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MAJOR ARTICLE

# Patient and Epidemiological Factors Associated With Influenza Testing in Hospitalized Adults With Acute Respiratory Illnesses, 2016–2017 to 2019–2020

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***Background.*** Data are limited on influenza testing among adults with acute respiratory illness (ARI)–associated hospitalizations. We identified factors associated with influenza testing in adult ARI-associated hospitalizations across the 2016–2017 through 2019–2020 influenza seasons.

***Methods.*** Using data from 4 health systems in the United States, we identified hospitalizations that had an ARI discharge diagnosis or respiratory virus test. A hospitalization with influenza testing was based on testing performed within 14 days before through 72 hours after admission. We used random forest analysis to identify patient characteristics and influenza activity indicators that were most important in terms of their relationship to influenza testing.

***Results.*** Across 4 seasons, testing rates ranged from 14.8%–19.4% at 3 pooled sites and 60.1%–78.5% at a fourth site with different testing practices. Discharge diagnoses of pneumonia or infectious disease of noninfluenza etiology, presence of ARI signs/symptoms, hospital admission month, and influenza-like illness activity level were consistently among the variables with the greatest relative importance.

***Conclusions.*** Select ARI diagnoses and indicators of influenza activity were the most important factors associated with influenza testing among ARI-associated hospitalizations. Improved understanding of which patients are tested may enhance influenza burden estimates and allow for more timely clinical management of influenza-associated hospitalizations.

**Keywords.** acute respiratory illness; clinical testing; hospitalization; influenza.

Seasonal influenza causes significant morbidity and mortality in the United States (US), with estimates of 400 000–810 000 influenza-associated hospitalizations each season between 2016–2017 and 2019–2020 [1]. Influenza testing is a critical component of public health surveillance and response but is not systematic [2, 3] and therefore may lead to bias in estimates of influenza burden. Data are limited on the frequency of influenza testing in hospitals, the characteristics of tested patients, and whether testing patterns have changed over time. Better understanding of testing patterns and potential biases could inform public health strategies to prevent community transmission, ensure appropriate and early clinical management of patients at increased risk of severe outcomes, and improve understanding of disease burden.

The Centers for Disease Control and Prevention, in conjunction with 4 US healthcare systems, established the VISION Network to utilize electronic health records (EHRs) to better understand influenza risk, complications, and vaccine effectiveness. Using these data, we differentiated between hospitalizations in adults with acute respiratory illness (ARI) who were and were not tested for influenza using patient-level characteristics and state-level influenza activity during the 2016–2017 through 2019–2020 influenza seasons.

## METHODS

### Study Population and Design

The VISION Network was comprised of 4 health systems: HealthPartners (Minnesota and Wisconsin), Kaiser Permanente Northwest (Oregon and Washington), the Southern California Consortium (SCC; includes University of California campuses in Irvine, Los Angeles, and San Diego), and the University of Colorado (UCO). Data on patient characteristics, hospitalizations, and respiratory virus testing were extracted from EHRs and claims across 87 hospitals. For each influenza season (defined as 1 September through 31 May of

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the following year), a retrospective patient cohort included persons aged ≥18 years based on prior healthcare utilization in the year before 1 September (look-back period) and active membership/insurance eligibility [4].

Data were collected on ARI-associated hospitalizations during the influenza season, defined as persons with respiratory virus testing performed (identified using Logical Observation Identifiers Names and Codes or *Current Procedural Terminology* codes) or diagnosed with acute respiratory illness (identified using *International Classification of Diseases, Ninth or Tenth Revision* [*ICD-9* or *-10*] codes, Supplementary Table 1). Hospitalizations were included if admission occurred during influenza season and length of stay was ≥24 hours. Data from readmissions within 30 days of discharge from a previous ARI hospitalization were combined and analyzed as a single encounter.

#### Definitions

The outcome was receipt of an influenza test (rapid antigen, molecular assay, viral culture, serology, or fluorescent antibody) (Supplementary Table 2) captured by the health system within 14 days before through 72 hours after admission. Due to site differences in testing approaches and rates, we pooled data from HealthPartners, Kaiser Permanente Northwest, and SCC (hereafter referred to as the pooled sites) for analysis and performed separate analyses for UCO (Supplementary Methods).

We identified independent variables at the patient level and pertaining to local influenza activity. Demographic variables included patient sex, age, race/ethnicity, insurance type, and Social Vulnerability Index quartile [5]. Underlying conditions were identified based on the presence of an *ICD-9* or *-10* discharge code for ≥1 inpatient or outpatient encounter during the look-back period (Supplementary Table 3). Immunosuppressive medications (using RxNORM and National Drug Codes) prescribed during the look-back period were used in addition to discharge codes to identify immunocompromising conditions (Supplementary Table 4). We also captured intensive care unit (ICU) admissions during hospitalization.

ARI discharge diagnoses were selected with input from clinicians at participating health systems to enable the analysis of the relationship between ARI diagnosis and receipt of influenza testing using a broad range of ARI categories. These diagnoses were categorized into 13 mutually exclusive categories: chronic lung disease, coronavirus disease 2019 (COVID-19), exacerbation of chronic lung disease, infectious diseases of noninfluenza etiology (eg, pertussis, respiratory syncytial virus), influenza, lower respiratory tract infection, otitis media, pneumonia (any etiology), viral or respiratory illness complicating pregnancy, screening for/exposure to communicable diseases excluding influenza, signs/symptoms related to febrile and/or respiratory illness (eg, cough, shortness of breath, stridor, wheezing, fever, chills), upper respiratory infection, and other (eg, pneumothorax, acute or chronic respiratory failure and pulmonary collapse) (Supplementary Table 1). All eligible ARI diagnoses were assigned to a category; a single encounter with multiple ARI diagnoses may therefore be classified in >1 ARI category.

Three variables captured local influenza activity: (1) hospital admission month, (2) state-level influenza-like illness (ILI) activity level, and (3) state-level influenza test percent positivity (Supplementary Methods). ILI activity and percent positivity were matched to the state(s) of each VISION site and the *Morbidity and Mortality Weekly Report* week of the encounter based on the date of the influenza test or hospital admission if no influenza test was performed (Supplementary Methods).

#### Statistical Analysis

To identify which variables were more important in terms of their relationship to influenza testing, we utilized random forest analysis for its ability to handle many predictors, both high dimensional and nonlinear [6]. Random forest analysis is a method of ensemble learning that constructs and combines multiple decision trees for a single result (Figure 1). It allows for evaluation of variable contribution to the model, that is, variable importance (Supplementary Methods). Multiple imputation was used to handle the few variables with 1% missing observations.

The main random forest models used balanced training data and permutation variable importance (hereafter referred to as balanced, unconditional) for the pooled sites and UCO separately for each influenza season. To identify the most influential variables, we calculated variable importance values, defined as the difference in model prediction accuracy (ie, the number of observations classified correctly) before and after permuting a variable averaged across all fitted trees. A larger importance value indicates a greater reduction in model accuracy when the variable is randomly permuted, and therefore higher explanatory power for the original variable. Variable importance was calculated by setting all negative values to zero and dividing each variable importance value by the sum of all variable importance values. We selected 5% as the threshold for identifying important variables. We used the area under the receiver operating characteristic curve (AUC) as the indicator of model accuracy [7]; AUCs range from 0.5 to 1, with values closer to 1 indicating better accuracy.

Five sensitivity analyses were conducted for the pooled sites and UCO for the 2019–2020 influenza season. First, we compared 3 other types of models to the main balanced, unconditional model: (1) a conditional variable importance on the balanced trained model (balanced, conditional) to see if accounting for correlation between variables impacted results [8], (2) an imbalanced version of the conditional variable importance (imbalanced, conditional) to assess whether balancing

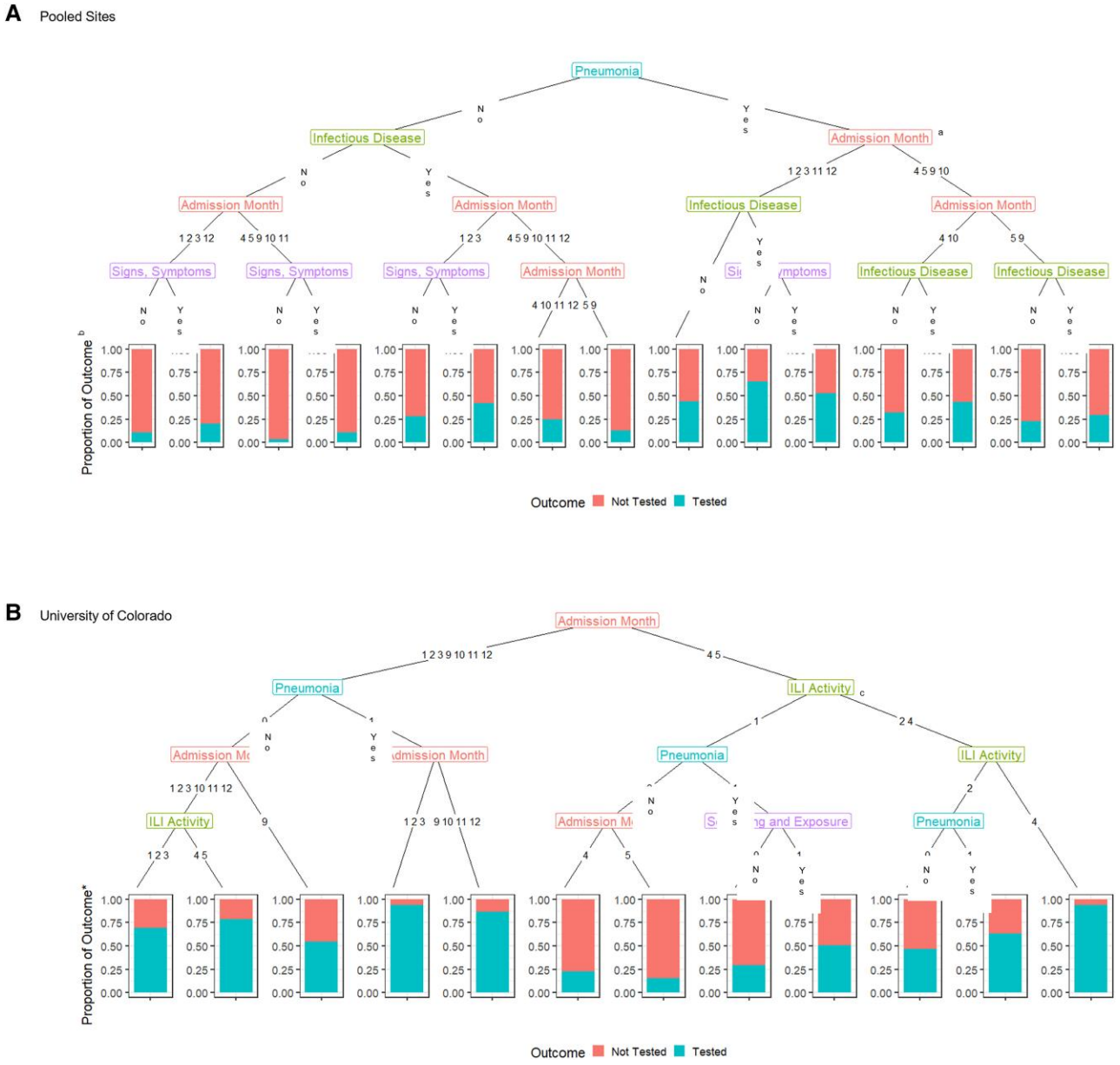



**Figure 1.** Example random forest tree constructed within the random forest using the unconditional balanced model for pooled sites (*A*) and University of Colorado (*B*) for the 2019–2020 influenza season. [a]Admission month numbers correspond to calendar months (1, January; 2, February, etc). [b]The lower portion of each shaded box represents the proportion of hospitalizations that were tested; the upper portion represents the proportion of hospitalizations that were untested. [c]Influenza-like illness (ILI) activity numbers correspond to ILI activity levels (1, minimal; 2, low; 3, moderate; 4, high; 5, very high).

impacted the potential for correlation adjustment, and (3) an unconditional variable importance on the imbalanced version (imbalanced, unconditional). The goal of these models was to validate the stability of the variables identified in the main model as important and provide insight into the best model choice based on underlying data. Second, we fit balanced, unconditional models to understand whether factors associated with testing differed by select patient-level or influenza activity characteristics. Models were fit after restricting to hospitalizations occurring during peak influenza months (Supplementary Methods) and to encounters with a pneumonia or influenza discharge diagnosis, and each was compared to the main results. We also compared results between patients with or without underlying conditions and by age group (<65 years vs ≥65 years). Third, we incorporated data on vital signs collected nearest to the time of hospital admission to assess whether they helped discriminate between encounters with and without influenza testing. Due to data availability, this analysis was restricted to SCC and UCO. Fourth, we used a narrower set of ARI discharge diagnoses (excluding viral or respiratory illness

complicating pregnancy, screening/exposure, otitis media, and chronic lung disease). Fifth, we restricted the model to January–May 2020 to examine whether testing practices changed early in the COVID-19 pandemic.

All analyses were conducted using SAS version 9.4 software (SAS Institute) or R software version 4.1.2 (R Core Team). This study was reviewed and approved by the Westat, Inc institutional review board (45 Code of Federal Regulations [C.F.R.] part 46; 21 C.F.R. part 56).

## RESULTS

### Influenza Testing Rates

Influenza testing among eligible hospitalizations at the pooled sites increased from 14.8% to 19.4% across the 4 seasons (Table 1). Testing rates were consistently higher at UCO than at the pooled sites but decreased from 75.0%–78.5% in earlier seasons to 60.1% in 2019–2020. More than 90% of tests performed at all sites across all seasons were molecular assays. Rapid antigen tests accounted for the majority of the remaining influenza tests, whereas viral culture, serology, and fluorescent antibody tests accounted for ≤0.5% of overall tests in each season. Most influenza testing (91.3%) was performed during hospitalization, including 58.7% on the day of admission and 25.9% on the day after admission. Testing before admission was documented in 8.7% of hospitalizations, including 5.8% of tests performed the day before admission.

### Characteristics of Hospitalizations With Influenza Testing

During the 2019–2020 season, the proportion of eligible hospitalizations with influenza testing at the pooled sites was similar between men (20.3%) and women (18.7%), by age group (18.0%–20.7%) and by racial/ethnic group (18.7%–25.6%) (Table 2). Testing was performed more often in persons with underlying conditions (20.9%–30.1%), particularly immunocompromising conditions, compared with persons with no reported underlying conditions (10.8%). At UCO, the overall proportion of tested encounters was higher. Men were tested more frequently than women (65.4% vs 57.1%), and patients aged 18–49 years were tested less frequently than those aged ≥50 years (47.6% vs 66.5%). Testing was performed more often in persons with underlying conditions (64.1%–77.0%). Across all sites, testing rates were higher in January–March (pooled sites, 27.0%–30.7%; UCO, 84.0%–87.2%), when ILI activity was high or very high (pooled sites, 24.3%–28.5%; UCO, 84.1%–84.5%), and when percent positivity was ≥5% (pooled sites, 21.3%–28.2%; UCO, 80.2%–83.9%). Testing patterns were similar in previous seasons (Supplementary Tables 5–7).

Nearly all ARI-associated hospitalizations (94.6% across all seasons) had an ARI discharge diagnosis; the remaining 5.4% of encounters had respiratory virus testing but no ARI discharge diagnosis. During the 2019–2020 season, 1.1% of encounters across all sites had respiratory virus testing performed but no ARI diagnosis. Compared to all ARI-associated hospitalizations, a larger proportion of eligible encounters without an ARI diagnosis occurred among patients aged 18–49 years, and a smaller proportion occurred among encounters with ICU admission during the hospitalization. There were also differences in the frequency of underlying conditions. Eligible encounters without an ARI discharge diagnosis occurred more frequently during periods of higher influenza activity compared to all hospitalizations (Supplementary Table 8). These differences were consistent across sites.

### Main Random Forest Analysis Results

In the 2019–2020 season at the pooled sites, pneumonia diagnosis had the highest relative importance (24.7%), followed by infectious disease of noninfluenza etiology diagnosis (13.9%), signs/symptoms related to febrile and/or respiratory illness (10.3%), hospital admission month (9.8%), and ILI activity (7.2%). Diagnoses of pneumonia and infectious disease of noninfluenza etiology along with hospital admission month consistently remained among the most important variables in previous seasons (Figure 2). The AUC ranged from 0.72 to 0.74 across the 4 seasons.

At UCO in the 2019–2020 season, hospital admission month and ILI activity had the highest relative importance (26.3% and 23.7%, respectively), followed by pneumonia diagnosis (9.7%), percent positivity (8.6%), and screening/exposure (5.4%). However, in all prior seasons, pneumonia and exacerbation of chronic lung disease consistently had the highest relative importance (range, 16.9%–20.9% and 15.3%–18.7%, respectively). Hospital admission month, ILI activity, infectious disease of noninfluenza etiology diagnosis, signs/symptoms, age, and race/ethnicity were important variables in ≥2 prior seasons (Figure 2). The relative importance of hospital admission month and ILI activity monotonically increased across seasons (4.1% to 26.3% and 1.4% to 23.7%, respectively). The AUC increased slightly from earlier seasons (0.72–0.74) to 2019–2020 (0.78).

### Sensitivity Analyses

In the first sensitivity analysis, the important variables were generally consistent across all models at the pooled sites (Figure 3). The balanced models had a higher AUC than the imbalanced models (0.72 vs 0.55). At UCO, the imbalanced unconditional model yielded similar results as the main balanced unconditional model. However, in the conditional models, percent positivity fell below the 5% threshold, whereas exacerbation of chronic lung disease, signs/symptoms, noninfluenza infectious diseases, and age exceeded the 5% threshold in 1 or both conditional models (Figure 3). The AUCs at UCO were similar between balanced (0.78) and imbalanced (0.77) models.

**Table 1. Proportions of Acute Respiratory Illness–Associated Hospitalizations[a] Tested for Influenza Virus Across Sites From 1 October 1 Through 31 May, by Season and Sensitivity Analysis**

| | Pooled Sites | | HealthPartners | | KPNW | | SCC | | UCO | |
|---|---|---|---|---|---|---|---|---|---|---|
| Season and Testing Rates | Tested/ Hospitalizations | (% Tested) | Tested/ Hospitalizations | (% Tested) | Tested/ Hospitalizations | (% Tested) | Tested/ Hospitalizations | (% Tested) | Tested/ Hospitalizations | (% Tested) |
| Season | | | | | | | | | | |
| 2016–2017 | 3925/26 470 | (14.8) | 509/2681 | (19.0) | 1088/8176 | (13.3) | 2328/15 613 | (14.9) | 3432/4575 | (75.0) |
| 2017–2018 | 5592/28 794 | (19.4) | 602/2788 | (21.6) | 1316/8262 | (15.9) | 3674/17 744 | (20.7) | 4028/5130 | (78.5) |
| 2018–2019 | 5446/29 810 | (18.3) | 495/3087 | (16.0) | 1282/8499 | (15.1) | 3669/18 224 | (20.1) | 4052/5288 | (76.6) |
| 2019–2020 | 5903/30 389 | (19.4) | 649/3014 | (21.5) | 1305/8728 | (15.0) | 3949/18 647 | (21.2) | 5175/8485 | (60.1) |
| Testing rates by sensitivity analyses, 2019–2020 season | | | | | | | | | | |
| Peak season | 1851/6722 | (27.5) | … | … | … | … | … | … | 1528/1812 | (84.3) |
| Pneumonia or influenza diagnosis | 2797/6411 | (43.6) | … | … | … | … | … | … | 2361/2924 | (81.0) |
| Age <65 y | 2815/14 742 | (19.1) | … | … | … | … | … | … | 2635/4613 | (57.1) |
| Age ≥65 y | 3088/15 647 | (19.7) | … | … | … | … | … | … | 2540/3872 | (66.0) |
| No underlying conditions | 395/3514 | (11.2) | … | … | … | … | … | … | 630/1373 | (46.0) |
| Any underlying condition | 5047/22 467 | (22.5) | … | … | … | … | … | … | 4545/7112 | (64.0) |
| Restricted ARI categories | 5664/26 207 | (21.6) | … | … | … | … | … | … | 4810/6774 | (71.0) |

Abbreviations: ARI, acute respiratory illness; KPNW, Kaiser Permanente Northwest; SCC, Southern California Consortium; UCO, University of Colorado.

[a]ARI-associated hospitalizations include hospitalizations with an ARI discharge diagnosis and/or respiratory virus testing.

In the second sensitivity analysis examining whether factors associated with testing differed by patient-level or influenza activity characteristics, testing rates at all sites were higher when restricted to encounters with a pneumonia or influenza diagnosis, lower when restricted to encounters among patients with no underlying conditions, and otherwise comparable to rates in the main model (Table 1).

When restricted to encounters at the pooled sites that occurred during the 2-month peak influenza season in the 2019–2020 season, hospital admission month and ILI activity no longer reached the 5% threshold, whereas pneumonia, signs/symptoms, and infectious disease diagnoses maintained or increased in importance compared to the main results (Figure 4). At UCO, pneumonia diagnosis increased in relative importance from 9.7% in the main model to 20.5% in the peak season model. Several variables no longer reached the 5% threshold in the peak season model, but the relative importance of infectious disease, age, race/ethnicity, and exacerbation of chronic lung disease increased to exceed the 5% threshold (range, 10.3%–14.7%). The AUC at UCO decreased from 0.78 in the main model to 0.70 in the peak season model.

After restricting the model to encounters with a pneumonia or influenza discharge diagnosis, pneumonia and signs/symptoms no longer met the 5% threshold at any site, which differed from the main results. However, ICU admission and Social Vulnerability Index at the pooled sites and screening/exposure and COVID-19 at UCO increased in importance and exceeded the 5% threshold. The AUC for this model compared to the main model decreased at the pooled sites (0.63 vs 0.72) but remained similar at UCO (0.79 vs 0.78).

When stratified by presence or absence of any underlying condition, the relative importance of pneumonia at the pooled sites was greater among patients with any underlying conditions (36.2%) than among patients with no underlying conditions (19.3%), whereas the relative importance of signs/symptoms was lower among patients with underlying conditions (10.3%) than those without (24.6%). At UCO, the relative importance of hospital admission month was lower among patients with no underlying conditions (19.7% vs 27.1%). Models stratified by age group yielded consistent results between age groups and were similar to results from the main analysis at all sites (Figure 4).

In the third sensitivity analysis, results incorporating vital signs at UCO and SCC were consistent with those from the main models. Respiratory rate at SCC was the only vital sign to exceed the 5% threshold (5.3%).

In the fourth sensitivity analysis limiting ARI diagnosis categories, testing rates were similar at the pooled sites (limited categories: 21.6% vs main model: 19.4%) and higher at UCO (limited categories: 71.0% vs main model: 60.1%). Results of the random forest analysis were consistent with the main analysis at both UCO and the pooled sites (Figure 5).

Finally, models restricted to January–May 2020 showed no differences at the pooled sites but did show an increase in the importance of ILI activity and percent positivity at UCO (Figure 5).

## DISCUSSION

Among 115 463 ARI-associated hospitalizations in adults across 4 US healthcare systems from 2016–2017 through

**Table 2. Patient Characteristics and Indicators of Influenza Activity Among Acute Respiratory Illness–Associated Hospitalizations[a] in Adults Aged ≥18 Years, 2019–2020**

| | 2019–2020 Influenza Season | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | Pooled Sites | | | | Colorado | | | |
| | All Hospitalizations | | Tested for Flu | | All Hospitalizations | | Tested for Flu | |
| Characteristic | No. | (Column %) | No. | (Row %) | No. | (Column %) | No. | (Row %) |
| Hospitalizations | 30 389 | (100.0) | 5903 | (19.4) | 8485 | (100.0) | 5175 | (60.1) |
| Sex | | | | | | | | |
| Male | 14 556 | (47.9) | 2948 | (20.3) | 3964 | (46.7) | 2592 | (65.4) |
| Female | 15 832 | (52.1) | 2954 | (18.7) | 4520 | (53.3) | 2582 | (57.1) |
| Missing | 1 | (0.0) | 1 | (100.0) | 1 | (0.0) | 1 | (100.0) |
| Age, y | | | | | | | | |
| 18–49 | 6831 | (22.5) | 1227 | (18.0) | 2462 | (29.0) | 1172 | (47.6) |
| 50–64 | 7911 | (26.0) | 1588 | (20.1) | 2151 | (25.4) | 1463 | (68.0) |
| 65–74 | 7106 | (23.4) | 1319 | (18.6) | 1757 | (20.7) | 1162 | (66.1) |
| ≥75 | 8541 | (28.1) | 1769 | (20.7) | 2115 | (24.9) | 1378 | (65.2) |
| Race/ethnicity | | | | | | | | |
| White, non-Hispanic | 18 913 | (62.2) | 3532 | (18.7) | 5902 | (69.6) | 3671 | (62.2) |
| Black, non-Hispanic | 1988 | (6.5) | 509 | (25.6) | 798 | (9.4) | 548 | (68.7) |
| Other, non-Hispanic | 2998 | (9.9) | 578 | (19.3) | 357 | (4.2) | 218 | (61.1) |
| Hispanic | 5221 | (17.2) | 1025 | (19.6) | 1162 | (13.7) | 666 | (57.3) |
| Unknown | 1269 | (4.2) | 259 | (20.4) | 266 | (3.1) | 72 | (27.1) |
| Insurance[b] | | | | | | | | |
| Medicare | 11 710 | (38.5) | 2140 | (18.3) | 2845 | (33.5) | 1918 | (67.4) |
| Medicaid | 6067 | (20.0) | 1265 | (20.9) | 2459 | (29.0) | 1534 | (62.4) |
| Private insurance | 3752 | (12.3) | 583 | (15.5) | 3705 | (43.7) | 2282 | (61.6) |
| Uninsured | 164 | (0.5) | 13 | (7.9) | 770 | (9.1) | 489 | (63.5) |
| Other insurance | 8754 | (28.8) | 1852 | (21.2) | 368 | (4.3) | 215 | (58.4) |
| Unknown insurance | 0 | (0.0) | 0 | (0.0) | 833 | (9.8) | 374 | (44.9) |
| Social Vulnerability Index, overall | | | | | | | | |
| 0–0.25 (lowest vulnerability) | 7284 | (24.0) | 1535 | (21.1) | 1464 | (17.3) | 908 | (62.0) |
| 0.2501–0.5 | 7114 | (23.4) | 1324 | (18.6) | 1070 | (12.6) | 668 | (62.4) |
| 0.5001–0.75 | 6352 | (20.9) | 1134 | (17.9) | 487 | (5.7) | 290 | (59.5) |
| 0.7501–1 (highest vulnerability) | 6295 | (20.7) | 1216 | (19.3) | 626 | (7.4) | 380 | (60.7) |
| Unable to geocode | 3139 | (10.3) | 656 | (20.9) | 4410 | (52.0) | 2659 | (60.3) |
| Missing | 205 | (0.7) | 38 | (18.5) | 428 | (5.0) | 270 | (63.1) |
| Underlying conditions[c] | | | | | | | | |
| No underlying conditions recorded | 3722 | (12.2) | 403 | (10.8) | 1373 | (16.2) | 630 | (45.9) |
| Blood disorders | 2947 | (9.7) | 754 | (25.6) | 844 | (10.0) | 562 | (66.6) |
| Any lung disease[d] | 12 526 | (41.2) | 2864 | (22.9) | 3559 | (41.9) | 2413 | (67.8) |
| Any heart disease[e] | 16 225 | (53.4) | 3509 | (21.6) | 4832 | (57.0) | 3223 | (66.7) |
| Liver disease | 4860 | (16.0) | 1025 | (21.1) | 162 | (1.9) | 111 | (68.5) |
| Any metabolic disease | 19 459 | (64.0) | 4120 | (21.2) | 3484 | (41.1) | 2429 | (69.7) |
| Neuromuscular | 10 655 | (35.1) | 2376 | (22.3) | 1786 | (21.1) | 1215 | (68.0) |
| Renal disease | 9678 | (31.8) | 2021 | (20.9) | 2816 | (33.2) | 1806 | (64.1) |
| HIV/AIDS (excluding asymptomatic HIV), hematologic malignancy, or other intrinsic immune conditions | 4233 | (13.9) | 1273 | (30.1) | 422 | (5.0) | 290 | (68.7) |
| Solid malignancy or organ transplantation | 3777 | (12.4) | 1071 | (28.4) | 0 | (0.0) | 0 | (0.0) |
| Rheumatologic or other inflammatory conditions | 3512 | (11.6) | 898 | (25.6) | 61 | (0.7) | 47 | (77.0) |
| Admitted to ICU during hospitalization | | | | | | | | |
| Missing | 1 | (0.0) | 0 | (0.0) | 113 | (1.3) | 56 | (49.6) |
| No | 23 489 | (77.3) | 4774 | (20.3) | 6372 | (75.1) | 3874 | (60.8) |
| Yes | 6899 | (22.7) | 1129 | (16.4) | 2000 | (23.6) | 1245 | (62.3) |
| ARI discharge diagnosis category[f] | | | | | | | | |
| Influenza | 432 | (1.4) | 285 | (66.0) | 237 | (2.8) | 228 | (96.2) |
| COVID-19 | 391 | (1.3) | 134 | (34.3) | 488 | (5.8) | 263 | (53.9) |

**Table 2. Continued**

| Characteristic | 2019–2020 Influenza Season | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | Pooled Sites | | | | Colorado | | | |
| | All Hospitalizations | | Tested for Flu | | All Hospitalizations | | Tested for Flu | |
| | No. | (Column %) | No. | (Row %) | No. | (Column %) | No. | (Row %) |
| Upper respiratory infection | 1142 | (3.8) | 524 | (45.9) | 438 | (5.2) | 358 | (81.7) |
| LRTI | 800 | (2.6) | 324 | (40.5) | 338 | (4.0) | 288 | (85.2) |
| Infectious diseases of noninfluenza etiology[g] | 8201 | (27.0) | 2861 | (34.9) | 3102 | (36.6) | 2386 | (76.9) |
| Otitis media | 86 | (0.3) | 20 | (23.3) | 20 | (0.2) | 18 | (90.0) |
| Pneumonia (of any etiology) | 6188 | (20.4) | 2654 | (42.9) | 2794 | (32.9) | 2236 | (80.0) |
| Signs/symptoms related to febrile and/or respiratory illness[h] | 17 258 | (56.8) | 4338 | (25.1) | 4764 | (56.2) | 3394 | (71.2) |
| Exacerbation of chronic lung disease[i] | 5686 | (18.7) | 1347 | (23.7) | 2023 | (23.8) | 1545 | (76.4) |
| Other | 15 658 | (51.5) | 3424 | (21.9) | 3724 | (43.9) | 2725 | (73.2) |
| Screening/exposure[j] | 5226 | (17.2) | 774 | (14.8) | 3169 | (37.4) | 1199 | (37.8) |
| Viral or respiratory illness complicating pregnancy[k] | 437 | (1.4) | 35 | (8.0) | 96 | (1.1) | 37 | (38.5) |
| Chronic lung disease | 1857 | (6.1) | 473 | (25.5) | 678 | (8.0) | 465 | (68.6) |
| Month of admission | | | | | | | | |
| September | 3895 | (12.8) | 407 | (10.4) | 477 | (5.6) | 302 | (63.3) |
| October | 3552 | (11.7) | 594 | (16.7) | 571 | (6.7) | 432 | (75.7) |
| November | 3263 | (10.7) | 632 | (19.4) | 604 | (7.1) | 465 | (77.0) |
| December | 3477 | (11.4) | 819 | (23.6) | 819 | (9.7) | 654 | (79.9) |
| January | 3679 | (12.1) | 1062 | (28.9) | 915 | (10.8) | 772 | (84.4) |
| February | 3030 | (10.0) | 818 | (27.0) | 893 | (10.5) | 750 | (84.0) |
| March | 2753 | (9.1) | 845 | (30.7) | 989 | (11.7) | 862 | (87.2) |
| April | 2955 | (9.7) | 455 | (15.4) | 1483 | (17.5) | 589 | (39.7) |
| May | 3785 | (12.5) | 271 | (7.2) | 1734 | (20.4) | 349 | (20.1) |
| ILI activity level[l] | | | | | | | | |
| Minimal | 15 113 | (49.7) | 1966 | (13.0) | 3867 | (45.6) | 1412 | (36.5) |
| Low | 3071 | (10.1) | 618 | (20.1) | 721 | (8.5) | 484 | (67.1) |
| Moderate | 1028 | (3.4) | 234 | (22.8) | 316 | (3.7) | 237 | (75.0) |
| High | 9291 | (30.6) | 2647 | (28.5) | 1476 | (17.4) | 1242 | (84.1) |
| Very high | 1673 | (5.5) | 407 | (24.3) | 2105 | (24.8) | 1800 | (85.5) |
| Unknown | 213 | (0.7) | 31 | (14.6) | 0 | (0.0) | 0 | … |
| Percent positivity[m] | | | | | | | | |
| <5% | 15 985 | (52.6) | 2262 | (14.2) | 5024 | (59.2) | 2314 | (46.1) |
| ≥5% to <20% | 6152 | (20.2) | 1312 | (21.3) | 1172 | (13.8) | 940 | (80.2) |
| ≥20% | 8252 | (27.2) | 2329 | (28.2) | 2289 | (27.0) | 1921 | (83.9) |

Abbreviations: ARI, acute respiratory illness; COVID-19, coronavirus disease 2019; HIV, human immunodeficiency virus; ICU, intensive care unit; ILI, influenza-like illness; LRTI, lower respiratory tract infection.

[a]ARI-associated hospitalizations include persons with an ARI diagnosis and/or respiratory virus testing.

[b]Insurance column percentages do not sum to 100% because patients could have >1 insurance type.

[c]Underlying conditions column percentages do not sum to 100% because patients could have >1 underlying condition.

[d]Any lung disease included chronic lung disease, asthma, chronic obstructive pulmonary disease (COPD), endemic mycoses, and pulmonary tuberculosis.

[e]Any heart disease included heart disease, congenital heart disease, heart failure, and ischemic heart disease.

[f]ARI discharge diagnoses column percentages do not sum to 100% because patients could have discharge diagnoses in >1 category.

[g]Examples of infectious disease of noninfluenza etiology included whooping cough, cytomegaloviral disease, Coxsackie virus, and respiratory syncytial virus.

[h]Examples of signs and symptoms related to febrile and/or respiratory illness included cough, shortness of breath, stridor, fever, and chills.

[i]Examples of exacerbation of chronic lung disease included COPD and asthma.

[j]Screening and exposure included screening and observation for communicable diseases (excluding influenza).

[k]Viral or respiratory illness complicating pregnancy included women aged 18–44 years.

[l]ILI activity reflects state-level ILI.

[m]Percent positive reflects the proportion of positive influenza tests by epidemiological week.

2019–2020, influenza testing was not universally performed for hospitalized patients with ARIs during influenza season and varied widely between healthcare systems, ranging from 14.8% to 19.4% at 3 pooled sites and 60.1% to 78.5% at a fourth site. Indicators of local influenza activity and select ARI diagnoses, especially pneumonia, had the greatest relative importance among predictors of influenza testing, and were largely consistent between the pooled sites and UCO. Indicators of

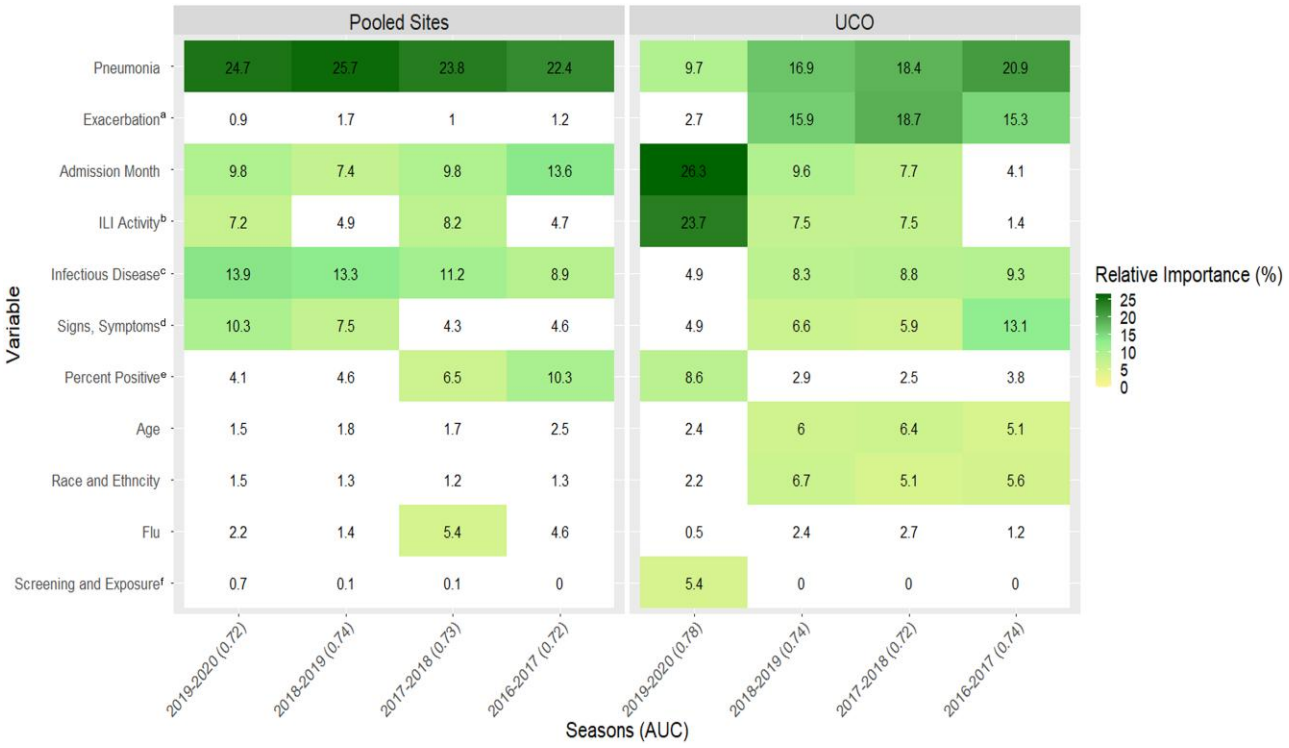



**Figure 2.** Variables that exceeded the 5% threshold of relative importance in distinguishing between hospitalizations with and without influenza testing performed using the balanced, unconditional model for the pooled sites and University of Colorado, by influenza season. [a]Examples of exacerbation of chronic lung disease included chronic obstructive pulmonary disease. [b]Influenza-like illness (ILI) activity reflects state-level ILI and is comprised of 5 categories: minimal, low, moderate, high, and very high. [c]Examples of infectious disease of noninfluenza etiology included whooping cough, cytomegaloviral disease, Coxsackie virus, and respiratory syncytial virus. [d]Examples of signs and symptoms related to febrile and/or respiratory illness included cough, shortness of breath, stridor, fever, and chills. [e]Percent positive reflects the proportion of positive influenza tests by epidemiological week and is comprised of 3 categories: <5%, ≥5% to <20%, and ≥20%. [f]Screening and exposure included screening and observation for communicable diseases (excluding influenza). Abbreviations: AUC, area under the receiver operating characteristic curve; ILI, influenza-like illness; UCO, University of Colorado.

influenza activity were generally more important at UCO, where testing was recommended among all hospitalized patients with ILI and overall testing rates were higher, whereas select ARI diagnoses were generally more important at the pooled sites where testing was recommended among more limited groups and often clinician-driven with lower testing rates.

VISION testing rates among eligible hospitalized patients were generally within the range of rates from other data sources. When restricted to hospitalizations with a pneumonia or influenza diagnosis, VISION testing rates were 33%–44% at the pooled sites and 81%–91% at UCO. Within the Influenza Hospitalization Surveillance Network (FluSurv-NET), a population-based surveillance platform focused on laboratory-confirmed influenza hospitalizations, testing rates in adults hospitalized with pneumonia or influenza ranged from 49% to 75% from 2010–2011 through 2017–2018 (unpublished data) [2]. Similarly, within the Hospitalized Adult Influenza Vaccine Effectiveness Network, testing rates among hospitalized adults with ARI along with ILI, pneumonia, or other evidence of respiratory involvement, acute respiratory distress, or cardiopulmonary conditions were 21%–79% from 2015–2016 through 2017–2018 (unpublished data).

Across all models, ARI diagnoses (particularly pneumonia, signs/symptoms, and infectious disease of noninfluenza etiology) and indicators of influenza activity (particularly hospital admission month and ILI activity) were consistently the most important across seasons of varying severity, including the more severe 2017–2018 season [9]. Indicators of influenza activity were incorporated to capture the epidemiological context in which encounters occurred, recognizing that local activity could impact testing decisions. Incorporating surveillance data into models was a novel addition that enabled us to identify potential drivers of influenza testing beyond patient-level factors. At UCO, indicators of influenza activity were more important than ARI diagnoses. Given that UCO's algorithm recommends testing all patients presenting with ILI (personal communication), testing differences by ARI diagnoses may be lessened, whereas influenza activity may have a greater influence on testing decisions. In contrast, at the pooled sites, ARI diagnoses were more important than influenza activity indicators. At all sites, ARI diagnoses maintained or increased in

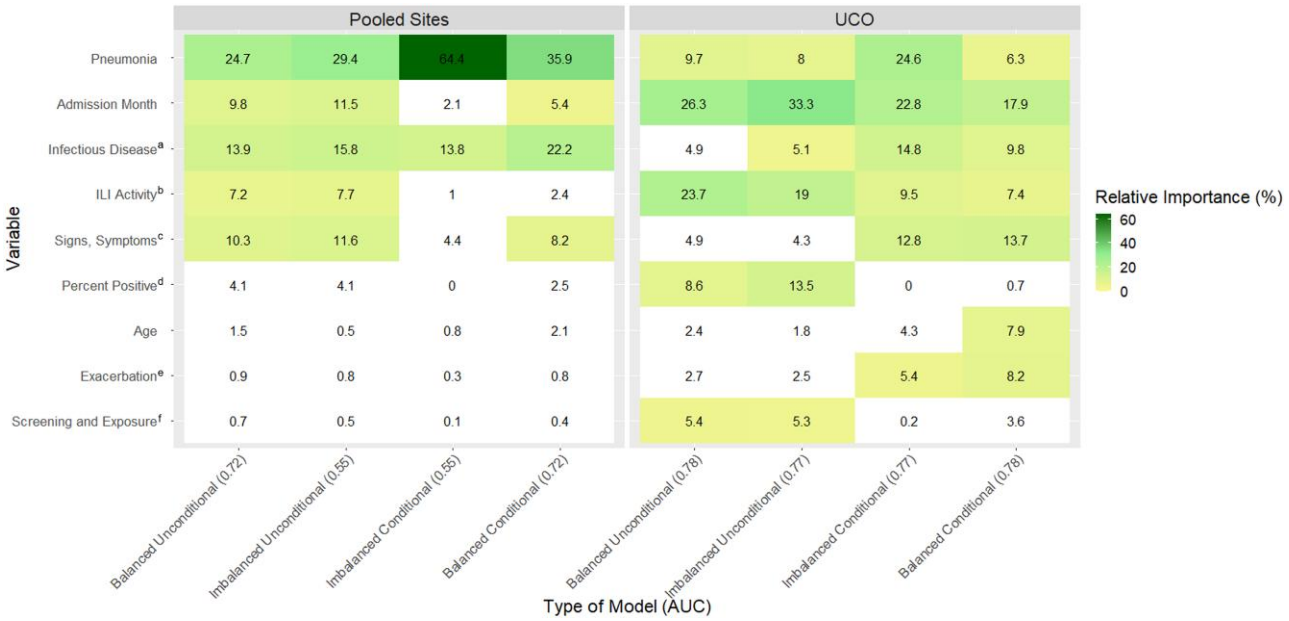



**Figure 3.** Variables that exceeded the 5% threshold of relative importance in distinguishing between hospitalizations with and without influenza testing performed for the 2019–2020 influenza season for the pooled sites and University of Colorado, by type of random forest model. [a]Examples of infectious disease of noninfluenza etiology included whooping cough, cytomegaloviral disease, Coxsackie virus, and respiratory syncytial virus. [b]ILI activity reflects state-level ILI and is comprised of 5 categories: minimal, low, moderate, high, and very high. [c]Examples of signs and symptoms related to febrile and/or respiratory illness included cough, shortness of breath, stridor, fever, and chills. [d]Percent positive reflects the proportion of positive influenza tests by epidemiological week and is comprised of 3 categories: <5%, ≥5% to <20%, and ≥20%. [e]Examples of exacerbation of chronic lung disease included chronic obstructive pulmonary disease and asthma. [f]Screening and exposure included screening and observation for communicable diseases (excluding influenza). Abbreviations: AUC, area under the receiver operating characteristic curve; ILI, influenza-like illness; UCO, University of Colorado.

importance when the analysis was restricted to the peak season. The consistent importance of ARI diagnoses aligns with current Infectious Diseases Society of America guidelines, which recommend testing for all hospitalized patients with ARI during periods of influenza activity to guide appropriate clinical management and antiviral treatment [10]. However, the overall testing rates at the pooled sites were still low and only marginally increased during the peak of the 2019–2020 season and among encounters with pneumonia and/or influenza diagnoses, suggesting there are still gaps in adherence to testing guidelines. Hospitalized patients with suspected influenza are recommended to be treated with influenza antivirals as soon as possible, without waiting for the results of clinical testing [10, 11], but empiric treatment without influenza testing is rare among hospitalized patients [12]. Opportunities for antiviral treatment of some hospitalized patients with influenza may be missed without more systematic testing.

Understanding influenza testing practices among adults hospitalized with ARI may enhance influenza disease burden estimates, which the Centers for Disease Control and Prevention produces weekly during influenza season and at the end of each season. These estimates are based on laboratory-confirmed influenza hospitalization rates from FluSurv-NET, adjusted in part for underdetection of influenza among ARI-associated hospitalizations, and are used to estimate influenza illness, medical visits, and deaths [13].

Although age and race/ethnicity were not among the variables with the highest relative importance in their association with influenza testing in our analysis, estimating disease burden by these demographic characteristics may still be beneficial. Burden estimates could account for higher influenza testing (and thus lower underdetection) in children compared to adults. Furthermore, adjusting for testing rates by race/ethnicity in estimating disease burden may shed light on whether and how burden differs across racial/ethnic groups. Relatedly, as use of multiplex panels increases, it is possible that hospitalized persons presenting without ARI may be tested and subsequently test positive for influenza, and it would be important to understand the implication of such hospitalizations that may be unrelated to a respiratory infection on influenza disease burden estimates.

This analysis is subject to several limitations. First, geographic or institutional factors associated with these 4 healthcare systems may result in findings that are not generalizable to the entire US. Second, indicators of influenza activity were only available at the state level and thus may not capture the granularity of local influenza dynamics. Third, collection of influenza vaccination data was likely incomplete in at least some sites and

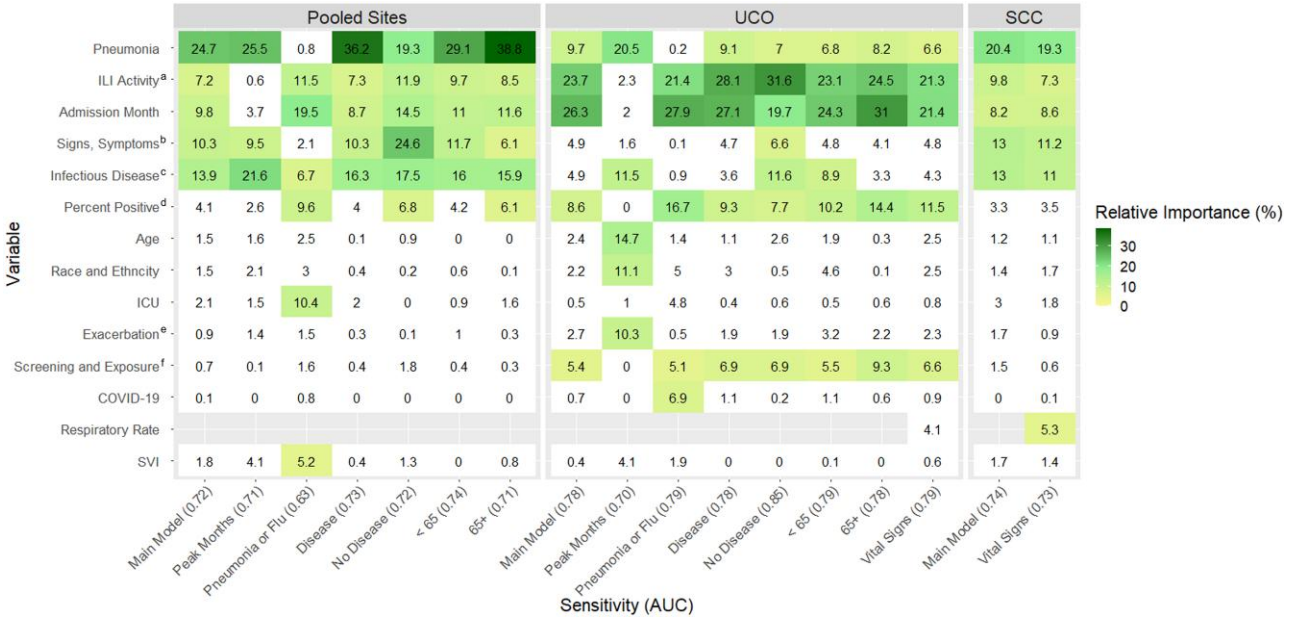
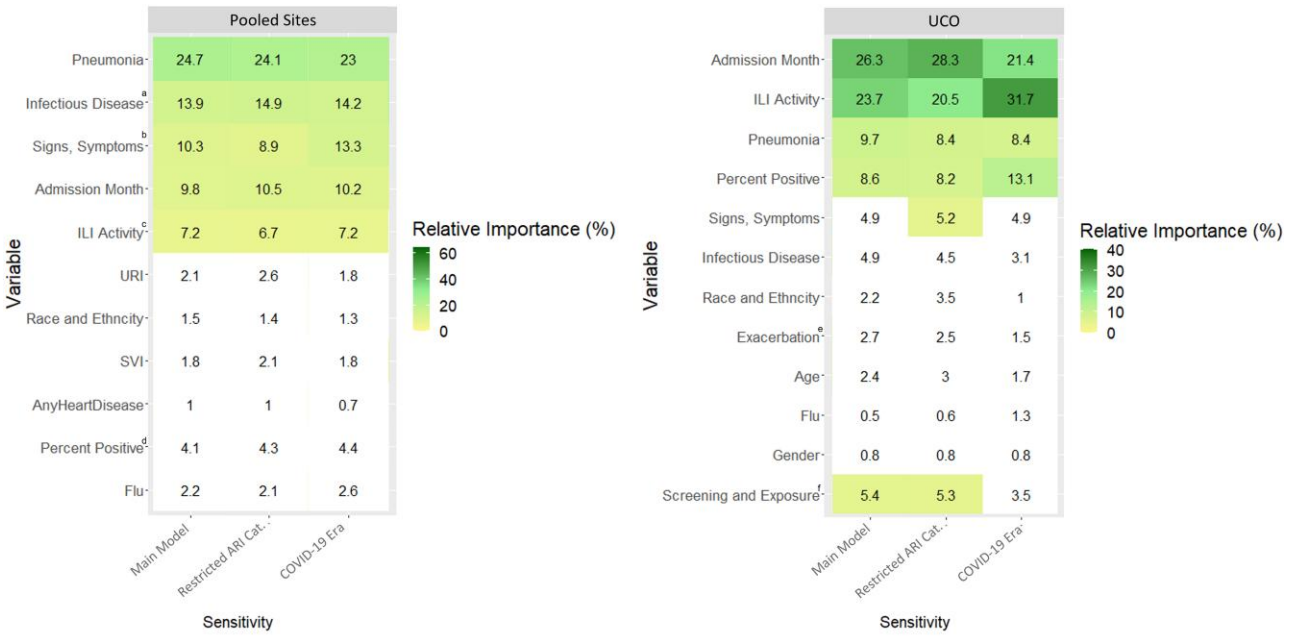



**Figure 4.** Variables that exceeded the 5% threshold of relative importance in distinguishing between hospitalizations with and without influenza testing performed using the balanced, unconditional model for the 2019–2020 influenza season, by sensitivity analysis. [a]ILI activity reflects state-level ILI and is comprised of 5 categories: minimal, low, moderate, high, and very high. [b]Examples of signs and symptoms related to febrile and/or respiratory illness included cough, shortness of breath, stridor, fever, and chills. [c]Examples of infectious disease of noninfluenza etiology included whooping cough, cytomegaloviral disease, Coxsackie virus, and respiratory syncytial virus. [d]Percent positive reflects the proportion of positive influenza tests by epidemiological week and is comprised of 3 categories: <5%, ≥5% to <20%, and ≥20%. [e]Examples of exacerbation of chronic lung disease included chronic obstructive pulmonary disease and asthma. [f]Screening and exposure included screening and observation for communicable diseases (excluding influenza). Abbreviations: AUC, area under the receiver operating characteristic curve; COVID-19, coronavirus disease 2019; ILI, influenza-like illness; SCC, Southern California Consortium; SVI, Social Vulnerability Index; UCO, University of Colorado.




[a]Examples of infectious disease of non-influenza etiology included whooping cough, cytomegaloviral disease, Coxsackie virus, and RSV.
[b]Examples of signs and symptoms related to febrile and/or respiratory illness included cough, shortness of breath, stridor, fever, and chills.
[c]ILI activity reflects state-level influenza-like illness and is comprised of 5 categories: minimal, low, moderate, high, and very high.
[d]Percent positive reflects the proportion of positive influenza tests by epidemiological week and is comprised of three categories: <5%, ≥5% to <20%,and ≥20%.
[e]Examples of exacerbation of chronic lung disease included COPD and asthma.
[f]Screening and exposure included screening and observation for communicable diseases (excluding influenza).

**Figure 5.** Variables that exceeded the 5% threshold of relative importance in distinguishing between hospitalizations with and without influenza testing performed using the balanced, unconditional model for the 2019–2020 influenza season, limited acute respiratory illness categories, and COVID-19 era. Abbreviations: ARI, acute respiratory illness; COVID-19, coronavirus disease 2019; ILI, influenza-like illness; SVI, Social Vulnerability Index; UCO, University of Colorado; URI, upper respiratory infection.

was therefore not included in our models. Fourth, we could not capture testing that occurred outside the healthcare systems, potentially leading to an underestimate of testing. Fifth, ARI diagnosis codes may have been influenced by test results, therefore reflecting rather than predicting testing. Sixth, this analysis focused on patient characteristics and influenza activity as predictors of testing. Other factors not routinely captured in EHR data may also affect testing practices.

The variability in influenza testing rates among sites suggests the need to develop innovative strategies for monitoring testing across different surveillance platforms to capture differences in testing and better inform influenza disease burden estimates. It also suggests the importance of identifying and focusing on the stakeholders who establish testing guidelines for large healthcare systems and reevaluating how guidelines are communicated to facilitate consistent implementation. These steps may help contextualize or improve potential underascertainment of severe influenza disease and the attendant implications for antiviral use and public health policy.

## Supplementary Data

Supplementary materials are available at *Open Forum Infectious Diseases* online. Consisting of data provided by the authors to benefit the reader, the posted materials are not copyedited and are the sole responsibility of the authors, so questions or comments should be addressed to the corresponding author.

## Notes

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***Patient consent.*** Patient consent was not required for this analysis.

***Disclaimer.*** The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.

***Potential conflicts of interest.*** All authors: No reported conflicts.

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