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# Department of Defense Influenza Surveillance and Mid-Season Vaccine Effectiveness

Anthony C. Fries, PhD\*

\*Representing DoD CONUS/OCONUS lab-based influenza surveillance activities

March 13, 2025

# Disclaimer

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# Briefing Outline

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- Purpose: To provide an update to on DoD influenza surveillance activities for 2024–2025
  - Program Descriptions
  - Vaccine Effectiveness in DoD Populations
    - ✓ DoD Beneficiaries
    - ✓ DoD Active Component Service members
  - DoD Phylogenetic Analyses
  - DoD Antigenic Characterization



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# Influenza Surveillance in the DoD: Overview

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- Global Influenza Surveillance
  - Approximately 400 locations in over 30 countries
    - ✓ Military, local government/academic
  - Extensive characterization capabilities within the DoD
    - ✓ Culture, PCR, sequencing, serology
  - Rapid sharing of results with CDC and/or regional WHO reference centers
- Comprehensive Epidemiology and Analysis Capabilities
  - Over 12 million Active Component records (health care utilization, immunizations, deployment, reportable diseases, etc.)
    - ✓ Produce *Medical Surveillance Monthly Report (MSMR)*, ad-hoc requests, studies/analyses
    - ✓ Weekly influenza reports
    - ✓ Vaccine safety and effectiveness studies



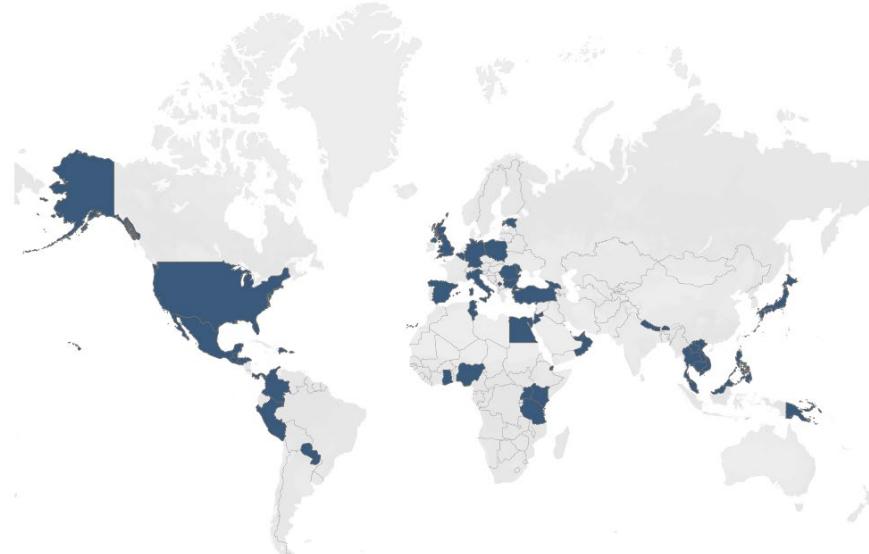
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# Influenza Surveillance in the DoD: GEIS

- The Global Emerging Infectious Surveillance (GEIS) partner laboratories form a wide-reaching network across the globe.
- Influenza surveillance activities in the DoD complement other existing global efforts:
  - Surveil some locations where data do not otherwise exist (e.g., Djibouti, Tanzania)
  - Surveil service members and their beneficiaries, U.S. civilians, and foreign national populations
  - The DoD service member population is highly vaccinated and widely distributed across the globe.

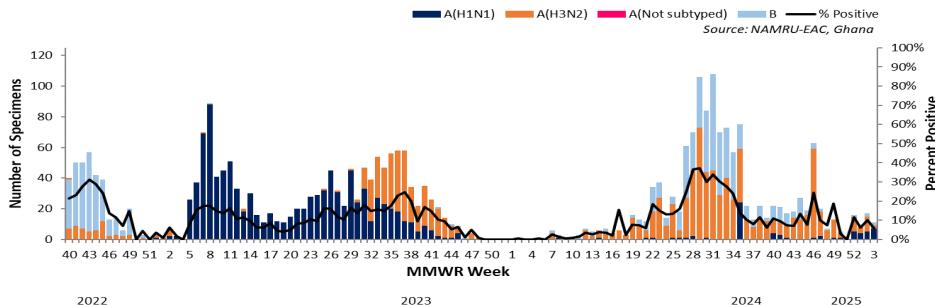
GEIS-Funded Laboratory Influenza Surveillance Footprint



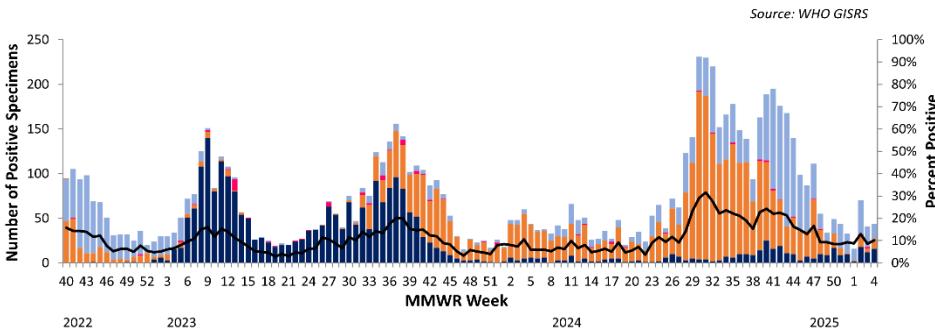
# Influenza Surveillance: Subtype Circulation – West Africa

- Data collected from the GEIS surveillance network typically mirrors what is seen in WHO FluNet and in some cases may be the primary source of data.

## DoD Surveillance

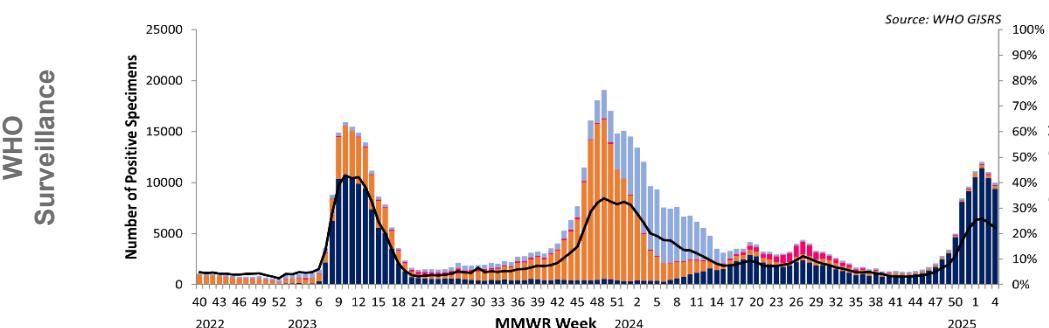
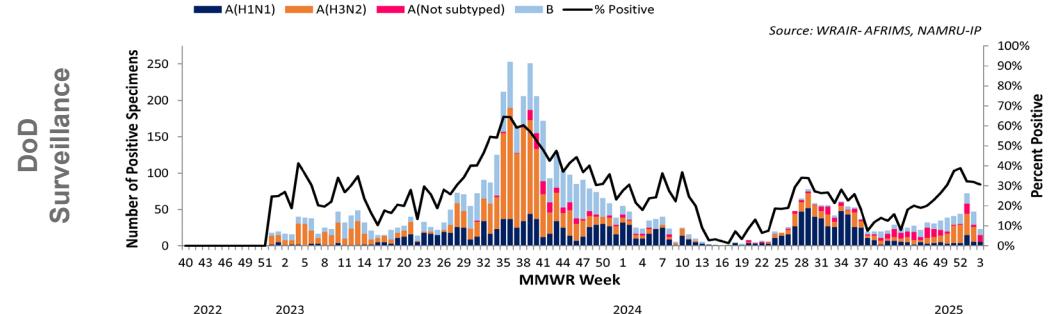


## WHO Surveillance



# Influenza Surveillance: Subtype Circulation – Asia

- Differences highlight the importance of using this surveillance stream to identify key samples for sequencing and advanced characterization.



# DoD Influenza Mid-Season Vaccine Effectiveness (VE) (1)

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## Case-Control Study of DoD TRICARE Beneficiaries



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# Beneficiary VE: Study Design and Case Definition

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- Adjusted Estimates of Vaccine Effectiveness
  - Population: DoD TRICARE beneficiaries, excluding service members
  - VE against medically-attended (outpatient), influenza-like illness (ILI), laboratory-confirmed influenza cases
  - Time period: November 24, 2024–March 1, 2025 (Weeks 48–09)
- Influenza-like illness case definition:
  - Fever ( $\geq 100.4^{\circ}\text{F}$ ) and cough, or
  - Fever ( $\geq 100.4^{\circ}\text{F}$ ) and two or more additional symptoms (fatigue, body aches, sore throat, headache, sinus congestion, shortness of breath, chills, runny nose, loss of taste or smell, nausea/vomiting/diarrhea, acute respiratory distress), or
  - Physician-diagnosed ILI



# Beneficiary VE: Analyses

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- Adjusted Estimates of Vaccine Effectiveness
  - Adjusted for age, month of illness, and region
- Analyses by:
  - Influenza (overall) all dependents
  - Influenza (overall) children (6 months-17 years)
  - Influenza (overall) adults (18–64 years)
  - Influenza A (overall) all dependents
  - Influenza A (overall) children (6 months-17 years)
  - Influenza A (overall) adults (18-64 years)
  - Influenza A (H1N1)pdm09 all dependents
  - Influenza A (H1N1)pdm09 children (6 months-17 years)
  - Influenza A(H3N2) all dependents
  - Influenza A(H3N2) children (2–17 years)
  - Influenza A(H3N2) adults (18-64 years)



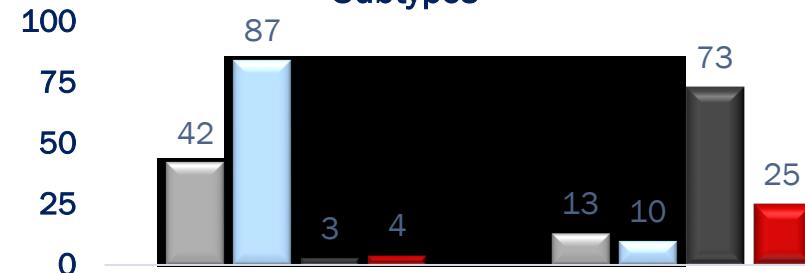
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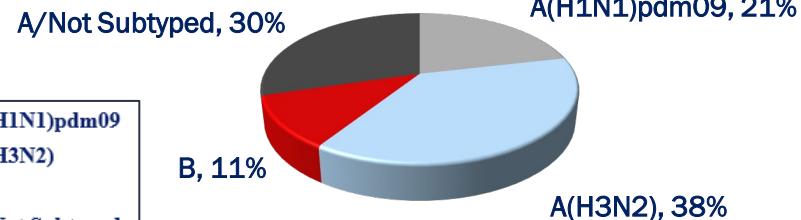
# Breakdown of Data for VE analyses

- Laboratories contributing to analyses:
  - USAFSAM: n=687 (65%)
  - Landstuhl Regional Medical Center (LRMC): n=362 (35%)
  - Incirlik AB: n=1 (<1%)
- Cases: n=257 (25%)
  - 174 (68%) vaccinated
  - 83 (32%) unvaccinated
- Controls: n=793 (75%)
  - 533 (67%) vaccinated
  - 260 (33%) unvaccinated

## Location Breakdown of Influenza USA Subtypes



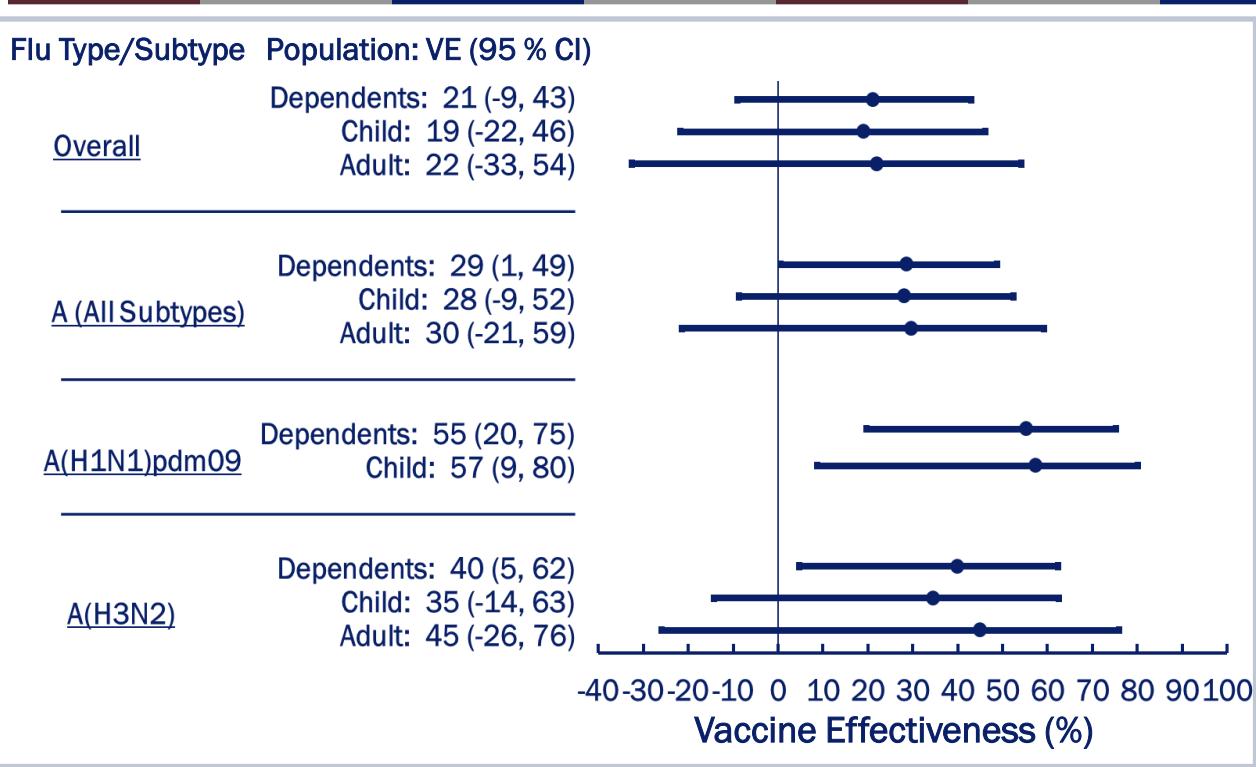
## Frequency of Influenza Subtypes



- A(H1N1)pdm09
- A(H3N2)
- B
- A/Not Subtyped



# Beneficiary VE: 2024-2025 Mid-Season Influenza Estimates (2 of 2)



- VE ranged from 19% to 57% against medically-attended ILI in children, adults, and dependents.
- Overall, VE was not significant and produced lower estimates in all populations.
- Influenza A (all subtypes), VE was slightly higher but not significant.
- A(H1N1)pdm09, VE was moderately protective and significant among all dependents (55%) and children (57%).
- A(H3N2), VE was higher among adults (45%) than in children (35%), but not significant. The dependents population was protective and significant at 40%.



# DoD Influenza Mid-Season Vaccine Effectiveness (2)

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Case Test-Negative Control Design: Ambulatory Care  
U.S. Active Component Service Members



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# U.S. Service Members VE: Study Design (Ambulatory)

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- Case test-negative control design (ambulatory subjects only)
- Population: Active component service members
- Army, Navy, Air Force, Marine Corps, Coast Guard, and Space Force
- Time Period: December 1, 2024 – February 18, 2025
- Lab-confirmed flu cases: positive by rapid, RT-PCR, or culture assays
- Test-negative Controls: negative by RT-PCR or culture assays (subjects with negative rapid excluded)
- Models adjusted for sex, age category, prior vaccination (yes or no in previous 5 years), and month of diagnosis



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# U.S. Service Members VE: Vaccination & Cases (Ambulatory)

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- Vaccination
  - Vaccination types included inactivated (73%), cell-based (7%), and other (19%)
  - 97% of subjects had prior flu vaccine in previous 5 years
- Cases
  - Influenza A (any subtype) = 5,167
  - Influenza A(H3N2) = 438
  - Influenza A(H1N1)pdm09 = 192
  - Influenza B = 331



# U.S. Service Members VE: Interim Estimates (Ambulatory)

Influenza Type	Vaccination Status	Cases No. (%)	Controls No. (%)	Crude VE (95% CI)	Adjusted VE (95% CI)*
A	Vaccinated	4,337 (84)	11,881 (83)	-6 (-16, 3)	14 (6, 22)
	Unvaccinated	830 (16)	2,411 (17)		
A(H1N1)pdm09	Vaccinated	152 (79)	11,881 (83)	23 (-1, 46)	39 (12, 57)
	Unvaccinated	40 (21)	2,411 (17)		
A(H3N2)	Vaccinated	336 (77)	11,881 (83)	33 (16, 47)	46 (31, 57)
	Unvaccinated	102 (23)	2,411 (17)		
B	Vaccinated	261 (79)	11,881 (83)	24 (1, 52)	32 (9, 49)
	Unvaccinated	70 (21)	2,411 (17)		

\*Adjusted for sex, age category, 5-year prior vaccination (Y/N), and month of diagnosis



# DoD Sequencing & Phylogenetic Analyses – Outline

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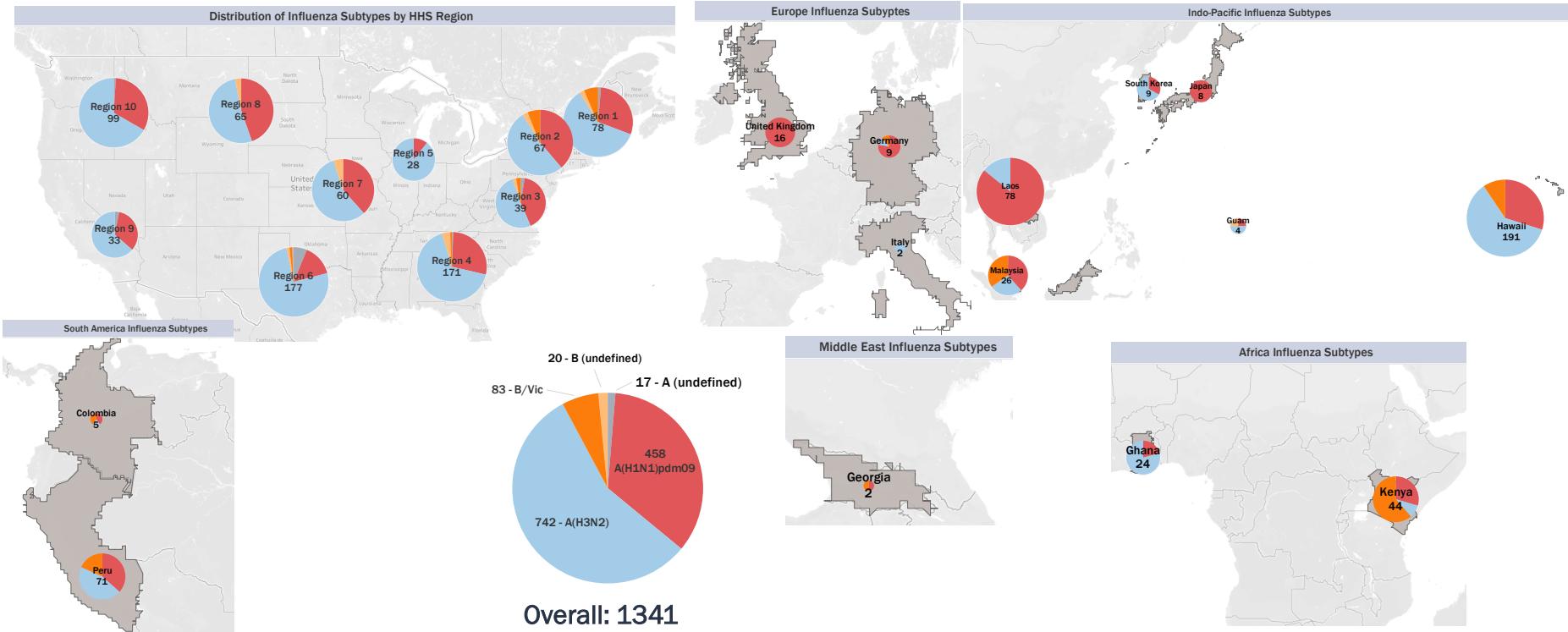
- Geographical distribution of all influenza viruses characterized for the DoD
- Influenza A(H1N1)pdm09 clade proportions and phylogeny
- Influenza A(H3N2) subclade proportions and phylogeny
- Influenza B subclade proportions and phylogeny
- Summary



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# Geographical Distribution of 2024–2025 DoD Influenza Sequence Data



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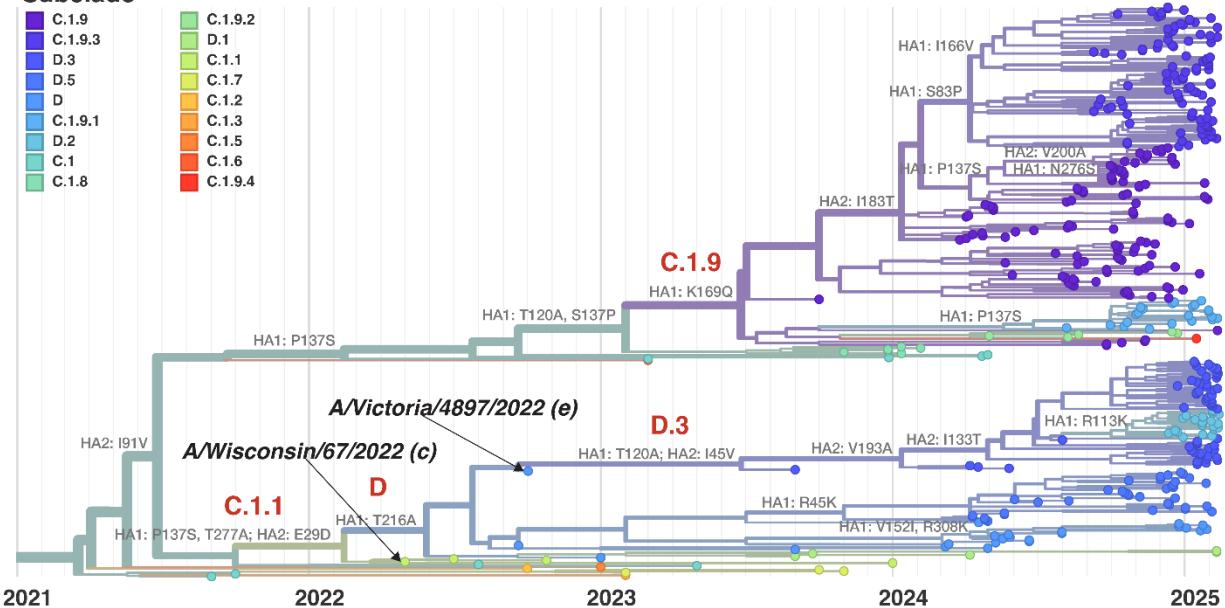


# DoD Phylogenetic Analyses – A(H1N1)pdm09 HA

## Subclade

- C.1.9
- C.1.9.3
- D.3
- D.5
- D
- C.1.9.1
- D.2
- C.1
- C.1.6
- C.1.8
- C.1.9.4

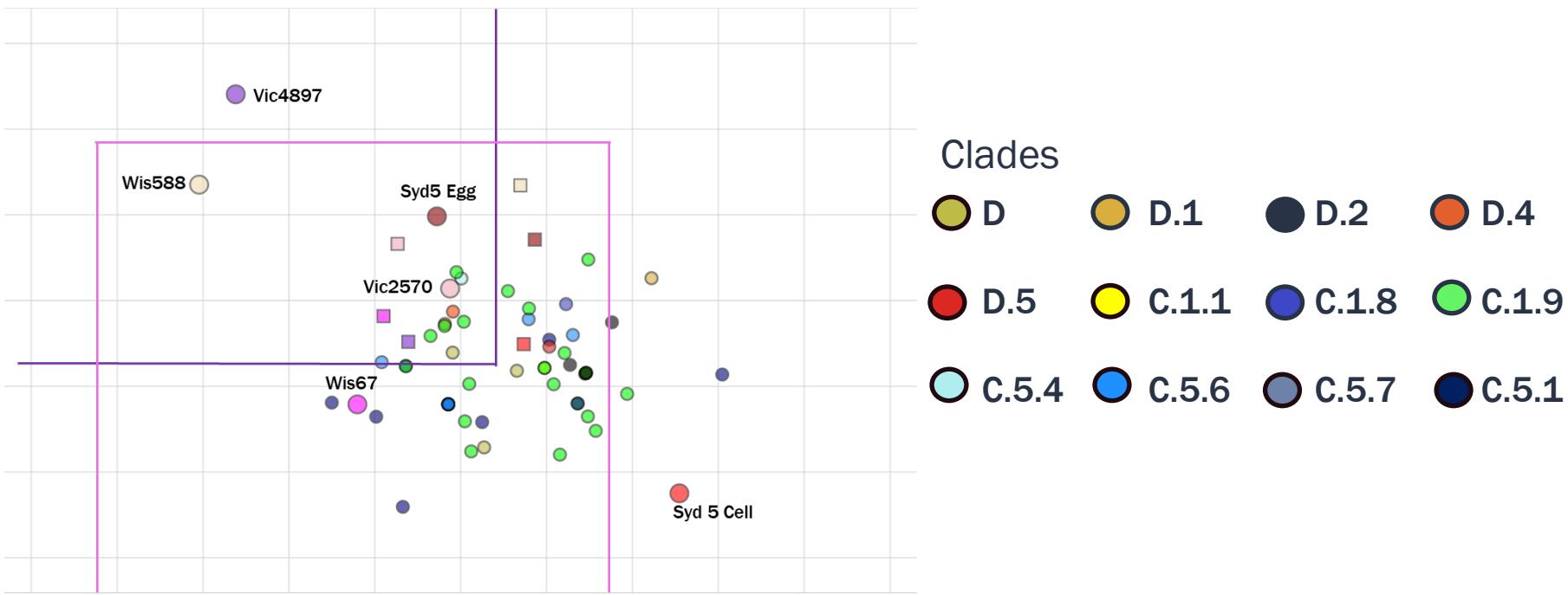
- C.1.9.2
- D.1
- C.1.1
- C.1.7
- C.1.2
- C.1.3
- C.1.5
- C.1.6
- C.1.8
- C.1.9.4



Clade/Subclade	No.	%
5a.2a	269	63.7%
C.1	4	1.5%
C.1.8	5	1.9%
C.1.9	124	46.1%
C.1.9.1	23	8.6%
C.1.9.2	4	1.5%
C.1.9.3	108	40.1%
C.1.9.4	1	0.4%
5a.2a.1	153	36.3%
D	17	11.1%
D.1	3	2.0%
D.2	2	1.3%
D.3	91	59.5%
D.5	40	26.1%

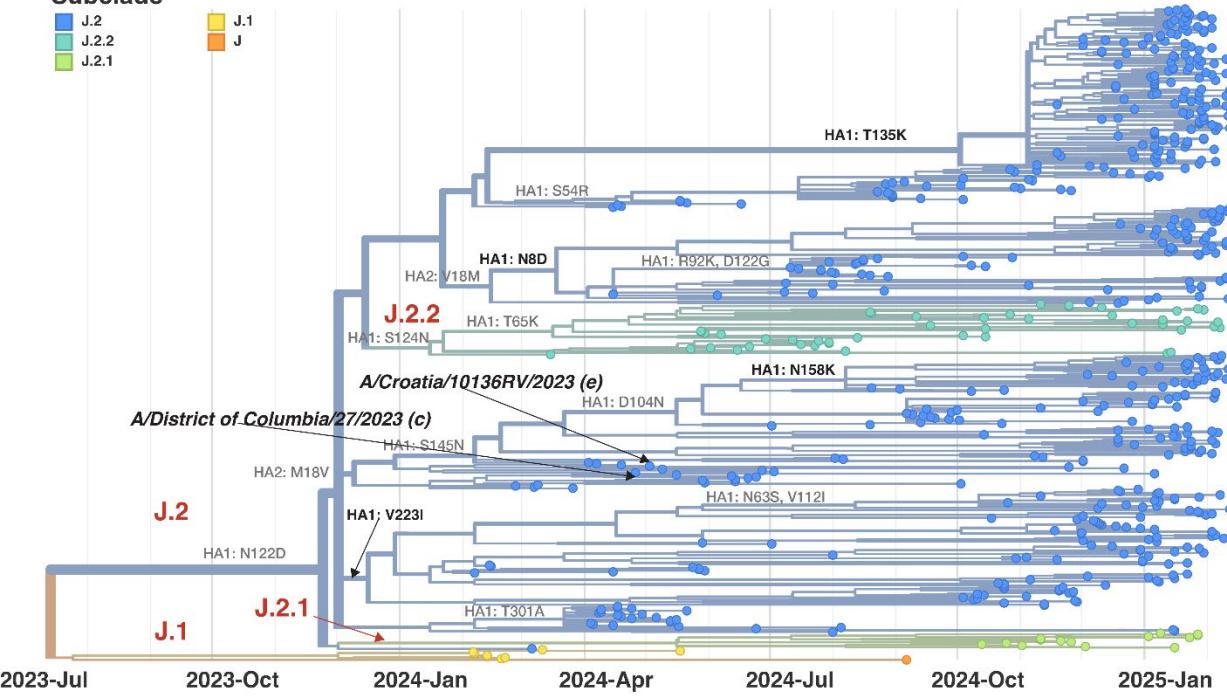


# DoD Antigenic Cartography: Influenza A/H1N1 isolates



# DoD Phylogenetic Analyses – A(H3N2) HA

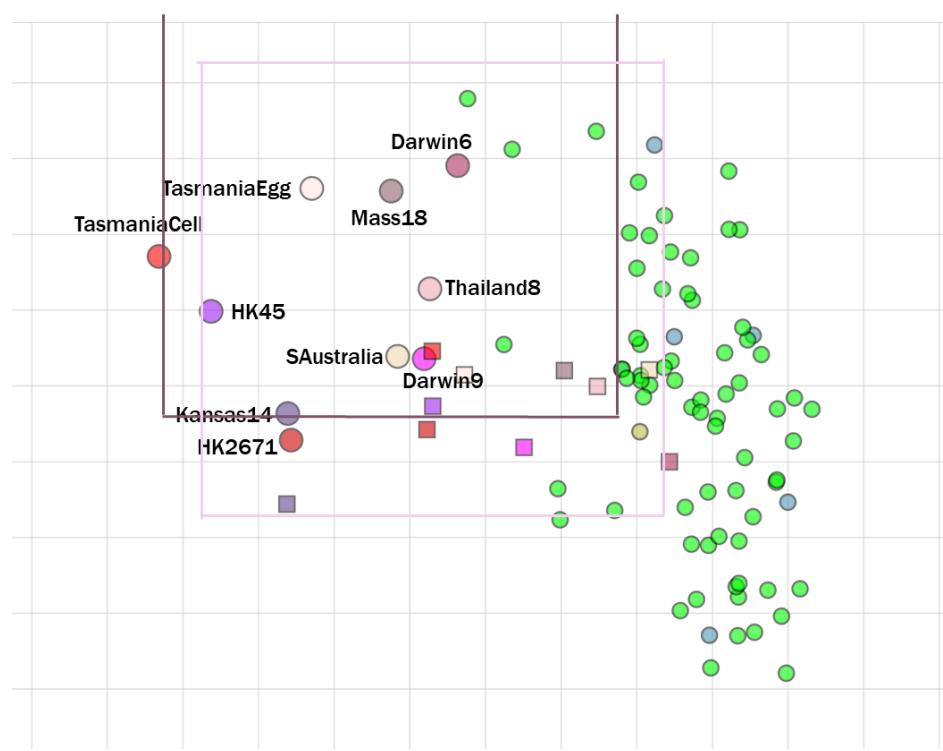
## Subclade



Clade/Subclade	No.	%
2a.3a	1	0.1%
G.1.3.1	1	100%
2a.3a.1	667	99.9%
J.1	9	1.3%
J.2	591	88.6%
J.2.1	14	2.1%
J.2.2	53	7.9%



# DoD Antigenic Cartography: Influenza A/H3N2 Isolates



Clades

● J.2   ● J.2.1   ● J.1



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# DoD Influenza Sequencing Summary

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- 422 Influenza A(H1N1)pdm09 sequences were characterized, of which 63.7% were HA clade 5a.2a. The dominant HA subclade was C.1.9, and the dominant NA clade was C.5.3.1.
- 668 Influenza A(H3N2) sequences were characterized, of which 99.9% were HA clade 2a.3a.1. The dominant HA subclade was J.2, and the dominant NA clade was B.4.2.
- 86 Influenza B/Victoria sequences were characterized, all of which were HA clade V1A.3a.2. The dominant HA subclade was C.5.1, and the dominant NA clade was B.7.
- Sequence data were contributed by DCPH-D, AFRIMS, NAMRU-EAC (Ghana), NAMRU-IP, NAMRU-S, NHRC, TAMC, WRAIR Africa, and WRAIR Europe-Middle East.
- Our data agree with the WHO Northern Hemisphere influenza vaccine strain selections.



# Questions?

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Department

CDR Shayne Gallaway, PhD

Respiratory Focus Area Lead, AFHSD-Global Emerging Infections  
Surveillance Branch



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# Back-up Slides

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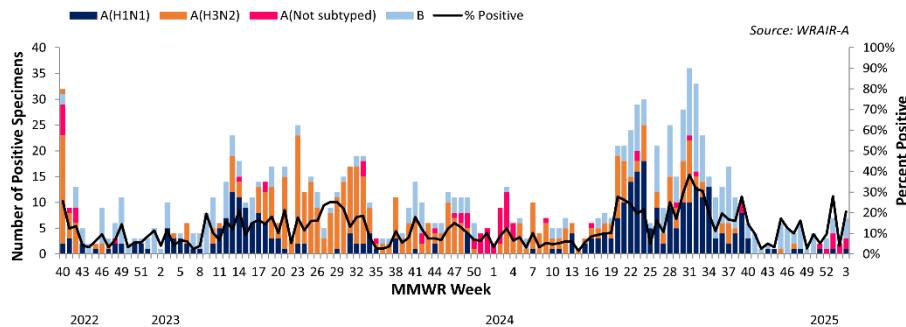
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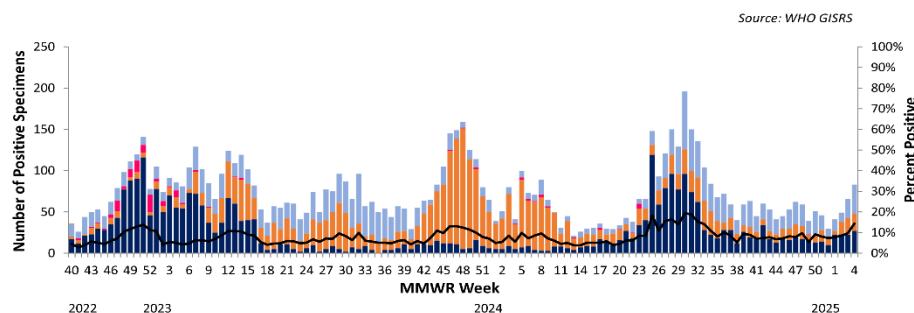
# Influenza Surveillance: Subtype Circulation - East Africa

- Data collected from the GEIS surveillance network typically mirror what is seen in WHO FluNet and, in some cases, may be the primary source of data.
- Differences highlight the importance of using this surveillance stream to identify key samples for sequencing and advanced characterization.

## DoD Surveillance



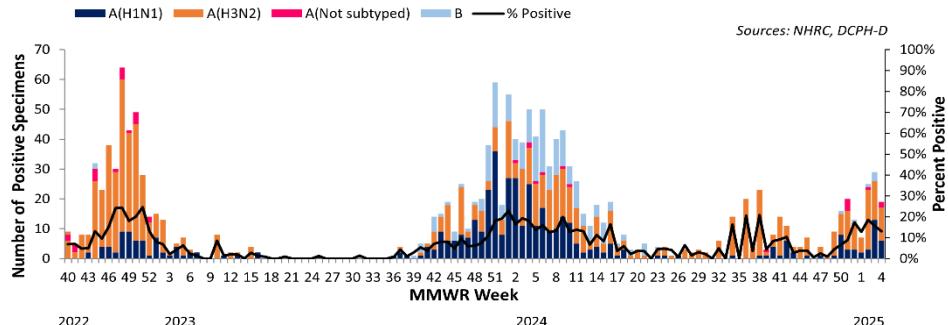
## WHO Surveillance



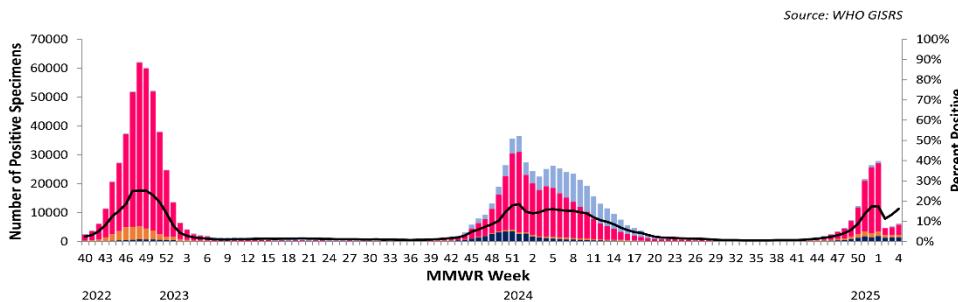
# Influenza Surveillance: Subtype Circulation - North America

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## DoD Surveillance



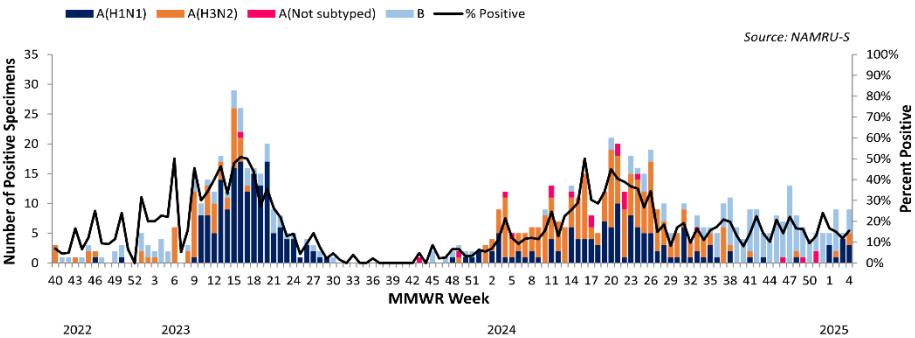
## WHO Surveillance



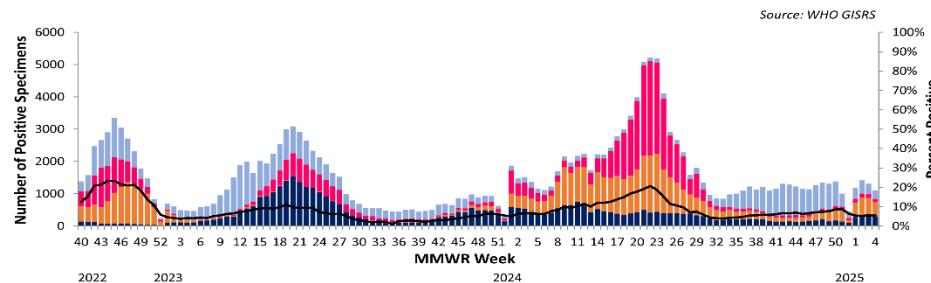
# Influenza Surveillance: Subtype Circulation - South America

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## DoD Surveillance



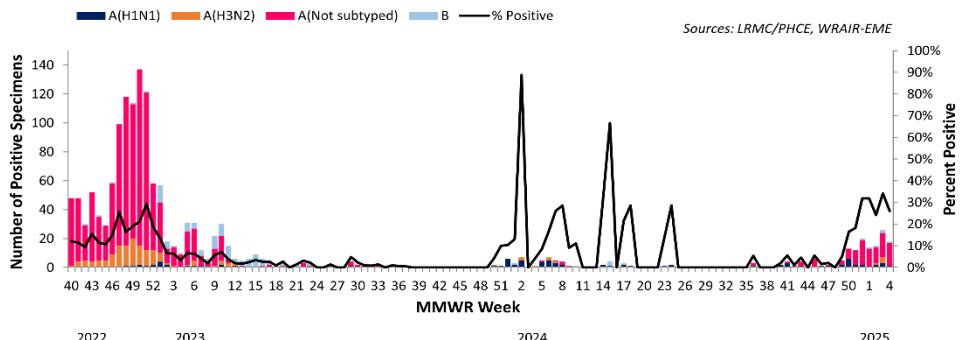
## WHO Surveillance



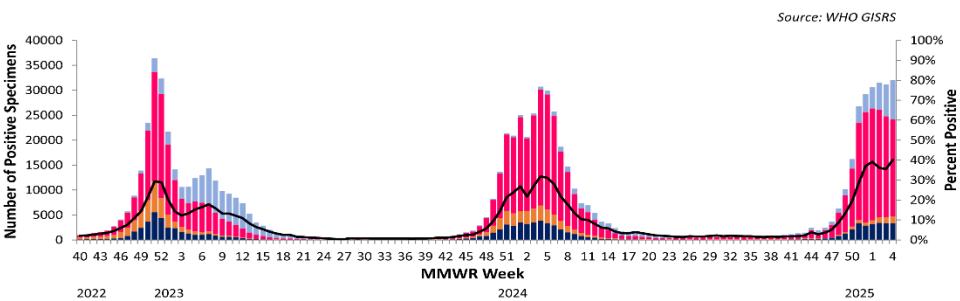
# Influenza Surveillance: Subtype Circulation - Europe

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## DoD Surveillance



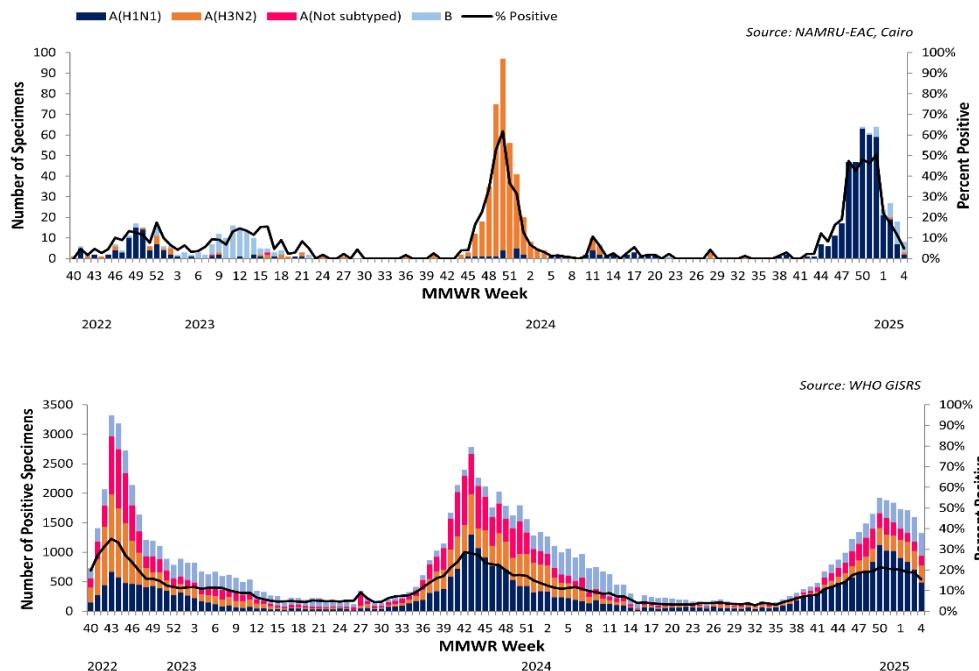
## WHO Surveillance



# Influenza Surveillance: Subtype Circulation - Middle East

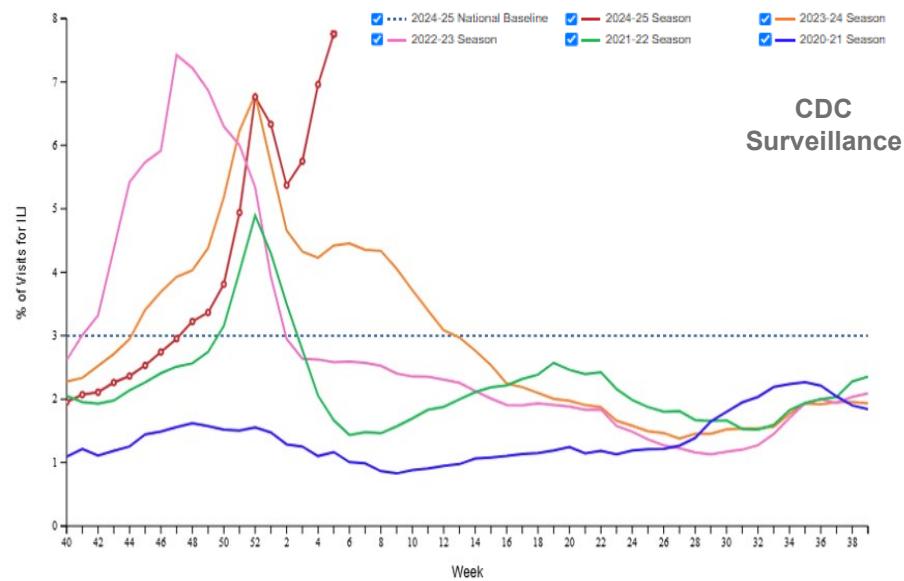
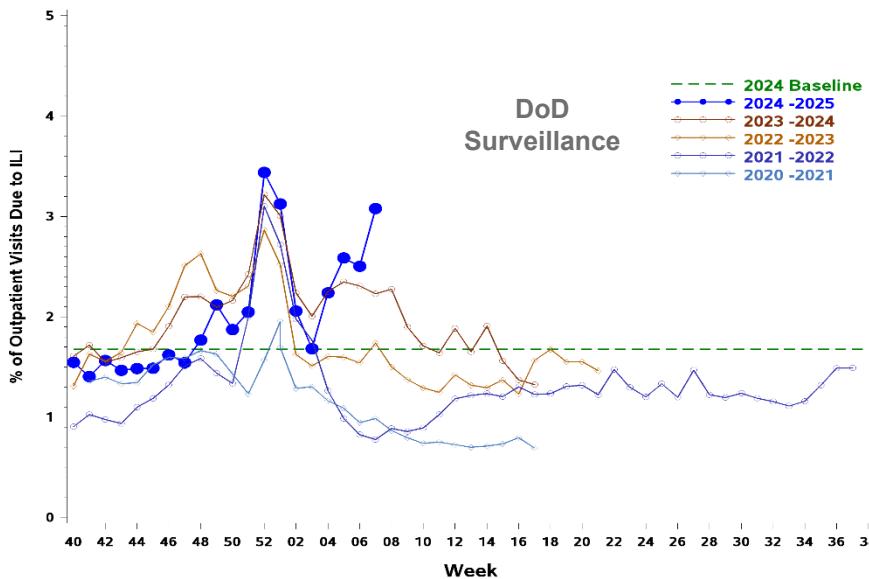
- Data collected from the GEIS surveillance network typically mirror what is seen in WHO FluNet and, in some cases, may be the primary source of data.
- Differences highlight the importance of using this surveillance stream to identify key samples for sequencing and advanced characterization.

DoD  
WHO Surveillance



# Influenza Surveillance in the DoD: MHS vs. CDC

- Even more broadly, the data collected across the Military Health System (MHS) typically mirror trends observed by the CDC.



# DoD Biosurveillance Wastewater Surveillance (WWS) Program

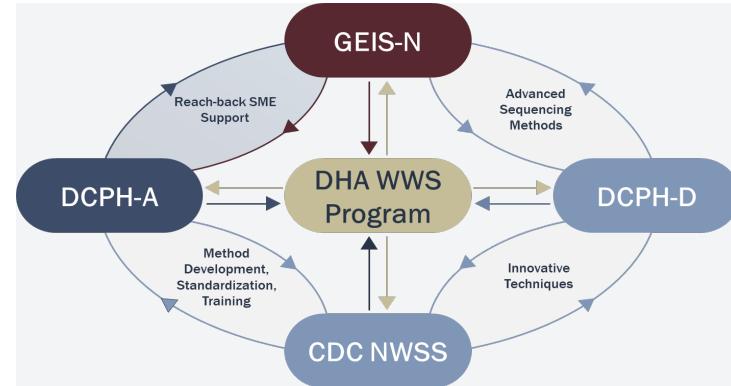


Aim: Establish a centralized, flexible, and scalable WWS framework for global pathogen detection, data integration, and response across DoD components.



- A non-invasive, cost-effective tool for early warning and monitoring pathogens (e.g., influenza) at the population level
- Enables DoD federated incorporation of data
- Advances bio-threat detection and enhanced situational awareness through the integration of environmental, epidemiological, and laboratory data

*The DoD WWS Program's Collaborative Network*



## Dual Surveillance Strategy

- **Steady-State Surveillance:** Implement validated WWS protocols across DoD components for routine data collection and analysis, enabling rapid pathogen detection and response.
- **Adaptive Innovation:** Develop and validate novel WWS methods to address evolving biological threats.

# Beneficiary VE: Case/Control Characteristics (1 of 2)

Characteristic		Cases	Controls	p-Value
		n= 257 No. (%)	n= 793 No. (%)	
Sex	Male	115 (44.75)	320 (40.35)	0.2139
	Female	142 (55.25)	473 (59.65)	
Age	2-5	75 (29.18)	297 (37.45)	0.0094
	6-9	51 (19.84)	97 (12.23)	
	10-17	53 (20.62)	129 (16.26)	
	18-24	7 (2.72)	33 (4.16)	
	25-44	45 (17.50)	151 (19.04)	
	45-64	26 (10.11)	86 (10.84)	
Beneficiary Category	Child (2-17)	179 (69.65)	523 (65.95)	0.2738
	Adult (18-64)	78 (30.35)	270 (34.05)	
Month of Illness	November	1 (0.39)	38 (4.79)	<0.0001
	December	41 (15.95)	294 (37.07)	
	January	98 (38.13)	236 (29.76)	
	February	114 (44.36)	224 (28.25)	
	March	3 (1.17)	1 (0.13)	



# Beneficiary VE: Case/Control Characteristics (2 of 2)

Characteristic		Cases	Controls	p-Value
		n= 257 No. (%)	n= 793 No. (%)	
Geographic Region	Eastern U.S.	67 (26.07)	191 (24.09)	0.8006
	Western U.S.	69 (26.85)	223 (28.12)	
	Other	121 (47.08)	379 (47.79)	
Vaccination Status	Vaccinated	174 (67.70)	533 (67.21)	0.8840
	Unvaccinated	83 (32.30)	260 (32.79)	
Influenza Status	Influenza	55 (21.40)	0 (0)	<0.0001
	Influenza A(H3N2)	97 (37.74)	0 (0)	
	Influenza A/not	76 (29.57)	0 (0)	
	Influenza B	29 (11.28)	0 (0)	
	Not Influenza	0 (0)	793 (100)	

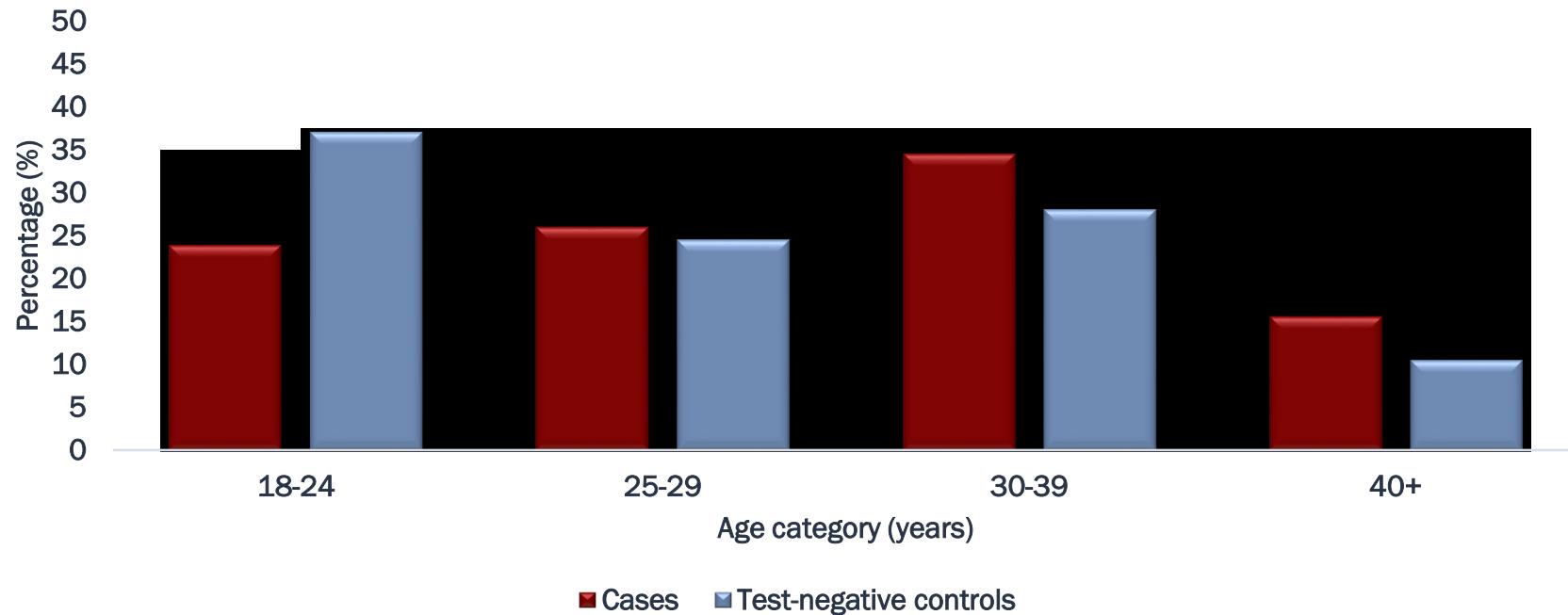


# Beneficiary VE: 2024-2025 Mid-Season Influenza Estimates (1 of 2)

Type	Population	Vaccine Status	Cases (%)	Controls (%)	Crude VE (95% CI)	Adjusted VE (95% CI)
Overall	Dependents	Yes	174 (17)	533 (51)	-2 (-38, 24)	21 (-9, 43)
		No	83 (8)	260 (25)		
Overall	Children	Yes	126 (18)	357 (51)	-11 (-60, 24)	19 (-22, 46)
		No	53 (8)	166 (24)		
Overall	Adults	Yes	48 (14)	176 (51)	15 (-44, 49)	22 (-33, 54)
		No	30 (9)	94 (27)		
A	Dependents	Yes	147 (14)	533 (52)	11 (-21, 35)	29 (1, 49)
		No	81 (8)	260 (25)		
A	Children	Yes	106 (16)	357 (52)	5 (-39, 35)	28 (-9, 52)
		No	52 (8)	166 (24)		
A	Adults	Yes	41 (12)	176 (52)	24 (-29, 56)	30 (-21, 59)
		No	29 (9)	94 (28)		
A(H1N1)pdm09	Dependents	Yes	25 (3)	533 (63)	59 (29, 77)	55 (20, 75)
		No	30 (4)	260 (31)		
A(H1N1)pdm09	Children	Yes	16 (3)	357 (64)	59 (17, 79)	57 (9, 80)
		No	18 (3)			
A(H3N2)	Dependents	Yes	48 (5)	533 (60)	52 (27, 69)	40 (5, 62)
		No	49 (6)	260 (29)		
A(H3N2)	Children	Yes	36 (6)	357 (60)	49 (16, 69)	35 (-14, 63)
		No	33 (6)	166 (28)		
A(H3N2)	Adults	Yes	12 (4)	176 (59)	60 (12, 82)	42 (-26, 76)
		No	16 (5)	94 (32)		



# U.S. Service Members VE: Age Breakdown (Ambulatory)



# DoD Influenza Mid-Season Vaccine Effectiveness (3)

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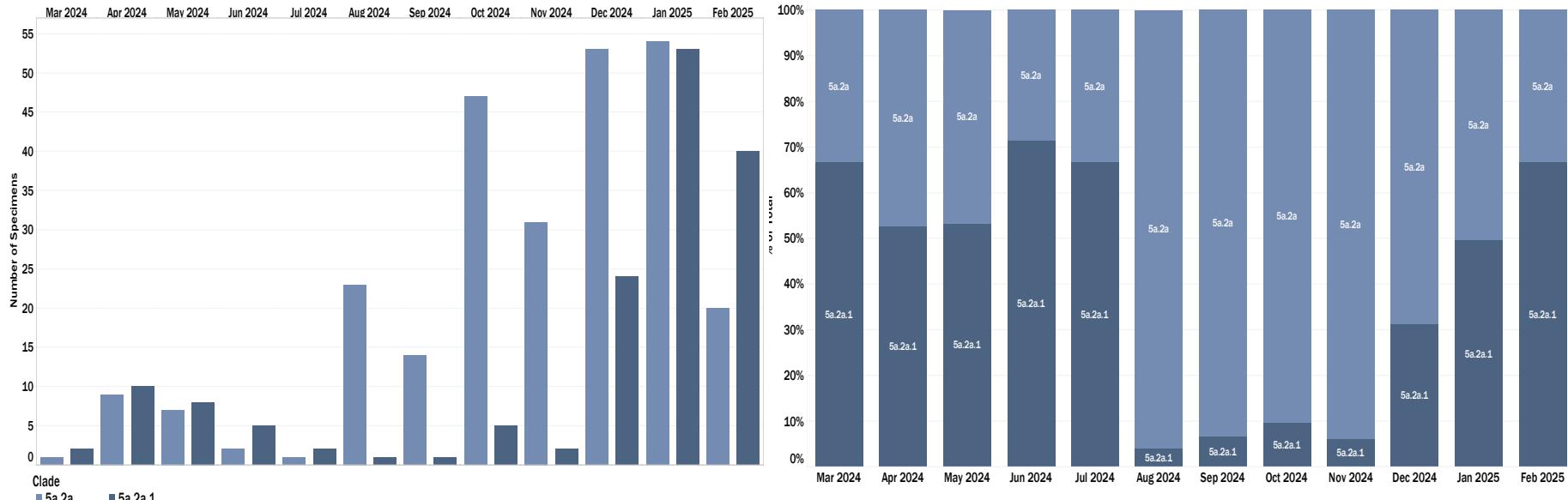
Cohort Study Design – Hospitalizations U.S. Active Component Service Members



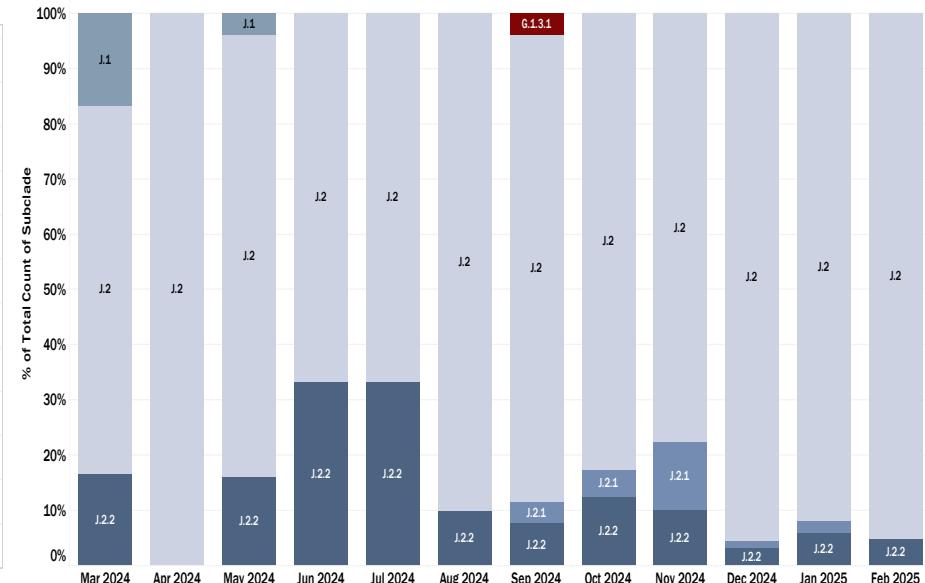
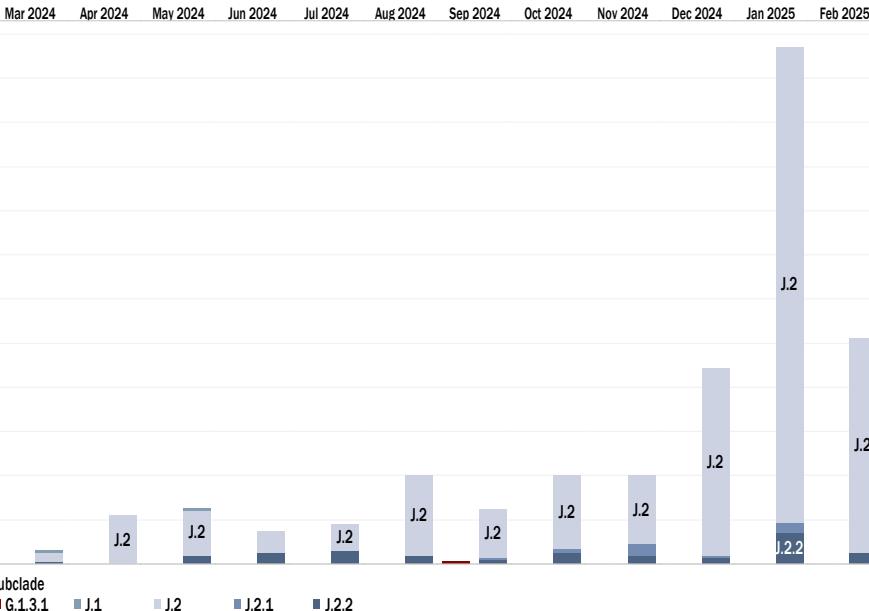
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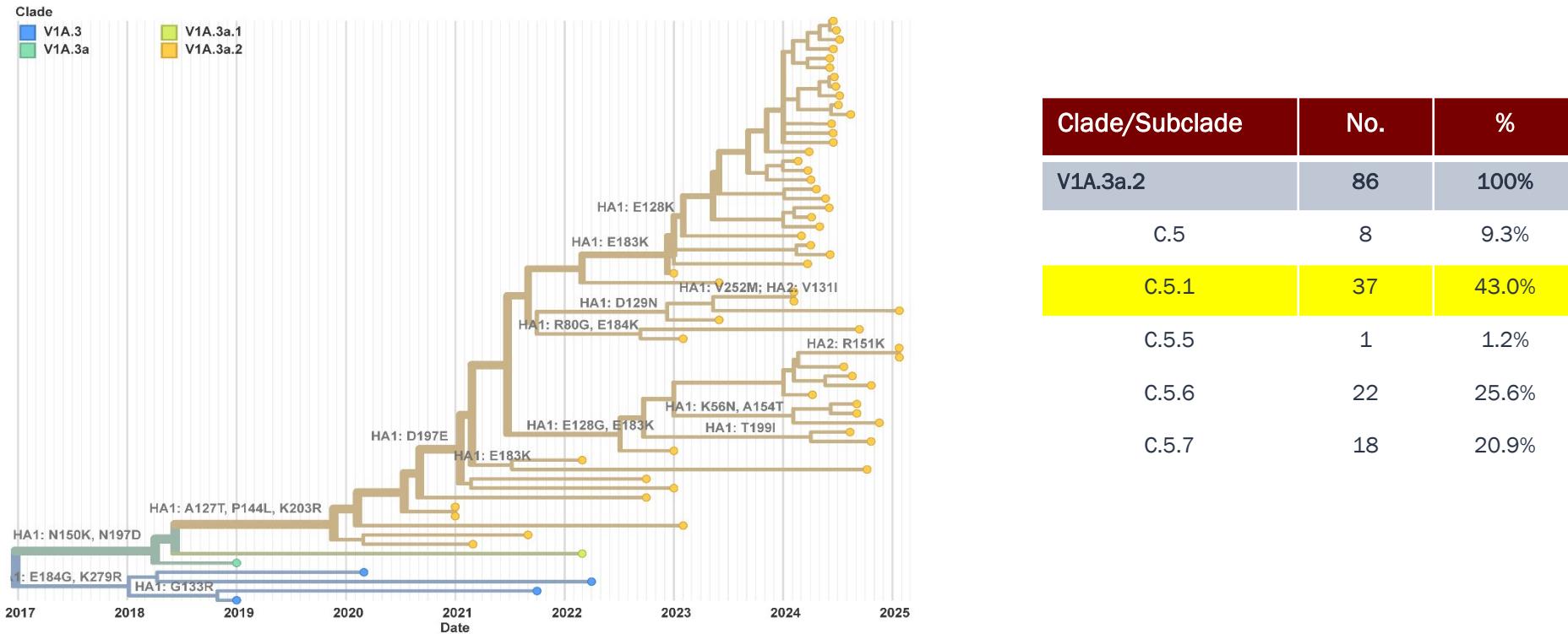
# A(H1N1)pdm09 Clade Dynamics



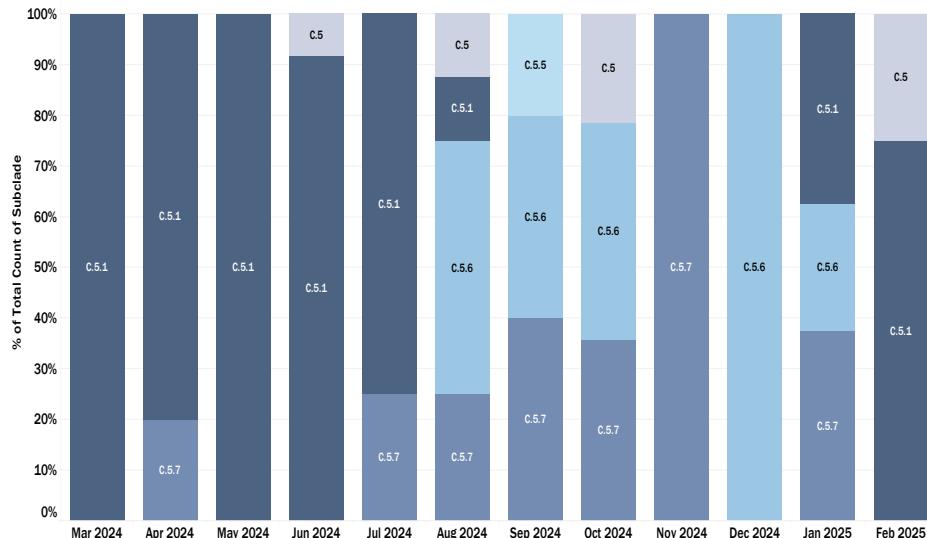
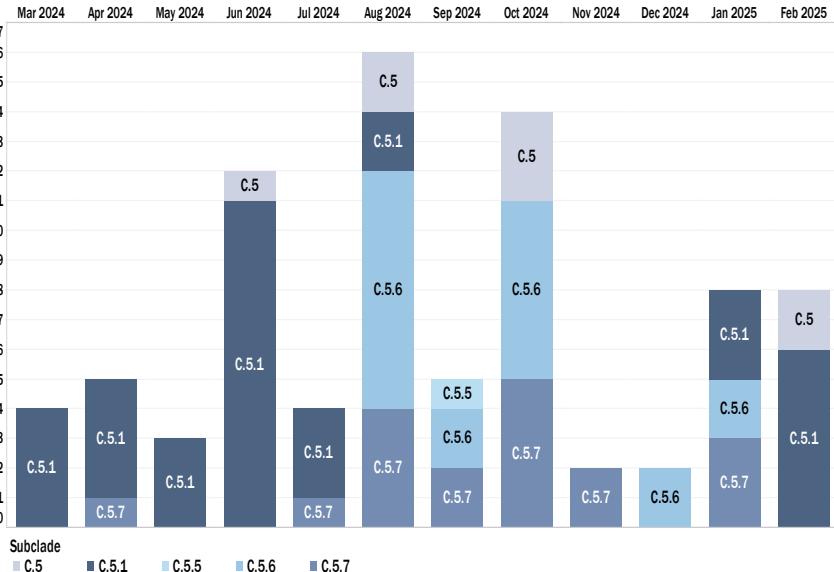
# A(H3N2) Subclade Dynamics



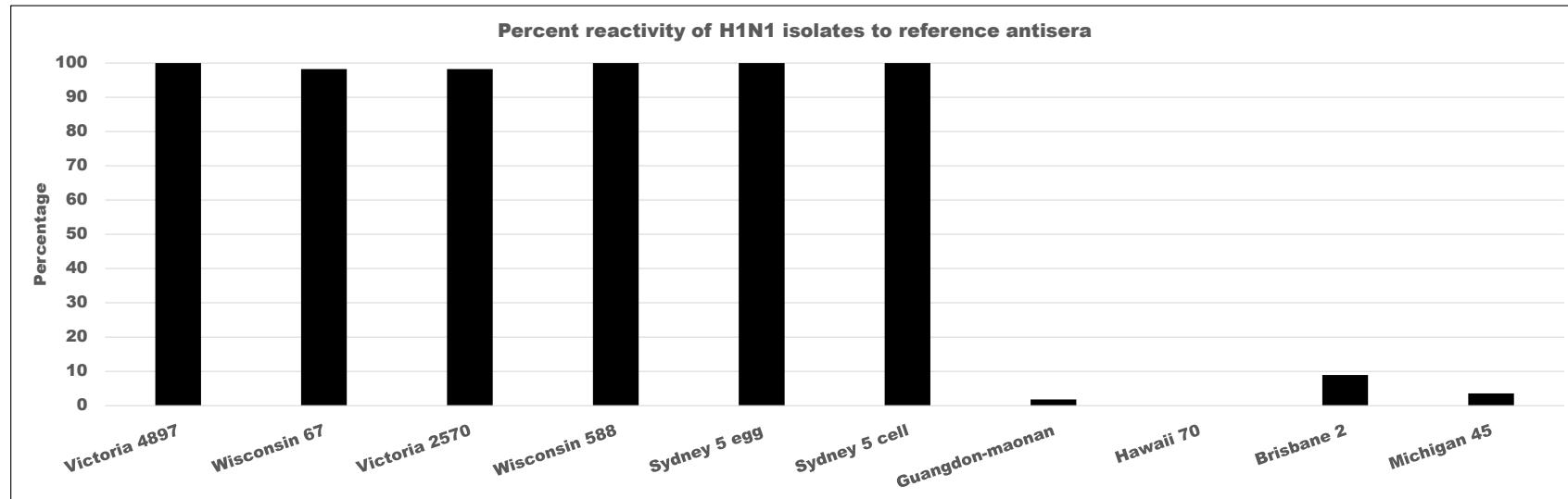
# DoD Phylogenetic Analyses – B/Victoria HA



# B/Vic Subclade Dynamics



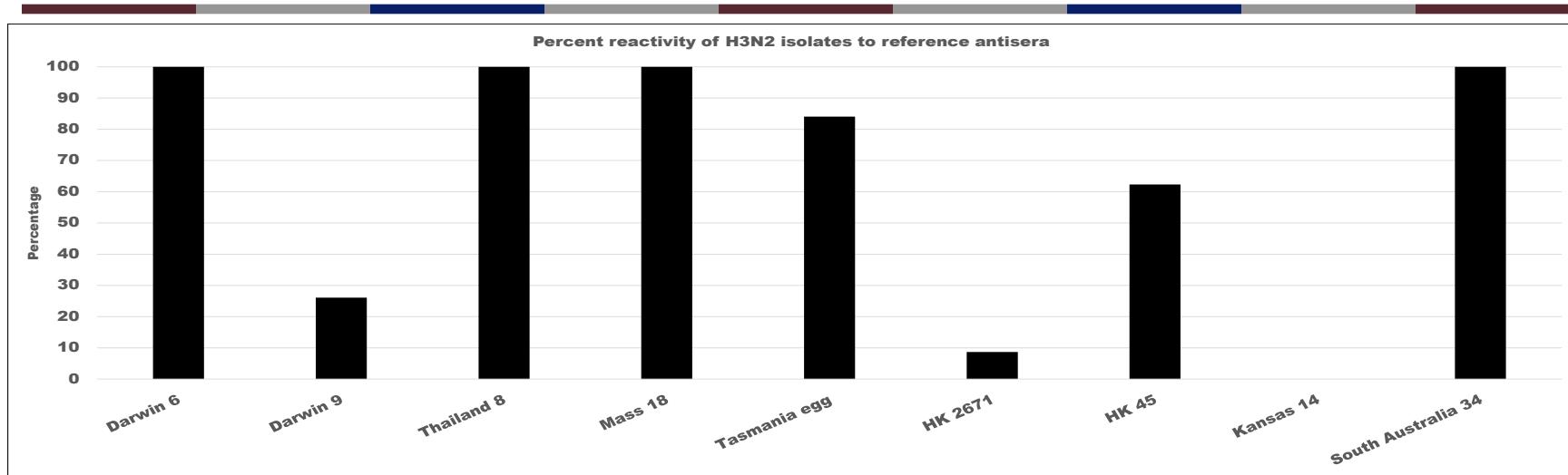
# Reactivity of Influenza A/H1N1 Isolates to Reference Antisera



	Victoria 4897	Wisconsin 67	Victoria 2570	Wisconsin 588	Sydney 5 egg	Sydney 5 cell	Guangdon-maonan	Hawaii 70	Brisbane 2	Michigan 45
Percent reactivity (within 4-fold change from the homologous titers)	100	98	98	100	100	100	2	0	9	4
Percent with higher titers than the homologous strain	100	13	2	2	23	46	0	0	0	0



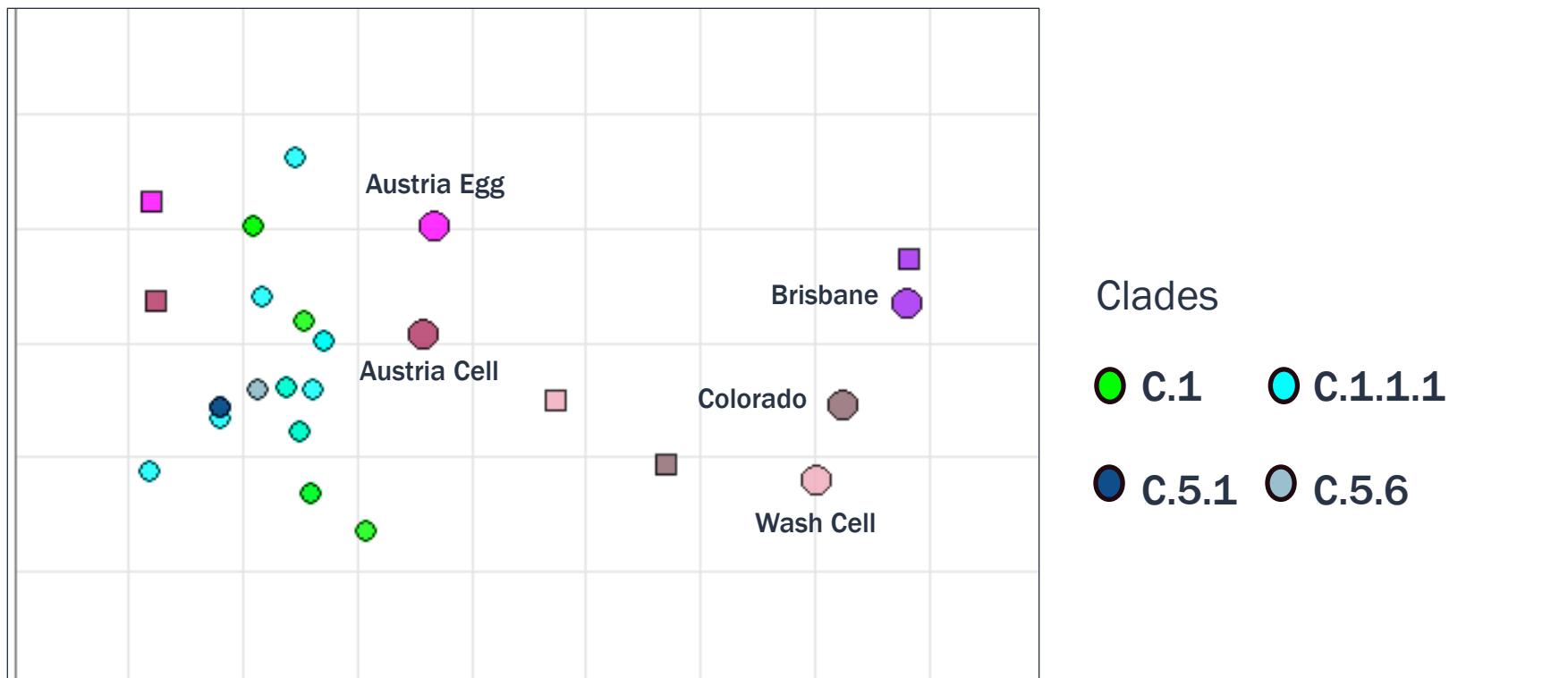
# Reactivity of Influenza A/H3N2 Isolates to Reference Antisera



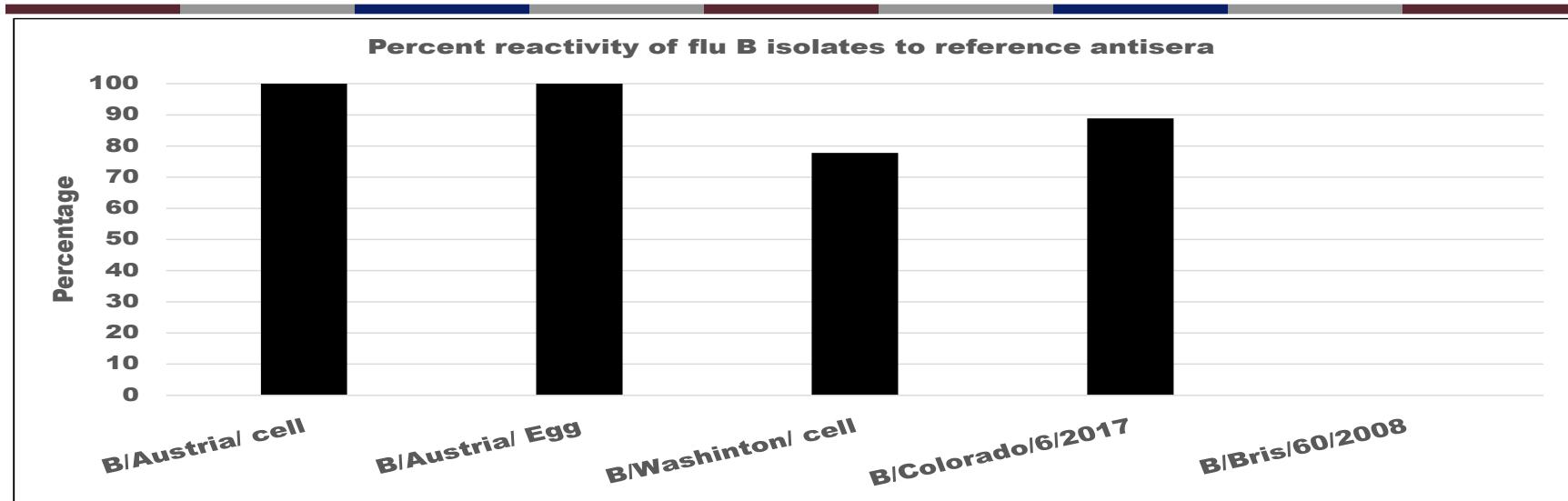
	Darwin 6	Darwin 9	Thailand 8	Mass 18	Tasmania egg	HK 2671	HK 45	Kansas 14	South Australia 34
Percent reactivity (within 4-fold change from the homologous titers)	100	26	100	100	84	9	62	0	100
Percent with higher titers than the homologous strain	100	0	62	97	19	0	12	0	72



# DoD Antigenic Cartography: Influenza B isolates



# Reactivity of Influenza B Isolates to Reference Antisera



	B/Austria/ cell	B/Austria/ Egg	B/Washington/ cell	B/Colorado/6/2017	B/Bris/60/2008
Percent reactivity (within 4-fold change from the homologous titers)	100	100	78	89	0
Percent with higher titers than the homologous strain	93	85	0	0	0

