Ontario influenza vaccine effectiveness study: respiratory virus surveillance

Jonathan Gubbay
Romy Olsha
Anne Winter
October 18, 2011
Background, methods and benefits of the influenza VE study

Anne Winter
What is the VE study?

A multi-provincial system aiming to:

- monitor circulating influenza viruses
- estimate influenza vaccine effectiveness (VE) against laboratory confirmed influenza
- assist WHO in selection of vaccine components for the next influenza season
- monitor the contribution of other circulating respiratory viruses to ILI
- rehearse and refine capacity for pandemic response
Which provinces participate in the VE study?

- BC launched a pilot study in 2004 to monitor influenza circulation and measure influenza VE

Other provinces joined the sentinel network:

- Alberta in 2006/07
- Quebec in 2007/08
- Ontario joined the sentinel network in the 2008/09 influenza season
- Manitoba joined for the 2011/12 season
- Coordinated by BC CDC
- Funded by CIHR (ends in March 2012), and In Kind support from PHOL

This is the last season of CIHR funding
Ontario Influenza VE study team
VE study objectives

• Detect the evolution and spread of new influenza variants as early as possible and directly correlate this with timely estimates of vaccine performance

• To monitor the circulation of respiratory viruses in community settings
Study design

• Case Control Study
• Cases are participants who test positive for influenza virus
• Controls are those who test negative for influenza
• Eligible participants are Ontario residents who provide consent AND present to sentinel physicians with symptoms of ILI within 7 days of onset
• ILI Definition: Acute onset of respiratory illness with fever and cough and with one or more of the following: sore throat, arthralgia, myalgia or prostration
• Nasal or Nasopharyngeal swabs are collected and sent to PHOL -Toronto
• VE study requisition collects information on: ILI onset and specimen collection data, patient’s TIV vaccine history for current and two previous consecutive years, chronic conditions and ILI symptoms
VE Study working hypothesis:

- With a good match between circulating influenza strains and vaccine components, trivalent influenza vaccine effectiveness will range between 70-90% after adjustment for age and chronic conditions.

- During a season of poor vaccine match, influenza vaccine effectiveness will be lower and will vary depending upon the antigenic distance between circulating strains and vaccine components, likely between 30-60%.
Methods/Data analysis

- (Anonymized) Data analyses are performed at the project coordinating center at the BC CDC in Vancouver
- ONLY respiratory specimens collected from patients meeting the eligibility criteria are included in analysis
- VE adjusted for other variables such as: age, sex, chronic conditions and interval between symptom onset and specimen collection
Unique features of the VE study

• Provides a snapshot of all circulating respiratory viruses around the province including rhinovirus, enterovirus, parainfluenza, coronavirus, RSV etc.

• Provides laboratory confirmation of respiratory viruses which cause ILI

• Informs vaccine composition as NML performs antigenic characterization (HAI test)

• Monitors antiviral resistance (NML and PHOL) to inform antiviral recommendations
Unique features of the VE study con’t

- Tracks viral evolution by performing sequencing on early/middle/end of season isolates
- Sentinels in the VE study are the only community HCPs in the province able to test patients with ILI regardless of symptom severity
Relevance for seasonal and pandemic respiratory virus surveillance

Public Health Needs
Annual Evaluation
Pandemic Preparedness
Emerging Surveillance Needs

Network for Seasonal and Pandemic Respiratory Virus Surveillance
Provincial & National links

Integration of Laboratory & Epidemiologic Data
Systematic testing of influenza and respiratory pathogens
Real time tracking of influenza virus evolution
VE estimation with lab-confirmed influenza,
Publications


Results from the influenza VE study, 2010/2011 season

Romy Olsha
VE study activities

Pre Season

- Lessons Learned
- REB Renewal, Amendments & Approvals (UofT)
- Recruit Sentinel Physicians College of Family Physicians
- Mail out Study materials & Specimen collection kits

SEASON

- Sentinel physicians sample eligible patients
- Specimen testing PHO Lab
- Data management Statistical analysis
- Data transfer Communicate w/ MOHLTC
- Knowledge Exchange w/ Physicians
Work flow

Recruitment (Info package) → Consent
Work flow

Recruitment (Info package) → Consent → Study supplies
Work flow

Recruitment (Info package) → Consent → Study supplies

- Transport media
- Swabs
- Ice-packs
- Biohazard bags
- Safe-T-Packs
- Requisition + consent forms
- Documents and labels
**Work flow**

- Recruitment (Info package)
- Consent
- Study supplies
- Patient recruitment, Sample and data collection
Work flow

Recruitment (Info package) → Consent → Study supplies → Patient recruitment, Sample and data collection → Sample and Data → Lab testing and data entry
Work flow

- Recruitment (Info package)
- Consent
- Study supplies
- Patient recruitment, Sample and data collection
- Sample and Data
- Lab testing and data entry
Work flow

Recruitment (Info package) → Consent → Study supplies → Patient recruitment, Sample and data collection

Report Results to Sentinel and pt’s PHU

Sample and Data

Lab testing and data entry
Work flow

Recruitment (Info package) → Consent → Study supplies → Patient recruitment, Sample and data collection

- Surveillance reports
to sentinels
weekly dissemination of results through PHO’s lab-based respiratory pathogen surveillance report

Report Results to Sentinel and pt’s PHU

Lab testing and data entry
Work flow

Recruitment (Info package) → Consent → Study supplies → Patient recruitment, Sample and data collection

Lab testing and data entry → Aggregate data to BC CDC for analysis

Publications

Report Results to Sentinel and pt’s PHU

Surveillance reports to sentinels + weekly dissemination of results through PHO’s lab-based respiratory pathogen surveillance report
Methods/Laboratory identification

• Respiratory specimens are being tested in PHL for:
  • Flu A, Flu B (by rRT-PCR) and the presence of other respiratory viruses (by multiplex PCR; pending funding)
  • Viral culture is performed for Influenza PCR Positive Specimens
  • Positive isolates are sent to NML for strain characterization and antiviral resistance.
Ontario VE Sentinels by Postal Code and Sample Submission
2010 - 2011

Legend

Physician Samples Nurse Practitioner Samples
0
1 - 9
> 10
> 10

Health Unit Boundary

Notes:
Physicians = 145
Nurse Practitioners = 5

Data Source: VE study, Ontario arm

Code | Name
-----|------
ALG  | Algoma District
BRN  | Brant County
CHK  | Chatham-Kent
DUR  | Durham Regional
ELG  | Elgin-St. Thomas
EOH  | Eastern Ontario
GBO  | Grey Bruce
HAL  | Halton Regional
HAM  | City of Hamilton
HDN  | Halton-Muskoka
HKP  | Kawartha-Pine Ridge District
HPE  | Hastings and Prince Edward Counties
HUR  | Huron County
KFL  | Kingston-Frontenac and Lennox and Addington
LAM  | Lambton
LGL  | Leeds-Grenville and Lanark District
MSL  | Middlesex-London
NIA  | Niagara Regional Area
NPS  | North Bay Parry Sound District
NWR  | Northwestern
OTT  | City of Ottawa
OXF  | Oxford County
PDH  | Perth District
PEE  | Peel Regional
POPG | Porcupine
PTC  | Peterborough County-City
REN  | Renfrew County and District
SMD  | Simcoe Muskoka District
SUD  | Sudbury and District
THB  | Thunder Bay District
TOR  | City of Toronto
TSK  | Timiskaming
WAT  | Waterloo
WDG  | Wellington-Dufferin-Guelph
WEC  | Windsor-Essex County
YRK  | York Regional
Demographics

VE (Ontario) Age and Sex distribution of cases and controls.
5 October 2010 - 25 August 2011

Age Group

Male
Female
Demographics

VE (Ontario), PCR result by Sex, 05 October 2010 - 25 August 2011.
Vaccine uptake for the 2010-11 season, VE study

**VE (Ontario) Vaccine Uptake and PCR Result**

- **2010-2011 TIV vaccine**
  - Yes: 63 (PCR-POS: 107, PCR-NEG: 0)
  - No: 385 (PCR-POS: 299, PCR-NEG: 22)
  - Unknown: 0

**VE (Ontario) pH1N1 Vaccine Uptake and PCR Result by Current Year Cases**

- **pH1N1 Vaccine**
  - No: 229 (PCR-POS: 22, PCR-NEG: 33)
  - Unknown: 0

---

**Vaccine uptake for the 2010-11 season, VE study**

**VE (Ontario) Vaccine Uptake and PCR Result**

- **2010-2011 TIV vaccine**
  - Yes: 63 (PCR-POS: 107, PCR-NEG: 0)
  - No: 385 (PCR-POS: 299, PCR-NEG: 22)
  - Unknown: 0

**VE (Ontario) pH1N1 Vaccine Uptake and PCR Result by Current Year Cases**

- **pH1N1 Vaccine**
  - No: 229 (PCR-POS: 22, PCR-NEG: 33)
  - Unknown: 0
Distribution of Flu Positive Samples from the VE Study - Ontario Arm, by Public Health Unit

October, 2010

Notes:
Total Positive Samples = 1

Data Source: VE study, Ontario arm

Legend
Flu Positive Samples
0
1 - 10

Code | Name
-- | --
ALG | Algoma District
BRN | Brant County
CHK | Chatham-Kent
DUR | Durham Regional
ELG | Elgin-St. Thomas
EOH | Eastern Ontario
GBO | Grey Bruce
HAL | Halton Regional
HAM | City of Hamilton
HDN | Haliburton-North
HKB | Haliburton-Kawartha-Pine River District
HPE | Hastings and Prince Edward Counties
HUR | Huron County
KFL | Kingston-Frontenac and Lennox and Addington
LAM | Lambton
LGL | Leeds-Grenville and Lanark District
ML | Middlesex-London
NIA | Niagara Regional Area

Code | Name
-- | --
NPS | North Bay Parry Sound District
NWR | Northwestern
OTT | City of Ottawa
OXF | Oxford County
PDH | Perth District
PEE | Peel Regional
PQP | Porcupine
PTC | Peterborough County-City
RFP | Renfrew County and District
SMD | Simcoe Muskoka District
SUD | Sudbury and District
THB | Thunder Bay District
TOR | City of Toronto
TSK | Timiskaming
WAT | Waterloo
WGP | Wellington-Dufferin-Guelph
WEC | Windsor-Essex County
YRK | York Regional
Distribution of Flu Positive Samples from the VE Study - Ontario Arm, by Public Health Unit

November, 2010

Notes:
Total Positive Samples = 29
Data Source: VE study, Ontario arm

Legend
Flu Positive Samples
- 0
- 1 - 10
- 11 - 20

Ontario
Agency for Health Protection and Promotion

Public Health Ontario
Santé publique Ontario
PARTNERS FOR HEALTH
PARTENAIRES POUR LA SANTÉ

Code Name
ALG Algoma District
BRN Brant County
CHK Chatham-Kent
DUR Durham Regional
ELG Elgin-St. Thomas
EOH Eastern Ontario
GBO Grey Bruce
HAL Halton Regional
HAM City of Hamilton
HDN Halton-Muskoka
HKP Haliburton-Kawartha-Pine Ridge District
HPE Hastings and Prince Edward Counties
HUR Huron County
KFL Kingston-Frontenac and Lennox and Addington
LAM Lambton
LGL Leaside-Grenville and Lanark District
MSL Middlesex-London
NIA Niagara Regional Area

Code Name
NPS North Bay Parry Sound District
NWR Northwestern
OTT City of Ottawa
O XF Oxford County
PDH Perth District
PEE Peel Regional
PQP Porcupine
PTC Peterborough County-City
REN Renfrew County and District
SMD Simcoe Muskoka District
SUD Sudbury and District
THB Thunder Bay District
TOR City of Toronto
TS K Timiskaming
WAT Waterloo
WDG Wellington-Dufferin-Guelph
WE C Windsor-Essex County
YRK York Regional
Distribution of Flu Positive Samples from the VE Study - Ontario Arm, by Public Health Unit

December, 2010

Legend

Flu Positive Samples

0
1 - 10
11 - 20
21 - 30

Notes:
Total Positive Samples = 95

Data Source: VE study, Ontario arm

Code | Name
--- | ---
ALG | Algoma District
BRN | Brant County
CHK | Chatham-Kent
DUR | Durham Regional
ELG | Elgin-St. Thomas
GEO | Eastern Ontario
GBO | Grey Bruce
HAL | Halton Regional
HAM | City of Hamilton
HAN | Haliburton-Kawartha-Pine Ridge District
HPR | Hastings and Prince Edward Counties
HUR | Huron County
KFL | Kingston-Frontenac and Lennox and Addington
LAM | Lambton
LGL | Leeds-Grenville and Lanark District
MSL | Middlesex-London
NIA | Niagara Regional Area
NYK | York Regional

Code | Name
--- | ---
NPS | North Bay Parry Sound District
NWR | Northwestern
OTT | City of Ottawa
OXF | Oxford County
PDH | Perth District
PEE | Peel Regional
PQP | Porcupine
PTC | Peterborough County-City
REN | Renfrew County and District
SMD | Simcoe Muskoka District
SUD | Sudbury and District
THB | Thunder Bay District
TOR | City of Toronto
TSK | Timiskaming
WAT | Waterloo
WDG | Wellington-Dufferin-Guelph
WEC | Windsor-Essex County

Ontario
Agency for Health Protection and Promotion

Public Health Ontario
PARTNERS FOR HEALTH

Santé publique Ontario
PARTENAIRES POUR LA SANTÉ
Distribution of Flu Positive Samples from the VE Study - Ontario Arm, by Public Health Unit
January, 2011

Notes:
Total Positive Samples = 146
Data Source: VE study, Ontario arm

Legend
Flu Positive Samples
0
1 - 10
11 - 20
21 - 30

Code | Name
--- | ---
ALG | Algoma District
BRN | Brant County
CHK | Chatham-Kent
DUR | Durham Regional
ELG | Elgin-St. Thomas
EOH | Eastern Ontario
GBO | Grey Bruce
HAL | Halton Regional
HAM | City of Hamilton
HDP | Halton-Regionality
HKP | Halliburton-Kawartha-Pine Ridge District
HPE | Hastings and Prince Edward Counties
HUR | Huron County
KFL | Kingston-Frontenac and Lennox and Addington
LAM | Lambton
NIA | Niagara Regional Area
MSL | Middlesex-London
PEE | Peel Regional
OTT | City of Ottawa
OXF | Oxford County
PDH | Perth District
REN | Renfrew County and District
SMD | Simcoe Muskoka District
SUD | Sudbury and District
THB | Thunder Bay District
WAT | Waterloo
WDG | Wellington-Dufferin-Guelph
WEC | Windsor-Essex County
YRK | York Regional
Distribution of Flu Positive Samples from the VE Study - Ontario Arm, by Public Health Unit

February, 2011

Notes:
Total Positive Samples = 68

Data Source: VE study, Ontario arm

Legend
Flu Positive Samples
0
1 - 10
11 - 20

Code  Name
ALG  Algoma District
BRN  Brant County
CHK  Chatham-Kent
DUR  Durham Regional
ELG  Elgin-St. Thomas
EOH  Eastern Ontario
GBO  Grey Bruce
HAL  Halton Regional
HAM  City of Hamilton
HDN  Halton-Medford
HKB  Haliburton-Kawartha-Pine Ridge District
HPE  Hastings and Prince Edward Counties
HUR  Huron County
KFL  Kingston-Frontenac and Lennox and Addington
LAM  Lambton
LGL  Leeds-Grenville and Lanark District
MSL  Middlesex-London
NIA  Niagara Regional Area

Code  Name
NPS  North Parry Sound District
NWR  Northwestern
OTT  City of Ottawa
OXF  Oxford County
PDH  Perth District
PEE  Peel Regional
PQP  Porcupine
PTC  Peterborough County-City
REN  Renfrew County District
SMD  Simcoe Muskoka District
SUD  Sudbury and District
THB  Thunder Bay District
TOR  City of Toronto
TSK  Timiskaming
WAT  Waterloo
WDG  Wellington-Dufferin-Guelph
WEC  Windsor-Essex County
YRK  York Regional
Distribution of Flu Positive Samples from the VE Study - Ontario Arm, by Public Health Unit

March, 2011

Notes:
Total Positive Samples = 26

Data Source: VE study, Ontario arm
Distribution of Flu Positive Samples from the VE Study - Ontario Arm, by Public Health Unit
April, 2011

Notes:
Total Positive Samples = 5
Data Source: VE study, Ontario arm

Legend
Flu Positive Samples
0
1 - 10

Code   Name
ALG Algoma District
BRN Brant County
CHK Chatham-Kent
DUR Durham Regional
ELG Elgin-St. Thomas
EOH Eastern Ontario
GBO Grey Bruce
HAL Halton Regional
HAM City of Hamilton
HDN Halton-North Norfolk
HKG Huron-Kinross District
HPE Hastings and Prince Edward Counties
HUR Huron County
KFL Kingston-Frontenac and Lennox and Addington
LAM Lambton
LGL Leeds-Grenville and Lanark District
MLD Middlesex-London
NIA Niagara Regional Area

Code   Name
NPS North Bay Parry Sound District
NWR Northwestern
OTT City of Ottawa
OXF Oxford County
PDH Perth District
PEP Peel Regional
PEP Porcupine
PTC Peterborough County-City
REN Renfrew County and District
SMD Simcoe Muskoka District
SUD Sudbury and District
THB Thunder Bay District
TBR City of Toronto
TSK Timiskaming
WAT Waterloo
WDG Wellington-Dufferin-Guelph
WEC Windsor-Essex County
YRK York Regional
### VE (Ontario) Flu A and B detection by date of onset - 23 September 2010 to 23 August 2011

<table>
<thead>
<tr>
<th>Date of symptom onset</th>
<th>Flu A</th>
<th>Flu B</th>
<th>Negative</th>
</tr>
</thead>
<tbody>
<tr>
<td>23/09/2010</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>07/10/2010</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>21/10/2010</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>04/11/2010</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>18/11/2010</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>02/12/2010</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>16/12/2010</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>30/12/2010</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>13/01/2011</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>10/01/2011</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>27/01/2011</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>10/02/2011</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>24/02/2011</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>10/03/2011</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>24/03/2011</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>07/04/2011</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>21/04/2011</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>05/05/2011</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>19/05/2011</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>02/06/2011</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>16/06/2011</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>30/06/2011</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>14/07/2011</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>28/07/2011</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>11/08/2011</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
VE (Ontario) Flu A and B detection by date of onset -
23 September 2010 to 23 August 2011

Date of symptom onset

Number of cases

- Flu A
- Flu B
- Negative

Dates:
- 23/09/2010
- 07/10/2010
- 21/10/2010
- 04/11/2010
- 18/11/2010
- 02/12/2010
- 16/12/2010
- 30/12/2010
- 13/01/2011
- 27/01/2011
- 10/02/2011
- 24/02/2011
- 10/03/2011
- 24/03/2011
- 07/04/2011
- 21/04/2011
- 05/05/2011
- 19/05/2011
- 02/06/2011
- 16/06/2011
- 30/06/2011
- 14/07/2011
- 28/07/2011
- 11/08/2011
VE (Ontario) Flu A and B detection by date of onset -
15 October 2010 to 01 May 2011
VE (Ontario) - Influenza Type and Subtype Results
5 October, 2010 - 25 August, 2011

- Flu A - H3: 270
- Flu A - pH1N1: 36
- Flu B: 63
VE (Ontario) Multiplex Viral Panel detection by date of onset - 15 October 2010 to 01 May 2011
VE (Ontario) Multiplex Viral Panel detection by date of onset -
15 October 2010 to 01 May 2011
VE (Ontario) Multiplex Viral Panel detection by date of onset - 15 October 2010 to 01 May 2011

Date of symptoms onset

Number of detections

RSV
RHINO
PARAINFLUENZA
METAPNEUMO
CORONA
ADENO
Overview of Recently Described and Emerging Respiratory Viruses: Rhinovirus, Metapneumovirus, and Bocavirus,
Jonathan Gubbay
Medical Microbiologist OAHPP
Respiratory viruses – key players

• Influenza A, B
• Respiratory Syncytial Virus
• Parainfluenza virus 1-4
• Rhinovirus (and enteroviruses)
• Adenovirus

• More recently described respiratory viruses:
  • Human metapneumovirus.
  • Multiple coronaviruses: SARS, 229E, NL63, OC43, HKU1.
  • Human bocavirus
  • Polyomaviruses KI, WU
921 Respiratory Outbreaks Tested by PHLs from September 1, 2010 to April 30, 2011.

<table>
<thead>
<tr>
<th>Respiratory viruses detected</th>
<th>LTC</th>
<th>Hospital</th>
<th>School/Daycare</th>
<th>Other settings*</th>
<th>No setting</th>
<th>Total</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Influenza A/H3</td>
<td>182</td>
<td>11</td>
<td>7</td>
<td>1</td>
<td>74</td>
<td>275</td>
<td>29.9</td>
</tr>
<tr>
<td>Entero/Rhinovirus</td>
<td>131</td>
<td>3</td>
<td>0</td>
<td>0</td>
<td>41</td>
<td>175</td>
<td>19.0</td>
</tr>
<tr>
<td>Coronavirus</td>
<td>52</td>
<td>2</td>
<td>0</td>
<td>0</td>
<td>7</td>
<td>61</td>
<td>6.6</td>
</tr>
<tr>
<td>Respiratory Syncitial</td>
<td>33</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>10</td>
<td>44</td>
<td>4.8</td>
</tr>
<tr>
<td>Parainfluenza</td>
<td>32</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>7</td>
<td>39</td>
<td>4.2</td>
</tr>
<tr>
<td>Metapneumovirus</td>
<td>28</td>
<td>0</td>
<td>2</td>
<td>1</td>
<td>7</td>
<td>38</td>
<td>4.1</td>
</tr>
<tr>
<td>Influenza A (H3)/Entero/Rhinovirus</td>
<td>23</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>6</td>
<td>30</td>
<td>3.3</td>
</tr>
<tr>
<td>Influenza A (H3)/Coronavirus</td>
<td>19</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>9</td>
<td>29</td>
<td>3.1</td>
</tr>
<tr>
<td>Influenza A (H3)/Respiratory Syncytial</td>
<td>10</td>
<td>0</td>
<td>1</td>
<td>0</td>
<td>5</td>
<td>16</td>
<td>1.7</td>
</tr>
<tr>
<td>Influenza A (H3)/Parainfluenza</td>
<td>12</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>13</td>
<td>1.4</td>
</tr>
<tr>
<td>Entero/Rhino/Parainfluenza</td>
<td>8</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>4</td>
<td>12</td>
<td>1.3</td>
</tr>
<tr>
<td>Influenza B</td>
<td>5</td>
<td>1</td>
<td>2</td>
<td>0</td>
<td>1</td>
<td>9</td>
<td>1.0</td>
</tr>
<tr>
<td>Metapneumovirus/Respiratory Syncytial</td>
<td>6</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>2</td>
<td>8</td>
<td>0.9</td>
</tr>
<tr>
<td>Coronavirus/Entero/Rhinovirus</td>
<td>6</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>6</td>
<td>0.7</td>
</tr>
<tr>
<td>Parainfluenza/Respiratory Syncytial</td>
<td>4</td>
<td>1</td>
<td>0</td>
<td>1</td>
<td>0</td>
<td>6</td>
<td>0.7</td>
</tr>
<tr>
<td>Influenza A (H3)/Metapneumovirus</td>
<td>4</td>
<td>0</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>5</td>
<td>0.5</td>
</tr>
<tr>
<td>Other viruses**</td>
<td>44</td>
<td>0</td>
<td>0</td>
<td>3</td>
<td>17</td>
<td>64</td>
<td>6.9</td>
</tr>
<tr>
<td>No virus detected</td>
<td>66</td>
<td>6</td>
<td>0</td>
<td>0</td>
<td>20</td>
<td>90</td>
<td>9.8</td>
</tr>
</tbody>
</table>
| **Total**                                         | 665  | 27       | 13             | 5               | 211        | 921   | 100.0
921 Respiratory Outbreaks Tested by PHLs from September 1, 2010 to April 30, 2011.

• Influenza A or B was detected in 44.8% of the outbreaks

• In 29.9% of all influenza positive outbreaks, at least one other virus was detected.
Rhinovirus

- Largest genus in *Picornaviridae* family
  - Name derived from adaptation to growth in nasal passages.
  - First discovered in 1956;
  - at least 100 serotypes described; 3 genetic groups (A, B, C).

- Implicated in 30% to 50% of all cases of acute respiratory disease
  - Single most important causative agent of common colds.
  - More recently recognised as a cause of LRTIs, including severe disease with significant morbidity/mortality.
Rhinovirus

- Incidence of infection in US approx 0.75 infections/person/year
  - In children 1.25 infections/person/year.

- 25% of infections asymptomatic.

- Cause early fall peak of colds in September in temperate northern hemisphere.
  - Often peak around 2 weeks after school opening in Sept.
  - Prevalence then falls in late fall, winter, early spring.
  - Second period of increased activity in late spring, April and May.
  - Accounts for 50% of colds in summer months.

- Occurs year round in tropical climates
Rhinovirus

- Infectious dose lower when given as droplet particles vs aerosols
  - Implies preference for nasopharynx vs LRT.
- Direct contact main mode of transmission.
  - Survives several hours on skin; 3-4 days on nonporous surfaces.
  - Small particle aerosols not big contributors to transmission
  - Large particle aerosols (cough, sneeze) may be involved.
Rhinovirus – Incubation Period and Shedding

• Recovered from nasal washes of experimentally infected volunteers at a median 10hrs after inoculation.
  • Throat sore/scratchy 10 to 12 hours after inoculation.
  • Shedding peaks 48 to 72hrs after viral challenge, then rapidly declines.
  • Usually no longer recoverable after 3 weeks.
    • Prolonged or persistent infection may occur in immunocompromised.
Rhinovirus

• Median duration of illness 7 days (1 to 33 days)
  • 25% last 2 weeks.

• Sinus involvement inherent feature of colds
  • All rhinovirus colds are viral rhinosinusitis. Sinus cavity abnormalities on CT in 87% of adults with self-diagnosed colds.
  • Middle ear and eustachian tube abnormalities common
    • Abnormal middle ear pressure, middle ear fluid common.
    • Recovered alone or with bacteria in 24% of OM cases.
Rhinovirus Complications

- Acute bacterial sinusitis (in 0.5% to 8% common colds)
- Acute bacterial OM (2% and 30% of colds in adults and children respectively)
- Exacerbations of chronic bronchitis (40% associated with rhinovirus infection)
- Asthma (rhinovirus associated with 60% to 70% of asthma exacerbations in school aged children).
- Other LRT syndromes (detected in varying % of persons with LRTI in hospital - <10% to 25%)
- Infections in immunocompromised – detected in a low % of LRT in immunocompromised
Human Metapneumovirus

- Discovered in 2001, causes RTI in all age groups.
- RNA virus
- hMPV and RSV in *Pneumovirinae* subfamily of the *Paramyxoviridae* family.
- Four major genotypes (A1,A2, B1,B2)
  - 2 major antigenic subgroups (A and B).
- Detected in serum from 1958.
Human Metapneumovirus: Epidemiology

• Transmission likely by droplet spread.
  • Healthcare associated infections documented

• Annual epidemics late winter, early spring.
  • Coincides/overlaps with RSV season.
  • Sporadic infection year round.

• Incubation period 4 to 9 days (usually 3-5 days)

• Viral shedding 1 to 2 weeks.
  • Immunocompromised may shed for months.
Human Metapneumovirus: Clinical Manifestations

- Bronchiolitis, asthma exacerbations, croup.
- URIs with concomitant OM.
- Most healthy children mild URI, some severe LRTI.
- Immunosuppressed at increased risk severe disease.
- All children infected at least once by 5yo.
  - Recurrent infections throughout life.
- Potential antiviral treatment: susceptible to ribavirin in vitro - no controlled clinical studies as yet.
“Newer” respiratory viruses: Human Metapneumovirus

• Children <5yo with URI, 1982-2001:
  • hMPV RNA in 3% of 2710 URI episodes (5% of 2384 culture neg.)
    • RSV in 6%, influenza in 6%, PIV in 7%.
  • Mean age hMPV+ 20 months
  • 78% from Dec-May.
  • Acute otitis media (AOM) in 50% (similar to influenza, RSV, PIV).
  • 54% febrile (vs 84% with influenza febrile)
    • Williams et al. JID 2006; 193:387–95

• Detected in 2.2% of 405 samples from community patients with ILI negative for influenza/RSV (1.3% of all samples submitted).
Human Metapneumovirus

Table 1. Clinical features at presentation of 118 children with human metapneumovirus upper respiratory tract infections.

<table>
<thead>
<tr>
<th>Symptom/sign</th>
<th>Children with symptom/sign, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fever</td>
<td>54</td>
</tr>
<tr>
<td>Coryza</td>
<td>82</td>
</tr>
<tr>
<td>Cough</td>
<td>66</td>
</tr>
<tr>
<td>Hoarseness</td>
<td>8</td>
</tr>
<tr>
<td>Otalgia</td>
<td>31</td>
</tr>
<tr>
<td>Rhinitis</td>
<td>79</td>
</tr>
<tr>
<td>Conjunctivitis</td>
<td>3</td>
</tr>
<tr>
<td>Pharyngitis</td>
<td>44</td>
</tr>
<tr>
<td>Abnormal tympanic membrane</td>
<td>63</td>
</tr>
</tbody>
</table>

Table 2. Summary of approximate reported frequency of symptoms and signs of hMPV lower RTI in young children from selected references [31,55,59,62,75,77,81,85]

<table>
<thead>
<tr>
<th>Clinical manifestation</th>
<th>Frequency range (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fever</td>
<td>45–100</td>
</tr>
<tr>
<td>Rhinorrhea</td>
<td>40–90</td>
</tr>
<tr>
<td>Cough</td>
<td>50–90</td>
</tr>
<tr>
<td>Retractions</td>
<td>40–80</td>
</tr>
<tr>
<td>Wheezing</td>
<td>30–50</td>
</tr>
<tr>
<td>Crackles</td>
<td>10–60</td>
</tr>
<tr>
<td>Tachypnea</td>
<td>60–90</td>
</tr>
<tr>
<td>Difficulty feeding</td>
<td>40–60</td>
</tr>
<tr>
<td>Abnormal tympanic membrane</td>
<td>10–40</td>
</tr>
<tr>
<td>Vomiting</td>
<td>10–30</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>10–40</td>
</tr>
<tr>
<td>Irritability</td>
<td>40–60</td>
</tr>
<tr>
<td>Conjunctival erythema</td>
<td>7–10</td>
</tr>
<tr>
<td>Rash</td>
<td>5–10</td>
</tr>
</tbody>
</table>

hMPV, human metapneumovirus; RTI, respiratory tract infection.

Case fatality rates of 10% reported in LTCF metapneumovirus outbreaks

Human Bocavirus

- Nonenveloped, singled strand DNA virus, family parvoviridae; first identified in 2005 in children with acute RTI.
- Name derives from similarity to bovine parvovirus 1 and canine minute virus.
- No data regarding antigenic variation or distinct serotypes.
- Detection only described in humans.
- Transmission presumed respiratory secretions; fecal-oral also possible.
- Duration of shedding variable: 50% <1 week, 25% over one month (1 record of 402 days).
- Circulates worldwide and throughout the year.
Bocavirus: 4 Clades

- HBoV1 (2009), HBoV3 (2009), HBoV4 (2010) more recently described
- Clades 2 to 4 first identified in stool
- No HBoV2 in >6000 respiratory samples
  - HBoV1 in 3 to 14%
    - Chieochansin et al. EID 15(9):1503-4, 2009
- HBoV2 in 4% NPA (Song et al. EID, 16(2):324-7, 2010)
- HBoV2B most common HBoV found in stool.
  - Evidence is HBoV2 associated with GI disease (not as strong as other GI viruses).
  - HBoV1 not associated with clinical GI disease
HBoV1 Clade 1 most common in respiratory tract

- HBoV associated with pneumonia/hospitalization when detected as part of coinfection (Adj. OR 3.87; 1.16-12.91)
  - Association gone when look at HBoV infection without viral coinfection (Adj. OR 0.58; 0.15-2.28)
    - Fry et al. JID 2007;195:1038-1045

- Factors complicating association with resp illness
  - Frequency of coinfection with other respiratory viruses
  - Duration of HBoV1 shedding in resp tract.
Human Bocavirus

• Prominent symptoms: cough, rinorrhea, fever.
• Associated with episodes of wheezing.
• Detected in 5% to 10% of all children with acute upper and lower RTI.
• Role as a pathogen confounded by simultaneous detection of other viruses in up to 80%.
  • Has been detected in resp tract, blood and stool of some ill children.
  • Seroconversion documented after symptomatic disease.
• Infection ubiquitous – all children seropositive by 5yo.
Human Bocavirus

• Laboratory Detection
  • HBoV PCR and serology mostly used by research labs.
  • Now included in commercial multiplex assays.

• Treatment – no specific therapy available.
Impact of Molecular Methods on Respiratory Viral Diagnostics

• Much greater sensitivity vs culture and DFA.
  • Better understanding of epidemiology of respiratory viruses.
  • Fewer infections where don’t identify a virus
  • Potential impacts on clinical care: less antibacterial therapy, shorter hospital stay, reduced mortality if earlier use of antivirals for influenza.

• Faster turnaround time – greater opportunity to guide therapy.

• Discovery of new viruses in respiratory tract in last decade
  • Metapneumovirus
  • Multiple coronaviruses: SARS, 229E, NL63, OC43, HKU1.
  • Human bocavirus
  • Polyomaviruses KI, WU

Viral coinfections recognised as a relatively common entity.
Acknowledgements

• Danuta Skowronski and the national VE team
• Natasha Crowcroft
• Respiratory Surveillance Team (Erik Kristjanson, Adriana Peci, Alex Marchand-Austin, Eddie Chong-King)
• Elizabeth Balogun
• Molecular Diagnostics department
• Virus Isolation department
• Yan Li and team at NML
• The College of Family Physicians of Canada
• Our sentinels

Thank You!