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Hospital Influenza Admissions as a Harbinger for Nursing Home Influenza Cases

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A B S T R A C T

Objectives: To determine temporal associations of local measures of influenza morbidity and mortality by the Centers for Disease Control and Prevention (CDC) with influenza hospitalizations in nursing home residents.
Design: Retrospective, longitudinal panel study.
Setting and participants: Long-stay nursing home residents, aged 65 years or older in 823 nursing homes from 2011 to 2015.
Measures: CDC-reported rates of influenza and pneumonia mortality and laboratory-confirmed influenza hospitalizations. We compared the CDC measures to nursing home resident hospitalizations due to (1) all-cause, (2) a primary diagnosis of respiratory or circulatory illness, and (3) a primary diagnosis of pneumonia or influenza based on Medicare Part A Claims data.
Results: Our final sample included 273,743 unique residents in 819 nursing homes in 108 cities. National laboratory-confirmed influenza-associated hospitalizations for the group aged 65 and older occurred 0 to 1 week prior to nursing home resident influenza-related hospitalizations (Spearman $\rho = 0.54$). CDC reported influenza hospitalizations occurred 3 weeks prior to CDC-reported influenza deaths ($\rho = 0.59$). Nursing home resident influenza hospitalizations occurred 2 weeks before local CDC-reported pneumonia and influenza deaths occurred ($\rho = 0.44$).
Conclusions/implications: Publicly reported CDC measures correlate well with nursing home hospitalizations for pneumonia and influenza. Rates of laboratory-confirmed influenza hospitalizations (as reported by the CDC) may be a useful surrogate for nursing home influenza outbreaks but should be considered along with local indicators of disease outbreaks. Early community signals could be clinically leveraged as a trigger for increased infection control measures in nursing homes.

Influenza illness has recently been associated with 600,000 hospitalizations (2016-2017 season) and 12,000 to 56,000 annual deaths.[1] Nursing home residents are particularly susceptible to influenza, and, if infected, risk hospitalization and death.[2-5] Protecting nursing home residents from influenza is therefore important.

Staff, visitors, and transfers into the home can introduce influenza into the nursing home. Once introduced, influenza can spread and result in outbreaks absent aggressive measures to reduce person-to-person viral transmission.[6-8] Established infection control guidelines for the long-term care setting to limit viral transmission include hand hygiene, social distancing, use of personal protective equipment, influenza vaccination for residents and staff, and antiviral chemoprophylaxis and early treatment of new cases.[9,10] Despite extensive efforts, influenza remains a problem in the long-term care setting.

Seasonal signals for influenza activity could be helpful in anticipating a rising risk for upcoming nursing home outbreaks.[11] Examples of potential seasonal signals for influenza risk to nursing homes include community measures of morbidity and mortality such as pneumonia and influenza hospitalizations, deaths in the community, community laboratory testing results, and hospital transfers to or from nursing homes with respiratory illness during influenza season. Some of these measures may be useful as early indicators of activity or as measures of the extent of severe infection. We would expect that hospital admission diagnoses of community and nursing home admissions with respiratory illness could serve as a proxy for influenza activity, and severity and increasing activity could presage outbreaks in community nursing homes. An alert from the hospital for rising respiratory illness activity could serve nursing home leadership to know when to redouble efforts aimed at enhancing influenza control measures, such as to improve surveillance for new illness; maximize vaccination; enhance hand hygiene; and enforce respiratory etiquette for staff, visitors, and residents.[12-14] However, it is unknown if localized hospital-level respiratory illness and influenza activity are necessary or a broad national measure is sufficient for monitoring and anticipating local risk.

Our aim was to assess whether rises in community influenza morbidity and mortality signal an imminent rise in influenza hospitalizations for local nursing home residents. Specifically, we were interested in determining whether local measures of influenza morbidity and mortality [Centers for Disease Control and Prevention (CDC)-reported deaths by city] or national measures (laboratory-confirmed hospitalizations) were temporally associated with influenza hospitalizations in nursing home residents.

Methods

We conducted a retrospective post hoc analysis of “long-stay” (prior residence of at least 100 days in the home with no more than 10 days out) fee-for-service residents of 823 nursing homes enrolled in an influenza vaccine trial (NCT01815268).[15] This study was approved by the Institutional Review Board. Nursing homes were randomized to offer either high-dose (Fluzone High-Dose; Sanofi Pasteur, Swiftwater, PA) or standard-dose (Fluzone, Sanofi Pasteur) vaccine to their residents and standard-dose influenza vaccine to their staff as standard of care for 2013-2014 influenza season (A/H1N1-predominant season) and followed for a primary outcome of hospitalization due to respiratory illness.15 Evaluating the relationship between the nursing home and community rates of influenza was a pre-planned analysis and the high-dose trial only recruited homes within 50 miles of a city where the CDC monitors influenza hospitalizations and mortality.[16] For each home, a running count of the weekly number of long-stay (LS) residents, their rates of influenza and pneumonia, and respiratory hospitalizations and citywide influenza deaths was determined for the 2011-2012, 2012-2013, 2013-2014, and 2014-2015 influenza seasons. We utilized Minimum Data Set assessments, version 3.0, linked to the Medicare enrollment record, to identify the weekly count of long-stay residents aged > 65 years, who were enrolled in part A for at least 6 months and without HMO enrollment for all participating nursing homes from 2011-2015. Each resident was linked to Medicare claims, and additional hospitalization

measures were obtained from the Medicare Provider and Analysis Review(MedPAR inpatient files) and eligibility data from the Medicare enrollment record.

Local CDC reports on influenza and pneumonia mortality, as well as national laboratory-confirmed influenza hospitalizations for those > 65 years of age, were used to assess the association between community influenza illness and nursing home influenza illness. Mortality data contain information from US cities in which the CDC identifies morbidity and mortality due to influenza from vital statistics data.[16] Data included weekly counts of pneumonia and influenza deaths (aggregated, not person-level) as a marker of city-wide influenza morbidity. The raw count of influenza and pneumonia deaths were population adjusted to determine deaths per 100,000 individuals using the 2013 estimates for each city from the US Census.[17] Each study nursing home was matched to its nearest (defined by Haversine distance, ie, shortest point) CDC-monitored city using Google Maps API and the "ggmap" R package.[18] We evaluated data from 108 cities (12 dropped because of no nearby eligible nursing homes, and 2 cities dropped because of incomplete reporting during the study time period, 2011-2015). After linkage, the total number of patients and hospitalizations was aggregated to the city level for comparison with CDC rates, and we calculated their weekly rate of influenza deaths per 100,000 population. Laboratory-confirmed influenza-associated hospitalizations are reported nationally as the Influenza Hospitalization Surveillance Network (FluSurv-NET).[19] FluSurv-NET covers > 70 counties in the 10 Emerging Infections Program (EIP) states (California, Colorado, Connecticut, Georgia, Maryland, Minnesota, New Mexico, New York, Oregon, and Tennessee) and additional states (varying by year) as part of the Influenza Hospitalization Surveillance Project (IHSP) states.

We compared the CDC community data to 3 measures of morbidity in the nursing home: (1) overall hospitalization rate, (2) hospitalizations with a primary diagnosis of respiratory or circulatory illness [International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) codes 390-519],[20,21] and (3) hospitalizations with a primary diagnosis of pneumonia or influenza ICD-9 diagnosis of 480.xx-488.xx.[22,23] Influenza illness can sometimes precipitate other acute illnesses through deconditioning, inflammation, or respiratory failure, or simply be misclassified (e.g., acute respiratory failure or myocardial infarction). Broad respiratory/circulatory case definition (2) and all-cause measure (3) were included to evaluate whether hospitalizations indirectly related to an NH index influenza case were correlated with CDC-reported measures.

Our primary objective was to determine the strength of correlation between nearby cities' pneumonia and influenza mortality rates and nursing home-specific measures of influenza as well as national rates of influenza hospitalization. We evaluated for a temporal association, the presence of a lag- or lead-in period between influenza in the community and influenza in nursing home residents.

The strength of association between the CDC and NH influenza measures was tested first using simple, cluster-adjusted correlation statistics (Spearman rho rank correlation) to identify which nursing home measure was most associated with community rates. We then computed cross-correlation measures with a 5-week lag/lead test to determine if the rise in influenza in the community was associated with the rise in influenza in nursing home settings. All analyses were conducted in R, version 3.4.3.[24]

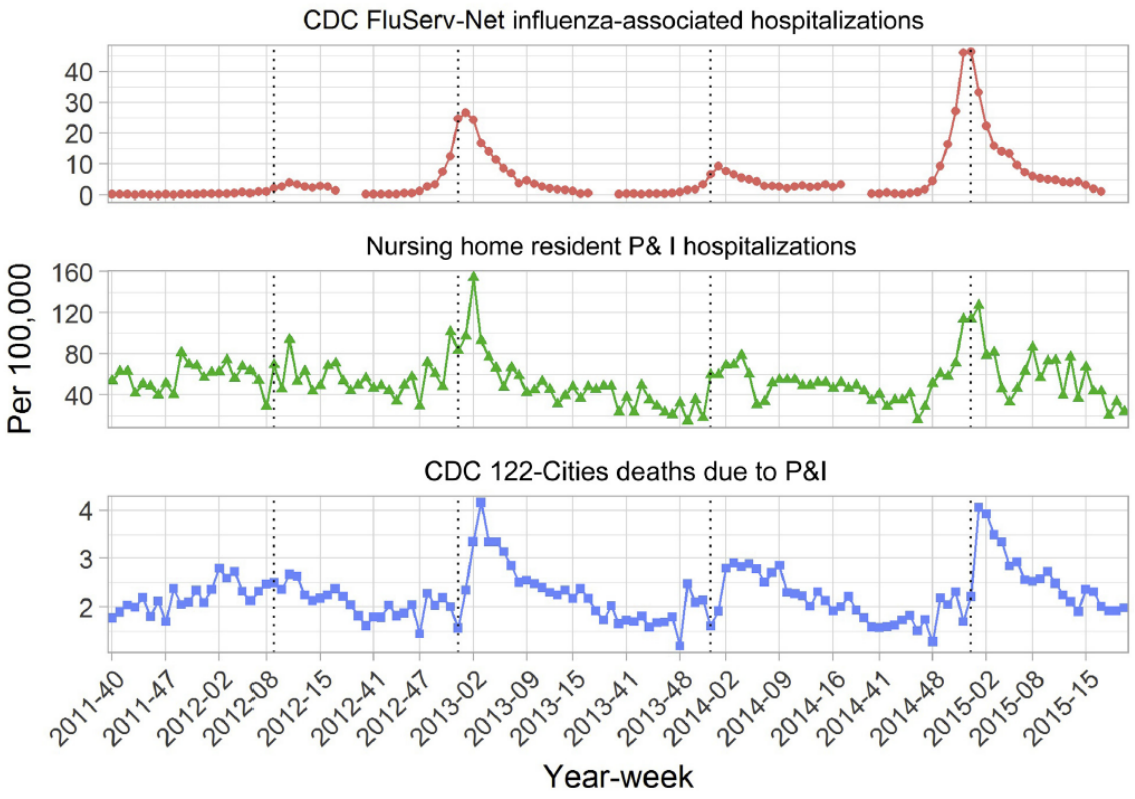

Fig. 1. Weekly nursing home hospitalizations from 2011 to 2015, nursing home residents vs publicly reported measures. The top figure shows laboratory-confirmed influenza hospitalizations among those aged > 65 years from CDC surveillance data. All measures are reported as no./100,000. The middle figure shows reported nursing home hospitalizations with a primary diagnosis of pneumonia and influenza (480.xx-488.xx). The bottom figure shows CDC-reported deaths due to pneumonia and influenza from the CDC 122 Cities data set. All measures are reported as no./100,000. The dotted lines represent the peak influenza week reported by the Centers for Disease Control for that season. P&I, pneumonia and influenza.

Results

After excluding homes with no eligible long-stay residents, 819 nursing homes in 108 cities were included in the analysis. Among these homes, 968,077 unique residents had at least 1 day in a participating nursing home from 2011-2015. After limiting to age $\geq$ 65 years (n = 837,753) and long-stay residents, the final sample included 273,743 residents. On average, there were 8 homes per city with a mean 345 residents (interquartile range of 119-437). The mean bed occupancy rate was 84% and 63% of patients were on Medicaid. Local nursing home hospitalization rates were derived from 91,844 patient-years of exposure time in 819 nursing homes. Overall, there were 40,452 all-cause, 12,474 respiratory/circulatory, and 2584 pneumonia and influenza hospitalizations identified during the 2011-2012, 2012-2013, 2013-2014, and 2014-2015 influenza seasons. The 2012-2013 influenza season had the highest average pneumonia and influenza hospitalizations per week, 58.3 per 100,000 residents.

Figure 1 shows the Centers for Disease Control 122 Cities (mortality) and FluServ-Net (hospitalizations) measures over time compared with long-stay NH resident hospitalizations for pneumonia and influenza. The Spearman rho (ρ) correlation statistic between the local 122 Cities mortality data and long-stay NH resident hospitalizations

demonstrated a moderate correlation overall. The highest was for all-cause hospitalizations (0.41, P < .001), then pneumonia and influenza (0.38, *P* < .001), and lastly respiratory and circulatory hospitalizations (0.25, *P* = .006). The Spearman ρ correlation statistic between the national CDC FluServ-Net laboratory-confirmed influenza-associated hospitalizations for those aged > 65 years in the community and NH resident hospitalizations was moderately correlated with pneumonia and influenza hospitalizations (0.44, *P* < .001), and less correlated for any respiratory or circulatory diagnoses (0.25, *P* = .006), and all-cause hospitalizations (0.27, *P* < .001).

Figure 2 illustrates the temporal relationship between CDC influenza measures and NH resident hospitalizations with a primary diagnosis of pneumonia or influenza for up to 5weeks before and after the index week. FluServ-Net laboratory-confirmed influenza-associated hospitalizations were most strongly correlated 0-1 weeks prior (ρ = 0.44; Figure 2, top panel) to long-stay NH resident hospitalizations for pneumonia or influenza. FluServ-Net influenza hospitalizations were most strongly correlated 3 weeks prior to CDC 122 Cities reported deaths due to pneumonia and influenza (ρ = 0.59; Figure 2, middle panel). The NH resident hospitalizations were most strongly correlated 2 weeks before CDC 122 Cities pneumonia and influenza deaths (ρ =0.54; Figure 2, bottom panel).

Discussion

In an assessment of 108 US cities and 819 nearby nursing homes, we found a moderately strong correlation between community influenza metrics and a number of measures of influenza morbidity in the nursing home. We noted that rates of community hospitalizations in those aged > 65 years slightly precede or occur with hospitalizations in nursing home residents followed by influenza morbidity/mortality (Figure 2). This observation supports the hypothesis that outbreaks of influenza in the community lead to the introduction of influenza (staff, visitors, new residents) into the nursing home in the immediate future, which is in turn associated with deaths 2 weeks afterward. All US nursing homes that receive Medicare funds are required to have formalized infection prevention programs by 2020. One function of these programs is to reduce exposure of residents to contagious diseases that may be introduced into the nursing home. Our data suggest that close monitoring of community hospitalization rates could serve to alert nursing home staff to consider escalating prevention and control strategies in their nursing homes to reduce the residents' risk for developing influenza.

However, this approach may be problematic as hospitalization rates measured by the CDC (FluServ-Net) are not provided publicly at a very granular local level. Alternatively, regional and local influenza activity is tracked by the state health departments and local hospitals. Department of health and hospital partnerships with nursing homescould take advantage of local hospital respiratory illness activity to keep vigil for imminent threats of high influenza exposure. Such a partnership could produce reports to complement publicly available influenza trend information. This approach could offer another tool to improve early signal detection. Although we observe that the even the national rates correlate with local disease, it would be ideal to have a direct community measure to signal nursing home administration. Also, there may be an opportunity to use more advanced analytical methods to improve early signal detection via automated machine learning and prediction methods using local, sparse data.

Additionally even if a local measure of influenza hospitalization were provided, it may be too infrequent in certain locations to be a useful signal-especially if there is a delay in reporting. In the absence of high-quality hospitalization data for a community, a potential approach would be to leverage local influenza testing laboratories (institutional, clinic-based, or individual) to identify early signals.

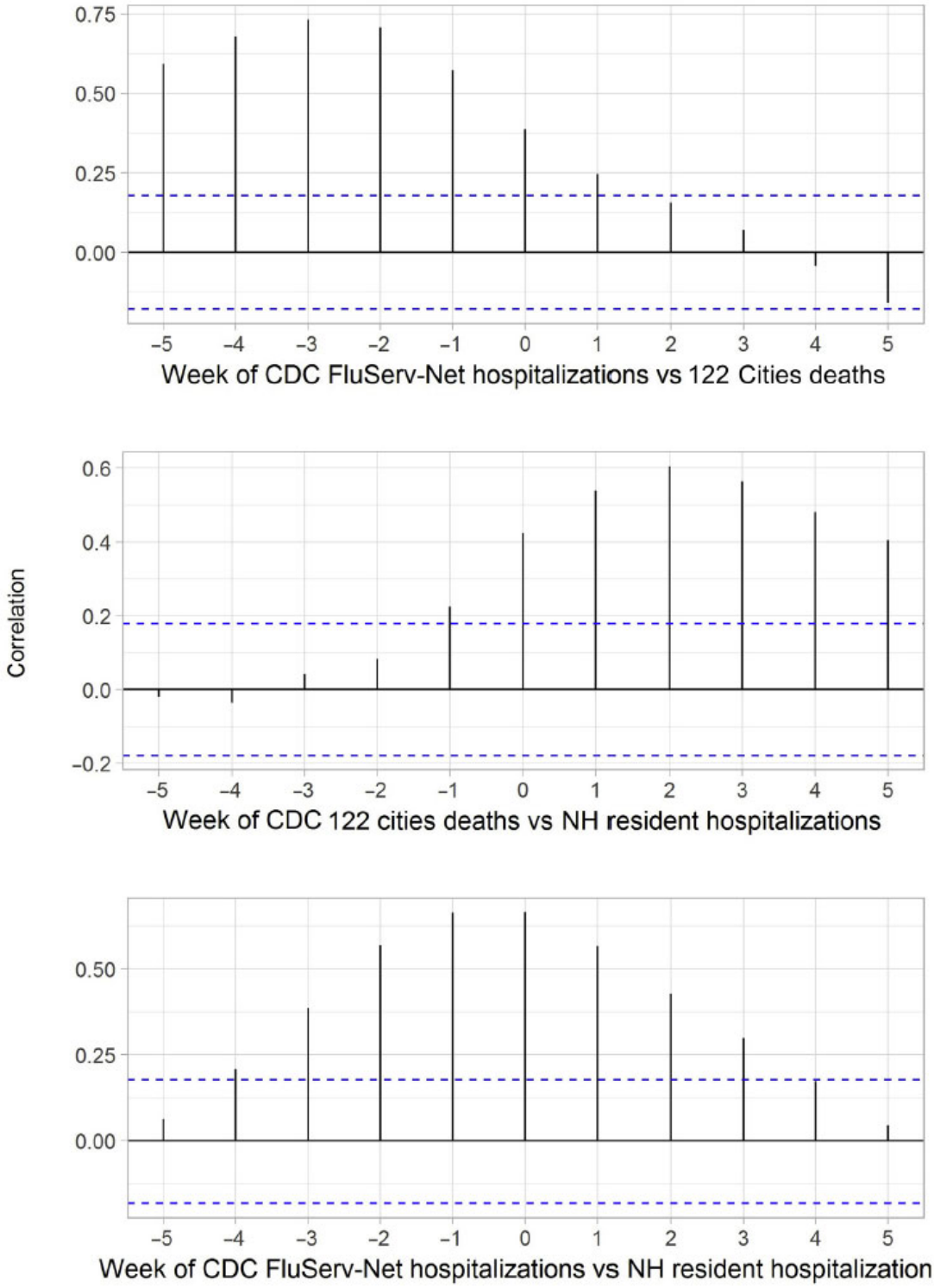

Fig. 2. Cross-correlation plots showing lag-times and lead-times across four influenza seasons (2011-2015). Top: Relationship between CDC FluServ-Net laboratory-confirmed influenza hospitalizations aged > 65 years and CDC 122 Cities deaths due to pneumonia and influenza showing hospitalizations were most strongly associated with deaths 3 weeks in the future. Middle: Relationship between CDC 122 Cities deaths due to pneumonia and influenza and NH resident hospitalizations due to pneumonia and influenza showing local pneumonia and influenza deaths were most strongly correlated 2 weeks after NH resident hospitalizations. Bottom: Relationship between CDC FluServ-Net laboratory-confirmed influenza hospitalizations and NH hospitalizations due to

pneumonia and influenza showing the community hospitalizations were most strongly correlated to NH resident hospitalizations that occurred in the same week or 1 week afterward. Blue dashed lines represent coverage probability for the 95% confidence interval. NH, nursing home.

Assuming a suitable measure is found, it is important to involve local nursing homes in the early signal warnings and interventions to mitigate outbreaks. There are many prevention measures that could be employed, including staff and patient vaccination for influenza (including increasingly common mandatory employee vaccination programs); respiratory hygiene stations and enforcement/encouragement of respiratory etiquette, including masking for symptomatic patients; declining visitation by symptomatic visitors; and sending ill staff home under a working well policy.25-30 As a practical approach, a period of nursing home epidemicity indicated by publicly reported CDC measures could instigate more stringent adherence to policies during a window of high risk. Although a collective group of prevention strategies is important, vaccination may be particularly impactful because influenza can be mild and even asymptomatic but still transmissible.[15,30]

Additionally, a future opportunity may be nursing home influenza morbidity as its own publicly reported measure. Publicly reported community measures seem to broadly follow nursing home morbidity, and therefore community warning signals may be sufficient in the home, especially in locations with few nursing homes and low event rates. However, areas with a large long-term care population and multiple nursing homes (i.e., larger cities) could benefit from local sentinel event monitoring partnerships where they systematically deploy point-of-care tests or leverage a partnership with their contracted laboratory, emergency department, or hospital for timely influenza testing. A cluster of nursing homes could potentially avoid outbreaks with such a proactive system. This system would have additional benefits beyond reporting vaccination rates, as the effectiveness of the vaccine varies significantly by season and identifying sentinel events could help with infection control even when the vaccine is less effective.

Our study was limited by the availability of publicly reported data on influenza disease in the general and nursing home population. We could not determine which nursing home residents had laboratory-confirmed cases of influenza-associated hospitalizations, or identify less acute cases that did not lead to hospitalization. We also analyzed aggregated influenza rates over time, not individual cases, adjusting for potential confounders. Therefore, potential sources of bias exist, particularly including misclassification of influenza disease. The associations reported here support the hypothesis that community outbreaks of influenza precede influenza introduction into the nursing home setting, and subsequent mortality. However, the practical impact of this finding may be limited by a lack of frequent hospitalizations or local data for particular communities. Our data originated from 823 nursing homes that were enrolled in a vaccination clinical trial.[15] This large, nationwide sample should allow generalizability to the broader nursing home population. Treatment assignment was random and included 2 commonly used vaccines in the older adult population. We evaluated a time-frame that included influenza seasons before and after the primary study dates to reduce the potential that study enrollment may have biased our results.

Conclusion

We found that publicly reported CDC measures of influenza hospitalizations precede nursing home hospitalizations for pneumonia and influenza, which precede community deaths due to influenza and pneumonia. Rates of laboratory-confirmed influenza hospitalizations (as reported by the CDC) may be a useful surrogate for nursing home influenza outbreaks, but should be considered along with local indicators of disease outbreaks. Early community signals could be clinically leveraged as a trigger for increased infection control measures in nursing homes.

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Potential Conflicts: S.S.H. conducts studies for Stryker (Sage Products), Monlycke 3M, Clorox, Xttrium, and Medline. L.G.M. conducts studies for Stryker (Sage Products), 3M, Clorox, Xttrium, and Medline; has received grants from Gilead Sciences, Achaogen, Merck, Abbott, and Cepheid; and has served as a consultant for Tetraphase for the conduct of other studies. J.A.M. conducts studies for Stryker (Sage Products), 3M, Clorox, Xttrium, and Medline; received grants and personal fees from Achaogen and Allergan; and grants from Cempra, Melinta, Science37, Theravance, and Thermo Scientific for the conduct of other studies. T.I.S. has received advisory board honorarium from Pfizer for unrelated work. V.M. holds stock in PointRight, Inc, and chairs the Independent Quality Committee for HRC Manor Care, Inc, and a scientific advisory committee for NaviHealth. Companies contributing product have no role in the design, conduct, analysis, or publication of the studies.

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