UNIVERSITY of OTAGO

Te Whare Wānanga o Otāgo

Using linked health data to better understand the causes of acute rheumatic fever and other post-streptococcal diseases

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Outline

- **Group A Streptococcus (GAS) infections**
- **Post-streptococcal autoimmune sequelae**
- **Methods**
- **Results - Sequelae of:**
  - GAS+ve throat swabs
  - GAS+ve skin swabs
  - Hospitalisations for streptococcal infections
- **Conclusions / Implications**
- **Limitations / Further work**

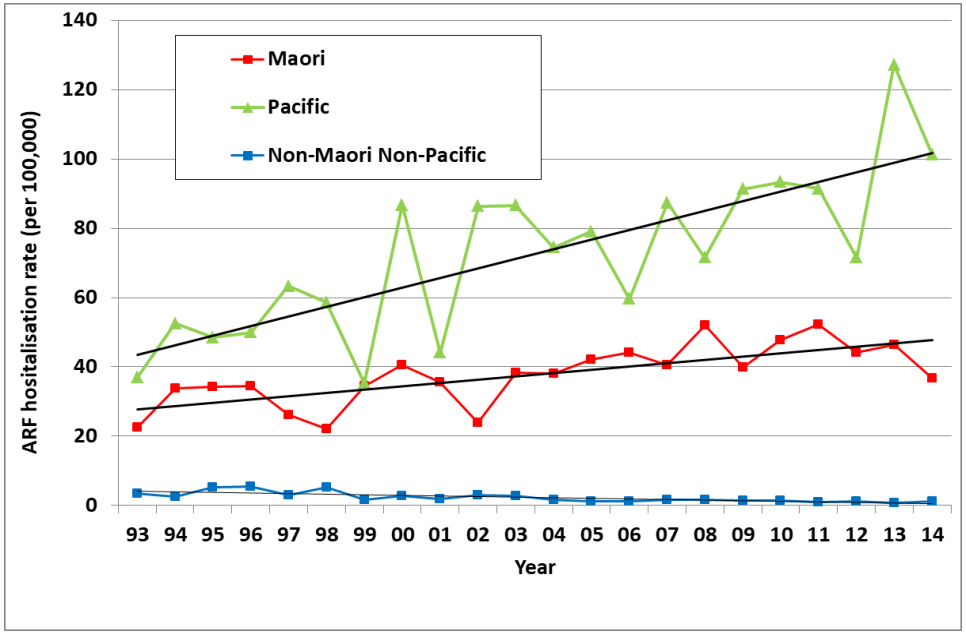
Background

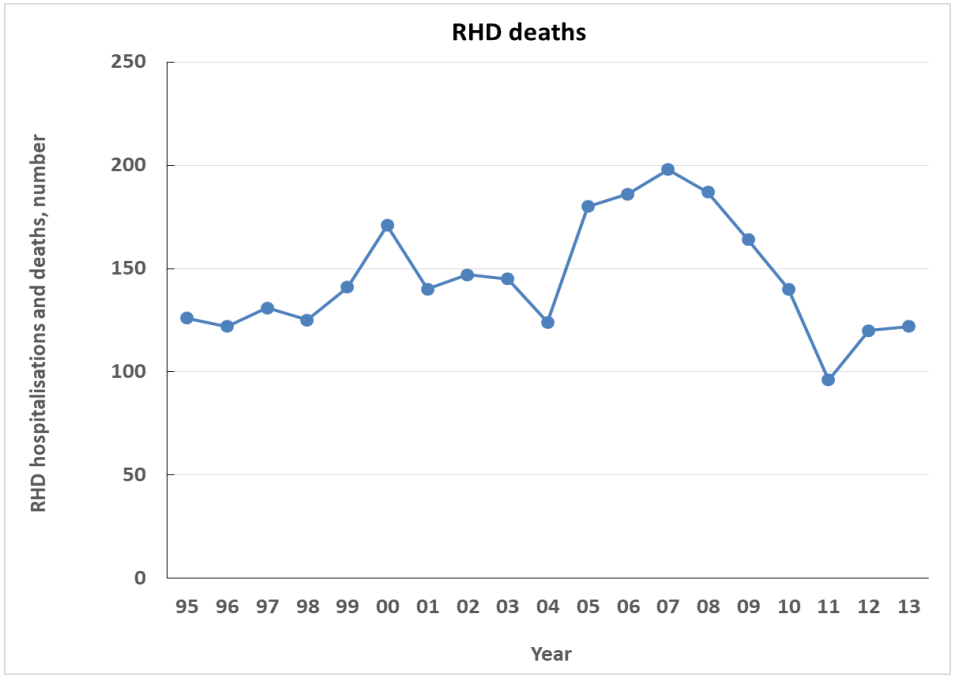
Group A Streptococcus (GAS):

- **Superficial infection**
  - **Pharyngitis**
  - **Impetigo, Pyoderma**
- **Invasive diseases**
  - **Septicaemia, Pneumonia, Osteomyelitis…**
  - **Necrotising fasciitis**
- **Toxin mediated diseases**
  - **Scarlet fever**
  - **Streptococcal toxic shock syndrome**
- **Post-streptococcal autoimmune sequelae**
  - **Acute Rheumatic Fever (ARF) → Rheumatic Heart Disease (RHD)**
  - **Acute Post-streptococcal glomerulonephritis (APSGN)**

Background

- RHD is one of NZs biggest ID killers (~140 deaths pa)
- Large cause of health iniquities with most ARF/RHD cases in Maori and Pacific





Background

Conventional wisdom

GAS (Strep) sore throat

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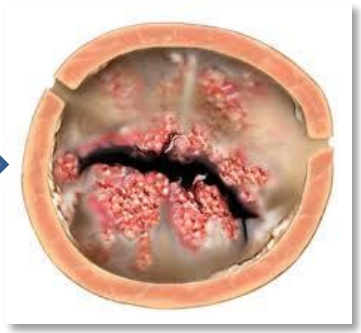
Acute Rheumatic fever (ARF)



Rheumatic heart disease (RHD)

GAS skin infection eg Impetigo

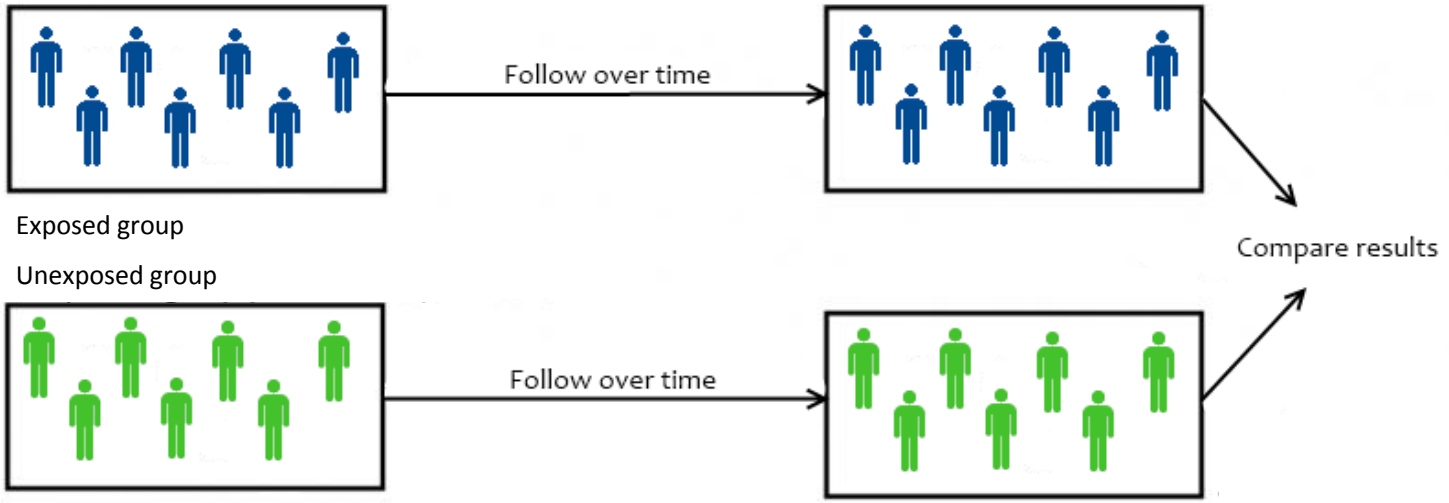
Acute Post Streptococcal Glomerulonephritis (APSGN)

Methods

- **GAS exposure data sources**
  - Laboratory throat swab and skin swab test data, community labs (Labtests), Auckland Region (pop= 1.5 million), 2009-2016
  - Hospitalisations for specific clinical conditions (eg Strep pharyngitis, skin infections) NZ (pop=4.5 million), 2001-15
- **Disease outcome data sources**
  - Hospitalisation data on first admissions for ARF (ICD.10 I00, I01, I02) APSGN (ICD.10 N00, N05)
  - Linked to exposure using unique patient number (encrypted NHI)

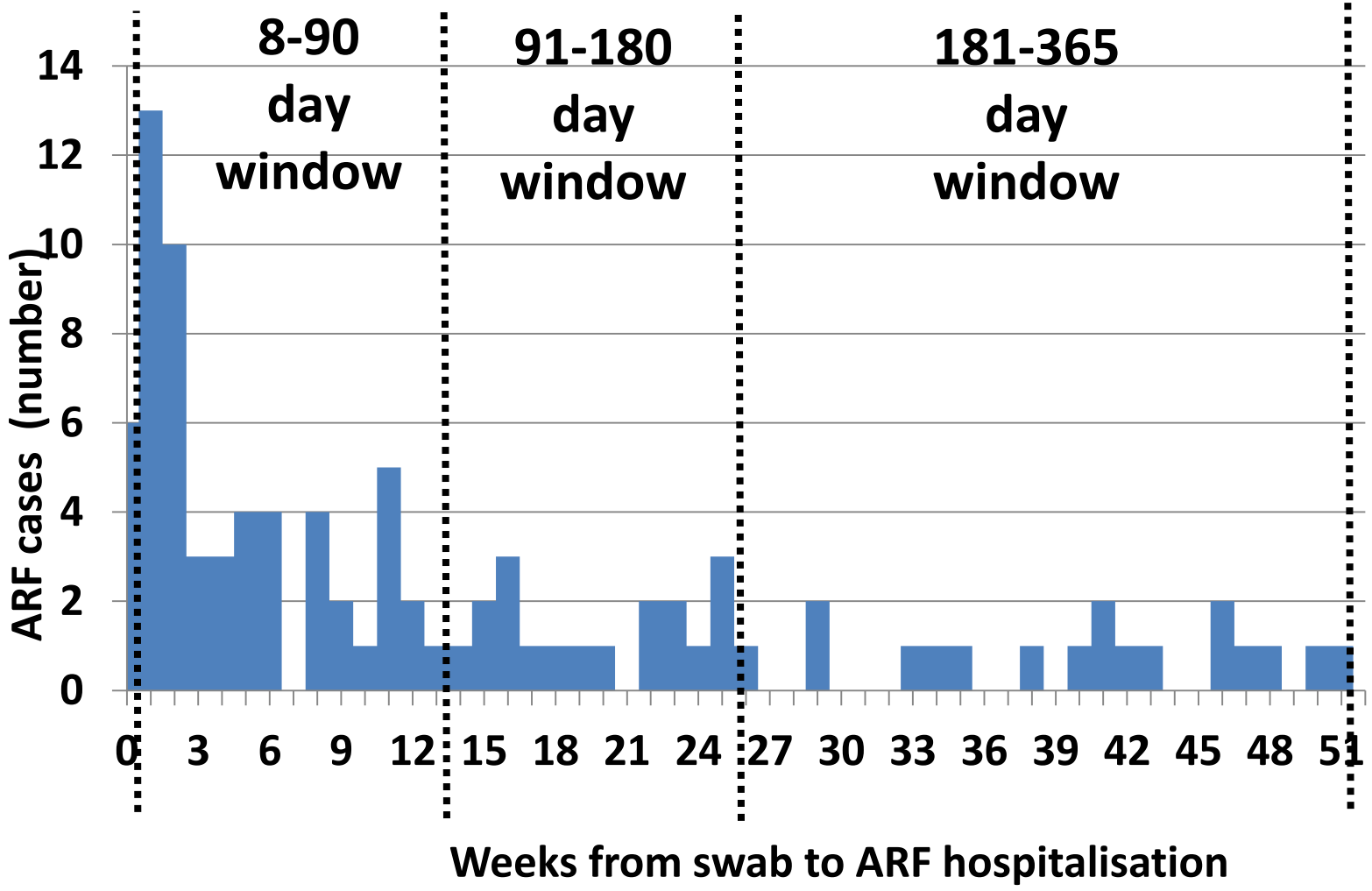
Methods

- **Analytic method**
  - Calculation of disease rates in cohorts:
    - Exposed (test +ve) vs. unexposed (test –ve)
    - Exposed (following hosp for Strep. disease) vs. Unexposed (same population 12 months later ie case-cross over design)
  - RR and 95%CI across cohorts, stratified by time intervals and other characteristics



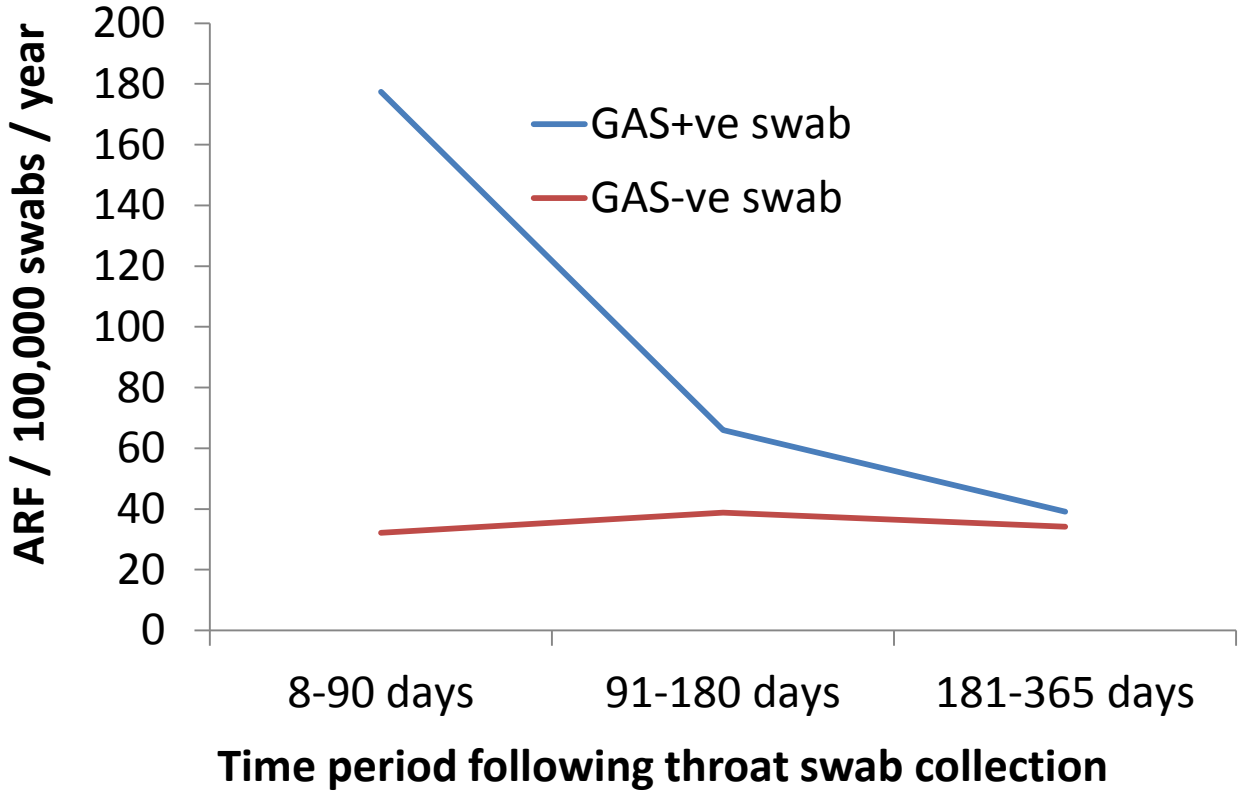
Methods - Time window

ARF (N=165 cases) incidence by week, following GAS+ve throat swab test results, Auckland 2009-16



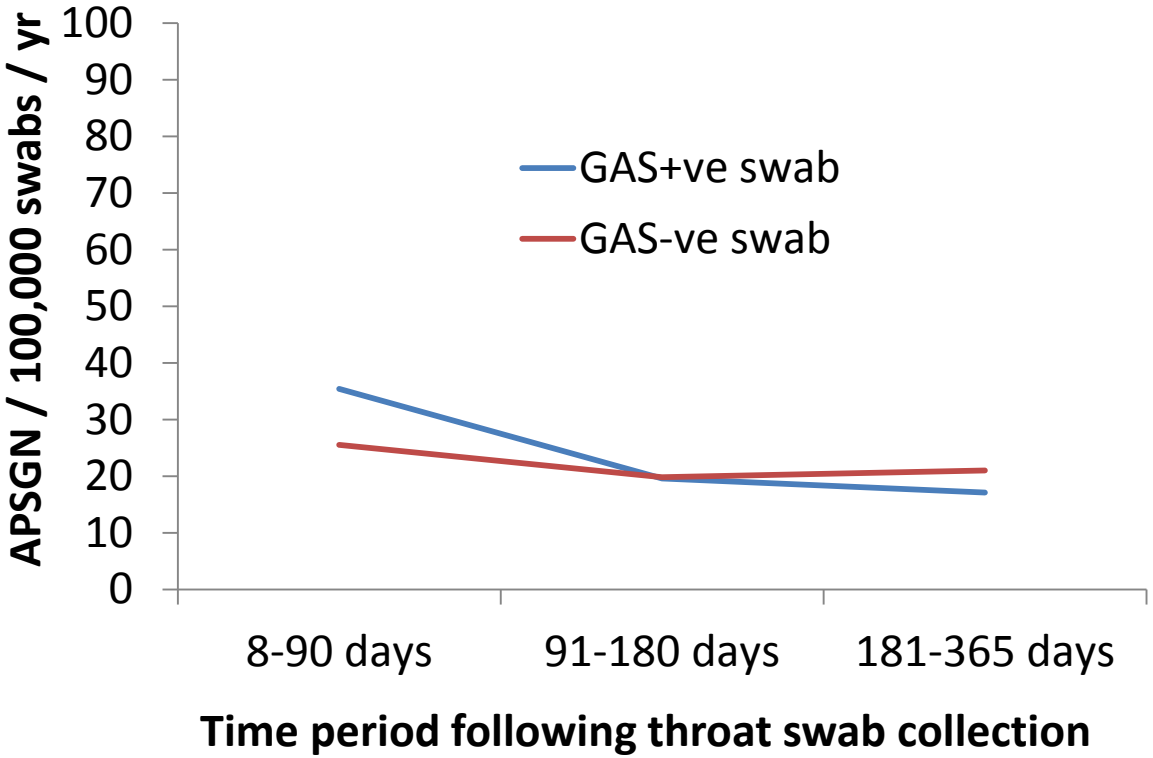
Results - ARF following GAS +ve throat swab

- ARF cases (N=155) in 365 days following GAS+ve throat swabs vs. risk ARF (N=378) following GAS & Group C/G -ve throat swabs
- All ages, 8-90 days, **RR elevated significantly**
  - Total 5-19 years, 8-90 days, **RR elevated significantly**
  - Māori 5-19 years, 8-90 days, **RR elevated significantly**
  - Pacific 5-19 years, 8-90 days, **RR elevated significantly**



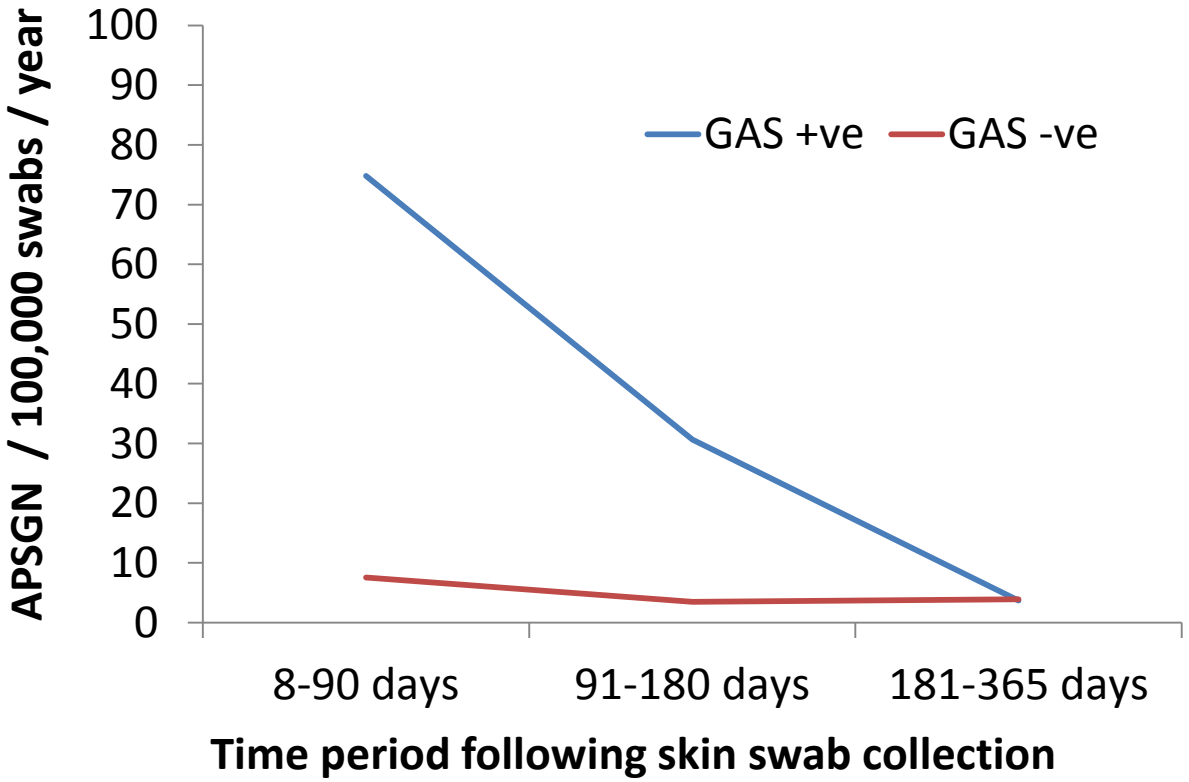
Results - APSGN following GAS+ve throat swab

- APSGN cases (N= 44) in 365 days following GAS+ve throat swabs vs. risk APSGN (N=233) following GAS & Group C/G -ve throat swabs
- All ages, 8-90 days, RR no significant effect
  - Total 5-19 years, 8-90 days, RR no significant effect
  - Māori 5-19 years, 8-90 days, RR no significant effect
  - Pacific 5-19 years, 8-90 days, RR no significant effect



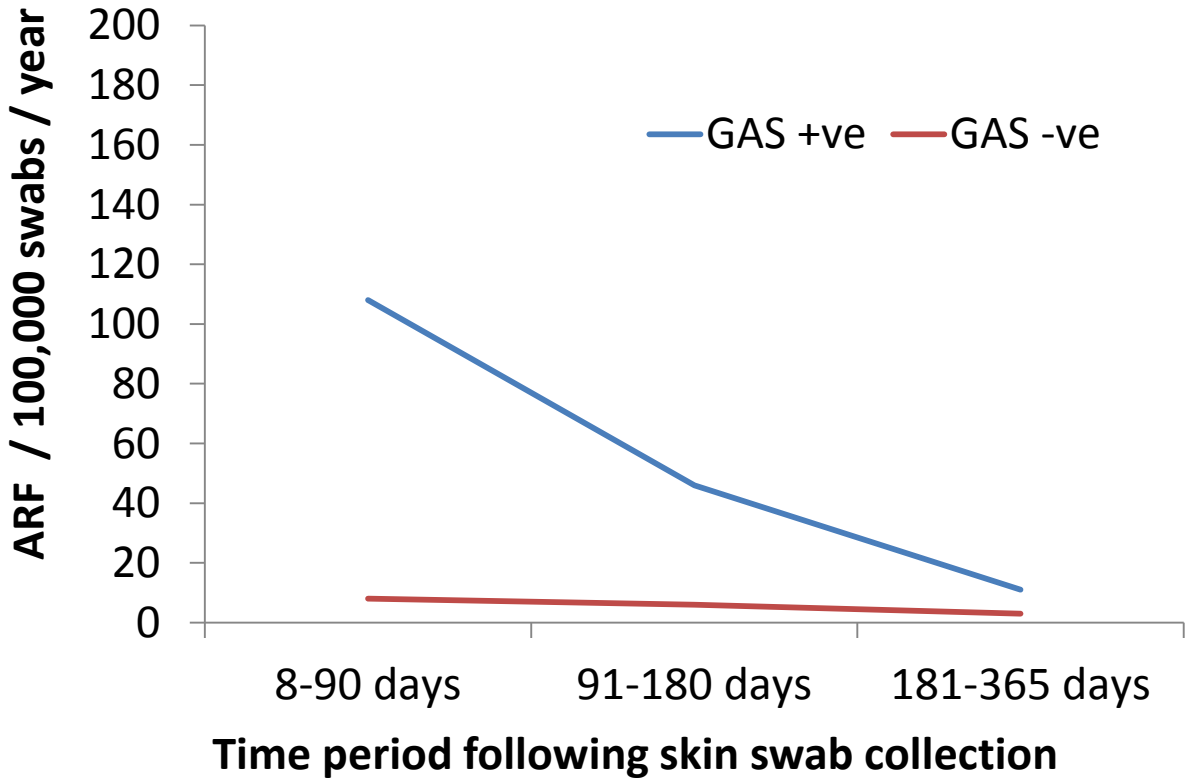
Results - APSGN following GAS +ve skin swab

- APSGN cases (N=18) in 365 days following GAS +ve skin swabs vs. risk APSGN (N=17) following GAS & Group C/G -ve skin swabs
- All ages, 8-90 days, **RR elevated significantly**
  - Total 5-19y olds, 8-90 days: **RR elevated significantly**
  - Māori 5-19y olds, 8-90 days: RR elevated, CI overlaps 1.00
  - Pacific 5-19y olds, 8-90 days: RR elevated, CI overlaps 1.00



Results - ARF following GAS +ve skin swab

- ARF cases (N= 23) in 365 days following GAS +ve skin swab vs. risk ARF (N= 18) following GAS & Group C/G -ve skin swabs
- All ages, 8-90 days, **RR elevated significantly**
  - Total 5-19y olds, 8-90 days: **RR elevated significantly**
  - Māori 5-19y olds, 8-90 days: RR elevated, CI overlaps 1.00
  - Pacific 5-19y olds, 8-90 days: RR elevated, CI overlaps 1.00



Results - ARF risk following hospitalisations for potentially causal infections

Hosp condition	Hosp admits[1]	ARF 8-90 days (N)	ARF 366-731 days (N)	RR (95%CI)
Strep pharyngitis & tonsillitis	4 657	4	0	NC
Skin infection	20 955	8	15	**Elevated significantly**
IDs (total)	100 814	61	51	**Elevated significantly**

[1] Māori and Pacific aged 5-19 years, admitted 2001-15

[2] Rate of subsequent initial ARF per 100,000 person years, two time periods: 8-90 days, and 366-731 days (baseline)

Results - APSGN risk following hospitalisations for potentially causal infections

Hosp condition	Hosp admits[1]	APSGN 8-90 days (N)	APSGN 366-731 days (N)	RR (95%CI)
Strep pharyngitis & tonsillitis	4 657	2	0	NC
Skin infection	20 955	4	5	**Elevated significantly**
IDs (total)	100 814	25	32	**Elevated significantly**

[1] Māori and Pacific aged 5-19 years, admitted 2001-15

[2] Rate of subsequent initial ARF per 100,000 person years, two time periods: 8-90 days, and 366-731 days (baseline)

Conclusions and Implications

Conventional wisdom

GAS (Strep) sore throat

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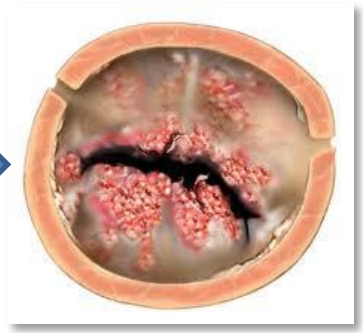
Acute Rheumatic fever (ARF)



Rheumatic heart disease (RHD)

GAS skin infection eg Impetigo

Acute Post Streptococcal Glomerulonephritis (APSGN)

Conclusions and Implications

- Risk of **ARF** is markedly elevated in 90 days following a **GAS+ve throat swab and GAS+ve skin swab** (and following related hospitalisations)
- Risk of ARF not significantly elevated following Group C/G+ve throat swab (small numbers)
- Risk of APSGN is markedly elevated following a GAS+ve skin swab (but not GAS+ve throat swab)
- **⇒ Support for treatment of GAS+ve skin infections as part of ARF** (and APSGN) **prevention programmes**

Children participating in RF prevention programme

Limitations and further work

(1) GAS exposure effects reduced by antibiotic use

→ Study of GP cases with linked antibiotic data to measure risk in treated and untreated cohorts

(2) Limits of observational data

→ Study of immune response to GAS throat and skin infections (HRC funded project underway)

Treating Group A streptococcal sore throats (based on 2014 Heart Foundation guidelines)

First line treatment	
Amoxicillin orally for 10 days	< 30 kg: 750 mg daily ≥ 30 kg: 1000 mg
Benzathine penicillin G, intramuscular injection, single dose	< 30 kg: 450 mg (600,000 Units ≥ 30 kg: 900 mg (1,200,000 Units)
Definite or possible anaphylaxis to penicillin or amoxicillin	
Erythromycin ethyl succinate orally for 10 days	40 mg/kg/day in 2 – 3 doses

Note:

- Decrease in maximum dose of amoxicillin from 1500mg to 1000mg
- Maximum dose for erythromycin ethyl succinate – 3200 mg (Medsafe datasheet) to 4000 mg (New Zealand Paediatric Formulary)

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Labtests