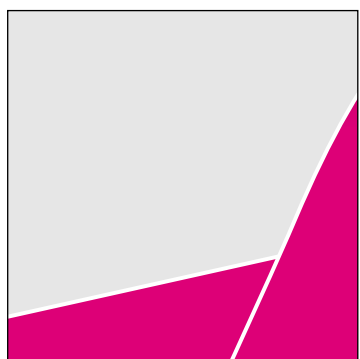


# Consultation on STD interventions for preventing HIV: what is the evidence?



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Consultation on STD  
interventions  
for preventing HIV:  
what is the evidence?

Geneva, Switzerland  
2000



Joint United Nations Programme on HIV/AIDS  
**UNAIDS**  
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# 1. Background

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The consultation was called in response to recent research findings in sexually transmitted disease (STD) treatment and its effect on the transmission of human immunodeficiency virus (HIV). The interrelationship between HIV infection and other STDs has become increasingly clear over the last decade. Clinical manifestations of some STDs are altered in the presence of HIV infection. This has particularly been the case with conditions such as chancroid (which becomes more aggressive and relatively more recalcitrant to standard therapeutic doses), genital herpes sores (whose recurrence rate becomes more frequent and/or the sores become persistent without anti-viral treatment), genital warts (which present as large lesions with no spontaneous resolution), and molluscum contagiosum (which becomes more florid very rapidly).

More recently, the focus has been on the role of these other STDs in facilitating HIV transmission. In 1995, a community-based STD intervention trial, which improved STD management and condom promotion in a rural district of the United Republic of Tanzania demonstrated evidence that STD treatment can substantially decrease HIV incidence. Three years later in a rural district of Uganda, another community-based trial providing mass STD treatment to the community did not demonstrate any impact on HIV incidence.

Numerous other studies showed an association between STD control and HIV transmission. However, many confounding factors such as risky sexual behaviour, frequency of partner change, and the prevalence of HIV and other STDs in the study population made a causal relationship difficult to substantiate.

At about the same time, however, a number of investigators started to report on the biological plausibility of the association between HIV and other STDs, and to suggest the potential biological mechanisms for it. Some studies among patients with STDs showed increased HIV viral copies in genital fluids in both men and women. Treatment of the STD in these patients resulted in reduced concentration of viral copies in the genital fluid compartment.

Therefore, it became necessary that a critical mass of researchers, scientists, donors, and programme managers review all this information in order to determine its programmatic importance and significance. With this in mind, a consultation comprising experts from various disciplines in the fields of STD and HIV was convened in Geneva from 14-16 October 1998. The aim of this meeting was to review and discuss these research findings in order to consolidate and strengthen strategies for STD control for the prevention of HIV infection. Additionally, it was important to review and discuss what is already known, and how existing knowledge should determine the focus for future programme policy and research.

## 1.1 Consultation objectives and expected outcomes

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The objectives of the consultation were:

1. To review evidence for STD as a cofactor in HIV transmission (including viral shedding data);
2. To review intervention studies addressing 'STD control to reduce HIV incidence' both in community and specific groups;
3. To identify further research needs in STD control for the prevention of HIV transmission.

The expected outcomes of the meeting were:

1. A document stating the role of STD control for HIV prevention and highlighting research needs in the area of STD control to prevent/reduce HIV transmission;
2. A statement regarding whether intervention trials are needed, and, if so, an identification of which type;
3. Proposals for change (if any) in the present policies and principles for STD control to prevent HIV infection in the general population and specific groups, and priority areas for action.

The focus of discussions was on studies conducted in various countries, looking specifically at:

- Impact of improved treatment of sexually transmitted diseases on HIV infection;
- Improved treatment services to reduce the prevalence of STDs;
- Information, education and communication (IEC) trials and STD interventions;
- Association of various STDs with the transmission of HIV;
- Policy and programmatic considerations.

## 2. Overview

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Data from a large number of biological and epidemiological studies conducted in four continents provide compelling evidence that STD is a co-factor for HIV transmission. This suggests that STD control has the potential to play an important role in the reduction of sexually acquired HIV transmission.

### 2.1 Review of evidence from epidemiological studies

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#### **STD/HIV cofactor hypothesis**

The existence of an association between STDs and HIV infection has been observed in many cross-sectional and case-control studies since the mid-1980s. This observation led to the hypothesis that STD enhances HIV transmission (STD/HIV co-factor hypothesis). However, the association is difficult to interpret because the sexual transmission of HIV and other classical STDs share the same risk factors. In cross-sectional studies, it is also difficult to determine the time sequence of the infections.

#### **Longitudinal observational studies**

Some of these methodologic problems can be partly overcome in longitudinal observational (cohort) studies. A number of such studies have contributed substantial evidence for the existence of the STD/HIV co-factor effect, with relative risks ranging from 1.5 to 8.5 depending on the STD under observation. A list of selected studies documenting STDs as risk factors for HIV transmission is given in Table 1.

*Studies on STDs as risk factors for HIV transmission*

Table 1

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

The increase in transmission probability for HIV infection per single sexual act is probably much higher than the relative risks observed in cohort studies because study participants are not continuously affected by STD during the follow-up period. The co-factor effect seems to be higher for ulcerative diseases, but in some populations, the proportion of HIV infections attributable to non-ulcerative STDs may be higher than that for ulcerative diseases. This may be because non-ulcerative STDs occur much more frequently.

### Intervention studies in high risk groups

In recent years, intervention studies have added much weight to the STD/HIV co-factor hypothesis. In a non-controlled study among sex workers from Kinshasa, regular STD treatment combined with condom promotion led to a significant decline in the incidence of HIV infection and several STDs (gonorrhoea, trichomoniasis and genital ulcers) as compared with the period prior to the start of the intervention. HIV incidence was more than halved. The risk factors most significantly associated with HIV seroconversion were gonorrhoea, trichomoniasis and irregular condom use (adjusted relative risks 2.3, 1.7, and 1.6 respectively).

In a study among sex workers from Abidjan with a high HIV incidence (16.5/100 person years) before the intervention, monthly STD case-findings based on clinical signs reduced the incidence to 7.9/100py. A more elaborate approach using speculum examination and microscopy was associated with a further reduction in incidence to 5.5/100py.

### Community-based randomized controlled trials

#### The Mwanza study

In a trial from Mwanza, the United Republic of Tanzania, the provision of improved treatment services was integrated into the existing primary health care (PHC) facilities. The impact was measured in a cohort recruited from 12 matched communities. This community-randomized trial in rural Tanzania showed that strengthened STD case management of symptomatic persons, using the syndromic approach provided through the existing PHC system, led to an estimated 38% (adjusted rate ratio = 0.62, confidence interval 0.45-0.85) reduction in HIV incidence over two years in the general adult population. The intervention comprised training of health care providers, regular supervision, provision of drugs and supplies, establishment of a reference centre, and promotion of improved treatment-seeking behaviour. Significant reductions were also observed in the prevalence of newly-acquired syphilis and of symptomatic urethritis in men, but no effect was seen on the prevalence of STDs in antenatal clinic (ANC) attendees.



### The Rakai study

A community-randomized trial in Rakai, Uganda, provided home-based mass treatment at ten-monthly intervals with single oral dose, broad-spectrum antibiotics. Treatment in the intervention arm was provided for gonorrhoea, chlamydial infection, trichomoniasis, bacterial vaginosis and chancroid (see Table 2). All RPR seroreactive individuals in the intervention arms were treated for syphilis and those in the control arm were referred for care.

*Medication used for mass treatment for intervention and control groups in Rakai*

Table 2	Intervention clusters (n=7871)	Control clusters (n =7256)
	Treatment provided:	
	- azithromycin 1000mg - ciprofloxacin 250mg - metronidazole 2g	-mebendazole 100mg - iron-folate tablet - low dose multi-vitamin

*Note: Intervention clusters were screened and treated for syphilis, whereas control clusters were provided with serological results and referred for treatment.  
Free treatment for symptomatic STDs through "Project Mobile Clinics" was also provided during treatment rounds.*

No difference in HIV incidence was seen between study arms (adjusted rate ratio = 0.97, confidence interval 0.81-1.16). There were significant reductions in the prevalence of bacterial vaginosis, trichomoniasis and syphilis, and in the incidence of trichomoniasis. In pregnant women, trichomoniasis, gonorrhoea, chlamydial infection and bacterial vaginosis were significantly reduced (the average interval between treatment and STD testing was 4.5 months).

## 2.2 Review of evidence from biological studies

During recent years, some of the biological mechanisms by which STDs act as co-factors for HIV transmission have been postulated. These include:

- An increase in HIV infectiousness due to an increase in viral shedding in genital secretions in the presence of STDs;
- An increase in susceptibility to HIV due to:
  - a disruption of the epithelial barrier;
  - an increase in cell receptivity to HIV (in vitro data);
  - an increased number of receptors per cell.

### Increase in infectiousness

Various studies have investigated the shedding of HIV into genital fluids. In a study of men infected with HIV in Malawi, the concentration of HIV copies was strongly enhanced in men with urethritis compared to those without urethritis. This concentration decreased after treatment of the urethritis. Studies in HIV-infected women from Abidjan demonstrated that the proportion of women with cervico-vaginal HIV shedding increased substantially in the presence of genital ulcers and gonococcal and chlamydial infection, but not trichomoniasis. In this study, the increase of HIV in genital

fluids in the presence of STDs was independent of the level of viral load in blood plasma.

A number of other studies have identified some STD-related correlates associated with increased HIV shedding in both men and women (see Table 3).

*Various STD-related correlates of increased HIV genital shedding*

Table 3

Female (cervico-vaginal secretions)	Male (semen)
Mucopurulent cervicitis	-
Cervical ulcer	-
Vaginal ulcer	-
Increased leukocytes	Increased leukocytes
<i>Neisseria gonorrhoeae</i>	<i>N. gonorrhoeae</i>
<i>Chlamydia trachomatis</i>	-

### 2.3 An operational model for STD control

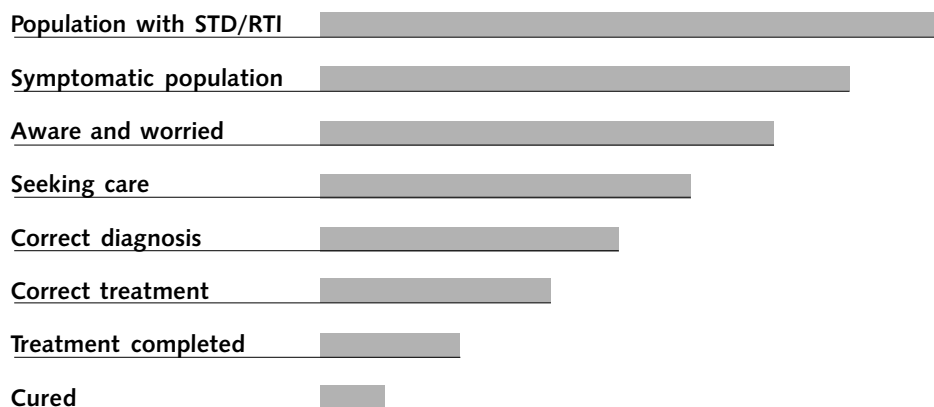
In any population, only a certain proportion of those with symptomatic STDs will be cured by the health services. This cure rate depends on a set of factors (proportions or probabilities):

- number of persons with symptomatic STDs/reproductive tract infections (RTIs);
- proportion of these aware and worried;
- proportion seeking care;
- proportion correctly diagnosed;
- proportion receiving correct treatment;
- proportion completing treatment;
- proportion cured.

As shown in the hypothetical example of Figure 1, the fraction achieving cure may be very small because at each step patients are 'lost'. However, it must be noted that each step is different for different population groups, as well as for their particular environmental circumstances.

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

Figure 1



The overall goal of interventions designed to address this operational model is to increase the number of patients with STD who attain cure. This can be achieved by making the population aware of disease symptoms (where present), and encouraging them to seek adequate care early, thus helping improve patients' treatment-seeking behaviour. Furthermore, improving the diagnostic skills of health workers and their prescription practices can strengthen case management. The availability of effective drugs is also essential, as is the provision of health education messages aiming at better compliance in completing prescribed drug treatment regimens.

## 3. Intervention studies addressing STD control to reduce HIV incidence

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### 3.1 Mwanza intervention trial

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This randomized study was conducted to evaluate the impact of improved sexually transmitted disease case management at primary health care level on the incidence of HIV infection in the rural Mwanza region of the United Republic of Tanzania.

#### **Objective**

To establish whether improved STD case management and treatment-seeking behaviour have an impact on HIV transmission and STD at a population level.

#### **Design**

Twelve large rural communities from Mwanza Region, the United Republic of Tanzania, six in the intervention arm and six in the comparison arm. Matched design: six pairs of communities with HIV prevalence expected to be similar within pairs. Randomization to intervention and comparison arms within each matched pair. Catchment population in each arm was about 150 000.

#### **Intervention**

Improved (syndromic) STD case management services integrated into the existing primary health care system of the United Republic of Tanzania. Components: training of health workers, regular and frequent supervision and in-service training, provision of effective low-cost drugs, and campaigns to improve the treatment-seeking behaviour of the population. In the comparison arm, continuation of existing services. Extension of the intervention into the comparison arm at the end of the trial. In addition, for ethical reasons, injections to treat syphilis were provided at baseline and follow-up to all persons in both arms with serological evidence of infection.

#### **Impact evaluation**

- Cohort study of about 1000 adults (15-54 years) from each of the 12 communities, follow-up period of two years. Outcomes: HIV incidence, syphilis incidence (measured by *Treponema pallidum* hemagglutination assay (TPHA), prevalence of active syphilis, prevalence of urethritis in men;

- Two repeated cross-sectional surveys in 100 ANC attendees from the same communities. Outcomes: prevalence of syphilis and gonococcal, chlamydial and trichomonal infections.

### **Laboratory methods employed**

Enzyme-linked immunosorbent assay (ELISA) for HIV infection, Western blot for indeterminate samples. TPHA and RPR test for syphilis. Leukocyte esterase dipstick test (LED) in urine in men as screening test for urethritis. Gram stain for gonococcal infection and enzyme immunoassay (EIA) for chlamydial infection in men with discharge or positive LED result. Wet preparation, gonococcal culture and chlamydial EIA in ANC attendees. No etiologic diagnosis from ulcers.

### **Operational results**

During the trial, 11 632 STD syndromes were treated at 25 health facilities. Partners were treated for 30-35% of patients. Reported clinical cure rates were above 95%, and 89% in patients who did not return for a clinical examination but who were followed to their homes.

### **Impact results**

Cohort study: coverage 85% at baseline, 71% at follow-up. Baseline HIV prevalence 4%, HIV incidence in the intervention group was 0.6% and in the comparison arm 0.9% per year. Significant reduction of HIV incidence by 42% in the intervention arm (38% after adjustment for possible confounding factors).

Syphilis: non-significant 30% reduction of syphilis incidence measured by TPHA. A significant reduction of active syphilis prevalence reported.

Urethritis: borderline significant 49% reduction of symptomatic urethritis in men. No reduction of overall urethritis (symptomatic plus asymptomatic), or of gonococcal and chlamydial infections in men, or of any STD in ANC attendees. No substantial differences in self-reported sexual behaviour between arms or over time.

### **Cost-effectiveness**

The intervention has been shown to be highly cost-effective. The cost of averting one case of HIV infection through this intervention has been estimated at US\$ 218, and at \$10 per disability-adjusted life year (DALY) saved. In a sensitivity analysis of factors influencing cost-effectiveness, the cost per DALY saved ranged from \$2.50 to \$48.00. These estimates compare favourably with those of other public health interventions.

### **Constraints**

Asymptomatic STDs were not covered except through partner treatment. In spite of the improved services, some patients still sought treatment from traditional healers or from drug sellers. Occasionally, drugs were misused by some health workers for financial gain, which was largely attributable to the difficult economic situation. Some trained staff were transferred, requiring retraining of others.

## **3.2 Rakai intervention trial**

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The Rakai study was a community-based randomized controlled, single-blinded efficacy trial.

### **Objectives**

1. To determine whether 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 (mass therapy chosen because of lack of infrastructure in the Rakai area).

### Design

The Rakai study for AIDS prevention was conducted in a rural area with high rates of HIV, STD and genital tract infections (GTIs). The study provided broad-spectrum antibiotic mass treatment in the intervention arm in order to cover both asymptomatic and symptomatic infections in persons and their formal and informal partners. The strategy covered multiple infections and permitted rapid treatment of the entire community. Symptomatic control arm subjects and those with positive syphilis serology were referred for syndromic STD management. The sampling goal was to achieve a 35% reduction in incidence in the intervention arm. It was designed this way in order to reduce re-introduction of STD into communities. Hence, the clusters were designed to group social interaction and, presumably, sexual interaction. Permanent residents were fully enrolled with a complete data set. The study also treated transients and spouses who lived outside the home. Data were collected on these individuals. There were five clusters each in treatment and control groups.

### Intervention

Home visits were conducted every 10 months. Questionnaires and samples were the same for everyone in the intervention and control groups. Intervention group received azithromycin, ciprofloxacin and metronidazole, regardless of symptoms. The control arm was given mebendazole (treatment for worms), iron and vitamins.

Sera were taken from both the control and the intervention arms. In the intervention arm, syphilis seroreactive positive participants received benzathine penicillin in their home, and in the control group, participants were referred to the health centre, which was stocked with benzathine penicillin. Sera, urine, self-administered vaginal swabs from women, and swabs of all reported genital ulcer disease in men were taken in the home. Women who reported genital ulcer disease were sent to clinics for ulcer swabs.

Between study visits, in both intervention and control arms, all symptomatic patients were advised to attend government clinics for treatment.

### Evaluation

HIV incidence was measured either between Visits 1 and 2, or Visits 2 and 3. For those persons who did not provide a Visit 2 sample, incidence was measured between Visits 1 and 3. STD prevalence was presented at each of the rounds (conservative analysis). In the STD cohort, all HIV positive and negatives were included. Baseline STD prevalences were: syphilis 10%, bacterial vaginosis 50%, *Trichomonas vaginalis* 25%, *Neisseria gonorrhoeae* 1.5%, *Chlamydia trachomatis* 3 % and HIV 16%.

### Summary of results

1. The study achieved the operational objective of reducing the prevalence of STD exposure in the intervention arm relative to the control arm;
2. No difference in HIV incidence was observed;
3. There was no difference in duration of symptoms between intervention and control;
4. Significant reductions in prevalence of syphilis and *T. vaginalis* were seen in the general population. A critical question is whether the ethically mandated STD services offered to control subjects might have resulted in convergence of treatment intensity between arms and possibly diluted an effect on HIV incidence.

## Constraints

Government services in both intervention and control arm communities were very limited, with frequent manpower and drug shortages in local health units. The project provided free penicillin to the units, but no training or other service delivery improvements.

## 3.3 Masaka intervention trial

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### Objectives

1. To determine the impact of behavioural change brought about by IEC alone compared to IEC with improved STD management on HIV incidence in a rural Ugandan population;
2. To evaluate the cost-effectiveness of the interventions and to assess whether they could assist in HIV control in other settings.

### Design

The study was a randomized controlled community trial with three arms:

- Arm A: IEC alone;
- Arm B: IEC with improved STD management;
- Arm C: Control community.

All three arms included social marketing of condoms, HIV testing, and counselling. For each arm, six parishes with 4000 adults each were enrolled. Randomization of the parishes considered:

- quality of health facilities available;
- level of staffing;
- type or size of road passing through the parish;
- distance from the district capital, Masaka.

### Interventions

#### 1. IEC package

The health promotion component aimed at promoting:

- correct knowledge on AIDS and STD;
- positive attitudes and compassion for people with AIDS and for their families;
- safer sexual behaviours such as reduction in numbers of sexual partners and the adoption of safer sexual practices (condom use);
- improved treatment-seeking behaviour for people with symptoms of STD.

#### 2. Improved STD management

The aim was to improve:

- knowledge and skills of health care providers;
- quality of STD care in the study arm.

#### 3. Comparison arm activities

In this arm, the focus was on non-HIV/STD public health measures such as immunization activities, malaria control and sanitation.

### Outcome measures

The primary outcome measure was HIV incidence. Other indicators included:

- STD incidence (*T. pallidum*, herpes simplex type 2, gonococcal infection and *C. trachomatis*);
- condom uptake;
- sexual behaviour change.

### Baseline data

The baseline prevalence of HIV overall was 8.7% in males and 10.9% in females. The prevalence varied from parish to parish (range 4-21%), with the highest rates observed in females aged 20-34 and males aged 25-44 (Table 4). So far only 4000 baseline rapid plasma reagin tests (RPRs) have been done. The overall rate is 11% (11.4% in males and 10.5% in females). TPHA confirmation of the results is still pending.

*Baseline prevalence of HIV in the three arms in Masaka, Uganda*

Table 4

	Arm A	Arm B	Arm C	Total
Total subjects enrolled	7109	7066	7031	21 206
% tested	70%	68%	70%	70%
HIV prevalence	9%	10%	11%	9.9%

### Results

The implementation started in the first health unit of Arm B in September 1994. By September 1995, all six parishes had been fully incorporated in the intervention.

1. A total of 5813 STD cases were reported from the six health units (2124 males, 3689 females). The sex differential could be due to pregnancy-related STD picked up during antenatal visits.
2. Of the STD syndromes, 54% were genital discharges and 32% were genital ulcers (23% of males and 7% of females with genital ulcers also had discharges).
3. The proportion of STD cases seeking care from private practitioners was 13%.
4. The overall return rate for STD cases has been less than 20%, of whom 67% reported to have been cured.
5. Overall results from follow-up of seronegatives (from three triplets) indicate an HIV incidence of 7.6% per 1000 person years (6.4 among males and 8.6 among females).

### Discussion

1. The baseline survey, which included parish assessment and preparations, was completed in November 1996 and round two of the study finished in December 1998. The last survey will be completed in June 2000. The results of the study will be available at that time.
2. The IEC-STD trial has been established with interventions in place that appear to be adequate.
3. The role of private practitioners in the trial is important. They have been trained and are supervised in a similar way to those in the public sector. The quality of service is not different from the public sector.

4. To determine the etiology of genitourinary disease (GUD), plans have been made to conduct an etiologic study using a clinic-based cohort. However, to obtain HSV-2 incidence with an estimated prevalence of 36% in males and 72% in females, this will need to be restricted to the youngest age group.
5. The lower than expected HIV incidence implies that the follow-up would ideally be longer than expected. However, this is unlikely to be feasible.
6. Because it is a service-based study, the sample was taken from populations in close proximity to the clinics. It is also important to see how the effect of the interventions has diffused.
7. Since no intervention operates in isolation, it is important to assess whether other projects taking place in the area will have a diluting effect.
8. Comparison of Arm A and Arm C is one of the few trials assessing the link between IEC and STD and HIV outcomes, making it particularly important. There is a poor utilization of HIV testing and counselling services. Only about 10% come for results in every arm. All residents in each arm will be tested as part of the house-to-house survey. Although the impact of testing and counselling at the individual level has had a variable impact, there are few data on community impact.

### 3.4 Mwanza and Rakai trials compared

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The differences in the results of the Mwanza and Rakai trials have raised a number of important programmatic and research questions.

#### Interventions

The Mwanza trial focused on enhanced syndromic diagnosis of symptomatic STDs. There was provision of continuous access to STD treatment, regular supervision and a consistent drug supply. After 24 months, the intervention in Mwanza resulted in a 38% reduction in HIV incidence in the intervention communities compared with the control communities.

In Rakai, Uganda, where a different approach of directly-observed mass treatment for curable STDs at 10-monthly intervals was tested, HIV incidence was similar in the intervention and control communities at the end of 20 months (i.e. second round of mass treatment).

Multiple factors may have contributed to the divergent results of these two trials. Some of the potential explanations for the results are outlined in points 1-3 below.

#### 1. Type of intervention

The Mwanza trial provided continuous access to STD treatment, regular supervision of health workers and a consistent supply of drugs. In Rakai, on the other hand, the intervention was mass treatment administered only every ten months to both symptomatic and asymptomatic study populations. It is plausible that continuous access to improved STD treatment services might be more effective than intermittent mass treatment. For example, persons infected soon after the round of mass treatment would have had access to the clinical services in prior existence, possibly with inadequate clinical care facilities (Table 5).



*Description of interventions*

Table 5

	<b>Rakai</b>	<b>Mwanza</b>
<b>Design</b>	Community-based randomized, controlled single-blinded in open cohort	Community-based randomized, controlled, unblinded trial in cohort
<b>Intervention</b>	STD mass treatment in home, directly observed	Syndromic treatment of symptomatic STDs through access to improved clinic-based service (and intramuscular penicillin to all RPR positives at baseline in both study arms)
<b>Measures taken in control communities</b>	Anthelmintic/vitamin/iron-folate. Mass treatment and referral for STD symptoms or positive syphilis test	Same intervention began two years later
<b>Frequency of intervention</b>	Baseline 10-monthly	Continuous
<b>Follow-up duration</b>	20 months	24 months
<b>Treatment of partners</b>	Presumed covered by mass treatment	Patient referral (about 30% presented to clinics for care)
<b>Measurement</b>	Entire population in the intervention and control communities (aged 15-59 years)	Randomly selected community cohort (aged 15-54 years) and antenatal clinic sample

**2. Stage of HIV epidemic**

In the later stage of an HIV epidemic, the relative contribution of curable STD to HIV transmission may decline, and the importance of viral STD may increase. The prevalence data from both sites show that Mwanza had a baseline HIV prevalence of 4% while the Rakai background HIV prevalence was 16% (Table 6). In the latter, an increased proportion of individuals is biologically and behaviourally susceptible to HIV infection, independent of a co-factor effect of STD. Thus, the proportion of new HIV infections attributable to a co-factor effect of curable STD may decline as the HIV epidemic matures.

**3. STD prevalence and profiles**

Different test methodologies were used to estimate the prevalence of STD in the two trials. In Rakai, the STD detection methods were more extensive than those used in Mwanza. Nevertheless, some comparisons can be made from sub-sample data. Syphilis prevalence rates were similar (Rakai 10%, Mwanza 7-9%). Gonorrhoea and chlamydia combined prevalence seems to have been comparable (Mwanza 2.4-3.2% and Rakai 3%). However, 31% of men and 61% of women in Rakai had HSV-2 infection, compared with 12% and 35% in Mwanza. High prevalence of incurable or difficult to treat STDs/RTIs (especially HSV-2 and bacterial vaginosis) may play a role that nullifies the effect of treating curable STDs at a population level (Table 6).

Table 6

	Rakai	Mwanza
Participation	77% of all those eligible	85% of all those eligible
Follow-up	73-75%	71%
Randomization	Effective at cluster level	Effective at community level
<b>Baseline HIV prevalence</b>	15.9%	4.1%
HSV-2	31.2% men 60.9% women	12.1% 35.6%
<b>Baseline STD prevalence</b>		
Syphilis seropositive	10	7-9%
Gonorrhoea	1-2%	2.4–3.2% (men - gonorrhoea and chlamydia)
Chlamydia	2-4%	
Trichomoniasis	24%	not reported
Genital ulcer symptoms	8-9%	not reported
Discharge symptoms	6-7%	1-2% (men)
Dysuria symptoms	10%	not reported
Bacterial vaginosis	50%	not reported

*Note: Rakai baseline rates refer to a 6-month period, not point prevalence of symptoms.*

Furthermore, untreated symptomatic STDs may be more important than asymptomatic ones for HIV transmission (asymptomatic STDs may be key to STD spread and related complications). It is conceivable that the STD/HIV co-factor effect of asymptomatic STDs may be lower than that of symptomatic STDs. Biologically, symptomatic STDs are more likely to be associated with inflammation and ulceration, and these correlates have been shown to be associated with inflammation with increased HIV shedding. The intervention in Mwanza dealt more with symptomatic infections than the Rakai intervention trial.

Intervention impact on STDs in Mwanza (Tables 7 and 8)

- Borderline significant reductions in the incidence of syphilis in the intervention communities;
- Significant reductions in the prevalence of serologic syphilis in the intervention communities;
- The prevalence of symptomatic urethritis in men was reduced by 50% in the intervention communities;
- Non-significant 30% reduction in TPHA seroconversion was documented.

#### **Intervention impact on HIV in Mwanza**

- In Mwanza, there was a 38% reduction in HIV incidence in the intervention communities compared with the controls.

Follow-up findings: HIV and STD incidence

Table 7

	Rakai		Mwanza	
		Adj RR* (CI**)		Adj RR (CI)
<b>HIV incidence</b>				
Intervention group	1.5	0.97 (0.81-1.16)	0.58	0.62 (0.45-0.85)
Control group	1.5		0.93	
<b>HIV incidence (with dysuria)</b>				
Intervention group	1.3	0.63 (0.4-1.01)	(N/A)	-
Control group	1.8			
<b>HIV incidence (with NG)</b>				
Intervention group	2.9	(N/A)	(N/A)	-
Control group	9.1			
<b>STD incidence</b>				
<b>Syphilis: TPHA seroconversion</b>				
Intervention group			3.0	0.69 (0.35-1.38)
Control group			4.1	
<b>New cases of active syphilis</b>				
Intervention group	1.7	0.65 (0.06-6.82)	2.2	0.62 (0.30-1.02)
Control group	2.2		3.4	
<b>Trichomoniasis</b>				
Intervention group	4.8	0.52 (0.35-0.79)	N/A	
Control group	9.1			

\*Adj RR = adjusted relative risk \*\*CI = Confidence Interval

Follow-up findings: STD prevalence

Table 8

	Rakai		Mwanza	
		Adj RR* (CI**)		Adj RR (CI)
<b>STD prevalence</b>	(%)		(%)	
<b>Syphilis seropositive</b>				
Intervention group	5.6	0.80 (0.71-0.89)	5.0	0.71 (0.54-0.93) RPR <sup>3</sup> 1:8
Control group	6.8		7.0	
<b>Gonorrhoea (NG)</b>				
Intervention group	0.8	0.66 (N/A)	-	-
Control group	1.2			
<b>Chlamydia (CT)</b>				
Intervention group	2.4	0.88 (0.50-1.53)	-	-
Control group	2.6			
<b>NG/CT</b>				
Intervention group	-	0.59 (0.38-0.91)	2.5	0.96 (0.50-1.85)
Control group			3.0	

→

## Follow-up findings: STD prevalence (con't.)

Table 8

	Rakai		Mwanza	
		Adj RR* (CI**)		Adj RR (CI)
<b>Trichomoniasis</b>				
Intervention group	9.3	1.02 (0.80-1.29)	-	
Control group	14.4			
<b>Genital ulcer symptoms</b>				
Intervention group	5.7	1.01 (0.93-1.31)	-	All symptoms: men Intervention group 11.5% RR 0.94 Control group 12.2% (0.59-1.559) All symptoms: women Intervention group 6.1% RR 1.00 Control group 6.5% (0.58-1.72) (0.25-1.03) men only
Control group	5.3			
<b>Discharge symptoms</b>				
Intervention group	6.5	1.12 (0.89-1.41)		
Control group	6.0			
<b>Dysuria symptoms</b>				
Intervention group	6.4	-		
Control group	5.7			
<b>Symptomatic urethritis</b>				
Intervention group	-	-	1.8	
Control group	-			3.2

\*Adj RR = adjusted relative risk \*\*CI = Confidence Interval

## Intervention impact on STDs in Rakai (Tables 7 and 8)

After three mass treatment rounds spanning 20 months, including two follow-up intervals, the following results were noted:

- Significant reductions in the prevalence of serologically diagnosed syphilis in intervention communities;
- Significant reductions in the prevalence and incidence of *T. vaginalis* in intervention communities;
- Borderline significant reductions in the prevalence of bacterial vaginosis.

**Intervention impact on HIV in Rakai**

In Rakai, HIV incidence was similar in the intervention and control communities overall.

**Issues for further discussion and research**

The Rakai team had carefully investigated and documented the sexual networks in the trial communities, and had tried to define the size of the trial communities accordingly. However, between 8% and 13% of the cohort participants reported having had a sexual partner outside the community, and about 45% of the cohort population reported having travelled outside the Rakai District during the follow-up period. About 83% of all enumerated residents were present at the time of the study visit to the community. Of these, about 93% consented to enrolment. The proportion accepting treatment was more than 90%. Thus, mass treatment coverage was about 77% of all eligible residents. Some discussants suggested that defaulters and non-participants may have been more mobile and may have engaged in high-risk behaviour more frequently than people who participated in the intervention.

Despite the mass treatment, STD prevalence was substantial at follow-up after 10 months, suggesting that reinfection must have been significant. The Rakai team underlined that the strong and significant reduction observed for trichomoniasis argues against the assumption that there was rapid reinfection.

In Rakai, effects of the population-attributable-risk (PAR) of incident HIV associated with STD were determined. In this exercise, the researchers noted that the relative risk of incident HIV was increased among persons with STD symptoms, particularly current symptoms. However, the prevalence of symptoms was low, and the PAR% was 9.5% for HIV acquisition for any one symptom and less than 20% for combinations of symptoms. Thus, in this high HIV prevalence setting, the attributable risk of HIV acquisition associated with STD symptoms was low. This, however, was at community level. Within the community, there may be subpopulations in whom the effect of STD on HIV acquisition is high. It is important to note that adolescents come under this category, and STD control in such a group will be critically important, even in a high HIV prevalence and low STD prevalence setting.

Some discussants pointed out that random variation might have contributed to the different results in Rakai and Mwanza. The confidence intervals around the impacts on HIV incidence observed were 0.81-1.16 for Rakai (rounds 1-3) and 0.45-0.85 for Mwanza. This means that the results were consistent with a reduction in HIV incidence of up to 19% in Rakai and from 15% to 55% in Mwanza, so that the discrepancy between the results of the trials may possibly be smaller than suggested by the two central estimates. Random error in trial results may have resulted in a possible overestimation of the effect in Mwanza and a possible underestimation of the effect in Rakai (Table 7).

In addition, some researchers have questioned the size and the implications of the changes in STD prevalence achieved in the Rakai trial:

- The main reductions achieved in Rakai were those in serologic syphilis (most of which was latent syphilis) and in trichomoniasis. There is no evidence to date that latent syphilis contributes to HIV transmission. The magnitude of the cofactor effect of trichomoniasis on HIV transmission is unknown and may be small.
- The STD detection methods were more advanced in Rakai than those used in Mwanza. This makes direct comparisons difficult. However, some data suggest that gonorrhoea and chlamydia may have been slightly higher in Mwanza, while the proportion of ulcers due to herpes simplex virus (HSV-2) was substantially higher in Rakai.
- For both gonococcal and chlamydial infection, the prevalence had been substantially higher in the intervention arm than in the comparison arm at baseline, but was almost identical in both arms *after* mass treatment. Therefore, it remains unclear what level of exposure to these STDs existed during the follow-up period in both arms, and whether this exposure had been differential.
- Candida infection was not covered by mass treatment. It may be possible that antibacterial treatment led to an increase in candidiasis in the intervention arm as a result of a reduction of vaginal lactobacilli. *Candida albicans* infection has recently been shown to be associated with HIV infection. Mass treatment may possibly have enhanced HIV transmission in some subjects. However, the Rakai research team stressed that there was no evidence that *C. albicans* infections increased in the population during the trial.

## Conclusion

Participants agreed that the epidemiological and biological evidence for an enhancing effect of STD on HIV transmission is overwhelming. There has been strong evidence for the effectiveness of STD interventions on HIV transmission in several studies. All participants agreed that effective control of STD should continue to be a key component for AIDS control programmes, especially in areas or subpopulations where STDs are highly prevalent.

Further research is needed to address the role of asymptomatic STDs and to investigate operational aspects of STD interventions in order to identify the best intervention approaches under different circumstances. Evidence documenting the efficacy of STD mass treatment in areas with late HIV epidemics and low STD rates is needed. More research is also needed on the impact of treating asymptomatic STDs among 'core' transmitters in areas with substantial STD rates and increasing HIV rates. Other research issues for consideration are:

- investigating the impact which can be achieved on health-seeking behaviour;
- collecting data on STD incidence and STD duration;
- improving diagnostic options for the assessment of symptom status;
- linking STD/HIV data with sexual network analyses;
- improving laboratory diagnosis of STD.

The intervention studies currently suggest that intermittent mass treatment alone, delivered to the general population, is not an effective approach to STD control for HIV prevention. However, targeted mass treatment (e.g. among high-frequency transmitters or others with high STD incidence and prevalence), at relatively short intervals, deserves examination and consideration for future operational research.

### 3.5 Comparative analysis of East African trials: Computer simulations of the intervention study results

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#### Background

The comparative analysis of the East African STD intervention trials showed differences in the various outcomes. Explanations for the differences found include:

- differences in the stage of the HIV epidemic;
- differences in the STD profiles;
- differences in the interventions and their effects.

To explore these differences, two options exist. The first is to conduct further laboratory analysis and the second is to use computer modelling approaches using the empirical data.

#### Rationale for computer simulation of STD interventions

The three East African trials have been rigorously designed and conducted. This ensures *internal validity*. Each trial gives valid estimates of effectiveness of specific interventions *within* that study population. The three trials are assessing four interventions in three different populations (Table 9). Since there are differences in the trials, such as stage of the epidemic, STD profiles, differences in the interventions, and random error in trial results, and possibly for other reasons (e.g. differences in sexual behaviour, circumcision, viral subtypes), the results of these trials are not directly comparable. Both the absolute and the

relative effectiveness of different interventions may vary in different populations. Using a sufficiently sophisticated computer model, it would be possible to simulate each intervention in turn in each of the populations, and thus to compare their effectiveness (and cost-effectiveness).

*Types of interventions being assessed in East African trials*

Table 9

Intervention trial	Intervention type
1 Mwanza	Syndromic treatment services
2 Rakai	Mass STD treatment
3(a) Masaka	IEC
3(b) Masaka	IEC and syndromic treatment services

### 3.6 STDSIM simulation model and application to East African trials data

STDSIM is a model which was developed at the Erasmus University, Rotterdam, with support from the EU. It is a stochastic simulation model of HIV and four STDs, namely, syphilis, chancroid, gonorrhoea and chlamydial infection. The transmission dynamics and natural history of each infection can be simulated. Each individual in a population can be tracked with respect to sexual partnerships and acquisition of infection (Table 10). Model outputs include HIV and STD prevalence and incidence over time by age and sex. The model allows the introduction of different interventions at specified points of time. The effects of different interventions can be modelled.

*Selected model assumptions concerning transmission and natural history of infections, cofactor effects and performance of treatment*

Table 10

Parameter		HIV	Gonorrhoea	Chlamydia	Syphilis	Chancroid
Transmission probability per contact	M® F	0.003	0.22	0.20	0.30	0.15
	F® M	0.0008	0.15	0.12	0.20	0.10
Relative increase in per-contact HIV transmission probability due to STD	Susceptibility		10	10	100	100
	Infectiousness		10	10	100	100
Annual risk of infection by contacts from outside study population	M	$5.4 \times 10^{-5}$	$2.1 \times 10^{-3}$	$2.4 \times 10^{-3}$	$7.2 \times 10^{-4}$	$4.8 \times 10^{-4}$
	F	$6.1 \times 10^{-5}$	$1.2 \times 10^{-3}$	$1.5 \times 10^{-3}$	$4.1 \times 10^{-4}$	$2.7 \times 10^{-4}$
Probability that infection becomes symptomatic	M	1.0	0.50	0.30	0.95	0.95
	F	1.0	0.20	0.15	0.50	0.70
Mean duration of infectious stage if not treated (weeks)	M	400	9	12	26	16
	F	400	13	16	26	16
Mean duration of infectious stage if treated	M	NA	2	3	2	2
	F	NA	8	10	2	2

→

*Selected model assumptions concerning transmission and natural history of infections, cofactor effects and performance of treatment (con't.)*

Table 10

Parameter		HIV	Gonorrhoea	Chlamydia	Syphilis	Chancroid
Mean duration of latent stage (weeks)	M F				520 520	
Fraction of symptomatic STD episodes cured by unimproved services	M F	0.05 0.05	0.05 0.05	0.05 0.05	0.05 0.05	0.05 0.05
Fraction of symptomatic STD episodes cured by improved services	M F	0.5 0.5	0.5 0.5	0.5 0.5	0.5 0.5	0.5 0.5
Fraction of steady partners of STD patients notified and cured*	M F	0.28 0.28	0.28 0.28	0.28 0.28	0.28 0.28	0.28 0.28
Fraction of STD cured by mass treatment	M F	0.95 0.95	0.95 0.95	0.95 0.95	0.95 0.95	0.95 0.95

M = male; F = female; NA = not applicable under conditions prevailing in rural Mwanza

\*Assumed to be zero unless services improved

The Department for International Development of the United Kingdom is now funding a research project using STDSIM to compare the effectiveness of the interventions studied in the three East African trials. This will be a collaborative effort of scientists from Erasmus University Rotterdam, London School of Hygiene and Tropical Medicine, and the research teams from the three trials.

### Study design

STDSIM will be fitted to each study population, using the available extensive empirical data sets to guide parameter choice. Using three different data sets will impose strong constraints on variability of parameter choice. The model will then be adjusted to ensure good fit to baseline prevalence of HIV and STD. The model will be used to predict the impact of interventions, and then further adjusted to match the empirical impact data from each site. The final model will be used to assess (cost-) effectiveness of all four interventions in all three populations. STDSIM may also be used to identify optimized intervention strategies for other settings.

### Preliminary results from modelling

#### 1. The SimulAIDS fitted to data from Masaka

The projected proportion of HIV infections attributable to STD at different phases of the epidemic using data from rural Uganda is shown in Table 11. The results support the hypothesis that the proportion of HIV infections attributable to the cofactor effect of STD may decline as HIV epidemics mature.



*Simulation results of the percentage (95% CI\*) of adult HIV infections attributable to STD during 1980, 1990 and 2000 for low and high STD cofactor scenarios*

Table 11

Scenario	Ulcerative STD	Non-ulcerative STD	Both STDs
<b>Low cofactor</b>	% CI	% CI	% CI
1980	68 (52-83)	17 (1-99)	86 (78-92)
1990	22 (16-31)	10 (4-20)	29 (23-36)
2000	16 (13-20)	3 (1-12)	17 (12-23)
<b>High cofactor</b>			
1980	95 (92-98)	4 (0-100)	100 (98-100)
1990	71 (66-75)	15 (4-50)	81 (77-85)
2000	51 (47-55)	4 (0-57)	58 (55-62)

\* CI = Confidence Interval

## 2. STDSIM fitted to data from Mwanza

STDSIM has been fitted to data from Mwanza. Simulations have then been performed to compare the predicted impact of syndromic management and single-round mass treatment. Results show that a single round of mass treatment simulated in the Mwanza population would lead to a rapid and substantial, but temporary, decline of STD prevalence and HIV incidence. Syndromic treatment services would lead to a slow but steady decline of HIV incidence, reaching a reduction of more than 60% within 10 years, compared to the levels expected without intervention. The combination of a single round of mass treatment with syndromic case management would result in a *rapid and sustained reduction* in HIV incidence, reaching a cumulative reduction of more than 60% within one year in this model simulation (Table 12).

*Cumulative percentage of HIV infections averted by three intervention strategies (using STDSIM model projections fitted to data from Mwanza)*

Table 12

Time period	Syndromic treatment	Mass treatment	Syndromic + mass treatment
1 year	20%	45%	58%
2 years	32%	39%	60%
5 years	51%	31%	66%
10 years	64%	27%	72%

## Summary of discussion

1. Modelling can be used to explore the effectiveness of different interventions. More research is needed using currently available models. However, the available models are not yet sufficiently 'fine-tuned' and need further improvement.
2. The accuracy of predictions depends on the amount of empirical data fed into a model.
3. Preliminary data show that mass treatment may be effective in some populations under certain conditions.
4. The combination of a single round of mass treatment with continuous syndromic STD services may be particularly effective. This strategy could potentially be evaluated through a randomized controlled trial, in which improved syndromic services are provided as 'gold standard' in the comparison arm.

## 3.7 Specific vulnerable populations

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### 3.7.1 Sex workers project: Sonagachi, India

#### Background

This intervention project for sex workers, based at Sonagachi Clinic (Sonagachi, India), began in 1992, and focused on behavioural change to influence HIV transmission among sex workers. STD control was included in the project because from the community point of view, it was felt strongly that a STD service component was essential to HIV prevention efforts.

The intervention had three major components:

- STD management;
- IEC;
- condom provision.

#### Rationale for intervention

Accessibility and acceptability of services present problems for sex workers. One of the other major issues is that sex workers do not have control over their bodies and decisions. It is the inner structure of the sex trade that has a strong influence on all aspects of the service delivery. However, it is assumed that sex workers will utilize high-quality health services. The clinic in this project played a critical role in influencing quality of care, improving health care-seeking behaviour, and in empowering the sex workers.

#### Summary of intervention activities

The activities included:

1. Advocacy at community level to identify STD services;
2. Outreach work for condom promotion, including involvement of sex workers themselves;
3. IEC to improve health care-seeking behaviour;
4. Improving the quality of services offered at the clinic, including STD services, screening for syphilis, and how to improve compliance with treatment and follow-up;
5. Advocacy among sex workers to demand better services as an empowering process;
6. Training the sex workers to have some control over their bodies.

#### Baseline findings

The following were the major baseline findings in the sex worker population:

1. High illiteracy rate (84%);
2. High-risk exposure among sex workers (average of 4 clients per day);
3. Young age of sex workers (85% aged 15–29 years);
4. High prevalence of STDs (syphilis, gonorrhoea, *T. vaginalis* and candidiasis – 81%);
5. Low condom use (3%);
6. Good knowledge regarding HIV, STD and health care-seeking behaviour;
7. Fairly good attitude and high level of cooperation;
8. HIV prevalence 1.12%.

#### Implementation of intervention

The clinic initially started with clinical-pathological diagnosis for STD. As this became

logistically more difficult and unsustainable, the practice switched over to syndromic management. Health education and condom promotion were also offered and some sex workers were recruited as peer health educators.

For evaluation of the intervention, a two-stage sampling design was used, whereby a random sample was taken from three populations. The samples included both old and new sex workers (the latter having worked for less than three months in the area). About 20% of surveyed persons were new members. The project is based not on a cohort, therefore, but rather on repeated random samples.

## Results

The findings are illustrated in Table 13.

*Random sample STD and HIV findings in sex workers at Sonagachi Clinic*

Table 13

	1992 baseline	1993	1995	1998
% with genital ulcers	6.22	7.20	2.95	0.99
% VDRL + (1:8 & above)	25.4	26.2	14.3	11.92
<b>% Condom use</b>				
Always	1.1	47.2	50.1	50.4
Often	1.6	22.1	31.6	40.1
<b>Sex worker HIV prevalence</b>				
Total screened	442	607	582	505
Number HIV positive	5	7	28	28
Seroprevalence (95% CI)	1.13% (0.15-2.11)	1.15% (0.3-2.11)	4.81% (3.07-6.55)	5.53% (3.54-7.52)

Summary of discussions

A number of challenges were faced in the implementation of the project.

### Technical challenges

1. There was no proven strategy for STD control in sex workers;
2. There was rapid movement of sex workers from place to place;
3. No strategy was available to address sex workers' casual partners for STD treatment and counselling;
4. There was no availability of screening for asymptomatic subjects;
5. Overall there was a poor rate of treatment compliance.

### Social constraints

The sex worker population was still stigmatized.

### Recommendations for similar interventions

1. The strategy should be based on community participation, sustainability, and replicability;
2. Research questions must be integrated into service delivery;
3. Caution should be taken when presenting longitudinal data because of participation bias and drop-out rates. Higher risk individuals may have dropped out. Analytical approaches to adjust for this should be used.

### 3.7.2 Sex workers and miners project: Lesedi, South Africa

The aim of this project was to reduce the prevalence of curable STDs in a South African mining community through the provision of STD services, including periodic presumptive treatment to women at high risk in order to decrease HIV transmission in both women and men.

#### Intervention components

1. Mobile clinic staffed by a registered nurse and an assistant;
2. Peer educators from the same groups used to recruit women at high risk;
3. Presumptive treatment with azithromycin 1 gram orally at monthly intervals to all women at high risk;
4. Health education especially with respect to STD and HIV and condom promotion;
5. Syndromic management of STD.

#### Evaluation of impact of intervention

1. Changes in STD prevalence among local miners were assessed through comparison of prevalence rates in two cross-sectional samples of miners taken nine months apart;
2. Routine disease surveillance data from mine health facilities were monitored to compare rates among miners in the intervention area to those living farther away;
3. Computer modelling (AVERT) was used to estimate the impact on HIV infection and on cost-savings.

#### Baseline results

- 407 women used the services during the first nine months of the intervention;
- Baseline prevalence of *N. gonorrhoeae* and/or *C. trachomatis* in women was 24.9%, and 9.7% had clinical evidence of genital ulcer. Half the women had one of the above STDs or a reactive syphilis serology.

#### Follow-up results

After 9 months of the intervention:

- STD prevalence decreased significantly among women using the service, although incidence rates remained high;
- Among hostel-based miners in the area, the prevalence of *N. gonorrhoeae* and /or *C. trachomatis* fell from 10.9% at baseline to 6.2% at the 9-month follow-up ( $p < 0.001$ ). The prevalence of genital ulcer by clinical examination dropped from 5.8% at baseline to 1.3% at follow-up ( $p < 0.001$ );
- Rates of symptomatic STDs seen at mine health facilities decreased among miners in the intervention area compared to miners at increased distance with less exposure to the project;

- An estimated 41 HIV infections were averted among women (40% reduction) and 196 (48% reduction) among miners (AVERT model);
- The actual cost of the intervention was 268 000 South African rands (c. US\$ 45 000) annually. The medical costs alone of caring for 196 miners with HIV were estimated at over 2.3 million rands. Based on these projected cost savings, the Mine Company took over the running costs of the project.

**Future plans**

The intervention was expanded in 1997 to cover a population of over 100 000 including 6000 miners living in six hostels. An interim evaluation and further expansion are planned.

**Effect of treatment of reproductive tract infections (RTIs) on vaginal shedding: Johannesburg, South Africa**

**Study population**

A consecutive sample of 57 HIV seropositive women complaining of vaginal discharge attending a STD clinic in Johannesburg was recruited. The women were evaluated for vaginal shedding of HIV following treatment of reproductive tract infections.

**Intervention**

- All the women were assessed clinically, and a full laboratory investigation for STD was conducted;
- HIV virologic studies included plasma viral load (reverse transcriptase-polymerase chain reaction (RT-PCR), HIV vaginal shedding (RT-PCR), CD4 counts;
- Syndromic management for STD was applied;
- Drugs used for management of vaginal discharge were:
  - ciprofloxacin 500 mg single dose;
  - doxycycline 100 mg twice daily for 7 days;
  - metronidazole 400 mg twice daily for 7 days;
  - clotrimazole 200 mg vaginal tablet single dose;
  - valacyclovir 500 mg twice daily for 5 days (if clinically indicated).

**Results**

Table 14 presents the results of the effect of syndromic management on individual infections in HIV-positive women.

*Effect of syndromic management on infections in 57 HIV-infected women in South Africa*

Table 14

Infection	Pretreatment Number positive (%)	Post-treatment Number positive (%)
Bacterial vaginosis	41 (72)	18 (32)
Candida	36 (64)	26 (45)
<i>T. vaginalis</i>	16 (29)	2 (4)
Gonorrhoea (GC)	8 (14)	2 (4)
<i>C. trachomatis</i> (CT)	10 (18)	3 (6)
GC/CT	15 (27)	5 (9)
Herpes simplex virus	5*( 9)	1 (2)

\*4 out of 5 HSV positive cases of cervicitis were treated with valacyclovir in addition to syndromic management of other STDs.

### Summary of findings

1. In this subgroup, vaginal shedding was related to plasma viral load. This association was independent of CD4+ counts;
2. In patients with plasma viral loads <10 000 copies/ml, significantly less vaginal HIV shedding was detected than those with  $\geq$ 10 000 copies/ml (Table 15);
3. Treatment of reproductive tract infections (RTIs) in patients with plasma viral loads  $\geq$  10 000 copies/ml resulted in a 39% reduction in vaginal HIV shedding, compared to 15% in those with loads <10 000 copies/ml (Table 16);
4. In those patients with herpes cervicitis, treatment with valacyclovir resulted in reduction of HIV to undetectable levels (Table 17).

#### *Association of HIV vaginal shedding with plasma HIV viral load at initial visit: South Africa*

Table 15

Initial plasma viral load	n	Median HIV vaginal shedding Copies/ml (range)	Number of patients shedding viral copies	% shedding $\geq$ 400 HIV copies/ml
<10 000	26	138 (0-10237)	4	15%
$\geq$ 10 000	31	1062* (0-67640)	18	58% **
<b>Total</b>	<b>57</b>	<b>216 (0-67640)</b>	<b>22</b>	<b>39%</b>

\*Mann-Whitney test p = 0.001

\*\*X<sup>2</sup> test p = 0.00

#### *Influence of treatment of RTIs on vaginal HIV shedding: South Africa*

Table 16

Initial plasma load RNA copies/ml	Reduction in vaginal HIV RNA shedding	Non-reduction in vaginal HIV RNA shedding	n	% reduced
<10 000	4 (25%)	22	26	15%
$\geq$ 10 000	12 (75%)	19	31	39%
<b>Total</b>	<b>16 (100%)</b>	<b>41</b>	<b>57</b>	

X<sup>2</sup> test p = 0.05

*Effect of valacyclovir treatment on vaginal HIV shedding in herpes cervicitis: South Africa*

Table 17

Case number	CD4+	Mean HIV Plasma RNA Copies/ml	Pretreatment vaginal RNA Copies/ml	Post-treatment vaginal RNA Copies/ml
426	412	21 590	3277	UD*
424	294	89 088	1062	UD
440	49	178 798	858	UD
329	12	407 089	4734	UD
455**	258	178 606	2859	1820

\*UD = undetectable (<400 copies/ml)

\*\*Not treated

**Summary of discussion**

1. It would seem that treatment of RTIs in the phase of high plasma HIV load (early stage of the epidemic) results in greater reduction of vaginal HIV shedding than in the later phases (mature phase).
2. Since new HIV infections are occurring at all stages of the epidemic, especially among the young, their scenario is similar to that seen in Mwanza and, therefore, treatment of RTIs remains an important component in HIV prevention.
3. As the HIV epidemic matures, herpes will constitute a significant proportion of RTIs. Interventions will require specific anti-herpes management to reduce HIV shedding.
4. The AVERT model needs to be modified to incorporate the influence of plasma viral load RTI/HIV dynamics.
5. It is not known how long the effect of the herpes antiviral will last in terms of suppression of viral shedding, but it could be related to the level of immunosuppression.

**3.7.3 HIV and STD incidence in a sex worker cohort in Kenya**

**Background**

The Pumwani sex worker programme was initiated in 1985 as a STD research project pre-AIDS. It is a set up with target groups' participation in the governance. In mid-1985, an HIV infection rate of 60% was recognized. The project has evolved since then to become an intervention to test the sustainability and replication of a sex worker intervention in Nairobi. There is now fairly convincing evidence that STD and HIV transmission have been reduced.

**Evolution of the intervention**

- 1985: individual counselling and condom promotion (little effect), and STD management;
- 1986: peer education and condom distribution;
- 1991: introduction of facilitated groups involved in problem-solving meetings;
- 1991: more aggressive STD diagnosis and management.

## Analysis of programme impact

### Sexual behaviour

Women are surveyed regarding the number of sex partners per day and the percentage of clients using condoms. The mean number of sex partners and mean percentage condom use is shown for each calendar year for the period 1985-1997 (Figures 2 and 3).

### Incidence of STDs

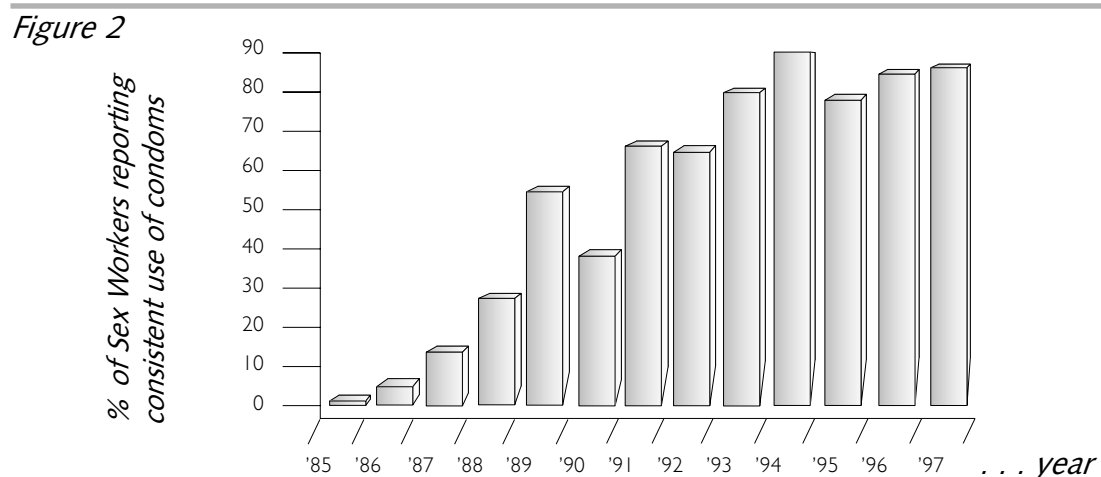
The mean percentage of visits positive for each calendar year was compared from 1985 to 1997 for gonorrhoea and from 1991 to 1997 for chlamydia. HIV-1 sero-incidence during the first 13 months of follow-up of the cohort was compared for each calendar year for the period 1985-1997 (Figures 4-6).

### Results

#### 1. Condom use

The proportion of sex workers self-reporting condom use increased and remained at a high level of over 80% for 5 years. During the period of observation, drops in use were noted and they were related to public misinformation regarding AIDS cures (Figure 2).

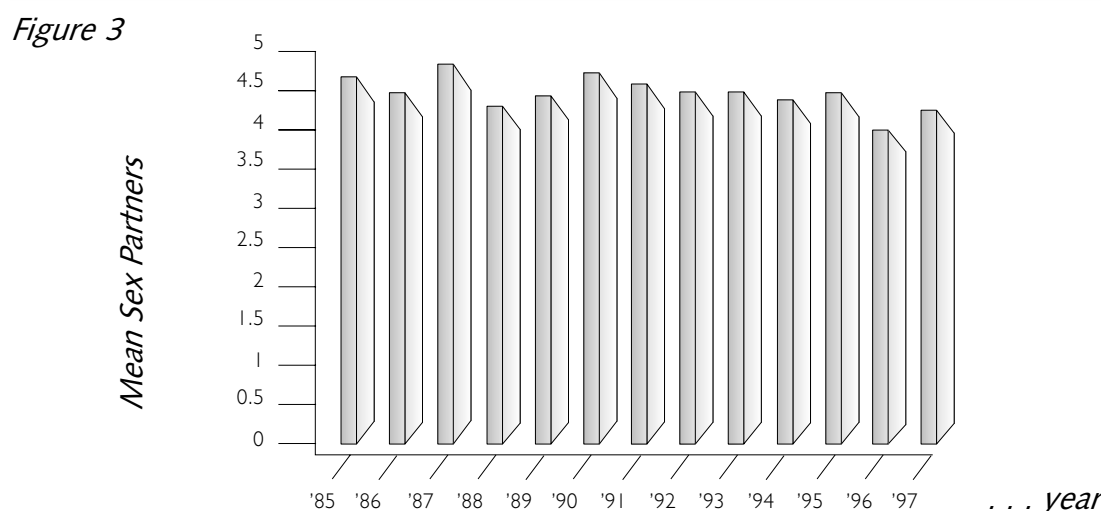
*Impact of the intervention on self-reported condom use*



#### 2. Sex partners

Virtually no change in the number of partners per day over the 12 years was found (Figure 3).

*Average sex partners per day by calendar year*



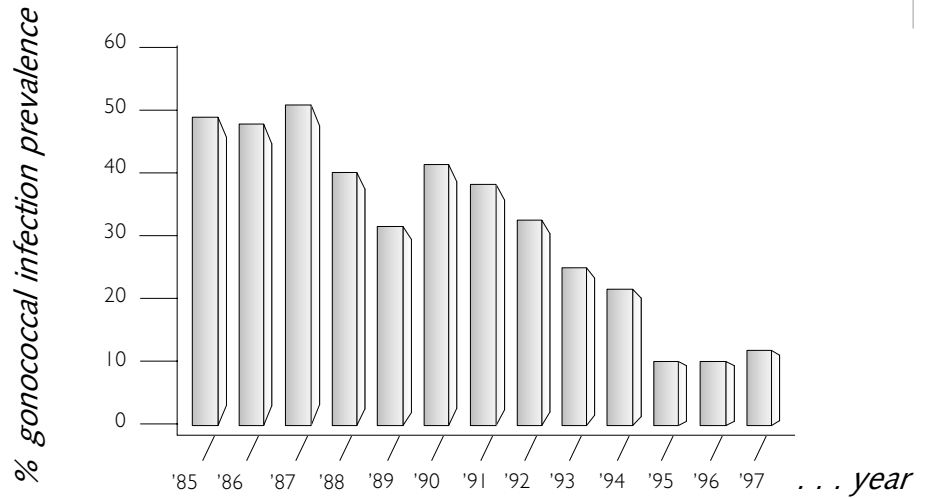


**3. STDs**

The prevalence of gonorrhoea was 50% in 1985 and 10% in 1997 (Figure 4).

*Intervention impact on gonococcal prevalence per visit*

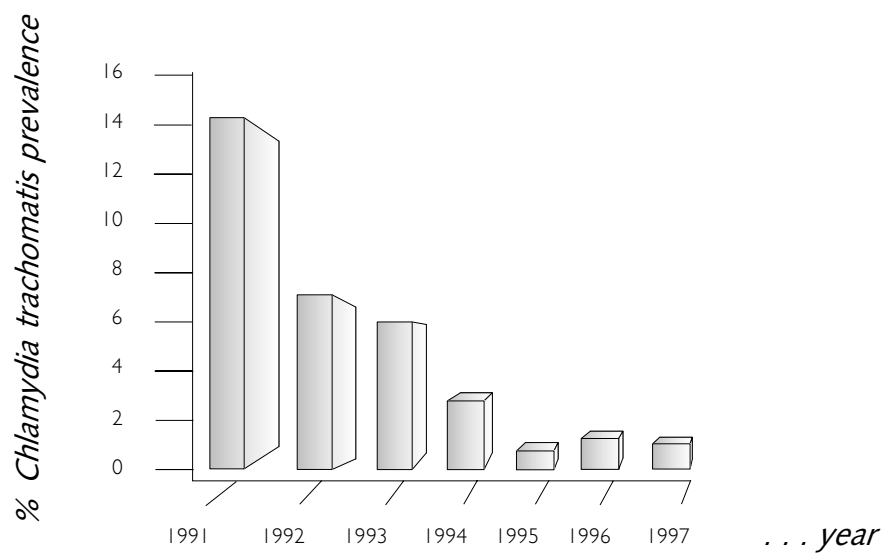
Figure 4



The prevalence of *C. trachomatis* was 14% in 1991 and 1% in 1997 (Figure 5).

*Impact on visit prevalence of Chlamydia trachomatis infection*

Figure 5

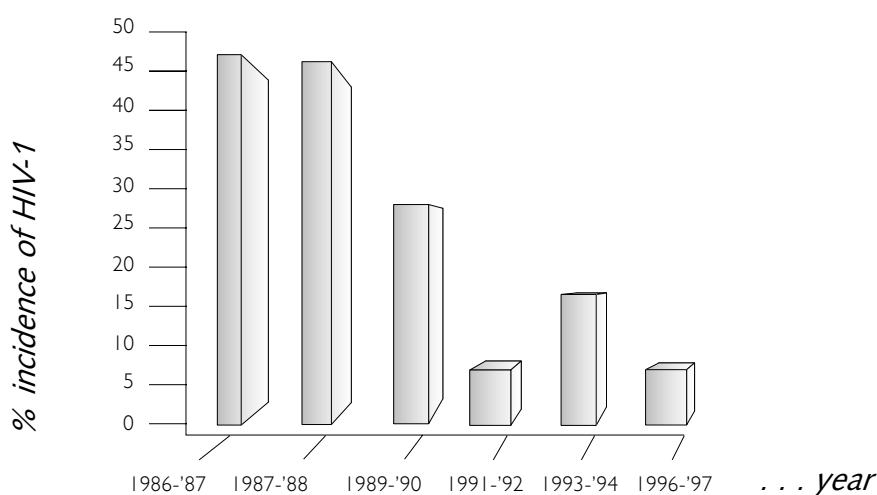


#### 4. HIV infection

HIV-1 sero-incidence during the first 13 months of follow-up of the cohort was compared for each calendar year 1985-1997. The HIV annual incidence was 45% from 1986 to 1987 and 6% from 1996 to 1997 (Figure 6).

*Impact on incidence of HIV-1 in the Pumwani sex worker cohort*

Figure 6



#### Programme replication

- Replication of this intervention model began in 1991;
- Modified intervention comprised community-based sex worker intervention plus strengthened STD management in public clinics;
- The programme now covers 20 health centres serving a catchment population of 1.5 million;
- Training for national replication is in progress;
- No separate services for sex workers and no different algorithms.

#### Other findings

- Changing prevalence of HIV-1 in ANC women, with 9% in 1992, 17% in 1994, 10% in 1996;
- Chancroid has essentially disappeared in Nairobi;
- In the general population, women are reporting fewer partners but no increase in condom use.

#### Constraints

- STD programme is being implemented in a rather erratic health system;
- Underpaid health workers;
- The unreliable drug supply has been a chronic issue, with donors supplying them to date. This is not sustainable;
- Inadequate supervision. Health workers need tools to supervise effectively.

## 4. Programmatic and Policy Issues

### 4.1 STD control for HIV prevention among adolescents

In examining strategies for the control of STD among adolescents, two questions form the basis for their selection:

1. In areas where HIV prevalence is high, will STD prevention and treatment programmes reduce the risk of HIV transmission for adolescents?
2. What priority should be given to STD prevention and treatment programmes for adolescents?

#### STD and HIV among adolescents

STD and HIV contribute major health risks to all sexually active adolescents. In both developed and developing countries, rising trends in the incidence and prevalence of STD/HIV among adolescents present a serious challenge to their health and well-being. Studies in Western countries, for example, have demonstrated that females under the age of 20 years are the population most likely to be infected with *C. trachomatis*. In the USA, the incidence of gonorrhoea declined markedly, but is now highest among 10-14 year olds, after adjusting for sexual activity.

Age- and sex-specific HIV prevalence data are available from sero-sentinel surveillance and several community studies. Globally, infection is not evenly distributed, and currently sub-Saharan Africa is disproportionately affected. Within the region itself, there is also much variation according to the stage of the epidemic. In some countries, the HIV epidemic seems to be levelling off, and as the disease becomes endemic, peak incidence shifts to younger age cohorts. This is diagrammatically represented in Figures 7 and 8. The reasons for this focus of infection in young people are complex, but include biological factors, sexual behaviour patterns and networks, epidemiological transmission dynamics, and treatment-seeking behaviour.

#### **Adolescents run special risks of exposure to STD/HIV:**

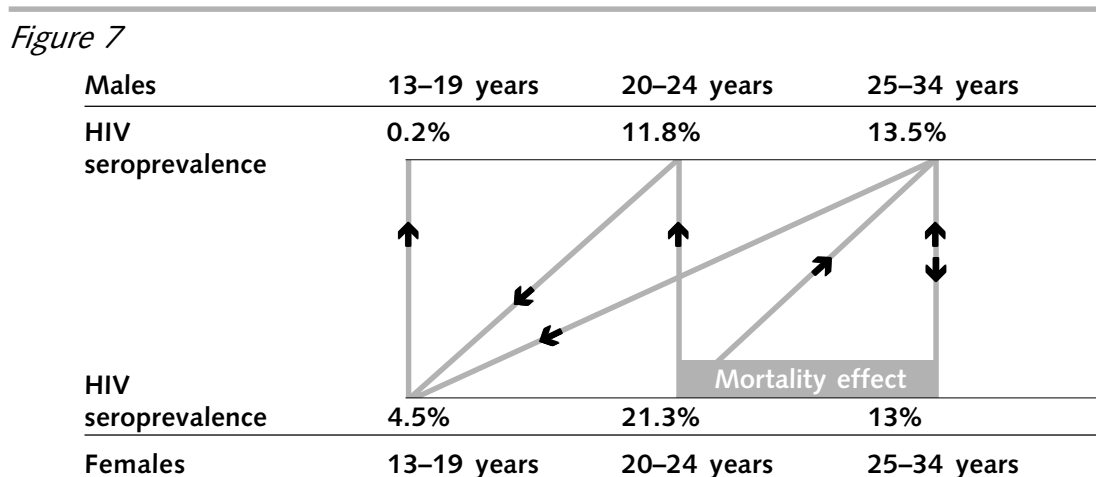
- Adolescents' sexual relations are often unplanned, sporadic and sometimes the result of pressure or force.
- Adolescent experimentation is a normal part of adolescent development. It assists in widening their horizons and in learning about adult roles and the responsibilities that they are likely to take on – it also exposes them to health risks.
- Adolescents' sexual relations typically occur before they have:
  - experience and skills in self-protection;
  - adequate information about STDs and how to avoid contracting these infections;
  - adequate access to services and supplies such as condoms.

#### **Adolescent girls are especially vulnerable:**

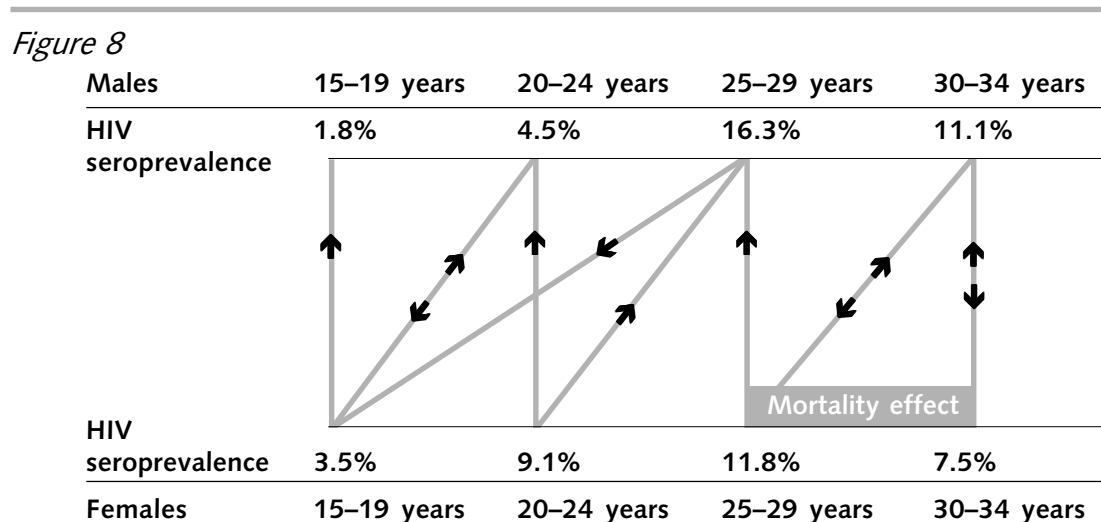
- Their inadequate mucosal defence mechanism and the immature lining of the cervix provide a poor barrier against infection;
- Young girls are more vulnerable than young men and adults for both social and economic reasons.

The diagrammatic presentation shows that younger girls seem to become infected from older males. As the younger girls become older, their sexual networks tend to be more of their age group and thus reverse the direction of infection. The mortality effect reduces the prevalence of HIV in the older females at the end of the scale.

*Model showing the main direction of HIV infection between partners of different ages: Uganda*



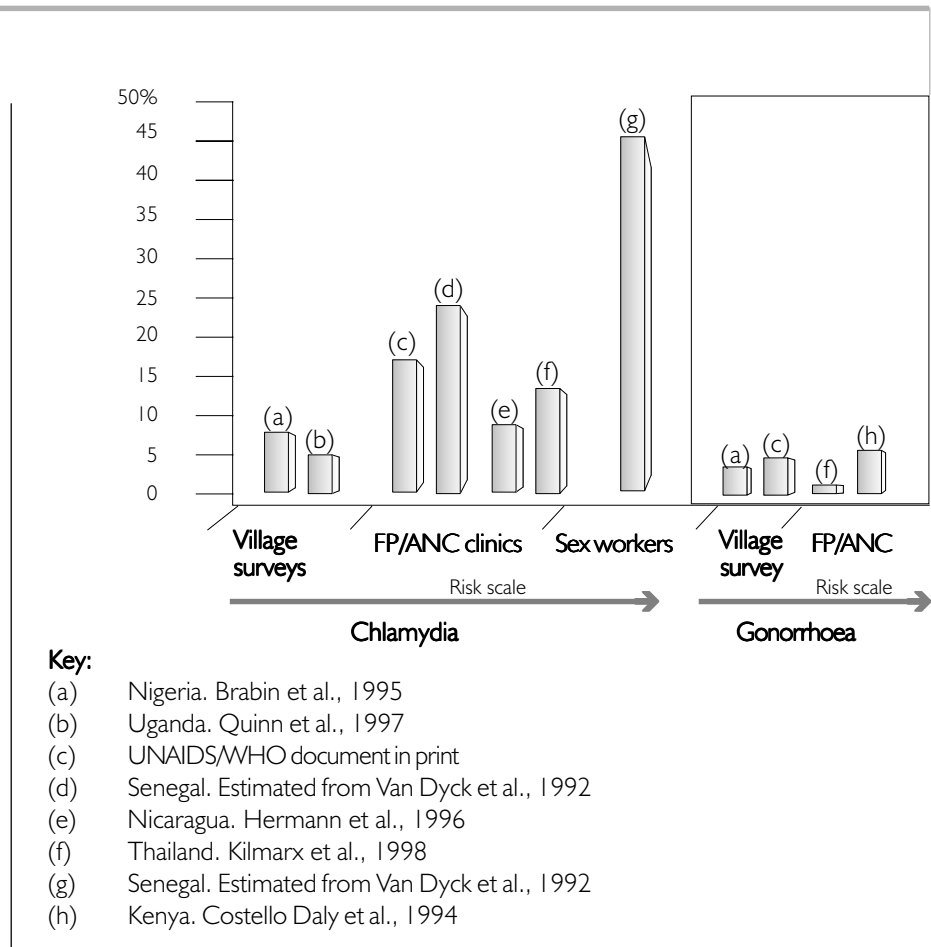
*Model showing the main direction of HIV infection between partners of different ages: Ethiopia*



Very little age- and sex-specific data are available for other STDs. A summary of the prevalence data for chlamydia and gonorrhoea in sexually active adolescent females is shown in Figure 9. What is striking is the very limited number of studies identified which report on chlamydia and gonorrhoea as separate infections in the age group of persons under 20 years.

*Prevalence of chlamydia and gonorrhoea in sexually active females < 20 years*

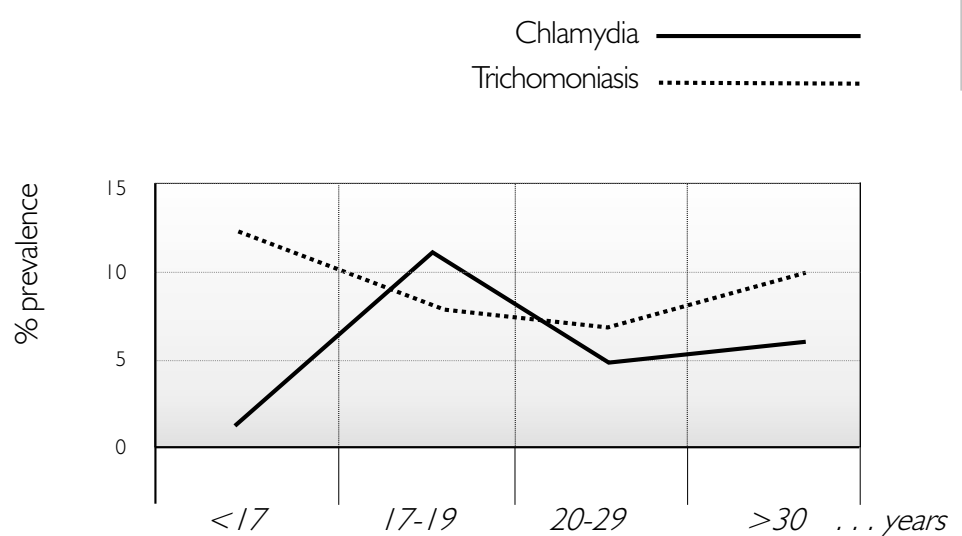
Figure 9



The prevalence data in Figure 9 are indicative of what is likely to be the pattern of chlamydia and gonococcal infection in adolescents in many countries. Prevalence is higher in subpopulations who are in regular sexual relationships, for example those who are pregnant or using non-barrier contraceptives or in sex work, compared to the general adolescent population.

*Prevalence of STIs in rural Nigerian females by age*

Figure 10



A rural population-based study in Nigeria remains one of the only studies from sub-Saharan Africa to have reported on several STDs by age. Chlamydia and trichomoniasis were the 'fections most commonly found. Chlamydia was most often detected in sexually active adolescents aged 17-19 years, and in line with many studies from developed countries, prevalence declined with increasing age. Without a doubt, chlamydia can be characterized as an adolescent infection. Prevalence of trichomoniasis in sexually active adolescent females was comparable to that found in older women. Its appearance in young adolescents who had only recently become sexually active suggested it might be a good marker of recent onset of sexual activity (Figure 10).

### **Preventing HIV infection in adolescents**

Strategies to prevent HIV infection in adolescents must be directed at:

- Strengthening the diagnosis and management of STDs among men and women in older age groups and among adolescents;
- Improving the quality and expanding the coverage of actions aimed at preventing HIV/STD transmission in adolescents (both from adults to adolescents and among adolescents).

### **What needs to be done**

Actions are needed in several different areas to improve the effectiveness of HIV/STD prevention activities directed at young people:

- More and better sustainable communication programmes are essential.
- Communication programmes should be linked to condom provision.
- HIV/STD prevention programmes should collaborate and, where appropriate, integrate with other relevant prevention programmes (for example those involved in teenage pregnancy prevention programmes).
- HIV/STD prevention programmes should tackle social, cultural and economic factors that fuel the transmission of STDs.
- Health facilities must be made more 'youth friendly'.
- Health workers need guidance and support to meet the needs of their younger patients more effectively and with greater sensitivity.

### **Challenges to STD diagnosis in adolescents**

- The STD may be asymptomatic in females.
- Adolescents may not be aware of the differences between normal and abnormal conditions (such as genital discharges) and hence do not seek advice and care.
- Adolescents often lack information about existing services (e.g. how to gain access, at what times the services operate, how much they cost or whether or not they are confidential).
- Even if adolescents know about services, they are often reluctant to seek help for diagnosis and treatment. This is due both to embarrassment and the possible associated stigma; they fear being seen as they wait to use STD services. They also fear negative reactions from health workers and lack of confidentiality.
- As adolescents often delay seeking services and the symptoms of some STDs disappear in time, they may believe that the disease has disappeared.
- Asymptomatic and mildly symptomatic STDs may be missed if health workers do not have adequate skills to undertake clinical examination or to elicit necessary information from adolescents, who are often not knowledgeable about their bodies.

**The constraints on effective treatment of STDs in adolescents:**

- There is often reluctance on the part of adolescents to use services (as above).
- Adolescents tend not to use services or medication because of inadequate information, access or money.
- Adolescents often have difficulty in complying with treatment because it may be lengthy (as in the case of chlamydia) or painful (as in the case of venereal warts), and sometimes there is a need to conceal medication so that the STD is not revealed to others.

**Different needs**

It is essential to remember that young people are a very heterogeneous group with different needs for health information and services, depending on their stage of development and their circumstances. Each of the following groups of young people has different needs:

- young people who are not yet sexually active;
- young people who are only occasionally sexually active;
- young people who are sexually active on a regular basis;
- young people who have health problems resulting from sexual activity (such as a STD or an unwanted pregnancy);
- young people who have been sexually abused.

The challenge is to set up a service that responds to these differing and evolving needs.

**Different strategies**

There is no 'single best' approach to reaching young people with the health information and services they need. An approach, such as a 'drop-in' youth centre, which serves a useful purpose in one setting, may not be successful in another setting for a variety of reasons. Even within the same setting, two or more approaches may be needed to reach different segments of the population group (for instance older and younger adolescents, male and female adolescents) and subgroups within the population (such as street youth).

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## **4.2 Summary of current strategies for STD control**

The current strategy for the prevention of sexual transmission of HIV has two components:

1. Promotion of adoption of safer sexual practices;
2. Reduction of incidence of curable STDs.

To implement STD prevention and care, five elements have been identified. They include:

- assessment;
- advocacy;
- strengthening STD activities;
- integration of STD prevention and care;
- Evaluation of interventions.

## Assessment

Assessment of the epidemiological situation and incorporation of the basic elements for prevention and care lead to an analysis of the gaps that exist, which, in turn, forms the basis for planning and execution of STD/HIV prevention programmes. The assessment will answer these questions:

1. Which populations are affected?
2. What are the main syndromes?
3. Where is care being provided?
4. What are the prevention and care activities currently in place?

Once an assessment is complete, organization of a response begins, taking into account horizontal execution and involvement of multiple partners.

## Advocacy

Advocacy for the inclusion of STD in the health care agenda should involve targeting politicians, decision-makers, donors and the communities themselves.

## Strengthening of STD activities

The following are the areas for strengthening STD activities: programme management, technical guidelines, access to STD drugs, laboratories, condom availability, training, planning and surveillance.

## Integration of STD prevention and care

Primary prevention includes the following components: integrated STD/HIV/AIDS health promotion, promotion of health care-seeking behaviour, antenatal care and condom provision. Care (for STDs) comprises the adaptation of flowcharts for management, syndromic management of symptomatic patients, care in public, private and informal sectors, targeting vulnerable populations, screening for asymptomatic patients, and provision of services for sexual partners.

## Evaluation of the interventions

This involves the development of indicators, monitoring, and evaluation of the interventions.

## Programmatic needs for implementation

- **Policy decision:** this refers to policies implemented mainly at the national level. In many settings, there are no policies, and where they do exist, they are often not adhered to.
- **Guidelines:** to guide practices, guidelines should be technically sound and should be reviewed frequently and revised when necessary.
- **Resources:** most successful programmes seen in industrialized countries operate with massive resources.
- **Training:** health care providers should receive basic training and have refresher courses.
- **Supervision:** health care providers should be supervised, especially in settings where they do not see many patients.
- **Consistent drug supplies:** often overlooked, drugs must be made available at all times.
- **Facility-based counselling/education:** this is an essential component and must include partner notification, compliance, condom use and risk reduction.



- **Implementation of strategies:** often insufficient attention has been paid to supportive activities that would ensure successful implementation of strategies.

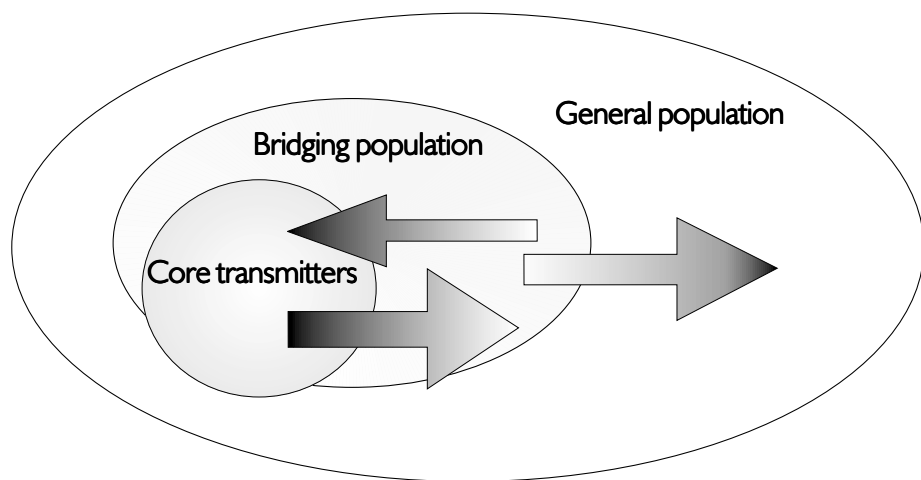
### 4.3 Public health approaches to STD prevention and care: Challenges, issues and opportunities

#### STD transmission dynamics

Figure 11 demonstrates the transmission dynamics of STDs in the general population. It shows those likely to transmit infection more frequently at the centre (*core transmitters*) and a *bridging population* between the core transmitters and the general population.

*STD transmission dynamics at population level*

Figure 11



#### Issues in case management

Issues in case management include:

- large number of asymptomatic infections especially in women;
- stigmatization and taboos;
- inadequate health care-seeking behaviour;
- lack of simple, rapid, cheap diagnostic tests for STDs;
- potential for blaming and violence;
- unavailability of effective drugs;
- counselling and communication.

#### Elements of STD control

For successful and sustained control of STD, the following three areas must be addressed:

##### 1. Primary prevention

This must include:

- reduction of number of partners;
- safer sex (including barrier use).

In primary prevention, there is a need to focus on youth, adolescents and women. Community awareness creation and destigmatization are key ingredients in primary prevention. It is also necessary to focus on behavioural change in high-

frequency transmitters (core transmitters), as well as on safer sex and promoting health care-seeking behaviour. Behavioural change and services for bridging populations are similarly important.

## 2. Case management

Diagnosis and treatment of symptomatic and asymptomatic infections are the key to case management. This should include those likely to perpetuate continuation of transmission (core transmitters and bridging populations) and those with the highest burden of complications (women, mostly asymptomatic), as well as adequate services for the general population.

## 3. Information, education and communication

IEC must be enhanced. Compliance with treatment, as well as partner notification, condom promotion, STD counselling and risk reduction should be included.

### Case management options

#### *Symptomatic infections*

In order to manage symptomatic infections, the syndromic approach and etiologic diagnosis and treatment must be considered.

#### *Asymptomatic infections*

It has become evident over the years that asymptomatic infections are more prevalent than previously thought. Strategies to deal with asymptomatic STDs include some form of screening or case-finding, and enhanced partner management services. Current research findings suggest that mass treatment in the general population has limited success and is not a recommended option. However, selective mass treatment<sup>1</sup> in specific population groups (periodic presumptive treatment), together with quality STD services for the general public, may be an option. Further research in this area is needed.

### Public health options

Public health options must consider both male and female core transmitters and women in the general population.

#### 1. Core transmitters (sex workers and their clients etc.)

- behaviour change, community development;
- periodic presumptive (mass) treatment;
- screening (generally not feasible);
- syndromic approach case management (in combination with risk assessment);
- service delivery needs (special clinics, timing, etc).

#### 2. Core transmitters (bridging population - clients of sex workers, long distance truck drivers, etc.)

- behaviour change including health care-seeking behaviour;
- syndromic approach case management;
- integrated service delivery (public and private sector);
- alternative service delivery options (pharmacies, drugs stores, etc).

#### 3. Women (general population)

- raise awareness of risks and promote health care-seeking behaviour;

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<sup>1</sup>Selective mass treatment is the application of epidemiological treatment, without examination or interview, to higher risk subpopulations such as sex workers, migrant workers, or military. The goal is coverage of all susceptible individuals within the subpopulation.

- syndromic approach for symptomatic vaginitis, genital ulcer disease and pelvic inflammatory disease (PID);
- integrated service delivery (mother and child health/family planning (FP), PHC);
- risk assessment/self assessment;
- selective laboratory screening;
- presumptive treatment.

### Policy decisions

It is important to decide on appropriate policy and plan accordingly. Policy decisions must be based on STD prevalence and incidence, dynamics of transmission, and resource availability (financial, human, infrastructure).

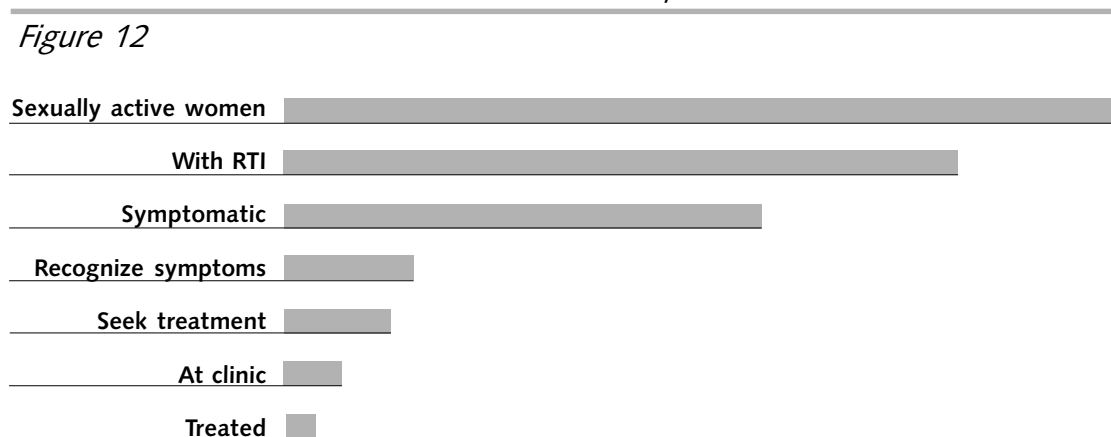
## 4.4 Reproductive tract infections (RTIs) in women

RTIs encompass three main groups of infection, particularly in women, and sometimes in men. These groups are:

- *Endogenous infections* of the female genital tract, such as candidiasis and bacterial vaginosis;
- *STDs* in both men and women;
- *Iatrogenic infections* which may be acquired through unsterile medical procedures or personal hygiene and cultural practices.

Symptom recognition, seeking treatment, partner referral and diagnosis (risk assessment) are necessary to improve the cure rate of women with RTI (Fig.12).

*Operational model for RTIs in women*



## 5. Recommendations

### 5.1 Introduction

STD detection and treatment should be essential components of HIV prevention programmes. To have maximal impact on HIV incidence, a combination of primary prevention and effective case management of STDs is required. It is also necessary to:

1. Improve access to quality STD clinical services;
2. Promote early and effective health care-seeking behaviour;
3. Establish surveillance systems to monitor STD and HIV trends, as well as their interaction, including the implementation of :
  - integrated/vertical surveillance systems;
  - prevalence studies;
  - incidence reporting;
  - monitoring etiology;
  - monitoring resistance.

To improve STD services, any service delivery programme should take into account the mix of public and private sector providers, and seek to involve both sectors to the extent possible and feasible. Particular attention should be paid to basic training, refresher training and supervision of service providers, to ensuring an uninterrupted supply of effective drugs, and to the attitudes of health care workers towards clients with STDs.

## 5.2 Evidence-based decisions for programming

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In order to facilitate and standardize decision-making based on evidence from field research, it is suggested that a rating system be used. One such system (based on that prescribed in the United States Preventive Services Task Force guidelines for the prevention of opportunistic infections), categorizes and weighs the quality of evidence supporting the recommendation on a scale of I-III and defines the strength of each recommendation from A-E as shown below.

**Rating system for the quality of evidence supporting recommendation for implementation**  
(based on US Preventive Services Task Force (USPHS/IDSA) guidelines for the prevention of opportunistic infections)

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The quality of evidence supporting the recommendation:

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<i>Category</i>	<i>Definition</i>
I	Evidence from at least one properly randomized controlled trial.
II	Evidence from at least one well-designed clinical trial without randomization, from cohort or case-control studies (preferably from more than one centre), from multiple time-series studies, or from dramatic results of uncontrolled experiments.
III	Evidence from opinions of respected authorities, based on clinical experience, descriptive studies, or reports of expert committees.

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The strength of each recommendation:

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<i>Category</i>	<i>Definition</i>
A	Both strong evidence for efficacy and substantial clinical benefit support recommendation for use; should always be offered.
B	Moderate evidence for efficacy – or strong evidence for efficacy, but only limited clinical benefit – supports recommendation for use; should generally be offered.

- C Evidence for efficacy is insufficient to support a recommendation for or against use, or evidence for efficacy may not outweigh adverse consequences such as cost of the approach; optional.
- D Moderate evidence for lack of efficacy or for adverse outcome supports a recommendation against use; should generally not be offered.
- E Good evidence for lack of efficacy or for adverse outcome supports a recommendation against use; should never be offered.

Thus, for example, findings from a piece of research with 'category IA' would be regarded as having high-quality scientific evidence. They would be strongly recommended for implementation in any programme and should always be offered.

### 5.3 Recommendations and their ratings for programmes

- ***STD control, including STD prevention and effective case management, is an essential component of HIV prevention and control programmes.***

Quality/strength: I/A

Evidence supporting this recommendation includes the results of a randomized community trial (Mwanza) that found that in communities receiving enhanced syndromic management of symptomatic STD cases, HIV incidence declined by almost 38% compared with communities receiving usual STD management. For that trial, key elements of STD control included syndromic case management based on etiologic assessment of prevalent STDs; the training of care providers in the appropriate use of syndromic algorithms; continuous supervision; an effective drug supply; and community-wide education about symptom recognition and available health care.

Results from several cohort studies noting associations between HIV acquisition and prior infection with specific STDs, particularly ulcerative infections, but also non-ulcerative ones, provide additional evidence supporting STD control for HIV prevention. In addition, numerous biological studies of HIV infected individuals have reported increased HIV genital shedding in the presence of ulcerative and non-ulcerative STDs.

Based on this evidence, case management of STDs should include, at a minimum, syndromic management of genital ulcer disease in men and women, urethral discharge in men, and vaginitis in women with vaginal discharge. Approaches to syndromic case management should take into account the local etiologies of these syndromes and the dynamic nature of STD prevalence in communities. Preferably, this would include routine periodic assessment of etiologies of prevalent STDs through the use of diagnostic tests. Decisions to include treatment for cervicitis in the management of vaginal discharge could be based on the local prevalence of *N. gonorrhoeae* and *C. trachomatis* infections. Studies assessing the efficacy of syndromic algorithms in various locations suggest that locally validated approaches to risk assessment, self-identification of risk, or use of additional symptoms and signs (e.g. swab of vaginal secretions to assess purulence) may be useful in identifying women with cervicitis. The international community, together with countries with relevant data, should develop guidelines and decision-making tools for country-specific strategies for the management of cervicitis in women with vaginal discharge.

Primary prevention strategies, focusing on reducing individual and population risk, consist of interventions aimed at reducing the number of sexual partners and on the promotion of safer sex practices, including the use of barriers such as the male or female condom. These strategies are identical to those developed and implemented for the primary prevention of sexually transmitted HIV infection and should thus be implemented as integrated HIV/STD prevention programmes.

- ***Effective STD and HIV prevention strategies include promotion of male latex condoms, skills building demonstrations aimed at correct condom use, and interactive individual or small group counselling aimed at reducing high-risk behaviours associated with HIV and other STDs.***

Quality/strength: II/A
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Prospective studies of HIV-discordant couples have consistently shown a strong protective effect of the male latex condom, when consistently used, against HIV. Condom efficacy against other STDs is less well studied. However, some prospective studies have found consistent condom use to be protective against gonorrhoea, chlamydia, and genital ulcer disease. Other mechanical (e.g. female condom, diaphragm) and chemical barriers (e.g. microbicides) have been less well studied. At least two well-conducted prospective studies of the microbicide nonoxynol-9 (N-9) found this agent to be protective against gonorrhoea and chlamydia.

Several studies, including some randomized trials, support the view that condom promotion at the population level and individual level can increase condom use. Observational studies from industrialized and non-industrialized nations have found that well-conducted condom promotion campaigns in general population settings were associated with increased condom use and, in some cases where this could be estimated, reduction in HIV incidence. Results from three small randomized controlled trials conducted among STD patients attending public clinics in the USA found that men who observed either an in-person or video demonstration illustrating specific steps to correct condom use had significantly fewer new STDs than those who were simply given condoms. In addition, two large multi-centre randomized controlled trials, and a smaller single-site trial, conducted among HIV-negative patients who attended publicly-funded STD clinics in the USA, have reported promising findings regarding efficacy of risk reduction counselling. In these trials, HIV-negative individuals assigned to personalized counselling interventions aimed at risk reduction (individual counselling for one trial and small group sessions for two of the trials) had significantly higher condom use and, in the two studies that measured this prospectively, significantly fewer new STDs compared with clients who received information alone. In one of these studies, a brief two-session individual counselling intervention had higher participant acceptance and was as effective in reducing new STDs as a longer four-session intervention. A randomized trial evaluating a brief HIV prevention counselling strategy modelled on this was also conducted in Kenya, the United Republic of Tanzania, and Trinidad. Reports of preliminary results indicate that the counselling approach was acceptable and achievable in resource-poor settings, and that persons assigned to the brief two-session interactive counselling sessions reported less risky behaviours. Although STD and HIV outcomes were collected as part of this trial, the results have not yet been reported.

- ***Antenatal screening of women for syphilis and, where feasible, cervicitis, is recommended.***

Quality/strength: II/A
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Although its role in HIV prevention remains uncertain, antenatal screening for syphilis and, where feasible, cervicitis, has been shown to decrease the incidence of complications of

pregnancy such as stillbirth, low birth weight, and premature rupture of membranes. Effective antenatal screening assumes appropriate treatment of asymptomatic women and presumptive treatment of their sex partners. In general, the Informal Consultation recommended that screening of pregnant women for syphilis, and treatment of all sero-reactive women and their partners, be implemented.

- ***Mass treatment of STDs as a strategy for HIV prevention is not recommended in general population settings.***

Quality/strength: I/A
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Results from a well-conducted randomized community trial in Rakai, Uganda, indicate that intermittent mass treatment as a means of STD control is probably not effective in decreasing HIV incidence in general population settings. While strong evidence supporting mass treatment for STDs among selected subgroups at high risk for HIV and other STDs is lacking, the role of such selective mass therapy, as a complement to continuous STD services, needs further exploration.

- ***Case management should include the identification and treatment of symptomatic and asymptomatic infections, in combination with facility-based counseling and education for prevention, treatment compliance, partner notification and promotion of condoms.***

Approaches to identification and management of infected individuals are syndromic or etiologic management of symptomatic patients, screening, and case-finding to detect symptomatic and/or asymptomatic individuals.

- ***Both primary prevention and case management strategies can be targeted at the general population and/or specific subgroups based on the estimated or confirmed prevalence of STDs and risk behaviours in these groups.***

To guide decisions with regard to the appropriate mix of intervention strategies, all HIV prevention and care programmes should assess the prevalence of STDs and of risk behaviours in sentinel populations. Examples of such populations are urban and rural antenatal or family planning clinic attendees, adolescents and sex workers, among others. To determine the etiologic spectrum of STDs, patients seeking care for STDs are a convenient sample. An understanding of the dynamics of STD transmission in a population and the importance of individuals with high rates of partner change is essential for rational decisions with regard to the allocation of scarce resources.

Various models and intervention studies have confirmed the importance of individuals with high rates of partner change and high rates of STD in maintaining STD and HIV epidemics. Typically, infections spread from these individuals to those with lower rates of partner change who, although vulnerable to infection, are themselves less likely to further transmit the infection. From the perspective of controlling STD in a community, interventions targeting high-frequency transmitters are likely to be more cost-effective than those interventions targeting the general population of individuals with little or no partner change. Yet, from the perspective of individual case management and to ensure credibility of service delivery systems, at the very minimum, services to treat symptomatic infections in both men and women should be made available. Services addressing symptomatic infections in women are not yet readily available in many countries. In addition, little attention has been given to improving the quality of services for men, which, although often available, are usually of poor quality.

- **STD control for prevention of HIV for specific groups.**

1. *Biological and epidemiological evidence*

There is sufficient evidence that interventions targeting specific groups in the population can have significant impact. To guide decisions in the planning and implementation of the interventions, assessments are required to determine the prevalence of various STD syndromes and risk behaviours.

2. *Core groups or high-frequency transmitters*

Various models and intervention studies have shown that individuals with high partner change rates and high rates of STD infection are important in the spread of both STDs and HIV to individuals who are at lower risk. Interventions that target this group are likely to have a major impact and can be cost-effective.

3. *Prioritization of options for STD interventions*

STD interventions should encompass the adaptation of the epidemiological situation and the health services in the community, community participation, and advocacy to ensure the community understands the nature of the interventions. The various groups that could be targeted in the community would include commercial sex workers, men who have sex with men, injecting drug users, migrant workers, transport workers and STD patients. STD syndromic management should be the *standard of care at the minimum*. The strategies should include: increasing STD awareness and improving health care-seeking behaviour, providing effective STD case management, and integrating STD services with other services so as to increase acceptability and accessibility.

## 6. Research Needs

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The need for further research on various aspects of STD diagnosis, treatment, prevention and care were highlighted throughout the consultation. The Informal Consultation has recommended that further research be conducted in the following areas: biology of STDs and their interaction with HIV, case management, screening and case-finding, and the implementation of STD prevention and care programmes.

### 6.1 Biological and sociocultural research

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There is a need to assess the protective effect of nonoxynol-9 (N-9) or other chemical barriers against HIV infection.

The role of asymptomatic STDs in HIV transmission also remains unclear, as does the role of other RTIs, for example bacterial vaginosis. Thus, further research is needed regarding the role and natural history of herpes simplex virus (HSV), bacterial vaginosis, serologic syphilis and genital candidiasis in HIV-positive and HIV-negative persons. Genital HIV shedding in symptomatic and asymptomatic persons has not been well documented and merits further research.

Several observations have been made with regard to the effect of **male circumcision** on HIV transmission. The quantification of a potential benefit that could be expected from



male circumcision as protection against HIV transmission is highly problematic. Studies conducted have pointed out four potential explanations as to why circumcised males may be more or less likely to acquire HIV/STD, including:

1. Exposed glans penis may develop a protective layer of keratin;
2. The foreskin may be especially susceptible to minor balanitis and trauma during intercourse, allowing movement of HIV through dermatologic intercourse;
3. Warm microclimate under the foreskin may permit microorganism survival, increasing exposure to potential infections;
4. Lack of circumcision may predispose to a co-infection with other STDs known to facilitate heterosexual HIV-1 transmission.

However, another study published in 1999 (*International Journal of STD and AIDS*) concluded that it would be incorrect to assert that circumcision prevents HIV transmission. Nevertheless, the association between male circumcision and HIV/STD transmission remains unclear and further research in this area is necessary before clear recommendations can be made.

Data regarding the effect of **female genital mutilation** (FGM) on the transmission of STD/HIV have not been well documented. A study reported in the *International Journal of Gynaecology and Obstetrics* identified the following risk factors for HIV infection related to FGM:

- Increased risk of inflammation and bleeding during coitus, leading to greater exposure to blood, which may enhance risk of infection;
- Abrasions may occur when attempting penetration;
- Greater risk of haemorrhage in childbirth, leading to an increased chance of receiving a blood transfusion and to greater risk of infection as universal blood supply screening has not been globally achieved;
- Use of unsterilized instruments in the performance of FGM;
- Increased anal intercourse when vaginal penetration is painful and difficult.

Further research in this area is needed.

## 6.2 STD case management research

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There is a need to develop new diagnostic tests for vaginal discharge and genital ulcers with greater sensitivity and specificity. The impact of guidelines and training materials, as well as of the training itself, must be evaluated and improved. How and when to adapt flowcharts to particular local contexts also needs to be determined.

The determinants of sexual behaviour among adolescents and of their health care-seeking behaviour must be adequately assessed, and this information must be utilized to improve services for young people. This is particularly important given the proportion of STDs occurring in those below the age of 25 years. In addition, research needs to be conducted on how to train health care providers working with adolescents to assure youth-friendly services.

## 6.3 Screening and case-finding research

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Appropriate screening criteria need to be identified. Field-testing of rapid diagnostics should take place in order to assess the effects of different screening and diagnostic approaches, and thus improve currently available services.

## 6.4 Research on the implementation of STD prevention and care

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Research needs in the implementation of STD prevention and care are many, and include areas such as:

- reduction of STD morbidity in women;
- health systems research on scaling-up interventions;
- collaboration with private sector, pharmacies and other relevant care givers;
- drug pricing, procurement and supply;
- trials of combined strategies: single mass treatment, selective periodic presumptive treatment, syndromic treatment;
- impact of different strategies in different population settings;
- measuring the effect of targeting regarding stigma;
- role of community in implementation and evaluation;
- advocacy for community ownership;
- prioritization of activities.

## 7. Conclusions

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On the basis of the collective evidence reviewed in this report, the Consultation considers that STD management continues to be an essential component of HIV prevention programmes and should continue to be a key component for AIDS control programmes, especially in areas where STDs are highly prevalent. There are sufficient scientific data pointing to the importance of STD control and the impact this can have on HIV transmission. Although it has been suggested that impact often depends on the epidemiology of STDs in the community and the stage of the HIV epidemic, studies from Kenya and other sites show that even in mature epidemics, interventions can have a significant impact.

Although further research is needed in many areas, in particular to address the role of asymptomatic STDs and to investigate operational aspects of STD interventions, the Consultation urges policy-makers not to hesitate in implementing STD control wherever possible. Emphasis should be given to interventions in persons with sexual behaviour likely to put them at higher risk of acquiring STDs, and to the improvement of STD services in the general population. Despite the need for further research, selective mass treatment for STD may still be an option for STD control under certain conditions, targeted towards people with high-risk sexual behaviour.

# Annex 1

## Common Usage of Different STD Control Strategies

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### **Mass STD treatment**

This is the application of epidemiological treatment, without examination or interview, to general populations based on high overall community prevalence. The goal is coverage of all susceptible individuals.

### **Selective mass treatment**

Selective mass treatment is the application of epidemiological treatment, without examination or interview, to higher-risk subpopulations such as sex workers, migrant workers, or military. The goal is coverage of all susceptible individuals within the sub-population.

### **Epidemiological treatment**

Epidemiological treatment is the presumptive treatment of individuals or populations with a high likelihood of having disease based on behavioural, clinical or epidemiological evidence.

### **Case management**

STD case management is the care of a person with a STD-related syndrome or with a positive test for one or more STD. The components of case management include: history; examination; correct diagnosis; early and effective treatment; advice on sexual behaviour; condoms; partner notification; case reporting; and clinical follow-up where appropriate.

# Annex 2

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## Annex 3

### Related Articles

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# Notes

Notes

The Joint United Nations Programme on HIV/AIDS (UNAIDS) is the leading advocate for global action on HIV/AIDS. It brings together seven UN agencies in a common effort to fight the epidemic: the United Nations Children's Fund (UNICEF), the United Nations Development Programme (UNDP), the United Nations Population Fund (UNFPA), the United Nations International Drug Control Programme (UNDCP), the United Nations Educational, Scientific and Cultural Organization (UNESCO), the World Health Organization (WHO) and the World Bank.

UNAIDS both mobilizes the responses to the epidemic of its seven cosponsoring organizations and supplements these efforts with special initiatives. Its purpose is to lead and assist an expansion of the international response to HIV on all fronts: medical, public health, social, economic, cultural, political and human rights. UNAIDS works with a broad range of partners – governmental and NGO, business, scientific and lay – to share knowledge, skills and best practice across boundaries.



Joint United Nations Programme on HIV/AIDS

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