Relative Effectiveness of Cell-Based Versus Egg-Based Quadrivalent Influenza Vaccines in Children and Adolescents in the United States During the 2019-2020 Influenza Season

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**De-identification and Linkage Methodology**

De-identified datasets are created using an algorithm developed by Datavant which removes personally-identifiable information (PII; which includes but is not necessarily limited to protected health information, or PHI). As the algorithm de-identifies a patient record, tokens are generated based on PII in the record using fields such as name, date of birth, and gender. Matching tokens are used to deterministically link a patient’s record in the EMR database with a record for the same patient in the claims database. This linked de-identified dataset is then made available for research use. Research staff are not involved in preparation of datasets containing PHI or the actual running of the algorithm.
Supplementary Table 1. List of CPT, CVX, and NDC codes used to identify influenza vaccines from the Veradigm EMR dataset.

| Influenza vaccine type | CPT   | CVX  | NDC                                      |
|------------------------|-------|------|------------------------------------------|
| IIV4e                  | 90685, 90686, 90687, 90688 | 150, 158, 161 | 19515-0897-01, 19515-0897-11, 19515-0906-41, 19515-0906-52, 33332-0219-20, 33332-0219-21, 33332-0319-01, 33332-0319-02, 33332-0419-10, 33332-0419-11, 49281-0419-10, 49281-0419-50, 49281-0419-58, 49281-0419-88, 49281-0519-00, 49281-0519-25, 49281-0631-15, 49281-0631-78, 58160-0896-41, 58160-0896-52 |
| IIV4c                  | 90674, 90756 | 153, 171, 186 | 70461-0319-03, 70461-0319-04, 70461-0419-10, 70461-0419-11 |

CPT, current procedural terminology; CVX, code for vaccine administered; NDC, national drug code.
Supplementary Table 2. Outcome case definitions

| ICD-10-CM Codes                                                                 | ICD-9-CM Codes                                                      |
|---------------------------------------------------------------------------------|---------------------------------------------------------------------|
| J09 (influenza due to certain identified influenza viruses)                      |                                                                     |
| J09.X (influenza due to identified novel influenza A viruses)                    |                                                                     |
| J09.X1 (influenza due to identified novel influenza A virus with pneumonia)      | 488.0 (influenza due to identified avian influenza virus)            |
|                                                                                 | 488.01 (influenza due to identified avian influenza virus with pneumonia) |
|                                                                                 | 488.8 (influenza due to novel influenza A)                            |
|                                                                                 | 488.81 (influenza due novel influenza A with pneumonia)               |
| J09.X2 (influenza due to identified novel influenza A virus with other respiratory manifestations) | 488.02 (influenza due to identified avian influenza virus with other respiratory manifestations) |
|                                                                                 | 488.82 (influenza due to novel influenza A with other respiratory manifestations) |
| J09.X3 (influenza due to identified novel influenza A virus with gastrointestinal manifestations) | 488.09 (influenza due to identified avian influenza virus with other) |
|                                                                                 | 488.1 (influenza due to 2009 H1N1 influenza virus)                   |
| J09.X9 (influenza due to identified novel influenza A virus with other manifestations) | 488.19 (influenza due to identified 2009 H1N1 influenza virus with other manifestations) |
|                                                                                 | 488.89 (influenza due to novel influenza A with other manifestations)  |
| J10 (influenza due to other identified influenza viruses)                         |                                                                     |
| J10.0 (influenza due to identified novel influenza A viruses)                    |                                                                     |
| J10.00 (influenza due to other identified influenza virus with unspecified type of pneumonia) | 487.0 (influenza with pneumonia)                                      |
| J10.01 (influenza due to other identified influenza virus with the same other identified influenza virus pneumonia) | 487.1 (influenza with other respiratory manifestations)               |
|                                                                                 | 487.0 (above)                                                       |
| ICD-10-CM Codes                                                                 | ICD-9-CM Codes                                                                 |
|--------------------------------------------------------------------------------|--------------------------------------------------------------------------------|
| J10.08 (influenza due to other identified influenza virus with other specified pneumonia) | 488.11 (influenza due to identified 2009 H1N1 influenza virus with pneumonia) |
| J10.1 (influenza due to other identified influenza virus with other respiratory manifestations) | 487.1 (above)                                                                 |
| J10.2 (influenza due to other identified influenza virus with gastrointestinal manifestations) | 487.8 (influenza with other manifestations)                                    |
| J10.8 (influenza due to other identified influenza virus with other manifestations) |                                                                                |
| J10.81 (influenza due to other identified influenza virus with other manifestations with encephalopathy) |                                                                                |
| J10.82 (influenza due to other identified influenza virus with other manifestations with myocarditis) |                                                                                |
| J10.83 (influenza due to other identified influenza virus with other manifestations with otitis media) |                                                                                |
| J10.89 (influenza due to other identified influenza virus with other manifestations) |                                                                                |
| J11 (influenza due to unidentified influenza virus)                                |                                                                                |
| J11.0 (influenza due to unidentified influenza virus with pneumonia)             |                                                                                |
| J11.00 (influenza due to unidentified influenza virus with unspecified type of pneumonia) | 487.0 (above)                                                                 |
| J11.08 (influenza due to unidentified influenza virus with specified pneumonia)  |                                                                                |
| J11.1 (influenza due to unidentified influenza virus with other respiratory manifestations) | 487.1 (above)                                                                 |
| J11.2 (influenza due to unidentified influenza virus with gastrointestinal manifestations) | 487.8 (above)                                                                 |
| J11.8 (influenza due to unidentified influenza virus with other manifestations)  |                                                                                |
| J11.81 (influenza due to unidentified influenza virus with encephalopathy)       |                                                                                |
| J11.82 (influenza due to unidentified influenza virus with myocarditis)          |                                                                                |
| J11.83 (influenza due to unidentified influenza virus with otitis media)         |                                                                                |
| ICD-10-CM Codes                                      | ICD-9-CM Codes                                      |
|-----------------------------------------------------|-----------------------------------------------------|
| J11.89 (influenza due to unidentified influenza virus with other manifestations) |                                                     |
Supplementary Table 3. Subjects with a record of each health condition included in the Charlson comorbidity index in the 12 months prior to the date of vaccination.

| Comorbidity                          | IIV4c (n=60,480) | IIV4e (n=1,240,990) |
|--------------------------------------|------------------|---------------------|
| Chronic pulmonary disease            | 6,410 (10.6)     | 180,757 (14.6)      |
| Diabetes without chronic complication| 458 (0.8)        | 7,959 (0.6)         |
| Hemiplegia or paraplegia             | 149 (0.2)        | 4,896 (0.4)         |
| Mild liver disease                   | 105 (0.2)        | 3,336 (0.3)         |
| Any malignancy                       | 67 (0.1)         | 2,030 (0.2)         |
| Rheumatic disease                    | 45 (0.1)         | 869 (0.1)           |
| Renal disease, mild to moderate      | 44 (0.1)         | 1,559 (0.1)         |
| Congestive heart failure             | 39 (0.1)         | 1,109 (0.1)         |
| Dementia                             | 31 (0.1)         | 706 (0.1)           |
| Peptic ulcer disease                 | 31 (0.1)         | 568 (0.0)           |
| Cerebrovascular disease              | 22 (0.0)         | 820 (0.1)           |
| Peripheral vascular disease          | 20 (0.0)         | 484 (0.0)           |
| Diabetes with chronic complication   | 18 (0.0)         | 376 (0.0)           |
| Severe renal disease                 | 17 (0.0)         | 334 (0.0)           |
| HIV infection, no aids               | 11 (0.0)         | 142 (0.0)           |
| Metastatic solid tumor               | 3 (0.0)          | 195 (0.0)           |
| Moderate to severe liver disease     | 2 (0.0)          | 138 (0.0)           |
| Myocardial infarction                | 2 (0.0)          | 59 (0.0)            |
| AIDS                                 | 1 (0.0)          | 14 (0.0)            |

Abbreviations: IIV4c, cell-based inactivated quadrivalent influenza vaccine; IIV4e, egg-based inactivated quadrivalent influenza vaccine; SMD, standardized mean difference.
Supplementary Figure 1. Unadjusted relative vaccine effectiveness (rVE) of IIV4c compared with IIV4e among individuals aged 4 through 17 years in the 2019-2020 influenza season. IIV4c, cell-based inactivated quadrivalent influenza vaccine; CI, confidence interval; IIV4e, egg-based inactivated quadrivalent influenza vaccine; IRME, influenza-related medical encounter.

| Event rate, n (%) | IIV4c (n=60,480) | IIV4e (n=1,240,990) | rVE (95% CI) IIV4c vs IIV4e |
|-------------------|------------------|---------------------|-----------------------------|
| Any IRME          |                  |                     |                             |
| Inpatient IRME    |                  |                     |                             |
| (admitting diagnosis) | 502 (0.8)      | 12,377 (1.0)        | 16.9 (9.1 to 24.0)        |
| Inpatient IRME    |                  |                     |                             |
| (any diagnosis)   | 601 (1.0)        | 14,870 (1.2)        | 17.2 (10.2 to 23.8)       |
| Outpatient IRME   |                  |                     |                             |
|                   | 2,335 (3.9)      | 61,748 (5.0)        | 23.3 (20.0 to 26.5)       |
Supplementary Figure 2. Influenza positive tests reported to CDC by public health laboratories overlapped with incidence of influenza-related medical encounters in the study cohort. *Influenza positive tests reported to CDC for the 5- to 24-year age group overlapped with influenza-related medical encounters in the 4- to 17-year study cohort. From: Centers for Disease Control and Prevention. FluView summary ending on September 26, 2020. Available at: https://www.cdc.gov/flu/weekly/weeklyarchives2019-2020/Week39.htm. Accessed March 25, 2021.