*Epidemiology and Infection*

Influenza vaccination status and outcomes among influenza-associated hospitalizations in Columbus, Ohio (2012-2015)

P.N. Zivich, L. Tatham, K. Lung, J. Tien, C.E. Bollinger, J.K. Bower

Supplement Figure S1: Inclusion/Exclusion criteria of study population

Supplement Table S1: Demographics by vaccination status by influenza season

Supplement Table S2: Odds of severe influenza hospitalization

Supplement Table S3: Odds of pneumonia by time between vaccine receipt and hospitalization

Supplement Table S4: Sensitivity analysis, excluding individuals without a date for receipt of the influenza vaccine

Supplement Table S5: Demographics by vaccination status of those who did not receive antivirals

Supplement Table S6: Odds of severe influenza hospitalization and pneumonia among those without antiviral treatment

SUPPLEMENT FIGURE S1: Derivation of the study population and exclusions



Exclusion process and number of patients excluded and included. 2071 of 2818 were included in the analytical sample.

|  |
| --- |
| SUPPLEMENT TABLE S1: Characteristics of influenza-associated hospitalized patients who received antivirals by season (Ohio, 2012-2015) \* |
|  |  | 2012-2013 Influenza Season |   | 2013-2014 Influenza Season |  | 2014-2015 Influenza Season |
|  |  | Overall (n=474) | Vaccinated (n=199) | Unvaccinated (n=275) | p \* |  | Overall (n=524) | Vaccinated (n=232) | Unvaccinated (n=292) | p \* |  | Overall (n=1073) | Vaccinated (n=655) | Unvaccinated (n=418) | p \* |
| Female | 247 (52.1) | 98 (49.2) | 149 (54.2) | 0.29 |  | 270 (51.5) | 113 (48.7) | 157 (53.8) | 0.25 |  | 575 (53.6) | 344 (52.5) | 231 (55.3) | 0.38 |
| Age group |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
|  | 0.5-4 years | 42 (8.9) | 11 (5.5) | 31 (11.3) | <0.0001 |  | 28 (5.3) | 5 (2.2) | 23 (7.9) | <0.0001 |  | 51 (4.7) | 15 (2.3) | 36 (8.6) | <0.0001 |
|  | 5-24 years | 33 (7.0) | 16 (8.0) | 17 (6.2) |  |  | 30 (5.7) | 14 (6.0) | 16 (5.5) |  |  | 81 (7.5) | 49 (7.5) | 32 (7.7) |  |
|  | 25-64 years | 194 (40.9**)** | 58 (29.1) | 136 (49.4) |  |  | 297 (56.7) | 105 (45.3) | 192 (65.7) |  |  | 339 (31.6) | 157 (24.0) | 182 (43.5) |  |
|  | 65+ years | 205 (43.2) | 114 (57.3) | 91 (33.1) |  |  | 169 (32.2) | 108 (46.5) | 61 (20.9) |  |  | 602 (56.1) | 434 (66.3) | 168 (40.2) |  |
| Race |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
|  | White | 326 (70.0) | 158 (80.6) | 168 (62.2) | <0.0001 |  | 326 (63.5) | 168 (72.7) | 158 (56.0) | <0.0001 |  | 780 (74.0) | 503 (78.5) | 277 (67.1) | <0.0001 |
|  | Other | 140 (30.0) | 38 (19.4) | 102 (37.8) |  |  | 187 (36.4) | 63 (27.3) | 124 (44.0) |  |  | 274 (26.0) | 138 (21.5) | 136 (32.9) |  |
|  | Missing | 8 |  |  |  |  | 11 |  |  |  |  | 19 |  |  |  |
| BMI ‡ |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
|  | Not obese (<18.5 - 29.9 kg/m2) | 306 (65.7) | 133 (68.6) | 173 (63.6) | 0.17 |  | 317 (60.6) | 149 (64.5) | 168 (57.5) | 0.0334 |  | 696 (65.1) | 427 (65.5) | 269 (64.5) | 0.92 |
|  | Obese (30.0 - 39.9 kg/m2) | 109 (23.4) | 46 (23.7) | 63 (23.2) |  |  | 144 (27.5) | 64 (27.7) | 80 (27.4) |  |  | 280 (26.2) | 168 (25.8) | 112 (26.9) |  |
|  | Morbidly Obese (>40 kg/m2) | 51 (10.9) | 15 (7.7) | 36 (13.2) |  |  | 62 (11.8) | 18 (7.8) | 44 (15.1) |  |  | 93 (8.7) | 57 (8.7) | 36 (8.6) |  |
|  | Missing | 8 |  |  |  |  | 1 |  |  |  |  | 4 |  |  |  |
| Medical Condition |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
|  | Asthma | 111 (23.4) | 45 (22.6) | 66 (24.0) | 0.72 |  | 155 (29.6) | 70 (30.2) | 85 (29.1) | 0.79 |  | 240 (22.4) | 145 (22.1) | 95 (22.7) | 0.82 |
|  | Cardiovascular disease | 232 (48.9) | 112 (56.3) | 120 (43.6) | 0.0066 |  | 280 (53.4) | 146 (62.9) | 134 (45.9) | 0.0001 |  | 717 (66.8) | 476 (72.7) | 241 (57.7) | <0.0001 |
|  | Chronic lung disease | 173 (36.5) | 89 (44.7) | 84 (30.5) | 0.0016 |  | 239 (45.6) | 121 (52.2) | 118 (40.4) | 0.0073 |  | 449 (41.8) | 288 (44.0) | 161 (38.5) | 0.0775 |
|  | Chronic metabolic disease | 198 (41.8) | 103 (51.8) | 95 (34.5) | 0.0002 |  | 205 (39.1) | 104 (44.8) | 101 (34.6) | 0.0171 |  | 513 (47.8) | 353 (53.9) | 160 (38.3) | <0.0001 |
|  | Neurologic disease | 124 (26.2) | 62 (31.2) | 62 (22.5) | 0.0353 |  | 224 (42.7) | 114 (49.1) | 110 (37.7) | 0.0084 |  | 522 (48.6) | 343 (52.4) | 179 (42.8) | 0.0023 |
|  | Immunosuppression | 104 (21.9) | 52 (26.1) | 52 (18.9) | 0.0608 |  | 107 (20.4) | 58 (25.0) | 49 (16.8) | 0.0204 |  | 206 (19.2) | 135 (20.6) | 71 (17.0) | 0.1415 |
|  | Blood disorder | 18 (3.8) | 12 (6.0) | 6 (2.2) | 0.0305 |  | 159 (30.3) | 86 (37.1) | 73 (25.0) | 0.0028 |  | 286 (26.6) | 188 (28.7) | 98 (23.4) | 0.0575 |
|  | Renal disease | 102 (21.5) | 51 (25.6) | 51 (18.5) | 0.0640 |  | 120 (22.9) | 66 (28.4) | 54 (18.5) | 0.0071 |  | 263 (24.5) | 181 (27.6) | 82 (19.6) | 0.0029 |
|  | Liver disease | 8 (1.7) | 3 (1.5) | 5 (1.8) | 1.00 † |  | 26 (5.0) | 13 (5.6) | 13 (4.4) | 0.55 |  | 52 (4.8) | 29 (4.4) | 23 (5.5) | 0.42 |
|  | ≥ 1 condition | 437 (92.2) | 193 (97.0) | 244 (88.7) | 0.0009 |  | 494 (94.3) | 225 (97.0) | 269 (92.1) | 0.0174 |  | 1027 (95.7) | 639 (97.6) | 388 (92.8) | 0.0002 |
| Alcohol abuse § |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
|  | Current | 16 (3.4) | 4 (2.0) | 12 (4.4) | 0.20 |  | 23 (4.4) | 10 (4.3) | 13 (4.4) | 0.18 |  | 33 (3.1) | 10 (1.5) | 23 (5.5) | 0.0007 |
|  | Former | 10 (2.1) | 6 (3.0) | 4 (1.4) |  |  | 24 (4.6) | 15 (6.5) | 9 (3.1) |  |  | 22 (2.0) | 16 (2.4) | 6 (1.4) |  |
|  | Never | 448 (94.5) | 189 (95.0) | 259 (94.2) |  |  | 477 (91.0) | 207 (89.2) | 270 (92.5) |  |  | 1018 (94.9) | 629 (96.0) | 389 (93.1) |  |
| Smoking status § |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
|  | Current | 122 (25.7) | 30 (15.1) | 92 (33.4) | <0.0001 |  | 210 (40.1) | 77 (33.2) | 133 (45.5) | 0.0009 |  | 212 (19.8) | 107 (16.3) | 105 (25.1) | <0.0001 |
|  | Former  | 124 (26.2) | 70 (35.2) | 54 (19.6) |  |  | 121 (23.1) | 70 (30.2) | 51 (17.5) |  |  | 334 (31.1) | 233 (35.6) | 101 (24.2) |  |
|  | Never | 228 (48.1) | 99 (49.7) | 129 (46.9) |  |  | 193 (36.8) | 85 (36.6) | 108 (37.0) |  |  | 527 (49.1) | 315 (48.1) | 212 (50.7) |  |
| Influenza virus type |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
|  | Influenza A | 346 (73.0) | 146 (73.4) | 200 (72.7) | 0.28 † |  | 363 (69.3) | 140 (60.3) | 223 (76.4) | 0.0004 |  | 786 (73.2) | 500 (76.3) | 286 (68.4) | 0.0064 |
|  | Influenza B | 124 (26.2) | 53 (26.6) | 71 (25.8) |  |  | 147 (28.0) | 83 (35.8) | 64 (21.9) |  |  | 271 (25.3) | 149 (22.7) | 122 (29.2) |  |
|  | Influenza A&B | 4 (0.8) | 0 (0) | 4 (1.4) |  |  | 14 (2.7) | 9 (3.9) | 5 (1.7) |  |  | 16 (1.5) | 6 (0.9) | 10 (2.4) |  |
| Severe influenza ‡  | 110 (23.2) | 50 (25.1) | 60 (21.8) | 0.40 |  | 138 (26.3) | 59 (25.4) | 79 (27.0) | 0.68 |  | 200 (18.6) | 116 (17.7) | 84 (20.1) | 0.33 |
| Diagnosis of pneumonia § | 138 (29.1) | 66 (33.2) | 72 (26.2) | 0.10 |  | 214 (40.8) | 86 (37.1) | 128 (43.8) | 0.12 |  | 366 (34.1) | 232 (35.4) | 134 (32.1) | 0.26 |
| Antiviral Treatment |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
|  | Prompt (≤ 2 days) | 444 (93.7) | 187 (94.0) | 257 (93.4) | 0.82 |  | 496 (94.7) | 218 (94.0) | 278 (95.2) | 0.53 |  | 1044 (97.3) | 639 (97.6) | 405 (96.9) | 0.51 |
|   | Late (> 2 days) | 30 (6.3) | 12 (6.0) | 18 (6.5) |   |   | 28 (5.3) | 14 (6.0) | 14 (4.8) |   |   | 29 (2.7) | 16 (2.4) | 13 (3.1) |   |
| \* Chi-squared test unless indicated otherwise |
| † Fisher’s exact test  |
| ‡ Severe influenza is defined as either admission to the intensive care unit or death  |
| § Diagnosis of pneumonia is defined as a chest x-ray indicating pneumonia and either diagnosis of pneumonia at discharge or ICD-9 discharge code for pneumonia (480-487.0). |

|  |
| --- |
| SUPPLEMENT TABLE S2a: Odds of severe influenza with respect to vaccination status by influenza season\*,† |
|  | Overall |  | 2012-2013 |  | 2013-2014 |  | 2014-2015 |
|  | OR | 95% CI |  | OR | 95% CI |  | OR | 95% CI |  | OR | 95% CI |
| Unadjusted | 0.89 | 0.72, 1.10 |  | 1.20 | 0.78, 1.85 |  | 0.92 | 0.62, 1.36 |  | 0.86 | 0.63, 1.17 |
| Adjusted ‡ | 0.87 | 0.69, 1.10 |  | 1.12 | 0.71, 1.76 |  | 0.79 | 0.52, 1.21 |  | 0.82 | 0.59, 1.14 |
| \* Severe influenza is defined as admission to the ICU or death during hospitalization. An odds ratio less than one implies that patients who received the influenza vaccine has decreased odds of severe influenza relative to patients who were not vaccinated. OR: odds ratio, 95% CI: 95% confidence interval. |
| † Age is modeled as a continuous variable. |
| ‡ Adjusted by all factors (season-vaccine interaction term, prompt treatment with antivirals, age, race, sex, obesity, asthma, CVD, CLD, CMD, neurological disease, blood disorders, renal disease, liver disease, immunosuppression, alcohol abuse, smoking status, and virus type)  |
|  |

|  |
| --- |
| SUPPLEMENT TABLE S2b: Odds of severe influenza with respect to vaccination status by age categories\*,† |
|  | Overall |  | 0.5-4 years old |  | 5-24 years old |  | 25-64 years old |  | 65+ years old |
|  | OR | 95% CI |  | OR | 95% CI |  | OR | 95% CI |  | OR | 95% CI |  | OR | 95% CI |
| Unadjusted | 0.89 | 0.72, 1.10 |  | 1.19 | 0.48, 2.96 |  | 0.75 | 0.37, 1.54 |  | 0.99 | 0.71, 1.38 |  | 0.96 | 0.68, 1.35 |
| Adjusted ‡ | 0.86 | 0.68, 1.09 |  | 0.80 | 0.31, 2.10 |  | 0.62 | 0.29, 1.31 |  | 0.85 | 0.59, 1.21 |  | 0.95 | 0.66, 1.35 |
| \* Severe influenza is defined as admission to the ICU or death during hospitalization. An odds ratio less than one implies that patients who received the influenza vaccine has decreased odds of severe influenza relative to patients who were not vaccinated. OR: odds ratio, 95% CI: 95% confidence interval. |
| † Age is modeled as a categorical variable. |
| ‡ Adjusted by all factors (age category-vaccine interaction term, prompt treatment with antivirals, age, race, sex, obesity, asthma, CVD, CLD, CMD, neurological disease, blood disorders, renal disease, liver disease, immunosuppression, alcohol abuse, smoking status, and virus type). |

|  |
| --- |
| SUPPLEMENT TABLE S3a: The association of timing between vaccination and hospital admission (<100 days, ≥100 days) with pneumonia by season |
|  | Overall |  | 2012-2013 |  | 2013-2014 |  | 2014-2015 |
|  | OR | 95% CI |  | OR | 95% CI |  | OR | 95% CI |  | OR | 95% CI |
| Unadjusted | 0.89 | 0.66, 1.18 |  | 0.60 | 0.30, 1.18 |  | 1.02 | 0.54, 1.95 |  | 0.92 | 0.63, 1.34 |
| Adjusted \* | 0.79 | 0.57, 1.08 |   | 0.58 | 0.29, 1.18 |   | 0.95 | 0.48, 1.88 |   | 0.82 | 0.54, 1.22 |
|  Time is modeled as an indicator variable. The variable indicates whether it has been ≥100 days between vaccination and hospitalization. An odds ratio > 1 suggests that patients with at least 100 days between vaccination and hospitalization have increased odds of pneumonia, relative to patients with less than 100 days between vaccination and hospitalization. OR: odds ratio, 95% CI: 95% confidence interval |
| \* Adjusted for the following confounders: age (in years), prompt treatment with antivirals, race, sex, obesity, asthma, CVD, CLD, CMD, neurological disease, blood disorders, renal disease, liver disease, immunosuppression, alcohol abuse, smoking status, and virus type. |
|  |

|  |
| --- |
| SUPPLEMENT TABLE S3b: The association of timing between vaccination and hospital admission (continuous) with pneumonia by season |
|  | Overall |  | 2012-2013 |  | 2013-2014 |  | 2014-2015 |
|  | OR | 95% CI |  | OR | 95% CI |  | OR | 95% CI |  | OR | 95% CI |
| Unadjusted | 0.99 | 0.96, 1.01 |  | 0.96 | 0.91, 1.01 |  | 0.97 | 0.92, 1.01 |  | 1.00 | 0.97, 1.03 |
| Adjusted \* | 0.97 | 0.95, 1.00 |   | 0.95 | 0.90, 1.01 |   | 0.96 | 0.92, 1.01 |   | 0.99 | 0.95, 1.02 |
|  Time is modeled as a continuous variable. The variable indicates how many weeks have occurred between vaccination and hospitalization. An odds ratio > 1 suggests that patients have increased odds of pneumonia, relative to patients with one week less between vaccination and hospitalization. OR: odds ratio, 95% CI: 95% confidence interval |
| \* Adjusted for the following confounders: age (in years), prompt treatment with antivirals, race, sex, obesity, asthma, CVD, CLD, CMD, neurological disease, blood disorders, renal disease, liver disease, immunosuppression, alcohol abuse, smoking status, and virus type. |
|  |

|  |
| --- |
| SUPPLEMENT TABLE S3c: The of association timing between vaccination and hospital admission (<100 days, ≥100 days) with pneumonia by season among 25-64 year olds |
|  | Overall |  | 2012-2013 |  | 2013-2014 |  | 2014-2015 |
|  | OR | 95% CI |  | OR | 95% CI |  | OR | 95% CI |  | OR | 95% CI |
| Unadjusted | 1.49 | 0.86, 2.58 |  | 0.68 | 0.18, 2.62 |  | 2.23 | 0.78, 6.38 |  | 1.44 | 0.67, 3.12 |
| Adjusted \* | 1.44 | 0.75, 2.77 |   | 0.48 | 0.10, 2.20 |   | 3.20 | 0.93, 10.98 |   | 1.29 | 0.51, 3.22 |
|  Time is modeled as an indicator variable. The variable indicates whether it has been ≥100 days between vaccination and hospitalization. An odds ratio > 1 suggests that patients with at least 100 days between vaccination and hospitalization have increased odds of pneumonia, relative to patients with less than 100 days between vaccination and hospitalization. OR: odds ratio, 95% CI: 95% confidence interval  |
| \* Adjusted for the following confounders: age (in years), prompt treatment with antivirals, race, sex, obesity, asthma, CVD, CLD, CMD, neurological disease, blood disorders, renal disease, liver disease, immunosuppression, alcohol abuse, smoking status, and virus type. |

|  |
| --- |
| SUPPLEMENT TABLE S3d: The association of timing between vaccination and hospital admission (continuous) with pneumonia by season among 25-64 year olds |
|  | Overall |  | 2012-2013 |  | 2013-2014 |  | 2014-2015 |
|  | OR | 95% CI |  | OR | 95% CI |  | OR | 95% CI |  | OR | 95% CI |
| Unadjusted | 1.02 | 0.98, 1.07 |  | 0.92 | 0.81, 1.05 |  | 1.01 | 0.94, 1.09 |  | 1.05 | 0.99, 1.11 |
| Adjusted \* | 1.01 | 0.96, 1.07 |   | 0.88 | 0.76, 1.02 |   | 1.03 | 0.94, 1.13 |   | 1.04 | 0.97, 1.13 |
|  Time is modeled as a continuous variable. The variable indicates how many weeks have occurred between vaccination and hospitalization. An odds ratio > 1 suggests that patients have increased odds of pneumonia, relative to patients with one week less between vaccination and hospitalization. OR: odds ratio, 95% CI: 95% confidence interval.  |
| \* Adjusted for the following confounders: age (in years), prompt treatment with antivirals, race, sex, obesity, asthma, CVD, CLD, CMD, neurological disease, blood disorders, renal disease, liver disease, immunosuppression, alcohol abuse, smoking status, and virus type. |

|  |
| --- |
| SUPPLEMENT TABLE S4a: Odds of severe influenza with respect to vaccination status by influenza season, excluding those missing date of vaccination \*, †, ‡ |
|  | Overall |  | 2012-2013 |  | 2013-2014 |  | 2014-2015 |
|  | OR | 95% CI |  | OR | 95% CI |  | OR | 95% CI |  | OR | 95% CI |
| Unadjusted  | 0.96 | 0.77, 1.20 |  | 1.21 | 0.77, 1.89 |  | 0.89 | 0.57, 1.37 |  | 0.98 | 0.70, 1.35 |
| Adjusted § | 0.92 | 0.72, 1.17 |  | 1.12 | 0.70, 1.78 |  | 0.75 | 0.47, 1.20 |  | 0.92 | 0.65, 1.30 |
|  \* Those without recorded vaccination times were excluded to determine if bias was introduced by the assumption that those without recorded vaccination times received the vaccine at least fourteen days before hospitalization. An odds ratio less than one implies that patients who received the influenza vaccine has decreased odds of severe influenza relative to patients who were not vaccinated. OR: odds ratio, 95% CI: 95% confidence interval |
| † Severe influenza is defined as admission to the ICU or death during hospitalization. |
| ‡ Age is modeled as a continuous variable. |
| § Adjusted by all factors (season-vaccine interaction term, prompt treatment with antivirals, age, race, sex, obesity, asthma, CVD, CLD, CMD, neurological disease, blood disorders, renal disease, liver disease, immunosuppression, alcohol abuse, smoking status, and virus type) and includes an interaction term between season and vaccine.  |

|  |
| --- |
| SUPPLEMENT TABLE S4b: Odds of severe influenza with respect to vaccination status by age categories, excluding those missing date of vaccination \*, †, ‡ |
|  | Overall \*\*\* |  | 0.5-4 years old |  | 5-24 years old |  | 25-64 years old |  | 65+ years old |
|  | OR | 95% CI |  | OR | 95% CI |  | OR | 95% CI |  | OR | 95% CI |  | OR | 95% CI |
| Unadjusted  | 0.96 | 0.77, 1.20 |  | 1.33 | 0.52, 3.39 |  | 0.75 | 0.36, 1.55 |  | 1.04 | 0.72, 1.49 |  | 1.04 | 0.72, 1.48 |
| Adjusted † | 0.90 | 0.70, 1.15 |  | 0.91 | 0.34, 2.46 |  | 0.65 | 0.30, 1.38 |  | 0.87 | 0.59, 1.28 |  | 1.00 | 0.68, 1.45 |
|  \* Those without recorded vaccination times were excluded to determine if bias was introduced by the assumption that those without recorded vaccination times received the vaccine at least fourteen days before hospitalization. An odds ratio less than one implies that patients who received the influenza vaccine has decreased odds of severe influenza relative to patients who were not vaccinated. OR: odds ratio, 95% CI: 95% confidence interval |
| † Severe influenza is defined as admission to the ICU or death during hospitalization. |
| ‡ Age is modeled as a categorical variable. |
| § Adjusted by all factors (age category-vaccine interaction term, age category, prompt treatment with antivirals, race, sex, obesity, asthma, CVD, CLD, CMD, neurological disease, blood disorders, renal disease, liver disease, immunosuppression, alcohol abuse, smoking status, and virus type) and includes an interaction term between season and vaccine.  |

|  |
| --- |
| SUPPLEMENT TABLE S4c: Odds of pneumonia diagnosis with respect to vaccination status by influenza season, excluding those missing date of vaccination \*, †, ‡ |
|  | Overall |  | 2012-2013 |  | 2013-2014 |  | 2014-2015 |
|  | OR | 95% CI |  | OR | 95% CI |  | OR | 95% CI |  | OR | 95% CI |
| Unadjusted  | 1.02 | 0.83, 1.24 |  | 1.27 | 0.83, 1.94 |  | 0.75 | 0.50, 1.10 |  | 1.11 | 0.84, 1.47 |
| Adjusted † | 0.89 | 0.72, 1.11 |  | 1.08 | 0.69, 1.67 |  | 0.57 | 0.37, 0.87 |  | 1.02 | 0.76, 1.37 |
| OR: odds ratio, 95% CI: 95% confidence interval |
|  \* Those without recorded vaccination times were excluded to determine if bias was introduced by the assumption that those without recorded vaccination times received the vaccine at least fourteen days before hospitalization. An odds ratio less than one implies that patients who received the influenza vaccine has decreased odds of pneumonia relative to patients who were not vaccinated. OR: odds ratio, 95% CI: 95% confidence interval |
| † Pneumonia is defined as a chest x-ray indicating pneumonia and either diagnosis of pneumonia at discharge or ICD-9 discharge code for pneumonia (480-487.0).  |
| ‡ Age is modeled as a continuous variable. |
| § Adjusted by all factors (season-vaccine interaction term, prompt treatment with antivirals, age, race, sex, obesity, asthma, CVD, CLD, CMD, neurological disease, blood disorders, renal disease, liver disease, immunosuppression, alcohol abuse, smoking status, and virus type) and includes an interaction term between season and vaccine.  |

|  |
| --- |
| SUPPLEMENT TABLE S4d: Odds of pneumonia with respect to vaccination status by age categories, excluding those missing date of vaccination \*, †, ‡ |
|  |  | Overall |  | 0.5-4 years old |  | 5-24 years old |  | 25-64 years old |  | 65+ years old |
|  |  | OR | 95% CI |  | OR | 95% CI |  | OR | 95% CI |  | OR | 95% CI |  | OR | 95% CI |
| 2012-2013 | Unadjusted  | 1.27 | 0.83, 1.94 |  | 0.33 | 0.03, 3.16 |  | 1.08 | 0.18, 6.32 |  | 1.37 | 0.64, 2.92 |  | 1.03 | 0.57, 1.87 |
|  | Adjusted † | 0.79 | 0.48, 1.31 |  | 0.19 | 0.02, 1.97 |  | 0.77 | 0.12, 5.02 |  | 0.89 | 0.38, 2.10 |  | 0.86 | 0.45, 1.65 |
|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| 2013-2014 | Unadjusted  | 0.75 | 0.50, 1.10 |  | 0.28 | 0.03, 2.97 |  | 2.19 | 0.45, 10.21 |  | 0.70 | 0.40, 1.24 |  | 0.70 | 0.35, 1.42 |
|  | Adjusted † | 0.64 | 0.41, 1.02 |  | 0.20 | 0.02, 2.40 |  | 3.17 | 0.62, 16.28 |  | 0.57 | 0.30, 1.08 |  | 0.61 | 0.29, 1.29 |
|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| 2014-2015 | Unadjusted  | 1.11 | 0.84, 1.47 |  | 1.33 | 0.28, 6.26 |  | 0.94 | 0.33, 2.64 |  | 1.22 | 0.74, 2.01 |  | 0.93 | 0.63, 1.37 |
|  | Adjusted † | 1.10 | 0.80, 1.51 |  | 1.60 | 0.31, 8.26 |  | 0.76 | 0.26, 2.24 |  | 1.47 | 0.87, 2.51 |  | 0.96 | 0.63, 1.45 |
|  \* Those without recorded vaccination times were excluded to determine if bias was introduced by the assumption that those without recorded vaccination times received the vaccine at least fourteen days before hospitalization. An odds ratio less than one implies that patients who received the influenza vaccine has decreased odds of pneumonia relative to patients who were not vaccinated. OR: odds ratio, 95% CI: 95% confidence interval |
| † Pneumonia is defined as a chest x-ray indicating pneumonia and either diagnosis of pneumonia at discharge or ICD-9 discharge code for pneumonia (480-487.0).  |
| ‡ Age is modeled as a categorical variable. Each season is modeled separately. |
| § Adjusted by all factors (age category-vaccine interaction term, age category prompt treatment with antivirals, race, sex, obesity, asthma, CVD, CLD, CMD, neurological disease, blood disorders, renal disease, liver disease, immunosuppression, alcohol abuse, smoking status, and virus type) and includes an interaction term between season and vaccine.  |

|  |
| --- |
| SUPPLEMENT TABLE S5: Characteristics of influenza-associated hospitalized patients who did not receive antivirals (Ohio, 2012-2015) |
|  |  | Overall |
|  |  | Overall (n=221) | Vaccinated (n=90) | Unvaccinated (n=131) | p\* |
| Female | 112 (50.7) | 48 (53.3) | 64 (48.8) | 0.51 |
| Age group |  |  |  |  |
|  | 0.5-4 years | 22 (9.9) | 5 (5.6) | 17 (13.0) | 0.0004 |
|  | 5-24 years | 20 (9.0) | 6 (6.7) | 14 (10.7) |  |
|  | 25-64 years | 104 (47.1) | 34 (37.8) | 70 (53.4) |  |
|  | 65+ years | 75 (33.9) | 45 (50.0) | 30 (22.9) |  |
| Race |  |  |  |  |
|  | White | 144 (66.7) | 73 (81.1) | 71 (56.3) | 0.0001 |
|  | Other | 72 (33.3) | 17 (18.9) | 55 (43.6) |  |
|  | Missing |  |  |  |  |
| BMI ‡ |  |  |  |  |
|  | Not obese (<18.5 - 29.9 kg/m2) | 153 (70.2) | 58 (65.2) | 95 (73.6) | 0.36 |
|  | Obese (30.0 - 39.9 kg/m2) | 53 (24.3) | 26 (29.2) | 27 (20.9) |  |
|  | Morbidly Obese (>40 kg/m2) | 12 (5.5) | 5 (5.6) | 7 (5.4) |  |
|  | Missing | 3 |  |  |  |
| Medical Condition |  |  |  |  |
|  | Asthma | 43 (19.5) | 23 (25.6) | 20 (15.3) | 0.06 |
|  | Cardiovascular disease | 112 (50.7) | 56 (62.2) | 56 (42.7) | 0.0044 |
|  | Chronic lung disease | 71 (32.1) | 30 (33.3) | 41 (31.3) | 0.75 |
|  | Chronic metabolic disease | 79 (35.7) | 43 (47.8) | 36 (27.5) | 0.0020 |
|  | Neurologic disease | 78 (35.3) | 44 (48.9) | 34 (25.9) | 0.0005 |
|  | Immunosuppression | 51 (23.1) | 24 (26.7) | 27 (20.6) | 0.29 |
|  | Blood disorder | 38 (17.2) | 26 (28.9) | 12 (9.2) | 0.0001 |
|  | Renal disease | 46 (20.8) | 25 (27.8) | 21 (16.0) | 0.035 |
|  | Liver disease | 16 (7.2) | 5 (5.6) | 11 (8.4) | 0.42 |
|  | ≥ 1 condition | 194 (87.8) | 89 (98.9) | 105 (80.1) | <0.0001 |
| Alcohol abuse § |  |  |  |  |
|  | Current | 15 (6.8) | 1 (1.1) | 14 (10.7) | 0.0207 |
|  | Former | 5 (2.3) | 2 (2.2) | 3 (2.3) |  |
|  | Never | 201 (90.9) | 87 (96.7) | 114 (87.0) |  |
| Smoking status § |  |  |  |  |
|  | Current | 61 (27.6) | 19 (21.1) | 42 (32.1) | 0.0119 |
|  | Former  | 52 (23.5) | 30 (33.3) | 22 (16.8) |  |
|  | Never | 108 (48.9) | 41 (45.6) | 67 (51.1) |  |
| Influenza virus type |  |  |  |  |
|  | Influenza A | 152 (68.8) | 64 (71.1) | 88 (67.2) | 0.61 |
|  | Influenza B | 68 (30.8) | 26 (28.9) | 42 (32.1) |  |
|  | Influenza A&B | 1 (0.4) | 0 (0.0) | 1 (0.8) |  |
| Season |  |  |  |  |
|  | 2012-2013 | 82 (37.1) | 23 (25.6) | 59 (45.0) | 0.0100 |
|  | 2013-2014 | 60 (27.1) | 31 (34.4) | 29 (22.1) |  |
|  | 2014-2015 | 79 (35.7) | 36 (40.0) | 43 (32.8) |  |
| Severe influenza † | 28 (12.7) | 14 (15.6) | 14 (10.7) | 0.29 |
| Diagnosis of pneumonia ‡ | 49 (22.2) | 18 (20.0) | 31 (23.7) | 0.52 |
|  \* Chi-squared test |
| † Severe influenza is defined as either admission to the intensive care unit or death |
| ‡ Diagnosis of pneumonia is defined as a chest x-ray indicating pneumonia and either diagnosis of pneumonia at discharge or ICD-9 discharge code for pneumonia (480-487.0). |
|  |

|  |
| --- |
| SUPPLEMENT TABLE S6: Odds of severe influenza and pneumonia with respect to vaccination status among patients not treated with antivirals (2012-2015, n=221), † |
|  |  | Overall |
|  |  | OR | 95% CI |
| Severe Influenza ‡ |  |  |
|  | Unadjusted  | 1.54 | 0.69, 3.41 |
|  | Adjusted # | 1.26 | 0.44, 3.59 |
| Pneumonia § |  |  |
|  | Unadjusted  | 0.81 | 0.42, 1.55 |
|  | Adjusted # | 0.60 | 0.25, 1.41 |
| \* Only patients who were not treated with antivirals are included in this analysis. There were as 221 patients who were not treated with antivirals from 2012-2015. An odds ratio less than one suggests that vaccinated patients have decreased odds of the outcome, relative to unvaccinated patients. OR: odds ratio, 95% CI: 95% confidence interval |
| † Age is modeled as a continuous variable. |
| ‡ Severe influenza is defined as admission to the ICU or death during hospitalization. |
| § Pneumonia is defined as a chest x-ray indicating pneumonia and either diagnosis of pneumonia at discharge or ICD-9 discharge code for pneumonia (480-487.0).  |
| # Adjusted by all factors (prompt treatment with antivirals, age, race, sex, obesity, asthma, CVD, CLD, CMD, neurological disease, blood disorders, renal disease, liver disease, immunosuppression, alcohol abuse, smoking status, and virus type) and includes an interaction term between season and vaccine.  |