**Supplementary tables:**

**Supplementary table 1. International Classification of Diseases (ICD) codes used to define high-risk conditions**

|  |  |  |
| --- | --- | --- |
| **High-risk conditions**  | **ICD-9 codes** | **ICD-10 codes** |
| Asthma  | 493 | J45 |
| Blood disorder | 282-284 | D55, D56.0-D56.2, D56.4,D56.5, D56.9, D57.0- D57.2,D57.4, D57.8, D58-D61,D64.0-D64.4, D64.8, D65-D68 |
| Cerebrovascular disease  | 431-434, 437, 438  | I60-I63, I68, I69 |
| Chronic obstructive pulmonary diseases and other lung diseases | 011, 012, 031.0, 135, 277.0,277.6, 491-496, 500-506, 508,514-517, 518.1-518.3, 518.6,518.83, 519.0, 748.4,-748.6,759.3, 770.2, 770.7, V42.6 | A15, A31.0, B39-B41, B44,B45, B46.0, D86.0, E84,E88.01, J18.2, J41-J45, J47,J60-J70, J80-J82, J84-J86,J95.0, J96, J98.1, J99, P25-P28,Q33, T86.3, T86.8, Z94.2 |
| Diabetes | 250, 251, 648.0, 357.2, 362.0,362.11, 36.41 | E08-E11, E13, O24 |
| Heart diseases | 448, 093, 391, 393-398, 402, 404, 410-414, 416, 417, 423-426, 427.1-427.8, 429, 440-444, 446, 447, 745-747, V241, V450, V4582, V42.1, V45.0, V45.81,V45.82 | I50, A52.0, I01, I02,I05-I09, I11, I13, I20-I28, I31, I33-I44, I46, I48, I51-I52, I97.0, I97.1, M31, Q20-Q28, Q89.3, R00.1, Z94.1, Z95, Z98.61 |
| Immunosuppressive conditions | 042, 136.3, 279, 288.0, 288.1,288.2, 288.4, 446, 710.0,710.1, 710.2, 710.3, 710.4,714, V08, V42.2, V42.7, V42.8, V42.9, V42.1, V42.6, V42.0, V58.0, V58.1, 140-172, 174-208 | B20, B59, B97.3, D47.Z1, D70-D73, D76, D80-D84, D89,M05-M08, M30-M34, M35.0,M35.9, Q89.0, T45.1X1, Z21,Z48.2, Z51.0, Z51.1, Z94,C00-C26, C30-C34, C37-C41,C43-C58, C60-C86, C88, C90-C96, C4A, C7A, C7B, D03, D46, Z85 |
| Kidney diseases | 403, 581-583, 585-587, 588.0,588.1, 590.0, V42.0, V45.1,V56 | I12, N01-N08, N11, N14-N18,N25, N26, N28, Q27.1, Q27.2,Q60, Z49, Z91.15, Z94.0, Z99.2 |
| Liver diseases  | 571, 572.2-572.8  | B18, K70-K77 |
| Neurological conditions  | 290, 294.1, 318.1, 318.2, 330-332, 333.0, 333.4-333.9, 334-336, 340-343, 344.0, 358.0,358.1, 359, 756.1, 756.3-756.6, 768.5, 780.72 | H49.81, M12.0, M30, M36.0,A17.0, E75.02, E75.19, E75.4,F01-F03, F71-F73, F84.2, G10- G14, G20, G21, G23-G26, G30-G32, G35-G37, G40, G45, G46, G60-G64, G70, G71, G73, G80-G83, G90.3, G91, G93, G94,G95, G99.2, P91, Q00-Q07,Q76, Q77-Q79, Q85, Q87.4,Q90-Q93, Q96, R41, R53.2,R54 |

We used ICD codes assigned to medical encounters or inpatient stay in the year prior to enrollment to define the presence/absence of a high-risk condition that may increase the risk of severe influenza disease for each enrollee. ICD version 9 was used prior to October 2015, and ICD version 10 was used after October 1 2015.

**Supplementary table 2. US Flu VE Network population characteristics by influenza infection status and presence of high-risk conditions, 2012‒2016**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|   | Patients without high-risk conditions |   |  Patients with any high-risk conditions |   |
|  |  |
|  Characteristics | Total | Number of influenza positive (%) |   | Total | Number of influenza positive (%) | *P*-value |
| Site |   |   |   |   |   |   |
| Seattle, WA | 3516 | 629 (18) |  | 2763 | 502 (18) | 0.78 |
| Marshfield, WI | 3513 | 1142 (33) |  | 1911 | 587 (31) | 0.18 |
| Temple, TX | 2982 | 731 (25) |  | 1741 | 317 (18) | < .01 |
| Ann Arbor and Detroit, MI  | 2594 | 767 (30) |  | 1520 | 374 (25) | < .01 |
| Pittsburgh, PA | 3121 | 899 (29) |  | 1708 | 433 (25) | 0.01 |
| Age (years) |  |  |   |   |   |
| 0.5–17  | 6565 | 1705 (26) |  | 2227 | 478 (22) | < .01 |
| 18–49 | 6235 | 1643 (26) |  | 2679 | 581 (22) | < .01 |
| 50–64 | 2220 | 640 (29) |  | 2465 | 618 (25) | 0.03 |
| ≥65 | 706 | 180 (26) |  | 2272 | 536 (23) | 0.42 |
| Sex |   |  |   |   |   |   |
| Female | 9131 | 2323 (25) |  | 5748 | 1272 (22) | < .01 |
| Male | 6595 | 1845 (28) |  | 3895 | 941 (24) | < .01 |
| Race/ethnicity a |  |  |   |   |   |
| White, non-Hispanic | 11777 | 3114 (26) |  | 7296 | 1723 (24) | < .01 |
| Black, non-Hispanic | 1142 | 354 (31) |  | 877 | 210 (24) | < .01 |
| Hispanic | 1377 | 369 (27) |  | 752 | 146 (19) | < .01 |
| Other, non-Hispanic | 1391 | 322 (23) |  | 692 | 130 (19) | 0.02 |
| Vaccination status |  |  |   |   |   |
| Vaccinated  | 6224 | 1207 (19) |  | 6032 | 1216 (20) | 0.28 |
| Unvaccinated | 9502 | 2961 (31) |  | 3611 | 997 (28) | <0.01 |
| Influenza season |  |  |   |   |   |
| 2012–13 | 3790 | 1409 (37) |  | 2064 | 703 (34) | 0.02 |
| 2013–14 | 3195 | 764 (24) |  | 1862 | 318 (17) | < .01 |
| 2014–15 | 4974 | 1234 (25) |  | 3307 | 778 (24) | 0.18 |
| 2015–16 | 3767 | 761 (20) |  | 2410 | 414 (17) | < .01 |
| Interval from onset to enrollment |  |   |   |   |
| 0–2 days | 5163 | 1793 (35) |  | 2884 | 898 (31) | < .01 |
| 3–4 days | 6198 | 1587 (26) |  | 3771 | 853 (22) | < .01 |
| 5–7 days | 4365 | 788 (18) |   | 2988 | 462 (16) |  < .01 |

a Race/ethnicity of 65 persons was unknown.

**Supplementary table 3. Adjusted influenza vaccine effectiveness against influenza A (H3N2) virus by high-risk condition, for patients aged ≥18 years, by seasonal vaccine match to circulating viruses**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|   | Influenza positive patients |   | Influenza negative patients | Vaccine effectiveness |   |
| Characteristics | Number of vaccinated/total (%) |   | Number of vaccinated/total (%) | Adjusted a % (95% CI) | *P*-value for interaction |
| **2014**–**2015 season** |  |  |  |  |  |
| Patients without high-risk conditions | 259/546 (47) |   | 990/2057 (48) | 2 (−20, 19) | – |
| Patients with any high-risk conditions |  358/499 (71) |  | 1304/1845 (71) | 7 (‒19, 28) | 0.93 |
| Asthma | 133/189 (70) |   | 499/734 (68) | 0 (−48, 33) | 0.63 |
| Diabetes | 115/155 (74) |   | 369/465 (79) | 38 (−3,63) | 0.19 |
| Heart diseases | 147/187 (79) |   | 526/669 (79) | 5 (−49, 40) | 0.80 |
| Immunosuppressive conditions | 52/70 (74) |   | 254/305 (83) | 51 (2, 76) | 0.12 |
| Renal diseases | 62/74 (84) |   | 185/215 (86) | 34 (–54, 72) | 0.51 |
| Cerebrovascular diseases | 19/25 (76) |   | 70/86 (81) | – | – |
| COPD and other lung diseases | 32/38 (84) |   | 161/205 (79) | – | – |
| Liver diseases | 20/30 (67) |   | 70/89 (79) | – | – |
| Neurologic conditions | 23/34 (68) |   | 124/154 (81) | – | – |
| **All other seasons b** |  |  |  |  |  |
| Patients without high-risk condition  | 191/517 (37) |   | 2149/4641 (46) | 33 (17, 46) |  |
| Patients with any high-risk condition  | 241/390 (62) |   | 2608/3836 (68) | 41 (13, 54) | 0.78 |
| Asthma | 77/135 (57) |   | 941/1450 (65) | 37 (4, 59) | 0.81 |
| Diabetes | 77/111 (69) |   | 713/984 (73) | 33 (–8, 58) | 0.74 |
| Heart diseases | 92/144 (64) |   | 1000/1325 (76) | 50 (26, 67) | 0.10 |
| Immunosuppressive conditions | 45/62 (73) |   | 494/656 (75) | 29 (‒34, 62) | 0.47 |
| Cerebrovascular diseases | 15/22 (68) |   | 136/163 (83) | ‒ | ‒ |
| COPD and other lung diseases | 32/45 (71) |   | 385/510 (76) | ‒ | – |
| Liver diseases | 9/16 (56) |   | 130/179 (73) | ‒ | ‒ |
| Neurologic conditions | 22/30 (73) |   | 289/386 (75) | ‒ | – |
| Renal diseases | 30/41 (73) |   | 327/405 (81) | ‒ | ‒ |

High-risk categories with fewer than 5 vaccinated influenza or non-influenza patients are not listed.

*P*-value for interaction for each specific high-risk conditions is calculated by comparing patients with the specific high-risk condition with patients without high-risk conditions.

a Adjusted for site, age, influenza season, interval from symptom onset to enrollment, calendar time (4 weeks).

b 2012–2013, 2013–2014, and 2015–2016 seasons.