NIHR | Newcastle In Vitro Diagnostics Co-operative

NIHR Newcastle MIC Industry Showcase:

Roche RSV study

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The Newcastle upon Tyne Hospitals NHS
NHS Foundation Trust

THE great north CHILDREN'S HOSPITAL

CHILDREN'S RESPIRATORY GROUP CRG

Newcastle University
Institute of Cellular Medicine

Disclosures

- **Roche Diagnostics**
  - **Funding for investigator-led Newcastle NIHR DEC evaluation of POC RSV test (CI)**
  - **Honoraria to Newcastle University**
- Novartis
  - Honorarium to Newcastle University
- Pfizer
  - Funding for investigator-led community-acquired pneumonia study (CI)
- Boehringer Ingelheim and Vertex
  - Travel and accommodation for academic meetings
- Teva
  - Honoraria to Newcastle University

Overview

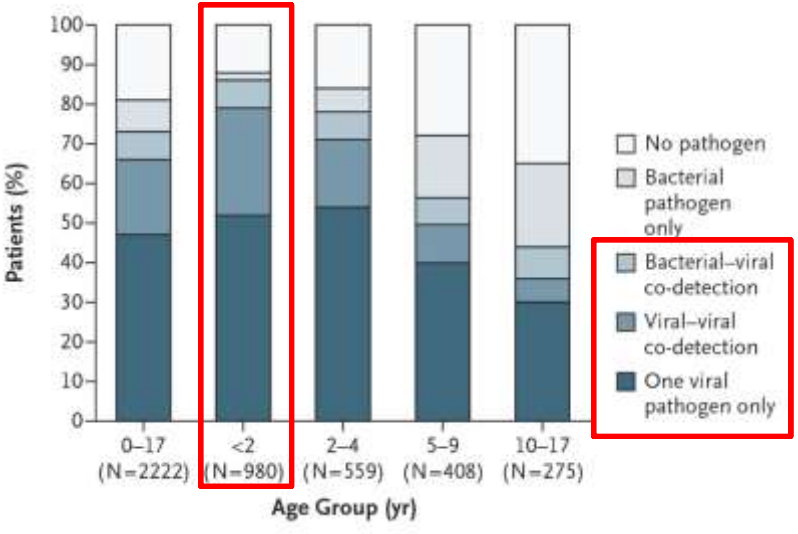
1. Clinical background – the problem
2. Why test for RSV and influenza?
3. Why use a Point of Care approach?
   - Evaluating a Point of Care test for RSV in a real-life NHS pediatric clinical setting using robust methodology
     - *the DEC-RSV study*
4. Summary
5. Reflections on the project

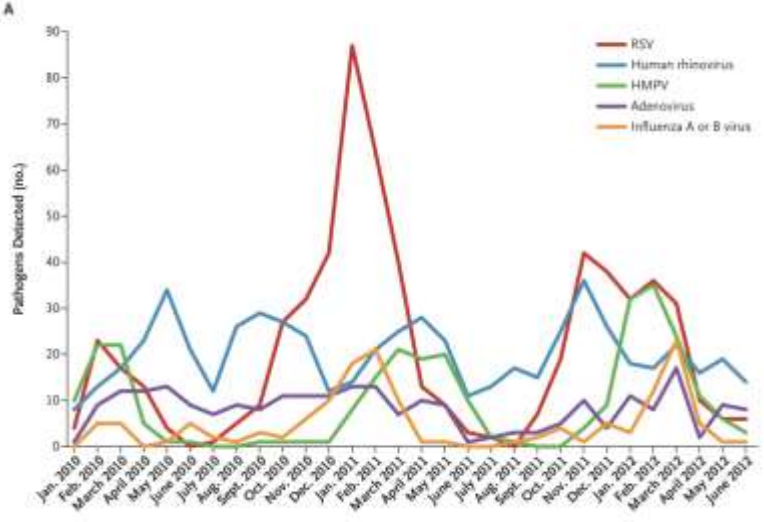
Paediatric respiratory medicine

http://www.scancrit.com/2012/01/27/snotty-children-anaesthesia/

Respiratory viruses in children

Community-Acquired Pneumonia Requiring Hospitalization among U.S. Children (large prospective study) Jain *et al.* N Engl J Med 2015; 372:835-845

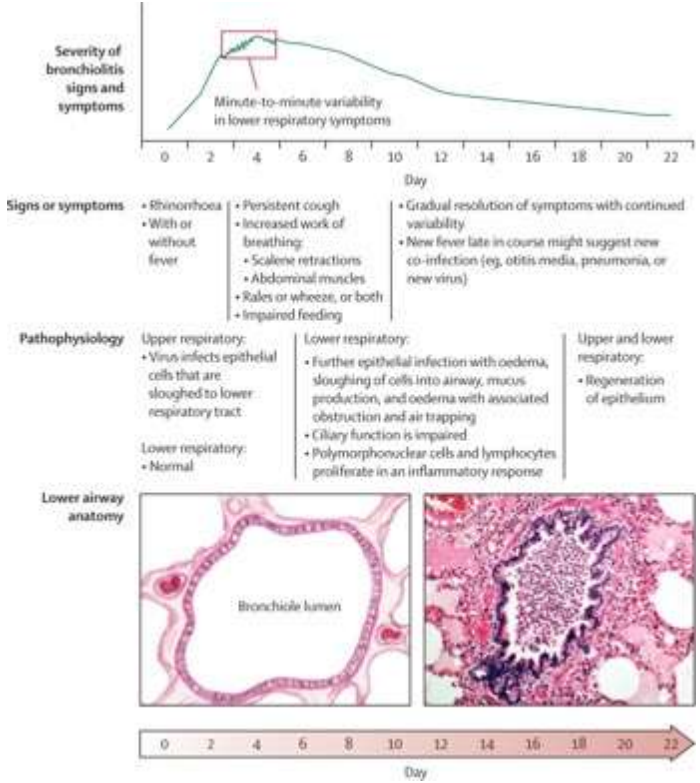




RSV bronchiolitis

- Annually RSV lower respiratory tract infection
  - 34 million children <5 years
  - 3.4 million hospital admissions
  - 200,000 deaths

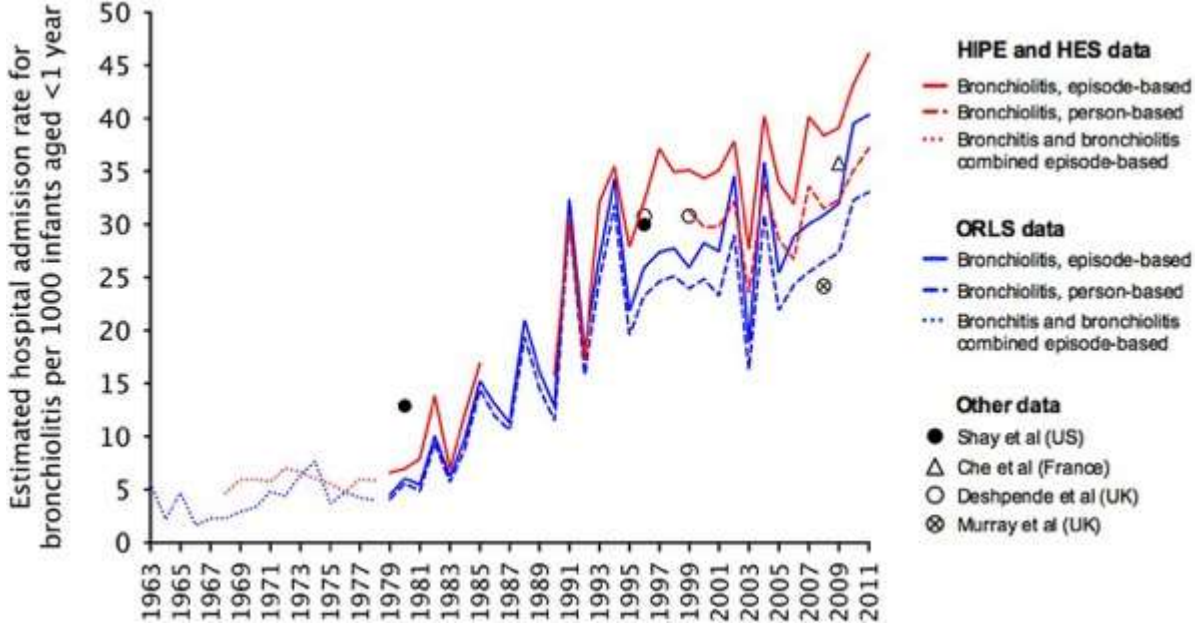
- In developed countries is the most common reason for admission to hospital in the first year of life



Florin *et al.* Viral bronchiolitis. *Lancet* 2016 http://dx.doi.org/10.1016/S0140-6736(16)30951-5

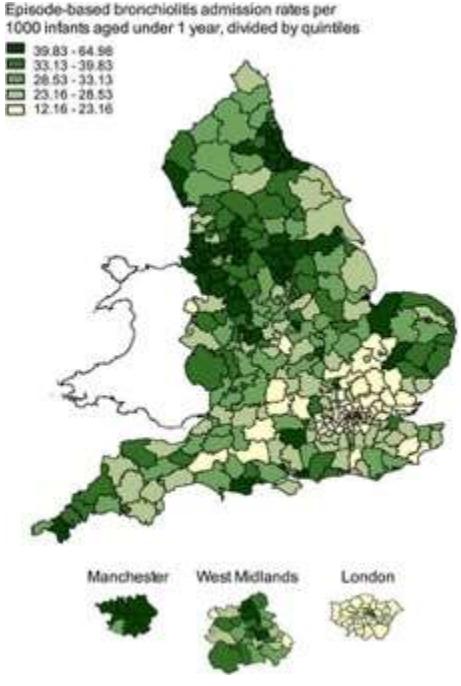
Increasing bronchiolitis admissions

Point estimates for the annual average episode and person-based hospital admission rate for bronchiolitis per 1000 infants aged <12 months from 1979 to 2011, episode-based combined acute bronchitis and bronchiolitis rates from 1965 to 1979 and bronchitis before 1965.



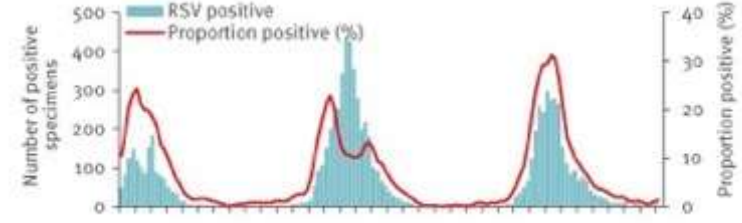
Christopher A Green et al. *Arch Dis Child*
doi:10.1136/archdischild-2015-308723

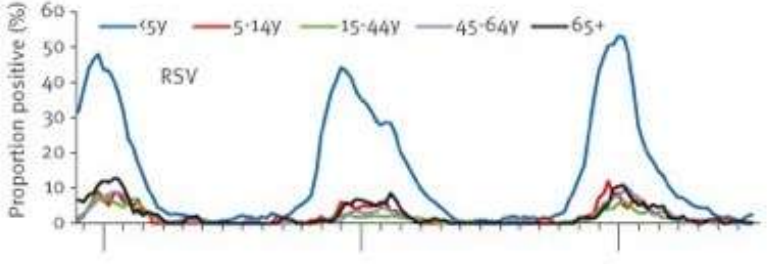
National and seasonal variation



National variation in person-based bronchiolitis hospital admission rates, 1999–2011.

Christopher A Green et al. *Arch Dis Child*
doi:10.1136/archdischild-2015-308723





http://www.diseasecast.com

Why test for RSV and influenza?

Allow targeted treatment

Epidemiology

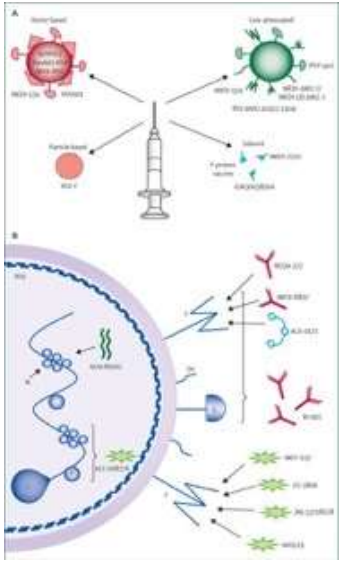
Avoid other investigations

Inform families and care givers

Infection control

Avoid unnecessary treatment

Prognosticate



Near future:

- Next generation anti-virals
- RSV vaccines

Mazur *et al.* Lower respiratory tract infection caused by respiratory syncytial virus: current management and new therapeutics. *Lancet Resp Med.* 2015;3:888-900

What the guidelines suggest

	NICE (UK), 2015*	AAP (USA), 2014*	CPS (Canada), 2014*	SIGN (Scotland), 2006*	Italy, 2014*	Spain, 2010*	Australia, 2008*	France, 2012*
Diagnostic testing								
Pulse oximetry	No mention about continuous vs intermittent checks should be performed in all children	Not recommended if supplemental oxygen is not required, or if oxyhaemoglobin saturation >90%	Not recommended unless high-risk patients in acute phase of disease; intermittent checks appropriate	Intermittent pulse oximetry should be performed on every child who presents to hospital	No mention	Intermittent pulse oximetry, no clear recommendation for continuous monitoring	No mention	No mention
Chest radiography	Not routinely recommended; consider when intensive care is proposed	Not routinely recommended; consider in severe disease requiring intensive care or signs of airway complication (eg, pneumothorax)	Not routinely recommended; consider when diagnosis is unclear, rate of improvement not as expected, or disease severity indicates other diagnoses	Not routinely recommended; consider with diagnostic uncertainty or atypical disease course	Not routinely recommended	Not routinely recommended; consider if diagnostic uncertainty, atypical presentation, severe disease, or progressive disease course	Not routinely recommended; might be warranted if diagnostic uncertainty, severe respiratory distress, or high risk for severe illness	Not routinely recommended; consider if asymmetrical breath sounds are found, diagnostic uncertainty, cardiac disease, chronic lung disease, and
Viral testing	No mention	Not routinely recommended	Not routinely recommended	Rapid respiratory syncytial virus testing recommended for admitted infants to guide cohorting	Respiratory syncytial virus antigen recommended in hospital setting for cohorting and potentially decreasing	Not routinely recommended; respiratory syncytial virus testing might assist with cohorting	Not routinely recommended; consider if diagnostic uncertainty or young febrile infants	Not routinely recommended

Florin *et al.* Viral bronchiolitis. *Lancet* 2016 http://dx.doi.org/10.1016/S0140-6736(16)30951-5

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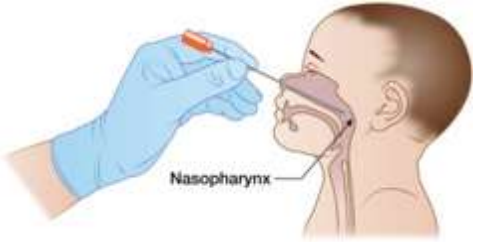
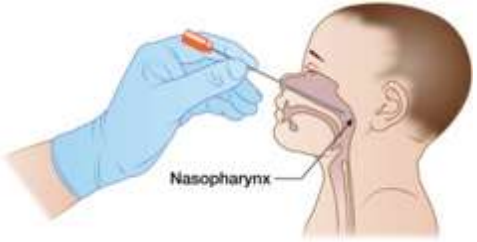
Current models of investigation



To lab

Time

Current models of investigation



To lab

PoC

Time

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- “Point Of Care”
- Validated for influenza A+B and Gp A Strep
- PCR-based test
- Time to result 15-20 mins

http://link.videoplatform.limelight.com/media/?mediaId=1c9fcd5b98e64c7f8d35ebc2c211ec1f&width=1026&height=576&autoplay=true&playerForm=HoverPlayer

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How to comprehensively evaluate point of care tests?

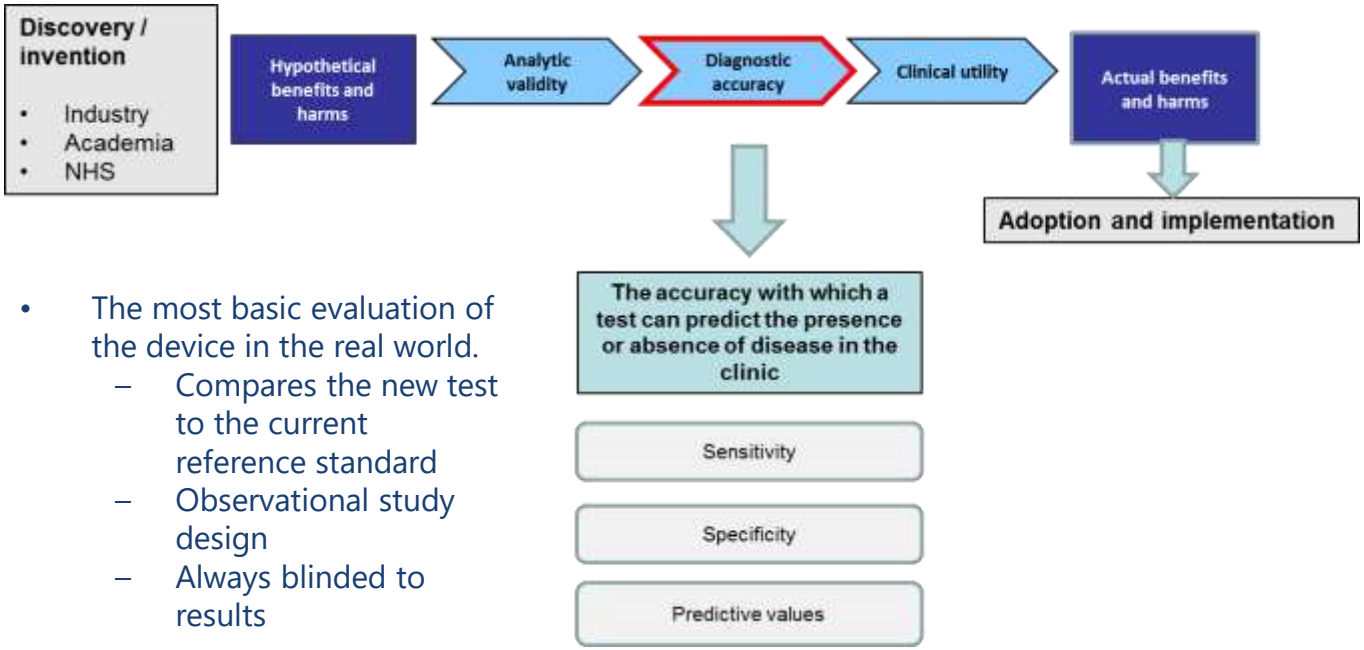
What are the MICs?

- 11 NIHR MICs across England established in January 2018, replacing the HTCs and DECs

- Some MICs focus on the development of new medical technologies (MedTech)

- Other MICs help to generate evidence and evaluate in vitro diagnostic tests

Diagnostic accuracy



- The most basic evaluation of the device in the real world.
  - Compares the new test to the current reference standard
  - Observational study design
  - Always blinded to results

The DEC-RSV study

The DEC-RSV study

Clinical diagnostic accuracy evaluation of the Respiratory Syncytial Virus (RSV) component of the Roche cobas Liat® system on paediatric patients presenting with an acute respiratory illness and possible RSV cause

Primary outcome measure: diagnostic accuracy of RSV component

Secondary outcome measures: time to result and modelling of the potential impact of the rapid test

Evaluate the test under standard UK NHS conditions

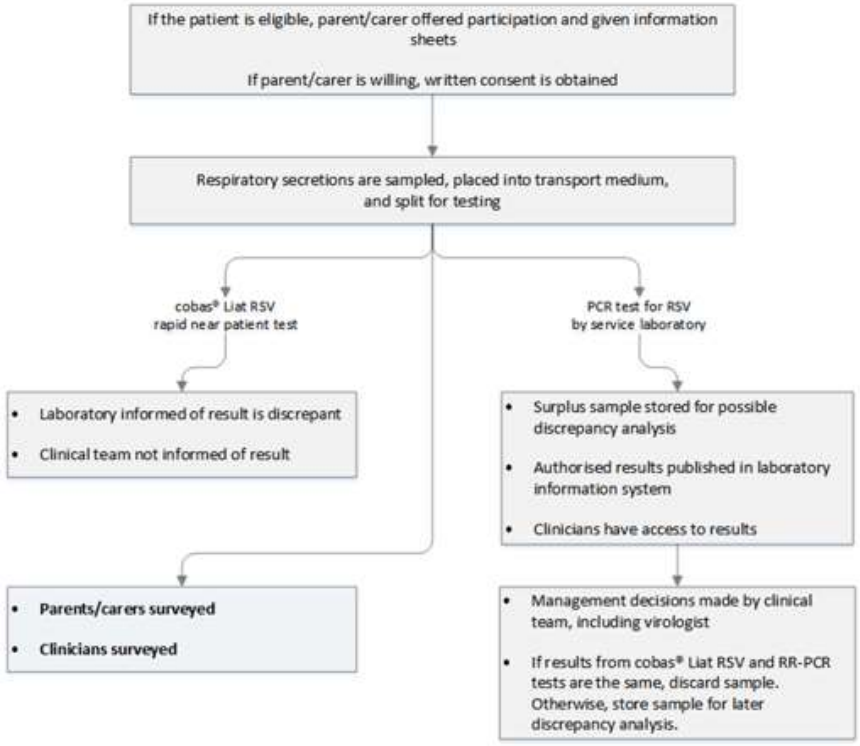
Study design

- **Population:**

  Children <2 years old that

  - Present with an acute respiratory illness AND
  - The attending clinicians consider that RSV infection is in the differential diagnosis

- **Comparator test(s):** Luminex® NxTAG respiratory pathogen panel OR Argene® respiratory panel

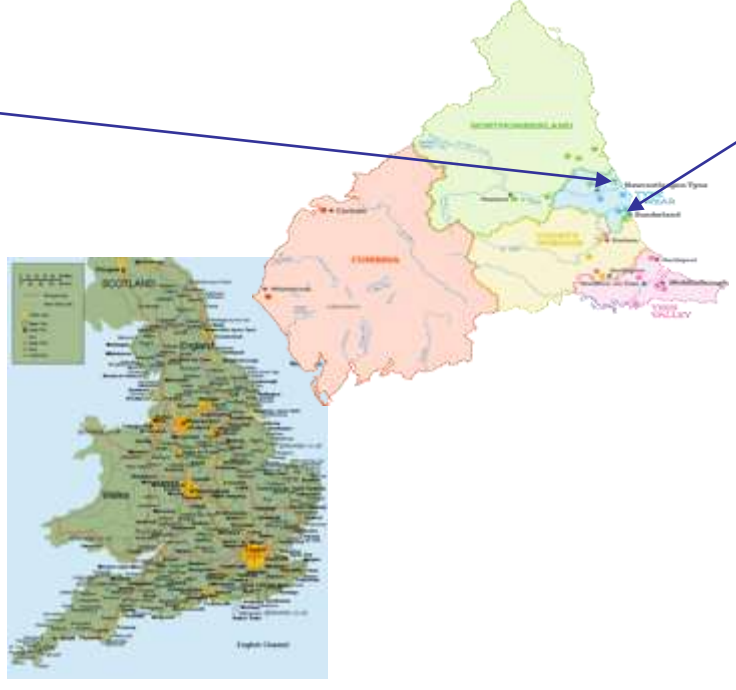


Sites

GNCH, Newcastle

Near by virology lab

Luminex



SRH, Sunderland

Offsite virology lab

Argene

Summary

- RSV is a common and major issue in paediatric medicine
- Roche cobas Liat® system for RSV
  - Excellent diagnostic accuracy
  - Improved time to result compared to laboratory-based testing
  - *[Publication in progress]*
- Healthcare professionals and families “like to have a diagnosis” but the results also enable infection control measures to be optimized and have the ability to aid with antimicrobial stewardship.
- Point of Care testing needs to be justified in each model of care terms of cost-benefit and actual impact on changes in clinical management

Reflections on the study

- Close working with Roche team throughout essential
  - Newcastle NIHR DEC/MIC offers a unique bespoke service
  - Offers experience and insight at the interface between industry/NHS/academia
  - More than just diagnostic accuracy – PPI, health economics, etc
- A large but enjoyable piece of work – impossible for me without the supporting team
  - Newcastle DEC
  - GNCH Research Unit
  - Sunderland team

Acknowledgements

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- Newcastle upon Tyne Hospitals NHS Trust Virology
  - Sheila Waugh

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