



# HIV/AIDS & STI NEWS

From the DFID Knowledge Programme on HIV/AIDS & STI

**MRC**  
Medical Research Council

No. 3, October 2002

## From the editorial board



This is the **third newsletter** from the DFID\* Knowledge Programme on HIV/AIDS and STIs. The Programme is funded by the Department for International Development, UK, and based at the London School of Hygiene and Tropical Medicine (LSHTM) and the Medical Research Council (MRC), Social and Public Health Sciences Unit, University of Glasgow. It has five areas of research: 1) Determinants of sexual behaviour; 2) Biological risk factors for HIV and STI transmission; 3) Factors affecting use and effectiveness of care and prevention services for HIV/AIDS and STIs; 4) Impact and cost-effectiveness of interventions against HIV and STIs; and 5) HIV/AIDS and STI prevention and care priorities and policies.

These newsletters provide a forum for the exchange of research within the Programme and introduce other relevant research from Programme members. They form a useful means to exchange information such as updates on projects underway, conferences, new grants, etc. Initially, the selected articles reflect the contents of our bi-annual scientific meetings

in London or Glasgow, but contributions from Programme members are invited. Please email your suggestions and comments to: [Tamsin.Kelk@lshtm.ac.uk](mailto:Tamsin.Kelk@lshtm.ac.uk). Also see the Programme's website: <http://www.lshtm.ac.uk/dfid/aids/>

*Philippe Mayaud, David Mabey, Graham Hart and Tamsin Kelk*

## In this issue

- **STI prevention and care:** including emerging issues in STI care; syphilis and pregnancy outcome; behavioural research for HIV/STI prevention and control; and the integration of STI care into reproductive health services.

- **New Programme Publications**

Newsletter editor: Tamsin Kelk, Health Policy Unit, London School of Hygiene and Tropical Medicine, Keppel Street, London, WC1E 7HT, UK. Email: [Tamsin.Kelk@lshtm.ac.uk](mailto:Tamsin.Kelk@lshtm.ac.uk)

# STI prevention and care

## Introduction

The prevention and care of STIs is of significant public health importance in decreasing the complications and sequelae of STI, decreasing prevalence and incidence of STI and decreasing HIV incidence. The role of health services in STI control is:

- To provide correct diagnosis, correct treatment and enhance treatment completion of those seeking care;
- To reach those aware and worried but not seeking care;
- To reach those with asymptomatic STIs, or those with STIs but unaware of their condition;
- To prevent STI among those uninfected.

The *integration* of STI care and prevention into primary health care services is an important strategy promoted by many agencies, which, however, deserves evaluation.

The Knowledge Programme (KP) is conducting research on several aspects of STI control, both in terms of development and evaluation of the impact and cost-effectiveness of these interventions, as well as operational research to monitor the performance of STI control strategies in "real-life situations" (KP Outputs 1, 3, 4 & 5). Some of this ongoing research is presented here.

## Emerging issues in STI care

There are several challenges facing STI control:

- 1) Selection of an appropriate and effective case management approach according to context, 2) Developing suitable diagnostic tests, 3) Evaluation of new drugs and new treatment approaches, and 4) Monitoring drug effectiveness.

### 1. STI case management

Syndromic management (SM) is a key STI management strategy promoted by the WHO. It provides immediate and

standardized treatment, has proven validity and cost-effectiveness, *but* it can result in over-treatment, its acceptability is often challenged by the medical establishment and thus, it has to be adapted to context. **Formative and operational research, and evaluation studies** are essential.

Despite its value, SM is not yet widely applied in many countries that would need it, particularly in those which are experiencing fast-growing epidemics of STI and HIV, such as China, India and former Eastern European countries. Moreover, the epidemiological contexts are constantly changing, prompting the need for regular re-evaluation of the algorithms. The KP is therefore involved in several studies seeking to (re)evaluate various STI algorithms, including their feasibility and cost-effectiveness.

### Genital Ulcer Syndrome (GUS) evaluation studies

SM has been effective in the management of GUS where bacterial infections such as *Treponema pallidum* (TP, causing syphilis) and *Haemophilus ducreyi* (HD, causing chancroid) are prevalent. However, recent data have shown that the proportion of *Herpes simplex virus* type 2 (HSV-2) has been increasing in many developing countries, particularly in areas of high HIV prevalence, resulting in increasing treatment failures. Initially, WHO's GUS algorithms recommended simultaneous treatment of syphilis and chancroid, with the addition, from 1994, of a separate genital herpes management arm, based on typical clinical presentation (vesicles) and history of recurrences, as hallmark features of genital herpes. The WHO recommendations did not include dispensation of expensive antivirals (i.e. acyclovir).

The KP has supported studies of GUS aetiologies in Uganda and China in 2000-01, using sensitive multiplex polymerase chain reaction (PCR) assays, seeking to evaluate the WHO algorithms, and possibly alternative ones. In Uganda, a study by the MRC in Masaka found that a minority

of 150 ulcers were caused by TP or HD (6% of all aetiologies), whilst HSV-2 was found in nearly 50% of cases and 31% of ulcers had no identifiable causes. Many ulcers were also infected with common bacteria, such as staphylococci. The WHO 1991 and 1994 algorithms appeared inappropriate and would result in over-treatment. A cost-effectiveness analysis of various algorithms will be undertaken.

In China, a study in two provinces among 227 GUS patients did not find a single case of chancroid, with syphilis (50%) and HSV (32%) being the dominant aetiologies. However, the most recent WHO algorithm with a separate arm for management of herpes would miss 11% of cases of syphilis, due to combined infections with HSV.

Based on these and other studies' findings, a WHO Expert Meeting in November 2001 recommended revisions of the GUS algorithm, which should combine herpes management (using acyclovir) with that of syphilis and chancroid, in areas where HSV may constitute >30% of GUS aetiologies. Aetiological studies and operational evaluation of the new algorithm will be an important priority for WHO. Since HSV may be particularly prevalent among HIV+ patients, management of GUS patients should provide an opportunity to promote HIV voluntary confidential counselling and testing services.

### Genital discharge (GDS) evaluation studies

The current algorithm (WHO 1999) for management of vaginal discharge recommends the use of risk assessment for the management of cervical infections with *N gonorrhoeae* (NG) and *C trachomatis* (CT), based on a combination of the factors: age <21, single, >1 partner in last 3 months, new partner in last 3 months, partner symptomatic.

In 3 studies in Uganda, The Gambia, and Bulgaria (the latter by Médecins Sans Frontières Switzerland), supported by the KP, cervical infections (NG/CT) were found in 9–11% of women presenting with vaginal discharge. In all studies, vaginal infections constituted the majority of infections (70%), with bacterial vaginosis (BV) being the most prevalent condition (32–48%).

| Prevalence of STI pathogens |                     |                     |                       |
|-----------------------------|---------------------|---------------------|-----------------------|
|                             | Uganda<br>F (n=177) | Gambia<br>F (n=226) | Bulgaria<br>F (n=296) |
| NG                          | 9.4                 | 6.3                 | 0.7                   |
| CT                          | 0.6                 | 4.5                 | 8.8                   |
| TV                          | 28.2                | 11.1                | 3.4                   |
| CA                          | 26.1                | 37.6                | 19.9                  |
| BV                          | 48.1                | 47.9                | 32.8                  |
| Multiple                    | 33.9                |                     | 4.0                   |
| No aetiology                | 27.7                |                     | 44.0                  |
| Syphilis                    | NA                  | 2.3                 | 2.7                   |
| HIV                         | NA                  | 12.4                | 0                     |

Risk factors for NG/CT infections varied by locality and a single risk-assessment strategy cannot fit all local contexts. Cost-effectiveness and operation feasibility studies will be useful for policy advocacy in Bulgaria. These findings were broadly in line with findings in many other parts of the world in similar populations (i.e. not directly high-risk populations such as sex workers, in whom NG/CT prevalence may be higher). Thus, adaptation of WHO algorithms to the local epidemiological context local is of paramount importance. The role of *Mycoplasma* spp. should be considered in expanded definitions of cervical infections in further studies.

### 2. STI diagnostics

Rapid point-of-care (POC) diagnostic tests are needed due to the high prevalence of asymptomatic STI (NG, CT), the lack of lab facilities in many 'first contact' clinics, and as a possible aid to case management. The ideal STI diagnostic test should be: sensitive; specific; easy to perform; rapid; stable; non-invasive;

affordable; and require none/minimal equipment and internal quality control. We collaborate with the STD Diagnostics Initiative of the WHO in several ways to develop and test such POC tests.

### Research focus of the KP

- *Mathematical modelling* – to predict cost-effectiveness and impact of POC tests depending on levels of prevalence and test characteristics (studies by Watts, Alary et al).
- *Test development* – NG and CT are the priority; for syphilis, using whole blood, and ability to distinguish between active and previous infection.
- *Test evaluation* – several KP partners have been selected as WHO SDI testing sites to conduct field evaluation of rapid POC (syphilis mainly). In addition, colleagues in The Gambia have evaluated the FemExam® (Litmus Concept, CA, USA) test for bacterial vaginosis (BV). FemExam® is a rapid colorimetric assay using two plastic cards for detection of elevated pH, amines and presence of *Gardnerella*. The study among 492 rural women (BV prevalence 38%) and 220 STI female clinic attenders (BV prevalence 48%) found the cards' sensitivity and specificity to be equivalent to that of conventional Amsel's clinical criteria, compared to a gold standard diagnosis of BV by Nugent score. The cards have the advantage of being rapid, less subjective and easily performed. Cutting their cost to \$1/card would provide wider accessibility.

### 3. New STI drugs and new treatment approaches

Studies supported by the KP are underway (or planned) on:

- Syphilis – RCT of azithromycin for primary and latent syphilis in a cohort of sex workers in Mbeya, Tanzania (Riedner, Grosskurth et al.)
- Herpes – RCT of acyclovir for episodic treatment of GUS in addition to syndromic management in Ghana and Central African Republic (Belec, Mayaud et al.)
- Gonorrhoea and Chlamydia – RCT of presumptive periodic treatment with azithromycin in a cohort of sex workers in Ghana and Benin (Alary, Pepin et al.)
- Vaginal infections (planned studies) – RCT of metronidazole (MTZ) for male partner management in Ghana (Adu-Sarkodie et al.); possible RCT of MTZ during pregnancy in The Gambia.

### 4. Monitoring STI drug effectiveness

STI case management depends on effective treatment regimens. The Gonococcal Antimicrobial Susceptibility Programme (GASP) was created by WHO in 1990 to monitor patterns and trends in NG susceptibility. GASP has had success in the American, Western Pacific and SE Asian regions of WHO, but not in Africa where antimicrobial resistance of NG to common antibiotics is high.

**GASP-WAR** (the West African Region network) is an initiative by Senegal (PNLS) and The Gambia (MRC), supported by the KP. An initial workshop was held in The Gambia (September 2001) involving Benin, Burkina Faso, Gambia, Ghana, Liberia, Nigeria, Senegal and Togo, and the network was later joined by Mali and Cote d'Ivoire. Next steps include: capacity building and needs assessment; conducting and analysing surveys; developing email/website/newsletter; linking with other regional/international networks.

*Philippe Mayaud (Clinical Research Unit, LSHTM)*

### Publications

- Mabey D et al (2001) Rapid and simple point of care diagnostics for STIs. *Sex Transm Inf*, 77: 397-401.
- Mayaud P et al (2002) GASP-WAR: West African network to tackle gonorrhoea. *Lancet*; 359: 173.
- West B et al. Evaluation of a new rapid diagnostic kit (FemExam®) for bacterial vaginosis in patients with vaginal discharge syndrome in The Gambia. *Sex Transm Dis* (in press).

### Syphilis and pregnancy outcome in Mwanza, Tanzania

In some parts of Africa, over 5% of antenatal clinic (ANC) attenders have syphilis. Screening for syphilis with the Rapid Plasma Reagin (RPR) test is simple and cheap, but is not done in most ANC clinics in much of Africa. Syphilis can cause stillbirth, low birth weight and premature delivery. The impact on pregnancy outcome of the WHO-recommended treatment, single dose benzathine penicillin, has not been evaluated.

This study aimed at determining: 1) the proportion of adverse pregnancy outcomes due to syphilis in Mwanza, and 2) whether a single dose of benzathine penicillin prevents adverse pregnancy outcomes due to syphilis. It involved: 1) a case-control study of women delivering in 3 hospitals in Mwanza Region who had not been screened for syphilis, and 2) a prospective study of pregnant women attending 2 ANC clinics in Mwanza Region, screened on site and treated with single dose benzathine penicillin if they were RPR-positive.

In the first study (retrospective), 1809 previously unscreened women were tested, of whom 144 (8%) were RPR+. 138 RPR+ and 242 RPR- women were recruited in the case control study. Syphilis was found responsible for:

- 11% of low birth weight deliveries
- 23% of pre-term births
- 50% of stillbirths
- 17% of all adverse pregnancy outcomes.

In the prospective study, 19,878 ANC clinic attenders were screened, of whom 1522 were RPR+ (7.7%). 556 RPR+ and 1127 RPR- women were recruited and their pregnancies were dated by ultrasound. RPR+ women were treated with benzathine penicillin 2.4m units IM-STAT. Other STIs were treated according to Tanzanian national guidelines. Results were as follows:

|           | Total | Adverse outcome | OR   | 95% CI   |
|-----------|-------|-----------------|------|----------|
| RPR-      | 826   | 17%             | 1    |          |
| RPR+ ≥1:8 | 99    | 15%             | 0.85 | 0.5 -1.5 |
| RPR+ <1:8 | 204   | 15%             | 0.86 | 0.6 -1.3 |
|           | Total | Stillbirth      | OR   | 95% CI   |
| RPR-      | 950   | 2.5%            | 1    |          |
| RPR+ ≥1:8 | 133   | 2.3%            | 0.89 | 0.3-3.0  |
| RPR+ <1:8 | 249   | 4.8%            | 1.95 | 0.96-4.0 |

### Conclusions

In Mwanza Region, syphilis is responsible for 50% of stillbirths and 17% of all adverse pregnancy outcomes in unscreened women. A single intramuscular dose of benzathine penicillin 2.4 million units reduces the risk of stillbirth to that seen in uninfected women. Syphilis screening and treatment should be included in programmes for the prevention of mother-to-child-transfer of HIV.

*Debby Watson-Jones (Clinical Research Unit, LSHTM)*

### Publications

Watson-Jones D et al (2002) Syphilis in pregnancy in Tanzania. I. Impact of maternal syphilis on outcome of pregnancy. *J Infect Dis* 186: 940-7.

Watson-Jones D et al (2002) Syphilis in pregnancy in Tanzania. II. The effectiveness of antenatal syphilis screening and single dose benzathine penicillin treatment for the prevention of adverse pregnancy outcomes. *J Infect Dis* 186: 948-57.

### Behavioural research for HIV/STI prevention and control in the Caribbean

It is estimated that nearly 2% aged 15-49 in the Caribbean are infected with HIV, the highest rate in the Western hemisphere and second highest in the world after sub-Saharan Africa. Transmission is primarily heterosexual. The female/male ratio

and proportion of perinatal transmission is the highest outside sub-Saharan Africa. HIV/AIDS is the leading cause of death in 25-44 year olds. Accordingly, the Special Programme on STI and HIV/AIDS within the Caribbean Epidemiology Centre (CAREC) has been supporting research and intervention programmes. One study took place in Guyana, one of the countries with the highest HIV prevalence in the Caribbean.

### HIV infection and risk practices among female sex workers in Georgetown, Guyana

The objectives of the survey were: to estimate the prevalence of HIV and behaviours associated with HIV risk among female sex workers (FSW) in Georgetown, to provide IEC for FSW, and to design interventions for and with FSW.

Research methods included: recruitment of study subjects (n=299) through snowballing sampling during day and night sessions; structured in-depth interview; HIV anonymous but linked testing using oral fluid. Red Thread (a women's NGO) trained sex workers as fieldworkers and supervised fieldwork.

### Results

HIV prevalence was 3%. Regarding *sexual behaviour*, in reported condom use, 84% "always use" condoms with clients; 91% used a condom during last intercourse with a client; and 37% "always use" condoms with boyfriend, husband or regular partner. But, only 45% showed a condom to the interviewer and 9% had sex with the last client who refused to use a condom. Regarding *substance use and abuse*, in the past 12 months, 7% had exchanged sex for drugs and 1% had used injectable drugs.

*Factors statistically associated with HIV status were:*

*Work location:* women living downtown (poorer area) were more likely to be HIV+ than those uptown (36.2 vs. 13.3%).

*Client pick-up location:* street and brothel based workers had a higher rate of HIV than those finding clients in discos/elsewhere (37.2 vs. 15.5%).

*Alcohol use:* women who regularly get high on alcohol were more likely to be HIV+ (51.2 vs. 28.2%).

*Coke/crack use:* women who have used crack cocaine were more likely to be HIV+ (45.3 vs. 27.1%).

*Anal sex:* women who have had anal sex were more likely to be HIV+ (42.9 vs. 29.2%).

*Syphilis:* those who reported having treatment for syphilis in the last year had a higher rate of HIV (52.9 vs. 28.6%).

### Conclusions

- Training sex workers to conduct research, and use of oral fluid sampling were both successful research strategies.
- Interventions targeting FSW on the streets and in hotels/brothels should be sustained. Periodic screening and treatment of STIs among FSW may reduce the incidence of STI and HIV. Sexual health promotion should address the dangers of anal sex.
- Joint prevention/care strategies should be developed between providers of substance abuse/addiction and HIV-related services.

*Caroline Allen (MRC Glasgow)*

### Integration of STI care in reproductive health services in Tanzania

In an integrated system, essential curative and preventive services should be available to a client in one visit. The question is, can "integration" close the gap between the current state of services and the goal of comprehensive quality reproductive health (RH) care? This study, conducted in 9 districts over 3 regions of Tanzania, aimed at better understanding the barriers and opportunities that inhibit or promote the provision of comprehensive RH services and STI care.

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### Barriers to the provision of comprehensive RH care:

**Lack of supplies:** for family planning (FP) methods, STI drugs, syphilis RPR testing kits.

**Organisation of space:** In 9 health facilities examined there were 86 rooms, 76 of which were used for patient care (58% adequate for physical examination), of which only 24 were attributed for a range of RH services, but not simultaneously.

**Time management:** Client flow analyses revealed that patients spend on average 70 minutes at the health care facility, with only 7 minutes of direct contact with at least one clinician, having queued on average twice for clinical care. Little time was actually spent by clinicians on RH care on a daily basis (10-15 minutes/day/trained health worker).

**Training:** No facilities had a staff member trained in all aspects of RH care (ie from FP to STI care and ANC/MCH care). Nurses represented 17% of staff trained in STI care and 73% of staff trained in RPR testing.

**Supervision:** A frequent shortcoming found our research. As one clinical officer put it: "Supervision is helpful when they bring us new ideas and teach us things we did not know... But sometimes they just come...and sign the book and continue their supervision trip."

**Incomplete care:** Over 1000 clinical outpatient (OPD), ANC and STI encounters were observed. Personal details, general symptoms and parity were taken in nearly all cases; relevant history was taken in nearly 60%, particularly for obstetric or FP risk factors, but sexual or RH history were collected only in 30%, and specific STI risk factors in under 10% of consultations. Regarding physical examinations, ANC clients were most likely to be examined (77%), with STI, OPD and FP clients considerably less so (37%, 32%, 9%, respectively).

**Partner notification:** Of 30 STI observations, 23 (77%) received information on partner notification, 14 (44%) received notification slips. From a total of 1127 STI cases across 9 sites in 4 months, 202 (18%) contact males and 112 (10%) contact females were treated.

**Condom promotion:** Condoms were seldom discussed or provided. An average of 6.1 (range 0-19.5) condoms are distributed to FP clients per month.

**Where do men go for care?** Men form the majority of clients in private pharmacies - due to secrecy, speed, proximity and their easier access to cash (compared to women). But, 77% of pharmacies are primarily attended by a nurse auxiliary or attendant; no attendants are trained in STI syndromic management.

### Opportunities for the provision of comprehensive RH care:

**Pre-service training schools and tutors** are in place and can be strengthened through support to tutors and new training approaches.

**Sufficient workforce exists for service provision** but motivation is lacking. Living wages, time management training and core incentives are needed.

**Overwhelming agreement exists among all stakeholders that supervision needs enhancing** – it must be ongoing, regular and comprehensive; role of district management teams.

**Qualified staff are in place to be utilised to their full potential** – using prescriptive authority Nursing Officers and Nurse Midwives to increase access to comprehensive care.

**Community is keen to take responsibility in overseeing aspects of the health services** – e.g. facility infrastructure and cost sharing; partnership in health.

**Men want to re-address the imbalance in their access to RH care and information** – focus on providing men with access to quality preventive/curative STI care in places they choose to go.

**Policy arena is opening up to new voices** – civil society groups and grass-root NGOs can play a major role in conveying community views to decision-makers and donors.

Monique Oliff (Clinical Research Unit, LSHTM)

### Publications

Oliff M (2002) DrPH thesis. Evaluation of the integration of sexually transmitted diseases/infection services within reproductive health services in Tanzania: an analysis of barriers and achievements. University of London.

Oliff M et al. Corn, cattle, coconuts, and condoms. Video of the project.

### Useful websites

AIDS Treatment News internet directory:  
<http://www.aidsnews.org>

International Union against STIs (IUSTI): <http://www.iusti.org>  
Medical Society Study Venereal Diseases (MSSVD), UK:  
<http://www.mssvd.org>

World Health Organization, Dept of HIV/AIDS:  
[http://www.who.int/HIV\\_AIDS/](http://www.who.int/HIV_AIDS/)

### Selected New Publications

Elwy AR, Hart GJ, Hawkes S, Petticrew M (2002) Effectiveness of interventions to prevent sexually transmitted infections and human immunodeficiency virus in heterosexual men: a systematic review. *Arch Intern Med* 9: 1818-30. *Research Output No. 4*

Hong S, Xin C, Qianhong Y, Yanan W, Wenyan X, Peeling RW, Mabey D (2002) Pelvic inflammatory disease in the Peoples' Republic of China: aetiology and management. *Int J STD AIDS* 13: 568-72. *Research Output No. 3*

Korenromp EL, Bakker R, de Vlas SJ, Robinson NJ, Hayes R, Habbema JD (2002) Can behaviour change explain increases in the proportion of genital ulcers attributable to herpes in sub-Saharan Africa? A simulation modelling study. *Sex Transm Dis* 29: 228-38. *Research Outputs Nos. 1 and 5*

Mabey D, Richens (2002) Sexually transmitted infections. In: Cook GC, Zumla A (eds). *Manson's Tropical Diseases*, 21st edition. London: WB Saunders. *Research Output No. 3*

Wang QQ, Peeling RW, Mabey D et al (2002) Validation of syndromic algorithm for the management of genital ulcer diseases in China. *Int J STD AIDS* 13: 469-74. *Research Output No. 4*

Watts C, Zimmerman C (2002) Violence against women: global scope and magnitude. *Lancet* 359: 1232-7. *Research Output No. 1*

*Details of Programme research areas are given on page 1. A more extensive list of publications is available on our website: <http://www.lshtm.ac.uk/dfid/aids/>*

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Name \_\_\_\_\_ Email: \_\_\_\_\_

Mailing address \_\_\_\_\_