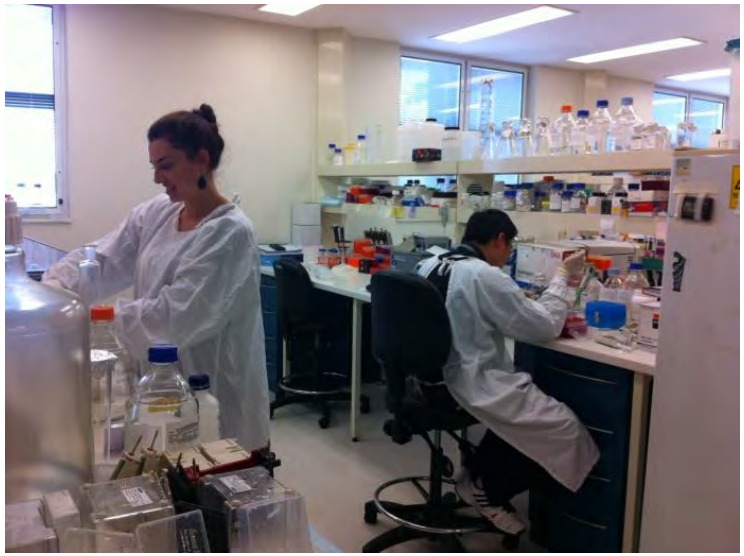
Point of Care Tests for respiratory viruses: impact on clinical outcomes of patients

Dr Sacha Stelzer-Braid

Postdoctoral Scientist

Virology Research Laboratory (VRL), UNSW and POWH

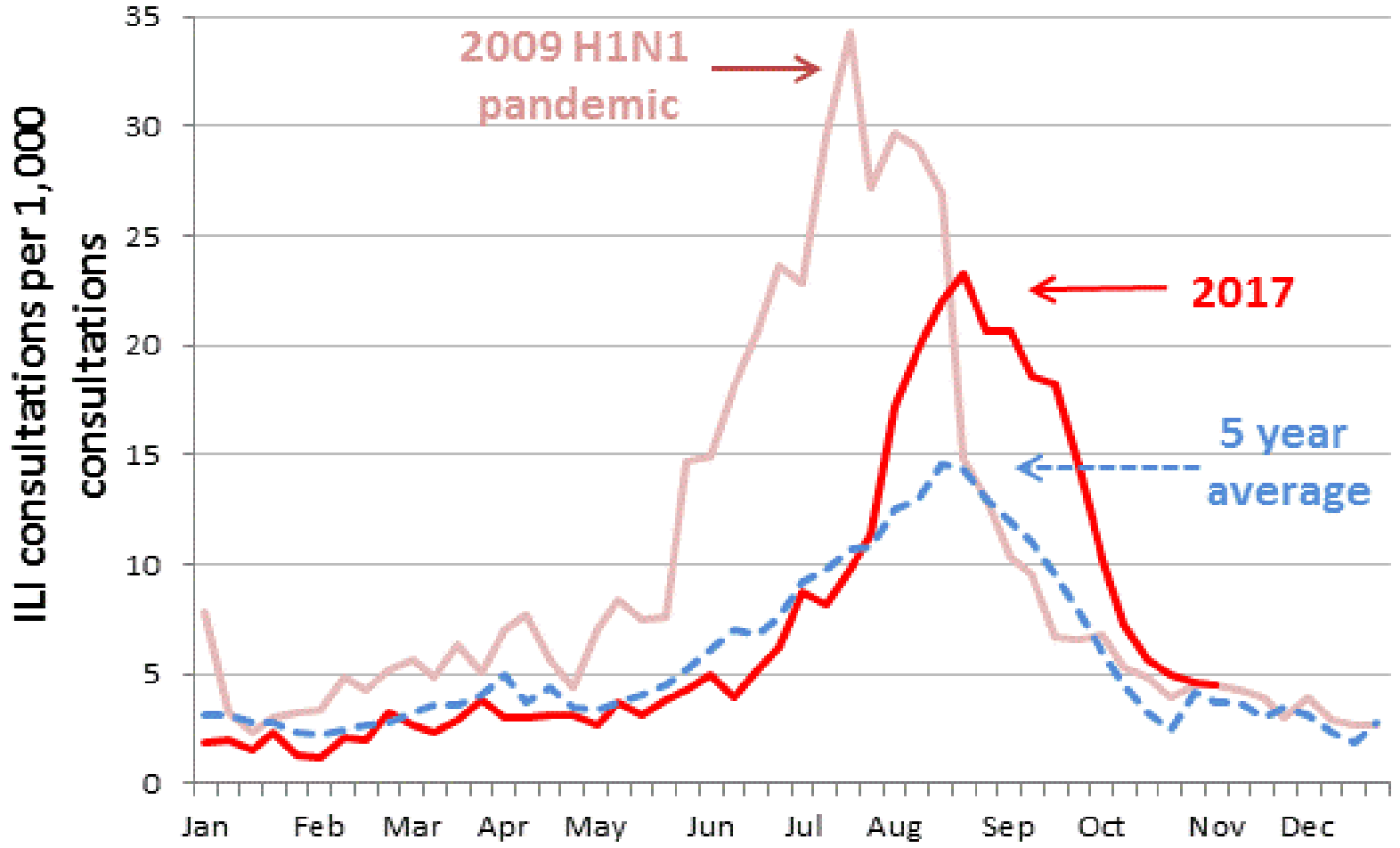


Outline

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

virology diagnosis . research . teaching

Integrated Systems for Epidemic Response

UNSW AUSTRALIA

Respiratory viral infections cause exacerbations

- Chronic respiratory disease: asthma, cystic fibrosis (CF) and chronic obstructive pulmonary disease (COPD)
- Worsened during exacerbations
  → <u>influenza and rhinovirus</u>

- Flu vaccine → 33% effective in 2017 (Sullivan *et al.*, 2017)
  → 11% in people ≥65 y.o.

- Antivirals available but **time critical**

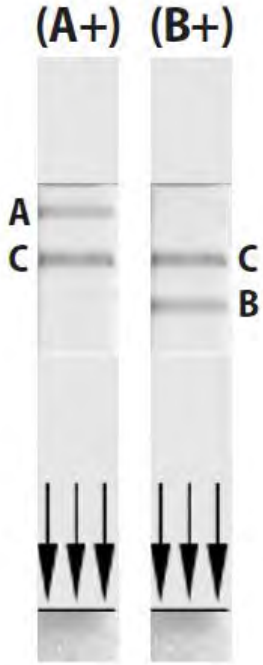
Sullivan *et al.*, 2017 Euro Surveill. 2017 Oct;22(43).

virology
diagnosis . research . teaching

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 ≤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

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

NP=nasopharyngeal

virology diagnosis . research . teaching

Integrated Systems for Epidemic Response

UNSW AUSTRALIA

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

Babady 2014 Expert Rev Mol Diagn. 2013 Nov;13(8):779-88.

virology diagnosis . research . teaching

Integrated Systems for Epidemic Response

UNSW AUSTRALIA

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

S

N
e
J

P
a
J

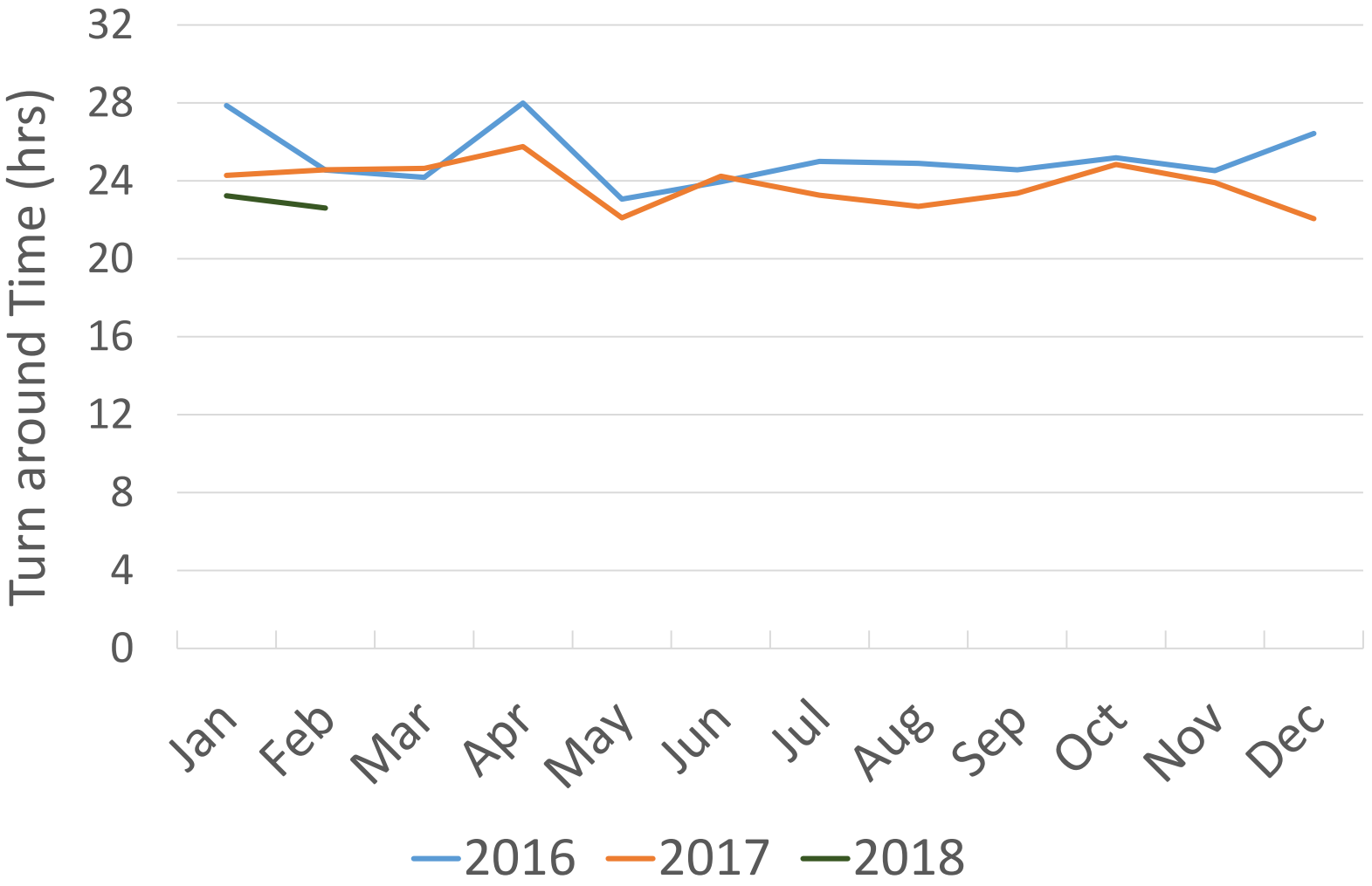
NP=nasopharyngeal

virology
diagnosis . research . teaching

INTEGRATED SYSTEMS FOR
Epidemic Response

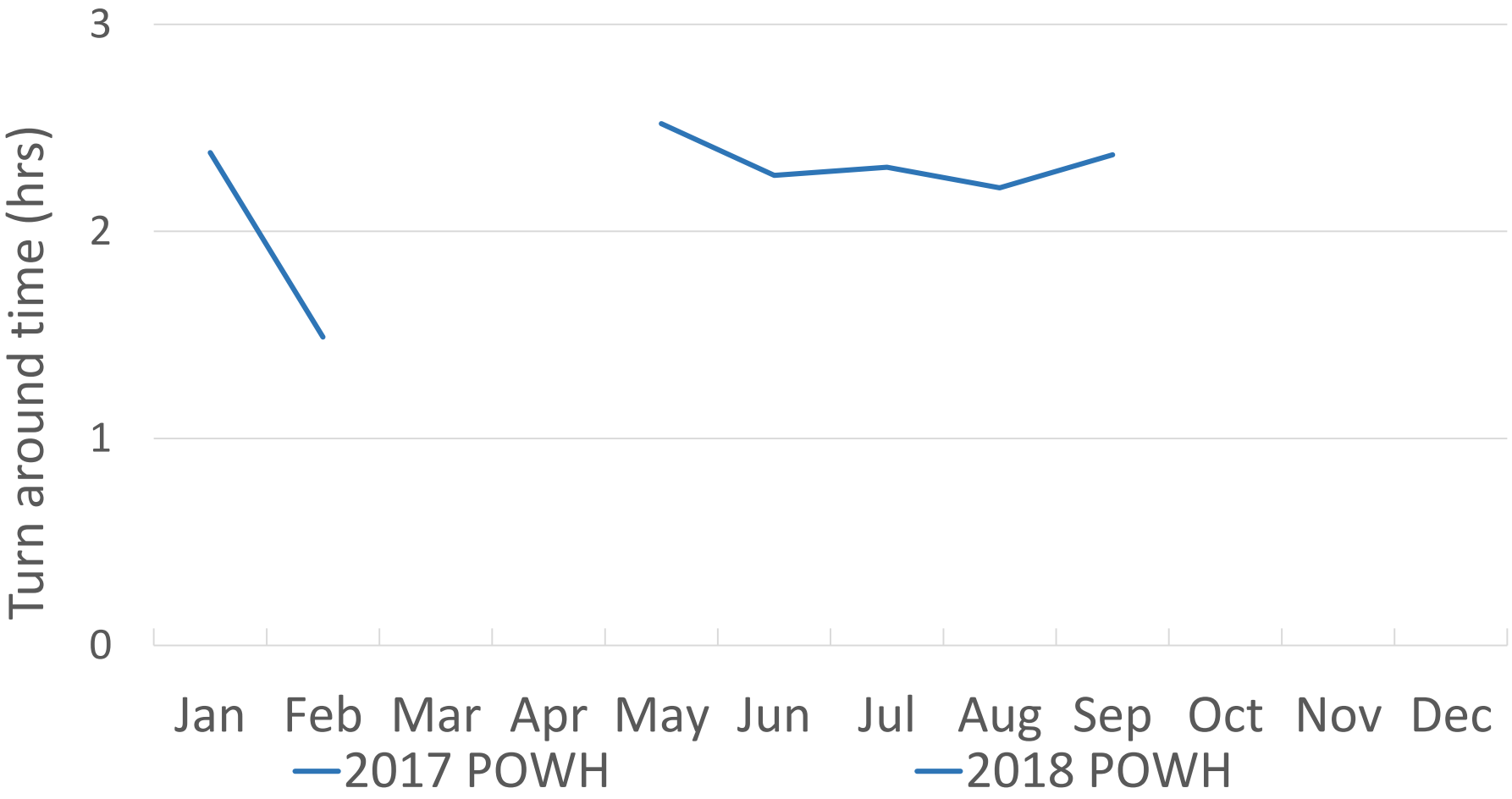
UNSW
AUSTRALIA

POWH PCR Testing



Thanks to Ryan Pratama, NSW Health Pathology

POWH Cepheid GeneXpert



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?

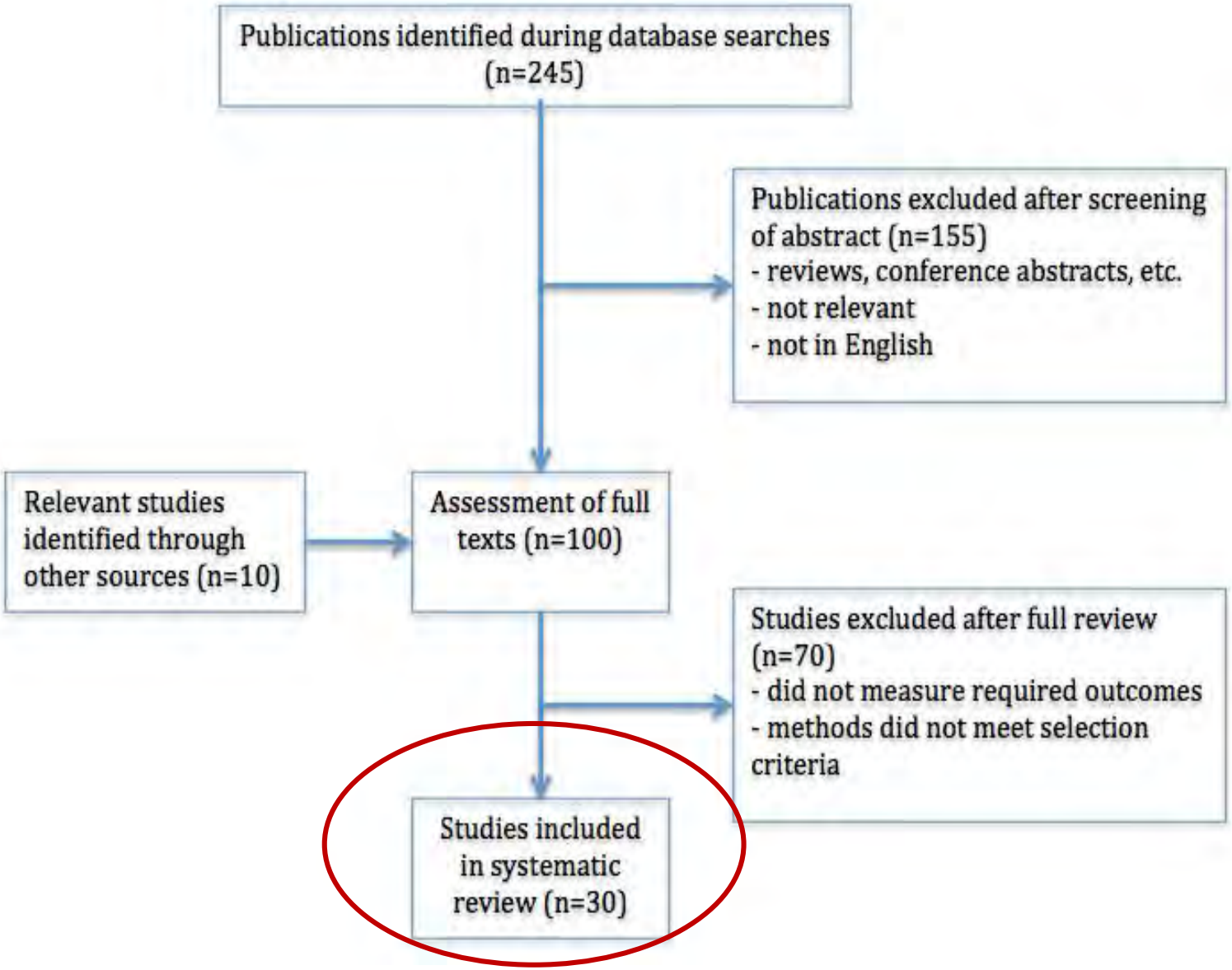
- Systematic review:
  i) antiviral prescription
  ii) antibiotic prescription
  iii) patient length of stay in the ED

- 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

↑ 12/14 (86%)

- Antibiotic prescription: 26 studies

↓ 20 / 26 (77%)

Egilmezer *et al.,* 2018, Reviews in Medical Virology, *provisionally accepted*

Studies using POCT – what are the real-world outcomes?

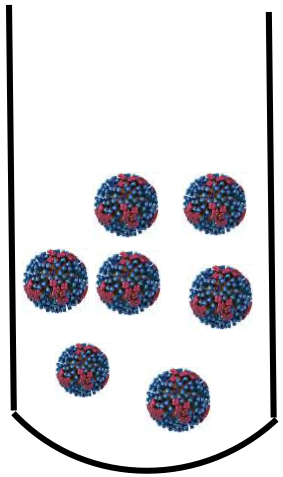
- Time spent in ED: 9 studies

  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)

NSSN
NSW Smart Sensing Network

→ Reduce overuse of antibiotics
→ antibiotic resistance

virology
diagnosis . research . teaching

Integrated Systems for Epidemic Response

UNSW AUSTRALIA

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

Images: Wikipedia

Developing New POCT

Published in final edited form as:
Anal Chem. 2015 August 4; 87(15): 7872–7879. doi:10.1021/acs.analchem.5b01594.

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

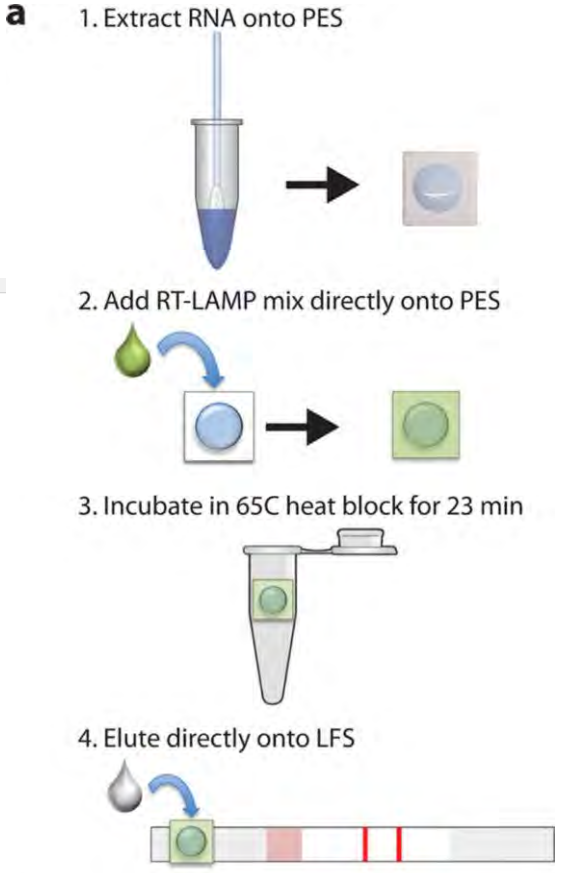
Natalia M. Rodriguez[†], **Jacqueline C. Linnes**[†], **Andy Fan**[†], **Courtney K. Ellenson**[†], **Nira R. Pollock**[‡], and **Catherine M. Klapperich**[†,*]

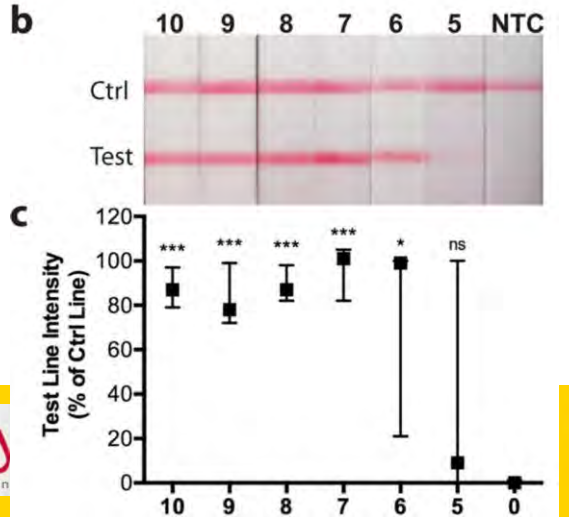
[†]Department of Biomedical Engineering, Boston University, Boston, Massachusetts 02215, United States

[‡]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 high-lighted 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

virology
diagnosis . research . teachin

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

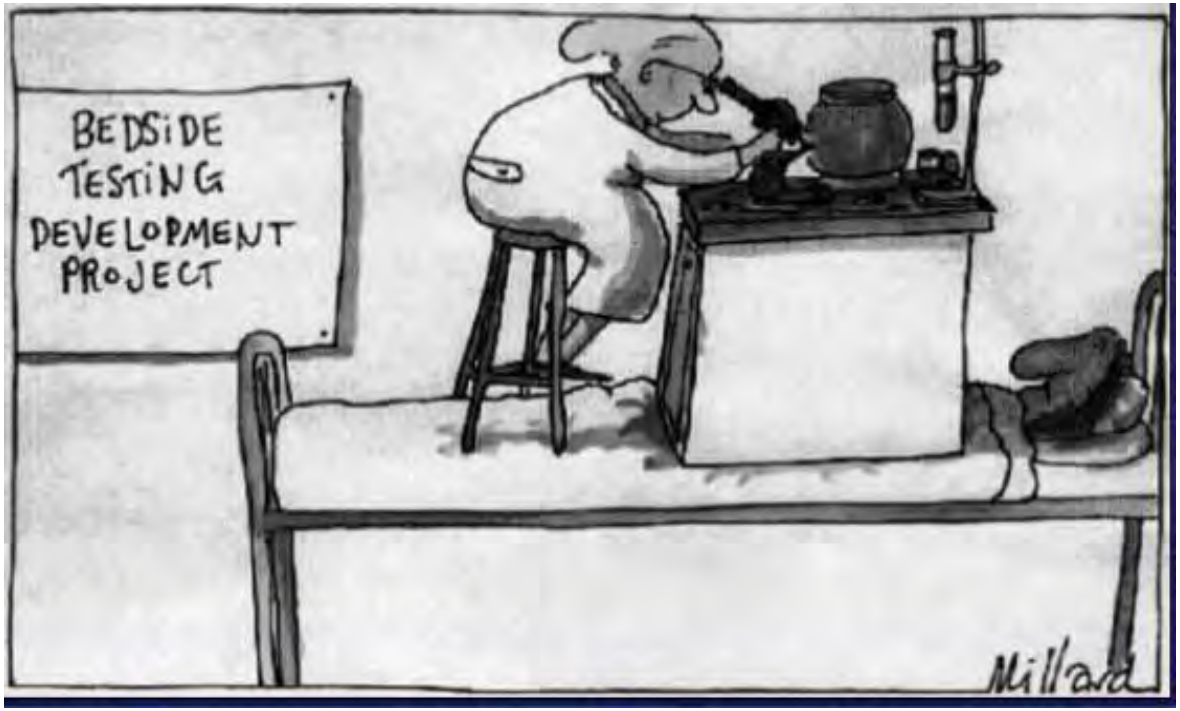
- Gregory Walker
- Ece Egilmezer

UNSW Chemistry

- Prof Justin Gooding
- Dr Padma Bakthavathsalam
- Danielle

Integrated Sciences

- Dylan Warby



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

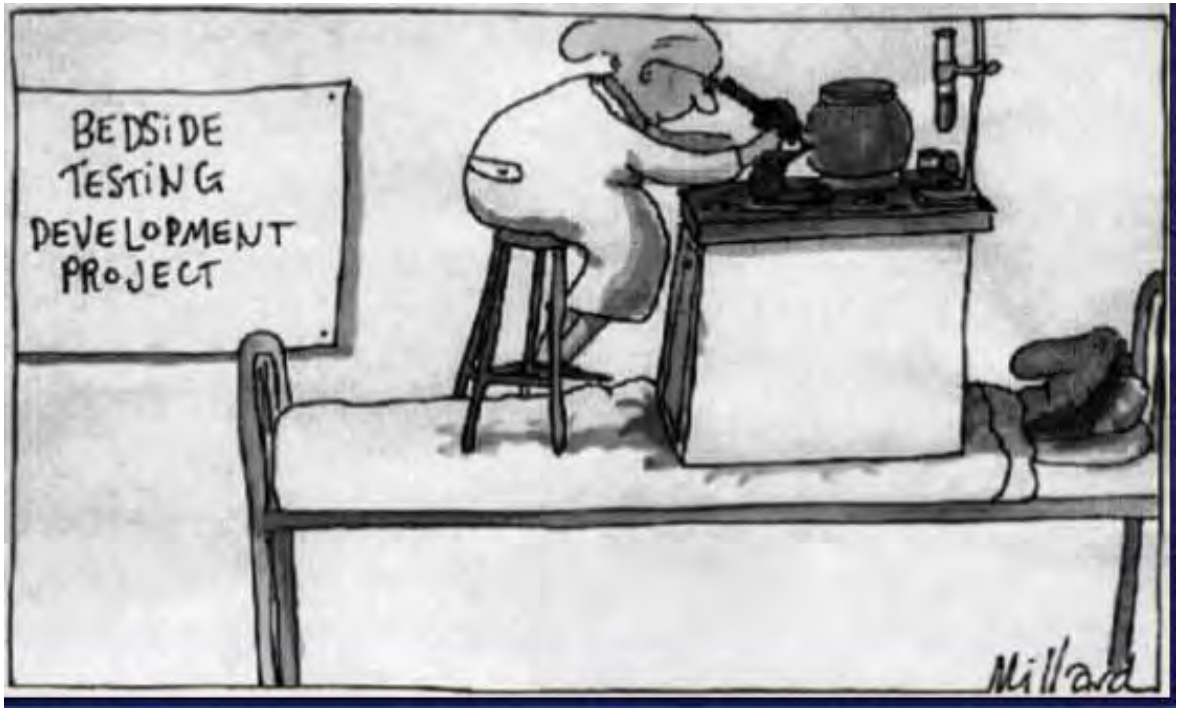
- Gregory Walker
- Ece Egilmezer

UNSW Chemistry

- Prof Justin Gooding
- Dr Padma Bakthavathsalam
- Danielle

Integrated Sciences

- Dylan Warby



Journals

Efficacy and Mechanism Evaluation

Health Services and Delivery Research

Health Technology Assessment

Programme Grants for Applied Research

Public Health Research

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

Nicholson K G, Abrams K R, Batham S, Medina M J, Warren F C, Barer M, Bermingham A, Clark T W, Latimer N, Fraser M, Perera N, Rajakumar K & Zambon M.

▶ 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)

Toolkit

Download report PDF

Print

Download report documents

Alerts & updates

Purchase hard copy

Responses to this report(0)

Permissions information

VIEW PROJECT

Share

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

Natalia M. Rodriguez[†], **Jacqueline C. Linnes**[†], **Andy Fan**[†], **Courtney K. Ellenson**[†], **Nira R. Pollock**[‡], and **Catherine M. Klapperich**[†,*]

[†]Department of Biomedical Engineering, Boston University, Boston, Massachusetts 02215, United States

[‡]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 high-lighted 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 negative rates. An accurate, sensitive, and specific molecular diagnostic that is also rapid, low-cost, and independent of laboratory infrastructure is needed for effective point-of-care detection and epidemiological control in these developing regions. We developed a paper-based assay that allows for the extraction and purification of RNA directly from human clinical nasopharyngeal specimens through a poly(ether sulfone) paper matrix, H1N1-specific *in situ* isothermal amplification directly within the same paper matrix, and immediate visual detection on lateral flow strips. The complete sample-to-answer assay can be performed at the point-of-care in just 45 min, without the need for expensive equipment or laboratory infrastructure, and it has a clinically relevant viral load detection limit of 10^6 copies/mL, offering a 10-fold improvement over current

GenePOC

Instrument

Characteristics

- **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)

PIE

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

Slide: Dylan Warby, Integrated Sciences

Quidel Quickvue

Study	Study Population	Sample type	Sensitivity	Specificity
Koul *et al*., 2015 Indian J Med Microbiol.	Adult and pediatric	600 N/T swabs	Flu A- 22.7% Flu B- 23.6%	Flu A-100% Flu B-100%
Lucas *et al*., 2011 Clin Infect Dis	Adult and pediatric	1538 nasal wash	Flu A- 15% $H1N1_{09}$-20% Flu B- 31%	Flu A- 99% $H1N1_{09}$- 99% Flu B- 99%
Velasco et al., 2010 J Clin Virol.	Adult and pediatric	360 nasal swabs	Flu A $H1N1_{09}$- 63%	Flu A $H1N1_{09}$ - 96%
Company Reported		Nasal swab	FluA – 94% Flu B – 70%	FluA – 90% Flu B – 97%