

STIs, Bacterial vaginosis & HIV in Pregnancy

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WHO Geneva 2008

Acknowledgments: Drs Sarah Hawkes (LSHTM)
Saiqa Mullick (Pop Council)



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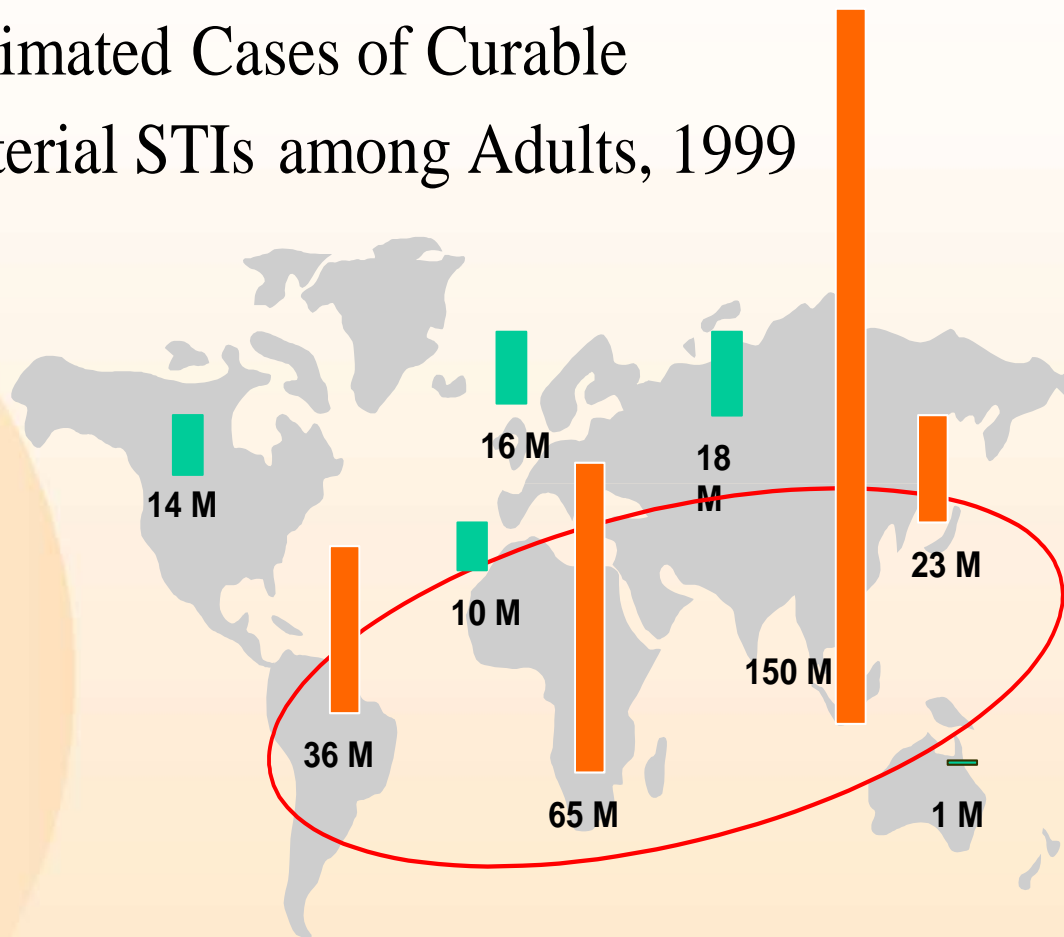
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Overview of talk

- Global epidemiology of STIs/RTIs
- Population-based prevalence of RTIs
- Sequelae of STIs
- TV & Bacterial vaginosis in pregnancy
- Syphilis in pregnancy
- HIV in pregnancy
- Options for prevention and care



Estimated Cases of Curable Bacterial STIs among Adults, 1999



Incidence bacterial STIs: ~340 million



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Reminder

RTIs= Reproductive Tract Infections

- Endogenous infections
- Iatrogenic infections
- Sexually transmitted infections (STIs)



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Purpose of surveillance

- To assess magnitude of STI burden at global, regional & country levels
- To identify vulnerable population groups
- To provide data to advocate for resources for intervention activities
- To monitor impact of intervention activities



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Problems with STI surveillance

Technical problems

- capturing asymptomatic infection (esp. in women)
- health-care seeking mainly outside surveillance sites (in private sector)
- differences in risk and epidemiology for specific STIs

Health-care system problems

- Logistical requirements
- Financial requirements

Consequence

- very few STI surveillance programmes in resource-poor countries



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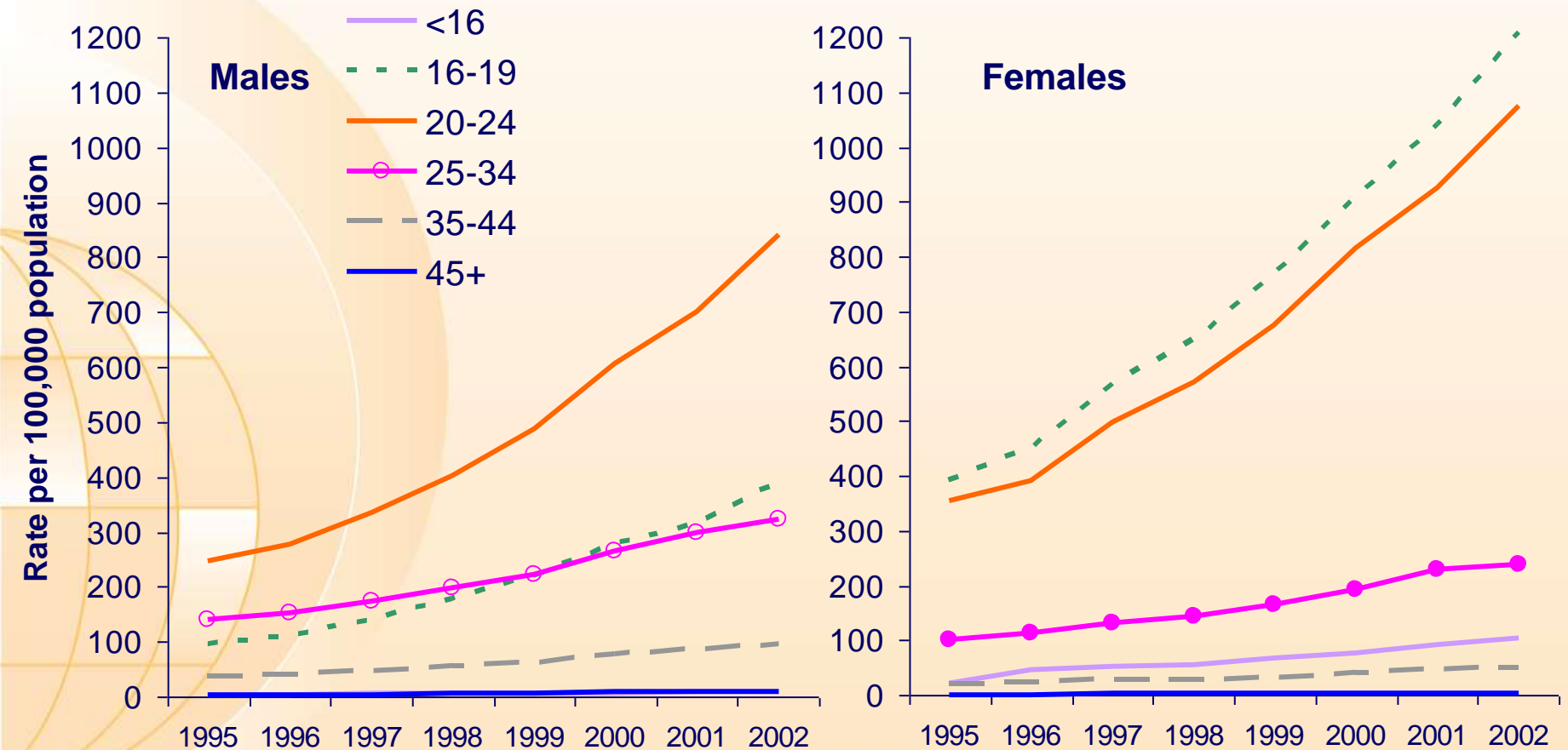


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Diagnoses of uncomplicated genital chlamydial infection in GUM clinics by sex and age group, UK: 1995-2002*



*Data are currently unavailable from Scotland for 2001 and 2002.

Source: HPA, UK



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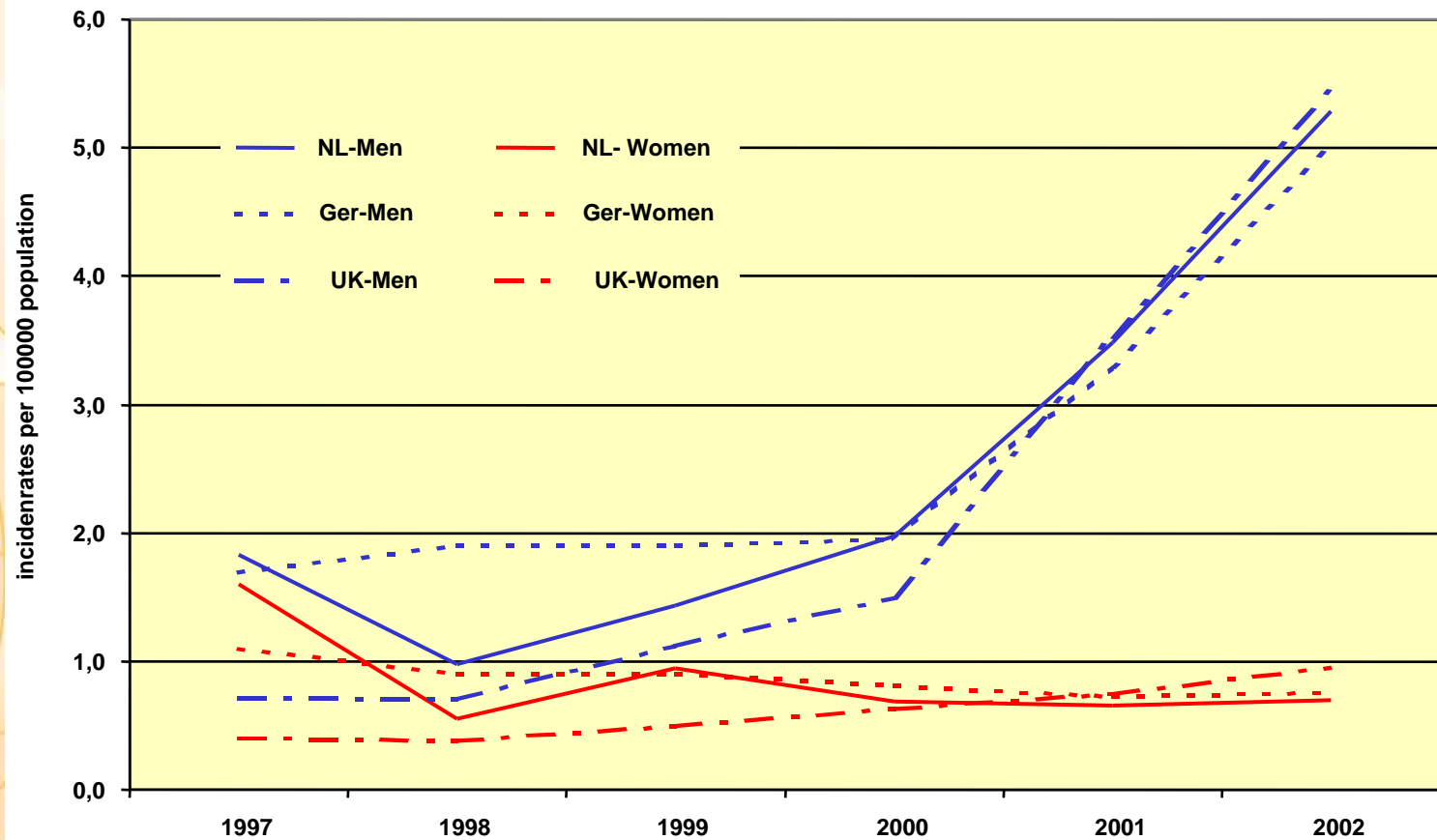


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Resurgence Syphilis 1997-2003 by sex UK, NL, Germany



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Measuring STIs in Resource Poor Settings

- Problem: lack of surveillance systems, or [gender-specific] problems with existing surveillance
- Solution: use results from “special studies” at national or international level
- Action: results are used to calculate burden of disease (important for planning and resource allocation)



Population-based prevalence of RTIs in resource poor countries

- Results from a systematic review of published and unpublished community-based studies of RTIs (1966-2000)
 - 28 studies identified
 - 10 countries represented
 - 17 studies women only
 - 3 studies men only
 - 8 studies men and women (not reported here)

(Elias, Low and Hawkes, 2003)



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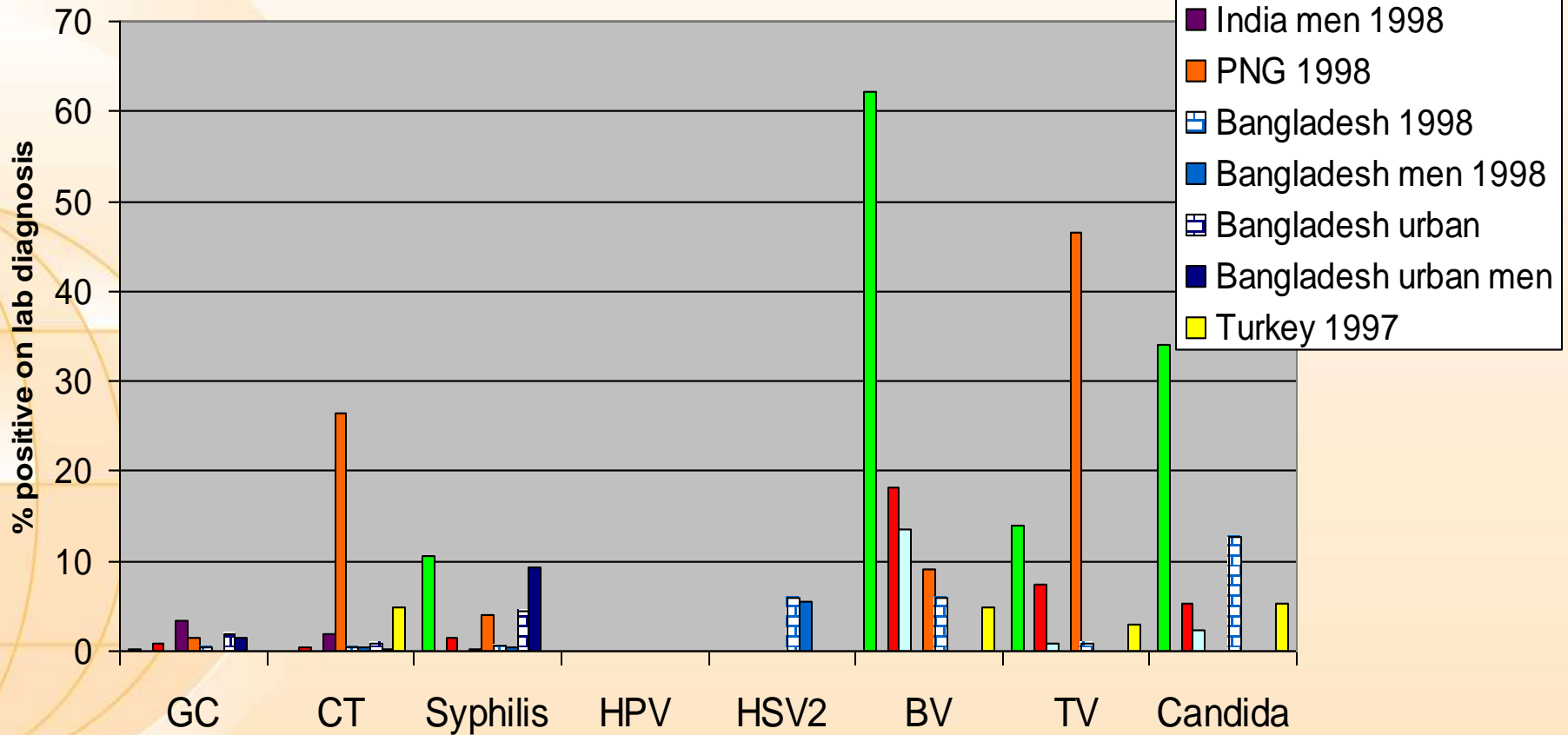


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Population-based prevalence of RTIs, Asian Region 1989-2000



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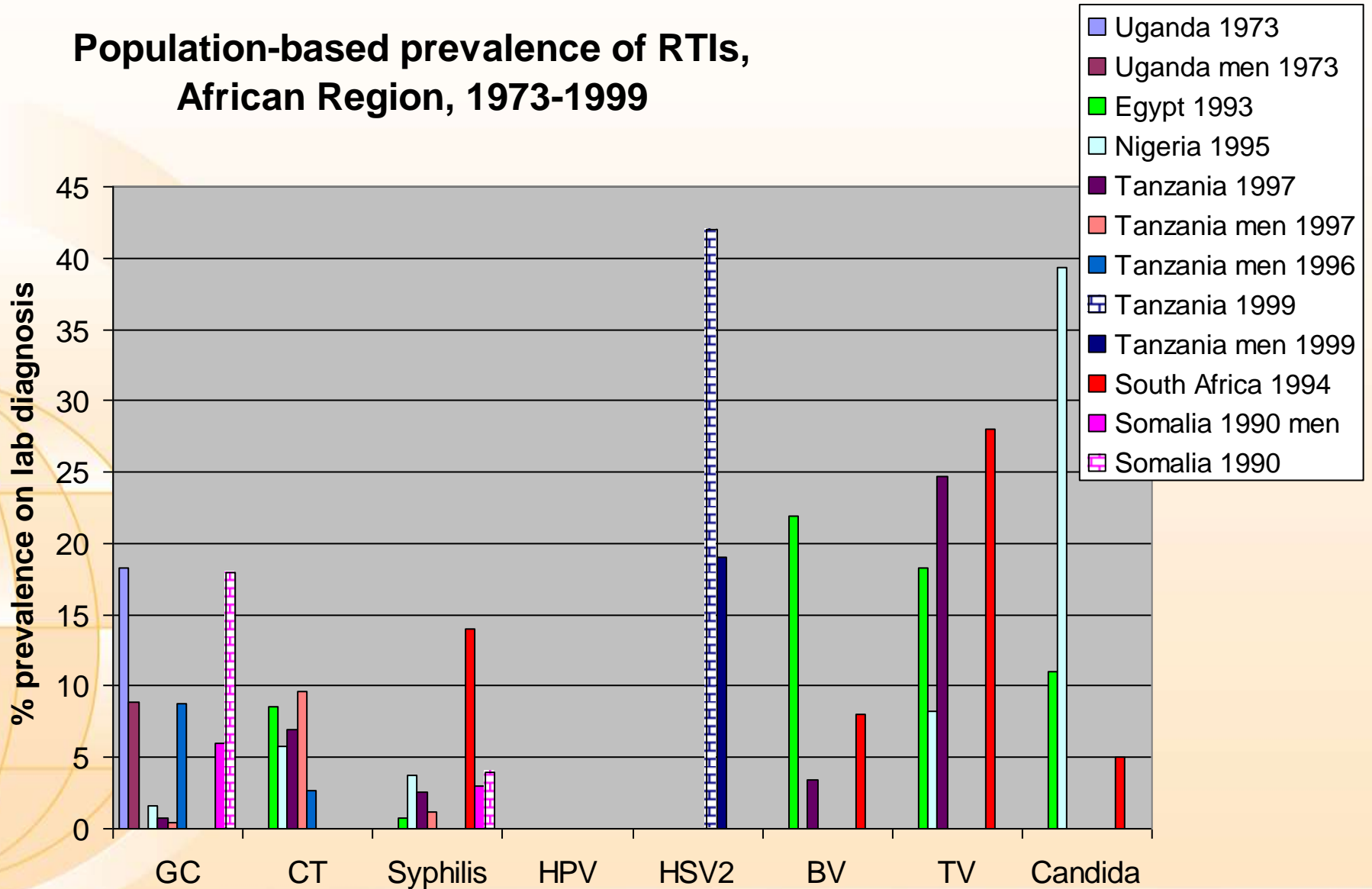


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Population-based prevalence of RTIs, African Region, 1973-1999



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What are the complications and sequelae of RTIs?

In adults

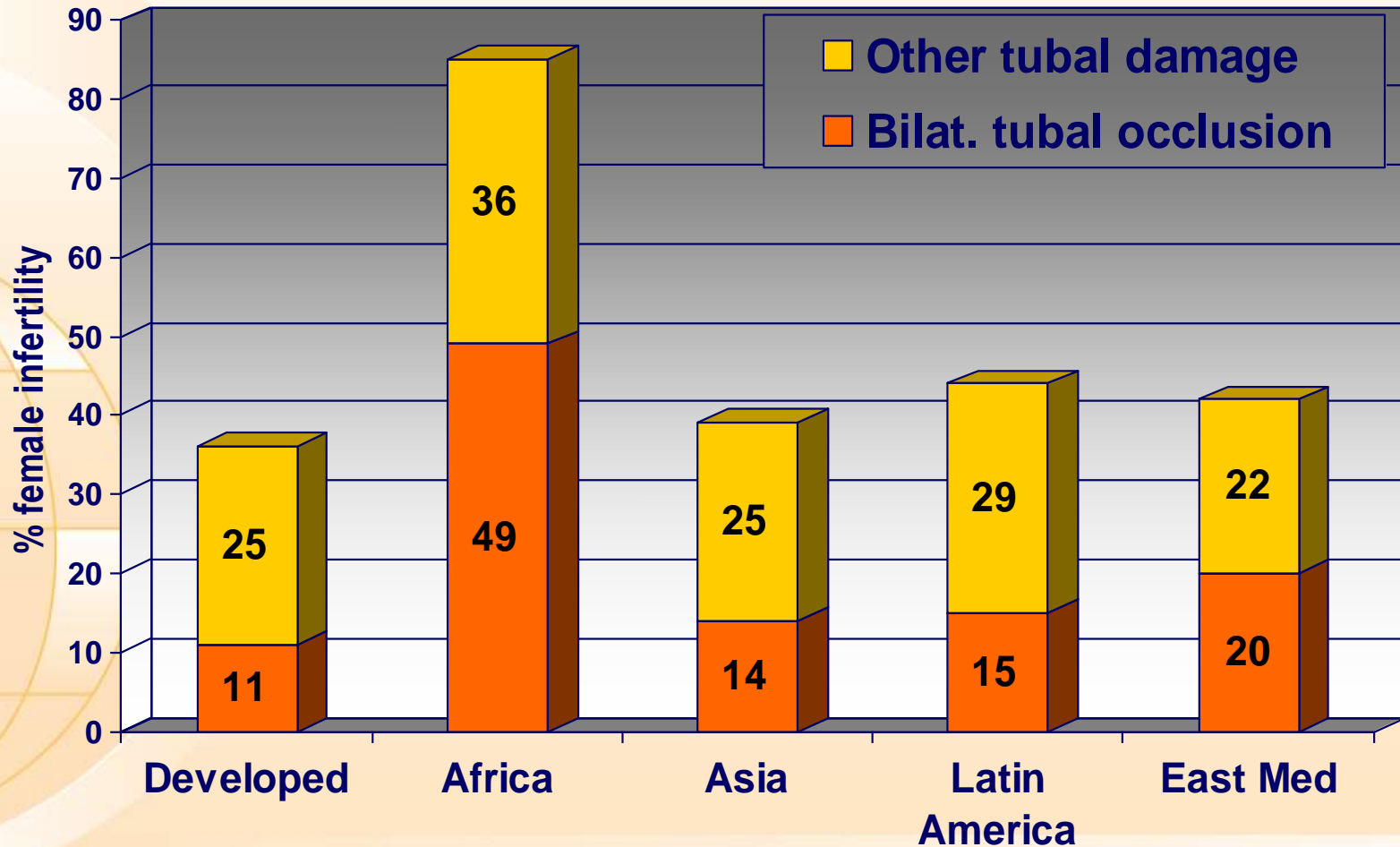
- Pelvic inflammatory disease (PID)
- Ectopic pregnancy
- Spontaneous abortions
- Post-partum infections
- Infertility (male & female)
- Cancers (cervical, anal, penile, liver)
- Increased HIV transmission

In children

- Stillbirths
- Prematurity, low birth weight
- Congenital syphilis
- Conjunctivitis and blindness
- Pneumonia



Fallopian tube damage as a cause of female infertility in the world



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Cates W et al, *Lancet*, 1985

Trichomoniasis

- Caused by *Trichomonas vaginalis*
- Is usually sexually transmitted
- Incubation period 3-28 days
- Affects women more than men
- Presents with a vaginal discharge
 - Scanty to profuse, usually yellow-green tinted
 - can be atypical depending on host factors



Trichomoniasis

- Can present with vulval erythema, oedema and excoriations
- Cervix may be involved – "strawberry cervix"
- Asymptomatic in 50% of cases
- Accounts for 15-20% of cases of vaginitis
- Associated with a 2-6 fold increase in risk of HIV transmission*

*Van Der Pol et al. JID 2008, 197:548–54



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Trichomonas vaginalis and Pregnancy

- Associated with low birth weight
- Preterm delivery
- Preterm delivery of low birth weight baby
- Perinatal transmission – only with female offspring in about 5% of cases
 - May present with Vg discharge in infant
 - Usually self-limiting in the infant (3-4 weeks)



Trichomonas vulvitis



- acute inflammation of the vulva, perineum and perianal area (intertrigo secondary to associated vaginal discharge)
- common manifestation - vulvitis, oedema, excoriations and severe pruritus



Trichomoniasis

A profuse greyish-white discharge, with a green tint, resulting from infection with *T. vaginalis*



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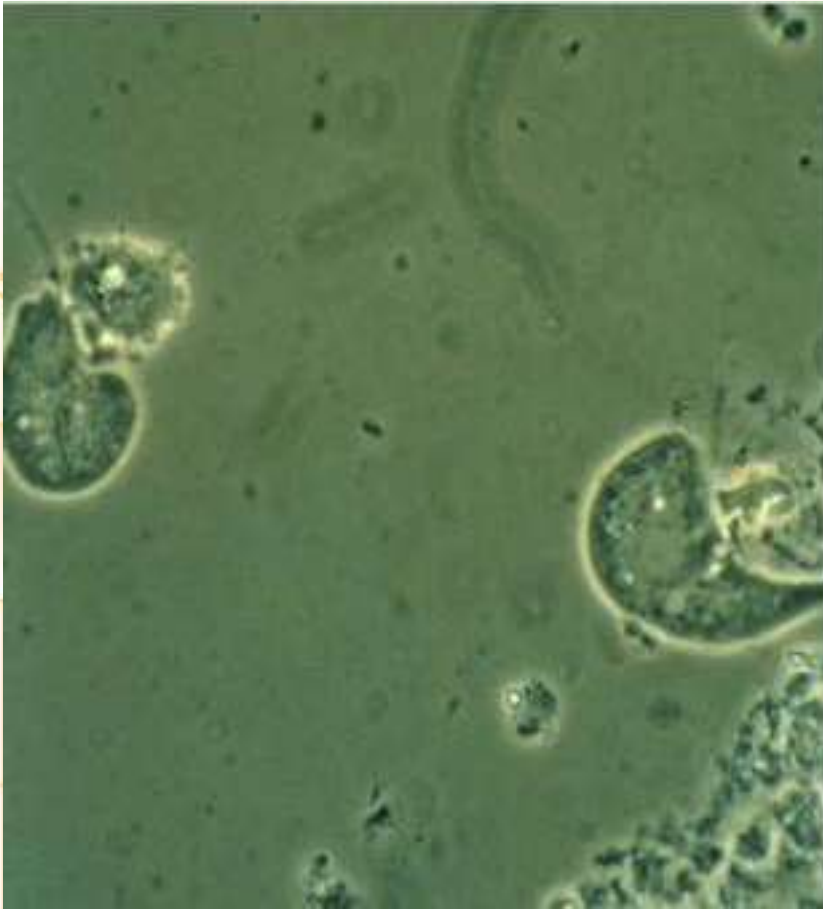


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Trichomonas vaginalis



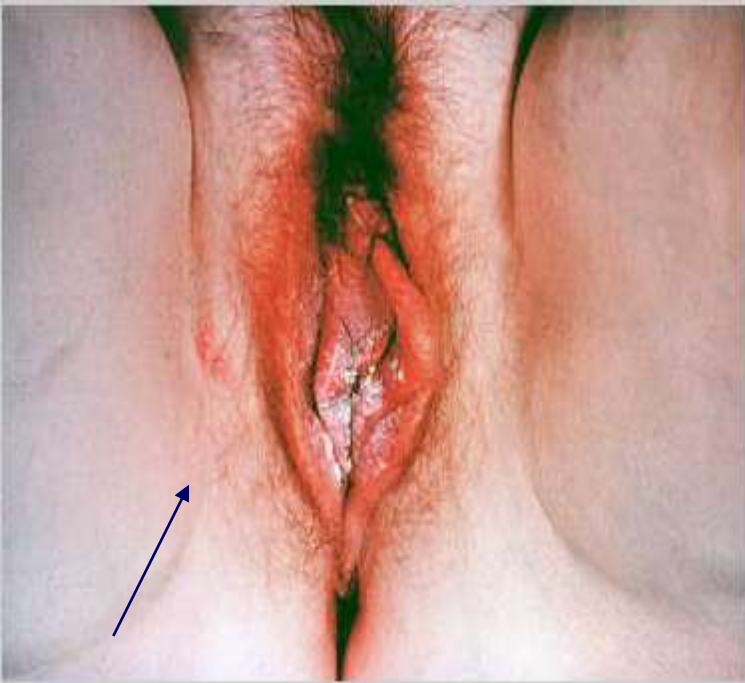
Wet mount

- *T. vaginalis* - a polymorphic organism - changing shape as it moves in amoeboid fashion
- usually recognized from the movement of the flagellae



Candida vulvitis

- Characteristic, floccular, white vaginal discharge
- Labia are swollen and erythematous
- commonly associated with acute pruritus and vaginal discharge
- Discharge - minimal to copious,
- often severe erythema of the vulva.
- Cervix is not affected



NB. Three satellite lesions on top of the right thigh



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intertrigo



Candida vulvitis with crural intertrigo

- Labia are swollen and erythemaous
- Erythema spreading to the inguinal and perianal regions
- No visible vaginal discharge

NB Papular erythematous rash on the upper thighs



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Bacterial vaginosis

- A clinical polymicrobial syndrome characterized by:
 - an increase in gram-negative anaerobic bacteria (Gardnerella vaginalis, Mobiluncus spp, Prevotella spp, Bacteroides, Peptostreptococcus, Fusobacterium, Porphyromonas, Mycoplasma hominis, etc.)
 - a reduction in the concentration of Lactobacilli
- It is the most common cause of abnormal vaginal discharge in women of reproductive age
 - asymptomatic in about 50% of women



Bacterial vaginosis



Cervix covered with a discharge associated with BV

- white to grey, homogeneous (nonfloccular),
- thin and adherent



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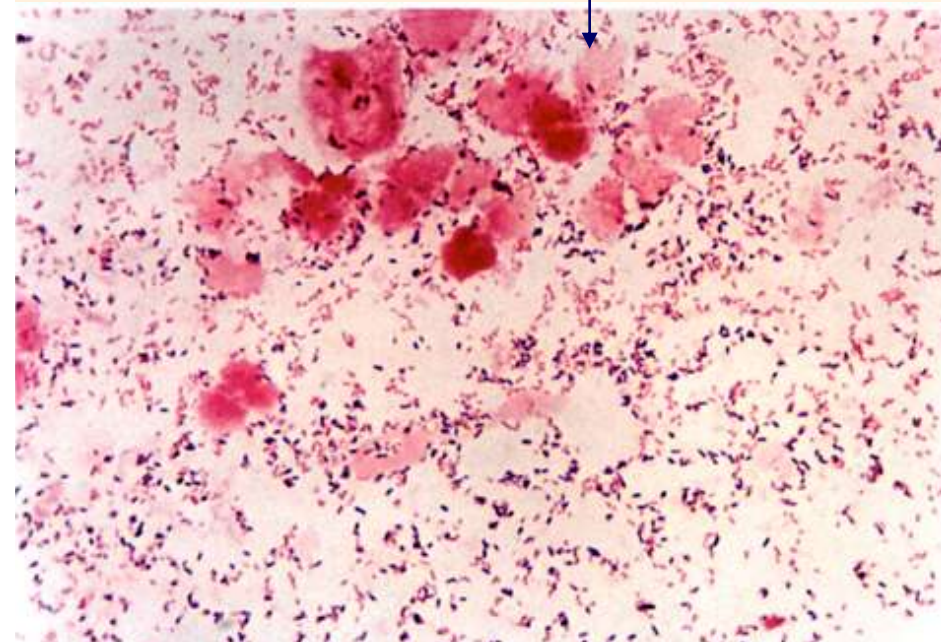
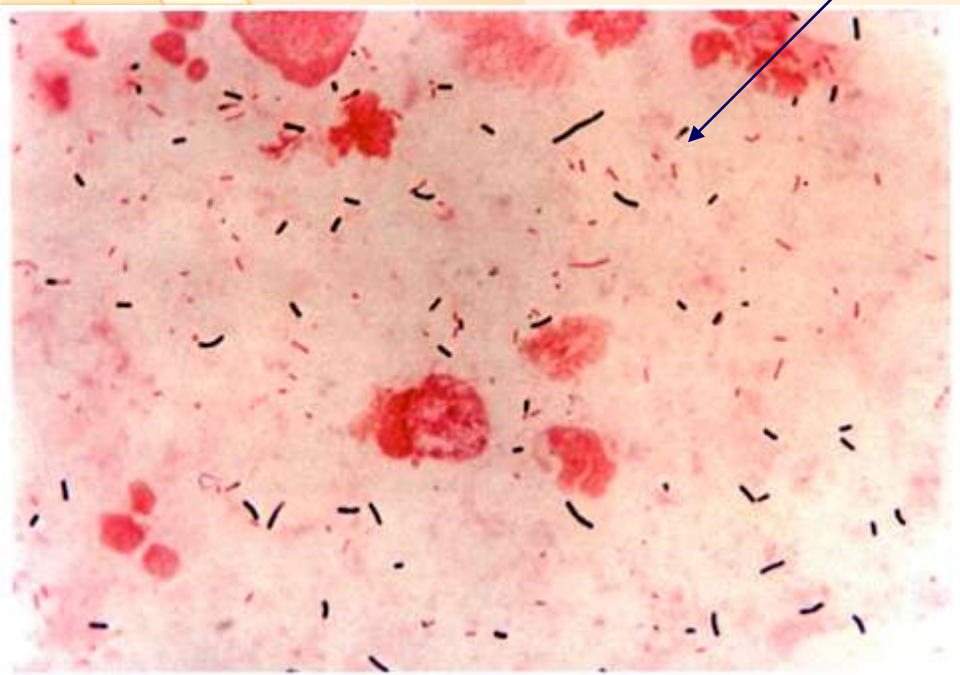


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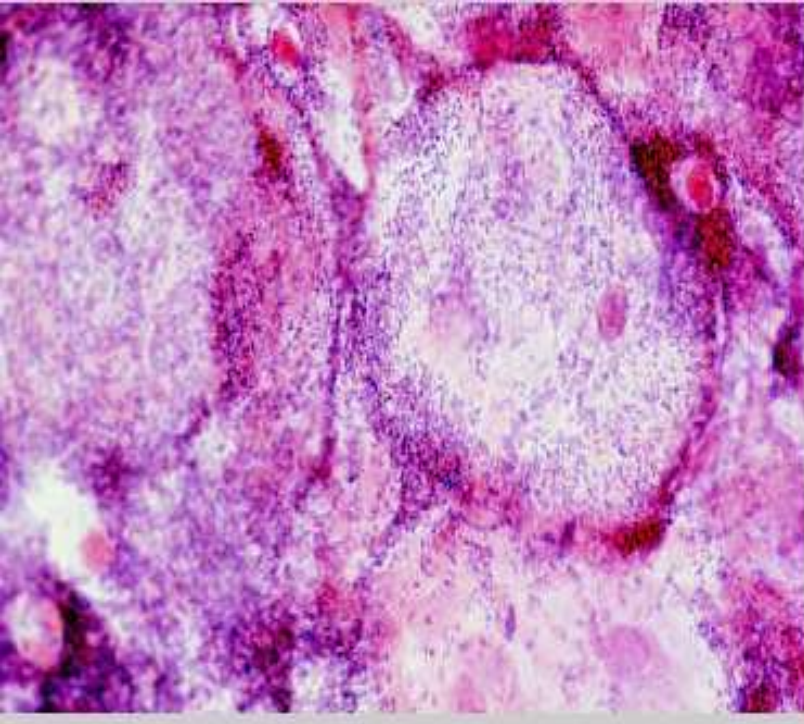
Normal flora:
Gram-stained smear showing
a pure flora of Gram-positive rods
of lactobacilli

Gram-stained smear showing mixed
intermediate flora - Gram-positive
and Gram-negative organisms

**Bacterial vaginosis (Probably Nugent
score = 8)**



Bacterial vaginosis



Gram-stained smear showing mixed bacterial flora associated with severe BV. (Probably Nugent score = 10)

- a "salt and pepper" appearance from the mixture of Gram-negative and Gram-positive bacteria.
- No lactobacilli seen.

Diagnosis of Bacterial Vaginosis

Clinical criteria

Amsel's criteria (3 of 4)

- Homogeneous thin vaginal discharge
- Vaginal pH > 4.5
- “Fishy” odour upon contact of the sample with KOH 10% (positive whiff test)
- Epithelial cells covered with bacteria (Clue cells)

Amsel R, 1983 Am J of Medicine, 74:14



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Diagnosis of Bacterial Vaginosis

Clinical criteria

Nugent's criteria- assigns a score of 0-10 based on different bacterial morphotypes seen in the stained smear.

A score of:

0-3 Normal

4-6 intermediate

7-10 is consistent with bacterial vaginosis

- Good intra-observer agreement
- High reproducibility
- Sensitivity of 85-90%
- Specificity of more than 90%



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Bacterial vaginosis and pregnancy

Evidence of an association between BV

- first trimester miscarriage
- mid-trimester (16-20 wk) abortion
- preterm birth - specifically preterm delivery < 30 wk that results in births of newborns < 1000 g
- Preterm rupture of membranes
- chorioamnionitis
- Postpartum endometritis
- Post-abortion infections
- Post-procedural infections

Kurki T 1992 Obstet Gynecol 80: 173,

Meis P 1995 Am J Obstet Gynecol 173:1231

Hillier S 1988 N Engl J Med 319: 972



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Bacterial vaginosis and pregnancy

It has been speculated that BV

- facilitates access of bacteria into the amniotic cavity
- remains in the uterine cavity as a chronic infection

Kurki T 1992 Obstet Gynecol 80: 173,
Meis P 1995 Am J Obstet Gynecol 173:1231
Hillier S 1988 N Engl J Med 319: 972



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Managing asymptomatic BV infection in pregnant women

We should

NOT

screen for bacterial vaginosis in asymptomatic women since there is no difference in the rate of pre-term birth?



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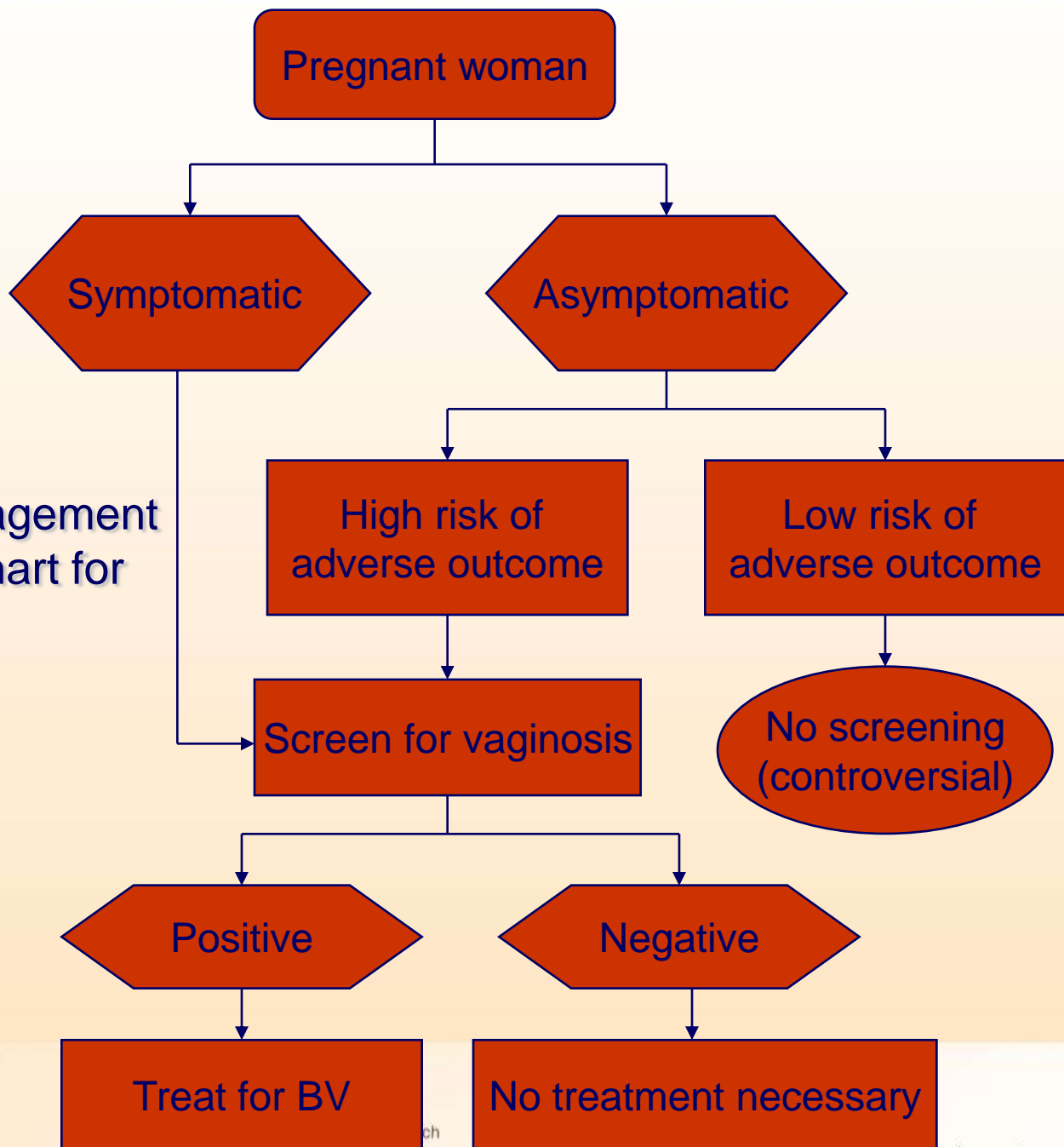
Managing asymptomatic BV infection in pregnant women

Some studies show that treatment of pregnant women with BV, who have a history of preterm delivery (high risk), might reduce the risk for prematurity

- Screening and treating in pregnancy
 - might be beneficial for asymptomatic, high risk women
 - should be conducted at the earliest part of the 2nd trimester to be of benefit



Simplify decision and management with a locally agreed flowchart for health workers



Is BV still important for pregnant women?



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BV and HIV

Evidence that BV and HIV are related

- Theoretical basis
- Epidemiological observations
- Therapeutic intervention studies



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Theoretical basis

BV characterised by:

- absence of Lactobacilli
- low H_2O_2
- high pH

Conditions believed to be conducive to increased susceptibility to HIV infection



Epidemiological Observations

Epidemiological association found in cross-sectional and prospective studies

- Relationship is dose-dependent
 - severe BV is associated with increasing risk of HIV infection
 - relative risk of HIV acquisition = 2 to 4

Cohen et al. AIDS 1995; Sewankambo et al. Lancet 1997; Taha et al. AIDS 1998; Martin et al. JID 1999.



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Therapeutic intervention studies

- One study (Uganda):
 - No difference in HIV acquisition in either treatment or control groups

BUT

 - BV therapy is not highly effective (cure rates at one month or more post-therapy)

Wawer et al. Lancet 1999



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Association between BV and HIV acquisition?

Community study in Rakai, Uganda

- 4718 women 15-59 years
- Nugent criteria for diagnosis of BV

HIV: 14.2 % in women with normal flora

26.7 % in women with severe BV (Nugent 9-10)
 $p < 0.001$

Sewankambo, N Lancet 1997 350: 546a



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Bacterial Vaginosis: Need to switch the direction of our research ?

- There is an association between BV and preterm birth, but it is not cause-effect.
- The association between BV and a higher acquisition rate for HIV suggests that the loss of lactobacilli or the presence of BV could increase susceptibility
- There is a difference in local immunity response in women with BV: Alteration in the balance between sialidase and IL-8?

(Cauci, Culhane)



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Vaginal and iatrogenic infections

Vaginal infections

- are most common cause of RTIs in women
- are associated with adverse outcomes of pregnancy
- are associated with increased susceptibility to HIV infection
- are associated with high health-care costs to individual women and to health-care system
- due to iatrogenic infections, contribute heavily to burden of maternal morbidity and mortality (**true magnitude unknown**)



Syphilis in pregnancy



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Transmission

- Syphilis is considered most infectious for sexual transmission in the primary, secondary and early latent stages.
- Estimates of the proportion of sexual contacts who become infected range from 6 to 62% for contacts of early syphilis cases.
- Little data on transmission probabilities for men-to-women and vice versa or on how infectious the late stages of syphilis are.



Secondary syphilis

- The second stage of infection, during which the infection is widely disseminated, develops after approximately 6 weeks to 6 months
- Classically there is a widespread macular rash over the trunk and limbs and sometimes over the palms and soles.
- Soft, papular lesions, known as condylomata lata, develop in moist areas such as the genitals and axillae.



Secondary syphilis cont

- Mucous patches, also called snail-track ulcers, are painless erosions and occur in the mouth and genitals.
- Condylomata lata and snail-track ulcers contain *T. pallidum* and are highly infectious.
- Systemic involvement can result in headache, laryngitis, bone pains and inflammation in the liver and kidneys leading to syphilitic hepatitis and the nephrotic syndrome.
- The symptoms and signs all resolve after a few weeks to 12 months.







Results of implementing antenatal syphilis screening

- Survey of 22 MoH in sub-Saharan Africa:
 - vast majority have ANC syphilis screening policies
 - most pregnant women do not get screened
 - estimated 2,000,000 or more women with active syphilis are pregnant each year - 1,640,000 have their infection undetected during pregnancy.
 - syphilis is the leading cause of perinatal mortality, causing 21% of perinatal mortality.
- More than 500,000 fetal deaths a year, globally, from congenital syphilis

Source: Schmid G. *Bulletin of the World Health Organization*, June 2004, 82(6)



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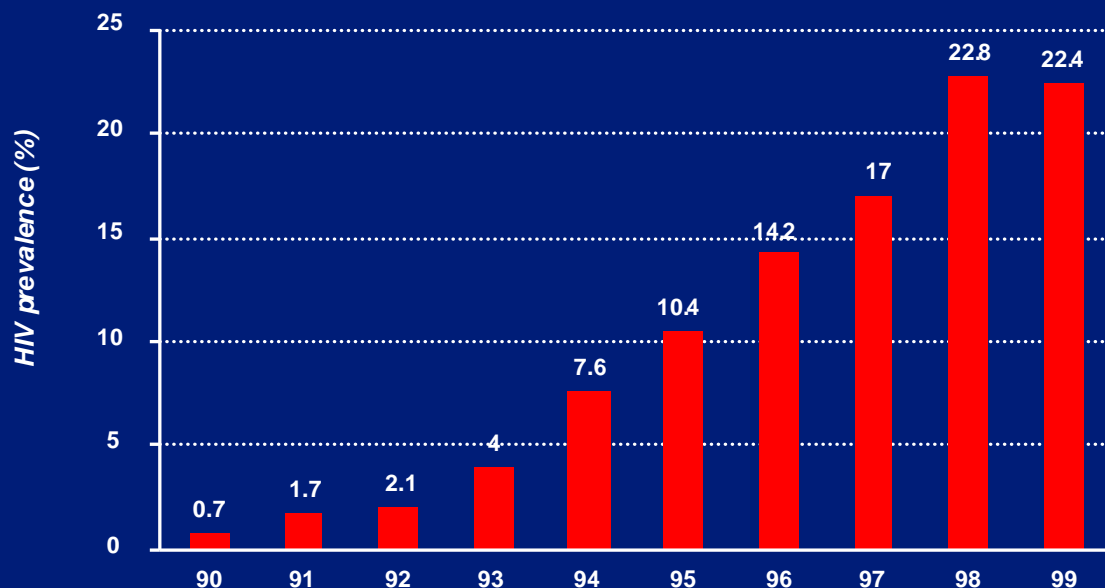


This is an anteroposterior (AP) radiograph of a human pelvis and the proximal femurs. The image shows the bony structures of the pelvic girdle, including the iliac, ischial, and pubic bones, as well as the femoral heads and necks. The femoral shafts are visible extending downwards. A small white label with the letter 'M' is positioned on the right side of the image, near the top of the femur. The overall image has a slightly grainy texture and a yellowish tint, characteristic of older radiographic prints.

M

Burden of HIV in pregnancy

HIV prevalence among pregnant women in South Africa, 1990 to 1999



00001-E-13-27 June 2000

Source: Department of Health, South Africa



Effect of pregnancy on HIV

- **HIV-positive women do not seem to have a worse prognosis from HIV on account of becoming pregnant**
- **Short-course treatments to prevent infection of a newborn are not the best choice for the mother's health**
- **Medications taken only during labour and delivery may precipitate resistance to future treatment options for the mother**
- **Combination therapies are the standard treatment**



Complications of pregnancy and delivery found among HIV positive (mainly symptomatic) women compared to HIV negative women: 1990-99

- **More frequent and severe reproductive tract infections**
- **More severe and more frequent blood loss, sepsis and delayed wound healing after caesarean section, and induced abortion**
- **Lower fertility rate ratios**
- **Insufficient weight gain in pregnancy**



Complications of pregnancy and delivery found among HIV positive (mainly symptomatic) women compared to HIV negative women: 1990-99

- **Higher rates of ectopic pregnancy**
- **Greater risk of post-partum haemorrhage and post-partum sepsis**
- **More frequent and severe anaemia and malaria, and possibly tuberculosis.**
- **Complications of AIDS-related conditions, such as bacterial pneumonia**



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The variable risk of MTCT of HIV (with and without preventive interventions)

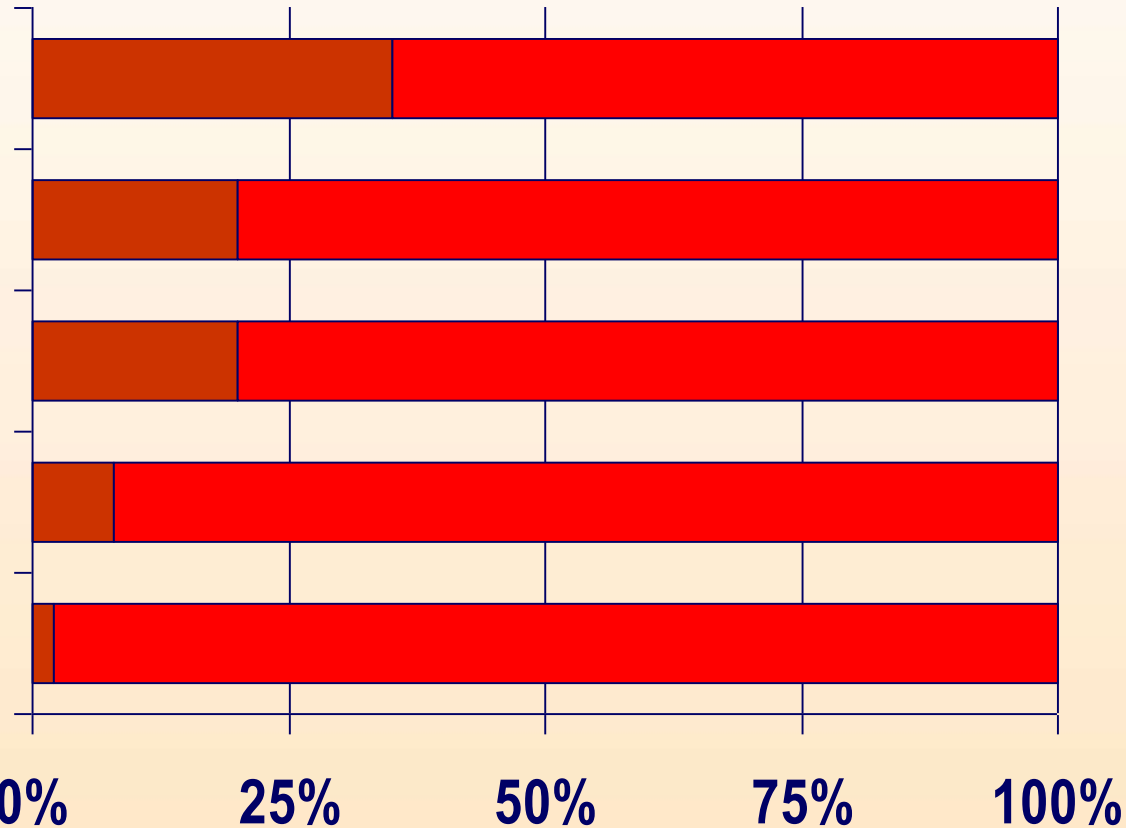
no ARV, prolonged breastfeeding

ARV, prolonged breastfeeding

no ARV, no breastfeeding

ARV, no breastfeeding

ARV, no breastfeeding, C-section



■ Infected

■ Uninfected

0%

25%

50%

75%

100%



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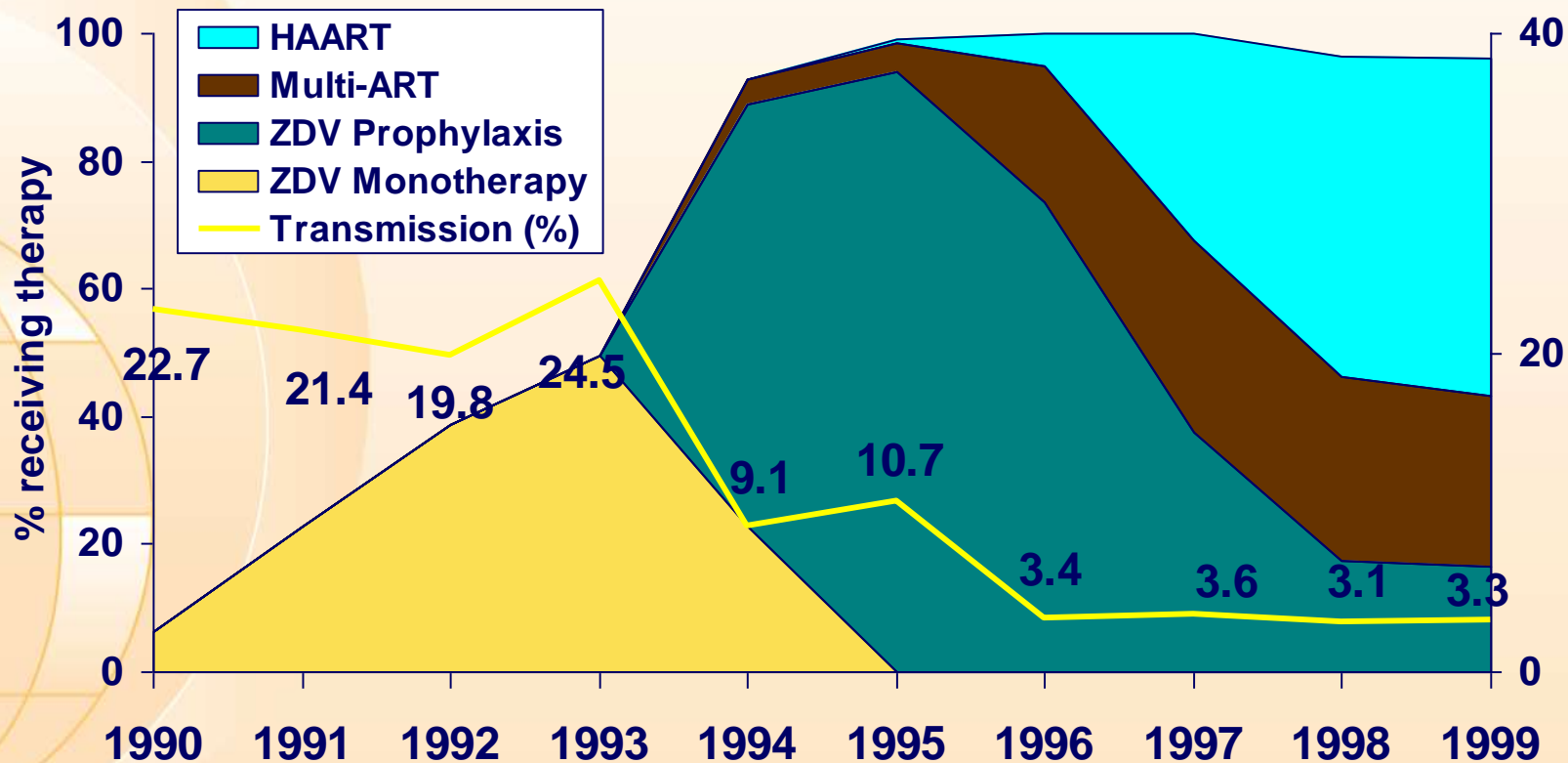


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ARV Use and HIV Transmission (WITS, USA)



Source: Blattner, Durban 2000, Int Conf AIDS Jul 9-14; (abstract no. LbOr4)



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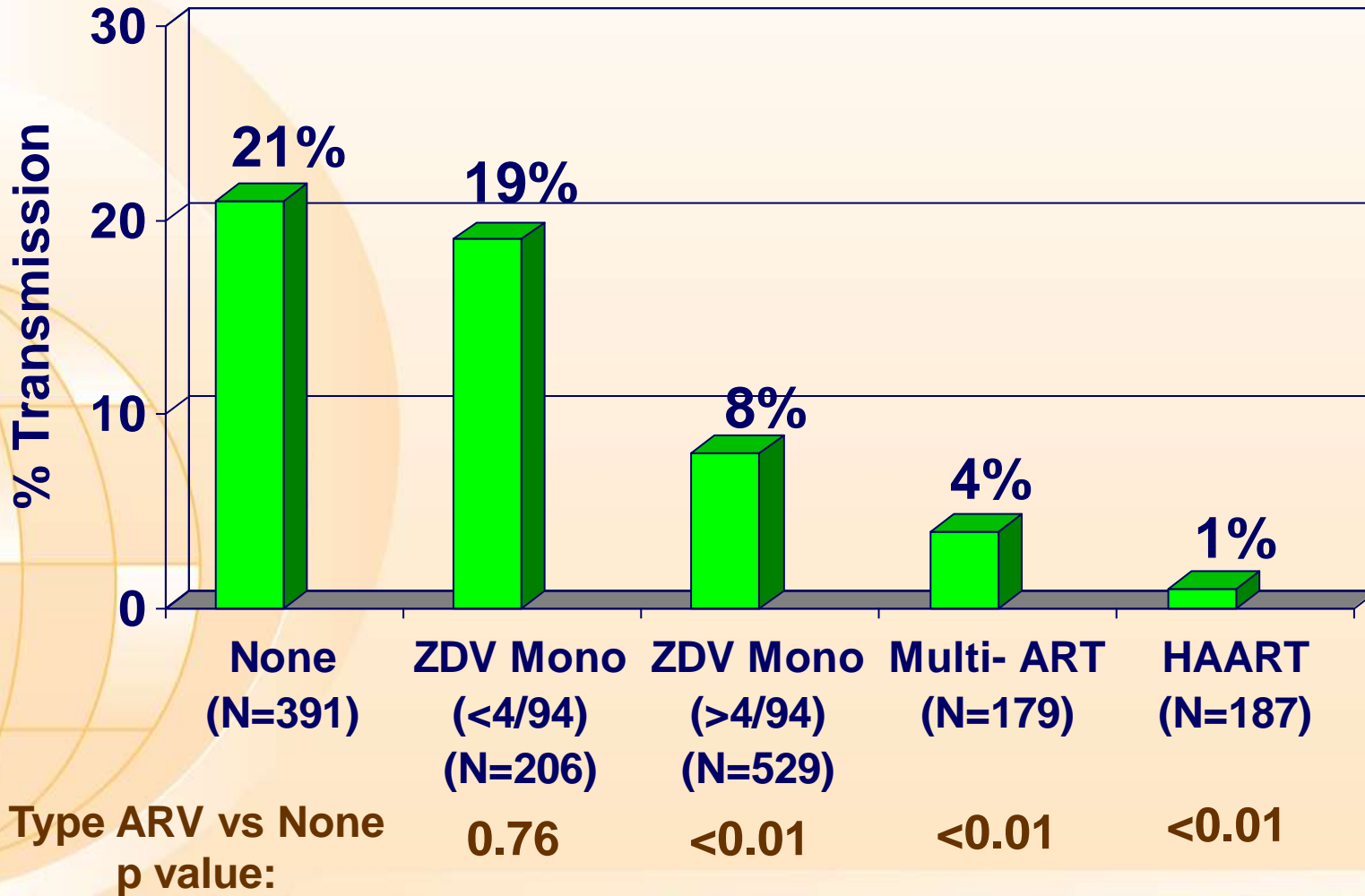
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Antenatal Antiretroviral Treatment and Perinatal Transmission in WITS, 1990-1999

Blattner W. XIII AIDS Conf, July 2000, Durban S Africa (LBO4)



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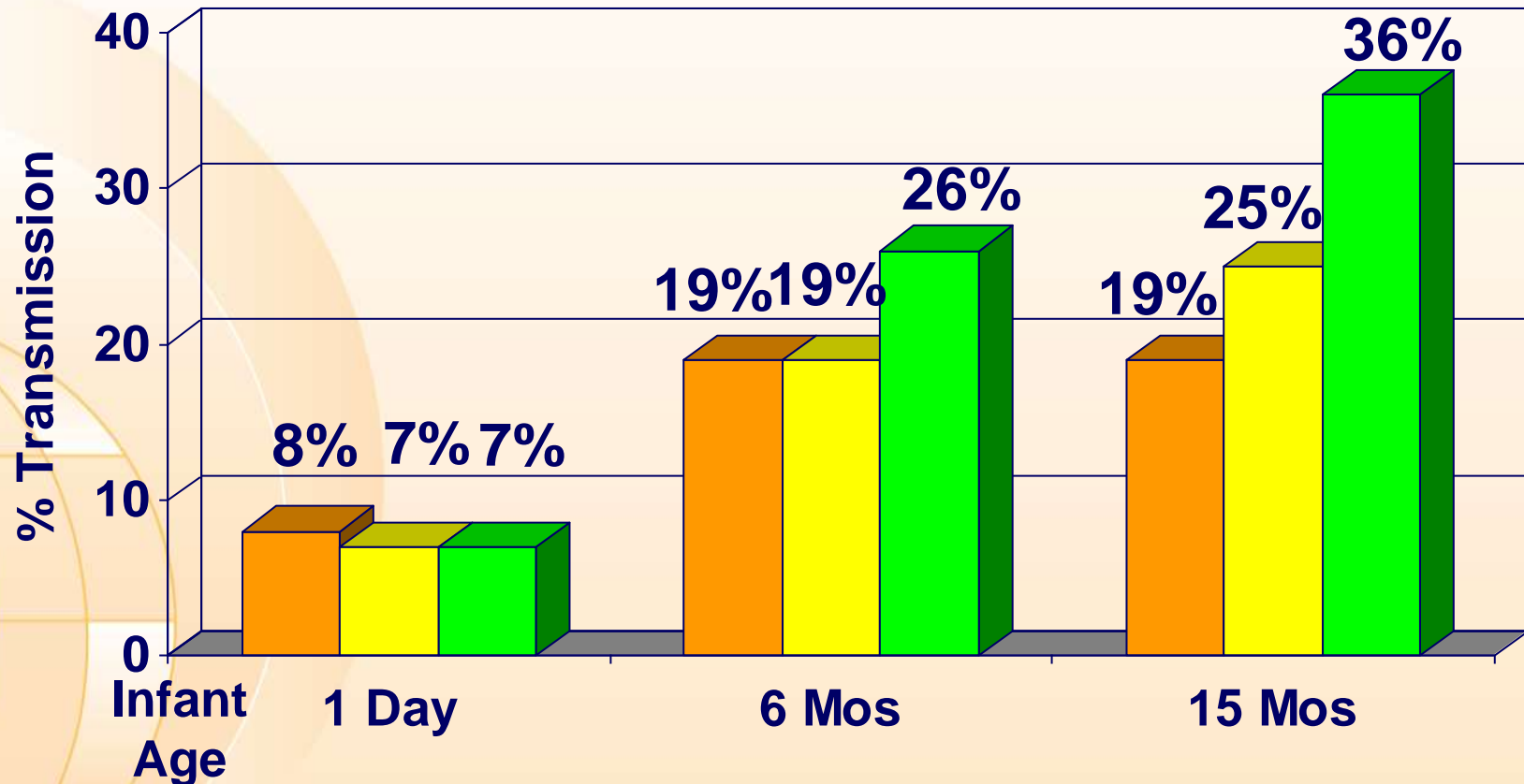
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Method of Infant Feeding and HIV Transmission in Breastfeeding Children

Coutsoudis A. XIII AIDS Conf, July 2000, Durban S Africa (LbOr6)



■ Never Breastfed (N=157)
■ Exclusive Breastfed (N=118)
■ Mixed Feeding (N=276)

At 6 months:
 Exclusive vs Mixed: 0.6 (0.3-1.0)
 Exclusive vs Never: 1.2 (0.6-2.2)

RTIs and HIV and adverse outcome of pregnancy

RTI	Possible Outcome				
	Spontaneous Abortion	Stillbirth	Pre-term rupture of membranes	Prematurity & Low birthweight	Congenital or neonatal infection
Bacterial vaginosis			X	X	
Syphilis	X	X		X	X
Gonorrhoea / Chlamydia			X	X	X
Trichomoniasis			X	X	
Herpes Simplex Virus				X	X
HIV/AIDS		X	X	X	X



What can be done to reduce adverse outcomes of pregnancy associated with RTIs?



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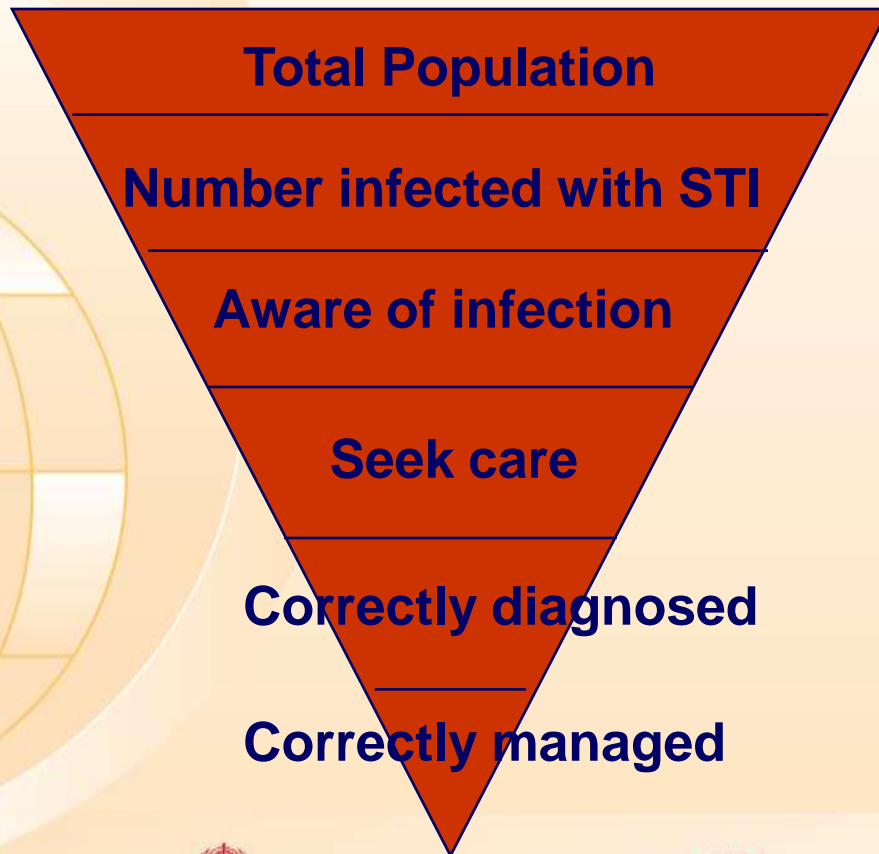


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A public health perspective on STI prevention and care



Primary prevention efforts

Vaccination

**Selective mass treatment
(PPT)**

Screening

Improve HCSB

Improve diagnosis

Improve case management

Improve partner management



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