Three Essays on Modeling Complex Dynamic Problems in Health and Safety

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Dissertation submitted to the faculty of the Virginia Polytechnic Institute and State University in partial fulfillment of the requirements for the degree of

Doctor of Philosophy
In
Industrial and Systems Engineering

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May 2, 2011
Falls Church, VA

Keywords: Literature synthesis method; Dynamic disease models; Disease transmission; Outbreak response; Individual-based (IB) model

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(ABSTRACT)

Essay #1 – Factors influencing the risk of falls in the construction industry: a review of the evidence

Falls are a significant public health risk and a leading cause of nonfatal and fatal injuries among construction workers worldwide. A more comprehensive understanding of casual factors leading to fall incidents is essential to prevent falls in the construction industry. However, an extensive overview of causal factors is missing from the literature. In this paper, 536 articles on factors contributing to the risk of falls were retrieved. One hundred twenty-one (121) studies met the criteria for relevance and quality to be coded, and were synthesized to provide an overview. In lieu of the homogeneity needed across studies to conduct a structured meta-analysis, a literature synthesis method based on macro-variables was advanced. This method provides a flexible approach to aggregating previous findings and assessing agreement across those studies. Factors commonly associated with falls included working surfaces and platforms, workers' safety behaviors and attitudes, and construction structure and facilities. Significant differences across qualitative and quantitative studies were found in terms of focus, and areas with limited agreement in previous research were identified. Findings contribute to research on the causes of falls in construction, developing engineering controls, informing policy and intervention design to reduce the risk of falls, and improving research synthesis methods.

Essay #2 – Review of quantitative studies of interventions for responding to infectious disease outbreaks

We reviewed the modeling and retrospective literature on responding to outbreaks of infectious diseases in humans and animals. Unlike routine immunization and control efforts, outbreak response activities require rapid reactive actions to address an urgent or emergent situation. We focused our review on characterizing the types of diseases analyzed, the interventions used, and the models employed. Out of the 211 studies identified, we find that the majority focus on a few diseases (influenza, foot and mouth disease, smallpox, measles, and hepatitis). We identified 34 distinct interventions explored in these studies that fall under the general categories of vaccination, prophylaxis, quarantine/isolation, contact restriction, exposure reduction, killing/slaughtering, and surveillance. A large number of studies (141) use simulation/analytical models to analyze outbreak response strategies. We identify key factors contributing to the effectiveness of different interventions that target high-risk individuals, trace infected contacts, or use a ring to delineate geographical boundaries for an intervention.

Essay #3 – Development of an individual-based model for polioviruses: implications of the selection of network type and outcome metrics

We developed an individual-based (IB) model to explore the stochastic attributes of state transitions, the heterogeneity of the individual interactions, and the impact of different network structure choices on the poliovirus transmission process in the context of understanding the dynamics of outbreaks. We used a previously published differential equation-based model to develop the IB model and inputs. To explore the impact of different types of networks, we implemented a total of 26 variations of six different network structures in the IB model. We found that the choice of network structure plays a critical role in the model estimates of cases and the dynamics of outbreaks. This study provides insights about the potential use of an IB model to support policy analyses related to managing the risks of polioviruses and shows the importance of assumptions about network structure.

Dedication

To my parents, Maohai Hu and Xiulan Ma

献给我的父母，胡茂海和马秀兰

To my husband, Yinan Li and my daughter, Zifei Li

献给我的丈夫，李一楠，和女儿，李梓霏

Acknowledgements

Towards the end of this journey, I feel grateful to many individuals who have made my graduate experience the one that I will cherish forever. This dissertation was hardly possible without the help and inspiration of my committee members during the past four years, and the endless care and love of my parents and husband. It is a chance of a lifetime to put in words the gratitude I feel in my heart.

I have been fortunate to have Dr. Hazhir Rahmandad as my advisor. He first sparked my interests in the research problem of complex systems, led me to the attractive field of epidemiological modeling, and thus inspired the course of my dissertation's work. During this journey, he steered me towards insightful references and modeling toolboxes; taught me how to question thoughts and express ideas; held me to a high research standard; enforced strict validations for each research result; and explored opportunities in many ways to train me to be a mature researcher. His technical and editorial advice was essential to the completion of this dissertation. For me, Hazhir was not only my academic mentor, but also a friend who often offered emotional support when I encountered difficulties. He helped me adjust to a new country and inspired me to have a fruitful life outside of school throughout my graduate studies. I hope that one day I will become as good a person and researcher as Dr. Rahmandad.

I owe sincere and earnest thanks to my committee members for their contributions and support. Dr. Triantis admitted me to the Grado Department of Industrial and Systems Engineering at Virginia Tech in 2007. He continually provided his insightful suggestions about studies and life from his wisdom and all-round knowledge. Without his consistent guidance, caring, and encouragement, I would not have gotten this far.

I would like to acknowledge Dr. Smith-Jackson for her practical advice in the field of construction safety. She generously gave her time and expertise to better my work and helped me gain a different perspective to the research problem.

This dissertation would not have been possible if I had not meet Dr. Thompson and Dr. Radboud J. Duintjer Tebbens in 2009. They found time in their very tight schedules to help develop my background in epidemiology and gave me constructive feedback all along the way. I'd like to thank Dr. Thompson, who contributed her efforts to improve the quality of this dissertation, and for her willingness to follow her comments with concrete assistance which showed a strong dedication to my graduate education. Her wisdom, knowledge and commitment to the highest academic standards always inspired and motivated me. Though Dr. Radboud J. Duintjer Tebbens is not a member of my dissertation committee, I would like to express my deepest gratitude to him for preparing me with good-spirited discussions relating to the work in my doctoral thesis.

I feel grateful to my husband, Yinan Li, who unwavering understood and loved me despite the enormous work pressures we were facing as we moved towards graduation together. He was always there to cheer me up and stood by me through the good times and bad. His support and encouragement was what made this dissertation possible.

My daughter, Zifei Li, who was born right before this dissertation was completed and who spent many days with my parents and Yinan to allow me to focus on my research and writing. I am deeply sorry for the time we spent apart but felt lucky to have her at this moment of time because her smiles and even cries supported me to pass the stressful time before the defense.

Most importantly, none of this would have been possible without the unflagging love and dedication of my parents, Maohai Hu and Xiulan Ma. They have unconditionally supported me during my past studies that provided the foundation for this work, in all my endeavors while I have been thousands miles away from them, and so lovingly and unselfishly cared for Zifei which enabled me to focus on the dissertation. Whatever I have achieved is theirs, and they are the most important part of my life. 最重要的是，没有我的父亲胡茂海和母亲马秀兰无尽的爱和无私的奉献，我的论文工作不可能顺利完成。他们无条件地在我过去的学习生涯中支持我，使我能够为今天博士论文的成文奠定坚实的基础，他们远在千里之外的中国鼓励我努力坚持学业，他们在美国对梓霏无私的爱与悉心的照料使得我能专心地完成论文的写作。我今天的成就应归功于他们，他们是我生活中最重要的一部分。

Last but not the least, I would like to express my heartfelt gratitude to all my friends. I have to give a special mention for the emotional and editing support given by Dr. Paul Renard and Mrs. Kathryn Pieplow.

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CHAPTER 1 Introduction

1.1 Problem Context

Many challenging problems related to population health and safety are dynamic and complex because they involve multiple stakeholders, competing goals, and causal factors that unfold over time (Hedley et al. 2004; Jones et al. 2006; Midgley 2006). Multiple qualitative and quantitative approaches can facilitate our understanding and management of health and safety challenges. Among those approaches, dynamic simulation models provide a useful tool when qualitative reasoning falls short due to complexity (Auchincloss & Roux 2008; Sterman 1994, 2006).

Building a dynamic model can be an effective way to capture feedback in a complex system and assist learning in dynamic tasks (Homer & Hirsch 2006; Leischow et al. 2008; Sterman 2000). For example, health scientists increasingly use simulation models to examine outbreak response strategies to combat epidemics (Eubank et al. 2004; Longini et al. 2007; Longini et al. 2005). Researchers face a number of challenges in building useful dynamic simulation models. A single perspective on a problem and its associated data could be biased. It is important to bring together perspectives of stakeholders from different research areas, such as biology, economics, epidemiology, and psychology (Midgley 2006). Conducting a model-based analysis requires synthesizing knowledge from the literature and practical cases in order to completely understand the problem context and the relevant causal relationships. Other challenges arise in selecting appropriate model boundaries, levels of aggregation, and model inputs.

This thesis contributes to a better understanding of distinct complex dynamic problems in health and safety, including safety-related engineering designs in Essay #1 (Chapter 2, (Hu et al. 2011)) and epidemiological modeling work covered in Essay #2 (Chapter 3) and Essay #3 (Chapter 4, (Rahmandad et al. 2010)). The thesis addresses the above-mentioned challenges in dynamic modeling by offering literature synthesis methods that help with crossing disciplinary boundaries, and providing insights about selecting the appropriate modeling assumptions for the specific application. In the next section, I provide a summary of the three essays constituting my dissertation, followed by a discussion of the common themes unifying them.

1.2 Research Contributions

1.2.1 Essay #1

Our study examines causal factors for the risk of falls in the construction industry relevant to a full range of construction stakeholders (e.g., contractors, sub-contractors, managers, policy makers, and workers) and provides the first qualitative summary of the factors influencing those risks. The findings contribute to research on the causes of falls in construction, the development of engineering controls, the design of policies and interventions to reduce the risk of falls, and improvement in research synthesis methods.

A comprehensive understanding of causal factors is critical to building simulation models that can facilitate the goal of minimizing risk and preventing falls and injuries. We observed a significant gap in the literature about causal factors of falls—the primary cause of fatal and non-fatal injuries in the construction industry. Therefore, we proposed a systematic method to synthesize the previous literature in a formal and methodical fashion, and included previous research which was too heterogeneous to allow any formal meta-analysis. In fact our literature synthesis method based on macro-variables (i.e., the general categories used to aggregate diverse factors discussed in the literature) can be used in many different contexts, and provides a flexible approach to aggregating previous findings and identifying areas of agreement across those studies.

1.2.2 Essay #2

We reviewed the modeling and empirical studies in the literature on responding to outbreaks of infectious diseases in humans and animals. Unlike routine immunization and control efforts, outbreak response activities require rapid reactive actions to address an urgent or emergent situation. We focused our review on characterizing the types of diseases analyzed, the interventions used, and the models employed. Out of the 211 studies identified, we found that the majority focused on a few diseases (e.g., influenza, foot-and-mouth disease, smallpox, measles, and hepatitis). We identified 34 distinct interventions explored in these studies that fall under the general categories of vaccination, prophylaxis, quarantine/isolation, contact restriction, exposure reduction, killing/slaughtering, and surveillance. A large number of studies (141) use simulation/analytical models to analyze outbreak response strategies. We identified key factors

contributing to the effectiveness of different interventions that target high-risk individuals, trace infected contacts, or use a ring to delineate geographical boundaries for an intervention.

1.2.3 Essay #3

We developed the first individual-based (IB) model of the poliovirus transmission process to explore the stochastic attributes of state transitions, the heterogeneity of individual interactions, and the impact of different network structure choices in the context of understanding the dynamics of outbreaks. In this thesis, the terms IB and agent-base (AB) are used interchangeably. The input data of the basic immunity and infectiousness states of the model were based on a previously published differential equation (DE) model (Duintjer Tebbens et al. 2005). To explore the impact of different types of networks, we implemented a total of 26 variations of six different network structures in the IB model. We find that the choice of network structures plays a critical role in the model estimation of cases and the dynamics of outbreaks. This study provides insights into the potential use of an IB model to support policy analyses related to managing the risks of polioviruses and shows the importance of assumptions about network structures.

1.3 Contributions to Dynamic Modeling in Health and Safety

Simulation models of problems related to health and safety help examine the dynamic evolution of variables of interest in a controlled environment and within an internally consistent framework. This is an important contribution to enable better decisions, because the interactions relevant in a complex problem are often not easily interpreted and predicted by human mental models (Homer & Hirsch 2006; Sterman 1994, 2006). Dynamic modeling work is capable of capturing complex causal relationships (Anderson & Armstead 1995; Candib 2007; Diez-Roux 2000; Glass & McAtee 2006; Koopman & Weed 1990; Krieger 2001), including multiple, concurrent outcomes (Jones et al. 2006), and allowing utilization of different qualitative and quantitative data sources (Best et al. 2007).

The three essays summarized above relate to modeling complex dynamic problems in health and safety across quite different topics. Besides their unique contributions stated in Section 1.2, there are unifying themes in these essays which address common challenges faced by modelers. Each of these key themes is discussed below.

1.3.1 Bringing together multiple disciplines, stakeholders, and sources of data

The complexity of building a dynamic model is partly due to the requirement to draw on multiple disciplines, stakeholders, and sources of data (Hedley et al. 2004; Ritter 2007). For example, the risk of falls in the construction industry could involve different levels of causal factors: institutional factors (e.g., safety culture), individual factors (e.g., age, gender, psychological condition, and personal experience), geographical factors (e.g., terrain and weather), and societal factors (e.g., safety climate). Furthermore, data associated with those factors are often gathered by different types of studies and measurement instruments, and spread across different disciplinary studies. The multiple stakeholders—ranging from workers, contractors, designers, and owners to regulatory agencies—all play a role in the complex system in which falls are embedded. As a result, it is challenging to extract and manage large quantities of information from such different sources to inform relevant and effective model-based analyses. Essays #1 (Hu et al. 2011) and #2 contribute to the development of systematic methods for extracting information from diverse literature sources.

The literature synthesis method presented in Essay #1 provides an effective way of synthesizing a heterogeneous body of knowledge from different information sources and varying stakeholders' perspectives in the literature. Specifically, the approach helps identify causal factors contributing to the risk of falls from multiple sources, and reduces the complexity of that information by aggregating over five hundred factors into 21 macro-variables. The aggregated macro-variables enable us to build an intuitive causal map to capture the interactions of factors leading to falls. Rather than restricting our analysis to studies that employ a single method or data source, the research described in Essay #1 offers a way to include a large range of views and zoom in on sub-groups with a specific characterization when needed. This method provides a flexible approach to aggregating findings and locating areas of agreement across studies in various disciplines which can then be applied to study dynamic issues in health and safety.

Essay #2 provides another instance of incorporating a wide range of different perspectives by reviewing outbreak response studies focusing on a diverse set of diseases from different research standpoints. We obtained useful insights by comparing and contrasting modeling studies with different assumptions (i.e., the heterogeneity of populations and the selection of network structures) being used to analyze outbreak response strategy. We

documented a large amount of variability in the types of models, interventions considered, and evaluation criteria applied. We find that comparing studies for specific diseases yields meaningful insights, which we describe in Chapter 3.

1.3.2 Exploring Alternative Modeling Assumptions

The extensive knowledge gained from review studies is important, but insufficient for drawing policy conclusions (Milstein 2008). Well-structured dynamic models assist researchers in understanding dynamic challenges, testing different scenarios and intervention options, considering different costs and risks, and selecting better solutions among different alternatives (Anderson & Armstead 1995; Birckmayer et al. 2004; Candib 2007; Diez-Roux 2000; Glass & McAtee 2006). Many assumptions go into building such models, including the type of model (e.g., DE models and AB/IB models), the network structures (e.g., random or scale-free networks), levels of aggregation, appropriate model boundaries and model inputs. We explore these assumptions below.

1) Modeling approaches and the level of aggregation

Most dynamic models in health and safety rely on DE or IB models (Auerhahn 2008; Homer & Hirsch 2006; Sterman 2000). Making the choice between DE and IB modeling techniques often dependent on assumptions about the heterogeneity of the population, as well as the level of aggregation that a study intends to capture and investigate (Rahmandad & Sterman 2008). Yet this could be a difficult decision, with no obvious best solution apparent beforehand.

DE and IB models are complementary and have their own costs and benefits. If the complex systems are depicted and studied by DE models, targeted populations are treated as being in different compartments and are assumed to have perfect mixing within each compartment (homogeneity) (Sterman 2000). For example, people in the same age group are represented in one stock variable and are indistinguishable. In contrast, IB models typically consider each person as a unique individual. Each agent can be defined to carry specific characteristics that distinguish it from others (e.g., age, immunity profile, and infectiousness status). This requires additional model inputs (e.g. distributions of different agents characteristics) and modeling resources (e.g., computational resources) (Rahmandad & Sterman 2008). In addition, agents in IB models are capable of interacting with each other, which enables

the integration of network structures (e.g., small-world, scale-free, and mixing-site types). DE and IB models are likely to yield different insights—in part due to the differences in their abilities to capture network structures and population heterogeneity (Rahmandad et al. 2010).

Epidemiological modeling is a cornerstone of studying the dynamic transmission of communicable diseases in a manner that is fast, safe, and inexpensive (Midgley 2006). This method has attracted extensive attention in both practical and theoretical fields, especially after several severe disease outbreaks and risks in the past decade, such as the risk of potential bioterrorism using smallpox virus after the September 11, 2001 terrorist attacks (Eubank et al. 2004; Halloran et al. 2002; Kaplan et al. 2003; Meltzer et al. 2001), SARS in 2003 (Day et al. 2006; House & Keeling 2008; Pourbohloul et al. 2005; Xu & Sui 2009), and H1N1 in 2009 (Baguelin et al. 2010; Flahault et al. 2009; Gojovic et al. 2009; Hsieh 2010; Lee et al. 2010). Essays #2 and #3 provide insights into the applications of both DE and IB modeling techniques. Essay #2 compares a variety of models of outbreak response planning for potential infectious disease outbreaks. Essay #3 provides a concrete example of assessing a key modeling assumption (i.e., network structures) in the context of polioviruses transmission.

Essay #2 reviews previous modeling work and compares studies employing both DE and IB modeling toolboxes. We identify the specific modeling techniques used in a comprehensive database and categorize each according to their levels of aggregation (i.e., individual humans or animals vs. groups of humans or animals) and network assumptions (i.e., homogeneous mixing vs. heterogeneous mixing). This categorization helps us to better compare and contrast the various model types. The analysis reveals the preference of reviewed articles for the use of different modeling methods to study a specific disease (e.g., models of heterogeneous mixing groups are often used to study animal diseases), and the importance of understanding different types of models and the role of social network structures in the transmission of infections. We also note that the use of IB models of disease diffusion has increased in the last decade.

Essay #3 provides an example of using an IB model to study poliovirus transmission and outbreaks. We base our IB model on a previously published DE model (Duintjer Tebbens et al. 2005), and document the differences and similarities between the two approaches in Chapter 4. This study enables us to openly explore the impact of common assumptions made regarding the appropriate modeling approach. In addition, Essay #3 reveals important considerations

regarding the challenges of building reliable IB models. Using an IB model appropriately depends on obtaining high-quality information about the nature of diseases, immunity, and social interactions. For example, we need a more detailed understanding of the process that creates *Who Acquires Infection From Whom* (WAIFW) patterns in a specific population of interest. Nevertheless, even without such detailed information, our analyses of alternative network structures still provide a baseline about the range of dynamics one could expect from this system. At the same time, our IB model shows that the computational time for transmission simulation and data recording could be a challenge. This time-scale is approximately linear with the population size, and simulating very large populations (e.g., millions of individuals) requires specialized computer clusters. In addition, the necessity of conducting comprehensive sensitivity analyses could add another significantly large dimension to the computational time.

2) Selecting network structures

Implementing an IB model requires the selection of network structures to explicitly capture the interactions among individuals (Rahmandad et al. 2010). Several metrics are used to characterize the properties of interactions and categorize different networks: degree distribution, mean shortest path, and clustering coefficient. However, the characterization of the exact contact network structure in a human population remains difficult (Edmunds & Brisson 2002), and can be a significant factor in the dynamics of interest. For example, high-degree nodes (i.e., hubs) are a major contributor to the diffusion of diseases in a network because they can transmit the disease to many different agents in far-off network locations. Disease diffusion slows as contact networks become more tightly clustered. Nevertheless, in the absence of reliable network data, with the IB model, we are able to explore the behavior of models under different network alternatives in order to learn about key characteristics of networks that matter in each problem setting. Such findings can help focus future data collection and specify the range of uncertainty associated with network structures.

Essay #2 explores how some of the key characteristics of network structures influence appropriate outbreak responses by comparing a variety of modeling studies in the literature. We note that long-range links in a network can reduce the viability of ring interventions, such as interventions targeting a subpopulation based on setting a ring around a geographical boundary

(Stone et al. 2010; Thornley & France 2009); and higher clustering can facilitate tracing interventions, as seen when individuals are targeted based on contact tracing in a social network.

Essay #3 illustrates a comparison between a published DE model (Duintjer Tebbens et al. 2005) and an IB model which implements different network settings. This study examines the impact of individual heterogeneity and different network topologies, including fully-connected, random, small-world, scale-free, all-in-range, and mixing-site networks. The controlled experiments suggested that the type of network structure could be of importance in determining the outcome of polio outbreaks (Barabasi & Albert 1999; Davis 1991; Watts & Strogatz 1998). Specifically, small-world networks, while causing slower outbreaks, could lead to a larger number of total paralytic cases; scale-free networks could lead to the fastest epidemics but not the highest number of paralytic cases; and all-in-range and some types of mixing-site networks could lead to relatively slow outbreaks with smaller final epidemic sizes.

3) Model boundary

Modelers are often forced to trade off between the disaggregation of details and the breadth of model boundary because of limited time, budgetary, and computational resources (Rahmandad & Sterman 2008). The boundary is defined here as the richness of the feedback structure endogenously captured in the model (Sterman 2000). Yet the right choice about appropriate boundaries for analyses is often unclear. Therefore, studies that compare the different insights of previous research when including different model boundaries, or comparative studies that change a specific boundary parameter to explore its impact on the results are helpful in informing the choice of model boundary for future research in the same area.

By providing a comprehensive literature review, Essay #1 outlines the broad boundary of the issues relevant to falls in construction based on the previous literature. This information can help researchers decide what factors they should include in their models and inform their choices about model boundaries. While we did not explicitly discuss model boundaries in Essay #2, the interventions considered in each study reflects various choices of model boundaries.

4) The development of model inputs

My thesis also addresses the challenge of selecting model inputs. First, the material provided in Essay #1 is a good starting point for getting estimates for many parameters relevant to risk factors of falls. In fact these parameter values are extracted from the reviewed papers and provided in a public online database. In Essay #2, we discuss how uncertainty in the model inputs for the disease may impact the attractiveness of alternative interventions (e.g. mass vs. tracing interventions (Elderd et al. 2006)). Finally, Essay #3 demonstrates the importance of model input assumptions for polio outbreak modeling. Specifically, to model transmissions at the individual level, we need to specify the detailed mechanisms for who meets whom in the population. Beyond the contact process, the infectivity of each type of contact is also relevant to the dynamics. The results suggest some of these assumptions could be important and lead to notable differences across simulations. More empirical work is required to fully specify the real world mechanisms.

Overall, these essays not only come together as instances of research to address complex dynamic problems in health and safety, but also provide methodological and process insights to help build better dynamic models. These insights span different challenges faced by modelers, from synthesizing different sources in the literature and contrasting perspectives, to exploring alternative assumptions regarding appropriate modeling methods, levels of aggregation, network structures, model boundaries, and model inputs.

1.4 Future Work

Several possibilities for future work arise from these essays. One possibility is to build dynamic models of the risk of falls in the construction industry. Essay #1 offers an opportunity to bound the value of parameters which could potentially feed into a quantitative dynamic model in the future. Future research based on the work presented in Essay #2 could study the impact of different modeling assumptions regarding outbreak response (e.g., behavioral responses) on the results of different models. The IB model developed for Essay #3 could be applied to test and compare viable response interventions for evaluating different response interventions.

1.5 A Few Personal Reflections

The work presented in this dissertation was not designed to lay out a single cohesive study. Rather, it integrates a broad range of topics, from the construction industry to epidemiology and methodological contributions to dynamic modeling efforts. These studies

reflect the twisting path of my research during the Ph.D. program, largely determined by funding availability and my advisor's focus. A large amount of time has been spent on acquiring the background knowledge in each new field when tackling a new problem, and understanding and incorporating multiple perspectives in a new study. Extensive learning efforts are required when attempting to answer those research questions in each essay—obtaining a sufficient level of domain expertise in a new area by studying literature, communicating with field experts, and participating in conferences and seminars. This may not have been the most common pathway to complete a Ph.D., yet the efforts have been fruitful. The research initiatives have made me familiar with several research communities (epidemiology, modeling and simulation, behavioral science, and safety), paving the way for conducting subsequent researches in cross-disciplinary teams. Furthermore, the quality of work presented in this dissertation has led to several publications. A journal article from the material in Essay #1, coauthored with Professors Rahmandad, Smith-Jackson, and Winchester, is accepted for publication in *Construction Management and Economics* (Hu et al. 2011). The review paper in Essay #2, coauthored with Drs. Rahmandad, Duintjer Tebbens, and Thompson is under review at *Epidemiology and Infection*. A third article coauthored with Drs. Rahmandad, Duintjer Tebbens, and Thompson from the material in Essay #3 is accepted for publication in *Epidemiology and Infection* (Rahmandad et al. 2010). Another journal publication with Dr. Rahmandad from material not discussed in this dissertation has been published in *System Dynamics Review* (Rahmandad & Hu 2010).

Despite these achievements, I understand that my dissertation has some weaknesses. First, while the above themes bring different essays together, the coherence of the dissertation as a single document is less than that in dissertations focusing on just one topic. The depth of my expertise in each domain is also inevitably less than what it would have been had I focused all my research efforts on a single project. In spite of these shortcomings, this research represents a meaningful contribution to the accumulated knowledge about my subject, and is particularly important due to the cross-disciplinary, integrative qualities of the work.

CHAPTER 2 Factors Influencing the Risk of Falls in the Construction Industry: a Review of the Evidence

Abstract

Falls are a significant public health risk and a leading cause of non-fatal and fatal injuries among construction workers worldwide. A more comprehensive understanding of casual factors leading to fall incidents is essential to prevent falls in the construction industry. However, an extensive overview of causal factors is missing from the literature. In this paper, 536 articles on factors contributing to the risk of falls were retrieved. One hundred and twenty-one (121) studies met the criteria for relevance and quality to be coded, and were synthesized to provide an overview. In lieu of the homogeneity needed across studies to conduct a structured meta-analysis, a literature synthesis method based on macro-variables was advanced. This method provides a flexible approach to aggregating previous findings and assessing agreement across those studies. Factors commonly associated with falls included working surfaces and platforms, workers' safety behaviors and attitudes, and construction structure and facilities. Significant differences across qualitative and quantitative studies were found in terms of focus, and areas with limited agreement in previous research were identified. The findings contribute to research on the causes of falls in construction, developing engineering controls, informing policy and intervention design to reduce the risk of falls, and improving research synthesis methods.

Keywords: Literature synthesis methods; Causal map; Safety; Accident causes

1.0 Introduction

The construction industry faces many occupational injuries and fatality risks, making it both unique and challenging to study. Construction is always risky because of outdoor operations (Hsiao and Simeonov, 2001; Imriyas, Pheng *et al.*, 2007), working at heights (Lipscomb, Glazner *et al.*, 2006), and often working in dynamic and complex environments (i.e., diverse construction methods (Hsiao and Simeonov, 2001), working conditions and materials (Chi, Chang *et al.*, 2004; Imriyas, Pheng *et al.*, 2007)). Equipment operation coupled with workers' attitudes, behaviors, and physical characteristics relevant to safety also contribute to the relatively higher risk context in this industry (Hsiao and Simeonov, 2001; Sa *et al.*, 2009). In theory, most construction injuries can either be prevented or controlled. Unfortunately, achieving this goal has been very slow in practice (Gambatese *et al.*, 2008). Hazard prevention and control in construction is a persistent and global challenge, with construction having one of the worst safety records among diverse economic sectors, including high-risk industries such as chemical, mining, electrical, and transportation (Lehtola *et al.*, 2008; Sa *et al.*, 2009; Hallowell, 2010a). The U.S. construction industry accounts for 19% of all occupational fatalities, and despite a gradual decline, remains the highest source of fatal occupational accidents (Bureau of Labor Statistics, 2010). The construction fatality rate in the United Kingdom has risen over recent years to constitute 21.5% of total occupational fatalities (Health and Safety Execute, 2010) while reportable non-fatal injuries averaged 16 per 1000 workers between 2004 and 2009, significantly higher than the average of 10 per 1000 workers overall (Labour Force Survey, 2009). Construction incidents account for more than one third of all industrial incidents over the last 10 years in China (Chua and Goh, 2004, Li and Wang, 2004, Tam et al., 2006, Liao and Perng, 2008). In addition to the loss of life and reduction in the quality of life of construction workers, construction incidents lead to project delays (Meerding *et al.*, 2006; Gavious *et al.*, 2009), increased project costs (Lipscomb *et al.*, 2003a; Horwitz and McCall, 2004), medical burden (Lipscomb *et al.*, 2003a), and other negative consequences. The direct effect may be billions of dollars annually (Hallowell, 2010b); while indirect costs of incidents are estimated to be six times more than the direct costs (Gavious *et al.*, 2009). For example, the estimated costs related to disabling injuries in the American construction industry were estimated at $15.6 billion (The Construction Chart Book, 2008).

Falls are a primary cause of construction injuries. Despite modest overall reduction, in the U.S., between 1992 and 2006, falls accounted for 32% of fatal occupational injuries in general (Dong *et al.*, 2009) and 50% of fatalities in construction (2009 data; Bureau of Labor Statistics, 2010). Internationally, falls from heights in New Zealand are the leading cause of occupational injuries (Department of Labour, New Zealand, 2010). Falls account for approximately 51% of injuries in China's construction industry (Yung, 2009). In Hong Kong, falling from heights represented more than 47% of the total fatal incidents (Chan *et al.*, 2008). As a result, falls are the most costly occupational hazard in many countries (Gavious *et al.*, 2009). In the U.S., the annual costs of fall-related occupational injuries were approximately six billion dollars in 2000 (Courtney *et al.*, 2001). The total compensation for injuries due to falls from heights reached the peak of HK$39,643,353 in 2008 in Hong Kong (Li and Poon, 2009). In the Netherlands, total health care costs due to work-related injuries were €1.15 billion in 2004, from which 44% of injuries resulted from falls (Meerding *et al.*, 2006). Overall, similar statistics across many different countries indicate that work-related falls represent an extraordinary global financial burden. Consequently, the prevention of falls is an important priority in the construction industry (Chi *et al.*, 2004; Winn *et al.*, 2004; Bentley *et al.*, 2006; Lehtola *et al.*, 2008).

Key construction stakeholders, including policy makers, owners, contractors, workers, engineers, and researchers, could benefit from an overall understanding of factors contributing to falls in the construction industry. To direct safety intervention efforts, construction safety practitioners need such an overview (Arboleda and Abraham, 2004). This knowledge can support policy makers in designing and evaluating policy, construction owners and contractors in investing in safety interventions, and workers in conducting their day-to-day activities. However, many diverse factors are relevant to understanding the causes of work-related falls in the construction industry. Different types of studies including surveys, interviews, questionnaires, case studies, accident/incident records, observations, and controlled laboratory experiments in various disciplines have been conducted to elaborate these factors. Given the multiplicity of factors involved, the volume of studies, and the diverse methods of research used, building an overall understanding that benefits different stakeholders is challenging. Previous review articles have focused on narrower questions such as factors influencing balance (Hsiao and Simeonov, 2001) or fall prevention interventions (Rivara and Thompson, 2000). A review of this literature

that captures the diversity of studies, assists with in-depth scholarly investigations, and also provides an aggregate overview of the knowledge domain for practitioners can fill an important research and practice gap.

2.0 Objective

This paper focuses on a study conducted to review and integrate existing knowledge domains relevant to factors that influence the risk of falls in the construction industry. Three specific goals distinguish the contributions of this research effort. First, in this review, a wide range of previous studies with different methods and approaches are covered. Second, we advance a causal mapping methodology to provide a comprehensive overview of casual factors related to falls for practitioners in the construction industry. Third, to make the results useful for researchers, a framework for synthesizing the causal factors is created and the raw review data is provided, which can be used for further analyses and aggregations.

3.0 Methods

To achieve the above goals, a four-step approach was followed. These steps included:

(1) Conducting a literature search to identify potentially relevant studies;

(2) Selecting studies that contributed to understanding the factors influencing falls in construction industry and ensuring the selected studies were of acceptable scientific quality;

(3) Coding the findings of each study;

(4) Synthesizing the results of the coded data.

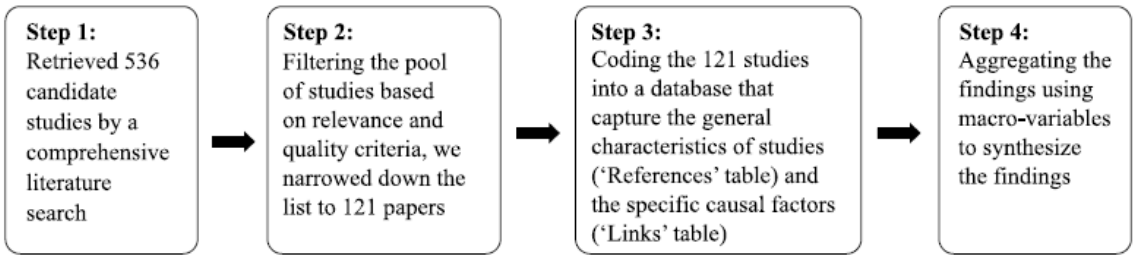

Figure 2-1 Process model of causal factor extraction

These steps are illustrated in Figure 2-1 and detailed in the subsequent sections.

3.1 Step 1: Comprehensive Literature Search

Potentially relevant papers were first retrieved from multiple databases and literature collections of published, peer-reviewed research articles and reports. Keyword bibliographic searches were conducted in electronic databases including Web of Science (AKA: "ISI Web of Knowledge"), MedLine, Engineering Village, ScienceDirect, PubMed, and Google Scholar. We began with a few proverbial keywords related to the topic as seeds, including combinations of "risk(s) of fall(s)", "fall(s)", "injury/injuries", "risk(s)", "fall(s) factor(s)/factor(s) of fall(s)" and "construction industry". By reviewing retrieved papers in the literature, a few new keywords were obtained and the search was expanded. A few rounds of this iterative method led to additional search keywords: "falls from heights/ladder/scaffolds/supporters/to a lower level/into a hole", "construction/industrial safety", "construction accidents/incidents", "construction/ occupational falls", "construction/occupational injuries", "non-fatal/fatal falls/injuries", "occupational accidents/incidents", "hazard of falls", "falls protection", "slips", "trips" "construction ergonomics", "safety climate", "safety culture", "high-risk group in construction", and "fatal occupational falls" and so forth. We also contacted several scholars in a variety of related domains to track additional relevant studies including working articles that could not be found through online databases. Finally, search results were augmented through back-referencing potentially relevant citations in the identified papers.

The resulting sample includes 536 studies and reports in the literature and covers more than 50 journals and conference proceedings. The major contributing journals to this sample include *Safety Science, Ergonomics, Injury Preventions, Journal of Construction Engineering and Management, International Journal of Industrial Ergonomics, Applied Ergonomics, American Journal of Industrial Medicine, Accident Analysis and Prevention, International Journal of Occupational Safety and Ergonomics, and Journal of Safety Research* with impact factors ranging between 0.410 to 1.721 (details available in the Online Supplement).

3.2 Step 2: Filtering and Categorization of the Sources

The identified studies were filtered and categorized in a two-step procedure by two reviewers (A doctoral student and a faculty member, both from the field of Industrial and

Systems Engineering). First, based on the abstract review, the studies were narrowed down according to the following criteria:

(1) The study was reported in English, and published no earlier than 1980 .

(2) The research focused on the casual factors contributing to falls in the construction industry (commercial and residential building sectors, and roadway construction sector were included).

(3) Given our purpose, more macro factors, papers reporting medical evidence on factors inside the body relevant to falls (e.g., investigating the impact of blood pressure and the rate of heartbeat) and studies on medical impact of injuries of falls (e.g., impact of different fall-related trauma on body) were excluded.

(4) Opinion-based or anecdotal papers not supported by empirical evidence or previous literature were excluded.

(5) Editorials, commentaries, letters to the editor, and news items were excluded.

The resulting pool of studies was reduced to 279 papers. In the second step, we reviewed the full papers and grouped them into different categories according to study type and quality. Then the following three categories were selected: 1) Well-designed quantitative papers, i.e., statistical estimation of impact or probability of risk associated with one or more factors related to the risk of falls in construction industry (17 papers); (2) Quantitative papers with the estimation of effects but lacking detailed controls to isolate different factors (40 papers); (3) Papers discussing causes of falls based on qualitative data and quantitative papers without an empirically strong estimation process, e.g. counts and histograms, and mathematical cost models (e.g. insurance studies) (64 papers). This step led to a final sample of 121 studies, where most of the excluded papers in the second step lacked empirical basis. The citations for the full sample of 121 papers are reported in Appendix A (from number [1] to [121]).

3.3 Step 3: Data Extraction

Full papers were coded by the same doctoral student to extract direct and indirect causal factors for the risk of falls, as well as the magnitude and statistics of estimated relationships, where available. This information was recorded in a database within two tables (i.e., “Reference”

and “Links”). The “Reference” table includes information about each article coded and the “Links” table includes the information about the causal relationships extracted from the articles. Data extracted from each coded paper in the “Reference” table include: year, reference authors, and full reference, study type, sample size, sample selection method, construction sector, and geographical location of sampled population (see one sample in Table 2-1). In “Links” table, the “Initial” and “Final” variable fields were used to denote the independent and dependent variables in each causal relationship captured; the types and units of these variables were specified in this table as well (see one sample in Table 2-2). Where available, the type of statistical tests, effect sizes, and standard deviations were recorded in the “Links” table as well.

In this coding process, the same variable names were extracted and recorded, verbatim, as used in the original studies. We also included all the causal links reported rather than simply those with dependent variables related to the risk of falls. The coding system therefore covers the full causal chain of the risk of falls as discussed in the sample papers. For instance, if worker training impacts safety behavior and that in turn impacts the risk of falls, two different causal links should be included in the database.

Table 2-1 An example record in the “Reference” table of the database (complete “Reference” table is publicly available online for interested readers. See the URL in “Online Supplement” section at the end.)

Year	Authors	Full reference	Study type	Sample size	Sample selection method	Sample population	Construction sector
2003	Lipscomb HJ, Dement JM, Nolan J, Patterson D, Li LM, Cameron W..	Lipscomb HJ, Dement JM, Nolan J, Patterson D, Li LM, Cameron W. Falls in residential carpentry and drywall installation: Findings from active injury surveillance with union carpenters. Journal of Occupational and Environmental Medicine 2003, 45(8): 881-890.	on-site interview	5137 carpenters	partnership with the Carpenters' District Council of Greater St. Louis and the Homebuilders Association of Greater St. Louis	St Louis, USA	residential construction

Table 2-2 An example from the "Links" table of the database (complete "Links" table is publicly available online for interested readers. See the URL in "Online Supplement" section at the end.)

Initial variable (cause)	Final variable (effect)	Reference number	Link sign (+ or -)	Initial type	Initial unit	Final type	Final unit	Significance test	Estimated effect
Fall protection program	Falls from heights	120 (Sa *et al.*, 2009)	-*	0-1 variable	dimensionless	0-1 variable	Dimen-sionless	Log-binomial regression (examines prevalence ratios (PRs))	P< 0.001

*Negative relationship between the initial and final variables means that by increasing the initial variable we expect a decrease in the final variable, and vice versa.

3.4 Step 4: Synthesis of Data

The data extracted from the empirical studies in Step 3 includes 534 variables with different names and definitions, many variable types, and statistical and non-statistical metrics. One of the most common practices to aggregate results of previous research is to conduct a formal meta-analysis that pools results from multiple studies to judge the strength of different causal links. A systematic meta-analysis requires consistent variable definitions and comparable statistical methods, so that data can be pooled from different studies to inform the overall strength of one (or more) causal relationship(s). However, the lack of homogeneity in the sample of studies reviewed makes it premature to conduct a quantitative meta-analysis for most of the causal relationships identified. To address this challenge, a set of macro-variables were used to aggregate the diverse variables into more general categories. In this method, we benefited from the previous contribution of Derzon and Lipsey (1999) who applied summary categories to different variables that they identified in their review of tobacco use predictors. We extended their approach to developing qualitative causal maps, which may make the analysis more useful to future researchers by formatting the raw data to allow for alternative macro-variable definitions.

Specifically, the similar variables and concepts were merged into 21 summary categories or macro-variables (see details in Appendix B). For example, "falls from heights", "falls from ladders", "falls from scaffolds", "falls", "slips, trips and falls", and "fatal falls", as well as a few others were merged into a single macro-variable: "risk of falls and injuries". Once the macro-variables were created, the causal links connecting the original variables within two macro-variables were aggregated to one causal macro-links that connect macro-variables. Through this

procedure, the 866 links were synthesized in the "Links" table into 32 macro-links. Appendix B describes macro-variables we chose and the full set of initial variables that were grouped together.

The use of macro-variables in this context helps synthesize commonalities across the diversity of definitions and the heterogeneity of disciplines from which the studies originated. In this way, the relationships captured in previous studies are demonstrated in a concise overview map of the aggregated factors (i.e., macro-variables). However, the categorization of original variables into macro-variables is both subjective and context dependent. Depending on the goals of the research, one could select more macro-variables to capture the nuances across a range of closely related concepts, e.g. separating working surface and working platform macro-variables, whereas we currently have a single macro-variable for both concepts. Researchers may also wish to restrict the review to a more homogenous subset of the current studies, thus aggregating over fewer original variables. Moreover, different researchers may partition the original variables into somewhat different macro-variables. To overcome these limitations, we publicly and freely provide the full coded data (see the URL in section of Online Supplement) so that other researchers can use alternative categories of macro-variables to synthesize the data. In this review study, one set of aggregated results is provided to be consistent with the purpose of the review, which is to help create an aggregate overview of the causes of falls in the construction industry.

4.0 Results

4.1 Characteristics of Coded Studies

4.1.1 Sectors of the Construction Industry Studied

Three distinct sectors in the construction industry were identified in our data: residential building, commercial building, and roadway construction. A large fraction of the coded papers (56 out of 121 papers) reported studies on risk factors based on data from the construction sector of commercial building. Thirty-two (32) papers analyzed fall-related causal factors in the residential building construction industry, focusing especially on residential roofing. Only two coded papers (Mungen and Gurcanli, 2005; Chau *et al.*, 2007) relied solely on data from the road and railway construction. The remaining 31 papers reported data from all sectors in the construction industry as a whole. Given the significant variations of construction tasks, practices,

and organizational arrangements across these sectors, additional sector-specific research especially in heavy roadway and railway construction is warranted. Detailed information on the industry is also available in the "Reference" table (see details in Online supplement).

4.1.2 Geographic Distribution

Data from 16 different countries and districts, covering five continents, were reported in the studies summarized in this review. The distribution of the countries in the coded sample is illustrated in Table 2-3. More than half of the research was based on data from the U.S. potentially due to higher research volume in the States, better surveillance and data availability in developed countries, and our focus on papers published in English. Moreover, upon a closer examination, only a handful of states, namely Washington, California, and West Virginia, contributed the majority of the U.S. data. As a result, current research may not capture all country- or state-specific factors (such as weather, terrain, industry standards, legal frameworks, and worker's safety norms). This suggests that additional research with a focus on local factors (such as weather, cultural, and institutional factors) may be warranted for many countries and regions around the world.

Table 2-3 Geographic distribution of data informing the coded papers (percentages represent proportions of the papers in the final sample (i.e., 121 studies) from a particular population)

Country Name	Occurrence
Australia	2
Canada	3
China (Hong Kong, Taiwan)	11
Denmark	6
Finland	3
France	6
Jordan	1
N.A.	6
New Zealand	2
South africa	1
South Korea	1
Sweden	5
Spain	1
The Netherlands	1
Turkey	2
UK	4
USA	66
Total:	121

N.A.: not available

4.1.3 Study Types and Variables

The current literature on risk factors of falls offers an array of sampling methods, variable definitions, and estimation techniques. Looking at the nature of analysis informing each link in the database (see Figure 2-2), 506 of the 866 links were identified using qualitative methods. The quantitative analyses also included many different types of statistical tests, including Mortality Ratios, ANOVAs, Odds Ratios, among others (also see Figure 2-2). This diversity is partly due to different study types used to gather the data. The majority of studies used data from archival sources (most used data sources are government and research institute data bases of falls). Other study types include controlled laboratory experiments, analytical models based on empirical data, on-site and telephone interviews, and questionnaires by mail or online. (See Table 2-4 for a summary of study types).

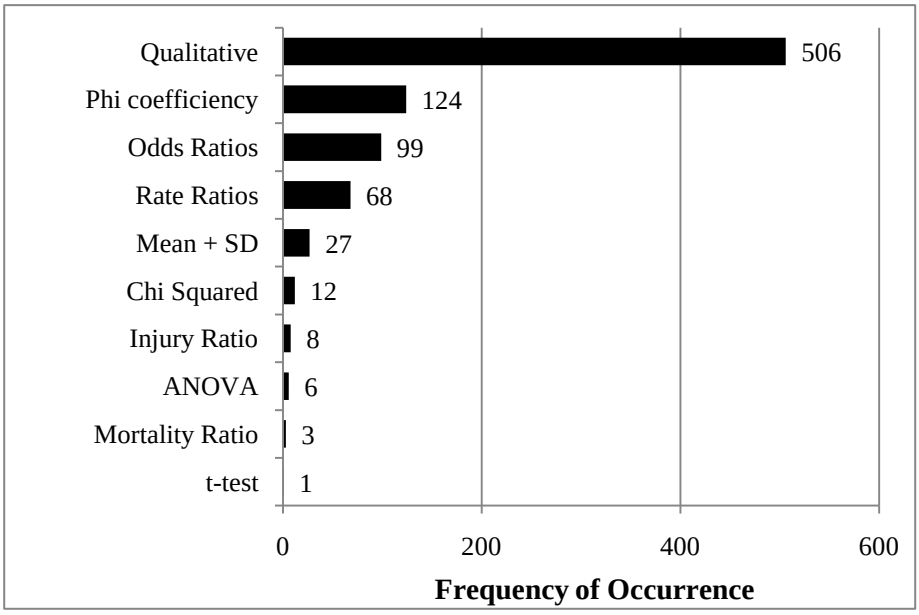

Figure 2-2 Frequency of the occurrence of the nature of statistical test for causal links reported in coded studies

Table 2-4 Sample selection methods reported in coded papers in the literature

Study types	Occurrence
Analytical model based on empirical data	6
Archived data _ doctor's first reports	2
Archived data _ insurance compensation claims	12
Archived data _ literature review	10
Archived data _ research institutes (e.g., National Institute for Occupational Safety and Health, Occupational Safety and Health Administration and so on)	60
Controlled laboratory experiment	12
On-site or phone interview	9
Questionnaire by mail or online	12
Total:	123*

*2 papers used 2 types of studies.

5.0 Summary of Causal Factors Identified

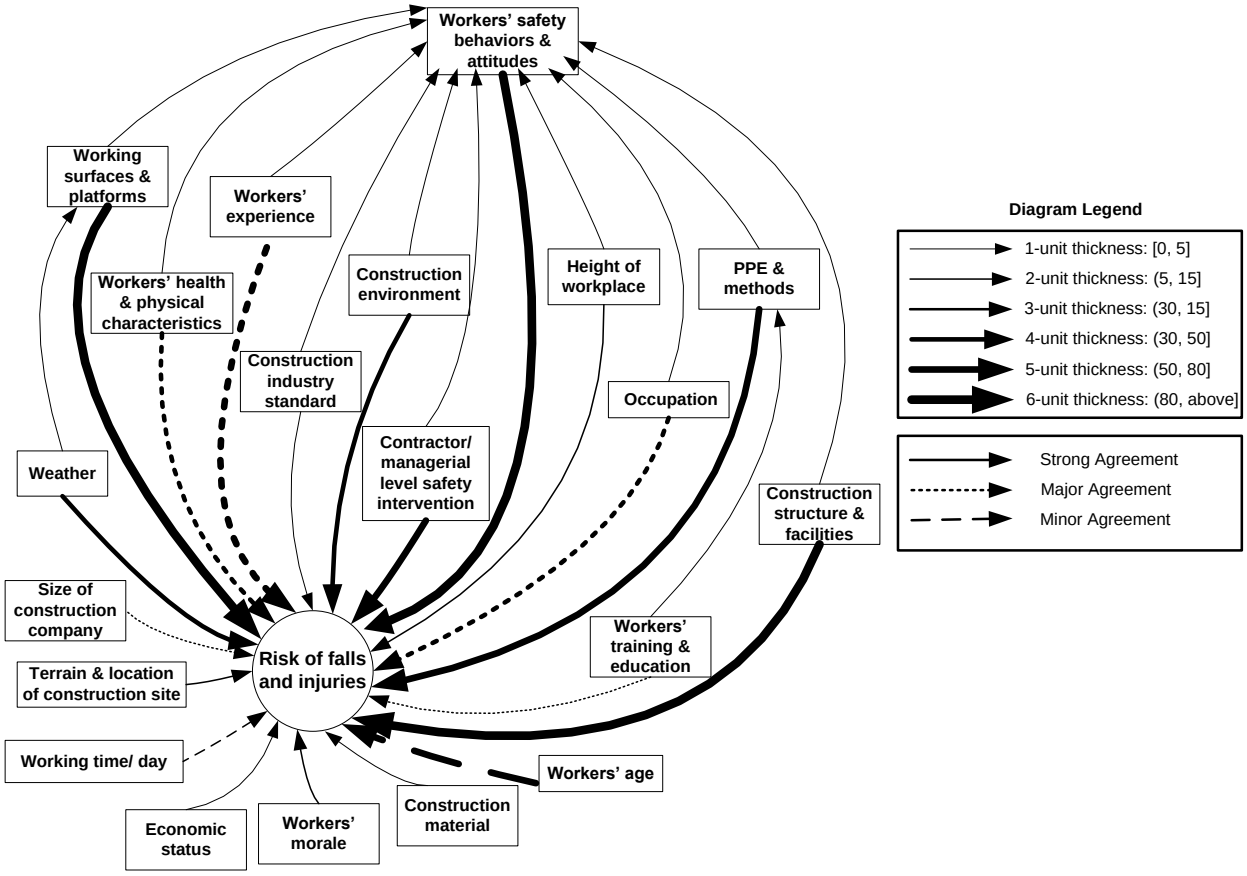

Figure 2-3 Causal relationships of macro-variables supported by qualitative and quantitative studies (ranges in legend represent the number of instances obtained from the literature on macro-variable relationships and consequences, and agreement consistency of causal relationships are summarized from coded studies by different line-styles)

Figure 2-3 illustrates the summary of synthesis of causal factors. Following the aforementioned synthesis method, all the results in the sample of papers are captured within 21 macro-variables and 32 causal links among them in order to present an overview of the causal pathways. Given that each link in this graph represents aggregation of multiple original links in previous studies, two additional characteristics of these links are used to further elaborate on the results. First, the thickness of each link represents the number of instances in the previous literature where a causal link has been identified among (the original variables defining) the macro-variables. Note that this representation does not capture the magnitude of impact for the link, rather, the emphasis in the previous literature on that link which may simply be the result of

the ease of data collection for some variables. The pattern of the link (i.e., solid, dotted and dashed lines) further elaborates on the level of agreement in the previous literature on the sign of the causal link. Where the literature consistently provides a positive/negative causal link, a solid-line is used. Where inconsistencies are observed in the previous findings, we use dotted or dashed lines. For example, the dotted-line between "workers' experience" and "risk of falls and injuries" suggests that there is some agreement that as a worker's experience in a sector increases, he/she faces a reduced risk of falls (Cellier *et al.*, 1995; Hsiao and Simeonov, 2001; Lipscomb *et al.*, 2003c; Bobick, 2004; Bentley *et al.*, 2006; Choudhry and Fang, 2008; Lipscomb *et al.*, 2008). However, the literature is not unequivocal on this connection, for example Haslam, *et al.* (2005) and Kaskutas, *et al.* (2009a) argued that experienced workers may become over confident and more likely to face fall-related risks resulting from carelessness and oversight.

Table 2-5 The number of link occurrences (instances) in the literature originating from macro-variables directly influencing the "risk of falls and injuries".

Ranking	Macro-variables of factors	Consistency of agreement	Number of link occurrences
1	Working surfaces and platforms	Strong	128
2	Workers' safe behaviors and attitudes	Strong	127
3	Construction structure and facilities	Strong	96
4	Contractors/managerial level safety intervention	Strong	55
5	Workers' age	Minor	53
6	PPE and methods	Strong	51
6	Workers' experience	Major	51
8	Workers' health and physical characteristics	Strong	50
9	Occupation	Major	45
10	Construction environment	Strong	40
11	Weather	Strong	32
12	Workers' training and education	Major	24
13	Size of construction company	Major	20
14	Workers' morale	Strong	16
15	Working time/day	Minor	10
16	Construction industry standard	Strong	9
17	Terrain and location of construction site	Minor	7
18	Height of workplace	Strong	6
19	Construction material	Strong	5
20	Economic status	Strong	4

Table 2-5 sorts the macro-variables directly influencing the "risk of falls and injuries" variable in decreasing order of the number of links, and provides the consistency from the previous work. The three most mentioned causes of falls in this literature include: (1) working surfaces and platforms (e.g., slippery surfaces, improper concrete surfaces, slippery roof, use of

platforms, bamboo scaffold, and slip of ladder base) (2) workers' safety behaviors and attitudes (e.g., safety procedure, perceived risk, evaluation of risk, operation at unsafe speed, or horseplay while working), and (3) construction structure and facilities (e.g., the stability of the building's framework, and the reliability of the construction equipment). The agreement across these links is strong in the literature.

The other highly studied and consistently rated factors contributing to risks of falls include the safety behavior at the contractor/managerial level, the use of personal protective equipment (PPE) and methods, the workers' health and physical characteristics, and the environment at the construction site. Factors such as age, workers' experience, and occupation of workers are also discussed frequently, but the agreement about their impact is somewhat modest. The experience effect is complicated through the direct effect of experience on improved safety and the indirect effect of experience due to over confidence, which can reduce adherence to safety procedures (Cellier *et al.*, 1995; Hsiao and Simeonov, 2001; Lipscomb *et al.*, 2003c; Bobick, 2004; Haslam *et al.*, 2005; Bentley *et al.*, 2006; Choudhry and Fang, 2008; Lipscomb *et al.*, 2008; Kaskutas *et al.*, 2009a). The age effect is confounded by experience (which is correlated with age), and health characteristics which are negatively correlated with age. As a result, the overall picture of the impact of age on the risk of falls is not very clear. Two variables, work time (of day/month) and construction site terrain, show little consistency among findings across different studies. While several studies found an impact for the time of the day and the day of the month on risks of falls, the results are not consistent across different studies (Pollack *et al.*, 1996; Kines, 2002; Chan *et al.*, 2008). Similarly, the location and terrain of the construction site is mentioned as an impact factor on the risk of falls; yet there is no general agreement across the current studies on the details of this impact (Buchner *et al.*, 1997; Lipscomb *et al.*, 2003b).

"Workers' safety behaviors and attitudes" is the top influencing variable in terms of the number of studies that found a relationship from this variable to the risk of falls. Moreover, this variable is influenced by many other direct causes of risks of falls shown in Figure 2-3. Therefore the literature suggests many causal factors, such as "contractor/managerial level safety intervention", "PPE and methods", and "workers' experience" having both a direct and an indirect effect on the risk of falls. However, most of these direct vs. indirect influence pathways

come from different studies. Therefore this finding may be partially due to different levels of aggregation in the original studies. Where the investigators have explicitly included workers' safety behaviors and attitudes, this has become a direct contributor to the risk of falls while many other variables influence this intermediate cause. In lieu of including this intermediate cause, studies found a direct impact for many of those secondary causes. A few longer causal chains are also observable in Figure 2-3. Specifically, "workers' training and education" influences "PPE and methods" while "weather" influences "working surface and platforms". Both these latter variables subsequently have an impact on "workers' safety behavior and attitudes", which, in turn, influences "risk of falls and injuries".

If the same synthesis of results is repeated using only the quantitative studies with a statistical test (total of 298 links) an interesting picture emerges. Many organizational and psychological concepts such as "workers' behavior and attitudes" rarely appear in the quantitative studies. For example, in this alternative synthesis, there is no more than a single mention of the macro-variable "contractor/managerial level safety intervention", even though it is the fourth most cited item in the full sample. Other factors that rarely show up in quantitative studies include "workers' training and education", "workers' morale", and "construction industry standards". This is not entirely surprising given that softer variables are harder to measure quantitatively and to trace in large-sample studies that provide a reliable statistical power.

6.0 Methodological Contributions

Besides summarizing the factors contributing to the risk of falls and injuries in construction, this paper makes a methodological contribution to the review of heterogeneous bodies of literature. Specifically, by capturing the coding and synthesis results in tables of a database, this method offers the researcher the flexibility to move across different levels of aggregation, or focus on different subsets of results, without the need to rework. This additional flexibility is now feasible through the digital appendices that could be included online with published work. We freely provide the full database in the URL reported at the end of the paper (i.e., Online supplement).

Varying levels of aggregation of the data could be achieved by using different macro-variables. In one extreme, each original variable could be seen as a unique macro-variable, providing much specificity in terms of variable definition and precision, but lacking a real

synthesis of previous findings. On the other extreme, by aggregating all closely related variables, a broad outline of the literature could be synthesized at the cost of reduced precision in the definition of concepts used. We selected a point towards the more aggregate part of this continuum, but the data provides other researchers with the ability to modify these macro-variables or define new ones, and rapidly generate a picture that is appropriate for their purpose. The only hard rule in creating such alternative macro-variables is that every original variable in the sample of interest should be included as part of one and only one macro-variable. The quality of the resulting synthesis also depends on the conceptual homogeneity of the variables included in each macro-variable. If those variables conceptually differ significantly, the resulting causal map (which would be parallel to Figure 2-3) would potentially be uninformative and confusing.

Another point of flexibility that results from this method concerns the selection of relevant causal links. The discussions so far focus on an overview perspective where all studies identified are included. Some differences exist across different study contexts which may require a more specific set before the aggregation of results. For example, a researcher may be interested in studying only the results from quantitative studies with specific statistical tests. Other researchers may be interested in examining the impact of studies that only include residential, or commercial sector, or some other criteria. The raw data provided in the database tables includes the details required for such alternative inclusion criteria. For example, consider studying the causes of falls and subsequent injuries among residential roofers. Figure 2-4 provides the overview of the literature based on the same macro-variables as before, but this time coding only the studies that are based on the residential roofing construction industry. Here "contractor/managerial level safety intervention" was most frequently reported as a major cause of the risk of falls (Hsiao and Simeonov, 2001; Lipscomb *et al.*, 2003b; Lipscomb *et al.*, 2003d; Shah *et al.*, 2003; Kaskutas *et al.*, 2009a; Kaskutas *et al.*, 2009b; Sa *et al.*, 2009), followed by "workers' safety behaviors and attitudes" (Hsiao and Simeonov, 2001; Lipscomb *et al.*, 2008; Sa *et al.*, 2009; Kaskutas *et al.*, 2009a; Kaskutas *et al.*, 2009b), "construction structures and facilitates" (Hsiao and Simeonov, 2001; Lipscomb *et al.*, 2003d; Kaskutas *et al.*, 2009b; Sa *et al.*, 2009) and "working surfaces and platforms" (Hsiao and Simeonov, 2001; Kaskutas *et al.*, 2009a; Kaskutas *et al.*, 2009b; Sa *et al.*, 2009). This figure is easily generated from the data given the connection between the two tables through the reference number: once a filtering criterion is defined (e.g. only residential sector and only roofers as sample population), the subset of relevant

links can be automatically retrieved and an alternative overview picture can be created using that data.

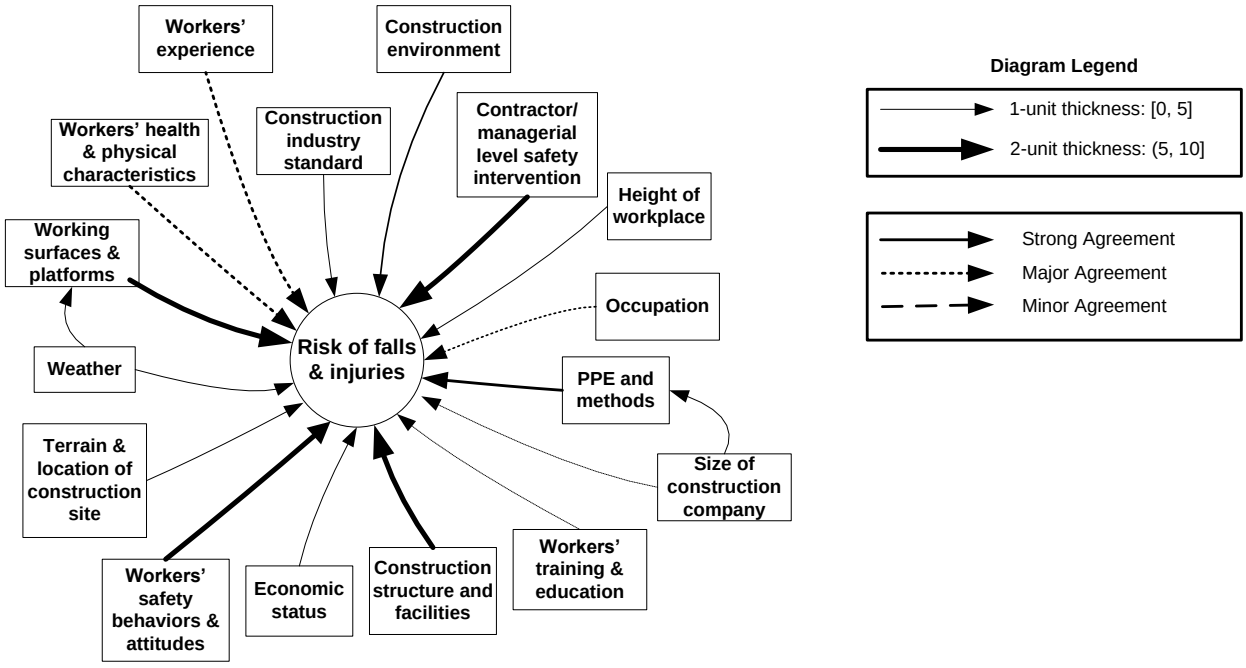

Figure 2-4 Subset-causal relationships of macro-variables for an instance on how to better utilize our coded online data to facilitate interested researchers in certain specific research fields – residential roofing industry

7.0 Discussion and Conclusions

Our analysis makes a number of contributions to understanding the risk of falls in construction. We provided a methodical compilation of the relevant research on the causes of and contributors to construction falls. The results can assist future researchers and practitioners in doing more relevant research and in designing more effective safety interventions that can help to reduce work-related falls. For example, our study points to the gap between qualitative and quantitative research on the causes of falls, where more quantitative studies are needed to assess the ultimate impact of psychological and organizational factors and how they tie into managerial interventions. Better estimation of different pathways is needed for analyzing the cost effectiveness of different managerial and engineering interventions. For instance, both "workers' safety behaviors & attitudes", and "working surfaces & platforms" are significant drivers of falls. Whereas "contractor/managerial level safety intervention" is expected to influence the former,

"PPE & methods" are likely to tackle the second source. Yet the expected reduction in fall or fatality hazard from a dollar of investment in one intervention or another is not clear from the current literature. Both these observations point to fertile areas for future research.

We also proposed a systematic method for aggregating data from multiple types of studies into a coherent causal network, even in the absence of homogeneity needed for formal meta-analysis. This framework is general and can be used in research in other areas of interest. Moreover, the framework provides a flexible architecture, in that it allows researchers to define their own macro-variables (how to partition the original variables into different sets for macro-variables) and compile summaries of the literature at different levels of analysis without much rework. The detailed database is provided openly online (see Online supplement).

A fairly complex picture is found about causes of the "risk of falls and injuries" in this review, in which different types of phenomena (e.g. weather, industry types, psychological factors) and different levels of analysis (e.g. individual, organizational, and geographical, and cultural) interact in determining the fall-related outcomes. While feasibility and research design concerns require researchers to break down this complex picture into smaller chunks that could be empirically assessed, these chunks should later be brought together to provide a holistic picture where one can assess the impact of different interventions, many of which cross different domains or levels of aggregation. One major challenge is in moving across these different levels of aggregation, from focused empirical studies to systematic synthesis of those results. The result indicates few previous attempts at building such holistic maps, and we anticipate this first attempt can lead to more nuanced and refined future work. Indeed, safety policy analysis for a construction firm requires simultaneous examination of different causes of injuries associated with falls as well as other types of injuries in selecting effective safety enhancing actions. We hope this method provides a blueprint that can promote the accumulation and utilization of research findings.

This literature review can inform the development of simulation models to predict fall injuries and inform prevention initiatives. The data gathered from this review could serve as input to a simulation model of incident causation for risks of falls. Such a simulation model will provide feedback to construction stakeholders to aid in the prevention of injuries and for efficient planning of safety initiatives. A holistic systems model can help with the direction for follow-up

research in many fields such as ergonomics (e.g., optimizing the design of safety training and its implementation, creating safe workplaces or systems), biomedicine (e.g., improving fall arresting/protection methods), materials science (e.g., creating new materials of shoes to prevent slipping), and medical science (e.g., to conduct quantitative experiments on influencing the specific factors).

The methods used and the results of our analyses can assist consensus among standards committees. For instance, standards committees often need to understand trends in larger bodies of research to ensure standards revisions are timely in addressing prevention and control practices. We have provided a process that can be replicated at minimal costs and used by individuals and groups who need to examine trends in the knowledge domain. This method and results can impact the effectiveness of policy setting as well. One should be cautious in drawing policy conclusions from this paper however, because the wide range of methods and variables did not allow a quantitative assessment of the magnitude of the impact of different causal factors. Therefore, the fact that one variable or the other is associated with the risk of falls and injuries in many studies does not necessarily mean the impact of that factor is great in magnitude. With this caveat in mind, it is still useful to summarize the major policy levers that are seen to have an impact on reducing the risk of falls and injuries based on this review. These levers include: 1) focusing on proper working platforms/surfaces. Ladders, scaffolds, and working platforms and surfaces should be dry, and stabilized; 2) sufficient and timely safety training along with close supervision and guidance, e.g. through safety consultants, safety checking, focusing on reducing the anxiety and rush to unsafe working speed; 3) a proper fall arresting system and other PPEs can reduce the injuries due to falls significantly; 4) targeting the safety culture in construction companies as well as the safety climate in the whole industry could provide additional leverage; 5) ergonomics of the worksite, from e.g. comfortable temperature, modest humidity, enough but not too much lighting/luminance level, low level of noise, are all expected to help with reducing falls or their impact.

Governments and labor organizations within various countries use data to determine allocations of funds in occupational safety and health. The systematic method applied in this study could be used in a variety of different occupations to produce information about trends in a specific occupational setting. This information, will in turn, help agencies evaluate budget and

impact measures over time. Researchers and funding agencies who set research agendas can employ our systematic method to identify gaps in research in occupational safety and health in terms of specific research topics and gaps in research within and between nations.

Moreover, as means by which information and communication technologies could address onsite safety challenges emerged and are more actively sought; the insight offered by the presented synthesis of causal factors, for example, could spur more innovative design and research explorations. The causal chain depicted in Figure 2-3 illustrates this notion. As "workers' training and education" influences "PPE and methods" with latter implications on "workers' safety behavior and attitudes" and thus "risk of falls and injuries", investigations of the role of smartphones, often ubiquitous onsite, and other mobile technologies (e.g. tablet computers such as the iPad) as delivery platforms in providing in situ, possibly tailored, training are availed. These types of efforts could offer new directions in intervention design in impacting the incidences of falls.

Finally, the database designed can be standardized and used as a repository of current knowledge for other fields of study focusing on different safety risks. It can be made open to the research community for editing through a wiki-like technological platform. This democratization of accumulated knowledge could have a significant effect on the speed and efficiency of research reviews and intervention design implementations.

8.0 Online Supplement

The full coded data are available in online tables from the URL below:

http://spreadsheets.google.com/pub?key=t4oRPwkps6BeqIkyUQhJQrQ&output=html

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Appendix A Complete list of coded papers

We report here the full list of 121 papers that were selected in step 2 and coded during step 3 (refer to Figure 2-1).

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Appendix B Table of macro-variables and their original variable mappings

Macro-variable	Original variable in 'Links' table in the database
Risk of falls and injuries	"falls from heights", "falls", "slips, trips and falls", "falls on the level", "fall from ladder", "slip on footstep of the ladder", "falls to a lower-level", "falls from loading platforms or into shafts", "falls through structures", "falls from scaffolds", "fall and slip injuries", "fatal falls", "falls risk", "falls and trips risk", "slips and falls injuries", "fatality death", "fatal injuries", "non-fatal injuries", "accident in construction industry", "construction injuries", "construction accident", "construction incident", "injury occurrence", "STF (slip, trip and falls) accidents", "male construction worker lost-time-injury elevation falls", "ladder-related injuries", "occupational fatal accidents", "construction falls accident", "falls from extension ladders", "fatal occupational injuries", "falls from roofs", "falls into holes in ground", "falls from moveable platforms".
Working surfaces and platforms	"grass/wet", "slippery underfoot condition", "uneven and damaged paving", "obstacles on the walking surface", "opening/holes", "heavy construction/improper surface", "improper plumbing and heating surface", "improper painting surface", "improper carpentry surface", "improper concrete surface", "floor condition bad", "work area condition - slippery surface", "serve surface condition of working place, such slippery surface and so on", "slippery roof", "slip of ladder base", "good roof surface condition", "good type of surface", "slippery underfoot condition", "place of falls - ladder", "place of falls-scaffolds", "place of falls-bamboo scaffold", "strong cover", "platform", "strength of roof", "connection of platform", "fixation of platform", "steps and stairways".
Workers' safe behaviors and attitudes	"failure to use safety equipment", "safety procedure", "perceived risk", "evaluation of risk", "attention/vigilance", "limiting injury seriousness", "lack of orderliness at the workplace or unsecure climbing devices", "fainting-fit, loss of balance", "stability of balance", "tipping of ladder top", "correct placement and protection of ladder", "stability of user on the scaffolds", "stability of user on the roof", "stability of user

	near a hole in ground", "movement control", "failed to secure and warn", "horseplay", "operated equipment without authority", "operated at unsafe speed", "remove safety device", "took unsafe position or posture", "Safe behavior", "taking risks (taking hazardous short cuts and entering hazardous areas)", "diverted attention", "satisfactory safety level", "construction safety", "condition of vestibular system".
Construction structure and facilities	"the utilization of the design for construction safety concept", "construction structure factors", "shortcomings with equipment", "poor structure", "good construction design and processes", "collapse of scaffolding", "collapse of structure", "quality and availability of equipment", "equipment fails", "good condition of equipment, such as good shape, structural weakness, ladders, scaffolds and vehicles", "ladder structure failure", "strength of ladder", "stability of ladder", "strength of scaffolds", "stability of scaffolds", "anchoring of scaffolds on buildings or structures", "foundation base structure", "scaffold floor condition", "strength of support", "machinery/hoisting", "stability of support machinery", "condition of lift/support/hoisting", "foundation".
Contractor/managerial level safety intervention	"relevance to both researchers and industry practitioners", "management's support, involvement and commitment in safety", "occupational organizations-activity", "originating influences-inadequacies with risk management", "good project management", "good risk management", "adjustment strategies to confront the risk of falling or balance disturbance in occupational situation", "requirements for contractors", "limited choice offered to workers", "PPE availability", "assigning blame", "responsibility of employer demands", "ineffective communication styles", "poor access to resource", "poor compensation/pay", "high demand of pace of work", "not responding to injury", "size of company", "construction trade: general contractor", "accepted hazardous work conditions by management level person", "safety monitors", "availability of safety professions".
Workers' Age	"age: 15-24", "age: 45-54", "age: < 30 years", "age: < 30 years", "younger than 35", "age_35 years and older", "age>30", "age < 30", "age", "age > 45", "age group: <16", "age group: 16-19", "age group: 20-24", "age group: 25-29", "age group: 30-34", "age group: 35-39", "age group: 40-44", "age group: 45-49", "age group: 50-54", "age group: 55-59", "age group: >59", "age: 16-24", "age: 25-34", "age: 35-44", "age: 45-54", "age: 55-64", "age: 65-79".
PPE and methods	"use of passive personal fall protective equipment", "fall prevention equipment/personal", "fall arresting systems", "preventing balance disturbance", "slip resistant shape", "fall protection", "edge protection to the scaffold worker", "personal fall injury protection", "concrete/damaged fall protection", "fall protection not attached", "personal fall arrest systems", "scaffold object protection", "good falling project protection", "hole-edge protection", "edge protection to platform worker", "personal protective methods", "safety nets", "warning line", "guardrails", "slides guard", "personal fall arrest".
Workers' experience	"less than 10 years work experience", "experience", "worker and work-team capabilities factors", "work experience", "inexperience", "experienced worker", "good ability of user to stay on ladder", "user ability to stay on scaffold", "user ability to stay on roof", "user ability", "apprentice carpenters".
Worker's health & physical characteristics	"hearing disorders", "sleep disorder", "current smoker", "no sporting activity", "chronic or acute pathologies", "alcohol (Intrinsic factors)", "drugs (Intrinsic factors)", "physical status (Intrinsic factors)", "weakness (Intrinsic factors)", "fatigue (Intrinsic factors)", "heart rate", "trauma", "fracture", "fractures sustained", "male", "female".
Occupation	"mason", "carpenters", "roofers", "plumber", "electricians", "civil-engineering

	workers", "other employees", "construction trade: carpentry", "construction trade: electrical work", "construction trade: plumbing", "construction trade: masonry", "construction trade: painting", "construction trade: insulating", "construction trade: glazier work", "construction trade: scaffolding", "roofers", "framing workers".
Construction environment	"inadequate lighting", "skylights", "good working environment", "environment-too bright or insufficient lighting", "surrounding activities, such as falling objects, heavy equipment traffic", "work area condition/poor lighting", "objects struck against", "falling load", "bad work situation (such as work surface, time)", "external condition", "source of injury-environment", "environment/ slope sharp", "environment/ non-terrain slippery".
Weather	"temperature (50 F)", "temperature (32 to 50 F)", "temperature (32 F and under)", "ice/snow", "temperature - < 32 F (< 0 C) to > 50 F (> 10 C)", "temperature -> 10 C (50 F)", "temperature -> 0-10 C (32 - 50 F)", "temperature - 0 C (32 F) and under", "weather conditions", "weather bad", "Winter", "summer-hot", "raining/snowing".
Workers' training and education	"job security and education", "language and cultural problem", "job-specific formal safety orientation and training", "safety education and training", "proper preparation and training", "effect of experience and training", "work technology", "employers are aware of fall protection standard".
Size of construction company	"firm size/employees : 0", "firm size/employees : 1-4", "firm size/employees : 5-9", "firm size/employees : 10-19", "firm size/employees : 20-49", "firm size/employees : 50-99", "firm size/employees : 100+", "company size <30", "company size 30-100", "company size >100", "company with less than 10 employees", "site size 10 or more workers", "union workers company", "nonunion workers company"
Workers' morale	"psychological feature (feel comfortable with supervisors who care for their safety)", "self-esteem", "performance pressure", "feeling invulnerable", "good relationship with 'boss'", "being treated fairly", "non-material incentives", "material incentive".
Working time/day	"time of injury-afternoon", "date of accident/ 21 to 25 days of a month", "data of accident-Friday", "time of accident- 14:01-16:00", "afternoon working time".
Construction industry standard	"change in the fall standard for the construction industry", "effectiveness/enforcement of safety fall protection standard", "regulation in construction industries", "poor regulatory and legal issues/ ladder regulations", "poor regulatory and legal issues/ worker protection standard", "poor regulatory and legal issues/ immigration law".
Terrain and location of construction site	"bad condition of the terrain", "face to south", "face to north", "southern hemisphere".
Height of workplace	"heights of fall", "height", "height of fall-below 15 m of height", "elevation", "height of falling", "less than 6 feet", "7 to 10 feet", "11 to 20 feet", "21 to 25 feet".
Construction materials	"construction material", "poison materials", "dangerous construction materials".
Economic status	"economic influences", "economic feature".

CHAPTER 3 Review of Quantitative Studies of Interventions for Responding to Infectious Disease Outbreaks

Abstract

We reviewed the modeling and retrospective literature on responding to outbreaks of infectious diseases in humans and animals. Unlike routine immunization and control efforts, outbreak response activities require rapid reactive actions to address an urgent or emergent situation. We focused our review on characterizing the types of diseases analyzed, the interventions used, and the models employed. Out of the 211 studies identified, we find that the majority focus on a few diseases (influenza, foot and mouth disease, smallpox, measles, and hepatitis). We identified 34 distinct interventions explored in these studies that fall under the general categories of vaccination, prophylaxis, quarantine/isolation, contact restriction, exposure reduction, killing/slaughtering, and surveillance. A large number of studies (141) use simulation/analytical models to analyze outbreak response strategies. We identify key factors contributing to the effectiveness of different interventions that target high-risk individuals, trace infected contacts, or use a ring to delineate geographical boundaries for an intervention.

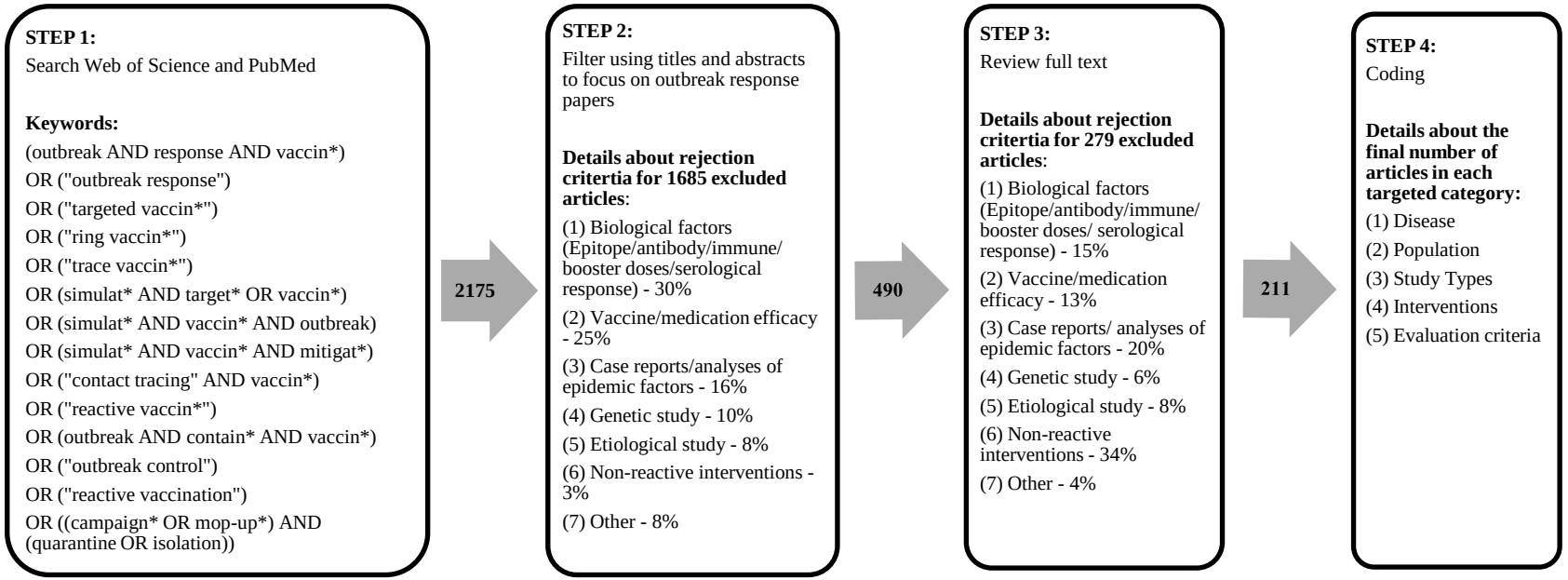
Keywords: Outbreak response; Dynamic disease models; Targeted intervention; Contact tracing; Vaccination

1.0 Introduction

Effective planning to respond to actual or potential outbreaks of infectious diseases requires a detailed understanding of the infectious disease, specific population, health system, and the available options, which analysts often synthesize in the context of quantitative assessments [1-211]. In contrast to ongoing surveillance and routine measures (e.g., immunization) used to prevent regularly occurring infectious diseases (i.e., disease control), outbreak response efforts typically require rapid mobilization of resources in response to an urgent or emergent situation in which the potential exists for widespread transmission of the disease. Thus, although outbreak response efforts tend to use the same tools as those used for control (e.g., vaccines, if available), outbreak response interventions tend to target specific populations. Several reviews provide a perspective on interventions targeting specific diseases [e.g., 212, 213], the role of contact network structure in disease evolution [e.g., 214, 215], targeted vaccination coverage (e.g., [216]), and use of social network analysis in epidemiology [e.g., 217]. However, no existing review of the outbreak response literature provides insights about the different types of interventions and their appropriateness for different types of outbreaks. This paper seeks to fill the void.

2.0 Methods

Figure 3-1 Flowchart of literature search and selection process

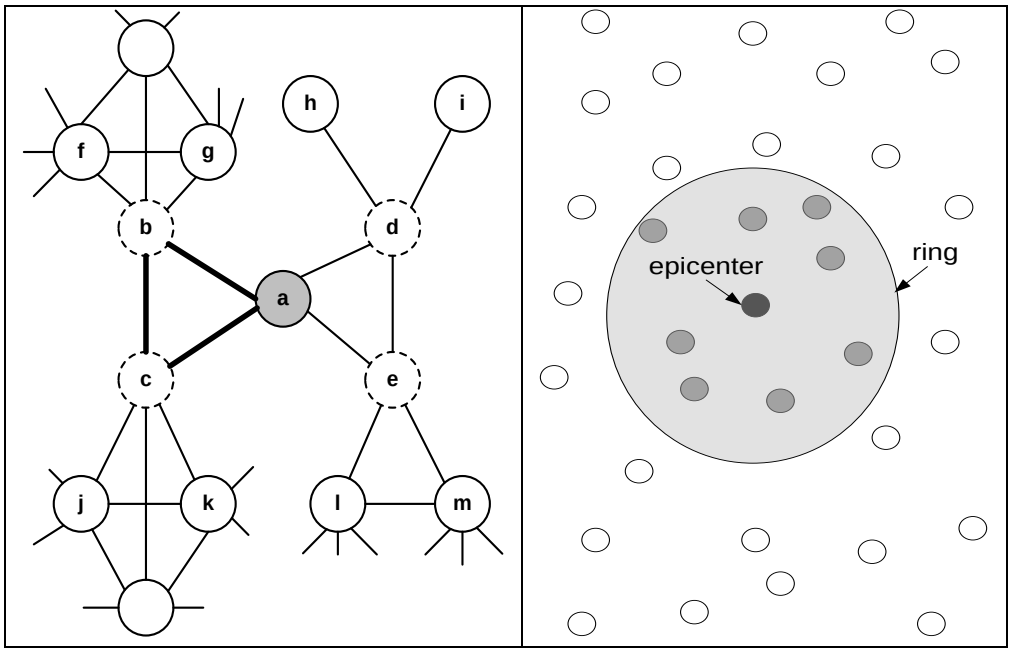


We conducted a comprehensive search of the literature to identify all quantitative outbreak response studies that analyzed alternative interventions based on empirical data from retrospective analysis or derived results for potential or actual outbreaks using analytical or simulation models. Figure 3-1 provides the specific terms we used to search PubMed and the Web of Science databases for studies published in English between January 1, 1980 and January 1, 2011. We reviewed all of the abstracts of 2,175 studies and the full text of 490 studies to determine relevance for our review. We excluded studies that focused on biological factors (e.g. epitope/antibody/immune/serological response), vaccine/medication efficacy, case reports/ analyses of epidemic factors, genetics, etiology, non-reactive interventions (i.e., those actions taken in the absence of a signal of an outbreak, including disease control efforts undertaken to address a gap in population immunity in the absence of an outbreak), and other biomedical/biological studies. After this screening process, we reviewed and coded 211 studies. We determined the disease(s), population(s), and outbreak response study type. The main study types included empirical retrospective quantitative analysis of an actual outbreak response that occurred, and modeling studies. For the modeling studies, we identified the specific modeling methods used and categorized them according to their level of aggregation (i.e., individual humans or animals vs. groups of humans or animals) and network/mixing assumptions (i.e., homogeneous mixing vs. heterogeneous mixing), which led to 4 categories: individuals homogeneously mixing (e.g., micro-simulation models and Markov models with explicit individuals but random mixing), individuals heterogeneously mixing (e.g., typical agent-based or individual-based (IB) models of individuals with explicit contact networks), groups homogeneously mixing (e.g. differential equation based (DEB) models, including Susceptible-Infected-Removed (SIR) models and variations), and groups heterogeneously mixing (e.g., model variables aggregated at the level of animal farms with explicit contact network among those farms). We captured descriptions of the models based on the information reported in the paper with respect to major structural types, but we categorized the types of models into the four categories above, which helped us to better compare and contrast the various model types.

Table 3-1 Definitions and categorization of specific interventions coded

Intervention category Specific intervention	Abbreviation	Definition	Targeting	Number of occurrences
Vaccination (V)				
Mass	VM	Target the entire population		47
Fractional mass	VF(XX%)	Target a specified percentage (XX%) of the total population		14
Susceptible	VS	Target all susceptible members of the population	TRisk	4
Health care worker	VW	Target health care workers (HCWs)	TRisk	17
High-risk people (non HCW)	VC	Target people with a specific risk factor (non HCWs)	TRisk	63
High-risk farms/animals	VA	Target high-risk farms or animals on farm	TRisk	8
Pregnant women	VP	Target pregnant women	TRisk	2
Traveler	VI	Target individuals traveling internationally to and/or from endemic areas	TRisk	1
Household	VH	Target members of households of infected individuals	TTrace	2
Institution	VK	Target members of a specific workplace (including schools, restaurants)	TRisk	7
Ring	VR	Target people based on their distance from the epicenter of an outbreak	TRing	44
Trace (non Household)	VT	Target individuals who (potentially) contacted an identified (index) case	TTrace	36
Random/acquaintance	VN	Target random neighbors of random nodes based on local network information	TTrace	6
Prophylaxis (non-vaccine) (e.g., antibiotics, rehydration therapy) (P)				
General medical	PM	Given in the absence of symptoms to the general public		32
Household medical	PH	Given in the absence of symptoms to specific household(s)	TTrace	7
Health care worker	PW	Given in the absence of symptoms to health care workers	TRisk	4
Quarantine/isolation (Q)				
Mass	QM	Target the entire population		37
Household	QH	Target household members of infected individuals	TTrace	3
Institutional	QK	Target co-workers of infected individuals	TRisk	4
Farm	QF	Target high-risk farms based on animal composition and/or characteristics	TRisk	7
Traveler/boarder	QT	Target travelers	TRisk	1
High-risk	QR	Target high-risk people with a specific risk factor (non HCW)	TRisk	6
Single case	QS	Target single case/cases		23
Contact restriction/limit contacts (C)				
School closure	CS	School closure	TRisk	14
Institution closure	CK	Workplace closure	TRisk	5
Farm closure	CF	Farm closure	TRisk	2
Self/cautious	CC	Individual actions to isolate themselves (behavioral changes)		2
Travel restriction	CT	Travel restrictions	TRisk	24
Exposure reduction measures (E)				
Personal protective equipment	EP	Wearing personal protective equipment (e.g., face masks, gloves)		7
Hygiene (vigilance, caution)	EH	Frequently washing hands, attention to personal and institutional hygiene		11
Killing/culling/slaughtering animals (K)				
Culling/slaughtering	KL	Slaughtering/culling animals	TTrace	44
Surveillance, data gathering, and reporting of cases (S)				
Mass surveillance	SM	Monitor outbreak/progression in a mass population		8
Clinic examination	SE	Serology testing of animals (biosecurity)		13
Contact tracing	ST	Tracing the contacts of infected cases	TTrace	43
No intervention	NO	Do nothing (i.e., no intervention)		63

Figure 3-2 Distinction between trace and ring vaccination: (a) Trace vaccination targets the first layer of contacts (individuals b-e) of the index case (individual a), and potentially the secondary contacts (individuals f-m) and (b) Ring vaccination targets all individuals within some radius (darker dots) of the index case (black dot).



We identified and defined the specific interventions used in these studies as shown in Table 3-1, which categorizes the interventions as: vaccination (V), prophylaxis (P), quarantine/isolation (Q), contact restriction (C), exposure reduction (E), surveillance (S), and animal killing/culling/slaughtering (K). As shown in Table 3-1, we denote the specific interventions using two letters, for which the first letter indicates the category. We noted explicit inclusion of a "do nothing" option (i.e., no intervention) as NO, and implicit inclusion of a do nothing option as NO*. We further classified the specific interventions according to the type of targeting that they imply. Targeted interventions that focus on a sub-population based on some risk factor (TRisk) independent of contact with an exposed individual include: vaccination of susceptible individuals (VS), health care workers (VW), high-risk groups (VC), high risk animals/farms (VA), pregnant woman (VP), and institutions (VK); and non-vaccine prophylaxis of health care workers (PW); quarantine/isolation of institutions (QK), farms (QF) and high-risk groups (QR); as well as contact restriction in schools (CS), institutions (CK), among travelers (CT) and farms (CF). Targeted interventions that rely on tracing the network of individuals

(depicted in Figure 3-2a) (TTrace) include: vaccination of households (VH), traced contacts (VT), travelers (VI), and random contacts (VN); non-vaccine prophylaxis of households (PH); quarantine/isolation of households (QH), travelers (QT), and single cases (QS); killing of infected animals (KL); and tracing the contact of infected cases (ST). Finally, targeted interventions that rely on geographical boundaries around selected, identified cases to guide the intervention (TRing) (Figure 3-2b) include vaccination of geographical rings around an epicenter (VR).

We recognized the opportunity to combine and/or use multiple interventions, and we noted that most studies include evaluation of the effectiveness of the interventions. Consequently, we coded the complete set of interventions evaluated in each study and we noted the evaluation criteria used by each study related to any comparisons among interventions: No comparisons (NOC), effectiveness of intervention(s) compared to doing nothing (EFC), effectiveness of interventions compared to each other (ECC), and cost-effectiveness of interventions evaluated (CEC). For example, the study by Bates et al. [19] of foot-and-mouth disease (FMD) examines culling/slaughtering (KL) and ring vaccination (VR) interventions separately, and also tests another intervention that combines killing (KL), clinical examination (SE) and travel restriction (CT) (i.e., KL+SE+CT). The study compares these three interventions according to their effectiveness with respect to limiting the size and duration of the outbreak (ECC), but it does not consider cost-effectiveness. We carefully applied our definitions consistently across different studies, and consequently some of the terms we used may differ from those used in the original papers (e.g., we coded trace vaccination for some studies that referred to the activity as “targeted vaccination”).

3.0 Results

Table 3-2 Breakdown of quantitative outbreak response assessments for different diseases with reference numbers in each category

Disease	Subjects	Empirical retrospective	Homogenously mixing groups	Heterogeneously mixing groups	Homogeneously mixing individuals	Heterogeneously mixing individuals
Bovine brucellosis	Animals	[1]				
Bovine herpes virus type I (BHVI)	Animals					[2]
Chickenpox	Human	[3, 4]				
Cholera	Human	[5]				
Classical swine fever (CSF)	Animals		[6, 7]			[8]
Foot-and-mouth disease (FMD)	Animals	[9-16]	[17-22]	[23-35]	[36]	[21, 37-42]
Hepatitis A	Human	[43-50]	[51]		[52]	[53, 54]
Hepatitis B	Human		[55-57]			[58]
HIV	Human		[57, 59]			
Influenza-avian	Animals		[60]	[61, 62]		
Influenza-general	Human	[63-67]	[59, 68-73]		[74]	[41, 75-81]
Influenza-H1N1	Human	[82-86]	[87-92]			[93-95]
Influenza-H5N1	Human or animals		[96, 97]			[98-100]
Influenza-pandemic	Human					[101-103]
Influenza-seasonal	Human		[104, 105]			
Measles	Human	[106-122]	[123-125]			[126, 127]
Meningococcal	Human	[128-133]	[134]			
Mumps	Human	[135]				
Pertussis	Human	[136-139]	[140]			[141]
Pneumonic Plague	Human				[142]	
Polio	Human	[143-145]	[146]			
Rabies	Animals			[147]		[148, 149]
SARS	Human	[150, 151]	[59, 152-159]			[41, 160-162]
Smallpox	Human		[59, 155, 163-169]			[170-182]
Staphylococcus aureus	Human		[183]			
Teschovirus encephalomyelitis	Animals	[184]				
Tuberculosis	Human	[185]				
Varicella	Human	[186, 187]				
Yellow fever	Human	[188, 189]				

We identified 141 studies (66.8%) that modeled outbreak responses prospectively using quantitative methods, and 70 studies (33.2%) that provided empirical retrospective assessments. Table 3-2 shows the breakdown of the 211 studies that we coded by disease and type of study. We found that several diseases accounted for the bulk of the quantitative assessments of outbreak response, with 48 on different types of influenza, 35 on foot-and-mouth disease (FMD), 23 on smallpox, 22 on measles, 15 on SARS, and 12 on hepatitis A. We also found fewer than 10 studies of the following diseases: meningococcal disease (7), pertussis (6), hepatitis B (4), polio (4), classic swine fever (CSF) (3), rabies (3), chickenpox (2), HIV (2), tuberculosis (2), varicella (2), yellow fever (2), pneumonic plague (1), cholera (1), bovine brucellosis (1), bovine herpes virus I (1), staphylococcus aureus (1), and teschovirus encephalomyelitis (1). The studies we reviewed used a wide range of modeling approaches with disease characteristics significantly impacting the methods used. For example, many of the FMD studies modeled groups of animals on farms heterogeneously mixing (assuming homogeneous mixing within farms), because infections spread rapidly within a farm and studying ring vaccination strategies requires separately modeling individual farms and their geographical contact network.

Table 3-3 Characterization of disease, population, model, intervention types, and evaluation criteria for disease-specific studies

Disease (Ref)	Population studied †	Model Description	Intervention	Evaluation criteria
Bovine brucellosis ([1])	Animals (Spain)	Empirical retrospective	VA+KL VA+KL+QT VS EH	ECC
Bovine herpes virus type I (BHV1) ([2])	Animals (The Netherlands)	IB (named Inter IBR programmed in Borland C++) (geographic location of individual farms, n=25,000 farms)	CT+EH KL CT+EH+VC	CEC
Chickenpox ([3])	Human (US)	Empirical retrospective	VW PM+QR	NOC
Chickenpox ([4])	Human (Prisoners, Switzerland)	Empirical retrospective	ST VS QK	NOC
Cholera([5])	Human (India)	Empirical retrospective	QS QM EH	NOC
Classical swine fever ([6])	Wild boar and domestic pig herds (Denmark)	Stochastic disease-event model with Monte Carlo simulation model (software program InterSpread Plus version) (spatial distribution structure, n=12,275)	KL KL+ST KL+ST+VR	ECC
Classical swine fever (CSF) ([7])	Wild boar and domestic pig herds (Denmark)	Stochastic disease-event model with Monte Carlo simulation model (software program InterSpread Plus version) (spatial distribution structure, n=12,275)	KL(500m radius)+SE+CT KL(500m radius)+SE+CT+TC TC+QM+CT KL(1km radius) VR+KL	CEC
Classical swine fever ([8])	Cattle (The Netherlands)	IB	KL+ST+CT KL (1km radius) VR (1, 2, 5 km)	ECC
FMD ([9])	Pig (Malaysia)	Empirical retrospective	VM CT	NOC

FMD ([10])	Animals (most European countries)	Empirical retrospective	KL VR+KL	ECC
FMD ([11])	Animals (Republic of Krorea)	Empirical retrospective	CT+KL+VR NO*	EFC
FMD ([12])	Animals (The Netherlands)	Empirical retrospective	SE+VR+KL NO*	EFC
FMD ([13])	Cattle (Fresno, Kings and Tulare counties of California)	Empirical retrospective	SE+CT SE+VR+KL SE+KL	CEC
FMD ([14])	Animals (Botswana and Zimbabwe)	Empirical retrospective	SE+QM+VR+CT SE+SM+VR+KL SE+VR+QF+VM SE+SM+KL	ECC
FMD ([15])	Animals (UK)	Empirical retrospective	KL NO*	EFC
FMD ([16])	Animals (UK)	Empirical retrospective	KL VR VR+KL	ECC
FMD ([17])	Cattle (Saudi Arabia)	DEB	ST+QF ST+KL VR	ECC
FMD ([18])	Cattle (Fresno, Kings and Tulare counties of California)	Monte Carlo simulation model (spatial distribution structure, n=2,238 herds and 5 sale yards)	VR VA KL	ECC
FMD ([19])	Cattle (Fresno, Kings and Tulare counties of California)	Monte Carlo simulation model (spatial distribution structure, n=2,238 herds representing beef, dairy, swine, goats and sheep and 5 sale yards in CA, US)	KL+CT+SE VR KL	ECC
FMD ([20])	Animals (UK)	Using the modeling parameter: first-fortnight incidence predict both the prevalence and duration of FMD	VM VA KL	ECC
FMD ([21])	Wild pig	IB and DEB (comparison). A review paper	KL	NOC
FMD ([22])	Animals (UK)	DEB	CT KL VR	ECC
FMD ([23])	Animals (UK)	Spatial simulation model (geospatial distribution of farms, n=6,000 farms)	KL VR KL+VR	ECC
FMD ([24])	Animals (UK)	Farms located on a hexagonal lattice	KL ST+KL VR+KL	ECC
FMD ([25])	Animals (US)	IB (different geographic areas considered: (1) a county in the south-central US (2) a county in the north-central US; and (3) a county in the western US.	VT+KL VR KL CT VR+CT	CEC
FMD([26])	Animals (UK)	Mathematical models were used to guide the UK foot-and-mouth disease (FMD) control policy during the 2001 epidemic	KL VR	ECC
FMD ([27])	Animals (Australia)	Spatial model (Monte Carlo method) called AusSpread (geographic information for spatial network, n sufficient to accommodate 7 default farm 'types')	VT+KL VR VA QF+CT	CEC
FMD ([28])	Animals (French farms)	IB (stochastic farm-based model) (geospatial distribution of farms, n=280,000 French farms)	KL VR	ECC
FMD ([29])	Animals (Republic of Korea)	IB (stochastic and spatial simulation) (spatial distribution of the farms, n=3,731 farms)	SE+KL+CT SE+KL+VR	ECC
FMD ([30])	Animals (Central Valley, CA)	Dynamic optimization model (n=1.8 million)	KL+CT KL+VA+CT	CEC

FMD([31])	Animals (UK)	Model (heterogeneously mixing groups) to simulate the reactive vaccination and culling strategies	VR KL	ECC
FMD ([32])	Animals (UK)	IB (stochastic spatial FMD model) (n=100,000)	KL (different regions/radius)	ECC
FMD ([33])	Animals (US)	Two-component stochastic framework (epidemiologic model and economic modules)	VR VA	CEC
FMD ([34])	Animals (Central Valley, CA)	Dynamic optimization model (n=1.8 million)	KL CT VR+KL	CEC
FMD ([35])	Animals (UK)	IB (n=1,000 farms in a 50* 50 km area)	KL VR QF	ECC
FMD ([36])	Cattle and pig herds (The Netherlands)	Markov Chain model (n=1,000 farms)	KL KL+VR ST+KL	CEC
FMD ([37])	Animals (Australia)	IB	KL ST+KL KL+VR(early) KL+VR(late)	CEC
FMD ([38])	Animals (Hannover, Germany)	Particle (spatial) model (a fix, finite but larger contact N*N square lattice graph)	VM VR+KL+CF NO	ECC
FMD ([39])	Cattle and sheep	IB (small world , n=10,000)	KL+VR NO*	EFC
FMD ([40])	Animals (UK)	IB (n=100,000)	VM VR VA VM+KL	ECC ()
FMD ([41])	Human or animals	Mathematical model (branching process, means that epidemic can be regarded as a growing tree) (contact tree)	ST+QM NO*	EFC
FMD ([42])	Animals (UK)	IB (n=100,000)	VR VR+KL	ECC
FMD ([21])	Wild pig	Review paper comparing IB and DEB	KL	NOC
Hepatitis A([43])	Human (Sydney)	Empirical retrospective	VC(homosexual men)	NOC
Hepatitis A ([44])	Human (Sioux City, Iowa)	Empirical retrospective	VT VC	ECC
Hepatitis A ([45])	Human (Atlanta, GA)	Empirical retrospective	VC	NOC
Hepatitis A ([46])	Human (Hamburg, Germany)	Empirical retrospective	VC NO*	EFC
Hepatitis A ([47])	Human (central Italy)	Empirical retrospective	VT NO*	EFC
Hepatitis A ([48])	Human (Boston, MA)	Empirical retrospective	VC	NOC
Hepatitis A ([49])	Human (London, UK)	Empirical retrospective	VT NO*	EFC
Hepatitis A ([50])	Human (Korea)	Empirical retrospective	VC VT	ECC
Hepatitis A ([51])	Human (US)	Using Monte Carlo simulation models to study the economics of vaccinating restaurant workers against hepatitis A	VK	CEC
Hepatitis A ([52])	Human (Israel)	Markov Model (MS Excel 97 package) (n=65,000)	VM VW	CEC (cost-utility)
Hepatitis A ([53])	Human (Canada)	Dynamic (age structured SEIRV model) and economic model	VC (different age groups)	CEC (cost utility)
Hepatitis A ([54])	Human (Italy)	Individual based model with dynamic social contact network (census data on population, household size and type, demographic school and industry)	VC QS QK QS+QK EH	ECC
Hepatitis B ([55])	Human (UK)	DEB of sexual and perinatal transmission of HBV to compare the effectiveness among heterosexual and	VC (infant)+VF (90%) VC (patient in clinic)+VF (90%)	CEC

		homosexual populations of programs of mass infant vaccination and targeted immunization of genitourinary medicine (GU) clinic attendees.		
Hepatitis B ([56])	Human (The Netherlands)	DEB (n=156,420)	VC (different high-risk groups including MSM, children of immigrants, highly active heterosexuals, infants, adolescents,)	ECC
Hepatitis B ([57])	Human (US, Asian & Pacific Islanders)	DEB (n=12 million)	ST+PM	CEC
Hepatitis B ([58])	Human (US)	IB	VC (MSM, patients with STD, prisoner)	ECC
HIV ([59])	Human	DEB	ST+QM NO*	EFC
HIV ([57])	Human	DEB (n=12 million)	ST+PM	CEC
Influenza-Avian ([60])	Cattle (The Netherlands)	DEB (n=4447 farms)	KL CT SE VR	ECC
Influenza-Avian ([61])	Animals (small poultry farm sector)	A conceptual model (incorporate SIR model) for the analysis of avian influenza mitigation options with cost-effectiveness analysis	CF (contact rates of asymptomatic and symptomatic flocks)	CEC
Influenza-Avian ([62])	Poultry (Korea)	Constructed a spatio-temporal multi-agent model of chickens and ducks in poultry farms in South Korea (76 (37.5 km ×37.5 km) unit squares)	QF KL	ECC
Influenza-general ([63])	Human (Hong Kong, China)	Empirical retrospective	NO VM VC(elderly, children and working age people)	CEC
Influenza-general([64])	Human (Michigan, U.S.)	Empirical retrospective study in a well-vaccinated nursing home populations	PM	NOC
Influenza-general ([65])	Human (US)	Empirical retrospective	PW QS+EP PM	ECC
Influenza-general ([66])	Human	Empirical retrospective	VM NO*	EFC
influenza-general ([67])	Human (Sydney, Australia)	Empirical retrospective	VC NO*	EFC
Influenza-general ([59])	Human	DEB	ST+QM NO*	EFC
Influenza-general ([68])	Human (France)	Monte Carlo simulation model (n=59.6 million)	VW+PW	CEC
Influenza-general ([69])	Human	DEB (n=20 million)	ST+PM NO*	EFC
Influenza-general ([70])	Human (San Antonio, Texas)	DEB	NO QM QM+PM QM+PM+VT	ECC
Influenza-general ([71])	Human (US)	Stochastic decision analytic computer simulation model constructed to simulate the decision of maternal immunization for an influenza epidemic and/or pandemic	NO VP	CEC
Influenza-general ([72])	Human	Age structured DEB (SEIRS model)	VC	NOC
Influenza-general ([73])	Human (Australia)	DEB (n=300,000)	VM ST+PM VW	ECC
Influenza-general ([74])	Human	IB (n=up to 1 million)	VC PM QM	CEC
Influenza-general ([75])	Human	IB ("small-world-like" network, n=10,000)	VM CS+CK ST+PM PH	ECC
Influenza-general ([76])	Human (UK and US)	IB (n=58.1 million)	CT CS QS+QH PM PM(50%)+PH+CS	ECC
Influenza-general ([41])	Human or animals	Mathematical model (branching process, means that epidemic can be regarded as a growing tree) (contact tree)	ST+QM NO*	EFC

Influenza-general ([77])	Human (US)	IB (mixing site type social contact network, n=10,000)	CS QM QH PH ST+PH	ECC
Influenza-general ([78])	Human (Italy)	IB (mixing site type network with households, schools and workplaces, n=57 million)	CT+VI VT PH CT QM	ECC
Influenza-general ([79])	Human (Allegheny County, PA)	IB (mixing site type network, n=1,242,755)	QS CS	ECC
Influenza-general ([80])	Human (Iowa, US)	Agent-based simulation for social network analysis	VW	ECC
Influenza-general ([81])	Human (Seattle and Miami, US)	Individual based network model with age structure (n=2095627 for Miami and = 3,211,727 for Seattle).	VC	ECC
Influenza-H1N1([82])	Human (Israel)	Empirical retrospective (an outbreak on a military base)	VK NO*	EFC
Influenza-H1N1 ([83])	Human (Queensland, Australia)	Empirical retrospective	VM ST+PM QM CS	ECC
Influenza-H1N1 ([84])	Human (Singapore military camps)	Empirical retrospective	PM QM	ECC
Influenza-H1N1 ([85])	Human (Mexico)	Empirical retrospective	VT VC	ECC
Influenza-H1N1 ([86])	Human (UK)	Empirical retrospective	EH NO*	EFC
Influenza-H1N1 ([87])	Human (US)	DEB	VM VF	CEC
Influenza-pandemic ([88])	Human (UK)	DEB (SEIR) (n=51.4 million (8.6 million of high risk group, 0.5 million of pregnant woman and 42.3 million non-risk people))	VC NO*	EFC
Influenza-H1N1 ([89])	Human (Taiwan)	DEB	VC NO*	EFC
Influenza-H1N1 ([90])	Human (Canada)	DEB (n=13,000,000)	VM NO*	EFC
Influenza-H1N1 ([91])	Human (Hong Kong)	DEB on evaluating two-group population (a mask wearing group and a non-mask wearing group)	EP NO*	EFC
Influenza-H1N1 ([92])	Human (Canada)	DEB (n=100,000)	VC NO*	EFC
Influenza-H1N1 ([93])	Human (Mexico)	Quantified the networks of 52 major cities, and using a stochastic SEIR model	VM VF(30%) VF(50%)	ECC
Influenza-H1N1 ([94])	Human (Ontario , Canada)	IB (mixing site type, n=10,391)	NO VC(30%) VC(60%) VF(30%) VF(60%) PM CS	ECC
Influenza-H1N1 ([95])	Human (Washington, DC)	IB (mixing site type network, n=7,414,562)	VP+VC+VW NO*	EFC
Influenza-H5N1 ([96])	Human or animals	Stochastic simulation of network model on simple classical deterministic compartmental models (n=K)	VM PM	ECC
Influenza-H5N1 ([97])	Animals (birds in India)	DEB model to understand the spread of the virus among birds and the effect of control measures on the dynamics of its spread	NO KL	ECC
Influenza-H5N1 ([98])	Human (Thailand)	IB (geo-graph distribution representing the contact connectivity of a typical rural SE Asian population, the close contact groups consist of household, schools and workplace and etc, n=500,000)	VT+PM VC VT+QR	ECC

Influenza-H5N1 ([99])	Human (US)	IB (n=281 million)	NO PH VM CS CT PH+CS+CT CT+QM VC+QM+CT+CS	ECC
Influenza-H5N1 ([100])	Animals (The Netherlands)	Spatial farm-based model (geospatial distribution of farms, n=185 farms)	KL NO*	EFC
Influenza-pandemic ([101])	Human (US)	IB (mixing site type of network with household, school, etc, n=2,000)	ST+PM NO*	EFC
Influenza-pandemic ([102])	Human (US)	Network model (mixing site type social contact network (within each group, some are fully connected, ring network or random network), n=10,000)	CS NO*	EFC
Influenza-pandemic ([103])	Human (US)	Using a stochastic agent-based model to simulate pandemic influenza in the community.	NO PH PM VF(70%) CS PH+CS PM+CS VF(70%)+CS	CEC
Influenza-seasonal ([104])	Human (US, Australia, and France)	DEB (SEIR) (n=NA (defined by N(t)=S(t)+E(t)+I(t)+P(t)))	VC	NOC
Influenza-seasonal ([105])	Human (Minnesota, US)	DEB	VF(0%) VF(20%) VF(40%) VF(60%)	ECC
Measles ([106])	Human (west island of Montreal)	Empirical retrospective	VC NO*	EFC
Measles ([107])	Human (North Wales)	Empirical retrospective	VT NO*	EFC
Measles([108])	Human (Zimbabwe)	Empirical retrospective	VM NO*	EFC
Measles ([109])	Human (Quebec, Canada)	Empirical retrospective	VC NO*	EFC
Measles ([110])	Human (Santa Cruz, Bolivia)	Empirical retrospective	VC NO*	EFC
Measles([111])	Human (Micronesia)	Empirical retrospective	VM	NOC
Measles ([112])	Human (Juneau, Alaska)	Empirical retrospective	NO VC VM	ECC
Measles ([113])	Human (Sydney, Australia)	Empirical retrospective	VC NO*	EFC
Measles ([114])	Human (Singapore)	Empirical retrospective	VC NO*	EFC
Measles ([115])	Human (Clark County, Washington)	Empirical retrospective	VW NO*	EFC
Measles ([116])	Human (Israel, military)	Empirical retrospective	VK NO*	EFC
Measles ([117])	Human (Sirnak Province, Turkey)	Empirical retrospective	VC SE	NOC
Measles([118])	Human (Niger and DRC)	Using previous surveillance data on reported measles cases from Kinshasa and Niamey to conduct the analysis	VM VR	ECC
Measles ([119])	Human (Duisburg city, Germany)	Empirical retrospective	VM NO*	EFC
Measles ([120])	Human (Qassim, Saudi Arabia)	Empirical retrospective	VM NO*	EFC
Measles ([121])	Human (Australia)	Empirical retrospective	ST+QM VC	ECC

Measles ([122])	Human(US)	Empirical retrospective	VT VC	NOC
Measles([123])	Human (Montana, US)	Cost-effectiveness analysis among six different response strategies using a mathematical model	VC (15months and older) VC(12-15months) VC(6months) VC(revaccinate 12-14months) VK VC(15-28months)	CEC
Measles ([124])	Human (Canada)	Empirical retrospective	VC NO*	EFC
Measles ([125])	Human (Niamey, Niger)	DEB (n=800,000)	VC NO*	EFC
Measles ([126])	Human	Using a stochastic model to test the heterogeneous transmission of communicable disease (n=1000)	CS CK VM VN VT	ECC
Measles ([127])	Human (Niamey, Niger)	IB (n=346,254 (45% of 769,454))	VC NO*	EFC
Meningococcal Disease ([128])	Human (the Czech Republic)	Empirical retrospective	VM VC	ECC
Meningococcal Disease ([129])	Human (Czech Republic)	Empirical retrospective	VC	NOC
Meningococcal Disease ([130])	Human (north Nottinghamshire, UK)	Empirical retrospective	VC	CEC
Meningococcal Disease([131])	Human	Report the retrospective cases and compare the effectiveness of different response intervention	VM VC PM	ECC
Meningococcal Disease ([132])	Human (Allgaeu, Germany)	Empirical retrospective	VT VC	ECC
Meningococcal Disease ([133])	Human (Brooklyn, NYC)	Empirical retrospective	VT VC	ECC
Meningococcal Disease ([134])	Human (Ghana)	Using a mathematical model and historical data from an outbreak of meningococcal disease in northern Ghana in 1997 to conduct the comparison between the routine fraction vaccination and fraction vaccination after the onset of the epidemic.	VF (85%) VF (72)	ECC
Mumps([135])	Human (US)	Empirical retrospective	QS PW PM	NOC
Pertussis([136])	Human (US)	Empirical retrospective	QS PW PM SM	ECC
Pertussis ([137])	Human (King County, Washington)	Empirical retrospective	ST+QM VW	CEC
Pertussis ([138])	Human (UK)	Empirical retrospective	VW+VC	NOC
Pertussis ([139])	Human (UK)	Empirical retrospective	VW NO*	EFC
Pertussis ([140])	Human (US)	DEB (n=100,000)	VT VC	ECC
Pertussis ([141])	Human (Toronto, Canada)	IB (n=1,000)	VW NO*	EFC
Pneumonic plague([142])	Human (France)	A mathematical compartment model was used to describe the geo and temporal spread of pneumonic plague epidemic in Paris, France	ST+PM PM CK EP	ECC
Polio([143])	Human (Albania)	Empirical retrospective	VC(aged 19-25 years)	NOC
Polio ([144])	Human (The Sultanate of Oman)	Empirical retrospective	VC QR	NOC
Polio ([145])	Human (China)	Empirical retrospective	VM VC	NOC
Polio ([146])	Human	Using an existing DEB to evaluate the impact of different aspects of immunization campaigns in response to polio outbreaks occurring in previously polio-free areas	VC VF(25%) VF(50%) VF(75%)	CEC

Rabies ([147])	Fox (Central Europe)	Individual based spatial explicit model for fox groups	VM VR (on the ring and solid area within the circle)	ECC
Rabies ([148])	Fox (UK)	IB model to evaluate efficacy of culling, oral vaccination, and oral vaccination and fertility control	KL VR	ECC
Rabies ([149])	African wild dogs	IB	VM NO*	EFC
SARS ([150])	Human (Global)	Empirical retrospective	ST+PM QR ST+QM CT	ECC
SARS([151])	Human (Singapore)	Empirical retrospective	SM+QS+ST ST SM EP	NOC
SARS ([59])	Human	DEB	ST+QM NO*	EFC
SARS ([152])	Human	DEB	VM QM VC	ECC
SARS([153])	Human (China)	A compartment model that mimics the SARS control strategies implemented by the Chinese government after the middle of April 2003:	QM QM(with time delay)	ECC
SARS ([154])	Human	DEB (n=100)	ST+QM CT	ECC
SARS ([155])	Human	DEB	ST+QM VW	NOC
SARS ([156])	Human	DEB (n=1000)	VM QS+EP	ECC
SARS ([157])	Human	DEB	VH PH	ECC
SARS([158])	Human (Singapore)	Using an differential equation model to evaluate the optimal control strategies for emerging infectious disease using SARS' parameters	QS PM EP	ECC
SARS ([159])	Human	A deterministic quarantine/isolation model with time delay	QS QR	NOC
SARS ([160])	Human	Mathematical model of the heterogeneous patterns of interpersonal contacts (mixing site type network (households, schools, workplaces, hospitals and other public venues), n=5,154)	VT QM	ECC
SARS([161])	Human	Using branching process to study the effectiveness of isolation and quarantine during SARS epidemics	QM QS,	ECC
SARS ([41])	Human	Mathematical model (branching process, means that epidemic can be regarded as a growing tree) (contact tree)	ST+QM NO*	EFC
SARS ([162])	Human	IB (small-world network, n=1,515,271 (41,860,740 social contacts))	VM VN VC	ECC
Smallpox ([163])	Human (large US city)	DEB (Large city, Homogeneous mixing population, no network applied, n=10 million)	VM VT ST+QS	ECC
Smallpox ([164])	Human (large US city)	DEB (Homogeneous mixing population, no network applied, n=10 million)	VT VM QM	ECC
Smallpox ([59])	Human	DEB	ST+QM NO*	EFC
Smallpox ([165])	Human	DEB	VT ST+QM	ECC
Smallpox ([166])	Human (Paris, France)	DEB (n=2.15 million)	VR VT ST+QS	ECC
Smallpox ([167])	Human	DEB (n=50,000)	NO EH VH+EH VK+EH VH+VK+EH QK+EH QH+EH CC PM	ECC

			PM+VH PM+QK PM+QH PM+VH+QH PM+CC PM+VH+QH+QK PM+QH+CC PM+VH+QH+CC PM+VH+QH+QK+CC PM+VH+QH+VK+QK+CC	
Smallpox ([168])	Human (large US city)	DEB (n=10 million)	VM VT	ECC
Smallpox ([155])	Human	DEB	ST+QM VW	NOC
Smallpox ([169])	Human (US)	DEB with socially/spatially structure (spatial structure, n=hypothetical contemporary US communities of 6000, 50,000 and 1.6 million in "village", "town" and "city")	VC(10%)+VS(30%) VC(10%)+VS(30%)+QR VC(10%)+VS(30%)+QR+VT+VC(95%) VC(10%)+VS(30%)+QR+VT+VC(95%)+VW(10%) VC(10%)+VS(30%)+QR+VT+VC(95%)+VW(50%) VC(10%)+VS(30%)+QR+VT+VC(95%)+VW(10%)+CS+VF(40%) VC(10%)+VS(30%)+QR+VT+VC(95%)+VW(50%)+CS+VF(40%) VC(10%)+VS(30%)+QR+VT+VC(95%)+VW(10%)+CS+VF(80%) VC(10%)+VS(30%)+QR+VT+VC(95%)+VW(50%)+CS+VF(80%) VC(10%)+VS(30%)+QR+VT+VC(95%)+VW(10%)+CS	ECC
Smallpox([170])	Human	Constructed an individual based model to describe the spread of smallpox after a deliberate release of the virus	VM QM VM+QM	ECC
Smallpox ([171])	Human (US)	IB (mixing site type , n=2,000)	VC(30%) VC(50%) VC(80%) VF(80%) VT	ECC
Smallpox ([172])	Human	IB	VT QS	ECC
Smallpox ([173])	Human	IB (mixing site type social contact network)	VM VT	ECC
Smallpox ([174])	Human (US)	IB (human contact network is strongly connected small-world-like graph with a well-defined scale for the degree distribution and locations graph is scale-free)	VM VT	ECC
Smallpox ([175])	Human	IB ("small-world" type network, n=10,000)	VT QM	ECC
Smallpox ([176])	Human	IB (mixing site type network, n=6000/50,000)	NO SE ST VW(10%) VW(50%) VW(10%)+CS VW(10%)+CS+VF(40%) VW(50%)+CS+VF(40%) VW(10%)+CS+VF(80%) VW(50%)+CS+VF(80%)	ECC
Smallpox ([177])	Human	Bayesian statistics to estimate the uncertainty in the parameters, later using a vaccination model developed by (Kaplan, et al., 2002)	VM VT	ECC
Smallpox ([41])	Human	Mathematical model (branching process, means that epidemic can be regarded as a growing tree) (contact tree)	ST+QM NO*	EFC
Smallpox ([178])	Human (Great Britain)	IB (Socio-spatial contact network (consistent with demographic and commuting data) was generated by a Markov chain Monte-Carlo algorithm)	QS VT VF(75%)+VT	ECC
Smallpox ([179])	Human (Great Britain)	Stochastic meta-population model consisting of the 459 districts of Great Britain in 1991 (mixing site type network (census data of travelling to work))	VM VT ST+QS	ECC

Smallpox ([180])	Human (US)	IB (mixing site type of network, n=50000 (with subpopulation of 2000 people mixing in household))	QS SM+VW(10%) SM+VW(50%) SM+VW(10%)+CS+VF(40%) SM+VW(50%)+CS+VF(40%) SM+VW(10%)+CS+VF(80%) SM+VW(50%)+CS+VF(80%) SM+VW(10%)+CS NO	ECC
Smallpox ([181])	Human (Sweden)	IB model	VR VW VC+VR VM	ECC
Smallpox ([182])	Human (Great Britain)	IB ("mathematical model that incorporates both information on individual contact structure and large-scale patterns of movements across a range of spatial scales") (individual contact structure, n=2,400,000)	QS ST+QS VT QS VR	ECC
Staphylococcus aureus ([183])	Human (Los Angeles, US)	Constructed a mathematical model to analysis the transmission of the emerging pathogen in a LA jail	QK QS EH PM	NOC
Teschovirus encephalomyelitis ([184])	Pigs (Czechoslovakia)	Empirical retrospective	VR KL+EH QF	NOC
Tuberculosis([185])	Human (San Francisco, US)	Empirical retrospective	QS ST+SE PM	NOC
Varicella([186])	Human (US)	Empirical retrospective	VK(school)	ECC(routine immunization)
Varicella([187])	Human (Philadelphia, US)	Empirical retrospective	VK(school, second dose)	NOC
Yellow fever([188])	Human (Kenya)	Empirical retrospective	VM QS SM	NOC
Yellow fever([189])	Human (Imatong, southern Sudan)	Empirical retrospective	VC	NOC

Abbreviations (see Table 1 for intervention abbreviations):
DEB=differential equation-based; FMD=foot-and-mouth disease; HIV=human immunodeficiency virus; IB=individual-based; MSM=men who have sex with men; SARS=Severe acute respiratory syndrome; CEC=Cost Effectiveness Criteria; ECC= Effectiveness Comparison Criteria; EFC=Effectiveness Only Criteria; NOC=No Comparison;
† If the study uses generic or fictitious population groups no specific population groups are specified and only general category (human or animal) are identified.
* Indicates implicit inclusion of the intervention (e.g., NO*)

Table 3-3 reports the results of detailed coding of the disease-specific studies, which varied in the number and types of interventions that they considered. Our review showed the frequent targeting of outbreak response efforts based on a specific risk factor (TRisk), potential contact with an exposed individual or index case (TTrace), and/or based on geographic proximity to an index case (TRing). TRisk interventions emerged as the most common type of intervention in our review, consistent with the large number of specific interventions associated with this type

of targeting. Overall 129 studies in our review targeted one or more high-risk groups, including health care workers (21 studies), high-risk farms (15 studies), those attending schools (14 studies) and other institutions (11 studies), pregnant women (2 studies), and others (e.g., infants, elderly, hospital patients, people with severe disease or chronic conditions, people who previously received a low-efficacy vaccine, men who have sex with men (MSM), homeless individuals, and injection drug users) (63 studies). We find that studies tend to either target individuals likely to contract and pass on the disease (such as healthcare workers), and/or individuals likely to experience the most severe outcomes (e.g., the elderly). TTrace interventions most commonly use IB models, which provide a straightforward way to capture the impact of tracing quantitatively. Common targets in tracing interventions include households (5 studies), random acquaintances (6 studies) and general social and sexual connections (36 studies). TRing interventions largely focus on diseases that infect livestock due to limited mobility of animals. The majority of TRing intervention studies on animals use a herd, flock, or farm as the unit of analysis, rather than individual animals. Outbreak response efforts tend to occur dynamically, such that targets change as information becomes available from the field. In addition, an effort that begins as a TTrace intervention may evolve to a TRing strategy if early tracing efforts reveal more widespread infection in the local area, and some combined interventions include components of one or more types of targeting.

Most studies (69%) included multiple interventions for comparison. We found 70 studies that only included a single intervention, and all of these studies made no comparisons of effectiveness (NOC). We found 50 studies that made statements of effectiveness based on implicit comparison to doing nothing (NO*). Only 29 studies performed cost-effectiveness analysis of different interventions.

We found comparisons between studies for specific diseases yielded some interesting insights and we summarize these insights here.

Influenza

The largest group of studies in our sample (48 studies) focuses on different types of influenza including general (21), seasonal (2) and pandemic (3) outbreak response for different strains, including H1N1 (14), H5N1 (5), and avian (3). Compared to other diseases, these studies

explore the widest range of interventions, including: VM, VW, VT, VC, VI, VP, VF, VR, CS, CK, PM, PH, PW, QM, QS, QF, KL, EH, EP, ST, and SE.

Outbreaks of seasonal (annual) influenza commonly occur in institutions, and many studies focus on interventions that target high-risk institutionalized populations (TRisk). In hospitals and nursing homes, studies report attack rates as high as 60% and case-fatality rates as high as 50% [218]. Doyle et al. [68] use a Monte Carlo simulation model to study the impact of vaccination of elderly people with chronic disease (VC), and show reductions of 24% in deaths and 40% in hospitalizations. Monto et al. [64] find the use of antiviral drugs to be effective in reducing transmission of seasonal flu in nursing homes. Balicer et al. [82] study influenza transmission in a confined population and find rapid mass vaccination response to an outbreak (VM) to be an effective intervention. Hsieh [89] analyzes pandemic influenza with a compartmental model and recommends vaccination of the elderly (VC) given higher estimated transmission probability per contact. Tuite et al. [92] use simulations of a deterministic, age-structured compartmental model of influenza transmission to recommend vaccine allocation to groups with a high risk of contact (VC), regardless of age, followed by age groups at increased risk of severe outcomes. An IB model by Lee et al. [95] suggests that vaccination in response to the detection of an outbreak should prioritize pregnant women, healthcare workers, young children, and people at risk for influenza complications due to underlying medical conditions. Longini et al. [98, 101] examine the success of targeting contacts (TTrace) with antivirals to contain H5N1 pandemics, and they suggest that tracing a sizeable fraction of contacts (VT) could prove as successful as vaccinating 80% of the population. Carrat et al. [75] use an IB model to assess the impact of vaccination (VM), treatment/prophylaxis with neuraminidase inhibitors (PM, PH), quarantine (QK), contact tracing (ST) and closure of schools (CS) or workplaces (CK) in stopping influenza pandemics. Ferguson et al. [76] find limited impact from travel restrictions (CT) following detection of a novel influenza strain outbreak while prophylaxis for half of the population along with school closure (CS) could reduce attack rates by half. Germann et al. [99] similarly suggest the need for multiple interventions (e.g., VC+QM+CT+CS) to contain an outbreak for relatively high transmissibility of the virus (i.e., high basic reproductive number or R0) in the absence of a vaccination option. Glass et al. [102] find significant impact from targeting children and schools (CS) in fighting a new influenza virus. Several studies [76, 94, 102] evaluate the effectiveness of school closure (CS) and suggest increased effectiveness if

applied early in the outbreak. The social costs of these closures may represent an important consideration, particularly under conditions of high population immunity and/or with access to a relatively inexpensive vaccine [94]. Baguelin et al. [88] conducted a cost-effectiveness study of H1N1 response in England and suggested that vaccination of the high-risk groups (VC) (i.e., the elderly with chronic diseases and school-age children) appears both effective in containing the epidemic and cost-effective. Sander et al. [90] demonstrated similar cost-effectiveness of an H1N1 vaccination program (VM) in Ontario, Canada. McCaw and McVernon [69] find that prophylaxis (ST+PM) represents a better use of a limited stockpile of antivirals than treatment of those already infected, and suggest that early intervention could provide the time needed to develop a vaccine for a new strain. Collectively, these studies suggest the need to tailor intervention strategies to specific population characteristics [62, 71, 80, 81, 99, 100].

Severe Acute Respiratory Symptom (SARS)

A few studies focus on response to the SARS outbreak. Xu and Sui [162] compare three intervention strategies (VM, VN, and VC) in response to the SARS outbreak using an IB model with a small world network and find the greatest impact from targeting the most well-connected individuals in the modeled network. Hsu and Hsieh identify contact tracing (ST) and quarantine (QM) as relatively successful [154], while Gjeorgjieva et al. [152] explore the impact of mass vaccination (VM), vaccination of high risk groups (VC) and isolation (QM). Pourbohloul et al. [160] assess the effectiveness of different interventions (i.e., VT and QM) for respiratory pathogens such as SARS using an IB model with mixing sites based on the Vancouver census. They find that isolation of infected people and quarantine of their close contacts (QM) appears effective for mildly transmissible diseases, but high basic reproductive number (R0) could pose a logistical challenge. Finally James et al. [151] review the interventions used in Singapore to control the SARS outbreak including prevention and control within healthcare settings, communities. and at the borders.

Hepatitis A

The majority of hepatitis A studies discuss empirical case studies of outbreaks in different locations across the world [44-50]. After retrospectively studying patients in a community-wide hepatitis A outbreak in 1996, Hutin et al. [44] identified methamphetamine

injectors, emergency room regular patients, and family members of relatives (VT) that visited a Women, Infants, and Children program (WIC) as high-risk groups to prioritize for vaccination (VC) in case of an outbreak. Analysis of a 2004 immunization campaign in response to a hepatitis A outbreak in Boston targeted people in health centers, detoxification centers, and homeless shelters (VC) [48]. Other studies of hepatitis A suggest targeting of subcategories of health care workers (VW) [52], travelers to high-risk countries (VI) [46], child immigrants from high and medium endemic countries (VC), and highly sexually-active individuals (VC) [43, 56]. On the other hand Meltzer et al. [51] find that vaccinating restaurant workers is not cost-effective from the perspective of a restaurant owner, even with bankruptcy representing a very likely outcome if a hepatitis A case in one or more customers traces back to an unvaccinated employee. Vaccination is cost-effective only from a societal (not restaurant owner) perspective and only when outbreak response activities begin after detection of an outbreak.

Hepatitis B

Four modeling studies explore response to hepatitis B outbreaks [55-58]. Kretzchmar et al. [56] compare the effectiveness of vaccination of children of immigrants from endemic countries, highly sexually-active risk groups (VC), and mass vaccination (VM) and find the greatest effectiveness for VC, with medium effectiveness of VM as it allows for significant reduction of new cases, but at relatively high costs. Armbruster and Brandeau [57] use a DEB model to find the optimum allocation of health care resources to screen for antiviral treatment of infected individuals (PM) and trace their contacts (ST). They find that after optimization and in the absence of binding logistical constraints the two strategies yield the same cost per identified infectious individual.

Measles

Our review found a relatively large proportion of empirical retrospective studies for measles. DeSerres et al. [109] recommend reactive measles vaccination of infants aged 6 to 11 months (VC) as an effective intervention based on relative attack rates between infants vaccinated after the start of an outbreak and those not vaccinated. Similarly, another study finds revaccination of school children in response to an outbreak effective in containing the epidemic [106]. Steingart et al. [115] recommend targeting HCWs (VW) in pediatric hospitals. “Catch up”

vaccinations of school children (VC) helped contain measles outbreaks in Singapore [114] and in Canada [124]. Gdalevich et al. [116], building on Israeli military experience, recommend mass vaccination at crowded institutions after detection of an outbreak. One study used an IB model calibrated to data from an outbreak in Niger to assess the impact of outbreak response vaccination [127] and found that early vaccination of children between 6 months and 15 years old (VC) can reduce the number of cases by as much as 90%. However, timely response is key [118], for example the impact of outbreak response vaccination in a Niger outbreak proved lower due to delays in the administration of the vaccine [127].

Smallpox

Not surprisingly given that global smallpox eradication occurred in 1979, all 23 studies that discussed response for potential reintroduction of smallpox (i.e., bioterrorism) and resulting outbreaks base their findings on simulation modeling. Meltzer et al. [170] recommend a combination of case quarantine (QS) and mass vaccination (VM) to control an outbreak. Kaplan et al. [163] used a DEB model of a smallpox bioterrorism attack in a large population and concluded that mass vaccination (VM) represents the best policy. In contrast, Halloran et al. [171] found in their individual based (IB) model of a smaller community that vaccination of contacts (VT) can achieve comparable results with lower costs.

Halloran et al. [171] and others [176, 180, 181] suggest that vaccination of hospital workers (VW) and trace vaccination of the population (VT) represent the best strategies for containing a smallpox bioterrorism attack. Aldis et al. [167] use a DEB model to test the effects of different interventions including VH, VK, PM, QH, QK, CC and EH during a smallpox outbreak, and conclude that quarantining high-risk household members (QH) can bring the outbreak under control. However, typical models assume students stay at home following school closure (CS), but violation of this assumption (e.g., if shopping malls replace schools as mixing site) could significantly reduce the effectiveness of school closure (CS). Finding similar results to those reported by Eichner [172], Porco et al. [175] use an IB model with a small-world-like network structure and mixing sites to model connections between individuals in a population of 10,000 people. They find that vaccination of contacts (VT) can control a smallpox bioterrorism attack, but stress the importance of sufficient tracing and vaccination capacity as a prerequisite. Legrand et al. [166] test the ability of trace vaccination within (VT) to stop a smallpox

bioterrorism attack and analyze the sensitivity of the results to R0, fraction of contacts identified, and delay in response. They find that the effectiveness of different strategies depends strongly on R0 and the intervention start time, and moderately on other factors (e.g., contingency plan). Kretzschmar et al. [165] use a group homogenously mixing model and they find that trace vaccination (VT) appears effective if case detection occurs quickly and vaccinators achieve high coverage of contacts. Eubank et al. [174] compare VM and VT in stopping a smallpox outbreak, and using a detailed IB model of Portland OR they find similar effectiveness for the two interventions in containing the epidemic, with lower vaccination side-effects anticipated for VT. Elderd et al. [177] study the impact of uncertainty in model inputs using a DEB model and suggest that mass vaccination (VM) offers a safer option given the long tail of high-cost outcomes that may occur with vaccination of contacts. Kress [168] suggests that VM+VT represents a better intervention that VM or VT alone based on number of infected cases. Riley and Ferguson [178] compare different interventions for smallpox in a detailed IB model of England and find QS and VT to be sufficient to contain the epidemic, unless significant logistical challenges exist which favor VM to VT. Longini et al. [180] extend their original 2002 paper [171] to larger populations (50,000) and find that single case isolation (QS), vaccination of their close contacts (VT), and conduct of VW control a large smallpox outbreak without needing to resort to more costly VM intervention. They find limited benefit from school closure in this case.

Foot and mouth disease (FMD)

Several models and a few empirical retrospective studies analyze FMD outbreak response interventions, mainly including VR and KL. Most papers that analyze VR focus on FMD among cattle and sheep [17-19, 36] and several modeling studies use detailed data from recent European outbreaks. Keeling et al. [40] explored VR of all farms that fall within some radius of a farm with a confirmed case. The number of cases goes down almost linearly with the radius of the ring, but the benefits remain moderate because cases escape the ring due to significant delays in implementing vaccination and opportunities for long distance jumps of the disease. Tildesley et al. [42] analyze the economics of VR to stop FMD and find that the optimum ring radius appears more robust to variation of disease model inputs than logistical bottlenecks. They also find that targeting the whole circle (rather than an annulus) (VR) makes the best use of resources, possibly because they start the vaccination from the outside of ring and go in, which prioritizes farms with

the minimum distance from recently-infected farms and eases implementation by eliminating the requirement for an explicit ring. Hutber et al. [20] propose the expected outbreak size by the second week of outbreak as a good metric for deciding on the cost-effectiveness of national vaccination programs as outbreaks that are likely to die out in this time period are not worth the vaccination costs. In a recent study, Tildesley et al. [35] show that county level data resolution appears good enough to support robust policy conclusions regarding optimum ring size. Other theoretical studies in this domain focus more on analytical approximations than practical insights [39, 168]. Criticisms of the ring vaccination results [38] include the lack of consistency in policy recommendations across different studies that use roughly the same types of models [40, 42].

Other Diseases

A few studies analyzed other diseases, including bovine brucellosis [1], bovine herpes virus type 1 (BHV-1) [2], chickenpox [3, 4], cholera [5], classical swine fever (CSF) [6-8], HIV [57, 59], meningococcal disease [128-134], mumps [135], pertussis [136-141], pneumonic plague [142], polio [143-146], rabies [147-149], staphylococcus aureus [183], teschovirus encephalomyelitis [184], tuberculosis [185], varicella [186, 187], and yellow fever [188, 189]. Given the limited number of studies for each of these, we do not detect noteworthy generalizations.

Table 3-4 Characterization of model and intervention types for each non-disease-specific study

Title (Ref)	Population studied	Model Description	Intervention	Evaluation criteria
Effectiveness of vaccination strategies for infectious diseases according to human contact networks ([190])	Human or animals	IB (random and scale free networks (average degree of either 10 or 100), n=10,000 or 100,000)	VR KL+EH QF	ECC
Optimal control of deterministic epidemics ([191])	Human or animals	Compare different deterministic optimal control models for epidemics characterized by an SIR model to assess the effectiveness of vaccination, quarantine, screening and health promotion campaigns	VM QM SM	ECC
Predictive models of control strategies involved in containing indoor airborne infections ([192])	Human	Mathematical model (Wells-Riley mathematical model, competing-risks model, and Von Foerster equation)	VT QM EH+EP	ECC
Epidemic control in a hierarchical social network ([193])	Human or animals	IB (mixing size type network with 2 different networks: residential neighbors and work neighbors, which share a common set of nodes, n=100,000)	PM QM CT+EH+VC CS+CK	CEC
A new SEIR epidemic model with applications to the theory of eradication and control of diseases, and to the calculation of R-0 ([194])	Human or animals	DEB model to test time-dependent control measures	VM ST QS	NOC
The impact of contact tracing in clustered populations (STD) ([195])	Human	Ordinary DEB model, starting with mean-field approaches and moving on to pairwise models, (pairwise network (homogeneous random network), n=100,000)	ST NO*	EFC
Efficient mitigation strategies for epidemics in rural regions ([196])	Human or animals	SEIR model on the contact network	VN VC	ECC

Epidemic models with heterogeneous mixing and treatment ([197])	Human	Heterogeneous mixing epidemic two-group model (n=N1+N2)	PM	NOC
Contact tracing and epidemics control in social networks ([198])	Human or animals	IB (stochastic simulation model and the mean-field equation) (random and small-world networks, n=1,000)	VC NO*	EFC
Contact tracing and disease control (STD and new invading pathogens) ([199])	Human	Pairwise-approximation method and full stochastic simulation (unstructured network where everyone has an equal number of contacts, and heterogeneous network in which individuals have differing numbers of contacts, n=100,000)	ST+PM ST+QM	ECC
Controlling disease spread on networks with incomplete knowledge ([200])	Human or animals	IB (Small-world networks (one dimension ring and a two dimensional regular lattice both with the addition of shortcuts leading to small-world topologies) and scale-free networks, n=2,500)	VM VT QM	ECC
Optimising control of disease spread on networks ([201])	Human or animals	IB (Small-world networks (one dimension ring and a two dimensional regular lattice both with the addition of shortcuts leading to small-world topologies) and scale-free networks, n=2,500)	VM VR VC	CEC
Superspreading and the effect of individual variation on disease emergence([202])	Human	Using an integrated theoretical and statistical analysis of the influence of individual variation in infectiousness on disease emergence with contact tracing data, showing that individual-specific control measures outperform populations wide measures	ST; VT	NOC
Effectiveness of realistic vaccination strategies for contact networks of various degree distributions ([203])	Human or animals	IB (random and scale free networks (average degree of either 10 or 100), n=10,000 or 100,000)	VM VR	ECC
A novel dynamic immunization strategy for computer network epidemics ([204])	Human or animals	IB	NO VN VR PM (in the ring)	ECC
What is the best control strategy for multiple infectious disease outbreaks? ([205])	Human or animals	DEB (n=10,000)	VM VR VN	ECC
Epidemic dynamics on scale-free networks with piecewise linear infectivity and immunization ([206])	Human or animals	IB (scale-free networks)	VR PM (in the ring)	ECC
Networks, epidemics and vaccination through contact tracing ([207])	Human or animals	IB (random network, n=1000)	VC NO*	EFC
Imperfect targeted immunization in scale-free networks ([208])	Human or animals	IB (Scale-free and Autonomous system (AS) level internet model (comes from the real-life data collected in the National Lab for Applied Network Research))	VT NO*	EFC
Modeling epidemics dynamics on heterogeneous networks ([209])	Human	Dynamics of the SIS process on heterogeneous networks, where different local communities are connected by airlines	CT	ECC
The dynamics of spreading and immune strategies of sexually transmitted diseases on scale-free network (STD) ([210])	Human	SIRS model on scale free network	VC VF	ECC
Comparative effects of avoidance and vaccination in disease spread on a dynamic small-world network ([211])	Human or animal	Individual based network model with dynamic small world contact networks (n=10,0000)	VN VS	ECC

Abbreviations (see table 1 for intervention abbreviations):
DEB=differential equation-based; IB=individual-based; SEIR=susceptible-exposed-infectious-recovered model of disease; SIRS=susceptible-infectious-removed-susceptible model of disease; SIS=susceptible-infectious-susceptible model of disease; STD= Sexually transmitted disease; CEC=Cost Effectiveness Criteria; ECC= Effectiveness Comparison Criteria; EFC=Effectiveness Only Criteria; NOC=No Comparison;* Indicates implicit inclusion of the intervention (e.g., NO*)

Table 3-4 reports the details of non-disease-specific studies, which tend to focus on offering insights about model behavior based on theoretical arguments that combine disease transmission and network structure [e.g. 195, 199] or different types of transmission (e.g., sexually transmitted diseases (STDs) [e.g. 210] and airborne infections [e.g. 192]). For example, one study focuses on the hubs in a scale-free (SF) network [208] while others focus on SIR

transmission models [204, 206]. Takeuchi and Yamamoto [203] analyze VM, VR, and VN for 3 random networks of scale-free, exponential, and constant degree distributions and find VM best suited for scale-free networks in which the existence of hubs make it very hard to contain the epidemic with VR. Eames and Keeling [199] provide approximations for contact tracing (ST) effectiveness needed to control diseases in SIR and SIS type models using pair-wise approximation of networks, which represent important considerations with respect to the transmission of STDs that spread through partnerships. They find relationships that connect the required contact tracing (ST) effectiveness to R0 and to the number of connections per individual, and their results show high levels of consistency when compared to IB simulations. They also find that network clustering reduces the effectiveness of trace vaccination (VT) required for containment, which may explain some differences between the results from IB and DEB models in other studies [192, 200, 208]. Benchke [191] analyzes optimal control strategies for SIR-type models of disease transmission and finds that for a wide range of interventions maximum effort should be focused in a short period early in the course of epidemic. Day et al. [161] find quarantine measures to be most cost-effective when surveillance and isolation are not complete (e.g., due to high asymptomatic cases). Lloyd-Smith et al. find significant variations in transmission due to differences in individuals, which point to additional value of interventions that target "super-spreaders" [202]. Fraser et al. [59] provide a good discussion of the likely effectiveness of ST+QM. Insufficient quantitative studies of non-pharmacologic interventions (e.g., social distancing (CS, CK, CF, CC and CT), wearing face masks (EP), frequently washing hands (EH)) exist to generalize their impacts.

A few studies analyze targeted intervention for animal diseases [18, 19, 24], however, targeting specific individual animals instead of farms often remains too expensive given the large number of animals involved and the speed of transmission within each farm. Morris et al. [23] offer a spatial simulation model for animal disease and response analysis, including ring vaccination (VR) and slaughtering (KL). Dybiec et al. [200] explore VR effectiveness on 1- and 2-dimensional small-world and scale-free networks, and for small-world networks they find an optimal ring size that balances the costs of vaccination with costs of the outbreak. They also find that in scale-free networks VR cannot stop outbreaks given the dominance of long-range links.

4.0 Discussion

Outbreak response efforts typically seek to minimize the health and financial costs following the detection of an outbreak. Our review of the empirical and modeling studies reveals a wide range of different interventions. Table 3-5 summarizes key factors that appear to influence the desirability of various types of targeted interventions that we identified in the context of this review.

Table 3-5 Overview of findings regarding factors influencing the effectiveness of different targeted interventions

Type of interventions	Factors relevant to the relative desirability of interventions	Model considerations	Other considerations
Targeted based on risk factors (TRisk)	Greater variability in susceptibility and/or ability to contribute to transmission [52, 175, 219] Greater differential disease burden and costs for high-risk population compared to general population [71] Greater ability to identify subpopulations important to transmission or those at higher risk of disease burden [68, 89] Lower costs of preferential targeting due to smaller intervention size	Different modeling approaches that capture high-risk groups or individuals	Constraints on access, privacy, and cultural concerns
Targeted based on network tracing (TTrace)	Lower R0 [59, 199] Lower proportion of asymptomatic to total infections [59, 199] Higher clustering [59] Higher coverage (ability to detect through tracing and intervene) [59, 199] More rapid response and lower costs of case detection [175] Less uncertainty in disease parameters [177]	Heterogeneously mixing or homogenously mixing with approximations [163, 199]	Surveillance and tracing logistics important
Targeted based on geographical boundaries (TRing)	Lower R0 [38, 39] Greater ability to detect first case [38, 39] More rapid response [127, 146, 221] Absence of long-range links [22, 211]	Spatially heterogeneous models that account for long-range links	Need to supplement ring intervention with movement restrictions, models can consider different designs regarding inward-outward rings and/or multiple case detections

The effectiveness of targeting interventions based on risk factors (TRisk) depends on several factors. First, the relative importance of different subpopulations in the transmission of infection and disease represents a critical factor. If identifiable subpopulations differ with respect to contact patterns and risk factors that lead them to participate significantly more in transmission than others, then these subpopulations provide a clear target for intervention [52, 175, 219]. Issues related to identifying such subpopulations and the costs of preferential targeting affect cost-effectiveness and the ability to successfully implement targeted interventions based on risk factors [44, 176, 220]. Targeting some subpopulations may become

more challenging than other strategies due to constraints related to identification, access, privacy, cultural concerns, and other issues [45, 56, 216]. The differential mortality and costs of disease for different subpopulations represent another consideration [71]. If wide variations exist across different subpopulations in their susceptibility to the disease or costs if infected, then this motivates targeting those most vulnerable, although identification, access, and logistics moderate the feasibility of this option [68, 89].

The effectiveness of vaccine interventions that trace contacts (TTrace) depends on several factors. The vaccination interventions (VT, VH) depend on the ability to prohibit sufficient numbers of susceptible contacts from participating in transmission. Higher R0 diminishes the probability that we can reduce the number of transmissions per infected individual below one [59, 199]. Also, larger proportions of infections that occur undetected (i.e., greater silent circulation) lowers the effectiveness of interventions that involve tracing [59, 199]. The nature of individual contact networks plays an important role, with higher clustering coefficients increasing the chances that targeted individuals come in contact with multiple index cases, which suggests more effective use of intervention resources [199]. High clustering also usually correlates with reduced costs of intervention per targeted individual, because local links dominate in highly-clustered networks. Both of these factors increase the cost-effectiveness of interventions that trace contacts in highly-clustered networks, compared to networks with many long-range links. The fraction of successfully traced individuals provided with the intervention will influence overall cost and effectiveness [59]. Furthermore, decreasing the times to identify the first case, mobilize the intervention resources, and intervene with contacts increases the chances of success for interventions that trace contracts [146, 175]. Finally, higher uncertainty in the model inputs for the disease may reduce the attractiveness of TTrace interventions compared to mass interventions, because uncertainty increases the chance that TTrace will not provide enough control to stop the outbreaks, even if it appears sufficient based on the most likely scenario [177].

Implementing TRing interventions (VR) requires specifying assumptions related to: (1) the screening process (and success rate) for identifying index cases, (2) the radius of ring(s) within which the intervention will occur, (3) the priority for targeting individuals inside the ring, (4) the intervention capacity and its coverage (probability of missing an individual), and (5) the

existence of any movement restrictions between the ring and outside. TRing interventions share some common success factors with TTrace interventions, including R0, the fraction of infections generated by asymptomatic contacts, and the time to identify the first case and mobilize the intervention resources [38, 39]. The relative sensitivity of VR to the fraction of cases generated by asymptomatic contacts appears lower than for VT. The effectiveness of VR depends on the absence of long-range links (i.e., the absence of contacts that connect individuals outside of the ring, which may include travel and commerce) [22, 211]. Consequently, a successful ring intervention in many cases requires movement restrictions (CT). Research to date far does not indicate clear superiority of conducting ring interventions inward (from periphery to center) or outward (from center to periphery), with only one FMD study raising the question and showing limited sensitivity [42].

Choosing the most effective targeted intervention requires considering not only potentially cost-effective interventions, but also the expected intervention time and expected logistical bottlenecks for the intervention. Disease characteristics and contact network patterns may constrain the achievable intervention effectiveness and the optimal intervention. Timely detection and response to outbreaks can contain the outbreak before it grows so large that it overwhelms available resources [127, 146], and minimizing response time should play a major role in assessing alternative interventions [221]. Response time depends on surveillance coverage, reporting delays, intervention implementation, logistical delays and the time until the intervention removes susceptibles from potentially participating in transmission (e.g., time until the vaccine confers immunity to transmission of infection) [146]. Those interventions that rely on very strong surveillance (i.e., SM, SE and ST) to identify index cases (ST) quickly will need to consider the true quality of available surveillance information. Interventions that rely on tracing (ST) require rapid response, presence on the ground, and good coordination in the health care system, which may not exist in all countries.

Overall, we find a wealth of studies that provide insights related to response planning for potential infectious disease outbreaks, and a large amount of variability in the types of models, interventions considered, and evaluation criteria applied. Further research will help to better define critical factors, but this review should provide useful context for those interested in the literature on outbreak response.

5.0 Acknowledgments

The authors received support from a grant to Kid Risk, Inc. from the World Health Organization Polio Research Committee. The findings and conclusions in this report are those of the authors and do not necessarily represent the views of the World Health Organization.

6.0 Declaration of Interests

None.

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CHAPTER 4 Development of an Individual-based Model for Poliovirus: Implication of the Selection of Network Type and Outcome Metrics

Abstract

We developed an individual-based (IB) model to explore the stochastic attributes of state transitions, the heterogeneity of the individual interactions, and the impact of different network structure choices on the poliovirus transmission process in the context of understanding the dynamics of outbreaks. We used a previously published differential equation-based model to develop the IB model and inputs. To explore the impact of different types of networks, we implemented a total of 26 variations of six different network structures in the IB model. We found that the choice of network structure plays a critical role in the model estimates of cases and the dynamics of outbreaks. This study provides insights about the potential use of an IB model to support policy analyses related to managing the risks of polioviruses and shows the importance of assumptions about network structure.

Keywords: Disease transmission; Individual-based model; Outbreak response; Poliovirus

1.0 Introduction

Global efforts to eradicate wild polioviruses continue, with types 1 and 3 wild polioviruses remaining endemic in four countries (Nigeria, India, Afghanistan, and Pakistan) and causing fewer than 2,000 global cases of paralytic polio annually.[1] While wild polioviruses circulate in these areas, the rest of the world must continue to keep polio vaccination levels very high,[2] due to the risk of outbreaks among susceptible people in polio-free countries. In addition, post-eradication policy planning must anticipate that outbreaks (defined as one or more cases of paralytic polio) will occur after the successful disruption of wild poliovirus transmission,[3-4] largely due to the risks of circulating vaccine-derived polioviruses (cVDPVs).[5] Most people infected with poliovirus do not show any symptoms, which necessitates modeling the transmission of infections,[5] but approximately one out of 200 susceptible people becomes paralyzed from a wild poliovirus infection.[6-8] The costs of outbreaks include both health costs experienced by paralyzed individuals plus the impacts on their families, and the financial costs associated with treating patients and responding to the outbreak with vaccine campaigns to reduce transmission.[9-11] Two vaccines provide protection from disease (paralytic poliomyelitis), but incomplete protection from infection: live oral poliovirus vaccine (OPV) and inactivated poliovirus vaccine (IPV). OPV represents the vaccine of choice for the Global Polio Eradication Initiative because of its low cost, ease of administration, induction of mucosal immunity, and ability to provide secondary protection (i.e., spread to contacts). However, OPV can cause vaccine-associated paralytic polio in rare cases and lead to outbreaks with cVDPVs in populations with large numbers of susceptibles, and consequently following the successful eradication of wild polioviruses global health leaders plan to eliminate the use of OPV.[12] Minimizing the risks of outbreaks will require coordination of OPV cessation, creation of a global vaccine stockpile, and development of specific plans for outbreak response.[13,14] Many countries will also consider switching from OPV to IPV because it carries no risk of vaccine-associated polio paralysis, but IPV represents a relatively expensive choice and its ability to prevent poliovirus transmission in some settings (notably low income areas with relatively poor hygiene and inadequate health systems) remains uncertain.[3,4]

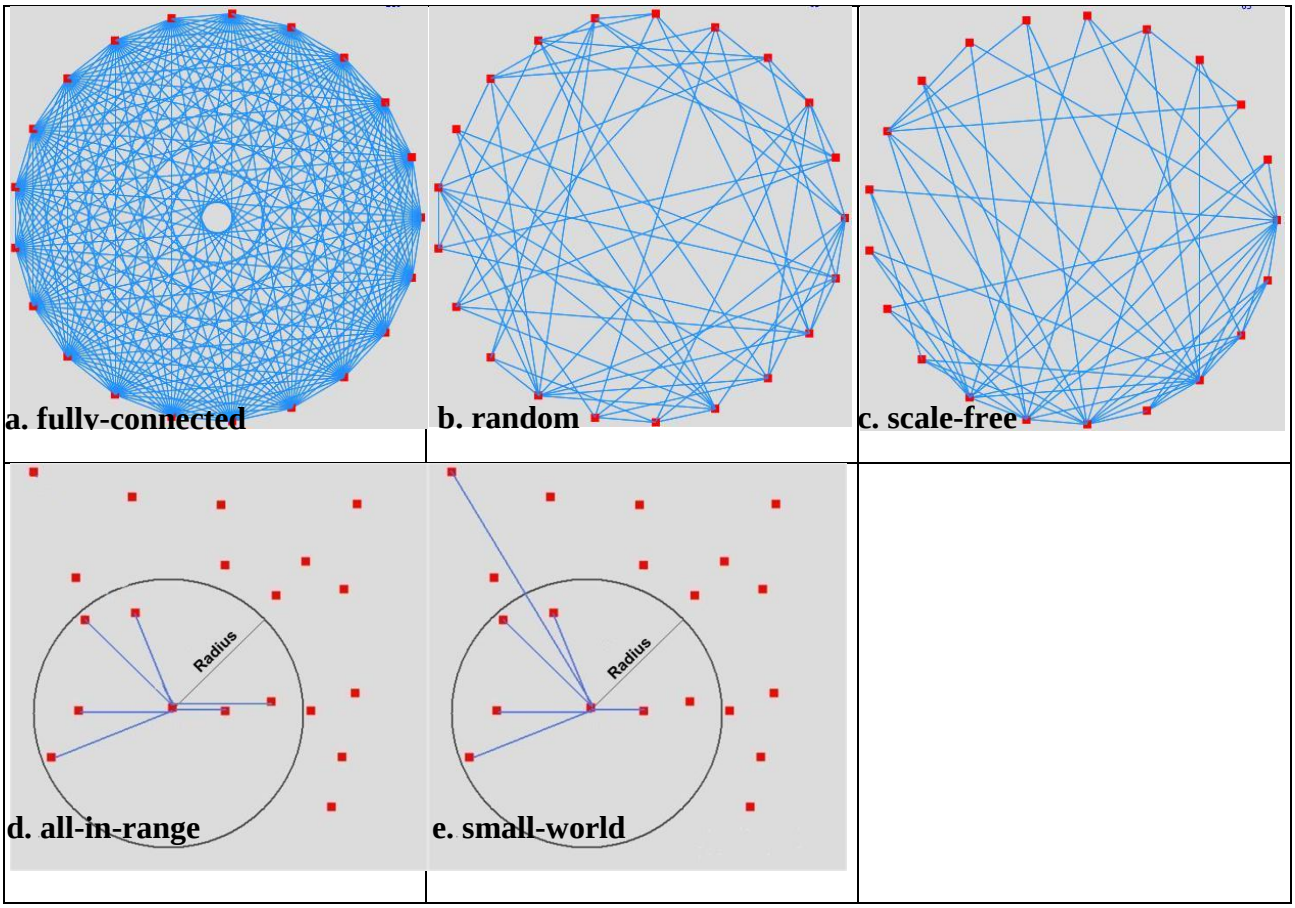
Prior work by two of the authors (RDT and KT) developed a differential equation-based (DEB) model [9] to explore the dynamics of poliovirus infection outbreaks and response strategies.[15] This model yields useful insights, but we recognize the opportunity to address

different questions using a stochastic, individual-based (IB) (or agent-based) modeling approach that explicitly considers the network structure of individuals and the stochastic interactions among them.

Prior studies identified the selection of the network structures as a critical assumption,[16-22] and show that DEB and IB models can yield different insights, in part due to the differences in their abilities to capture network structures and population heterogeneity.[22] In contrast to the assumption of homogenous mixing in DEB models, IB models typically require a network structure that governs the interactions of individuals. Analysts must identify links between individuals (nodes in the network) that specify "who acquires infection from whom" (WAIFW) to mimic the interaction patterns of individuals in a real population [23-24].

We identified five major theoretical network structures in the literature: fully-connected, random,[25] small-world,[26] scale-free,[27] and all-in-range (local).[28] Figure 4-1 provides a graphical representation of example networks from each category. The literature also includes examples of empirical networks, which seek to closely mimic individual contact patterns determined through: (1) contact tracing of individuals,[29-30] or (2) capturing physical locations (mixing sites) in which individuals spend time with others (e.g. schools, workplaces, recreation centers, and shopping malls) that determine interactions based on emerging co-location patterns [31].

Despite the importance of network structure, IB models remain limited with respect to the available information about WAIFW in real populations.[32] Consequently, identifying the critical network parameters that influence outbreak dynamics is essential to develop appropriate IB models to address policy questions and guide data collection.[24, 33] This study describes our efforts to develop an IB model to characterize poliovirus outbreaks at the level of interactions among individuals and explore the impacts of network choices. The IB model explicitly captures immunity states and transition rates similar to those developed earlier,[9] but focuses on stochastic attributes of state transitions and the impact of different network structures on the transmission process.



* The initial layouts of nodes in the networks shown in panels a-c appear as a ring, but the reasonable representation of the initial structure for the networks shown in panels d-e require random distribution of nodes. The network obtained in panel e results from rewiring the network in panel d as described in the text.

Figure 4-1 Examples of the five different theoretical network structures, with each network including 20 individuals (nodes) (N=20) and each node connecting to 6 other nodes on avearge (K=6)*

2.0 Methods

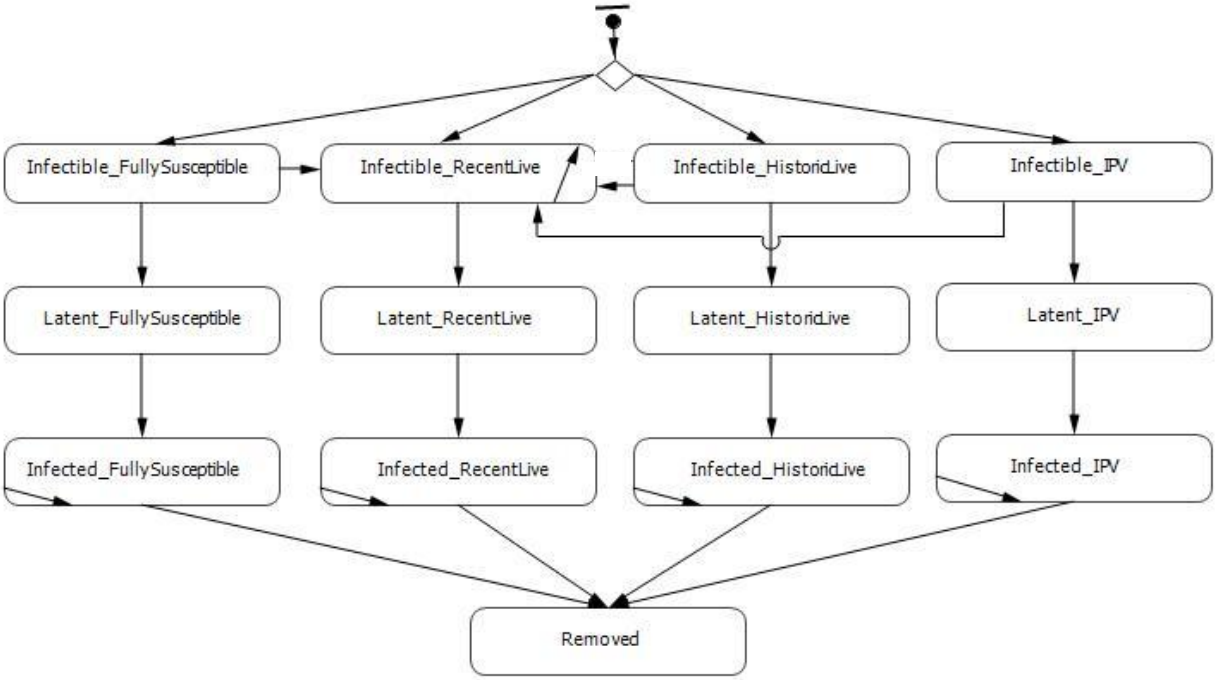


Figure 4-2 Immunity and infectiousness states based on [9] along with possible transitions in the IB model

We developed an IB model for a hypothetical outbreak in a low-income country setting, corresponding to the prospectively modeled outbreak in Figure 4-2 of Duintjer Tebbens et al.[9] The model assumes complete eradication of wild polioviruses and starts the outbreak with a single poliovirus introduction 5 years after cessation of all polio vaccinations. We explored multiple different network structures, including the five theoretical networks shown in Figure 4-1 and several empirical mixing-site networks. Figure 4-2 shows the basic structure of the immunity states from the DEB model[9] and individual state transitions in our IB model for poliovirus infections. The 13 different states modeled capture infectible people (top row), people with latent infections (second row), infected people (third row), and removed people (bottom). The model captures four different types of immunity: (1) "fully susceptibles" - never exposed to live or killed poliovirus, (2) "recent live" partially infectibles - individuals recently infected with live poliovirus, (3) "historic live" partially infectibles - individuals historically, but not recently, infected with live poliovirus, and (4) "IPV" - individuals never infected with live poliovirus but vaccinated with IPV.[9] Although not shown in Figure 4-2, the DEB and IB models also include 25 different age groups,[9] which influences the network patterns in mixing-site settings. We

define inputs to the IB model with a fully-connected network parallel to the DEB model and keep the same basic reproduction number (R_0) across both models (see appendix). To model transmissions at the individual level rather than at the population level in the DEB model, we disaggregate the concept of R_0 into separate inputs for contact rate (C) and infectivity (i) of a contact (i.e., the probability of a contact leading to infection). Specifically, we start with the equation $R_0=C*i*d$ for each type of infectious and infectible person, using d as the average duration of infectiousness for "fully susceptible" individuals, and we calculate i based on an assumed value of C = 5 contacts per day and the values of R_0 and d in the DEB model.[9] The choice of C does not impact R_0 as long as i adjusts to C. We confirmed that we obtained the expected R_0 in the simulations by calculating the average number of individuals directly infected by a single infectious individual introduced in a fully susceptible population (see appendix).

Consistent with the DEB model [9], which begins with a population immunity profile that distributes members in the population to appropriate initial immunity states, the IB model begins by assigning each individual to an initial state as susceptible or partially infectible. The initial population immunity profile follows the projected age distribution for low-income countries and places all children under age 5 years old in the "infectible-fully susceptible" state given the assumption of cessation of all polio vaccination five years prior to the outbreak.[9] We assigned members of the population over age 5 years old to the "infectible-historic live" or "infectible-fully susceptible" state according to assumptions about the historical OPV vaccination rates.[9] Given the assumed lack of IPV or OPV use prior to the outbreak, none of the individuals start in the "infectible-IPV" or "infectible-recent live" states.

Table 4-1 Summary of model inputs for an individual-based model that differ from those used for the differential equation based model [9] via different types of social contact networks

Theoretical networks		
Network	Construction rule	Notes
Fully-connected	Connect every node to every other node (K does not apply)	Structure consistent with the assumption of homogeneous mixing and represents a discrete, stochastic equivalent of the DEB model
Random	Randomly select $K*N/2$ of the $N(N-1)/2$ possible links among N nodes, leading to a Poisson degree distribution (the distribution for the number of links per node) with mean K [25]	Not very realistic for most human interaction patterns given the low clustering of contacts, but one of the

		earlies and most commonly used networks
Scale-free	Select *K* initial nodes with *K***K*/2 randomly assigned links among them, then add new nodes to the network (until *N* nodes are reached), each with *K*/2 links to be connected to previous nodes based on a preferential attachment, such that the probability of connecting to a node is proportional to the number of existing links to that node [27] (the degree distribution of connections follows a power law ($P(k=x) \sim x^{M}$)	Relatively small number of highly-connected individuals and many individuals with limited connections, such that the average distance between individuals is fairly small
All-in-range	Randomly assign people to locations on a square grid, then assign contacts locally (i.e., limited to local geographical neighbors within a given radius), and select the radius of interaction to obtain an average number of connections equal to *K*	Realistic structure when intimate interaction is required for diffusion and the nodes cannot move
Small-world	Begin with the all-in-range network, and then with probability *p*, detach each link from one end and rewire it to a random other node in the population (with duplicate links not allowed)	High clustering and small average distance between individuals [26]
Empirical networks		
Mixing-site 1	Assumes (1) all individuals link to an average of six others in their households between 5 pm and 9 am, (2) all children between 3 and 15 years old and two-thirds of adults (i.e., 16 years and older) go to a randomly selected workplace or school between 9 am and 5 pm, where they are connected with *W* co-workers or *S* classmates, respectively, (3) all other individuals (i.e., very young children and one-third of adults) remain connected at home between 9 am and 5 pm, (4) same contact rate (*C*) applies for homes, workplaces, and schools	
Mixing-site 2	Same as mixing-site 1, except assumes contact rate at home (C_h) twice the rate used for workplace or school (C_w), with the overall expected number of contacts in the population (*C*) kept the same as other networks by adjusting C_h and C_w	
Mixing-site 3	Assumes (1) one hundred different villages, each with one thousand villagers (randomly selected), (2) individuals spend their time in their isolated villages, except for half a day per week when sub-groups of them attend one of ten randomly selected community centers (e.g., a market or place of worship) and interact with people from other villages, (3) the subgroup mixing in the community center includes children between 3 and 15 years old and two-thirds of adults (16 years and older) (similar to mixing-site 1).	

We compare the transmission dynamics across all five of the major theoretical network categories from the literature and three empirical mixing-site networks. The top of Table 4-1 describes the construction rules applied to create the theoretical networks, and the bottom of Table 4-1 provides the assumptions used to create three mixing-site networks, which reflect

possible scenarios to bring individuals into contact at identifiable locations (e.g., home, work, school). Although modeling real population interactions using mixing-sites requires significant data and detailed information about types of contacts leading to infection,[34] we determined that in the absence of specific data we could still learn about how mixing-site networks function by considering the scenarios in Table 4-1. We chose to model two basic types of empirical mixing site networks: one that focuses on workplaces and schools as hubs of transmission within a large population (mixing-sites 1 and 2) and one that focuses on modeling the population as a collection of villages from which individuals connect periodically (mixing site 3). While the selection of network type and model inputs may lead to different results and infinitely many options exist for developing empirical network strucutres, we focused our analysis on demonstrating the differences between a range of typical empirical and theoretical networks. In order to explore networks consistently, we used the same total number of individuals (nodes, agents) (N), and the same average number of connections per individual (K) when comparing networks that use K as an input. However, recognizing the uncertainty in the network parameters, we repeated comparisons for three different values of K. Table 4-2 summarizes the specific inputs values used for the networks.

Table 4-2 Summary of model inputs for the IB model that differ from those used for the DEB model[9] for the different networks structures described in Table 4-1

Model input (units), Abbreviation	Value	Notes
Total population (people), N	100 000	Number of individuals
Daily number of contacts per individual (people/day), C	5	Assumed value used to calculate the rate of sending the infection message for a given R_0 (see text)
Average connections per individual (connections/individual), K	10, 50, 100	
Random rewire probability of small-world network (dimensionless), p	0.1, 0.05, 0.01	
Power law input for scale-free network, M	2.6	
Age of adulthood (yr)	16	
Age of school entry (yr)	4	
Proportion of children under age 4 years old in the population (proportion)	0.07	These children stay at home in mixing-sites 1 and 2
Proportion of students in the	0.26	

population(proportion)		
Proportion of working adults in the population(proportion)	0.45	Two-third of adults work during daytime for mixing-sites 1 and 2
Proportion of adults staying at home in the population (proportion)	0.22	One-third of adults not working
Number of students per school (people/place), S_1 S_2 S_3	 51 345 711	For mixing-sites 1 and 2, correspond to: K=10 K=50 K=100
Number of coworkers per workplace (people/place), W_1 W_2 W_3	 17 115 237	For mixing-sites 1 and 2, correspond to: K=10 K=50 K=100
Contact rate at home (people/day), C_h	6.4	For mixing-site 2
Contact rate at workplace or school (people/day), C_w	3.2	For mixing-site 2
Number of community meeting places (places)	100	For mixing-site 3
People per village (people)	1000	For mixing-site 3

Each simulation of the IB model begins by creating a population of N=100 000 individuals. The IB model distributes the individuals into their age and initial immunity groups and then sets up the chosen network structure to connect individuals using a construction rule. During the simulation births occur and susceptible newborns enter the network with connections created by applying the same construction rule used to create the initial network, with the net effect of increasing the potential number of people who could become infected to over 100 000. Consistent with the original model designed for outbreaks of short duration,[9] this model ignores deaths. Thus, the network is dynamic in the sense that new individuals get added and wired to the rest of the population, but the existing connections do not change dynamically (e.g. because of self-quarantine).

We introduce the first, randomly selected, infectious individual (patient zero) into the population at time zero of each simulation to initialize the infection process. The outbreak may die out if the patient is removed before infecting others. However, an outbreak occurs in the

population when the imported poliovirus establishes effective transmission among individuals (presumably primarily via the fecal-oral route and possibly to some extent via the oral-oral route [35]) and infects enough people to cause at least one paralytic case.[9] Infection depends on the existence of connections between infectious and infectible individuals in the network and the contact rate (C). Not every contact between an infected individual and an infectible individual leads to infection, and the probability of infection following contact (i) depends on the individual's immunity state.

We performed repeated analyses for three different average numbers of connections per individual (K=10, 50, and 100) to explore a range given limited knowledge about how contacts lead to poliovirus transmission. We also explored all five of the theoretical networks in the top of Table 4-1, and for the small-world network, we explored the impact of three different values for the probability of random rewiring of the local links (p=0.01, 0.05, 0.1), which makes a total of seven simulated theoretical networks. We note that the random, small-world(s), and all-in-range networks represent a continuum of different levels of clustering and average distances between nodes. The clustering and distances decrease as we increase p, because a small-world network with p=1 yields a random network, while setting p=0 yields an all-in-range network. To facilitate some comparison between the seven simulated theoretical networks and the three simulated mixing-site networks, we selected the number of coworkers per workplace (W) and students per class (S) such that time-weighted average connections per person (K) remain the same as the value used for other network settings, noting that K does not exist for the fully-connected and mixing-site 3 networks. We used the same contact rate (C) for all networks, except for mixing-site 2, for which we used twice the contact rate for home than that for schools and workplaces to explore the impact of differential contact intensity in different locations while also maintaining the same R_0, as noted in Table 4-2.

We projected the trajectory of potential polio outbreaks and we compared the results across different network and model inputs using the AnyLogic™ (XJ Technologies, Russia) simulation environment. We record an outbreak upon detection of the first paralytic case, which occurs stochastically in approximately one out of 200 infections of "fully susceptible" individuals.[9] We track the trajectory of the outbreak until it finishes (i.e. no latent or infected individuals remain in the population) or until day 2000, whichever comes first. Each simulation started with

construction of a new network consisting of 100 000 initial individuals, and a randomly selected patient zero. Due to the stochastic nature of the simulations, we ran 100 simulations for each of the 10 simulated networks times 3 different values of *K* (for networks that include *K*) for a total of 26 combinations (i.e., the fully-connected and mixing-site 3 networks do not include *K*). During the simulation, we capture the following metrics:

- Die out fraction (dimensionless): The fraction of simulations that do not lead to an outbreak, defined as detection of a paralytic case.
- Detection day (day): The day that the first paralytic case occurs.
- Peak time (day): The day with the highest number of infections observed within the duration of poliovirus diffusion.
- Epidemic Duration (day): The time it takes for the outbreak to end (i.e. the time until no latent or infectious individual remains), which we record as >2000 days if transmission would continue beyond the maximum simulation length.
- Number of infections (number of people): The cumulative number of people who become infected and get removed (recover or die from the infection) at the end of the simulation.
- Number of paralytic cases (number of people): The total number of paralytic cases accumulated by the end of the simulation.
- Peak infections (number of people): The number of people infected at the peak time.

If the event captured by the first metric occurs (i.e., the transmission of infection dies out and does not lead to an outbreak), then the remaining metrics do not provide interesting or meaningful information, and consequently we report their results for only the subsets of 100 simulations that did not die out. For these metrics we found statistically robust means with the sample of 100 simulations. We performed 1000 simulations to characterize the die out fraction results to obtain more statistically robust estimates.

3.0 Results

Table 4-3 reports the results of the fraction of "die out" cases for different network structures and numbers of connections per individual (*K*) based on 1000 simulations. One of the significant advantages of IB models compared to a DEB model emerges simply from the ability to characterize the stochastic possibility of die out. For example, although the comparable DEB model with the relativley high R_0 of 13 predicts an outbreak, the IB model with a fully-connected

network dies out by chance approximately 15% of the time, because the infection does not go beyond the first (few) patient(s) who get removed before infecting a larger population.

Table 4-3 Results of 1000 simulations of the fraction of "die out" cases (dimensionless) for 26 combinations of different network structures and numbers of connections between individuals (K)

K	Network	Mean	Lower 95% confidence limit	Upper 95% confidence limit
NA	fully-connected	0.14	0.12	0.17
10	random	0.21	0.18	0.24
50	random	0.16	0.14	0.17
100	random	0.17	0.14	0.19
10	scale-free	0.12	0.10	0.14
50	scale-free	0.12	0.09	0.15
100	scale-free	0.12	0.10	0.14
10	all-in-range	0.98	0.97	1.00
50	all-in-range	0.17	0.14	0.19
100	all-in-range	0.18	0.15	0.21
10	small-world (p = 0.01)	0.27	0.24	0.30
50	small-world (p = 0.01)	0.13	0.11	0.15
100	small-world (p = 0.01)	0.15	0.12	0.17
10	small-world (p = 0.05)	0.16	0.14	0.17
50	small-world (p = 0.05)	0.16	0.14	0.18
100	small-world (p = 0.05)	0.12	0.09	0.15
10	small-world (p = 0.10)	0.16	0.15	0.18
50	small-world (p = 0.10)	0.14	0.12	0.15
100	small-world (p = 0.10)	0.13	0.10	0.15
10	mixing-site 1	0.46	0.42	0.46
50	mixing-site 1	0.44	0.40	0.48
100	mixing-site 1	0.43	0.40	0.46
10	mixing-site 2	0.44	0.41	0.46
50	mixing-site 2	0.43	0.40	0.45
100	mixing-site 2	0.45	0.40	0.50
NA	mixing-site 3	0.20	0.18	0.22

Table 4-3 shows some differences in die out behavior as a function of the type of theoretical network structure and number of connections (K). The random network for K = 50 and 100 behaves similarly to the fully-connected network because relatively low clustering (i.e., neighbors of same individual are not that likely to be connected to each other) leads to quick propagation of infection throughout the network, reducing the chance of die out compared to a highly clustered population. However, with fewer connections per individual (K = 10) we

observe a larger die out fraction (~21%), because the Poisson distribution of *K* implies a relatively large fraction of individuals with very few connections and thus a relatively lower probability of pushing the virus beyond patient zero. Notably, if patient zero is one of the relatively poorly connected individuals, then the outbreak is more likely to die out. For the scale-fee network, we see a relatively small die out fraction (~10%-13%), which indicates that the few "hubs" of highly-connected individuals serve as relatively effective spreaders, because they connect most people in the population with small distance between individuals. Thus, although the fixed number of connections (*K*) requires the existence of many individuals with relatively few connections to average out the hubs (for all three values of *K*), in most cases patient zero infects a hub directly, and then the hubs infect each other and much of the rest of the population fairly quickly. The all-in-range network behavior depends heavily on *K*. With *K*=10, only a small number of outbreaks occurred in the 1000 simulations, given the highly localized nature of interactions, which implies that nearly all of the infections died out prior to causing a paralytic case. Individuals in the all-in-range network share many connections with their neighbors, which lessens the impact of infection of two connected people since they likely share many contacts, and this overlap reduces their ability to transmit the virus to new people. However, as *K* increases, the all-in-range network goes through a phase shift, in which the larger radius of interaction makes the progression of virus viable and die out drops to approximately 18%. For the small-world network, we generally see low die out fractions (i.e., 12-16%), because long-range connections seed the virus in multiple locations and therefore reduce die out. However, for the small-world network with p=0.01 and *K*=10, we see the same type of phase shift as occurred with the all-in-range network with *K*=10, which appears consistent with prior observations of such a phase transition.[26]

For mixing-sites 1 and 2, which move individuals between home and work or school, we observe a significant increase in the fraction of simulations that die out (i.e., 40-50%) compared to what we found for most of the theoretical networks (i.e., 12-19%, with the notable exceptions of the results of the random, all-in-range, and small-world networks with *K*=10). We believe that this may occur because: (1) most contacts happen in highly clustered family units, which limits transmission beyond the family in the relatively fewer contacts between infectious members of the household and their co-workers/school-mates, and (2) one-third of adults and young children stay at home, which reduces opportunities for transmission. The young age of fully susceptibles

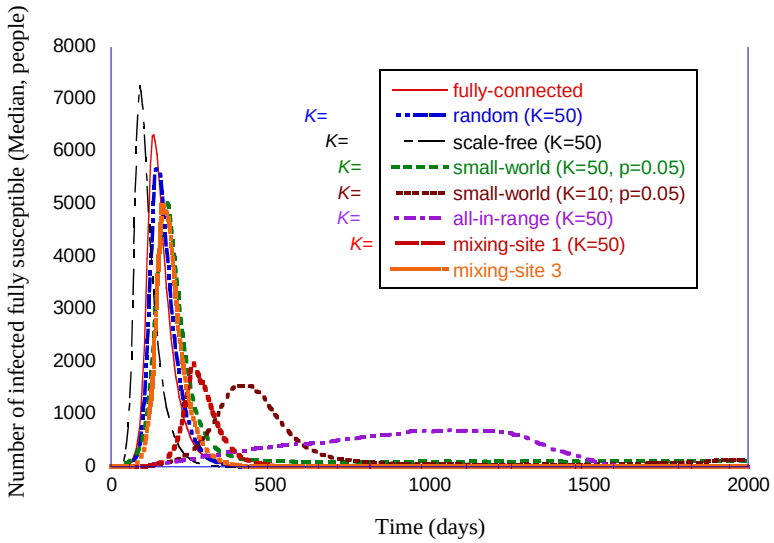
(with relatively higher infectivity) further increases the importance of the mixing-site dynamics. In contrast, the contact pattern in mixing-site 3, which is independent of *K*, shows a much lower die out fraction (approximately 20%). For mixing-site 3, people connect to each other across 1000-member villages, in which the virus can spread with no restriction if the virus gets transmitted during the limited weekly mixing time at community centers (e.g., markets or places of worship).

Table 4-4 Results of 100 simulations for outbreak metrics for 26 combinations of different networks and values of *K* based on the subsets of simulations in which outbreaks did not die out (robust simulation mean, in units indicated for each metric)

K	Network	Detection day (day)	Peak time (day)	Duration (day)	Infection (1000s of people)	Peak infections (1000s of people)	Paralytic cases (people)
NA	fully-connected	82	133	585	95	19	82
10	random	123	198	580	74	10	64
50	random	92	145	541	92	17	77
100	random	90	142	562	93	18	79
10	scale free	67	116	471	72	15	74
50	scale free	57	99	456	82	18	80
100	scale free	58	99	463	84	19	79
10	all-in-range*	NA	NA	NA	NA	NA	NA
50	all-in-range	214	1068	1808	99	1.8	104
100	all-in-range	160	688	1304	98	3	99
10	small-world (p = 0.01)	471	1499	1921	11	0.36	28
50	small-world (p = 0.01)	100	238	>2000	97	10	113
100	small-world (p = 0.01)	78	190	>2000	105	12	143
10	small-world (p = 0.05)	202	417	1932	62	4	80
50	small-world (p = 0.05)	87	172	>2000	99	14	120
100	small-world (p = 0.05)	73	152	>2000	105	15	140
10	small-world (p = 0.10)	142	284	1901	76	6	98
50	small-world (p = 0.10)	82	154	>2000	102	15	132
100	small-world (p = 0.10)	72	139	>2000	106	16	143
10	mixing-site 1	165	283	729	57	6	56
50	mixing-site 1	159	258	709	59	6	59
100	mixing-site 1	157	253	699	59	7	58
10	mixing-site 2	170	284	769	63	6	63
50	mixing-site 2	163	265	808	66	7	64
100	mixing-site 2	154	251	764	66	7	63
NA	mixing-site 3	105	178	637	86	14	83

*** No outbreaks observed in 100 simulations**

(a)



(b)

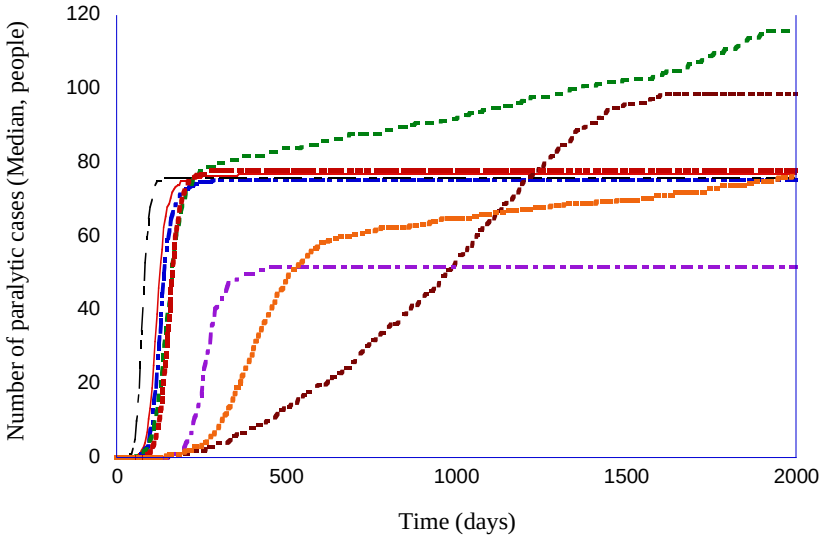


Figure 4-3 Visual representation of the behavior of outbreaks for 8 selected simulated networks as a function of time: (a) number of infections occurring in fully susceptible people as a function of time, and (b) accumulated number of paralytic cases as a function of time.

Table 4-4 shows the results for the metrics that provide insights about the nature of the simulated outbreaks that do not die out, and Figure 4-3(a) provides a visual representation of the outbreak dynamics by showing the number of infected fully susceptibles as a function of time.

The detection day of the first paralytic case provides an indication of the speed of the transmission of infections among "fully susceptible" individuals under different network structures. The peak day provides an indication of the overall speed of transmission in the whole population. The outbreak duration provides insight about how quickly the infection passes through the entire population, and indicates whether the outbreak could continue for more than 2000 days absent intervention. The total number of infections serves as an indicator of the impact of the network on the extent to which infection spreads through the population. The peak infections allow us to see the maximum numbers of people infected simultaneously, which reflects the maximum intensity of the transmission of infection under the different types of network structures. The last column of Table 4-4 provides the estimated number of paralytic cases, which would typically represent the only observable outcome, and Figure 4-3(b) shows big differences in the accumulation of these cases over time for various network structures.

Table 4-4 shows some important differences in the outbreaks depending on the assumptions about the network. In contrast to the stochatic variation that we observed related to die out fractions (Table 4-3), we observed negligible stochastic variation across for the outbreak metrics in Table 4-4 relative to the number of significant figures supported by the model, and consequently Table 4-4 reports only the robust mean values for these metrics. On average, the outbreaks that occur with the fully-connected network take off relatively quickly (e.g., detection day=82, peak time=133, compared with detection day=78, peak time=128 for the DEB model[9]). At its peak, the typical outbreak with the fully-connected network involves over 18,000 infected individuals and the rapid spread of infection limits the overall duration of the epidemic to 585 days on average, with over 95% of the population becoming infected and an average of 82 paralytic cases. The results with the random network show similar behavior, although the average outbreak occurs relatively later (detection day=123), proceeds more slowly (peak time=178), and leads to lower numbers of infected individuals (74% of the population gets infected) and paralytic cases (64). For the scale-free network, we see a very fast take off for the outbreak, which increases the peak infections and reduces the duration of the outbreak. As noted above, patient zero typically infects a hub directly or with one degree of separation in the scale-free network, which leads to rapid infection of all of the hubs, which then infect most of the population. However, the existence of some poorly-connected individuals means that the outbreak fails to reach all of the individuals, such that between 72-84% of the population gets

infected, depending on *K*. Higher *K* values appear to speed up the outbreak slightly, but do not have a large impact because enough hubs exist with *K*=10 to start and support widespread transmission. For the all-in-range network, the outbreak depends heavily on *K*, with essentially no outbreaks for *K*=10, and relatively slow outbreaks for *K*=50 and 100 that move through the population in a wave-like progression from the location of patient zero outwards. Given the slower diffusion with *K*=50, this setting leads to larger peak time, detection date, and duration than does the setting with *K*=100. Notably, slower diffusion actually increases the total number of infections because it extends the epidemic to affect more newborn babies over time. For the small-world network, we generally observe high numbers of infections, except for the network with mainly local connections for *K*=10 and *p*=0.01. We observe the highest numbers of infections and paralytic cases for the all-in-range network with *K*=50, 100 with outbreaks that continue beyond 2000 days in most cases, because the slow transmission that results from largely local links (see the large peak time) essentially matches the speed of entry of fully susceptible newborns.

For mixing-sites 1 and 2, the outbreaks that take off appear relatively insensitive to *K* and *C*. For these mixing-site networks, we see a slow outbreak (e.g., later detection day and peak times than most other network types) that affects the majority of the population before ending after approximately 700-770 days. Shifting the weight of the contacts more toward homes (mixing-site 2) leads to slightly higher numbers of infections and faster outbreaks, presumably because household links act as a bottleneck on transmission for mixing-site 1. By increasing the relative speed of transmission in the home for mixing-site 2, the one-third of household members who do not mix outside of the home become more prone to infection. In contrast to mixing-sites 1 and 2, the contact pattern in mixing-site 3 allows infection to spread through the whole population, only slightly slower than the fully-connected network, with the majority of people getting infected at the end of the outbreak, which occurs within a few months.

4.0 Discussion

Prior research demonstrates the importance of structural and model input assumptions for other diseases,[36, 37] but this paper presents the first IB model for polio outbreaks. By developing this model, we create the opportunity to both represent the stochastic nature of polio outbreaks and consider the impact of different network structures to model heterogeneous human

interactions. With realistic network structures, IB models may show behaviors that differ significantly from the parallel DEB models, and offer opportunities to characterize interventions that target specific types of individuals or parts of networks. We anticipate that IB models could play a valuable role in evaluating different polio outbreak response strategies, such as comparing mass vaccination and ring vaccination options.

Despite the potential uses of IB models, our results suggest important considerations. The computation time, which includes both network setup and transmission dynamics, increases significantly with population size. Notably, the scale-free network we modeled required approximately 30 minutes per simulation just to set up the network on an Intel Core™ 2 CUP 6400 @ 2.13 GHz desktop. The computation times for transmission simulation and data recording scale approximately linearly with population size. Thus, simulating very large populations (e.g., millions of individuals) would require specialized computer clusters, although improved hardware and algorithms continue to reduce computational barriers.[32,34,38] The necessity of conducting comprehensive sensitivity analyses to characterize the impacts of uncertain assumptions adds another dimension of computational time. However, sensitivity analyses reveal critical insights and help analysts address the false certainty and precision projected through the use of detailed IB models,[39] and our analyses suggest that the level of stochastic uncertainty may differ across outcome metrics. We note that the closed-source nature of the AnyLogic™ modeling tool makes it difficult to evaluate the impact of software algorithms and programming choices that could affect the results. We do not believe that choosing a different software program would change the insights that we obtained here related to our comparisons between networks, but we mention this as a limiation because we only compared our results to the prior DEB and we did not compare results between open and closed-source software tools.

Our analysis of various options for network structures, which underly all IB models, highlights the importance of choices related to both model structure and inputs. Prior studies indicate that scale-free and small-world networks might make the most sense for infections transmitted through individual-to-individual networks, like sexually-transmitted diseases (STDs).[40-41] In contrast, mixing-site networks may provide a better representation for airborne diseases such as flu.[24, 31, 42] For poliovirus infections, we expect that using mixing-

sites may also offer the best strategy, but even with a limited set of scenarios for these we found potentially large differences in the behavior of outbreaks. In this regard, we expect that improvement of IB models for polioviruses will require a more detailed understanding of the processes that create WAIFW patterns in specific populations of interest, and that additional insights about the relative importance of fecal-oral versus oral-oral transmission pathways may also help to influence choices about network structures and contact rates both within and between mixing sites. Epidemiologic investigations could provide important insights that would significantly improve our ability to model outbreaks. As long as live polioviruses continue to circulate, the opportunity exists to better characterize the role of potential mixing sites in poliovirus transmission in low-income countries, including markets, schools, places of worship, sewage, rivers, and workplaces. The role of migrant populations also represents an important consideration, and data on population movement in countries of highest concern for poliovirus transmission could provide significant insights with respect to developing appropriate networks. While polioviruses can spread over long distances,[43] the relative frequency of short-distance to long-distance poliovirus infectious contacts remains unknown and requires further investigation.

Several observations also suggest the need for additional development of the IB model. First, we observed persistent transmission as a result of a reintroduction in small-world networks, which suggests the need to include age-dependent mortality rates and waning of immunity. Second, if we seek to use the model to evaluate specific outbreak response strategies, then we would need to use serotype-specific model inputs and explicitly characterize the transmission and evolution of OPV viruses to address questions related to the development of circulating vaccine-derived polioviruses. Thus, although this work suggests that IB modeling offers an important opportunity to better characterize the actual dynamics of the spread of infection, using IB models appropriately for polio outbreaks will depend on obtaining high quality information about the nature of polioviruses, immunity, and social interactions.

5.0 Note

Supplementary material accompanies this paper on the Journal's website (http://journals.cambridge.org/hyg).

6.0 Acknowledgments

The authors received support from a grant to Kid Risk, Inc. from the World Health Organization Polio Research Committee. The findings and conclusions in this report are those of the authors and do not necessarily represent the views of the World Health Organization.

7.0 Declaration of Interests

None

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Appendix

Table 4-5summarizes the model inputs taken from the prior differential equation based model [1] for use in the individual-based model.

Figure 4-4 summarizes the results of our analysis of the R_0 achieved in the simulations for the different network structures, which shows how close the models came to using an R_0 of 13. To generate the histograms shown in Figure 4-4, we assume that all the individuals remain fully susceptible (i.e., in the upper-left state in Figure 2) except patient zero, which implies that all individuals can be infected repeatedly until patient zero moves to the Removed state. The x-axis gives the number of infections observed before the patient zero goes to the Removed state, and the y-axis gives the proportion of infected cases with this result in the sample of 500 runs.

Table 4-5 Summary of model inputs taken from the differential equation based model [1].

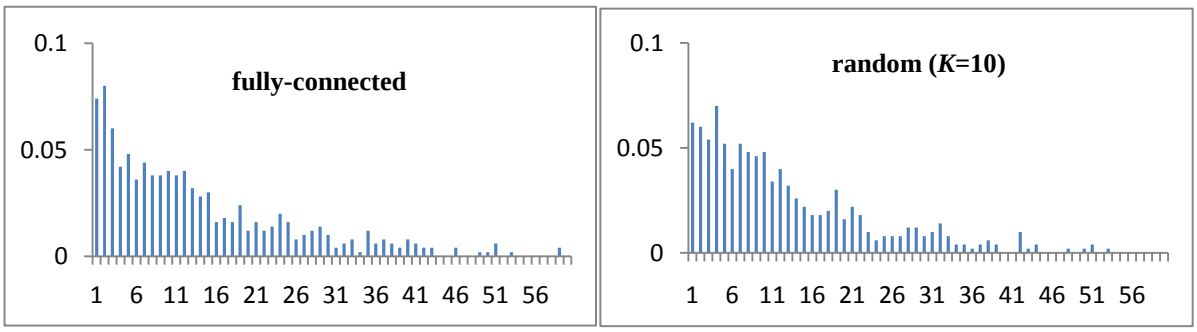
Model input (units)	Value	Sources [ref. nos.]	Notes
Basic reproductive number, R_0	13	[1-3]	Average number of secondary infections caused by one infection introduced to an entirely susceptible population assuming a low-income country [1]
Average duration of infection (days) For fully susceptibles For recent live For historic live For IPV only	 35 7 9 20	 [4-9] [5, 10-11] [6, 12] [5, 10-11]	
Relative susceptibility (proportion)			Probability that a partially infectible

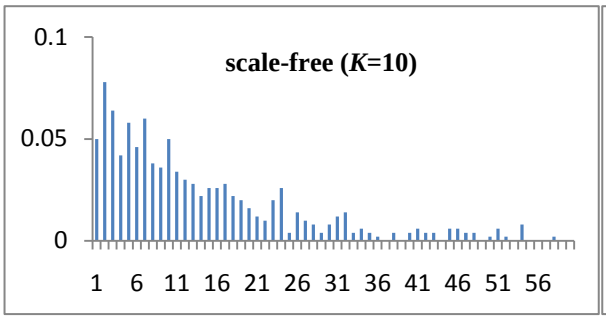
For fully susceptibles For recent live For historic live For IPV only	1 0.25 0.8 0.95	 [5, 10] [5, 10]	person in group acquires infection divided by the probability that a fully susceptible person acquires infection in an identical situation [1]
Relative infectiousness (proportion) For fully susceptibles For recent live For historic live For IPV only	 1 0.1 0.5 0.75	 [5, 10] [5, 10]	Probability that a partially infectible person in a group infects others divided by the probability that a fully susceptible person passes the virus to others in an identical situation [1]
Average duration of latent period (days)	2	[6, 10-11, 13-15]	
Average duration of incubation period (days)	10	[4, 13, 16]	Time from infection to onset of paralysis
Detection trigger for acute flaccid paralysis surveillance (cases)	1	[1]	
Half-life of secondary OPV infection rate after the response (days)	13.1	[1]	

Table 4-6 Summary of results of analyses performed to explore actual R_0 implied by different network and input choices used. Mean and standard error from a sample of 500 simulations are reported for each setting.

Network	**R_0 mean (standard error)**
differential equation based model	13
fully-connected	13.36 (0.60)
random (*K*=10)	12.73 (0.59)
scale-free (*K*=10, *p*=0.05)	13.13 (0.61)
small-world (*K*=10)	12.7 (0.56)
all-in-range (*K*=10)	13.41 (0.64)
mixing-site 1 (*S1=51, W1=17*)	12.94 (0.55)
mixing-site 1 (*S2=345, W2=115*)	12.99 (0.59)
mixing-site 1 (*S3=711, W3=237*)	12.97 (0.58)
mixing-site 2 (*S1=51, W1=17*)	13.05 (0.56)
mixing-site 2 (*S2=345, W2=115*)	13.10 (0.66)
mixing-site 2 (*S3=711, W3=237*)	13.23 (0.59)
mixing-site 3	13.01 (0.62)

Figure 4-4 Histograms of simulations exploring R_0 for networks, see Table 4-6 for a summary of the statistics.

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0.1
0.05
0
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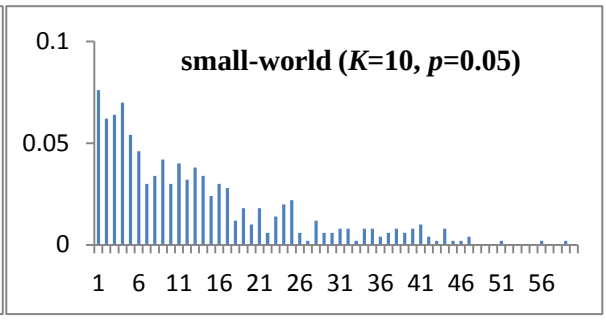
small-world (K=10, p=0.05)
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0.05
0
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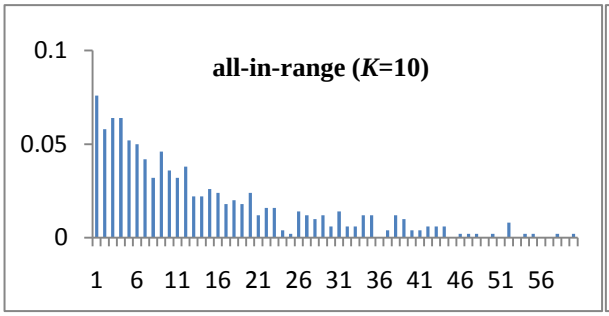
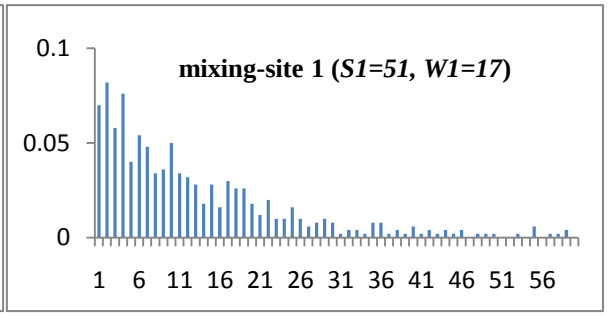

all-in-range (K=10)
0.1
0.05
0
1 6 11 16 21 26 31 36 41 46 51 56


mixing-site 1 (S1=51, W1=17)
0.1
0.05
0
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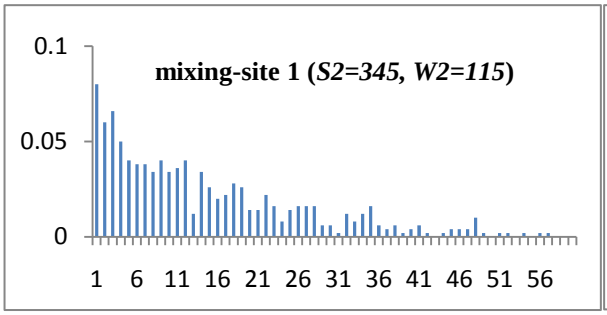
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0.1
0.05
0
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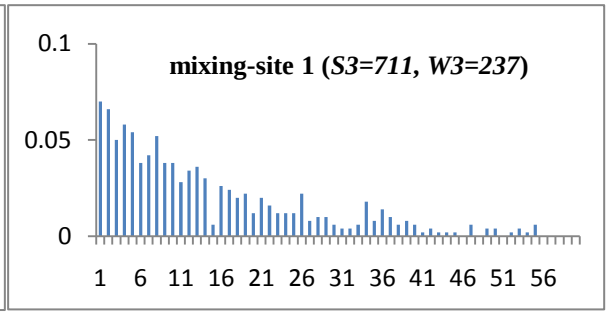
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0.05
0
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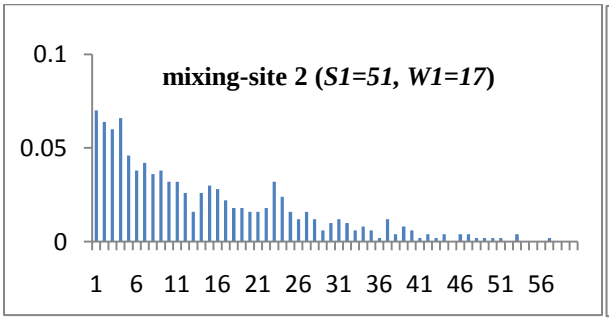
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0.05
0
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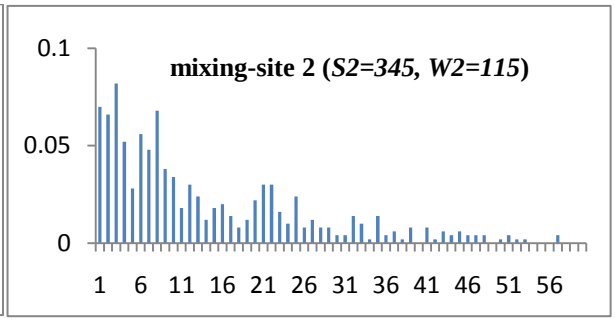
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0.1
0.05
0
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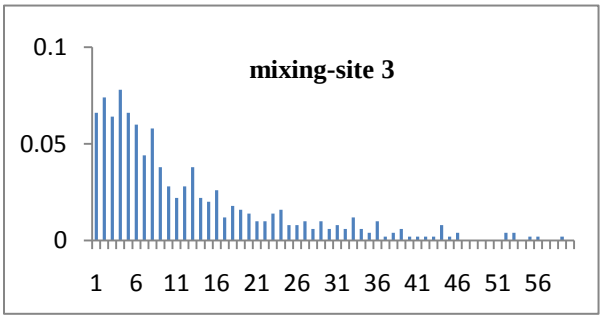
mixing-site 3
0.1
0.05
0
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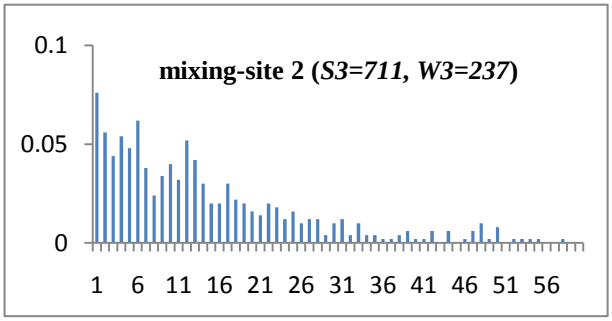
mixing-site 2 (S3=711, W3=237)
0.1
0.05
0
1 6 11 16 21 26 31 36 41 46 51 56

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