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Varicella Infection Modeling

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Abstract

Infectious diseases can spread rapidly through healthcare facilities, resulting in widespread illness among vulnerable patients. Computational models of disease spread are useful for evaluating mitigation strategies under different scenarios. This report describes two infectious disease models built for the US Department of Veteran Affairs (VA) motivated by a Varicella outbreak in a VA facility. The first model simulates disease spread within a notional contact network representing staff and patients. Several interventions, along with initial infection counts and intervention delay, were evaluated for effectiveness at preventing disease spread. The second model adds staff categories, location, scheduling, and variable contact rates to improve resolution. This model achieved more accurate infection counts and enabled a more rigorous evaluation of comparative effectiveness of interventions.

ACKNOWLEDGEMENTS

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NOMENCLATURE

ACIP	Advisory Committee on Immunization Practices
CASoS	Complex Adaptive System-of-Systems (concerning a specific system) or Complex Adaptive Systems-of-Systems (concerning the field of systems)
CDC	Centers for Disease Control and Prevention
CLC	Community Living Center
CSV	Comma Separated Value
Cust	Custodian
DIN	Dining room
DOH	Department of Health
FSW	Food Service Worker
GUI	Graphical User Interface
HCW	Health Care Worker
HOSP	Hospice unit
Hosp NA	Hospice Nurse's Aide
Hosp Nur	Hospice Nurse
Hosp Pat	Hospice Patient
LTC	Long term care unit
LTC NA	Long-Term Care Nurse's Aide
LTC Nur	Long-Term Care Nurse
LTC Pat	Long-Term Care Patient
MICU	Medical Intensive Care Unit
Med Off	Medical Officer
MMRV	measles, mumps, rubella, and varicella
NCIRD	National Center for Immunization and Respiratory Diseases
NS	Nurse's station
RN	Registered Nurse
Sandia	Sandia National Laboratories
SEIR	Susceptible, Exposed, Infectious and Recovered (disease progression)
SME	Subject Matter Expert
STC	Short-Term Care unit
STC NA	Short-Term Care Nurse's Aide
STC Nur	Short-Term Care Nurse
STC Pat	Short-Term Care Patient
VA	Department of Veteran's Affairs
VHA	Veterans Health Administration
VAMC	VA Medical Center
VZIG	varicella zoster immune globulin
VZV	varicella zoster virus

1 Introduction

The Office of Public Health, United States (US) Veterans Health Administration (VHA) is engaged in a collaborative research program with the Complex Adaptive System of Systems (CASoS) Engineering group at Sandia National Laboratories (Sandia). The current program continues the long-standing research partnership between the institutions aimed at applying advanced modeling and simulation methods to large-scale emerging problems in public health and healthcare management. In 2012, the second year of the current research program, work has focused on leveraging the modeling capability developed in the first year to address policy issues of current interest to VHA leadership. This document describes current status of research efforts as of December 15, 2012.

Prompt actions by VHA officials effectively curbed a varicella infection in a VA hospital in San Juan, Puerto Rico and prevented a large-scale outbreak. The current work seeks to develop an analysis framework to evaluate several potential intervention actions to curb the spread of in-facility infections and to quantify the reliability and robustness of these interventions for a range of patient populations.

The multi-level approach used in this Varicella infection modeling effort gives decision makers the flexibility to answer a variety of questions based on the outbreak scenario, interventions under consideration, and the available data. This approach also allows for comparison of the effectiveness of models of varying levels of resolution.

The most aggregate-level model focuses on infection propagation through a notional and approximately static contact network, with very little detail about the specific environment. Development on this model is complete.

The more intermediate-resolution model, a dynamic patient/staff mixing model, is an agent-based representation of the dynamic interactions of individuals, each of which belongs to one of several different classes of people. Although the Sandia CASoS group frequently utilizes this style of agent-based modeling, for this research activity the approach has been extended so that the contact patterns are dynamic, reflecting the arrival and departure of patients and staff. It is also capable of explicit representation of specific locations throughout a facility (or group of facilities) and the likelihood that individuals from each class of people will be in each location by time period across the analysis horizon. These capabilities allow for higher-resolution contact estimates, evaluation of different staffing models, and examination of more complex interventions (e.g. closing the dining room and delivering trays to rooms). Development on this model has also been completed.

The most detailed model, a discrete-event simulation-based operations model, includes explicit representation of specific locations and the probabilistic movement of patients (including transfers between units and use of medical testing facilities) and different types of staff between these locations across the analysis horizon. It has a detailed representation of shifts for staff as well as detailed tracking and maintenance of patient-to-staff ratios across wards and units. This model has been designed as a discrete event simulation because it is primarily an operations-style model. This model has been designed but not yet fully implemented. Although the approach here mirrors the real world quite closely it carries a significantly high data burden. One intent of this documentation is to inform Sandia-VHA discussions on the relevance of pursuing this level of

detailed modeling and, if interest exists, the creation of a plan to acquire the necessary data. Hence, this document emphasizes descriptions of the model structure, the types of questions it is designed to address, and data requirements in contrast with the less detailed modeling approaches. All three levels of models can provide value through differing capabilities and data requirements.

1.1 Background on Varicella Outbreak Event in San Juan

In December 2011, the San Juan VA Medical Center (VAMC) experienced an outbreak of Varicella within the Community Living Center (CLC) and the Medical Intensive Care Unit (MICU). The first signs of the outbreak came on December 12 when two nurses from the CLC called in sick with symptoms of chickenpox. Two days later, a CLC resident developed a rash and fell seriously ill with chicken pox (Wentzell, 2012). Between the 13th and 19th days after the resident fell ill, 11 more staff and two other patients fell ill, for a total of 13 confirmed cases of chickenpox.

The San Juan VAMC immediately screened all patients and staff within the affected units (and later all staff) and sent potentially-exposed employees who did not have immunity to chickenpox home on administrative leave (furlough). They also controlled entry to affected units. There was a coordinated effort between the VISN-8 Emergency Management Office, VHA leadership (both regional and Central Office), the Centers for Disease Control and Prevention (CDC), US Department of Health (DOH), and Puerto Rico Department of Health to help control the outbreak. Almost 900 doses of vaccine were needed for 429 staff. Replacement staff (11 registered nurses [RNs]) had to be found to avoid having to turn away patients (Wentzell, 2012). The final case was reported on December 31.

During the outbreak, the US Department of Veteran's Affairs (VA), Veterans Health Administration (VHA) requested decision support from Sandia National Laboratories' (SNL's) Complex Adaptive Systems of Systems (CASoS) Engineering group. The VHA's immediate concern was that the aggressive nature of the virus, the immunocompromised patient population, and staff cultural norms and demographics might combine in non-linear ways to create a major infectious disease outbreak. Analysis was performed to identify critical leverage mechanisms in the disease propagation system and potential tipping points that could be exploited by decision makers to contain the infection. Conference calls between SNL modelers and VHA physicians began on Monday, December 19 while the outbreak was in progress.

1.2 Overview of Varicella

Varicella (Chickenpox) is a highly contagious, acute disease caused by the varicella zoster virus (VZV). The related recurrent infection is herpes zoster, more commonly known as shingles (Centers for Disease Control and Prevention [CDC], 2012). Primary infection (varicella) usually results in a generalized blistered rash with about 250-500 lesions and a mild fever (American Academy of Pediatrics [AAP], 2006). Serious complications of varicella include dehydration, pneumonia, bleeding problems, encephalitis, bacterial infections of the skin, sepsis, toxic shock syndrome, and bone or joint infections (CDC, 2011a). Varicella can be fatal. Individuals at increased risk for complications include infants, adolescents, adults, pregnant women, and immunocompromised people (CDC, 2011a).

Exposure occurs through close contact with an infectious person, either face-to-face or close indoor contact. The exact duration of contact necessary for transmission of the virus is the subject of some debate, but most experts agree that transitory contact is not sufficient (AAP, 2006). VZV enters the body through the respiratory tract and conjunctiva and has a typical incubation period of 14-16 days (CDC, 2012). The range for the incubation period is 10 to 21 days (CDC, 2012). The period during which an infected person is contagious ranges from approximately 1-2 days before the onset of the rash until after all the lesions have crusted over (typically 4 -7 days after onset of the rash) (CDC, 2007).

The single-antigen live attenuated vaccine for Varicella (VARIVAX®) was licensed for use in the United States in 1995 (CDC, 2012); a combination measles, mumps, rubella, and varicella (MMRV) vaccine (ProQuad®) was licensed for healthy children aged 12 months to 12 years in 2005 (CDC, 2007). Adults receive a two-dose regimen, with the second dose 4-8 weeks after the first (Merck & Co., Inc., 2012). Immunity develops over approximately 6 weeks (42 days). Varicella disease occurring more than 42 days after vaccination (breakthrough varicella) is usually mild, with fewer lesions, low or no fever, and a shorter duration of illness. However, approximately 25-30% of breakthrough cases are not mild, exhibiting clinical features more closely resembling those of unvaccinated cases (CDC, 2007). Vaccinated patients infected with varicella exhibiting fewer than 50 lesions have been shown to be one third as contagious as unvaccinated patients; however, those with 50 or more lesions were as contagious as unvaccinated patients (Seward, Zhang, Maupin, Mascola, & Jumaan, 2004).

For unvaccinated individuals known to have been exposed to an infected person (for example, a health care worker who has been treating an inpatient with Varicella), administration of the vaccine as soon as possible after exposure provides one potential mitigation strategy. Post-exposure vaccination appears to be effective in preventing full-blown varicella in children. There have been few published studies on the effectiveness of such vaccinations, but existing studies indicate a >90% chance of either preventing or reducing the severity of the disease when children are vaccinated within three days of exposure. This positive effect may not necessarily translate to adults, a population exhibiting a weaker immunological response to the first dose of varicella vaccine (Seward, Marin, & Vázquez, 2008). For those who cannot receive the vaccination and are at risk of severe complications, varicella zoster immune globulin (VZIG) can be administered to prevent or modify illness (CDC, 2007).

The Advisory Committee on Immunization Practices (ACIP) recommends that all healthcare workers be immunized against varicella at the start of employment (CDC, 2011b). If exposure occurs, the CDC's National Center for Immunization and Respiratory Diseases (NCIRD) recommends that healthcare workers without evidence of immunity should be offered the varicella vaccine within 3-5 days of exposure to the rash and should be furloughed from days 8 to 21 after exposure (Lopez & Marin, 2011).

2 Static Contact-Network Infection Model

As mentioned above, three models have been designed and two developed to examine the potential impacts of varicella infection-control strategies for the San Juan VA CLC. The use of a multi-level modeling approach to address this problem was discussed in the INFORMS presentation of Moore et al., (2012, p. 419). The first of our multi-level models is an aggregate-level, static contact-network infection model.

Social-network models can be used to examine the likely spread of disease through a region or facility by generating realistic contact patterns and simulating transmission between individuals. Examples of the use of social network models to study infection propagation include Meyers, Newman, Martin and Schrag (2003) and Christley et al., (2005). Social networks are represented using nodes and arcs, with nodes representing individuals and arcs representing connections between individuals. Nodes with large numbers of connections to other nodes are referred to as "highly connected." In the San Juan implementation for Varicella, staff members are represented as network nodes with a high degree of connectedness and patients are represented as nodes with lesser degrees of connectedness. The network structure for the San Juan analysis is described in greater detail in Section 2.2.

The contact-network infection model for San Juan implemented traditional SEIR infection dynamics using transition probabilities, attack rates, and R0 estimates from literature sources and personal communication with VA physicians. In the absence of information on staffing patterns and patient to patient and patient to staff interactions, notional contact networks were constructed algorithmically. These static contact networks were designed to enable different levels of connectivity among staff members, among patients, and between staff and patients. Varying parameters, thereby controlling the connectivity of each network component enabled evaluation of likely rates of propagation across each category of contact. These approximations of possible contact network structures within a facility were used to test alternative interventions for slowing the spread of varicella through the facility population.

The contact-network infection model is conceptually similar to the pandemic influenza model proposed by Davey and Glass (2008). Both models link three principal components to form a configurable simulation of infection spread and mitigation options.

1. SEIR infection dynamics
2. Contact network to approximate social interactions among members of the populations
3. Interventions to limit the spread of disease across the contact network

The Davey pandemic model was designed to simulate a different pathogen spreading across larger-scale community structures, so simple re-parameterization of that model to represent an individual health care facility as needed for the San Juan varicella case was not possible. The new contact-network infection model was developed to investigate the spread of varicella infections within a facility and identify relevant mitigations. It also includes a variety of potential interventions specific to the varicella case, including staff replacement and vaccination. The user interfaces for controlling parameters in this model are presented in Appendix A.

2.1 SEIR Infection Manifestation

A discrete variation of the traditional SEIR process was used to model infection progression for each individual in the simulation. The simulation proceeds by evaluating every potential person-to-person contact once per hour. Contacts between infectious and susceptible persons result in the susceptible person being exposed to the disease with a probability assigned as an input parameter. Exposed persons progress sequentially to the infectious and recovered phases. In this simulation, the time of residence of each person in each disease stage is assigned stochastically using a truncated normal distribution for which the mean and standard deviation in the stage duration are shown in Table 1. The disease stage names shown in Table 1 were selected to match the terminology used by VHA infectious disease physicians in exchanges during the San Juan incident. The stage duration distributions are shown in Figure 1. Distributions for modeled disease durations from initial exposure to end of infectious phase (scabbing of lesions) are illustrated in Figure 2.

Table 1: Disease stage start and duration times

Disease Stage	Expected Stage Start		Time in Stage, hours				Infectious
	Days	Hours	Mean	Min	Max	St.Dev.	
Susceptible	N/A	N/A	N/A	N/A	N/A	N/A	No
Latent	0	0	312	252	372	20.0	No
Pre-symptomatic	13	312	48	40	56	2.67	Yes
Symptomatic	15	360	120	100	160	6.67	Yes
Resistant	20	480	N/A	N/A	N/A	N/A	No
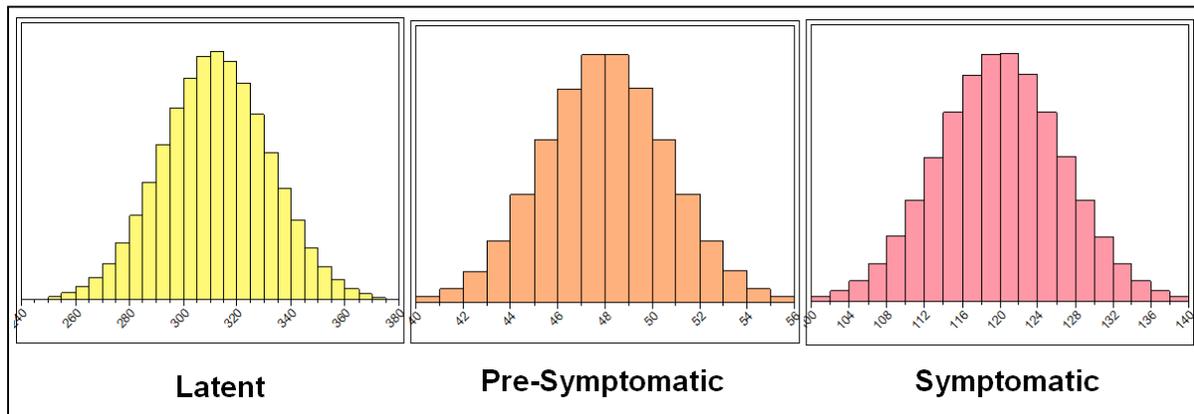
Figure 1: Histograms showing normal distributions of duration times in hours for modeled disease stages

Figure Note: X-axis represents time, Y-axis indicates frequency, and the height is frequency, N (the number of replicates) =1,000,000

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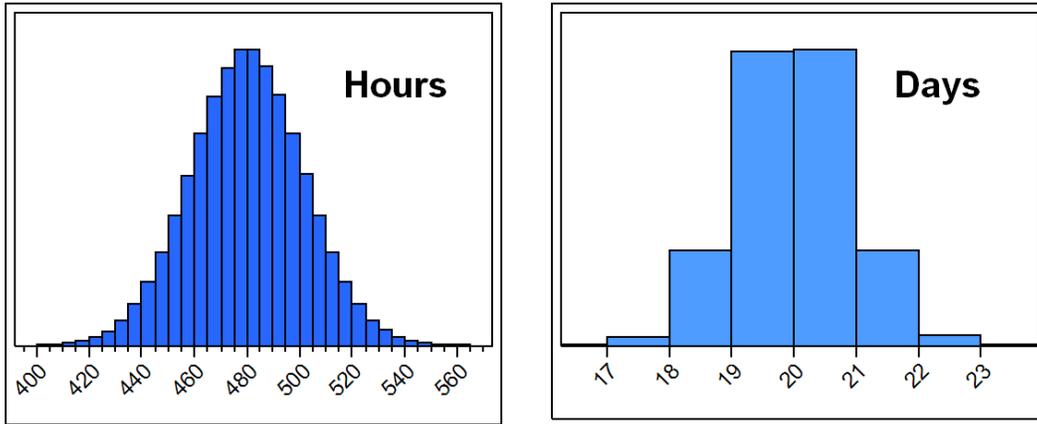
Figure 2: Histograms showing normally distributed disease process duration. Duration values include all stages from initial exposure to infectious stage termination.

Figure Note: X-axis represents time, Y-axis indicates frequency, and the height is frequency, N (the number of replicates) =1,000,000

2.2 Contact Network

The contact network for the San Juan facility model represents staff members as network nodes with a high degree of connectedness and patient as nodes with lesser degrees of connectedness (Figure 3). In designing the model, network concepts previously applied to other social networks composed of a densely-connected component joined to a sparsely-connected component, such as Pashtun tribal dynamics (Schubert, Moore, Finley, Hammer, & Glass, 2011) and gendered social networks (Moore, Finley, Hammer, & Glass, 2012) were incorporated.
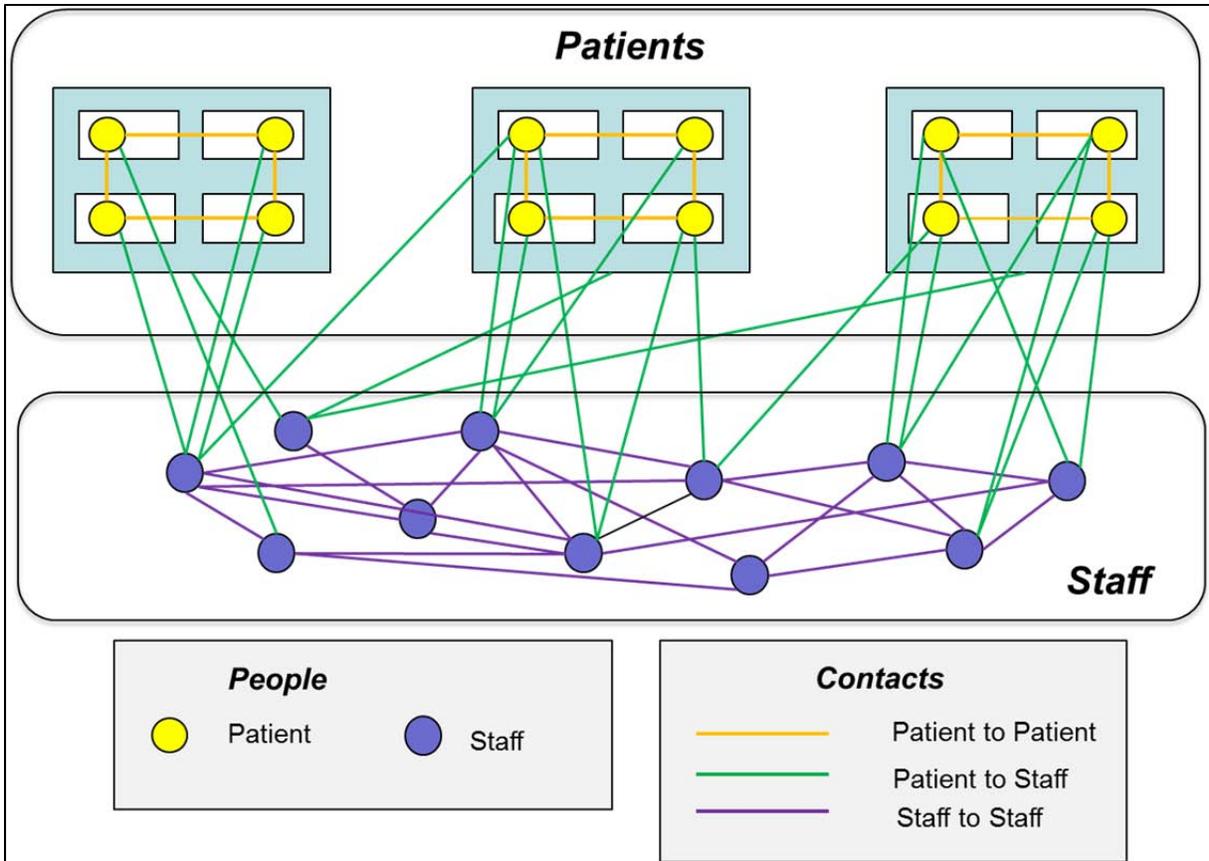
Figure 3: Schematic diagram showing notional view of contact network.

Figure Note: Staff-to-staff connections are more numerous than patient-to-patient connections.

The contact network was constructed at scales representative of the Community Living Center (CLC) units from which varicella cases were reported. Patient loads were assigned to match the census reported for the Long Term Care (LTC) unit at the San Juan facility (74 patients). Since exact staff counts were not available, we assigned variable values for staff count (36 to 75). While staffing differences between shifts would be expected to have an effect on disease transmission within the facility, shifts were not explicitly represented in this version of the model.

The network construction mechanism creates connections (edges) between nodes (which represent staff and patients). Connections are assigned according to a rule set with user defined input values. There are two components to this input, used in a similar way for the creation of all connection types (patient-patient, staff-patient, etc.). The first component is a goal, or expected number, of connections between pairs of individuals of specific types. These goals are based on subject matter expert guidance, and can be adjusted by the user if needed. The simulation will continue to add connections randomly between pairs of nodes until the mean number of connections for each type of relationship has approximately reached the goal. Since this process by itself could result in too few connections for some of the individuals (for example, an individual patient could have no contacts and this requirement could still be satisfied), a user-defined minimum number of connections may be set for each individual of a certain type. This

ensures that nurses are serving at least some patients and patients have someone taking care of them, to make the contact pattern more realistic.

Baseline counts for each contact type are assigned by surveying subject matter experts. Nursing professionals and LTC administrators familiar with LTC staffing standards and procedures provided estimates of expected staff and patient contact counts. The minimum and expected contact counts obtained from these experts are listed in Table 2. Average per-node connection counts obtained on 100 contact networks created by the above procedure are also shown in Table 2.

Table 2: Baseline connectivity values for LTC unit simulation
(Patient Count = 74, Staff Count = 36, 100 stochastic realizations)

Contact Type	Based on SME Input		Values Calculated via Simulation	
	Minimum	Expected/Goal	Mean	Std. Dev.
Roommate	1	1	1	0
Patient-Patient	1	16	16.34	4.47
Staff-Staff	2	22	19.46	4.78
Staff-Patient	2 per staff member	18 per staff member	17.91	4.20
Patient-Staff	3 per patient	6 per patient	8.72	2.04

2.3 Interventions

Sandia analyzed the impact of possible interventions on disease progression through a facility using this model. Following the theme of Sandia's prior work on pandemic influenza modeling, consideration was given both to single intervention strategies and also to potentially synergistic interactions when multiple interventions are combined to form a layered strategy. Interventions include targeted vaccination, furloughing of susceptible staff, cohort isolation of exposed patients, and application of improved infection control procedures.

2.3.1 Vaccination

The vaccination intervention in this model applies a delayed transition to immune state to selected persons within the simulations. Data on timing of onset of immunity following varicella vaccinations in adults are scant. Lopez and Marin (2011) indicated that a high percentage of immunity is probably exhibited by adults between 5 and 7 weeks following administration of the first of a two-dose regimen. In the absence of more detailed estimates of healthcare workers (HCW) and LTC patient development of resistance after immunization, the onset of immunity was modeled as a truncated normal distribution with a mean of 1008 hours (6 weeks) and a standard deviation of 56 hours, providing an approximate range from 5 to 7 weeks with a mean time to development of immunity of 6 weeks following immunization.

2.3.2 Staff Furlough

The staff furlough intervention removes selected susceptible members of the facility staff until they develop immunity or the disease outbreak is over. Two styles of furlough interventions were designed into the model: Furlough with Replacement and Furlough without Replacement.

Furlough with Replacement

Furloughing with replacement simulates staffing changes available to administrators when sufficient replacement staff members are available. In this intervention, selected nodes within the staff network are replaced by a staff node not previously a part of the network. The replacement node inherits the network connections previously held by the replaced node. The replaced node is disconnected from the facility network of staff-to-staff and staff-to-patient contacts and is marked as being located offsite. The model continues to process the disease progression of offsite nodes as well as their progress toward immunity if they have been vaccinated. As depicted in Figure 4, this intervention option maintains the same contact count per node after the intervention as was present before the intervention.
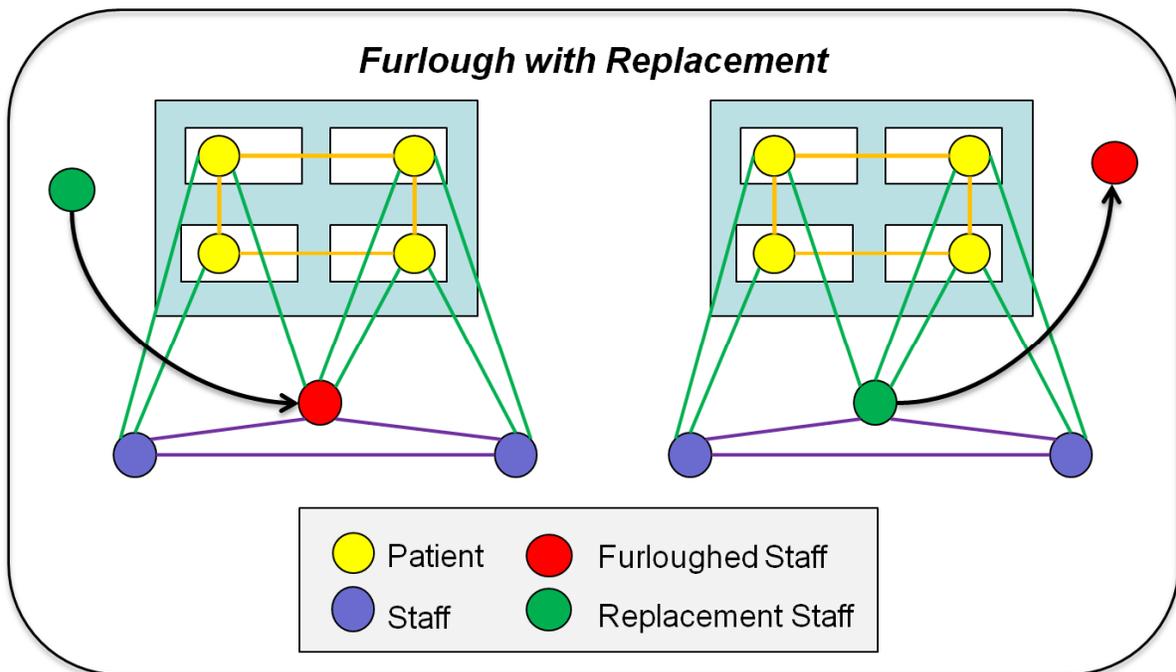
Figure 4: Diagram showing the operation of the furlough with replacement intervention.

Figure Note: The number and pattern of connections remains the same after intervention.

Furlough without Replacement

Furloughing without replacement simulates staffing changes required when replacement staff members are not available. In this intervention, selected nodes within the staff network are removed from the network, but no replacement nodes are inserted in their places. Existing contacts which formerly included the removed staff node are assigned to nearby nodes (Figure

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5). The replaced node, now disconnected from the facility network of staff-to-staff and staff-to-patient contacts, is marked as being located offsite. The model continues to process the disease progression of offsite nodes as well as their progress toward immunity if they have been vaccinated. As shown in Figure 5, this intervention option maintains the same contact count per patient node, but increases the contact count for each staff node. It is important to realize that this intervention may lead to unacceptably high patient-to-staff ratios. This outcome is one of the motivating factors for the creation of the more detailed agent-based patient/staff mixing model described in the next section.
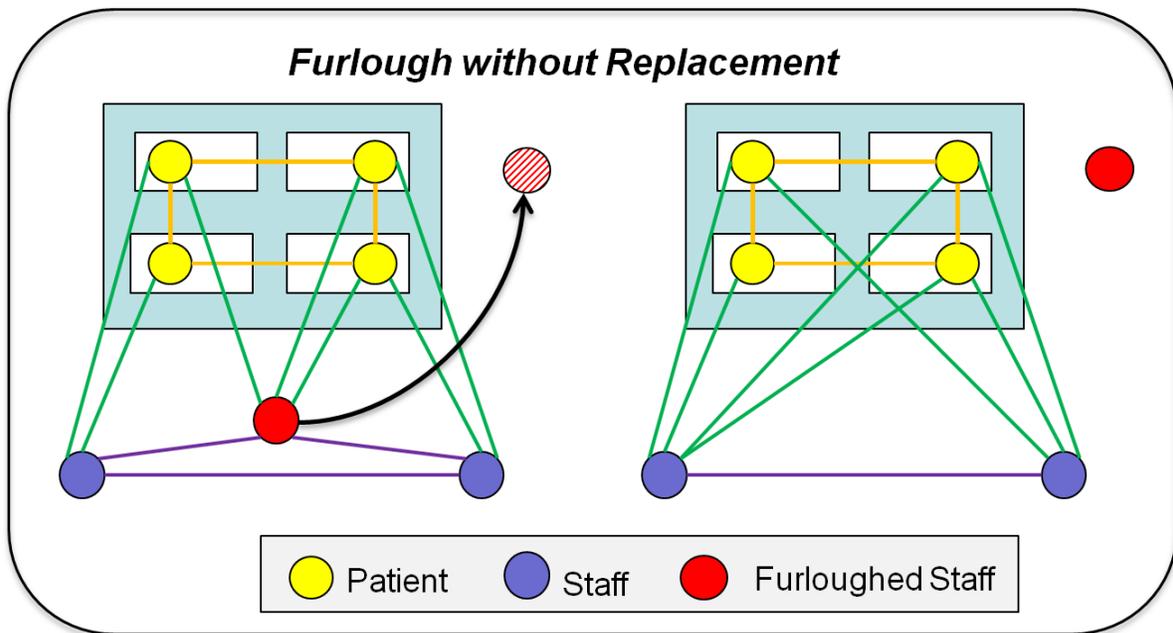
Figure 5: Diagram showing the operation of the furlough without replacement intervention

Figure Note: The number of connections to patients remains fixed while the number of connections between staff and patients increases after intervention.

2.3.3 Patient Cohort Isolation

The cohort isolation intervention creates groups of patients with similar disease status to avoid the spread of disease from infected to susceptible patients. Practices to keep sick-with-sick and well-with-well are common in nursing and epidemiology. Most often, cohort isolation takes the form of moving infected patients into a single room or ward to enable staff to care for them more effectively and to restrict their contact with patients who are believed not to have contracted the disease. Subject matter experts with whom we discussed varicella interventions discounted the potential effectiveness of physically moving infected patients between rooms as a way of combatting spread of the disease. In their judgment, the two- to three-day non-symptomatic infective state through which varicella patients pass before the appearance of lesions means that the roommate of a symptomatic patient has already been exposed by the time the rash becomes

visible. Shifting symptomatic patients into specific rooms while rooming non-symptomatic cases together was thought by our SME's to be ineffective at decreasing exposures. Such movement was projected to possibly increase patient exposure to infection, since a non-symptomatic infectious person could be inadvertently lodged alongside an unexposed patient.

To address these concerns, cohort isolation was implemented as two distinct stages (Figure 6). The first stage, termed "Isolate" in Figure 6, severs patient-patient contacts with all patients other than the symptomatic individual and his roommate. This operation effectively isolates the pair from interactions which could directly spread the disease to other patients. Operationally, this would be accomplished by restricting movement outside patients' rooms by for example delivering meal trays to the room, rather than allowing either patient to visit the dining room. The second phase, denoted as "Segregate" in Figure 6 entails moving patients so that two symptomatic individuals are collocated while their possibly-exposed roommates are collocated. Breaking the intervention into two stages permits us to evaluate the effectiveness of moving patients compared to simply instituting in-place isolation procedures for containing disease spread.
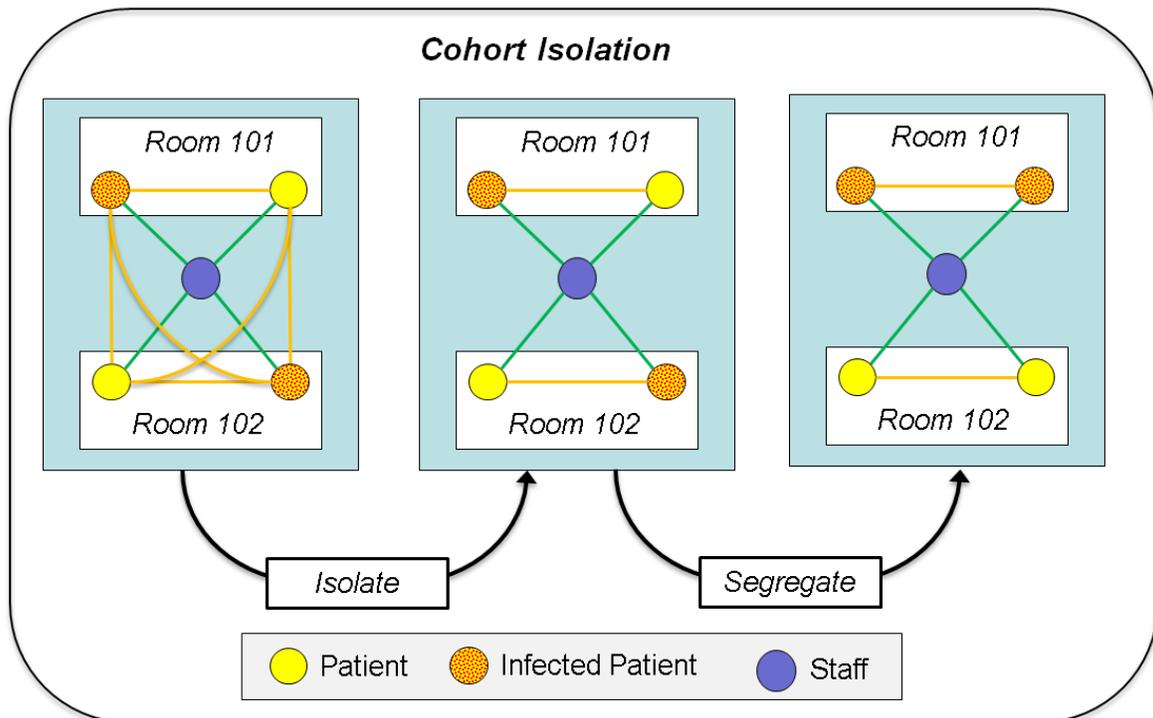
Figure 6: Diagram showing the operation of the cohort isolation intervention.

Figure Note: In the Isolate stage, patient-patient contacts are eliminated between sets exposed patients. In the Segregate phase, patients are transferred to co-locate persons with similar disease stages.

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2.3.4 Enhanced Infection Control

A range of infection control procedures can slow or limit the spread of disease in a facility through reducing exposures. These measures can take the form of PPE (gloves, masks, gowns, etc.), disinfectant gel, and disinfectant swabbing of keyboards and counter surfaces. We implement the enhanced infection control intervention in the model by diminishing (attenuating) the strength of the connections between patients and staff and between staff and staff (Figure 7).
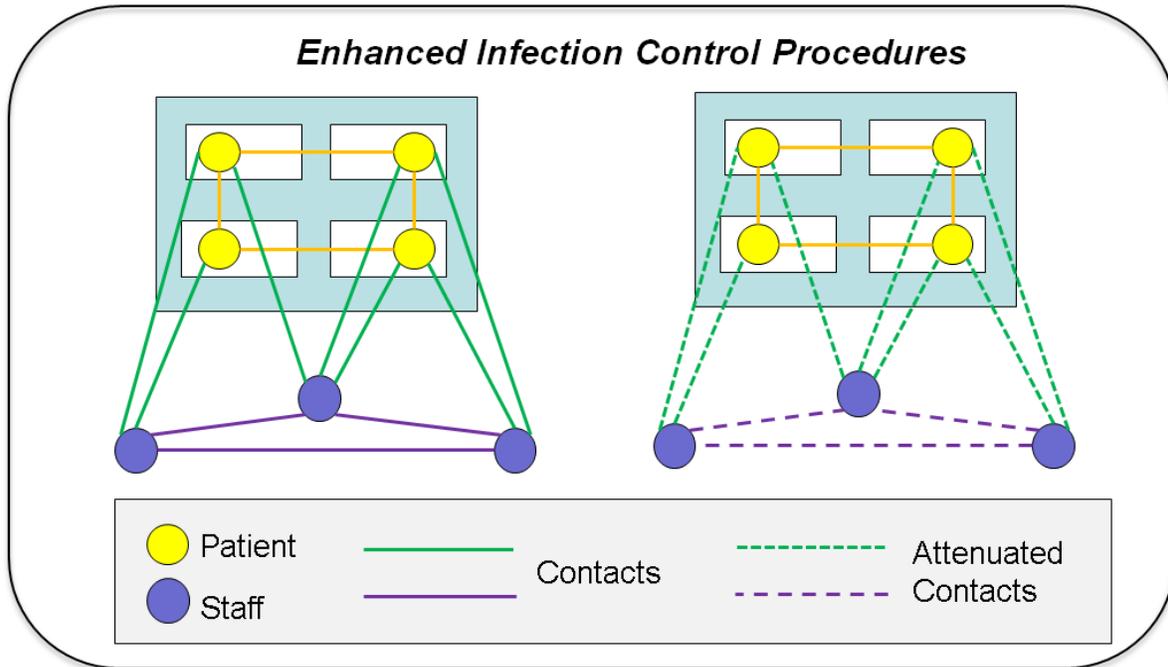
Figure 7: Diagram showing the operation of the enhanced infection control intervention

2.4 Input Parameters

We use variable input parameters to calibrate the model to correspond to clinical conditions and to experimentally examine the effects of these parameters on the progress of the modeled disease spread. Principal parameters used in the model are listed in Table 3.

Table 3: Runtime input parameters controlling infectivity

Parameter Name	Description	Baseline Value
Staff Turnover Per Month	Percentage of staff who are replaced in a month	4
Patient Turnover Per Month	Percentage of patients who are replaced in a month	15
Staff Immunity Rate	Mean immunity rate for staff members	0.85
Patient Immunity Rate	Mean immunity rate for patients	0.92
Max Generation	Number of infection generations at which simulation ends	10
Initial Patients Infected	Number of patients infected at start of simulation	1
Initial Staff Infected	Number of staff infected at start of simulation	2
Initial Generation	Generation number assigned to initial infected nodes	0

The contact network influences the number of infected individuals and the rate at which infection spreads through a facility. Parameters listed in Table 4 control the size, contact density and topology of the facility contact network.

Table 4: Runtime Input Parameters Controlling the Contact Network

Parameter Name	Description	Baseline Value
Staff Node Count	Number of staff members	36
Patient Node Count	Number of patients	74
Remote Probability	Exposure probability remote contacts	0.002
Close Probability	Exposure probability for close contacts	0.005
Int Probability	Exposure probability for intimate contacts	0.02
Combined Probability	Exposure probability for all contacts. (setting this parameter to non-zero applies single value to all remote, close, and intimate contacts)	0.02
Min Staff Connectivity	Minimum number of contacts each staff member has with other staff members	2
Min Staff To Patient Connectivity	Minimum number of contacts each staff member has with patients	2
Min Patient Connectivity	Minimum number of contacts each patient has with other patients	1
Min Patient To Staff Connectivity	Minimum number of contacts each patient has with staff members	3
Staff Connectivity	Expected number of contacts each staff member has with other staff members	18
Staff To Patient Connectivity	Expected number of contacts each staff member has with patients	18
Patient Connectivity	Expected number of contacts each patient has with other patients	18
Patient To Staff Connectivity	Expected number of contacts each patient has with staff members	6

2.5 Initial Modeling results

We ran the model to determine which interventions are most effective at reducing varicella infections in a facility. Additionally, we were able to examine the importance of rapid application of interventions. The remainder of this section describes the key insights gained from those experiments.

2.5.1 Intervention Effectiveness

All interventions reduce the number of infections over the base case (Figure 8). Interventions vary in effectiveness ranging from approximately two infections prevented by isolation and cohort segregation up to approximately five infections prevented by enhanced infection control.
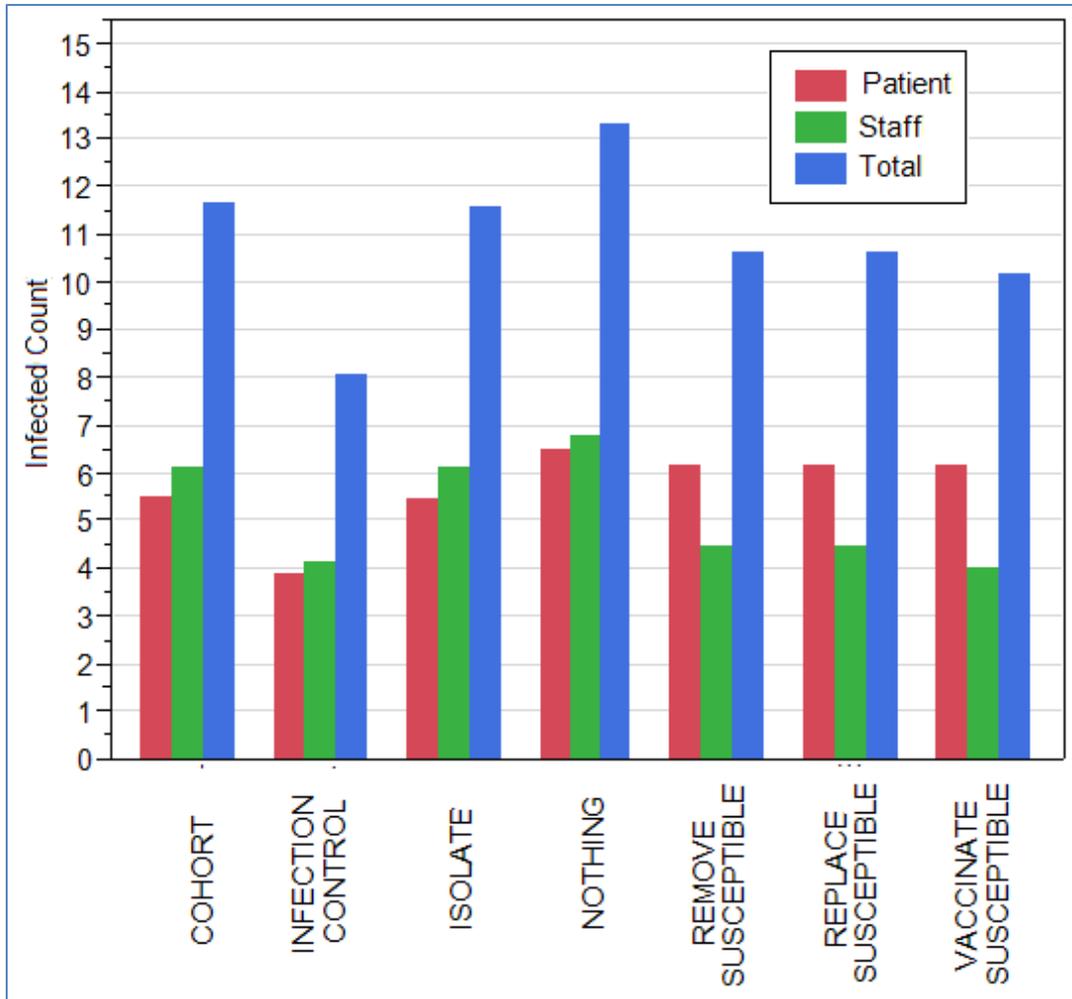
Figure 8: Effect of interventions on numbers of infections

Figure Note: Each bar represents the mean value of 100,000 replicates with input values from Tables 3 and 4.

Although the most effective single intervention is enhanced infection control, its advantage over other interventions may be illusory. The infection control intervention assumes a 25% improvement in infection control effectiveness among staff members and between staff members and patients. While the 25% improvement estimate is arbitrary, the dramatic improvement in outcomes due to enhanced infection control suggests that increased vigilance paid to simple procedures such as hand washing, hand gel, surface disinfection and PPE can yield significant improvements.

Isolation of infected patients and segregation of symptomatic and non-symptomatic cohorts have similar effectiveness. Each is slightly more effective within patient populations than for staff populations. Although these interventions generate essentially identical responses at the modeled input parameters, cohort segregation often performs less effectively than simple isolation at other reasonable input settings. In these cases, presumably the advantage of segregation is outweighed

by the chance of transferring an exposed but non-symptomatic person to a room with susceptible patients.

Furloughing of staff members is shown to be effective in all tested variants. As expected, the greatest benefit of furloughing is fewer staff infections, although each intervention reduces mean patient infections to a certain degree.

2.5.2 Initial Infection Count

The modest improvement in infection prevention shown by interventions in Figure 8 is in part due to the seeding scheme adopted in the base case runs. To more closely match the reported conditions at the San Juan CLC, the model was run with three initial infections, two staff and one patient. Seeding the model with three infected individuals (the three-point case) results in substantial spread of the infection before the index cases become symptomatic and interventions can be initiated. To illustrate this point, we duplicated the model runs shown in Figure 8 with a single patient and a single staff member serving as the index cases. Initializing the model with a single infected individual (center and right-hand panels of Figure 9) results in fewer total infections across all interventions. Additionally, the effectiveness of each intervention is enhanced relative to the base case (labeled "NOTHING" in Figures 8 and 9) when the model is initiated with a single point of infection.
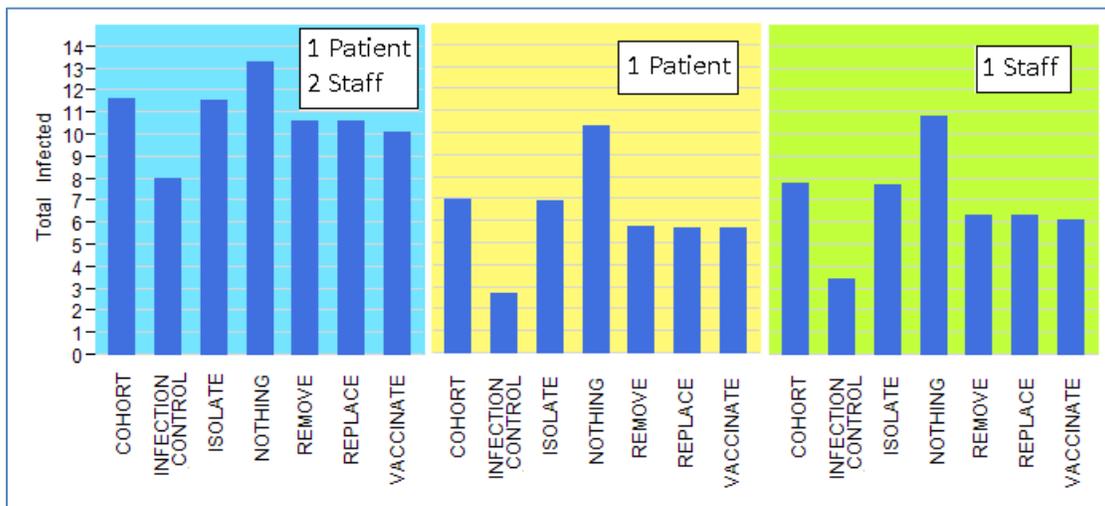
Figure 9: Effect of initial infection configuration on effectiveness of interventions.

We interpret the pattern shown in Figure 9 to indicate the importance of early intervention action. The three-point initial condition shown in the left-hand panel of the figure can be thought of as initiating the simulation at one generation farther along than the single point source examples shown. That is, the true point source for the three-point case is unknown, and the infection has spread substantially through the facility by the time the three index cases become symptomatic. For the three-point case the mean effectiveness of the interventions (excluding enhanced infection control) is 2.4 infections prevented. For the single point source cases the mean intervention effectiveness is 4.1 infections prevented. Thus, applying interventions when the actual index case appears nearly doubles the effectiveness of all interventions compared to waiting until the next generation becomes symptomatic.

2.5.3 Intervention Delay

Delaying the start of intervention increases the number of infections generated by model runs (Figure 12). In the case of a three-point source initial configuration (Figure 12, Left), beginning furloughing immediately upon detection of the first symptomatic individual results in a mean intervention effectiveness of 2.3 infections prevented. Delaying intervention for five days halves the intervention's effectiveness. Delays of 18 or more days obviate the beneficial effects of the intervention. The single point source initial configuration shows that immediate intervention can prevent 5.5 infections, while waiting until 30 days after the first appearance of symptoms yields little useful improvement from furloughing interventions. These results indicate that immediate application of accepted interventions is needed to generate useful benefit from those interventions.
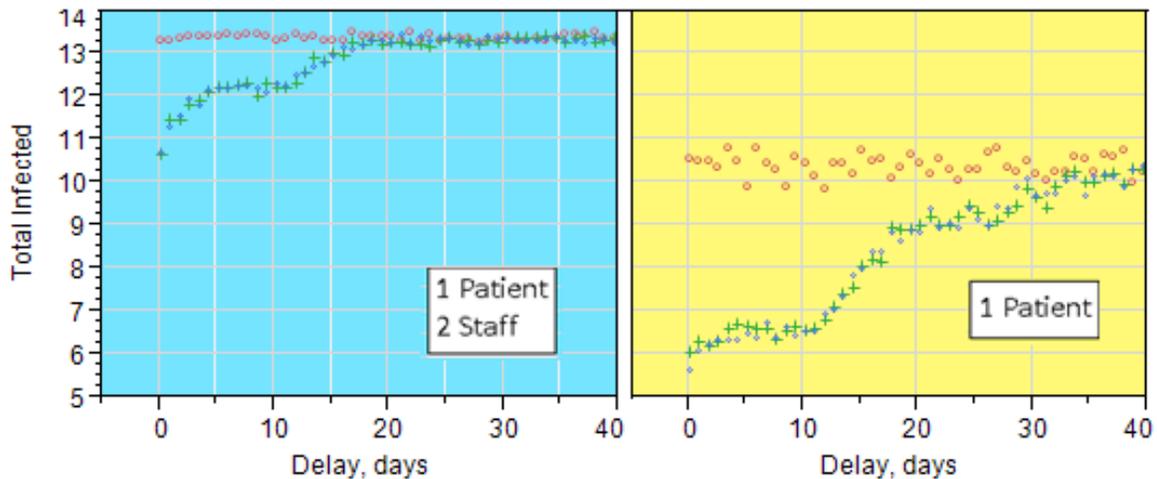
Figure 10: Impact of intervention delay on effectiveness of interventions

Figure Note: Panels represent different initial infection configurations. Red circles represent infected individuals in the absence of interventions. Green plus signs represent infected individuals when the furlough intervention is applied.

2.6 Advantages of Moving to a More Detailed Model

The model described in this section has the advantage that it does not require a great deal of facility-specific data. However, there are several drawbacks to the use of a high-level model for this type of analysis, which made a more detailed model desirable. The dynamic patient/staff mixing model, described in the upcoming section, was developed to meet this need.

The more detailed model includes explicit representation of specific locations throughout a facility (or group of facilities) and the likelihood that individuals from each class of people will be in each location by time period across the analysis horizon. This allows for a higher resolution contact estimate, evaluation of different staffing models, and examination of more complex interventions (e.g. closing the dining room and delivering trays to rooms) based on a newfound understanding of where the transmission risks are greatest. The more detailed model also includes a more realistic representation of staff shifts, reflecting the number of people really in

the system (and the associated changed in interaction patterns) more accurately. Another key addition in the patient/staff mixing model is the representation of different types of staff (for example, custodians versus nurses). Their interaction with each other and with patients would be very different, so the ability to represent staff types separately is key to developing realistic contact patterns.

Finally, the more detailed model allows representation of different units for patients within the CLC. This makes it possible to vary the immunity rates by individual unit population and assign different activity patterns to patients from different units. For example, a hospice patient is likely to be less mobile than a patient in long-term care, and might therefore spend a higher proportion of time in their room.

3 Dynamic Patient/Staff Mixing Model

In the more aggregate contact network infection model described in Section 2 for Varicella, the hospital contact network was generated algorithmically to represent different contact rates for patient-patient, patient-staff, and staff-staff contacts. In this dynamic model, the concept of location has been included to help generate patient and staff contact patterns. Patients and staff move from location to location probabilistically based on SME estimation of typical time spent in each area. This allows for higher resolution contact estimates, evaluation of different staffing models, and examination of more complex interventions (e.g. closing the dining room and delivering trays to rooms).

3.1 Cases for Analysis

Six scenarios were analyzed using this model: a Base case with no interventions; Furloughing all susceptible staff without replacement; Furloughing all susceptible staff with replacement; Furloughing all susceptible staff with return; Specialized nurses versus team nursing model; Isolation of patients based on immune/susceptible/infected status.

3.1.1 Base case

The baseline case represents normal operations within the CLC. Patient, staff, and immunity rate data used in this analysis are derived from actual VHA data for the San Juan CLC facility in December 2011 where available (for example, patient census, arrival rate, and average length of stay). Where actuals were not available, realistic estimates were made. Immunity rates for patients are based on email exchanges with VHA staff at the time of the incident.

Patients considered in this analysis include approximately 112 patients, divided into three units (long term, short term, hospice)

- A mean of 74 "long term" patients
  - mean arrival rate of 139 per year (Poisson arrivals)
  - mean length of stay of 193 days (exponential distribution)
  - *92% vaccinated or immune to varicella*
- A mean of 25 "short term" patients
  - mean arrival rate of 225 per year (Poisson arrivals)
  - mean length of stay of 40 days (exponential distribution)
  - *97% vaccinated or immune to varicella*
- A mean of 13 "hospice" patients
  - mean arrival rate of 180 per year (Poisson arrivals)
  - mean length of stay of 25 days (exponential distribution)
  - *41% vaccinated or immune to varicella*

We assume that patients are admitted directly to one of the CLC facility's three units and are eventually discharged from that same unit. There are no transfers between these units.

For staff, the numbers below show the number "on duty" at any given time. Depending on how many shifts are implemented, the total population numbers are 3-4 times higher. Exact shift

schedules and staff numbers of these types specifically for the San Juan CLC were not available, so simplified estimates were used.

- 20 nurses (three 8-hour shifts, 7 days a week)
    – 12 "long term care" nurses
    – 6 "short term care" nurses
    – 2 "hospice care" nurses
- 5 medical officers (two 12-hour shifts, 7 days a week)
- 5 food service workers (two 12-hour shifts, 7 days a week)
- 2 custodians (three 8-hour shifts, 7 days a week)
- 30 nurse's aides (three 8-hour shifts, 7 days a week)
    – 19 "long term care" nurse's aides
    – 7 "short term care" nurse's aides
    – 4 "hospice care" nurse's aides

A vaccinated or immune rate of 85% was used where not specifically defined.

Varicella follows a Susceptible, Exposed, Infectious and Recovered progression (SEIR). In this model, the terminology used for each state is Latent, Pre-Symptomatic, Symptomatic, and Recovered. Recovered individuals are considered immune. VZV enters the body through the respiratory tract and conjunctiva, and has a typical incubation period of 14-16 days (CDC, 2012).The range for the incubation period is 10 to 21 days (CDC, 2012). The period during which an infected patient is contagious ranges from about 1-2 days before the onset of the rash until after all the lesions have crusted over (typically 4-7 days after the onset of the rash) (CDC, 2007). Given this information about the progression of the illness, mean times in each disease state are:

- Latent: 13 days
- Pre-Symptomatic: 1.5 days
- Symptomatic: 5 days
- Recovered: all days thereafter

It is assumed for the purpose of this model that time spent in each disease state is exponentially distributed.

Individuals have two labels with regard to their susceptibility. The first is their actual susceptible versus immune status as determined by an initial draw from a probability distribution. The second involves whether they have been *identified* as susceptible. The two labels are not necessarily the same in every case, since there is some error associated with oral history and serological screening. Identification of susceptible staff has an error rate determined by a parameter for the run. In the results that follow, the error rate used is 0.05. Screening is limited by a "bandwidth" scenario parameter, to reflect the fact that testing and/or interviewing takes time and only a certain number can be completed per day. The bandwidth parameter used for the results in the following analyses was 200. There is also assigned an "identification delay" factor associated with the time it takes to get test results back, which in this case is set to 2 days. A "mitigation delay" factor is assigned to account for the time it takes for a mitigation strategy decision to be made once the first individual becomes symptomatic.

The locations represented in the model include:

- Long-term care unit (LTC) with 50 rooms
- Short-term care unit (STC) with 30 rooms
- Hospice unit (HOSP) with 20 rooms
- Dining room (DIN)
- Nurse's station (NS)
- Off duty or away (no transmission or infection occurs here)

The patients and staff represented include:

- Long-Term Care Patients (LTC Pat)
- Short-Term Care Patients (STC Pat)
- Hospice Patients (Hosp Pat)
- Long-Term Care Nurses (LTC Nur)
- Short-Term Care Nurses (STC Nur)
- Hospice Nurses (Hosp Nur)
- Long-Term Care Nurse's Aides (LTC NA)
- Short-Term Care Nurse's Aides (STC NA)
- Hospice Nurse's Aides (Hosp NA)
- Medical Officers
- Food Service Workers
- Custodians

In the base case, nurses have an equal likelihood of being in any of the rooms within their unit, but will very rarely go to rooms in another unit. Nurse's aides also only work within a specific unit. Both nurses and nurse's aides can be in their units or in the nurse's station.

The simulation monitors the nurse-patient ratios to ensure that the ratios do not drop below legally required levels as nurses become ill or are furloughed. If the ratios get too low, existing patients are not discharged, but new patients are turned away until the ratio becomes acceptable again. The simulation tracks the number of patients turned away due to reduced staffing levels if applicable.

The model determines the location of each individual during a given time period (in this case, one hour) based on the probability of that type of person being in a given location during a certain "type" of time period. In this case, the time period "types" are daytime non-meal times (default), meal times (6am-8am, 11am-1pm, 5pm-7pm), and nighttime (8pm-5am). The probabilities used for our analysis are shown in tables presented in Appendix B.

Since time spent in these locations may vary and there is uncertainty around the values given, the values in this table are used as mean values. A Dirichlet distribution is used to represent the uncertainty in these values. This distribution allows the probabilities within each row (representing a "draw" from the distribution) to vary while ensuring that the probabilities still add up to 1. An example of the resulting distributions is illustrated in Figure 11, below.
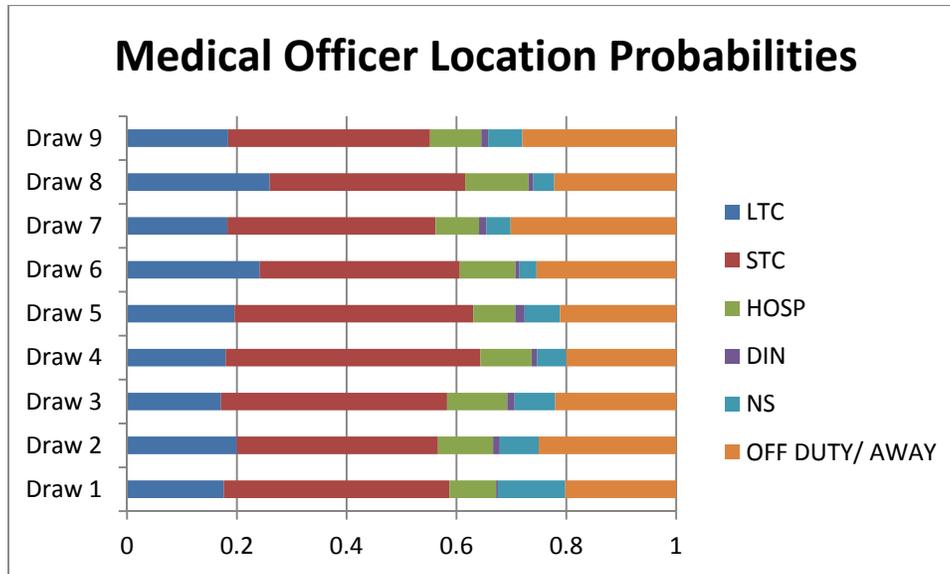
Figure 11: Example of draws from the Dirichlet Distribution for Medical Officer Location probabilities

Figure Note: These draws are used to incorporate uncertainty around the actual location probabilities for different types of people in the model. Each draw represents a location probability distribution assigned to an individual when they enter the model. Note that while the probabilities vary, they still add up to 1 for each draw.

Once the set of individuals in a given location during the current time period is determined, a probability of interaction is used to determine whether actual contact occurs. Since this level of detail was unavailable for the San Juan facility, summary data from Polgreen, Tassier, Pemmaraju and Segre (2010) was used to estimate the probabilities. Their research effort, which attempted to prioritize vaccination of healthcare workers against influenza, recorded 6,654 contacts by 148 workers in 15 categories by observing their movements throughout the day. Contacts were defined as approaches within approximately 0.9m. (Polgreen et al., 2010). Using data shown in Table 1 of the Polgreen paper, the number of contacts per hour per person between each pair of employee types and patients was generated (contact table is presented in Appendix C).

Given that two people have made contact, two additional factors impact the probability of transmission. The first is the default probability of transmission given that two individuals interact, a likelihood defined by the modeler (the default used is .85 to reflect a reasonable attack rate for varicella). The second is the disease state and/or susceptibility of the interacting individuals (recovered or immune, symptomatic, etc.).

3.1.2 Furloughing all susceptible staff without replacement

In this scenario, all of the workers who are not vaccinated or immune at the start of the simulation are sent home for the duration of the outbreak (from the time of the first infected individual's arrival through the end of the simulation after all infected individuals have recovered, with a delay built in to reflect time to diagnose the infected patient and identify individuals who are not immune). ACIP recommends furloughing unvaccinated health care

providers who have no evidence of immunity and who are exposed to VZV. Exposed susceptible individuals are potentially infective 8-21 days after exposure (CDC, 2011b, p. 23). The furloughing of staff without replacement is likely to put nurse-patient ratios below acceptable levels: this potential consequence is tracked in the model as the number of new patients that must be turned away (if any) due to inadequate staffing.

3.1.3 Furloughing all susceptible staff with replacement

In this scenario, all workers who are not vaccinated or immune at the start of the simulation are sent home for the duration of the outbreak (from the time of the first infected individual's arrival through the end of the simulation, with a delay built in to reflect time to diagnose the infected patient and identify individuals who are not immune). Susceptible staff members are replaced by staff with immunity. ACIP states that recently vaccinated health care providers do not require any restriction on their work activities (CDC, 2011b, p. 23).

3.1.4 Furloughing all susceptible staff with return

In this scenario, all workers who are not vaccinated or immune at the start of the simulation are vaccinated and then sent home for the duration of the outbreak (from the time of the first infected individual's arrival through the end of the simulation, with a delay built in to reflect time to diagnose the infected patient and identify individuals who are not immune). Susceptible individuals who have been vaccinated are not replaced but are considered immune after 6 weeks (42 days) and may then return to work. ACIP recommends that health care providers without evidence of immunity receive two doses of vaccine administered 4-8 weeks apart (CDC, 2011b, p. 23).

3.1.5 Specialized nurses versus team nursing staffing model

There is an assumption that contact patterns have significant impacts on the spread of airborne diseases (Salathé et al., 2010). There is no consensus on the duration of contact required to become infected through close proximity: experts suggest anywhere from five minutes to an hour (CDC, 2011b, p. 23). However, it is rational to assume that a person will experience more contagious events (e.g., sneeze or cough) during longer periods of close contact than for shorter ones. Hashemian, Stanley and Osgood (2012) have shown that incorporating a micro-contact dataset (daily inter-person contact patterns) with infectious disease models can yield results consistent with case counts found in a study population. Meyers et al., (2003) and Ueno and Masuda (2008) have identified doctors and other health care providers as the main transmitters of diseases in hospitals and recommend restricting the visits of these staff members to different wards.

In this scenario, the comparative impacts of nurses serving patients in all CLC units versus serving a specific ward (long term care, short term care, or hospice) were explored. This scenario is analyzed using a "team nursing" model in which nurses work across any of the care units, making them equally likely to be in any patient "rooms" when not at the nurse's station. The default scenario under which this does not occur is referred to as "specialized nursing."

3.1.6 *Isolation of patients based on immune/susceptible/infected status*

For this scenario, the model is configured with an isolation unit for infected patients. Once identified as infected, patients are moved to a unit in which only immune (serologically verified) or infected patients reside. Only immune staff can serve this population. In this analysis, the roommates of infected patients are not placed in isolation in response to their presumed exposure (as they were in the static contact network model Patient Cohort Isolation scenario). However, both types of isolation can be represented in either model.

A simulation by Laskowski et al., (2011) demonstrated that patient-oriented policies (e.g. masking infected patients) tended to have a larger effect on controlling the spread of infection compared to health care provider-oriented policies (masking or furloughing infected nurses), suggesting that extending this scenario to examine more detailed patient-level interventions could be quite valuable.

Since a decision to isolate symptomatic patients is a likely first step during outbreaks of highly-contagious viruses, this intervention is evaluated in conjunction with other mitigation strategies.

3.2 Results from the Dynamic Patient/Staff Mixing Model

Users are able to define a number of parameters before initiating a set of model runs (see Table 5, below). Three of these inputs define the mitigation strategy combination to be used. In the table below, these inputs are reflected in the first three columns. Specialized nursing is set to "TRUE" where the specialized nursing strategy is used and "FALSE" when team nursing is in place. The user can also select up to two additional mitigation strategies (seen in Table 5 columns for "First Mitigation" and "Second Mitigation"). In this case, the first column is used solely to reflect the "isolation of patients" strategy as True (on) or False (off).

Table 5: Comparison of Total Infected Across Different Mitigation Strategies

Specialized Nursing	First Mitigation	Second Mitigation	Total Infected			
			Max	Median	Min	Mean
True	No mitigation	No mitigation	61	42	3	41.02
True	Isolation of patients	No mitigation	58	42	3	39.24
True	Isolation of patients	Furlough w/o replacement	23	8	3	8.41
True	Isolation of patients	Furlough w replacement	23	7	3	9.45
True	Isolation of patients	Furlough w return	23	7.5	3	8.19
False	No mitigation	No mitigation	70	46	28	46.46
False	Isolation of patients	Furlough w replacement	30	9	3	9.72
False	No mitigation	Furlough w replacement	36	11	3	12.49

The total numbers of infections are higher when using this model versus the Contact Network model, in large part because the other model does not include staff shifts. That results in a smaller overall population that can potentially become infected. This model also includes more staff types; the prior model was focused on generic staff reflective of nurses and nurse's aides.

As might be expected, the no mitigation cases (representing the worst case scenario) result in the highest number of infections. The number infected with no mitigation is higher under the team nursing plan than under the specialized nursing plan, which is to be expected given the increased mixing that occurs under a team nursing environment.

The isolation of symptomatic patients does offer some benefit, although the decrease is relatively small. For example, under team nursing and furloughing with replacement, isolating sick patients results in a mean total infected of 9.72 versus 12.49.

The three different furloughing options (furlough with replacement, furlough without replacement, and furlough with return) result in very similar infection counts. However, there are operational considerations that must be taken into account in addition to controlling disease spread. For example, furloughing staff without replacement results in lower staff-patient ratios, forcing the facility to turn away a larger number of patients than it otherwise would. The impact on numbers of patients turned away can be seen in Table 6 below. For all three strategies, isolation of patients and specialized nursing were used.

Table 6: Patients Turned Away Under Different Furlough Strategies

Furlough Strategy	Patients Turned Away			
	Max	Median	Min	Mean
Furlough w/o replacement	25	1	0	2.64
Furlough w replacement	8	0	0	0.59
Furlough w return	12	1	0	2.21

It is also useful to examine the locations where transmission is occurring most frequently in order to understand the physical locations where interventions might be most effective. The modeled results of average numbers of total infections (transmissions) that occur in each of the main locations are shown in Table 7.

Table 7: Average Total Infections Occurring in Given Locations

Mitigation Strategy	Average Total of Infections Occurring in LTC Unit	Average Total of Infections Occurring in STC Unit	Average Total of Infections Occurring in Hospice Unit	Average Total of Infections Occurring in Nurse's Station	Average Total of Infections Occurring in Dining Unit	Average Total of Infections Occurring in Isolation Unit
Specialized Nursing, No Mitigation	12.61	5.28	11.1	3.29	7.19	0
Specialized Nursing, Patient Isolation, No Mitigation	12.36	5.31	11.06	3.79	5.17	0
Specialized Nursing, Patient Isolation, Furlough with Return	2.51	0.97	1.34	0.98	0.84	0
Specialized Nursing, Patient Isolation, Furlough with Replacement	2.94	1.17	1.68	1.12	0.99	0
Specialized Nursing, Patient Isolation, Furlough without Replacement	2.56	0.98	1.47	0.96	0.89	0
Team Nursing, No Mitigation	9.22	5.48	21.47	3.03	5.78	0
Team Nursing, Patient Isolation, Furlough with Replacement	2.81	1.31	4.06	1.13	1.7	0
Team Nursing, Patient Isolation, Furlough without Replacement	2.14	1.26	2.97	1.13	0.74	0

These results show the greatest numbers of infections occur in the Hospice unit and the LTC unit. This is because the susceptibility rate of the hospice patients is much higher and because the LTC unit has a larger population of patients and staff. These results are important to note because they imply that interventions focused on protecting Hospice patients and reducing contacts within the Long Term Care unit will provide the greatest opportunity for containing infection. The Dining Unit is also the site of significant infection transmission: in some simulations more infections occurred in the Dining Unit than in the Short Term Care unit, implying that mitigation strategies limiting access to the dining hall could improve overall infection counts.

It is also useful to examine disease progression over time in each scenario. Average numbers of infections across all of replicates of each scenario by day for two scenarios are illustrated in Figures 12 and 13, below.

Specialized Nursing, Isolation of Patients, No Mitigation
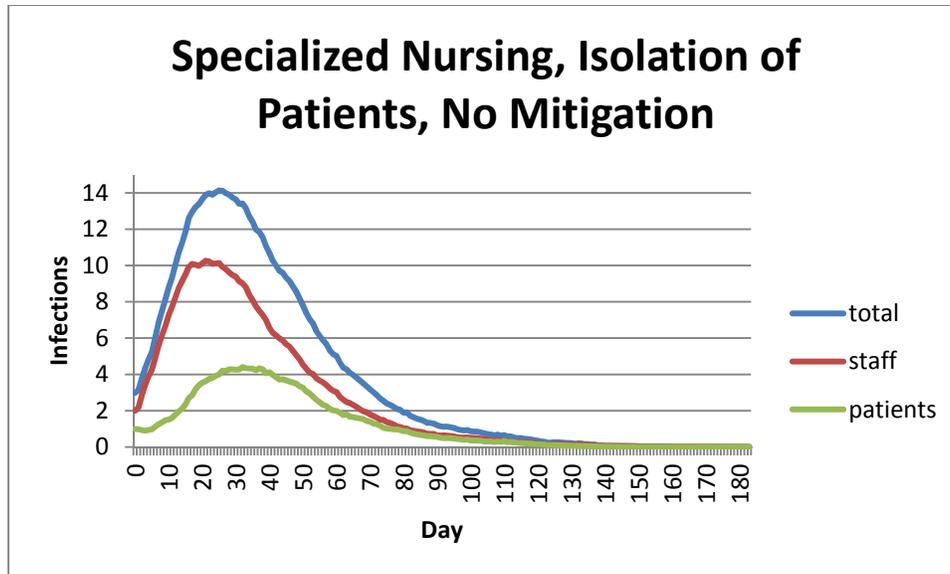
Figure 12: Average infections by day across multiple runs under specialized nursing, with isolation of patients and no other mitigation

Specialized Nursing, Islolation of Patients, Furlough with Replacement
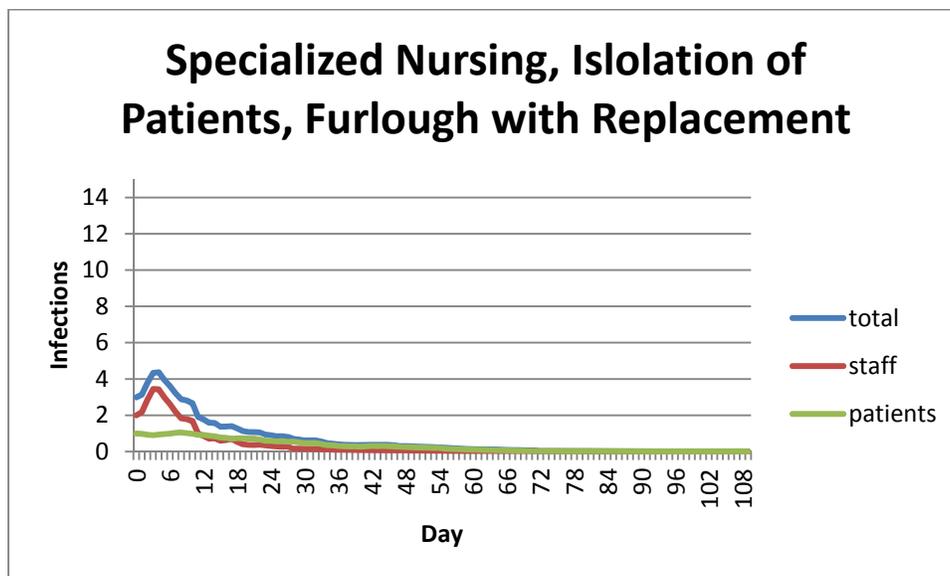
Figure 13: Average infections by day across multiple runs under specialized nursing, with isolation of patients and furloughing with replacement

Not only do the infection counts differ between the two scenarios, the shapes of the curves are also different. The first scenario results in a much higher number of staff infections than patient infections. In the second scenario, the average number of infected staff members starts out higher than the number of patients infected: the two lines eventually cross and remain close together through time, most likely due to the furloughing of susceptible staff.

It is important to note that the actual course of the outbreak that occurred in San Juan was just one possible outcome (one "replicate") of a scenario. The average numbers of infections for the scenario that most closely resembles the mitigation actions taken in San Juan during the outbreak

of December 2011 (Specialized Nursing, Isolation of Patients, Furlough with Replacement) are lower than the actual numbers seen during the outbreak. The average seen in the replicates under that scenario (9.23) was lower than the observed number of infections (13), implying that the outbreak resulted in a slightly worse than average outcome given a set of mitigation strategies, but was well within the range of potential outcomes predicted using the model (minimum of 2 and maximum of 23 infections).

The average number of infections transmitted to patients by staff as modeled under differing mitigation strategies are shown in Table 8. The modeling provides this insight for all types of staff and patients. However, patient safety is the primary goal of this study, so in this discussion we focus on transmissions only to this group. It is useful to notice that nurses' aides are the largest transmitters to patients, most likely due to their relatively large numbers and their higher patient contact rate. Food service workers also appear to be effective transmitters given their relatively small population. This stems from the breadth of individuals that use the dining facilities. This result is consistent with Polgreen et al., (2010) where it is demonstrated that more effective prevention stems from vaccinating in declining order of social contact.

Table 8: Average infection transmission counts between different types of people

Mitigation Strategy	Average patient to patient infections	Average nurse to patient infections	Average nurse aide to patient infections	Average custodian to patient infections	Average medical officer to patient infections	Average food service to patient infections
Specialized Nursing, No Mitigation	3.01	1.39	7.68	0.07	1.11	2.56
Specialized Nursing, Patient Isolation, No Mitigation	1.47	1.5	8.03	0.08	1.12	2.81
Specialized Nursing, Patient Isolation, Furlough with Return	1.16	0.14	0.19	0.01	0.06	0.16
Specialized Nursing, Patient Isolation, Furlough with Replacement	1.08	0.18	0.52	0.01	0.07	0.2
Specialized Nursing, Patient Isolation, Furlough without Replacement	1.13	0.19	0.29	0.01	0.11	0.18
Team Nursing, No Mitigation	2.63	1.08	13.27	0.04	0.78	1.95
Team Nursing, Furlough with Replacement	1.84	0.13	1.3	0	0.12	0.35
Team Nursing, Patient Isolation, Furlough with Replacement	1.11	0.1	0.62	0	0.05	0.31

The output results shown in Table 8 indicate that nurses' aides and food service workers were infecting patients at relatively higher rates. The value of selectively applying a furlough intervention is illustrated by the graph in Figure 14, where the curves represent the progression of infection spread over time if one were to furlough only nurse's aides, only food service workers, no one, or all susceptible staff. As expected, furloughing all susceptible staff provides the greatest benefit, but selective furloughing can also provide some benefit. Furloughing only the nurse's aides that are susceptible, for example, significantly reduces the peak number of infections.
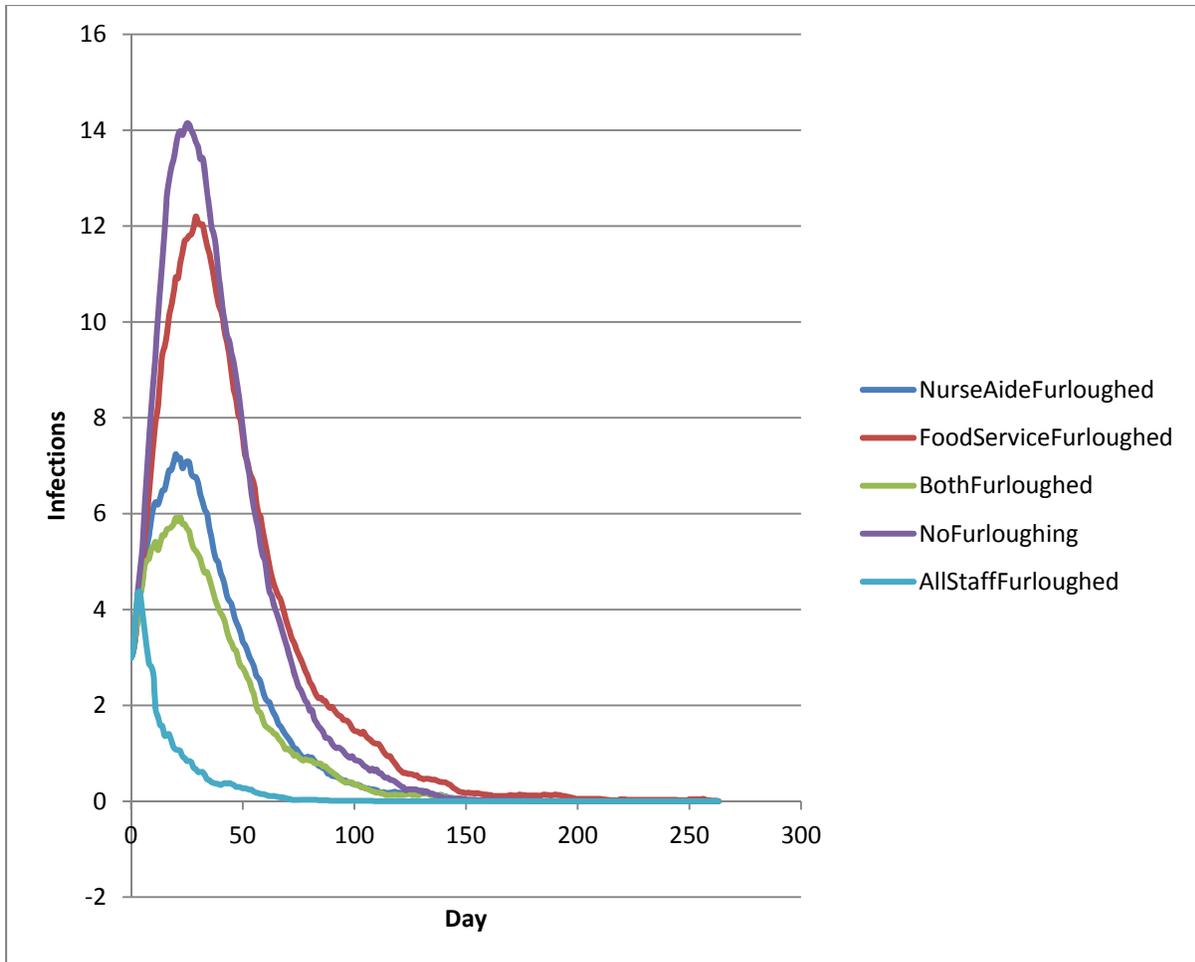
Figure 14: Infections over Time under Selective Furloughing Options

3.3 Future Additions to the Model

In the future, adding more detailed structure regarding the facilities' semi-private and private rooms to the model would enable us to better represent the closer degree of contact between roommates versus casual contact within the unit (Hashemian, et al., 2012). It would also be beneficial to include more locations within the model, such as hallways, bathing facilities, and other common spaces in addition to correlation in the locations of each patient over time. Increased fidelity regarding the operation and location of individual areas of the facility will also improve the accuracy of model results. Implementing these refinements would require data on the location and schedule of dining spaces, specific staff schedules, and more accurate hourly schedules for patients and staff. Ideally, visitor data would also be incorporated.

The development of enhanced metrics for quickly gauging the differences between operational and disease transmission impacts across different mitigations strategies is also a potential area for future development.

4 Discrete Event Simulation: Operations Modeling Approach

The design of the two social network-based models discussed above is grounded in the perspective that the core behavior driving the spread of disease is social contact: hence, those two modeling structures are tied to that dynamic. The proposed discrete-event operations model is instead focused on accurately representing the activities taking place within the CLC (for example, provision of patient care and meals) and simply overlaying transmission through the contact that occurs as a result of the provision of those services.

The dominant methodology for addressing health care operations problems is discrete event simulation. Discrete-event simulation is especially helpful in this problem space due to its ability to represent wait time for services and resources when the demand for that service or resource exceeds an institution's capacity (Roberts, 2011). The preliminary simulation designed for San Juan is a stochastic discrete-event simulation, with simulation steps using pseudo-random numbers to represent real-world uncertainty. Sensitivity analysis can be used to explore the potential range of different outcomes and the sensitivity of the model to different variables.

We built an initial simulation of the San Juan CLC facility in FlexSim Healthcare, a commercial package designed for the easy representation of activities that occur in hospital settings. This initial version was created using available data on staff, patient load, and operations. Given a detailed representation of facility operations, it would be possible to measure the impacts of different mitigation strategies on patient experience and cost. That information could then be used to evaluate trade-offs between infection control and impacts to hospital operations.

Arrival rates and processing times (length of stay) for patients are uncertain. When available, these rates can be based on actual length of stay and admissions/discharges data, utilizing draws from a statistical distribution fitted to the real data to allow for uncertainty. This modeling approach also enables analysts to assign specific staff to different shifts in the simulation.

Processing times and patient paths through the system are defined by "patient tracks" with associated probabilities of branching into various options. The model also provides "global processes" to represent staff activities that are not direct patient care.

The admissions/discharges/transfers (ADT) data needed to create an accurate representation of patient tracks through the facility are not available to Sandia at the present time. Similarly, detailed information on staff activities throughout the day at the San Juan facility has not been made available. Information at this level of granularity is essential for deriving meaningful results from this type of model.

Since data on the real flow of patients between CLC care units are not available to Sandia, we currently assume, for the purposes of modeling, that patients are admitted from home/the hospital into a particular unit within the CLC and, once treated or deceased, discharged either to home, the hospital, or the morgue. In this configuration, the length of stay distribution does not vary based on where patients come from or where they exit to. Additionally, patients remain assigned to a single CLC unit for the duration of their stay in the CLC.

With access to Admissions/Discharges/Transfers (ADT) data or other patient chart data, it would be possible to complete the patient tracks. That information, combined with data on daily staff activities and shift assignments, would make it possible to measure impacts of mitigation

strategies at a more detailed level than the previous two models. For example, one could calculate impacts to staff workload and patient wait times.

5 Discussion

Computational modeling provides valuable information to be used in developing intervention policies for healthcare facility-based infections. Models which provide accurate estimation of disease spread and the effects of intervention strategies can be run many times with a range of scenarios to represent not only the historical case, but alternative outcomes which may have taken place. These alternative outcomes, which were not observed in the historical case, are a product of random processes, differing assumptions, and varied mitigation strategies. The goal of modeling-based studies of infectious disease mitigation is to generate intervention policies which balance the often disparate requirements of disease spread reduction and reliability in that reduction, minimization of disruptions to patient care and cost. These robust intervention policies aim to reduce the number of infection cases while minimizing the uncertainties associated with application of the policies across multiple facilities in different regions while protecting patient care.

Models range in complexity from simple mathematical calculations to highly-accurate simulations of all significant factors thought to influence outcomes. Simple models are quick to design and build, and potentially useful results are comparably easy to derive. Simple models can generate useful general-purpose intervention policies which require little time or effort to customize to unique properties of a given outbreak. More detailed models take into account more factors and ideally can generate more accurate results. However, they require more effort to create and require a relatively large amount of input data to generate meaningful results. The art of modeling infectious disease mitigation effectively involves balancing the speed and generality advantages of simple models against the expense and complexity of high resolution approaches.

While complex models can provide appropriate information on the system which they were designed to simulate, overfitting a detailed model to the exemplar case can result in a model which captures one system nearly perfectly, but is ill-suited to general application as a policy design and evaluation tool. Model studies often start with the goal of constructing a simple computational simulation to address general cases. However, the need to validate such a model by showing that it can match historical instances often requires successively complex additions to the elegantly simple modeling core. Often, models which have become incrementally more complex are unable to adequately assess intervention strategies for diseases, populations, or communities other than the typical cases. Such progressively overfit models are of limited usefulness and are often not promoted into general use.

This study directly addresses this tradeoff between simplicity and complexity in an infectious disease intervention model by using multiple models to independently design policies for mitigation of disease spread in a facility. This report describes our investigation of three types of modeling approaches developed to gain insight into the spread of infectious disease in a nursing home setting. Two of those models were implemented and run to generate simulation results, while the third type has not yet been developed sufficiently to generate useful simulation results.

The three infection-spread models differ in the fidelity of the simulation and in the amount of facility-specific data needed to parameterize the models. The Static Contact-Network Infection Model is the most abstract, modeling potential disease transmission paths as static connections between nodes of randomly generated networks. This more general model of infection process requires minimal facility data to model the San Juan CLC: staffing levels, patient census, and susceptibility values. The potential contact counts which determine the rate of infection spread in

the model are based on estimates provided by experts in long-term care nursing and administration. The second model, the Patient/Staff Mixing model, simulates the San Juan facility at a higher resolution while using more detailed facility data, such as patient resident times, staffing shift changes, and staff role differences. The third modeling motif investigated involved a very high-resolution Discrete Event Simulation, which models the detailed day-to-day interactions of the unit. This highly-detailed model has the potential to attain the most accurate re-creation of facility disease spread patterns, but requires highly-detailed data collection and a lengthy setup and calibration procedure.

The analysis performed using a combination of actual and notional data for the San Juan scenario yields useful information on the types of interventions that would be most effective at curbing the spread of the disease. The Patient/Staff Mixing model results showed the greatest numbers of infections occurring in the hospice unit and the long term care unit, implying that interventions focused on protecting the vulnerable hospice patients and reducing contacts within the long term care unit would be very useful. The results also showed that while furloughing all susceptible staff would provide the greatest benefit, selective furlough of susceptible nurse's aides would be a good option if trying to limit operational impacts while reducing disease spread. Specialized nursing is also the best option for limiting the spread in the scenarios that were analyzed.

Much of the data used to populate the models is reflective of real parameters but is not exact. However, even with that critical caveat, the two implemented models do illustrate some important insights. First, uncovering the presence of diseases of this nature quickly is very important, as is the quick formulation of a strategy to address them. Delays in identification and decision making significantly increase the difficulties of containment. Second, mitigation strategies need to prioritize treatment of the most vulnerable patients and the health care workers with the most extensive contact networks. Often, there are significant logistical challenges, including lab testing capacity, that prevent the immediate testing of all potentially-susceptible staff. Understanding on whom to first focus scarce resources can significantly control infection spread. Also, acquisition of replacement staff can present significant challenges depending on the numbers needed and the skills required. Under some circumstances, furloughing staff can significantly disrupt patient care (even when replacements can be identified). Hence, it is critical to consider both the benefits of containment and the disruption in care that will occur when deciding who to furlough. This final point illustrates the importance of modeling disease spread and care disruptions simultaneously.

There are several areas in which further development of these modeling tools could be useful to the VHA. The analysis done this year using these models was focused on Varicella, but there is a clear benefit to having the capability to apply these modeling techniques to other diseases. Disease spread within a facility is of concern from both health and logistics perspectives: understanding the relevant trade-offs for different interventions is key to informed decision making. This type of analysis can inform both policy for preventing potential incidents and mitigation strategies in reaction to an event.

To derive the greatest benefit from the combined social contact and operations models, more detailed data about VHA operations and patient activities (activities, discharges, transfers, etc.) at a "typical" VHA facility of concern would be extremely useful. Data of this nature would allow for completion of a more detailed logistics model for weighing impacts to operations against containment benefits. The ability to combine social network modeling and logistics modeling to paint a more complete picture of both disease spread and the impacts of mitigation strategies to

operations would provide a key capability to decision makers for future questions. This fuller representation would enable stakeholders to more easily understand the potential impacts of interventions on their work and the activities they engage in.

This phase of the investigation has focused on creating two models which can independently generate estimates of disease spread when a variety of interventions are implemented. We intend the follow-on phase to provide the VA with (1) the ability to generate priority-ranked recommendations for single interventions and layered intervention combinations, and (2) estimates of the advantages and drawbacks of applying more complex modeling motifs to disease mitigation questions.

6   CONCLUSION

This report summarizes investigations by Sandia National Laboratories' Complex Adaptive System of Systems team into the applicability of computational modeling to mitigating infectious disease spread within a healthcare facility. This work was begun in response to a varicella infection among patients and staff at the San Juan VA Medical Center. The operational response phase of the work proceeded coincident with the outbreak in December 2011. That brief, high-intensity modeling phase produced a number of potential modeling methodologies which held promise for use in future outbreaks. The present study has involved a build-out of two of the most promising modeling methodologies, and a proof-of-concept evaluation of a third. The static contact-network model is easy to parameterize and generates rational estimates of projected outbreak dynamics. Additionally, the simple model demonstrates the value of quick response to stopping the spread of the disease. The more detailed mixing model generates estimates which are better grounded to the operation of a VA CLC and enable us to examine more involved intervention strategies. Future work to directly compare the model outputs and policy suites derived from the outputs could yield both recommendations for operational interventions and better understanding of the level of modeling effort needed to answer such questions.

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