**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.