



# New Respiratory Pathogens

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# Research work on ARI and Dengue 3 decades ago...





Southeast Asian J Trop Med Public Health. 1994 Dec;25(4):684-7.

## **Etiology of acute lower respiratory infection in Filipino children under five years.**

Capeding MR<sup>1</sup>, Sombrero LT, Paladin FJ, Suzuki H, Numazaki Y, Sanjel MC.

- ARI is a major cause of morbidity and mortality
- Low sensitivity and specificity of diagnostic tests
- Viral etiology studies are uncommon



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## **Etiology of acute lower respiratory infection in Filipino children under five years.**

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- ARI is a major cause of morbidity and mortality
  - Pneumonia remains a leading cause of death
- Low sensitivity and specificity of diagnostic tests
  - Novel molecular techniques enabled identification of etiologic agents
- Viral etiology studies are uncommon
  - Respiratory viruses are extensively researched

J Med Virol. 2010 May;82(6):1071-4. doi: 10.1002/jmv.21763.

**Detection of novel respiratory viruses from influenza-like illness in the Philippines.**

Furuse Y<sup>1</sup>, **Suzuki A**, Kishi M, Galang HO, Lupisan SP, Olveda RM, Oshitani H.



estimated the worldwide incidence of Respiratory Tract Infections (RTIs) to be 450 million cases, with approximately 4 million RTI-related deaths, accounting for 7% of all disease-related deaths (2011)

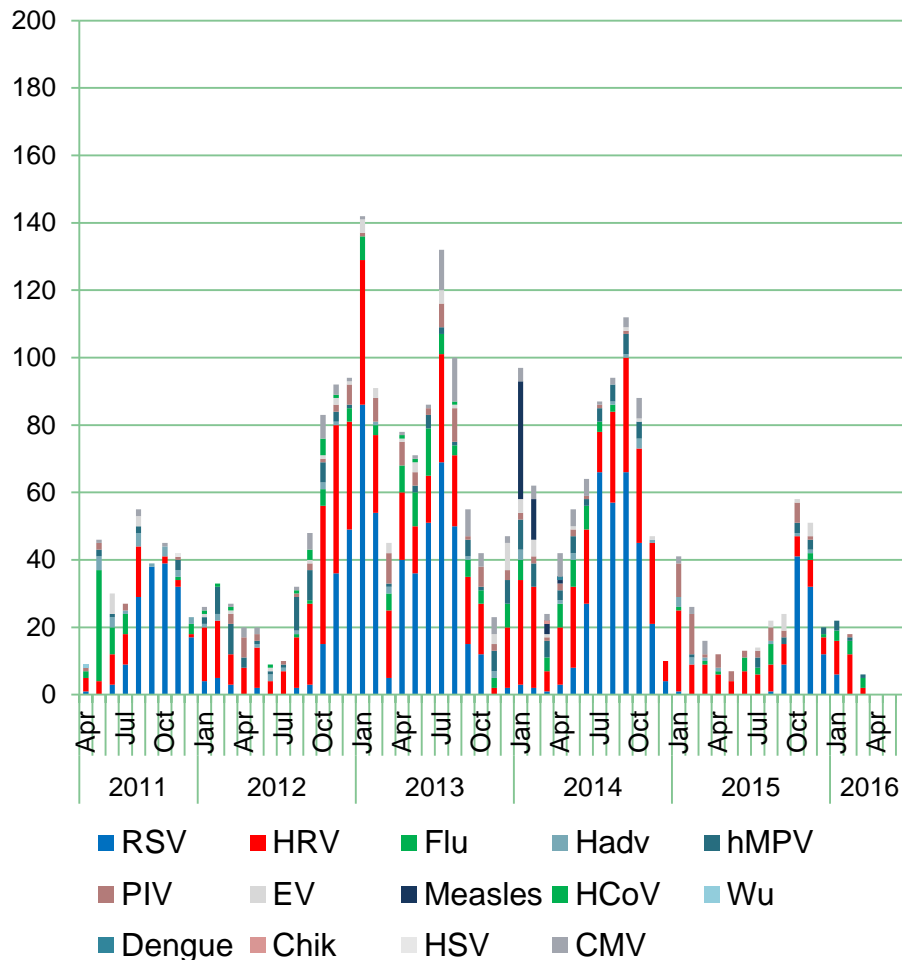


**Scientific  
Collaborations**  
(Local and  
International)



# Viral pathogens from patients with severe Pneumonia

## Hospital Sentinel Sites, 2011-2016



Virus	Frequency (%)
RSV (Respiratory Syncytial Virus)	1026 (25)
HRV (Rhinovirus)	736 (18)
Influenza	152 (3.7)
<b>hMPV (Metapneumovirus)</b>	<b>132 (3.2)</b>
PIV (Parainfluenza)	118 (2.9)
HEV (Enterovirus)	61 (1.5)
Measles	56 (1.4)
HAdV (Adenovirus)	41 (1.0)
<b>HCoV (Coronavirus)</b>	<b>13 (0.3)</b>

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Viral Pathogens in severe pneumonia has come into prominence as the role of bacterial infection decreases through early case detection, appropriate antibiotic treatment and introduction of conjugate vaccines





# RSV (Respiratory Syncytial Virus)

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- Important cause of severe ALRI
- Major cause of hospital admissions in young children
- 45% of hospital admissions and RSV-deaths occur in children younger than 6 months
- Substantial proportion with RSV-related death had co-morbidities



# RSV (Respiratory Syncytial Virus)

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- Perinatal immunization strategies for children age younger than 6 months will have substantial impact on RSV-related child mortality
- The lack of vaccine and limited antiviral options highlights the need for novel therapeutic strategies such as drugs that target host factors required for viral replication



# HRV (Rhinovirus)

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- An important viral pathogen in severe pneumonia or one of the main pathogens causing upper RTIs
- Etiological role still controversial because it has also been detected in healthy individuals



# hMPV (Metapneumovirus)

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- Identified in 2001 to patient with symptoms similar to those infected with RSV and several patients required hospitalization and mechanical ventilation
- Most common presentation in children includes rhinorrhoea cough and fever; acute otitis media also frequently reported; conjunctivitis, rash, diarrhea and vomiting are reported but infrequently
- Bronchiolitis, pneumonia, asthmatic exacerbations are most frequent lower respiratory tract complications compared to other respiratory viruses



# hMPV (Metapneumovirus)

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- Second most frequently identified virus in respiratory tract infections
- Pathogenesis is strongly affected by bacterial co-infections with pneumococcus, infection with hMVP facilitates adhesion of pneumococcus to the mucosal membrane
- Study showed administration of pneumococcal conjugate vaccine is sufficient to reduce the incidence of hMPV



# hMPV (Metapneumovirus)

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- Has a worldwide distribution and affects all age groups but predominantly affects the young, elderly and immunocompromised patients (underlying or chronic conditions such as asthma, congenital heart disease, cancer and COPD)
- Infection occurs through out the year but seasonal prevalence in colder months and co-insights with the peak of RSV infection



# HCoV (Coronavirus)

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- A first recognized as animal pathogens in the 1930s, 30 years later identified as human pathogens
- In 2003 SARS-CoV was identified as a novel virus responsible for the 2002-2003 global outbreaks of SARS which lasted for 9 months, infected 8,096 people and resulted in 774 deaths. This sparked a renewed interest in research and 2 years later HCoV was newly recognized



# HCoV (Coronavirus)

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- The incubation period is 2-5 days, most likely to be transmitted during the first few days of illness, when symptoms and respiratory viral loads are at their highest
- Associated frequently with common cold, URTI characterized by rhinorrhea, nasal congestion, sore throat, cough that may be associated with fever





# HCoV (Coronavirus)

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- Symptoms are self limiting and typically peak on day 3 or 4 of illness
- Have been associated with bronchiolitis, croup and pneumonia primarily in infants and immunocompromised children
- May be associated with acute otitis media or asthma exacerbations



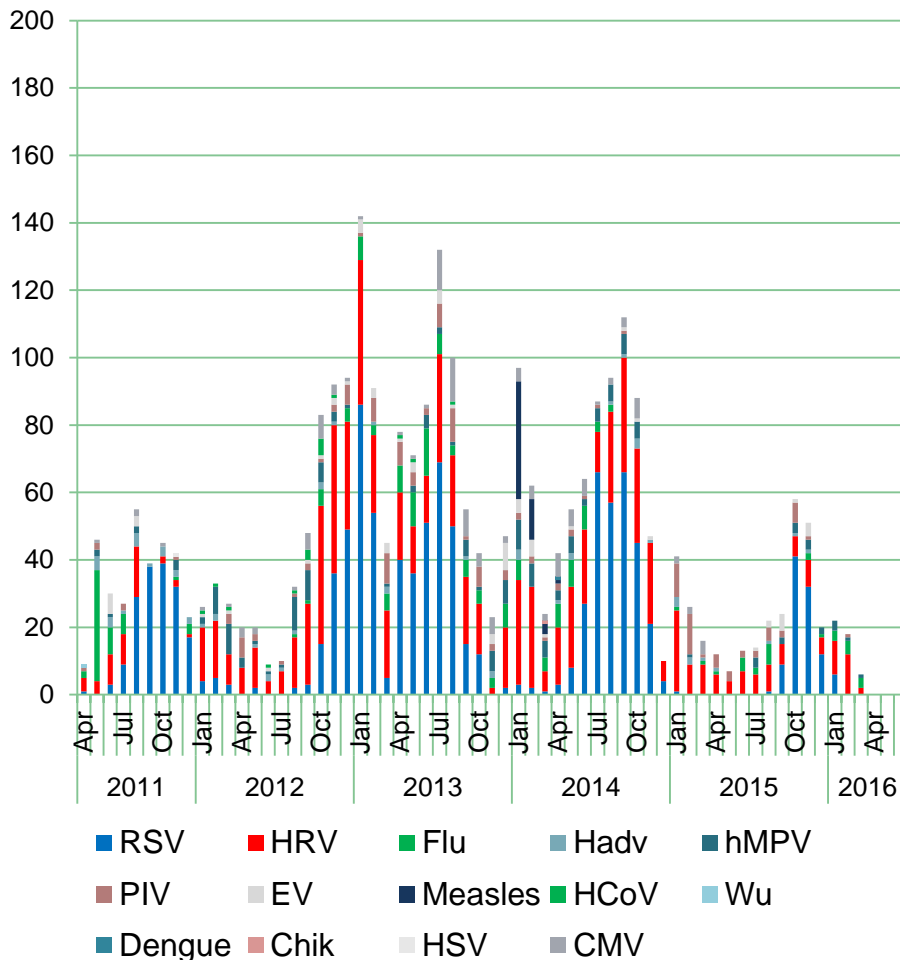
# Respiratory Viruses

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- Different behavioural habits, environments and degrees of immunity are experienced at different ages
- Half lives of antibodies that recognize different pathogens vary resulting differences in severity according to age
- Studies showed 100% of 6 year old children have been infected with one or more respiratory pathogens however, infections do not result in effective long-term immunity, so children can be repeatedly infected by the same viruses

# Viral pathogens from patients with severe Pneumonia

## Hospital Sentinel Sites, 2011-2016



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HCoV (Coronavirus)	13 (0.3)
<b>2 viruses</b>	<b>241 (5.9)</b>
<b>3 viruses</b>	<b>4 (0.1)</b>
<b>4 viruses</b>	<b>1 (0.02)</b>

# Co-infection

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- Overall co-infection rate (CIR) around 18%
- Higher in the 7-14 year old subgroup than in any other age group
- Except RSV, all pathogens showed higher CIR in pediatric patients than in adult patients
- 4 pathogens with highest CIR were HCoV (47%), HBoV (45%), EV (42%) and PIV (35%)
- Lower CIRs observed for RSV, ADV and IAV



# Co-infection

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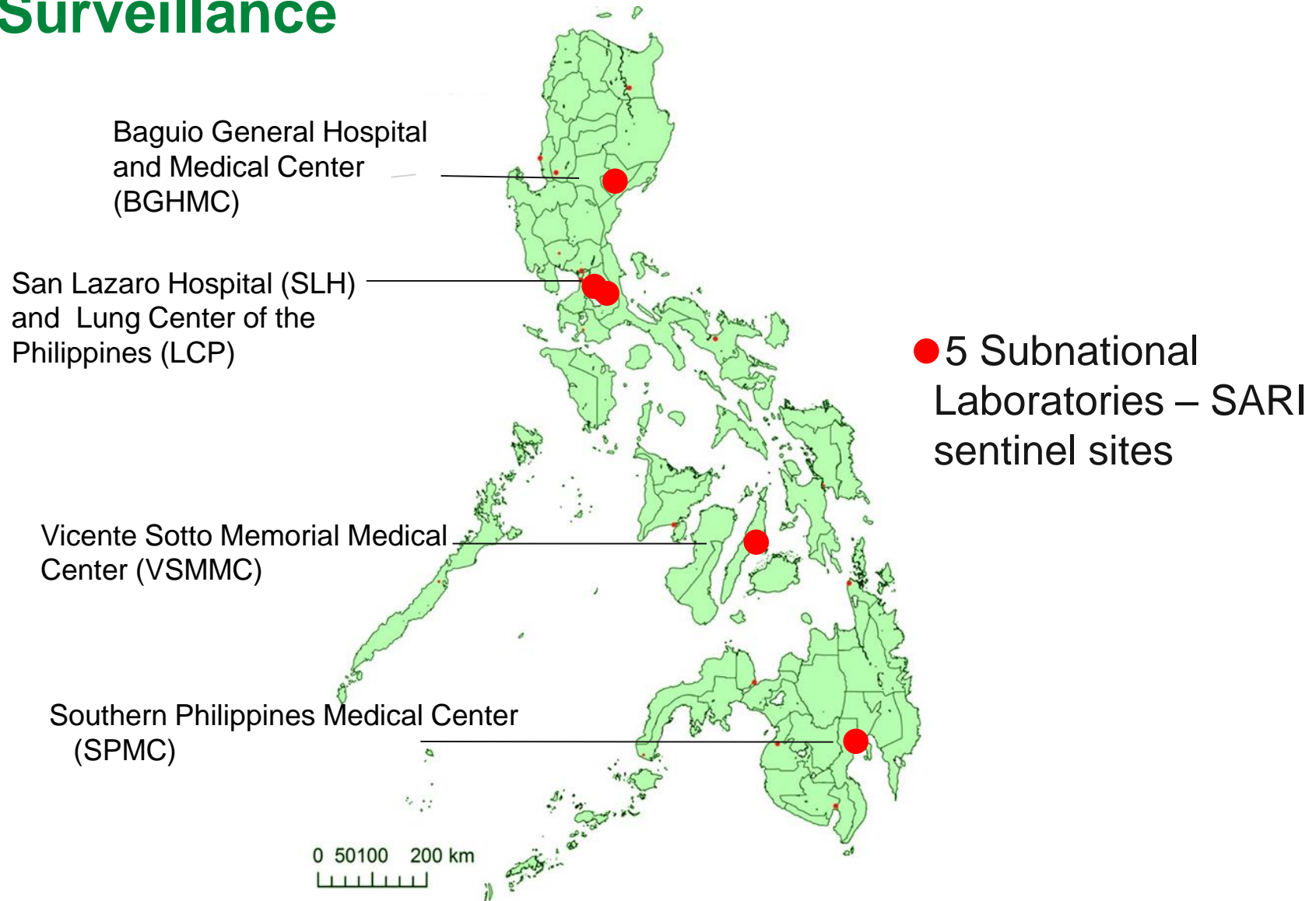
- Human rhinovirus, parainfluenza, adenovirus, *S. pneumoniae* and *K. pneumoniae* had significant involvement in co-infections
- Clinical symptoms range from negligible to severe

# Laboratory Tests

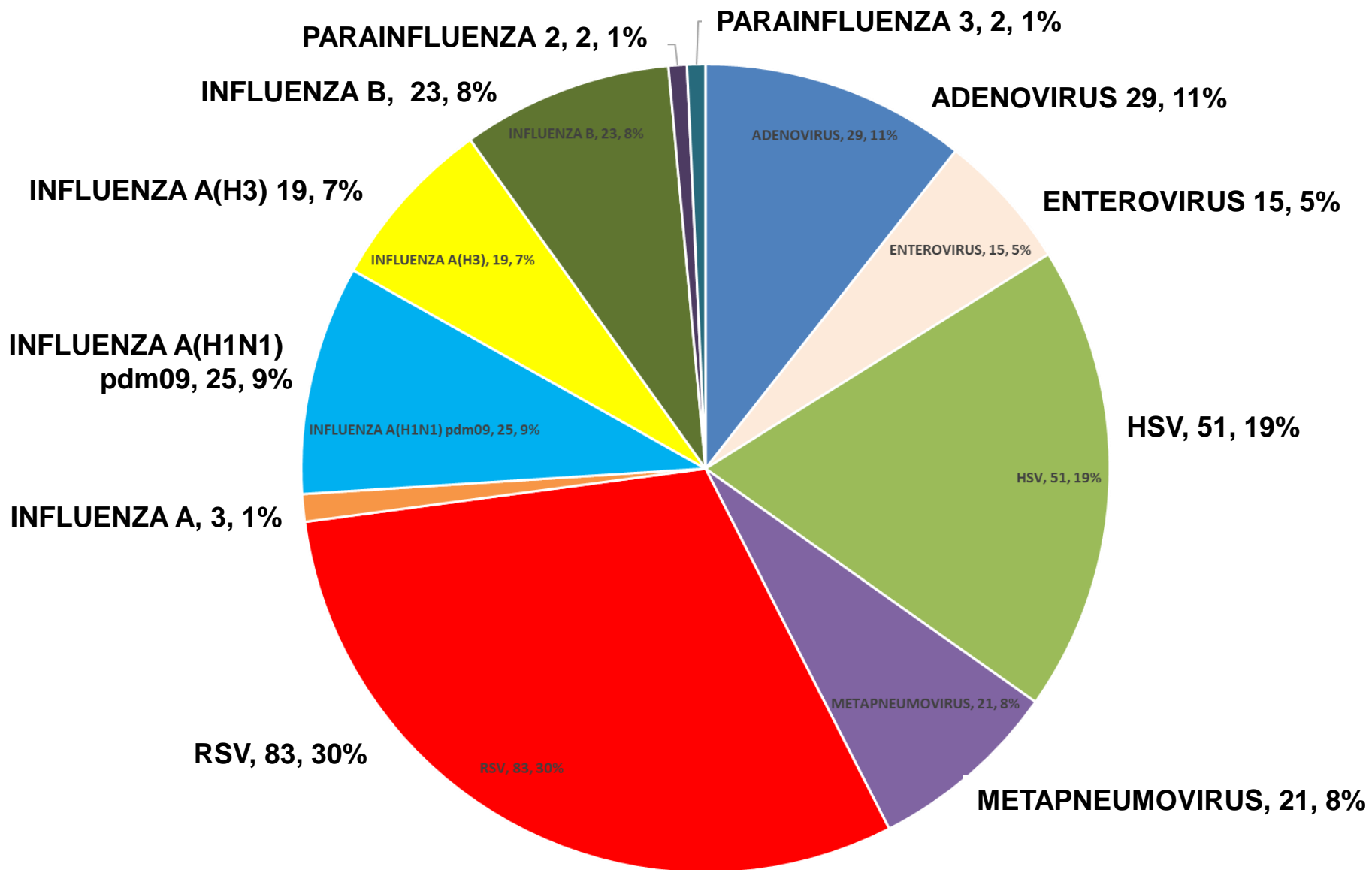
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- Collection of nasopharyngeal swabs in viral transport medium (VTM) stored at 4°C until transport to RITM or other laboratories and tested by Real Time PCR within 10 days after sample collection
- The gold standard for diagnosis of viral infection is virus isolation however, novel viruses cannot be isolated and demonstrating the presence of the viral genome is the only available detection method

# Severe Acute Respiratory Infection (SARI) Surveillance



# Respiratory viruses detected by PCR in the SARI Surveillance 2015-2016 (N=911)





# Weekly U.S. Influenza Surveillance Report



2017-2018 Influenza Season Week 6 ending February 10, 2018

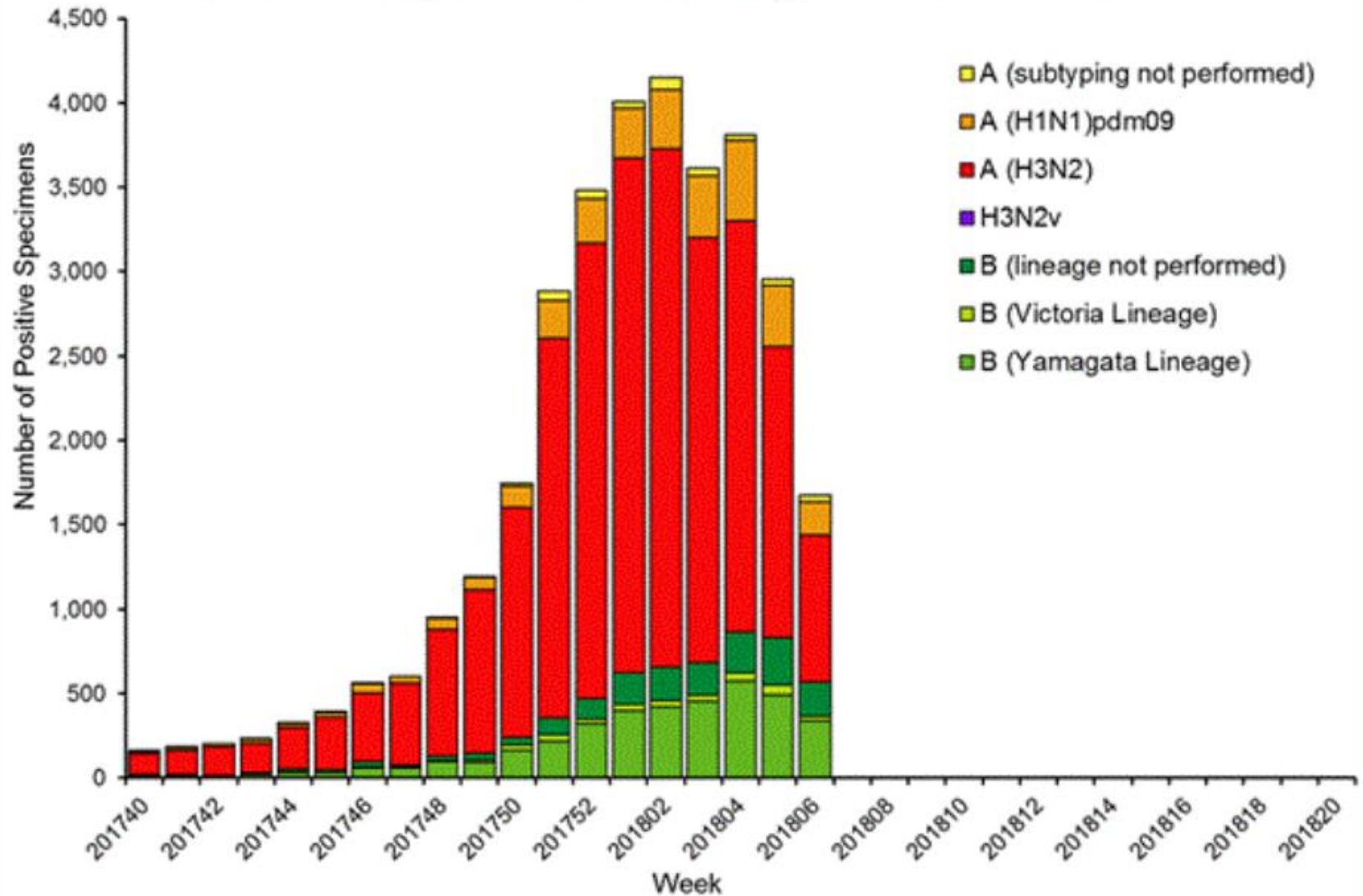
*All data are preliminary and may change as more reports are received.*

## Synopsis:

During week 6 (February 4-10, 2018), influenza activity remained elevated in the United States.

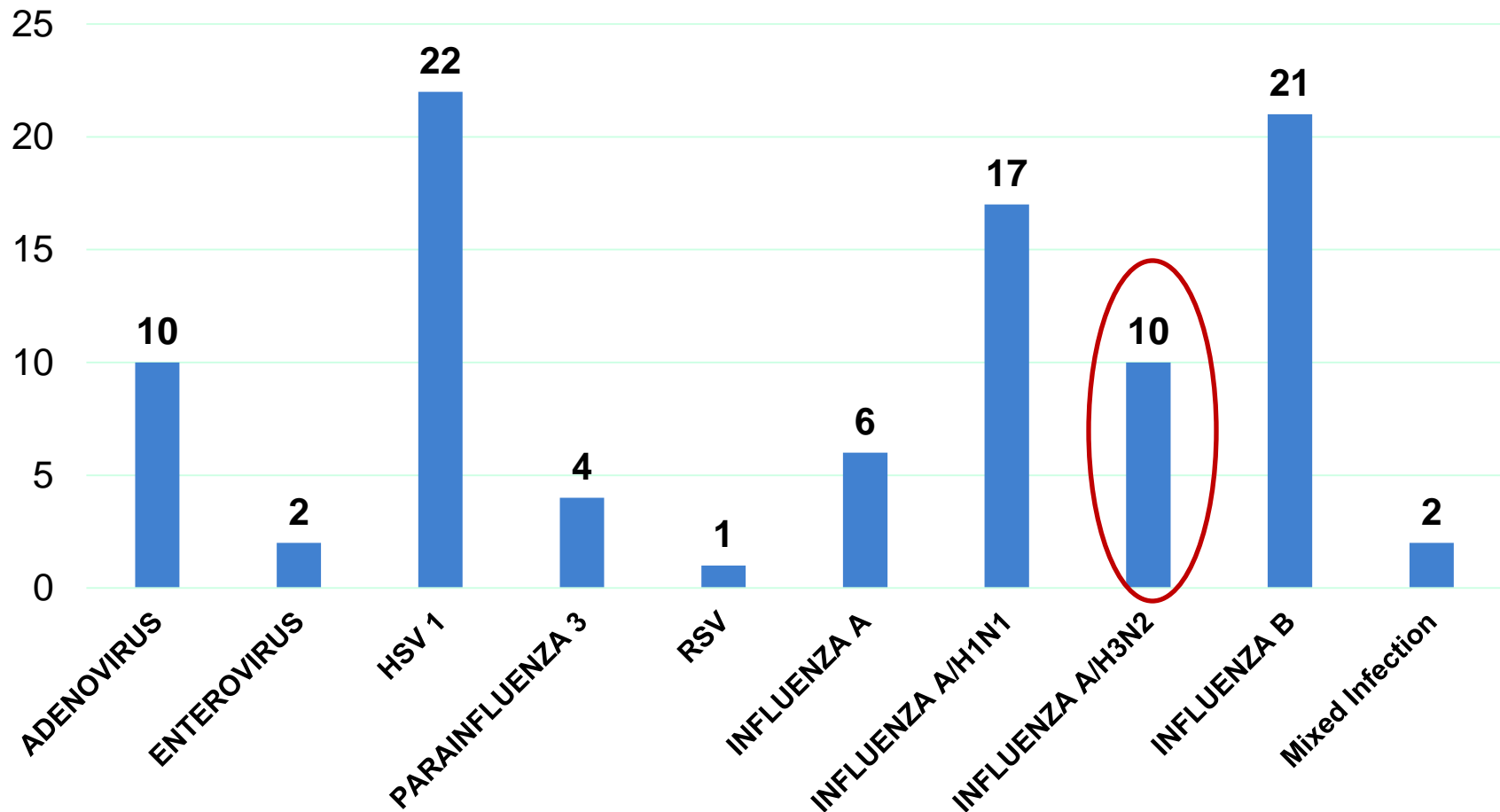
- **Viral Surveillance:** The most frequently identified influenza virus subtype reported by public health laboratories during week 6 was influenza A(H3). The percentage of respiratory specimens testing positive for influenza in clinical laboratories remained elevated.
- **Pneumonia and Influenza Mortality:** The proportion of deaths attributed to pneumonia and influenza (P&I) was above the system-specific epidemic threshold in the National Center for Health Statistics (NCHS) Mortality Surveillance System.
- **Influenza-associated Pediatric Deaths:** Twenty-two influenza-associated pediatric deaths were reported.
- **Influenza-associated Hospitalizations:** A cumulative rate of 67.9 laboratory-confirmed influenza-associated hospitalizations per 100,000 population was reported.
- **Outpatient Illness Surveillance:** The proportion of outpatient visits for influenza-like illness (ILI) was 7.5%, which is above the national baseline of 2.2%. All 10 regions reported ILI at or above region-specific baseline levels. New York City, the District of Columbia, Puerto Rico and 43 states experienced

## Influenza Positive Tests Reported to CDC by U.S. Public Health Laboratories, National Summary, 2017-2018 Season





# Respiratory viruses isolated in the SARI Surveillance 2015-2016 (N=911)





# GUIDELINES ON VERIFICATION OF MEASLES ELIMINATION IN THE WESTERN PACIFIC REGION



2013

 **World Health  
Organization**  
Western Pacific Region

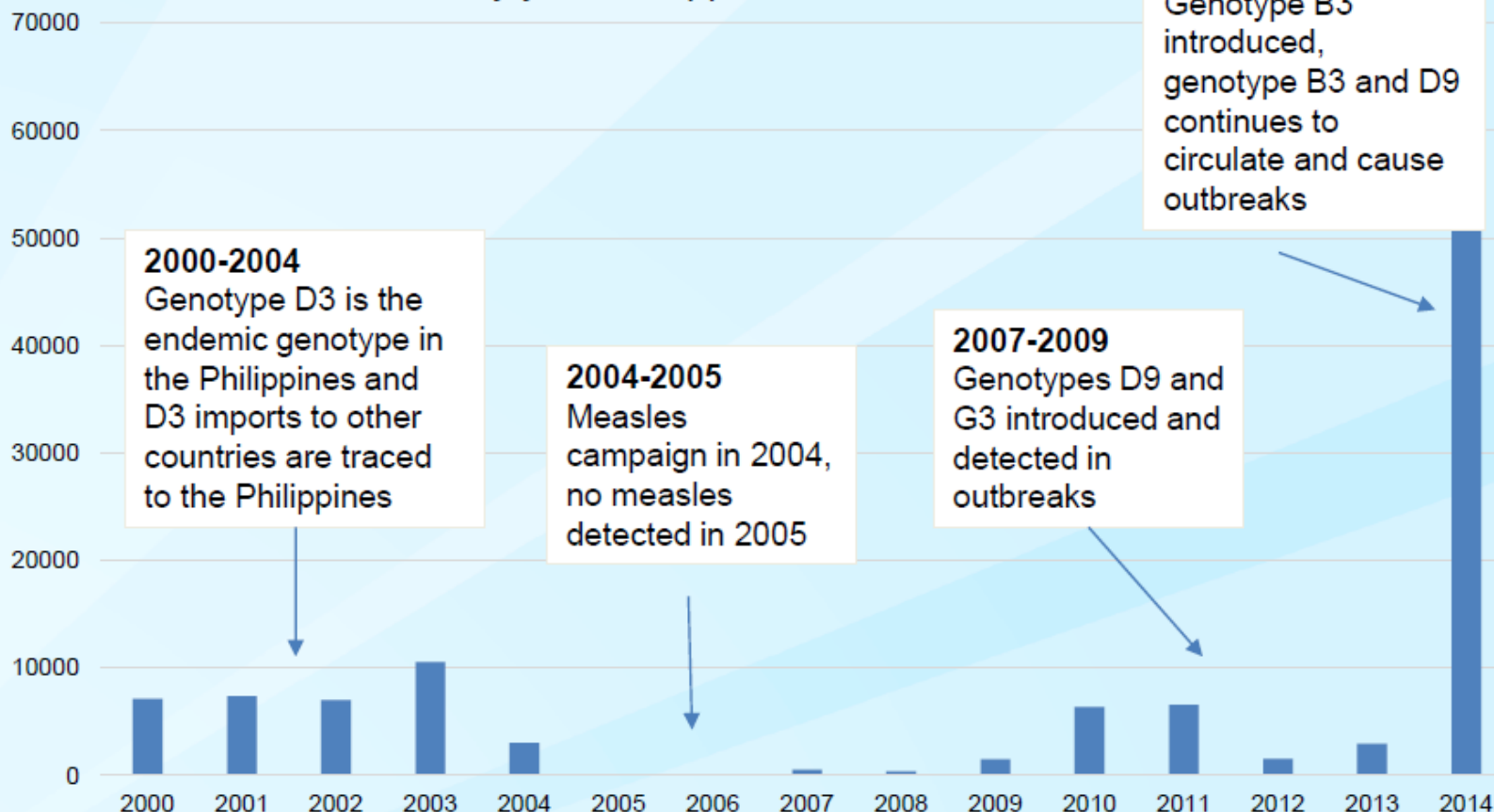
Western Pacific Region  
Research Institute for Tropical Medicine

# Summary of progress towards elimination

	Categories	Countries, Areas, Epidemiological Blocks
1	Verified as having achieved measles elimination in 2014-2017	Australia, Brunei Darussalam, Cambodia, Hong Kong SAR, Japan, Macao SAR, Republic of Korea, New Zealand (n=8)
2	Verified as having achieved rubella elimination in 2017	New Zealand, Republic of Korea (n=2)
4	Approaching measles elimination, but with surveillance gaps	Lao People's Democratic Republic, Pacific Islands, Singapore (n=3)
5	Re-established measles transmission	Mongolia (n=1)
6	Endemic measles virus transmission	China, Malaysia, Papua New Guinea, Viet Nam, the Philippines (n=5)

# Measles Genotypes In the Philippines

Measles cases by year, Philippines, 2000-2014



## 2000-2004

Genotype D3 is the endemic genotype in the Philippines and D3 imports to other countries are traced to the Philippines

## 2004-2005

Measles campaign in 2004, no measles detected in 2005

## 2007-2009

Genotypes D9 and G3 introduced and detected in outbreaks

## 2014-2015

Genotype B3 introduced, genotype B3 and D9 continues to circulate and cause outbreaks

Genotype D3 not detected globally after 2004

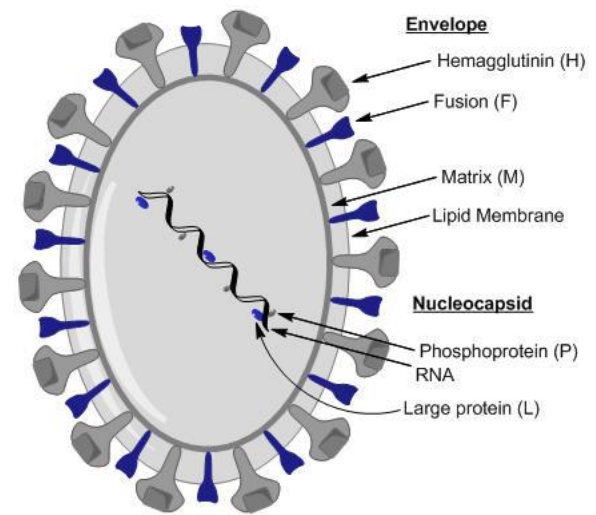
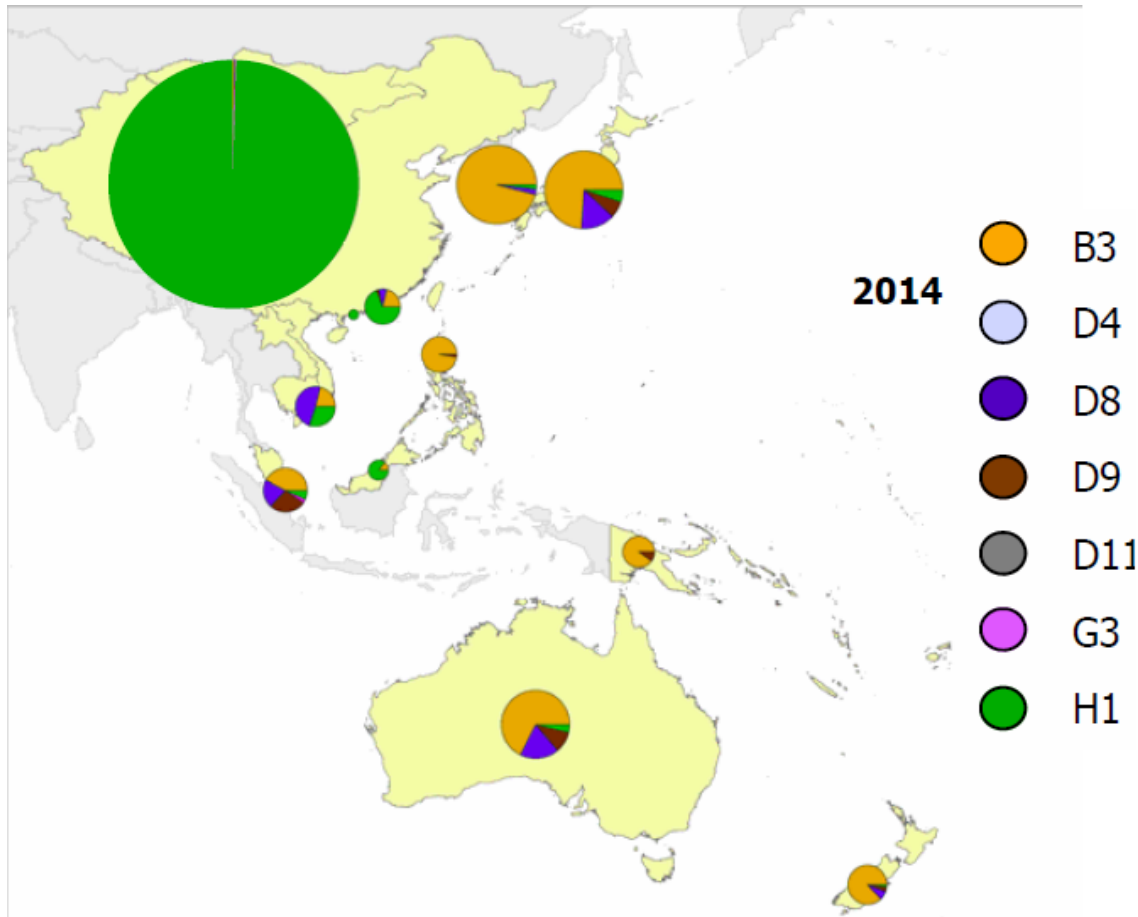
Mapping Transmission Pathways Following the Outbreak in the Philippines in 2014: Tracking  
Genotype B3 “Harare”

Importation of genotype B3                      Importation of genotype D9



**Global transmission of measles viruses  
from the Philippines, 2014**

# Measles Genotype Distribution of Cases in WPR, 2014



Measles Virus



# Bacterial Pathogens

## Major Pathogens Isolated

Pathogen	No of Isolates
<i>Streptococcus pneumoniae</i>	4 (0.4%)
<i>Hemophilus influenzae</i>	1 (0.1%)
* <i>Methicillin Resistant Staphylococcus aureus (MRSA)</i>	4( 0.4%)
<i>Salmonella group C1</i>	1 (0.1%)
<i>Staphylococcus aureus</i>	1 ( 0.1%)
<i>Pseudomonas aeruginosa</i>	1 (0.1%)
<i>Enterobacter cloacae</i>	1 (0.1%)
<i>Escherichia coli</i>	1 (0.1%)
<b>Total</b>	<b>14 (1.4%)</b>

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# Serotype Distribution of *S. pneumoniae*

Total number of  
invasive isolates: 34  
Blood: 21  
CSF: 13

Age population  
Pediatric: 19  
Adult: 8  
No data yet: 7

<b>Vaccine Serotypes</b>	<b>No.</b>	<b>Non-vaccine Serotypes</b>	<b>No.</b>
<b>1</b>	<b>8</b>	<b>15</b>	<b>2</b>
<b>3</b>	<b>2</b>	<b>23A</b>	<b>2</b>
<b>4</b>	<b>1</b>	<b>12F</b>	<b>1</b>
<b>5</b>	<b>4</b>	<b>20</b>	<b>1</b>
<b>6A</b>		<b>10A</b>	<b>1</b>
<b>6B</b>	<b>1</b>	<b>35B</b>	<b>1</b>
<b>7F</b>			<b>8 (23%)</b>
<b>9V</b>			
<b>14</b>	<b>2</b>	others	
<b>18C</b>	<b>1</b>	<b>6A/B/C/D</b>	<b>1</b>
<b>19A</b>	<b>1</b>	<b>18A/B/C/F</b>	<b>1</b>
<b>19F</b>	<b>1</b>	<b>25F/25A</b>	<b>1</b>
<b>23F</b>	<b>2</b>		
	<b>23 (68%)</b>		<b>3 (9%)</b>
<b>TOTAL</b>	<b>34</b>		



# MRSA

- Has increased prevalence worldwide as both a healthcare-associated and community-associated pathogen
- Frequently causes skin and soft tissue infections however, is also associated with invasive infections particularly pneumonia
- The incidence of invasive MRSA pneumonia in children remains low



# Conclusion

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- The rapid advancement of molecular tools in the past 15 years has allowed discovery of new respiratory viruses and led to the discovery of hMPV and HCoV
- The isolation of viral pathogens demonstrate its potential important role in the etiology of severe pneumonia among children
- The data on etiologic bacterial agents of lower respiratory tract infections still remain low and elusive inspite of improved diagnostic methods

*Thank you!*

