# STIs, Bacterial vaginosis & HIV in Pregnancy

Dr. Francis J. Ndowa
WHO Geneva 2009

Training Course in Sexual and Reproductive Health Research
Geneva, February 2009

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# Overview of talk

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



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# Reminder

| | source | cause | examples |
|---|---|---|---|
| RTIs: STI | Sexual partner with STI | Sexual contact | gonorrhoea, chlamydia, syphilis, HIV, herpes simplex virus infection |
| RTIs: Endogenous | Normally found in vagina | Hormonal, medication, etc | candidiasis, bacteria vaginosis |
| RTIs: Iatrogenic | Inside or outside the vagina | Self or medical instrumentation | Staphylococcal septicaemia, etc. |



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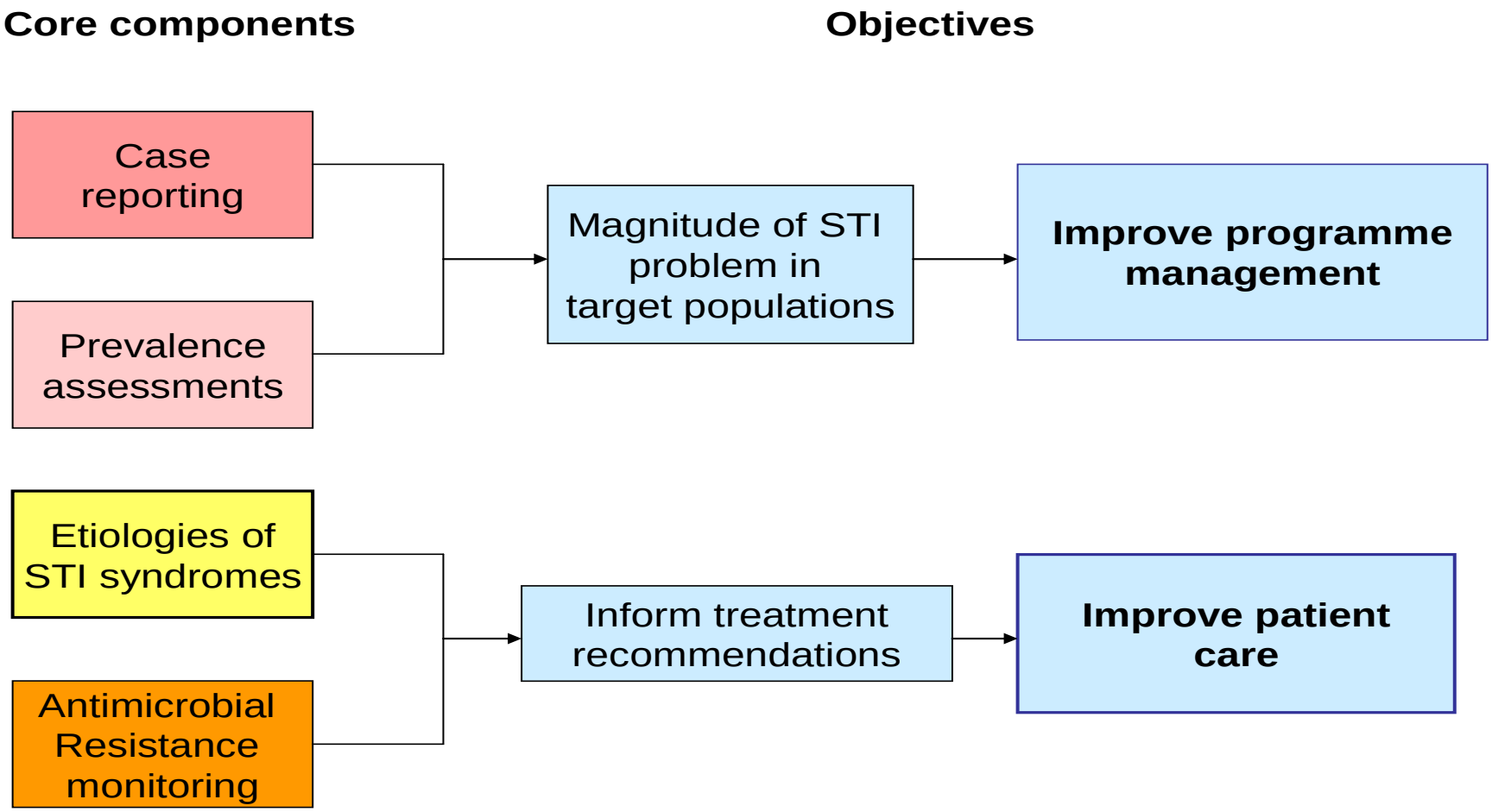
# Purpose of surveillance

- 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

# Objectives and core components of STI surveillance



# STI Surveillance: current status

## Case reporting

- Overall weakness in IDS
- Under-reporting
  - Poor Coverage
  - Poor Representation
  - Poor Motivation
- Health seeking behaviour
  - Private (GP/Pharmacy/Traditional)
  - Self-medication
- Asymptomatic/Inapparent

## Prevalence assessments

- Opportunistic data collection
- Ad hoc/Sporadic Implementation
- No Institutionalised System/Policy
- No Standard Study Design
- No Standard Laboratory Methods
- Sustainable (Lack of resources)



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# STI surveillance – basic

- Case reporting – syndromic (male urethral discharge, male/female genital ulcer disease)
- STI prevalence assessment and monitoring – high risk populations
- Antimicrobial resistance monitoring
- Assess and monitor etiology of syndromes
- Special studies



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# STI surveillance – advanced

- Case reporting – etiologic (syphilis, gonorrhoea, chlamydia, congenital syphilis)
- STI prevalence assessment and monitoring – high risk populations and general population
- Antimicrobial resistance monitoring
- Assess and monitor etiology of syndromes
- Special studies



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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

## Consequences

- very few STI surveillance programmes in resource-limited countries



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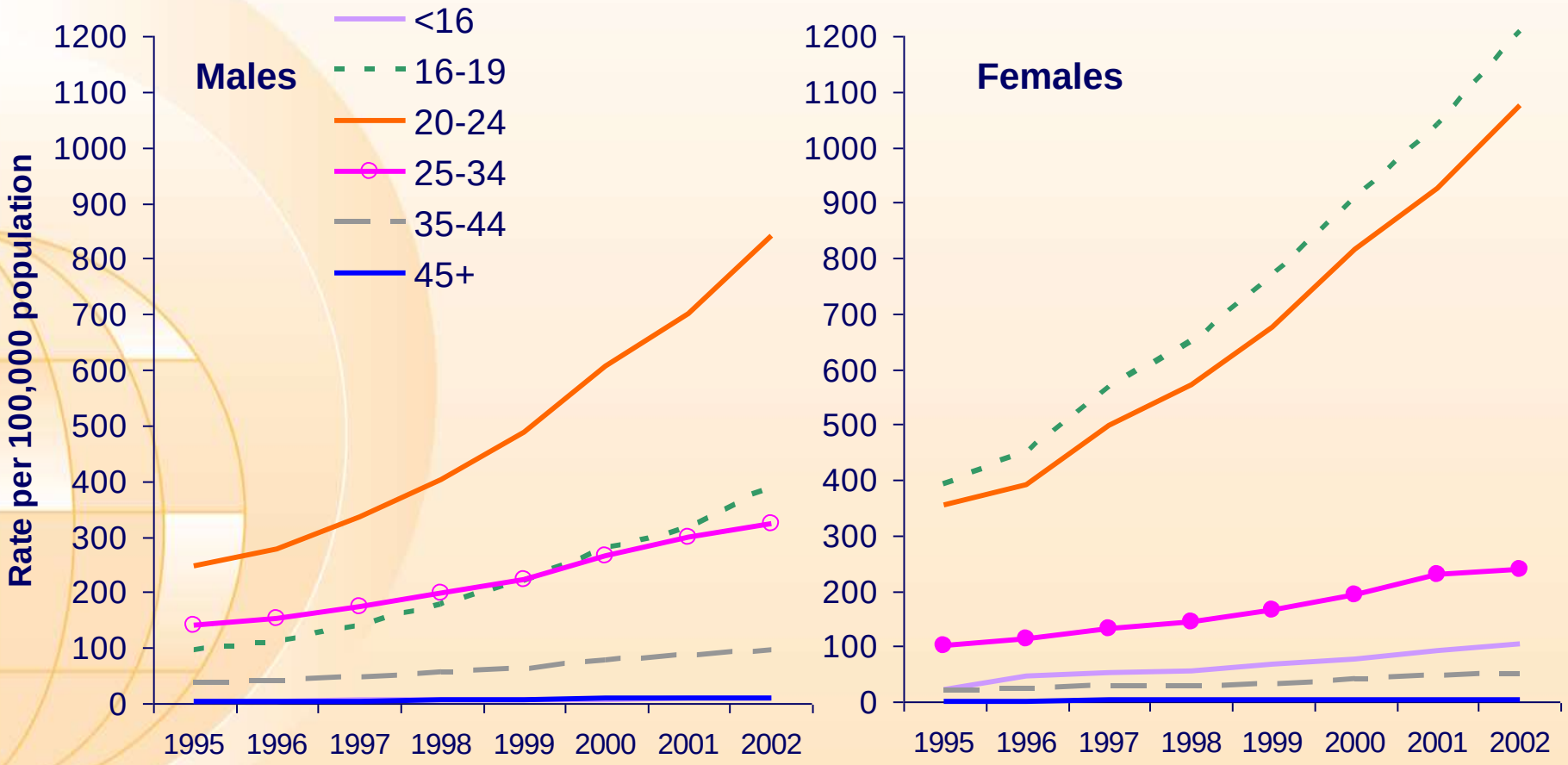
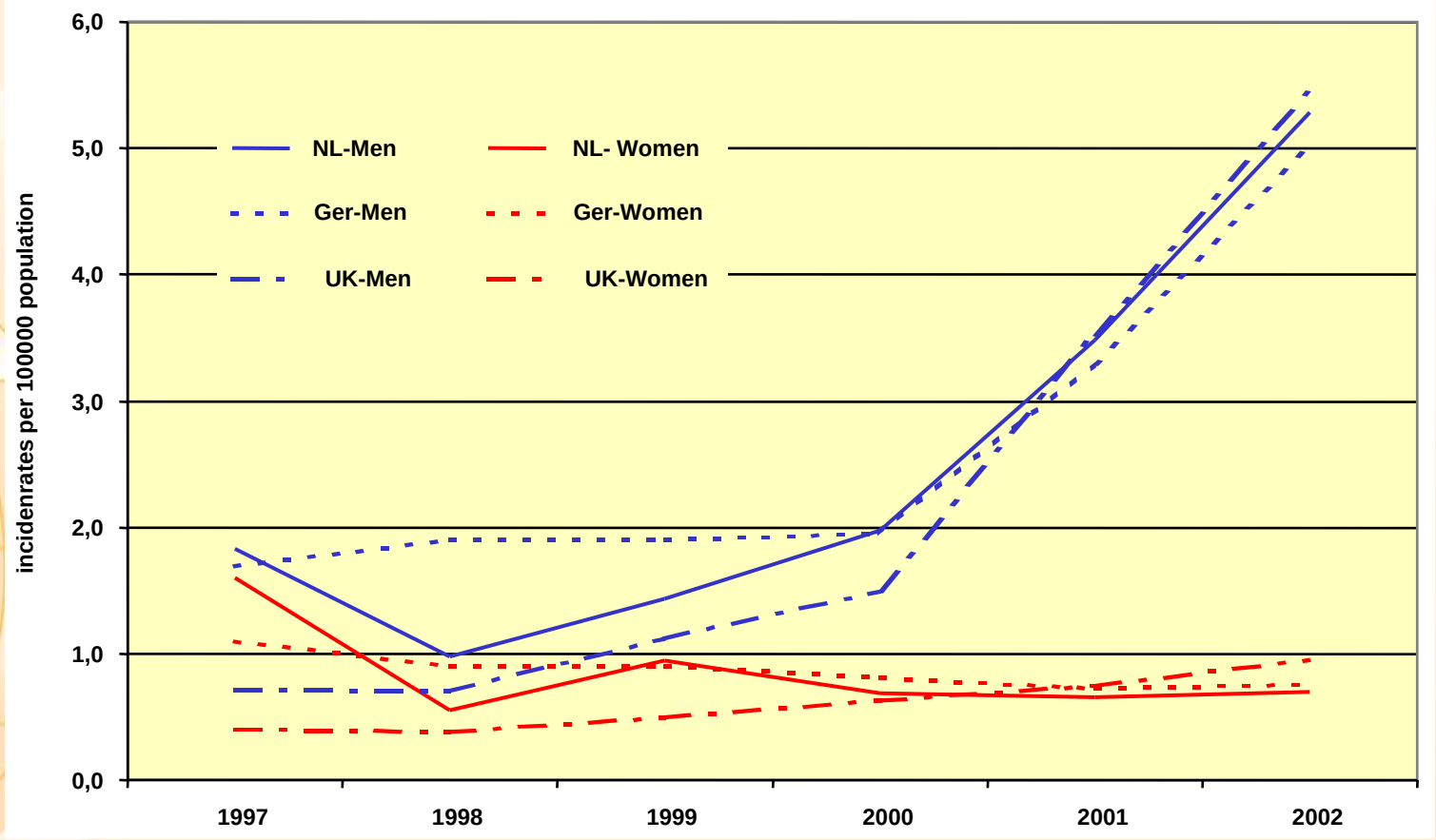
# Diagnoses of uncomplicated genital chlamydial infection in GUM clinics by sex and age group, UK: 1995-2002*




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

Source: HPA, UK

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



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# Population-based prevalence of RTIs in resource-constrained 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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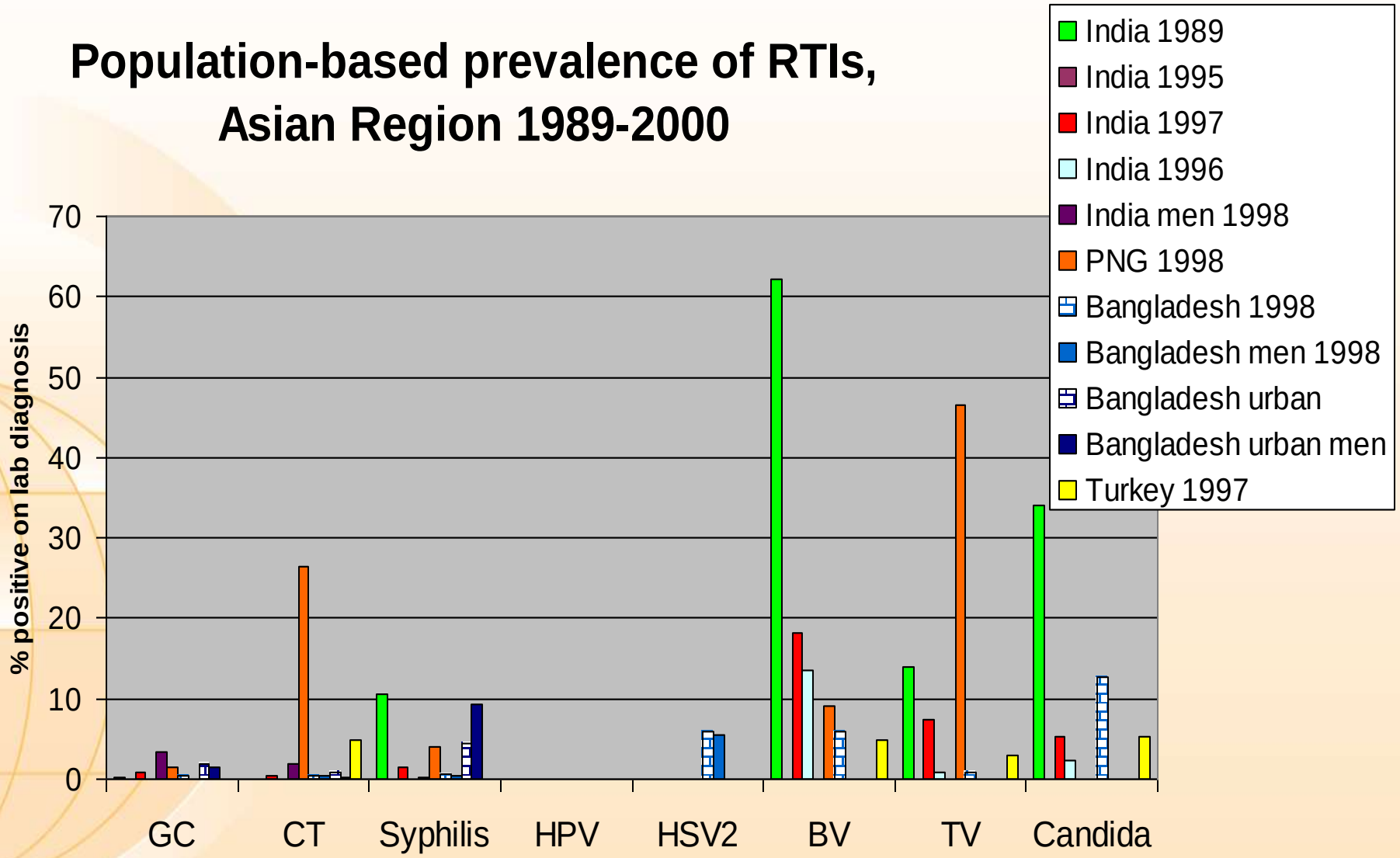
# Population-based prevalence of RTIs, Asian Region 1989-2000



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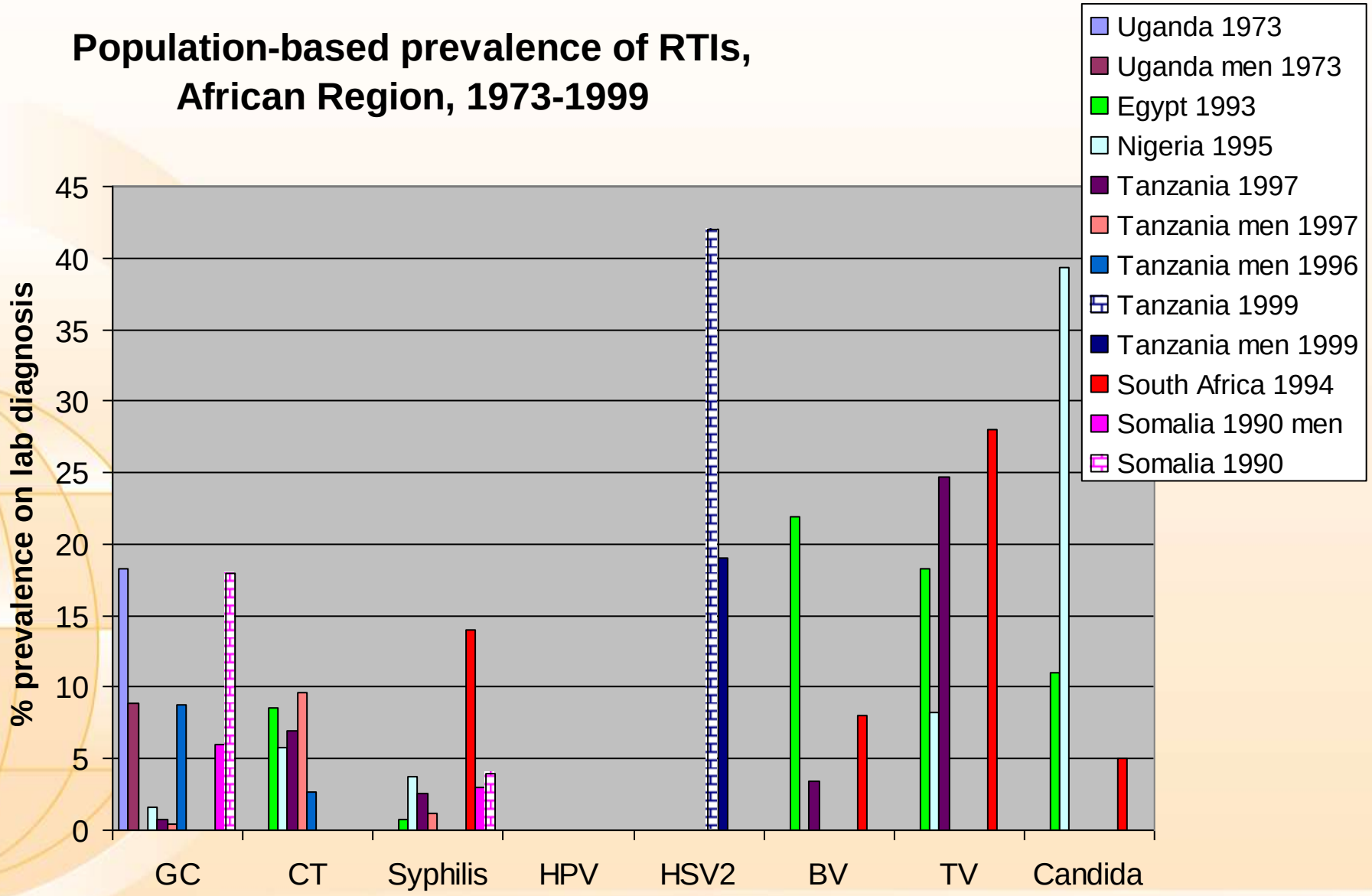
# Population-based prevalence of RTIs, African Region, 1973-1999



# 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



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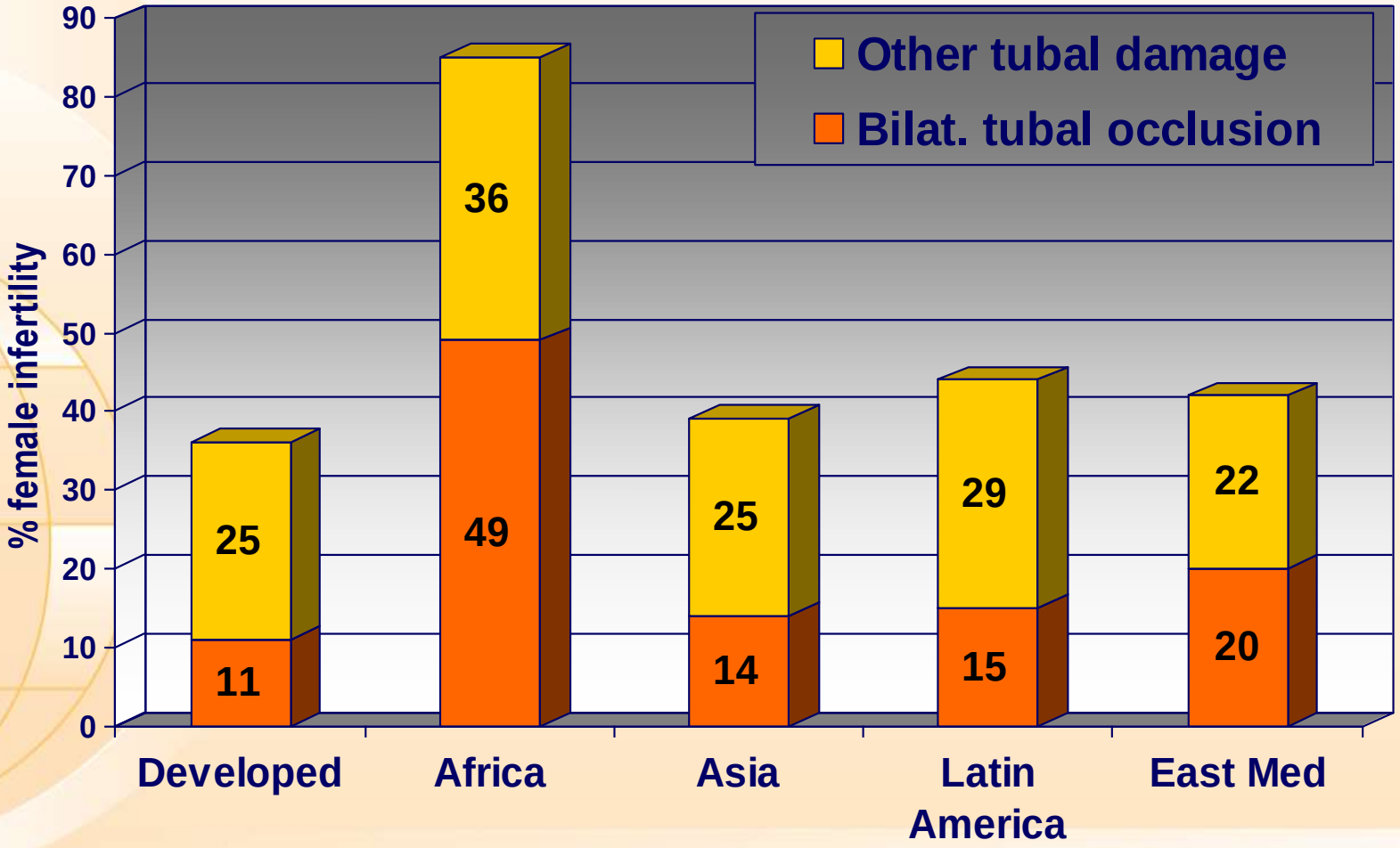
# Fallopian tube damage as a cause of female infertility in the world




Cates W *et al*, *Lancet*, 1985

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# 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



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# 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)



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# 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



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# Trichomoniasis

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



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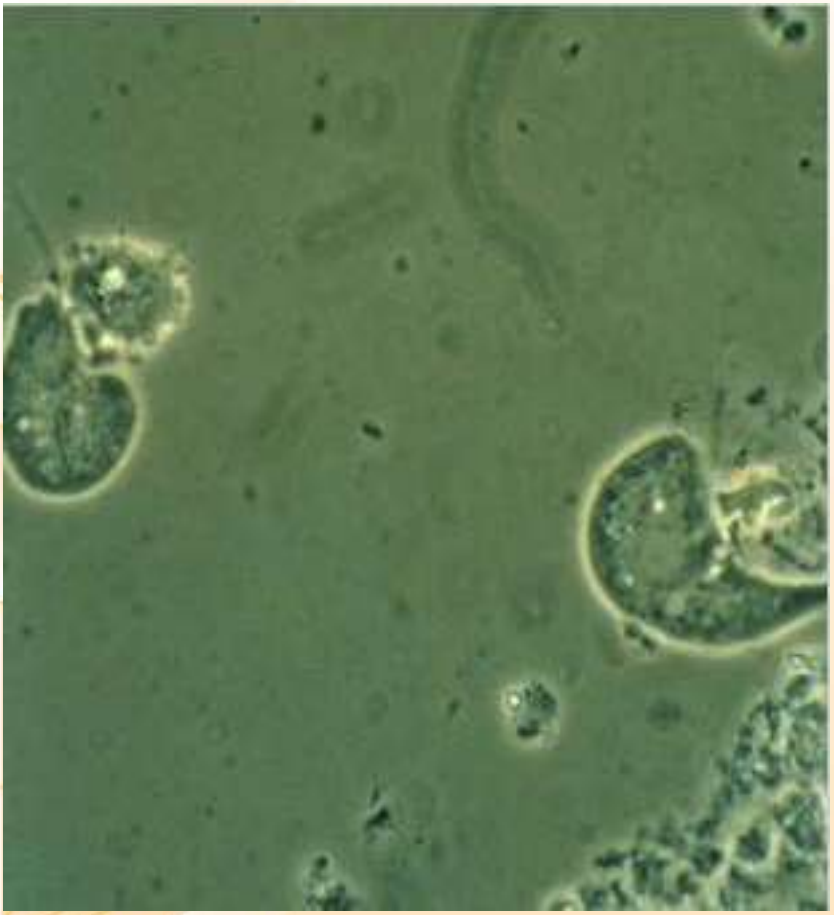
# Trichomonas vaginalis



*Wet mount*

- T. vaginalis - a polymorphic organism - changing shape as it moves in amoeboid fashion

- usually recognized from the movement of the flagellae



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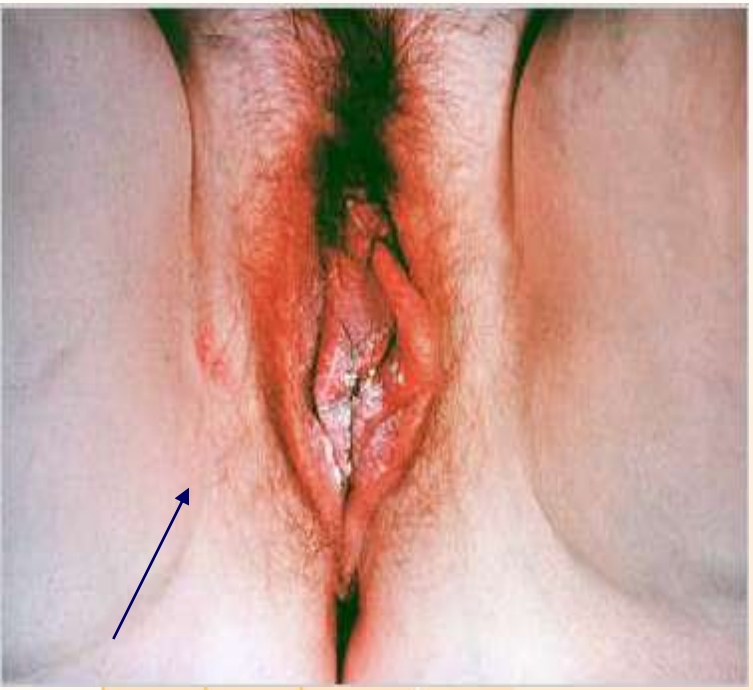

## Candida vulvitis

- 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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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



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# Bacterial vaginosis

Cervix covered with a discharge associated with BV

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



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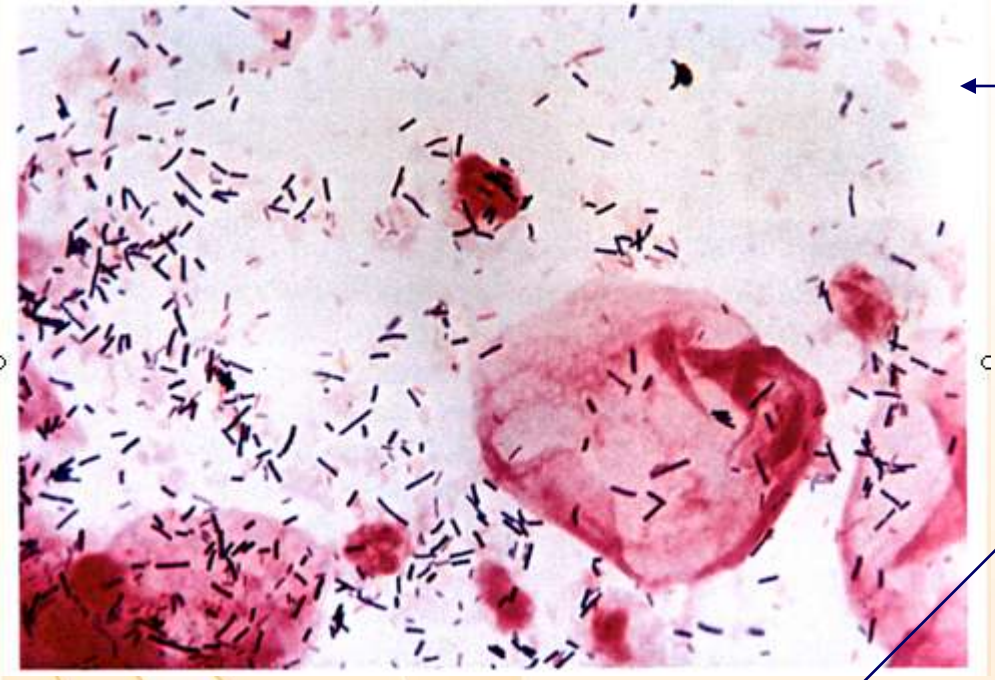
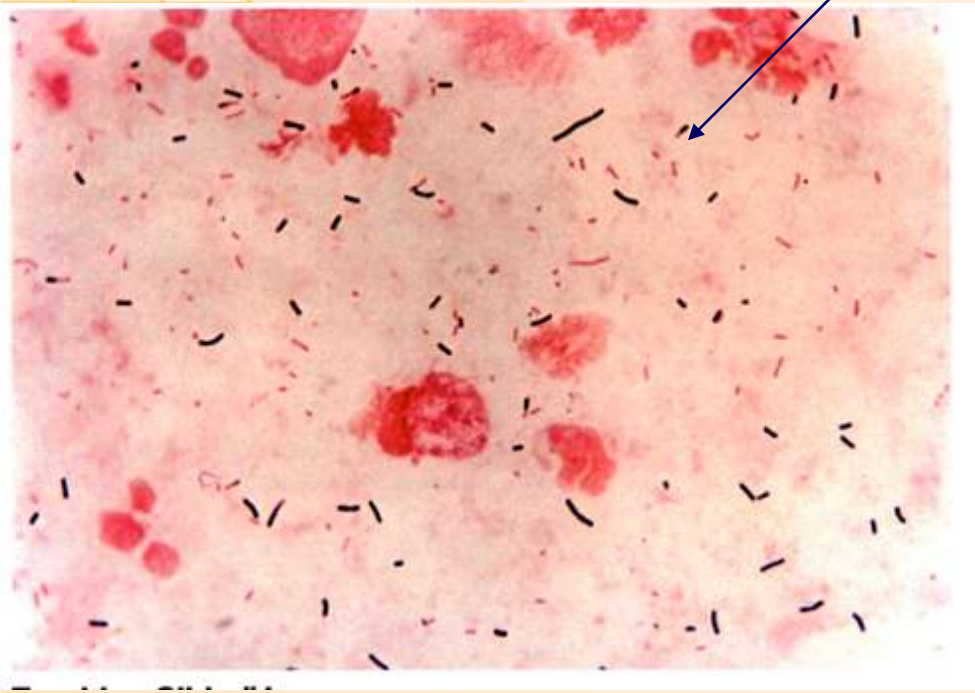
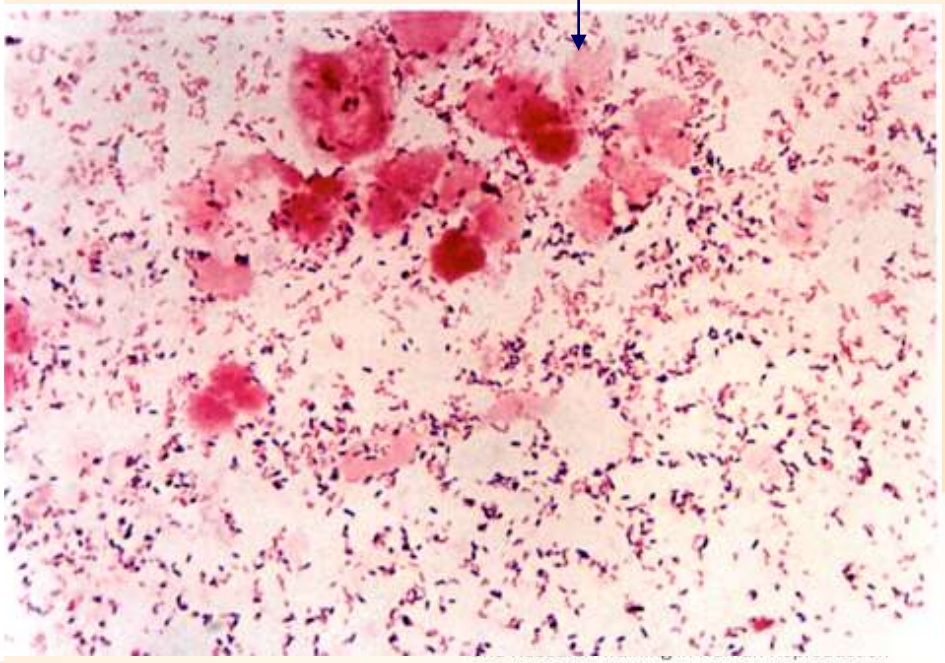


**Normal flora:**
**Gram-stained smear showing a pure flora of Gram-positive rods of lactobacilli**

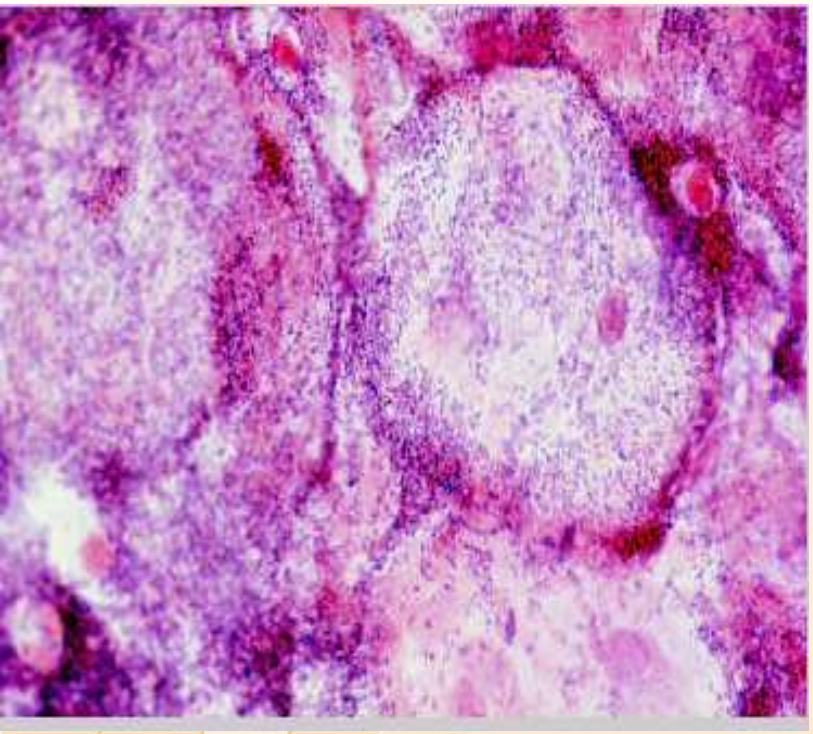
**Gram-stained smear showing mixed intermediate flora - Gram-positive and Gram-negative organisms**



**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.



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# 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

# 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



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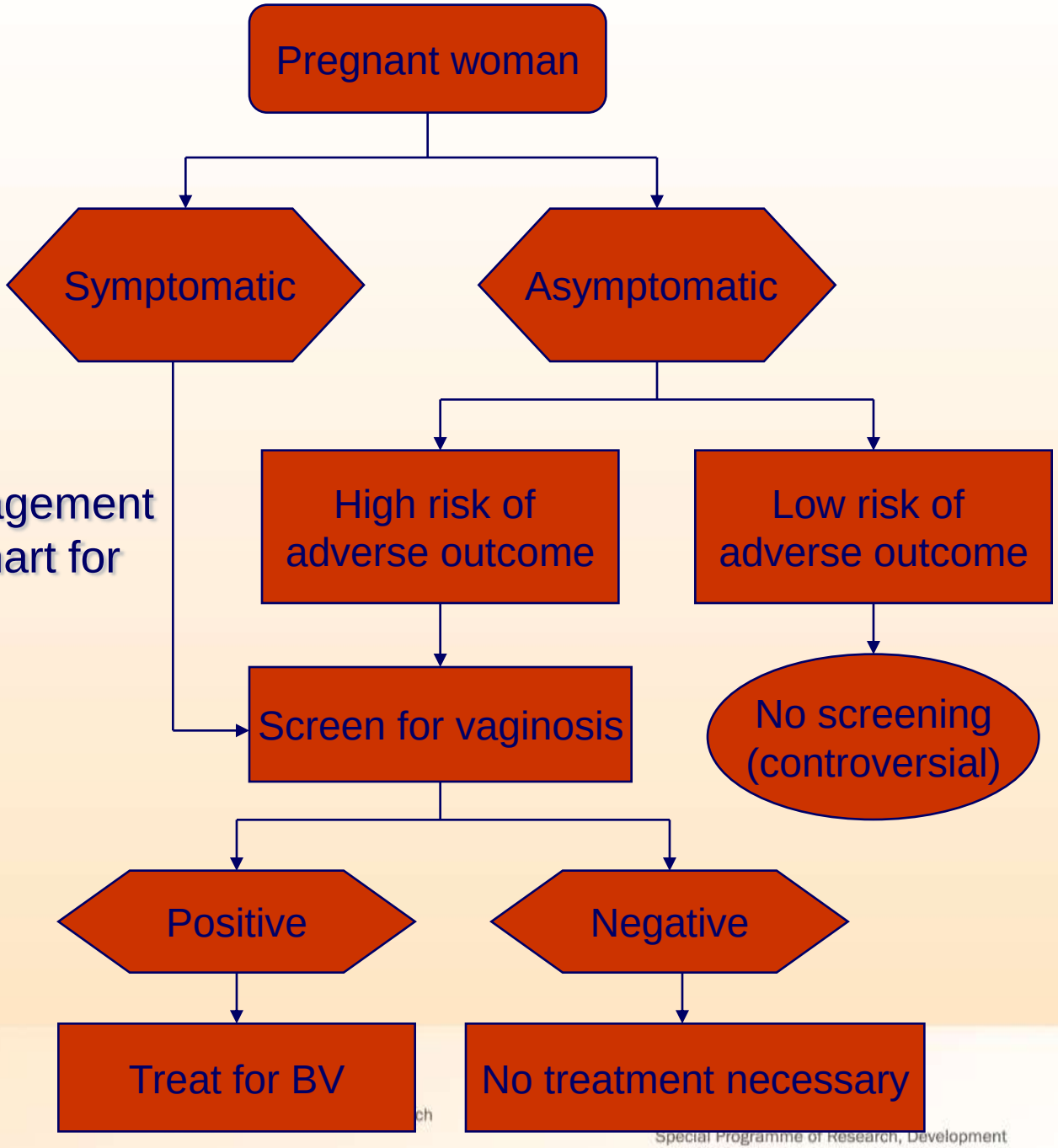
Simplify decision and management with a locally agreed flowchart for health workers



# 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.

# 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

# 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

# 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)

# 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**)



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# 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.



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# 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, mucous membranes
- Soft, papular lesions, known as condylomata lata, develop in moist areas such as the genitals and axillae.



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# Implementation of 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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# 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**



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# 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**



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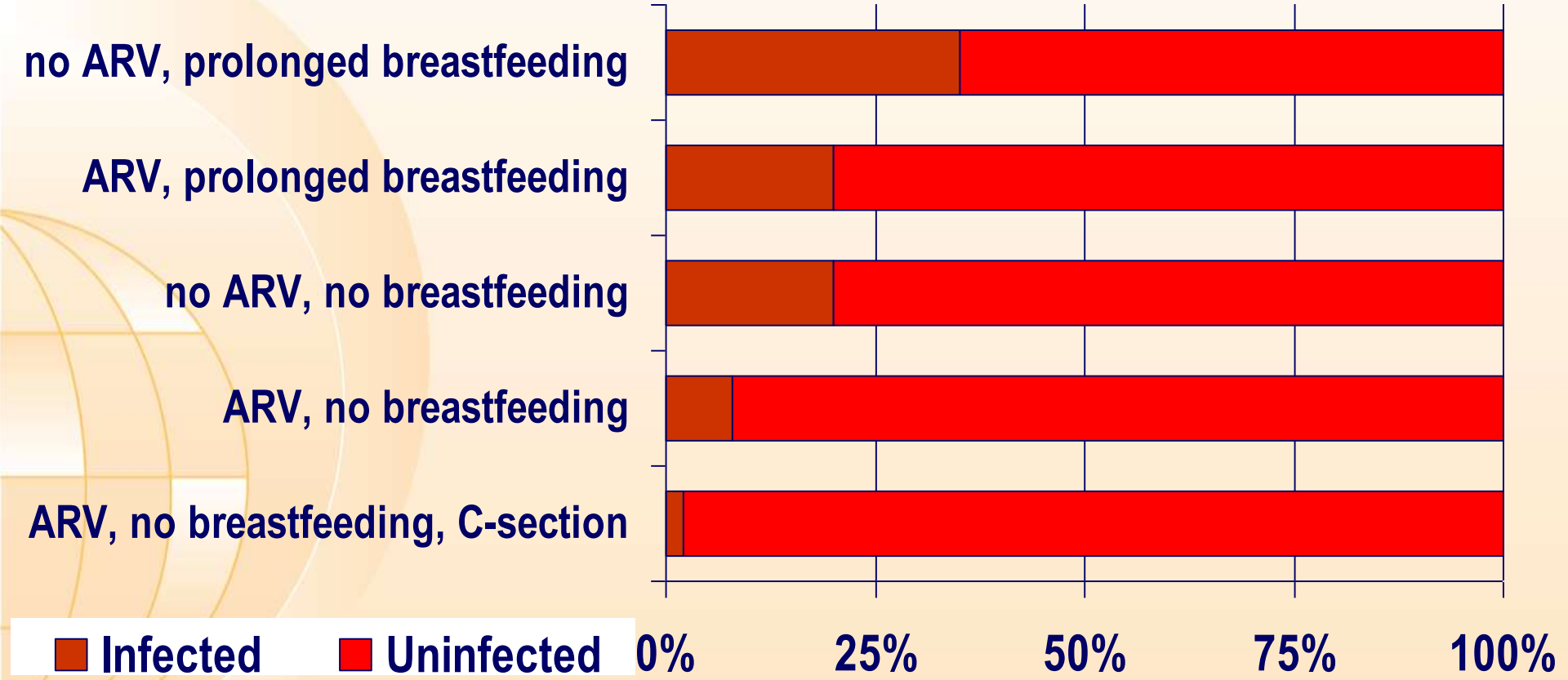
# The variable risk of MTCT of HIV (with and without preventive interventions



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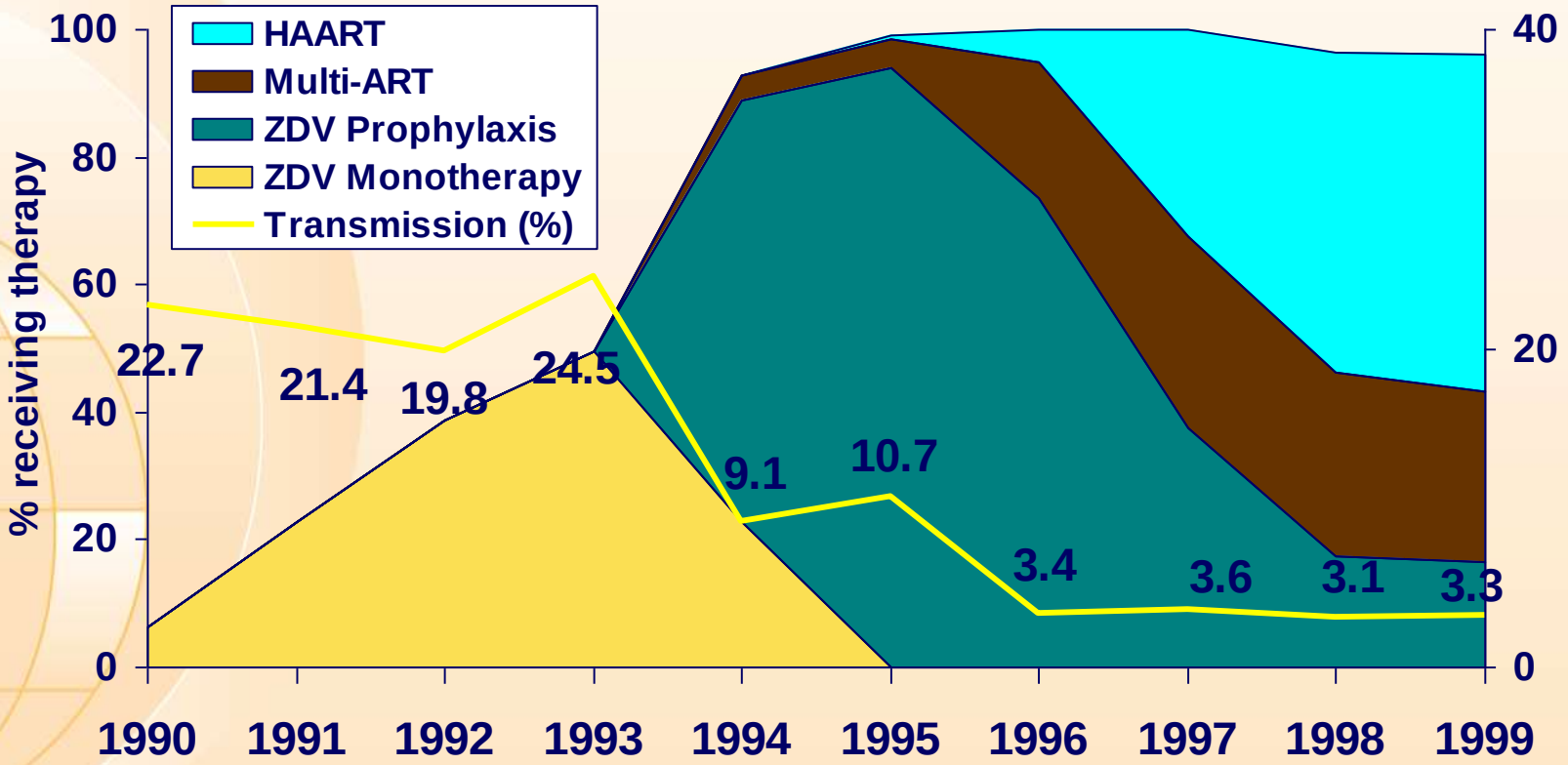
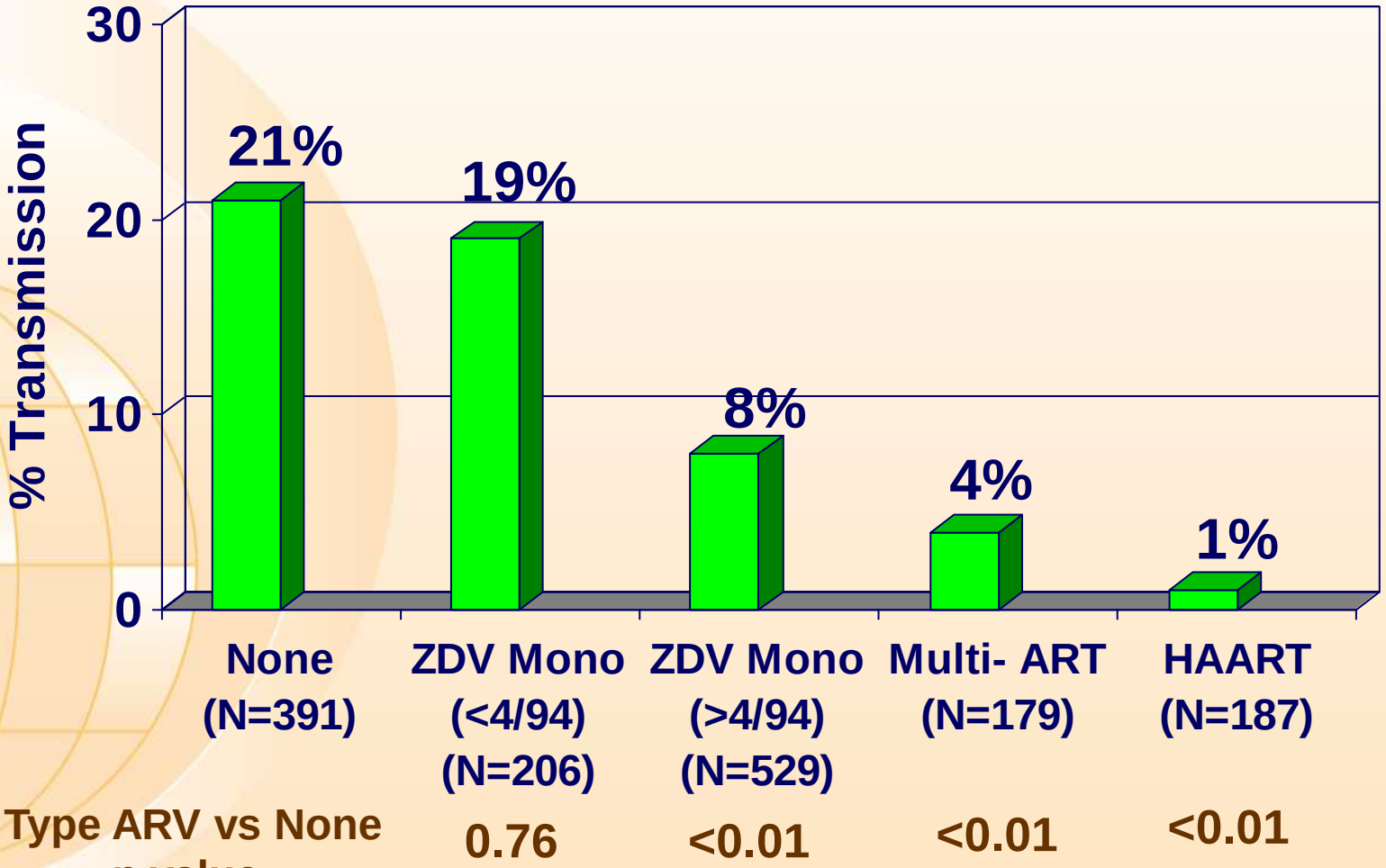
# ARV Use and HIV Transmission
## (WITS, USA)




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

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

*Blattner W. XIII AIDS Conf, July 2000, Durban S Africa (LBOr4)*




| Type ARV vs None p value: | ZDV Mono (<4/94) (N=206) | ZDV Mono (>4/94) (N=529) | Multi- ART (N=179) | HAART (N=187) |
|---|---|---|---|---|
| | 0.76 | <0.01 | <0.01 | <0.01 |



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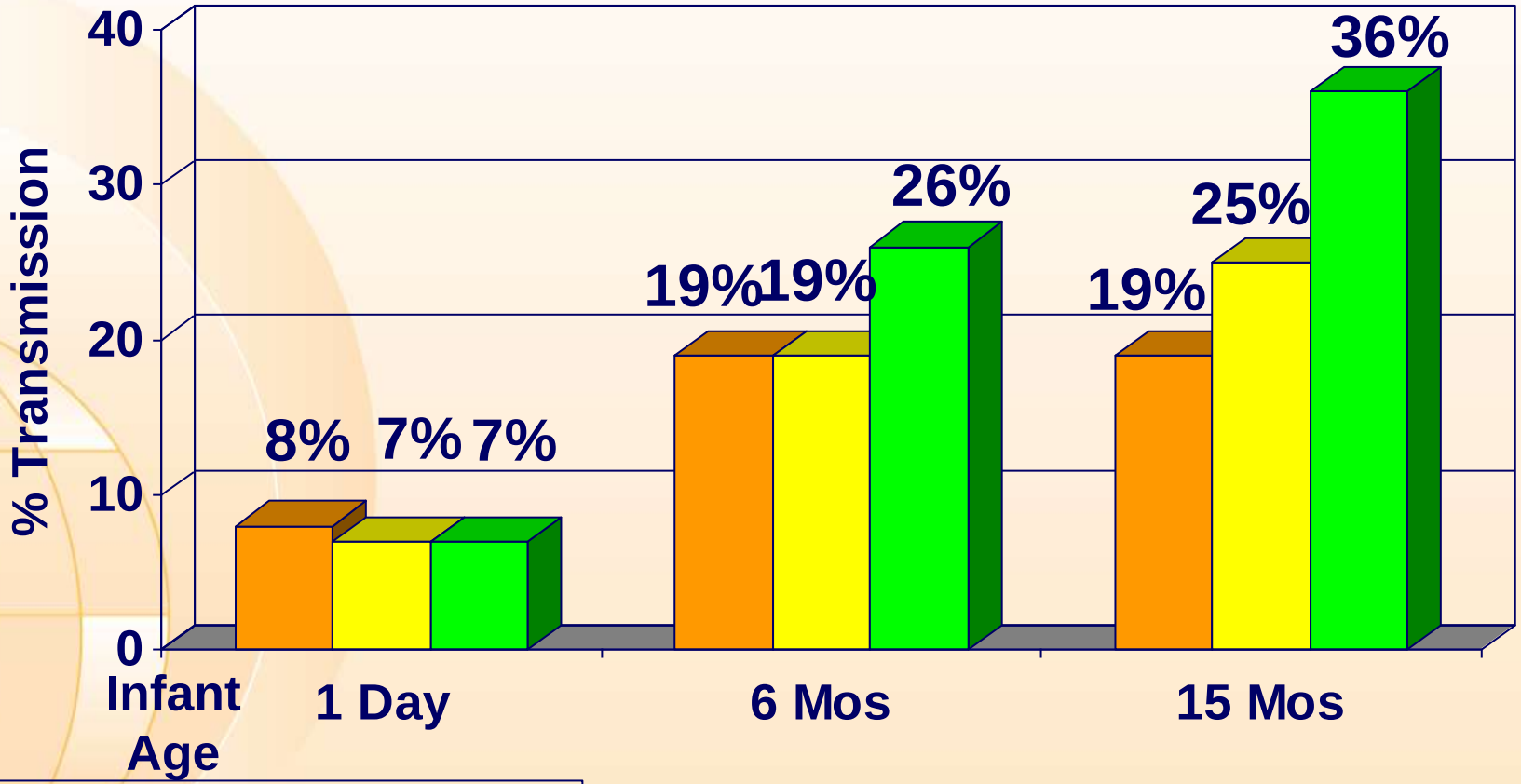
# Method of Infant Feeding and HIV Transmission in Breastfeeding Children *Coutsoudis A. XIII AIDS Conf, July 2000, Durban S Africa (LbOr6)*




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



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# 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 |



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



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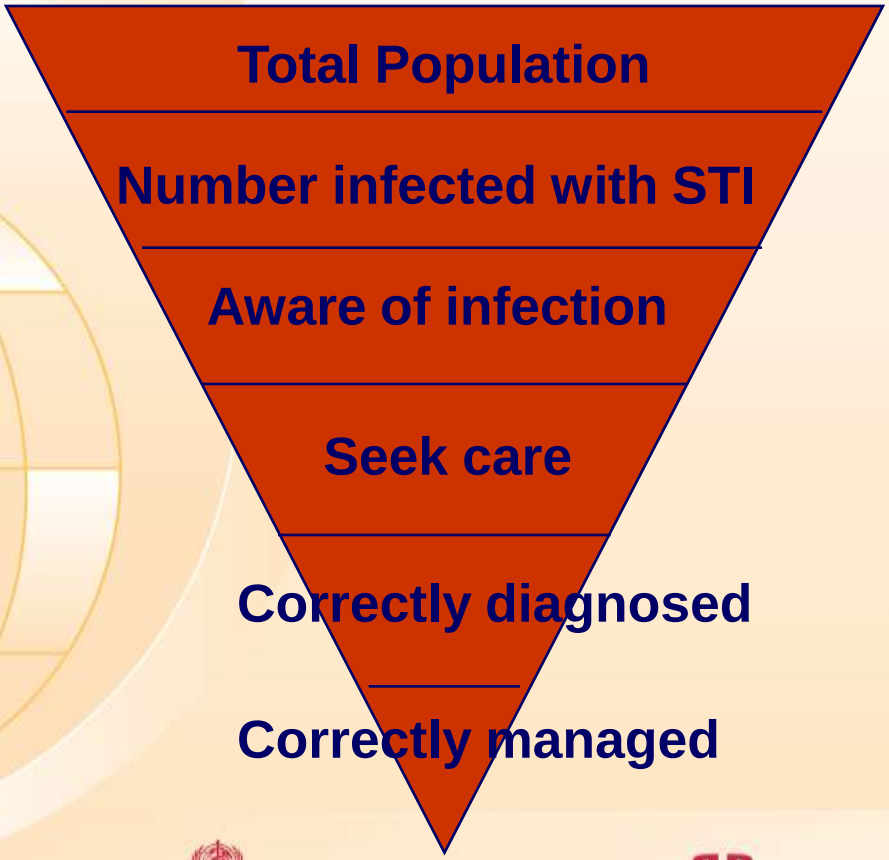
# A public health perspective on STI prevention and care




**Primary prevention efforts**

**Vaccination**

**Selective mass treatment (PPT)**

**Screening**

**Improve HCSB**

**Improve diagnosis**

**Improve case management**

**Improve partner management**



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