Malawi Medical Journal; 18(4) 176 -190 December 2006

Epidemiology of reproductive tract infections (RTIs) in Malawi

Adamson Muula[1] and Eveline Geubbels[2]

[1]Department of Community Health, College of Medicine, Blantyre, Malawi
[2]Center for Reproductive Health, Department of Community Health, College of Medicine, Malawi

Methods for the review

We searched for references of published literature about Malawi through Pubmed and obtained full text papers from HINARI, Popline, EBSCO, journals' open access initiatives and local libraries. The Cochrane library was used (through the free WHO Reproductive Health Library) for information on the current state of effective interventions for STD's. We contacted the Reproductive Health Unit (RHU) and the Health Management Information Unit of the Ministry of Health for information on guidelines and health care delivery regarding STD's.

General introduction

Microbiological, immunological and pathogenic aspects

Reproductive tract infections (RTIs) include endogenous infections, iatrogenic infections and sexually transmitted infections (STIs). Endogenous infections result from an overgrowth of organisms normally present in the vagina, and are the most common RTIs worldwide. They may or may not be transmitted through sex. Iatrogenic infections occur when a medical procedure (e.g. insertion of an intra uterine device (IUD), or induced abortion) introduces a micro organism into the reproductive tract, e.g. because of improperly sterilised surgical instruments or by pushing an already existing lower reproductive tract infection into the upper reproductive tract. Sexually transmitted diseases, previously referred to as venereal (Greek goddess of love, Venus) diseases, are an important cause of morbidity in Malawi and globally. The World Health Organisation (WHO) estimated that 340 million new cases of syphilis, chlamydia, trichomoniasis and gonorrhoea occurred in 1999[1]. Most of the RTIs, except HIV, HPV related cervical cancer and peritonitis from pelvic inflammatory disease (PID) are unlikely to cause death but are responsible for considerable morbidity. Long-term effects such as infertility due to salpingitis or epididymo-orchitis have diverse socio-cultural ramifications. As discussed in the Chapter on HIV and AIDS, RTIs have received particular attention in recent years on account of the role they play in facilitating HIV transmission and acquisition [2,3].

The most common RTIs are described below:

Ulcerative RTIs

- Syphilis is caused by the spirochete Treponema pallidum and results in acute disease, characterised by a primary painless ulcer within 21 days of acquisition and in one third of untreated cases a generalised secondary eruption of a maculopapular rash with associated lymphadenopathy in approximately 90 days. About one third of untreated secondary cases become clinically latent. Neurosyphilis may occur in secondary syphilis or during the latency period. Foetal infection occurs often when mothers have an untreated infection. Laboratory diagnosis is made by serologic tests of blood, usually using rapid tests with non-treponemal antigens (e.g. RPR, VDRL) and confirmation by tests that use treponemal antigens (e.g. FTA-Abs, MHA-TP or TPHA).
- Chancroid is caused by the bacterium Haemophilus ducreyi and in men results in a single or multiple painful necrotizing ulcers in the genital area often with painful unilateral swelling and suppuration of the regional lymph nodes (bubo). In women the infection is asymptomatic or results in minimally symptomatic lesions in the vaginal wall or cervix. Diagnosis is made by isolation of the organism from lesion exudates, by PCR or by serology.
- Genital Herpes is usually caused by herpes simplex virus type 2. It occurs as primary or recurrent infection with or without symptoms. If symptomatic in primary disease small ulcers appear on the cervix and vulva in women and penile gland and prepuce in men characterized by itching and burning sensation followed by clustered blisters that eventually break into ulceration. Recurrent disease may involve the perineal skin, legs, buttocks, vulva and mouth, depending on sexual practices. Recurrence is commonly associated with HIV immunosuppression. Herpes is generally diagnosed using ELISA, viral isolation or PCR.

Non-ulcerative RTIs

- Gonorrhoea is caused by the bacterium Neisseria gonorrhoeae. In men infection is characterised by acute purulent discharge from the urethra with dysuria within 3-5 days of acquisition. In women the infection causes mucupurulent cervicitis, which is often asymptomatic and symptoms can take up to three weeks to manifest but may result in abnormal discharge, dysparunia and vaginal spotting after intercourse. Gonorrhoea can lead to infertility or ectopic pregnancy. Disseminated gonococcal infections have been reported resulting in oesophageal infections, neonatal ophthalmic and perinatal ulcerative infections. Diagnosis is made by gram stain of discharges, bacteriologic culture or tests that detect nucleic acid (like NAAT or PCR).
- Chlamydia is caused by the bacterium Chlamydia trachomatis. Chlamydia often coexists with gonorrhoea. Clinical manifestations mimic gonorrhoea in the first 10-14 days. However, in men burning sensation followed by a thin purulent discharge appear. Up to 70% of infections in women are asymptomatic. Chlamydia in women may lead to salpingitis, chronic infection of fallopian tubes or endometrium with ectopic pregnancy, infertility or chronic pelvic pain as consequences. In men it may lead to orchitis and epididymitis. Diagnosis is by direct immunoflorescence test with monoclonal antibody of intraurethral or endocervical swab material, EIA, DNA probe, nucleic acid amplification test or cell culture.
- Trichomoniasis is caused by the protozoa Trichomonas vaginalis and in women is characterised by vaginitis with petecchiae and thin, foamy, greenish-yellow discharge with a foul smell. Vulva soreness has been reported as a result of women crushing the vaginal vestibule. In men trichomoniasis often results in only mild symptoms of the penile prepuce manifesting as balanitis in uncircumcised men. Trichomoniasis is often a co-infection of gonorrhoea or other STIs. Diagnosis is by microscopic examination of discharge (wet mount), by culture or PCR.
- Human papilloma viruses (HPV) are sexually transmissible viruses that are the most common cause of genital warts. These can appear on the cervix, inside the vagina, on the penis, in the urethra and around the anus. HPV infection is often asymptomatic. However, a proportion of women and men infected with HPV also develop ano-genital cancers. Cervical cancer is the most common type of cancer in women in the developing world and some HPV subtypes (e.g. HPV types 16 and 18) have been found to be more important than other subtypes in the development of cervical intra-epithelial neoplasm (CIN), a precursor of cervical cancer. Other terms used for CIN are cervical dysplasia, carcinoma in situ (CIS), precancerous lesions or squamous intra-epithelial lesions (SIL). Whereas HPV warts can be directly observed, CIN often can not. A promising technique to detect CIN on the cervix in low-resource settings is visual inspection with acetic acid, which turns the affected tissue to a white colour ('aceto-white lesions'). Microscopic diagnosis using Papanicolaou staining (Pap smears) is also an option, but needs pathologist expertise and is therefore seldom a sustainable option in low-income countries. The HPV virus can be detected using HPV DNA detection assays, of which the polymerase chain reaction assay is the most sensitive.

Endogenous RTIs

- Candidiasis is most often caused by Candida albicans yeast strains and usually presents as vulvar pruritis with or without vaginal discharge of varying character. Most patients may be diagnosed using direct microscopy of vaginal secretions (wet mount) which show mycelia. Some patients only will be diagnosed through vaginal culture. Candidiasis can be distinguished from other causes of vaginitis (like bacterial vaginosis (BV) and trichomoniasis) in that it is not associated with increased vaginal pH or large numbers of white blood cells.
- Bacterial vaginosis is characterized by the disturbance of normal vaginal flora where there is resultant loss of lactobacilli. It is a very common condition worldwide. Diagnosis can be done using the presence of three of four of the following clinical signs (Amsel criteria): 1) homogeneous white adherent discharge; 2) vaginal fluid pH > 4.5; 3) release of fishy amine odour when mixed with 10% KOH solution; 4) > 20% clue cells (squamous epithelial cells covered with vaginal bacteria like Garderella and Mobilincus species) in a wet mount preparation. Microscopy of gram-stained slides using scoring systems like the Nugent scoring is more sensitive and specific, but has to be performed by an experienced microscopist while the Amsel criteria can be used in most clinical settings.

Background to diagnosis and treatment of RTIs in Malawi

In the early seventies, only syphilis and gonorrhoea were used as diagnoses for STIs in Malawi [4]. Several studies have shown that the presence of STI's both

ulcerative and non-ulcerative significantly increases the transmission of HIV [2,3]. Thus the control of STIs has become critical. In the early 1990s the Ministry of Health in Malawi with guidance from WHO conducted STI case management and antimicrobial resistance pattern studies to assess the knowledge and practice of health providers in the management of STIs and to monitor the pattern of antimicrobial resistance. Based on the findings of the clinical trials and surveys the Malawi Government adopted the Syndromic Management Approach to STIs in 1992 (Chilongozi et al 1996)[5] and revised them in 2004 [6]. With this approach empirical treatment is based on the disease category with which a patient may present and not on laboratory results.

The syndromes included in the syndromic management flowcharts are cervical cancer, genital ulcer disease (GUD), urethral discharge (UD), persistent or recurrent urethral discharge, abnormal vaginal discharge, lower abdominal pain in women, scrotal swelling, inguinal bubo, balanitis and neonatal conjunctivitis.

In the guidelines, the Ministry acknowledges that syndromic management has its drawbacks: the rate of resistance of the causative organisms to drugs is likely to increase rapidly, making the drugs ineffective after a short time of use. The increase in resistance means that there is need to find new and usually more expensive drugs, which will make the approach difficult to sustain. There will be considerable over-diagnosis and over-use of antibiotics treatment especially in the case of abnormal vaginal discharge because many women will have endogenous infections, not an STI. Clients may not be satisfied when they are treated ineffectively and hence may find alternative modes or places for treatment. However, with a good reference laboratory periodically monitoring antibiotic resistance patterns, a syndromic approach remains the first choice in the management of STIs in resource poor settings. Even in communities where laboratory support is either inadequate or non-existent, the syndromic approach is considered cost-effective[7].

Syndromic management cannot be used to find asymptomatic cases, which disproportionately occur in women with STIs. Unless laboratory investigations are available, the patient may be considered not infected, and thus will not be treated[8]. So where resources are not limited available laboratory resources should be used, as is done for example in research settings.

Distribution of disease

Most of the studies on STI prevalence in Malawi have been conducted among selected groups such as commercial sex workers, antenatal clinic attendees, prisoners, HIV infected subjects and STI clinic attendees. One study from Mangochi reported age-specific community based prevalence data on gonorrhoea and Chlamydia [9]. Other community based STI prevalence studies have been conducted by the University of Pennsylvania in collaboration with UNC Project in Mangochi, Mchinji, Balaka and Rumphi. These studies have demonstrated lower prevalence of STIs in these population than in the studies of special groups[10]. Only the HMIS data (health facility based) and two studies reported data on STI incidence.

When comparing data from different studies one has to take into account that the use of different diagnostic definitions of STIs (e.g. syndromic versus lab-based diagnosis), biological samples (e.g. semen versus urine) and laboratory methods (e.g. culture versus PCR for gonorrhoea) results in different likelihood of diagnosing the STI. For instance, Kaydos-Daniels et al [11] e.g. reported that semen was more sensitive than urine or urethral swab in the determination of Trichomonas vaginalis among men attending Lilongwe Central Hospital (LCH).

Only one study on bacterial vaginosis was found on the occurrence of endogenous RTIs and one other on the prevalence of HPV infection. Sexual transmission does not appear to be a major mode of transmission of hepatitis B in Malawi [12] and is not included in this chapter.

Incidence

As stated above, there is paucity of data on the incidence of RTI among the general population. Taha et al[13] reported the 6 month incidence (measured in 1989-1990) of lab-confirmed gonorrhoea, trichomoniasis and syphilis to be 1.8%, 14.1% and 3.7% respectively among HIV positive postpartum women and 1.3%, 10.2% and 2.8% respectively among HIV negative postpartum women. These incidences were measured between 6 and 12 months after delivery, a time when many women who have followed the cultural norms to be sexually abstinent for the first months postpartum resume sexual activity. Because their partners may have turned elsewhere for sex in this period, it may constitute an especially high risk period for postpartum women. Zachariah et al[14], in their study of 4229 prisoners, reported 50 (1.2% per year) with incident STIs acquired within the prison (syndromic diagnosis). The prison environment in Malawi is mainly a male dominated area with the total number of females being less than one percent. This high incidence of STIs suggests that there is frequent sexual contact between prisoners.

Malawi's Health Management Information System's Annual Report[15] estimated the sexual active population

Table 1 Prevalence of gonorrhoea and chlamydia in the community, by sex and age.

	Gonorrhoea (urine PCR)		Chlamydia (urine PCR)	
	Men	Women	Men	Women
15-19	Not assessed	2.4%	Not assessed	5.4%
20-24	5.7%	4.5%	6.3%	5.4%
25-29	2.6%	3.5%	9.5%	3.9%
30-34	10.7%	3.4%	5.3%	5.5%
35-39	6.6%	Not assessed	4.9%	Not assessed
40-44	8.7%	Not assessed	0%	Not assessed
Total	6.1%	3.5%	6.1%	5.0%

Source – Center for Social Research, Save the Children Federation USA, Malawi Ministry of Health and Population, MEASURE Evaluation. Avoiding unwanted pregnancy and sexually transmitted infections: a rural Malawi district study. Chapel Hill, NC: MEASURE Evaluation, 2004.

of the country in the period July 2004 to June 2005 to be 6,047,173, with 207,136 visits for STI reported by health facilities, resulting in a cumulative incidence of 3.4%. Rates of reported STIs for this period ranged from a low of 0.9% in Karonga to a high of 5.9% in Nsanje. This range probably may reflect differences in real incidence but also differences in reporting and access to facilities.

Prevalence

The results from the Mangochi community study showed high proportions of gonorrhoea and chlamydia in men and women (Table 1).

More data on RTI prevalence are presented in Table 2 and 3 below, sorted by population group and pathogen or syndromic group.

Of the available data, those concerning pregnant women and male sugar estate workers probably reflect closest the prevalence among women and men in the community (Table 2). They show that STIs are extremely common, with STIs found among 7.5% (in 1994) and 16.8% (in 1998) of male estate workers upon visual inspection. As can be expected from the incidence data in pregnant women reported above, trichomoniasis was extremely common, with around one third of pregnant women infected in the early nineties. One tenth of people in these cohorts had positive syphilis serology, but more recent (2004) sentinel surveillance data give a prevalence of only 2.7%. Other ulcerative STIs were also quite common with around 5% of pregnant women suffering from genital ulcer disease.

Data on occurrence of active herpes simplex type 2 lesions were not found, but results from the male sugar estate workers cohort suggest that around three quarters of men have been infected at sometime during their life. Gonorrhoea was found among 3% of pregnant women. No data were available from the male estate workers cohort.

The data by Taha[16] of cohorts of women attending ANC services at QECH show a decline in prevalence of all STDs from 1990 to 1995/1996. In the same period no increase in reported condom use was observed. The decrease is therefore possibly a result of better access to STI treatment or changes in sexual risk behaviour. In these same cohorts, 30% of the women had bacterial vaginosis, 59% had mild or moderate disturbance of vaginal flora, and only 11% had normal vaginal flora.

Miotti et al described that among a sample of 268 women 31% had HPV infection and 10% had CIN[17].

Table 3 shows the prevalence of STI in patient populations. The STI studies by University of North Carolina and LCH among men with urethritis showed that, although gonorrhoea was by far the most common pathogen identified, Trichomonas vaginalis often existed as co-infection or as only infection (21% of cases).

Three studies showed independently that Chlamydia trachomatis is seldom diagnosed in Malawian men with urethritis [8,23,24].

In a study of men presenting with GUD to the STI clinic in 1995, Behets et al noted that 26.2% of the men had Haemophilus ducreyi while 29.2% had treponemes [25]. Dual infection with HIV delayed wound healing following treatment. Both these diseases (chancroid and syphilis) are covered in the current syndromic treatment guidelines. Cotrimoxazol, which was used to treat chancroid at the time the study was carried out, has now been replaced with the more effective erythromycin.

Table 2 Prevalence of RTIs / syndromes among pregnant women, male sugar estate workers, prisoners and commercial sex workers, with lab-confirmed versus syndromic diagnosis.

Study	Population	STI / syndrome	Diagnostic method	Year	Prevalence (%)
Pregnant women, lab-confirmed diagnosis					
Watson	ANC women	Syphilis	RPR + TPHA	Not reported, but before 1985	13.7 (9.5-19.5)
Taha et al[16]	ANC women	Syphilis	RPR +THPA / FTA-Abs	1990	13.4 (12.6-14.2)
Taha et al[16]	ANC women	Syphilis	RPR + THPA or FTA-Abs	1993	12.1 (10.8-13.6)
Taha et al[16]	ANC women	Syphilis	RPR + THPA or FTA-Abs	1995	12.1 (9.9-14.1)
Taha et al[16]	ANC women	Syphilis	RPR + THPA or FTA-Abs	1996	11.1 (9.0-13.2)
National Sentinel Surveillance	ANC women	Syphilis	VDRL	2004	2.7 (2.3-3.7)
McCallum et al	Pregnant or post partum women	Trichomoniasis	Wet mount and Gram stain	1971	19.0 (12.5-27.8)
Taha et al[16]	ANC women	Trichomoniasis	Wet mount	1990	32.5 (31.4 – 33.6)
Taha et al[16]	ANC Women	Trichomoniasis	Wet mount	1993	28.6 (26.7 - 30.1)
Taha et al[16]	ANC Women	Trichomoniasis	Wet mount	1995	23.8 (20.9 - 26.7)
Taha et al[16]	ANC Women	Gonorrhoea	Culture	1990	4.9 (4.4 - 5.4)
Taha et al[16]	ANC Women	Gonorrhoea	Culture	1993	2.5 (1.8 - 3.2)
Taha et al[16]	ANC Women	Gonorrhoea	Culture	1995	2.5 (1.4 - 3.6)
Taha et al	ANC women	BV		1990-1993	30.0
Pregnant women, syndromic diagnosis					
Taha et al[16]	ANC Women	GUD	Visual inspection	1990	6.8 (6.2 - 7.4)
Taha et al[16]	ANC Women	GUD	Visual inspection	1993	6.7 (5.6 - 7.8)
Taha et al[16]	ANC Women	GUD	Visual inspection	1995	3.4 (2.1 - 4.7)
Taha et al[16]	ANC Women	Genital warts	Visual inspection	1990	4.8 (4.3 - 5.3)
Taha et al[16]	ANC Women	Genital warts	Visual inspection	1993	3.1 (2.4 - 3.8)
Taha et al[16]	ANC Women	Genital warts	Visual inspection	1995	2.5 (1.4 - 3.6)
Occupational or special cohorts, lab confirmed diagnosis					
Sutcliffe[12]	Male estate workers	HSV	Serology	1998	88.1 in HIV+ 64.3 in HIV -
Kumwenda	Male estate workers	Syphilis	RPR only	1994	6.5 (5.3-7.7)
Kumwenda[21]	Male estate workers	Syphilis	RPR only	1998	10.4 (8.9 - 12.2)
Male estate workers	Syphilis	RPR only	1998		
Occupational or special cohorts, syndromic diagnosis					
Kumwenda[21]	Male estate workers	Any STD	Physical exam	1994	7.5 (6.3-8.8)
Kumwenda[21]	Male estate workers	Any STD	Physical exam	1998	16.8 (14.9 - 18.9)
Zachariah	Commercial sex workers	Abnormal vagi nal discharge	Syndromic diagnosis	2000-2001	13.0 (11.6-14.7)
Zachariah[22]	Commerical sex workers	PID	Syndromic diagnosis	2000 - 2001	6.4 (5.3 - 7.6)
Zachariah[22]	Commercial sex workers	GUD	Syndromic diagnosis	2000 - 2001	5.6 (4.6 - 6.8)
Zachariah[14]	Prison inmates	Urethtral dis charge	Syndromic diagnosis	2000 - 2001	2.0 (1.6 - 2.4)
Zachariah[14]	Prison inmates	Genital ulcer dis ease	Syndromic diagnosis	2000 - 2001	1.4 (1.1 - 1.8)
Zachariah[14]	Prison inmates	Epididymo-or chitis	Syndromic diagnosis	2000 - 2001	0.8 (0.6 - 1.1)

Table 3 Prevalence of STIs / syndromes among patient populations, with lab-confirmed versus syndromic diagnosis.

Study	Population	STI / syndrome	Diagnostic method	Year	Prevalence
Patient populations, lab confirmed diagnosis					
McCallum[19]	Female ophthalmic inpatients	Trichomoniasis	Wet mount and Gram stain	1971	35.8 (24.3-49.3)
	Infertile women	Trichomoniasis	Wet mount and Gram stain	1971	39.5 (25.6-55.3)
Hobbs	Urethritis patients at STI clinic	Gonorrhoea	Not reported	1996	65.7 (58.5-72.3)
Dallabetta[8]	Men at STI clinic with UD or dysuria, without GUD	Gonococcal urethritis	Culture	1992-1993	71.8 (66.7-76.4)
Zachariah[23]	Patients with UD at STI clinic	Gonorrhoea	Ligase chain reaction on urine	2000 / 2001	82.7 (74.6-88.7)
Price[24]	Urethritis patients at STI clinic	Gonorrhoea	PCR or Gram stain	Not reported	73.5 (69.0-77.5)
Dallabetta[8]	Men at STI clinic with UD or dysuria, without GUD	Chlamydial urethritis	EIA	1992-1993	4.0 (2.3-6.6)
Zachariah[23]	Urethritis patients at STI clinic	Chlamydia	Ligase chain reaction on urine	2000 / 2001	1.8 (0.5-6.4)
Price[24]	Urethritis patients at STI clinic	Chlamydia	Ligase chain reaction	Not reported	0.6 (0.1-2.5)
Hobbs[26]	Urethritis patients at STI clinic	Trichomoniasis	Either PCR or Wet mount / Culture	1996	20.8 (15.5-27.3)
Price[24]	Urethritis patients at STI clinic	Trichomoniasis	PCR or culture	Not reported	17.3 (13.9-21.2)
Hobbs[26]	Asymptomatic men at dermatology clinic	Trichomoniasis	Either PCR or Wet mount / Culture	1996	12.1 (7.4-19.4)
Behets[25]	GUD patients at STI clinic	Chancroid	Culture	1992-1993	26.2 (23.3-29.4)
Behets[25]	GUD patients at STI clinic	Syphilis	RPR confirmed with MHA-TP	1992-1993	29.2 (25.9-32.8)
Price[24]	Urethritis patients at STI clinic	Syphilis	RPR	Not reported	5.1 (3.4-7.7)
Patient populations, syndromic diagnosis					
Kristensen	Unselected outpatients	Symptomatic STIs	Self report + physical examination	1989	4.3 (4.0-4.7)
Maher	Medical inpatients	Discrete ulcer	Visual inspection	23 June 1994	11.4 (6.9-18.2)
Maher[28]	Medical inpatients	Non-discrete ulcer	Visual inspection	23 June 1994	1.6 (0.4-5.7)
Maher[28]	Medical inpatients	Genital warts	Visual inspection	23 June 1994	7.3 (3.9-13.3)
Maher[28]	Medical inpatients	Urethral discharge	Visual inspection	23 June 1994	9.7 (4.5-19.5)
Komolafe	STD clinic attendees	GUD	Syndromic diagnosis	1996-1998	40.9 (40.3-41.4)
Komolafe[29]	STD clinic attendees	Genitourinary symptoms in women (high risk)	Syndromic diagnosis	1996-1998	20.5 (20.0-20.9)
Komolafe[29]	STD clinic attendees	Genitourinary symptoms in women (low risk)	Syndromic diagnosis	1996-1998	2.2 (2.1-2.4)
Komolafe[29]	STD clinic attendees	Urethral discharge	Syndromic diagnosis	1996-1998	15.6 (15.2-16.1)
Komolafe[29]	STD clinic attendees	PID	Syndromic diagnosis	1996-1998	13.4 (13.0-13.8)
Komolafe[29]	STD clinic attendees	Scrotal swelling	Syndromic diagnosis	1996-1998	2.4 (2.3-2.6)
Komolafe[29]	STD clinic attendees	Bubo	Syndromic diagnosis	1996-1998	2.0 (1.9-2.2)
Komolafe[29]	STD clinic attendees	Balanitis	Syndromic diagnosis	1996-1998	0.3 (0.3-0.4
Zachariah	Male STI clinic attendees	GUD	Syndromic diagnosis	Not reported	49 (43-55)
Zachariah[30]	Male STI clinic attendees	Urethral discharge	Syndromic diagnosis	Not reported	42 (36-49)
Zachariah[30]	Female STI clinic attendees	Abnormal vaginal discharge	Syndromic diagnosis	Not reported	50 (44-56)
Zachariah[30]	Female STI clinic attendees	GUD	Syndromic diagnosis	Not reported	27 (22-33)
Zachariah[30]	Female STI clinic attendees	PID	Syndromic diagnosis	Not reported	18 (14-23)

Summary – Incidence / Prevalence

- Community based prevalence of gonorrhea is 2.7% in women and 4.8% in men
- Community based prevalence of chlamydia is 4.0% in women and 4.4% in men
- Antenatal surveillance based prevalence of syphilis is 2.7% in women in 2003
- Annually 3.4% of the sexually active population attends health facilities because of STIs
- 30% of pregnant women had bacterial vaginosis, 24% trichomoniasis, 3.4% ulcerative disease and 2.5% genital warts in the mid 1990s
- 10% of male estate workers had syphilis in 1998
- One third of women has HPV, half of which are subtype 16 and 18, the subtypes against which future vaccines are directed. One tenth of women has a precancerous lesion of the cervix
- GUD and vaginal discharge are the most common reasons for visiting an STI clinic
- Gonorrhea and trichomoniasis (not chlamydia) are most common causes of urethral discharge
- Herpes is the commonest cause of genital ulceration followed by chancroid and then syphilis
- Data on active genital herpes were not found, but three quarters of male estate workers have evidence of infection in the past. No data on HSV 2 serology were found for women

The study by Behets among men only, showed that Genital Ulcer Disease (GUD) accounted for 60% of visits [25]. The study by Komolafe et al of all visits to the QECH STI clinic over a three year period also showed that GUD was by far the most common reason for attending the clinic (accounting for 40.9% of all visits by men and women) [29].

A study by Zachariah also found GUD to be the most common reason for attending the STI clinic, but for men only. For female STI clinic attendees, abnormal vaginal discharge was most frequent [30]. Current research based at KCH/UNC Project finds herpes is the commonest cause (60%) of GUD syndrome. Details will be reported in the next edition.

Lay diagnoses of sexually transmitted infections include: Chinzonono (gonorrhoea or vaginal discharge), chindoko (Chancroid or syphilis), mabomu (chancroid with inguinal involvement or buboes.)[31] Vaginal discharge could also be described as mauka.

Distribution of determinants

Several biological, behavioural and social determinants are known to affect the distribution of STIs worldwide. Many of these determinants impact on sexual behaviour and thus increase the risk for both HIV and other STIs. These are dealt with extensively in the HIV/AIDS chapter. In the subsequent section, we will present information specific for STIs.

Biological determinants

Sex

In the early studies of STI patients presenting for care, there was preponderance for males. Wynendaele et al[32] in their study at two STI clinics reported that between 60% and 74% of the clinic attendees were males. Kristensen found that of outpatients who had an STI 81.7% were men [27]. But later data showed that as many women as men attended STI clinics [29,30,33]. This may indicate a relative increase in prevalence of STI in women as compared to men, but may also just reflect changes in accessibility to the clinic by the two sexes.

Age

Most studies in STI clinics have reported that the majority of clients are between 20 and 30 years old [8, 25,29,30,32,33]. This is perhaps not surprising as young adults are likely to be more sexually active than older adults. It may also suggest that younger adults and adolescents may not have acquired the knowledge and skills that enable them to protect themselves from unsafe sex.

HIV

STI patients are likely to be co-infected with HIV and STIs facilitate the transmission of HIV.

The association between HIV and STIs has been described fully in the chapter on HIV and AIDS.

Use of traditional vaginal agents

Preference for dry sex is a common observation in southern Africa. The practice involves women putting various absorbents such as wads of cloth, cotton or herbs in order to absorb 'extra' lubrication in order to increase friction when having sex. This is perceived as more pleasurable. Herbs may also be used to 'tighten' the introitus, again encouraging perception of pleasurable sex. The role of vaginal agents in facilitating STI transmission is not known. However, it is reasonable to expect these agents to interfere with the integrity of condoms leading to condom breakages and therefore

facilitate STI transmission. Dry sex also has potential to promote the spread of STIs, including HIV by the fact that it may encourage the development of abrasions through trauma experienced during sex. Lastly, vaginal agents could potentially be vehicles for the introduction of pathogens (not necessarily STIs) into the vagina. Dallabetta et al[34] studied 6603 antenatal women of which 13% reported use of traditional vaginal agents for vaginal tightening while 34% had used these agents for self treatment of vaginal itch or discharge.

Behavioural determinants

As with many other communicable diseases, personal and group behaviours are important determinants of STIs.

Number of sexual partners and abstinence

Apart from vertical transmission of STIs (as in the case of ophthalmia neonatorum) the bulk of STIs are transmitted through sex. Sexual abstinence therefore removes the possibility of being infected with STIs through sex. Having multiple sexual partners is a risk factor for STIs. Although researchers on STI among clinic attendees have reported multiple sexual partners among clients[24,33], the risk for STIs associated with multiple partners has not been quantified. Also refer to the HIV/AIDS chapter.

Condom use

Condoms, if used correctly and consistently for penetrative peno-vaginal and/or peno-anal sex are an effective tool in the prevention of transmission of sexually transmitted infections. However a study in post partum women in QECH found no relation between reported condom use and incidence of STIs, possibly due to bias in reporting condom use.

In Malawi, the male latex condom is the commonly used type as compared to the female condom.

Controversy surrounds the promotion of condoms in Malawi. While there is agreement amongst the scientific community that use of condoms can contribute to the reduction of STIs, society is divided on the morality and effectiveness of condom use, especially among young unmarried persons. Condom promotion in prisons, where homosexual practices are reported is also not permissible as the practice (homosexuality) is illegal [14]. Although prostitution is illegal in Malawi, use of condoms among commercial sex workers (CSWs) is permitted.

Zachariah et al[35] carried out a study to assess the acceptability of the female condom among commercial sex workers in Thyolo. Overall, 80% of the sex workers indicated preference of the female condom over the male condom. Despite the high approval rating of the female condom, several technical problems were reported and these include discomfort (86%), too much lubrication (32%), perception that the condom was too large (32%), noise during intercourse (11%) and difficulties with insertion of the inner ring (10%). In 3.4% of the CSWs, the female condom was re-used on consecutive clients without washing while 12.5% had re-used after washing.

Among CSWs, Zachariah et al reported the following factors as being associated with no condom use during a symptomatic period with an STI: 1) involvement of commercial sex work outside a known rest house or bar; 2) presence of genital ulcer disease; 3) having fewer than two clients per day; 4) alcohol use; 5) having had no prior medication for STI symptoms [22].

More data on the frequency of condom use in Malawi can be found in the HIV/AIDS chapter.

Commercial sex

Commercial sex work by its nature involves having multiple and casual sexual partners. Non-use of condoms may increase risk as there are reports that some clients of CSWs offer higher pay when no condom is used. The prevalence of STIs in CSWs is therefore generally estimated to be higher than in the general population, but the scanty data available from Malawi do not lend much support for this hypothesis [22,35].However, no study directly compared the prevalence of STIs in CSWs compared with non CSWs using the same diagnostic methods. Also refer to the paragraphs on transactional and commercial sex in the HIV/AIDS Chapter.

Delays in seeking care.

Effective prevention and control of STIs requires prompt identification, treatment, partner tracing and behavioural change. Many STI clients seek care from grocery shops, traditional healers and some may not even receive treatment at all. Dallabetta et al[8] reported a mean duration of presentation after development of symptoms as 8.7 days (range 1-85 days), Zachariah et al reported 14 days delay[30] and in men with urethral discharge even 27 days [23]. About half of patients had sought treatment elsewhere before attending the STI clinic, most frequently at the traditional healer.

Sanitation

Lack of adequate sanitation could potentially facilitate transmission where genital contact of infected genital fluids occurs when sharing bath towels and toilet seats. McCallum and Tozer[19] proposed that the prevalence

of genital infections amongst Malawian women could be due to inadequate perineal sanitation, high ambient temperature and humidity. However it is generally assumed that such transmission of STIs in Malawi is not responsible for the high prevalence observed.

Socio-cultural and environmental determinants

The environment, health and disease are inextricably linked. Sexually transmitted diseases thrive in an environment of gender inequality, poverty, lack of effective and prompt STI care, and hopelessness. Again, these factors are touched upon below but are more extensively discussed in the chapter on HIV and AIDS.

Poverty

Poverty has often times presented as an important reason some CSWs engage in the practice but they may also not use condoms for penetrative sex in an effort to obtain more money from clients who prefer non-condom use.

Initiation, fisi and other cultural practices

Cultural factors are often mentioned as important determinants in the spread of STIs. Please refer to chapter on HIV/AIDS.

Economic envir onment (trade centres, tr ansport routes)

There is anecdotal evidence to suggest that major trade routes in Malawi could be epicentres of STIs as has been described in other countries. In the southern region, these are the Blantyre-Thyolo, Mulanje-Muloza route and the Blantyre-Lunzu-Mwanza route. In the central region, the Lilongwe-Mchinji-Chipata route and the Lilongwe-Kasungu route are likely to facilitate STI transmission. In the north, the Mzuzu, Ekwendeni-Karonga route is another route that may be considered facilitative for STI transmission.

Like HIV/AIDS, syphilis is more prevalent in the Southern region than in the Central and Northern regions.

Table 4 Syphilis prevalence in pregnant women, by region

Region	Total sampled	Syphilis +	% Syphilis +	95% CI
North	2288	22	1.0	0.6 - 1.5
Centre	2740	64	2.3	1.8 - 3.0
South	2949	127	4.3	3.6 - 5.1
Total	7,977	213	2.7	2.3 – 3.7

Source – National antenatal surveillance 2003.

Education

Education accords the individual and communities the opportunity to access health information and choice. Education also affords opportunity to travel and money and casual sex. Education may also result in increased access to prompt and effective treatment for STIs. The table below shows that the overall result for pregnant women, for syphilis at least, is a higher prevalence in women with less education.

Table 5 Syphilis prevalence in pregnant women, by education level

Education level	Total Sampled	Syphilis +	% Syphilis +	95% CI
None	1921	70	3.6	2.9 - 4.6
Primary	4631	121	2.5	2.1 - 3.0
Secondary	1227	21	1.7	1.1 - 2.7
Post Secondary	68	1	1.5	0.0 - 7.9
Total	7,977	213	2.7	2.3 – 3.7

Source – National antenatal surveillance 2003.

Access to adequate diagnosis and treatment

Several studies (all in STI clinics) have shown that between 50 and 60% of patients attending STI clinics first seek care outside the formal health care system, most often at traditional healers (table 3.) [23,25,30,31] An ethnographic study on STI health seeking behaviour was conducted in Ntchisi, Nkhata-Bay and Lilongwe with almost similar findings[36]. Traditional healers are viewed as less expensive, more sympathetic, more confidential and more accessible than biomedical treatment. On the other hand the latter is seen as faster and more powerful than traditional care [31].

Table 6 Sources of prior STI care for STI clinic attendees

Baseline evaluations of STD case management in 39 health facilities were carried out in 1994 after the first version of syndromic management guidelines was introduced but before providers were comprehensively trained. It showed that correct assessment and treatment of STD (syndromes) was rare and that only a quarter of patient was correctly counselled on condom use, partner referral and the increased risk of transmission of HIV associated with having an STD. At least one third of patients did not receive effective treatment. In addition, overtreatment was frequent[5]. Whereas this failure may sometimes have been caused by lack of drugs, it was more likely due to insufficient or incorrect

Reference	Study Population	Traditional healer/herbalists	Pharmacists	Private clinics	Several	Others
Dallabetta8	Men with urethritis	36.5%	31%	22.7%		29.7%
Behets25	Men with GUD	23.3%	16.7%	12.2%		23.5%
Zachariah23	Men with urethral discharge	30%	21%	4%	15%	-
Zachariah30	STD patients (both sexes)	37%	24.0%	21%	18%	

knowledge [7]. Female STD patients received less comprehensive diagnosis, care and counselling than male patients. After the publication of the 2003 revised Malawian Syndromic Management Guidelines, the RHU trained over 1000 health care providers on syndromic management and further training is being organized by districts.

Impact of STIs

Life expectancy

Most STIs while responsible for substantial sequelae and morbidity do not lead to death. Exceptions include peritonitis from PID and HPV associated cervical cancer. Data about mortality associated with these diseases have not been found.

Infant morbidity and mortality in STI affected mothers

Maternal STIs can be transmitted to the baby in-utero (syphilis for instance) or during delivery. Ophthalmia neonatorum occurs when a neonate suffers from purulent conjunctivitis having acquired the infection through passage in an infected birth canal. Crede's prophylaxis with 1% silver nitrate was the recommended practice of new born care several years ago but this has reduced in use over the years. Among the shortfalls of Crede's prophylaxis was the irritation of the cornea following administration of silver nitrate of high concentration. All parents with baby suffering from ophthalmia neonatorum are invited for STI management.

All pregnant women in Malawi are supposed to be screened for syphilis using the Determine syphilis test. When the test is positive, the woman and her spouse are treated for syphilis. The baby is also treated with penicillin within a week of birth and observed in the out patient's department thereafter.

Economic

The burden that STIs exacts on the economy is related to medical costs, absenteeism from work due to clinic attendances and, rarely, death. The majority of STIs however do not result in eventual death. There is paucity of data on the economic cost of STIs on the Malawi economy.

Health services

From July 2004 to June 2005 207,136 cases of STI were treated at Malawian health facilities.15 This represents 2% of all out-patients attendances. Apart from these visits to the conventional health care system, likely at least another 100,000 consultations for STIs are sought of traditional healers.

Summary - Determinants

- Both sexes seek care in equal numbers but women receive quality care less often than men
- Majority of clients to STI clinics are young adults
- Condom use by CSWs is higher than in the general population
- CSWs prefer female condom above male condom, and use it frequently when available
- The risk of STIs associated with cultural practices is unknown
- Delays in seeking care are long and sex during the symptomatic period is common. More than half of clients first seek care outside the conventional health care system
- Before syndromic management of STIs was introduced, correct assessment, treatment and risk reduction counseling for STIs was rare

Summary - Impact

- Data on mortality associated with PID and cervical cancer have not been found
- Data about impact on infants of STI affected mothers are lacking
- Data on economic impact of STIs are not available
- At least 300,000 consultations for STIs are sought annually, both inside and outside the conventional health care system

Effective interventions

Biological interventions

Male circumcision

There has been global interest in male circumcision as tool for the prevention of HIV and other STIs. A recent randomised clinical trial showed that male circumcision reduced the HIV incidence by 60%[37]. One observational study showed a reduced risk of GUD (particularly chancroid and syphilis) associated with male circumcision, but no evidence from clinical trails is available [38]. More information on the prevalence of male circumcision in Malawi is presented in the chapter on HIV and AIDS.

Screening for syphilis at ANC

Treatment of syphilis during pregnancy with penicillin effectively cures syphilis in the mother and prevents congenital syphilis in the baby. The Ministry of Health's policy on syphilis is that all women attending antenatal care receive syphilis screening through a universal Determine syphilis test. Those women who test positive are treated and their male partners are invited for assessment and treatment. The baby is also treated presumptively at delivery. Although ANC attendance is high in Malawi, according to the 2000 MDHS data, a blood sample for syphilis testing is drawn in only 43% of women (ranging from 23% in Karonga district to 57% in Lilongwe district). Another challenge of this policy is the fact that many women who attend ANC still deliver outside of the health sector, and thus presumptive treatment of the baby is not possible.

Syndromic management of STIs

A cluster randomized controlled trial was carried out in Mwanza, Tanzania to assess the effect of strengthened syndromic management of STIs versus usual care on prevention of HIV and other STIs. The intervention consisted of training health workers in syndromic STI case management as recommended by WHO providing inexpensive but effective drugs, making regular supervisory visits to health facilities and conducting village campaigns to improve treatment-seeking behaviour. This package resulted in a 28% reduction in serologically diagnosed syphilis prevalence and a 49% decrease in reported urethritis, but no significant reduction in gonorrhoea, chlamydia or overall urethritis. It also reduced the HIV incidence by 40% [39,40].

Current Malawian syndromic management guidelines for urethritis use drugs directed against C. trachomatis, N. gonorrhoea, Ureaplasma and Mycoplasma species, but not T. vaginalis, and treatment failure is high [41]. In a randomized clinical trial in LCH, metronidazole treatment for T. vaginalis did not decrease persistent urethritis detected one week after treatment (possibly because inflammation resolves slowly), but did clear T. vaginalis effectively and reduced the excretion of HIV in semen [24]. In Malawi, metronidazole is given only to men with persistent urethral discharge. However that clinical trial suggests the value of inclusion of metronidazole in the treatment of urethral discharge syndrome.

Susceptibility testing of N. gonorrheae isolates in men with urethritis showed decreased susceptibility for gentamicin, the drug currently included in the treatment guidelines for urinary discharge. Whereas in 1993 susceptibility was still 95%[41], it declined to 92% in 1996 and 85% in 2000/2001 [23]. However, in 2003 the susceptibility was back at 96%[42] and in 2004 at 95%[43]. Dallabetta et al[8] reported that 90% of men who had the combined symptoms of discharge and dysuria had laboratory confirmed urethritis, either due to N. gonorrhoea or Chlamydia trachomatis. The specificity of dysuria alone or discharge alone was lower at 78% and 77% respectively. Dysuria has since been added to the entry criteria for the syndromic management flow chart of urethritis.

The effect of syndromic management versus usual care for STIs depends on the country-specific situation. The high prevalence of treatable STIs in Malawi and the low quality of the STI care that existed before syndromic management was introduced suggest that properly executed syndromic management has the potential to reduce the prevalence of STIs considerably. This was confirmed in a formal evaluation of the in-service training in syndromic management in 1997. The evaluation found that 56% of the diagnostic algoriths were followed accurately in pilot sites, 67% of treatments

were correctly prescribed, examinations were correctly performed in 69% of males and 89% of females, partner notification slips were handed out to 87% patients, and condoms were available in 96% of sites[44].

Mass community treatment

There is some interest globally on the possibility of community mass treatment against STIs in order to curb the incidence of STIs and thereby reduce HIV spread. Three rounds of mass treatment were carried out in Rakai, Uganda, with a treatment interval of 10 months. Single doses of azithromycin, ciprofloxacin and metronidazole were given to consenting adults in the intervention group and vitamins and anti-helminths to participants in the control group. Whereas there was no effect on incident HIV infection (RR 0.97; confidence interval 0.81-1.16), a reduction of 20% was seen for syphilis, 41% for trichomoniasis and 13% for bacterial vaginosis[45]. Community mass treatment for STI has not been tried in Malawi.

Vaccination for Human Papilloma Virus

Pharmaceutical companies are developing HPV vaccines. They have already shown high vaccine efficacy in phase III effectiveness trials [46,47]. Most are at least directed against subtypes 16 and/or 18. It will take a few more years before these vaccines are available on the market, but when they are, they could have an enormous impact on the occurrence of cervical cancer in the country. How effective they may be in Malawi depends on the subtypes that circulate in the population and on the adequacy of the vaccination program. One study has been found, which showed that subtype 16 and 18 constitute only half of all HPV infections in Malawi [17].

Screening and treatment of cervical intra-epithelial neoplasia

Studies done in India, Kenya, South Africa, Peru and Thailand show that a screening algorithm for cervical intra-epithelial neoplasia (CIN) based on visual inspection of the cervix with acetic acid (VIA) and same day treatment is cost effective[48]. Several different techniques are in use for the subsequent surgical treatment of CIN. A Cochrane review did not identify one single surgical technique as superior to treat CIN. Of the commonly used techniques, large loop excision of the transformation zone (LLETZ, or LEEP in the USA) appears to yield the best specimen for histopathological assessment. The equipment required for LLETZ is less expensive than that for laser excision and vaporisation, making LLETZ a more favoured technique. Cryotherapy appears to be effective treatment for low grade CIN lesions but not for high grade lesions. Cold knife cone biopsy has a place when endocervical glandular disease is suspected, or when early invasive cervical cancer is suspected on cytology but when no visible lesion is noted on the cervix[49].

In Malawi, some experience has been gained with VIA and subsequent LLETZ through the Project Hope cervical cancer screening and treatment program. Malawi has now introduced a national screening and treatment programme for cervical cancer of VIA with subsequent cryotherapy. Currently, services are provided at 13 sites. The 5 year strategic plan's target is to provide the services at all districts hospitals and 10% of health centres by 2010.

Behavioural interventions

Partner notification

Sexual partners of patients with STIs are likely to be infected, in which case they should be treated for their own benefit, to prevent re-infection of the current patient and transmission of the STI to others.

Several strategies exist to notify those partners who may have an STI, e.g. patient referral (in which the index patient informs the partner and refers him/her for care, provider referral (in which healthcare staff notifies the partner) and contact referral (in which the index patient notifies the partner with the understanding that health care staff will contact the partner when s/he has not visited the clinic by a certain date. There is limited evidence that provider referral or a choice between the index patient and provider referral is more effective than the index patient referral in bringing partners to health services for treatment[50]. The commentary to this Cochrane review concluded that: 'in view of the limited number of available trials, the poor methodological quality of the trials and limited data from low-income countries, it is not possible to recommend one partner notification strategy above the other. More trials comparing the effects of various notification strategies in developing countries (especially those with high HIV and STI rates) are needed. These trials should be carefully designed to limit bias (for example, through adequate allocation concealment and blinding of outcome assessments). Studies should assess a broader range of outcomes including re-infection rates, incidence of STIs, costs and harmful effects[51]. There is no active partner tracking in Malawi. Instead, the index patient is given a partner notification slip to give to his/her partner/s. The slip asks them to come to the health care facility. It is unknown to what extent this is done in practice, although STI clinics have these partner notification slips.

Summary - Interventions

- Syndromic management has the potential to improve the treatment of STIs in Malawi, but an evaluation of its effectiveness has not been performed since 1997
- Although Trichomoniasis vaginalis is a frequent cause of urethritis, current recommended drugs for primary urethral discharge do not cover T .vaginali
- Susceptibility of N. gonorrhoea to gentamicin has been increasing from 85% in 2001 to 95% in 2004
- Syphilis screening and subsequent treatment can be significantly improved because a test is performed in only 43% of women attending antenatal care (DHS2000)
- Vaccination for HPV may prevent a substantial number of cases of cervical cancer in the future
- An adequate partner notification method is advocated in Malawi but it is not known to what extent it is used in practice
- Training for traditional healers to refer STI patients for effective care has successfully been implemented in two sites but has not been expanded nationally

Peer education programmes

Please refer to the chapter on HIV/AIDS.

Socio-cultural interventions

Social marketing of condoms

Please refer to the chapter on HIV/AIDS.

Social marketing of behaviour change

Please refer to the chapter on HIV/AIDS.

Special clinics for Commercial Sex Workers

Please refer to the chapter on HIV/AIDS.

Training for traditional healers

Many STI patients consult traditional healers either as the first line of care or when already on medication obtained at an STI clinic. As part of the HIV prevention strategies, the Ministry of Health advocates co-operation with traditional healers who may refer their patients to conventional health care facilities. In some areas of the country, such as Thyolo and Chiradzulu, traditional healers have been trained in the recognition of STIs and referral of cases to health facilities where effective STI care can be provided.

References

1. Sangani P, Rutherford G, Wilkinson D. Population-based intervention for reducing sexually transmitted infections, including HIV infection. Cochrane Data Base of Systematic Reviews, 2004; 2: CD001220
2. Cameron DW, Simonsen JN, D'Costa LJ, Ronald AR, Maitha GM, Gakinya MN et al. Female to male transmission of human immunodeficiency virus type 1: risk factors for seroconversion in men. Lancet 1989;ii:184-9.
3. Laga M, Manoka A, Kivuvu M, Malele B, Tuliza M, Nzila N et al. Non-ulcerative sexually transmitted diseases as risk factors for HIV-1 transmission in women: results from a cohort study. AIDS 1993;7:95-102.
4. Rampen F. Venereal syphilis in tropical Africa. Br J Ven Dis 1978; 54: 364-8
5. Chilongozi DA, Costello Daly C, Franco L, Liomba NG, Dallabetta G. Sexually transmitted diseases: a survey of case management in Malawi. Int J STD AIDS 1999; 7: 269-275.
6. Reproductive Health Unit, Ministry of Health, Malawi. Management of Sexually Transmitted Infections using Syndromic Approach. Guidelines for Service Providers. Second edition V0.03. Lilongwe, May 2004.
7. Costello Daly C, Franco L, Chilongozi DAT, Dallabetta G. A cost comparison of approaches to sexually transmitted disease treatment in Malawi. Health Pol Plan 1998; 13: 87-93
8. Dallabetta G, Behets F, Lule G, Hoffman I, Hamilton H, Wangel AM, Moeng S, Cohen M, Liomba G. Specificity of dysuria and discharge complaints and presence of urethritis in male patients attending an STD clinic in Malawi. Sex Transm Inf 1998; 74: (Suppl 1) S 34-S37
9. Center for Social Research, Save the Children Federation USA, Malawi Ministry of Health and Population, MEASURE Evaluation. Avoiding unwanted pregnancy and sexually transmitted infections: a rural Malawi district study. Chapel Hill, NC: MEASURE Evaluation, 2004.
10. Thornton R, Bula A, Chavula K, Bigname-Van Assche S, Watkins SC. Reactions to voluntary counseling and testing in rural Malawi (submitted for publication). Accessed on 6 June 2006 at http://www.malawi.pop.upenn.edu/Level%203/Papers/PDF-files/thornton-et-al-2005.pdf
11. Kaydos-Daniels SC, Miller WC, Hoffman I, Price MA, Martinson F, Chilongozi D, Namakwha D, Gama S, Phakati S, Cohen MS, Hobbs MM. The

use of specimens from various genitourinary sites in men, to detect Trichomonas vaginalis infection. J Infect Dis, 2004 15: 1926-31.

12. Sutcliffe S, Taha TE, Kumwenda NI, Taylor E, Liomba GN. HIV-1 prevalence and herpes simplex 2, Hepatitis C virus and Hepatitis B virus infections among male workers at a sugar estate in Malawi. J Acquir Immune Defic Syndr 2002; 31: 90-97.
13. Taha TET, Canner JK, Chiphangwi JP, Dallabetta GA, Yang LP, Mtimavalye LAR et al. Reported condom use is not associated with incidence of sexually transmitted diseases in Malawi. AIDS 1996;10:207-12.
14. Zachariah R, Harries AD, Chantulo AS, Yadidi AE, Nkhoma W, Maganga O. Sexually transmitted infections among prison inmates in a rural district of Malawi. Trans R Soc Trop Med Hyg 2002;96: 617-9
15. Ministry of Health, Planning Department, Health Management Information Unit. Health Management Information System Bulletin July 2004 – June 2005. Lilongwe, September 2005.
16. Taha TE, Dallabetta GA, Hoover DR, Chiphangwi JD, Mtimavalye LAR, Liomba GN, Kumwenda NI, Miotti PG. Trends of HIV-1 and sexually transmitted diseases among pregnant and postpartum women in urban Malawi. AIDS 1998; 12: 197-203
17. Miotti PG, Dallabetta GA, Daniel RW, Canner JK, Chiphangwi JD, Liomba GN et al. Cervical abnormalities, human papillomavirus, and human immunodeficiency virus infections in women in Malawi. J Infect Dis 1996; 173:714-7.
18. Watson PA. The use of screening tests for sexually transmitted diseases in a third world community: a feasibility study in Malawi. Eur J Sex Transm Dise 1985;2:63-5.
19. McCallum M and Tozer RZ. Vaginal flora in Malawian women. Centr Afr J Med 1973; 19: 176-178.
20. Taha TE, Gray RH, Kumwenda NI, Hoover DR, Mtimavalye LA, Liomba GN et al. HIV infection and disturbances of vaginal flora during pregnancy. J Acquir Immune Defic Syndr Hum Retrovirol 1999;20:52-9.
21. Kumwenda NI, Taha TE, Hoover DR, Markakis D, Liomba GN, Chiphangwi JD, Celentano DD. Three surveys of HIV-1 prevalence and risk factors among men working at a sugar estate in Malawi. Sex Transm Dis 2002;29:366-71.
22. Zachariah R, Spielmann MP, Harries AD, Nkhoma W, Chantulo A, Arendt W. Sexually transmitted infections and sexual behaviour among commercial sex workers in a rural district of Malawi. Int J STD AIDS 2003; 14: 185-88
23. Zachariah R, Harries AD, Nkhoma W, Arendt V, Nchingwa D, Chantulo A et al. Behavioural characteristics, prevalence of Chlamydia trachomatis and antibiotic susceptibility of Neisseria gonorrhea in men with urethral discharge in Thyolo, Malawi. Trans R Soc Trop Med Hyg 2002;96:232-5.
24. Price MA, Zimba D, Hoffman JF, Kaydos-Daniels SC, Miller WC, Martinson F et al. Addition of treatment for trichomoniasis to syndromic management of urethritis in Malawi: a randomised clinical trial. Sex Transm Dis 2003;30:516-22.
25. Behets FM, Liomba G, Lule G, Dallabetta G, Hoffman IF, Halmiton HA, Moeng S, Cohen MS. Sexually transmitted diseases and humandeficiency virus control in Malawi: a field study of genital ulcer disease. J Infect Dis 1995; 171: 541-5
26. Hobbs MM, Kazembe P, Reed AW, Miller WC, Nkata E, Zimba D, Costello Daly C, Chakraborty H, Cohen MS, Hoffman I. Trichomonas vaginalis as a cause of urethritis in Malawian men. Sex Transm Infect 1999;26:381-7.
27. Kristensen JK. The prevalence of symptomatic sexually transmitted diseases and human immunodeficiency virus infection in outpatients in Lilongwe, Malawi. Genitourin Med 1990;66:244-6.
28. Maher D, Hoffman I. Prevalence of genital infection in medical inpatients in Blantyre, Malawi. J Infect 1995;31:77-8.
29. Komolafe OG, Nkumba J, Makoka M, Makhalira A, Bonongwe P. Sexually transmitted diseases at Queen Elisabeth Central Hospital, Blantyre, Malawi. East Afr Med J 2000;77:644-7.
30. Zachariah R, Nkhoma W, Harries AD, Arendt V, Chantulo A, Spielmann MP, Mbereko MP, Buhendwa L. Health seeking and sexual behaviour in patients with sexually transmitted infections: the importance of traditional healers in Thyolo, Malawi. Sex Transm Infect 2002;78:127-9.
31. Dallabetta G. Understanding STDs in Malawi. Africa Health; Nov 1994:21-22.
32. Wynendaele B, Bomba W, M'manga W, Bhart S, Fransen L. Impact of counselling among STD patients in Malawi. International Journal of STD and AIDS 1995; 6: 105-9
33. Lule GS, Moses A, Bandawe C. Characteristics and sexual behaviour of individuals attending the sexually transmitted diseases clinic at Queen Elisabeth Central Hospital, Blantyre, Malawi. Centr Afr J Med 1997;43:6-11.
34. Dallabetta GA, Miotii PG, Chiphangwi JD, Liomba G, Canner JK, Saah AJ. Traditional vaginal agents: use and association of HIV infection in Malawian women. AIDS 1995; 9: 293-7

35. Zachariah R, Harries AD, Buhendwa L, Spielman MP, Chnatulo A, Bahali E. Acceptability and technical problems of the female condom amongst commercial sex workers in a rural district in Malawi. Trop Doct 2003;33:220-4.
36. Support to AIDS and family health (STAFH) Project. Health seeking behaviour and partner notification by clients with sexually transmitted diseases (STDs) in Malawi: an ethnographic approach. STAFH / JSI, Lilongwe, December 1997.
37. Auvert B, Taljaard D, Lagarde E, Sobngwi-Tambekou J, Sitta R, et al. Randomized, Controlled Intervention Trial of Male Circumcision for Reduction of HIV Infection Risk: The ANRS 1265 Trial. PLoS Med 2005; 2:e298.
38. Quigley MA, Weiss HA, Hayes RJ. Male circumcision as a measure to control HIV infection and other sexually transmitted diseases. Current Opinions Infect Dis 2001;14:71-5.
39. Grosskurth H, Mosha F, Todd J, Awijaruba E, Klokke A, Senkoro K, et al. Impact of improved treatment of sexually transmitted diseases on HIV infection in rural Tanzania: randomised controlled trial. Lancet 1995; 346:530-6.
40. Mayaud P, Mosha F, Todd J, Balira R, Mgara J, West B, Rusizoka M, Mwijarubi E, Gabone R, Gavyole A, Grosskurth H, Hayes R, Mabey D. Improved treatment services significantly reduce the prevalence of sexually transmitted diseases in rural Tanzania: results of a randomised controlled trial. AIDS 1997; 11:1873-1880.
41. Lule G, Behets FTM, Hoffman IF, Dallabetta G, Hamilton HA, Moeng S, Liomba G, Cohen MS. STD / HIV control in Malawi and the search for affordable and effective urethritis therapy: a first field evaluation. Genitourin Med 1994;70:384-8.
42. Costello Daly C, Hoffman I, Hobbs M, Maida M, Zimba D, Davis R, Mughogho G, Cohen MS. Development of an antimicrobial susceptibility surveillance system for Neisseria gonnorrhoeae in Malawi: comparison of methods. J Clin Microb 1997;35:2985-8.
43. Chilongozi D, LCH/UNC project, 5 May 2006, personal communication.
44. Klouda A, Kachiza C, Kaponda C, Mgawi M, Kazembe A. Evaluation In-service training in Syndromic Management of STDs. STAFH Project. Malawi 1997
45. Wawer MJ, Sewankambo NK, Serwadda D, Quinn TC, Paxton LA, Kiwanuka N et al. Control of sexually transmitted diseases for AIDS prevention in Uganda: a randomised community trial. Rakai Project Study Group. Lancet 1999;353:525-35.
46. Harper DM, Franco EL, Wheeler C, Ferris DG, Jenkins D, Schuind A et al. Efficacy of a bivalent L1 virus-like particle vaccine in prevention of infection with human papillomavirus types 16 and 18 in young women: a randomised controlled trial. Lancet 2004;364:1757-65.
47. Koutsky LA, Ault KA, Wheeler CM, Brown DR, Barr E, Alvarez FB, Chiacchierini LM, Jansen KU. A controlled trial of a human papillomavirus type 16 vaccine. N Engl J Med 2002;347:1645-51.
48. Goldie SJ, Gaffikin L, Goldhaber-Fiebert JD, Gordillo-Tobar A, Levin C, Mahe C, Wright TC; Alliance for Cervical Cancer Prevention Cost Working Group. Cost-effectiveness of cervical-cancer screening in five developing countries. N Engl J Med 2005; 353:2158-68.
49. Martin-Hirsch PL, Paraskevaidis E, Kitchener H. Surgery for cervical intraepithelial neoplasia (Cochrane Review). In: The Reproductive Health Library, Issue 8, 2005. Oxford: Update Software Ltd. Available from http://www.rhlibrary.com.
50. Mathews C, Coetzee N, Zwarenstein M, Lombard C, Guttmacher S, Oxman A et al. Strategies for partner notification for sexually transmitted diseases (Cochrane Review). In: The Reproductive Health Library, Issue 8, 2005. Oxford: Update Software Ltd. Available from http://www.rhlibrary.com.
51. Volmink J. Partner notification strategies for reducing transmission of sexually transmitted infections: RHL commentary (last revised: 11 November 2002). The WHO Reproductive Health Library, No 8, Update Software Ltd, Oxford, 2005.