Quantifying Influenza Exposure Within Hospitals And Nursing Homes

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Quantifying Influenza Exposure within Hospitals and Nursing Homes

Drew Dickinson

Year Completed: 2019

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Master of Public Health

Yale School of Public Health, Department of Epidemiology of Microbial Diseases

First Reader: Louise-Marie Dembry, MD MS MBA

Second Reader: Susan Huang, MD MPH
Abstract

**Background:** Influenza acquisition in hospitals and nursing homes (NHs) highlights the need for infection prevention to protect patients from contagious diseases while under the care of a healthcare facility. We quantified influenza exposure in both settings and compared facility-onset influenza rates in order to determine if risks of acquiring influenza differed by type of healthcare facility since infection prevention practices are less standardized and less rigorous in NHs.

**Methods:** We conducted a retrospective cohort study of California hospital and NH inpatients during the 2015-2016 influenza season, defined as the peak influenza month, plus the two adjacent months, using claims data. Exposure-days per average daily census were quantified by summing influenza exposure-days per facility and then dividing by the average daily census of each facility. Hospital-onset influenza (HOI) and nursing home-onset influenza (NHOI) rates were calculated by dividing the number of facility-onset cases by patient-days at-risk, excluding the first two days of stay. NHOI rates were based upon recently admitted patients (first fourteen days of stay) due to the less frequent reporting of claims codes for longer stay residents.

**Results:** We evaluated events from December 2015 to April 2016. Across 343 hospitals and 1,048 NHs, we calculated 55,970 days of influenza exposure in hospitals and 3,451 days of influenza exposure in NHs. There was a mean of 1.0 (SD: 0.9) influenza hospital exposure-days per average daily census versus a mean of 0.02 (SD: 0.06) influenza NH exposure-days per average daily census during the influenza season (p<0.001). The mean HOI rate was 0.04 (SD: 0.08) influenza cases per 1,000 patient-days and the mean NHOI rate was 0.10 (SD: 0.21) cases per 1,000 recently admitted resident-days (p=0.011) (OR=10.8, 95% CI: 6.2 to 18.9).

**Conclusion:** Despite having greater influenza exposure, hospitals had nearly an eleven-fold lower rate of facility-onset influenza than NHs, suggesting opportunity for improved infection prevention activities in NHs. Validation of administrative data are needed.
Acknowledgements

I would like to thank Dr. Susan Huang of the University of California Irvine School of Medicine for her generous mentoring and guidance through this project. I would like to thank Dr. Louise-Marie Dembry of the Yale School of Public Health for sparking my interest in the field of healthcare epidemiology and for her assistance in editing this manuscript. I would also like to thank Dr. Stefan Gravenstein of Brown University for his comments in preparation of this manuscript. Lastly, I would like to thank Jiayi He and Gabrielle Gussin of the University of California Irvine School of Medicine for their help and patience with data collection and analysis. This project would not have been completed without them.
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Table 1. Characteristics of hospitals and nursing homes.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Hospitals Median (IQR)</th>
<th>Nursing Homes Median (IQR)</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>343</td>
<td>1,048</td>
</tr>
<tr>
<td>Total Annual Admissions</td>
<td>6,316 (2,287 - 11,239)</td>
<td>384 (223 - 605)</td>
</tr>
<tr>
<td>Average Daily Census During</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Influenza Season</td>
<td>114 (46 - 201)</td>
<td>224 (146 - 293)</td>
</tr>
<tr>
<td>Mean Length of Stay (days)</td>
<td>6 (5 - 7)</td>
<td>117 (65 - 214)</td>
</tr>
<tr>
<td>Mean Age (years)</td>
<td>59 (55 - 63)</td>
<td>76 (72 - 80)</td>
</tr>
<tr>
<td>% Male</td>
<td>42 (38 - 48)</td>
<td>42 (36 - 50)</td>
</tr>
<tr>
<td>% White</td>
<td>76 (56 - 89)</td>
<td>57 (39 - 78)</td>
</tr>
<tr>
<td>% Medicare</td>
<td>48 (39 - 55)</td>
<td>40 (22 - 56)</td>
</tr>
<tr>
<td>% Medicaid</td>
<td>24 (12 - 36)</td>
<td>35 (18 - 52)</td>
</tr>
<tr>
<td>Mean Elixhauser Comorbidity Score</td>
<td>3 (3 - 3)</td>
<td>1 (1 - 1)</td>
</tr>
</tbody>
</table>

Note: IQR, interquartile range
Table 2. Facility-level characteristics associated with facility-onset influenza in bivariate and multivariate negative binomial regression.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Bivariate</th>
<th>Multivariate³</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Odds Ratio (95% CI)</td>
<td>P Value</td>
</tr>
<tr>
<td>Facility Type</td>
<td></td>
<td></td>
</tr>
<tr>
<td>(Nursing Home vs Hospital)</td>
<td>2.6 (2.1, 3.3)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Influenza Exposure-</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Days per Average</td>
<td>0.9 (0.8, 1.0)</td>
<td>0.16</td>
</tr>
<tr>
<td>Daily Census</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Facility Mean Age in Years per 10 Year Change</td>
<td>1.6 (1.4, 1.7)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Facility % White Race per 10% Change</td>
<td>1.02 (0.97, 1.06)</td>
<td>0.50</td>
</tr>
<tr>
<td>Facility % Male per 10% Change</td>
<td>0.8 (0.7, 0.9)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Facility Mean Length of Stay in Days per 10 Day Change</td>
<td>1.00 (0.99, 1.01)</td>
<td>0.48</td>
</tr>
</tbody>
</table>
Note. CI, confidence interval.

\(^a\)Multivariate analysis: Medicare and Medicaid usage were collinear with age. Annual admissions and comorbidity score (Elixhauser score) were collinear with facility type. Average daily census during influenza season was collinear with influenza exposure-days per average daily census.
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**Figure 4.** Incidence rate of hospital-onset influenza (A) and nursing home-onset influenza (B) per 1,000 patient and resident-days, respectively, across California counties. Unadjusted rate ratio comparing facility-onset influenza in nursing homes to hospitals across California counties (C). NA signifies that a rate ratio could not be calculated, either because data on that county could not be collected or because the hospital-onset influenza incidence rate was 0.
**Body of Thesis**

**Specific Aims & Hypotheses**

*Primary Study Aim & Hypothesis*

1. **Aim:** Quantify the proportion of hospital and nursing home days with potential risk of influenza exposure to other patients/residents, visitors, and staff.

   **Hypothesis:** Patients hospitalized with influenza are significant sources of influenza exposure to patients hospitalized for other reasons. I hypothesize that hospitals will have a greater proportion of influenza exposure-days compared to nursing homes as more individuals present to the hospital specifically for influenza care.

*Secondary Study Aim & Hypothesis*

2. **Aim:** Quantify facility-onset influenza rates, comparing the rate of hospital-onset influenza to nursing home-onset influenza.

   **Hypothesis:** I hypothesize that rates of nursing home-onset influenza will be greater compared to hospital-onset influenza even when accounting for increased age and comorbidities of nursing home residents, driven by less stringent infection prevention measures compared to hospitals.

**Background**

Influenza is a highly seasonal viral illness that infects between 5% and 20% of the United States population every year.¹ Common symptoms of influenza include fever, pharyngitis, and myalgias. While less common, complications from influenza can arise such as pneumonia,
secondary infections, myocarditis, and sepsis. Transmission of the virus is mediated through the contact of respiratory droplets with mucosal surfaces, such as the mouth, nose, and throat, and occurs with a peak in the winter and early spring months. This seasonality has been attributed to both virologic and human host factors. Decreased humidity in winter months may increase the virus’ survival in the environment while winter months are associated with increased human crowding and the use of indoor heating which has the possibility of recycling dry air.2,3

Influenza acquired in healthcare settings may be an important contributor to seasonal morbidity and mortality. Roughly 200,000 individuals are hospitalized due to influenza or influenza-related complications annually.4 This large, seasonal concentration of influenza cases within healthcare settings increases the likelihood of transmission to uninfected individuals with at least 15% of influenza cases having their onset in healthcare facilities.5

Individuals within healthcare facilities may be at particularly high risk of contracting influenza due to proximity to other ill patients, shared healthcare personnel (HCP), and presence of multiple comorbidities. Moreover, HCP, visitors, and other patients can import influenza from the community, with as many as half of HCP who are infected with influenza working while mildly symptomatic (i.e. upper respiratory symptoms in the absence of fever).6,7

Outbreaks of hospital-onset influenza (HOI) are quite heterogenous. A review conducted by Salgado and colleagues found that nosocomial influenza outbreaks can have attack rates as high as 50% and last for several months.8 Conversely, analyses over multiple influenza seasons suggest that many cases of HOI are singular events with clustering sparsely occurring during peak influenza season.9,10 The heterogeneity of HOI outbreaks may be partially attributed publication bias whereas the most extensive outbreaks are likely to be published despite their relative rarity and in contrast to what systematic assessments find for attributable risk.
On the other hand, outbreaks of influenza in nursing homes (NHs) have been widely reported in the United States. The comorbidities and increased age of residents substantially increases this population’s risk of acquiring influenza, even in the face of high vaccination rates.\textsuperscript{11-13} Those over 65 years of age have been estimated to account for approximately 90\% of influenza deaths nationally, with risk of death increasing as age increases.\textsuperscript{4,14,15} In contrast to hospitals, outbreaks in NHs have shown high clustering and attack rates ranging from 5\%-50\%.\textsuperscript{16-19} In fact, clustering of cases occurs commonly not only within NHs, but also across multiple NHs.\textsuperscript{20,21}

Hospitals and NHs have a duty to protect their patients and residents from influenza. Hospitals are a setting for patients to recover under the care of medical experts; therefore, a case of HOI that extends care and increases acuity is antithetical to a hospital’s primary mission.\textsuperscript{4,22,23} Similarly, NHs are primarily residential facilities aiding in the care of a sub-acute and chronically ill population.\textsuperscript{22} NH-onset influenza (NHOI) is a highly concerning event that not only disrupts the residential environment but unnecessarily increases morbidity and mortality within this vulnerable population. NHOI events are also antithetical to an NH’s primary mission to uphold health and resident safety.

The paucity of published influenza outbreak reports in hospitals compared to NHs may be related to system factors. The higher ratio of clinical staff to patients and the implementation of robust infection prevention measures (e.g. droplet precautions, single rooms, hand hygiene) in hospitals may reduce the likelihood of transmission of influenza and other contagious pathogens compared to NHs. However, data comparing the risk of HOI and NHOI between interconnected facilities are lacking. This study involves an analysis of facility-onset influenza in hospitals and neighboring NHs to assess whether different risks of influenza exist by setting.
Methods

Days of exposure engendered by patients/residents who have influenza and require hospitalization or NH care were quantified. The risks of hospital and NH-onset influenza were calculated using administrative data from statewide databases and compared while adjusting for influenza exposure and facility-level risk factors for influenza infection.

1. Study Design

This is a comparative study of two retrospective cohorts: adult patients in 343 California general acute care hospitals and adult NH residents in 1,048 California NHs.

2. Study Period

The study period included the 5-month 2015-2016 influenza season, defined as the peak influenza month plus the two preceding and subsequent months.

3. Study Population

The hospital cohort consisted of all adult patients hospitalized in California adult general acute care hospitals during the 5-month influenza season. The NH cohort consisted of all adult NH residents in California licensed NHs that accept any reimbursement from the Centers for Medicare and Medicaid Services (CMS) during the 5-month influenza season.

Under the primary aim of quantifying influenza exposure, the NH cohort included all NH residents. Under the secondary aim of quantifying facility-onset influenza rates, the NH cohort consisted solely of recently admitted residents. Recently admitted
residents were define as all residents during their first fourteen days of stay. NH resident assessments in MDS are performed five days and fourteen days after admission, followed by monthly assessments in order to qualify for Medicare billing. Due to reduced fidelity of coding practices after the first fourteen days of stay, influenza cases may be underreported and underestimated after this period.

A length of stay restriction was not applied to hospitalized patients. Daily assessments performed in hospitals means that the detection of influenza is just as likely during longer hospital stays as it is for shorter stays.

4. Data Sources

Data was collected using databases from California’s Office of Statewide Health Planning and Development (OSHPD) and CMS’ Minimum Data Set (MDS) for NHs.\textsuperscript{24,25} OSHPD collects mandatory patient-level data on all hospitalizations from California hospitals. The MDS is a national database that collects detailed data on all residents in NHs receiving any payment from CMS. Influenza diagnoses of hospital patients and NH residents were abstracted from OSHPD and the MDS, respectively, according to \textit{International Statistical Classification of Disease, Tenth Revision} (ICD-10) codes.

5. Outcomes (Dependent Variables)

Under the primary aim of quantifying influenza exposure in California healthcare facilities, we quantified influenza exposure-days by summing all of the inpatient-days for hospitalized patients with influenza diagnoses, either present on admission or acquired during the hospital stay. This reflected the total number of potential days that the
institution may expose other patients to influenza in the absence of robust infection prevention activities. We first assumed that patients remained infectious for the entire duration of their hospital stay. This is plausible because most patients are hospitalized less than the typical ten-day infectious period for influenza, and also because those with longer stays may have prolonged viral shedding due to their severity of infection and compromised health status. As a sensitivity analysis, we quantified exposure-days under the assumption that cases are infectious for ten days or until discharge, whichever is sooner. Any calendar day on which a patient was hospitalized and within the infectious period was counted as an exposure-day. Patients admitted to the hospital with influenza were assumed to be infectious upon admission. Patients whose influenza diagnosis was not present on admission were assumed to be infectious starting at the midpoint of their hospital stay.

Quantification of influenza exposure-days within NHs was performed similarly to hospitals to the extent that administrative coding would allow. Specifically, NH data do not include the same number of diagnostic codes (10 for NHs vs 24 for acute care hospitals), and NH data do not include an indicator of whether a diagnosis is present on admission. Due to the longer stay of NH residents, residents with influenza were assumed to be infectious for a maximum of ten days or until discharge, whichever sooner. Because it was not possible to determine whether influenza was present on NH admission, cases of influenza in NH residents that were not diagnosed in a preceding hospital visit were assumed to start at the midpoint of the NH stay. Patients who were hospitalized with influenza and transferred to an NH while still infectious had any remaining period of the ten-day infectious period attributed to the NH.
Influenza exposure-days per average daily census were calculated as a means to normalize across facilities of various sizes. Exposure-days for each facility were summed and divided by the average daily census for each facility during the influenza season. Average daily census was calculated by summing the daily census for each facility during the influenza season and dividing it by the number of days in the 5-month season.

Under the secondary aim of calculating the rate of facility-onset influenza, cases of hospital-onset influenza (HOI) were summed among those with influenza diagnoses that were designated as not present on admission and among patients who had hospital lengths of stays of at least three days. Analysis was limited to those staying at least three days as the first 48 hours after admission is generally allotted for the identification and work-up of community-acquired infections that were incubating upon admission. Cases of HOI were assumed to have a date of onset at the midpoint of a patient’s hospital stay. Any date of onset that fell within the prescribed influenza study period was included. Cases of influenza that were diagnosed within 48 hours of admission to an NH after transfer from a hospital were attributed to the previous hospital stay.

Diagnoses of influenza are rarely made within NHs. Therefore, cases of nursing home-onset influenza (NHOI) would be underestimated if only influenza cases diagnosed in an NH were summed. To account for this underestimation, cases of influenza present on hospital admission after transfer from an NH were summed along with the number of influenza diagnoses made in an NH. Similar to hospitals, residents diagnosed with influenza in an NH were assumed to acquire influenza at the midpoint of admission and the most recent assessment period associated with an influenza diagnosis. Cases that were diagnosed upon transfer to a hospital were assumed to acquire influenza on the date of admission.
transfer. Cases were included if the date of influenza acquisition fell within the influenza season and within the previously defined recent admission period. This included those who were transferred to a hospital between day three and fourteen of their NH stay where influenza was diagnosed upon admission.

HOI rates were calculated per 1,000 at-risk patient-days. Hospital patient-days during influenza season among all hospitalized patients starting from the third day of stay through discharge were totaled. Patient-days from those who presented to the hospital with influenza present on admission were excluded.

Similarly, NHOI rates were calculated per 1,000 at-risk recently admitted resident-days, as well. Recently admitted resident-days at risk consisted of all NH-days from the third to fourteenth day. Resident-days from those that were diagnosed with influenza in a hospital and then transferred to an NH were excluded.

6. **Independent Variables**

Collection of facility-level characteristics included number of annual admissions, mean daily census during influenza season, facility mean length of stay, mean facility age, percentage of male patients/residents in facility, percentage of White patients/residents in facility, percentage of patients/residents with Medicare in facility, percentage of patients/residents with Medicaid in facility, and mean facility Elixhauser score.29

7. **Statistical Analysis**
Descriptive characteristics of facilities in the hospital and NH cohort were reported for the entire year. Median values and interquartile ranges were reported for continuous variables. Mean values across hospital and NH subgroups were compared using a two-sided Wilcoxon two-sample test.

Mean exposure-days per average daily census across hospital and NH subgroups were compared using a two-sided Wilcoxon two-sample test. Mean facility-onset influenza rates across facility type were also compared using a two-sided Wilcoxon two-sample test.

The association between facility type (NH compared to hospital) and facility-onset influenza rates were evaluated using a negative binomial regression model controlling for influenza exposure and facility-level characteristics. A negative binomial distribution was used due to the overdispersion of facilities in which the facility-onset influenza count was zero. Adjusted comparisons to assess the effect of facility type on facility-onset influenza rate were performed controlling for influenza exposure-days per average daily census and facility characteristics (number of annual admissions, mean daily census during influenza season, facility mean length of stay in days, mean facility age in years, percentage of male patients/residents in facility, percentage of White patients/residents in facility, percentage of patients/residents with Medicare in facility, percentage of patients/residents with Medicaid in facility, and mean facility Elixhauser score). Age, race, sex, and length of stay were scaled to reflect changes by ten units in negative binomial regression.
All analyses were performed in SAS, version 9.4 (SAS Institute, Cary, NC). All confidence intervals were reported with 95% confidence and all reported p-values were reported at $\alpha=0.05$ and were two-sided.

Results

We evaluated influenza cases from December 2015-April 2016 in 343 hospitals and 1,048 NHs in California. Facility characteristics are shown in Table 1. Compared to hospitals, NHs had significantly fewer mean annual admissions (454 (range: 11 to 2203) vs 7,915 (range: 20 to 42,159), p<0.001), a significantly lower mean facility Elixhauser comorbidity score (1 (range: 0 to 6) vs 3 (range: 0 to 5), p<0.001), as well as significantly lower percentages of white residents in the facility (57% (range: 0% to 100%) vs 70% (range: 1% to 99%), p<0.001) and residents on Medicare in the facility (40% (range: 0% to 100%) vs 48% (range: 0% to 88%), p<0.001). Compared to hospitals, NHs had a significantly greater mean daily census during influenza season (241 (range: 1 to 2,337) vs 143 (range: 1 to 797), p<0.001), facility mean length of stay (173 days (range: 1 day to 3,262 days) vs 10 days (range: 3 days to 275 days), p<0.001), mean facility age (75 years (range: 8 years to 90 years) vs 59 years (range: 31 to 78 years), p<0.001), and percentage of residents on Medicaid in the facility (37% (range: 0% to 100%) vs 26%, (range: 0% to 77%), p<0.001). Hospitals and NHs did not significantly differ on the percent of male patients or residents in the facility.

Using influenza present on hospital admission as a proxy for community-onset influenza, influenza cases peaked in mid-February of 2016 (Figure 1). We evaluated influenza cases from December 2015-April 2016.
The peak of HOI cases occurred during the week of February 16, 2016 with a total of 26 cases. This peak of HOI cases coincided with the peak of community-onset cases. The peak of NHOI cases occurred during the following week of February 23, 2016 with a total of 113 cases.

In California hospitals, 8,583 patients contributed 55,970 hospital-days of influenza exposure. In NHs, 413 residents contributed 3,451 NH-days of influenza exposure. There was a median of 5 (interquartile range (IQR): 3 to 7) days of infectiousness per hospitalized influenza patient and a median of 10 (IQR: 7 to 10) days of infectiousness per NH resident with influenza. This translated to a mean of 1.0 (standard deviation (SD): 0.9) influenza hospital exposure-days per average daily census versus a mean of 0.02 (SD: 0.06) influenza NH exposure-days per average daily census during influenza season (p<0.001) (Figure 2). Upon sensitivity analysis, the mean influenza hospital exposure-days per average daily census decreased to 0.9 (SD: 0.7). However, hospitals continued to demonstrate greater mean exposure compared to NHs (p<0.001).

Despite higher exposure, hospitals had a lower facility-onset influenza rate. Among all 343 hospitals, 91 (27%) had at least one case of HOI, and among all 1,048 NHs, 297 (28%) had at least one case of NHOI. There were 180 cases of HOI in 91 hospitals and 468 cases of NHOI in 297 NHs (Figure 3). Among all facilities, this translated to a mean HOI rate of 0.04 (SD: 0.08) influenza cases per 1,000 patient-days and a mean NHOI rate of 0.10 (SD: 0.21) cases per 1,000 recently admitted resident-days (p=0.011). Among facilities with at least one case of facility-onset influenza, the mean HOI rate was 0.13 (SD: 0.11) influenza cases per 1,000 patient-days and the mean NHOI rate was 0.36 (SD: 0.26) cases per 1,000 recently admitted resident-days (p<0.001). In bivariate analysis, NHs had 2.6 (95% CI: 2.2 to 3.3) times the rate of facility-onset influenza compared to hospitals (Figure 2). In adjusted analysis, NHs had 10.8 (95% CI: 6.2 to
18.9) times the rate of facility-onset influenza compared to hospitals (Table 2). Adjusted analysis controlled for the facility characteristics of mean facility age in years, percent White patients/residents in the facility, percent male patients/residents in the facility, mean facility length of stay in days, and influenza exposure-days per occupied bed. The proportion of Medicare and Medicaid patients/residents in the facility was collinear with mean facility age. Annual admissions and mean facility Elixhauser score were collinear with facility type. Average daily census during influenza season was collinear with influenza exposure-days per average daily census.

Both hospitals and NHs had a wide range of facility-onset influenza rates. Cases of HOI occurred across 22 counties and cases of NHOI occurred across 33 counties (Figure 4). Throughout 56 counties, the average HOI rate per county was 0.02 (SD: 0.04) HOI cases per 1,000 patient-days. Thirty-four counties containing 78 hospitals had no cases of HOI based on diagnostic administrative codes while 22 counties containing 265 hospitals had a mean HOI incidence of 0.06 (SD: 0.04) HOI cases per 1,000 patient-days (Fig 2). Of note, these 22 counties contain 85% of California’s population according to 2017 projections based upon the 2010 California census.\(^3\)0\)

The average NHOI rate per county was 0.12 (SD: 0.15) NHOI cases per 1,000 recently admitted resident-days. Eighteen counties containing 53 NHs had 0 cases of NHOI compared to 33 counties containing 993 NHs which had at least one case of NHOI. The mean incidence of NHOI in these 33 counties was 0.20 (SD: 0.14) NHOI cases per 1,000 recently admitted resident-days. Only two counties (El Dorado and Merced) had a facility-onset rate ratio below 1.00. The remaining 20 counties in which both HOI and NHOI were non-zero had a mean NHOI rate that was 3.5 (SD: 2.3) times as high as the HOI rate.
Discussion

In this study, we calculated nearly 60,000 of days of healthcare influenza exposure to other patients and residents in California hospitals and NHs during influenza season. Despite having lower monthly exposure-days per average daily census, NHs had nearly eleven-fold the rate of facility-onset influenza during a resident’s first two weeks of stay compared to hospitals. Importantly, the reported risks of influenza are likely underestimated due to imperfect testing in both NHs and hospitals. Nevertheless, hospitals generally perform more medical testing than NHs, thus the differences may in fact be even greater than reported here.

Hospitals had over 50 times the amount of influenza exposure-days per average daily census compared to NHs. This significant difference in influenza exposure persisted in sensitivity analysis. The greater amount of influenza exposure in hospitals is likely attributed to the presentation of patients directly to the hospital specifically for influenza-related care. The presentation and resolution of patients with influenza within the hospital greatly confines influenza exposure to hospitals. This risk of direct admission for influenza care is much lower in NHs, and both settings have similar risks related to exposure from healthcare workers or visitors from the community who may be contagious with influenza. Thus, even with the underestimation, it is likely that there is a truly higher risk of influenza exposure in hospitals.

The elevated rate of facility-onset influenza in NHs compared to hospitals is concerning. Residents in NHs are often a subset of patients that were previously hospitalized. The increased risk upon transfer to an NH suggests there are facility-level differences that increase one’s risk of acquiring influenza in an NH. Furthermore, the increase in the odds ratio of facility-onset influenza after adjustment for characteristics of the facility population suggests there are systematic facility differences between hospitals and NHs.
Structural differences between facility types may account for this difference. For example, as hospitals trend toward single-occupancy rooms, many NHs maintain multi-occupancy rooms. This crowding in rooms has been suggested to increase one’s risk of acquiring influenza. Differences in infection prevention programs between the facility types may also help explain these differences in influenza rates. NHs have only been recently mandated by CMS to establish infection prevention programs, many of which have yet to reach their full potential in terms of scope and staffing. Those facilities that do implement standard precautions may apply them less commonly or less consistently given the nature of the setting. Additionally, NHs are meant to resemble a home setting. Droplet precautions and isolation may be not used, or even desired, to the extent they are in a hospital setting. Limited staffing within NHs may also prevent proper oversight of compliance of residents, staff, and visitors to recommended precautions. The limited infection prevention measures are evidenced by data suggesting nearly ninety percent of California NHs received a citation from CMS regarding infection prevention between 2014 and 2017. Unfortunately, these citations are rarely followed up on, and NHs often incur no fine. As these incipient programs develop over time, NH-onset infection rates will likely fall to resemble those of hospitals. In the meantime, it is imperative that NHs are actively supported in their efforts to strengthen their infection prevention efforts and are kept accountable for citations they may receive.

In addition, we found the peak of HOI to coincide with the peak of community-onset influenza. Retrospective studies of HOI have observed a similar relationship between influenza peaks. Conversely, we observed the peak of NHOI to follow the hospital and community-onset peak. In an analysis of four influenza seasons in Northern Ireland, influenza outbreaks for three seasons were also found to occur after the community peak. The differences in the timing
of the two peaks may be attributed to patient movement and infection prevention. Community influenza cases likely present directly to the hospital, acting as a source of influenza exposure during the same time as outbreaks within the community. After clinical resolution, these hospitalized individuals may be transferred to an NH while still infectious, serving as a source of exposure in the NH after the community peak has passed. Infection prevention measures that do not properly prevent transmission from previously hospitalized residents recovering from influenza in an NH may lead to further NHOI cases later on.

Furthermore, facility-onset influenza cases displayed clustering. As demonstrated in Figure 3A, cases of HOI tended to co-locate in areas with cases of NHOI. However, of note, spatial analysis was not performed to formally test for the presence of statistically significant clusters. Robust sharing networks of patients between facilities within counties may account for this clustering trend.\(^{38}\) Hospitals can contribute to a substantial amount of infectious disease exposure in NHs.\(^ {39}\) Due to the relatively short hospital lengths of stay and the prolonged infectiousness of patients with influenza requiring hospitalization, there is a high probability that patients hospitalized for influenza are discharged to NHs while still infectious. Thus, hospitals and NHs that share a patient network should work together to ensure infection prevention activities are followed through among facilities.

Our study has several limitations. First, administrative data need validation for this purpose. Assessment of influenza cases in NHs is limited as the number of diagnostic codes available in NH administrative datasets are reduced compared to hospitals (10 for NHs vs 24 for acute care hospitals). This may cause a differential underestimation of influenza exposure and cases in NHs. Second, we could not account for differing indications to test for and diagnose influenza between facility types, leading to possible ascertainment bias. Hospitals are required to
perform daily patient assessments, potentially facilitating frequent detection and recording of an influenza diagnosis. In contrast, NH resident assessments are required five and fourteen days after admission, followed by monthly assessments. The prolonged time between formal assessment periods means a higher chance of failing to detect a case of influenza arising during interim-assessment periods. Additionally, many NHs may lack resources to test or access to facilities that readily test for influenza antigen, reducing the likelihood of influenza diagnoses in this setting.\textsuperscript{40} Such differences in influenza diagnosis may further underestimate influenza exposure in NHs and the rate of NHOI. Similarly, facilities that presumptively diagnose and treat influenza in the absence of diagnostic tests may risk overestimation of their facility exposure and facility-onset influenza rate. It is not possible to know the collective magnitude or direction of such bias in our dataset because we do not have access to laboratory results, only administrative claims. Third, our algorithm (based on the OSHPD encrypted identifier which relies upon date of birth, gender, and social security number) to track patients between hospitals and to generate linkers into the MDS NH dataset may have mismatches. However, we would anticipate that such mismatches would be non-differential to the question we are asking. Nevertheless, matching of the hospital database to the NH database was performed on a county basis to limit mismatches to a specific region.

Our results have important implications for infection prevention. Hospitals and NHs both have the duty of continuing to care for sick patients while protecting others from transmission. Due to higher influenza exposure within hospitals and the primary presentation of individuals specifically to hospital for influenza care, hospitals have a greater exposure burden to protect against. The primary goal of NHs, on the other hand, should be to reduce their facility-onset rate through reducing exposure from those recently transferred from a hospital.
Healthcare facilities should maximize attention to influenza symptoms and institute infection prevention responses (e.g. pre-emptive vaccination, droplet precautions, single room if available, restricting ill visitors) to minimize any chance of facility-onset influenza exposure during influenza season.\textsuperscript{41,42} Importantly, these infection prevention measures have been demonstrated to have a larger reduction in influenza risk when bundled together as opposed to being used individually.\textsuperscript{43}

CDC-recommended attentiveness to influenza includes assessing for influenza symptoms followed by testing upon facility admission and ensuring symptomatic HCP and visitors stay home when ill, even when mildly symptomatic.\textsuperscript{1,44} Unique to NH residents is the possibility that influenza presents with atypical signs and symptoms such as behavior changes and may warrant clinical testing.\textsuperscript{45} In order to prevent transmission within facilities, the CDC recommends vaccination of both patients, residents, and HCP, the use of droplet precautions and hand hygiene, plus restricting visitation for ill persons.\textsuperscript{1,45} Vaccination is especially important for individuals over 65 years of age before the onset of the influenza season. In fact, CMS mandates the offering of influenza vaccination to residents.

Importantly, patients and facilities are quite diverse across California. This is demonstrated in the heterogeneity of facility-onset influenza rates in the choropleth in Figure 4. Interventions to limit exposure, therefore, should be targeted for the specific needs of hospitals and NHs in individual regions. However, we analyzed a single influenza season. While the 2015-2016 influenza season in California was classified as moderate,\textsuperscript{46} more severe influenza seasons may expect to have decreased heterogeneity between facility-onset influenza rates across the state. Further longitudinal analyses of facilities over several influenza seasons may elucidate on this heterogeneity and expose regions that chronically struggle with facility-onset influenza.
Nevertheless, all facilities can benefit from attentiveness to influenza symptoms and infection prevention and containment strategies, but certain facilities may require more targeted interventions to reduce their known high risk.

In conclusion, healthcare facilities serve as a substantial source of influenza exposure to patients/residents, staff, and visitors. Use of administrative diagnosis databases identified that a significantly greater proportion of influenza exposure occurs in hospitals; yet, the rate of facility-onset influenza is greater in NHs. Moreover, these administrative data likely underestimate this difference. These data are provocative. The recent mandate of formalized infection prevention programs in NHs may have a positive impact in future years. We hope this study serves as a call to action for better assessment and response to influenza cases to reduce facility-onset cases to their lowest possible level.
References


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