Invasive Group A Streptococcal Disease (iGAS) update

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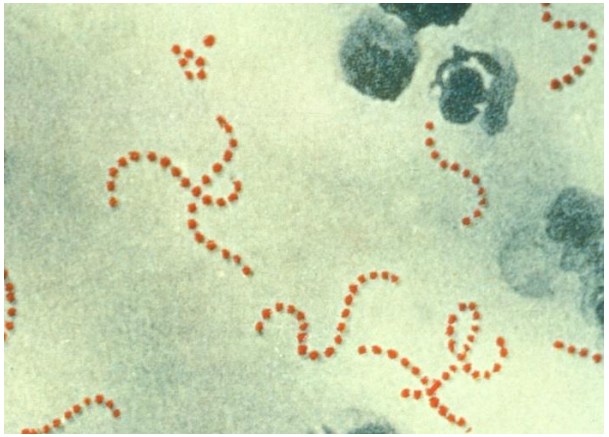
Overview

- Aetiology, clinical manifestations
- Complications
- Transmission
- Epidemiology
- Public health response
- Prevention and management in primary care

Aetiology, clinical manifestations

Group A streptococcus

- Streptococcus pyogenes
- Gram-positive cocci
- Penicillin sensitive



Disease

- Non-invasive: tonsillitis/pharyngitis (strep throat), impetigo, cellulitis, scarlet fever
- Invasive (iGAS): bacteraemia, necrotising fasciitis, streptococcal toxic shock syndrome, maternal sepsis, meningitis, bone/joint infections, pneumonia

Clinical presentation of invasive infections

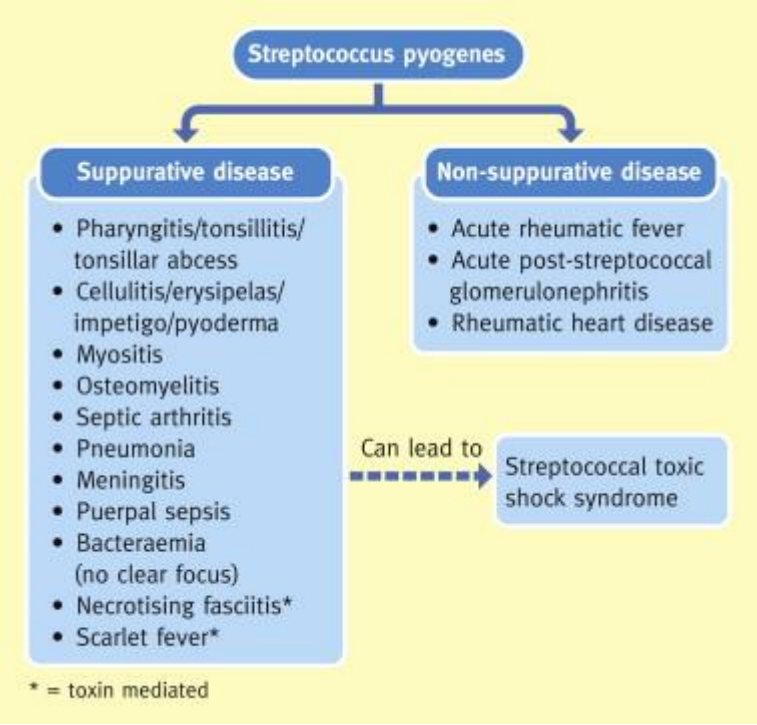
Vary depending on the site of infection, often non-specific:

- Fever, chills, dizziness, shortness of breath, chest pain, headache, neck stiffness, nausea, vomiting, red/warm/painful/rapidly spreading skin infection which may have pus or ulceration, abdo pain/bleeding/purulent vaginal discharge in maternal sepsis.

In children, often non-specific and difficult to distinguish from a viral infection

- Fever, erythematous rash, cold or mottled limbs, limb pain, not wanting to walk, poor feeding, abdominal pain, vomiting, lethargy, throat infection, chest infection, oliguria.

Complications of Group A Strep Infection



REVISED JONES CRITERIA

2002-2003 WHO Criteria for the Diagnosis of RF and RHD

MAJOR MANIFESTATIONS:

- **Carditis**
- **Polyarthritis**
- **Chorea**
- **Erythema Marginatum**
- **Subcutaneous Nodules**

MINOR MANIFESTATIONS:

- **Clinical: fever, polyarthralgia**
- **Labs: elevated ESR, C-reactive protein (Acute Phase Reactants)**
- **ECG: prolonged P-R interval**

SUPPORTING EVIDENCE OF A PRECEDING STREPTOCOCCAL INFECTION W/IN THE LAST 45 DAYS:

- **Elevated or rising anti-streptolysin O or other streptococcal antibody, *or***
- **(+) Throat culture, *or***
- **Rapid antigen test for group A streptococcus**

Harrison's Principles of Internal Medicine, 17th ed.

Transmission

Person to person

- Respiratory droplets, skin contact, fomites
- Colonises throat, skin, genital and rectal mucosa
- Transmission from carriers can occur
- Infection occurs via respiratory tract or broken skin

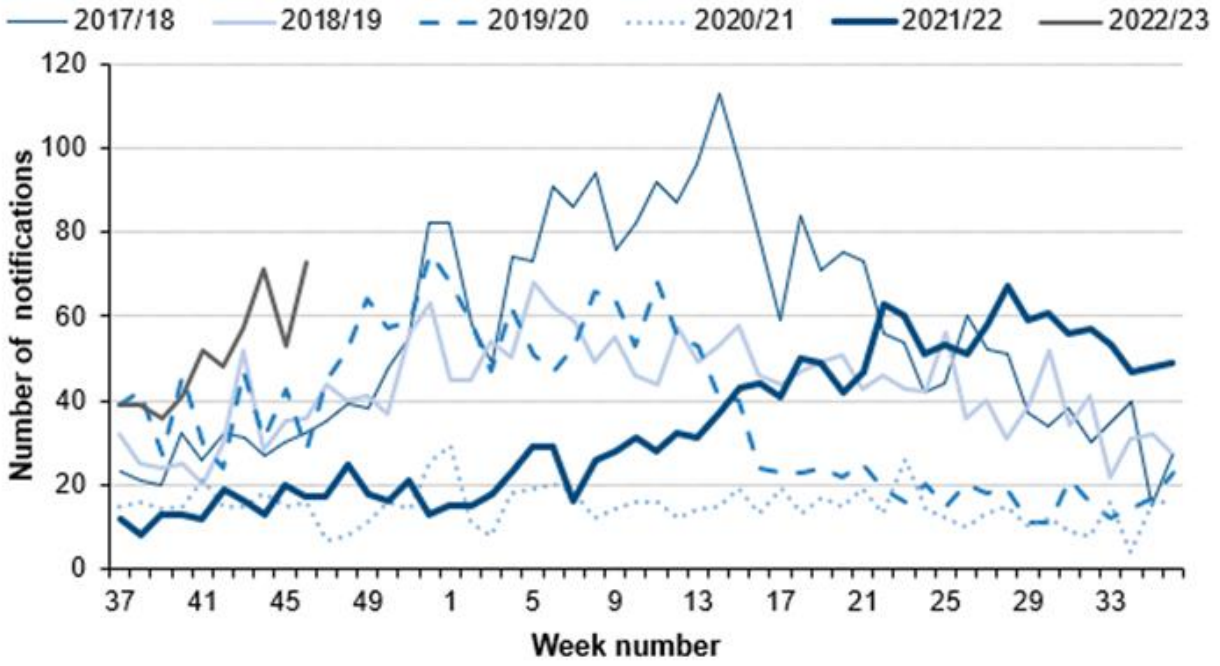
- Infectious: from ~7 days prior to symptoms until ~24hr after commencing antibiotics
- Incubation: typically 1-4 days. Occasionally prolonged (up to 30 days).

iGAS epidemiology - Risk factors

- Household contacts
- Age >65 or <5 years
- Aboriginal and/or Torres Strait Islander people, people from the Pacific Islands
- Injecting drugs
- Homelessness or overcrowding
- Chronic disease
- Immunocompromise
- Pregnancy and post-partum state
- Acute viral infection in children (influenza, other respiratory viruses, varicella).

iGAS epidemiology - UK

Weekly lab iGAS notifications by season



iGAS – Global Picture

Global Incidence over double the usual incidence

- Multiple European countries (France, Netherlands, Ireland, Sweden, UK) and USA have seen an increase in cases in the second half of 2022
- Associated with a significant increase in the number of deaths

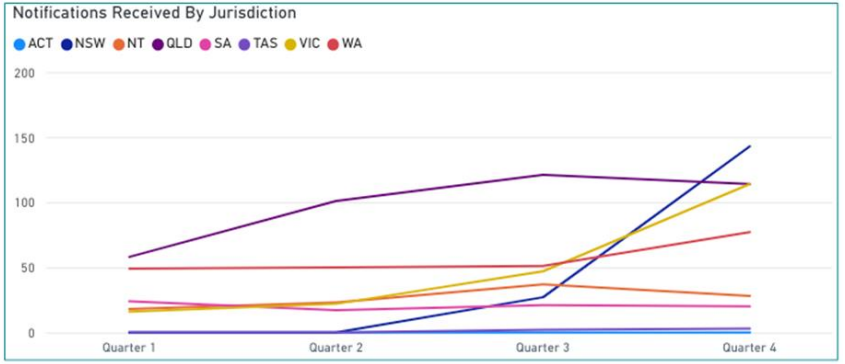
Predominately affecting:

- Adults > 50 years
- Children aged 10 years and younger
- Coincided with an increase in RSV and influenza circulation and incidence of scarlet fever GP consultations

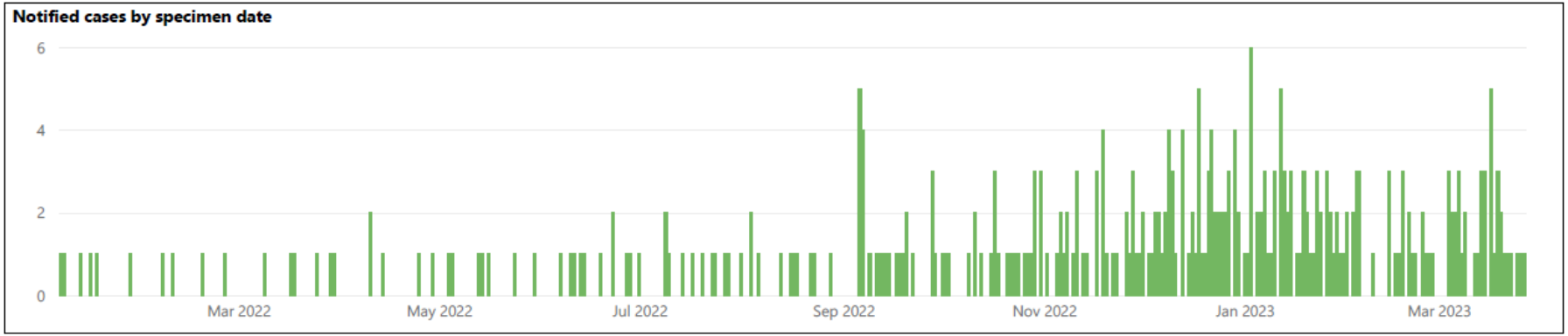
iGAS – Australian / Local Epidemiology

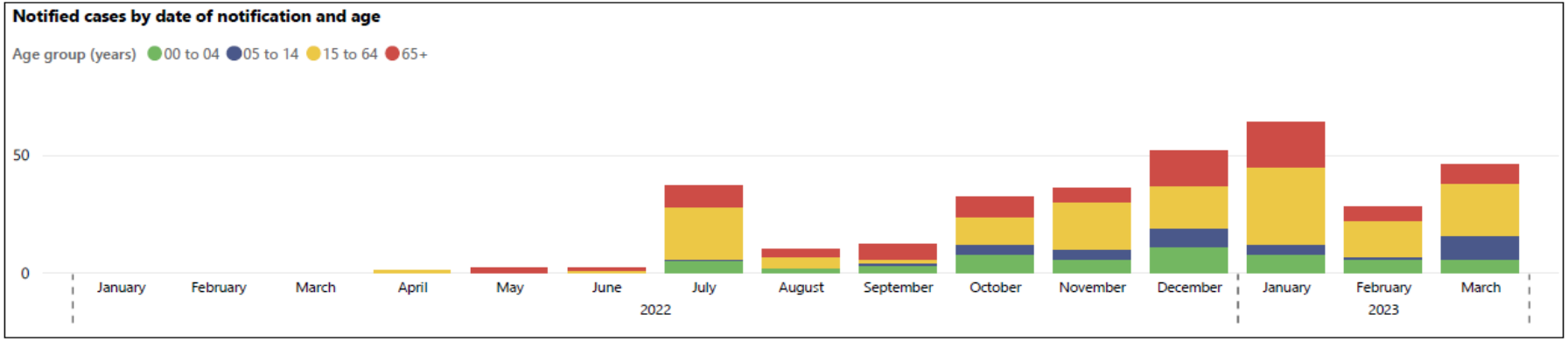
- Disproportionate impact of the disease among Aboriginal and Torres Strait Islander peoples
- NT: 2011 – 2021 – 74% of iGAS notifications
- Notification of iGAS cases by laboratories was made mandatory nationally from July 2021

- 2022: 184 notifications of iGAS were reported in Victoria
- 1 Jan – 9 Mar 2023: 101 notifications in Victoria
- Some severe paediatric cases



iGAS epidemiology - Victoria





Hypotheses for increased trend

- Co-circulation of winter viruses (e.g. RSV, influenza)
- Reduced GAS exposure during pandemic → reduced accrual of natural immunity → increased susceptibility
- Seasonal increase?
- More virulent strains?

iGAS treatment

- Requires hospital admission
- Sepsis management
  - Rapid fluid resuscitation / vasopressor support
  - Intravenous antibiotics
    - Penicillin is drug of choice (usually IV benzyl penicillin)
    - Cefazolin IV is used if immediate non-severe or delayed non-severe hypersensitivity to penicillins
    - Vancomycin IV is used if immediate severe or delayed severe hypersensitivity to betalactams
    - **PLUS clindamycin** to stop inhibit production, suppression of penicillin-binding proteins and long-term post-dose effects
- Surgical debridement may be critical
- Close monitoring

Image: A Melbourne child in ICU with iGAS, 6 hours after first presenting with symptoms

Public health response

- iGAS is a “routine” notifiable condition in Victoria – laboratories required to notify within 5 working days.
- National guideline for public health management (SoNG) under development through CDNA.
- The Department has commenced enhanced data collection for iGAS notifications.
- Intent for iGAS to become “urgent” and both doctor and lab notifiable
- Clinical Practice Guidelines : Invasive group A streptococcal infections: management of household contacts (rch.org.au)

Recommendations for clinicians (1)

- Consider strep throat or scarlet fever in children presenting with sore throat +/- rash.
    - Collect throat swab and commence empiric antibiotics if indicated (see RCH “sore throat” guideline) https://www.rch.org.au/clinicalguide/guideline_index/Sore_throat/
- Exclude children with strep throat or scarlet fever from school/childcare until recovered and treated with antibiotics for >24hr.
- Encourage seasonal influenza immunisation, especially for children.
- Advise parents/guardians of children presenting with suspected viral illnesses to be alert to the signs and symptoms of serious bacterial infection and when to seek immediate medical care.

Prescribing decisions in the setting of antimicrobial stewardship

Sore Throat Guideline:

- Only scarlet-fever type rash discriminates between GAS and viral aetiologies
- Viral illness is the most common cause of sore throat
- GAS rare under age 4
- Antibiotics recommended for high-risk gps: ATSI people, Maori and Pacific Islander people, history of RF or RHD, FHx of RF or RHD, immunosuppressedT

Red Flags in Primary Care

- Unwell/toxic appearance
- Respiratory distress
- Stridor
- Trismus
- Drooling
- “Hot potato” voice (muffled voice associated with pharyngeal/peritonsillar pathology)
- Torticollis
- Neck stiffness/fullness
- Inability to swallow (from Centor)

Refer to hospital

Centor Score for Strep pharyngitis

- Age 3-14
- Fever (>38 degrees)
- Tonsillar exudate
- Tender, enlarged, anterior cervical lymph nodes
- Absence of cough

Things that point to EBV

- Fatigue
- Age
- Duration of symptoms
- Splenomegaly/LUQ tenderness

TREATING INDIVIDUAL SORE THROATS DOES NOT PREVENT iGAS

Throat swab for Strep

Empiric antibiotics based on the scenario

Recommendations for clinicians (2)

- Be alert to the elevated risk of iGAS:
  - Evaluate all patients with a clinically compatible illness
  - Be alert to paediatric patients who are more unwell than you would expect with viral illness, or who have viral illness and then became more unwell
  - Identify sick children: cold or mottled limbs, limb pain, not wanting to walk, poor feeding, abdominal pain, vomiting, lethargy, throat infection, chest infection, oliguria.
- Management: urgently refer patients with suspected iGAS to hospital, early resuscitation, empiric Abx.

Current Antibiotic Shortages

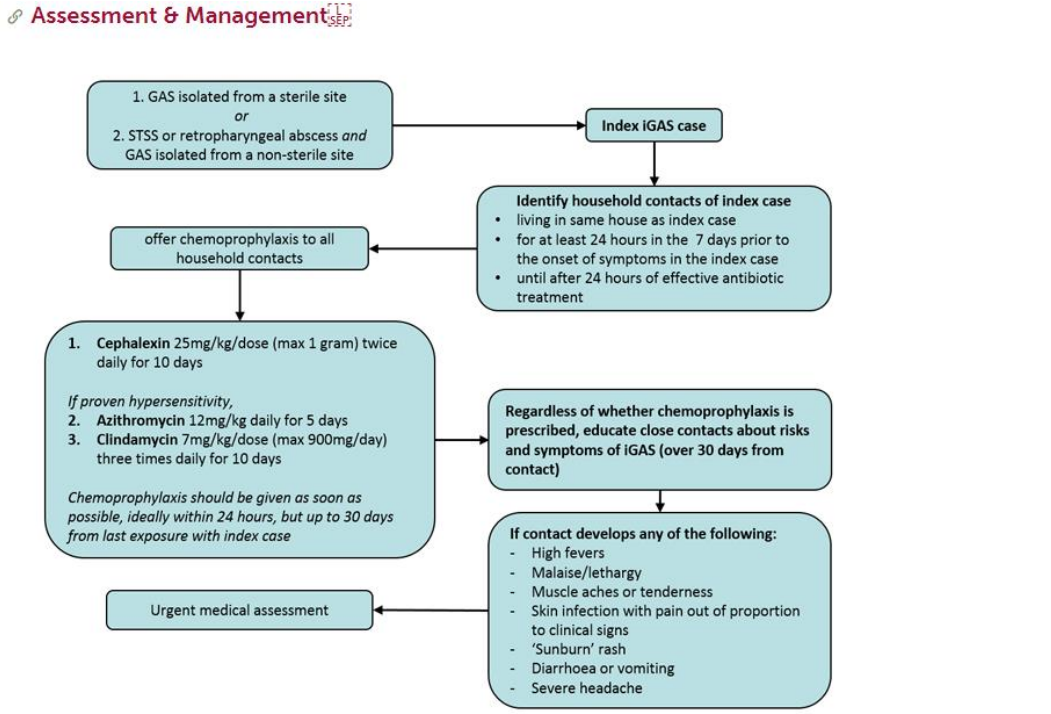
- **Oral, first line antibiotics (incl oral liquids) are affected. Main shortages include:**
  - amoxicillin
  - amoxicillin/clavulanic acid
  - Cefaclor and cefalexin
  - phenoxymethylpenicillin
  - sulfamethoxazole/trimethoprim
  - Trimethoprim

Do not change your prescribing practice to second-line antibiotics without strong clinical indications for doing so. The situation is improving.

iGAS Contact management

- RCH Invasive group A streptococcal infections: management of household contacts

- Therapeutic Guidelines: Prevention of invasive group A streptococcal infection



Rationale for making Acute Rheumatic Fever & Rheumatic Heart Disease routine notifiable conditions in Victoria

RHD and ARF are planned to become notifiable conditions in Victoria. This aims to:

- Improve local epidemiological and surveillance data; contribute to national data
- Systematically identify cases and ensure cases are linked in to clinical care (for follow-up and secondary prophylaxis)
- Reduce health inequities
- Utilise our new networked public health system
- **And ultimately, reduce morbidity and mortality**

Notification parameters in other jurisdictions

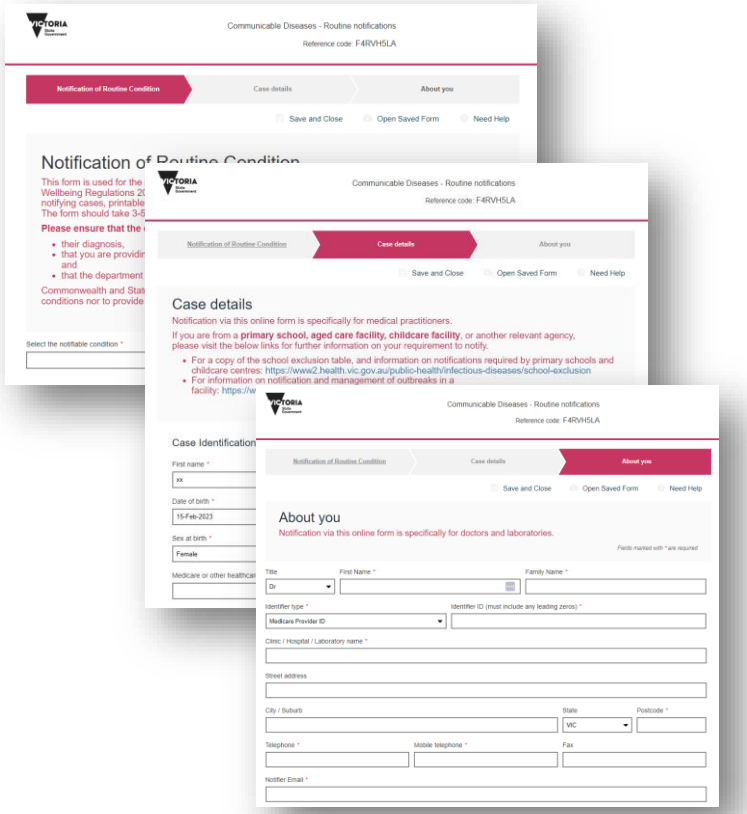
A summary of RHD/ARF registers & control programs in Australia

- **Vic, ACT and Tasmania are the only Australian jurisdictions without:**
  - An RHD control program
  - ARF and RHD being notifiable
  - An ARF/RHD register (provides patient reminders for prophylaxis and tracks patients)

What does routine notification involve?

- **Complete a written notification within 5 days of diagnosis,** using the existing online “Notification of Routine Condition” form (time to complete 3-5 mins) or through faxing a hardcopy notification form to the department

- The notification may be followed by a request to complete a short enhanced surveillance form to collect further targeted information (e.g., symptoms/signs, lab evidence, diagnostic testing)



ARF admissions

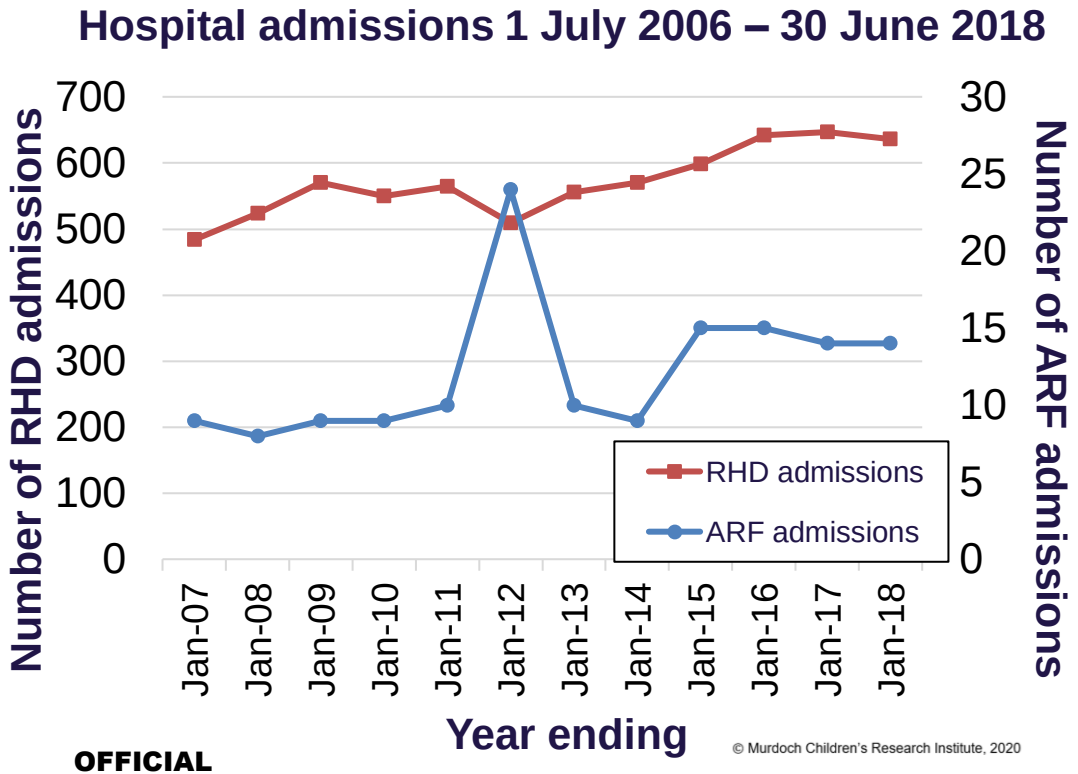
- **0.4 per 100,000 resident population aged <40 years**
  95% CI: 0.3-0.5 (146 admissions; 107 people; 8-24 per year)

- **1.2 per 100,000 aged 10-14 yrs**
  95% CI: 0.9-1.6 (48 admissions)

RHD admissions

- **9.9 per 100,000**
  95% CI: 9.7-10.2
  (6,861 admissions;
  5,167 people; 484-647 per year)

- **1.1 per 100,000 aged <40 years**
  95% CI: 1.0-1.3 (428 admissions)



ARF

146 ARF admissions for 107 Victorians aged <40yo, 1 July 2006 – 30 June 2018

- **Males:** 88 admissions (60%)
- **Indigenous Australians:** 8 admissions (5.5%)
- **Reside in metro LGA:** 106 admissions (73%)

Risk of ARF hospitalisation for Victorian residents aged <40 years		
Univariate analysis	**IRR**	**95% CI**
Males	1.5	1.2-2.1
Indigenous Australian	4.9	2.4-10.0
Loddon Mallee*	1.8	1.1-3.0

* Compared to North and West Metro (64 admissions)

RHD

6,861 RHD admissions for 5,167 Victorians, 1 July 2006 – 30 June 2018

- **Females:** 3,842 admissions (56%)
- **Indigenous Australians:** 46 admissions (0.7%; 128 unknown status)
- **Reside in metro LGA:** 4,515 admissions (66%)
- **Aged <40yo:** 428 admissions (6%)

Risk of RHD hospitalisation for Victorian residents		
Univariate analysis	**IRR**	**95% CI**
Females	1.2	1.2-1.3
Population aged <40 years		
Indigenous Australian	3.8	2.4-6.2

ARF and RHD among children and adolescents in Victoria, Australia

- 811 potential cases ➡179 eligible patients
  - RCH 147
  - MCH 24
  - Both 8

- 108 Victorian, 71 non-Victorian

J Paed Child Health 2022;59:352-359

Victorian residents (108)

- Median age 10.2y (IQR 7.9-12.6)
  - Only 1 case <5yo
- 10% ATSI
- 45% Pacific (33% Samoan)
- 20% Not recorded

- 9% refugee-like background
- 80% Major city
- Concentration of cases NW Melb
- 70% in lower 3 SES quintiles

Victorian residents - Rheumatic Fever (n=45)

- 83 Victorian residents had at least one episode of ARF (45 had ARF only)
- Clinical presentation: joints 64%, carditis 57%, chorea 19%
- Recurrence rate of ARF: 13.3%

	Cases	**Population**	**Annual incidence* (per 100,000)**	**Incidence rate ratio** (95% CI)
Aboriginal and/or Torres Strait Islander	4	10410	3.8	**9.8** (2.5 – 28.3)
Pacific Islander	24	7486	32.1	**82.1** (45.4 – 147.9)
All other ethnicities	27	691802	0.39	Ref
TOTAL	55	709698	0.77	-

*Estimated incidence ARF, 5-14 years
Low-risk population defined as incidence < 2 per 100,000

Resources for clinicians

Health.vic webpage: https://www.health.vic.gov.au/infectious-diseases/streptococcal-disease-group-a-beta-haemolytic-streptococcus

RCH Invasive group A streptococcal infections: management of household contacts - https://www.rch.org.au/clinicalguide/guideline_index/Invasive_group_A_streptococcal_infections__management_of_household_contacts/

RCH Sore throat - https://www.rch.org.au/clinicalguide/guideline_index/Sore_throat/

RCH Febrile child - https://www.rch.org.au/clinicalguide/guideline_index/Febrile_child/

RHD Australia e-Learning: https://www.rhdaustralia.org.au/e-learning-discussion-forum