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Exempted: Spatial Clustering of Intentionally Unvaccinated Children in California and its Potential Consequences for Measles Transmission

A dissertation submitted in partial satisfaction of the

requirements for the degree Doctor of Philosophy

in Sociology

by

Ashley Renee Gromis

2017

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ABSTRACT OF THE DISSERTATION

Exempted: Spatial Clustering of Intentionally Unvaccinated Children in California and its Potential Consequences for Measles Transmission

by

Ashley Renee Gromis

Doctor of Philosophy in Sociology

University of California, Los Angeles, 2017

Professor Ka Yuet Liu, Chair

Rates of non-medical vaccine exemptions have been increasing in the U.S. since the early 1990s. These exemptions tend to be spatially clustered rather than randomly occurring in the population. In contrast to long-standing public health findings, under-vaccination due to non-medical exemptions tends to be found among children with educated, affluent, non-Hispanic white parents rather than those with relatively disadvantaged backgrounds. This dissertation uses data on Personal Beliefs Exemptions (PBEs) in schools in California from 1998-2014 and an empirically-calibrated large-scale simulation experiment to understand how spatial clusters of these exemptions form and their potential consequences for measles transmission.

This dissertation emphasizes the importance of interaction in social networks in structuring both the local context surrounding parents' vaccine decisions and the patterns of

physical contact through which disease spreads. Major findings show that residential sorting of parents into neighborhoods and schools based on socio-demographic characteristics associated with school-level PBE rates provides only a partial explanation for broader patterns of clustering. Additional analyses provide evidence of spillover effects between PBE rates and socio-demographic characteristics, particularly percent non-Hispanic white children, on PBE rates in nearby schools.

A large-scale simulation of measles transmission using a synthetic population of youth in California in 2014 is then used to examine the potential consequences of PBEs for disease spread. Schools serve as hotspots for measles transmission regardless of the spatial locations of PBEs, although clustering of these exemptions within households and charter schools increase the opportunities for infections. Surprisingly, spatial pockets of PBEs may provide slight protection against measles transmission when outbreak sizes are small and the disease is introduced randomly into the population. Yet, clustering of exemptions can reduce protective effects of herd immunity to large measles epidemics, even when overall vaccination coverage in the population is high.

This dissertation concludes by drawing connections between findings in the empirical chapters and linking the results to the larger theoretical context of social interaction in networks. Practical implications for vaccine policy and efforts to control vaccine-preventable disease are discussed. Overall, this project seeks to illustrate how decisions perceived as personal by parents contribute to collective health outcomes.

The dissertation of Ashley Renee Gromis is approved.

Gabriel Rossman

William G. Roy

Edward T. Walker

Peter Bearman

Ka Yuet Liu, Committee Chair

University of California, Los Angeles

2017

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ACKNOWLEDGMENTS

When I enrolled in college as an enthusiastic undergraduate over a decade ago, I had never heard of sociology. I grew up in a small town where "that's just the way things are" was a constantly recurring answer to my constantly recurring questions centering on some variant of "why are things like this" or "why do we have to do things this way". So you can imagine my excitement when, after enrolling in an introductory course my sophomore year, I discovered the ways in which sociology seeks to look under the surface of social behavior. Dream careers as a computer scientist, radio DJ, band t-shirt designer, or the meteorologist who names tropical storms were set aside for a degree in sociology, an offer of admission to the graduate program at UCLA, and a one-way plane ticket to Los Angeles.

Several years have now passed; I will not bore you with the specifics (or second thoughts about alternative career paths as an architect, folklorist, professional story-teller, or Ira Glass' assistant on *This American Life*). When finishing up this dissertation, I saved the acknowledgments until the very end because this is the section I most looked forward to writing. It provides me with a chance to thank all the people without whom the journey from discovery of sociology to PhD would not have been possible.

I first thank my adviser and committee chair, Ka Liu. I was first her teaching assistant, then her research assistant, before formally becoming her student. I am appreciative of the many, many hours she has devoted—in person, via Skype, and by email—to helping me think through solving methodological problems, framing research questions, communicating my ideas in writing, and employing myself post-grad school. Her perspective was down-to-earth, her advice was practical and I would not be in the position I find myself in as I leave UCLA without her.

The guidance she has provided me with is not only reflected in this dissertation, but also in my secondary research projects and how I approach sociological inquiry more generally.

I also must thank my other committee members—Gabriel Rossman, Bill Roy, Ed Walker, and Peter Bearman. Bill and Gabriel have advised me since I first came to UCLA. My understanding of how to think sociologically about the empirical questions presented in this project (and others) has benefited enormously from conversations with Bill. Gabriel provided important direction in my development as a computational sociologist, and has fielded many methodological questions on both this and other projects. Ed has been generous with his guidance on this and other research, and the way I think about building and working through projects is much indebted to him. This project has also benefited substantially from Peter's insightful comments and suggestions.

Many other professors have played important roles in the development of my research and methodological skills. At UCLA, this is particularly true of Jacob Foster, Mike Lens, and Robert Rhoads. I would not have made it to UCLA without John McCarthy's advising and Pat Rafail's mentorship when I was an undergraduate at Penn State University.

Support comes in many forms in graduate school. I thank the Hellman Fellows Fund, California Center for Population Research, and National Institute of Health for providing me with financial support as a research assistant. I also need to acknowledge the Hoffman2 Shared Computing Cluster provided by the UCLA Institute for Digital Research and Education. Without access to their computing resources and the help of their excellent support personnel, I would still be waiting on the results of the spatial models and simulation experiments presented in Chapters 4, 5 and 6. For help with the many administrative and bureaucratic hurdles to be overcome in a graduate program, I thank Wendy Fujinami.

I spent much of my time at UCLA as a teaching assistant. I owe sincere thanks to the many graduate students who passed through 3 iterations of Sociology 210A, 4 iterations of Sociology 210B, and 2 iterations of Sociology 210C for making the 210 sequence a teaching commitment I truly enjoyed. My own understanding of statistics is much better for having served in that role, and, more importantly, it provided me with the initial connections that grew into important friendships and other sources of support in the program.

The most important source of support during my time as a graduate student was the other students in the program. This department is filled with graduate students who are kind, willing to help, generous with their time, and act as sources of both professional and personal support. I thank Winston Chou, Stephanie D'Souza, Becca DiBennardo, Yewon Lee, Laura Loeb, Tala Oszkay, Corey O'Malley, Chase Raymond, Casandra Salgado, Anup Sheth, Isaac Speer, Phi Su, Anne White, and so many more. I owe six particular debts of gratitude: I cannot imagine making it through the program without the endless support provided by Nicole Iturriaga (my academic life partner), Mirian Martinez-Aranda, and Ariana Valle. Chris Rea and Kevin Shih were the two most trusted sources of feedback on both my own work and understanding of social networks, institutions, and influence. Kyle Nelson is a trusted collaborator and served as an important voice of reason at two critical junctures in my graduate career.

I owe an enormous thanks to my family for all of their support after I decided to run off to Los Angeles to pursue yet more schooling. My mother, father, and sister, Brittany, have been endlessly encouraging. I must acknowledge my mother in particular—more than anyone else on the outside of academia, she has patiently listened to the ups and downs of graduate school throughout the past several years and never stops believing in me, even when I am ready to. I thank my Aunt Marilyn, my Grandmother Mattie, and my Aunt Sue and Uncle Bill for their

support and encouragement as well. I also must acknowledge the quiet supervision that Peeks provided for the initial work on this project.

Many friends have also played major roles in my support network. I thank Renea Romesberg and Kate Ascah for keeping me grounded. They have provided a very important respite from my academic life, and with them I am reminded of where I have been, where I am going, and who I want to be. Finally, I thank Greg Schwartz, who has been one of the most important sources of support and stability as I complete this dissertation. He challenges me to look at things from new, and larger, perspectives, knows that I understand concepts best when they are graphed, and makes me a more balanced person. He also assisted with proof-reading the final copies of Chapters 1, 2, and 7 presented here.

VITA

EDUCATION

2012 M.A., Sociology — University of California, Los Angeles
Committee: William Roy (chair), Gabriel Rossman

2010 B.A., Sociology & History (Highest Distinction) — Pennsylvania State University
Honors in Sociology, supervised by John D. McCarthy

PUBLICATIONS

William G. Roy and **Ashley Gromis**. *Forthcoming*. "Non-lyrical Dimensions of Protest Music" in *Oxford Handbook of Protest Music*. Oxford University Press.

Gromis, Ashley. 2013. "From 'Tippecanoe and Tyler, Too' to 'Born in the U.S.A.': The Transformation of the Campaign Song in Presidential Elections in the United States". *Research in Political Sociology* 21:129-157.

Gromis, Ashley and William G. Roy. 2013. "Music and Social Movements." In *The Wiley-Blackwell Encyclopedia of Social and Political Movements*. David A. Snow, Donatella Della Porta, Bert Klandermans, and Doug McAdam (eds.) Malden, MA: Wiley-Blackwell.

McCarthy, John D., Patrick Rafail and **Ashley Gromis**. 2013. "The Trend of Public Protest in America: Increasingly Local, Domesticated and Strategic." In *Advances in Social Movement Research*. Bert Klandermans, Conny Roggeband and Jacquelien van Stekelenburg (eds.) Minneapolis, MN: University of Minnesota Press.

DATABASES

Public Court Records of Eviction in Los Angeles County, California, 2014. (33,420 observations)
- *Constructed by scraping the Superior Court of California website and using text extraction to code case information, including geographical location (address-level) and court outcomes.*

Synthetic Youth Population (ages 0-17), California, 2014. (9,059,020 observations)
- *Empirically calibrated state-wide youth population used for large-scale agent-based simulations; constructed using data from: 2010 US Census, 2014 American Community Survey, California Department of Education, California Department of Public Health, and California Birth Master File.*

Popular Music Recordings on 78 rpm Records, 1868-1961 (370,783 observations)
- *Cleaned user-generated data to create consistent listing of artists, titles, and release dates.*

CONFERENCE PAPERS (selected)

Ashley Gromis and Kayuet Liu. 2016. "Explaining Spatial Clustering of Non-Medical Exemptions from School Vaccination Requirements in California, 1992-2014." Annual meeting, Population Association of America, Washington DC.

Gromis, Ashley. 2013. "From 'Tippecanoe and Tyler, Too' to 'Born in the U.S.A.': The Transformation of the Campaign Song in Presidential Elections in the United States." Annual meeting, American Sociological Association, New York, NY.

Rafail, Patrick, John D. McCarthy, and **Ashley Gromis**. 2011. "Explaining the Spatial Distribution of the 2009 Tax Day Tea Parties." Annual meeting, American Sociological Association, Las Vegas, NV.

RESEARCH EXPERIENCE

"LA County Eviction Court Survey", with Prof. Michael Lens, UCLA Department of Urban Planning, and Kyle Nelson, UCLA Department of Sociology, June 2016 – Present.

- *Designed and implemented data mining strategy to collect eviction court records for quantitative analyses of neighborhood prevalence and case outcomes in Los Angeles County, CA.*

"Diffusion of Non-Medical Exemptions to School Vaccine Requirements in California", with Prof. Ka-Yuet Liu (P.I.), UCLA Department of Sociology, April 2013 – Present.

- *Constructed a longitudinal dataset of kindergartens and neighborhood characteristics and a synthetic youth population from multiple administrative data sources; performed data analysis using multi-level regression, spatial models, latent class analysis, and large-scale agent-based modeling.*

"Reproduction and diffusion in Trajectories of Campus Activism, 1960-1995", January 2014 – Present.

- *Organized and supervised research team of 13 undergraduates assisting with data collection of newspaper articles covering student protest; project uses natural language processing in Python to examine how discourse of student activism on college campuses evolves over time.*

"Estimating the Mortality Rates of Unauthorized Mexican Immigrants in California", with Prof. Ka-Yuet Liu (P.I.), UCLA Department of Sociology, May 2015 – June 2016.

- *Compiled a consistent dataset for the California Statistical Death Master File for 1970-2013 (9.3 million observations, 4.6 GB)*

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TEACHING EXPERIENCE

Instructor of Record
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Sociology 210B: Intermediate Statistical Methods II (graduate), Prof. Ka-Yuet Liu (4 quarters)
Sociology 210C: Intermediate Statistical Methods III (graduate), Prof. Megan Sweeney (2 quarters)
Sociology 180A: Sociology of Cheating (undergraduate), Prof. Rick Grannis (1 quarter)
Sociology 133: Collective Behavior (undergraduate), Prof. Edward Walker (2 quarters)

FELLOWSHIPS AND AWARDS

2016 Departmental Fellowship, UCLA Department of Sociology
2014 Excellence in Teaching Award, UCLA Department of Sociology
2013 Excellence in Teaching Award, UCLA Department of Sociology
2012 Excellence in Teaching Award, UCLA Department of Sociology
2012 Graduate Summer Research Mentorship Award, UCLA Graduate Division
2010 Distinguished Graduating Senior, Penn State Department of Sociology

Chapter 1: Introduction

Many children in the United States and across the world dream of a trip to Disneyland, the self-declared "Happiest Place on Earth." But in late December 2014, "It's a Small World," took on increased meaning beyond just the name of one of the theme park's most iconic attractions after more than 40 visitors were infected with the measles (Harriman 2015). One or more international visitors among the tens of thousands of daily attendees at the Disney parks[1] likely introduced the disease (McCarthy 2015) before it was carried back to local communities across the U.S. and into neighboring countries.

The resulting outbreak, with 147 confirmed cases in 7 U.S. states[2], 159 in Canada, and 1 in Mexico, was larger than usual for North America in recent years and raised questions regarding the effectiveness of measles control efforts (Blumberg et al. 2015). Once a common childhood illness, the measles was declared non-endemic[3] in the U.S. in 2000 and domestic transmission is now relatively rare. The measles is not the only childhood disease that has experienced a significant reduction in prevalence in the past 100 years. Widespread vaccination in the U.S. has resulted in the drastic reduction in diseases with significant mortality rates and long-term health consequences in children since the beginning of the 20th century, including smallpox, poliomyelitis, tetanus, diphtheria, pertussis (whooping cough), mumps, rubella, and haemophilus influenzae type b (Centers for Disease Control and Prevention 1999).

Yet over the past two decades, the number of children entering schools without meeting mandated vaccination requirements in the U.S. for non-medical reasons has increased

[1] The exposures occurred at both Disneyland and the adjoining Disney California Adventure Park. The source patient for the outbreak was never officially identified.

[2] California, Arizona, Utah, Nebraska, Washington, Colorado, and Oregon

[3] Non-endemic diseases are those not continuously transmitted for a period of 1 year or more in a geographical area (Orenstein and Papania 2004).

significantly (Centers for Disease Control and Prevention 2016; Omer et al. 2009). States that allow exemptions on the basis of parental "personal" beliefs and permit relatively easy access to these exemptions tend to have higher rates of exempted children (Omer et al. 2006). These increases come despite continued efforts to increase vaccination coverage nationally and eradicate serious vaccine-preventable diseases by the Centers for Disease Control and Prevention (CDC) and the American Academy of Pediatrics (AAP) (Centers for Disease Control and Prevention 2015; Pediatrics 2010).

A similar trend in non-compliance to recommended childhood vaccines has been observed in other high-income countries as well. Internationally, vaccine hesitancy has been investigated as a cause of declining vaccination rates in the United Kingdom (UK) (Brown et al. 2011; Hobson-West 2003; Velan 2011), the Netherlands (Hak et al. 2005), Italy (Profeta, Ferrante, and Porro De' Somenzi 1986), France (Verger et al. 2015), Greece (Danis et al. 2010), Romania and Croatia (European Center for Disease Prevention and Control 2015), Nigeria (Babalola 2011), Sweden, Turkey, Japan, Australia (Gangarosa et al. 1998), and Canada (McGirr, Tuite, and Fisman 2013). As in the U.S., these increases in vaccine refusals come despite continued efforts to increase vaccine coverage and eliminate vaccine-preventable disease globally (Andre et al. 2008). The World Health Organization's (WHO) Strategic Advisory Group of Experts on Immunization formed the Working Group on Vaccine Hesitancy in 2011 to specifically target populations with increasing vaccine concerns and refusals (SAGE Working Group on Vaccine Hesitancy 2014). In Europe, both overall measles incidence and indigenous

transmission of the disease are higher in countries with suboptimal rates of vaccine coverage compared to countries with consistently high vaccine coverage (Muscat et al. 2009).[4]

The measles outbreak that began at Disneyland in December 2014 heightened tensions in debates surrounding vaccine compliance and permitted exemptions after unvaccinated children were identified as playing a significant role in the outbreak (Clemmons et al. 2015; Harriman 2015; Majumder et al. 2015; Zipprich et al. 2015). Even though measles was declared non-endemic in 2000, the number of reported cases has been increasing in recent years, with incidence spiking in 2008, 2011, 2013, and 2014 (Centers for Disease Control and Prevention 2013, 2017b). Children with non-medical exemptions have been significant contributors to this upward trend in cases (Centers for Disease Control and Prevention 2013; Phadke et al. 2016). Previous research has also linked low measles vaccination coverage to disease outbreaks in Canada (Dubé, Vivion, and MacDonald 2015). In California, where the Disneyland outbreak began and the majority of cases were reported, increased media attention was given not only to the increasing number of vaccine refusals, but also ongoing efforts by parents to minimize exposure of their own children to those who are unvaccinated (Foxhall 2015; Kaplan 2015).

Previous research has shown that children with non-medical vaccine exemptions tend to be (non-Hispanic) white, have parents with higher levels of education, and come from relatively more affluent households (Atwell et al. 2013; Birnbaum et al. 2013; Carrel and Bitterman 2015; Richards et al. 2013; Safi et al. 2012; Smith, Chu, and Barker 2004; Wei et al. 2009). This is in contrast to long-standing public health findings that under-immunization in children tended to be associated with minority racial or ethnic backgrounds, single-parent families, lower socio-economic status, and lower maternal education (Bobo et al. 1993; Ehresmann et al. 1998;

[4] According to the minimum 95% two dose vaccination coverage recommended by the WHO. Countries with suboptimal rates of vaccine coverage are Switzerland, Germany, Italy, UK, and Romania. Those with consistently high vaccine coverage are Iceland, Finland, Slovenia, Slovakia, and Hungary.

Hughart et al. 1999; Kenyon, Matuck, and Stroh 1998; Luman et al. 2003; Smith et al. 2004; Williams et al. 1995). Children from disadvantaged backgrounds face systematic health care barriers, including lack of consistent access to private sources of routine care, which can decrease the likelihood of being up-to-date with vaccinations (Bates and Wolinsky 1998).

Yet, lack of access to healthcare resources is unlikely to be the mechanism underlying vaccine refusal by white, educated, relatively affluent parents. Parents who refuse vaccines for their children have been portrayed as uninformed, irrational, and easily manipulated (Senier 2008), acting out of ignorance (Allen 2008), and perceived as lacking credibility in making decisions (Carpiano and Fitz 2017). These explanations are not supported by studies of parents who choose to delay or refuse vaccines, who are generally aware of vaccine information and recommendations touted by most public health and medical professionals (Gust et al. 2003; Meszaros et al. 1996; Reich 2016; Senier 2008).

Rather these parents likely feel personal responsibility for and efficacy in managing health decisions for their children and weigh perceived potential costs and benefits of vaccination before making these decisions (Funk, Salathé, and Jansen 2010; Kennedy, Basket, and Sheedy 2011; Reich 2016; Ropeik 2013; Sansom et al. 2001). Although parents may view their choices as asserting individual parental prerogative over the health of their children (Reich 2016), vaccine decisions are rarely made in isolation (Brunson 2013b) and perceived costs and benefits of vaccination are vulnerable to influence from the social environment (Bauch and Bhattacharyya 2012; Brunson 2013a). Vaccine decisions are located at the intersection of cultural processes and social networks (Mische 2011), which affect perceptions of social norms toward and support of vaccination (Wang et al. 2014). Recognizing this interdependence in

vaccine decisions is important for understanding where children with non-medical exemptions are likely to be found.

Children with non-medical exemptions tend to be geographically clustered rather than randomly distributed throughout the population (Atwell et al. 2013; Buttenheim, Jones, and Baras 2012; Ernst and Jacobs 2012; Lieu et al. 2015; Omer et al. 2008). This clustering creates spatial pockets without sufficient levels of herd immunity to prevent disease outbreaks. Across the U.S. and abroad, increasing vaccine hesitancy and refusal has been associated with the resurgence of vaccine-preventable diseases (Omer et al. 2006; Phadke et al. 2016; Salathé and Bonhoeffer 2008). Children with vaccine exemptions for non-medical reasons have not only an increased individual risk of infection, but also create an elevated risk for other children, both vaccinated and unvaccinated, in their local communities (DeBolt et al. 2002; Feiken et al. 2000; Imdad et al. 2013; Omer et al. 2008, 2009; Salmon et al. 1999).

Research Questions

How do we explain increasing rates and geographical clustering of children with non-medical vaccine exemptions? How do these trends affect how disease spreads? First, to understand increasing rates of non-medical exemptions we need to look beyond traditional understandings of under-vaccination to address the reversing trend in demographic characteristics associated with non-immunization. Specifically, how do social processes of residential sorting and local spillover effects contribute to generating geographical clusters of non-medical vaccine exemptions across space? The implications of this question extend beyond understanding associations between socio-demographic characteristics and individual health behaviors to community-level risk of disease spread. Does clustering of unvaccinated children

affect the locations in the local community where measles infections are likely to be transmitted? How much do these clusters affect the overall potential for measles outbreaks?

While previous research has presented evidence for the positive association between non-Hispanic white population, educational attainment, and other socio-economic status (SES) indicators and non-medical exemptions at the school-level, this work investigates how social processes may contribute to associations over broader geographical areas. Membership in particular social categories is not itself a mechanism[5] (Hedström and Swedberg 1996), nor are individual characteristics alone likely responsible for the clustering of decisions against vaccination (Crossley 2010; Emirbayer 1997). This work emphasizes the roles that both social selection and influence play in parents' decisions to obtain non-medical exemptions, resulting in their spatial clustering, and network processes that connect clusters of exemptions to the biological transmission of vaccine-preventable disease.

Personal Belief Exemptions in California

Empirically, this project focuses on non-medical vaccine exemptions to school-mandated vaccination requirements in California from 1998 to 2014. There is no individual mandate for vaccination or federal immunization law[6] in the U.S. Vaccination regulations apply to enrollment of children in schools and licensed childcare and are legislated at the state level. As of 1999, all 50 U.S. states had laws requiring proof of immunization against diphtheria, measles, rubella, and polio (Orenstein and Hinman 1999); additional vaccine requirements vary by state. In California,

[5] E.g. Identifying racially as non-Hispanic white does not itself cause you to be more skeptical of vaccines; the association is rather the observed evidence of other individual-level mechanisms.

[6] Although the right of states to require vaccinations for school-entry has been upheld by the Supreme Court on two occasions: *Jacobson v. Massachusetts*, 197 U.S. 11 (1905) and *Zucht v. King*, 260 U.S. 174 (1922). Additionally, the Court ruled that states are not required to permit non-medical exemptions to vaccination requirements in *Prince v Massachusetts*, 321 US 158 (1944).

compliance with vaccination requirements is reported to the Immunization Branch of the Department of Public Health (CDPH). This project uses the statewide, school-level data on Personal Beliefs Exemption (PBE) rates released annually by CDPH.[7]

In California, children are required to provide proof of immunization when entering childcare, kindergarten, and seventh grade (California Department of Public Health, Immunization Branch 2016b). California has had compulsory immunization legislation requiring measles and polio vaccination prior to school enrollment since 1967 (Jackson 1969). Diphtheria, pertussis, and tetanus were added to the regulations in the 1970s. Enforcement of and penalization for not meeting vaccination requirements varied significantly during this period (Robbins, Brandling-Bennett, and Hinman 1981). Serious enforcement of immunization requirements for school-attendance increased following a large measles outbreak in Los Angeles County in 1977 (Orenstein and Hinman 1999).

Immunization requirements shift over time as new vaccines are developed. Proof of adequate immunization against polio, tetanus, diphtheria, pertussis, measles, and haemophilus influenzae type b[8] has been a requirement of childcare and/or school registration in California since at least 1989, covering the full period of analysis here (California Department of Public Health, Immunization Branch 2016b; Kizer and Allenby 1989). Two additional vaccinations were also added to the kindergarten requirements since then—Hepatitis B, beginning in August 1997, and Variacella (chicken pox) in the 2001-2002 school year (Belshe 1996; California Department of Health Services, Immunization Branch 2003).

[7] Data on vaccine exemptions is not available at the individual level due to privacy concerns. Studies that examine vaccine coverage outside of the school setting typically audit medical records at a particular medical practices (e.g. Hughart et al. 1999; Lieu et al. 2015) or use random samples of parents, such as the National Immunization Survey (e.g. Luman et al. 2003; Smith, Chu, and Barker 2004). For analyses over larger geographical areas, such as states, school-level PBE data is the most complete source for general locations of exempted children.

[8] The haemophilus influenzae type b vaccine has been required of licensed childcare centers since 1978; however, immunization regulations were updated in 1996 to also require vaccine for licensed home-based childcare programs.

Beginning in the early 1990s, California experienced a substantial increase in the percentage of children entering schools without meeting these vaccination requirements. Prior to 2016, parents could enroll children in childcare and schools in California without fulfilling vaccination requirements by filing either a permanent medical exemption (PME), granted with documentation from a physician stating that the child cannot be vaccinated due to vaccine allergies, being immunocompromised, or other serious medical conditions (Salmon, Sapsin, et al. 2005), or a non-medical Personal Beliefs Exemption. Initially, parents needed only to sign a pre-prepared form stating their aversion to obtaining all the required vaccines for their children on personal/philosophic grounds to obtain a PBE (Salmon et al. 1999; Salmon, Sapsin, et al. 2005). Rates of children in California kindergartens with PBEs increased from .48% in 1992 to a high of 3.15% in 2013[9], as shown in Figure 1.1.

During this same period, the state experienced a significant increase in reported pertussis cases, including epidemics with more than 9,000 reported cases in 2010 (Winter et al. 2012) and 2014 (Winter et al. 2014). Spatial clustering of non-medical exemptions in California was shown to be correlated with elevated incidence of pertussis in 2010 (Atwell et al. 2013). In 2008, intentionally unvaccinated children were identified as playing a significant role in a measles outbreak in San Diego after a child with a PBE contracted the disease in Switzerland and exposed over 800 people to the illness upon returning the U.S., resulting in 11 additional cases and a significant containment effort to prevent additional infections by public health officials (Sugerman et al. 2010).

These increases in disease outbreaks prompted the signing of Assembly Bill 2109 (AB 2109) in 2012, which increased restrictions on obtaining PBEs. Effective January 2014, parents

[9] While there was some fluctuation in the rate of PMEs in California during the same period, the changes were quite small, non-monotonic, and the overall rate never exceeded 0.20% in any year (California Department of Public Health, Immunization Branch 2008, 2010, 2011, 2012, 2013, 2015, 2016a).

had to obtain a physician's signature confirming that they had been informed of the risks of refusing or delaying childhood vaccinations before being granted a PBE. Presumably, this requirement did have some effect on PBEs as the statewide rate dropped from a high of 3.15% in the 2013-2014 school year to 2.54% in the 2014-2015 school year (California Department of Public Health, Immunization Branch 2016a). Still, as shown in Figure 1.2, rates of kindergarteners entering schools with these exemptions remained high in several California counties, particularly in the northern region of the state.

The Disneyland outbreak in December 2014 had far-reaching implications for non-medical vaccine exemptions in California. First, it may have resulted in a further reduction in the percentage of children entering kindergarten with PBEs in the 2015-2016 school year (to 2.38% statewide) (California Department of Public Health, Immunization Branch 2016a). More significantly, however, it also served as the impetus for Senate Bill No. 277 (SB 277), which outlawed PBEs in California beginning in the 2016-2017 school year (Yang, Barraza, and Weidenaar 2015). Currently, all children are now required to fulfill vaccination requirements to enroll in licensed childcare, kindergarten, or seventh grade in private or public facilities, unless granted a PME by a physician[10]. Children not meeting these requirements must be homeschooled.

This policy change moves California from one of the more lenient U.S. states with regards to accessing non-medical exemptions (Omer et al. 2006) to among the states with the most restrictive policies against allowing children who do not meet vaccination requirements to enroll in schools. Some exemptions to vaccination requirements are available in every state, but vary significantly in both the types of exemptions that are available and the ease in acquiring

[10] There was a larger-than-usual increase in PMEs reported in the 2016-2017 school year, particularly among children enrolling in private school kindergartens, raising questions about compliance with SB 277 (California Department of Public Health, Immunization Branch 2017).

them (Orenstein and Hinman 1999; Rota et al. 2001; Salmon et al. 1999; Salmon, Omer, et al. 2005; Salmon, Sapsin, et al. 2005; Yang, Barraza, et al. 2015; Yang and Silverman 2015). All states allow medical exemptions and, until 2016, all but two states[11] permitted some type of non-medical exemptions. The remaining 48 states allowed exemptions for religious reasons, 20 of which allowed additional exemptions on the basis of vaccination violating parents' personal, moral, or philosophical beliefs (Yang and Silverman 2015). Following changes in immunization laws in California and Vermont in 2016, those numbers are now 47 and 18 states, respectively[12].

PBEs in California serve as an important case study on non-medical vaccine exemptions. The relative ease of obtaining these exemptions prior to 2014, and their continued allowance until 2016, permitted a significant increase in children enrolling in schools without meeting vaccine requirements, a trend that has been noted elsewhere across the U.S. and in other high-income countries internationally. The resulting interaction between decreasing rates of vaccination and increases in disease incidence serves as an important example to the many other states with recent attempts to change policies addressing access to non-medical exemptions (Mello, Studdert, and Parmet 2015; Yang, Barraza, et al. 2015). Allowing exemptions to vaccination requirements for personal or philosophical reasons can significantly increase state medical and non-medical costs associated with disease outbreak (Sugerman et al. 2010; Wells and Omer 2012). Examining the social processes that result in and consequences that result from spatial clustering of PBEs in California from 1998-2014, is informative to active debates surrounding vaccine compliance in both the national and international arenas.

It should be noted that PBEs are not a direct, consistent indicator of vaccination status; children with PBEs can be entirely unvaccinated, partially vaccinated, or even fully vaccinated.

[11] Mississippi and West Virginia

[12] Vermont still permits exemptions for religious reasons.

PBE data released by the CDPH does not distinguish which, if any, vaccines exempted children have, nor do the CDPH annual immunization reports include students with PBEs, even if partially or fully vaccinated, in estimates of coverage for specific antigens (California Department of Public Health, Immunization Branch 2017). That said, an in-depth analysis of immunization records among children with PBEs in California shows that while coverage varies substantially by vaccine, the modal number of total vaccines among these children was zero (Buttenheim et al. 2015). Children with PBEs in schools with high PBE rates tended to have lower partial vaccination levels than those in schools with typical PBE rates (Buttenheim et al. 2015). Examinations of vaccine coverage among exempted children in other states have shown significant variation as well; 75.5% of parents of children with non-medical exemptions surveyed across four U.S. states[13] reported that they had consented to at least one vaccination (Salmon, Moulton, et al. 2005), while inspection of vaccination records of exempted children in Arkansas revealed the opposite—70.8% reported no vaccines at all (Safi et al. 2012). All three of these studies suffer from missing data, incomplete records, and lack of verification with physician records.[14] For these and other reasons, it is difficult to ascertain the true vaccination status of exempted children (Buttenheim et al. 2015). In this project, no assumptions are made about partial vaccination for children with PBEs. Treating these children as unvaccinated is consistent with previous research investigating vaccination coverage (Buttenheim et al. 2012; Omer et al. 2008, 2009; Sugerman et al. 2010) and the link between unvaccinated children and disease risk (Atwell et al. 2013; Ernst and Jacobs 2012; Feiken et al. 2000; Imdad et al. 2013).

[13] Colorado, Massachusetts, Missouri, and Washington

[14] Buttenheim et al (2015) do use the official immunization records submitted to schools, but any vaccination without a noted date is recorded as missing, which could be an artifact of record keeping rather than refusal. Data presented by Reich (2016) demonstrate that parents may prefer to submit a blank immunization record, even if a child is partially vaccinated, lest the partial record call into question claims that vaccination violates personal beliefs.

Outline of Chapters

The following chapter provides the background for the empirical analyses in this project by presenting the rationale for why discussions of adherence to vaccine requirements and access to non-medical exemptions should be concerned with social networks and spatial processes. Although California is the empirical focus of this project, my goal in Chapter 2 is to present a larger theoretical argument that highlights how selection and social influence create homophily among parents' vaccination decisions. Local clustering of these decisions then creates unintended consequences for biological contagion across wider geographical areas. I argue that non-medical vaccine exemptions and their consequences are located at the intersection of social and biological contagion; both of these processes occur over the larger social network and interact in ways that cannot be clearly understood by parents making decisions within local contexts. This chapter concludes by laying the groundwork for the hypotheses advanced in the subsequent empirical chapters.

Chapter 3 maps the broader patterns of spatial clustering of PBEs across schools in California. Previous examinations of spatial clustering of non-medical vaccine exemptions are mostly focused at the school-level; while school-level associations are briefly investigated in Chapter 3, the analysis primarily uses spatial scan statistics to identify factors associated with broader patterns of clustering across schools. In particular, does residential sorting explain large geographical pockets of PBEs? If parents select into schools and communities based on a stable set of socio-demographic and neighborhood characteristics associated with PBEs at the school level, this could create larger areas with elevated rates of non-medical exemptions.

Chapter 4 continues the investigation of the spatial clustering of PBEs across schools by examining spatially dependent processes. In particular, I shift the level of analysis to yearly data

to examine the spatial and temporal stability in covariate effects on PBE rates. I use spatial econometrics models to estimate spatial heterogeneity in covariate effects, as well as adjudicate whether spatial autocorrelation in PBE rates should be attributed to spillover processes between schools or spatial correlation in unmeasured covariates. Do characteristics and PBE rates of schools affect the PBE rates of others nearby?

Chapter 5 moves to the second half of the project by examining the effect of geographical clustering of PBEs on locations of measles transmission. The analyses use an empirically calibrated synthetic population of children in California in 2014, built to reflect empirical distributions of socio-demographic and neighborhood characteristics, school enrollment, and school-level PBE rates. This population is used to conduct a large-scale simulation experiment to examine how focal points of interaction contribute to disease spread. Many existing epidemiological simulation models of disease spread include these local and community interaction foci; however, to my knowledge, this is the first attempt to incorporate empirical data on vaccine exemptions to specifically investigate how the geographical structure of social interaction interacts with spatial pockets of unvaccinated children to influence biological contagion. Therefore, this chapter combines insights from epidemiological examinations of measles outbreaks with understandings of social interaction in networks to investigate this question: Does spatial clustering of non-medical vaccine exemptions affect the focal points of interaction where measles transmission is most likely to occur?

Chapter 6 uses agent-based simulation models to examine how spatial clustering of non-medical vaccine exemptions affects the potential for measles outbreaks. This chapter particularly seeks to understand how the spatial clustering, not just the increasing rates of exemptions over time or the overall prevalence of these exemptions, influences the possibility of outbreaks.

Simulation models with varying spatial and temporal patterns of PBES are used to ask: Does it matter that PBEs are spatially clustered? Or it is just overall increasing rates of exemptions that may be contributing to increased measles incidence in the U.S.?

Chapter 7 then summarizes the findings of the four empirical chapters. I connect these findings back to the theoretical motivations outlined in Chapter 2 and discuss the methodological implications of using administrative data on PBEs and empirically calibrated simulation experiments to examine these research questions. I also briefly discuss the relevance of the findings to public health strategies to address the formation and consequences of spatial clusters of children with non-medical vaccine exemptions.

Significance

Fundamentally, this project raises questions concerning how social processes underlying homophily, particularly residential sorting and social influence, shape spatial patterns of non-medical vaccine exemptions that can have serious implications for biological contagion. Although parents may view vaccines as a question of individual decision-making for their children, these choices affect the entire community, often in ways they cannot discern. For this reason, research into the formation of spatial clusters of vaccine exemptions over time is needed to understand how vaccine policy and local interaction in social networks can increase potential for disease spread. This project contributes to a growing literature that examines this intersection of social processes and biological contagion and emphasizes the importance in understanding how local social norms and influence can have serious consequences for the introduction, spread, and containment of communicable disease (Bauch and Galvani 2013; Dodds and Watts 2005).

Figures

Figure 1.1: Statewide PBE rate in California kindergartens by school type, 1992-2014

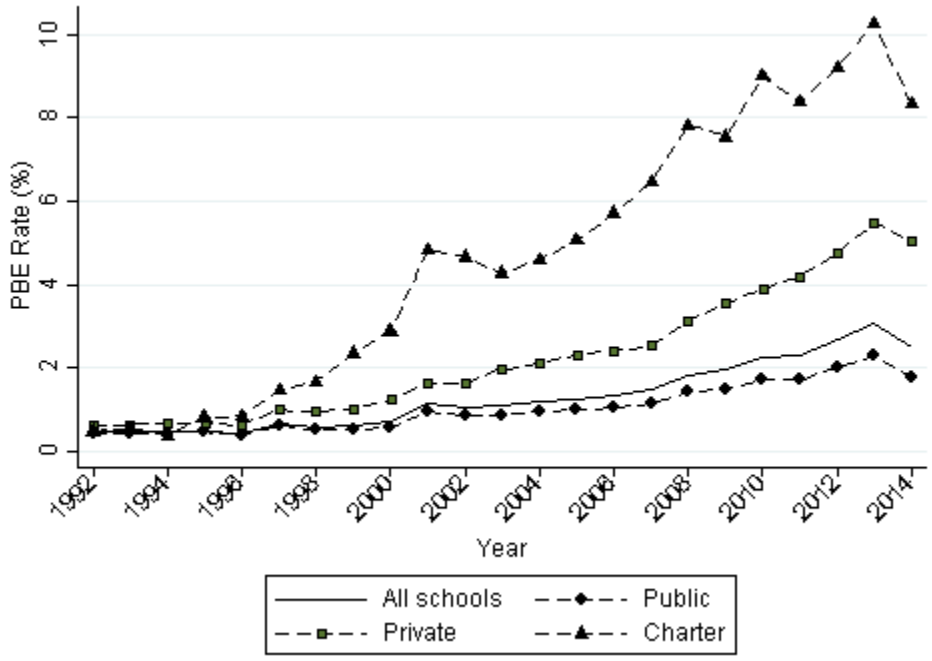
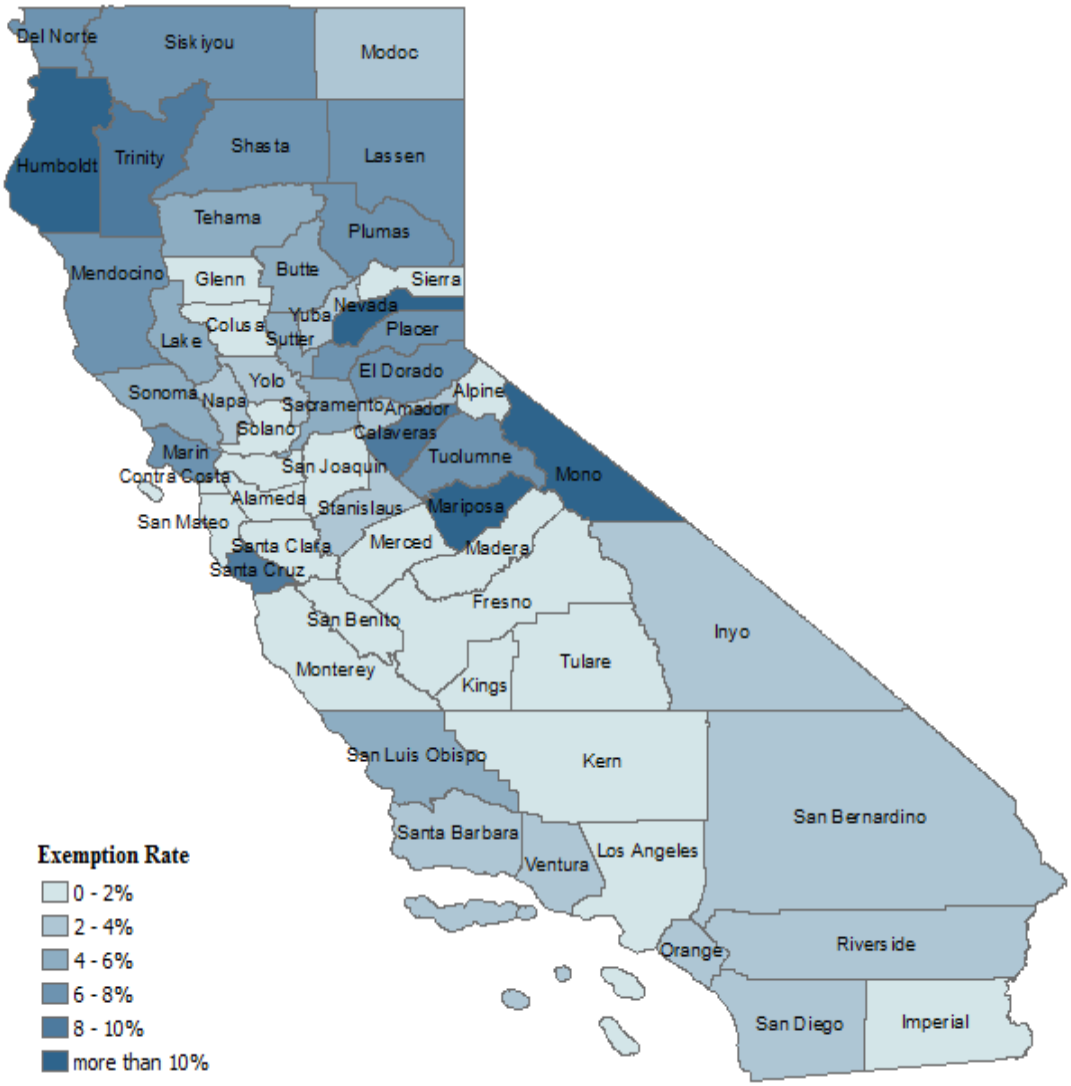


Figure 1.2: County PBE rates in California kindergartens, 2014-2015 school year



Chapter 2: The Importance of Social Networks and Space in Vaccine Refusals Debates

Abstract

Previous research shows many parents view vaccine decisions as individual choices made in the interest of their children. Reduction in the prevalence of vaccine-preventable disease, erosion of trust in healthcare institutions, and social influence all contribute to perceptions of costs and benefits of vaccination. Vaccination decisions are vulnerable to the same social processes that result in homophily of other health behaviors, such as selection into schools accepting of alternative views toward vaccines and social influence from others with anti-vaccine beliefs. As social networks also structure physical contact, these social behaviors shape larger patterns of biological contagion. This chapter examines the ways in which social processes contribute to clustering of unvaccinated children and how these clusters influence disease spread in local communities.

Chapter Introduction

Increasing rates and geographical clustering of non-medical vaccine exemptions across the U.S. and other high-income countries suggest that more research is needed to understand how areas of low vaccination coverage form. Why are vaccine refusals increasing in some areas and not others? Qualitative research on vaccine hesitancy has demonstrated that parents engage in decision-making processes that weigh costs and benefits of vaccination (Reich 2016; Sansom et al. 2001). This project seeks to connect these understandings of vaccine decision-making to macro-level spatial patterns in locations of vaccine exemptions by emphasizing how social networks can affect perceptions of risks associated with vaccination, and how the resulting spatial patterns of vaccine exemptions shape biological contagion.

Vaccine Decisions

Traditional public health understandings of the causes of under-immunization typically focus on lack of access to health care and lack of information. This type of strategy assumes that barriers to immunization can be overcome if parents are informed of the benefits of vaccines and provided with opportunity to vaccinate their children. Yet, interviews with parents who have chosen to delay or refuse childhood vaccines generally show that parents are aware of public health recommendations for vaccines and have spent time seriously considering these decisions (Asch et al. 1994; Meszaros et al. 1996; Reich 2016; Senier 2008).

Previous studies undertaken to identify concerns of vaccine hesitant parents have shown contradictory results. Some of these studies find that parents who refuse vaccines and parents who vaccinate share similar knowledge of vaccines and beliefs about vaccination (Bardenheier et al. 2004; Gust et al. 2004). At the same time, parents who express the greatest number of concerns about vaccines do not share socio-demographic characteristics with those most likely to

seek non-medical exemptions (Gilkey et al. 2014; Shui, Weintraub, and Gust 2006).[15] Furthermore, a nationally representative survey showed that 22% of parents who vaccinated their children thought the recommended schedule was *not* the best choice (Dempsey et al. 2011). This suggests that decisions to refuse vaccines cannot be simply reduced to awareness of recommendations or socio-demographic characteristics, but how vaccine information is evaluated and acted on. Three important components of this decision-making process are evaluation of risk, trust in healthcare institutions, and influence from social networks.

Evaluation of Risk

Most interventions targeting vaccine compliance focus at the individual level and are primarily based on increasing awareness of the benefits vaccination and serious health consequences of vaccine-preventable disease (Jarrett et al. 2015; Nyhan et al. 2014; Sadaf et al. 2013; Silverman 2003). For example, a government-led pro-vaccine campaign in the U.K. following the now-discredited claim linking the Measles Mumps and Rubella (MMR) vaccine to development of autism emphasized 'the facts' associated with risks of measles infections in children (Hobson-West 2003).[16] This focus on individual risk can be problematic for several reasons, including lack of discussion of costs when considering herd immunity and the assumption that all parents calculate risks in the same manner as public health officials (Hobson-West 2003).

[15] Certainly, many studies show that *more* concerns about vaccine safety and anti-vaccine beliefs are associated with decreased likelihood of vaccination (Allred et al. 2005; Asch et al. 1994; Gaudino and Robison 2012; Humiston et al. 2005; Prislin et al. 1998). These results only demonstrate that it can be difficult to reduce vaccine refusals to associations with individual concerns and characteristics alone.

[16] The MMR-autism vaccine scare began in 1998 following the publication of an article in a British medical journal linking the MMR vaccine to the development of autism in some children.

Higher levels of vaccination result in fewer susceptible individuals in a population, significantly reducing the ability of a disease to spread. This collective benefit is referred to as herd immunity. Herd immunity is a public good. Public goods are non-excludable and non-rivalrous; this means that people can neither be prevented from using a good, nor prevent its use by others (Olson 1965). Under herd immunity, everyone in the population, vaccinated or unvaccinated, benefits from decreased risk of infection due to lower disease prevalence.

As Olson (1965) points out, however, even if all people in a group acknowledge that a public good is in their collective interest, not all individuals will be compelled to contribute resources it. Because public goods are non-excludable and non-rivalrous, individuals are able to "free-ride" off of the contributions of others. In fact, from a game-theoretic perspective, it can be individually rational to not contribute to a public good when its cost is non-zero and others are contributing. Herd immunity also operates under this principle. Not everyone must be vaccinated; the proportion of the population that needs to be vaccinated in order to achieve herd immunity depends on the infectiousness of the disease. It is higher (92-96%) for highly infectious diseases, such as measles or pertussis, and slightly lower (84-88%) for those that are less infectious, such as the mumps (Anderson and May 1985).

The cost of vaccination is non-zero. It usually requires visiting a healthcare professional, which may consume both time and monetary resources. There are also small risks of reactions to the injection or vaccine itself. People certainly have an incentive to be vaccinated—the expected acquisition of personal immunity to a disease—but when herd immunity has already been achieved in the population, this benefit may seem less important. However, when too many people opt out of vaccines, herd immunity is lost and disease risk increases for *everyone* in the community, even those who have been vaccinated, as no vaccine is 100% effective.

Although there are situations where it may seem in a parent's best interest not to vaccinate from an individually rational perspective (Hobson-West 2003; Rogers and Pilgrim 1996; Wing 1990), it is unclear how helpful this perspective is for understanding vaccine decisions in practice. Assessment of costs and benefits of individual behaviors are vulnerable to the influence of many social factors besides those explicitly incorporated into these types of calculations (Oberschall and Leifer 1986), which can make it difficult to attribute individual vaccine decisions directly to this type of calculus. There are also questions about the extent to which parents understand herd immunity. While parents explaining decisions not to vaccinate their children generally understood that vaccines have an important role in reducing the prevalence of serious childhood diseases, it was unclear whether they understood how their choices affect herd immunity (Meszaros et al. 1996; Quadri-Sheriff et al. 2012; Reich 2016).[17] Similarly, physicians who promote alternative vaccine schedules emphasize that parents should prioritize their own children's health when making vaccine decisions even though they acknowledge the collective benefits of herd immunity (Sears 2011).

The reduction of disease prevalence due to herd immunity may also affect parents' perceptions of overall disease risk. The success of vaccines in significantly reducing disease prevalence has led to underestimations of the seriousness of these diseases (Callender 2016). Herd immunity reduces disease incidence to such low levels that the perceived risks of vaccination appear higher than risks of infection (Bauch and Bhattacharyya 2012). Previous studies show that vaccine beliefs and decisions are responsive to the salience of disease risks and outbreaks (Bauch 2005; Bauch and Bhattacharyya 2012; Funk et al. 2010; Horne et al. 2015). In interviews, parents of unvaccinated children have explicitly mentioned that their decision was

[17] For example, parents made comments such as "If those kids that are vaccinated are truly protected…why would you be threatened by my child who is not vaccinated" (Reich 2016:236). These types of comments ignore the risks to those who are not able to be vaccinated and vaccine failures.

influenced by feeling that their children were not at risk for infection due to the vaccination of other children (Benin et al. 2006). Simulations of vaccine decision-making also show these effects: When individuals rely on anecdotes from the media and their social networks to form opinions of disease risk, beliefs about the necessity of vaccines can be biased by only a few examples of people who refused vaccines and suffered no adverse effects. In these cases, vaccine coverage in the population often falls well below what would be predicted if everyone were able to perceive actual disease risk (Fu et al. 2011).

Low disease prevalence is related to other forms of bias in decision-making. Omission bias occurs when parents think that it is worse to vaccinate and have harmful side effects than to refuse vaccines and risk possible future infection (Asch et al. 1994; Brown et al. 2010; Ritov and Baron 1990). This can be the case even when risks from an infection may be more harmful overall (Asch et al. 1994). Furthermore, vaccine decisions are also influenced by parents' perceptions of their ability to control their child's risk of exposure to a disease (Meszaros et al. 1996; Senier 2008; Walker and Rea 2016).

These findings suggest that some parents feel a great sense of individual responsibility for children's health when making vaccine decisions (Poltorak et al. 2005; Reich 2016; Senier 2008). In particular, parents may want to exercise control when they fear a health risk with origins that are not well defined, such as autism (Reich 2016; Ropeik 2013). A sense of control also affects perceptions of risks associated with vaccination in other ways as well. Risks that are imposed may cause more concerns than those voluntarily accepted (Calman, Bennett, and Corns 1999; Ropeik 2013). The source of the imposed risks also matter: those imposed by institutions seen as untrustworthy, such as the government or the pharmaceutical industry, may seem particularly threatening (Ropeik 2013). Trust in healthcare institutions can act as a significant

modifier of how risks associated with vaccines and vaccine-preventable disease are assessed (Hobson-West 2003, 2007).

Trust in Healthcare Institutions

As mentioned above, vaccination decisions cannot be reduced to availability of information. The source of vaccine information affects parents' decisions as well. Distrust in the government or official public health agencies, such as the Centers for Disease Control and Prevention (CDC) and Food and Drug Administration (FDA), is also associated with vaccine refusals in the U.S. (Lee et al. 2016; Offit and Moser 2009; Salmon, Moulton, et al. 2005). While some parents feel that the true risks of vaccines are unknown or intentionally hidden by the government and public health officials, other parents are concerned that official recommendations are one-size-fits-all and ignore risks to individual children in favor of the collective (Reich 2016).

Parents have expressed particular concern over the associations between vaccines and the pharmaceutical industry. Some parents suspect that the pharmaceutical industry has vested interest in vaccine safety research and is involved in public health vaccination recommendations (Dubé et al. 2016). Suspicion over ingredients used in vaccines (Reich 2016) and the profit from developing and patenting vaccines (Offit and Moser 2009) are also contributors to vaccine hesitancy. Vaccine scares, such as the discredited MMR-autism link or unsafe mercury exposure from vaccines administered to infants in the U.S., create increased suspicion of pharmaceutical companies that can have lasting effects on public trust in vaccines (Gross 2009; Ludlow et al. 2015).

Many studies of vaccine hesitancy emphasize that trust in healthcare occurs at two levels: trust in the larger medical establishment and trust in personal practitioners. While physicians are representative of the larger institution of medicine and associated health agencies, personal relationships with physicians influence how parents assess vaccine risks (Senier 2008). Physicians are still viewed as one of the most trusted sources of healthcare information (Freed et al. 2011; Gaudino and Robison 2012; Kennedy, LaVail, et al. 2011; Kennedy and Gust 2005; Sadaf et al. 2013), and physician reassurance has had positive effects on addressing concerns of vaccine hesitant parents (Fredrickson et al. 2004; Gust et al. 2008). Many intervention strategies for increasing vaccine uptake focus on physicians as playing a crucial role in reassuring parents of the benefits of vaccination and encouraging compliance (Berry et al. 2017; Caskey, Lindau, and Alexander 2009; Fredrickson et al. 2004; Gust et al. 2004; Kempe et al. 2011; Larson et al. 2011; MacDougall et al. 2016; Omer et al. 2009).

Trusted relationships with alternative health practitioners can have the opposite effect on vaccination. Parents with alternative health beliefs were more likely to have misconceptions about the safety of vaccines (Gellin et al. 2000) and parents of children with vaccine exemptions were more likely to report confidence in alternative health practitioners than parents of vaccinated children (Benin et al. 2006; Salmon, Moulton, et al. 2005). Some alternative views toward vaccines include the belief that natural infection or immunity is preferable to synthetic vaccines, as the latter may overwhelm the immune system (Fredrickson et al. 2004; Luthy et al. 2012; Reich 2016; Ropeik 2013; Senier 2008).

Parents seeking alternative sources of vaccine information may also use the Internet. While the amount of available information makes the Internet an attractive resource, the lack of verification or review comprises its quality (Cline and Haynes 2001). Although the 2002-2003

Health Information National Trends Survey found that physicians were still the most trusted source of health information overall, 63.7% of respondents who reported using the Internet had searched for health information in the previous 12 months (Hesse et al. 2005). More notably, while approximately 50% of respondents indicated that they wanted to consult their physician first for health information, only 11% reported doing this; 49% of respondents reported that they actually went online to retrieve health information first (Hesse et al. 2005). In a 2009 survey, 24% of parents identified the Internet in the three most important sources of information on childhood vaccination (Kennedy, LaVail, et al. 2011).

Healy and Pickering (2011) highlight the role of non-verified sources on the Internet in spreading anti-vaccine rhetoric. As the authors point out, stories that garner attention may be those that are novel, controversial, or generally "newsworthy" rather than those that present the most research-supported aspects of vaccination. Parents with less trust in healthcare providers are more likely to use the Internet as a source of vaccine information, and parents who used the Internet were more likely to have children with non-medical exemptions and lower perceptions of vaccine safety and effectiveness (Jones et al. 2012). Research has also shown that younger and more educated parents are more likely to use the Internet as a source of vaccine information (Cotten and Gupta 2004; Jones et al. 2012).

Other parents are also common sources of vaccine information: some parents rely primarily on the advice of others when making vaccine decisions (Brunson 2013a). The characteristics of one's social networks were found to be more predictive of vaccination decisions than individual attributes (Brunson 2013b). Parents who chose not to vaccinate their children were more likely to have trusting relationships with people who did not believe in

vaccination (Benin et al. 2006). Taking cues for vaccination decisions from social networks is particularly important for understanding why vaccination status clusters over geographical space.

Homophily in Social Networks

Clustering of children with non-medical vaccine exemptions within schools is an example of homophily. Homophily is the tendency of people with similar characteristics to share ties or cluster in the same areas in a social network and is generated through three social processes. First, parents can choose to associate with one another due to the shared refusal to vaccinate their children. In other words, they selectively associate due to the behavior of interest. Second, parents could associate due to another characteristic that is correlated with refusing vaccines. This has a confounding effect as the homophily in vaccination behavior is a result of selection on the correlated characteristic rather than the behavior itself. Third, parents can directly influence one another to refuse vaccines. I discuss each of these processes in turn below.

(i) Selection

Selection has been shown to be an important determinant of homophily of other health behaviors in networks. Selection of friends with similar smoking status was an important source of homophily of smoking behavior in adolescent friendships in Finland, the U.S., and the U.K. (Mercken et al. 2012; Schaefer, Haas, and Bishop 2012). Without properly accounting for selection into social relationships, the effects of other social processes resulting in homophily, such as social influence, can be significantly overestimated (Kandel 1978).

For parents who file non-medical exemptions, effects of selection would represent choosing to associate with or live in the same areas as other parents who are also exempting their

children. Selection may be an important factor in clustering of exempted children if parents intentionally seek out locations in which alternative beliefs toward vaccination are accepted. Parents who refuse vaccines may face stigma from vaccinating parents who view their decisions as lacking credibility and ignorant of public health (Carpiano and Fitz 2017). Alternatively, parents who consider protection provided by herd immunity when refusing vaccines (e.g. Benin et al. 2006) may be less likely to intentionally select into schools or neighborhoods that already have a high proportion of exempted children.[18]

(ii) Confounding Effects

Clustering of other health outcomes has been generated not by selecting on the behavior of interest, but on factors correlated with the behavior. For example, poorer health outcomes among migrants in Sweden was associated with selecting into social networks predominantly composed of other migrants (Rostila 2010). The authors suggested this effect was likely due to the reinforcement of social norms and attitudes that promoted unhealthy behaviors in these networks. In a study of interaction in an online health community, ties tended to be formed based on similarities in age, gender, and body mass index—characteristics that are often sources of similarity in offline social ties—rather than the fitness and exercise characteristics of user profiles related to health behaviors (Centola and van de Rijt 2015).

Clustering of non-medical exemptions could also be generated by parents selecting into particular schools or neighborhoods on characteristics related to vaccine behavior rather than the behavior itself. Residential sorting into certain kinds of neighborhoods based on socio-economic factors associated with non-medical vaccine exemptions—racial/ethnic background, parental

[18] This would be making the assumption that parents understand that herd immunity has a local quality. As discussed above, even when parents acknowledge that vaccination has collective benefits, they may not understand how herd immunity operates in practice.

education, and household income—could also produce clustering of exempted children, even if parents did not intend that outcome. Socio-economic factors related to racial/ethnic background, education, and social class are strong predictors of residential sorting (Bayer, Ferreira, and McMillan 2007; Massey 1990). Even if parents select into neighbors for other reasons, local social norms surrounding vaccine skepticism may develop and counteract influence from dominant cultural norms that would otherwise support vaccine compliance (Benin et al. 2006).

(iii) Social Influence

While selection into neighborhoods or schools contributes to the structure of social networks, behaviors within the network can also produce homophily in health outcomes. Social influence occurs when the behavior of others subsequently affects an individual's own behavior. In this case, parents with unvaccinated children can influence other parents to choose not to vaccinate their children (Sobo 2015). Even without the ability to directly solicit the opinions of others, we perceive their actions as conferring information about the quality or value of behaviors (Banerjee 1992; Bikhchandani, Hirshleifer, and Welch 1992; Salganik 2006; Strang and Meyer 1993). We make the assumption that, like ourselves, others weigh decisions before acting. Their behavior then is the visible outcome of a decision-making process in which there were more favorable than unfavorable considerations for that action.[19] For example, the "bandwagon effect" was the most significant factor in influencing college students to agree to an optional flu-like vaccine (Hershey et al. 1994), demonstrating that knowledge of peer behavior can influence vaccine decisions.

[19] Although this type of process does not necessarily result in arriving at "correct" outcomes, individuals decisions in these behavior cascades can be shown to be rational given available signals (Easley and Kleinberg 2010).

Social influence also contributes to the establishment of collective attitudes toward health behavior. Group norms and social support surrounding healthy behaviors were found to be an important component of the positive SES gradient in health (Chang and Lauderdale 2009; Link and Phelan 1995; Phelan, Link, and Tehranifar 2010). For example, diffusion mediated by social status was shown to be a significant predictor of smoking behavior in the U.S. and across European countries (Christakis and Fowler 2008; Pampel 2001, 2002).

The puzzle, however, is why vaccine refusals are more common among socially advantaged parents who are attentive to other healthy lifestyle behaviors, such as good nutritional practices (Gilkey, McRee, and Brewer 2013). The reversing gradient in association between SES and unvaccinated children may be partially the result of changing cultural attitudes. Over time, the positive associations between higher SES groups and high cholesterol (Chang and Lauderdale 2009), smoking (Pampel 2005), and cocaine use (Miech 2008) have reversed as social norms surrounding these behaviors have become more negative, and higher social strata individuals were more responsive to the cultural redefinitions and subsequent behavior modification. The association of vaccines with health risks rather than benefits may be promoting shifts in attitudes toward vaccination among health conscious, high SES parents.

Social networks are important influencers of health; they serve as channels for the diffusion of information and create systems of reinforcement of behaviors (Pampel, Krueger, and Denney 2010; Smith and Christakis 2008). Diffusion has been studied in many social settings in addition to health practices, including organization structures in firms (DiMaggio and Powell 1983) and government (Hedström, Sandell, and Stern 2000; Knoke 1982; Tolbert and Zucker 1983), advances in technology (David 1985; Ryan and Gross 1943) and medicine (Burt 1987), and tactics in social movements (Andrews and Biggs 2006; Givan, Roberts, and Soule 2010;

Soule 1997; Tilly 1978; Wang and Soule 2012). To understand why non-medical exemptions cluster spatially, it is important to understand how who we are connected to in our networks affect the spread of health behaviors.

Social Ties

Social ties are the connections among people in social networks. Neighbors are the people with whom we share direct ties. Even though we are often aware of practices in our networks outside of our own neighbors, we may give more weight to the information, opinions, and behavior of those we are directly connected to when making decisions. For example, while people may be aware of upcoming protest events, they are most influenced to attend when other people they know are also participating (Bond et al. 2012; Klandermans and Oegema 1987).

The strength—strong or weak—of social ties affects social influence in networks. Granovetter (1973) provides two related, but distinct conceptions of tie strength: the first is the combination of amounts of time, emotional intensity, intimacy, and reciprocity that characterizes the interaction and the second is how the tie relates to overall network structure. In practice, this project focuses most on the second definition to examine how ties affect different types of contagion processes in social networks. Although I spend less time discussing the first definition explicitly, it is important to note here because people who share strong ties tend to be similar (Granovetter 1973). This homophily can encourage the increased amounts of time, interaction, and investment that tend to characterize strong ties, or result from it.

Structurally, strong ties tend to demonstrate triadic closure,[20] while weak ties tend to provide bridges between local clusters of ties (Friedkin 1980; Granovetter 1973).[21] Ties can be clustered geographically (Kleinberg 2006; Liben-Nowell et al. 2005) or with respect to other social characteristics, such as racial/ethnic background, socio-economic class, hobbies, educational affiliation, occupation, or organizational membership (Killworth and Bernard 1978; Watts 2004; Watts, Dodds, and Newman 2002). This clustering can be good for reinforcing behaviors, but creates redundancy in the circulation of information or opinions. Bridges provided by weak ties, on the other hand, allow for information and disease to spread more rapidly beyond local clusters (Centola and Macy 2007; Granovetter 1973, 1983; Watts 2004; Watts and Strogatz 1998). This is why removal of weak ties tend to be more damaging to the overall connectivity of a network than removal of strong ties (Granovetter 1983; Onnela et al. 2007).

To illustrate the important role of weak ties in diffusion, Granovetter (1973) demonstrated that people often learned of new job opportunities from acquaintances or friends of friends rather than close friends or family. Weak ties have also been shown to facilitate knowledge sharing between units within an organization (Hansen 1999),[22] in online communities (Zhao, Wu, and Xu 2010), and across neighborhoods in the Philippines (Liu and Duff 1972). Weak ties can also be effective sources of new information among strangers that come into contact due to membership in the same organization. For example, employees receive technical

[20] If person A has a strong tie to person B and person A has another strong tie to person C, it is likely that persons B and C will become friends as well. This observation was also made in previous studies of the structure of social networks (Rapoport 1953; Rapoport and Horvath 1961).

[21] Bridges are ties that, if removed, would break the network into separate components. Rather than acting as true bridges, many weak ties act as local bridges, whose removal do not break the network into separate components but does significantly increase the distance between two nodes.

[22] Although complex knowledge diffusion benefits from strong ties.

advice from others through a large company network, even though they do not know each other personally (Constant, Sproull, and Kiesler 1996).

Strong ties, on the other hand, promote the establishment and enforcement of social norms and aid in the adoption of new behaviors. Individuals may look to others that seem similar to themselves when making decisions. The spread of obesity in a social network was more likely to occur among same-sex contacts (Christakis and Fowler 2007). Much of our daily interaction occurs locally and spatial proximity is a common component of social diffusion (Rogers 2003; Strang and Soule 1998). Happiness can spread dynamically across social networks, but the influence decreases as people in the network become more geographically distant (Fowler and Christakis 2008). In particular, happiness was shown to increase after a next-door neighbor, nearby friend or sibling, or co-resident spouse reported increased happiness.

Spatial proximity has also been shown to be important for the spread of practices among governments, organizations, and firms. Political affiliation and support can also diffuse among nearby populations, as demonstrated with support for the trade union movement in Sweden (Hedström 1994) and presidential candidate Salvador Allende in Chile (Petras and Zeitlin 1967). Protest events and riots can spread to nearby cities, potentially due to event coverage in the local news media (Andrews and Biggs 2006; Myers 1997), while the adoption of new organizational structures may spread to local governments, hospitals, and corporations from those located nearby (Burns and Wholey 1993; Davis and Greve 1997; Knoke 1982).

Diffusion may occur spatially not only due to the increased ability to observe the behavior of others in close physical proximity (Hedström 1994) but also because the clustering of ties creates multiple connections of reinforcing influence (Centola and Macy 2007). Social diffusion involves a conscious decision for adoption. It is assumed that an individual will adopt a

practice after his/her threshold is met; the threshold is the number of previous adoptions an individual must witness before he/she is convinced to adopt (Granovetter 1978). In simple contagion, thresholds are low and it is possible for adoption to occur after only one contact with the practice (Centola and Macy 2007).[23] In many cases, however, the threshold for adoption is greater than one exposure.

Complex contagion requires two or more sources of contact with a practice before an individual adopts (Centola and Macy 2007). This has important consequences for how the practice spreads. Complex contagion often characterizes practices that are perceived as risky or not yet proven, and has been demonstrated in collective action that involves substantial commitment for participation (McAdam 1988; McAdam and Paulsen 1993; Zhao 1998), partnerships that require reliability and trust (Nelson 1989; Ruef, Aldrich, and Carter 2003), the promotion of collective efficacy (Morenoff, Sampson, and Raudenbush 2001), adoption of new medical technology (Coleman, Katz, and Menzel 1966), decisions to go to college (Berg 1970), and leaving social gatherings (Granovetter 1978). In many cases, the source of the exposure also influences likelihood of adoption (Centola and Macy 2007) While many farmers in Iowa first heard about a new type of hybrid seed corn from agricultural salesmen, the adoption of the seed corn by their neighbors was more important for influencing farmers to plant the new seeds themselves (Ryan and Gross 1943).

Complex contagion may characterize the spread of non-medical vaccine exemptions as the decision refusal vaccines still contradicts prevailing medical and public health advice. Therefore, parents may require multiple reinforcements before deciding not to vaccinate. As

[23] Two of the most straightforward examples of simple contagion are the spread of information and disease. It only requires coming into contact with an infectious measles case once to acquire the disease, just as it only requires one person informing you of a measles outbreak at Disneyland for you to be aware that it has occurred.

discussed above, behaviors that require multiple affirmations may show increased spatial concentration as physical proximity to other adopters increases the likelihood that higher adoption thresholds are met (Burns and Wholey 1993; Centola and Macy 2007; Davis and Greve 1997; Gould 1991; Hedström 1994; McAdam 1988; Myers 1997; Petras and Zeitlin 1967; Rogers and Kincaid 1981; Whyte Jr 1954; Zhao 1998).

Understanding spatial patterns of non-medical exemptions requires investigation not only of residential sorting into schools or neighborhoods, but the extent to which spatially dependent processes, such as complex social contagion, facilitate the spread of exemptions among geographically proximate parents. Social networks and space are important for debates around vaccine refusals because social processes associated with homophily can create spatial clusters of health behaviors, including vaccination decisions. Beyond influencing health behaviors, however, social networks also structures physical contact, which shapes biological contagion.

Biological Contagion

Biological contagion refers the spread of disease and occurs through physical contact. The structure of our social networks affects who we are likely to come into contact with, and, therefore, the paths through which disease spreads. As social diffusion and biological contagion are both rooted in our social networks, spatial clusters of non-medical exemptions have consequences for biological contagion of vaccine-preventable diseases. As two empirical chapters of this project examine measles transmission, I will provide a brief review of how disease spreads, how social ties contribute to the creation of disease epidemics, and, finally, how social behavior shapes biological contagion more generally.

The first important way that biological contagion differs from social diffusion is that the adoption is a complex, unintentional biological process that does not depend on socially constructed thresholds. Certainly, the spread of disease is affected by susceptibility both at the individual and population levels. However, after accounting for specific factors that can affect individual susceptibility[24] and transmission properties of a disease,[25] the process of infection is so complex that it is often assumed to be random when modeling of disease spread (Easley and Kleinberg 2010). It should be noted that there are a few cases in which individuals intentionally attempt to acquire a disease. For example, parents may expose young children to chickenpox to minimize risks associated with contracting the disease as an adult.

The second important way that biological contagion differs is that the "search" process the disease conducts in spreading through the network disregards social characteristics of the contact. Diseases seek to infect anyone who has sufficient contact with a contagious individual. This process is referred to as broadcast search, and is the most efficient way for a disease to continue to propagate itself (Watts 2004). Disease spread usually occurs via simple contagion, although some previous research suggests that multiple contacts can influence some biological contagion outcomes (Dodds and Watts 2005).

Spatial clustering of non-medical vaccine exemptions creates pockets of individuals with decreased protection to infection. When a disease reaches these pockets of unvaccinated individuals, it can more easily broadcast itself through the local area. While some diseases require physical contact with bodily fluids (e.g. Ebola or HIV) to spread, highly infectious diseases that spread through airborne pathogens, such as the measles, pertussis, or flu, can infect individuals that come into contact with the air around an infected individual, even without

[24] Such as immunity acquired from vaccination or previous infection.

[25] Including sufficient contact to spread the infection, probability of infection given contact, etc.

directed interaction.[26] This magnifies the ability of these diseases to spread when unvaccinated individuals are clustered in close spatial proximity.

Disease Spread in Small-Worlds

As mentioned above, weak ties are structurally important for the spread of disease in social networks. Long-range weak ties between local clusters contribute to the "small-worlds" property exhibited by many large social networks. Social networks exhibit significant local clustering, due in part to triadic closure, as well as short average distances between distant individuals[27] (Watts and Strogatz 1998). Long-range weak ties extend outside of the interactions patterned by membership in social groups, such as family, work, school, or close friendships.

Weak ties connect otherwise disparate parts of the larger network and play important roles in reaching socially and geographically distant individuals (Travers and Milgram 1969). Infections in small worlds networks were observed to spread more quickly and at higher rates than those in traditional lattice or reaction-diffusion models (Kuperman and Abramson 2001; Moore and Newman 2000).[28] Epidemiological modeling on small worlds networks produced oscillating epidemics consistent with observed patterns of infection over time (Grassly and Fraser 2006). Large-scale simulations of disease spread often explicitly model long-range weak ties as travel or interaction in focal points outside the local neighborhood, and examine how they contribute to both introduction of a disease into populations from external sources and spread of the disease internally (Chao et al. 2010; Eubank et al. 2004; Fu et al. 2011; Germann et al. 2006).

[26] This effect is even more pernicious in the case of measles as it remains in the air and can be transmitted for a limited period even after an infected individual is no longer present (de Jong and Winkler 1964).

[27] Distance is defined as the shortest path between two nodes in a network.

[28] Lattice models have networks with regular, non-random structures. Reaction-diffusion models allow disease to spread outward in multiple directions from a central infection point.

Robustness of Networks to Disease Spread

The different structural characteristics of strong and weak ties also affect the robustness of networks to failure—the ability of processes on the network to continue operating after one or more the nodes has been removed or becomes inoperable. Many networks, including real world social networks, are characterized by power law degree distributions[29] (Watts 2004). These networks contain hubs, which have a disproportionately high number of ties compared to most nodes in the network. The presence of hubs in a network can affect its robustness to failures. Random "attacks" in these networks are much more likely to hit peripheral nodes with low degrees and have little effect on the overall functionality of the network; however, many "attacks" are not random but target highly connected hubs and have serious implications for network functionality (Callaway et al. 2000; Watts 2004). Therefore, hubs in networks may increase robustness to failure in random attacks, but render the network less robust when attacks are targeted (Watts 2004).[30]

Spatial pockets of unvaccinated children may serve as hubs for disease spread in social networks. More specifically these pockets may act as epidemiological disease cores. Disease cores are areas of the network characterized by high interconnectivity (Bearman, Moody, and Stovel 2004) that can be very influential in sustaining disease transmission and creating outbreaks in a population (Hethcote, Yorke, and Nold 1982; St. John and Curran 1978; Yorke, Hethcote, and Nold 1978). While disease cores are typically applied to the study of sexually

[29] The degree of a node is its number of ties. A degree distribution just shows the degrees of all nodes in a network.

[30] Targeted attacks need not be malicious in nature; they may also occur due to increased probability for internal problems. An example: Mechanical problems, passenger incidents, or schedule delays at primary metro centers, such as 30th Street Station in Philadelphia, affect transportation more than these incidents at smaller metro stations that only serve one or two lines along the route, and are, therefore, more consequential to continued functioning of the network. However, 30th Street Station may also be more likely to experience these types of events as (1) there are just more trains, passengers, and lines running through that station than the others, increasing the underlying rate of opportunity for these problems, and (2) someone wishing to intentionally disrupt the metro system in Philadelphia may intentionally target 30th Street Station as it would create the most disadvantage in the network overall.

transmitted diseases rather than those spread through casual physical contact, such as the measles or pertussis, frequent interaction among unvaccinated children may play a similar role of sustaining disease transmission in an otherwise highly vaccinated population.

If spatial clusters of children with non-medical exemptions create disease cores that act as hubs in the transmission of disease in social networks, they could have two contradictory effects on epidemics. Most schools in California do not have high rates of unvaccinated children,[31] and so there are a limited number of local areas that function as disease cores. On one hand, if a vaccine-preventable disease is introduced into the population randomly, it may be unlikely that it occurs in a pocket with high exemption rates. Outside the spatial clusters of exemptions, the disease will encounter resistance to propagation from local herd immunity due to high levels of vaccination. On the other hand, if the disease is introduced into a pocket of unvaccinated children, or reaches a pocket of unvaccinated children early in the disease infection cycle, the disease may gain increased momentum. These scenarios may be comparable to random and targeted attacks in networks. In the first scenario, random introduction of the disease could potentially lead to fewer overall infections. In the second scenario, however, the clustering of exempted children could create much larger outbreaks of the disease facilitated by the lack of local herd immunity, increasing risk of infection for everyone in the community.

Social Behavior and Biological Contagion

Disease transmission is affected by more than just the structure of social networks; however, it is also shaped directly by social behaviors in the network. Vaccine scares lead to lower vaccination rates, which in turn increase opportunity for disease spread due to loss of herd immunity (Bauch and Galvani 2013). The whole-cell pertussis vaccine scare in the U.K. in the

[31] This is discussed in greater detail in Chapter 3.

1970s resulted in increased pertussis outbreaks; the same pattern may also be emerging with the scare surrounding the discredited MMR-autism link and increasing rates of measles (Bauch and Bhattacharyya 2012). The cyclical pattern between protective behavior and disease outbreak is also evident in HIV transmission. The AIDS epidemic initially curtailed risky sexual behavior in the gay community; however, the development and diffusion of highly effective anti-viral drugs was followed by declines in perceptions of risk associated with unprotected sex (Crepaz, Hart, and Marks 2004). This resulted in the resurgence of risky sexual behavior in some communities (Ferguson 2007). At the community level, the prevalence of vaccination, practice of risky behaviors, or adoption of other preventative measures, such as covering one's mouth when coughing, can all be influenced by social norms (Bauch and Galvani 2013).

Patterns in social interaction also affect disease transmission throughout the population. Contact between individuals does not occur randomly; rather individuals mix assortively based on many different characteristics, including age, racial/ethnic background, or tendency to form connections with like others (Newman 2003). Sexual partners are selected non-randomly, contributing significantly to transmission patterns of sexually transmitted infections, including HIV/AIDS (Klovdahl 1985; Laumann et al. 1989) and gonorrhea (Yorke et al. 1978). Mapping overall patterns of interaction in networks, including social norms that organize dating behavior in schools, can be particularly important for understanding risk of sexually transmitted infections that extend beyond individual-level characteristics, such as number of sexual partners (Bearman et al. 2004). Friendship networks influence not only probability of contact with particular individuals, but also the practice of protective behaviors against infection during those interactions (Youm and Laumann 2002). Contact behavior in social networks is crucial to

understanding population-level transmission patterns and risk of disease outbreak (Berkman et al. 2000; Ferguson 2007).

Efforts to contain in-process epidemics also depend on social behaviors. Compliance with mandated outbreak control measures, such as booster vaccination and quarantines, affect the ability to contain epidemics (Cava et al. 2005; DiGiovanni et al. 2004). Just as important as mandated control measures are the voluntary behavior changes made by individuals based on perceptions of disease risk amidst outbreaks (Ferguson 2007; Funk et al. 2010). Awareness of information regarding an epidemic can influence individuals to either modify contact patterns or seek treatment earlier to prevent risk of subsequent infections (Kiss et al. 2010). Information diffusion can be particularly effective when both the epidemic and spread of information occur on overlapping social networks (Funk et al. 2009). The myriad of ways in which individual behavior and biological contagion interact before, during, and following disease outbreaks create feedback that fundamentally alter both social behavior and disease transmission (Funk et al. 2010).

Conclusion

Spatial clustering of non-medical vaccine exemptions and its consequences are located at the intersection social behavior and biological contagion. The goal of this project is to connect previous findings on how parents make vaccine decisions to broader patterns in locations of children with these exemptions. Certainly, there are many factors that influence vaccine decisions. The micro-level interactions that affect how parents weigh and justify these decisions are out of the scope of this project. I also do not discuss the influence of the media, political orientations, or larger trends in health policy in shaping these decisions, although they matter

too. My primary intention here is to highlight how social processes and local contexts can create clustering in vaccine refusals, which many parents perceive as individual decisions, and how these spatial clusters can alter patterns of disease spread.

Chapter 3 investigates how residential sorting contributes to spatial clusters of children with non-medical exemptions in California. The discussion of parental decision-making presented here is extended into formal hypotheses to test associations between PBE rates and factors that should affect perceived costs and benefits of vaccines in the local area. I then investigate the extent to which spatial clusters across schools can be explained by selection of parents into particular schools based on SES and other neighborhood characteristics.

Chapter 4 continues the examination of clustering of PBEs across schools but shifts focus to effects of spatially dependent social processes. Although residential sorting and selection contribute to homophily (Gimpel and Hui 2015; Mouw and Entwisle 2006; Schelling 1978), local contexts, social interaction, and endogenous processes, such as diffusion, can produce outcomes that are not consistent across individuals or communities that share similar characteristics (Sampson, Morenoff, and Gannon-Rowley 2002). PBE rates may be influenced not only by the characteristics of a school and its surrounding area, but also by others nearby.

Chapter 5 turns attention to the consequences of spatial clusters of children with PBEs. Specifically, I examine how clustering of PBEs affects the focal points of social interaction where measles transmission is likely to occur. Although the small-worlds model emphasizes the importance of weak ties in disease transmission, strong ties may contribute substantially to disease spread when a disease is non-endemic and susceptible children are spatially clustered.

Chapter 6 then investigates how spatial clustering of exemptions affects the robustness of the larger social network to disease spread. In particular, I examine the extent to which the

spatial clustering of exemptions, rather than the overall number, renders the network less robust to disease outbreaks. If spatial clusters of unvaccinated children serve as hubs for disease outbreaks, the protective effects of herd immunity could be comprised, even if most parents continue to vaccinate.

Chapter 3: Clustering of Personal Belief Exemptions across Kindergartens in California, 1998-2014

Abstract

The shifting socio-demographic profile of unvaccinated children requires new research to understand why these parents refuse vaccines. Residential sorting into neighborhoods based on factors associated with increased PBE rates in schools could generate larger clusters of these exemptions across schools. However, use of spatial scan statistics on a longitudinal dataset of PBEs in California from 1998-2014 demonstrates that this mechanism cannot fully explain the broader spatial patterns of PBEs. Significant spatial pockets of PBEs remain even after accounting for the effects of factors that increase the likelihood of PBEs in schools, including alternative health practitioners and prevalence of autism. Racial/ethnic composition in the local area around the school exerts the greatest influence on clustering of PBEs across schools, and a series of indirect tests show that this effect is likely operating independently of socio-economic status. While selection into private and charter schools has a strong influence on clustering of PBEs in these locations, additional social processes must be investigated to understand how larger spatial pockets of children with vaccine exemptions are formed.

Chapter Introduction

The development and routinization of childhood vaccination have played a significant role in declining early-life mortality, both in the U.S. and around the world (Plotkin and Plotkin 2012). Significant public health attention has been focused on identifying factors associated with children who are not up-to-date on vaccinations in an effort to increase vaccine uptake. The reversal in the association between socio-demographic characteristics and lack of vaccination due to vaccine refusals (Smith et al. 2004) requires new perspectives on the social processes underlying these decisions.

Rather than lacking access to healthcare or being unaware of physician and public health recommendations, parents weigh perceived costs and benefits before deciding not to vaccinate (Reich 2014, 2014; Senier 2008). Spatial distributions of factors associated with how parents evaluate costs and benefits may help explain the geographical clustering observed in non-medical exemptions to school vaccine requirements. Residential sorting, or the selection of parents into particular neighborhoods, can be generated by multiple factors, including socio-economic status (SES), racial/ethnic composition, or other neighborhood-level factors.

Previous research on non-medical exemptions has primarily focused on identifying factors related to higher rates of these exemptions in schools. The focus of this analysis, however, is to understand how high rates of children with vaccine exemptions aggregate across schools. Does residential sorting of parents based on characteristics correlated with non-medical exemptions at the school level explain larger spatial clusters of these exemptions? While clustering of unvaccinated children within schools may increase very local incidence of disease, clustering across schools with high non-medical vaccine exemption rates may have serious implications for the risk of disease outbreaks that span larger geographical areas.

Multiple types of analyses are used to separate within and across school effects on PBE rates in California kindergartens from 1998-2014. First, multi-level regression models are used to examine school-level correlates, including presence of physicians, prevalence of alternative health practitioners, local incidence of autism, socio-economic conditions, and racial composition of the local area around a school. Second, spatial scan statistics are used to investigate the ability of school-level associations to explain the clustering of high rates of PBEs across schools. Third, a series of indirect tests will be used to further unpack the primary finding that racial/ethnic composition—particularly percent non-Hispanic white—of children located in the local area around the school has the greatest contribution to clustering of PBEs across schools. While residential sorting may have some effect on the broader patterns of PBEs across California schools during this period, the significant spatial clustering left unexplained by socio-economic and neighborhood characteristics suggests that other spatially dependent processes, such as social diffusion through networks, are likely at work.

Personal Belief Exemptions

Prior to 2014, California was one of the most lenient states with regard to school vaccine policy in the U.S. (Omer et al. 2006; Yang, Barraza, et al. 2015; Yang and Silverman 2015). Parents needed only to sign a statement refusing some or all of the required vaccinations due to personal beliefs on the school immunization form. As shown in Figure 1, average rates of PBEs increased across non-charter public, private, and charter[32] kindergartens[33] from the early 1990s through 2014.

[32] In the U.S., charter schools are state funded, but operate independently of the local public school system. They provide additional schooling options for parents, and often emphasize alternative pedagogies or academic focuses.

Beginning in 2014, California vaccine policy was amended to require a physician's signature with the PBE request stating that the parents had been made aware of the risks of refusing childhood vaccinations. As shown in Figure 3.1, this change did result in a modest reduction of PBEs. In 2014, the statewide exemption rate for children entering kindergarten was 2.54%, still more than double the <1% observed in 1992. This reduction could be partially attributed to parents who were previously filing PBEs for the sake of convenience due to misplaced or slightly incomplete vaccination records. Requiring a visit to a physician may have encouraged parents not holding strong beliefs against vaccination to either request copies of records or complete immunization requirements for their child. The spatial patterns of PBEs in 2014 will be of primary interest to this analysis as these parents would have continued to refuse school-mandated immunizations for their child, even after consulting with a medical professional.

As Figure 3.1 demonstrates, overall vaccination coverage across California kindergartens remains high, yet the public, private, and charter schools within the top 5% of the PBE distributions have approximately 10%, 20%, and 45% of students exempted, respectively. Vaccine beliefs are likely not fixed; as parents encounter new information and opinions about vaccination and vaccine-preventable disease, they may revise their stance. In particular, parents may be influenced by behaviors and information within the media or local social contexts (Fu et al. 2011). Behaviors of other parents may be themselves taken to confer information about the prudence of vaccination, even if the issue itself is not formally discussed (Banerjee 1992). Alternatively, local media coverage of vaccine safety concerns or outbreaks of vaccine preventable disease may make these issues more salient for parents, influencing their vaccination

[33] In California, proof of immunization is required for children entering licensed childcare centers, kindergarten, and the 7th grade. This research will focus on PBEs filed when children enter kindergarten, although some attention will also be given to where exemptions have been observed in childcare centers from 2010-2014.

decisions (Bauch and Bhattacharyya 2012; California Department of Public Health, Immunization Branch 2016a; Healy and Pickering 2011).

Costs and Benefits of Vaccination

(a) Healthcare

First, as mentioned in Chapter 1, children with non-medical exemptions tend to come from relatively more advantaged socio-demographic backgrounds (Smith et al. 2004). This contradicts previous findings showing an association between under-vaccination and relatively disadvantaged social positions, particularly lack of access to healthcare (Allred, Wooten, and Kong 2007). In principle, every child in the U.S. should have access to free vaccination, either through health insurance or federally funded programs (Centers for Disease Control and Prevention 2012c). Providing low-income families with access to government healthcare programs increases use of preventative care services, including immunization (Kempe et al. 2000; Kim et al. 2007; Santoli et al. 1999). Previous research on PBEs in California kindergartens did not show a significant association with health insurance coverage (Walker and Rea 2016).

Yet fewer physicians in the local neighborhood could have contributed to PBEs, particularly before they required a physician's signature. Even if the costs associated with the vaccines themselves should not be a barrier to immunization, visits to physicians may incur other inconveniences, including time commitments or access to transportation. Parents may have found it easier to file PBEs than visit physicians to obtain copies of lost immunization records or complete a few remaining vaccines (Rota et al. 2001). In part, lack of physicians locally may contribute to the higher rates of PBEs observed in rural areas (Richards et al. 2013). If fewer

local physicians contributed to the relative convenience of filing an exemption, PBEs should be more common in schools located in areas with few or no physicians.

Hypothesis 1: Fewer physicians in the local area increases the school PBE rate.[34]

(b) Socio-economic status

Vaccine refusals tend to be associated with children from relatively higher SES backgrounds; however, previous research on under-immunization in California has shown variation in these findings. A review of electronic health records of children born between 2000 and 2011 in Northern California showed that higher incomes were associated with higher immunization coverage, while higher levels of education were associated with lower immunization coverage in neighborhoods (Lieu et al. 2015). This same pattern of associations was shown in a statewide examination of PBEs between 1994 and 2009 (Richards et al. 2013). This contrasts with findings showing that higher community levels of education and income were associated with higher rates of PBEs between 2005 and 2010 (Atwell et al. 2013). Given the focus of this research on a more recent period during which the state experienced its highest PBE rates,[35] with particular attention paid to 2014 following the policy change requiring a physician's signature to file a PBE, I expect PBEs to be correlated at the school level with both higher levels of education and affluence. I use mother's level of education in particular as

[34] For these analyses, all covariates are calculated for the same vicinity around a school (discussed in greater detail below). Some covariates may have more local effects than others. As I have no individual-level data on where children in schools seek medical care or socio-demographics characteristics of children with PBEs specifically, I make no assumptions about the relative size of the local areas in which these covariates should exert effects. The following chapter will specifically address whether covariate values in neighboring schools matter for a school's own PBE rate.

[35] The highest statewide PBE rates were observed in 2010-2013, as shown in Figure 3.1.

mothers are often the parents most responsible for vaccine decisions (Carpiano 2009; Reich 2014; Senier 2008).[36]

> Hypothesis 2a: Higher average levels of maternal education in the local area increases school-level PBE rates.

Hypothesis 2b: Schools in areas with higher mean property values have higher PBE rates. Previous research on PBEs in California consistently indicates that PBEs were more likely to be found in more rural areas (Atwell et al. 2013; Richards et al. 2013).

Hypothesis 2c: Schools in areas of lower population densities have higher PBE rates. Finally, lower percentages of racial or ethnic minorities tends to be associated with higher SES and higher incidence of PBEs in California (Atwell et al. 2013; Carrel and Bitterman 2015; Richards et al. 2013). While this finding was not consistent for overall under-immunization in Northern California (Lieu et al. 2015) nor non-medical exemptions in Michigan (Omer et al. 2008), it is consistent with clustering of non-medical exemptions in both Arizona and Arkansas (Birnbaum et al. 2013; Safi et al. 2012).

> Hypothesis 3: Schools with higher percentages of non-Hispanic white children in the local area have higher PBE rates.

The specific mechanisms underlying the trend in vaccine refusals among white, college-educated, and relatively affluent parents remain to be explained. It could be that these parents are not overall more likely to be vaccine skeptics, just that they feel more personally responsible for weighing costs and benefits of vaccines and making individually informed decisions for their child's health (Reich 2016). Material highlighting vaccine safety concerns found on the Internet may contribute to this SES association. Younger, more highly educated parents are more likely to use the Internet as a source of vaccine information than their counterparts (Jones et al. 2012).

[36] Mothers are also the parents held most responsible for children's health generally in the U.S.

While there are also ample online resources presenting evidence that vaccines are safe, stories promoting more novel and/or surprising vaccine safety concerns may generate more attention (Healy and Pickering 2011). In particular, parents who do not consider healthcare providers as reliable sources of vaccine information may seek out alternative vaccine materials online (Jones et al. 2012). Educated parents with resources to invest in debates over vaccine safety may be more compelled to act on their distrust of the medical profession (Mechanic 1996) and refuse vaccines for their child (Gaudino and Robison 2012; Jones et al. 2012; Sobo 2015). This would be consistent with the finding that non-white parents, those with lower income, and those with lower educational attainment report having more vaccine safety concerns, but still vaccinate their children (Freed et al. 2010; Shui et al. 2006).[37]

(c) Vaccine Skepticism

The recent wave of vaccine safety concerns began after Wakefield et al. made the now-discredited claim that the MMR vaccine causes autism in 1998. Increasing numbers of autism diagnoses without straightforward medical explanation (review in Eyal et al. 2010; King and Bearman 2009; Liu, King, and Bearman 2010) has contributed to the popularity of the vaccine-autism link (Bearman 2009). Despite many studies demonstrating that vaccines do not cause autism (review in Taylor, Swerdfeger, and Eslick 2014), 25% of parents in a 2009 survey strongly agreed with the statement "some vaccines cause autism in healthy children" (Freed et al. 2010). The hypotheses on how vaccination may be related to autism have constantly shifted as they have been refuted by medical studies and epidemiological evidence (Plotkin, Gerber, and Offit 2009). Yet, suspicion of the for-profit pharmaceutical industry, lack of trust in medical

[37] It could also be that parents of different racial/ethnic backgrounds have different concerns related to childhood health (Pew Research Center 2015) or different perceptions of the prevalence, risk, or seriousness of vaccine-preventable infectious disease (Walker and Rea 2016). Lower perceived disease risk has been shown to be associated with increased likelihood of vaccine exemptions (Jones et al. 2012; Salmon, Moulton, et al. 2005).

professionals, prevalence of misinformation on the Internet, and sensationalized stories in the media claiming adverse illnesses resulting from vaccines has continued to fuel vaccine hesitancy, its (supposed) link to autism, and the popularity of alternative vaccine schedules (Dempsey et al. 2011; Offit and Moser 2009).[38] Although many different organized factions are present in the promotion of anti-vaccine beliefs, the purported MMR-autism link made by Wakefield and his colleagues has been cited as perhaps providing the biggest boost to the anti-vaccine movement in recent years (Daley and Glanz 2011). Prevalence of children diagnosed with autism in the local area may contribute to awareness of the developmental disorder and alleged link to vaccines, increasing the likelihood of vaccine refusals.

> Hypothesis 4a: Increases in the number of children diagnosed with autism in the local area increases school-level rates of PBEs.

Alternatively, autism advocacy organizations in the local area may also increase awareness of the autism-vaccine controversy.

> Hypothesis 4b: Presence of autism advocacy organizations in the county in which a school is located increases school-level rates of PBEs.

Another source of vaccine skepticism may come from alternative health practitioners. For example, a vocal minority of chiropractors continue to be skeptical of the necessity and effectiveness of vaccines, choosing instead to believe disease is caused by misalignments within the body (Campbell, Busse, and Injeyan 2000; Colley and Haas 1994). Previous studies of non-medical vaccine exemptions have shown that parents of exempted children are more likely to put confidence in alternative health practitioners than parents without exempted children (Benin et al. 2006; Ernst 2001; Lehrke et al. 2001; Salmon, Moulton, et al. 2005), report seeking

[38] In addition, during a televised debate in 2015, multiple Republican presidential candidates either explicitly endorsed the disputed link between vaccines and autism or refused to strongly refute it (Miller 2015).

chiropractic care for their children (Gaudino and Robison 2012), or live in Primary Care Service Areas with increased rates of naturopaths and midwives (Walker and Rea 2016).

> Hypothesis 5: Higher prevalence of alternative healthcare practitioners, particularly chiropractors and acupuncturists, in the local area is associated with increased school-level PBE rates.

Outbreaks of vaccine-preventable disease could have the opposite effect, increasing the perceived benefit of vaccination. Low perceived risk of infection of vaccine-preventable diseases or their consequences has been cited as an important component of vaccine hesitancy and seeking vaccine exemptions (Offit and Moser 2009; Ropeik 2013; Salmon, Moulton, et al. 2005). In a 2004 survey, a majority (72%) of parents who reported having serious vaccine safety concerns yet still had their child vaccinated attributed their decision to the risk of their child contracting a disease if not vaccinated (Shui et al. 2006). Historical data demonstrate that vaccination rates increase following disease outbreaks (Bauch and Bhattacharyya 2012). Additionally, an online experiment showed that exposure to information on consequences of vaccine-preventable childhood diseases can lead to increases in pro-vaccine attitudes (Horne et al. 2015).[39] Here, I examine pertussis (whooping cough) rates in particular as it remains relatively common compared to other vaccine-preventable diseases that predominantly affect young children. As I am specifically interested in variation of PBEs across space, pertussis outbreaks may be likely to have a more local effect on awareness of vaccine-preventable disease than less common, but more newsworthy outbreaks of diseases such as the measles.[40]

> Hypothesis 6: Local incidence of pertussis increases the perceived level of risk of an infectious disease in the local area and decrease PBE rates in schools.

[39] Increase in pro-vaccine attitudes was demonstrated in comparison not only to the control group but also a condition presenting information from the Centers for Disease Control and Prevention (CDC) refuting the vaccine-autism link.

[40] As discussed in Chapter 1, serious outbreaks of the measles garner more public attention and may have a greater effect on vaccine exemptions for the state overall rather than just in the local area where an outbreak occurs.

Clustering of PBEs across Schools

In addition to clustering at the school-level, parental decisions to not vaccinate their child may create clustering of PBEs across schools as well. As shown in Figure 3.2A, this is indeed the case in California: the shaded regions on the map indicate pockets of schools with higher relative risks of PBEs than the state as a whole.[41] It is important to understand how this clustering is generated as these areas may be particularly vulnerable to disease outbreaks.

The homophily, or similarity, of vaccination status across geographical space could have been formed by several processes. Given understandings of school-level correlates of PBEs, however, the most straightforward explanation is residential sorting. Residential sorting is the process of households selectively residing in particular areas due to some desired neighborhood characteristic or context.[42] Parents need not choose their residential neighborhoods based directly on the vaccination status of other children to create these clusters. Rather, it is likely that parents are choosing neighborhoods, and, by extension, school districts, based on factors correlated with vaccine exemptions. In particular, school-level associations of SES and exemptions may be important as socio-demographic factors related to racial/ethnic background, education, and social class have been shown to be strong predictors of residential sorting (Bayer et al. 2007; Massey 1990). In this case, it would be expected that the factors associated with PBEs at the school-level discussed above help explain the significant clustering of PBEs across schools as well.

> Hypothesis 7: Accounting for factors associated with higher PBE rates at the school level, and particularly socio-demographic characteristics, will help explain clustering of high PBE rates across schools.

[41] This map was generated using spatial scan analysis, discussed in more detail in the methods section below.

[42] Residential sorting typically assumes selection, albeit however constrained, on the part of individuals to move to a particular location; however, there are certainly examples of forced relocation that also contribute to distributions of characteristics across neighborhoods (e.g. Desmond 2012).

At the school level, higher rates of non-medical exemptions have been shown in charter and private schools than in non-charter public schools (Birnbaum et al. 2013; Brennan et al. 2016; Carrel and Bitterman 2015; Sobo 2015; Yang, Delamater, et al. 2015). Thus, even after accounting for SES and neighborhood characteristics, higher PBE rates should be observed in private and charter schools than non-charter public schools due to the sorting of children by parents into these types of schools. Parents may select into these types of schools due to alternative pedagogical orientations from the more standardized local public schools. Enrollment in private and charter schools in California is based on parental decisions rather than residence in a particular school district. Educated parents who choose to enroll their children in these educational alternatives to the traditional public school system may also perceive an important role of self-education regarding child health (Sobo 2015). This may prompt them to investigate and share alternative orientations toward health practice, including distrust of the medical industry or increased interest in alternative medicine.

> Hypothesis 8: Even after accounting for SES and other neighborhood characteristics, private and charter schools still have higher PBE rates than non-charter public schools.

Data and Methods

To examine clustering first within and then across schools, analyses will be conducted in two stages. First, multi-level negative binomial regression models will be used to estimate school-level correlations. Then, spatial scan statistics will be used to identify spatial clustering across schools and test associations of school-level variables. The outcome is counts of PBEs per school by year. When possible, covariates are measured in the immediate vicinity around the school. This is defined as a 500-child radius drawn around the school (or childcare center), and represents its “catchment” area (Liu and Bearman 2015). The 500-child radius was determined

based on population interpolation using Census estimates. This approach was used to establish a comparable local geographical unit around a school across areas of the state with very different population densities (e.g. the radius of a school neighborhood is much smaller in urban Los Angeles than in the rural counties along the northern Oregon border). County is used as a tertiary level of geography for two measures, pertussis incidence and autism advocacy organizations, due to data availability. All covariates used in the analysis were lagged 6 and 3 years for kindergartens and childcare centers, respectively. These lags are appropriate as the timing of many vaccine decisions in accordance with the schedule recommended by the CDC occur in the first 0-15 months of life. Lagging the independent covariates by 5 years does not substantially change the results (Table A3.1 in Appendix). As PBEs are filed upon school entry and represent the final decision point for exemptions, a model without the independent covariates lagged was also estimated; again, the results remain substantially unchanged (Table A3.2 in Appendix).

Data

PBEs. Data on Personal Belief Exemptions from 1998 to 2014 for kindergartens in public and private schools with student enrollments greater than 10 is available from the California Department of Public Health (CDPH). PBE data for licensed childcare centers with more than 10 students were available for 2010-2014. Students in California are required to provide proof of meeting vaccination requirements when enrolling in licensed childcare centers, kindergarten, and 7th grade. The PBE data were matched to public and private school enrollment records available from the California Department of Education (CDE) for information on school characteristics.

SES measures. SES is measured by average education and property values in the 500-kid radius around the school. Education was measured as the highest year of schooling completed

by the mother at time of birth, and averaged across the 500-child school radius. Information on maternal education was obtained from the California Birth Statistical Master File (BSMF) for 1992 to 2007.[43] Data on median property values and population density were interpolated for the full analysis period using data from the 1990 and 2000 U.S. Censuses at the block group level, averaged across the school's 500-child radius, and logged due to skew. Property values are used as a measure of SES in the local area due to their relationship to property taxes, which can reflect the level of wealth in an area and partially fund K-12 education in California.

Racial/Ethnic Background. Racial composition is represented as the percentage non-Hispanic white among children in the 500-child radius around the school, and was calculated from the BSMF. Public school records from the CDE provide enrollment breakdowns by race and ethnicity. Segregation measures, specifically isolation indices, were calculated at the school district level. In this case, the isolation index represents the extent to which non-Hispanic white students are exposed only to one another in schools within the district. Due to the size of the Los Angeles Unified School District, schools were separated by the eight school boards within the district, and isolation indices were calculated at the school board level.

Physicians. Presence of physicians was measured as counts of general, family, and pediatric physicians in the 500-child radius around the school. Addresses of physicians were collected and geo-coded from the yearly American Medical Association Directory of Physicians.

Autism. Incidences of autism diagnoses within the 500-child school radius were taken from the California Department of Developmental Services (DDS) data from 1992 to 2011. The DDS provides services to a large majority of individuals with a full syndrome autism disorder in

[43] Maternal education was preferred to a measure of paternal education for two reasons. First, mothers are often most responsible for children's vaccine decisions (Benin et al. 2006; Senier 2008). Second, mother's years of education are less likely to be missing in the BSMF data. A robustness check using father's years of education on a restricted subset of the data did not show meaningful differences in covariate effects.

California. Further details of the DDS data are described elsewhere (Liu et al. 2010). Knowing a child with an autism diagnosis may have a more local effect than the other variables in the area around a school due to reasonable range of neighborhood social interaction for children. To examine broader influence of awareness of the autism-vaccine link, the count of autism advocacy organizations was collected from records of tax-exempt organizations kept by the Internal Revenue Service and recorded at the county level.

Alternative Health Practitioners. Counts of alternative health practitioners, specifically chiropractors and acupuncturists, in the 500-child radius around the school were measured using licensing records from the California Department of Consumer Affairs. To ensure these variables were not simply picking up proximity to local business areas, count of veterinarians in the school neighborhood were also calculated, as well as a set of random business addresses with the same prevalence of chiropractors and acupuncturists.

Pertussis. Reported numbers of pertussis cases in California for 2000-2010 were obtained from the Immunization Branch of the CDPH. De-identified data on incidence were aggregated at the county level, and used in the analysis as rate per 1000 population.

Methods

School-Level Correlates. Effects of the independent covariates on counts of PBEs within schools are estimated using negative binomial regression with random effects clustering at the school level. Expected counts of PBEs (u_{ij}) are calculated as:

$$\log(u_{ij}) = \log(t_{ij}) + \alpha + \beta x_{ij} + \gamma z_j + \upsilon_{ij}$$

Here, schools are indexed by i and year by j, $\log(t_{ij})$ is the logged number of enrolled students (exposure), α is the constant, x_{ij} is a vector of independent covariates measured by

school and year while β is estimated covariate effects, z is a set of indicator variables for year with γ estimated effects, and υ_{ij} is the error term, composed of $\nu_i \sim N(0,\sigma_\nu^2)$ and $\varepsilon_{ij} \sim N(0,\sigma^2)$. Negative binomial models are estimated due to over-dispersion in the PBE data. Three-level mixed-effects Poisson models with random effects at the school and county levels are used when county-level predictors (pertussis and autism advocacy organizations) are included in the model.[44]

The models presented in this chapter do not incorporate spatial autocorrelation in PBE rates. This is a concern because schools located in close geographical proximity may have correlated PBE rates. If autocorrelation is not taken into account, regression assumptions of error independence may be violated and covariate effects may be inflated. To address this concern spatial lag models were estimated in R using standardized inverse weighted distance between schools in 2014. In addition to independent covariate effects, spatial lag models also estimate a spatial correlation term (ρ) for the dependent variable. While the spatial dependency parameter was significant in the model, the covariate effects were not significantly different (spatial models will be discussed in much greater detail in Chapter 4). I present the results of the negative binomial regression model here as the residual spatial clustering of PBE rates across schools is of particular interest to the second part of the analysis, and will be examined in depth using spatial scan statistics.

Clustering across schools. Statistically significant spatial clustering of high PBE rates across public schools in 2014 was identified using the Kulldorff Spatial Scan Statistic, implemented in SaTScan (Kulldorff 1999). Counts of PBEs in schools are assumed to be distributed as Poisson random variables. Maximum likelihood estimation is used to identify

[44] Using an ordinary least squares model with logged PBE rate as the dependent variable does not substantively change the findings reported in this chapter. Results shown in Table A3.3 in Appendix.

circular geographical areas (of varying sizes, see below) that encompass schools with increased likelihoods of PBEs compared to the statewide rate in California in 2014. Likelihood ratios for the circular clusters are calculated by comparing observed numbers of PBEs in schools with expected numbers of PBEs based on kindergarten enrollments (assuming the overall statewide PBE rate). Statistical significance is assessed through 9999 Monte Carlo randomizations. Only statically significant (using α=.05) clusters of increased relative risk of PBEs compared to the statewide rate are included in the analyses here. Spatial scan statistics have been used previously to examine both the clustering of non-medical vaccine exemptions (Atwell et al. 2013; Omer et al. 2008) and other health outcomes, such as autism (Mazumdar et al. 2010).

Spatial clusters of increased rates of PBEs across schools were first analyzed without adjusting for any covariates. Figure 3.2A shows the pattern of spatial clustering of PBEs among public kindergartens unadjusted for the spatial distributions of the covariates. Spatial clusters were then sequentially adjusted individually and finally jointly for covariates, including: demographic characteristics (logged median property values, logged population density, mother's highest level of education, and percent non-Hispanic white), count of physicians, incidence of autism (counts of children with autism diagnoses), and prevalence of alternative health practitioners (counts of chiropractors and acupuncturists). The shaded regions of the maps show geographical areas with schools that have statistically significantly higher relative risk of PBEs than the state overall. If distributions of covariates are responsible for these broader patterns of spatial clustering in PBEs across schools, the shaded circles should disappear (i.e. the increased relative risk of PBE should be reduced) once the covariate is taken into account. Not every school within a cluster necessarily has statistically significantly higher PBE rates; the goal is to identify geographical areas with high rates of unvaccinated children. Being located within a

cluster increases the exposure of all children, vaccinated or not, to unvaccinated children, which can have serious implications for risk of disease spread (Buttenheim et al. 2012).

As shown in the results below, racial composition in the 500-child radius around the school has the largest effect on clustering of PBE rates across schools. To understand why this might be the case, particularly compared to the limited findings for other SES indicators, a series of indirect tests are estimated to examine possible explanations for this result. First, the effect of neighborhood racial composition, measured as percent non-Hispanic white, is estimated among a homogenous population with regard to SES—Head Start participants. Head Start is a government-funded program that provides education, nutrition and health services to young children from low-income families. In general, families must earn less than 100% of the federal poverty level to be eligible. If neighborhood racial composition is merely picking up the effect of another unmeasured effect of SES, there should be no additional effect of neighborhood racial composition in this population.

Second, Moran I's spatial autocorrelation statistics was calculated for census block group-level racial composition and maternal education across California. If residential sorting explains larger spatial clustering of PBEs across schools, it could be that some covariates have more uneven distributions across the state, producing the observed uneven distribution of PBEs. Inverse weighted distance was calculated between the centroids of each Census block group and statewide autocorrelation was estimated.

Third, the correlation of PBE rates across school district boundaries is examined to investigate whether PBE rates across schools can be attributed to school-district specific factors. If PBE rates in childcare centers and private schools located geographically near public schools with statistically significantly higher PBE rates (compared to the state overall) also have

increased PBE rates, this suggests that school-district specific factors are not increasing rates only in schools located within the administrative boundary. This logic reflects tests for proximity effects used in examining social influence in the spread of autism diagnoses (Liu et al. 2010).

Fourth, the effect of racial segregation on PBE rates is used to further investigate how the concentration of racial composition the local area around a school may influence rates independently of SES or overall neighborhood racial composition. If non-Hispanic white parents are the most likely to act on concerns over vaccine safety, children living in more segregated areas may have higher PBE rates even after controlling for the effects of other socio-demographic variables. This may also suggest high PBE rates are not observed due to a selection process alone but through reinforcement of these behaviors by similar parents in the local community.

Results

School-level Correlates. Table 3.1 shows associations of covariates with PBEs at the school-level. Each additional physician in the 500-child radius around the school increases PBE rates by a factor of 1.004, net of the other variables in the model. Lack of convenient access to physicians should result in a negative association if this was driving PBEs rates. This is the opposite relationship predicted by Hypothesis 1—lack of physicians in the local area does not appear to explain high PBE rates in schools.

Rather than lack of access to physicians, it could be that selective access to physicians contributes to discrepancies in PBE rates. Physicians themselves could vary in their attitudes toward vaccination or activeness in encouraging skeptical parents to vaccinate their children (Freed et al. 2004; Walker and Rea 2016). Consistent with these results, when physicians are

divided by specialty, count of pediatricians in the school neighborhood decreased PBE rates, while counts of family and general practitioners increased PBE rates, controlling for other socio-demographic and neighborhood characteristics (Table A3.4 in Appendix). The association between PBEs and physicians then may depend on the type of health practitioner, and the counseling and options that they provide with regards to childhood vaccination (Freed et al. 2004).[45]

The socio-demographic variables mostly have the hypothesized effects. A one year increase in average mother's educational attainment in the school neighborhood is associated with a 20% in expected number of PBEs, controlling for other socio-demographic and neighborhood characteristics. Property values initially have a positive effect on PBE rates, although this relationship becomes insignificant once other socio-demographic variables are accounted for.[46] Consistent with previous findings, higher population densities in a school neighborhood are associated with a reduction in the number of PBEs. Finally, a 10% increase in percent non-Hispanic white in a school neighborhood is associated with a 22% increase in expected number of PBEs, net of other model covariates. These findings suggest that PBEs in California from 1998-2014 were more likely to be located in schools in neighborhoods with higher education levels (supports Hypothesis 2a), lower population densities (supports

[45] The effect for count of pediatricians in the school neighborhood does not retain significance when northern California is excluded from the analysis (this is not true of the other covariates of interest discussed here). For this analysis, the correlation with PBEs at the school level could be, in part, a product of lack of pediatricians in school neighborhoods in less populated areas (e.g. Northern California). This may contribute to the higher rates of PBEs observed in schools there, but also may be influenced by a lower likelihood for specialized practitioners to be in these areas than general or family practitioners.

[46] Controlling for percent renters does not affect this finding for property values, or substantially change the effects of other covariates included in the model, as shown in Table A3.5 in Appendix. The percent renters variable was constructed by averaging the percent of households renting in the Census block group across the 500-child radius around a school. Furthermore, Table A3.6 in Appendix shows that using logged household income instead of property values shows a negative association with PBEs in the full model. This is opposite the expected finding; net of other model covariates, increases in logged household income decrease PBE rates. As when controlling for percent renters, however, the effects of the other covariates in the model remain largely unchanged.

Hypothesis 2c), and higher percentage non-Hispanic white population (supports Hypothesis 3). Support was not found for Hypothesis 2b—after controlling for other SES and neighborhood characteristics, measures of affluence do not show a significant positive relationship with school-level PBE rates.

For the hypotheses on factors that might affect perceived costs and benefits of vaccination, the results were mixed. Counts of children with autism diagnoses in the school neighborhood had the expected positive effect on PBEs, although the effect was modest: an additional child in the school neighborhood diagnosed with autism increased expected PBE rate in the school by 0.8%, controlling for other factors. The presence of autism advocacy organizations in the county in which the school was located, however, did not have a significant relationship with school PBE rates, as shown in Table 3.2. Although these findings provide support for Hypothesis 4a stating that children with autism diagnoses in the local area around a school should increase PBE rates, the effects are modest. Hypothesis 4b, specifying that autism awareness organizations should have a broader effect on PBE rates, is not supported. This measure only records the presence of an advocacy organization though, not any particular outreach activities or approach to creating awareness. It could be that the organizations have worked to dispel the discredited link between vaccines and autism, or that this concern is more likely to spread in networks among parents than it is through general autism outreach.

Counts of alternative health practitioners were also positively associated with PBE rates in schools, although only the effect of chiropractors remains significant once the other covariates are included in the model. For each additional chiropractor in the local area around a school, the PBE rate is expected to increase by 2.7%, net of the other covariates in the model. This effect cannot be explained by the potentially confounding effect of proximity to business areas: a

variable created to measure proximity to the same number of random business addresses does not have statistically significant effects on PBEs (Table A3.7 in Appendix). This provides some evidence for Hypothesis 5 that parents who seek PBEs are more likely to live in school neighborhoods where alternative medicine practices are more common. Yet, this finding is far from straightforward; Table A3.7 in the Appendix shows that the count of veterinarians also has a significant, positive effect on PBEs. The association between alternative medicine and PBEs could also be spurious and instead picking up the effect(s) of another unmeasured neighborhood-level characteristic or process.

Finally, pertussis incidence at the county level does not appear to be significantly associated with school-level PBEs. While the covariate effect is in the direction predicted by Hypothesis 6, indicating that as pertussis cases (per 1000) increase, school PBE rates decrease, it is not statistically significant ($p=0.086$). The availability of this data at the school neighborhood level may have provided a more direct test of this relationship.

Clustering Across Schools. I now turn to the question of whether the school-level correlates discussed above provide explanatory power for clustering of high PBE rates across schools in California, as was predicted by Hypothesis 7. As discussed above, if a covariate is responsible for the clustering of PBEs across schools, the shaded clusters of high PBE rates shown on the maps in Figure 3.2 should significantly decrease or disappear after adjusting for the covariate. Figure 3.2A shows the unadjusted statistically significant clusters of PBEs across public kindergartens in 2014. Unadjusted PBE clusters are located in the rural northern region near the Oregon border, along the coast around San Francisco, Santa Cruz, Santa Barbara, Los Angeles, and the northern suburbs outside San Diego, and finally in the central inland areas.

At the school level, presence of physicians had a positive effect on PBEs. Adjusting for the positive effect of physicians has almost no impact on the spatial clusters of PBEs across schools (Figure 3.2B). On the other hand, controlling for logged population density largely explains away the cluster of high PBEs in the rural areas near the Oregon border (Figure 3.2C). Traditionally, clustering of unvaccinated children in rural areas may have been attributed to lack of healthcare resources, but the positive effect of physician presence in the local area around a school found in the school-level models suggests this is not the mechanism here. Residing in a rural area itself is unlikely to influence vaccination decisions; the effect of population density on clustering of high PBE rates across schools here is likely picking up the effect of another mechanism yet to be explained.

Somewhat surprisingly, the strong effect of mother's education at the school level does not seem to contribute explanatory power to clustering of PBE rates across schools. Controlling for average years of mother's education in the area around the school has very little effect on reducing spatial clustering of PBEs across schools (Figure 3.2D). Likewise, distributions of property values across schools do not appear to have significant effects of broader clustering of PBEs either (Figure 3.2E); adjusting for property values produces little effect beyond modest reductions in some of the clusters in urban areas along the coast (Figure 3.2B). Likewise, the distributions of neither counts of autism diagnoses (Figure 3.2F) nor alternative health practitioners (Figure 3.2G) have significant effects on reducing the clustering of PBEs across schools.

As shown in Figure 3.2H, however, percent non-Hispanic white appears to have the most significant effect of any of the covariates in reducing the size and prevalence of spatial clusters of PBEs across schools in both the rural northern and urban coastal areas. While some significant

clusters still remain to be explained, this reduction may indicate that racial composition is associated with the formation of clusters of PBEs across schools, and cannot be attributed to unmeasured characteristics of SES. This finding will be explored in greater detail below.

Overall, controlling for school-level correlates of PBE rates does not provide adequate explanatory power for clustering across schools, as predicted by Hypothesis 7. This suggests that residential sorting into neighborhoods may leave important mechanisms unexplained. As detection of these clusters may be vulnerable to the influence of a small number of schools in a particular year, spatial scan statistics were estimated across multiple years; results remain largely unchanged over time (Figure A3.1 in Appendix).

Before moving on, however, there may be other sorting processes generating clustering of PBEs across schools that are not attributable to residential sorting, but to selection into particular schools. Results in Table 3.3 show support for Hypothesis 8—compared with public schools, private and charter schools have significantly higher predicated PBE rates, even after adjusting for socio-demographic covariates. Compared to non-charter public schools, private schools increase expected PBE rates by a factor of 2.162, while charter school status increases expected PBE rates by a factor of 3.066, accounting for socio-demographic covariates.[47] The effect of mother's years of education and non-Hispanic white in the school neighborhood remain approximately the same after controlling for school type; however, the effect of logged property values on PBEs appears to be mediated through school type. This finding is consistent with previous research showing selection into particular charter or private schools with alternative pedagogies or norms sympathetic to non-vaccination by parents who file PBEs for their children (Brennan et al. 2016; Sobo 2015).

[47] Including school neighborhood characteristics (counts of physicians, acupuncturists, chiropractors, or autism diagnoses) does not significantly alter these results.

Neighborhood Racial Composition. The above findings suggest that selection by parents into certain schools increases PBE rates, even after controlling for other school-level factors, but that residential sorting into particular neighborhoods by SES does not adequately explain PBE clustering across schools. Furthermore, the distribution of percent non-Hispanic white in the 500-child radius around schools across the state seemed to provide more explanatory power for clustering of PBEs across schools than measures of SES. This suggests that the effect of neighborhood racial composition on PBEs may indicate the presence of a mechanism that is independent of SES and residential sorting. Race/ethnicity itself does not act (and is, therefore, not the mechanism), but may indicate the presence of other processes that are associated with racial composition of the local area.

Several indirect tests were estimated to further investigate this finding for non-Hispanic white population. As shown in Figure 3.3, The effect of percent non-Hispanic white in the school neighborhood was estimated across types of kindergartens (public, private, charter) and licensed childcare centers (day care centers, Head Start Centers) to examine whether the effect was consistent. Head Start Centers were of particular interest as they represent a population that is homogeneous with regard to SES. If percent non-Hispanic white was simply picking up an unmeasured effect of SES, percent non-Hispanic white population around the childcare center should have no effect on PBEs in Head Start Centers. The opposite is found: Among Head Start Centers, a 10% increase in percent white in the neighborhood is associated with a 37% increase in the expected PBE rate, controlling for other SES and neighborhood covariates.

Results presented in Table 3.4 also indicate that racial composition of the area around the school has a significant effect beyond simple selection. Controlling for other socio-demographic and neighborhood characteristics, a non-Hispanic white isolation index has a positive effect on

PBE rates; specifically, a 1% increase in the isolation index is associated with a 1.3% expected increase in school PBE rates. This finding suggests that, even after controlling for percent non-Hispanic white and other SES characteristics, schools with increased segregation of non-Hispanic white students have increased exemption rates. This could magnify the effect of concentration of anti-vaccine attitudes and its influence in some neighborhoods that exhibit increased homophily along lines of race and ethnicity.

As a robustness check for these findings, Moran's I was calculated for the distributions of mother's education level and percent non-Hispanic white by Census block group across California. It could be that racial/ethnic composition of a neighborhood shows an increased association with PBE rates because it is more geographically segregated and clusters of non-Hispanic white children happen to overlap with clusters of PBEs. Moran's I results suggest that this is not the case. Both percent non-Hispanic white (observed = 0.170, expected < 0.001, $p < 0.001$) and mother's education level (observed= 0.174, expected < 0.001, $p < 0.001$) have similarly statistically significant uneven spatial distributions across the state, while only percent non-Hispanic white seems to have an effect on clustering of PBEs across schools. This suggests that the unevenness of underlying spatial distributions of the socio-demographic characteristics themselves cannot explain the non-Hispanic white finding.

Additionally, to rule out that this effect could be generated by school- or school district-specific factors, PBE rates in childcare centers and private schools located near public schools in significant spatial PBE clusters were compared to those that were not similarly located near these clusters. As shown in Figure 3.4, being located closer to a public kindergarten in a PBE cluster increased the expected rate of PBEs within the childcare center. However, this could be due to children in the local kindergarten having younger siblings in the nearby childcare centers who

share similar vaccination status. It seems less likely that one child would attend public kindergarten while another sibling attended kindergarten in a private school, yet the effect remains: spatial proximity to a public kindergarten located in a PBE cluster has a significant, positive effect on expected PBE rates in the private kindergarten. Clustering of PBEs in a neighborhood appears to reach beyond administrative boundaries in the local area.

Finally, Figure 3.2I demonstrates that statistically significant PBE clusters across schools remain after controlling for all school-level covariates. Effects of demographic, socio-economic, and neighborhood characteristics investigated here are not able to adequately account for larger pockets of exempted children.

Discussion

These analyses align with previous findings of increasing rates of unvaccinated children in the U.S. (Smith et al. 2004): Traditional public health understandings of lack of access to healthcare cannot explain the rising PBE rates in California over the past two decades. Schools with high PBE rates are likely to be located in neighborhoods with relatively higher levels of education and proportions of non-Hispanic white population. Addressing this increase in unvaccinated children requires a new perspective on who is most vulnerable to under-immunization and how parents are making decisions to refuse vaccines for their children.

This chapter makes two contributions to understating the increasing rates of children with PBEs in California. First, in addition to socio-demographic factors linked to increasing rates of unvaccinated children in the U.S., characteristics of the local area that could affect perceptions of costs and benefits of vaccination are investigated to understand their influence on school-level PBE rates. In particular, proximity to children with autism diagnoses and reported cases of

pertussis were investigated to determine if vaccine skepticism attributable to the discredited vaccine-autism link or disease incidence influenced the number of children with vaccine exemptions. Prevalence of children diagnosed with autism in the area around the school was associated with a modest, statistically significant increase in PBE rates in schools; however, county-level rates of pertussis incidence and presence of autism advocacy organizations did not appear to have significant effects. Access to data on pertussis incidence at a more local level would likely shed additional light on how disease incidence may be related to requests for PBEs. Previous research has linked PBE rates in local areas to increased incidence of pertussis (Imdad et al. 2013; Omer et al. 2008) and measles (Feiken et al. 2000; Salmon et al. 1999). Further research could establish if vaccine uptake increased in these areas following disease outbreak.

Second, PBE rates across schools were analyzed to understand how larger pockets of exemptions are formed. Clustering of PBEs across schools can have significant consequences for all children located within these clusters, as it increases exposure to unvaccinated children (Buttenheim et al. 2012) and vaccine exemptions increase community level risk of disease spread, not just individual-level risk for those with exemptions (Atwell et al. 2013; Feiken et al. 2000; Imdad et al. 2013; Omer et al. 2008, 2009). While sorting into alternative, non-public schools had significant effects on PBE rates net of other SES and school neighborhood covariates, residential sorting into neighborhoods based on statistically significant school-level correlates could not adequately explain clustering across schools.

Yet, racial composition of the school neighborhood was shown to have effects that were independent of other measures of SES, suggesting that other important mechanisms may help explain larger pockets of PBEs and the unevenness in the distribution of PBEs across schools. The finding that percent non-Hispanic white in the area around the school contributed to broader

spatial clustering of PBEs across schools did not appear to be attributable to (1) unmeasured indicators of SES; (2) the underlying spatial distribution of race or ethnicity in California; (3) school- or school district-specific factors; or (4) distributions of race or ethnicity within schools districts (in fact, non-Hispanic white students concentrated in particular schools within a district increased PBE rates).

Conclusion

Other mechanisms generating these broader patterns of clustering could be spatially dependent and endogenous processes, such as diffusion. The potential spillover effects of vaccine skepticism in social networks and spread of exemptions outside alternative charter or private schools to nearby public schools warrants additional investigation. Although autism diagnoses in the school neighborhood are not associated with broader patterns of PBE clusters across schools, it could be that the now-discredited vaccine-autism link was sufficient to spark the recent wave of vaccine skepticism that has spread well beyond communities where clusters of autism cases were initially found. This chapter focused on identifying spatial clustering of PBEs across schools in California, the following chapter will build on this analysis to investigate how the influence of factors associated with PBEs may spread between schools, creating the broader spatial patterns observed here.

Tables

Table 3.1: Correlates of PBEs among public school kindergartens, 1998-2014[1]

	Unadjusted[2] IRR[3]	Sig.	95% C.I.		Adjusted IRR	Sig.	95% C.I.	
Mother's education	1.560***	0.000	1.533	1.588	1.195***	0.000	1.168	1.222
Property values (ln)	1.715***	0.000	1.637	1.796	0.995	0.854	0.947	1.046
Pop. density (ln)	0.671***	0.000	0.656	0.688	0.776***	0.000	0.760	0.793
% white[4]	1.346***	0.000	1.336	1.356	1.218***	0.000	1.206	1.230
Physicians	1.011***	0.000	1.009	1.013	1.004***	0.000	1.002	1.006
Acupuncturists	1.043***	0.000	1.035	1.050	0.999	0.886	0.992	1.007
Chiropractors	1.051***	0.000	1.045	1.056	1.027***	0.000	1.022	1.033
Autism diagnoses	1.015***	0.000	1.009	1.021	1.008*	0.012	1.002	1.014

Note:
[1] 2-level random intercept negative binomial regression model, N= 89,063 school-years. Year indicator variables included not shown. All independent variables lagged 6 years. †p ‹ .10; *p ‹ .05; **p ‹ .01; ***p ‹ .001
[2] Adjusted for year indicator variables.
[3] Incidence Rate Ratio
[4] Measured in 10% increments (deciles)

Table 3.2: Three-level model for correlates of PBEs among public school kindergartens, 2006-2014[1]

	IRR	Sig.	95% C.I.	
Mother's education	1.257***	0.000	1.222	1.293
Property values (ln)	1.294***	0.000	1.186	1.411
Population density (ln)	0.910***	0.000	0.884	0.937
% white[2]	1.158***	0.000	1.143	1.174
Physicians	0.999	0.166	0.997	1.001
Acupuncturists	0.970***	0.000	0.962	0.978
Chiropractors	1.030***	0.000	1.025	1.036
Autism diagnosis	1.007*	0.025	1.001	1.012
Autism advocacy orgs (county)	0.996	0.105	0.992	1.001
Pertussis rate, ages 0-6 (county)	0.962†	0.086	0.921	1.006

Note:
[1] 3-level random intercept Poisson model, N= 49,153 school-years. Year indicator variables included but not shown. All independent variables lagged 6 years. †p ‹ .10; *p ‹ .05; **p ‹ .01; ***p ‹ .001
[2] Measured in 10% increments (deciles)

Table 3.3: Effects of school type on PBEs among kindergartens, 1998-2014[1]

	Model 1				Model 2			
	IRR	Sig.	95% C.I.		IRR	Sig.	95% C.I.	
School type[2]								
Private schools					2.162***	0.000	2.063	2.266
Charter schools					3.066***	0.000	2.832	3.320
Mother's education	1.147***	0.000	1.121	1.173	1.144***	0.000	1.119	1.169
Property value (ln)	1.110***	0.000	1.057	1.165	1.049*	0.044	1.001	1.010
Pop. density (ln)	0.821***	0.000	0.804	0.839	0.787***	0.000	0.771	0.803
% White[3]	1.213***	0.000	1.201	1.225	1.206***	0.000	1.195	1.217

Note:

[1] 2-level random intercept negative binomial regression model, N= 116,351 school-years. Year indicator variables included but not shown. Demographic variables lagged 6 years. †p ‹ .10; *p ‹ .05; **p ‹ .01; ***p ‹ .001.

[2] Reference category: public, non-charter schools.

[3] Measured in 10% increments (deciles)

Table 3.4: Effect of racial segregation on PBEs rates among public kindergartens[1]

	Adjusted IRR[2]	Sig.	95% C.I.	
Mother's education	1.195***	0.000	1.168	1.223
Property values (ln)	1.003	0.895	0.954	1.056
Population density (ln)	0.795***	0.000	0.778	0.813
% white[3]	1.138***	0.000	1.124	1.152
Physicians	1.005***	0.000	1.003	1.007
Acupuncturists	1.002	0.579	0.995	1.010
Chiropractors	1.023***	0.000	1.017	1.029
Autism diagnoses	1.007*	0.021	1.001	1.013
White isolation Index*100	1.013***	0.000	1.011	1.014

Note:

[1] 2-level random intercept negative binomial regression model, N= 83,825 school-years. Demographic variables lagged 6 years. †p ‹ .10; *p ‹ .05; **p ‹ .01; ***p ‹ .001.

[2] Yearly indicator variables included but not shown.

[3] Measured in 10% increments (deciles)

Figures

Figure 3.1: PBE rates in California kindergartens, 1992-2014

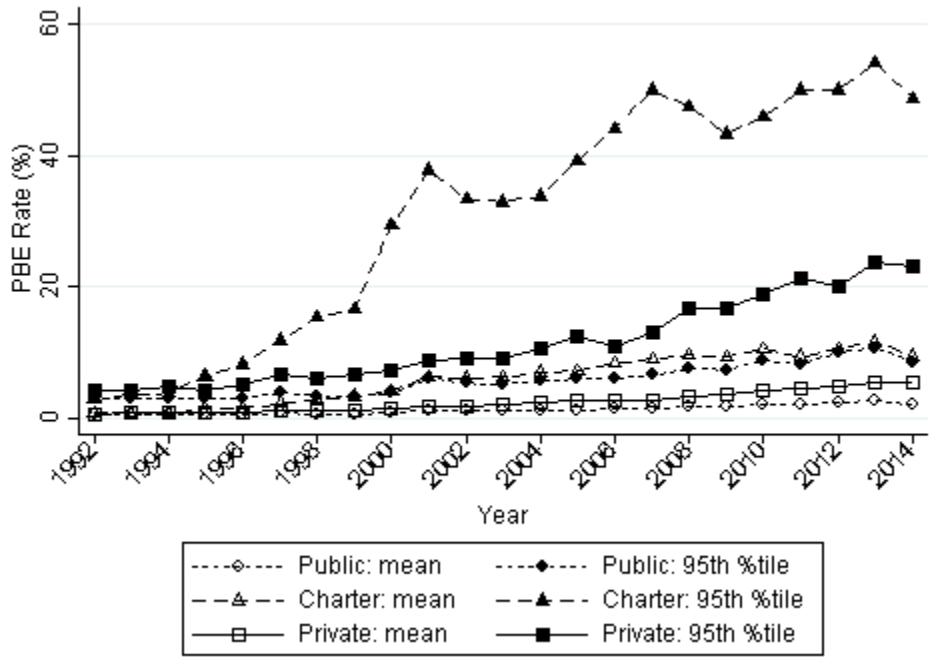
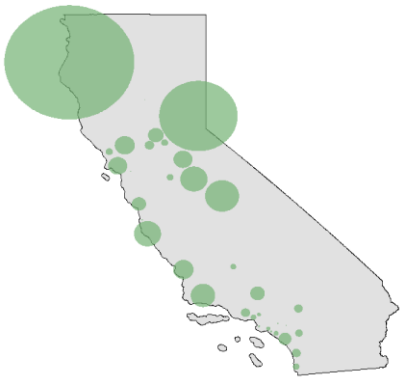
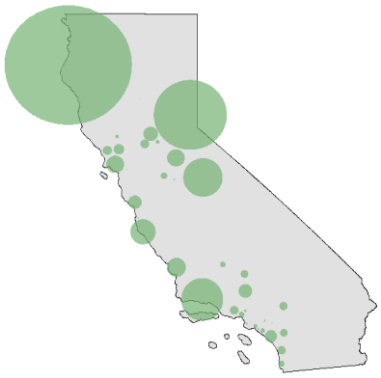


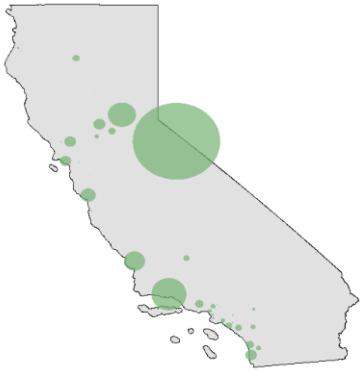
Figure 3.2: Adjusted spatial clusters of PBEs across public schools, 2014



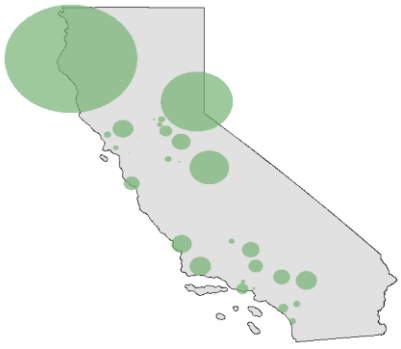
A. Unadjusted



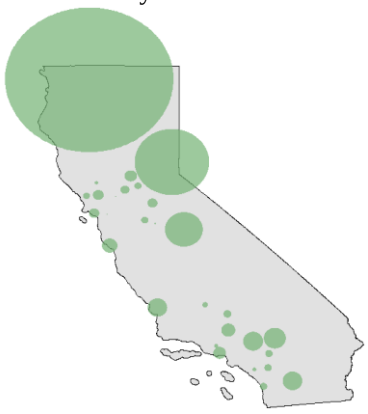
B. Physician count



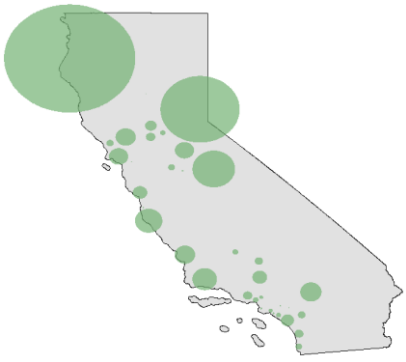
C. Population density (logged)



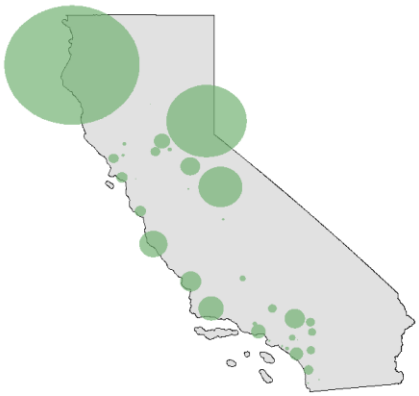
D. Mother's education



E. Property values (logged)

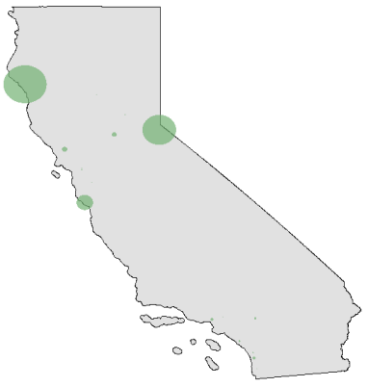


F. Autism diagnoses



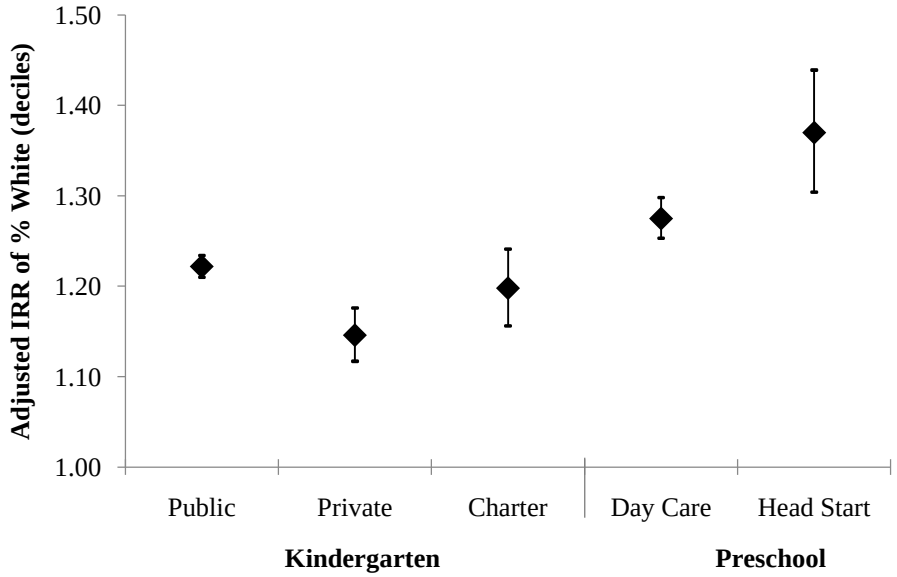
G. Alternative health practitioners

H. Percent non-Hispanic white



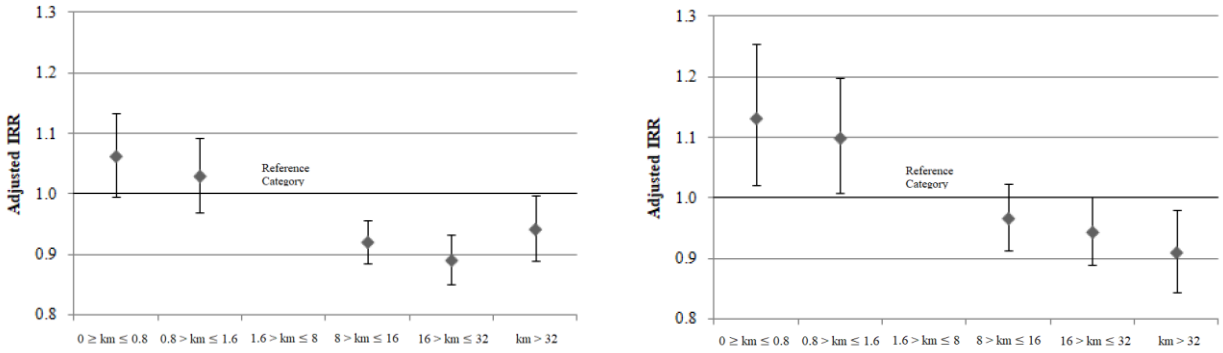
I. All covariates

Figure 3.3: Effect of percent non-Hispanic white by school type



Note: Kindergarten analyses include data from 1998-2014, while childcare center analyses include data from 2010-2014. IRRs estimated via negative binomial regression and adjusted for mother's education, logged property values, logged population density, counts of physicians, chiropractors, acupuncturists, and autism diagnoses, and yearly indicator variables. Public schools: N=84,303; private schools: N=27,378; charter schools: N=5,247; day care centers: N=30,801; Head Start centers: N=6,049.

Figure 3.4: Effect of distance to nearest public school kindergarten in PBE cluster on PBE rates in childcare centers and private schools



Note: IRRs estimated via negative binomial regression and adjusted for mother's education, logged property values, logged population density, % white, counts of physicians, chiropractors, acupuncturists, autism diagnoses, and yearly indicator variables; N=36,850. Public schools in clusters only include those with statistically significantly higher relative risk of PBEs after adjusting for covariates.

Appendix

Table A3.1: Correlates of PBEs among public school kindergartens, 5 year lag, 1998-2014[1]

	Unadjusted IRR[2]	Sig.	95% C.I.		Adjusted IRR	Sig.	95% C.I.	
Mother's education	1.535***	0.000	1.508	1.563	1.186***	0.000	1.159	1.214
Property values (ln)	1.673***	0.000	1.596	1.753	0.989	0.670	0.940	1.040
Pop. density (ln)	0.669***	0.000	0.655	0.684	0.776***	0.000	0.759	0.792
% white[3]	1.344***	0.000	1.334	1.354	1.221***	0.000	1.208	1.233
Physicians	1.009***	0.000	1.007	1.011	1.004***	0.001	1.002	1.006
Acupuncturists	1.036***	0.000	1.029	1.043	0.998	0.509	0.991	1.005
Chiropractors	1.040***	0.000	1.035	1.045	1.026***	0.000	1.021	1.032
Autism Diagnoses	1.010***	0.000	1.004	1.016	1.004	0.184	0.998	1.010

Note:
[1] 2-level random intercept negative binomial regression model, N= 89,550 school-years. Year indicator variables included but not shown. All independent variables lagged 5 years. †p ‹ .10; *p ‹ .05; **p ‹ .01; ***p ‹ .001.
[2] Adjusted for year indicator variables.
[3] Measured in 10% increments (deciles)

Table A3.2: Correlates of PBEs among public school kindergartens, 1998-2010[1]

	Unadjusted IRR[2]	Sig.	95% C.I.		Adjusted IRR	Sig.	95% C.I.	
Mother's education	1.659***	0.000	1.623	1.695	1.181***	0.000	1.149	1.215
Property values (ln)	1.846***	0.000	1.743	1.945	0.978	0.466	0.921	1.038
Pop. density (ln)	0.599***	0.000	0.583	0.616	0.748***	0.000	0.729	0.768
% white[3]	1.403***	0.000	1.392	1.415	1.256***	0.000	1.241	1.272
Physicians	1.011***	0.000	1.009	1.014	1.003*	0.020	1.000	1.005
Acupuncturists	1.071***	0.000	1.062	1.080	1.027	0.000	1.019	1.036
Chiropractors	1.054***	0.000	1.047	1.061	1.019***	0.000	1.013	1.025
Autism Diagnoses	1.016***	0.000	1.009	1.023	1.005	0.138	0.998	1.012

Note:
[1] 2-level random intercept negative binomial regression model, N= 67,336 school-years. Year indicator variables included but not shown. Independent variables not lagged. Model only estimated through 2010 due to availability of data on autism diagnoses †p ‹ .10; *p ‹ .05; **p ‹ .01; ***p ‹ .001.
[2] Adjusted for year indicator variables.
3 Measured in 10% increments (deciles)

Table A3.3: Correlates of logged PBE rates among public school kindergartens, 1998-2010[1]

	Unadjusted IRR[2]	Sig.	95% C.I.		Adjusted IRR	Sig.	95% C.I.	
Mother's education	0.342***	0.000	0.327	0.358	0.075***	0.000	0.055	0.095
Property values (ln)	0.531***	0.000	0.480	0.581	0.103***	0.000	0.054	0.153
Pop. density (ln)	-0.444***	0.000	-0.467	-0.420	-0.272***	0.000	-0.295	-0.250
% white[3]	0.253***	0.000	0.247	0.260	0.170***	0.000	0.160	0.179
Physicians	0.009***	0.000	0.006	0.012	0.000	0.786	-0.003	0.002
Acupuncturists	0.053***	0.000	0.044	0.062	0.017***	0.000	0.008	0.025
Chiropractors	0.070***	0.000	0.063	0.076	0.037***	0.000	0.030	0.043
Autism Diagnoses	0.030***	0.000	0.024	0.037	0.021***	0.000	0.014	0.028

Note:
[1] 2-level random intercept linear regression model, N= 89,063 school-years. Dependent variable logged to adjust for skew. Year indicator variables included but not shown. Independent variables lagged 6 years. †p ‹ .10; *p ‹ .05; **p ‹ .01; ***p ‹ .001.
[2] Adjusted for year indicator variables.
3 Measured in 10% increments (deciles)

Table A3.4: Physician effects on PBEs, by physician type, 1998-2014[1]

	Adjusted IRR[2]	Sig.	95% C.I.	
Mother's education	1.193***	0.000	1.166	1.220
Property values (ln)	0.975	0.336	0.927	1.026
Population density (ln)	0.782***	0.000	0.766	0.799
% white[3]	1.216***	0.000	1.204	1.229
Family Practitioners	1.008***	0.000	1.004	1.011
Pediatricians	0.995*	0.040	0.991	0.999
General Practitioners	1.021***	0.000	1.010	1.032
Acupuncturists	0.995	0.206	0.988	1.003
Chiropractors	1.028***	0.000	1.022	1.033
Autism diagnoses	1.006*	0.037	1.001	1.012

Note:
[1] 2-level random intercept negative binomial regression model, N= 89,550 school-years. All covariates lagged 6 years. †p ‹ .10; *p ‹ .05; **p ‹ .01; ***p ‹ .001.
[2] Yearly indicator variables included but not shown.
[3] Measured in 10% increments (deciles)

Table A3.5: Percent renters effects on PBE rates in public kindergartens, 1998-2014[1]

	Adjusted IRR[2]	Sig.	95% C.I.	
Mother's education	1.218***	0.000	1.190	1.246
Property values (ln)	1.036	0.176	0.984	1.089
Percent renters	1.006***	0.000	1.005	1.007
Population density (ln)	0.747***	0.000	0.730	0.764
% white[3]	1.223***	0.000	1.211	1.235
Physicians	1.003**	0.002	1.001	1.005
Acupuncturists	0.995	0.245	0.988	1.003
Chiropractors	1.024***	0.000	1.018	1.030
Autism diagnoses	1.008**	0.008	1.002	1.014

Note:
[1] 2-level random intercept negative binomial regression model, N= 89,063 school-years. All covariates lagged 6 years. †p ‹ .10; *p ‹ .05; **p ‹ .01; ***p ‹ .001.
[2] Yearly indicator variables included but not shown.
[3] Measured in 10% increments (deciles)

Table A3.6: Effect of household income on PBE rates in public kindergartens, 1998-2014[1]

	Adjusted IRR[2]	Sig.	95% C.I.	
Mother's education	1.281***	0.000	1.250	1.312
Household Income (ln)	0.711***	0.000	0.659	0.766
Population density (ln)	0.782***	0.000	0.766	0.798
% white[3]	1.222***	0.000	1.210	1.234
Physicians	1.004***	0.000	1.002	1.006
Acupuncturists	0.998	0.619	0.991	1.006
Chiropractors	1.025***	0.000	1.020	1.031
Autism diagnoses	1.007*	0.026	1.001	1.013

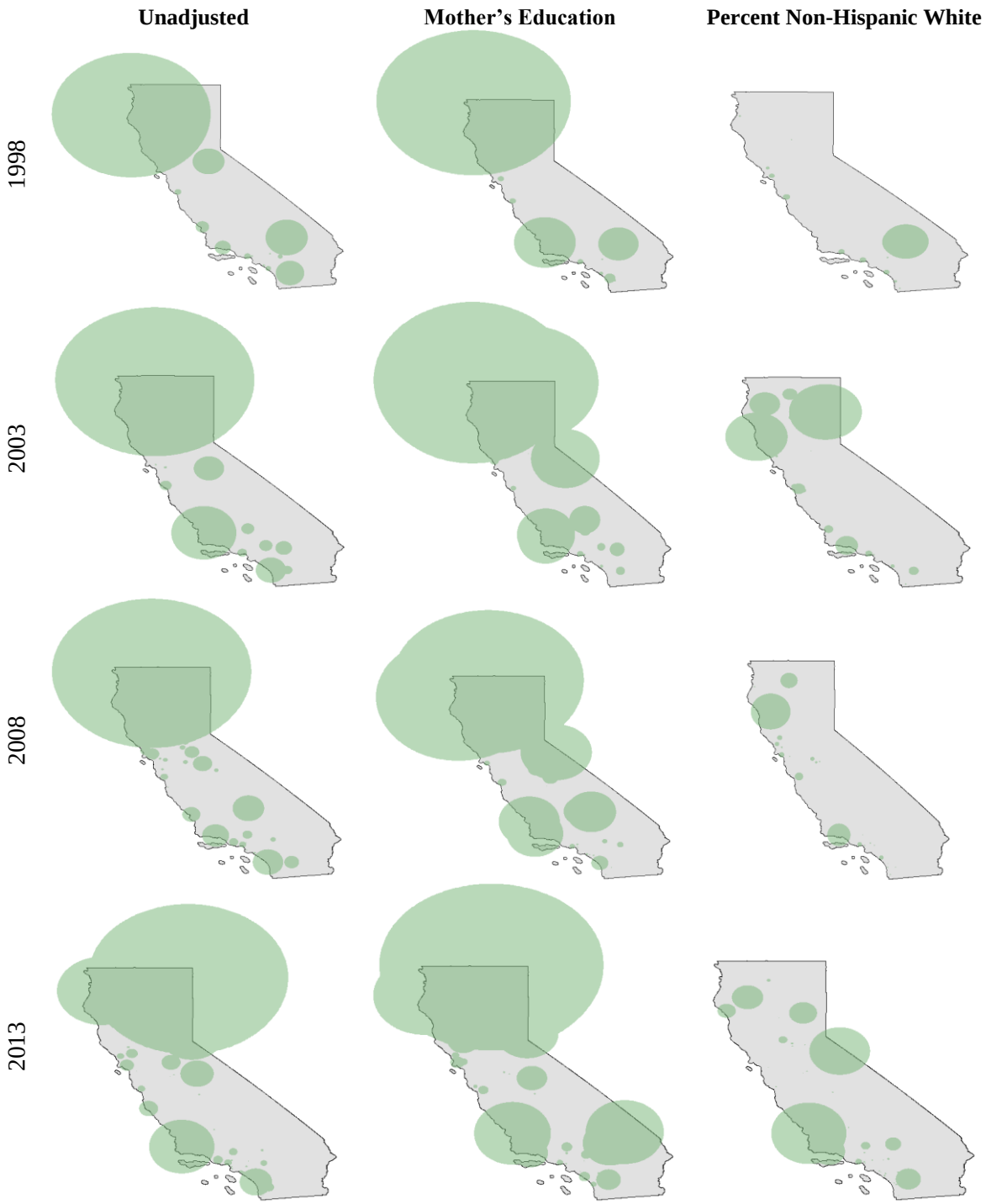
Note:
[1] 2-level random intercept negative binomial regression model, N= 89,063 school-years. All covariates lagged 6 years. †p ‹ .10; *p ‹ .05; **p ‹ .01; ***p ‹ .001.
[2] Yearly indicator variables included but not shown.
[3] Measured in 10% increments (deciles)

Table A3.7: Correlates among public school kindergartens, additional local business variables, 1998-2014[1]

	IRR	Sig.	95% C.I.	
Mother's education	1.191***	0.000	1.164	1.219
Property values (ln)	0.963	0.152	0.916	1.014
Population density (ln)	0.786***	0.000	0.770	0.803
% white[2]	1.214***	0.000	1.202	1.227
Physicians	1.004***	0.000	1.002	1.006
Acupuncturists	0.994	0.154	0.987	1.002
Chiropractors	1.026***	0.000	1.021	1.032
Autism diagnosis	1.006*	0.035	1.001	1.012
Random addresses (N=Chiropractors)	1.002	0.420	0.997	1.007
Random addresses (N=Acupuncturists)	0.997	0.476	0.989	1.005
Veterinarians	1.016***	0.000	1.009	1.023

Note:
[1] 2-level random intercept negative binomial regression model, N= 89,550 school-years. Year indicator variables included but not shown. All independent variables lagged 6 years. †p ‹ .10; *p ‹ .05; **p ‹ .01; ***p ‹ .001.
[2] Measured in 10% increments (deciles)

Figure A3.1: Adjusted spatial clusters of PBEs by mother's education and percent non-Hispanic white, 1998-2013



Chapter 4: The Structure of Spatial Dependence in Yearly Personal Beliefs Exemption Rates across Kindergartens in California, 1998-2014

Abstract

Social interaction among parents can generate shared attitudes toward vaccines. Instead of the static effects of socio-demographic and neighborhood characteristics that would be expected to result from residential sorting, this type of process can create local variation in the influence of these factors on PBEs. Results from spatial regression analyses support that PBE rates in California are influenced not only by the conditions in the area immediately surrounding a school, but also those in neighboring areas. In particular, higher proportions of non-Hispanic white population and numbers of alternative health practitioners are associated with higher PBE rates in nearby schools. Being located near schools with high PBE rates in the previous year also has a positive effect on school PBE rates. These findings suggest that spatially dependent processes, such as spatial diffusion, that are not addressed in standard regression analyses may play a key role in generating broader spatial clusters of children with non-medical vaccine exemptions.

Chapter Introduction

What if geographical clusters of schools with high PBE rates are generated not only by parents selecting into particular neighborhoods, but also through interaction among parents in nearby areas? Previous studies have shown that local social norms and networks contribute to the disparity in rates of children with non-medical vaccine exemptions across schools and communities (Gaudino and Robison 2012; Sobo 2015). These processes of social influence are more dynamic that residential sorting because conditions in one neighborhood can spill over its boundaries to affect outcomes in surrounding areas. This creates variation in effects that are difficult to capture with standard regression approaches that assume a given set of characteristics reproduce the same outcomes across space.

Results from the previous chapter indicate that socio-demographic and neighborhood characteristics correlated with PBE rates at the school level cannot fully account for large PBE clusters that span schools. Spatially dependent processes, such as spatial diffusion of vaccine skepticism and other spillover effects from characteristics in the surrounding neighborhoods, can contribute to the formation of large pockets of PBEs. In this scenario, it is the relationship between nearby covariate values that contributes PBE clustering beyond what can be explained by residential sorting. Alternatively, the models I estimate could be missing important factors associated with PBE rates that are not distributed evenly across space. Any spatial correlation of these missing factors can produce the residual clustering of PBE rates after accounting for the other covariates in the model.

In this chapter, I use spatial econometrics models to investigate whether spatial dependence in PBE rates across schools is likely attributable to omitted, spatially correlated variations or local spillover. I begin with a brief review of previous literature pointing to the

importance of spillover processes in generating spatial clustering. I then discuss how spatial econometrics models can help identify processes that generate underlying spatial autocorrelation in outcomes (Anselin 1988b; Haining 1978). Next, I apply these models to the longitudinal dataset of PBEs in kindergartens in California from 1998-2014 described in the previous chapter. The results suggest that PBE rates and characteristics of one school have spillover effects on the prevalence of PBEs in nearby schools. The chapter concludes with a discussion of the importance of spatially dependent social context in vaccine decisions.

Spatial Dependence in PBE Rates

PBE rates are not equally distributed across schools in California. Figures 4.1A and 4.1B present Lorenz curves for PBE rates across public, private and charter kindergartens in 1998 (1A) and 2014 (1B). Lorenz curves are used to display the cumulative share of a good[48] by the cumulative share of the population. In 1998, approximately 80% of PBEs were concentrated within 10% of the student population in charter and private schools and 15% of the student population in public schools. Concentration of PBEs within the student population decreases over time; by 2014, approximately 80% of PBEs are found in 25% of the student population, regardless of school type.

This concentration is consistent with the increasing dispersion of PBEs across schools over time shown in Figure 4.1C. Dispersion measures the percent of schools that had at least one enrolled student with a PBE (Cohen and Tita 1999). Between 1998 and 2014, the percentage of kindergartens with any exempted children steadily increased. For public and charter schools, percentages of kindergartens with any exempted children almost doubled (percentages increased by approximately 90% in both cases), while the percentage of private schools more than tripled,

[48] Lorenz curves are most commonly used to model inequality in income.

from 14% to 46% of kindergartens. Over the same period, the *average* percentage of children with PBEs in charter and private kindergartens increased from approximately 7.5% to 12%, while public schools had a more limited increase from an average of 2% in 1998 to 4% in 2014.

Interestingly, simultaneous with this dispersion of PBEs in schools over time, the spatial autocorrelation of PBEs has increased. Spatial autocorrelation is the spatial dependence between an observation in one location and others nearby (Cliff and Ord 1981; Ord and Getis 1995). Figure 4.1D demonstrates that the global autocorrelation in PBE rates across all kindergartens, as measured by Moran's I[49], increased from 0.21 to 0.36 between 1998 and 2014. These patterns—a highly uneven distribution of PBEs across schools, the dispersion of PBEs to a greater proportion of schools along with increasing spatial autocorrelation warrant the investigation of spatially dependent processes, which may explain why PBE rates cluster across space.

Spatial Heterogeneity

Spatial heterogeneity refers to local differences in relationships between independent covariates and dependent outcomes across space (Getis 1994). This variation is also known as non-stationarity. Non-stationarity in relationships between covariates and outcomes can be observed for a variety of reasons, including unmeasured, spatially correlated covariates that are not included in the model and spillover effects among nearby observations (Fotheringham, Brunsdon, and Charlton 2003). Certainly, some variation will be observed in relationships across space when examining social outcomes, even if only through random processes. Models that examine spatial heterogeneity, such as Geographically Weighted Regression, specifically

[49] Moran's I is commonly used measure spatial correlation among observations. Values range from -1 to 1; statistically significant positive values indicate assortative spatial correlation, while significant negative values indicate disassortative spatial correlation. Statistically insignificant values indicate lack of spatial patterns. Random permutations are used to compare significance against the value expected if the observations did not exhibit any spatial patterns. Moran's I was estimated using the `spdep` package in R.

investigate statistically significant variation in relationships between covariates and outcomes across space (Brunsdon, Fotheringham, and Charlton 1996; Fotheringham et al. 2003; Getis 1994).

Unmeasured Covariates

Perhaps the most straightforward explanation for spatial dependence in outcomes after controlling for covariates of interest is omitted, spatially correlated covariates. Standard regression analyses assume a well-specified model. If the model is missing important variables that are not evenly distributed across space, their unmeasured effects will create spatial dependence in the error terms. For example, PBE rates may be increased by the presence of anti-vaccine organizations in the local area. If anti-vaccine groups are only located in some areas across California and the model does not control for their presence, predicted PBE rates in schools in these areas will have similar (and correlated) residual values. The presence of these types of effects could also be attributable to selection into certain neighborhoods, and would not require the specification of additional spillover processes between schools to explain clustering of PBEs.

Spatial Externalities

But again, it is not unreasonable to expect that parents' interaction in their neighborhood and others nearby may also help spread vaccine skepticism locally. Spatial externalities refer to the influence that characteristics of one neighborhood have on outcomes in other nearby areas (Anselin 2003; Morenoff 2003). Spatial externalities create spatially dependent relationships because an outcome in one neighborhood depends not only on conditions in that neighborhood

but also in those nearby. These externalities may result from social behavior that crosses neighborhood boundaries (Caughy et al. 2013) or indirect effects of behaviors that are not contained locally. For example, high crime rates in one neighborhood can produce negative externalities by increasing stress in surrounding neighborhoods (Morenoff 2003).

Spatial externalities of covariates in nearby schools may be partially responsible for spatial patterns of PBEs. For example, previous research has shown that increased confidence in and use of alternative medicine is positively associated with vaccine skepticism (Gaudino and Robison 2012; Gellin et al. 2000; Salmon, Moulton, et al. 2005). Alternative health practitioners in one local area may create interest in these practices and draw patients from nearby neighborhoods as well. This could increase PBE rates not only in the schools immediately surrounding offices of alternative health practitioners, but also other schools nearby. Schools, particularly those whose enrollment is not determined by residence in a particular school district, may enroll children from other nearby neighborhoods with characteristics associated with higher PBEs rates.

Spatial Diffusion

A specific type of spatial externalities indicates a spatial diffusion process: when PBEs rates in one school directly affect the subsequent likelihood of PBEs in nearby schools. Under a diffusion mechanism, an individual's decision to adopt a practice is not only a product of own preferences, but also the behavior of others around them. Erosion of trust in health care providers has prompted some parents to look beyond physicians for credible information on vaccine safety (Hilton, Petticrew, and Hunt 2007). In a 2009 survey, 82% of parents reported having "some" or "a lot" of trust in vaccine safety information provided by family and friends (Freed et al. 2010).

In qualitative interviews with new mothers, both local cultural norms and trusting relationships with other parents holding anti-vaccine beliefs emerged as influences on vaccination intentions (Benin et al. 2006).

Diffusion creates a dynamic process in which populations with almost identical sets of characteristics and preferences can have very different distributions of adoptions (Granovetter 1978). In the case of PBEs, some initial selective decisions to not vaccinate children within in a school community may influence other parents to refuse vaccines as well (Bikhchandani et al. 1992; May and Silverman 2003). For instance, previous research has shown that social interaction can spread anti-vaccine beliefs to parents who had previously vaccinated older children (Sobo 2015).

Diffusion of vaccine concerns though spatially embedded social networks could result in the severe disparities in PBE rates across schools in California. Spatial proximity is an important contributor to local clustering of ties in social networks (Bullock, Barnett, and Di Paolo 2010; González, Hidalgo, and Barabási 2008; Herrmann, Barthélemy, and Provero 2003). Diffusion of risky or unproven behaviors tends to require multiple reinforcements before an individual adopts (Centola and Macy 2007). Although parents with anti-vaccine beliefs may perceive vaccines as risky (Gust et al. 2004), refusal of recommended childhood vaccination still conflicts with prevailing recommendations from pediatricians and school immunization requirements in all U.S. states (Committee on Practice and Ambulatory Medicine et al. 2016). Deciding not to vaccinate after witnessing others in a local area making the same decision may increase spatial concentration of children with PBEs, as observed in other complex contagion outcomes (Centola and Macy 2007; Hedström 1994) and spread of health behaviors in social networks (Fowler and

Christakis 2008). An opinion formation process that requires affirmation from multiple sources intensifies the spatial clustering of vaccine exemptions (Salathé and Bonhoeffer 2008).

Homophily can increase the likelihood of diffusion (Centola 2010, 2011; Centola and Macy 2007). Racial or ethnic background has been identified as the greatest source of homophily in social networks in the U.S. (McPherson, Smith-Lovin, and Cook 2001), and plays a strong role in the creation of social ties (Currarini, Jackson, and Pin 2010; Smith, McPherson, and Smith-Lovin 2014). Tendency for racially homophilous ties in social networks can shape health risks, such as frequency of opiate use (Rowe et al. 2017). Similarity in racial composition of neighborhoods can also influence spatial diffusion of other behaviors, such as the spread of non-youth homicides among Pittsburgh census tracts in the early 1990s (Cohen and Tita 1999). Homophilous adoption decisions may also be prompted by others who share cultural (Chaves 1996; Soule 1997, 2004) or structural (Burt 1987; Strang and Tuma 1993) similarities.

Adoption influenced by homophily can also render geographically near, but socially unlike individuals *less* influential. Observation of like others may result in "hierarchical" diffusion in which spread occurs not through spatial contiguity, but via imitation of behavior observed in others that one wishes to emulate (Bale 1978; Centola 2011; Cohen and Tita 1999) or perceives as peers (Soule 1997). While concentrations of unvaccinated children in home-schooling programs (Kennedy and Gust 2005; Khalili and Caplan 2007) and Montessori (Brennan et al. 2016) or other charter or private schools (Carrel and Bitterman 2015) may depend heavily on selecting into programs with more lenient policies and collective attitudes toward vaccination, these parents may also become more skeptical toward vaccines after observing rising rates of vaccine refusals among parents with similar educational practices, even if they are located farther away. Therefore, when examining spillover effects between schools, it is

important to consider how a school's neighbors are defined and test alternative specifications in the spatial models.

In summary, non-stationarity in relationships between independent covariates and dependent outcomes can be caused by many factors. One such factor is unmeasured, spatially correlated covariates that are not included in the model. But complex interactions within and across neighborhoods can lead to instability in social processes and inconsistent outcomes across individuals or communities that share similar characteristics (Sampson et al. 2002). Spillover processes reflex these dynamic processes, and could be contributing to differences in the prevalence of PBEs in schools that may otherwise have very similar socio-demographic and neighborhood profiles.

Individual level data are needed to directly test specific mechanisms of spillovers and diffusion. As discussed in the previous chapter, the longitudinal dataset of PBEs in California kindergartens does not include individual-level measures of vaccination status or social networks. However, by describing the overall spatial patterns of associations between covariates and PBEs, we can infer whether observed trends in school PBE rates are consistent with some social processes more so than others. Specifically, spatial econometrics models are used here to gather indirect evidence to help adjudicate between spatial dependency due to unmeasured covariate effects and spillover processes. These spillover processes can occur as both spatial externalities of covariate effects and spatial diffusion of PBEs through local social networks.

Data

The analyses in this chapter again utilize the school-level dataset of PBE rates in California kindergartens for the 1998-2014 period. The dependent variable for these analyses is

logged[50] yearly PBE rates in California public, charter, and private year kindergartens with more than 10 enrolled students, as reported by the California Department of Public Health. PBE reports are matched to enrollment records from the California Department of Education. Covariates include the following measures for the 500-child radius around a school: logged mean property values, household income, and population density[51] from the U.S. Census; average mother's years of education and percent non-Hispanic white children from the California Statistical Birth Master File; count of local physicians from the American Medical Association Directory of Physicians; count of autism diagnoses from the California Department of Developmental Services; and counts of licensed acupuncturists and chiropractors from the California Department of Consumer Affairs. Full details of the construction of this dataset are presented in the previous chapter. Table A4.1 in Appendix shows the yearly counts of schools included in the following models.[52]

Analytic Strategy

A series of spatial analyses were conducted to examine spatial trends in covariate effects on school PBE rates over time. Models were estimated yearly to assess how covariate effects and model fit varied over time. Standard spatial panel econometric models do not allow inclusion of time-lagged covariates or examine dynamic time trends (Millo and Piras 2012); however, random effect spatial panel models are estimated for robustness purposes and included in the Appendix.

[50] Rates have a positively skewed distributed and were logged to adjust for this.

[51] Measured at the Census block group level.

[52] Unless otherwise noted, all models for the same year have the same number of observations. For the sake of space, I report the Ns in Table A4.1 rather than including them in the footnotes of each separate figure.

First, Geographically Weighted Regression (GWR) models were estimated yearly to test local non-stationarity (spatial heterogeneity) in regression coefficients. Non-spatial regression models assume covariate effects are consistent across space; GWR models test the plausibility of this by estimating covariate effects locally at each observation. In addition to coefficients, standard errors and significance tests are also estimated locally. The results presented here are restricted to only those effects that were statistically significant. Including statistically insignificant effects may capture variation that is non-systematic and attributable to random processes. For the GWR models, all covariates were allowed to vary geographically.[53]

The GWR spatial kernel is estimated using an adaptive Gaussian k-nearest neighbor (k-NN) approximation; multiple values of *k* were fitted to select the optimal number of neighbors (bandwidth). For the results presented here, the bandwidth was 0.01, presenting the approximately 60 nearest schools.[54] Model fit was assessed by comparing Akaike Information Criterion (AIC) values from the GWR models to those obtained from Ordinary Least Squares (OLS) models (Nakaya et al. 2016). Models were estimated using the `spgwr` package in R (Bivand et al. 2009). Results from these models allow us to assess whether there is statistically significant local variation in covariate effects on school PBE rates across California.

As discussed above, local variation in covariate effects can be generated by spatial externalities of covariates, other endogenous processes, such as diffusion of vaccine skepticism across neighborhoods, or bias due to spatially correlated, omitted variables. Spatial econometrics models can be used to help identify processes that generate spatial autocorrelation in outcomes (Anselin 1988b; Haining 1978) and contribute to spatial heterogeneity in covariate effects.

[53] Allowing some coefficients to vary locally while others are held constant at their global mean can create bias in both local coefficient estimates and relative improvement shown by comparisons of model fit statistics.

[54] The exact numbers of schools including in this bandwidth each year can be directly calculated by multiplying the yearly counts presented in Table A4.1 by 0.01.

Specifications of relationships between measured covariates, unmeasured covariates, and outcomes vary in these models. Figure 4.2 provides an illustration of the spatial relationships in these models, and I discuss each of

Spatial error models[55] (Figure 4.2A) attribute spatial autocorrelation in the dependent outcome to unmeasured, spatially correlated covariates. The omission of these covariates from the model creates correlation in the error terms of OLS regression models.[56] This correlation is demonstrated by the multi-directional arrows with dashed lines in Figure 4.2A. In this case, spatial dependency in PBE rates is assumed to result from unmeasured covariates, such as presence of anti-vaccine organizations. If these factors could be measured and included in the model, it is assumed that the spatial dependence would disappear. Formally, the spatial error model estimates a school's logged PBE rate (y_i) as:

$$y_i = \alpha + \beta X_i + \lambda W\varepsilon + u_i$$

Here, schools are indexed by i, α is the constant, X_i is a vector of independent covariates for each school, β is estimated covariate effects, W is the weights matrix, while ε represents spatially correlated errors due to omitted covariates, λ the strength of the spatial dependency in these errors, and u_i the random, school-specific error.[57]

Alternatively, spatial lag models[58] (Figure 4.2B) assume a spillover process in which events at one location increase the likelihood of observing similar events in nearby locations (Anselin 1988b). This model is more consistent with a diffusion process. Spatial lag models have been used in previous research to examine spillover effects in the production of knowledge and

[55] Sometimes referred to as spatial disturbance models.

[56] Thus violating the independence of errors assumptions in OLS models and creating potential bias in coefficients.

[57] As models are estimated yearly, these terms are not indexed by *t*.

[58] Sometimes referred to as spatial effects models.

innovative activity across European countries (Moreno, Paci, and Usai 2005), behavior problems among adolescent peers (Caughy et al. 2013), and county homicide rates in the U.S. (Baller et al. 2001).

In the case of PBE rates, use of a spatial lag model suggests that schools are influenced by the PBE rates of other schools nearby. A school's PBE rate then is influenced not only by its covariates, but also PBE rates in neighboring schools. For example, vaccine refusals may flow through parental social networks that cross schools, creating spatial dependency in PBE rates in nearby schools. The spatial lag model estimates a school's logged PBE rate (y_i) as:

$$y_i = \rho W y + \alpha + \beta X_i + \varepsilon_i$$

Here, schools are again indexed by i, ρ is the spatial dependency parameter, W is the weights matrix, y presents the PBE rates in nearby schools (and is multiplied by the weights matrix), α is the constant, X_i is a vector of independent covariates for each school, β is estimated covariate effects, and ε_i is the individual error term. As others have pointed out, an important caveat is that spatial lag models do not specify temporal order while diffusion occurs over time (Morenoff 2003). For this reason, spatial lag models capture the spatial patterns that may result from diffusion rather direct evidence of the process itself.[59] As discussed in more detail below, I do create a secondary measure of temporally lagged PBE rates in neighboring schools to further examine the possibility of diffusion.

As discussed above, influence from covariates in nearby schools may also spillover, creating spatial externalities in their effects. In theory, spatial externalities in covariates are captured in the spatial dependency (ρ) term in spatial lag models. This is because spatially lagged

[59] While spatial lag models can capture the spatial dependency in outcomes resulting from dynamic diffusion processes, they do not directly allow for estimation of a secondary spatial dependency parameter for time-lagged outcomes (Anselin 2001). More generally though, even if we could specify the temporal order, caution is still needed in making claims about causation based on spatial correlation.

dependent variables capture not only direct correlation between outcomes but also spillover effects of covariates in nearby locations (Morenoff 2003). Spatial Durbin models can be used to estimate these indirect, or spatially lagged, effects of the covariate terms.

Figure 4.2 illustrates that the difference between the spatial Durbin model and a spatial lag model is that the Durbin model has an additional set of spatially lagged covariate terms.[60] Spatial Durbin models are assumed to produce unbiased coefficient estimates even if the true process generating the spatial dependency is spatially lagged effects of the dependent variable or spatial correlation in the error due to omitted covariates (Elhorst 2010; LeSage and Pace 2009).[61] To reiterate the example above, the presence of acupuncturists in the local area surrounding a school may have a positive spatially lagged effect on nearby neighborhoods if parents of children in those schools also visit those practitioners.

Direct effects of spatial Durbin models used here estimate influence of a school's own covariates on its PBE rate,[62] while indirect effects estimate the influence that spills over from covariates in neighboring schools[63] (Elhorst 2010; Golgher and Voss 2016; LeSage and Pace 2009). Here, a school's logged PBE rate (y_i) is estimated as:

$$y_i = \rho Wy + \alpha + \beta_d X_i + \beta_s WX + \varepsilon_i$$

This is the above equation for the spatial lag model, with the exception that the covariate effects are now separated into a set of direct effects (β_d) of a school's covariate values (X_i) and indirect

[60] This is the standard spatial Durbin model and it provides the best fit for this data. There is also a less commonly used spatial Durbin error model, which I also tested. It produced slightly higher values of AIC but similar estimates of direct and indirect effects of the covariates. As the number of neighbors included in the weights matrices increases, the AIC values for the spatial Durbin models and spatial Durbin error models converge.

[61] This is because both the spatial lag and spatial error models are special cases of the spatial Durbin model.

[62] This can also pick up feedback effects if there is spillover between PBEs rates in neighboring schools.

[63] These spillover effects can be interpreted in two ways: (1) the average change in all neighboring school PBE rates produced by a one-unit change in covariate *x* at school *j*, or (2) the average change in school *j*'s PBE rate that accrues from a one-unit change in covariate *x* in all neighboring schools. Mathematically, the results are the same. There is a nice discussion of this in LeSage and Pace (2009), which includes the algebraic equations.

effects (β_s) from covariate values of neighboring schools (WX). Also, ρ now measures the effect of PBE rates in nearby schools after controlling for the indirect effects of covariates. All spatial econometrics models were estimated using the `spdep` package in R.

To summarize, spatial lag models are generally assumed to be more consistent with diffusion process and spatially lagged effects of covariates, while spatial error models tend to indicate bias due to omitted variables. Evidence of externalities in particular covariates from spatial Durbin models can further suggest potential mechanisms responsible for spillover effects between schools. Relative fit of spatial lag and spatial error models for school PBE rates is compared using Lagrange Multiplier tests and AIC (Anselin 2003; Baller et al. 2001). Lagrange multiple tests examine spatial autocorrelation in residuals from an OLS model using the same independent covariates. Formulas differ slightly for calculation of test statistics for spatial lag and spatial error models, and larger test statistics indicate more evidence for a particular model (Anselin 1988a). Lower values of AIC indicate better model fit (Akaike 1974; Fotheringham et al. 2003; Nakaya et al. 2016; Snipes and Taylor 2014).

Spatial Neighbors

Spatial neighbors can be defined in many ways (Anselin, Syabri, and Kho 2006), which can affect results of spatial analyses (Lee et al. 2014). K-Nearest Neighbors (k-NN) weighting was used for this analysis; this method was preferred to both spatial contiguity weighting, which is more appropriate for areal units[64], and weighted distance matrices, which are more appropriate for data with relatively even distribution of points across space (Anselin et al. 2006; Nakaya et al. 2016). Schools in California are not evenly distributed across space—schools are clustered in

[64] Areal units aggregate point-based data into larger spatial geographies (e.g. Census tracts or counties), but choice of aggregating unit can influence results of statistical tests (Fotheringham and Rogerson 2008).

urban areas and relatively far apart in the more sparsely populated northern counties. As I had no theoretical basis for defining how many neighbors should be included in the analyses, I tested NN matrices for the nearest 5, 10, and 15 neighbors, with additional robustness checks for up to 50 nearest neighbors, in increments of 5.

As mentioned above, a caveat of using spatial lag models to investigate diffusion processes is that they do not specify temporal order. To address this, I created an indicator variable to record whether a school had a high PBE rate in the previous year. Schools with high PBE rates were defined as those with rates more than 2 standard deviations above the mean standardized PBE rate across the 1998-2014 period. The mean rate over the full period was used to account for increasing PBE rates over time (Cohen and Tita 1999), although standardized rates by year were also calculated and used for robustness tests. When used in spatial Durbin models, this indicator variable estimates both the direct influence of a school having a high PBE rate in the previous year and the indirect effects of having neighboring schools with high PBE rates in the previous year. Time-lagged dependent variables were not used directly as covariates due to the bias this can create in the effects of other covariates (Achen 2000; Keele and Kelly 2006; Millo and Piras 2012).[65] To estimate these effects, only schools with PBE data recorded for the previous year were included in the analyses. Robustness checks for these results were conducted using a balanced panel spatial lag model with random effects for schools. This model was estimated using the `splm` package in R.

The analytic strategy so far has assumed that spillover effects through covariates or PBE rates or covariates occur across spatially proximate schools. The modification of diffusion effects by homophily suggests that all school may not be equal in their influence others nearby.

[65] Although this variable is created from the dependent variable value in the previous year, it does not meaningfully change the values or significance of direct or indirect effects of the other covariates when included in the model.

Spillover effects may be most pronounced across schools of the same type. For example, parents of students in charter schools may be more attentive to PBE rates in other nearby charter schools, rather than vaccination trends in nearby public schools. To investigate whether it is the geographically nearest schools or the nearest schools of the same type that most influence a school's PBE rate, two sets of NN weights matrices were created. The first included the nearest schools across all school types. The second included the nearest schools of the same type only.[66]

Results

As discussed above, the presence of spatial externalities, which can be produced by spillovers in covariate effects, endogenous processes, or omitted variables, will produce local variation in covariate effects. Results from the GWR models presented in Figure 4.3 provide the evidence of this spatial heterogeneity. Figure 4.3A shows that allowing local variation in coefficients leads to better fitting model, as indicated by statistically significant reduction in AIC compared to an OLS model. Figures 4.3B-4.3I present the distribution of significant local effects for each covariate over time, as well as the percentage of schools that had significant local effects.

Consistent with findings in the previous chapter, count of physicians in the local area surrounding a school has only a small percentage of significant local effects and very small effect sizes (4.3B). Count of chiropractors also has a relatively small percentage of significant local effects and little variation in effect size (Figure 4.3C). Count of acupuncturists has a greater proportion of local significant effects, but most of the variation is in the tails, rather than center, of the distribution of effect sizes (Figure 4.3D). This is an interesting finding given that the effect

[66] Effects for all schools were still estimated in the same model, but rows in the weight matrices corresponding to charter schools could only contain other charter schools, etc.

of acupuncturists was insignificant in the full model in the previous chapter. Effects of autism diagnoses in the local area surrounding a school become more positive over time, consistent with what might be expected given the MMR-autism vaccine scare in the late 1990s; however, these effects are only significant for a very small percentage of schools (Figure 4.3E).

The socio-demographic variables appear to have greater local variation and a higher percentage of locally significant coefficients. Logged household income, in particular, exhibits significant variation over time, but, again, in no year do more than 20% schools show significant local effects (Figure 4.3I).[67] Logged block group density consistently has negative local effects on school PBE rates, although there are some positive local effects for some schools, as shown in the tail of the distribution (Figure 4.3H). The percentage of significant local coefficients does not change systematically across the 1998-2014 period. The local effects of average mother's education (Figure 4.3F) and percent non-Hispanic population in the local area surrounding a school (Figure 4.3G) are similar in that they both show increases in the percentage of statistically significant local effects over time. Percentage non-Hispanic white seemingly exhibits less variation than average mother's education, but the variation that does occur is consistently positive across almost all years.

Local variation in the effects of private and charter school status show different, but interesting effects. Private school status appears to have the most consistent effects on PBE rates across schools in this period (Figure 4.3J). The effects are consistently positive, and the covariate maintains more than 50% of local effects are significant in all years. Charter school status also consistently has positive effects on PBE rates, but exhibits more variation over time than private schools (Figure 4.3K). In particular, the percentage of statistically significant local effects for

[67] Property values were insignificant after controlling for other covariates in the model.

charter schools increases substantially over time. This provides additional support for charter schools as a significant influence in increasing PBE rates in California kindergartens.

In summary, results from the GWR models demonstrate that there is local variation in covariate effects, but that the distributions of local effects vary across covariates. The ability of covariates to produce positive and negative local effects indicates that the influence of covariates is likely modified by other spatially dependent process or omitted variables. Covariates that produce consistently positive and statistically significant local effects, such as percent non-Hispanic white and private school status, may be particularly important to spatially dependent relationships.

Spatial econometrics models were then estimated to examine the potential underlying processes of spatial dependence in PBE rates. Improvement in model fit, as measured by reduction in AIC, produced by spatial lag and spatial error models are presented in Figure 4.4. An OLS model that does not incorporate spatial dependency is used for the baseline comparison for values of AIC. Figure 4.4 suggests two findings. First, spatial lag models generally provide improved fit over spatial error models, which suggest spatial spillover in PBE rates. As the number of nearest neighbors included in the spatial weights matrix increases, the AIC values generally decrease, but inconsistently and with decreasing returns after 15-NN.[68] The reduction in AIC for k-NN values of 20 through 50 is shown in Figure A4.1 in Appendix. Table A4.2 in Appendix shows that Lagrange Multiplier tests also indicate that spatial lag models generally provide better specification for the spatial dependence in the data. Second, Figure 4.4 also shows that using all nearest schools as neighbors provides a significantly better fit than using only the nearest schools of the same type. This is at least partially attributable to the increased distance of

[68] The difference between AIC values for spatial lag and spatial error models also decreases as the number of neighbors included in the weights matrix increases, as might be expected from a local spillover process.

the nearest neighbors when restricting the weights matrix to only other schools of the same type. But if parents were looking primarily to parents in peer schools for cues on vaccine decisions, geographical proximity may not be the most important factor, as observed in other studies on diffusion (Soule 1997).

To examine the potential indirect effect of covariates, spatial Durbin models were estimated using a 15-NN weights matrix for all nearest schools.[69] I chose to estimate the spatial Durbin models for 15-NN as it provided a lower value of AIC than for 5-NN or 10-NN and Lagrange Multiplier tests showed no significant spatial dependence in the spatial lag model residuals for most years.[70] Figure 4.5 presents these results. These results provide insight into whether spatial heterogeneity shown in the GWR models can be attributed to spillover effects of covariates in neighboring schools.

First, the variables that were shown to have lower proportions of significant local effects, particularly counts of physicians (Figure 4.5A) and autism diagnoses (Figure 4.5D), also do not show many significant direct or indirect effects in the spatial Durbin model. Interestingly, alternative health practitioners, particularly acupuncturists (Figure 4.5C), are more likely to have statistically significant indirect rather than direct effects over this period. Chiropractors also have small indirect effects, but they are only significant in a few years (Figure 4.5B). This suggests that the effects of these practitioners may span larger areas than just in the schools located most nearby. The result for acupuncturists in particular may be responsible for the greater proportion

[69]As shown in Figure A4.1 in Appendix, AIC does continue to reduce slightly until approximately 30 NN. The magnitude of reduction decreases as NN increases over 15. I examined results from spatial Durbin models for many values of NN, particularly those between 25 and 35; the results do not substantially change.

[70] There was one exception—the model for 1998 showed mildly significant spatial dependence in residuals. Ideally, after spatial dependency is properly incorporated into regression models, the residual terms should not show significant spatial autocorrelation.

of significant local effects shown in the GWR results yet the insignificant findings in the previous chapter.[71]

More importantly, the only socio-demographic variable that exhibits consistent indirect spatial spillover effects is percent non-Hispanic white, particularly after 2003. Although percent non-Hispanic white (Figure 4.5F) and mother's education (Figure 4.5E) have similar direct effects on school PBE rates, only percent non-Hispanic white has statistically significant indirect effects. This suggests that racial/ethnic composition matters not only in the local area around a school, but also in the surrounding neighborhoods.

Logged block group density also shows significant indirect effects, but only in the first few years (Figure 4.5G). This indicates that PBE rates were initially higher in more rural areas. Property values (Figure 4.5H) do not show consistent significant direct or indirect effects over time, although, interestingly, direct effects tend to be positive and indirect effects negative. Some of the variation in local covariates shown in the GWR models could be attributable to the opposite signs in direct and spillover effects, although it is difficult to draw these conclusions when effects are only significant in a handful of years.

Despite the strong positive effects shown by school type in the GWR models, neither private (Figure 4.5I) nor charter (Figure 4.5J) school status shows consistent indirect effects on PBE rates in neighboring schools. Surprisingly, the few statistically significant indirect effects shown for charter school status in later years are *negative* rather than positive. Based on the GWR results and increasing PBE rates over time, I suspected there might be a positive spillover effect on PBE rates from private and charter schools to nearby public schools, yet results are not consistent with this hypothesis. Rather, if anything, private and charter schools may be attracting

[71] The lack of direct effects in some years may be influenced by the increased likelihood of PBEs in rural areas. Acupuncturists may influence PBE rates in the general area, but not necessarily in the local business district where the office is located.

vaccine hesitant parents over time, increasing the disparities between PBE rates in these schools and neighboring public schools.[72] For this data, this could be in part a result of parents of children selecting into charter schools in neighboring communities.

Finally, to further examine possible diffusion of PBEs, spillover effects of having neighboring schools with high PBE rates in the preceding year are shown in Figure 4.6. Using an indicator of high PBE rates in the previous year preserves the temporal order assumed in diffusion processes. These results are net of the direct impact of whether the school itself had a high PBE rate and both the direct and indirect effects of the other covariates described above. The strongest effects are shown when neighbors are defined as nearest schools of all types (Figure 4.6A). Using nearest schools of the same type instead (Figure 4.6B) also has some positive effects, albeit smaller and not consistently statistically significant. This is consistent with the results above demonstrating that the nearest schools of any type most influence PBE rates. Again, this could be a product of increased distance between schools of the same type, but emphasizes that the spillover effects on PBE rates are likely occurring in spatially local areas and are not confined within particular types of schools.

As shown in Figure 4.6A, as the number of neighbors included in the model increases, there are decreasing returns on the positive effects on school PBE rates. In other words, the nearest 5 to 10 schools provide the greatest influence on PBE rates. Using the 15 or 20 nearest neighbors continues to show positive effects, but it is largely capturing the effects present when only 10 neighbors are included in the model. These results are also generally consistent with those obtained from a panel spatial lag model with random effects over the full analysis period demonstrating that high PBE rates in the most nearby schools in the previous school year has a positive effect on PBE rates (Figure A4.3 in Appendix).

[72] To be fair though, the negative indirect effects for charter schools are only statistically significant in 2011.

Discussion

As PBE rates have increased in California kindergartens over time, PBEs have been observed in a greater percentage of schools and spatial autocorrelation of PBE rates has also increased. Results in the previous chapter suggested that the broader spatial clustering of PBEs in California could not be attributed to selection processes based on school-level correlates. The spatial econometrics analyses presented in this chapter extend this discussion to examine how spatial externalities in covariate effects and endogenous processes, such as diffusion, may be responsible for the high inequality in PBE rates across schools. Separating this type of social process from residential sorting is important for understanding how pockets of unvaccinated children are formed and may be targeted in intervention strategies.

Significant local variation in covariates effects PBE rates, as shown in the GWR models, suggests the neighborhood characteristics do not uniformly affect PBE rates over space. Investigation of whether local variation in the covariate effects could be attributed to spatial spillover effects showed mixed results. Only percentage non-Hispanic white had consistent indirect effects. Acupuncturists also showed indirect effects, which may explain the local variation in its effects, despite the insignificant result in the full model in the previous chapter. Furthermore, school type failed to show significant spillover effects, despite strong positive local effects.

Improved model fit for spatial lag over spatial error models is consistent with spillover effects of PBE rates. This was also supported by positive effects of having nearby schools with high PBE rates in the previous year. The positive indirect effects of percent non-Hispanic white children in nearby schools suggest that these parents play a significant role in the increasing rates of non-medical vaccine exemptions. As many social ties in the U.S. are racially/ethnically

homophilous, the indirect effects of percent non-Hispanic white may be picking up effects of spatial diffusion of vaccine hesitancy across nearby schools with high proportions of non-Hispanic white children.

These findings are limited by the use of administrative data. Data is not available for individual-level locations of PBEs, boundaries for school enrollment, and parental networks. The local area around a school is defined here as a 500-kid radius. If school neighborhoods actually span wider areas, this may affect the findings of the spatial models.[73] The challenge is to fit models at a geographical level that captures spatial variation without fitting too much to local idiosyncrasies. The macro-level results presented here suggest the presence of spatially dependent processes in generating clusters of PBE rates across local school areas. Future research on micro-level processes is needed to uncover how socio-demographic characteristics, such as race/ethnicity, consistently contribute to generating these larger spatial patterns of non-medical exemptions.

These results were also limited by the use of year cross-sectional data to examine dynamic processes that unfold over time. Existing spatial panel methods do not yet allow incorporation of temporally lagged effects (Millo and Piras 2012; Parent and LeSage 2012). Regression modeling of both spatial and temporal dependency can be difficult due to endogeneity and potential non-stationarity in both time trends and spatial dependency, which can produce biased estimates of parameters. More sophisticated dynamic space-time models estimated via simulation (Lee et al. 2014) could be used to better estimate expected patterns of

[73] As discussed in the methods section above, how you define neighbors in spatial econometrics models can meaningfully affect your results. In practice, the definition of the size of the school neighborhood could also affect the results presented here. Like number of neighbors included in the spatial weights matrices, I suspect that substantial increases in the size of the school neighborhood will decrease differences in fit between spatial lag and spatial error models, as well as decrease reduction in AIC compared to standard OLS models. As the geographical area under examination increases, it would be expected that some of the differences over space average out and estimates tend more toward the global averages presented in standard regression models.

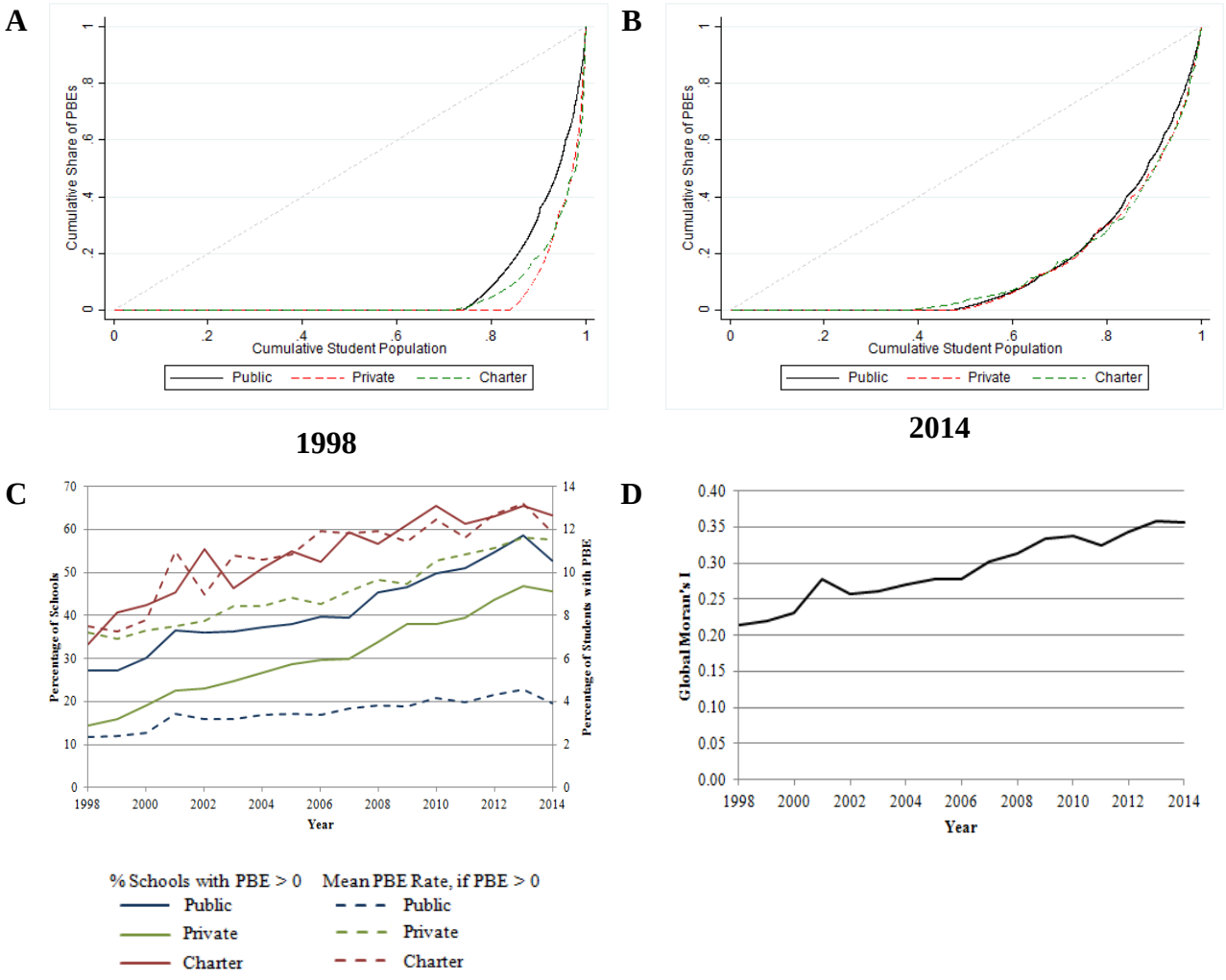
particular diffusion processes over time. Event history analysis could also offer insights specifically into the dispersion of PBEs over time by examining time-varying effects on the hazard rate of a school having at least one enrolled child with a PBE.

Conclusion

The results presented here move beyond a static representative of social determinants and emphasize the importance of investigating local spillover to better understand underlying processes that may be responsible for the spatial patterns of non-medical vaccine exemptions across schools. Examining how spatially dependent social processes generate these local effects is an important step in identifying the merging of social and spatial patterns in vaccine exemptions (Wang et al. 2014). The results are consistent with qualitative research that suggests that parents are aware of social norms toward vaccination and are influenced by others in their social networks (Attwell and Freeman 2015; Gaudino and Robison 2012; Sobo 2015). Social marketing campaigns that target specific segments of the population while addressing local social norms and misconceptions associated with vaccination may be more effective in influencing hesitant parents to vaccinate (Chiprich and White 2011; Opel et al. 2009). The results presented here and in the previous chapter demonstrate that significant spatial dependence exists in locations of children with PBEs in California. The next two chapters will examine the consequences of this clustering on local measles risk.

Figures

Figure 4.1: Spatial concentration and dispersion of PBE rates in California kindergartens, 1998-2014



Note: Concentration of PBEs within schools has decreased slightly over time, although the distribution remains highly uneven regardless of school type, as shown in Lorenz curves for 1998 (A) and 2014 (B). If PBEs were evenly distributed across the student population, the lines should fall on the diagonal (as shown by the light gray dashed line). The proportion of schools with at least one enrolled child with a PBE has increased over time, regardless of school type, as has the mean PBE rate in all schools with at least one exemption (C). Not only is the mean PBE rate higher in charter and private schools, it has also experienced a steeper gradient of mean increase across this period. Finally, the spatial autocorrelation among PBE rates in neighboring schools, measured by global Moran's I, has increased over time (D). All values of Moran's I are statistically significant at $\alpha < .001$.

Figure 4.2: Diagrams of spatial relationships in autocorrelation among school PBE rates in spatial error (A), spatial lag (B), and spatial Durbin lag (C) models

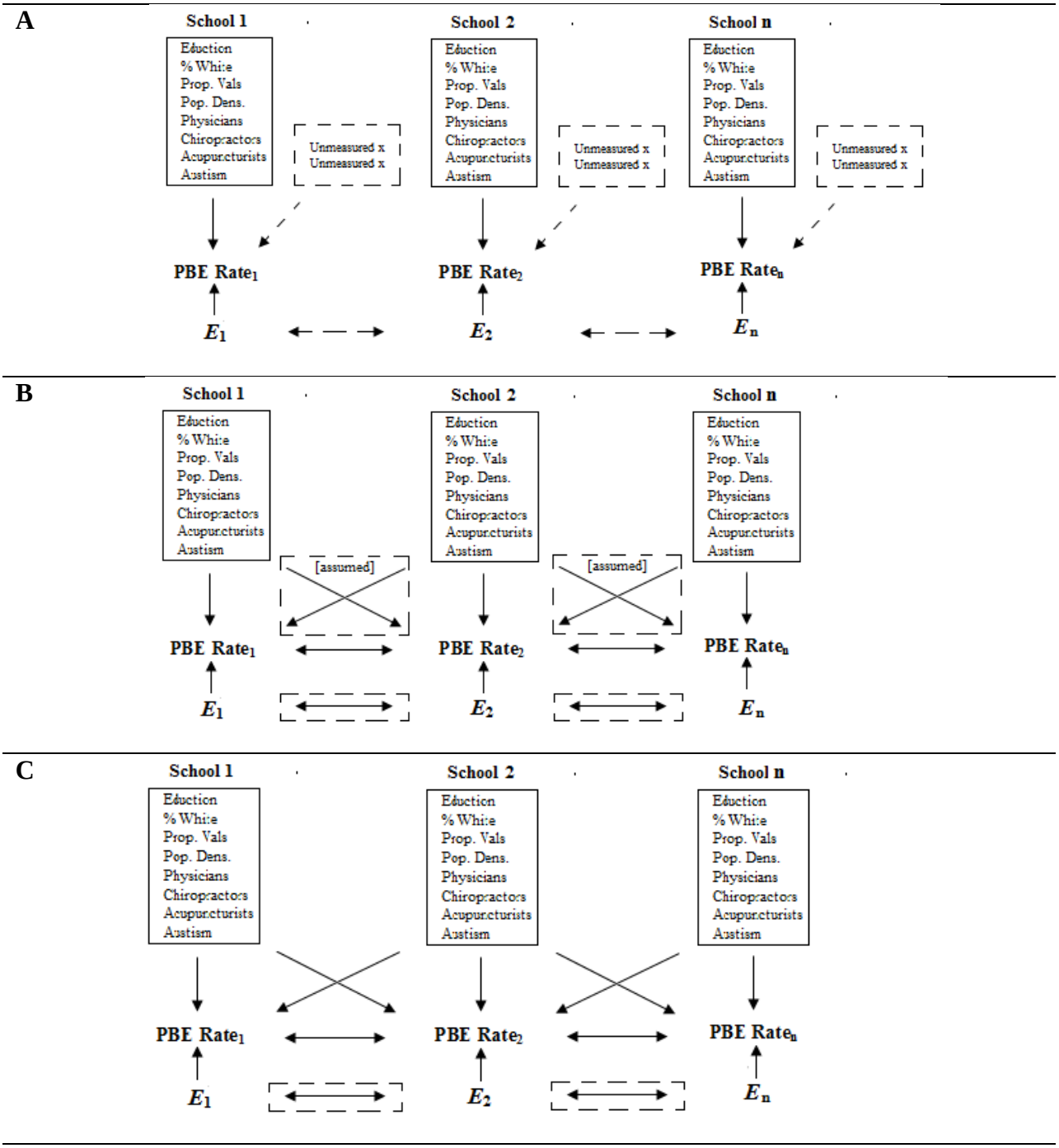
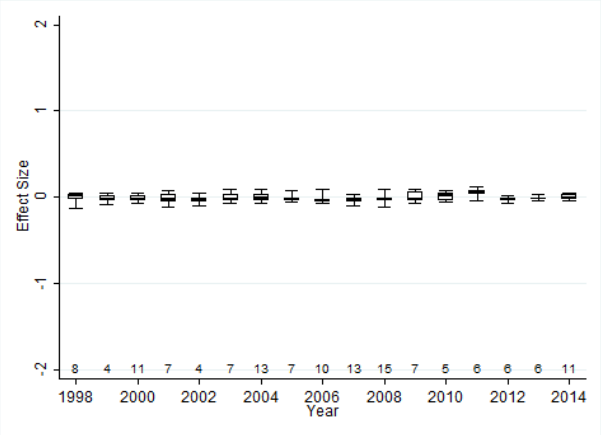
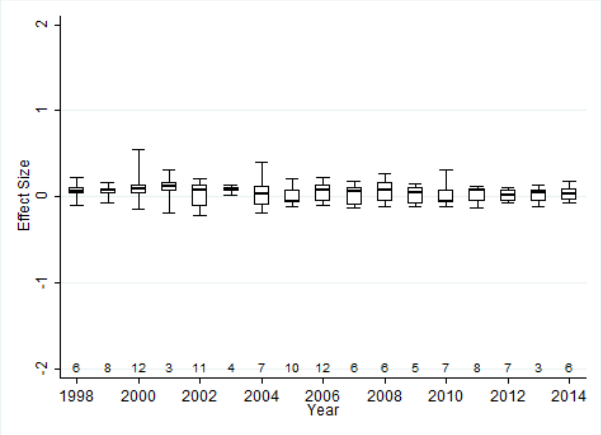


Figure 4.3: Local variation in covariate effects in GWR models, 1998-2014

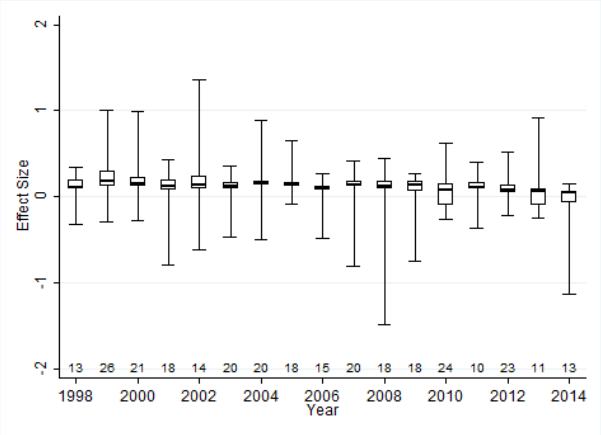
A. Reduction in AIC for GWR Models



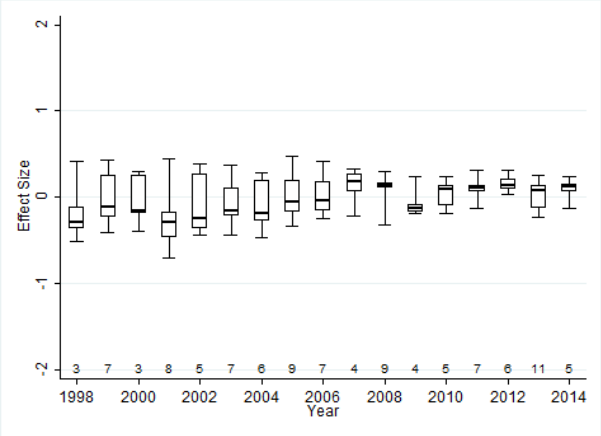
B. Physicians



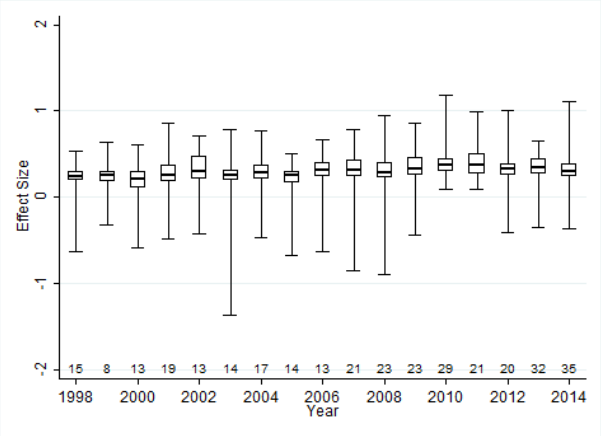
C. Chiropractors



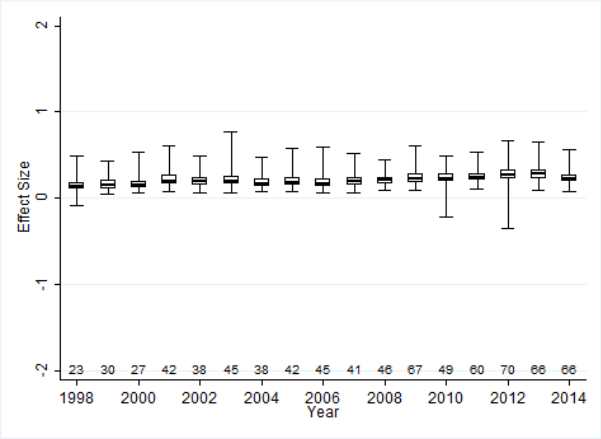
D. Acupuncturists



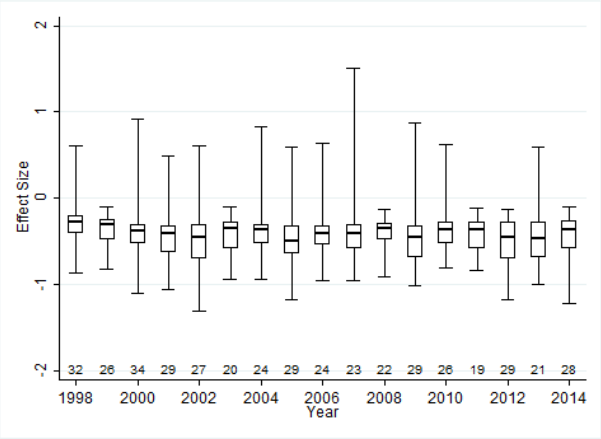
E. Autism cases



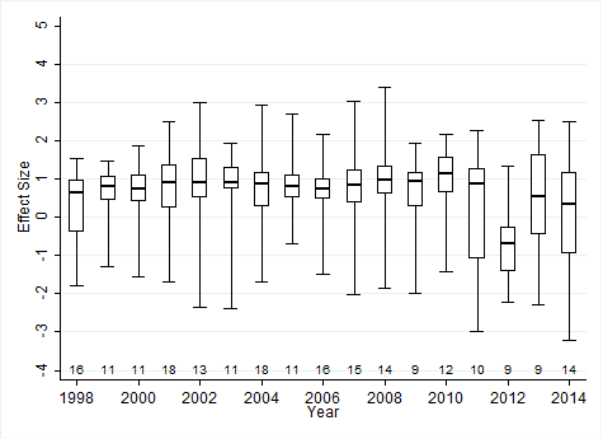
F. Mother's education



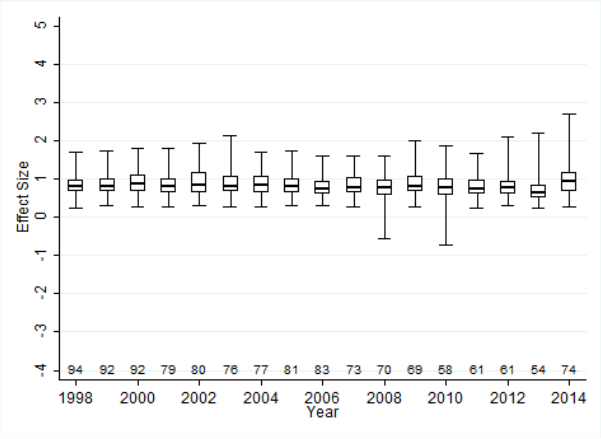
G. Percent non-Hispanic white



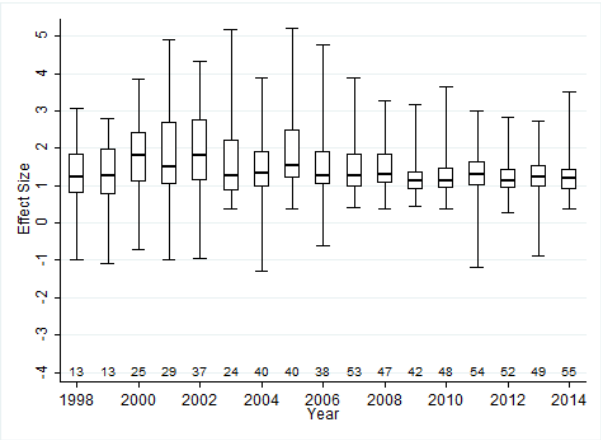
H. Block group density (logged)



I. Property values (logged)



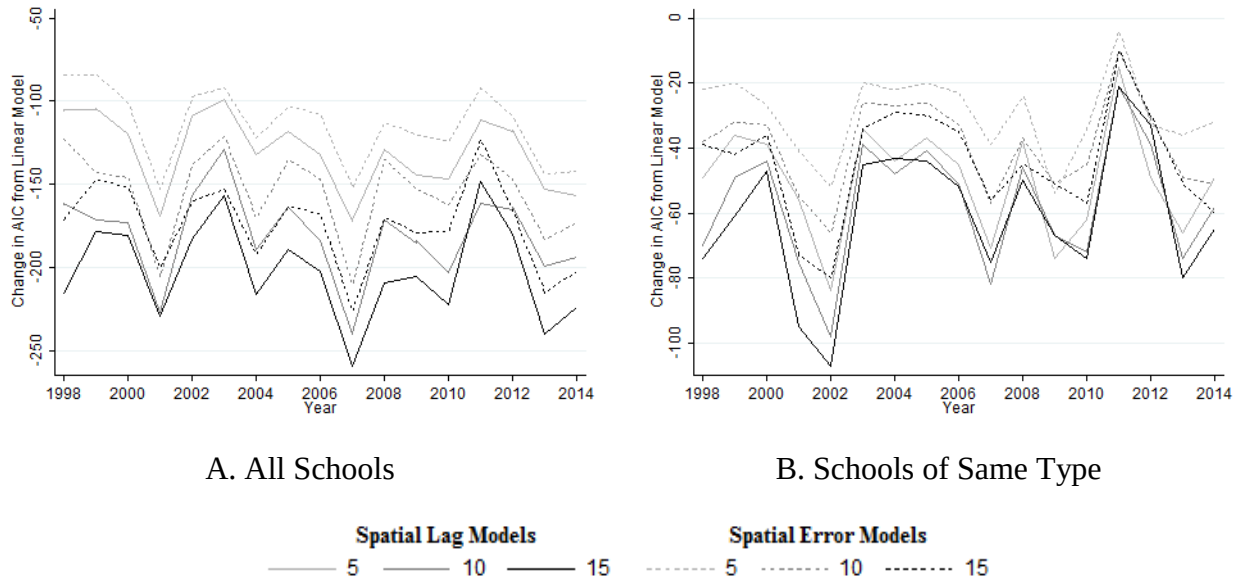
J. Private school status



K. Charter school status

Note: Percent of locally significant coefficients shown above the x-axis. The box plots include only statistically significant ($\alpha < 0.05$) local coefficients; the values shown are the minimum effect size (lower whisker), 25th percentile (lower bound of box), median (midpoint of box), 75th percentile (upper bound of box), and maximum (upper whisker). Bandwidth set at 0.01. Figure 3A reports the reduction in AIC in GWR models as compared to OLS models.

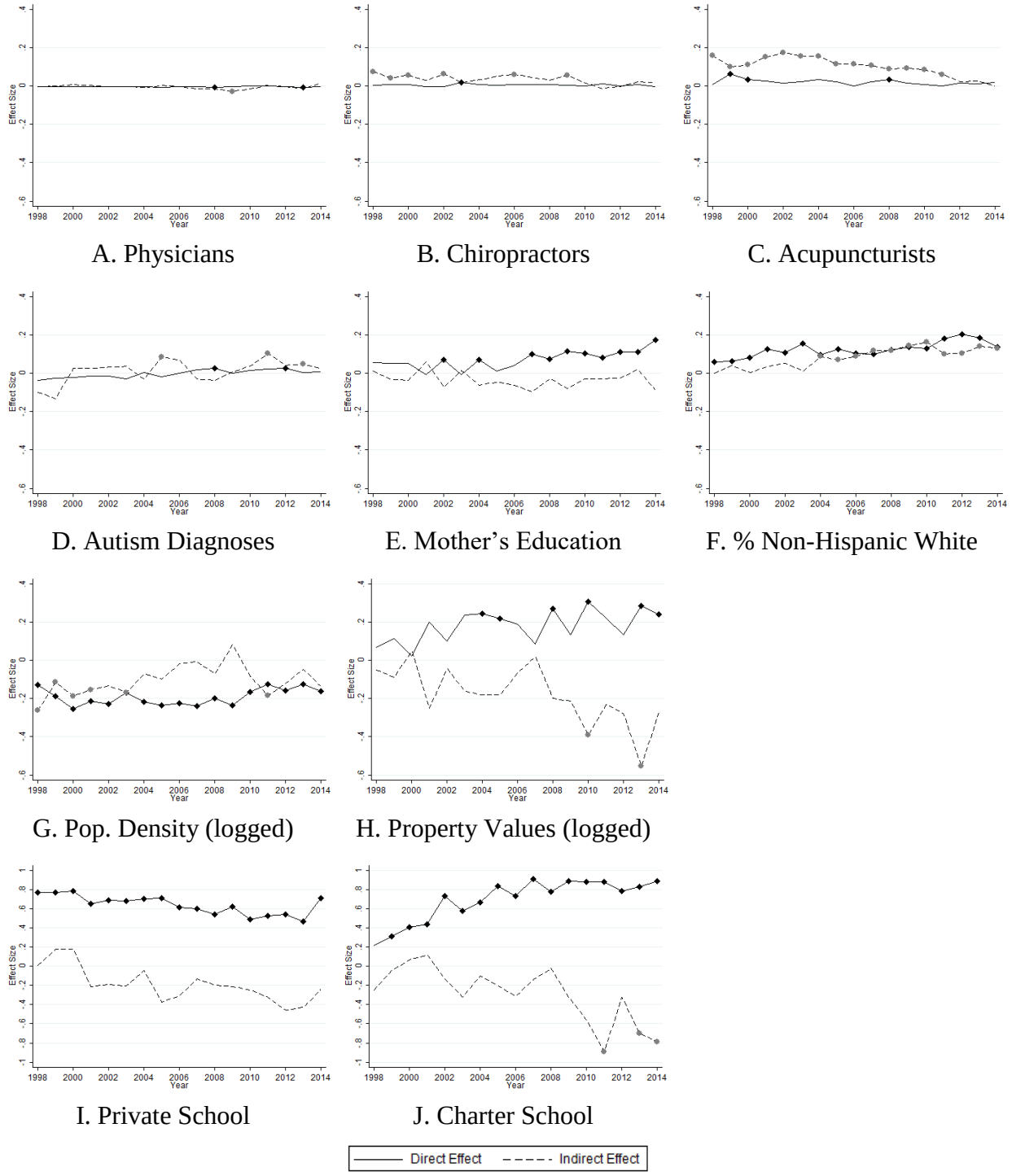
Figure 4.4: Reduction in AIC (compared to OLS models) for spatial autocorrelation models



Note: Results are shown for models with 5, 10 and 15 nearest neighbors for both all nearest schools (A) and nearest schools of the same type (B). These comparisons demonstrate that: 1) Spatial lag models generally fit the data better than spatial error models, indicating a spillover effect between PBE rates in neighboring schools. 2) Defining neighbors as all nearest schools results in a better fit than assigning neighbors as the nearest schools of the same type (notice differences in the scale of the y-axis). The preferred models support that PBE rates may be a result of a local spillover process among geographically nearby schools. Although some of the differences in AIC look quite small, very small reduction in AIC can be used as evidence of a significantly better model fit (Fotheringham et al. 2003).[74] Models were estimated independently for each year; dependent variable is logged school PBE rate and covariates include: mother's years of education, percent non-Hispanic white, Census block group density (logged), average property values (logged), count of physicians, acupuncturists, chiropractors, and children diagnosed with autism in the school's 500-child radius and dummy variables representing school type. Nearest neighbor values of 5 through 50 (in increments of 5) were tested for each year and neighbor type (Figure A4.1 in Appendix).

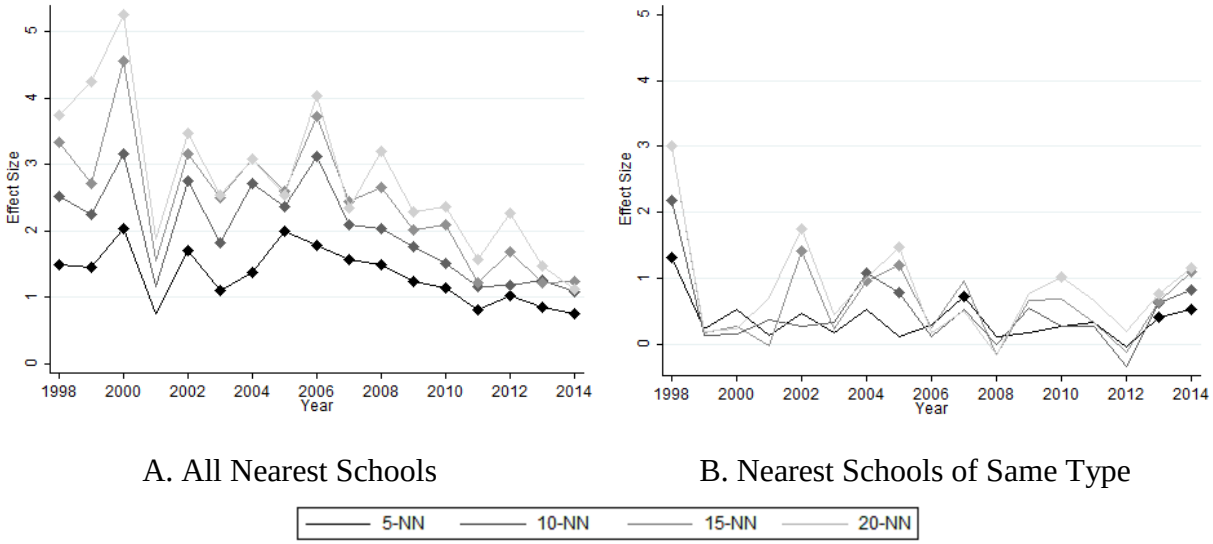
[74] Fotheringham et al (2003) suggest that an absolute difference of 3 in AIC is sufficient evidence to prefer one model over another.

Figure 4.5: Direct and indirect effects of covariates



Note: Covariates with spatial externalities have indirect as well as direct influence. Effect sizes estimated using spatial Durbin models with 15-NN for all nearest schools. Lines show all estimated effect sizes; points mark only those statistically significant using $\alpha < .05$. Covariates with spatial externalities should have indirect as well as direct influence. Effects of charter and private school status are separated in the fourth row due to differences in axis scales.

Figure 4.6: Effect of having neighboring schools with high PBE rates in the previous year



A. All Nearest Schools

B. Nearest Schools of Same Type

Note: High PBE rates in the geographically nearest neighbors, regardless of school type (A), has a more consistent positive effect on PBE rates in a school than nearest schools of the same type (B), controlling for the direct effect of a school itself having a statistically significantly higher PBE rate in the previous year. Nearest neighbors are grouped in increments of 5 to show decreasing returns on positive effects as distance increases. Lines show all effect sizes; points represent only those statistically significant at $\alpha < .05$. Effects were estimated using spatial Durbin models, controlling for mother's years of education, percent non-Hispanic white, Census block group density (logged), average property values (logged), count of physicians, acupuncturists, chiropractors, and children diagnosed with autism in the school's 500-child radius, indicator variables representing school type, and the direct effect of a school itself having a high PBE rate in the previous school year. Results using yearly standardization are generally consistent with those presented here, as shown in Figure A4.2.

Appendix

Table A4.1: Yearly observations, by school type

Year	Public	Private	Charter	Total
1998	4537	1826	124	6487
1999	4616	1738	131	6485
2000	4666	1769	146	6581
2001	4737	1749	166	6652
2002	4772	1644	181	6597
2003	4814	1509	199	6522
2004	4806	1450	204	6460
2005	4869	1419	213	6501
2006	4931	1404	223	6558
2007	4957	1368	235	6560
2008	4924	1236	241	6401
2009	4974	1155	277	6406
2010	4930	1189	290	6409
2011	4961	1163	323	6447
2012	4948	1186	388	6522
2013	4932	1205	409	6546
2014	4952	1126	446	6524

Note: These yearly counts serve as the N for all the spatial models presented in this chapter, unless otherwise noted.

Table A4.2: LaGrange Multiplier tests for spatial dependence, 1998-2014

Year	LM Error	LM Lag	Robust LM Error[1]	Robust LM Lag[2]
1998	241.28***	319.47***	0.26	78.45***
1999	218.09***	262.57***	1.87	46.34***
2000	219.59***	258.61***	3.17	42.19***
2001	303.98***	336.55***	10.77**	43.35***
2002	226.79***	256.96***	6.81**	36.98***
2003	227.71***	221.95***	21.67***	15.91***
2004	288.40***	309.75***	15.91***	37.27***
2005	231.74***	266.95***	9.03***	44.24***
2006	241.61***	283.44***	6.56**	48.39***
2007	356.86***	386.02***	21.76***	50.93***
2008	255.08***	295.55***	11.96***	52.42***
2009	265.24***	278.50***	23.97***	37.24***
2010	255.41***	301.70***	11.00***	57.29***
2011	173.96***	197.66***	9.90***	33.61***
2012	252.05***	247.76***	30.73***	26.44***
2013	330.84***	334.94***	38.05***	42.15***
2014	307.92***	309.21***	37.72***	39.01***

Note: Models estimated for 15 nearest schools (all types). Values shown are $\chi^2(1)$ test statistics, with significance represented as *** $p < .001$; ** $p < .05$.
[1]Robust LM error model tests for presence of spatial dependency in errors after accounting for spatial lag process.
[2]Robust LM lag model tests for presence of significant spatial lag after account for spatial dependency in errors.

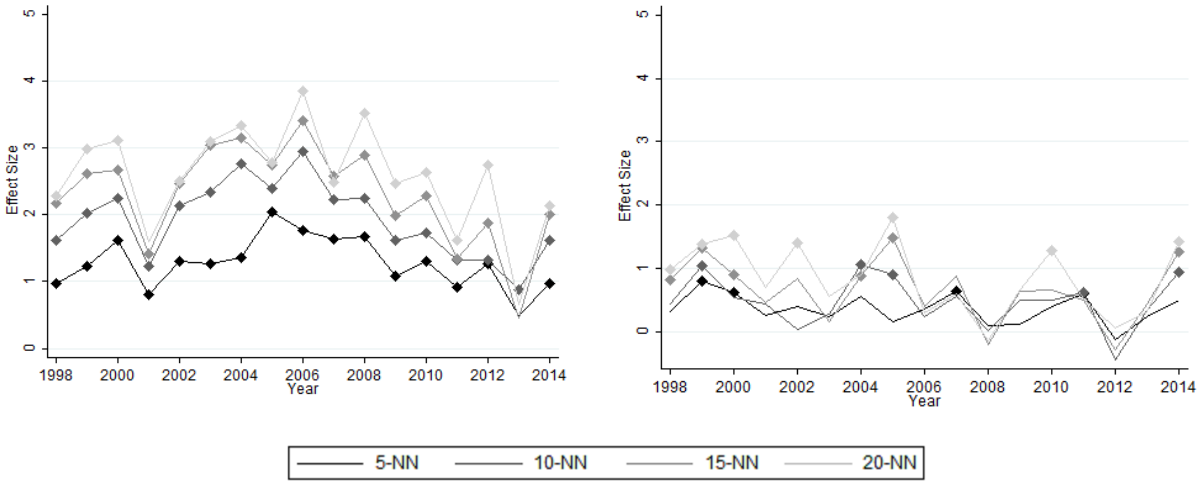
Figure A4.1: Reduction in AIC (compared to OLS) for spatial autocorrelation models, nearest 5 to 50 neighbors for all schools (A) and schools of the same type (B)

A

B

Note: Note differences in y-axis scale—defining nearest neighbors as all schools rather than nearby schools of the same type almost always results in a larger reduction in AIC, regardless of specification of *k*. The best fitting models should produce the lowest values of AIC; however, as shown in the graphs above, there is no value of *k* that consistently produces the best fit across all years. The best fitting models (i.e. lowest values of AIC) are generally produced when including from 15 to 35 neighbors, although, overall, there are diminishing returns on reduction to AIC for increasing the number of neighbors above 15.

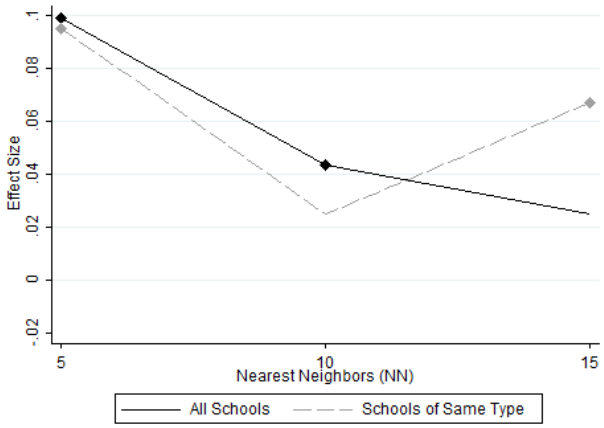
Figure A4.2: Effect of having neighboring schools with high PBE rates in the previous year, as measured by yearly standardized rates



A. All Nearest Schools B. Nearest Schools of Same Type

Note: Models were estimated independently for each year using spatial Durbin models, controlling for mother's years of education, percent non-Hispanic white, Census block group density (logged), average property values (logged), count of physicians, acupuncturists, chiropractors, and children diagnosed with autism in the school's 500-child radius, indicator variables representing school type, and the direct effect of a school itself having a high PBE rate in the previous school year.

Figure A4.3: Effect of neighboring schools with high PBE rates in the previous year, 1998-2014



Note: High PBE rates were defined as having a PBE more than 2 standard deviations above the standardized mean. Results were obtained from a balanced panel spatial lag model using 15-NN weights, and controlling for having a high PBE rate in the school in the previous year, mother's years of education, percent non-Hispanic white, Census block group density (logged), average property values (logged), count of physicians, acupuncturists, chiropractors, and children diagnosed with autism in the school's 500-child radius, dummy variables representing school type, and dummy indicators for year; yearly n= 4,373, overall N= 74,341.

Chapter 5: How Spatial Clustering of Non-Medical Vaccine Exemptions Affects Locations of Measles Transmission in Social Networks

Abstract

Physical contact in social networks structures transmission of infectious disease. The small-worlds model emphasizes the role of weak ties in disease spread by facilitating transmission between local clusters in the network. Yet, for diseases in highly vaccinated populations, such as measles in the U.S., contact with strong ties—those we interact with frequently—may play an important role in disease transmission among unvaccinated children. An empirically calibrated simulation model using 9,059,060 children shows that, with or without spatial clustering of PBEs, schools are predominant sites of measles infections. Yet, clustering of PBEs in charter schools increases the opportunity for transmission. Additionally, households only become important transmission settings when siblings share vaccination status. Community interaction results in a smaller percentage of infections overall, yet does reduce outbreak size when eliminated from the model. Physician offices are the most frequent sites of community infections due to exposure of infants too young to be vaccinated. These findings emphasize the important role strong ties play in disease transmission when children who lack vaccination are clustered within social networks and have implications for containment strategies.

Chapter Introduction

Disneyland grabbed headlines in early January 2015[75], when it emerged as the common exposure setting in an escalating measles outbreak. Infections spread to 7 U.S. states, Canada, and Mexico (Zipprich et al. 2015), sparking intense debate over vaccines (Blumberg et al. 2015; Radzikowski et al. 2016) and vaccine refusals (Yang, Barraza, et al. 2015). However, visits to Disneyland during the initial exposure period accounted for only 32% of the cases reported in California; infections acquired at the Disney theme parks were carried back to local communities where the disease continued to spread (Harriman 2015).

This chapter transitions from investigating social processes that influence spatial clustering of children with non-medical vaccine exemptions to examining its effect on disease spread. Examining how outbreaks move through social networks is important for understanding the ways in which social processes shape patterns of biological contagion and have implications for disease prevention and containment strategies. How does spatial clustering of non-medical vaccine exemptions affect the types of social ties through which measles is transmitted? Like social diffusion, biological contagion is heavily influenced by the structure of contact in social networks (Granovetter 1973; Newman, Barabási, and Watts 2006). While weak social ties, those that reach outside local clusters of interaction, likely introduce measles infections to new areas of a network (Watts 2004; Watts and Strogatz 1998), this chapter demonstrates that the clustering of vaccination exemptions makes strong ties play a crucial role in continued transmission in local communities due to their ability to connect unvaccinated children.

This chapter begins with a discussion of contact and disease spread in social networks. I then introduce a cross-sectional synthetic population of California youth in 2014 and an agent-

[75] While visitors to the park contracted measles in December 2014, cases were not reported to the California Department of Public Health until early January 2015.

based simulation model I built to examine the role of social ties in measles transmission. Vaccine-preventable disease outbreaks are highly stochastic events, particularly in developed countries where a disease is no longer endemic[76] (Bjørnstad, Finkenstädt, and Grenfell 2002). The simulation experiment models disease transmission as a dynamic, stochastic process to understand the variation in outcomes that can result from identical populations and transmission parameters (Bolker and Grenfell 1993; Bruch and Atwell 2015; Rahmandad and Sterman 2008). I conclude with a discussion of why interaction among unvaccinated children is an important component of understanding localized disease risk.

Social Contact and Disease Spread in Networks

Social networks affect health not only through social processes of diffusion, residential sorting, and establishing local norms, but also by providing paths for biological contagion. Unlike social influence, which can occur via many channels, networks shape biological contagion through structuring physical contact (Smith and Christakis 2008). Contact in networks is assortative; people tend to interact with like others, such as those who are of similar age, speak the same language, or share the same affiliations (Newman 2003), and these mixing patterns correspond with local community structure in large social networks (Newman and Girvan 2003; Newman and Park 2003). Human mobility patterns tend to be geographically local; high regularly and repeated interaction in local neighborhoods shapes opportunities for contagion (González et al. 2008; Mossong et al. 2008), particularly for disease spread through casual physical contact (Ferguson 2007).

[76] Again, non-endemic diseases are those not continuously transmitted for a period of 1 year or more in a geographical area. Measles has been non-endemic in the U.S. since 2000, a result of maintaining sufficient herd immunity to prevent continuous transmission in the population (Hinman, Hutchins, Bellini, et al. 2004; Orenstein and Papania 2004).

Even though much of our physical interaction tends to occur with those who share socio-demographic characteristics and are geographically proximate, disease outbreaks have the ability to quickly transform from local clusters of cases into global epidemics (Watts 1999, 2004). This is due to the small-worlds properties of real-world social networks. Small-worlds models contain both local clustering resulting from regular and overlapping social interaction (usually associated with strong social ties) and more long-range connections formed through less frequent interaction outside local clusters in our networks (typically attributed to weak social ties) (Watts 2004; Watts and Strogatz 1998).

Small-worlds properties in social networks increase disease spread through a combination of global and local efficiency. The local clustering in small-worlds networks provide sufficient redundancy that permits flow among proximate nodes even if some nodes in the cluster are removed (local efficiency) while the long-range ties allow relatively short, navigable paths between more distant nodes (global efficiency) (Latora and Marchiori 2001). The long-range ties, in particular, allow disease to spread more quickly across local clusters in the network (Moore and Newman 2000). Having even only a small proportion of social ties extend outside local clusters to distant parts of the network significantly reduces both the level of infectiousness required to infect half of a population and, in cases of highly infectious diseases, significantly reduces the time necessary to completely saturate the population (Watts and Strogatz 1998).

While long-distance travel creates opportunities for the introduction of disease to new areas (Chen et al. 2010; Sugerman et al. 2010), patterns of interaction in social networks sustain transmission locally. Contact with strong ties, those we interact with regularly based on membership in enduring social structures, such as households and schools, may limit the reach of the disease, while weak tie interaction, the infrequent contact with others who may or may not be

previously known to us in the neighborhood and larger community, may extend it. For non-endemic diseases in highly vaccinated populations, such as measles in the U.S., the actual distributions of unvaccinated children modify these patterns of transmission via strong or weak ties. Empirically calibrated simulation models allow examination of the aggregate effects of individual decisions against vaccination that is not otherwise possible with abstract models or in real-world settings (Hedström and Åberg 2005).

Measles Transmission

Measles is easily spread through casual physical contact (Ferguson 2007) or airborne transmission (de Jong and Winkler 1964). Infections occur most commonly in children; this was the case both before (Top 1938) and after routine vaccination (Markowitz et al. 1989).Children not only tend to interact with others close to their own age(Del Valle et al. 2007; Del Valle, Hyman, and Chitnis 2013; Longini, Ackerman, and Elveback 1978; Schenzle 1984), but are also more likely to have contact adequate for transmission of diseases spread through casual physical contact compared to adults (Del Valle et al. 2007). Significant amounts of children's contact with family members in the household and other children who attend the same school (Del Valle et al. 2007; Longini et al. 1982; Mossong et al. 2008; Viboud et al. 2004). Schools and childcare centers in particular have been dominant transmission settings for many measles outbreaks (Centers for Disease Control and Prevention 2004; Chen et al. 1989; Davis et al. 1987; Feiken et al. 2000; Gustafson et al. 1987; Hull et al. 1985; Markowitz et al. 1989; Marks, Halpin, and Orenstein 1978; McCombie et al. 1988; Nkowane et al. 1987; Wassilak et al. 1985). Outbreaks in schools can be carried to back to households, where siblings are exposed (Gindler et al. 1992; Markowitz et al. 1989), and into the wider community (Longini et al. 1982; Viboud et al. 2004).

In the vaccine era, when transmission in the general population is less common, children under five years of age are particularly vulnerable to measles infections (Gindler et al. 1992; Hinman, Hutchins, Baughman, et al. 2004). In some outbreaks, the highest attack rates[77] are experienced among infants under one year of age that are not yet eligible for vaccination (McCormick, Halsey, and Rosenberg 1977). Increased susceptibility to measles infection has been observed among children with mothers born after 1963 due to reduced levels of inherited maternal immunity (Papania et al. 1999).[78] Medical settings, particularly pediatrician offices, contribute significantly to exposure to the disease for children under five years of age in the larger community (Davis et al. 1986; Gindler et al. 1992) and serve as a common locations for measles infections (Bloch et al. 1985; Markowitz et al. 1989).

Few previous epidemiological studies have documented how transmission settings are affected by patterns of selective vaccine refusal.[79] Locations of measles transmission are a product of not only where physical contact is likely to occur, but also where vulnerable children can be reached. The previous two chapters demonstrate that children with PBEs are not distributed randomly across geographical space. The simulation model used here can examine how PBE clusters alter risk of infections in locations of frequent contact among children, which will have implications for containment strategies.

[77] Attack rates are the proportion of exposed individuals who become infected.

[78] Mothers who were born after license of the measles vaccine in 1963 are less likely to have been infected by the measles as a child; mothers who have experienced a previous measles infection develop and pass on higher antibody titers than those who have acquired immunity through immunization (Papania et al. 1999).

[79] Buttenheim et al (2013) present results from simulation experiments demonstrating that heterogeneity in physician policies toward unvaccinated children can create clustering of susceptible individuals in certain offices. This suggests increased risk of infection in these locations that may spillover into the local community; however, the simulation experiments do not explicitly model disease spread.

Hypotheses

Unvaccinated children are at higher risk for measles infection, and spatial clustering of unvaccinated children contributes to increased community-level risk of disease transmission (Feiken et al. 2000; Omer et al. 2009; Salmon et al. 1999). Schools and childcare centers are likely to be important transmission settings for measles regardless of PBEs due to the predominance of contact among children which occurs there; however, clustering of PBEs in these locations may increase their importance in measles transmission during outbreaks.

> Hypothesis 1A: Measles infections should be more common in schools when PBEs are spatially clustered than if PBEs were randomly distributed in the population.

Private schools and charter schools have higher PBE rates than non-charter public schools (Birnbaum et al. 2013; Brennan et al. 2016; Carrel and Bitterman 2015; Sobo 2015), which could create increased opportunity for measles transmission in these types of schools in particular.

> Hypothesis 1B: Charter and private schools should produce high percentages of infections relative to student enrollment than non-charter public schools.

As mentioned above, households are also an important setting for contact among children. Although the number of unique contacts in the household is limited, regular contact among siblings and the tendency to share vaccination status (Liu et al. 2015; Sugerman et al. 2010) likely contributes to increased risk of measles infection in this setting.

> Hypothesis 2: Higher percentages of infections should occur in households when PBEs are spatially clustered than would be expected if PBEs were distributed randomly.

As predicted by the small-worlds model, weak tie interaction may serve as important pathways through which new infections are sustained in the population due to redundancy in contact among strong ties in households and schools. At some point, exposure and infection

among susceptible individuals in these locations will become saturated. To sustain itself in the population long-term, the disease must travel outside local clusters into the larger network. Even if weak tie contact generates a small proportion of total measles cases, interaction in community settings, including neighborhoods, physician offices, and other public places such as shopping malls, may play a crucial role in spreading infections between strong tie settings (schools, childcare, and households).

> Hypothesis 3: Eliminating contact in community settings should significantly reduce the overall size of outbreaks, even if the percentage of infections generated in these locations is relatively low.

Synthetic Population

The synthetic population includes all children ages 0-17 in California in 2014. The foremost goal of creating this population was to capture where children with PBEs are located in California and the focal points where they are likely to interact with other children (Liu and Bearman 2015). The base population was built from age-year estimates by race/ethnicity for Census block groups in 2014 from 2015 ESRI Business Analyst.[80] Children were assigned household incomes and mother's level of education and employment status based on 2014 Census block group-level data from 2015 ESRI Business Analyst and the 2014 American Community Survey. Children were aggregated into families using predicted sibship size and sibling age gaps by race/ethnicity, mother's level of education, and geographical location[81] as informed by data from the 2000 California Birth Statistical Master File. Children were assigned

[80] Supplemental data from the 2010 Census was used to separate population counts of Hispanic/Latino children due to assignment as an ethnicity by the Census and a racial category by the California Department of Education.

[81] At the three-digit zip code level.

point-level geographical locations from population density estimates at the block level from the 2010 Census.

Children were assigned to schools based on 2014 enrollment records from the California Department of Education (CDE). School type (public, charter, private, or home school) was predicted by grade level based on race/ethnicity, mother's education level and employment status, and household income using data from the 2012 National Household Education Surveys Program.[82] Enrollment in licensed childcare was assigned for children ages 3-4 years using the same method with data from the California Department of Social Services.[83] Students were enrolled in schools based on distance and enrollment availability (Wheaton et al. 2009). For public schools (including charters schools) enrollment proportions by race/ethnicity were maintained. Race/ethnicity enrollment for private schools was informed by the 2012 Private School Universe Survey.[84] Grade assignment was based on age. Table 1 provides descriptive statistics for enrollments in the synthetic population.

Children were also assigned to neighborhood and community interaction locations. I define neighborhoods as the 2010 Census block group the child resided in. Use of block groups as neighborhoods is consistent with previous health research examining walkability (Frank et al. 2010) and access to resources of adolescents local areas (Gordon-Larsen et al. 2006).[85] Interaction points in the larger community occurred in two locations: physician offices and

[82] The National Household Education Surveys Program provides descriptive statistics on childcare and K-12 educational enrollment in the U.S. population.

[83] Childcare enrollment percentages for children ages 3-4 were consistent with state-level statistics available in the 2014 American Community Survey.

[84] Available from the National Center for Education Statistics; enumerates and provides descriptive statistics for U.S. private schools. CDE does not provide private school enrollment by race/ethnicity.

[85] Neighborhoods are also often defined as Census tracts in health research (e.g. Saelens et al. 2003), but preference was given to constituting neighborhoods as block groups in this population as all the agents are children and may not be expected to traverse as large of a daily "neighborhood" as adults.

shopping malls. Physician offices were included due to their noted role as transmission settings in epidemiological studies of measles infections, as discussed above. Children were assigned to a local physician[86] using standardized inverse weighted distance and location data from the American Medical Association's 2012 Directory of Physicians. Shopping malls were chosen to represent a general community location in which children may come into contact (Liu and Bearman 2015). There is nothing special about social contact in malls for disease spread in particular; they serve a more theoretical role in the model to represent community contact. Children in the population were assigned identifiers for the three nearest shopping malls. Shopping mall locations were collected from the Directory of Major Malls. Unlike neighborhoods and physicians, which can be expected to remain relatively constant for the simulation period, families visit many different locations in the larger community in relatively short periods of time. For this reason, before each visit, children were randomly[87] assigned to one of their three possible malls.

In addition to using an empirically informed synthetic population, this simulation experiment is novel in its use of reported PBE data[88] to assign children immunization status. PBE statistics are typically provided by the California Department of Public Health (CDPH) for students entering kindergarten and the 7th grade. Kindergarten and 7th grade PBEs in the synthetic population were assigned by school according to the 2014 data. Other grades were assigned PBE rates that are consistent with those reported in that school in their kindergarten or 7th grade year. Kindergarten rates were used for elementary grades, while 7th grade rates were

[86] Includes pediatricians, family and general practitioners.

[87] There is some bias toward closer malls if there is substantial difference in distances to the three nearest malls.

[88] Children with PBEs may be entirely unimmunized or may only be missing one or two required vaccines. Again, for this project, no assumptions are made about partial vaccination.

used for middle school grades. For the 2011-2012 school year, PBE statistics were reported for the 7th through 12thgrades; these rates were used to determine appropriate PBE rates in high school grades. Schools and grades with missing PBE data[89] were assigned average PBE rates of that school type (public, private, charter) in the same school district.[90] Home-schooled children were assigned PBEs rates in private schools located in the same county.[91] Licensed childcare PBE rates were assigned as reported in 2014, and those missing data were assigned rates of the same center type (daycare or Head Start) within the same county. Children ages 0-4 not in licensed childcare were assigned to have the same PBE rates as children in childcare in the same county. Infants under 1 year of age were considered to be unvaccinated as the CDC does not typically recommend the first dose of the MMR vaccine until ages 12-15 months (Centers for Disease Control and Prevention 2017a). Siblings were given preference for similar PBE status[92] to reflect the tendency of hesitant parents to make selective vaccination decisions for all of their children (Reich 2016); consistent with previous research (Liu et al. 2015) I will show that clustering of PBEs in households can have a substantial effect on measles transmission.

Simulation Model

Contact parameters for interaction in families, childcare, schools, neighborhoods, and malls were adapted from empirically calibrated influenza simulations (Chao et al. 2010;

[89] PBE data is only available for schools with 10 or more students and some grades were not able to be matched to with school data for the appropriately lagged year.

[90] After assigning PBE rates in all schools, including those with missing data, I confirmed that the overall PBE rates by grade level were consistent with those released in annual CDPH immunization reports for the corresponding year.

[91] Rates of PBEs among homeschooled children tend to be particularly high (Khalili and Caplan 2007), and this may under-estimate the actual rates of vaccine refusals among these children.

[92] The model prioritized PBEs for other siblings if another child in the household was assigned to be unvaccinated, however, there is a small proportion of siblings that do not share vaccination status.

Germann et al. 2006). Previous measles simulations have also adapted contact networks developed for influenza transmission (e.g. Grefenstette et al. 2013) and the age-structured contact rates used here are comparable to those used in other measles simulation experiments (Liu et al. 2015). These parameters reflect: (1) the tendency of children to interact with others of similar age (assortative mixing), (2) differences in the number of potential contacts due to the size[93] of the focal points in this population, and (3) the frequency/intensity of interaction. For example, students are more likely to have adequate contact for disease transmission with other children sharing the same classrooms than in the overall school population (Del Valle et al. 2007). Within-grade contact was estimated to be five times that of within-school contact (Cauchemez et al. 2011). Contact in schools is of particular interest as PBEs are reported at the school-level,[94] and vaccination coverage within schools can significantly influence opportunities for measles outbreaks in local areas (Mossong and Muller 2000). Probability of contact at a physician office was calibrated from epidemiological reports of measles exposure (Sugerman et al. 2010) and adjusted to reflect the higher probability of contact with other children at pediatricians than in family/general practitioner offices.[95] Table 1 above includes the age-structured contact probabilities for each type of focal point. It is important to note that robustness checks confirm that these contact probabilities, together with empirical transmission parameters (described below), can successfully reproduce the expected basic reproduction number for measles (R_0 = 12-18; see Fine 1993) in an entirely susceptible population.

[93] In other words, the number of other children also assigned to that particular interaction point.

[94] As previously mentioned, individual-level PBE data is unavailable due to privacy concerns.

[95] This was achieved using the relative proportions of children assigned to pediatricians versus general/family practitioners in the synthetic population.

Similarly, the model's disease transmission parameters are grounded in epidemiological findings. First, probabilities of transmission in the pre-vaccine era (Top 1938) are used to represent the probability of infect given exposure.[96] These probabilities are age-dependent to reflect the protection afforded by maternal immunity for the first 6-12 months of life (Papania et al. 1999). Second, the overall vaccine efficacy is set at 96.9% based on previous research (Davis et al. 1987). Vaccine failure is modeled as an exponentially decreasing function across number of exposures to reflect that the initial exposures likely pose greater risk of infection than subsequent exposures.[97] Third, previous research shows that the average time from exposure to first symptoms for measles is 14 days and that individuals are most infectious 2 days before and after the appearance of symptoms, such as a rash (Papania et al. 1999). Therefore, I set the incubation period at 12 days, with an individual becoming infectious the 13th day after exposure. The individual remains infectious for 3 days—assumed to be 2 days prior to and the first day of the appearance of symptoms. On the third day, it is assumed the child visits a physician, receives a measles diagnosis, and is quarantined.[98]

A discrete time Susceptible-Exposed-Infected-Recovered (SEIR) model is used to simulate measles transmission. SEIR models are appropriate for the modeling of measles transmission (Allen et al. 1990; Grenfell 1992; London and Yorke 1973) due to the extended latent period between exposure and appearance of symptoms (E) and immunity from re-infection

[96] Estimates based on data collected after introduction of the measles vaccine are confounded by both the prevalence of vaccination and probability of contact between children with different vaccination statuses. Nor can estimates of force of infection be used as they incorporate both infectiousness and age-dependent contact.

[97] If an individual has been vaccinated but not developed measles seropositivity, the failure would be expected to occur within the initial exposure(s) (i.e. probability of vaccine failure is not uniform across exposures). Using a function in which the risk of failure exponentially decreases with number of exposures results in an overall vaccine efficacy rate more consistent with reported efficacy rates than if vaccine failure were set uniformly at 96.9%.

[98] The simplifying assumption is made that the first visit to the physician results in an accurate diagnosis and initiates separation from the population. Empirically, failure to diagnose measles on the initial healthcare visit can result in longer exposure in the population and increase likelihood of further transmission (Blumberg et al. 2015). This can particularly be a problem at the beginning of an epidemic (e.g. Sugerman et al. 2010).

after a case has recovered (R) (Markowitz et al. 1990). The SEIR model was run with a daily time step.[99] At the beginning of each simulation trial, 10 children were randomly selected to serve as the initial infections—these seeded infections represent external introduction points of the disease into the population. After the three-day infectious period, children recovered and were considered to be immune from re-infection.[100] The analysis period was 36 weeks, the typical length of a school year in the U.S.[101]

Each weekday, children have contact in households, childcare centers, schools, neighborhoods, and at the mall. On weekends, contact occurs in households, neighborhoods, and malls. Possibility of transmission begins when the child becomes infectious after the incubation period. As mentioned above, on the third day children are contagious, symptoms appear, and they visit the physician and can expose a small number of other children visiting the same physician.

Infections occur probabilistically. For each interaction location, a child is assigned a random number of exposures based on the probability of contact and the number of infectious children in that location. For unvaccinated children, the probability of infection, p_u, is:

$$p_u = 1-(1-\beta_a)^{\tau}$$

where β_a is the age-dependent rate of transmission and τ is the number of exposures to infectious children in that location. For vaccinated children, the probability of infection, p_v, is:

[99] Due to the incubation period, weekend contact was rendered unimportant in early generations of cases in the model. Children were permitted to have contact in households, neighborhoods, and the larger community—locations where weekend contact could occur—daily in the simulation.

[100] Immunity is typically considered to be lifelong, although in rare cases measles has been re-acquired later in life (Markowitz et al. 1990). Here it is assumed (reasonably) that after infection children are immune for the remainder of the 36-week period.

[101] The model does not account for holidays. Holidays would likely decrease measles transmission as school closure can be an effective intervention strategy for reducing contact for disease spread (Germann et al. 2006), although long-term investigation of measles transmission showed the drop in contact rates during holidays averaged out over time (London and Yorke 1973).

$$p_v = 1-(1-(\beta_a * \gamma)^{\tau}$$

where β_a is the age-dependent rate of transmission, γ is the vaccine efficacy[102] and τ is the number of exposures to infectious children in that location. Here, efficacy is calculated as:

$$\gamma = \pi_0/2^T$$

where π_0 is the overall probability of vaccine failure and T is the total number of exposures up to and including that location. If exposed, children become infected randomly based on their probability of infection.

Results

Figure 5.1 provides the transmission settings of measles infections in the synthetic population. Figure 5.1A shows the locations where children in the simulation experiment contract measles when PBEs are distributed as observed.[103] Approximately 83% of all transmission occurs through contact with strong ties—siblings, schoolmates, and children in the same childcare center. Interaction in the local neighborhood (Census block group) and larger community, including malls and physician offices, accounts for significantly fewer direct infections overall. Among these locations, physician offices are responsible for the majority of infections. Results from simulations with 1 and 40 seeded infections show that these findings are generally robust to the number of initial infections introduced into the population (Figure A5.1 in Appendix).

[102]Probability that the vaccine does not fail.

[103] Here, "observed" refers to assignment consistent with empirical PBE data, as described above.

Figure 5.1B shows results from a comparison population in which PBEs were redistributed throughout the population at random.[104] When PBEs are randomly assigned, most infections are still generated by contact with strong ties (~76%, as compared to ~83%), and a majority of the weak tie infections occur in physician offices. That said, even though contact with strong ties may account for a larger percentage of infections, weak tie interactions could play an important role in transmitting the disease between locations, substantially affecting the overall level of infections. This would be consistent with findings from the small-worlds model that redundancy in contact among strong ties limits new exposures, while weak ties carry the disease outside local clusters. These effects are investigated by simulating outbreaks in conditions in which contact in each focal point is eliminated while the other interaction points remain active. Results for each of the contact settings in these models are discussed below.

Schools and Childcare Centers

Schools were the most common transmission setting in the simulation. When PBEs were assigned as observed, schools accounted for 57% of all infections across 1000 replications (Figure 5.1A). This percentage includes infections generated by contact both within the same grade and in the larger school population. This result is consistent with epidemiological studies and previous measles simulation models, which have identified schools as hotspots for measles transmission (Becker et al. 2016; Markowitz et al. 1989; Sugerman et al. 2010).

Surprisingly, when PBEs were distributed randomly, schools accounted for an even higher proportion of infections (67%) across 1000 replications (Figure 5.1B). Although the

[104] Therefore, this comparison population has the same overall number of PBEs but they are not clustered spatially. PBEs were not randomly assigned to children aged < 1 year as they are considered too young for vaccination. The next chapter will discuss the logic behind random assignment of PBEs in greater detail.

absolute number of school infections is higher when PBEs are distributed as observed,[105] the percentage of transmissions is higher in schools when PBEs are randomly distributed due to the frequency of daily contact among children that occurs in this setting. This result seems to contradict Hypothesis 1A, which predicted that measles infections would be more common in schools when PBEs are spatially clustered than if randomly distributed. Regardless of the spatial clustering of PBEs, the percentage of infections transmitted in schools increases as the overall outbreak size increases. This suggests that contact in schools presents opportunities for larger outbreaks of disease, but that spatial clustering of PBEs can create larger outbreaks overall.

Panels C and D in Figure 5.1 present the percentage reduction in the number of cases when contact settings are removed across the distribution of outbreak sizes. As shown in Figure 5.1C, removing contact in schools reduces the number of cases across the entire distribution of outbreak sizes, but with a disproportionate effect among the largest outbreaks in the right tail of the distribution. Unlike the other interaction points, removing contact within schools continues to have a strong effect even in the largest outbreaks and eliminates over 95% of cases. Figure 5.1D shows a similar effect of removing contact in schools when PBEs are randomly distributed in the population, although the reduction in cases in the largest outbreaks is only approximately 90%. This difference in the effects of removing schools when PBEs are clustered rather than randomly distributed reflects the extent to which the spatial concentration of PBEs intensifies schools' efficiency as hotspots of measles transmission. The model shows that the importance of these clusters is not necessarily in the percentage of infections that occur there, but in the higher number of infections produced overall. In short, my results provide only mixed support for Hypothesis 1A—a higher percentage of infections occur in schools when PBEs are randomly distributed; however, PBE clusters in schools can produce larger outbreaks overall.

[105] Spatial clustering of PBEs creates larger possible maximum outbreak sizes, as discussed in the next chapter.

The effect of contact in schools, moreover, varies by school type. Figure 5.2 reports the ratio between the percentage of infections and the percentage of children enrolled by school types. When PBEs are distributed as observed, the percentage of infections transmitted in public schools is about 90% of what we would expect given the proportion of children enrolled in public schools. When PBEs are distributed randomly, percentages of infections more closely reflect average school sizes. Public schools have the largest average enrollment sizes (Table 1), and, as a result, have approximately 10% more infections than the proportion of children enrolled in public schools alone would suggest when PBEs are distributed randomly.

Figure 5.2 shows that charter schools are responsible for more infections than what would be expected given the proportion of children enrolled. This is primarily due to the high PBE rates in charter schools: if PBEs are distributed randomly, charter schools are shown to have fewer, rather than more, infections than their over enrollment proportion would suggest. This is because the smaller average size of charter schools suppresses transmission. Similarly, Figure 5.2 shows that very low percentages of infections occur in private schools when PBEs are distributed randomly. The small average enrollment size of private schools is sufficient to decrease infection rates despite their relatively high PBE rates.

These findings provide qualified support for Hypothesis 1B. School types with higher PBE rates, and particularly those with higher average enrollment sizes, are more prone to measles transmission. Similar results are observed for childcare centers. Infections occur less frequently in Head Start programs than daycare centers, as Head Starts tend to have lower PBE rates than daycare centers (California Department of Public Health, Immunization Branch 2007, 2008; see Table 1 for rates in synthetic population).

Figure 5.1A demonstrates that childcare centers account for only a small percentage of measles infections, and removing childcare contact only reduces outbreak size approximately 20% between the85th and 95th percentiles of the outbreak distribution. Removing contact in childcare has almost no effect on reducing outbreak sizes in large epidemics. Yet, among children ages 3-4, 38.2% of infections are acquired in childcare centers. This population likely underestimates the risk of childcare transmission as only licensed centers for pre-school age children are included. Measles transmission in the U.S. may be particularly likely in centers that serve infants too young to be vaccinated (Centers for Disease Control and Prevention 2004).

Households

As shown in Figure 5.1A, only about 23% of measles infections are transmitted in households. However, when household contact is removed, there are substantial reductions in outbreak size. Figure 5.1C shows that removing household contact has the second greatest overall effect on reducing outbreak size (after schools).Removing sibling contact exerts the most influence around the 90th percentile of the outbreak distribution when it reduces outbreak sizes by approximately 80%.

Removing household contact produces a substantial effect because siblings with shared exemption status act as *bridges* between other interaction locations. Removing household contact has only a very weak effect when PBEs are assigned randomly (Figure 5.1D). Figure 5.3 further illustrates that it is the tendency for siblings to share vaccination status rather spatial clustering alone that produces this result. The middle box in Figure 5.3 shows outbreaks sizes from a model in which PBEs are spatially clustered as observed in schools, but siblings do not have a tendency to share the same vaccination status. This reduces outbreak size in the top 50% of the

distribution. Outbreak sizes at the 75th percentile and above are more similar to those generated when household contact is removed entirely (left-hand box) than when permitted and siblings tend to share vaccination status (right-hand box). When siblings do not share vaccination status, the percentage of infections transmitted via household contact reduces to just over 9% (Figure A5.2 in Appendix), comparable to the percentage of infections transmitted in households when PBEs are assigned randomly (8%, Figure 5.1B). This provides support for Hypothesis 2; contact in households results in a greater percentage of infections when siblings tend to share vaccinations status.

My results are consistent with existing findings that households have served as important transmission settings in many measles outbreaks, especially following increasing rates of non-medical exemptions. Figure 5.4A shows that sibling contact was an important source of infections in the 2008 San Diego measles outbreak that primarily affected unvaccinated children. Similarly, households were an important transmission setting in the Disneyland outbreak (Harriman 2015; Zipprich et al. 2015) and measles infections generally in the U.S. in recent years (Figure 5.4B), while it has a less important role to measles transmission prior to the rise of non-medical exemptions (Figure 5.4C).[106]

Physicians

As mentioned above, physician offices were the most frequent transmission setting in weak tie interaction. Contact in physician offices accounted for 15% of all measles infects when

[106] Caution is needed when comparing transmission settings in the Disneyland outbreak and cases reported in Figures 4B and 4C to those obtained in the synthetic population as the former include both children and adults while the latter includes only children. Differences in contact patterns among children and adults can result in important differences in transmission settings (Mossong et al. 2008). Yet, epidemiological accounts of measles infections in the U.S. demonstrate that household contact plays a significant role in transmission, particularly among unvaccinated siblings.

PBEs were spatially clustered, and 21% when PBEs were distributed randomly. In both conditions, infections acquired in physician offices disproportionately affected children too young to be vaccinated (Figure 5.5C), consistent with epidemiological findings (Gindler et al. 1992; Sugerman et al. 2010). As shown in Figure 5.5A, on average, approximately 23% of secondary measles infections in the simulation occurred in children less than 1 year of age. Epidemiological reports of infections in infants less than 1 year of age also presented in Figure 5.5A show that this percentage is generally consistent with that observed in actual outbreaks. In fact, infants too young to be vaccinated are often the age cohort with the highest attack rates in measles outbreaks (Bloch et al. 1985; Hinman, Hutchins, Baughman, et al. 2004; Papania et al. 2014; Phadke et al. 2016). Figure 5.5B demonstrates that medical settings and households are the most common sources of infections for infants in the simulation, consistent with epidemiological accounts of risk of measles exposure for children under age 5, and particularly those under 16 months of age (Gindler et al. 1992). Eliminating interaction in physician offices significantly reduces outbreak size despite its relatively small share in terms of direct transmissions, particularly when PBEs are spatially clustered. As shown in Figure 5.1C, outbreak size is reduced more than 60% between the 80^{th} and 95^{th} percentiles as outbreak size begins to increase rapidly when PBEs are spatially clustered. Unlike removing contact in schools, however, removing contact at physician offices has only limited impact on reducing infections in the largest outbreaks.

Neighborhoods and Malls

Very few direct infections occurred through contact in Census block groups (neighborhoods) and malls. Whether PBEs were spatially clustered or distributed randomly,

interaction in these locations only accounted for 1-2% of infections (Figures 1A and 1B). Despite this lower overall number of infections, interaction in these locations could still be important for spreading infections between sites that generate many infections, such as schools and households. Removing contact in these locations does lower the number of cases, but only when outbreak size is within a narrow range. As shown in Figure 5.1C, eliminating contact in malls begins to limit outbreaks sizes only around the 75th percentile (when outbreak sizes begin to noticeably increase), and has the greatest effect around the 80th percentile, when outbreak sizes are reduced by approximately 30%. In larger outbreaks with higher proportions of infections in school, removing contact in malls has little impact in reducing overall size. In comparison, eliminating contact in neighborhoods also begins to reduce outbreak sizes around the 75th percentile, but has the largest effect around the 90th percentile, again reducing outbreak sizes by approximately 30%.

Undoubtedly, the choice of contact probabilities in these locations affects these results. A series of additional models were estimated to test how results vary with changes in probabilities of contact. First, it could be that the relative amount of contact in these two locations affects the overall "weakness" of ties. Perhaps a greater proportion of weak tie contact in malls than in neighborhoods will lead to increased transmission overall due to increasing contact spanning wider areas. To investigate this, I held the overall expected number of ties in neighborhoods and malls constant, but varied the relative amount of expected ties in each location.[107] As shown in Figure 5.6, while increasing the relative share of contact in malls (Figure 5.6A) and neighborhoods (Figure 5.6B) increases the percentage of infections acquired in those locations,

[107] This entails compensating the increase in the probability of contact in one of these locations (either neighborhoods or malls) with a proportional decrease in the other. This results in the same overall number of ties in these two settings, but varies which setting the majority of ties occur in. Increasing the overall number of contacts increases the reproduction number and outbreak sizes, which makes it difficult to isolate the effects of increases in contact within one setting in particular.

respectively, there is no consistent relationship between the share of weak tie interaction in either type of location and the overall outbreak size. This is the case with or without spatial clustering of PBEs. Thus, the lack of substantial results for contact in malls and neighbors cannot be attributed to the relative "weakness" of ties in these locations.

Second, I increased the probability of contact in neighborhoods and malls separately (Figure 5.6C) and jointly (Figure 5.6D), without holding the overall number of expected ties constant, to examine how outbreak size is affected if overall contact in these locations is actually higher. Surprisingly, increasing the probability of contact does not produce a substantial effect on size of outbreaks, either separately or jointly, until approximately 5-fold increases. A 5-fold increase in contact probability in these locations necessitates that on average, every child, including infants aged less than 1, must have 30 minutes of close, i.e. school-level, contact in neighborhoods or malls every day of the week, which may not be empirically plausible.

When contact in neighborhoods is increased 5-fold, the most noticeable increase is in the maximum outbreak size. Alternatively, when contact in malls is increased 5-fold, outbreak sizes increase more in the 3rd quartile of the distribution (between the 50th and 75th percentiles). This difference can likely be attributed to the clustering of PBEs in neighborhoods. Some block groups have substantial percentages of children with PBEs; increasing neighborhood contact then presents greater opportunity for larger outbreaks in those neighborhoods when the disease happens to reach them. Malls, on the other hand, provide ties that extend outside local neighborhoods, increasing the likelihood of reaching more distant children with PBEs, but not necessarily linking large clusters of children with PBEs. Jointly increasing probability of contact in neighborhoods and malls (Figure 5.6D) produces increases both in the middle 50% (between the 25th and 75th percentiles) and the maximum outbreak sizes.

These findings provide mixed support for Hypothesis 3, which predicts that the elimination of contact in neighborhoods, malls, and physician offices should significantly reduce the overall size of outbreaks. Eliminating contact in physician offices does have a substantial effect on reducing outbreak sizes, and primarily affects children too young to be vaccinated. Interaction in neighborhoods and malls, on the other hand, neither generates significant percentages of direct infections, nor has substantial impact on reducing overall outbreak size outside a very limited range of the distribution.

Overall, while eliminating contact in all interaction points has some effect on initially reducing outbreak sizes when PBEs are spatially clustered, model results show that only the removal of contact in schools is sufficient to prevent large outbreaks. Removing contact in other locations, particularly households and physician offices, reduces connectivity and makes it more difficult to reach PBE clusters; however, ultimately, as long as contact is permitted in schools and PBEs are spatially clustered, large epidemics are possible. Although the percentage of infections in schools increases as outbreak size increases regardless of distribution of PBEs, spatial clustering of PBEs attenuates this trend and produces much larger outbreaks overall.

Discussion

Social networks structure physical contact, which, in turn, structures disease transmission. This simulation experiment demonstrates that the overlap between locations of frequent, routine social contact and concentrations of children who lack measles protection due to non-medical vaccine exemptions elevate the risk of disease transmission in these settings. While weak ties may play important roles in the introduction of a disease to new areas of the contact network (Watts 1999, 2004; Watts and Strogatz 1998), strong ties play an important role

in infecting local clusters of vulnerable children. The following chapter will extend this analysis to examine how interaction in these clusters may increase disease risk for the network as whole.

Regardless of locations of PBEs, schools are the most common setting for measles transmission due to the amount of daily contact among children that occurs there. Schools have been sites of major measles outbreaks even when vaccination coverage among students has been very high (Chen et al. 1989; Gustafson et al. 1987; Nkowane et al. 1987). This chapter shows that the clustering of PBEs in certain types of schools, particularly charter schools, increases opportunity for measles transmission. Allowing parents to enroll children in charter schools by choice can increase PBE concentration in these schools beyond what might be expected by residence-based enrollment alone.[108] Moreover, my results show that parental decisions against vaccination also create increased opportunity for measles transmission within the household through contact with unvaccinated siblings—those siblings then have the ability to carry the disease into new classrooms or schools (Sugerman et al. 2010).

Weak tie contact results in a smaller percentage of infections, but there is evidence that interaction in physician offices, neighborhoods, and malls increases connectivity between more common infection sites. When PBEs are spatially clustered, eliminating contact in these locations decreases outbreak sizes more than would be expected by simply eliminating the direct infections that occur there. Yet, an important finding of this study is that as long as paths to schools with high concentrations of PBEs exist, it is not possible to prevent large outbreaks by eliminating contact in these weak tie locations. That said, physician offices are the most common sites of infections in community contact and therefore a crucial site for intervention. Children infected with measles are very likely to seek medical attention (Davis et al. 1986), and lack of

[108] As mentioned in Chapter 3, enrollment in traditional public schools is based on residence in a particular district, while charter school enrollment does not have this restriction.

necessary preventative precautions or delay in obtaining a correct diagnosis can significantly increase transmission risk in medical settings (Blumberg et al. 2015; Chen et al. 2011).

This study has several limitations. First, the synthetic population includes only youth under18 years of age as the effects of clustering of PBEs in schools were of primary interest. This may underestimate transmission risk in households, neighborhoods, or other locations where contact between children and adults is common. Although measles infections are most common in children due to increased likelihood of sufficient contact for disease spread, adults have constituted a substantial proportion of cases in some recent U.S. outbreaks (Chen et al. 2011; Harriman 2015; Parker Fiebelkorn et al. 2010). Spatial concentration of PBEs in schools most likely affects measles transmission risks among children, yet use of populations that include adults may be better able to assess overall population transmission risk in these shared settings.

Second, the intention of this study was only to capture the general contours of the contact network among children to evaluate the effects of PBE clusters on measles outbreaks. Even very detailed simulation models cannot predict the timing, location, or severity of outbreaks. The exact definitions and inclusion of interaction locations influence where simulated transmission occurs. For example, heterogeneity in contact probabilities and vaccination status within schools and neighborhoods can affect results. Nonetheless, the simulation results presented here are generally consistent with existing epidemiological findings. Furthermore, the simulation model provides an opportunity to evaluate the roles of strong and weak ties across various outbreak sizes as well as hypothetical scenarios, which is not possible to observe in the real world.

Third, PBE rates were estimated for all ages except children in kindergarten and the 7th grade. More complete reporting of vaccination coverage in all school grades would help to more accurately assess where children with PBEs are clustered and how this affects disease

transmission. Fourth, PBE reports used here did not indicate levels of MMR vaccination specifically. Actual rates of MMR coverage among children with PBEs vary significantly across schools (Buttenheim et al. 2015), and likely exert influence on where actual measles outbreaks are most likely to occur. To my knowledge, however, previous simulation experiments of disease spread have not incorporated empirical data on PBEs. The use of this type of data can help examine how current prevalence and spatial patterns of PBEs affect locations of measles transmission beyond models without empirical grounding.

Conclusion

These results demonstrate that schools remain important sites of measles transmission, and suggest that intervention strategies focusing on eliminating transmission in schools may be most effective in containing disease epidemics (Germann et al. 2006; Ogbuanu et al. 2012; Painter et al. 2010). Easily obtained non-medical vaccine exemptions and school choice allow clustering of unvaccinated children in charter schools, which may be particularly vulnerable to measles outbreaks (e.g. Sugerman et al. 2010). Exposure to other unvaccinated children in schools is particularly high for children with PBEs in California (Buttenheim et al. 2012). Policies that limit exposure to intentionally unvaccinated children in the community, such as physician policies against high proportions of unvaccinated children in their practice, may reduce risk to susceptible children, particularly those too young to be vaccinated (Buttenheim, Cherng, and Asch 2013; Freed et al. 2004). Results in this chapter suggest that the spatial clustering of PBEs in schools results in the potential for large measles epidemics. The next chapter will specifically address this finding by examining the overall effect of spatial clustering on the size of measles outbreaks.

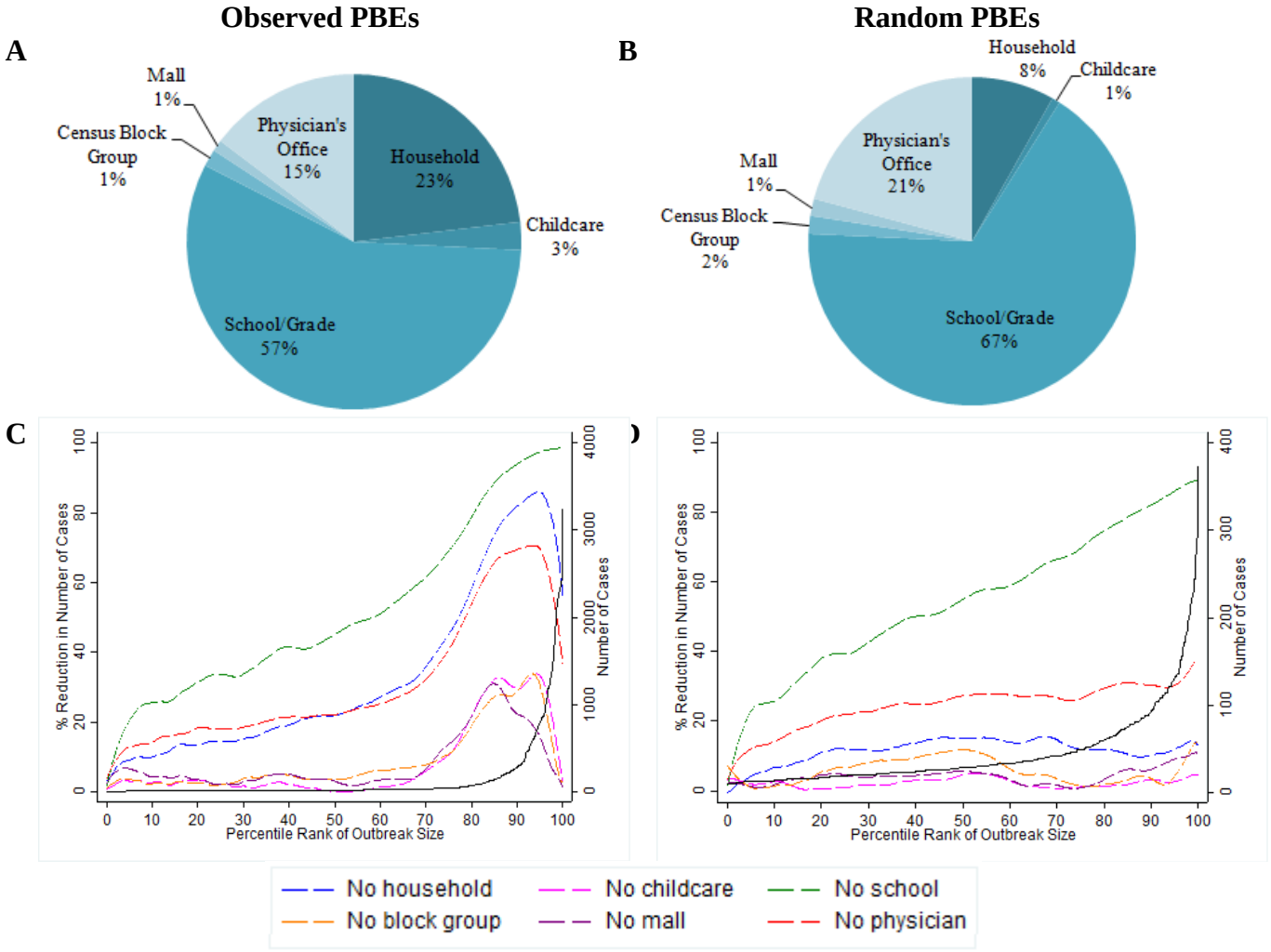
Tables

Table 5.1: Descriptive Statistics of Synthetic Population

			Focal Point Size			% Unvaccinated (μ)		Contact Probabilities	
Foci	Type	N	Mean	Std. Dev.	% Enrolled	PBE	Age < 1	Ages 0-4	Ages 5-17
Families	Siblings	5,895,518	1.54	0.79	100.00	1.97	5.48	0.8	0.8
Childcare	Daycare	9,599	43.66	31.75	5.95	3.41	0	0.04	
	Head Start	1,586	49.75	44.56	1.12	0.25			
School: Type	Public	8,757	607.06	497.77	75.42	1.72			
	Private	3,174	153.99	205.64	6.93	3.68	0		
	Charter	1,079	427.41	408.81	6.54	4.09			
School: Grades	Elementary	48,441	60.28	42.38					0.01999
	Middle	16,230	88.49	121.83	[same as below]	[same as below]	0		0.02234
	High	13,521	140.81	196.70					0.01576
School: Levels	Elementary	8,935	387.31	274.52	32.25	2.27			0.00399
	Middle	7,509	419.45	350.20	15.90	1.36	0		0.00447
	High	3,840	543.99	746.27	21.02	0.96			0.00315
Neighborhood	Block Groups	23,112	391.96	311.81	100.00	2.27	5.48	0.0000653	0.0001958
Community	Physicians	19,247	470.67	299.86	100.00	2.31	5.54	0.0000024	0.0000073
	Malls	801	12078.69	7868.75	100.00	2.28	5.38	0.005	0.0025
	Total	9,059,020				1.91	5.74		

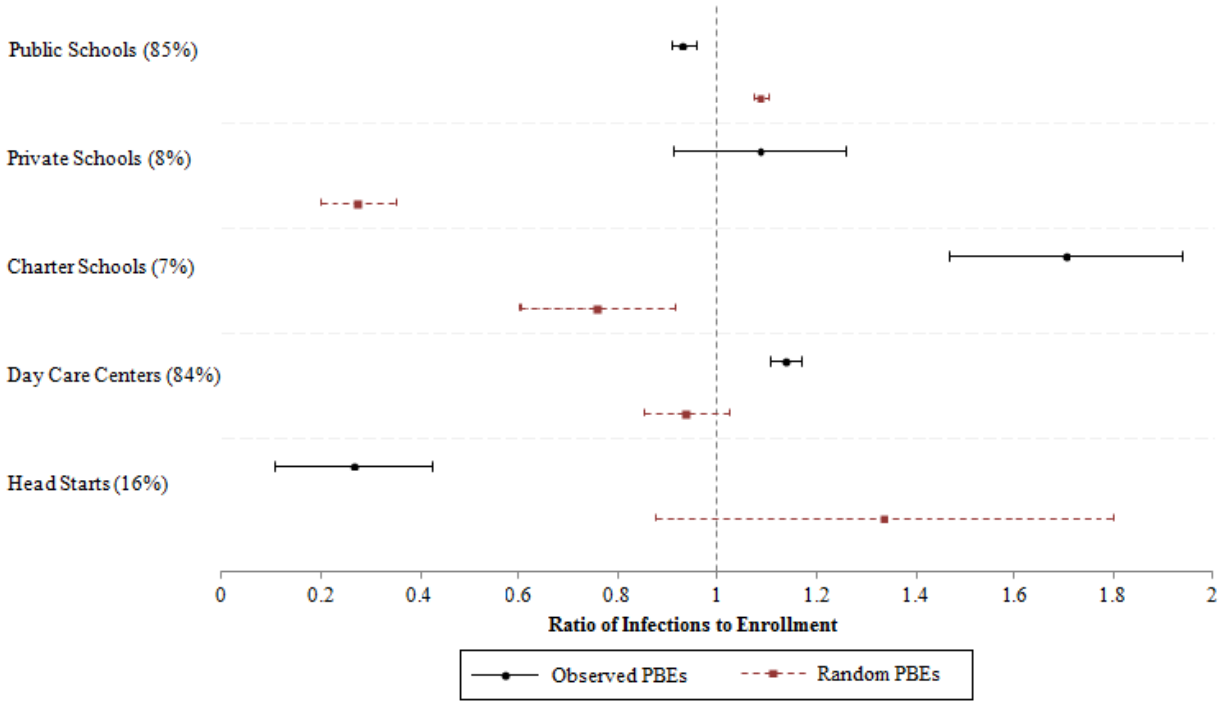
Figures

Figure 5.1: Transmission settings for measles infections



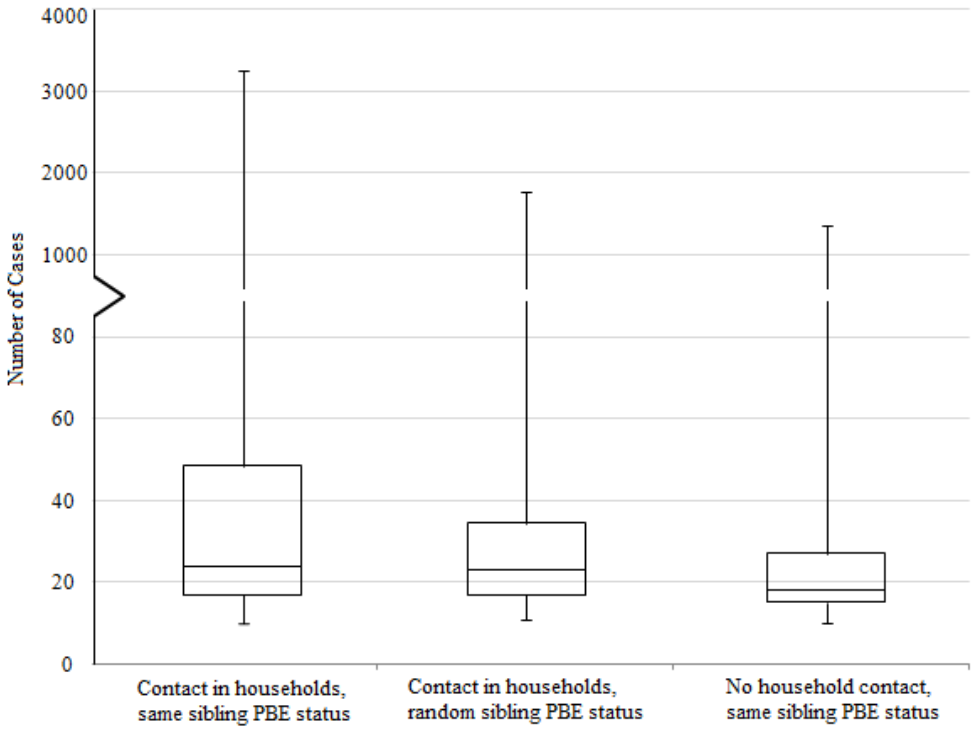
Note: Panels A and B compare percentages of infections acquired in each of the contact locations when PBEs are distributed as observed in California (A) to what would be expected if PBEs were distributed randomly in the population (B). While this demonstrates where infections are likely to occur overall, Panels C and D show how measles outbreaks sizes are affected by removing interaction points from the model. Contact in some locations may provide important channels for disease spread, even if infections directly acquired in that setting is relatively low. When PBEs are distributed as observed (C), removing interaction settings can reduce the size of outbreaks by making it more difficult for the disease to reach pockets with high numbers of unvaccinated children, as shown by the reduction in outbreak sizes in the 85th to 95th percentiles of the distribution. However, a steep decrease in these effects is observed above the 95th percentile in Panel C, indicating that this reduction in connectivity is not sufficient to fully prevent large potential measles outbreaks as long as children are permitted to have contact in schools with high PBE rates. Alternatively, removing interaction points when PBEs are distributed randomly over space creates more uniform reductions in the size of outbreaks across the distribution (D). In Panels C and D, the x-axis plots 1000 trials ranked from least to greatest by the total number of infections across the 36-week simulation period. The primary y-axis shows the % reduction in measles infections produced by eliminating contact in a setting at that simulation rank. The secondary y-axis and solid black line show the total number of cases per trial in that rank.

Figure 5.2: Ratio of percentage of infections to percentage of children enrolled in school and childcare centers



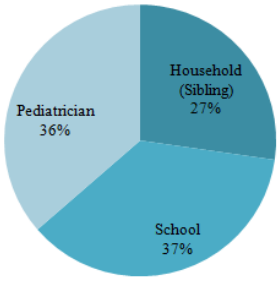
Note: While schools serve as primary transmission settings both when PBEs are spatially clustered and randomly distributed in the population, charter schools are more frequent settings of school transmissions when PBEs are distributed as observed. Charter schools have only 7% of the student population in the simulation, yet experience almost 13% of the school infections (1.7 times higher than expected). Alternatively, Head Start programs enroll 16% of children ages 3-4 in childcare, but experience only 4% of all childcare center infections (only 0.27 times what would be expected). This is due to the higher average rates of children with PBEs in charter schools (and very low PBE rates in Head Start programs) (see Table 1). When PBEs are distributed randomly, percentage of infections depends more heavily on average enrollment size. Private schools have fewer infections than expected based on the percentage of student population enrolled due to smaller average grade and school sizes, while public schools have more infections than expected based on enrollment proportion due to higher average grade and school sizes, see Table 1). Percentage of school and childcare center population enrolled in that institution type shown in parenthesis following label; points show mean estimates, error bars show 95% confidence intervals.

Figure 5.3: Distribution of outbreak sizes with and without shared vaccination status among siblings

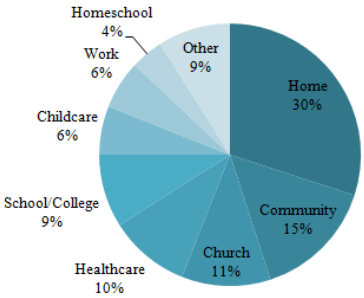


Note: Frequent contact between infectious children and unvaccinated siblings in the household contributes to increased infections across the distribution of outbreak sizes. Outbreak sizes when contact within the household is permitted but siblings do not share vaccination status (Plot 2) is more similar to outbreak sizes when there is no household contact (Plot 3) than with household contact among siblings with shared vaccination status (Plot 1). PBEs distributed as observed in all trials. Values shown in box plots are the minimum number of cases (lower whisker), 25th percentile (lower bound of box), median (midpoint of box), 75th percentile (upper bound of box), and maximum (upper whisker).

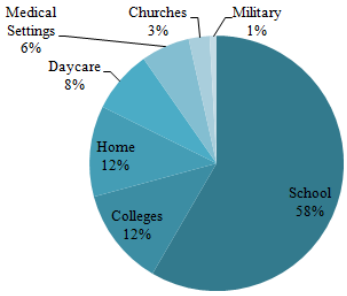
Figure 5.4: Prominence of household transmission in reported measles outbreaks



A. San Diego Outbreak, January 2008[109]



B. U.S. Acquired Infections, 2001-2008[110]



C. U.S. Outbreak Settings, 1985-1986[111]

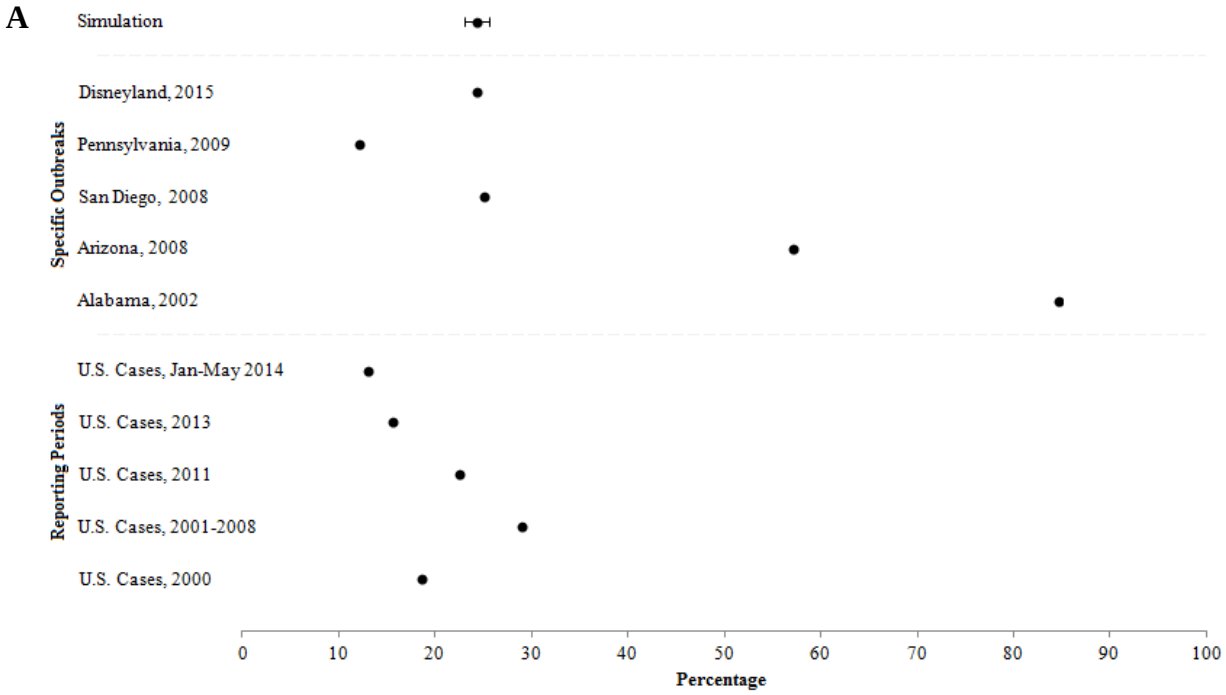
Note: In the San Diego outbreak (A), 1 infected child generated 11 additional child infections, 3 transmitted via sibling contact. Household transmission constituted a similar portion of all secondary measles cases with known transmission settings in the U.S. from 2001-2008 (B). Prior to the rise of non-medical vaccine exemptions in the U.S., the household may have played an important though slightly less prominent role (C). It should be noted that transmission settings of cases in (B) and (C) include both adults and children.

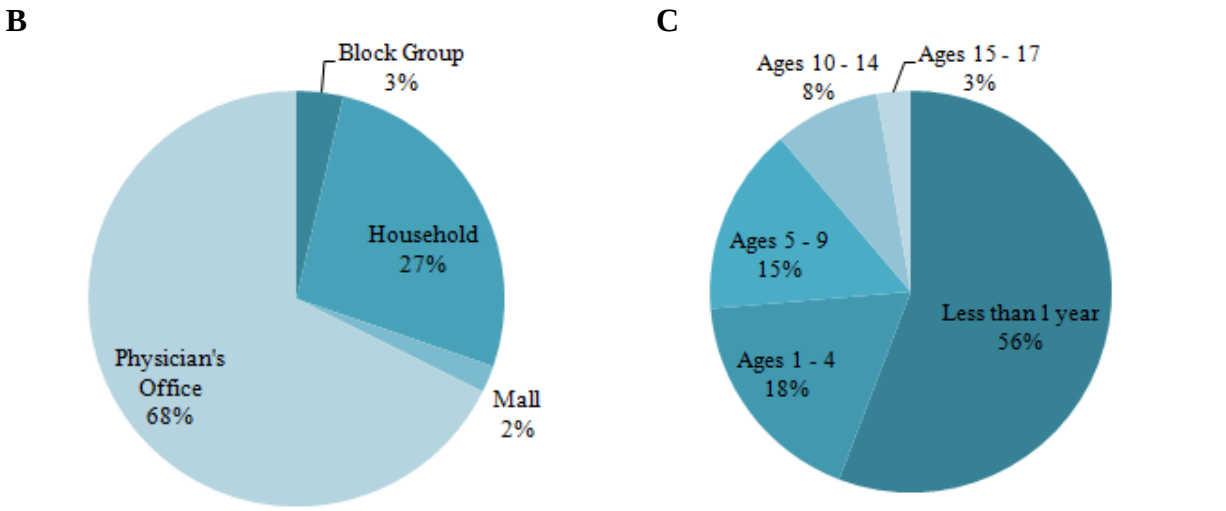
[109] Data from (Sugerman et al. 2010). 1 infection acquired in Switzerland generated 11 secondary cases in children in California.

[110] Settings known in 235 (72%) of the 325 cases acquired in children and adults in the U.S. from 2001-2008. Data in (Parker Fiebelkorn et al. 2010).

[111] Known settings reported for 113 of the 152 outbreaks in 1985-1986. Outbreaks include cases in both children and adults. Data from (Markowitz et al. 1989).

Figure 5.5: Infections in children aged < 1 year

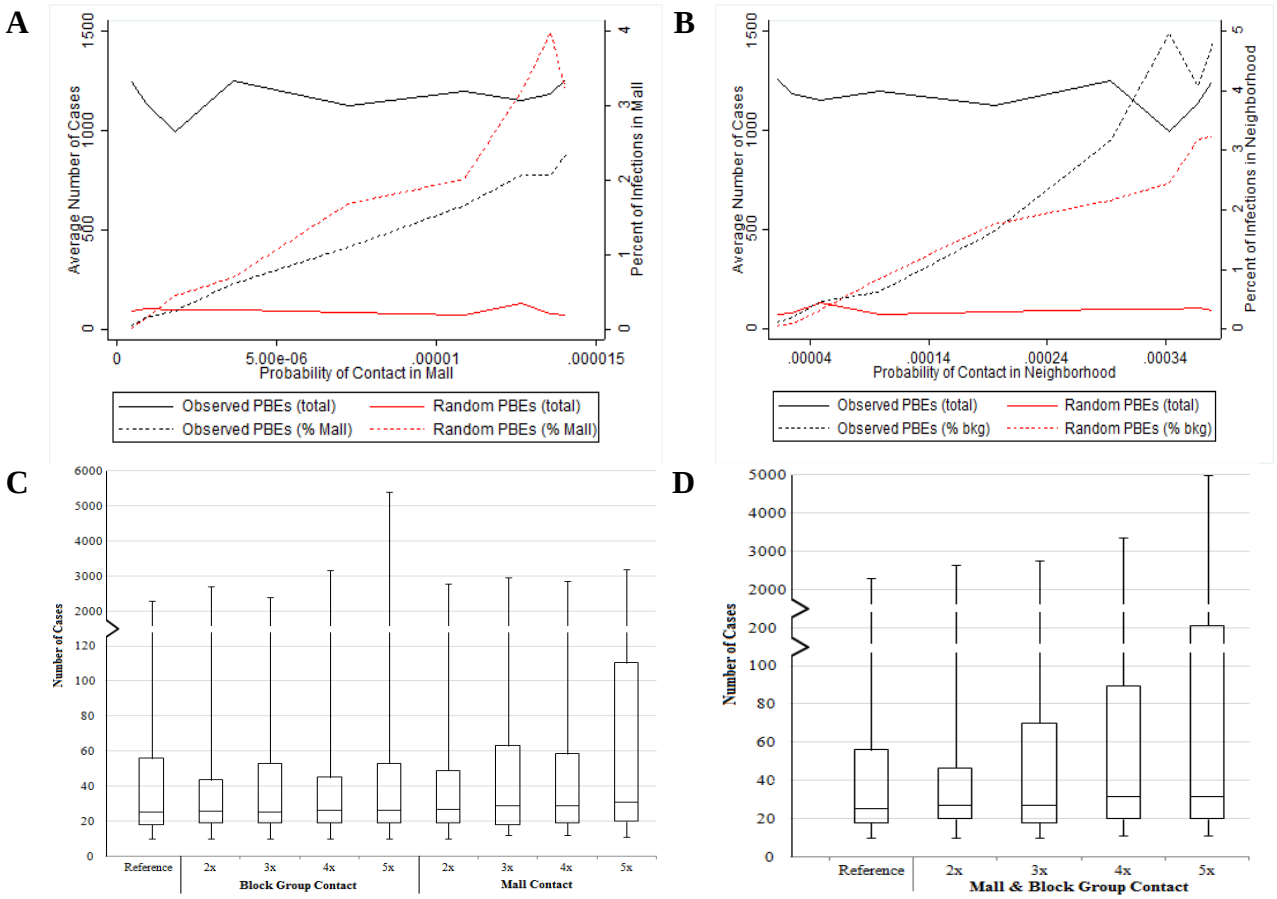




Transmission settings for children aged < 1 **Infections in physician's offices**

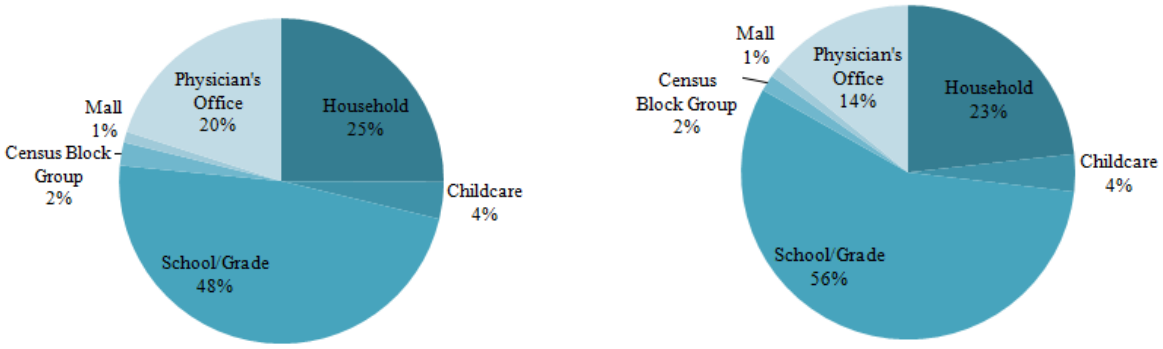
Note: (A) Percentage of infections occurring in children aged< 1 year (children too young to be vaccinated). The top line shows the average percentage of secondary infections in children aged < 1 in the simulation experiment (1000 trials); error bars show 95% confidence interval around the mean. This finding is compared to percentage children aged < 1 year (of all infections in children) in actual outbreaks and reporting periods (data from Centers for Disease Control and Prevention 2002, 2004, 2012a, 2012b, 2013; Chen et al. 2011; Gastañaduy et al. 2014; Harriman 2015; Parker Fiebelkorn et al. 2010; Sugerman et al. 2010). The percentage of simulated infant infections is generally consistent with actual measles outbreaks. (B) Transmission settings among infected children aged <1 year (1000 trials). Contact with infected siblings and other children in physician offices are important sources of exposure for infants. (C) Age distribution of infections in physician offices. Infections generated in physician offices disproportionately affect infants, which is consistent with epidemiological accounts of exposure in medical settings (Gindler et al. 1992; Papania et al. 1999).

Figure 5.6: Average number of overall infections and percentage of infections acquired in malls (A) and neighborhoods (Census block groups) (B) as proportion of contact increases



Note: In order to hold the combined number of expected contacts in these locations constant, as probability of contact in the mall increases, probability of contact in the neighborhood decreases, and vice versa. This demonstrates that although the percentage of infections acquired in these locations responds to increases in the probability of contact there, the relative share of contact in malls versus the local neighborhood has very little effect on the overall outbreak size. The second two panels show the outbreak distribution as contact probability is increased separately (C) and jointly (D) in block groups and malls, without holding constant the overall number of contacts. Increasing probability of contact in these locations does not initially have a substantial effect on size of outbreaks, either separately or jointly until approximately 5-fold increases. At that point, there is a noticeable effect on outbreak sizes in both locations, albeit in different parts of the distribution. When probability of contact is increased 5-fold within block groups, the greatest effect is in the tail (the maximum size of outbreaks), while increasing probability of contact 5-fold within malls has more effect on 50^{th}-75^{th} percentiles of the distribution. This difference is likely due to locations of PBEs; PBEs are more clustered within some block groups, leading to larger potential outbreaks in those neighborhoods when probability of contact is increased. Weak tie connections in malls may link geographically distant children with PBEs but may not provide easily searchable links to large PBE clusters.

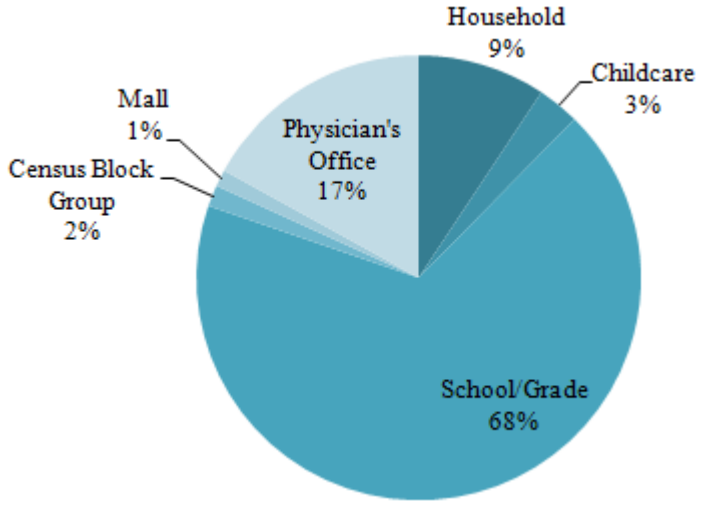
Figure A5.1: Transmission settings for measles infections, using 1 and 40 initial infections.



A. 1 infectious child **B. 40 infectious children**

Note: PBEs distributed as observed. Results over 100 trials.

Figure A5.2: Transmission settings for measles infections, when PBEs are distributed as observed by siblings do not have the tendency to share vaccination status



Note: Results over 1000 trials.

Chapter 6: Effects of Non-Medical Vaccine Exemptions on Overall Size of Measles Outbreak

Abstract

Clustering of non-medical vaccine exemptions allows children to act as multiple transmitters in disease cores, increasing the effective reproduction number of measles in an otherwise highly vaccinated population. An empirically calibrated simulation experiment with 9,059,020 children in California demonstrates that the observed spatial concentration of PBEs increases maximum outbreak size over ten-fold while offering slight protection against transmission during small outbreaks. As expected, spatial clustering of PBEs weakens herd immunity, allowing large outbreaks at approximately 93% population vaccination comparable to what would be expected at only 90% population vaccination if PBEs were spatially random. These small differences in vaccination coverage close to the levels necessary for herd immunity determine whether a disease is non-endemic. Spatial clustering of vaccine exemptions may force us to reevaluate levels of overall levels of population vaccination necessary to secure the benefits of herd immunity.

Chapter Introduction

This chapter addresses the puzzle of why measles incidence has been increasing in the U.S., despite high overall levels of vaccination coverage in the population. The measles outbreak that began at Disneyland in December 2014 came at the end of a year in which the U.S. experienced its highest measles incidence since the disease was declared non-endemic (Centers for Disease Control and Prevention 2017b).[112] Vaccine refusals have been identified as playing a significant role in many of these recent outbreaks (Centers for Disease Control and Prevention 2017b; Harriman 2015; Majumder et al. 2015; Zipprich et al. 2015). Nonetheless, adequate MMR vaccination[113] coverage among children entering kindergarten in California in 2014 was reported at 92.6% (California Department of Public Health, Immunization Branch 2015), within estimated levels of population measles vaccination necessary for herd immunity (Anderson and May 1985).

The previous chapter presented evidence from an empirically calibrated simulation experiment that concentrations of unvaccinated children in households, charter schools, and physician offices create increased opportunity for measles transmissions in these locations. This chapter again uses simulation modeling to address how spatial clusters of children with PBEs can affect overall sizes of measles outbreaks. Large-scale empirically calibrated simulation models that incorporate data on both locations of PBEs and interaction in social networks are better able to examine how current levels and locations of potentially unvaccinated children can affect the probability of severity of disease outbreaks (Chao et al. 2010; Eubank et al. 2004; Germann et al. 2006; Halloran et al. 2008; Hethcote 1997). This chapter examines larger implications of non-

[112] Again, measles was declared non-endemic in the U.S. in 2000; this indicates that measles transmission is not sustained domestically for at least 1 year or more currently in the U.S.

[113] Defined as 2+ doses.

medical exemptions by asking: can the current level of spatial clustering of PBEs being observed in California increase the potential of measles outbreaks? To the best of my knowledge, this is the first large-scale simulation model that utilizes observed data on vaccine exemptions to evaluate their potential effects on outbreaks.

Specially, this chapter asks whether the spatial pockets of children with high rates of non-medical vaccine exemptions constitute cores of disease transmission, sustaining contagion in an otherwise highly vaccinated population. These cores create the potential for measles outbreaks comparable to what would be expected with lower vaccination coverage in the population. As discussed in the previous chapter, social interaction tends to be spatially local, allowing infectious children in these core areas to transmit the disease to multiple other unvaccinated children, amplifying the average reproductive rate. Investigating effects of spatial clustering of unvaccinated children on disease outbreak potential is crucial as it may force us to re-think standard guidelines (e.g. Anderson and May 1985) for levels of population vaccination required to achieve herd immunity.

Following a brief review of previous work on disease cores and the formation of disease epidemics, I will use the synthetic population and simulation model outlined in the previous chapter to compare measles outbreak potential in populations with the same overall levels of vaccination but different spatial and temporal clustering in the locations of PBEs. Specifically, I examine effective reproduction numbers and the overlap of outbreak locations with spatial clusters of PBEs to investigate whether children with non-medical vaccine exemptions may be constituting disease cores of measles transmission in the population. I conclude by discussing why this work is informative to on-going debates surrounding state-level policies toward vaccine requirements and permitted exemptions (Yang and Silverman 2015).

Spatial Clusters of PBEs as Disease Cores

Spatial clusters of unvaccinated children create pockets in the contact network that can be particularly vulnerable to disease outbreak. In these areas, an infectious child has the opportunity to expose and infect multiple other susceptible children through regular patterns of local social interaction. The ability of an infectious individual to create multiple subsequent infections, therefore serving as a "multiple transmitter", can constitute an epidemiological disease core (Thomas and Tucker 1996).The concept of disease cores was defined and continues to be used primarily in the context of sexually transmitted diseases (STDs). It was first introduced by York et al (1978) to capture the dynamics and persistence of the transmission of gonorrhea. Disease cores allow a relatively small subset of the population who are highly interconnected (share direct ties) to infect one another and sustain transmission of a disease beyond what would be expected if all members of a population interacted randomly (Bearman et al. 2004; Hethcote et al. 1982; Yorke et al. 1978). A small proportion of individuals constituting the core can be disproportionately responsible for sustaining an epidemic.

Typically, diseases spread through casual physical contact, such as the measles, pertussis, and flu, are assumed to propagate via random mixing in contact networks that does not depend on disease cores (Liljeros, Edling, and Amaral 2003).While multiple transmitters were first identified as key players in the epidemiology of gonorrhea, it is applicable here as it emphasizes the important role that individuals who infect multiple others play in maintaining an effective reproduction number (R_{eff}) above 1 (Over and Piot 1993). R_{eff} is the expected number of new infections generated by each infectious individual (Anderson and May 1990).[114] For an epidemic to be created and sustained, R_{eff} must be maintained above 1 (Dietz 1993; MacDonald 1952,

[114] The effective reproduction number differs from the basic reproduction number in that the latter assumes a completely susceptible population, whereas the former does not.

1957). If R_{eff} is less than 1, each infectious case is failing to reproduce itself and the epidemic is expected to die out. Multiple infections in a local area can push R_{eff} above the critical threshold of 1, which can spillover into other neighborhoods through interaction points located in the larger community (e.g. physician offices or malls) or more distant geographical areas (e.g. amusement parks or airports).

Hypotheses

Most children in California continue to fulfill school-mandated vaccination requirements; however, there are distinct spatial and temporal trends in those that have PBEs. First, children with PBEs tend to be spatially clustered (Atwell et al. 2013; Carrel and Bitterman 2015; Richards et al. 2013). Second, the overall rate of PBEs in the state has been increasing over time, from less than 1% of children entering kindergarten in 1992 to a peak of 3.15% in 2013[115](California Department of Public Health, Immunization Branch 2016a). In the general population then, younger school-aged children would be expected to have lower overall levels of vaccination than older adolescents. Assortative mixing by age in social networks (Mossong et al. 2008; Newman 2003) could increase disease outbreak potential, primarily among younger age groups, even if PBEs were randomly distributed across space. To understand how exempted children may be serving as cores for the transmission of vaccine-preventable disease in the population, it is important to separate spatial effects from the overall temporal trends that cluster exemptions within different age cohorts. To examine how the spatial clustering of PBEs affects measles transmission in California in 2014, three possible "worlds" were modeled in the simulation experiment.

[115] PBEs decreased slightly to 2.54% of the kindergarten population in 2014 due to a change in state law that mandated that PBE requests be accompanied by a physician's signature.

1. “Observed”: PBEs are distributed as empirically observed across both age and geographical space, retaining both temporal and spatial trends.
2. “Spatially random”: PBEs are distributed randomly across geographical space, but each age retains the number of PBEs observed. In other words, kindergarten-aged children are assigned more PBEs overall than high school-aged children because exemption rates for children entering kindergarten in California were much higher in 2014 than in the early 2000s when current high school students would have been entering kindergarten.
3. “Spatially and temporally random”: PBEs are distributed randomly across age and geographical space. The total number of PBEs in the population remains the same as in the other two scenarios, but no temporal or space trends are retained.

> Hypothesis 1: Due to assortative mixing by age and geographical proximity, the largest outbreaks should occur in the observed condition, followed by the spatially random condition, and then the spatially and temporally random condition.

The largest outbreaks should be observed in the observed condition due to clusters of children with PBEs operating as disease cores.

> Hypothesis 2: In the observed condition, the effective reproduction number—the average number of infections generated by a single infectious child—should continually increase as the number of infectious children with PBEs increases.

Additionally, if unvaccinated children are playing important roles in measles transmission, there should be a spatial relationship between PBEs and measles cases.

> Hypothesis 3: Clusters of measles cases should overlap spatially with PBE clusters.

Initially, I retain the same overall level of vaccination in the population in 2014 for all three of the PBE conditions. Regardless of spatial patterns in vaccine exemptions, lower vaccination coverage in the population would be expected to increase potential for disease spread (Anderson, May, and Anderson 1992; Anderson et al. 1992). To assess whether measles

incidence may be increasing in the U.S. because of loss of effective herd immunity due to spatial clusters of vaccine refusals, I then compare outbreak sizes in the observed condition with that in the spatially random condition at lower levels of vaccination.

> Hypothesis 4: Spatial clustering of PBEs in the observed condition allows outbreak sizes that are only generated in the spatially random condition at lower overall levels of vaccination coverage in the population.

Data and Methods

Population. This chapter again uses the synthetic population of youth ages 0-17 in California in 2014. The inclusion of children of all ages in the population, including those too young to be vaccinated and older children with higher overall vaccination rates, allows for a better estimation of the community-level risk of PBEs. Again, data from the Census, American Community Survey, and California Birth Master Files records was used to create a population representative of the age, race/ethnicity, parental education, and sibship size distributions of the 2014 Californian population at the Census block-group level. Enrollment records from the California Department of Education, as well as data from the National Household Education Survey and Private School Universe Survey, were used to assign children to schools. Approximately 50% of the children ages 3-4 were assigned to licensed childcare consistent with data on enrollment and capacity in these centers available from the California Departments of Public Health and Social Services, respectively. Full details of the construction of demographic characteristics and school assignment for the population are provided in the previous chapter.

Prevalence of PBEs. Vaccination status is assigned in the three separate PBE conditions described above as follows:

Observed. PBEs[116] were assigned within schools and licensed childcare consistent with reported prevalence rates from the Immunization Branch of the California Department of Public Health as described in the previous chapter; siblings were given preference for the same vaccination status. Children aged less than 1 year were considered unvaccinated. As vaccination information is typically collected when a child enters licensed childcare, kindergarten, and the 7thgrade, I assign PBEs in other grades consistent with school-specific rates for the year the children would have entered kindergarten or 7th grade. This maintains the observed state-wide percentages of PBEs across school grades. For schools without recorded data, PBEs were assigned the average rate by school type at the district level. Children younger than age 5 and not in licensed childcare were assigned PBEs at a rate consistent with childcare centers in the same county.

Spatially Random. PBE assignments from the observed condition were randomly re-shuffled within age. The overall number of PBEs for each age is the same as the observed condition, but assignment occurs randomly across schools and geographical space.

Spatially and temporally random condition. PBEs were randomly shuffled through the entire population, removing both the spatial clustering and temporal trend in prevalence by age. Consistent with the observed and spatially random conditions, PBEs are not assigned to children less than 1 year of age. As discussed in the previous chapter, these children are assumed to be unvaccinated due to the CDC recommended vaccine schedule and ineligible for PBEs in the synthetic population.

Network Structure Details of network structure and interaction are discussed at length in the previous chapter. For only the briefest review: Interaction was possible in six contact

[116] As discussed in Chapter I, children with PBEs may be entirely unimmunized or may only be missing one or two required vaccines; for this project, no assumptions are made about partial vaccination.

settings: households, childcare, schools, neighborhoods, malls, and physician offices. Probabilities of contact in the home, school, neighborhood, and mall settings were adapted from an empirically calibrated influenza simulation (Chao et al. 2010) and were adjusted to reflect school, community, and neighborhood sizes in the synthetic population. Probabilities of physician contact were calibrated to reflect exposures in epidemiological accounts of measles transmission in California (Sugerman et al. 2010). Contact probabilities were age-structured; not accounting for the increased tendency of children to interact with others their own age (Cauchemez et al. 2011; Mossong et al. 2008; Wallinga, Edmunds, and Kretzschmar 1999) can lead to under-estimation of R_{eff} (Mossong and Muller 2000) and less well-performing models of measles transmission (Schenzle 1984).

Disease Transmission Model parameters were informed by epidemiological studies of measles transmission. First, probability of transmission given contact is age-structured to reflect variations in susceptibility (Top 1938). Second, the incubation period is set to 12 days and the infectious period is 2 days prior to and 1 day following the onset of symptoms, after which it is assumed the child is quarantined (Papania et al. 1999). Third, overall vaccine efficacy is set at 96.9% (Davis et al. 1987), and, fourth, the probability of vaccine failure is modeled as an exponentially decreasing function of the number of exposures to an infectious individual.[117]

Using parameters informed by epidemiological accounts allows a plausible simulation experiment; robustness checks show that when used with the network structure described above in a completely susceptible population, the chosen parameters successfully reproduce basic reproduction numbers typical for the measles (R_0 = 12-18) (Anderson et al. 1992; Fine 1993). Epidemic trajectories can be influenced by the baseline reproduction numbers for a disease

[117] As discussed in the previous chapter, using a function in which risk of failure decreases exponentially with the number of exposures results in an overall vaccine efficacy rate more consistent with reported efficacy rates than if vaccine failure was set uniformly at 96.9% across exposures.

(Germann et al. 2006) making a realistic R_0 an important foundation for examining effects of PBEs on R_{eff}. An SEIR model using a daily time step over a 36-week period with 10 seeded infections was again used for the simulation. All results presented below were obtained using the same synthetic population and model parameters; variation was only introduced in assignment of PBEs, as described above.

Results

Measles outbreak sizes in the observed, spatially random, and spatially/temporally random conditions are presented in Figure 6.1. In each of the conditions, overall vaccination coverage in the population is 92.6%.[118] First and foremost, as shown in Figure 6.1, serious epidemics, i.e. those with thousands of infections, occurred only in the observed condition. While both the spatially and spatially/temporally random conditions show a similar increase in outbreaks in the right tail of the distribution, the magnitude of the outbreaks is substantially lower than in the observed condition.

This result is robust to the specific contact probabilities in the model; the previous chapter showed that eliminating contact in particular interaction locations still resulted in larger outbreaks when PBEs were distributed as observed rather than randomly (with the exception of completely prohibiting contact in schools, which is a burdensome intervention policy in real-world settings (Germann et al. 2006)) and previous work has shown that increasing or decreasing contact in any interaction location (including households, schools, workplaces, and neighborhoods) is not sufficient to mitigate measles outbreaks when vaccine coverage is low (Liu et al. 2015).

[118] This includes children aged < 1 who are too young to be vaccinated and children assigned PBEs.

Figure 6.1 illustrates two important points about the potential for measles outbreaks. First, it is the spatial clustering of PBEs that contributes substantially to increased sizes of outbreaks, rather than just increasing rates of PBEs over time. If it were the overall time trend that most influenced outbreak sizes, the spatially random condition should show comparable outbreak sizes to those in the observed condition. Compared with the random conditions, the maximum outbreaks are more than ten times larger when PBEs are distributed as observed.

Second, as shown in the middle 50% of the outbreak distribution (from the 25th to 75th percentiles) in Figure 6.1, it is the spatially/temporally random condition that experiences the largest outbreaks. The absolute difference in average outbreak size between the temporally/spatially random condition and the observed and spatially random conditions within this segment of the distribution is approximately 5 cases. In regards to measles transmission, 5 cases constitutes an epidemiological outbreak (Feiken et al. 2000; Markowitz et al. 1989).[119] This provides mixed support for Hypothesis 1: while outbreaks above the 75th percentile are substantially larger in the observed condition, *more* cases are generated initially in the spatially/temporally random condition.

This result may be attributed to spatial pockets of unvaccinated children acting similarly to hubs in networks. Hubs are nodes with a disproportionately high number of ties compared to the remainder of the network, which affects the robustness of a network to failure (Albert, Albert, and Nakarado 2004; Albert, Jeong, and Barabási 2000; Barabási 2009). Previous research has demonstrated that networks with hubs are generally robust with regard to random removal of nodes; however, targeted removal or attacks on hubs can significantly impair the network and render it less robust (Callaway et al. 2000; Pastor-Satorras and Vespignani 2001a, 2001b; Wang and Chen 2002; Watts 2004). Introducing measles cases into the population through randomly

[119] Others define an outbreak as only 3 related cases (e.g. Clemmons et al. 2015)

selected children mirrors this: Reaching unvaccinated children facilitates measles transmission. Randomly distributing exemptions throughout the population makes it easier for infections to reach unvaccinated children; however, those infected children are not connected to the significant numbers of unvaccinated children necessary for a large-scale outbreak. Spatial clustering of PBEs provides the opposite effect: it may be slightly more challenging initially to reach unvaccinated children, but, once a cluster is encountered, multiple infections in that area can provide a substantial boost to continued transmission overall.

In other words, spatial clusters of PBEs may provide some initial protection against measles transmission; however, any initial protective effects are obliterated by the rapid reproduction of infections once a PBE cluster is reached. In practice, protective effects of spatial clustering of PBEs in the population are possibly compromised for this and two additional reasons: 1) the introduction of measles into the population may be likely to come from an unvaccinated individual who acquires an infection externally and then introduces directly into a cluster;[120] and 2) measles infections do not need to originate in a PBE cluster to start an outbreak, only sustain minimal transmission until a cluster is reached. Models with 50 and 100 randomly seeded infections reinforce this point (Figure A1 in Appendix). While incidence is still slightly higher initially in the spatially/temporally random condition than the observed condition, as the number of seeded infections increases, so does the ability of the disease to reach pockets of unvaccinated children and the overall outbreak size.

The dynamics of measles transmission over time in each of the three conditions is shown in Figure 6.2. Initially, in the first generation of measles transmission resulting from the 10 seeded infections, each of the PBE conditions has approximately the same average R_{eff}

[120] The 2008 San Diego measles outbreak was started by an intentionally unvaccinated child that acquired the disease on a family trip to Switzerland and then infected two siblings, two classmates at a charter elementary school, and four infants at a pediatrician's office (Sugerman et al. 2010).

(observed: 0.56[121]; spatially random: 0.61; temporally/spatially random: 0.64). Beginning in the 3rd generation, the average R_{eff} begins to diverge. By the 5th generation, the average R_{eff} has exceeded the critical value of 1 in the observed condition, and remains at or above 1 among active transmissions for almost all of the remaining generations. In both the spatially and temporally/spatially random conditions, the average R_{eff} never reaches 1. This indicates that even while transmission may be continuing, the outbreak is, on average, always in a state of decline. By the end of the 36-week period, measles transmission has ended in approximately 85% of trials in the observed condition and over 95% of trials in both random conditions. Not only is an outbreak more likely to be active at the end of the 36-week period when PBEs are spatially clustered as observed, but sustained epidemics ($R_{eff} \geq 1$) are only witnessed in this condition, generating the differences in outbreak sizes observed in Figure 6.1.

Figure 6.3 presents evidence to support Hypothesis 2 that exempted children act as multiple transmitters when PBEs are spatially clustered. The average R_{eff} steadily increases as the number of infectious children with PBEs increases only in the observed condition. In particular, when six or more of the infectious children have PBEs, the average R_{eff} exceeds 1. The average R_{eff} never reaches 1 in the random conditions, even when multiple infectious children have PBEs. These results support that spatial clusters of children with vaccine exemptions constitute disease cores with increased likelihood of generating multiple subsequent infections.

In the observed condition, an average of 68.7% of the secondary infections are unvaccinated—44.4% had PBEs while the remaining cases were infants (aged < 1 year). The overall percentage of unvaccinated infections in the simulation is slightly higher than that reported for measles outbreaks in the U.S. between 2000-2015, which found that 56.8% of

[121] This average R_{eff} is very close to that observed for actual measles transmission in the U.S. from 2001-2011, estimated at 0.52 (95% CI: 0.44 – 0.60) (Blumberg et al. 2014)

infected cases were unvaccinated (Phadke et al. 2016). However, this is a conservative estimate as it excludes the 28.8% of cases that had "unknown" or "unvaccinated or unknown" status. Furthermore, 41.8% of confirmed unvaccinated cases had non-medical vaccine exemptions (Phadke et al. 2016), comparable to the 44.4% in the simulation.

Unvaccinated children also constitute a significant proportion of infected cases in the random conditions. Cases in both the spatially and spatially/temporally randomly conditions involved similar proportions of unvaccinated children.[122] It is not that lack of vaccination does not affect transmission when PBEs are distributed randomly; rather the lack of spatial clustering prevents the larger outbreaks present in the observed condition.

In all conditions, infants aged less than 1 year account for a larger proportion of cases than would be expected given the age distribution in the population. As discussed in the previous chapter, infants less than 1 year of age account for 24.3% of the secondary infections when PBEs are spatially clustered. This comparable to the 25% of infections in children too young to be vaccinated reported in actual outbreaks (Papania et al. 1999; Sugerman et al. 2010).[123]

Figure 6.4 shows the spatial clusters of PBEs and measles cases in the synthetic population. As shown in Figure 6.4A, clusters of schools and childcare centers in the synthetic population with statistically significantly higher risk of PBEs compared to the overall population rate were concentrated in the northwestern region near the Oregon border, the inner central region near Lake Tahoe, and in some of the coastal urban cities, e.g. Santa Cruz, Santa Barbara, Santa Monica, and suburbs around San Diego (spatial clusters of reported PBEs in public

[122] The distribution of percent of unvaccinated cases in the observed condition is more skewed than that in the random conditions, and increases more sharply as the number of cases increases. In the top 10% of outbreaks in the observed condition, an average of 84.60% of cases are unvaccinated due to PBEs or age < 1 year.

[123] Both of these epidemiological accounts of measles outbreaks included children aged 0 to 15 months as the MMR vaccine is not recommended until ages 12-15 months. In the synthetic population, infants too young to be vaccinated are only those aged < 1 year. The simulation results presented here are percentage of secondary infections, and potentially underestimate the risk posed to infants by PBEs among older children.

kindergartens in 2014 are presented in Figure A2 in Appendix) . Figure 6.5C shows clusters of schools and childcare centers with statistically significantly higher risk of measles infections in the observed condition. There is a lack of infections in the northern and some central parts of the state, where PBEs tend to be very common. This is likely due to lack of overall population in those regions (Figure 6.4B shows population density of synthetic children in California). Spatial clusters of PBEs are particularly vulnerable to disease outbreaks in areas with higher concentrations of people, such as the densely population coastal areas around Malibu, Los Angeles, and in the suburbs above San Diego. This provides qualified support for Hypothesis 3: spatial clusters of PBEs and measles cases do show some overlap, but primarily in areas with higher population densities.

Finally, measles infections were simulated at varying levels of population vaccination with PBEs distributed spatially randomly. Figure 6.5 presents these results. With the observed 92.6% vaccination coverage in the population, spatial clustering of PBEs allows maximum outbreak sizes comparable to those expected at approximately 90% vaccination coverage if PBEs are spatially random. This suggests that even when taking into account that PBEs are more common among younger children due to increasing exemption rates over time, spatial clustering alone lowers effectiveness of herd immunity in the population. Levels of population vaccination necessary for herd immunity are estimated to be between 92-96% (Anderson and May 1985); failing to maintain vaccination coverage at these levels locally allows disease outbreaks that create greater risk of disease transmission in the larger population. Although the absolute difference between 92.6% and 90% vaccination coverage may seem small, minor changes in coverage can generate large differences in epidemic sizes as shown more generally in Figure 6. These results provide support for Hypothesis 4 and indicate that PBEs clusters reduce

effectiveness of herd immunity. Even though overall vaccination levels in the population remain high, this alone is not sufficient to prevent serious outbreaks when there are spatial pockets of PBEs.

Discussion

This simulation experiment examines the effects of spatial clustering of PBEs in California on potential for measles outbreaks. To the best of my knowledge, this is the first model of measles transmission that has been calibrated with (1) fine-grained locational data of focal points of interaction, (2) disease transmission parameters from epidemiological studies and (3) observed spatial and temporal distributions of non-medical vaccine exemptions. As the findings demonstrate, due to the non-linear nature of epidemics, the spatial patterns of reported PBE have a substantial impact on outbreak sizes beyond what one would expect given relatively low levels of exemptions in high-income places, such as California. Moreover, examination of counterfactual scenarios shows that neither the increasing rates of PBEs over time alone, nor their overall prevalence in the population can account for these effects.

In particular, spatial pockets of children with high PBE rates may act as disease cores in the spread of vaccine-preventable illness. In these local areas, infected children are able to expose clusters of susceptible children and generate multiple subsequent infections. It is much harder for children outside these clusters to serve as multiple transmitters due to fewer susceptible, unvaccinated children in the local area. Therefore, the ability to infect multiple other children is a product not only of an individual's own behavior (lack of vaccination) but their network neighbors' decisions against vaccination as well. This is consistent with results of previous abstract simulation studies showing that clusters of anti-vaccine beliefs created through

social influence in networks increase the risk of disease outbreak (Eames 2009; Salathé and Bonhoeffer 2008).

As such, spatial clustering of children with PBEs renders the population less robust to disease spread and decreases the effectiveness of herd immunity. While major measles outbreaks were still the exception when PBEs were spatially clustered, overall outbreak sizes were significantly higher than when PBEs were spatially and/or temporally random. Spatial clustering of PBEs creates outbreaks comparable to those expected with lower vaccination coverage in the population should PBEs be distributed randomly, even when temporal trends in increasing rates over time are retained. Separating the effects of spatial and temporal trends demonstrates that spatial concentration may be particularly concerning for increasing measles incidence.

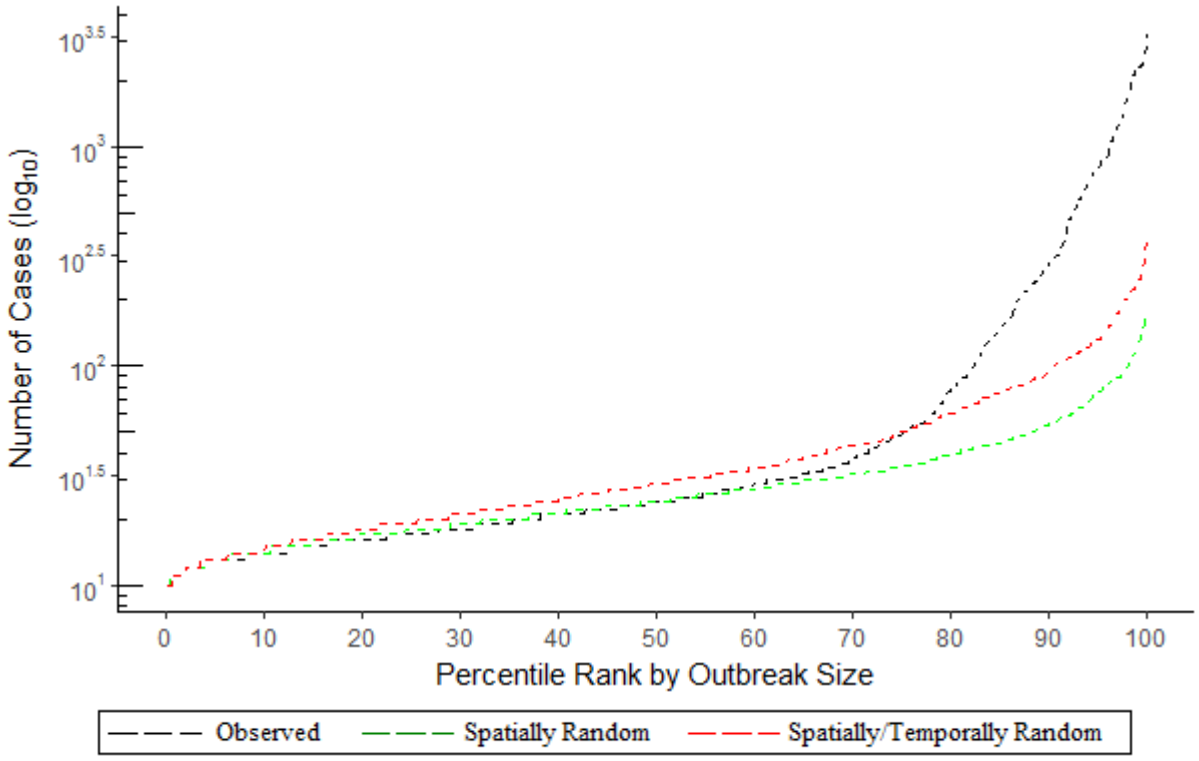
The results presented here are not intended to make a definitive statement on locations of spatial clusters of children lacking MMR vaccination or where measles outbreaks may be likely to occur in California, but are rather a more general illustration of unintended consequences of policies toward non-medical vaccine exemptions. This work is limited by lack of specific data on MMR vaccination among children with PBEs. Previous research has shown, however, that MMR coverage was relatively low among children with PBEs in California schools in 2009, particularly in schools with schools with high PBE rates (Buttenheim et al. 2015). Additionally, in the scenario presented here, measles transmission was allowed to continue to spread through the population unabated. When measles outbreaks occur in the real world, significant steps are taken to limit transmission through vaccination and quarantine programs.

Conclusion

Increasing rates of PBEs and incidence of vaccine-preventable disease are creating serious debates over vaccine policies (Yang, Barraza, et al. 2015; Yang and Silverman 2015). As increasing measles incidence in the U.S. and results of this simulation experiment suggest, focusing efforts on maintaining overall levels of vaccination in the population are not sufficient to prevent disease transmission. Spatial pockets of unvaccinated children are threatening to reverse the elimination of endemic measles transmission in the U.S. (Blumberg et al. 2015; Jansen et al. 2003; Omer et al. 2009; Papania et al. 2014). Voluntary vaccination programs allow for the creation of these partially vaccinated pockets of individuals that increase the risk of network-wide epidemics (Perisic and Bauch 2009). Modeling of STD transmission in networks mirroring properties of those observed in the real world demonstrated that preventive interventions were most effective when directly targeting individuals most active in the behaviors that led to disease transmission (Newman 2002). Debates surrounding vaccination policy and efforts to increase vaccination must recognize this discrepancy: population-wide protection against disease outbreaks depends not only on overall vaccine compliance, but on spatial locations of non-compliance.

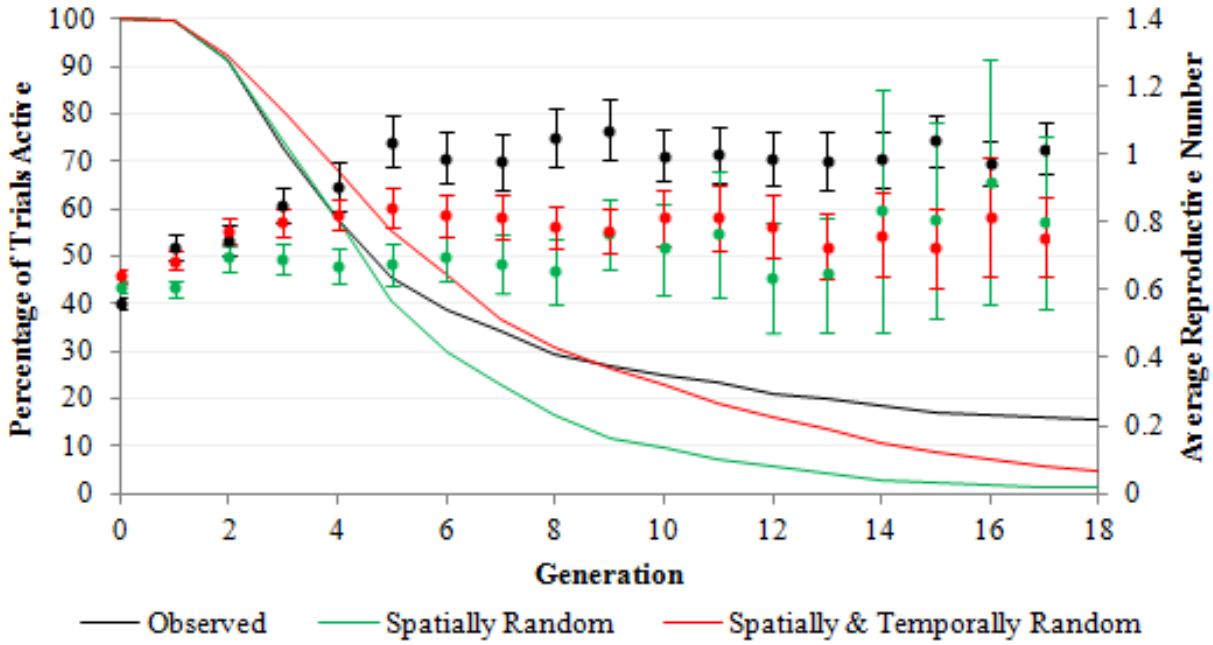
Figures

Figure 6.1: Simulated measles outbreak potential



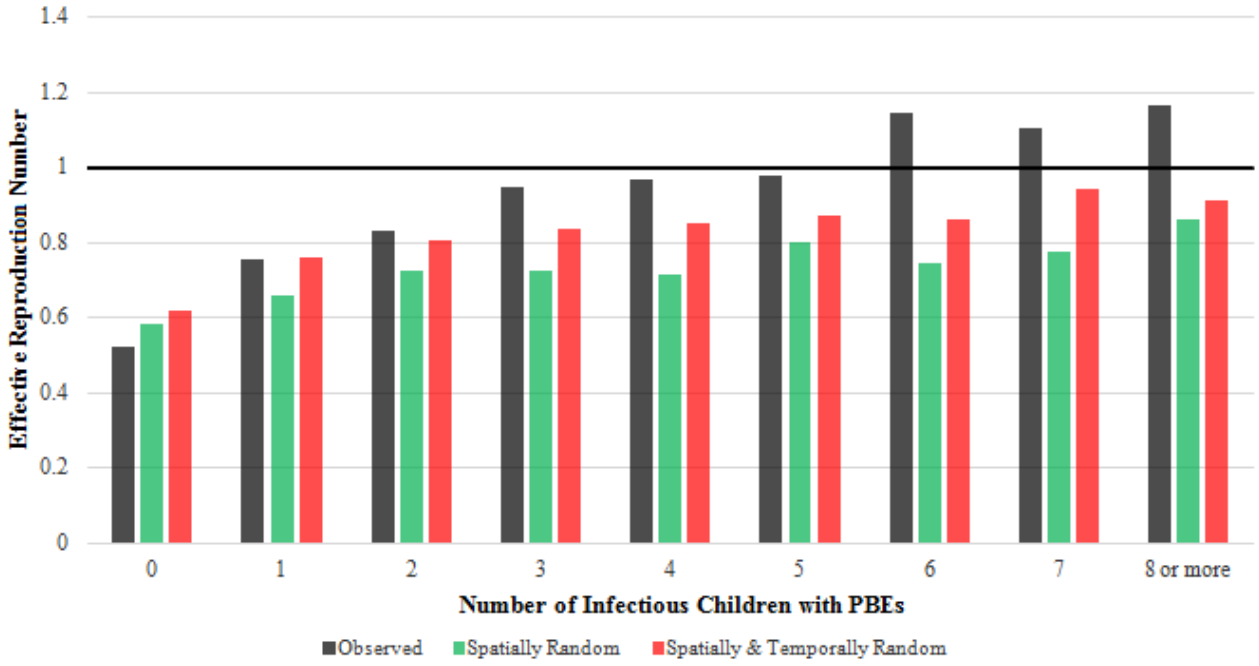
Note: Results averaged over 1000 trials.

Figure 6.2: Percent active trials and average R_{eff} in active trials across case generations



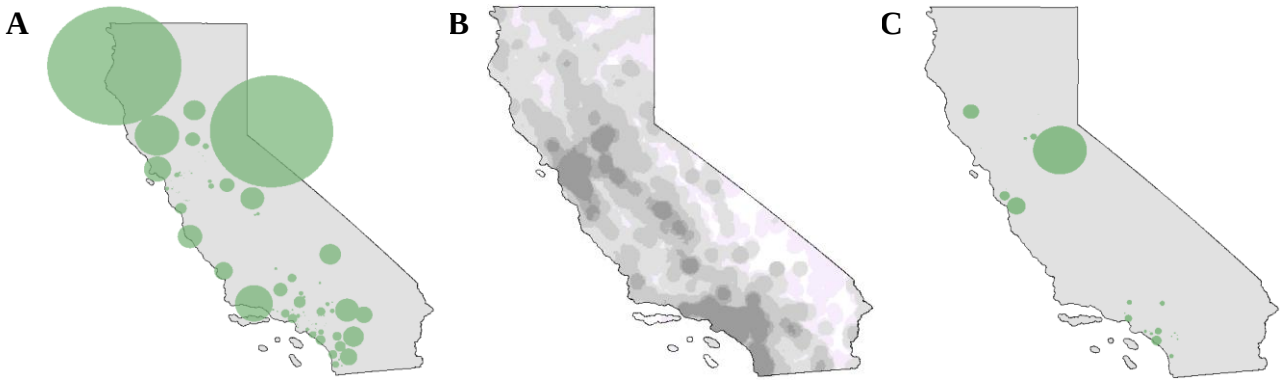
Note: Percent active trials shown by lines corresponding to the primary y-axis and average R_{eff} in active trials shown by points and corresponds to secondary y-axis. Lines show the percentage of trials still active in each generation of measles transmission. Measles transmission ceases before the full 36-week period in most trials, regardless the distribution of PBEs; however, there are approximately twice as many active transmissions continuing through the end of the 36-week period when PBEs are distributed as observed, than in either random PBE condition. Mean R_{eff} in active trials, plotted on the secondary y-axis, demonstrate that the average $R_{eff}$is at or above the critical value of 1 in the observed PBE condition after approximately the 5th generation of cases. Average R_{eff}in the random PBE conditions fail to reach this critical value at any point across generations of cases. Error bars show 95% confidence interval around the mean; the confidence intervals widen in the last few generations due to the small number of active trials, particularly in the random conditions. On average, spatial clustering of children with PBEs allows longer continuous measles transmission and produces higher R_{eff} after the first 4 generations of tranmission, which contribute to larger outbreak sizes than when PBEs are distributed randomly.

Figure 6.3: Effective reproduction number by number of infectious children with PBEs



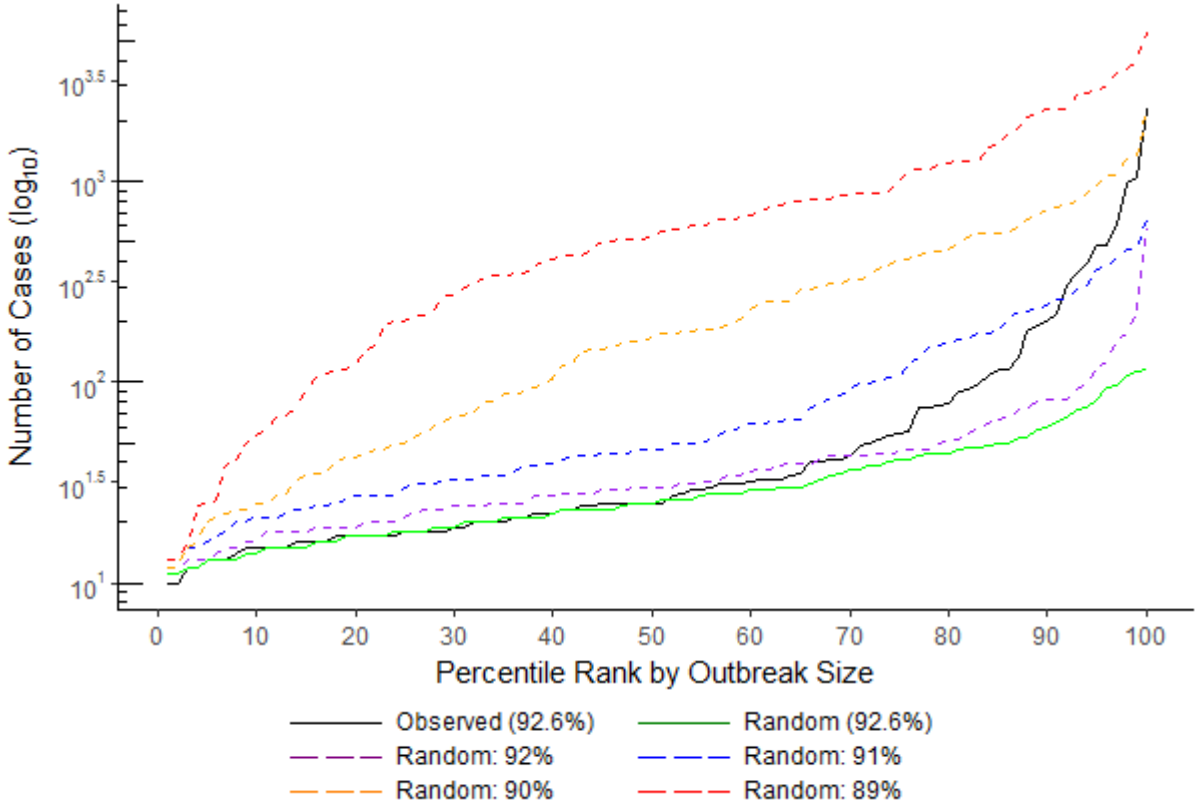
Note: R_{eff} steadily increases with the number of infectious children with PBEs, surpassing the critical value of 1 when there are six or more infectious children with PBEs. The same trend is not observed in either of the random conditions, and R_{eff} never reaches 1. $R_{eff}$is calculated by dividing the number of new infections by the number of infectious cases in a generation; numbers shown here are averaged across 1000 trials. The horizontal line marks the critical value of $R_{eff} = 1$; values above 1 are needed to sustain the epidemic, while those below 1 indicate declining disease spread.

Figure 6.4: Locations of synthetic measles infections



Note: (A) Spatial clusters of schools and childcare centers in the synthetic population with statistically significantly higher relative risk of PBEs than in the overall population. (B) Population density of synthetic children. (C) Spatial clusters of schools and childcare centers with statistically significantly higher relative risk of measles infections when PBEs are distributed as observed (across 1000 trials). Not all clusters of children with PBEs overlap with areas of significantly higher risk of measles infections; those that do tend to be in areas with higher population density. Higher population densities likely increase the ability for the disease to spread between smaller clusters of children with PBEs in these areas. Maps were created using Spatial Scan Statistics (see Kulldorff 1999).

Figure 6.5: Spatial clustering of PBEs reduces effective herd immunity in population



Appendix

Figure A6.1: Size of measles outbreaks with 50 (A) and 100 (B) randomly seeded infections

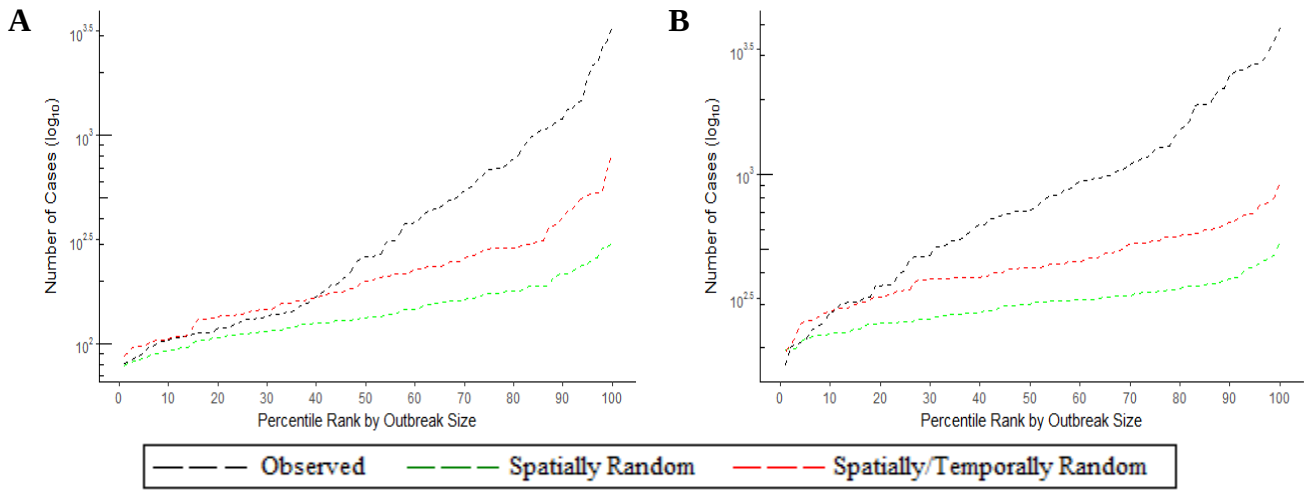
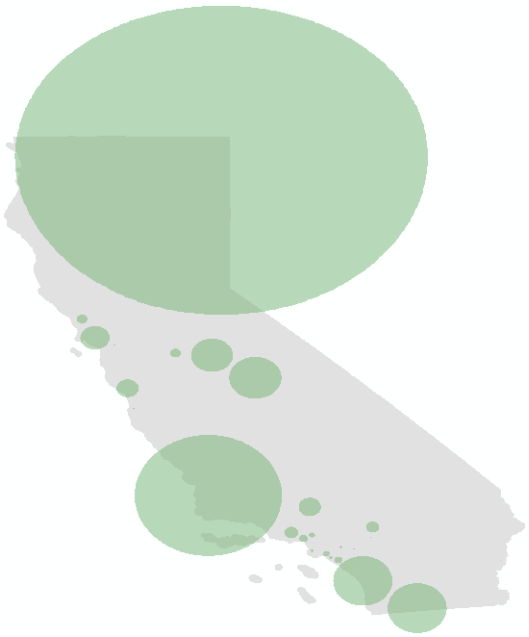


Figure A6.2: Clusters of kindergartens with statistically significantly higher relative risk of PBEs compared to the state-wide rate in kindergartens, 2014



Note: Data from the California Department of Public Health.

Chapter 7: Summary and Conclusion

Online articles on rising rates of vaccine refusals or outbreaks of vaccine preventable disease in the U.S. garner hundreds of comments. Debates rage over vaccine safety, suspicion of alternative motives in promoting vaccination, clear evidence for vaccines in preventing illness, and risks posed to others by unvaccinated children. Most of these discussions boil down to some variant on the following: should parents be able to refuse vaccines for their children?

As mentioned in **Chapter 1**, many vaccine hesitant parents assert the right to make individual decisions for the health of their child (Reich 2016; Senier 2008). Currently, parents who file non-medical vaccine exemptions rather than meet school vaccine requirements are a relatively small minority. As long as most parents in the U.S. and other high income countries continue choosing to vaccinate, how much do we really need to be concerned about the small number of parents that do not?

The problem with defining vaccine refusals as an individual parental choice is that when we look at the larger population we see that these decisions are isolated neither in determinants nor consequences. As discussed in **Chapter 2**, parents' perceptions of costs and benefits of vaccines are affected by many cultural forces beyond simple calculations of the efficacy of vaccines in preventing disease and risks associated with vaccine-preventable infections. Rather, how parents weigh these decisions depends on relationships with health professionals and others in their social networks. This renders vaccine decisions vulnerable to the social processes that create clustering in many other health outcomes.

The interdependence of vaccine decisions form pockets of low immunization. In turn, the structure of our social networks and patterns of social behavior affect the ability of diseases to reach susceptible hosts. As individuals, we cannot see the ways in which our interactions and

decisions aggregate in the larger network. And for this reason it is very difficult to reduce vaccine decisions to individual prerogative and consequences. So where do these clusters of non-medical vaccine exemptions form? And, more importantly, is the current level of clustering serious enough to influence how disease spreads?

Interestingly, previous research shows that parents who seek non-medical exemptions do not tend to fit the traditional profile of relative disadvantage associated with unvaccinated children (Smith et al. 2004). Rather these parents tend to be non-Hispanic white, well educated, and relatively affluent (Atwell et al. 2013; Birnbaum et al. 2013; Richards et al. 2013; Safi et al. 2012; Wei et al. 2009). Many hold alternative health beliefs (Gaudino and Robison 2012; Gellin et al. 2000; Reich 2016), and choose to send their children to private or charter schools (Brennan et al. 2016; Carrel and Bitterman 2015; Sobo 2015).

Chapter 3 demonstrates that although many of these factors have the expected school-level associations with PBEs in California, it is the percent non-Hispanic white children in the local area around the school that has the strongest association with clustering of PBEs across schools. Socio-economic status characteristics (SES), such as mother's level of education, have strong associations with PBEs within schools, but do not show substantial relationships to broader patterns of clustering. Although race/ethnicity is commonly seen as reflecting unmeasured effects of SES, these findings suggest that race/ethnicity can have effects on PBEs that are independent of SES.

Sorting of parents into schools based on race/ethnicity, SES, and other local neighborhood characteristics, such the presence of alternative health practitioners, does explain some, but not all, of the spatial clustering of PBEs across public kindergartens in California.

How can the remaining clustering be accounted for? Certainly, one possible reason is that parents sort themselves based on another, unmeasured characteristic associated with PBE rates.

More dynamic social processes could be at work as well. It could be that socio-demographic characteristics matter not only in the local vicinity around a school, but also in the surrounding neighborhoods. In other words, both a school's characteristics and the characteristics of schools nearby affect the likelihood of PBEs.

The influence from others could be more direct as well. Parents who refused to vaccinate their children could directly influence others around them to make similar choices. Qualitative studies of vaccine exemptions have shown that parents' social networks influence their decisions (Brunson 2013b, 2013a; Sobo 2015). This is consistent with other sociological studies demonstrating that diffusion of behaviors that require higher levels of commitment can create spatial pockets of adoptions (Centola and Macy 2007).

Investigation of these alternative social processes requires statistical models that examine dynamic, rather than static, effects across space. For this purpose, **Chapter 4** uses a set of spatial econometric models designed to incorporate the underlying spatial processes that generate clustering in outcomes. Spatial heterogeneity in the effects of socio-demographic, neighborhood, and school characteristics on school PBE rates showed local variation that is usually missed in models that only estimate average effects.

Spatial externalities occur when covariate characteristics of one school affect the PBE rates in other nearby schools. Percent non-Hispanic white in the local area around the school showed consistently significant, positive effects on PBE rates in nearby schools. Although mother's level of education and percent non-Hispanic white had similar direct effects on a

school's own PBE rate, mother's level of education did not show a significant effect on PBE rates nearby.

Spatial diffusion is also an externality, but it occurs when PBE rates in neighboring schools directly influence one another. The best fitting spatial models showed that spillover between PBE rates in neighboring schools better represented the spatial clustering of PBEs than unmeasured covariates not included in the model. These findings suggest that dynamic social processes, such as diffusion, likely affect clusters of PBE clustering across schools.

Future research is needed to examine why higher proportions of non-Hispanic white parents in the areas surrounding a school have such strong effects on clustering of PBEs. Effects of race/ethnicity independent those of SES and the indirect spillover effects would both be consistent with these parents playing a particularly important role in the diffusion of vaccine refusals through local social networks. Individual-level data on vaccine refusals and social networks could help determine if this was the case.

As discussed in **Chapter 2**, parents do not evaluate costs and benefits associated with vaccines free from the influence of others around them. Spatially dependent processes can contribute to the formation of local cultures where alternative views toward vaccines become normative as more parents decide to exempt their children. Decreasing trust in healthcare institutions and physicians to provide the most reliable information on vaccine safety could have amplified these trends.

The practical implication of the results in **Chapters 3 & 4** is that preventing spatial pockets of children with vaccine exemptions from forming may require interventions that target parents' social networks rather than taking an individualistic approach. Although most intervention strategies are conducted at the individual level, reviews have revealed that this

approach is limited in its effectiveness (Sadaf et al. 2013). Perceived support for vaccination among family and friends affects decisions to vaccinate (Allen et al. 2010). Identifying where these spatial pockets of unvaccinated children are likely to occur and local concerns surrounding vaccines in those areas may help us craft more effective intervention strategies.

Theoretically, **Chapters 3 & 4** demonstrate that selection into particular schools and neighborhoods alone is not enough to explain spatial pockets of PBEs. While there is a tendency to assume that differences in outcomes across space is the result of compositional effects, these findings suggest a more dynamic process. Permissive policies toward non-medical vaccine exemptions allow the creation of spatial pockets of unvaccinated children to form through social interaction among parents. This is an important illustration of how feedback effects in micro-level individual behaviors have the ability to reshape macro-level patterns. Here, social interaction serves as a transformational mechanism (Hedström and Swedberg 1996) that aggregates individual-level preferences into aggregate outcomes (Coleman 1986).

Methodologically, the contribution of this research is in showing that spatial methods can be used to help identify sociological meaningful differences in the locations of vaccine exemptions over space. Others have also used these models to understand how low birth weights cluster over space (Morenoff 2003) and how crime rates and locations of homicides within a city result from spatial diffusion into neighboring areas (Baller et al. 2001; Cohen and Tita 1999). Although the data and methods used here do not allow us to directly test for diffusion, they illuminate larger spatial patterns and associations that are not visible in individual-level data. These findings suggest where it might be productive for future research to look for these mechanisms.

But how concerned should we be about current levels of vaccine exemptions and their locations? Recent epidemiological investigations of measles and pertussis have shown that unvaccinated children are not only at increased risk for infection themselves, but also increase the risk of disease transmission to others in the surrounding community (Atwell et al. 2013; Feiken et al. 2000; Imdad et al. 2013; Omer et al. 2008). Abstract simulation models also suggest that spatial clustering of vaccine refusals increases disease spread (Eames 2009; Liu et al. 2015; Salathé and Bonhoeffer 2008).

It is reasonable to expect that the size and locations of clusters condition the level of consequences for disease spread. To my knowledge, no previous work has examined the risks of disease outbreak given the actual numbers and locations of vaccine exemptions. Yet, simulation experiments with empirically calibrated data on both the location of PBEs and local focal points of interaction are important for understanding potential macro-level consequences of real-world behaviors (Hedström and Åberg 2005).

Schools have served as hotspots for measles transmission, including in highly vaccinated populations. The clustering of exemptions within schools and the amount of physical contact that occurs among children there may make these locations even more vulnerable to measles transmission. Contact in the community within larger clusters of exemptions may play an important role in spreading the disease between schools.

Yet, the simulation experiments presented in **Chapter 5** show the opposite results. A greater percentage of measles cases occur in schools when PBEs are *not* spatially clustered. When PBEs are spatially clustered, however, charter schools become particularly important settings for measles transmission due to higher average PBE rates. Similarly, contact within

households plays a much bigger role in measles transmission when siblings share vaccination status.

Surprisingly, contact within neighborhoods and malls were not responsible for large percentages of measles infections nor did they appear to serve as the most important channels for measles transmission between schools. Contact within physician offices generated more infections than these locations, and disproportionately affected children too young to be vaccinated. Prohibiting contact in all interaction focal points did show some initial effects in reducing the number of infections. However, only eliminating contact in schools was sufficient to prevent large outbreaks entirely.

Even though a larger percentage of infections occurred in schools when PBEs were not spatially clustered, a larger number of total infections were transmitted in schools when PBEs were allowed to cluster spatially as observed in the population. Could the spatial clustering of vaccine exemptions in particular be to blame for increasing measles incidence in the U.S.?

Chapter 6 demonstrates that maximum measles outbreak sizes were 10 times larger when PBEs were spatially clustered than when PBEs were assigned at random. Surprisingly, spatial clustering of PBEs *reduced* the number of cases in smaller outbreaks. In other words, spatial clustering of exemptions appears to provide some initial slight protection against measles infections because it is more difficult for the disease to find unvaccinated children. Once the disease reaches one unvaccinated child, however, the search becomes much easier and many more unvaccinated children can be infected nearby.

This is because spatial pockets of unvaccinated children serve as disease cores in measles transmission. Within these areas, contagious children are able to generate many subsequent infections, which increase the effective reproduction number of the disease. This boost in

transmission allows infections to spread outside these clusters and into the larger community. This lowers the effectiveness of protection against disease spread provided by herd immunity, even when overall vaccination coverage is high in the population.

These findings emphasize that it is the spatial clustering of vaccine exemptions rather than their overall prevalence in the population that most affects potential measles outbreaks. Parents making these decisions should be made aware of the collective consequences of seemingly individual decisions. The ability to accurately perceive disease risk has important implications for social behavior in networks (Bauch and Bhattacharyya 2012).

Policies that allow easy access to non-medical vaccine exemptions can increase their prevalence and allow these spatial pockets to form. Findings from **Chapter 5** in particular remind us that the pairing of school choice and the ability of parents to refuse vaccines magnify the risk of vaccine-preventable disease transmission in charter schools. Offering incentives (Buttenheim and Asch 2013) or resources to schools to keep exemption rates low can also help prevent large disease outbreaks in these locations.

Theoretically, results from **Chapters 5 & 6** contribute to our awareness of the strength of strong ties in creating disease cores that are able to increase disease spread in populations with high overall rates of vaccination. The tendency for children with non-medical exemptions to be located in the same households and schools means that frequent social interaction between unvaccinated children is likely to occur via strong ties. In other words, if weak ties provide bridges for diseases to travel into new areas of the network, strong ties can supply pockets of susceptible children to fuel a few initial cases into large outbreaks.

Understanding that pockets of unvaccinated children can function as disease cores also highlights the threat that non-medical exemptions pose to the ability to maintain non-endemic

status for measles in the U.S. As foreshadowed in **Chapter 2**, clusters of unvaccinated children can have two different effects on network robustness to disease spread. When the disease is introduced randomly and most children are vaccinated, the network is more robust to small outbreaks. Yet, non-random introduction of a disease, or the ability of the disease to quickly reach clusters of unvaccinated children, has the opposite effect—the network is less robust and outbreak sizes increase. This distinction helps us look past blanket views that all clustering necessarily has negative effects on disease spread. This can inform future research that investigates how the size of spatial clusters specifically affects outbreaks.

Using simulation experiments that combine empirical data on locations of children, vaccine exemptions, and interaction points in the local community with epidemiological models of disease spread allow sociological insight into how social networks shape biological contagion. These models allow specification of counterfactual scenarios that are not able to be observed in the real world. At the same time, the model's empirical grounding improves our ability to use the findings to inform real world puzzles.

Much attention has been given to potential threats to public health posed by increasing rates of non-medical vaccine exemptions. As a whole, this project maps out the concrete ways in which parents' vaccination decisions contribute to collective health outcomes. My findings illustrate how our social networks shape both the contexts in which we make health decisions and the patterns of physical contact through which disease travels. This intersection of social behavior and biological contagion shapes both perceptions of vaccine-preventable disease risk and how actual risks of infections accumulate in the community. Although parents may perceive vaccine decisions for their children as personal and individualistic, they are fundamentally communal and collective in their consequences.

Bibliography

Achen, Christopher H. 2000. "Why Lagged Dependent Variables Can Suppress the Explanatory Power of Other Independent Variables." in *Annual Meeting of the Political Methodology Section of the American Political Science Association*. Los Angeles, CA.

Akaike, Hirotugu. 1974. "A New Look at the Statistical Model Identification." *IEEE Transactions on Automatic Control* 19(6):716–23.

Albert, Réka, István Albert, and Gary L. Nakarado. 2004. "Structural Vulnerability of the North American Power Grid." *Physical Review E* 69(2):025103.

Albert, Réka, Hawoong Jeong, and Albert-László Barabási. 2000. "Error and Attack Tolerance of Complex Networks." *Nature* 406(6794):378–82.

Allen, Arthur. 2008. *Vaccine: The Controversial Story of Medicine's Greatest Lifesaver*. Reprint edition. New York: W. W. Norton & Company.

Allen, Jennifer D. et al. 2010. "Parental Decision Making about the HPV Vaccine." *Cancer Epidemiology and Prevention Biomarkers* 19(9):2187–98.

Allen, Linda, Truman Lewis, Clyde F. Martin, and Mark Stamp. 1990. "A Mathematical Analysis and Simulation of a Localized Measles Epidemic." *Applied Mathematics and Computation* 39(1):61–77.

Allred, Norma J., Kate M. Shaw, Tammy A. Santibanez, Donna L. Rickert, and Jeanne M. Santoli. 2005. "Parental Vaccine Safety Concerns: Results from the National Immunization Survey, 2001–2002." *American Journal of Preventive Medicine* 28(2):221–24.

Allred, Norma J., Karen G. Wooten, and Yuan Kong. 2007. "The Association of Health Insurance and Continuous Primary Care in the Medical Home on Vaccination Coverage for 19- to 35-Month-Old Children." *Pediatrics* 119(Supplement 1):S4–11.

Anderson, Roy M. and Robert M. May. 1985. "Vaccination and Herd Immunity to Infectious Diseases." *Nature* 318(6044):323–29.

Anderson, Roy M. and Robert M. May. 1990. "Immunisation and Herd Immunity." *The Lancet* 335(8690):641–45.

Anderson, Roy M., Robert M. May, and B. Anderson. 1992. *Infectious Diseases of Humans: Dynamics and Control*. Reprint edition. Oxford: Oxford University Press.

Andre, Francis E. et al. 2008. "Vaccination Greatly Reduces Disease, Disability, Death and Inequity Worldwide." *Bulletin of the World Health Organization* 86(2):81–160.

Andrews, Kenneth T. and Michael Biggs. 2006. “The Dynamics of Protest Diffusion: Movement Organizations, Social Networks, and News Media in the 1960 Sit-Ins.” *American Sociological Review* 71(5):752–777.

Anselin, Luc. 1988a. “Lagrange Multiplier Test Diagnostics for Spatial Dependence and Spatial Heterogeneity.” *Geographical Analysis* 20(1):1–17.

Anselin, Luc. 1988b. *Spatial Econometrics: Methods and Models*. Boston, MA: Kluwer Academic Publishers.

Anselin, Luc. 2003. “Spatial Externalities, Spatial Multipliers, And Spatial Econometrics.” *International Regional Science Review* 26(2):153–66.

Anselin, Luc, Ibnu Syabri, and Youngihn Kho. 2006. “GeoDa: An Introduction to Spatial Data Analysis.” *Geographical Analysis* 38(1):5–22.

Asch, David A. et al. 1994. “Omission Bias and Pertussis Vaccination.” *Medical Decision Making* 14(2):118–23.

Attwell, Katie and Melanie Freeman. 2015. “I Immunise: An Evaluation of a Values-Based Campaign to Change Attitudes and Beliefs.” *Vaccine* 33(46):6235–40.

Atwell, Jessica E. et al. 2013. “Nonmedical Vaccine Exemptions and Pertussis in California, 2010.” *Pediatrics* 132(4):624–30.

Babalola, Stella. 2011. “Maternal Reasons for Non-Immunisation and Partial Immunisation in Northern Nigeria.” *Journal of Paediatrics and Child Health* 47(5):276–81.

Bale, J. R. 1978. “Geographical Diffusion and the Adoption of Professionalism in Football in England and Wales.” *Geography* 63(3):188–97.

Baller, Robert D., Luc Anselin, Steven F. Messner, Glenn Deane, and Darnell F. Hawkins. 2001. “Structural Covariates of U.s. County Homicide Rates: Incorporating Spatial Effects.” *Criminology* 39(3):561–88.

Banerjee, Abhijit V. 1992. “A Simple Model of Herd Behavior.” *The Quarterly Journal of Economics* 107(3):797–817.

Barabási, Albert-László. 2009. “Scale-Free Networks: A Decade and Beyond.” *Science* 325(5939):412–13.

Bardenheier, Barbara et al. 2004. “Are Parental Vaccine Safety Concerns Associated With Receipt of Measles-Mumps-Rubella, Diphtheria and Tetanus Toxoids With Acellular Pertussis, or Hepatitis B Vaccines by Children?” *Archives of Pediatrics & Adolescent Medicine* 158(6):569–75.

Bates, Ann S. and Fredric D. Wolinsky. 1998. “Personal, Financial, and Structural Barriers to Immunization in Socioeconomically Disadvantaged Urban Children.” *Pediatrics* 101(4):591–96.

Bauch, Chris T. 2005. “Imitation Dynamics Predict Vaccinating Behaviour.” *Proceedings of the Royal Society of London B: Biological Sciences* 272(1573):1669–75.

Bauch, Chris T. and Samit Bhattacharyya. 2012. “Evolutionary Game Theory and Social Learning Can Determine How Vaccine Scares Unfold.” *PLOS Computational Biology* 8(4):e1002452.

Bauch, Chris T. and Alison P. Galvani. 2013. “Social and Biological Contagions.” *Science* 342(6154):47–49.

Bayer, Patrick, Fernando Ferreira, and Robert McMillan. 2007. “A Unified Framework for Measuring Preferences for Schools and Neighborhoods.” *Journal of Political Economy* 115(4):588–638.

Bearman, Peter. 2009. “Just-so Stories: Vaccines, Autism, and the Single-Bullet Disorder.” *Social Psychology Quarterly* 73:112–15.

Bearman, Peter S., James Moody, and Katherine Stovel. 2004. “Chains of Affection: The Structure of Adolescent Romantic and Sexual Networks.” *American Journal of Sociology* 110(1):44–91.

Becker, Alexander D. et al. 2016. “Estimating Enhanced Prevaccination Measles Transmission Hotspots in the Context of Cross-Scale Dynamics.” *Proceedings of the National Academy of Sciences* 113(51):14595–600.

Belshe, S.Kimberly. 1996. *California Immunization Handbook: A Guide to Implementing the School and Child Care Entry Immunization Requirements of the California School Immunization Law*. DIANE Publishing.

Benin, Andrea L., Daryl J. Wisler-Scher, Eve Colson, Eugene D. Shapiro, and Eric S. Holmboe. 2006. “Qualitative Analysis of Mothers’ Decision-Making About Vaccines for Infants: The Importance of Trust.” *Pediatrics* 117(5):1532–41.

Berg, Ivar. 1970. *Education for Jobs; The Great Training Robbery*. New York: Columbia University Press.

Berkman, Lisa F., Thomas Glass, Ian Brissette, and Teresa E. Seeman. 2000. “From Social Integration to Health: Durkheim in the New Millennium.” *Social Science & Medicine* 51(6):843–57.

Berry, Nina J. et al. 2017. “When Parents Won’t Vaccinate Their Children: A Qualitative Investigation of Australian Primary Care Providers’ Experiences.” *BMC Pediatrics* 17:19.

Bikhchandani, Sushil, David Hirshleifer, and Ivo Welch. 1992. "A Theory of Fads, Fashion, Custom, and Cultural Change as Informational Cascades." *Journal of Political Economy* 100(5):992–1026.

Birnbaum, Michael S., Elizabeth T. Jacobs, Jennifer Ralston-King, and Kacey C. Ernst. 2013. "Correlates of High Vaccination Exemption Rates among Kindergartens." *Vaccine* 31(5):750–56.

Bivand, Roger, Danlin Yu, Tomoki Nakaya, and Miquel-Angel Garcia-Lopez. 2009. "Spgwr: Geographically Weighted Regression." *R Package Version 0.6–19. Available Online: Http://Cran.r-Project.org/Web/Packages/Spgwr/Spgwr.pdf*.

Bjørnstad, Ottar N., Bärbel F. Finkenstädt, and Bryan T. Grenfell. 2002. "Dynamics of Measles Epidemics: Estimating Scaling of Transmission Rates Using a Time Series Sir Model." *Ecological Monographs* 72(2):169–84.

Bloch, Alan B. et al. 1985. "Measles Outbreak in a Pediatric Practice: Airborne Transmission in an Office Setting." *Pediatrics* 75(4):676–83.

Blumberg, Seth et al. 2015. "Assessing Measles Transmission in the United States Following a Large Outbreak in California." *PLOS Currents Outbreaks* 7.

Blumberg, Seth, Wayne T. A. Enanoria, James O. Lloyd-Smith, Thomas M. Lietman, and Travis C. Porco. 2014. "Identifying Postelimination Trends for the Introduction and Transmissibility of Measles in the United States." *American Journal of Epidemiology* 179(11):1375–82.

Bobo, Janet Kay, James L. Gale, Purushottam B. Thapa, and Steven G. F. Wassilak. 1993. "Risk Factors for Delayed Immunization in a Random Sample of 1163 Children From Oregon and Washington." *Pediatrics* 91(2):308–14.

Bolker, B. M. and B. T. Grenfell. 1993. "Chaos and Biological Complexity in Measles Dynamics." *Proceedings of the Royal Society of London B: Biological Sciences* 251(1330):75–81.

Bond, Robert M. et al. 2012. "A 61-Million-Person Experiment in Social Influence and Political Mobilization." *Nature* 489(7415):295–98.

Brennan, Julia M. et al. 2016. "Trends in Personal Belief Exemption Rates Among Alternative Private Schools: Waldorf, Montessori, and Holistic Kindergartens in California, 2000–2014." *American Journal of Public Health* 107(1):108–12.

Brown, Katrina et al. 2011. "Attitudinal and Demographic Predictors of Measles-Mumps-Rubella Vaccine (MMR) Uptake during the UK Catch-Up Campaign 2008–09: Cross-Sectional Survey." *PLOS ONE* 6(5):e19381.

Brown, Katrina F. et al. 2010. “Omission Bias and Vaccine Rejection by Parents of Healthy Children: Implications for the Influenza A/H1N1 Vaccination Programme.” *Vaccine* 28(25):4181–85.

Bruch, E. and J. Atwell. 2015. “Agent-Based Models in Empirical Social Research.” *Sociological Methods & Research* 44(2):186–221.

Brunsdon, Chris, A.Stewart Fotheringham, and Martin E. Charlton. 1996. “Geographically Weighted Regression: A Method for Exploring Spatial Nonstationarity.” *Geographical Analysis* 28(4):281–98.

Brunson, Emily K. 2013a. “How Parents Make Decisions about Their Children’s Vaccinations.” *Vaccine* 31(46):5466–70.

Brunson, Emily K. 2013b. “The Impact of Social Networks on Parents’ Vaccination Decisions.” *Pediatrics* 131(5):2012–2452.

Bullock, Seth, Lionel Barnett, and Ezequiel A. Di Paolo. 2010. “Spatial Embedding and the Structure of Complex Networks.” *Complexity* 16(2):20–28.

Burns, Lawton R. and Douglas R. Wholey. 1993. “Adoption and Abandonment of Matrix Management Programs: Effects of Organizational Characteristics and Interorganizational Networks.” *The Academy of Management Journal* 36(1):106–38.

Burt, Ronald S. 1987. “Social Contagion and Innovation: Cohesion Versus Structural Equivalence.” *American Journal of Sociology* 92(6):1287–1335.

Buttenheim, Alison, Malia Jones, and Yelena Baras. 2012. “Exposure of California Kindergartners to Students with Personal Belief Exemptions from Mandated School Entry Vaccinations.” *American Journal of Public Health* 102(8):e59-67.

Buttenheim, Alison M. et al. 2015. “MMR Vaccination Status of Children Exempted from School-Entry Immunization Mandates.” *Vaccine* 33(46):6250–56.

Buttenheim, Alison M. and David A. Asch. 2013. “Making Vaccine Refusal Less of a Free Ride.” *Human Vaccines & Immunotherapeutics* 9(12):2674–75.

Buttenheim, Alison M., Sarah T. Cherng, and David A. Asch. 2013. “Provider Dismissal Policies and Clustering of Vaccine-Hesitant Families.” *Human Vaccines & Immunotherapeutics* 9(8):1819–24.

California Department of Health Services, Immunization Branch. 2003. *California Immunization Handbook: School and Child Care Immunization Requirements for Schools and Child Care Programs*. 7th ed. Richmond, CA.

California Department of Public Health, Immunization Branch. 2007. *Vaccine-Preventable Diseases and Immunization Coverage in California, 2001-2006*. Retrieved

(https://www.cdph.ca.gov/programs/immunize/Documents/Complete%20Report_Vaccine_Preventable%20Diseases%20and%20Immunization.pdf).

California Department of Public Health, Immunization Branch. 2008. *Childhood Immunization Coverage in California, 2006-08*. Retrieved (https://www.cdph.ca.gov/programs/immunize/Documents/ChildhoodImmunizationCoverageCA2006-08.pdf).

California Department of Public Health, Immunization Branch. 2010. *2009-2010 Kindergarten Immunization Assessment Report*.

California Department of Public Health, Immunization Branch. 2011. *2010-2011 Kindergarten Immunization Assessment Report*.

California Department of Public Health, Immunization Branch. 2012. *2011-2012 Kindergarten Assessment Results*.

California Department of Public Health, Immunization Branch. 2013. *2012-2013 CA Kindergarten Immunization Assessment*.

California Department of Public Health, Immunization Branch. 2015. *2014-2015 Kindergarten Immunization Assessment Results*. Retrieved (https://www.cdph.ca.gov/programs/immunize/Documents/2014-15%20CA%20Kindergarten%20Immunization%20Assessment.pdf).

California Department of Public Health, Immunization Branch. 2016a. *2015-2016 CA Kindergarten Summary Report*. Retrieved (https://www.cdph.ca.gov/programs/immunize/Documents/2015-16_CA_KindergartenSummaryReport.pdf).

California Department of Public Health, Immunization Branch. 2016b. *California Immunization Handbook: School and Child Care Immunization Requirements for Schools and Child Care Programs*. 9th ed. Richmond, CA.

California Department of Public Health, Immunization Branch. 2017. *2016-2017 Kindergarten Immunization Assessment – Executive Summary*. Retrieved (https://archive.cdph.ca.gov/programs/immunize/Documents/2016-17_CA_KindergartenSummaryReport.pdf).

Callaway, Duncan S., M. E. J. Newman, Steven H. Strogatz, and Duncan J. Watts. 2000. "Network Robustness and Fragility: Percolation on Random Graphs." *Physical Review Letters* 85(25):5468–71.

Callender, David. 2016. "Vaccine Hesitancy: More than a Movement." *Human Vaccines & Immunotherapeutics* 12(9):2464–68.

Calman, K. C., P. G. Bennett, and D. G. Corns. 1999. "Risks to Health: Some Key Issues in Management, Regulation and Communication." *Health, Risk & Society* 1(1):107–16.

Campbell, James B., Jason W. Busse, and H.Stephen Injeyan. 2000. “Chiropractors and Vaccination: A Historical Perspective.” *Pediatrics* 105(4):e43–e43.

Carpiano, Richard M. 2009. “Come Take a Walk with Me: The ‘Go-Along’ Interview as a Novel Method for Studying the Implications of Place for Health and Well-Being.” *Health & Place* 15(1):263–272.

Carpiano, Richard M. and Nicholas S. Fitz. 2017. “Public Attitudes toward Child Undervaccination: A Randomized Experiment on Evaluations, Stigmatizing Orientations, and Support for Policies.” *Social Science & Medicine* 185:127–36.

Carrel, Margaret and Patrick Bitterman. 2015. “Personal Belief Exemptions to Vaccination in California: A Spatial Analysis.” *Pediatrics* 136(1):80–88.

Caskey, Rachel, Stacy Tessler Lindau, and G.Caleb Alexander. 2009. “Knowledge and Early Adoption of the HPV Vaccine Among Girls and Young Women: Results of a National Survey.” *Journal of Adolescent Health* 45(5):453–62.

Cauchemez, Simon et al. 2011. “Role of Social Networks in Shaping Disease Transmission during a Community Outbreak of 2009 H1N1 Pandemic Influenza.” *Proceedings of the National Academy of Sciences* 108(7):2825–30.

Caughy, Margaret O’Brien, Tammy Leonard, Kurt Beron, and James Murdoch. 2013. “Defining Neighborhood Boundaries in Studies of Spatial Dependence in Child Behavior Problems.” *International Journal of Health Geographics* 12:24.

Cava, Maureen A., Krissa E. Fay, Heather J. Beanlands, Elizabeth A. McCay, and Rouleen Wignall. 2005. “Risk Perception and Compliance With Quarantine During the SARS Outbreak.” *Journal of Nursing Scholarship* 37(4):343–47.

Centers for Disease Control and Prevention. 1999. “Achievements in Public Health, 1900-1999 Impact of Vaccines Universally Recommended for Children -- United States, 1990-1998.” *Morbidity and Mortality Weekly Report* 48(12):243–48.

Centers for Disease Control and Prevention. 2002. “Measles--United States, 2000.” *Morbidity and Mortality Weekly Report* 51(6):120–23.

Centers for Disease Control and Prevention. 2004. “Measles Outbreak Associated with an Imported Case in an Infant — Alabama, 2002.” *Morbidity and Mortality Weekly Report* 53(2):30–33.

Centers for Disease Control and Prevention. 2012a. “Hospital-Associated Measles Outbreak - Pennsylvania, March-April 2009.” *Morbidity and Mortality Weekly Report* 61(2):30–32.

Centers for Disease Control and Prevention. 2012b. “Measles - United States, 2011.” *Morbidity and Mortality Weekly Report* 61:253–57.

Centers for Disease Control and Prevention. 2012c. *VFC Program Distribution of Pediatric Vaccines*. Atlanta, Georgia. Retrieved (https://www.cdc.gov/vaccines/programs/vfc/about/distribution.html).

Centers for Disease Control and Prevention. 2013. "Measles — United States, January 1–August 24, 2013." *Morbidity and Mortality Weekly Report* 62(36):741–43.

Centers for Disease Control and Prevention. 2015. *Epidemiology and Prevention of Vaccine-Preventable Diseases*. 13th ed. edited by J. Hamborsky, A. Kroger, and C. Wolfe. Washington D.C.: Public Health Foundation.

Centers for Disease Control and Prevention. 2016. *2015-16 School Year Vaccination Exemption Reports*. Retrieved (https://www.cdc.gov/vaccines/imz-managers/coverage/schoolvaxview/data-reports/exemptions-reports/2015-16.html).

Centers for Disease Control and Prevention. 2017a. *Child and Adolescent Schedule*.

Centers for Disease Control and Prevention. 2017b. *Measles Cases and Outbreaks*. Atlanta, Georgia. Retrieved (https://www.cdc.gov/measles/cases-outbreaks.html).

Centola, Damon. 2010. "The Spread of Behavior in an Online Social Network Experiment." *Science* 329(5996):1194–1197.

Centola, Damon. 2011. "An Experimental Study of Homophily in the Adoption of Health Behavior." *Science* 334(6060):1269–72.

Centola, Damon and Michael Macy. 2007. "Complex Contagions and the Weakness of Long Ties." *American Journal of Sociology* 113(3):702–34.

Centola, Damon and Arnout van de Rijt. 2015. "Choosing Your Network: Social Preferences in an Online Health Community." *Social Science & Medicine* 125:19–31.

Chang, Virginia W. and Diane S. Lauderdale. 2009. "Fundamental Cause Theory, Technological Innovation, and Health Disparities: The Case of Cholesterol in the Era of Statins." *Journal of Health and Social Behavior* 50(3):245–60.

Chao, Dennis L., M.Elizabeth Halloran, Valerie J. Obenchain, and Ira M.Longini Jr. 2010. "FluTE, a Publicly Available Stochastic Influenza Epidemic Simulation Model." *PLOS Computational Biology* 6(1):e1000656.

Chaves, Mark. 1996. "Ordaining Women: The Diffusion of an Organizational Innovation." *American Journal of Sociology* 101(4):840–73.

Chen, Robert T., Gary M. Goldbaum, Steven G. F. Wassilak, Lauri E. Markowitz, and Walter A. Orenstein. 1989. "An Explosive Point-Source Measles Outbreak in a Highly Vaccinated Population Modes of Transmission and Risk Factors for Disease." *American Journal of Epidemiology* 129(1):173–82.

Chen, Sanny Y. et al. 2011. “Health Care–Associated Measles Outbreak in the United States After an Importation: Challenges and Economic Impact.” *The Journal of Infectious Diseases* 203(11):1517–25.

Chen, Tai-Ho et al. 2010. “Measles Outbreak Associated With an International Youth Sporting Event in the United States, 2007.” *Pediatric Infectious Disease Journal* 29(9):794–800.

Chiprich, Jennifer and Akisha White. 2011. “Implementation and Evaluation of the ‘I Choose’ Campaign to Promote Adult Immunization in South Los Angeles.”

Christakis, Nicholas A. and James H. Fowler. 2007. “The Spread of Obesity in a Large Social Network over 32 Years.” *New England Journal of Medicine* 357(4):370–79.

Christakis, Nicholas A. and James H. Fowler. 2008. “The Collective Dynamics of Smoking in a Large Social Network.” *New England Journal of Medicine* 358(21):2249–58.

Clemmons, Nakia S., Paul A. Gastanaduy, Amy Parker Fiebelkorn, Susan B. Redd, and Gregory Wallace. 2015. “Measles — United States, January 4–April 2, 2015.” *Morbidity and Mortality Weekly Report* 64(14):373–76.

Cliff, Andrew David and J.Keith Ord. 1981. *Spatial Processes: Models & Applications*. London: Pion.

Cline, Rebecca J. W. and Kevin M. Haynes. 2001. “Consumer Health Information Seeking on the Internet: The State of the Art.” *Health Education Research* 16(6):671–92.

Cohen, Jacqueline and George Tita. 1999. “Diffusion in Homicide: Exploring a General Method for Detecting Spatial Diffusion Processes.” *Journal of Quantitative Criminology* 15(4):451–93.

Coleman, James S. 1986. “Social Theory, Social Research, and a Theory of Action.” *American Journal of Sociology* 91(6):1309–35.

Coleman, James Samuel, Elihu Katz, and Herbert Menzel. 1966. *Medical Innovation: A Diffusion Study*. New York: Bobbs-Merrill Co.

Colley, F. and M. Haas. 1994. “Attitudes on Immunization: A Survey of American Chiropractors.” *Journal of Manipulative and Physiological Therapeutics* 17(9):584–90.

Committee on Practice and Ambulatory Medicine, Committee on Infectious Diseases, Committee on State Government Affairs, Council on School Health, and Section on Administration and Practice Management. 2016. “Medical Versus Nonmedical Immunization Exemptions for Child Care and School Attendance.” *Pediatrics* 138(3):e2016-2145.

Constant, David, Lee Sproull, and Sara Kiesler. 1996. “The Kindness of Strangers: The Usefulness of Electronic Weak Ties for Technical Advice.” *Organization Science* 7(2):119–35.

Cotten, Shelia R. and Sipi S. Gupta. 2004. “Characteristics of Online and Offline Health Information Seekers and Factors That Discriminate between Them.” *Social Science & Medicine* 59(9):1795–1806.

Crepaz, Nicole, Trevor A. Hart, and Gary Marks. 2004. “Highly Active Antiretroviral Therapy and Sexual Risk Behavior: A Meta-Analytic Review.” *Journal of the American Medical Association* 292(2):224–36.

Crossley, Nick. 2010. *Towards Relational Sociology*. New York, N.Y.: Routledge.

Currarini, Sergio, Matthew O. Jackson, and Paolo Pin. 2010. “Identifying the Roles of Race-Based Choice and Chance in High School Friendship Network Formation.” *Proceedings of the National Academy of Sciences* 107(11):4857–61.

Daley, Matthew F. and Jason M. Glanz. 2011. “Straight Talk about Vaccination.” *Scientific American* 305(3):32, 34.

Danis, K., T. Georgakopoulou, T. Stavrou, D. Laggas, and T. Panagiotopoulos. 2010. “Socioeconomic Factors Play a More Important Role in Childhood Vaccination Coverage than Parental Perceptions: A Cross-Sectional Study in Greece.” *Vaccine* 28(7):1861–69.

David, Pa. 1985. “Clio and the Economics of Qwerty.” *American Economic Review* 75(2):332–37.

Davis, Gerald F. and Henrich R. Greve. 1997. “Corporate Elite Networks and Governance Changes in the 1980s.” *American Journal of Sociology* 103(1):1–37.

Davis, Ronald M. et al. 1986. “Transmission of Measles in Medical Settings: 1980 Through 1984.” *Journal of the American Medical Association* 255(10):1295–98.

Davis, Ronald M. et al. 1987. “A Persistent Outbreak of Measles Despite Appropriate Prevention and Control Measures.” *American Journal of Epidemiology* 126(3):438–49.

DeBolt, Charla A., Krista Rietberg, Nita Heimann, David Bibus, and Jeffrey S. Duchin. 2002. “School Exemption Data and Geocoding as Tools for Assessing the Relationship of Pertussis Clusters to High Exemption Rates for Pertussis-Containing Vaccines in School Districts.”

Del Valle, Sara Y., James M. Hyman, and Nakul Chitnis. 2013. “Mathematical Models of Contact Patterns Between Age Groups for Predicting the Spread of Infectious Diseases.” *Mathematical Biosciences and Engineering* 10(0):1475–97.

Del Valle, Sara Y., James M. Hyman, Herbert W. Hethcote, and Stephen G. Eubank. 2007. “Mixing Patterns between Age Groups in Social Networks.” *Social Networks* 29(4):539–554.

Dempsey, Amanda F. et al. 2011. “Alternative Vaccination Schedule Preferences Among Parents of Young Children.” *Pediatrics* 128(5):848–56.

Desmond, Matthew. 2012. “Eviction and the Reproduction of Urban Poverty.” *American Journal of Sociology* 118(1):88–133.

Dietz, K. 1993. “The Estimation of the Basic Reproduction Number for Infectious Diseases.” *Statistical Methods in Medical Research* 2(1):23–41.

DiGiovanni, Clete, Jerome Conley, Daniel Chiu, and Jason Zaborski. 2004. “Factors Influencing Compliance with Quarantine in Toronto During the 2003 SARS Outbreak.” *Biosecurity and Bioterrorism: Biodefense Strategy, Practice, and Science* 2(4):265–72.

DiMaggio, Paul J. and Walter W. Powell. 1983. “The Iron Cage Revisited: Institutional Isomorphism and Collective Rationality in Organizational Fields.” *American Sociological Review* 48(2):147.

Dodds, Peter S. and Duncan J. Watts. 2005. “A Generalized Model of Social and Biological Contagion.” *Journal of Theoretical Biology* 232(4):587–604.

Dubé, Eve et al. 2016. “‘Nature Does Things Well, Why Should We Interfere?’ Vaccine Hesitancy Among Mothers.” *Qualitative Health Research* 26(3):411–425.

Dubé, Eve, Maryline Vivion, and Noni E. MacDonald. 2015. “Vaccine Hesitancy, Vaccine Refusal and the Anti-Vaccine Movement: Influence, Impact and Implications.” *Expert Review of Vaccines* 14(1):99–117.

Eames, Ken T. D. 2009. “Networks of Influence and Infection: Parental Choices and Childhood Disease.” *Journal of the Royal Society Interface* 6(38):811–14.

Easley, David and Jon Kleinberg. 2010. *Networks, Crowds, and Markets: Reasoning about a Highly Connected World*. New York: Cambridge University Press.

Ehresmann, K. R. et al. 1998. “A Statewide Survey of Immunization Rates in Minnesota School Age Children: Implications for Targeted Assessment and Prevention Strategies.” *Pediatric Infectious Disease Journal* 17(8):711–16.

Elhorst, J.Paul. 2010. “Applied Spatial Econometrics: Raising the Bar.” *Spatial Economic Analysis* 5(1):9–28.

Emirbayer, Mustafa. 1997. “Manifesto for a Relational Sociology.” *American Journal of Sociology* 103(2):281–317.

Ernst, E. 2001. “Rise in Popularity of Complementary and Alternative Medicine: Reasons and Consequences for Vaccination.” *Vaccine* 20:S90–93.

Ernst, Kacey and Elizabeth T. Jacobs. 2012. “Implications of Philosophical and Personal Belief Exemptions on Re-Emergence of Vaccine-Preventable Disease: The Role of Spatial Clustering in under-Vaccination.” *Human Vaccines & Immunotherapeutics* 8(6):838–41.

Eubank, Stephen et al. 2004. “Modelling Disease Outbreaks in Realistic Urban Social Networks.” *Nature* 429(6988):180–84.

European Center for Disease Prevention and Control. 2015. *Vaccine Hesitancy among Healthcare Workers and Their Patients in Europe: A Qualitative Study*. Stockholm: European Center for Disease Prevention and Control.

Eyal, Gil, Brendan Hart, Emine Onculer, Neta Oren, and Natasha Rossi. 2010. *The Autism Matrix*. Malden, MA: Polity Press.

Feiken, Daniel R. et al. 2000. “Individual and Community Risks of Measles and Pertussis Associated with Personal Exemptions to Immunization.” *Journal of the American Medical Association* 284(24):3145–50.

Ferguson, Neil. 2007. “Capturing Human Behaviour.” *Nature* 446(7137):733–733.

Fine, Paul EM. 1993. “Herd Immunity: History, Theory, Practice.” *Epidemiologic Reviews* 15(2):265–302.

Fotheringham, A.Stewart, Chris Brunsdon, and Martin Charlton. 2003. *Geographically Weighted Regression: The Analysis of Spatially Varying Relationships*. John Wiley & Sons.

Fotheringham, A.Stewart and Peter A. Rogerson. 2008. *The SAGE Handbook of Spatial Analysis*. SAGE.

Fowler, James H. and Nicholas A. Christakis. 2008. “Dynamic Spread of Happiness in a Large Social Network: Longitudinal Analysis over 20 Years in the Framingham Heart Study.” *BMJ* 337(a2338):1–9.

Foxhall, Emily. 2015. “Parents Take Extreme Steps to Keep Their Kids from the Unvaccinated.” *Los Angeles Times*, March 9. Retrieved (http://www.latimes.com/local/california/la-me-measles-extreme-parents-20150310-story.html).

Frank, L. D. et al. 2010. “The Development of a Walkability Index: Application to the Neighborhood Quality of Life Study.” *British Journal of Sports Medicine* 44(13):924–33.

Fredrickson, Doren D. et al. 2004. “Childhood Immunization Refusal: Provider and Parent Perceptions.” *Family Medicine* 36(6):431–439.

Freed, Gary L., Sarah J. Clark, Amy T. Butchart, Dianne C. Singer, and Matthew M. Davis. 2010. “Parental Vaccine Safety Concerns in 2009.” *Pediatrics* 125(4):654–59.

Freed, Gary L., Sarah J. Clark, Amy T. Butchart, Dianne C. Singer, and Matthew M. Davis. 2011. “Sources and Perceived Credibility of Vaccine-Safety Information for Parents.” *Pediatrics* 127(Supplement 1):S107–12.

Freed, Gary L., Sarah J. Clark, Beth F. Hibbs, and Jeanne M. Santoli. 2004. “Parental Vaccine Safety Concerns: The Experiences of Pediatricians and Family Physicians.” *American Journal of Preventive Medicine* 26(1):11–14.

Friedkin, Noah. 1980. “A Test of Structural Features of Granovetter’s Strength of Weak Ties Theory.” *Social Networks* 2(4):411–22.

Fu, Feng, Daniel I. Rosenbloom, Long Wang, and Martin A. Nowak. 2011. “Imitation Dynamics of Vaccination Behaviour on Social Networks.” *Proceedings of the Royal Society of London B: Biological Sciences* 278(1702):42–49.

Funk, Sebastian, Erez Gilad, Chris Watkins, and Vincent A. A. Jansen. 2009. “The Spread of Awareness and Its Impact on Epidemic Outbreaks.” *Proceedings of the National Academy of Sciences* 106(16):6872–77.

Funk, Sebastian, Marcel Salathé, and Vincent A. A. Jansen. 2010. “Modelling the Influence of Human Behaviour on the Spread of Infectious Diseases: A Review.” *Journal of The Royal Society Interface* 7(50):1247–1256.

Gangarosa, Eugene J. et al. 1998. “Impact of Anti-Vaccine Movements on Pertussis Control: The Untold Story.” *The Lancet* 351(9099):356–361.

Gastañaduy, Paul A. et al. 2014. “Measles - United States, January 1-May 23, 2014.” *Morbidity and Mortality Weekly Report* 63(22):496–99.

Gaudino, James A. and Steve Robison. 2012. “Risk Factors Associated with Parents Claiming Personal-Belief Exemptions to School Immunization Requirements: Community and Other Influences on More Skeptical Parents in Oregon, 2006.” *Vaccine* 30(6):1132–42.

Gellin, Bruce G., Edward W. Maibach, Edgar K. Marcuse, and for the National Network for Immunization Information Steering Committee‖. 2000. “Do Parents Understand Immunizations? A National Telephone Survey.” *Pediatrics* 106(5):1097–1102.

Germann, Timothy C., Kai Kadau, Ira M. Longini, and Catherine A. Macken. 2006. “Mitigation Strategies for Pandemic Influenza in the United States.” *Proceedings of the National Academy of Sciences of the United States of America* 103(15):5935–40.

Getis, Arthur. 1994. “Spatial Dependence and Heterogeneity and Proximal Databases.” Pp. 105–20 in *Spatial Analysis And GIS*, edited by A. S. Fotheringham and P. Rogerson. Philadelphia, Pa.: Taylor & Francis.

Gilkey, Melissa B. et al. 2014. “The Vaccination Confidence Scale: A Brief Measure of Parents’ Vaccination Beliefs.” *Vaccine* 32(47):6259–65.

Gilkey, Melissa B., Annie-Laurie McRee, and Noel T. Brewer. 2013. “Forgone Vaccination during Childhood and Adolescence: Findings of a Statewide Survey of Parents.” *Preventive Medicine* 56(3):202–6.

Gimpel, James G. and Iris S. Hui. 2015. “Seeking Politically Compatible Neighbors? The Role of Neighborhood Partisan Composition in Residential Sorting.” *Political Geography* 48:130–42.

Gindler, Jacqueline S., William L. Atkinson, Laurie E. Markowitz, and Sonja S. Hutchins. 1992. “Epidemiology of Measles in the United States in 1989 and 1990.” *Pediatric Infectious Disease Journal* 11(10):841–46.

Givan, Rebecca Kolins, Kenneth M. Roberts, and Sarah A. Soule. 2010. *The Diffusion of Social Movements: Actors, Mechanisms, and Political Effects*. New York: Cambridge University Press.

Golgher, André Braz and Paul R. Voss. 2016. “How to Interpret the Coefficients of Spatial Models: Spillovers, Direct and Indirect Effects.” *Spatial Demography* 4(3):175–205.

González, Marta C., César A. Hidalgo, and Albert-László Barabási. 2008. “Understanding Individual Human Mobility Patterns.” *Nature* 453(7196):779–82.

Gordon-Larsen, Penny, Melissa C. Nelson, Phil Page, and Barry M. Popkin. 2006. “Inequality in the Built Environment Underlies Key Health Disparities in Physical Activity and Obesity.” *Pediatrics* 117(2):417–24.

Gould, Roger V. 1991. “Multiple Networks and Mobilization in the Paris Commune, 1871.” *American Sociological Review* 56(6):716.

Granovetter, Mark. 1978. “Threshold Models of Collective Behavior.” *American Journal of Sociology* 83(6):1420.

Granovetter, Mark. 1983. “The Strength of Weak Ties: A Network Theory Revisited.” *Sociological Theory* 1:201–33.

Granovetter, Mark S. 1973. “The Strength of Weak Ties.” *American Journal of Sociology* 78(6):1360–80.

Grassly, Nicholas C. and Christophe Fraser. 2006. “Seasonal Infectious Disease Epidemiology.” *Proceedings of the Royal Society B: Biological Sciences* 273(1600):2541–50.

Grefenstette, John J. et al. 2013. “FRED (a Framework for Reconstructing Epidemic Dynamics): An Open-Source Software System for Modeling Infectious Diseases and Control Strategies Using Census-Based Populations.” *BMC Public Health* 13:940.

Grenfell, B. T. 1992. “Chance and Chaos in Measles Dynamics.” *Journal of the Royal Statistical Society. Series B (Methodological)* 54(2):383–98.

Gross, Liza. 2009. “A Broken Trust: Lessons from the Vaccine–Autism Wars.” *PLOS Biology* 7(5):e1000114.

Gust, Deborah A. et al. 2003. “Parental Perceptions Surrounding Risks and Benefits of Immunization.” *Seminars in Pediatric Infectious Diseases* 14(3):207–12.

Gust, Deborah A. et al. 2004. “Underimmunization among Children: Effects of Vaccine Safety Concerns on Immunization Status.” *Pediatrics* 114(1):E16–22.

Gust, Deborah A., Natalie Darling, Allison Kennedy, and Ben Schwartz. 2008. “Parents With Doubts About Vaccines: Which Vaccines and Reasons Why.” *Pediatrics* 122(4):718–25.

Gustafson, Tracy L. et al. 1987. “Measles Outbreak in a Fully Immunized Secondary-School Population.” *New England Journal of Medicine* 316(13):771–74.

Haining, Robert P. 1978. “A Spatial Model for High Plains Agriculture.” *Annals of the Association of American Geographers* 68(4):493–504.

Hak, E., Y. Schönbeck, H.De Melker, G. A.Van Essen, and E. A. M. Sanders. 2005. “Negative Attitude of Highly Educated Parents and Health Care Workers towards Future Vaccinations in the Dutch Childhood Vaccination Program.” *Vaccine* 23(24):3103–7.

Halloran, M.Elizabeth et al. 2008. “Modeling Targeted Layered Containment of an Influenza Pandemic in the United States.” *Proceedings of the National Academy of Sciences* 105(12):4639–44.

Hansen, Morten T. 1999. “The Search-Transfer Problem: The Role of Weak Ties in Sharing Knowledge across Organization Subunits.” *Administrative Science Quarterly* 44(1):82–111.

Harriman, Kathleen. 2015. “2014-2015 California Measles Outbreak: It’s a Small World After All.” Retrieved (https://www.hhs.gov/sites/default/files/nvpo/nvac/meetings/pastmeetings/2015/2014-2015_california_measles_outbreak.pdf).

Healy, C.Mary and Larry K. Pickering. 2011. “How to Communicate With Vaccine-Hesitant Parents.” *Pediatrics* 127(Supplement 1):S127–33.

Hedström, Peter. 1994. “Contagious Collectivities: On the Spatial Diffusion of Swedish Trade Unions, 1890-1940.” *American Journal of Sociology* 99(5):1157–79.

Hedström, Peter and Yvonne Åberg. 2005. “Quantitative Research, Agent-Based Modelling and Theories of the Social.” Pp. 114–144 in *Dissecting the Social: On the Principles of Analytical Sociology*. Cambridge University Press.

Hedström, Peter, Rickard Sandell, and Charlotta Stern. 2000. “Mesolevel Networks and the Diffusion of Social Movements: The Case of the Swedish Social Democratic Party.” *American Journal of Sociology* 106(1):145–72.

Hedström, Peter and Richard Swedberg. 1996. “Social Mechanisms.” *Acta Sociologica* 39(3):281–308.

Herrmann, Carl, Marc Barthélemy, and Paolo Provero. 2003. “Connectivity Distribution of Spatial Networks.” *Physical Review E* 68(2):026128.

Hershey, John C., David A. Asch, Thi Thumasathit, Jacqueline Meszaros, and Victor V. Waters. 1994. “The Roles of Altruism, Free Riding, and Bandwagoning in Vaccination Decisions.” *Organizational Behavior and Human Decision Processes* 59(2):177–87.

Hesse, Bradford W. et al. 2005. “Trust and Sources of Health Information: The Impact of the Internet and Its Implications for Health Care Providers: Findings From the First Health Information National Trends Survey.” *Archives of Internal Medicine* 165(22):2618–24.

Hethcote, Herbert W. 1997. “An Age-Structured Model for Pertussis Transmission.” *Mathematical Biosciences* 145(2):89–136.

Hethcote, Herbert W., James A. Yorke, and Annett Nold. 1982. “Gonorrhea Modeling: A Comparison of Control Methods.” *Mathematical Biosciences* 58(1):93–109.

Hilton, Shona, Mark Petticrew, and Kate Hunt. 2007. “Parents’ Champions vs. Vested Interests: Who Do Parents Believe about MMR? A Qualitative Study.” *BMC Public Health* 7:42.

Hinman, Alan R., Sonja S. Hutchins, William J. Bellini, et al. 2004. “Population Immunity to Measles in the United States, 1999.” *The Journal of Infectious Diseases* 189(Supplement 1):S91–97.

Hinman, Alan R., Sonja S. Hutchins, Andrew L. Baughman, et al. 2004. “Vaccination Levels Associated with Lack of Measles Transmission among Preschool-Aged Populations in the United States, 1989–1991.” *The Journal of Infectious Diseases* 189(Supplement 1):S108–15.

Hobson-West, Pru. 2003. “Understanding Vaccination Resistance: Moving beyond Risk.” *Health, Risk & Society* 5(3):273–83.

Hobson-West, Pru. 2007. “‘Trusting Blindly Can Be the Biggest Risk of All’: Organised Resistance to Childhood Vaccination in the UK.” *Sociology of Health & Illness* 29(2):198–215.

Horne, Zachary, Derek Powell, John E. Hummel, and Keith J. Holyoak. 2015. “Countering Antivaccination Attitudes.” *Proceedings of the National Academy of Sciences* 112(33):10321–24.

Hughart, N. et al. 1999. “The Relation of Parent and Provider Characteristics to Vaccination Status of Children in Private Practices and Managed Care Organizations in Maryland.” *Medical Care* 37(1):44–55.

Hull, Harry F., Jean M. Montes, Patricia C. Hays, and Robert L. Lucero. 1985. “Risk Factors for Measles Vaccine Failure Among Immunized Students.” *Pediatrics* 76(4):518–23.

Humiston, Sharon G., E.Brooke Lerner, Elizabeth Hepworth, Taura Blythe, and Julius G. Goepp. 2005. “Parent Opinions About Universal Influenza Vaccination for Infants and Toddlers.” *Archives of Pediatrics & Adolescent Medicine* 159(2):108–12.

Imdad, Aamer et al. 2013. “Religious Exemptions for Immunization and Risk of Pertussis in New York State, 2000–2011.” *Pediatrics* 132(1):37–43.

Jackson, C. L. 1969. “State Laws on Compulsory Immunization in the United States.” *Public Health Reports* 84(9):787–95.

Jansen, V. a. A. et al. 2003. “Measles Outbreaks in a Population with Declining Vaccine Uptake.” *Science* 301(5634):804–804.

Jarrett, Caitlin, Rose Wilson, Maureen O’Leary, Elisabeth Eckersberger, and Heidi J. Larson. 2015. “Strategies for Addressing Vaccine Hesitancy – A Systematic Review.” *Vaccine* 33(34):4180–90.

Jones, Abbey M. et al. 2012. “Parents’ Source of Vaccine Information and Impact on Vaccine Attitudes, Beliefs, and Nonmedical Exemptions.” *Advances in Preventive Medicine* 2012:e932741.

de Jong, J. G. and K. C. Winkler. 1964. “Survival of Measles Virus in Air.” *Nature* 201:1054–55.

Kandel, Denise B. 1978. “Homophily, Selection, and Socialization in Adolescent Friendships.” *American Journal of Sociology* 84(2):427–36.

Kaplan, Karen. 2015. “Vaccine Refusal Helped Fuel Disneyland Measles Outbreak, Study Says.” *Los Angeles Times*, March 16. Retrieved (http://www.latimes.com/science/sciencenow/la-sci-sn-disneyland-measles-under-vaccination-20150316-story.html).

Keele, Luke and Nathan J. Kelly. 2006. “Dynamic Models for Dynamic Theories: The Ins and Outs of Lagged Dependent Variables.” *Political Analysis* 14(2):186–205.

Kempe, Allison et al. 2000. “Quality of Care and Use of the Medical Home in a State-Funded Capitated Primary Care Plan For Low-Income Children.” *Pediatrics* 105(5):1020–28.

Kempe, Allison et al. 2011. “Prevalence of Parental Concerns About Childhood Vaccines.” *American Journal of Preventive Medicine* 40(5):548–55.

Kennedy, Allison, Michelle Basket, and Kristine Sheedy. 2011. “Vaccine Attitudes, Concerns, and Information Sources Reported by Parents of Young Children: Results From the 2009 HealthStyles Survey.” *Pediatrics* S92–99.

Kennedy, Allison, Katherine LaVail, Glen Nowak, Michelle Basket, and Sarah Landry. 2011. “Confidence About Vaccines In The United States: Understanding Parents’ Perceptions.” *Health Affairs* 30(6):1151–59.

Kennedy, Allison M. and Deborah A. Gust. 2005. “Parental Vaccine Beliefs and Child’s School Type.” *The Journal of School Health* 75(7):276–80.

Kenyon, Thomas A., Michael A. Matuck, and George Stroh. 1998. “Persistent Low Immunization Coverage Among Inner-City Preschool Children Despite Access to Free Vaccine.” *Pediatrics* 101(4):612–16.

Khalili, Donya and Arthur Caplan. 2007. “Off the Grid: Vaccinations Among Homeschooled Children.” *The Journal of Law, Medicine & Ethics* 35(3):471–77.

Killworth, Pd and Hr Bernard. 1978. “Reversal Small-World Experiment.” *Social Networks* 1(2):159–92.

Kim, Sam S., Jemima A. Frimpong, Patrick A. Rivers, and Jennie J. Kronenfeld. 2007. “Effects of Maternal and Provider Characteristics on Up-to-Date Immunization Status of Children Aged 19 to 35 Months.” *American Journal of Public Health* 97(2):259–66.

King, Marissa and Peter Bearman. 2009. “Diagnostic Change and the Increased Prevalence of Autism.” *International Journal of Epidemiology* 38(5):1224–34.

Kiss, Istvan Z., Jackie Cassell, Mario Recker, and Péter L. Simon. 2010. “The Impact of Information Transmission on Epidemic Outbreaks.” *Mathematical Biosciences* 225(1):1–10.

Kizer, Kenneth W. and Clifford L. Allenby. 1989. *California Immunization Handbook: School and Child Care Entry Health Requirements*. Fourth. Berkeley, CA: Immunization Unit, California Department of Health Services.

Klandermans, Bert and Dirk Oegema. 1987. “Potentials, Networks, Motivations, and Barriers: Steps Towards Participation in Social Movements.” *American Sociological Review* 52(4):519–31.

Kleinberg, Jon. 2006. “Complex Networks and Decentralized Search Algorithms.” Pp. 1019–1044 in *Proceedings of the International Congress of Mathematicians (ICM)*, vol. 3. Retrieved (https://pdfs.semanticscholar.org/a1df/b772c176330c52b36dc3ea3ea03c9fdaa69d.pdf).

Klovdahl, Alden S. 1985. “Social Networks and the Spread of Infectious Diseases: The AIDS Example.” *Social Science & Medicine* 21(11):1203–16.

Knoke, David. 1982. “The Spread of Municipal Reform: Temporal, Spatial, and Social Dynamics.” *American Journal of Sociology* 1314–1339.

Kulldorff, Martin. 1999. “Spatial Scan Statistics: Models, Calculations, and Applications.” Pp. 303–22 in *Scan Statistics and Applications, Statistics for Industry and Technology*, edited by J. Glaz and N. Balakrishnan. Birkhäuser Boston. Retrieved (http://link.springer.com/chapter/10.1007/978-1-4612-1578-3_14).

Kuperman, Marcelo and Guillermo Abramson. 2001. “Small World Effect in an Epidemiological Model.” *Physical Review Letters* 86(13):2909–12.

Larson, Heidi J., Louis Z. Cooper, Juhani Eskola, Samuel L. Katz, and Scott Ratzan. 2011. “Addressing the Vaccine Confidence Gap.” *The Lancet* 378(9790):526–535.

Latora, Vito and Massimo Marchiori. 2001. “Efficient Behavior of Small-World Networks.” *Physical Review Letters* 87(19):198701.

Laumann, E. O., J. H. Gagnon, S. Michaels, R. T. Michael, and J. S. Coleman. 1989. “Monitoring the AIDS Epidemic in the United States: A Network Approach.” *Science* 244(4909):1186–89.

Lee, Charlotte, Kathryn Whetten, Saad Omer, William Pan, and Daniel Salmon. 2016. “Hurdles to Herd Immunity: Distrust of Government and Vaccine Refusal in the US, 2002–2003.” *Vaccine* 34(34):3972–78.

Lee, Jay, Jinn-Guey Lay, Wei Chien Benny Chin, Yu-Lin Chi, and Ya-Hui Hsueh. 2014. “An Experiment to Model Spatial Diffusion Process with Nearest Neighbor Analysis and Regression Estimation.” *International Journal of Applied Geospatial Research (IJAGR)* 5(1):1–15.

Lehrke, Philipp, Matthias Nuebling, Friedrich Hofmann, and Ulrich Stoessel. 2001. “Attitudes of Homoeopathic Physicians towards Vaccination.” *Vaccine* 19(32):4859–64.

LeSage, James and Robert Kelley Pace. 2009. *Introduction to Spatial Econometrics*. Boca Raton, FL: Chapman and Hall/CRC.

Liben-Nowell, David, Jasmine Novak, Ravi Kumar, Prabhakar Raghavan, and Andrew Tomkins. 2005. “Geographic Routing in Social Networks.” *Proceedings of the National Academy of Sciences of the United States of America* 102(33):11623–28.

Lieu, Tracy A., G.Thomas Ray, Nicola P. Klein, Cindy Chung, and Martin Kulldorff. 2015. “Geographic Clusters in Underimmunization and Vaccine Refusal.” *Pediatrics* 135(2):280–89.

Liljeros, Fredrik, Christofer R. Edling, and Luis A.Nunes Amaral. 2003. “Sexual Networks: Implications for the Transmission of Sexually Transmitted Infections.” *Microbes and Infection* 5(2):189–96.

Link, Bruce G. and Jo Phelan. 1995. “Social Conditions As Fundamental Causes of Disease.” *Journal of Health and Social Behavior* 80–94.

Liu, Fengchen et al. 2015. “The Role of Vaccination Coverage, Individual Behaviors, and the Public Health Response in the Control of Measles Epidemics: An Agent-Based Simulation for California.” *BMC Public Health* 15:447.

Liu, Kayuet and Peter S. Bearman. 2015. “Focal Points, Endogenous Processes, and Exogenous Shocks in the Autism Epidemic.” *Sociological Methods & Research* 44(2):272–305.

Liu, Ka-Yuet, Marissa King, and Peter S. Bearman. 2010. “Social Influence and the Autism Epidemic.” *American Journal of Sociology* 115(5):1387.

Liu, William T. and Robert W. Duff. 1972. “The Strength in Weak Ties.” *The Public Opinion Quarterly* 36(3):361–66.

London, Wayne P. and James A. Yorke. 1973. “Recurrent Outbreaks of Measles, Chickenpox and Mumpsi. Seasonal Variation in Contact Rates.” *American Journal of Epidemiology* 98(6):453–68.

Longini, Ira M., Eugene Ackerman, and Lila R. Elveback. 1978. “An Optimization Model for Influenza A Epidemics.” *Mathematical Biosciences* 38(1):141–57.

Longini, Ira M., James S. Koopman, Arnold S. Monto, and John P. Fox. 1982. “Estimating Household and Community Transmission Parameters for Influenza.” *American Journal of Epidemiology* 115(5):736–51.

Ludlow, Martin, Stephen McQuaid, Dan Milner, Rik L. de Swart, and W.Paul Duprex. 2015. “Pathological Consequences of Systemic Measles Virus Infection.” *The Journal of Pathology* 235(2):253–65.

Luman, Elizabeth T., Mary Mason McCauley, Abigail Shefer, and Susan Y. Chu. 2003. “Maternal Characteristics Associated With Vaccination of Young Children.” *Pediatrics* 111(Supplement 1):1215–18.

Luthy, K. E., R. L. Beckstrand, L. C. Callister, and S. Cahoon. 2012. “Reasons Parents Exempt Children From Receiving Immunizations.” *The Journal of School Nursing* 28(2):153–60.

MacDonald, George. 1952. “The Analysis of Equilibrium in Malaria.” *Tropical Diseases Bulletin* 49(9):813–29.

MacDonald, George. 1957. *The Epidemiology and Control of Malaria*. London: Oxford University Press.

MacDougall, Donna M. et al. 2016. “Knowledge, Attitudes, Beliefs, and Behaviors of Pregnant Women Approached to Participate in a Tdap Maternal Immunization Randomized, Controlled Trial.” *Human Vaccines & Immunotherapeutics* 12(4):879–85.

Majumder, Maimuna S., Emily L. Cohn, Sumiko R. Mekaru, Jane E. Huston, and John S. Brownstein. 2015. “Substandard Vaccination Compliance and the 2015 Measles Outbreak.” *JAMA Pediatrics* 169(5):494–95.

Markowitz, Lauri E. et al. 1989. “Patterns of Transmission in Measles Outbreaks in the United States, 1985–1986.” *New England Journal of Medicine* 320(2):75–81.

Markowitz, Lauri E., Stephen R. Preblud, Paul E. M. Fine, and Walter A. Orenstein. 1990. "Duration of Live Measles Vaccine-Induced Immunity." *Journal* 9(2):101–10.

Marks, James S., Thomas J. Halpin, and Walter A. Orenstein. 1978. "Measles Vaccine Efficacy in Children Previously Vaccinated at 12 Months of Age." *Pediatrics* 62(6):955–60.

Massey, Douglas S. 1990. "American Apartheid: Segregation and the Making of the Underclass." *American Journal of Sociology* 96(2):329–57.

May, Thomas and Ross D. Silverman. 2003. "'Clustering of Exemptions' as a Collective Action Threat to Herd Immunity." *Vaccine* 21(11–12):1048–51.

Mazumdar, Soumya, Marissa King, Ka-Yuet Liu, Noam Zerubavel, and Peter Bearman. 2010. "The Spatial Structure of Autism in California, 1993–2001." *Health & Place* 16(3):539–46.

McAdam, Doug. 1988. *Freedom Summer*. New York: Oxford University Press.

McAdam, Doug and Ronnelle Paulsen. 1993. "Specifying the Relationship Between Social Ties and Activism." *American Journal of Sociology* 99(3):640–67.

McCarthy, Michael. 2015. "Measles Cases Exceed 100 in US Outbreak." *BMJ : British Medical Journal (Online)* 350.

McCombie, S. C., R. D. Worrell, B. W. Porter, J. A. Browning, and C. G. Ray. 1988. "Risk for Measles Related to Immunization Status in Two Tucson High Schools." *Public Health Reports* 103(2):162–66.

McCormick, Joseph B., Neal Halsey, and Robert Rosenberg. 1977. "Measles Vaccine Efficacy Determined from Secondary Attack Rates during a Severe Epidemic." *The Journal of Pediatrics* 90(1):13–16.

McGirr, Ashleigh A., Ashleigh R. Tuite, and David N. Fisman. 2013. "Estimation of the Underlying Burden of Pertussis in Adolescents and Adults in Southern Ontario, Canada." *PLoS ONE* 8(12):e83850.

McPherson, Miller, Lynn Smith-Lovin, and James M. Cook. 2001. "Birds of a Feather: Homophily in Social Networks." *Annual Review of Sociology* 27:415–44.

Mechanic, David. 1996. "Changing Medical Organization and the Erosion of Trust." *The Milbank Quarterly* 74(2):171–89.

Mello, Michelle M., David M. Studdert, and Wendy E. Parmet. 2015. "Shifting Vaccination Politics — The End of Personal-Belief Exemptions in California." *New England Journal of Medicine* 373(9):785–87.

Mercken, Liesbeth, Christian Steglich, Philip Sinclair, Jo Holliday, and Laurence Moore. 2012. "A Longitudinal Social Network Analysis of Peer Influence, Peer Selection, and

Smoking Behavior among Adolescents in British Schools." *Health Psychology* 31(4):450–59.

Meszaros, Jacqueline R. et al. 1996. "Cognitive Processes and the Decisions of Some Parents to Forego Pertussis Vaccination for Their Children." *Journal of Clinical Epidemiology* 49(6):697–703.

Miech, Richard. 2008. "The Formation of a Socioeconomic Health Disparity: The Case of Cocaine Use during the 1980s and 1990s." *Journal of Health and Social Behavior* 49(3):352–66.

Miller, Michael E. 2015. "The GOP's Dangerous 'debate' on Vaccines and Autism." *The Washington Post*. Retrieved (https://www.washingtonpost.com/news/morning-mix/wp/2015/09/17/the-gops-dangerous-debate-on-vaccines-and-autism/).

Millo, Giovanni and Gianfranco Piras. 2012. "Splm: Spatial Panel Data Models in R." *Journal of Statistical Software* 47(1):1–38.

Mische, Ann. 2011. "Relational Sociology, Culture, and Agency." Pp. 80–98 in *The SAGE Handbook of Social Network Analysis,* edited by J. Scott and P. J. Carrington. London: SAGE Publications.

Moore, Cristopher and M. E. J. Newman. 2000. "Epidemics and Percolation in Small-World Networks." *Physical Review E* 61(5):5678–82.

Moreno, Rosina, Raffaele Paci, and Stefano Usai. 2005. "Spatial Spillovers and Innovation Activity in European Regions." *Environment and Planning A* 37(10):1793–1812.

Morenoff, Jeffrey D. 2003. "Neighborhood Mechanisms and the Spatial Dynamics of Birth Weight." *American Journal of Sociology* 108(5):976–1017.

Morenoff, Jeffrey D., Robert J. Sampson, and Stephen W. Raudenbush. 2001. "Neighborhood Inequality, Collective Efficacy, and the Spatial Dynamics of Urban Violence." *Criminology* 39(3):517–58.

Mossong, J. and C. P. Muller. 2000. "Estimation of the Basic Reproduction Number of Measles during an Outbreak in a Partially Vaccinated Population." *Epidemiology & Infection* 124(02):273–278.

Mossong, Joël et al. 2008. "Social Contacts and Mixing Patterns Relevant to the Spread of Infectious Diseases." *PLOS Medicine* 5(3):e74.

Mouw, Ted and Barbara Entwisle. 2006. "Residential Segregation and Interracial Friendship in Schools." *American Journal of Sociology* 112(2):394–441.

Muscat, Mark, Henrik Bang, Jan Wohlfahrt, Steffen Glismann, and Kåre Mølbak. 2009. "Measles in Europe: An Epidemiological Assessment." *The Lancet* 373(9661):383–89.

Myers, Daniel J. 1997. “Racial Rioting in the 1960S: An Event History Analysis of Local Conditions.” *American Sociological Review* 62(1):94–112.

Nakaya, Tomoki, Martin Charlton, Jing Yao, and A.Stewart Fotheringham. 2016. *GWR4.09 User Manual*. Department of Geography, Ritsumeikan University.

Nelson, Reed E. 1989. “The Strength of Strong Ties: Social Networks and Intergroup Conflict in Organizations.” *The Academy of Management Journal* 32(2):377–401.

Newman, M. E. J. 2002. “Spread of Epidemic Disease on Networks.” *Physical Review E* 66(1):016128.

Newman, M. E. J. 2003. “Mixing Patterns in Networks.” *Physical Review E* 67(2):026126.

Newman, M. E. J. and M. Girvan. 2003. “Mixing Patterns and Community Structure in Networks.” Pp. 66–87 in *Statistical Mechanics of Complex Networks, Lecture Notes in Physics*. Springer, Berlin, Heidelberg. Retrieved June 28, 2017 (https://link.springer.com/chapter/10.1007/978-3-540-44943-0_5).

Newman, M. E. J. and Juyong Park. 2003. “Why Social Networks Are Different from Other Types of Networks.” *Physical Review E* 68(3):036122.

Newman, Mark, Albert-László Barabási, and Duncan J. Watts. 2006. *The Structure and Dynamics of Networks*. Princeton: Princeton University Press.

Nkowane, B. M., S. W. Bart, W. A. Orenstein, and M. Baltier. 1987. “Measles Outbreak in a Vaccinated School Population: Epidemiology, Chains of Transmission and the Role of Vaccine Failures.” *American Journal of Public Health* 77(4):434–38.

Nyhan, Brendan, Jason Reifler, Sean Richey, and Gary L. Freed. 2014. “Effective Messages in Vaccine Promotion: A Randomized Trial.” *Pediatrics* 133(4):e835–42.

Oberschall, Anthony and Eric M. Leifer. 1986. “Efficiency and Social Institutions: Uses and Misuses of Economic Reasoning in Sociology.” *Annual Review of Sociology* 12(1):233–53.

Offit, Paul A. and Charlotte A. Moser. 2009. “The Problem With Dr Bob’s Alternative Vaccine Schedule.” *Pediatrics* 123(1):e164–69.

Ogbuanu, Ikechukwu U. et al. 2012. “Impact of a Third Dose of Measles-Mumps-Rubella Vaccine on a Mumps Outbreak.” *Pediatrics* 130(6):e1567–74.

Olson, Mancur. 1965. *The Logic of Collective Action: Public Goods and the Theory of Groups*. Cambridge, MA: Harvard University Press.

Omer, Saad B. et al. 2006. “Nonmedical Exemptions to School Immunization Requirements: Secular Trends and Association of State Policies With Pertussis Incidence.” *Journal of the American Medical Association* 296(14):1757–63.

Omer, Saad B. et al. 2008. “Geographic Clustering of Nonmedical Exemptions to School Immunization Requirements and Associations With Geographic Clustering of Pertussis.” *American Journal of Epidemiology* 168(12):1389–96.

Omer, Saad B., Daniel A. Salmon, Walter A. Orenstein, M.Patricia deHart, and Neal Halsey. 2009. “Vaccine Refusal, Mandatory Immunization, and the Risks of Vaccine-Preventable Diseases.” *New England Journal of Medicine* 360(19):1981–88.

Onnela, J. P. et al. 2007. “Structure and Tie Strengths in Mobile Communication Networks.” *Proceedings of the National Academy of Sciences* 104(18):7332–36.

Opel, Douglas J., Douglas S. Diekema, Nancy R. Lee, and Edgar K. Marcuse. 2009. “Social Marketing as a Strategy to Increase Immunization Rates.” *Archives of Pediatrics & Adolescent Medicine* 163(5):432–37.

Ord, J.Keith and Arthur Getis. 1995. “Local Spatial Autocorrelation Statistics: Distributional Issues and an Application.” *Geographical Analysis* 27(4):286–306.

Orenstein, Walter A. and Alan R. Hinman. 1999. “The Immunization System in the United States — The Role of School Immunization Laws.” *Vaccine* 17(Supplement 3):S19–24.

Orenstein, Walter A. and Mark J. Papania. 2004. “Defining and Assessing Measles Elimination Goals.” *The Journal of Infectious Diseases* 189(Supplement 1):S23–26.

Over, Mead and Peter Piot. 1993. “Health Sector Priorities Review: HIV Infection and Sexually Transmitted Diseases.” Pp. 455–527 in *Disease Control Priorities in Developing Countries*, edited by D. T. Jamison, W. H. Mosley, A. R. Measham, and J. L. Bobadilla. New York, N.Y: Oxford University Press.

Painter, Julia E. et al. 2010. “Development, Theoretical Framework, and Lessons Learned From Implementation of a School-Based Influenza Vaccination Intervention.” *Health Promotion Practice* 11(Supplement 1):42S–52S.

Pampel, F. C. 2001. “Cigarette Diffusion and Sex Differences in Smoking.” *Journal of Health and Social Behavior* 42(4):388–404.

Pampel, Fred C. 2002. “Inequality, Diffusion, and the Status Gradient in Smoking.” *Social Problems* 49(1):35–57.

Pampel, Fred C. 2005. “Diffusion, Cohort Change, and Social Patterns of Smoking.” *Social Science Research* 34(1):117–39.

Pampel, Fred C., Patrick M. Krueger, and Justin T. Denney. 2010. “Socioeconomic Disparities in Health Behaviors.” *Annual Review of Sociology* 36:349–70.

Papania, Mark et al. 1999. “Increased Susceptibility to Measles in Infants in the United States.” *Pediatrics* 104(5):e59–e59.

Papania, Mark J. et al. 2014. “Elimination of Endemic Measles, Rubella, and Congenital Rubella Syndrome From the Western Hemisphere: The US Experience.” *JAMA Pediatrics* 168(2):148–55.

Parent, Olivier and James P. LeSage. 2012. “Spatial Dynamic Panel Data Models with Random Effects.” *Regional Science and Urban Economics* 42(4):727–38.

Parker Fiebelkorn, Amy et al. 2010. “Measles in the United States during the Postelimination Era.” *The Journal of Infectious Diseases* 202(10):1520–28.

Pastor-Satorras, Romualdo and Alessandro Vespignani. 2001a. “Epidemic Dynamics and Endemic States in Complex Networks.” *Physical Review E* 63(6):066117.

Pastor-Satorras, Romualdo and Alessandro Vespignani. 2001b. “Epidemic Spreading in Scale-Free Networks.” *Physical Review Letters* 86(14):3200–3203.

Pediatrics, Committee on Practice and Ambulatory Medicine and Council on Community. 2010. “Increasing Immunization Coverage.” *Pediatrics* 125(6):1295–1304.

Perisic, Ana and Chris T. Bauch. 2009. “Social Contact Networks and Disease Eradicability under Voluntary Vaccination.” *PLOS Computational Biology* 5(2):e1000280.

Petras, James and Maurice Zeitlin. 1967. “Miners and Agrarian Radicalism.” *American Sociological Review* 32(4):578–86.

Pew Research Center. 2015. *Parenting in America: Outlook, Worries, Aspirations Are Strongly Linked to Financial Situation*.

Phadke, Varun K., Robert A. Bednarczyk, Daniel A. Salmon, and Saad B. Omer. 2016. “Association Between Vaccine Refusal and Vaccine-Preventable Diseases in the United States: A Review of Measles and Pertussis.” *Journal of the American Medical Association* 315(11):1149.

Phelan, Jo C., Bruce G. Link, and Parisa Tehranifar. 2010. “Social Conditions as Fundamental Causes of Health Inequalities: Theory, Evidence, and Policy Implications.” *Journal of Health and Social Behavior* 51(Supplement 1):S28–40.

Plotkin, Stanley, Jeffrey S. Gerber, and Paul A. Offit. 2009. “Vaccines and Autism: A Tale of Shifting Hypotheses.” *Clinical Infectious Diseases* 48(4):456–61.

Plotkin, Susan L. and Stanley A. Plotkin. 2012. “A Short History of Vaccination.” in *Vaccines*, edited by S. A. Plotkin, W. A. Orenstein, and P. A. Offit. Philadelphia, Pa.: Saunders.

Poltorak, Mike, Melissa Leach, James Fairhead, and Jackie Cassell. 2005. “‘MMR Talk’ and Vaccination Choices: An Ethnographic Study in Brighton.” *Social Science & Medicine* 61(3):709–19.

Prislin, R., J. A. Dyer, C. H. Blakely, and C. D. Johnson. 1998. “Immunization Status and Sociodemographic Characteristics: The Mediating Role of Beliefs, Attitudes, and Perceived Control.” *American Journal of Public Health* 88(12):1821–26.

Profeta, M. L., P. Ferrante, and C. Porro De’ Somenzi. 1986. “A Survey on Factors Affecting Acceptance of Measles Vaccine.” *European Journal of Epidemiology* 2(2):128–33.

Quadri-Sheriff, M. et al. 2012. “The Role of Herd Immunity in Parents’ Decision to Vaccinate Children: A Systematic Review.” *Pediatrics* 130(3):522–30.

Radzikowski, Jacek et al. 2016. “The Measles Vaccination Narrative in Twitter: A Quantitative Analysis.” *JMIR Public Health and Surveillance* 2(1). Retrieved (http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4869226/).

Rahmandad, Hazhir and John Sterman. 2008. “Heterogeneity and Network Structure in the Dynamics of Diffusion: Comparing Agent-Based and Differential Equation Models.” *Management Science* 54(5):998–1014.

Rapoport, Anatol. 1953. “Spread of Information through a Population with Socio-Structural Bias: I. Assumption of Transitivity.” *The Bulletin of Mathematical Biophysics* 15(4):523–33.

Rapoport, Anatol and William J. Horvath. 1961. “A Study of a Large Sociogram.” *Behavioral Science* 6(4):279–91.

Reich, Jennifer A. 2014. “Neoliberal Mothering and Vaccine Refusal: Imagined Gated Communities and the Privilege of Choice.” *Gender & Society* 28(5):679–704.

Reich, Jennifer A. 2016. *Calling the Shots: Why Parents Reject Vaccines*. New York: NYU Press.

Richards, Jennifer L. et al. 2013. “Nonmedical Exemptions to Immunization Requirements in California: A 16-Year Longitudinal Analysis of Trends and Associated Community Factors.” *Vaccine* 31(29):3009–13.

Ritov, Ilana and Jonathan Baron. 1990. “Reluctance to Vaccinate: Omission Bias and Ambiguity.” *Journal of Behavioral Decision Making* 3(4):263–77.

Robbins, Kb, Ad Brandling-Bennett, and Ar Hinman. 1981. “Low Measles Incidence - Association with Enforcement of School Immunization Laws.” *American Journal of Public Health* 71(3):270–74.

Rogers, Anne and David Pilgrim. 1996. “The Risk of Resistance: Perspectives in the Mass Childhood Immunization (MCI) Programme.” Pp. 73–90 in *Medicine, Health and Risk: Sociological Approaches,* edited by J. Gabe. Oxford: Wiley-Blackwell.

Rogers, Everett M. 2003. *Diffusion of Innovations, 5th Edition*. 5th edition. New York: Free Press.

Rogers, Everett M. and D.Lawrence Kincaid. 1981. “Communication Networks: Toward a New Paradigm for Research.” Retrieved March 8, 2017 (http://www.popline.org/node/400732).

Ropeik, David. 2013. “How Society Should Respond to the Risk of Vaccine Rejection.” *Human Vaccines & Immunotherapeutics* 9(8):1815–18.

Rostila, Mikael. 2010. “Birds of a Feather Flock Together – and Fall Ill? Migrant Homophily and Health in Sweden.” *Sociology of Health & Illness* 32(3):382–99.

Rota, J. S. et al. 2001. “Processes for Obtaining Nonmedical Exemptions to State Immunization Laws.” *American Journal of Public Health* 91(4):645–48.

Rowe, Christopher, Glenn-Milo Santos, Henry F. Raymond, and Phillip O. Coffin. 2017. “Social Mixing and Correlates of Injection Frequency among Opioid Use Partnerships.” *International Journal of Drug Policy* 41:80–88.

Ruef, Martin, Howard E. Aldrich, and Nancy M. Carter. 2003. “The Structure of Founding Teams: Homophily, Strong Ties, and Isolation among U.S. Entrepreneurs.” *American Sociological Review* 68(2):195–222.

Ryan, Bryce and Neal C. Gross. 1943. “The Diffusion of Hybrid Seed Corn In Two Iowa Communities.” *Rural Sociology* 8(1):15–24.

Sadaf, Alina, Jennifer L. Richards, Jason Glanz, Daniel A. Salmon, and Saad B. Omer. 2013. “A Systematic Review of Interventions for Reducing Parental Vaccine Refusal and Vaccine Hesitancy.” *Vaccine* 31(40):4293–4304.

Saelens, Brian E., James F. Sallis, Jennifer B. Black, and Diana Chen. 2003. “Neighborhood-Based Differences in Physical Activity: An Environment Scale Evaluation.” *American Journal of Public Health* 93(9):1552–58.

Safi, Haytham et al. 2012. “Vaccine Policy and Arkansas Childhood Immunization Exemptions.” *American Journal of Preventive Medicine* 42(6):602–5.

SAGE Working Group on Vaccine Hesitancy. 2014. *Report of the SAGE Working Group on Vaccine Hesitancy*. Retrieved (http://www.who.int/immunization/sage/meetings/2014/october/SAGE_working_group_revised_report_vaccine_hesitancy.pdf?ua=1).

Salathé, Marcel and Sabastian Bonhoeffer. 2008. “The Effect of Opinion Clustering on Disease Outbreaks.” *Journal of The Royal Society Interface* 5(29):1505–8.

Salganik, Matthew J. 2006. “Experimental Study of Inequality and Unpredictability in an Artificial Cultural Market.” *Science* 311(5762):854–56.

Salmon, Daniel A. et al. 1999. “Health Consequences of Religious and Philosophical Exemptions from Immunization Laws - Individual and Societal Risk of Measles.” *Journal of the American Medical Association* 282(1):47–53.

Salmon, Daniel A., Saad B. Omer, et al. 2005. “Exemptions to School Immunization Requirements: The Role of School-Level Requirements, Policies, and Procedures.” *American Journal of Public Health* 95(3):436–40.

Salmon, Daniel A., Lawrence H. Moulton, et al. 2005. “Factors Associated With Refusal of Childhood Vaccines Among Parents of School-Aged Children: A Case-Control Study.” *Archives of Pediatrics & Adolescent Medicine* 159(5):470–76.

Salmon, Daniel A., J. W. Sapsin, et al. 2005. “Public Health and the Politics of School Immunization Requirements.” *American Journal of Public Health* 95(5):778–83.

Sampson, Robert J., Jeffrey D. Morenoff, and Thomas Gannon-Rowley. 2002. “Assessing ‘Neighborhood Effects’: Social Processes and New Directions in Research.” *Annual Review of Sociology* 28(1):443–78.

Sansom, Stephanie L., Lawrence Barker, Phaedra S. Corso, Cedric Brown, and Robert Deuson. 2001. “Rotavirus Vaccine and Intussusception: How Much Risk Will Parents in the United States Accept to Obtain Vaccine Benefits?” *American Journal of Epidemiology* 154(11):1077–85.

Santoli, Jeanne M., Lance E. Rodewald, Edmond F. Maes, Michael P. Battaglia, and Victor G. Coronado. 1999. “Vaccines for Children Program, United States, 1997.” *Pediatrics* 104(2):e15–e15.

Schaefer, David R., Steven A. Haas, and Nicholas J. Bishop. 2012. “A Dynamic Model of US Adolescents’ Smoking and Friendship Networks.” *American Journal of Public Health* 102(6):e12–18.

Schelling, Thomas C. 1978. *Micromotives and Macrobehavior*. New York: Norton.

Schenzle, Dieter. 1984. “An Age-Structured Model of Pre- and Post-Vaccination Measles Transmission.” *Mathematical Medicine and Biology* 1(2):169–91.

Sears, Robert W. 2011. *The Vaccine Book: Making the Right Decision for Your Child*. New York: Little, Brown and Company.

Senier, Laura. 2008. “‘It’s Your Most Precious Thing’: Worst-Case Thinking, Trust, and Parental Decision Making about Vaccinations.” *Sociological Inquiry* 78(2):207–29.

Shui, Irene M., Eric S. Weintraub, and Deborah A. Gust. 2006. “Parents Concerned About Vaccine Safety: Differences in Race/Ethnicity and Attitudes.” *American Journal of Preventive Medicine* 31(3):244–51.

Silverman, Ross D. 2003. “No More Kidding Around: Restructuring Non-Medical Childhood Immunization Exemptions to Ensure Publi Health Protection.” *Annals of Health Law* 12:277–94.

Smith, Jeffrey A., Miller McPherson, and Lynn Smith-Lovin. 2014. “Social Distance in the United States: Sex, Race, Religion, Age, and Education Homophily among Confidants, 1985 to 2004.” *American Sociological Review* 79(3):432–56.

Smith, Kristen P. and Nicholas A. Christakis. 2008. “Social Networks and Health.” *Annual Review of Sociology* 34(1):405–29.

Smith, Philip J., Susan Y. Chu, and Lawrence E. Barker. 2004. “Children Who Have Received No Vaccines: Who Are They and Where Do They Live?” *Pediatrics* 114(1):187–95.

Snipes, Michael and D.Christopher Taylor. 2014. “Model Selection and Akaike Information Criteria: An Example from Wine Ratings and Prices.” *Wine Economics and Policy* 3(1):3–9.

Sobo, Elisa J. 2015. “Social Cultivation of Vaccine Refusal and Delay among Waldorf (Steiner) School Parents.” *Medical Anthropology Quarterly* 29(3):381–99.

Soule, Sarah A. 1997. “The Student Divestment Movement in the United States and Tactical Diffusion: The Shantytown Protest.” *Social Forces* 75(3):855.

Soule, Sarah A. 2004. “Diffusion Processes within and across Movements.” Pp. 294–310 in *The Blackwell Companion to Social Movements*, edited by D. A. Snow, S. A. Soule, and H. Kriesi. Malden, MA: Blackwell.

St. John, Ronald K. and James W. Curran. 1978. “Epidemiology of Gonorrhea.” *Sexually Transmitted Diseases* 5(2):81–82.

Strang, David and John W. Meyer. 1993. “Institutional Conditions for Diffusion.” *Theory and Society* 22(4):487–511.

Strang, David and Sarah A. Soule. 1998. “Diffusion in Organizations and Social Movements: From Hybrid Corn to Poison Pills.” *Annual Review of Sociology* 24(1):265–290.

Strang, David and Nancy Brandon Tuma. 1993. “Spatial and Temporal Heterogeneity in-Diffusion.” *American Journal of Sociology* 99(3):614–39.

Sugerman, David E. et al. 2010. “Measles Outbreak in a Highly Vaccinated Population, San Diego, 2008: Role of the Intentionally Undervaccinated.” *Pediatrics* 125(4):747–55.

Taylor, Luke E., Amy L. Swerdfeger, and Guy D. Eslick. 2014. “Vaccines Are Not Associated with Autism: An Evidence-Based Meta-Analysis of Case-Control and Cohort Studies.” *Vaccine* 32(29):3623–29.

Thomas, James C. and Myra J. Tucker. 1996. “The Development And Use Of The Concept Of A Sexually Transmitted Disease Core.” *The Journal of Infectious Diseases* 174(Supplement 2):S134–43.

Tilly, Charles. 1978. *From Mobilization to Revolution*. Reading, MA: Addison-Wesley Publishing Company.

Tolbert, Pamela S. and Lynne G. Zucker. 1983. “Institutional Sources of Change in the Formal Structure of Organizations: The Diffusion of Civil Service Reform, 1880-1935.” *Administrative Science Quarterly* 28(1):22.

Top, Franklin H. 1938. “Measles in Detroit, 1935—I, Factors Influencing the Secondary Attack Rate Among Susceptibles at Risk.” *American Journal of Public Health and the Nations Health* 28(8):935–943.

Travers, J. and S. Milgram. 1969. “Experimental Study of Small World Problem.” *Sociometry* 32(4):425–43.

Velan, Baruch. 2011. “Acceptance on the Move: Public Reaction to Shifting Vaccination Realities.” *Human Vaccines* 7(12):1261–70.

Verger, Pierre et al. 2015. “Vaccine Hesitancy Among General Practitioners and Its Determinants During Controversies: A National Cross-Sectional Survey in France.” *EBioMedicine* 2(8):891–97.

Viboud, Cécile et al. 2004. “Risk Factors of Influenza Transmission in Households.” *British Journal of General Practice* 54(506):684–89.

Walker, Edward T. and Christopher M. Rea. 2016. “Pediatric Care Provider Density and Personal Belief Exemptions From Vaccine Requirements in California Kindergartens.” *American Journal of Public Health* 106(7):1336–41.

Wallinga, Jacco, W.John Edmunds, and Mirjam Kretzschmar. 1999. “Perspective: Human Contact Patterns and the Spread of Airborne Infectious Diseases.” *Trends in Microbiology* 7(9):372–77.

Wang, Dan J. and Sarah A. Soule. 2012. “Social Movement Organizational Collaboration: Networks of Learning and the Diffusion of Protest Tactics, 1960–1995.” *American Journal of Sociology* 117(6):1674–1722.

Wang, Eileen, Jessica Clymer, Cecilia Davis-Hayes, and Alison Buttenheim. 2014. “Nonmedical Exemptions From School Immunization Requirements: A Systematic Review.” *American Journal of Public Health* 104(11):e62–84.

Wang, Xiao Fan and Guanrong Chen. 2002. “Synchronization in Scale-Free Dynamical Networks: Robustness and Fragility.” *IEEE Transactions on Circuits and Systems I: Fundamental Theory and Applications* 49(1):54–62.

Wassilak, Steven G. F., Walter A. Orenstein, Peggy L. Strickland, Carol A. Butler, and Kenneth J. Bart. 1985. "Continuing Measles Transmission in Students Despite a School-Based Outbreak Control Program." *American Journal of Epidemiology* 122(2):208–17.

Watts, Duncan J. 1999. *Small Worlds: The Dynamics of Networks Between Order and Randomness*. Princeton, N.J.: Princeton University Press.

Watts, Duncan J. 2004. *Six Degrees: The Science of a Connected Age*. New York: W. W. Norton & Company.

Watts, Duncan J., Peter Sheridan Dodds, and M. E. J. Newman. 2002. "Identity and Search in Social Networks." *Science* 296(5571):1302–5.

Watts, Duncan J. and Steven H. Strogatz. 1998. "Collective Dynamics of 'small-World' Networks." *Nature* 393(6684):440–42.

Wei, Feifei et al. 2009. "Identification and Characteristics of Vaccine Refusers." *BMC Pediatrics* 9:18.

Wells, Katelyn B. and Saad B. Omer. 2012. "The Financial Impact of a State Adopting a Personal/Philosophical Belief Exemption Policy: Modeling the Cost of Pertussis Disease in Infants, Children and Adolescents." *Vaccine* 30(41):5901–4.

Wheaton, William et al. 2009. *Synthesized Population Databases: A US Geospatial Database for Agent-Based Models*. Research Triangle Park, NC: RTI Press. Retrieved (http://www.rti.org/pubs/mr-0010-0905-wheaton.pdf).

Whyte Jr, William H. 1954. "The Web of Word of Mouth." *Fortune* 50(5):140–143.

Williams, Ian T., Jack D. Milton, James B. Farrell, and Neil M. H. Graham. 1995. "Interaction of Socioeconomic Status and Provider Practices as Predictors of Immunization Coverage in Virginia Children." *Pediatrics* 96(3):439–46.

Wing, Kenneth R. 1990. *The Law and the Public's Health*. 7th edition. Ann Arbor, MI: Health Administration Press.

Winter, Kathleen et al. 2012. "California Pertussis Epidemic, 2010." *The Journal of Pediatrics* 161(6):1091–96.

Winter, Kathleen, Carol Glaser, James Watt, and Kathleen Harriman. 2014. "Pertussis Epidemic — California, 2014." *Morbidity and Mortality Weekly Report* 63(48):1129–32.

Yang, Tony Y., Leila Barraza, and Kim Weidenaar. 2015. "Measles Outbreak as a Catalyst for Stricter Vaccine Exemption Legislation." *Journal of the American Medical Association* 314(12):1229–1230.

Yang, Tony Y., Paul L. Delamater, Timothy F. Leslie, and Michelle M. Mello. 2015. "Sociodemographic Predictors of Vaccination Exemptions on the Basis of Personal Belief in California." *American Journal of Public Health* 106(1):172–77.

Yang, Tony Y. and Ross Silverman. 2015. "Legislative Prescriptions for Controlling Nonmedical Vaccine Exemptions." *Journal of the American Medical Association* 313(3):247–48.

Yorke, James A., Herbert W. Hethcote, and Annett Nold. 1978. "Dynamics and Control of the Transmission of Gonorrhea." *Sexually Transmitted Diseases* 5(2):51–56.

Youm, Yoosik and Edward O. Laumann. 2002. "Social Network Effects on the Transmission of Sexually Transmitted Diseases." *Sexually Transmitted Diseases* 29(11):689–697.

Zhao, Dingxin. 1998. "Ecologies of Social Movements: Student Mobilization during the 1989 Prodemocracy Movement in Beijing." *American Journal of Sociology* 103(6):1493–1529.

Zhao, Jichang, Junjie Wu, and Ke Xu. 2010. "Weak Ties: Subtle Role of Information Diffusion in Online Social Networks." *Physical Review E* 82(1):016105.

Zipprich, Jennifer et al. 2015. "Measles Outbreak — California, December 2014–February 2015." *Morbidity and Mortality Weekly Report* 64(6):153–54.