**Supplemental Tables**

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| **Supplemental Table 1. Outcome influenza A with vaccine status SD-IIV3/4 versus HD-IIV3 (ref. SD-IIV3/4)** |
| **Variable** | **Unadjusted β1** | **Adjusted β1**  | **((Adj. β - Unadj β)/ Unadj β)\*100** | **Effect Modifier** |
| Vaccination status (ref. SD-IIV3/4) | -0.0977 | --- | --- | --- |
| Adjusted by |  |  |  |
| Age on Sept.1, years | -0.0955 | 2 | No |
| Female sex | -0.0968 | 1 | No |
| Race | -0.0844 | 14 | **Yes** |
| Non-smoker, ref.=ever smoker | -0.0997 | 2 | No |
| Site, ref. = Pennsylvania | 0.0250 | 125 | **Yes** |
| Season, ref. = 2015-2016 | -0.1659 | 70 | **Yes** |
| Interval from onset to enrollment | -0.0296 | 70 | **Yes** |
| Any prior high-risk condition | -0.0954 | 2 | No |
| Prior vaccination status | -0.1021 | 4 | No |
| Healthcare utilization-prior | -0.1778 | 82 | **Yes** |
| Health care utilization-post (30 days) | -0.0911 | 7 | No |
| Outpatient frequent (prior) healthcare utilization | -0.0982 | 1 | No |
| Days between vaccination and illness onset | -0.1105 | 13 | **Yes** |
| Number of high-risk conditions | -0.1028 | 5 | No |
| Timing of vaccination (weeks) | -0.1117 | 14 | **Yes** |

*1Unadjusted and adjusted estimate (****β)*** *for vaccination status*

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| **Supplemental Table 2. Checking the causal effect (confounders) with outcome influenza A and exposure vaccination status (SD-IIV3/4 versus HD-IIV3)** |
| **Characteristics** | ***P* value** | **Confounder** |
| **SD-IIV3/4****versus HD-IIV3** | **Influenza A status** |
| Age on Sept.1, years | 0.346 | 0.166 | No |
| Female sex | 0.615 | 0.287 | No |
| Race | <.001 | 0.444 | No |
| Non-smoker, ref.=ever smoker | 0.341 | 0.128 | No |
| Site | <.001 | <.001 | **Yes** |
| Season | <.001 | <.001 | **Yes** |
| Interval from onset to enrollment | <.001 | <.001 | **Yes** |
| Any prior high-risk condition | 0.471 | 0.051 | No |
| Prior vaccination status | <.001 | 0.752 | No |
| Health care utilization-Prior | 0.123 | 0.238 | No |
| Health care utilization-post (30 days) | 0.004 | 0.149 | No |
| Outpatient frequent (prior) healthcare utilization | 0.020 | 0.914 | No |
| Days between vaccination and illness onset | <.001 | 0.049 | No |
| Number of high-risk conditions | 0.118 | 0.055 | No |
| Timing of vaccination (weeks) | <.001 | 0.828 | No |

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| **Supplemental Table 3. Propensity Score Method – Checking for balance using standardized effect size.** |
| **Variables** | **Unweighted** | **Weighted**  |
| **Standardized Effect Size** | ***P* value** | **Standardized Effect Size** | ***P* value** |
| Age on Sept. 1 | 0.033 | 0.362 | 0.052 | 0.228 |
| Race |  | <.001 |  | 0.772 |
| White, non-Hispanic | -0.157 |  | 0.0 |  |
| Black, non-Hispanic | 0.1 |  | 0.027 |  |
| Other race, non-Hispanic | 0.185 |  | 0.007 |  |
| Hispanic, any race | -0.066 |  | -0.039 |  |
| Sex |  | 0.603 |  | 0.819 |
| Female | 0.019 |  | 0.011 |  |
| Male | -0.019 |  | -0.011 |  |
| Site |  | <.001 |  | 0.045 |
| Michigan | 0.246 |  | 0.01 |  |
| Pennsylvania | -0.105 |  | -0.025 |  |
| Texas | -0.316 |  | -0.041 |  |
| Washington | 0.787 |  | 0.133 |  |
| Wisconsin | -0.807 |  | -0.113 |  |
| Season |  | <.001 |  | 0.938 |
| 2015-2016 | -0.188 |  | -0.026 |  |
| 2016-2017 | 0.051 |  | -0.005 |  |
| 2017-2018 | -0.019 |  | 0.022 |  |
| 2018-2019 | 0.132 |  | 0.007 |  |
| Interval from onset to enrollment |  | <.001 |  | 0.967 |
| 0-2 days | -0.138 |  | -0.01 |  |
| 3-4 days | -0.025 |  | -0.003 |  |
| 5-7 days | 0.144 |  | 0.011 |  |
| Any prior high-risk condition |  | 0.387 |  | 0.422 |
| No | 0.032 |  | -0.037 |  |
| Yes | -0.032 |  | 0.037 |  |
| Prior vaccination status |  | <.001 |  | 0.300 |
| No | -0.222 |  | -0.047 |  |
| Yes | 0.222 |  | 0.047 |  |
| Timing of vaccination (weeks) | -0.558 | <.001 | -0.105 | 0.037 |

*Vaccination status (SD-IIV3/4 versus HD-IIV3) = age, race/ethnicity, sex, site, season, interval from onset to enrollment (0-2 days, 3-4 days, 5-7 days), any prior high-risk condition, prior vaccination status, timing of vaccination and three way interactions*

*Weighted: Effect size average treatment effect*

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| **Supplemental Table 4. Unadjusted relative vaccine effectiveness (rVE) of high dose influenza vaccine compared with standard dose influenza vaccine (HD-IIV3 versus SD-IIV3/4) – Sensitivity analysis, excluding one site at a time** |
|  | **Excluding Michigan** | **Excluding Pennsylvania** | **Excluding** **Texas** | **Excluding Washington** | **Excluding Wisconsin** |
| *SD-IIV3/4 vs. HD-IIV3* |
| Any Influenza A | 14 (-4, 30) | 7 (-13, 24) | 7 (-12, 23) | 11 (-13, 30) | 1 (-23, 20) |
| Influenza A/H1N1 | 20 (-17, 46) | -29 (-90, 12) | -1 (-45, 29) | -12 (-72, 27) | 2 (-49, 35) |
| Influenza A/H3N2 | 14 (-8, 31) | 17 (-4, 33) | 12 (-9, 29) | 16 (-10, 36) | 1 (-28, 22) |
| *2015-16/2016-17*  |
| Any Influenza A | -6 (-44, 22) | -6 (-46, 23) | -12 (-53, 18) | -5 (-60, 31) | -35 (-92, 6) |
| Influenza A/H1N1 | 22 (-71, 65) | 10 (-102, 60) | 3 (-103, 54) | -51 (-260,36) | -5 (-145, 55) |
| Influenza A/H3N2 | -9 (-52, 22) | -6 (-50, 25) | -11 (-55, 21) | 1 (-58, 37) | -43 (-112, 4) |
| *2017-18/2018-19*  |
| Any Influenza A | **27 (5,43)** | 18 (-5, 36) | 19 (-3, 36) | 23 (-2, 43) | 20 (-6, 39) |
| Influenza A/H1N1 | 24 (-19, 51) | -28 (-100, 18) | 4 (-45, 36) | 9 (-49, 45) | 11 (-44, 44) |
| Influenza A/H3N2 | **28 (3, 46)** | **31 (8, 48)** | **25 (1, 43)** | **28 (0, 48)** | 23 (-6, 44) |

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| **Supplemental Table 5. Adjusted1 relative vaccine effectiveness (rVE) of high dose influenza vaccine compared with standard dose influenza vaccine (HD-IIV3 versus SD-IIV3/4) – Sensitivity analysis, excluding one site at a time** |
|  | **Excluding Michigan** | **Excluding Pennsylvania** | **Excluding****Texas** | **Excluding Washington** | **Excluding Wisconsin** |
| *SD-IIV3/4 versus HD-IIV3* |
| Any Influenza A | 13 (-11, 32) | 1 (-27, 23) | -3 (-30, 19) | 15 (-13, 35) | 11 (-13, 31) |
| Influenza A/H1N1 | 2 (-56, 38) | -42 (-128, 19) | -42 (-119, 8) | -13 (-87, 32) | -7 (-71, 33) |
| Influenza A/H3N2 | 14 (-13, 36) | 12 (-17, 34) | 8 (-20, 30) | 22 (-7, 44) | 17 (-11, 37) |
| *2015-16/2016-17*  |
| Any Influenza A | 17 (-26, 45) | 15 (-32, 45) | -4 (-56, 31) | -14 (-90, 32) | 3 (-47, 35) |
| Influenza A/H1N1 | -26 (-229, 52) | -42 (-288, 48) | -84 (-356, 26) | -71 (-393, 41) | -63 (-320, 37) |
| Influenza A/H3N2 | 24 (-22, 53) | 28 (-19, 56) | 13 (-39, 46) | -2 (-85, 44) | 13 (-39, 46) |
| *2017-18/2018-19*  |
| Any Influenza A | 9 (-24, 33) | -4 (-42, 23) | -4 (-40, 22) | 22 (-10, 44) | 14 (-17, 37) |
| Influenza A/H1N1 | 8 (-59, 46) | -44 (-147, 16) | -35 (-124, 19) | 1 (-80, 46) | 2 (-69, 43) |
| Influenza A/H3N2 | 7 (-33, 35) | 6 (-34, 34) | 6 (-32, 33) | 17 (-7, 51) | 18 (-17, 43) |
| **1***A priori variables = age, race/ethnicity, sex, site, season, interval from onset to enrollment (0-2 days, 3-4 days, 5-7 days), any prior high-risk condition, and bi-week (indicator variable of 2-week blocks of calendar time)* |