Brief Report

Department of Defense Midseason Vaccine Effectiveness Estimates for the 2017–2018 Influenza Season

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The 2017–2018 influenza season has been a topic of interest in the media and among the general public due to concerns about the protective nature of the 2017–2018 influenza vaccine. During the Southern Hemisphere's winter influenza season in mid-2017, Australia's overall influenza vaccine effectiveness (VE) was surprisingly low at 33% (95% CI, 17%–46%).[1] More specifically, Australia reported an influenza A(H3) VE of 10% (95% CI, -16%–31%), which was not statistically significantly different from zero.[1] These findings prompted concerns about the prospect of a similarly low VE during the subsequent influenza season in the Northern Hemisphere, as Australia and the U.S. selected identical vaccine strains. The Department of Defense (DoD) conducts VE analyses to determine the extent of matching between the recommended seasonal vaccine and the circulating strain. This article reports the results of DoD VE mid-season estimates determined by the Armed Forces Health Surveillance Branch (AFHSB) Air Force (AFHSB-AF) satellite at the U.S. Air Force School of Aerospace Medicine; Naval Health Research Center (NHRC); and the AFHSB.

METHODS

The AFHSB-AF satellite branch is a sentinel site-based program that requests weekly submissions of six to 10 specimens accompanied by a completed questionnaire from each site. Vaccination status was verified through immunization records obtained from the Air Force Complete Immunization Tracking Application, medical records from the Aeromedical Services Information Management System, or self-reported data from the questionnaire. Individuals were considered to be vaccinated if they were vaccinated at least 14 days prior to symptom onset. Those who were vaccinated less than 14 days prior to symptom onset were excluded from the study.

NHRC's population included civilians who sought care at outpatient clinics near the U.S.–Mexico border through the febrile respiratory illness program.Vaccination status was obtained through medical record reviews and self-report, if available.[2] NHRC classified cases and controls to have been vaccinated if symptom onset started 14–180 days after receiving the vaccine.[2]

AFHSB's VE study used data obtained via the Defense Medical Surveillance System and Navy and Marine Corps Public Health Center. The high vaccination rate is attributable to the fact that annual influenza vaccination is required for service members.[2]

All three VE estimates were derived using a test-negative case-control study design although each organization utilized different study populations (i.e., AFHSB-AF satellite, DoD dependent data; NHRC, civilians near the U.S.–Mexico border; AFHSB, active component service member data). All studies calculated crude and adjusted VE using odds ratios (ORs) and 95% CIs obtained from multivariable logistic regression models **(Table)**. Statistical data analyses were performed using SAS version 9.4 (2013, SAS Institute, Cary, NC). VE was calculated as (1−OR) × 100. AFHSB-AF's adjustment variables were age group, time period, and geographic region. NHRC's only adjustment variable was age group. AFHSB's adjustment variables were age group, sex, month of illness, and 5-year vaccination status. For summary purposes, vaccine effects were considered statistically significant if 95% CIs around point estimates of VE did not include zero.

Inactivated influenza vaccine was the only vaccine type analyzed, because the live, attenuated influenza vaccine was not recommended or used during the 2017–2018 season. Cases were laboratory-confirmed influenza positives and controls were influenza test negatives. Influenza positives from the AFHSB-AF satellite and NHRC were confirmed through reverse transcription polymerase chain reaction (RT-PCR) and/or viral culture, while AFHSB used RT-PCR and/or viral culture as well as positive rapid tests, excluding individuals with rapid test negatives.

RESULTS

From 1 October 2017 through 10 February 2018, the AFHSB-AF's VE study included 1,160 cases and 1,383 controls, with 36% and 47% having been vaccinated, respectively. Overall, the adjusted VE was 51% (95% CI, 41%–59%). The adjusted VE for influenza A(H3N2) was low at 37% (95% CI, 22%–49%) **(Figure)**. Influenza A(H1N1) pdm09 and influenza B had higher adjusted VE estimates of 79% (95% CI, 67%–86%) and 60% (95% CI, 49%–70%), respectively **(Figure)**. Adjusted VE estimates were similar among children (aged 2–17 years) and adults **(data not shown)**.

From 13 November 2017 through 8 January 2018, the NHRC's VE study included 201 cases and 114 controls, with 13% and 24% having been vaccinated, respectively. For the NHRC's study, the overall adjusted VE was 55% (95% CI,

TABLE. Department of Defense midseason influenza vaccine effectiveness (VE) estimates, 2017–2018

Population		Cases		Controls[a]					
	Influenza type	No. of cases	% vaccinated	No. of controls	% vaccinated	Crude VE (%)	95% CI	Adjusted VE (%)[b]	95% CI
Dependents (AFHSB-AF)									
	Overall	1,160	16	1,383	25	36	25–45	51	41–59
	Influenza A(H3N2)	610	12	1,383	32	21	5–35	37	22–49
	Influenza A(H1N1)	153	2	1,383	42	71	56–81	79	67–86
	Influenza B	390	8	1,383	36	39	23–52	60	49–70
Border civilians (NHRC)									
	Overall	201	13	114	24	52	13–74	55	17–75
	Influenza A(H3N2)	156	13	114	24	50	6–73	52	9–75
	Influenza B	41	12	114	24	55	-25–84	63	-5–87
Active component service members (AFHSB)									
	Overall	2,926	89	2,557	90	9	-8–24	19	3–33
	Influenza A	2,539	89	2,557	90	9	-9–24	19	2–33
	Influenza A(H3N2)	301	89	2,557	90	15	-25–42	27	-9–50
	Influenza B	383	89	2,557	90	12	-25–37	25	-8–48

CI, confidence interval; AFHSB-AF, Armed Forces Health Surveillance Branch-Air Force satellite cell; NHRC, Naval Health Research Center; AFHSB, Armed Forces Health Surveillance Branch

[a]All studies used unmatched, influenza test-negative controls.

[b]AFHSB-AF adjusted for age group, month of illness, and region; NHRC adjusted for age group; and AFHSB adjusted for sex, age group, month of illness, and 5-year prior vaccination status (Y/N).

17%–75%). For influenza A(H3N2), VE was 52% (95% CI, 9%–75%). For influenza B, VE was 63% but not statistically significant (95% CI, -5%–87%) **(Figure)**.

From 1 December 2017 through 10 February 2018, the AFHSB's study included 2,926 cases and 2,557 controls, with 89% and 90% having been vaccinated, respectively. After adjustment, VE for active component service members was statistically significant at 19% (95% CI, 3%–33%). For influenza A(H3N2) and influenza B, the adjusted VE estimates were 27% (95% CI, -9%–50%) and 25% (95% CI, -8%–48%), respectively **(Figure)**; neither adjusted VE estimate was statistically significant.

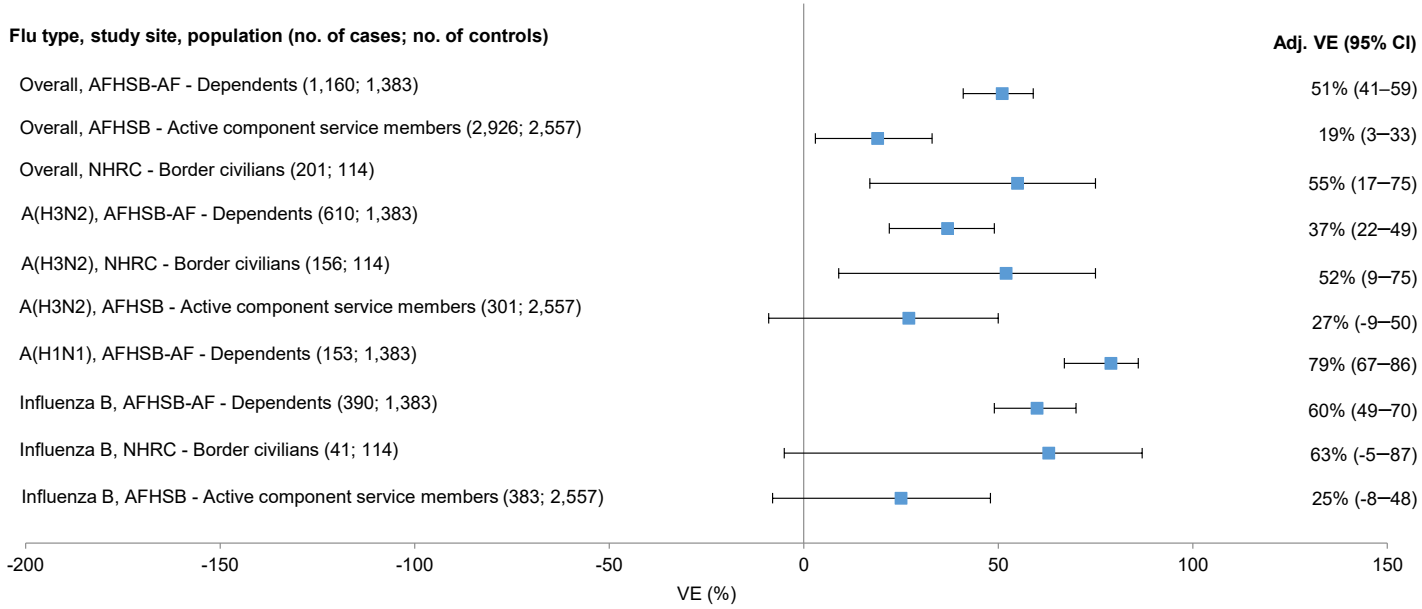
EDITORIAL COMMENT

Overall, adjusted VE estimates for DoD studies were moderately protective for the dependent population. The AFHSB-AF satellite's overall adjusted VE was statistically significant and conferred moderate to high protection; NHRC's adjusted VE was statistically significant overall and was moderately protective for influenza A(H3N2); and AFHSB's active component adjusted VE was statistically significant overall and provided some protection.

All of the VE studies had limitations. For example, specimens were obtained from those seeking care at a medical treatment facility or meeting the influenza-like illness case definition; therefore, less severe cases that did not seek medical attention were not included in the analyses. Individuals included in the DoD studies were younger than the general population, so VE could not be analyzed for older, higher-risk populations. Active component members are a highly immunized population, which may have a negative impact on VE estimates due to methodologic validity (i.e., limited unvaccinated controls) and biologic effects (i.e., repeated vaccination). Lower sample size could have contributed to the reduction of statistical power in some DoD analyses.

The Centers for Disease Control and Prevention (CDC) reported lower VE at 36% (95% CI, 27%–44%), compared with all DoD studies with a dependent population. The CDC's adjusted VE for influenza A(H3N2) was low at 25% (95% CI, 13%–36%), 67% (95% CI, 54%–76%) for influenza A(H1N1)pdm09, and 42% (95% CI, 25%–56%) for influenza B.[3] Midseason results for the CDC did not closely match DoD midseason VE estimates. This difference in VE estimates may be due, at least in part, to differences in the types of influenza vaccine used in DoD and in civilian populations. More than half of the influenza vaccine purchased and administered by the DoD was derived from cell culture propagation rather than from egg propagation.[3] A rapid decline of VE for the vaccine component influenza A(H3N2) that was egg-propagated has been seen in the past few years.[4] Zost et al. reported that the current circulating influenza A(H3N2) viruses possess a new glycosylation site in antigenic site B of the hemagglutinin, and that the current egg-adapted A(H3N2) component of the vaccine does not have this mutation, which is hypothesized to

FIGURE. Department of Defense midseason influenza vaccine effectiveness (VE), 2017–2018



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

diminish antigenicity.[5] Additional research is needed to assess whether VE against circulating A(H3N2) viruses varies by vaccine propagation type.

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