STIs, Bacterial vaginosis & HIV in Pregnancy

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Saiqa Mullick (Pop Council)

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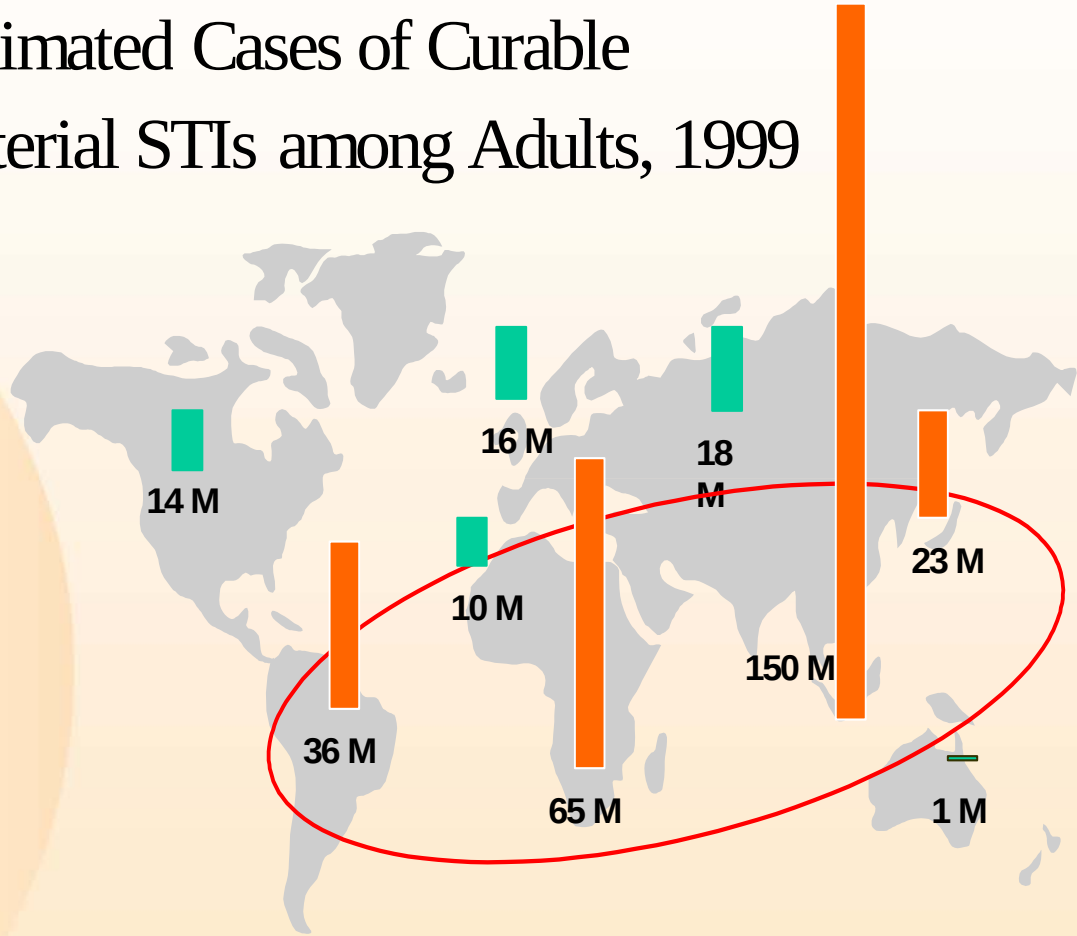
Overview of talk

- 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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Models of STI surveillance

- Routine systematic recording and reporting
  - of STI patients at health-care facilities
  - of specific diseases
  - of syndromes and associated sequelae

- Special studies
  - proportions of persons infected with STIs in different population groups
  - most common microbial causes of STI syndromes
  - monitoring prevalence of antimicrobial resistance

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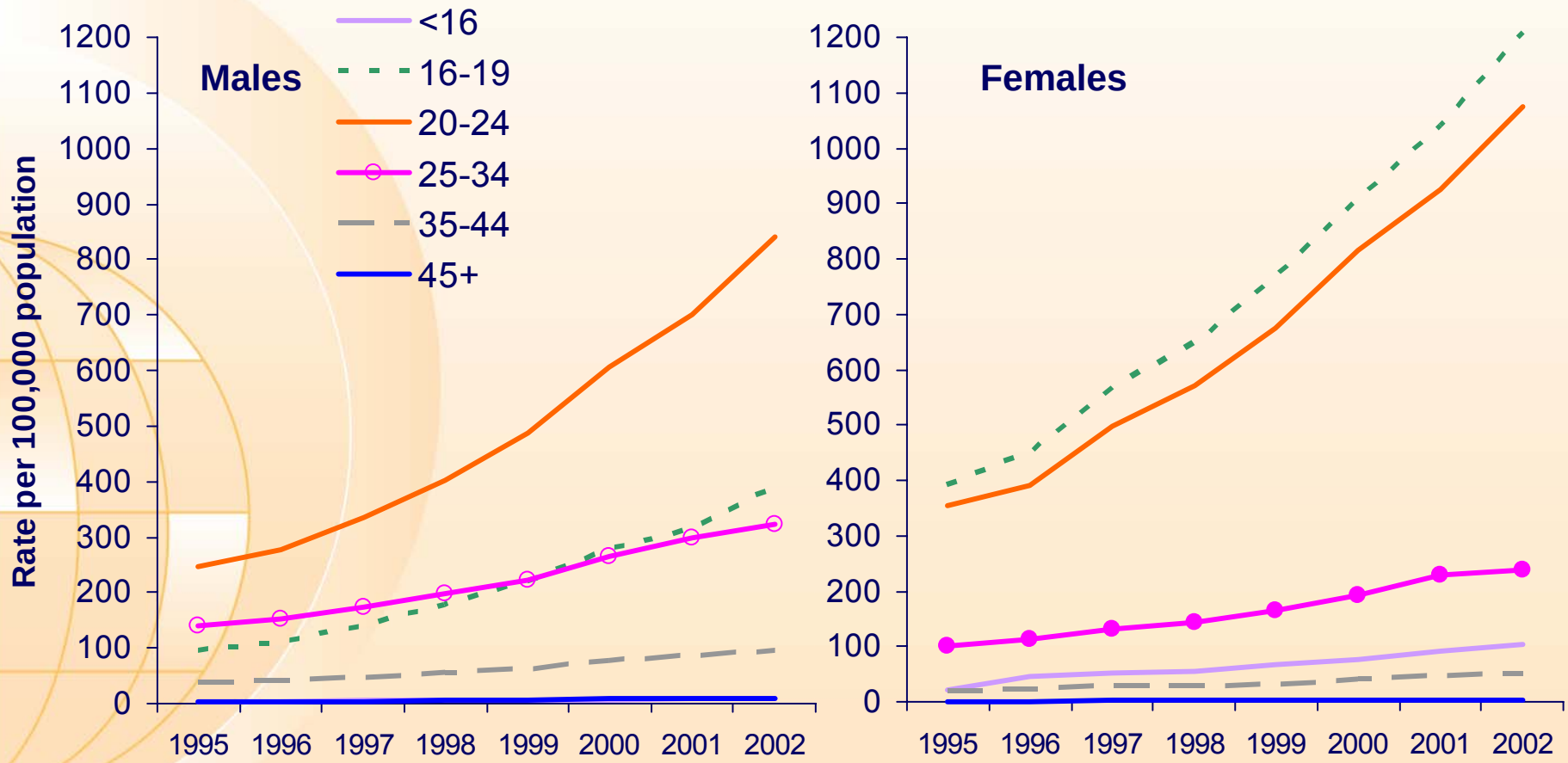
Diagnoses of uncomplicated genital chlamydial infection in GUM clinics by sex and age group, UK: 1995-2002*



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

Source: HPA, UK

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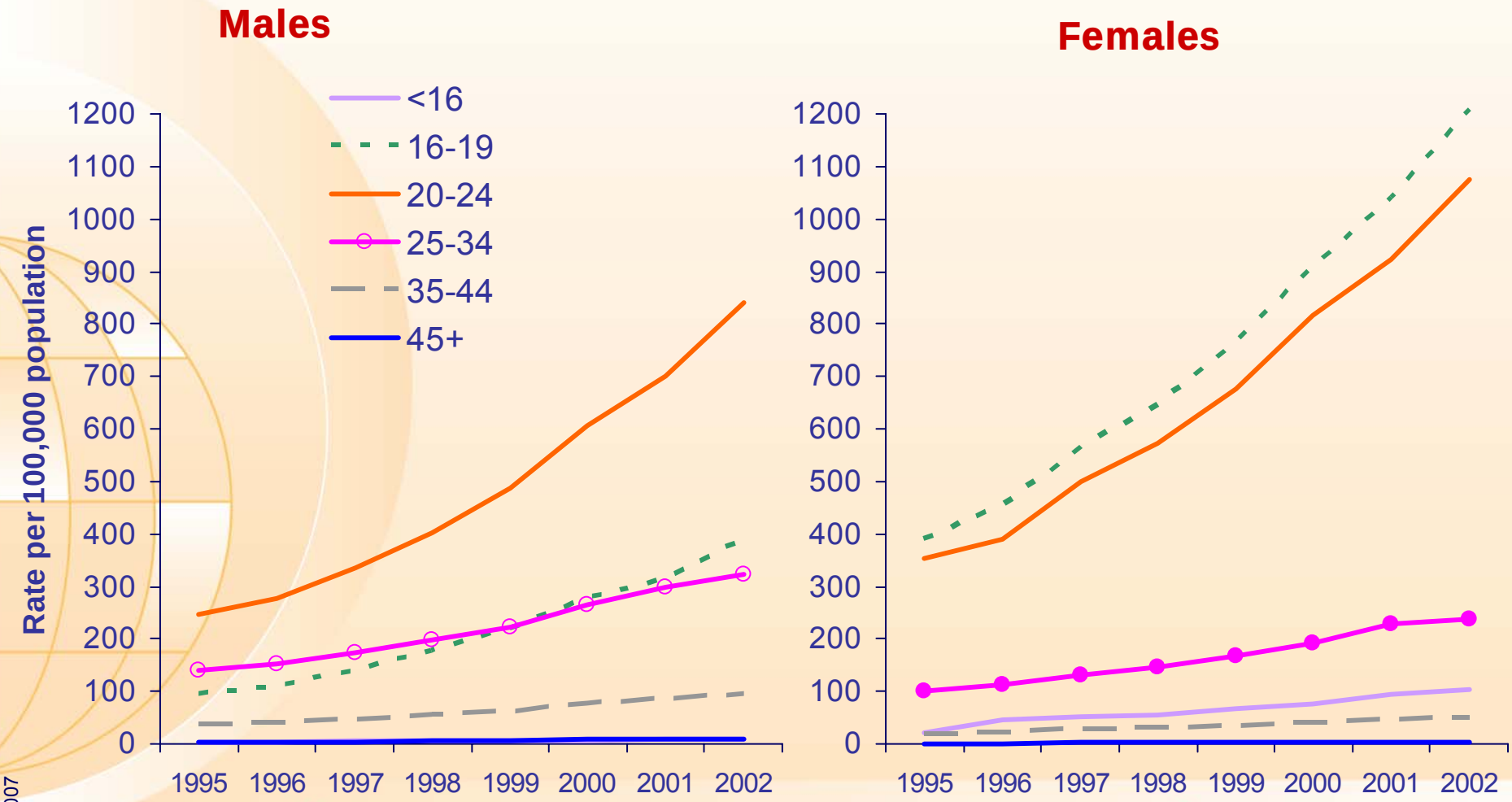
Diagnoses of uncomplicated gonorrhoea in GUM clinics by sex and age group, UK: 1995-2002*



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*Data are currently unavailable from Scotland for 2000, 2001. Source: HPA, UK

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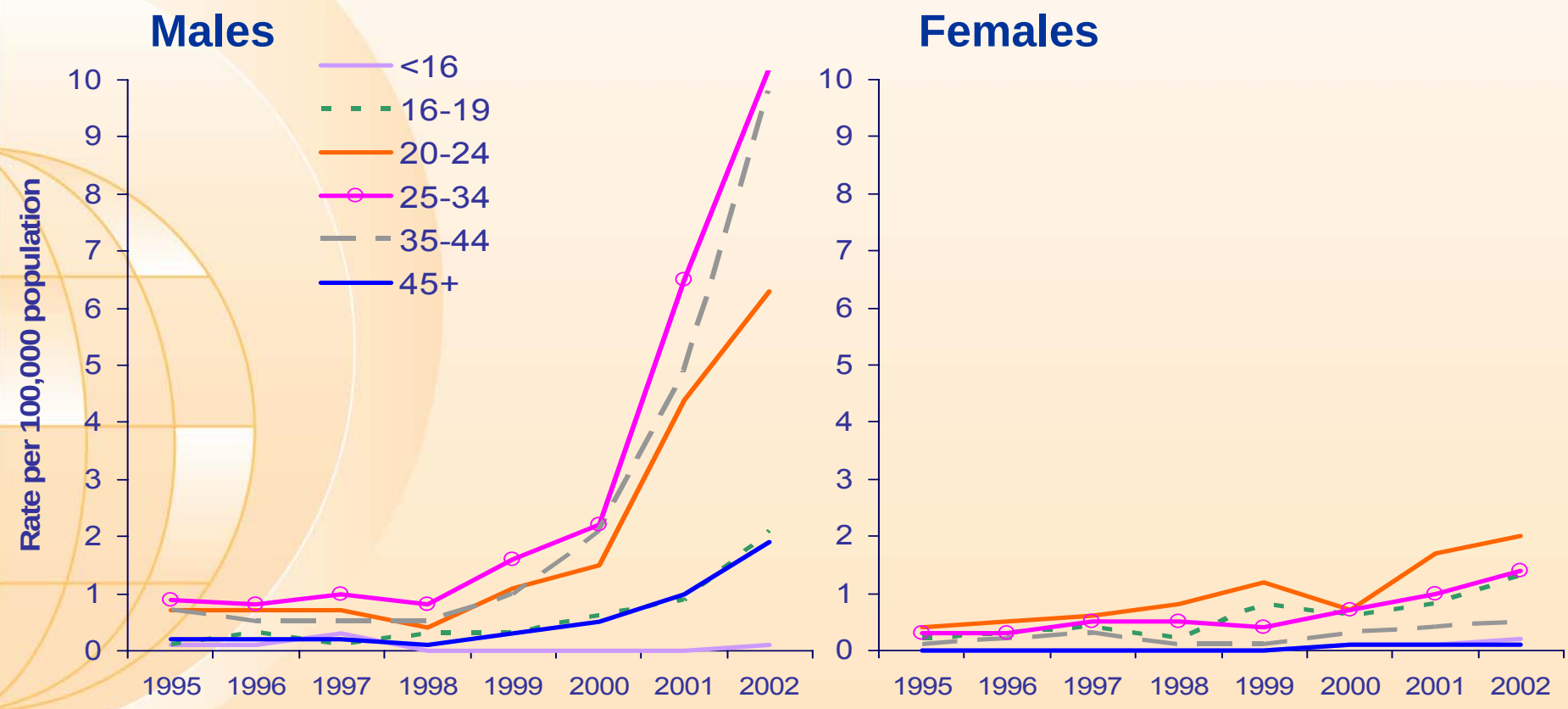
Rates of diagnoses of infectious syphilis (primary & secondary) by sex and age group, GUM clinics, United Kingdom*, 1995 - 2002



* Data are currently unavailable from Scotland for 2001 and 2002
Data source: KC60 statutory returns and ISD(D)5 data. HPA, UK.

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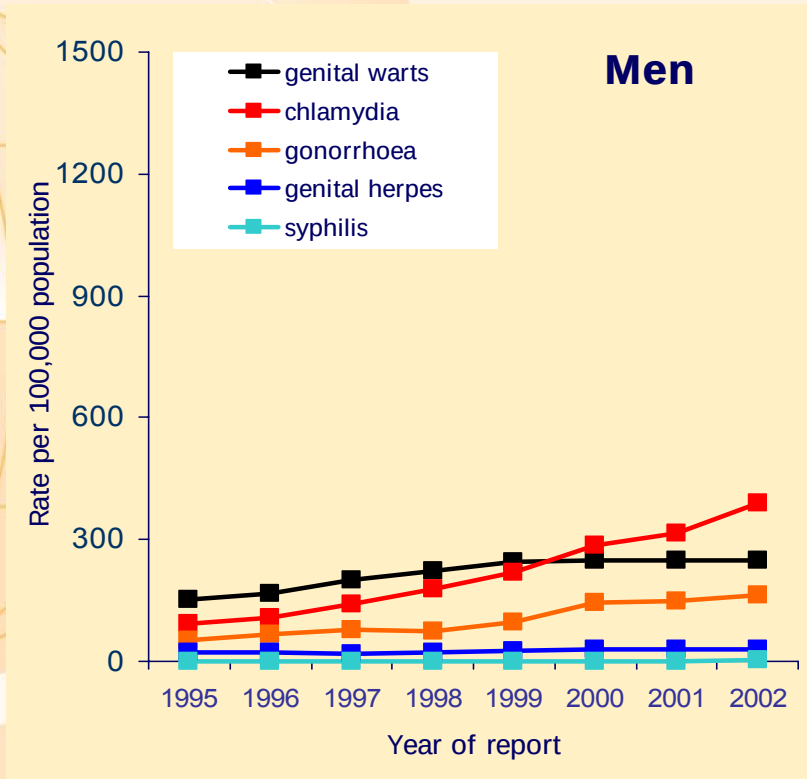
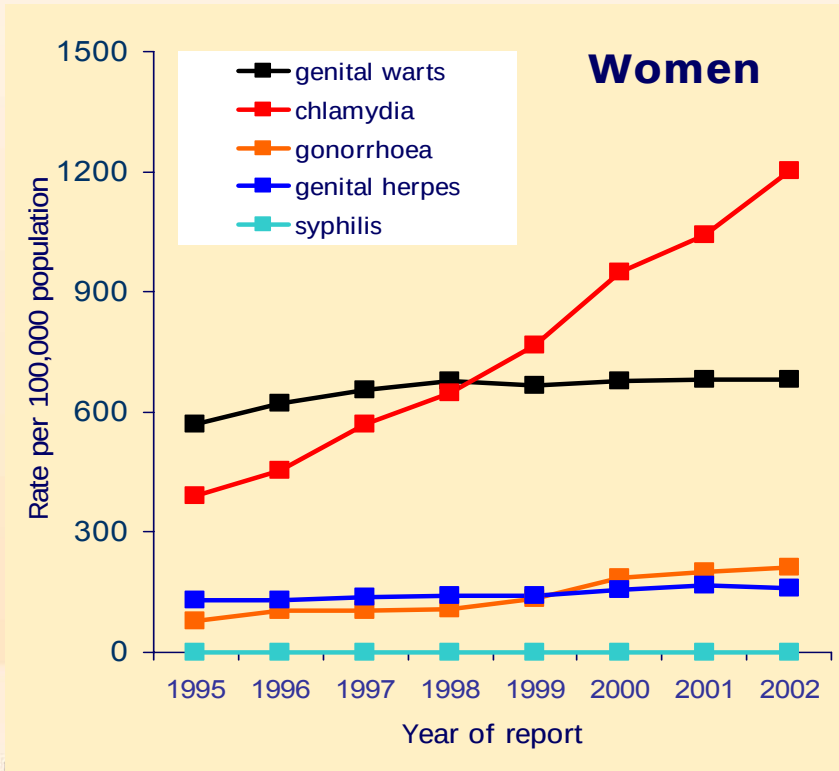
STIs in young people in the UK –increasing trends

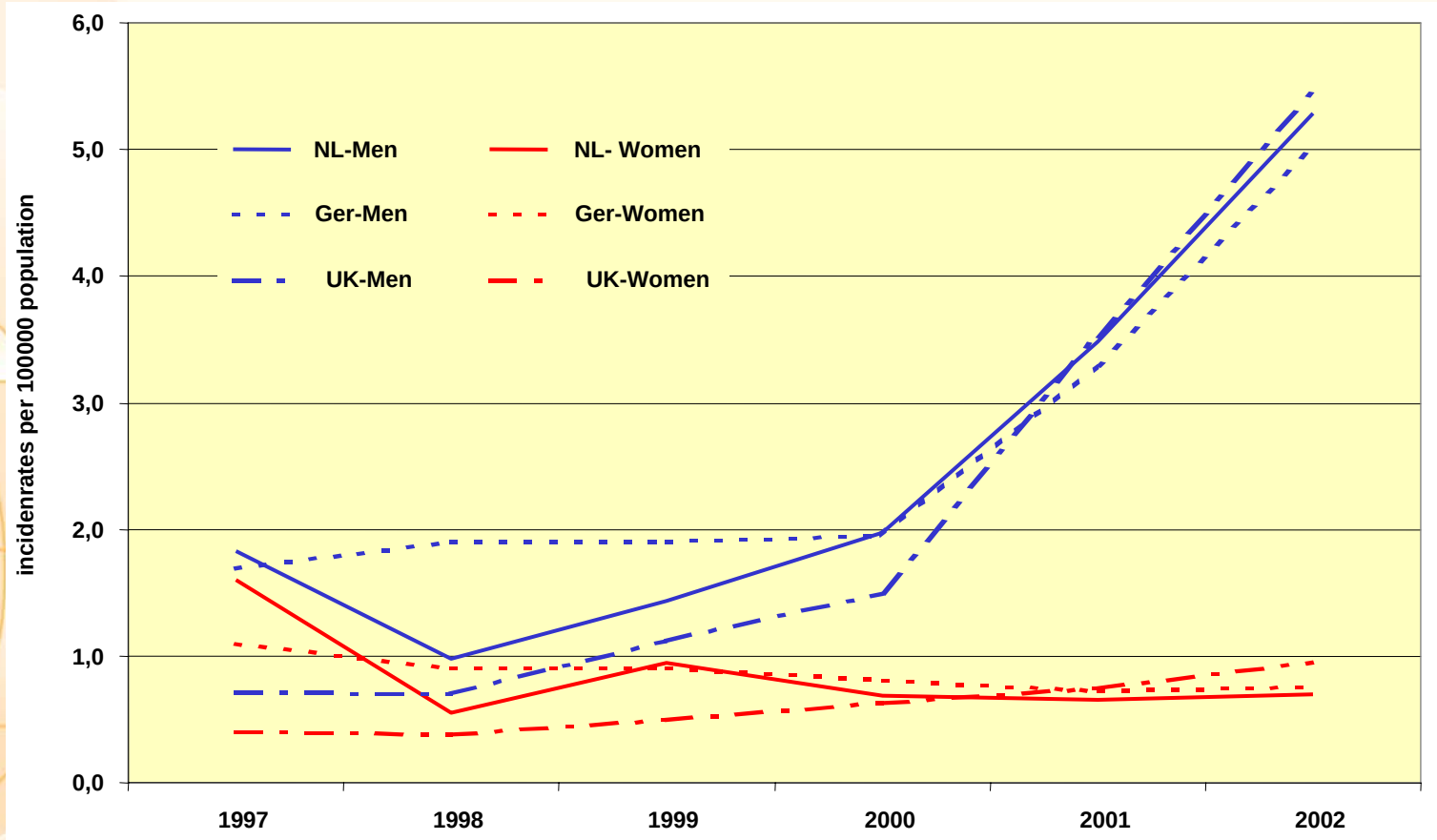
Fig 3. Recent trends in major acute STIs in young people, 16-19 years. E, W &NI.





Source: HIV/STI Division, CDSC

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)

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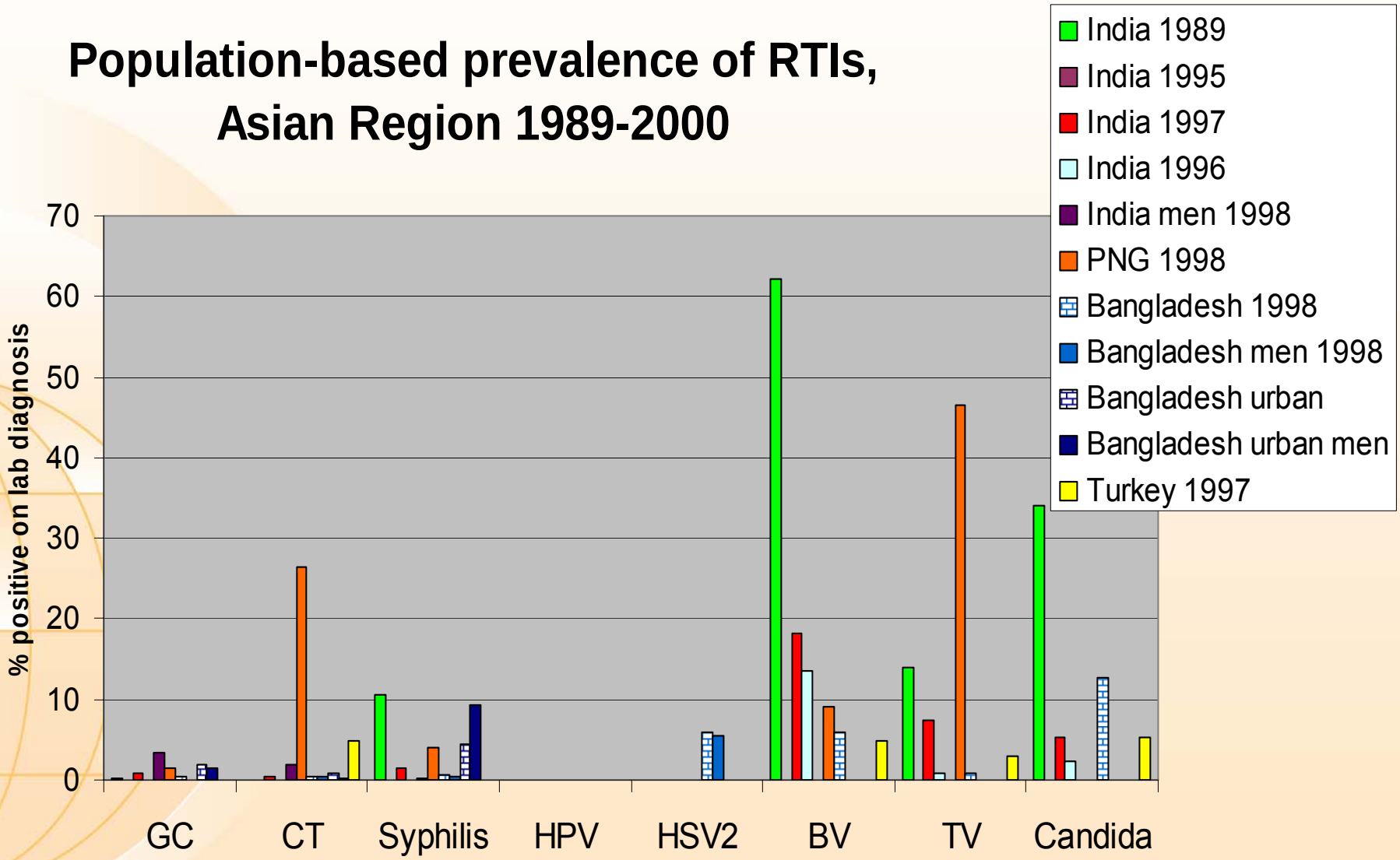
Population-based prevalence of RTIs, Asian Region 1989-2000



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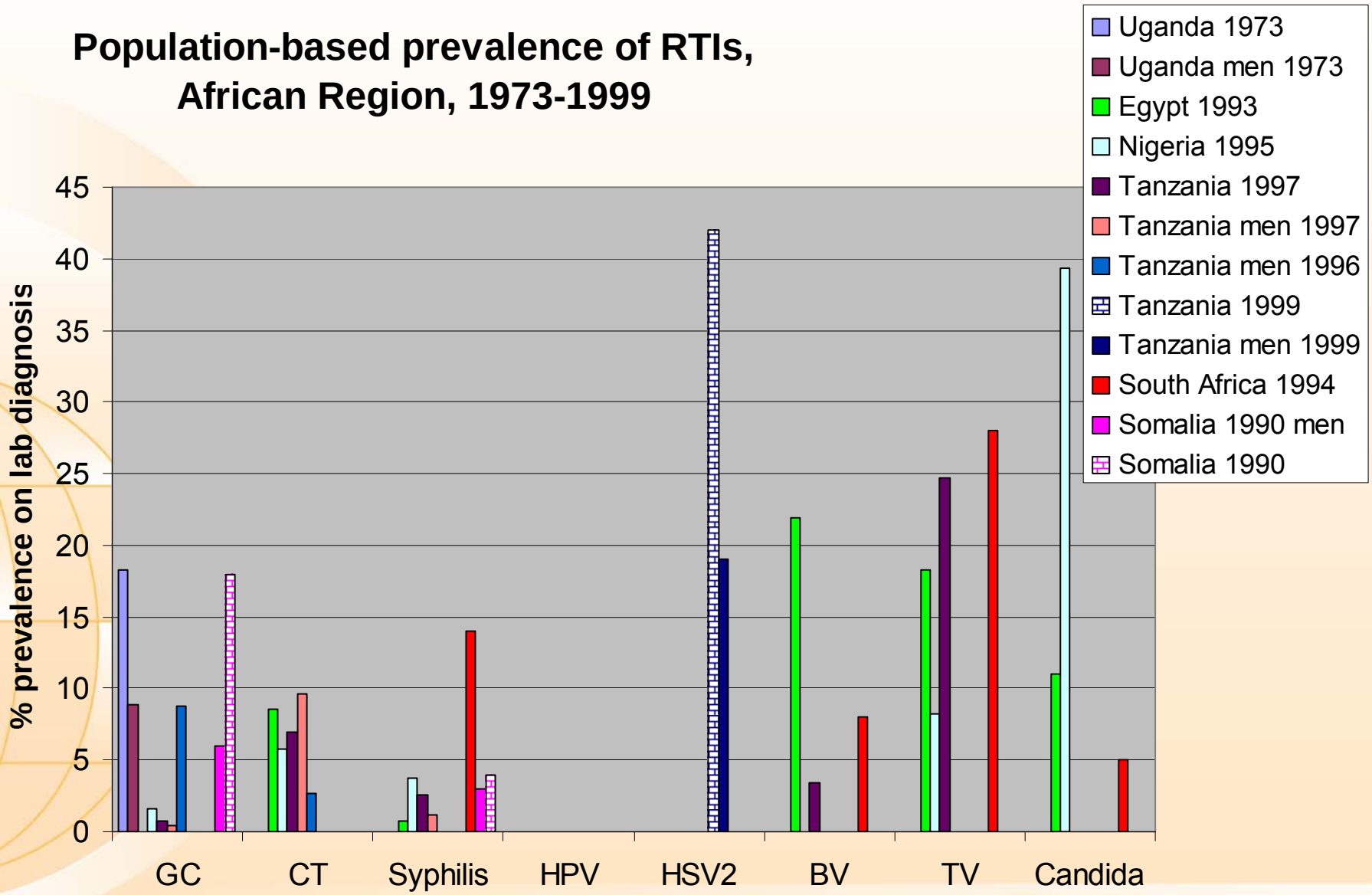
Population-based prevalence of RTIs, African Region, 1973-1999



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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

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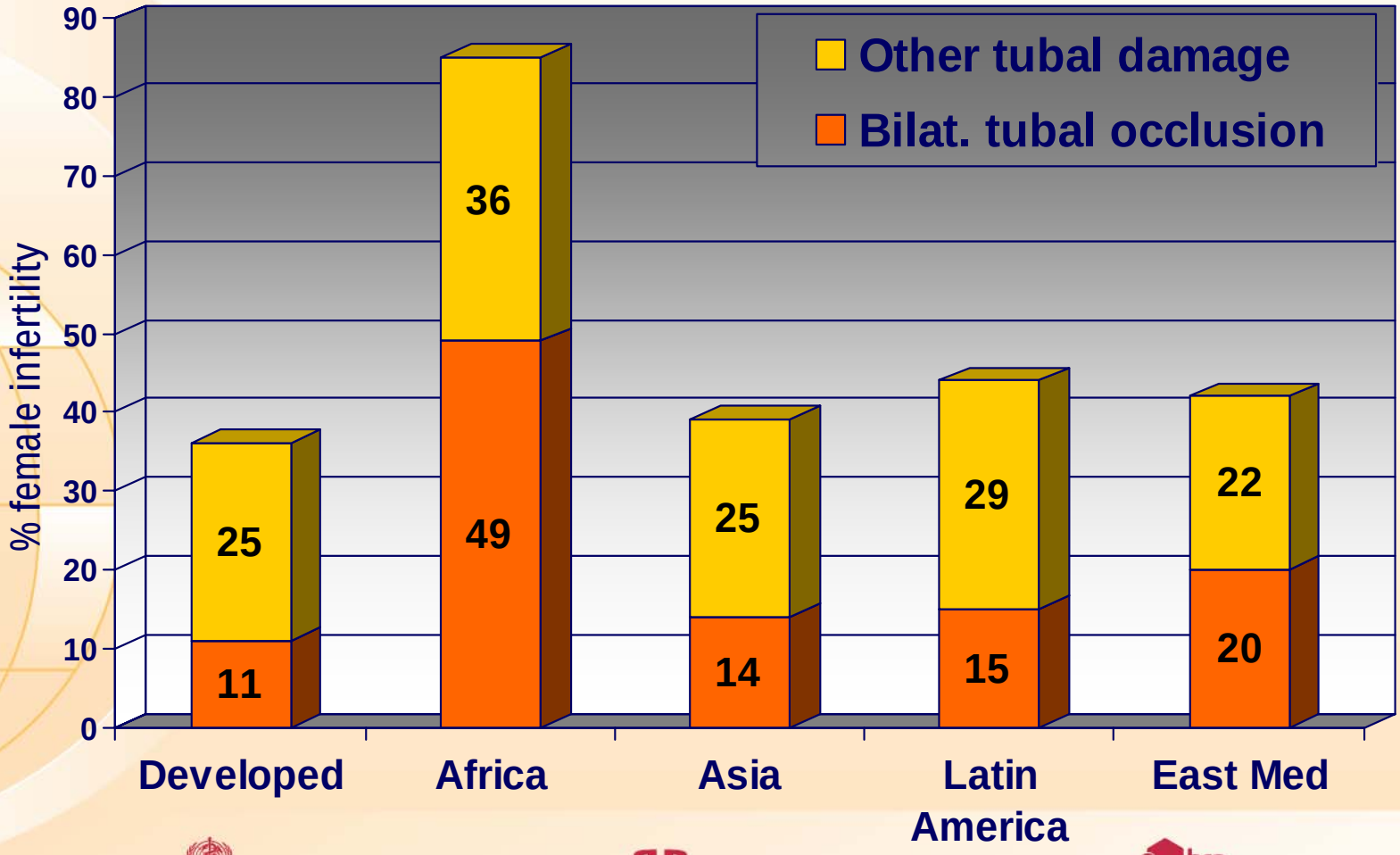
Fallopian tube damage as a cause of female infertility in the world



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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

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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

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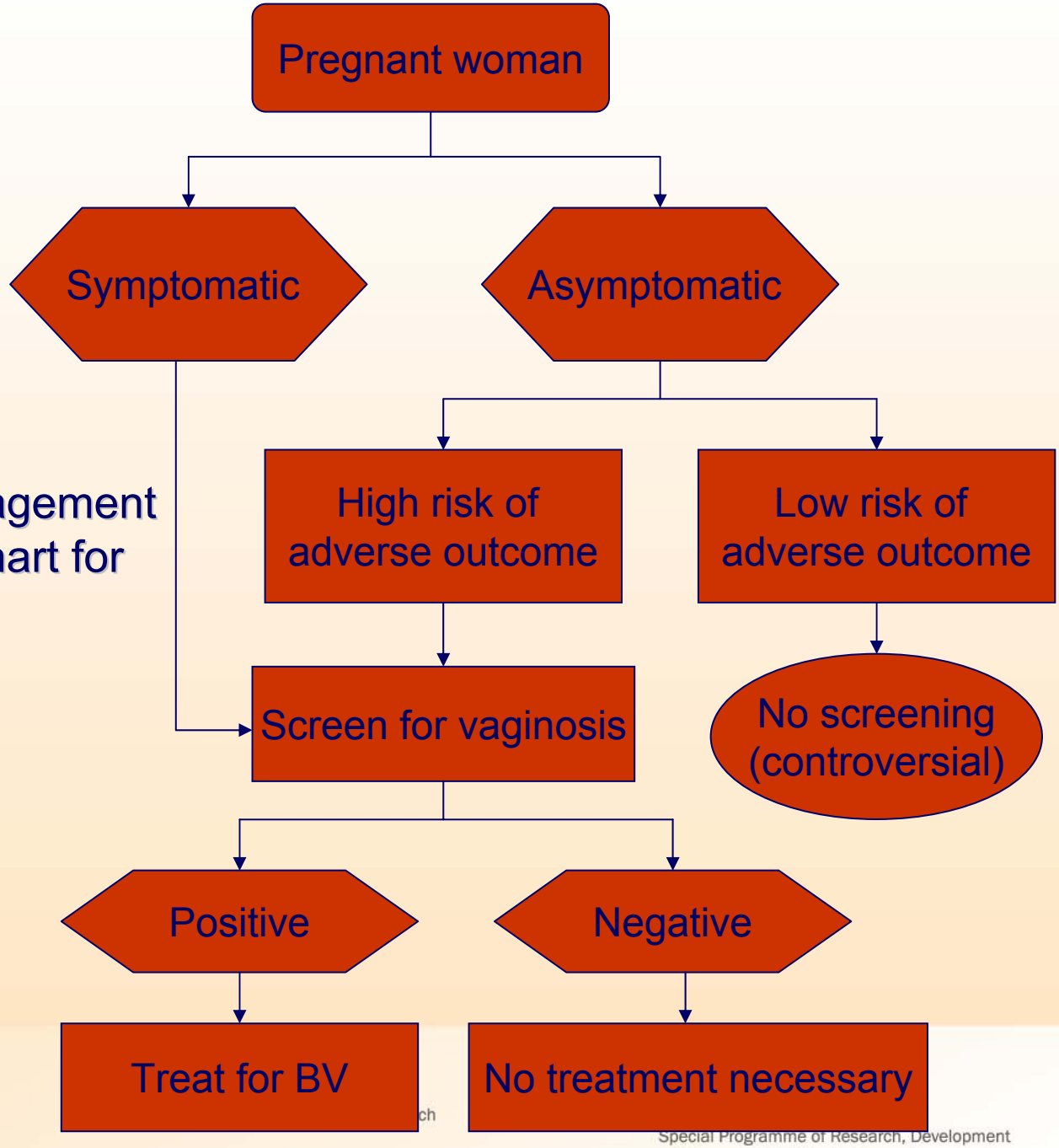
Simplify decision and management with a locally agreed flowchart for health workers



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.

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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

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)

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

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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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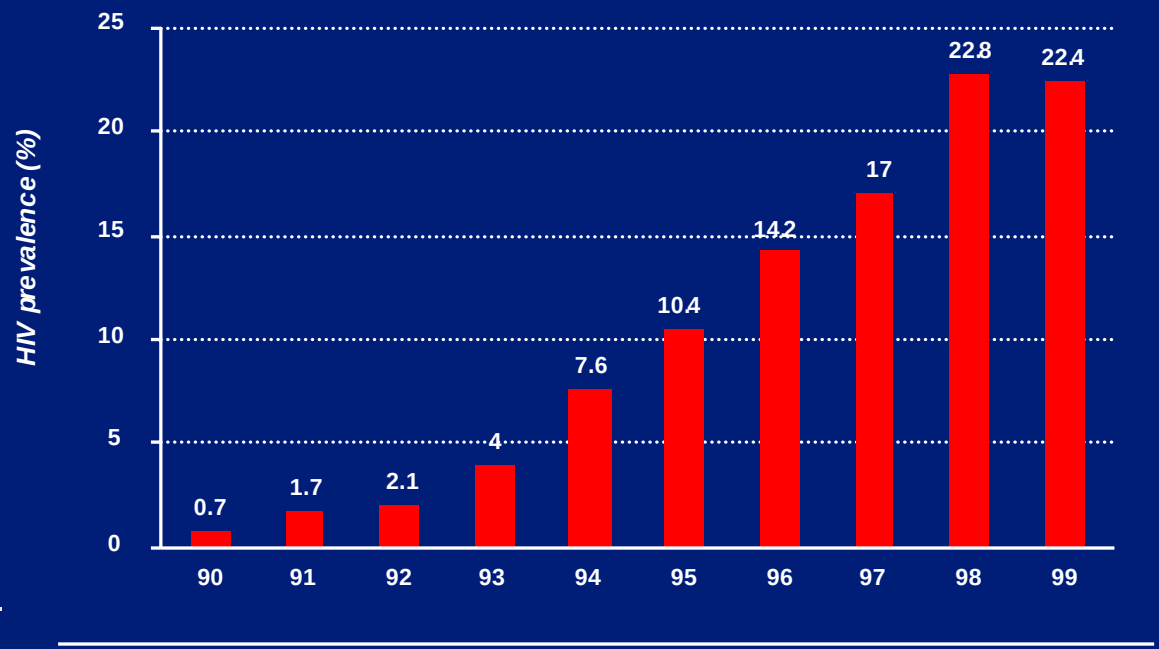
Burden of HIV in pregnancy

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



00001-E-13- 27 June2000

Source: *Department of Health, South Africa*

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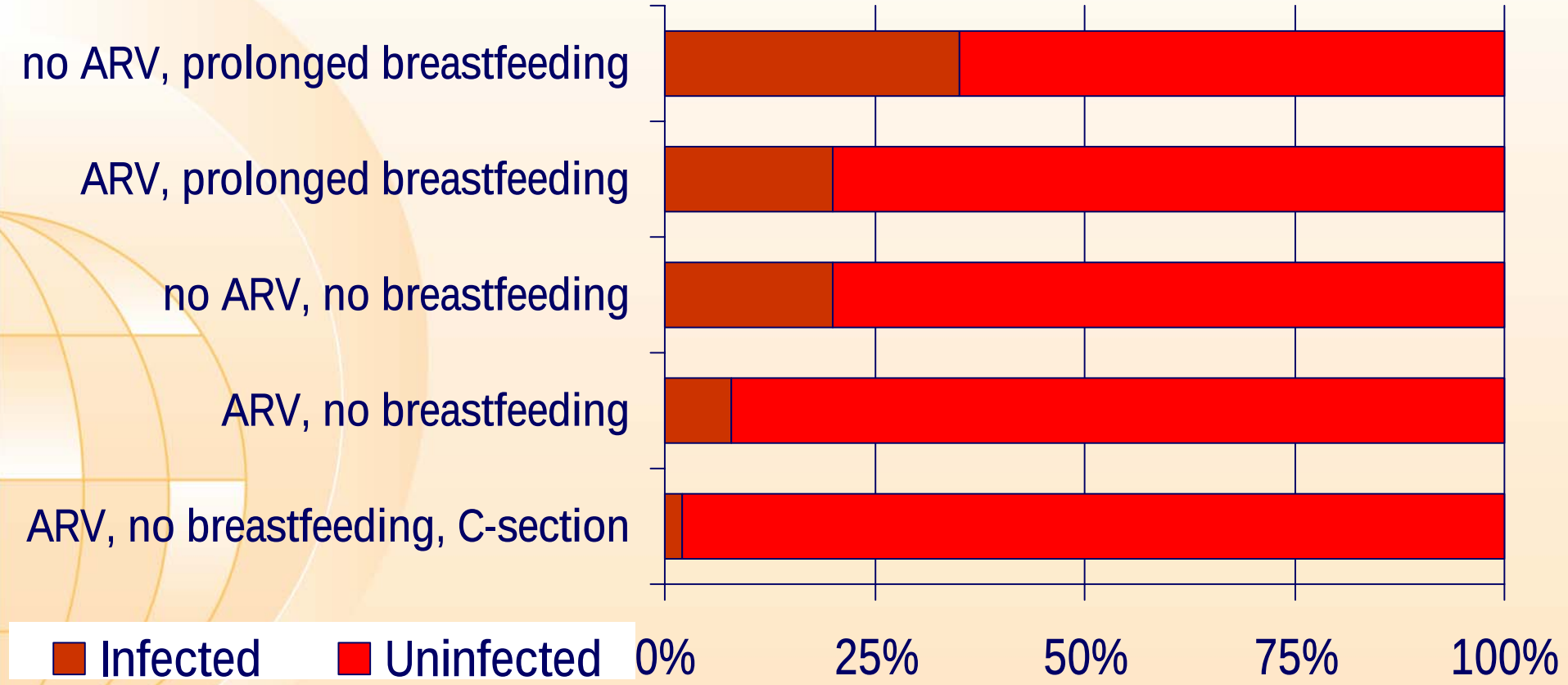
The variable risk of MTCT of HIV (with and without preventive interventions



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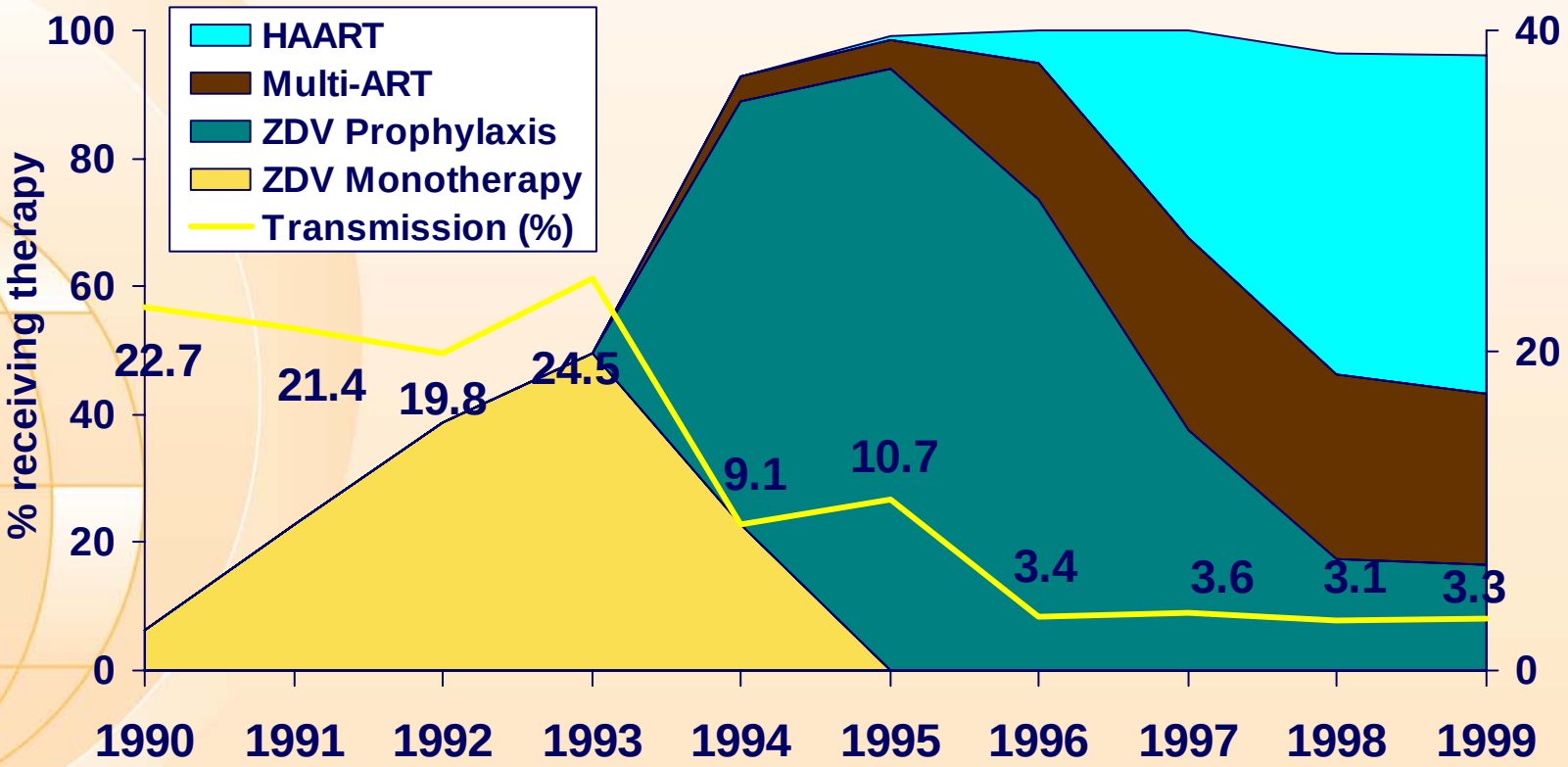
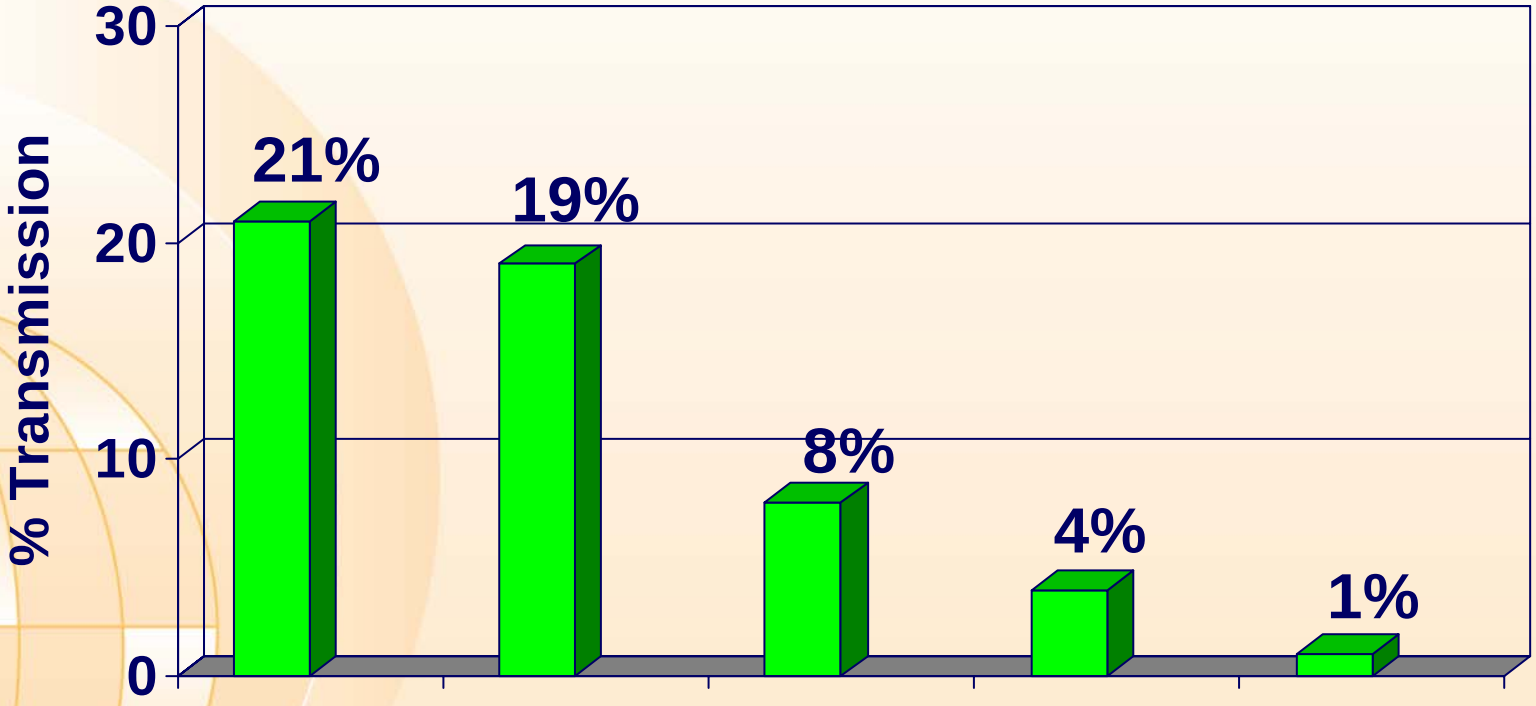
ARV Use and HIV Transmission
(WITS, USA)



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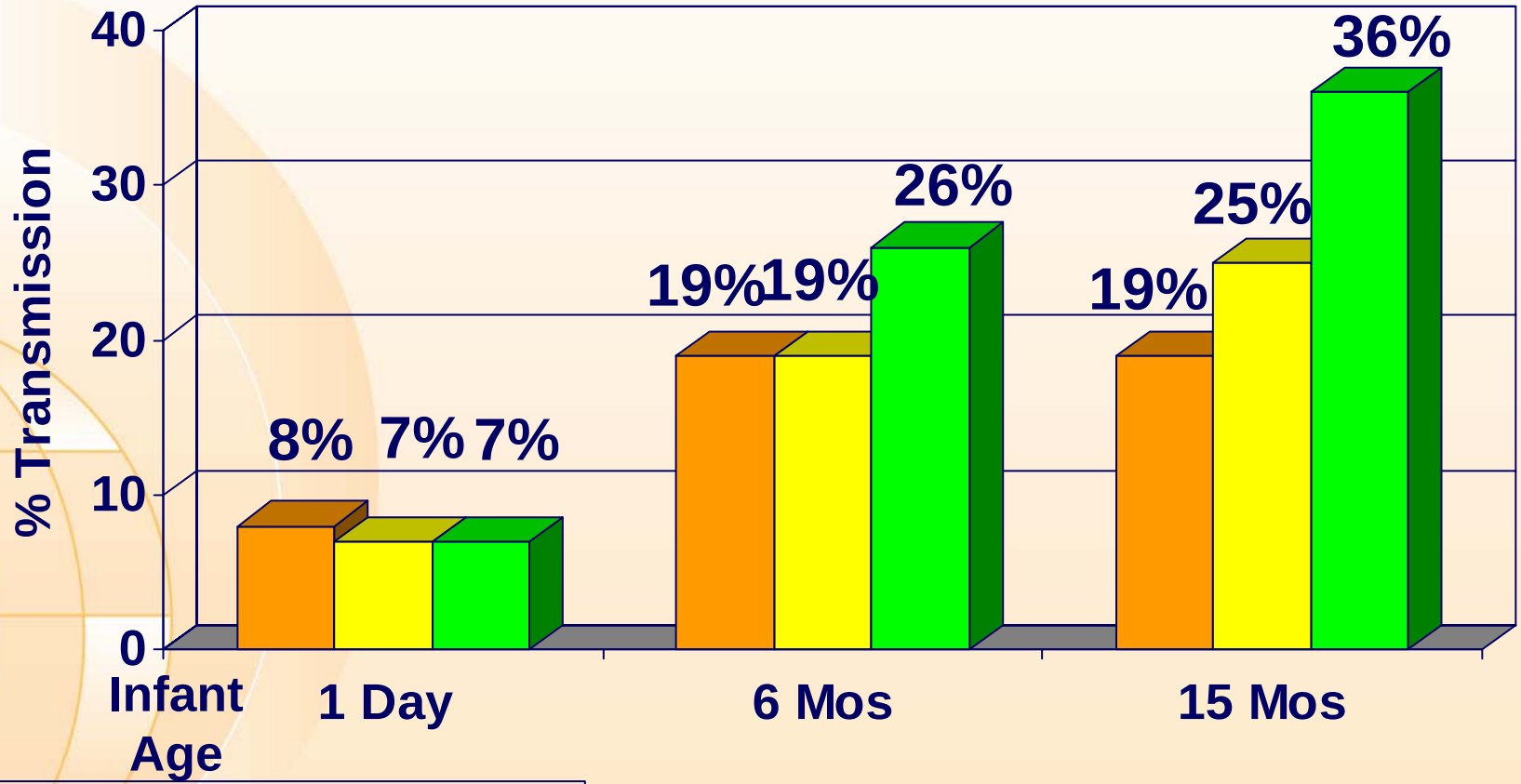
Method of Infant Feeding and HIV Transmission in Breastfeeding Children *Coutsoudis A. XIII AIDS Conf, July 2000, Durban S Africa (LbOr6)*



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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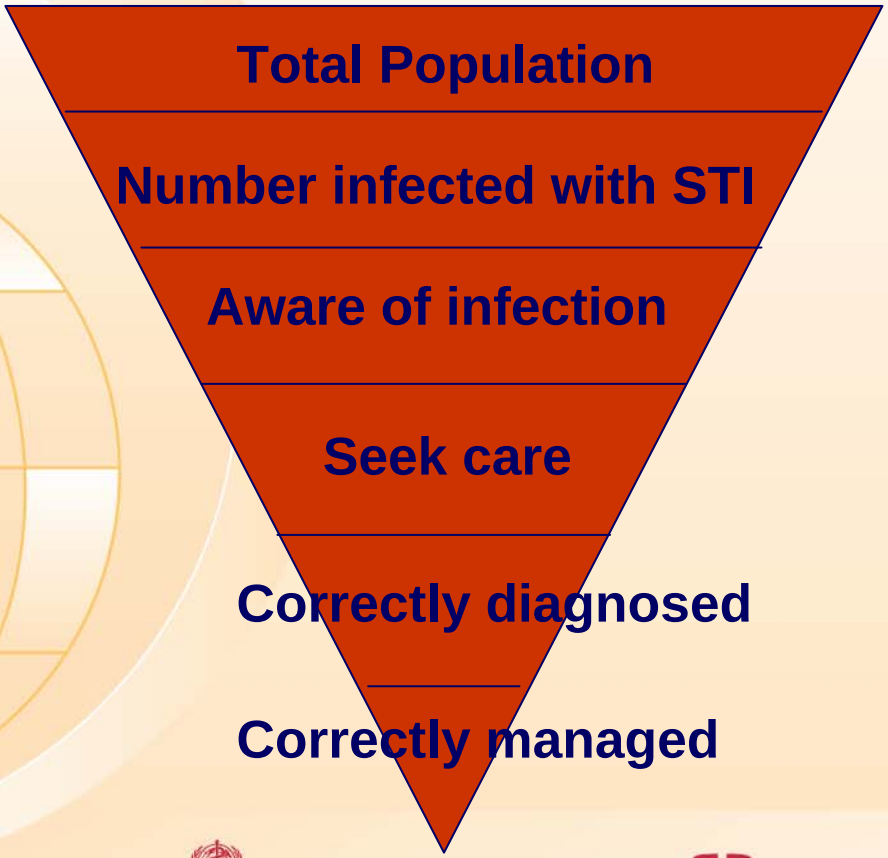
A public health perspective on STI prevention and care



Primary prevention efforts

Vaccination

Selective mass treatment (PPT)

Screening

Improve HCSB

Improve diagnosis

Improve case management

Improve partner management

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