JB DST

ARTIGO ESPECIAL

SYNDROMIC MANAGEMENT OF SEXUALLY TRANSMITTED DISEASES AT PRIMARY HEALTH CARE LEVEL IN TANZANIA

Effectiveness And Impact

PHILIPPE MAYAUD[1], EZRA MWIJARUBI[2], AWENE GAVYOLE[3*]

RESUMO

A epidemia do HIV tem aumentado com gravidade em muitas partes da África sub-saariana , com a prevalência entre adultos passando de 20% em alguns centros urbanos e com uma prevalência menor , porém constantemente crescente, nas áreas rurais, onde vive a maioria dos africano. Muitos estudos sugeriram que a transmissão sexual do HIV pode ser consideravelmente aumentada com a presença de outras DST, que são muito prevalentes em muitas partes da África, devido ao menos em parte à má qualidade dos serviços de tratamento das DST. A Organização Mundial de Saúde (OMS), portanto, tem promovido a melhoria dos serviços de DST para poder reduzir a prevalência das DST na população, reduzindo assim a transmissão do HIV. A medição do impacto, exeqüibilidade e da relação custo-eficácia de tal programa foi realizada em um teste de comunidade randomizada, levado a cabo na região de Mivanza, na Tanzânia. A abordagem sindrômica das DST foi bem aceita pelo corpo médico e pelos pacientes. Este tipo de tratamento foi capaz de curar pacientes com dst sintomáticos e foi superior às práticas anteriores utilizadas nestes locais. A implementação bem sucedida dependeu de forma crucial de treinamento com qualidade, de supervisão dos trabalhadores de saúde e de um fornecimento constante de medicamentos. Esta intervenção produziu um impacto significativo sobre a soroconversão para o HIV ao longo de 2 ano, com redução de aproximadamente 40% (incidência de 1.2% de HIV nas comunidade sob intervenção e de 1.9% nas comunidade de comparação, com $P = 0.007$) nestas taxas. Além disso, a intervenção reduziu a prevalência da sífilis nas comunidades sob intervenção (títulos de Rapid Plasma Reagin [RPR] ou Ensaio de Hemoaglutinação de Treponema pallidum [TPHA] positivo), em 30% (de 7.0% para 5.0%, $P<0.02$) e a prevalência de uretrite sintomática em homens em aproximadamente 50% (de 3.2% para 1.8%, $P=0.008$). A intervenção teve boa relação custo-eficácia, com um custo anual per capita de US$ 0.39 e um custo por ano vida corrigido para incapacidade poupado (DALY) de US$ 10/DALY, quando se considera apenas o impacto do HIV. Estes resultados são melhores do que outras intervenções de saúde. Recomenda-se agora que os serviços de tratamento de DST sejam um componentes essencial dos programas de controle de AIDS/DST; entretanto, documentamos que a abordagem sindrômica tem várias limitações: (i) não houve impacto sobre as infecções assintomáticas, que foram altamente prevalentes nesta população tanto em homens quanto em mulheres; (ii) não houve impacto sobre a prevalência de DST entre mulheres grávidas vivendo nas mesmas; (iii) apesar da ênfase nos serviços de aconselhamento durante o treinamento dos trabalhadores primários, houve um impacto limitado sobre a aceitação do condom e sobre a notificação de parceiros nestas áreas rurais. Várias opções para o fortalecimento do impacto do controle das DST devem ser combinadas e são discutidas neste trabalho.

Unitermos: *DST/HIV/AIDS, Abordagem Sindrômica, HIV/AIDS, África – cuidados primários de saúde, relação custo-eficácia, impacto, ensaio controlado randomizado.*

1 – Dr. Philippe Mayaud, M.D., M.Sc., is a Lecturer at the Department of Infectious Tropical Diseases, London School of Hygiene & Tropical Medicine (LSHTM), London, UK. He worked from 1991-1997 with the STD/HIV Intervention & Research Programme, Mwanza Region, Tanzania, jointly run by the African Medical & Research Foundation (AMREF) and LSHTM.
2 – Mr Ezra Mwijarubi, Medical Assistant, is an STD/HIV Intervention Officer and Trainer with AMREF Tanzania since 1991. He previously worked for the Regional Medical Office, Mwanza, and was attached to the STD/HIV Intervention & Research Programme, Mwanza Region, Tanzania.
3 – Dr. Awene Gavyole, M.D., is the current Programme Manager of AMREF (since 1996). He previously was the Regional Medical Officer, Mwanza Region (1993-1996), overseing the implementation of the joint project.

**This paper is based on an oral presentation (Symposia CS4) made at the XI Congreso Latinoamericano de Enfermedades de Transmision Sexual and V Conferencia Panamericana de Sida, Lima, Peru, 3-6 December 1997.*

SUMMARY

The HIV epidemic has been increasing in severity in many parts of sub-Saharan Africa, adult prevalence exceeding 20% in some urban centres, with lower but steadily increasing prevalence in rural areas where the majority of Africans live. Several studies have suggested that the sexual transmission of HIV may be considerably enhanced in the presence of other STDs which are highly prevalent in many parts of Africa, due at least partly to the poor quality of STD treatment services. The WHO therefore has been promoting improvement of STD services in order to reduce the prevalence of STDs in the population, thereby reducing the transmission of HIV. Measurement of the impact, feasibility and cost-effectiveness of such a programme has been provided in a randomised-communit trial conducted in the Mwanza Region of Tanzania.

Syndromic management of STDs was well accepted by staff and patients. Management was effective in curing symptomatic STD patients and superior to formerly prevailing treatment practices. Successful implementation depended crucially on quality training and supervision of health workers and on the regular supply of drugs.

The intervention produced a significant impact on HIV seroconversion over 2 years with a reduction of about 40% (1.2% HIV incidence in intervention communities and 1.9% in comparison communities, P=0.007). In addition the intervention reduced the prevalence of serological syphilis in intervention communities (rapid plasma reagin [RPR] titre ≥1:8 and *Treponema pallidum* haemagglutination assay [TPHA] positive) by 30% (from 7.0% to 5.0%, P < 0.02) and the prevalence of *symptomatic* urethritis in males by about 50% (from 3.2% to 1.8%, P=0.08). The intervention was very cost-effective with an annual cost per capita of US$ 0.39 and a cost per disability-adjusted life year saved of US$ 10/DALY when considering only the impact on HIV. This compares favourably with other health interventions.

It is now recommended that STD treatment services be an essential component of AIDS/STD control programmes, however we documented that syndromic management had several limitations: (i) there was no impact on asymptomatic infections which were highly prevalent in this population both in men and women; (ii) there was no impact on STD prevalence among pregnant women living in the same communities; (iii) despite emphasis on counselling services during the training of primary care workers, there was a limited impact on condom acceptance, and partner notification in these rural areas. Several options for strengthening the impact of STD control should be combined and are discussed in the paper.

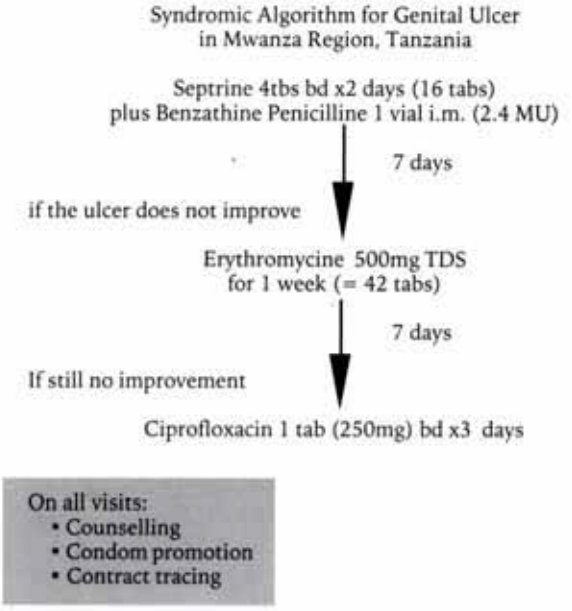
Key words: sexually transmitted diseases, syndromic case management, HIV/AIDS, Africa, primary health care, cost-effectiveness, impact, randomised controlled trial.

The HIV epidemic has been increasing in severity in many parts of sub-Saharan Africa.

RATIONALE FOR AN STD INTERVENTION

HIV infection continues to occur at high levels in sub-Saharan Africa, the region which has suffered the most since the onset of the HIV/AIDS epidemic.[1] Adult prevalence often exceed 20% in some urban centres, with lower but steadily increasing prevalence in rural areas where most Africans still live. The majority of adult HIV infections in Africa are acquired through heterosexual contact,[1] and most efforts at preventing HIV transmission have focused on health education to reduce risky sexual behaviour or to increase condom use.

Figure 1



An increasingly recommended prevention strategy is the management of sexually transmitted diseases (STDs),[2-5] since many epidemiological studies have suggested that the presence of STDs may enhance the sexual transmission of HIV.[6-8] However, in many parts of sub-Saharan Africa where STDs are a major public health problem[9-12] and lead to severe complications,[13,15] resources are unavailable for proper diagnosis with laboratory tests and many patients consult at the first level of primary health care where even basic training of health workers in STD management is lacking. Therefore, the World Health Organisation (WHO) has been promoting the syndromic management of STDs, which offers immediate diagnosis and treatment without requiring expensive and time-consuming laboratory tests[16].

Although this strategy has been promoted for some years and may be a very costeffective intervention,[17,18] its likely impact on the HIV epidemic had remained unclear. It was against this background that we decided to

conduct an communityrandomised intervention trial in Tanzania to obtain direct empirical data on the impact of this intervention strategy on HIV incidence, STD prevalence, and on its feasibility and cost-effectiveness.

This paper will review briefly the rationale for syndromic management of STDs and will present the design and main results of the intervention trial, most of which have already been published.[19-27]

It is now recommended that STD treatment services be an essential component of AIDS/STD control programmes.

SYNDROMIC CASE MANAGEMENT OF STDS

When using syndromic management, the health care provider bases his/her diagnosis and treatment on 'syndromes', which are groups of patients symptoms and clinical findings, instead of specific diseases identified through testing. Treatment is provided for all (or most) pathogens or conditions that could cause the 'syndrome'. For example, in Mwanza, the treatment of 'Genital Ulcer syndrome' (Figure 1) would combine treatment covering *Treponema pallidum*, causing syphilis, with an injection of long-acting benzyl-penicillin, and *Haemophilus ducreyi*, agent of chancroid, with trimethoprim-sulfamethoxazole (first line therapy), erythromycin (second line therapy) or ciprofloxacin (third line therapy),[28] given that these two bacterial pathogens are the most common etiological agents causing genital ulcers in this part of Africa.[29] Since all possible treatments are offered, the likelihood of a cure for the STD causing the symptoms is increased. To assist the provider, flowcharts which map out the steps to take when determining symptoms and treatment, are available. Ideally, the flowcharts would reflect the prevalence of various STD pathogens, antimicrobial susceptibility pattern and drug availability in the appropriate region.

The advantages of the syndromic approach include: (i) a lower dependency on expensive, time-consuming or unavailable laboratory tests; (ii) treatment is given at first encounter and more time can be spent on counselling and condom advice; (iii) treatment is standardized which can facilitate training, supervision and surveillance.

The main disadvantage of syndromic approach is the over-treatment of many patients, leading to increased drug costs. Moreover, in order to be effective, syndromic guidelines must rely on local data of STD prevalence, syndromic etiological pattern, antibiotic resistance (essential for *Neisseria gonorrhoeae* and when possible for *Haemophilus ducreyi*), and drug availability, which may be difficult to obtain and this step may not always be fulfilled. Finally, syndromic management entails allowing the prescription of certain drugs that may not otherwise be allowed for certain levels of health care providers. For these reasons, syndromic management has often been resisted by the medical establishment.

However, the WHO and several researchers have highlighted that this approach may be the only possible alternative in resource-constrained health systems, if the goal of proper STD case management and eventual control of STDs is to be attained.[11,30] A WHO 'desk study' has also suggested that syndromic management may be more cost-effective than approaches based on etiological diagnosis or based on clinical judgment.[31]

INTERVENTION COMPONENTS AND MONITORING OF STD TREATMENT EFFECTIVENESS IN MWANZA, TANZANIA[19,24-26]

Improvement of STD services at primary care level was implemented in the Mwanza Region, in Northern Tanzania. Six rural communities (defined as the catchment population served by a health centre and its 3-4 satellite dispensaries) received improved STD case management and 6 other communities served as 'comparison' where usual STD services were provided. Communities were matched in pairs based on pre-intervention STD attendance rates and location. An earlier survey had shown that HIV prevalence was higher along

Table 1

Cure rates of genital discharge and genital ulcer syndromes in urban and rural areas of Mwanza Region, Tanzania

Populations	STD Syndromes: Male GDS No. cases	Male GDS % cured	Female GDS No.cases	Female GDS % cured	GUS all No.cases	GUS all % cured
Urban clinic returners (return rate 75-80%) [1]	797	86%	1227	76%	429	60%
Rural clinics retumers (return rate 32-35%) [1]	3,662	99%	3,046	96%	2,216	98%
Rural clinics non-returners [2]	89	69%	97	53%	106	70%
Combined rural clinics [3]	–	79%	–	70%	–	78%
Comparison health units [4]		15-25%		15 - 30%		35%

GDS: Genital Discharge Syndrome; GUS: Genital Ulcer Syndrome
[1] Data obtakned from clinic regisfers (STD reference clinic + 25 rural clinics)
[2] Special survey among non-retuning STD patients
[3] Sum of the products of cure rafes by the proportion of retuming and non-returning patients for each syndrome
[4] Estimated drug efficacy from 4, 000 prescriptions of 18 comparison hea/th units

the main roads and the shores of Lake Victoria than in the more remote villages.[32] The intervention was randomly attributed to one community in each pair.[19]

A reference clinic and laboratory were established in the main town to carry out the necessary preliminary work on syndromic etiological and antibiotic susceptibility patterns, and flowcharts for management of the main syndromes were designed. Effective, but affordable, drugs were selected for treatment. Health workers from a total of 25 health units underwent a 3-week theoretical and practical training course, during which they studied proper case management of STD patients following flowcharts, proper health education and counselling, condom promotion, partner referral and basic record keeping. STD drugs were supplied during regular supervision visits at 6-8 weekly intervals which also provided an opportunity for inservice training and data collection. Education campaigns promoted prompt utilisation of health services for STDs in the communities served by these health units STD syndromes treated were recorded, with their outcome. Over a 2-year period, 11,632 STD cases were treated in the intervention health units. 47% were males; two thirds presented with genital discharge, and 27% with genital ulcers. 53% were females; genital discharge accounted for half of the syndromes and lower abdominal pain (pelvic inflammatory disease) for 36%.

Health workers from a total of 25 health units underwent a 3-week theoretical and practical training course.

Treatment effectiveness for three main syndromes (male and female genital discharge syndromes [M-GDS; F-GDS], genital ulcer syndrome [GUS]) was monitored through a combination of clinical and (in the reference clinic) biological criteria. The observed cure rates were high (Table 1), and complete treatment failures with second or third line therapy were observed in only very few cases. Unfortunately, many patients did not return for a complete follow-up assessment in rural areas so that a definitive result could not be recorded in many cases. To overcome this problem, a separate study of non-returning patients was conducted, which revealed lower cure rates (Table 1), though many patients had improved temporarily. Actually, many of these patients with relapses failed to comply with therapy or to refer their sexual partners for treatment. Combining data from returning and non-returning STD patients in rural areas, we estimated that treatment effectiveness was about 80% on clinical criteria. These results are comparable to those found by Hanson et al in Zambia.[33]

Table 2

Resistance levels of isolates of *Neisseria gonorrhoeae* by Minimum Inhibitory Concentration (MIC) method and E-test, in Mwanza, Tanzania, 1992-1996.

Antibiotics	1992 (n = 130) % resistant	1994 (n= 100) % resistant	1996 (n= 109) % resistant
Penicillin	63	58	60
Tebacyclin	35	98	96
TMP-SMX *	4	5	9
Ciprofloxacin	0	0	0
Cefuroxime	0	0	0
Ceftriaxone	NT	NT	0
Erythromycin	NT	NT	12
Spectinomycin	0	NT	0
Chloramphenicol	NT	NT	7

1992: MIC results (ref 26); 1994: E-tesf results; 1996: correlated MIC and E-test results (ref 24)
* TMP-SMX = trimethoprim-sulfamethoxazole (cotrimoxazole) at high dose
NT= not tested

Table 3

Baseline and follow-up incidence and prevalence of HIV-1 and sexually transmitted (STD) markers and relative risk in intervention and comparison groups in a cohort of 12,534 adults and two crosssectional studies of 1,200 pregnant women (ANC) in Mwanza Region, Tanzania

HIV/STD markers *	Baseline Intervention %	Baseline Comparison %	P-value	Follow-up Intervention %	Follow-up Comparison %	Adjusted RR *	Relative Risk 95% Confidence Interval	P-value
HIV-1	3.8	4.4	NS	1.2	1.9	0.57	0.42 - 0.79	0.007
TPHA	15.8	15.1	NS	3	4.1	0.69	0.35 - 0.93	NS
TPHA/RPR≥ 1:8	6.2	6.2	NS	5	7	0.71	0.54 - 0.93	<0.02
New cases RPR >1:8	–	–	–	2.2	3.4	0.62	0.38 - 1.02	0.06
Male Urethritis [1]	10.2	10.7	NS	5.8	7	0.87	0.50 - 1.49	NS
Urethritis+symptoms [2]	1.4	1.8	NS	1.8	3.2	0.51	0.25 - 1.03	0.08
Any STD (ANC)	37.3	41.3	NS	34.4	32.3	1.07	0.79 - 1.43	NS

** HIV-1 and TPHA prevalence are given at Baseline and the 2-year incidence at Follow-Up; New RPR are incidence rates at Follow-up; all other measurements are prevalence figures*
TPHA: Treponema pallidum *haemagglutination assay; RPR: rapid plasma reagin*
\# Analysis adjusted for age, sex, community pair, circumcision in men, travel during the follow-up period, history of STD prior to baseline survey and the community prevalence of STD marker at basiline
baseline
[1] Urethritis: N.gonorrhoeae *on urethral Gram smear and/or* C.trachomatis *by ag detection of urethral swab and/or presence of ≥ 5 PMN/HPF on urethral Gram smear*
[12] Urethritis + symptoms: reported symptoms over past one year or at time of interview

Data were also collected on STD treatment regimens provided in 18 rural clinics without improved STD case management

Data were also collected on STD treatment regimens provided in 18 rural clinics without improved STD case management. Health workers in these units did not have a standardised way of prescribing and lacked effective drugs for STD treatment. It was estimated, using a panel of international STD experts, that only 1535% of all STDs were effectively treated in these health units (Table 1).

Gonococcal isolates were obtained from urethral and cervical samples from men and women attending the reference clinic in Mwanza. Over the time of the intervention (1992-1996), we observed high levels of resistance to penicillin (50%), increasingly high levels of resistance to tetracycline (35% to 96) with the emergence of plasmid-mediated tetracycline resistance.[26] Sensitivity to high dose trimethoprimsulphamethoxazole (TMP-SMX) and to ciprofloxacin remained high throughout the study period (Table 2). Continued monitoring of antimicrobial susceptibility of local strains of *N.gonorrhoeae* by accurate methods will be essential.

Patients were given referral slips to encourage sexual partners to come for treatment but only 25-30% of index patients did send their partners (more men did so). Condom use was promoted and condoms were offered but take-up rate was only 1% in rural areas; this was in contrast with take up rates in the urban area (70%).

We also evaluated the referral system from dispensaries (lowest level of peripheral health unit) where drug reserved for treatment failures (ciprofloxacin) could not be stocked. There were only 97 referrals in 2 years, but only 25 of those arrived at the referral centre — a finding that underscores the need to treat STDs at the first point of encounter with the health system.

Despite tremendous improvement in patients' management, our experience of syndromic treatment of STDs in rural highlighted the following constraints: (i) asymptomatic infections cannot be covered by an approach which relies on the self reporting of patients; (ii) some patients in rural areas still choose alternative sources of treatment, such as traditional healers or drug sellers, sometimes in combination with 'Western' medication; (iii) service delivery could be affected by staff transfers or sickness; (iv) occasional misuse of drugs was observed. The latter problem was usually overcome by regular supervision visits.

IMPACT STUDY ON HIV AND STDS[19-23]

In order to measure the impact of the programme on HIV incidence and STD prevalence and incidence a cohort of about 1,000 in the 12 matched communities was followed for two years.[19] A total of 12,534 randomly selected men and women aged 15-54 years were interviewed and tested for HIV and other STDs before the start of the intervention and two years later.[21] In order to detect any changes in sexual behaviour, an in-depth survey was randomly administered to one in every eight participants at baseline and follow-up.[22]

The main results are presented in Table 3, Figure 2 and Figure 3. At baseline, rates of HIV prevalence in the intervention and comparison communities were 3.8%

Figure 2

HIV seroconversion over two years in six paired communities,

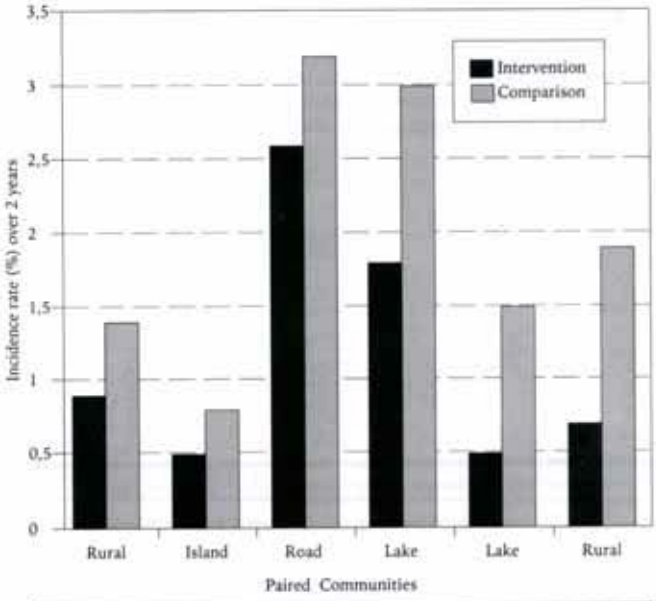
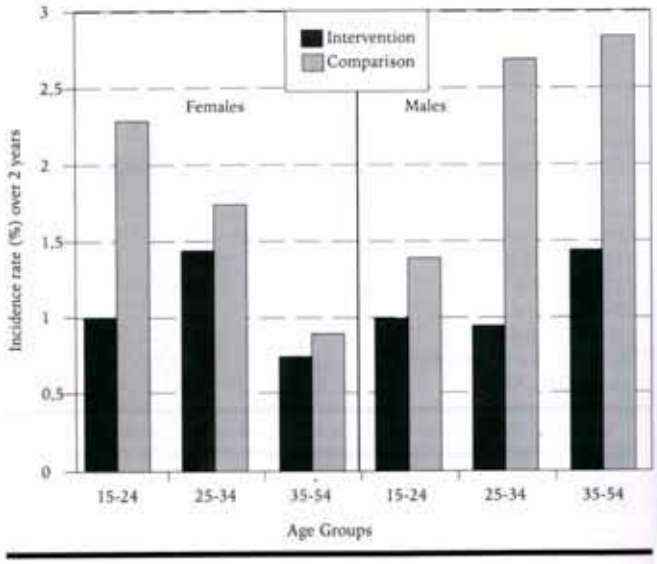


Figure 3

HIV seroconversion over two years by age, sex and community in Mwanza Region, Tanzania



and 4.4% respectively.[20] HIV seroconversion was 1.2% (48/4149) over 2 years in intervention communities and 1.9% (84/4400) in comparison communities. This corresponds to a decreased risk of seroconversion of 42% [adjusted risk ratio (RR), 0.58, P=0.007] after adjustment for age, sex, history of travel, baseline STD prevalence and male circumcision.[21]

The decreased seroconversion rate was observed for each matched-pair (Figure 2) and for all age and sex groups (Figure 3) with the largest reduction found among females aged 15-24 years and in males aged 25-34 years who represented peak incidence sub-groups.[21]

Responses to the sexual behaviour questionnaires revealed differences between men and women but not between intervention and comparison groups.[22] There was little change in number of partners (whether casual or regular) among participants in both groups between baseline and follow-up surveys. Condom use was very limited with only 2.4% of men and 2.3% of women saying that they had used a condom with an extramarital partner during the two-year follow-up period.[21]

The prevalence of serological syphilis (rapid plasma reagin [RPR] titre > 1:8 and *Treponema pallidum* haemagglutination assay [TPHA] positive) was 6.2% in both intervention and comparison communities at baseline. At follow-up it was 5.0% in the intervention communities and 7.0% in the comparison communities (adjusted RR = 0.71, P < 0.02). The prevalence of urethritis in males (defined by the presence of *N.gonorrhoeae* and/or more than 5 polymorphonuclear cells per HPF on a urethral gram smear and/or a positive *C. trachomatis* antigen-detection assay of a urethral swab) did not differ significantly between intervention and comparison groups at follow-up, but the prevalence of *symptomatic* urethritis was reduced was reduced by about 50% [adjusted RR=0.51, P=0.08] (Table 3). There was no reduction in prevalence of any STD in repeated concurrent cross-sectional studies of pregnant women attending antenatal services at the 12 health centres from the same communities (Table 3).[23]

COST EFFECTIVENESS OF STD SYNDROMIC MANAGEMENT[27]

We used the 'ingredients approach' to costing, in which estimates of the volume of inputs are multiplied by unit prices. We separated out the costs of the intervention from the research costs of the evaluation study. Capital costs accounted for about a third of the total costs. The total annual cost of the intervention was US$ 59,060 (at December 1993 prices) equivalent to US$ 0.39 per head of population served based on a catchment population of 25,000 per community. Deducting treatment costs for STDs in the comparison areas, the incremental cost of improved services was US$ 54,839.

During the 2 years of the trial, 11,632 STD cases were treated in the intervention health units implying a cost-per case treated of about US$ 10, of which US$ 2 was the cost of drugs. Using HIV incidence data from our study we estimated that 252 HIV infections were averted each year in the intervention communities, giving an incremental cost of US$ 218 per HIV infection averted.

We used the 'ingredients approach' to costing, in which estimates of the volume of inputs are multiplied by unit prices

To compute the disability-adjusted life-years (DALYs) lost through an HIV infection, we used life expectancies both for rural Tanzania and those assumed in the World Development Report[17] as well as mortality data from a study of the natural history of HIV-1 in rural Uganda,[34] a setting similar to that of rural Mwanza. We assumed that patients infected at an average age of 28 years would live an average of seven years, six years with only a slight disability, and a final year with major disabling disease. On this basis, the incremental cost per DALY saved was around US$ 9 to US$ 10. Our intervention therefore compared very favourably with other health interventions generally regarded as highly cost-effective in low-income countries, such as tuberculosis chemotherapy (US$ 3-5/DALY), measles immunization (US$ 15-19/DALY), MCH services (US$ 30-50/DALY).[17,26]

LESSONS LEARNED FROM THE MWANZA TRIAL

This is the first time a randomised trial has been used to provide empirical data on the impact and cost-effectiveness of an HIV intervention in the general population. The trial has shown that improved STD treatment in a rural African population was highly effective in reducing HIV incidence and compared favourably with other cost-effective interventions.

Treatment of STDs using the syndromic approach was an acceptable approach to both staff and patients and it was highly effective in curing STDs. Supportive supervision and on-site training were essential components to keep the system working.

The European Commission has meanwhile supported the extension of syndromic STD case management to cover almost all health units in Mwanza Region and is supporting its introduction to other Regions of Tanzania. Implementation at a much larger scale, outside the research environment, may reduce effectiveness since it may be more difficult to maintain the same level of supervision and an efficient drug supply. Costs, however, are likely to be reduced since fixed costs can be shared over a much wider population and recurrent costs do not increase linearly.

Additional STD control strategies have been added to STD control efforts in Tanzania such as screening and case finding of STDs among women attending antenatal or Maternal & Child health services following WHO guidelines for greater integration of STD services.[11,35] Although the cost-effectiveness and simplicity of syphilis screening strategies have been demonstrated,[18,36,37] few developing countries have actually put it into practice with consistency. Control of cervical infections which are often asymptomatic is proving even more problematic despite intensive research in this area[39,42] and a simple, cheap and reliable method to diagnose cervical infections is desperately lacking.[43] In some settings where prevalence of STDs is high among pregnant women, mass antimicrobial therapy has been proven to be of benefit in terms of decreased complications and low birthweight rates.[44]

Additional STD control strategies have been added to STD control efforts in Tanzania.

The trial revealed two other important findings. Firstly, young people are at particularly high risk for STD/HIV and may benefit even greater of targeted STD/HIV interventions. Yet, there have been no controlled trial to measure the effectiveness of such interventions outside industrialised countries.[45] A new community-randomized trial is underway in Mwanza Region to evaluate the impact, feasibility and cost-effectiveness of a sexual and reproductive health intervention targeting adolescents at primary school level.[46,47]

Secondly, we noted a very high rate of asymptomatic STD infections in both men and women. There is no evidence that these infections will be adequately reduced by an intervention based on voluntary report of symptoms by patients. Possible solutions may include: (i) strategies that increase partner notification of symptomatic patients; (ii) the use of simple screening tests based on non-invasive sampling, such as detection of leukocytes in urine to screen for urethritis in men;[48,49] (iii) regular STD screening or prophylactic treatment in population sub-groups at increased risk for STDs/HIV, such as commercial sex workers and their partners, people living in mining, trading or fishing centres, uniformed forces or prison inmates; (iv) mass treatment of STDs at population level.

Any of these approaches will require careful evaluation. For example, a large trial is being conducted in the Rakai district of Uganda[50] with preliminary promising results on the reduction of STDs.[51] The importance of properly conducted randomised-controlled trials to measure the impact and cost-effectiveness of health interventions that may lead to strategic health policy decisions cannot be over-emphasized.[52]

ACKNOWLEDGMENTS

The Mwanza trial was a collaborative study between the following institutions: the African Medical & Research Foundation (AMREF), Mwanza, Tanzania; the Regional Medical Office, Mwanza; the Municipal Health Office, Mwanza; the National Institute for Medical Research (NIMR), Mwanza; the London School of Hygiene & Tropical Medicine, London, UK; the Institute of Tropical Medicine, Antwerp, Belgium. Overall supervision rested with the National AIDS Control Programme of Tanzania.

The authors wish to acknowledge the work of their colleagues in Tanzania and Europe, particularly Drs. A.Buve, R.Gabone, L.Gilson, H.Grosskurth, G.ka-Gina, J.Killewo, F.Mosha, K.Mugeye, A.Nicoll, and R.Swai, Messrs. J.Changalucha, J.Cornelissen, A. Klokke, J. Newell, K.Senkoro, J.Todd, B.West, and Professors R.Hayes, M.Laga, and D.Mabey, as well as staff at Sekou Toure Hospital, Mwanza, the National Institute for Medical Research, Mwanza and the African Medical & Research Foundation (AMREF), Mwanza.

The Mwanza trial was supported by the Commission of the European Communities (DG VIII and DG XII), the Overseas Development Administration (ODA), UK, the Medical Research Council (MRC), UK and the Centre for International Migration and Development (CIM), Germany.

Address for correspondence:
Dr. Philippe Mayaud Clinical Research Unit Department of Infectious & Tropical Diseases, London School of Hygiene and Tropical Medicine. Keppel Street, London WC1E 7HT, UK tel: (0044) 171-927.2291 fax: (0044) 171-637.4314 e-mail: p.mayaud@lshtm.ac.uk

REFERENCES

1. World Health Organization (WHO). The current global situation of the HIV/AIDS pandemic. *Weekly Epidemiol Rec* 1996;71:207-08.
2. Laga M, Diallo M, Buve A. Inter-relationship of sexually transmitted diseases and HIV: where are we now? *AIDS* 1994;8(suppl 1): S119-S124.
3. Mertens TE, Hayes RJ, Smith PG. Epidemiological methods to study the interaction between human immunodeficiency virus infection and other sexually transmitted diseases. *AIDS* 1990;4:57-65.
4. Pépin J, Plummer FA, Brunham RDet al. The interaction of HIV and other sexually transmitted diseases: an opportunity for intervention. *AIDS* 1989; 3:3-9.
5. Wasserheit JN. Epidemiologic synergy: interrelationships between human immunodeficiency virus infection and other sexually transmitted diseases. *Sex Transm Dis* 1992; 19: 61-77.
6. Cameron DW, Simonsen NJ, D'Costa LJ, *et al*. Female to male transmission of human immunodeficiency virus type 1: risk factors for seroconversion in men. *Lancet* 1989;2:403-7.
7. Plummer FA/ Simonsen JN, Cameron DW, *et al*. Cofactors in male-female sexual transmission of HIV-1. *J Infect Dis* 1991;163:233-9.
8. Laga M, Manoka A, Kivuvu M, *et al*. Non-ulcerative sexually transmitted diseases as risk factor for HIV-1 transmission in women: Results from a cohort study. *AIDS* 1993;7:95-102.
9. Arya OP, Lawson JB. Sexually transmitted diseases in the tropics. *Trop Doctor* 1977;7:51-56.
10. De Schryver A, Meheus A. Epidemiology of sexually transmitted diseases: the global picture. *Bull WHO* 1990;68:639-654.
11. Piot P, Islam MQ. Sexually transmitted diseases in the 1990s. Global epidemiology and challenges for control. *Sex Transm Dis* 1994:21(2 Suppl):S7-S13.

WHO/GPA. Global prevalence and incidence of selected curable sexually transmitted diseases: overview and estimates. Geneva: WHO, 1996.

13. Muir DG, Belsey MA. Pelvic inflammatory disease and its consequences in the developing world. *Am J Obstet Gynecol* 1980;138:913-28.
14. Schulz KF, Cates W, O'Maura PR. Pregnancy loss, infant death and suffering: legacy of syphilis and gonorrhoea in Africa. *Genitourin Med* 1987;62:320-5.
15. Wasserheit J. The significance and scope of reproductive tract infections annong third world women. *Int J Gyn Obs* 1989; 3(suppl):145-163.
16. WHO/GPA. *Management of sexually transmitted diseases*. WHO/GPA/TEM/94.1, Geneva: WHO 1994.
17. World Bank. *World Development Report 1993: Investing in Health*. Oxford University Press, New York, 1993.
18. Over M, Piot P. *HIV infection and sexually transmitted diseases*. In: Jamison DT, Mosley WH, Measham AR, Borbadilla JL (eds). Disease control priorities in developing countries. New York: Oxford University Press, 1993:455-527.
19. Hayes R, Mosha F, Nicoll A, *et al*. A Community trial of the impact of improved STD treatment on the HIV epidemic in rural Tanzania: 1. Design. *AIDS* 1995;9:919-26.
20. Grosskurth H, Mosha F, Todd J, *et al*. A Community trial of the impact of improved STD treatment on the HIV epidemic in rural Tanzania: 2. Baseline survey results. *AIDS* 1995;9:927-34.
21. 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;346:530-6.
22. Quigley M, Munguti K, Grosskurth H, *et al*. Sexual behaviour patterns and other risk factors for HIV infection in a rural Tanzania: a case-control study. *AIDS* 1997;11:237-48.
23. Mayaud P, Mosha F, Todd J, *et al*. Improved treatment services significantly reduce the prevalence of sexually transmitted diseases in rural Tanzania: Results of a randomised controlled trial. *AIDS* 1997;11:1873-80.
24. Mayaud P, Cleophas B, West B, *et al*. Monitoring STD syndromic treatment effectiveness: experience of an integrated programme in Mwanza, Tanzania. Abstract 0105. International Congress of Sexually Transmitted Diseases, Seville, 19-22 Oct 1997.
25. Mwijarubi E & Mayaud P. Tanzania: integrating STD management. *Lancet* 1997;349(suppl):SIII28.
26. 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.
27. Gilson L, Mkanje R, Grosskurth *H, et al*. Cost-effectiveness of improved STD treatment services as a preventive intervention against HIV in Mwanza Region, Tanzania. *Lancet* 1997;350:1805-09.
28. Plummer FA, Nsanze H, Karasira P, *et al*. Epidemiology of chancroid and *Haemophilus ducreyi* in Nairobi Kenya. *Lancet* 1989;ii:1293-5.
29. Naamara W, Plummer F, Greenblatt RM, D'Costa LJ, Ronald AR. Treatment of chancroid with ciprofloxacin: a prospective, randomised clinical trial. *Am J Med* 1987;82(suppl 4A):317-20.
30. Van der Veen FH, Ndove I, Guindo S, *et al*. Management of STDs and cost of treatment in primary health care centres in Pikine, Senegal. *Int J STD & AIDS* 1994;5:262-267.
31. WHO/GPA (Islam, M). Analysis of the cost-effectiveness of approaches to STD. Informal Technical Working Group Meeting on STD Activities in GPA. Agenda Item No. TV. Background Paper No. 4, Geneva, February 1993.
32. Barongo LR, Borgdorff MW, Mosha FF, *et al*. The epidemiology of HIV-1 infection in urban areas, roadside settlements and rural villages in Mwanza Region, Tanzania. *AIDS* 1992;6:1521-8.
33. Hanson S, Sunkutu RM, Kamanga J, *et al*. STD care in Zambia: an evaluation of the guidelines for case management through a syndromic approach. *Int J STD & AIDS* 1996;7:324-32.
34. Mulder DW. The epidemiology of HIV-1 in a rural Ugandan population. Proefschrift ter verkrijging can de graad van doctor aan de Erasmus Universiteit Rotterdam. Rotterdam, 1996:108.
35. WHO/GPA (Van Praag, E). Provision of STD services in Maternal and Child Health and Family Plarming settings. Informal Technical Working Group Meeting on STD Activities in GPA. Agenda Item No. IV. Background Paper No. 7, Geneva, February 1993.
36. Hira S, Bhat GJ, Chikamata DM, *et al*. Syphilis intervention in pregnancy: Zambian demonstration project. *Genitourin Med* 1990; 66: 159-164.
37. Temmerman M, Mohamedali F & Fransen L. Syphilis prevention in pregnancy: an opportunity to improve reproductive and child health in Kenya. *Health Pol & Plan* 1993; 8(2):122-7.
38. 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 Inf Dis* 1993;17:82-8.
39. Thomas T, Choudhri S, Kariuki C, Moses S. Identifying cervical infection among pregnant women in Nairobi, Kenya: limitations of risk-assessment and symptom-based approaches. *Genitourin Med* 1996;72:334-8.
40. Mayaud P, Grosskurth H, Changalucha J, *et al*. Risk assessment and other screening options for gonorrhoea and chlamydial infections in women attending rural Tanzanian antenatal clinics. *Bull WHO* 1995;73 (5):621-630.
41. Mayaud P, ka-Gina G, Cornelissen J, *et al*. Validation of a WHO algorithm with risk-assessment for the clinical management of vaginal discharge in Mwanza, Tanzania. *Suppl. Sex Transm Inf* (former *Genitourin Med*), 1998 (in press).
42. Mayaud P, Uledi E, Cornelissen J, *et al*. Risk scores to detect cervical infections in urban antenatal clinic attenders in Mwanza, Tanzania. *Suppl. Sex Transm Inf* (former *Genitourin Med*), 1998 (in press).
43. Chernesky M. How can industry, academia, public health authorities and the Sexually Transmitted Diagnostics Initiative (SDI) work together to help control sexually transmitted diseases in developing countries? *Sex Transm Dis* 1997;24 (2):61-3 and *Genitourin Med* 1997;73:1-2
44. Temmerman M, Njagi E, Nagelkerke N, *et al*. Mass antimicrobial treatment in pregnancy: A randomized, placebo-controlled trial in a population with high risk of sexually transmitted diseases. *J Reprod Med* 1995;40:176-80.
45. Oakley A, Fullerton D, Holland J, *et al*. Sexual health education interventions for young people: a methodological review. *BMJ* 1995; 310: 158-62.
46. Nyamwaya D, Biseko S, Gabone R, *et al*. Prevention of HIV infection and enhancement of reproductive health among adolescents in rural Tanzania: a community randomised trial. Part 1: Rational and design of the intervention. Abstract 543 International Congress of Sexually Transmitted Diseases, Seville, 19-22 Oct 1997.
47. Obasi A, Biseko S, Gabone R, *et al*. Prevention of HIV infection and enhancement of reproductive health among adolescents in rural Tanzania: a community randomised trial. Part 2: Design of the impact evaluation. Abstract 544. International Congress of Sexually Transmitted Diseases, Seville, 19-22 Oct 1997.
48. Mayaud P, Changalucha J, Grosskurth*H, et al*. The value of urine specimens in screening for male urethritis and its microbial aetiologies in Tanzania. *Genitourin Med* 1992;68:361-5.
49. Watson-Jones D, Buve A, Mosha *F, et al*. Is asymptomatic urethritis in men an obstacle to effective STD control? A community study in Mwanza, Tanzania. (Oral presentation) Abstract MoC341. XIth International AIDS Conference, Vancouver, July 7-12, 1996.
50. Waver M, Gray RH, Ouinn TC. AIDS intervention in Uganda [letter]. *Scienze.* 1995; 270: 564.
51. Waver MJ, Sewankambo NK, Gray RH, *et al*. Community-based trial of STD control for AIDS prevention, Rakai district, Uganda. Abstract 540. International Congress of Transmitted Diseases, Seville, 19-22 Oct 1997.
52. Hayes R. Waver M, Gray Rr *et al*. Randomized trials of STD treatment for HIV prevention: report of an international workshop. *Genitourin Med* 1997;73:432-43.