# 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**


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


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# Briefing Outline

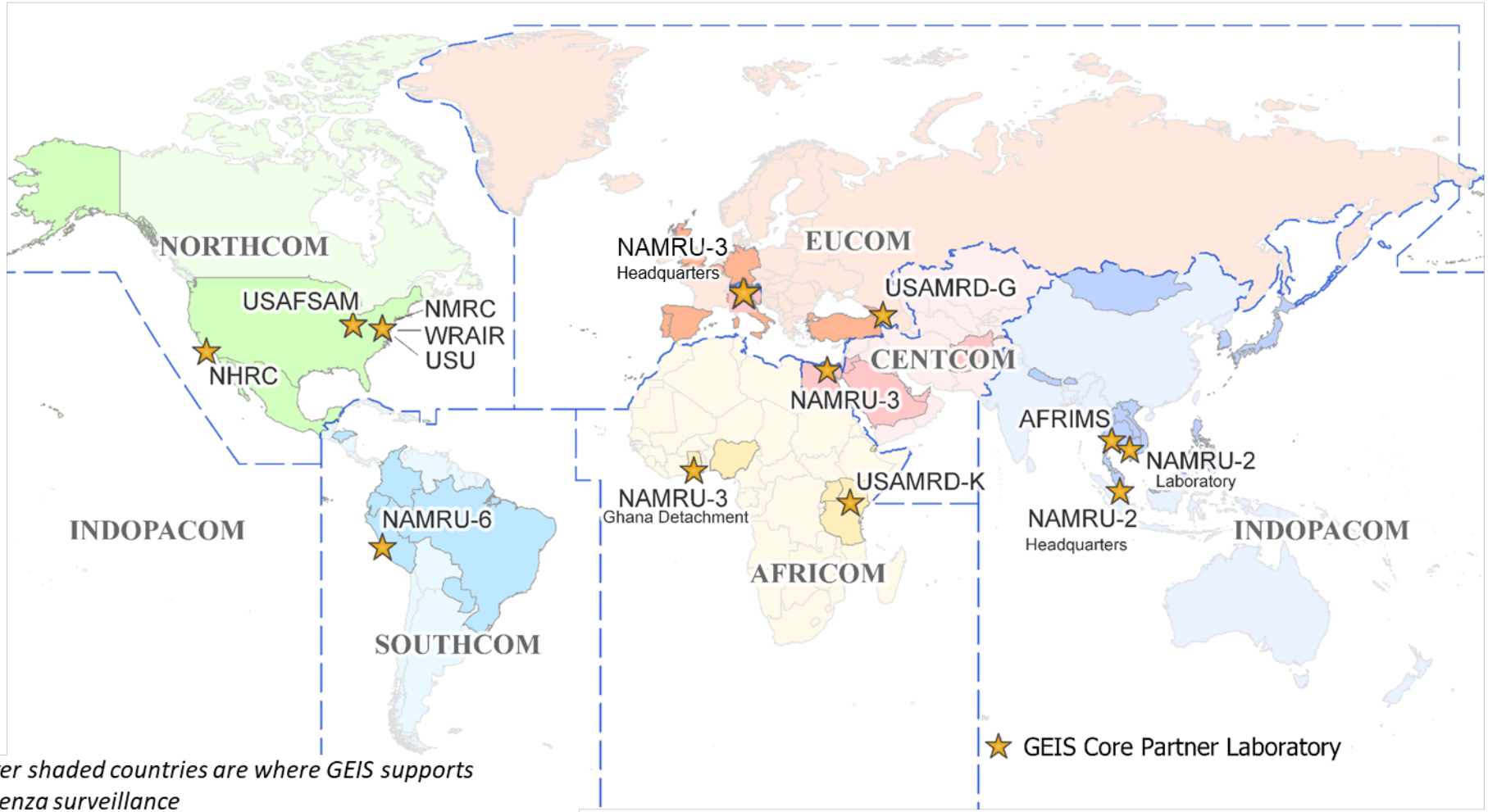
**Purpose: Provide an update to the VRBPAC on DoD influenza surveillance activities for 2020 -2021**

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

# GEIS-Supported Influenza Surveillance Footprint




*Darker shaded countries are where GEIS supports influenza surveillance*

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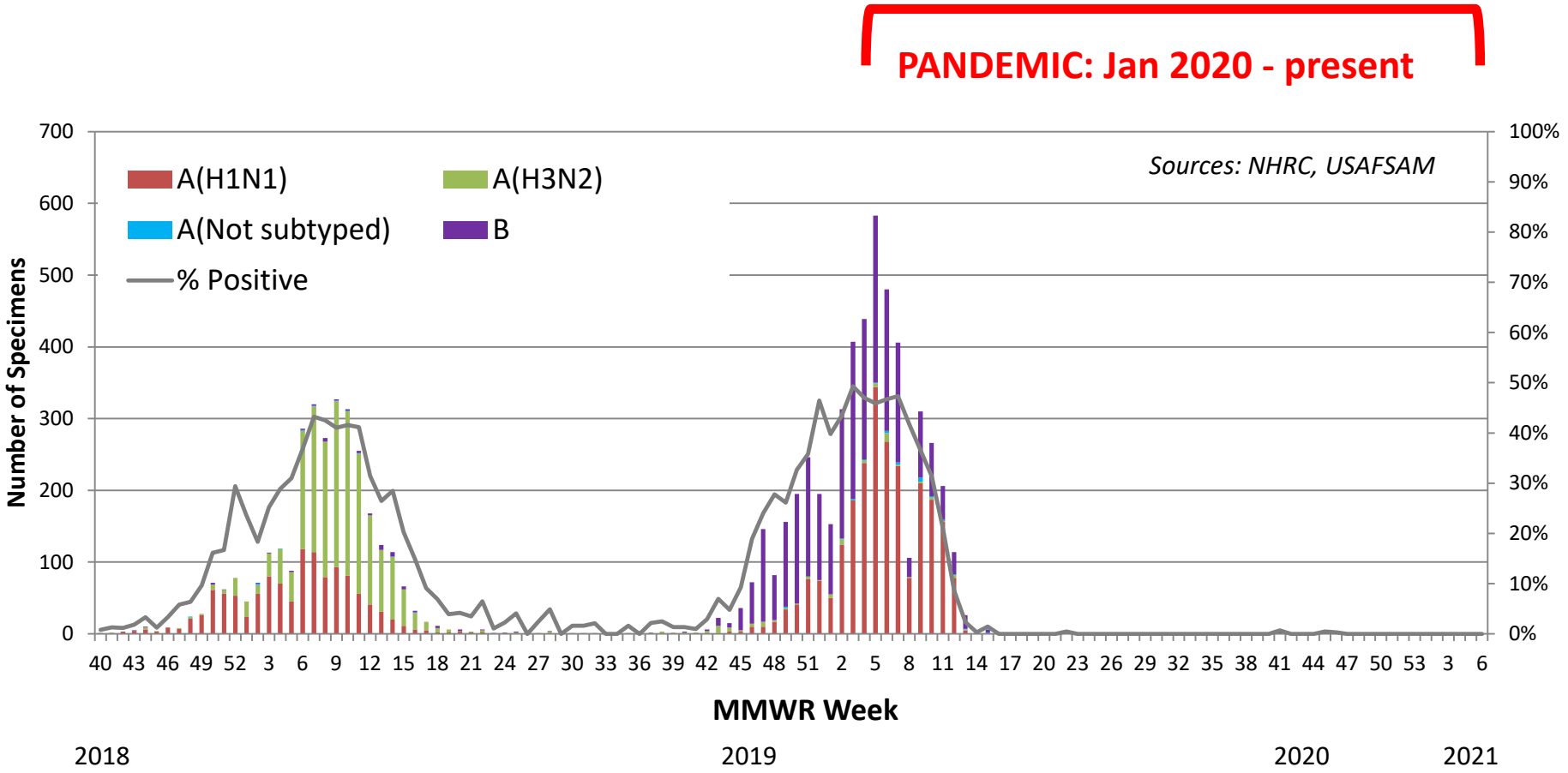
# DoD Influenza Subtype Circulation

- **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

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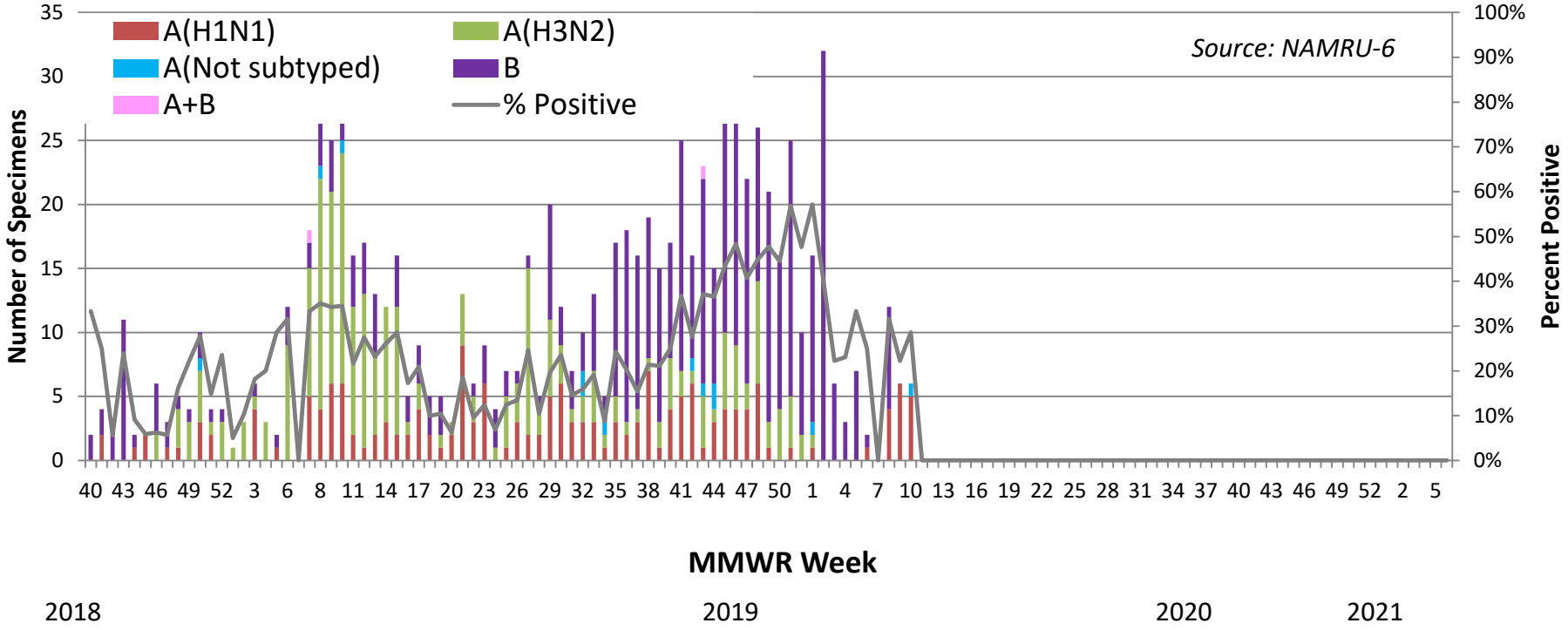
# Subtype Circulation: South America

Number and Proportion of Specimens Positive for Influenza by Subtype

**PANDEMIC: Jan 2020 - present**

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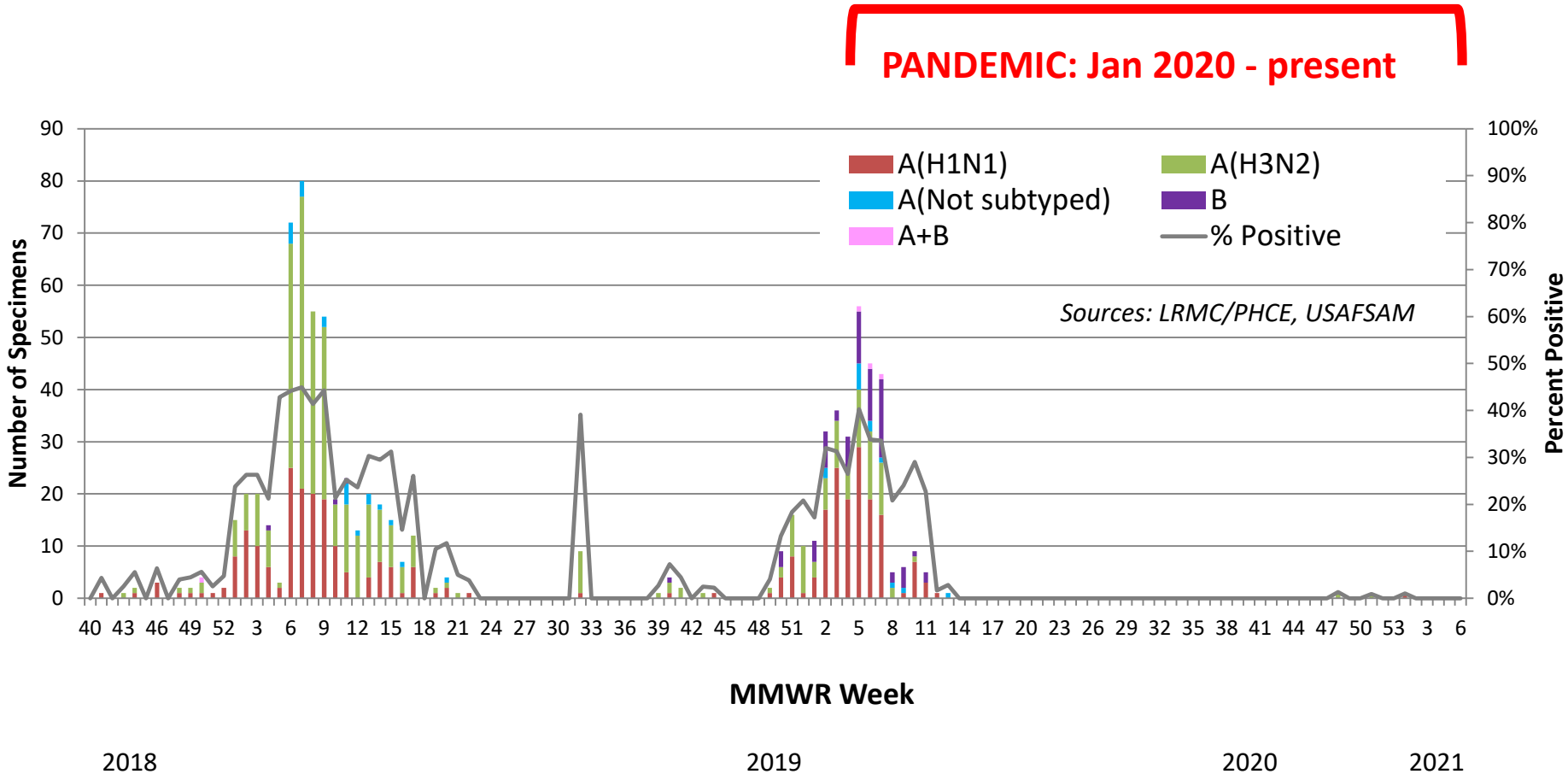
# Subtype Circulation: Europe

Number and Proportion of Specimens Positive for Influenza by Subtype

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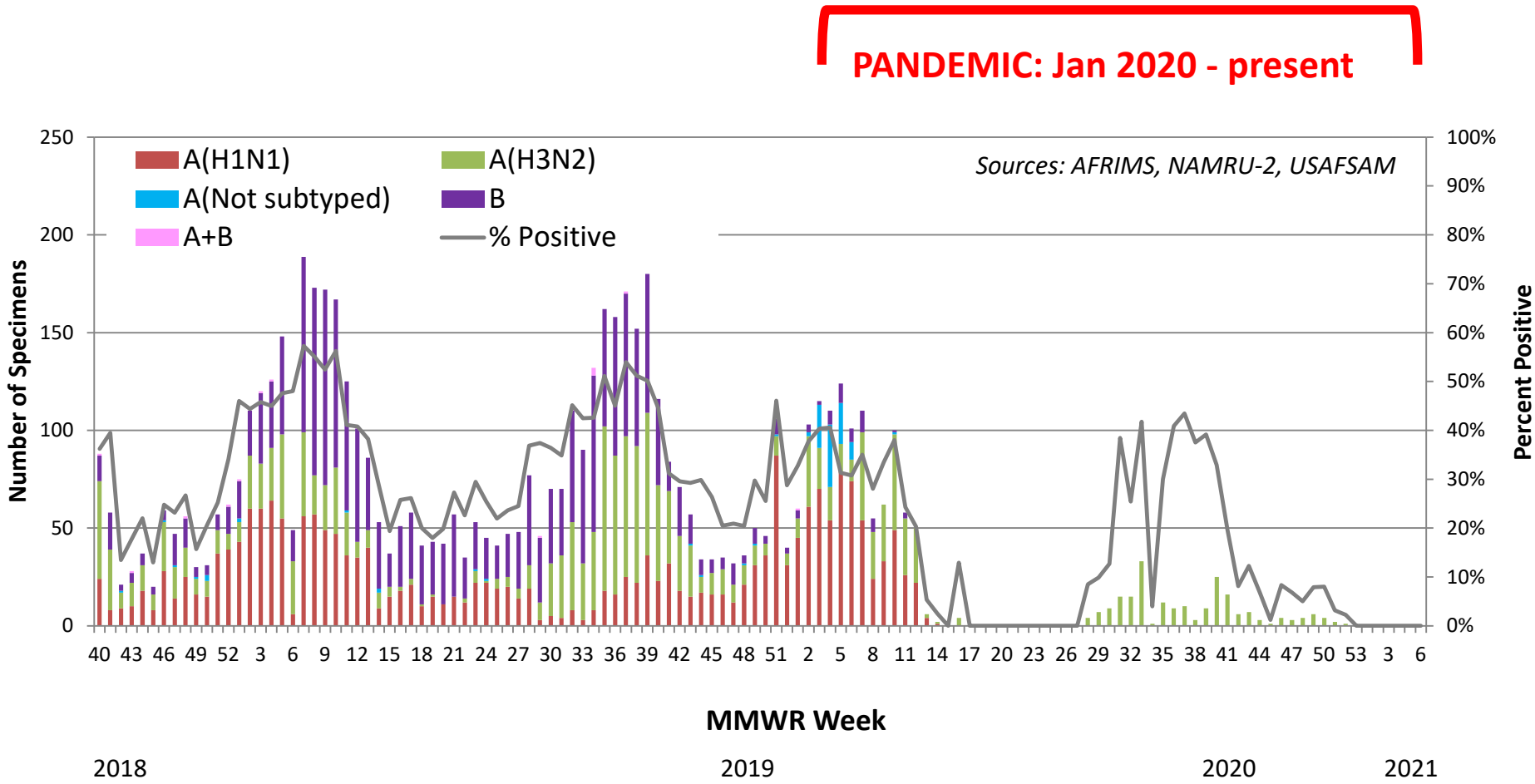
# Subtype Circulation: Asia

Number and Proportion of Specimens Positive for Influenza by Subtype

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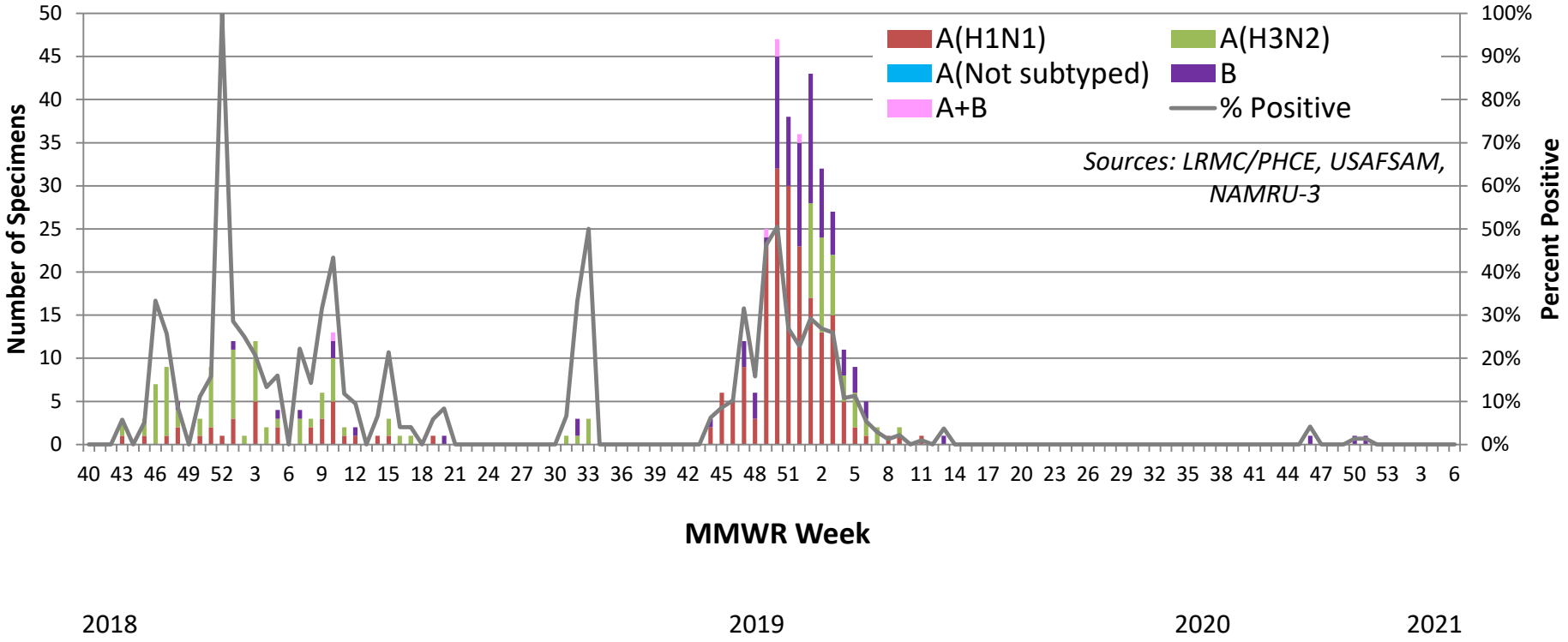
# Subtype Circulation: Middle East

Number and Proportion of Specimens Positive for Influenza by Subtype

**PANDEMIC: Jan 2020 - present**

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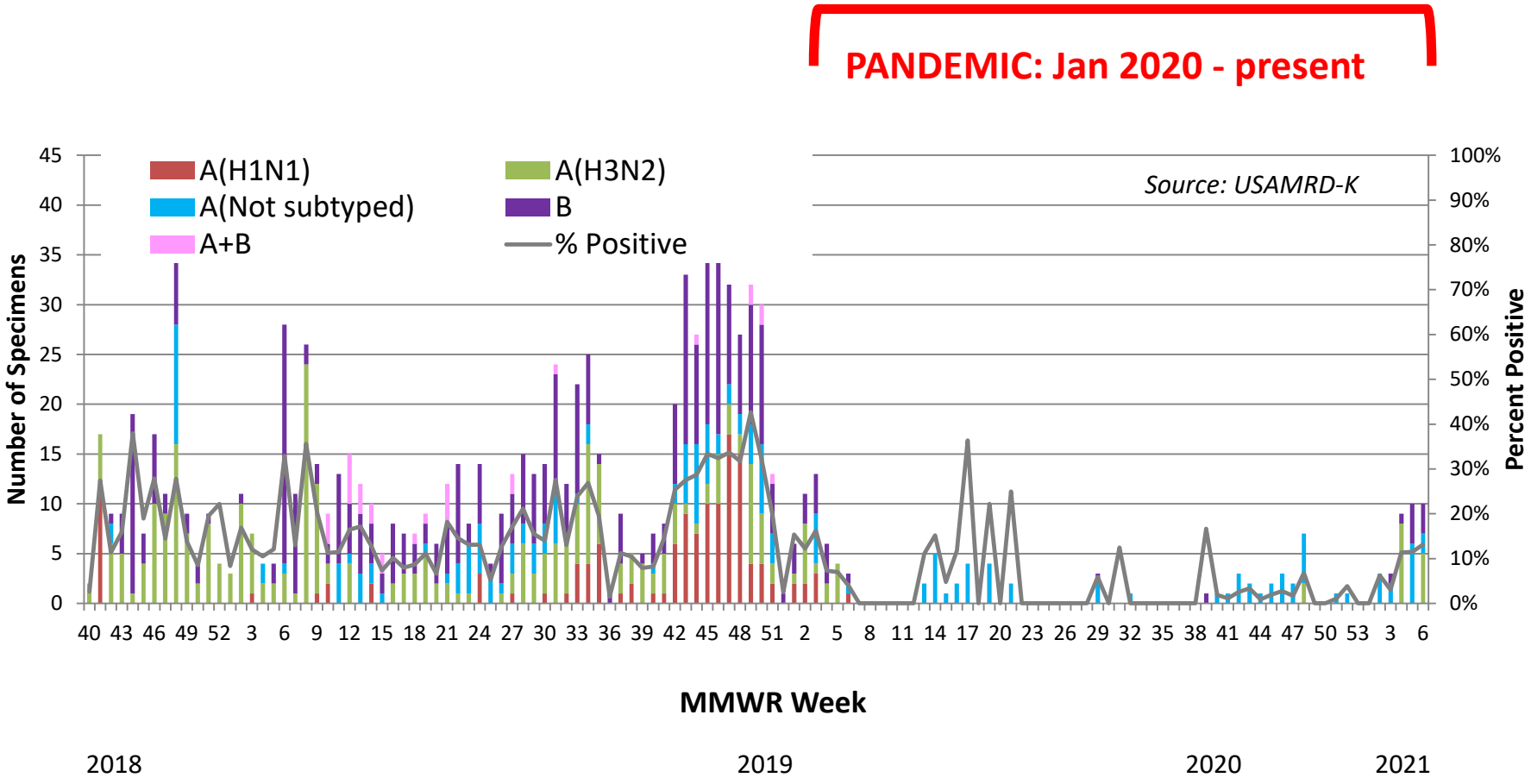
# Subtype Circulation: East Africa

Number and Proportion of Specimens Positive for Influenza by Subtype

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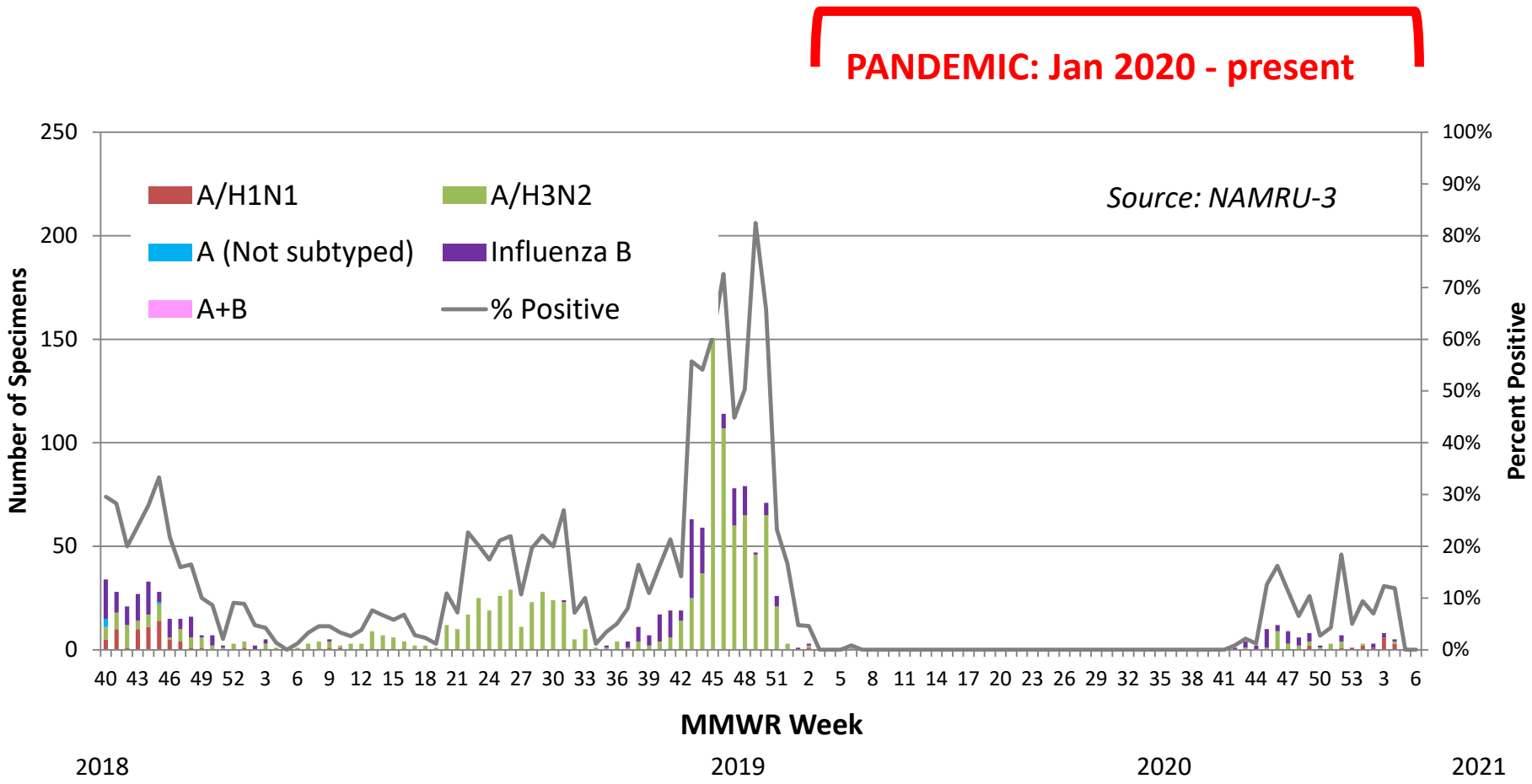
# Subtype Circulation: West Africa (Ghana)

Number and Proportion of Specimens Positive for Influenza by Subtype

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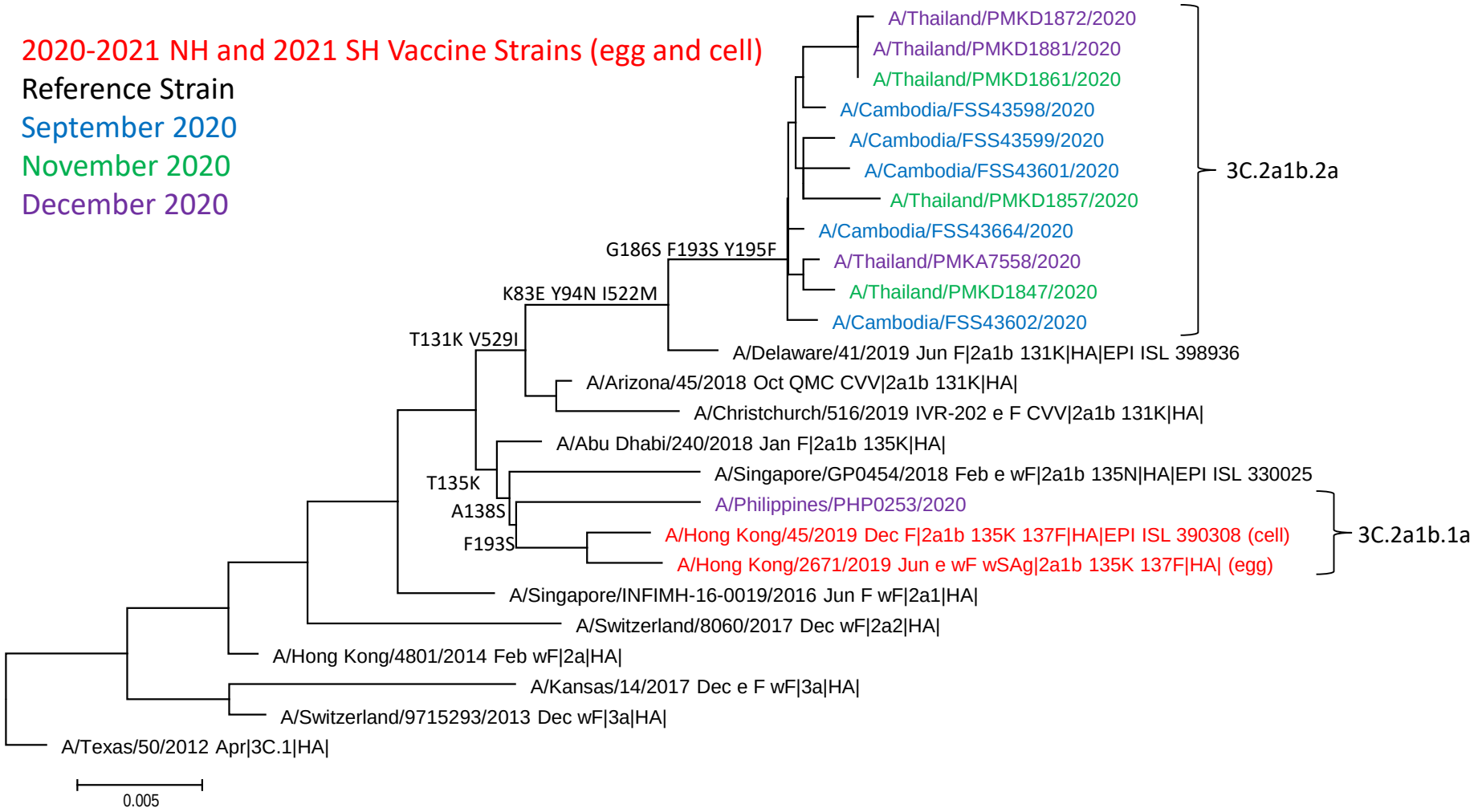
# Summary of Circulating Subtype 2020-2021 Influenza Season

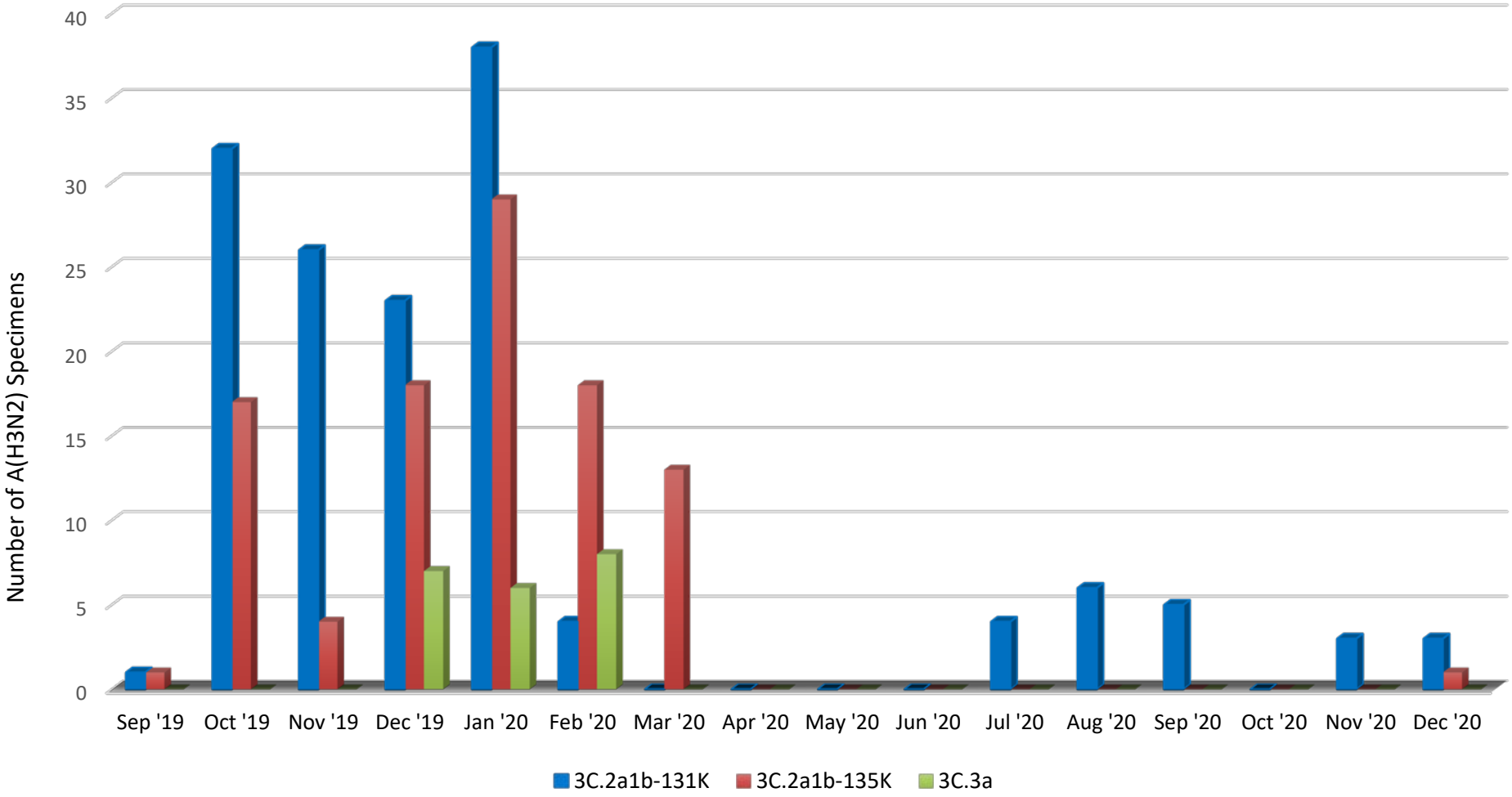
- Influenza surveillance has been **limited** during the 2020-2021 season and positivity is much lower compared to previous seasons
  - **North America:** no positive cases reported in the past several weeks
  - **South America:** no positive cases reported in the past several weeks
  - **Europe:** reduced 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)



# A(H3N2) HA Clades
# Sep 2019-Dec 2020



# 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

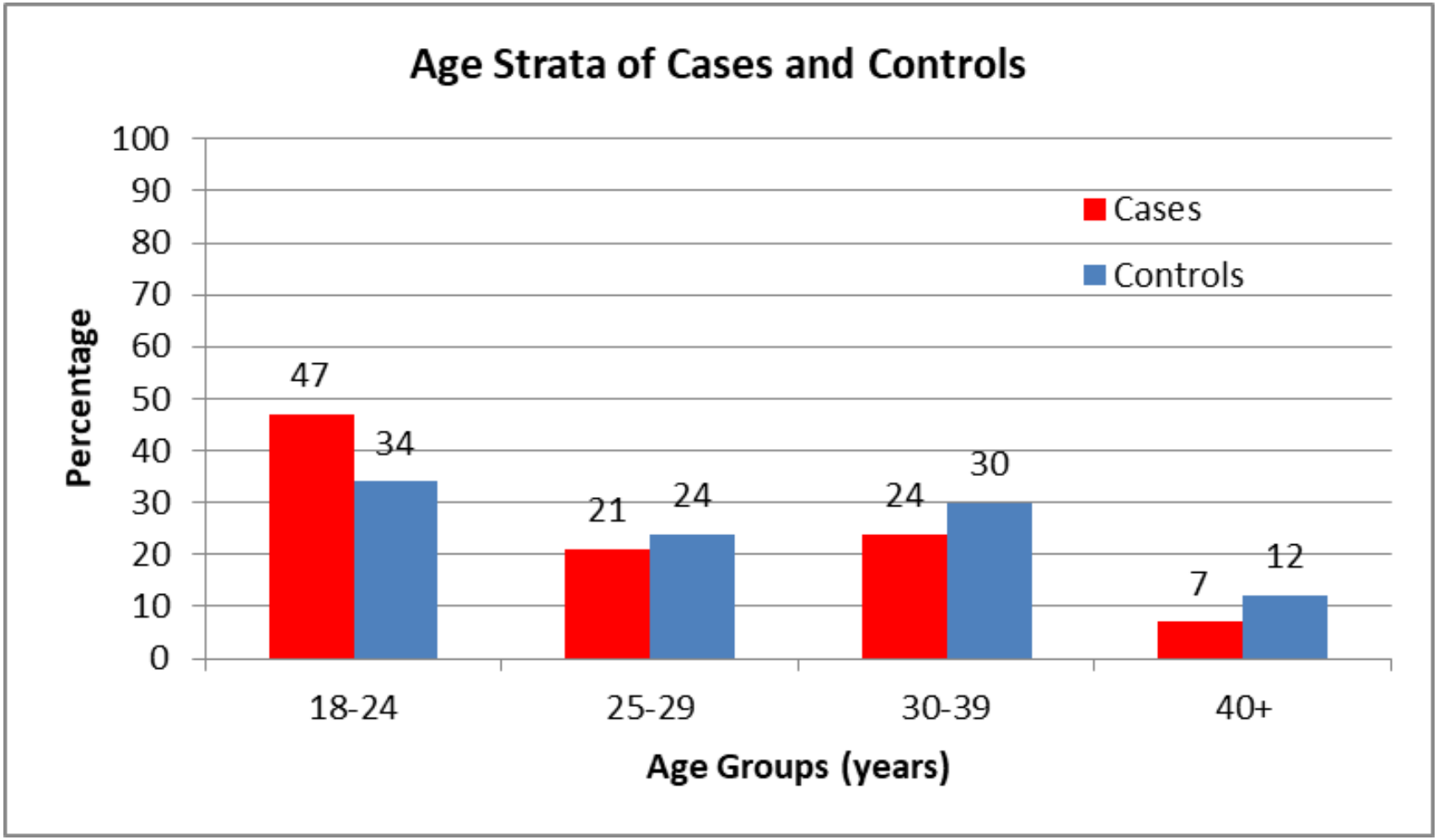
# Study Design

- 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



# 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

# Limitations

- 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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# Questions?

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