Emergence of the SARS-CoV-2 Omicron Variant in the Pragmatic Assessment of Influenza Vaccine Effectiveness in the Department of Defense (PAIVED) Study

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Background

Novel SARS-CoV-2 (SCV2) variants may differ in epidemiology and clinical impact. Omicron is considered to cause less severe illness than prior variants; however, the severity of symptoms for all variants is also related to vaccination status, history of prior infections, age, and other health conditions.

PAIVED is a randomized trial comparing the effectiveness of 3 different platforms of inactivated influenza vaccines (egg-based, cell-based, and recombinant) in adult military health system beneficiaries. PAIVED actively surveils participants for influenza-like illness (ILI), including COVID-19, and conducts targeted investigations among those who develop ILI.

The most recent season (2021/22) offered an opportunity to assess symptomatology associated with emerging SCV2 variants in this prospective cohort.

Methods

Primary objective

- Compare demographics and severity between those ILIs in which Delta and Omicron variants of SCV2 were identified

Participants

- DoD healthcare beneficiaries aged 18+
  - Active duty (AD), dependents, and retirees

Locations

San Diego, CA (NMCSD/MCRD); Annapolis, MD (USNA); Bethesda, MD (WRNMMC, USU); Fort Bragg, NC (WAMC); San Antonio, TX (BAMC, WHASC); Portsmouth, VA (NMCP); Tacoma, WA (MAMC)

Study Procedures

- Randomized (1:1:1) to receive 1 of 3 licensed influenza vaccine formulations (egg-based, recombinant, or cell-culture derived)
- Weekly surveys throughout the influenza season querying the development of **influenza like illness (ILI),** defined as:
  - Cough or sore throat, **and**
  - Feverish or having chills, **or**
  - Body aches or fatigue
- When ILI identified, participants completed:
  - Daily symptom diary (Flu-Pro) x 7 days
  - 2 visits (virtual or in person), 4 weeks apart
    - Nasal swab for viral PCR (acute)
      - SCV2 genome sequencing, as applicable
    - Blood sample (acute & convalescent)

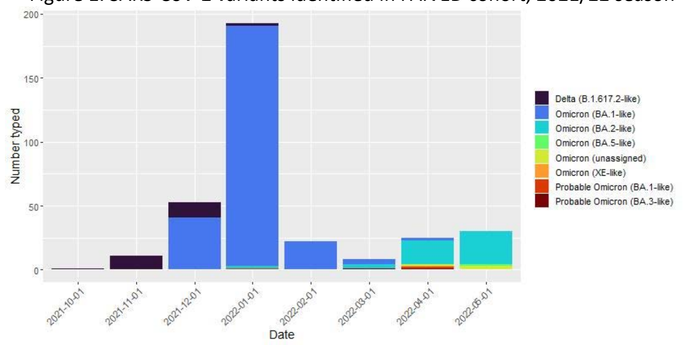
Results

Table 1. PAIVED SARS-CoV-2 summary, 2021/22 season

	Delta (N=21)	Omicron (N=306)	Total (N=327)[1]	p value
Male: N (%)	14 (66.7%)	169 (55.2%)	183 (56.0%)	0.31
> high school education	16 (76.2%)	251 (82.0%)	267 (81.7%)	0.50
Race/ethnicity				< 0.01
Asian	0 (0.0%)	23 (7.5%)	23 (7.0%)	
Black	7 (33.3%)	26 (8.5%)	33 (10.1%)	
Hispanic	3 (14.3%)	56 (18.3%)	59 (18.0%)	
Multiple races	2 (9.5%)	13 (4.2%)	15 (4.6%)	
Unknown/Other	0 (0.0%)	5 (1.6%)	5 (1.5%)	
White	9 (42.9%)	183 (59.8%)	192 (58.7%)	
Military status				0.96
Active duty	17 (81.0%)	251 (82.0%)	268 (82.0%)	
Dependent	2 (9.5%)	31 (10.1%)	33 (10.1%)	
Retired military	2 (9.5%)	24 (7.8%)	26 (8.0%)	
Worst symptom severity				0.36
None	0 (0.0%)	22 (7.2%)	22 (6.7%)	
Mild	8 (38.1%)	116 (37.9%)	124 (37.9%)	
Moderate	12 (57.1%)	123 (40.2%)	135 (41.3%)	
Severe	1 (4.8%)	37 (12.1%)	38 (11.6%)	
Very severe	0 (0.0%)	8 (2.6%)	8 (2.4%)	
Age: Mean (SD)	39.3 (10.6)	37.0 (9.6)	37.2 (9.6)	0.32
Duration of illness	11.8 (7.0)	10.3 (5.5)	10.4 (5.6)	0.32
Days off work	3.5 (3.9)	3.9 (3.6)	3.9 (3.7)	0.49
Days with limited activities	5.7 (4.2)	5.4 (4.1)	5.4 (4.1)	0.87
Days with fever	3.2 (3.1)	2.4 (2.1)	2.5 (2.2)	0.45
Days on fever reducer	3.6 (3.4)	3.3 (3.0)	3.3 (3.1)	0.73
Number of FLU-PRO surveys returned	5.6 (1.9)	5.4 (1.7)	5.4 (1.7)	0.24
Days since symptom onset	6.4 (4.4)	6.4 (2.9)	6.4 (3.0)	0.52
Maximum nose score	2.0 (1.0)	1.9 (0.9)	1.9 (0.9)	0.55
Maximum throat score	1.4 (0.9)	1.5 (1.1)	1.5 (1.1)	0.92
Maximum eyes score	0.9 (0.9)	0.7 (0.8)	0.7 (0.8)	0.08
Maximum systemic score	1.7 (0.9)	1.4 (0.9)	1.4 (0.9)	0.14
Maximum respiratory score	1.3 (0.6)	1.3 (0.7)	1.3 (0.7)	0.91
Maximum Gastrointestinal score	0.6 (0.5)	0.5 (0.6)	0.5 (0.6)	0.16
Maximum senses score	1.3 (1.5)	0.8 (1.2)	0.8 (1.2)	0.11
Maximum total score (including senses)	1.3 (0.5)	1.1 (0.6)	1.1 (0.6)	0.13

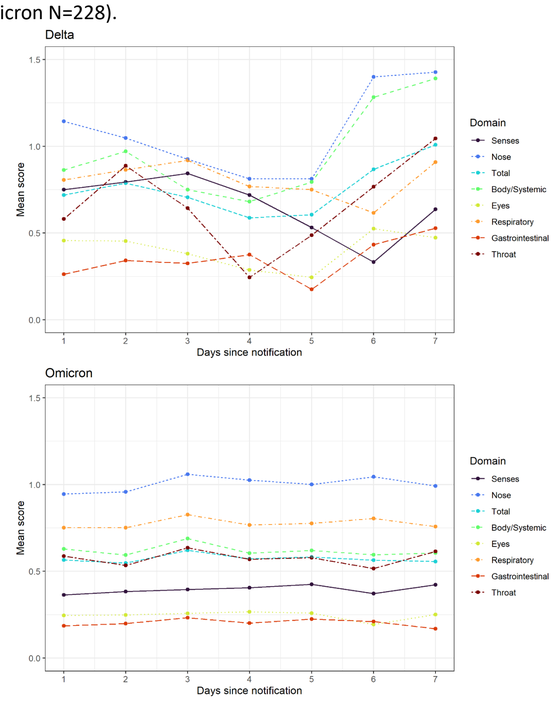
[1] One participant is included twice in this table who was infected in separate ILIs with Delta and Omicron variants in November 2021 and January 2022, respectively. Ten participants did not fill out any FLU-PRO Plus surveys and were not included in this table.

Figure 1. SARS-CoV-2 variants identified in PAIVED cohort, 2021/22 season



All 24 Delta identifications were B.1.617.2-like; Omicron infections were: BA.1-like (257), BA.2-like (48), BA.3-like (2), BA.5-like (1), XE-like (1) and unassigned (4).

Figure 2. Mean FLU-PRO Plus domain scores, by variant (Delta and Omicron) and days since ILI notification. Participants who responded to at least 5 days of FLU-PRO surveys included in this plot (Delta N=17, Omicron N=228).



Results (continued)

- During the 2021/22 season, 336 participants (7.2% of active cohort; 26.0% of those who reported ILI) tested positive for SCV2
  - 24 Delta (B.1.617.2-like)
  - 313 Omicron variants: 257 BA.1-like, 48 BA.2-like, 2 BA.3-like, 1 BA.5-like, 1 XE-like, and 4 unassigned (Figure 1)
- One participant tested positive for Delta in November 2021 and for Omicron (BA.1) in January 2022
- Among the 326 participants with sequenced SCV2 and symptom data assessed using the FLU-PRO Plus survey, 56% were male, 59% were white, and 82% were active-duty military (Table 1)
- Peak symptom severity was classified as mild to moderate in 79.2% of cases, fever duration averaged 2.5±2.2 days, and there were activity limitations for a mean of 5.4±4.1 days
- No differences in maximum symptom scores (total or by domain) were detected for participants infected with Omicron compared to Delta
- Among the domains, nose scores were highest throughout in both Delta and Omicron variant infections, whereas the senses domain scores appeared higher early in Delta infections than in Omicron infections (Figure 2)

Conclusions

Omicron emerged as the predominant SCV2 variant causing ILI in our cohort this season, typically manifesting with mild to moderate symptoms. Further exploration of potential differences in ILI experience between SCV2 variants and other ILI causes (including co-infections), plus the impact of vaccination, will add insight into the relative contribution of such factors on SCV2 symptomatology.

Acknowledgments

Disclaimer
Views expressed are those of the author(s) and do not reflect the official policy/position of USUHS, DoD, Department of the Army, Navy, or Air Force, or the DHA, Henry M. Jackson Foundation for the Advancement of Military Medicine, Inc. (HJF), BAMC, MAMC, WRNMMC, US Army Medical Dept, US Army Office of the SG, or the USG. Investigators followed human subjects protection 45CFR46 policies.

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