

DoD Influenza Surveillance and Mid-Season Vaccine Effectiveness

Armed Forces Health Surveillance Division (AFHSD)

Naval Health Research Center (NHRC)

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) – 5 March 2021**

LTC Kevin Taylor, MD, MTM&H**

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



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Briefing Outline



Purpose: Provide an update to the VRBPAC on DoD influenza surveillance activities for 2020 -2021

1. Program Description
2. DoD Strain Circulation
3. **Limited** Molecular Analyses
4. Vaccine Effectiveness **in US Service Members**

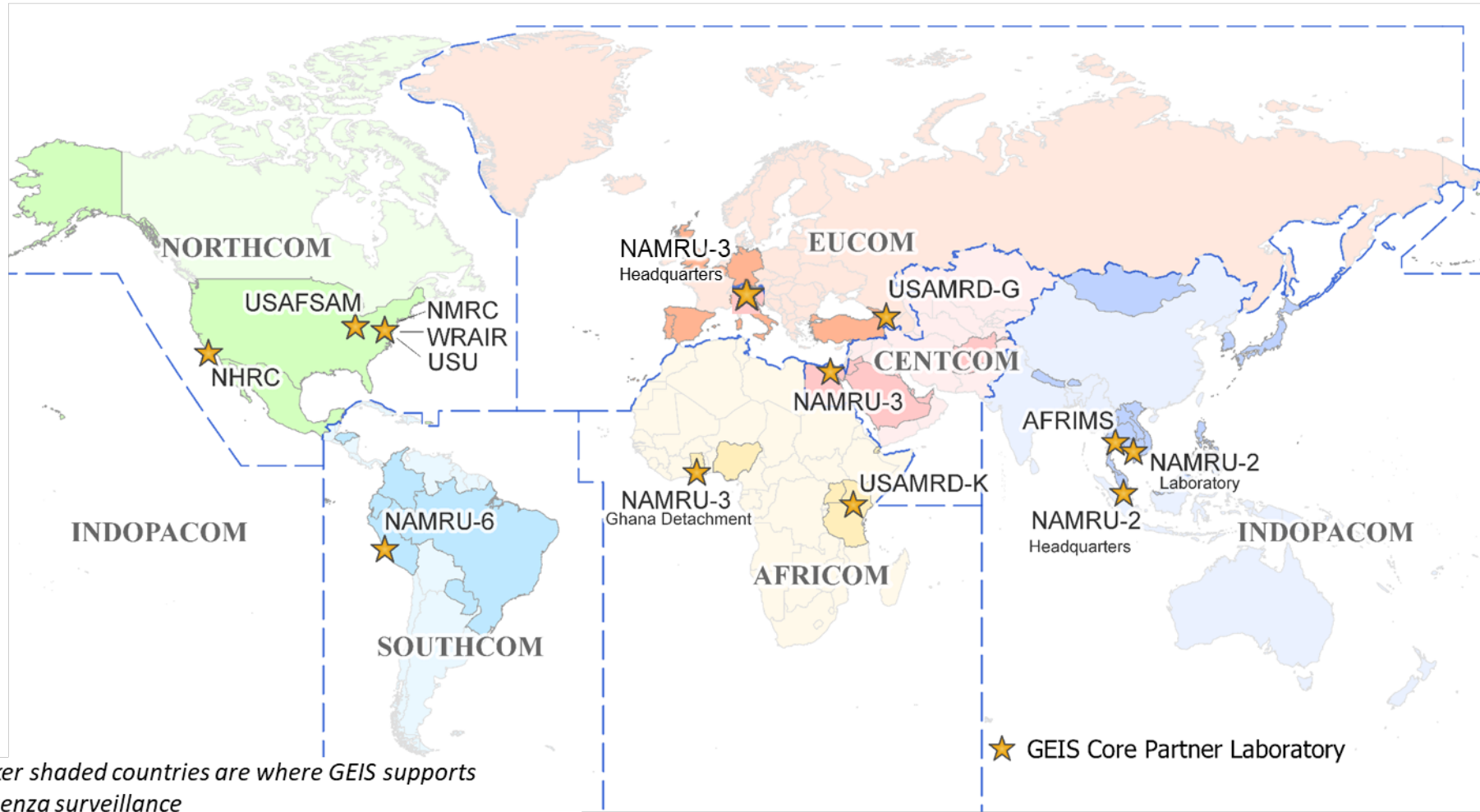
Breadth of DoD Influenza Surveillance



- **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
 - Yearly average: ~30,000 samples collected and analyzed each year
- **Comprehensive Epidemiology and Analysis Capabilities**
 - 1.33 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

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GEIS-Supported Influenza Surveillance Footprint



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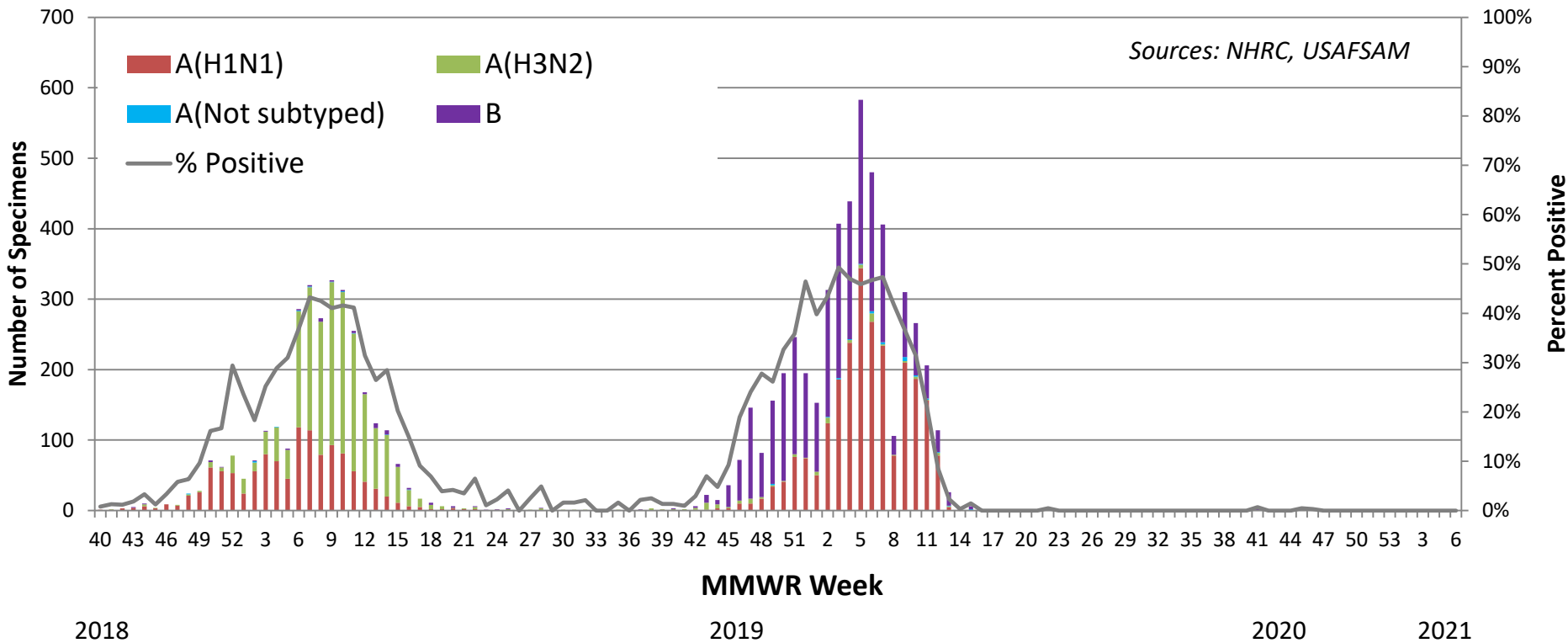
- **Common themes for the 2020-2021 season**
 - ALL laboratories and nations affected by the SARS-CoV-2 pandemic
 - Extensive restrictions and lockdowns (as well as high viral transmissibility) resulted in reagent shortages, shipping delays, staffing reductions, and low enrollment
 - Shift to testing and assay validation for SARS-CoV-2 over influenza
 - Surveillance estimates for DoD on the next few slides are dramatically lower than usual, and data was unable to be obtained for some countries
- **Country-specific examples**
 - Peru: nationwide shutdowns
 - Kenya/Tanzania: delay in shipments of reagents
 - Republic of Georgia: border shutdown

Subtype Circulation: North America



Number and Proportion of Specimens Positive for Influenza by Subtype

PANDEMIC: Jan 2020 - present



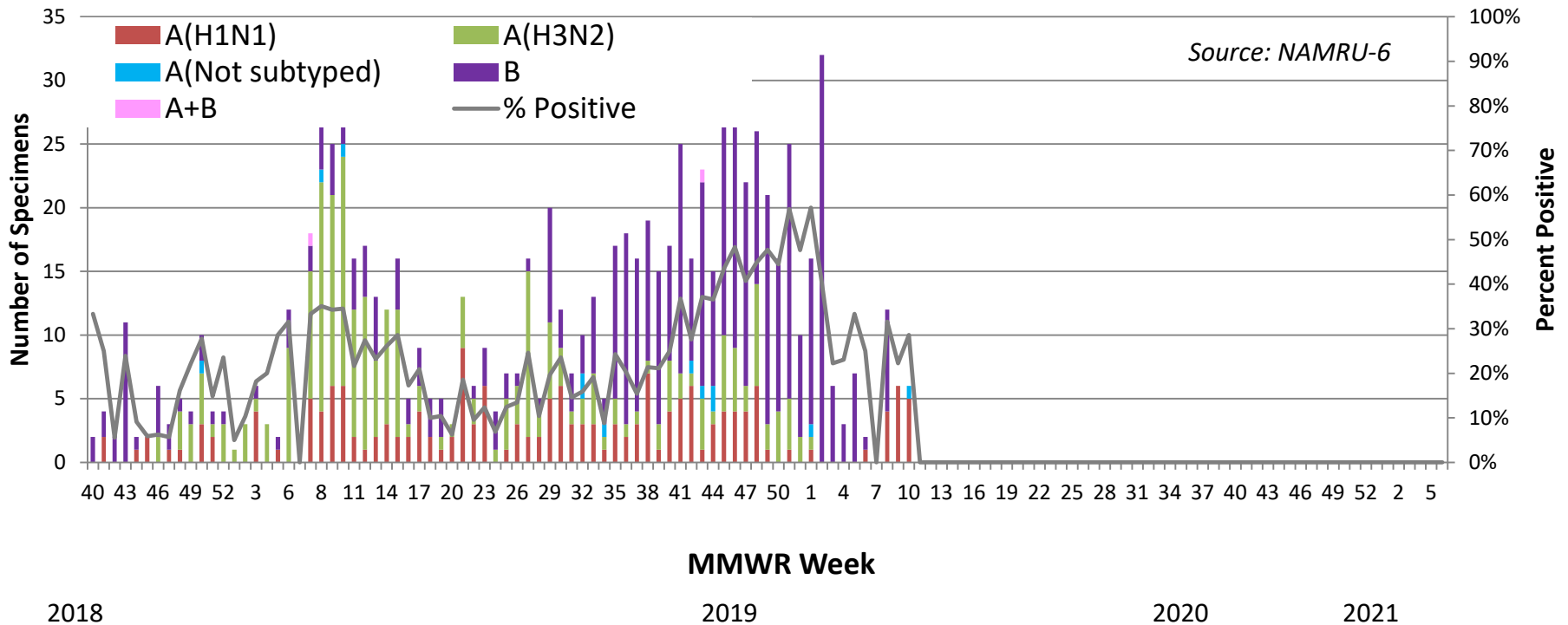
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Subtype Circulation: South America



Number and Proportion of Specimens Positive for Influenza by Subtype

PANDEMIC: Jan 2020 - present

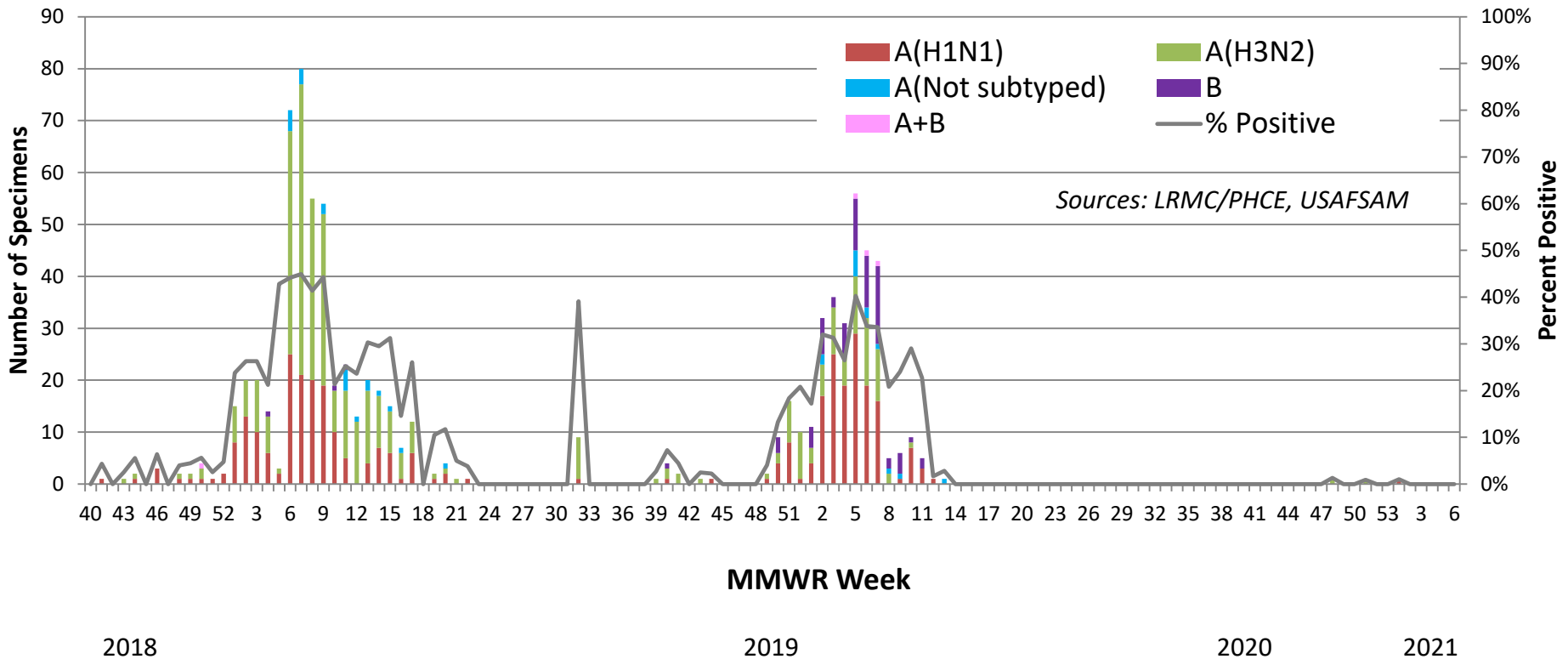


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Subtype Circulation: Europe

Number and Proportion of Specimens Positive for Influenza by Subtype

PANDEMIC: Jan 2020 - present



Sources: LRM/PHCE, USAFSAM

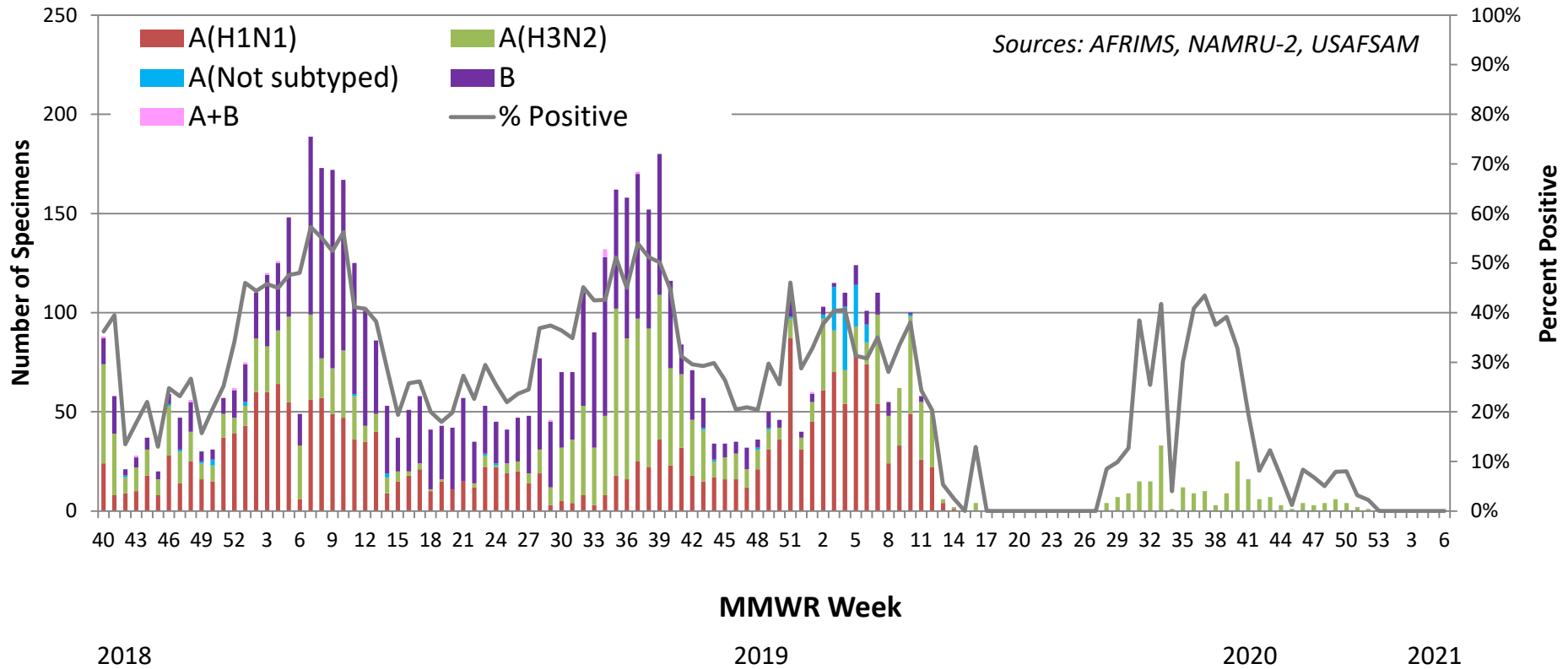
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Subtype Circulation: Asia



Number and Proportion of Specimens Positive for Influenza by Subtype

PANDEMIC: Jan 2020 - present



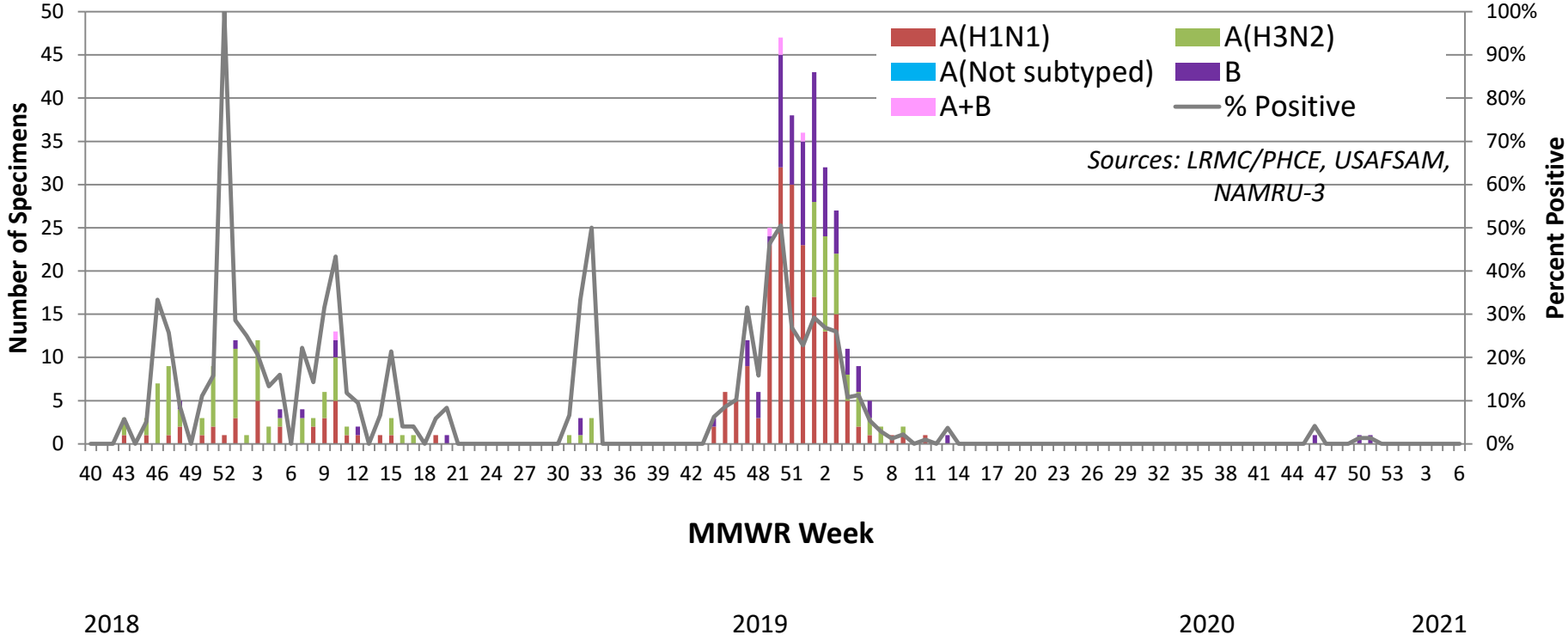
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Subtype Circulation: Middle East



Number and Proportion of Specimens Positive for Influenza by Subtype

PANDEMIC: Jan 2020 - present



Sources: LRMC/PHCE, USAFSAM, NAMRU-3

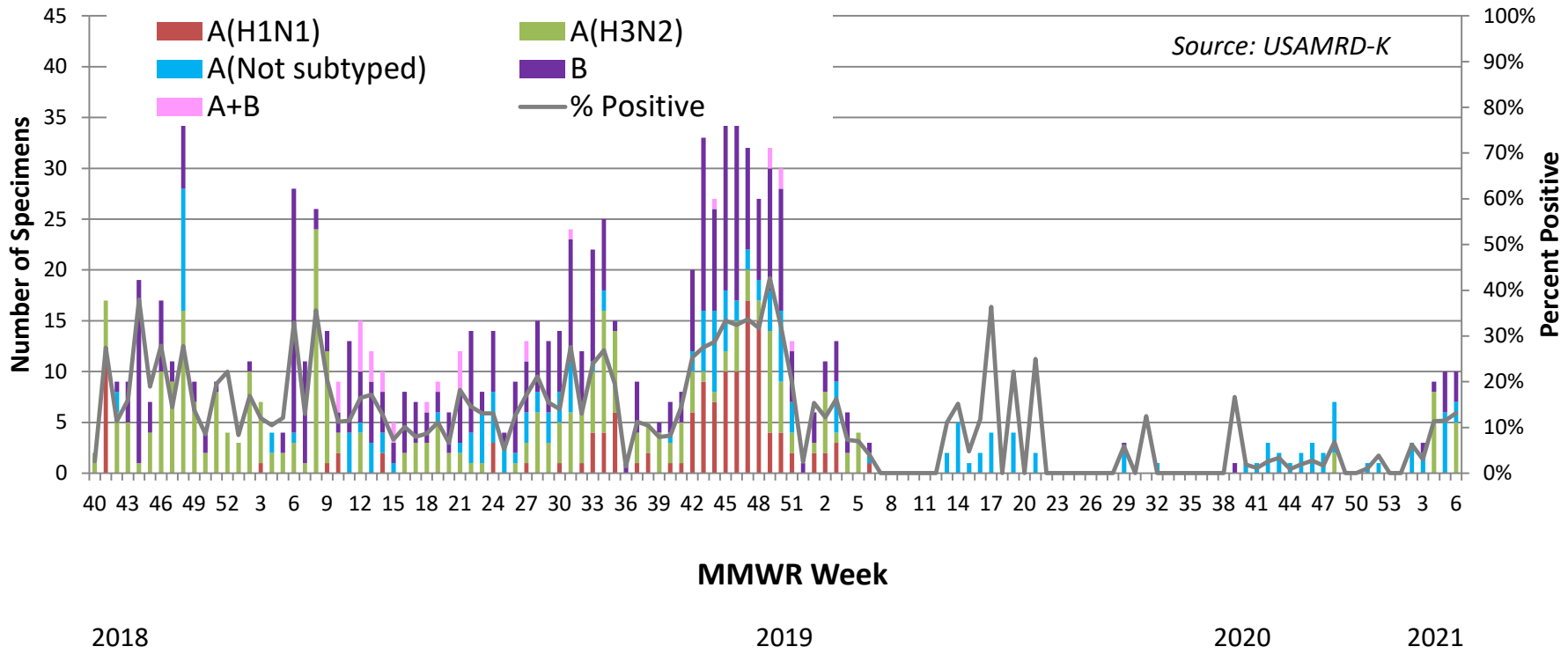
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Subtype Circulation: East Africa



Number and Proportion of Specimens Positive for Influenza by Subtype

PANDEMIC: Jan 2020 - present



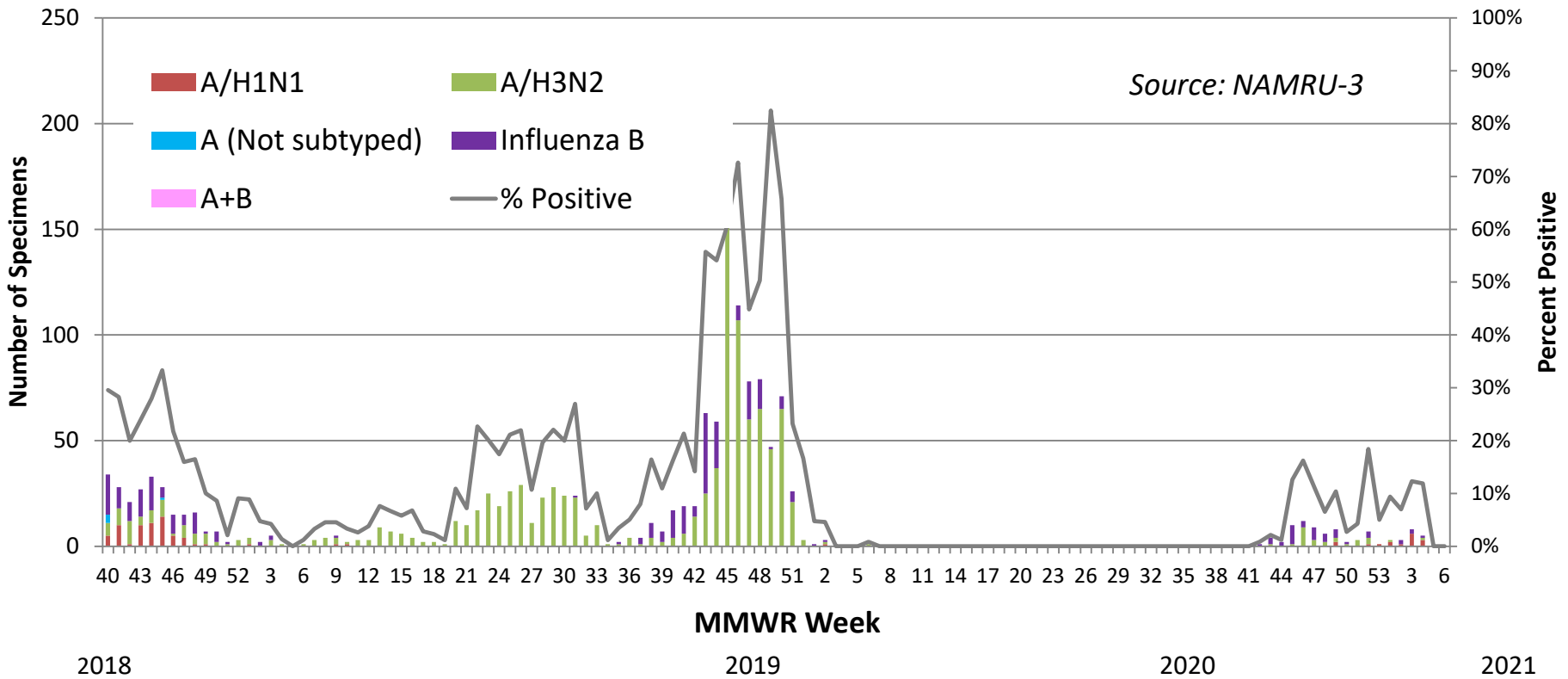
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Subtype Circulation: West Africa (Ghana)



Number and Proportion of Specimens Positive for Influenza by Subtype

PANDEMIC: Jan 2020 - present



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Summary of Circulating Subtype 2020-2021 Influenza Season



- Influenza surveillance has been **limited** during the 2020-2021 season and positivity is much lower compared to previous seasons
 - **North America:** no positive cases reported in the past several weeks
 - **South America:** no positive cases reported in the past several weeks
 - **Europe:** reduced testing with few **influenza A** cases
 - **Asia:** shows **A(H3N2)** predominating at lower levels in weeks 29-42, but disappearing after week 52
 - **Middle East:** limited testing with sparse **influenza B**
 - **East Africa:** shows **influenza A** predominating at lower levels with **influenza B** beginning to circulating after week 5
 - **West Africa:** shows **A(H3N2)** and **influenza B** predominating at lower levels compared to previous season

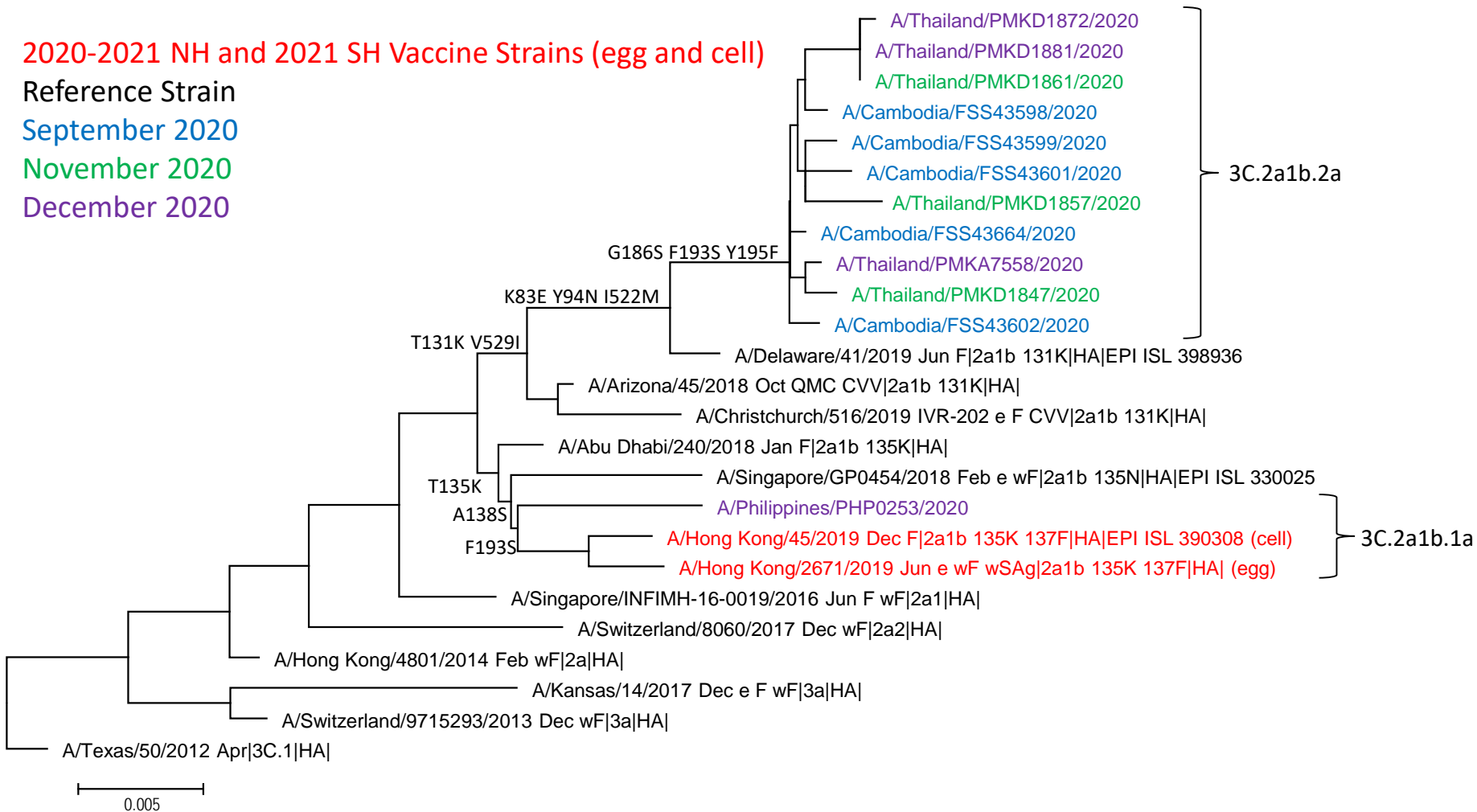
DoD / USAFSAM Phylogenetic Analysis 2020-2021 Influenza Season

2020-2021 A(H3N2) HA Phylogenetic Tree (n=12)



2020-2021 NH and 2021 SH Vaccine Strains (egg and cell)

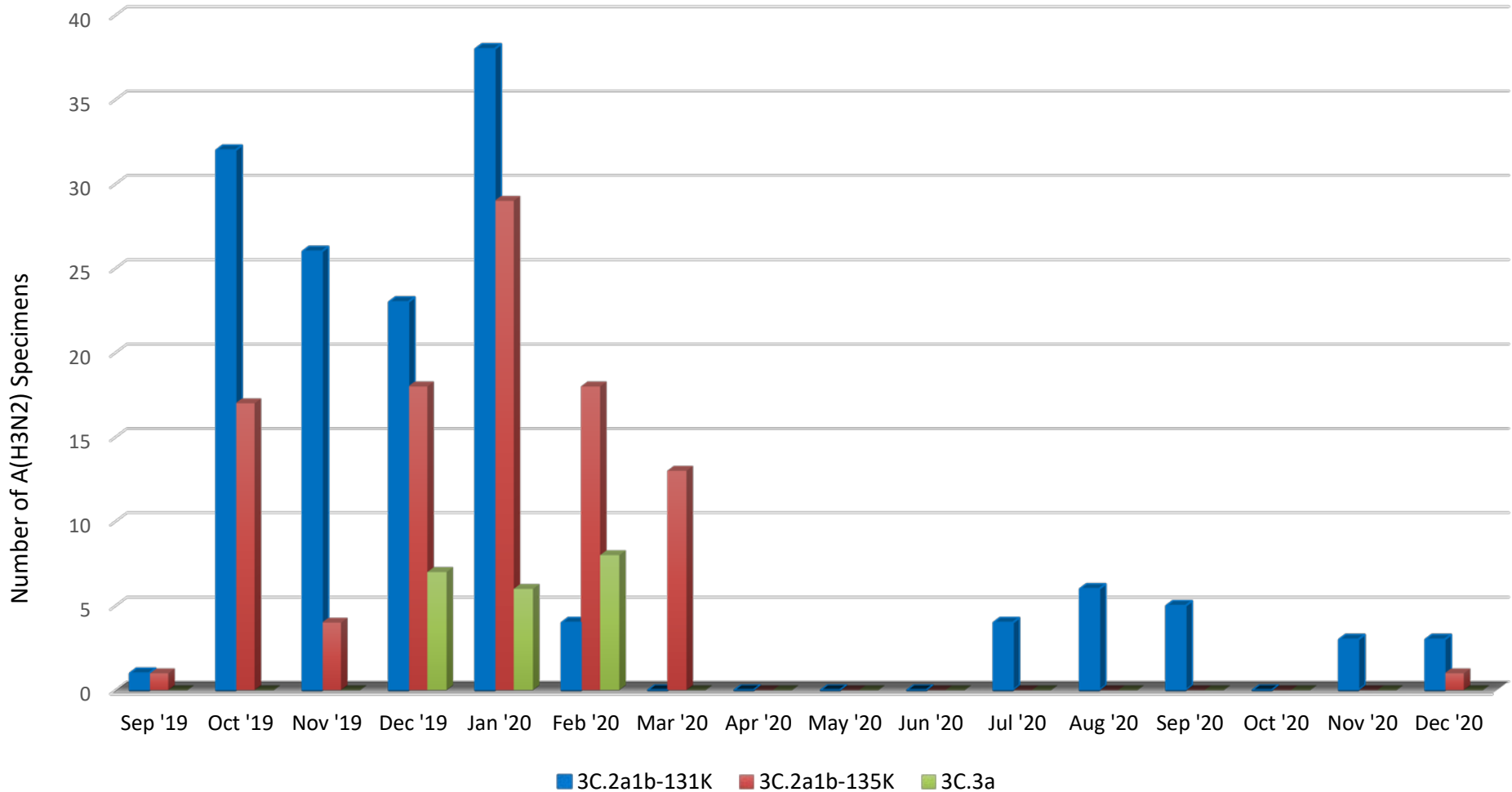
Reference Strain
September 2020
November 2020
December 2020



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A(H3N2) HA Clades

Sep 2019-Dec 2020



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Discussion



- Influenza rates were very low in the 2020-2021 season, resulting in only 12 influenza A(H3N2) sequences from the INDOPACOM region available for analysis
- All influenza A(H3N2) HA sequences resided in the 3C.2a1b clade with the majority (92%) in subgroup T131K (3C.2a1b.2a) with the remaining sequence in the T135K group (3C.2a1b.1a)
- The WHO strain recommendation for the 2021-2022 Northern Hemisphere influenza vaccine A(H3N2) component, A/Cambodia/e0826360/2020 for the egg-based and cell- or recombinant-based vaccine, inhibit viruses in the 3C.2a1b.1a and 3C.2a1b.2a clades well
- No influenza A(H1N1)pdm09, B/Victoria, or B/Yamagata sequence data were available for the 2020-2021 season, however the strain clades circulating in the USAFSAM/DoD data at the end of the 2019-2020 season were consistent with the WHO strain recommendations for the 2021-2022 Northern Hemisphere influenza vaccine

Vaccine Strain Recommendations



Based on both the 2019-2020 and 2020-2021 seasons, our genetic data align well with the following WHO recommendations for the 2021-2022 Northern Hemisphere influenza vaccine:

- For the 2021-2022 influenza vaccine A(H1N1) component: A/Victoria/2570/2019-like virus for the egg-based vaccine and A/Wisconsin/588/2019-like virus for the cell- or recombinant-based vaccine
- For the 2021-2022 influenza vaccine A(H3N2) component: A/Cambodia/e0826360/2020-like virus for the egg-based and cell- or recombinant-based vaccine
- For the 2021-2022 influenza vaccine B/Victoria component: B/Washington/02/2019 for the egg-based and cell- or recombinant-based vaccines
- 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

DoD / AFHSD Service Member Vaccine Effectiveness (VE) Estimates

Analysis Overview



- Mid-year estimates provided by:
 - AFHSD AF Satellite - US Air Force School of Aerospace Medicine (USAFSAM)
 - Naval Health Research Center (NHRC)
 - AFHSD Epidemiology and Analysis Section (E&A)
- Case test-negative control studies used to estimate VE
 - All studies used case test-negative control method
 - Each influenza infection from USAFSAM and NHRC was confirmed by RT-PCR or viral culture; AFHSD also used positive rapid tests (but excluded rapid test negatives)
 - Analyses performed for influenza types and subtypes

Study Design



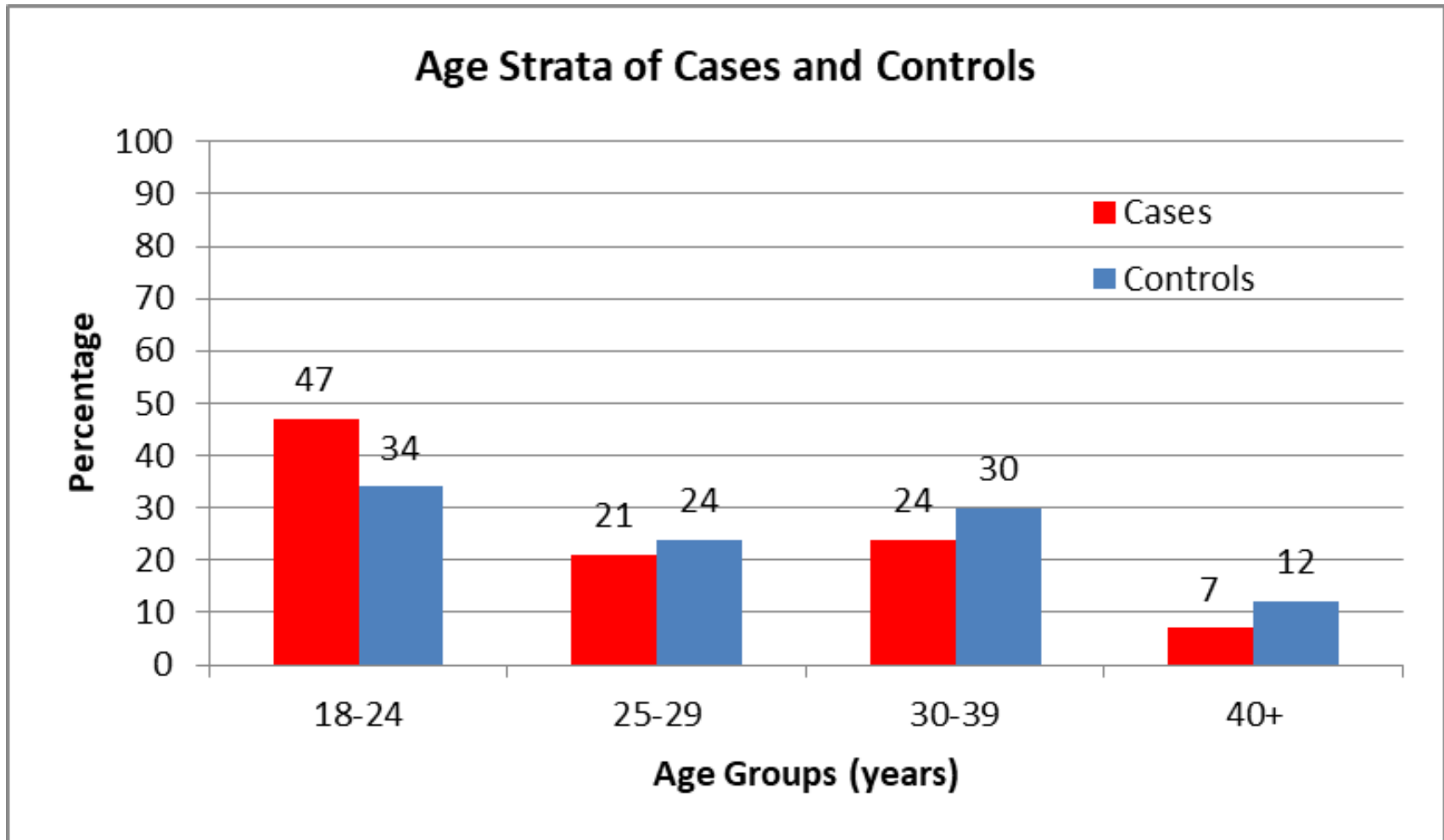
- Case / Test-negative control design
- Population: Active component Service Members
 - Army, Navy, Air Force, Marines
 - CONUS and OCONUS
- Time Period: October 4, 2020 – February 13, 2021
- Lab-confirmed flu cases: positive by rapid, RT-PCR, or culture assays
- Test-negative Controls: negative by RT-PCR or culture assays (subjects with negative rapid excluded)
- Models adjusted for sex, age category, prior vaccination, and month of diagnosis
- Overall and type-specific VE calculated (data did not support sub-type analysis)

Vaccination Information & Case Subtypes



- Vaccination
 - IIV was the only vaccine type among the study subjects
 - 95% of subjects had prior flu vaccine in previous 5 years
- Cases
 - Influenza A (any subtype) = 219
 - Influenza A(H3N2) = 0
 - Influenza A(H1N1) = 1
 - Influenza B = 171

Cases and Controls by Age Group



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Interim VE Estimates 2020-2021



Influenza Type	Vaccination Status	Cases N (%)	Controls N (%)	Crude VE (95% CI)	Adjusted VE (95% CI)*
Any Influenza	Vaccinated	141 (38)	7049 (56)	54 (43, 62)	29 (9, 44)
	Unvaccinated	234 (62)	5432 (44)		
Influenza A	Vaccinated	74 (34)	7049 (56)	61 (48, 70)	15 (-18, 39)
	Unvaccinated	145 (66)	5432 (44)		
Influenza B	Vaccinated	74 (43)	7049 (56)	41 (20, 57)	40 (16, 57)
	Unvaccinated	97 (57)	5432 (44)		

*Adjusted for sex, age, and month of diagnosis

Summary of DoD VE Results



- Statistically significant VE estimates indicated an overall midseason VE of **29% in Service members only**
 - VE for influenza B was 40%, indicating moderate protection
 - VE for influenza A was low, but not statistically significant (15%)
 - VE was unable to be calculated for other populations due to insufficient case numbers

- Generalizability
 - Subjects were medically attended; did not assess vaccine impact on less severe cases
 - Active Duty military population is highly immunized; this could have a negative impact on VE (potential method issues and biological effects such as attenuated immune response with repeated exposures)
 - Populations are younger; did not assess vaccine impact in older, high-risk populations

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Ms. Kathy Bush
Mr. Joshua Cockerham
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COL Mark Fukuda
COL John Maza
COL Norm Waters
LTC Stefan Fernandez
MAJ Katie Poole-Smith
Dr. Chonticha Klungthong
Ms. Thipwong Tipawan
Ms. Tippa Wongstitwilairoong

LRMC/PHC-Europe

COL Rodney Coldren
COL Alexander Kayatani
CPT Cole Anderson
SSgt Brianne Holdbrook
Dr. Michael Koenig
Mr. Fritz Castillo

NAMRU-2

CAPT Patrick Blair
LCDR Robert Hontz
LCDR Jose Garcia
CDR Frederick Stell
Mr. John Brooks
Mr. Vireak Heang
Mr. Agus Rachmat
Ms. Chenda Yi

NAMRU-3

LCDR Michael Gregory
LCDR David Wolfe
Dr. Hala Bassaly
Dr. Anne Fox
Dr. Emad Mohareb
Dr. Mayar Said
Dr. Tamer Saied
Mr. Ehab Amir

NAMRU-6

LT Eugenio Abente
Dr. Sonia Ampuero
Dr. Max Grogl
Dr. Yeny Tinoco
Dr. Marita Silva
Dr. Giselle Soto
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Ms. Vumilia Mwalongo

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Dr. William Ampofo
Dr. Ivy Asante
Ms. Augustina Arjarquah
Mr. Erasmus Kotey

Questions?



LTC Kevin Taylor, MD, MTM&H
Focus Area Chief, AFHSD-Global Emerging Infections Surveillance Branch
Tel: 301-319-3248
E-mail: kevin.m.taylor4.mil@mail.mil

COL Douglas Badzik, MD, MPH
Chief, Armed Forces Health Surveillance Division
E-mail: douglas.a.badzik.mil@mail.mil

CAPT Guillermo Pimentel, PhD
Chief, AFHSD-Global Emerging Infections Surveillance Branch
E-mail: guillermo.pimentel2.mil@mail.mil