

Right-Sizing Surveillance What does it mean?

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Several Definitions of Right-Sizing

- Right-sizing toward sustainability (financial limits)
- Right-sizing toward limited highly functional sites (really good data)
- Right-sizing toward statistical significance-looking at the right number of viruses to meet objectives

Activities Regarding Right-Sizing

- **2011-U.S starts to discuss virologic right-sizing and implemented new guidance to states for 2015-16 season—more later**
- **June 2014 -Global working group Optimal Size meeting at WHO—discussed various public health objectives**
 - About 20 people from around the globe
 - More discussions with WHO June 2015
- **Presentation and discussion at Improving Vaccine Strain Selection Meeting November 2015, Hong Kong**
- **Preliminary discussions CDC/PAHO in Feb 2016 for how right-sizing might be considered in the Americas**
- **Slow baby steps.....new territory.....some considerations**

Evaluation of Sentinel Sites

- How to consider geography?
- How to manage sites and evaluate performance?
- What criteria should sites meet as minimum standards?

Right Size Parameter Decisions

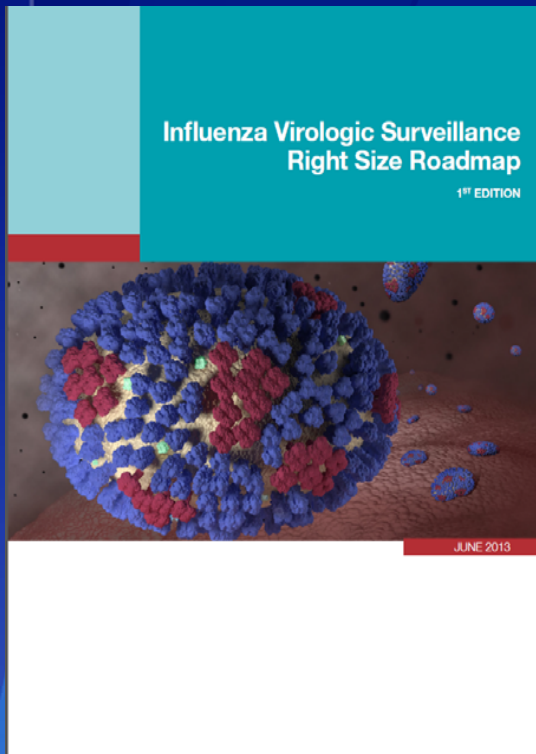
- **What question are you trying to answer?**
- **At what confidence level / margin of error?**
- **At what geographic level?**
- **Over what timeframe?**
- **What is the appropriate data to use?**

Influenza Virologic Surveillance Right Size Project – U.S. Rationale

- **The Right Sizing project is a proactive effort to show exactly what is needed for the degree of accuracy required**
- **Need evidence-based decisions**
 - Statistical, systematic approach lacking
 - Up to now capacity has been the driver of testing decisions
- **Funding/Sustainability**
 - Justify and optimize resources
- **Create scalable approach to meet outbreak or pandemic surge needs**

The Influenza Virologic Surveillance Right Size Roadmap

Roadmap to achieve an effective virologic surveillance system:



- Requirements: define state and national virologic surveillance needs of public health laboratories.
- Implementation Guidance/toolkit for CDC, health departments and public health laboratories.
- Modeling tools to determine effective sample size needed to detect/monitor key virologic surveillance objectives.

U.S. Right Size Objectives

U.S. objectives are all virologic:

- **Situational awareness**
- **Novel virus detection**
- **Antiviral resistance monitoring and investigation**
- **Vaccine strain selection and vaccine candidate development**

Situational Awareness: Sample Size Calculator

- **Surveillance objective: Determine the beginning & end of the influenza season & monitor the prevalence and spread of influenza viruses throughout the year.**
- **Surveillance question: How many specimens from patients with ILI does the laboratory need to test per week to determine that the prevalence of Flu+ specimens among ILI patients tested is x% (e.g. 10%) at a specified confidence level and error rate?**
- **State level statistical significance**

Calculators

Calculator A: Situational Awareness for Seasonal Influenza

Medically Attended ILI (MA-ILI) **2%**

Total Population **317,581,124**

Expected prevalence of Flu+/MA-ILI **10%**

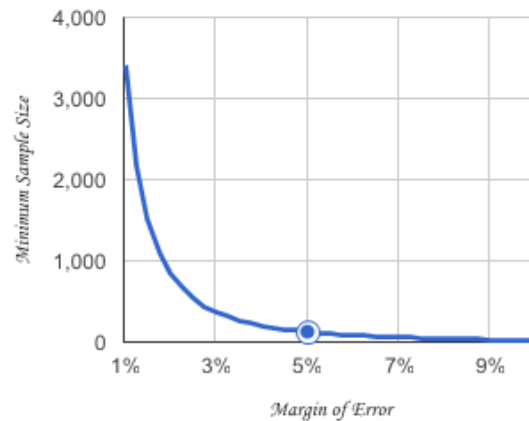
Sample Size

Sample Size Table

Data Confidence

Confidence level **95%**

The graph, table, and output language below describe the **minimum sample size** (of unscreened MA-ILI specimens) needed to estimate the fraction of Flu+/MA-ILI with a specified **margin of error** and confidence level of **95%**. This calculation is based on the estimated inputs provided above and assumes that the estimated level of Flu+/MA-ILI will be close to **10%** and the total population under surveillance is **317,581,124**. Use the mouse to view values in the sample size graph and scroll through sample size table.



Margin of Error	Minimum Sample Size
1%	3415
1.25%	2195
1.5%	1527
1.75%	1124
2%	861
2.25%	681
2.5%	576
2.75%	496
3%	430
3.25%	375
3.5%	330
3.75%	293
4%	262
4.25%	235
4.5%	211
4.75%	190
5%	172
5.25%	157
5.5%	144
5.75%	133
6%	124
6.25%	116
6.5%	109
6.75%	103
7%	98
7.25%	93
7.5%	89
7.75%	85
8%	81
8.25%	78
8.5%	75
8.75%	72
9%	70

A sample size of **138** unscreened MA-ILI specimens is needed in order to be **95%** (+/- **5%**) confident that the true prevalence of Flu+/MA-ILI is **10%**.

Surveillance Question of Other Calculators

- **Novel event detection**
 - How many specimens do you need to test to detect a rare/novel influenza virus at a given prevalence with 95% confidence
- **Antiviral resistance**
 - How many specimens do you need to test to detect at least one resistant influenza virus within a given subtype/lineage at given prevalence with 95% confidence
- **Vaccine strain selection**
 - How many influenza positives of each subtype/lineage does CDC need to test to detect a drift variant at a given prevalence and then, once detected, develop a vaccine candidate strain?

US Right Size Parameter Decisions for Vaccine Strain Selection

- **What question are you trying to answer?**
 - How many influenza positives of each subtype/lineage need to be tested to detect at least 1 drift variant if the prevalence is $\geq 3\%$
- **At what confidence level / margin of error?**
 - 95% confidence
- **At what geographic level?**
 - National
- **Over what timeframe?**
 - Per month
- **What is the appropriate data to use?**
 - Characterization data from viruses of each subtype/lineage

Right Size Objectives

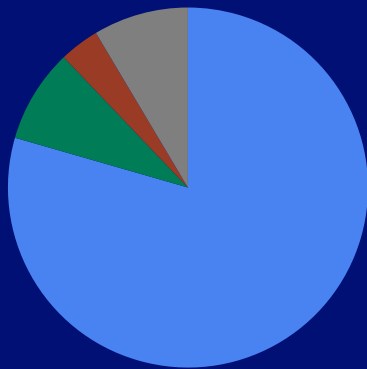
Objective	State/national	# needed	What?	Time
Situational awareness start of season	State	~ 135	Non pre-screened ILI samples	weekly
Situational awareness peak	State	~320	Non pre-screened ILI samples	weekly
Novel event detection	National	2095 598 or 11	Any influenza positive tested at PHL	weekly
Novel event detection	State # for national goals	1-251 depending on time of season and size of state	Any influenza positive tested at PHL	weekly
Antiviral resistance (detection)	National	59	Positives of each subtype/lineage	monthly
Antiviral resistance (investigation)	National	200	Positive of the subtype/lineage of concern	monthly
Vaccine strain selection	National	99	Positives of each subtype/lineage	monthly

US Right Size Parameter Decisions

- **Another question arose as we were modifying our submission guidance to states**
 - Are all viruses of equal concern?
 - Developed guidance assuming that they are

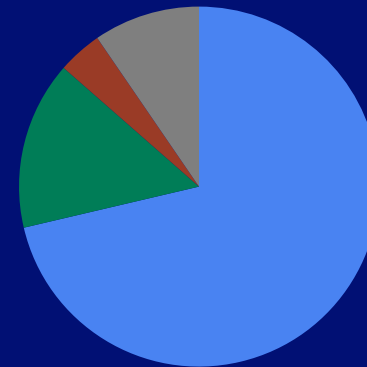
Proportion of Influenza Virus Type/Subtype/Lineages 2013-14 Season, United States

number reported



■ H1 ■ H3 ■ B Vic ■ B Yam

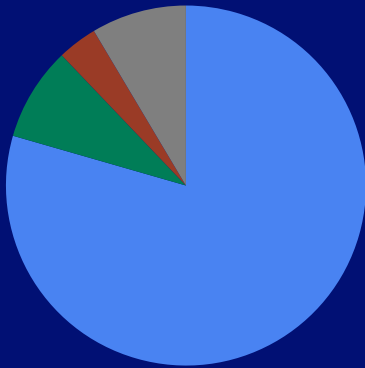
number characterized



■ H1 ■ H3 ■ B Vic ■ B Yam

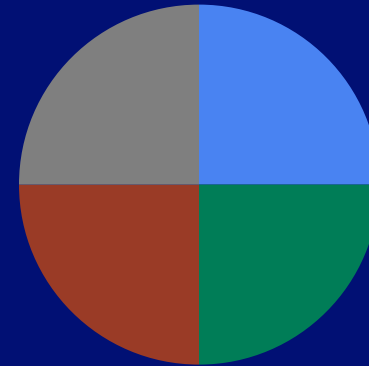
But This Year it Will Look More Like This

number reported



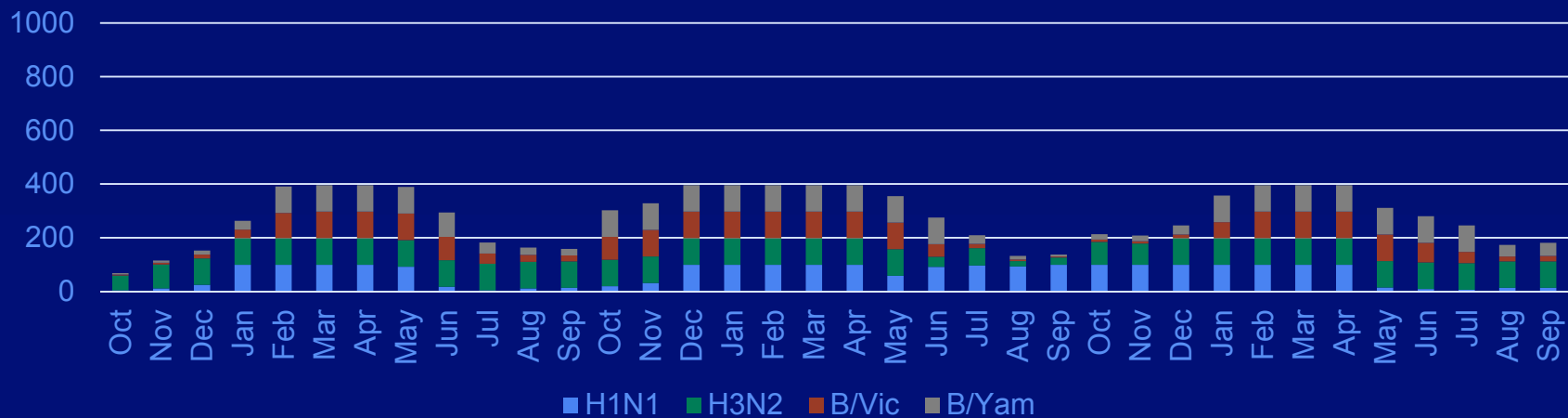
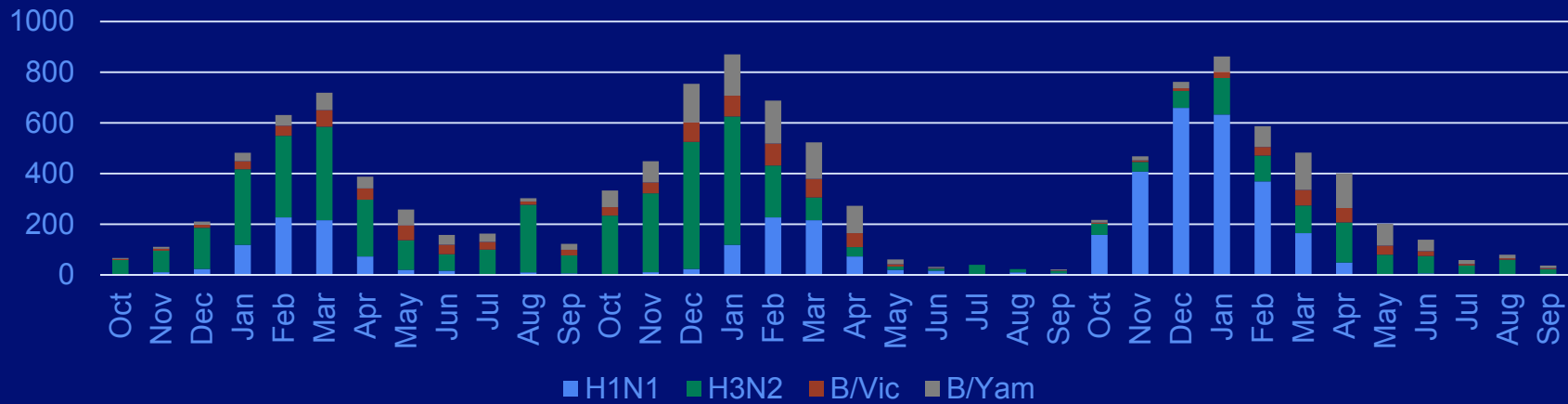
■ H1 ■ H3 ■ B Vic ■ B Yam

number characterized

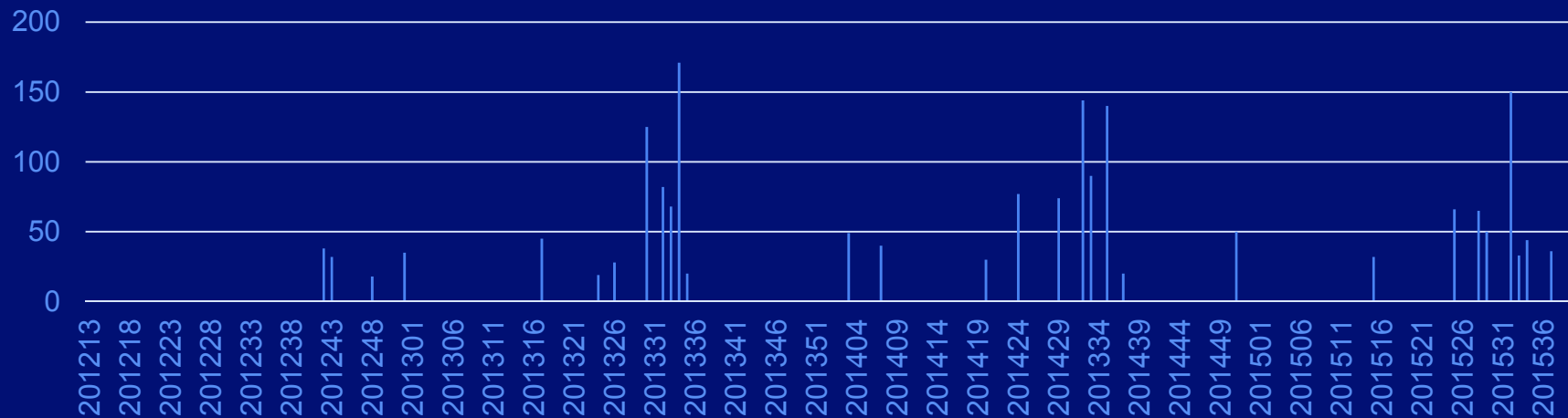


■ H1 ■ H3 ■ B Vic ■ B Yam

US Influenza Viruses Received for Characterization at CDC and Potential Impact of Guidance Changes 2011-12 to 2013-14 Seasons



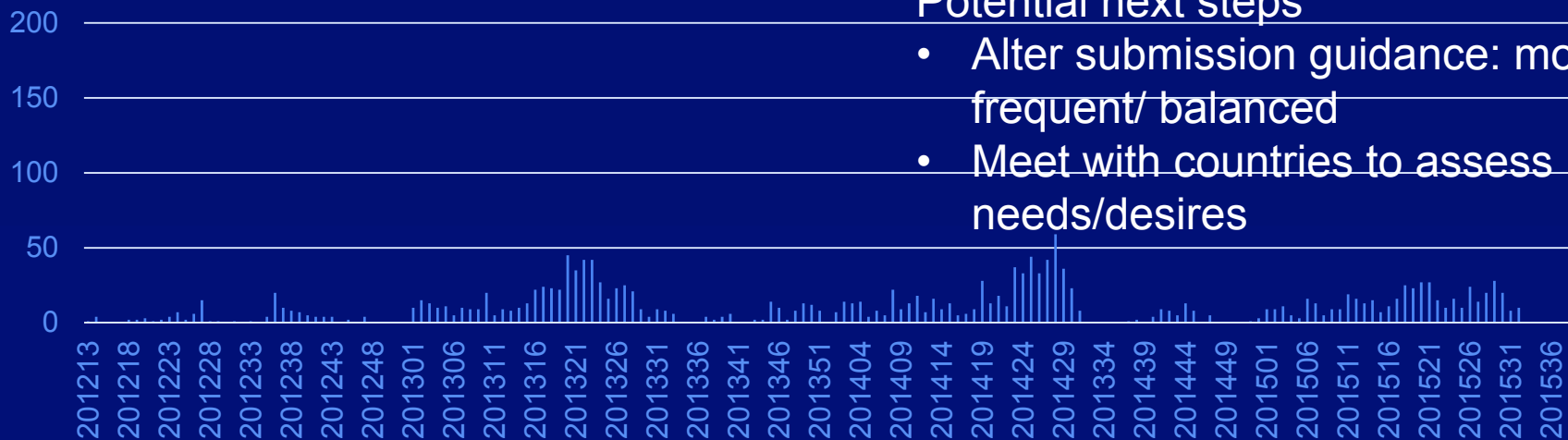
PAHO Example: South American Samples by Date Received at CDC and Date Collected



■ Received

Potential next steps

- Alter submission guidance: more frequent/ balanced
- Meet with countries to assess needs/desires



■ Collected

Challenges and Considerations

- **Can we combine genetic and antigenic characterization data in a way that allows genetic data to fill a gap?**
- **Submission guidance would need to be modified**
 - Much more complex on an international level
- **Monitoring of submissions would be needed**
 - Participation reminders
 - Need to know what is available and what is being tested
 - Need to be able to actively solicit samples of lower prevalence viruses if goals aren't being met

Advantages

- **Better understanding of the statistical strength of data going into vaccine virus selection**
- **Improved geographic representativeness of data going into vaccine component decisions**
 - All areas meet goals for statistical significance when possible
 - Not intended to reduce surveillance in any area
- **With increased frequency of shipments, follow up and investigation of unusual viruses would be more feasible**
 - Allows for more time for analysis

Right-Sizing Depends on your Goals and Objectives

What are your national goals for surveillance?

How does your Influenza Platform support your goals?

All this needs to be considered as part of sustainability and advocacy

If a global project, decisions on global goals would need to be reached

Acknowledgements

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Thank you!

<http://www.aphl.org/aphlprograms/infectious/influenza/Page/Influenza-Virologic-Surveillance-Right-Size-Roadmap.aspx>

Google “Right size influenza virologic surveillance”