Kingdom of Cambodia

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Ministry of Health

Concept Note on
The Same Day ART Initiation in Cambodia

National Center for HIV/AIDS, Dermatology and STD

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Contents

Abbreviations

3TC	Lamivudine
ART	Antiretroviral Therapy
ARV	Antiretroviral
CBC	Complete Blood Count
CI	Confidence Interval
CTX	Cotrimoxazole Prophylaxis
DTG	Dolutegravir
HBV	Hepatitis B virus
HCV	Hepatitis
HIV	Human Immunodeficiency Virus
EFV	Efavirenz
OI	Opportunistic Infection
PCP	Pneumocystis Carinii Pneumonia
PEP	Post Exposure Prophylaxis
PI	Protease Inhibiter
PrEP	Pre-Exposure Prophylaxis
PLHIV	People Living with HIV
RNA	Ribonucleic Acid
TDF	Tenofovir
TPT	Tuberculosis Prevention Therapy
UNAIDS	United Nations Programme on HIV and AIDS
VCCT	Voluntary Confidential Counseling and Testing
WHO	World Health Organization

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I. Background and rationale

The *Cambodian National HIV Clinical Management Guidelines*, adapted from WHO guidelines aim to provide better and more effective care to PLHIV in Cambodia. Cambodia has successfully implemented the "treat all" WHO recommendation of 2018 with most individuals testing HIV positive promptly starting anti-retroviral treatment (ART).

In July 2017, WHO issued guidelines for rapid initiation of antiretroviral therapy that states "Rapid ART initiation should be offered to all people living with HIV following a confirmed HIV diagnosis and clinical assessment". Rapid initiation is defined as within seven days from the day of HIV diagnosis; people with advanced HIV disease should be given priority for assessment and initiation. Furthermore, the guidelines recommend ART initiation should be offered on the same day to people who are ready to start.

There are several studies showing the benefits of rapid or same-day ART. In a study by Rosen S showed that those randomized to receive immediate ART on the day of diagnosis were significantly more likely than those randomized to usual care (three to five additional visits with adherence counseling over 2 to 4 weeks prior to ART initiation) to be virally suppressed at 10 months (64% vs. 51%). In the rapid arm, 119/187 patients (64%) initiated treatment and were virally suppressed at 10 months, compared to 96/190 (51%) in the standard arm (relative risk [RR] 1.26 [1.05-1.50]).

Similar improvements in both the proportion of participants retained in care achieving viral suppression and survival at the end of 1 year were recently reported in a randomized controlled trial of same-day ART initiation conducted in Haiti. The unadjusted risk ratio (RR) of being retained at 12 months with HIV-1 RNA <50 copies/ml was 1.21 (95% CI: 1.04, 1.38; p = 0.015) for the same-day ART group compared to the standard ART group, and the unadjusted RR for being retained with HIV-1 RNA <1,000 copies was 1.18 (95% CI: 1.04, 1.31; p = 0.012).

However, a study conducted by Chan AK, Kanike E, Bedell R, et al in Malawi, showed that after ART initiation, a greater proportion of people were lost to follow-up in the same-day start group, although the trial sample size was small and differences were not significant. In Malawi, same-day ART initiation in pregnant women with HIV was associated with reduced retention, because many women reportedly struggled with initiating ART on the same day as learning their HIV status

Another study by Pilcher, et al. concluded that the treatment for HIV infection can be started on the day of diagnosis without impacting the safety or acceptability of ART. Same-day ART may shorten the time to virologic suppression.

Treating HIV early can help keep level of viral load low and protecting the patients' health by preserving immune function and reducing the risk for severe opportunistic infections. For patients rapid ART or same-day ART will help them:

- Stay healthier longer by preserving the immune system by maintaining high CD4 cell counts
- Reducing risk of opportunistic infections and other diseases,
- Reducing or nearly eliminating the chance of transmitting HIV to other people
- Increasing access to other services they need such as social support, addiction recovery, and mental health.

II. Objectives

The main objectives of this document are:

- To provide the public health and HIV program rationale for rapid or same-day ART,
- To provide a practical guide for ART teams, HIV care related team, and planning team for rapid or same-day ART implementation.

III. Definition of same day ART initiation

Initiation ART at ART clinic on the same day of HIV confirmation at VCCT for adolescents and adults who are no contraindication to the criteria of the same day ART initiation.

IV. Eligibility for same day ART initiation

Anyone with a new confirmed HIV diagnosis:

- New HIV infected adolescents and adults enrolled in ART clinic
- No experience using ART, except ARV prophylaxis such as PEP, PrEP and PMTCT.
- Asymptomatic infection
- No use of nephrotoxic drugs
- No history of renal failure

V. Reasons for possible non-eligibility for same day ART initiation

Patients for whom the same day ART might be medically complicated and need prior well managed active opportunistic infection before initiating ART[1] .

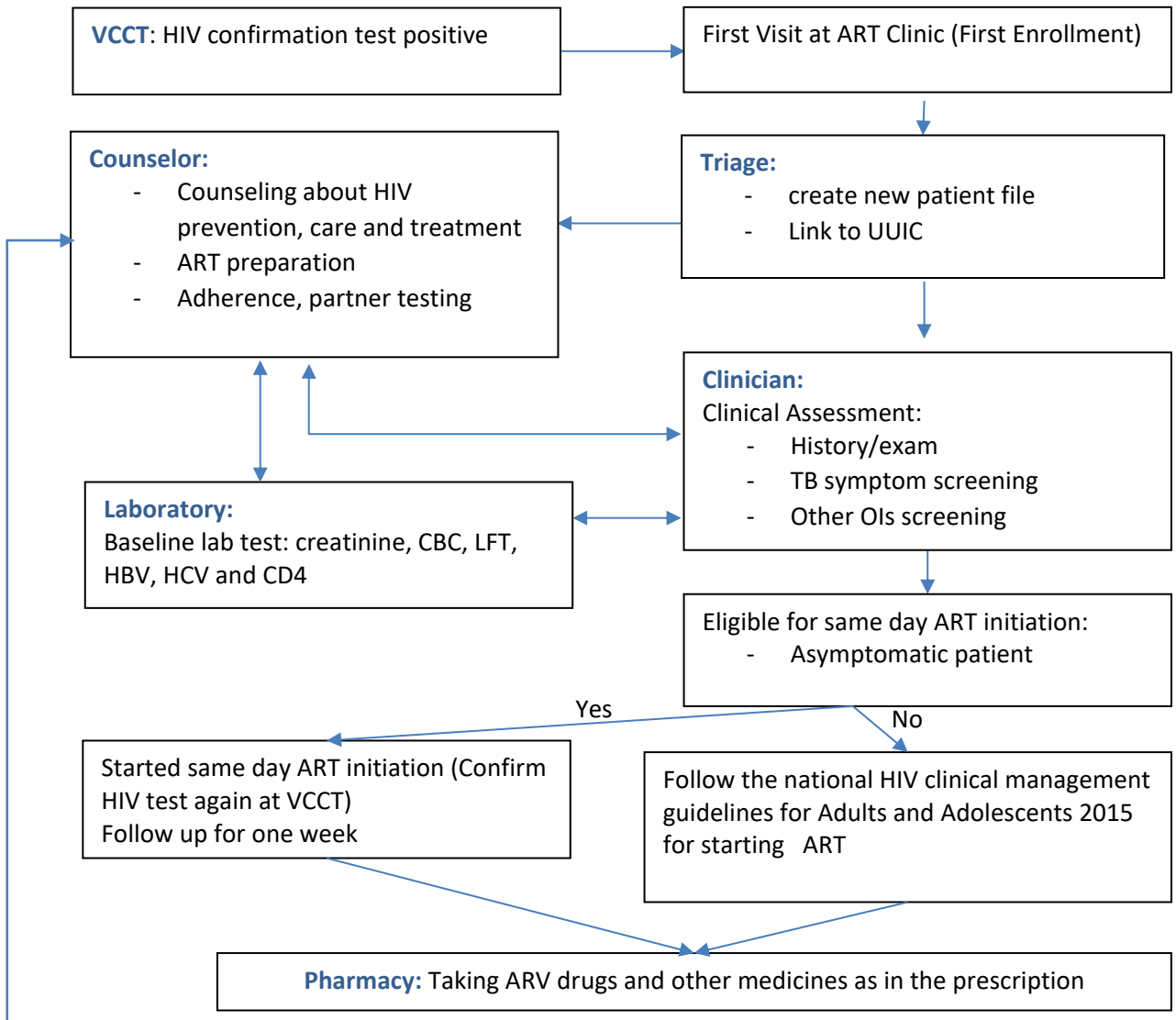
[1] Please refer to Table 8-3 page 53 in current National HIV Clincial Management guideline for Adult and adolescent 2015.

- TB symptoms or TB screen positive
- Suspected PCP, cryptococcal meningitis or other severe OIs
- Patient had experience on ART for HIV/AIDS
- Use of nephrotoxic drugs
- Patient with drug use, high toxicity and could not provide counseling

Note: If the patient presents with one or more risk factors above, **a blood test for serum creatinine levels** and calculate the creatinine clearance. **Only initiate patients to TDF if creatinine clearance is equal or greater than 60 ml/min.**

VI. Process of the same day ART initiation

6.1 Patient flow at ART clinic



6.2 Clinical Assessment:

- History/exam to assess for OI's (TB symptom screening, PCP, meningitis and other OIs)
- If asymptomatic and no contraindication to same day ART initiation, then okay to start same day ART

6.3 Counseling:

Drug counselor at ART clinic provides counseling on the benefit of the same day ART treatment, important of adherence, family planning, partner testing, HIV prevention, care and treatment and ART preparation including explanation of possible side-effects. Female patients of childbearing age who will be taking dolutegravir (DTG) will need a pregnancy test and counseling on effective and adhere to family planning methods. If she is pregnant or desires to get pregnant, non-DTG containing regimens should be offered.

6.4 Laboratory:

Nurse takes blood from the patient for baseline lab test, creatinine, CBC, liver function test, HBV, HCV test and CD4 count. Female patients of child bearing age need to be checked for pregnancy before starting. The cryptococcal antigen test will be done at laboratory if CD4 count of the patient ≤100 cell/mm3. Patients can be contacted and return to clinic based on laboratory results.

VII. ARV regimen

The preferred first-line regimen for nearly all populations are: **TDF+3TC+DTG***

<table>
<tr><th>Population</th><th>Preferred</th><th>Alternatives**</th></tr>
<tr><td>Adult men and adolescent boys</td><td rowspan="3">TDF+3TC+DTG</td><td rowspan="3">TDF+3TC+EFV600

TDF+3TC+EFV400</td></tr>
<tr><td>Pregnant (> 8 weeks after conception) and breastfeeding women and adolescent girls</td></tr>
<tr><td>Women and adolescent girls using effective contraception or not of childbearing potential</td></tr>
</table>

Women and adolescent girls of childbearing potential who want to become pregnant or are not effective contraception	TDF+3TC+EFV600	TDF+3TC+EFV400 TDF+3TC+PI

*More detailed information about DTG use, see operational guidance: Use of Dolutegravir (DTG) for adults and adolescents in Cambodia, December 2018.

**For special situations, ARV side effect, renal insufficiency, see in detail in the *National HIV Clinical Management Guidelines for Adults and Adolescents,* Chapter 10. Monitoring and Substitutions for ART Toxicity, page 57.

VIII. Follow up

Clinicians have to make sure that the next follow-up visit is in accordance with the follow-up schedule below.

Day/week	Clinical	Adherence counseling	Laboratory	Drugs
Day 0	×	×	×	Start ART Start CTX
Week 1 (7 days after first visit)	×	×	See result	Stop CTX if CD4 ≥ 350. Start Fluconazole prophylaxis if indicated based on CD4.
Week 2	×	×		Start TB preventive therapy (TPT) if clinically screen negative for active TB and there is no contra-indication to start TPT[2]
Follow up every month for TPT. TPT guidelines and SOP is being updated and treatment regiments can be either of Rifapentine and isoniazid weekly for 3 months (3HP) or Rifampicin plus isoniazid daily for 3 months (3HR) to be offered as alternative to current Isoniazid monotherapy for 6 months (6H).				

[2] Refer to Chapter 6 table 6.2 page 46 of National HIV clinical management guidelines for adults and adolescent ,2015

When patient has finished TPT but still on CTX prophylaxis, see the *National HIV Clinical Management Guidelines for Adults and Adolescents*, Table 2-1 Clinic visit routine schedule on page 29 and for routine laboratory investigation see Table 2-3 Routine Laboratory investigation on page 30 (English version).

IX. Monitoring

To ensure the program is collecting, documenting and reviewing necessary data to see the progress of the same-day ART, indicators below will be monitored.

Indicator 1: Percentage of patients initiating same-day ART s

Indicator 2: Percentage of patients who come for follow-up visit as scheduled

Indicator 3: Percentage of patients have VL results suppression at the first 6 months

Indicator 4: Percentage of patients who retained on ART at 12 months

Indicator 5: Percentage of patients lost to follow-up after ART initiation

Indicator 6: Percentage of patients were stopped ART treatment because of ARV side effect

Indicator 1: Percentage of patients have same-day ART initiation	
Definition	Number ART patients who have ART initiated on the same day as their HIV confirmatory test divided by the total number of patients enrolled at the ART clinic in the reporting period.
Purpose	To measure the percentage of same-day ART initiation.
Method of Measurement	Count the number of patients who have ART initiation date the same as HIV confirmatory test date, then compute for percentage using numerator and denominator below.
Frequency	Monthly
Numerator	Number ART patients who have ART initiation date the same as HIV confirmatory date in the reporting period.
Denominator	Total number of patients enrolled at the ART clinic in the reporting period.
Disaggregation(s)	Same Day ART Initiation (0 day) Not Same Day ART Initiation
Source of data	ART database
Interpretation	Of the total patient load, how many clients have initiated same-day ART?

Indicator 2: Percentage of same day initiation patients who come for follow-up visits as scheduled	
Definition	Number same-day ART initiation patients who came for follow-up visit as scheduled divided by the total number of same-day ART initiation patients enrolled at the ART clinic.

Purpose	To measure the "discipline" of same-day ART initiation patients.
Method of Measurement	Count the number of patients who have same-day ART initiation and came for the follow-up visit as scheduled, then compute for percentage using numerator and denominator below.
Frequency	Monthly
Numerator	Number of same-day ART initiation patients who came for follow-up as scheduled in the reporting period.
Denominator	Total number of same-day ART initiation patients enrolled at the ART clinic in the reporting period.
Disaggregation(s):	Early On the schedule Within buffer (1-5 days) Beyond the buffer (> 5 days) NCHADS: "drug buffer is never more than 5 days"
Source of data	ART database.
Interpretation	How "disciplined" are same day initiation patients?

Indicator 3: Percentage of patients have viral load suppressed at month 6th (From month 5 through month 7) after ART initiation	
Definition	Number of patients with viral load suppression after 6 months of ART divided by the total number of patients initiating ART for the same period.
Purpose	To monitor the efficacy of ART treatment among same-day (rapid) ART initiation patients.
Method of Measurement	Count number of patients at the ART site in the reporting period who have been initiated ART in the past six months (From month 5 through month 7), then compute for percentage using numerator and denominator below.
Frequency	Six months
Numerator	Number of patients who have viral load suppression 6 months after the same day ART initiation (within 210 days).
Denominator	Total number of patients initiating ART the same day at the site during the same period.
Disaggregation(s)	Same Day ART Initiation (0 day) Not Same Day ART Initiation
Source of data	ART database
Interpretation	What is the difference between viral load suppression rate among same-day (rapid) and non-rapid ART initiation?

Indicator 4: Percentage of patients who retained on ART at 12 months	
Definition	Number of patients who are still active (on ART in the clinic) after 12 months of ART initiation divided by the total number of patients initiating ART in the 12 months prior the reporting period.
Purpose	To monitor the proportion of HIV infected patients on ART and actively followed by ART clinics.
Method of Measurement	Count number of registered patients at the ART site 12 months prior the beginning of reporting period, count number of active patients, dead, and lost to follow-up, then compute for percentage using numerator and denominator below.
Frequency	Annually
Numerator	Number of patients who are still receiving ART during the selected 12 months after ART initiation (excluding those who were lost-to-follow-up, died, and transferred out).
Denominator	Total number of patients initiating ART in the 12 months prior to the beginning of the current reporting period (including those who were transferred in)
Disaggregation(s)	Same Day ART Initiation (0 day) Not Same Day ART Initiation
Source of data	ART database
Interpretation	Is the retention rate among rapid ART initiation clients less, equal or greater than the retention rate among not SD/Rapid ART initiation?

Indicator 5: Percentage of patients lost to follow-up after ART initiation	
Definition	Number of patients who are lost to follow-up divided by total number of patients on ART (active patients + LTF + died + transfer out) at the end of the reporting period
Purpose	To monitor the proportion of HIV infected patients on ART and actively followed up by ART clinics.
Method of Measurement	Count number of registered patients at the ART site in the reporting period who have received ART, then compute for percentage using numerator and denominator below.
Frequency	Quarterly
Numerator	Total number of patients who were lost to follow up during the reporting period. *"Lost to follow up" is defined by the NCHADS patients who did not come for the visit at ART site more than 90 days after missing the "next appointment" date.*
Denominator	Total number of patients on ART at the end of the reporting period (active patients + LTF + died + transfer out)
Disaggregation(s)	Same Day ART Initiation (0 day) Not Same Day ART Initiation

Source of data	ART database Patient register
Interpretation	Is the lost to follow-up rate among same day (SD) ART initiation less, equal or greater than the lost to follow-up rate among not SD ART initiation?

Indicator 6: Percentage of patients were stopped ART treatment because of ARV side effect	
Definition	Number of patients who started same day ART then stop at least one drug due to side effects divided by total number of patients started same day ART in the reporting period.
Purpose	To monitor the proportion of HIV patients stop ART treatment due to side effects of the drugs.
Method of Measurement	Count number of registered patients started same day ART in the reporting period then compute for percentage using numerator and denominator below.
Frequency	Quarterly
Numerator	Patient who start same day ART then stop at least one drug because of side effect during the reporting period.
Denominator	Total number of patients start same day ART in the reporting period
Disaggregation(s)	Same Day ART Initiation (0 day) Not Same Day ART Initiation
Source of data	ART database Patient register
Interpretation	Is the rate of stopping treatment among SD ART initiation less, equal or greater than the stopping treatment rate among not SD ART initiation?

X. References

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