Supplemental Table 2: Literature search strategy

|  |  |
| --- | --- |
| **Database** | **Strategy** |
| **Medline**  **(OVID)**  **1946-** | Influenza, Human/ OR \*Respiratory Tract Infections/ep OR ((influenza\* OR flu) ADJ3 season\*).ti,ab.  AND  ((Lab\* ADJ3 (confirm\* OR report\* OR test\*)) OR (serologic\* ADJ2 (confirm\* OR test\*)) OR ((hospital\* OR public health) ADJ3 lab\*) OR (positive ADJ2 test\*) OR (vaccin\* ADJ2 effective\*) OR (negative ADJ2 test\*) OR swab\* OR specimen\* OR sample\* OR polymerase chain reaction OR PCR OR RT-PCR OR (rapid ADJ3 test\*) OR (diagnos\* ADJ2 (test\* OR assay\*)) OR hospitalization OR (sensitivity ADJ2 specificity) OR antigen detection OR (molecular ADJ2 (assay\* OR test\*)) OR culture\* OR secretion\* OR antibody staining OR antibody titer\* OR nucleic acid detection OR bronchial wash OR nasal wash OR aspirate OR sputum).mp  AND  (Epidemiology OR surveillance OR clinical trial\* OR cohort stud\* OR household stud\* OR controlled trial\* OR observational stud\* OR randomi?ed trial\* OR prospective stud\* OR (vaccin\* ADJ2 effective\*) OR (communit\* ADJ2 cohort\*)).mp  NOT  Exp animals/ NOT exp humans/  Limit English; 1998- |
| **Embase**  **(OVID)**  **1996-** | Influenza/ OR \*Respiratory Tract Infection/ep OR ((influenza\* OR flu) ADJ3 season\*).ti,ab.  AND  ((Lab\* ADJ3 (confirm\* OR report\* OR test\*)) OR (serologic\* ADJ2 (confirm\* OR test\*)) OR ((hospital\* OR public health) ADJ3 lab\*) OR (positive ADJ2 test\*) OR (vaccin\* ADJ2 effective\*) OR (negative ADJ2 test\*) OR swab\* OR specimen\* OR sample\* OR polymerase chain reaction OR PCR OR RT-PCR OR (rapid ADJ3 test\*) OR (diagnos\* ADJ2 (test\* OR assay\*)) OR hospitalization OR (sensitivity ADJ2 specificity) OR antigen detection OR (molecular ADJ2 (assay\* OR test\*)) OR culture\* OR secretion\* OR antibody staining OR antibody titer\* OR nucleic acid detection OR bronchial wash OR nasal wash OR aspirate OR sputum).mp  AND  (Epidemiology OR surveillance OR clinical trial\* OR cohort stud\* OR household stud\* OR controlled trial\* OR observational stud\* OR randomi?ed trial\* OR prospective stud\* OR (vaccin\* ADJ2 effective\*) OR (communit\* ADJ2 cohort\*)).mp  NOT  Exp animals/ NOT exp humans/  Limit English; 1998- ; exclude Medline journals |
| **CINAHL**  **(Ebsco)**  **1982-** | (MH "Influenza, Human") OR (MJ "Respiratory Tract Infections"/EP) OR ((influenza\* OR flu) N3 season\*)  AND  ((Lab\* N3 (confirm\* OR report\* OR test\*)) OR (serologic\* N2 (confirm\* OR test\*)) OR ((hospital\* OR public health) N3 lab\*) OR (positive N2 test\*) OR (vaccin\* N2 effective\*) OR (negative N2 test\*) OR swab\* OR specimen\* OR sample\* OR polymerase chain reaction OR PCR OR RT-PCR OR (rapid N3 test\*) OR (diagnos\* N2 (test\* OR assay\*)) OR hospitalization OR (sensitivity N2 specificity) OR antigen detection OR (molecular N2 (assay\* OR test\*)) OR culture\* OR secretion\* OR antibody staining OR antibody titer\* OR nucleic acid detection OR bronchial wash OR nasal wash OR aspirate OR sputum)  AND  (Epidemiology OR surveillance OR clinical trial\* OR cohort stud\* OR household stud\* OR controlled trial\* OR observational stud\* OR randomi?ed trial\* OR prospective stud\* OR (vaccin\* N2 effective\*) OR (communit\* N2 cohort\*))  Limit English; 1998- ; Humans; exclude Medline records |
| **Cochrane**  **Library** | [mh "Influenza, Human"] OR [mh "Respiratory Tract Infections"] OR ((influenza\* OR flu) NEAR/3 season\*)  AND  ((Lab\* NEAR/3 (confirm\* OR report\* OR test\*)) OR (serologic\* NEAR/2 (confirm\* OR test\*)) OR ((hospital\* OR public health) NEAR/3 lab\*) OR (positive NEAR/2 test\*) OR (vaccin\* NEAR/2 effective\*) OR (negative NEAR/2 test\*) OR swab\* OR specimen\* OR sample\* OR polymerase chain reaction OR PCR OR RT-PCR OR (rapid NEAR/3 test\*) OR (diagnos\* NEAR/2 (test\* OR assay\*)) OR hospitalization OR (sensitivity NEAR/2 specificity) OR antigen detection OR (molecular NEAR/2 (assay\* OR test\*)) OR culture\* OR secretion\* OR antibody staining OR antibody titer\* OR nucleic acid detection OR bronchial wash OR nasal wash OR aspirate OR sputum)  AND  (Epidemiology OR surveillance OR clinical trial\* OR cohort stud\* OR household stud\* OR controlled trial\* OR observational stud\* OR randomi?ed trial\* OR prospective stud\* OR (vaccin\* NEAR/2 effective\*) OR (communit\* NEAR/2 cohort\*))  Limit English; 1998- ; Humans; exclude Medline records |

Supplemental Table 3. Definitions of quality levels and numbers of studies included in meta-analyses (n=15 studies)

|  |  |  |  |
| --- | --- | --- | --- |
| Quality indicator | Study Quality Level | | |
| High | Intermediate | Low |
| Geographic representativeness | Multi-city and includes non-university cities  (n=8) | Multi-city but includes only university cities  (n=1) | Single city  (n=6) |
| Age representativeness | Includes entire child (0-17 years, 18 year span) and adult (18-64 years, 47 year span) age span  (n=6) | Ages included span ≥9 years for children or ≥23.5 years for adults\*  (n=7) | Age span not specified or includes <9 years for children or <23.5 years for adults \*  (n=2) |
| General representativeness | Randomly or systematically chosen subjects  (n=0) | General population volunteers, may exclude those with high risk of influenza complications  (n=15) | Includes only members of a specific group (e.g., college students)  (n=0) |
| Adequacy of follow-up | Active follow-up: contacts subjects at least every week to ask about symptoms  (n=9) | Active follow-up: contacts subjects at least every two weeks  (n=3) | Passive follow-up: instructs subjects to contact study staff if have symptoms  (n=3) |
| Sensitivity of symptoms prompting laboratory testing | Does not require any one specific symptom  (n=10) | Requires one specific symptom; or includes URI without listing specific symptoms  (n=3) | Requires ≥2 specific symptoms  (n=2) |
| Laboratory method | RT-PCR with or without culture  (n=8) | Viral culture without RT-PCR  (n=7) | Methods other than RT-PCR or culture  (n=0) |

Abbreviation: RT-PCR, reverse-transcription polymerase-chain reaction; URI, upper respiratory infection.

\*Age representativeness examples: a study that included adults 18-49 years (span 32 years) covered >23.5 years of the 47-year adult age span and was rated “intermediate”; a study that included children 15-85 months (or 1.3-7.1 years, span 5.8 years) covered <9 years of the 18-year child age span and was rated “low”

Supplemental Table 4. Quality levels for 15 studies included in meta-analyses\*

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| First author, year published | Age-group (s) | No. of seasons | Geographic representation | Age representation | General represenation | Follow-up | Sensitivity of symptoms | Laboratory method |
| Barrett 2011[1] | Adult | 1 | High | Intermediate | Intermediate | Low | High | Intermediate |
| Belshe 2000[2] | Children | 2 | High | Low | Intermediate | High | High | Intermediate |
| Hoberman 2003[3] | Children | 2 | Low | Low | Intermediate | Intermediate | Intermediate | Intermediate |
| Jackson 2010[4] | Adult | 2 | High | Intermediate | Intermediate | High | Low | Intermediate |
| Langley 2011[5] | Adult | 1 | High | High | Intermediate | Intermediate | Low | Intermediate |
| Monto 2009[6] | Adult | 1 | Intermediate | Intermediate | Intermediate | Low | High | High |
| Monto 2014[7] | Children, adult, all ages | 1 | Low | High | Intermediate | High | High | High |
| Ohmit 2006[8] | Adult | 1 | High | Intermediate | Intermediate | Intermediate | High | High |
| Ohmit 2008[9] | Adult | 1 | High | Intermediate | Intermediate | Low | High | High |
| Ohmit 2013[10] | Children, adult, all ages | 1 | Low | High | Intermediate | High | High | High |
| Ohmit 2015[11] | Children, adult, all ages | 1 | Low | High | Intermediate | High | High | High |
| Ohmit 2016[12] | Children, adult, all ages | 1 | Low | High | Intermediate | High | High | High |
| Smithgall 2016[13] | All ages | 1 | Low | High | Intermediate | High | High | High |
| Treanor 2007[14] | Adult | 1 | High | Intermediate | Intermediate | High | Intermediate | Intermediate |
| Treanor 2011[15] | Adult | 1 | High | Intermediate | Intermediate | High | Intermediate | Intermediate |

\*Definitions of low, intermediate, and high quality levels are in Supplemental Table 3.

Supplemental Table 5. Adjustment of infection rates among unvaccinated persons determined by meta-analysis to estimate infection rate in a population with median vaccine coverage and effectiveness, 2010-2016

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | Children 0-17 years | | | Adults ≥18 years | | | All ages | | |
| Season | VE | VC | VExVC | VE | VC | VExVC | VE | VC | VExVC |
| 2010-11 | 0.594 | 0.495 | 0.294 | 0.503 | 0.346 | 0.174 | 0.506 | 0.423 | 0.214 |
| 2011-12 | 0.477 | 0.499 | 0.238 | 0.471 | 0.328 | 0.154 | 0.467 | 0.411 | 0.192 |
| 2012-13 | 0.652 | 0.549 | 0.358 | 0.670 | 0.351 | 0.235 | 0.615 | 0.440 | 0.271 |
| 2013-14 | 0.487 | 0.572 | 0.278 | 0.570 | 0.362 | 0.206 | 0.531 | 0.451 | 0.239 |
| 2014-15 | 0.097 | 0.577 | 0.056 | 0.100 | 0.376 | 0.038 | 0.102 | 0.464 | 0.047 |
| 2015-16 | 0.511 | 0.576 | 0.294 | 0.411 | 0.357 | 0.147 | 0.434 | 0.448 | 0.194 |
| Median |  |  | 0.286 |  |  | 0.164 |  |  | 0.204 |

Abbreviations: VE, vaccine effectiveness; VC, vaccine coverage

Data sources: United States Influenza Vaccine Effectiveness Network[16], FluVaxView[17]

Vaccine effectiveness and coverage values were estimated by weighing values for smaller age groups by population size to arrive at summary values for children (0-17 years), adults 18-64 years), and all ages

The product of VE x VC indicates the decrease in infection rate expected for the given vaccine effectiveness and coverage, i.e., median decreases of 28.6% for children, 16.4% for adults, and 20.4% overall