Point of Care Tests for respiratory viruses: impact on clinical outcomes of patients

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Outline

1. Importance of respiratory viral infections
2. POCT tests available
3. Studies using POCT – what are the real-world outcomes?
4. New developments in POCT
5. Summary
Importance of respiratory viral infections
Importance of respiratory viral infections

Source: ASPREN and VIDRL

Australian data, Li-Kim-Moy et al., Communicable Diseases Intelligence 2016
Respiratory viral infections cause exacerbations

- Chronic respiratory disease: asthma, cystic fibrosis (CF) and chronic obstructive pulmonary disease (COPD)
- Worsened during exacerbations → influenza and rhinovirus
- Flu vaccine → 33% effective in 2017 (Sullivan et al., 2017) → 11% in people ≥65 y.o.
- Antivirals available but time critical

Types of POCT for respiratory viruses

• Lateral flow POCT

Quidel Quickvue
Types of POCT for respiratory viruses

• Lateral flow POCT

Positives:
• Easy-to-use
• Results in $\leq 15$ minutes
• Excellent specificity
• Compatible with multiple transport options
• Long shelf-life

Negatives:
• ↓ sensitivity
• Influenza B sensitivity lower than influenza A
• Influenza A virus subtype?
• Limited multiplex
### BinaxNOW

<table>
<thead>
<tr>
<th>Study</th>
<th>Study Population</th>
<th>Sample type</th>
<th>Sensitivity</th>
<th>Specificity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hassan et al., 2014</td>
<td>Pediatric</td>
<td>200 frozen NP swabs &amp; washes</td>
<td>Flu A- 72.8%</td>
<td>Flu A- 100%</td>
</tr>
<tr>
<td>J Clin Micro</td>
<td></td>
<td></td>
<td>Flu B- 70.8%</td>
<td>Flu B- 100%</td>
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<tr>
<td>Cho et al., 2013</td>
<td>Adult and pediatric</td>
<td>253 frozen NP swabs</td>
<td>Flu A- 71%</td>
<td>Flu A-100%</td>
</tr>
<tr>
<td>J Virol Methods</td>
<td></td>
<td></td>
<td>Flu B- 37.2%</td>
<td>Flu B- 100%</td>
</tr>
<tr>
<td>DiMaio et al., 2012</td>
<td>Adult and pediatric</td>
<td>200 frozen NP samples</td>
<td>Flu A-62.2%</td>
<td>Flu A-100%</td>
</tr>
<tr>
<td>J Virol Methods</td>
<td></td>
<td></td>
<td>Flu B- 54.5%</td>
<td>Flu B- 100%</td>
</tr>
<tr>
<td>Booth et al., 2006</td>
<td>Adult and pediatric</td>
<td>224 frozen NPA &amp; N/T swabs</td>
<td>Flu A-80%</td>
<td>Flu A- 99%</td>
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<tr>
<td>J Med Virol</td>
<td></td>
<td></td>
<td>Flu B- 47%</td>
<td>Flu B-100%</td>
</tr>
</tbody>
</table>

NP=nasopharyngeal
Types of POCT for respiratory viruses

- Lab in a capsule POCT
- All-in-one machines

GenePOC and PIE
Up to 12 targets

- Cdiff
- VRE
- Staph. Aureus
- Multi-Drug Resistance CRE
- GBS
- Pharyngeal strep
- Flu/RSV
- HIV-HBV-HCV
- Enteric Panels
- Respiratory Panels
- Mycobacterium
- CT/GC/TV/MG
- Vaginitis Panel
- HSV

Types of POCT for respiratory viruses

- Lab in a capsule POCT

**Positives:**
- Excellent specificity and sensitivity
- Traceability
- Influenza A subtyping
- Other viruses

**Negatives:**
- Expensive
- Require specialised equipment
Cepheid GeneXpert

NP=nasopharyngeal
POWH PCR Testing

Turn around Time (hrs)

2016 2017 2018

Thanks to Ryan Pratama, NSW Health Pathology
POWH Cepheid GeneXpert

Turn around time (hrs)

Jan Feb Mar Apr May Jun Jul Aug Sep Oct Nov Dec

2017 POWH

2018 POWH

Thanks to Ryan Pratama, NSW Health Pathology
Potential benefits of POCT

- ↑ prescription of antivirals
- ↓ prescription of antibiotics
- ↓ length of hospital stay
- ↓ exacerbations

Does this happen in practice?
Studies using POCT – what are the real-world outcomes?

• Systematic review:
  i) antiviral prescription
  ii) antibiotic prescription
  iii) patient length of stay in the ED

• Comprehensive search of all primary research papers available that meet search criteria

Egilmezer et al., 2018, Reviews in Medical Virology, provisionally accepted
Studies using POCT – what are the real-world outcomes?

• Clearly defined eligibility criteria & methodology

• Medline & Embase

• “influenza, point-of-care test, antivirals, antibiotics, length of stay”
Egilmezer et al., 2018, Reviews in Medical Virology, provisionally accepted
Studies using POCT – what are the real-world outcomes?

• Antiviral prescription: 14 studies
  \[\uparrow \quad 12/14 \ (86\%)\]

• Antibiotic prescription: 26 studies
  \[\downarrow \quad 20 / 26 \ (77\%)\]

Egilmezer et al., 2018, Reviews in Medical Virology, provisionally accepted
Studies using POCT – what are the real-world outcomes?

• Time spent in ED: 9 studies

  5/9 (55.6%) ↓

• More research needed
Developing New POCT

• Aim: develop methods to rapidly detect pathogen nucleic acid using "everyday" devices

• Low-middle income countries

Target antigen binding, triggering release of fluorescent molecules. → Readouts using commonly available equipment
Developing New POCT

- Prof Justin Gooding
- Dr Padma Bakthavathsalam
- NSW Smart Sensing Network (NSSN)

→ Reduce overuse of antibiotics
→ antibiotic resistance
What are the features of new POCT devices?

- Simple
  - clear instructions, straightforward read-out
- Cheap
- No specialised machinery
- Robust reagents and consumables
- Concordance with established laboratory methods – sensitive and specific
- Low sample volume
- Safe (devices, reagents, disposal)
- Traceability
Developing New POCT

Paper-Based RNA Extraction, \textit{in Situ} Isothermal Amplification, and Lateral Flow Detection for Low-Cost, Rapid Diagnosis of Influenza A (H1N1) from Clinical Specimens

Natalia M. Rodriguez\textsuperscript{†}, Jacqueline C. Linnes\textsuperscript{†}, Andy Fan\textsuperscript{†}, Courtney K. Ellenson\textsuperscript{†}, Nira R. Pollock\textsuperscript{‡}, and Catherine M. Klapperich\textsuperscript{†,*}

\textsuperscript{†}Department of Biomedical Engineering, Boston University, Boston, Massachusetts 02215, United States

\textsuperscript{‡}Division of Infectious Diseases, Beth Israel Deaconess Medical Center, Harvard Medical School, Boston, Massachusetts 02115, United States

Abstract

The 2009 Influenza A (H1N1) pandemic disproportionately affected the developing world and highlighted the key inadequacies of traditional diagnostic methods that make them unsuitable for use in resource-limited settings, from expensive equipment and infrastructure requirements to unacceptably long turnaround times. While rapid immunoassay diagnostic tests were much less costly and more context-appropriate, they suffered from drastically low sensitivities and high false

PES- poly(ether sulfone) paper matrix
Summary

• Improved clinical outcomes:
  • ↑ prescription of antivirals
  • ↓ prescription of antibiotics
  • ? stay in ED

• Improved prognostic data

• Potential use of new POCT for control of outbreaks of known and emerging respiratory viruses
Thank you

Virology Research Lab
• Gregory Walker
• Ece Egilmezer

UNSW Chemistry
• Prof Justin Gooding
• Dr Padma Bakthavathsalam
• Danielle

Integrated Sciences
• Dylan Warby

@DrSachaSB
Questions

• Does anyone currently use POCT?

• What system do you use?

• What would be the ideal POCT if we could design from scratch?
Thank you

Virology Research Lab
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UNSW Chemistry
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Randomised controlled trial and health economic evaluation of the impact of diagnostic testing for influenza, respiratory syncytial virus and Streptococcus pneumoniae infection on the management of acute admissions in the elderly and high-risk 18- to 64-year olds


*Detailed Author information*

*Health Technology Assessment Volume: 18, Issue: 36, Published in May 2014*

https://doi.org/10.3310/hta18360

*Citation: Nicholson K, Abrams K, Batham S, Medina M, Warren F, Barer M, et al.* Randomised controlled trial and health economic evaluation of the impact of diagnostic testing for influenza, respiratory syncytial virus and Streptococcus pneumoniae infection on the management of acute admissions in the elderly and high-risk 18- to 64-year olds. *Health Technol Assess* 2014;18(36)
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GenePOC

**Instrument**

- **Compact / Portable**
- **Easy to use** (2 min hands on time)
- **Fast** (70m turnaround time)
- **Innovative** (multiplexing up to 12 targets)
- **Flexible** (up to eight samples and 8 different assays per run)

**Characteristics**

**Menu of Assays**

- Cdiff
- VRE
- Staph. Aureus
- Multi-Drug Resistance CRE
- GBS
- Pharyngeal strep
- Flu/RSV
- HIV-HBV-HCV
- Enteric Panels
- Respiratory Panels
- Mycobacterium
- CT/GC/TV/MG
- Vaginitis Panel
- HSV

**PIE**

Slide: Dylan Warby, Integrated Sciences
## Quidel Quickvue

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<td><strong>Koul et al., 2015</strong>&lt;br&gt; Indian J Med Microbiol.</td>
<td>Adult and pediatric</td>
<td>600 N/T swabs</td>
<td>Flu A - 22.7%</td>
<td>Flu A- 100%</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>Flu B - 23.6%</td>
<td>Flu B- 100%</td>
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<tr>
<td><strong>Lucas et al., 2011</strong>&lt;br&gt; Clin Infect Dis</td>
<td>Adult and pediatric</td>
<td>1538 nasal wash</td>
<td>Flu A - 15%</td>
<td>Flu A- 99%</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>H1N1&lt;sub&gt;09&lt;/sub&gt;- 20%</td>
<td>H1N1&lt;sub&gt;09&lt;/sub&gt;- 99%</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Flu B - 31%</td>
<td>Flu B- 99%</td>
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<tr>
<td><strong>Velasco et al., 2010</strong>&lt;br&gt; J Clin Virol.</td>
<td>Adult and pediatric</td>
<td>360 nasal swabs</td>
<td>Flu A H1N1&lt;sub&gt;09&lt;/sub&gt;- 63%</td>
<td>Flu A H1N1&lt;sub&gt;09&lt;/sub&gt; - 96%</td>
</tr>
<tr>
<td><strong>Company Reported</strong></td>
<td>Nasal swab</td>
<td>FluA – 94%</td>
<td>FluA – 90%</td>
<td></td>
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<tr>
<td></td>
<td></td>
<td>Flu B – 70%</td>
<td>Flu B – 97%</td>
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