DEFENSE HEALTH AGENCY • DEPARTMENT OF DEFENSE •

PRO CURA MILITIS

DoD Influenza Surveillance and Mid-Season Vaccine Effectiveness

Armed Forces Health Surveillance Division (AFHSD)
Naval Health Research Center (NHRC)
Naval Medical Research Center (NMRC)
United States Air Force School of Aerospace Medicine (USAFSAM)
DoD Global Respiratory Pathogen Surveillance Program Partners

Presentation to the Vaccines and Related Biological Products Advisory Committee (VRBPAC) – 7 March 2023

Anthony C. Fries, PhD**

**Representing the DoD CONUS and OCONUS lab-based influenza surveillance activities

Briefing Outline

- **Purpose:** Provide an update to the VRBPAC on DoD influenza surveillance activities for 2022 -2023

    - Program Descriptions
    - Vaccine Effectiveness in DoD Populations
        - ✓ DoD Beneficiaries
        - ✓ DoD Active Duty Service Members
    - DoD Phylogenetic Analyses
    - DoD Antigenic Characterization

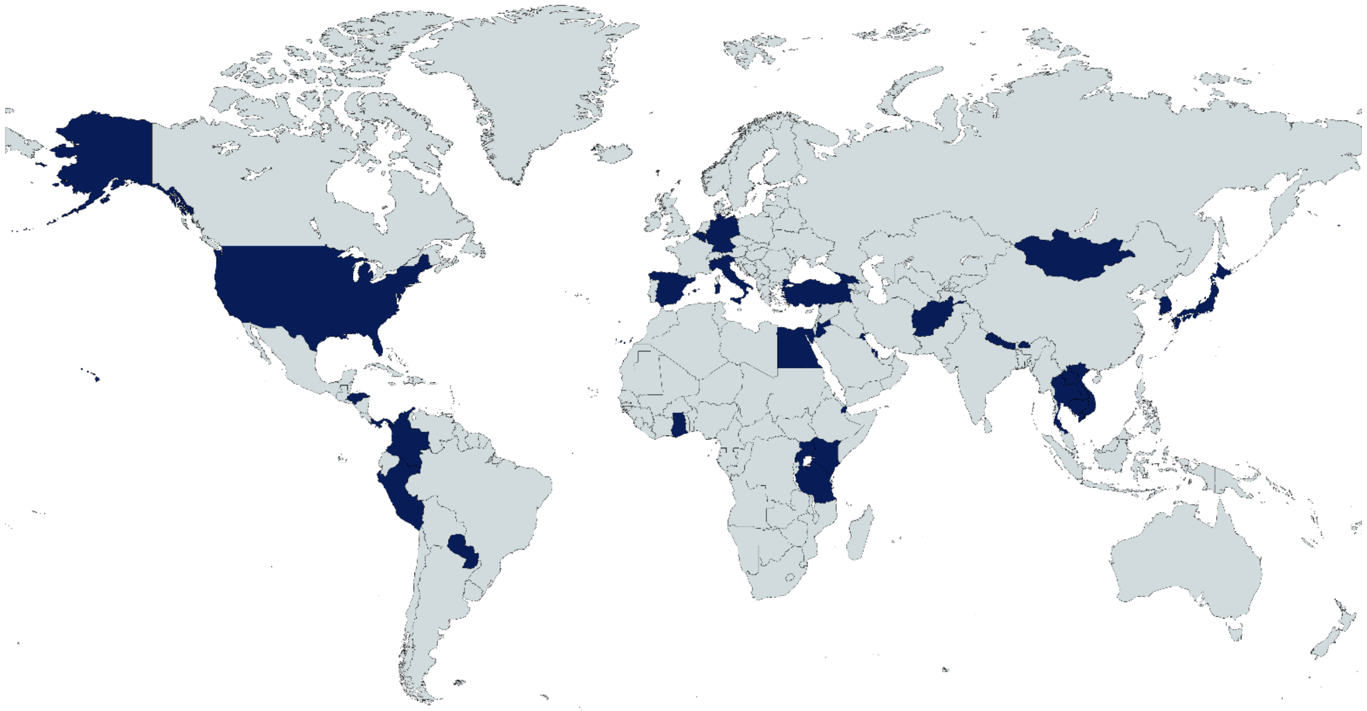
Influenza Surveillance in the DoD

- **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 Duty 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

Influenza Surveillance in the DoD

- The Global Emerging Infections Surveillance (GEIS) partner laboratories form a wide-reaching network across the globe
- Influenza surveillance activities in the DoD complement existing WHO efforts
  - Can surveil in some locations where data does not exist otherwise (Djibouti, Tanzania)
  - Surveil Service members and their beneficiaries, U.S. civilians and foreign national populations
  - DoD Service member population is highly vaccinated and widely distributed across the globe

GEIS-Funded Laboratory Influenza Surveillance Footprint

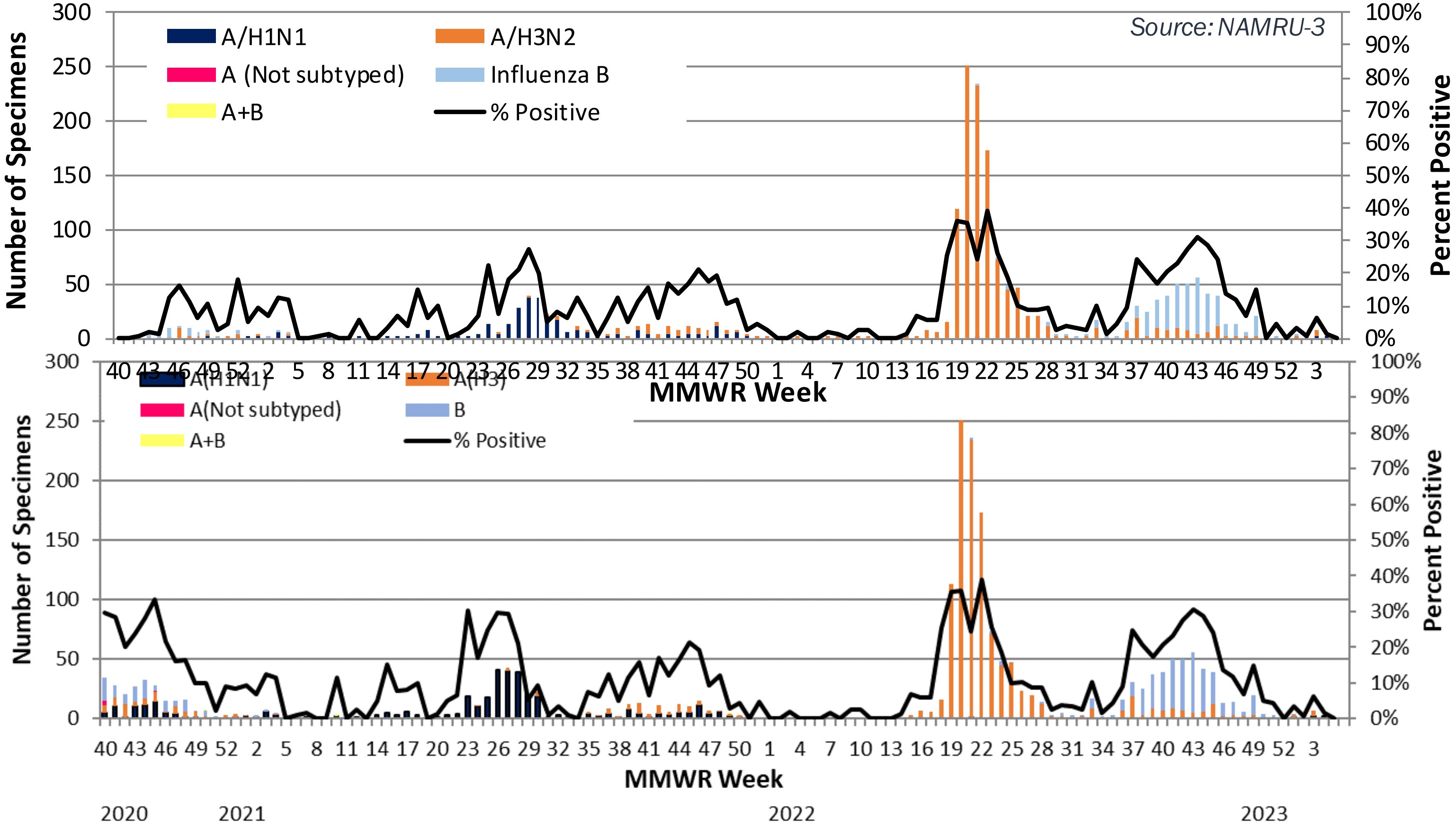


Influenza Surveillance in the DoD

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

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

Positive Flu Test Results in Ghana: GEIS-funded (top) and WHO (bottom)



Source: NAMRU-3

Source: WHO GISRS

Vaccine Effectiveness in DoD Populations

Influenza Mid-Season Vaccine Effectiveness
Matched Case-Control Study
DoD TRICARE Beneficiaries

USAFSAM 2022-2023 Mid-Season Influenza VE Analysis

- Case, test-negative control study design
    - Population: DoD TRICARE beneficiaries, excluding Service Members
    - VE against medically-attended (outpatient), influenza-like illness (ILI) laboratory-confirmed influenza cases
    - Time period: October 2, 2022 – February 18, 2023 (Weeks 40-07)

- Influenza-like illness case definition:
    - Fever (≥100.4 °F) and cough or
    - Fever (≥100.4 °F) and 2 or more additional symptoms (fatigue, body aches, sore throat, headache, sinus congestion, shortness of breath, chills, runny nose, loss of taste or smell, acute respiratory distress) or
    - Physician diagnosed ILI

USAFSAM 2022-2023 Mid-Season Influenza VE Analysis

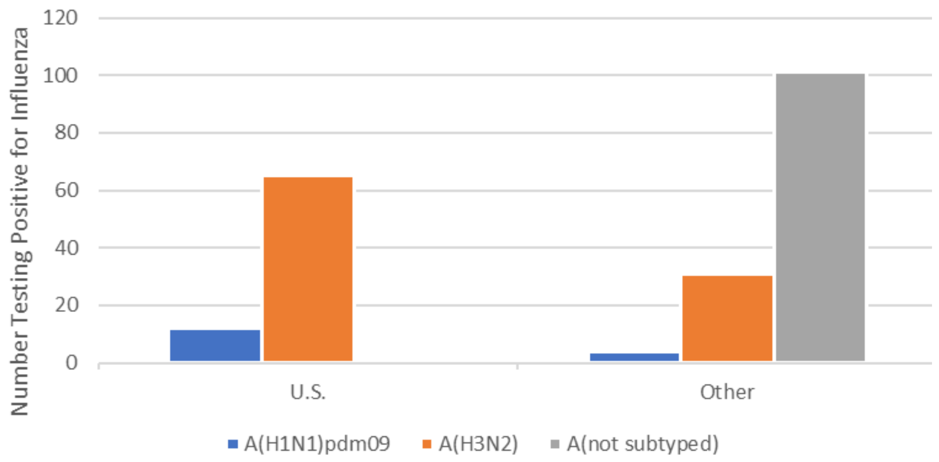
- Controls matched to cases by specimen collection time period
  - Matched 1 case to 3 controls in childrens analysis
  - Matched 1 case to 4 controls in dependents, adults, and influenza A(H3N2) analysis

- Analyses by:
  1. Influenza A (overall) **all dependents**
  2. Influenza A (overall) **children** (6mo – 17 years)
  3. Influenza A (overall) **adults** (18-64 years)
  4. Influenza A(H3N2) all dependents

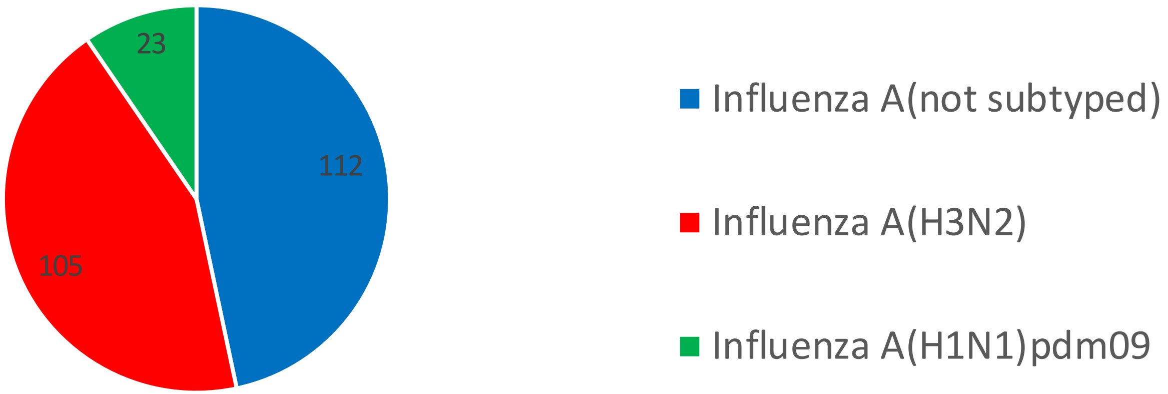
USAFSAM 2022-2023 Mid-Season Influenza VE Analysis

- Laboratories contributing to analyses:
  - Landstuhl Regional Medical Center (LRMC): n=630 (52%)
  - USAFSAM: n=570 (47%)
- Cases: n=240 (20%)
  - 113 (47%) vaccinated
  - 127 (53%) unvaccinated
- Controls: n=960 (80%)
  - 561 (58%) vaccinated
  - 399 (42%) unvaccinated

Location Breakdown of Influenza Subtypes



Frequency of Influenza Subtypes



Characteristics of laboratory confirmed influenza (RT-PCR)

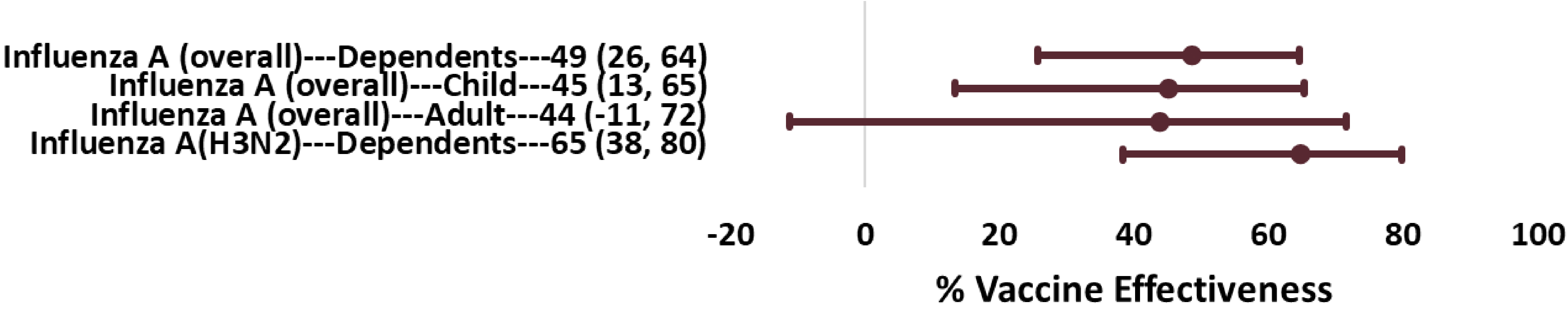
Characteristic		Cases n= 240 No. (%)	Controls n= 960 No. (%)	p-Value
Gender				0.5628
	Male	116 (48.33)	444 (46.25)	
	Female	124 (51.66)	516 (53.75)	
Age				<.0001
	0-5	54 (22.50)	350 (36.45)	
	6-9	58 (24.16)	110 (11.45)	
	10-17	65 (27.08)	121 (12.60)	
	18-24	14 (5.833)	101 (10.52)	
	25-44	37 (15.41)	211 (21.97)	
	45-64	12 (5.00)	67 (6.98)	
Beneficiary Category				<.0001
	Adult (18-64)	63 (26.25)	379 (39.47)	
	Child (0-17)	177 (73.75)	581 (60.52)	
Month of Illness				<.0001
	October	28 (11.66)	218 (22.70)	
	November	71 (29.58)	191 (19.89)	
	December	120 (50.00)	254 (26.45)	
	January	14 (5.833)	201 (20.93)	
	February	7 (2.916)	96 (10.00)	
Geographic Region				0.0012
	Eastern U.S.	47 (19.58)	122 (12.70)	
	Western U.S.	40 (16.66)	249 (25.93)	
	Other	153 (63.75)	589 (61.35)	
Vaccination Status				0.0015
	Vaccinated	113 (47.08)	561 (58.43)	
	Unvaccinated	127 (52.91)	399 (41.56)	
Influenza Status				<.0001
	Influenza A(H1N1)pdm09	23 (9.58)	0 (0)	
	Influenza A(H3N2)	105 (43.75)	0 (0)	
	Influenza A/not subtyped	112 (46.66)	0 (0)	
	Not Influenza	0 (0)	960 (100)	

USAFSAM 2022-2023 Mid-Season Influenza VE Estimates

Type	Population	Vaccine Status	Cases (%)	Controls (%)	Crude VE (95% CI)	Adjusted VE (95% CI)
Influenza A	Adults	Yes	36 (11)	168 (53)	43 (-11, 71)	44 (-11, 72)
		No	27 (9)	84 (27)		
Influenza A	Children	Yes	77 (11)	275 (39)	40 (9, 61)	45 (13, 65)
		No	100 (14)	256 (36)		
Influenza A	Dependents	Yes	113 (9)	561 (47)	50 (29, 65)	49 (26, 64)
		No	127 (11)	399 (33)		
Influenza A(H3N2)	Dependents	Yes	39 (7)	250 (48)	73 (54, 84)	65 (38, 80)
		No	66 (13)	170 (32)		

- Notes:
- VE was calculated as VE = (1 - odds ratio) x 100%
- Subjects were considered vaccinated if the vaccine was received at least 14 days prior to specimen collection date
- Controls were matched to cases by specimen collection time period up to the following ratios (Case:Control) : Dependents and Children 1:3, Adults & A(H3N2) 1:4
- Adjusted VE was calculated using conditional multivariable logistic regression and adjusted for 1) age (categorical), 2) Geographic Region (Eastern US, Western US, OCONUS)
- The relative standard error (RSE) is above 30% in the adult (60%) and children (38%) analysis. An RSE above 30% indicates unreliable results and caution should be taken with interpretation of results.
- Children 6 months – 2 years were included in the study and may lead to an underestimation of VE since they may only be partially vaccinated/protected.

USAFSAM 2022-2023 Mid-Season Influenza VE Estimates



- Overall, influenza A VE was higher among children (45%) than in adults (44%) and was statistically significant (not in adults).
- VE was highest among the A(H3N2) analysis at 65%.
- VE increased in influenza A (overall) children [53% (25, 71)], all dependents [53% (30, 68)], and influenza A(H3N2) [71% (48, 83)] analyses when including children 6 months -2 years of age (18 cases were added).

Vaccine Effectiveness in DoD Populations

Influenza Mid-Season Vaccine Effectiveness
Matched Case-Control Study
U.S. Active Component Service Members

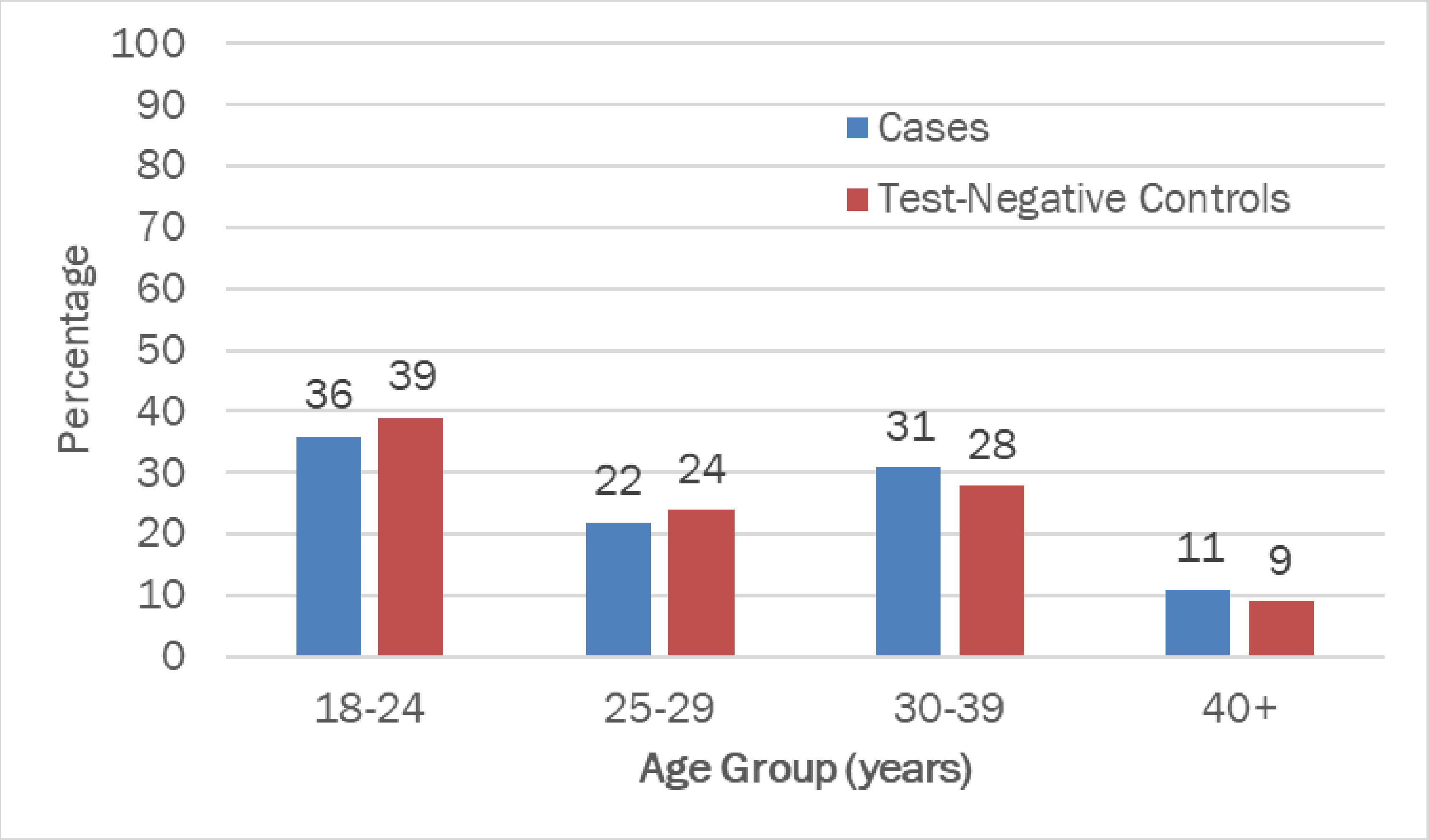
U.S. Service Members: Study Design

- Case / Test-negative control design
- Population: Active component Service Members
  - Army, Navy, Air Force, Marines
  - CONUS and OCONUS
- Time Period: September 1, 2022 – February 4, 2023
- 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, and month of diagnosis
- Type and subtype-specific VE calculated

U.S. Service Members: Vaccination Information & Case Subtypes

- Vaccination
  - Quadrivalent IIV was the only vaccine type among the study subjects
  - 94% of subjects had prior flu vaccine in previous 5 years
- Cases
  - Influenza A (any subtype) = 4,639
  - Influenza A(H3N2) = 574
  - Influenza A(H1N1) = 73
  - Influenza B = 274
- Sample size too small to calculate inpatient-only VE (only 12 cases)

Cases and Test-Negative Controls: Age Groups



U.S. Service Members:
Interim VE Estimates 2022-2023

Influenza Type	Vaccination Status	Cases N (%)	Controls N (%)	Crude VE (95% CI)	Adjusted VE (95% CI)*
Influenza A	Vaccinated	2,170 (47)	12,639 (54)	25 (20, 30)	35 (30, 40)
	Unvaccinated	2,469 (53)	10,794 (46)		
A/H1N1	Vaccinated	41 (57)	12,639 (54)	-16 (-84, 27)	14 (-46, 49)
	Unvaccinated	31 (43)	10,794 (46)		
A/H3N2	Vaccinated	170 (30)	12,639 (54)	64 (57, 70)	64 (55, 70)
	Unvaccinated	404 (70)	10,794 (46)		
Influenza B	Vaccinated	155 (57)	12,639 (54)	-11 (-41, 13)	21 (-6, 40)
	Unvaccinated	119 (43)	10,794 (46)		

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

U. S. Service Members: Interim VE Summary

- The 2022-2023 Influenza vaccine provided:
    - Low protection against Influenza A (35%)
    - Moderate protection against Influenza A/H3N2 (64%)
    - Low protection against Influenza B (21%): non-significant

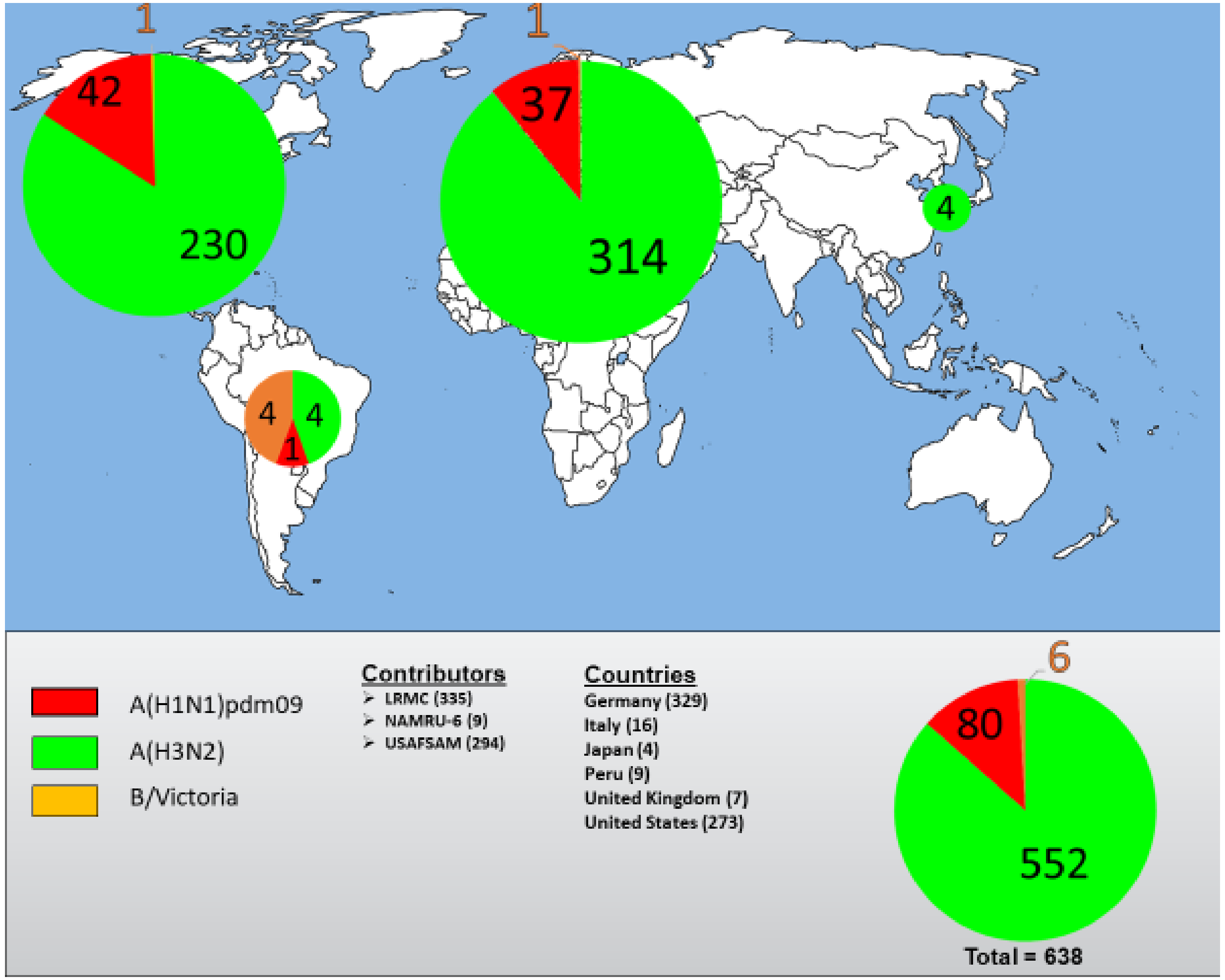
✓ Note: Moderate protection (54%) was found against hospitalized influenza A in a cohort designed study.

DoD Phylogenetic Analyses

DoD Phylogenetic Analyses

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

Geographical Distribution of 2022-2023 Influenza

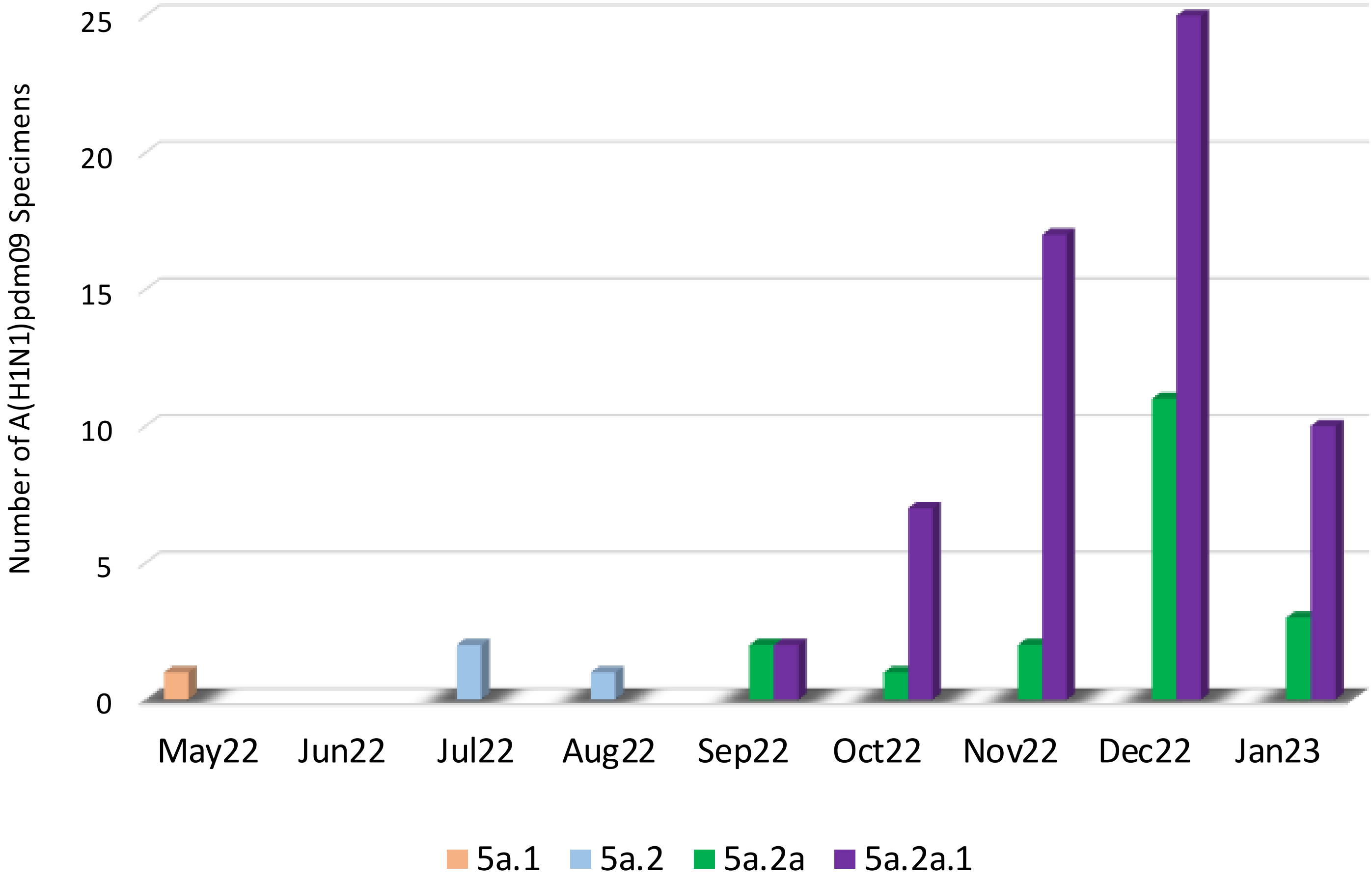


Contributors
- LRMC (335)
- NAMRU-6 (9)
- USAFSAM (294)

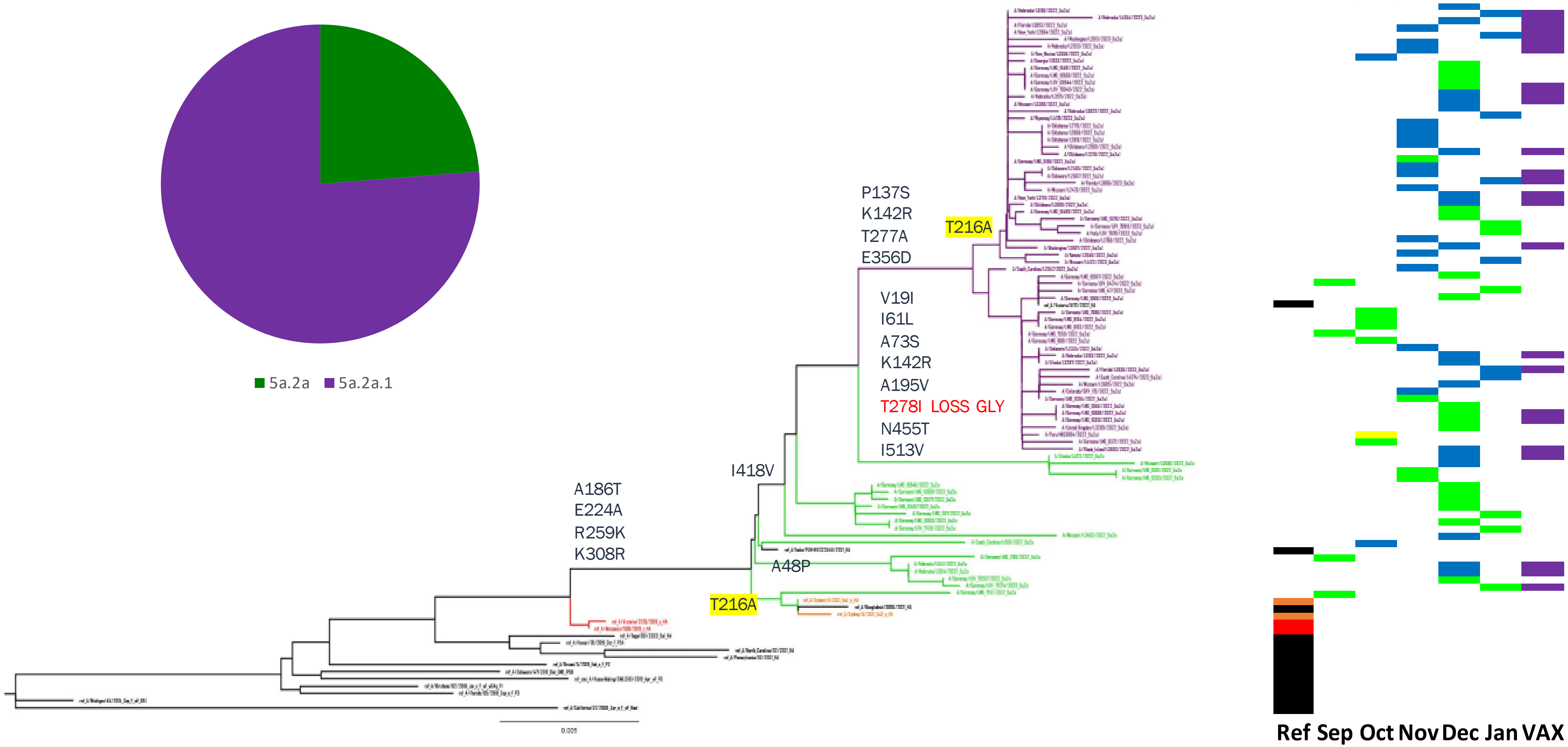
Countries
Germany (329)
Italy (16)
Japan (4)
Peru (9)
United Kingdom (7)
United States (273)

Influenza A(H1N1)pdm09

6B.1A Sub-Clade	#	%	Key Clade Substitutions Rel. to Vaccine
5a.2a	19	23.8%	K54Q A186T Q189E E224A R259K K308R
5a.2a.1	61	76.3%	P137S K142R T277A E356D I418V N451H



Influenza A(H1N1)pdm09 HA



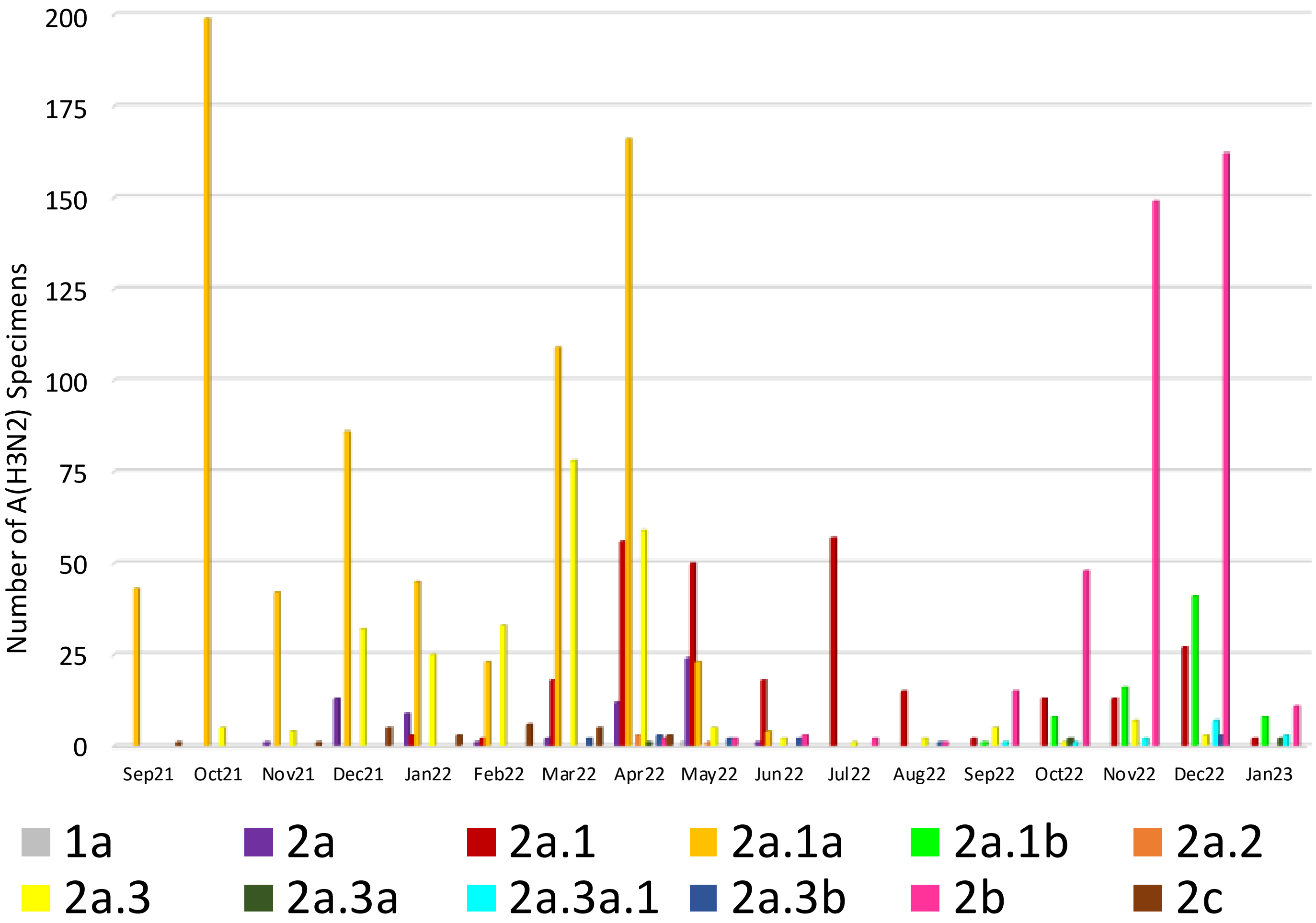
CLADE	CLADE TOTAL	% VACCINATED
5a.2a	19	21.1%
5a.2a.1	61	32.8%
ALL	**80**	**30.0%**

Side Bar Legend

🟩	EUCOM
🟦	NORTHCOM
🟨	SOUTHCOM
⬛	REFERENCE
🟥	NH VACCINE
🟧	SH VACCINE
🟪	VACCINATED

Influenza A(H3N2)

3C.2a1b.2a2 Sub-Clade	#	%	Key Clade Substitutions Rel. to Vaccine
2a.1	57	10.3%	**D53G** D104G K276R
2a.1b	74	13.4%	**D53G** D104G I140K K276R R299K
2a.3	16	2.9%	**D53N** N96S I192F N378S
2a.3a	4	0.7%	**D53N** E50K N96S I192F I223V N378S
2a.3a.1	14	2.5%	**D53N** E50K N96S I140K I192F I223V N378S
2a.3b	3	0.5%	**D53N** N96S I140M I192F N378S
2b	384	69.6%	**E50K** F79V I140K **S156H**



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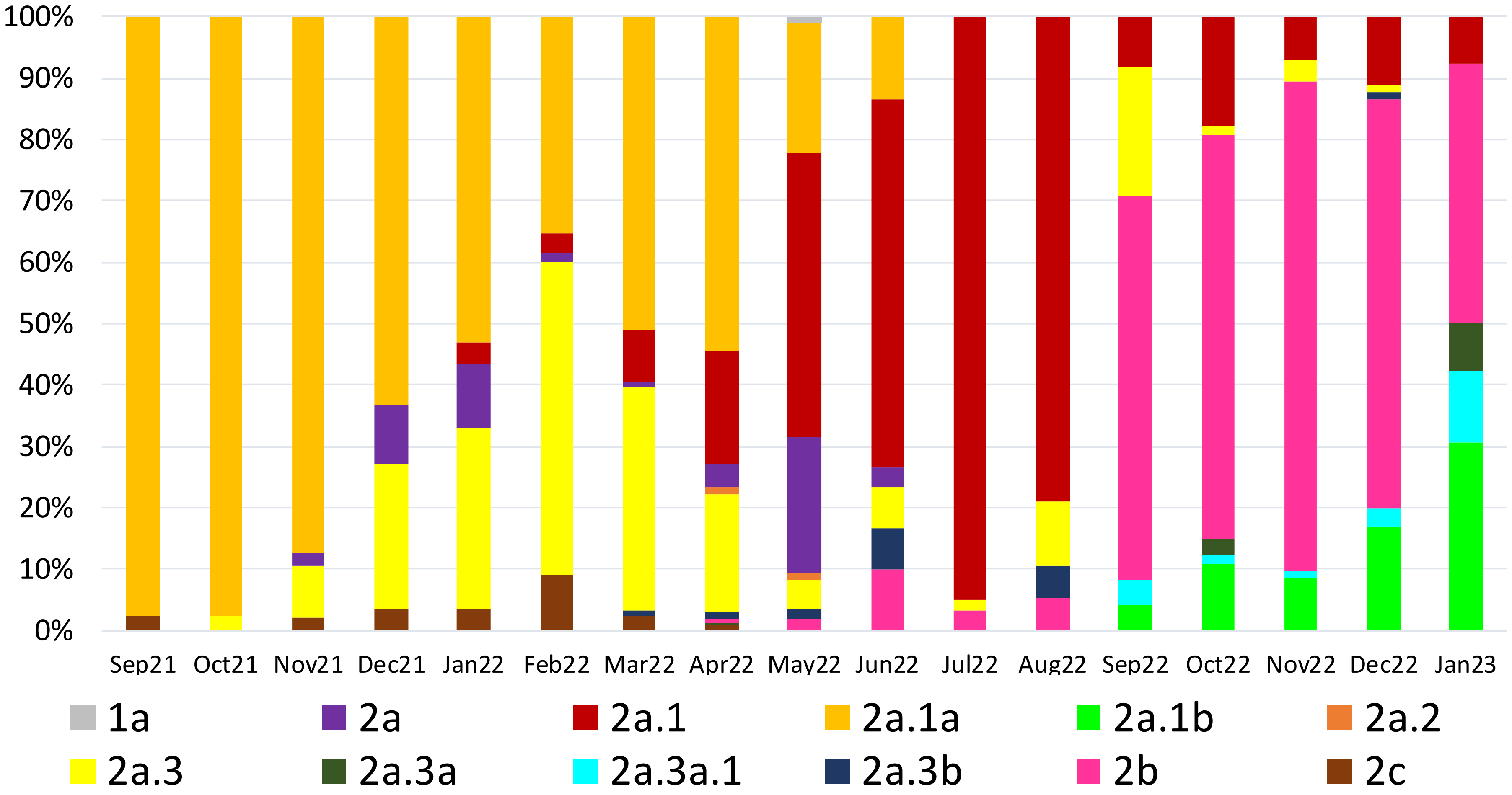
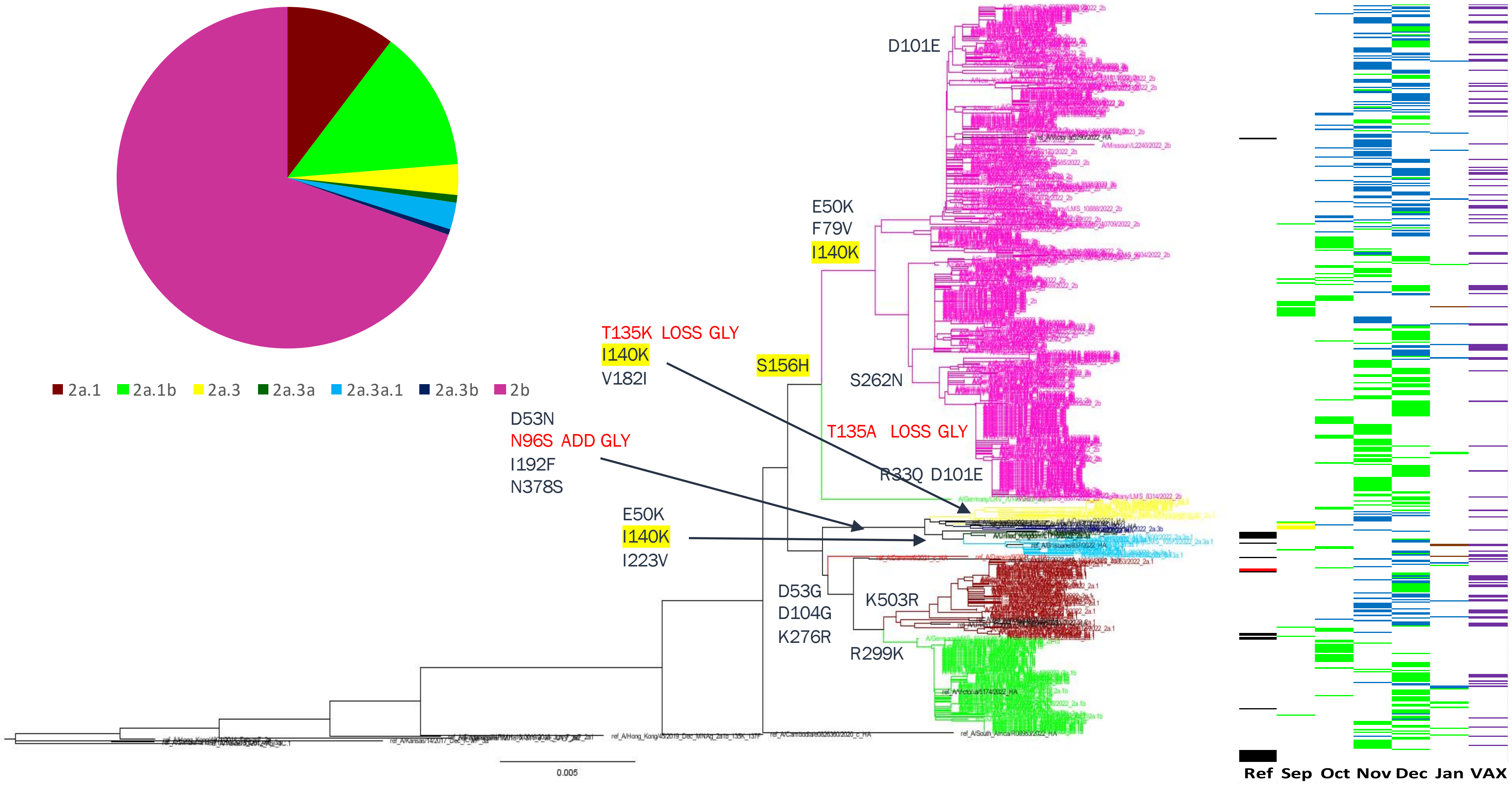
Influenza A(H3N2)



Influenza A(H3N2) HA

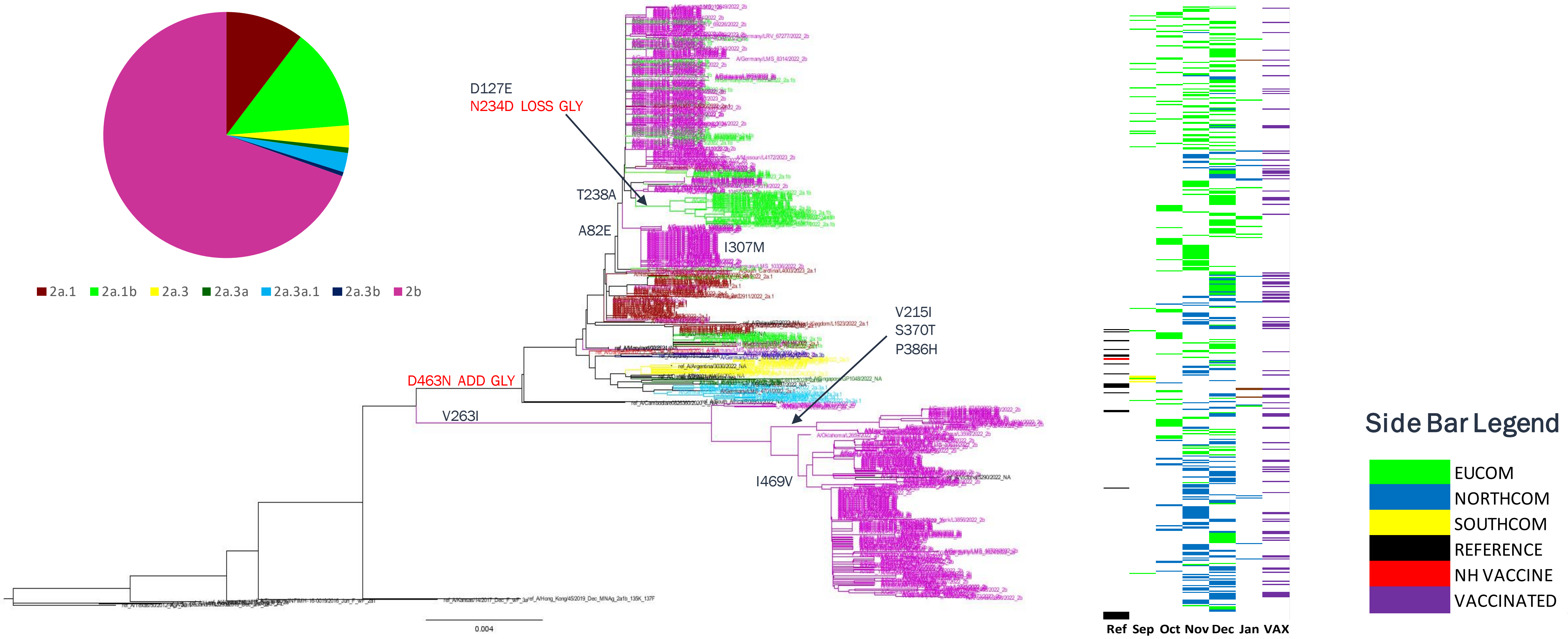


CLADE	CLADE TOTAL	% VACCINATED
2a.1	57	33.3%
2a.1b	74	14.9%
2a.3	16	12.5%
2a.3a	4	50.0%
2a.3a.1	14	35.7%
2a.3b	3	0.0%
2b	384	16.1%
ALL	**552**	**18.3%**

Side Bar Legend

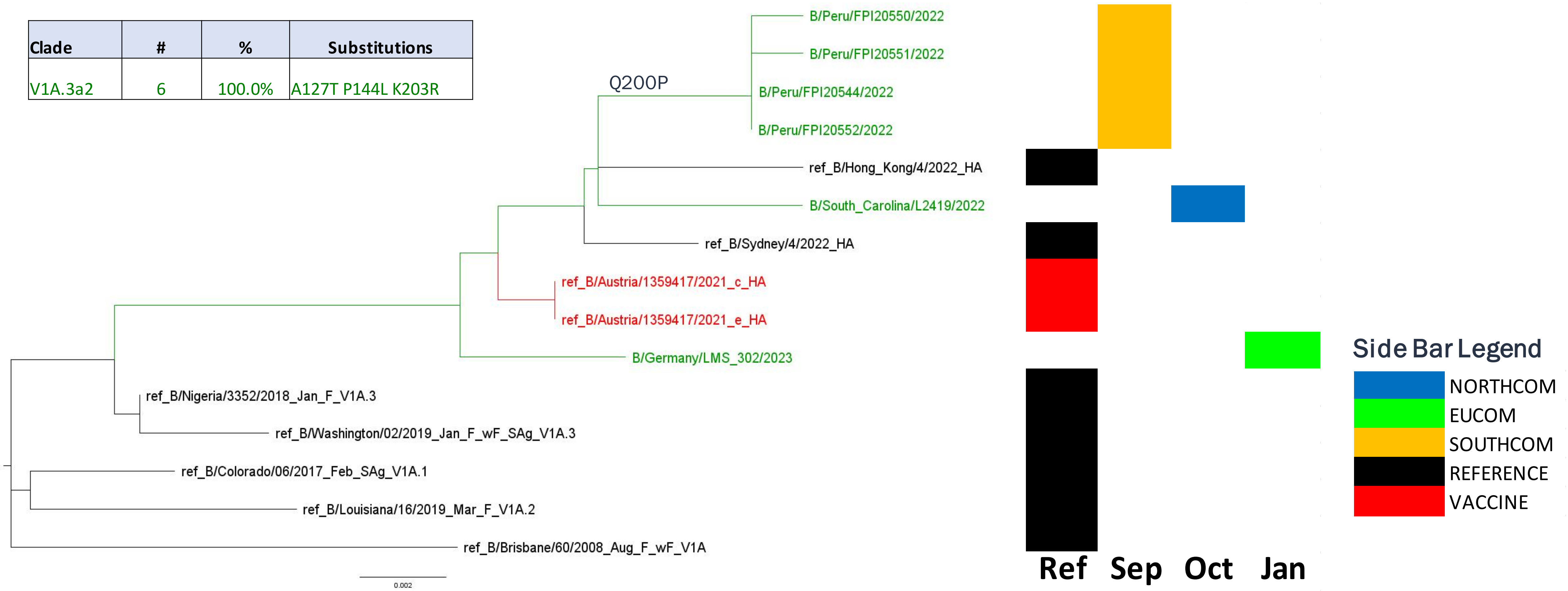
🟩	EUCOM
🟦	NORTHCOM
🟨	SOUTHCOM
⬛	REFERENCE
🟥	NH VACCINE
🟪	VACCINATED

Influenza A(H3N2) NA



Influenza B/Victoria HA

Clade	#	%	Substitutions
V1A.3a2	6	100.0%	A127T P144L K203R

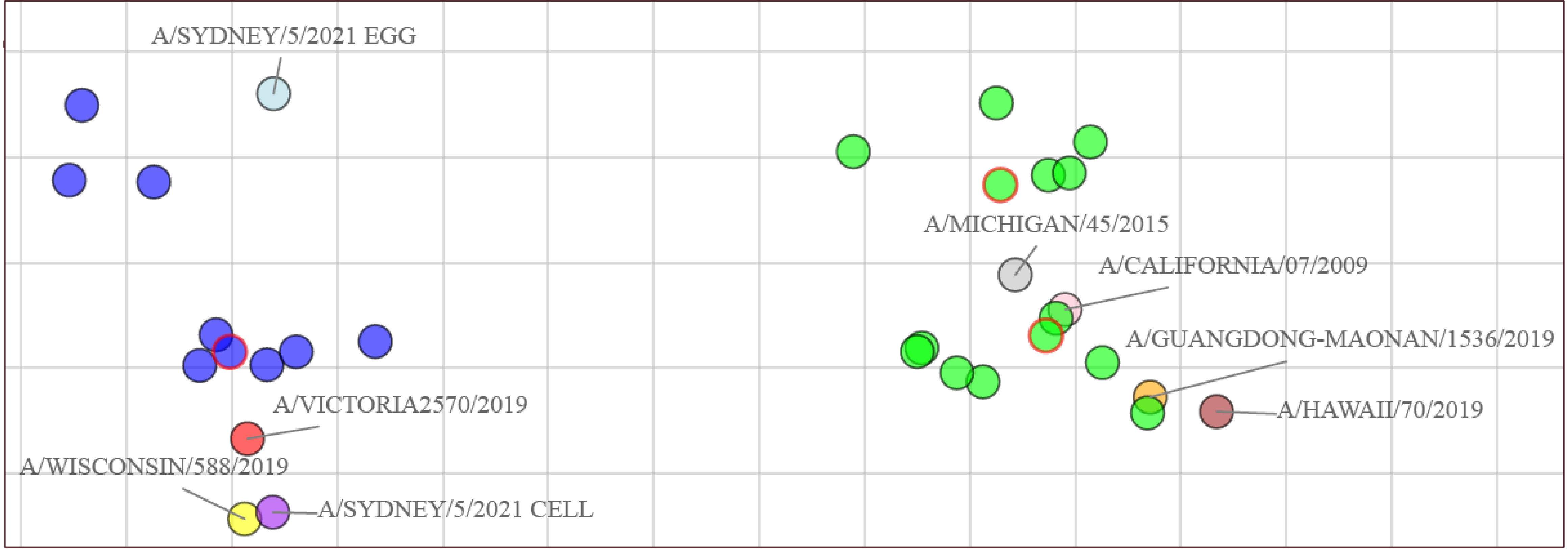


Summary

- DoD surveillance provided sequence data for 638 influenza specimens, mostly centered on the U.S. and western Europe.
- 80 influenza A(H1N1)pdm09 HA sequences indicate 76% in clade 5a.2a.1 and 24% in clade 5a.2a. A similar structure is observed in NA with one potential reassortment.
- 552 influenza A(H3N2) HA sequences indicate 70% in clade 2b, 13% in 2a.1b, 10% in 2a.1, 3% each in 2a.3 and 2a.3a.1, and 1% each in 2a.3a and 2a.3b. Many potential reassortments were observed in NA, particularly among 2b and 2a.1b viruses.
- 6 influenza B HA sequences were all characterized as V1A.3a.2, with very little difference in structure to NA.

DoD Antigenic Characterization

Influenza A(H1N1)pdm09 Antigenic Cartography



- Isolates were grown in MDCK cells and tested by HINT assay
- Neutralization titer 50 was used for developing the antigenic map using ACMACS (Red borders indicate OCONUS samples)
- Antisera: A/Victoria2570/2019; A/Wisconsin/588/2019; A/Sydney/5/2021 egg; A/Sydney/5/2021 cell; A/Hawaii/70/2019; A/Guangdong-Maonan/1536/2019; A/Michigan/45/2015; A/California/07/2009

Influenza A(H1N1)pdm09 Antigenic Cartography

	A/Victoria2570/2019	A/Wisconsin/588/2019	A/Sydney/5/2021 egg	A/Sydney/5/2021 cell	A/Guangdong-Maonan/1536/2019	A/Hawaii/70/2019	A/Michigan/45/2015	A/California/07/2009	Clade	Mutations	
A/Victoria2570/2019	20480	20480	14482	81920	160	320	640	160			
A/Wisconsin/588/2019	14482	20480	7241	57926	160	320	640	80			
A/Sydney/5/2021 egg	10240	10240	10240	20480	80	320	640	160			
A/Sydney/5/2021 cell	10240	20480	10240	81920	320	640	640	80			
A/Guangdong-Maonan/1536/2019	160	160	80	320	40960	40960	81920	81920			
A/Hawaii/70/2019	40	80	40	160	40960	81920	40960	81920			
A/Michigan/45/2015	640	320	1280	640	10240	20480	40960	81920			
A/California/07/2009	640	80	1280	640	20480	28963	40960	81920			
Test antigens											
H1032210	640	640	640	320	10240	20480	10240	20480	5a.1	N129D T185I	
H1032217	160	320	640	160	5120	10240	20480	20480	5a.1	N129D T185I	
H1032209	640	320	320	320	10240	20480	10240	20480	5a.1	N129D T185I D187A Q189E	
H1032220	160	640	320	320	10240	10240	20480	20480	5a.1	N129D T185I D187A Q189E	
H1032212	1810	1810	640	1280	20480	40960	20480	40960	6B.1A.5b	K130N K160M	
H1032215	905	12280	320	640	20480	40960	20480	28963	6B.1A.5b	K130N K160M	
H1032201	1280	1280	640	1280	40960	81920	40960	81960	6B.1A.5b	K130N K160M	
H1032216	453	905	320	453	28963	40960	40960	57926	6B.1A.5b	K130N P137S K160M	
H1032213	453	640	226	453	20480	40960	40960	40960	6B.1A.5b	K130N P137S K160M	
H1032214	320	640	640	320	5120	10240	10240	10240	6B.1A.5b		
H1032203	1280	2560	640	1280	5120	5120	10240	10240	6B.1A.7	K130N	
H1032207	453	453	160	226	28963	40960	57926	57926	6B.1A.7	L161I	
H1032208	113	640	80	160	28963	57926	57926	57926	6B.1A.7	L161I	
H1032204	1280	2560	905	905	20480	81920	40960	81960	6B.1A.7	L161I E506D	
H1032211	40960	57926	20480	327680	113	226	320	80	5a.2	N129D K130N N156K L161I	
H1032219	10240	10240	5120	20480	20	40	320	40	5a.2	T185I V250A E506D	
H1221107	28963	57926	28963	163840	320	640	640	80	5a.2a		
H1230102	40960	40960	40960	163840	160	160	640	40	5a.2a.1	K54E D274N N451H	P137S K142R A186T Q189E E224A R259K T277A K308R E356D I418V
H1230103	40960	40960	40960	163840	320	1280	1280	80	5a.2a.1	K54Q T216A	
H1230104	20480	20480	40960	163840	640	320	320	80	5a.2a.1	K54Q T216A	
H1230105	40960	40960	40960	81920	2560	1280	640	320	5a.2a.1	K54Q T216A	
H1230107	10240	10240	20480	40960	80	160	320	40	5a.2a.1	K54Q T216A H399Q	
H1230108	10240	10240	10240	40960	40	40	160	40	5a.2a.1	K54Q T216A	

Influenza A(H3N2) Antigenic Cartography

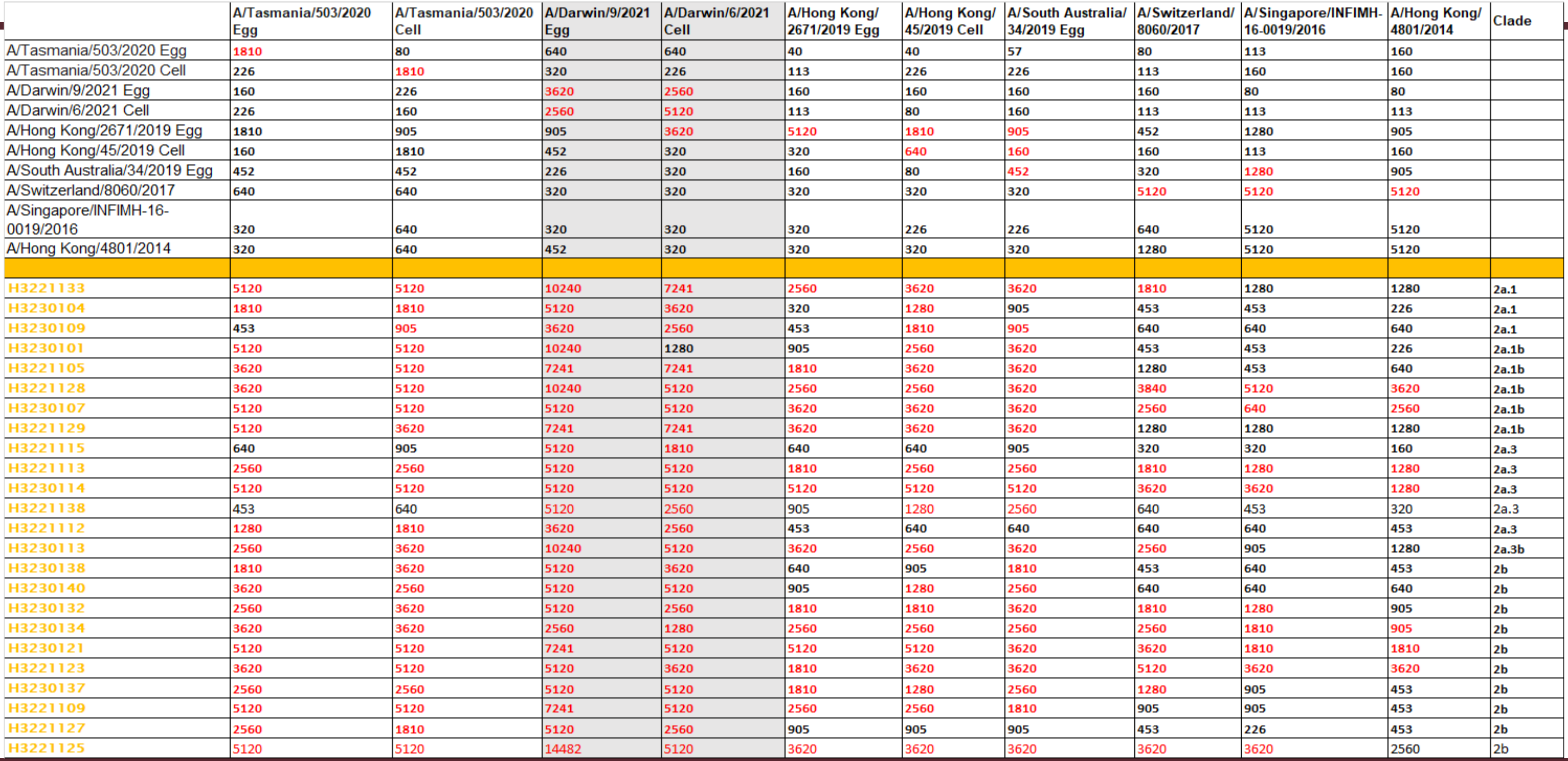
- H3N2 Isolates were grown in MDCK cells and tested by HINT assay
- Neutralization titer 50 was used for developing the antigenic map using ACMACS
- Red borders indicate EUCOM samples
- 3 clusters are observed

- Antisera:
  - A/Tasmania/503/2020 Egg
  - A/Tasmania/503/2020 Cell
  - A/Darwin/9/2021 Egg
  - A/Darwin/6/2021 Cell
  - A/Hong Kong/2671/2019 Egg
  - A/Hong Kong/45/2019 Cell
  - A/South Australia/34/2019 Egg
  - A/Switzerland/8060/2017
  - A/Singapore/INFIMH-16-0019/2016
  - A/Hong Kong/4801/2014

A(H3N2) (Cluster 1) - cross-reactive to all tested antisera

	A/Tasmania/503/2020 Egg	A/Tasmania/503/2020 Cell	A/Darwin/9/2021 Egg	A/Darwin/6/2021 Cell	A/Hong Kong/2671/2019 Egg	A/Hong Kong/45/2019 Cell	A/South Australia/34/2019 Egg	A/Switzerland/8060/2017	A/Singapore/INFIMH-16-0019/2016	A/Hong Kong/4801/2014	Clade
A/Tasmania/503/2020 Egg	1810	80	640	640	40	40	57	80	113	160	
A/Tasmania/503/2020 Cell	226	1810	320	226	113	226	226	113	160	160	
A/Darwin/9/2021 Egg	160	226	3620	2560	160	160	160	160	80	80	
A/Darwin/6/2021 Cell	226	160	2560	5120	113	80	160	113	113	113	
A/Hong Kong/2671/2019 Egg	1810	905	905	3620	5120	1810	905	452	1280	905	
A/Hong Kong/45/2019 Cell	160	1810	452	320	320	640	160	160	113	160	
A/South Australia/34/2019 Egg	452	452	226	320	160	80	452	320	1280	905	
A/Switzerland/8060/2017	640	640	320	320	320	320	320	5120	5120	5120	
A/Singapore/INFIMH-16-0019/2016	320	640	320	320	320	226	226	640	5120	5120	
A/Hong Kong/4801/2014	320	640	452	320	320	320	320	1280	5120	5120	
H3221126	1280	905	1810	640	320	453	640	640	320	320	2b
H3221110	905	905	1810	453	453	905	640	453	226	453	2b
H3221111	640	640	905	640	320	640	640	640	320	320	2b
H3221119	905	905	1280	640	640	905	640	905	640	640	2b
H3221120	640	905	1280	640	640	640	320	640	453	640	2b
H3221121	640	1280	2560	905	640	1280	1280	905	640	640	2b
H3230124	905	1810	1810	905	905	905	320	640	640	640	2b
H3230127	1280	905	1810	905	640	905	905	905	453	453	2b
H3230119	453	1810	2560	905	640	1280	453	1280	905	640	2b
H3230130	1810	905	2560	905	905	1810	1810	1280	640	640	2b
H3230136	1280	1810	1810	905	1280	1280	1280	1280	1280	640	2b
H3230143	905	1280	2560	640	1280	1280	1280	905	1810	905	2b
H3230117	640	640	2560	905	905	1280	640	640	640	453	2b
H3230118	905	1280	1810	1810	905	905	453	905	905	905	2b
H3230116	1280	1280	3620	1280	905	1810	905	905	1280	905	2b
H3230120	905	905	2560	1810	905	1810	1810	905	1810	905	2b
H3221117	453	1280	2560	1280	960	1280	453	1280	1280	905	2b
H3230123	1280	905	1810	1280	1280	1810	1280	1280	1280	1280	2b

A(H3N2) (Cluster 2) - high reactivity to A/Darwin/9/2021 Egg and A/Darwin/6/2021 Cell based antisera and cross-reactive to most antisera tested



	A/Tasmania/503/2020 Egg	A/Tasmania/503/2020 Cell	A/Darwin/9/2021 Egg	A/Darwin/6/2021 Cell	A/Hong Kong/ 2671/2019 Egg	A/Hong Kong/ 45/2019 Cell	A/South Australia/ 34/2019 Egg	A/Switzerland/ 8060/2017	A/Singapore/INFIMH-16-0019/2016	A/Hong Kong/ 4801/2014	Clade
A/Tasmania/503/2020 Egg	1810	80	640	640	40	40	57	80	113	160	
A/Tasmania/503/2020 Cell	226	1810	320	226	113	226	226	113	160	160	
A/Darwin/9/2021 Egg	160	226	3620	2560	160	160	160	160	80	80	
A/Darwin/6/2021 Cell	226	160	2560	5120	113	80	160	113	113	113	
A/Hong Kong/2671/2019 Egg	1810	905	905	3620	5120	1810	905	452	1280	905	
A/Hong Kong/45/2019 Cell	160	1810	452	320	320	640	160	160	113	160	
A/South Australia/34/2019 Egg	452	452	226	320	160	80	452	320	1280	905	
A/Switzerland/8060/2017	640	640	320	320	320	320	320	5120	5120	5120	
A/Singapore/INFIMH-16-0019/2016	320	640	320	320	320	226	226	640	5120	5120	
A/Hong Kong/4801/2014	320	640	452	320	320	320	320	1280	5120	5120	
H3221133	5120	5120	10240	7241	2560	3620	3620	1810	1280	1280	2a.1
H3230104	1810	1810	5120	3620	320	1280	905	453	453	226	2a.1
H3230109	453	905	3620	2560	453	1810	905	640	640	640	2a.1
H3230101	5120	5120	10240	1280	905	2560	3620	453	453	226	2a.1b
H3221105	3620	5120	7241	7241	1810	3620	3620	1280	453	640	2a.1b
H3221128	3620	5120	10240	5120	2560	2560	3620	3840	5120	3620	2a.1b
H3230107	5120	5120	5120	5120	3620	3620	3620	2560	640	2560	2a.1b
H3221129	5120	3620	7241	7241	3620	3620	3620	1280	1280	1280	2a.1b
H3221115	640	905	5120	1810	640	640	905	320	320	160	2a.3
H3221113	2560	2560	5120	5120	1810	2560	2560	1810	1280	1280	2a.3
H3230114	5120	5120	5120	5120	5120	5120	5120	3620	3620	1280	2a.3
H3221138	453	640	5120	2560	905	1280	2560	640	453	320	2a.3
H3221112	1280	1810	3620	2560	453	640	640	640	640	453	2a.3
H3230113	2560	3620	10240	5120	3620	2560	3620	2560	905	1280	2a.3b
H3230138	1810	3620	5120	3620	640	905	1810	453	640	453	2b
H3230140	3620	2560	5120	5120	905	1280	2560	640	640	640	2b
H3230132	2560	3620	5120	2560	1810	1810	3620	1810	1280	905	2b
H3230134	3620	3620	2560	1280	2560	2560	2560	2560	1810	905	2b
H3230121	5120	5120	7241	5120	5120	5120	3620	3620	1810	1810	2b
H3221123	3620	5120	5120	3620	1810	3620	3620	5120	3620	3620	2b
H3230137	2560	2560	5120	5120	1810	1280	2560	1280	905	453	2b
H3221109	5120	5120	7241	5120	2560	2560	1810	905	905	453	2b
H3221127	2560	1810	5120	2560	905	905	905	453	226	453	2b
H3221125	5120	5120	14482	5120	3620	3620	3620	3620	3620	2560	2b

A(H3N2) (Cluster 3) - reactive to A/Darwin/9/2021 Egg and A/Darwin/6/2021 Cell based antisera (low cross-reactivity to other antisera for some samples)

	A/Tasmania/503/2020 Egg	A/Tasmania/503/2020 Cell	A/Darwin/9/2021 Egg	A/Darwin/6/2021 Cell	A/Hong Kong/ 2671/2019 Egg	A/Hong Kong/ 45/2019 Cell	A/South Australia/ 34/2019 Egg	A/Switzerland/ 8060/2017	A/Singapore/INFIMH-16-0019/2016	A/Hong Kong/ 4801/2014	Clade
A/Tasmania/503/2020 Egg	1810	80	640	640	40	40	57	80	113	160	
A/Tasmania/503/2020 Cell	226	1810	320	226	113	226	226	113	160	160	
A/Darwin/9/2021 Egg	160	226	3620	2560	160	160	160	160	80	80	
A/Darwin/6/2021 Cell	226	160	2560	5120	113	80	160	113	113	113	
A/Hong Kong/2671/2019 Egg	1810	905	905	3620	5120	1810	905	452	1280	905	
A/Hong Kong/45/2019 Cell	160	1810	452	320	320	640	160	160	113	160	
A/South Australia/34/2019 Egg	452	452	226	320	160	80	452	320	1280	905	
A/Switzerland/8060/2017	640	640	320	320	320	320	320	5120	5120	5120	
A/Singapore/INFIMH-16-0019/2016	320	640	320	320	320	226	226	640	5120	5120	
A/Hong Kong/4801/2014	320	640	452	320	320	320	320	1280	5120	5120	
H3230106	453	453	5120	3620	320	905	905	453	1280	905	2a.1
H3221130	640	905	5120	2560	320	640	453	320	320	320	2a.1
H3221131	640	640	5120	1280	320	320	320	320	226	113	2a.1
H3221132	640	640	5120	3620	320	453	453	453	320	320	2a.1
H3221104	320	453	1810	1810	320	320	320	320	160	160	2a.1
H3221101	905	905	5120	5120	640	905	640	640	640	453	2a.1a
H3221107	640	453	3620	2560	453	1810	453	226	453	320	2a.1a
H3221103	640	640	5120	1810	320	453	640	640	453	453	2a.1a
H3221106	320	320	2560	1280	226	226	453	320	453	320	2a.1a
H3230108	1280	905	5120	2560	453	453	1280	1280	453	1280	2a.1b
H3221114	1280	905	5120	1810	640	905	905	905	453	453	2a.3
H3221136	1280	640	5120	2560	453	640	640	320	320	320	2a.3a
H3230133	1280	1280	5120	1810	1280	1280	640	1280	1280	905	2b
H3230139	1810	1280	2560	1280	453	640	905	453	453	453	2b
H3230122	1280	1280	3620	1280	1280	1810	640	1810	1810	1280	2b
H3230115	640	1280	1810	905	905	905	1280	1280	905	640	2b
H3221118	905	640	1810	640	640	905	640	905	453	453	2b
H3230131	640	640	1280	905	453	905	640	453	640	640	2b
H3221122	905	640	905	453	226	320	453	453	320	320	2b

Antigenic Characterization Summary

- Ferret antisera against both 5a.2 (A/Wisconsin/588/2019 & A/Victoria/2570/2019) and 5a.2a (A/Sydney/5/2021) viruses neutralized our circulating A(H1N1)pdm09 viral isolates in our surveillance network.

- Ferret antisera generated against 2a (A/Darwin/6/2021 & A/Darwin/9/2021) viruses neutralized our circulating A(H3N2) viral isolates in our surveillance network.

Notes on Vaccine Strain Recommendations

- The WHO influenza vaccine strain recommendations for the 2023-2024 Northern Hemisphere season are:
  - For the 2023-24 influenza vaccine A(H1N1) component: **A/Victoria/4897/2022-like** virus for the egg-based vaccine and **A/Wisconsin/67/2022-like** virus for the cell- or recombinant-based vaccine
    - ✓ **Based on our 2022-23 genetic and antigenic data, we agree with this recommendation**
  - For the 2023-24 influenza vaccine A(H3N2) component: **A/Darwin/9/2021-like** virus for the egg-based vaccine and **A/Darwin/6/2021-like** virus for the cell- or recombinant-based vaccine
    - ✓ **Based on our 2022-23 genetic and antigenic data, we agree with this recommendation**
  - For the 2023-24 influenza vaccine B/Victoria component: **B/Austria/1359417-like** virus for the egg-based and cell- or recombinant-based vaccines
    - ✓ We do not have 2022-23 data to agree or disagree with this recommendation
  - The above three influenza strains are recommended for the trivalent vaccine, and for the quadrivalent vaccine to include these three in addition to the B/Yamagata component, **B/Phuket/3073/2013-like** virus for the egg-based and cell- or recombinant-based vaccines
    - ✓ We do not have 2022-23 data to agree or disagree with this recommendation

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Recruit Surveillance Sites

Marine Corps Recruit Depot San Diego
Marine Corps Recruit Depot Parris Island
Recruit Training Command Great Lakes
Fort Leonard Wood
Fort Benning
Fort Jackson
Lackland Air Force Base
Coast Guard Training Center Cape May

CDC-California Department of Health Border Infectious Disease Surveillance Sites

Clinica de Salud del Pueblo Brawley
Clinica de Salud del Pueblo Calexico
Clinica de Salud del Pueblo El Centro
San Ysidro Health Center
Pioneers Memorial Healthcare
El Centro Regional Medical Center
Sharp Chula Vista Hospital
Mexicali General Hospital

DoD Beneficiary Surveillance Sites

Branch Health Clinic/ Marine Corps Air Station Yuma
Naval Hospital Camp Pendleton
Captain James A. Lovell Federal Health Care Center (Naval Hospital Great Lakes)
Robert E. Bush Naval Hospital Twenty Nine Palms
Naval Training Center San Diego
Naval Medical Center San Diego
Naval Branch Health Clinic Kearny Mesa
Naval Health Clinic Lemoore
Naval Hospital Yokosuka
Naval Branch Health Clinic Naval Base San Diego
Naval Medical Center Portsmouth
Boone Branch Health Clinic
Oceana Branch Health Clinic

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Extra Slides

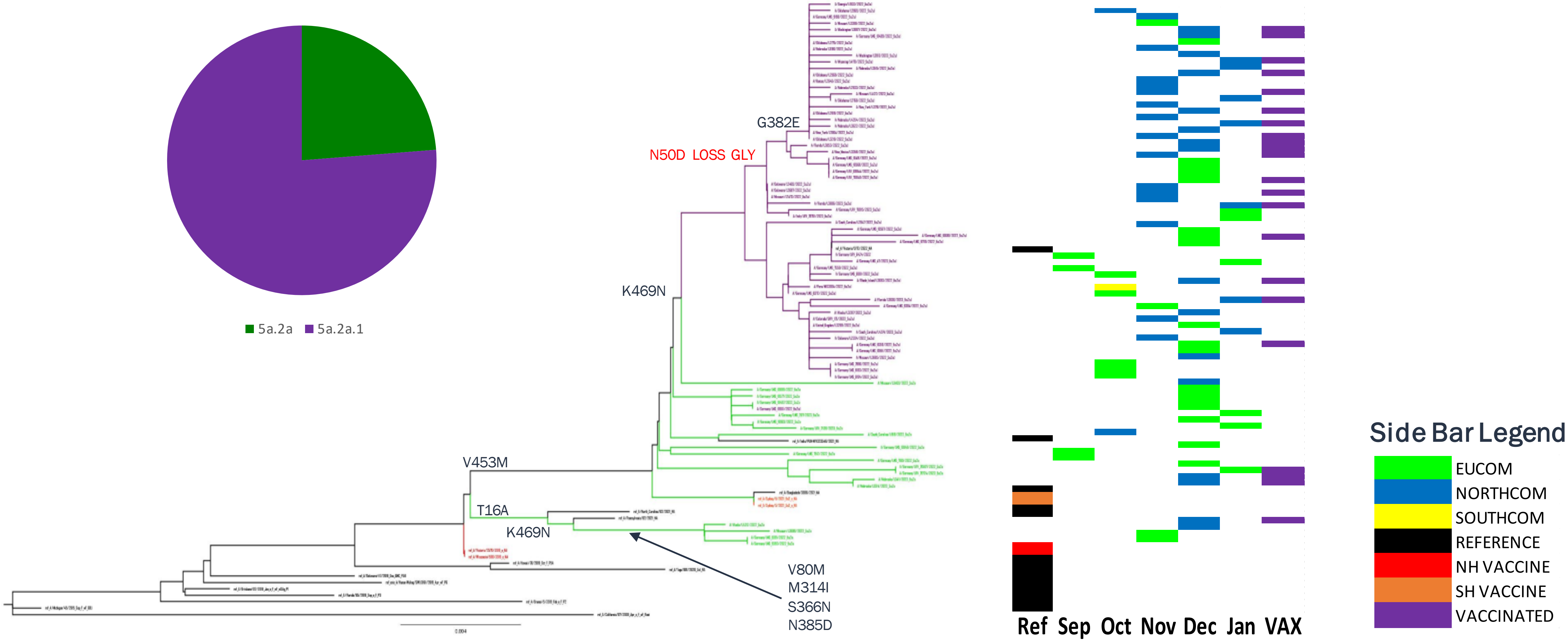
U.S. Service Members:
Cohort Study Design – Inpatient VE

- Same study parameters as case test-negative study except:
  - Cohort study design
  - Time Period: September 1, 2022 – January 7, 2023
  - Outcome: lab-confirmed influenza (rapid/PCR/culture) indicating hospitalization or inpatient stay with 1st or 2nd ICD-10-CM code for Influenza (J09-J11)
- Results:

Outcome	Vaccination Status	Case N (%)	Person-Years (PY)	Incidence Rate per 10,000 PY	Adjusted IRR (95% CI)*	Adjusted VE (95% CI)*
Lab-confirmed	Vaccinated	4 (18)	157,039	0.03	0.42 (0.14, 1.24)	58 (-24, 86)
	Unvaccinated	18 (82)	299,465	0.06		
Lab-confirmed & inpatient flu diagnosis	Vaccinated	8 (20)	157,039	0.05	0.46 (0.21, 1.00)	54 (0, 79)
	Unvaccinated	33 (80)	299,039	0.11		

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

Influenza A(H1N1)pdm09 NA



Influenza B/Victoria NA