

HIV and General Medical Presentations of STIs

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Topics

- HIV
- Syphilis
- Disseminated Gonococcal Infection (DGI)
- SARA
- LGV
- Enteric STI
- Hepatitis
- Herpetic Encephalitis

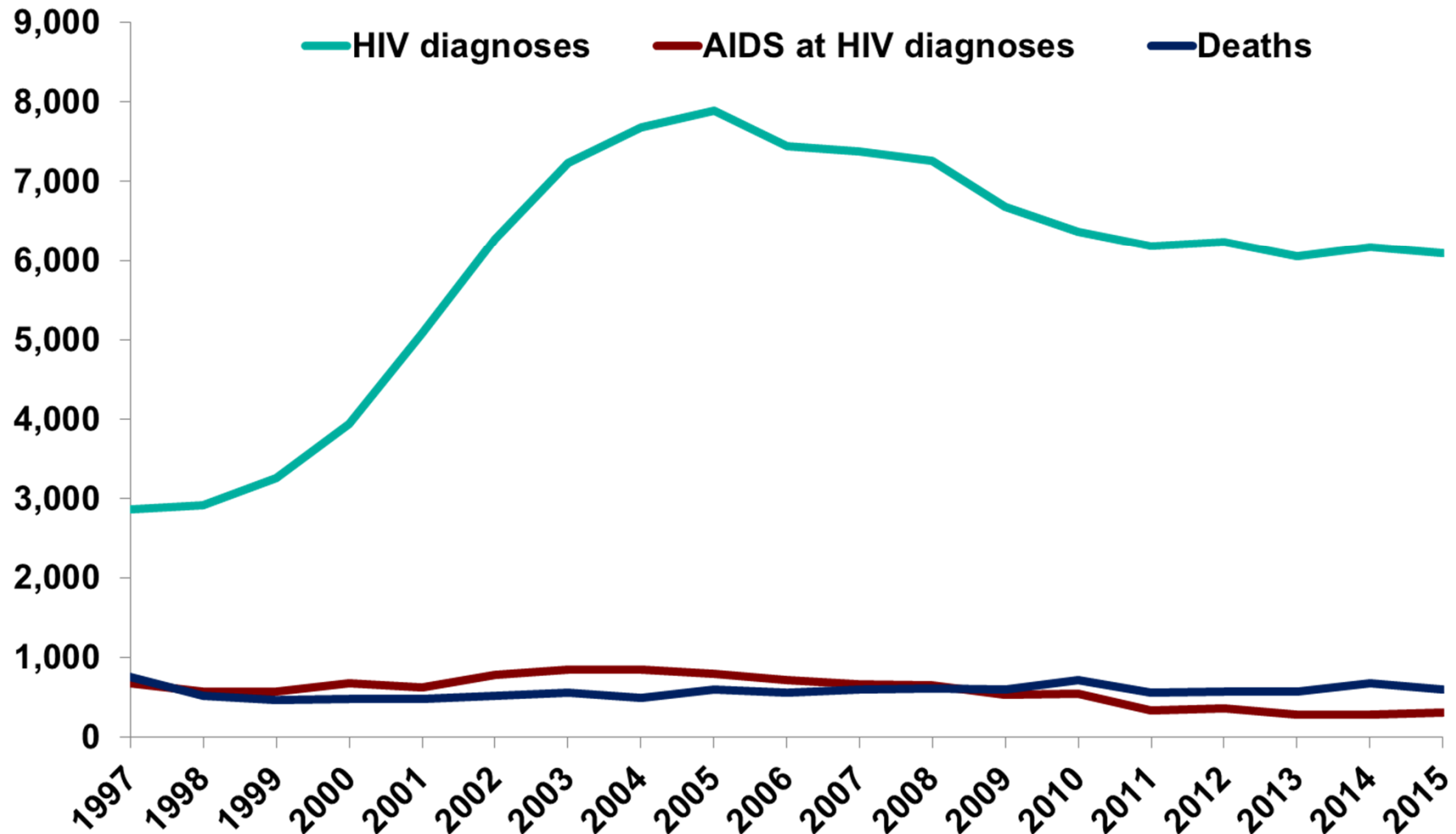
HIV Epidemic --- What has worked

- ART availability
- ART for pregnant women
- Male circumcision in Africa
- Early start of treatment
- PEP
- PrEP



Number of people newly diagnosed with HIV and AIDS, and all-cause deaths among people with HIV in the ART era:

United Kingdom, 1997 - 2015



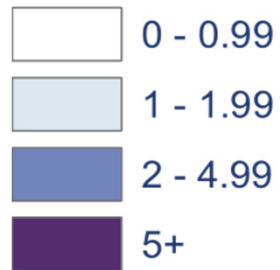
AIDS at HIV diagnoses is within 3 months of HIV diagnoses.



Public Health
England

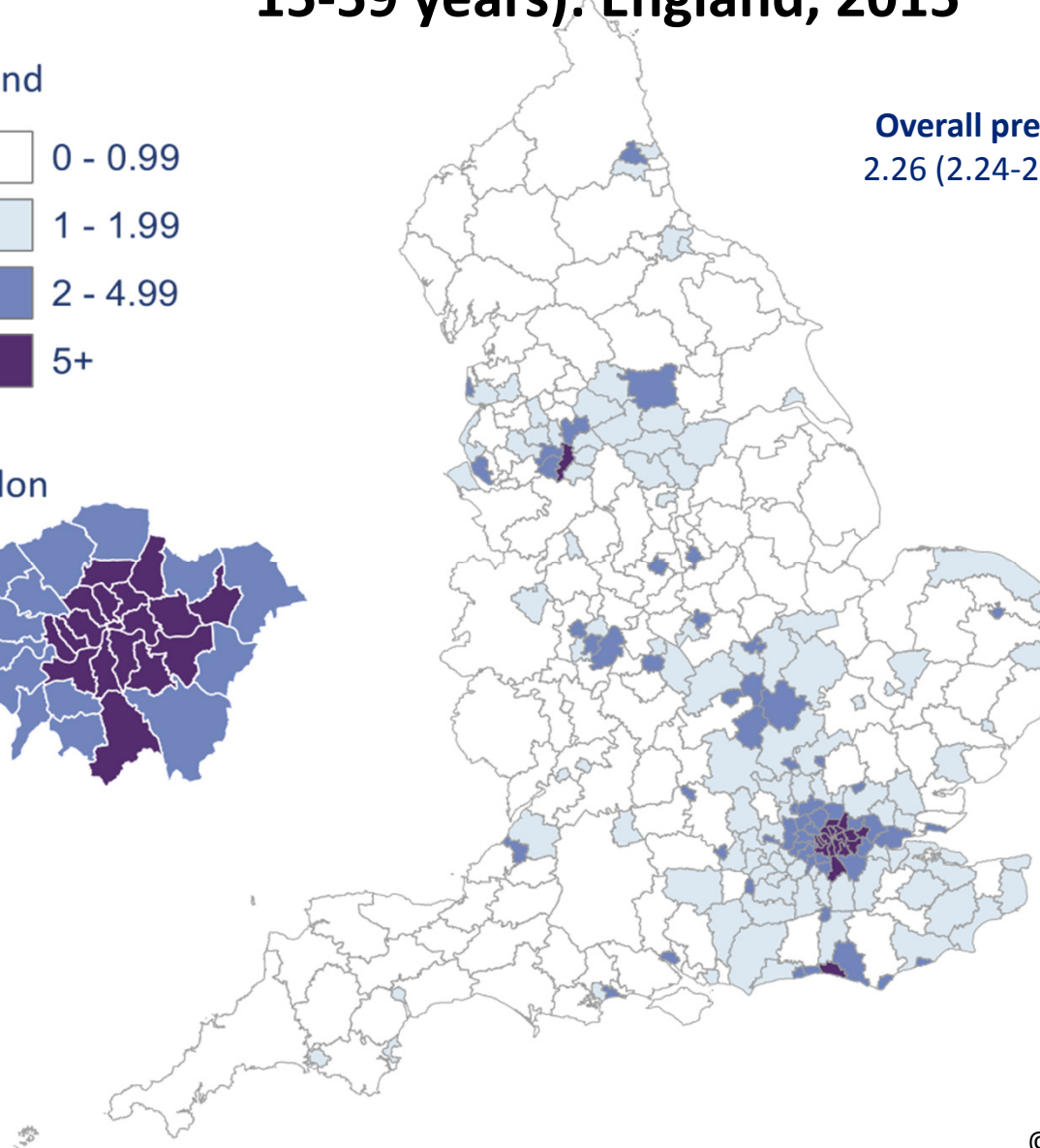
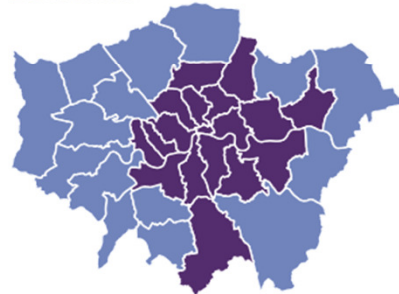
Diagnosed HIV prevalence (per 1,000 population aged 15-59 years): England, 2015

Legend



Overall prevalence rate:
2.26 (2.24-2.27) per 1,000

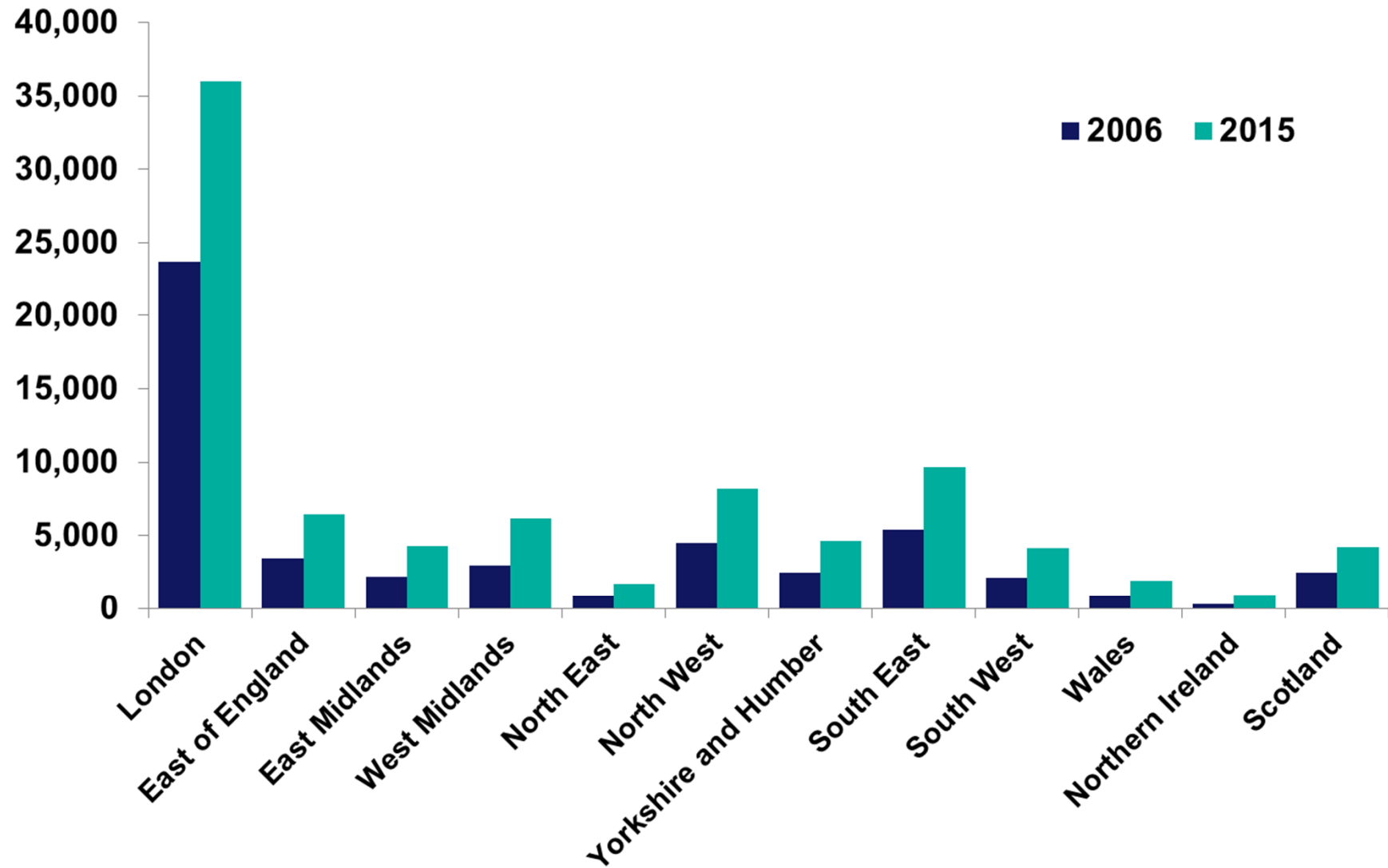
London





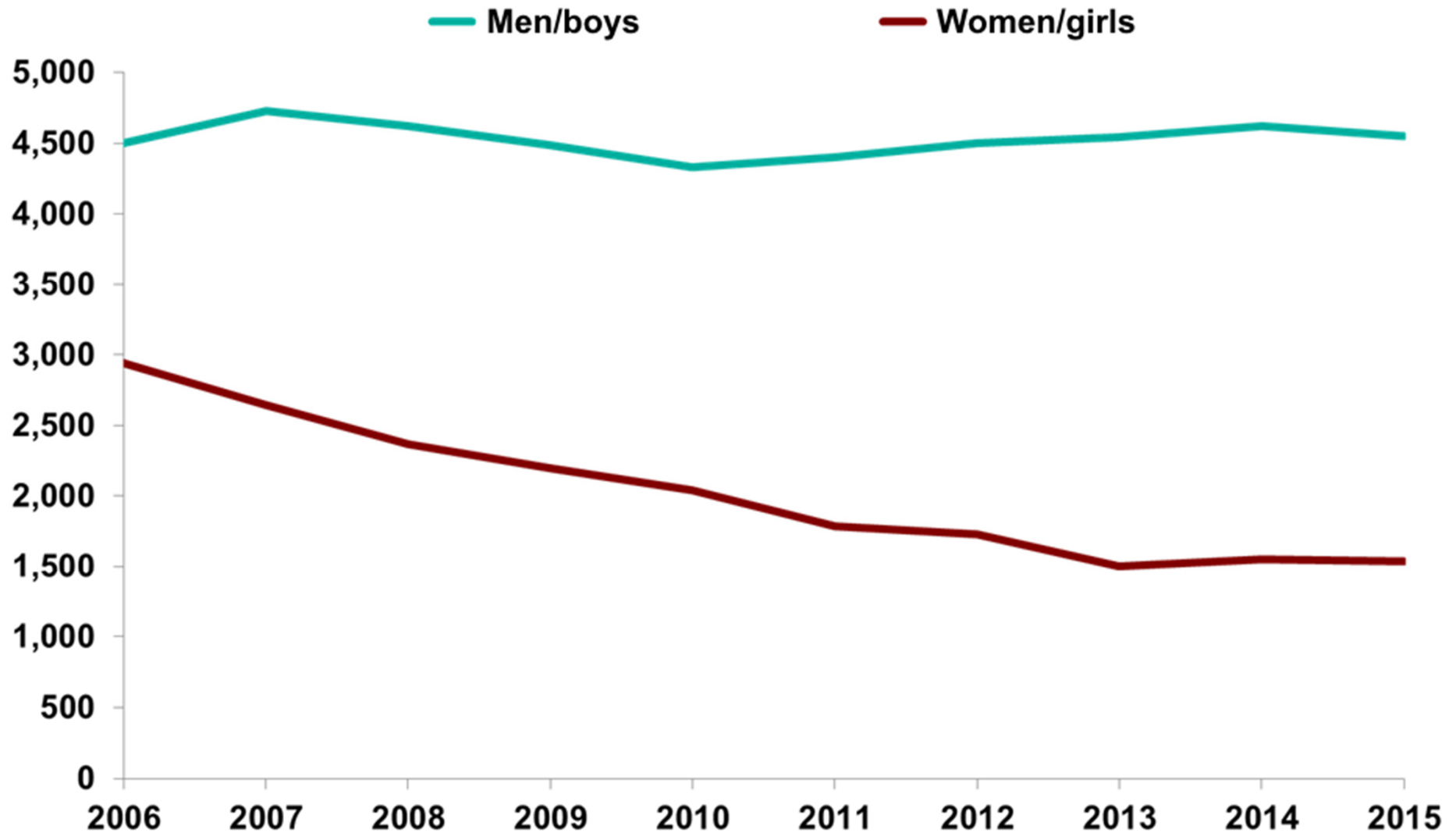
Public Health
England

Number of people who accessed HIV care by PHE centre of residence: United Kingdom, 2006 and 2015



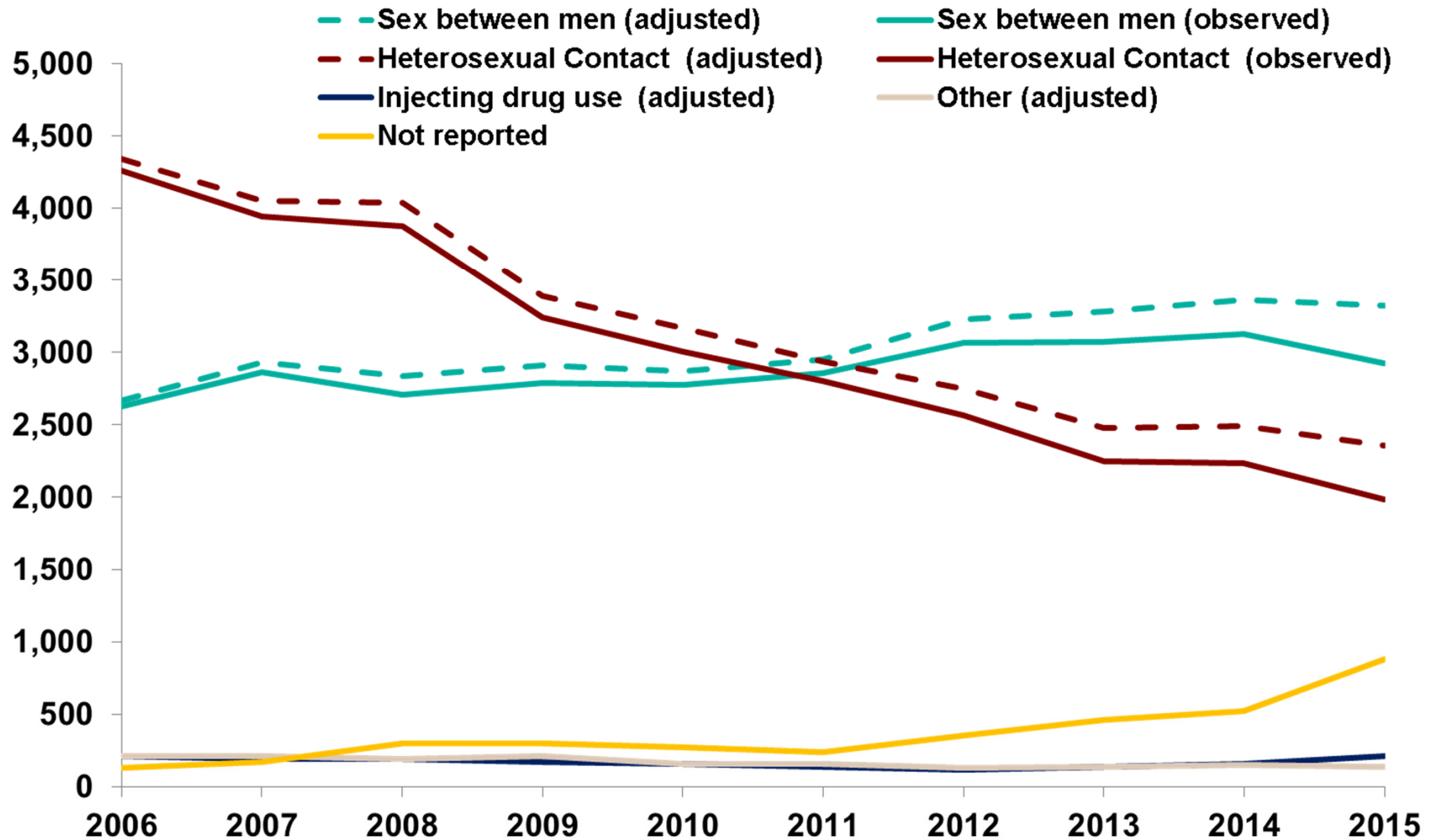


Number of men/boys and women/girls newly diagnosed with HIV: United Kingdom, 2006 - 2015





Number of people newly diagnosed with HIV by exposure category: United Kingdom, 2006 - 2015



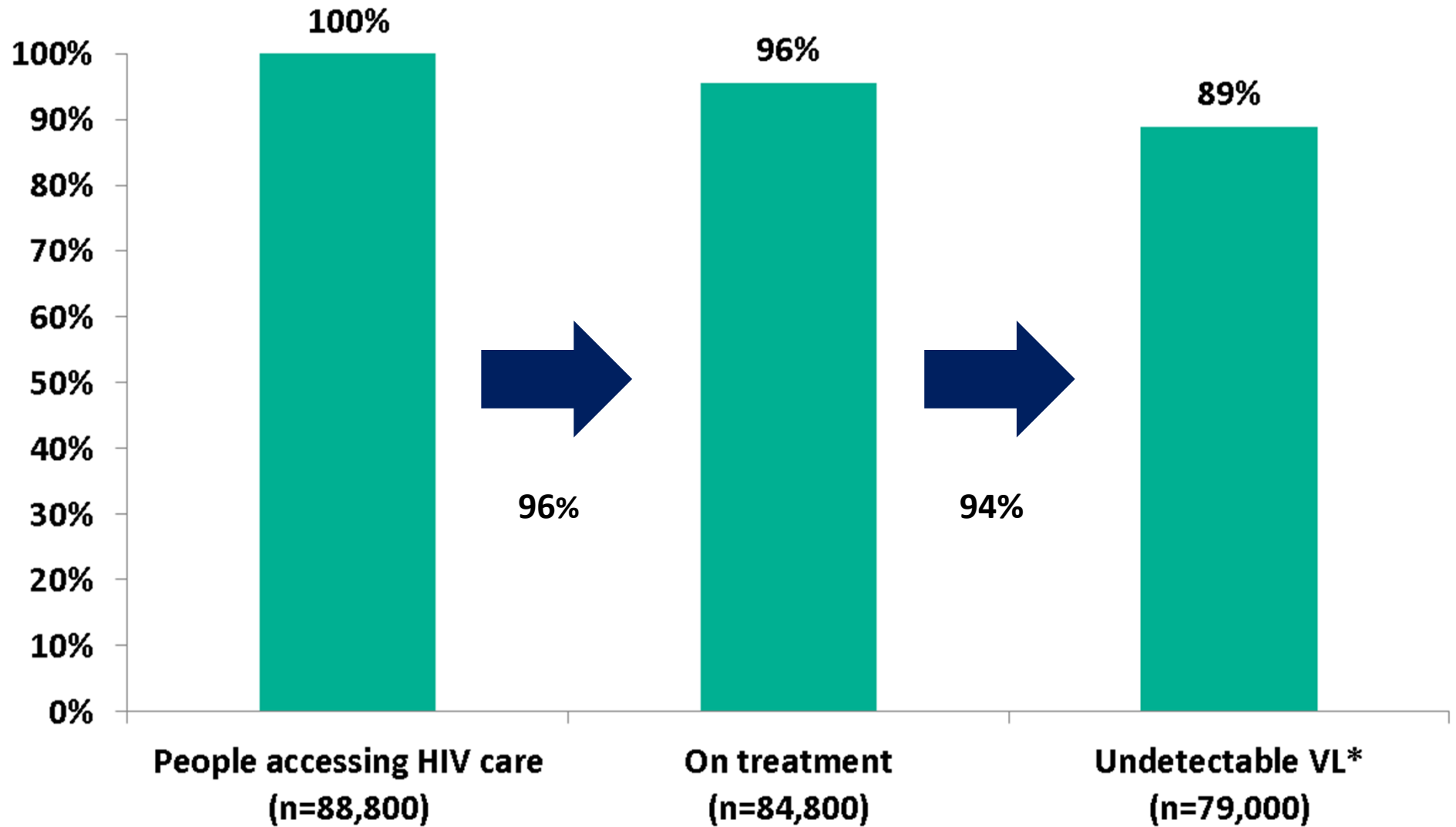


Estimated number of people living with HIV, undiagnosed rate and prevalence rate by exposure category: UK, 2013

Exposure category	Total HIV infection (credible interval)	% Undiagnosed (credible interval)	HIV prevalence per 1,000 population (credible interval)
Men who have sex with men	43,500 (40,200, 48,200)	16% (10, 25%)	59 (52, 68)
People who inject drugs	2,400 (2,100, 2,600)	10% (6, 16%)	6.7 (5.5, 8.3)
Heterosexuals	59,500 (54,700, 66,00)	31% (25, 38%)	1.6 (1.5, 1.8)
Men	24,000 (21,600, 27,400)	34% (27, 42%)	1.3 (1.2, 1.5)
<i>Black African ethnicity</i>	13,600 (11,800, 16,700)	38% (29, 50%)	41 (35, 49)
<i>Non black-African ethnicity</i>	10,200 (9,100, 12,300)	27% (18, 39%)	0.6 (0.5, 0.7)
Women	35,500 (32,700, 28,900)	29% (23, 36%)	1.9 (1.7, 2.0)
<i>Black African ethnicity</i>	25,100 (22,400, 28,900)	31% (23, 40%)	71 (63, 81)
<i>Non black-African ethnicity</i>	10,300 (9,400, 11,700)	23% (16, 32%)	0.6 (0.5, 0.6)
Total	107,800 (101,600, 115,800)	24% (20, 29%)	3.7 (3.5, 4.0)



Continuum of HIV care: United Kingdom, 2015



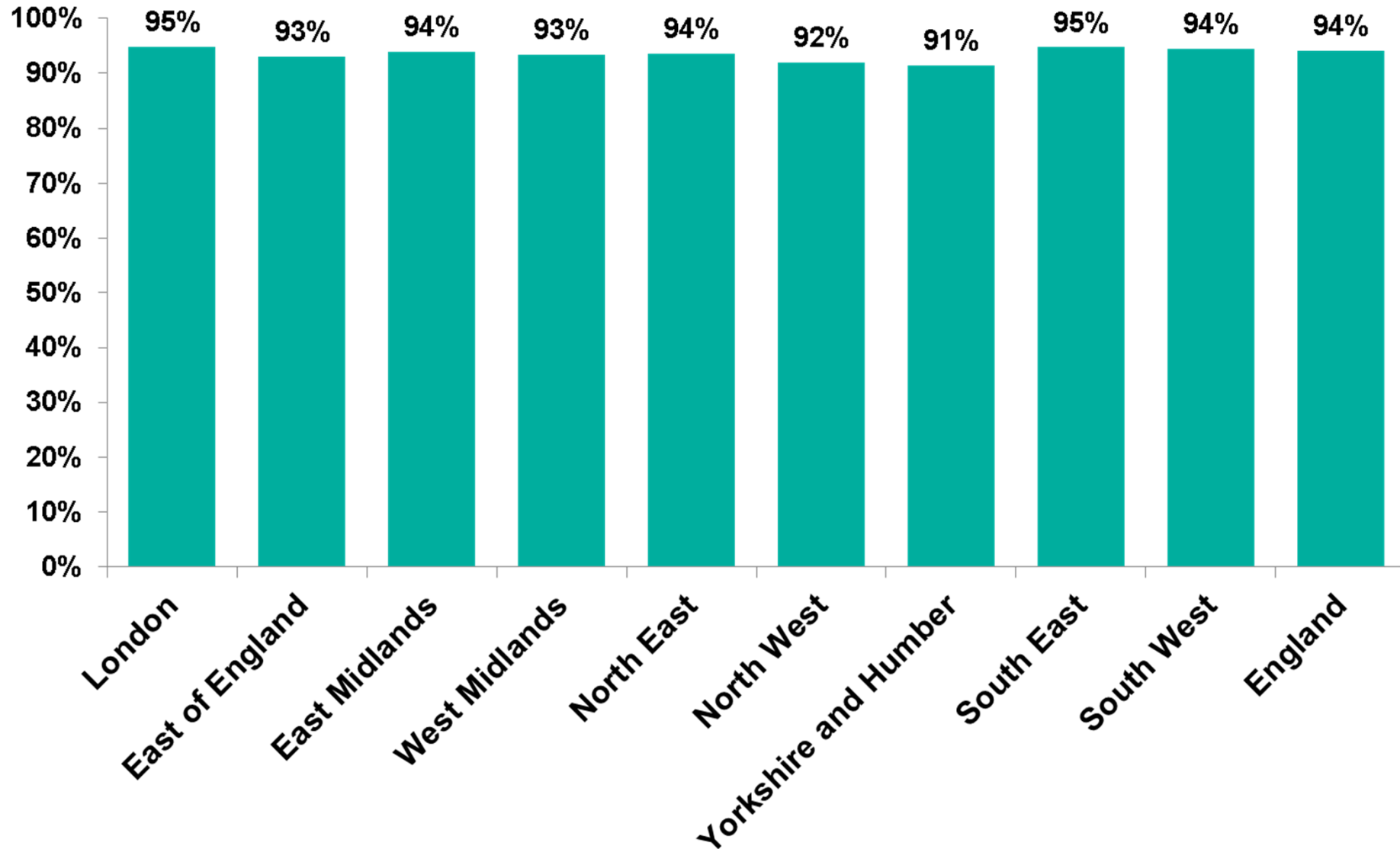
*Viral load (VL) ≤ 200 copies/mL

Excludes those with a missing viral load (14%)



Public Health
England

Proportion of people on antiretroviral therapy with a viral load <200 copies/mL: England, 2015



Excludes those with a missing viral load (14%)

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What is Late Diagnosis

- If CD4 count < 350 == Late diagnosis
- If CD4 count is < 200 === Very late diagnosis
- Currently in NE 35 - 50% of the diagnosis are late diagnosis

2008 CDC Case Definition for HIV Infection: AIDS-Defining Clinical Conditions

- Candidiasis (trachea, bronchia, or lung)
- Candidiasis (esophageal)
- Cervical cancer (invasive)
- Coccidioidomycosis (disseminated or extrapulmonary)
- Cryptococcosis (extrapulmonary)
- Cryptosporidiosis (intestinal, for longer than 1 month)
- Cytomegalovirus disease (other than liver, spleen, or nodes)
- Cytomegalovirus retinitis (with loss of vision)
- Encephalopathy (HIV-related)
- Herpes simplex: chronic ulcers (present for longer than 1 month)
- Herpes simplex: bronchitis, pneumonitis, or esophagitis
- Histoplasmosis (disseminated or extrapulmonary)
- Isosporiasis (intestinal, for longer than 1 month)
- Kaposi's sarcoma
- Lymphoma, Burkitt's (or equivalent term)
- Lymphoma, immunoblastic (or equivalent term)
- Lymphoma, primary of brain
- *Mycobacterium avium* complex, disseminated or extrapulmonary
- *Mycobacterium kansasii*, disseminated or extrapulmonary
- *Mycobacterium tuberculosis*; any site (pulmonary or extrapulmonary)
- *Mycobacterium*, other species or unidentified species, disseminated or extrapulmonary
- *Pneumocystis carinii* pneumonia
- Recurrent pneumonia (≥ 2 episodes in 1-year period)
- Progressive multifocal leukoencephalopathy
- Salmonella (recurrent septicemia)
- Toxoplasmosis (brain)
- Wasting syndrome due to HIV: $>10\%$ involuntary weight loss plus either chronic diarrhea (≥ 2 stools per day for at least 30 days) or chronic weakness and documented fever (for at least 30 days) in the absence of a concurrent illness or condition other than HIV that could explain this finding.

HIV-Associated Malignancies

- Increased risk of:
 - Kaposi sarcoma
 - High grade B cell non-Hodgkin lymphoma
 - Invasive cervical cancer
 - Anal cancer
 - Hodgkin lymphoma
 - Multicentric Castleman's disease
 - Testicular germ cell cancer
 - Non-small cell lung cancer
 - Hepatocellular cancer
 - Other cancers

Why more HIV Testing

- Advantages

- Reduce AIDS
- Reduce patient morbidity and mortality
- Reduce Horizontal and Vertical transmission
- May whip out HIV infection from humans

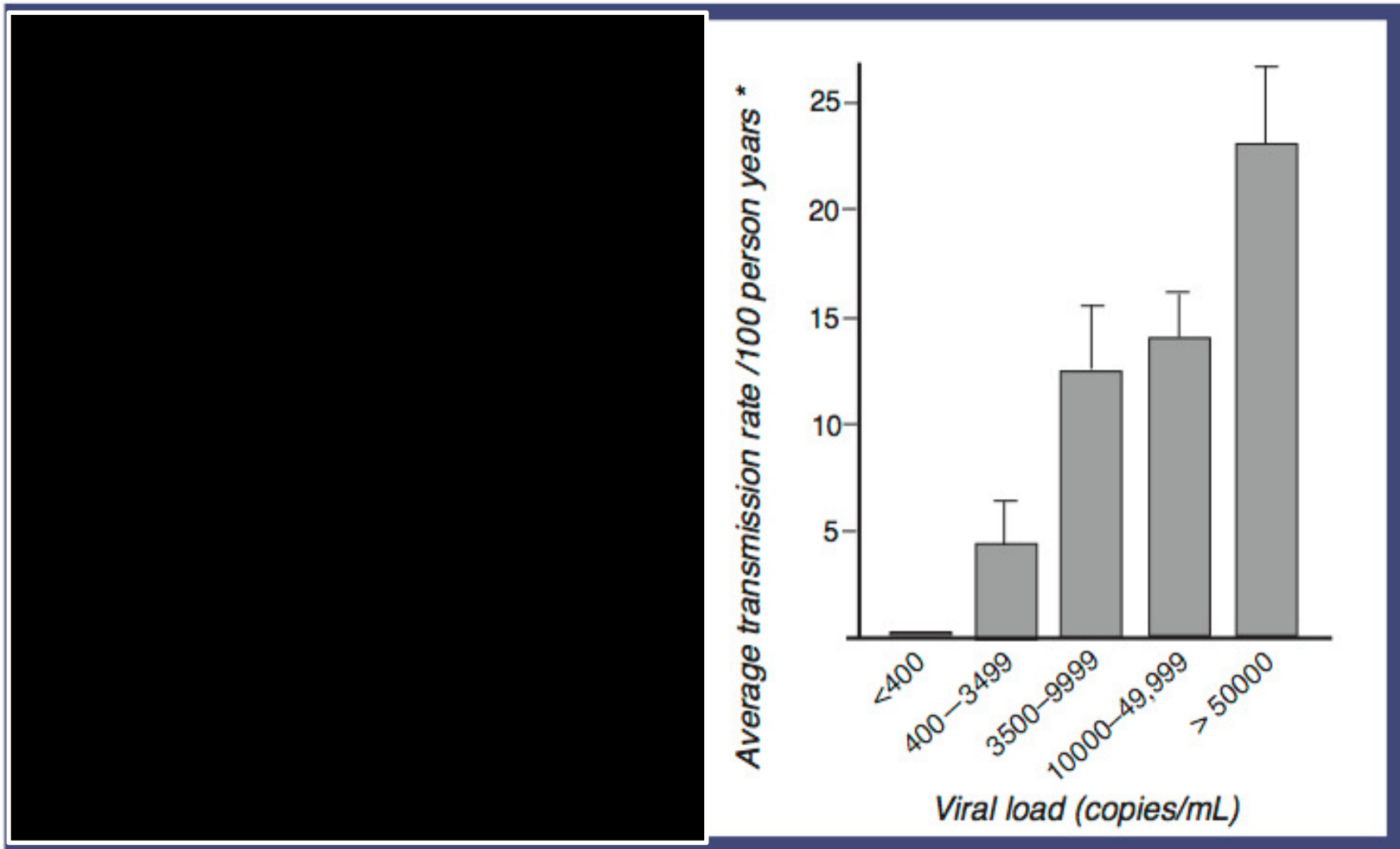
- Disadvantages

- Expensive
- Psychological Issues – trauma of a false positive
- Other specialities may call for funding for extra testing

Consequences of Late Diagnosis

CD4 COUNT	Probability of AIDS	Mortality
> 500	< 2%	0.5%
350 – 500	2 – 4%	0.9%
200 – 350	6 – 9%	1.7%
< 200	13 – 20%	6%

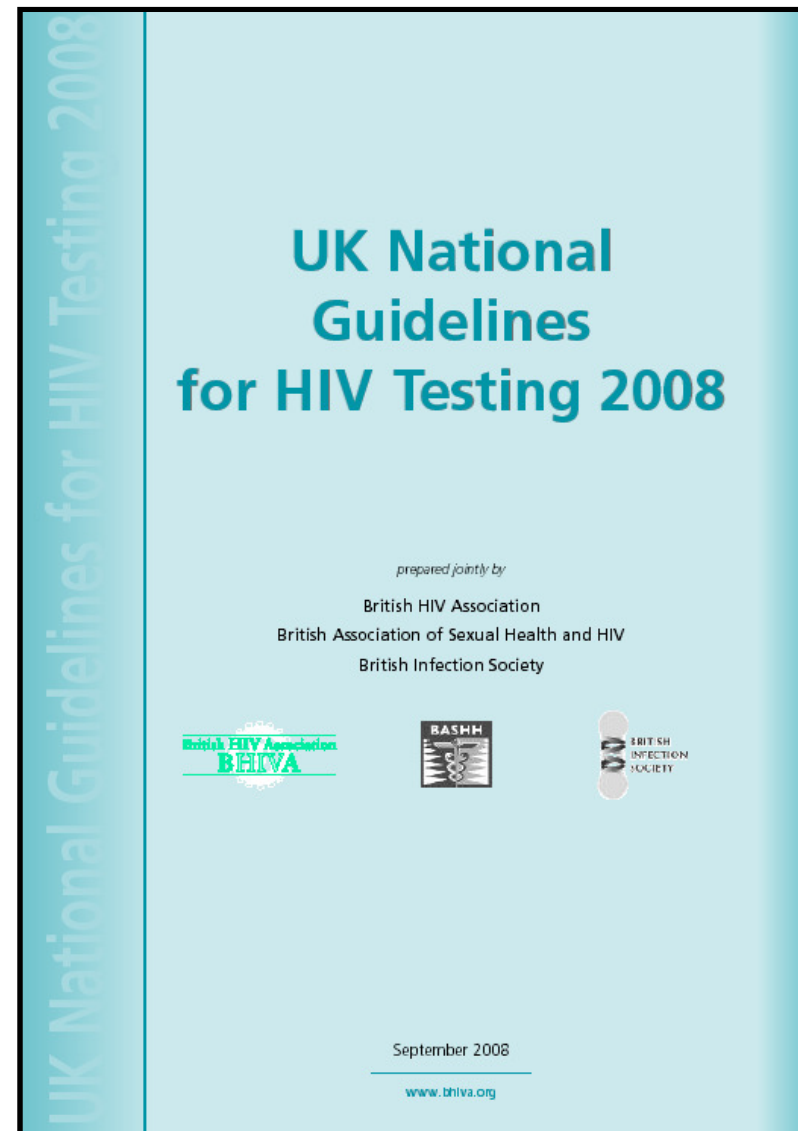
Probability of HIV Transmission



Early Diagnosis enables HIV Prevention



How to Increase HIV Testing



Case Report 1

- Male age 34
- Symptoms started April 2015
- Rectal bleeding/ Anal pain/ constipation/ diarrhoea/ mucousy rectal discharge

- Referred to surgeons January 2016
- Flexi Sigmoidoscopy ---- Haemorrhoids and ulcerated eroded area in the anal canal

Case Report 1

- Haemorrhoidectomy and biopsy ---- showed Treponema Pallidum.
- GUM clinic
- History MSM
- Never had HIV test or STI screen
- Casual Sex in Edinburgh (April 2015)

Case Report 1

- Results
- HIV Type 1 positive
- Syphilis Positive
- Rectal chlamydia positive
- CD4 count ---- 267
- HIV VL ----- 67,450
- **Was this a delayed diagnosis**

Case Report 2

- Mr JPW ---- age 39
- March 2015 --- fever, night sweats, cervical lymphadenopathy, skin rash
- Seen by GP
- Diagnosed as viral infection
- Symptomatic treatment ---- recovered

Case Report 2

- Attended PRIDE July 2015
- STI screen
- HIV and Chlamydia positive
- CD4 count ---- 625 (23%)
- HIV VL --- 10,761
- Started treatment ---- STRIBILD (Sept 2015)
- Latest CD4 ---- 700
- Latest VL --- < 20 (undetectable)
- **Missed Diagnosis!!!!**

Where is most HIV diagnosis
missed ---- BHIVA 2010 Audit

Where is most HIV diagnosis missed --- - BHIVA 2010 Audit

- Gastroenterology (unexplained bowel symptoms)
- Haematology (blood dyscrasia)
- General Practice (flue like / viral illness / unexplained lymphadenopathy)



14 European countries

Terrence
HIGGINS
TRUST



1,166
couples



one HIV positive
and on treatment,
one HIV negative



58,000
acts of sex
without condoms

ZERO

HIV transmissions

BHIVA guidelines for starting Treatment

- CD4 count < 350
- HIV and Hepatitis B/C co-infection
- HIV related symptoms
- AIDS
- TASP (Treatment AS Prevention)
- HIV seroconversion illness
- Discordant Relationship
- Patient wishes

Simple method of assessing risk of HIV Infection

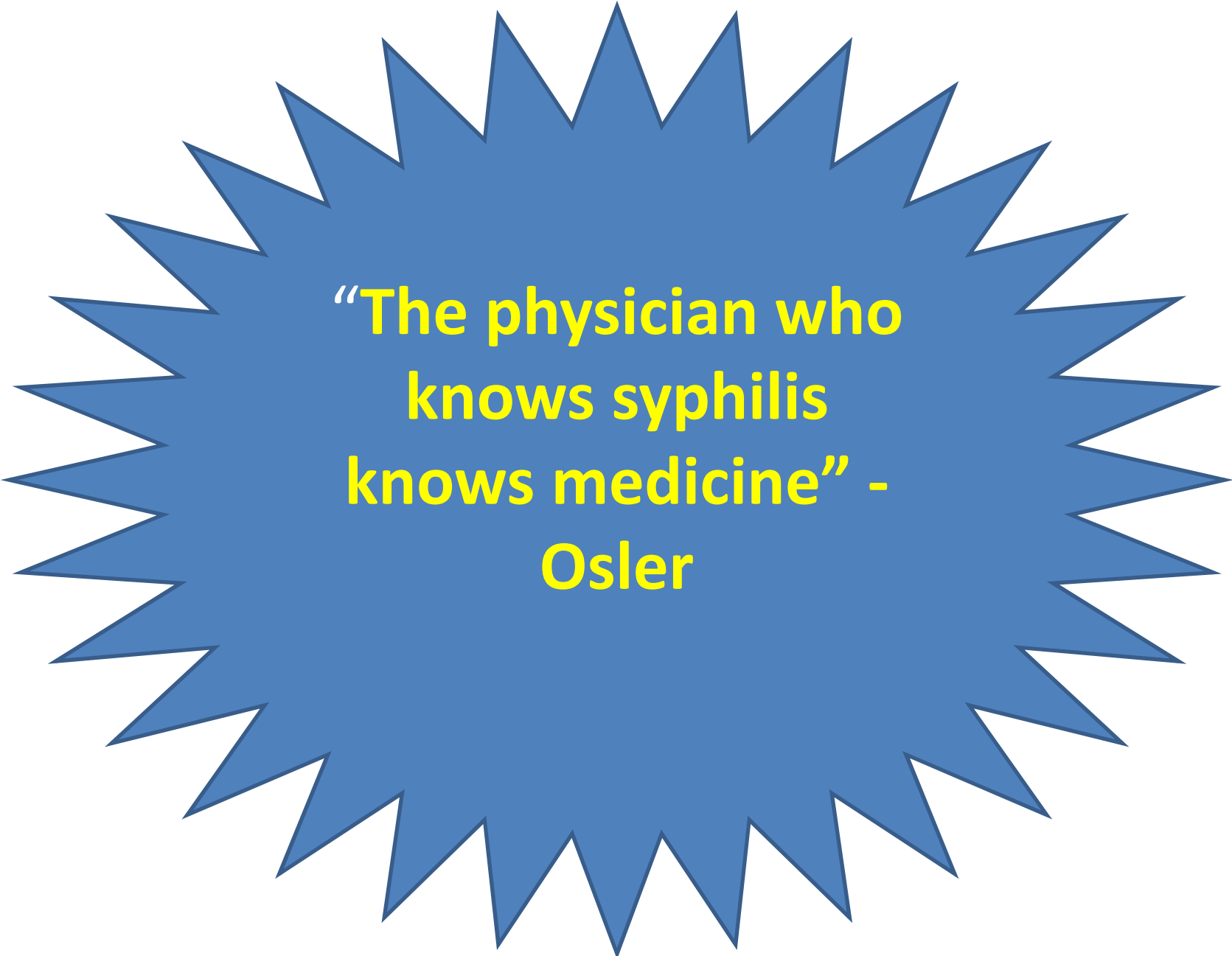
- Ask if patient has sex with men, women or both. **If gay do an HIV test.**
- Ask if patient has / had sex with someone from high risk country or comes from a high risk country. **If yes, do an HIV test.**

Simple method of assessing risk of HIV Infection

- Ask if patient is a past or current IVDA.
- **If yes do an HIV test.**

- Ask if patient has had sex with a sex worker, received blood transfusion, injections from contaminated needles or had unprofessional tattoos.
- **If yes, do an HIV test.**



A blue starburst shape with many sharp points, centered on a white background. Inside the starburst, the text is written in a bold, yellow, sans-serif font.

**“The physician who
knows syphilis
knows medicine” -
Osler**

National Syphilis Epidemiology

- Majority of diagnoses of infectious syphilis are in MSM (around 75%)
- Median age in males is 36 years
- Median age in females is 28 years
- Two fifths of female cases <25 years old

Syphilis Classification

Early Infectious syphilis (first 2 years of infection)

Primary	9 – 90 days after infection
Secondary	6 – 12 weeks after infection --- may last for 2 years
Early latent	<2 years

Clinical presentation

Primary

- Characterised by ulcer (chancre) and regional lymphadenopathy
- Chancre classically in anogenital region, single, painless, indurated with clean base
- Can be multiple or other atypical presentation, including asymptomatic

Secondary

- Characterised by multisystem involvement within first two years of infection
- Often a rash (typically often affecting palms/soles), can be mucocutaneous lesions, lymphadenopathy, patchy alopecia, uveitis, meningitis, cranial nerve palsies, hepatitis, splenomegaly
- Hearing impairment and vertigo: neuritis (mimics Meniere's syndrome).

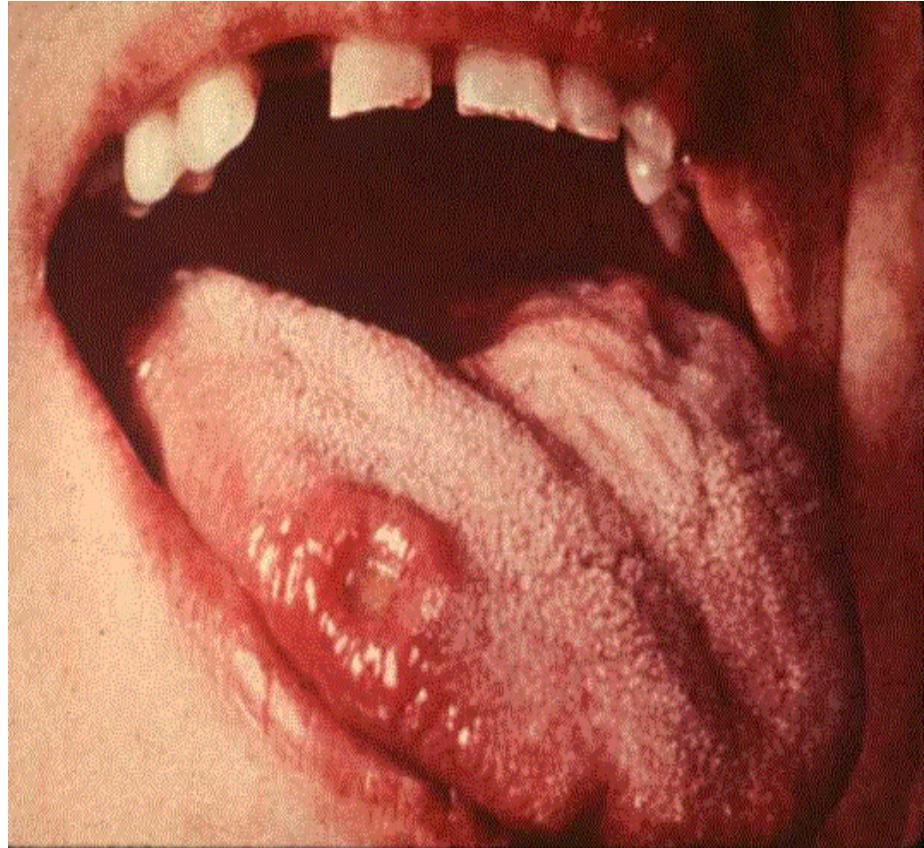
Classical primary chancre



Vulval Primary Chancre



Primary Chancre on tongue





Secondary
Syphilis
Rash





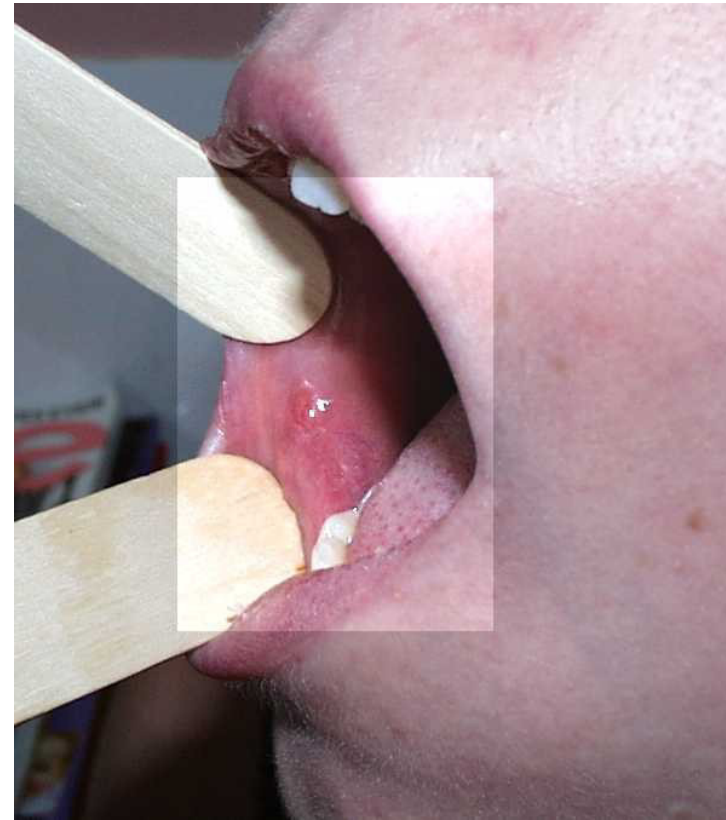
Patchy alopecia



Snail track ulcers



Mucosal patches



Secondary syphilis

Visual symptoms: episcleritis; uveitis; iritis; chorioretinitis; optic neuritis and perioptic neuritis.



Condylomata Lata



Late Syphilis --- Late Latent

- Cardiovascular
 - Syphilitic aortitis
- Neurosyphilis
 - Meningitis
 - Tabes dorsalis
 - Paresis
- Gummatous
 - Formation of chronic gummas

Syphilis Tests

- Direct identification
 - Dark ground microscopy
 - PCR swab
- Serological tests
 - Syphilis screening test (STS)

Diagnosis - serology

- Non treponemal (non specific) tests
 - VDRL
 - RPR
- Treponemal (specific) tests
 - TPHA
 - TPPA
 - EIA
 - FTA-Abs
 - IgM EIA

Disseminated Gonococcal Infection

- 0.5 - 3 % of gonorrhoea cases
- Commoner in women.
- Bacteraemia probably begins 7 to 30 days after infection

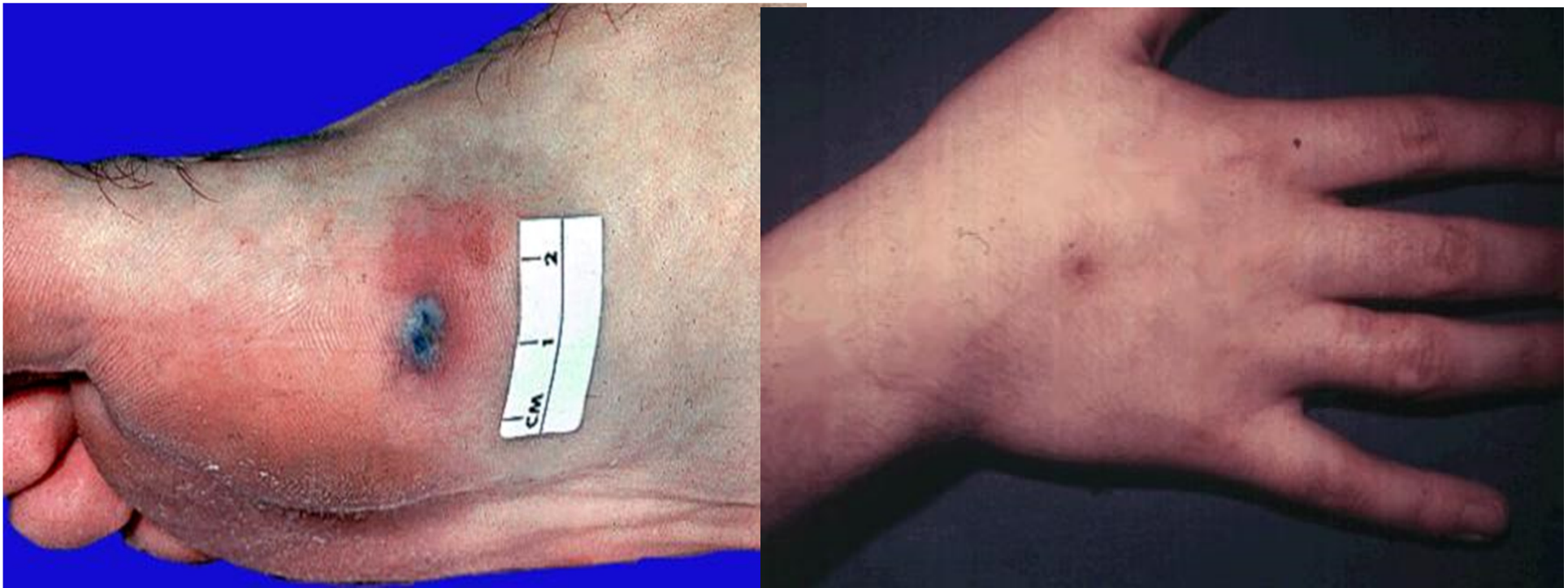
Clinical Features

- Joint pain ---- septic arthritis
- Tenosynovitis
- Skin lesions
- Conjunctivitis

- Meningitis (< 25 cases in literature)
- Endocarditis (1 – 3% of DGI)
- Hepatitis
- Fitz-Hugh Curtis Syndrome
- Abscess formation

Skin lesions

Tender necrotic pustule on an erythematous base



Tenosynovitis - 68%



DGI - Diagnosis

- Clinical presentation
 - index of suspicion
 - systemic illness milder than with meningococcal septicaemia
 - up to 40% afebrile
- Microbiological (Culture and PCR)

DGI - Diagnosis

- Microbiological
 - Joint aspirate culture +ve in 30-40%
 - Blood culture +ve in 20-30%
 - less commonly from skin lesions
- Overall <50% +ve from joint, blood or skin lesions

DGI - Diagnosis

- Microbiological
- >95% +ve from genital swabs
- N.B
- +ve genital and -ve extra genital results with clinical features = probable DGI

DGI - Treatment

- Refer to ID and Sexual Health
- IV / IM Ceftriaxone + Azithromycin
- STI screen

Chlamydia

- Sexually Acquired Reactive Arthritis (SARA)
- Conjunctivitis
- Pneumonitis
- Infertility
- Prostatitis
- Epididimo-orchitis
- Fitz – Hue Curtis Syndrome (peri-hepatitis)

SARA

- Chlamydia (35 – 70%)
- Gonococcus (16%)
- Ureaplasma urealyticum

- M > F ---- 10:1
- HLA-B27 ---- 50x more likely to get SARA

- Immune response to urogenital organisms at distant sites

HLA-B27

- Ankylosing spondylitis : 90-95%
- Reiter's disease : 70-85%
- Psoriatic Arthritis : 54%
- Inflammatory Bowel Arthritis : 50%
- Acute Anterior Uveitis : 52%

- Europeans : 7-10%
- Northern Scandinavia : 26-50%
- Blacks : <2%

Clinical Symptoms

- Young adults (usually 18-50 years)
- Usually starts 10-30 days after new sexual contact
- Most initial episodes resolve in 12 weeks
- At least 50% recur - from 3 months to 36 years

Clinical Symptoms

- Arthritis (asymmetrical, 1 to 5 lower limb joints, rarely upper limbs)
- Urethral discharge
- Enthesitis / Fascitis (40%)
- Tenosynovitis (30%)
- Dactylitis (16%)
- Sacro-ilitis (10%)
- Conjunctivitis (20 – 50%)
- Iritis (2 – 11%)
- Malaise / Fatigue / Fever (10%)

Conjunctivitis - in 30% cases.



- Anterior Uveitis/Iritis- in 8%.
 - Occurs late in initial severe episode or recurrence.
 - Rarely maybe presenting feature



Joints involved in initial SARA

- Knee - 80%
- Ankle - 64%
- Interphalangeal - 36%
- Wrist - 24%
- Tarsometatarsal - 20%
- Hip - 18%
- Sacro-iliac - 10%



Muco-cutaneous lesions

- Keratoderma blennorrhagica : 21%
- Mucosal lesions : 10-39%
- Nail lesions : 9%



Keratoderma blennorrhagica

MUCOSAL LESIONS

- Genital : 25-39%
 - Circinate balanitis in 25% - well-defined red macules with polycyclic margin



NAIL LESIONS

- Nails become opaque, thickened, ridged, brittle
- If severe nails turn brown, are shed from base and shed



VISCERAL LESIONS

- Cardiovascular
 - Pericarditis <5%
 - Myocarditis <5%
 - Aortitis - very rare
 - Thrombophlebitis (deep veins leg) - about 3%
- Pleurisy - about 8%

VISCERAL LESIONS

- Lymphadenopathy in <1%
- Nervous system <2%
 - Meningoencephalitis, peripheral neuropathy, amyotrophic lateral sclerosis
- Amyloid - very rare

Investigations and Management

- Multidisciplinary team management
- GUM / Rheumatologist / Ophthalmologist/
Dermatologist
- **Essential**
- Full screening for STIs, including HIV.
- FBC, CRP, ESR.
- Urinalysis.
- Liver and kidney function tests.

Investigations and Management

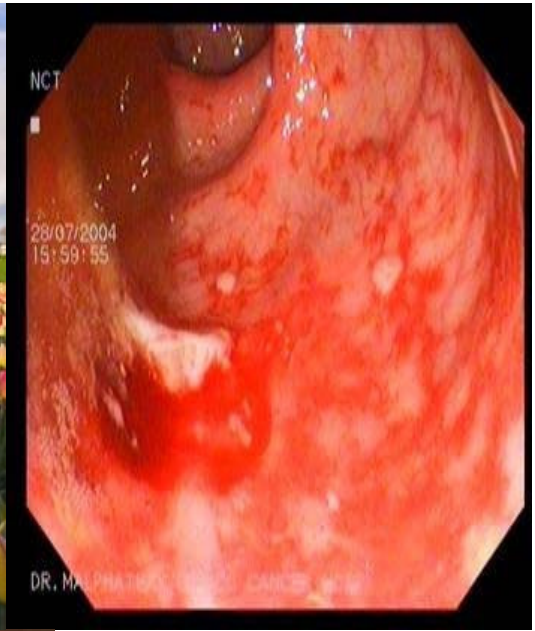
- **Useful**
- HLAB27.
- Xrays of affected joints and sacroiliac joints.
- Electrocardiogram.
- Echocardiogram.
- Ophthalmic evaluation including slit lamp assessment.

Other Investigations

- Blood cultures.
- Stool culture (if enteritic organisms suspected).
- Ultrasonography of affected joints or entheses.
- Magnetic resonance imaging of sacroiliac joints.
- Synovial fluid analysis for cell count, Gram stain, crystals, culture.
- Synovial biopsy.
- Exclusion tests for other diseases with rheumatological features, for example, rheumatoid factor (rheumatoid arthritis), autoantibodies (systemic lupus erythematosus), plasma urate (gout), chest Xray and serum angiotensin converting enzyme (ACE) level (sarcoidosis).

MANAGEMENT

- Urethritis (Doxycycline 100mg bd for 2-3 weeks)
- Eyes
 - Conjunctivitis - self limiting ; no treatment
 - Iritis ; mydriasis (atropine) + Betamethasone
- Arthritis
 - Non-Steroidal Anti-Inflammatories
 - If very severe ; Sulphasalazine, Methotrexate
- Balanitis - self limiting ; usually no treatment but if severe steroid with antimicrobial
- Keratoderma blennorrhagica ; no specific treatment



LGV

Case Report

- Male
- Painful defecation with fresh PR bleeding since Dec 2004
- Abdomen - unremarkable
- PR - craggy, ulcerated area - posterior and immediately above anal canal
 - Proctoscopy: limited view; 2 biopsies taken
- “.. told Mr P”: rectal cancer suspected but inflammatory process is also possible

Biopsy Report

No evidence of malignancy or dysplasia

Moderate to severe active chronic inflammation with focal granuloma formation.

G1

Possibility of inflammatory bowel disease of Crohn's type

Slide 81

G1

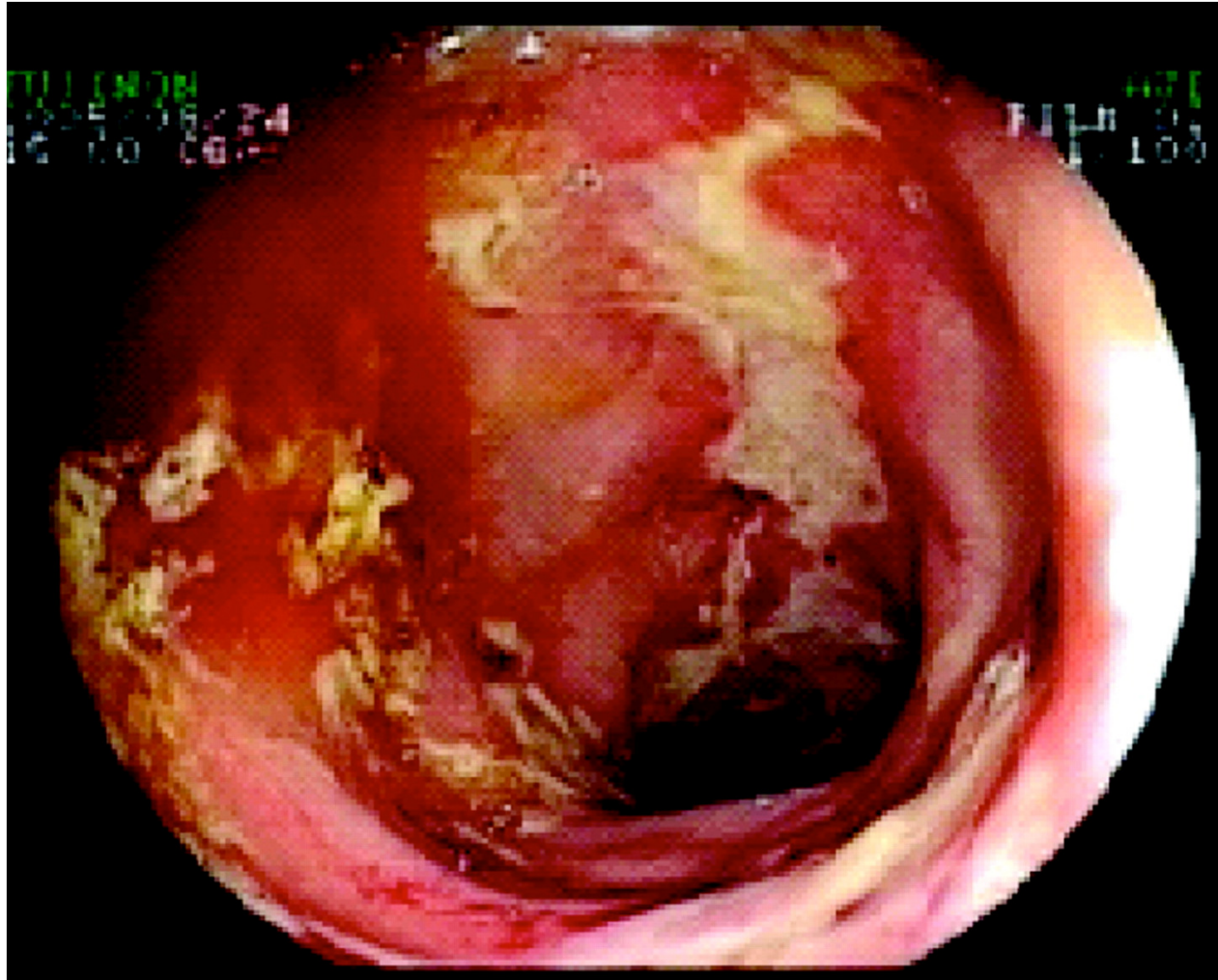
occasional crypt abscess

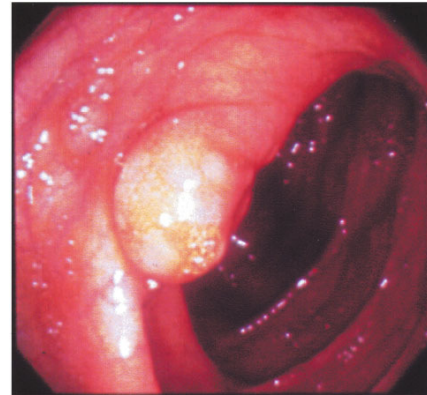
GUM, 11/06/2006

- Barium follow through – no evidence of small bowel disease
- Asacol and Predsol for >1 month
- Symptoms unabated.
- Started oral prednisolone 30 mg daily
- Symptoms not improving
- Referred to ID
- HIV test Negative

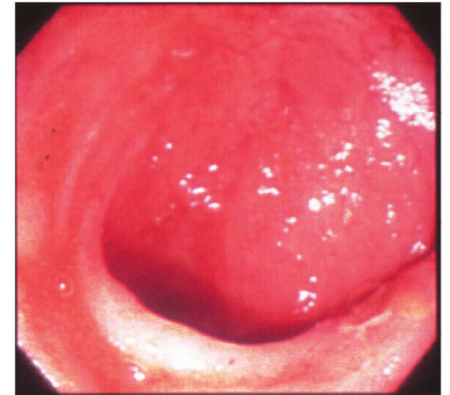
- GUM
- Gay with multiple sexual partners
- Rectal Chlamydia Positive
- LGV ---- Positive
- Symptoms - dramatic improvement with prednisolone and doxycycline
- Completed 3 weeks of doxycycline
- L2 Serovar identified

Proctitis

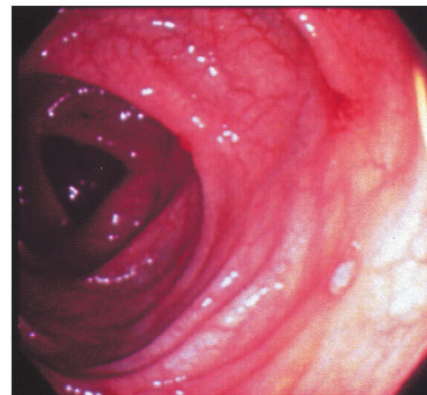




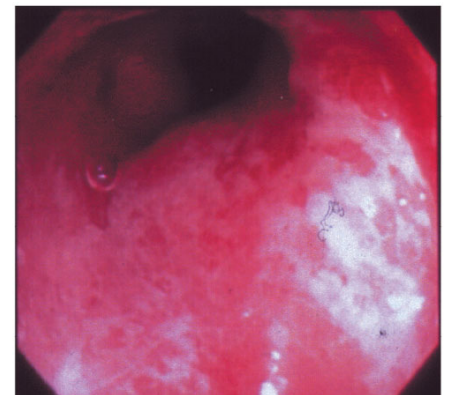
A



B



C



D

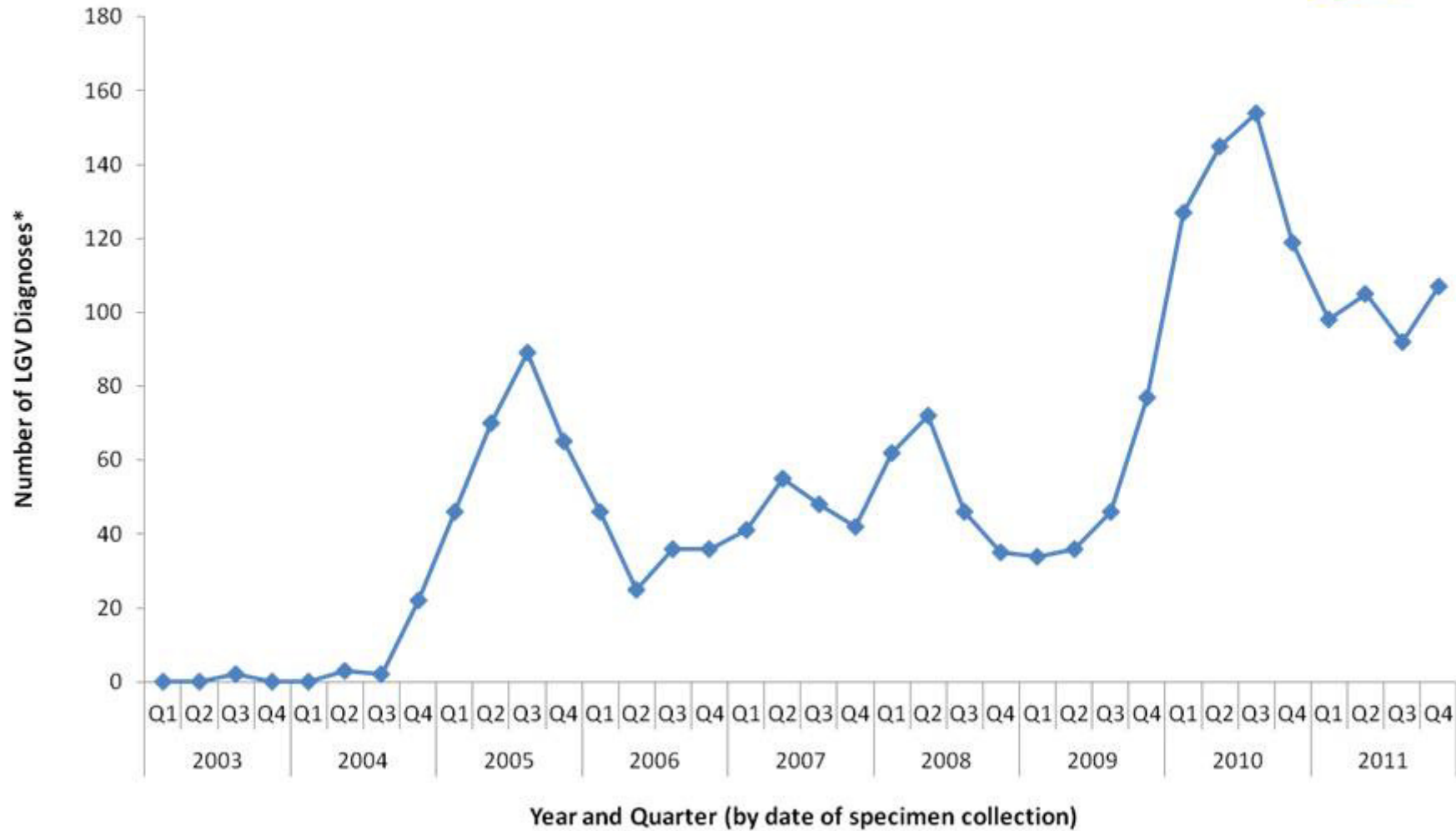
Presentation – Anorectal (n=228)

	N (%)
Rectal discharge	179 (79)
Rectal pain	157 (69)
Rectal bleeding	133 (58)
Tenesmus	65 (29)
Constipation	56 (25)
3 or more local symptoms	116 (50.9)
Systemic symptoms	68 (30)

LGV and other STI Co-infection

- HIV
- Hepatitis C
- Other STI

Number of LGV diagnoses by quarter, UK: 2003-2011



Data source: *STBRL; Sexually Transmitted Bacterial Reference Laboratory

Sexual behaviour

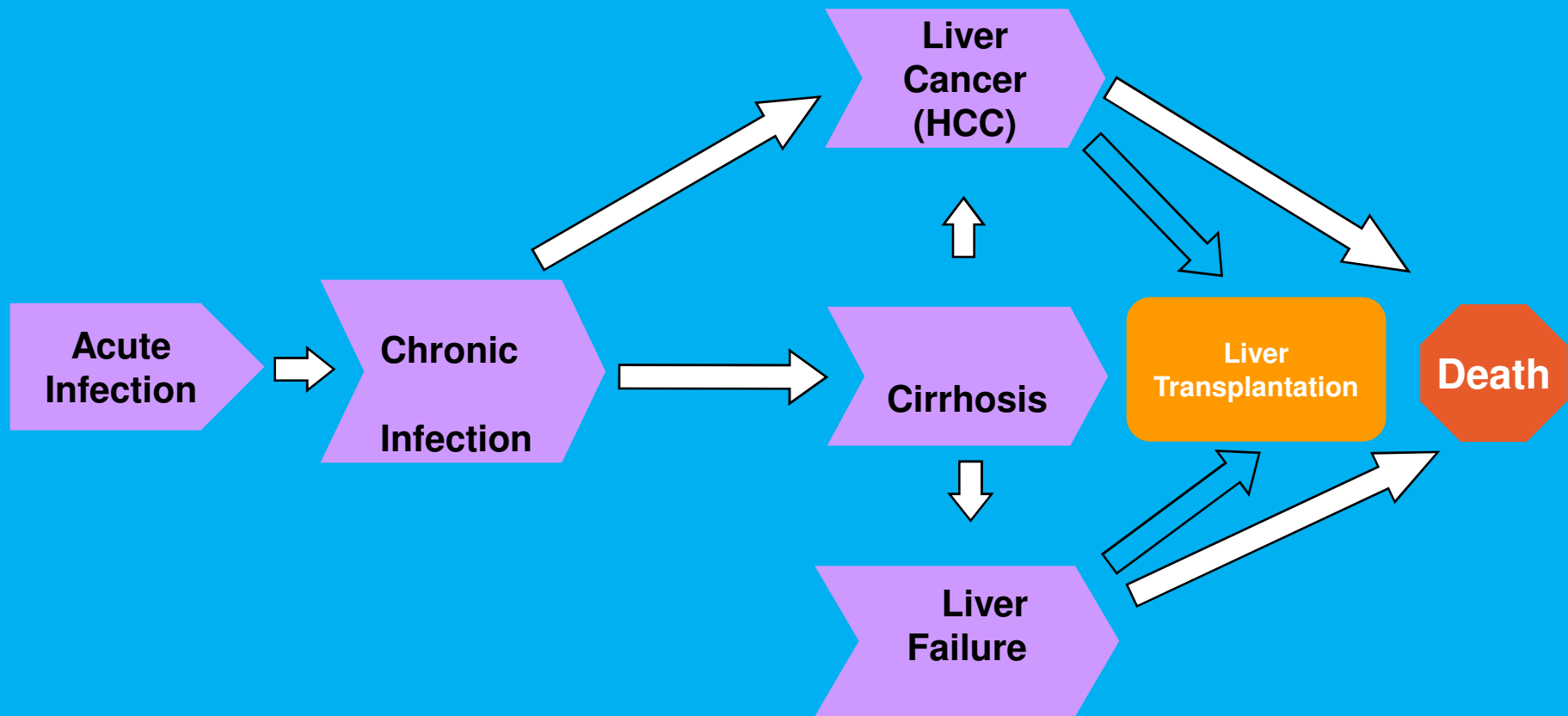
- Multiple Partners
- Unprotected anal intercourse
- Fisting
- Sex toys

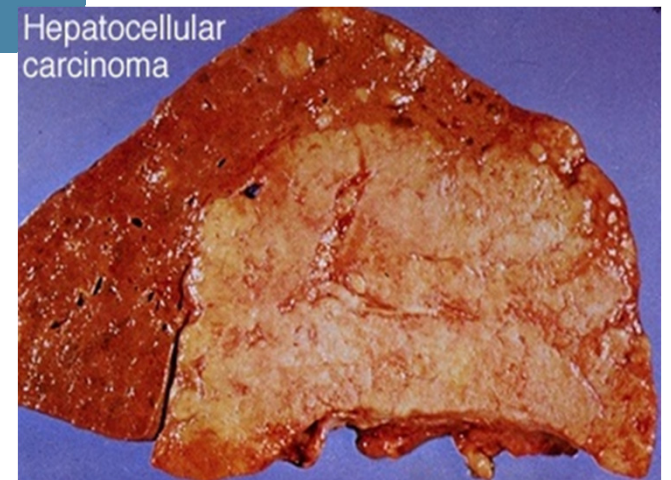
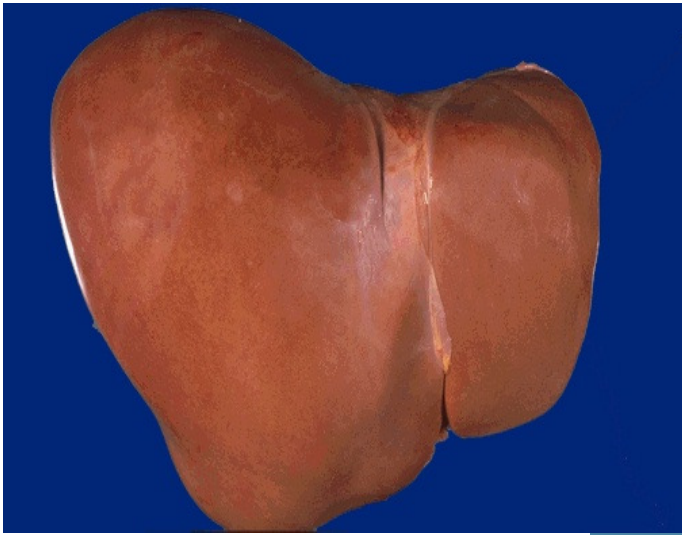
Diagnosis and Treatment

- Chlamydial PCR Swab
- Doxycycline 100mg bd for 3 weeks

Hepatitis B and C

Natural History of Hepatitis Infection





HCV Infection: extrahepatic manifestations

Hematologic

- Mixed cryoglobulinemia
- Aplastic anemia
- Thrombocytopenia
- Non-Hodgkin's β -cell lymphoma

Dermatologic

- Porphyria cutanea tarda
- Lichen planus
- Cutaneous necrotizing vasculitis

Renal

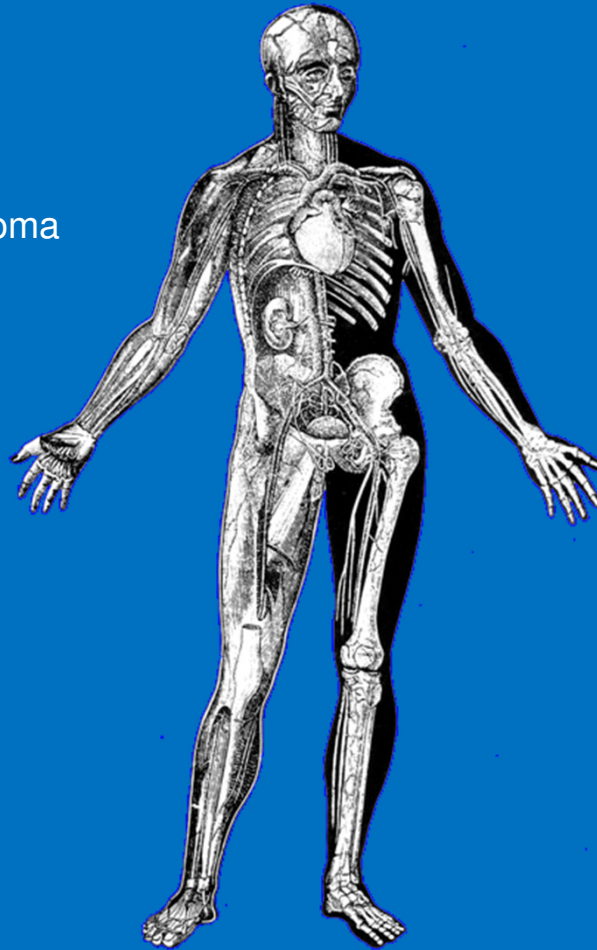
- Glomerulonephritis
- Nephrotic syndrome

Endocrine

- Anti-thyroid antibodies
- Diabetes mellitus

Salivary

- Sialadenitis



Ocular

- Corneal ulcer
- Uveitis

Vascular

- Necrotizing vasculitis
- Polyarteritis nodosa

Neuromuscular

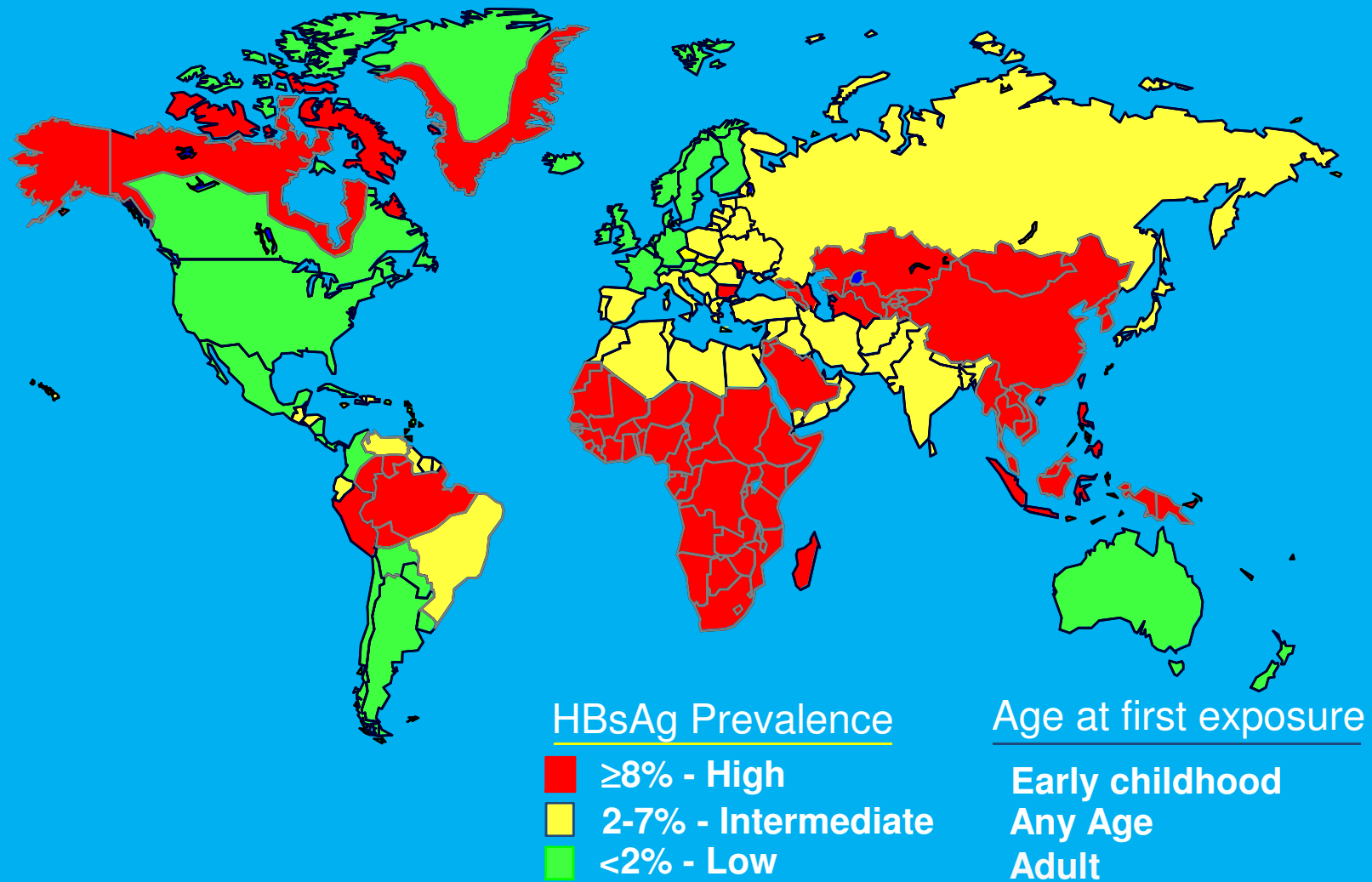
- Weakness/myalgia
- Peripheral neuropathy
- Arthritis/arthritis

Autoimmune Phenomena

- CREST syndrome

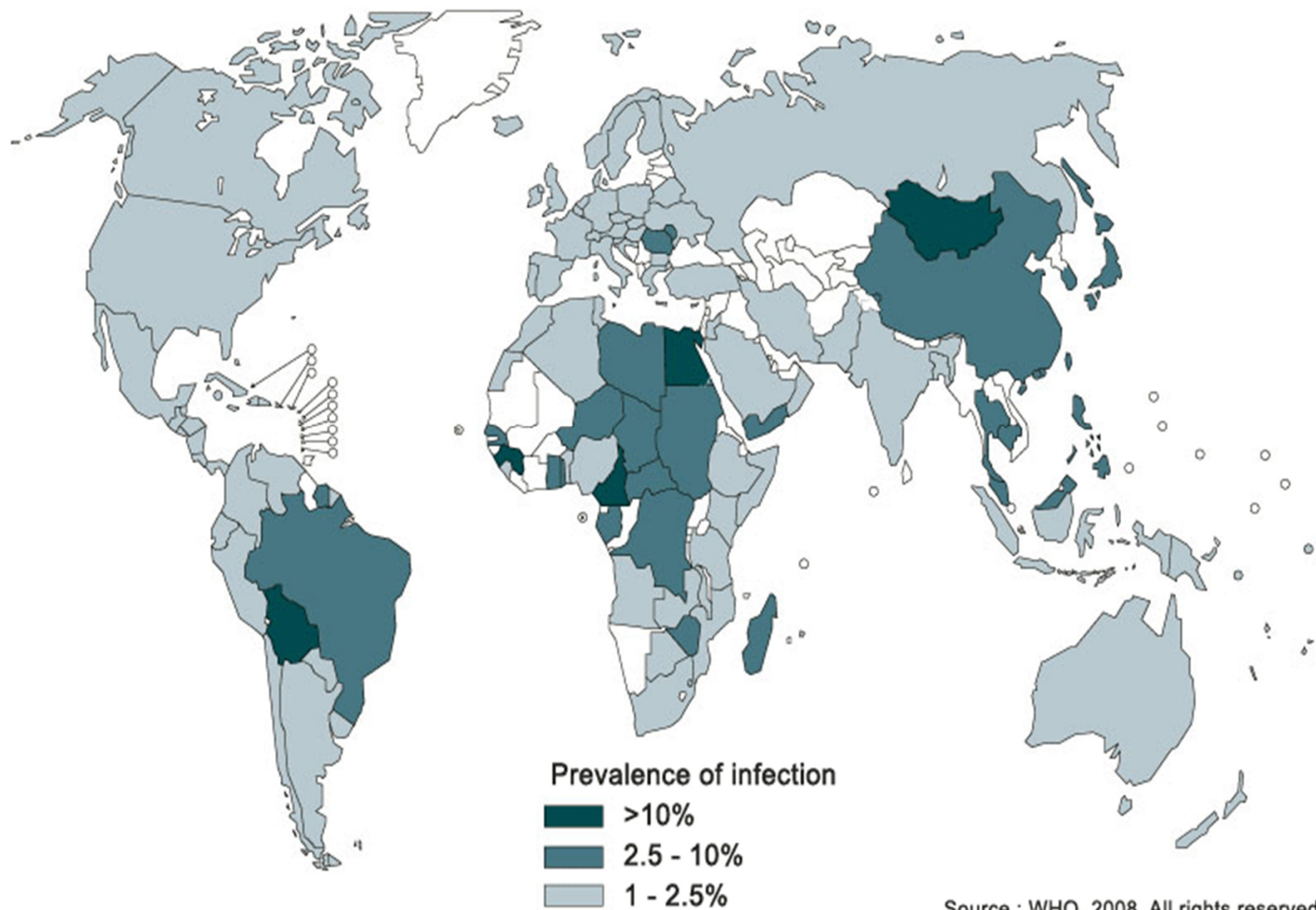
Fatigue

Geographic distribution of Chronic HBV



Source: CDC and Prevention

Hepatitis C, 2007



Source : WHO, 2008. All rights reserved.

Indications for screening

- Any history of injection or intranasal drug use
- Blood transfusion or solid organ transplant before July 1992
- Blood product for clotting problem produced before 1987
- Long term dialysis
- **Any elevation of ALT**
- **FATIGUE**
- HIV infection
- MSM
- Contact of Hepatitis C
- From areas of high Hep C prevalence

Herpes

- Proctitis
- Meningitis / Encephalitis
- Herpetic keratitis
- Pneumonitis
- Hepatitis

Herpetic Encephalitis

- 5% to 10% of encephalitis worldwide
- Both HSV1 and HSV2
- 90% HSV 1
- 10% HSV2

Herpetic Encephalitis

- Symptoms :-
- Fever (90%)
- Headaches (81%)
- Psychiatric symptoms (71%)
- Seizures (67%)
- Vomiting (60%)
- Focal weakness (33%)
- Memory loss (24%)
- Lethargy, confusion, delirium

Herpetic Encephalitis

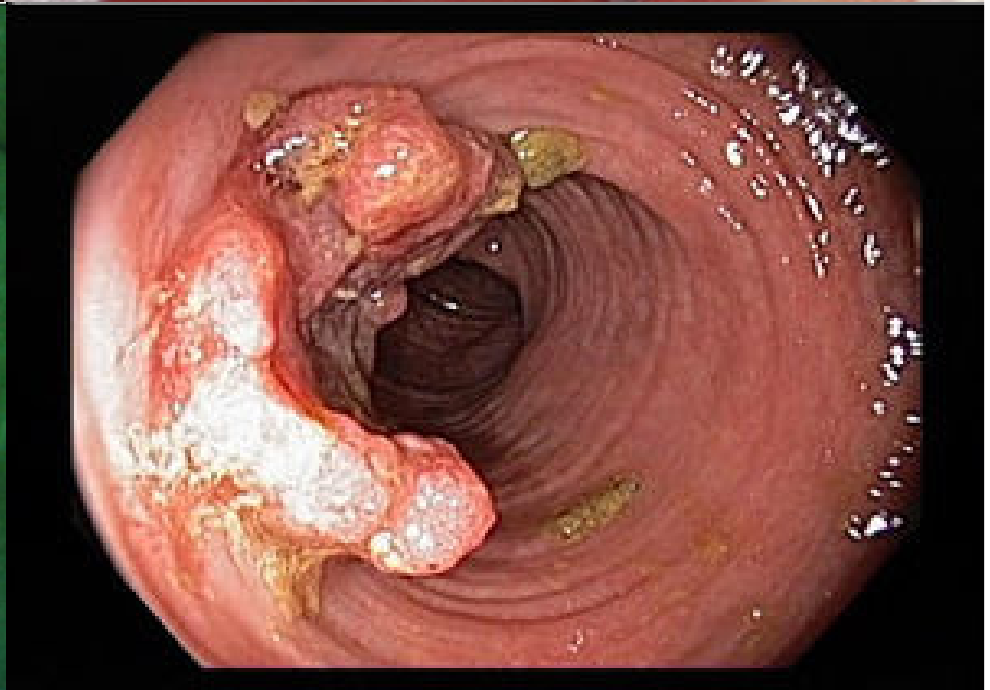
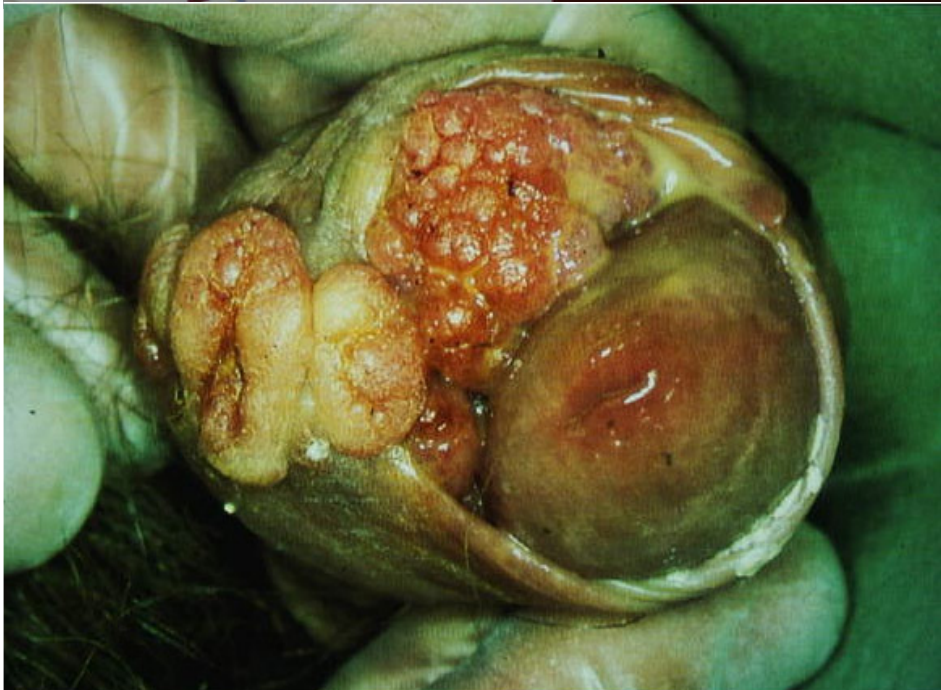
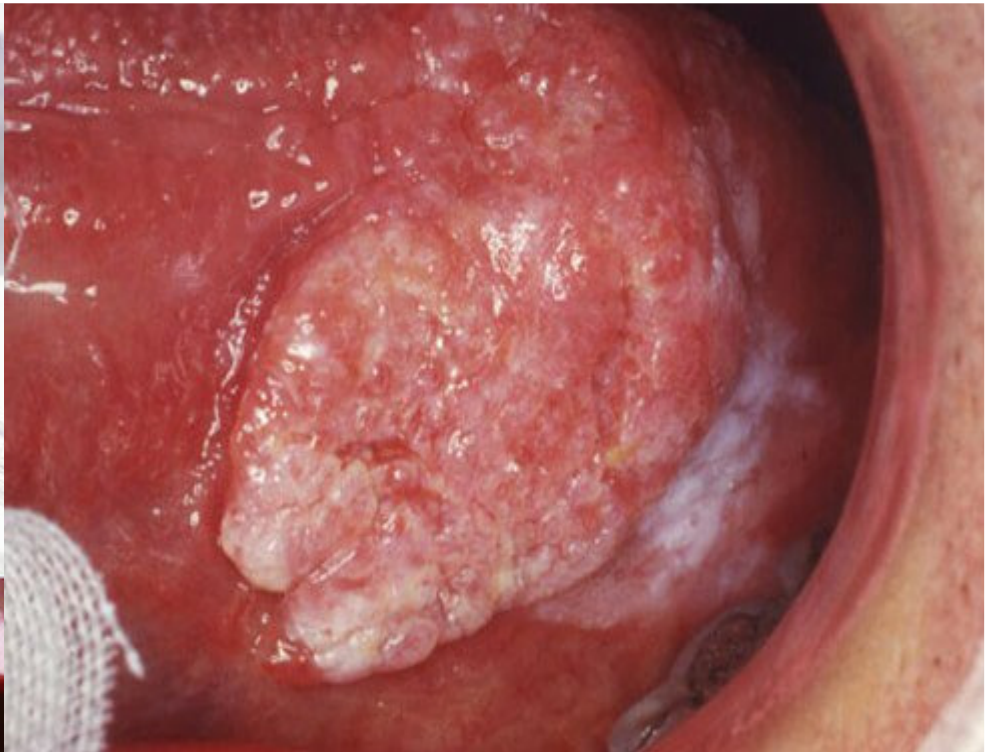
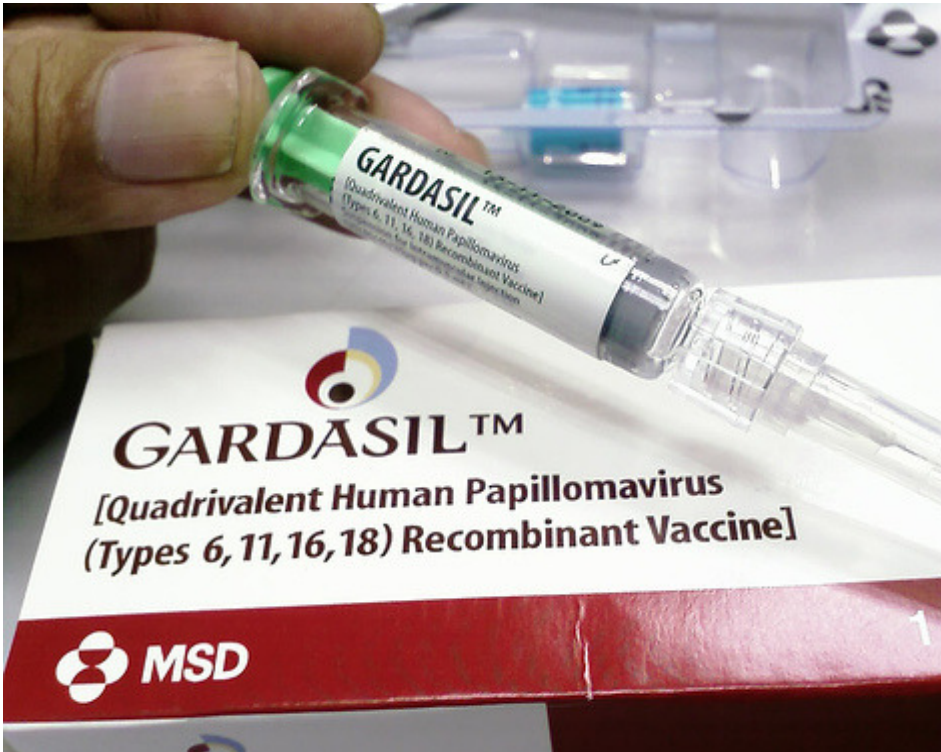
- Management guided by Infectious diseases and Neurologist
- Diagnosis
- High Index of suspicion
- CT / MRI
- LP
- PCR on CSF for HSV, enterovirus, VZV, C+S
- HIV test
- Treatment with IV acyclovir for 14 to 21 days

HSV Diagnosis

- History
- CLINICAL
- HSV positive on PCR

HPV

- Carcinoma (Oral, genital, anal)
- Laryngeal Papillomas



Sexually Transmissible Enteric Infections

Hepatitis A
Shigella.



Transmission – six 'F's ?

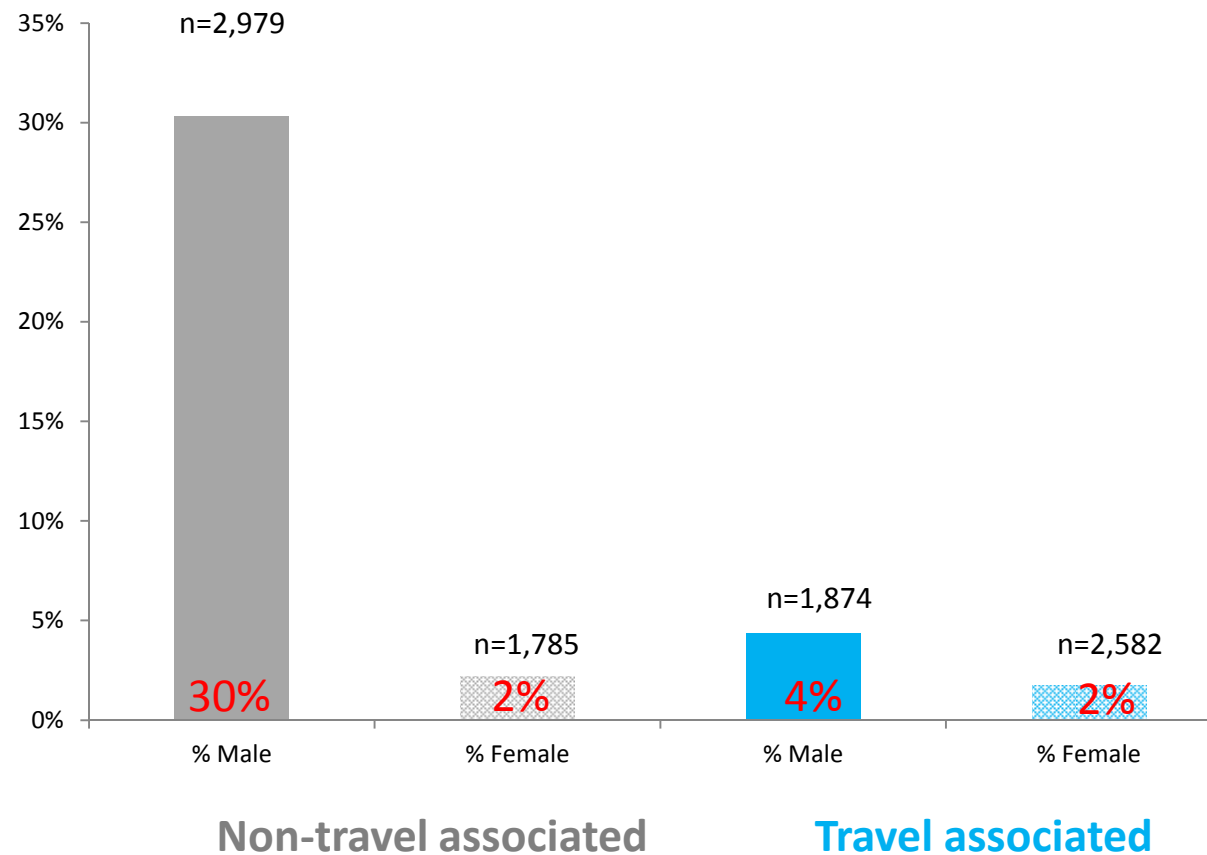
- Fingers
- Faeces
- Flies
- Food
- Fluids
- ... ~~Fucking~~ Oral-anal contact

Shigella

- MSM
- HIV infected
- Rimming, fisting
- High numbers of partners
- Dense sexual network
- Low awareness of enteric infections
- Chemsex
- Sex parties
- Meeting through social media apps
- Severe illness in some cases

(Gilbart, et al. STI. 2015 and Cresswell, et al. STD. 2015)

Shigella cases, % known to be HIV+



Summary

- Early diagnosis of HIV is IMPORTANT
- Have a low threshold for undertaking a HIV antibody test
- Syphilis should be considered in the differential diagnosis of different medical presentations.
- Other STI can rarely present medically.
- Sexual History is important when considering if there is a possibility of HIV, BBV and STI in the general medical presentation.