Pragmatic Assessment of Influenza Vaccine Effectiveness in the DoD (PAIVED): Updates from Year 3 of Multi-Site Trial

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Background

The SARS-CoV-2 pandemic has spotlighted respiratory infections and the value of effective vaccines. The dramatic success of new SARS-CoV-2 vaccines is in contrast to the suboptimal efficacy of existing influenza vaccines, particularly among military populations. The Pragmatic Assessment of Influenza Vaccine Effectiveness in the DoD (PAIVED) study compares 3 FDA-licensed influenza vaccine types (egg-based, cell-based, and recombinant) to assess differences in immunogenicity and effectiveness in adults.

Methods

Primary objective: Compare the relative effectiveness of 3 types of licensed influenza vaccines over 3 influenza seasons (2018/19, 2019/20, 2020/21)

- Vaccine effectiveness: prevention of laboratory-confirmed influenza

Participants: DoD healthcare beneficiaries aged 18+

- Active duty (AD), dependents, and retirees were randomized to receive 1 of 3 licensed influenza vaccine formulations (egg-based, recombinant, or cell-culture derived)

Locations: San Diego, CA (NMCSD/MCRD), Annapolis, MD (USNA), Bethesda, MD (WRNMMC, USU), Fort Bragg, NC (WAMC), Fort Hood, TX (DAMC), San Antonio, TX (BAMC, LAFB), Portsmouth, VA (NMCP), and Tacoma, WA (MAMC).

Surveillance: Participants completed weekly surveys throughout the influenza season (excluding recruits, who reported directly to clinic when ill). When an ILI was identified, participants participated in two visits (virtual or in person) four weeks apart, during which participants reported symptom severity and duration, and provided a nasal swab and blood sample.

Influenza-like illness (ILI) definition: Cough or sore throat, **and** feverish or having chills, **or** body aches or fatigue (updated, previously required all 3 symptoms)

Outcomes: In participants reporting ILI:

- Nasal swab for viral PCR to determine if influenza is the cause of illness, and
- ILI symptom/severity

Results

Table 1. PAIVED summary

	2018/19	2019/20	2020/21
# military bases	5	9	10
# participants enrolled	1,623	5,879	3,269
# in sub-study	200	379	319
# with at least 1 ILI	298	1,656	314
Total ILIs	316	2,017	356
Mean duration (days)	11.4	12.3	9.6
Mean days of limited activity	2.5	2.9	3.0
Mean days of missed work	0.6	0.7	1.6

Figure 1. PAIVED summary flow chart

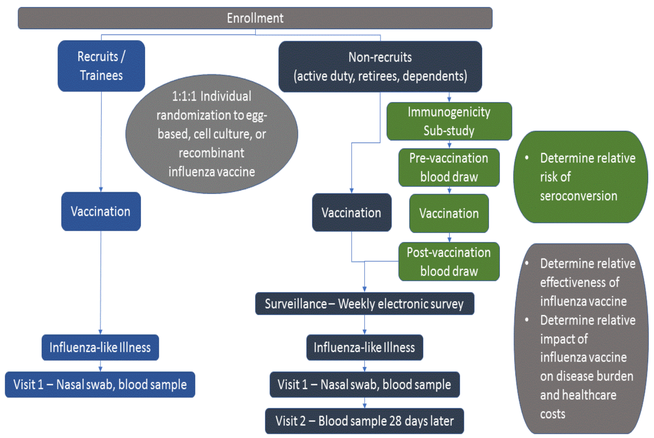
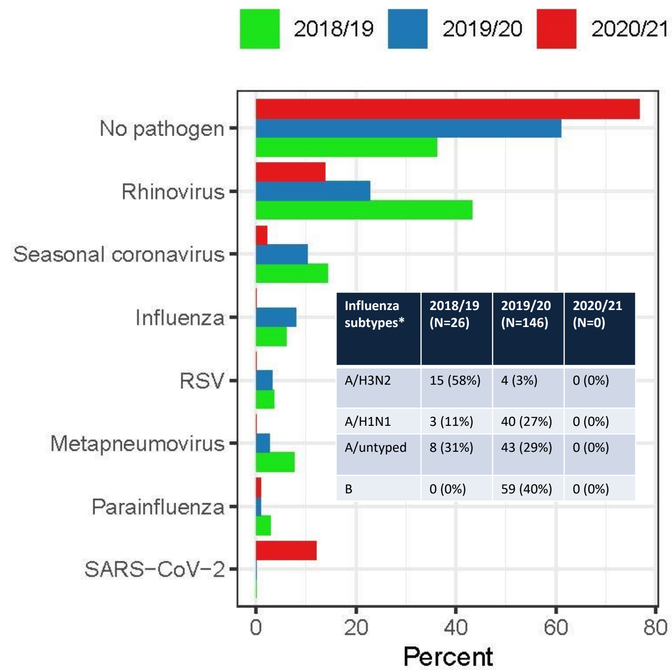


Figure 2. Pathogens identified in ILI samples



Influenza subtypes*	2018/19 (N=26)	2019/20 (N=146)	2020/21 (N=0)
A/H3N2	15 (58%)	4 (3%)	0 (0%)
A/H1N1	3 (11%)	40 (27%)	0 (0%)
A/untyped	8 (31%)	43 (29%)	0 (0%)
B	0 (0%)	59 (40%)	0 (0%)

*Influenza subtype numbers include ILI samples and diagnoses from the Military Health record for 2018/19 and 2019/20; Military Health record data are not yet available for 2020/21.

Table 2. PAIVED demographics

	Total enrolled (N=10,771)
Age	
Mean (SD)	33.9 (14.8)
Range	17.9 – 91.6
Male	7493 (69.6%)
Race	
Asian	696 (6.5%)
Black	1180 (11.0%)
Hispanic	2168 (20.1%)
Multiple races	409 (3.8%)
Unknown/Other	143 (1.3%)
White	6175 (57.3%)
Military status	
Active duty	8151 (75.7%)
Dependent	1260 (11.7%)
Missing	17 (0.2%)
Retired military	1343 (12.5%)

Conclusions

There have been relatively low rates of ILI identified in this study during this season (2020/21), with only 10% of the participants reporting an ILI, consistent with low rates of non-COVID-19 ILI reported elsewhere. Planned analyses include calculating comparative influenza vaccine effectiveness to inform future vaccine purchasing decisions, as well as comparing serological response to the different vaccines. PAIVED will continue during the 2021/22 season.

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The investigators have adhered to the policies for protection of human subjects as prescribed in 45CFR46.

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