# Significant Increases In Pharyngeal *Neisseria gonorrhoeae* Positivity And Cases Isolated To The Pharynx, 2011-2015: The ACCESS Project

Comninos NB[1], Rutherford A[2], Garton LM[3], Callander D[4], Guy RJ[5], Donovan B[6], Fairley CK[7], Goddard SL[8], Grulich AE[9], Templeton DJ[10]; on behalf of the ACCESS collaboration.

**Affiliations**: [1]RPA Sexual Health, Sydney; [2]School of Public Health and Community Medicine, University of New South Wales, [3]Illawarra Sexual Health Service, NSW; [4] The Kirby Institute, University of New South Wales, [5]Sydney Sexual Health Centre, [6]Melbourne Sexual Health Centre, [7]Alfred Hospital, [8]Monash University; [9]Central Clinical School, University of Sydney.

Disclosures: none

Health
NSW GOVERNMENT
Sydney
Local Health District

## Overview

**Introduction**
- key issues informing research
- Background: pharyngeal gonorrhoea

**Aims and objectives**

**Methods**
- design
- analysis

**Results**
- main findings

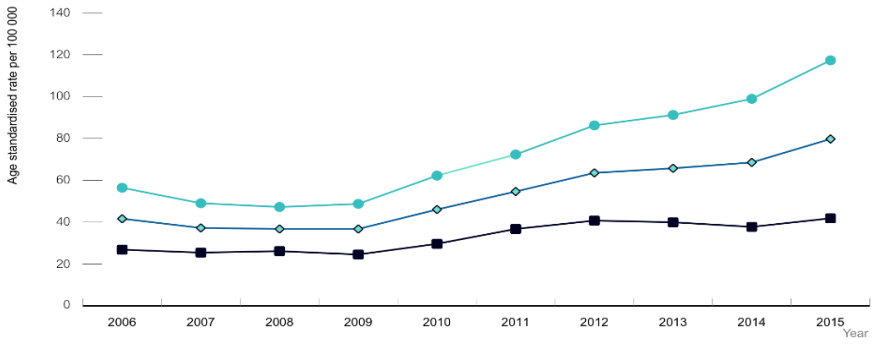
**Conclusion and discussion**
- Interpretation of findings
- Limitations
- Explaining main findings

Health
NSW GOVERNMENT
Sydney
Local Health District

# Introduction: Gonorrhoea in Australia

Notifications nearly doubling for males and females over the past decade

Figure 89 Gonorrhoea notification rate per 100 000 population, 2006 – 2015, by sex




| | 2006 | 2007 | 2008 | 2009 | 2010 | 2011 | 2012 | 2013 | 2014 | 2015 |
|---|---|---|---|---|---|---|---|---|---|---|
| Female | 26.8 | 25.4 | 26.1 | 24.5 | 29.6 | 36.7 | 40.7 | 39.9 | 37.7 | 41.8 |
| Male | 56.4 | 49.0 | 47.2 | 48.7 | 62.2 | 72.3 | 86.2 | 91.2 | 98.9 | 117.3 |
| Total | 41.6 | 37.2 | 36.7 | 36.7 | 46.0 | 54.6 | 63.5 | 65.7 | 68.5 | 79.7 |

Source: Australian National Notifiable Diseases Surveillance System

# Introduction: Why worry?

**Gay and bisexual men:**

**-disproportionately affected**

**-most likely to be diagnosed with HIV**

## STIs increase HIV transmission

| | Adjusted HR | 95% CI | P trend value |
|---|---|---|---|
| Anal NG (NAAT) | | | 0.002 |
| No | 1 | --- | |
| Yes | 7.12 | 2.04-24.79 | |
| Anal warts (self-reported) | | | 0.002 |
| No | 1 | --- | |
| Yes | 3.63 | 1.62-8.14 | |
| HSV-1 (Prevalent) | | | 0.095 |
| No | 1 | --- | |
| Yes | 2.42 | 0.86-6.83 | |
| Insertive UAI HIV unknown | | | 0.761 |
| Insertive UAI HIV positive | | | 0.013 |
| Receptive UAI withdrawal HIV unknown | | | 0.002 |
| Receptive UAI withdrawal HIV positive | | | 0.108 |
| Receptive UAI ejaculation HIV unknown | | | 0.551 |
| Receptive UAI to ejaculation HIV positive | | | 0.004 |

HR, hazard ratio; CI: confidence interval

Jin et al. JAIDS 2010;53:144-9

# Introduction: why worry?

**Multi-drug resistant gonorrhoea is a vitally important clinical and public health challenge**

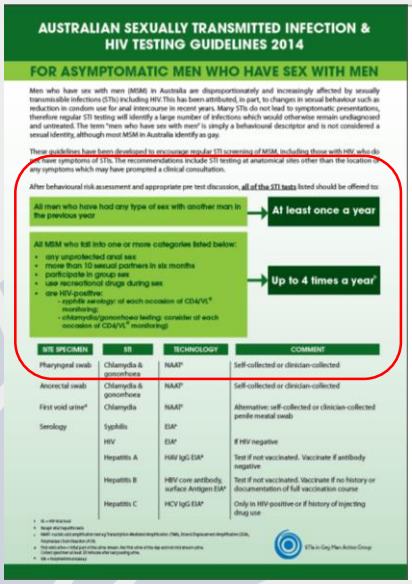
- **WHO 'Call to Action' - July 2017**

"To control gonorrhoea, we need new tools and systems for better prevention, treatment, earlier diagnosis, and more complete tracking and reporting of new infections, antibiotic use, resistance and treatment failures," Dr Marc Sprenger, Director of Antimicrobial Resistance at WHO (2017).

NSW GOVERNMENT Health Sydney Local Health District

# The coming crisis: Multi-drug resistant Gonorrhoea


# What we should be doing…and what we are doing



AUSTRALIAN SEXUALLY TRANSMITTED INFECTION & HIV TESTING GUIDELINES 2014

FOR ASYMPTOMATIC MEN WHO HAVE SEX WITH MEN

Men who have sex with men (MSM) in Australia are disproportionately and increasingly affected by sexually transmissible infections (STIs) including HIV. This has been attributed, in part, to changes in sexual behaviour such as reduction in condom use for anal intercourse in recent years. Many STIs do not lead to symptomatic presentations, therefore regular STI testing will identify a large number of infections which would otherwise remain undiagnosed and untreated. The term "men who have sex with men" is simply a behavioural descriptor and is not considered a sexual identity, although most MSM in Australia identify as gay.

These guidelines have been developed to encourage regular STI screening of MSM, including those with HIV, who do not have symptoms of STIs. The recommendations include STI testing at anatomical sites other than the location of any symptoms which may have prompted a clinical consultation.

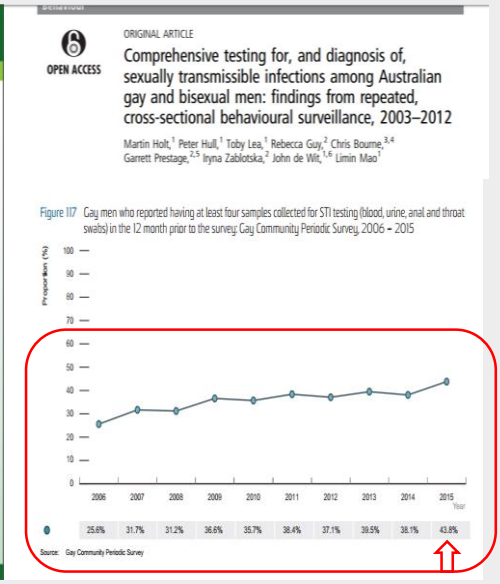
After behavioural risk assessment and appropriate pre test discussion, all of the STI tests listed should be offered to:

All men who have had any type of sex with another man in the previous year → At least once a year

All MSM who fall into one or more categories listed below:
- any unprotected anal sex
- more than 10 sexual partners in six months
- participate in group sex
- use recreational drugs during sex
- are HIV-positive:
  - syphilis serology: at each occasion of CD4/VL* monitoring;
  - chlamydia/gonorrhoea testing: consider at each occasion of CD4/VL* monitoring)

→ Up to 4 times a year*

| SITE SPECIMEN | STI | TECHNOLOGY | COMMENT |
|---|---|---|---|
| Pharyngeal swab | Chlamydia & gonorrhoea | NAAT* | Self-collected or clinician-collected |
| Anorectal swab | Chlamydia & gonorrhoea | NAAT* | Self-collected or clinician-collected |
| First void urine* | Chlamydia | NAAT* | Alternative: self-collected or clinician-collected penile meatal swab |
| Serology | Syphilis | EIA* | |
| | HIV | EIA* | If HIV negative |
| | Hepatitis A | HAV IgG EIA* | Test if not vaccinated. Vaccinate if antibody negative |
| | Hepatitis B | HBV core antibody, surface Antigen EIA* | Test if not vaccinated. Vaccinate if no history or documentation of full vaccination course |
| | Hepatitis C | HCV IgG EIA* | Only in HIV-positive or if history of injecting drug use |



OPEN ACCESS

ORIGINAL ARTICLE

Comprehensive testing for, and diagnosis of, sexually transmissible infections among Australian gay and bisexual men: findings from repeated, cross-sectional behavioural surveillance, 2003–2012

Martin Holt,[1] Peter Hull,[1] Toby Lea,[1] Rebecca Guy,[2] Chris Bourne,[3,4] Garrett Prestage,[2,5] Iryna Zablotska,[2] John de Wit,[1,6] Limin Mao[1]

Figure 117 Gay men who reported having at least four samples collected for STI testing (blood, urine, anal and throat swabs) in the 12 month prior to the survey: Gay Community Periodic Survey, 2006 – 2015



# Introduction: Pharyngeal gonorrhoea

**Pharyngeal gonorrhoea:**

- Disproportionately affects gay & bisexual men[1], female sex workers[2]
- Asymptomatic short-lived infection (median duration 6-12wks)[3]
- Treatment failures seen[4], may be more common than at anogenital sites[5]
- Transmissible to anogenital sites[6]
- Younger age and oral sex practices[7]
- Reservoir of emerging antimicrobial resistance[8]

1 .Trebach, Chaulk, Page, Tuddenham, Ghanem, *Sex Transm Dis* 2015
2. Mc Grath-Lone, Marsh, Hughes, Ward, *sex transm Infect* 2014; Park, Marcus, Pandori, Snell, Philip, Bernstein, *Sex Transm Dis* 2012; Diaz et al., *BMC Pub Health* 2013
3. Chow, Camilleri, Ward et al., *Sex Health* 2016; Chow, Lee, Tabrizi et al.,*Sex Transm Infect* 2016; Apewokin, Geisler, Bachmann, *Sex Transm Dis* 2010
4. Read, Limnios, McNulty, Whiley, Lahra, *Sex Health* 2013, Ohnishi et al. *Antimic Ag Chemo*, 2017
5. Moran, *Sex Transm Dis* 2009
6. Bernstein et al. Clin Infec Dis, 2009; Kinghorn,*Sex Transm Infect* 2010; Chow, Cornelisse, Read et al. *Sex Transm Infect*, 2015; Marcus, Kohn, Barry, Philip, Bernstein,*Sex Transm Infect* 2011, Temleton, Read, Varma, Bourne, *Sex Health* 2016
7. Morris SR, Klausner JD, Buchbinder SP et al. *Clin Infect Dis*, 2006; Templeton, D. J., Jin, F., McNally, L. P et al. *Sex Transm Infect*, 2010.
8. Deguchi, Yasuda, Ito, *Antimic Ag Chemo* 2014

NSW GOVERNMENT Health Sydney Local Health District

# Introduction: Pharyngeal gonorrhoea

**BUT:**

**-Strong surveillance systems**

**-New opportunities for frequent testing: PrEP**

**-Promising prevention & eradication strategies:**
- **antiseptic mouthwash**
- **future vaccines**
- **novel / alternative antimicrobials**



# Introduction: Research Aims and Questions

**Gay and bisexual men (GBM) and Female sex workers (FSW)**

**Testing at sexual health clinics across Australia**

**5 year period (2011-2015)**

**Aims:**

- ***To explore temporal trends in pharyngeal gonorrhoea test positivity***
- ***To contrast these trends with trends in anogenital gonorrhoea test positivity***
- ***To explore factors associated with pharyngeal gonorrhoea***

NSW GOVERNMENT Health
Sydney Local Health District

## Methods: Study Design

- **Cross-sectional design**
- **Ethics approval:** ACCESS* Project has multi-site approval, concept sheet and proposal approved by committee
- Data from **42 sexual health clinics across Australia**

**ACCESS Project: Australian Collaboration for Coordinated Enhanced Surveillance of Sexually Transmitted Infections and Blood Borne Viruses*

- *Commenced 2008*
- *Collects data from sexual health clinics and other sites across Australia*
- *Such data provides insight into trends in testing practices, disease patterns and risk factors for STIs*

Health
NSW GOVERNMENT | Sydney Local Health District

## Methods: Analysis

**"Positivity": proportion of all tests with a positive result**

**STATA: Line listed, de-identified data: testing occasions**

**Univariate & Multivariate Analyses**

***Random Effects Model – Clustering***

***Temporal trends*** in pharyngeal gonorrhoea positivity

***Factors*** associated with positive pharyngeal tests

Health
NSW GOVERNMENT | Sydney Local Health District

# Methods: Analysis

**Factors associated with positive pharyngeal gonorrhoea tests**

**Variables Included:**

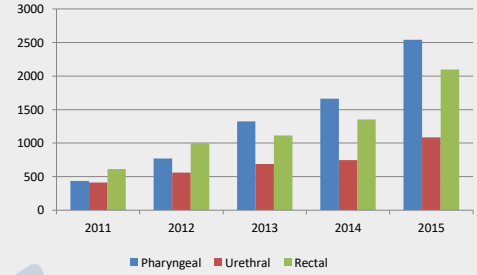
**Calendar year of testing**
**Age**
**Testing site location (region of Australia)**
**Aboriginal/Torres Strait Islander status**
**Country of birth**
**Injecting drug use** (reported, in the previous 12 months)
**Contact with an STI** (reported, not specifically gonorrhoea)
**Sex work** (reported in the 12 months prior to consultation)
**HIV status**
**Anogenital symptoms**
**Number of sexual partners** (non paying) in the previous 6 months.

**Excluded**
**Condom use**

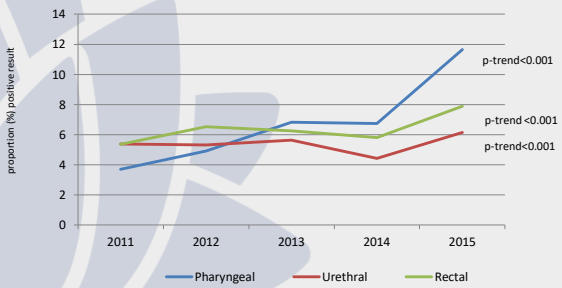
Health
NSW GOVERNMENT | Sydney Local Health District

# Results: Gay and bisexual men

**Number of positive *Neisseria gonorrhoeae* tests**




**Trend in *Neisseria gonorrhoea* test positivity**




**Pharyngeal positivity increased by over 300%** (p- trend<0.001).

**Anogenital positivity: smaller increases**

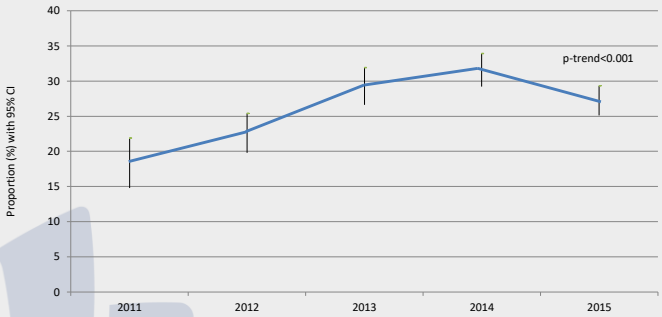
**Independent predictors of a positive pharyngeal test:**

- **younger age** (p-trend<0.001)
- **more partners** (p-trend<0.001)
- **STI contact** (p<0.001)
- **injecting drug use** (p<0.001)
- **anogenital symptoms** (p<0.001)
- **HIV-positive status** (p=0.005)

Health
NSW GOVERNMENT | Sydney Local Health District

# Result: Gay and bisexual men

**Proportion of positive three-site tests where positive result isolated to pharynx**

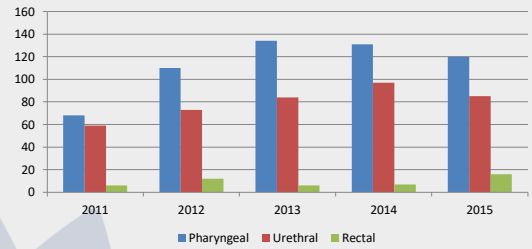



**'Isolated' pharyngeal positivity** (without anogenital co-infection) **increased by almost 50%** (p-trend<0.001)

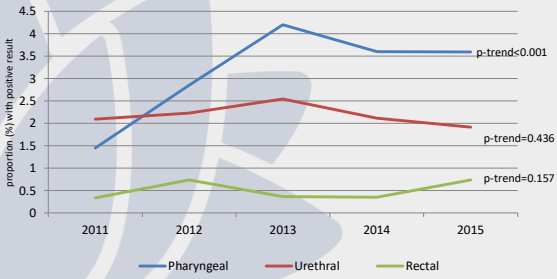
Health
NSW GOVERNMENT
Sydney
Local Health District

# Results: Female sex workers

**Number of positive Neisseria gonorrhoeae tests**




**Temporal Trend *Neisseria gonorrhoeae* test positivity**




**Pharyngeal positivity increased by almost 250%** (p-trend <0.001)

**No significant increase in anogenital positivity**

**But**: Adjusted (Multivariate) analysis:

→*Odds of a positive pharyngeal result for FSW did **not** significantly increase over time*
(OR=1.06; 95% CI 1.0-1.2; p-trend=0.134)

**Independent predictor (+) pharyngeal test:**

**-STI contact (p<0.001)**

Health
NSW GOVERNMENT
Sydney
Local Health District

# Results: Discussion and Interpretation

## Strengths

**First nation-wide study:**

**Significant temporal increase in pharyngeal gonorrhoea positivity**

**Significant temporal increase in "isolated" pharyngeal cases**

**Several factors associated with positive pharyngeal gonorrhoea test in our study also predicted incident pharyngeal gonorrhoea in the HIM study[1]**

- **Younger age**
- **More partners**
- **STI contact**

**Among both GBM and FSW: STI contact associated with positive pharyngeal test**

8. Templeton, D. J., Jin, F., McNally, L. P et al., *Sex Transm Infect* 2010.

Health
NSW GOVERNMENT | Sydney Local Health District

# Results: Discussion and Interpretation

## Limitations

- Study Type
- Missing Data, Power (FSW)
- Condom use

***Repeat testers***

***Different testing methods*** across clinics (culture vs more sensitive NAAT[9])

*Culture swabs to NAAT→increase positivity*[10]

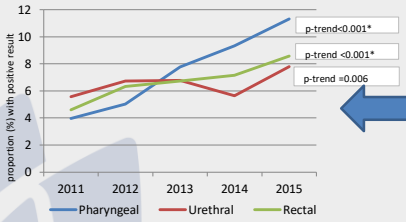
9. Smith, D. W., Tapsall, J. W., Lum, G., *Comm Dis Intell* 2005.
10. Cornelisse, V. J., Chow, E. P., Huffam, S et al., *Sex Transm Dis* 2017.

Health
NSW GOVERNMENT | Sydney Local Health District

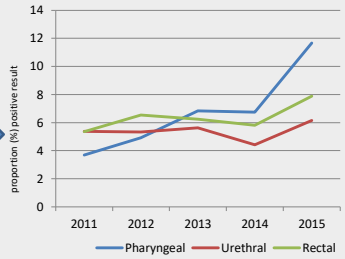
# Results: Discussion and Interpretation

***Sub-analysis: dealing with Repeat testers and NAAT vs Culture***

**GBM: First visits, NAATs only**




**GBM: All visits, NAATs and Culture swabs:**




**Temporal trend remains highly significant and greater in the pharynx than at anogenital sites**

**Same factors associated with positive pharyngeal test (except injecting drug use)**

- younger age (p-trend<0.001)
- more partners (p-trend=0.004)
- STI contact (p<0.001)
- anogenital symptoms (p<0.001)
- HIV-positive status (p=0.004)

NSW GOVERNMENT Health Sydney Local Health District

# Conclusion: Discussion, Interpretation

**May partially (but not wholly explain)**

*Repeat testing throughout the period*

*Culture to NAAT (one clinic)*

*More frequent testing in more recent years*

**First visits, NAATs only: Temporal trend appears to remain highly significant**

NSW GOVERNMENT Health Sydney Local Health District

## Conclusion: Discussion and Interpretation

**Explaining these findings: research priorities, areas of active research**

?Increasingly effective contact tracing

?Increasingly engaging at-risk GBM (younger, more partners, STI contact)

?Changing oral sex practices

?Treatment failures

?Pharynx to pharynx transmission

Health
NSW GOVERNMENT
Sydney Local Health District

## Conclusion: Recommendations

**Pharyngeal gonorrhoea may be a key driver of increasing gonorrhoea notifications in Australia**

**<u>Urgent need for:</u>**

**-increased testing frequency → frequent pharyngeal testing in at-risk groups**

**-Maintain and strengthen surveillance, contact tracing, engagement of at risk GBM**

**-Novel strategies to combat pharyngeal gonorrhoea**

Health
NSW GOVERNMENT
Sydney Local Health District

# Acknowledgements

**Study investigators:** Margaret Hellard, Mark Stoové, Carol El-Hayek (Burnet Institute); Rebecca Guy, Basil Donovan, Denton Callander (Kirby Institute); Wayne Dimech (NRL)

**Operational Committee:** Jason Asselin, Lucy Watchirs Smith, Clarissa Moreira, Gijo Thomas, Long Nguyen, Caroline van Gemert

**Advisory Committee**: Scott McGill, Stella Pendle, Ben Wilcock, Melanie Walker, Scott Bowden, Deborah Bateson, Helen Tyrrell, Philip Reed, Christopher Fairley, Aaron Cogle, Christine Selvey, Norm Roth, David Nolan, Catherine O'Connor, Jules Kim, Mark Boyd, Jane Hocking, Michael West, Nicola Stephens, Lisa Bastian

**Site investigators:** Sarah Martin, Stephen Davies, David Baker, Alison Nikitas, Katherine Brown, Mark Bloch, Nathan Ryder, Debbie Allen, Philip Reed, David Smith, Christopher Carmody, Christopher Fairley, Eva Jackson, Catherine O'Connor, Frederick Lee, Josephine Lusk, Andrew Carr, John McAllister, Anna McNulty, Robert Finlayson, David Lewis, Andrew Small, Jen Kok, Philip Cunningham, Bradley Forssman, Nicholas Doong, Stella Pendle, Wendle Rosevear, Graham Neilsen, Craig Atkinson, Julian Langton-Lockton, Darren Russel, Maree O'Sullivan, Cheryn Palmer, Krispin Hajkowicz, Arun Menon, Goran Pervan, Alison Ward, Charlotte Bell, Eugene Athan, Jennifer Hoy, Ian Woolley, Norm Roth, BK Tee, Sally Rowell, Lewis Marshall, Jenny McCloskey, Manoji Gunathilake, Louise Owen, Mark Wilson, Justin Manuel, Bill Kefalas, David Townson.

**Funding:** Core funding for ACCESS comes from the Australian Department of Health.

# Acknowledgements

- Associate Professor David Templeton
- Dr Denton Callander
- Dr Alison Rutherford
- Linda Garton
- Associate Professor Anna McNulty
- Professor Rebecca Guy
- Professor Basil Donovan
- Professor Christopher Fairley
- Dr Sian Goddard
- Professor Andrew Grulich
- Associate Professor Catherine O'Connor
- Dr Georgia Carins
- Dr Heulwen Rees