

9 Support for Sexual and Reproductive Health in People Living with HIV/AIDS

Clinical Protocol for the WHO European Region



EUROPE

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Edited by:
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Abbreviations

3TC	lamivudine
ABC	abacavir
AIDS	acquired immunodeficiency syndrome
APV	amprenavir
ART	antiretroviral treatment
ARV	antiretroviral
ASC-H	atypical squamous cells, cannot exclude HSIL
ASC-US	atypical squamous cells of undetermined significance
ATV	atazanavir
AUC	area under concentration-time curve
BID	twice daily
BV	bacterial vaginosis
CIC	combined injectable contraceptive
CIN	cervical intraepithelial neoplasia
C _{max}	maximum blood concentration
C _{min}	minimum blood concentration
CNS	central nervous system
COC	combined oral contraceptive
CSF	cerebrospinal fluid
Cu-IUD	copper-releasing IUD
ddI	didanosine
DMPA	depot medroxyprogesterone acetate
DNA	deoxyribonucleic acid
the DTs	delirium tremens
EE	ethinylestradiol
EFV	efavirenz
FIGO	Fédération Internationale de Gynécologie Obstétrique (International Federation of Gynecology and Obstetrics)
FPV	fosamprenavir
FSH	follicle-stimulating hormone
FTC	emtricitabine
GC	gonococci
HAART	highly active antiretroviral therapy
HBV	hepatitis B virus
HCV	hepatitis C virus
HIV	human immunodeficiency virus
HIV/STIs	HIV and other STIs
HPV	human papilloma virus
HR	harm reduction
HSIL	high-grade squamous intraepithelial lesion
HSV	herpes simplex virus
IDU	injecting drug user
IDV	indinavir
IUD	intrauterine device
IV	intravenous or intravenously
LEEP	loop electrosurgical excision procedure
LGV	lymphogranuloma venereum

LH	luteinizing hormone
LNG	levonorgestrel
LNG-IUD	levonorgestrel-releasing IUD
LPV/r	lopinavir/ritonavir
LSIL	low-grade squamous intraepithelial lesion
MSM	men who have sex with men
MTCT	mother-to-child transmission (of HIV)
NE	norethindrone
NET-EN	norethisterone-enantate
NFV	nelfinavir
NGU	non-gonococcal urethritis
NNRTI	non-nucleoside reverse transcriptase inhibitor
NVP	nevirapine
OD	once daily
PEP	post-exposure prophylaxis
PI	protease inhibitor
PID	pelvic inflammatory disease
PLWHA	people living with HIV/AIDS
PMTCT	prevention of mother-to-child transmission
PO	per os (orally)
POC	progestogen-only contraceptive
POP	progestogen-only pill
Q	every (e.g. Q8H = every 8 hours)
QID	four times daily
QOD	every other day
RNA	ribonucleic acid
RPR	rapid plasma reagin
RTI	reproductive tract infection
RTV	ritonavir
RH	reproductive health
S&RH	sexual and reproductive health
SQV	saquinavir
STI	sexually transmitted infection
TB	tuberculosis
TDF	tenofovir
THC	tetrahydrocannabinol
TID	three times daily
Tmax	time of peak concentration
TMP/SMX	trimethoprim-sulfamethoxazole (co-trimoxazole)
TSH	thyroid-stimulating hormone
VDRL	venereal disease research laboratory slide test
VIA	visual inspection of the cervix
VVC	vulvovaginal candidiasis
WHO	World Health Organization
ZDV	zidovudine

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I. Introduction

As the health and well-being of people living with HIV/AIDS (PLWHA) improves due to antiviral treatment (ART), it has become necessary to reconsider many previous policies concerning their sexuality and reproduction. A rights-based approach to caring for their sexual and reproductive health (S&RH) is needed to:

- empower them as individuals;
- ensure that they consider themselves capable of healthy and satisfying sexual lives through the effective management of their HIV infection; and
- address other S&RH concerns effectively.

The purpose of this protocol is to assist health care providers at every level during consultations with PLWHA (whether or not on ART) on sexual and reproductive health. The present protocol includes steps that should be taken during such consultations, based on WHO documents and available evidence.

II. Background

Reproductive health (RH) is concerned with the reproductive system and its processes and functions at every stage of life. The term implies that people should be able to have a satisfying, responsible and safe sex life, and that they should be able to reproduce and freely decide whether, when and how often to do so (1).

Reproductive health overlaps but is not synonymous *sexual health* (2). Sexual health encompasses positive aspects of sexuality and sexual relationships, as well as problems with power dynamics in these relationships, including coercion, violence and discrimination. It concerns “the enhancement of life and personal relations, and not merely counselling and care related to reproduction and sexually transmitted diseases” (1).

In order to attain and maintain S&RH, people must be empowered to exercise control over their sexuality and reproduction and have access to related health services (2). S&RH services are offered by a variety of providers – from primary care physicians in western Europe to obstetricians, gynaecologists, urologists, dermatovenerologists and sexologists in eastern Europe – at venues that include family planning centres, youth-friendly health centres and STI centres.

Reproductive health care providers should use any opportunity to promote voluntary testing and counselling for HIV infection and strive to improve access to care for PLWHA. HIV specialists should be informed of the reproductive rights and choices of PLWHA and refer them to appropriate RH services for quality assistance.

In Europe, reproductive health services for drug-using women are particularly important. Female injecting drug users (IDUs) are difficult to reach through the usual RH services and may mistakenly perceive themselves as infertile because of drug-related amenorrhea.

III. Principles of Sexual and Reproductive Health Services for PLWHA

1. General principles

- Provision of reproductive health services should follow the human rights principles of non-discrimination, participation and accountability.
- Services should be comprehensive and client-oriented, addressing all the needs of PLWHA during their lifetime.
- There should be no discrimination towards PLWHA, irrespective of any risk behaviours.
- Women should not be forced to have an abortion because of their HIV status.
- Confidentiality is to be a guiding principle in all services for PLWHA, including S&RH services.

These principles are based on recognition of the needs of PLWHA:

- to obtain complete and correct information regarding their S&RH choices
- to have or not have children and to make informed decisions about the choice
- to have access to the same full range of S&RH services as HIV-negative people
- to be treated without stigmatization or discrimination in health care settings
- to expect confidentiality and respect for their human rights from health care providers
- to be involved in the formulation of policies and programmes that affect them.

2. Principles of HIV testing and counselling

HIV testing and counselling should be offered to clients and their partners during:

- testing for or treatment of reproductive tract infections (RTIs) and sexually transmitted infections (STIs);
- contraceptive counselling, with an emphasis on the benefits of knowing one's status when choosing a method of contraception;
- pre-conception, for planned pregnancy and childbirth to minimize mother-to-child transmission (MTCT);
- prenatal care, to maximize care for the mother and the prevention of MTCT (PMTCT);¹
- newborn care, to facilitate safe choices regarding feeding options when HIV status is unknown;
- consultation regarding options for unwanted pregnancies;
- screening consultation for cervical cancer; and
- outreach work, especially among groups at high risk of infection (e.g. IDUs, men who have sex with men (MSM) or sex workers).

3. Patient counselling

Every HIV-infected patient attending S&RH services should receive appropriate counselling on sexual and reproductive health issues, such as:

- reduction of risky sexual behaviour and safer sex negotiation, for both HIV-discordant and -concordant partners;
- the causes and management of sexual dysfunction;
- family planning and contraception;
- cervical cancer screening;
- STIs;

¹ For more information please refer to Protocol 10, *Prevention of HIV transmission from HIV-infected mothers to their infants*.

- hepatitis B vaccination;
- substance use;
- interactions between ARVs and other drugs; and
- interactions between contraceptives and illicit drugs.

Psychological support should be provided during counselling, with referrals for further assistance as required.

IV. Sexual health of PLWHA

Sexual health is affected by a variety of issues (3), including:

- sexual well-being (satisfaction, pleasure and freedom from dysfunction)
- HIV, other STIs and RTIs
- mental health
- violence related to gender and sexuality
- physical disabilities and chronic illnesses
- unintended pregnancy and unsafe abortion
- infertility.

1. Taking a sexual health history

A sexual history should be included when obtaining the medical history of PLWHA. It will help equip the provider to discuss risk-reduction strategies for preventing further transmission, such as reducing the number of sexual partners or using condoms, and make appropriate referrals (4, 5).

Health care providers should be non-judgemental of the range and diversity of their patients' sexual practices and backgrounds. A provider's attitude will affect the quality and effectiveness of care provided to PLWHA. Providers should:

- be open and able to discuss sex and other sensitive issues
- be prepared to take a comprehensive sexual history
- be able to manage debilitating S&RH problems that patients face (4)
- be sensitive to the needs of PLWHA who may have suffered violence
- have current information and refer patients to appropriate support (5, 6).

It is a fundamental duty of all health workers to use their professional skills ethically and be aware of the laws in their country. The main ethical principles of the health care profession are:

- do no harm
- respect the rights of the patient
- assure informed consent
- maintain the highest degree of patient confidentiality.

A list of recommended topics and suggested questions to use in obtaining a sexual history is provided in Annex 1.

2. Sexual well-being

While many of the sexual health issues faced by PLWHA are similar to those faced by their non-infected peers, some issues are particular to those living with HIV/AIDS.

2.1. Sexual dysfunction among women

The limited evidence available suggests that sexual dysfunction is common in women following disclosure of HIV infection. It may be attributed to:

- psychological factors (including post-diagnosis depression, anxiety, irritability, loss of self-esteem, altered/disturbed body image, change of roles in couple relationship, social isolation and fear of infecting others);
- medical factors (such as endocrinopathies and autonomic and peripheral neuropathies, gastrointestinal symptoms and headache);
- previous violence and associated fear and trauma;

- lipodystrophy, a side-effect of ART that can result in stigmatization and sexual isolation (7–9); and/or
- infrequent sex, avoidance and non-communication (10).

2.2. Sexual dysfunction among males

Among HIV-infected males, ART has been associated with low libido, erectile dysfunction and increased serum estradiol levels (11).

TABLE 1.		CLINICAL SIGNS OF MALE SEXUAL DYSFUNCTION	
Clinical signs		Possible cause	
<i>Historical</i>			
Abrupt onset		Psychogenic impotence (HIV diagnosis, performance anxiety)	
Absent nocturnal/early morning erections		Vascular or neurological disease	
Loss of erection after penetration		Anxiety or vascular steal	
<i>Exam</i>			
Reduced femoral or peripheral pulse		Vascular disease	
Testicular atrophy/loss of muscle bulk/loss of facial or body hair		Hypogonadism	
<i>Laboratory</i>			
Low serum-free testosterone, high prolactin or abnormal thyroid-stimulating hormone (TSH) levels		Endocrinologic dysfunction	
Abnormal lipids		Atherosclerosis	

Source: Colson & Sax, 2000 (12).

2.3. Interactions between erectile dysfunction drugs and ARVs

Sexual dysfunction, including a decrease in sexual interest, has been noted in both females and males receiving ART regimens with PIs (13, 14). Switching HIV-infected patients to regimens that do not contain PIs may alleviate some symptoms associated with sexual dysfunction (15), while among some male patients, sildenafil or apomorphine hydrochloride may improve erections (16). Recreational use of Viagra (sildenafil) is common among some groups (17, 18). Prescription of ARVs and erectile dysfunction agents should be based on possible side-effects and drug interactions.

TABLE 2.		INTERACTIONS BETWEEN ERECTILE DYSFUNCTION AGENTS AND ANTIRETROVIRAL DRUGS					
Erectile dysfunction agent	Agent dose	ARV	ARV dose	Agent effect on ARV levels	ARV effect on agent levels	Potential clinical effects	Management
Sildenafil (Viagra)	—	Amprenavir	—	—	Not studied; may increase sildenafil levels	Increased sildenafil effects (hypotension, priapism)	Initiate sildenafil at 25 mg QOD-OD and adjust dose as indicated; not recommended to exceed 25 mg in a 48-hour period.
	25 mg x 1 dose	Indinavir	800 mg TID	Indinavir AUC: increased 11%; Cmax: increased 48%	Sildenafil AUC: increased 340%; Cmax: increased 300% (levels exceeded those achieved by a 100 mg single dose)	Increased sildenafil effects (hypotension, priapism)	Initiate sildenafil 30–45 minutes before sex and adjust dose as indicated; not recommended to exceed 25 mg in a 48-hour period.
	—	Lopinavir/ritonavir	—	—	Not studied; may increase sildenafil levels	Increased sildenafil effects (hypotension, priapism)	Initiate sildenafil 30–45 minutes before sex and adjust dose as indicated; not recommended to exceed 25 mg in a 48-hour period.
	—	Nelfinavir	—	—	Not studied; may increase sildenafil levels.	Increased sildenafil effects (hypotension, priapism)	Initiate sildenafil 30–45 minutes before sex and adjust dose as indicated; not recommended to exceed 25 mg in a 48-hour period.
	25 mg x 1 dose	Nelfinavir	1250 mg Q12H	Not studied	No significant change	—	No dose adjustment necessary.
	100 mg x 1 dose	Ritonavir	300 mg, 400 mg and 500 mg BID on Days 2, 3 and 4–8, respectively	—	Sildenafil AUC: increased 1000%; Cmax: increased 290%; Tmax: delayed 3 hours	Increased sildenafil effects (hypotension, priapism)	Initiate treatment at a 25 mg dose; do not exceed 25 mg in 48-hour period.
	—	Saquinavir	—	—	Sildenafil AUC: increased 200–1100%	Increased sildenafil effects (e.g. headache, flushing, priapism)	Initiate sildenafil 30–45 minutes before sex and adjust dose as indicated; not recommended to exceed 25 mg in a 48-hour period.

Erectile dysfunction agent	Agent dose	ARV	ARV dose	Agent effect on ARV levels	ARV effect on agent levels	Potential clinical effects	Management
Tadalafil (Cialis)	—	Lopinavir/ ritonavir	—	—	Not studied; may increase tadalafil levels.	Increased tadalafil effects (e.g. hypotension, priapism)	Do not coadminister. Suggested alterna- tive agents: sildenafil, vardenafil.
	20 mg x 1 dose	Ritonavir	200 mg BID	—	—	Increased tadalafil effects	Do not exceed 10 mg tadala- fil every 72 hours.
Vardenafil (Levitra)	10 mg x 1 dose	Indinavir	800 mg Q8H	Not studied	Vardena- fil AUC: increased 16- fold; Cmax: increased 7-fold; half- life: increased 2-fold	Increased vardena- fil effects (hypoten- sion, nausea, priapism, syncope)	Consider initiating vardenafil at lower dose and titrate to effect. Dose should not exceed 2.5 mg in any 24- hour period.
	—	Lopinavir/ ritonavir	—	—	Not studied; may increase vardenafil levels	Increased vardenafil effects (hy- potension, priapism, etc.)	Initiate vardenafil at 5 mg OD and adjust dose as indicated; not recommended to exceed 20 mg in a 48- hour period.

AUC: area under concentration-time curve; Cmax: maximum blood concentration; Tmax: time of peak concentration; OD: once daily; BID: twice daily; TID: three times daily; QOD: every other day; Q: every (Q8H= every 8 hours)

Source: Adapted from HIV InSite, 2005 (19).

2.4. Substance use

When asking about sexual practice it is important to list all medications taken by a patient, including recreational, illicit and herbal/alternative drugs. Substance use by PLWHA may increase risky sexual behaviour and HIV transmission. If HIV-infected patients also receive ART or are about to initiate it, potential drug interactions should be considered and discussed with them. Table 3 summarizes some interactions between alcohol and ARVs and between marijuana and ARVs. (For more information about illicit drugs and ARV interactions please refer to Protocol 5, *HIV/AIDS treatment and care for injecting drug users.*)

TABLE 3. INTERACTIONS BETWEEN ARVs AND ALCOHOL/MARIJUANA							
Substance	ARV	ARV dose	Substance dose	Substance effect on ARV levels	ARV effect on substance levels	Potential clinical effects	Management
Alcohol	Abacavir	600 mg QD	0.7 g/kg body weight	Abacavir AUC: increased 41%; half-life: increased 26%	No significant change	—	No dose adjustment necessary
	Amprenavir	—	—	—	—	Propylene glycol toxicity (acidosis, central nervous system (CNS) depression)	Use of alcoholic beverages is not recommended with amprenavir oral solution. Suggested alternative: amprenavir capsules.
Marijuana (THC – tetrahydrocannabinol)	Indinavir	800 mg Q8H x 21 days (pharmacokinetics measured at 14 days)	4% THC cigarettes	Indinavir AUC: no significant change; Cmax: no significant change; Cmin: decreased 34%	Not clinically significant	—	No dose adjustment necessary
	Nelfinavir	750 mg TID	4% THC cigarettes or 2.5 mg dronabinol TID	Nelfinavir AUC: no significant change; Cmax: decreased 17%; Cmin: no significant change	Not clinically significant	—	No dose adjustment necessary

AUC: area under concentration-time curve; Cmax: maximum blood concentration; Cmin: minimum blood concentration; THC: tetrahydrocannabinol.

Source: HIV InSite, 2005; New York State Department of Health AIDS Institute, 2006 (19, 20).

2.5. Aspects of mental health

Depression after HIV diagnosis may be a reason for sexual dysfunction in PLWHA. Appropriate psychological support should be an essential part of sexual dysfunction management, as not all PLWHA will need antidepressant therapy, and such support can facilitate a healthy sexual life. Some patients who have been referred for psychotherapy and prescribed antidepressants after their HIV diagnosis experience side-effects that include sexual dysfunction. More recently developed antidepressants with minimal drug interactions can be used when sexual dysfunction has been attributed to the older agents (6).

TABLE 4. ANTIDEPRESSANT AGENTS WITH SEXUAL DYSFUNCTION SIDE-EFFECTS (MEN AND WOMEN)		
Antidepressant	Therapeutic dosage	Potential clinical effects due to ARV interactions
Fluoxetine (Prozac)	10–40 mg/day	Increased delavirdine, ritonavir effects; possibly increased fluoxetine effects
Paroxetine (Paxil)	10–40 mg/day	Decreased paroxetine effect with fosamprenavir
Sertraline (Zoloft)	50–100 mg/day	Drug interactions unlikely with ARVs
Venlafaxine XR (Effexor XR)	75–375 mg/day	Increases in serum level of venlafaxine possible with RTV coadministration
<i>Possible substitutions for individuals experiencing sexual dysfunction from other antidepressant agents</i>		
Bupropion sustained release (Wellbutrin SR)	Not to exceed 400 mg/day (in divided doses) due to increased risk of seizures, particularly in individuals who have other risk factors for seizures	Clinically important drug interactions with PIs unlikely (preliminary in vitro data show weak inhibition by ritonavir)
Mirtazapine (Remeron)	15–45 mg/day	Increases in serum level of mirtazapine possible with ritonavir coadministration.

Sources: HIV/AIDS Bureau, 2003; Colson & Sax, 2000; Anderson, 2005 (6, 12, 21).

3. STIs and RTIs

Management of STIs and RTIs should include the following components:

- medical and sexual history
- informed consent for testing and exam procedures
- physical examination
- testing for STIs and RTIs
- preventive measures (such as hepatitis B vaccination)
- treatment as needed, with consideration for potential ARV interactions
- for STIs, partner notification and fulfilment of any public health obligations
- counselling on risk reduction, and referral as appropriate
- scheduling of follow-up visits and consultations.

In general, the management of RTIs and non-HIV STIs for PLWHA is similar to that for other patients, with several differences.

- The clinical presentation of STIs may vary with HIV disease stage.
- Longer therapeutic courses may be needed.
- Potential drug interactions with ARV drugs should be evaluated.
- Enhanced surveillance is necessary due to the rapid progress and frequent recurrence of infections in PLWHA.

There are special considerations for the management of syphilis, vulvovaginal candidiasis and bacterial vaginosis in PLWHA; see Annexes 2–4.

Among HIV-infected women, higher rates and/or greater severity of the following STIs and RTIs and their complications have been noted than among HIV-negative women:

- pelvic inflammatory disease (PID)²
- human papillomavirus (HPV) infection, causing cervical dysplasia (22–24)
- cervical intraepithelial neoplasia (CIN)³
- vaginal yeast infections.

² PID is sometimes noted as a co-epidemic of HIV in some urban populations of reproductive age (6).

³ Rates are substantially higher among women in the advanced stages of HIV/AIDS (25).

Among MSM, increased levels of rectal chlamydial infection, syphilis, gonorrhoea, herpes simplex virus (HSV), lymphogranuloma venereum (LGV), anal dysplasia and genital herpes are common regardless of HIV status (26–32). In addition, anal cancer is strongly associated with HPV infection, and it is significantly more likely among MSM who are HIV-infected (33, 34).

Testing procedures vary depending on resources and particular STI prevalence. Health care providers should accordingly consult local STI management guidelines for further advice.

TABLE 5. STI TESTING FOR PLWHA			
Test	Rationale or risk group	Result	Recommended action
Venereal disease research laboratory slide test (VDRL) or rapid plasma regain (RPR)	Syphilis screening	Negative	Repeat every 3–6 months, counsel on prevention of STIs.
		Positive	Follow <i>European STD guidelines</i> (http://www.iusti.org/guidelines.pdf) for the management of syphilis (35). See also Annex 2.
Pap smear	Detection of cell changes	See section VIII	Cf. section VIII and Annex 5 below.
Gonococci (GC) and <i>Chlamydia</i> testing	For all women with initial Pap smear, and for any symptomatic men	Negative	Counsel on prevention of STIs; repeat if necessary.
		Positive	Treat patient; refer partner(s) of previous 60 days for evaluation and treatment.
GC and <i>Chlamydia</i> testing, urethral	MSM	Negative	Retest annually, counsel on prevention of STIs.
		Positive	Treat patient; refer partners of previous 60 days.
GC and <i>Chlamydia</i> testing, pharyngeal	Men and women who have oral-genital sex	Negative	Retest annually, counsel on prevention of STIs.
		Positive	Treat patient; refer partners of previous 60 days.
GC and <i>Chlamydia</i> testing, rectal	Women and men who have receptive anal sex	Negative	Re-test annually, counsel on prevention of STIs
		Positive	Treat patient; refer partners of previous 60 days.
Lymphogranuloma venereum (LGV)	MSM	Positive	Treat patient; refer partners of previous 30 days.

GC: gonococci; RPR: rapid plasma regain; VDRL: venereal disease research laboratory slide test.

Source: United States Department of Health and Human Services HIV/AIDS Bureau, 2003 (6).

3.1. Partner notification

It is essential that every effort be made to treat the partners of those HIV-infected people diagnosed with other STIs; otherwise, the likelihood of STI reinfection is high. Following a safety assessment to consider the implications of notifying sexual partners (i.e. a risk assessment for intimate partner violence), and in accordance with local protocols and regulations, patients should be encouraged to ensure that their sexual partners are evaluated and treated. Partner management strategies are based on the premise that the sexual partners of people with STIs are likely to be infected with the same STIs, but that they may be asymptomatic, and that they may not otherwise seek care. The various options for partner notification and treatment should be discussed with the patient. Depending on the resources of the provider and the individual situation of the patient, options include:

- the patient informing and accompanying a partner for testing;
- provider-assisted notification followed by testing and treatment; and
- in rare cases, expedited partner treatment in which the patient delivers medication to a partner without a clinical examination (36–38)⁴.

⁴ This is not the preferred option due to the possibility of the partner's coinfection with multiple STIs including HIV, implications for drug interactions or allergies and medicolegal issues.

3.2. Interactions of STI/RTI drugs and ARVs

If PLWHA are on ART, possible drug interactions with other STI treatment drugs should be considered and discussed with them.

TABLE 6.		INTERACTIONS BETWEEN ARVs AND OTHER STI/RTI DRUGS						
STI/RTI agent	STI/RTI agent dosage	ARV	ARV dosage	Agent effect on ARV levels	ARV effect on agent levels	Potential clinical effects	Management	Suggested alternative agent(s)
Azithromycin	600 mg x 1 dose	EFV	400 mg x 7 days	No significant change	Azithromycin AUC: no significant change; Cmax: ↑ 22%	—	No dose adjustment necessary	—
	1200 mg x 1 dose	IDV	800 mg TID	No significant change	—	—	No dose adjustment necessary	—
Ciprofloxacin	750 mg Q12H x 3 days	ddI	200 mg (buffered formulation) Q12H x 3 days	ddI AUC: ↓ 16%; Cmax: ↓ 28%	Ciprofloxacin AUC: ↓ 15-fold (with simultaneous ddI dosing); ↓ 26% when ciprofloxacin is dosed 2 hours before or 6 hours after ddI tablets.	↓ ciprofloxacin effects	Consider ddI enteric coated capsule or administer ddI tablets/suspension 6 hours prior to or 2 hours after ciprofloxacin administration	—
	750 mg x 1 dose	ddI	400 mg (enteric coated capsule) x 1 dose	Not studied	No significant change	—	No dose adjustment necessary	—
Co-trimoxazole (TMP/SMX)	160/800 mg Q12H x 1 week	IDV	400 mg Q6H x 1 week	No significant change	TMP AUC: ↑ 19%; SMX AUC: no significant change	—	No dose adjustment necessary	—
Erythromycin base (E-Base, Ilosone, E-Mycin, Eryc, Ery-Tab)	—	APV	—	Not studied; may ↑ APV levels	Not studied; may increase erythromycin levels	—	Dose adjustment not established	Azithromycin, clarithromycin
	250 mg QID x 7 days	SQV	1200 mg TID	In HIV-infected patients, SQV AUC: ↑ 99%; Cmax: ↑ 106%	—	↑ SQV effects	Dose adjustment not established	—
Famciclovir (Famvir)	500 mg x 1 dose	FTC	200 mg x 1 dose	No significant change	—	No significant change	No dose adjustment necessary	—

STI/RTI agent	STI/RTI agent dosage	ARV	ARV dosage	Agent effect on ARV levels	ARV effect on agent levels	Potential clinical effects	Management	Suggested alternative agent(s)
Metronidazole (Flagyl)	—	APV	Oral solution (contains propylene glycol)	—	—	Propylene glycol toxicity (acidosis, CNS depression)	Do not coadminister with APV oral solution	Amprenavir capsules
	—	LPV/r	Oral solution (contains alcohol)	—	—	Disulfiram reaction (hypotension, headache, nausea, vomiting)	Do not coadminister; consider LPV/r capsules	—
	—	RTV	Oral solution (contains alcohol) and capsules	—	—	Disulfiram-like reaction (headache, hypotension, flushing, vomiting)	Do not coadminister	—
Sufamethoxazole	1000 mg x 1 dose	ddI	200 mg (buffered formulation) x 1 dose	No significant change	No significant change	—	No dose adjustment necessary	—
	Trimethoprim (Trimplex)	200 mg x 1 dose	ddI	200 mg (buffered formulation) x 1 dose	ddI AUC: no significant change; Cmax: ↑ 17%	TMP AUC: no significant change; Cmax: ↓ 22%	—	No dose adjustment necessary

↑: increase; ↓: decrease; QID: four times daily

Source: HIV InSite, 2005 (19).

4. Violence related to gender and sexuality

Gender- and sexuality-related violence has a detrimental effect on a victim's physical, emotional and social life. By understanding the range of complications he or she may be experiencing, health care providers are able to offer more effective HIV/AIDS treatment. In many cases the victim, who is most often female, will not only be infected with HIV by the perpetrator, but also, due to feelings of low self-worth, socioeconomic factors or oppressive tactics, she will not be diagnosed until a later stage of the disease (39, 40).

Treating PLWHA who have been subjected to violence requires the provider to do the following things (39, 41–44).

- Routinely evaluate the possibility of violence for all female (and male when indicated) HIV-infected patients.
- Keep the health and welfare of the patient as the first priority. “Safety first” and “do no harm” should be guiding principles.
- Avoid retraumatizing the patient with questions that are likely to provoke a strong or emotional reaction, cause distress or insinuate a negative judgement.
- Be prepared to respond to distress and highlight the patient's strengths.
- Be prepared to provide appropriate care, follow-up and support services (referrals).
- Maintain confidentiality.

- With respect to partner notification, take into account the harm that may occur if an abuser is notified. Where such notification is mandatory, the patient should be informed about the consequences of disclosure prior to identifying the partner.
- Agree with the person who has suffered violence upon any action that is to be taken with respect to the abuser or perpetrator. Respect the patient's wishes, as her or his consent is essential. In accordance with legal obligations, exceptions may need to be made for suspected abuse of minors.
- Be prepared for emergency intervention if a patient or a patient's dependants feel they are in imminent danger.
- Provide psychological support or refer the patient to a specialist for such support, as well as for legal counselling if appropriate.
- Counsel the patient on post-exposure prophylaxis (PEP) (for prevention of STIs, emergency contraception, etc.) (Please refer to Protocol 13, *Post-exposure prophylaxis for HIV infection* for further information.)

5. Impact of disabilities and chronic illnesses on sexual health

Compared to non-disabled people, individuals with a physical, sensory, intellectual or mental health disability are often at increased risk for contracting and transmitting HIV, for substance abuse and for restricted access to services and interventions (45, 46). While PLWHA with physical disabilities and chronic illnesses contend with the same sexual health issues as their non-disabled peers, they often face additional barriers to care, such as:

- difficulty accessing treatment centres due to lack of mobility or independence;
- ineffective communication (lack of interpreters – including sign language – confused, complicated explanations, too technical language, etc.); and
- homophobia, HIV stigma and the misconception among professional health providers that the physically disabled do not have sex.

Disabled individuals, especially women, may also be at an increased risk for gender-based violence due to factors such as:

- increased physical vulnerability
- need for attendant care
- social isolation
- lack of economic independence
- decreased access to health care
- less education about safer sexual behaviours
- difficulty being believed (47–49).

Health care providers should ensure that PLWHA with disabilities or chronic illnesses have the same support, treatment and access to care as the non-disabled population. The range of possible mental and physical disabilities and chronic illnesses is broad, as are the specific sexual health concerns that may need to be addressed. Providers should be prepared to:

- ensure patients have full access to information, care and treatment support;
- address substance use;
- address gender-based violence;
- provide referrals to disability support organizations, substance use centres, institutions for gender-based violence, etc.;
- determine the individual's knowledge of and negotiation skills for safer sex;
- determine the level of support available from other care providers and family members for contraception and safer sex practices;
- adapt safer sex messages for the use of the disabled;
- address contraindications for ART and other drugs needed to treat a patient's physical disability/chronic illness; and
- coordinate with other health care providers.

V. Contraception

The recommendations for contraceptive methods in this section are based on a comprehensive manual of recommendations on eligibility criteria for contraceptive use (50). The manual includes HIV/AIDS as a factor in determining eligibility for each major contraceptive method.

1. Preliminary visit

In addition to medical eligibility criteria, the patient's social, cultural and behavioural context must also be considered. Contraceptive recommendations should be individualized for each woman and couple, based on disease stage and treatment as well as lifestyle and personal desires. Each woman is best placed to interpret the risks and benefits the available methods may have for her. It should be the patient who makes the final selection of contraceptive method. To make an informed choice, she requires information on:

- the method's effectiveness
- its correct use
- its risks and benefits
- common side-effects
- signs and symptoms that would necessitate a return to the clinic
- cost and convenience issues
- the method's effect on transmission of STIs, including HIV.

Counselling should help women living with HIV/AIDS to make decisions about their fertility. It should therefore include information on:

- effective contraceptive methods to prevent pregnancy and STI transmission;
- the effects of HIV disease progression on health;
- the effectiveness and availability of ARVs;
- the services that provide ART;
- the interactions between ARVs and contraceptives;
- the risk of HIV transmission to an uninfected partner while trying to become pregnant;
- the possible impact of HIV on pregnancy, including adverse pregnancy outcomes;
- the risk of MTCT and the risks and benefits of strategies to reduce it, including ARV prophylaxis, caesarean section and bottle-feeding⁵; and
- the possible birth defects associated with the use of some ARVs.

2. Medical eligibility criteria for contraceptive use by women living with HIV/AIDS

Most contraceptive methods are safe and effective for use by women with asymptomatic HIV infection as well as for women with developed HIV/AIDS disease (50). However, transmission of HIV and other STIs (HIV/STIs) warrants special consideration during family planning counselling because preventing transmission is as important as preventing pregnancy. Since condoms are the only contraceptive method shown to protect against acquiring and transmitting HIV/STIs, family planning services should strongly encourage and facilitate their consistent and correct use (51).

⁵ For more information, please refer to Protocol 10, *Prevention of HIV transmission from HIV-infected mothers to their infants*.

3. General contraceptive methods

3.1. Barrier methods and spermicides

3.1.1. Dual protection

- Dual protection is defined as the simultaneous prevention of STI transmission and unwanted pregnancy. It can be achieved by the consistent use of latex condoms, either alone or in combination with another method.
- Dual protection is also achieved by avoidance of penetrative sex, particularly in situations of high risk.
- Dual protection may be indicated to compensate for a reduction in the effectiveness of hormonal contraceptives due to interactions between ART and hormonal contraception (see section V.4.1 below).
- Dual protection strategies should be part of the counselling and support provided by all reproductive health services (52).

3.1.2. Male latex condoms

- When used consistently and correctly, male latex condoms⁶ protect against female-to-male, male-to-male and male-to-female transmission of HIV, as shown in studies of HIV-discordant couples⁷ (53).
- In HIV-infected couples, condoms can offer individuals protection against new HIV strains. Limited evidence suggests that infection with more than one strain of HIV may accelerate the progression of HIV disease (54).
- Laboratory studies have demonstrated the impermeability of latex condoms to infectious agents, including the smallest viruses, contained in genital secretions.
- Latex condoms may be less effective in protecting against those STIs not transmitted by semen or fluid (such as herpes, human papillomavirus and syphilis), since the infected areas may not be covered by the condom (51).
- Clear instructions on correct condom use are essential. To provide optimum protection against infection, they must be of good quality and be used consistently and correctly.
- Emergency contraception can be offered as a backup in case a condom breaks or slips (see section V.3.6 below).
- For serodiscordant couples, information and access to post-exposure prophylaxis for uninfected partners should be offered if a condom breaks or slips.
- Despite the method's efficacy, low rates of condom use have been reported, even following disclosure of positive HIV status to sexual partners (55).
- Use of condoms to prevent HIV/STI transmission should be emphasized in cases where prevention of pregnancy is not a concern, such as pregnancy or any kind of infertility, e.g. due to sterilization or menopause.

3.1.3. Female condoms

- Available data indicate that female condoms, used correctly and consistently, provide protection against STIs, including HIV (56–58).
- The limited data available suggest they may be slightly less effective than male condoms for the prevention of pregnancy (59). However, they offer several advantages, including:
 - the possibility of insertion prior to intercourse;
 - no necessity for removal immediately after ejaculation; and
 - greater female control, though some degree of negotiation and male cooperation is still required.

⁶ Condoms made of animal membranes do not protect against HIV, as such when the term condom is used in this document, it refers to latex condoms unless otherwise stated.

⁷ Couples with discordant serostatus – those in which one sexual partner is HIV-positive and the other HIV-negative – may require special support. Protected sex using a condom is the only way to ensure PLWHA that HIV-negative sexual partners can remain uninfected.

3.1.4. Other barrier methods (diaphragms, cervical caps)

Women for whom pregnancy is an unacceptable risk should be advised that other contraceptive barrier methods (diaphragms and cervical caps) may not be appropriate because of their relatively higher typical-use failure rates for those who cannot use them consistently and correctly. It should also be stressed that they do not protect against the transmission of HIV or other STIs.

3.1.5. Spermicides

- Since nonoxynol-9 may cause some side-effects, condoms lubricated with it should no longer be promoted; nevertheless, it is better to use a nonoxynol-9-lubricated condom than no condom (60).
- The safety concerns with nonoxynol-9 also apply to other spermicidal products marketed for contraception. Spermicides should not be used by women living with HIV/AIDS, neither alone or with other barrier methods such as diaphragms or cervical caps.
- There is no evidence that nonoxynol-9-lubricated condoms provide any more protection against pregnancy or sexually transmitted infections than condoms lubricated with silicone.

3.2. Low-dose combined oral contraceptives (COC)

TABLE 7. LOW-DOSE COC ($\leq 35 \mu\text{g}$ OF ETHINYLESTRADIOL (EE)) FOR WOMEN LIVING WITH HIV/AIDS		
Status	Category ^a	Comment
High risk of HIV	1	Overall, evidence is inconsistent regarding whether there is any increased risk of HIV acquisition among COC users.
HIV/AIDS without ART	1	Limited evidence suggests no association between COC use and changes in RNA levels or CD4 counts among HIV-infected women. There is also limited evidence showing no association between COC use and female-to-male HIV transmission, and mixed results regarding increased risk of HIV and HSV shedding among HIV-infected women using hormonal contraception.
HIV/AIDS + ART	2	For women on ART, refer to the section on drug interactions below (V.4.1). As there may be drug interactions between hormonal contraceptives and ARVs, such use is classified as Category 2.
Drug interactions		
ARVs	2	It is important to note that ARV drugs have the potential to decrease or increase the bioavailability of steroid hormones in hormonal contraceptives. The limited data available suggest that interactions between many ARVs (particularly some NNRTIs and PIs) and hormonal contraceptives may alter the safety and effectiveness of both. For women initiating or continuing hormonal contraceptive use while on ART, the consistent use of condoms is recommended for preventing HIV transmission; it may also compensate for any possible reduction in the effectiveness of the hormonal contraceptive. See section V.4 below.

^a Category 1: no restrictions for use of contraceptive method; use in any circumstances. Category 2: advantages of using method generally outweigh theoretical or proven risks. Generally advisable to use the method.

Note: COCs do not protect against HIV/STIs. If there is risk of HIV/STIs, the correct and consistent use of condoms is recommended, either alone or with another contraceptive method. Male latex condoms are proven to protect against HIV/STIs.

Source: WHO, 2004 (50).

There are concerns that women may have a greater risk of acquiring STIs when using hormonal contraceptives, possibly due to decreased condom usage. Yet the evidence is inconsistent regarding whether hormonal contraceptive users have greater risk of acquiring HIV than non-users (50).

3.3. Progestogen-only contraceptives (POCs)

Progestogen-only contraceptives include progestogen-only pills (POPs), injectable progestogens (depot medroxyprogesterone acetate (DMPA) and norethisterone-enantate (NET-EN)) and progestogen implants (levonorgestrel implants (Norplant and Jadelle) and etonogestrel implants (Implanon)).

TABLE 8. PROGESTOGEN-ONLY CONTRACEPTIVES FOR WOMEN LIVING WITH HIV/AIDS				
Condition	Category ^a			Comment
	POP	D/NE	LN/ETG	
High risk of HIV	1	1	1	Overall, evidence is inconsistent as to any increased risk of HIV acquisition among POC users.
HIV/AIDS without ART	1	1	1	Studies conflict over whether there is increased risk of HIV and HSV shedding among HIV-infected women using DMPA.
HIV/AIDS + ART	2	2	2	For women on ART, refer to the section on drug interactions (V.4.1 below). As there may be interactions between hormonal contraceptives and ARVs, it is classified as Category 2.
Drug interactions				
ARV	2	2	2	ARVs have the potential to decrease or increase the bioavailability of steroid hormones in hormonal contraceptives (see section V.4.1 below). It is not known whether the contraceptive effectiveness of injectable POCs (such as DMPA and NET-EN) would be compromised, as they provide higher blood hormone levels than other POCs and COCs. Studies are underway to evaluate potential interactions between DMPA and selected PI and NNRTI drugs. For women initiating or continuing hormonal contraceptive use while on ART, the consistent use of condoms is recommended for preventing HIV transmission; it may also compensate for any possible reduction in the effectiveness of the hormonal contraceptive.

D/NE: depot medroxyprogesterone acetate (DMPA)/norethisterone enantate (NET-EN); LNG/ETG: levonorgestrel implants (Norplant and Jadelle) and etonogestrel implants (Implanon); POP: progestogen-only pill.

^a Category 1: no restrictions for use of contraceptive method; use in any circumstances. Category 2: advantages of using method generally outweigh theoretical or proven risks. Generally advisable to use the method.

Note: POCs do not protect against HIV/STIs, though neither has the use of POCs been associated with HIV acquisition or transmission (61). If there is risk of HIV/STIs, the correct and consistent use of condoms is recommended, either alone or with another contraceptive method. Male latex condoms are proven to protect against HIV/STIs.

Source: WHO, 2004 (50).

3.4. Combined contraceptives in injectable, patch and ring form

For women living with HIV/AIDS, there are no restrictions on the use of combined injectable contraceptives (CICs), combined contraceptive patches or combined contraceptive vaginal rings.

- CICs provide for the release of a natural estrogen plus a progestogen. Two CIC formulations, both given at four-week intervals, are considered here: Cyclofem (medroxyprogesterone acetate 25 mg plus estradiol cypionate 5 mg) and Mesigyna (norethisterone enantate 50 mg plus estradiol valerate 5 mg).
- The combined contraceptive patch is a 20 cm², three-layer patch applied to the buttocks, torso, abdomen or upper arm to release ethinylestradiol and a progestogen (norelgestromin) transdermally. The combined contraceptive patch currently available is Evra (17-deacetyl norgestimate (norelgestromin) 150 µg plus ethinylestradiol 20 µg). A new patch has to be applied once a week for three consecutive weeks each month.
- The combined contraceptive vaginal ring releases ethinylestradiol and a progestogen (etonogestrel) from a 54 mm ethylene vinyl acetate copolymer ring. The vaginal ring formulation currently available is NuvaRing (etonogestrel 120 µg plus ethinylestradiol 15 µg). It is inserted once a month, taken out after 21 days to allow the normal menstrual cycle, and a new ring is inserted after a 7-day break.

The contraceptive effect of CICs, patches and vaginal rings is achieved by inhibiting ovulation. These contraceptive methods are new, with little epidemiological data on their long-term effects.

TABLE 9. CICs AND COMBINED CONTRACEPTIVE PATCHES AND RINGS FOR WOMEN LIVING WITH HIV/AIDS				
Status	Category ^a			Comment
	CIC	Patch	Ring	
High risk of HIV	1	1	1	—
HIV/AIDS without ART	1	1	1	Relatively limited information is available on the safety of the combined contraceptive patch and vaginal ring. At present, there are no restrictions on the use of CICs, patches or vaginal rings for women living with HIV/AIDS.
HIV/AIDS + ART	2	2	2	For women on ART, refer to the section on drug interactions (V.4.1 below). As there may be interactions between hormonal contraceptives and ARVs, this use is classified as Category 2.
<i>Drug interactions</i>				
ARVs	2	2	2	ARVs have the potential to decrease or increase the bioavailability of steroid hormones in hormonal contraceptives (see section V.4.1 below). The limited data available suggest that potential drug interactions between many ARVs, particularly some NNRTIs and PIs, and hormonal contraceptives may alter safety and effectiveness of both. For women initiating or continuing hormonal contraceptive use while on ART, the consistent use of condoms is recommended for preventing HIV transmission; it may also compensate for any possible reduction in the effectiveness of the hormonal contraceptive.

^a Category 1: no restrictions for use of contraceptive method; use in any circumstances. Category 2: advantages of using method generally outweigh theoretical or proven risks. Generally advisable to use the method.

Note: CICs, patches and rings do not protect against HIV/STIs. If there is risk of HIV/STIs, the correct and consistent use of condoms is recommended, either alone or with another contraceptive method. Male latex condoms are proven to protect against HIV/STIs.

Source: WHO, 2004 (50).

3.5. Intrauterine devices

IUDs can be safely used by women living with HIV/AIDS, whether asymptomatic, on ART or clinically well, but such users should be closely monitored for pelvic inflammatory disease (PID). IUDs are not usually recommended for women living with AIDS who are not on ART if more appropriate contraceptive methods like condoms or steroid hormonal contraceptives are available and acceptable.

While physicians should be wary of over-diagnosing PID, it is highly probable with IUD-wearers when one or more of the following symptoms are observed:

- lower genital tract infection
- cervical motion tenderness
- adnexal tenderness
- enlargement of one or both Fallopian tubes, a tender pelvic mass
- direct or rebound tenderness
- elevation of temperature (temperature may be normal in many cases of PID).

Hospitalization of patients with acute PID should be seriously considered when:

- the diagnosis is uncertain
- surgical emergencies such as appendicitis and ectopic pregnancy cannot be excluded
- a pelvic abscess is suspected
- severe illness precludes management on an outpatient basis
- the patient is pregnant
- the patient is unable to follow or tolerate an outpatient regimen
- the patient has failed to respond to outpatient treatment.

The levonorgestrel-releasing intrauterine device (LNG-IUD) releases 20 µg of levonorgestrel (LNG) daily, directly into the uterus. Because LNG suppresses endometrial growth, users can expect a marked reduction in the amount of menstrual blood. Many women experience little or no bleeding (amenorrhea) within a year of beginning use. In sexual relations where the recommended condoms are not used, a reduction of menstrual blood loss may be regarded as a means of decreasing the risk of female-to-male HIV transmission.

TABLE 10. IUDs FOR WOMEN LIVING WITH HIV/AIDS					
Condition	Category ^a (I: initiation, C: continuation)				Comment
	Cu-IUD		LNG-IUD		
	I	C	I	C	
High risk of HIV	2	2	2	2	Among women at risk of HIV, copper-releasing IUD (CU-IUD) use did not increase risk of HIV acquisition.
HIV/AIDS without ART	2	2	2	2	Limited evidence shows no increased risk of overall or infection-related complications among IUD users when comparing HIV-infected women with non-infected women. Furthermore, it shows no association between IUD use among HIV-infected women and increased risk of transmission to sexual partners. IUD users with AIDS should be closely monitored for PID.
HIV/AIDS + ART	3	2	3	2	IUD users with AIDS should be closely monitored for PID.
Clinically well on ART	2	2	2	2	—
Drug interactions					
ARVs	2/3	2	2/3	2	There are no known drug interactions between ARVs and IUDs. However, IUD use by AIDS patients is classified as Category 3 for insertion and Category 2 for continuation, unless the woman is clinically well on ART, in which case both insertion and continuation are classified as Category 2.

Cu-IUD = copper-releasing IUD; LNG-IUD = levonorgestrel-releasing IUD (20 µg/24 hours),

^a Category 1: no restrictions for use of contraceptive method; use in any circumstances. Category 2: advantages of using method generally outweigh theoretical or proven risks. Generally advisable to use the method. Category 3: method not usually recommended unless other more appropriate methods are not available or not acceptable (theoretical or proven risks usually outweigh the advantages of using the method).

Note: IUDs do not protect against HIV/STIs. If there is risk of HIV/STIs, the correct and consistent use of condoms is recommended, either alone or with another contraceptive method. Male latex condoms are proven to protect against HIV/STIs.

Source: WHO, 2004 (50).

3.6. Emergency contraception

Emergency contraception can prevent pregnancy when:

- a contraceptive method fails
- no method was used
- sex was forced.

Emergency contraceptive pills inhibit or delay ovulation, and prevent implantation and fertilization or transport of sperm/ova by altering the endometrium.

When used within 72 hours after sex:

- the Yuzpe regimen (COC) prevents about 74% of expected pregnancies (62);
- POPs prevent 85% of expected pregnancies under typical use and 89% under correct use (63); and
- POPs produce fewer side-effects than COCs.

3.6.1. Emergency contraceptive pill regimens

- One of the best-studied progestogen-only regimes consists of 1.5 mg of levonorgestrel (two pills containing 0.75 mg taken either in a single dose or at a 12-hour interval). Ideally, the pills should be taken within 72 hours of unprotected intercourse.
- If low-dose pills containing 30 µg ethinylestradiol and 150 µg levonorgestrel are used, four pills should be taken in a first dose as soon as convenient, but no later than 72 hours after unprotected intercourse. These should be followed by a second dose of four pills 12 hours later.
- The standard regimen (the Yuzpe method) consists of the combined oral pills containing 50 µg ethinylestradiol and 250 µg levonorgestrel. Two pills should be taken in a first dose as soon as convenient, but no later than 72 hours after unprotected intercourse. These should be followed by a second dose of the same pills 12 hours later.

The most common side-effects of hormonal emergency contraception are nausea and vomiting. The Yuzpe regimen is associated with a 42% incidence of nausea and a 16% incidence of vomiting (64). These problems were significantly less common among users of the levonorgestrel regimen, at 23% and 6%, respectively (63). The Yuzpe regimen can be used if levonorgestrel or mifepristone are not available.

Several observations should be made about the management of side-effects.

- Taking the pills with food or at bedtime may help reduce nausea.
- If vomiting occurs within two hours of taking the pills, the dose should be repeated. In cases of severe vomiting, the repeat dose may be administered vaginally.
- The majority of women will have their menstrual period on time or slightly early. If there is a delay of more than one week, a pregnancy test should be performed.
- A single dose simplifies the use of levonorgestrel for emergency contraception without increasing side-effects.
- Breast tenderness, headache, dizziness and fatigue may occur.

Hormonal emergency contraception may have side-effects in women living with HIV/AIDS.

- There are no studies of side-effects in women living with HIV/AIDS, neither on ART or off. Nausea and vomiting are side-effects with some ARTs and may be intensified when taking emergency contraceptive pill regimens.
- The Yuzpe regimen should be avoided in women taking indinavir, atazanavir, amprenavir or efavirenz since it raises estradiol levels, which may increase the risk of thrombo-embolic disease (see section V.4.1 below).

3.6.2. IUDs as emergency contraceptives

- A copper-releasing IUD can also be used within five days of unprotected intercourse as an emergency contraceptive.
- When the time of ovulation can be estimated, the Cu-IUD may be inserted more than five days after intercourse if necessary, as long as the insertion does not also occur more than five days after the earliest estimated ovulation.

3.6.3. Mifepristone

- Orally administered mifepristone (10 mg), an antiprogesterin, offers high efficacy with few side-effects when taken within 120 hours (five days) of unprotected intercourse (65).
- Mifepristone can delay menstruation, which may in turn increase patient anxiety.
- There are no studies about the efficacy or side-effects of mifepristone in women living with HIV/AIDS, either with or without ART.

3.7. Surgical sterilization procedures

Given that sterilization is a surgical procedure intended to be permanent, special care must be taken to ensure that every patient who chooses it is making a voluntary informed choice. All patients, irrespective of HIV status, must understand the permanence of sterilization and be informed of alternative contraceptive methods. The indications and contraindications for sterilization are the same as for HIV-negative patients.

As sterilization provides no protection against STI acquisition or HIV transmission, it is essential to stress the importance of condom use, particularly as sterilization has been associated with a decrease in condom use. The national laws and existing norms for sterilization procedures must also be considered in the decision process.

The general health of any PLWHA who opt for this procedure must be examined carefully before any elective surgery is undertaken. A decision to proceed depends on any existing AIDS-related illnesses that may compromise the patient.

3.8. Fertility-awareness methods and coitus interruptus

Fertility-awareness methods and coitus interruptus are characterized by higher typical-use failure rates than other methods and should not be routinely recommended for either HIV-positive or -negative women.

3.9. Lactational amenorrhea method

This method is not recommended due to the need to avoid HIV transmission in serodiscordant couples and breastfeeding infants. Replacement feeding is recommended where acceptable, feasible, affordable, sustainable and safe. Otherwise, exclusive breastfeeding is recommended during the first months of life and should then be discontinued as soon as feasible.

Mothers living with HIV/AIDS should be helped to make the best choice for feeding their infants in accordance with their circumstances, and to carry out their decision. They should thus receive counselling that includes information about the risks and benefits of various infant feeding options (based on local assessments), and support to carry out their choice safely and appropriately.

3.10. Future prospects

Developmental work on microbicides, which could provide an invaluable method of dual protection, is underway. Such products are inserted into the vagina before sexual intercourse to prevent transmission of HIV/STIs and would be thus under the control of the woman. Although some microbicides aim to provide dual protection against unintended pregnancies and HIV/STIs, others are only intended to prevent the latter. So far, no microbicides have been shown to decrease MTCT effectively, nor are any microbicial products on the market for the prevention of sexual transmission of HIV or other STIs. Until effectiveness trials demonstrate safety and efficacy, microbicide use should not be promoted.

4. Contraception for women on ARV

WHO recommends using highly active antiretroviral therapy (HAART) for PLWHA who are eligible for ART in accordance with the WHO clinical staging system (for more information please see Protocol 1, *Patient evaluation and antiretroviral treatment for adults and adolescents*).

ARV regimens recommended by the WHO Regional Office for Europe for first- and second-line therapy are shown in Table 11.

TABLE 11. RECOMMENDED FIRST- AND SECOND-LINE HAART REGIMENS FOR ADULTS AND ADOLESCENTS	
First-line regimen	Second-line regimens
ZDV + 3TC ^a + EFV ^b or NVP	LPV/r ^c + ddI + ABC LPV/r ^c + TDF + ABC LPV/r ^c + TDF + (ZDV + 3TC) ^d
TDF + FTC ^a + EFV or NVP	LPV/r ^c + ddI + ABC LPV/r ^c + ddI + ZDV
ABC + 3TC ^a + EFV or NVP	LPV/r ^c + ddI + ZDV LPV/r ^c + (ZDV + 3TC) ^d

^a 3TC (lamivudine) and FTC are considered interchangeable agents, given their activity, tolerance and resistance profiles. They are both listed in this table as a reflection of the commonly available FDCs.

^b For the purpose of this table, treatment failure on an NVP- or EFV (efavirenz)-based regimen is considered to result in NNRTI class cross-resistance.

^c LPV/r is listed as the preferred RTV-boosted protease inhibitor (PI) in this table, but other boosted PIs can be substituted based on individual programme priorities. ATV/r, SQV/r, FPV/r and IDV/r are all possibilities. In the absence of a cold chain, NFV can be employed as the PI component, but it is considered less potent than a boosted PI.

^d ZDV + 3TC is listed here for “strategic” use, as resistance to both drugs is predicted to be present following failure on the respective first-line regimen listed. ZDV may prevent or delay the emergence of the K65R mutation; 3TC will maintain the M184V mutation, which may decrease viral replicative capacity as well as induce some degree of viral re-sensitization to ZDV. It must be stressed that the clinical efficacy of this strategy in this situation has not been proven.

4.1. Interactions between ARVs and steroids in hormonal contraceptives

The limited data available suggest that several ARVs, especially NNRTIs and PIs, have the potential to either decrease or increase the bioavailability of steroid hormones in hormonal contraceptives. These drug interactions may alter the safety and effectiveness of both the hormonal contraceptives and the ARVs. The possible interactions between ARVs and COCs, as well as the suggested alternatives, should be taken into consideration and discussed with the patients.

Table 12 summarizes the most recent evidence regarding ARVs and steroids in COCs and provides management recommendations regarding use of the latter (66).

TABLE 12. INTERACTIONS BETWEEN ARVs AND ETHINYLESTRADIOL (EE)/ NORETHINDRONE (NE) ACETATE		
ARVs	Effect of coadministration on EE, NE acetate and ARV levels	Recommendations
<i>Protease inhibitors (PIs)</i>		
Atazanavir (ATV)	EE ↑ 48%, NE ↑ 110%	Use the lowest effective dose or an alternative method.
Fosamprenavir (FPV)	EE and NE ↑, FPV ↓ 20%	Do not coadminister, alternative contraceptive methods recommended.
Indinavir (IDV)	EE ↑ 24%, NE ↑ 26%	No dose adjustment required.
Lopinavir/ritonavir (LPV/r)	EE ↓ 42%	Use an alternative or additional method.
Nelfinavir (NFV)	EE ↓ 47%, NE ↓ 18%	Use an alternative or additional method.
Ritonavir (RTV)	EE ↓ 40%	Use an alternative or additional method.
Saquinavir (SQV)	No data	—
<i>Non-nucleoside reverse transcriptase inhibitors (NNRTIs)</i>		
Efavirenz (EFV)	EE ↑ 37%	Use an alternative or additional method.
Nevirapine (NVP)	EE ↓ 20%	Use alternative contraceptive methods.

No data are available for interactions between ARVs and levonorgestrel. It is not known whether the contraceptive effectiveness of progestogen-only injectable contraceptives (such as DMPA and NET-EN) would be compromised – these methods provide higher blood hormone levels than other progestogen-only contraceptives or combined oral contraceptives.

4.2. Interactions between ARVs and IUDs

There are no known interactions between ARVs and either the copper- or the levonorgestrel-releasing IUDs.

4.3. Teratogenicity of EFV

- EFV is considered potentially teratogenic and should be avoided for women trying to conceive or not using effective contraception.
- It is recommended that women have a pregnancy test prior to initiating treatment with EFV.
- For women using effective contraception, EFV is a viable option for the NNRTI component of an ARV treatment regimen.

4.4. Adherence to contraception and HIV/AIDS treatment

HIV-positive women may need to take several pills each day for ART, prophylaxis or treatment of opportunistic infections, symptomatic relief or treatment of concurrent illnesses. In addition to potential drug interactions, the impact of pill burden on adherence to contraception and HIV-related therapies should be considered. A hormonal contraceptive method that requires daily administration will increase pill burden. Women need to be aware of these considerations when they select a contraceptive method.

5. Contraceptive methods for women on both ART and TB treatment

- For women receiving ART and tuberculosis (TB) treatment, drug interactions with certain hormonal contraceptives can reduce the effectiveness of hormonal contraception.
- Due to drug interactions, a non-hormonal method of contraception is preferable for women receiving both ART and TB treatment.

- If hormonal contraception is the only option, low-dose (<35 µg) estrogen COC is usually not recommended for women receiving rifampicin. Although evidence is limited, use of an oral contraceptive pill containing a higher dose of estrogen (50 µg) may be considered unless the patient is taking EFV, IDV, APV or ATV.
- DMPA can generally be used with rifampicin.
- The effectiveness of LNG-IUDs is unlikely to be reduced.

6. Considerations for the most vulnerable populations

Sexual and reproductive health services should strive to create a supportive and non-discriminatory environment for specific vulnerable populations. Due to the stigma attached to these populations, they often do not seek health care through conventional channels. It is therefore important for outreach to be part of the strategy for all S&RH programmes in order to improve access for these groups.

6.1. Sex workers (male and female)

- Consistent condom use should be recommended to sex workers for use with clients and their regular partners to prevent HIV transmission to the uninfected partner.
- Pending evidence on the reuse of female condoms, it is recommended that they be used only once.

6.2. MSM

- MSM should be advised to use water-based or silicone-based lubricants during anal sex to maintain condom integrity.

6.3. IDUs

- Drug-related amenorrhea is not an indication of infertility. It is thus important to advise women who are injecting drug users on regular use of contraception to prevent unintended pregnancy.
- Links should be reinforced between RH and harm reduction (HR) services.

7. Recommendations for contraceptive methods

- Discussion of family planning should be initiated during post-test HIV counselling and continued in follow-up sessions and at regular intervals throughout care.
- All staff should understand that they have a professional responsibility to maintain HIV confidentiality.
- In addition to medical eligibility criteria, the social, cultural and behavioural context should also be considered, and recommendations for contraceptive methods should be tailored to the individual, based on disease stage, treatment, lifestyle and personal wishes.
- Transmission of HIV and other STIs warrants special consideration during family planning counselling. Family planning services should strongly encourage and facilitate the consistent and correct use of condoms as the only contraceptive method that protects against HIV and other STIs. Furthermore, all reproductive health services should provide support for dual protection.
- Links between harm-reduction services for IDUs and HIV/AIDS treatment and care services should be established and strengthened to provide better continuity of care.

VI. Safe abortion

Preventing unintended pregnancies and unsafe abortions is essential for improving the reproductive health of all women, including those living with HIV/AIDS. Even where contraceptive services are available, unintended pregnancies still happen for a variety of reasons – contraceptives may fail, male partners may oppose using condoms or other forms of contraception, people may not use contraceptives for fear of side-effects, unprotected sex may be coerced or forced, etc. – and many women will seek termination of these pregnancies.

In case HIV infection is diagnosed during pregnancy, the woman may seek termination of pregnancy even if the pregnancy was planned or wanted. For whatever reason women living with HIV/AIDS want to terminate a pregnancy, they should have access to safe abortion.

When induced abortion is performed by qualified people using correct techniques in sanitary conditions, it is a safe procedure. Restrictive abortion legislation is associated with a high incidence of unsafe abortion, performed by unskilled providers and/or in unhygienic conditions. On the other hand, abortion should not be presented as a method of family planning. Every woman has the right to – and should have the opportunity to make – informed choice regarding her pregnancy and should not be coerced, either into terminating the pregnancy or carrying it to term.

1. Abortion counselling

If a woman's HIV status is unknown, HIV testing and counselling should be offered during counselling on unwanted pregnancy; however, a HIV test should not be mandatory, and refusal to be tested should not affect her access to safe abortion services. Neither should HIV testing be requested in order to protect staff, as universal infection control precautions should be taken for every abortion.

Non-directive, non-judgemental, confidential counselling should be provided by a professional trained in pregnancy termination and well informed on the subject of HIV infection in pregnancy. Complete and accurate information, given respectfully in understandable language, will assist women in making the best decisions about their pregnancies. In cases of minors or people mentally incapable of informed consent, assistance should be provided according to national regulations. If drug use is involved, additional expertise may be required.

If sexual intercourse between an HIV-negative woman and an HIV-positive man results in pregnancy, HIV infection is unlikely to have occurred in the woman if the HIV antibody screening test is negative one month after exposure and can be excluded if negative six months after exposure. If an early diagnosis is needed, HIV infection should be highly suspected if there is:

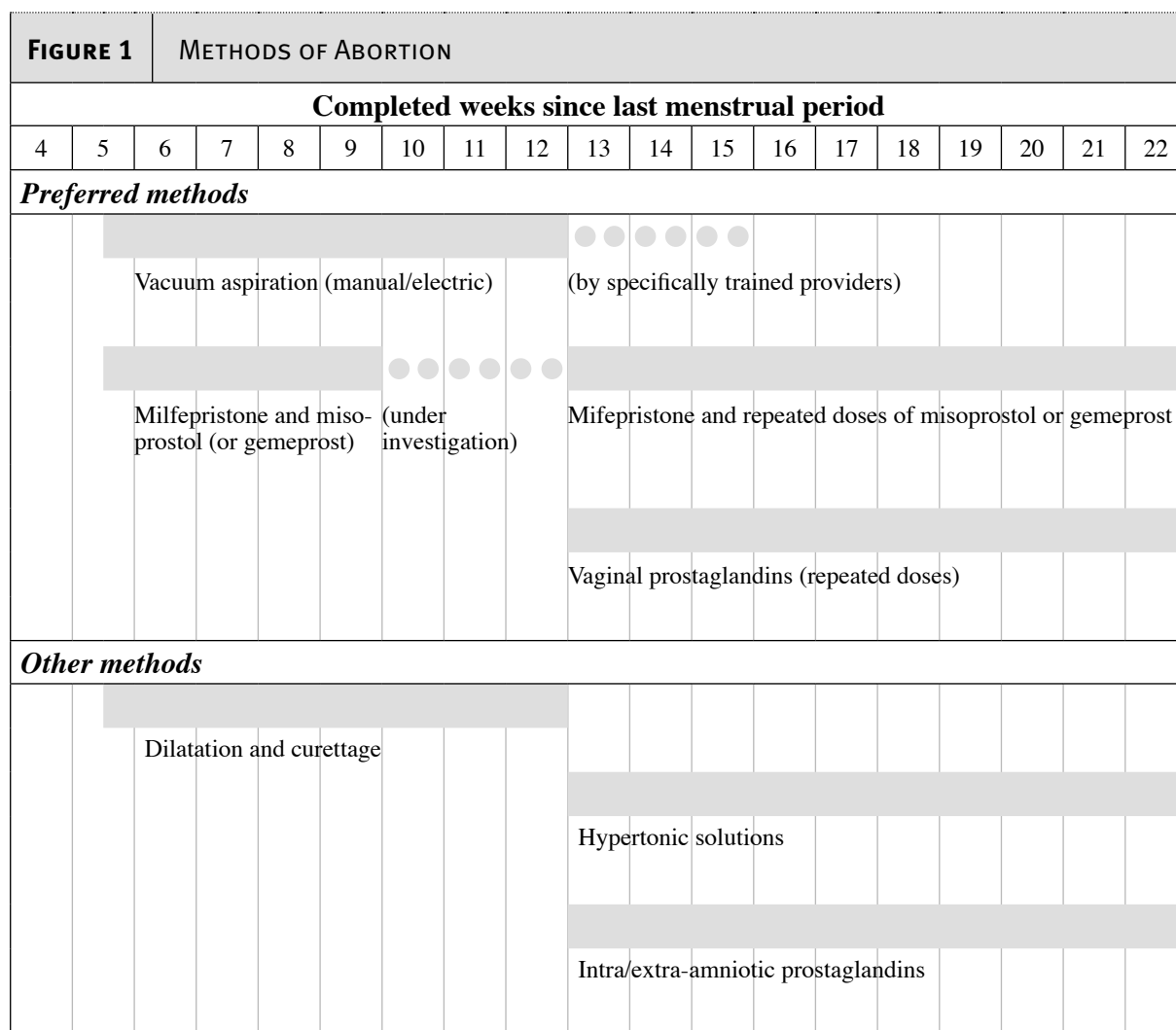
- a positive detection of HIV RNA, starting 15 days post-exposure;
- p24 antigenaemia, starting 18 days post-exposure; or
- a positive HIV-antibody screening test, starting three weeks post-exposure (subject to confirmation and expert advice).

Counselling for HIV-infected women should include:

- the risks of pregnancy to her own health
- the risks of transmission to the newborn
- the effectiveness of ARVs and other interventions in reducing MTCT
- the potential side-effects of such interventions, including ARV toxicity.

2. Surgical and medical methods of abortion

Abortion methods used for women living with HIV/AIDS do not differ from those used for HIV-negative women. Both surgical and medical methods of abortion are safe. See Fig. 1 for the recommended methods at various stages of gestation.



Source: WHO, 2004 (67).

- The complication rate is low for abortions that meet international standards (67).
- Haemoglobin should be measured and anaemia treatment initiated in accordance with etiology.
- The presence of infection in the lower reproductive tract at the time of abortion is a risk factor for post-procedural RTIs.
- The routine use of antibiotics at the time of abortion has been reported to reduce the post-procedural risk of infection by half. However, safe abortion can still be performed when antibiotics are not available for prophylactic use (67).
- There is currently no data available about the effectiveness of the recommended dosages of mifepristone, misoprostole and gemeprost in women living with HIV/AIDS, so the recommended dosages of these drugs for medical abortion (67) does not differ from those for HIV-negative women.
- There are currently no data available about potential interactions between mifepristone, misoprostole and ARVs in HIV-positive women.

3. Post-abortion care and family planning

Ensuring confidentiality is a key issue in post-abortion care. Post-abortion care for HIV-infected women should include:

- evaluation and treatment of any complications;
- minimizing transmission of HIV and other STIs in the post-abortion period, including from uterine bleeding;
- family planning counselling and services; and
- referrals for continuing HIV/AIDS treatment, care and support.

In settings where HIV and/or abortion are stigmatized, women living with HIV/AIDS may need additional counselling and psychosocial support. Otherwise, post-abortion and family planning counselling should be the same, regardless of HIV status.

Most contraceptive methods can be started immediately post-abortion.

4. Recommendations

- Non-directive, non-judgemental, unbiased and confidential counselling about termination of pregnancy should be provided by a trained person (to the extent allowed by law).
- In countries where abortion is not against the law, safe termination of pregnancy should be available and accessible to women living with HIV/AIDS.
- Family planning counselling and services should be essential components of post-abortion care, as they assist women in avoiding unintended pregnancies and reducing repeat abortions.

VII. Natural or medically assisted reproduction

Most PLWHA are of childbearing age and may desire to have children. They should have access to the same S&RH counselling and services as other people. Nor is there, in cases of couple infertility, any reason to exclude couples with HIV from accessing reproduction technology.

1. Reproductive counselling for couples with HIV

The aims of reproductive counselling for couples with HIV include:

- reducing the risk of transmission to both the uninfected partner in HIV serodiscordant couples and their offspring;
- enabling informed reproductive choices;
- informing couples about the risks of HIV transmission and chances of pregnancy in both natural and medically assisted conception;
- preparing couples for the psychological impact of assisted conception, addressing the issues of:
 - availability
 - duration of treatment
 - failure
 - logistics;
- discussing the possibility of foster or adoptive parenting where available to couples with HIV; and
- informing and advising couples about hepatitis B (HBV) and C (HCV), including the risks of sexual transmission (HBV) and vertical transmission (HBV and HCV).

2. Fertility

Women

- Most women living with HIV/AIDS menstruate about every 25–35 days, suggesting monthly ovulation (68).
- So far, the impact of ART on fertility has not been explored in women living with HIV/AIDS.
- Drugs, including methadone and psychotherapeutic medications, may contribute to menstrual disorders in women living with HIV/AIDS (69).
- HIV may not affect a woman's reproductive potential, unless she is highly immunosuppressed and presents with opportunistic infection. Nevertheless, fertility is lower in HIV-infected women than in the general population (70).

Men

- HIV can be identified in the semen of men living with HIV/AIDS regardless of the viral load in the blood.
- Many men living with HIV/AIDS have normal semen analyses for fertility (71).
- Healthy men living with HIV have semen fertility analyses similar to those of HIV-negative men, while AIDS patients have grossly abnormal semen (72).
- Some ARV drugs may have an effect on spermatogenesis (73).
- Men infected with HIV may experience sexual dysfunction including erectile dysfunction.

3. Pregnancy duration and outcome

- Women living with HIV/AIDS have a greater risk of certain adverse pregnancy outcomes (intra-uterine growth retardation, pre-term delivery, low-birth-weight infants, etc.) than HIV-negative women (74).
- Although data are limited, several studies have suggested there is an increased risk of spontaneous abortion and stillbirth among women living with HIV/AIDS (74).

- The effects of HIV infection on pregnancy outcomes are likely to be more pronounced among women with symptomatic HIV infection (75).
- Pregnancy does not have an effect on HIV disease progression or mortality (76, 77).
- The risk of opportunistic infections among women with HIV does not appear to be altered by pregnancy.

4. Counselling before conception

Assisting people living with HIV/AIDS in decisions about childbearing requires counselling on:

- the risk of HIV transmission to the partner, and interventions that can reduce it (see the next section);
- effects of HIV on pregnancy, including increased risk of certain adverse outcomes;
- the safety of ARVs during pregnancy, and their possible side-effects;
- the risk of birth defects while receiving particular ARVs; and
- the effectiveness of ARV prophylaxis, caesarean section and bottle-only feeding in reducing the risk of MTCT.

5. Reducing the risk for sexual transmission of HIV during conception

Special support should be considered for couples with discordant serostatus wishing to conceive.

- They need reproductive counselling and assistance to limit the risk of HIV transmission to the uninfected partner in unprotected sexual intercourse.
- Even though some serodiscordant couples have started pregnancies through timed unprotected intercourse without infecting the negative partner, this practice is unsafe and is not recommended.
- Specific methods of sperm preparation and testing can substantially reduce the chance of HIV transmission to the female partner (78, 79). Male-positive discordant couples who want to have a child should be informed of risk-reduction techniques and encouraged to seek assistance at institutions that can provide the most effective methods of sperm preparation.

5.1. Sperm-washing and virological determination of HIV in semen

Sperm washing can be carried out in any laboratory providing assisted reproduction services to infertile couples. It is a three-step semen processing method consisting of:

1. gradient centrifugation to isolate motile spermatozoa and reduce the number of potentially infected non-spermatozoa cells;
2. repeated washing of the cell preparation to eliminate cell-free virus; and
3. spontaneous migration to obtain an aliquot of motile virus-free spermatozoa (80, 81).

It is recommended that all processed samples be tested for HIV prior to insemination using polymerase chain reaction techniques (82). HIV genome detection in semen requires special technical equipment and skills. The use of universal infection control procedures and specific training should be provided to laboratory staff to avoid HIV infection when handling potentially infectious semen.

6. Assisted reproductive technology in case of HIV infection

Fertility screening and STI diagnosis and treatment of both partners are needed before assisted reproductive technology can be considered. A history of fertility, HIV-related parameters (including CD4 count and viral load) and ART should be established.

Basic fertility assessment includes a clinical evaluation of ovulation, hormonal parameters (follicle-stimulating hormone (FSH), luteinizing hormone (LH) and prolactin) and tubal patency for women and a sperm analysis (count, motility, progression and morphology) for men.

6.1. Fertile couples

In serodiscordant fertile couples with an HIV-positive woman, the use of artificial insemination should be encouraged. Home artificial insemination – introducing sperm collected in a condom into the vagina after intercourse using a simple syringe or other clean receptacle, after advice on recognizing and identifying the fertile period – can provide a means of conception that prevents the male partner from becoming infected.

A number of serodiscordant couples with HIV-positive men wish to have children. There is no risk-free method for ensuring safe conception in this situation. However, the use of sperm-washing (see section VII.5.1 above) to reduce levels of HIV in semen has allowed many men living with HIV/AIDS to father seronegative children (83). In fact, with washed sperm of undetectable viral load, there is minimal risk of transmission of HIV to the female partner and children (84).

If both the man and woman are HIV-positive, sperm washing can also be used to limit the woman's risk of HIV superinfection.

6.2. Infertile couples

After one year of repeated attempts at home artificial insemination without pregnancy, couples may be referred to infertility counselling and treatment. Artificial insemination and assisted reproductive technology are available in some places. Foster or adoptive parenting should also be considered.

For issues related to pregnancy in HIV-infected people and prevention of MTCT, please refer to Protocol 10, *Prevention of HIV transmission from HIV-infected mothers to their infants*.

VIII. Cervical intraepithelial lesions and cervical cancer

Cervical cancer is one of the most common types of cancer, causing deaths among women worldwide. The estimated number of new cases per year is 500 000 (85). Human papillomavirus infection with oncogenic genotypes is the etiologic agent in the development of premalignant and malignant lower genital tract disease, including cervical cancer. The development of cancer from precursor lesions is a long process and may take up to 20 years, a process that has been the basis for the development of cytological screening programmes to detect pre-invasive disease (see Annex 5) (86).

The relative risk for cervical intraepithelial neoplasia (CIN) is 5–10 times higher for women living with HIV/AIDS than for other women (87, 88).

1. Initial and follow-up evaluation

- Women should have a complete gynaecological examination, including a Pap test and pelvic examination, as part of their initial HIV evaluation.
- HIV-positive women are more likely to have genital warts and squamous intraepithelial neoplasia of the external genitalia than those who are HIV-negative (89); careful physical examination of the external genitalia of women living with HIV/AIDS is crucial.
- Cytology screening is effective in women living with HIV/AIDS.
- Cervical cancer screening should be offered to women living with HIV/AIDS at least once a year, using the same test offered to uninfected women (see Annexes 5–7).
- If an HIV-positive woman has been treated for precancerous lesions, she should have Pap smears every 4–6 months until at least three negative results have been obtained (89).
- A high-risk HPV deoxyribonucleic acid (DNA) detection test can be performed in case of a Pap smear with either atypical squamous cells of undetermined significance (ASC-US) or atypical squamous cells where a high-grade squamous intraepithelial lesion (HSIL) cannot be ruled out (ASC-H) (89).
- Examination of the entire lower genital tract, including vagina, vulvae and perianal areas, colposcopy and biopsy of cervix, to confirm cytological and visual abnormalities recommended in case of:
 - abnormal cytology (persistent low-grade squamous intraepithelial lesions (LSILs), ASC-US or HSILs);
 - an oncogenic HPV type; or
 - a history of untreated abnormal Pap smear (89).

2. General management of patients with CIN

The general management of CIN among women living with HIV/AIDS should not differ from that for the general population. Despite a modest effect of ART on spontaneous regression of CIN, follow-up of women on ART should be the same as follow-up of women not receiving ART.

Observation without specific intervention is recommended for biopsy-proven CIN 1 unless one of the following condition obtains:

- lesions persist over an 18–24 month period
- lesions evolve to CIN 2 or worse
- there is poor adherence to routine monitoring (89, 90).

3. Treatment of cervical intraepithelial lesions

- HIV-infected women should be counselled before pre-cancer treatment to ensure that they understand the need for close follow-up and the possibility for repeated treatments.

- Cone biopsy can be done under local anaesthesia on an outpatient basis using a cold knife technique or a loop electrosurgical excision procedure (LEEP).
- CIN 2 and 3 require excisional or ablative treatment.
- Women living with HIV/AIDS have a high rate of recurrence/persistence (40–60%) and progression of CIN 2 and 3 after treatment, and should therefore be monitored every six months after treatment. Prompt re-treatment should be provided when persistent, recurrent or progressive high-grade lesions are detected (90).
- Hysterectomy is contraindicated as a pre-cancer treatment in the absence of other indications (90).
- Treatment for CIN should not be modified for patients receiving ART.
- ART should not be instituted or modified for the purpose of treating CIN.
- Abstinence from sexual intercourse is recommended following treatment; if this is not possible, condoms should be used consistently and correctly.

4. Management of invasive cancer

- The International Federation of Gynecology and Obstetrics (FIGO) classification system is recommended for determining the cancer stage (91).
- For women with a CD4 count <200 cells/mm³, surgery is the preferred option when appropriate, or attenuated treatment with radiation or chemotherapy (90).
- Women with advanced HIV disease have a poor prognosis with all treatment modalities. For women with a CD4 count >200 cells/mm³, standard treatment modalities may be used.
- Comprehensive palliative care programmes are essential for improving the quality of life for women with cervical cancer (see Protocol 3, *Palliative care for people living with HIV/AIDS*).

5. Anal screening

There is no medical consensus about the use of anal Pap smear screening at this time.

IX. Suggested minimum data to be collected at the clinical level

The suggested minimum data to be collected is important in the development of key indicators on access to services and their success. Such indicators assist managers in decision-making on ways to strengthen and expand these services to all who need them.

The following data should be collected at the clinical level on a regular basis (e.g. monthly, quarterly or semi-annually):

- number of HIV-infected women of reproductive age having sexual intercourse during the last six months;
- number of HIV-infected women (cumulative) using modern contraceptive methods;
- number of pregnant HIV-infected women;
- number of terminated pregnancies in HIV-infected women;
- number of HIV-infected people tested for STIs;
- number of HIV-infected people diagnosed with STIs;
- number of HIV-infected people who have received STI treatment;
- number of HIV-infected women tested for cervical cancer within the past three years;
- number of deliveries to couples with at least one HIV-positive partner; and
- number of deliveries after medically assisted conception in couples with at least one HIV-positive partner.

Data collection methods should follow the principles of confidentiality and should not lead to the disclosure of identifiable patient information inside or outside the clinical setting.

Annex 1. Suggested topics and questions for taking a sexual history

Begin the sexual history component by stating:

“Since sex is an important part of overall health, we ask everyone the following questions. Please give only answers that you feel comfortable with me knowing.”

Sexual orientation/identity

1. Do you have sex with men, women or both?
2. Do you consider yourself heterosexual, homosexual, bisexual or other?
3. If applicable: do you consider yourself male or female?
 - a. Have you ever had hormone therapy?
 - b. Have you had or considered having a sex change?
 - c. Have you had or considered having any sex-change surgery?

Sexual practices and sexual well-being

1. What kind of sex do you have:
 - a. oral sex?
 - b. vaginal sex?
 - c. anal sex?
 - d. other?
2. How do you protect yourself from HIV/STIs?
3. Do you ever use condoms or other barrier methods?
4. If yes, for what kind of sex?
5. If MSM:
 - a. Are you more often the receptive or insertive partner?
 - b. What protection do you use for each role?
6. When was the last time you had unprotected sex?
7. Do you use alcohol or drugs before or during sex?
8. How do you think alcohol or drugs affects your decisions and abilities to have safer sex?
9. Are you satisfied with your sexual life?
10. Do you have any kind of problem when having sex (sexual dysfunction)?
11. If so, what kind?
12. Do you now or have you in the past suffered from depression?

Prevention

1. Have you made any changes in your sexual behaviour because of HIV/STIs?
2. How do you protect your sex partner(s) from HIV?

3. What percentage of the time do you and your partner(s) use condoms (or other barriers such as diaphragms or cervical caps)?

Sex trading

1. Have you ever exchanged sex for food, shelter, drugs or money?
2. Are you earning an income by sex work?

Contraception

1. For heterosexual/bisexual patients:
 - a. What method of birth control do you use?
 - b. How long have you been using it?
 - c. Do you use any additional barriers?
2. Are you interested in becoming pregnant?
3. If yes, do you have any plans for when? Are you interested in birth control?

Sexually transmitted infections (STIs)

1. Have you ever been treated for:
 - a. syphilis
 - b. gonorrhoea
 - c. proctitis
 - d. vaginitis
 - e. genital herpes
 - f. *Chlamydia*
 - g. non-gonococcal urethritis (NGU)
 - h. pelvic inflammatory disease
 - i. genital warts
2. Note site, date, treatment and compliance
3. Have you ever had a Pap smear?
 - a. When was the last time?
 - b. To your knowledge, have any been abnormal?

Substance use

1. Do you smoke or chew tobacco?
 - a. How many cigarettes/how much smokeless tobacco (chewing or snuff) do you consume per day?
 - b. How long have you used tobacco?
2. How often do you drink alcohol? How many drinks per week on average?
 - a. Have you ever drunk so much that the next day you didn't remember what you did ("blackouts")?
 - b. Have you ever experienced withdrawal symptoms (cravings, "the shakes", "the DTs" (delirium tremens))?
 - c. Are you ever worried about your alcohol use?
3. Do you use drugs for fun?
 - a. What kinds of drugs?
 - b. How often do you take these drugs (daily, weekly, monthly, occasionally)?
 - c. For how long have you been taking them?
 - d. Have you ever taken so much that the next day you didn't remember what you did?
 - e. Are you ever worried about your drug use?

4. Are you on any medicine to help you sleep or relax? If so, what?
5. Are you on any pain relievers? If so, which ones?
6. Have you ever injected drugs (including steroids or vitamins)?
7. If so, have you ever shared needles or works, even just once?
8. Have any of your current or past sex partners ever injected drugs?

Intimate partner or gender-based violence

(Read section IV.4. of this protocol first to help avoid causing unnecessary stress for the patient.)

1. Have you ever been sexually abused, assaulted or raped?
2. In your adult life, have you ever lived in a situation with physical violence or intimidation?
3. If yes to either of the above, when did they occur?
4. Are you currently encountering discrimination, humiliation or physical or sexual violence?
5. Are you afraid for your safety now? For example, are you physically forced to have sexual intercourse against your will? Do you have sexual intercourse because you are afraid of what your partner may do?
6. Have you been forced to do something sexual that you found degrading or humiliating?

Annex 2. Management of syphilis in PLWHA

- Cell-mediated and humoral immunity may modify the natural course of syphilis infection in HIV-coinfected individuals.
- The diagnostic and treatment of syphilis-coinfected PLWHA may be different due to a rapid clinical course with unusual manifestations, including increased risk of neurological manifestations and increased treatment failure rates (6).
- The recommended treatment for early syphilis does not change for PLWHA. When possible, the cerebrospinal fluid (CSF) should be examined and a more intensive treatment be administered, regardless of the clinical stage of syphilis (92).
- Clinical and serological evaluations of syphilis-coinfected patients should occur at 3, 6, 9, 12 and 24 months.
- In case of treatment failure, re-treatment should be undertaken as appropriate (6).

Annex 3. Management of vulvovaginal candidiasis in women living with HIV/AIDS

The controversy over whether vulvovaginal candidiasis (VVC), particularly recurrent VVC, is more common in women living with HIV/AIDS than in matched control HIV-negative women remains largely unresolved (93). Thus, it may be inappropriate to propose HIV testing in women with recurrent VVC.

In women living with HIV/AIDS, candidiasis frequently involves several sites, including the vulva and vagina. It is often severe and frequently relapses.

The microbiological spectrum of VVC appears similar in HIV-positive and HIV-negative women (93). Treatment involves topical application of a wide variety of imidazoles (miconazole, clotrimazole, econazole, butoconazole, terconazole, etc.) or nystatin. Although more expensive, imidazoles require shorter courses of treatment and appear to be more effective than nystatin (94).

Treatment principles are identical to those for HIV-negative women. There is no evidence of refractory VVC responding to conventional antifungal treatment. Repeated treatment may be required for women living with HIV/AIDS. It is recommended that any predisposing factors such as antibiotic use, the use of antiseptic/antibiotic vaginal preparations or vaginal douching be reduced or eliminated. Simultaneous treatment of rectal focuses with oral nystatin or fluconazole is useful in preventing recurrences. Although treatment of sexual partners is not recommended, it may be considered for women who have recurrent infection.

TABLE 13. TREATMENT OF VULVOVAGINAL CANDIDIASIS FOR WOMEN LIVING WITH HIV/AIDS				
Antifungal agent	Dose	Frequency	Route	Duration
<i>First-line</i>				
Fluconazole	100 mg	Single dose	PO	Once
Clotrimazole	500 mg	Single dose	Vaginal	Once
<i>Second-line</i>				
Ketoconazole	200 mg	BID	PO	3 days
Ketoconazole	200 mg	OD	PO	7 days
<i>Maintaining treatment of recurrent candidiasis</i>				
Nystatin	2000–4000 mg	BID	PO	10 days
<i>or:</i>				
Fluconazole	50–200 mg	OD	PO	10 days
<i>Second-line</i>				
Ketoconazole	200 mg	OD	PO	Depends on response; usually 7–10 days
Amphoterecin B	From 0.1 mg/kg/day up to 0.5 mg/kg/day	BID	IV	
Intraconazole	100 mg	OD	PO	

PO: per os (orally)

Annex 4. Management of bacterial vaginosis in women living with HIV/AIDS

Bacterial vaginosis (BV) is a clinical syndrome resulting from replacement of the normal hydrogen peroxide-producing *Lactobacillus sp.* in the vagina by high concentrations of anaerobic bacteria, such as *Gardnerella vaginalis* or *Mycoplasma hominis*. Additional studies are needed to confirm the relationship between altered vaginal microflora and the acquisition of HIV.

- Treatment of sexual partners has not been demonstrated to be beneficial.
- It is recommended that predisposing factors, such as the use of antiseptic/antibiotic vaginal preparations or vaginal douching, be reduced or eliminated.
- The recommended regimen for BV is metronidazole 400 mg or 500 mg PO BID for seven days. Patients taking metronidazole should be cautioned not to consume alcohol while they are taking the drug or within 24 hours of taking the last dose.
- Alternative regimens:
 - metronidazole 2 g PO as a single dose
 - clindamycin 2% vaginal cream 5 g intravaginally at bedtime for seven days
 - metronidazole 0.75% gel 5 g intravaginally BID for five days
 - clindamycin 300 mg PO BID for seven days (93).

Annex 5. Cervical cancer screening methods

1. The classic screening test for cervical cancer is the Pap smear. A single Pap test may have a false negative rate of 10–25% (90). Accuracy is significantly improved with regular periodic screening. Controlled studies have not demonstrated a decrease in Pap test sensitivity or specificity in HIV-positive women. To use Pap tests as a screening method, basic infrastructure to perform cervical cytology screening should be available at all health care levels. The Bethesda system of classification is recommended for both HIV-positive and HIV-negative patients (95). (See Annex 6 below.)
2. Alternative methods include visual inspection of the cervix (VIA) after application of 3–4% acetic acid, to differentiate normal cervical appearance from cervical lesions. This test is not recommended in settings where Pap smear is available.
3. Newer cervical screening techniques using liquid-based cytology increase sensitivity, albeit at greater cost, and offer the possibility of direct HPV DNA testing. The utility of this test in women living with HIV/AIDS has not been assessed.
4. HPV testing using a high-risk HPV DNA test allows for the detection of oncogenic/non-oncogenic types and is recommended in case of borderline Pap results (ASC-US or ASC-H).

Annex 6. PAP smear report, in accordance with the 2001 Bethesda system

The Bethesda system of Pap smear classification is recommended for both HIV-negative and HIV-positive women (95).

TABLE 14. PAP SMEAR REPORT (IN ACCORDANCE WITH THE 2001 BETHESDA SYSTEM)	
Specimen adequacy	Satisfactory for evaluation Unsatisfactory for evaluation
General categorization	Negative for intraepithelial lesion or malignancy Epithelial cell abnormality Other
Interpretation	Negative for intraepithelial lesion or malignancy Epithelial cell abnormalities <i>Squamous cell</i> Atypical squamous cells of undetermined significance (ASC-US) Low-grade squamous intraepithelial lesion (LSIL), including HPV changes and mild dysplasia/CIN 1 High-grade squamous intraepithelial lesions (HSIL), including moderate and severe dysplasia, CIN 2, CIN 3, carcinoma in situ Squamous cell carcinoma <i>Glandular cell</i> Glandular cell abnormalities

Source: Solomon et al., 2002 (95).

Annex 7. Recommended management for abnormal Pap smears

TABLE 15. RECOMMENDED MANAGEMENT FOR ABNORMAL PAP SMEARS	
Pap smear result	Management (based on histology)
Unsatisfactory for evaluation	Repeat smear, correct the reason for unsatisfactory evaluation.
LSIL or ASC-US	Repeat smear in six months to one year: <ul style="list-style-type: none"> • if normal, continue with screening schedule as per national policy • if LSIL, ASC-US or HSIL, refer for colposcopy.
HSIL or ASC-H	Refer for colposcopy.
Invasive carcinoma	Refer to hospital for further investigation and management.

Source: WHO, in press (90).

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