DoD Influenza Surveillance and Mid-Season Vaccine Effectiveness

Armed Forces Health Surveillance Branch (AFHSB)
Naval Health Research Center (NHRC)
United States Air Force School of Aerospace Medicine (USAFSAM)
DoD Global Influenza Network Partners

Presentation to the Vaccines and Related Biological Products Advisory Committee (VRBPAC) – 9 March 2017

CAPT Michael Cooper, PhD**

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

“Medically Ready Force...Ready Medical Force”
Disclaimer

The views expressed in this presentation are those of the author and do not necessarily reflect the official policy or position of the Department of Defense or the U.S. Government.
Briefing Outline

- PURPOSE: Provide a concise update to the VRBPAC on DoD influenza surveillance activities, 2016-2017

1. Program Description
2. Strain Circulation
3. Molecular Analyses
4. Vaccine Effectiveness
My name is Michael Cooper and I am the Lead for respiratory infection surveillance at the Armed Forces Health Surveillance Branch in the division of Global Emerging Infection Surveillance and Response. We are a DoD asset.

Today I will be presenting data on the 2016-17 influenza season from our influenza surveillance network. Included here will be surveillance data from our partners in North America, Africa, Asia and Europe. In addition, surveillance data will also be presented on military recruits.

I will also be presenting a brief summary of phylogenetic analyses developed by US Air Force School of Aerospace Medicine.

In addition, I’ll be presenting three mid-year estimates of vaccine effectiveness developed from the Naval Health Research Center (NHRC), the United States Air Force School of Aerospace Medicine (USAFSAM and the Armed Forces Health Surveillance Branch.
**Breadth of DoD Influenza Surveillance**

- **Global Virus 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
    - ~300 sequences submitted to GenBank in fiscal year 2016

- **Comprehensive Epidemiology and Analysis Capabilities**
  - 1.4 Million Active Duty records (health care utilization, immunizations, deployment, reportable diseases, etc)
    - Produce Medical Surveillance Monthly Reports, Ad-hoc requests, Studies/analyses,
    - Weekly influenza reports
    - Vaccine safety and effectiveness studies
I just want to take a moment to give some background on my organization and our influenza surveillance network. Again, we are a DoD asset dedicated to the surveillance of infectious disease primarily, but not exclusively, in the military community. Our influenza surveillance program extends to over 400 locations in over 30 countries. In addition to monitoring US military personnel our partners have relationships with foreign governments including ministries of health, ministries of defense and academic institutions which provide disease surveillance data on local national populations.

Our laboratories have extensive characterization capabilities including cell culture, PCR and sequencing capabilities.

On average, about 30,000 respiratory samples are collected and analyzed each year within our surveillance network and approximately 300 sequences are submitted to GenBank.
In 2017:
--Over 30 countries
--Over 400 sites
United States Military Recruits
Number and Proportion of Specimens Positive for Influenza by Subtype
Week 40, 2014 - Week 5, 2017

Source: NHRC
Epi week is along the X axis and the percentage of positive samples is along the right hand side. The number of specimens submitted is along the Y axis on the left hand side.

The data for the current flu season is located at the right hand side of the graph (starting with week 40). Different colors indicate the different sub-types.

Military Recruits are particularly vulnerable to respiratory infections due to factors such as crowded living conditions and stressful work environment. Historically, up to 20% of recruit classes might be hospitalized for respiratory infections during the two months of recruit training. In addition, recruits are a highly vaccinated population. Surveillance on them gives us information on what viruses might be evading current vaccines.

These data come from eight recruit training sites throughout the United States. So far, recruits have experienced low levels of influenza infection. Influenza A H3N2 has been the dominate subtype with low levels of flu B reported. Sample submission and the number of positive samples for recruits peaked (so far) in week 5. Note the outbreaks of H3N2 during May and July of last year. Benefit and need for year-round surveillance.

Ft Benning Georgia, Ft Jackson, SC, Ft Leonard Wood (Missouri), Naval Recruit Training Center, Great Lakes (Illinois), Lackland AFB (Texas), Marine Corps Recruit Depots, Paris Island (SC) and San Diego, Coast Guard Training Center, Cape May NJ

Army = 10 wks, Navy 8 weeks, Marines = 13 weeks, AF 8 weeks
North America
Number and Proportion of Specimens Positive for Influenza by Subtype
Week 40, 2014 - Week 6, 2017

Source: USAFSAM, NHRC
This graph represents surveillance data for military members and their dependents residing within the United States and select civilian populations along the Mexico border. So far, in North America, flu levels have been fairly low with H3/N2 as the dominant sub-type.
Europe
Number and Proportion of Specimens Positive for Influenza by Subtype
Week 40, 2014 - Week 7, 2017

Source: LRMC/PHCR-Europe
This graph represents surveillance data for military members and their dependents residing in one of seven countries in Europe (Belgium, Germany, Italy, Spain, Turkey, United Kingdom, Portugal). Flu activity for this population is relatively low and dominated by H3N2.
Latin America
Number and Proportion of Specimens Positive for Influenza by Subtype
Week 40, 2014 - Week 6, 2017

Source: NAMRU-6
These surveillance data come from select local national populations within Peru, Paraguay, Columbia Nicaragua, and Honduras. Relatively low flu activity with a mix of H3N2 and flu B. These countries fall within in the tropics band so we don’t expect peaks at this time.
Asia
Number and Proportion of Specimens Positive for Influenza by Subtype
Week 40, 2014 - Week 8, 2017

Source: AFRIMS, NAMRU-2, 65th Med Brigade, NH Yokosuka
These data represent US military personnel and dependents stationed in ASIA and select local national populations. Our surveillance in Asia indicates moderate influenza activity with a mix of H3, H1 and flu B reported between weeks 28 and 40 (early July through early October).

Countries:
Bhutan Cambodia Japan Indonesia Nepal Philippines South Korea Thailand Pakistan
East Africa

Number and Proportion of Specimens Positive for Influenza by Subtype

Week 40, 2014 - Week 6, 2017

Source: USAMRU-K
Moderate activity from week 22 through 37 (late May through early September) with a mix of H1, H3 and flu B. In recent months activity has been low with mixed flu types. These countries are located within the tropics.

Countries: Kenya, Uganda, Tanzania
Summary of Circulating Strain Activity to date

- In North America and Europe, military members and dependents have experienced low to moderate flu activity so far; positive samples have been primarily H3N2

- Globally, a mix of H3N2 and H1N1 has been detected in the DOD network
USAFSAM/DoD Phylogenetic Analysis
2016-2017 Influenza Season
Distribution of Sequenced Influenza A/H1N1pdm09, A/H3N2, and B Specimens within the DoD, 2016-2017

Contributors
AFRIMS
Deployed Laboratories
Landstuhl Regional Medical Center
NAMRU-2
NAMRU-6
Naval Health Research Center – San Diego, CA
USAMRD-K
USAFSAM – Wright-Patterson AFB, Ohio
WRAIR

Countries
Cambodia
Country 1
Country 2
Egypt
Germany
Italy
Japan
Kenya
Nigeria
Paraguay
Peru
Philippines
South Korea
Thailand
Turkey
United States

Total Sequences
412

A(H1N1)pdm09
A(H3N2)
B Victoria
B Yamagata

United States Air Force School of Aerospace Medicine (USAFSAM/PHE)
2510 5th Street, Wright-Patterson AFB OH 45433
For these analyses a total 412 sequences were collected, 341 (83%) were influenza A(H3N2), 19 (5%) were influenza A(H1N1)pdm09, 39 (10%) were influenza B Victoria, and 13 (3%) were influenza B Yamagata. These sequences come from 16 countries on five continents. A(H3N2) was the predominant subtype in all regions collected from except for Africa and southeast Asia, where B Victoria was either equal to or greater than the number of A(H3N2) sequences.
Geographical Distribution of Sequences

- Of a total of 412 sequences collected to date, 341 (83%) were influenza A(H3N2),
- 19 (5%) were influenza A(H1N1)pdm09,
- 39 (10%) were influenza B Victoria,
- 13 (3%) were influenza B Yamagata

- Sequences collected from 16 countries over 5 continents
- A(H3N2) was the predominant subtype in all regions collected from except for Africa and southeast Asia (B Victoria)
• All 19 of the H1N1 sequences collected were in clade 6B; 15 of them (79%) were in subclade 6B.1

• *A/Michigan/45/2015-like virus* is the recommended A(H1N1)pdm09 component of the 2017-2018 influenza vaccine.
DoD Influenza H3N2

Selected 2016-2017 Influenza A(H3N2)
HA Phylogenetic Analysis
VRBPAC 2017
N = 150
Sequences were selected to be representative of the total distribution of H3N2 specimens sequenced

2016-2017 A(H3N2)
Vaccine strain: A/Hong Kong/4801/2014
Reference Strain
July 2016
August 2016
September 2016
October 2016
November 2016
December 2016
January 2017
ADD GLY: Create Glycosylation Motif
LOSS GLY: Loss of Glycosylation Motif
wF – WHO Doc Reference Antigen
SAg - CDC Serology Antigen
CSAg – CDC Serology Antigen
wSAg – WHO Doc. Serology Antigen
e Egg isolate

Total 2016-2017 A(H3N2)
N = 341

3C.2a1 64.9%
3C.2a2 11.4%
3C.2a Only 16.1%
3C.3a 7.3%

Proposed 3C.2a2

3C.2a

3C.3a

3C.2a1
• 150 of the 341 influenza A(H3N2) sequences collected for the 2016-2017 season were selected to represent the clade proportions as well as geographical and temporal distribution
• 7% of sequences were in clade 3C.3a, 65% were in subclade 3C.2a1, 11% were in clade 3C.2a2, and 16.1% were in clade 3C.2a with no further subclade designation

• A/Hong Kong/4801/2014-like virus is the recommended as A(H3N2) component of the 2017-2018 vaccine.
Substitution Frequencies of H3N2 Key Amino Acids
These graphs highlight the genetically dynamic nature of A(H3N2). The frequency plots show the amino acid substitutions at either consistently low levels (I58V, N122D), spiking at some point in the analysis (S144K, R142G), increasing at the end of the analysis (T135K), or variable throughout the analysis time period (N171K, N121K).

- The bottom right graph shows the number of sequences by month
2016-2017 Influenza B Victoria
HA Phylogenetic Analysis
VRBPAC 2017

N = 39

Current 2016-2017 B Victoria vaccine strain:
B/Brisbane/60/2008-like virus

Reference Strain
July 2016
August 2016
September 2016
October 2016
November 2016
December 2016
January 2017

ADD GLY  Create Glycosylation Motif
LOSS GLY  Loss of Glycosylation Motif
F  –  CDC Reference Antigen
SAg  –  CDC Serology Antigen
wF  –  WHOcc Reference Antigen
CSAg  –  CDC Serology Antigen
wSAg  –  WHOcc Serology Antigen
e  Egg Isolate
LR  Low Reactor to B/Brisbane/60/2008 (≥ 8 fold)

B/Ohio/01/2005 Feb e LR F

0.005
• All 39 of the influenza B Victoria sequences were in clade 1A; - Three strains were found to have a deletion at amino acid positions 162 and 163

• Either -B/Texas/02/2013-like virus or B/Brisbane/60/2008-like virus is recommended for the 2017-18 flu season.
2016-2017 Influenza B Yamagata
HA Phylogenetic Analysis
VRBPAC 2017
N = 13

Current 2016-2017 B Yamagata vaccine strain: B/Phuket/3073/2013
Reference Strain
- July 2016
- August 2016
- October 2016
- November 2016
- December 2016
- January 2017
- F – CDC Reference Antigen
- SAg - Serology Antigen
- wF – WHOcc Reference Antigen
- wSAg – WHOcc Serology Antigen
- e Egg Isolate

K48R  A182T
A108P  N203S
N116K  G230D
S150I  K299E
N166Y  E313K

B/Massachusetts/02/2012 Mar F wF

B/New York/2000/2017
B/New York/2001/2017
B/Virginia/1224/2017
B/Montana/1988/2017
B/Illinois/NHRC 18462/2016
B/Nevada/283/2016
vidrl B/South Auckland/14/2016 Jul wSAg

vidrl B/Townsville/6/2016 Feb

V177I
B/Nebraska/1736/2017
B/California/NHRC 27794/2016

B/Arizona/10/2015 Nov SAg wSAg

B/Cambodia/FSS33766/2016
B/Turkey/2013/2017
B/Peru/CFI3361/2016

crick B/Hamburg/1/2016 Jan wSAg

V90A
B/Ohio/w230/2016
B/Germany/x24/2016

B/Phuket/3073/2013 Nov e F wF SAg wSAg

Y3
- All 13 of the influenza B Yamagata specimens were in clade 3

-B/Phuket/3073/2013-like virus is the recommended influenza B Yamagata component of the 2017-2018 quadrivalent influenza vaccine
Summary of Recommendations

• For the 2017-2018 influenza trivalent vaccine:
  - A(H1N1)pdm09 component: A/Michigan/45/2015-like virus
  - A(H3N2) component: A/Hong Kong/4801/2014-like virus
  - B Victoria component: B/Brisbane/60/2008-like virus, OR B/Texas/02/2013-like virus (depending on production)

• For the 2017-2018 quadrivalent vaccine:
  - B Yamagata component: B/Phuket/3073/2013-like virus
Vaccine Effectiveness (VE)
To this point, the flu season has been relatively mild in most regions covered by the DoD influenza surveillance network

- Not enough cases for detailed sub-analyses

Simplified Analyses

- No LAIV use
- Very little H1N1
VE Preview

• Mid-year estimates provided by
  – US Air Force School of Aerospace Medicine (USAFSAM)
  – Naval Health Research Center (NHRC)
  – AFHSB, Epidemiology and Analysis

• Case-Control studies, logistic regression used to estimate VE
  – Two studies used control-test negative method
  – Epidemiology and Analysis used Health Controls
  – No analyses by flu “A” subtype; H3 dominant season
  – Each influenza infection was confirmed by PCR or viral culture
Testing Criteria for ILI

- Fever ≥100.5°F (38°Celsius) AND
- Cough and/or Sore Throat

Specimens should be collected within 72 hours of onset symptoms.
- surveillance sites are asked to submit up to 10 specimens per week, giving priority to the sickest or hospitalized patients.
USAFSAM Case-Control Analyses
• Adjusted Estimates of Vaccine Effectiveness
  – Population: DoD healthcare beneficiaries (excluding Active Duty)
  – Time period: October 2, 2016 – February 18 2017
  – Analysis by influenza subtype/type (H3N2 and B) and by age group (children and adults)
  – Adjusted for age, month of illness and region
  – Cases: n=534 ; confirmed by RT-PCR or viral culture
  – Controls: n=838 ; test-negative; RATIO NOT OPTIMAL
  – Vaccination rates: cases 32%, controls 36%
  – Of total cases:
    • 89% were influenza A (H3N2)
    • 1% were influenza A(H1N1)pdm09
    • 10% were influenza “B”
USAFSAM: Cases and Controls by Age Group

Cases and Controls by Age Group (USAFSAM)

- <18:
  - Cases: 60.1%
  - Controls: 66.0%

- 18+:
  - Cases: 39.9%
  - Controls: 34.0%
USAFSAM: Cases and Controls by Age Group

Cases and Controls by Age Group (USAFSAM)

- <18: 60.1% Cases, 66.0% Controls
- 18-49: 22.3% Cases, 22.2% Controls
- 50+: 17.6% Cases, 11.8% Controls
• Adjusted Estimates of Vaccine Effectiveness

  – H3N2: overall adjusted VE was moderately protective and statistically significant for influenza A(H3N2) (VE = 42%)
    – Significantly protective for children
    – Not significantly protective for adults

  – Flu “B”: overall adjusted VE was moderately protective and statistically significant for influenza “B” (VE = 53%)
    – 77% of subjects under 18
## VE by Influenza Type and Subtype

<table>
<thead>
<tr>
<th>Type</th>
<th>Population</th>
<th>Vaccine Type</th>
<th>Cases (%)</th>
<th>Controls (%)</th>
<th>Crude VE (95% CI)</th>
<th>Adjusted VE (95% CI)*</th>
</tr>
</thead>
<tbody>
<tr>
<td>A (H3N2)</td>
<td>All dependents</td>
<td>IIV</td>
<td>154 (32)</td>
<td>299 (36)</td>
<td>14 (-9, 32)</td>
<td>42 (24, 56)</td>
</tr>
<tr>
<td></td>
<td>Unvaccinated</td>
<td>IIV</td>
<td>323 (68)</td>
<td>539 (64)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Adults (&gt;18)</td>
<td>IIV</td>
<td>78 (39)</td>
<td>114 (40)</td>
<td>5 (-38, 34)</td>
<td>32 (-3, 55)</td>
</tr>
<tr>
<td></td>
<td>Unvaccinated</td>
<td>IIV</td>
<td>123 (61)</td>
<td>171 (60)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Children (&lt;18)</td>
<td>IIV</td>
<td>76 (28)</td>
<td>185 (33)</td>
<td>24 (-4, 45)</td>
<td>48 (25, 64)</td>
</tr>
<tr>
<td></td>
<td>Unvaccinated</td>
<td>IIV</td>
<td>200 (72)</td>
<td>368 (67)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>B</td>
<td>All dependents</td>
<td>IIV</td>
<td>14 (26)</td>
<td>299 (36)</td>
<td>35 (-21, 65)</td>
<td>53 (11, 75)</td>
</tr>
<tr>
<td></td>
<td>Unvaccinated</td>
<td>IIV</td>
<td>39 (74)</td>
<td>539 (64)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

IIV=inactivated influenza vaccine; VE=vaccine effectiveness; CI=confidence interval; VE=(1-odds ratio) x 100.

*VE adjusted for age group (<9, 9-17, 18-49, 50-64, 65+), month of illness and region (CONUS v. OCONUS). Influenza B analysis was only adjusted for month of illness.
NHRC Case-Control Analyses
Adjusted Estimates of Vaccine Effectiveness

- Population: Civilians only
  - DoD dependents in Southern California, Arizona, and Illinois outpatient clinics
  - Civilians at outpatient clinics near US-Mexico border (CDC and CA State collaboration)
- Adjusted for: age and study population (military dependents VS US-Mexico border civilians)
- Cases: n=75; confirmed by RT-PCR
- Controls: n=224; test-negative 3:1 ratio
- Vaccination Rates: cases 33%, controls 48%
- 93% of cases were A/H3
- 4% were flu B
- 3% were A/H1
Naval Health Research Center

Cases and Controls by Age Group (NHRC)

<table>
<thead>
<tr>
<th>Age Groups (Years)</th>
<th>Cases</th>
<th>Controls</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-17</td>
<td>68.0%</td>
<td>64.0%</td>
</tr>
<tr>
<td>18-64</td>
<td>32.0%</td>
<td>36.0%</td>
</tr>
<tr>
<td>65+</td>
<td>0.0%</td>
<td>0.0%</td>
</tr>
</tbody>
</table>
Adjusted Estimates of Vaccine Effectiveness

- VE against H3 was moderately protective and statistically significant
- VE for children (0-17, H3 only) was moderately protective but not statistically significant
# NHRC: Estimates of Vaccine Effectiveness

## 299 ILI cases enrolled between DEC 29 2016 and FEB 16 2017

<table>
<thead>
<tr>
<th>Type</th>
<th>Population</th>
<th>Vaccine Type</th>
<th>Cases (%)</th>
<th>Controls (%)</th>
<th>Crude VE (95% CI)</th>
<th>Adjusted VE (95% CI)*</th>
</tr>
</thead>
<tbody>
<tr>
<td>A (H3N2)</td>
<td>All</td>
<td>IIV</td>
<td>23 (33)</td>
<td>107 (48)</td>
<td>47 (6, 70)</td>
<td>46 (6, 70)</td>
</tr>
<tr>
<td></td>
<td>Unvaccinated</td>
<td>IIV</td>
<td>47 (67)</td>
<td>117 (52)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Children (&lt;18)</td>
<td>IIV</td>
<td>15 (31)</td>
<td>67 (47)</td>
<td>48 (-4, 74)</td>
<td>48 (-4, 74)</td>
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<td>IIV</td>
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IIV=inactivated influenza vaccine; VE=vaccine effectiveness; CI=confidence interval; VE=(1-odds ratio) x 100.

*VE adjusted for age group and population (DoD dependents, civilians near US-Mexico border)
AFHSB
Epidemiology and Analysis
Case-Control Analyses
• Matched Case Health-Control Study of VE
  – Population: Active component service members
    • Army, Navy, Air Force, Marines
    • CONUS and OCONUS
  – Lab-confirmed flu cases (n=987)
    • Rapid, RT-PCR, or culture
• Health Controls (n=3709)
  • Medical encounter for injuries or mental health conditions with no ILIs reported at encounter
  • No medical encounters for influenza during season
  • Matched to cases by sex, age, date of encounter (+/- 3 days), and location
• Models adjusted for 5-yr vaccination status (Y/N)
Cases and Controls by Age Group (AFHSB)

<table>
<thead>
<tr>
<th>Age Groups (Years)</th>
<th>Cases</th>
<th>Controls</th>
</tr>
</thead>
<tbody>
<tr>
<td>18-24</td>
<td>29.4%</td>
<td>29.5%</td>
</tr>
<tr>
<td>25-29</td>
<td>18.8%</td>
<td>18.7%</td>
</tr>
<tr>
<td>30-39</td>
<td>37.1%</td>
<td>37.8%</td>
</tr>
<tr>
<td>40+</td>
<td>14.7%</td>
<td>14.0%</td>
</tr>
</tbody>
</table>
• Vaccination Status
  – Cases: 91% vaccinated
  – Controls: 89% vaccinated

• Cases
  – Influenza A (unsubtyped) = 636*
  – Influenza A H3N2 = 261
  – Influenza A H1N1 = 12
  – Influenza B = 79

• 93% of cases and 95% of controls had prior flu vaccine in previous 5 years

• IIV was the only vaccine used by DoD this season
AFHSB Mid-Season 2016-2017 Case Health Control VE Study (Active Component)

Cases and Controls by Age Group (AFHSB)

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<th>Age Groups (Years)</th>
<th>Cases</th>
<th>Controls</th>
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<tbody>
<tr>
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<tr>
<td>30-39</td>
<td>37.1%</td>
<td>37.8%</td>
</tr>
<tr>
<td>40+</td>
<td>14.7%</td>
<td>14.0%</td>
</tr>
</tbody>
</table>
Active Duty Vaccine Effectiveness 2016-2017

- VE estimates for Flu “A” were very low and not statistically significant
- Wide CIs, low power due to relatively small numbers and very high vaccination rates (90%)
- For Flu “B” numbers were too small to produce reliable estimates
# AFHSB Mid-Season 2016-2017 Case Health Control VE Study (Active Component)

<table>
<thead>
<tr>
<th>Influenza Type/Subtype</th>
<th>Vaccine Type</th>
<th>Cases (%)</th>
<th>Controls (%)</th>
<th>Crude VE (95% CI)</th>
<th>Adjusted VE (95% CI)*</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Influenza A</strong></td>
<td>IIV</td>
<td>823 (91)</td>
<td>3109 (91)</td>
<td>5 (-23, 27)</td>
<td>3 (-25, 25)</td>
</tr>
<tr>
<td></td>
<td>Unvaccinated</td>
<td>86 (9)</td>
<td>315 (9)</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>A/H3N2</strong></td>
<td>IIV</td>
<td>228 (87)</td>
<td>898 (91)</td>
<td>32 (-6, 57)</td>
<td>33 (-6, 57)</td>
</tr>
<tr>
<td></td>
<td>Unvaccinated</td>
<td>33 (13)</td>
<td>93 (9)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

OR = Odds Ratio; IIV = inactivated influenza vaccine; *Adjusted for sex, age, month of diagnosis, and vaccination status in 5 years prior (Y/N)
## Summary of VE Results

<table>
<thead>
<tr>
<th>Flu Type</th>
<th>Study Site</th>
<th>Population</th>
<th>Cases</th>
<th>Controls</th>
<th>VE</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>A(H3N2)</td>
<td>USAFSAM</td>
<td>DoD Dependents</td>
<td>477</td>
<td>838</td>
<td>42</td>
<td>[24, 56]</td>
</tr>
<tr>
<td>A(H3N2)</td>
<td>NHRC</td>
<td>DoD Dependents and Civilians</td>
<td>70</td>
<td>224</td>
<td>46</td>
<td>[6, 70]</td>
</tr>
<tr>
<td>A(H3N2)</td>
<td>AFHSB*</td>
<td>Active Duty</td>
<td>261</td>
<td>991</td>
<td>33</td>
<td>[-6, 57]</td>
</tr>
<tr>
<td>B</td>
<td>USAFSAM</td>
<td>DoD Dependents</td>
<td>53</td>
<td>838</td>
<td>53</td>
<td>[11, 75]</td>
</tr>
</tbody>
</table>

*A FSHB VE results from case health control study design*
Summary of VE Results

• For Dependents and Civilians overall:
  – VE against H3N1 was moderately protective and statistically significant
  – VE against Flu “B” was moderately protective and statistically significant

• For Active Duty Military:
  – VE was not statistically significant for Flu “A”
Discussion-Limitations

• Generalizability
  – Subjects were sick enough to seek medical attention, can’t comment on vaccine impact for 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)
Discussion-Limitations

– Populations are younger; cannot comment on vaccine impact in older, high-risk pops
– USAFSAM analyses was limited by a suboptimal control : case ratio
– NHRC analyses were limited by small numbers
– AFHSB analyses were limited by high vaccination rates
  – Low statistical power
Thanks
Acknowledgements

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Mr. Agus Rachmat
Mr. Vireak Heang

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Mr. Jeffrey Thervil  
Ms. Elizabeth Toure  
Mr. Scott Wallace  
Carol Garrett  
Matt Couch  
Matt Sanders  
Matt Levine  
Aleta Yount  
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Sgt Ashley Seaton

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Mr. Silvanos Opana  
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Back-up slides (USAFSAM)
# USAFSAM: Adjusted Estimates of Vaccine Effectiveness 2016-2017

## VE Overall (all Influenza Types)

<table>
<thead>
<tr>
<th>Type</th>
<th>Population</th>
<th>Vaccine Type</th>
<th>Cases (%)</th>
<th>Controls (%)</th>
<th>Crude VE (95% CI)</th>
<th>Adjusted VE (95% CI)*</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Overall (all influenza types)</strong></td>
<td></td>
<td>IIV</td>
<td>169 (32)</td>
<td>299 (36)</td>
<td>17 (-5, 34)</td>
<td>42 (24, 55)</td>
</tr>
<tr>
<td>All dependents</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Unvaccinated</td>
<td></td>
<td>IIV</td>
<td>365 (68)</td>
<td>539 (64)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Adults (&gt;18)</td>
<td>IIV</td>
<td>82 (39)</td>
<td>114 (40)</td>
<td>6 (-35, 35)</td>
<td>34 (0, 56)</td>
</tr>
<tr>
<td>Unvaccinated</td>
<td>Adults (&gt;18)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Children (&lt;18)</td>
<td>IIV</td>
<td>87 (27)</td>
<td>185 (33)</td>
<td>26 (0, 45)</td>
<td>47 (24, 62)</td>
</tr>
<tr>
<td>Unvaccinated</td>
<td>Children (&lt;18)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

IIV=inactivated influenza vaccine; VE=vaccine effectiveness; CI=confidence interval; VE=(1-odds ratio) x 100.

*VE adjusted for age group (<9, 9-17, 18-49, 50-64, 65+), month of illness and region (CONUS v. OCONUS).
*Strengthen Our Role as a Combat Support Agency
*Fortify Our Relationship with the Services

- Respond to Immediate Mission Needs (W2)
- Support Service Needs for Data, Reporting, and Analytics (W7)
- Improve System of DHA Accountability (W9)
- Leverage Strategic Partnerships (W10)
## Characteristics of laboratory confirmed influenza cases and test-negative controls from October 2, 2016 –February 18, 2017

US Air Force School of Aerospace Medicine’s DoD Global, Laboratory-based, Influenza Surveillance Program

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Cases (n=534)</th>
<th>Controls (n=838)</th>
<th>p-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No.(%)</td>
<td>No.(%)</td>
<td></td>
</tr>
<tr>
<td><strong>Gender</strong></td>
<td></td>
<td></td>
<td>0.385</td>
</tr>
<tr>
<td>Male</td>
<td>246 (46.1)</td>
<td>366 (43.7)</td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>288 (53.9)</td>
<td>472 (56.3)</td>
<td></td>
</tr>
<tr>
<td><strong>Age (years)</strong></td>
<td></td>
<td></td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>&lt;9</td>
<td>151 (28.3)</td>
<td>406 (48.5)</td>
<td></td>
</tr>
<tr>
<td>9-17</td>
<td>170 (31.8)</td>
<td>147 (17.5)</td>
<td></td>
</tr>
<tr>
<td>18-49</td>
<td>119 (22.3)</td>
<td>186 (22.2)</td>
<td></td>
</tr>
<tr>
<td>50-64</td>
<td>74 (13.9)</td>
<td>64 (7.6)</td>
<td></td>
</tr>
<tr>
<td>65+</td>
<td>20 (3.7)</td>
<td>35 (4.2)</td>
<td></td>
</tr>
<tr>
<td><strong>Beneficiary Category</strong></td>
<td></td>
<td></td>
<td>0.008</td>
</tr>
<tr>
<td>Child</td>
<td>321 (60.1)</td>
<td>553 (66.0)</td>
<td></td>
</tr>
<tr>
<td>Adult (18-49)</td>
<td>119 (22.3)</td>
<td>186 (22.2)</td>
<td></td>
</tr>
<tr>
<td>Adult (50+)</td>
<td>94 (17.6)</td>
<td>99 (11.8)</td>
<td></td>
</tr>
<tr>
<td><strong>Month of Illness</strong></td>
<td></td>
<td></td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>October</td>
<td>4 (0.7)</td>
<td>101 (12.1)</td>
<td></td>
</tr>
<tr>
<td>November</td>
<td>10 (1.9)</td>
<td>188 (22.4)</td>
<td></td>
</tr>
<tr>
<td>December</td>
<td>90 (16.9)</td>
<td>181 (21.6)</td>
<td></td>
</tr>
<tr>
<td>January</td>
<td>211 (39.5)</td>
<td>242 (28.9)</td>
<td></td>
</tr>
<tr>
<td>February</td>
<td>219 (41.0)</td>
<td>126 (15.0)</td>
<td></td>
</tr>
<tr>
<td><strong>Geographic Region</strong></td>
<td></td>
<td></td>
<td>0.945</td>
</tr>
<tr>
<td>CONUS</td>
<td>510 (95.5)</td>
<td>801 (95.6)</td>
<td></td>
</tr>
<tr>
<td>OCONUS</td>
<td>24 (4.5)</td>
<td>37 (4.4)</td>
<td></td>
</tr>
<tr>
<td><strong>Vaccination Status</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vaccinated</td>
<td>169 (31.6)</td>
<td>299 (35.7)</td>
<td></td>
</tr>
<tr>
<td>Unvaccinated</td>
<td>365 (68.4)</td>
<td>539 (64.3)</td>
<td></td>
</tr>
<tr>
<td><strong>Influenza Type</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>B</td>
<td>53 (9.9)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>A(H1N1)</td>
<td>4 (0.8)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>A(H3N2)</td>
<td>477 (89.3)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

---

*aSpecimen collection began during Week 40 (October 2, 2016) and continued through Week 7 (February 18, 2017).

*bCONUS=continental United States, OCONUS=outside of continental United States

*cVaccination status was determined by electronic medical records and plausible self-report at enrollment

*dVaccination status is the exposure of interest, see VE tables
Note: The last few weeks still had pending results which are not included in the analysis and are not shown here; percent positivity is affected by this and may be artificially inflated.
Overall Summary of DoD VE Results

Summary of VE Results (w/AFHSB test-negative results)

<table>
<thead>
<tr>
<th>Flu Type</th>
<th>Study Site</th>
<th>Population</th>
<th>Cases</th>
<th>Controls</th>
<th>VE [95% CI]</th>
</tr>
</thead>
<tbody>
<tr>
<td>A(H3N2)</td>
<td>USAFSAM</td>
<td>DoD Dependents</td>
<td>477</td>
<td>838</td>
<td>42 [24, 56]</td>
</tr>
<tr>
<td>A(H3N2)</td>
<td>NHRC</td>
<td>DoD Dependents and Civilians</td>
<td>70</td>
<td>224</td>
<td>46 [6, 70]</td>
</tr>
<tr>
<td>A(H3N2)</td>
<td>AFHSB*</td>
<td>Active Duty</td>
<td>264</td>
<td>1299</td>
<td>23 [-15, 49]</td>
</tr>
<tr>
<td>B</td>
<td>USAFSAM</td>
<td>DoD Dependents</td>
<td>53</td>
<td>838</td>
<td>53 [11, 75]</td>
</tr>
</tbody>
</table>

*AFSHB VE results from test-negative case-control study design
Back-up slides (USAFSAM)
Alternate age stratification
### VE by Influenza Type and Subtype

<table>
<thead>
<tr>
<th>Type</th>
<th>Population</th>
<th>Vaccine Type</th>
<th>Cases (%)</th>
<th>Controls (%)</th>
<th>Crude VE (95% CI)</th>
<th>Adjusted VE (95% CI)*</th>
</tr>
</thead>
<tbody>
<tr>
<td>A (H3N2)</td>
<td>All dependents</td>
<td>IIV</td>
<td>154 (32)</td>
<td>299 (36)</td>
<td>14 (-9, 32)</td>
<td>42 (24, 56)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Unvaccinated</td>
<td>323 (68)</td>
<td>539 (64)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Children (&lt;18)</td>
<td>IIV</td>
<td>76 (28)</td>
<td>185 (33)</td>
<td>24 (-4, 45)</td>
<td></td>
<td>48 (25, 64)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Unvaccinated</td>
<td>200 (72)</td>
<td>368 (67)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Adults (18 - 49)</td>
<td>IIV</td>
<td>35 (31)</td>
<td>64 (34)</td>
<td>14 (-41, 48)</td>
<td></td>
<td>38 (-7, 65)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Unvaccinated</td>
<td>78 (69)</td>
<td>122 (66)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Adults (50+)</td>
<td>IIV</td>
<td>43 (49)</td>
<td>50 (51)</td>
<td>6 (-66, 47)</td>
<td></td>
<td>22 (-48, 59)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Unvaccinated</td>
<td>45 (51)</td>
<td>49 (49)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>B</td>
<td>All dependents</td>
<td>IIV</td>
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<td>299 (36)</td>
<td>35 (-21, 65)</td>
<td>53 (11, 75)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Unvaccinated</td>
<td>39 (74)</td>
<td>539 (64)</td>
<td></td>
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</tbody>
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IIV = inactivated influenza vaccine; VE = vaccine effectiveness; CI = confidence interval; VE = (1 - odds ratio) x 100.

*VE adjusted for age group (<9, 9-17, 18-49, 50-64, 65+), month of illness and region (CONUS v. OCONUS). Influenza B analysis was only adjusted for month of illness.
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- Leverage Strategic Partnerships (W10)
VE by Influenza Type and Subtype

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<thead>
<tr>
<th>Flu Type</th>
<th>Population</th>
<th>Cases</th>
<th>Controls</th>
<th>VE [95% CI]</th>
</tr>
</thead>
<tbody>
<tr>
<td>A (H3N2)</td>
<td>All Dependents</td>
<td>477</td>
<td>838</td>
<td>42 [24, 56]</td>
</tr>
<tr>
<td>A (H3N2)</td>
<td>Adults</td>
<td>201</td>
<td>285</td>
<td>32 [-3, 55]</td>
</tr>
<tr>
<td>A (H3N2)</td>
<td>Children</td>
<td>276</td>
<td>553</td>
<td>48 [25, 64]</td>
</tr>
<tr>
<td>B</td>
<td>All Dependents</td>
<td>53</td>
<td>838</td>
<td>53 [11, 75]</td>
</tr>
</tbody>
</table>