

Lymphogranuloma venereum in the UK



Guy's and St Thomas'



NHS Foundation Trust

John White

Dept of Genitourinary Medicine
Guy's & St Thomas' Hospital Trust

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Chlamydia trachomatis

- “Obligate intracellular parasite”
- Sexually transmissible
- Different *serovars*
- A, B, B₁ & C = trachoma
- D to K = genital infection
- L₁, L₂ & L₃ = lymphogranuloma venereum (LGV)

LGV Epidemiology

- Classical LGV endemic in parts of
 - Africa, India, SE Asia, Caribbean & Central/South America
- Uncommon cause of GUD (<10%)
 - recent studies suggest more
- Rarely diagnosed in UK until 2004



LGV Recent Developments

Rotterdam – Sept 2004

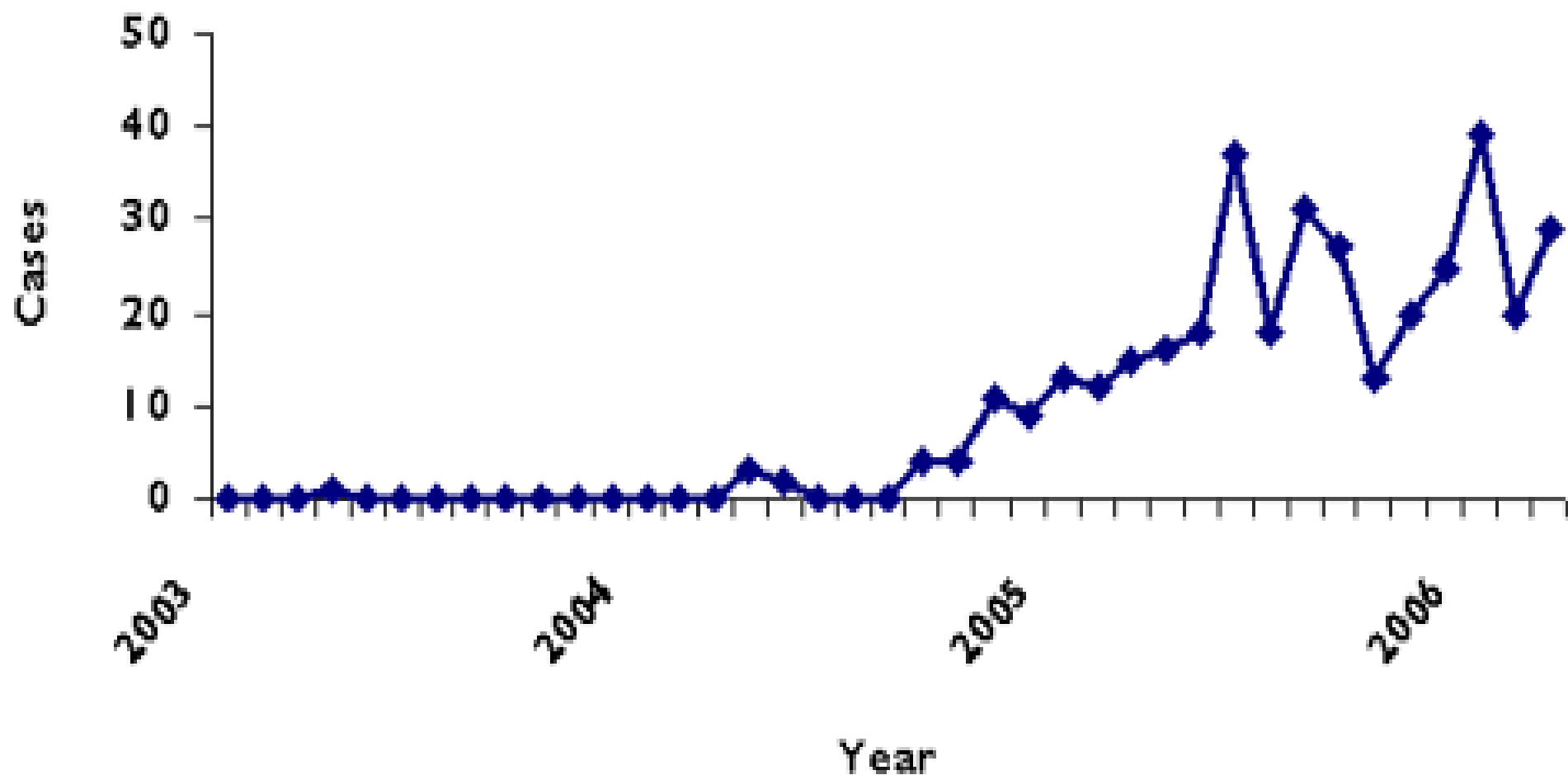
- Cluster of 92 MSM LGV cases
- All **proctitis**; no inguinal or urethral disease
- All **white**, age >25, 77% **HIV positive**
- Other **STIs** prevalent, new **HIV & HCV**
- MSM sex parties, leather scene, sex clubs/saunas: UPASI, fisting, enemas
- Other reports from Europe and then UK in late 2004, then USA & Canada, Australia...

LGV Recent Developments - UK

- UK response via HPA – Oct 2004
- Increase awareness, improve diagnosis & surveillance
- Confirmatory testing
- Enhanced surveillance from all cases
- UK LGV cases = **500** to May 2007



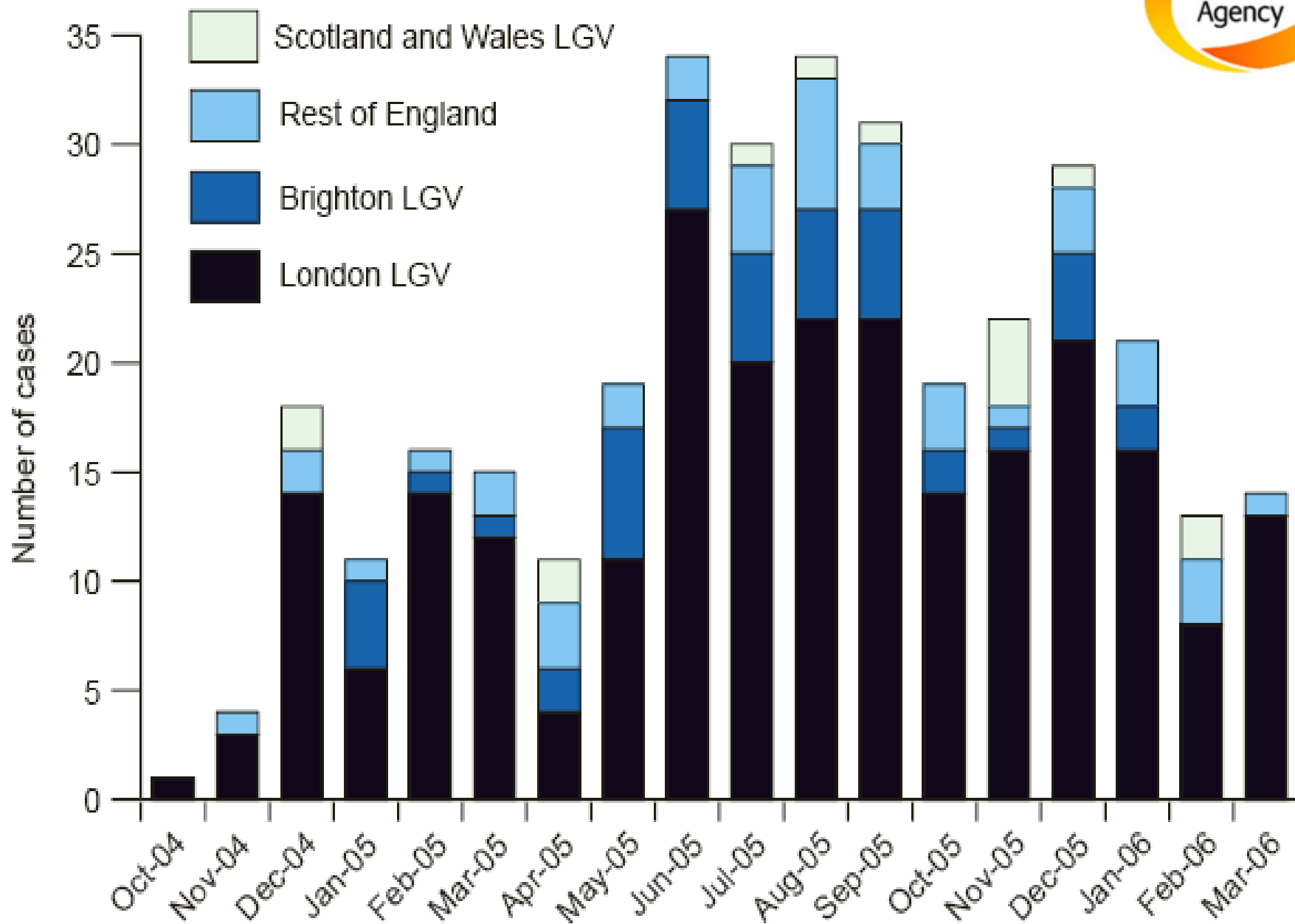
Confirmed cases of LGV with epidemiological data, United Kingdom, January 2003 - September 2006



LGV Recent Developments - UK

- UK data is consistent with rest of Europe:
 - 99% **MSM**; predominantly **white** (95%) and **HIV positive** (74%); median age **38** (21-65)
 - almost exclusively **anorectal** disease
 - high levels of **concurrent STIs**
 - both **HIV and HCV** seroconversions seen
 - most in **London** (69%) & **Brighton** (15%) but wide geographic distribution
 - frequent **misdiagnosis & delays** before treatment in early cases

Figure 2 Laboratory confirmed cases of LGV, UK : 2004 to 2006



LGV Secondary Stage

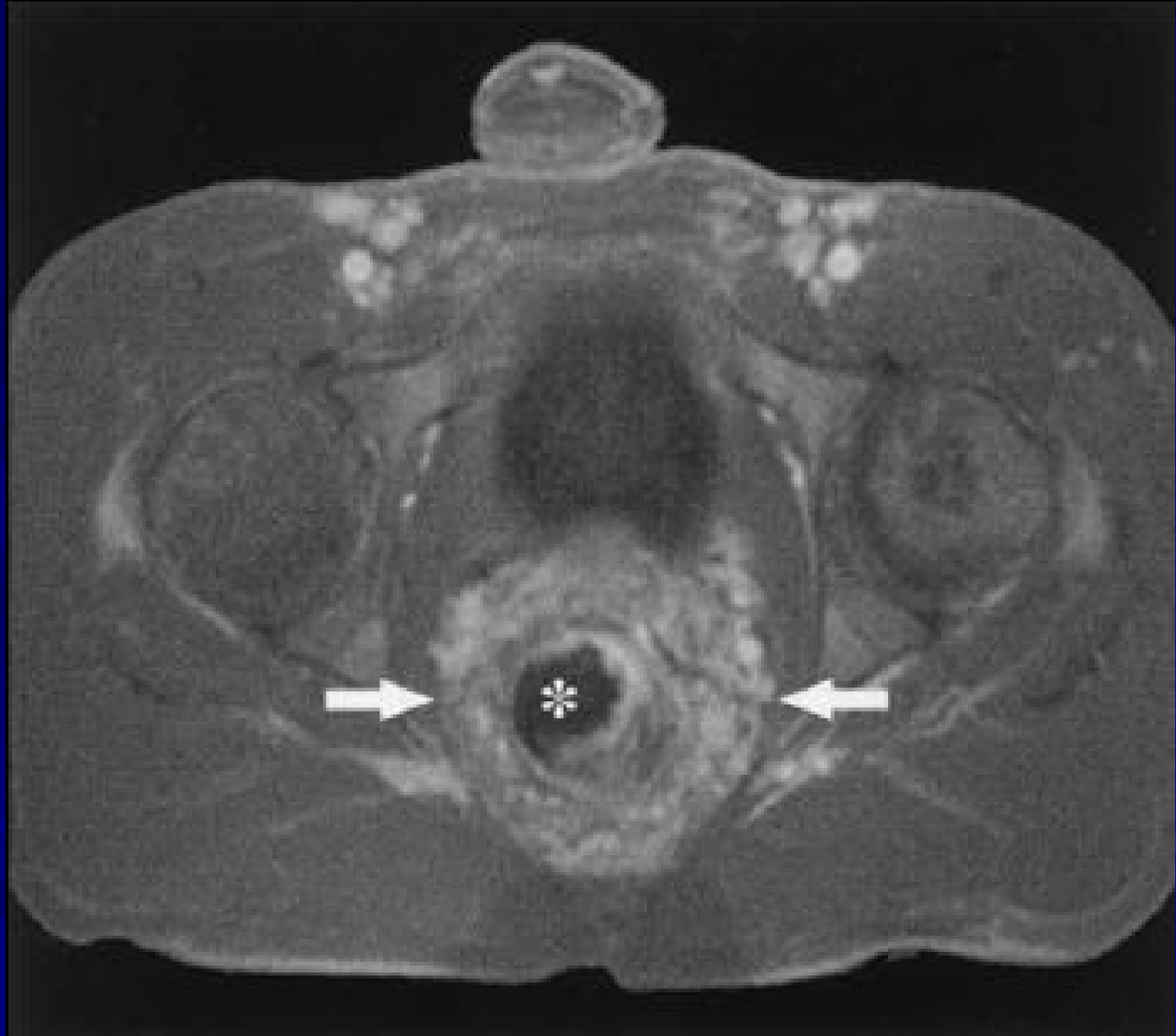
- Anorectal involvement can cause **acute haemorrhagic proctitis**
- Wide spectrum of presenting symptoms:
 - perianal irritation, mucopurulent discharge, rectal pain, tenesmus, constipation, PR bleeding, bloody diarrhoea, abscess, fistulae +/- systemic features
- **Proctoscopy** – granular or ulcerative distal proctitis similar to IBD

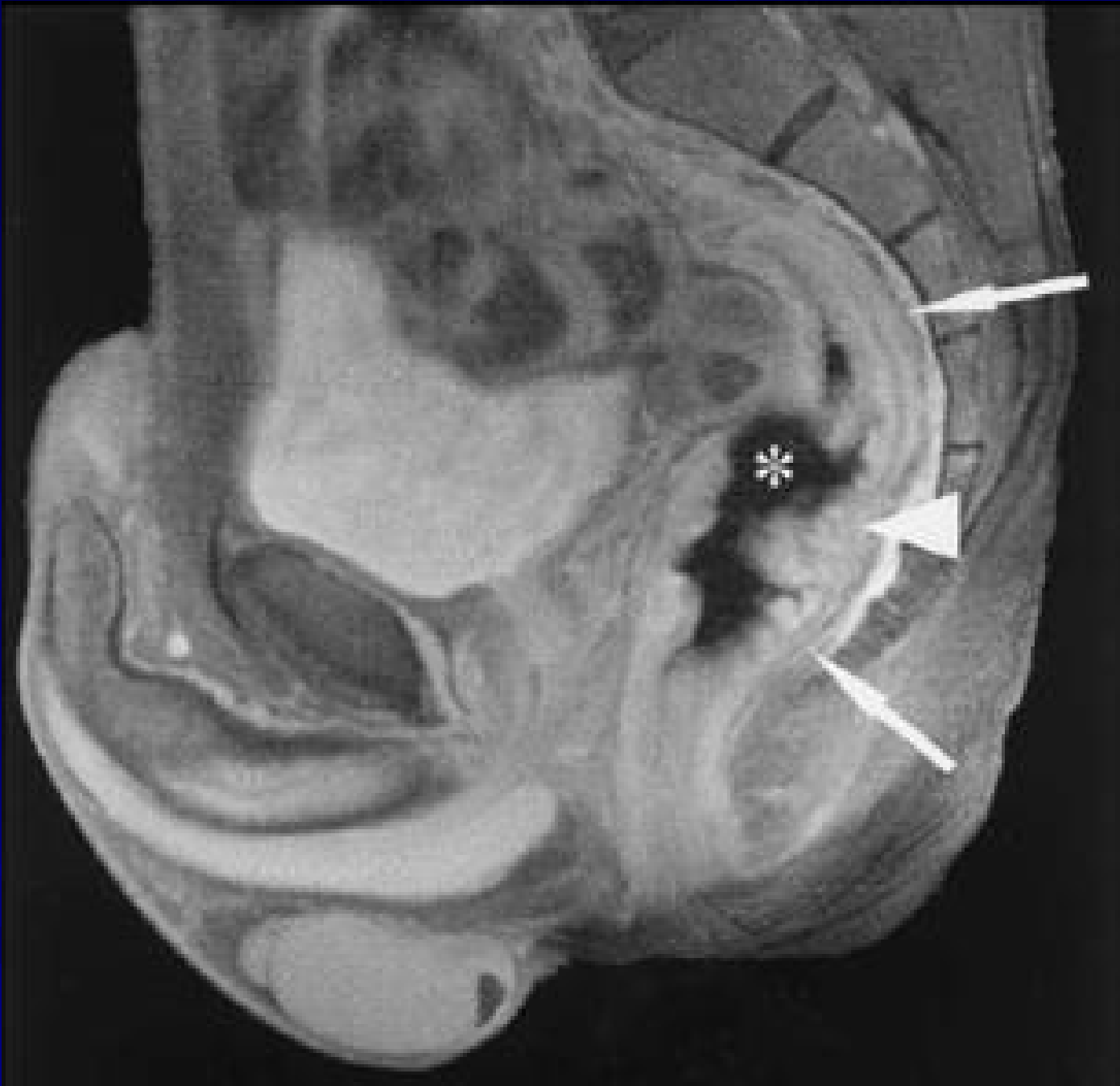


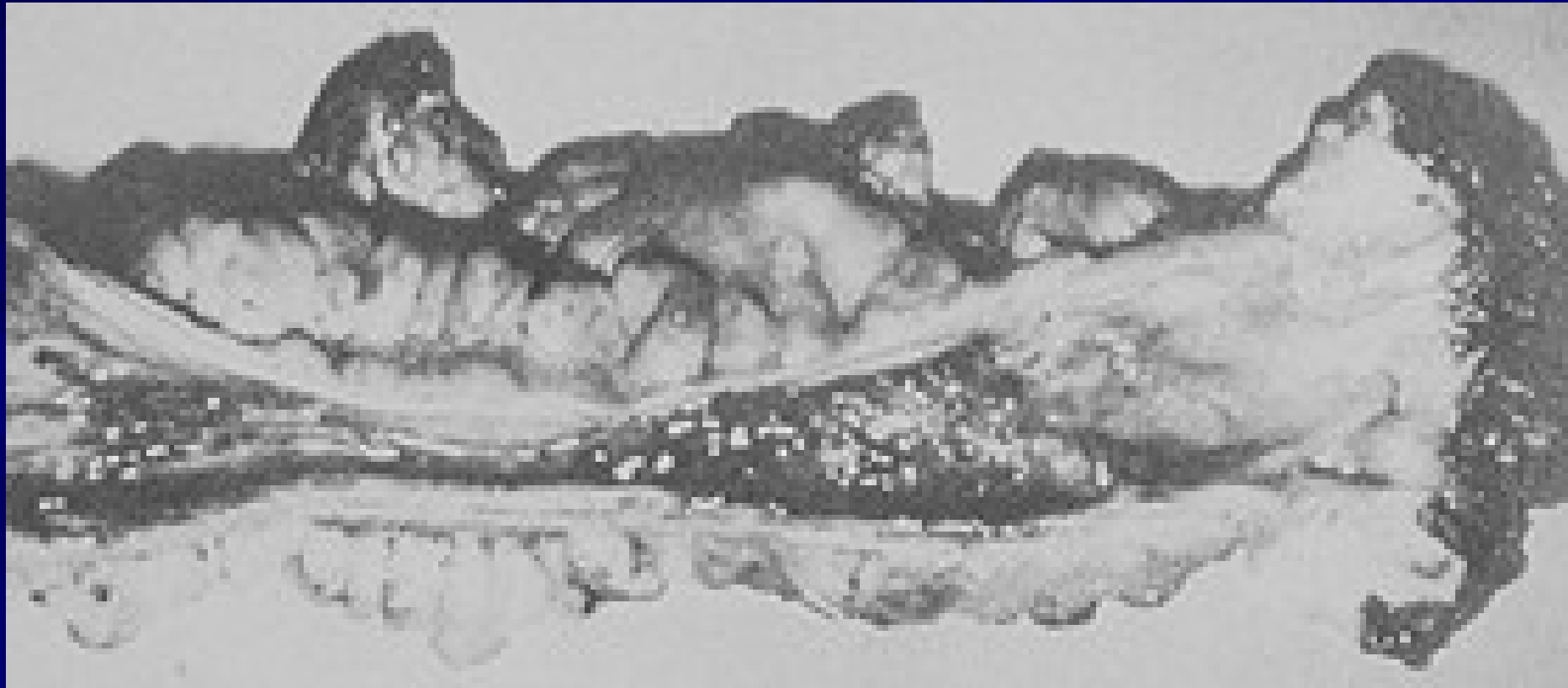
**LGV
Proctitis**



LGV proctitis and ulcer





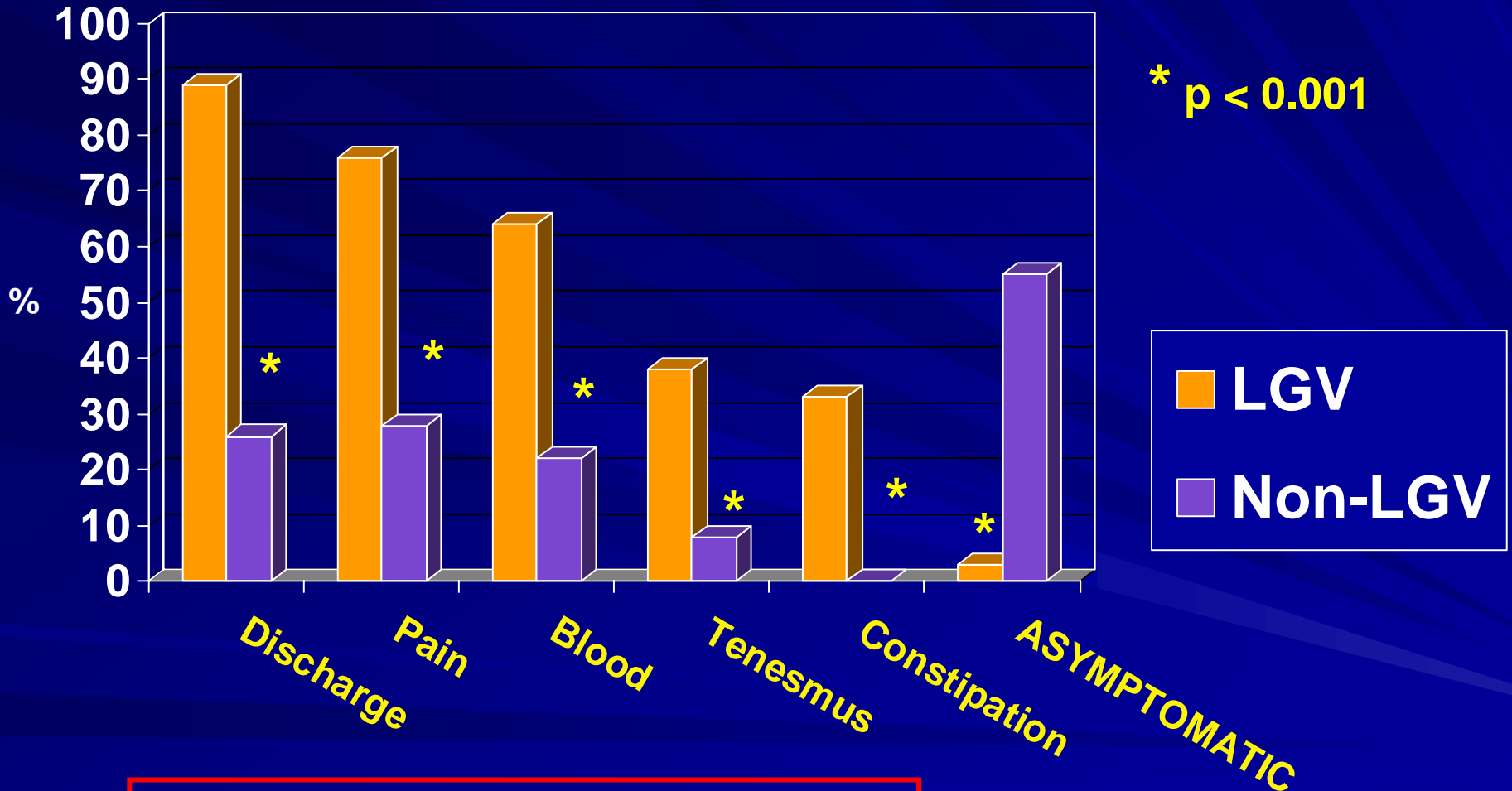


Rectal Stricture - LGV

Risk factors

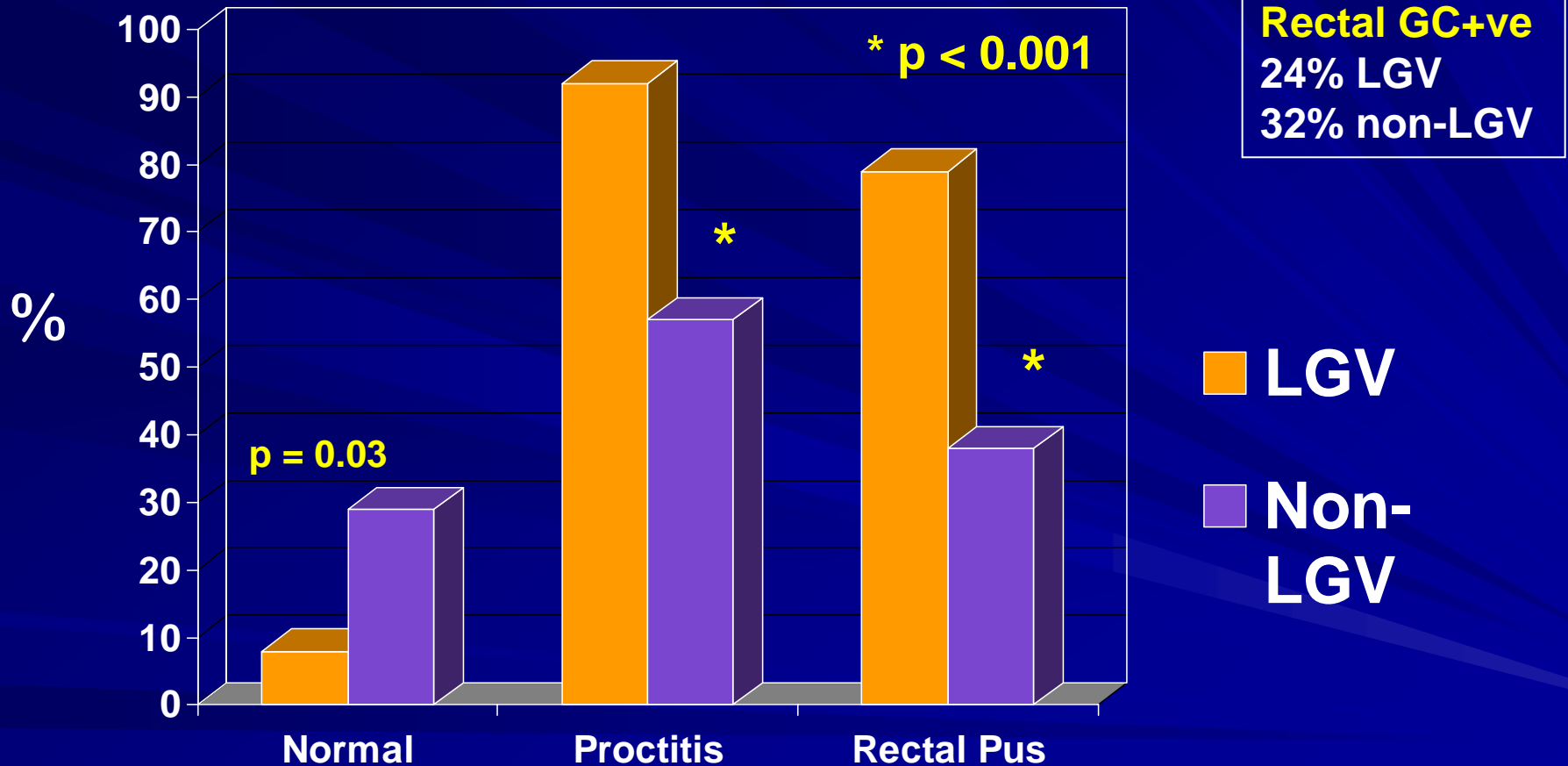
	LGV	Non-LGV	P value
Median age	39	32	0.0001
HIV +ve	60 %	32 %	0.006
Unprotected RAI _{6/12}	82 %	64 %	0.047
Receptive Fisting _{6/12}	22 %	0 %	0.001
Rectal GC	24%	32 %	n.s.

Symptoms in GSTT cohort



HPA: No differences HIV+ve vs. -ve

Proctoscopic findings (%)



GSTT: No differences HIV+ve vs. -ve

LGV Diagnosis: Identification of organism

- Serology, culture and older tests...
- **NAATs**
 - Swab from ulcer, rectum, bubo pus
- **STBRL** types CT⁺ samples using LGV-specific rtPCR
 - All **L2** serovar so far
- **94%** rectal CT⁺ NAATs confirmed to date

LGV: Histopathological Features

- 12 HIV+ MSM had **endoscopy** and **rectal biopsy**
- Most had suspected diagnoses of inflammatory bowel disease prior to LGV diagnosis
- **Biopsy findings:**
 - Cryptitis & crypt abscesses common
 - Distortion of crypt architecture not prominent
 - More consistent with an infective aetiology
- No pathognomonic histology associated with LGV

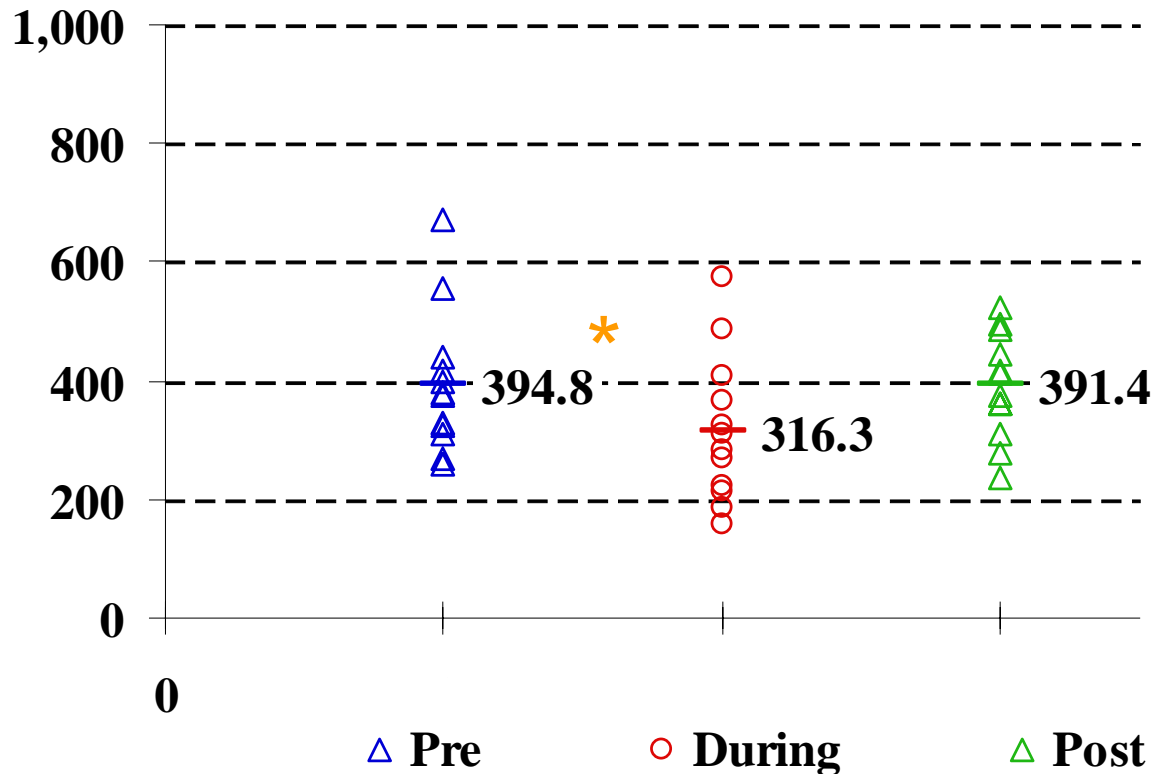
Prevalence of rectal chlamydia?

Lloyd MSM Clinic: 4/05-4/06

- **29/395** rectal samples tested
chlamydia positive = **7.3 %**
 - c.f. urethral chlamydia +ve = **2.8%**
- 6 were LGV = **1.5 %**
- 23 were Non-LGV = **5.8 %**
- Rectal CT in patients without symptoms of proctitis = **4.9 %**
- Urethral CT in patients without symptoms of urethritis = **1.1 %**

Mean CD4 count pre & post LGV infection in HIV+ MSM not on HAART

n = 12

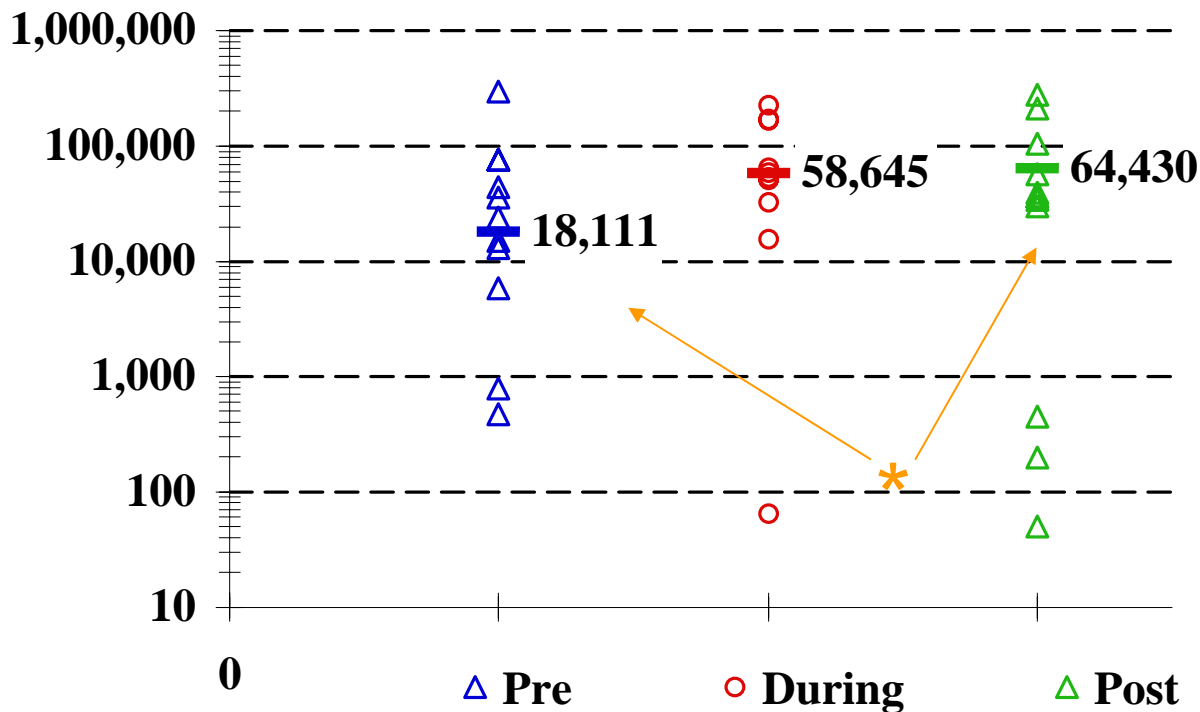


* Difference = statistically significant ($P = 0.017$)

Pre- and post-CD4 counts were not significantly different.

Mean HIV viral load pre & post LGV infection in HIV+ MSM not on HAART

n = 12



* Difference = statistically significant (P = 0.0361)

Pre- and during viral loads were not significantly different.

(P = 0.0737).

Treatment efficacy

- NO RCTs in database
- 3/52 **doxycycline 100mg bd** achieves “symptomatic resolution”
- Use of **azithromycin** for LGV and non-LGV ?evidence ?dose

Treatment efficacy

- Single dose **azithromycin 1g** for **non-LGV rectal chlamydia**
- N = 101; 91% asymptomatic (anorectal)
- 86/101 Rx with stat dose AZI
- TOC in 75/86 - >3/52 since Rx
- **9/75** positive = **12% Rx failure**
- ?reinfection ?TOC too soon

■ Steedman N, McMillan A - BASHH May 2007

Clinical review: LGV

- **45** LGV patients attended for follow-up assessment
- Resolution of proctitis symptoms had occurred in all men, taking up to **eight weeks** in long-standing infections

Treatment & follow-up

■ All LGV cases treated:

doxycycline 100mg bd

for at least 2 weeks (most 3/52):

- Well-tolerated
- All completed course (self-reported)
- No discontinuations

Test of cure

- **36/45** (80%) had at least one rectal swab for *C. trachomatis* at follow-up
- Median of **5 weeks** (range 1- 43 weeks) after completion of doxycycline therapy
- All tested **negative**
- Two men remained symptomatic from **anal fistulae** complicating their LGV and these required surgical management

Relapse or reinfection?

- 5/52 men presented with repeat episodes of symptomatic proctitis 2-8 months after treatment of their initial LGV
- All had been symptom-free for at least 2 months since completing treatment
- None had attended scheduled follow-up
- All reported high risk sexual practices during the period since their initial treatment
- Each had a positive rectal *C. trachomatis* test for their new episode

Relapse or reinfection?

- Three were confirmed as **LGV**
- Two were typed as **non-LGV serovars**
- The three LGV cases responded to 3 weeks further doxycycline treatment
- One **LGV** case returned for follow-up and had a negative rectal chlamydia swab 4 weeks after treatment

Control of LGV

- Recognition of LGV as cause of **proctitis**, **anogenital ulcer** & **inguinal bubo** both within and outside of GUM
- **More info** needed on:
 - Asymptomatic LGV
 - Urethral LGV
 - LGV GUD/inguinal syndrome
 - Fists, toys, enemas etc. as vectors of infection
- Improved access to rectal chlamydia testing
- Behavioural interventions
- Importance of venues & core groups

Acknowledgements

- GSTT clinic & laboratory staff
- STBRL/HPA Colindale
- UK LGV incident group