

Febrile Respiratory Illness (FRI) Surveillance Update

Operational Infectious Diseases, Naval Health Research Center, San Diego, CA



2017 Week 2 (through 14 January 2017)

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Influenza

NHRC Laboratory-Confirmed Influenza Cases, US Military Basic Trainees

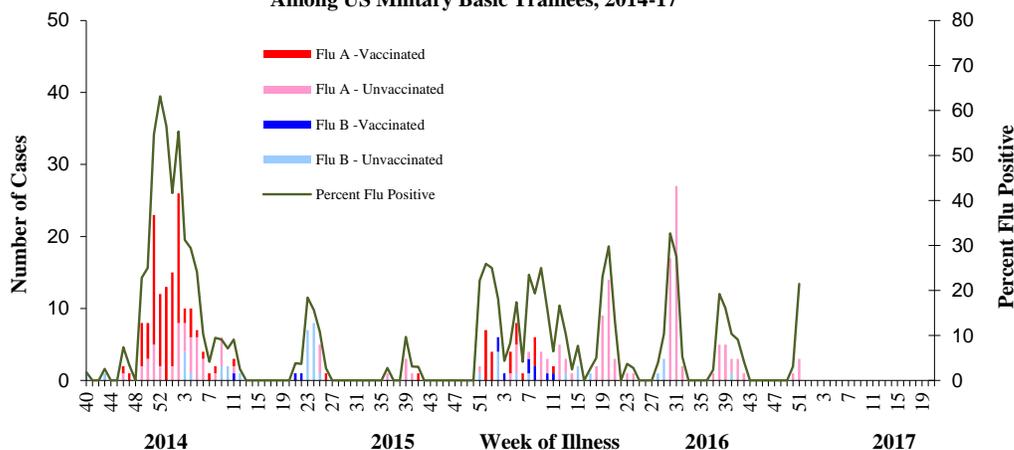
Site	Current Week*				Since Oct.1, 2016				No. Tested
	A/ Untyp.	A/H3	A/H1	B	A/ Untyp.	A/H3	A/H1	B	
Ft. Benning									69
Ft. Jackson						6			67
Ft. Leonard Wood									11
NRTC Great Lakes						1		1	43
Lackland AFB									8
MCRD Parris Island						3			17
MCRD San Diego									70
CGTC Cape May									30
Total	0	0	0	0	0	10	0	1	315

- NHRC also conducts shipboard FRI surveillance that includes large-deck ships of the US Fleet Forces (Atlantic), 3rd (Pacific), and 7th (Far East) Fleets.
- NHRC conducts FRI surveillance among (non-active duty) DoD beneficiaries in Illinois and San Diego (details on page 7).
- NHRC-CDC-BIDS collaborative border FRI/SARI surveillance program is ongoing at 7 US-Mexico border sites in San Diego (2) and Imperial (5) counties in California. Details on page 8.
- For more information about NHRC FRI surveillance programs, please [contact NHRC](#).

Items of Note

- Elevated FRI rate at MCRD San Diego
- NHRC is able to test for novel influenza strains, MERS coronavirus, enterovirus EV-68, Ebola virus, and Zika virus

Vaccination Status of Confirmed Influenza Cases Among US Military Basic Trainees, 2014-17

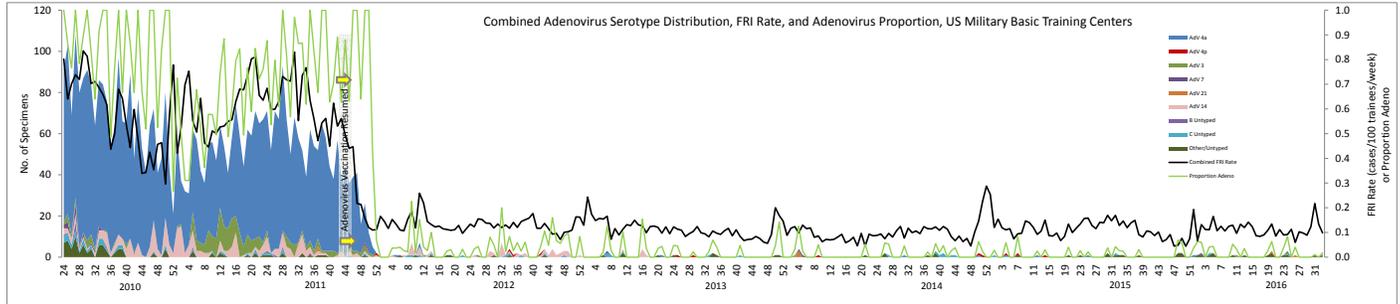


Other Items of Interest

- NHRC is conducting laboratory-based surveillance for meningococcal disease. The program's purpose is to track and characterize meningococcal cases among DoD medical beneficiaries. For more information and the most recent data, [view the Quarterly Meningococcal Report](#).

Adenovirus

- Vaccination against types 4 and 7 adenovirus was instituted at all basic training centers by mid-November 2011.
- FRI rates and the proportion of FRI cases positive for adenovirus have decreased markedly since vaccine was reintroduced.
- Sporadic adenovirus cases at basic training centers 2012-16. FRI rates remain low in general.



FRI Rates

- FRI surveillance is ongoing at 8 U.S. military basic training centers, representing all service branches. As each week’s FRI count is reported, [FRI Rate Status](#) is classified into one of 3 categories:
 - At or below expected value (expected value shown as dashed line)
 - Moderately elevated
 - Substantially elevated

Week ending 14 January 2017:

- **At or below expected value:**

[Fort Benning](#)

[Fort Jackson](#) (data through 31 Dec.)

[Fort Leonard Wood](#)

[Naval Recruit Training Command, Great Lakes](#) (data through 31 Dec.)

[Marine Corps Recruit Depot, Parris Island](#)

[Lackland Air Force Base](#) (data through 31 Dec.)

[Coast Guard Training Center, Cape May](#)

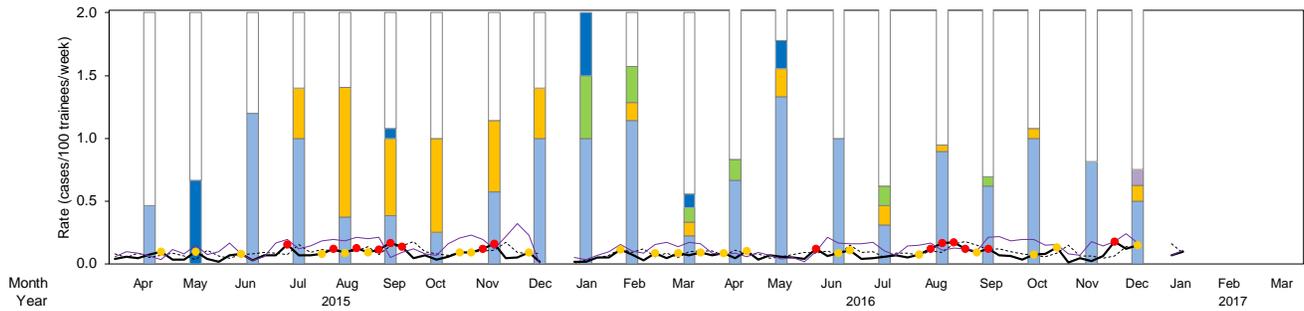
• **Moderately elevated:**

[Marine Corps Recruit Depot, San Diego](#)

• **Substantially elevated:**

None

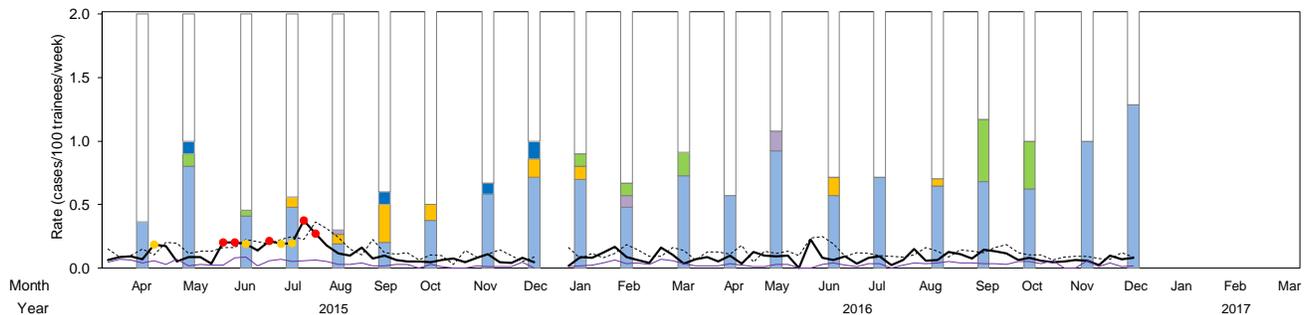
Ft. Benning FRI Rates and Diagnostic Test Results
 Shaded bars represent monthly proportions of each pathogen (clear = no pathogen identified)



Samples Received		13	6	10	20	27	26	24	35	10	4	14	18	12	9	26	13	38	26	26	27	16	
Adenovirus			33%				4%				25%		6%		11%								
Influenza											25%	14%	6%	8%		8%		4%					
RSV																							
C. pneumo																							6%
M. pneumo				20%	52%	31%	38%	29%	20%		7%	6%		11%		8%	3%		4%			6%	
Rhinovirus		23%	60%	50%	19%	19%	13%	29%	50%	50%	57%	11%	33%	67%	50%	15%	45%	31%	50%	41%	25%		
Influenza Subtype	B										0%	100%	100%	100%		100%		0%					
	A/H3										0%	0%	0%	0%		0%		100%					
	A/pH1										100%	0%	0%	0%		0%		0%					
	Untyped										0%	0%	0%	0%		0%		0%					

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Ft. Jackson FRI Rates and Diagnostic Test Results
 Shaded bars represent monthly proportions of each pathogen (clear = no pathogen identified)

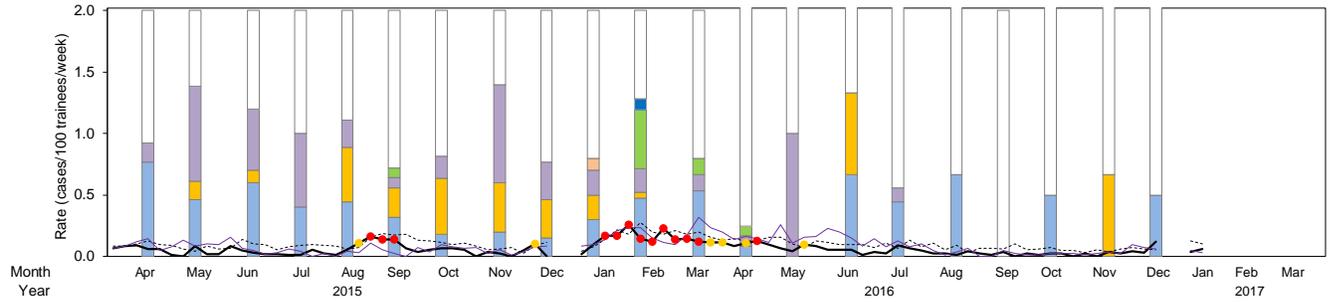


Samples Received		33	20	44	50	53	20	16	24	14	20	21	11	21	13	14	14	34	41	32	22	14	
Adenovirus			5%				5%		4%	7%													
Influenza			5%	2%							5%	5%	9%						24%	19%			
RSV																							
C. pneumo						2%						5%		8%									
M. pneumo					4%	4%	15%	6%		7%	5%					7%	3%						
Rhinovirus		18%	40%	20%	24%	9%	10%	19%	29%	36%	35%	24%	36%	29%	46%	29%	36%	32%	34%	31%	50%	64%	
Influenza Subtype	B		100%	100%							0%	0%	0%						0%	0%			
	A/H3		0%	0%							0%	0%	0%						100%	100%			
	A/pH1		0%	0%							100%	100%	100%						0%	0%			
	Untyped		0%	0%							0%	0%	0%						0%	0%			

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– Observed FRI rate (expected rate = dashed line) • Moderately elevated • Substantially elevated — Pneumonia rate (incl. afebrile)

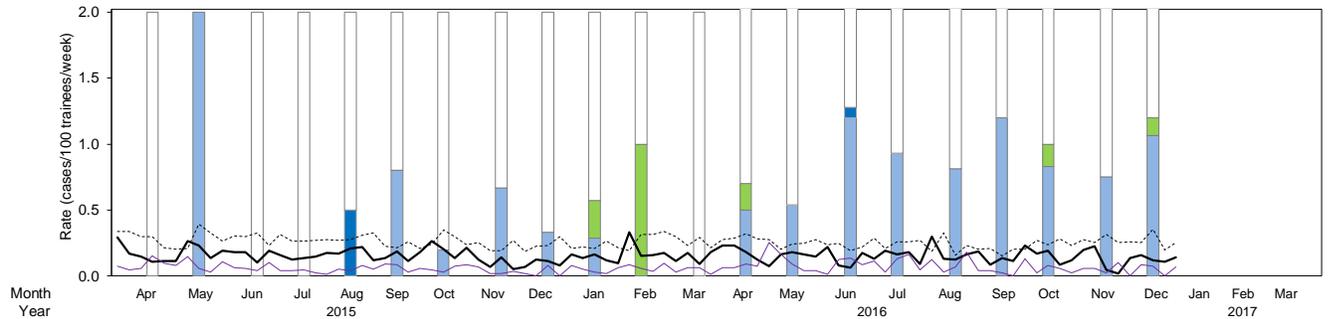
Ft. Leonard Wood FRI Rates and Diagnostic Test Results
 Shaded bars represent monthly proportions of each pathogen (clear = no pathogen identified)



Samples Received	26	13	20	10	9	25	22	10	13	20	42	15	24	6	3	18	3	1	4	3	4		
Adenovirus											5%												
Influenza					4%						24%	7%	4%										
RSV										5%													
C. pneumo	8%	38%	25%	30%	11%	4%	9%	40%	15%	10%	10%	7%	4%	50%		6%							
M. pneumo		8%	5%		22%	12%	23%	20%	15%	10%	2%					33%					33%		
Rhinovirus	38%	23%	30%	20%	22%	16%	9%	10%	8%	15%	24%	27%	4%			33%	22%	33%		25%	25%		
Influenza Subtype					B					0%	20%	100%	100%										
					A/H3					100%	10%	0%	0%										
					A/pH1					0%	70%	0%	0%										
					Untyped					0%	0%	0%	0%										

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Great Lakes FRI Rates and Diagnostic Test Results
 Shaded bars represent monthly proportions of each pathogen (clear = no pathogen identified)

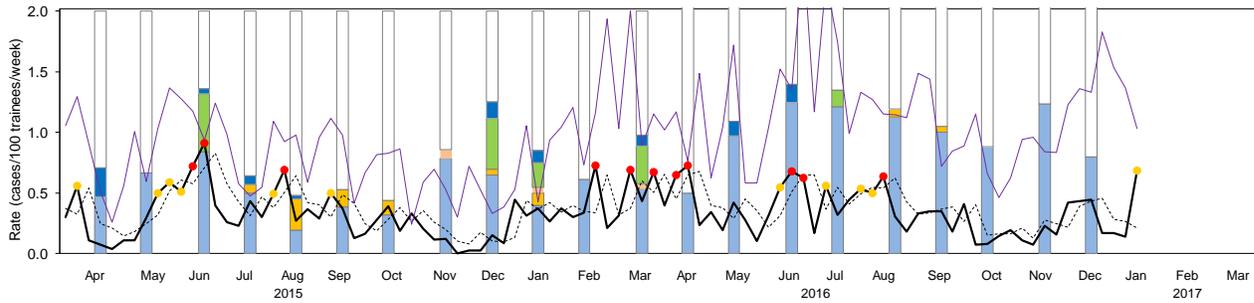


Samples Received	1	1	1	3	4	5	10	3	6	7	2	3	20	26	25	30	32	15	12	8	15	
Adenovirus					25%										4%							
Influenza										14%	50%		10%						8%			7%
RSV																						
C. pneumo																						
M. pneumo																						
Rhinovirus	100%				40%	10%	33%	17%	14%				25%	27%	60%	47%	41%	60%	42%	38%	53%	
Influenza Subtype					B					0%	0%	50%					100%	0%				
					A/H3					0%	0%	0%					0%	100%				
					A/pH1					100%	100%	50%					0%	0%				
					Untyped					0%	0%	0%					0%	0%				

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— Observed FRI rate (expected rate = dashed line) ● Moderately elevated ● Substantially elevated — Pneumonia rate (incl. afebrile)

MCRD SD FRI Rates and Diagnostic Test Results
 Shaded bars represent monthly proportions of each pathogen (clear = no pathogen identified)

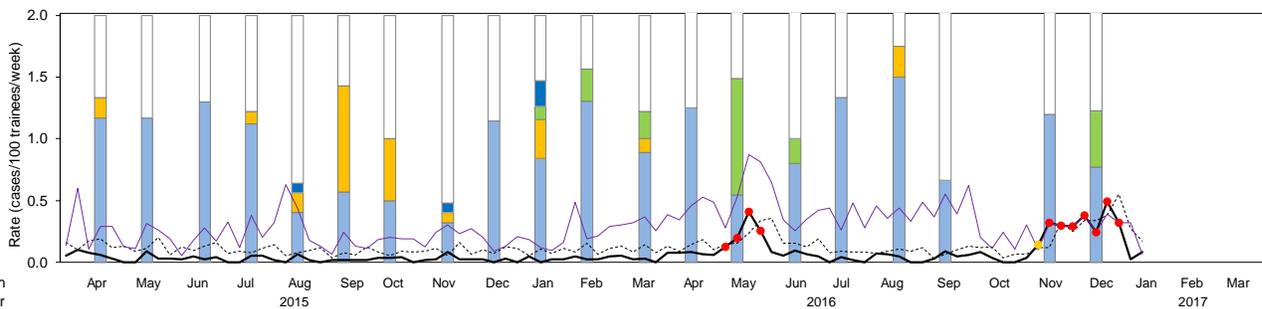


Samples Received	34	42	88	56	62	57	50	28	43	40	13	45	48	33	53	43	62	40	25	21	5	
Adenovirus	12%		2%	4%	2%				7%	5%		4%		6%	8%							
Influenza			24%						21%	10%		16%				7%						
RSV								4%		3%	2%											
C. pneumo																						
M. pneumo				4%	13%	7%	6%		2%	5%							3%	3%				
Rhinovirus	24%	33%	42%	25%	10%	19%	16%	39%	33%	20%	31%	27%	25%	48%	62%	60%	56%	50%	44%	62%	40%	

Influenza Subtype	B		76%						11%	0%		0%										100%
	A/H3		24%						89%	100%		86%										0%
	A/pH1		0%						0%	0%		14%										0%
	Untyped		0%						0%	0%		0%										0%

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MCRD PI FRI Rates and Diagnostic Test Results
 Shaded bars represent monthly proportions of each pathogen (clear = no pathogen identified)



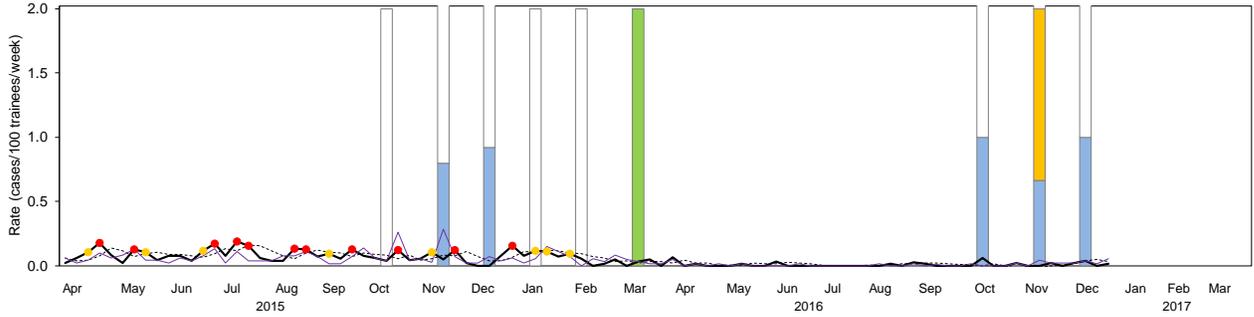
Samples Received	12	12	20	41	25	14	4	25	7	19	23	18	8	59	20	6	8	3	0	5	13	
Adenovirus					4%			4%		11%												
Influenza										5%	13%	11%		47%	10%							23%
RSV																						
C. pneumo																						
M. pneumo	8%			5%	8%	43%	25%	4%		16%	6%											13%
Rhinovirus	58%	58%	65%	56%	20%	29%	25%	16%	57%	42%	65%	44%	63%	27%	40%	67%	75%	33%		60%	38%	

Influenza Subtype	B									0%	0%	0%		0%	0%							0%
	A/H3									0%	0%	0%		100%	100%							100%
	A/pH1									100%	100%	100%		0%	0%							0%
	Untyped									0%	0%	0%		0%	0%							0%

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— Observed FRI rate (expected rate = dashed line) ● Moderately elevated ● Substantially elevated — Pneumonia rate (incl. afebrile)

Lackland AFB FRI Rates and Diagnostic Test Results
Shaded bars represent monthly proportions of each pathogen (clear = no pathogen identified)

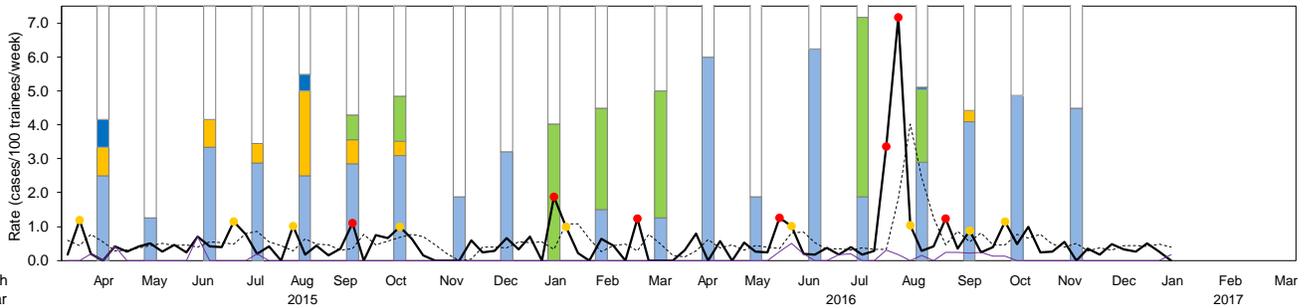


Samples Received	0	0	0	0	0	0	1	5	13	3	2	2					2	3	4	
Adenovirus																				
Influenza												100%								
RSV																				
C. pneumo																				
M. pneumo																				67%
Rhinovirus								40%	46%								50%	33%	50%	

Influenza Subtype	B	A/H3	A/pH1	Untyped
		50%	0%	50%
			50%	0%
				0%

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Cape May FRI Rates and Diagnostic Test Results
Shaded bars represent monthly proportions of each pathogen (clear = no pathogen identified)



Samples Received	9	6	9	13	15	21	17	4	7	13	5	6	5	12	6	24	101	22	20	10
Adenovirus	11%				7%												1%			
Influenza						10%	18%			54%	40%	50%				71%	29%			
RSV																				
C. pneumo																				
M. pneumo	11%	11%	8%	33%	10%	6%												5%		
Rhinovirus	33%	17%	44%	38%	33%	38%	41%	25%	43%		20%	17%	80%	25%	83%	25%	39%	55%	65%	60%

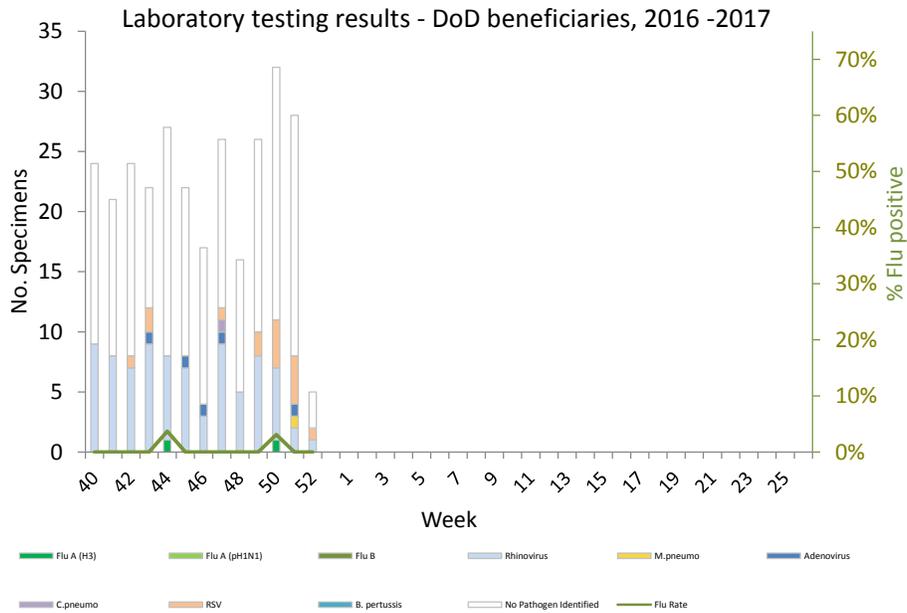
Influenza Subtype	B	A/H3	A/pH1	Untyped
		0%	0%	100%
		100%	100%	0%
		0%	0%	100%
		0%	0%	0%
				0%
				7%

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— Observed FRI rate (expected rate = dashed line) ● Moderately elevated ● Substantially elevated — Pneumonia rate (incl. afebrile)

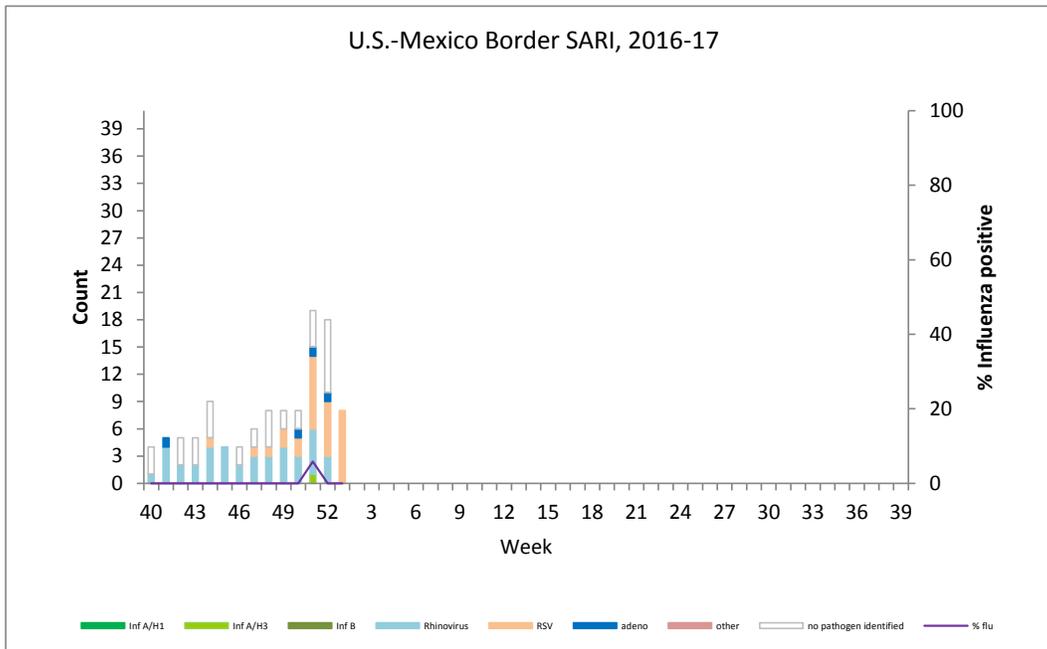
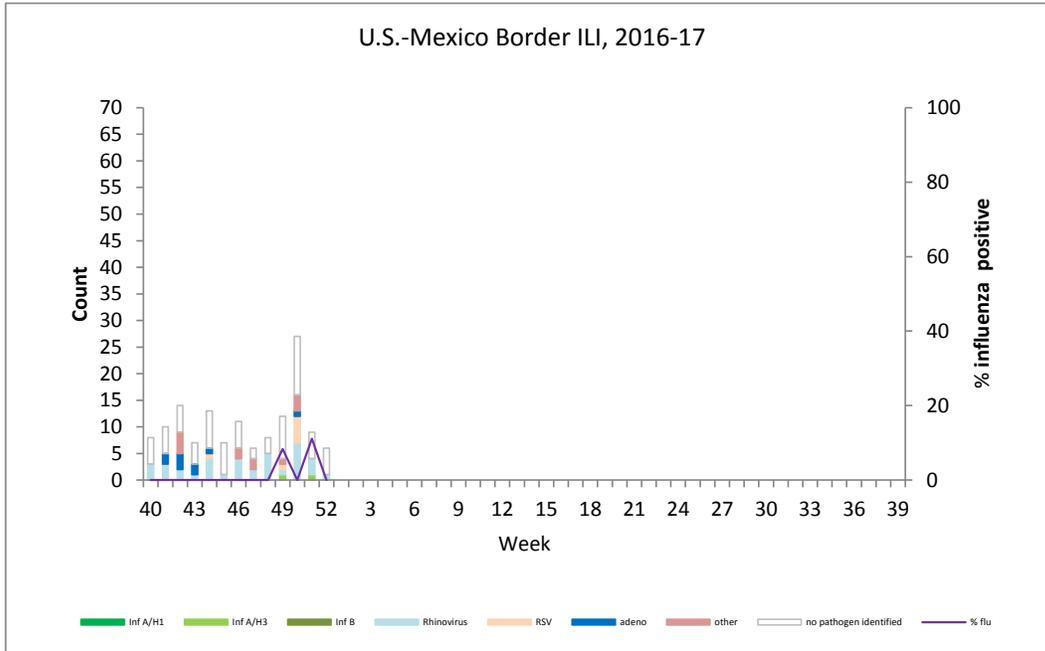
DoD Beneficiary Surveillance

- NHRC conducts FRI surveillance among (non-active duty) DoD beneficiaries at Lovell FHCC (Great Lakes, IL) and in 4 NMC San Diego facilities: the Emergency Department, Pediatric Department, Naval Branch Health Clinic Kearny Mesa, and NH Camp Pendleton.
- For questions regarding surveillance in this population, please contact the principal investigators at NHRC-FRI_Ben@med.navy.mil.



US-Mexico Border Surveillance

- In collaboration with the CDC Border Infectious Disease Surveillance program and San Diego/Imperial Counties, NHRC performs laboratory testing for FRI cases among civilians near the US-Mexico border. Both outpatient (FRI) and inpatient (Severe Acute Respiratory Illness; SARI) cases are included in the program. Current sites are located in San Diego (2) and Imperial (5) counties in California.



Phylogenetic Comparison of Influenza A (H3N2) HA and NA Protein Sequences

- 3 analyzed H3N2 HA sequences were derived from MDCK isolates and 19 were derived from clinical specimen.
- 2 analyzed H3N2 NA sequences were derived from MDCK isolates and 16 were derived from clinical specimen.
- Phylogenetic trees for both HA and NA protein sequences were generated by Clustal V method using DNASTAR® Lasergene Megalign software.
- Amino acid changes shown are with respect to 2010 vaccine strain **A/Perth/16/2009-like virus** for HA sequences and **A/Norway/1186/2011** for NA sequences

Summary of Influenza A (H3N2) Protein Homology When Compared with 2016-2017 Vaccine Strain

Segment	No.	2016-2017 Vaccine Strain	Protein Homology
H3N2 HA	22	A/HongKong/4801/2014	97.8-98.6%
H3N2 NA	18	A/HongKong/4801/2014	97.3-98.1%

Summary of Influenza A (H3N2) N-Linked Glycosylation Mutations

- Loss or gain of N-linked glycosylation sites affect host innate immune system recognition and the ability to induce adaptive immune response thus altering its viral antigenicity.¹ Predicted loss or gain of N-linked glycosylation of protein sequences were calculated using CBS NetNGlyc 1.0 Server <http://www.cbs.dtu.dk/services/NetNGlyc/>

A/H3N2 Segment	Mutation	
	ADD GLY	LOSS GLY
HA	K160T	S124G, T135K
NA	S245N	

1. Sun X, Jayaraman A, Mainprasad P, Raman R, Houser K, Pappas C, ...Tumpey T. (2013). N-Linked Glycosylation of the Hemagglutinin Protein Influences Virulence and Antigenicity of the 1918 Pandemic and Seasonal H1N1 Influenza A Viruses. *Journal of Virology* 8756-8766.

Phylogenetic Comparison of Influenza B (Victoria and Yamagata) HA and NA Protein Sequences

- 1 analyzed Influenza B HA sequence was derived from MDCK isolate and belonged to the Y3 clade of the Yamagata lineage.
- 1 analyzed Influenza B NA sequence was derived from MDCK isolate and belonged to the Y3 clade of the Yamagata lineage.
- Phylogenetic trees for both HA and NA protein sequences were generated by Clustal V method using DNASTAR® Lasergene Megalign software.
- Amino acid changes shown (both HA and NA sequences) are with respect to previous vaccine strain, B/Florida/04/2006-like virus.

Summary of Influenza B Protein Homology When Compared with 2016-2017 Vaccine Strain

Segment	No. Isolates	2016-2017 Vaccine Strain	Protein Homology
B/Yamagata HA	1	B/Phuket/3073/2013	99.3%
B/Yamagata NA	1	B/Phuket/3073/2013	98.7%

Summary of Influenza B N-Linked Glycosylation Mutations

- Loss or gain of N-linked glycosylation sites affect host innate immune system recognition and the ability to induce adaptive immune response thus altering its viral antigenicity.¹ Predicted loss or gain of N-linked glycosylation of protein sequences were calculated using CBS NetNGlyc 1.0 Server <http://www.cbs.dtu.dk/services/NetNGlyc/>

INF B Segment	Mutation	
	ADD GLY	LOSS GLY
HA		
NA		

1. Sun X, Jayaraman A, Mainprasad P, Raman R, Houser K, Pappas C, ...Tumpey T. (2013). N-Linked Glycosylation of the Hemagglutinin Protein Influences Virulence and Antigenicity of the 1918 Pandemic and Seasonal H1N1 Influenza A Viruses. *Journal of Virology* 87:56-8766.

2. Lee H, Tang J, Kong D, Loh T, Chiang D, Lam T, Koay E. (2013). Comparison of Mutation Patterns in Full-Genome A/H3N2 Influenza Sequences Obtained Directly from Clinical Samples and the Same Samples after a Single MDCK Passage. *PLoS One*.

Evolutionary Relationships Among Influenza A (H3N2) Neuraminidase (NA) Genes 2016-2017 Influenza Season

Vaccine Strain

Reference Strain

2015-16 Consensus (37 strains)

July-Sept 2016 (14 strains)

Oct-Dec 2016 (4 strains)

LOSS GLY: predicted loss of glycosylation

ADD GLY: predicted addition of glycosylation

NHRC: Naval Health Research Center

BRD: US/Mexico Border outpatient

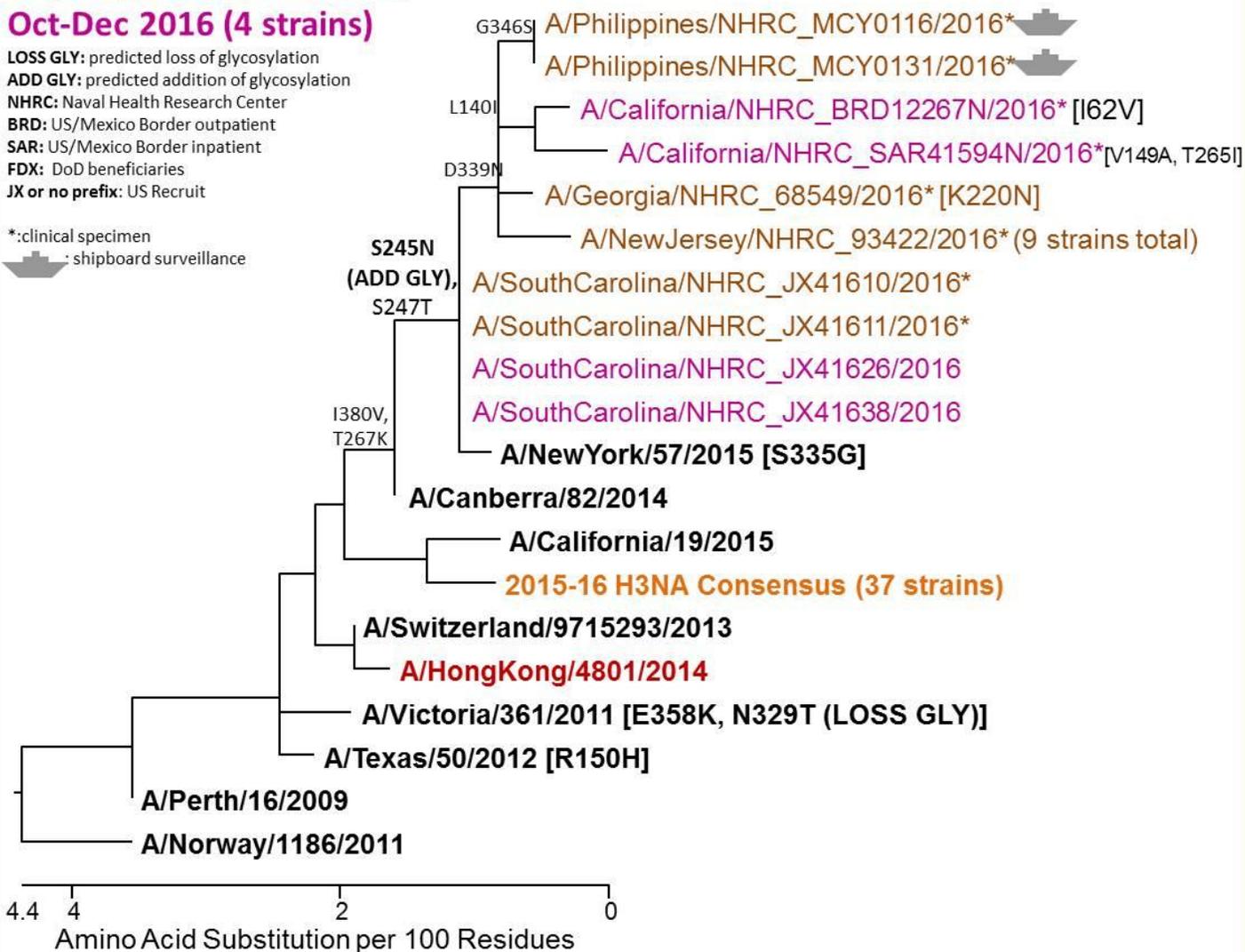
SAR: US/Mexico Border inpatient

FDX: DoD beneficiaries

JX or no prefix: US Recruit

*: clinical specimen

🚢: shipboard surveillance



Evolutionary Relationships Among Influenza B (Yamagata Lineage) Hemagglutinin (HA) Genes 2016-2017 Influenza Season

Vaccine Strain

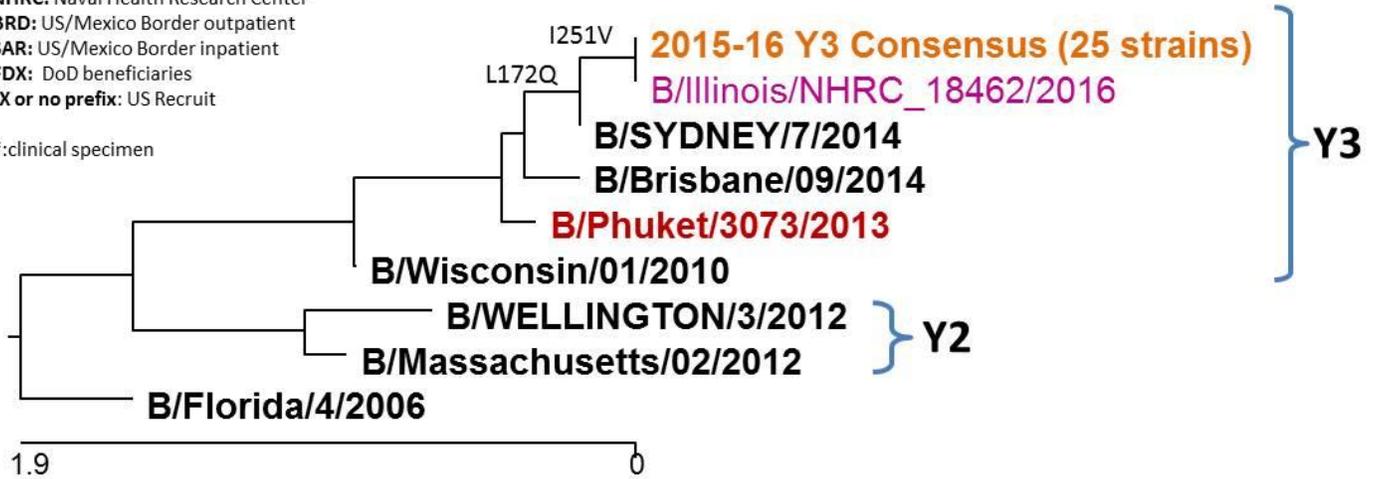
Reference Strain

2015-16 Consensus (25 strains)

Oct 2016 (1 strain)

LOSS GLY: predicted loss of glycosylation
ADD GLY: predicted addition of glycosylation
NHRC: Naval Health Research Center
BRD: US/Mexico Border outpatient
SAR: US/Mexico Border inpatient
FDX: DoD beneficiaries
JX or no prefix: US Recruit

*:clinical specimen



Evolutionary Relationships Among Influenza B (Yamagata Lineage) Neuraminidase (NA) Genes 2016-2017 Influenza Season

Vaccine Strain

Reference Strain

2015-16 Consensus (26 strains)

Oct 2016 (1 strain)

LOSS GLY: predicted loss of glycosylation
 ADD GLY: predicted addition of glycosylation
 NHRC: Naval Health Research Center
 BRD: US/Mexico Border outpatient
 SAR: US/Mexico Border inpatient
 FDY: DoD beneficiaries
 JX or no prefix: US Recruit

*:clinical specimen

