 2010).

The demand side of vaccine supply is more uncertain, and is influenced by many factors, including the severity of the influenza season, vaccine financing and cost to consumer (including insurance factors), providers under-purchasing vaccine to avoid loss, multiple sites of vaccination, and state-to-state variability in requirements, among others (Orenstein & Schaffner, 2008; Penfold et al., 2011). Solutions to many of these issues have been suggested at federal, state, and local levels (Penfold et al., 2011): (1) collaboration and coordination of vaccine purchasing and distribution (to achieve discounts in pricing, ensure equitable and efficient distribution, and alleviate provider competition and uncertainty surrounding demand); (2) collaboration between public and private entities administering and reimbursing for vaccination (to minimize staffing demands and financial risk, and utilize economies of scale in contracting and billing with health plans and payers); (3) enhancement of financial coverage of vaccines through healthcare reform (specifically to require coverage of all preventive services without cost sharing; see the following paragraph for an update); and (4) using health information technology (to improve communication between stakeholders as well as demonstrate shared savings).

Perhaps the largest demand-side factor influencing influenza vaccine supply, availability, and ultimately uptake, is the individual's means and decision to receive the vaccine. Historically, most health insurance plans have covered the cost of influenza vaccination, which has been cheap (on the high end, generally under $20 per dose for providers: Orenstein, Mootrey, Pazol, & Hinman, 2007). Since 1994, underinsured or uninsured children have been eligible to receive vaccination (including influenza vaccination) at no cost through the Vaccines for Children (VFC) program (Centers for Disease Control and Prevention, 2014b). For adults without private insurance, publicly-financed options providing influenza vaccination include Medicare, TRICARE, and most state Medicaid agencies (Centers for Disease Control and Prevention, 2014c). Adults aged 19-64 not eligible for these services, however, have historically had to self-pay for influenza vaccination and though the out-of-pocket costs are still relatively small, a large chunk of this population faces financial challenges to do so (Orenstein et al., 2007) and out-of-pocket cost is still seen as a barrier to population-level vaccine coverage (Jacob et al., 2016). Fortunately, the passage of the Affordable Care Act has alleviated much of this remaining out-of-pocket cost barrier by greatly expanding insurance coverage to the previously uninsured and by requiring new health plans to cover all routinely recommended preventive services (including influenza vaccination) without any cost sharing (U.S. Department of Health and Human Services, 2012).

Young children: high-risk for influenza, high-priority for vaccination

As aforementioned, influenza is a significant health problem for children under the age of 5 years (henceforth known as "young children") in the United States. Young children are a particularly vulnerable population group due to increased risk of severe influenza complications simply because of their age, even if they are otherwise healthy (Neuzil, Zhu, et al., 2002). This risk is greatest in children under the age of 2 years, but children between 2 and 5 years of age are still more likely than healthy older children to be taken to a doctor, urgent care center, or the emergency room because of influenza (Centers for Disease Control and Prevention, 2013b; Thompson et al., 2004). Young children experience increased morbidity due to influenza disease – the estimated number of hospitalizations among 0-4 year olds in recent influenza seasons ranged from 9,992 to 15,203 with the exception of the 2009-2010 season which had an estimated 37,671 hospitalizations; this was mostly due to the H1N1 influenza pandemic which caused morbidity separate from that season's seasonal influenza virus (Kostova et al., 2013). This is a substantial portion of the total hospitalization morbidity of the entire US population, representing a risk of hospitalization of 100 per 100,000 in healthy children and 500 per 100,000 in children with underlying medical conditions (Centers for Disease Control and Prevention, 2015a). Other population-level estimates suggest the hospitalization rate associated with influenza in young children may be even as high as 900 per 100,000 children (Poehling et al., 2006). Consequently, the US federal government has long considered young children a “high risk” population. While children 5 through 18 years are not considered at such increased risk, they experience the highest rates of influenza infection and serve as a major source of influenza transmission within communities, the impact of which particularly affects children’s schools, medical offices, and families (Centers for Disease Control and Prevention, 2015a; Fiore et al., 2010).

Despite the risks of influenza to children risks, despite the continued safety, efficacy, effectiveness, availability and affordability of influenza vaccines in children, and despite long-standing childhood vaccination programs, uptake of influenza vaccination in US children remains sub-optimal and substantially lower than uptake of other routinely-recommended childhood vaccines. For example, annual influenza vaccination rates of young children rose from about 40% or lower where it had largely plateaued just prior to the universal influenza vaccine recommendation (Centers for Disease Control and Prevention, 2009b) to roughly 70% where it has now plateaued for the past couple seasons since the universal recommendation (Centers for Disease Control and Prevention, 2015a, 2015b). The unvaccinated population contains millions of young US children and in some states represents as high as 50% of all young US children (National Foundation for Infectious Diseases, 2015). Further, “full coverage” among young children – having received the appropriate number of influenza vaccinations for the child’s age – is generally much lower, peaking around 45% in children aged 6-23 months according to the most recent estimates (Santibanez, Grohskopf, Zhai, & Kahn, 2016) and quickly diminishing in older age groups (Centers for Disease Control and Prevention, 2010b). The federal government, in their Healthy People 2020 objectives, originally established 80% uptake as the goal for influenza vaccination, though recently they changed this objective to 70% for unstated reasons (U.S. Department of Health and Human Services, 2015). Regardless, that many states fail to hit even 70% overall uptake annually and that complete influenza vaccine uptake is much lower in the youngest, most vulnerable children – especially compared to the substantially higher uptake rates in children for other routinely-recommended childhood vaccines (Elam-Evans, Yankey, Singleton, Kolasa, & Centers for Disease Control and Prevention, 2014) – indicates a significant public health problem with adverse consequences both to children (Centers for Disease Control and Prevention, 2013) and communities at large (Jordan et al., 2006).

Thus, the overarching research objective of this dissertation is to better understand influenza vaccination of US children, with a particular focus on young children. To accomplish the objective, this dissertation has three aims, summarized below and then detailed in the following chapters. The first is to better understand differences in determinants of uptake in US children for influenza vs. other vaccinations, using nationally-representative, provider-verified data from the National Immunization Survey. It will examine differences in determinants in young children who are up-to-date on both, either, or neither influenza vaccines and a recommended series of other vaccines across a plethora of factors thought to influence health services use, including the incorporation of restricted data pertaining to parental perceptions surrounding vaccination and vaccine-preventable diseases and intersectionality theory to examine the interaction of disadvantaged social statuses. The second aim is to quantify for the first time using nationally-representative data, the association of child's vaccination status with household adult work loss in the US. It will use the National Health Interview Survey to do so, linking children to adults in the household to examine if child vaccination status is associated with household adult missed work time due to illness or injury, and if this is moderated by paid sick leave status. The final aim is to perform a policy analysis of system-level policy alternatives to improve influenza vaccination rates in children. It will evaluate two policy alternatives through which state and/or local governments can improve influenza vaccine uptake of young US children – both a mandatory approach (creating annual influenza vaccination requirements for preschool and childcare) and a comparable voluntary approach (offering in-facility vaccination in preschools and licensed organized childcare facilities) – and how the federal government can encourage states to adopt such policies.

Chapter 2

A hidden vulnerable population: determinants of young children up-to-date on vaccine series recommendations but not those for influenza vaccines

Abstract

Background: Children under 5 (especially under 2) years old are at increased risk for influenza-related complications. Children 6 months or older in the US are recommended to receive flu vaccination annually, yet uptake is substantially lower than other routinely-recommended vaccines. Few nationally-representative studies have examined factors influencing flu vaccine uptake in young US children. Further, most rely on parent-reported vaccination and do not consider factors known to be crucial to vaccine uptake. Moreover, none consider intersectionality of social disadvantage or how flu vaccine determinants differ from those of other vaccines.

Methods: This nationally-representative study examines provider-verified data on 7,246 children aged 6-23 months from the most recent (2011) National Immunization Survey to include the restricted Parental Concerns module (which contains crucial variables on parent perceptions of vaccines and vaccine-preventable diseases). Focusing on children up-to-date (UTD) on a series of vaccines (the 4:3:1:3:3:1:4 series) but not flu vaccines ("hidden vulnerability to flu"), linear probability regression examines disparities by an array of factors thought to influence health services use, including intersectionality of child's race/ethnicity, and mother's education and marital status.

Results: In this study, 71% of children were UTD on the series yet only 33% on flu vaccine recommendations by their second birthday; 44% had hidden vulnerability to flu. In multivariate models, parental history of vaccine refusal was associated with 9.9% (95% CI: 4.2-15.7) higher probability of hidden vulnerability to flu, though also with 5.2% (0.2-10.1) higher probability of children being UTD on neither series nor flu vaccines. By contrast, parental history of delaying vaccination was associated with 7.5% (2.6-12.5) lower probability of hidden vulnerability to flu despite being associated with 15.5% (10.8-20.2) higher probability of being UTD on neither the series nor flu vaccines. Intersectionality revealed that mother's college education is associated with increased hidden vulnerability to flu only among Hispanic and non-Hispanic Black children. Further, Hispanic children with married, college-educated mothers had the highest predicted probability (60.3%: 48.9-71.7) relative to non-Hispanic White children with college-educated mothers regardless of the mother being married (36.6%: 31.9-41.3) or not (29.5%: 16.6-42.4). The direction of interaction coefficients indicated this to be unique to hidden vulnerability to flu.

Conclusions: Independent of parental history of vaccine refusal and a myriad of health services use factors, we find that no parental history of vaccine delay was uniquely associated with child's hidden vulnerability to flu. Providers must be aware that general parental compliance with child vaccine recommendations and lack of vaccine hesitancy may not indicate parent choice to vaccinate their child against flu and thus must specifically engage all parents annually about flu vaccines. Further, examination of intersectionality of social disadvantage suggests that maternal college education may not confer improved preventive health service use behavior among non-Hispanic Black and especially Hispanic children despite that it does for non-Hispanic White children. Policymakers and researchers from public health, sociology, and other sectors need to collaborate to further examine how vaccine hesitancy and intersectional social disadvantage interact to affect influenza vaccine uptake in young US children.

Introduction

Background

Young children are considered to be "high risk" for influenza simply because of their age, even if they are otherwise healthy (Centers for Disease Control and Prevention, 2015b; Neuzil, Zhu, et al., 2002). They are at increased risk of influenza-related doctor visits, urgent care visits, ER visits, and hospitalizations (Centers for Disease Control and Prevention, 2013; Thompson et al., 2004) and make up a substantial portion of influenza morbidity in the total US population (Centers for Disease Control and Prevention, 2015a). Influenza in children also has significant implications for their families and communities at large, as it affects family members and caregivers (Teo et al., 2005), causes substantial parental work absenteeism (Fraaij & Heikkinen, 2011), and fuels community epidemics (Jordan et al., 2006). Influenza vaccination is the most effective means of preventing influenza (Cox & Subbarao, 1999) and the CDC recommends it for all persons 6 months of age and older (Fiore et al., 2010). Influenza vaccines have continually demonstrated a great safety profile (Centers for Disease Control and Prevention, 2013), have a high efficacy in children (Osterholm et al., 2012), and are effective at preventing numerous adverse outcomes in children, including doctor visits (Centers for Disease Control and Prevention, 2014a), febrile illnesses (Belshe et al., 1998), and hospitalizations (Ferdinands et al., 2014). Further, influenza vaccines have historically been the most affordable and available to children relative to other population groups thanks to the Vaccines for Children program and other public programs (Centers for Disease Control and Prevention, 2014b).

Despite all of this, uptake of influenza vaccination in US children remains sub-optimal. For example, though national estimates of yearly influenza vaccination uptake in young US children increased after the 2010 universal influenza vaccine recommendation, it has plateaued around 70% (Centers for Disease Control and Prevention, 2015a, 2015b) – as low as 50% in some states – representing millions of unvaccinated children (National Foundation for Infectious Diseases, 2015). Further, many fewer children receive “full coverage” – the most important measure of coverage, defined as having received the appropriate number of influenza vaccinations for the child’s age; full coverage peaked at 45% in children 6-23 months old according to the most recent estimates (Santibanez et al., 2016), and quickly diminishes with age (Centers for Disease Control and Prevention, 2010b).

By contrast, uptake of other childhood vaccines is generally much higher. For example, over the past several years, the percent of children 19-35 months old who were up to date on various vaccination recommendations at their age was: 84.6% for the diphtheria-tetanus-acellular pertussis (DTaP) vaccine, 93.9% for the poliovirus vaccine, 91.9% for the measles-mumps-rubella (MMR) vaccine, 82.0% for the *Haemophilus influenza* type B (Hib) vaccine, 92.4% for the Hepatitis B (HepB) vaccine, 91.2% for the varicella vaccine, and 84.4% for the pneumococcal conjugate vaccine (PCV). Moreover, the percent who were up-to-date on *all* of the above recommendations (the “4:3:1:3:3:1:4” series[1]) peaked at 70.4% (Elam-Evans et al., 2014).

Statement of research aims

The first research aim of this dissertation is to, in a single model, understand the unique determinants of young children that obtain compliance to a large series of recommended vaccines yet are not compliant on the recommended number of seasonal influenza vaccinations. It will elucidate what is known about young children henceforth referred to as having “hidden vulnerability to flu” – i.e., young children who are up-to-date on a wide variety of vaccine

[1] The 4:3:1:3:3:1:4 series refers to the child being UTD on 7 routine child vaccination recommendations, spanning 11 vaccine-preventable diseases at 36 months of age: (1) ≥4 doses of DTaP/DTP vaccine; (2) ≥3 doses of polio vaccine; (3) ≥1 dose of MMR vaccine; (4) ≥3 doses of Hib vaccine; (5) ≥3 doses of hepatitis B vaccine; (6) ≥1 dose of varicella vaccine; and (7) ≥4 doses of PCV7.

recommendations (the 4:3:1:3:3:1:4 series) and would thus appear to be broadly protected against vaccine-preventable diseases but yet who are simultaneously not protected against influenza. This may allow practitioners and policy makers to take more calculated steps to improve influenza vaccination coverage and reduce morbidity and mortality associated with influenza in young children by identifying the many children with hidden vulnerability to flu.

Literature review

As aforementioned, despite the increased risk and burden of influenza in young children and that children in the US are afforded the most vaccine coverage options (through public programs unique to children, such as Vaccines For Children [VFC], and greater inclusion in programs such as Medicaid), influenza vaccination uptake in young children in the US remains sub-optimal. Research on predictors and determinants of influenza vaccination in the US, however, has tended to focus more on adult populations, particularly elderly populations, and substantially less on child populations (Malosh et al., 2014; Poehling et al., 2001). This is a general limitation of the literature that may hinder our ability to understand sub-populations of young children that may be increased risk and factors related to young children and their parents that may guide approaches to improving vaccination in young children. Extending a recent unpublished review (Meng, 2013), Table 2-1 below is a summary of the literature on influenza vaccination determinants in US children.

Table 2-1. Summary of published literature on factors associated with higher influenza vaccination uptake in US children.

Level	**Determinant**	**Source**
Child	Presence of high risk medical conditions placing child at increased risk for influenza-related complications	(Centers for Disease Control and Prevention, 2005; Gnanasekaran, Finkelstein, Lozano, et al., 2006; Kramarz et al., 2000; Ma et al., 2006; Poehling et al., 2001, 2010; Santibanez et al., 2014)
Child	Younger child age	(Gnanasekaran, Finkelstein, Hohman, et al., 2006; Gnanasekaran, Finkelstein, Lozano, et al., 2006; Marshall et al.,

		2002; Poehling et al., 2001, 2010; Santibanez et al., 2014; Santibanez, Santoli, Bridges, & Euler, 2006)
Child	Higher number of recent visits to provider	(Gaglani, Riggs, Kamenicky, & Glezen, 2001; Marshall et al., 2002; Poehling et al., 2001, 2010; Uwemedimo, Findley, Andres, Irigoyen, & Stockwell, 2011)
Child	Race/ethnicity Non-Hispanic White or Asian relative to Non-Hispanic Black or Hispanic Non-Hispanic Black relative to Hispanic (Note that there were no significant racial/ethnic differences nationally in most recent influenza seasons)	(Santibanez et al., 2016, 2006)) (Uwemedimo et al., 2011) (Santibanez et al., 2014)
Child	Having a practice visit during the flu season	(Ma et al., 2006; Poehling et al., 2001, 2010)
Child	Hospitalization	(Gnanasekaran, Finkelstein, Lozano, et al., 2006; Kramarz et al., 2000)
Child	Child covered with private health insurance	(Daley et al., 2005)
Parent/family	Belief that receiving the vaccine is a smart idea/provides benefits	(M. A. Allison et al., 2010; Flood et al., 2010; Gnanasekaran, Finkelstein, Hohman, et al., 2006; Lin, Nowalk, et al., 2006; Malosh et al., 2014; Nowalk et al., 2005, 2007)
Parent/family	Belief that the vaccine is safe/ not worrying about its safety	(M. A. Allison et al., 2010; Flood et al., 2010; Gnanasekaran, Finkelstein, Hohman, et al., 2006; Szilagyi, Rodewald, Savageau, Yoos, & Doane, 1992)
Parent/family	Higher parental education	(Daley et al., 2006; Gnanasekaran, Finkelstein, Lozano, et al., 2006; Santibanez et al., 2006)
Parent/family	Perception of influenza risk	(Daley et al., 2005; Flood et al., 2010; Malosh et al., 2014)
Parent/family	Belief that vaccination is a social norm	(M. A. Allison et al., 2010; Daley et al., 2006, 2007)
Parent/family	No perception of high barriers to vaccination	(Daley et al., 2006, 2007; Malosh et al., 2014)
Parent/family	Living in an a more urbanized area	(Poehling et al., 2010; Santibanez et al., 2006)
Parent/family	Having relatives recommend the flu shot	(Lin, Nowalk, et al., 2006; Lin, Zimmerman, et al., 2006)
Parent/family	Family income above the poverty line	(Santibanez et al., 2006)
Parent/family	Parental worry about child's asthma	(Szilagyi et al., 1992)
Parent/family	Having family members who received the vaccine	(Ma et al., 2006)
Parent/family	Increased maternal age	(Uwemedimo et al., 2011)
Parent/family	English proficiency in mother	(Uwemedimo et al., 2011)
Parent/family	Perception of easy access to the doctor's office for a flu	(Lin, Nowalk, et al., 2006)
Provider	Physician recommendation of the vaccination	(M. A. Allison et al., 2010; Daley et al., 2005, 2006; Flood et al., 2010; Gnanasekaran, Finkelstein, Hohman, et al., 2006; Hemingway & Poehling, 2004; Lin, Nowalk, et al., 2006; Lin, Zimmerman, et al., 2006; Ma et al., 2006; Mirza et al., 2008; Nowalk et al., 2005, 2007; Poehling et al., 2001)
Provider	Having recall/reminder systems in place	(Daley et al., 2004; Gaglani et al., 2001; Kempe et al., 2005; Lin, Nowalk, et al., 2006; Lin, Nowalk, Toback, & Ambrose, 2013; Moore & Parker, 2006; Nowalk et al., 2007; Stockwell et al., 2012; Szilagyi et al., 1992)
Provider	Non-rural practice site	(Lin et al., 2013; Poehling et al., 2001, 2010)
Provider	Evening/weekend vaccination clinic hours	(Lin et al., 2013; Poehling et al., 2001, 2010)

Provider	Private or hospital provider type	(Santibanez et al., 2006; Uwemedimo et al., 2011)
Provider	Lower patient volume	(Lin et al., 2013; Poehling et al., 2010)
Provider	Longer duration of vaccine availability	(Lin et al., 2013; Paul et al., 2006)
Provider	Higher vaccination coverage among practice staff	(Lin et al., 2013)
Other	Positive media coverage	(Gnanasekaran, Finkelstein, Hohman, et al., 2006; Ma et al., 2006)

Recent studies of predictors and determinants of *other* vaccinations in US children confirm that many of the above factors as well as others are important. At the child level, this includes child's race and ethnicity, and number of siblings; at the parent/family level, this includes poverty status and urbanicity; mother's educational attainment, marital status, and age; and at the provider level, this includes number of vaccination providers, type of providers (public/private), and provider participation in the VFC program (Zhao & Luman, 2010). From 2001-2010, significant progress was made in reducing disparities in these other vaccinations in many of the above domains of US children largely in part to the VFC program, though significantly lower vaccination was still observed in several populations: children with multiple siblings or who were not first born; children who obtained vaccination through public coverage; and non-Hispanic white children relative to Hispanic children (Zhao & Smith, 2013).

There are three primary limitations to the literature on predictors and determinants of influenza vaccination uptake in US children. The first is that almost all of studies focus on certain child subpopulations, such as those who were hospitalized, those at high-risk for influenza, or children from one particular part of the US or a particular health system or health facility. By contrast, only a few studies examined factors influencing the uptake of influenza vaccination generalizable to the general pediatric population in the US (Centers for Disease Control and Prevention, 2005; Flood et al., 2010; Santibanez et al., 2014, 2006). Further, as none of these nationally-representative studies explicitly examined predictors and determinants, none of them utilized a conceptual framework to ground their selection of covariates that could affect influenza vaccination uptake in US children, though Flood et al. (2010) did suggest that the Health Behavior Model could appropriately serve such a function in future studies.

Second, there has been no explicit comparison in predictors and determinants between children who are up-to-date (UTD) for their influenza vaccination vaccinations and children who are UTD on *other* recommended series of vaccines. Given that influenza vaccination uptake in US children is much lower than uptake of other routinely-recommended childhood vaccinations, and that the influenza virus and vaccine are both relatively unique compared to other vaccine-preventable diseases and other vaccines (e.g., the flu vaccine has to be given annually, circulating viruses can vary substantially from year to year), it is likely that there may be unique factors affecting the uptake of influenza vaccination. Concordantly, there is reason to believe that, relative to other childhood vaccines, there are (1) differences in the populations exhibiting influenza vaccination disparities and (2) differences in determinants of health services use affecting influenza vaccination in US children. One study of influenza vaccination in US children conducted sensitivity analyses regarding uptake of other vaccines in the study population and briefly reported that children who were up-to-date on other vaccination series had higher odds of also receiving the influenza vaccination (Santibanez et al., 2006). However, this was not a focus of the study and there were no comparisons of determinants or disparities of uptake between the two outcomes.

Third, the existing literature is limited in its ability to examine determinants of childhood influenza vaccination in a comprehensive manner. Most studies and available datasets do not have the ability to adjust for many of the constructs noted in the full literature as associated with uptake – e.g., some contain a wide variety of socioeconomic and demographic variables but have little to no information on provider and system level factors nor parental perceptions of vaccines, and vice versa. Further, to my knowledge, there have been no studies of influenza vaccination in the US that consider the interacting effects of multiple disadvantages social statuses.

Intersectionality theory, which originates in black feminist theory (Crenshaw, 1989), posits that social statuses like race/ethnicity, gender, and social class cannot be disaggregated as they reinforce each other in producing and maintaining a variety of health outcomes across the life span (P. H. Collins, 1990, 2000; Dill & Zambrana, 2009; Schulz & Mullings, 2006). A general criticism of prior health research is that it has tended to treat such disadvantaged statuses as separate constructs, which not only potentially obscures important health differences but impairs efforts to reduce health disparities; the application of intersectionality theory directly addresses this issue and has greatly enhanced our understanding of health outcomes (Warner & Brown, 2011). Only a handful of studies apply intersectionality theory examining vaccination (Branković, Verdonk, & Klinge, 2013; Canales, 2010; Carpenter & Casper, 2009; Gottvall, Tydén, Larsson, Stenhammar, & Höglund, 2011; Joe, 2014; Monforti & Cramer, 2014; Salad, Verdonk, de Boer, & Abma, 2015; J. Vardeman-Winter, Tindall, & Jiang, 2013; Jennifer Vardeman-Winter, 2012), though none examine influenza vaccination or are generalizable to young US children. However, these studies uncovered findings that would not have otherwise been observed in purely additive models that did not examine the interacting effects of disadvantaged social statuses, providing additional justification for the added value that the application of intersectionality theory will contribute to better understanding the determinants of influenza vaccination in US children.

The study described below directly addresses these gaps in the literature using provider-verified vaccination data in a sample nationally-representative of young children in the US that includes major constructs across all domains noted in the literature and examines interactions of social disadvantage. In particular, it comprehensively identifies children who are up-to-date on a large series of vaccine recommendations – who would otherwise not seem like a population vulnerable to vaccine-preventable disease nor suggest they would have tendencies to refuse vaccination – but who are not up-to-date on their influenza vaccine recommendations. These young children are thus a hidden vulnerable population.

Methods

Data source

Data for this study come from the 2011 National Immunization Survey (NIS), the most recent NIS to include the Parental Concerns (PC) module, a restricted supplement to the NIS that is necessary for this study given the aforementioned associations noted in the literature of vaccine uptake with attitudes, perceptions, beliefs, and behaviors surrounding vaccines and vaccine-preventable diseases. The NIS is developed and produced by the National Center for Immunization and Respiratory Disease (NCIRD), National Center for Health Statistics (NCHS), and the National Opinion Research Center (NORC) at the University of Chicago. The NIS has monitored vaccination uptake among young children in the US since 1994 (Elam-Evans et al., 2014). The target population for the NIS is children aged 19 to 35 months living in US households at the time of the interview (Centers for Disease Control and Prevention & NORC at the University of Chicago, 2012). The PC module was merged with publicly-accessible variables by NCHS analysts and this merged, restricted dataset was accessed at the Penn State Federal Statistical Research Data Center, a Census Bureau facility housed at Penn State that meets all physical and information security requirements for accessing restricted federal data. Data collection for NIS was approved by the NCHS Research Ethics Review Board (ERB). Analysis of de-identified data from the survey is exempt from the federal regulations for the protection of human research participants. Analysis of restricted data through the Research Data Center is also approved by the NCHS ERB. The findings and conclusions in this paper are those of the author and do not necessarily represent the views of the Research Data Center, the National Center for Health Statistics, or the Centers for Disease Control and Prevention. Additionally, the proposed research of this study was reviewed by the Pennsylvania State University Institutional Review Board who deemed it Not Human Research.

The NIS uses random digit dialing telephone survey methodology to identify households containing children in the target age range. The adult who is the most knowledgeable about the child's vaccinations is interviewed. Historically, the survey was landline only, but in 2011, a cell-phone component was added to address the rapid rise of houses only using a cell phone. Samples of telephone numbers are independently drawn within selected geographical strata each calendar quarter. The design of the 2011 NIS makes it possible to produce annual estimates of vaccination uptake levels for each state and the US Virgin Islands, as well as for 9 sub-state urban city/county areas (including the District of Columbia). For the 2011 NIS, household interviews were conducted between January 6, 2011 and February 8, 2012 for the landline sample and January18, 2011 to February 18, 2012 for the cell phone sample. The response rate for the landline sample was 61.5% and for the cell phone sample was 25.2% via the CASRO method. With consent of the child's parent or guardian, the NIS then contacts the child's health care provider(s) by mail to request vaccination information from the child's medical records. Provider data collection occurred from February 2011 to April 2012; 79.5% of landline cases and 75.0% of cell phone cases gave consent to contact their children's vaccination providers, and 95.2% and 93.8%, respectively, of providers returned the questionnaires. The 2011 NIS public-use data file contains 26,741 children with completed household interview data, and 19,144 with provider-verified data (excluding the Virginia Island sample). Overall, the CASRO response rate was 61.6% and 72.3% of these household children had adequate provider data (Centers for Disease Control and Prevention & NORC at the University of Chicago, 2012). Of these 19,144 children with adequate provider-verified data, 13,358 (69.8%) were flagged to receive the restricted PC module, and 12,559 of them (94.0%) completed it (unpublished data from NCHS). This study uses data from children with provider-verified data, a completed PC module, and eligible for influenza vaccination up-to-date indicators (discussed below) in order to have the most accurate available estimates with generalizability to children in the 50 US states plus the District of Columbia.

Dependent variable

Given that the study aim is to compare factors associated with determinants of young children being UTD for influenza vaccine recommendations with those UTD for a recommended series of other vaccinations (the "4:3:1:3:3:1:4" series), there are three dependent variables of interest: (1) young children UTD for *neithe*r their recommended number of influenza vaccines *nor* the 4:3:1:3:3:1:4 series; (2) young children *only* UTD on their 4:3:1:3:3:1:4 series (not UTD on their recommended number of influenza vaccines); and (3) young children UTD for *both* their recommended number of influenza vaccines *and* the 4:3:1:3:3:1:4 series. The operationalization of these outcomes is through the use of combinations of two binary variables (0 = "no," 1 = "yes"). The first variable represents whether a child at 24 months of age during the survey period was up to date on their recommended influenza vaccinations (i.e., received the correct amount of influenza vaccinations given the number of influenza seasons they have experienced by their second birthday). By design, this NIS-constructed measure excludes children who were not 6-23 months of age during the entire span of September 1 to December 31 as "not eligible" for this outcome. This variable was designed to capture children with the highest risk for severe influenza-related complications (<24 months old) who were eligible to receive the vaccine (6+ months old) during almost all of the influenza season (September 1 through December 31, when most influenza infection occurs). The second variable captures whether or not the same child is UTD on the 4:3:1:3:3:1:4 series. Referring to the comparison groups above, three corresponding binary outcomes were generated: (1) "both" (a "yes response" to both UTD questions); (2) "series but not flu" (a "yes" response to the series question; a "no" to the flu question); and (3) "neither" (a "no" response for both UTD question). These terms are used throughout the paper.

Determinants of influenza vaccination

Given that influenza vaccination uptake is the use of a health service, the selection of predictors or determinants of influenza vaccination examined in this study is grounded in Andersen's Behavioral Model of Health Services Use (Andersen, Rice, & Kominski, 2007), a conceptual model of individual- and contextual-level determinants of health services utilization. It divides individual-level determinants into three major components: (1) *predisposing factors* (e.g., child's race/ethnicity, parental education and marital status, parental vaccine attitudes and beliefs); (2) *enabling factors* (e.g., family income, health insurance); and (3) *need factors* (e.g., objective and perceived measure of general health, functional state, need for medical care). The model also accounts for how intermediate-level individual health behavior influences health services use (e.g., personal health practices, such as children being breastfed or fed breast milk). Andersen's model has been used extensively in studies investigating health services use across several realms of the healthcare system and in the context of a variety of diseases (Babitsch, Gohl, & von Lengerke, 2012).

All variables from the data set that pertained to elements of the Behavioral Model of Health Services Use or to other previous determinants from the literature review were investigated as determinants of child influenza vaccination status in this study.

Seven variables represent constructs of contextual level factors (at the family or practice level) pre-disposing, enabling, or creating need for influenza vaccination and other health services use – (1) *education of the mother* (college graduate vs. not); (2) *age group of the mother* (≤19 years; 20-29 years; ≥30 years); (3) *marital status of the mother* (married vs. never married, widowed, divorced, separated, or deceased); (4) *language* (English vs. Spanish or other); (5) *housing arrangement* (owned or being bought; rented; or other arrangement); (6) *area of residence* (59 geographical strata described in "Data source" excluding the U.S. Virgin Islands), and (7) *provider facility type* (public/WIC; hospital; private; military/other facilities; or mixed).

Seven variables represent constructs of parental perceptions, beliefs, and context surrounding vaccines and vaccine-preventable diseases: (1) vaccines are necessary to protect child health (scale 0-10; where 10 is highest agreement); (2) vaccines do a good job at preventing their respective diseases (scale 0-10); (3) vaccines are safe (scale 0-10); (4) vaccine-preventable diseases are serious and can hurt children (scale 0-10); (5) the strength of physician recommendation for vaccination (scale 0-10); (6) parental history of refusing or deciding not to get, for their children, any vaccine (binary); and (7) parental history of delaying or putting off getting, for their children, any vaccine (binary). Accessed through the Research Data Center, these variables came from the restricted NIS Parental Concerns module and were necessary for adjusting for parental vaccine concerns.

Five variables represent constructs of individual (child) level factors pre-disposing, enabling, or creating need for influenza vaccination and other health services use – (1) *sex of the child* (male vs. female); (2) *race/ethnicity of the child* (Hispanic; non-Hispanic White only; non-Hispanic Black only; or non-Hispanic other + multiple race); (3) *first born status of the child* (no vs. yes); (4) *receipt of benefits from the Women, Infants, and Children program* (currently receiving vs. not); as well as (5) whether the child was *uninsured* at any time during the year.

Lastly, one variable represents a proxy construct for the child's health behavior environment – *whether the child was ever breast fed or fed breast milk* (yes vs. no).

Initially a variable for family income as a percentage of the poverty line was to be included in this study. A correlation matrix was first conducted on all covariates, however, and the variable for family income as a percentage of the federal poverty line exhibited concerns of multicollinearity with ever use of WIC (r=-0.77). Because WIC use has less missingness and because WIC eligibility includes family income as a consideration but also other considerations relevant to vulnerability or disadvantaged status of the child or the child's family (i.e., child nutrition risk as determined by a licensed health professional, or child or family eligibility for Medicaid, Temporary Assistance for Need Families, or other state-administered programs; see: Food and Nutrition Service, United States Department of Agriculture, 2016), the WIC use variable was retained and the family income variable was not included. After excluding family income, there were no concerns of multicollinearity between the remaining 20 covariates. Of the 190 pairwise comparisons of these covariates, only 9 (4.7%) were greater than r=+/- 0.40 (the highest being r=-0.58) and the vast majority were under r=+/-0.10. This indicates that the selected covariates represent different constructs and should not unnecessarily inflate the standard errors in multivariate regression.

Study population

Respondents were eligible for this study if they had provider-verified data (required for determination of up-to-date status of the 4:3:1:3:3:1:4 series and influenza vaccinations, the two variables that comprise the outcome variables of this study), if they were eligible for the influenza up-to-date questions (age/date restrictions were put in place by NCHS to ensure capture of the most vulnerable, influenza-vaccine eligible children during the influenza season), and if the parents responded to the Parental Concerns Module (contains key covariates that were not asked to all respondents). This eligible sample contained 8,065 children. Complete case analysis (i.e., listwise deletion; excluding cases missing on any variables in the analysis) was performed. Only 10% of the eligible sample were not complete cases; the complete case analytic sample contains 7,246 children (89.8% of the eligible sample). Sensitivity analyses were conducted to determine if being in the complete case analytic sample was associated with any variables utilized in the study. There was no association between being in the complete case sample with the “series but not flu” UTD status variable, the key outcome of interest. Being in the complete case analytic sample was not associated with 15 of the 20 covariates, though complete case respondents were more likely to be college-educated, slightly less likely to delay or put off vaccination, and slightly more likely to agree that vaccines do a good job at preventing disease, that vaccines are safe, and that their child's healthcare provider encouraged them to vaccinate their child. The choice of complete case analysis is reinforced for two reasons. First, the association of missingness from the complete case analytic sample with a few variables indicates missingness was not completely at random – a key assumption required for multiple imputation. Second, our complete case sample is relatively large (N=7,246), and the complete case missingness is relatively low (N=819), not associated with our outcome of interest, and only associated with few covariates (the associations of which are relatively small in magnitude), all of which suggest listwise deletion may be less biased than (or at worst, as biased as) other methods of dealing with missingness (P. D. Allison, 2014).

Analysis

For each of the three outcome variables separately, bivariate associations between UTD status and each determinant were first examined. Then, each outcome was regressed onto all determinants using robust-adjusted Linear Probability Model (LPM) regression to generate multivariate results. Main (additive) effects estimated from regression, however, are neither useful nor appropriate from an intersectional perspective (Veenstra 2013). Thus, to quantitatively incorporate intersectionality, hierarchical interaction terms for child’s race/ethnicity, mother’s education, and mother’s marital status were added (i.e., in addition to variables for these constructs separately, adding in all possible two-way interaction terms and the three-way interaction term) to examine the intersectional (multiplicative) effects of disadvantaged social statuses. These measures of social status likely also carry the effects of others not included in the interaction terms given that education also influences two other important dimensions of class – occupation and income/wealth (Herd, Goesling, & House, 2007).

Logistic regression is often used for the examination of bivariate outcomes. This study does not use logistic regression, however, for two primary reasons. First, most of the outcomes are anticipated to be non-rare and odds ratios from logistic regression can mislead readers to overestimate relative risk effect sizes when used to examine non-rare outcomes (Bauer, 2014; J. Lee, 1994). Second, and most importantly for the purposes of this study, logistic regression does not produce results conducive to straightforward interpretation of interaction terms given the coefficient are either log odds or odds ratios (Ai & Norton, 2003; Bauer, 2014). Thus, this study used LPM regression – i.e., Ordinary Least Squares regression of a binary outcome. LPM regression, by comparison, makes interpretation of coefficients (including of interaction terms) much more straightforward given that LPM coefficients are interpreted as changes in probability of observing the "1" response of the outcome (UTD vaccination status) associated with changes in the explanatory variables. Moreover, the use of LPM regression is motivated by the literature (Aldrich & Nelson, 1984; Angrist, 2001; Heckman & Snyder, 1997) and has been used in influential studies (Angrist & Pischke, 2009; Currie & Gruber, 1996). Given that coefficients of each construct of the hierarchical interaction terms are not themselves directly interpretable (Brambor, Clark, & Golder, 2006), marginal probabilities of UTD status from interaction term subgroups of interest from the multiplicative model are calculated and graphed. This allows for the interpretation and comparison of UTD vaccination probabilities among two-term subgroups (i.e., child's race/ethnicity*mother's education groups, child's race/ethnicity*mother's marital status groups, and mother's education*marital status groups) and among three-term interaction subgroup (i.e., child's race/ethnicity*mother's education*marital status groups) as predicted by the model adjusting for all covariates and incorporating intersectionality theory.

All analyses were performed using Stata/SE 13.1 statistical software (StataCorp LP, 2013) and use Stata's *svy* commands to apply NIS-provided sample weights to generate national-representativeness adjusting for complex survey design, ratio, non-response, post-stratification adjustments, and heteroscedasticity.

Results

Table 2-2 contains weighted, descriptive statistics of the complete case analytic sample, nationally-representative of U.S. children 6-23 months of age. Overall, 33% of children were UTD on their recommended influenza vaccinations, and 71% were UTD on the 4:3:1:3:3:1:4 vaccine series by the age of 24 months. Examining the cross-section of these UTD variables reveals that over 27% of children were UTD on both the series and influenza vaccines, 23% were UTD on neither, 44% were UTD on the series but not flu vaccines, and the remaining 6% were UTD on influenza vaccines but not the series (not examined elsewhere in the study due to small sample size and not being relevant to the research question). Overall, most sample children were: male sex; non-Hispanic White race/ethnicity; not first-borns; WIC "ever" users; and breastfed or fed breast milk. Most sample children lived: in English-speaking households; in households owned or being bought; with married mothers; with mothers without a college degree; and with mothers who generally highly agreed that vaccines are necessary, safe, effective, and prevent harmful diseases (ratings of agreement ranging from 8.3 to 9.4 out of 10). Last, most sample children saw private providers and mothers perceived that their child's physician provided a strong recommendation for the child to receive vaccinations in general. Despite the positive average parental perception of vaccines and vaccine-preventable disease and strong physician recommendations, however, over 15% of parents had ever refused or decided not to have their child vaccinated, and one third had ever delayed or put off having their child vaccinated.

Table 2-2. Descriptive statistics of study population, U.S children aged 6-23 months old (N=7,246), 2011 NIS.

Variable	**Percent**	**N**
Outcome variables		
Total up-to-date on influenza vaccine(s) at 24 months old		
No	66.7	4602
Yes	33.3	2644
Total up-to-date on 4:3:1:3:3:1:4 vaccine series		
No	28.9	2048
Yes	71.1	5198
*Up-to-date on BOTH influenza vaccine(s) AND 4:3:1:3:3:1:4 vaccine series		
No	72.5	5042
Yes	27.6	2204
**Up-to-date on ONLY 4:3:1:3:3:1:4 vaccine series; not influenza vaccine(s)		
No	56.5	4252
Yes	43.5	2994
Up-to-date on ONLY influenza vaccine(s); not 4:3:1:3:3:1:4 vaccine series		
No	94.3	6806
Yes	5.8	440
*Up-to-date on NEITHER influenza vaccine(s) NOR 4:3:1:3:3:1:4 vaccine series		
No	76.8	5638
Yes	23.2	1608
Independent variables	**Percent**	**N**
Child's sex		
Female	48.2	3503
Male	51.8	3743
Child's race/ethnicity		
Non-Hispanic White only	50.8	4629
Non-Hispanic Black only	12.5	690
Non-Hispanic other or multiple race	9.2	757
Hispanic	27.5	1170
Child's first born status		
First born	40.6	2399
Not first born	59.4	4847
Child ever received benefits from the *Women, Infants, and Children* program		
No	47.8	4325
Yes	52.2	2921
Child uninsured		
No	91.9	6755
Yes	8.1	491
Mother's education		
Less than a college graduate	63.8	3706
College graduate	36.2	3540
Mother's age group		
≤19 years	2.6	121

20-29 years	41.6	2144
≥30 years	55.9	4981
Mother's marital status		
Married	67.9	5506
Never married, widowed, divorced, separated, or deceased	32.1	1740
Language		
English	87.0	6712
Spanish or other	13.0	534
Housing arrangement		
Owned or being bought	57.1	5153
Rented	39.5	1889
Other arrangement	3.4	204
Provider facility type		
Public/WIC	11.4	751
Hospital	10.5	836
Private	60.5	4464
Military/other facilities	3.9	242
Mixed	13.7	953
Child was ever breastfed or fed breast milk		
No	22.4	1406
Yes	77.6	5840
Parent ever refused or decided not to have their child vaccinated		
No	84.6	6052
Yes	15.4	1194
Parent ever delayed or put off having their child vaccinated		
No	66.6	4852
Yes	33.4	2394
	Mean (SD)	**N**
Parent belief that vaccines are necessary to protect children's health	9.4 (1.3)	7246
Parent belief that vaccines do a good job at preventing their diseases	9.1 (1.6)	7246
Parent belief that vaccines are safe	8.3 (2.1)	7246
Parent belief that vaccine-preventable diseases are serious and can hurt children	9.2 (2.1)	7246
Parent perception of strength of physician's vaccine recommendation	9.3 (1.7)	7246

Source: 2011 National Immunization Survey (NIS) data, children represented in the Parental Concerns module with provider-verified vaccination data and eligible for the influenza vaccination up-to-date question who are not missing any covariates. Means and percentages weighted to be nationally-representative. N un-weighted to show actual number of observations in each cell. For the last 5 covariates (parent beliefs/perceptions), the scale is 0-10 where 0 is disagree and 10 is agree.

*Outcome variables in this study

**Main outcome of interest in this study, "series but not flu" (i.e., "hidden vulnerability to flu")

Bivariate (unadjusted) results

Table 2-3 shows weighted bivariate statistics: the correlation between UTD outcomes and each covariate (Column 1 is UTD on “both” the series and influenza vaccines, Column 2 is UTD on the “series but not flu” vaccines, and Column 3 is UTD on “neither”). Increased vulnerability across the columns is noted by: lower “yes” percentage in Column 1 (lower likelihood of being UTD on “both”); higher “yes” percentage in Column 2 (higher likelihood of not being UTD on influenza vaccines despite being UTD on the series); and higher “yes” percentage in Column 3 (higher likelihood of being UTD on “neither”).

Looking across all three columns in Table 2-3, these findings suggest that, unadjusted for other covariates, young children of Hispanic ethnicity and/or from non-English speaking households and/or who have never delayed vaccination have “hidden vulnerability to flu” – i.e., they may appear to have vaccine uptake behavior comparable to other young children on most vaccines but are uniquely less likely to be UTD on influenza vaccine recommendations. First, the only determinant that uniquely exhibited vulnerability in the “series but not flu” outcome but not the other outcomes was household language: children in households speaking Spanish or another language were 9 percentage points more likely to be in the “series but not flu” group than children in households English. Further, Hispanic children had the highest percentage of “series but not flu” despite showing very little difference from non-Hispanic Whites in the “neither” (most vulnerable) outcome. Otherwise, traits associated with children being more likely to be “series but not flu” were: child race/ethnicity other than non-Hispanic White (especially Hispanic children); WIC recipients; non-college graduate mothers; and history of refusing vaccination, though, counterintuitively, history of not delaying or putting off vaccination had the opposite unadjusted association. All of these groups were also significantly vulnerable to the comparison vaccine UTD outcomes in Columns 1 and 3, except for the vaccine delay finding.

Table 2-3. Correlates of vaccination up-to-date variables, U.S children aged 6-23 months old (N=7,246), 2011 NIS.

	Up-to-date status (combinations of seasonal influenza and the 4:3:1:3:3:1:4 series)								
	"BOTH" Both flu and 4:3:1:3:3:1:4 series			**"SERIES BUT NOT FLU" 4:3:1:3:3:1:4 series, not flu**			**"NEITHER" Neither flu, 4:3:1:3:3:1:4 series**		
	72.5%	**27.6%**		**56.5%**	**43.5%**		**76.8%**	**23.2%**	
	No %	**Yes %**	**p**	**No %**	**Yes %**	**p**	**No%**	**Yes %**	**p**
Child's sex									
Female	72.7	27.3		57.4	42.6		75.8	24.2	
Male	72.3	27.8	0.8430	55.6	44.4	0.4609	77.8	22.2	0.3583
Child's race/ethnicity									
Non-Hispanic White only	68.4	31.6		59.3	40.7		78.6	21.4	
Non-Hispanic Black only	82.5	17.5		56.9	43.1		68.0	32.0	
Non-Hispanic other/multiple race	68.9	31.1	0.0002	57.9	42.2	0.0220	78.8	21.3	0.0113
Hispanic	76.6	23.4		50.5	49.5		77.0	23.0	
Child's first born status									
First born	70.1	29.9		54.1	45.9		82.1	18.0	
Not first born	74.1	25.9	0.0572	58.1	41.9	0.1026	73.3	26.7	0.0002
Child ever received WIC benefits									
No	65.9	34.1		59.3	40.7		81.3	18.7	
Yes	78.4	21.6	<0.0001	53.9	46.1	0.0210	72.8	27.2	<0.0001
Child uninsured									
No	71.8	28.2		56.4	43.6		77.7	22.3	
Yes	79.6	20.4	0.0270	56.9	43.1	0.9200	67.4	32.6	0.0099
Mother's education									
Less than a college graduate	77.3	22.7		54.4	45.6		73.5	26.5	
College graduate	63.9	36.1	<0.0001	60.0	40.0	0.0141	82.8	17.2	<0.0001
Mother's age group									
≤19 years	83.2	16.8		44.0	56.0		73.3	26.7	
20-29 years	77.8	22.2	<0.0001	55.6	44.4	0.1680	72.5	27.5	
≥30 years	68.0	32.0		57.7	42.3		80.3	19.8	0.0010
Mother's marital status									
Married	69.0	31.0		58.0	42.0		79.1	20.9	
Never married, widowed, divorced, separated, or deceased	79.8	20.2	<0.0001	53.2	46.8	0.0579	72.1	27.9	0.0019
Language									
English	72.1	27.9		57.6	42.4		76.3	23.7	
Spanish or other	75.0	25.0	0.445	48.6	51.4	0.0228	80.3	19.7	0.2179

Housing arrangement									
Owned or being bought	69.5	30.5	0.0017	56.6	43.4	0.7133	80.0	20.0	0.0013
Rented	75.6	24.4		56.6	43.4		73.0	27.0	
Other arrangement	85.3	14.7		41.4	48.6		68.6	31.4	
Provider facility type									
Public/WIC	82.0	18.0	0.0003	53.2	46.8	0.5188	67.1	32.9	<0.0001
Hospital	76.6	23.4		58.0	42.0		75.9	24.1	
Private	69.6	30.4		57.6	42.4		78.9	21.1	
Military/other facilities	85.5	14.6		58.7	41.3		57.6	42.4	
Mixed	70.2	29.8		52.3	47.7		82.2	17.8	
Child was ever breastfed or fed breast milk									
No	79.5	20.5	<0.0001	53.3	46.7	0.1333	73.3	26.7	0.0500
Yes	70.4	29.6		57.4	42.6		77.9	22.1	
Parent ever refused/decided not to have their child vaccinated									
No	70.1	29.9	<0.0001	57.4	42.6	0.0340	78.5	21.5	<0.0001
Yes	85.4	14.6		51.1	48.9		67.8	32.3	
Parent ever delayed or put off having their child vaccinated									
No	69.3	30.7	0.0003	53.9	46.1	0.0032	82.6	17.4	<0.0001
Yes	78.7	21.3		61.6	38.4		65.4	34.6	
	No mean (se)	**Yes Mean (se)**	**p**	**No mean (se)**	**Yes Mean (se)**	**p**	**No mean (se)**	**Yes Mean (se)**	**p**
Parent believes vaccines are necessary to protect children's health	9.33 (0.03)	9.58 (0.04)	<0.0001	9.36 (0.04)	9.46 (0.04)	0.0775	9.50 (0.03	9.08 (0.08)	<0.0001
Parent believes vaccines do a good job at preventing their diseases	9.02 (0.05)	9.21 (0.07)	0.0252	9.01 (0.06)	9.15 (0.05)	0.0658	9.18 (0.04)	8.73 (0.11)	0.0001
Parent believes vaccines are safe	8.16 (0.06)	8.63 (0.07)	<0.0001	8.26 (0.06)	8.34 (0.09)	0.4618	8.43 (0.06)	7.83 (0.11)	<0.0001
Parent believes vaccine-preventable diseases are serious and can hurt children	9.13 (0.07)	9.27 (0.09)	0.2228	9.20 (0.07)	9.12 (0.08)	0.4880	9.20 (0.06)	9.07 (0.14)	0.4125
Parent perceived strength of physician vaccine recommendation	9.32 (0.04)	9.41 (0.12)	0.5055	9.33 (0.07)	9.36 (0.06)	0.7548	9.37 (0.06)	9.27 (0.07)	0.2852

Source: 2011 National Immunization Survey (NIS) data, children represented in the Parental Concerns module with provider-verified vaccination data and eligible for the influenza vaccination up-to-date question who are not missing any covariates. Means and percentages weighted to be nationally-representative. For the last 5 covariates (parent beliefs/perceptions), the scale is 0-10 where 0 is disagree and 10 is agree. Shaded cells indicate most vulnerable groups among those with statistically significant differences in each UTD outcome.

Multivariate (fully-adjusted) results

Table 2-4 shows weighted results from the multivariate LPM regression models of each UTD outcome onto the hierarchical interaction terms of interest (child's race/ethnicity, mother's education, and mother's marital status) and all covariates. Covariates represent marginal probabilities of being in each outcome group, and similar to Table 2-3, increased vulnerability across the columns is noted by: negative marginal probability in Column 1 (lower probability of being UTD on "both" vaccine); and higher marginal probabilities in Columns 2 and 3 (higher probability of being UTD on "series but not flu" or "neither," respectively).

Comparing all models in Table 2-4, several patterns emerge. Although the "both" and "neither" outcomes had significant bivariate findings across most covariates (Table 2-3), many determinants lost significance after adjustment in Table 2-4 (e.g., insurance, strength of belief that vaccines are good at preventing their diseases). Ever receiving WIC was significant across all outcomes in the bivariate model (Table 2-3) but lost significance across all outcomes in the adjusted model suggesting its association with vaccine uptake vulnerability is explained entirely by other factors. Several significant findings remained in the adjusted model, however. Similar to the bivariate findings, the "both" and "neither" uptake outcomes had significant differences by mother's age group (older mothers were less likely to have children receiving "both," but the least likely to receive "neither"), and provider facility type (children who saw providers at public/WIC and military/other facilities were less likely to be UTD on "both," more likely to be UTD on "neither"). Last, findings observed across all models indicate the strongest determinants of young childhood vaccine vulnerability to be parental history of vaccine refusal or delay as well as some intersectional combination of mother's education and child's race/ethnicity as evident in the significant interaction terms (intersectional findings interpreted in a section to follow).

Highlighting the outcome of interest, “series but not flu” (Column 2), findings suggest that intersecting social status, having ever refused a vaccine for one’s child and having never delayed or put off vaccination are independently associated with hidden vulnerability to flu. First, factors that lost significance in this adjusted model compared to the bivariate model include ever use of WIC and household language, suggesting they are explained by other determinants in the model. Second, one finding that appeared only after controlling for all covariates was that children with parents who ever refused or decided not to get their child vaccinated had a 9.9 percentage point (95% confidence interval: 4.2-15.7) higher probability of being in the “series but not flu” group. Third, counterintuitively, parental history of delaying or putting off vaccination was associated with reduced probability of being in the “series but not flu” group by 7.5 percentage points (2.6-12.5). Further, the direction of this finding was not observed in the other two outcomes, indicating it is unique to hidden vulnerability to influenza. Last, the social statuses of mother’s education and child’s race/ethnicity have some intersectional significance and again, the direction of the coefficients of significant interaction terms is different than what would be expected from the direction of the “both” and “neither” outcomes, indicating that intersectionality plays a role in hidden vulnerability to flu. Because the magnitudes of interaction term coefficients are not directly interpretable, however, they are examined in more detail in the following section using model-predicted probabilities.

Table 2-4. Change in predicted probabilities of up-to-date vaccine status, multivariate linear probability model regression, U.S children aged 6-23 months old (N=7,246), 2011 NIS.

Up-to-date status (combinations of seasonal influenza and the 4:3:1:3:3:1:4 series)						
	"BOTH" Both flu and 4:3:1:3:3:1:4 series		"SERIES BUT NOT FLU" 4:3:1:3:3:1:4 series, not flu		"NEITHER" Neither flu, 4:3:1:3:3:1:4 series	
	β	**95% CI**	**β**	**95% CI**	**β**	**95% CI**
Child's race/ethnicity (ref: non-Hispanic White)						
Non-Hispanic Black	-0.041	-0.174, 0.092	-0.040	-0.145, 0.092	0.038	-0.090, 0.165
Non-Hispanic other or multiple race	0.007	-0.107, 0.121	0.001	-0.018, 0.105	-0.015	-0.128, 0.097
Hispanic	0.044	-0.070, 0.158	-0.027	-0.155, 0.157	-0.017	-0.120, 0.086
Mother is a college graduate (ref: education less than a college graduate)	***0.116	0.062, 0.170	*-0.083	-0.150, -0.016	*-0.059	-.0115, -0.002
Mother never married, widowed, divorced, separated, or deceased (ref: married)	0.004	-0.064, 0.071	0.009	-0.090, 0.108	-0.007	-0.102, 0.088
Child's race/ethnicity*mother's education						
(Ref: non-Hispanic White with college graduate mother)						
Non-Hispanic Black with college graduate mother	-0.161	-0.325, 0.003	0.121	-0.094, 0.336	0.130	-0.097, 0.357
Non-Hispanic other/multiple race with college graduate mother	-0.050	-0.195, 0.095	0.058	-0.122, 0.238	0.022	-0.111, 0.155
Hispanic with college graduate mother	**-0.208	-0.350, -0.065	**0.263	0.104, 0.422	-0.032	-0.153, 0.088
Child's race/ethnicity*mother's marital status						
(Ref: non-Hispanic White; mother never married, widowed, divorced, separated, or deceased)						
Non-Hispanic Black; mother never married, widowed, divorced, separated, or deceased	-0.044	-0.201, 0.113	0.022	-0.157, 0.202	0.030	-0.128, 0.187
Non-Hispanic other/multiple race; mother never married, widowed, divorced, separated, or deceased	0.063	-0.107, 0.234	-0.042	-0.253, 0.169	-0.023	-0.190, 0.143
Hispanic; mother never married, widowed, divorced, separated, or deceased	-0.080	-0.211, 0.051	0.068	-0.082, 0.217	0.004	-0.124, 0.133
Mom is college graduate*never married/widowed/divorced/separated/deceased (ref: mom is college graduate*married)	0.011	-0.156, 0.177	-0.080	-0.240, 0.081	0.114	-0.074, 0.302
Child's race/ethnicity*mother's education*mother's marital status						
(Ref: non-Hispanic White; mom is college graduate; never married, widowed, divorced, separated, or deceased)						
Non-Hispanic Black; mom is college graduate; never married, widowed, divorced, separated, or deceased	0.119	-0.160, 0.398	0.086	-0.258, 0.430	-0.253	-0.588, 0.083
Non-Hispanic other/multiple race; mom is college graduate; never married, widowed, divorced, separated, or deceased	0.141	-0.368, 0.649	0.076	-0.357, 0.510	-0.202	-0.498, 0.094

Hispanic; mom is college graduate; never married, widowed, divorced, separated, or deceased	-0.046	-0.290, 0.197	-0.115	-0.475, 0.244	0.140	-0.232, 0.512
Child is male	0.004	-0.034, 0.043	0.010	-0.034, 0.053	-0.013	-0.050, 0.024
Child is first born	0.036	-0.001, 0.073	0.041	-0.006, 0.087	***-0.082	-0.122, -0.041
Child ever received WIC benefits	-0.028	-0.081, 0.026	0.025	-0.045, 0.095	0.002	-0.066, 0.070
Child uninsured	-0.013	-0.077, 0.050	-0.032	-0.119, 0.056	0.054	-0.021, 0.130
Mother's age group (ref: ≥30 years)						
≤19 years	-0.057	-0.174, 0.060	0.078	-0.083, 0.239	0.032	-0.104, 0.169
20-29 years	*0.051	-0.100, -0.002	-0.006	-0.060, 0.047	*0.050	0.007, 0.093
English language (vs. Spanish or other)	-0.021	-0.119, 0.078	0.061	-0.035, 0.157	-0.037	-0.115, 0.041
Housing arrangement (ref: owned or being bought)						
Rented	0.014	-0.032, 0.060	-0.050	-0.103, 0.003	0.041	-0.007, 0.088
Other arrangement	*-0.090	-0.164, -0.016	0.010	-0.111, 0.130	0.082	-0.019, 0.183
Provider facility type (ref: Private)						
Public/WIC	*-0.068	-0.134, -0.002	0.017	-0.061, 0.095	*0.081	0.014, 0.148
Hospital	-0.051	-0.108, 0.005	-0.009	-0.085, 0.067	0.016	-0.043, 0.075
Military/other facilities	*-0.113	-0.196, -0.030	-0.032	-0.155, 0.091	**0.174	0.054, 0.293
Mixed	0.017	-0.042, 0.076	0.036	-0.032, 0.104	-0.048	-0.099, 0.003
Child was never breastfed nor fed breast milk (ref: ever)	*-0.056	-0.100, -0.015	0.033	-0.023, 0.088	0.018	-0.030, 0.066
Parent ever refused/decided not to have their child vaccinated (ref: never)	***-0.130	-0.173, -0.087	**0.099	0.042, 0.157	*0.052	0.002, 0.101
Parent ever delayed or put off having their child vaccinated (ref: never)	***-0.083	-0.124, -0.042	**-0.075	-0.125, -0.026	***0.155	0.108, 0.202
Parent belief that vaccines are necessary to protect children's health	*0.015	0.002, 0.028	0.008	-0.011, 0.026	**-0.022	-0.038, -0.006
Parent belief that vaccines do a good job at preventing their diseases	-0.009	-0.026, 0.008	0.012	-0.005, 0.030	-0.007	-0.023, 0.009
Parent belief that vaccines are safe	*0.014	0.003, 0.024	0.000	-0.012, 0.013	*-0.011	-0.022, -0.001
Parent belief that vaccine-preventable diseases are serious, can hurt children	-0.000	-0.010, 0.001	-0.006	-0.018, 0.007	0.004	-0.006, 0.015
Parent perception of strength of physician vaccine recommendation	-0.004	-0.022, 0.015	0.002	-0.014, 0.019	0.005	-0.006, 0.017

Source: 2011 National Immunization Survey (NIS) data, children represented in the Parental Concerns module with provider-verified vaccination data and eligible for the influenza vaccination up-to-date question who are not missing any covariates. Coefficients (predicted probabilities) are weighted to be nationally-representative. Standard errors used to calculate 95% confidence intervals are adjusted for complex survey design. Also controls for area of residence. *p<0.05 **p<0.01 ***p<0.001

For the last 5 covariates (parent beliefs/perceptions), the scale is 0-10 where 0 is disagree and 10 is agree.

For the "series but not flu" outcome, shaded cells represent significant coefficients indicating vulnerability unique to the "series not flu" outcome or in a direction different than suggested from the "both" or "neither" outcomes.

Intersectional (fully-adjusted) results

Table 2-5 shows, for each UTD outcome, model-predicted probability of being UTD among all hierarchical combination of interactions terms for child’s race/ethnicity, mother’s education, and mother’s marital status. These predicted probabilities use the multivariate LPM models from Table 2-4 to predict UTD probabilities and 95% confidence intervals adjusted for all covariates in order to interpret the interactions. Focusing on just the “series but not flu” outcome of interest, recall from Table 2-4 that the coefficient for mother’s education and the two-way term interaction of mother’s education with child’s race/ethnicity (Hispanic) were both significant, indicating the mathematical presence of significant intersectionality. There were no significant differences within the predicted probabilities of each sole intersectional construct (see Figure 2-1). That said, though differences by mother’s education or marital status were very small in size, Hispanic children had about 9 percentage points higher “series but not flu” than non-Hispanic whites, a large, nearly significant size (the confidence intervals barely overlapped).

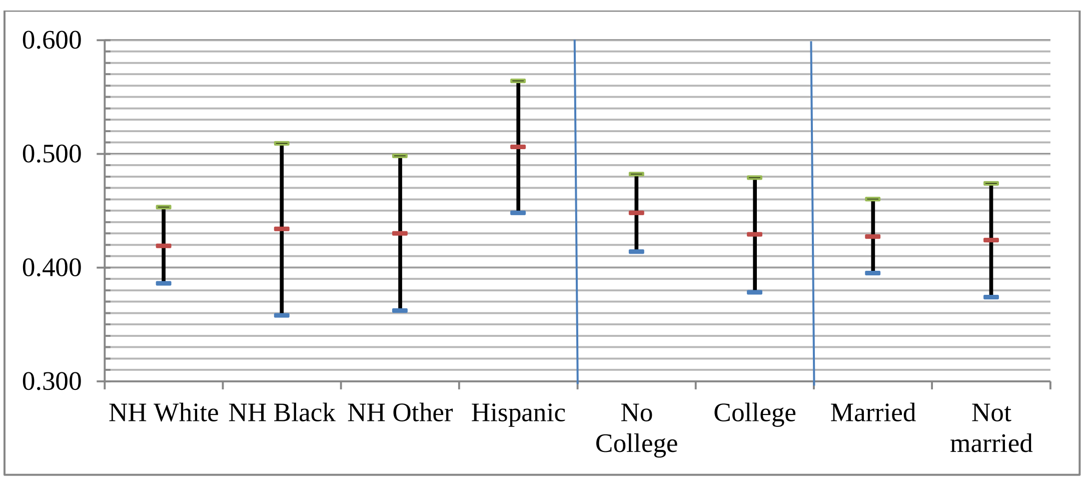

Figure 2-1. Model-predicted probability (with 95% confidence intervals) of “series but not flu” outcome among main coefficients from Table 2-5.

Table 2-5. Predicted probabilities of up-to-date vaccine outcomes among intersectional interaction term subgroups, multivariate linear probability model regression, U.S children aged 6-23 months old (N=7,246), 2011 NIS.

Up-to-date status (combinations of seasonal influenza and the 4:3:1:3:3:1:4 series)						
	" BOTH" Both flu and 4:3:1:3:3:1:4 series		**"SERIES BUT NOT FLU" 4:3:1:3:3:1:4 series, not flu**		**"NEITHER" Neither flu, 4:3:1:3:3:1:4 series**	
Main coefficient subgroups	**Prob**	**95% CI**	**Prob**	**95% CI**	**Prob**	**95% CI**
Child's race/ethnicity						
Non-Hispanic White only	0.295	0.270, 0.321	0.419	0.386, 0.453	0.230	0.200, 0.260
Non-Hispanic Black only	0.186	0.126, 0.246	0.434	0.358, 0.509	0.315	0.236, 0.395
Non-Hispanic other or multiple race	0.309	0.251, 0.368	0.430	0.362, 0.498	0.208	0.158, 0.258
Hispanic	0.237	0.186, 0.288	0.506	0.448, 0.564	0.207	0.163, 0.251
Mother's education						
Less than a college graduate	0.250	0.222, 0.278	0.448	0.414, 0.482	0.248	0.220, 0.276
College graduate	0.296	0.259, 0.332	0.429	0.378, 0.479	0.225	0.178, 0.272
Mother's marital status						
Married	0.284	0.254, 0.314	0.427	0.395, 0.460	0.229	0.200, 0.258
Never married, widowed, divorced, separated, or deceased	0.276	0.229, 0.324	0.424	0.374, 0.474	0.259	0.208, 0.309
Two-way interaction term subgroups						
Child's race/ethnicity*mother's education						
Non-Hispanic White child; non-college graduate mother	0.253	0.220, 0.286	0.452	0.407, 0.498	0.247	0.205, 0.289
Non-Hispanic White child; college graduate mother	0.372	0.316, 0.429	0.344	0.291, 0.396	0.225	0.163, 0.287
Non-Hispanic Black child; non-college graduate mother	0.198	0.106, 0.290	0.419	0.323, 0.516	0.294	0.212, 0.377
Non-Hispanic Black child; college graduate mother	0.194	0.115, 0.274	0.460	0.331, 0.589	0.321	0.180, 0.462
Non-Hispanic other or multiple race child; non-college graduate mother	0.280	0.199, 0.362	0.439	0.335, 0.544	0.224	0.152, 0.296
Non-Hispanic other or multiple race child; college graduate mother	0.395	0.240, 0.550	0.413	0.284, 0.543	0.159	0.087, 0.232
Hispanic child; non-college graduate mother	0.272	0.193, 0.350	0.447	0.370, 0.524	0.232	0.170, 0.293
Hispanic child; college graduate mother	0.168	0.100, 0.236	0.565	0.447, 0.683	0.222	0.116, 0.329
Child's race/ethnicity*mother's marital status						
Non-Hispanic White child; married mother	0.294	0.264, 0.324	0.419	0.375, 0.464	0.228	0.183, 0.273
Non-Hispanic White child; never married, widowed, divorced, separated, or deceased mother	0.301	0.236, 0.367	0.399	0.332, 0.466	0.262	0.190, 0.335
Non-Hispanic Black child; married mother	0.194	0.105, 0.284	0.423	0.320, 0.526	0.313	0.211, 0.415
Non-Hispanic Black child; never married, widowed, divorced, separated, or deceased mother	0.201	0.131, 0.271	0.457	0.360, 0.553	0.285	0.210, 0.360
Non-Hispanic other or multiple race child; married mother	0.283	0.210, 0.356	0.441	0.346, 0.536	0.221	0.156, 0.285
Non-Hispanic other or multiple race child; never married, widowed, divorced, separated, or deceased mother	0.404	0.227, 0.582	0.407	0.258, 0.555	0.158	0.069, 0.248

Hispanic child; married mother	0.263	0.190, 0.336	0.488	0.415, 0.561	0.200	0.144, 0.255
Hispanic child; never married, widowed, divorced, separated, or deceased mother	0.173	0.113, 0.234	0.494	0.377, 0.611	0.289	0.172, 0.406
Mother's education*mother's marital status						
Mother is not a college graduate; married	0.260	0.220, 0.299	0.437	0.393, 0.481	0.248	0.209, 0.287
Mother is not a college graduate; never married, widowed, divorced, separated, or deceased	0.241	0.202, 0.281	0.463	0.411, 0.516	0.244	0.199, 0.288
Mother is a college graduate; married	0.294	0.258, 0.330	0.447	0.396, 0.498	0.199	0.157, 0.240
Mother is a college graduate; never married, widowed, divorced, separated, or deceased	0.301	0.206, 0.396	0.380	0.270, 0.490	0.296	0.176, 0.417
Three-way interaction term subgroups						
Child's race/ethnicity*mother's education*mother's marital status						
Non-Hisp. White child; mother is not college grad; married	0.252	0.211, 0.292	0.449	0.391, 0.508	0.249	0.190, 0.308
Non-Hisp. White child; mother is not college grad; never married/widowed/divorced/separated/deceased	0.256	0.200, 0.311	0.458	0.382, 0.534	0.242	0.178, 0.306
Non-Hisp. White child; mother is college grad; married	0.368	0.329, 0.406	0.366	0.319, 0.413	0.191	0.153, 0.228
Non-Hisp. White child; mother is college grad; never married/widowed/divorced/separated/deceased	0.382	0.231, 0.533	0.295	0.166, 0.424	0.297	0.129, 0.466
Non-Hisp. Black child; mother is not college grad; married	0.211	0.081, 0.341	0.409	0.276, 0.543	0.287	0.172, 0.402
Non-Hisp. Black child; mother is not college grad; never married/widowed/divorced/separated/deceased	0.170	0.102, 0.239	0.441	0.351, 0.530	0.309	0.234, 0.385
Non-Hisp. Black child; mother is college grad; married	0.165	0.072, 0.259	0.448	0.286, 0.609	0.358	0.166, 0.550
Non-Hisp. Black child; mother is college grad; never married/widowed/divorced/separated/deceased	0.255	0.108, 0.401	0.485	0.275, 0.696	0.242	0.085, 0.399
Non-Hisp. other/multiple race child; mother is not college grad; married	0.259	0.154, 0.364	0.450	0.308, 0.592	0.234	0.141, 0.327
Non-Hisp. other/multiple race child; mother is not college grad; never married/widowed/divorced/separated/deceased	0.326	0.207, 0.444	0.417	0.292, 0.542	0.204	0.095, 0.313
Non-Hisp. other/multiple race child; mother is college grad; married	0.325	0.237, 0.413	0.425	0.333, 0.518	0.197	0.123, 0.271
Non-Hisp. other/multiple race child; mother is college grad; never married/widowed/divorced/separated/deceased	0.543	0.097, 0.988	0.388	0.040, 0.737	0.079	0.000, 0.239
Hispanic child; mother is not college grad; married	0.296	0.191, 0.402	0.423	0.325, 0.520	0.232	0.155, 0.310
Hispanic child; mother is not college grad; never married/widowed/divorced/separated/deceased	0.220	0.149, 0.291	0.499	0.411, 0.588	0.230	0.158, 0.302
Hispanic child; mother is college grad; married	0.204	0.123, 0.286	0.603	0.489, 0.717	0.142	0.067, 0.216
Hispanic child; mother is college grad; never married/widowed/divorced/separated/deceased	0.092	0.000, 0.209	0.485	0.206, 0.763	0.393	0.098, 0.687

Source: 2011 National Immunization Survey (NIS) data, children represented in the Parental Concerns module with provider-verified vaccination data and eligible for the influenza vaccination up-to-date question who are not missing any covariates from main analysis. Coefficients represent predicted linear probabilities of vaccination up-to-date outcomes among all hierarchical interaction term subgroups from multivariate linear probability regression models (Table 2-4).

Examining the predicted probability among the child's race/ethnicity*mother's education subgroups elucidates the significant interaction term coefficients. First, examining differences in predicted probabilities (Table 2-5), Hispanic children with college-educated mothers have the highest probability (0.565: 0.447-0.683) of "series but not flu," significantly higher than non-Hispanic White children with college-educated mothers (0.344: 0.291-0.396) despite that the former had one of the lowest predicted probabilities of the "both" outcome. Second, examining the pattern of how child's race/ethnicity modifies the relationship between mother's education and "series but not flu" (Figure 2-2, trend lines) shows that mother's education only appears to be associated with reduced "series but not flu" probability among non-Hispanic White and non-Hispanic Other children, but with increased probability among non-Hispanic Blacks and Hispanics. Non-Hispanic Black and Hispanic children, however, have relatively low prevalence of the "both" outcomes relative to non-Hispanic White children (Table 2-5), strengthening the argument that attainment of a college degree is associated with hidden vulnerability to being UTD on large series of vaccines but not influenza among Black and Hispanic children only.

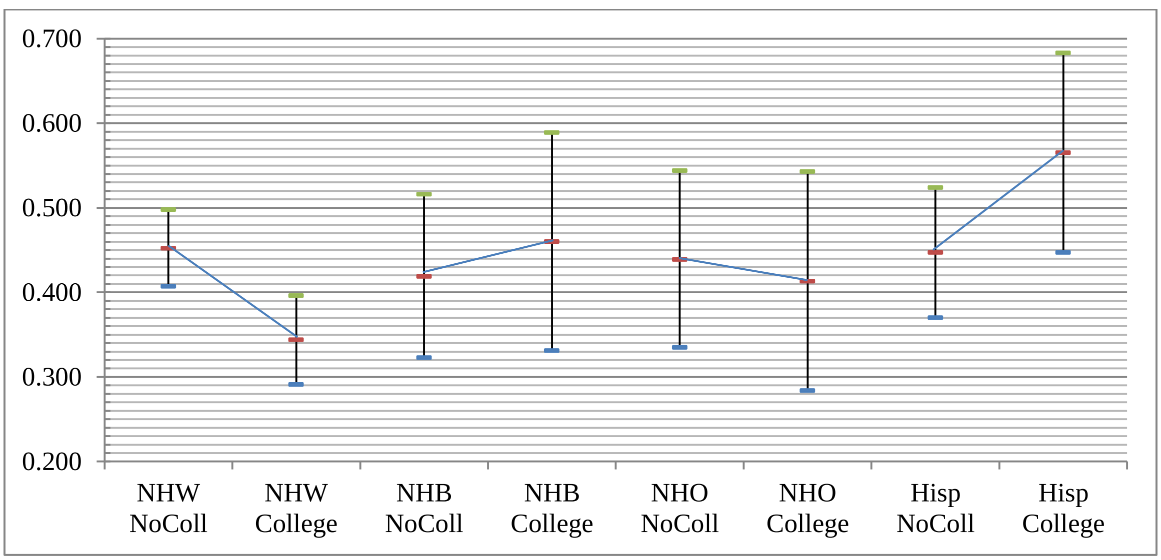

Figure 2-2. Model-predicted probability (with 95% confidence intervals) of "series but not flu" outcome among two-way interaction term subgroups: child's race/ethnicity*mother's education From Table 2-5.

For the other two-way interactions in the “series but not flu” outcome – child’s race/ethnicity*mother’s marital status and mother’s education*mother’s marital status – there were neither significant interaction term coefficients from Table 2-4 nor significant differences in predicted probabilities of intersectional subgroups in Table 2-5. This indicates no two-way intersectionality involving mother’s marital status.

There were also no significant coefficients among the triple-interaction term coefficients in Table 2-4, though there was one significant difference in predicted “series but not flu” among the triple interaction subgroups (Table 2-5), again involving Hispanic children: Hispanic children with married, college-educated mothers were significantly more likely to be in the “series but not flu” group (0.603: 0.489-0.717) than non-Hispanic White children with college-educated mothers regardless of whether the mother was married (0.366: 0.319-0.413) or never married, widowed, divorced, separated, or deceased (0.295: 0.166-0.424). This is elucidated by quick examination of the graphical representation of the triple interaction (Figure 2-3), which shows how race/ethnicity modifies the relationship between mother’s education and “series but not flu” stratified by mother’s marital status. The patterns seen among married mothers (top panel of Figure 2-3) closely mimics the unstratified relationship depicted in Figure 2-2. Looking at the pattern among mother’s never married, widowed, divorced, separated, or deceased (bottom panel of Figure 2-3), however, reveals a divergence in Hispanic women. From this, compared to Figure 2-2, the triple interaction clarifies that attainment of a college degree is associated with hidden vulnerability to being UTD on large series of vaccines but not influenza Hispanic children *only with married Hispanic mothers*. Hispanic mothers not in the married group appear to have the same education interaction as non-Hispanic White and non-Hispanic Other/multiple race children. The direction of the interaction term coefficient suggests this is unique to “series but not flu” vulnerability.

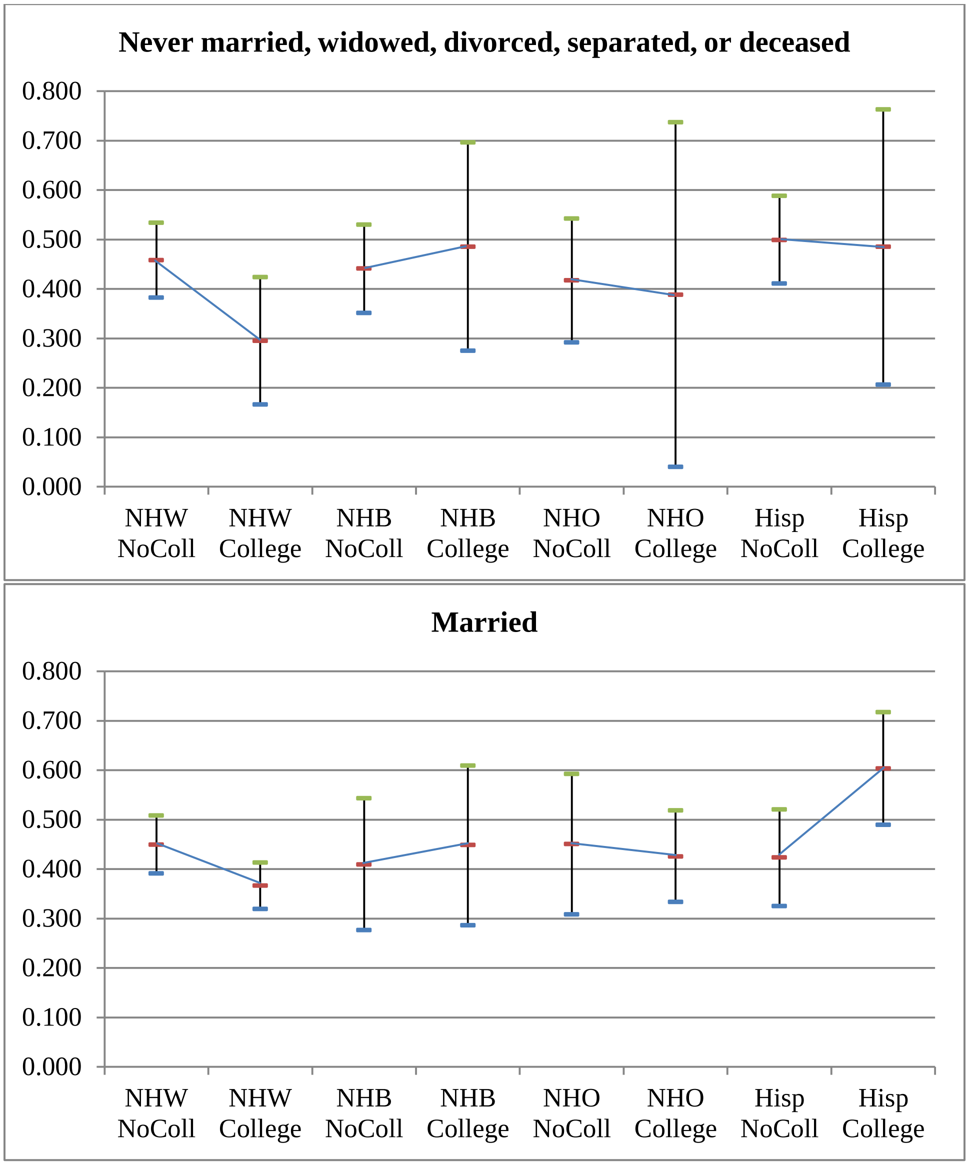

Figure 2-3. Model-predicted probability (with 95% confidence intervals) of “series but not flu” outcome among three-way interaction term subgroups: child’s race/ethnicity*mother’s education, stratified by mother’s marital status from Table 2-5.

Discussion

The overarching motivation of this study is tri-fold. First, few studies have examined factors influencing the uptake of influenza vaccination generalizable to the general US pediatric population, none of which grounded their analyses in a conceptual framework. Second, and related, literature examining influenza vaccination in children is limited in its ability to do so comprehensively, mostly relying on parent-reported vaccination without simultaneous, analytic consideration of many determinants known to be important to vaccine uptake or potential effects of intersectionality. The third and perhaps most important motivation for this study, however, is that the literature suggests influenza vaccination and its determinants are distinct from other vaccines and their respective determinants yet provides no comparison between the two in the same population of children. Consequently, the literature is unable to confidently and comprehensively identify and understand the determinants of young US children with "hidden vulnerability" to influenza: those who are up-to-date on a large series of vaccine recommendations – who would otherwise not seem like a population vulnerable to vaccine-preventable disease nor suggest they would have tendencies to refuse vaccination – but yet who are not up-to-date on their influenza vaccine recommendations.

To the first two motivations, this study adds that, in a nationally-representative sample of young children adjusting for intersectionality and a wide array of conceptually-grounded health services use and vaccine determinants at multiple levels, "hidden vulnerability" to low influenza vaccine uptake is associated with parents ever refusing any vaccine for their child, but interestingly enough, also with parents never having delayed or put off vaccinating their child. Additionally, intersectional consideration of social (dis)advantage revealed that a college education in mothers is associated with increased "hidden vulnerability" of influenza only among non-Hispanic Black and Hispanic children. The opposite association was found in non-Hispanic

White children, suggesting the benefits of parental college education to their child's vaccine uptake are not the same among racial/ethnic minorities that have historically been socially disadvantaged. To the third motivation, this study adds that the direction of the latter two findings above (vaccine delay and intersectionality) are unique to children with "hidden vulnerability" to influenza compared to children in the "both" or "neither" outcomes.

One robust finding from this study is that parental history of ever refusing a vaccine for their child was associated with reduced vaccination across all uptake outcomes. What is particularly interesting, however, is that this study found a unique predictor of "hidden vulnerability" to influenza to be parental history of never delaying vaccination. This may reflect the rise in vaccine hesitancy noted in the literature (Salmon, Dudley, Glanz, & Omer, 2015) in a way not observed before – that parents of children who appear to be up to date on their shots and thus appear to support the concept of vaccination are uniquely hesitant or skeptical about the influenza vaccine. This finding may indicate that the prevalence of vaccine hesitancy is deeper than anticipated and functions differently surrounding influenza. Vaccine hesitancy is complex; it is heavily grounded in myths about vaccines and their respective diseases, as well as interwoven with broader contexts such as socioeconomic circumstances, social norms, health beliefs, the media, and institutional trust (Chatterjee & O'Keefe, 2010; Larson, Jarrett, Eckersberger, Smith, & Paterson, 2014; Poland & Jacobson, 2001; Salmon et al., 2015; Schwartz & Caplan, 2011). Further research is needed into how these contexts may differ as they relate to vaccine hesitancy for influenza vaccines vs. other vaccines.

Intersectionality is a fundamental concept not just as it pertains to social disadvantage but also as it pertains to health (P. H. Collins, 1990, 2000; Dill & Zambrana, 2009; Schulz & Mullings, 2006), yet it has unfortunately been largely neglected in the health literature (Warner & Brown, 2011). Health policy researchers have simultaneously placed increasing recognition on the notion that health considerations must be incorporated into decision-making across many sectors and policy areas given that health is influenced by social, physical, and economic environments. The “Health in All Policies” approach, first published in 2013, recognizes that these social determinants of health drive health outcomes and inequities and advocates that the examination of health involve, among other things, promoting equity and health, and creating change at the structural level (Rudolph, Caplan, Ben-Moshe, & Dillon, 2013). Intersectionality and the “Health in All Policies” approach describe related phenomenon, and this study applies the lessons of both to describe a case of interacting patterns of social disadvantage and their relation to health vulnerability. For example, other recent studies of incomplete vaccine uptake among very young children from the NIS found nearly identical influenza vaccine uptake as the present study, as well as lower complete influenza vaccine uptake among Hispanics and non-Hispanic black children persisting across a decade of data (Santibanez et al., 2016). However, they offer no discussion of how social disadvantage may relate to these disparities, thus not connecting the concept of disparities with health inequities, nor do they examine how social statuses may be interacting, reinforcing the aforementioned criticisms coming from both sociologists and public health professionals.

Intersectional results from this study help to elucidate this gap – they appear to support the postulate that the attainment of a college degree in mothers is associated with higher uptake of both a large series of vaccines as well as the influenza vaccine in young children of racial/ethnic groups except for non-Hispanic Black and Hispanic children. By comparison, attainment of a college degree in mothers of non-Hispanic Black and Hispanic young children appears to be associated with “hidden vulnerability” of the young child to influenza. In other words, mother’s college education is associated with higher probability of the young child receiving a large series of vaccines and thus creating the appearance that the mother is accepting of vaccines yet the young child is simultaneously not up-to-date on influenza vaccines. Further, the direction of the interaction term coefficients suggests that this process is unique to children with “hidden vulnerability" but not to children vulnerable to other vaccines. This raises a larger point - higher parental education is generally associated higher vaccine uptake in US children (Daley et al., 2006; Gnanasekaran, Finkelstein, Lozano, et al., 2006; Santibanez et al., 2006), though this study provides evidence that the benefits from attainment of college education may be different in minorities and may contribute to disparities in influenza vaccination (and perhaps other health and health services outcomes, as well). Studies examining the education gradient and health have found that the returns of higher education may differ by race/ethnicity, particularly with regards to health behavior (Williams & Collins, 1995). For example, Perna (2005) found that post-secondary education increased the likelihood of having health insurance more for blacks than for whites, but found no differences in other health behaviors by race, though this contradicts our findings that college education is associated with increased "hidden vulnerability" of influenza only among non-Hispanic Black and Hispanic children. Additional research is needed to better elucidate the relationship between education and specific preventive health behaviors/utilization and how it differs by race.

These findings should be interpreted within the study's limitations. First, the provider-verified influenza vaccine UTD variable used to construct the outcome variables of this study does not capture influenza vaccinations that occurred after December 31st for the first dose or through the date of the interview or January 31st for the second dose (Centers for Disease Control and Prevention & NORC at the University of Chicago, 2012). This means it does not capture *all* provider-verified influenza vaccine doses given in any given season. However, influenza vaccine distribution is usually complete near the end of November or early in December (Centers for Disease Control and Prevention, 2014f). Indeed, in the 2011-2012 influenza season, approximately 131.2 million influenza vaccines were distributed by December 31st out of a total of 132.1 million on the year (99.2%) (Centers for Disease Control and Prevention, 2012). Since the influenza vaccine variable can contain up to three seasons of data depending on the child's birthdate, 99.2% compounded over three years is 97.7%, meaning we may reasonably estimate we are missing 0.8-2.3% of vaccine doses per child in our data, making the concern minimal. Further, the alternative measure, household-reported influenza vaccination of child within the previous 12 months, was not available in the 2011 NIS, would have only spanned one season and thus not have been able to portray child UTD on all influenza vaccines received by age 24 months, and would be subject to recall bias. Second, by design, key variables in this study require provider-verified data and thus exclude children without provided-verified data. Some of these children may be lacking this type of data because they lack a usual source of care, which has been linked to lower preventive care use in adults (DeVoe, Fryer, Phillips, & Green, 2003). Because this is a survey limitation, this is unavoidable, though because those that are excluded may use less preventive services, the implication is that our findings are likely conservative. Third, there is concern of non-response bias with the NIS. For example, the overall household response rate was 61.6% with 72.3% of these respondent households having adequate provider data, the implication being that over a third of eligible houses are not captured in the NIS and of those captured, over a quarter did not have adequate provider data necessary for this analysis. Of these remaining respondent households with adequate provider data, 69.8% were flagged to receive the PC module and though this is not due to non-response, an additional small percentage of households were lost due to a 94% PC module completion rate. Of all respondent household children with adequate provider-verified data and a completed PC module, about 64.2% were eligible for the influenza up-to-date variables; again, though this is due to age during the influenza season and is not a non-response issue, it does lower study power. Overall, the implication is that more than half of eligible children are lost due to NIS non-response issues, introducing concerns of non-response bias. This is a limitation of the data source itself that needs to be addressed in future surveys and warrants investigation of non-response effects. Though this study's findings must be interpreted with this in mind, the NIS still provides the only opportunity to examine nationally-representative, provider-verified uptake of multiple vaccines in young children that includes key constructs for parental attitudes, perceptions, and beliefs surrounding vaccination and vaccine-preventable diseases. Fourth, this analysis is cross-sectional and thus cannot make causative claims; all findings are associative in nature. That said, one of the main identifying strategies of this study was to use only provider-verified vaccine outcomes and to include in one model a set of conceptually-grounded covariates more comprehensive than other literature, including a wide variety of socioeconomic and demographic constructs at the child, parent, and family/household levels, provider facility type, strength of physician recommendation for vaccination, a health environment proxy, history of vaccine refusal or delay, and parental perceptions and attitudes surrounding vaccine necessity, effectiveness, safety, and disease risk. Moreover, despite that parental perceptions and attitudes toward vaccines and their diseases have repeatedly been recognized as important determinants of vaccine uptake, they have seldom been utilized in nationally-representative examinations of vaccine uptake given their limited availability in national data and the restricted access required to obtain them. Further, though we cannot definitively rule out the possibility of bidirectionality in our findings, we believe this possibility to be less likely. Referring back to Andersen's model, the aforementioned constructs included are thought to temporally precede the decision to use a health service. This is noticeably true for the significant factors noted in this study: pre-disposing (child's race/ethnicity) and enabling factors (mother's education), as well as their intersectionality, precede historical personal health services use factors at the behavior level (history of vaccine refusal and/or delay), which precede health services utilization (vaccine uptake).

This study discusses the importance of "hidden vulnerability to flu" – a phenomenon where 44% of very young US children are up to date on a large series of vaccines which appears to indicate excellent preventive health services uptake yet are not completely immunized against influenza. Independent of an expansive set of confounders, the most important factor predicting presence of such hidden vulnerability is history of vaccine refusal, though public health policymakers, practitioners, and researchers need to be aware that there was also a significant association with never having delayed vaccination. In other words, healthcare providers in general need to have conversations surrounding vaccine hesitancy even with the parents of children who appear to be broadly up to date on their shots and generally support the concept of vaccination – these parents are unlikely to give any indication to the doctor of their skepticism of the influenza vaccine yet their child may likely go unvaccinated. Providers thus must specifically engage all parents on the topic of influenza vaccination regardless of their other decisions regarding their child's vaccinations. Pediatricians and other healthcare providers who see children should consider adding questions to their history and physical protocols pertaining to parental history of refusing or delaying vaccination, as well as pertaining to vaccine hesitancy both generally and specifically to influenza in order to systematically include these conversations in their medical evaluations of child patients. Further, this study documents an association suggesting that college education may not translate into improved preventive service behavior among children of historically-disadvantaged race or ethnicity despite that it does for non-Hispanic White children. As such, it is yet again clear that policymakers and researchers from public health, sociology, and other sectors need to collaborate to examine both how preventive health services use functions in the context of interacting social disadvantage, and how social policies ensuring equitable social advantage indeed lead to equitable health – the calling of Health in All Policies.

Chapter 3

The association of child influenza vaccination status with household adult work loss due to illness

Abstract

Background: As it pertains to influenza, children cause substantial household transmission and parental work absenteeism, and contribute to community epidemics. All persons over 6 months of age are recommended annually to receive an influenza vaccine. The association of influenza vaccination in young children with reduced household adult work loss, however, has rarely been studied. Although a few studies in Europe and one of US school-based vaccination provide proof of concept, conceptual grounding and generalizability to all working US adults is very limited.

Methods: This study uses data nationally-representative of working US adults with household children (N=7,938) from the most recent (2014) National Health Interview Survey. Using zero-inflated negative binomial regression, it examines the association of child influenza vaccination with household adult work loss days due to illness or injury and the moderating role of paid sick leave, adjusted for a variety of occupation, socioeconomic, demographic, and health confounders.

Results: On average, working US adults with children in the household missed 3.64 days of work in the previous year due to illness or injury, 54% had paid sick leave, and 52% of sample children in the household received an influenza vaccine in the previous year. Adjusting for confounders, adults without paid sick leave had almost no difference in missed work time by household child influenza vaccination status (0.17 less missed work days than with unvaccinated household

children: 2.93 [2.13-3.72] vs. 3.10 [2.34-3.85]), though in those with paid sick leave, this difference was much larger although still not statistically significant (0.96 less missed work days than those with unvaccinated household children: 4.32 [3.28-5.35] vs. 5.28 [4.08-6.49]).

Conclusions: For working adults with paid sick leave, having a household child vaccinated for influenza (versus not) may be associated with one less lost work day due to illness in the previous year, though this was not statistically significant. The lack of significance may be due to several reasons, including that the work loss measure was not illness-specific and included injuries, that only one child was sampled for households with multiple children, or due to design effects. We suggest evaluation in a larger sample given the magnitude's plausible consistence with other studies showing child influenza illness to be associated with one or more parental work loss days and with limited studies examining parental work loss reduction due to child influenza vaccination. Further, this association was over five times smaller among working adults without paid sick leave. Because paid sick leave is distributed inequitably to those with lower income or educational attainment, this suggests that those without paid sick leave are not only likely less able to take off work when they or their child are sick, but also are likely bringing their illness to work because they cannot afford to take off.

Introduction

Background

It is well-established that young children (under the age of 5 years old) are a high risk population group as it relates to influenza. They are at increased risk of doctor visits, urgent care visits, ER visits, and hospitalizations due to influenza (Centers for Disease Control and Prevention, 2013; Thompson et al., 2004), and represent a substantial portion of all influenza-related morbidity for the total US population (Centers for Disease Control and Prevention, 2015a). The broader impacts of influenza in young children on their surrounding environments have also been the subject of research, though the findings are less well-established. For example, published literature reviews of the impact of influenza in children note that it affects family members and caregivers (Teo et al., 2005), causes substantial parental work absenteeism (Fraaij & Heikkinen, 2011), and contributes to community epidemics (Jordan et al., 2006), though more evidence is needed.

The CDC recommends that all persons 6 months of age and older receive influenza vaccination (Fiore et al., 2010) as the best preventive measure against influenza (Cox & Subbarao, 1999). One particular gap in the literature of the impact of influenza in children, however, is that our understanding of the broader effects of influenza vaccination in children, especially as it relates to their contacts, is limited and requires better characterization (B. Y. Lee & Shah, 2012; Teo et al., 2005). Pertaining to parental absenteeism from work, this gap in knowledge is particularly important for several reasons: (1) influenza vaccination uptake in US children remains sub-optimal and substantially lower than that of other childhood vaccines (National Foundation for Infectious Diseases, 2015; Santibanez et al., 2016); (2) influenza infection in children is known to cause parental work absenteeism (Fraaij & Heikkinen, 2011);

and (3) it is estimated that influenza infection in the US results in over $87 billion in economic burden each year in the US, $16.3 billion of which is due to lost earnings (Molinari et al., 2007). Thus, better understanding the extent to which childhood influenza vaccination prevents parental work loss would significantly contribute toward the research gap in our understanding of its indirect effects on families and society.

Statement of research aims

The second research aim of this dissertation is to understand the association of child vaccination status on work loss of other adults living in the same household in a nationally-representative sample. It will also examine how this relationship is moderated by the adult having or not having paid sick leave and how this varies and has different implications across determinants of interest such as race and ethnicity, education, occupation, and marital status. The findings will contribute to the gap in the literature on direct and indirect effects of child influenza vaccination by examining its potential association directly on family work status and by extension, indirectly on the economic burden of influenza in the US. It will help build the case for practitioners and policymakers as to why influenza vaccination of children is not just important for protecting child health but also for maintaining a strong and healthy work force and minimizing billions of dollars of annual economic burden due to influenza.

Literature Review

Multiple studies show that seasonal influenza infection in children is associated with transmission in the household; it has even been argued that the presence of children in the household is the *most* important predictor of secondary influenza illness within other family members (Principi & Esposito, 2004). For example, household contacts of children with influenza had a 1.85 hazard ratio of influenza infection within 5 days in a nation-wide prospective study in France (Viboud et al., 2004); a prospective study of children who went to the Emergency Department in Milan, Italy with confirmed influenza found that 18.3% of their household contacts had similar disease (highest among mothers and siblings: Esposito et al., 2005); and three prospective studies over the previous several decades from Seattle, Washington demonstrate that having a child in the house predicted secondary infection among family members (Fox, Hall, Cooney, & Foy, 1982; Foy, Cooney, & Allan, 1976; Neuzil, Hohlbein, & Zhu, 2002). None of these studies are nationally-representative to the United States, but the evidence strongly suggests that household contacts of US children with influenza are at risk for secondary influenza illness.

Moreover, there is also evidence in the literature that having a child with influenza or influenza-like-illness (ILI) symptoms in the household is significantly associated with significant parental work day loss (Fraaij & Heikkinen, 2011; King et al., 2012). A prospective study of children treated in an emergency department in Boston, MA for influenza infections showed that 64% of the children's parents missed at least 1 work day; the authors extrapolated these findings to national hospitalization rates and estimated that parents of children infected with influenza in the US miss nearly 247,000 work days a year (Bourgeois, Valim, McAdam, & Mandl, 2009); a systematic review of studies in Western Europe found that parents of children with laboratory-confirmed influenza missed 1.3-6.3 days of work (Antonova, Rycroft, Ambrose, Heikkinen, & Principi, 2012); a prospective study in Turkey estimated that for every 100 children infected with influenza, there were nearly 200 parental work loss days, equating to a mean duration of 3.2 days lost (Heikkinen et al., 2004); and a prospective survey of adults from three large US employers found that employees with household members with ILI symptoms missed 0.6 more work days (significant) relative to those with children without such illness and estimated that nearly a tenth of work absenteeism was due to acute respiratory infection in household members during the flu season (Palmer, Rousculp, Johnston, Mahadevia, & Nichol, 2010). There is also evidence that parental work loss due to *any* child illness is significantly higher during the influenza season: a prospective study in Seattle estimated that 20 days were lost for every 100 children who missed a school day for *any* illness during the flu season (Neuzil, Hohlbein, et al., 2002).

By comparison, the association of influenza *vaccination* in children with parental work loss has rarely been studied (Jefferson, Rivetti, Di Pietrantonj, Demicheli, & Ferroni, 2012) and the few studies found have no generalizability to the general US population. For example, a prospective study of parents of 303 children in Italy missed significantly less work days when the child had received the influenza vaccine vs. not (1.56 less days missed for mothers and 0.42 less days missed for fathers on average) (Principi, Esposito, Marchisio, Gasparini, & Crovari, 2003a); an industry-funded study of children attending day care in various sites across Western Europe found that the parents of children who received the live-attenuated nasal spray vaccine had 47.5% less missed work days compared to parents of unvaccinated children (Vesikari et al., 2006); and a study of Maryland schools found that offering influenza vaccination through school-based programs significantly reduced lost parental workdays relative to control schools (King et al., 2005, 2006).

Methods

Data source

Data for this study come from most recent (2014) National Health Interview Survey (NHIS), developed by the National Center Health Statistics (NCHS) of the CDC. The NHIS was created in 1957 as a response to the National Health Survey Act of 1956 and is considered to be the cardinal source of health information of the civilian, non-institutionalized US population (target population). Since 1957, the NHIS was been periodically updated, and the most recent major revision occurred in 1997 with small modifications made each year thereafter. The NHIS is a cross-sectional household interview survey of the target population living in the US at the time of the interview that uses a multistage area probability design to generate a nationally-representative sampling of occupied housing units and non-institutional group residences (e.g., college dormitories) (Division of Health Interview Statistics, National Center for Health Statistics & Centers for Disease Control and Prevention, 2015).

The content of the NHIS consists of four "Core" components that are largely unchanged from year to year as well as a variety of supplementary sections. The first Core component is the Household Compositions section, which contains basic demographic and relationship information from all persons in each sampled occupied housing unit. The second Core component is the Family Core section, which is administered separately for every family within each sample housing unit (there can be more than one family per housing unit) and collects information on all persons in the family related to sociodemographic characteristics, basic indicators of health status, activity limitations, injuries, health insurance coverage, and access and utilization of health services. The NHIS defines a family as an individual or a group of two or more related persons who are living together in the same household, which also includes unmarried couples who are living together. Within each family, if there are any children (17 years or younger), one child is randomly selected. A knowledgeable adult answers questions about the child, and these responses comprise the third Core component – the Sample Child section. The knowledgeable adult then answers questions about themselves, which comprises the fourth Core component – the Sample Adult section. Both the Sample Child and Sample Adult sections contain basic questions on health status, health services, and health behaviors, though the majority of questions are unique to health issues pertinent to adults and children separately (Division of Health Interview Statistics, National Center for Health Statistics & Centers for Disease Control and Prevention, 2015).

This analysis also contains a restricted variable indicating respondent's FIPS code (household state of residence). This variable was merged with the publicly-accessible NHIS variables by NCHS analysts and this merged, restricted dataset was accessed at the Penn State Federal Statistical Research Data Center, a Census Bureau facility housed at Penn State that meets all physical and information security requirements for accessing restricted federal data. Data collection for NHIS was approved by the NCHS Research Ethics Review Board (ERB). Analysis of de-identified data from the survey is exempt from the federal regulations for the protection of human research participants. Analysis of restricted data through the Research Data Center is also approved by the NCHS ERB. The findings and conclusions in this paper are those of the author and do not necessarily represent the views of the Research Data Center, the National Center for Health Statistics, or the Centers for Disease Control and Prevention. Additionally, the proposed research of this study was reviewed by the Pennsylvania State University Institutional Review Board who deemed it Not Human Research.

Dependent variable

The outcome variable in this study is self-reported number of work loss days in the past 12 months from the Sample Adult section. The exact question asked was, "During the past 12 months, that is, since [12-months before interview date], about how many days did you miss work at a job or business because of illness or injury (do not include maternity leave)?"

Independent variables of interest

The independent variable of interest is adult-reported influenza vaccination status of the child within the previous 12 months (binary) from the Sample Child section. This includes both receipt of the shot or the nasal spray vaccine. Another independent variable of interest in terms of its possible interacting effects on the relationship between child influenza vaccination status and parental work loss is whether or not the adult has paid sick leave (from the Sample Adult section).

Covariates

Three covariates directly related to parental work status were included from the Sample Adult file to control for confounding. These include: (1) *worker class* (employee of a private company for wages; a federal government employment; a state government employee; a local government employee; or self-employed in own business, professional practice, or firm or working without pay in a family-owned business); (2) *paid by the hour* (whether the respondent was paid by the hour at their current or most recent job or business); and (3) *simplified occupation code* (23 mutually-exclusive categories as derived by U.S. Census Bureau and the Bureau of Labor Statistics classifications; not shown in tables due to large number of categories).

Nine socioeconomic and demographic characteristics related to work, social position, and general health were also included from the Sample Adult, Family, Person, or Imputed Income File sections. These include: (1) *sex* (male or female); (2) *race/ethnicity* (recoded from the Office of Management and Budget's race classifications and a Hispanic ethnicity variable: non-Hispanic White only; non-Hispanic Black/African American; non-Hispanic Asian; non-Hispanic other or multiple race; or any Hispanic); (3) *age category* (18-24; 25-34; 35-44; 45-54; 55-64; 65+); (4) *self-rated health* (excellent; very good; good; fair; or poor); (5) *highest family educational attainment* (<high school; high school or GED; Associate's degree or some college but no degree; and Bachelor's degree or higher); (6) *family income relative to poverty threshold* (<100%; 100-199%; ≥200%); (7) *family size* (2; 3; 4; 5; or 6+); (8) *family type* (one adult with children; or multiple adults with children); and (9) *household location of residence* (FIPS state codes; this is a restricted variable accessed through the Research Data Center that was necessary for adjusting for state-level employment policy and other state-level policy contexts).

Given that the focus of this study is to investigate whether or not parental work loss is influenced by child influenza vaccination status, we also control for *adult influenza vaccination status* (whether the adult reported receiving either the shot or nasal spray influenza vaccine in the previous 12 months, from the Sample Adult file).

A correlation matrix was conducted on all covariates and there were no concerns of multicollinearity, indicating that the selected covariates represent different constructs that should not unnecessarily inflate the standard errors in multivariate regression.

Study population

The present study matches children with a knowledgeable adult respondent in their family by linking together multiple NHIS Core sections together by combinations of unique identifiers for the household, family, and/or person because the outcome variable is at the adult level, the independent variable of interest is at the child level, and important covariates are needed at both the adult and family levels. The weighting variable used in this study is the final annual Sample Adult weight provided by NHIS because the unit of analysis is adults. The 2014 NHIS contained data on 36,697 adults, and the total household response rate was 73.8% (Division of Health Interview Statistics, National Center for Health Statistics & Centers for Disease Control and Prevention, 2015).

The study sample was restricted to the 23,555 adults eligible for the outcome of interest – those who indicated they had a job last week or had no job last week but did have a job in the past 12 months. Because the independent variable of interest is at the child level (child influenza vaccination status), the study sample was then restricted to the 8,413 working adults with children in the household who completed the Sample Child component; the conditional response rate for the Sample Child component was 91.2% (Division of Health Interview Statistics, National Center for Health Statistics & Centers for Disease Control and Prevention, 2015). Of these working adults with child respondents in the household, 8,192 were not missing responses on the dependent, independent, and moderator variables of interest (missed work days, household child influenza vaccine, and paid sick leave questions) and thus comprise the total eligible sample.

Complete case analysis (i.e., listwise deletion; excluding cases missing on any variables in the analysis) was performed. Nearly 97% of the eligible sample were complete cases across all variables (n=7,938). Sensitivity analyses were conducted to determine if being in the complete case analytic sample was associated with any variables utilized in the study and there was no association with work loss, child influenza vaccination status, nor paid sick leave, though complete case respondents were slightly more likely to be government employees and 18-24 or 55-64 years old. Given that missingness was not completely at random, that our complete case sample is relatively large, and that complete case missingness is very low and not associated with any key variables nor most covariates, listwise deletion is appropriate and likely less biased than other methods of dealing missingness (P. D. Allison, 2014).

Analysis

Bivariate analyses were conducted to examine if significant differences in the mean number of household adult work days lost differed by values of each covariate separately. Then, parental work loss days was regressed on child influenza vaccination status and paid sick leave status in a series of multivariate analyses: first with all direct occupation covariates, then adding in socioeconomic and demographic covariates, and finally adding in adult influenza vaccination status (Models 1 through 3). An interaction term between child vaccination status and paid sick leave status was then added (Model 4) to see if having paid sick leave moderates the fully-adjusted relationship between child influenza vaccination status and parental work loss days, given the direct role paid sick plays in the ability of a working adult to miss work due to illness or injury. Because the work loss outcome is an overdispersed and zero-inflated count variable, zero-inflated negative binomial (ZINB) regression is utilized to appropriately model it (Long & Freese, 2006; UCLA: Statistical Consulting Group, 2011). Last, to interpret the interaction term coefficients, work loss days are predicted from Model 4 for all interaction subgroups (by household child's influenza vaccination status, by paid sick leave status, and by the four combinations of the two binary variables).

All analyses were performed using Stata/SE 13.1 statistical software (StataCorp LP, 2013) and use Stata's *svy* commands to apply NHIS-provided final annual Sample Adult weights to generate national-representativeness of non-institutionalized US adults adjusting for complex survey design, ratio, non-response, post-stratification adjustments, and heteroscedasticity.

Results

Table 3-1 contains weighted, descriptive statistics of the complete case analytic sample, nationally-representative of working US adults with children in the household. On average, respondents missed 3.64 days in the previous year due to illness or injury (not including maternity leave), and 54% had paid sick leave at their job. Respondents reported that a little over half (52%) of child respondents living in these households received an influenza vaccination in the previous year. Overall, average respondents were: employees of private companies; and paid by the hour. They mostly: were non-Hispanic Whites; were 35 years or older; of very good or excellent self-reported health; reported receipt of an influenza vaccination in the previous year; lived with families with at least another adult; had 4 or more family members; had family income at least twice the poverty line; had highest family educational attainment of less than a bachelor's degree.

Table 3-1. Descriptive statistics of study population, working US adults with children in the household (N=7,938), 2014 NHIS

Variable		
Outcome variable	**Mean (sd)**	**N**
Work loss day to injury or illness, previous 12 months	3.64 (17.27)	7938
Independent variables of interest	**Percent**	**N**
Child influenza vaccination status, previous 12 months		
Unvaccinated	51.8	4105
Vaccinated	48.2	3833
Paid sick leave status		
No	46.0	3728
Yes	54.0	4210
Covariates	**Percent**	**N**
Worker class		
Employee of a private company for wages	77.2	6082
Federal government employee	2.6	225
State government employee	5.2	452
Local government employee	6.8	532
Self-employed or in family-owned business	8.2	647
Paid by the hour		
No	39.3	2960
Yes	60.7	4978
Sex		
Female	49.8	4466
Male	50.2	3472
Race/ethnicity		
Non-Hispanic White	58.2	4282
Non-Hispanic Black or African American	11.9	1027
Non-Hispanic Asian	6.1	442
Non-Hispanic other or multiple race	2.0	201
Hispanic	21.9	1986
Age category (years)		
18-24	11.6	670
25-34	25.2	2257
35-44	35.3	2930
45-54	22.4	1667
55-64	4.6	338
65+	1.0	76
Highest family educational attainment		
<High school	6.2	671
High school or GED	16.9	1441
Associate's degree or some college (no degree)	33.1	2696
Bachelor's degree or higher	43.9	3130

Family income as a percentage of the Federal Poverty Line		
<100%	13.1	1330
100-199%	21.1	1816
≥200%	65.8	4792
Family size		
2	4.6	776
3	25.8	2252
4	36.4	2782
5	20.1	1384
6+	13.1	744
Family type		
One adult with 1+ children	9.3	1559
Multiple adults with 1+ children	90.7	6379
Reported health status		
Excellent	35.9	2688
Very good	34.6	2727
Good	24.2	2031
Fair	4.9	453
Poor	0.5	39
Adult influenza vaccination status, previous 12 months		
Yes	63.5	5044
No	36.5	2894

Source: 2014 National Health Interview Survey (NHIS) data, working adult respondents with child respondents in the household and not missing on covariates. Means and percentages weighted to be nationally-representative of working adults with children in the household. N un-weighted to show actual number of observations in each cell.

Bivariate (unadjusted) results

Table 3-2 shows weighted bivariate statistics, the unadjusted difference in mean work loss days among respondents across all covariates. Having a child in the household with an influenza vaccination was non-significantly associated with 0.37 fewer missed work days than having an unvaccinated household child (3.45 vs. 3.82, p=0.4967). Similarly, paid sick leave was non-significantly associated with 0.68 more missed work days (3.95 vs. 3.27, p=0.2316). There was only one covariate significantly associated with differences in mean missed work – self-rated health, which exhibited a clear gradient of more missed work days associated with decreasing self-rated health (p<0.0001).

Table 3-2. Bivariate statistics of work loss days stratified by covariates, working US adults with children in the household (N=7,938), 2014 NHIS

	Work loss days	
Independent variables of interest	**Mean (se)**	***p***
Child influenza vaccination status, previous 12 months		
Unvaccinated	3.82 (0.31)	
Vaccinated	3.45 (0.34)	0.4967
Paid sick leave status		
No	3.27 (0.45)	
Yes	3.95 (0.34)	0.2316
Covariates		
Worker class		
Employee of a private company for wages	3.62 (0.34)	
Federal government employee	4.46 (0.96)	
State government employee	3.39 (0.59)	0.1014
Local government employee	4.59 (0.81)	
Self-employed or in family-owned business	2.55 (0.52)	
Paid by the hour		
No	3.08 (0.27)	
Yes	4.00 (0.43)	0.0787
Sex		
Female	3.76 (0.38)	
Male	3.52 (0.39)	0.6603
Race/ethnicity		
Non-Hispanic White	3.77 (0.43)	
Non-Hispanic Black or African American	3.45 (0.43)	
Non-Hispanic Asian	2.62 (0.44)	0.1992
Non-Hispanic other or multiple race	5.41 (1.51)	
Any Hispanic	3.52 (0.50)	
Age category (years)		
18-24	3.36 (1.02)	
25-34	3.89 (0.70)	
35-44	3.44 (0.27)	
45-54	3.24 (0.40)	0.8577
55-64	6.54 (2.88)	
65+	2.87 (2.20)	
Highest family educational attainment		
<High school	3.02 (0.94)	
High school or GED	3.59 (0.51)	
Associate’s degree or some college (no degree)	4.45 (0.59)	0.3135
Bachelor’s degree or higher	3.14 (0.39)	
Family income as a percentage of the Federal Poverty Line		
<100%	3.77 (0.59)	
100-199%	4.19 (0.72)	0.5901
≥200%	3.44 (0.32)	
Family size		

2	4.22 (0.81)	0.1212
3	3.24 (0.36)	
4	3.97 (0.48)	
5	4.16 (0.95)	
6+	2.53 (0.37)	
Family type		
One adult with 1+ children	4.09 (0.50)	0.4027
Multiple adults with 1+ children	3.59 (0.30)	
Reported health status		
Excellent	1.96 (0.19)	<0.0001
Very good	2.74 (0.24)	
Good	4.12 (0.37)	
Fair	14.37 (3.60)	
Poor	62.04 (28.06)	
Adult influenza vaccination status, previous 12 months		
No	3.47 (0.31)	0.4308
Yes	3.94 (0.52)	

Source: 2014 National Health Interview Survey (NHIS) data, working adult respondents with child respondents in the household and not missing on covariates. Means and percentages weighted to be nationally-representative of working adults with children in the household. P-values of mean differences calculated using standard errors adjusted for complex survey design.

Multivariate (adjusted) results

Table 3-3 shows incidence rate ratios (IRRs) of work loss days due to illness or injury in the previous year from ZINB regression models. Model 1 shows the relationship of work loss days with household child influenza vaccination status and paid sick leave controlling only for factors directly related to household adult occupation. Having a vaccinated household child vaccinated resulted in a modest 0.95 times the incidence of work loss days than having an unvaccinated child (not statistically significant; 95% confidence interval: 0.72-1.26). In this model, having paid sick leave was also associated non-significantly with less missed work days (0.89: 0.57-1.37). Models 2 (adding socioeconomic and demographic covariates) and 3 (then adding adult influenza vaccination status) had nearly identical results. In both, the magnitude of the IRR of work loss associated with household child influenza vaccination increased to 0.90, though still non-significant (0.75-1.09 in Model 2, 0.74-1.09 in Model 3). Paid sick leave, however, was significantly associated with a 1.31 (1.04-1.65; Model 2) to 1.32 (1.05-1.65; Model 3) times higher incidence of missed work time. Model 4 incorporates an interaction between paid sick leave and household child influenza vaccination status. Similar to Models 2 and 3, paid sick leave remained significant and household child influenza vaccination non-significant; the interaction was also non-significant. Three other covariates remained significantly associated with higher IRRs of missed work time across Models 2 to 4 – relative to private employees, state government employees (IRRs 1.49-1.51 across models); relative to non-Hispanic Whites, non-Hispanic other or multiple race (IRRs 2.26-2.38 across models); and last, relative to excellent self-reported health, working adults of very good, good, fair, or poor health (IRRs 1.36-1.37, 2.00, 6.88-6.98, and 46.01-48.40, respectively, across models). A sensitivity analysis interacting these factors with household child influenza vaccination found no significant interaction term coefficients.

Table 3-3. Incident Rate Ratios of work loss days from multivariate zero-inflated negative binomial regression, working US adults with children in the household (N=7,938), 2014 NHIS

Categorical variables	**Incident Rate Ratios (IRRs) Lost Work Days due to illness or injury, previous 12 months**							
	Model 1		**Model 2**		**Model 3**		**Model 4**	
Independent variables of interest	**Adj. IRR**	**95% CI**	**Adj. IRR**	**95% CI**	**Adj. IRR**	**95% CI**	**Adj. IRR**	**95% CI**
Child received influenza vaccination, previous 12 months	0.95	0.72, 1.26	0.90	0.75, 1.09	0.90	0.74, 1.09	1.02	0.70, 1.51
Has paid sick leave	0.89	0.57, 1.37	*1.31	1.04, 1.65	*1.32	1.05, 1.65	*1.46	1.03, 2.06
Child vaccinated*Paid sick leave	--	--	--	--	--	--	0.82	0.50, 1.34
Covariates								
Worker class (ref: employee of private company for wages)								
Federal government employee	1.30	0.77, 2.22	1.33	0.88, 2.00	1.34	0.89, 2.02	1.35	0.90, 2.04
State government employee	1.13	0.81, 1.57	1.28	0.94, 1.75	1.28	0.94, 1.74	1.28	0.94, 1.73
Local government employee	1.43	0.97, 2.12	*1.49	1.01, 2.21	*1.50	1.02, 2.22	*1.51	1.02, 2.23
Self-employed or in family-owned business	1.01	0.55, 1.84	1.51	0.97, 2.35	1.50	0.95, 2.35	1.56	0.99, 2.45
Not paid by the hour (vs. paid by the hour)	0.78	0.59, 1.04	0.90	0.71, 1.14	0.91	0.72, 1.14	0.91	0.73, 1.15
Male	--	--	0.99	0.81, 1.21	0.99	0.81, 1.20	0.98	0.81, 1.20
Race/ethnicity (ref: Non-Hispanic White)								
Non-Hispanic Black or African American	--	--	1.01	0.74, 1.39	1.00	0.73, 1.38	1.01	0.73, 1.38
Non-Hispanic Asian	--	--	0.91	0.63, 1.33	0.92	0.64, 1.33	0.92	0.64, 1.33
Non-Hispanic other or multiple race	--	--	**2.26	1.28, 3.99	**2.27	1.28, 4.02	**2.38	1.34, 4.24
Any Hispanic	--	--	1.14	0.76, 1.69	1.15	0.77, 1.71	1.14	0.77, 1.69
Age category (years) (ref: 35-44)								
18-24	--	--	1.00	0.63, 1.59	1.01	0.64, 1.61	1.01	0.64, 1.58
25-34	--	--	0.96	0.78, 1.20	0.97	0.78, 1.20	0.97	0.78, 1.21
45-54	--	--	0.94	0.70, 1.28	0.94	0.70, 1.27	0.94	0.70, 1.27
55-64	--	--	1.08	0.66, 1.77	1.08	0.66, 1.76	1.08	0.66, 1.76
65+	--	--	1.63	0.31, 8.65	1.60	0.30, 8.47	1.62	0.29, 8.90
Highest family educational attainment (ref: ≥Bachelor's)								
<High school	--	--	0.73	0.45, 1.18	0.74	0.46, 1.20	0.76	0.47, 1.23
High school or GED	--	--	1.16	0.82, 1.64	1.17	0.83, 1.66	1.17	0.83, 1.65
Associate’s degree or some college (no degree)	--	--	1.23	0.91, 1.65	1.24	0.92, 1.66	1.24	0.93, 1.67
Family income as % of the Federal Poverty Line (ref: ≥200%)								
<100%	--	--	1.35	0.94, 1.95	1.34	0.92, 1.93	1.36	0.94, 1.98
100-199%	--	--	1.22	0.92, 1.61	1.23	0.93, 1.63	1.24	0.94, 1.64
Family size (ref: 4)								
2	--	--	0.97	0.56, 1.68	0.96	0.56, 1.66	0.96	0.56, 1.66
3	--	--	1.06	0.81, 1.40	1.05	0.80, 1.39	1.05	0.80, 1.38

5	--	--	0.90	0.68, 1.19	0.90	0.68, 1.19	0.90	0.68, 1.19
6+	--	--	0.79	0.55, 1.14	0.81	0.57, 1.17	0.81	0.57, 1.61
One adult with 1+ child (vs. Multiple adults with 1+ child)	--	--	1.16	0.78, 1.73	1.17	0.79, 1.73	1.16	0.78, 1.72
Reported health status (ref: excellent)								
Very good	--	--	*1.36	1.07, 1.73	**1.37	1.08, 1.74	*1.36	1.07, 1.73
Good	--	--	***2.00	1.50, 2.66	***2.00	1.50, 2.67	***2.00	1.49, 2.67
Fair	--	--	***6.89	4.07, 11.65	***6.88	4,03, 11.72	***6.98	4.11, 11.85
Poor	--	--	***48.24	14.32, 162.46	***48.4	14.31, 163.76	***46.01	13.81, 153.26
Adult received influenza vaccination, previous 12 months	--	--	--	--	1.00	0.82, 1.23	1.01	0.83, 1.23

Source: 2014 National Health Interview Survey (NHIS) data, working adult respondents with child respondents in the household and not missing on covariates. Adjusted incidence rate ratios are weighted to be nationally-representative of working adults with children in the household. Standard errors used to calculate 95% confidence intervals are adjusted for complex survey design. All models model the relationship of work loss days due to illness or injury in the previous 12 months and both the influenza vaccination status of household children and adult's paid sick leave status. Model 1 only controls for occupation covariates. Model 2 adds in socioeconomic and demographic covariates of the working adult, their family, and their household. Model 3 adds in the working adult's influenza vaccination status. Model 4 is the same as Model 3 but includes an interaction term between child vaccination status and paid sick leave status to see if having paid sick leave moderates the relationship between child influenza vaccination status and household adult work loss days. All models also control for the Bureau of Labor Statistics' 23-category simplified occupation code, and household location of residence (FIPS state code).

*p<0.05; **p<0.01; ***p<0.001

Table 3-4 shows model-predicted mean missed work days among all combinations of interactions terms for respondent paid sick leave and household child influenza vaccination. Multivariate ZINB regression from Table 3-3 (Model 4) is used to predict mean missed work time and 95% confidence intervals adjusted for all covariates. Those with paid sick leave did have significantly more missed work days than those without (4.83 [3.85-5.81] vs. 3.02 [2.42-3.63]), though there was no significant difference by those with a vaccinated household child (3.54 [2.79-4.29]) vs. an unvaccinated child (4.11 [3.32-4.90]). Examining the two-way interaction subgroups decomposes these overall differences. The pattern observed is that those without paid sick leave had almost no difference in missed work time by household child influenza vaccination status (0.17 less missed work days than with unvaccinated household children: 2.93 [2.13-3.72] vs. 3.10 [2.34-3.85]), though in those with paid sick leave, this difference was much larger (0.96 less missed work days than those with unvaccinated household children: 4.32 [3.28-5.35] vs. 5.28 [4.08-6.49]). Neither of these differences were statistically significant as evident in the overlapping confidence intervals. Sensitivity analyses were conducted surrounding the significant covariates from Models 2 to 4 of Table 3-3 (worker class, race/ethnicity, and self-reported health). In these sensitivity analyses, we stratified the interaction interpretation output from Table 3-4 (predicted work loss days of paid sick leave, household child's influenza vaccination status, and their interaction) by worker class, race/ethnicity, and reported health status. There were no changes to the main findings – the association of less missed work days with household child’s influenza vaccination status still remained among those with and without paid sick leave, though still statistically insignificant when stratified by worker class, race/ethnicity, and reported health status.

Table 3-4. Predicted work loss days due to illness or injury (previous 12 months) among interaction term subgroups from Table 3 (Model 4), working US adults with children in the household (N=7,938), 2014 NHIS

	Work loss days	
	Mean	**95% CI**
Child influenza vaccination status, previous 12 months		
Unvaccinated	4.11	3.32, 4.90
Vaccinated	3.54	2.79, 4.29
Paid sick leave status		
No	3.02	2.42, 3.63
Yes	4.83	3.85, 5.81
Two-way interaction term subgroups		
Child unvaccinated, no paid sick leave	3.10	2.34, 3.85
Child vaccinated, no paid sick leave	2.93	2.13, 3.72
Child unvaccinated, paid sick leave	5.28	4.08, 6.49
Child vaccinated, paid sick leave	4.32	3.28, 5.35

Source: 2014 National Health Interview Survey (NHIS) data, working adult respondents with child respondents in the household and not missing on covariates. Predicted work loss days due to injury or illness (previous 12 months, excluding maternity leave) from the full multivariate zero-inflated negative binomial regression model (Table 3-3, Model 4). Weighted to be nationally-representative of working adults with children in the household. Standard errors used to calculate 95% confidence intervals are adjusted for complex survey design.

Discussion

Influenza in children is known to affect family members and caregivers, causing substantial parental work loss and contributing to community epidemics (Fraaij & Heikkinen, 2011; Jordan et al., 2006; Teo et al., 2005). The main motivation of this study is that despite these known secondary risks of influenza in children to their contact, better characterization is needed of the degree to which childhood influenza vaccination can prevent such secondary risks (B. Y. Lee & Shah, 2012; Teo et al., 2005). In a nationally representative study of US children, this study investigated the association of working adult work loss due to illness or injury with influenza vaccination status of children in the same household, adjusting for a wide variety of confounding factors.

The primary finding of this study is that, among individuals with paid sick leave, having a household child vaccinated against influenza may result in about one less lost work day in the previous year compared to those with unvaccinated children in the household. Though this finding was not statistically significant, it is consistent with the magnitude of multiple studies showing that child influenza illness is associated with at least one missed day of work among household contacts (Antonova et al., 2012; Bourgeois et al., 2009; Heikkinen et al., 2004), and comparable in magnitude to the few European studies investigating reduction of parental work loss associated with child influenza vaccination (Principi, Esposito, Marchisio, Gasparini, & Crovari, 2003b; Vesikari et al., 2006), indicating our findings to be of plausible magnitude that may be significant in larger studies. There are many causes of work loss and this finding likely reflects this in combination with power issues. Yet, at the same time, one less missed work day is fairly large in magnitude especially given it is due to something as simple as making sure a household child is vaccinated against influenza and future studies with a larger sample size may find this to be a true association.

The second principle finding is that the association was over five times smaller among working adults without paid sick leave. Those without paid sick leave are likely less able to take off work when their child is sick or when they themselves are sick, indicating both the importance of paid sick leave in caring for children but also in preventing working adults without paid sick leave from bringing their illness to work because they cannot afford to take off. Paid sick leave is distributed unequally and there is evidence that Hispanic workers and workers with low pay or low education are the least likely to have it (Potepan, 2008).

This study has three limitations. First, the work loss question asks about work loss due to any illness or injury (but excluding maternity leave); having a question just asking about illness or even asking specifically about reasons related to influenza-like illness would likely capture a more specific association. Similarly, the question asks about the previous year but a more accurate question would be asked at the end of the influenza season about just the period of time encompassed by the influenza season. Moreover, ideally vaccine uptake data would be provider-verified. These suggestions would both reduce recall bias and improve the specificity and accuracy of the question. Second, examining work loss requires that individuals must have worked within the previous year, which inherently excludes non-working adults who likely have different contexts for not working (e.g., a stay at home spouse vs. a perpetually-unemployed adult) and thus also have different health contexts. While it is impossible to capture work loss of these adults nor is this the objective of this study, other studies may consider investigating the benefits of household child influenza vaccination in preventing other negative health outcomes that perhaps pertain to a wider variety of US household adult contacts. Last, these data are cross-sectional, and do not allow for causal claims. It is possible that respondent work loss occurred prior to reported household child influenza vaccination, though even in cases where this is true, the child was likely vaccinated the previous year, too, given that prior vaccine history is indicative of future vaccine behavior. Regardless, future studies should address these limitations in a larger sample.

This study is the first to investigate the association of child influenza vaccination with reduction of missed work time due to illness in working US adults. Though the main results were statistically non-significant, reported magnitudes of prevented work loss time are plausible in the context of related literature, and may represent a significant association in a larger sample. Consequently, vaccinating children in the household may prevent work loss in household adults who have paid sick leave, adding to the literature on the indirect benefits of childhood influenza vaccination to household contacts. Further, given that the observed association was over five times smaller among adults without sick leave, and that sick leave is distributed inequitably to those with lower income or education in the United States, further investigation is required. Those without sick leave are already at social and economic disadvantage and this study adds that they are likely less able to take off work when they or their child has the flu and thus more likely to bring it with them to work.

Chapter 4

System-level policy alternatives for improving influenza vaccine uptake in young U.S. children

Abstract

Background: Influenza vaccine uptake among young US children is substantially lower than other recommended childhood vaccines despite the increased risk of flu complications among young children and affordable, available, safe and effective vaccines. Compared to the past, individuals have limited experience with vaccine diseases and fear has shifted away from disease burden to misguided concerns, especially about vaccine safety. There is a concurrent rise in anti-vaccine and vaccine-hesitant views. Economic theory suggests low uptake may be due to the fact that an individual's choice to vaccinate meets conditions that can cause market failure: some have better information about vaccines and their diseases (asymmetric information), and high uptake creates herd immunity (both a positive externality and a public good). These contexts apply to all vaccines, however. A feature of this policy problem that could account for the discrepancy between uptake of flu vs. other vaccines in young children might be the lack of system-level government intervention for improving flu vaccination relative to other childhood vaccines.

Methods: Guided by Collins' health policy adaptation of Bardach's "eightfold path" for policy analysis, this study performs an empirical analysis of system-level policies that local and/or state governments can use to improve flu vaccine uptake of US children under the age of 5. Three states recently implemented mandatory annual flu vaccine entry requirements for children aged 6-59 months for childcare and/or pre-school (allowing for approved religious exemptions), marking the first time flu vaccines were included in any school entry requirement. Thus, national expansion of this was the first alternative evaluated (Alternative 1). A comparable voluntary option (Alternative 2) was evaluated – offering state-wide, in-facility vaccination in preschools and licensed organized childcare facilities. Using the best available evidence, alternatives were evaluated by projected impact, feasibility, and stakeholder reception. Following Collins' tool, projected impact was considered the main concern and was evaluated in terms of six projected indicators relative to status quo (70% uptake, where national uptake has plateaued in young children): increased flu vaccine uptake, reduced flu cases (illness), and reduced doctor's visits, hospitalizations, deaths, and economic burden due to flu in young US children.

Results: Alternatives 1 and 2 would result in estimated increased national flu vaccine uptake of 9-18%, and 1.3-4.5% above status quo, respectively, corresponding to annual reduction of 4.8-9.6%, and 0.7-2.4% of flu cases and related outcomes, respectively. Thus, the overall contribution to the health of young US children was rated as high and modest/unclear, respectively. While all alternatives would require some level of difficulty to administer and investment in flu vaccine administration infrastructure, it was clear that Alternative 2 would capitalize on the least existing resources and structures and would be the most difficult to administer and to sustain. Stakeholder reception would be relatively strong for both alternatives, though likely strongest in Alternative 1. Considering the above, it was clear that Alternative 2 was the least preferable in terms of projected impact, feasibility, and stakeholder reception. Hence, it is the recommendation of this policy analysis that states pursue Alternative 1. Discussed are lessons learned and best practices from three states with existing influenza vaccine requirements and mechanisms through which the federal government could incentivize states to enact such policy.

Introduction

Background

Although the adverse effects of routinely recommended vaccination programs are markedly outweighed by their benefits, such risk will always involve public concern. Although concern over risks of recommended health interventions is not unwarranted, it is by a public not trained to carefully weigh the risks and benefits of vaccination (Jacobson, Zabel, & Poland, 2002). Moreover, in recent times there has been a rise in “anti-vaccine” and “vaccine-hesitant” sentiment in the United States (Salmon et al., 2015). Vaccine hesitancy recognizes a spectrum of beliefs ranging from total vaccine acceptance to total vaccine refusal and is a complex and contextual issue requiring approaches at multiple levels, including to individuals, providers, health systems, and the nation (Larson et al., 2014; Salmon et al., 2015). While largely grounded in myths about vaccine-preventable diseases and their corresponding vaccines unsupported by scientific evidence (Chatterjee & O’Keefe, 2010; Poland & Jacobson, 2001; Schwartz & Caplan, 2011), vaccine hesitancy is also entwined with broader social and political factors such as institutional trust, socioeconomic context, the media, social norms, and health beliefs, among others (Larson et al., 2014; Salmon et al., 2015). These scenarios coupled with the success of vaccines at preventing disease present a central challenge whereby the current low incidence of most vaccine-preventable diseases has created a misleading public perception that the risk of these diseases is also low and subsequently that the costs/risks of the vaccines are relatively high, resulting in low participation in vaccination programs compared to historical participation (van Panhuis et al., 2013). In other words, where once fear of vaccine-preventable diseases motivated many individuals to participate in vaccine programs, most individuals today have limited or no experience with the diseases and the fear has shifted to misguided concerns that promote lower uptake, particularly surrounding vaccine safety, despite that high vaccination uptake is required to maintain low disease incidence (Chatterjee & O'Keefe, 2010).

Unlike the incidence of many other vaccine-preventable diseases, the incidence of influenza is *not* low due to several factors, most notably the nature of the influenza virus and its ability to rapidly mutate and causing annual epidemics (Centers for Disease Control and Prevention, 2015a). This might lead one to believe that some of the aforementioned modern challenges to participation in vaccination programs might be mitigated as they pertain to influenza vaccination. This is not congruent with the reality of influenza vaccination uptake in the US, however, which has remained substantially below federal objectives for many years despite well-established influenza vaccination programs (Centers for Disease Control and Prevention, 2010b; Lu et al., 2013; Setse et al., 2011). In fact, many of the reasons behind relatively low participation in vaccination programs for other vaccines are persistently cited as reasons for forgoing influenza vaccination. For example, people who choose not to receive influenza vaccines persistently cite reasons not grounded in evidence – e.g., that influenza is not that dangerous, that influenza vaccines are largely ineffective, and that influenza vaccines are not safe and can actually cause the disease ("The myths surrounding influenza and vaccination," 2012). The lack of significant progress in vaccination uptake – especially among young children, whom are a high-risk population at increased risk of severe complication due to influenza (Neuzil, Zhu, et al., 2002) – is particularly concerning considering that influenza vaccines are very safe (Centers for Disease Control and Prevention, 2013), immunologically efficacious and effective at preventing numerous outcomes (Osterholm et al., 2012), and widely available and increasingly affordable for children (Centers for Disease Control and Prevention, 2014b).

Economic theory offers several factors for which to assess if government intervention may be necessary due to market failure – externalities, information asymmetry, and whether the "product" at hand is a public good (Rosen & Gayer, 2010). Applying these considerations to better understand reasons potentially explaining why participation in influenza vaccination programs is so low elucidates that perhaps so many individuals opt not to receive the vaccine or vaccinate their children because influenza vaccination exists in a failed market. First, there are significant externalities present in the decision to vaccinate. Herd immunity is a hidden benefit of high vaccination uptake given that no one can see or own herd immunity. Conversely, individuals fail to consider that choosing not to vaccinate has negative implications beyond one's self – it puts others at risk, especially those who are unable to receive the vaccine, including children under the age of 6 months. Thus, from the externality perspective, there are hidden benefits of high uptake and hidden costs of low uptake that many individuals fail to consider when choosing to vaccinate or not. Second, there is asymmetric information present in how individuals understand influenza disease and vaccination, as is evident in the aforementioned persistent misconceptions offered by those refusing vaccination. Thus, from the information asymmetry perspective, many individuals severely underestimate the risks of influenza and benefits of vaccination when choosing vaccinate or not. Last, herd immunity – the product of sufficiently high vaccination uptake – is a public good because it is non-excludable (none can be excluded from its benefits) and also non-rival (one person's "use" of herd immunity does not prevent another's). Thus, from the public good perspective, some individuals may be misled to believe that herd immunity is a product that they can use but do not need to contribute to (though others may do this in full knowledge that they are reaping benefits of vaccination without incurring the known small risks of vaccination nor what they incorrectly see as larger risks of vaccination). In sum, low participation in influenza vaccination programs may be due to an influenza vaccine "market failure" requiring government policy intervention.

Further, the policy, legal and political context surrounding influenza vaccination provides potential insight as to why influenza vaccine uptake in the US is lower than that of other recommended vaccines. One key difference is that influenza vaccination programs have not been subject to government intervention to nearly the same extent that other vaccines have. Perhaps the most prominent example is that they have not yet been included in state mandated school vaccine requirements. The US Supreme Court case *Jacobson v. Massachusetts* (1905) ruled that states (though not the federal government) have authority to enforce compulsory vaccination laws of any citizens under the rational that the freedom of the individual must sometimes be subordinated to the common welfare and states have this Constitutional right via state police power clauses. This decision was reaffirmed by the Supreme Court in *Adams v. Milwaukee* (1913) which also ruled that states can delegate compulsory vaccination power to local municipalities in order to enforce public health regulations. Then, in *Zucht v. King* (1922), the Supreme Court ruled that states can make vaccination uptake a legal requirement for attendance at both public and private schools and can decide how to enforce such laws (including the construction of exemptions from the law). Currently, every state and the District of Columbia has a law that requires children to provide documentation that they have met their state's immunization requirement prior to entering school, and states typically use the CDC's immunization schedule to determine which vaccines to include (Cole & Swendiman, 2014).

Though very recently some states and cities newly require young children to receive the influenza vaccine to enter preschool or daycare, no states include influenza vaccination as part of their state mandated school vaccine requirements (Cole & Swendiman, 2014). New Jersey was the first entity to enact any form of mandatory influenza vaccination when, in 2008, they began requiring children aged 6-59 months (i.e., children eligible for the vaccine and considered high-risk for influenza) to receive annual influenza vaccination prior to enrolling in child care, and two other states have since done the same: Connecticut as of January 2011, and Rhode Island as of August 2015 (Rhode Island also extended the requirement to children enrolled in pre-school) (Immunization Action Coalition, 2015). New York City passed a similar requirement to the one in Rhode Island which was to take effect in January 2016 but it was struck down by a judge in the

NY State Supreme Court in December 2015; the basis of the ruling was not that the City did not have the right to mandate vaccination, but that they had yet to add influenza to a list of mandated vaccines in NY state's public health law and could not enforce the influenza vaccine requirement until the that occurred (Santora, 2015). Influenza vaccination was not routinely recommended for all children until 2010 (see: Fiore et al., 2010), and most existing school vaccine requirements were the result of measles outbreaks in in the 1960s and 1970s (Cole & Swendiman, 2014), which may explain why influenza vaccines have only recently been included in three states' preschool and/or childcare entry requirements but not others.

Inclusion of influenza vaccination into pre-school and/or child care requirements are, of course, not the only options for government to improve childhood influenza vaccination rates at the system level. Perhaps one of the most important system-level changes occurred in 2010 when the CDC updated their recommendation, for the first time, to be universal – i.e., to include all persons 6 months or older annually – given improvements in cost and supply of the vaccines and their continued safety and effectiveness (Fiore et al., 2010). This had an important effect on uptake of influenza vaccination nationally, raising annual influenza vaccination rates of children 6-59 months from about 40% or lower where it had largely plateaued just prior to the universal recommendation (Centers for Disease Control and Prevention, 2009b) to up to roughly 70% where it has now plateaued for the past couple seasons since the universal recommendation (Centers for Disease Control and Prevention, 2015a, 2015b). The remaining 30% represents millions of unvaccinated young US children that in some states is as high as 50% (National Foundation for Infectious Diseases, 2015); clearly new policy is needed to reach rates comparable to those of other routinely-recommended childhood vaccinations (see: Elam-Evans, Yankey, Singleton, Kolasa, & Centers for Disease Control and Prevention, 2014) for this population at increased risk of morbidity and mortality to influenza. All things considered, the aforementioned historical and politicolegal contexts point to a lack of government intervention for improving influenza vaccination compared to that of other childhood vaccinations.

Statement of research aims

The third research aim of this dissertation is to perform a policy analysis evaluating several mechanisms through which influenza vaccination of children at high risk for influenza complications (under 5 years old) can be improved at the system level (local and/or state governments). This policy analysis will thus consider system-level mechanisms both voluntary (preschool and childcare on-site vaccination) and mandatory (immunization requirements for participation in child care and/or pre-school). The political window of opportunity to add and evaluate such policy options related to influenza vaccination may be more open than it has ever been, given that (1) as of 2010, the federal government now recommends influenza vaccination for all children 6 months of age and older, and (2) since 2008, three states (Connecticut, New Jersey, and Rhode Island) have set precedent for successful state-wide childcare and/or preschool influenza vaccine requirements. Further, in his 2013 State of the Union address, President Obama asked Congress to expand access to preschool (Office of the Press Secretary & The White House, 2013), convening a plethora of stakeholders at the state and local level in December 2014 to announce a planned investment of over $1 billion (The White House, n.d.). As such, the potential for state and local governments to reach young children through school systems is increasing. The findings from this policy analysis will help gather and assess evidence as to the potential effects aforementioned policy alternatives could have nation-wide on child influenza vaccination uptake and associated outcomes, as well as their feasibility and stakeholder reception.

Methods

This policy analysis is partially guided by Collins' simple tool for health policy analysis (T. Collins, 2005), which is a health policy adaption of Bardach's "eightfold path" for policy analysis (Bardach, 2012). The first half of Collins' tool was conducted in the introductory discussion of this paper. The social, historical, and political contexts behind participation in vaccination programs in the US have been defined. The problem has been stated – influenza vaccination uptake among children in the US is sub-optimal and substantially lower than uptake of other vaccinations. Evidence has been reviewed to identify significant features of the policy problem that could account for the discrepancy between childhood influenza vaccination uptake and uptake of other vaccines. Most notably, this is the lack of system-level intervention for improving influenza vaccination relative to that of other childhood vaccinations. Finally, multiple policy options – both voluntary and mandatory, structured to be comparable – are being considered that can affect change at the system level (elucidated below).

To carry out the remainder of the policy analysis, this analysis is guided by the second half of Collins' framework and based in published literature and reports of similar policy contexts. For each policy alternative, projections will be made evaluating the potential impact. Projected impact is considered the main concern of the policy analysis (Bardach, 2012; T. Collins, 2005), and in this study, projections are made in terms of a variety of outcomes related to influenza – improvements in influenza vaccine uptake, and reduced influenza cases, healthcare visits, hospitalizations, deaths, and overall economic burden. That said, the feasibility of the alternatives will be also evaluated in terms of material, financial, and human resource expenditure and stakeholder reception will be evaluated for or a variety of relevant stakeholders to understand the likely support for and opposition to each alternative. Lastly, a recommendation will be made for which policy to pursue based on projected impact, feasibility, and stakeholder reception.

Policy alternatives

Definitions of relevant terms

Preschool

The term “preschool” refers to a specific type of childcare that is part of early childhood education. It is discussed here separately from other childcare definitions in more detail given that it is often delineated from childcare in many policy settings, including the discussion of existing influenza vaccination requirements for young US children. The term “preschool” can refer to a wide variety of licensed public or private education facilities for children prior to the start of compulsory education, including kindergartens, pre-kindergartens (“pre-K”), compensatory education programs (such as Head Start), and nursery schools that operate under education guidance (Kamerman & Gatenio-Gabel, 2007). In this study, we will refer to “preschools” as all of the above except kindergarten because kindergarten is almost entirely comprised of children who are already 5 years of age and thus are not the target population of these policies (they are no longer considered high risk as it relates to influenza).

Childcare

The terms “childcare” and “daycare” have been used interchangeably to refer to settings that provide care for children younger than five years of age while their parents work. This can include care given by relatives and non-relatives in unlicensed or licensed settings. The definition of “childcare” used in this study refers to a variety of licensed/regulated childcare settings, which mostly includes “organized child care facilities” in non-residential settings – daycare centers, childcare centers, nursery schools, preschools, and Head Start programs for children ages 0 to 4 years (Kamerman & Gatenio-Gabel, 2007; Laughlin, 2013). This definition generally excludes school/enrichment activities (e.g., sports, lessons, clubs, and after- and before-school programs). The most recent Census estimates on childcare arrangements estimate that, of a total of 20.404 million children aged 0-4 years, 12.499 million (61.3%) were in a regular childcare arrangement, and 4.797 million (23.5%) in an organized care facility (2.726 million [13.4%] in a daycare center, 1.231 million [6.0%] in a nursery or preschool, and 1.140 million [5.6%] in a Head Start or other school program) (Laughlin, 2013). Definitions vary by state; one example from New Jersey (the first state to implement childcare influenza vaccine requirements), considers a child care center any facility that provides care for six or more children younger than 13 years who attend less than 24 hours a day, and these facilities are required to be licensed by state law every 3 years (Department of Children and Families, State of New Jersey, 2016).

That said, these estimates only include data on organized childcare facilities, though the definition of childcare also includes “family child care,” which refers to childcare at residential locations by a caregiver who is not a relative of the child and that is regulated by states through licensing or registration (Kamerman & Gatenio-Gabel, 2007). Referring back to the previous example, New Jersey defines “family child care homes” as those residences that provide care for five or less children 13 and under; there is voluntary registration required but no licensing and these facilities are not included in the childcare influenza vaccination requirements (Department of Children and Families, State of New Jersey, 2016). By comparison, Rhode Island, the most recent of the three states with influenza childcare requirements, *does* include home-based child care centers in their requirement (Rhode Island Department of Health, 2015a), defining “family child-care homes” as any home other than the child’s home that four or more children are cared for at the same time by a caregiver not related to the children, and *does* require them to be licensed (Department of Children, Youth and Families, State of Rhode Island, 2014). It is estimated that over 11% (2.286 million) of children under 5 years of age receive childcare in these settings, and these children are included in the definition of childcare used in the projections of this policy analysis (Kamerman & Gatenio-Gabel, 2007; Laughlin, 2013). Thus, the most accurate estimate for the number of children aged 0-4 years in the US in licensed childcare settings that could be regulated by states (including family care settings and preschool) used in this study is over 7 million total (~35%) (Laughlin, 2013). These data, though the most recent Census estimates with the smallest margins of error, are from 2008. The present day number is likely larger given the push to increase early childhood education and Head Start but for the purposes of this study, this is an accurate, conservative estimate.

Medical exemption

The term “medical exemption” to vaccination refers to a legal exemption from state-mandated vaccine requirements due to the presence of valid medical contraindications to receiving the influenza vaccine. The CDC defines the following valid medical contraindications to receiving any influenza vaccine: a history of a severe (anaphylactic) allergic reaction to an influenza vaccine component (having an egg allergy that only involves urticaria is not a valid contraindication); a history of Guillain-Barré syndrome within 6 weeks following a vaccine dose; and currently having moderate or severe acute illness (persons should return when acute illness is mild or gone) (Centers for Disease Control and Prevention, 2015a). There are additional contraindications pertaining only to the LAIV, including children younger than the age of 2 years, children younger than 5 years with recurrent wheezing, adults 50 years or older, persons with certain chronic medical conditions (including asthma, a recent wheezing episode, reactive airways disease or other chronic pulmonary or cardiovascular conditions, metabolic disease such as diabetes, renal disease, or hemoglobinopathy, such as sickle cell disease), children or adolescents receiving long-term therapy with aspirin or aspirin-containing therapy, because of the association of Reye syndrome with wild-type influenza infection, persons immunosuppressed (including from HIV or receiving immunosuppressive therapy), pregnant women, those who have been administered influenza antiviral medications within 48 hours, and those with a history of severe allergies to eggs or any other vaccine component (Centers for Disease Control and Prevention, 2015a). Obtaining a medical exemption generally involves submitting a letter from a licensed MD, DO, or other advanced medical practitioner (e.g., NP, PA) stating the valid reason as outlined by an official body (typically the ACIP or the American Academy of Pediatrics).

Religious exemption

The terms “religious exemption” refers to a type of non-medical exemption to vaccination requirements based upon the principle that vaccination violates the individual’s religious liberties. All states and the District of Columbia (DC) allow them with the exception of California, Mississippi, Vermont, and West Virginia, which only allow valid medical exemptions (California and Vermont removed their religious exemptions beginning July 1, 2016) (Immunization Action Coalition, 2016a; National Conference of State Legislatures, 2016). Prior to California and Vermont repealing their religious exemption legislation, a literature review showed that the 31 states (including DC) that prior to July 1, 2016 only allowed religious nonmedical exemptions (not philosophical exemptions) had nonmedical exemption rates ranging from ~0.0% (Delaware) to 6.4% (Oregon), though only 6 of the 31 were higher than 1.5% (Wyoming [1.9%], Missouri [2.1%], New Hampshire [2.3%], Montana [3.0%], Alaska [4.0%], Illinois [4.8%], and Oregon [6.4%]). Though demographics, culture, and context vary across states and account for some of these differences, the literature consistently shows that states with easier exemption requirements (in terms of the effort and paperwork required) have higher exemption rates, and vice versa (Wang, Clymer, Davis-Hayes, & Buttenheim, 2014). New Jersey, one of the three states with influenza vaccination requirements for young children for entering a childcare/preschool facility, allows religious exemptions to the requirement and defines this as a written statement signed by the parent or guardian that their child's free exercise of religious rights is interfered with by the proposed vaccination; as long as the statement includes the words, "religion," or "religious," or a similar reference, the religious exemption will be automatically granted (Department of Health and Senior Services, State of New Jersey, 2008). By comparison, to obtain religious exemptions in Rhode Island, one of the other three states with the influenza vaccine childcare requirement, parents must get a form from their child's school, complete it (including acknowledging that their child could be excluded from the facility during an outbreak), and have it signed by the school nurse and school administrative head (Rhode Island Department of Health, 2015b). Their religious exemption rates to school requirements are 1.2% and 0.7%, respectively (Wang et al., 2014).

Philosophical or personal belief exemption

The term "philosophical exemption" (also known as a "personal belief exemption") is a type of non-medical exemption to vaccination requirements. It is defined as a "provision in the state law, which allows parents to exempt their children from the school vaccine requirement if it contradicts parental beliefs beyond those considered religious or spiritual beliefs. These exemptions can include moral, philosophical, or personal beliefs that relate to vaccines" (Diekema, 2014, p. 277). Currently there are 18 states that allow some type of philosophical exemption to vaccine requirements (National Conference of State Legislatures, 2016). Among states allowing philosophical exemptions, nonmedical exemption rates range from 0.5% (Louisiana) to 5.7% (Vermont; note that Vermont repealed philosophical exemptions as of July 1, 2016: National Conference of State Legislatures, 2016), though a majority of nonmedical exemption rates in these states were above 3% (Wang et al., 2014). Further, whereas religious exemptions tend to produce low exemption rates in most states and can be minimized to only those truly desiring them by strengthening the process to obtain them, philosophical exemptions increasingly comprise an “overwhelming majority” of all exemptions (Wang et al., 2014, p. e80) and thus have more dire effects on the health of young US children.

Policy Alternative 1 – a mandatory approach: influenza vaccine requirements for preschool and childcare

The mandatory policy alternative being evaluated to increase influenza vaccination uptake in young US children at the system-level is creating annual influenza vaccination requirements for preschool and childcare. This will be referred to as “Alternative 1.” The basic premise is that all children 6-59 months of age in any recognized form of childcare or preschool must provide proof of immunization by a cutoff date (typically, December 31st of each calendar year[2]). Those who do not must be excluded (not allowed to attend child care or preschool) for the duration of influenza season (e.g., March 31), until they receive at least one dose of the influenza vaccine or until they turn 60 months of age. Children enrolling in child care or preschool after December 31 must provide documentation of receiving the current seasonal influenza vaccine before being allowed to enter school; those enrolling after March 31 are not required to receive the flu vaccine. This policy includes the opportunity for parents to claim religious exemptions

[2]This date is ideal for several reasons. First, seasonal influenza typically peaks in February (Centers for Disease Control and Prevention, 2014), so it ensures that the requirement of vaccination occurs before most seasonal influenza incidence. Second, the first lots of influenza vaccines generally become available at the beginning of August with production and availability peaking in October or November and rapidly declining thereafter, though vaccines continue to be available later in the influenza season (Centers for Disease Control and Prevention, 2014), so the vaccines will still be in supply by the cutoff date and parents have ample time to have their child receive it. Third, it is a convenient date: it is easier for parents to remember that the cutoff is the last day of the calendar year, and as it relates to the operation of preschools and daycare centers, they can check child vaccination status and notify parents who have yet to comply prior to the first period of operation in the new calendar year.

that are appropriately rigorous to obtain seeing as this is present in all but 4 states overall, including in all 3 states that currently have influenza vaccine preschool/childcare requirements. This policy evaluation will not evaluate the potential benefits of only allowing medical exemptions due to the nonviable nature of such a policy alternative in almost every state. Further, in lieu of the literature reviewed above pertaining to philosophical exemptions showing that they comprise an overwhelming portion of all nonmedical exemptions and particularly affect young children unable to receive certain vaccinations, philosophical exemptions will not be evaluated as an evidence-based component of this alternative in this policy analysis.

Policy Alternative 2 – a voluntary approach: on-site influenza vaccination in preschool and licensed organized childcare facilities

The comparable voluntary policy alternative being evaluated to increase influenza vaccination uptake in young US children at the system-level is to offer in-facility vaccination in preschools and licensed organized child care facilities. The basic premise is that the vaccination is not required annually for childcare or preschool continuation by a cutoff date but instead is offered by a licensed healthcare professional at the childcare or school facility. The rationale is that parents and guardians do not have to take time off of work to get the child vaccinated, thus reducing the barrier to voluntary childhood vaccination and increasing the convenience and odds that the parent opts to have their child receive it. While all states have some regulatory requirements for preschools, not all states require regulation or licensure of childcare offered in settings other than organized child care facilities. For example, there is considerable variation across states as to what constitutes different types of childcare, what types of childcare must be subject to staffing and quality standards (or if not subject to such standards, whether or not the type of childcare is even subject to a registration process requiring some form of regular/random check-in or inspection), and state resources for enforcement of any regulations or standards, etc. (Koch Consulting, 2005). The central issue as it pertains to this policy analysis, as hinted above, is that “nonregulated” childcare providers – which includes relatives, non-relative in-home providers, some family childcare home providers who care for less than the number of children in their state requiring licensure, and some center programs that operate part-day or part-year and do not meet their state’s requirements for regulation/licensure – are not required to meet state childcare requirements nor are subject to other state enforcement activities (United States General Accounting Office, 2000). That said, to avoid this issue, the proposed policy alternative would extend to all preschools but only to licensed organized childcare facilities in each state.

Projected impact

Assumptions

A few evidence-based assumptions are made in order to project the national impact of the proposed policy alternatives to young children (aged 0-4 years). The first assumption is the number of children aged 0-4 years in the United States. The most recent complete US Census (2010) estimated that there were 19,976,606 young children in the 50 states plus DC, and the most recent projection from these estimates is that this number is 19,680,478 as of July 1, 2014 (Population Division, U.S. Census Bureau, 2015). For the purposes of this study, we will conservatively assume that there are 19.6 million young children in the US. The second assumption is that the national uptake of influenza vaccination in young children is roughly 70% where it has now plateaued for the past couple seasons since the universal influenza vaccine recommendation (Centers for Disease Control and Prevention, 2015a, 2015b); this will serve as a baseline uptake rate for comparison. The third assumption is the age-specific effectiveness of influenza vaccination in young children. Kostova et al. (2013) specifically investigated this using a variety of influenza vaccine effectiveness estimates from six recent influenza seasons, where "vaccine effectiveness" refers to the percentage reduction in risk of influenza illness (i.e., cases) that is attributable to vaccination. Their mean vaccine effectiveness estimate in children aged 0-4 years was 53.4%, which will be used in this study.

The fourth assumption relates to the vaccine uptake expected due to implementation of Alternative 1. As aforementioned, there are three states that have implemented preschool and/or childcare influenza vaccine requirements for children aged 6-59 months – Connecticut, New Jersey, and Rhode Island. All three states allow religious exemptions, and none allow philosophical exemptions, so their experiences implementing these policies provide real world examples of direct influence on influenza vaccine uptake to use for projecting potential effects of Alternative 1. New Jersey implemented their program in September 2008 (Immunization Action Coalition, 2015). The season before New Jersey implemented their requirement, uptake among young children was just below the national average by 1 percentage point (Centers for Disease Control and Prevention, 2009a). The season they implemented the requirement, however, uptake was over 8 percentage points higher than the national average (Centers for Disease Control and Prevention, 2009b), and the most recent estimates from the 2014-2015 season – 6 seasons after implementation – show New Jersey's influenza vaccination rate of young children to be nearly 9 percentage points above the national average (79.1% vs. 70.4%), the fifth highest of all 50 states plus DC (Centers for Disease Control and Prevention, 2015e). It is also worth noting that this was not the largest advantage New Jersey had after implementation - in the 2012-2013 season, New Jersey's uptake rate for young children was 88%, which was 18 percentage point higher than that year's national average (National Foundation for Infectious Diseases, 2015). Connecticut first implemented their policy January 2011 (Immunization Action Coalition, 2015). The season before implementation, uptake was about 10 percentage points above the national average for young children, and the season after implementation it was about 16 percentage point above the national average (Hadler et al., 2014). In the most recent estimates from the 2014-2015 season Connecticut's influenza vaccination rate of young children was 82.4%, the second highest of all 50 states plus DC (Centers for Disease Control and Prevention, 2015e). Last, Rhode Island implemented their requirement in August 2015 (Immunization Action Coalition, 2015), though vaccine uptake data for the 2015-2016 season is not yet available so no pre-post comparisons can be made. From these data, it is reasonable to assume that Alternative 1 could generate influenza vaccine uptake among 6-59 months olds of 9-18 percentage points above the current national average of 70% (status quo) – i.e., to 79-88% national average uptake. The effect may likely be larger among states below the national average, but this is a conservative assumption regarding potential average effects nationally.

The last assumption relates to the vaccine uptake expected due to implementation of Alternative 2. One limitation of the literature is that there has been no published evaluation of in-facility vaccination in preschools or other childcare settings. There is some literature investigating school-based influenza vaccination programs for school-aged children, though these estimates cannot reliably be generalized to in-facility preschool or organized childcare because there are near universal rates of K-12 participation whereas it is estimated that less than a quarter of all children 0-4 years old receive childcare in licensed organized childcare facilities nationally (D. Wilson, Sanchez, Blackwell, Weinstein, & El Amin, 2013). That said, at best, the literature pertaining to K-12 school-based influenza vaccination programs can only be expected to apply to a quarter of our target population. Perhaps the best comparison is when Hawaii offered state-wide in-school influenza vaccination to all children in kindergarten through eighth grade (5-13 years old) with 90% of all the public and private schools statewide participated (132,775 total children) in the 2007-2008 season (Effler et al., 2010). In that program, Hawaii achieved 46% vaccination. No state-level uptake was available, though among all 5-12 year olds for that season nationally, the uptake was 28.4% (Santibanez et al., 2014) and the authors of the Hawaii study reported a previous pilot study of their study had a vaccination rate among 5-13 year olds as 35% (Effler et al., 2010). Otherwise, the best evidence of school-based influenza vaccine programs comes from several recent clinical trials in the US that showed similar uptake (Davis, King, Moag, Cummings, & Magder, 2008; Gaglani, 2014; King et al., 2006), and one which showed uptake at only 25%, which was 5% greater than counties in the same state not participating in the intervention (King et al., 2012). Considering these data – even though they are not greatly generalizable to preschools and organized childcare, nor to the same age group of children, and considering they had lower baseline uptake which would be easier to affect than the current baselines of 70% – the best reasonable assumption regarding increased uptake from status quo is 5-18% of children in elementary and middle school. Applying the assumption from earlier that only a quarter of children attend preschool or organized licensed childcare facilities compared to nearly all school-aged children attending elementary or middle school brings this number down to 1.25-4.5%. This will serve as the reasonable assumption of the percentage points above the current national average of 70% influenza vaccine uptake among all 6-59 months olds nationally (status quo) that Alternative 2 could generate – i.e., to 71.3-74.5% national average uptake

Reduced influenza cases (illness)

Recall that the average influenza vaccine effectiveness (reduced influenza cases due to vaccination) assumed in this study for children aged 0-4 years old is 53.4% and that there are approximately 19.680 million young US children. These assumptions can be used to project the number of reduced influenza cases due to the projected effects of the policy alternatives.

In the case of Alternative 1, we reasonably projected expected influenza vaccination uptake in the target population to increase by 9-18%. Multiplying these numbers by the average

age-specific vaccine effectiveness results in an expected reduction of 4.8-9.6% of influenza cases beyond the status quo, times the estimated number of children in the target population, is an estimated prevention of 945,000 to 1,889,000 cases of influenza in the United States annually compared to current policy.

In the case of Alternative 2, we reasonably projected influenza vaccination uptake in the target population to increase by 1.25-4.5%. Multiplying these numbers by the average age-specific vaccine effectiveness results in an expected reduction of 0.67-2.4% of influenza cases beyond the status quo, times the estimated number of children in the target population, is an estimated prevention of 132,000-472,000 cases of influenza in the United States annually compared to current policy.

Reduced influenza-related healthcare visits

The CDC recently investigated the number of cases of influenza-like illness that prompted the parent to seek medical care (i.e., “medically attended” cases) that were averted by influenza vaccination (Reed et al., 2014). They estimated that 440,660 influenza-related healthcare visits were averted for children aged 4 or younger.

In the case of Alternative 1 where we estimated a reduction of 4.8-9.6% of influenza cases compared to status quo, we would expect a commensurate reduction of influenza-related healthcare visits. Thus, we reasonably expect such healthcare visits to decrease by 21,152 to 42,303 among US children under 5 per year on average nationally compared to current policy.

In the case of Alternative 2 where we estimated a reduction of 0.67-2.4% of influenza cases compared to status quo, we would expect a commensurate reduction of influenza-related healthcare visits. Thus, we reasonably expect such healthcare visits to decrease by 2,952 to 10,576 among US children under 5 per year on average nationally compared to current policy.

Reduced influenza-related hospitalizations

The estimated number of hospitalizations among 0-4 year olds from six recent influenza seasons ranged from 9,992 to 15,203 with the exception of the 2009-2010 season which had an estimated 37,671 hospitalizations; this was mostly due to the H1N1 influenza pandemic which caused morbidity separate from that season's seasonal influenza virus (Kostova et al., 2013). Excluding the 2009-2010 season given the atypical context of the pandemic, the mean estimated hospitalizations among 0-4 year olds was about 13,672 annually.

In the case of Alternative 1 where we estimated a reduction of 4.8-9.6% of influenza cases compared to status quo, we would expect a commensurate reduction of hospitalizations. Thus, we reasonably expect hospitalizations to decrease by 656 to 1,313 among US children aged 0-4 years per year on average nationally compared to current policy.

In the case of Alternative 2 where we estimated a reduction of 0.67-2.4% of influenza cases compared to status quo, we would expect a commensurate reduction of hospitalizations. Thus, we reasonably expect hospitalizations to decrease by 92 to 328 US among children aged 0-4 years per year on average nationally compared to currently policy.

Reduced influenza-related mortality

It is difficult to directly attribute mortality to influenza for a variety of reasons but primarily relating to the use of different outcomes, different methods, the lack of laboratory testing to confirm infection in many cases, and that even when influenza infection is confirmed and related to death, it is rarely reported on death certificates (Centers for Disease Control and Prevention, 2011; Curwen et al., 1990; Thompson et al., 2009). That said, these limitations have been known for decades and statistical modeling has been developed specifically to better understand influenza-associated deaths (Thompson et al., 2009). There are few age-specific estimates of influenza-associated deaths in the US, as most are aggregated into large age groups or reported as population totals. Thompson et al. (2003) estimated the mortality as 0.3 and 0.2 per 100,000 for children aged <1 and 1-4 years, respectively, based on over 20 years of surveillance data through 1999. The most recent National Vital Statistics Reports data estimates the comparable mortality as 0.5 and 0.2 per 100,000 for children aged <1 and 1-4 years, respectively, comprising a total of 52 deaths to influenza across children aged 0-4 (Xu, Murphy, Kochanek, & Bastian, 2016). Since the estimates of mortality rates are very similar but the latter source is more recent and reports the total number of deaths for all young children, we will consider 52 deaths in young children to be a reasonable assumption.

In the case of Alternative 1 where we estimated a reduction of 4.8-9.6% of influenza cases compared to status quo, we would expect a commensurate reduction of mortality. Thus, we reasonably expect influenza-associated deaths to decrease by 3 to 5 among US children aged 0-4 years per year on average nationally compared to current policy.

In the case of Alternative 2 where we estimated a reduction of 0.67-2.4% of influenza cases compared to status quo, we would expect a commensurate reduction of mortality. Thus, we reasonably expect influenza-associated deaths to decrease by 0 to 1 among US among children aged 0-4 years per year on average nationally compared to currently policy.

Reduced influenza-related economic burden

The total economic burden of influenza in children under 5 years old in the United States, including direct and indirect medical costs (including lost earnings and loss of life) is projected at $2.192 billion (Molinari et al., 2007). These estimates are in 2003 US dollars. Using the US

Department of Labor's consumer price index inflation calculator (Bureau of Labor Statistics, 2016) to adjust this number to 2016 US dollars results in a total economic burden of $2.84 billion.

In the case of Alternative 1 where we estimated a reduction of 4.8-9.6% of influenza cases compared to status quo, we would expect a commensurate reduction of total economic burden. Thus, we reasonably expect influenza-associated economic burden due to young US children to decrease by $136.32 to $272.64 million per year on average nationally compared to current policy.

In the case of Alternative 2 where we estimated a reduction of 0.67-2.4% of influenza cases compared to status quo, we would expect a commensurate reduction of total economic burden. Thus, we reasonably expect influenza-associated economic burden due to young US children to decrease by $19.028 to $68.160 million per year on average nationally compared to current policy.

Feasibility

For Alternative 1, though there is undoubtedly necessary administrative, financial, and human resource expenditure required to implement preschool and licensed childcare influenza vaccine requirements, the idea of school vaccine requirements at the state level is not new – every state as well as DC has them and has for many decades (Cole & Swendiman, 2014; National Foundation for Infectious Diseases, 2015). The benefit here is that such policies can capitalize on existing infrastructure, precedents, methods, and resources from implementation of other school vaccine requirements. Further, the challenges of these policies are well known and lessons well described. The National Foundation for Infectious Diseases (NFID) worked with program administrators from New Jersey, Connecticut, and New York City to learn from their experiences and publish a list of 9 key elements in planning for implementing such policies: (1) prepare and implement a comprehensive communications plan to communicate early and often with all stakeholders, including well before implementation; (2) address educational/awareness barriers to all stakeholders (especially parents with children new to preschool or childcare) surrounding the impact of influenza in young children, vaccine safety and efficacy; (3) locate and assess tools that can help overcome attitudinal, awareness, motivational, and access barriers to the vaccine (the NFID provides some on their website); (4) recognize that influenza vaccination has unique challenges related to supply and timing (provide ample time for childcare centers and preschools to prepare and meet requirements); (5) though existing infrastructure can be utilized, consider expanding infrastructure specifically for influenza vaccination (i.e., consider expanding capacity for the vaccines to be provided at locations other than private healthcare professionals' offices); (6) learn from the unintended consequences experienced in New Jersey and Connecticut (e.g., higher religious exemptions were observed relative to other vaccines so consider strengthening the process to obtain them, increase efforts to educate parents on influenza disease and vaccines); (7) the timing for tracking influenza vaccination may not coincide with that of other childhood vaccines, so more time may be necessary to capture uptake data and to validate compliance; (8) ensure that there is an enforcement mechanism (consider citations, fines, and/or exclusion from school, but allow time to enforce compliance through education prior to penalties); and (9) work closely with all relevant stakeholders at all phases from planning through implementation and evaluation (National Foundation for Infectious Diseases, 2015). Overall, the ability to capitalize on existing vaccine requirement infrastructure with the possibility of expanding infrastructure specific to influenza vaccination administration options therefore makes the feasibility of Alternative 1 as having "some difficulty" (certainly less than Alternative 2, explored below).

Alternative 2 requires a comparably higher level of administrative, financial, and human resource expenditure to implement and sustain at the state or local level, and unlike Alternative 1, there is not existing infrastructure for these programs, so Alternative 2 requires a lot of planning and startup costs. Effler et al. (2010) described in a fair amount of detail how the program worked when Hawaii implemented their statewide K-8 school-based influenza vaccination program during the 2007-2008 season. In sum, they had to obtain written consent from each child's parent or guardian, which involved sending out information packets (in several languages) with an explanatory letter, Vaccine Information Statements, and a consent form. The consent form asked about potential contraindications to each vaccine, and vaccines previously received within the previous year, which introduced recall bias. They distributed the packets at school when it began in August and requested a response within 4 weeks to allow for planning. They placed all information online, as well. The vaccines were administered cost-free and families received no incentive for participation. The state Department of Health (DOH) provided the vaccine and all clinic supplies (school faculty and staff were also offered influenza vaccination at no cost through school clinics). The vaccines were given at school during normal school hours from October 15, 2007, through January 31, 2008. School clinic dates and times required dialogue with administrators of each school to schedule and each school was required to provide a large room for up to 4 hours (two sessions, six weeks apart for elementary schools so children who had never yet received a dose could receive the two doses required; this particularly applies to Alternative 2). Schools also had to then notify parents of the scheduled clinics and escort students to and from them. State DOH staff transported clinic supplies from state offices to each school a day before the clinic and this required assistance from contracted courier services. The state DOH paid for all vaccines in advance using both state and federal funds. Additionally, the DOH arranged and paid for all of the clinic staffing (each school clinic required a clinic manager, at least one registration person, and at least one licensed healthcare professional to provide the vaccine; the licensed healthcare personnel had to be verified by the DOH as in good standing). These staffing requirements had to be determined in advance to ensure availability. All state personnel, volunteers, and contracted staff had to receive training tailored to their responsibilities and the training had to be developed by the DOH (volunteers were considered state employees for liability purposes). Hawaii estimated the total operation costs as $2,480,493 (over half was spent on costs other than purchasing the vaccines), with a total cost estimate of $27.37 per administration (including purchase, healthcare staff resources, printing costs, data management, media promotion, and participation reward). Last, it is worth nothing that these estimates may represent the *best case scenario* for implementing a state-wide school-based influenza vaccination program given that Hawaii's population is concentrated in a relatively small area and is mostly urban; extrapolating these results to areas other than cities means adding in challenges of reaching facilities in areas with less than high population density.

Stakeholder reception

The major stakeholders for vaccine policy and the vaccine delivery system in the United States comprise ten primary groups: (1) the federal government (specifically the US Department of Health and Human Services); (2) states and sub-state governments (specifically state and local health departments and other health and public health officials); (3) professional health organizations (such as the American Academy of Pediatrics, American Nurses Association, American Public Health Association, Association for Professionals in Infection Control and Epidemiology, Infectious Disease Society of America, National Association of County and City Health Professionals, among others); (4) private healthcare providers and facilities; (5) preschools and licensed/regulated childcare entities (including family childcare homes); (6) health plans/payers; (7) the medical industry (especially vaccine manufacturers); (8) non-health groups representing stakeholders (especially teachers' unions); (9) other relevant advocacy organizations, especially anti-vaccine or vaccine-hesitant organizations; and (10) families, parents, and implicitly their young children.

The federal government would likely respect and support states' decisions to enact any of these policy alternatives without a preference of one over the other and doing so may even open states up to receive federal immunization infrastructure grants, which the federal government would support (to be discussed later; see the Prevention and Public Health Fund).

States and sub-state governments would also likely support both alternatives, though they would likely prefer Alternative 1 over Alternative 2 given the lessened impact and greater difficulty in implementing of the latter option, especially since the major burden of Alternative 2 falls upon the state to implement whereas the burden of implementing Alternative 1 falls more on providers.

Professional health organizations would likely strongly support all of the alternatives but would likely prefer Alternative 1 over Alternative 2 given the larger projected impact and that many of these organizations have published official policy statements in strong support of influenza vaccination requirements for healthcare personnel, a related but more contentious topic (Immunization Action Coalition, 2016b).

Private health providers and facilities would likely support both options. On one hand, they might have a preference for Alternative 2 given it places less of the onus of administration on them. However, given that Alternative 1 has a much larger projected impact on reducing healthcare visits due to influenza, they may also prefer these alternatives.

Preschools and licensed/regulated childcare entities would likely favor Alternative 1 over Alternative 2 because the former would have a greater impact in protecting their populations and the latter would involve a lot more responsibility and resource expenditure on their behalf for less projected impact.

Health plans and payers would likely be indifferent to these alternatives given they have likely already planned and budgeted for the increased vaccination associated with the Affordable Care Act requirements of provision of immunizations with no cost sharing. Though Alternative 2 might put less stress on vaccine financing, it would also require added interaction with new entities for reimbursement (i.e., mainly an increase in reimbursement to the state, which may indirectly involve interaction with preschool and childcare entities) whereas Alternative 1 would function mainly through existing reimbursement mechanisms but at a higher volume.

The medical industry would likely support all alternatives considering they would all increase demand for influenza vaccines, which has been unpredictable in the past. Alternative 1 would generate greater demand, so they would likely have stronger support for this alternative because the increased demand for their products without worry of supply concerns given that vaccine supply was deemed suitable for the universal recommendation in 2010.

Non-health groups representing stakeholders – namely teachers' and childcare providers unions – may be hesitant to support or even against supporting Alternative 2 given it places large responsibilities on their constituents and unions have historically opposed requirements made of their constituents without formal negotiations. They would likely be indifferent to Alternative 1.

Other relevant advocacy organizations, namely anti-vaccine or vaccine-hesitant organizations, would likely oppose both alternatives with stronger opposition to Alternative 1. That said, New York City noted that concerns of opposition from these groups, while expected, was much smaller than anticipated and was manageable: "In a city of more than eight million people, only 19 commented at the public hearings held to discuss the proposed flu vaccine requirement. Another 276 submitted written comments. Those who spoke in person, and most of those who submitted comments in writing, appeared to be mobilized by anti-vaccine groups. Nearly half of the letters submitted were an identical form letter and 25 percent of those who commented were not city residents" (National Foundation for Infectious Diseases, 2015, p. 5).

Last, the reaction from families, parents, and implicitly their young children will likely be mixed depending on vaccine history, attitudes, perceptions, and beliefs. Though vaccine-hesitant sentiment has risen in the United States (Salmon et al., 2015), a recent national poll shows that three-quarters of parents want childcare providers to check vaccination records annually and 41% even support policies that remove unvaccinated children from childcare (University of Michigan C.S. Mott Children's Hospital, 2014). That said, a vast majority of families and parents would likely support both alternatives, though there would probably be more support for Alternative 2 given it does not require parents to independently get their child vaccinated but rather gives an option for it to occur at the child's location of preschool and/or license childcare facility.

Recommendation and discussion

Table 4-1 contains a high-level comparison of the components of this policy evaluation – the projected impact, feasibility, and stakeholder reception of each alternative's annual average national effect relative to the status quo.

Table 4-1. High-level summary of projected national impact, feasibility, and stakeholder reception of proposed policy alternatives relative to status quo (70% national uptake)

	Alternative 1	Alternative 2
Projected impact (annual national effect)		
Increased percentage of influenza vaccine uptake	9.0-18.0	1.25-4.5
Reduced influenza cases (%)	4.8- 9.6	0.67-2.4
Reduced influenza cases (millions)	0.945-1.889	0.132-0.472
Reduced influenza-related doctor's visits	21,152-42,303	2,952-10,576
Reduced influenza-related hospitalizations	656-1,313	92-328
Reduced influenza-related deaths	3-5	0-1
Reduced economic burden (million $USD)	136.32-272.64	19.028-68.160
Overall contribution to health of target population	*High*	*Modest/unclear*
Feasibility (level of difficulty to administer)	*Some difficulty*	*Difficult*
Stakeholder reception		
Federal government	Support	Support
State and sub-state governments	Most support	Some support
Professional health organizations	Strong support	Support
Private health providers and facilities	Support	Support
Preschools and regulated organized childcare	Most support	Some support
Health plans/payers	Indifferent	Indifferent
Medical industry	Most support	Support
Teachers' and childcare providers' unions	Indifferent	Oppose
Anti-vaccine/vaccine-hesitant organizations	Strongly oppose	Oppose
Families, parents, and implicitly young children	Support	Most support
Overall stakeholder support	*Strongest*	*Strong*

Looking across all the information in Table 4-1 results in several overall findings. Alternative 1 achieves projected effects much larger than Alternative 2. Though feasibility and stakeholder reception are important considerations, projected impact is considered to be the most important dimension of evaluation in the model used to guide this policy analysis (Bardach, 2012; T. Collins, 2005) and it is clear that Alternative 2 is projected to produce substantially less health impact than Alternative 1.

That said, examining feasibility and stakeholder reception results in a similar conclusion. While the overall feasibility of Alternative 1 does require some difficulty to implement and additional investment in influenza vaccine administration infrastructure, there is existing precedent for such requirements and existing vaccine infrastructure for which to expand upon. Further, Alternative 1 is more feasible at a system-level than Alternative 2 given most states will have to invest significant material, financial, and human resources to create and enforce entirely new system-level on-site vaccination infrastructure at preschools and licensed childcare facilities for Alternative 2. While Alternative 2 may have marginally better stakeholder reception among parents and less opposition from anti-vaccine or vaccine-hesitant advocacy groups, Alternative 1 likely has higher stakeholder reception among state and local governments, professional health organizations, preschools and regulated organized childcare entities, and the medical industry and would likely face no opposition from unions representing teachers and childcare providers.

Additionally, there are three limitations to Alternative 2 worth formal discussion. First, even if there is significant preschool expansion in the near future, most children 2 years and under (and many children 3 years and under) will still be a difficult-to-reach population through state-regulated means given these children have limited access to preschool due to age and that only a minority of them will be captured in licensed, organized childcare facilities (many will remain in unregulated residential childcare settings). This is an important limitation given that getting parents to vaccinate their kids helps to establish habits of future vaccination (Verani, Irigoyen, Chen, & Chimkin, 2007); not only would Alternative 1 begin this habit earlier than Alternative 2 but it has a greater chance of initiating this process within the first year of the child's life, reducing the chance of vaccine refusal altogether. Second, there is significant concern that Alternative 2 will not be able to have much improvement beyond the current national average of 70% uptake given vaccine uptake in the literature reviewed on school-based influenza vaccine programs was generally well below recommended rates even in intervention groups. Third, there are also concerns over the sustainability of in-preschool or in-childcare program due to the higher level of material, financial, and human resources startup costs necessary and a lack of existing infrastructure for states and localities to run these programs relative to Alternative 1.

All things considered, it is the recommendation of this policy analysis that states pursue Alternative 1 – enacting legislation requiring all children 6-59 months of age in preschool or licensed childcare settings to provide proof of influenza immunization by December 31st of each calendar year, allowing for valid, documented medical or religious exemptions, else they face exclusion from such settings until the cessation of the influenza season or until the child turns 5, whichever comes first.

As aforementioned, states can maximize the impact of this policy in several ways. First, there has been research on how to effectively allow nonmedical exemptions to be claimed by only those who really want them and not to those who are ambivalent but would opt to claim them simply due to the ease of their obtainment. When implemented in such a way, individuals still maintain autonomy of the decision to opt out of vaccination if it poses a serious threat to their religious practice, but the law is structured in a way that discourages such easy-to-obtain ambivalent exemptions, thus allowing only a very minimal amount of overall exemptions and maximizing the chance of herd immunity in the general population. For example, states can maximize the protective strength of exemption law by strengthening the rigor of the application process and frequency of exemption submission, educating parents at the point of exemption, and applying penalties for violation of exemption law (Yang & Silverman, 2015). Thus, states can minimize the amount of nonmedical exemption to very low rates while still allowing religious autonomy. Second, states can expand the projected impact of this policy alternative by regulating (if they do not, already) and including family child care homes in the requirement. It is estimated that this policy has the potential to prevent, each year in young US children, up to 1.8 million influenza cases, 42,000 influenza-related sick doctor visits, 1,300 hospitalizations due to influenza, 5 deaths, and $272,000,000 in total economic burden compared to status quo. Last, it is also worth noting that the live, attenuated influenza vaccine (LAIV) has higher vaccine effectiveness in young children. The estimates in this policy analysis, however, are based off of the inactivated influenza vaccine ("the shot") to err on the side of caution as well as to reflect that inactivated influenza vaccines comprise a vast majority of influenza vaccines administered. Though the LAIV can only be given to children 2 or older, if the production of LAIV could be scaled up or target children in these policies aged 2-4, the projected impact would increase.

The federal government can play a role in encouraging states to enact such a policy. Though *Mack and Printz v. United States* (1997) made it explicit that the federal government cannot impose a penalty on states for not enacting legislation, they can provide incentives or withhold existing funding as encouragement to comply. The federal government should consider using such a mechanism to reward or leverage existing federal funding. One potential mechanism is the Prevention and Public Health Fund, part of the Affordable Care Act (ACA). The Fund began in 2010 by providing $500 million annually to build public health efforts, with the goal of building up to $2 billion per year by 2015, a significant chunk of which (currently, over $25 million) goes to states for improving vaccine infrastructure and programs to improve vaccination rates (Forsberg & Fichtenberg, 2012; U.S. Department of Health and Human Services, 2016).

One criticism of such policy is that the mortality due to influenza in young children is relatively low. The first response to this criticism is that mortality is only one measure of the burden of a public health problem, and that we must include discussion of other important dimensions such as morbidity, doctor's office utilization, and economic burden, among others. To facilitate this discussion, comparisons are made to motor vehicle injuries for children aged 0-4 years old given it is an example of a public health problem that resulted in mandatory preventive policy being enacted. By 1986, all 50 states had adopted laws requiring the use of child car restraint devices, though empirical evidence supporting the protective effect of such devices had existed in the early 1970s (Bae, Anderson, Silver, & Macinko, 2014). In 1975, the fatality rate of motor vehicle accidents for US children under the age of 5 years was 4.50 per 100,000, which had dropped to 3.78 by 1987 (when all 50 states had enacted restraint legislation) and most recently was 1.25 in 2014. The only age group with a lower mortality rate was children aged 5-9, whereas adult age groups had fatality rates over 10 times higher. Children under 5 years had the lowest injury rate of all population groups – currently, this rate is 228 per 100,000 in 2014, down from 417 in 1988 (earliest available national data) (National Highway Traffic Safety Administration, 2015). Returning to mortality to influenza, it is true that the mortality burden is highest among the elderly and low among children under 5 years old; estimates suggest the rate varies somewhere around 0.2-0.5 per 100,000 children aged 0-4 (Thompson et al., 2003; Xu et al., 2016) in the presence of current national vaccine uptake of roughly 70% for these young children. However, the morbidity due to influenza among young children is comparatively very high. As discussed in Chapter 1, the estimated number of hospitalizations among 0-4 year olds in recent influenza seasons ranged from 9,992 to 15,203 with the exception of the 2009-2010 season which had an estimated 37,671 hospitalizations; this was mostly due to the H1N1 influenza pandemic which caused morbidity separate from that season's seasonal influenza virus (Kostova et al., 2013). This is a substantial portion of the total hospitalization morbidity of the entire US population, representing a risk of hospitalization of 100 per 100,000 in healthy children and 500 per 100,000 in children with underlying medical conditions (Centers for Disease Control and Prevention, 2015a). Other population-level estimates suggest the hospitalization rate associated with influenza in young children may be even as high as 900 per 100,000 children (Poehling et al., 2006). This range of hospitalization rates is comparable to or higher than recent estimates of injury rates due to motor vehicle accidents for this age group meaning that, in many recent years, more young children are *hospitalized* due to influenza than are just *injured* (not necessarily hospitalized) due to motor vehicle accidents. This suggests that the age-specific morbidity of influenza is a more significant issue than age-specific morbidity due to motor vehicle accidents. To further the discussion, the second response to this criticism is that varicella, another vaccine-preventable disease, has a lesser morbidity burden than influenza yet all 50 states include varicella in elementary school entry requirements and all but 2 states require varicella vaccination for childcare entry (Immunization Action Coalition, 2016). For example, by 2012, examining all hospitalizations in CT, hospitalization rates due to varicella had dropped to 0.8 and 3.6 per 100,000 children aged 1-4, and <1 years, respectively, down from 20.5 and 33.7 prior to routine immunization (Humes, Weinberger, Kudish, & Hadler, 2015). In this case, it is clear that even the *pre-vaccination* age-specific hospitalization rates due to varicella were substantially less than the current hospitalization rates due to influenza with 70% vaccine uptake.

Without systemic approaches such as the policy recommended in this analysis, the United States will likely continue to spend resources on isolated small-scale interventions to improve influenza vaccine uptake that will have insufficient effects. Under these circumstances, not only will young children continue to experience high morbidity and sick visits due to influenza, but young children will continue to serve as the major source of transmission of influenza to families and the community and to the overall economic burden. Communities will continue to have to resort to use of disruptive non-pharmaceutical interventions during influenza pandemics and harsh epidemics, such as temporarily closing schools and postponing or canceling mass gatherings (Centers for Disease Control and Prevention, 2016). Building off of the precedent of

New Jersey, Connecticut, and Rhode Island, and while the political window of preschool expansion is open, it is the ideal time for states to enact preschool and childcare influenza vaccine requirements for young children to protect the future of our nation's health.

Chapter 5

Concluding remarks

The overarching objective of this dissertation was to better understand determinants of hidden vulnerability to, indirect benefits to household contacts of, and system-level policy for influenza vaccination of children in the United States, with a focus on young children. The central motivation, as outlined in Chapter One, is the present reality that influenza vaccine uptake in children in the United States is substantially lower than uptake of other childhood vaccines and has plateaued in recent years. This is despite that young children are at increased risk for influenza complications, comprising a large portion of influenza morbidity and hospitalizations, despite that all children contribute to household and community influenza transmission, including causing substantial parental work absenteeism, and despite that influenza vaccines are safe, effective, available, affordable, and recommended for all children aged 6 months or older.

As it relates to the first objective of this dissertation, few nationally-representative studies have examined factors influencing influenza vaccine uptake in young US children. Further, most rely on parent-reported vaccination, do not contain factors known to be crucial to vaccine uptake, and none consider intersectionality of social disadvantage or how influenza vaccine determinants differ from those of other vaccines. Chapter Two contributes to the literature by directly addressing these limitations. Using provider-verified data nationally-representative of children under the age of 2 years, it examines, in detail, children with “hidden vulnerability to flu” – i.e., those up-to-date on a wide range of vaccine recommendations (the 4:3:1:3:3:1:4 series) but not up-to-date on complete influenza vaccination. In addition to including a plethora of publicly-available factors thought to influence vaccination and health services use more broadly, it includes federally-restricted variables on parent perceptions of vaccines and vaccine-preventable diseases, constructs which are known to be crucial to understanding vaccine disparities but have seldom been used in nationally-representative data. Further, using the linear probability model, which is ideal for examining interactions, the study incorporates intersectionality by including hierarchical interaction terms for child's race/ethnicity and mother's education and marital status. The study uncovered that 44% of all children under the age of 2, who are at greatly increased risk for severe influenza complications, had hidden vulnerability to flu. The principle findings were that, independent of parental history of vaccine refusal and aforementioned confounders, no parental history of vaccine delay was uniquely associated with child's hidden vulnerability to flu, indicating that providers must both be aware that general parental compliance with child vaccine recommendations and lack of vaccine hesitancy may not necessarily indicate parent choice to vaccinate their child against flu and they thus should specifically engage all parents annually about flu vaccines. Further, the examination of intersectionality of social disadvantage suggested that maternal college education may not confer improved influenza vaccination behavior for non-Hispanic Black and Hispanic children despite that it does for non-Hispanic White children.

As it relates to the second objective of this dissertation, it is known that influenza in children causes substantial household transmission and parental work absenteeism, and contributes to community epidemics, though the association of influenza vaccination in young children with reduced household adult work loss has only been examined in a handful of studies with no nationally-representative generalizability to US children. Chapter Three contributes to the literature by directly addressing this limitation, linking data nationally-representative of working US adults to children in their household to examine the association of prevented work loss due to illness with influenza vaccination of household children and its potential moderation by paid sick leave status. For working adults with paid sick leave, having a household child vaccinated for influenza (versus not vaccinated) may be associated with one less lost work day due to illness in the prior year. Though this was not statistically significant, it is worth re-evaluation in a larger cohort given that the observed association was of plausible magnitude compared to the limited literature examining the association of parental work loss with either child influenza illness or influenza vaccination. Notably, the association of reduced work time in the analysis in Chapter Three was over five times smaller among working adults without paid sick leave. Because paid sick leave is distributed inequitably to those with lower paying positions or educational attainment, findings suggest that those without paid sick leave may be likely less able to take off work when they or their child are sick and thus likely bringing influenza to the workplace.

As it relates to the third and final objective of this dissertation, though there are historical, social, political, and economic contexts underlying the recent relatively low participation in vaccine programs in the United States, none uniquely explain why influenza vaccine uptake is much lower than that of other vaccines. A significant feature of this policy problem that could account for this discrepancy in young children, however, might be the lack of system-level government intervention for improving influenza vaccination relative to other childhood vaccines. Chapter Four contributes to the literature by performing a systematic policy analysis evaluating a mandatory system-level alternative (enacting annual influenza vaccine requirements for children 6-59 months prior to entering daycare and/or preschool) and a comparable voluntary system-level alternative (offering state-wide, in-facility vaccination in preschools and licensed organized childcare facilities) compared to status quo. Using the best available evidence to evaluate each alternative in terms of projected impact, feasibility, and stakeholder reception, the recommendation was for states to enact mandatory an annual childcare and pre-school influenza vaccination entry requirement for young children, allowing sufficiently rigorous-to-obtain religious exemptions. Relative to the status quo of 70% national uptake of influenza vaccination among children 6-59 months, this policy alternative is projected to reach national average uptake of 79-88%, corresponding to the prevention, each year, of an additional 950,000 to 1,900,000 cases of influenza, 21,000 to 42,000 influenza-related doctor's visits, 650-1,300 influenza-related hospitalizations, 3-5 influenza-related deaths, and $130 million to $270 million in economic burden while having the best relative feasibility and stakeholder reception. Lessons learned and best practices from three states with existing such requirements and mechanisms through which the federal government could incentivize states to enact such policy were discussed.

All things considered, this dissertation achieved its objectives. First, in a nationally-representative, provider-verified sample controlling for a wide variety of confounders including crucial restricted variables, it identified factors related to vaccine hesitancy and intersectional social disadvantage of maternal education and child's race/ethnicity that are uniquely associated with a child having hidden vulnerability to influenza. Second, in a nationally-representative sample of working US adults, it identifies a potential indirect effect of child vaccination to household contacts – possible reduction of illness-related work loss for adults with paid sick leave, though further investigation in a larger cohort is required. Last, based on the best available evidence, a systematic policy analysis identified that states have a timely political opportunity to capitalize on existing vaccine infrastructure and legislative precedent by adding annual influenza vaccination to preschool and daycare entry requirements for young children.

Although the empirical analyses presented in this dissertation significantly contribute to the literature on influenza vaccination of US children and offer policy solutions, there remain areas requiring further investigation. First, though this dissertation identifies unique disparities in children with hidden vulnerability to influenza, the causes of disparities in influenza vaccination are likely multifactorial and complex and research elucidating the mechanisms underlying disparities is limited (Fiscella, Dressler, Meldrum, & Holt, 2007; Logan, 2009). Hypothesized explanations include, among others, lower healthcare access, distrust of physicians, resistant attitudes and beliefs , and discrimination in healthcare settings (Bleser, Miranda, & Jean-Jacques, 2016; Fiscella, 2005; Hebert, Frick, Kane, & McBean, 2005), though much of this work has focused on adult patients. In particular, despite that vaccine hesitancy and intersectional social disadvantage are both hypothesized to be crucial to understanding disparities (Dubé, Vivion, & MacDonald, 2015; Larson et al., 2014; Salmon et al., 2015; Warner & Brown, 2011) – including connections to the increasing prevalence of complementary and alternative medicine and its association with vaccine hesitance (Ali, Calabrese, Lee, Salmon, & Zwickey, 2014; Bleser, Elewonibi, Miranda, & BeLue, Forthcoming; Busse, Wilson, & Campbell, 2008; Ernst, 2001; Gellin, Maibach, & Marcuse, 2000; Salmon et al., 2005; K. Wilson, Mills, Boon, Tomlinson, & Ritvo, 2004) – research on these topics is limited and requires further investigation. Further, as noted in Chapter 3, there is sparse literature examining the relationship between adult work loss and child vaccination status and that literature is limited mainly to parents, who are often not the only working adults in the household, and to studies with no national generalizability to adults or young children in the US. Further research is required both investigating this relationship generally as well as how paid sick leave may play a role in allowing working adults to capitalize on prevent health services use, especially vaccination, to protect themselves and their children and to improve work productivity.

The implications of the findings of this dissertation and the discussed future research directions underscore that policymakers and researchers from interdisciplinary fields – namely, those in the fields of public health, health services, demography, sociology, education, and labor, among others – need to collaborate to understand and solve these issues. In particular, vaccine hesitancy, intersectional social disadvantage, and health-related work loss all involve complex social, cultural, philosophical, and economic phenomena that cannot be understood or solved by any one discipline alone. For example, vaccine hesitancy is typically studied by public health and health services researchers but cannot wholly be understood from the perspective of these fields alone given that vaccine hesitancy involves changing dynamics in social and cultural norms, viewpoints, and moods, trust in physicians and institutions, and the media, among others (Salmon et al., 2015). In this case, to avoid treating just the symptoms of vaccine hesitancy, those versed in social and fundamental causes of health must also be involved in order to connect complex upstream causes with behavioral level decisions that ultimately affect downstream health outcomes (see: Braveman, Egerter, & Williams, 2011; Embrett & Randall, 2014; Link & Phelan, 1995; Phelan, Link, & Tehranifar, 2010). Similarly, social scholars have long argued that the intersectionality of social statuses like race/ethnicity, gender, and social class cannot be disentangled as they reinforce each other in affecting health outcomes across the life span (P. H. Collins, 1990, 2000; Crenshaw, 1989; Dill & Zambrana, 2009; Schulz & Mullings, 2006), so further study into disparities in vaccination and other health services use cannot continue to neglect complex social causes or it will continue the criticism that prior health research has hindered our ability to holistically understand health disparities (Warner & Brown, 2011). Health policy researchers have recently pushed for the same concept but from their “side” – that upstream research and policy not previously connected to health should fundamentally incorporate health. Doing so will help build the case of the “Health in All Policies” approach, that social determinants of health drive health outcomes and inequities and the examination of health involves, among other things, promoting equity and health, and creating change at the structural level (Rudolph et al., 2013). In closing, it is the hope that this dissertation, which is an intentional effort to connect fundamental/social cause theory, intersectionality, and the “Health in All Policies” approach in order to understand a complex health and health services policy problem and the web of upstream factors that contribute to it, inspires others to do the same. A complete understanding of how to reduce health inequities depends on the ability to do so.

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Zucht v. King, 260 US 176 (1922).

VITA

William Killington Bleser

RELEVANT WORK EXPERIENCE

Research Assistant | University Park, PA | The Pennsylvania State University

Health Policy & Administration; Demography — Aug. 2015 – Present

- Performs and disseminates research related to public health, health disparities, social causes, etc.

Aligning Forces for Quality (AF4Q) evaluation — Aug. 2011 – Aug. 2015

- Assisted in research, mixed-methods evaluation of a large, community quality improvement initiative

Patient-Centered Medical Home (PCMH) project — Oct. 2011 – Aug. 2012

- Coordinated and assisted with research on the first regional rollout of a state-wide PCMH initiative

Vaccine Safety Fellow | Washington, DC — Aug. 2010 – July 2011

U.S. Department of Health and Human Services, National Vaccine Program Office

- Coordinated Working Groups of the National Vaccine Advisory Committee related to vaccine safety and policy
- Data Manager for the U.S. Guillain-Barré Syndrome Meta-Analysis project

EDUCATION

Doctor of Philosophy: Health Policy and Administration; Demography (dual-title). GPA: 3.92 — Aug. 2016

The Pennsylvania State University (PSU) | University Park, PA

Robert W. Graham Endowed Graduate Fellowship

Master of Science in Public Health: Global Disease Epidemiology & Control — May 2011

The Johns Hopkins University Bloomberg School of Public Health (JHSPH) | Baltimore, MD

Bachelor of Science: Neuroscience (Pre-Medicine track)

The College of William and Mary (W&M) | Williamsburg, VA — May 2009

William Edward and Sophie Robinson Croxton Scholarship

PUBLICATIONS

Bleser W.K., Miranda P.Y., Jean-Jacques M. Racial/Ethnic Disparities in Influenza Vaccination of Chronically Ill US Adults: The Mediating Role of Perceived Discrimination in Health Care. *Med Care*. 2016;54(6):570-577

Bleser, W. K., Young, S. I., & Miranda, P. Y. Disparities in Patient- and Family-Centered Care during U.S. Children's Healthcare Encounters: A Closer Examination [in press in *Academic Pediatrics*].

Bleser, W. K., Elewonibi, B. R, Miranda, P. Y., & BeLue, R. Complementary and Alternative Medicine and Influenza Vaccine Uptake in US Children. [Provisional acceptance in *Pediatrics*].

McHugh, M., Shaw, B., Wolf, L., **Bleser, W.**, & Duckett, P. (2016). Advancing Payment Reform at the Community Level. *Quality Management in Health Care*, 25(2), 111–120.

Hearld, L. R., **Bleser, W. K.**, Alexander, J. A., & Wolf, L. J. (2016). A Systematic Review of the Literature on the Sustainability of Community Health Collaboratives. *Medical Care Research and Review: MCRR*, *73*(2), 127–181.

Bleser, W. K., Miller-Day, M., Naughton, D., Bricker, P. L., Cronholm, P. F., & Gabbay, R. A. (2014). Strategies for Achieving Whole-Practice Engagement and Buy-in to the Patient-Centered Medical Home. *Annals of Family Medicine*, 12(1), 37–45.

Salmon, D. A., Proschan, M., Forshee, R., Gargiullo, P., **Bleser, W.**, … H1N1 GBS Meta-Analysis Working Group. (2013). Association between Guillain-Barré syndrome and influenza A (H1N1) 2009 monovalent inactivated vaccines in the USA: a meta-analysis. *The Lancet*, 381(9876), 1461–1468.

ACTIVITIES, AWARDS & LEADERSHIP

Medical Care Student Research Award. American Public Health Association.	2015
Ad hoc journal article reviewer. Medical Care	2015 – Present
Graduate Student Demographic Methods Workshop. Executive Board, PSU	2013 – Present
AcademyHealth, Penn State Chapter. Vice President/President, PSU	2012/13 – Present
International Health Student Group. Executive Board, JHSPH	2009 – 2010
Up 'til Dawn (St. Jude's Children's Hospital fundraiser). Outreach Chairman, W&M	2007 – 2008
Alpha Tau Omega, Virginia Kappa Kappa Chapter. W&M. Awards received as President:	
▪ Excellence in Scholarship Award ▪ Upper alpha award for fostering alumni relations	2007 – 2008