

## Mid-Season Influenza Vaccine Effectiveness Estimates for the 2016–2017 Influenza Season

Elizabeth Toure, MPH; Angelia A. Eick-Cost, PhD, ScM; Anthony W. Hawksworth; Michael J. Cooper, PhD (CAPT, USPHS); Zheng Hu, MS; Christopher A. Myers, PhD; Peter E. Kammerer, MD; Michelle N. Ricketts; Susan Federinko, MD, MPH (Lt Col, USAF)

The Department of Defense (DoD) conducts year-round influenza surveillance for military healthcare beneficiaries and select civilian populations. Data from routine respiratory surveillance are used to estimate midseason influenza vaccine effectiveness (VE) and findings are shared annually at the Food and Drug Administration's advisory committee meeting on U.S. influenza vaccine strain selection. DoD VE estimates from the Defense Health Agency Armed Forces Health Surveillance Branch (AFHSB) and Naval Health Research Center (NHRC) are presented in this report.

### METHODS

The AFHSB–Air Force Satellite Cell (AFHSB-AF) conducted a test-negative case-control study using data from the U.S. Air Force School of Aerospace Medicine's worldwide sentinel site-based program, the DoD Global, Laboratory-Based, Influenza Surveillance Program. Respiratory specimens were collected from DoD dependents presenting to outpatient military treatment facilities with influenza-like illness (ILI). Influenza cases were identified using reverse transcription–polymerase chain reaction (RT-PCR) or viral culture; controls were ILI patients who tested negative for influenza. From 2 October 2016 through 18 February 2017, a total of 534 cases and 838 test-negative controls were identified. Vaccination status was ascertained via electronic immunization records (Air Force Complete Immunization Tracking Application and the Aeromedical Services Information Management System) and self-report from patient questionnaires. Individuals were considered vaccinated if they received the current

season's vaccine at least 14 days before illness onset. Those who were vaccinated within 14 days of illness onset were excluded.

NHRC's study utilized a test-negative case-control design using data from their febrile respiratory illness (FRI) surveillance program, which included outpatient DoD dependents in Southern California, Arizona, and Illinois, as well as outpatient civilians presenting at clinics in California near the U.S.–Mexico border. Cases were identified using RT-PCR; controls were FRI patients who tested negative for influenza. From 29 December 2016 through 16 February 2017, a total of 75 cases and 224 test-negative controls were identified. Vaccination status was ascertained by medical chart review when possible and self-report when necessary. Individuals were considered vaccinated if illness occurred between 14 and 180 days since vaccination.

AFHSB conducted a matched case-control study using data from the Defense Medical Surveillance System (DMSS) and Standard Ancillary Service–processed laboratory data from the Navy and Marine Corps Public Health Center to evaluate VE among active component, nonrecruit service members worldwide, across all services. Cases were defined as service members with influenza-positive laboratory tests (rapid antigen tests, RT-PCR or culture). Healthy controls were identified using medical encounters for injuries or mental health conditions without any ILIs reported at the encounter and no medical encounters for influenza during the season. Healthy controls were matched to cases by sex, age, date of encounter ( $\pm 3$  days), and treatment facility. From 1 December 2016 through 25 February 2017, a total of 909 cases and 3,424 matched healthy controls were identified. Vaccination status was ascertained by electronic immunization records from DMSS.

Multivariable logistic regression was used to calculate adjusted odds ratios (AORs) using SAS 9.3 (SAS Institute Inc., Cary, NC). VE was calculated as  $(1 - \text{AOR}) \times 100$ . Given the predominance of influenza A(H3N2), VE analyses against influenza A(H1N1)pdm09 were not possible, and only one study (AFHSB-AF) was able to conduct an influenza B VE analysis. All analyses evaluated the effectiveness of inactivated influenza vaccines because the live attenuated influenza vaccine was not used during the 2016–2017 influenza season in the U.S.<sup>1</sup> AFHSB-AF adjusted for age group, month of illness, and region for the overall and influenza A(H3N2) analyses; the influenza B analysis was adjusted for month of illness only. NHRC adjusted for age group and surveillance population. AFHSB adjusted for 5-year influenza vaccination history (at least one influenza vaccination in the previous 5 years vs. no influenza vaccinations during the previous 5 years). Control selection methods varied between the studies and were chosen based on the characteristics of the population and the data available.

### RESULTS

Adjusted VE for dependents and civilians against all influenza types was similar across studies and showed statistically significant protection (Table). AFHSB-AF found that, for all influenza types, VE was 42% (95% CI: 24%–55%), similar to NHRC's overall VE of 45% (95% CI: 5%–68%). VE against influenza A(H3N2) for dependents and civilians was also similar across studies with AFHSB-AF estimating influenza A(H3N2) VE at 42% (95% CI: 24%–56%) and NHRC estimating influenza A(H3N2) VE at 46% (95% CI: 6%–70%). VE against influenza B was slightly higher at 53% (95%

**TABLE.** Mid-season influenza vaccine effectiveness (VE) estimates, 2016–2017

| Population                               | Influenza type           | No. of cases | % vaccinated | No. of controls | % vaccinated <sup>a</sup> | Crude VE | 95% CI   | Adjusted VE | 95% CI <sup>b</sup> |
|--|--------------------------|--------------|--------------|-----------------|---------------------------|----------|----------|-------------|---------------------|
| Dependents (AFHSB-AF)                    | Overall                  | 534          | 32           | 838             | 36                        | 17       | (-5–34)  | 42          | (24–55)             |
|  | Influenza A(H3N2)        | 477          | 32           | 838             | 36                        | 14       | (-9–32)  | 42          | (24–56)             |
|  | Influenza B              | 53           | 26           | 838             | 36                        | 35       | (-21–65) | 53          | (11–75)             |
| Dependents and civilians (NHRC)          | Overall                  | 75           | 33           | 224             | 48                        | 45       | (6–68)   | 45          | (5–68)              |
|  | Influenza A(H3N2)        | 70           | 33           | 224             | 48                        | 47       | (6–70)   | 46          | (6–70)              |
| Active component service members (AFHSB) | Influenza A <sup>c</sup> | 909          | 91           | 3,424           | 91                        | 5        | (-23–27) | 3           | (-25–25)            |
|  | Influenza A(H3N2)        | 261          | 87           | 991             | 91                        | 32       | (-6–57)  | 33          | (-6–57)             |

AFHSB-AF, Armed Forces Health Surveillance Branch–Air Force Satellite Cell; NHRC, Naval Health Research Center; AFHSB, Armed Forces Health Surveillance Branch

<sup>a</sup>AFHSB-AF and NHRC used unmatched, influenza test–negative controls; AFHSB used healthy controls (matched to cases by sex, age, date [+/- 3 days] and location).

<sup>b</sup>AFHSB-AF adjusted for age group, month of illness and region (overall and influenza A[H3N2]). Influenza B analysis adjusted for month of illness only; NHRC adjusted for age group and surveillance population; AFHSB adjusted for 5-year prior vaccination status (Y/N).

<sup>c</sup>Cases and controls include all influenza A–positive cases, subtyped and not subtyped.

CI: 11%–75%), as estimated by AFHSB-AF. Adjusted VE estimates for active component service members were not statistically significant. The AFHSB analysis found that VE against all influenza A was 3% (95% CI: -25%–25%) and VE against influenza A(H3N2) was 33% (95% CI: -6%–57%).

## DISCUSSION

Mid-season influenza VE estimates indicated that vaccination reduced the odds of medically attended influenza infection by approximately 45% among DoD dependents and civilians. These results were consistent with other studies, which have also found moderate VE this season.<sup>2,3</sup> Additionally, the DoD's findings were similar to VE estimates from previous influenza A(H3N2)–predominant seasons without vaccine mismatch.<sup>4,5</sup>

VE estimates for active component service members are frequently lower than those for civilians.<sup>6,7</sup> There are many factors that could lead to decreased VE among military personnel, including their high influenza vaccination rates (approximately 90%), annual (repeat) vaccinations, and early-season vaccination.<sup>6</sup> Studying VE in a highly vaccinated population adversely affects the

statistical power of the analysis given the limited number of unexposed cases and controls. Additionally, repeated vaccination has been shown in some studies to reduce VE and potentially diminish antibody response to influenza.<sup>5,8–10</sup> Lastly, military personnel may experience waning immunity due to the fact that the U.S. military tends to start influenza vaccinations very early in the season.<sup>11–13</sup> Further research is necessary to determine how these factors might influence VE in the military population.

Limitations included a relatively small number of cases, which decreased the power of the studies and prevented VE estimation against influenza A(H1N1)pdm09 and, for two of the studies, influenza B. Additionally, these studies were limited in that only ILI cases severe enough to seek medical care were included, and the study populations tended to be younger than the general population. Therefore, it is difficult to comment on VE in less severe cases or among older populations.

*Author affiliations:* Defense Health Agency/ Armed Forces Health Surveillance Branch–U.S. Air Force School of Aerospace Medicine, Wright-Patterson AFB, OH (Ms. Toure, Lt Col Federinko); Armed Forces Health Surveillance Branch, Silver Spring, MD (Dr.

*Eick-Cost, CAPT Cooper, Ms. Hu); Naval Health Research Center, San Diego, CA (Dr. Myers, Mr. Hawksworth, Dr. Kammerer, Ms. Ricketts); Oak Ridge Institute for Science and Education, Oak Ridge, TN (Ms. Toure); and the Henry M. Jackson Foundation for the Advancement of Military Medicine Inc., Bethesda, MD (Mr. Hawksworth, Dr. Kammerer, Ms. Ricketts).*

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**Erratum:** Armed Forces Health Surveillance Branch. Update: Heat illness, active component, U.S. Armed Forces, 2016. *MSMR*. 2017;24(3):9–13. On p. 12, the footnote in Table 2 should read “One heat illness per person per year.” The footnote text was corrected in each online version of the *MSMR*'s annual heat illness updates for 2013–2017.

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