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The Effect of Individual Movements and Interventions on the Spread of Influenza in Long-Term Care Facilities

Mehdi Najafi, PhD, Marek Laskowski, PhD, Pieter T. de Boer, MSc, Evelyn Williams, MD, Ayman Chit, PhD, Seyed M. Moghadas, PhD

Background. Nosocomial influenza poses a serious risk among residents of long-term care facilities (LTCFs). **Objective.** We sought to evaluate the effect of resident and staff movements and contact patterns on the outcomes of various intervention strategies for influenza control in an LTCF. **Methods.** We collected contact frequency data in Canada's largest veterans' LTCF by enrolling residents and staff into a study that tracked their movements through wireless tags and signal receivers. We analyzed and fitted the data to an agent-based simulation model of influenza infection, and performed Monte-Carlo simulations to evaluate the benefit of antiviral prophylaxis and patient isolation added to standard (baseline) infection control practice (i.e., vaccination of residents and staff, plus antiviral treatment of residents with symptomatic infection). **Results.** We calibrated the model to attack rates of 20%, 40%, and 60% for the baseline scenario. For data-driven movements, we found that the largest reduction in attack

rates (12.5% to 27%; ANOVA $P < 0.001$) was achieved when the baseline strategy was combined with antiviral prophylaxis for all residents for the duration of the outbreak. Isolation of residents with symptomatic infection resulted in little or no effect on the attack rates (2.3% to 4.2%; ANOVA $P > 0.2$) among residents. In contrast, parameterizing the model with random movements yielded different results, suggesting that the highest benefit was achieved through patient isolation (69.6% to 79.6%; ANOVA $P < 0.001$) while the additional benefit of prophylaxis was negligible in reducing the cumulative number of infections. **Conclusions.** Our study revealed a highly structured contact and movement patterns within the LTCF. Accounting for this structure—instead of assuming randomness—in decision analytic methods can result in substantially different predictions. **Key words:** nosocomial influenza; agent-based modelling; interventions; contact patterns; simulations. (*Med Decis Making* 2017;37:871–881)

Nosocomial influenza outbreaks continue to inflict substantial morbidity and mortality, with significant associated healthcare costs.¹ Residents of long-term care facilities (LTCFs) are particularly vulnerable to influenza due to underlying health conditions,^{2,3} and possible congregation during daily activities, creating high exposure to infection. Furthermore, some residents may be cognitively impaired and unable to follow basic hygiene precautions. Outbreaks of influenza in LTCFs occur even in the presence of high vaccination rates of both residents and staff, with attack rates (i.e., the proportion of population at risk infected throughout the outbreak) that vary from 5% to 60% and case

fatality rates as high as 55%.^{3,4} Although vaccination has shown to reduce the risk of severe outcomes,^{5,6} infection can still occur because of the lower vaccine efficacy among geriatric populations as compared with other age-groups.^{1,7,8,9}

In addition to annual vaccination campaigns, a number of strategies are implemented to prevent infection and its spread among residents of LTCFs. These include non-pharmacological infection control measures (e.g., isolation, restriction of visitation during the outbreak, hand hygiene and masks) and antiviral drugs for treatment and prophylaxis.^{10–12} Despite the implementation of these strategies to varying degrees, frequent outbreaks are declared in LTCFs and early containment remains challenging, as the source of infection is often unknown. Furthermore, a sizeable portion of individuals may experience asymptomatic infection without presenting clinical symptoms while being capable of transmitting the infection.

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Although a number of factors contribute to the complexity of nosocomial outbreaks, the interactions among residents, visitors, and staff can significantly influence the outcome of prevention and control measures in LTCFs.^{1,3} In this study, we developed a discrete-time agent-based simulation model to evaluate the effect of various intervention strategies where transmission dynamics is parameterized based on interactions among individuals. To the best of our knowledge, this study presents the first modeling framework that uses movement data to determine the network of interactions within an LTCF. We collected such data in Canada's largest veteran's LTCF, using wearable tags that exchange ultra-low-power radio signals between individuals in a prescribed proximity. Using such data, we constructed a transition probability matrix to simulate the movement and interactions between individuals throughout the LTCF modeled in this study, and evaluated the effect of several intervention strategies that are commonly practiced to contain influenza outbreaks in these settings.

Agent-based modeling has increasingly been applied to study disease dynamics and gauge the impact of prevention and control measures in population and healthcare settings, where the interactions between individuals are often modeled based on observations, plausible assumptions, or randomly.^{11,13–16} We compare our results using data-driven movements with those obtained from random movements. This comparison allows us to study the importance of individual movements in a closed

setting like an LTCF, and describe the dynamics and emergent properties of an outbreak that may be characterized by localized attributes, such as joint spatial, temporal, and behavioural interactions.

METHODS

Study Population

We collected movement data in the Veterans Centre located at Sunnybrook Health Sciences Centre, Toronto, the largest veterans LTCF in Canada. Our study took place in 2 sections of this facility with a total of 50 rooms, and 19 service locations and public arenas inside the center. Residents live in several units that are specialized according to their needs, including semi-private rooms and private rooms. The total number of staff working in the areas related to the study was 64 in all shifts, of which 63% participated in the study. The total number of residents in these areas during the data collection period was 52, of which 37% participated.

Ethical Approval

Ethics approval was received, and informed consent was obtained from participants (and when required from substitute decision makers for residents) before commencement of data collection. Ethical approval was obtained from York University office of research ethics, and Sunnybrook Health Sciences Centre research ethics board. Participation by staff members and residents was voluntary. Information on the data collection process was provided to all participants, including substitute decision makers for residents. No personal information was collected and participants were anonymous in the contact signals received during data collection using socio-metric wearable devices.

Data Infrastructure and Collection Process

The study comprised 2 periods of data collection in December 2015 and February 2016, each for a duration of 14 d. These periods fall within the typical influenza season in Canada, which generally peaks between December and March.¹⁷ The data were collected using wireless tags and receivers (Figure S1, Appendix) that were worn by all participants during daily activities (excluding resting time or bathing). Each tag was associated with a unique identifier digital code, which was used to determine

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the between-participant contacts of resident to resident, staff to staff, and resident to staff. Contact events were measured in frequency, location, and time duration within a spatial resolution up to 1.5 m for proximity between tags,^{18,19} and a temporal resolution of 15 sec for contacts. Exchange of radio packets between devices was only possible when participants were facing each other, as the human body acts as a shield at the radio frequency used. Similar to previous work,²⁰ our system detected and recorded close-range contacts during which a communicable disease could be transmitted; e.g., by coughing, sneezing, or physical contact.

Tags broadcast their unique identification number, as well as the identification number of the other tags in proximity to radio frequency identification (RFID) readers mounted in the environment (i.e., throughout the LTCF). The RFID reader forwarded any information received from the tags to a data server for further analysis. In addition to tags worn by participants, so-called ‘marker tags’ were placed in known locations throughout the environment to assist with locating participants in the LTCF.

The sensing system was tuned so that the recorded data included the start and end times of contacts between participants and their locations, with a temporal resolution of milliseconds. We used this information to determine the number of contacts for each participant, the duration of contacts, the cumulative time spent in contact among 2 or more participants, and the frequency and location of encounters during the data collection period. The corresponding distributions are broad: short durations were the most probable, but very long durations were also observed with a non-negligible probability. For diseases in which the transmission probability between 2 participants depends on their time in contact, different contacts might yield very different transmission probabilities. Many contacts are very short and correspond to a small transmission probability, but some are considerably longer than others, and could therefore play a crucial role in disease dynamics.

Data Analysis and Transition Probabilities

For analysis and eventual inclusion into the model, time-stamped data were separated into 2 categories. We compiled data sets that captured contacts between participants and marker tags, and data sets that captured contacts among 2 or more

participants. Data were aggregated along the temporal dimension into 15-sec slots to determine the location of each participant during each 15-sec slot. For each hour of the day, we counted the number of visits (for a slot in which a participant is at a particular location) each participant makes to any location from each starting location. This yields a matrix of Markov chain state transition probabilities, as shown in Figure 1, for each class of participants, which was used to parameterize the movement module of the model (see Appendix). The Markov chain model provides a simple way to capture sequential dependence of places visited by participants.

Agent-based Modeling Structure

A previously validated agent-based modeling framework was used as the basis for disease natural history and disease transmission between participants in the LTCF.²¹ Earlier models using this framework in the larger community presumed the activities of participants based on assumptions about behavioural patterns in an environment that includes homes, workplaces, schools, and other social contexts.^{21–23} We adapted this framework to represent resident rooms, common areas, and staff areas within the LTCF.

The agent-based approach used here is a discrete-time simulation model in which agents are situated and capable of movement throughout a discrete environment.^{24,25} A key component of our study is the model calibration for disease transmissibility (given a specific attack rate) using the data collected for the movement of participants in the LTCF. We characterized the movements of participants as a function of time, and counted the number of transitions made by participants between locations in the study area. This movement module was used to determine the current location of participants in the model, and the next location to which each individual agent will probabilistically move during daily activities. We also classified individual movements based on their functions in the LTCF as residents or staff. The transition probabilities derived from the collected data were then used to calibrate the model for the transmission probability.

For simulating disease dynamics, we built the model with compartments representing individual agents and their epidemiological health statuses, movements, and interactions between the

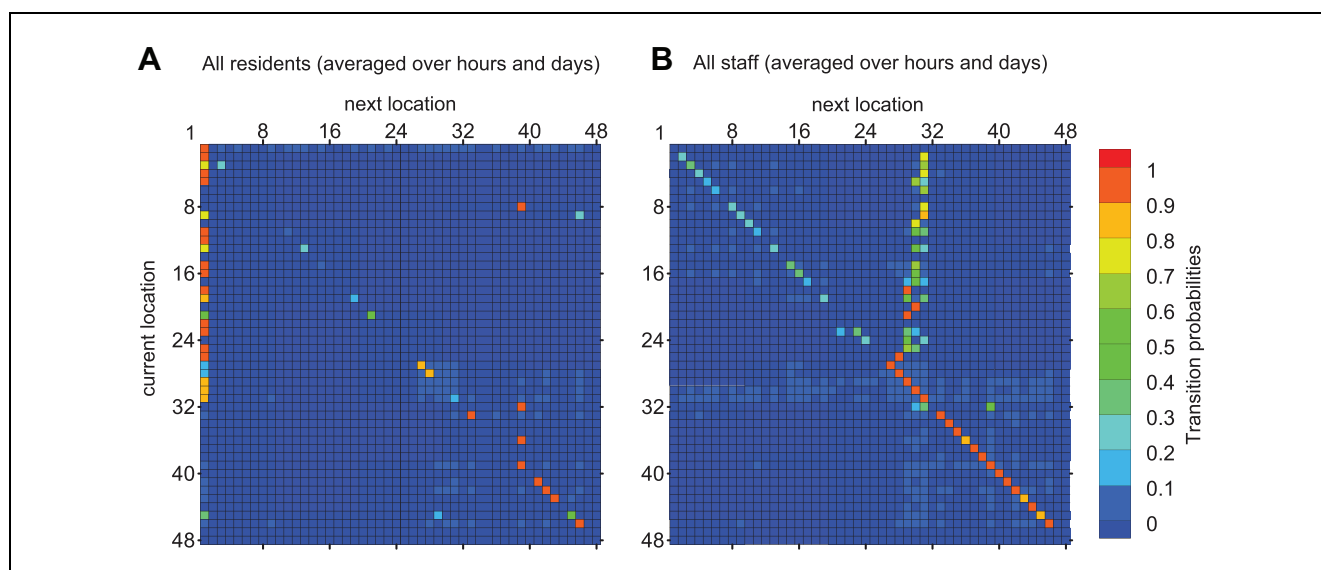


Figure 1 Transition probabilities for movements of residents (A) and staff (B) from the current location to the next location within 15 sec. Locations within the LTCF include resident rooms, service area, public area, and activity rooms (see Appendix).

compartments. The underlying structure of the model describes the dynamics of the clinical course of influenza infection, and includes state compartments of individuals as susceptible (S), exposed and infected but not yet infectious (E), pre-symptomatic and infectious without symptoms (P), asymptomatic and infectious without symptoms (A), infectious with symptoms (I), and recovered (R).

Disease transmission occurs as a result of contact between susceptible and infectious agents. We assumed a standard Markov chain process for disease progression in the model compartments. At any time during the simulation, agents are in one of these compartments according to their epidemiological status. In our model, each time-step in the simulation is associated with an independent Bernoulli trial for disease transmission:^{24,25}

$$P_{\text{transmission}} = 1 - (1 - \beta(1 - q_1)(1 - q_2)(1 - q_3)(1 - q_4))^t$$

where β is the transmission probability per person per time unit; q_1 is the reduction in transmissibility in pre-symptomatic or asymptomatic individuals; q_2 is the reduction in transmissibility due to antiviral treatment; q_3 is the reduction in susceptibility to infection as a result of vaccine-induced immunity (which depends on the vaccine efficacy); q_4 is the reduction in susceptibility to infection due to antiviral prophylaxis, and t is the amount of time spent at the same location with potentially infectious

contacts. The reduction in disease transmissibility represented by q_i , $i=1,2,3,4$, is applied only when the relevant interventions in simulation scenarios are implemented, and based on the characteristics of the susceptible and infectious agents that come into contact with each other within t amount of time. The time period t is governed by collected movement data imputed into a Markov model, sampled in increments of 15 sec as the time step used in the model.

If transmission occurs following exposure, a susceptible agent becomes infected and enters the latent stage. After the latent period has elapsed, the epidemiological status changes to pre-symptomatic or asymptomatic.²¹ Agents with asymptomatic infection remain infectious and can transmit the disease for the entire infectious period without presenting clinical symptoms. Those with pre-symptomatic infection will develop clinical symptoms while infectious. Infectious periods for pre-symptomatic, asymptomatic, and symptomatic infections are sampled from their associated distributions.²¹

Parameterization

The transmission rate, β , was iteratively modified through a series of trials²¹ to calibrate the model to cumulative attack rates of 20%, 40%, and 60% among residents in the baseline scenario.^{1,3} Each

Table 1 Intervention Strategies Used in Simulation Scenarios

Scenario Index	Residents and Staff	Residents	Staff
Baseline		Vaccination (100% coverage) + treatment of symptomatic residents	Vaccination (100% coverage)
S1	Baseline		Symptomatic staff sent home and replaced
S2	Baseline	Isolation of symptomatic residents	Symptomatic staff sent home and replaced
S3	Baseline	Isolation of symptomatic residents + prophylaxis of all residents ^a	Symptomatic staff sent home and replaced
S4	Baseline	Prophylaxis of all residents ^a	Symptomatic staff sent home and replaced

^aCorresponding to the outbreak control policy in the LTCF, prophylaxis of all residents started after 3 symptomatic cases were identified and the outbreak in the LTCF was declared.

trial used at least 1,000 randomly initialized simulation runs to generate an average attack rate.

We assumed that infected participants during pre-symptomatic and asymptomatic stages are (on average) 50% less infectious than during their symptomatic phase.²² The effect of antiviral treatment was included in the reduction of disease transmissibility following the initiation of treatment. We assumed that treatment reduces the infectiousness by 60% for those who did not receive prophylaxis.^{22,26} Prophylaxis was assumed to reduce susceptibility to infection by 30% and transmissibility (if infected) by 60%.²² Those who developed symptomatic infection while receiving prophylaxis continued with treatment, with an additional 60% reduction in infectiousness.^{22,27} The overall reduction in infectiousness for these participants following the start of treatment was 84% (given by $1 - (0.4 \times 0.4) = 0.84$). We assumed a probability of 0.65 that individuals receiving prophylaxis will have significantly milder symptomatic infection (if they developed illness).^{22,26,27} Vaccine effectiveness was included as reduced susceptibility to infection, and reduced infectiousness reflected in lower probability of developing symptomatic infection (if infected). For residents, vaccine effectiveness was uniformly sampled from the estimated range of 14% to 30%, with the mean of 22%.^{7,8} For staff, vaccine effectiveness was sampled for each individual in the range of 60% to 90%, with the mean of 80%.²⁸ For a vaccinated individual, the probability of developing symptomatic infection (if infection occurs) was reduced by the sampled vaccine effectiveness.

The duration of the latent period for each infected individual was drawn from a uniform distribution with a minimum of 1 d and a maximum of 2 d.²⁹ The pre-symptomatic period for each infected individual was drawn from a log-normal distribution with the scale parameter $\mu = -0.775$ d, and

shape parameter $\sigma^2 = 0.16$ d, giving an average of 0.5 d.^{21,22,26} The infectious period was sampled from a log-normal distribution (Figure S6, Appendix), with the scale parameter $\mu = 1$ d, and the shape parameter $\sigma^2 = 0.4356$ d, which has a mean of 3.38 d.^{21,22}

Simulation Scenarios

Simulations were implemented on Compute Canada’s mp-2 cluster, which features 39,168 CPUs available to users, and an overall performance of 240 TFLOP/s, with a total memory of 57.6 TB. We considered the baseline scenario to include pre-outbreak vaccination of residents and staff, and treatment of symptomatically infectious residents. For comparison purposes, we considered 4 additional scenarios that included measures in the baseline scenario and were consistent with outbreak control policies in the LTCF considered here. These policies included prophylaxis of all residents after the identification of 3 symptomatic cases. Residents with symptoms of influenza were typically isolated in their rooms without interactions with other residents; however, no formal quarantine procedures were practiced. Staff presenting symptomatic infection were removed from simulations and replaced with a healthy individual for the sampled duration of the infectious period. Staff replacement was included in all scenarios, reflecting the policy to send home the staff who are clinically infectious. The scenarios for a combination of intervention strategies are chosen based on outbreak responses in the LTCF studied here, and are summarized in Table 1. Each scenario was run for over 1,000 independent realizations using a different random seed each time, and a different random resident in the model was chosen as the initial case. The total population in the model is $n = 68$. This required 72,000 core hours of compute time. For presentation of the

Table 2 Average and 95% Confidence Intervals for Cumulative Infections among Residents for Different Attack Rates based on the Movement Profiles

Data-driven Movement	Average Cumulative Infections among Residents (95% CI)				
AR	Baseline	S1	S2	S3	S4
20%	4.8 (4.5–5.1)	4.5 (4.2–4.8)	4.6 (4.3–4.9)	3.6 (3.4–3.8)	3.5 (3.3–3.7)
40%	10.3 (9.9–10.8)	9.9 (9.5–10.4)	10 (9.5–10.4)	7.7 (7.3–8.0)	7.7 (7.3–8.0)
60%	15.2 (14.5–15.8)	14.9 (14.4–15.3)	14.8 (14.3–15.3)	13.3 (12.9–13.7)	13.2 (12.8–13.6)
Random Movement					
20%	5.2 (4.9–5.5)	4.7 (4.3–5.1)	1.5 (1.4–1.6)	1.5 (1.4–1.6)	3.7 (3.6–3.9)
40%	10 (9.7–10.4)	9.3 (8.9–9.6)	2.4 (2.3–2.6)	2.2 (2.0–2.3)	6.2 (5.9–6.4)
60%	15.1 (14.7–15.5)	14.3 (13.9–14.7)	4 (3.7–4.3)	3.1 (2.9–3.2)	9.2 (8.9–9.5)

The baseline scenario included vaccination (with 100% coverage) of residents and staff, plus treatment of symptomatic residents. Other scenarios (S1–S4, as described in Table 1) included additional measures to the baseline scenario. AR, attack rate.

results, we aggregated the simulation outputs on a daily basis. To evaluate the effectiveness of interventions, we compared the model results of data-driven movements with those obtained using random movements. In the random movement scenarios, visiting any locations within the model was equally likely for staff while working on shift. For residents, the same rule applied from 7 AM to 11:59 PM; however, they remained in their rooms between midnight and 6:59 AM.

RESULTS

To compare the effect of interventions, we simulated the model and aggregated the results to obtain the daily incidence of infection, from which we estimated the cumulative number of infections over the course of an outbreak (Table 2). Using the transition probabilities for individual movements derived from data, we estimated the post-intervention attack rates for both residents and the total study population (i.e., residents and staff) in all strategy scenarios. Figure 2 illustrates the cumulative number of infections among residents over a 7-wk period for both data-driven and random movements in the population setting. Not surprisingly, the highest attack rates occurred in the baseline scenario of interventions (Figure 2, black curves). When movements are compelled by data (Figure 2A–C), replacement of staff with symptomatic infection (scenario S1; red curves) alone or combined with isolation of residents with symptomatic infection (scenario S2; cyan curves) has little or no effect on the reduction in attack rates among residents (Table 3). The largest reduction in attack rates was achieved for scenarios S3 (magenta curves) and S4

(blue curves) for which all residents were offered antiviral prophylaxis for the duration of the outbreak (Table 3). These observations hold true for the range of attack rates simulated here. The percentage reduction in the cumulative number of infections amongst residents for each scenario compared with the baseline strategy is presented in Table 3.

When movement of individuals was random (Figure 2D–F), we observed significant differences in the outcomes of simulated scenarios. In contrast to the outcomes for data-driven movements, the lowest attack rates were obtained for scenarios S2 (cyan curves) and S3 (magenta curves), in which the isolation of residents with symptomatic infection was implemented. Given that the outcome of scenario S4 (blue curves) had higher attack rates than that in scenarios S2 and S3, a strategy with isolation outperforms the strategy with prophylaxis for all residents (Table 3). Similar to the case of data-driven movements, the replacement of staff with symptomatic infection (scenario S1; red curves) has the lowest impact in reducing attack rates among residents. We obtained similar results for the cumulative number of infections among residents and staff (Figure S7; Appendix). These findings underscore the importance of movement and contact patterns in the outcomes of intervention strategies in close settings, such as an LTCF.

To account for variability in individual movements, we performed a sensitivity analysis using a sampling-based approach to generate new transition matrices. In this approach, we considered the data-driven transition frequency matrices for movements of participants between different locations as the mean of Poisson distributions, and generated 100 samples, resulting in new transition matrices. For

Table 3 Percentage Reduction in Cumulative Infections among Residents for Each Scenario Compared with the Baseline Strategy

Data-driven Movement	Percentage Reduction in Cumulative Infections among Residents (ANOVA <i>P</i> value)		
AR	20%	40%	60%
Baseline	0	0	0
S1	6.8 (0.109)	3.8 (0.218)	1.9 (0.689)
S2	4.2 (0.333)	3.6 (0.241)	2.3 (0.589)
S3	26.6 (<0.001)	25.7 (<0.001)	13.1 (<0.001)
S4	25.3 (<0.001)	25.8 (<0.001)	12.4 (<0.001)
Random movement			
Baseline	0	0	0
S1	9.3 (0.043)	7.7 (0.003)	4.8 (0.012)
S2	69.6 (<0.001)	75.7 (<0.001)	73.4 (<0.001)
S3	70.8 (<0.001)	78.5 (<0.001)	79.6 (<0.001)
S4	27.9 (<0.001)	38.6 (<0.001)	38.8 (<0.001)

One-way ANOVA was done between the mean values of cumulative infections achieved in the baseline and other simulation scenarios. The baseline scenario included vaccination (with 100% coverage) of residents and staff, plus treatment of symptomatic residents. Other scenarios (S1–S4) included additional measures to the baseline scenario, as described in Table 1. AR, attack rate.

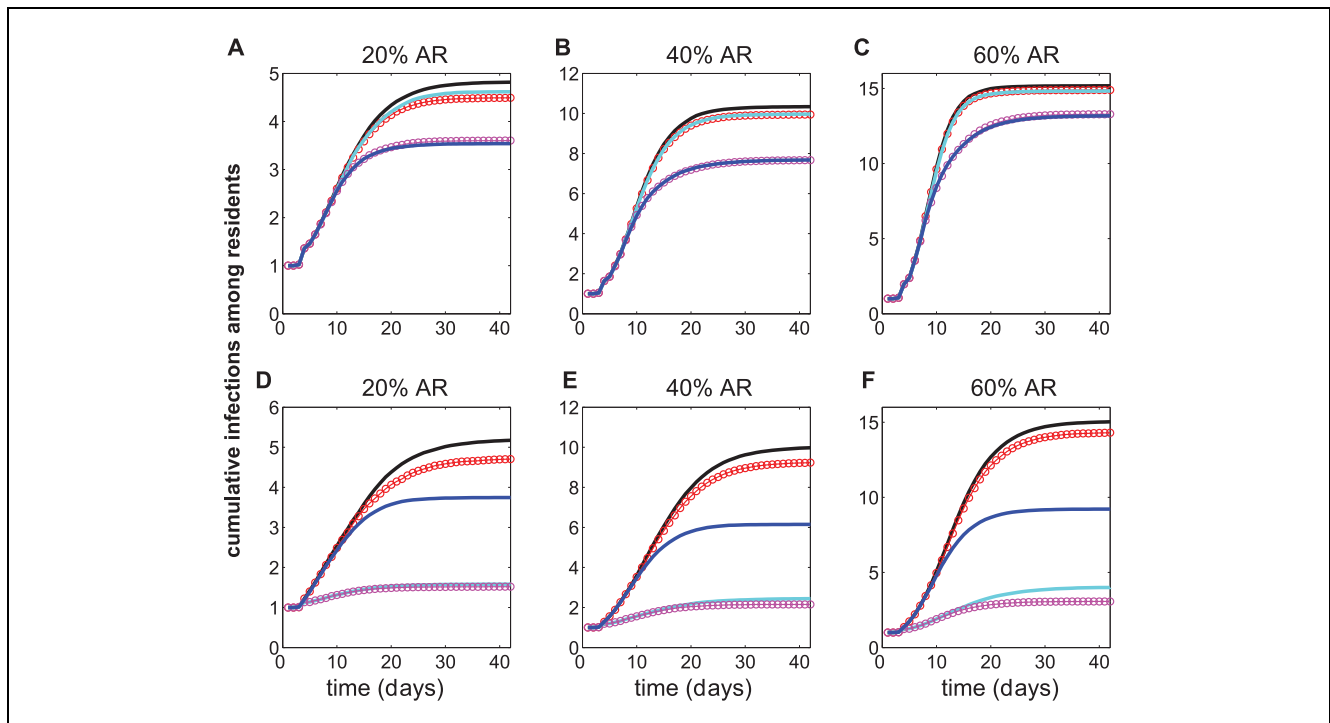


Figure 2 Cumulative infection curves for residents during 7 wk of nosocomial influenza infection outbreak with data-driven movements (A, B, C) and random movements (D, E, F). Color curves correspond to baseline (black) and intervention scenarios: S1 (red), S2 (cyan), S3 (magenta), and S4 (blue), as described in Table 1. AR, attack rate.

each sample, we ran a complete set of simulations for all of the scenarios described in Table 1. Figure 3 illustrates boxplots for the variation in the cumulative number of infections averaged over

independent realizations for each scenario. These simulations show the robustness of our results delineated above with respect to variations in movements.

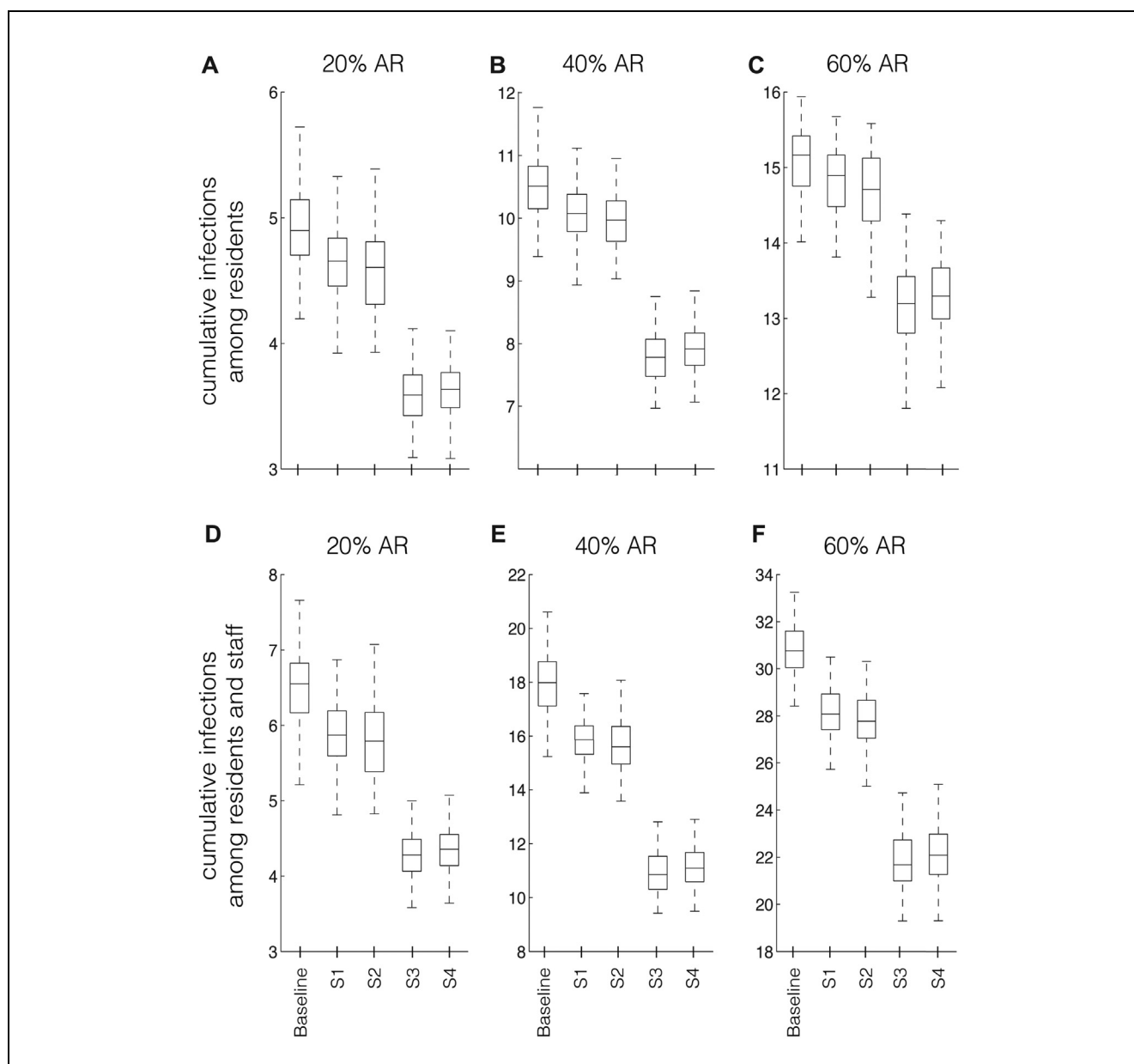


Figure 3 Variations in the cumulative number of infections among residents (A, B, C) and total infections (D, E, F) through the simulation of nosocomial influenza infection outbreak scenarios in the LTCF based on the Poisson sampling of transition matrices for individual movements. AR, attack rate.

DISCUSSION

In this study, we investigated the effect of movement and contact patterns of participants on the outcomes of prevention and control strategies against nosocomial influenza in an LTCF. The significance of our study relates to the integration of movement data into an agent-based modeling

approach to establish a framework for the evaluation of intervention strategies. A novel aspect of this study is the application of Internet of Things to collect data on individual movements and parameterize an *in silico* population that more closely resembles the actual setting. The integration of data processing with simulations enabled us to observe significant differences in the outcomes of scenarios

when movements in the LTCF are assumed to be random and when movements are compelled by data based on location and interactions. The analysis of such data suggests that the movements and contact patterns within this setting are indeed highly structured.

In comparing strategy outcomes, we observed that a measure that reduces the susceptibility to infection (i.e., prophylaxis) has the largest impact on reducing attack rates among residents when movements are data-driven. This corroborates previous findings of a systematic review on control practices and the effectiveness of interventions in LTCFs,³⁰ suggesting that antiviral prophylaxis remains the most effective pharmaceutical measure for influenza control in the context of reduced vaccine efficacy. In contrast, for random movements, we observed that isolation of clinically infectious patients leads to the largest reduction in attack rates. In the context of random movements, participants tended to have contacts with a greater variety of distinct individuals with a possibly shorter duration. Since the effectiveness of prophylaxis in infection prevention is imperfect, the interruption of virus spread from infectious individuals becomes paramount in reducing the attack rate. However, when movements are highly structured, individuals are more likely to encounter the same infectious contact repeatedly, and therefore measures to protect at-risk individuals are of critical importance. These findings suggest that, in well-confined settings, such as LTCFs, where interactions are clustered, preventive measures, such as vaccines with improved efficacy, are attractive strategies for institutional management of nosocomial influenza, as they are analogous with the use of prophylaxis.

There have been a number of modeling studies to evaluate the effect of intervention strategies, either individually or combined, on the control of nosocomial infections in hospital settings and LTCFs.^{11,13–16} Although these models rely on movement patterns derived from observations, plausible assumptions, or averaging over time and selected groups of individuals, none has evaluated the effect of such movements on infection control strategies. We considered this objective, and integrated the model with actual movement data collected in an LTCF. However, similar to previous studies, our model has a number of limitations. For example, our model does not consider all possible locations that LTCF residents may access during daily activities. Similarly, based on the process of data collection, we did not include possible

interactions that staff may encounter with any individuals from outside while being off-shift from the LTCF. Furthermore, given the short period of an outbreak, the model was implemented without visitation to the LTCF, and therefore infection was introduced only once at the start of the simulation. We did not have access to patient data for influenza infection during the study period or outbreaks at any other point in time, and therefore no comparison was made between the model outputs and the incidence of infection in the LTCF. Within the model, we assumed an immediate detection of illness for symptomatic cases, with the start of intervention measures according to the simulated scenario. We assumed that isolation of residents is 100% effective against transmission to other residents, and the only possible transmission route was through healthcare workers being infected through contact with isolated patients. However, cognitively impaired residents may not adhere to the practice of isolation during their illness, which may reduce the effectiveness of patient isolation in preventing disease transmission. Furthermore, we assumed 100% vaccine coverage in residents and staff (note: data from the LTCF indicated over 90% vaccine coverage for both staff and residents). Since our objective was to evaluate the effect of resident and staff movements on the outcomes of various intervention strategies, a number of the model parameters (e.g., effectiveness of vaccine and antiviral prophylaxis, reduction in disease transmissibility for pre-symptomatic and asymptomatic infections) were extracted from the published literature, which are subject to variations and may depend on the individual health status. Given these parameters, we investigated the effect of variation in movement patterns on the model outcomes through a sensitivity analysis. Our model does not include the effect of other non-pharmaceutical interventions, such as personal protective equipment and hand hygiene, and their effectiveness in these settings is not well documented.³⁰ We also did not consider the effect of fomites nosocomial transmission, and assumed uniform mixing of air in locations where there are multiple individuals. Despite these limitations, which merit further investigation, our results, combined with the sensitivity analysis for the individual movements, demonstrate that the strategy outcomes are highly dependent on the contact patterns in the particular facility. Tag and sensor studies can provide a low-cost way to collect facility-specific contact data, which can be used to parameterize decision models.

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REFERENCES

- Matheï C, Niclaes L, Suetens C, Jans B, Buntinx F. Infections in residents of nursing homes. *Infect Dis Clin North Am*. 2007;21:761–72.
- Arden NH. Control of influenza in the long-term-care facility: a review of established approaches and newer options. *Infect Control Hosp Epidemiol*. 2000;21:59–64.
- Simor AE. Influenza outbreaks in long-term-care facilities: how can we do better? *Infect Control Hosp Epidemiol*. 2002;23:564–7.
- Thompson WW, Shay DK, Weintraub E, et al. Mortality associated with influenza and respiratory syncytial virus in the United States. *JAMA*. 2003;289:179–86.
- Powers DC. Effect of age on serum immunoglobulin G subclass antibody responses to inactivated influenza virus vaccine. *J Med Virol*. 1994;43:57–61.
- Arden NH, Patriarca PA, Fasano MB, et al. The roles of vaccination and amantadine prophylaxis in controlling an outbreak of influenza A (H3N2) in a nursing home. *Arch Intern Med*. 1988;148:865–8.
- Jefferson T, Rivetti D, Rivetti A, Rudin M, Di Pietrantonj C, Demicheli V. Efficacy and effectiveness of influenza vaccines in elderly people: a systematic review. *Lancet*. 2005;366:1165–74.
- Jefferson T, Di Pietrantonj C, Al-Ansary LA, Ferroni E, Thorning S, Thomas RE. Vaccines for preventing influenza in the elderly. *Cochrane Database Syst Rev*. 2010:CD004876.
- Nichol KL, Nordin JD, Nelson DB, Mullooly JP, Hak E. Effectiveness of influenza vaccine in the community-dwelling elderly. *N Engl J Med*. 2007;357:1373–81.
- Centers for Disease Control and Prevention. Interim guidance for influenza outbreak management in long-term care facilities. Atlanta: CDC; 2011.
- Van den Dool C, Hak E, Bonten MJ, Wallinga J. A model-based assessment of oseltamivir prophylaxis strategies to prevent influenza in nursing homes. *Emerg Infect Dis*. 2009;15:1547–55.
- Ye M, Jacobs A, Khan MN, et al. Evaluation of the use of oseltamivir prophylaxis in the control of influenza outbreaks in long-term care facilities in Alberta, Canada: a retrospective provincial database analysis. *BMJ Open*. 2016;6:e011686.
- Barnes S, Golden B, Wasil E. MRSA transmission reduction using agent-based modeling and simulation. *INFORMS J Comput*. 2010;22:635–46.
- Jaramillo C, Taboada M, Epelde F, Rexachs D, Luque E. Agent based model and simulation of MRSA transmission in Emergency Departments. *Procedia Comput Sci*. 2015;51:443–52.
- Blanco N, Eisenberg MC, Stillwell T, Foxman B. What transmission precautions best control influenza spread in a hospital? *Am J Epidemiol*. 2016: kwv293.
- Rubin MA, Jones M, Leecaster M, et al. A simulation-based assessment of strategies to control clostridium difficile transmission and infection. *PLoS ONE*. 2013;8:e80671.
- NACI, Canadian Immunization Guide Chapter on Influenza and Statement on Seasonal Influenza Vaccine for 2016-2017. Ontario: Public Health Agency of Canada. Available from: URL: <http://www.phac-aspc.gc.ca/naci-ccni/flu-2016-grippe-eng.php>. [Accessed on 30 January, 2017].
- Schünemann HJ, Hill SR, Kakad M, et al. WHO Rapid Advice Guidelines for pharmacological management of sporadic human infection with avian influenza A (H5N1) virus. *The Lancet Infect Dis*. 2007;7:21–31.
- World Health Organization. Limiting the spread of pandemic, zoonotic, and seasonal epidemic influenza; 2010. Available at: URL: http://www.who.int/influenza/resources/research/research_agenda_influenza_stream_2_limiting_spread.pdf, [Accessed 7 September, 2016].
- Salathé M, Kazandjieva M, Lee JW, Levis P, Feldman MW, Jones JH. A high-resolution human contact network for infectious disease transmission. *Proc Natl Acad Sci U S A*. 2010;107:22020–5.
- Laskowski M, Xiao Y, Charland N, Moghadas SM. Strategies for early vaccination during novel influenza outbreaks. *Sci Rep*. 2015;5. doi:10.1038/srep18062.
- Laskowski M, Greer AL, Moghadas SM. Antiviral strategies for emerging influenza viruses in remote communities. *PLoS ONE*. 2014;9:e89651.
- Laskowski M, Duvvuri VR, Buckeridge DL, Wu G, Wu J, Moghadas SM. Influenza H3N2 variant viruses with pandemic potential: preventing catastrophe in remote and isolated Canadian communities. *Prevent Med*. 2013;57:910–3.
- Laskowski M, Moghadas SM. A general framework for agent-based modelling with applications to infectious disease dynamics. *Proc Int Symp Math Comput Biol*. 2014;9:318–39.
- Mostaço-Guidolin LC, Demko AB, Pizzi NJ, Moghadas SM. A software development framework for agent-based infectious disease modelling. *INTECH Open*. 2011;33:641–64.
- Ferguson NM, Cummings DA, Cauchemez S, et al. Strategies for containing an emerging influenza pandemic in Southeast Asia. *Nature*. 2005;437:209–14.
- Yang Y, Longini IM Jr, Halloran ME. Design and evaluation of prophylactic interventions using infectious disease incidence data from close contact groups. *J R Stat Soc*. 2006;55:317–30.
- Jefferson TO, Rivetti D, Di Pietrantonj C, Rivetti A, Demicheli V. Vaccines for preventing influenza in healthy adults. *Cochrane Database Syst Rev*. 2007;CD001269.
- Lessler J, Reich NG, Brookmeyer R, Perl TM, Nelson KE, Cummings DA. Incubation periods of acute respiratory viral infections: A systematic review. *Lancet Infect Dis*. 2009;9:291–300.
- Rainwater-Lovett K, Chun K, Lessler J. Influenza outbreak control practices and the effectiveness of interventions in long-term care facilities: a systematic review. *Influenza Other Respir Viruses*. 2014;8:74–82.

31. Hightower J, Borriello G. A Survey and Taxonomy of Location Systems for Ubiquitous Computing, Technical Report 2001-UW-CSE01-08-03. Seattle: University of Washington, Computer Science and Engineering; 2001.
32. Saxena M, Gupta P, Jain BN. Experimental Analysis of RSSI-based Location Estimation in Wireless Sensor Networks, Communication Systems Software and Middleware and Workshops. 3rd IEEE/Create-Net International Conference on Communication System Software and Middleware (COMSWARE '08). Bangalore; 2008. p 503–10.
33. Stehlé J, Voirin N, Barrat A, et al. Simulation of an SEIR infectious disease model on the dynamic contact network of conference attendees. *BMC Med.* 2011;9.
34. Cattuto C, Van den Broeck W, Barrat A, Colizza V, Pinton JF, Vespignani A. Dynamics of person-to-person interactions from distributed rfid sensor networks. *PLoS ONE.* 2010;5:e11596.
35. Stehlé J, Voirin N, Barrat A, et al. High-resolution measurements of face-to-face contact patterns in a primary school, *PLoS ONE.* 2011;6:e23176.
36. Isella L, Romano M, Barrat A, et al. Close encounters in a pediatric ward: Measuring face-to-face proximity and mixing patterns with wearable sensors. *PLoS ONE.* 2011;6:e17144.
37. Vanhems P, Barrat A, Cattuto C, et al. Estimating potential infection transmission routes in hospital wards using wearable proximity sensors. *PLoS ONE.* 2013;8:e73970.
38. Anderson RM, May RM, Anderson B. Infectious diseases of humans: dynamics and control. Oxford: Oxford University Press; 1992.
39. Pastor-Satorras R, Vespignani A. Epidemic spreading in scale-free networks. *Phys Rev Lett.* 2001;86:3200.
40. Lloyd-Smith JO, Schreiber SJ, Kopp PE, Getz WM. Super-spreading and the effect of individual variation on disease emergence. *Nature.* 2005;438:355–9.