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Concept Note on Treatment as Prevention (TasP) as a Strategy for Elimination of New HIV Infections in Cambodia

December 2012

National Center for HIV/AIDS Dermatology and STD
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Preface

Antiretroviral therapy as HIV prevention is an important component of the strategy for elimination of new HIV infections among sero-discordant couples. This approach complements the strategy for continuum of HIV/AIDS prevention to care and treatment to achieve the goal of elimination of new HIV infections in Cambodia by 2020.

The Ministry of Health through the National Centre for HIV/AIDS, Dermatology and STD and development partners has developed the Concept Note on Treatment as Prevention (TasP) as a Strategy for Elimination of New HIV Infections in Cambodia to guide efficient stepwise implementation of this approach.

The Ministry of Health is confident that all concerned stakeholders participating in the implementation of the approach will consider all steps in this concept paper in developing detailed practical implementation plan that suits the local needs.
Acknowledgments

The National Center for HIV/AIDS, Dermatology and STD would like to express its appreciation and great gratitude to the Core Group of the Steering Committee for the Continuum of Care for People Living with HIV that made all necessary efforts in developing the Concept Note on Treatment as Prevention as a Strategy for Elimination of New HIV Infections in Cambodia.

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Phnom Penh, 24 December 2012

[Signature]
Director
National Center for HIV/AIDS,
Dermatology and STD
CONCEPT NOTE ON TREATMENT AS PREVENTION (TASP) AS A STRATEGY FOR ELIMINATION OF NEW HIV INFECTIONS IN CAMBODIA

1 Introduction

In the mid-1990s Cambodia faced one of the fastest growing HIV rates in Asia and the Pacific, but in just a little over a decade became one of the few countries to reverse the spread of the epidemic. In 2010, Cambodia received a millennium development goal (MDG) award from the United Nations as a global recognition of the country’s efforts to cut HIV prevalence from an estimated 1.75% (among adults aged 15-49) in 1998 to a projected 0.7% in 2012 (2011 HIV Estimation and Projection). The country has also achieved the universal access target for treatment, with over 80% of adults and children in need (CD4 ≤ 350 cells/mm$^3$) receiving antiretroviral therapy (ART).1

In June 2011, Cambodia expressed its support to the “Three Zeros” UN goals and targets including intensifying efforts to eliminate new HIV infections. In line with the Three Zeros and current global control efforts (e.g. Treatment 2.0), the National Center for HIV/AIDS, Dermatology and STD (NCHADS) of the Ministry of Health (MOH) is working in close partnership with Cambodian referral hospitals and NGO clinics, local and international NGOs, the UN and donor governments to eliminate new HIV infections using a range of strategies. In keeping with the Three Zeros goals, Cambodia is launching the Cambodia 3.0 initiative which includes the boosted Linked Response for elimination of mother to child transmission (eMTCT) of HIV and congenital syphilis, the boosted Continuum of Prevention to Care and Treatment (CoPCT) and treatment as prevention (TasP).

The effectiveness of early initiation of antiretroviral therapy (ART)2 in preventing sexual transmission of HIV among sero-discordant couples was demonstrated in the HPTN 052, a randomized controlled clinical trial of 1,763 sero-discordant couples that was conducted in nine countries.3 The study illustrated that ART given to HIV-infected patients with a CD4 count of between 350 and 550 cells/mm$^3$ decreased HIV transmission by 96% to the uninfected partner. Furthermore, the HPTN 052 study demonstrates a 41% reduced risk of HIV-related clinical events, extra-pulmonary tuberculosis in particular, among patients that were initiated on ART with CD4 count between 350 and 550.4 The findings of this important clinical trial corroborate findings from more than ten years of observational and basic science studies showing the impact of ART to prevent HIV transmission through control of viral replication.5,6 Following the dissemination of this breakthrough evidence, WHO recently released new guidance on ART as

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2 “Early initiation” was defined in this study as immediate enrolment on therapy for HIV-1 infected patients with CD4 count between 350 and 500/mm$^3$.


4 Grinsztejn, B et al. Effects of early versus delayed initiation of antiretroviral therapy (ART) on HIV clinical outcomes: results from the HPTN 052 randomized controlled clinical trial (Late breaker abstract). IAS 2012.


prevention on couples HIV testing and ARV therapy for treatment and prevention in sero-discordant couples.\textsuperscript{7}

WHO is consolidating its ARV treatment Guidelines that will cover all aspects of HIV treatment including treatment as prevention with special considerations on ART among MARPS and pregnant women. The Guidelines are expected to be released in 2013.\textsuperscript{8}

In regards to eMTCT, WHO issued a recent programmatic update on the use of ARVs for Prevention of Mother to Child Transmission (PMTCT) of HIV which includes an Option B+, in addition to the existing Options A and B. Option B+ comprises a triple ARV regimen which is not discontinued after delivery (like in Option B) but maintained for the rest of the woman’s life regardless of CD4 count level.\textsuperscript{9} The advantages of Option B+ include greater simplification of ARV regimens and service delivery for PMTCT, protection from MTCT in future pregnancies, prevention of transmission to sero-discordant partners and eliminating the challenge of starting and stopping ARV regimens, potentially multiple times in case of multiple pregnancies.

In keeping with the programmatic and guidelines updates provided by WHO in April 2012, the Ministry of Health, through NCHADS and development partners, is considering early initiation of ART as prevention in Cambodia. This concept note describes the priority program strategies necessary to implement TasP.

2 Rationale

According to the national HIV prevalence estimations and projections analyses conducted in 2011 by NCHADS and its development partners,\textsuperscript{10} projected HIV incidence is rapidly decreasing from its peak with 20,978 new HIV infections in 1995, down to 1,780 in 2010 and expected as low as 1,007 in 2015. The 2011 HIV estimation and projection exercise conducted by NCHADS indicated around 1,350 new transmissions in 2012 with 37% occurring between wife and husband and 30% during sex work. Another 10% of infections are attributable to vertical transmission from HIV-infected mothers to their infant (MTCT). While the number of infections attributable to MTCT is comparatively low, HIV-infected pregnant women are a strategic target population for TasP in Cambodia in view of the initiative to eliminate MTCT of HIV.

PLHIV with highest risk behaviors are more likely to spread the virus and less likely to be on ART. Findings from the 2010 BSS indicate that PLHIV are still sexually active and may not always use a condom with their partner. The study found that 47.1% of female PLHIV in care, but not on ART, and 46.2% of male PLHIV, reported having sex with a sweetheart in the previous six months. Of those, 87.5%

\textsuperscript{7} WHO. Guidance on HIV Testing and Antiretroviral Treatment and Prevention in Sero-discordant Couples. April, 2012.

\textsuperscript{8} WHO. Programmatic Update: Use of Antiretroviral Drugs for Treating Pregnant Women and Preventing HIV Infection in Infants. April 2012.

\textsuperscript{9} WHO. Programmatic Update: Use of Antiretroviral Drugs for Treating Pregnant Women and Preventing HIV Infection in Infants. April 2012.

reported condom use with their sweetheart the last time they had sex.\textsuperscript{11} Among Pre-ART men who reported having sex with a sex worker, only 52.4\% reported using a condom the last time they had sex with a sex worker. Focusing efforts to initiate ART among HIV positive populations at higher risk may have a greater impact on reducing new HIV infections at the population level, by mitigating the most common modes of transmission.

Since 1995 HIV testing and counseling center has been expanded in the form of Voluntary Confidential Counseling Testing (VCCT). In 2011, there were 255 VCCT sites spread out over the country’s 24 provinces and cities. Of these VCCT sites 226 are supported directly by the government, 29 by NGOs. In 2006, Cambodia launched Health Provider-Initiated Testing and Counseling (HPITC) targeting TB, STI, ANC clinic attendees, HIV exposed infants and patients in infectious disease wards. Community and Peer Initiated Testing and Counseling (C/PITC) targeting MARPs populations were launched in 2011 to address the low uptake of HIV testing services among EWS, MSM and transgenders (TG). Peer networks educate and mobilize their members to improve the demand for HIV testing and counseling and to attend meetings at the Drop in Centers (DIC). DICs are used as MARP-friendly venues for outreach HTC provision by health center staff.

Cambodia has already achieved exceptionally high coverage of ART among eligible PLHIV. Based on HIV prevalence estimations conducted in 2011, there were an estimated 53,166 adults (with a CD4 count of <350 cells/mm\textsuperscript{3}) in need of ART in Cambodia at the start of 2012. By 30 June 2012 the national program had achieved more than 80\% coverage, providing ART for 43,285 adults living with HIV.\textsuperscript{12} As of the end of June 2012, there were 7,081 PLHIV actively followed in pre-ART care with 1,276 patients being newly enrolled during Q2 2012.\textsuperscript{13} In parallel with ARV treatment scale up, the median CD4 count at ART initiation has increased from an average of 119 cells/mm\textsuperscript{3} in 2006 to around 200 cells/mm\textsuperscript{3} in 2011. This median CD4 count at ART initiation is on a par with the median CD4 levels found in upper middle income countries, and above those found in most low and lower-middle income countries.\textsuperscript{14}

In addition, Cambodia has achieved a successful scale up of PMTCT services through the Linked Response approach with HIV-infected Pregnant Women (PW) being targeted to receive a triple ARV regimen from week 14 of pregnancy. In 2011, 856 women received a triple ARV regimen, 747 of them had a CD4 less than 350 cells/mm\textsuperscript{3} \textsuperscript{15} and 107 women for triple ARV prophylaxis. The Linked Response, which ties HIV services to antenatal care services, contributed to increased coverage of HIV testing among pregnant women and coverage of HIV positive pregnant women receiving ARV for PMTCT, from 21\% in 2008 to 63\% in 2011.

In view of the declining incidence of HIV, high treatment coverage and other contextual factors, Cambodia is deemed ready to implement ART as prevention for those who have higher level of CD4, focusing in phase 1 on sero-discordant couples and HIV-infected pregnant women, and then in a phase 2 addressing TasP among MARPS in accordance with forthcoming WHO recommendations.

\textsuperscript{11} NCHADS. Behavioural Sentinel Surveillance, 2010.
\textsuperscript{12} NCHADS. Facility ART Report, Quarter 2 2012, 8 August 2012.
\textsuperscript{13} NCHADS. Facility Pre-ART Report, Quarter 2 2012, 8 August 2012.
\textsuperscript{15} NCHADS, NMCHC. Linked Response and PMTCT Report, 2011.
3 Goals and Objectives

3.1 The goal of TasP in Cambodia is to reduce sexual HIV transmission within discordant partnerships, including MARPs and their sexual partners, and to reduce vertical transmission by HIV-infected pregnant women to their infants.

3.2 Specific programmatic objectives include:

3.2.1 To increase HIV case detection by increasing HIV testing among MARPS and their partners, partners of PLHIV who are on Pre-ART and partners of HIV infected pregnant women, and identify sero-discordant couples [as is outlined in the SOPs for both Standard Operating Procedure for Implementation of the Boosted Linked Response between HIV, SRH and TB Services for Elimination of New Pediatric HIV Infections and Congenital Syphilis in Cambodia and the Boosted Continuum of Prevention to Care and Treatment (COPCT)];
3.2.2 To provide early/immediate ART to HIV-infected individuals within identified sero-discordant couples, including MARPS and their sexual partners, PLHIV in Pre-ART and their partners;
3.2.3 To identify all HIV-infected pregnant women and enroll them on ART according to new PMTCT recommendations (option B+);
3.2.4 To improve retention in care and adherence for all those initiated on ART using innovative active follow-up mechanisms;
3.2.5 To enhance ART patient monitoring to capture TasP outcomes and related adverse effects.

4 Strategic Framework

To achieve the goal of elimination of new HIV infections will require accelerating HIV case detection among MARPs, pregnant women, and partners of PLHIV and ensuring that they are enrolled early in care and treatment. NCHADS must also consider several clinical, ethical and programmatic aspects of TasP that must inform strategy development and implementation. These include patient well-being considerations including the use of optimal and less toxic treatment regimens, the importance of equitable treatment of PLHIV, incremental costs associated with this strategy and supply chain management challenges.

As TasP is implemented, it is critical that the quality of the whole continuum of care is optimum to achieve appropriate impact on the community. Continuous technical assistance at CoC sites to ensure quality of care will be part of the implementation of the recent SOPs through strengthened mentoring activities to support clinicians and other health care providers in charge of following adult and children living with HIV. Integrated with the Boosted-Linked Response and the Boosted-CoPCT, particular attention will be paid to improve the quality of services and reduce patient loss at the key steps along the HIV care cascade in order to achieve sustained reductions in viral load (see figure 1).
Cambodia will build on its prior successful strategies to increase access to care and treatment and PMTCT services when implementing TasP. Program strategies along the HIV Care Cascade will include the following:

### 4.1 Accelerated HIV case detection

- **HIV testing and counseling (HTC) services** have been provided through Voluntary Confidential Counseling and Testing (VCCT), health provider initiated testing and counseling (HPITC) especially for TB cases, pregnant women and children born to HIV positive mothers, and community/peer initiated testing and counseling (CPITC) targeting MARPs.
- To further accelerate uptake of HTC, active HIV case finding will be explored targeting partners of MARPs, HIV positive pregnant women and PLHIV who are on pre-ART and ART, as described in the Cambodia 3.0 conceptual framework.
- Moreover, HPITC will be expanded to health facilities serving population with high HIV prevalence such as health posts in prisons and methadone maintenance therapy (MMT) sites.
- CPITC will also be expanded in hot spots where MARPs are concentrated.
- HIV-infected pregnant women will be encouraged to bring their husbands and partners for HIV testing with support from community based prevention, care and support networks.

### 4.2 Increased identification of sero-discordant couples

A number of sero-discordant couples are already enrolled in Community Based Prevention, Care and Support (CBPCS), and are accessing the necessary services. However, many sero-discordant
couples, including EW, hidden MSM and TG, and their partners and other, have not yet been identified. Active case detection and Partner Tracing Strategies under the Boosted CoPCT SOP must be implemented to increase identification of HIV-infected individuals and to encourage partners to come for HIV testing. Such an approach includes:

- Identification of sero-discordant couples among PLHIV through CBPCS network, among MARPS through CPITC approach in accordance with the Boosted CoPCT, Boosted LR and HTC SOPs.
- Individuals who have already been diagnosed and enrolled in pre-ART should be encouraged to recruit their partners for HIV testing. Negative partners should return for Couples HIV Testing and Counseling (CHTC) and HIV test every three months.
- Couples and partners should be offered HIV testing and counseling on a voluntary basis with support for mutual disclosure.
- Refresher trainings of HIV testing counselors to strengthen partner disclosure counseling will be conducted using the recently finalized Comprehensive Counseling Curriculum, which contains a module on positive prevention and partner disclosure counseling.

4.3 Strengthen referral of PLHIV and their partners from HTC to Pre-ART/ART services to reduce delays and ensure enrollment

- Active referral will be conducted by peers from PLHIV community networks.
- Other approaches to active referral will also be tested.
- Reinforced monitoring systems will be developed to follow newly diagnosed PLHIV and partner from HTC services to Pre-ART/ART service.

4.4 Ensure early/immediate ART initiation of identified PLHIV engaged in discordant couples

- HIV-positive partners with CD4 cells $>$350 / mm$^3$ and $<$500/ mm$^3$ in sero-discordant couples should be offered ART to reduce HIV transmission to uninfected partners.
- Pre-ART/ART clinicians will be trained for TasP in discordant couples and revised ART guideline.
- First line regimen for TasP will be available at pilot sites according to the present concept note.

4.5 Strengthen the retention of PLHIV in care and strengthen positive prevention

- Peer case management approach integrated with HBC and PLHIV networks will be implemented to reduce loss to follow-up in pre-ART as well as ART.
- Reinforced monitoring system to follow-up newly enrolled PLHIV and partner at Pre-ART/ART service will be developed.
- The quality of Pre-ART/ART counseling will be reinforced through refresher trainings using the Comprehensive Counseling Curriculum finalized in 2012.
- Condom use by discordant couples will be strongly encouraged and condoms will be made available on sites.
- Positive prevention among sero-discordant couples will be strengthened in accordance with the SOP in positive prevention.
4.6 Implementing PMTCT Option B+ to HIV+ pregnant women to achieve eMTCT of HIV as well as proper syphilis treatment of pregnant women to achieve eMTCT of Syphilis

- The newly designed Boosted-Linked Response approach in 2012 is planned to increase the coverage of HIV testing among pregnant women and PMTCT.
- PMTCT counseling will be reinforced at ANC and delivery services using Comprehensive Counseling Curriculum.
- Clinicians at pre-ART/ART sites will be trained on the PMTCT option B+ to optimize its implementation.
- Under the boosted-LR, pregnant women tested will also be tested for syphilis.
- Availability of syphilis treatment will be strengthened at FHC and STI services of referral hospitals and NGO clinics to ensure proper treatment of all positive pregnant women.

4.7 Enhancing ART adherence in the context of TasP

- Refresher trainings for Drug counselors and peers will be conducted using the Comprehensive Counseling Curriculum’s module on treatment adherence counseling.
- Case management approach by peer will be used to identify and support adherence among PLHIV and will be used for active linkages of PLHIV to PLHIV networks as well as additional psychosocial services supporting reductions in risk behaviors for MARPs (community support, PLHIV network, prevention programs) or improving the economic livelihoods of PLHIV.
- Viral load test at 6 months will be used to detect early poor adherence and then according to the routine monitoring described in the revised ARV guideline for adults and adolescents to detect treatment failures.
- Early detection and management of ARV adverse effects will be strengthened according to the current ART guideline and the present concept note (see below under TasP ARV regimen).
- Positive Prevention messages will be provided to PLHIV according to the positive prevention SOP to reinforce adherence and improve choices and quality of life.

4.8 Optimization of drug regimens and management of treatment failure

TasP requires that patients take potentially toxic, lifelong drug regimens to prevent transmission to their partner. To reduce the risk of harm to the patient from early initiation of ART, the proposed first line regimen will be TDF/3TC/EFV, which is known to be well tolerated and is the first line regimen recommended by WHO.

- All patients initiated on ART under the TasP strategy (CD4 count between 350 and 500 cells/mm$^3$) will start an ARV regimen with: TDF/3TC/EFV.
- The limited biological monitoring approach as described in the current ART guideline for detection of adverse effects will be applied to all patients initiated on TasP.
• Since updated data suggest that there is no increased risk of birth defects associated with EFV if used during the first trimester in pregnancy, the recommended ARV regimen for HIV-infected pregnant women under the PMTCT Option B+ will also be TDF/3TC/EFV.  

Comparative costing analyses have been conducted to explore the budget implications of the updated strategy (Annex 2). The national forecasting working group (FWG) will be tasked with revising the assumptions behind the semi-annual drug forecast. Given the current low number of new infections each year and the current number of serodiscordant couples and HIV-infected pregnant women accessing services every year, resources can be best mobilized to support the implementation of TaSP using an optimal regimen.

This guidance is expected to be incorporated into the 2013 revision of Cambodia’s national guidelines on the use of ARVs for prevention, care and treatment.

4.9 Strategy on Boosted CoPCT for MARPS (to support Phase 2 implementation)

• “Active case detection” as described in section 4.1 above includes counseling for partner involvement, tracing of sexual contacts, innovative social network methods, in addition to the current MARPS peer network approach.

• For MARPS and partners, key approaches and operations will be defined in the SOP on Boosted COPCT among MARPs.

• For the phase 2 of the implementation of TaSP, according to forthcoming WHO recommendations, appropriate strategies will be developed by the TaSP TWG to efficiently link HIV+ MARPs to pre-ART/ART services in order to provide strengthened HIV and drug counseling, positive prevention including risk reduction and early/immediate ART initiation as TaSP.

• Appropriate coverage of given MARPs populations will have to be reached to reduce HIV transmission at the community level.

• Specific methods will be developed to monitor the impact of TaSP within given MARPs populations and the reduction of HIV transmission.

5 Implementation Road Map

Treatment as Prevention (TaSP), as a Strategy for Elimination of New HIV Infections in Cambodia, will be implemented according to the following roadmap starting in Quarter 3, 2013. The implementation phases planned are as below:

5.1 Finalization of key documents and approval by the MoH:


17 Regimen guidance in Annex 2 includes context for the TDF/3TC/EFV regimen choice and the product selection based on availability, cost and convenience of dual and triple Fixed Dose Combinations for the selected regimen.
• Conceptual Framework for Elimination of New HIV infections in Cambodia by 2020: as part of the Health Sector Response towards “Three Zeros” (“Cambodia 3.0”): December 2012
• SOP on HIV Testing and Counseling in Cambodia: September 2012
• Concept Note on Treatment as Prevention (TasP) as a Strategy for Elimination of New HIV Infections in Cambodia: December 2012
• Standard Operating Procedures (SOP) for Implementation of the Boosted Linked Response between HIV, SRH and TB Services for Elimination of New Pediatric HIV Infections and Congenital Syphilis in Cambodia: December 2012
• SOP on Boosted Continuum of Prevention to Care and Treatment among MARPS: January 2013.
• SOP on Continuous Quality Improvement (CQI) for CoC Service): November 2012.
• Comprehensive Counseling Training Curriculum: December 2012.
• SOP for Boosted Continuum of Care for PLHIV: February 2013.

5.2 Start implementation of the Cambodia 3.0 Initiative, including TasP, at OD level (TasP Phase 1 during Quarters 3 and 4, 2013, targeting discordant couples and pregnant women)

• Semester 2, 2013:
  o Battambang OD, Battambang Province ("HIV Free OD for ASEAN" by 2015)
  o Kampong Siam OD, Kampong Cham Province
  o Siam Reap OD, Siam Reap Province
  o Tbong, Cheung and Lech ODs in Phnom Penh
  o O Chrov OD (including Poipet City), Banteay Mean Chey Province

• 2014: Nationwide Expansion of TasP

5.3 Review of the progress of the Cambodia 3.0 initiative including TasP evaluation (End of 2013)

5.4 National Scale-up of the Cambodia 3.0 initiative, including TasP, to all the 32 High Risk ODs (TasP Phase 2 from 2014, targeting discordant couples, pregnant women and MARPs) (see the list of the High Risk ODs decided by the National Program and development partners in Annex 3).

6. Logistics

Implementation of this strategy will require a revised approach to ARV forecasting for the ART cohort. Key changes to assumptions behind forecasting demand for ARV products include:

6.1 Starting number of patients on ART:
  • In the initial implementation phase:
    • The impact on the total number of patients should be minimal. Among the sero-discordant couples, the program will identify the HIV-infected individuals who are not yet in treatment and add this number of new patients to the total expected patient numbers. According the CBPCS report by KHANA, up to June 2012, there were 1, 657 sero-discordant couples, of whom only 157 positive partners are on pre-ART. This represents 9% while other 91% are already on ART.
    • All those enrolled in pre-ART (in Q1 2012 there were 7,594 people enrolled in pre-ART) will be put on ART.
7 Monitoring and Evaluation

There is substantial evidence that ART as Prevention is extremely effective in preventing transmission of HIV in sero-discordant couples. Nevertheless, measuring outcomes and impact of the TasP approach in Cambodia and progress towards elimination of new HIV infections will be critical to the success of the strategy when scaling up TasP in phase 2. Routine monitoring, evaluations and quality improvement approaches (linked to the existing CQI strategy) will be required along the implementation process to review progresses, gaps in service coverage, challenges and to incorporate the lessons learned into programming decisions.

A series of monitoring Indicators should be routinely collected and evaluated to track program achievements:

7.1 Indicators for active HIV case finding and detection of discordant couples and HIV+ pregnant women

- Number of newly diagnosed HIV infections
- Number of partners from newly diagnosed HIV patient tested
- Number of partners from newly diagnosed HIV patient tested positive
- Number of identified discordant couples
- Percent of eligible PLHIV patients in discordant couples accepting early ART (Enrollment)
- Number of HIV-infected pregnant women not yet on ART being initiated on ART under PMTCT Option B+
- Number of PLHIV started on TasP

7.2 Indicators for follow-up of patients on TasP

- Percent of patients initiated on TasP lost to follow up
- Percent of patients initiated on TasP who die
- Percent of patients initiated on TasP who stop treatment
- Number and percentage of TasP retained on treatment after 12, 24, 36 months
- Number of TasP patients with undetectable viral load at 6 months (early adherence)
- Number and rate of TasP patients who have to change ARV regimen because of adverse events
- Rate of TasP patients coming on-time at their follow-up appointments for regular drug pick up
- Number of TasP patients who were diagnosed with TB and start TB treatment during the first year of TasP
- Rate of consistent condom use at last sex among sero-discordant couples initiated on TasP
- Rate of treatment failure at 1 year, 2 years among patients initiated on TasP

• ART regimens for new and existing patients: All new patients should begin ART with a TDF-based first line regimen. This will lead to substantial changes in the required quantities of d4T and TDF.
7.3 Impact indicators of TasP

- Transmission rate among partners of PLHIV who initiated TasP (impact indicator)
- Transmission rate from mother-to-child (modeled)
- Changes of Community viral load among EW at given areas at 1 year, 2 years compared to baseline community viral load at the start of the TasP intervention in this population
- Changes of Community viral load among MSM at given areas at 1 year, 2 years compared to baseline community viral load at the start of the TasP intervention in this population

Annex 1: Regimen optimization through provision of Tenofovir based ART

By starting patients on TDF the likelihood of a toxicity-drive regimen change is reduced. Evidence shows that patients on tenofovir experience fewer adverse events than patients on d4T or AZT, and may have better adherence as a consequence. In a study among 1,124 patients on tenofovir (TDF), zidovudine (AZT) or stavudine (d4T), patients on AZT were more than twice as likely to require drug substitution due to toxicity compared with patients on TDF, while patients on stavudine were nearly six times as likely to require a drug substitution.  

There is further evidence that adherence among patients on Tenofovir will be better compared with other regimens due to the new Fixed Dose Combination formulations that are available. Two optimal TDF based FDC products are now available in Cambodia 1) TDF/3TC/EFV and 2) TDF/3TC (which can be taken in combination with Efavirenz once daily). Using option 1) one FDC pill is taken once daily and using option 2) two pills are taken once daily.

In a 2009 meta-analysis of 11 randomized, controlled trials (total number of subjects, 3029), it was shown that the “adherence rate was better with once-daily regimens (+2.9%; 95% confidence interval, 1.0%-4.8%; P < .003) than with twice-daily regimens. This modest effect was more pronounced at the time of treatment initiation and for regimens for which all medications were taken once per day” (484).  

This study indicates that there is a small but existent difference in adherence between patients who take their medications once daily rather than twice or more daily. But for the purposes of a debate over the efficacy of triple TDF/3TC/EFV vs. dual TDF/3TC plus EFV, this finding is not of direct relevance, as both the one-pill and two-pill regimen are taken once a day.

As the price of TDF-based products have declined it is now feasible to consider using TDF in the first line.  

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20 According to the 2011 revision of the national adult treatment guidelines the recommended first line regimens are d4T or AZT based and TDF is reserved for second line. The majority of patients in Cambodia are on first line d4T and AZT-based regimens. The program must maintain the principle of “equity of benefit” to ensure that PLHIV in Cambodia have equitable access to optimal treatment regimens. When TasP is implemented, TDF-based regimens should be promoted as first line therapy to ensure patients benefit from the clinical and convenience advantages of the regimen. In line with this principle, NCHADS is initiating a
regimen comprising a fixed dose combination of TDF/3TC plus single Efavirenz (EFV) are now on par with costs of a once per day AZT based regimen. The national program recommends a once daily regimen of TDF/3TC plus EFV for patients eligible for TasP.

<table>
<thead>
<tr>
<th>Regimen</th>
<th>Formulation</th>
<th>Cost per Patient per Year</th>
</tr>
</thead>
<tbody>
<tr>
<td>TDF/3TC/EFV</td>
<td>Triple FDC</td>
<td>$159</td>
</tr>
<tr>
<td>TDF/3TC/EFV</td>
<td>Dual FDC TDF/3TC + Single EFV</td>
<td>$125</td>
</tr>
</tbody>
</table>

Annex 2: Comparative cost analysis of three ART regimens for use in TasP

The comparative cost of implementing TasP using three different first line regimens has been analyzed and is presented in the following figure. The regimens considered in this analysis include:

1) AZT/3TC/NVP
2) TDF/3TC+EFV and
3) TDF/3TC/EFV

proactive drug switch for all patients on d4T as part of their first line therapy in 2013. The adult treatment guidelines will be revised to recommend TDF as first line for all new patients.

Annex 3: List of HIV High Risk Cities or Districts in Cambodia

<table>
<thead>
<tr>
<th>No</th>
<th>Province/Municipality</th>
<th>City/District</th>
<th>MARP</th>
<th>HIV rate among ANC in 2011*</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Phnom Penh</td>
<td>1.1 OD Tbaung (Mean Chey)</td>
<td>EW, MSM TG PWID PWUD</td>
<td>0.38%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>1.2 OD Leach (Po Sen Chey &amp; Daung Kor)</td>
<td></td>
<td>0.25%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>1.3 OD Kandal (Chamkar Mennon &amp;7 Makara)</td>
<td></td>
<td>0.43%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>1.4 OD Choeung (Torl Kok, Reussey Keo, Sen Sok)</td>
<td></td>
<td>0.75%</td>
</tr>
<tr>
<td>2.</td>
<td>Battambang</td>
<td>2.1 OD Battambang</td>
<td>EW, MSM TG PWUD</td>
<td>0.14%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>2.2 OD Sampeo Laun</td>
<td></td>
<td>0.55%</td>
</tr>
<tr>
<td>3.</td>
<td>Banteay Mean Chey</td>
<td>3.1 OD Serey Sophon</td>
<td>EW, MSM TG PWUD</td>
<td>0.33%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>3.2 OD O Chrev including Poipet City</td>
<td></td>
<td>0.27%</td>
</tr>
<tr>
<td></td>
<td>Province</td>
<td>District 1</td>
<td>District 2</td>
<td>District 3</td>
</tr>
<tr>
<td>---</td>
<td>----------------</td>
<td>---------------------</td>
<td>---------------------</td>
<td>---------------------</td>
</tr>
<tr>
<td>4.</td>
<td>Pailin</td>
<td>4.1 OD Pailin</td>
<td>EW, MSM,TG</td>
<td>PWUD</td>
</tr>
<tr>
<td>5.</td>
<td>Seam Reap</td>
<td>5.1 OD Seam Reap</td>
<td>EW, MSM TG</td>
<td>PWUD</td>
</tr>
<tr>
<td>6.</td>
<td>O Dor Mean Chey</td>
<td>6.1 OD Samrong</td>
<td>EW, MSM TG</td>
<td>PWUD</td>
</tr>
<tr>
<td></td>
<td></td>
<td>6.2 OD Aung Long Veng</td>
<td></td>
<td></td>
</tr>
<tr>
<td>7.</td>
<td>Preah Vihear</td>
<td>7.1 OD Preah Vihear</td>
<td>EW, MSM</td>
<td>PWUD</td>
</tr>
<tr>
<td></td>
<td></td>
<td>including Sam Em</td>
<td></td>
<td></td>
</tr>
<tr>
<td>8.</td>
<td>Kandal</td>
<td>8.1 OD Takmao</td>
<td>EW,MSM TG</td>
<td>PWUD</td>
</tr>
<tr>
<td></td>
<td></td>
<td>8.2 OD Kean Svay</td>
<td></td>
<td></td>
</tr>
<tr>
<td>9.</td>
<td>Kg Speu</td>
<td>9.1 OD Chbar Monn</td>
<td>EW, MSM</td>
<td>PWUD</td>
</tr>
<tr>
<td>10.</td>
<td>Takeo</td>
<td>10.1 OD Daun Keo</td>
<td>EW, MSM</td>
<td>PWUD</td>
</tr>
<tr>
<td>11.</td>
<td>Kampot</td>
<td>11.1 OD Kampot</td>
<td>EW, MSM</td>
<td>PWUD</td>
</tr>
<tr>
<td>12.</td>
<td>Preah Sihanouk</td>
<td>12.1 OD Preah Sihanouk</td>
<td>EW, MSM</td>
<td>PWUD</td>
</tr>
<tr>
<td>13.</td>
<td>Koh Kong</td>
<td>13.1 OD Smach Mean Chey</td>
<td>EW, MSM</td>
<td>PWUD</td>
</tr>
<tr>
<td>14.</td>
<td>Pursat</td>
<td>14.1 OD Sampeo Meas</td>
<td>EW, MSM</td>
<td>PWUD</td>
</tr>
<tr>
<td>15.</td>
<td>Kg Chhnaing</td>
<td>15.1 OD Kg Chhnaing</td>
<td>EW, MSM</td>
<td>PWUD</td>
</tr>
<tr>
<td>16.</td>
<td>Svay Rieng</td>
<td>16.1 OD Svay Chrum</td>
<td>EW, MSM</td>
<td>PWUD</td>
</tr>
<tr>
<td></td>
<td></td>
<td>16.2 OD Chi Phou/ Bavet City</td>
<td></td>
<td></td>
</tr>
<tr>
<td>17.</td>
<td>Prey Veng</td>
<td>17.1 OD Kg Leav</td>
<td>EW, MSM</td>
<td>PWUD</td>
</tr>
<tr>
<td></td>
<td></td>
<td>17.2 OD Neak Loeung</td>
<td></td>
<td></td>
</tr>
<tr>
<td>18.</td>
<td>Kg Cham</td>
<td>18.1 OD Kg Seam-Kg Cham</td>
<td>EW, MSM</td>
<td>PWUD</td>
</tr>
<tr>
<td></td>
<td></td>
<td>18.2 OD Memot</td>
<td></td>
<td></td>
</tr>
<tr>
<td>19.</td>
<td>Kg Thom</td>
<td>19.1 OD Kg Thom</td>
<td>EW, MSM,PWUD</td>
<td></td>
</tr>
<tr>
<td>20.</td>
<td>Kratie</td>
<td>20.1 OD Kratie</td>
<td>EW, MSM</td>
<td>PWUD</td>
</tr>
<tr>
<td>21.</td>
<td>Stung Treng</td>
<td>21.1 OD Stung treng</td>
<td>EW, MSM</td>
<td>PWUD</td>
</tr>
<tr>
<td>22.</td>
<td>Ratanakiri</td>
<td>22.1 OD Ratanakiri</td>
<td>EW, PWUD MSM</td>
<td></td>
</tr>
<tr>
<td>23.</td>
<td>MondolKiri</td>
<td>23.2 OD Mondolkiri</td>
<td>EW, PWUD</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Total: 22 Provinces 1 Municipality</td>
<td>32 ODs</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*data reported by the Linked response OD in 2011, reflecting new HIV infections*