Review and Update GAS and Influenza

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Objectives

- To review the epidemiology of invasive GAS infections in Ontario
- To provide an update on recent GAS outbreaks and emm74 emergence
- To discuss news in influenza and influenza prevention for Ontario

Group A streptococcal infection
Overall disease burden

Each year

- 1.8 million new cases of serious infection
- at least 500,000 deaths
- 110 million cases of STI
- 610 million cases of pharyngitis

At least 18 million people suffer the consequences of serious GAS diseases

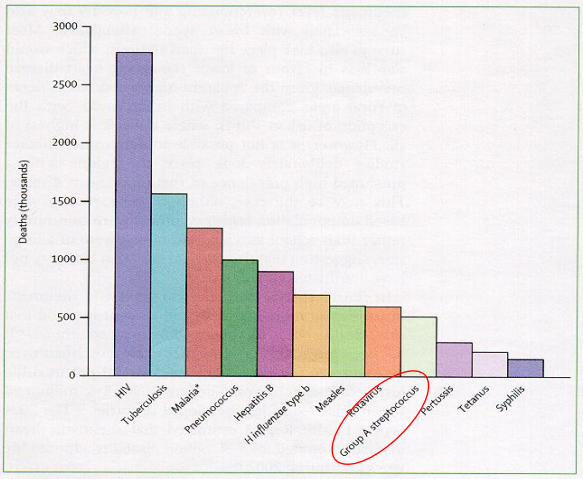
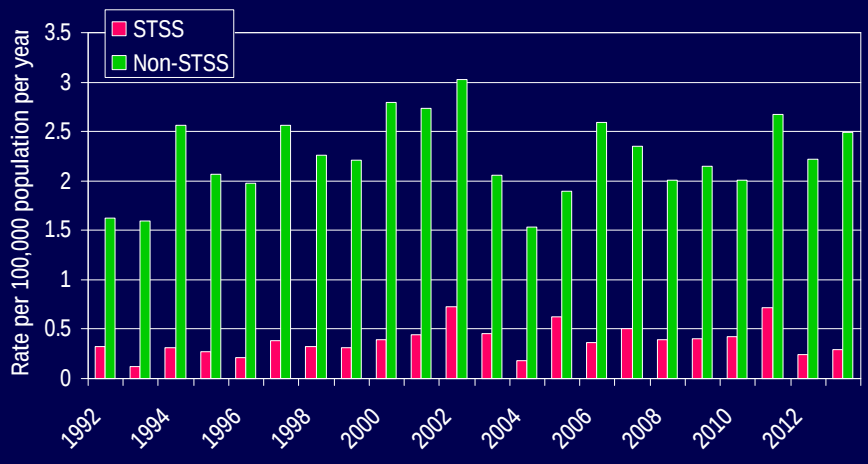


Figure 3: **Estimated global mortality from individual pathogens in 2002**
Data from the 2004 World Health Report[65] and various estimates found in fact sheets on the WHO website (http://www.who.int). Estimates are vague, often based on inadequate data, and should be considered a general guide only. *Almost all malaria mortality is due to *Plasmodium falciparum*.

Invasive GAS disease
Metropolitan Toronto/Peel Region, 1992-2013



Epidemiology of IGAS Ontario

- 50% skin/soft tissue infections, 16% primary bacteremia, 12% pneumonia, 10% arthritis
  - 15% with STSS
  - 8-10% with necrotizing fasciitis
- 70% with positive blood cultures
  - 30% other sterile site (eg. synovial fluid, pleural fluid, tissue)
- 26% required ICU admission (17% vented)
- 32% required surgery
- 18% case fatality rate

Epidemiology of IGAS Ontario

- Median age: 48 years (range 0-101)
  - 15% children (<16), 33% older adults (>65)
  - 54% male
- 62% with chronic underlying illness
  - 18% with cardiac disease, 14% lung disease, 11% diabetes, 10% cancer, 9% alcohol abuse
- 11% nosocomial, 7% from nursing homes
- 3.6% homeless
- 2.5% with recognized contact with another case of GAS infection

Risk factors for IGAS in children

Risk factor	Cases	Controls	Odds ratio	P value
# rooms in house (mean)	6.4	7.4	.67 (.51,.88)	.03
≥1 other child in house	33 (87%)	43 (57%)	17 (3.9,73)	.0002
≥1 person with runny nose	4 (11%)	26 (34%)	.09 (.01,.4)	.002
New use NSAIDS	9 (24%)	7 (9%)	11 (2.1,55)	.005

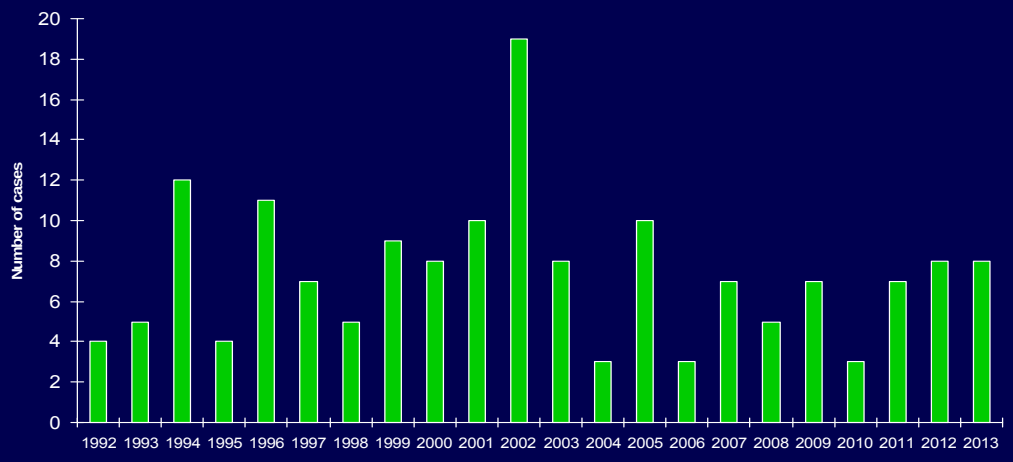
Factor, EID, July 2003

Risk factors for IGAS in adults

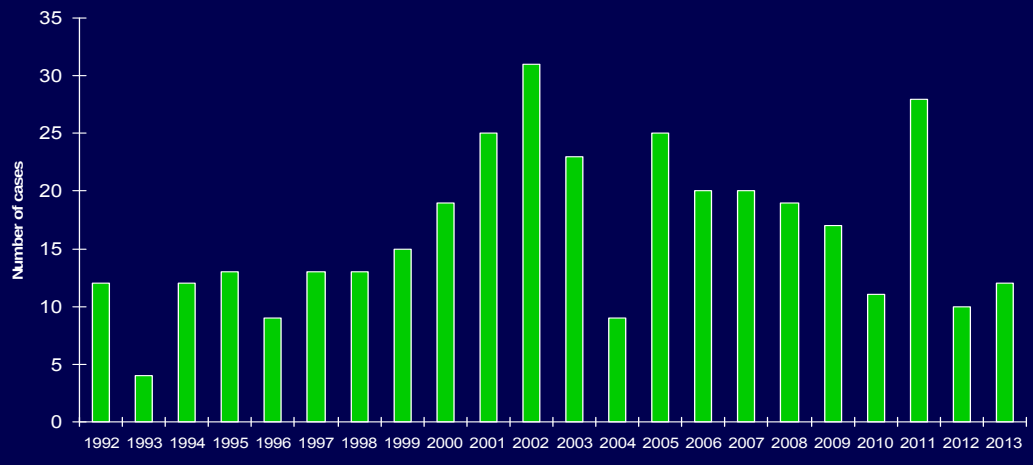
Risk factor	Odds ratio	P value
Exposure to children with sore throat	4.9 (1.2,20)	.02
Number of persons in household	2.7 (1.4,5.3)	.004
IV drug use	15 (2.5,86)	.003
HIV infection	15 (1.0,207)	.004
Diabetes, cardiac disease, corticosteroid therapy, cancer	2.2 to 5.2	.005

Factor, EID, 2005

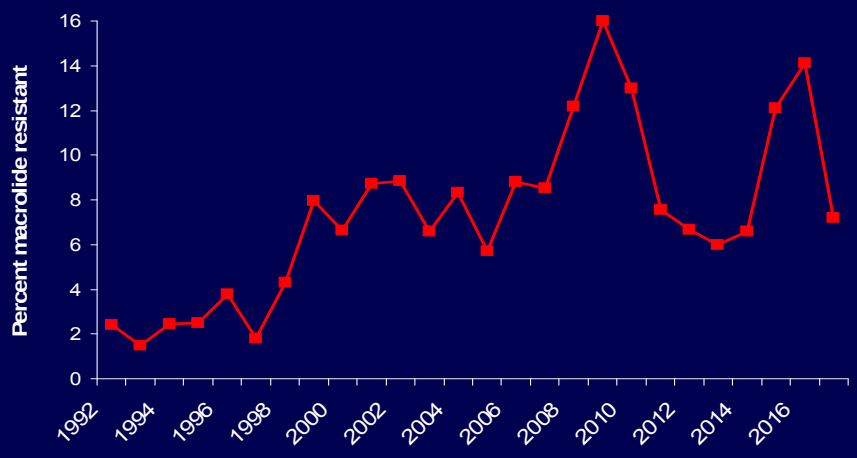
Number of episodes of NF per year Metropolitan Toronto/Peel region 1992-2013



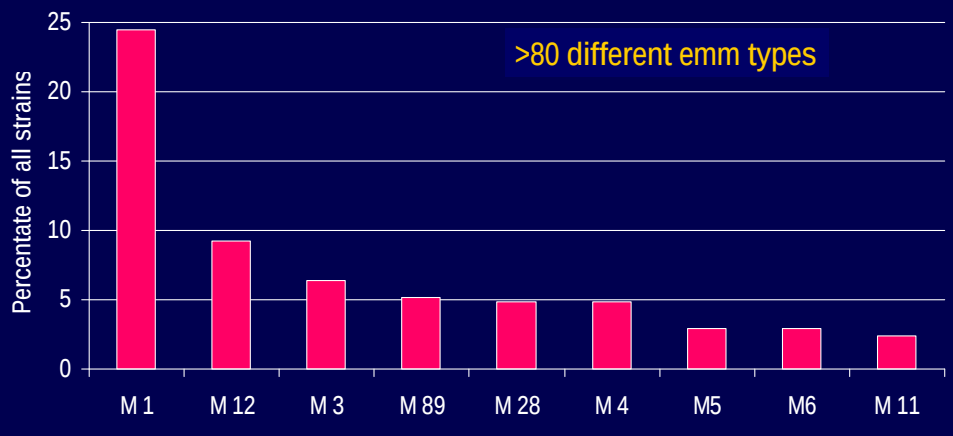
Number of episodes of STSS per year Metropolitan Toronto/Peel region 1992-2013



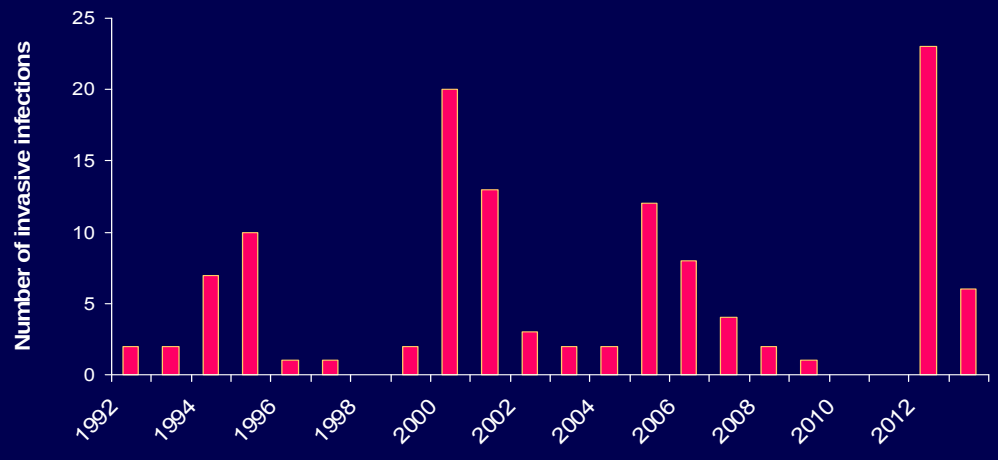
Macrolide resistance in invasive GAS Ontario, 1992-2017



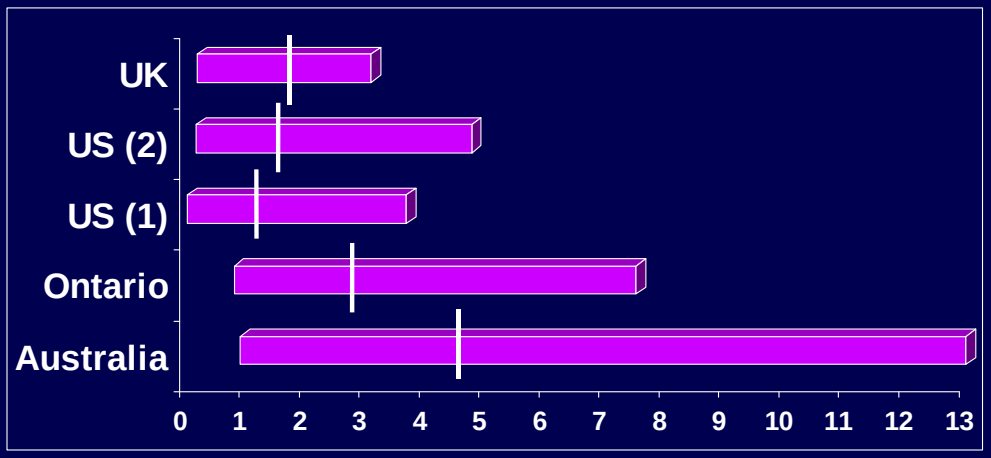
iGAS, Toronto/Peel, 1992-2013 Most common Mtypes



Number of episodes of iGAS due to M type 3 Metropolitan Toronto/Peel region 1992-2013



Risk of secondary disease
Rate invasive disease/1000 household contacts



Summative results – household contact

- 11 subsequent invasive cases
  - 6 husband-wife pairs
  - 1 pair brothers
  - 1 father-daughter (2 months)
  - 3 maternal-neonatal pairs (all British)
- Estimated risk
  - 11/4748, or 1 per 430 household contacts

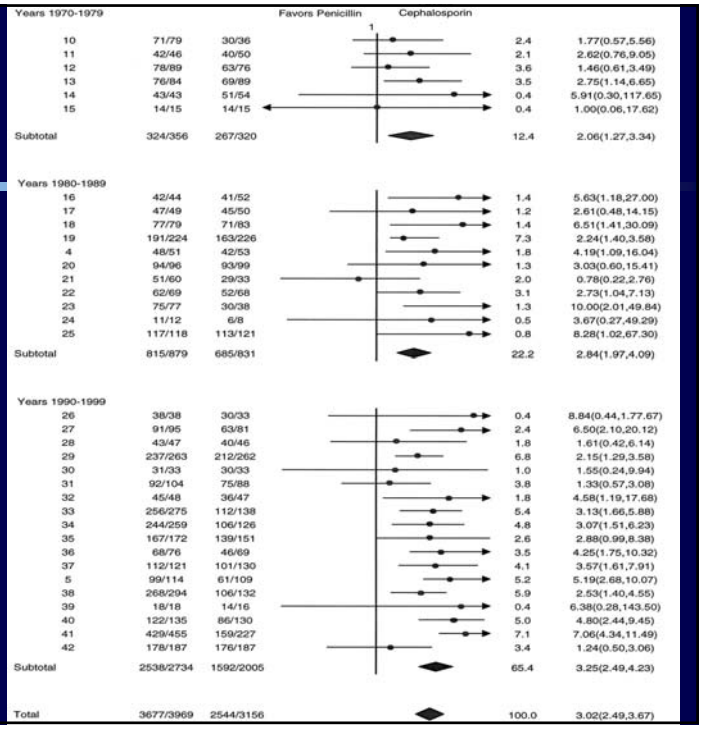
Does prophylaxis work?

- Household contacts of pharyngitis cases randomized to: placebo vs. penicillin vs. cephalosporin
- Rate of disease
  - 5.3% (26/492) placebo
  - 4.3% (19/447) amoxicillin
  - 1.8% (9/507) cephalosporin (P=.003)
  - *5 days of prophylaxis more effective than 3 or 4*

Kikuta PIDJ 2007;26:139-41

Pencillin is effective for treating infections

Cephalosporins are more effective in eradicating carriage

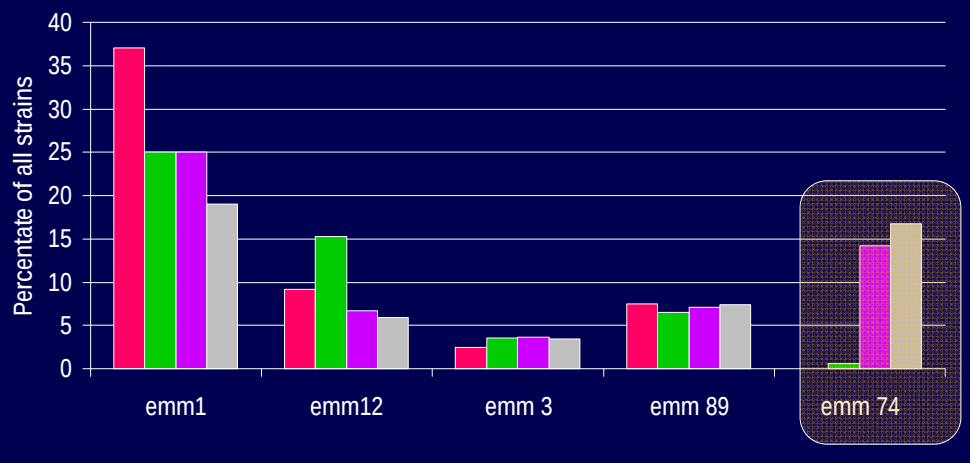


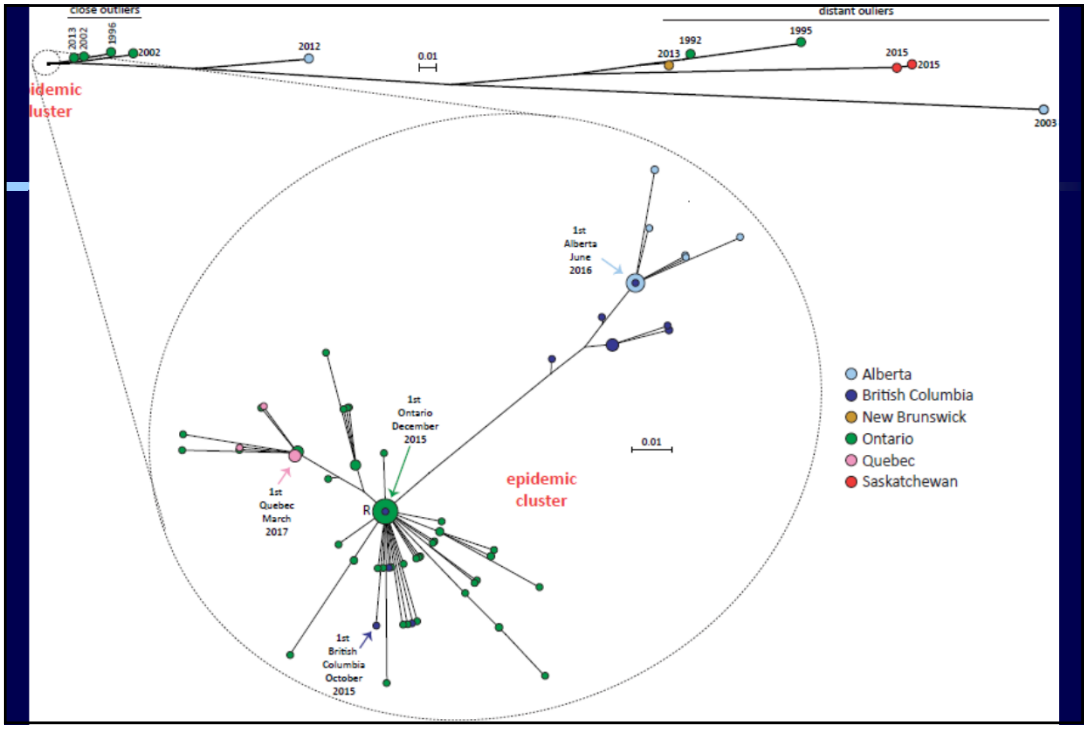
Opportunities for prevention

- Nursing home and hospital transmission
  - Mostly long term care/ALC wards
- Post-partum and surgical site infections associated with colonized or infected satff

What is new?

iGAS, Toronto/Peel, 2014-2017
Emm type variability





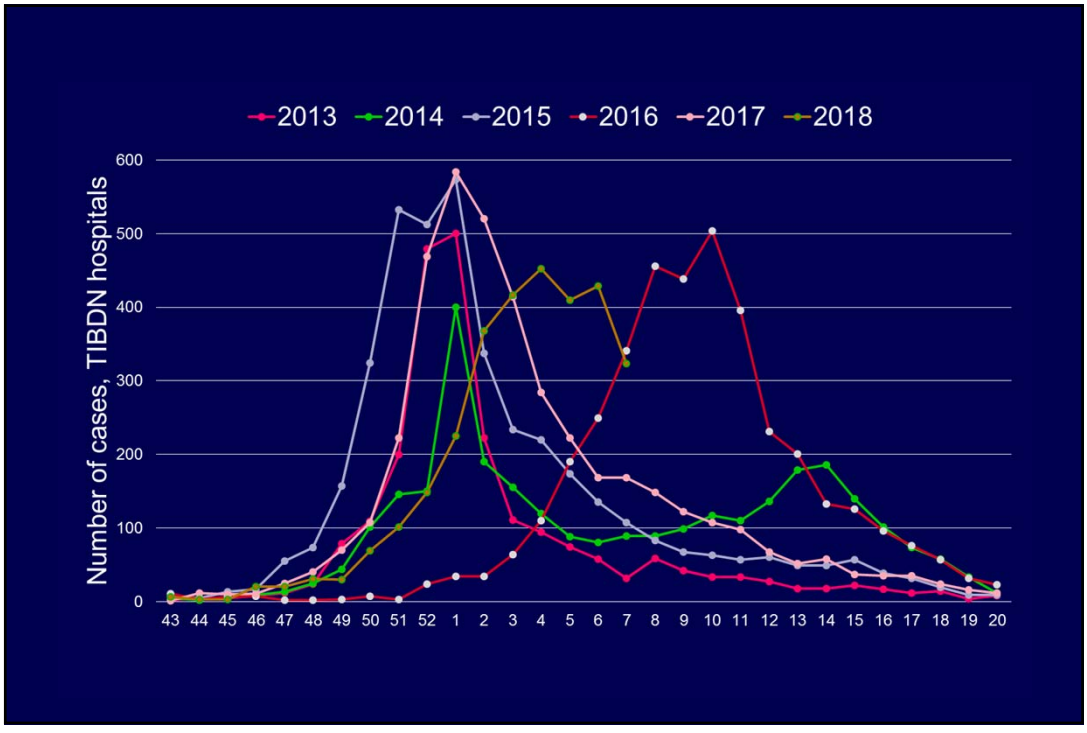
Many vaccine candidates

All still early in development

Development status of current vaccine candidates (*approaching trials).

Candidate name/Identifier	Stage of development			Reference
	Pre-clinical	Phase I	Phase II	
M protein: 6-valent N-terminal	X	X		[36]
M protein: 26-valent N-terminal	X	X	X	[32]
M protein: 30-valent N-terminal	X	*		[33]
M protein: minimal epitope J8	X	X		[34]
M protein: minimal epitope J14/p145	X			[45]
M protein: C-repeat epitope (StreptInCor)	X	*		[38]
M protein: C-repeat epitopes	X			[46]
Three conserved antigens (Combo)	X			[43]
GAS carbohydrate	X			[47]
GAS carbohydrate defective for GlcNAc side-chain	X			[48]
GAS C5a peptidase	X			[49]
Fibronectin-binding protein	X			[50,51]
Streptococcal protective antigen	X			[32]
Serum opacity factor	X			[52]
Streptococcal pyrogenic exotoxin A/B/C	X			[53–55]
Streptococcal pili (T antigen)	X			[56,57]
Serine protease (SpyCEP)	X			[58]

What's new with flu?



Influenza season, 2017/18

- Single, spread out wave
  - Mixed influenza A(H3N2) and influenza B
    - Almost equal number of each
  - Overall vaccine efficacy estimate 42%
    - Against influenza B – 55%
    - Against influenza A(H3N2) – 17-23%
- Vaccine not great – **BUT BETTER THAN NOTHING**