

Influenza vaccine effectiveness wanes over the influenza season: Results from five military treatment facilities

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Background

Influenza vaccination can reduce influenza burden, but questions have arisen about the duration of vaccine protection. Vaccine effectiveness can vary depending on the match between circulating and vaccine strains, as well as the time since vaccination. While the timing of vaccination varies for military personnel, annual influenza vaccination is mandated; therefore, this is a highly vaccinated population in which one can consider duration of protection associated with influenza vaccine. This is a secondary analysis that utilizes data from the ARI Consortium Natural History Study (ARIC NHS), a longitudinal, observational study conducted at five sites (San Diego, CA (NMCS), Bethesda, MD (WRNMMC), San Antonio, TX (BAMC), Portsmouth, VA (NMCP), and Tacoma, WA (MAMC)) that occurred from 2009 to 2018.

Methods

Primary objective: Determine if influenza vaccine effectiveness decreases over time

Secondary objective: Determine whether repeated influenza vaccination (4+ influenza vaccinations in past 5 years) is associated with increased risk of influenza

Participants: DoD healthcare beneficiaries

- Otherwise healthy active duty (AD), dependents, retirees seeking healthcare for an influenza-like illness (ILI) (temperature $\geq 100.4^{\circ}$ F and sore throat or one of the following: cough, sputum production, shortness of breath, or chest pain)

Sample collection: NP swabs were collected at enrollment, and on days 3, 7, and 28; swabs were tested for a variety of different pathogens (e.g., influenza, rhinovirus, seasonal coronaviruses, adenovirus, RSV, parainfluenza, etc.) and are considered positive if any of the samples had a positive test result.

Data collection: Demographics, symptom information, history of influenza vaccination, and other data related to the illness were recorded

Retained participants for this study: Have complete demographics, influenza vaccination in previous two years, and influenza, rhinovirus, and coronavirus test results for current ILI

Outcome identification:

- Nasal swab for viral PCR to determine if influenza, rhinovirus, and/or coronavirus is present

Model:

- Multivariate logistic regression
- Odds of influenza/rhinovirus/seasonal coronavirus identification according to:
 - Time since vaccination (90-day periods)
 - Age, race, month of diagnosis, influenza season
 - Vaccinated 4+ times in past 5 years

Results

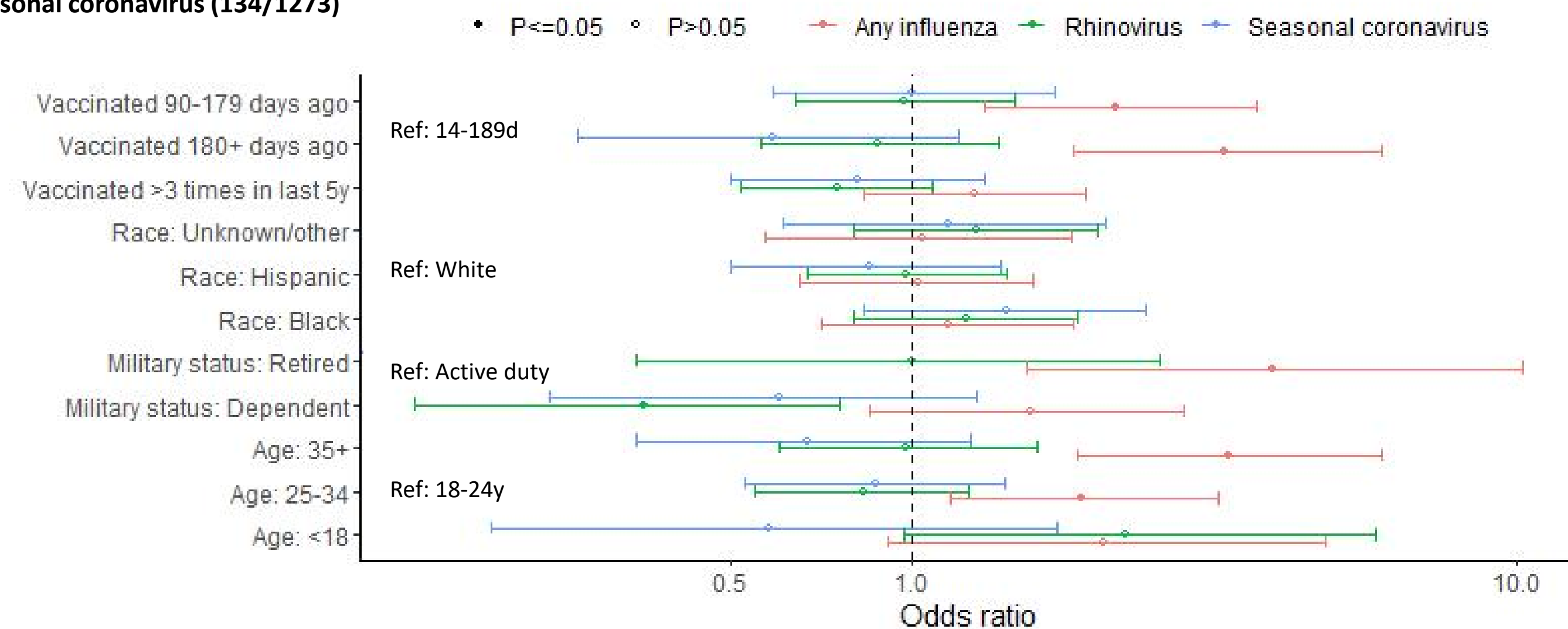
Table 1. Characteristics of individuals included in the analysis of waning influenza vaccine effectiveness in the ARIC study (p-values calculated from chi-square test)

	Influenza A (N=160)	Influenza B (N=32)	No influenza (N=1081)	p value
Age group				< 0.01
<18	17 (10.6%)	14 (43.8%)	155 (14.3%)	
18-24	29 (18.1%)	5 (15.6%)	437 (40.4%)	
25-34	65 (40.6%)	2 (6.2%)	319 (29.5%)	
35+	49 (30.6%)	11 (34.4%)	170 (15.7%)	
Race				0.3
Black	33 (20.6%)	3 (9.4%)	152 (14.1%)	
Hispanic	32 (20.0%)	10 (31.2%)	230 (21.3%)	
Unknown/Other	16 (10.0%)	4 (12.5%)	120 (11.1%)	
White	79 (49.4%)	15 (46.9%)	579 (53.6%)	
Military status				< 0.01
Active duty	111 (69.4%)	10 (31.2%)	845 (78.2%)	
Dependent	41 (25.6%)	16 (50.0%)	220 (20.4%)	
Retired	8 (5.0%)	6 (18.8%)	16 (1.5%)	
Days since influenza vaccination				< 0.01
<90	19 (11.9%)	8 (25.0%)	286 (26.5%)	
90-179	96 (60.0%)	12 (37.5%)	506 (46.8%)	
180+	45 (28.1%)	12 (37.5%)	289 (26.7%)	
# of last 5 years vaccinated				0.01
1	23 (14.4%)	7 (21.9%)	282 (26.1%)	
2	15 (9.4%)	4 (12.5%)	132 (12.2%)	
3	13 (8.1%)	5 (15.6%)	111 (10.3%)	
4	21 (13.1%)	2 (6.2%)	82 (7.6%)	
5	88 (55.0%)	14 (43.8%)	474 (43.8%)	

Table 2. Multivariate logistic regression results from model using influenza diagnosis as the outcome variable. Also included in the model are season and month of diagnosis (results not shown).

	Any influenza	Influenza A	Influenza B
Vaccinated <90 days ago	Ref	Ref	Ref
Vaccinated 90-179 days ago	2.2 (1.3, 3.7)	2.4 (1.4, 4.4)	1.1 (0.4, 3.4)
Vaccinated 180+ days ago	3.3 (1.9, 6.0)	4.1 (2.1, 8.2)	1.2 (0.4, 3.5)
Active duty	Ref	Ref	Ref
Dependent	1.6 (0.8, 2.8)	1.5 (0.8, 2.7)	1.3 (0.2, 5.7)
Retired	4.0 (1.6, 10.2)	1.5 (0.5, 4.0)	12.2 (2.8, 56.3)
Age <18	2.1 (0.9, 4.8)	1.3 (0.5, 3.3)	4.9 (0.9, 46.0)
Age 18-24	Ref	Ref	Ref
Age 25-34	1.9 (1.2, 3.2)	2.3 (1.4, 4.0)	0.3 (0.0, 1.6)
Age 35+	3.3 (1.9, 6.0)	3.5 (1.9, 6.5)	1.9 (0.5, 8.3)
Vaccinated 4+ times in last 5y	1.3 (0.8, 1.9)	1.3 (0.8, 2.0)	1.2 (0.5, 3.1)
Race: White	Ref	Ref	Ref
Race: Black	1.1 (0.7, 1.9)	1.3 (0.8, 2.1)	0.5 (0.1, 1.7)
Race: Hispanic	1.0 (0.7, 1.6)	0.9 (0.6, 1.5)	1.6 (0.6, 4.0)
Race: Unknown/other	1.0 (0.6, 1.8)	1.0 (0.5, 1.8)	1.3 (0.3, 4.0)

Figure 1. Multivariate logistic regression results for models with outcomes of a) Any influenza (192/1273), b) Rhinovirus (265/1273), and c) Seasonal coronavirus (134/1273)



Conclusions

Influenza vaccination was most protective against influenza 14-89 days post-vaccination and effectiveness decreased thereafter; when the analysis was done with rhinovirus and seasonal coronavirus as the outcomes, no effect of time since vaccination was observed, increasing confidence that the effects seen in the study on influenza infection are not associated with changing seasons. Given that influenza season often lasts ~3 months, these results indicate that influenza vaccination may not be effective throughout the season and early influenza vaccination is not recommended. One explanation for this finding may be waning immunity; however, the results may be associated with a poorer match between vaccine and circulating strains due to influenza virus evolution. Repeated influenza vaccination was not significantly associated with influenza identification. The waning effectiveness of influenza vaccination indicates additional consideration be given to the timing of vaccination.

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