HIV/AIDS Prevention and Care Newsletter

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This was formerly known as the Antiretroviral Newsletter. The aim of this biannual newsletter is to provide health workers in the Region with a brief, up-to-date summary of the latest developments in HIV prevention and in the management of HIV infection, including antiretroviral therapies and co-morbidities (or associated conditions).

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PART A UPDATE ON PREVENTION OF HIV TRANSMISSION

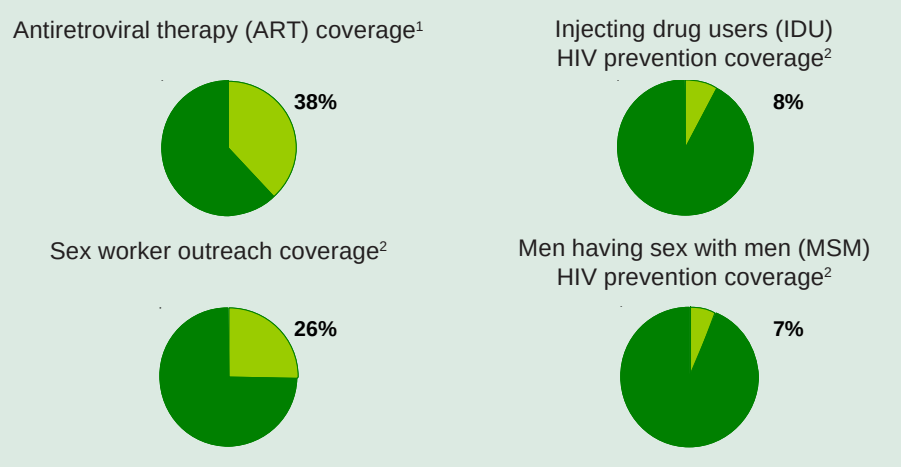
Provider-initiated Testing and Counselling (PITC)

Traditional Voluntary Counselling and Testing (VCT) is client initiated. This means the process is started by the client, who decides for whatever reason to take an HIV test. Coverage of client-initiated HIV testing and counselling service is inadequate in both high-income and resource-constrained settings.[1] It is estimated that worldwide only 12%–25% of people living with HIV/AIDS (PLHA) know their status.[2] Approximately 72% of those who require antiretroviral therapy (ART) are not receiving it because they do not know that they are HIV positive.[3] Coverage of all interventions for HIV prevention is low and the number of new infections remains high.[4] Increased access to HIV testing and counselling is essential to promote earlier diagnosis of HIV infection and earlier treatment before HIV-related illnesses occur and to allow PLHA to receive information to prevent HIV transmission to others.

The strategy of Provider-initiated Testing and Counselling (PITC) in health care facilities aims to increase the number of people accessing testing and counselling services and the benefits of knowing their HIV status. PITC is initiated by health care providers for people attending health care facilities as part of a standard programme of medical services. Attendance at any health facility offers a unique opportunity to integrate discussions of HIV and HIV testing into routine medical care. For example, the PITC approach could be used in settings where pregnant women receive services for the prevention of mother-to-child transmission (PMTCT), and in tuberculosis and sexually transmitted infection clinics. The recently published *Guidance on Provider-initiated HIV Testing and Counselling in Health Facilities* (WHO/UNAIDS May 2007)[5] recommends this approach be extended to all health facilities with consideration to the type of epidemic, local knowledge and understanding, and the availability of resources, including qualified staff and infrastructure.

In September 2006, the United States Centers for Disease Control also issued revised recommendations for HIV serologic screening in the United States of America.[1] It is now recommended to offer HIV serologic screening as a routine component of medical evaluations.

Figure 1. Access to HIV prevention and care in countries in the Western Pacific



[1] WHO Western Pacific Regional Office, [2] Coverage Survey Report 2005

Box 1. Simplified pre-test counselling in the PITC model

When recommending HIV testing and counselling to a client, the health care provider should provide the client with the following information:

- risks for transmission
- how HIV can be prevented
- benefits and consequences of an HIV test
- testing process
- meaning of the test results in understandable language
- where to obtain other services
- test result is confidential
- client has the right to decline the test
- declining an HIV test will not affect the client's access to services that do not depend on knowledge of HIV status
- if the HIV test is positive, the client will be encouraged to disclose this to other persons who may be at risk of exposure to HIV
- an opportunity to ask questions

The culture of "HIV exceptionalism", driven in the past by stigma and lack of effective treatment, is no longer applicable.[1] While stigma remains a real issue in many societies, the availability of life-prolonging treatment argues in favour of people knowing their status. There are three important caveats: HIV test results should be confidential; antiretroviral therapy should be available; and people should be able to opt out of testing. In an "opt-out" approach, clients, after receiving simplified counselling (Box 1) initiated by the health provider, must specifically decline the HIV test if they do not want it to be performed.[5] The HIV test will be performed unless the client refuses it. This approach may not be suitable for all situations where disclosure and discrimination may cause harm to the client.

PITC must not coerce clients to be tested and does not mean compulsory testing. Providers need to be trained to counsel clients not only in the significant benefits of testing but also other possible transmitted infections. Such individuals may have HIV and may benefit from knowing their HIV-positive status in order to receive specific preventive and/or therapy services. Depending on the HIV prevalence in the country or in the outcomes, including disclosure of HIV status, stigma and discrimination, and the availability of social support. Clients must be assured that their results will be kept confidential.[6]

An "opt-in" approach, traditionally part of client-initiated VCT, where clients specifically give consent to be tested rather than specifically refusing a test, may merit consideration for highly vulnerable populations.[5]

PITC has two main objectives:

1. To confirm the HIV status of patients with suspected HIV-related symptoms

   This enables clinical decisions to be made and medical services to be offered that would not be possible

Table 1. PITC recommendations based on HIV prevalence

Definition	Description	Recommendations
All epidemic settings	Low-level, concentrated and generalized HIV epidemic	PITC is recommended for all adults, adolescents and children who present to health facilities with signs and symptoms suggestive of underlying HIV infection, including tuberculosis, and to children born to HIV-positive mothers.
Low-level HIV	HIV prevalence has not consistently exceeded 5% in any defined sub-population. Recorded infection is largely confined to clients with higher-risk behaviour (sex workers, drug injectors and men who have sex with men [MSM]).	Priority should be to ensure that HIV testing and counselling is recommended to all clients with signs and symptoms suggestive of underlying HIV infections. Decisions about whether and how to implement PITC in low-level and concentrated epidemics should be guided by an assessment of the epidemiological and social context of the local situation. Based on that assessment, consideration may be given to the implementation of PITC on STI services, health services for most-at-risk populations, testing services and antenatal, childbirth and postpartum services.
Concentrated HIV epidemic	HIV prevalence is consistently over 5% in at least one defined sub-population but is below 1% in pregnant women in urban areas. HIV has spread rapidly in a defined sub-population, but is not well established in the general population.	
Generalized HIV epidemic	HIV prevalence is consistently over 1% in pregnant women. HIV is firmly established in the general population.	All adults and adolescents attending any health facility. All children born to HIV-positive mothers.

without knowledge of the person's HIV status. If clients present to health facilities with symptoms or signs of illness that could be attributable to HIV, it is the responsibility of health care providers to recommend HIV testing as part of the patient's routine clinical management.

2. To enable people with HIV who have no symptoms to know their HIV status

   Health care providers may recommend HIV testing to clients in some settings even if they do not have obvious HIV-related symptoms or signs. This includes recommending HIV testing to all pregnant women, patients diagnosed or suspected of having tuberculosis and those presenting with sexually transmitted infections. Such individuals may have HIV and may benefit from knowing their HIV-positive status in order to receive specific preventive and/or therapeutic services. Depending on the HIV prevalence in the country or in the community served by the health facility, HIV testing and counselling may be recommended by the health care provider as part of a package of services provided to all clients during all clinical interactions in the health facility.[5]

Implementation of PITC, which requires country-level adaptation, should be undertaken in consultation with all stakeholders, including civil society and self-support groups, be backed by epidemiological data and information, and should consider the risks and benefits to the client and the adequacy of social and legal protections available.

Biomedical Approaches to Preventing HIV Transmission

A wide range of promising new HIV prevention approaches are being tested in clinical trials, including male circumcision, cervical barriers, pre-exposure prophylaxis with antiretroviral drugs, herpes suppression, microbicides and HIV vaccines.[7]

2.1 Male circumcision

Countries with higher rates of male circumcision have lower rates of HIV infection.[8] A meta-analysis of 15 observational studies showed that an uncircumcised man is approximately 2.5 times more likely to become infected with HIV than a circumcised man. The biological basis for this is that the foreskin increases risk of HIV infection due to the high density of HIV target cells (Langerhans cells) and lack of keratinization (it is mucous membrane and not skin) of the inner mucosal surface.[9] Circumcision may reduce HIV risk directly, or by preventing other sexually transmitted diseases, such as syphilis, that facilitate HIV acquisition and transmission.

In 2005, the first randomized efficacy trial of male circumcision for HIV prevention, conducted in a community near Johannesburg, South Africa, showed that of the 3274 circumcised men enrolled in the study, 60% were less likely to become infected with HIV from their female partners than uncircumcised men.[10]

Two further trials were stopped early on the recommendation of the Data and Safety Monitoring Board because men in the circumcised group were significantly less likely to contract HIV compared to the uncircumcised group.

In a randomized controlled trial of 2784 men in Kisumu, Kenya, men were assigned to an intervention group (circumcision, 1391 men) or a control group (delayed circumcision, 1393 men). The trial was stopped early on 12 December 2006, by the Data and Safety Monitoring Board because the protective effect of circumcision was found to be 60%.[11] Adverse events occurred in 84 (3.6%) circumcisions; all were resolved with treatment. Behavioural disinhibition was not observed in the circumcised group.[12]

In the Rakai district of Uganda, 4996 uncircumcised, HIV-negative men aged 15–49 years who agreed to HIV testing and counselling were enrolled in this randomized trial. Men were randomly assigned to receive immediate circumcision (2474 men) or circumcision delayed for 24 months (2522 men). HIV testing, physical examination and interviews were repeated in follow-up visits at six, 12 and 24 months. As in the other trials, the protective effect of circumcision was 60%.[13]

Data from the South Africa study showed that male circumcision at the 60% efficacy level could prevent up to 220 000 cases and 8200 deaths in the country within a year and that male circumcision can significantly reduce the HIV burden in a community.[14]

Further modelling predicts that widespread implementation of male circumcision could avert 2 million HIV infections over the next decade in sub-Saharan Africa.[15]

Does male circumcision protect female partners from HIV acquisition?

Data were analysed from 4417 Ugandan and Zimbabwean women participating in a prospective study to assess whether male circumcision of the primary sex partner is associated with women's risk of HIV. At baseline, 74% reported uncircumcised primary partners, 22% had circumcised partners, and 4% had partners of unknown circumcision status. During 23 months of follow-up, 210 women acquired HIV (167, 34 and nine women whose primary partners were uncircumcised, circumcised or of unknown circumcision status, respectively). While circumcision of the male partner appeared to be protective, the effect was lost after adjustment for other risk factors, such as women who had multiple partners or were sex workers. The authors conclude that the potential protection offered by male circumcision for women recruited from high-risk settings warrants further investigation.[16]

Acceptability of circumcision

Thirteen studies of the acceptability of circumcision have been conducted in nine sub-Saharan countries, showing that approximately 65% of men are willing to be circumcised, a decision supported by 69% of female partners.[17] These numbers represent a high acceptance of this intervention.

Table 2. Current HIV prevention trials of antiretroviral drugs and microbicides				
HIV-negative volunteers				
Study drugs	Location	Number of participants	Start date	Projected completion
Tenofovir (TDF) + emtricitabine (FTC) or placebo	Botswana	1200	March 2007	
TDF + FTC or placebo	Ecuador, Peru	1400 men	In Development (two separate studies)	
TDF + FTC or placebo		1400 MSM		
TDF or placebo	Bangkok, Thailand	1600 IDUs	June 2005	June 2007
1% TDF gel or placebo gel	South Africa	980 women	May 2007	April 2010
Pharmacokinetics and Placental transfer of TDF 1% vaginal gel applied vaginally two hours prior to expected time of planned caesarean	United States of America	16 healthy pregnant women	Not started yet	
Prevention of mother-to-child transmission				
TDF + FTC or placebo	Cambodia Côte d'Ivoire, South Africa	30 mother infant pairs as PMTCT intervention	October 2006	July 2008
Single dose of TDF or TDF + FTC at the time of labour to HIV-infected pregnant women and to their newborn infants	United States of America	22	Currently recruiting subjects	
Single dose of TDF or TDF + FTC at the time of labour to HIV-infected pregnant women and to their newborn infants	Brazil Malawi	160		
Microbicides				
BufferGel PRO or 2000/5 vaginal gel	Malawi South Africa Tanzania United States of America Zambia Zimbabwe	3220 women	Currently recruiting subjects	
PRO 2000/5 Gel 0.5% PRO 2000/5 Gel 2%	South Africa Tanzania Uganda Zambia	9673 women	October 2005	March 2009
TDF topical gel women	India United States of America	200 women	-	Early 2008
TDF vaginal gel oral TDF, oral TDF/FTC or oral placebo in different combinations	Malawi South Africa Uganda Zambia Zimbabwe	4200 women	In Development	
Oral and vaginal gel preparations of TDF	South Africa Uganda United States of America	120 women		
VivaGel™	United States of America	40 women	Currently recruiting subjects	
Normosol-R Nonoxynol-9 rectally administered	United States of America	10 MSM		

Sources: www/clinicaltrials.gov and Microbicide Trials Network www.mtnstopshiv.org

Additionally, 71% of men and 81% of women would like their sons to be circumcised.

Safety of circumcision

The safety of male circumcision was studied by comparing circumcision-related adverse events in both HIV-infected and uninfected men in the Ugandan studies.[18] The investigators analysed results from two randomized clinical trials, one of which enrolled HIV-negative men who were willing to know their HIV status, whereas the other enrolled men who were either HIV-positive or declined to know their status. All 2326 HIV-negative men and 420 HIV-positive men were circumcised.

The rate of surgery-related adverse events was 6.0% in the HIV-positive men versus 7.7% among the HIV-negative men (no significant

difference). Infections were the most common adverse events: The rates of grade two infections were 1.9% in HIV-positive men versus 2.3% in HIV-negative men.

Joint statement

In December 2006, the World Health Organization (WHO), the United Nations Population Fund (UNFPA), the United Nations Children's Fund (UNICEF), the World Bank and the United Nations Joint Programme on HIV/AIDS (UNAIDS) Secretariat issued the following joint statement on circumcision:

> *"Although the results* [of clinical trials] *demonstrate that male circumcision reduces the risk of men becoming infected with HIV, the United Nations Agencies emphasize that it does not provide complete protection against HIV infection. Circumcised men can still become infected with the virus and, if HIV-positive, can infect their sexual partners. Male circumcision should never replace other known effective prevention methods and should always be considered as part of a comprehensive prevention package, which includes correct and consistent use of male or female condoms, reduction in the number of sexual partners, delaying the onset of sexual relations, and HIV testing and counselling."*[19]

2.2 Microbicides

Microbicides are topical substances, such as gels or creams, that are applied to the vagina or rectum to reduce HIV transmission. The success of circumcision trials has been matched by the failure of microbicide trials.

Two randomized clinical trials of cellulose sulfate microbicides were stopped prematurely by the Data and Safety Monitoring Board. These were presented at the International AIDS Society meeting in Sydney, Australia, in July 2007. The first trial was stopped because the rate of HIV transmission was higher in the women using the microbicide compared to the placebo (23 versus 11 HIV infections, representing a doubling of HIV transmission rate in the microbicide users). The second trial was stopped by the Data and Safety Monitoring Board because the first trial was stopped. An interim data analysis of this trial at the time it was stopped showed no difference between the microbicide and placebo groups.

This is the second time microbicides have failed in clinical trials. Studies of nonoxynol, a spermicide which also nonspecifically blocks HIV-1 infection, were not successful.[20, 21]

Other studies are evaluating topical antiretroviral agents. These agents include tenofovir and dapivirine.[22] The major concern regarding the use of antiretroviral agents as microbicides is the emergence of drug resistance, especially if the woman does not know that she is HIV-infected since systemic absorption of the antiretroviral would be the equivalent of monotherapy.

Other second- and third-generation microbicides that are under investigation in large efficacy trials[23] include vaginal acidifying agents that maintain a protective vaginal pH, such as BufferGel, and detergents or surfactants that inactivate viral particles, such as Savvy vaginal gel, probiotics such as lactin V capsules, and polyanions such as VivaGel.

2.3 Pre-exposure prophylaxis (PrEP) with antiretrovirals

Antiretrovirals have been used extensively for HIV post-exposure prophylaxis (occupational and non-occupational exposure) and for the prevention of mother-to-child transmission of HIV. Research in animals suggests that antiretrovirals may also be effective at preventing infection in HIV-uninfected adults. This is termed pre-exposure prophylaxis, or PrEP. Efficacy trials of this approach are under way in Botswana, Peru and Thailand.

The antiretroviral that has received the most attention for its potential as a PrEP drug is tenofovir. However, the use of tenofovir in PrEP clinical trials has been controversial. In August 2004, a clinical trial of tenofovir to prevent HIV infection in sex workers was stopped because of concerns that the trial's provisions for post-study care were inadequate and that prevention counselling was limited.

In the first published randomized clinical trial, conducted between June 2004 and March 2006 in Tema in Ghana, Douala in Cameroon, and Ibadan in Nigeria, researchers enrolled 936 HIV-negative women at high-risk of HIV infection to receive tenofovir 300 mg once daily or a placebo. There were eight HIV seroconversions, two in the tenofovir group and six in the placebo group. The researchers concluded that tenofovir was safe but the effectiveness in reducing HIV acquisition could not be conclusively evaluated because of the small number of HIV infections observed during the study. Currently, 12 further trials of tenofovir oral tablets or vaginal and rectal gels are ongoing.

2.4 Occupational and non-occupational exposure prophylaxis

The following is not intended to be a complete guide to post-exposure prophylaxis (PEP). It summarizes current best practices. Comprehensive guidelines are presented in *Management of HIV infection and antiretroviral therapy in adults and adolescents: A clinical Manual,* which was published by the WHO Regional Office for South-East Asia. PEP should be provided within 72 hours following exposure of non-intact skin (through percutaneous sharps injury or other exposure) or mucous membranes (through sexual exposure or splashes to the eyes, nose or mouth) to a potentially infected body fluid from an HIV-positive or unknown HIV status source. Body fluids which may transmit HIV include blood, genital secretions, and cerebrospinal, amniotic, peritoneal or pleural fluids. While PEP will be less effective or ineffective if delayed for more than 72 hours, it may be considered in circumstances where a significant potential exposure has occurred.

Occupational post-exposure prophylaxis

Since PEP is not 100% effective, health facilities should implement and strengthen workplace safety training especially universal precautions:

- training of all employees in handling and disposal of infectious material;
- provision of guidelines for prevention and control of infections;
- provision of equipment necessary for prevention and control of infections, such as educational materials, disposable gloves,

disposable syringes and needles, and sharps bins; and

- monitoring mechanism to ensure implementation.

Components of occupational PEP

- treatment of exposure site;
- assessment of risk;
- discussion of PEP and understanding of the benefits and side effects of antiretrovirals;
- voluntary counselling and testing;
- providing antiretrovirals, if indicated; and
- follow-up and documentation.

Counselling

- pretest counselling;
- test the health care worker for HIV, hepatitis B and hepatitis C (baseline tests);
- counsel the health care worker that they must not give blood and must practice safe sex and safe injecting practices until the outcome is known;
- provide post-test counselling and give baseline results;
- offer hepatitis B vaccination if HBsAg negative; and
- provide counselling on further HIV transmission including condom use, avoiding breastfeeding and not donating blood until the person is tested HIV negative three months after the exposure.

Antiretrovirals for post-exposure prophylaxis

There is no evidence that three drugs are superior to two drugs in the setting of PEP:[24]

- two drug regimen (for all potential exposures); and
- three or more drug regimen (for potential exposures where source is known or suspected to have ART resistance).

Antiretroviral therapy should be started as soon as possible and at the latest within 72 hours of the exposure. People presenting after 72 hours of exposure could also be considered for post-exposure prophylaxis. ARV should be continued for one month.

The drugs used in PEP should be aligned with the formulary adopted in the country. Zidovudine (AZT), lamivudine (3TC) and boosted protease inhibitor (PIs) are the most common ARV drugs used in these situations. Alternative non-nucleoside reverse transcpritase inhibitor (NNRTIs) that can be considered are stavudine (d4T) and didanosine (ddI). Nucleoside reverse transcriptase inhibitor (NRTIs) nevirapine (NVP) and efavirenz (EFV) should not be used for PEP. Nevirapine is not recommended for PEP due to the risk of severe reactions reported in these situations. Efavirenz should be avoided due to central nervous system side effects and should not be given to pregnant women or women of childbearing potential.

2.5 Non-occupation post exposure

Initiating non-occupation post exposure

Th same schedule is recommended as for occupational PEP; commence ARV as soon as possible after the exposure, within 72 hours, and continue for 28 days. There are no data to support the effectiveness of PEP started after 72 hours.

HIV status of the source

When the HIV status of the source is unknown, determine whether the source is available for HIV testing. If the risk associated with the exposure is considered substantial, nPEP can be started pending determination of the HIV status of the source and then stopped if the source is determined to be non-infected.

When the source is known to be from a group with a high prevalence of HIV infection (e.g. a homosexual or bisexual man, an injecting drug user or a sex worker), the risk of transmission is increased. In the case of sexual violence, the source person may not be identifiable. Where the HIV status of the source is unknown and cannot be determined, nPEP should be offered following risk evaluation and counselling of the exposed person by a trained health care worker.

If the source person is known to be HIV-positive, nPEP is indicated and a two-drug regimen should be given unless there is evidence that the source person has a current or past history of ARV use with poor adherence, or is known to have failed first-line ART. A three-drug PEP regimen is recommended in this case.

Non-occupation post exposure Counselling

The process of counselling is similar to PEP. There are two additional considerations: possible exposure to other sexually transmitted infections and emergency contraception. Additional blood tests should be taken for syphilis (Venereal Disease Research Laboratory [VDRL] and Treponema Pallidum Haemagglutination Test [TPHA]) and swabs taken for chlamydia and gonorrhoea, if possible.

Emergency contraceptive pills can be used for up to five days after unprotected sexual intercourse. Several regimens are available, using levonorgestrel or combined oral contraceptive pills.

Box 2. Guidelines for providing non-occupation post exposure (nPEP)

Situations where nPEP may be provided	Situations where nPEP should not be provided
▪ unprotected sexual exposure including rape ▪ needle sharing by injecting drug users ▪ injuries from needles discarded in public places ▪ human bite injuries	▪ persistent potential exposure to HIV such as discordant sex partners who rarely use condoms ▪ repeated unprotected sex with sex workers or other non-regular partners ▪ injecting drug users who often share injection equipment ▪ persons who engage in frequent, recurrent risk exposure behaviour should be counselled and provided with appropriate risk-reduction interventions

Table 3. Summary of recommendations for occupational and non-occupational post-exposure prophylaxis	
Starting PEP	As soon as possible after exposure and within one hour if possible; Not more the 72 hours after exposure if possible; Consider PEP > 72 hours after a high-risk exposure.
Duration of PEP	28 days
Which regimen to choose	Two nucleoside reverse transcriptase inhibitor (NRTIs) which are the same as the recommended NRTI backbone in the standard first-line WHO antiretroviral therapy in the country.
Preferred two-drug regimens	Zidovudine (AZT) 250 mg or 300 mg twice per day or stavudine (d4T) 30/40 mg twice per day + lamivudine (3TC) 150 mg twice per day.
Alternative two-drug regimens	Tenofovir (TDF) 300 mg once daily + (3TC 300 mg once daily or emtricitabine (FTC) 200 mg once daily). These ARVs can all be given once daily.
Three-drug regimens	Some countries have already implemented the three-drug PEP regimens. There are no prospective data regarding the relative efficacy of two or three drugs. In most cases where the source is unlikely to have ART-resistance, two drugs are likely to be sufficiently potent to prevent HIV transmission with only incremental increase in potency with the addition of a third drug. In cases where the source is known or suspected to have ART resistance, two NRTIs plus a protease inhibitor (PI) can be considered.
Preferred three-drug regimens	Two NRTIs as listed above + ritonavir (RTV) boosted PI chosen according to availability or indinavir (IDV) 800 mg thrice per day if RTV is not available.
Non-nucleoside reverse transcpritase (NNRTIs) in PEP	If a third drug is used, an NNRTI should not be used. Nevirapine is contraindicated for PEP due to risk of toxicities and the potential for development of resistance. Efavirenz should not be used in women who are pregnant or are of child-bearing age.
PEP in pregnant women	PEP should be provided if indicated. Pregnant women should not receive efavirenz, tenofovir or the combination of stavudine (d4T) + didanosine (ddI). The preferred PI in pregnancy is saquinavir/r.

2.6 Herpes suppression

Herpes simplex virus (HSV) infection is a recognized risk factor for both HIV acquisition and transmission.[25] However, results of clinical trials aimed at supressing HSV-2 as a means of reducing HIV trasmission have been mixed. In a case contol study conducted by the United States Army and Air Force, 30.3% of HIV-positive individuals were HSV-2 positive compared to 9.7% of HIV-negative controls. This is consistent with results from a 22-study meta-analysis of African studies and other Western studies.

A randomized, double-blind, placebo-controlled study enrolled 821 female sex workers in Mwanza, Tanzania, who were initially HIV-negative but HSV-2 seropositive. Four hundred women were randomized to acyclovir 400 mg twice daily and 421 women were randomized to placebo. After 30 months of follow-up, the incidence of HIV was equal in both arms. The study was hampered by high rates of drop out and poor adherence to acyclovir.[26]

Results of the HIV Prevention Trials Network (HPTN) 039 trial and several other ongoing trials will be needed to truly determine if suppressing HSV-2 reduces the incidence of HIV acquisition.[27]

PART B REVIEW OF NEW DRUGS AND CLASSES

Integrase inhibitors

The viral enzyme integrase plays an essential role in the viral life cycle. Integrase inhibitors function by blocking the integrase enzyme, which plays a key role in the incorporation of viral DNA into the host genome. Integrase inhibitors work by inhibiting the insertion of HIV DNA into human DNA by the integrase enzyme. On 12 October 2007, the United States Food and Drug Administration (FDA) granted accelerated approval to the first drug in the new class of integrase inhibitors.

Raltegravir (Isentress™) is approved for use in combination with other antiretroviral agents for the treatment of HIV-1 infection in treatment-experienced adult patients who have evidence of viral replication and HIV-1 strains resistant to multiple antiretroviral agents.

Raltegravir is administered as a single 400 mg tablet taken twice daily without regard to food and does not require boosting with ritonavir.

Common reported adverse experiences are diarrhoea (16.6%), nausea (9.9%), headache (9.7%) and fever (4.9%). Elevation of creatine kinase, myopathy and rhabdomyolysis have been reported. Raltegravir should be used with caution in patients at increased risk of myopathy or rhabdomyolysis, such as patients receiving concomitant medication known to cause these conditions.

No dose adjustment of raltegravir is required when co-administered with other antiretroviral agents. Rifampicin should be administered with caution due to reduced plasma concentrations of raltegravir.

Raltegravir is currently available worldwide to qualified patients through an expanded access clinical research programme. Information about the programme can be found at **www.benchmrk.com**

Elvitegravir is the second integrase inhibitor and it is currently in phase II of clinical development.

Chemokine receptor 5 inhibitors

Entry inhibitors block access of HIV into the host cell. Enfuvirtide (T20), a fusion inhibitor, was approved for use in 2003. Chemokine receptor 5 inhibitors (CCR5) antagonists disrupt crucial interactions between the virus and host cell surface, preventing virus binding and entry. A CCR5 antagonist, maraviroc was approved by the FDA in August 2007 and another, vicriviroc, is in advanced clinical development.

New non-nucleoside inhibitor

Etravirine (formerly known as TMC125) is an investigational second-generation NNRTI designed to retain activity against many viruses that are resistant to first-generation NNRTIs, such as efavirenz and nevirapine. While 13 NNRTI mutations have been identified which reduce susceptibility to etravirine, the K103N, which causes high-level resistance to both efavirenz and nevirapine, was not associated with reduced response to etravirine.

Darunavir, (formerly known as TMC114) was approved by the FDA on 23 June 2006, for use in combination with other antiretroviral agents for the treatment of HIV infection in antiretroviral-treatment experienced adults, such as those infected with HIV-1 strains resistant to more than one protease inhibitor. Darunavir is a second-generation PI that is highly active in vitro against both wild-type and PI-resistant HIV. The recommended daily dose of darunavir is 600 mg (two 300 mg tablets) taken with ritonavir 100 mg twice daily with food. Darunavir is classified by the FDA as pregnancy category B. There are no adequate and well-controlled studies conducted on pregnant women. The most common treatment-emergent adverse events reported with the use of darunavir were diarrhoea, nausea, headache and nasopharyngitis. Abnormal liver and pancreatic function tests, abnormally high cholesterol and triglyceride levels, and decreases in white blood cell counts have also been reported.

Kaletra (lopinavir/ritonavir) is now available as a heat-stable, film-coated tablet (also called Meltrex or Alluvia in some countries) that provides advantages over the currently marketed capsule formulation. Specifically, the tablet formulation does not require refrigeration and can be administered without regard to meals and has a decreased pill burden compared to the capsule formulation; two tablets [200 mg/50 mg] tablets replace three capsules [133.3 mg/33.3 mg]. Four tablets once daily are given in treatment-naive patients only.

Clinton Foundation HIV/AIDS Initiative

The objectives of the Clinton Foundation HIV/AIDS Initiative (CHAI) are:*

- To lower the costs of HIV drugs and diagnostics through negotiations with pharmaceutical companies.
- To partner with governments to implement large-scale treatment and prevention programmes. Currently, CHAI is working with 25 countries.
- To expand access to treatment in rural areas.
- To make treatment universally accessible to all children.

*Source: http://www.clintonfoundation.org/pdf/chai-faq-053007.pdf

Sixty-six countries have access to CHAI prices for ARV drugs and diagnostics, representing 90% of all AIDS cases in the developing world. Current ARV price list and suppliers are available at http://www.clintonfoundation.org/pdf/chai-arv-price-list-050807.pdf

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HIV/AIDS Prevention and Care Newsletter

Moving Towards Universal Access

World Health Organization
Western Pacific Region

This was formerly known as the Antiretroviral Newsletter. The aim of this biannual newsletter is to provide health workers in the Region with a brief, up-to-date summary of the latest developments in HIV prevention and in the management of HIV infection, including antiretroviral therapies and co-morbidities (or associated conditions).

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REVIEW ARTICLE: Second-line antiretroviral drugs: use, availability and cost with a focus on Western Pacific countries

The need for second line

In 2007, the World Health Organization (WHO) and the Joint United Nations Programme on HIV/AIDS (UNAIDS), in collaboration with Mexico's National Institute of Public Health and The Clinton Foundation HIV/AIDS Initiative (CHAI), published *Demand Forecast for Antiretroviral Drugs in Low- and Middle-Income Countries, 2007–2008*. With limited data to guide forecasting, the probability that people would need second-line antiretroviral therapy (ART) was estimated at 4% per year for Latin American countries and 2% per year for other developing countries.

Recent data from several large cohorts in Asia and Africa suggest that the need for second-line ART is closer to 1% per year. In 62 Medecins Sans Frontieres (MSF) programmes, rates and timing of first-line failure have been reported.[1] Among 48 338 adults, 370 (0.8%) switched to a second-line regimen after a median of 20 months (switch rate 4.8/1000 person-years).[1] According to data collected from centres in the TREAT Asia HIV Observational Database (TAHOD) (Figure 1), less than 3% of 1246 patients commencing stavudine (d4T)+ lamivudine (3TC) + nevirapine (NVP) changed to a protease inhibitor (PI)-containing regimen over two years of follow-up.[2]

Figure 1. Centres in the TREAT Asia HIV Observational Database (TAHOD)

In Cambodia, five out of 362 patients (1.4%) switched to second-line ART over 24 months of follow-up.[3]

In a cohort study from India, treatment failure, as defined by WHO immunological criteria, was reported in 3.9% of patients over 33 months of follow-up.[4] Projected to 2010, the mid-range estimate is that 17% of patients in this cohort will be on second-line ART (Figure 2).

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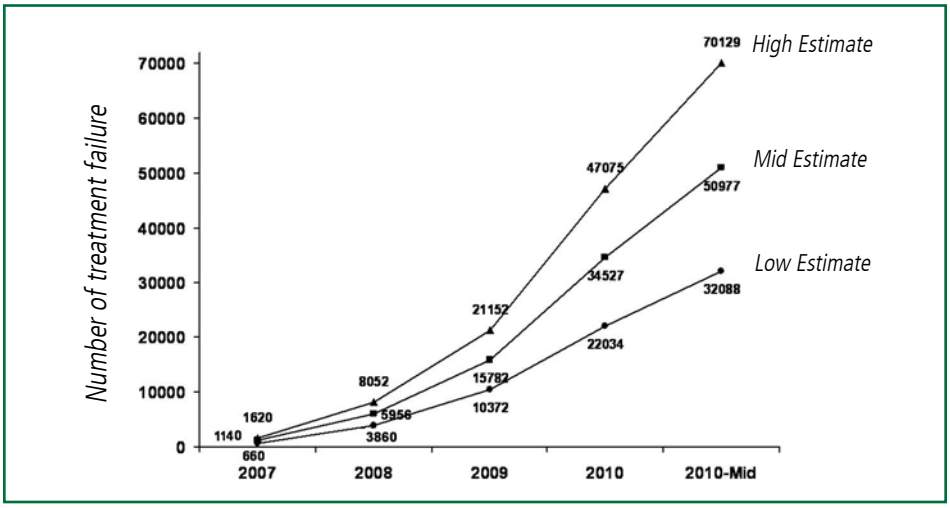
In a large African cohort in Botswana, 13 879 treatment-naive patients received zidovudine (AZT) + 3TC + efavirenz or nevirapine as first-line regimen and didanosine (ddI), d4T, and nelfinavir or lopinavir/ritonavir (LPV/r) as second-line therapy. Failure was defined as two consecutive viral load measurements >400 copies/ml. There were 209 failures (5.3%) over six years of follow-up.[5]

In resource-limited settings, WHO recommends clinical and immunological criteria be used in defining failure. If viral load is available, the appropriate threshold for switching regimens in resource-limited settings remains to be determined. Some evidence suggests that 5000 to 10 000 copies/ml may be an appropriate threshold.[6]

The drugs

WHO recommends that second-line ART should consist of a ritonavir-boosted protease inhibitor (PI/r) plus two nucleoside reverse transcriptase inhibitors (NRTIs), at least one of which is new and not used in the first-line regimen (Figure 3).[6] The preferred nucleoside/nucleotide drugs are abacavir (ABC), didanosine (ddI), lamivudine (3TC) and tenofovir (TDF). Lopinavir/r (LPV/r) and atazanavir/r (ATV/r) are the preferred boosted PIs.[7]

Figure 2. Projected demand for second-line ART in India



Choice of nucleoside reverse transcriptase inhibitor (NRTI)

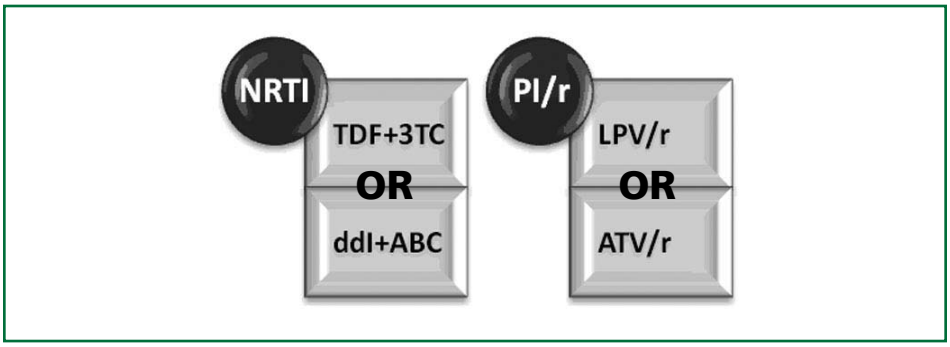
The combinations of ABC plus ddI or TDF + 3TC (or FTC) are recommended following failure of a d4T or AZT-containing regimen.[7,8,9] Didanosine levels are increased by 60% in the presence of TDF and there are reports of early virological failure in patients receiving this combination, particularly if associated with a non-nucleoside reverse transcriptase inhibitor (NNRTI) or another nucleoside. If used together with TDF, the dose of ddI should be adjusted (reduced to 250 mg/day if body weight > 60 kg and 200 mg/day if ≤ 60 kg) and the patients should be closely monitored.[10,11,12]

Tenofovir (TDF) is not recommended in pregnancy due to reports of reduced bone mineral density in children exposed to TDF *in utero*. Continuing 3TC in the presence of 3TC resistance maintains selective pressure on HIV harbouring the M184V mutation. This mutant virus is less "fit" than wild-type virus and, for this reason, many physicians keep 3TC in second-line in addition to NRTIs and PI/r.[13,14,15]

Choice of protease inhibitor (PI)

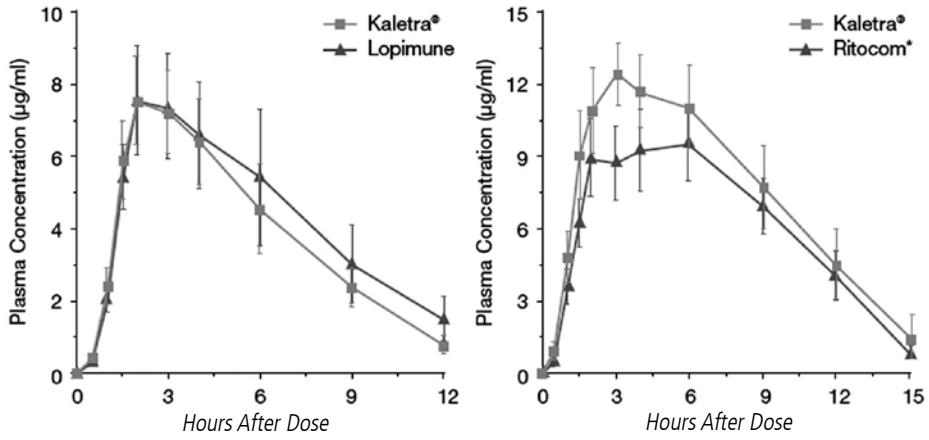
Lopinavir/ritonavir (LPV/r) has been used as the preferred PI in most national ART guidelines. It first became available as a soft gelatin capsule that required refrigeration. Recently, melt extrusion technology has been used to produce a heat stable tablet that does not require refrigeration. The LPV/r tablet (also marketed as Aluvia®) has been approved (or approval filed) in 154 developing countries. Heat-stable generic ATV/r will become available in 2008/2009 and is expected to be 50% less expensive than LPV/r because of the higher daily dose needed for LPV (800 mg) compared to ATV (300 mg).

Figure 3. WHO-recommended second-line Antiretrovirals (ARVs)



ABC = abacavir; ddI = didanosine; 3TC = lamivudine
TDF = tenofovir ; LPV/r=lopinavir/ritonavir ; ATV/r = atazanavir/ritonavir

Figure 4. Bioavailability of two generic versions of LPV/r tablet in an animal model



Source: Garren K, *et al.* 2nd Workshop on HIV Treatment, Pathogenesis and Prevention Research in Resource-Poor Settings. May 2008, Dakar, Senegal

Second-line generics

The Clinton Foundation HIV/AIDS Initiative (CHAI) Procurement Consortium, consisting of 69 countries, enables cost-saving through bulk purchasing. CHAI has agreements with seven generic Indian antiretroviral (ARV) manufacturers: Aurobindo, Cipla, Hetero, Zhejiang Huahai, Matrix, Ranbaxy and Strides. All of the WHO-recommended second-line ARVs are included in CHAI's pricing agreements.

Two generic LPV/r tablets from India show bioequivalence (BE) compared to the branded product in an animal model (Figure 4). Human bioequivalence studies have also been conducted. Results from a Thai BE study are expected in the third quarter of 2008.

In the generic market of other second-line drugs, ABC, 3TC, ddI (buffered and enteric coated formulations), saquinavir, nelfinavir and LPV/r currently are available. Many generic submissions are in the pipeline, including heat-stable ritonavir, TDF and ATV.

The cost

With current estimates, it is projected that by 2010, 60%–90% of the cost of ART will be for second-line drugs if prices are not reduced.

CHAI has made the following forecasts (Table 1). The cost of ATV

(continued on Page 4)

Table 1. The Clinton Foundation HIV/AIDS Initiative ARV price list (May 2008)

WHO-recommended drug		Ceiling price (US$/year)	Cipla	Matrix	Ranbaxy	Aurobinda	Strides
Adult Products							
Lopinavir/ritonavir tablets		513	✓			✓	
Tenofovir		149	✓				
Didanosine EC	250 mg caps	150				✓	
	400 mg caps	240				✓	
Didanosine	100 mg tabs	185*				✓	
Didanosine	200 mg tabs	181*				✓	
Abacavir		300	✓		✓	✓	
Lamivudine		36	✓	✓	✓	✓	✓
Paediatric Products							
LPV/r tablets 100 mg/25 mg		389		✓		✓	
ddI caps (125/200 mg)		67/81				✓	
ABC syrup (20 mg/ml)		225				✓	
3TC syrup (50 mg/ml)		35	✓				

*100 mg tabs = US$0.128/pill, 200 mg tabs=US$0.251/pill. Annual cost per patient is therefore similar.

Source: CHAI. Antiretroviral price list. Journal [serial on the Internet]. April 2008

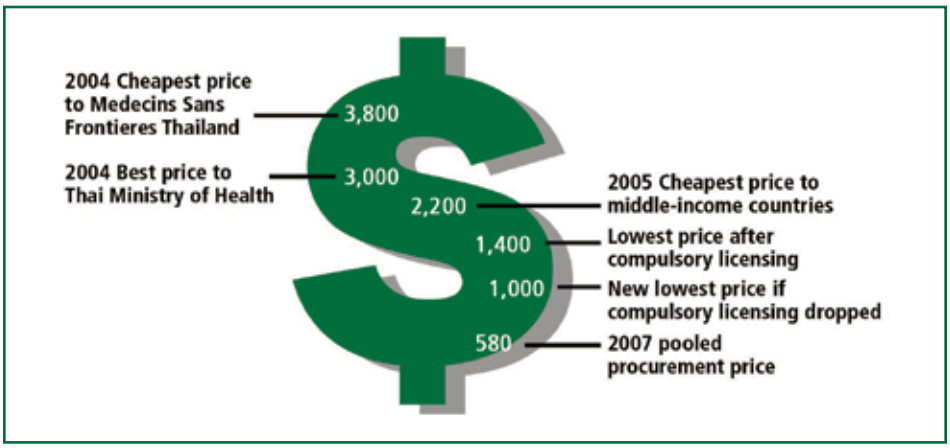
Available from: http://www.clintonfoundation.org/what-we-do/clinton-hiv-aids-initiative/information-center-resources

(continued from Page 3)

will fall and it will become available co-formulated with ritonavir. Considering these assumptions, CHAI projects that ATV will capture much of the future PI market based on the 40%–60% potential cost-saving compared to LPV/r. [16]

Further, TDF and ddI (enteric coated) prices will fall and their use in second-line treatment will increase. ABC use is projected not to change.

Figure 5. The impact of compulsory licensing in Thailand (prices in US$)



The politics

Compulsory licensing

Under the World Trade Organization (WTO) rules, countries may issue compulsory licenses for patented drugs to protect public health or increase access to any essential medicine, not just antiretrovirals.[17] In 2001, the United States Department of Health and Human Services authorized imports of generic ciprofloxacin when it was feared that terrorists would spread anthrax. In 2006, Thailand issued compulsory licenses for efavirenz (EFV), LPV/r and the antiplatelet drug, clopidogrel (Figure 5). The license permits the Thai Government's Pharmaceutical Organization to import generic versions of these drugs from India, where the drug is not patented, and to make the drugs itself. Branded EFV is still sold in Thailand and the originator receives a royalty payment. Indian generic EFV is also available through the Thai Universal Coverage health care scheme.

While LPV/r capsules are still marketed in Thailand, the new heat-stable tablet version will not be available. If Thailand wants LPV/r tablets, it must rely on a stable Indian generic supply or make its own. In May 2007, Brazil also issued its first ever compulsory license, for EFV.

India and Thailand have the largest generic drug manufacturing capacity in the region. Many Indian generics have WHO-prequalification and/or United States Food and Drug Administration (FDA) tentative approval. No Thai generics have comparable status, limiting their use outside Thailand to individual purchase for personal use and the "grey" cross-border market.

India, which did not issue patents on medicines until 2005 when it was required by the WTO, is the world's largest producer of generic drugs. However, patent applications are pending for TDF, LPV/r and ATV. If granted, generic manufacturers in India will need voluntary or compulsory licenses to continue production.

Voluntary licensing

Pharmaceutical companies may issue non-exclusive voluntary licenses to generic makers to produce patented medicines for sale in low-income countries.[17] This is the case with TDF, one of the key second-line drugs. The terms of the licenses include: production to WHO or United States FDA quality standards, agreement to purchase the active pharmaceutical ingredient (API) from approved suppliers, and 5% royalty.

In May 2008, delegates at the 61st World Health Assembly backed an initiative that aims to promote new approaches to pharmaceutical research and development (R&D). The approval of the Global Strategy on Public Health, Innovation and Intellectual Property promotes the notion that every country should contribute to global R&D, with differential obligations based on ability to pay. Products developed under this system would be issued a global patent.

Access and use in Western Pacific countries

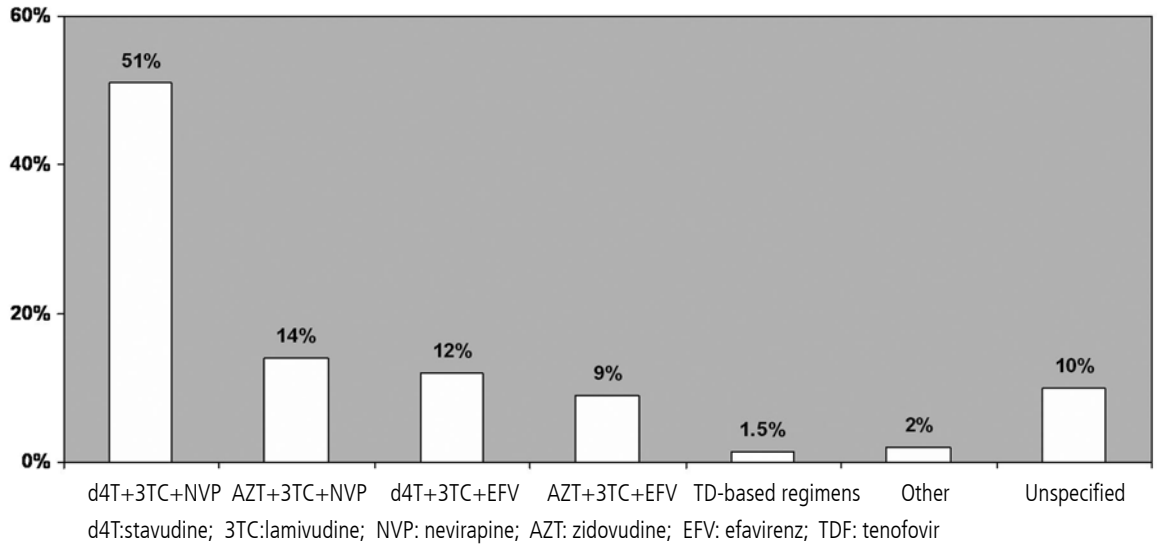
While good data are available on patterns of first-line ART use, both worldwide (Figure 6) and in Asia (Figure 7), there are fewer data on second-line use (Figure 8).

To better understand second-line ART use in the Region, an informal email survey was conducted in Western Pacific countries (June 2008). Seven countries responded (Cambodia, China, the Lao People's Democratic Republic, Mongolia, Papua New Guinea, the Philippines and Viet Nam) and all reported that the use of second-line ART was still limited.

Six out of seven countries had all WHO-recommended second-line NRTIs (ABC, ddI and TDF) available. Of the two WHO-recommended PIs, LPV/r was available in four countries and ATV was available in none. Indinavir and ritonavir were available in three countries, and saquinavir and nelfinavir in one.

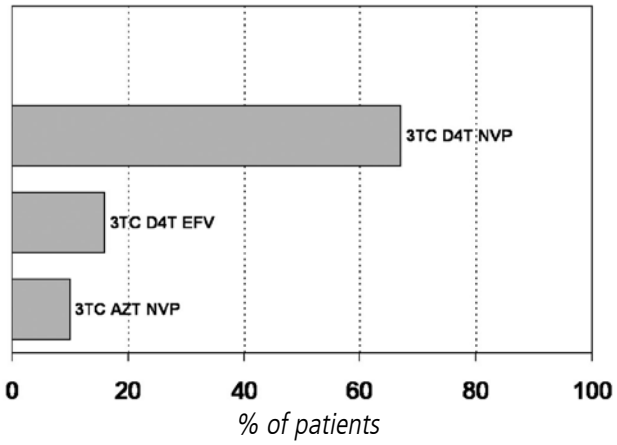
(For references, go to Page 12)

Figure 6. Use of first-line ART 2007



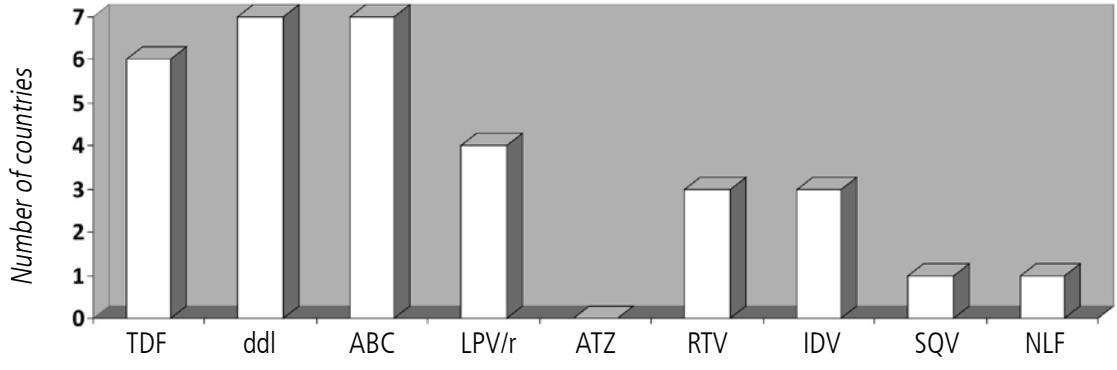
Source: WHO, UNAIDS. *Towards Universal Access: Scaling up priority HIV/AIDS interventions in the health sector*. Journal [serial on the Internet]. 2008 Date: Available from: http://www.who.int/hiv/pub/towards_universal_access_report_2008.pdf

Figure 7. Use of first-line ART in Asia



Source: Renaud-Thery F, *et al.* Use of antiretroviral therapy in resource-limited countries in 2006: distribution and uptake of first- and second-line regimens. *AIDS*, 2007, Jul; 21 Suppl 4:S89-95.

Figure 8. Access to second-line ART in Western Pacific countries (June 2008)



PROGRAMME MANAGER'S VIEWPOINT
Universal Access in a low prevalence country: opportunities and challenges for the Lao People's Democratic Republic

by Dr Chansy Phimphachanh, Director, Centre for HIV/AIDS and STI, Vientiane

The Lao People's Democratic Republic is a country of 6 million people, landlocked by China, Cambodia, Myanmar, Thailand, and Viet Nam. It ranks among the least developed countries. Since 2002, the country has experienced more than 6% economic growth per annum. There are many challenges ahead, as more than 80% of the population lives in rural and remote areas with limited access to services and the threat of unexploded ordnance (50% of the land and surface area and 15 out of 17 provinces are contaminated).

The prevalence of HIV in the general population is as low as 0.2%. It is estimated that 5500 people are living with HIV and most infections are sexually acquired. The HIV epidemic in the Lao People's Democratic Republic is driven mainly by unprotected sexual exposure between female sex workers and their clients. It is estimated that there are 8000 sex workers in the country. However, the rate of infection among female sex workers is still low (0.5% in 2008). In a cross-sectional HIV prevalence survey conducted in 2008 in Vientiane, 5.6% of 540 men having sex with men (MSM) were HIV positive. Future trends in HIV infection in the Lao People's Democratic Republic are difficult to predict as socioeconomic and behavioural factors are rapidly changing. Monitoring these changes is a priority of the national programme.

Since 2006, the National Strategy and Action Plan on HIV/AIDS (NSAP) has focused on scaling up Universal Access with a major emphasis on sex workers and their clients, MSM and sexually transmitted infections (STI). Medecins Sans Frontieres started providing antiretroviral therapy (ART) in 2003. In 2005, a second location was opened with nongovernmental organization support in Vientiane. Other ART sites in Vientiane, and in the north and south of the country, will open in 2008/2009. With Medecins Sans Frontieres phasing out in 2008, the Ministry of Health will manage all activities related to ART in the country, with the financial support of the Global Fund to Fight AIDS, Tuberculosis and Malaria and the technical assistance of partners. By the end of 2008, around 1000 patients in need of antiretroviral (ARV) treatment will receive it free and there is no waiting list. By 2012, it is expected that there will be 3500 patients on ARVs.

The Lao People's Democratic Republic is a small country with relatively fast decision-making processes; most of the technical decisions are taken at the national programme level allowing fast-track implementation of activities. The Lao People's Democratic Republic is considering to scaling up prevention activities among high-risk groups. Low levels of awareness and limited access to prevention services including condoms heighten the risk of transmission of HIV infection.

The Lao People's Democratic Republic is a low prevalence country. The priority is to keep HIV prevalence low. However, HIV may spread faster than anticipated as external factors such as development, migrations, and a market economy are constantly changing. There is a need to closely monitor this epidemic and its driving factors in order to respond quickly to new challenges. So far, the Lao People's Democratic Republic has adequately responded to these challenges, but it is necessary to sustain the response in the country based on a functional health system.

Lao People's Democratic Republic AIDS Statistics	
Estimated Total Population, July 2008	6 678 000
Estimated number of people living with HIV/AIDS, end 2007	5 500
Proportion of adults with HIV/AIDS who are women, end 2007	24%
Estimated adult prevalence of HIV/AIDS, end 2007	0.2%
Estimated number of AIDS deaths in 2007	<100

Source: *UNAIDS/WHO 2008 Report on the global AIDS epidemic*

Entertainment Establishment (EE) owners network sustains 100% Condom Use Programme for HIV/STI prevention among sex workers

A new lesson learned from the DFID/NORAD-funded Preventing HIV Project in Viet Nam

"The practice in Ha Long and other districts of Quang Ninh province demonstrates that, with increased condom use among sex workers supported by a EE owner network, there is a reduction in HIV, syphilis and other sexually transmitted infections, with no signs of an increase in sex work."

In Ha Long City in Quang Ninh province, an early pilot version of the 100% condom use programme (CUP) (2000–2002) was re-invigorated in 2004 and extended to districts in Quang Ninh and 21 provinces in total, with support from the United Kingdom Department of International Development (DFID) and the Norwegian Cooperation Development Agency (NORAD)-funded Preventing HIV Project (PHP) (2004–2008).

Sex work was prevalent in Quang Ninh, particularly in Ha Long City, the provincial capital, along with a booming tourism industry. Migrant workers seeking new job opportunities, and tourists demanding commercial sex have contributed to this situation, thus fuelling the risk of HIV sexual transmission in Ha Long. The Department of Labour, Invalids, and Social Affairs (DOLISA) estimates that there are 234 sex workers in Quang Ninh but it is believed that there could be as many as 2500 sex workers in the whole province, with 1585 sex workers in the four PHP districts according to mapping done in 2007. The number of clients for sex workers working in small guest houses is between 10-12 to 20 a day, and five per hour during peak times. HIV prevalence among sex workers peaked in 1996 at 7%.

What has been achieved in Quang Ninh so far?

- HIV among sex workers has decreased from 7% in 1996 to less than 3% in 2006, below the national average of 4.2% (National Sentinel Surveillance 2006). Rates of syphilis have decreased from 10% in 1998 to 0.6% in 2006 (2005-2006 IBBS).
- STI prevalence among sex workers has decreased from 40%–50% in 1996 to 5%–10% in 2007 (Quang Ninh Provincial AIDS Centre Report 2008).
- Reported condom use among sex workers at the last sexual encounter with male clients reached 98% in 2005 (2005-2006 IBBS) and was still 97% in 2007 (A Rapid Survey Report 2007).

Lessons learnt:

- A proactive response from the Local People's Committee and identifying open-minded advocates from the police and DOLISA were critical.
- Police support was key in creating an enabling environment for condom promotion and utilization. For example, in line with the promotion of the 100% CUP, carrying condoms was no longer considered evidence of engaging in sex work and therefore no longer persecuted.
- Education and support of sex workers for personal protection was provided by the entertainment establishment (EE) owners so that "Khong bao cao su, Khong choi" (No condom, no sex) became the norm for day-to-day business in the EEs.
- Provincial STI centres signed agreements with the EE owners, committing them to ensure regular check-ups of sex workers, to provide condoms to the EEs, and to provide on-site check-ups and educational materials.

Mobilizing EE owners to develop a peer network was key in convincing other EE owners to cooperate with implementing the 100% CUP and for providing education about safer sex. This included promoting the "no condom, no sex" principle, as well as monitoring non-compliance. This EE owner-based approach is the new lesson, which differs from traditional peer education involving only sex workers as peer educators who are usually vulnerable in front of the EE owners.

The way forward

- Revitalize the 100% CUP throughout Viet Nam to include coverage of large-size EEs and street-based sex workers and further expanding the norm of "no condom, no sex" in all sex work venues.
- Use STI clinic data to monitor non-use of condoms among male clients and identify and sanction the EE owners who fail to comply with the 100% CUP. Possible options for sanctions include verbal warning to EE owners, frequent inspection visits to identified EE, or sending a man wearing a police uniform to stand in front of the particular EE during business hours.
- Mobilize and coordinate resources for strengthening the EE owner network to sustain the implementation of CUP; ensure a sufficient supply of quality condoms and lubricants to all identified EEs; and monitor the impact through the national HIV and STI surveillance system.
- Conduct a broader and deeper evaluation of condom use programmes and their overall impact on the HIV and STI epidemic in Viet Nam .

The second global progress report Towards Universal Access: Scaling up priority HIV/AIDS interventions in the health sector

The second global progress report, *Towards Universal Access: Scaling up priority HIV/AIDS interventions in the health sector*, was released by WHO on 2 June 2008 in collaboration with UNICEF and UNAIDS.

Two main data sources were used in developing the report: (1) The WHO framework for global monitoring and reporting on the health sector's response to HIV/AIDS, and (2) the WHO/UNICEF report card on the prevention of mother-to-child transmission (PMTCT) and paediatric HIV care and treatment in low- and middle-income countries. The WHO framework contains 39 indicators designed to measure the availability, coverage and impact of high priority HIV interventions delivered by the health sector and key health system components required to support scale-up. In July 2007, this framework was introduced and validated for the Western Pacific Region through the Meeting on Strengthening of Strategic Information held in Manila. The data in the global report reflects the hard work of health ministries at the country level, who worked in collaboration with WHO and UNICEF representative offices and other implementing partners to coordinate data collection.

The global report reveals impressive achievements towards the goal of Universal Access to HIV prevention, treatment, care and support by 2010. Nearly 3 million people were receiving antiretroviral therapy in low- and middle-income countries at the end of 2007, a more than seven-fold increase over four years and finally reaching the 3 by 5 target. Approximately 33% of pregnant women with HIV received antiretrovirals to prevent mother-to-child transmission, and the availability of testing and counselling services increased in many countries. However, at the current pace of scale-up, most countries will not meet universal access targets by 2010. Only 31% of people in need of ART received it by the end of 2007. Countries continue to face a number of challenges in expanding and sustaining the response to HIV, such as weak health systems, a shortage of human resources and lack of long-term sustained financing. The annual number of new HIV infections continues to surpass the annual additional number of people who receive treatment. In 2007, about 2.5 million people were newly infected with HIV, but less than 1 million additional people received antiretroviral therapy in the same year.

In the Western Pacific Region, about 89 000 persons were receiving ART as of December 2007 out of an estimated 320 000 individuals in need of ART, resulting in an ART coverage rate of 28% (Table 2). ART coverage rates varied considerably in the Region, and only Cambodia and the Lao People's Democratic Republic achieved coverage rates above 65%. Significant progress has been made in scaling up testing and counselling services in many countries in the Region. For example, in Papua New Guinea, intensive efforts by the National Department of Health have resulted in a greater than seven-fold increase in the number of people tested for HIV in 2007, as compared to 2006. Much improvement is required for PMTCT in the Region. In 2007, only 13% of pregnant women living with HIV in the Western Pacific Region received antiretrovirals for preventing mother-to-child transmission (2100 out of the estimated 16 000 HIV-positive pregnant women needing ARVs for PMTCT).

Development of the second global progress report has exposed both successes and challenges. Data were received from many more countries than in the previous reporting period and data collection and validation were better coordinated with UNAIDS, UNICEF and other partners. However, there remains a paucity of comprehensive data in many critical areas such as prevention, testing and counselling, and access to services for most-at-risk populations. In addition, further investment and capacity are needed to ensure that the data being collected and reported by countries are being disseminated and used to further scale up and improve priority health sector interventions. The WHO Western Pacific Regional Office would like to thank countries for their hard work and efforts during this process and we look forward to continued successful collaboration and improvements in the years to come.

Table 2. Estimated numbers of people receiving and needing antiretroviral therapy and antiretrovirals for PMTCT and coverage percentages by countries in the Western Pacific Region, 2007

Western Pacific Region Countries	Estimated Number of people receiving antiretroviral therapy, December 2007	Estimated Number of people needing antiretroviral therapy based on UNAIDS/WHO methods, December 2007	Antiretroviral therapy coverage based on UNAIDS/WHO methods, December 2007	Antiretroviral therapy coverage based on country reports December 2007	Number of pregnant women living with HIV receiving antiretrovirals to prevent mother-to-child transmission, December 2007	Estimated number of pregnant women living with HIV needing antiretrovirals to prevent mother-to-child transmission, based on UNAIDS/WHO methods December 2007	Estimated number of pregnant women living with HIV receiving antiretrovirals to prevent mother-to-child transmission, 2007
Cambodia	27 000 (25 000–28 000)	40 000 (34 000–47 000)	67% (57%–80%)	83% £	505	1600 (1200–2000)	25%–41%
China	35 000 (33 000–37 000)	190 000 (120 000–290 000)	19% (12%–29%)	41%	593	6800 (4300–11 000)	6%–14%
Fiji	<100	<200			7	<100	82%–95%
Lao People's Democratic Republic	700 (500–900)	690 (<200–1200)	>95% (59%–>95%)		24	<200 (<100–<500)	9%–36%
Malaysia	6800 (6100–7400)	20 000 (14 000–28 000)	35% (24%–49%)		183	1300 (770–2200)	9%–24%
Mongolia	<100	<100		12%	0	<100	0%
Papua New Guinea	2300 (2100–2400)	5900 (5000–6800)	38% (33%–45%)	35%	84	1900 (1800–2100)	4% (3%–5%)
Philippines	<500	1100 (740–1500)	31% (22%–45%)	56%	1	<200 (<200–<500)	<1%
Viet Nam	17 000 (16 000–18 000)	67 000 (41 100–110 000)	26% (17%–42%)	35%	744*	3900 (2400–6400)	12%–31%
Western Pacific Region	89 000 (84 000–94 000)	320 000 (240 000–440 000)	28% (20%–37%)		2100	16 000 (12 000–21 000)	13% (10%–18%)

Source: Towards Universal Access: Scaling up priority HIV/AIDS interventions in the health sector, Progress Report 2008

* time period: Oct 06-Sep 07, £: coverage estimate for adults only

Report of the Commission on AIDS in Asia *Redefining AIDS in Asia:* relevance to the WHO HIV/AIDS Programme in the Western Pacific Region

The complexities of the AIDS epidemic in Asia and challenges in responses led to the creation of the independent Commission on AIDS in Asia in June 2006, which was assigned, during an 18-month period, to conduct an analysis of the developmental consequences of the epidemic in the region, its medium- to long-term implications on the socioeconomic environment, and to recommend strategies for a stronger response to HIV/AIDS.

The Commission, led by the Economic Advisory Council to the First Minister of India, included a member of the Chinese Center for Disease Control, a member of a Japanese Cooperation Center, parliamentarians, academics, researchers, activists, international organizations, and the UNAIDS Regional Director. Several papers were reviewed, studies were commissioned with involvement of more than 30 specialists and members of community-based organizations and civil society were surveyed. The commission received inputs from a number of subregional workshops and country missions as well as testimonies from representatives of government and civil society.

The report notes that, despite the progress in the region to confront the epidemic of HIV/AIDS, there is still a long way to go towards universal access. Further, enabling policies and legislation can be crucial steps to implementing interventions that can really make the difference. Stigma and discrimination are still barriers that need to be overcome, especially among most-at-risk populations such as people who inject drugs, men who have sex with men (MSM) and sex workers and their clients.

Report calls for a focus on most-at-risk populations (MARPs)

A great achievement of the report was the first attempt to emphasize responses to HIV/AIDS epidemics in the Asian context. The report indicated the common important characteristics of HIV epidemics in Asia—unprotected paid sex, sharing of contaminated needles and syringes, and unprotected sex among men who have sex with men. It mentioned that "currently, HIV epidemics in Asia are highly unlikely to sustain themselves in the 'general population' independently of commercial sex, drug injecting, and sex among men. And, most critically, it means that prevention efforts that drastically reduce HIV transmission among and between those most-at-risk populations will bring the epidemics under control."

For the past 10 years, the WHO Regional Office for the Western Pacific has been supporting Member States to implement targeted interventions, focusing on populations with most-at-risk behaviours. One such intervention is the 100% condom use programme, which was initiated in Sihanoukville province in Cambodia in October 1998, following the success of the strategy in Thailand. Cambodia is the only country in the Western Pacific Region that has clearly shown reduction of HIV prevalence among its general population as a result of coordinated prevention efforts including the 100% condom use programme among sex workers and their clients. In 2003, the WHO Regional Office for the Western Pacific first issued a statement on the need of preventing HIV/AIDS among and from people who inject drugs and developed a workplan to support harm reduction strategies. More attention was paid to countries such as China, Malaysia and Viet Nam, where HIV prevalence had been highest in injecting drug users. WHO proposed evidence-based and cost-effective strategies including the implementation of needle and syringe programmes; methadone substitution therapy; and treatment, care and support for people who inject drugs, with special attention on scaling up antiretroviral therapy (ART) for this segment of the population.

Dialogue and collaboration between public health and law enforcement sectors are crucial to the success of harm reduction interventions.

The WHO Western Pacific Regional Office is facilitating this synergy throughout the Region with special emphasis on Cambodia, the Lao People's Democratic Republic and Viet Nam through the implementation of related activities supported by funds provided by Swedish International Development Cooperation Agency (SIDA) Sweden, in view of the growing evidence that MSM may play a more important role in HIV transmission.

MSM are gaining increasing attention in the region. UNESCO, UNDP and national governments are prioritizing MSM as a target group for prevention, and WHO has been requested to provide technical support in the context of the health sector's response to the epidemic. A global consultation was organized in September 2008 in Geneva to steer health sector responses worldwide.

While the report was very supportive of ongoing programmes, it highlighted the need to ensure stronger leadership and political commitment with priority given to prevention in most-at-risk

populations. Governments are called to scale up programmes to a large enough level to face the epidemic and to involve all sectors including civil societies.

The report stated that "in addition to prevention programmes, ART is the most effective way to reduce the impact of the epidemic." It recommended that governments must assume responsibility for ensuring that free antiretroviral therapy is available and accessible to all who need it and that antiretroviral treatment programmes should be integrated into the general health care systems of countries.

The WHO Western Pacific Regional Office is providing technical assistance to countries to increase access to ART. A comprehensive treatment programme with a public health approach is being promoted, in line with one of the recommendations of the AIDS commission. However, as highlighted in the second global progress report, Towards Universal Access: Scaling up priority HIV/AIDS interventions in the health sector, ART coverage in the Western Pacific Region stands at 28% and standing current trends, it is unlikely that many countries could reach the universal access goal by 2010.

The report also recommended strengthening HIV/AIDS strategic information, in particular epidemiological and behavioural information systems. In addition to HIV prevalence data (as used for current UNAIDS/WHO classification of epidemics), it suggests that a better understanding of the epidemic will come from data on the behaviours that drive transmission and the evolution of epidemics.

The report used the "Asian Epidemic Model" with behavioural data from a number of countries to propose four epidemic scenarios: latent, expanding, mature, and declining epidemics. The report categorizes a latent epidemic as a very low prevalence in which early and effective action on prevention will avert a large-scale epidemic. An expanding epidemic is one where HIV prevalence is still relatively low but growing and without immediate and effective prevention, the epidemic is likely to grow to significant levels. A mature epidemic is one in which HIV prevalence has been rising for several years and HIV is spreading in the general population, requiring a broader prevention action. Finally, a declining epidemic is one that is under control but can be resurgent if there is a lack of effective prevention strategies, particularly in the most hidden populations.

As public health surveillance is the core function of national governments, the Western Pacific Regional Office continues to support more than 15 countries in the development of second-generation HIV surveillance including behavioural components.

As observed by the Commission, "HIV surveillance is often institutionally and geographically fragmented". In the region, while HIV surveillance has been continuously improved, there needs to be a further strengthening of data collection systems, with a focus on behavioural information from most-at-risk populations.

The AIDS Commission report is another important resource for HIV control in Asia. Recommendations are aligned with WHO ongoing activities and are supportive of future WHO assistance to Western Pacific countries.

The report, launched and extensively publicized in June 2008, was presented at WHO Western Pacific Regional Office in a "brown bag seminar" as part of a very intensive debate among colleagues based in Manila. The report is open for comments and suggestions at: http://health.groups.yahoo.com/group/AIDS_ASIA/.

2nd Asia-Pacific Regional Meeting on Universal Access to HIV Prevention, Treatment, Care and Support in Low Prevalence Countries

In October 2006, the 1st Regional Consultative Meeting on Universal Access to Prevention, Treatment, Care and Support in Low Prevalence Countries was organized in Ulaanbaatar, Mongolia. Sixty-two representatives from governments, civil society and international organizations came from 10 countries: Bangladesh, Bhutan, the Democratic People's Republic of Korea, Fiji, the Lao People's Democratic Republic, Malaysia, Maldives, Mongolia, the Philippines and Sri Lanka. Various United Nations and multilateral agencies were also present as resource persons and observers. The meeting made the following advocacy statements and recommendations under the banner "A Call for Action":

- There is a need for focused prevention efforts for people most at risk, including sex workers and their clients, injecting drug users, men who have sex with men and migrants and mobile populations, the majority of whom are young.
- Greater efforts are needed to raise general awareness about HIV/AIDS to help reduce AIDS-related stigma and discrimination.
- A priority for an effective response to the epidemic is improving surveillance systems, to gain better understanding of factors driving the epidemic and target interventions to those most at risk.
- Governments and international donors are urged to increase support for national HIV prevention programmes.

(Continued on Page 12)

(continued from Page 11)

The 2nd Regional Consultative Meeting on Universal Access to Prevention, Treatment, Care and Support in Low Prevalence Countries was hosted by the Philippine Government on 26-28 August 2008, in Manila. The objectives of the meeting were to:

- review progress of countries and identify steps to address gaps in the operationalization of the Ulaanbaatar 2006 Call for Action;
- identify emerging issues in scaling up comprehensive national AIDS responses towards Universal Access in line with the recommendations of the Commission on AIDS in Asia*, and measures to implement them; [18] and
- reaffirm political commitment among governments, civil society and international agencies by adopting concrete ways forward towards universal access to prevention, treatment, care and support.

The meeting consisted of 10 plenary sessions and six break-out sessions focusing on six thematic areas. These themes were based on the following obstacles identified during the first meeting:

- access to commodities and low-cost technology;
- human rights, stigma and discrimination;
- human resource and system constraints;
- sustainable financing;
- civil society participation; and
- delivering quality interventions and reaching coverage.

Participants shared challenges in implementation and lessons learnt and then identified achievable solutions to overcome these obstacles and challenges to adequately face the HIV/AIDS epidemic in low prevalence countries.

Dr Shigeru Omi, WHO Regional Director for the Western Pacific, officially welcomed the delegates on behalf of the United Nations family. Other colleagues from the WHO Regional Office, together with colleagues from other United Nations agencies, also participated in this meeting in different capacities (speakers, facilitators, organizing committee members).

*See *Report of the Commission on AIDS in Asia Redefining AIDS in Asia:* relevance to the WHO HIV/AIDS Programme in the Western Pacific Region in this newsletter.

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