

# Impact of virological multiplex testing on clinical management





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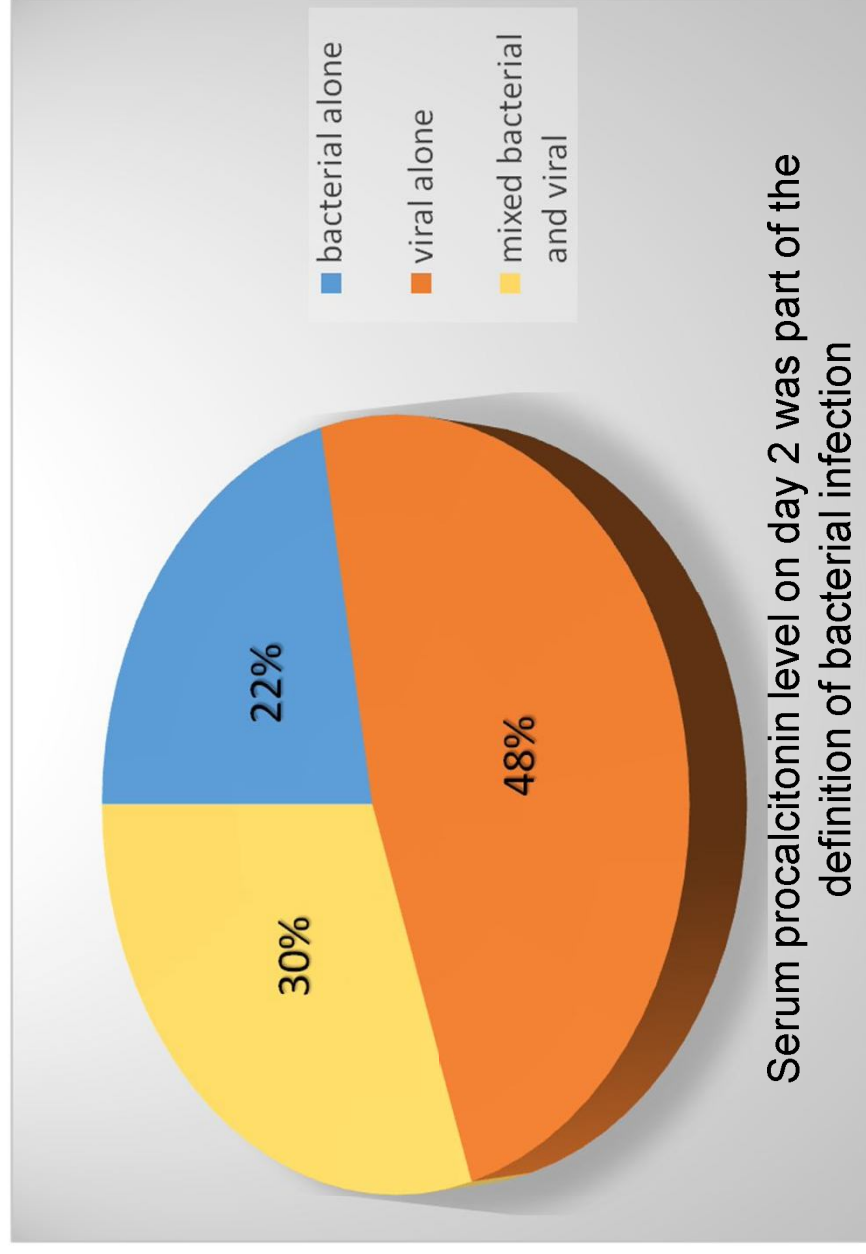
# Content

-  Are viral diseases frequent among hospitalised adult patients with acute respiratory illness ?
-  What is the accuracy of the clinical diagnosis
-  What is the influence of rapid identification of viral etiology on patient management
  - Withholding of antibiotic treatment
  - Initiation of antiviral therapy
  - Implementation of infection control measures to prevent transmission
-  Conclusions

# Bacterial Complications of Respiratory Tract Viral Illness: A Comprehensive Evaluation

Falsey et al JID 2013;208: 432

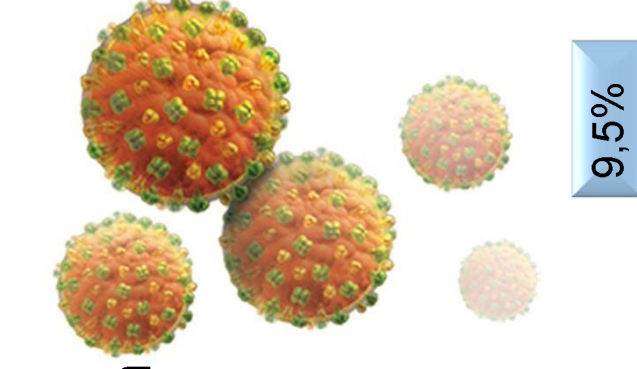
- 842 hospitalisation (771 adults pts) for acute respiratory tract infection
- 447 hospitalisations (53%) with microbiological diagnoses



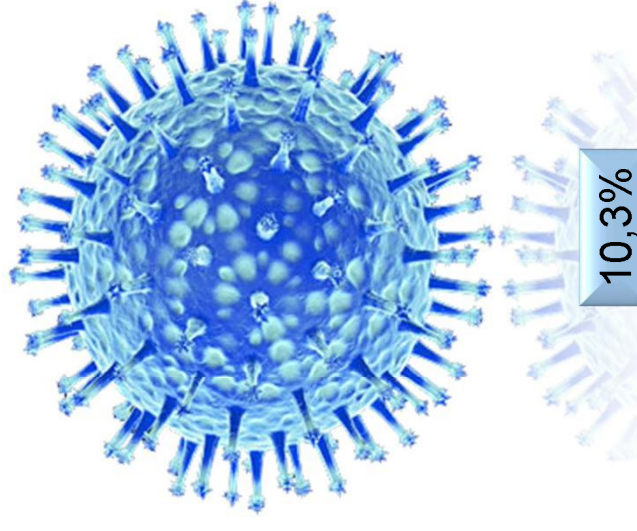
# Circulation of respiratory viral pathogens in adults

- Culture, PCR for RSV and Influenza
- **1388 adult patients** hospitalised with acute respiratory symptoms from november to april
- >65 years or with underlying cardiopulmonary diseases

Falsey et al NEJM 2005; 352: 1749



9,5%



10,3%

**1/5 patients with acute respiratory symptoms infected with Influenza or RSV infection**



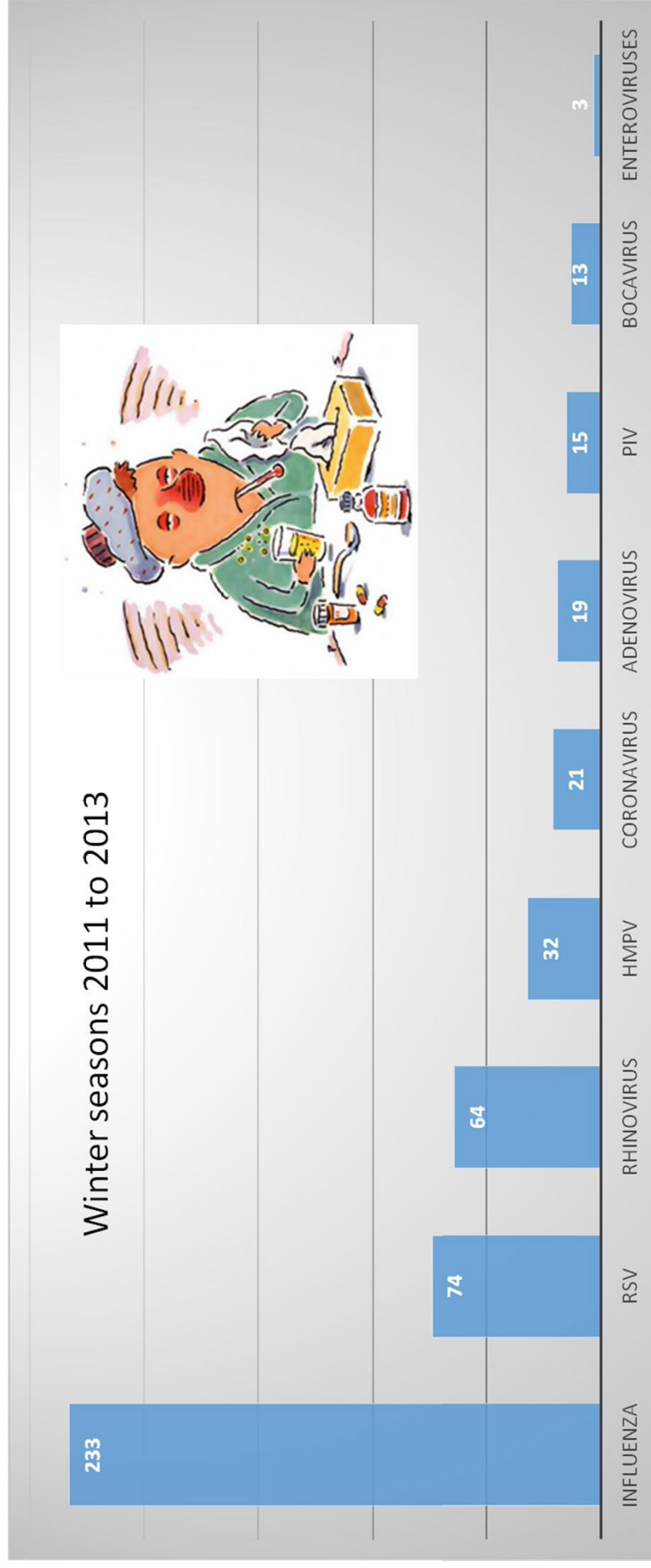
CHU Saint-Pierre

# Respiratory virosis among hospitalised adults with acute respiratory illness at CHU Saint-Pierre

Year	Total patient tested	% patient with viral pathogen*	Molecular biology technique	
2011	113	38	Rt-PCR home made	Only patients in ICU or immunosuppressed
2012	340	32	Microarray	All hospitalised patients
2013	942	32.5	Microarray	All hospitalised patients

\*Positive rapid test or culture or molecular biology

# Viral pathogens isolated among adult hospitalised patients at CHU Saint-Pierre during 3 years



# Sensitivity of clinical diagnosis of influenza among pts with laboratory confirmed Influenza.

Sensitivity % (95% CI)	Specificity % (95% CI)	Influenza number	Population	Reference
<b>36</b> (22-52)	78 (72-83)	42/270	Adults at the emergency department who meet CDC criteria to receive antiviral treatment	Dugas et al Am J Emerg Med 2015; 33:770
<b>29</b> (18-43)	92 (87-95)	53/258	Healthy adults with acute respiratory complain	Stein et al Ann Emerg Med 2005;46:412
<b>29</b>	-	504/4689	Adults (318) and children (186), in and out patients	Miller et al JID 2015;



Will providers respond to rapid diagnostic data with adjustment of empiric antibiotic treatment regimens ?

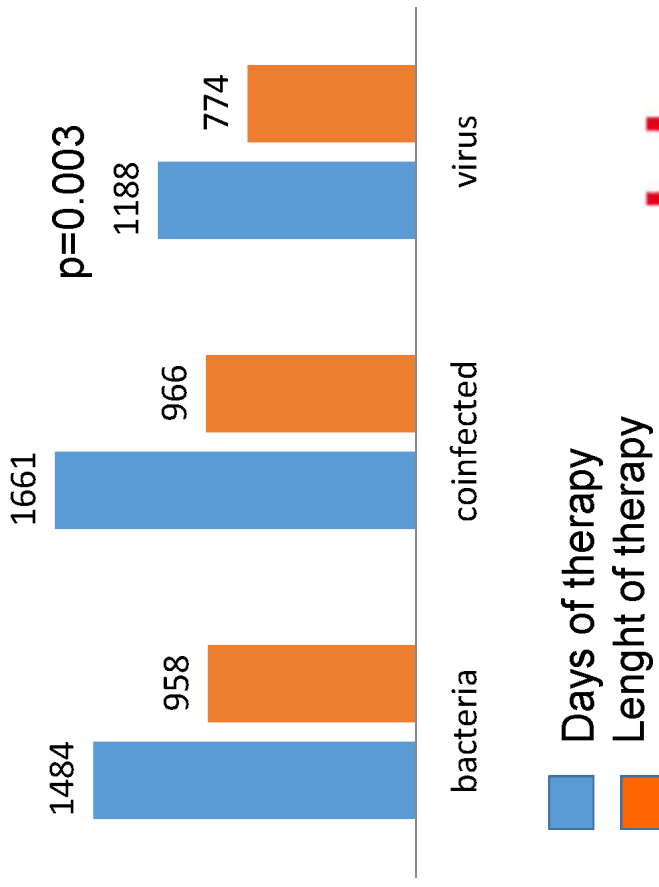
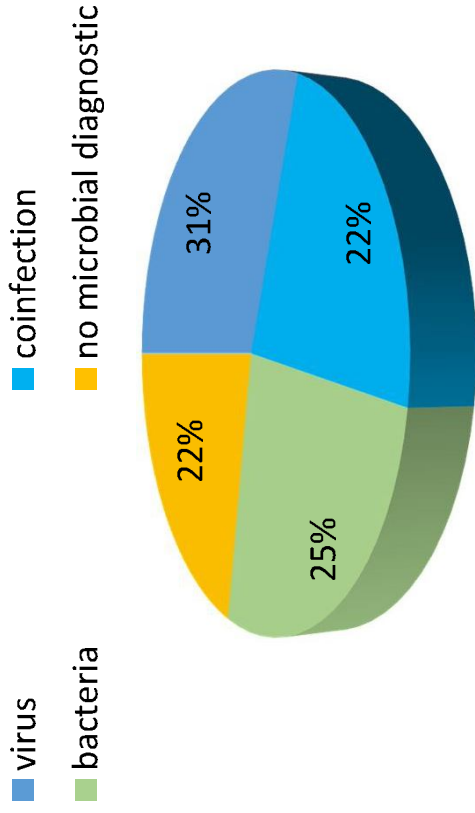


# The clinical impact of the detection of potential etiologic pathogens of community-acquired pneumonia

Gita Gelfer, James Leggett, Jillian Myers, Luan Wang, David N. Gilbert\*

Providence Portland Medical Center, Portland, OR, USA

- 59 hospitalised patients with CAP
- Common core diagnostic test bundle (blood culture, sputum, serum procalcitonin level, legionella urine antigen, nasopharyngeal swab for virus by molecular tests).



# Value of concurrent procalcitonin and viral testing to reduce unnecessary AB use

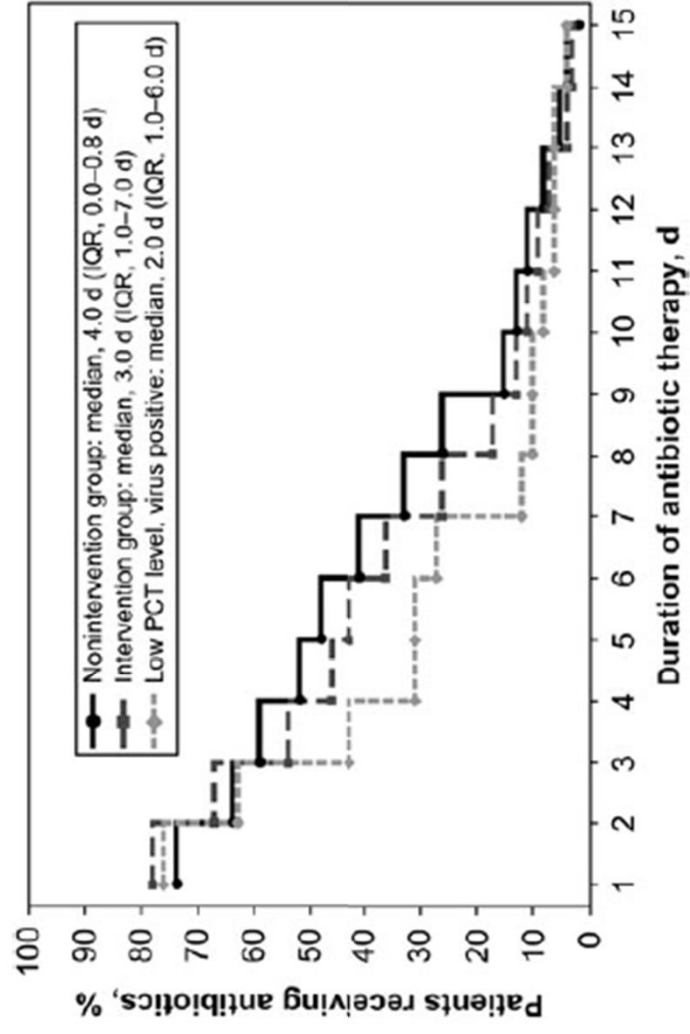
Branche et al J Inf Dis June 2015

- 300 adults hospitalised with non pneumonic LRTI
- Randomised 1:1 to standard care or procalcitonin guided care + multiplex viral PCR testing)

128 / 300  
48%  
with viral  
diagnostic

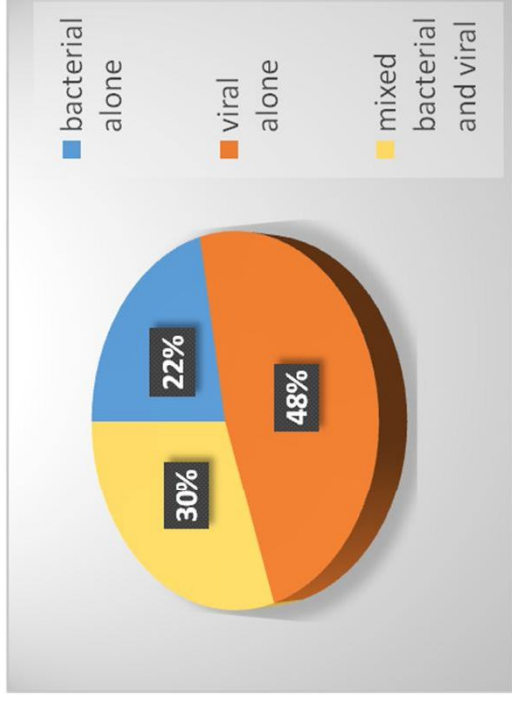
	Intervention sub group*	Control group	p
Subjects number	49	149	
Discharged receiving oral AB	10 (20)	64 (45)	0.002
AB use $\leq$ 48h	28 (57)	61 (41)	0.07
Total AB days	2 (0-3)	4 (0-8)	0.11

\*patient with the lowest risk for bacterial infection, ie pts tested positive for virus and with a low PCT level



348 patients hospitalised with a viral respiratory infection

Variable	Viral Alone	Mixed Viral-Bacterial	FDR <sup>a</sup>
In hospital	212 pts	136 pts	
ICU admission	13 (6)	19 (14)	0.08
Respiratory failure	9 (4)	12 (9)	0.26
Death	2 (1)	3 (2)	0.60
Length of stay, d	6.4 ± 9.5	12.3 ± 43.4	0.16
Length of illness, d	19.4 ± 11.2	22.4 ± 11.3	0.08
Antibiotic use			
Any inpatient antibiotics	191 (90)	125 (92)	0.83
Duration of inpatient use, d	4.2 ± 4.6	6.2 ± 9.0	0.04
Discharged receiving oral antibiotics	123 (58)	88 (65)	0.38
Antibiotic complications	71 (33)	74 (54)	0.002



# Impact of Rapid Detection of Viral and Atypical Bacterial Pathogens by Real-Time Polymerase Chain Reaction for Patients with Lower Respiratory Tract Infection

107 adult patients hospitalised with CAP

Multiplex real time PCR 5 virus + 3 atypical pathogens

Nov 2002 to March 2004

Patient randomised to

- Group 1: Results of PCR within 48h of admission (55 pts)
- Group 2: PCR results blinded (52 pts)

30 pts with viral pathogen

AB stopped  
11% of pts

28% of pts with influenza treated with oseltamivir

	Group 1	Group 2
Number of patients with viral pathogen	14	16
Median duration of AB (days)	10 (1-46)	9 (1-31)

# Antiviral treatment

- Among influenza hospitalised patients, antiviral therapy is associated with reduced
  - incidence of lower respiratory tract complications
  - Requirement of intensive care
  - Duration of viral shedding
  - Mortality
- Efficacy is greatest with early therapy but appears to be effective for at least 5 days after symptoms onset
- Oseltamivir is recommended by CDC for all influenza hospitalised patients



Dobson et al Lancet 2015  
Lee et al Clin Inf Dis 2012  
Louie et al Clin Inf Dis 2012  
Rodriguez et al J Antimicrob Chemother 2011

- What is cost effective: to test and to treat accordingly or to treat everybody?





# To Test or to Treat? An Analysis of Influenza Testing and Antiviral Treatment Strategies Using Economic Computer Modeling

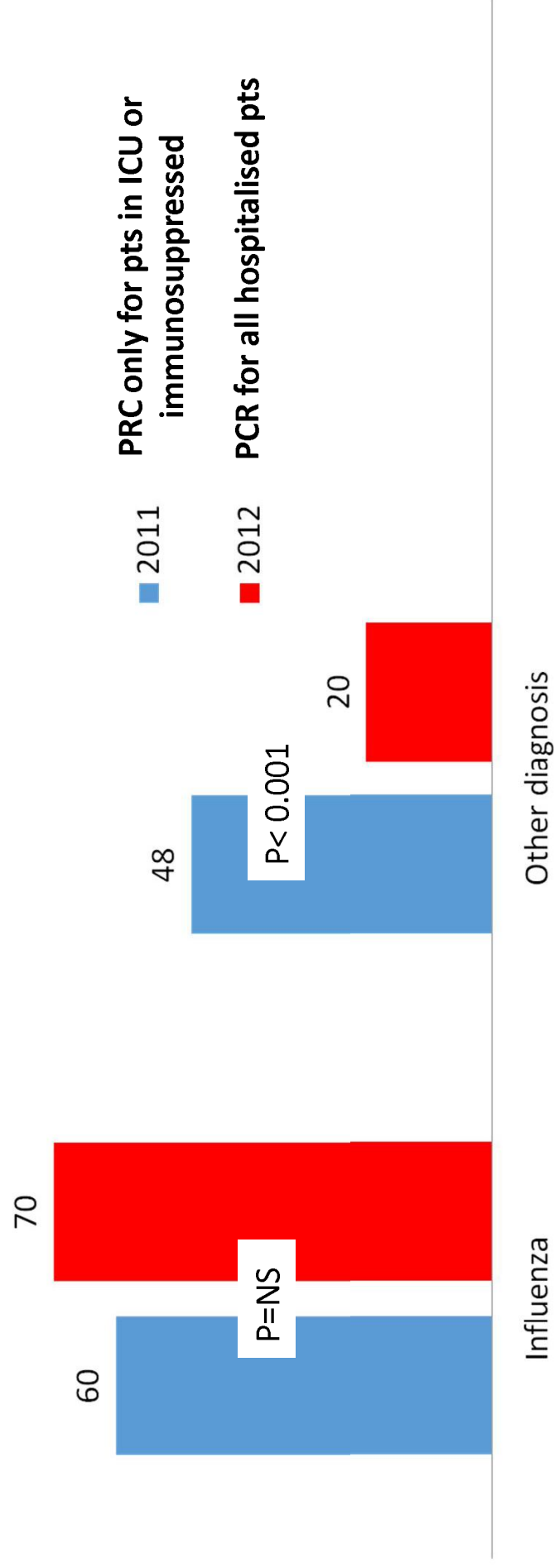
Bruce Y. Lee<sup>1,2,3\*</sup>, Sarah M. McGlone<sup>1,2,3</sup>, Rachel R. Bailey<sup>1,2,3</sup>, Ann E. Wirlinga<sup>1,2,3</sup>, Shanta M. Zimmer<sup>1</sup>, Kenneth J. Smith<sup>1</sup>, Richard K. Zimmerman<sup>4</sup>



« ..... For older adults ( $\geq 65$  year old), in both seasonal and pandemic influenza scenarios, employing PCR was the most cost effective option with the closest competitor being clinical judgment (when judgment accuracy  $\geq 50\%$ ) ..... »



# Use of Tamiflu in adult patients hospitalised with acute respiratory infection at CHU Saint-Pierre



# Infection control considerations

- Numerous outbreak of nosocomial influenza and other respiratory virosis have been described in acute care hospitals
- Health care workers but also patients may be the source of these outbreaks
- Timely institution of additionnal precautions are required for patients with ILI to prevent the nosocomail spread of the viruses
- Type of precautions to be used varied according to mode of transmission the virus

Eibach et al J Hosp Inf 2014; 86:188

Pagani et al J Am geriatr Soc 2015; 63: 739

Voirin et al Infect control Hosp Epidemiol 2015; 36:254

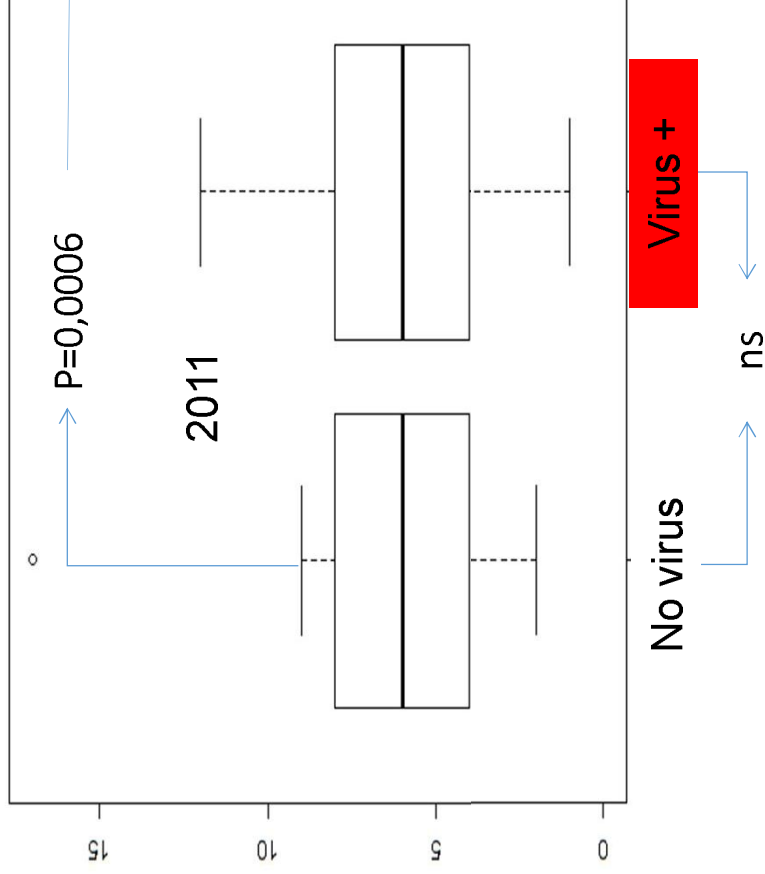
# Isolation precautions for acute respiratory illnesses

Virus	Type of precautions recommended
Human metapneumovirus	Contact
Influenza	Droplet Airborne precaution if performance of aerosol generating procedure
Parainfluenza virus	Contact
Adenovirus	Contact + droplet
Respiratory syncytial virus	Contact
Rhinovirus	Droplet
SARS / MERS Co virus	Airborne + contact + droplet

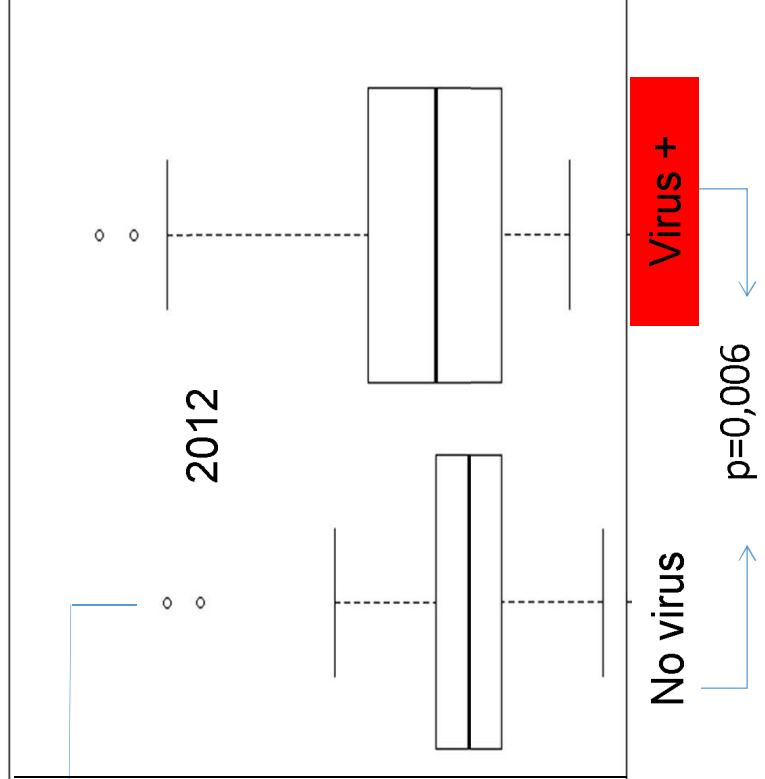
CDC 2007 Guideline for Isolation Precautions: Preventing Transmission of Infectious Agents in Healthcare Settings

# Duration of isolation precautions for respiratory virosis in hospitalised adults at CHU Saint-Pierre

PRC only for pts in ICU or immunosuppressed



PCR for all hospitalised pts



# Conclusions



Respiratory tract infections are one of the most common reason for hospitalisation among adults and molecular tests shows that in winter season, a significant proportion (→70%) of these illnesses are associated with viruses



Influenza and RSV are the most prevalent virus but other viral pathogens contribute to the swell of adult patients in hospitals during the winter months



Accurate clinical diagnostic of acute viral respiratory infection is challenging because of overlap of symptoms associated with the various viruses and overlap with symptoms associated with other illnesses

# Conclusion



Because of concern of bacterial co-infection, physician seems hesitant to discontinue AB even if PCR detect a virus. There appears to be a need for extended AB stewardship with direct and timely discussion of the results of diagnostic tests with patient caregivers. Serum biomarkers as procalcitonin coupled with molecular tests seems to be most helpful to guide AB decisions



Viral diagnostics based on molecular biology are also useful and cost effective to inform some treatment plan decisions

- Initiation or withholding of neuraminidase inhibitors treatment
- Initiation or interruption of infection control precautions

