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Improved treatment services significantly reduce the prevalence of sexually transmitted diseases in rural Tanzania: results of a randomized controlled trial

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Objective: To evaluate the impact of improved case management for sexually transmitted diseases (STD) at the primary health care level on the incidence and prevalence of STD.

Design: Community-randomized controlled trial.

Setting: Mwanza region, Tanzania.

Subjects: A random cohort of about 1000 adults aged 15–54 years from each of 12 communities, in six matched pairs. One member of each pair was assigned at random to receive the intervention, and the others served as a comparison community. This cohort was surveyed at baseline and at follow-up 2 years later. About 100 antenatal clinic attenders were also studied in each community on two occasions: the first shortly after the implementation of the intervention, and the second approximately 1 year later.

Intervention: Improved services were established for the management of STD, using the syndromic approach, in rural health units.

Results: A total of 12 534 individuals were enrolled in the cohort study, of whom 8844 (71%) were seen again 2 years later. The prevalence of serological syphilis (rapid plasma reagin titre ≥1:8, *Treponema pallidum* haemagglutinin assay positive) was 6.2% in both intervention and comparison communities at baseline. At follow-up it was 5.0% in the intervention community and 7.0% in the comparison community [adjusted relative risk (RR), 0.71; 95% confidence interval (CI), 0.54–0.93; $P < 0.02$]. The prevalence of urethritis in males did not differ significantly between intervention and comparison groups at follow-up, but the prevalence of symptomatic urethritis was reduced by about 50% (adjusted RR, 0.51; 95% CI, 0.24–1.10; $P = 0.08$). There was no significant difference between the groups in the incidence of self-reported STD symptoms over the last year of the follow-up period, or in the prevalence of any STD in antenatal clinic attenders.

Conclusion: The reduction in HIV incidence previously reported in this intervention study can be attributed to a reduction in the duration, and hence the prevalence of symptomatic STD.

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Key words: Sexually transmitted diseases, syndromic management, Africa, impact evaluation

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Introduction

Sexually transmitted diseases (STD) are among the most common presenting complaints at health facilities in sub-Saharan Africa accounting for, in some clinics, more than 10% of adult attenders [1,2]. Unfortunately in many countries they have been accorded low priority, so that health workers are not well trained in their management and are not supplied with appropriate drugs for their treatment. Failure to treat these diseases effectively and early has resulted in a high incidence of sequelae, affecting principally women and resulting in infertility, ectopic pregnancy and adverse pregnancy outcome [3,4].

Now that it is clear that treatable bacterial STD facilitate heterosexual HIV transmission, the control of these diseases has assumed even greater importance [5–8]. Strategies for STD control include health education, encouraging people to have fewer sexual partners and to use condoms for high-risk encounters, and prompt and effective treatment of cases and their sexual partners, which will reduce the pool of infected individuals and hence slow transmission.

The management of STD in rural health centres in Africa cannot depend on laboratory diagnosis, since laboratory facilities are not generally available. The World Health Organization has therefore recommended a syndromic approach, in which patients presenting with syndromes commonly associated with STD are treated for all the likely causes of that syndrome [9]. The advantage of this approach is that patients receive curative treatment at their first visit; the main disadvantage is that it inevitably leads to overtreatment, which may have important cost implications.

We have trained staff in the syndromic management of STD, and supplied them with drugs of proven efficacy for STD treatment in six rural health centres and their satellite dispensaries in Mwanza Region in northwestern Tanzania. We have compared the incidence and prevalence of STD, including HIV infection, in a cohort of approximately 1000 adults in each of these six communities with that in a cohort of adults from six comparison communities without improved services, over a 2-year period. We have previously reported that this intervention reduced the incidence of HIV infection by approximately 40% [8]. We report here the impact of the intervention on other STD.

Methods

Mwanza Region is on the southern shores of Lake Victoria, and has a population of about two million, of whom approximately 250 000 live in Mwanza municipality and the remainder in small towns and villag The design of the intervention and the evaluation its impact on HIV incidence, and preliminary d on selected STD indicators, have been describ previously [8,10]. The essential features are summariz below.

Intervention

The intervention had five components: establishm of a reference clinic, training of health care provid supply of effective drugs, regular supervision and hea education in the target communities to encourage in viduals with STD symptoms to seek treatment early.

The standard treatment recommendations used h been described in detail elsewhere [10]. They w based on the aetiology of the common syndromes the region, established at the STD clinic, and on antimicrobial susceptibility of local isolates of *Neiss gonorrhoeae*. Therapeutic regimens had been shown be more than 95% effective in the STD clinic [(unpublished data). Inspection of records revealed th in comparison, communities' health facilities ar pated cure rates of approximately 2% for chancro 15% for gonorrhoea and chlamydial infection and than 50% for syphilis. Health workers were encoura to counsel patients concerning risk reduction and serious consequences of STD and HIV infection, provide free condoms, and to advise patients to r their sexual partners for treatment, giving them a c to pass to each contact in order to facilitate this proc

Impact evaluation

Twelve large communities, each consisting of catchment population of a health centre and its satel dispensaries, were selected as the elements for rando ization. A previous survey of the region had dem strated substantial geographical variations in H prevalence. To help ensure comparability of the int vention and comparison communities with respect baseline HIV and STD prevalence and risk factors infection, the communities were matched into six pa as previously described [10]. In each matched pair, community was randomly chosen to receive the int vention immediately following the baseline surv whereas the comparison community received the int vention after the follow-up survey 2 years later.

Main cohort

The impact of the intervention on the incidence prevalence of STD was measured in a cohort approximately 1000 adults aged 15–54 years selected random from the population living within 90 min w of each health centre, using a cluster sampling meth described previously [12]. Data concerning history genital discharge and genital ulcer syndrome at basel and at follow-up 2 years later were collected from cohort using a standard questionnaire.

Venous blood was taken at each visit for syphilis serology. After separation of serum, a rapid plasma reagin (RPR) test (VD-25; Murex, Dartford, Kent, UK) was performed in the field, and subjects with a positive test were treated for syphilis with a single dose of 2.4×10^6 U of benzathine penicillin. *Treponema pallidum* haemagglutination assay (TPHA; Fujirebio, Tokyo, Japan) was performed in the laboratory in Mwanza. A RPR test (as above) was performed in the laboratory on all sera positive for TPHA, and the results of laboratory (rather than field) tests were used to assess the impact of the intervention. Titres (1:2–1:32) were determined for RPR-positive sera.

Male subjects were asked to provide a first-void urine sample, which was tested for the presence of leukocytes using the leukocyte esterase dipstick test (LED; Nephur-Test + Leuko; Boehringer-Mannheim, Lewes, Sussex, UK). Subjects reporting a urethral discharge, subjects with other complaints who were found to have a urethral discharge on examination and those with a positive LED test, were asked to permit the collection of an intra-urethral swab. The swab was smeared on a glass slide which was heat-fixed for subsequent Gram staining; the presence of intracellular Gram-negative diplococci was taken as evidence of *N. gonorrhoeae* infection. A second swab was inserted 2–3 cm inside the urethra, rotated and then placed in transport medium at +4°C for a maximum of 6 h before being frozen at −20°C and later tested for *Chlamydia trachomatis* using an antigen capture enzyme immunoassay (IDEIA Chlamydia; Novo Nordisk Diagnostika, Cambridge, Cambridgeshire, UK). Urethritis was defined as the presence of *N. gonorrhoeae* and/or *C. trachomatis* infection and/or five or more polymorphs per high power field of Gram-stained sample.

Antenatal study

In order to obtain further information on the impact of the intervention on STD in women, a sample of 100 consecutive women attending antenatal clinics in each of the 12 health centres was interviewed and examined with a speculum to collect vaginal and cervical swabs, as previously described [13]. A first survey was conducted 6 months after the beginning of the main cohort study, and a second survey 12 months later in the same communities (but with different antenatal clinic attenders), and the prevalence of STD compared in intervention and comparison communities.

Statistical methods

The intervention in this study was the provision of improved STD treatment services in health centres and dispensaries in the community. Thus the analysis of the impact of the intervention was carried out at the community level, within the matched pairs of the study. For each matched pair the relative risk (RR) of the outcome STD marker was calculated for the intervention community compared with the comparison community. The overall crude RR was calculated as the geometric mean of the RR from the six matched pairs. Statistical significance was assessed with the paired t test on the logarithms of the RR, and corresponding 95% confidence intervals (CI) for the RR were obtained.

To adjust for differences between the intervention and comparison communities that might bias the estimate of impact, a logistic regression model was fitted using data about individuals and including terms for the matched pair, age group (15–19, 20–24, 25–29, 30–34, 35–44, 45–54 years), sex, circumcision in men, travel out of the village during the 2-year follow-up period, reported history of STD (ever) at the baseline survey, and the community prevalence of the STD outcome at the baseline survey. By computing observed and expected numbers for each outcome in the intervention (O_i, E_i) and comparison (O_c, E_c) communities, an adjusted RR was obtained for each pair as $(O_i/E_i)/(O_c/E_c)$. Adjusted significance tests and confidence intervals were calculated as before.

Results

Implementation of intervention

The intervention programme was successfully implemented in six communities immediately after the baseline survey. Sixty staff were trained in the use of syndromic algorithms in six health centres and 20 satellite dispensaries. The remaining six communities served as comparison areas for the study, and the intervention was implemented in them after the final follow-up survey. Clinic records showed that 11 632 STD syndromes were treated in the intervention health units during the 2-year follow-up period: 5466 in men, and 6166 in women. During the study period: 3722 sexual partners were treated in the intervention communities (0.32 per index case), but only 104 STD patients were recorded as having accepted condoms (0.9%).

Coverage of the evaluation cohort

A total of 12 534 subjects were enrolled at the baseline survey, representing 85% of eligible individuals. Detailed results of the baseline survey have been presented previously [12], and are summarized in Table 1. Prevalence of HIV infection, STD and risk factors for HIV infection did not differ significantly between intervention and comparison communities, but there were small imbalances in the reported history of STD (ever), travel away from the village, and male circumcision; these variables were adjusted for in the analysis.

Seventy-one per cent (8844) of the cohort members were seen again at the follow-up survey 2 years later. The reasons for non-attendance have been reported

Table 1. Baseline and follow-up prevalence of sexually transmitted disease (STD) markers and relative risk in intervention and compa groups in a cohort of 12 534 adults.

	Baseline		Follow-up		Relative risk		
STD marker	Intervention %	Comparison %	Intervention (%)	Comparison (%)	Crude	Adjusted*	95% confide interval
TPHA†	15.8	15.1	108/3558 (3.0)	158/3864 (4.1)	0.70	0.69	0.35–1.3
Active syphilis‡							
RPR ≥ 1:2	8.7	8.3	452/4244 (10.7)	525/4528 (11.6)	0.90	0.90	0.79–0.9
RPR ≥ 1:4	7.3	7.1	316/4244 (7.4)	428/4528 (9.5)	0.77	0.77	0.67–0.8
RPR ≥ 1:8	6.2	6.2	214/4244 (5.0)	315/4528 (7.0)	0.69	0.71	0.54–0.9
RPR ≥ 1:16	4.8	4.7	136/4244 (3.2)	224/4528 (4.9)	0.62	0.63	0.43–0.91
RPR ≥ 1:32	3.3	3.4	91/4244 (2.1)	168/4528 (3.7)	0.56	0.58	0.38–0.9
New cases RPR ≥ 1:8			85/3893 (2.2)	141/4170 (3.4)	0.60	0.62	0.38–1.02
Urethritis	10.2	10.7	119/2052 (5.8)	152/2186 (7.0)	0.84	0.87	0.50–1.4
Symptoms in past year	1.4	1.8	37/2052 (1.8)	70/2186 (3.2)	0.48	0.51	0.25–1.03
Symptoms now	1.0	1.3	32/2052 (1.6)	54/2186 (2.5)	0.48	0.51	0.24–1.1
Neisseria gonorrhoeae and/or *Chlamydia trachomatis* infection	2.4	3.2	52/2052 (2.5)	66/2186 (3.0)	0.68	0.96	0.50–1.85
Symptoms in past year	0.4	0.7	21/2052 (1.0)	33/2186 (1.5)	0.47	1.14	0.46–2.83
Symptoms now	0.3	0.5	19/2052 (0.9)	26/2186 (1.2)	0.58	1.26	0.53–3.02

*Analysis adjusted for age, sex, community pair, circumcision in men, travel during the follow-up period, history of STD prior to baseline vey and the community prevalence of STD marker at baseline. †*Treponema pallidum* haemagglutination assay (TPHA) prevalence is give baseline, and the 2-year incidence at follow-up. ‡Active syphilis defined as TPHA-positive and positive rapid plasma reagin (RPR) t §Adjusted for overall baseline prevalence of urethritis (symptomatic and asymptomatic). ¶Adjusted for overall baseline prevalence *Neisseria gonorrhoeae* and *Chlamydia trachomatis* infections (symptomatic and asymptomatic).

elsewhere; coverage and reasons for non-attendance were similar in intervention and comparison communities [8].

Syphilis

A definitive TPHA and RPR result was available at follow-up for 8772 individuals, as 20 refused to give blood and 52 TPHA results could not be resolved. Inconsistencies with the initial publication result from retesting of sera for which TPHA results at baseline and follow-up were discordant. A further 11 subjects had a missing TPHA result at baseline, and 1339 had been TPHA-positive, giving a denominator of 7422 for TPHA seroconversion. Seven hundred and nine subjects had a confirmed positive RPR test at the baseline survey; exclusion of these subjects gave a denominator for 'new cases' of syphilis of 8063.

Results of serological tests for syphilis at baseline and follow-up in intervention and comparison communities are shown in Table 1. The prevalence of TPHA positivity at baseline was similar in intervention and comparison communities (15.8% and 15.1% respectively). The incidence of TPHA seroconversion over the 2-year follow-up period was 108 out of 3558 in the intervention communities (3.0%), and 158 out of 3864 in the comparison communities (4.1%; adjusted RR, 0.69; 95% CI, 0.35–1.38). After adjustment, this represented a reduction in incidence of 30% in the intervention communities, although the difference was not statistically significant at the 5% level ($P = 0.25$).

The prevalence of serological syphilis (RPR-positive, TPHA-positive) at follow-up was significantly lower in intervention than in comparison communities. If an RPR titre of ≥ 1:8 was taken as positive, the adjust relative risk was 0.71 (95% CI, 0.54–0.93; $P < 0.0$ but whichever titre of RPR is considered, the prev lence was significantly lower in the intervention co munities. The adjusted relative risk decreased wi increasing titre, from 0.90 at a titre of ≥ 1:2 to 0.58 a titre of ≥ 1:32. After excluding subjects with positi RPR and TPHA at baseline (many of whom remain RPR-seropositive in spite of adequate treatment), t prevalence of new cases of serological syphilis (RP ≥ 1:8, TPHA-positive) was 85 out of 3893 in the inte vention communities (2.2%), and 141 out of 4170 the comparison communities (3.4%; adjusted RI 0.62; 95% CI, 0.38–1.02; $P = 0.06$).

Urethritis

Urethral swabs were taken from 1144 men (96% those eligible). Of the 51 eligible men from who swabs were not obtained, 29 were in the interventio communities and 22 in the comparison communitie Six men refused to give a urine sample, none of who reported symptoms. All men from whom swabs we not taken were considered negative in the subsequer analysis.

The prevalence of urethritis and of *N. gonorrhoe* and/or *C. trachomatis* infection in men at follow-up shown in Table 1. The prevalence of urethritis and *N. gonorrhoeae*/*C. trachomatis* infection was lower in th intervention communities, but not significantly so. Th prevalence of confirmed urethritis in men wh reported having had a urethral discharge in the pas year was lower in the intervention communitie (adjusted RR, 0.51; 95% CI, 0.25–1.03; $P = 0.06$) The prevalence of confirmed urethritis in men report

ing urethral discharge at the time of examination was also reduced by approximately 50% (adjusted RR, 0.51; 95% CI, 0.24–1.10; $P = 0.08$). The reduction in the overall prevalence of urethritis in the intervention group was entirely accounted for by the reduction in symptomatic cases.

Self-reported STD symptoms

Of 2052 men in the intervention communities, 236 reported a genital discharge or ulcer in the past year at follow-up (11.5%), compared with 269 out of 2186 men in comparison communities [12.3%; crude RR, 0.90 (95% CI, 0.51–1.59); adjusted RR, 0.94 (95% CI, 0.57–1.56); difference not significant]. Among women, 137 out of 2234 complained of one of these symptoms in the past year at follow-up in intervention communities (6.1%), and 155 out of 2372 in comparison communities [6.5%; crude RR, 0.96 (95% CI, 0.54–1.72); adjusted RR, 1.00 (95% CI, 0.58–1.72); difference not significant].

Antenatal clinic attenders

A total of 1149 women were enrolled in the first survey. Of these, eight (0.7%) declined examination and were excluded from the analysis, leaving 575 women in the intervention and 566 in the comparison communities. Mean age was 25.0 years in both groups. At the second survey, 1239 women were enrolled, all of whom agreed to be examined and provided samples; 614 were from intervention, and 625 from comparison communities. Mean age was 25.0 and 24.9 years respectively.

The prevalence of STD in sampled antenatal clinic attenders at the first and second surveys are shown in Table 2. Approximately 40% had an STD, and there was no significant difference in the prevalence of any STD between intervention and comparison communities on either occasion. Analysis using different titres to define RPR positivity (from 1:2 to 1:32) failed to reveal any differences between the two groups (data not shown).

Discussion

We have previously reported that improved syndromic management of STD reduced the incidence of HIV infection in this population by 42% over a 2-year period [8], and postulated that this was achieved through a reduction in the duration of symptomatic bacterial STD, which can facilitate heterosexual HIV transmission. The initial publication failed to provide conclusive evidence in support of this hypothesis [8]. Since that time, the results of syphilis serology by RPR titre have become available, and we have performed an analysis of the impact on STD prevalence which was appropriately adjusted for the community prevalence of STD at baseline. By removing an important source of variation, the latter adjustment resulted in an appreciable increase in precision for certain outcome measures. We have demonstrated that after adjustment, there was a significant reduction in the prevalence of serological syphilis in the intervention communities, and that the prevalence of symptomatic urethritis in men was reduced by approximately 50%. We have also documented a reduction in TPHA seroconversion of approximately 30% in the intervention communities, although this did not achieve statistical significance.

As reported previously [8], we believe the impact of this intervention on HIV infection and other STD reflects improved access to effective STD treatment; this would be expected to reduce the duration, and hence the prevalence of symptomatic STD in the population; a reduced prevalence should, in turn, lead to a reduction in incidence, although this may not be immediately apparent if the main reservoir of infected individuals are not symptomatic. It seems unlikely that this intervention had a great impact on sexual behaviour (e.g., a reduction in the number of sexual partners, or increased use of condoms), as this was not its primary intention. At follow-up of the main cohort, the reported total number of sexual partners, and of casual partners, did not differ from baseline or between intervention and comparison communities [8]. Less than 1%

Table 2. Prevalence of sexually transmitted disease (STD) markers and relative risk in intervention and comparison groups in two random surveys of antenatal clinic attenders.

	First round		Second round		Relative risk, second round (95% confidence interval)	
STD marker	Intervention n = 575 (%)	Comparison n = 566 (%)	Intervention n = 614 (%)	Comparison n = 625 (%)	Crude	Adjusted*
Neisseria gonorrhoeae/ Chlamydia trachomatis prevalence†	7.0	9.9	6.7	6.6	0.91 (0.48–1.73)	0.93 (0.49–1.75)
Trichomonas vaginalis	28.5	28.6	25.4	23.2	1.08 (0.92–1.28)	1.09 (0.92–1.28)
Active syphilis prevalence‡	7.6	8.3	6.8	6.4	1.08 (0.68–1.73)	1.08 (0.66–1.79)
Any STD§	37.3	41.3	34.4	32.3	1.11 (0.88–1.39)	1.07 (0.79–1.43)

*Analysis adjusted for age only. †For baseline prevalence of *N. gonorrhoeae* and *C. trachomatis* n = 964; missing data are due to contaminated *N. gonorrhoeae* cultures. ‡Active syphilis defined as *Treponema pallidum* haemagglutination assay positive and rapid plasma reagin titre of ≥ 1:8. §Any STD is defined as *N. gonorrhoeae, C. trachomatis, T. vaginalis* or active syphilis.

of subjects were recorded as having accepted condoms in this rural population (in contrast to Mwanza town, where they are well accepted).

The intervention had no impact on the incidence of self-reported STD symptoms in the past year in either men or women, or on the prevalence of STD in antenatal clinic attenders. In the case of women, it is well known that there is a poor correlation between symptoms and the presence of sexually transmitted pathogens, since many women complaining of vaginal discharge have bacterial vaginosis or candidosis rather than STD. In the case of men it is initially more surprising that improved STD treatment services failed to reduce the incidence of reported genital discharge and ulceration. This may result in part from recall bias, as it is likely that the repeated health education campaigns conducted in intervention communities made people more aware of the importance of STD symptoms. Moreover, it became clear during the course of this study that asymptomatic infection with *N. gonorrhoeae* and *C. trachomatis* was prevalent among both men and women in this study population [13,14]. It is likely that asymptomatically infected people of both sexes constitute the main reservoir of these infections, implying that their incidence is not likely to be significantly reduced by an intervention which reaches only those with symptoms and a small proportion of their sexual partners. The correlation between reported symptoms and laboratory evidence of STD has been found to be poor in community-based surveys in both men and women in Mwanza Region [13–15]; in addition to individuals with proven infections but no symptoms, many were identified who complained of symptoms but in whom an STD could not be documented. It is possible that a significant proportion of urethral symptoms can be attributed to schistosomiasis, which is endemic in the region [15].

The failure of the intervention to have any impact on the prevalence of STD in antenatal clinic attenders after 1 year is disappointing. Improved syndromic management of symptomatic STD may have little impact on the prevalence of STD in antenatal clinic attenders, at least in the short-term. Although the prevalence of symptoms related to the reproductive tract is high in this population when they are directly questioned on the subject, few voluntarily present to the official health sector for treatment [16]. Moreover, we have shown that the prevalence of *N. gonorrhoeae* and *C. trachomatis* is identical in those who do and those who do not complain of a vaginal discharge [13]. It is clear that only through comprehensive screening programmes will the prevalence of STD be reduced in this vulnerable population. Yet even screening for syphilis, which is cheap, simple and cost-effective is not practised in most antenatal clinics in sub-Saharan Africa, for logistic and economic reasons [17,18].

In the absence of simple and cheap screening tests *N. gonorrhoeae* and *C. trachomatis*, we and others ha attempted to identify women at risk of these infecti through a simple questionnaire [13,19]. Unfortunat this approach does not appear very promising, giv sensitivities and specificities of at most 70%. Parti notification is another possible means of identify infected women, but in this study fewer than 30% contacts of symptomatic STD patients presented treatment. Presumptive treatment has been sugges for populations at high risk, but is likely to be expe sive, has not been validated and remains controvers Simple, cheap, and rapid diagnostic tests for *N. gon rhoeae* and *C. trachomatis*, using a non-invasive sam such as urine, are urgently needed, especially women.

The interpretation of serological tests for syphilis is ficult at the population level. Yaws was endemic Tanzania until the mass treatment campaigns of 1950s and 1960s, but is said to be seen no longer. have therefore assumed that positive treponemal se ogy (TPHA) is due to current or previous ven syphilis. We assumed initially that subjects with a po tive RPR test and TPHA had untreated syphilis, this assumption is open to question. A proportion these individuals may have a false positive RPR tes conjunction with a long-standing positive TPHA; may occur relatively frequently in populations such this, with a TPHA-positivity prevalence of 15% an high prevalence of malaria and other parasitic inf tions. Moreover, in some subjects, particularly th treated late in the course of the disease, the RPR not revert to negative even after successful treatm [20–22]. Since it is likely that such 'sero-fast' indivi als, as well as those with false positive RPR tests, have low RPR titres, we have compared prevalence of RPR positivity at various titres in intervention and comparison communities. expected, the impact appears greater the higher RPR titre used to define positivity, or when indivi als with a positive RPR and TPHA at baseline excluded from the analysis, since subjects identif according to these criteria are more likely to have b infected recently.

It is initially surprising that the intervention sho have significantly reduced the seroprevalence of syp in the main cohort, but not among antenatal cli attenders. However, in the case of antenatal cli attenders, a cohort was not followed; different wor were seen at follow-up. Whereas in the main coh RPR-positive subjects were treated at baseline, antenatal clinic attenders seen at the second survey not been treated in this way. Thus at the second sur most seropositive subjects in the main cohort rep sented infections acquired in the past 2 years, whe many antenatal seropositive results will have been

to long-standing infections; unfortunately antenatal screening for syphilis is not routinely performed in these rural health centres.

We have shown that it is possible to reduce the incidence of HIV infection by approximately 40% in a rural African population by improving the management of symptomatic STD at health centres and dispensaries. The intervention also reduced the prevalence of serological syphilis and of symptomatic urethritis in men. Our data suggest that a high proportion of HIV infections in sub-Saharan Africa may be attributed to the increased risk of heterosexual HIV transmission in the presence of a 'classical' STD. They also suggest that this cofactor effect is more pronounced for symptomatic than for asymptomatic STD. Recent data showing that symptomatic STD increase shedding of HIV in the genital tract provide a plausible biological mechanism for this interaction [23–25]. The implementation of improved services for the treatment of STD at the primary health care level should be given the highest priority.

If it were possible to reduce STD rates in developing countries to those prevailing in Northern Europe, this could have a dramatic impact on the heterosexual HIV/AIDS epidemic in Africa and Asia. At present, given the lack of appropriate screening tests and the high prevalence of asymptomatic infection in both men and women, mass treatment of STD may be the only feasible way to do this. Since HIV infection is now the leading cause of death among young adults in many African countries [26,27], and is spreading rapidly in some parts of Asia, there is an urgent need to measure the impact and cost-effectiveness of this approach; if it is shown to be effective, the international community must be mobilized to provide the resources needed to apply it on a wide scale.

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References

1. Arya OP, Lawson JB: Sexually transmitted diseases in the tropics. Epidemiological, diagnostic, therapeutic and control aspects. *Trop Doctor* 1977, 7:51–56.
2. De Schryver A, Meheus A: Epidemiology of sexually transmitted diseases: the global picture. *Bull WHO* 1990, 68:639–654.
3. Schulz KF, Cates W, O'Masra PR: Pregnancy loss, infant death, and suffering: legacy of syphilis and gonorrhoea in Africa. *Genitourin Med* 1987, 62:320–325.
4. Wasserheit JN: The significance and scope of reproductive tract infections among third world women. *Int J Gynecol Obstet* 1989, 3 (suppl):S145–S168.
5. Cameron DW, Simonsen JN, D'Costa LJ, *et al.*: Female to male transmission of human immunodeficiency virus type 1: risk factors for seroconversion in men. *Lancet* 1989, ii:403–407.
6. Pepin J, Plummer FA, Brunham RC, Piot P, Cameron DW, Ronald AR: The interaction of HIV and other sexually transmitted diseases: an opportunity for intervention. *AIDS* 1989, 3:3–9.
7. Laga M, Alary M, Nzila N, *et al.*: Condom promotion, sexually transmitted disease treatment, and declining incidence of HIV-1 infection in female Zairian sex workers. *Lancet* 1994, 344:246–248.
8. Grosskurth H, Mosha F, Todd J, *et al.*: Impact of improved treatment of sexually transmitted diseases on HIV infection in rural Tanzania: randomised controlled trial. *Lancet* 1995, 346:530–536.
9. World Health Organization: Recommendations for the management of sexually transmitted diseases. *WHO Advisory Group Meeting on Sexually Transmitted Diseases Treatments. WHO/GPA/STD/93.1*. Geneva: WHO; 1993.
10. Hayes R, Mosha F, Nicoll A, *et al.*: A community trial of the impact of improved sexually transmitted disease treatment on the HIV epidemic in rural Tanzania: 1. Design. *AIDS* 1995, 9:919–926.
11. West B, Changalucha J, Grosskurth H, *et al.*: Antimicrobial susceptibility, auxotype and plasmid content of *Neisseria gonorrhoeae* in Northern Tanzania: emergence of high level plasmid mediated tetracycline resistance. *Genitourin Med* 1995, 71:9–12.
12. Grosskurth H, Mosha F, Todd J, *et al.*: A community trial of the impact of improved sexually transmitted disease treatment on the HIV epidemic in rural Tanzania: 2. Baseline survey results. *AIDS* 1995, 9:927–934.
13. Mayaud P, Grosskurth H, Changalucha J, *et al.*: Risk assessment and other screening options for the identification of gonorrhoea and chlamydial infection in rural Tanzanian antenatal clinic attenders. *Bull WHO* 1995, 73:621–630.
14. Grosskurth H, Mayaud P, Mosha F, *et al.*: Asymptomatic gonorrhoea and chlamydial infection in rural Tanzanian men. *BMJ* 1996, 312:277–280.
15. Buvé A, Mosha F, Watson-Jones D, *et al.*: Is asymptomatic urethritis in men an obstacle to effective STD control? A community study in Mwanza, Tanzania. *XI International Conference on AIDS*. Vancouver, July 1996 [abstract Mo.C. 3411].
16. Newell J, Senkoro K, Mosha F, *et al.*: A population-based study of syphilis and sexually transmitted disease syndromes in North-Western Tanzania. 2. Risk factors and health seeking behaviour. *Genitourin Med* 1993, 69:421–426.
17. Hira SK, Bhat GJ, Chikamata DM, *et al.*: Syphilis intervention in pregnancy: Zambian demonstration project. *Genitourin Med* 1990, 66:159–164.
18. Temmerman M, Mohamed Ali F, Fransen L: Syphilis prevention in pregnancy: an opportunity to improve reproductive and child health in Kenya. *Health Policy Planning* 1993, 8:122–127.
19. Vuylsteke B, Laga M, Alary M, *et al.*: Clinical algorithms for the screening of women for gonococcal and chlamydial infection: evaluation of pregnant women and prostitutes in Zaire. *Clin Infect Dis* 1993, 17:82–88.
20. Larsen SA, Steiner BM, Rudolph AH: Laboratory diagnosis and interpretation of tests for syphilis. *Clin Microbiol Rev* 1995, 8:1–21.
21. Goeman J, Kivuvu M, Nzila N, *et al.*: Similar serological response to conventional therapy for syphilis among HIV positive and HIV negative women. *Genitourin Med* 1995, 71:275–279.