

# A new explanation for rising rates of anal cancer

## A SYNDEMIC INTERACTION

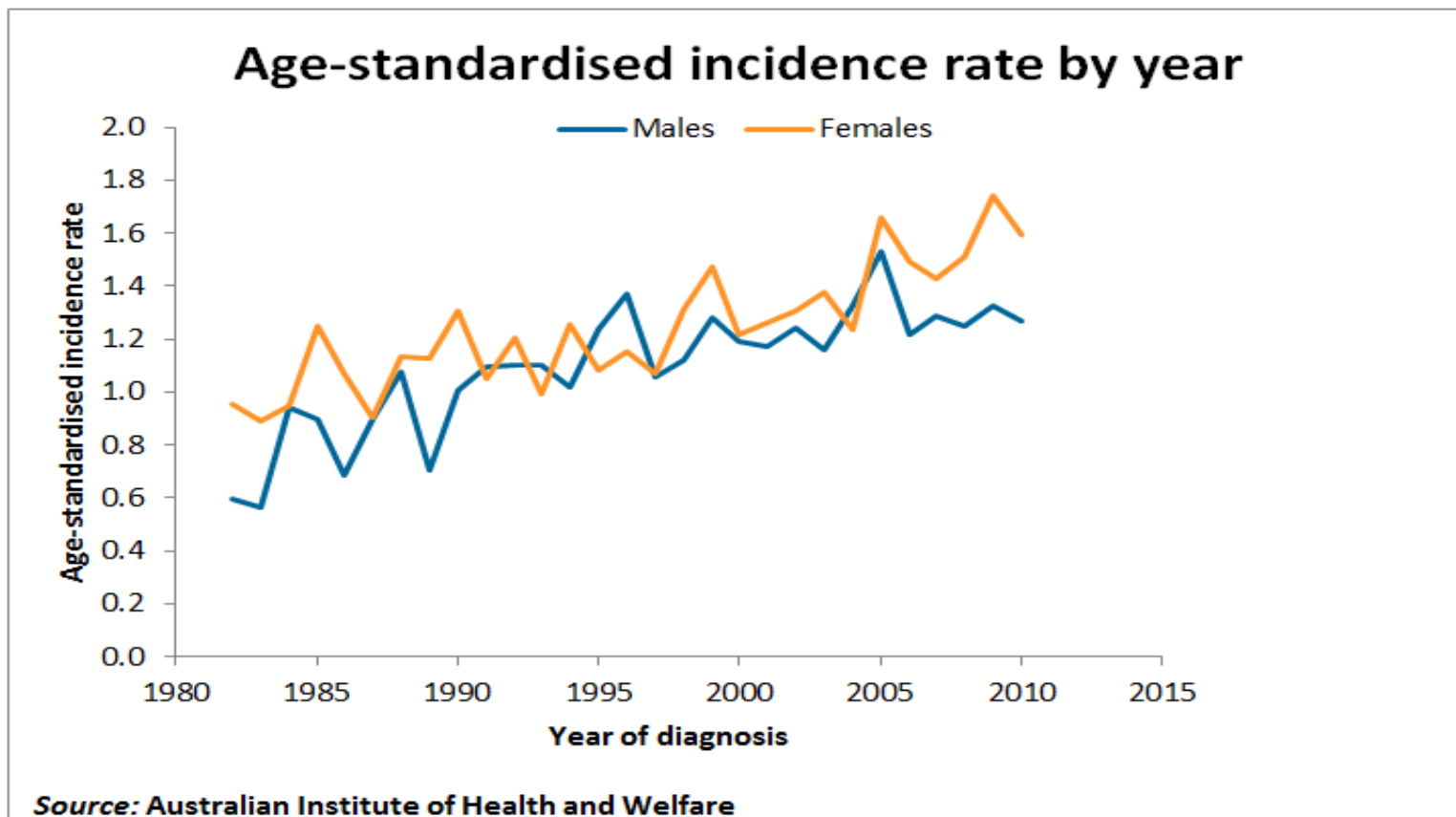
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# ANAL CANCER RATES ARE RISING IN MEN AND WOMEN WORLDWIDE



AIHW Australian Institute of Health and Welfare (AIHW) 2014. Australian Cancer Incidence and Mortality (ACIM) books: " & B10 & accessed 21/09/2014.  
<http://aihw.gov.au/>

# CO-FACTORS REPORTED WITH DEVELOPMENT OF ANAL CANCER



- Sexual intercourse before the age of 30
- Receptive anal sexual intercourse
- Lifetime number of sexual partners
- Female gender
- Current cigarette smoking
- Immune suppression after organ transplantation
- HIV infection
- Anal fistulae & epithelial trauma

## **Genital wart related associations**

- Patients with GW have significantly increased risk of anal cancer & other cancers e.g. head & neck cancers
- Anal warts- cancer seen to arise out of anal warts
- Persistence of HrHPV in Danish women with genital warts



# THE ROYAL PERTH HOSPITAL SURGICAL DATABASE : HIGH RATES OF HSIL IN WARTS

Established 1996

- a surgical data base of patients treated for anal warts in theatre
- epidemiological & histological data collected prospectively
- findings previously reported<sup>1,2</sup>
  - 52% high-grade in males with HIV
  - 20% high-grade in males without HIV
  - HIV rates of AIN at least double that of HIV negative population

1 McCloskey J, Metcalf C, French M, Flexman J, Burke V, Beilin L. The frequency of high-grade intraepithelial neoplasia in anal/perianal warts is higher than previously recognised. *Int J STD & AIDS* 2007; 18:538-42

2 McCloskey J, Phillips M, French M, Flexman J, McCallum D, Metcalf C. Update on the Royal Peth Hospital Anogenital Wart Database. In: Barros E, editor. *HIV Infection- Impact Awareness and Social Implications of Living with HIV/AIDS: In Tech*; 2011. p. 81-90.

# This study: 261 men; 53 women

- The majority of men (75%) were HPV positive compared with 40% of the women
- 80% of the MSM (most of the men) were HPV positive compared with only 47% of heterosexual men
- 40% of the men were HIV positive and HIV was strongly associated with HPV infection
- HPV positivity was associated with 6.5X increased risk of HSIL

# WHAT IS A SYNDEMIC?- THE WIKEPEDIA DEFINITION



- ‘A **syndemic** or synergistic epidemic is the aggregation of two or more concurrent or sequential epidemics or disease clusters in a population with biological interactions, which exacerbate the prognosis and burden of disease.<sup>1</sup>
- The syndemic approach departs from the biomedical approach to diseases to diagnostically isolate, study, and treat diseases as distinct entities separate from other diseases and independent of social contexts.’<sup>2</sup>

The term was developed by [Merrill Singer](#) in the mid-1990s. Syndemics develop under [health disparity](#), caused by [poverty](#), stress, or [structural violence](#) and are studied by [epidemiologists](#) and [medical anthropologists](#) concerned with public health, [community health](#) and the effects of social conditions on health.

<sup>1</sup> Tsai AC, Mendenhall E, Trostle JA, Kawachi I. Co-occurring epidemics, syndemics, and population health. The Lancet 2017;389:978-82

<sup>2</sup> <https://en.wikipedia.org/wiki/Syndemic> doi 20170905

# Variables included in the structural equation model showing the path to high-grade intra-epithelial neoplasia

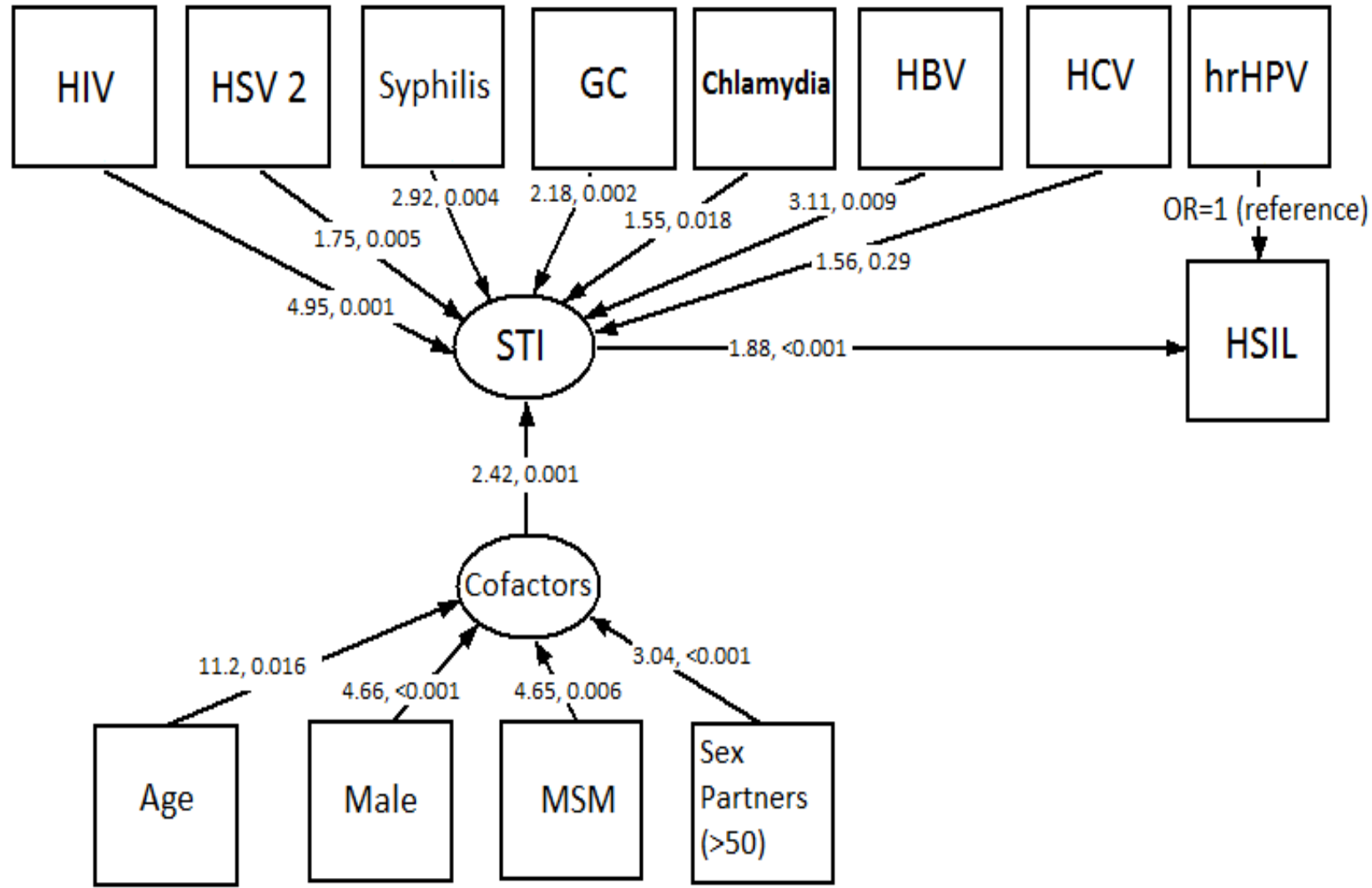
## **INDEPENDENT** variables:

- Warts and high-risk HPV
- HIV
- HSV2
- Gonorrhoea
- Chlamydia
- Hepatitis B infection
- Hepatitis C

## **COVARIATES:**

- Increasing age
- Males compared to females
- MSM & BSM compared to heterosexual
- Number of sexual partners  
(1-10, 11-49, 50 plus)

# High Grade AIN AS A SYNDEMIC OF STI'S AND OTHER COFACTORS



Squares indicate observed variables and ovals indicate unobserved latent variables.

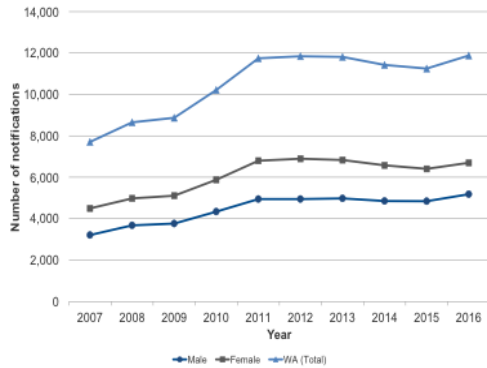
Arrows show hypothetical relationships established by this study.

Values show the odds ratio and *p*-values for each association indicated by an arrow.

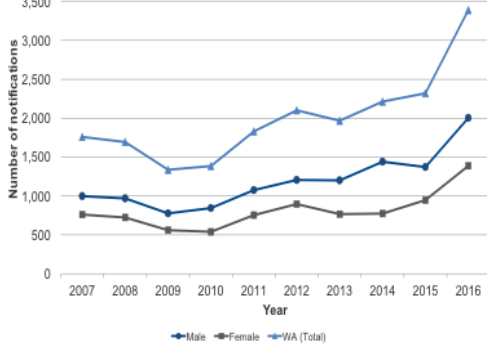


# STI's in WA 2007-2016

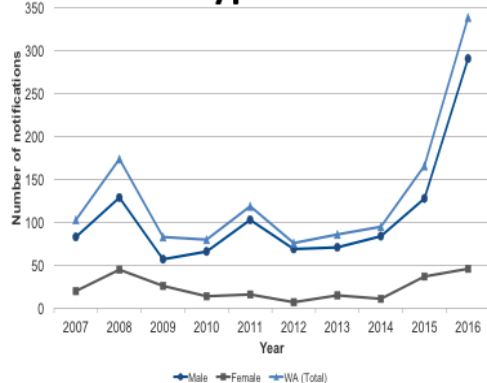
## Chlamydia



## Gonorrhoea



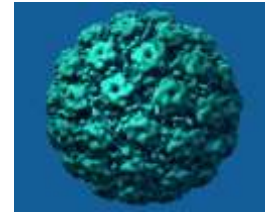
## Syphilis



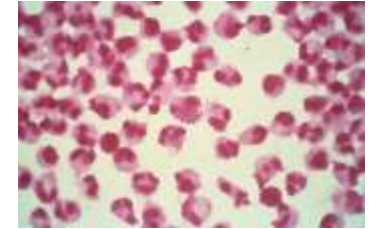
How can STI's act to increase the risk of HSIL?  
Increasing rates of STI's?



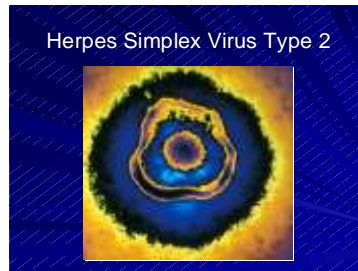
Chlamydia- persistence of HrHPV



Increases HrHPV replication



Gonorrhoea- inflammatory extracellular reaction



Herpes Simplex Virus Type 2

HSV2- a known mutagen, enables uptake of HPV



Syphilis- other evidence for cancer association



**Systemic action**

HIV

HBV

HCV

# Syndemic synergy of HPV and other sexually transmitted pathogens in the development of high-grade anal squamous intraepithelial lesions

Jenny C. McCloskey, W. Martin Kast, James P. Flexman, Dugald McCallum, Martyn A. French, Michael Phillips

*Papillomavirus Research*, 4: 90–98 (2017)

