



Febrile Respiratory Illness (FRI) Surveillance Update

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



2015 Week 38 (through 26 September 2015)

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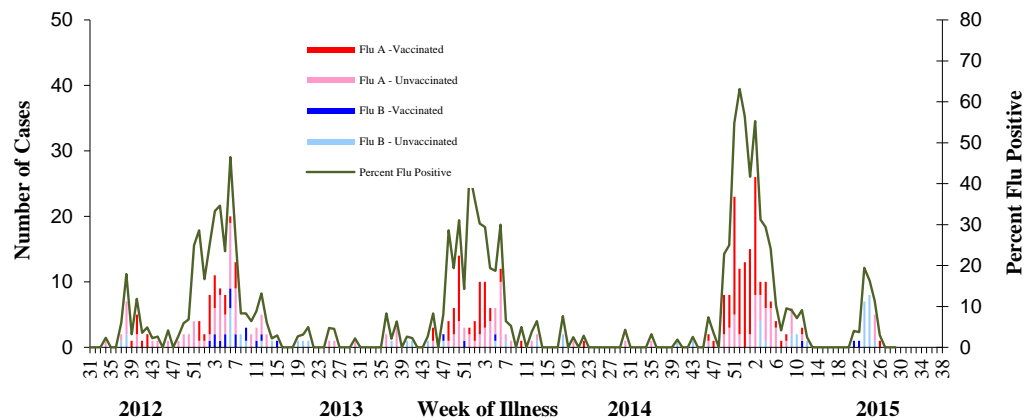
Influenza

NHRC Laboratory-Confirmed Influenza Cases, US Military Basic Trainees

Site	Current Week*				Since Oct.1, 2014				No. Tested
	A/Untyp.	A/H3	A/H1N1	B	A/Untyp.	A/H3	A/H1N1	B	
Ft. Benning						18		1	157
Ft. Jackson						17		3	386
Ft. Leonard Wood						13		1	181
NRTC Great Lakes						26		2	82
Lackland AFB									
MCRD Parris Island						12		2	240
MCRD San Diego					3	54		21	555
CGTC Cape May						5		1	76
Total	0	0	0	0	3	145	0	31	1677

- 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.
- Most A/H3 isolates from 2014-15 NHRC surveillance are in the “drifted” subclades that may not be well-matched by the 2014-15 vaccine (phylogenetic HA and NA trees on pages 9-16).
- For more information about NHRC FRI surveillance programs, please [contact NHRC](#).

Vaccination Status of Confirmed Influenza Cases
Among Military Basic Trainees, 2012-15



Other Items of Interest

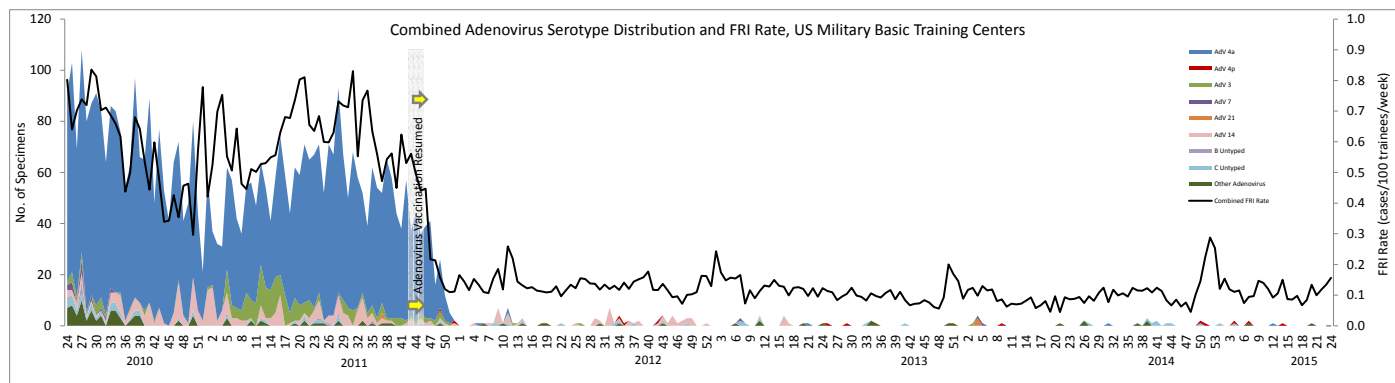
- NHRC is conducting laboratory-based surveillance for meningococcal disease. The program’s purpose is to track and characterize meningococcal cases among DoD medical beneficiaries. For more information and the most recent data, [click here](#).

Items of Note

- Elevated FRI rates at Fort Benning and CGTC Cape May
- NHRC has capability to test for novel H7N9 influenza virus, MERS coronavirus, enterovirus EV-68, and Ebola virus

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 2012-14. 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 26 September 2015:

- **At or below expected value:**

[Fort Jackson](#) (data through 19 September)

[Fort Leonard Wood](#)

[Naval Recruit Training Command, Great Lakes](#)

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

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

• **Moderately elevated:**

None

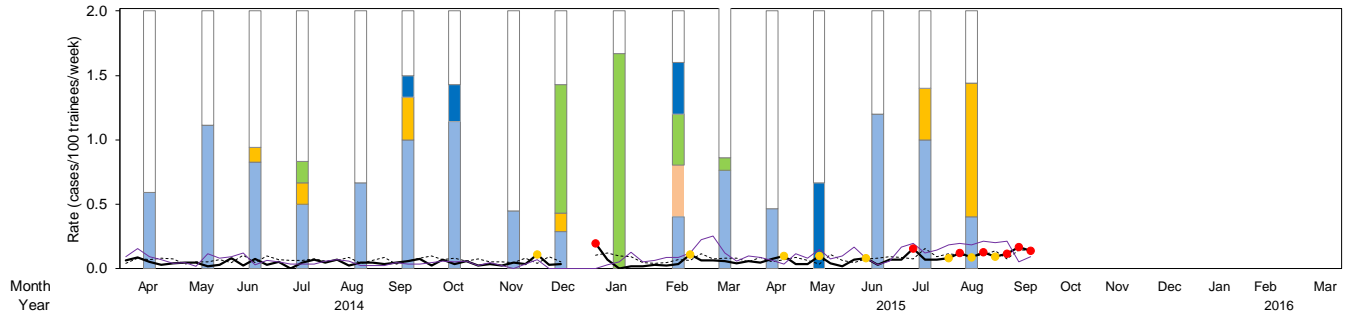
• **Substantially elevated:**

[Fort Benning](#)

[Coast Guard Training Center, Cape May](#) (data through 19 September)

[Lackland Air Force Base](#) (data through 18 July)

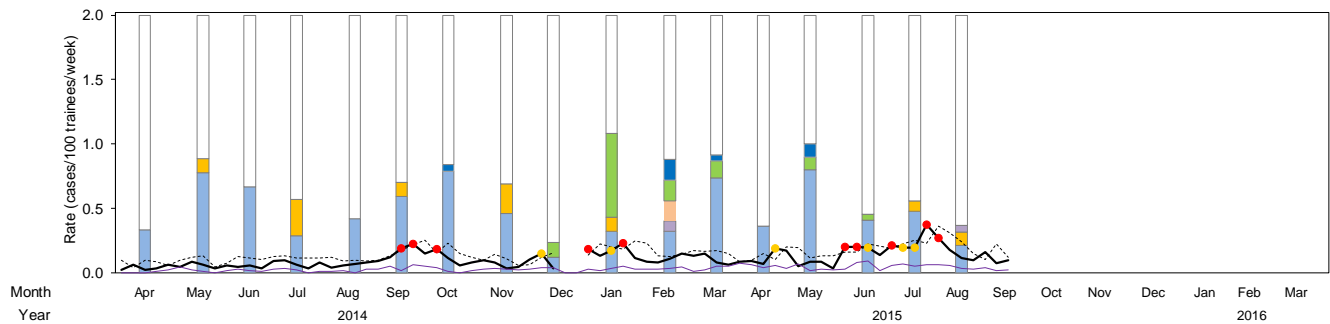
Ft. Benning FRI Rates and Diagnostic Test Results
 Shaded bars represent monthly proportions of each pathogen (clear = no pathogen identified)



Month Year	Apr	May	Jun	Jul	Aug	Sep	Oct	Nov	Dec	Jan	Feb	Mar	Apr	May	Jun	Jul	Aug	Sep
Samples Received	17	9	17	12	21	24	14	9	14	12	5	21	13	6	10	20	25	
Adenovirus						8%	14%				20%			33%				
Influenza				8%					50%	83%	20%	5%						
RSV											20%							
C. pneumo																		
M. pneumo			6%	8%		17%			7%							20%	52%	
Rhinovirus	29%	56%	41%	25%	33%	50%	57%	22%	14%		20%	38%	23%		60%	50%	20%	
Influenza Subtype	B			0%					0%	0%	0%	100%						
	A/H3			100%					100%	100%	100%	0%						
	A/pH1			0%					0%	0%	0%	0%						
	Untyped			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)

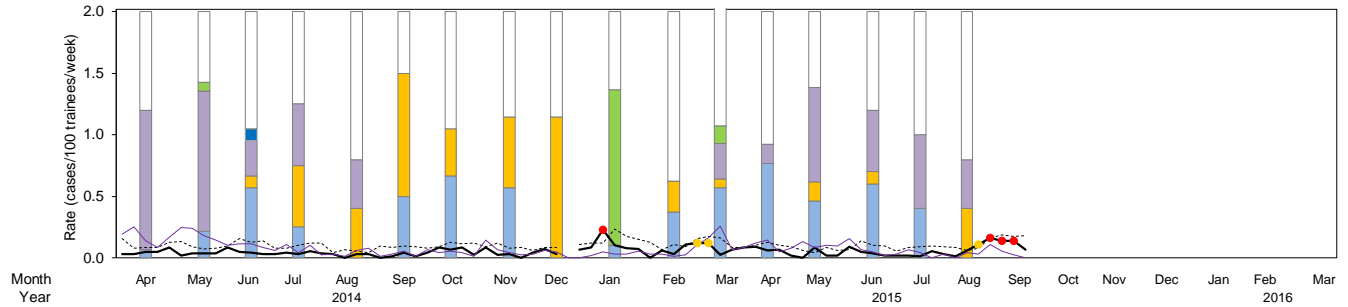


Month Year	Apr	May	Jun	Jul	Aug	Sep	Oct	Nov	Dec	Jan	Feb	Mar	Apr	May	Jun	Jul	Aug	Sep
Samples Received	6	18	12	14	19	54	38	26	17	37	25	46	33	20	44	50	38	
Adenovirus							3%				8%	2%		5%				
Influenza									6%	32%	8%	7%		5%	2%			
RSV																		
C. pneumo											4%							
M. pneumo		6%		14%		6%	12%			5%						4%	5%	
Rhinovirus	17%	39%	33%	14%	21%	30%	39%	23%	6%	16%	16%	37%	18%	40%	20%	24%	11%	
Influenza Subtype	B									0%	0%	0%	33%	100%	100%			
	A/H3									100%	100%	100%	67%	0%	0%			
	A/pH1									0%	0%	0%	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)

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

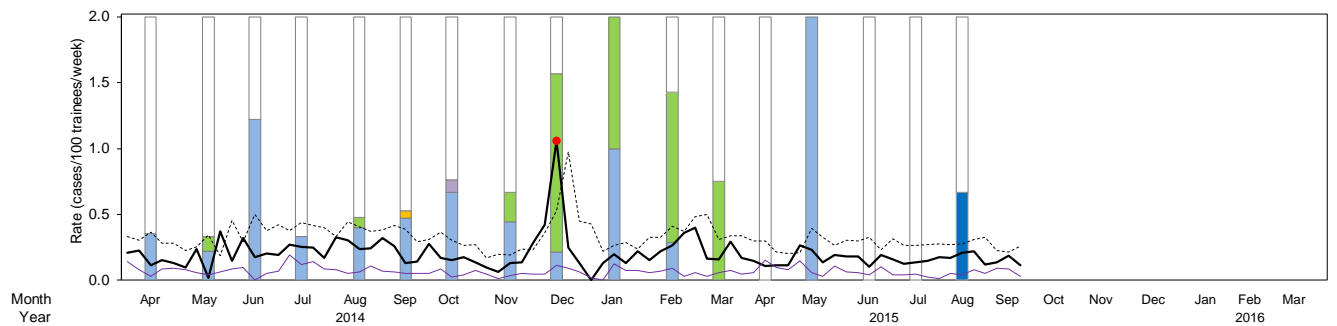


Samples Received	30	28	21	8	5	4	21	14	7	19	16	28	26	13	20	10	5
Adenovirus			5%														
Influenza		4%								63%		7%					
RSV																	
C. pneumo	57%	57%	14%	25%	20%							14%	8%	38%	25%	30%	20%
M. pneumo			5%	25%	20%	50%	19%	29%	57%		13%	4%		8%	5%		20%
Rhinovirus	3%	11%	29%	13%		25%	33%	29%		5%	19%	29%	38%	23%	30%	20%	

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



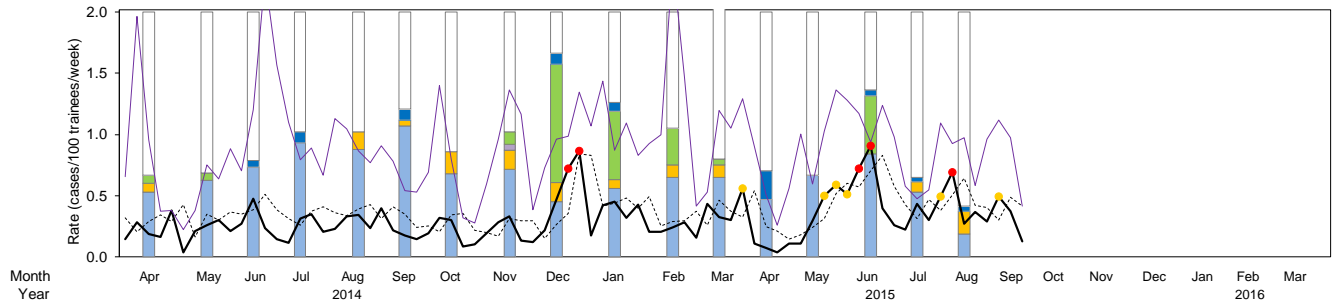
Samples Received	17	18	18	12	25	34	21	9	28	2	7	8	1	1	1	3	3
Adenovirus																	33%
Influenza		6%			4%			11%	68%	50%	57%	38%					
RSV																	
C. pneumo							5%										
M. pneumo						3%											
Rhinovirus	18%	11%	61%	17%	20%	24%	33%	22%	11%	50%	14%		100%				

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

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

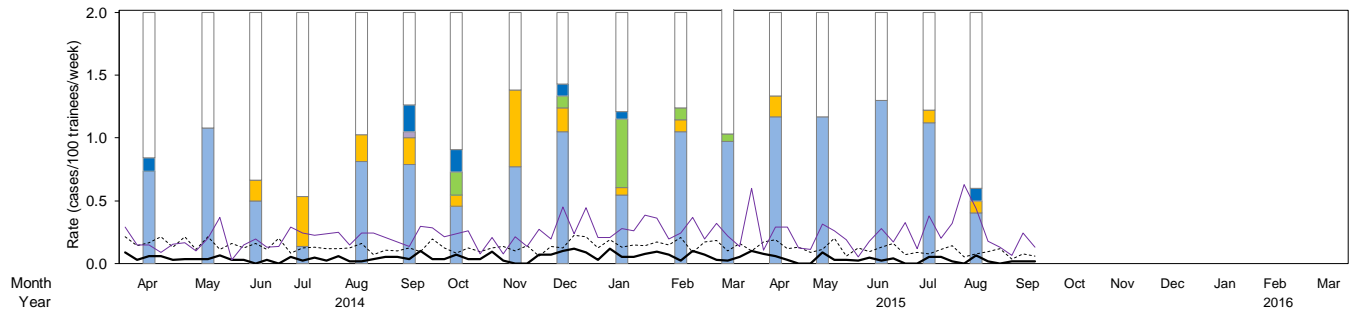
MCRD SD FRI Rates and Diagnostic Test Results
Shaded bars represent monthly proportions of each pathogen (clear = no pathogen identified)



Samples Received		30	32	38	43	41	43	44	39	66	57	40	40	34	42	88	49	43
Adenovirus				3%	5%		5%			5%	4%			12%		2%	2%	2%
Influenza		3%	3%						5%	48%	28%	15%	3%			24%		
RSV																		
C. pneumo									3%									
M. pneumo		3%			7%	2%	9%		8%	8%	4%	5%	5%				4%	9%
Rhinovirus		27%	31%	37%	47%	44%	53%	34%	36%	23%	28%	33%	33%	24%	33%	42%	27%	9%
Influenza Subtype	B	100%	100%						0%	0%	31%	0%	0%			76%		
	A/H3	0%	0%						100%	91%	69%	100%	100%			24%		
	A/pH1	0%	0%						0%	0%	0%	0%	0%			0%		
	Untyped	0%	0%						0%	9%	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)

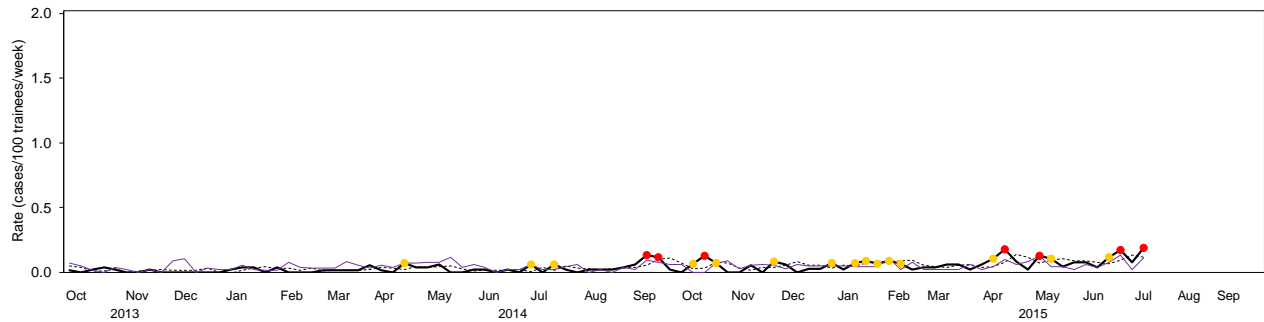


Samples Received		19	13	12	15	37	38	22	13	21	33	21	33	12	12	20	41	20
Adenovirus		5%					11%	9%		5%	3%							5%
Influenza								9%		5%	27%	5%	3%					
RSV																		
C. pneumo							3%											
M. pneumo				8%	###	11%	11%	5%	31%	10%	3%	5%		8%			5%	5%
Rhinovirus		37%	54%	25%	7%	41%	39%	23%	38%	52%	27%	52%	48%	58%	58%	65%	56%	20%
Influenza Subtype	B							100%		0%	0%	0%	0%					
	A/H3							0%	###	100%	100%	100%						
	A/pH1							0%	0%	0%	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)

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

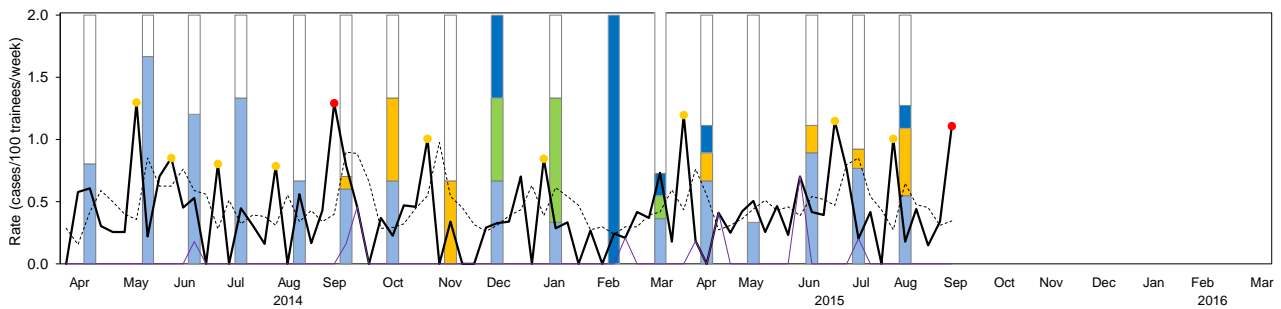


Samples Received	Oct	Nov	Dec	Jan	Feb	Mar	Apr	May	Jun	Jul	Aug	Sep	Oct	Nov	Dec	Jan	Feb	Mar	Apr	May	Jun	Jul	Aug	Sep
Adenovirus	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Influenza																								
RSV																								
C. pneumo																								
M. pneumo																								
Rhinovirus																								

Influenza Subtype	B	A/H3	A/pH1	Untyped
B				
A/H3				
A/pH1				
Untyped				

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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	Apr	May	Jun	Jul	Aug	Sep	Oct	Nov	Dec	Jan	Feb	Mar	Apr	May	Jun	Jul	Aug	Sep
Adenovirus									33%		100%	9%	11%				9%	
Influenza									33%	50%		9%						
RSV																		
C. pneumo																		
M. pneumo						5%	33%	33%					11%		11%	8%	27%	
Rhinovirus	40%	83%	60%	67%	33%	30%	33%		33%	17%		18%	33%	17%	44%	38%	27%	

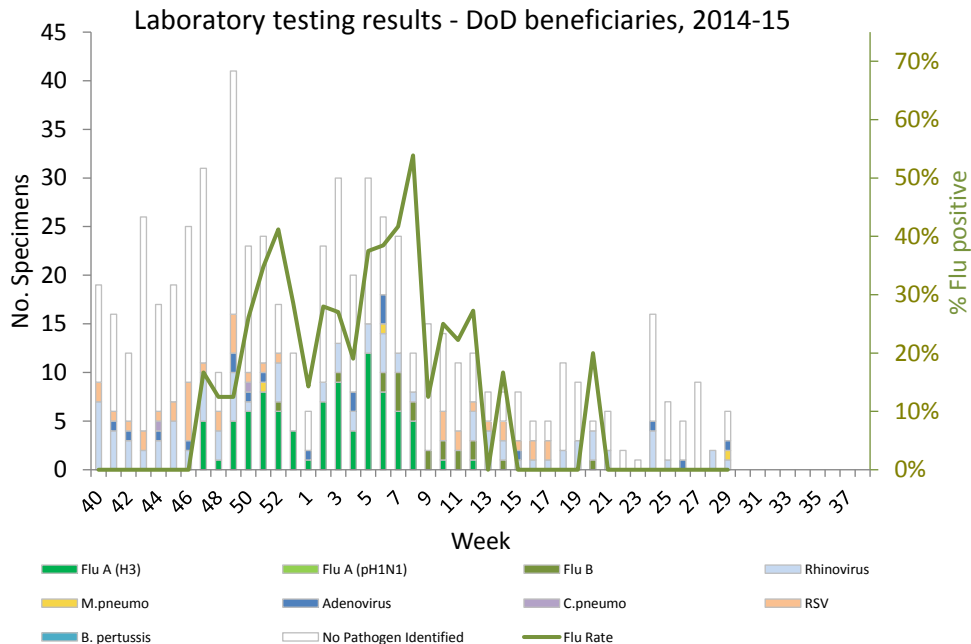
Influenza Subtype	B	A/H3	A/pH1	Untyped
B		0%	0%	100%
A/H3		100%	100%	0%
A/pH1		0%	0%	0%
Untyped		0%	0%	0%

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

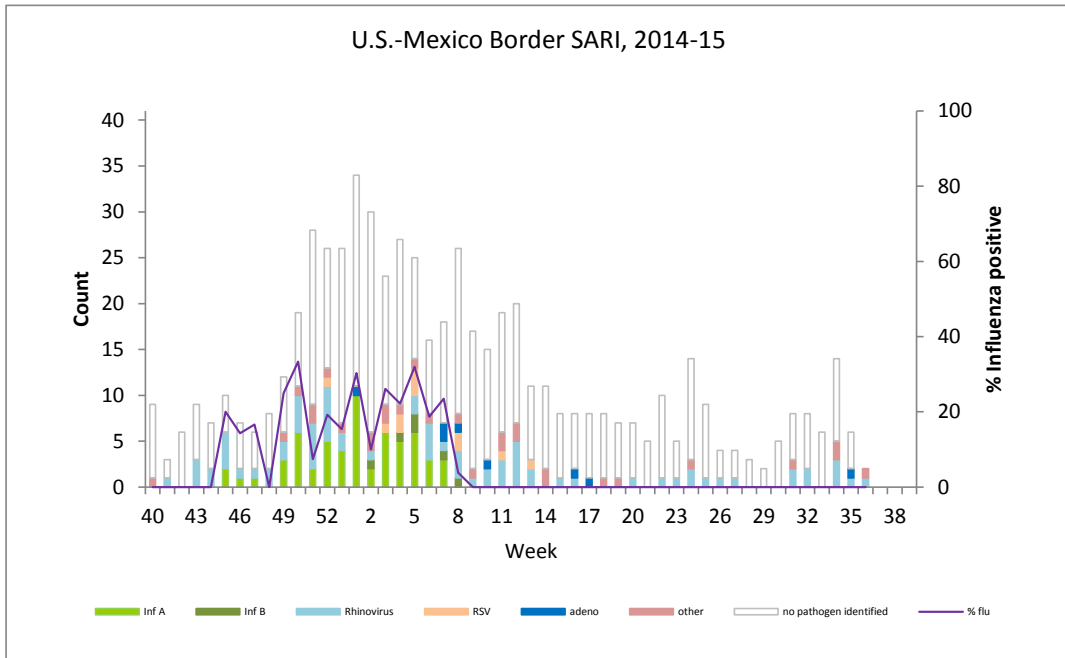
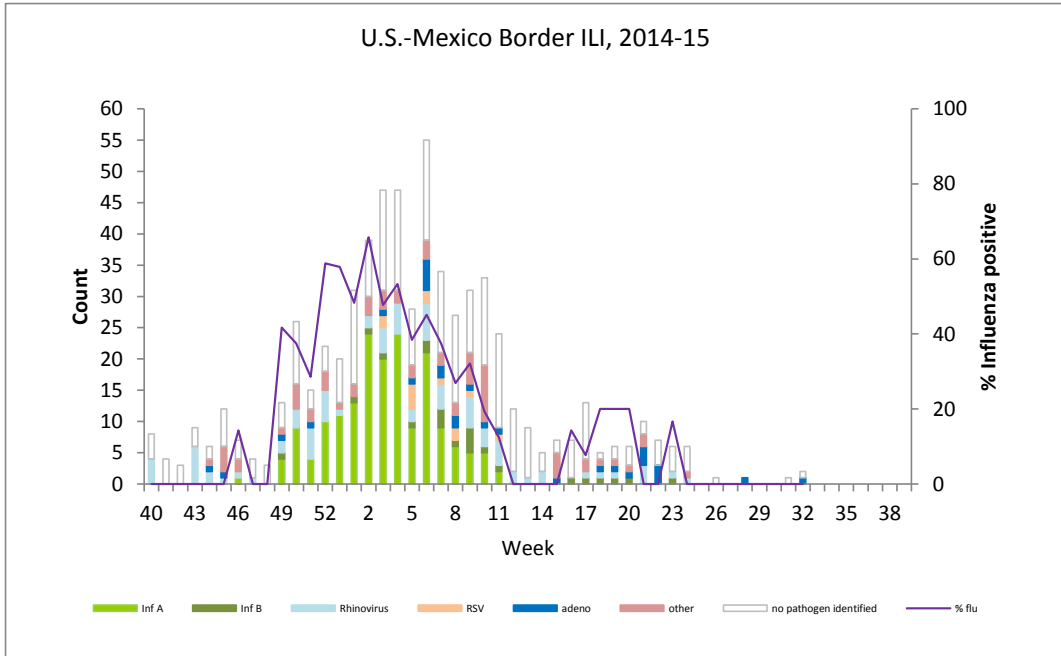
DoD Beneficiary Surveillance

- 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 investigator (Chris Myers, christopher.a.myers48.civ@mail.mil) or the study coordinator (Erin Hansen, erin.a.hansen.ctr@mail.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

- **140** analyzed H3N2 HA sequences were derived from MDCK isolates.
- **5** analyzed H3N2 HA sequences were derived from clinical samples.
- **130** analyzed H3N2 NA sequences were derived from MDCK isolates.
- 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 2010 vaccine strain **A/Perth/16/2009-like virus**

Summary of Influenza A (H3N2) Protein Homology When Compared to 2014-2015 Vaccine Strain

Segment	No. Specimens	2014-2015 Vaccine Strain	Protein Homology
H3N2 HA	145	A/Texas/50/2012	96.5-99.2%
H3N2 NA	130	A/Texas/50/2012	97.8-98.8%

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	N122D T128A N144S N158K N158H T160K T160I
NA	S245N D151N* N329I S331R	N86D N151G* S247T N329T

***This mutation may be an indicator of MDCK culture-induced changes.²**

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.

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*.

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

- 47 analyzed Influenza B HA sequences were derived from MDCK isolates. 18 (41%) isolates belong to the V1A clade of the Victoria Lineage and 26 (59%) belong to the Y3 clade of the Yamagata lineage.
- 44 analyzed Influenza B NA sequences were derived from MDCK isolates. 18 (42%) isolates belong to the V1A clade of the Victoria Lineage and 26 (58%) belong 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 strains B/Ohio/01/2005-like virus for B/Victoria specimens and B/Massachusetts/02/2012-like virus for B/Yamagata specimens.

Summary of Influenza B Protein Homology When Compared to 2014-2015 Vaccine Strain

Segment	No. Isolates	2014-2015 Vaccine Strain	Protein Homology
B/Victoria HA	20	B/Brisbane/60/2008	99.3-99.6%
B/Victoria NA	18	B/Brisbane/60/2008	98.5-99.4%
B/Yamagata HA	27	B/Massachusetts/02/2012	97.5-98.1%
B/Yamagata NA	26	B/Massachusetts/02/2012	96.1-97.0%

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	A199T	N197D N197S T199N
NA	D463N	N283S

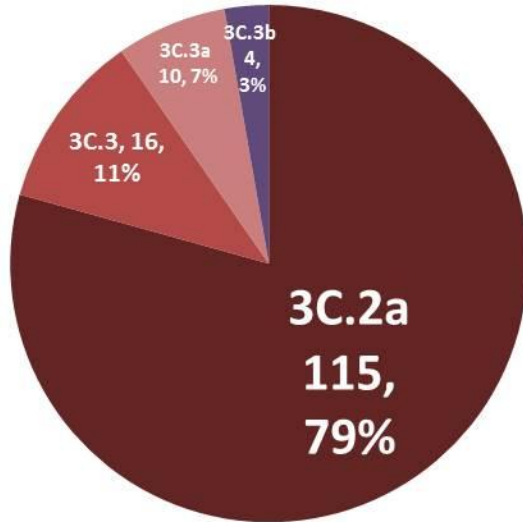
1. Sun X, Jayaraman A, Mainprasad P, Raman R, Houser K, Pappas C, ...Tumpey T. (2013).

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.

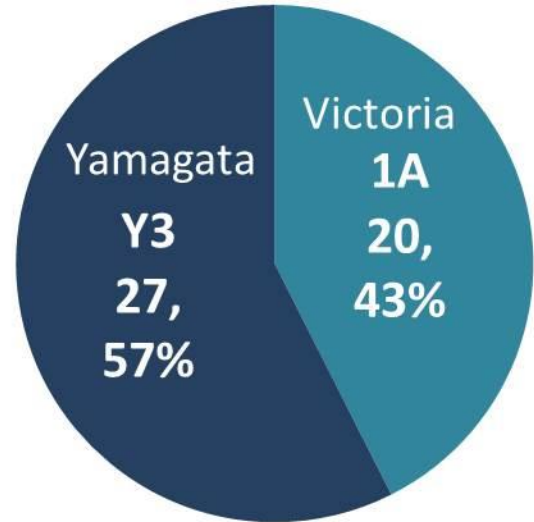
2. Lee H, Tang J, Kong D, Loh T, Chiang D, Lam T, Koay E. (2013). Comparison of Mutation Patterns in Full-Genome A/H3N2 Influenza Sequences Obtained Directly from Clinical Samples and the Same Samples after a Single MDCK Passage. *PLoS One*.

Summary of Influenza A/H3N2 and Influenza B Hemagglutinin (HA) Genetic Groups Sept 2014-June 2015

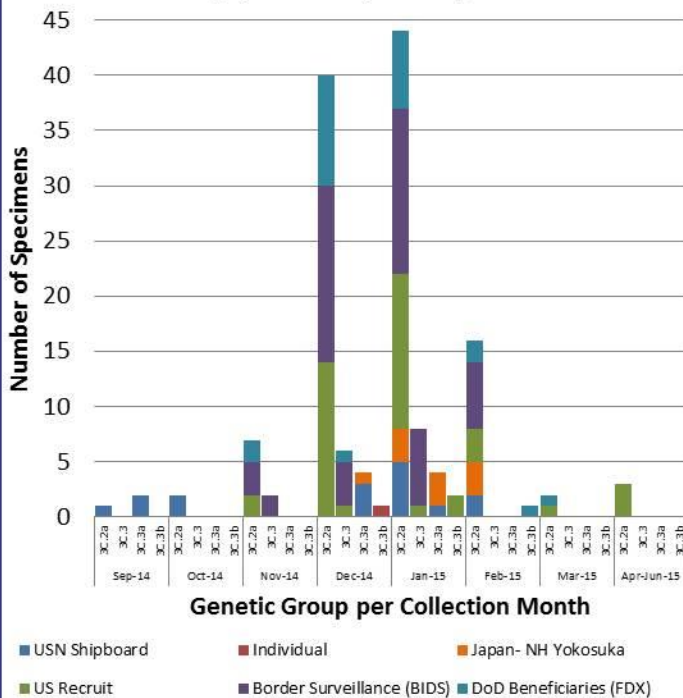
Influenza A/H3N2



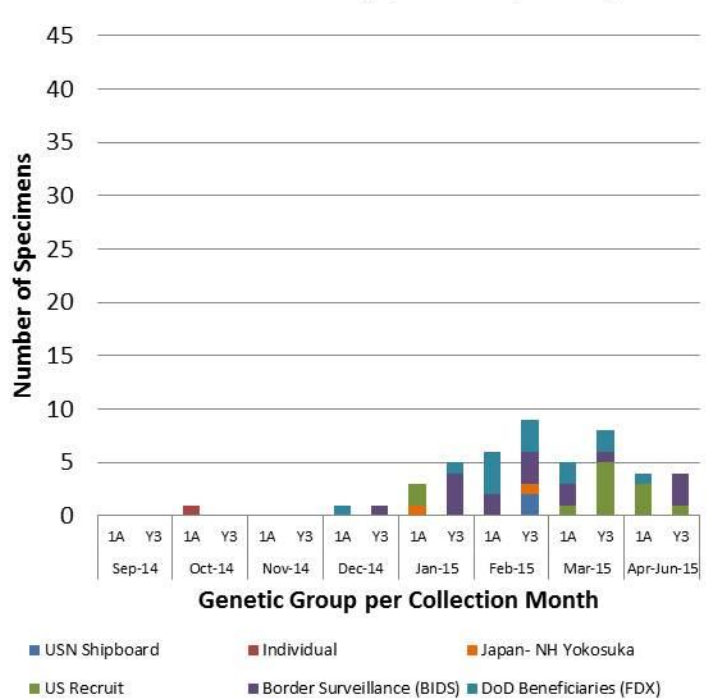
Influenza B



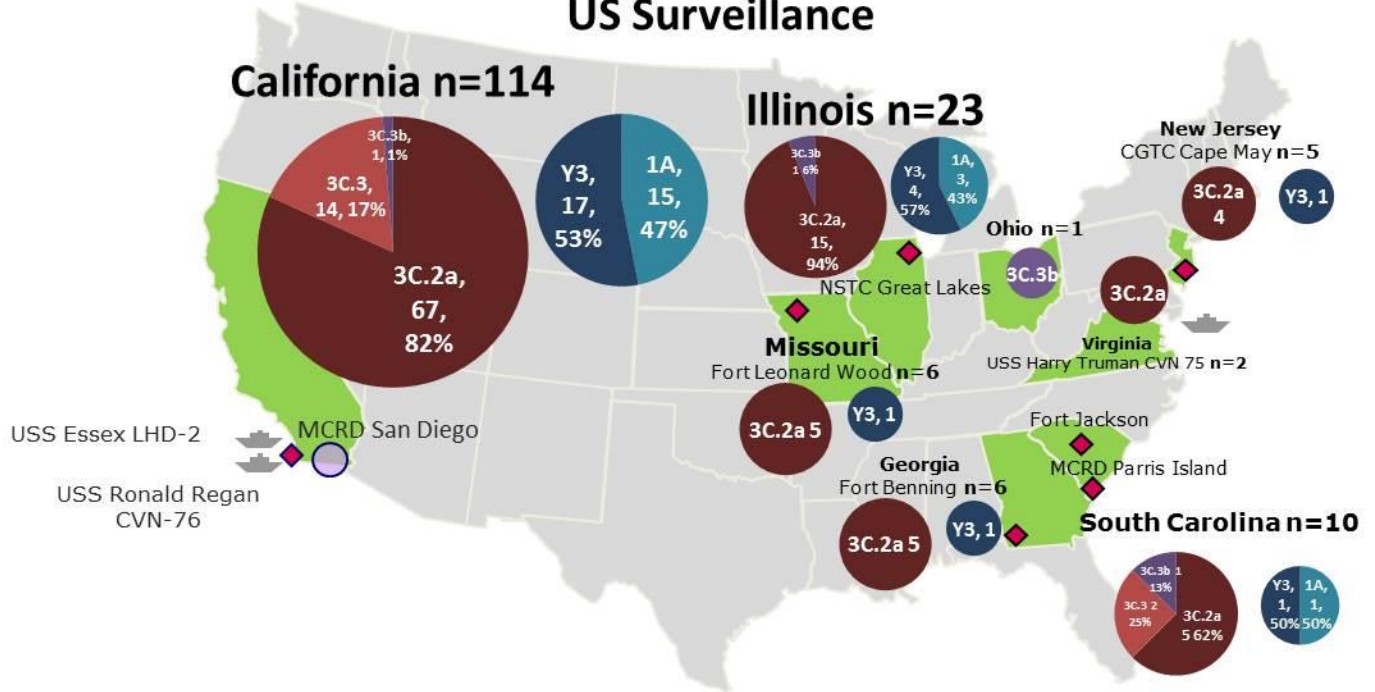
Distribution of Influenza A (H3N2) HA Genetic Groups by Collection Month (9/2014-6/2015)



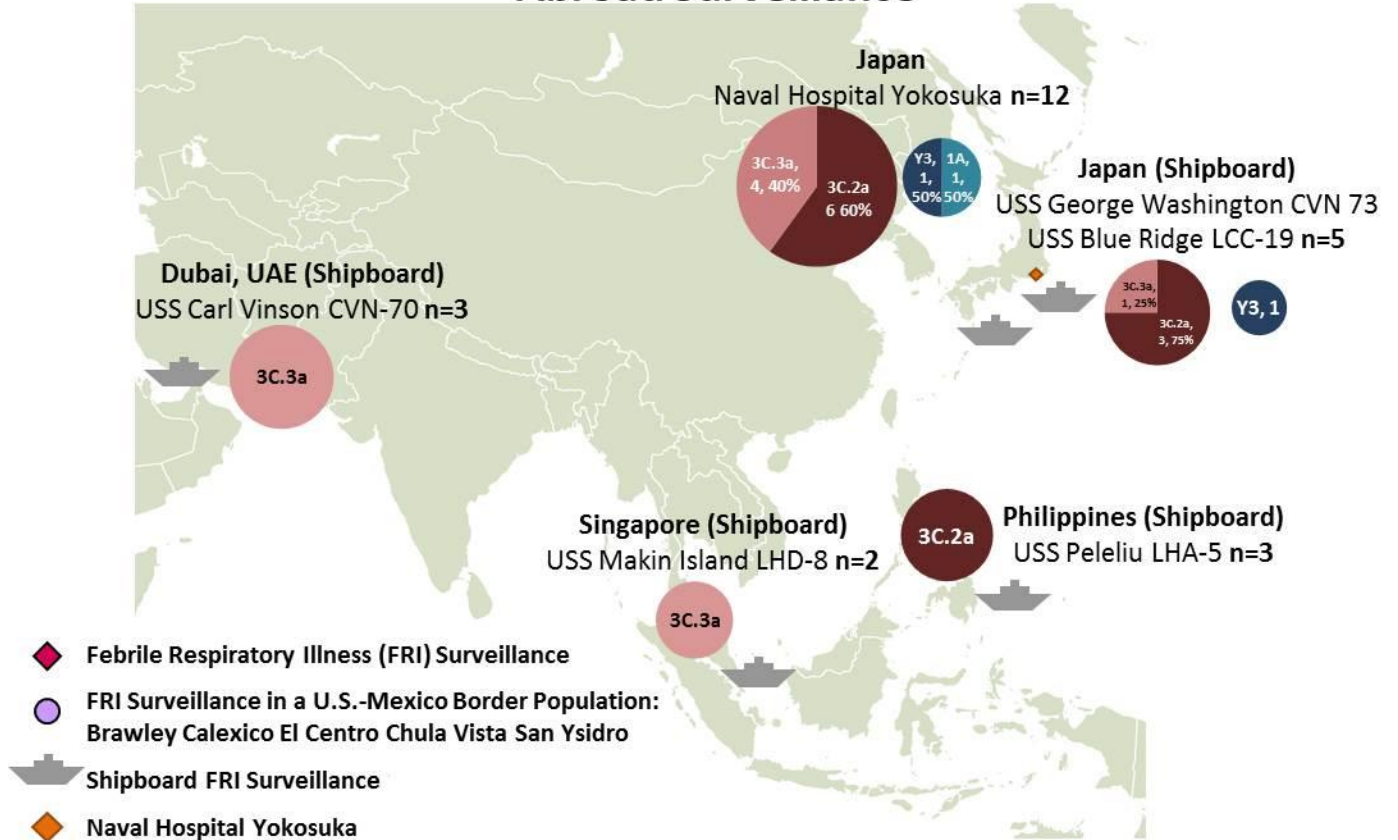
Distribution of Influenza B HA Genetic Groups (Yam. and Vict. Lineages) by Collection Month (9/2014-6/2015)



Geographic Distribution of Influenza A/H3N2 and Influenza B: US Surveillance



Geographic Distribution of Influenza A/H3N2 and Influenza B: Abroad Surveillance

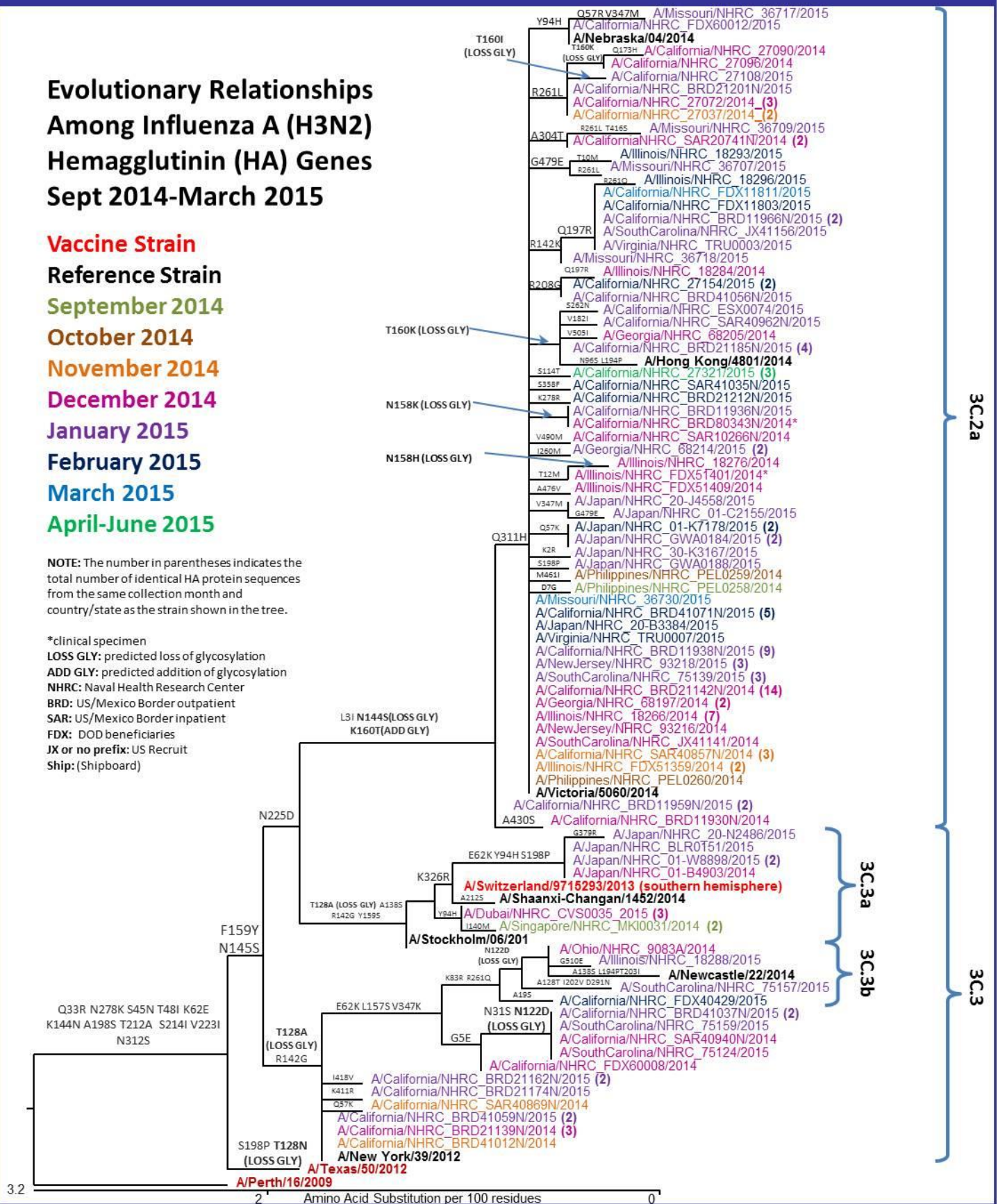


Evolutionary Relationships Among Influenza A (H3N2) Hemagglutinin (HA) Genes Sept 2014-March 2015

- Vaccine Strain**
- Reference Strain**
- September 2014
- October 2014
- November 2014
- December 2014
- January 2015
- February 2015
- March 2015
- April-June 2015

NOTE: The number in parentheses indicates the total number of identical HA protein sequences from the same collection month and country/state as the strain shown in the tree.

- *clinical specimen
- 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
- Ship: (Shipboard)

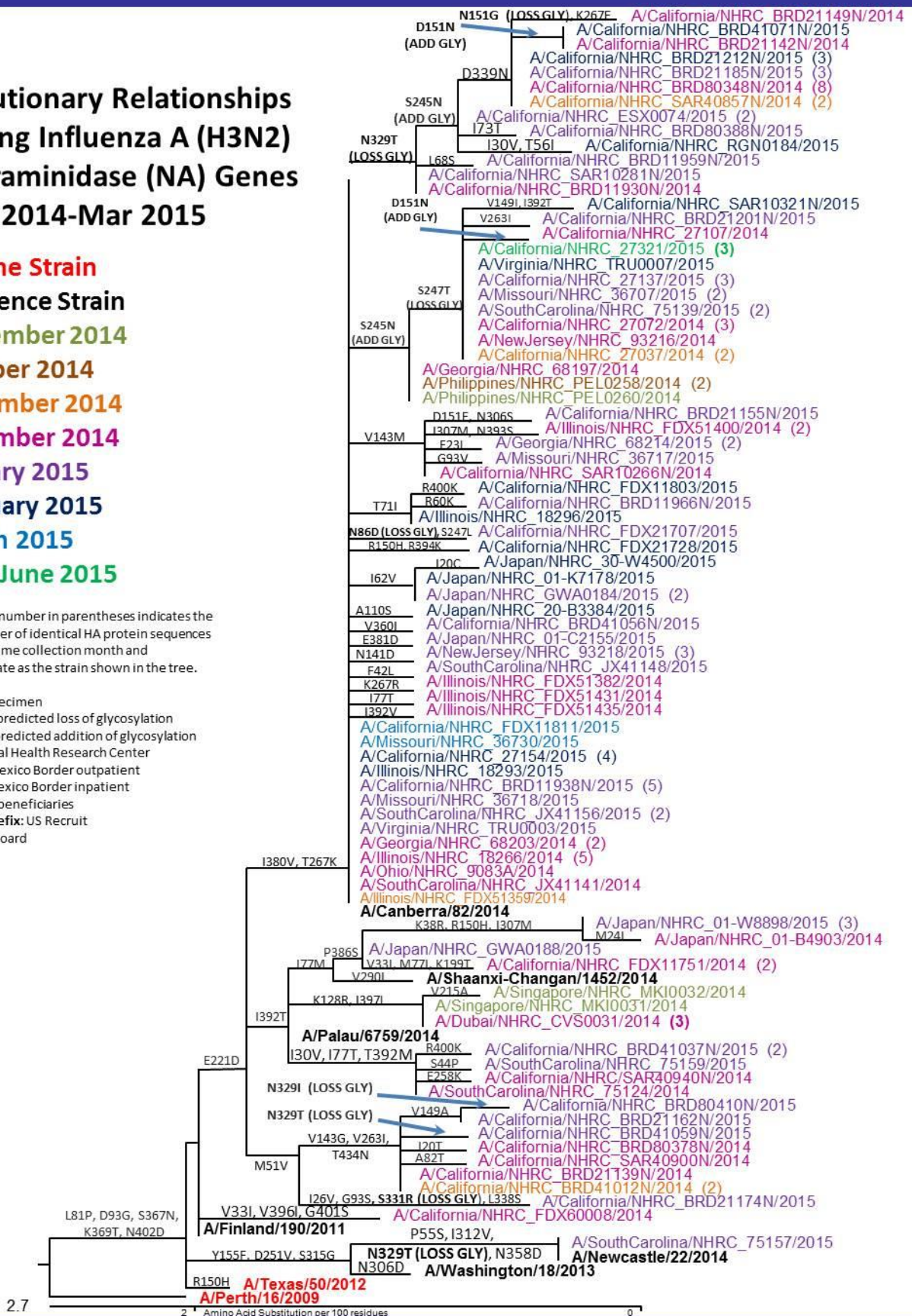


Evolutionary Relationships Among Influenza A (H3N2) Neuraminidase (NA) Genes Sept 2014-Mar 2015

- Vaccine Strain**
- Reference Strain**
- September 2014
- October 2014
- November 2014
- December 2014
- January 2015
- February 2015
- March 2015
- April-June 2015

NOTE: The number in parentheses indicates the total number of identical HA protein sequences from the same collection month and country/state as the strain shown in the tree.

- *clinical specimen
- 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
- Ship: Shipboard

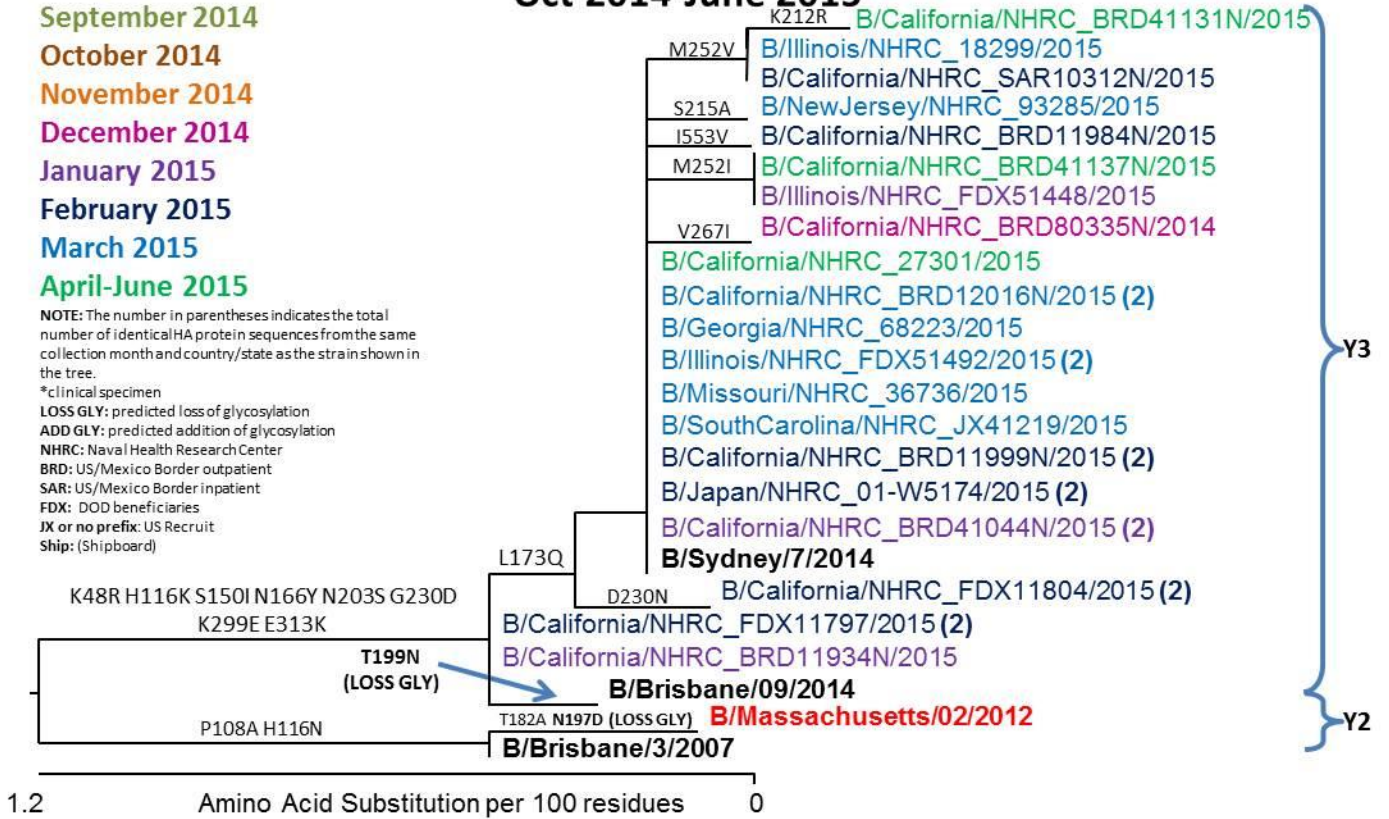


Evolutionary Relationships Among Influenza B Yamagata Lineage Hemagglutinin (HA) Genes Oct 2014-June 2015

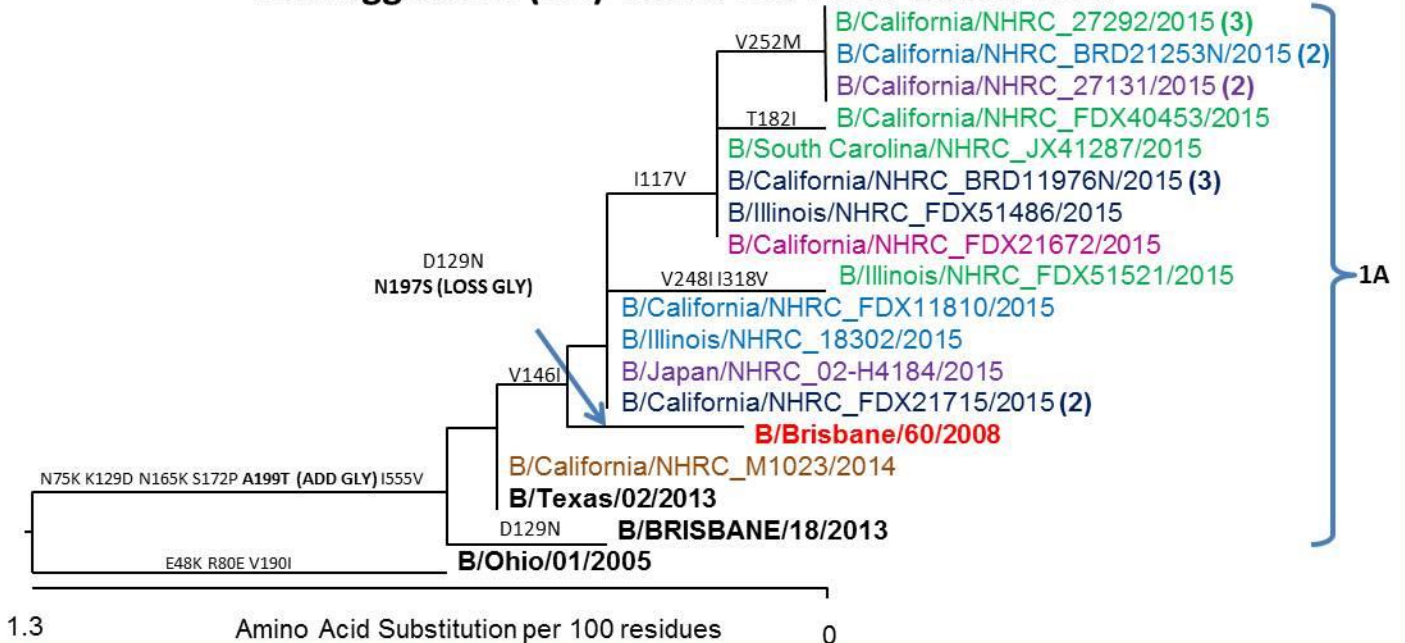
- Vaccine Strain**
- Reference Strain**
- September 2014
- October 2014
- November 2014
- December 2014
- January 2015
- February 2015
- March 2015
- April-June 2015

NOTE: The number in parentheses indicates the total number of identical HA protein sequences from the same collection month and country/state as the strain shown in the tree.

- *clinical specimen
- 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
- Ship: (Shipboard)



Evolutionary Relationships Among Influenza B Victoria Lineage Hemagglutinin (HA) Genes Oct 2014-March 2015

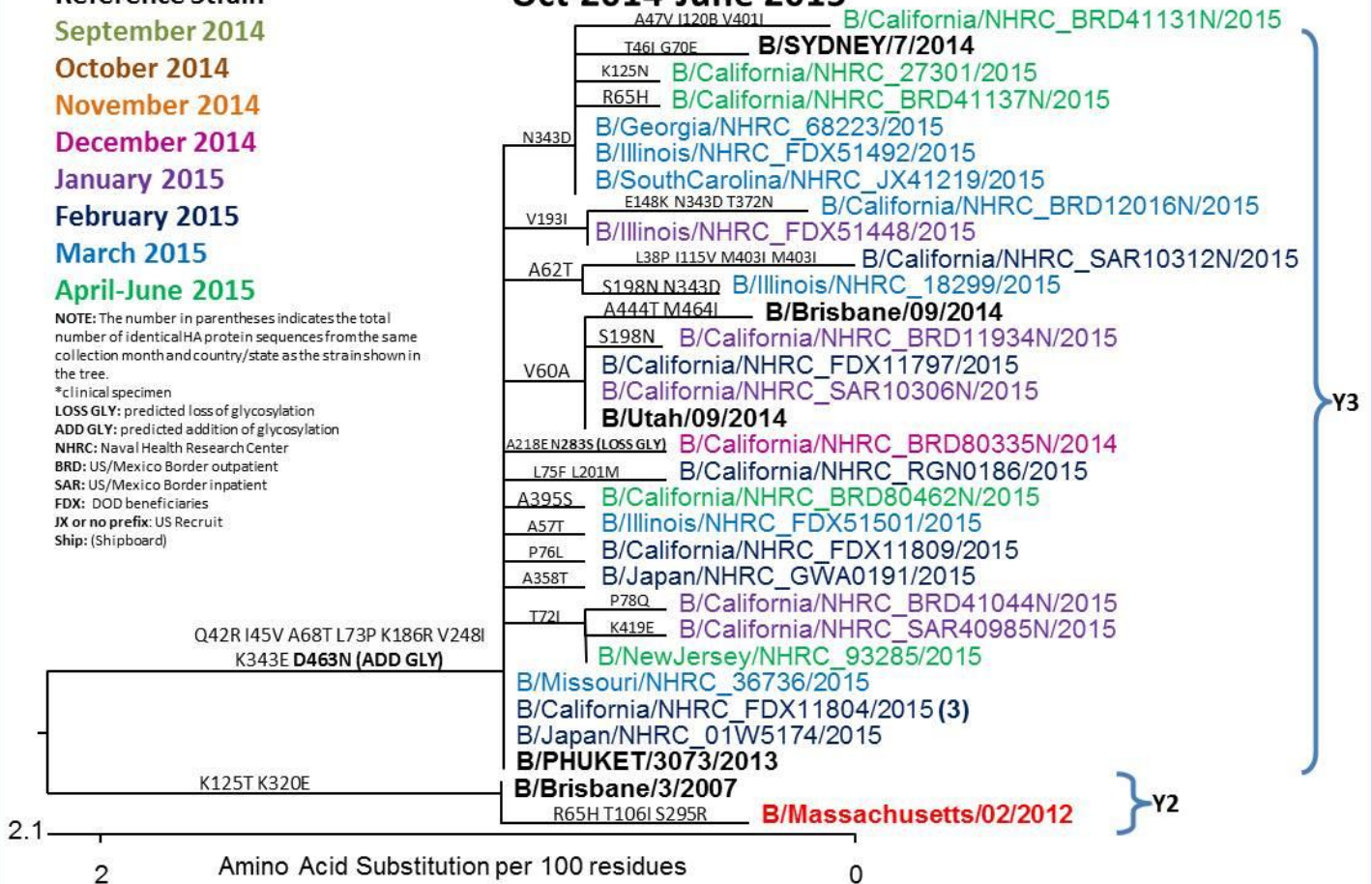


Evolutionary Relationships Among Influenza B Yamagata Lineage Neuraminidase (NA) Genes

- Vaccine Strain
- Reference Strain
- September 2014
- October 2014
- November 2014
- December 2014
- January 2015
- February 2015
- March 2015
- April-June 2015

Oct 2014-June 2015

NOTE: The number in parentheses indicates the total number of identical HA protein sequences from the same collection month and country/state as the strain shown in the tree.
 *clinical specimen
 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
 Ship: (Shipboard)



Evolutionary Relationships Among Influenza B Victoria Lineage Neuraminidase (NA) Genes

Oct 2014-April 2015

