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
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

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Subtype Circulation: North America

Number and Proportion of Specimens Positive for Influenza by Subtype

PANDEMIC: Jan 2020 - present

Sources: NHRC, USAFSAM
Subtype Circulation: South America

Number and Proportion of Specimens Positive for Influenza by Subtype

PANDEMIC: Jan 2020 - present

Source: NAMRU-6

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Subtype Circulation: Europe

Number and Proportion of Specimens Positive for Influenza by Subtype

PANDEMIC: Jan 2020 - present

Sources: LRMC/PHCE, USAFSAM

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Subtype Circulation: Asia

Number and Proportion of Specimens Positive for Influenza by Subtype

PANDEMIC: Jan 2020 - present

Sources: AFRIMS, NAMRU-2, USAFSAM

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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
Subtype Circulation: East Africa

Number and Proportion of Specimens Positive for Influenza by Subtype

PANDEMIC: Jan 2020 - present

Source: USAMRD-K
Subtype Circulation: West Africa (Ghana)

Number and Proportion of Specimens Positive for Influenza by Subtype

PANDEMIC: Jan 2020 - present

Source: NAMRU-3
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 \textit{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 \textit{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

Number of A(H3N2) Specimens

3C.2a1b-131K  3C.2a1b-135K  3C.3a

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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

Age Strata of Cases and Controls

Percentage

Cases

Controls

Age Groups (years)

18-24

21

34

47

25-29

24

30

24

30-39

40+

7

12

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## Interim VE Estimates 2020-2021

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

*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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LRMC/PHC-Europe
COL Rodney Coldren
COL Alexander Kayatani
CPT Cole Anderson
SSgt Brianne Holdbrook
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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

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