

DFID KNOWLEDGE PROGRAMME ON HIV/AIDS & STIs

COUNTRY RESEARCH

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Global

Title	<i>UNAIDS 5-year Evaluation</i>
Country	Global
LSHTM staff	Louisiana Lush, Patrick Vaughan, Charlotte Watts, Lilani Kumaranayake
Collaborators	ITAD, UK; KIT, Amsterdam
Funding	UNAIDS
Dates	September 2001 – September 2002

Summary

Thematic study of comparative global programmes to learn lessons for UNAIDS' governance and management. Participation in evaluation methodology development and country visits.

Title	<i>Enhancing access to antiretrovirals and other aspects of HIV/AIDS care</i>
Country	Global
LSHTM staff	Louisiana Lush
Collaborators	Royal Institute of International Affairs
Funding	DFID

Summary

As part of DFID AIDS/STI programme, analysis of political background to current international debate around enhancing access to drugs, with antiretrovirals at the centre. Paper written and conference on access to essential medicines organised jointly with the Royal Institute of International Affairs at Chatham House. Further work underway to investigate the role of private resources in enhancing access, including through public-private partnerships.

Sub-Saharan Africa

Title *Meta-analysis of male circumcision and HIV risk in sub-Saharan Africa*

LSHTM staff Helen Weiss, Maria Quigley, Richard Hayes

Funding UNAIDS

Summary

The hypothesis that male circumcision may reduce the risk of acquiring HIV infection was first suggested early in the HIV epidemic, and many epidemiological studies have since included circumcision status as a potential risk factor in studies of HIV infection. To evaluate the cumulative evidence for this association, a systematic literature review of studies was carried out. Papers including circumcision as a risk factor for HIV-1 infection among males in sub-Saharan Africa and published up to April 1999 were included. A random-effects meta-analysis was used to calculate a pooled relative risk (RR) and 95% confidence interval (CI) for all studies combined, and stratified by type of study population. Further analyses were conducted among those studies that adjusted for potential confounding factors.

A total of 27 studies were included. Of these, 21 showed a reduced risk of HIV among circumcised men. HIV risk among circumcised men was around half that in uncircumcised men (crude RR=0.52, CI 0.40-0.68). In the 15 studies that adjusted for potential confounding factors, the association was even stronger (adjusted RR=0.42, CI 0.34-0.54). The association was stronger among men at high risk of HIV (crude RR 0.27; adjusted RR=0.29, CI 0.20-0.41) than among men in general populations (crude RR 0.93; adjusted RR=0.56, CI 0.44-0.70).

The results show that male circumcision is associated with a significantly reduced risk of HIV infection among men in sub-Saharan Africa, particularly among men at high risk of HIV. These results suggest that consideration should be given to the acceptability and feasibility of providing safe services for male circumcision as an additional HIV prevention strategy in areas of Africa where men do not traditionally circumcise.

Benin – see also Kenya

Title	<i>Periodic presumptive treatment of sexually transmitted infections among female sex workers: a multicenter trial</i>
Countries	Benin and Ghana
LSHTM staff	Philippe Mayaud, David Mabey
Collaborators	Benin site (Annie-Claude Labbé, Honoré Meda, Cyriaque Gnintoungbe) Ghana site (Khonde Nzambi, Comfort Asamoah-Adu, Agnes Dzokoto) Centre hospitalier <i>affilié</i> universitaire de Québec, Université Laval, Canada (Michel Alary) Centre for International Health, Université de Sherbrooke, Canada (Jacques Pépin)
Funding	Canadian Agency for International Development (CIDA) and DFID
Dates	April 2001 – March 2002

Summary

In West Africa, female sex workers (FSW) and their clients constitute important core groups in the transmission of STI. There are no easy method to detect and screen common STI such as *Neisseria gonorrhoeae* (NG) and *Chlamydia trachomatis* (CT) in these groups. Treatment relies on the syndromic approach, which require that infected individuals at least display symptoms and signs, but these infections are often symptomless. An alternative approach, presumptive treatment, does not rely on diagnostic tests and offers the possibility of selecting core groups with high rates of both STIs and sexual partner change. This approach has been successfully used for syphilis control, but very few studies on selective treatment of NG and CT have been conducted:

The study is a community-randomised double-blinded placebo-controlled trial of periodic presumptive treatment (PPT) of NG/CT administered monthly for 9 months to FSWs in Benin and Ghana with the aims to determine the impact of this strategy on:

- NG/CT prevalence among the FSWs (main outcome)
- NG/CT prevalence among clients in the same areas
- HIV incidence among FSW
- bacterial drug resistance (antibiotics to be used are: ciprofloxacin and azithromycin).

Main results/outcomes

The project started by determination of sites for inclusion and preliminary clients study in January 2001 in Benin and October 2001 in Ghana. Baseline STI prevalence survey among FSW and enrolment in the trial and measurement of NG/CT prevalence started in April 2001 in Benin and December 2001 in Ghana. The project was completed in August 2002 and final analysis is taking place.

Brazil – see also Morocco

Title	<i>Molecular epidemiology of Human Herpes virus 8 (HHV-8) in AIDS associated Kaposi's sarcoma in Brazil</i>
Country	Brazil (Sao Paulo, Salvador, Manaus)
LSHTM staff	Philippe Mayaud, Helen Weiss
Collaborators	Maria Claudia Nascimento (PhD student), Claudio Pannuti (University of Sao Paulo Medical School, Brazil), Chris Boshoff (Wolfson Institute for Biomedical Research, University College London)
Funding	PhD support for MCN obtained for 4 years – Supported by CNPq (Brazil)
Dates	September 2000 – August 2004

Summary

Human herpes virus HHV-8 and strain variants have been identified in all clinical forms of Kaposi's sarcoma (KS) (classic, endemic, iatrogenic and epidemic- or AIDS-associated). KS is the most frequent cancer associated with HIV. However, the precise routes of transmission, strain classification and epidemiology of HHV-8 have not been studied extensively.

Given its extraordinary ethnic diversity, Brazil provides a unique opportunity to study HHV-8 strain variants in different populations. The study will try to characterise the main HHV-8 variants found in various subgroups in separate geographical locations, from various ethnic backgrounds, with or without HIV, and with or without AIDS-KS. The study will use novel serological techniques to detect anti-HHV-8 antibodies (or to screen for HHV-8 infection). The genetic diversity of HHV-8 will be analysed in different geographic regions of Brazil.

Preliminary results

A molecular analysis of 83 KS biopsies from AIDS patients in Sao Paulo has enabled us to type and classify the main circulating HHV-8 strains among AIDS patients in the southeast of Brazil. HHV-8 strains were also isolated and typed in peripheral blood of AIDS and renal transplant patients, enabling further large-scale epidemiological studies of HHV-8 using blood samples.

The study will now be extended to the Northeast (Bahia) and Amazonian regions of Brazil. The research will focus on determining the HHV-8 seroprevalence and risk factors for HHV-8 among blood donors in three Brazilian centres (Sao Paulo, Salvador and Manaus), and on determining HHV-8 molecular subtypes among AIDS patients with or without KS in those three centres.

Bulgaria

Title	<i>Evaluation of performance, costs and acceptability of different management approaches to vaginal discharge in Sofia, Bulgaria</i>
Country	Bulgaria
LSHTM staff	Philippe Mayaud, Fern Terris-Prestholt
Collaborators	Nadine Cornier and Arnaud Janin (Médecins Sans Frontières [MSF], Switzerland and Belgium), Philippe Cavailler (Epicentre, France and MSF Switzerland)
Funding	Swiss Cooperation, MSF
Dates	2001 – 2004

Summary

Background

Bulgaria has been experiencing tremendous sociological and structural changes rapidly which have affected the health sector. STI are soaring and STI management relies on outdated vertical and stigmatising public health services, whilst the simplified WHO-promoted syndromic approach is still resisted by many health professionals. MSF has been supporting the establishment of a model STI clinic in Sofia, which aims to offer confidential and quality reproductive and sexual health services to marginalised populations (gypsies, male and female sex workers, drug users), and Bulgarian youth.

Aims

Research will be conducted by the MSF team to evaluate the burden of STI and the operational and economic performance of syndromic management and current STI management practices in the Bulgarian context, through a series of studies:

- providing baseline information on the prevalence and risk factors of different STI at the MSF clinic
- evaluating the validity of various algorithms for the management of vaginal discharge and detection of cervical infections among symptomatic women presenting to the clinic
- evaluating the costs of the various approaches from the various providers perspective (MSF and Bulgarian public health system)
- evaluating the acceptability of syndromic management from the patients and providers' perspectives.

Preliminary results for study 1

Between September 2001 and July 2002, 424 women with confirmed vaginal discharge were enrolled in these studies. The prevalence of cervical infections (N gonorrhoeae and/or C trachomatis) was 9.5% and those of vaginal infections were: 2.5% for trichomoniasis, 35.5% for bacterial vaginosis, and 23% for candidiasis. In addition, 2.5% of women had active syphilis and 38% of women were found to harbour human papilloma virus (HPV) strains, most of which were of oncogenic types. 32 (27%) of 118 women with HPV had evidence of cervical dysplasia). This is the first study of HPV and dysplasia in Bulgaria.

Cameroon

Title	<i>Epidemiological modelling of microbicides impact and cost-effectiveness</i>
Countries	Cameroon, Uganda, South Africa, Zambia
LSHTM staff	Charlotte Watts, Peter Vickerman, Anna Foss
Collaborators	Clinical Trials Unit, MRC; Geoff Garnet, Imperial College; Scientists collaborating in microbicide trials (RHRU)
Funding	DFID/MRC
Dates	2001 – 2005

Summary

The Microbicides Development Programme will trial the impact of new microbicides for HIV prevention. In practise microbicide impact will be affected by many contextual factors, including patterns of sexual behaviour, condom use, and STD and HIV infection. Stochastic and deterministic mathematical models of HIV and STD transmission incorporating a microbicide will be used to:

- i) explore the population level impact and cost-effectiveness of vaginal-microbicides with different levels of efficacy, coverage and patterns of use;
- ii) investigate factors influencing the potential impact of a vaginal microbicide used in different settings;
- iii) identify optimal strategies for the use of a vaginal microbicide in combination with other methods of HIV prevention;
- iv) estimate the per sex-act efficacy of a vaginal microbicide, controlling for sexual behaviour, STD infection and condom use (using the Phase III trial behavioural, epidemiological and impact data).
- v) The models will include the role of other STDs in HIV transmission, the potential indirect protection provided by microbicides that are active against STDs, and the impact of concurrent forms of HIV prevention. The modelling will use behavioural data from the trial sites, and build upon work conducted by Watts and Vickerman (2000).

Central African Republic

Title	<i>Biological interrelationships between Herpes simplex virus type 2 (HSV-2) infection and HIV among women in Bangui, Central African Republic</i>
Countries	Bangui, Central African Republic, London and Paris
LSHTM staff	Philippe Mayaud, Helen Weiss, David Mabey, Richard Hayes
Collaborators	David Brown (ERNVL/PHLS, Colindale), Laurent Belec (Hopital Europeen Georges Pompidou and INSERM U430, Paris, France), Gerard Gresenguet (CNRMST, Bangui) Francois-Xavier Mbopi-Keou (PhD student)
Funding	GlaxoWellcome, R&D Department, UK; Royal Society ESEP exchange grant
Dates	July – November 1998 <i>and</i> April 1999 – October 2001 - completed

Summary

These series of studies combining field work at the Centre National de Reference des MST et du SIDA (CNRMST/SIDA) in Bangui and laboratory work in two centres in London (ERNVL/PHLS) and Paris (HEGP and INSERM U430) formed initially part of an MSc student's summer project in 1998. This was then extended during 1999 through grants supporting laboratory work by GlaxoWellcome R&D Department, UK. A Royal Society Exchange Grant was awarded to pursue the collaboration between the partner institutions, leading to development of new joint research proposals. The student (Francois-Xavier Mbopi-Keou) has now completed a PhD programme on the genital mucosal immunity to HSV-2 and HIV.

The aims of the study were:

- to measure the prevalence and genital shedding of HSV-2 in a female population in Bangui,
- to determine the role of HSV2 in possible co-transmission of HIV
- to study the correlates of HSV-2 and HIV shedding, in particular factors susceptible to influence mucosal immunity such as vitamin A and E
- to study the genital mucosal immunity to HSV-2 and HIV.

Main results:

- The study found that the prevalences of HSV-2 antibody (91% vs. 78%, $p=0.02$), HSV-2 shedding (43% vs. 22%, $p=0.03$) and levels of HSV-2 DNA ($p=0.01$) were all significantly higher among HIV-1 seropositive women (prevalence of 15%) than among HIV-1 seronegative women. There was a significant correlation between genital HIV-1 RNA and HSV-2 DNA levels ($p=0.02$) among the 23 dually HSV-2/HIV-1 seropositive who were shedding HSV-2 DNA. This was one of the first studies suggesting that HSV-2 genital shedding may play an important role in HIV transmission in Africa.
- The lack of association between cervicovaginal HSV-2 DNA and HIV-1 DNA shedding also found in this study supports the notion that HIV-1 replication in the female genital tract may be subcompartmentalized in distinct cellular reservoirs each with their separate turnover, and which may be influenced differently under the effect of genital HSV-2 replication.
- Vitamins A and E levels were not significantly altered in HIV seropositive women, women shedding HIV-RNA or HSV2-DNA in their genital tract. However, vitamin A deficiency was associated in an additive fashion with the number of genital tract infections or serological syphilis.
- It was also demonstrated that HSV-2 shedders did not exhibit HSV2 specific mucosal immunity, whilst non-shedders have high levels of locally produced neutralising antibodies.
- Protocols to optimise the testing of cervico-vaginal lavage samples for further shedding studies have been developed.

This collaboration has now extended into intervention studies against HSV2 in Bangui and Ghana (below).

NB. A profile of this research and participants can be found on the Royal Society website, launched in May 2003.

Title	<i>Anti-herpetic treatment with syndromic management of genital ulcer patients in Africa: clinical and biological evaluation on HIV-1 and HSV-2 genital shedding</i>
Countries	Central African Republic (Bangui), Ghana (Accra and Kumasi), London and Paris
LSHTM staff	Philippe Mayaud, Helen Weiss, David Mabey, Richard Hayes
Collaborators	David Brown (ERNVL/PHLS, Colindale), Laurent Belec, Hicham Bouhlal (Hopital Europeen Georges Pompidou and INSERM U430, Paris, France), Gerard Gresenguet (CNRMST, Bangui), Khonde Nzambi (WAPTCA, Ghana), Jacques Pepin (Centre Hospitalier Universitaire de Sherbrooke, Sherbrooke, Canada)
Funding	Agence Nationale de Recherche sur le SIDA (ANRS), France GlaxoSmithKline, R&D Department, UK
Dates	April 2002 – March 2004

Summary

Building on previous work on HSV-2 and HIV shedding in Bangui (above), the proposed project is a randomised placebo-controlled, double-blinded, multicentric therapeutic trial evaluating the association of antiherpetic treatment with the standard syndromic management of genital ulcers in Africa, and its impact on the genital shedding of HIV and of *Herpes simplex hominis* type 2 (HSV-2) virus.

The main objective of this trial will be to demonstrate that acyclovir treatment given during clinical episodes (episodic therapy) can reduce genital shedding of free- or cell-associated HIV, thereby contributing to a reduction of HIV infectiousness of dually infected individuals (HIV+/HSV-2). Given the present state of knowledge and hypotheses formulated around the possible role of HSV on the HIV epidemic in Africa, the proposed research will contribute to confirm or invalidate the existence of mutual reinforcement of HSV-2 and HIV replication. This will represent a study of biological plausibility for such an in vivo interaction. In addition the chosen intervention strategy has practical and operational implications in that it will allow the evaluation of a novel approach to syndromic management of genital ulcers in Africa that could later lead to revisions of management guidelines.

China

Title	<i>DFID Resource Centre</i>
Country	China
LSHTM staff	David Mabey, Philippe Mayaud, Duncan McCormick, Heiner Grosskurth, Lilani Kumaranayake, Charlotte Watts, Linda Morison, Susan Beckerleg, Gill Walt, Louisiana Lush
Collaborators	Family Health International; CDSC; Department of STD, UCL; Laboratory Centre for Disease Control, Canada
Funding	DFID
Dates	1998 – 2002

Summary

The School has worked with the Ministry of Health in Beijing, the National Centre for STDs in Nanjing, and the Municipal Health Department in Amsterdam to run a series of training and policy workshops on STDs in 6 provinces of China since 1995. Since 1998 this programme has included operational research projects evaluating syndromic STD management in Shanghai, Chengdu, Tianjin and Shenyang. A survey of sexual behaviour and STDs has also been undertaken among university students in Beijing.

In December 2000, the School set up a Resource Centre, with Family Health International, CDSC and the Academic Department of STDs at UCL, to provide technical support to a new DFID-funded programme on HIV/AIDS and STDs in the provinces of Yunnan and Sichuan. Expertise is being provided in the fields of epidemiology, surveillance, behavioural science, clinical medicine, microbiology and policy analysis. A situational assessment of sexual health will be undertaken in the two provinces in 2002, using methodology developed by Heiner Grosskurth and colleagues in India.

Title	Resource Centre for China-UK HIV/AIDS and STI in China
Country	China (Yunnan and Sichuan Provinces)
LSHTM staff	Philippe Mayaud, David Mabey, Susan Beckerleg, Lilani Kumaranayake, Louisiana Lush, Gill Walt, Heiner Grosskurth, Linda Morison (advisors: Ruairi Brugha, Jim Todd, Louisiana Lush)
Collaborators	China-UK HAPAC project (Cheng Feng, Billy Stewart), Beijing; National Centre for AIDS Control, Beijing; National STD Control Centre, Nanjing; Health bureaux of Yunnan and Sichuan Family Health International (FHI), Washington and Bangkok offices Dept of STD, University College London Medical School (John Richens, Robert Power)
Funding	DFID through subcontract from FHI
Dates	November 2000 – November 2002

Summary

The project is to provide technical consultancies during the inception phase of a large 5-year DFID bilateral project for HIV/AIDS Prevention and Care (HAPAC) in two provinces of China.

This demonstration project aims to set up best practice interventions for HIV/AIDS and STI prevention and care strategies targeting high-risk groups including commercial sex workers (CSWs), intravenous drug users (IDUs) and men who have sex with men (MSM), through the involvement of target groups and NGOs. The project has four outputs:

- 1) Strengthened strategic planning, management, and implementation capacity in key institutions in order to deliver more effective HIV/AIDS/STI policy and practice;
- 2) High-risk behaviours among primary target populations reduced through implementation of replicable models of HIV/STI prevention and STI treatment;
- 3) Care and support for people living with HIV/AIDS improved;
- 4) Project evaluation and system developed and operationalised.

The multi-disciplinary team of London-based consultants will provide input into:

- 1) Design of a comprehensive Situation Analysis of Sexual health (SASH) in the 2 project provinces;
- 2) Design of best practice interventions for HIV/AIDS & STI prevention and care targeting high-risk groups (CSW and IDU);
- 3) Design of second generation HIV surveillance systems;
- 4) Design of economics and policy analysis studies;
- 5) Training and study tours.

Main results/outcomes

In the two years of the project, consultants have:

- facilitated several workshops for the design of SASH and reviewed the initial stages of SASH implementation;
- prepared best practice documents and strategies for intervention among CSW and IDU;
- organised a policy study tour in Amsterdam and London;
- organised a policy training orientation course in London;
- organised workshops on policy and economic studies.

Title	<i>HAPAC China SASH and policy analysis</i>
Country	China
LSHTM staff	Louisiana Lush and Gill Walt (policy analysis only)
Collaborators	Family Health International
Funding	DFID
Dates	2001 – 2002

Summary

Policy analysis and training for support to the DFID and Family Health International HIV/AIDS Prevention and Care Project in China. Presentations made to study tour. Training visit supported for developing policy and economics skills. Future in-depth policy work planned.

Estonia – see Morocco

The Gambia

Title *The natural history of HIV-1, HIV-2 and dual infections in West Africa*

LSHTM staff Shabbar Jaffar

Collaborators Hilton Whittle et al, MRC laboratories, Fajara, The Gambia

Funding MRC

Summary

This study examined the rates of survival of HIV-1, HIV-2 and dually infected individuals, and the factors that predicted survival, including CD4 cell count and plasma viral load. Studies were conducted among hospital patients and among individuals living in a rural community. The studies have been completed and the data are currently being written up for publication.

Title	<i>Survey of reproductive morbidity in a rural area of The Gambia</i>
Country	The Gambia
LSHTM staff	Linda Morison, Philippe Mayaud
Collaborators	Gijs Walraven (PI); Katie Paine, Beryl West, Rosalind Coleman, Robin Bailey, Akum Aveika, Kunle Okenoye (MRC The Gambia); Leszek Borysiewicz, Caroline Scherf (Imperial College London).
Funding	MRC

Summary

Data on the epidemiology of reproductive health morbidity are urgently needed to guide effective interventions, to set health care priorities and to target future research. The aim of the study was to determine the prevalence of reproductive disease in a sample of rural Gambian women.

A reproductive health questionnaire was administered by field workers to women aged 15-54 years living in a rural area under demographic surveillance. A female gynaecologist questioned and examined the women, including speculum examination and bimanual pelvic examination. Vaginal swabs were taken for *Trichomonas vaginalis*, *Candida albicans* and bacterial vaginosis. Cervical smears were taken for cytology and cervical swabs for *Chlamydia trachomatis* PCR, and *Neisseria gonorrhoea* culture. A venous blood sample was tested for haemoglobin, HIV, HSV2, and syphilis serology.

1,348 women participated out of 1,871 eligible women (72%). Reproductive symptoms, particularly more intimate conditions, were more often reported to the gynaecologist (53% of the women) than to the field worker (26%). Menstrual problems, abnormal vaginal discharge and vaginal itching were the most commonly reported symptoms. Only a minority of women reported that they had sought health care for their symptoms. Results show a high prevalence of reproductive morbidity: menstrual dysfunction (34%), infertility (9.8%), reproductive tract infections (RTIs) (47%), pelvic tenderness (9.8%), cervical dysplasia (6.7%), masses (16%), and childbirth-related damage to pelvic structures (46%). 70% of the women had at least one reproductive morbidity condition.

For these rural women, whose lives are heavily dependent on their reproductive function, reproductive disease is a large burden. In inadequately resourced rural areas, with poor education, heavy agricultural and domestic labour and limited access to (quality) health care, many women are not able to attain and maintain reproductive health and wellbeing.

Full details available in Walraven *et al.* Lancet (2001) **357**: 1161-7.

Papers containing more detail on different aspects of the study are in preparation or submitted. For more detail on female circumcision see Morison *et al.* TMIH (2001) **6**(8): 643-53.

Title	<i>Evaluation of various methods for the diagnostic of bacterial vaginosis in Gambian women</i>
Country	The Gambia
LSHTM staff	Philippe Mayaud, Linda Morison
Collaborators	MRC Laboratories, Fajara, The Gambia: Edward Demba, Beryl West, Maarten Schim van der Loeff, Akum Aveika, and Robin Bailey
Funding	WHO – STI programme Litmus concepts, USA (donation of survey materials and tests)
Dates	March 2000 – July 2001

Summary

The study's aims were to:

- evaluate the WHO algorithm for management of vaginal discharge among symptomatic women presenting with vaginal discharge to an urban STD clinic in Fajara.
- obtain detailed microbial evaluation of vaginal flora and of various diagnostic procedures for bacterial vaginosis.
- evaluate a new rapid diagnostic kit (FemExam®, Litmus, USA) for bacterial vaginosis among symptomatic women attending an STI/GUM clinic.
- measure cure rates following syndromic treatment.

Main results

The prevalence of bacterial vaginosis in the women attending the GUM clinic with vaginal discharge symptoms was 49%. Diagnosis using Amsel's clinical criteria was 78% sensitive but only 58% specific and resulted in a 21% over treatment rate. Using either FemExam® Card 1 or Card 2 singly the sensitivities were similar, around 70% but with a higher specificity on Card 2 (81%). Either card resulted in similar over treatment rates. The best sensitivity (91%) was obtained using cards 1 and 2 combined but this led to more false positives and lower specificity. Using one FemExam® card is the best choice cost wise being cheaper than using Amsel's criteria. Using the two-card system at the proposed lower \$1price also becomes more feasible.

Title	<i>Evaluation of immuno-pathological effects of bacterial vaginosis and vaginal flora changes in Gambian women</i>
Country	The Gambia
LSHTM staff	Philippe Mayaud, Linda Morison
Collaborators	MRC Laboratories, Fajara, The Gambia (Edward Demba, Beryl West, Maarten Schim van der Loeff, Akum Aveika, and Robin Bailey)
Funding	MRC Laboratories, The Gambia
Dates	2001 – 2006 (part-time PhD with Open University)

Summary

The first part of the project is linked to the project titled "Evaluation of various methods for the diagnostic of bacterial vaginosis in Gambian women", aimed at defining the prevalence of BV in Gambian women attending a GUM clinic, and will establish the necessary methodology for determination of vaginal bacterial ecology, including appropriate culture systems and the use of molecular diagnostic techniques.

The second part of the project will aim at further characterising vaginal flora and BV in various populations (with/without symptoms, urban/rural, pregnant/non-pregnant) and better understand the immunopathological processes involved in BV through, for example:

- typing Lactobacilli strains;
- evaluating chemical composition of vaginal flora;
- evaluating the role of sperm on vaginal ecology;
- measuring levels of cytokines and quantitation of lactoferrin.

Main results/outputs

The first part of the study was conducted. Successful systems for the growth of aerobic and anaerobic flora have been established in the lab, and a first study looking at prevalence of BV and vaginal flora changes in symptomatic women has been conducted.

Title	<i>Evaluation of a diagnostic tests for bacterial vaginosis in a cohort of rural Gambian women</i>
Country	The Gambia
LSHTM staff	Philippe Mayaud, Linda Morison
Collaborators	MRC Laboratories, Farafenni and Fajara, The Gambia (Gijs Walraven, Beryl West, Edward Demba) Kurt Cook (LSHTM MSc student)
Funding	Litmus Concepts Inc., USA (donation of survey materials) LSHTM (to support an MSc student)
Dates	March – July 1999, analysis 2002

Summary

Evaluation of a new rapid diagnostic kit (FemExam®, Litmus, USA) for bacterial vaginosis in women, consisting of cards to detect amines and measure pH (card 1) and Gardnerella vaginalis (card2).

The project was conducted by an MSc Student (Kurt Cook) for his summer project nested within a larger reproductive morbidity survey (RMS) in rural Gambia.

Main results:

- The prevalence of BV prevalence was 38% by Nugent's (gram stain) criteria, and similar among women reporting and not reporting a symptom of vaginal discharge.
- When compared with Gram stain criteria, Amsel's clinical criteria had a sensitivity of 39.1% and specificity of 94.2%.
- Various combinations of the three individual FemExam® tests (card 1 for pH and amine test, or card 2 for Gardnerella vaginalis PIP test) gave sensitivities ranging from 44.5% to 65.4% and specificities ranging from 76.9% to 90.0%.
- Cost per patient and per true case ranged from \$0.69 and \$1.82 respectively for Gram stain diagnosis to \$8.09 and \$21.29 for FemExam® 2 card method.
- The FemExam® test compared favourably with conventional clinical diagnosis and has the advantage of being rapid, less subjective and easily performed in clinical settings of resource-poor countries. Cutting its cost would provide wider accessibility in developing countries.

Title	<i>Evaluation of a participatory behaviour change programme (Stepping Stones) for HIV prevention in The Gambia</i>
Country	The Gambia
LSHTM staff	Linda Morison
Collaborators	Matthew Shaw (PI); Katie Paine, Marianne van der Sande, Gijs Walraven, Beryl West, Robin Bailey, Isata Wurie, Michelle Jawo, M E Sowe, Akum Aveika, Keith McAdam (MRC The Gambia); Graham Hart (MRC Sociology Unit, Glasgow)
Funding	MRC

Summary

Stepping Stones is a community level, Participatory Learning and Action (PLA) programme, developed in Uganda for HIV prevention. The Gambian Government, UK Medical Research Council, Action Aid, Gambia Family Planning Association and a local mission collaborated to adapt the programme into an infertility prevention framework in order to discuss sensitive subjects related to reproductive health.

As part of this an STI survey was conducted amongst 15-34 year men and women from 18 villages in a rural area of The Gambia. Following written consent a brief questionnaire was administered and specimens were collected to test for STIs. 1076 participants provided a blood sample. 5% men and 28% of women were HSV2 positive and 2% men and 10% women were TPHA positive. Only 6/1030 urine samples tested positive for chlamydia. Older age, being married and being from the Jola ethnic group were all risk factors for STI. Women were less likely than men to seek treatment for STI symptoms.

An evaluation of Stepping Stones using 2 intervention and 2 comparison villages showed that knowledge of modes of transmission of HIV/STI and levels of risk awareness were raised following the intervention. Dialogue within marriage had increased resulting in a lower occurrence of disagreements and domestic violence. Women reported that they would insist on condom use for sex outside of marriage and even ask their husbands to use condoms for non-marital sex. Diffusion of the programme message had taken place.

Ghana – see also Central African Republic, Benin

Title	<i>The epidemiology of Trichomonas vaginalis and related infections</i>
Country	Ghana
LSHTM staff	David Mabey, Helen Weiss
Collaborators	Yaw Adu-Sarkodie, Komfo Anokye Teaching Hospital, Kumasi, Ghana; Anne Buvé, Tania Crucitti, Institute for Tropical Medicine, Antwerp
Funding	Association of Commonwealth Universities; DFID
Dates	2001 – 2004

Summary

We are studying the prevalence of and risk factors for vaginal, rectal and oral infections with *T. vaginalis* and the morphologically indistinguishable protozoal parasites *Pentatrichomonas hominis* and *Trichomonas tenax* in pregnant women, using a newly developed species specific polymerase chain reaction (PCR) assay. We are also comparing PCR with traditional diagnostic tests including microscopy, culture and antigen detection assays, and assessing the prevalence of *T. vaginalis* strains resistant to nitroimidazoles and their contribution to failure of standard treatment with metronidazole.

India – see also Morocco, Tanzania

Title	<i>The relationship between gynaecological morbidity and common mental disorders in Goa</i>
Country	India
LSHTM staff	Vikram Patel, Prof. David Mabey
Funding	The Wellcome Trust
Dates	October 2000 – October 2005

Summary

Gynaecological morbidity (GM) and Common Mental Disorders (CMD) are common and disabling health problems for women in South Asia. The commonest self-reported complaint associated with GM is abnormal vaginal discharge. A significant proportion of this GM is “medically unexplained”, i.e. not associated with laboratory confirmed Reproductive Tract Infections (RTI). There is a substantial literature demonstrating the important contribution of CMD such as depression and anxiety to medically unexplained somatic symptoms in developing countries, and its specific role in gynaecological symptoms such as pelvic pain in developed countries. Qualitative studies have shown that many women with the complaint of discharge associate it with mental stress and have co-existing symptoms typical of CMD such as tiredness and sleep problems. The symptom has been likened to the well-defined psychosomatic syndrome of *dhat* or “white discharge” in Asian men. This study aims to determine the relationship between CMD and GM, with the hypothesis that the prevalence of CMD are more likely to develop medically unexplained GM. The study will be the first systematic, population cohort study investigating the cross-sectional and longitudinal relationship between GM and CMD in South Asia. It will use the latest accepted laboratory techniques for gold standard diagnoses of RTI to define the medically unexplained group. It will include a qualitative component of in-depth interviews to explore the meaning and contexts of symptoms and views on appropriate intervention strategies. Economic and disability evaluations will enable the estimation of costs and impact of the illnesses. The findings will provide definitive information on the relationship between two common health problems of considerable public health significance in South Asia. Ultimately, the project will lead to the development of community-based interventions for GM which target both RTI and psychosocial factors that may lead to medically unexplained symptoms.

Title *Field evaluation of simple point-of-care tests for NG/CT*

Country India

LSHTM staff Heiner Grosskurth, David Mabey

Collaborators WHO TDR (STD Diagnostics Initiative - SDI)

Funding body SDI

Dates 2001 – 2002

Summary

Programme staff and collaborators at 5 sites in India submitted applications to run field and laboratory sites for the evaluation of new rapid, simple point-of-care tests for gonorrhoea and chlamydial infection. These were considered by the SDI panel in 2001 and the sites were among those selected. There are now several dipstick-type serological tests for these infections on the market in developing countries, but none has been independently evaluated. We will evaluate the use of these tests in support of syndromic management of vaginal discharge, in low prevalence populations.

Kenya

Title *Multicentre study on factors determining the differential spread of HIV infection in sub-Saharan African towns*

LSHTM staff Richard Hayes, Linda Morison, Helen Weiss, Judith Glynn

Collaborators The Study Group on Heterogeneity of HIV Epidemics in African Cities:
A Buvé (coordinator); M Laga, E Van Dyck, W Janssens, L Heyndricks (Institute of Tropical Medicine, Belgium); S Anagonou (Programme National de Lutte contre le SIDA, Benin); M Laourou (Institut National de Statistiques et d'Analyses Economiques, Benin); L Kanhonou (Centre de Recherche en Reproduction Humaine et en Demographie, Benin); Evina Akam, M de Loenzien (Institut de Formation et de Recherche Demographiques, Cameroon); S-C Abega (Université Catholique d'Afrique Centrale, Cameroon); L Zekeng (Programme de Lutte contre le SIDA, Cameroon); J Chege (The Population Council, Kenya); V Kimani, J Olenja (University of Nairobi, Kenya); M Kahindo (National AIDS/STD Control Programme, Kenya); F Kaona, R Musonda, T Sukwa (Tropical Diseases Research Centre, Zambia); N Rutenberg (The Population Council, USA); B Auvert, E Lagarde (INSERM U88, France); B Ferry, N Lydié (Centre français sur la population et le développement, France); NJ Robinson (Glaxo Wellcome, UK, formerly INSERM U88); M Caraël (UNAIDS, Switzerland)

Funding UNAIDS, Geneva, Switzerland; European Commission, Directorate General XII, Brussels, Belgium; Agence Nationale de Recherches sur le SIDA/ Ministère français de la coopération, Paris, France; DFID, London, UK; The Rockefeller Foundation, New York, USA; SIDACTION, Paris, France; Fonds voor Wetenschappelijk Onderzoek, Brussels, Belgium; Glaxo Wellcome, London, UK; BADC, Belgium; Development Cooperation, Nairobi, Kenya

Summary

The aim was to explore whether the differences in rate of spread of HIV in four urban populations in Africa could be explained by differences in sexual behaviour and/or factors influencing the probability of HIV transmission during sexual intercourse.

A cross-sectional, population based study was conducted in two towns with a high HIV prevalence (Kisumu in Kenya and Ndola in Zambia) and two towns with a relatively low HIV prevalence (Cotonou in Benin and Yaoundé in Cameroon). In each of these towns approximately 1,000 men and 1,000 women, aged 15-49 years, were randomly selected from the general population. Consenting men and women were interviewed about their socio-demographic characteristics and sexual behaviour. They were asked to provide biological samples, which were tested for HIV, syphilis, HSV-2, gonorrhoea, chlamydial infection and trichomoniasis (the latter for women only). In addition a survey was conducted among a representative sample of 300 sex workers in each town.

In these four African populations differences in sexual behaviour were outweighed by differences in factors that influence HIV transmission (for example, male circumcision and ulcerative STDs), in explaining the differences in rate of spread of HIV. This does not mean that interventions aimed at reducing risky sexual behaviour are not important. In all four sites high-risk behaviour patterns were identified and a high prevalence of HIV among young women calls for urgent interventions. The results have now been published in a supplement to AIDS.

Title	<i>Multicentre study to evaluate the accuracy of HIV surveillance using antenatal clinic attenders</i>
LSHTM staff	Judith Glynn
Collaborators	A Buvé (Institute of Tropical Medicine, Antwerp, Belgium); M Caraël (UNAIDS, Geneva, Switzerland); L Zekeng, I Macauley (Faculty of Medicine and Biomedical Sciences, University of Yaoundé, Cameroun); M Kahindo (National AIDS/STD Control Programme, Nairobi, Kenya); M Hawken (Nairobi, Kenya); R Musonda, (Tropical Diseases Research Centre, Ndola, Zambia); Members of the Study Group on Heterogeneity of HIV Epidemics in African Cities
Funding	UNAIDS - completed

Summary

The study is linked to the "Multicentre study on factors determining the differential spread of HIV infection in sub-Saharan African towns". It was carried out in 3 of the 4 towns used for that study in sub-Saharan Africa, 2 with high prevalence of HIV (Kisumu, Kenya and Ndola, Zambia) and 1 with stable low prevalence (Yaounde, Cameroon). The aim of this study was to use the general population seroprevalence and detailed population data collected in the parent study to compare with data on HIV prevalence obtained using sentinel surveillance techniques in antenatal clinics. The results show that HIV is associated with decreased fertility but that the differences between HIV prevalence in the antenatal clinic and in the population varied from site to site, making any standard adjustments difficult. We also found an association between long post partum abstinence and HIV positivity in Yaoundé. Further analyses will explore relationships between HIV and risk factors for abortion, and factors associated with time of antenatal clinic attendance.

Title	<i>Evaluation of HAPAC Kenya</i>
Country	Kenya
LSHTM staff	Louisiana Lush
Funding	The Futures Group Europe/DFID
Dates	July – August 2001

Summary

Consultancy to evaluate output 1 of the DFID and The Futures Group Europe HIV/AIDS Prevention and Care Project in Kenya. This output aimed to develop capacity at the national, provincial and local levels for planning, managing and delivering HIV/AIDS services throughout Kenya.

Malawi – see also South Africa, Uganda

Title	<i>HIV subtypes and history of the HIV epidemic in Northern Malawi</i>
Country	Malawi
LSHTM staff	Paul Fine, Judith Glynn, Lyn Bliss, Philip Broadbent, Keith Branson, Mia Crampin
Collaborators	Dr Jonathan Clewley, Dr Grace McCormack (PHLS)
Funding	The Wellcome Trust

Summary

Objectives

To characterise the early evolution and spread of HIV in Northern Malawi.

Methods

As part of the Karonga Prevention Study in Northern Malawi, blood samples were collected on filter papers in 1981-84 and 1987-89 from all individuals (more than 44,000) living in two areas of Karonga District, northern Malawi. The samples included 203 that were HIV-1 positive. We undertook a phylogenetic analysis of DNA sequences of the env and/or gag genes from all those from whom appropriate templates could be amplified (179).

Results

The first 4 HIV positive specimens were from 1982: one A, one D and two unclassifiable, possibly a new C sub-subtype. Of the 11 positive specimens from 1982-84, 6 (55%) were subtype C. By 1987-89, 152/168 (90%) of sequences were subtype C ($p=0.004$ compared with earlier period). Others were subtypes A (3) and D (6), AC (2), AD and DC recombinants, and the unclassifiable clade (3). The non-C subtypes were more common in the north of the district, near the Tanzanian border, where the first A and D specimens were seen. The subtype C specimens included clusters of closely related strains, indicating local spread, and more distantly related strains, indicating multiple introductions. Four of the early subtype C sequences were closely related and were found at the base of a large clade of low diversity that accounted for 40% of C sequences in the late 1980s.

This shows a significant increase in subtype C as a proportion of HIV subtypes in this area during the 1980s. This greater success of C, and the extensive spread of a single clade, could be due to a founder effect and/or to biological differences in transmissibility.

Further studies will look at more recent specimens and changes over time in individuals.

Title	<i>Antenatal clinic HIV surveillance in Northern Malawi</i>
Country	Malawi
LSHTM staff	Paul Fine, Mia Crampin, Judith Glynn, Lyn Bliss
Collaborators	Dr Bagrey Ngwira, Dr Frank Mwaungulu, Karonga Prevention Study National AIDS Control Programme
Funding	The Wellcome Trust

Summary

Objectives

- i) Assess the accuracy of ANC surveillance.
- ii) Monitor trends in HIV prevalence.

Methodology

As part of the Karonga Prevention Study in Northern Malawi, we are carrying out antenatal clinic HIV surveillance, in conjunction with the National AIDS Control Programme. These are compared with community HIV prevalence from case control studies in the district.

Results

Age, sex and area-standardized HIV prevalence in women aged 15-44 in the population was 4.3% in 1988-90, 12.7% in 1991-1993 and 14.4% in 1998-2001. For men, HIV prevalence was 4.0%, 9.1% and 11.6% in the same periods. The age and area adjusted HIV prevalence in the ANC in 1999-2001 was 9.8%. The underestimate can be largely explained by marriage and mobility. Reduced fertility in HIV-positives was demonstrated in both ANC and community populations. A previously recommended parity-based adjustment gave an estimated HIV prevalence of 14.7%.

Title	<i>Socio-economic impact of HIV on households in Northern Malawi</i>
Country	Malawi
LSHTM staff	Paul Fine, Mia Crampin, Sian Floyd, Judith Glynn, Lyn Bliss, Philip Broadbent, Keith Branson
Collaborators	Dr Bagrey Ngwira, (Karonga Prevention Study Malawi); Dr John Parry, Dr Jonathan Clewley, (PHLS); Dr Nyovani Madise, (Southampton)
Funding	The Wellcome Trust

Summary

Objectives

To measure the impact of HIV on individuals and households in Northern Malawi.

Methods

As part of the Karonga Prevention Study in Northern Malawi, filter paper blood samples from general population samples from the 1980s have been HIV tested. These form the basis of a retrospective cohort study. All (197) HIV positive individuals and 396 (initially) HIV negative matched individuals, and their families, were traced in 1998-2000. Possible seroconversion was assessed by tests, verbal autopsies and spouses' status. Interviews included information on children, morbidity and mortality and socio-economic status.

Results

Information was obtained on all but 11 index individuals. 10-year survival was 36% in HIV positives and 93% in (initially) HIV negatives. The age/sex-adjusted hazard ratio for mortality by HIV status, excluding seroconverters, was 15.2 (95% confidence interval 9.8-23.6). Survival time decreased with age, but relative survival, compared to HIV negatives, was similar across age groups. Spouses of initially HIV positive cases had 3.2 times the mortality of spouses of initially HIV negative cases, and survivors were 5.4 times as likely to be HIV positive. Among children with HIV positive mothers, infant mortality was 27% (95% confidence interval 19-38), under 5 mortality 46% (36-58) and under 10 mortality 49% (38-61). The corresponding figures for those with HIV negative mothers were 11% (9-13), 16% (13-19) and 17%(14-20). Further analyses are exploring the impact on socio-economic status of the households.

Title	<i>Epidemiology of mycobacterial and HIV infections in Northern Malawi</i>
Country	Malawi
LSHTM staff	Paul Fine, Mia Crampin, Judith Glynn, Sian Floyd, Lyn Bliss, Keith Branson
Collaborators	Dr Bagrey Ngwira, Frank Mwuangulu Karonga Prevention Study Malawi Dr Francis Drobniowski, PHLS Mycobacterium Reference Laboratory, Dulwich; Dr Sebastian Lucas, UMDS, St Thomas's Hospital
Funding	The Wellcome Trust, LEPR

Summary

Objectives

Studies of the relationship between HIV and mycobacterial disease.

Methods

The Karonga Prevention Study in Northern Malawi includes a case-control study of risk factors for tuberculosis and leprosy, including HIV. This started in 1988. Interim analyses showed the expected strong association with tuberculosis, but no association with leprosy. Further analyses will examine whether the association changes over time, with the proportion of HIV-infected individuals who are immunocompromised. A new phase of the case-control study is examining additional risk factors for TB. A retrospective cohort study also examined the association between HIV and TB in this population.

Title	<i>A randomised controlled trial of single-dose M vaccae in the immunotherapy of (HIV positive) pulmonary tuberculosis</i>
Countries	Malawi, Zambia
LSHTM staff	Paul Fine, Lyn Bliss, Judith Glynn, Mia Crampin
Collaborators	Dr Bagrey Ngwira (Karonga Prevention Study Malawi); Dr Ali Zumla, (University College London Medical School); Dr Janet Darbyshire, Dr Andrew Nunn (MRC HIV Clinical Trials Unit)
Funding	DFID – completed

Summary

Background

Mortality rates of HIV-infected patients treated for tuberculosis remain high. This study aimed to assess the effect on mortality of immunotherapy with single-dose SRL172 added to standard anti-tuberculosis chemotherapy in such patients.

Methods

The double-blind trial enrolled 1229 patients aged 18-60 years, who had never received antiretroviral treatment and who presented with newly diagnosed, sputum-smear-positive pulmonary tuberculosis to referral centres in Lusaka, Zambia and Karonga, Malawi. Both HIV-positive and HIV-negative patients were enrolled, to avoid stigmatisation. Participants were randomly assigned a single injection of SRL172 or matching placebo within 2 weeks of starting 8 months of anti-tuberculosis chemotherapy and followed up for at least 12 months. The primary endpoint was time to death in the HIV-infected population. Analyses were based on 760 HIV-positive patients after exclusion of 84 patients with errors in storage of the injection, no bacteriological confirmation, or no HIV result.

Findings

Of 760 HIV-infected patients, 374 received SRL172 and 386 received placebo. SRL172 did not cause any serious adverse events. The follow-up rate was 88% at 12 months in both groups. Of the HIV-positive patients, 109 (19.5 per 100 person-years) of 372 assigned SRL172 and 107 (19.3 per 100 person-years) of 386 assigned placebo died. In the Cox's regression analysis, stratified by centre, the hazard ratio of deaths (SRL172/placebo) was 1.03 (95% CI 0.79-1.35). There was no evidence of benefit to the group assigned SRL172.

Interpretation

Immunotherapy with single-dose SRL172 as an adjunct to standard anti-tuberculosis treatment in HIV-positive adults with pulmonary tuberculosis had no significant effect on survival or bacteriological outcome, though the treatment was safe and well tolerated.

Mali

Title	<i>RCT of the impact and cost-effectiveness of youth intervention through traditional gatekeepers in urban and rural areas</i>
Country	Mali
LSHTM staff	Sarah Castle
Collaborators	SPAP, Interventions among adolescent groups, CERPOD Bamako, INRSP Bamako, CPHL
Funding body	DFID and Rockefeller Foundation
Dates	September 2001 – March 2002

Summary

To date, formative research, together with evaluations of sexual health interventions in the Mopti region, have indicated that numerous barriers exist which prevent young people from improving their sexual health. Although general sexual health knowledge is often quite high, the quality of this information and young people's ability to apply it are frequently limited. Evidence suggests that simply providing information or appropriate services may not be sufficient to induce behaviour change. This collaborative project between Save the Children, the London School of Hygiene & Tropical Medicine and local research partners seeks to reinforce psychological and social resources for safe sexual behaviour.

Firstly, throughout the study population, the intervention will seek to improve the accessibility and acceptability of sexual health services. Concurrently, in selected sites, a series of original curricula addressing psychological factors and other life skills for better sexual health will be developed and implemented by adolescent peer educators. In addition, societal gatekeepers (religious leaders, caste members, praise singers) who ascribe gender roles and sexual norms will be actively recruited into a second peer education programme to promote reproductive rights.

A randomised controlled trial will be conducted to evaluate the effect of delivering a simple package of services focusing only on appropriate and accessible sexual health care versus a comprehensive package where services are accompanied by the two sets of peer education programmes. Behavioural and biomedical differences in sexual health outcomes will be measured to compare each type of intervention and cost-effectiveness will be assessed. In addition, process indicators for the two peer-education programmes relating to their acceptability, feasibility, efficacy and uptake will also be carefully monitored. The peer-led curricula, together with the methods of impact evaluation, will be disseminated at the end of the intervention with a view to their being implemented more widely in sub-Saharan Africa.

Morocco

Title	<i>Multicentre international seroepidemiology study of Herpes simplex virus (HSV) infection (HISS study)</i>
Countries	Morocco, Brazil, Estonia, Sri Lanka, India
LSHTM staff	Philippe Mayaud
Collaborators	Frances Cowan and Rebecca French (Department of STDs, UCLMS), David Brown (ERNVL/CPHL)
Funding	GlaxoWellcome, R&D Department, UK
Dates	September 1999 – December 2002

Summary

Background: The association between Herpes simplex virus type 2 (HSV-2) and Human Immunodeficiency virus (HIV) and the development of HSV vaccines have increased interest in the study of HSV epidemiology.

Objectives: To estimate the age- and gender-specific sero-prevalence of HSV-1 and HSV-2 infections in selected populations in Brazil, Estonia, India, Morocco, and Sri Lanka, countries with a relatively low HIV prevalence.

Methods: Serum samples were collected from various populations including children, antenatal clinic attenders, blood donors, hospital in-patients, and HIV-sentinel surveillance groups. STD clinic attenders were enrolled in Sri Lanka, male military personnel in Morocco. Sera were tested using a common algorithm by type-specific HSV-1 and HSV-2 antibody assay (HerpeSelect Focus California).

Results: 13,986 samples were tested, 45.0% from adult females, 32.7% from adult males, and 22.3% from children. The prevalence of HSV-1 varied by site ranging from 63.1% to 92.9% in adult males and from 73.4 to 90.1% in adult females. In all countries HSV-1 seroprevalence increased significantly with age ($p < 0.001$) in both men and women.

The prevalence of HSV-2 infection varied between sites. Brazil had the highest age-specific rates of infection for both men and women, followed by Sri Lanka for men and Estonia for women, the lowest rates being found in Estonia for men and India for women respectively. In all countries, HSV-2 seroprevalence increased significantly with age ($p < 0.01$) and adult females had higher rates of infection than adult males by age of infection.

Conclusions: HSV-1 and HSV-2 seroprevalence was consistently higher in women than men, particularly for HSV-2. Population-based data on HSV-1 and HSV-2 will be useful for designing potential HSV-2 vaccination strategies and for focusing prevention efforts for HSV-1 and HSV-2 infection.

Mozambique

Title	<i>Policy transfer in infectious diseases</i>
Countries	Mozambique and South Africa
LSHTM staff	Gill Walt, Louisiana Lush, Jessica Ogden
Collaborators	Centre for Health Policy, Witwatersrand University, Johannesburg; University of Mozambique
Funding	ESRC
Dates	January 2000 – December 2002

Summary

Investigation into international level development of policies for infectious diseases with case studies of syndromic management for sexually transmitted infections and DOTS for tuberculosis. Subsequent analysis of transfer of policies to national level in South Africa and Mozambique.

South Africa – see also Cameroon, Mozambique

Title	<i>Tuberculosis and HIV disease in mineworkers in South Africa</i>
Country	South Africa
LSHTM staff	Alison Grant, John Day, Katherine Fielding, Richard Hayes, Liz Corbett, Lilani Kumaranayake
Collaborators	Aurum Health Research, Welkom, South Africa; Lynn Morris and Clive Gray, National Institute for Virology, Johannesburg, SA; Dick Chaisson, Johns Hopkins University, Baltimore, USA; Kevin De Cock, CDC Kenya; Keith Klugman, SAIMR, Johannesburg, SA
Funding	Aurum Health Research
Dates	October 1998 – September 2002

Summary

This is a collaborative project to carry out a series of studies of tuberculosis and HIV disease in South African mineworkers. Studies specifically concerning HIV which are in progress include:

- 1) *Sentinel surveillance for HIV-infection among mineworkers.* A system of surveillance has been established using anonymous, unlinked testing of urine specimens among three groups: the general population of mineworkers, employees admitted to hospital and employees presenting with sexually transmitted diseases.
- 2) *Effect of preventive therapy on disease episodes among HIV-infected mineworkers.* HIV-infected employees have been recruited to a specialised clinical service delivering appropriate preventive therapies, in particular TB preventive therapy and cotrimoxazole. Using an incremental recruitment design, the efficacy of the preventive therapy in this population is being assessed in terms of its effect on hospital admissions (all-cause and cause-specific) and loss of working time. We also plan to assess the cost-effectiveness of the service.
- 3) *Adherence to preventive therapy.* A pilot study to investigate adherence to TB preventive therapy and cotrimoxazole among HIV-infected miners under operational conditions is currently being analysed.
- 4) *Evaluation of voluntary counselling and testing services.* VCT services within the mining health service were evaluated using a tool developed by UNAIDS. The results were used as the basis to implement major improvements to the service. A more recent survey has investigated attitudes of the workforce to VCT.
- 5) *Evaluation of the impact of a targeted core group intervention for women at high risk on HIV incidence among gold miners.* A programme of education and improved STI treatment for women at high risk of STI/HIV in the Welkom area is being implemented. This study will evaluate the impact of the programme on HIV incidence among mineworkers.
- 6) *A cohort study to investigate the effect of tuberculosis on the progression of HIV disease.* HIV-infected miners are followed before, during and after an episode of tuberculosis to determine the effect of tuberculosis on HIV disease progression, as measured by HIV viral load. In an extension to this study, the effect of an episode of TB on the range of HIV quasispecies will be investigated.
- 7) *Phenotypic and functional analysis of CD8+ T cells in patients with tuberculosis and/or HIV infection.* A cohort study to compare T cell receptor repertoires in HIV-infected and -uninfected patients with tuberculosis, to determine whether CD8+ T cell responses to HIV change during an episode of tuberculosis, and to assess whether abnormally expanded CD8+ T cells become exhausted in patients with an episode of tuberculosis.

Planned studies

- 1) *Continuous vs. intermittent antiretroviral therapy among HIV-infected individuals in a gold mining community in South Africa.* A randomised controlled trial to compare continuous vs. intermittent antiretroviral therapy (ART), and, using a factorial design, to compare self-administered vs. "supported" ART in a community of mine workers.
- 2) *Pharyngeal carriage and antimicrobial resistance in isolates of Streptococcus pneumoniae in HIV-infected miners.* A cross sectional study to examine the prevalence of nasopharyngeal carriage of pneumococci in HIV-infected and -uninfected individuals, the distribution of carriage serotypes in these groups and the effect of low-dose cotrimoxazole prophylaxis on the prevalence of carriage and of antimicrobial resistance.

Title	<i>The ProTEST Initiative</i>
Countries	South Africa, Malawi, Zambia, Uganda
LSHTM staff	Peter Godfrey-Faussett, Helen Ayles, Harry Hausler Lilani Kumaranayake, Fern Terris-Prestholt, Charlotte Watts
Collaborators	WHO, UNAIDS, Lusaka Urban District Health Management Team, Malawi National Tuberculosis Programme, South African Department of Health
Funding	WHO

Summary

The “ProTEST” initiative (coordinated by WHO in collaboration with UNAIDS, CIDA, NORAD, DFID and USAID) is investigating how to interrupt the sequence of events by which HIV infection fuels the tuberculosis epidemic, by promoting Voluntary Counselling and Testing (VCT) for HIV as an entry point to access to a range of HIV and tuberculosis prevention and care interventions. The establishment of pilot projects in different settings will enable assessment of the feasibility of operationalising the links between general health services and HIV and tuberculosis programmes necessary to provide access to a range of HIV and tuberculosis prevention and care interventions, with VCT for HIV as an entry point to access. The project outcomes are effectiveness, cost-effectiveness, affordability and acceptability.

WHO is establishing a steering group to provide oversight to the “ProTEST” projects in different sites. Projects are currently under way in South Africa (funded by CIDA), Malawi (funded by NORAD) and Zambia (funded by DFID). WHO plans to fund the implementation of projects in Uganda and another site in Zambia. The operational research projects currently under way require particular assistance in linking up technical areas (e.g. VCT for HIV, TB/HIV clinical management, TB preventive therapy), overall guidance in ensuring the measurement of the appropriate outcomes and evaluating impact, and data management.

LSHTM is involved with all aspects of the “ProTEST” initiative: membership of the steering group; co-ordination of the pilot projects in South Africa and Zambia (see separate entries in this booklet); regular supervisory visits to the sites in South Africa, Malawi and Zambia; economic evaluation; evaluation of impact.

Title	<i>Classical and molecular epidemiological studies of tuberculosis in the South African gold mines</i>
Country	South Africa
LSHTM	Pam Sonnenberg, Judith Glynn, Peter Godfrey-Faussett
Collaborators	Jill Murray (Pathologist, National Centre for Occupational Health), Stuart Shearer (Occupational Health Physician, Gold Fields SA), Raymond Glyn Thomas (Radiologist, University of the Witwatersrand)
Funding	Colt Foundation Fellowship ORS award

Summary

In the South African gold mining industry, the incidence of tuberculosis is amongst the highest in the world and the prevalence of HIV infection has increased to almost 30% on some mines. Extensive data, including DNA fingerprinting, has been collected since 1995 on all tuberculosis patients working on four mines in the Gauteng Province. A number of related studies, which address the natural history of tuberculosis and the interaction between tuberculosis and HIV infection are underway. These aim to estimate the effect of HIV infection on the incidence of (1) new tuberculosis and (2) recurrent tuberculosis due to relapse and reinfection.

Title	<i>The acceptability, feasibility and cost-effectiveness of rapid HIV testing, tuberculosis preventive therapy and cotrimoxazole prophylaxis in South African TB/HIV pilot districts</i>
Countries	South Africa
LSHTM staff	Harry Hausler, Peter Godfrey-Faussett, John Porter, Lilani Kumaranayake, Charlotte Watts, Jessica Ogden
Collaborators	Laura Campbell, Barbara Karpakis, Julia Kim, Thembela Masuku, Refiloe Matji, Pren Naidoo, Paul Pronyk, Jackie Sallet, Carol Sheard, Nono Simelela
Funding	South African Department of Health, Medical Research Council of Canada
Dates	April 1999 – December 2002

Summary

The aim of the project is to assess the acceptability, feasibility and cost-effectiveness of rapid HIV testing, tuberculosis preventive therapy (TBPT) and co-trimoxazole prophylaxis as part of a comprehensive package of HIV/AIDS/STD/TB prevention, care and support in South Africa. The project is being conducted in 4 districts including rural, peri-urban and urban sites.

Health workers were trained on voluntary HIV counselling testing (VCT) and the comprehensive package. Clients attending health facilities are informed in morning health education sessions that VCT is available, free and confidential. All clients with TB, STDs and those attending antenatal care are offered VCT by health workers. Rapid HIV testing is performed. HIV-positive clients are clinically staged and screened for symptoms of TB. Clients with no symptoms of TB are offered TBPT (isoniazid 300 mg daily for 6 months) and clients with WHO stage 3 or 4 are offered cotrimoxazole prophylaxis (960 mg daily for life). Clients on prophylaxis are followed monthly and monitored for adherence, side effects and hospitalisations.

Acceptability to clients and health workers will be assessed through measuring uptake and through focus group discussions and individual interviews. Feasibility will be measured through measures of adherence and time analyses. Costs will be measured from the client and provider perspective. Effectiveness will be estimated based on measured adherence and results of efficacy from past clinical trials. Cost-effectiveness will be calculated comparing rapid to lab testing, TBPT to no TBPT and cotrimoxazole prophylaxis compared to no cotrimoxazole prophylaxis.

Title	<i>The effect of HIV on morbidity and mortality in South African gold miners</i>
Country	South Africa
LSHTM	Pam Sonnenberg, Judith Glynn
Collaborators	National Centre for Occupational Health, and University of Witswatersrand, SA (Jill Murray); Gold Fields Ltd (Stuart Shearer, Andre Bester)
Funding	Colt Foundation
Dates:	2002 – 2004

Summary

Objective: Assess the impact of HIV infection on morbidity, mortality and health service use, by time since infection.

Method: Retrospective cohort study of miners with known dates of seroconversion to HIV.

Title	<i>Evaluation of antiretroviral therapy implementation for HIV-infected employees of Anglo American Group companies</i>
Country	South Africa
LSHTM	Alison Grant, Katherine Fielding, Lilani Kumaranayake
Collaborators	Aurum Health Research, South Africa
Funding	Aurum Health Research, South Africa
Dates:	October 2002 – September 2005

Summary

Objective: To evaluate ART provision in the mining industry and other industrial settings with respect to key feasibility issues and clinical outcomes

Method: Observational cohort.

Title	<i>Randomized, double-blind, placebo-controlled trial of Acyclovir for the reduction of HIV acquisition and transmission among high-risk HSV-2 seropositive women in South Africa</i>
Country	South Africa
LSHTM	Philippe Mayaud, Helen Weiss
Collaborators	Sinead Delany (PhD student) and Helen Rees (RHRU, Baragwanath Hospital, Johannesburg); Connie Celum et al (University of Washington, USA)
Funding	Wellcome Trust (submitted) (and NIH)
Dates:	2002 – 2006

Summary

There has been considerable interest for the potential role of Herpes simplex virus type-2 (HSV-2) - the main cause of genital herpes - in facilitating HIV acquisition (in HIV-negative individuals) or HIV transmission (in HIV-positive individuals). A recent UNAIDS/WHO workshop recommended that the impact of specific interventions against HSV-2 on HIV acquisition/transmission be urgently measured. These interventions might include: (1) treatment for patients infected with HSV and presenting for clinical episodes (episodic therapy); (2) prevention of clinical or sub-clinical recurrences among patients infected with HSV-2 (suppressive therapy); and (3) primary prevention of HSV-2 infection through specific vaccination, use of barrier methods (condoms and/or microbicides), safe sex education, etc.

A large multicentre phase III, randomized, double-blind, placebo-controlled trial of acyclovir (suppressive therapy) for the reduction of HIV acquisition among high-risk HSV-2 seropositive, HIV seronegative individuals will be set up by the University of Washington (USA) with NIH funding in several sites outside the US. The RHRU is applying to be one of the participating sites.

As part of her PhD studies, Sinead Delany (RHRU/LSHTM) will conduct a RCT of HSV suppressive therapy to determine the efficacy of anti-herpetic suppressive therapy on HIV acquisition in HSV-2 seropositive women at high risk for HIV infection, attending an STI clinic in downtown Johannesburg. Secondary objectives will be: (1) to measure the effect of anti-herpetic suppressive therapy on HIV viral shedding in HSV-2 seropositive women who are co-infected with HIV; and (2) to measure the effect of anti-herpetic suppressive therapy on the occurrence and frequency of HSV-2 viral reactivation in both HIV infected and uninfected women. Thus her study will include both HIV-seropositive and HIV-sero-negative women.

Preliminary research will also aim to determine the conditions of adherence to HSV-2 suppressive therapy, and evaluate the performance of various HSV serological assays including a rapid diagnostic test.

Title	<i>Microbicides Development Programme: Economic analysis to assess demand, cost-effectiveness and inform future distribution strategies</i>
Country	South Africa
LSHTM	Fern Terris-Prestholt, Charlotte Watts, Lilani Kumaranayake
Collaborators	Sheena McCormack and Andrew Nunn (MRC Clinical Trials Unit, London); Sinead Delany and Helen Rees (RHRU, Baragwanath Hospital, Johannesburg); Gita Ramjee (MRC, Durban); Prof Bhat (University Teaching Hospital, Lusaka)
Funding	DFID
Dates:	2002 – 2005

Summary

Microbicides are substances capable of reducing the transmission of HIV and other sexually transmitted diseases (STDs) when applied in the vagina. DFID has funded a programme of microbicide development that would provide women with an HIV prevention method they can control. A number of economic considerations will affect future interest in and uptake of microbicides.

Economic modelling and analysis will be used to:

- 1) estimate the potential demand and market for a microbicide in a couple sub-Saharan African countries;
- 2) assess the cost, accessibility and equity implications of different mechanisms of microbicide distribution;
- 3) empirically assess the cost-effectiveness of the Phase III microbicide trials;
- 4) estimate the cost-effectiveness of interventions promoting microbicide use in the trial countries.

Economic analysis of market supply and demand will be used to develop a framework for assessing the demand, willingness-to-pay, and production capacity for a microbicide. In a number of trial sites behavioural data collected by PSI will be used in combination with demographic, household and economic data to estimate the potential demand and market for a microbicide, and to assess the cost, accessibility and equity implications of different mechanisms of microbicide distribution. This work will build upon ongoing work on the economics of HIV/AIDS, and use available data on the costs of providing HIV prevention and family planning commodities. A full economic costing of the Phase III microbicide trials will be conducted, with a protocol developed using established cost methodologies. The cost data obtained will be used, in combination with the intervention outcome and impact data to consider the aggregate cost-effectiveness of the multi-site trial. In addition, the cost and output data will be used in combination with mathematical models of impact in other epidemiological contexts, to model the potential cost-effectiveness of scaled up interventions in the trial countries. All work will be conducted in collaboration with collaborating country economists.

Title	<i>Cost-effectiveness of brothel-based STI treatment for sexworkers in Hillbrow, South Africa</i>
Country	South Africa
LSHTM	Peter Vickerman, Fern Terris-Prestholt, Charlotte Watts, Lilani Kumaranayake
Collaborators	Sinead Delany and Helen Rees (RHRU, Baragwanath Hospital, Johannesburg)
Funding	DFID Innovations grant; DFID/LSHTM HEFP Knowledge Programme
Dates:	2000 – 2002

Summary

Hillbrow, the inner-city neighbourhood of Johannesburg, South Africa has high levels of sex-work and a highly mobile population. There is a high prevalence of STI, with surveillance data showing a prevalence of 5.9% and 45.7% for syphilis and HIV respectively, among STD clinic attendees.

There is a high turnover rate among the commercial sex-workers (CSWs), with many young women entering the trade. These young women are often unable to negotiate condom use with clients and/or boyfriends, and often do not seek prompt STI treatment at government health clinics. Since 2000, the Reproductive Health Research Unit (RHRU) has been implementing a brothel-based STI treatment intervention. This study estimated the cost-effectiveness of this intervention during its first year of activity.

Full annual financial and economic costs were collected using the standardised costing methodology layed out in the Costing Guidelines for HIV Prevention.. Costs for the start-up and implementation of the intervention were included, research cost were removed. Behavioural data was collected from sex workers, female family planning clients and male STD clients in Hillbrow, epidemiological and intervention related data was collected from sex workers attending the intervention, other relevant epidemiological data was collected from other populations from the nearby area. The data was used with an epidemiological model, POP 1.0, to project the patterns of HIV and STI transmission among the sex workers and the general population. The model projections were fit to available HIV and STI prevalence data from Hillbrow, and these simulations were used to estimate the number of cervical STIs and HIV infections averted by the project. The uncertainty in model parameters was used to obtain confidence intervals around the impact estimates.

Preliminary results

Total annual cost of the intervention was around \$100,000. The intervention reached 1431 women and provided 2523 visits during this time. Model estimates showed 252 HIV infections averted and 6273 cervical infection averted. Cost per HIV infection averted was around \$400, and cost per DALY saved was \$12. Although targeted interventions are especially recommended in early HIV epidemics this study shows targeted interventions can still be cost effective in established epidemics.

Sri Lanka – see Morocco

Tanzania

Title	<i>Adolescent reproductive health intervention trial, Mwanza: Strategies for the prevention of HIV infection and the enhancement of reproductive health among adolescents in rural Tanzania (MEMA kwa Vijana Project)</i>
Country	Tanzania
LSHTM staff	Alessandra Anemona, Dean Everett, Heiner Grosskurth, Richard Hayes, Lilani Kumaranayake, David Mabey, Angela Obasi, Mary Plummer, David Ross (Director), Fern Terris-Prestholt, James Todd
Collaborators	African Medical and Research Foundation (AMREF), Tanzania; Medical Research Council, Glasgow; Ministry of Education and Culture, Tanzania; Ministry of Health, Tanzania; National Institute for Medical Research (NIMR), Tanzania; University of Montreal, Canada
Funding	European Commission Co-funding: Ireland Aid; MRC, UK; DFID, UK; UNAIDS
Dates	October 1997 – September 2002

Summary

This project aims to develop and rigorously evaluate an intervention aimed at improving the reproductive health of adolescents in four rural districts of Mwanza Region, Tanzania.

The objective of the intervention is to reduce sexual risk behaviour and the prevalence and incidence of HIV and other STDs in adolescents, and to increase their use of effective contraceptive methods. An intervention package has been designed based on the curriculum of the Tanzanian Ministry of Education and is being implemented among adolescents attending the last three years of primary school in ten rural communities that include 62 primary schools and 18 health facilities. The intervention uses innovative learning methods, and includes teacher-led classroom sessions on reproductive health and risk reduction, peer education directed at adolescents who are both in and out of school, the provision of youth-friendly reproductive health and family planning services (both in health facilities and through youth condom promoters and distributors), and outreach activities in the community.

The impact is being evaluated through a community-randomised trial in which ten intervention and ten comparison communities are compared. In 1997-98, an initial survey was conducted among 9,436 adolescents aged 15-19 years to ensure comparability of the two groups through appropriate stratification of the study communities prior to randomisation. This survey showed that the prevalence of HIV rose from 0.2% in 15 year-old males to 1.0% in 19 year-old males. In females, the HIV prevalence rose from 0.9% to 4.6% over the same age range. The prevalence of *Chlamydia trachomatis* (CT) also increased with age and was lower in males than in females. In males, the prevalence of CT rose from 0.4% at 15 years to 1.7% at 19 years, and in females it increased from 1.8% at 15 years to 3.2% at 19 years.

In each community, a cohort of between 402 and 563 primary school pupils aged 14 and above was recruited in late 1998 (total 9,291 participants), and is being followed-up for three years. This cohort is being used to measure the impact of the intervention on the sero-incidence of HIV, syphilis and *Herpes simplex virus-2* infection, the prevalence of gonorrhoea and chlamydia and the incidence of pregnancy. Knowledge and attitudes related to sexual and reproductive health, sexual risk behaviour and use of contraceptive methods are being evaluated through a variety of methods (in collaboration with the MRC-funded Health & Lifestyles Research Programme in Mwanza). Feasibility and cost-effectiveness are being assessed, and a detailed process evaluation is an integral part of the project. The final follow-up survey of the trial cohort started in late September 2001, and the main trial results are expected by September 2002.

Title	<i>Sexual behaviour of adolescents in rural Tanzania and the impact of an innovative sexual health intervention: Health & Lifestyles Research (HALIRA) Programme</i>
Country	Tanzania
LSHTM staff	Alessandra Anemona, Heiner Grosskurth, Richard Hayes, Angela Obasi, Mary Plummer (Co-ordinator), David Ross, James Todd
Collaborators	African Medical and Research Foundation (AMREF), Tanzania; Medical Research Council, Glasgow; National Institute for Medical Research (NIMR), Tanzania
Funding	MRC, UK; Co-funding: DFID, UK; European Commission; Ireland Aid
Dates	January 1999 – June 2003

Summary

This programme of behavioural research is investigating the sexual behaviour of rural adolescents in Mwanza Region, Tanzania. It is closely linked to the Adolescent Reproductive Health Intervention Trial, Mwanza (MEMA kwa Vijana Project).

The programme is using three main qualitative and two main quantitative methods to investigate the sexual behaviour of rural adolescents:

- Participant observation, where young East African researchers each year spend 7 weeks in each of six selected villages, observing the social life of adolescents, including sexual negotiation, etc.
- In-depth interviews with adolescents who are selected based on their HIV and/or pregnancy status that are ascertained within the evaluation component of the MEMA kwa Vijana trial.
- Focus group discussions with young people, mainly about issues that have been found to be difficult to address in questionnaires, in-depth interviews and participant observation.
- Three rounds of face-to-face interviews to all ~10,000 members of the impact evaluation cohort of the MEMA kwa Vijana trial.
- Three rounds of self-completion questionnaire interviews by selected members of the impact evaluation cohort of the MEMA kwa Vijana trial and (in the first two rounds only) their younger peers (approximately 6,000 per round).

Title	<i>Behavioural, immunological and virologic correlations of HIV-1 infection and superinfection in rural Tanzania</i>
Country	Tanzania
LSHTM staff	Heiner Grosskurth, Gabriele Riedner, David Mabey, Richard Hayes, Brent Wolff
Collaborators	Michael Hoelscher, Frank von Sonnenburg, Oliver Hoffmann (University of Munich); Eligius Lyamuya, Fred Mhalu (Muhimbili University College of Health Sciences, Dar es Salaam); Leonard Maboko, Donan Mmbando, Titus Nkulila (Mbeya Region Research Board); Francine McCutchan (Henry Jackson Foundation); Carolyn Williamson (University of Cape Town)
Funding	European Commission
Dates	July 2000 – June 2005

Summary

HIV infection may potentially be protective against superinfection by a second HIV strain. Whilst co-infections with different HIV strains have been described, only few data are available on the circumstances of such superinfection. This study investigates the prevalence, incidence, and the virologic, immunological, clinical, and social factors associated with superinfection in a cohort of 600 highly exposed barworkers in a mostly rural region of Tanzania, where 3 HIV-1 subtypes co-circulate (A,C,D). The study will help to determine whether superinfection can occur in the presence of a fully developed immune response, will define its natural history and virologic outcomes, including emergence of recombinants, and will provide a new and innovative approach to define correlates of protective immunity for vaccine development. Within the collaborative arrangement, LSHTM contributes to the overall implementation of the study, and addresses behavioural and STD related research questions in particular.

Title	<i>The epidemiology and control of ulcerative STIs among sex workers in Mbeya, Tanzania and their interaction with HIV infection</i>
Country	Tanzania
LSHTM staff	Gabriele Riedner, Heiner Grosskurth, David Mabey, Richard Hayes
Collaborators	Eligius Lyamuya, Fred Mhalu (Muhimbili University College of Health Sciences, Dar es Salaam); Leonard Maboko, Donan Mmbando, Titus Nkulila (Mbeya Region Research Board); Michael Hoelscher, Frank von Sonnenburg, Oliver Hoffmann (University of Munich)
Funding	The Wellcome Trust
Dates	August 2000 – July 2003

Summary

Genital ulcers and other sexually transmitted infections (STI) have been shown to enhance the transmission of HIV infection, but many aspects of this interaction remain unclear. For example, it has been hypothesised that the prevalence and incidence of ulcers due to *Herpes simplex virus-2* (HSV-2) infection increase in mature HIV epidemics, and that HIV infected individuals with herpetic lesions excrete HIV more frequently than individuals without such lesions. It has further been suggested that the mass treatment of syphilis may lead to a paradoxical increase in HIV infection, because of an increase in the pool of individuals susceptible for syphilis. It would thus be important to investigate whether individuals treated for syphilis maintain some immunity against reinfection, and how long this may last. With respect to the control of ulcerative STI, a single dose oral treatment for syphilis that would have many advantages over the traditional treatment with penicillin injection has recently become available, but the feasibility and effectiveness of this strategy has not yet been evaluated in developing countries.

In the context of a study on HIV superinfection conducted in Mbeya, Tanzania, an opportunity has opened to address these research questions in an open cohort of 600 sex workers. Four interlinked studies are being performed: We aim to determine the prevalence and incidence of genital ulcers, and to compare the proportion of ulcers due to HSV-2 in HIV+ and HIV- individuals. The frequency of cervico-vaginal excretion of HIV in HIV infected women is being compared between women with and without HSV-2 lesions. Cohort members infected with syphilis receive treatment, and we aim to record the occurrence of and the time until reinfection. The treatment of syphilis with a single dose of oral azithromycin is being compared with the standard method through a randomised controlled trial.

Title	<i>Impact of syphilis on pregnancy outcome and evaluation of syphilis screening strategies to reduce adverse pregnancy outcomes in Mwanza, Tanzania</i>
Country	Tanzania
LSHTM staff	Deborah Watson-Jones, David Mabey, Richard Hayes, Helen Weiss, David Ross, James Todd; Lilani Kumaranayake; Fern Terris-Prestholt
Collaborators	National Institute of Medical Research (NIMR), Mwanza; Regional Medical Office, Mwanza; Bugando Medical Centre, Mwanza; Sengerema Designated District Hospital; Institute of Tropical Medicine, Antwerp; Universities of Montreal and Quebec, Canada; University of Newcastle
Funding	The Wellcome Trust

Summary

Reproductive tract infections (RTIs) during pregnancy, particularly syphilis, are believed to be one of the major risk factors for adverse pregnancy outcome. However, estimates of the impact of syphilis in pregnancy have given widely disparate results and few studies have controlled for the potential confounding effects of other factors associated with adverse pregnancy outcomes such as maternal malaria, anaemia and infection with other RTIs or HIV. The World Health Organisation and the Centers of Disease Control have recommended that screening and treatment for syphilis should be introduced as a routine part of antenatal clinic (ANC) services. However, there have been reported failures of single dose therapy to prevent congenital syphilis infection from Africa and the USA.

This study investigated the impact of untreated maternal syphilis on pregnancy outcome in a retrospective cohort of women, recruited at delivery in Mwanza Region, Tanzania, who did not have ANC syphilis screening. In total 380 women were recruited (138 RPR+, 242 RPR-). The study confirmed that syphilis still presents a major risk factor for poor birth outcome. 25% of women with high titre active syphilis had a stillbirth compared to 1% of women seronegative for syphilis ($p < 0.001$). Women with active syphilis had an 18-fold increased risk of stillbirth, a six-fold increased risk of preterm livebirths and four times the risk of any adverse pregnancy outcome.

The efficacy of treatment with single dose benzathine penicillin was evaluated in a prospective study of pregnant women screened for syphilis during pregnancy, adjusting for the above confounders for adverse pregnancy outcomes. In a prospective cohort of pregnant women recruited antenatally there was no evidence of any significant differences in pregnancy outcome between women treated for high titre active syphilis or low titre active syphilis and uninfected women, suggesting single dose treatment is effective in preventing adverse outcomes attributable to maternal syphilis. A cost-effective analysis of this intervention is now underway.

Title	<i>The impact and cost-effectiveness of HIV prevention strategies in sub-Saharan Africa: a comparative analysis of four strategies evaluated in three randomised trials (STDSIM Project)</i>
Countries	Tanzania and Uganda
LSHTM staff	Richard White, Kate Orroth, James Todd, David Ross, Alessandra Anemona, David Mabey, Heiner Grosskurth, Richard Hayes; Lilani Kumaranayake, Fern Terris-Prestholt
Collaborators	Eline Korenromp, Dik Habbema (Erasmus University Rotterdam); David Serwadda, Nelson Sewankambo, Fred Wabwire, Tom Lutalo, Ronald Gray, Maria Wawer (Rakai Research Programme of the Uganda Virus Research Institute and Johns Hopkins University); Anatoli Kamali, Jessica Nakiyingi, Lawrence Muhangi, Jimmy Whitworth (MRC Programme on AIDS, Uganda Virus Research Institute); Wambura Mwita (National Institute for Medical Research Tanzania)
Funding	DFID
Dates	December 1998 – May 2002

Summary

Resources for HIV prevention are limited, and policy-makers urgently need reliable information on the impact and cost-effectiveness of alternative control strategies. Three randomised trials, investigating the impact on HIV of four intervention strategies, have been published or are near completion in Mwanza (Tanzania), Masaka (Uganda) and Rakai (Uganda). In this collaborative project, cost data from the three trials are being standardised, and the cost and impact of the intervention strategies compared. Comparisons of impact are complicated by variations in HIV/STD prevalence and other differences between the three study populations. To address this problem, the simulation model STDSIM (Erasmus University, Rotterdam) is being fitted to the extensive data from the three trials in order to compare the impact of the different control strategies within each population. The study will thus provide information on the cost-effectiveness of alternative control strategies in a range of population settings.

Title *A randomised trial to evaluate the impact of regular malaria chemoprophylaxis on the progression of HIV in lactating women and the risk of post-natal mother-to-child transmission*

LSHTM staff Shabbar Jaffar

Collaborators Prof. Nkya, KCMC Tanzania, Dr Suzanne Filteau, ICH

Summary

The aim of this trial will be to examine whether malaria prophylaxis might retard the progression of HIV-1 and reduce the risk of HIV-1 transmission in lactating women. Approximately 400 women will be recruited over a period of about 2 years. Various ancillary studies will be conducted, including on adherence to prophylaxis.

Title *Field evaluation of simple point-of-care tests for syphilis*

Countries Tanzania, India

LSHTM staff David Mabey, Dean Everett

Collaborators WHO TDR (STD Diagnostics Initiative - SDI); NIMR, Mwanza, Tanzania

Funding SDI

Dates 2001 – 2003

Summary

Programme staff and collaborators in Mwanza, Tanzania submitted an application to run field and laboratory sites for the evaluation of new rapid, simple point-of-care tests for syphilis on behalf of the WHO STD Diagnostics Initiative. These were considered 2001 and the site was among the six selected. There are now several dipstick-type serological tests for syphilis on the market, some of which do not require separation of serum. None has been independently evaluated, and none is FDA approved. We will evaluate the tests for the screening of antenatal clinic populations.

Title	<i>Integration of STI prevention and care into reproductive health services in Tanzania: an analysis of barriers and opportunities</i>
Country	Tanzania
LSHTM staff	Philippe Mayaud, Monique Oliff (DrPH student) (advisors: Ruairi Brugha, Jim Todd, Louisiana Lush)
Collaborators	AMREF Tanzania (Vera Pieroth, Daraus Bukenya)
Funding	DFID (Innovations Grant)
Dates	June 2000 – June 2002

Summary

Operational study aiming at better understanding the barriers and opportunities at the national, regional, district and delivery levels that inhibit or promote the provision of comprehensive reproductive health services and STI care. The project was conducted by a DrPH student (Monique Oliff) for her research project. The DrPH was awarded in August 2002.

The study used a multi-disciplinary approach and consisted of:

- A review of national policy documents
- A stakeholder analysis and political mapping
- An analysis of service provision including interviews and observations in 9 randomly selected health facilities in 3 regions
- In-depth interviews with clients of reproductive services and health providers (including a sample of alternative care providers), and focus group discussions with community members.

Main results/outcomes

Many opportunities to improve the delivery of comprehensive reproductive health services to include STI prevention and care lie in:

- existing pre-service training infrastructure;
- workforce management and maximisation of the potential of existing staff;
- workforce supervision, role of district management teams;
- community responsibilities;
- involvement of men as clients;
- opening of policy arena to the influence of civil groups and NGOs.

A feedback workshop with key stakeholders was held in Tanzania using a very innovative participatory method involving the subjects of the research from the community having dialogue with the national policy-makers.

Title	<i>The role of mobility in the spread and control of STD and HIV</i>
Countries	Tanzania, Zimbabwe
LSHTM staff	Basia Zaba, Brent Wolff; Richard White
Collaborators	Dik Habbema, Helene Voeten Erasmus University Rotterdam; TANESA project (Tanzania); Manicaland project (Zimbabwe); Simon Gregson, Imperial College, London
Funding	European Commission

Summary

This project received approval from the EC in 2000, with Erasmus University as the lead partners.

The aim of this project is to study the impact of mobility on the spread of STD/HIV and the relative appropriateness of different interventions in settings differing in their pattern of mobility. A detailed data analysis will be undertaken of mobility data from two African study areas (one in Tanzania, one in Zimbabwe), followed by simulation modelling – it is hoped that this modelling exercise will yield results which will help in the interpretation of currently observed epidemic patterns, and to help plan strategies to increase the effectiveness of interventions in highly mobile populations.

Preliminary data analysis has been completed of mobility data already available for the two study sites, and an abstract prepared about this for presentation at the African AIDS conference in Ouagadougou. We have also completed a review of information on mobility contained in DHS data from all African surveys completed in the 80s and 90s.

Title	<i>AMREF Mine Health Project</i>
Country	Tanzania
LSHTM staff	Deborah Watson-Jones, David Ross
Collaborators	African Medical & Research Foundation (Meghan DiCarlo & Awene Gavyole), Kahama Mining Corporation, Geita Goldmine, National Institute of Medical Research, Mwanza
Funding	Kahama Mining Corporation, Geita Goldmine, African Mining Services, Stanley Mining
Dates:	2002 – 2003

Summary

Objectives

To develop and manage a sustainable of community-based health programmes minimize the impact of HIV, STIs, lung diseases and malaria among mineworkers, female bar workers and communities surrounding mining areas of the Lake Zone of Tanzania

Methodology

Key activities:

- 1) Mine site - Mineworker peer health educator (PHEs) scheme and HIV/STI/TB/Malaria Awareness programmes.
- 2) Community - Community health educators (CHEs) scheme, social marketing of condoms and insecticide-treated bednets, Annual Health Week, production of locally appropriate health promotion materials, focused interventions for high-risk groups e.g. female bar workers.
- 3) Health facilities - Health worker training and supervision of selected health units in partnership with District Health Authorities, establishment of community HIV Information Centres with voluntary counselling and testing (VCT) (joint venture with District health department also offering other sexual and reproductive health services and ongoing post-test counselling and support).

Results

Baseline cross-sectional surveys in two mining communities conducted in 2000 and 2001 demonstrated a 16% HIV prevalence in men and 18% in women, compared to 4-10% in male mine workers and 42% in female bar workers. Over 50% of men reported paying for sex during the previous year.

Project prevention activities started in 2001 including PHE schemes, condom promotion and bednet social marketing, focused interventions targeting bar workers and their male clients. HIV Information Centres offering VCT, syndromic STI management and family planning have been established in 2002.

A baseline survey for a third mine in North Mara, Tanzania, has recently been conducted.

Title	<i>Epidemiology of Human papilloma virus (HPV) infection and cervical dysplasia in Tanzania</i>
Country	Tanzania
LSHTM staff	Philippe Mayaud, David Mabey, Helen Weiss, Richard Hayes, David Ross
Collaborators	John Changalucha (NIMR/MEMA project, Mwanza); Charles Lacy, Dil Gill (St Mary's Hospital, London); Michael Hagensee (University of Louisiana, USA)
Funding	DFID KP
Dates:	2001 – 2003

Summary

Human papillomaviruses (HPV) are among of the most prevalent STI pathogens worldwide. High-risk oncogenic genital HPV have been shown to be the causative agents of cervical cancer and pre-cancer or squamous intra-epithelial lesions (SIL), which is the most common female cancer in sub-Saharan Africa, with age-standardised incidence rates being fourfold higher in Africa than in North America and Europe. However, detailed data on HPV epidemiology, strain distribution and natural history are scarce from African countries. The influence of HIV on the natural history of HPV and SIL is not well documented in Africa.

The objectives of this project, which will draw on previously or currently collected samples in the Mwanza region, will be:

- 1) To determine the prevalence, risk factors, strain characteristics of HPV infection among pregnant women in urban Mwanza;
- 2) To compare the prevalence of HPV 16 (most common oncogenic type) using serology and PCR test on cervical samples;
and if serological test is found useful:
- 3) To determine the prevalence and incidence of HPV-16 in a cohort of young people living in rural areas of Mwanza, and correlate with HIV acquisition and other risk factors, and residence in MEMA intervention or comparison site.

Title	<i>Vaginal microbicides for the prevention of HIV transmission: a feasibility study for Phase III trials in Mwanza Region, Tanzania</i>
Country	Tanzania
LSHTM staff	Richard Hayes, David Ross, Dean Everett, Andrew Vallely, Tobias Chirwa
Collaborators	African Medical & Research Foundation (AMREF), Tanzania; National Institute for Medical Research (NIMR), Tanzania; MRC Clinical Trials Unit, London; MRC Social and Public Health Sciences Unit, Glasgow
Funding	DFID/MRC
Dates:	October 2001 – September 2003

Summary

Objectives

The aim of this feasibility study is to investigate whether high-risk women in Mwanza City would be a suitable group for Phase III (efficacy) trials of vaginal microbicides such as dextrin sulphate, PRO 2000 or others.

The specific objectives of the feasibility study will be:

- To determine whether it is possible to recruit and follow-up sufficient numbers of high-risk women in this site;
- To estimate HIV incidence among these women;
- To estimate condom use among these women.

Methodology

This feasibility study will be linked to an AMREF Women's Reproductive Health Project which will be established in Mwanza City. Between 10 and 15 weekly women's reproductive health clinics will be set up in different areas of the city. The clinics will be run by mobile teams, and each clinic will operate on a fixed day each week. Women working in food and recreational facilities (bars, hotels, restaurants, discos etc.), who are assumed to be at high risk of HIV and other STIs, will be invited to participate in the project. Consenting women will be recruited at their nearest project clinic, and then followed up at routine clinic visits every three months. They will also be encouraged to attend the clinic at other times if necessary. Periodic serum samples, genital swabs and urine will be collected to measure the prevalence and incidence of HIV and other STIs including syphilis, HSV2, gonorrhoea, chlamydia, trichomoniasis and bacterial vaginosis. Detailed data will also be collected on the demographic and behavioural characteristics of the women. Recruitment commenced in September 2002.

A linked social science project will be carried out using a mix of quantitative and qualitative research methods. The main objectives will be to characterise sexual behaviour (including condom use) among high-risk women and their sexual partners; to determine the acceptability of vaginal gel and applicators among high-risk women and their sexual partners; and to identify the obstacles and facilitating factors to continued involvement in the microbicide research programme by high-risk women.

Title	<i>Clinical epidemiology of HSV-2 and the impact of HSV suppressive therapy to reduce HIV incidence in high risk women in Tanzania</i>
Country	Tanzania
LSHTM staff	Deborah Watson-Jones, Richard Hayes, Helen Weiss, David Ross, Dean Everett, Tobias Chirwa
Collaborators	African Medical & Research Foundation (AMREF), Tanzania; National Institute for Medical Research (NIMR), Mwanza; Regional Medical Office, Mwanza; Institute of Tropical Medicine, Antwerp; Hôpital Européen Georges Pompidou, Université Pierre & Marie Curie (Paris VI), Paris; University College Hospital, London; Kahama Mining Corporation Ltd.
Funding	DFID/MRC
Dates:	October 2001 – September 2003

Summary

Objectives

- To determine the current aetiology of genital ulceration in NW Tanzania.
- To determine whether HSV-2 suppressive therapy will reduce the incidence of HIV in women at high risk of acquiring HIV.
- To examine the interaction between HIV and HSV-2 shedding and the effect of HSV suppressive therapy on HIV and HSV viral shedding in high risk women (HRW).

Methodology

- Aetiology of genital ulcers will be measured in STI clinic attenders presenting with symptomatic genital ulceration in Mwanza.
- A placebo-controlled trial of HSV-2 suppressive therapy with aciclovir, as a strategy to reduce HIV incidence, HSV-2 and HIV viral shedding, will be carried out in a cohort of 860 HRW in communities neighbouring large-scale goldmines.
- The interaction between HIV and HSV-2 shedding will be examined in a sub-group of HRW from the cohort.

Results

Study will start fieldwork in 2003.

Thailand

Title	<i>The association between HSV-2 and HIV-1 infections among Thai hospital patients</i>
Country	Thailand
LSHTM staff	Shabbar Jaffar
Collaborators	Sukhum Jiamton, Puan Suthipinittharm (Mahidol University)
Funding	Glaxo-Wellcome
Dates	January 2000 – August 2003

Summary

The aim of this study was to examine whether *Herpes simplex* virus type-2 infection leads to a greater level of HIV-1 genital shedding. Approximately 140 HSV-2 seropositive, some of whom had a HSV-2 genital ulcer, some whom were HSV-2 positive but did not have an ulcer and some who were HSV-2 negative, were recruited. Analysis will examine rates of HIV genital shedding in these groups, taking clinical stage into account.

In this study, approximately 20 HIV-1 infected patients with genital ulcers, half women and half men, were followed longitudinally. The changes in genital shedding of HIV following healing of the ulcer, taking clinical stage into account, will be examined in these patients.

Title	<i>Impact of HIV on tuberculosis in Thailand</i>
Country	Thailand
LSHTM staff	Potjaman Siriarayapon (DrPH), Judith Glynn, Emilia Vynnycky
Collaborators	Dr H Yanai (RIT, Chiang Rai, Thailand)
Funding	WHO Thailand (completed)

Summary

That HIV increases the risk of tuberculosis is well known, but less is known about the magnitude of this increase and how this may vary over time and by age. Chiang Rai experienced an explosive HIV epidemic which was quickly reversed, a pattern which gives rise to complex changes in the incidence of tuberculosis. This was explored in a case-control study spanning nearly a decade. A model was developed to explore these changes further.

During the study period, the number of new TB cases in Chiang Rai Hospital increased more than 3-fold. The ORs increased over time for both sexes but did not have a clear age pattern. The proportion of TB cases attributable to HIV rose to 72.0% in males and 65.8% in females by 1998.

Despite the marked reduction in HIV incidence already seen in Chiang Rai, the HIV prevalence among TB cases and the proportion of cases attributable to HIV continue to rise.

Title *A randomised trial of micronutrient therapy among Thai HIV-infected patients*

Country Thailand

LSHTM staff Shabbar Jaffar

Collaborators Sukhum Jiamton, Puan Suthipinittharm (Mahidol University)

Funding Nestle Foundation

Summary

The aim of this study was to examine whether a comprehensive range of micronutrients that includes vitamins A, B6, B12, C and E and selenium, at doses higher than recommended daily allowance can slow the progression of HIV and reduce the level of HIV-genital shedding. 500 patients were recruited, randomised to receive the intervention or a placebo and then followed regularly for a period of 1-2 years. The main paper from this trial in impact on disease progression and mortality has been submitted and the a PhD thesis by Dr Jiamton is near completion. Analyses for further papers on a) the impact on HIV genital shedding and b) of the association between plasma levels of micronutrients and markers of HIV disease progression and transmission are underway. In addition, funds have been secured for a new follow-up of the study patients to assess whether the beneficial effects of micronutrients might be reproduced over a longer time frame - this is likely to lead to a further publication.

Uganda – see also Cameroon, South Africa, Tanzania

Title	<i>The aetiology of STI syndromes and evaluation of treatment algorithms in Masaka district, Uganda</i>
Country	Uganda (Masaka district)
LSHTM staff	Philippe Mayaud
Collaborators	MRC Programme on AIDS, Entebbe, Uganda (Anatoli Kamali, Peter Hughes, Delys Morgan, Jimmy Whitworth); University of Manitoba, Canada (Ian Maclean)
Funding	MRC Programme on AIDS, Uganda
Dates	January 2000 – June 2001 (completed)

Summary

Evaluation of the microbial aetiologies and validity and costs of the main STI syndromes in 3 rural health units in the Masaka District. This research supports the main Masaka community STD trial.

Main results/outputs

- Urethral discharge syndrome: the main pathogen was *N gonorrhoeae* (NG, 57% by urethral culture, 70% by LCR on a urine specimen) and *C trachomatis* (CT) was rarely found (<1%). 6% of men had a positive *T vaginalis* culture (often in association with NG).
- Vaginal discharge syndrome: most frequent were vaginitis-causing agents such as *T vaginalis* (28%), *C albicans* (27%) or bacterial vaginosis (48%); agents causing cervicitis were rarely found, NG (9.4%) and CT (<1%).
- Genital ulcer syndrome: using a multiplex PCR method, the study found that HSV-2 was the most prevalent STI pathogen (50%). *Haemophilus ducreyi* and *Treponema pallidum* were rarely found (around 3% each). A number of ulcers yielded Staphylococci or Streptococci-positive cultures. However, these micro-organisms could be secondary contaminants to the genital wound, rather than aetiological agents.

Broadly, the study supports the syndromic approach for male and female discharge syndromes, TV treatment may be added to the M-GDS algorithm. The study also confirms that HSV has become the number one pathogen in GUS. Antibiotic treatment targeting bacterial infections is unlikely to be beneficial (although it will help with secondary bacterial infections). Algorithms should be revised to include specific anti-herpes therapy for genital ulcers.

Title	<i>Bridging gaps between public and traditional health care sectors: a model to improve quality of STI/HIV/AIDS care in sub-Saharan Africa</i>
Country	Uganda and Zambia
LSHTM staff	Philippe Mayaud, Ruairi Brugha, James Todd, Monique Oliff
Collaborators	Elisabeth Faxelid and Roy Unge (IHCAR, Karolinska Insitutet, Stockholm, Sweden); Donna Kabatesi (THETA, Uganda); Freddie Ssengooba (IPH, Makerere University, Uganda); Phillimon Ndubani (INESCOR, University of Zambia); Rodwell Vongo (THPAZ, Zambia)
Funding	EC
Dates	2002 – 2006

Summary

The general objective of this research is to develop and evaluate innovative strategies to create mutual understanding and increased dialogue and collaboration between public and traditional health care providers in Uganda and Zambia. The purpose is to improve the quality and increase the uptake of STI/HIV/AIDS health care services, focusing particularly on the humanity of patient/provider interactions and effectiveness of public (preventive) health services in both sectors. By humanity is meant a) consumer satisfaction in relation to the care they receive, and b) quality of the communication, empathy, and sensitivity of providers. Public health dimensions will include promotion and uptake of key STI/HIV/AIDS related health services such as condom use, partner notification, voluntary counselling and testing (VCT) for HIV, awareness of STI symptoms and importance of STI treatment, and better access to quality services through both sectors.

A process oriented, country-specific intervention will be designed, implemented and evaluated. The intervention will build on earlier work and on-going activities related to collaboration between the traditional and public sectors in the two countries. Strategies to be agreed in the preliminary phase and tested through the intervention and evaluation will include: joint and separate training activities, interactive group discussions (involving public and traditional health care providers), and the development of provider peer influencing networks (PINs). Process indicators which will be developed to evaluate the intervention will, for example, assess: attitudes towards the opposite type of provider and towards collaboration, meetings/interactive sessions involving public and traditional health care providers, and referrals between the sectors. Outcome indicators (in both sectors) will assess: patient satisfaction with STI/HIV/AIDS care received, the delivery of health promotion activities, and uptake of the above mentioned key STI/HIV/AIDS related health services. The same indicators will be assessed in a quasi-experimental control arm to monitor secular effects.

Progress

The project started in September 2002 with review of practices regarding intersectoral collaboration in both countries, stakeholder consultations, and the collection of key information for site selection.

The first project workshop was held in Entebbe in January 2003. **Selected districts will be an urban XXX in Zambia (Kabwe and Ndola) and rural in Uganda (Luweero and Kibaale).** Baseline assessment of traditional healers and biomedical workers' practices will be undertaken in April-August 2003.

Title	<i>HIV impact on fertility – causes, consequences and measurement issues</i>
Countries	Uganda and Malawi
LSHTM staff	Basia Zaba, Susan Hunter, Sabine Litwinenko; Judith Glynn, Richard White
Collaborators	Ties Boerma (University of North Carolina); Lucy Carpenter (Oxford University); Simon Gregson, Geoff Garnett (Imperial College); Jimmy Whitworth, Jessica Nakiyinge (MRC Masaka); Mark Urassa (TANESA Project, Tanzania); Lindiwe Makubalo, Ntomboxolo Bikitsha (South Africa Department of Health)
Funding	DFID; USAID – Measure project

Summary

There are several on-going projects in this research area, all of them concerned with identifying the HIV-associated factors (behavioural and biological) which cause the fertility of HIV positive women to differ from that of their HIV negative counterparts, and in exploring how these differences affect HIV prevalence measures based on ante-natal surveillance. A common aim is to produce an algorithm for adjusting prevalence measures based on monitoring pregnant women to make them representative of the general female population in the child bearing ages.

One approach, the focus of the PhD investigation, is to use “proximate determinant” modelling of sexual behaviour and biological factors which determine age specific fertility and infection risk. Our links with the TANESA project and the MRC programme in Masaka allow us to test model predictions against empirical data, and to develop practical methods for adjusting data and interpreting biases. Two papers were published in AIDS last year - the first explains the results of a simulation study exploring the relationship between trends in HIV prevalence in young pregnant women (as would be observed in ANC clinics) under alternative classifications - age or parity - compared to trends in all women. The second paper shows how data from DHS surveys can be used to categorise populations by size of risk groups of women who were unlikely to become pregnant and would therefore be missed from ANC surveillance, and how to adjust prevalence estimates for these omissions. This approach has been validated in two recent studies, one in Manicaland, Zimbabwe the other in Mwanza region, Tanzania, as reported in papers by Gregson et al and Changalucha et al published this year in AIDS.

Title	<i>HIV and child mortality</i>
Countries	Uganda, Malawi
LSHTM staff	Basia Zaba, Andy Sloggett; Judith Glynn, Lyn Bliss, Sian Floyd, Mia Crampin
Collaborators	Michael Bracher (NIAS, the Hague); MRC centre Masaka, Uganda; TANESA project, Tanzania; Karonga Prevention Study, Malawi
Funding	UNICEF, USAID

Summary

This new study has two main aims, each with several subsidiary research questions:

- To ascertain current levels of child mortality in populations affected by HIV and assess the contribution of HIV to the burden of child mortality
- To propose methods for correcting the estimates of child mortality obtained using birth history and indirect approaches, which are subject to bias in the presence of HIV, due to a high correlation between maternal and child mortality.

After visits to all the collaborating sites, data sharing agreements were drawn up, and the necessary data editing completed to allow similar analyses of data from all three sites. Draft analyses have been prepared for each site, focussing on the relationship between maternal HIV infection, maternal survival and child mortality. We are hoping to turn these into papers for presentation at the next international AIDS conference. A meta analyses has also been made, and presented in a report to UNICEF.

The main new research finding so far, is that maternal mortality has a large effect on child survival that is independent of maternal HIV status. Child mortality is increased approximately by a factor of five in the year immediately following or preceding a mother's death. Mortality rates for children of HIV positive mothers are about three times those of HIV negative mothers. The association between maternal and child mortality causes five-year retrospective reports on child mortality by HIV positive mothers to under-estimate the true rates by around 8%. At the population level, this translates into an overall under-estimate of child mortality of the order of 4% in populations where HIV prevalence in females is around 10%.

Work is continuing on finalising the analyses, writing up these results, and on developing correction procedures for child mortality estimation.

Zambia – see also Cameroon, Kenya, Malawi, South Africa, Uganda

Title	<i>The natural history of HIV progression in a cohort of HIV infected Zambian adults</i>
Country	Zambia
LSHTM staff	Peter Godfrey-Faussett, Maria Hosp, Alwyn Mwinga, John Porter, Maria Quigley
Collaborators	University Teaching Hospital, Lusaka, Zambia
Funding	DFID
Dates	1992 until the present

Summary

A randomised double-blind placebo controlled trial was conducted to estimate the efficacy of preventive therapy for tuberculosis in HIV infected adults in Lusaka. The main outcome measures were the incidence of tuberculosis, mortality and adverse drug reactions. The trial has been analysed and the results have been written up. Follow-up of the cohort continues and the accumulated follow-up averages 3 years per person, with a maximum follow-up of 7 years. We have studied the correlation between CD4 count, neopterin, total lymphocyte count, and haemoglobin (1,2) and examined the long-term effect of preventive therapy (3). We are currently examining the natural history of HIV infection using clinical data and progression markers. The mortality rate and the decline of progression markers in this cohort is similar to other African and non-African cohorts.

Title *The prevention of HIV-associated TB in Lusaka, Zambia*

Country Zambia

LSHTM staff Helen Ayles, Peter Godfrey-Faussett, Maria Quigley

Collaborators School of Medicine, University of Zambia;
Kara counselling and Training Trust, Lusaka, Zambia;
Urban District Health Management Team, Lusaka, Zambia

Funding The Wellcome Trust

Dates October 1998 – September 2001

Summary

Overall Aim

To reduce the impact of HIV-associated tuberculosis (TB) on the health of the population of Lusaka.

Research Question

Is it feasible to administer TB preventive therapy (PT) safely to HIV infected individuals via the voluntary counselling and testing (VCT) clinics already established in Lusaka?

Overview

The majority of cases of tuberculosis in Lusaka are associated with HIV. Many of these HIV-associated TB cases could be prevented if people had access to HIV testing and preventive therapy. This study utilises existing counselling and testing facilities to investigate whether safe administration and monitoring of PT is possible. Previous studies have shown that individuals in the earlier stage of HIV disease benefit most from PT. They have also shown that individuals seeking testing are the most motivated to comply with PT. Subjects will be recruited from VCT centres and all subjects will receive 6 months isoniazid 300mg/day. Outcomes will be compliance with therapy, adverse events, development of isoniazid resistance and mortality. To address the question of reinfection vs inadequate sterilisation, a household transmission study using molecular epidemiology will be undertaken. Household members will be counselled for HIV and investigated for active TB. Any HIV-positive household contacts who do not have evidence of active TB, will be offered PT. Any cases of TB in the household contacts will be analysed using restriction fragment length polymorphism (RFLP) and the strain compared with that of the index case. Outcomes will be the clustering of TB strains within a household, indicating possible transmission and thus reinfection. Secondary outcomes will be the uptake of HIV counselling and testing using a method of "family counselling", uptake of HIV testing in the home compared to in the counselling centre, and uptake of PT in these household contacts.

Title	<i>Household studies on HIV and TB</i>
Country	Zambia
LSHTM staff	Helen Ayles, Peter Godfrey-Faussett, Maria Quigley
Collaborators	School of Medicine, University of Zambia; Kara counselling and Training Trust, Lusaka, Zambia; Urban District Health Management Team, Lusaka, Zambia
Funding	The Wellcome Trust
Dates	October 1998 – September 2001

Summary

Overall Aim

To reduce the impact of HIV-associated tuberculosis (TB) on the health of the population of Lusaka.

Research Questions

1. Can provision of HIV counselling and testing at a family level increase uptake of VCT and isoniazid TB preventive therapy for people living with HIV?
2. In HIV-positive individuals, recently exposed to TB, does TB preventive therapy sterilise latent infection only or does it also prevent re-infection?
3. How much TB is transmitted within households in Lusaka?

Overview

The majority of cases of tuberculosis in Lusaka are associated with HIV. Many of these HIV-associated TB cases could be prevented if people had access to HIV testing and preventive therapy.

Cases of smear positive TB will be approached and offered counselling on TB and HIV in their household on a family level. HIV counselling and testing will be offered either in the home or in the local VCT centre. Isoniazid preventive therapy will be offered to any household contact found to be HIV positive. To address the question of reinfection vs inadequate sterilisation, any cases of TB in the household contacts will be analysed using restriction fragment length polymorphism (RFLP) and the strain compared with that of the index case. Outcomes will be the clustering of TB strains within a household, indicating possible transmission and thus reinfection. Secondary outcomes will be the uptake of HIV counselling and testing using this method of "family counselling", uptake of HIV testing in the home compared to in the counselling centre, and uptake of PT in these household contacts.

Zimbabwe – see also Tanzania

Title	<i>A pilot study to assess the acceptability and feasibility of conducting a community randomised trial of an adolescent reproductive health intervention in Zimbabwe</i>
Country	Zimbabwe
LSHTM staff	Richard Hayes, Shabbar Jaffar, David Mabey
Collaborators	Mary Bassett, David Wilson (University of Zimbabwe) Frances Cowan, Judith Stephenson, Anne Johnson (UCL); David Brown (PHLS)
Funding	The Wellcome Trust
Dates	October 1999 – March 2001

Summary

Zimbabwe has seen an abrupt and violent HIV epidemic with prevalence of HIV among adults in some cities near 30%. The final aim of this research is to conduct a community-randomised trial to determine the effectiveness of a targeted adolescent sexual health intervention. The intervention will comprise an enhanced school-based sex education programme combined with provision of youth-friendly sexual health services. It is proposed to randomise 30 secondary schools to the intervention and comparison arms. A cohort of pupils aged 12 and over will be recruited and followed up for 4 years to measure the impact of the intervention on the incidence of HIV, STIs and unintended pregnancy.

An initial *pilot study* has been funded by the Wellcome Trust to assess the feasibility and acceptability of conducting the main trial, to develop and pre-test the intervention and data collection methods, and to collect data on HIV/STI prevalence rates and other variables that will help to refine the design of the main trial. In collaboration with PHLS, a urinary assay for HSV2 antibodies will be developed and validated.

Title	<i>A pilot study to assess the acceptability and feasibility of conducting a community randomised trial of a targeted HIV prevention intervention among sex workers</i>
Country	Zimbabwe
LSHTM staff	Richard Hayes, Shabbar Jaffar, David Mabey
Collaborators	David Wilson, Mary Bassett (University of Zimbabwe); Frances Cowan, Judith Stephenson, Anne Johnson, (UCL)
Funding	The Wellcome Trust
Dates	October 1999 – March 2001

Summary

Zimbabwe has seen an abrupt and violent HIV epidemic with prevalence of HIV among adults in some cities near 30%. The final aim of this research is to conduct a community randomised trial to test the effectiveness and cost-effectiveness of targeting HIV prevention interventions through sex workers (SWs). It is planned that about 20 communities will be randomised to either intervention or comparison arms of the study. The targeted intervention will consist of giving periodic presumptive treatment (PPT) of STIs to SWs via a community nurse, in addition to using peer educators to promote safer sex and maximise condom use among these women. By involving peer educators in intervention delivery we hope to make it sustainable and acceptable. The primary outcome measure would be difference in HIV incidence in male migrant workers between intervention and comparison communities after two years. Secondary outcome measures will include differences in rates of bacterial STIs in SWs and migrant workers and the population attributable fraction (PAF) for incident HIV infection associated with past or incident HSV-2 infection will be calculated.

The aims of this pilot study are: a) to determine the extent to which a mature HIV epidemic, such as the one in Zimbabwe, is driven by commercial sex, b) to develop an acceptable and sustainable HIV prevention intervention targeted through SWs, c) to determine the feasibility of undertaking a community randomised trial to test effectiveness and cost effectiveness of the targeted intervention in reducing HIV incidence in the wider population, and d) to develop and evaluate a urinary assay for HSV-2 antibody, to be used as a biomedical outcome measure in the proposed trial.

A cross-sectional survey was completed in 1405 men, working on commercial farms or in mines. Urine testing revealed an HIV prevalence of 27%, but a low prevalence of other STIs (chlamydia 1.5%, gonorrhoea 0.5%). 29% of men reported sex with a SW in the past year. HIV infection was more common in men reporting SW contact (OR 1.9, 95% CI 1.5-2.5).

Title	<i>Regai Dzive Shiri: a randomised trial of HIV/STD prevention among Zimbabwean youth</i>
Country	Zimbabwe
LSHTM staff	Richard Hayes, Shabbar Jaffar
Collaborators	University College London and University of Zimbabwe
Funding	NIH
Dates	September 2002 – August 2007

Summary

Zimbabwe has one of the most severe HIV epidemics in the world. The development of effective interventions to protect the next generation of young people from infection is a major public health priority. School-based interventions offer a potentially efficient method of reaching the target population, but their effectiveness needs to be evaluated before wide-scale implementation can be recommended.

The aim of the project is to implement and rigorously evaluate an exciting and innovative adolescent HIV/STD prevention programme involving school students, professional peer educators, teachers, parents, rural health clinics and the wider community, by means of a community randomised trial.

Primary objective

To measure the effectiveness of an adolescent HIV prevention intervention, delivered to secondary school pupils and the wider community, in reducing the incidence of HIV infection, the incidence and prevalence of other STIs and the incidence of unintended pregnancy among the students.

Secondary objectives

- 1) To use a combination of quantitative and qualitative research methods to explore the evolution of sexual behaviour in adolescents in rural Zimbabwe.
- 2) To assess the impact of the intervention on knowledge and attitudes regarding reproductive and sexual health, reported behaviour, and measures of self-efficacy.
- 3) To determine through rigorous process evaluation whether these programmes are delivered as intended.
- 4) To refine and assess the validity of research instruments for measuring sexual behaviour among Zimbabwean adolescents.
- 5) To examine through rigorous process evaluation the acceptability and feasibility of providing VCT in rural community settings.
- 6) To study the epidemiology of Herpes simplex virus type-2 (HSV2) infection among adolescents, and to measure the extent to which HSV2 facilitates acquisition of HIV infection.

Methods

30 communities (60 secondary schools) will be randomly allocated to either early or deferred programme implementation. Communities in the deferred arm will have HIV prevention as currently implemented. The impact of the programme will be measured in a cohort of 6,600 Form 2 secondary school pupils aged >12 (median age 15), who will be followed for 4 years (to median age 19). Participants will be surveyed at the start of the project, after 30 months and after 4 years. At each survey they will complete a questionnaire and provide a finger-prick blood sample (and a urine sample for girls). The impact of the programme on cumulative incidence of HIV and HSV2 infection, and unintended pregnancy as well as on reported sexual behaviour will be determined. A detailed process evaluation of the programme will be conducted to inform wider programme implementation.

ACRONYMS

AMREF	African Medical Research Foundation
ANRS	Agence Nationale de Recherche sur le SIDA
BADC	Belgian Administration for Development Cooperation
CDC	Centers for Disease Research
CDSC	Communicable Disease Surveillance Centre, UK
CERPOD	Centre for Applied Research on Population & Development, Mali
CIDA	Canadian Agency for International Development
CNPq	Conselho Nacional de Desenvolvimento Científico e Tecnológico, Brazil
CNRMST/SIDA	National Reference Centre for STD and AIDS, Central African Republic
CPHL	Central Public Health Laboratory, UK
DFID	Department for International Development, UK
DOTS	Directly Observed Treatment, Short course
ERNVL	Enteric, Respiratory and Neurological Virus Laboratory
ESRC	Economic and Social Research Council, UK
ESEP	European Science Exchange Programme
FHI	Family Health International
GUM	Genito-Urinary Medicine
HAPAC	HIV/AIDS Prevention and Care
ICH	Institute of Child Health, University of London
INRSP	National Institute for Research on Health and Population, Mali
INSERM	Institut National de la Santé et de la Recherche Médicale, France
ITAD	Information, Training and Development Ltd
KCMC	Kilimanjaro Christian Medical Centre, Tanzania
KIT	Royal Tropical Institute, Amsterdam
LEPRA	Leprosy Relief Association
LSHTM	London School of Hygiene and Tropical Medicine
MRC	Medical Research Council

MSF	Médecins Sans Frontières
NIAS	Netherlands Institute for Advanced Study
NIH	National Institutes for Health
NIMR	National Institute of Medical Research, Mwanza, Tanzania
NORAD	Norwegian Agency for Development Cooperation
PI	principal investigator
PHLS	Public Health Laboratory Service, UK
RHRU	Reproductive Health Research Unit, Johannesburg, South Africa
RIT	Research Institute of TB, Japan
SAIMR	South African Institute for Medical Research
SASH	Situation Analysis of Sexual Health
SPAP	Safe Passages to Adulthood Programme, LSHTM
UCL	University College, London University
UCLMS	University College London Medical School
UNAIDS	Joint United Nations Programme on HIV/AIDS
USAID	United States Agency for International Development
WAPTCA	West African Project to Combat AIDS
WHO TDR	World Health Organisation Technical Development & Research Programme