STI control as HIV prevention

Dr. Antonio Carlos Gerbase
WHO, Geneva

Reproductive Tract Infections (RTI)

- **Iatrogenic infections**
  - **e.g. post abortum**
- **Endogenous Infections**
  - **e.g. *Candida albicans and bacterial vaginosis***
- **Sexually Transmitted Infections (STI)**
  - **e.g. gonorrhea, syphilis, herpes**

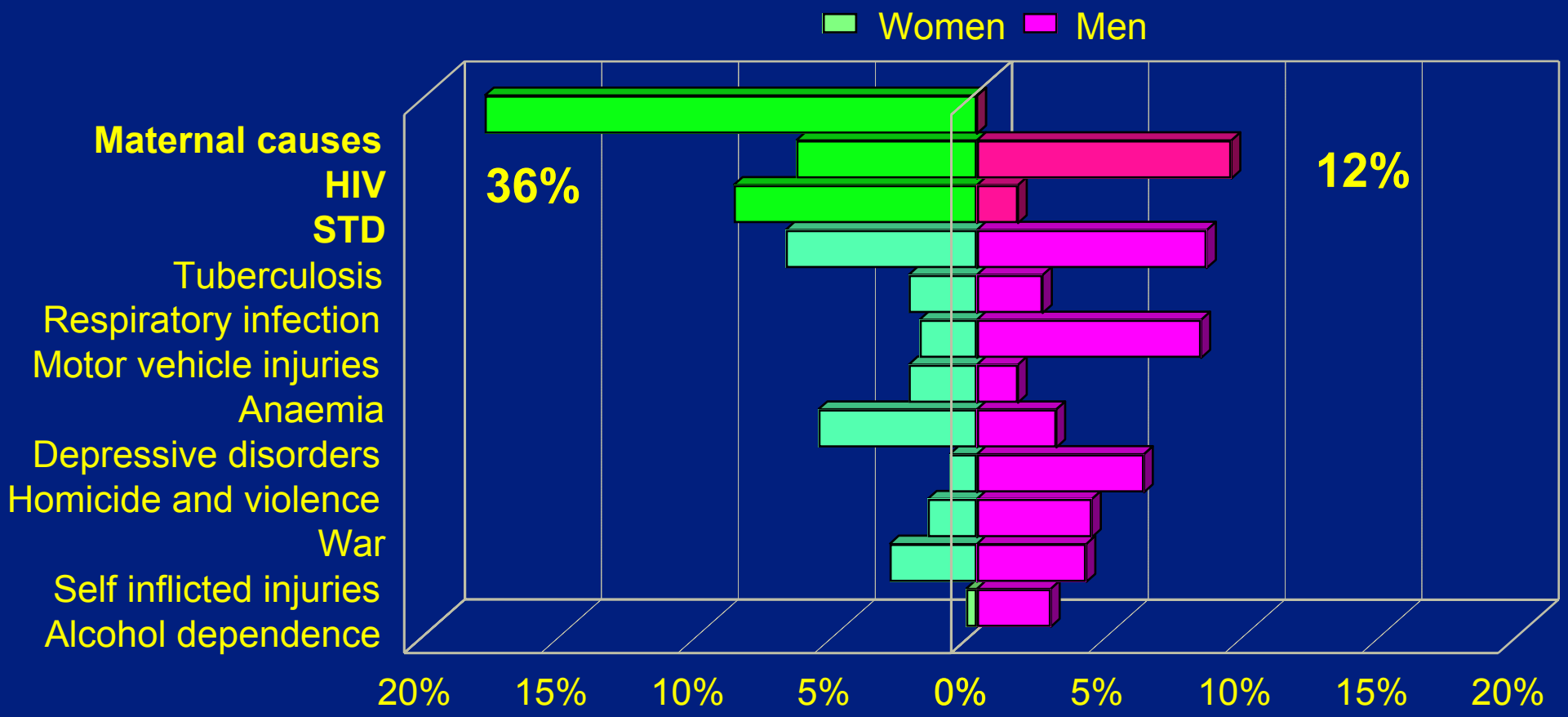
Sexually Transmitted Infections

- **Considerable morbidity**
- **High incidence and prevalence**
- **High rate of complications**
- **Bigger problem in women and young people**
- **Facilitate HIV transmission**

STI: complications and sequelae

- PID
- Ectopic pregnancy
- Infertility (male, female)
- Perinatal, infant infections
- Genito-anal cancers
- AIDS
- Death

Burden of disease in adults 15-44 years in the developing world by sex, 1990



Source: World development report 1993

How STIs disseminate?

Basic Reproductive rate

$$Ro = B \times c \times D$$

Transmission efficiency

Rate of sex partner change

Duration of infectiousness

How to control STIs ?

Decreasing Reproductive rate !

$$R_0 = B \times c \times D$$

Barriers and vaccines

Enhance resistance and reduce susceptibility

Health promotion

Alter sexual behaviour

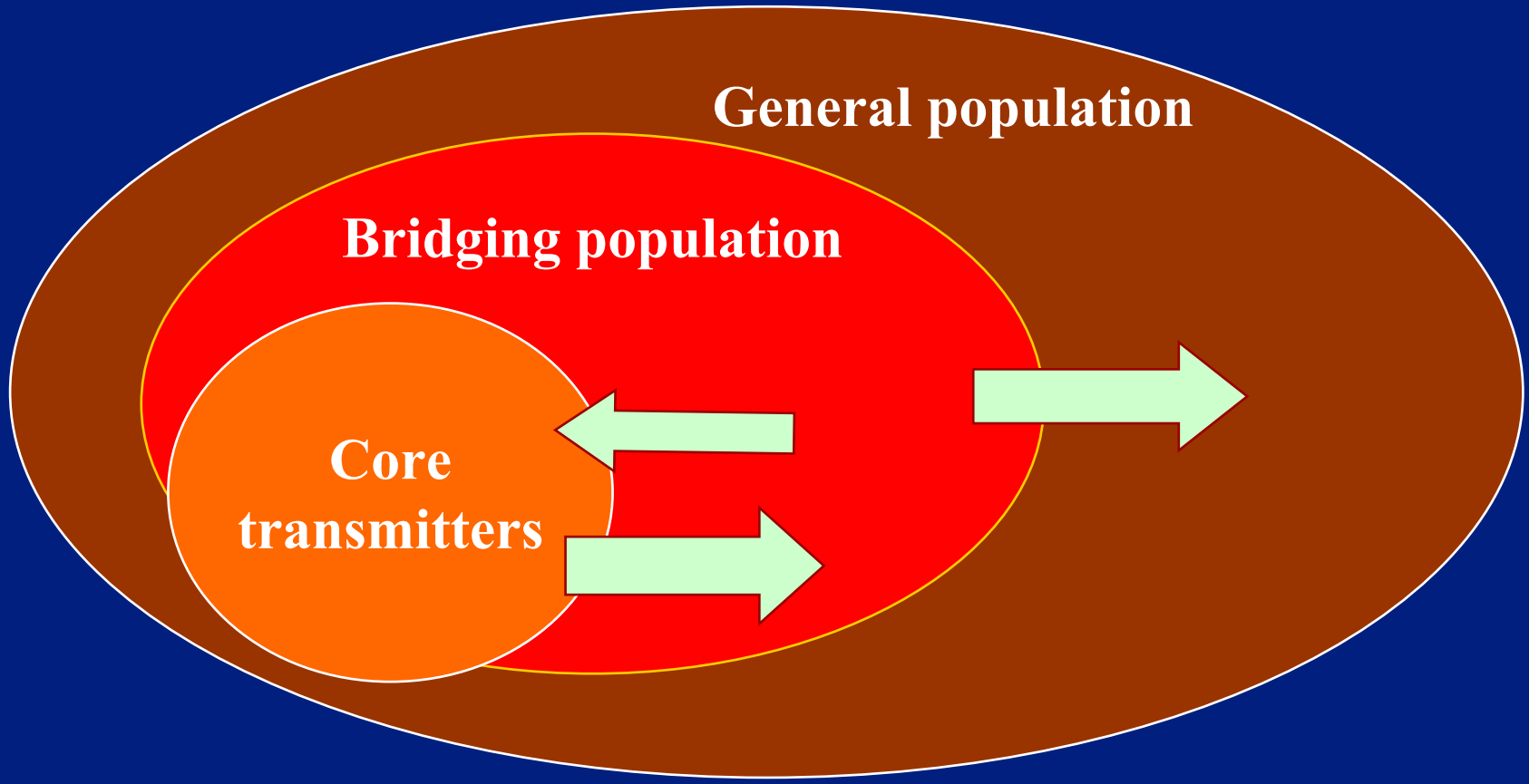
Case and partner management

Shorten duration of infection

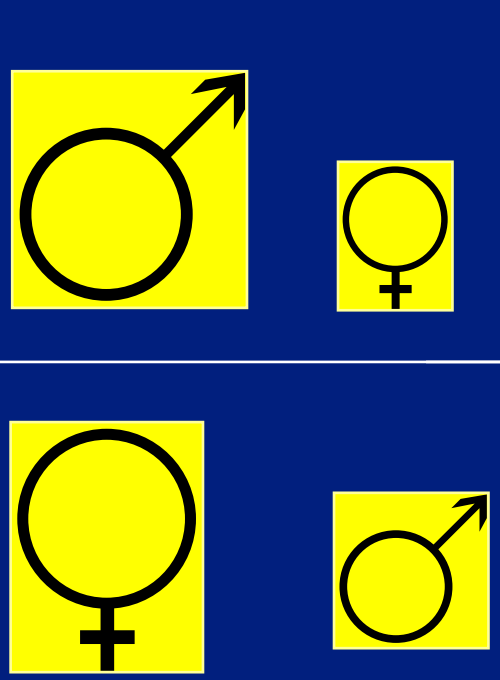
STI: social and demographic determinants

- **Socio-economic status (behaviour and health systems)**
- **M:F rates (migration, missing males)**
- **Age structure of the population**
- **Population density**

STI transmission dynamics at population level



Sexually Transmitted Diseases

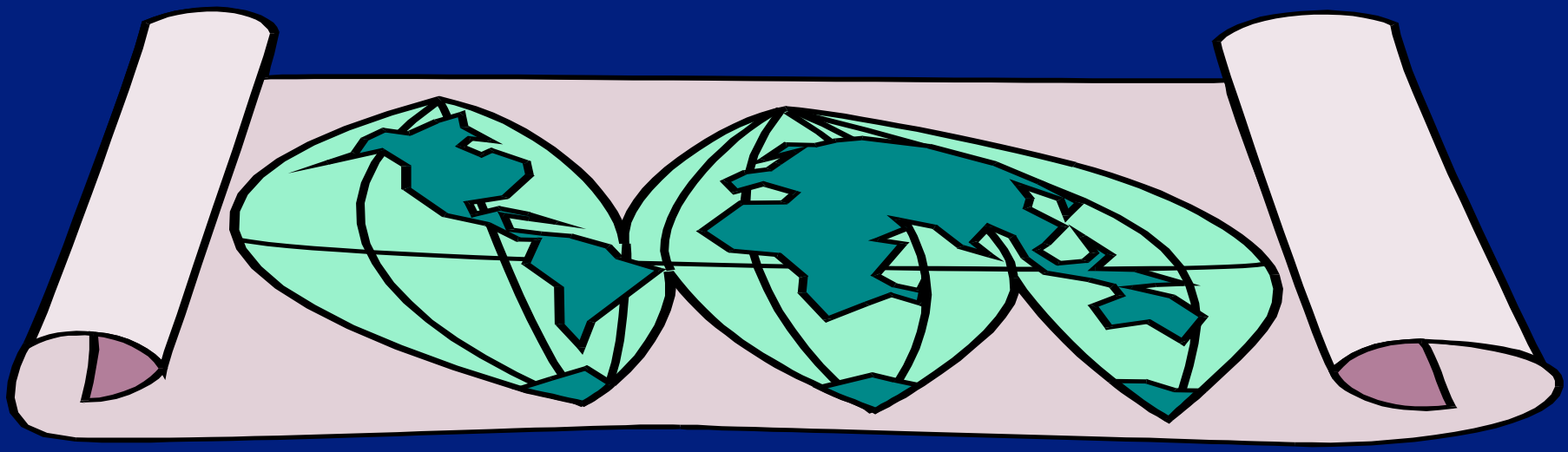


Symptomatic

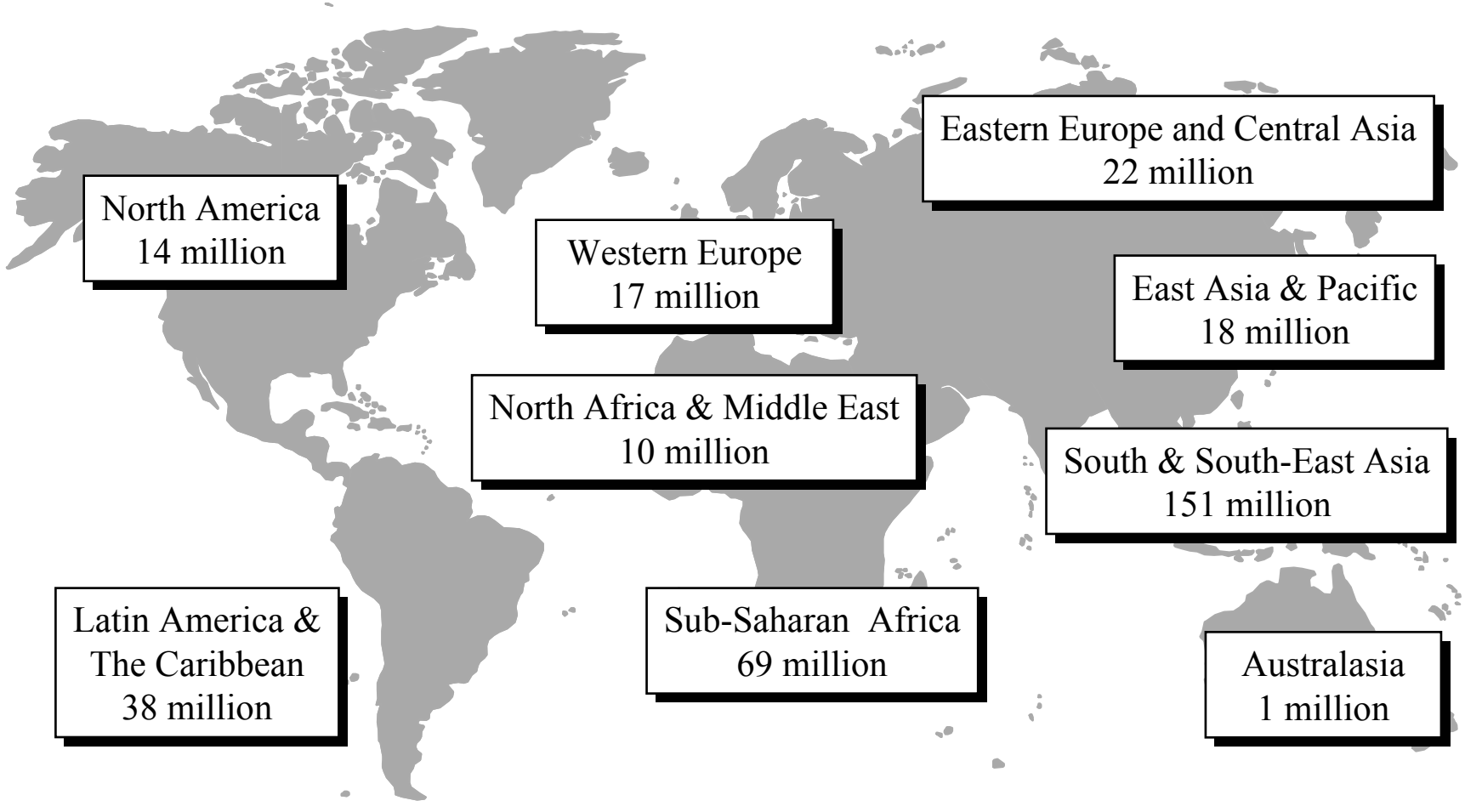
Asymptomatic

HIV/AIDS/STI Initiative

Global epidemiology



Estimated new cases of curable STI among adults, 1999*



Global total: 340 million

*** gonorrhoea, chlamydial infection, syphilis and trichomoniasis**

Estimates

- Starting from reporting and correcting for underreporting
- Delfi method
- Starting from prevalence (our choice):

$$Incidence = \frac{Prevalence}{Duration\ of\ infection}$$

STI Data

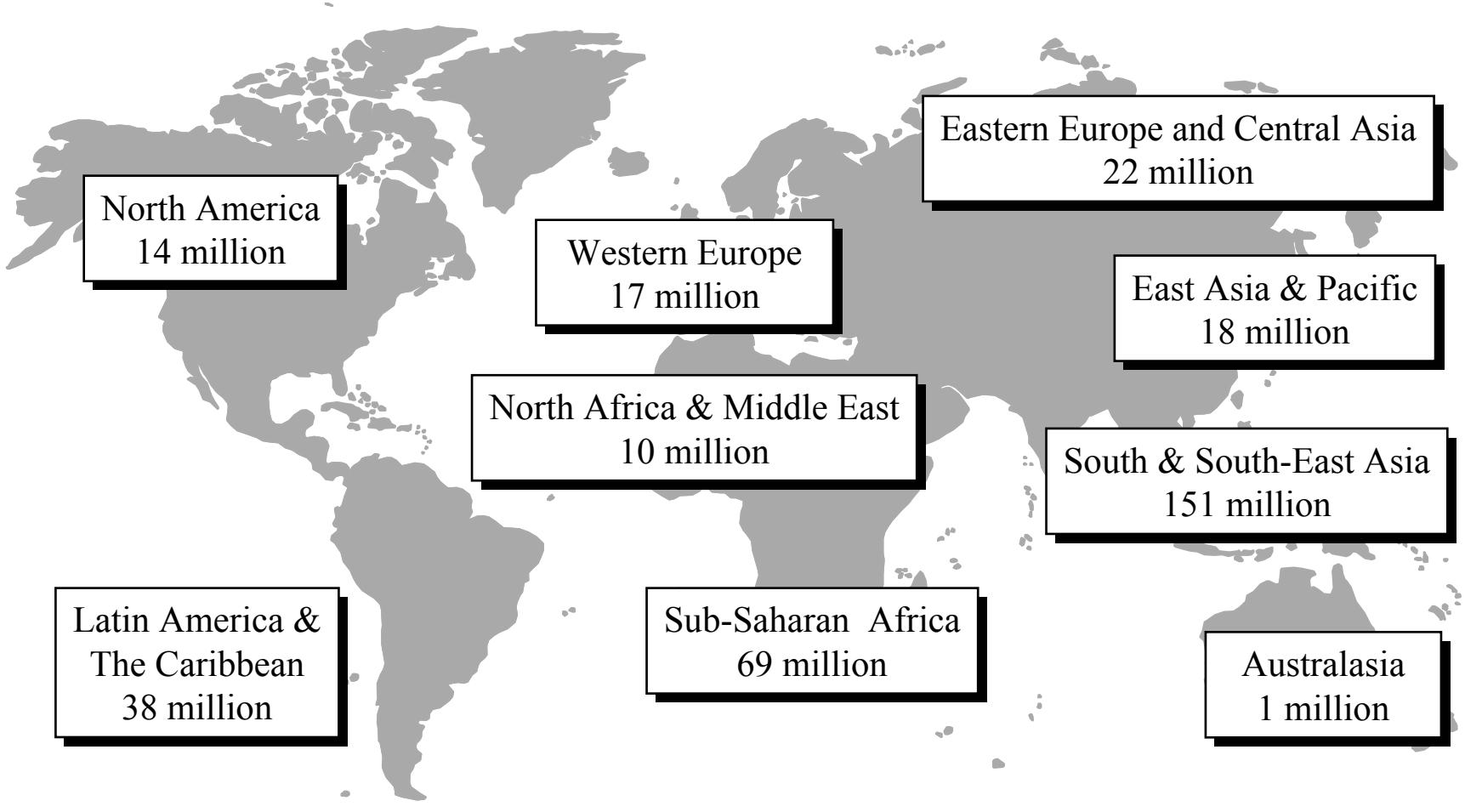
Prevalence and incidence of STIs may vary widely

- **within countries and between countries in the same region**
- **between urban and rural population**
- **in similar population groups.**

STI Prevalence

- Differences reflect social, cultural and economic factors and different access to care
- Higher in urban residents, unmarried and young adults

Estimated new cases of curable STI among adults, 1998*



Global total: 340 million

*** gonorrhoea, chlamydial infection, syphilis and trichomoniasis**

Global estimates of curable STI, 1999

	Incidence	Prevalence
Syphilis	0.41%	0.95%
Gonorrhoeae	2.09%	0.77%
Chlamydia	3.04%	2.89%
Trichomonas	5.76%	3.85%

Global estimates of curable STI, 1999

	New cases (million)
Syphilis	12
Gonorrhoeae	62
Chlamydia	92
Trichomonas	174

Syphilis 2000

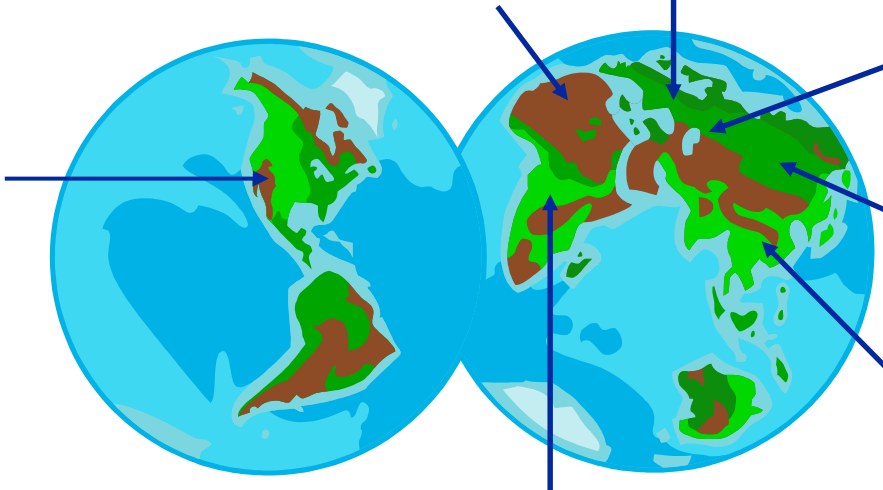
Low in Western Europe

Prevalence of 1.3% in Morocco

Epidemic in Eastern Europe and NIS

In USA declining rates since 1992

Congenital syphilis still a problem among minorities



Increase in Mongolia

In Asia and Pacific:High rates in Cambodia (4%), Papua New Guinea (3.5%) and South Pacific (8%)

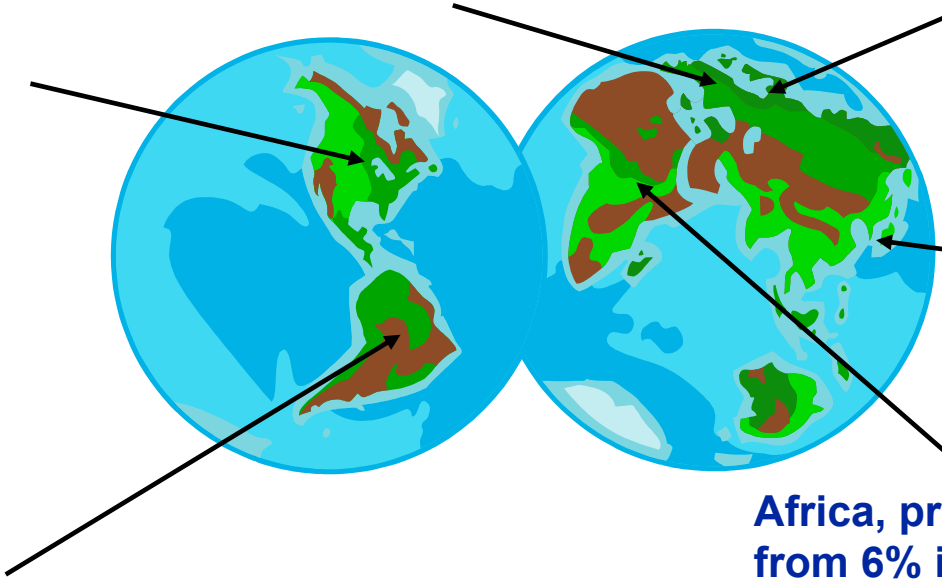
In Africa prevalence form 2.5% to 17.4% in PW

Chlamydia 2000

Low prevalence and incidence rates in the Nordic countries, following a wide scale screening programmes in the 1970s

Europe, prevalence in PW, from 2.7% in Italy to 8% in Iceland

USA: most common notifiable infectious disease (3 million/year)



In Asia and Western Pacific, prevalence in PW, 5.7% in Thailand up to 17% in India, One study in a rural population in Papua New Guinea showed a prevalence rate of 26%

Africa, prevalence in PW : from 6% in Tanzania to 13% in Cape Verde,

Latin America and Caribbean, prevalence rates from 1.9% amongst teenager in Chile, 2.1%, PW, in Brazil, and 12.2% attendees FP in Jamaica

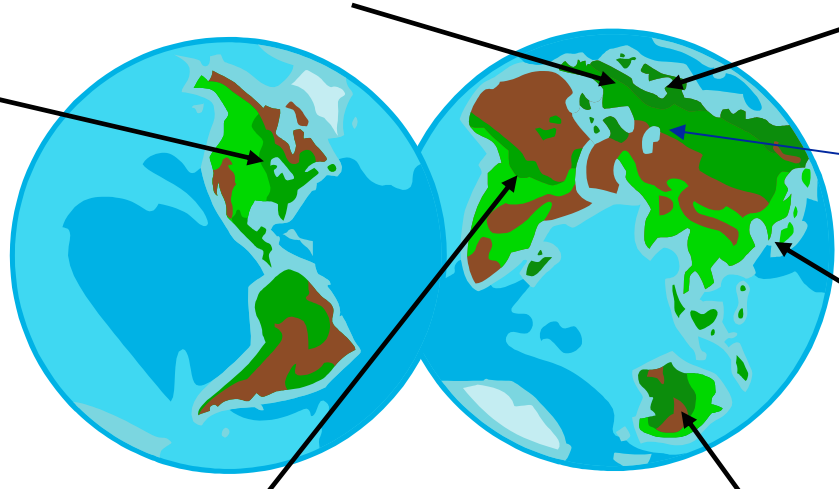
The higher prevalence female adolescents (24.1%-27%),

Gonorrhoea 2000

In Western Europe, a significant decline Outbraks and increase in London and Paris

Sweden: trends in the incidence of gonorrhoea showed a steady decline However, in 1997 the number of new cases was 17% higher than in 1996. First increase since 1976!

In USA, between 1981 and 1996 the incidence decreased 71.3%. Rates amongst blacks were 35% higher



An important increased in gonorrhoea rates has been seen in Eastern Europe, in the NIS

Western Pacific: prevalence rates for gonorrhoea (3% or greater) are found in Cambodia and Papua New Guinea

In Africa, prevalence rates in OW: 3.1% in Central African Republic and 7.8% in South Africa

Australia, notification of gonoccocal infection doubled since 1991.

The question is no longer whether STI detection and treatment should be an essential component of HIV prevention programs, but rather how this component should be implemented to have maximal impact on HIV incidence in specific populations.

MMWR 1998; 47 (No. RR-12): 1-24

STIs and HIV transmission

- **STIs are cofactors in HIV transmission**
- **STIs control reduces HIV transmission**

Epidemiological synergy established between HIV/STIs

- Biological evidence
- Seroconversion studies
- Intervention trials

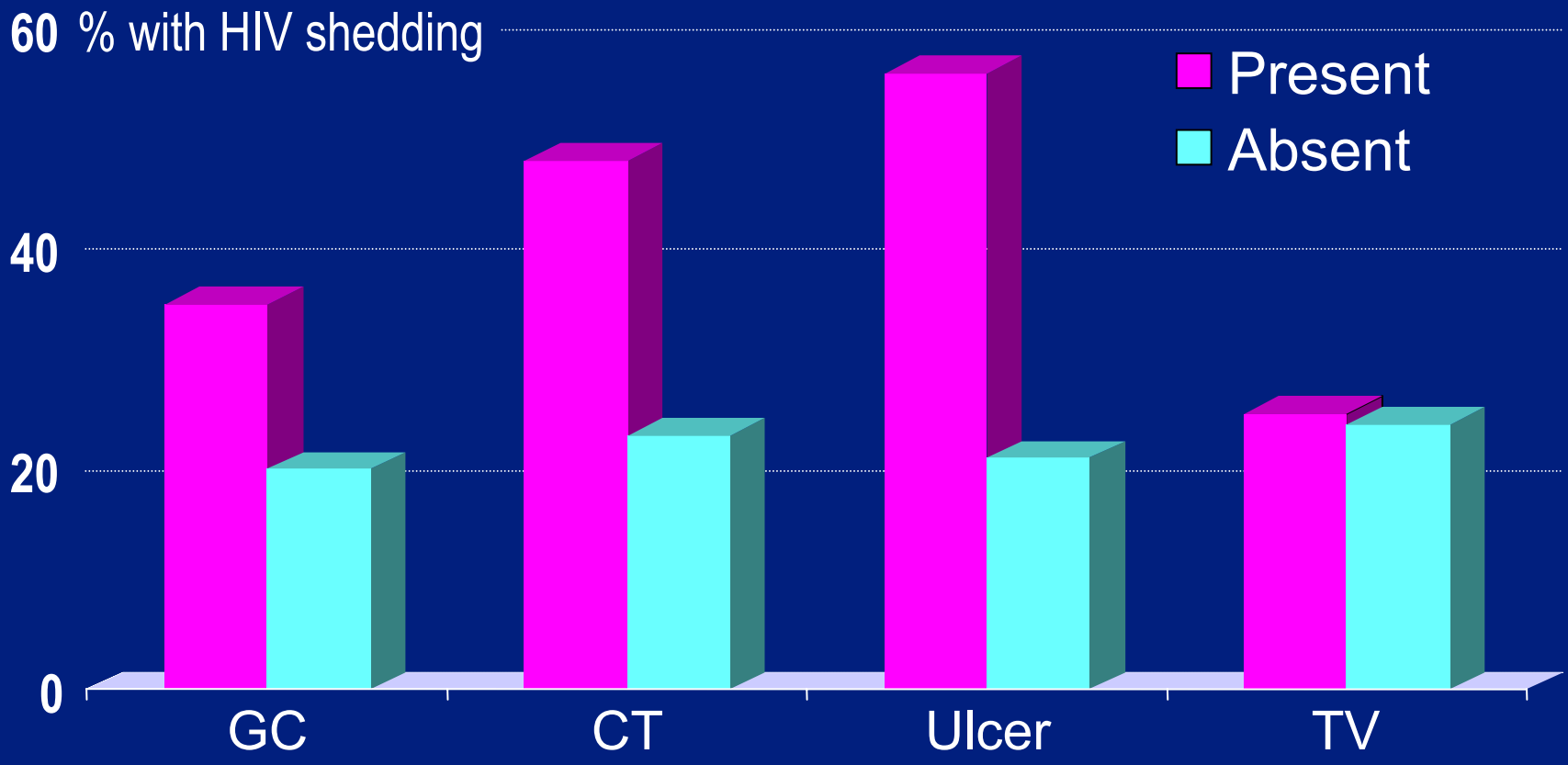
Epidemiological synergy established between HIV/STIs

Biological evidence

STD-related correlates of increased HIV genital shedding

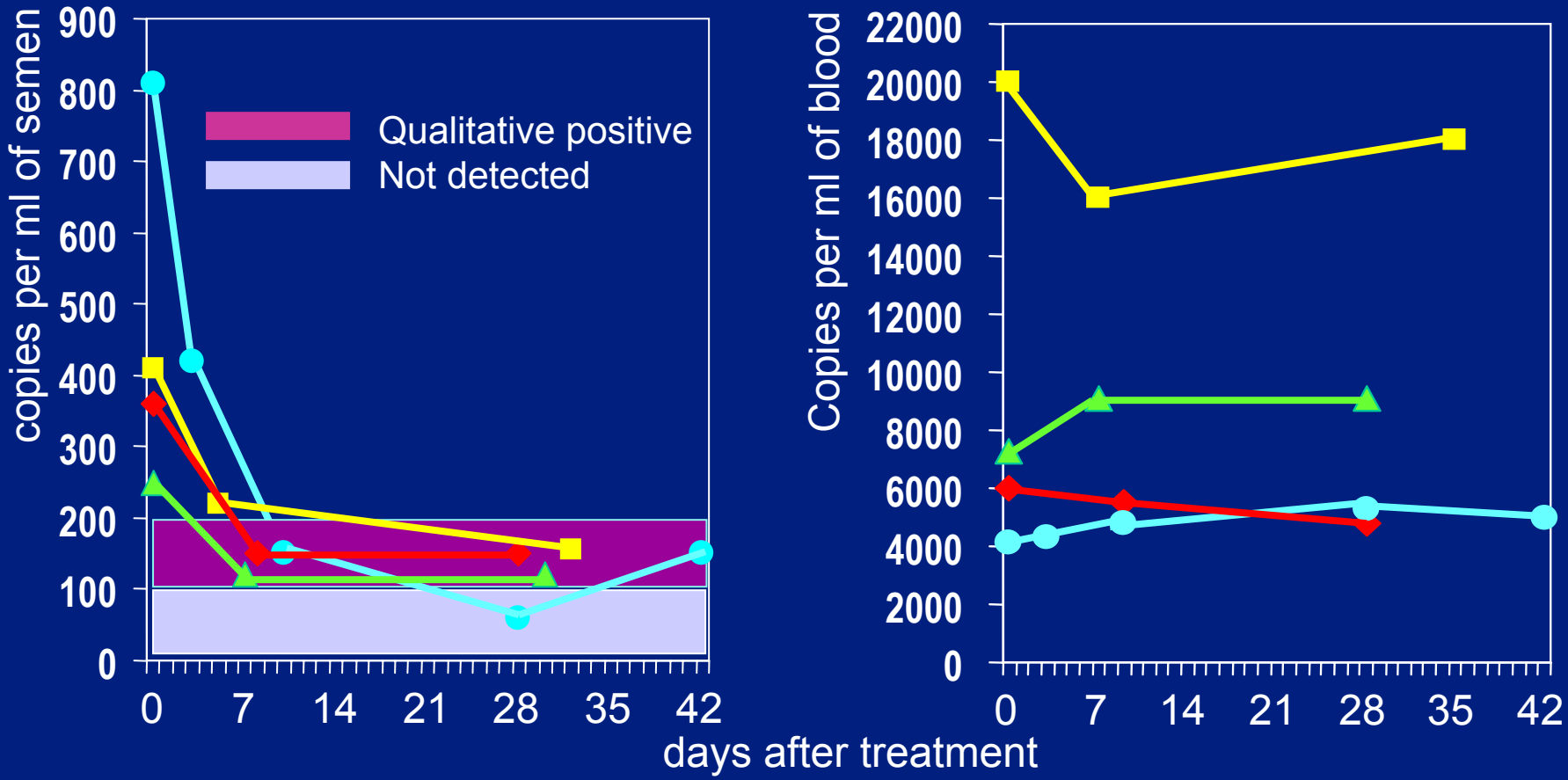
Cervico-vaginal secretions	*Semen*
• mucopurulent cervicitis	• urethritis
• cervical ulcer	
• vaginal ulcer	
• leucocytes ↗	• leucocytes ↗
• *N. gonorrhoea*	• *N. gonorrhoea*
• *C. trachomatis*	

Association between presence of STD and cervico-vaginal shedding of HIV–1



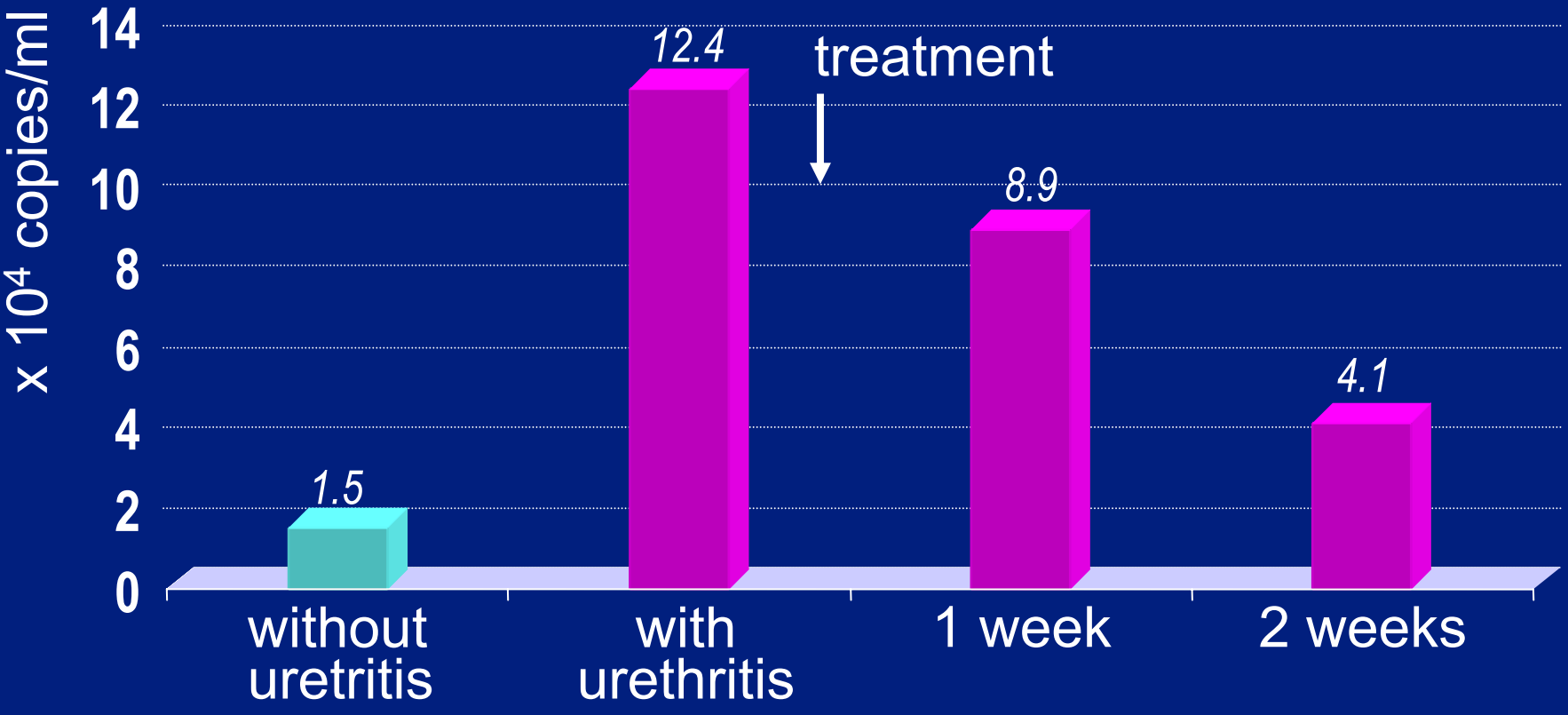
From Ghys *et al., AIDS,* 1997

Impact of HIV load in semen and blood in 4 patients receiving treatment for urethral discharge



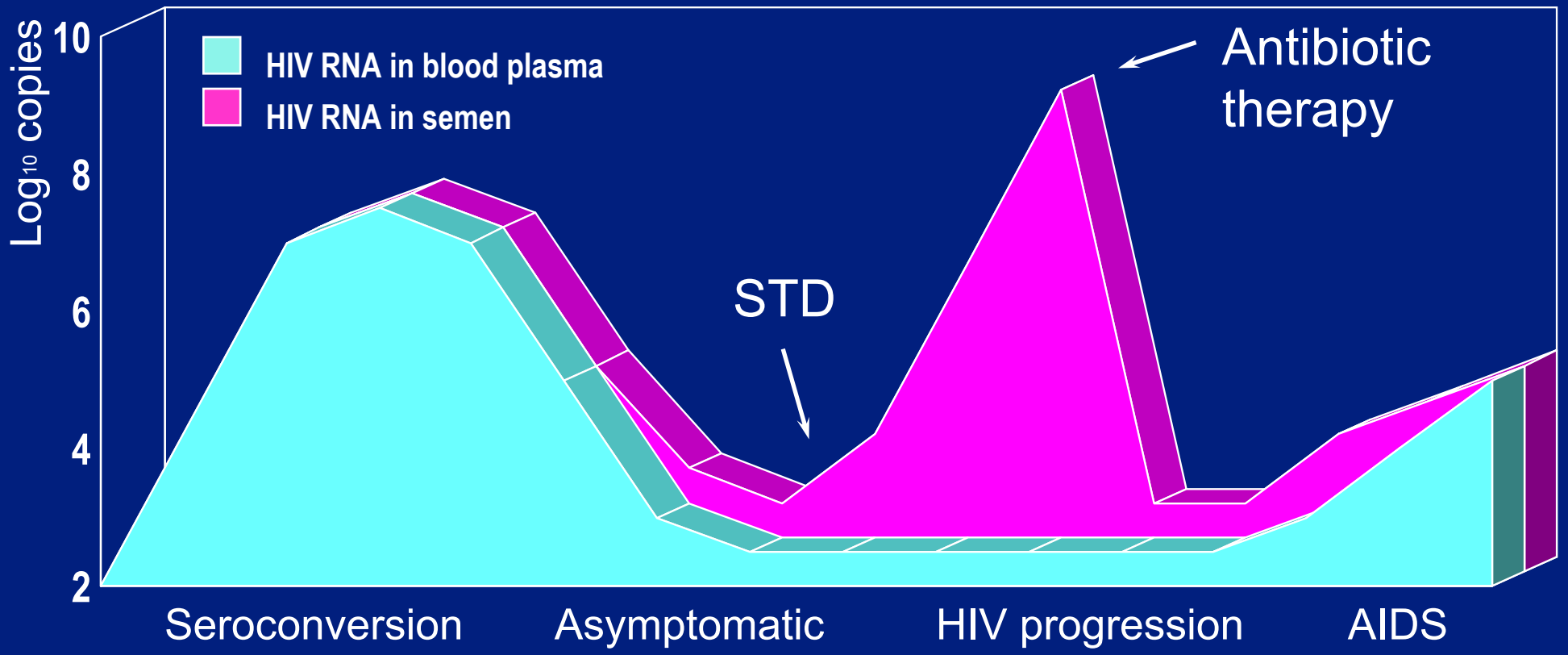
From Atkins *et al., British Medical Journal,* 1996

Median concentration of HIV-1 RNA in semen among 104 men with and without urethritis in Malawi



Cohen *et al., Lancet,* 1997

Hypothetical model of impact of STD on HIV genital shedding in men



From ISSTDR, Seville 1997; M. Cohen, plenary presentation

Epidemiological synergy established between HIV/STIs

Seroconversion studies

Longitudinal studies

Reference	Study population	STD studied	Relative risk
Cameron et al.	Heterosexual men, (Kenya)	Genital ulcer (mainly chancroid)	4.7
Darrow et al.	Homosexual men (U.S.A)	Syphilis	1.5-2.2
Holmberg et al.	Homosexual men (U.S.A)	Herpes	4.4
Laga et al.	Heterosexual women (Zaire)	Gonorrhoea Chlamydia infection Trichomoniasis	3.5 3.2 2.7
Stamm et al.	Homosexual men (U.S.A)	Herpes Syphilis	3.3-8.5 8.4-8.5

Epidemiological synergy established between HIV/STIs

Intervention trials

The Mwanza intervention

The Mwanza intervention

- Randomised study to assess impact of improved STI case management in HIV incidence, in Mwanza region, Tanzania

Mechanism of the Mwanza intervention

- Training and supervision
- Drug supply
- Health education on care seeking

HIV incidence over 2 years in intervention and control communities in the Mwanza trial

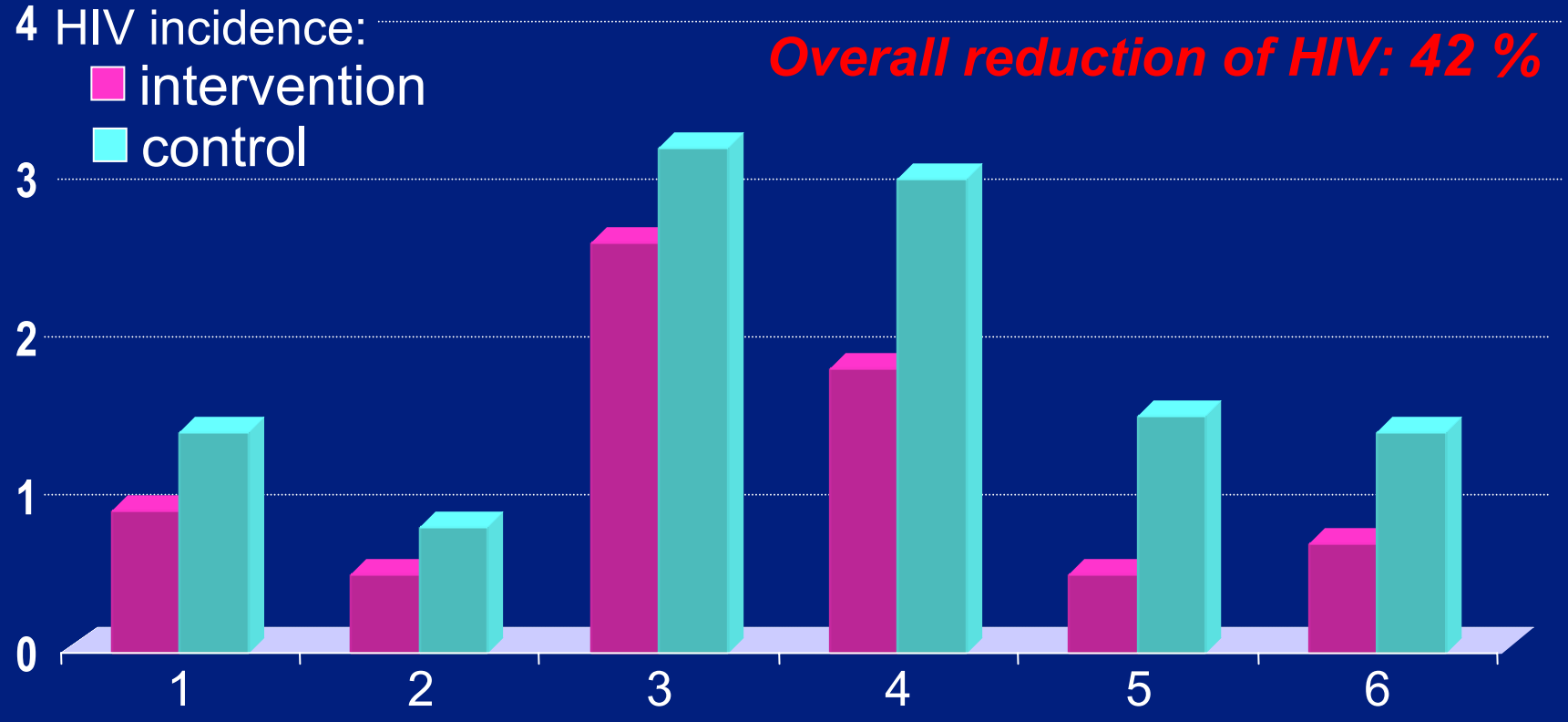
- Establishment of STD reference centre in Mwanza town
- Training of HCW in syndromic approach, health education and condom promotion
- Regular supply of effective STD drugs through a separate disbribution system
- Regular supervisory visits to health centres
- Periodic visits to the villages by health educators to promote prompt attendance to health centres for symptomatic STD

Cure rate of STD achieved by health services in Mwanza

Aware of symptoms	*Intervention*	*Control*
Attends health centre	80%	30%
Diagnosed as STD	77%	(77%)
Correct treatment prescribed & obtained	74%	20%
Compliant	83%	(83%)
Proportion of patients cured	38%	4%

From Buvé *et al.*, 1998

HIV incidence over 2 years in intervention and control communities in the Mwanza trial



From Grosskurth *et al., Lancet,* 1995

The Rakai Intervention

Objectives of Rakai Intervention

- 1. To determine if reductions in STD prevalence and incidence would result in decreased HIV transmission/acquisition;
- 2. To determine if reduction in STD incidence and prevalence could be achieved effectively by mass STD treatment (chose mass therapy because of lack of infrastructure in the Rakai area).

Elements of Rakai Intervention

- Home visits were conducted every 10 months
- Questionnaires and samples were the same for everyone (intervention and control group)
- Intervention group received Azithromycin, Ciprofloxacin and Metronidazole, regardless of symptoms
- The control arm was given Mebendazole (treatment for worms), iron and vitamins

Medication used for Mass treatment for intervention and control groups in Rakai.

Intervention clusters (n=7871)	Control clusters (n =7256)
Treatment provided:	
Azithromycin 1000mg	Mebendazole 100mg
Ciprofloxacin 250mg	Iron-folate tablet
Metronidazole 2g	Low dose multi-vitamin

The Rakai Intervention: results

- Significant reduction in prevalence of Syphilis
- Significant reduction in prevalence and incidence of Trichomoniais
- Borderline significant reductions in prevalence of Bacterial vaginosis
- No differences of HIV incidence in the intervention and control communities

Possible reasons for differences between Mwanza e Rakai - I

- Stage of the epidemics
  - The proportion of new HIV infections attributable to STIs may decline when the HIV epidemic matures
- Kind of prevalent STIs: proportion of treatable and non treatable STIs (specially HSV2 and Bacterial vaginosis)
- Differences in the interventions and in their effects

Possible reasons for differences between Mwanza e Rakai - II

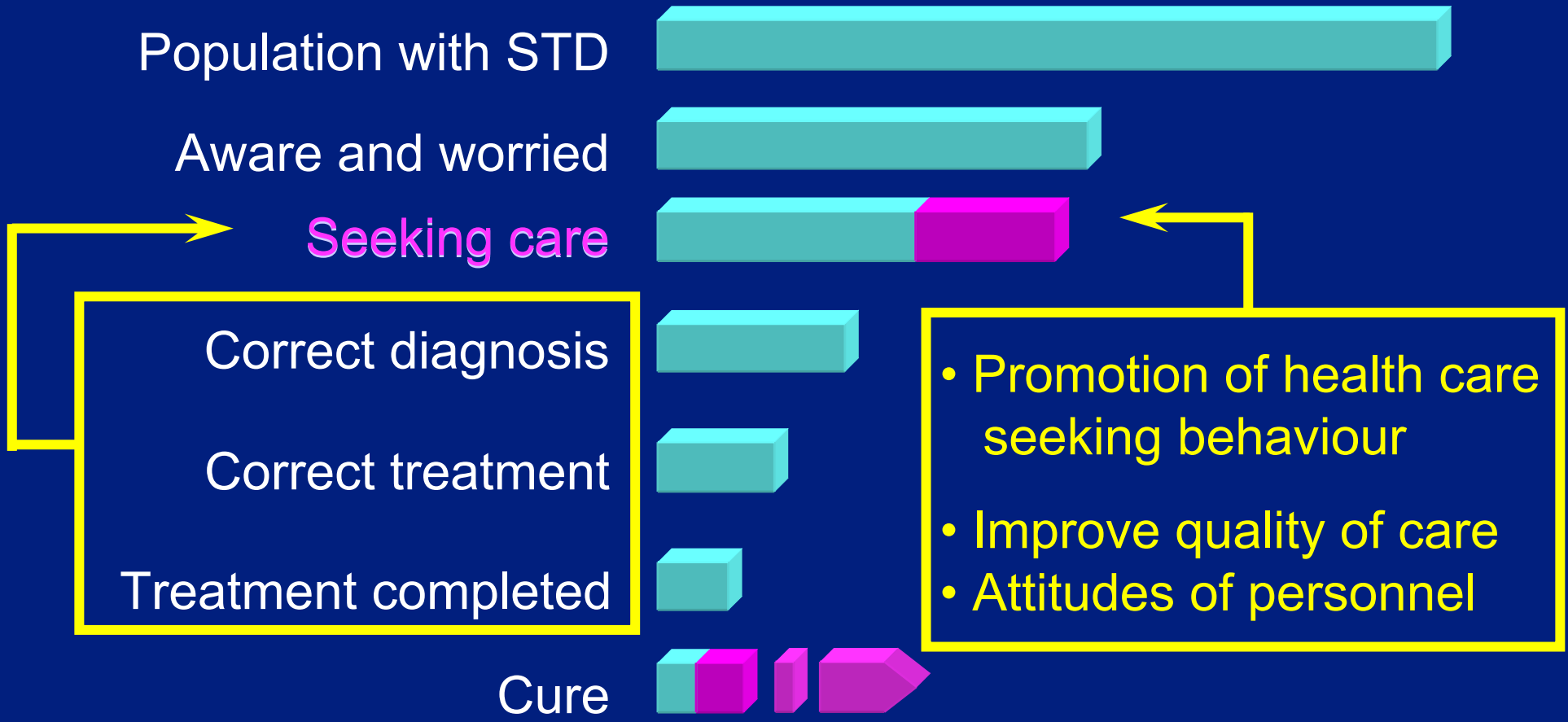
- Mass treatment: reintroduction rate depends on coverage, mobility and migration. Limited treatment available between rounds
- Syndromic management provides continuous control between episodes
- Relative importance of symptomatic and asymptomatic STIs in HIV transmission

Improving quality of STD case management at primary care level remains priority!

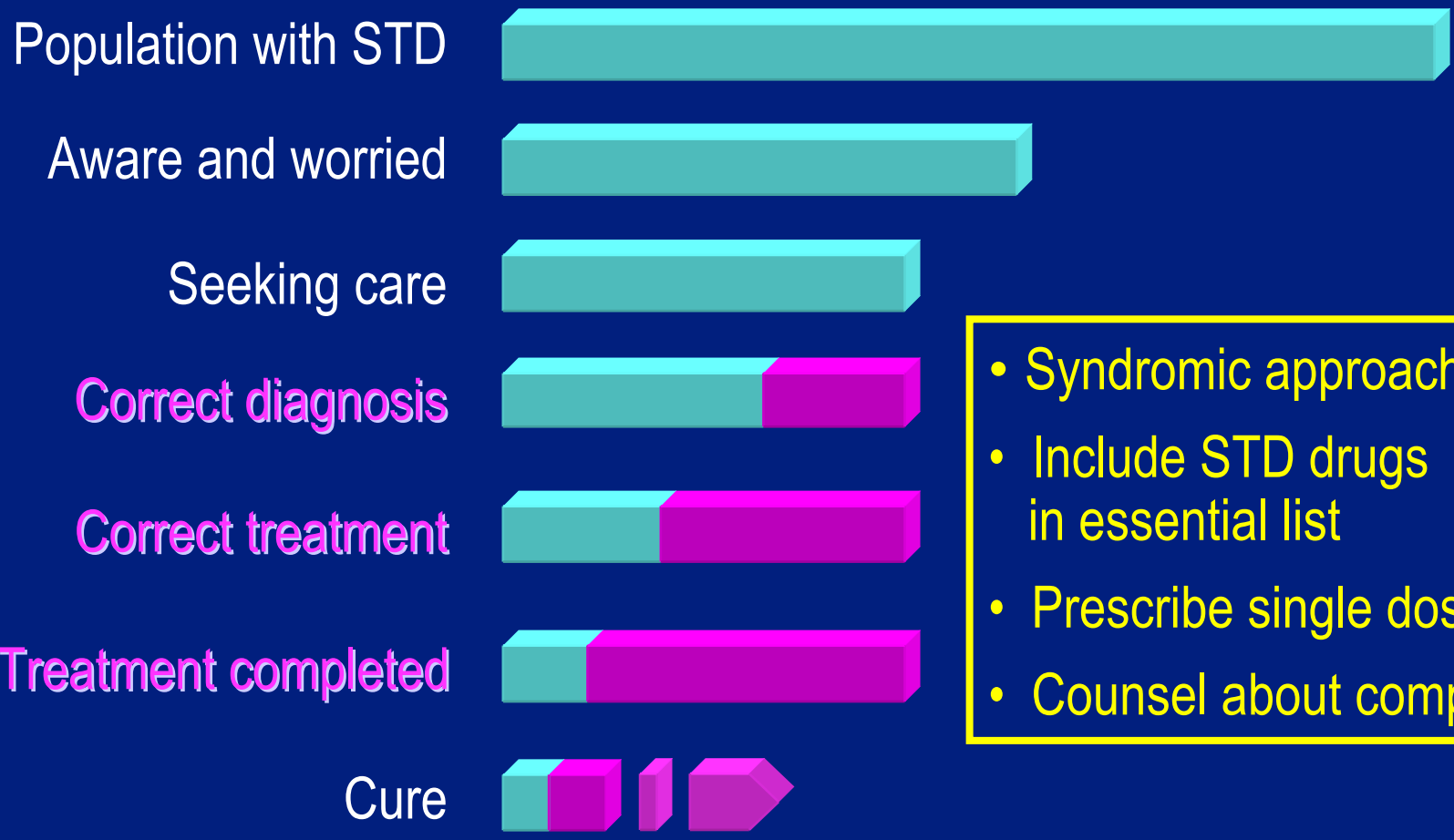
- Demand from patients
- Scope for improvement is enormous in most countries
- “Know how” is available
- Is effective in reducing HIV incidence (cf. Mwanza trial)
- Enhances prevention efforts in the clinic setting

Operational model of the role of health services in STD case management

Operational model of the role of health services in STD case management



Operational model of the role of health services in STD case management



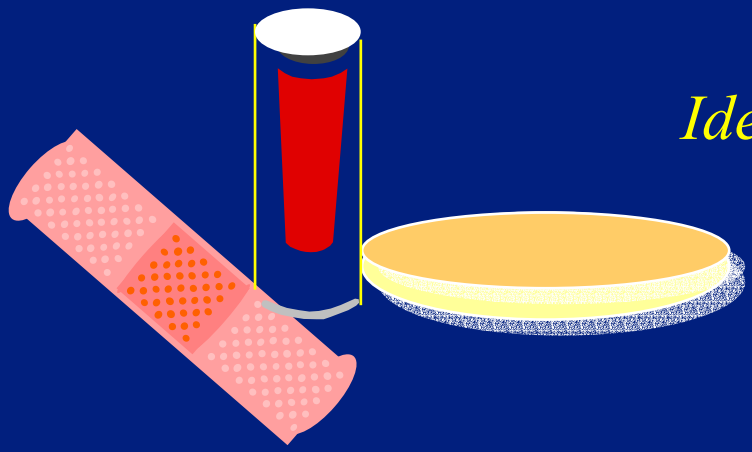
- Syndromic approach
- Include STD drugs in essential list
- Prescribe single dose
- Counsel about compliance

Clinical Diagnosis Approach

Identify the STD causing symptoms based on clinical experience

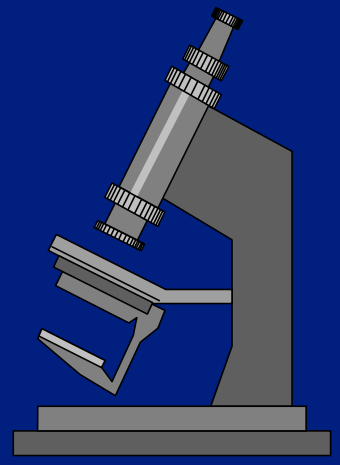
- even experienced STD providers often misdiagnose STDs
- miss mixed infections
- difficult for surveillance

Etiologic Diagnosis Approach

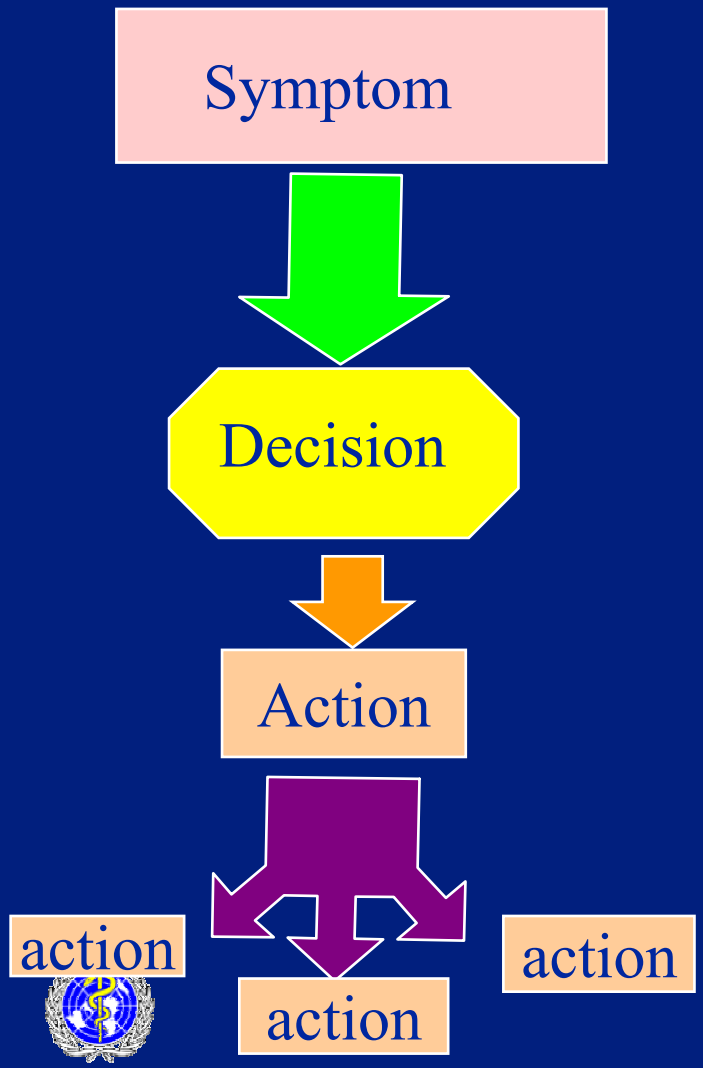


Identify the organism causing the symptoms with laboratory tests and microscopy

- tests can be time consuming and expensive
  e.g. cultures cost $12 - $40 & take up to six days
- even rapid tests (RPR) require equipment to obtain and separate venous blood
- dependent technician & lab accuracy



Syndromic Diagnosis Approach

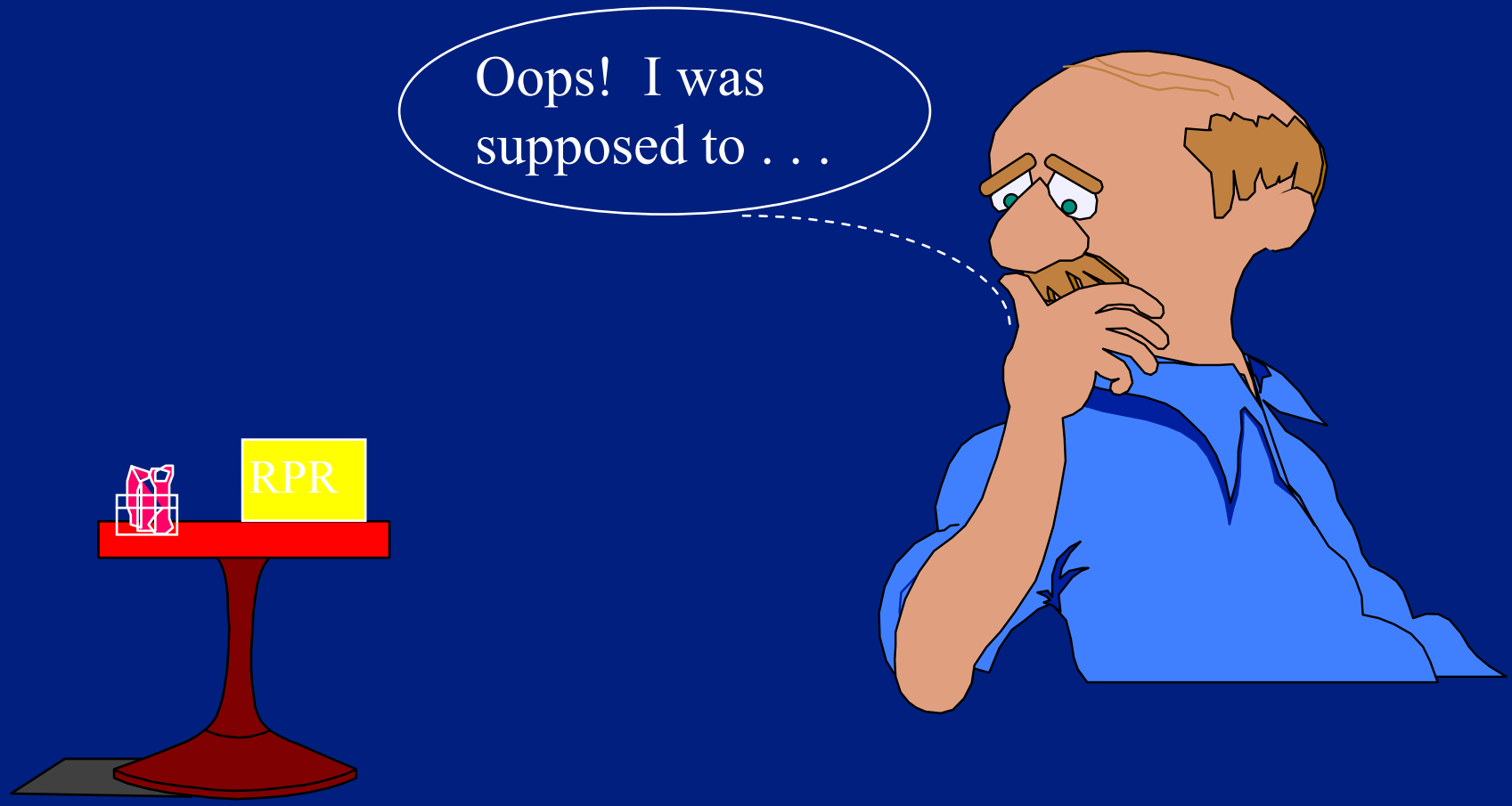


Identify all possible STDs that could cause syndrome and give recommended treatment based on epidemiologic and laboratory data

- Immediate treatment
  - decrease transmission
  - decrease complications
- Can do syndrome surveillance

- Need to weigh the ability to treat as many infected as possible (sensitivity) with the risks of overtreatment (specificity)
- resistance & stigma

THE SUPPOSED TO … APPROACH



Urethral discharge

Patient complains of urethral discharge or dysuria

Take history and Examine. Milk urethra if necessary

Discharge confirmed?

No

Ulcer(s) present?

No

- Educate and counsel
- Promote and provide condoms
- Depending on counselling capabilities offer HIV testing

Yes

Use appropriate flow chart

Yes

Treat for gonorrhoea and chlamydia

- Educate
- Counsel if needed
- Promote and provide condoms
- Depending on counselling capabilities offer HIV testing
- Partner management
- Advise to return in 7 days if symptoms persist

Persistent/ Recurrent Urethral Discharge in Men

NB.: This flowchart assumes effective therapy for Gonorrhoea and Chlamydia to have been received and taken by the patient prior to this consultation

Patient complains of persistent/recurrent urethral discharge or dysuria

Take history and Examine. Milk urethra if necessary

Discharge confirmed?

No → Ulcer(s) present?

No →
- •Educate and counsel
- •Promote and provide condoms
- •Depending on counselling capabilities offer HIV testing

Yes → Use appropriate flow chart

Yes

Reinfection or poor compliance

Yes → Repeat urethral discharge treatment

No

- **- Treat for Trichomonas vaginalis**
- - Educate
- - Counsel
- - Promote/provide condoms
- - Partner management
- - Return in 7days

Improved?

Yes →
- •Educate and counsel
- •Promote and provide condoms
- •Depending on counselling capabilities offer HIV testing

No

Refer

Genital ulcers

Patient complains of genital sore or ulcer

Take history and examine

Sore/Ulcer/Vesicle present?

No →
- Educate and counsel
- Promote and provide condoms
- Depending on counselling capabilities offer HIV testing

Yes

Vesicles or small ulcers with history of recurrent vesicles?

Yes →
- Management of herpes
- Educate
- Counsel on risk reduction
- Promote and provide condoms
- Depending on counselling capabilities offer HIV testing

No

YIELD

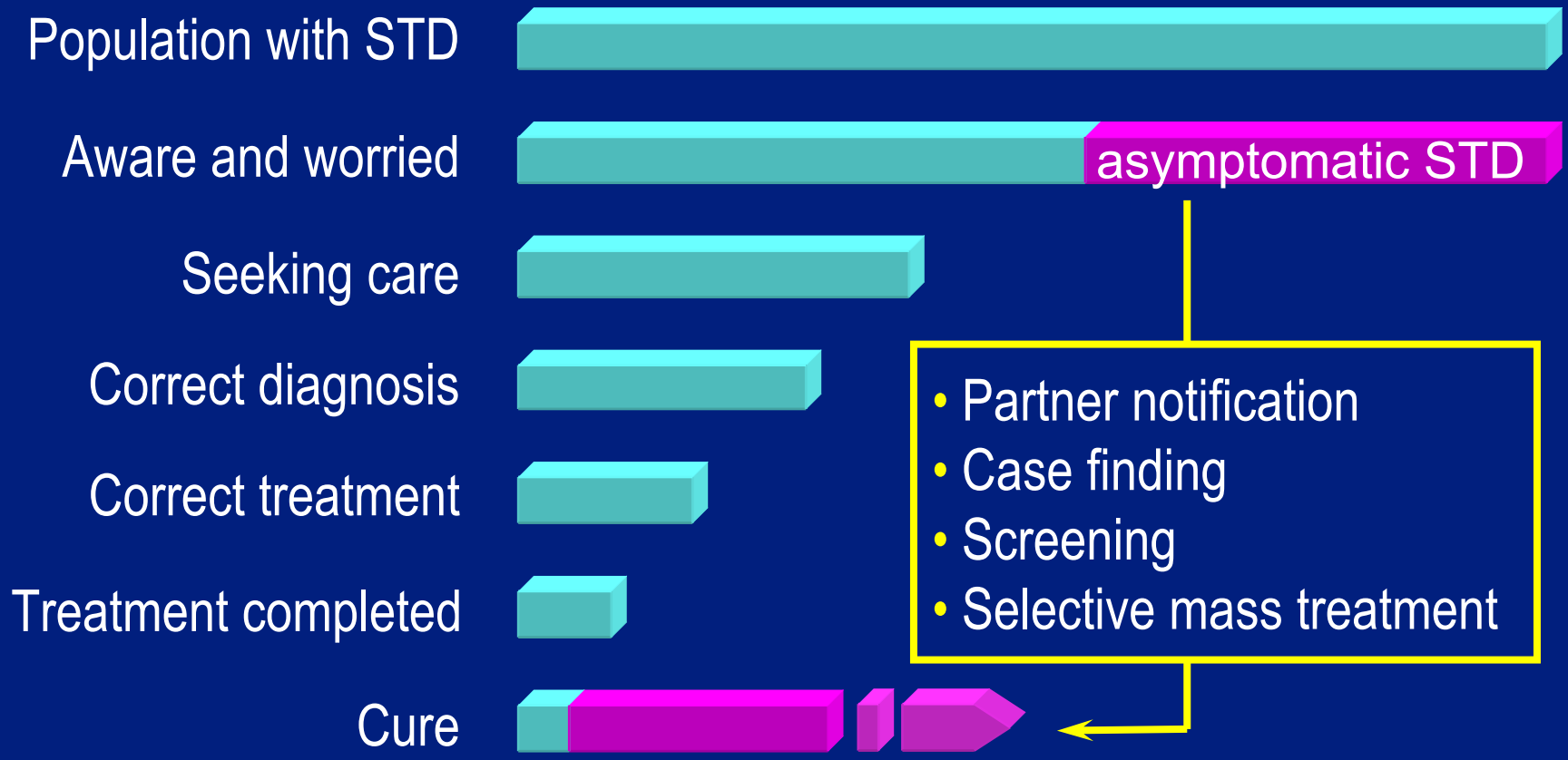
Treat for syphilis and chancroid
- Educate
- Counsel on risk reduction
- Promote and /provide condoms
- Depending on counselling capabilities offer HIV testing
- Partner management
- Advise to return in 7 days

← Yes

Clinical deterioration, or no improvement after one week?

YIELD : Needs adaptation to local epidemiological situation

Operational model of the role of health services in STD case management



What proportion of STD is asymptomatic?

Incidence studies

- 2% of incident infections with gonorrhoea remained asymptomatic for at least 2 weeks (Harrison *et al.*, New England Journal of Medicine, 1979)

Prevalence studies

• Screening pregnant women (GC/CT)	40%
• Screening FP clinic attenders (GC)	80%
• Male contact of clinical cases (GC)	29%
• Male contacts of cases detected through screening (GC)	76%

Where STD control is likely to have a maximum impact

- In settings with high prevalence of "relevant" STD (GUD, urethritis and cervicitis)
- Low quality of STD services
- At the earlier stages of the HIV epidemic

It is **NOT A MAGIC BULLET**, but an essential component of a package of multiple HIV prevention strategies

WHO core functions in STI control

- Policy and advocacy
- Knowledge management
- Technical assistance to countries
- Partnerships development
- Norms and standards
- New technologies and tools development

Strategic areas of action

- Improve access to quality STI care
- Promote early and effective health care seeking behaviour
- To establish simple and affordable surveillance systems to monitor trends and interrelations of HIV and STIs epidemics

Danke Merci

Merci Grazias

Obrigado

Thank you Danke

Grazias

Danke Thank you

Merci

HIV/AIDS/STI Initiative