Achieving Universal Access and Moving towards ending HIV epidemic in Cambodia by 2025:
Experiences of health sector response to HIV in the last 25 years

Mean Chhivun, MD, MPH
## Evolution of health sector response to HIV from 1991 to 2020

### Phase 1: 1991-2000

- **Cambodia 1.0**
  - % HIV peaked at 1.7 in 1998
  - HIV prevention among general population and MARP
  - 100% condom use in sex work settings
  - VCT in main cities
  - Few home-based care

### Phase 2: 2001-2010

- **Cambodia 2.0**
  - % HIV declined to 0.6 in 2010
  - Universal access to ART (CoC): (WHO award for 3 by 5 in 2005)
  - PMTCT (Linked Response) and TB/HIV (5 I strategy)
  - MARPs prevention and link to health services (CoPCT)
  - HTC: VCCT, PITC, CPICT
  - Continuous Quality Improvement (CQI) for HIV prevention and care services
  - UN award for MDG6 (HIV) in October 2010

### Phase 3: 2011-2020

- **Cambodia 3.0**
  - **Pre-Elimination** of new HIV infections by 2020:
    - Target: 90-90-90
    - B-IACM/PNTT linked to:
      - ART as prevention (TasP)
      - (T and T among KP)
      - Boosted CoC
      - Boosted LR for e-MTCT
      - Boosted CoPCT among KP
  - Strengthen Health/Community System including private sector to support IRIR
  - Monitoring and evaluation of impact including IACSS
Evolution of health sector response to HIV from 2021 to 2030
(Elimination of new HIV infections by 2025)

**Phase 4: Ending HIV epidemic**
2021-2025

**Cambodia 4.0**
- Indicators:
  - <300 HIV newly infections yearly
  - <5% of MTCT
- Target: 95-95-95 by 2025
- Streamline B-IACM/PNTT:
  - Active search among hard to reach and hidden;
  - Test and Treat for all with QA
- IACSS for individual follow up system country wide (Integrated in MOH/SI system)
- Integrated community based support system
- Domestic Investment.....%

**Phase 4: Post elimination**
2026-2030

**Cambodia 4.0**
Maintain all efforts put in the HIV elimination and integrated HIV care and treatment services in to health care system (e.g. LSPM, SI, service delivery);
- Domestic investment;
- Ownership of OD management team to control HIV epidemic and to retain PLHIV in HIV care and treatment service;
- Ownership of Community Networks (KP, PLHIV,...);
- ???
Phase 1: 1991-2000

- **Cambodia 1.0**
  - % HIV peaked at 1.7 in 1998
  - HIV prevention among general population and MARP
  - 100% condom use in sex work settings
  - VCT in main cities
  - Few home-based care
Situation of the HIV Epidemic in Cambodia

- Started ART scale-up
- Started VCCT scale-up
- condom social marketing started
- First brothel-based prevention projects
- Finger prick testing

Incident cases:
- Mother to child
- Needle sharing
- Wife->husband
- Husband->wife
- Sex work

HIV+ adults

Adults living with HIV

Incident HIV infections

- **Political will:** GOC and partners
  - Recognizing HIV epidemic: 1\textsuperscript{st} HIV detected
  - Building capacity for managing HIV program:
    - First TWG: short term plan
    - NAP and Bureau of AIDS: medium term plan
    - NCHADS: long term plan 5 Y strategic plan and AOCP
    - NAC and NAA to strengthen multi sectoral response
  - Good partnership: UN, WB, INGO and LNGO

- **Strategic priorities:**
  - Strong vertical HIV response
  - Changing socio-cultural: sex behavior
  - HIV awareness and condom use
  - Condom promotion: social marketing
  - 100% CUP at brothel (FSW) linked to STI case management:
    (Demonstration then rapid scale up)
  - Stand alone HIV services: VCCT, HBC
  - Strong HIV surveillance system:
    HSS, BSS and SSS, HIV estimations and projections (AEM)

- **Changed unsafe sex behaviors**
- **Stabilized HIV epidemic**
Sex behavioral, HIV and STI trends among brothel-based sex workers
Key Lessons Learned from Cambodia 1.0: How Cambodia stabilized HIV epidemic?

- **Political will:**
  - Recognized HIV epidemic from the first detected case
  - Swift responses

- **Strong HIV program:** leadership management at all levels
  - Know our HIV epidemic and response is utmost important:
  - Invest in strategic information: HSS, BSS, SSS
  - 100% cup in sex work setting (from demonstration site to country wide implementation within 2 years: clear road map and shared)
  - Started with *vertical response* is effective (efficiency and sustainability?)

- **Good partnership:** stewardship and mutual responsibility
Major challenges

- Changing socio-cultural norms:
  - Talk publicly about sex, condom use,…

- Changing unsafe sex behavior:
  - Abstinence, Be faithful, Condom use

HOW?
Phase 2: 2001-2010

Cambodia 2.0

- % HIV declined to 0.7 in 2010
- Universal access to ART (CoC) (WHO award for 3 by 5 in 2005)
- PMTCT (Linked Response) and TB/HIV (5 I strategy)
- MARPs prevention and link to health services (CoPCT)
- HTC: VCCT, PITC, CPICT
- Continuous Quality Improvement (CQI) for HIV prevention and care services
- UN award for MDG6 (HIV) in October 2010
Cambodia 2.0: Rapid Expansion
Strategic Expansion of HTC

Entry point for: HIV prevention and care

PITC for TB and PW in most Health facilities (HC)
Community/Peer Initiated Testing and Counseling for MARPs (late 2000)
Strategic Expansion of ART Sites

- ART sites in 55/77 ODs covering 92% of PLHIV found
- Indicating the need of Satellite ART sites
Not only expanding services, but systematically linking with the community and creating demand
Continuum of Care Framework
Facilitated Expansion of ART

- Reduced stigma and discrimination among health workers and general populations
- Community based
- Entry Point for HIV
- Enabling environment
- Health Service Delivery (District Level)
Number of people with HIV, in need of ART and on ART aged 15+ (2000-2015)

- People with HIV aged 15+
- In need of ART aged 15+
- On ART aged 15+

**ART Retention**
- 87% at 12M
- 83% at 24M
- 73.6% at 60M

**ART Coverage 82%**

*Source: NCHADS/DMU 2013*
“Linking Model”

2000
- PMTCT TWG (’99)
- PMTCT pilot (’01)
- PMTCT GL: SD-NVP (’02)

2005
- PMTCT GL rev: Dual prophyl (’05)
- PMTCT Review (’07)
- Linked Response (’08)

2010
- PMTCT GL rev: Option B (’10)

TB-HIV Sub-committee (’99)
- TB/HIV Framework (’02)
- TB/HIV pilot (’03)
- Joint Statement: Role & Responsibility (’03)
- SOPs PITC in TB cases (’06)
- CAMELIA and ID-TB/HIV results (’09)
- SOP, Joint Statement: 3I’s (’10)
- 3I’s Role Out (’11)
Facilitated expansion of PMTCT and TB/HIV

**HC**
- HCBC Team/NGO
- Community

**Satellite HC**
- VCCT
- HCBC Team/NGO
- Health worker/NGO

**RH (Hub)**
- Referral and Follow-up

**VCCT**
- Referral and Follow-up
20 HCs have only 2 VCCT sites, 1 OI/ART services

Linkages: Kirivong Operational District
14 HC refer blood samples to 5 sub-satellites & 1 satellite
Linking Model Demonstration Results (2007-9)

* Introduction of syphilis testing in the first quarter of 2009
** Percentage of pregnant women tested for HIV/ syphilis at antenatal care out of total expected pregnant women
PMTCT Coverage

- **2007**:%
Pregnant women tested for HIV (with known status, newly identified and previously known)

- **2008**:%
Pregnant women tested for HIV (with known status, newly identified and previously known)

- **2009**:%
Pregnant women tested for HIV (with known status, newly identified and previously known)

- **2010**:%
Pregnant women tested for HIV (with known status, newly identified and previously known)

- **2011**:%
Pregnant women tested for HIV (with known status, newly identified and previously known)

- **2007**:%
HIV+ pregnant women received triple ARV prophylaxis or ART

- **2008**:%
HIV+ pregnant women received triple ARV prophylaxis or ART

- **2009**:%
HIV+ pregnant women received triple ARV prophylaxis or ART

- **2010**:%
HIV+ pregnant women received triple ARV prophylaxis or ART

- **2011**:%
HIV+ pregnant women received triple ARV prophylaxis or ART

- **2007**:%
HIV exposed infants received ARV Prophylaxis for six weeks

- **2008**:%
HIV exposed infants received ARV Prophylaxis for six weeks

- **2009**:%
HIV exposed infants received ARV Prophylaxis for six weeks

- **2010**:%
HIV exposed infants received ARV Prophylaxis for six weeks

- **2011**:%
HIV exposed infants received ARV Prophylaxis for six weeks
TB/HIV Coverage

- % PLHIV in pre-ART screened for TB
- % TB cases tested for HIV
- % HIV+ TB cases started / continued on ART
Moving Towards Integration between HIV-MCH-TB
Responding to changing epidemics

- Overcoming political, legal and social barriers
- Reaching the most-at-risk populations
- Linking them to health services
Changing conditions (1)

1995

13,000 sex workers
70% direct, 30% indirect

1998
100% CUP

2008
AHT law

2010

36,000 sex workers
10% direct, 90% indirect

Direct

Indirect
Changing conditions (2)

- 2008 Law on Suppression of Human Trafficking
  - Massive brothel closure, poorly organized
  - Sex workers driven underground increasing vulnerability and risk
  - Virtual collapse of 100% CUP as key partners and structures disappear

- Increasing attentions to human rights marginalized populations
HIV concentrated among MARPs:

<table>
<thead>
<tr>
<th>Population Size</th>
<th>HIV prevalence</th>
</tr>
</thead>
<tbody>
<tr>
<td>EW (38,000)</td>
<td>10% (Clients &gt;7/w)</td>
</tr>
<tr>
<td>NGO report 2012</td>
<td>SSS 2011</td>
</tr>
<tr>
<td>MSM (16,000)</td>
<td>2.1%</td>
</tr>
<tr>
<td>NGO report 2012</td>
<td>Bros Khmer 2010</td>
</tr>
<tr>
<td>TG</td>
<td></td>
</tr>
<tr>
<td>PWID 1,300</td>
<td>25%</td>
</tr>
<tr>
<td>IBBS 2012</td>
<td>IBBS 2012</td>
</tr>
<tr>
<td>PWUD 13,000</td>
<td>4%</td>
</tr>
<tr>
<td>IBBS 2012</td>
<td>IBBS 2012</td>
</tr>
</tbody>
</table>
Continuum of Prevention to Care and Treatment: COPCT (2009-)
MARPs prevention and access to health services

Sex Workers

C/PITC

Peer Network
Peer Educator
NGO

Health service delivery at district level

HCBC Team
PHC network
CBO
NGO
Health Workers

MSM, TG, PWUD and PWID

Provider Initiated Counseling & Testing (PITC), VCCT, Pre-ART/ART
STI, ANC, SRH, Safe Abortion, Safe Delivery, EPI, Nutrition (children)
TB, Malaria
Laboratory
Current trends in HIV financing

Domestic vs. External Sources (millions of USD)

Source: NASA IV Report, 2013
Key Lessons Learned from Cambodia 2.0:

- Knowing our HIV epidemic and response remains key
- Moving from vertical response to diagonal (linking) then horizontal (integration):
  - Systematic linkages and integration to maximize resources
- Common service delivery frameworks coordinated by NCHADS involving all stakeholders for strategic expansion
  - Good partnership: harmonization and alignment
- Decentralization the HIV response to sub-national level (OD)
  - Use experience OD to support other OD
- Sharing resources among relevant programs with mutual benefit:
  - (HIV-MNCHC-CENAT, Pediatric care…)
- “Real” involvement of community (PLHIV and MARPs network)
Major Challenges

- Limited capacity to estimate the number of PLHIV who do not know their status by province (be used for the denominator)

- Changing conditions of the MARPs and related factors

- Bringing the strong vertical programs to work together
  - Competition for resources: project based among some key players (national programs and stakeholders)

- Scarcity resources (human, money)
Phase 3: 2011-2020

Cambodia 3.0

- **Pre-Elimination** of new HIV infections by 2020:
  - Target: 90-90-90
- B-IACM/PNTT linked to:
  - ART as prevention (TasP)
  - (T and T among KP)
  - Boosted CoC
  - Boosted LR for e-MTCT
  - Boosted CoPCT among KP
- Strengthen Health/Community System including private sector to support IRIR
- Monitoring and evaluation of impact including IACSS
Cambodia 3.0: Virtual elimination of new HIV infections by 2020

- **e-MTCT** (Boosted LR)
  - Pregnant Women and Sex Partners

- **KP Prevention and Links to Health Service** (Boosted COPCT)
  - MARP and Sex Partners

- **STI case management**

- **Boosted CoC**

- **VCCT, PITC (TB, ANC)**
  - Community Peer Initiated TC

- **Immediate ART (CD4≤500)**

- **PLHIV Partners**
  - PLHIV on Pre-ART

**ART as Prevention**
Key Populations: Prevention & Links to Health Services

(1) Sharper epidemiological targeting:

- PWID selling sex
- PWID
- Male/TG sex workers
- MSM ‘pleasure circuit’
- PWUD selling sex
- ‘EW (Massage, KTV, Beer promoters, etc)
- Casino workers, Migrants, etc.
(2) Reach unreached populations (MSM, TG, PWID, PWUD and their partners) and explore hidden populations

(3) Expand outreach finger prick HTC and link to STI and ART

(4) Expand NSP and MMT for PWID

(5) Strengthen strategic information and response; e.g. ‘rapid response mechanism’, Unique Identifier System (UIC)

First IR: PDI

Scaling up the implementation of the IR-IR strategic approaches
eMTCT and TasP

- Streamlining HTC procedures and referral
- Partner tracing and testing
- Active case management to maximize retention across HTC–PreART/ART–PMTCT–TB/HIV
- TasP (Discordant Couples → MARPs)
- PMTCT Option B+
Streamlining HTC procedures and referral

**Cambodia 2.0**

- Referral Hosp with VCT/ART
  - Pre-ART&ART
    - Patient Referral if (+)
  - Health Center with VCT
    - 1st Test, Confirmatory Test
      - Sample referral
      - 1st Test Result
      - Patient Referral if (+)
  - Health Center without VCT
    - Blood Taking

**Cambodia 3.0**

- Referral Hosp with VCT/ART
  - Confirmatory Test, PreART&ART
    - Patient referral if (+)
  - Every Health Center
    - First Test with Finger Prick

---

1st Test, Confirmatory Test
How Cambodia can achieve 90-90-90 target by 2020 (over the next 4 years: 2017-2020) ?

Test and Treat all
Early Testing: first IR strategy
Early ART and Retain: second IR strategy
Figure 2. B-IACM/PNTT at PHD level toward achieving 90-90-90 target by 2020

```
0 20 40 60 80 100 120

100 120

Denominator

100

90

70%

Estimated PLHIV (of people tested)
PLHIV tested
Reactive tests
Confirmed positive
Pre-ART/ART enrollment
PLHIV on ART
Viral load tested
VL suppressed

"First IR strategy"

"Second IR strategy"

IRIR (Identify-Reach-Intensify-Retain) strategic approaches

MCV, January 4, 2016
```
Active search for PLHIV who do not know their status at community level with high confidentiality, 2016-2020

(12000-15000?) **PLHIV are not in HIV system**

- **Target pop**
- **KP**
- **LTFU & D**
- **Hidden**

Who and Where are they? (Case profiling?)

- **By ART team and CA (NGO-FS, CV) key informants: local authority (at village level)**
- **By KP Networks: OW, key informants: brokers, (at KP locations), PDI**
- **By health workers at Health Facilities (PITC)**
  - Active search among targeted general populations
- **HC & RH**
  - ANC
  - Maternity
  - TB
  - OPD, IPD
- **Blood Bank**
- **Health Post:**
  - Factories
  - Casino
  - Plantation
  - Prison, closed settings

**MCV, January 4, 2016**
CA framework to operationalize IRIR

- **HC** (Health facility)
  - **VCCT** (VCT, Community Care and Treatment)
    - **Referral**
      - **ART facility** (Treat All)
        - **Enrolment**
          - **CV (2 VHSG, CSV)**
            - **OW-KP**
              - **PLHIV in need**
                - **Stable PLHIV**
                  - **Report FU**
                      - **PLHIV in need**
                        - **Stable PLHIV**
                          - **Referral**
                            - **Enrolment**
                              - **HC** (Health facility)
                                - **Detect**
                                  - **NGO-FS**
                                    - **Detect**
                                      - **Report FU**
                                        - **PLHIV in need**
                                          - **Stable PLHIV**
                                            - **Referral**
                                              - **Enrolment**
                                                - **VCCT** (VCT, Community Care and Treatment)
                                                  - **Referral**
                                                    - **HC** (Health facility)
                                                      - **Detect**
                                                        - **NGO-FS**
                                                          - **Detect**
                                                            - **Report FU**
                                                              - **PLHIV in need**
                                                                - **Stable PLHIV**
                                                                  - **Referral**
                                                                    - **Enrolment**
                                                                      - **VCCT** (VCT, Community Care and Treatment)
                                                                        - **Referral**
                                                                            - **HC** (Health facility)
                                                                              - **Detect**
                                                                                - **NGO-FS**
                                                                                  - **Detect**
                                                                                    - **Report FU**
                                                                                      - **PLHIV in need**
                                                                                          - **Stable PLHIV**
                                                                                                                                - **Referral**
                                                                                                                                 - **Enrolment**
                                                                                                                                                                      - **VCCT** (VCT, Community Care and Treatment)
                                                                                                                                                                                                 - **Referral**
                                                                                                                                                                                                                                              - **HC** (Health facility)
                                                                                                                                                                                                                                                                                                                                                                         - **Detect**
                                                                                                                                                                                                                                                                                                                                                                                             - **NGO-FS**
                                                                                                                                                                                                                                                                                                                                                                                                                     - **Detect**
                                                                                                                                                                                                                                                                                                                                                                                                                                                                       - **Report FU**
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             - **PLHIV in need**
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   - **Stable PLHIV**
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  - **Referral**
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       - **Enrolment**
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             - **VCCT** (VCT, Community Care and Treatment)
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           - **Referral**
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               - **HC** (Health facility)
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   - **Detect**
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   - **NGO-FS**
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     - **Detect**
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           - **Report FU**
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             - **PLHIV in need**
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             - **Stable PLHIV**
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             - **Referral**
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             - **Enrolment**
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        - **VCCT** (VCT, Community Care and Treatment)
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           - **Referral**
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             - **HC** (Health facility)
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       - **Detect**
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       - **NGO-FS**
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       - **Detect**
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       - **Report FU**
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       - **PLHIV in need**
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       - **Stable PLHIV**
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       - **Referral**
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       - **Enrolment**
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       - **VCCT** (VCT, Community Care and Treatment)
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           - **Referral**
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             - **HC** (Health facility)
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       - **Detect**
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       - **NGO-FS**
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       - **Detect**
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       - **Report FU**
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       - **PLHIV in need**
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       - **Stable PLHIV**
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       - **Referral**
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       - **Enrolment**
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       - **VCCT** (VCT, Community Care and Treatment)
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           - **Referral**
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             - **HC** (Health facility)
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       - **Detect**
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       - **NGO-FS**
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       - **Detect**
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       - **Report FU**
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       - **PLHIV in need**
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       - **Stable PLHIV**
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       - **Referral**
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       - **Enrolment**
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       - **VCCT** (VCT, Community Care and Treatment)
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           - **Referral**
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             - **HC** (Health facility)
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       - **Detect**
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       - **NGO-FS**
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       - **Detect**
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       - **Report FU**
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       - **PLHIV in need**
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       - **Stable PLHIV**
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       - **Referral**
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       - **Enrolment**
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       - **VCCT** (VCT, Community Care and Treatment)
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           - **Referral**
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             - **HC** (Health facility)
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       - **Detect**
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       - **NGO-FS**
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       - **Detect**
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       - **Report FU**
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       - **PLHIV in need**
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       - **Stable PLHIV**
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       - **Referral**
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       - **Enrolment**
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       - **VCCT** (VCT, Community Care and Treatment)
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           - **Referral**
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             - **HC** (Health facility)
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       - **Detect**
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       - **NGO-FS**
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       - **Detect**
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       - **Report FU**
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       - **PLHIV in need**
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       - **Stable PLHIV**
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       - **Referral**
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       - **Enrolment**
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       - **VCCT** (VCT, Community Care and Treatment)
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           - **Referral**
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             - **HC** (Health facility)
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       - **Detect**
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       - **NGO-FS**
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       - **Detect**
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       - **Report FU**
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       - **PLHIV in need**
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       - **Stable PLHIV**
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       - **Referral**
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       - **Enrolment**
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       - **VCCT** (VCT, Community Care and Treatment)
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           - **Referral**
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             - **HC** (Health facility)
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       - **Detect**
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       - **NGO-FS**
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       - **Detect**
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       - **Report FU**
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       - **PLHIV in need**
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       - **Stable PLHIV**
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       - **Referral**
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       - **Enrolment**
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       - **VCCT** (VCT, Community Care and Treatment)

**Key informants**
- Local authorities for General Population
- Community networks for Key populations

**Identify-Reach**
- Finger prick:
  - Outreach
  - Fixed sessions
  - Events
  - Social network

**Intensify-Retain**
1. Referrals of new reactive cases
2. Lost to follow-up
3. Support to PLHIV in greatest needs (poor PLHIV and still unstable on ART)
4. Community ARV delivery (stable PLHIV)

**Health Equity Fund**
- Adherence
- Retention
- VL suppression

**B-IACM**
- CMC/CMA, GOC
First IR strategy among KP

HIV services
VCCT and ART

GOC-OD

PASP Partners

Health facility

Community

Key informants
Remork drivers
Brokers
Peers...

HIV reactive

Community HTC

NGO-FS

Self testing?
For specific groups if available

HIV reactive

OW

OW

OW

Routine Outreach

High Technology

High risk Key Populations
(EW, MSM, TG, PWID/PWUD)

PDI
Community outreach finger prick testing among targeted general population
Streamlining HTC procedures and referral:
among targeted general populations, 2017-2020

Referral Hospital with VCCT/ART
(Confirmatory test and ART) “Test and Treat

PITC

Every Health Center/Health Post
“HIV finger prick testing”

Follow-up Refer

Targeted general populations

Community outreach “HIV finger prick testing by NGO-FS/CV (VHSG) (High Confidentiality)

Patient referral if (reactive)

Walk-in

Patient referral if
(reactive)
Main Challenges

- Reaching and serving highest risk populations (KP and targeted general populations)
- Partner notification/involvement
- Scarcity of resources (human, money)
- Fragmented health and community systems (PHC, TB, Malaria etc)
- Program efficiency, Cost effectiveness, Financial sustainability

How to scale rapidly B-IACM (IRIR strategic approach)?
កិច្ចប្រជ ុំផ្សព្វផ្ាយគោលការណ៍ ណណ ជាតិ ស្ដីព្ី ការណែទុំ - ព្ាបាលជុំងឺ កាស្និយ មនុស្ស ការ ព្ាបាលគោយ ឱស្ែប្រឆុំងគមគោគគេដស្៍ ស្ុំោរ់ មន ស្សគព្ញវ័យ គកេងជុំទង់ និង ក មារ ថ្ែៃទី ២ ៨ វិច្ឆិកា ឆ ន ុំ ២០១៦
Treat All Overview

Dr Laurent Ferradini
World Health Organization
“Treat All” to end AIDS

WHO Treat All policy uptake and practice

HIV management guidelines dissemination

Laurent Ferradini, WHO Cambodia
Phnom Penh, 28 Nov. 2016
### Global summary of the AIDS epidemic | 2015

<table>
<thead>
<tr>
<th>Number of people living with HIV in 2015</th>
<th>Total 36.7 million [34.0 million – 39.8 million]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adults</td>
<td>31.8 million [30.1 million – 33.7 million]</td>
</tr>
<tr>
<td>Women</td>
<td>16.0 million [15.2 million – 16.9 million]</td>
</tr>
<tr>
<td>Children (&lt;15 years)</td>
<td>3.2 million [2.9 million – 3.5 million]</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>People newly infected with HIV in 2015</th>
<th>Total 2.1 million [1.9 million – 2.4 million]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adults</td>
<td>1.9 million [1.7 million – 2.1 million]</td>
</tr>
<tr>
<td>Children (&lt;15 years)</td>
<td>240 000 [210 000 – 280 000]</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>AIDS deaths in 2015</th>
<th>Total 1.1 million [940 000 – 1.3 million]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adults</td>
<td>1.3 million [1.2 million – 1.5 million]</td>
</tr>
<tr>
<td>Children (&lt;15 years)</td>
<td>190 000 [170 000 – 220 000]</td>
</tr>
</tbody>
</table>
Decline in HIV incidence and mortality over time

- People dying from AIDS-related causes globally
- People newly infected with HIV/AIDS globally

Declines in HIV incidence are stalling.
Global 2020 and 2030 targets

Number of people dying from HIV

- 2005: 2.0m
- 2000/2010: 1.5m
- 2015: 1.1m
- 2020: <500k
- 2030: <400k

Number of people newly infected with HIV

- 2000: 3.2m
- 2005: 2.5m
- 2010: 2.2m
- 2015: 2.1m
- 2020: <500k
- 2030: <200k
Global ART coverage over time
Evolution of global ART coverage and eligibility criteria according to WHO guidelines (2013 – 2016)
Each successive guideline expansion was associated with a greater proportion of persons initiating ART at the original site of enrollment.

- Greater improvements observed in Burundi, especially when guidelines expanded from CD4<350 to 500
- Sites in Rwanda followed a similar pattern, except the improvements were not as pronounced when guidelines expanded from CD4<350 to 500

The time from enrollment to ART initiation shortened with guideline expansion. Patients are initiating ART sooner after enrollment under expanded guidelines.

- Slightly greater improvements among women when pregnancy criteria added, relative to men
CIPRA and SMART studies: ART start at CD4 ≤ 350 cells/mm³ led to improvements in HIV mortality, disease progression, & co-morbidities (TB)

Observational studies: ART start at CD4 > 350 cells/mm³ improved mortality, disease progression & non-AIDS events

TEMPRANO and START studies show that ART start at CD4 > 500 cells/mm³ markedly reduced transmission and lowered risk of TB

HPTN 052 showed that ART start at CD4 > 500 cells/mm³ markedly reduced transmission and lowered risk of TB

2005-2010

2010-2013

2015

Temprano/START represent the end of a chain of evidence that has led us to the point of universal ART
Temprano is one of the main studies that has driven the recommendation for universal ART

- Côte d’Ivoire (9 centres in Abidjan)
- HIV-infected adults with CD4 <800 cells/µL, not otherwise eligible for ART
- Multicentre randomised trial (4 arms) comparing:

<table>
<thead>
<tr>
<th>ART WHO-guided</th>
<th>No IPT</th>
<th>IPT</th>
</tr>
</thead>
<tbody>
<tr>
<td>WHO-guided ART, no IPT (N=511)</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>Immediate ART, no IPT (N=515)</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>WHO-guided ART, IPT (N=512)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Immediate ART, IPT (N=518)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

(Definitions of WHO-guided changed as the guidelines evolved so about half of the patients were enrolled under 2006 guidelines (<200 CD4) and half under the 2010 guidelines (<350 CD4))

Comparing early ART with deferred \( p=0.0002 \)

Early ART was beneficial in all and also those with CD4 ≥500

Comparing early ART with deferred \( p=0.027 \)

The START trial: When looking at the primary outcome (death or severe disease), immediate ART was protective

- Enrolled over 4000 people with CD4>500 at 211 sites in 35 countries
- Study design: patients randomized to either early start or waiting until CD4 fell below 350
- Overall there were 42 “events” in the immediate arm and 96 in the deferred arm (p<0.001)
- No difference in drug toxicities between arms and no evidence of harm caused by ART
- Trial was closed early by the DSMB because of higher than expected benefit of ART


Reach the Treatment targets by 2020
What’s new in the ARV Guidelines?

- **Treat all** - PLHIV of all ages and populations are eligible to start at any CD4 cell count

- **Using ARVs for Prevention** – Pre-exposure prophylaxis (PrEP) to prevent HIV among people at significant risk of HIV

- **Optimized ARV regimens** – new ARV drug classes and better formulations

- **Improved service delivery approaches** - to reach all people at all ages, differentiated care package

- **Health systems strengthening** – to avoid ARV stocks-out and risk the development of HIV drug resistance, service integration
Treat All - Challenge

Number of people receiving ART

- 2000: 770k
- 2005: 2.2m
- 2010: 7.5m
- 2015: 17m
- Mid-2016: 18.2 m [16.1 – 19.0 m]

2020: 30.0m

2030: 37.0m

End AIDS
Treat All: Treatment Gap

Global number of PLHIV ~ 37 M

CD4 > 500
+8 M

CD4 < 500
+12 M

17 M on ART

+20M Treatment gap with Treat all

Cost 31B USD per year by 2020 (50% treatment cost)
Treat All: a top priority for WHO

“TREAT ALL”
FROM POLICY TO ACTION — WHAT WILL IT TAKE?

THURSDAY, 9 JUNE, 13:00-14:30
CONFERENCE ROOM 11, UNITED NATIONS

CO-CHAIRS: Ren Minghui, WHO Assistant Director-General and Aaron Motsoaledi, Minister of Health, South Africa. SPEAKERS INCLUDE: Piyasakol Sakolsatayadorn, Minister of Public Health, Thailand; Raymonde Goudou Coffie, Minister of Health, Côte D’Ivoire; Marisol Touraine, Minister of Health, France; Ambassador Deborah Birx, PEPFAR, USA; Wu Zunyou, Department of Disease Control, China; and Loyce Maturu, Africanaid Zvandiri, Zimbabwe. MODERATED BY Gottfried Hlinschall, Director, WHO Department of HIV.

JOIN THE EVENT

COSPONSORED BY: CÔTE D’IVOIRE, SOUTH AFRICA, THAILAND, THE UNITED STATES OF AMERICA
Methods: Adoption and implementation of WHO Policy recommendations

- Triangulated baseline surveys from dissemination meetings, annual e-surveys with national MoH HIV Programme Managers (PM), peer reviewed literature, National Strategic plans and concept notes

- Compared to end **2015 Global AIDS Response Progress Reporting (GARPR)**; discrepancies verified at country level with HIV PMs

- Present adoption & implementation of priority policies through July 2016 for both 144 LMIC & 35 Fast Track Countries

- Housed in WHO Country Intelligence database
Movement to ‘Treat All’ is happening
Policy uptake for adults and adolescents, October 2016

85% of the 35 most heavily burdened (‘fast-track’) countries have adopted WHO treatment recommendations
Implementation is just getting underway and the majority of countries have not yet fully put the policy into practice for Treat All.
The success story of ‘treat all’ for pregnant women, July 2016

Uptake of Option B+ in the treatment of HIV positive pregnant women in low- and middle-income and Fast-Track countries (situation as of July 2016)

The boundaries and names shown and the designations used on this map do not imply the expression of any opinion whatsoever on the part of the World Health Organization concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. Dotted and dashed lines on maps represent approximate border lines for which there may not yet be full agreement.
Option B+ has been one of the most widely adopted WHO recommendations, July 2016

Overall, 88% of 144 LMICs have adopted the Option B+ approach to provide lifelong ART to pregnant and breastfeeding women.
“Treat All” and this shift is happening for children and adolescents

BUT WE STILL NEED TO DIAGNOSE SOONER AND TREAT BETTER
90% of LMIC adopted TDF + 3TC (or FTC) + EFV as the preferred first-line therapy

TDF/XTC/EFV adopted widely
July 2016
Framework for Differentiated approach to care and services

- WHO recognizes that one size for all will not work as HIV programmes continue to expand
- Differentiated services allow for a public health approach that maximizes the benefit for PLHIV and for the health care system

**Figure 6.1. Key factors in differentiated approaches to HIV care (5)**

- **Early**
  - Adherence & retention support

- **Advanced**
  - Minimal clinical package to reduce illness and death

- **Stable**
  - Simplified ART delivery - Differentiated Care Models

- **Unstable**
  - Adherence support vs Switching

- Service intensity
- Service frequency
- Health worker cadre
- Service location
- People living with HIV

- ART initiation and refills
- Clinical monitoring
- Adherence support
- Laboratory tests
- OI treatment
- Psychosocial support
- Monthly
- Biannually
- Every 3 months
- Every 6 months
- Physician
- Clinical officer
- Nurse
- Pharmacist
- Community health worker
- Patient, peers and family

World Health Organization
Improved service delivery through differentiated models of care

New recommendations for:

- Linkage to care with Rapid initiation of ART
- Adherence
- Retention
- “people-centered” integration with other services including TB, Hepatitis, STIs and NCDs

New policies to improve programme efficiency:

- Less frequent clinic visits
- Less frequent medication pick-up visits for stable patients
- Trained lay providers can distribute ART in the community
Uptake of Service delivery recommendations, July 2016
Uptake of Co-infection recommendations
July 2016

- Isoniazid preventive therapy (IPT) for people living...
- Intensified TB case finding in PLHIV
- Co-trimoxazole prophylaxis
- TB infection control in HIV health-care settings
- Hepatitis B screening in antiretroviral therapy clinics
- Hepatitis C management in antiretroviral therapy clinics
- Hepatitis B vaccination provided at antiretroviral...
- Hepatitis C treatment provided in antiretroviral...
- Other

Tuberculosis  
Hepatitis
Conclusions
WHO World AIDS Day 2016 Key messages

• Fewer people are dying from HIV due to the expansion of HIV treatment but *declines in HIV incidence are stalling.*

• Achieving the global target to end AIDS by 2030 will require rapid and effective implementation of the WHO "treat all" recommendations and *prevention efforts need to be revitalized.*

• Countries are rapidly adopting new WHO treatment recommendations but *full implementation still on the way.*

• *Certain populations continue to be left behind* (adolescent girls/young women and key population groups such as MSM, SW, PWID, TG people and others) in all regions.

• Reaching these groups requires innovations in the delivery of HIV services beyond health facilities, *including access to self-testing.*

• Lack of knowledge of HIV status is a major barrier to accessing treatment: WHO issuing *new guidelines to recommend HIV self-testing and partner notification services.*

• Innovations in HIV technologies, medicines and service delivery approaches provide opportunities for *accelerating the response.*
Acknowledgements

WHO team
- Gottfried Hirnschall
- Meg Doherty
- Deng Serongkea
- Linh-Vi Le
- Naoko Ishikawa
- Ying-Ru Lo

Thank you!
កិច្ចប្រជ ុំផ្សព្វផ្ាយគោលការណ៍ ណណ ជាតិ ស្ដីព្ីការណ៍ព្រះបាលនិងការព្រះបាលគោយ ការ អភិវឌ្ឍន៍ និងការអភិវឌ្ឍន៍រកប្រការ កសិកម្ម ការផ្តល់សេវាកម្ម ក្នុងប្រទេស និងការផ្តល់សេវាកម្មនៅក្នុងការប្រការ ក្នុងប្រទេស។

ប្រការឈឺបែបសម្រាប់ក្នុងឆ្នាំ ២០១៦ ប្រការឈឺបែបសម្រាប់ក្នុងឆ្នាំ ២០១៧
Summary of Guidelines: What’s New
Dr Ngauv Bora
NCHADS
Objective

• Summary of the key changes of the 3 revised guidelines for the clinical management of HIV infection in Cambodia:
  - National HIV Clinical Management Guidelines for Adults and Adolescents
  - Guidelines for Management of Common and Opportunistic Infections in HIV-infected Infants, Children and Adolescents in Cambodia
  - Guidelines for Diagnosis and Antiretroviral Treatment of HIV Infection in Infants, Children and Adolescents in Cambodia
Guideline development process

- The format, scope, and key content updates were agreed during series of NCHADS TWG meetings.
- Direct consultation with Cambodian HIV clinicians and observation at HIV treatment centres.
- Literature review and documentation:
  - Previous Cambodian guidelines
  - 2015 updated WHO guidelines for HIV, TB, Viral Hepatitis, and NCD
  - Other HIV guidelines from USA, Australia, Vietnam, Thailand, PNG, South Africa and MSF HIV TB guidelines
  - Relevant published international research, and direct communication with international experts
WHO guidelines:

Consolidated Guidelines on the use of ARV drugs for treating and preventing HIV infection

What’s New? Nov 2015
Second edition 2016
Key messages from the 2016 WHO guidelines

• Treat all (at any CD4) - PLHIV across all ages, but the sickest remain a priority (symptomatic disease and CD4 < 350)

• Phased introduction of optimised regimens (new drug class; optimised dosing and formulations)

• Differentiated care packages to optimise the care cascade (reduce late presentation, improve retention).

• PrEP recommended as an additional prevention choice for all people at substantial risk of HIV infection.
HIV Guidelines in Cambodia: Formats

• Adults and Adolescents:
  ✓ One consolidated guideline, including sections on antiretroviral therapy and opportunistic infections, which were previously contained in two separate documents.

• Infants, children and adolescents:
  ✓ Opportunistic infection guidelines
  ✓ ART guidelines
The scope of the adult and Adolescent guidelines has been expanded to meet the current clinical needs of PLHIV:

- ART
- OI
- Adolescent transition to adult care
- Viral hepatitis
- Monitoring and prevention of non-communicable diseases (NCD)
- Mental health, including HIV related dementia
- Post exposure prophylaxis (occupational + non occupational)
## Criteria to start antiretroviral therapy

### Adults and adolescents:

**Who should start ART**
- ALL regardless of CD4 count
- Priority should be given to:
  - PLHIV with WHO clinical stage III/IV or CD4 ≤ 350
  - Pregnant and breastfeeding women (Option B+)
  - PLHIV with HBV, and TB co-infections

**When to start ART**
- Within 2 weeks after enrolment following preparedness and completion of ART counseling.
- With some opportunistic infections, delay in ART initiation are required after initiating OI treatment
  - Cryptococcosis meningitis: 4-6 weeks
  - TB with CD4 > 50: 2-8 weeks

### Children:

TREAT ALL

*ALL CHILDREN REGARDLESS OF CD4 AND/OR CLINICAL STAGE SHOULD START ART AS SOON AS POSSIBLE, PREFERENCESLY WITHIN 2 WEEKS OF DIAGNOSIS*
When to start ART when active OI

<table>
<thead>
<tr>
<th>Opportunistic Infection</th>
<th>Time from start treatment for OI and start ART</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tuberculosis</td>
<td></td>
</tr>
<tr>
<td>CD4 &lt; 50 cells/mm³</td>
<td>Within 2 weeks</td>
</tr>
<tr>
<td>CD4 &gt; 50 cells/mm³</td>
<td>2 – 8 weeks</td>
</tr>
<tr>
<td>Cryptococcal meningitis (CM)</td>
<td>4 – 6 weeks</td>
</tr>
<tr>
<td>Cryptococcus non-meningeal disease including Cryptococcal Ag + CSF neg</td>
<td>Within 2 weeks</td>
</tr>
<tr>
<td>All other OI</td>
<td>Within 2 weeks</td>
</tr>
</tbody>
</table>
## 1st line ART

### Adults and adolescents:

<table>
<thead>
<tr>
<th>Age</th>
<th>Preferred first line</th>
<th>Alternative first line*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adults</td>
<td>TDF + 3TC + EFV</td>
<td>AZT+ 3TC + EFV (or NVP)</td>
</tr>
<tr>
<td>Including pregnant/ breastfeeding and with TB and HIV co-infection</td>
<td></td>
<td>TDF + 3TC + NVP</td>
</tr>
<tr>
<td><strong>Adolescents &gt; 35kg</strong></td>
<td>TDF + 3TC + EFV</td>
<td>AZT+ 3TC + EFV (or NVP)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>TDF + 3TC + NVP</td>
</tr>
<tr>
<td><strong>Adolescents &lt; 35kg</strong></td>
<td>TDF + 3TC + EFV</td>
<td>ABC + 3TC + NVP</td>
</tr>
</tbody>
</table>

*ABC or PI or when available Dolutegravir may be required in special situations as alternative 1st line agents. Consult with an expert.

### Children:

<table>
<thead>
<tr>
<th>Age</th>
<th>Preferred regimen</th>
<th>Alternative</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;3 years or &lt;10kg</td>
<td>ABC + 3TC + LPV/r</td>
<td>ABC/ AZT + 3TC + NVP</td>
</tr>
<tr>
<td></td>
<td>After 1 year, confirmed VL suppression and switch to: ABC/AZT + 3TC + NVP</td>
<td></td>
</tr>
<tr>
<td>≥ 3- &lt; 10 years and ≥10kg</td>
<td>ABC + 3TC + EFV</td>
<td>ABC/AZT + 3TC + NVP</td>
</tr>
<tr>
<td>≥ 10 years and &gt;35kg</td>
<td>TDF + 3TC + EFV</td>
<td>ABC/AZT + 3TC + NVP/EFV</td>
</tr>
</tbody>
</table>
### Monitoring antiretroviral therapy

#### Reducing the use of CD4 and scaling-up VL

When to start / continue and stop CD4 monitoring?

<table>
<thead>
<tr>
<th>Start / continue</th>
<th>Baseline CD4 then 6 monthly until stopping criteria are fulfilled</th>
</tr>
</thead>
<tbody>
<tr>
<td>Criteria to Stop CD4 monitoring*</td>
<td>On ART for at least 1 year and all of the following:</td>
</tr>
<tr>
<td></td>
<td>• No adverse drug reactions requiring regular monitoring,</td>
</tr>
<tr>
<td></td>
<td>• No current illness, and not on TB treatment</td>
</tr>
<tr>
<td></td>
<td>• Not pregnant</td>
</tr>
<tr>
<td></td>
<td>• Good understanding of lifelong adherence</td>
</tr>
<tr>
<td></td>
<td>• 2 x CD4 &gt; 350 cells/ mm³</td>
</tr>
<tr>
<td></td>
<td>• 2 x undetectable VL</td>
</tr>
<tr>
<td></td>
<td>• Routine VL monitoring is available</td>
</tr>
<tr>
<td>Check CD4 again</td>
<td>Virological failure → recommence CD4 algorithm</td>
</tr>
<tr>
<td></td>
<td>Pregnancy → recommence algorithm if &lt; 350 +/- or VL detectable.</td>
</tr>
</tbody>
</table>
CD4 testing

- CD4 at baseline and every 6 M whilst on cotrimoxazole
- If routine VL is available, no need for ongoing routine CD4.
- Repeat CD4 if VL failure confirmed.
Viral load

- Routine viral load monitoring
- M6 after start or change ART regimen
- Then every 12 months
- Pregnant women test VL M3 after start ART
- If on ART do VL early in pregnancy
- Control VL after 3 months adherence boosting when VL found detectable
2\textsuperscript{nd} line ART

- Switch to 2\textsuperscript{nd} line regimen if the control VL after 3 months adherence boosting is > 1,000 copies/ml (even if it has decreased +++)

- Check VL 6 months after starting 2\textsuperscript{nd} line regimen
### 2nd line ART

#### Adults and adolescents:

<table>
<thead>
<tr>
<th>Failed 1st line regimen</th>
<th>Preferred second line</th>
</tr>
</thead>
<tbody>
<tr>
<td>TDF + 3TC + NNRTI</td>
<td>AZT + 3TC + ATV/r</td>
</tr>
<tr>
<td></td>
<td>(if HBsAg negative)</td>
</tr>
<tr>
<td></td>
<td>TDF + 3TC + AZT + ATV/r</td>
</tr>
<tr>
<td>AZT (or d4T) + 3TC + NNRTI</td>
<td>TDF + 3TC + ATV/r</td>
</tr>
<tr>
<td>If failed 1st line including a PI</td>
<td>Consult an expert</td>
</tr>
</tbody>
</table>

#### Children:

<table>
<thead>
<tr>
<th>Children</th>
<th>First line</th>
<th>Preferred 2nd line regimen</th>
<th>Alternative 2nd line regimen</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>ABC/AZT+3TC+LPV/r</td>
<td>No change from first line regimen</td>
<td>AZT (or ABC) +3TC + NVP/EFV$</td>
</tr>
<tr>
<td></td>
<td>ABC/AZT+3TC+EFV or NVP</td>
<td>AZT (or ABC) + 3TC + LPV/r *</td>
<td>TDF+ 3TC + LPV/r *</td>
</tr>
<tr>
<td>Adolescents (&gt;10-19 y)</td>
<td>TDF/AZT+3TC+EFV</td>
<td>AZT/TDF# + 3TC + ATV/r (if &gt;40kg)*</td>
<td>AZT/TDF + 3TC + LPV/r*</td>
</tr>
</tbody>
</table>
ART key updates

- ART for all, regardless of CD4 count
- First line ART: TDF + 3TC + EFV (including PW)
- Second line ART: 2NRTI + ATV/r
- EFV 400mg equivalent to 600mg
  - Except pregnant women and rifampicin co-administration
  - Plan for transition once available
- ART monitoring:
  - Reduced use of CD4
  - Routine VL
## Clinic visit routine schedule

<table>
<thead>
<tr>
<th>Week</th>
<th>Clinical</th>
<th>Adherence counseling</th>
<th>Laboratory testing</th>
<th>Drugs start /Stop</th>
</tr>
</thead>
<tbody>
<tr>
<td>Week 0</td>
<td>✔</td>
<td>✔</td>
<td>✔</td>
<td>Start Cotrimoxazole</td>
</tr>
<tr>
<td>Week 1</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Week 2</td>
<td>✔</td>
<td>✔</td>
<td></td>
<td>Start cART</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Stop Cotrimoxazole if CD4 &gt; 350 and no TB</td>
</tr>
<tr>
<td>After start ART</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Week 2</td>
<td>✔</td>
<td>✔</td>
<td></td>
<td>Start IPT</td>
</tr>
<tr>
<td>Month 1</td>
<td>✔</td>
<td>✔</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Every 1 M whilst on IPT</td>
<td>✔</td>
<td>✔</td>
<td>✔ VL at month 567</td>
<td>Stop IPT after 6 months</td>
</tr>
<tr>
<td>After stop IPT, still on Cotrimoxazole</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Every 1 – 3 months (According to clinical status, + adherence)</td>
<td>✔</td>
<td>✔</td>
<td>✔ VL at M 567 then M 11132, M 232425 etc</td>
<td>Stop Cotrimoxazole according to criteria (see Error! Reference source not found. page 34 )</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>✔ CD4 every 567 M</td>
<td></td>
</tr>
<tr>
<td>After stop Cotrimoxazole</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Every 1 – 3 months</td>
<td>✔</td>
<td>✔</td>
<td>✔ VL at every 11132,13 Months</td>
<td></td>
</tr>
</tbody>
</table>
Objective:

• **Support transition to adult care, + provide adolescent appropriate care**
  - The adult HIV care service needs to cooperate with paediatric care providers at operational and individual patient levels to support the transition of adolescents into their care and to ensure their service is “adolescent friendly”.

• **The goals of successful transition**: are that the individual is retained in care, remains adherent to cART, develops the capacity to take measures to reduce the risk of onward transmission of HIV, and that they receive the clinical and psychosocial support required to transition into a physically and psychologically healthy adult.

---

### 4. ADOLESCENTS

| ORGANIZATIONAL ARRANGEMENTS FOR ADOLESCENT CARE IN ADULT HIV CLINICS | 31 |
| PSYCHOSOCIAL SUPPORT | 32 |
| SPECIFIC ISSUES TO ADDRESS WITH ADOLESCENTS | 32 |
| Clinical issues | |
PMTCT: What’s new?

- **HIV+ pregnant women:**
  - TDF +3TC (or FTC) + EFV (Fixed-Dose Combination) regardless of WHO stage and CD4 count and continue lifelong (option B+)

- **HEI:**
  - HIV DNA-PCR at birth
  - Infants should be vaccinated as per the Expanded Program on Immunizations (EPI) schedule, including BCG
  - Nevirapine (NVP) prophylaxis is given at birth for **6 weeks** to all HIV-exposed children in not in high-risk situations of HIV transmission
  - Dual Nevirapine (NVP) and Zidovudine (AZT) prophylaxis is given at birth to all HIV-exposed infants in high-risk situations.
### PMTCT: What’s new?

<table>
<thead>
<tr>
<th>Mother</th>
<th>Risk Status of HIV Exposed Infant HIV</th>
<th>Infant feeding status</th>
<th>Infant prophylaxis ( *)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Urgently initiate:</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>TDF +3TC (or FTC) + EFV (Fixed-Dose Combination)</strong></td>
<td>High Risk situations: 1- Mother on ART who have received less than 4 weeks of ART at the time of delivery or 2- Mother diagnosed HIV positive at delivery or during post partum period. 3- Mother with established HIV infection with VL &gt;1000 copies/mL in the 4 weeks before delivery, if VL available 4- Mother with incident HIV infection during pregnancy or breastfeeding</td>
<td>Formula feeding</td>
<td>Dual NVP and AZT for 6 weeks</td>
</tr>
<tr>
<td></td>
<td>Low Risk situations: Not fall in the high risk situations.</td>
<td>Breast feeding or formula feeding</td>
<td>NVP for 6 weeks</td>
</tr>
<tr>
<td></td>
<td>Breast feeding</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

- **Urgently initiate:**
  - TDF +3TC (or FTC) + EFV (Fixed-Dose Combination)
  - Regardless of WHO stage and CD4 count
  - And continue lifelong (option B+)

- **High Risk situations:**
  1. Mother on ART who have received less than 4 weeks of ART at the time of delivery.
  2. Mother diagnosed HIV positive at delivery or during postpartum period.
  3. Mother with established HIV infection with VL >1000 copies/mL in the 4 weeks before delivery, if VL available.
  4. Mother with incident HIV infection during pregnancy or breastfeeding.

- **Low Risk situations:**
  - Not fall in the high risk situations.

Formula feeding: Dual NVP and AZT for 6 weeks.
Breast feeding: Dual NVP and AZT for 6 weeks then continue NVP alone for another 6 weeks.
NVP for 6 weeks.
Breastfeeding:

- Mothers living with HIV should breastfeed for at least 12 months and can continue breastfeeding for up to 24 months or longer (as for the general population) while being fully supported for ART adherence.

- Mothers living with HIV and healthcare workers can be reassured that ARV treatment is effective at reducing the risk of postnatal HIV transmission in the context of mixed feeding and that mixed feeding in itself is not a reason to stop breastfeeding.

- Mothers living with HIV and healthcare workers can be reassured that shorter durations of breastfeeding less than 12 months are better than never initiating breastfeeding.
Definition of Lost to Follow-up

WHO consolidated Strategic Information Guidelines 2015:

Definitions of linkage, enrolment and retention in HIV care

Linkage to HIV care is defined as the duration of time starting with HIV diagnosis and ending with enrolment in HIV care or treatment.¹

Enrolment in HIV care begins when a person with HIV presents to the facility where HIV care is provided and a patient file or chart is opened. WHO recommends that all patients be enrolled in HIV care at their first facility visit following an HIV-positive diagnosis (which may take place on the same day as the HIV diagnosis).

Retention in HIV care describes when a patient who is enrolled in HIV care routinely attends these services, as appropriate to the need. This excludes people who have died or were lost to follow-up.

Lost to follow-up (LFU): Three months or more (90 days or more) since last missed appointment.

Definition of Lost to Follow-up

Current definition:

New definition in Cambodia:
Prevention of Opportunistic Infections What’s new?

1. TB screening and Isoniazid Preventive Therapy (IPT)
2. Cotrimoxazol (CTX)
3. Cryptococcoal antigen (CrAg) for cryptococcal prophylaxis
TB screening and IPT

WHO Algorithm for TB screening for Adult and Adolescent with HIV:

- Adults and adolescents living with HIV:
  - Screen for TB with any one of the following symptoms:
    - Current cough
    - Fever
    - Weight loss
    - Night sweats
  - If > 40kg: Isoniazid 300mg / day + pyridoxine 50mg / day
  - If ≤ 40kg: Isoniazid 200mg / day + pyridoxine 50mg / day

NOT NEW TO BE REINFORCED

Screen for TB regularly at each encounter with a health worker or visit to a health facility

IPT = 6 month course:
- If > 40kg: Isoniazid 300mg / day + pyridoxine 50mg / day
- If ≤ 40kg: Isoniazid 200mg / day + pyridoxine 50mg / day
Criteria to start, continue, and stop IPT:

<table>
<thead>
<tr>
<th>IPT</th>
<th>TB symptom screening should be performed at EVERY clinic visit</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>When to start IPT</strong></td>
<td>- All patients with TB symptom negative and no contraindications (Contraindications: peripheral neuropathy, heavy alcohol consumption, ALT/AST &gt; 3 x ULN).</td>
</tr>
<tr>
<td>(Adults and adolescents)</td>
<td>- Patients who TB symptom screen positive; start IPT after elimination of active TB.</td>
</tr>
<tr>
<td></td>
<td>- After completion of TB treatment (secondary prophylaxis)ADERE</td>
</tr>
<tr>
<td></td>
<td><em>Start IPT at the first follow up visit after commencing ART, provided the patient is tolerating ART and is clinically stable. Otherwise start as soon as stable on ART.</em></td>
</tr>
<tr>
<td><strong>Continue IPT</strong></td>
<td>- Complete 6 months (if treatment interruption, see below)</td>
</tr>
<tr>
<td><strong>When to stop IPT</strong></td>
<td>- If symptoms of hepatitis (anorexia, nausea, vomiting, abdominal pain, chills, icterus and dark urine), stop INH immediately and seek the HIV clinic</td>
</tr>
<tr>
<td></td>
<td>- If increase of ALT/AST under monitoring of patients with risk of liver disease:</td>
</tr>
<tr>
<td></td>
<td>▪ Asymptomatic and ALT/AST &gt; 5 x ULN or</td>
</tr>
<tr>
<td></td>
<td>▪ Symptomatic and ALT/AST &gt; 3 x ULN</td>
</tr>
<tr>
<td></td>
<td>- If persistent neuropathy after increase of pyridoxine to 100mg daily</td>
</tr>
<tr>
<td></td>
<td>- After completion of 6 months on IPT</td>
</tr>
</tbody>
</table>
Interruptions of IPT

• Patients should be advised strongly that it is critical that IPT be taken as prescribed, continuously for 6 months.

• However if there is one interruption to IPT, the following can be considered.
  – If interrupted for < 8 weeks, perform clinical TB screening and if negative continue INH and extend so total taken is equivalent to 6 months.
  – If interrupted for ≥ 8 weeks, perform clinical TB screening and if negative re-start treatment.

• If the patient interrupts IPT more than once, then do not try to reinstitute again.
Cotrimoxazole

- CD4 threshold increased to 350 cells / mm$^3$
- All adolescents until 20 years old

- Start at first visit (if CD4 unknown)
- Stop at week 2 visit if CD4 < 350 cells / mm$^3$ and no TB or WHO stage 3 or 4 conditions.

- Otherwise continue: until CD4> 350 cells / mm$^3$ 2 x 6 months apart and age ≥ 20 years old.
Cotrimoxazole

• **WHO 2014:** Moderate-quality evidence from nine observational studies supports the effectiveness of co-trimoxazole prophylaxis in reducing mortality risk among people starting ART with a CD4 cell count ≤350 cells/mm³

CD4 threshold increased to 350 cells / mm³

All adolescents (whatever CD4) until 20 year-old
Cotrimoxazole

Criteria for starting, continuing and stopping Cotrimoxazole for Adults and Adolescents including pregnant women:

<table>
<thead>
<tr>
<th>Cotrimoxazole</th>
<th>Adolescent (11-19)</th>
<th>Adults (≥20 years)</th>
</tr>
</thead>
</table>
| **When to start** | All regardless of CD4 count | · CD4 < 350 cells/mm³ *  
· All patients with TB  
· WHO stage 3 or 4 regardless of CD4 count |
| **When to continue** | ALL | · CD4 < 350 cells/mm³ and/or on TB treatment  
If history of PCP with CD4 count > 200 cells/mm³ (secondary prophylaxis indefinitely) |
| **When to stop** | Never stop (until adult age 20 ) | · CD4 count > 350 cells/mm³ on 2 measurements at least 6 months apart and undetectable VL and completed TB treatment |

* Start cotrimoxazole at the first visit, and if the CD4 is > 350 then cease it at the next visit two weeks later
Cotrimoxazole

Criteria for starting, continuing and stopping Cotrimoxazole for HIV-exposed infants and HIV-infected children:

<table>
<thead>
<tr>
<th>Cotrimoxazole</th>
<th>HIV-exposed infant</th>
<th>All HIV-infected infants and children regardless of age or clinical stage of disease</th>
</tr>
</thead>
</table>
| **When to start** | 4-6 weeks of age | - Immediately after HIV diagnosis for all child presenting for the first time at any age > 6 weeks  
- 4-6 weeks of age as for exposed infants, and continue after diagnosis of HIV has been confirmed  
- In children with PCP, subsequent to PCP treatment being completed |
| **When to continue** | ALL | ALL |
| **When to stop** | PCR or antibody negative 6 weeks after complete cessation of breastfeeding | - if the child is anemic (bone marrow suppression) or if Grade 3/4 toxicity rash  
- until children transition to adult care, regardless of ART or CD4 recovery |
Prevention of Cryptococcus
WHO 2011 and 2016

Prevention of cryptococcal disease
The routine use of antifungal primary prophylaxis for cryptococcal disease in HIV-infected adults, adolescents and children with a CD4 count less than 100 cells/mm³ and who are CrAg negative or where CrAg status is unknown is not recommended prior to ART initiation, unless a prolonged delay in ART initiation is likely (strong recommendation, high-quality evidence).

The use of routine serum or plasma CrAg screening in ART-naive adults, followed by pre-emptive antifungal therapy if CrAg positive to reduce the development of cryptococcal disease, may be considered prior to ART initiation in:

a. patients with a CD4 count less than 100 cells/mm³; and
b. where this population also has a high prevalence (>3%) of cryptococcal antigenaemia.

(conditional recommendation, low-quality evidence).

Screen and Treat strategy
Cryptococcal Ag screening

- Simplified low cost antigen detection methods for Cryptococcal antigen (CRAG) using a Lateral Flow Assay (LFA)

- Opportunity to screen PLHIV for cryptococcal infection

- Asymptomatic cryptococcal infection, detected by CRAG test may precede clinical disease by weeks – months
Advantages of CrAg screen and treat compared with $1^0$ fluconazole prophylaxis:

Avoid treating those who are at very low risk
- Drug complexity, toxicity
- Women of child bearing age and pregnant (Pregnancy Cat C)
- Antifungal drug resistance; candida, cryptococcus

Clinical benefit
- CRAG+ triggers close evaluation and LP to look for active infection (asymptomatic CM) requiring amphotericin
- More intensive treatment of CRAG+ isolated antigenaemia
- And close monitoring after start ART for IRIS

Pre-emptive treatment
- Treatment of asymptomatic (IPCA) is safer, more accessible, and less resource intensive (outpatient, fluconazole) than when symptomatic (hospitalization, amphotericin / repeated LP)
Cryptococcus Screening and Prevention

Fluconazole prophylaxis *when CRAG test is not available*:

| When to start Fluconazole prophylaxis | CD4 < 100 cells / mm³  
*and* Not in the 1⁰ trimester of pregnancy  
*and* AST/ALT < 3x ULN* |
|--------------------------------------|--------------------------------------------------|
| When to stop Fluconazole prophylaxis | CD4 > 100 on 2 occasions > 6 months apart  
*and* VL undetectable  
Or if emergence of hepatitis:  
• AST/ALT > 3 x ULN and symptomatic,  
• or AST/ALT > 5 x ULN and asymptomatic |

* Monitor AST/ALT at baseline, 1 and 2 months, then if clinically indicated. In case of HBV /HCV co-infection or abnormal at AST/ALT at baseline, continue to monitor AST/ALT monthly till month 4.
Screen and treat *when CRAG test is available*:

- Clinical scenarios at the time of diagnosis of CRAG + include:
  1. Symptomatic cryptococcal meningitis (CM) / other cryptococcal disease
  2. Asymptomatic cryptococcal meningitis (CM)
  3. Isolated positive cryptococcal antigenaemia (ICPA)
CRAG screening algorithm

NEW

NEW

NEW

NEW
For the induction phase of treatment in HIV-infected adults, adolescents and children with cryptococcal disease (meningeal and disseminated non-meningeal), the following two-week anti-fungal regimens are recommended in order of preference.

a. Amphotericin B + flucytosine
   [Strong recommendation, high quality of evidence]

b. Amphotericin B + fluconazole
   [Strong recommendation, moderate quality of evidence]

c. Amphotericin B short course (5-7 days) + high-dose fluconazole (to complete two weeks of induction) when a minimum package of pre-emptive hydration and electrolyte replacement and toxicity monitoring and management cannot be provided for the full two week induction period.
   [Conditional recommendation, low quality of evidence]

d. Fluconazole high dose + flucytosine, when amphotericin B is not available
   [Conditional recommendation, low quality of evidence]

e. Fluconazole high dose alone, when amphotericin B is not available
   [Conditional recommendation, low quality of evidence]
## 22. HEPATITIS B

<table>
<thead>
<tr>
<th>Topic</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>HIV HBV RELATIONSHIP</td>
<td>100</td>
</tr>
<tr>
<td>HBV TRANSMISSION AND PREVENTION</td>
<td>100</td>
</tr>
<tr>
<td>DIAGNOSIS OF HBV</td>
<td>100</td>
</tr>
<tr>
<td>HBV CLINICAL DISEASE AND NATURAL HISTORY</td>
<td>101</td>
</tr>
<tr>
<td>PREGNANCY AND HBV</td>
<td>102</td>
</tr>
<tr>
<td>MANAGEMENT OF HBV HIV CO INFECTION</td>
<td>102</td>
</tr>
</tbody>
</table>

## 23. HEPATITIS C

<table>
<thead>
<tr>
<th>Topic</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>HIV HCV RELATIONSHIP</td>
<td>103</td>
</tr>
<tr>
<td>HCV TRANSMISSION AND PREVENTION</td>
<td>103</td>
</tr>
<tr>
<td>HCV CLINICAL DISEASE AND NATURAL HISTORY</td>
<td>103</td>
</tr>
<tr>
<td>DIAGNOSIS OF HCV</td>
<td>104</td>
</tr>
<tr>
<td>MANAGEMENT OF HCV HIV CO INFECTION</td>
<td>104</td>
</tr>
</tbody>
</table>

## 24. CHRONIC LIVER DISEASE

<table>
<thead>
<tr>
<th>Topic</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>CLINICAL ASSESSMENT</td>
<td>105</td>
</tr>
<tr>
<td>LABORATORY ASSESSMENT</td>
<td>105</td>
</tr>
<tr>
<td>MANAGEMENT OF CHRONIC LIVER DISEASE</td>
<td>106</td>
</tr>
</tbody>
</table>
HIV-Hepatitis B co-infection

• It is important that all patients with HIV-HBV co-infection are commenced on TDF + 3TC/FTC containing cART, and they must be continued on TDF even if need to change to 2\textsuperscript{nd} line ART

• If just one of these drugs (particularly 3TC/FTC) are used, drug resistance will develop

• Standard 2\textsuperscript{nd} line ART for HBV-HIV co-infected patients will therefore include: AZT + 3TC/FTC + TDF+ ATV/r

• HBs-Ag is ideally measured prior to starting ART, however it is not routinely required whilst the preferred 1\textsuperscript{st} line ART contains both TDF and 3TC

• HBs-Ag must be tested if there is consideration to change to 2\textsuperscript{nd} line cART, and if clinically there are abnormalities in liver function tests
HIV-Hepatitis C co-infection

- Management of HCV has been traditionally with interferon-based regimens, which are very difficult to tolerate, and have limited efficacy.
- Emerging as standard treatment are new HCV antiviral agent known as Direct Acting Antiviral Agents (DAA) which are highly effective and well tolerated, include combination oral regimens requiring 8 – 24 weeks therapy.
- The DAA variably target specific genotypes, or are pan genotypic, and are becoming available in fixed dose combinations.
- The newer regimens are also highly effective and well tolerated in HCV HIV co-infection.
- Many DAA are becoming available globally, including protease inhibitors (Simepravir, Paritaprevir), NS5A inhibitors (Ledipasvir, Ombitasvir, Daclatasvir), and NS5B inhibitors (Sofosbuvir, Dasabuvir).
- A pilot project of HCV diagnosis and treatment among co-infected HIV patients will start in 2016 in Cambodia. It is expected that access to DAA and viral load testing for HCV treatment will improve rapidly in Cambodia.
- An algorithm for the diagnosis and assessment of HCV is included in Ch 51. ANNEX HCV diagnostic algorithm.
- Some guidance for the clinical management of HIV-HCV co-infection using DAA in Cambodia will be issued soon as an addendum of the current guidelines (on-going).
### 33. NUTRITION AND WEIGHT MANAGEMENT IN HIV INFECTED ADULTS AND ADOLESCENTS

<table>
<thead>
<tr>
<th>Section</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>KEY POINTS</strong></td>
<td>133</td>
</tr>
<tr>
<td><strong>DEFINITION OF MALNUTRITION:</strong></td>
<td>133</td>
</tr>
<tr>
<td><strong>NUTRITION SCREENING AND WEIGHT MANAGEMENT</strong></td>
<td>134</td>
</tr>
<tr>
<td><strong>INITIAL EVALUATION</strong></td>
<td>134</td>
</tr>
<tr>
<td><strong>WEIGHT EVALUATION EVERY VISIT</strong></td>
<td>134</td>
</tr>
<tr>
<td><strong>UNDERWEIGHT OR LOSS OF WEIGHT: ASSESSMENT AND MANAGEMENT.</strong></td>
<td>137</td>
</tr>
<tr>
<td><strong>OVERWEIGHT: ASSESSMENT AND MANAGEMENT.</strong></td>
<td>139</td>
</tr>
<tr>
<td><strong>NORMAL WEIGHT – AT INITIAL OR FOLLOW UP VISITS</strong></td>
<td>139</td>
</tr>
<tr>
<td><strong>FOOD AND MEDICATIONS</strong></td>
<td>139</td>
</tr>
<tr>
<td><strong>NUTRITION AND PREGNANCY</strong></td>
<td>140</td>
</tr>
<tr>
<td>Food handling and safety</td>
<td></td>
</tr>
</tbody>
</table>
### Chronic NCD in PLHIV

<table>
<thead>
<tr>
<th>Section</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>34. CHRONIC NON-COMMUNICABLE DISEASES IN PLHIV</td>
<td>1</td>
</tr>
<tr>
<td><strong>Key Points</strong></td>
<td>141</td>
</tr>
<tr>
<td><strong>NCD prevention: Healthy diet and lifestyle</strong></td>
<td>141</td>
</tr>
<tr>
<td>35. SMOKING CESSATION</td>
<td>1</td>
</tr>
<tr>
<td>36. HYPERTENSION</td>
<td>1</td>
</tr>
<tr>
<td><strong>Screening, and diagnosis hypertension in PLHIV</strong></td>
<td>143</td>
</tr>
<tr>
<td><strong>Management of hypertension</strong></td>
<td>143</td>
</tr>
<tr>
<td><strong>Drug interactions with antihypertensive medicines and cART</strong></td>
<td>144</td>
</tr>
<tr>
<td>37. TYPE 2 DIABETES</td>
<td>1</td>
</tr>
<tr>
<td><strong>Screening for Diabetes in PLHIV</strong></td>
<td>145</td>
</tr>
<tr>
<td><strong>Diagnosis of Type 2 Diabetes and Impaired Glucose Tolerance</strong></td>
<td>145</td>
</tr>
<tr>
<td><strong>Management of Impaired Glucose Tolerance</strong></td>
<td>146</td>
</tr>
<tr>
<td><strong>Management of Type 2 Diabetes</strong></td>
<td>146</td>
</tr>
<tr>
<td><strong>Drug interactions between diabetes medication and cART</strong></td>
<td>147</td>
</tr>
<tr>
<td>38. HYPERLIPIDAEMIA</td>
<td>1</td>
</tr>
<tr>
<td><strong>Screening for Hyperlipidemia in PLHIV</strong></td>
<td>148</td>
</tr>
<tr>
<td><strong>Management of Hyperlipidaemia</strong></td>
<td>148</td>
</tr>
<tr>
<td><strong>Drug interactions between lipid lowering medications and cART</strong></td>
<td>149</td>
</tr>
<tr>
<td><strong>Monitoring for adverse effects</strong></td>
<td>149</td>
</tr>
<tr>
<td>39. OSTEOPOROSIS</td>
<td>1</td>
</tr>
<tr>
<td>40. KIDNEY DISEASE</td>
<td>1</td>
</tr>
<tr>
<td><strong>Investigation of Kidney Disease</strong></td>
<td>151</td>
</tr>
<tr>
<td><strong>Acute Kidney Injury</strong></td>
<td>152</td>
</tr>
<tr>
<td><strong>Chronic Kidney Disease</strong></td>
<td>152</td>
</tr>
<tr>
<td><strong>Chronic kidney disease caused by hypertension + / or diabetes</strong></td>
<td>152</td>
</tr>
<tr>
<td><strong>HIV associated nephropathy (HIV AN)</strong></td>
<td>153</td>
</tr>
</tbody>
</table>
Chronic NCD in PLHIV: Key points

• With effective ART, **PLHIV live longer**, and uncontrolled VL, immunodeficiency and opportunistic infections are less of a problem

• However HIV itself, long term ARV, and advancing age puts PLHIV at **increased risk of NCDs**

• PLHIV are at increased risk of developing a range of **metabolic and non-communicable diseases (NCDs)**, including cardiovascular disease, diabetes, chronic lung disease and cancers

• It is important that **HIV clinicians are aware of NCD**, and regularly addresses issues of **prevention** with PLHIV during consultations

• In addition PLHIV on long-term ART should be **screened for NCD** (according to this guideline) and referred for appropriate care

• HIV clinician needs to check for any **drug interactions** between ART and medications prescribed either within or outside the HIV clinic, and to monitor for **toxicity**
Recommendations for prevention and management of NCD

<table>
<thead>
<tr>
<th>The emphasis on diet and lifestyle modification will vary depending on whether the patient is under/over/normal weight and other risk factors, HT, diabetes etc.</th>
</tr>
</thead>
</table>
| **Diet:** most people need to pay attention to eat
  - More protein (tofu, beans, chicken, fish)
  - More vegetables (5 x 400 – 500gm servings vegetables and fruit per day)
  - Less fat (avoid deep fried foods, cut/skin the fat of meats e.g. pork/chicken)
  - Less sugar (soft drinks, sweets, condensed milk).
  - Less salt (prohok, MSG, fish sauce, soy sauce and salted meat or fish) instead use other flavours (e.g. lemon juice, pepper) and herbs.
  - Minimize processed foods (usually high in salt, fat, sugar)
| **Weight:** Maintain BMI between 18.5 – 22.9 |
| **Alcohol:** maximum of 2 standard drinks per day, ≥ 2 alcohol free days. |
| **No smoking** |
| **Exercise:** 30 minutes per day (e.g. brisk walking) (more if need to lose weight) |
### Post Exposure Prophylaxis (PEP)

- **Expanded to victims of sexual assault (others?)**

- **3 drug regimen:**
  TDF + 3TC + ATV/r

### Post Exposure Prophylaxis Care Pathway

#### 1. Assessment and immediate management
- **First aid**
  - Oral exposure: spit out blood/body fluids and rinse with water.
  - Wounds: wash wounds /skin sites that had contact with blood / body fluids.
  - Mucous membranes and eyes: irrigate with water /saline (remove contact lenses).
  - Do not inject antiseptics or disinfectants into wounds.
  - Do not douche the vagina or rectum after sexual exposure
- **HIV testing of the exposed and the source** (if possible)
  - Do not delay initiation of PEP around testing, it can be started and ceased if source is found to be HIV negative, or exposed is found to be HIV positive
- **Assess risk and eligibility for PEP** based on the nature of the exposure and source HIV status

#### 2. Counselling re risks and options re PEP
- Explain the estimated risk of transmission (see above)
- Explain the risks and benefits of PEP:
  - PEP significantly reduces but does not eliminate the risk of transmission
  - PEP has to be taken continuously for 28 days
  - PEP ARV side effects
- Obtain verbal informed consent to initiate PEP

#### 3. Initiate PEP as soon as possible following exposure, TAKE THE FIRST DOSE NOW!
- Check for drug interactions with any concurrent medications
- Provide adherence counseling and drug information
- Do not delay PEP whilst gathering information or filling in paperwork
- Standard PEP ARV regimen:
  - TDF 300mg + 3TC 300mg + ATV/r 300/100mg once daily x 28 days
  - Take the first dose straight away.
  - Give initial prescription / supply for XXXX days

#### 4. Assess and provide emergency contraception and STI treatment in the context of sexual exposure.
- Presumptive treatment of STI with Azithromycin 1g and Cefixime 400mg stat.
- Emergency contraception, and baseline + follow up pregnancy testing.
The term *HIV-associated neurocognitive disorder* (HAND) encompasses a spectrum from mild impairment (minor neurocognitive disorder, MND) to HIV associated dementia (HAD).

- Risk factors for HAND: advanced HIV, a low nadir CD4 prior to starting cART, older age, vascular and metabolic disease such as diabetes and HT.
- Severe forms of HAND are much less common in the era of effective cART.

Mild forms of HAND are common and often go undiagnosed, however they may contribute to poor adherence to care and treatments including cART, mood disturbance, and reduced ability to function well within the family, work and community.

<table>
<thead>
<tr>
<th>Cognitive impairment;</th>
<th>Progressive memory loss, loss of concentration, confusion and slowing of thought.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Motor symptoms;</td>
<td>Loss of balance, clumsiness, change in handwriting, tremor, unsteady gait, incontinence</td>
</tr>
<tr>
<td>Behavioral changes;</td>
<td>Apathy, social withdrawal, loss of interest in what is going on, and their own well-being.</td>
</tr>
</tbody>
</table>
Useful screening questions for depression

• During the past month, have you felt like you were losing interest or pleasure in doing things?
• Have you felt down, depressed or helpless?
• If a patient appears depressed, it is important to assess their risk for suicide:
  • Have you ever thought about giving up?
  • Have you ever thought about ending your life?
• If yes, ask about what circumstances have they thought of this, and if they have any thoughts or plans to hurt themselves?
Orthotomus chaktomuk
Cambodian tailorbird
PLHIV lifetime clinical pathway

Health issues
- HIV stage 4 conditions
  - Tuberculosis, IRIS
  - Early drug toxicity
- Well +/- Pregnancy, trauma, other illness, mental health issues, etc...
- HT, glucose intolerance, hyperlipidaemia, ETOH, smoking obesity
  + long term HIV + cART
  - CVA, IHD, diabetes, kidney disease, cancer, HAND / dementia

Cotrimoxazole until CD4 > 350
- IPT 6M
- cART
- 2nd line cART
- Viral load monitoring M6, M12, M24, M36 etc
- CD4 monitoring 6 monthly
- Weeks, Months, Years, Decades

HIV clinic visits monthly (until off IPT) → Every 1 → 3 months
Need to address NCD

Health issues:
- HIV stage 4 conditions
  - Tuberculosis, IRIS
  - Early drug toxicity
- Well +/- Pregnancy,
  - trauma, other illness,
  - mental health issues, etc...

1° Prevention:
- HT, glucose intolerance,
  - hyperlipidaemia,
  - ETOH, smoking obesity

2° Prevention:
- CVA, IHD, diabetes,
  - kidney disease, cancer,
  - HAND / dementia

+ long term HIV + cART

HIV clinic visits monthly (until off IPT) → Every 1→3 months

2Wx4

Cotrimoxazole until CD4 > 350

IPT 6M

cART

2nd line cART

Viral load monitoring M6, M12, M24, M36 etc

↑VL

M6

CD4

CD4 monitoring 6 monthly

Weeks

Months

Years

Decades
Laboratory tests timed with clinical consultations

• Laboratory tests should be performed on the same day as clinical visits.
• Clinicians should anticipate when the next VL or CD4 is due, and schedule the next visit on a day when laboratory testing is possible.
• Laboratory testing may be performed within 1 month either side of the scheduled test: eg $5_{67}$ indicates the test planned for 6M can be performed at a clinic visit any time between 5 and 7 months.
• If, for whatever reason a patient misses their scheduled CD4, or VL test, it should still be performed as soon as possible.
កិច្ចប្រជ ុំផ្សព្វផ្ាយគោលការណ៍ ណណ ជាតិ ស្ដីព្ី ការ ណែទុំ ព្ាបាលជុំងឺ ឱ កាស្និយ ម និង ការ ព្ាបាលគោយ ឱ ស្ែប្រឆុំងគមគោគគេដស្៍ ស្ុំោរ់ មន ស្សគព្ញវ័យ គកេងជុំទង់ និង ក មារ ថ្ែៃទី ២ ៨ វិច្ឆិកា ឆ ន ុំ ២០១៦

មេរះ ចាប់ វិធី ព្រឹក ដំ បុរស
Cotrimoxazole Prophylaxis
# Criteria for Cotrimoxazole prophylaxis in Children

<table>
<thead>
<tr>
<th>Start Cotrimoxazole</th>
<th>Stop Cotrimoxazole</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>HIV-exposed infant</strong></td>
<td>4-6 weeks of age</td>
</tr>
<tr>
<td><strong>All HIV-infected infants and children regardless of age or clinical stage of disease</strong></td>
<td>• Immediately after HIV diagnosis made in a child presenting for the first time at any age &gt;4-6 weeks (Primary Prophylaxis) • In children with PCP, subsequent to PCP treatment being completed (Secondary Prophylaxis)</td>
</tr>
</tbody>
</table>
Criteria for starting, continuing and stopping Cotrimoxazole for Adults and Adolescents including pregnant women (1)

<table>
<thead>
<tr>
<th>When to start cotrimoxazole</th>
<th>Adolescent (11-19)</th>
<th>Adults (≥20 years)</th>
</tr>
</thead>
<tbody>
<tr>
<td>· All regardless of CD4 count</td>
<td>· CD4 &lt; 350 cells/mm3 *</td>
<td></td>
</tr>
<tr>
<td></td>
<td>· All patients with TB</td>
<td></td>
</tr>
<tr>
<td></td>
<td>· WHO stage 3 or 4 regardless of CD4 count</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>When to continue cotrimoxazole</th>
<th>Adolescent (11-19)</th>
<th>Adults (≥20 years)</th>
</tr>
</thead>
<tbody>
<tr>
<td>· ALL</td>
<td>· CD4 &lt;350 cells/mm3 and/or on TB treatment</td>
<td></td>
</tr>
<tr>
<td></td>
<td>· If history of PCP with CD4 count &gt; 200 cells/mm3 (secondary prophylaxis indefinitely)</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>When to stop cotrimoxazole</th>
<th>Adolescent (11-19)</th>
<th>Adults (≥20 years)</th>
</tr>
</thead>
<tbody>
<tr>
<td>· Never stop</td>
<td>· CD4 count &gt; 350 cells/mm3 on 2 measurements at least 6 months apart and undetectable VL and completed TB treatment</td>
<td></td>
</tr>
<tr>
<td>· (until adult)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Criteria for starting, continuing and stopping Cotrimoxazole for Adults and Adolescents including pregnant women (2)

• **Cotrimoxazole in pregnancy and lactation**
  – The WHO endorses cotrimoxazole use as a priority intervention in pregnant PLHIV, that there is **no conclusive evidence for teratogenicity** and that the benefits of cotrimoxazole prophylaxis outweigh any potential risk.
  – Cotrimoxazole prophylaxis regimens for PLHIV are non-inferior to intermittent preventive treatment (IPT) of malaria (do not use any additional malaria IPT).

• **Drug interactions**
  – *Drugs that cause potassium retention, e.g. ACE inhibitors*—increase risk of hyperkalaemia; monitor potassium concentration.
  – Cotrimoxazole may potentiate the effects of oral hypoglycaemic agents (monitor BSL)
Cryptococcus Antigen Screening & Fluconazole Prophylaxis
Cryptococcal meningitis (CM) is a significant cause of morbidity and mortality amongst Cambodian PLHIV. It occurs mostly in advanced disease in PLHIV with CD4 < 100 cells / mm3, with those with CD4 < 50 cells / mm3 at particularly high risk.

Two previous studies in Cambodia have found ~ 20% (symptomatic and asymptomatic), and ~ 8% (asymptomatic) patients with CD4< 100 were CRAG + at the time of entry into HIV treatment.

Asymptomatic cryptococcal infection risks developing clinical life threatening cryptococcal disease in the following weeks – months.

**Detection of Cryptococcal antigen (CRAG):** Simplified low cost antigen detection methods for Cryptococcal antigen (CRAG) using a Lateral Flow Assay (LFA) provides an opportunity to screen PLHIV for cryptococcal infection, and will be available soon in Cambodia.
• CRAG test enables detection of cryptococcal infection prior to the development of symptoms.

• The CRAG testing is for screening purposes only. If a patient has symptoms of meningitis they should proceed directly to LP rather than wait for CRAG test result.

• Cryptococcal disease is very rare in children, and earlier access to ART should ensure that even fewer children develop cryptococcal disease.

• Children presenting with symptoms of meningitis and CD4 <15% (<5 years of age) or CD4 <100 cells/mm² (≥ 5 years of age) should be investigated for cryptococcal disease as outlined in the National Guidelines for common and opportunistic infections in HIV infected children in Cambodia.
Figure 7-1 Cryptococcal Antigen screening

- Newly enrolled PLHIV
  - If symptomatic of meningitis do not wait for CRAG screening. Proceed to LP (see Ch 16 Meningitis)
  - If CD4 < 100, laboratory performs CRAG test

- CRAG positive
  - Contact patient for urgent follow up
  - Screen for meningitis*
  - Check AST/ALT < 3xULN
  - Pregnancy test negative

- CRAG negative
  - Initiate ART
  - No fluconazole

- Symptomatic*
  - Start Fluconazole 1200mg AND urgent referral for LP
  - LP: opening pressure, CCAG, glucose, Micro, India Ink.

- Asymptomatic
  - *Criteria for LP
  - Any symptoms potentially meningitis:
    - Headache
    - Neck pain, photophobia, neurological signs or confusion
  - LP negative
  - Outpatient, Fluconazole 800mg daily x 2 weeks
  - Hospitalise, LP large volume

- LP positive
  - Consolidation phase: Fluconazole 400g/day x 8 weeks
  - Maintenance: 200mg/day x 1 yr + VL undetectable, CD4> 100 x 6M

- Start ART after 4 – 6 weeks of antifungal therapy
  - Start ART within 2 weeks of antifungal therapy
Criteria for starting & stopping Fluconazole Prophylaxis(1)

- **For Adult:** Fluconazole prophylaxis (when CRAG test is not available)

<table>
<thead>
<tr>
<th>When to start Fluconazole prophylaxis</th>
<th>CD4 &lt; 100 cells / mm³ and Not in the 1st trimester of pregnancy and AST/ALT &lt; 3x ULN*</th>
</tr>
</thead>
</table>

<table>
<thead>
<tr>
<th>When to stop Fluconazole prophylaxis</th>
<th>CD4 &gt; 100 on 2 occasions &gt; 6 months apart and VL undetectable</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Or if emergence of hepatitis:</td>
</tr>
<tr>
<td></td>
<td>• AST/ALT &gt; 3 x ULN and symptomatic,</td>
</tr>
<tr>
<td></td>
<td>• or AST/ALT &gt; 5 x ULN and asymptomatic</td>
</tr>
</tbody>
</table>
Criteria for starting & stopping Fluconazole Prophylaxis (2)

• **Pregnant women:**
  – Women of childbearing age who screen CRAG positive should have a pregnancy test prior to starting fluconazole (teratogenic); those who are not pregnant and are started on fluconazole should be advised to avoid pregnancy during treatment.
  – CRAG-positive patients who are pregnant should be offered an LP and discussed with an expert before a decision is made regarding management.

• **For Children:** Fluconazole prophylaxis is no longer recommended as primary prophylaxis.

(*WHO Rapid advice: diagnosis, prevention and management of cryptococcal disease in HIV-infected adults, adolescents and children. December 2011*)
TB Screening & Isoniazide Prophylaxis
TB screening and Isoniazide Preventive Therapy (IPT)

• **TB screening:**
  – initial visit, prior to initiating ART and at every follow-up visit thereafter.
  – **Symptom screening** regardless of TB treatment history, done by counsellors, nurses or doctors for the following symptoms or conditions in the last 4 weeks

**For Children**

• Living with active TB patients or ex-patients
• Failure to thrive
• Fever
• Current cough
• Enlarged cervical lymph nodes
**TB screening and Isoniazide Preventive Therapy (IPT)**

**For Adolescents and adults:**

- Cough: any time, any duration
- Fever: anytime, any duration
- Drenching night sweats: 2 weeks and above
- Loss of weight? AND weight the patients at each visit and compare with the previous visit

- PLHIV who present with cough, fever, weight loss or night sweats may have active TB and should be evaluated for TB and other diseases as well.

- Those who do not report any one of the symptoms of current cough, fever, weight loss or night sweats are unlikely to have active TB and should be offered IPT.
Indication for starting IPT:

For Children
- If no symptoms: those over 12 months of age are eligible for IPT.
- Children less than 12 months old with a household TB contact
- All children living with HIV after a successful completion of TB disease treatment

For Adolescents and Adults
- All patients with TB symptom negative and no contraindications.
- Patients who TB symptom screen positive; start IPT after elimination of active TB.
- After completion of TB treatment (secondary prophylaxis)

- Start IPT at the first follow up visit after commencing ART, provided the patient is tolerating ART and is clinically stable. Otherwise start as soon as stable on ART.
Figure 4: Isoniazid preventive therapy in children

Child more than 12 months of age living with HIV

Screen for TB with one of the following symptoms:
- Poor Weight gain
- Fever
- Current Cough
- Cervical lymph node enlargement
- Recent TB exposure

No

Contraindications for IPT? (active hepatitis/generalized neuropathy)

No
- Start IPT Daily INH (10mg/kg) x 6 months + Pyridoxine

Yes
- Defer IPT

Yes

Investigate for TB and other diseases

Other diagnosis
- Give appropriate treatment consider IPT

Not TB
- Follow up consider IPT

TB
- Treat for TB

Screen for TB regularly at each encounter with health worker or visit to a health facility

IPT should not be started in case of the following contraindications:
- Active hepatitis (acute or chronic) with ALT ≥ 2 N
- Symptoms of peripheral neuropathy

Pyridoxine dose x 6 months:
- Age <5 years, 12.5 mg daily
- Age ≥5 years, 25 mg daily
Adults and adolescents living with HIV*

Screen for TB with any one of the following symptoms¹:  
Current cough  
Fever  
Weight loss  
Night sweats

No  Yes

Assess for contraindications to IPT³  Investigate for TB and other diseases³

No  Yes

Give IPT  Defer IPT  Other diagnosis  Not TB  TB

Give appropriate treatment and consider IPT  Follow up and consider IPT  Treat for TB

Screen for TB regularly at each encounter with a health worker or visit to a health facility
IPT: Interruption

- **Interruptions to IPT**
  - Patients should be advised strongly that it is critical that IPT be taken as prescribed, continuously for 6 months.

- However if there is one interruption to IPT, the following can be considered.
  
  - If interrupted for < 8 weeks, perform clinical TB screening and if negative continue INH and extend so total taken is equivalent to 6 months.
  
  - If interrupted for ≥ 8 weeks, perform clinical TB screening and if negative re-start treatment for 6 more months.

- If the patient interrupts IPT more than once, then do not try to reinstitute again.
<table>
<thead>
<tr>
<th></th>
<th>Criteria to initiate</th>
<th>Dose</th>
<th>Criteria to stop</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Cotrimoxazole</strong></td>
<td>See: Ch 5 Primary Prophylaxis for Opportunistic infections</td>
<td>· CD4 &lt; 350</td>
<td>Age ≥ 20 years and No active TB, and VL undetectable and CD4 &gt; 350 on two occasions &gt; 6 months apart.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>· TB at any CD4</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>· WHO stage 3 or 4</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>· All adolescents If not contraindicated</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>1 DS; (TMP-160mg, SMX-800mg) tablet daily or 2 SS; (TMP-80mg, SMX-400mg) tablets daily.</td>
<td></td>
</tr>
<tr>
<td><strong>Isoniazid preventive therapy (IPT)</strong></td>
<td>See: Ch 6 Screening for TB and assessment for Isoniazid Preventive Therapy (IPT)</td>
<td>All PLHIV (including pregnant women) without active TB should have IPT one course If not contraindicated.</td>
<td>After 6 months.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Isoniazid 300mg / day + pyridoxine 50mg/d (if weight &lt; 40kg Isoniazid 200mg / day)</td>
<td></td>
</tr>
<tr>
<td><strong>Fluconazole</strong></td>
<td>See: Ch 7 Cryptococcus screening and prevention</td>
<td>PLHA with CD4 &lt; 100 If not contraindicated</td>
<td>VL undetectable and CD4 &gt; 100 on two occasions &gt; 6 months apart.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Fluconazole 100mg/ day</td>
<td></td>
</tr>
</tbody>
</table>
កិច្ចប្រជ ុំផ្សព្វផ្ាយគោលការណ៍ ណណ ជាតិ 
ស្ដីព្ី ការណ៍-បកស្រាត់នឹងការមើលបើប្រក 
ការមើលបើប្រការារភ្នាក់ប្រមូលបន្លែ កប្រ ការារភ្នាក់ប្រមូលបន្លែ កប្រ 
ញ្ចក្តីបក្រញ្ចក្តីបក្រ 

សូមរក្សាទុកការប្រការ ត្រូវបាន 

ឯុទិត នឹងវិធីការសិក្សាចុងក្រោយ
Antiretroviral therapy

Joseph Harwell, MD, FAAP, FIDSA
Clinton Health Access Initiative
The Warren Alpert Medical School at Brown University
## Pediatric First Line ART

<table>
<thead>
<tr>
<th>Age</th>
<th>Preferred regimen</th>
<th>Alternative</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;3 years or &lt;10kg</td>
<td>ABC + 3TC + LPV/r</td>
<td>ABC/ AZT + 3TC + NVP</td>
</tr>
<tr>
<td></td>
<td>After 1 year, confirmed VL suppression and switch to: ABC/AZT + 3TC + NVP</td>
<td></td>
</tr>
<tr>
<td>≥ 3- &lt; 10 years and ≥10kg</td>
<td>ABC + 3TC + EFV</td>
<td>ABC/AZT + 3TC + NVP</td>
</tr>
<tr>
<td>≥ 10 years and &gt;35kg</td>
<td>TDF + 3TC + EFV</td>
<td>ABC/AZT + 3TC + NVP/EFV</td>
</tr>
</tbody>
</table>
LPV/r oral pellets are being piloted at NPH and will soon be available to everyone

- Not appropriate for infants under 3 months (syrup still needed for these children)
- Heat stable, no need for refrigeration
Pediatric First Line ART

New Formulation: ABC/3TC 120/60 mg

• To reduce pill burden, Mylan has produced a new dosing of ABC/3TC: 120/60 mg
• The tablet can be disbursed in liquid, and is scored (can be easily cut in half)
• The Inter-Agency Task Team (IATT) for PMTCT (a WHO body) has promoted the new formulation to Optimal Status

The new product reduces pill burden by 40-50%

<table>
<thead>
<tr>
<th>Weight Band (Kg)</th>
<th>ABC/3TC (60/30 mg)</th>
<th>ABC/3TC (120/60 mg)</th>
<th>ABC/3TC (600/300 mg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>3-5.9</td>
<td>2</td>
<td>1</td>
<td>N/R</td>
</tr>
<tr>
<td>6-9.9</td>
<td>3</td>
<td>1.5</td>
<td>N/R</td>
</tr>
<tr>
<td>10-13.9</td>
<td>4</td>
<td>2</td>
<td>N/R</td>
</tr>
<tr>
<td>14-19.9</td>
<td>5</td>
<td>2.5</td>
<td>N/R</td>
</tr>
<tr>
<td>20-24.9</td>
<td>6</td>
<td>3</td>
<td>N/R</td>
</tr>
<tr>
<td>25-34.9</td>
<td>1 adult tab (600/300mg)</td>
<td>1 adult tab (600/300mg)</td>
<td>1</td>
</tr>
</tbody>
</table>
## Adult First Line ART

<table>
<thead>
<tr>
<th>Age</th>
<th>Preferred first line</th>
<th>Alternative first line*</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Adults</strong></td>
<td>TDF + 3TC + EFV</td>
<td>AZT+ 3TC + EFV (or NVP)</td>
</tr>
<tr>
<td>Including pregnant/breastfeeding, and with TB and HIV co-infection</td>
<td></td>
<td>TDF + 3TC + NVP</td>
</tr>
<tr>
<td><strong>Adolescents &gt; 35kg</strong></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*ABC or PI or when available Dolutegravir may be required in special situations as alternative 1st line agents. Consult with an expert.
The WHO recommends TLE400 as an *alternative first-line regimen for adults and adolescents*, in combination with TDF+3TC

### Clinical Benefits of TLE400
- ENCORE study compared TLE400 vs TLE600.
- TLE400 patients had higher CD4 counts, significantly fewer adverse effects, and less treatment stoppage.

### Convenience of TLE400
- **Single tablet of TLE400mg per day**
- No increased pill burden by switching to TLE400 from TLE600

### Cost of TLE400
- One supplier will make TLE400 available for **$99 per patient per year**, or 6-8% less than the EFV600 price
Other new drugs

- **Dolutegravir (DTG)**
  - Integrase inhibitor
  - Currently considered a third line drug
  - A very inexpensive FDC containing DTG should be available next year for use in first line

- **Raltegravir (RAL)**
  - Integrase inhibitor
  - Currently considered a third line drug, occasionally used in second line
  - Relatively easy to develop resistance, likely will be replaced by DTG

- **Etravirine (ETV)**
  - NNRTI
  - Active against most NNRTI-resistant virus
  - *NOT* active against hepatitis B
  - Currently considered a third line drug

- **Darunavir**
  - Protease inhibitor
  - Currently considered a third line drug
  - Potential for use in second line in the future
Questions?
Treatment Monitoring & PMTCT

Dr. Ahmed Hassani
U.S. Centers for Disease Control & Prevention

Dr. Men Pagnaroat
AIDS HealthCare Foundation
<table>
<thead>
<tr>
<th>Adults and adolescents:</th>
<th>TREAT ALL</th>
</tr>
</thead>
</table>
| **Who should start ART** | • ALL regardless of CD4 count  
   • Priority should be given to:  
   - PLHIV with WHO clinical stage III/IV or CD4 \( \leq 350 \)  
   - Pregnant and breastfeeding women (Option B+)  
   - PLHIV with HBV, and TB co-infections |

| When to start ART | • Within 2 weeks after enrolment following preparedness and completion of ART counseling.  
   • With some opportunistic infections, delay in ART initiation are required after initiating OI treatment  
   - **Cryptococcosis meningitis**: 4-6 weeks  
   - TB with CD4 > 50**: 2-8 weeks |

<table>
<thead>
<tr>
<th>Children:</th>
<th>TREAT ALL</th>
</tr>
</thead>
</table>

**ALL CHILDREN REGARDLESS OF CD4 AND/OR CLINICAL STAGE SHOULD START ART AS SOON AS POSSIBLE, PREFERENCESLY WITHIN 2 WEEKS OF DIAGNOSIS**
<table>
<thead>
<tr>
<th>Opportunistic Infection</th>
<th>Time from start treatment for OI and start ART</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Tuberculosis</strong></td>
<td></td>
</tr>
<tr>
<td>CD4 &lt; 50 cells/mm³</td>
<td>Within 2 weeks</td>
</tr>
<tr>
<td>CD4 &gt; 50 cells/mm³</td>
<td>2 – 8 weeks</td>
</tr>
<tr>
<td><strong>Cryptococcal meningitis (CM)</strong></td>
<td>4 – 6 weeks</td>
</tr>
<tr>
<td><strong>Cryptococcus non-meningeal disease including</strong></td>
<td></td>
</tr>
<tr>
<td>Cryptococcal Ag + CSF neg</td>
<td>Within 2 weeks</td>
</tr>
<tr>
<td><strong>All other OI</strong></td>
<td>Within 2 weeks</td>
</tr>
</tbody>
</table>
**Monitoring antiretroviral therapy**

Reducing the use of CD4 and scaling-up VL

**When to start / continue and stop CD4 monitoring?**

<table>
<thead>
<tr>
<th>Start / continue</th>
<th>Baseline CD4 then 6 monthly until stopping criteria are fulfilled</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Criteria to Stop CD4 monitoring</strong>*</td>
<td>On ART for at least 1 year and all of the following:</td>
</tr>
<tr>
<td></td>
<td>• No adverse drug reactions requiring regular monitoring,</td>
</tr>
<tr>
<td></td>
<td>• No current illness, and not on TB treatment</td>
</tr>
<tr>
<td></td>
<td>• Not pregnant</td>
</tr>
<tr>
<td></td>
<td>• Good understanding of lifelong adherence</td>
</tr>
<tr>
<td></td>
<td>• 2 x CD4 &gt; 350 cells/ mm³</td>
</tr>
<tr>
<td></td>
<td>• 2 x undetectable VL</td>
</tr>
<tr>
<td></td>
<td>• Routine VL monitoring is available</td>
</tr>
</tbody>
</table>

| Check CD4 again | Virological failure → recommence CD4 algorithm |
|                | Pregnancy → recommence algorithm if < 350 +/or VL detectable. |
CD4 testing

- CD4 at baseline and every 6 M whilst on cotrimoxazole
- If routine VL is available, no need for ongoing routine CD4.
- Repeat CD4 if VL failure confirmed.

Whenever CD4 ≤ 350
Start / continue cotrimoxazole and monitor CD4 every 6 months.
When CD4 > 350 2 x in 6 months, and no TB, stop cotrimoxazole and if routine VL monitoring is available CD4 monitoring can be withheld, until VL failure.
If routine VL is not available, continue CD4 monitoring every 6 months, and do targeted VL test to confirm immunological failure if CD4 drops
**Viral load**

- Routine viral load monitoring
- M6 after start or change ART regimen
- Then every 12 months
- Pregnant women test VL M3 after start ART
- If on ART do VL early in pregnancy
- Control VL after 3 months adherence boosting when VL found detectable
• Switch to 2\textsuperscript{nd} line regimen if the control VL after 3 months adherence boosting is > 1,000 copies/ml (even if it has decreased +++)

• Check VL 6 months after starting 2\textsuperscript{nd} line regimen
### Adults and adolescents:

<table>
<thead>
<tr>
<th>Failed 1&lt;sup&gt;st&lt;/sup&gt; line regimen</th>
<th>Preferred second line</th>
</tr>
</thead>
<tbody>
<tr>
<td>TDF + 3TC + NNRTI</td>
<td>AZT + 3TC + ATV/r (if HBsAg negative)</td>
</tr>
<tr>
<td></td>
<td>TDF + 3TC + AZT + ATV/r (if HBsAg positive)</td>
</tr>
<tr>
<td>AZT (or d4T) + 3TC + NNRTI</td>
<td>TDF + 3TC + ATV/r</td>
</tr>
<tr>
<td>If failed 1&lt;sup&gt;st&lt;/sup&gt; line including a PI</td>
<td>Consult an expert</td>
</tr>
</tbody>
</table>

If failed 1<sup>st</sup> line including a PI, consult an expert.

### Children:

<table>
<thead>
<tr>
<th>First line</th>
<th>Preferred 2&lt;sup&gt;nd&lt;/sup&gt; line regimen</th>
<th>Alternative 2&lt;sup&gt;nd&lt;/sup&gt; line regimen</th>
</tr>
</thead>
<tbody>
<tr>
<td>Children</td>
<td>ABC/AZT+3TC+LPV/r</td>
<td>AZT (or ABC) +3TC + NVP/EFV$</td>
</tr>
<tr>
<td></td>
<td>ABC/AZT+3TC+EFV or NVP</td>
<td>TDF + 3TC + LPV/r *</td>
</tr>
<tr>
<td>Adolescents (&gt;10-19 y)</td>
<td>TDF/AZT+3TC+EFV</td>
<td>AZT/TDF# + 3TC + ATV/r (if &gt;40kg)*</td>
</tr>
<tr>
<td></td>
<td></td>
<td>AZT/TDF + 3TC + LPV/r*</td>
</tr>
<tr>
<td>Week</td>
<td>Clinical</td>
<td>Adherence counseling</td>
</tr>
<tr>
<td>--------------</td>
<td>----------</td>
<td>----------------------</td>
</tr>
<tr>
<td>Week 0</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Week 1</td>
<td>✓</td>
<td></td>
</tr>
<tr>
<td>Week 2</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>After start ART</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Week 2</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Month 1</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td><strong>Every 1 M whilst on IPT</strong></td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td><strong>After stop IPT, still on Cotrimoxazole</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Every 1 – 3 months (According to clinical status, + adherence)</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>After stop Cotrimoxazole</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Every 1 – 3 months</td>
<td>✓</td>
<td>✓</td>
</tr>
</tbody>
</table>
HIV+ pregnant women:
- TDF + 3TC (or FTC) + EFV (Fixed-Dose Combination) regardless of WHO stage and CD4 count and continue lifelong (option B+)

HEI:
- HIV DNA-PCR at birth
- Infants should be vaccinated as per the Expanded Program on Immunizations (EPI) schedule, including BCG
- Nevirapine (NVP) prophylaxis is given at birth for 6 weeks to all HIV-exposed children not in high-risk situations of HIV transmission

- Dual Nevirapine (NVP) and Zidovudine (AZT) prophylaxis is given at birth to all HIV-exposed infants in high-risk situations.
  - This is also highly effective in reducing MTCT through breast milk.
  - NVP and AZT should be administered once daily for at least 6 weeks for both breastfed and non-breastfed infants. Breastfed infants should continue infant prophylaxis with NVP alone for an additional 6 weeks (total of 12 weeks of prophylaxis).
**Urgently initiate:**

TDF +3TC (or FTC) + EFV (Fixed-Dose Combination) regardless of WHO stage and CD4 count and continue lifelong (option B+)

<table>
<thead>
<tr>
<th>Mother Risk Status of HIV Exposed Infant HIV</th>
<th>Infant feeding status</th>
<th>Infant prophylaxis</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>High Risk situations:</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1. <em>Mother on ART</em> who have received less than 4 weeks of ART at the time of delivery or</td>
<td>Formula feeding</td>
<td>Dual NVP and AZT for 6 weeks</td>
</tr>
<tr>
<td>2. <em>Mother diagnosed HIV positive at delivery or during post postpartum period.</em></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3. <em>Mother with established HIV infection with VL &gt;1000 copies/mL in the 4 weeks before delivery, if VL available</em></td>
<td>Breast feeding</td>
<td></td>
</tr>
<tr>
<td>4. <em>Mother with incident HIV infection during pregnancy or breastfeeding</em></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Low Risk situations:</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Not fall in the high risk situations.</td>
<td>Breast feeding or formula feeding</td>
<td>NVP for 6 weeks</td>
</tr>
</tbody>
</table>
Breastfeeding:

– Mothers living with HIV should breastfeed for at least 12 months and can continue breastfeeding for up to 24 months or longer (as for the general population) while being fully supported for ART adherence.

– Mothers living with HIV and healthcare workers can be reassured that ARV treatment is effective at reducing the risk of postnatal HIV transmission in the context of mixed feeding and that mixed feeding in itself is not a reason to stop breastfeeding.

– Mothers living with HIV and healthcare workers can be reassured that shorter durations of breastfeeding less than 12 months are better than never initiating breastfeeding.
កិច្ចប្រជ ុំផ្សព្វផ្ាយគោលការណ៍ ណណនុំជាតិស្ដីព្ីការណ៍ ឲ្យការណ៍ដឹកនាំ-ប្រការិកការប្រឈម និង ការប្រការិកឲ្យវិប្បនិិះមកដល់ជនប្រាកដនៃស្របព័រ ឲ្យធ្វើបាន ការប្រការិកឲ្យមកដល់ជនប្រាកដដ៏កើតមក និង ការប្រការិកឲ្យមកដល់ជនប្រាកដដ៏កើតមក់ ស្របព័រ ជីវភាពប្រការិក ឲ្យមកដល់ជនប្រាកដ។

ឈុតី ចុក ឯុតីក អាច ឬ នឹង

រាជរដ្ឋបាល សាលាភិបាល ស្រុកសំរាប់ការពារជាតិ
Co-morbidities
Dr. Chel Sarim
Dr. Deng Serongkea
Chronic non-communicable diseases in PLHIV

Dr. Chel Sarim
FHI 360

National HIV clinical management guidelines for Adults and Adolescents
4th Revision in 2015
Key points

Recommendations for prevention and management of NCD

Smoking cessation

Screening, diagnosis, management and drug interaction of
  – Hypertention
  – Diabetes type 2
  – Hyperlipidaemia
Key points of chronic non-communicable diseases in HIV

- With effective ART, PLHIV live longer, and uncontrolled VL, immunodeficiency and opportunistic infections are less of a problem.

- However HIV itself, long term ARV, and advancing age puts PLHIV at increased risk of NCDs.

- PLHIV are at increased risk of developing a range of metabolic and non-communicable diseases (NCDs), including cardiovascular disease, diabetes, chronic lung disease and cancers.

- It is important that the HIV clinician is aware of NCD, and regularly addresses issues of 1st and 2nd prevention with PLHIV during consultations.

- In addition PLHIV on long-term ART should be screened for NCD (According to this guideline) and referred for appropriate care.

- The HIV clinician needs to check for any drug interactions with ART and medications prescribed either within or outside the HIV clinic, and to monitor for toxicity on an ongoing basis.
**Recommendations for prevention and management of NCD**

### Table 34-1 Recommendations for prevention and management of NCD

<table>
<thead>
<tr>
<th>Recommendations</th>
</tr>
</thead>
<tbody>
<tr>
<td>The emphasis on diet and lifestyle modification will vary depending on whether the patient is under/over/normal weight and other risk factors, HT, diabetes etc.</td>
</tr>
</tbody>
</table>

**Diet:** most people need to pay attention to eat
- More protein (tofu, beans, chicken, fish)
- More vegetables (5 x 400 – 500gm servings vegetables and fruit per day)
- Less fat (avoid deep fried foods, cut/skin the fat of meats e.g. pork/chicken)
- Less sugar (soft drinks, sweets, condensed milk).
- Less salt (prohok, MSG, fish sauce, soy sauce and salted meat or fish) instead use other flavours (e.g. lemon juice, pepper) and herbs.
- Minimize processed foods (usually high in salt, fat, sugar)

**Weight:** Maintain BMI between 18.5 – 22.9

**Alcohol:** maximum of 2 standard drinks per day, ≥ 2 alcohol free days.

**No smoking**

**Exercise** 30 minutes per day (e.g. brisk walking) (more if need to lose weight)
Smoking cessation

WHO Counselling tool to assist individuals to quit smoking

A1: ASK
Do you use tobacco?
NO
Reinforce message that tobacco increases risk of heart disease
YES

A2: ADVISE
Advise to quit in a clear, strong and personalized manner
“Tobacco use increases the risk of developing a heart attack, stroke, lung cancer and respiratory diseases. Quitting tobacco use is the one most important thing you can do to protect your heart and health, you have to quit now.”

A3: ASSESS
Are you willing to make a quit attempt now?
YES
NO

A4: ASSIST
- Assist in preparing a quitting plan
  - Set quit date
  - Inform family and friends
  - Ask for their support
  - Remove cigarettes/tobacco
  - Remove objects/articles that prompt you to smoke
  - Arrange follow-up visit*

- Promote motivation to quit
  - Provide information on health hazards of tobacco and give leaflet to the patient

A5: ARRANGE
At follow-up visit
- Congratulate success and reinforce
- If patient has relapsed, consider more intensive follow-up and support from family

* Ideally second follow-up visit is recommended within the same month and every month thereafter for 4 months and evaluation after 1 year. If not feasible, reinforce counseling whenever the patient is seen for blood pressure monitoring.
Hypertension

- Screening, and diagnosis hypertension in PLHIV
  - All patients should have blood pressure taken at each visit
  - If BP > 140/90 on more than one occasion = hypertension

- Management of hypertension
  - See in detail of The Cambodian Clinical Practice Guidelines detail the management of hypertension
Hypertension requires both pharmacological and non-pharmacological management

- Patients should be advised how to reduce BP and risk of CVD:
  - Weight loss if overweight
  - Healthy diet and lifestyle as detailed in Table 34-1, with an emphasis on reduced sodium intake.
  - If mild hypertension e.g. up to SBP 159+ or DBP 99 try non-pharmacological measures for 3–6 months prior to considering antihypertensive therapy.
Hypertension requires both pharmacological and non-pharmacological management

Evaluate for other conditions associated with HT: Weight loss if overweight

- Cardiovascular disease (history, examination, ECG if available)
- Cerebrovascular disease – stroke, dementia
- Perform the following laboratory tests:
  - Diabetes – fasting glucose
  - Serum lipids – total cholesterol, HDL cholesterol, triglycerides
Hypertension (Cont.)

- Pharmacological management

Table 36-1 Cambodian guidelines for commencement of antihypertensive medicine

<table>
<thead>
<tr>
<th>Hypertensive Patient</th>
<th>Initiate pharmacologic treatment</th>
<th>BP goal</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥ 60 years*</td>
<td>SBP ≥ 150 mm Hg or DBP ≥ 90 mm Hg</td>
<td>SBP &lt; 150 mm Hg and DBP &lt; 90 mm Hg</td>
</tr>
<tr>
<td>&lt; 60 years</td>
<td>SBP ≥ 140 mm Hg or DBP ≥ 90 mm Hg</td>
<td>SBP &lt; 140 mm Hg</td>
</tr>
<tr>
<td>18-59 years</td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥ 18 years with</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CKD or/and Diabetes</td>
<td>SBP ≥ 140 mm Hg or DBP ≥ 90 mm Hg</td>
<td>SBP &lt; 140 mm Hg and DBP &lt; 90 mm Hg</td>
</tr>
</tbody>
</table>
Pharmacological management

The Cambodian Clinical Practice Guidelines recommend the following initial regimens:

- Patients > 55 years old - Thiazide diuretic
- Patients < 55 years old – Angiotensin converting enzyme inhibitor (ACE I)
- Diabetic or kidney disease (any age) - ACE I

If the BP is not controlled to the target level a second agent should be added, acceptable combinations are:

- Thiazide diuretic + ACE I
- Thiazide diuretic + calcium channel blocker
- ACE I + calcium channel blocker

Examples of drug doses: Please see in the National HIV clinical management guidelines for Adults and Adolescents 4th Revision in 2015 (Page 151)
Drug interactions with antihypertensive medicines and ART

Table 36-2 Antihypertensive drug interactions with ARV

<table>
<thead>
<tr>
<th>Drug</th>
<th>Interaction with ARV</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>ACEI</strong> : enalopril, captopril, ramipril;</td>
<td>No described interactions with NNRTI, NRTI or PI.</td>
</tr>
<tr>
<td><strong>Calcium channel blockers</strong></td>
<td>Levels of CCB are potentially decreased by NNRTI, and increased by PI → careful monitoring of BP and dose adjust.</td>
</tr>
<tr>
<td>including amilodipine, nifedipine;</td>
<td></td>
</tr>
<tr>
<td><strong>Beta blockers</strong> : atenolol, metoprolol, propranolol;</td>
<td>Potential interaction as both may prolong PR interval → careful monitoring of BP, and dose adjust, consider ECG.</td>
</tr>
<tr>
<td><strong>ARB</strong> (angiotensin 2 receptor blockers)</td>
<td>Losartan levels potentially decreased by NNRTI, and increased by PI → careful monitoring of BP and dose adjust</td>
</tr>
</tbody>
</table>
Type 2 Diabetes

- Screening for Diabetes in PLHIV
  - Overweight (BMI >23, +/- waist circumference in men ≥85cm and in women ≥ 80cm)
  - Family history of diabetes
  - Hypertension (BP >140/90)
  - Dyslipidaemia
  - History of stroke or ischaemic heart disease
  - Women with history of gestational diabetes or have given birth to a large baby (>3.5 kg)
  - Age over 35
  - Chronic renal impairment
  - Glycosuria on urine dipstick.

PLHIV commencing Protease Inhibitor containing ART: PLHIV should be screened for diabetes prior to starting a PI, as these can cause insulin resistance. Follow up screening at 3 months after commencing PI and every 12 months.
Diagnosis of Type 2 Diabetes and impaired glucose tolerance

**WHO diagnostic criteria for diabetes**

<table>
<thead>
<tr>
<th></th>
<th>Glucose concentration, mmol/l (mg/dl)</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Whole blood</td>
<td>Capillary</td>
</tr>
<tr>
<td><strong>Diabetes mellitus</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fasting</td>
<td>≥ 6.1 (110)</td>
<td>≥ 6.1 (110)</td>
</tr>
<tr>
<td>or</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2-hour post glucose load or both</td>
<td>≥ 10.0 (180)</td>
<td>≥ 11.1 (200)</td>
</tr>
<tr>
<td><strong>Impaired glucose tolerance</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fasting concentration (if measured) and 2 hours after glucose load</td>
<td>6.7-9.9 (120-179)</td>
<td>7.8-11.0 (140-199)</td>
</tr>
<tr>
<td><strong>Fasting hyperglycaemia</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fasting</td>
<td>5.6-6.0 (100-109)</td>
<td>5.6-6.0 (100-109)</td>
</tr>
<tr>
<td>2 hours (if measured)</td>
<td>≤ 6.7 (120)</td>
<td>≤ 7.8 (140)</td>
</tr>
</tbody>
</table>

Notes about testing for diabetes: Venous plasma is the preferred test however the blood must be tested within the hour, or collects in sodium fluoride tube to inhibit glycolysis and place the tube in ice-water until analysis. Corresponding capillary values are similar for fasting samples and differ only for the 2 hours.
Type 2 Diabetes (Cont.)

- Management of impaired glucose tolerance
  - Weight loss if overweight
  - Healthy diet and lifestyle as detailed in Table 34-1 of adults guideline 2015
  - Follow up testing in 12 months

- Management of Type 2 Diabetes
  - See the Cambodian National guidelines for comprehensive guidance on management of diabetes type 2 diabetes in 2015
  - If available the patient should be referred to a diabetes clinic.
Diabetes requires both pharmacological and non-pharmacological management:

- Non-pharmacological measures to reduce risk of complications of diabetes:
  - Healthy diet and lifestyle as detailed in Table 34-1 of adults guidelines in 2015
  - Modification of the diet ® diabetic diet. Most importantly reduce the portion size of carbohydrate, including rice. (see Figure 48-1 Food pyramid for Diabetes Type 2 in adults guidelines in 2015).

Patients should be evaluated for other conditions associated with diabetes:

(See in detail in adults guidelines in 2015)
Type 2 Diabetes (Cont.)

- Pharmacological management of diabetes:
  - First line: Metformin 500 – 2000mg divided into 2 doses with meals
  - Alternative first line: Gliclazide 40 – 320mg divided into 2 doses with meals
  - Second line: Metformin + sulfonylurea
  - Third line: basal or premix insulin + oral agent, or basal + meal time insulin

- Drug interactions between diabetes medication and ART

<table>
<thead>
<tr>
<th>Drug</th>
<th>Interaction with ARV</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gliclazide and Glimepiride;</td>
<td>Levels potentially decreased by PI, and increased by EVF. Careful monitoring and dose adjustment of the gliclazide may be required.</td>
</tr>
<tr>
<td>Glibenclamide</td>
<td>Levels potentially decreased by EFV and NVP and increased by PI.</td>
</tr>
<tr>
<td>Metformin and insulin</td>
<td>Not known to interact with NNRTI, NRTI PI, ART, however dolutegravir could potentially increase metformin concentrations.</td>
</tr>
</tbody>
</table>
Hyperlipidaemia

- Screening for hyperlipidemia in PLHIV
  - The risk of cardiovascular disease is increased with elevated low – density lipoprotein
  - cholesterol (LDL – C)
  - Lipid related risk for CVD is not reflected in the Total Cholesterol (TC) measurement
  - alone, as this is comprised of LDL-C and HDL – C
  - Triglyceride levels > 10 mmol/l increase the risk of pancreatitis
  - PLHIV who are taking PI based ART regimens are at risk of hyperlipidaemia, although less with ATV/r compared to LPV/r.
  - Indications for testing serum lipids, and thresholds for treatment with lipid lowering drugs depend on the patients overall cardiovascular risk.
PLHIV commencing PI containing ART

- All PLHIV should have fasting serum lipids checked prior to starting a PI containing ART
- Monitored after 3 months and then 12 monthly, as PI drugs can cause hyperlipidaemia
- PLHIV may have other indications for serum lipid levels – eg. diabetes.
Management of hyperlipidaemia: Hyperlipidaemia requires both pharmacological and non-pharmacological management

- Non pharmacological management:
  - Follow Table 34-1 of adults guidelines, which all impact on lipid levels directly or associated risk factors for NCD
  - Reduce saturated fats (animal fats), replace with mono/polyunsaturated fats.
  - Optimize diabetic control.

- Pharmacological management
  - Change from LPV/r to ATV/r. If predominantly raised LDL-C, prescribe Statin
  - Predominantly raised TG (>10mmol/l), especially if with a low HDL-C, prescribe Fibrate +/- or fish oil.
Target levels on therapy

- increase drugs within max safe doses to achieve the following:
  - Total Cholesterol < 4.0 mmol/L
  - HDL –C ≥ 1.0 mmol/L
  - LDL-C < 2mmol/L
  - TG < 2mmol/L
Drug interactions between lipid lowering medications and ART

<table>
<thead>
<tr>
<th>Statins</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Simvastatin and lovastatin are contraindicated with PI containing ART as there is a high risk of rhabdomyolysis.</strong></td>
<td></td>
</tr>
<tr>
<td>Other statins may be used with PI containing ART but at lower doses:</td>
<td></td>
</tr>
<tr>
<td>• Atorvastatin start 10mg → max dose with PI ART = 40mg</td>
<td></td>
</tr>
<tr>
<td>• Pravastatin start 20mg → max dose with PI ART = 40mg</td>
<td></td>
</tr>
<tr>
<td>• Rosuvastatin start 5mg → max dose with PI ART = 20mg</td>
<td></td>
</tr>
<tr>
<td><strong>Fibrates</strong></td>
<td></td>
</tr>
<tr>
<td>• Gemfibrozil:</td>
<td></td>
</tr>
<tr>
<td>• Drug levels may be lowered by PI ART</td>
<td></td>
</tr>
<tr>
<td>• Do not use in combination with a statin due to the risk of myositis</td>
<td></td>
</tr>
<tr>
<td>• Fenofibrate</td>
<td></td>
</tr>
<tr>
<td>• Monitor ALT/CK if in combination with statins due to increased risk of side effects</td>
<td></td>
</tr>
<tr>
<td><strong>Fish oils</strong> are not known to have interaction with ART</td>
<td></td>
</tr>
</tbody>
</table>
Monitoring for adverse effects

- Lipid lowering drugs can cause liver dysfunction and myopathy
- Patients should be warned of the symptoms of myopathy (pain, stiffness, weakness) and liver inflammation (abdominal pain, vomiting)

- Check ALT and creatinine kinase (CK) at baseline
- Check CK and ALT again if any symptoms
- Stop drug if persistent muscle pain or weakness, esp. if CK > 500 U/L
- Stop drug if CK > 1000 U/L with no symptoms.
- Stop drug if ALT increases to > 3 x ULN.
Thank you for your attention
កិច្ចប្រជ ុំផ្សព្វផ្ាយគោលការណ៍ ណណ
នុំ ជាតិ ស្ដីព្ី ការ ណែទុំ - ព្ាបាលជុំងឺ ឱកាស្និយ មនិង ការ ព្ាបាលគោយ ឱស្ែប្រឆុំងគមគោគគេដស្៍ ស្ុំោរ់ មន ស្សគព្ញវ័យ គកេងជុំទង់ និង កមារ ថ្ែៃទី ២ ៨ វិច្ឆិកា ឆ ន ុំ ២០១៦
Viral Hepatitis and Chronic Liver Disease in HIV-infected Persons

Dr. Chel Sarim

National HIV clinical management guidelines for Adults and Adolescents

4th Revision in 2015
<table>
<thead>
<tr>
<th>Table of content</th>
</tr>
</thead>
<tbody>
<tr>
<td>▪ HBV and HCV transmission and prevention,</td>
</tr>
<tr>
<td>▪ HBV and HCV diagnosis,</td>
</tr>
<tr>
<td>▪ The natural history of HBV and HCV mono-infection,</td>
</tr>
<tr>
<td>▪ The relationship between HIV and HBV &amp; HIV and HCV,</td>
</tr>
<tr>
<td>▪ The management of HIV/HBV and HIV/HCV co-infection,</td>
</tr>
<tr>
<td>▪ The management of complications of chronic liver disease.</td>
</tr>
</tbody>
</table>
Hepatitis B
It is estimated that worldwide, 2 billion people have evidence of past or present infection with HBV, and 240 million are chronic carriers of HBV surface antigen (HBsAg).

It is estimated that around 650 000 people die each year from the complications of CHB.

Overall, HBV accounts for around 45% of cases of HCC and 30% of cirrhosis, with much higher proportions in LMICs.

Cambodia is considered a high prevalence country with > 8% of the population HBV infected.
HBV infection can be either acute or chronic, and may range from asymptomatic infection or mild disease to severe or rarely fulminant hepatitis.

Acute hepatitis B is usually a self-limiting disease marked by acute inflammation and hepatocellular necrosis, with a case fatality rate of 0.5–1% (1).

Chronic hepatitis B (CHB) infection is defined as persistent HBV infection (the presence of detectable hepatitis B surface antigen [HBsAg] in the blood or serum for longer than six months), with or without associated active viral replication and evidence of hepatocellular injury and inflammation.
Age is a key factor in determining the risk of chronic infection.

**Chronicity:**

- is common following acute infection:
  - in *neonates* (90% of neonates born to hepatitis B e antigen [HBeAg]-positive mothers) and
  - in *young children* under the age of 5 years (20–60%), but
- occurs rarely (<5%) when infection is acquired in *adulthood*. 
Outcome of hepatitis B infection by age at infection

- Chronic infection
- Symptomatic infection

Legend:
- Symptomatic infections
- Chronic infections
• HBV is transmitted through infected blood or body fluids (semen, vaginal fluids);
• The virus can enter the bloodstream through mucous membranes or a break in the skin.

**Transmission of Hepatitis B**

- **Perinatal** (30 – 90% transmission risk)
- **Parenteral**
  - Injecting drug use (IDU): very high risk
  - Health care setting:
    - Transfusion
    - Medical procedures
    - Needle stick injury (~ 30% risk)
  - Household:
    - Child to child
    - Toothbrush, razors, etc.
    - Piercing, tattoos
- **Sexual** (including oral)

**Prevention of Hepatitis B transmission**

- **Vaccination**
  - Newborn (↓ by 70%)
  - HCW
  - Spouse
- **Universal precautions**
- **Blood screening**
- **Condoms**
- **Household precautions**
Diagnosis of HBV

- HBsAg positivity indicates current HBV infection
- If the HBsAg is negative but the HBsAb positive this indicates immunity to HBV due to vaccine or past infection.
- HBcAb is positive either due to previous exposure, or with a positive HBsAg due to persistent infection
- Further testing includes HBeAg (active replication and high infectivity), HBeAb, and HBV DNA Viral Load.
  - These assist in assessing the phase of the disease, which is important for determining when to initiate HBV antiviral therapy in HBV mono infected patients.
Natural History of untreated HBV mono infection

- Acute Infection
  - > 90% of infected infants progress to chronic disease
  - < 5% of infected immunocompetent adults progress to chronic disease

- Chronic Infection
- Cirrhosis
  - 30% of chronically infected individuals
  - 23% of patients decompensate within 5 yrs of developing cirrhosis

- Liver Cancer (HCC)
- Liver Failure ( Decompensation)
- Death
The four phases of chronic HBV infection

1. **Immune tolerance**: Little immune activation /response to the virus
   - Lasts decades when infected in infancy but mostly brief or absent in adults
   - Normal ALT, HBeAg positive, high viral load (HBV DNA)

2. **Immune clearance**:
   - Fluctuating ALT and HBV DNA levels
   - 5% - 10% / yr seroconvert from HBeAg → HBeAb which is associated with ↓↓ HBV VL.

3. **Immune control**: Non-replicative (latent) infection.
   - HBeAg negative, low or undetectable HBV DNA, normal ALT levels
   - Previously called “carrier” however this may be misleading as may reactivate.

4. **Immune escape**: Reactivation
   - Spontaneous reactivation occurs in 20% of people in the immune control phase
   - HBeAg negative, positive HBcAb, VL detectable (often high).
Extra hepatic manifestations of HBV

- Associated with deposition of circulating Ag-Ab immune complexes → inflammation:
  - Arthralgia and arthritis
  - Purpuric cutaneous lesions (leukocytoclastic vasculitis)
  - Glomerulonephritis
  - Polyarteritis nodosa (small/medium vessel vasculitis: skin, eyes, kidney, heart, CNS, etc.).
Pregnancy and HBV

- Mother to child transmission: rate 10% - 90% (dependent on DNA VL)
  - HBV vaccine to infant within 24 hours of birth reduces transmission by 70%.
  - Further reduction in transmission is expected if the woman is on antiviral therapy.
  - There is no indication for caesarean section.
  - There is no evidence of transmission from breast milk (although HBsAg and HBV DNA are detectable in breast milk)
- Pregnant woman with chronic hepatitis should be monitored closely for deterioration in liver disease.
- Monitor for a hepatitis flare up to 6 weeks after delivery (esp. if not on antiviral therapy)
HIV/HBV relationship

- HIV and HBV have common modes of transmission.
- HIV co-infection results in higher rates of progression of HBV to cirrhosis and hepatocellular carcinoma (HCC).
- There is some evidence to suggest that there is increase progression to HIV outcomes and all-cause mortality.
- HBV results in higher risk of liver toxicity with ART and other drugs.
- ART includes some drugs with anti HBV activity, and this influences the management of co infected patients.
- Immune reconstitution on ART may result in “flare” of hepatitis.
Management of HBV/HIV co-infection

• In mono-infected HBV patients antiviral medication is only indicated in the immune clearance, and immune escape phases of HBV infection, when there is a risk of progression to cirrhosis and HCC.

• Patients not in either of these phases should be monitored 6 – 12 monthly with HBV VL and liver function tests.
Management of HBV/HIV co-infection

• Now all HIV patients will be commenced on TDF + 3TC containing ART, this will automatically include treatment for HBV co-infection.

• It is important that all patients with HIV HBV co-infection commenced TDF + 3TC containing ART must continue both drugs even if they change to 2nd line ART.

• If just one of these drugs (particularly 3TC) is used, drug resistance will develop.

• Standard 2nd line ART for HBV/HIV co-infected patients will therefore include: AZT + 3TC + TDF+ ATV/r.

• HBsAg is ideally measured prior to starting ART, however it is not necessary for this to be routinely performed whilst the preferred 1st line ART contains TDF.

• A HBsAg test is essential if there is consideration to change to 2nd line ART, and is clinically indicated if there are any abnormalities in the liver function tests.
Hepatitis C
Burden of HCV infection and mortality

• A systematic review in 2013:
  – 185 million persons are HCV-antibody positive,
  – 130–150 million may be chronically infected (HCV RNA positive).

• A more recent systematic review:
  – 110 million persons are HCV-antibody positive,
  – 80 million have chronic infection.

• Between 10% and 30% of persons with chronic HCV infection have stage F3 or F4 fibrosis.
Burden of HCV infection and mortality

- Global prevalence of HIV/HCV coinfection
  - A frequently cited article: 4 million persons are coinfected,
  - One recent analysis indicates that 2.3 million persons may be coinfected globally,
  - An analysis from Africa estimated that 5.7% of persons with HIV were coinfected with HCV.

- Deaths per year due to HCV-related diseases:
  - 333,000 in 1990,
  - 499,000 in 2010,
  - 704,000 in 2013.
HCV Transmission and prevention

- There is no vaccination for HCV,
- Prevention relies on:
  - universal precautions,
  - blood screening in the health care setting,
  - harm reduction strategies with IVDU such as needle and syringe exchange,
  - household measures such as not sharing razorblades or toothbrushes.
- Sexual transmission is rare, but more likely with HIV co-infection and blood contact. Condoms may be advised.
- Perinatal transmission is ~5% in non-PLHIV.
- Hepatitis C is mostly transmitted via the parenteral route and is common in IVDU.
<table>
<thead>
<tr>
<th>Population</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Persons who inject drugs (PWID) (19)</td>
<td>PWID have the highest risk of infection. Globally, the prevalence of anti-HCV antibody is 67% among PWID.</td>
</tr>
<tr>
<td>Recipients of infected blood products or invasive procedures in health-care facilities with inadequate infection control practices (20–30)</td>
<td>Risk of HCV infection varies depending upon the frequency of medical procedures (i.e. number of injections/person/year) and level of infection control practices. A high frequency of injections and a low level of infection control can result in a high prevalence of HCV in the general population (e.g. prevalence of chronic HCV infection confirmed by nucleic acid testing was 4.0% in Egypt in 2015) (31).</td>
</tr>
<tr>
<td>Children born to mothers infected with HCV (30, 32–35)</td>
<td>HCV transmission risk is estimated as 4–8% among mothers without HIV infection. Transmission risk is estimated as 10.8–25% among mothers with HIV infection.</td>
</tr>
<tr>
<td>People with sexual partners who are HCV infected (36–40)</td>
<td>There is low or no risk of sexual transmission of HCV among HIV-uninfected heterosexual couples and HIV-uninfected men who have sex with men (MSM). The risk of sexual transmission is strongly linked to pre-existing HIV infection.</td>
</tr>
<tr>
<td>People with HIV infection (40–48)</td>
<td>Persons with HIV infection, in particular MSM, are at increased risk of HCV infection through unprotected sex.</td>
</tr>
<tr>
<td>People who use intranasal drugs (49)</td>
<td>Non-injecting drug use (e.g. through sharing of inhalation equipment for cocaine) is associated with a higher risk of HCV infection.</td>
</tr>
<tr>
<td>People who have had tattoos or piercings (50)</td>
<td>Tattoo recipients have higher prevalence of HCV compared with persons without tattoos (odds ratio = 2.24, 95%CI 2.01, 2.50)</td>
</tr>
</tbody>
</table>
### TABLE 2.3 WHO guidance on prevention of HCV infection in health-care settings

- Hand hygiene: including surgical hand preparation, hand-washing and use of gloves
- Safe handling and disposal of sharps and waste
- Safe cleaning of equipment
- Testing of donated blood
- Improved access to safe blood
- Training of health personnel

### TABLE 2.5 WHO recommendations for prevention of HCV infection among people who inject drugs

- Offer people who inject drugs the rapid hepatitis B vaccination regimen.
- Offer people who inject drugs incentives to increase uptake and complete the hepatitis B vaccination schedule.
- Implement sterile needle and syringe programmes that also provide low dead-space syringes for distribution to people who inject drugs.
- Offer peer interventions to people who inject drugs to reduce the incidence of viral hepatitis.
- Offer opioid substitution therapy to treat opioid dependence, reduce HCV risk behaviour and transmission through injecting drug use, and increase adherence to HCV treatment.
- Integrate the treatment of opioid dependence with medical services for hepatitis.

### TABLE 2.6 WHO guidance on prevention of sexual transmission of HCV infection

- Promotion of correct and consistent condom use
- Routine testing of sex workers in high-prevalence settings
- Integrated action to eliminate discrimination and gender violence, and increased access to medical and social services for vulnerable persons
Diagnosis of HCV

• Hepatitis C Ab remains detectable in all infected with HCV, even if the virus has been cleared spontaneously or with treatment.

• HCV RNA testing is required to diagnose current chronic HCV infection, and to monitor therapy.
Natural History of untreated HCV mono infection

- **Acute Infection**
  - ~75% of infected progress to chronic disease

- **Chronic Infection**

- **Cirrhosis**
  - 20% of chronically infected individuals develop cirrhosis after 40 yrs

- **Liver Failure ( Decompensation)**
  - Mortality (years after infection):
    - 1% at 20 years
    - 4% at 40 years

- **Liver Cancer (HCC)**

- **Death**
FIGURE 2.2 Natural history of HCV infection

- HCV infection
- Chronic infection (55–85%)
- Mild fibrosis
- Moderate to severe fibrosis
- Cirrhosis (15–30%)
- Decompensated cirrhosis

Spontaneous resolution (15–30%)

Hepatocellular carcinoma (2–4% per year in cirrhosis)
Natural History of untreated HCV mono infection

- Acute HCV infection is often asymptomatic, and chronic HCV often remains asymptomatic for many years.
- After many years chronic infection may progress to cirrhosis, liver cancer, and hepatic failure.
- Extra hepatic manifestations of chronic HCV infection include
  - dermatological conditions such as porphyria cutanea tarda, and vasculitic rashes associated with cryoglobulinaemia,
  - rheumatological conditions,
  - haematological abnormalities,
  - thyroid disorders.
HIV/HCV relationship

• Hepatitis C is mostly transmitted via the parenteral route and is common in IVDU.
• However the risk of sexual and perinatal transmission is higher in PLHIV than in non-PLHIV.
• HIV co-infection results in higher rates of progression of HCV to cirrhosis and hepatocellular carcinoma (HCC).
• HCV increases the risk of liver toxicity with ART and other drugs.
Management of HCV/HIV co-infection

- Management of HCV has been traditionally with interferon-based regimens, which are very difficult to tolerate, and have limited efficacy.
- Emerging as standard treatment are new HCV antiviral agent known as Direct Acting Antiviral Agents (DAA) which are highly effective and well tolerated, include combination oral regimens requiring 8 – 24 weeks therapy.
- The DAA variably target specific genotypes, or are pan genotypic, and are becoming available in fixed dose combinations.
- The newer regimens are also highly effective and well tolerated in HCV HIV co-infection.
Management of HCV/HIV co-infection

• Many DAA are becoming available globally, including:
  – protease inhibitors Simepravir and Paritaprevir,
  – NS5A inhibitors Ledipasvir, Ombitasvir, Daclatasvir,
  – NS5B inhibitors Sofosbuvir, and dasabuvir.

• A pilot project of HCV diagnosis and treatment among co-infected HIV patients will start in 2016 in Cambodia.
  – It is expected that access to DAA and viral load testing for HCV treatment will improve rapidly in Cambodia.
Chronic Liver Disease
Introduction

• The assessment and management of chronic liver disease is similar regardless of whether the disease is caused by HBV, HCV or alcohol.
Clinical assessment

- History: symptoms of acute and chronic liver disease, and extra hepatic manifestaion.
- Examination: signs of chronic liver disease + liver failure.
Laboratory assessment

- Markers of severity of chronic liver disease
  - ALT:
    - Some correlation with inflammation,
    - Poor correlation with fibrosis,
  - An inverted AST/ALT ratio (AST > ALT)
  - Low platelets (portal hypertension + hypersplenism)
  - Low albumin (synthetic function)
  - Raised prothrombin time (PT) (synthetic function)
  - Elevated direct bilirubin (secretory function)
  - Severe liver injury may be indicated if ALT falls and bilirubin rises.
Laboratory assessment

• Whilst biopsy has traditionally been used to assess the degree of hepatic fibrosis, non-invasive tests including Elastography (Fibro-scan) are increasingly taking this role.
Management of complications of chronic liver disease

- **General management** of complications of chronic liver disease due to any cause (including HBV, HCV an alcohol)
  - Avoid hepatotoxic drugs (e.g. NSAIDS, and traditional medicines),
  - Stop or minimize drinking alcohol.
  - Healthy diet: low in salt + saturated fat, adequate protein (1 – 1.5 g / kg body weight / day), fruit, vegetables.
  - Treat the underlying cause (HBV, HCV)
Management of complications of chronic liver disease

**Management of Ascites**

- Restrict dietary salt and water (e.g. 1 - 1.5 litre) intake
- Bed rest if significant fluid overload
- Diuretic: spironolactone preferred, dose: 25–200 mg /day
- +/- low dose furosemide (K+ supplements may be required)
- Monitor carefully:
  - Clinical: BP (lying + standing), HR, weight, peripheral oedema, CVS, ascites
  - Laboratory: K+, Na+, Creatinine, albumin
- Drainage of ascites may be necessary.
- There is often ↑ extravascular volume but with ↓ intravascular volume, so there is a risk of renal failure, esp. with diuresis, and large volume drainage of ascites.
Management of complications of chronic liver disease

- **Management of Spontaneous bacterial peritonitis (SBP)**
  - Usually associated with severe hepatic dysfunction
  - Suspect if ascites ↑, fever, abdominal pain and tenderness, encephalopathy.
  - **Ix:** ascitic tap - WCC > 500/mm³ +/or neutrophil > 250/mm³
  - Causative organisms mostly enteric Gram-negative bacilli eg E coli, + if on prophylaxis; streptococcal or enterococcus.
  - **Rx:** ceftriaxone 1g IVI daily, + if on antibiotic prophylaxis add amoxicillin/ ampicillin 1 g IV, 6-hourly.
  - **Prophylaxis** - cotrimoxazole 1 DS daily if:
    - GIT bleeding
    - Low ascitic protein (<10g / l)
    - Previous episode of SBP
Management of complications of chronic liver disease

• Management of portal hypertension
  – Ideally all patients with cirrhosis should have endoscopy to determine if varices are present, and if they are identified:
    ▪ Treatment of oesophageal varices (e.g. banding, sclerosis)
    ▪ Non selective beta-blocking agents to lower portal pressure (propranolol)
Management of complications of chronic liver disease

- Management of portal systemic encephalopathy
  - Look for underlying cause: HCC, SBP, renal failure etc.
  - If severe (grade 3 or 4)
    - Withhold protein for 24 – 28 hours then gradually increase to normal.
    - Empirically treat for sepsis with ceftriaxone 1 gm. IVI / daily
  - Maintain optimal fluid and electrolyte balance
  - Lactulose to both clear the colon and alter ammonia metabolism and diffusion.
  - Use doses to ensure two soft stools per day and continue long term
Thank you for your attention
Adolescent Transition to adult Pre and ART services

Dr. Deng Serongkea
World Health Organization
Outline

• Goal

• A- Transition from PAC site to Adult ART site - *Roles of PAC site*
  1. Support for Adolescents living with HIV/AIDS
  2. Preparing for transition in the adolescent care setting
  3. Evaluation before transition occurred
  4. Post-Transition Assessment

• B- After Transition to Adult ART site - *Roles of Adult ART site*
  1. Organizational arrangements for Adolescent care in Adult HIV clinics
  2. Psychosocial support
  3. Reproduction and sexual health
  4. Adherence and retention in care
  5. Clinical issues regarding Adolescent care
Objectives of transitions

• Both PAC & AAC are to support youth to:
  • retains in care, remains adherent, disclosure HIV status with partner and reducing HIV transmission to others,
  • receives the clinical and psychosocial support and to transition into a physically and psychologically healthy adult.
A- Transition from PAC site to Adult ART site

Roles of PAC Site:
1. Support for Adolescents living with HIV/AIDS
2. Preparing for transition in the adolescent care setting
3. Evaluation before transition occurred
4. Post-Transition Assessment
1. Support for Adolescents living with HIV/AIDS

- **Knowing their HIV status:**
  - **Disclosure to child** should be done prior to transition to adult service *(if not, please do it at adult site)*
  - Age of full disclosure: 6-12 y.o
  - If disclosure after puberty ≈12 y.o → depression, treatment non-adherence, poor retention in care.
  - **Disclosure to others: risks and benefits:**
    - **Benefits:** obtain support, safer sex/HIV prevention with partner
    - **Risks:** stigma, discrimination, abandonment and violence.
    - Adolescents will need to be empowered and supported to determine if, when, how and to whom to disclose.

- **Counseling for adolescents includes:**
  - sexual and reproductive education, support for intimate romantic relationships, disclosure to partners and significant others.
  - group counseling *(at clinic, support by skilled person):* to develop better self-esteem.
2. Preparing for transition in the adolescent care setting

Provider should:
– Developing a Transition Plan:
  • disclosure of HIV status.
  • Explain to patient /family about transition
  • Patient’s filing
  • Final appointment at PAC and new appointment at Adult site. Arrange with Adult site.
– Education and Skills Training for Adolescent Patients:
  • What patient need to know in the Adult site and evaluate the readiness for transition:
    • seeking medical care for symptoms or emergencies
    • Identify symptoms and describe them
    • Make, cancel, and reschedule appointments,
2. Preparing for transition in the adolescent care setting (cont.)

- Education and Skills Training for Adolescent Patients (cont.):
  - Arrive to appointments on time
  - Call ahead of time for urgent visits
  - Make sure that they have enough medication at home before medications run out before appointment date.
  - Understand the importance of health care follow up


  _Identifying adult care provider_: assist adolescent in choosing adult ART site best suit the individual. factors: distance, transportation, etc.
2. Preparing for transitioning patients in the adult care setting (cont.)

- **When to Transition patients:** when the patient:
  - Understood his/her disease and its management
  - Had ability to make and keep appointments
  - Known when to seek medical care for symptoms or emergencies
  - Clinically stable
2. Preparing for transitioning patients in the adult care setting (cont.)

- Communication between the Pediatric and Adult Care Provider:
  - Inform the transitional plan to ACP
  - Be ready to manage specific adolescents (..poor adherence..) with necessary skills
3. Evaluation before transition occurred

• Pre-Transition Assessment
  – The team of pediatric care provider should devise a plan to achieve the following on an ongoing basis:
    • Assessment: is adequately caring for his/her own health
    • Assessment: barriers, support needed, and who will provide this support
3. Evaluation before transition occurred (cont.)

- Checklist for Successful Transition
  - Accepted his or her HIV status
  - Knew how to negotiate appointments and has been introduced to the adult ART clinic
  - Be able to assume responsibility for his or her treatment and participate in decision-making
  - Psychosocial support needed after the transition are available.
  - Know who to call in case of an emergency, and that the patient should carry this information with them
  - Speak up and ask the physician or nurse counselor any questions needed.
  - Understand the medications...name and time taken..
4. Post-Transition Assessment

- **Post-Transition Assessment**
  - Patients still *continue to have contact with their PAC site*?
    - may create challenges in maintaining ongoing care at the adult site facility. Communication between PAC and adult providers is important to a successful transition process.
  - *rely on their pediatric care provider for emotional support*?
    - This is normal happening to lower the patient’s sense of loss.
    - The pediatric provider should defer clinical management decisions to the adult site and should be alert to the risk of hindering the patient from establishing a trusting relationship with the new adult site.
  - **Young patients who withdraw from care in an adult clinic will often return to their PAC site.**
    - the PAC provider should be prepared to help the patient identify services that can provide increased support and should encourage re-engagement at adult site.
Model for transition (modified from MAGNA Children at Risk)- a summary job aid.

**At pediatric service**
- Start preparation for transition **up to one year before the transfer**
- Help adolescents join mmm support groups for children or adolescents where transition is discussed
- Support groups for caregivers
- Assign case manager (case management supporter) over transition period – NGOs, mmm volunteer, AUA social worker, MAGNA, CPN+
- Help contact with Adult Site for the transfer and set up an appointment for the adolescent
- Help to complete the transfer form
- Explain to the Adolescent and caretaker where Adult services location (take them there for an initial visit)

**After Transition**
- Book the appointment in Adult Services
- Help with the registering the patient in Adult Services and transferring patient file
- Nurse counsellor or PLHIV volunteer to accompany patient for to the first visit in Adult sites
- Explain the patient about the new registration and pharmacy system at Adult site
- Reminders to the Adolescent about the next appointment date
- Nurse counsellor or PLHIV volunteer to link with community support volunteer (CSV) care to find the lost case
- Active Case Management can be used to follow-up with lost cases
- Case management supporter /Community support volunteer can visit adolescent (2 times per month) for first 6 months
- Case management supporter /Community support volunteer can visit adolescent (1 time per month) after 6 months
- Evaluation after 9 months
B- After Transition to Adult ART site

Roles of Adult ART site:

1. Organizational arrangements for Adolescent care in Adult HIV clinics
2. Psychosocial support
3. Reproduction and sexual health
4. Clinical issues regarding Adolescent care
5. Adherence and retention in care
1-O rganizational arrangements for Adolescent care in Adult HIV clinics

**Clinic level organizational arrangements for transition of adolescents to adult care:**

1. Identify a focal point for communication between the adult and pediatric services: oversee transition plan, answer concerns/questions.

2. Develop a specific orientation procedure to acquaint the newly transitioned patient to the adult clinic environment that includes:
   - Orientation to the physical layout of the clinic.
   - Introduction to clinic staff.
   - Explaining clinic visit flow.
   - Clearly explaining the policy for late arrivals and walk-ins.
   - Assignment one clinic staff member as point person for the patient, and have his/her contact information available, including hours when contact is possible.
1-Organizational arrangements for Adolescent care in Adult HIV clinics-(cont.)

Organizational arrangements for improving the “adolescent friendliness” of the clinic:

1. Create a specific clinic time each week for adolescent attendance.
2. Structure this clinic time for shorter waiting periods, and longer consultation times.
3. Invite a counsellor/PSW from the paediatric clinic to join this session.
4. Enable MMM (peer support) adolescent specific activities.
5. Ensure where possible that fees are not charged to the Adolescent.
6. Partner with NGOs to provide specific adolescent support to complement clinic services.
7. Foster a clinic culture where staff remains non-judgmental and respectful at all times.
2-Psychosocial support

• The Adult HIV clinic will be required to provide ongoing psychosocial support to adolescents, which may include:
  • Identifying and address crises (i.e., suicidal behaviour, homelessness).
  • Reproductive health and sexuality, and promotion of safer sex behaviours.
  • Providing access to benefits, entitlements, and services.
  • Supporting youth in self-care and life-enhancing practices.
  • Identifying and treating chronic problems (i.e., depression, substance abuse).
  • Promoting skills to live independently and to make the transition to adulthood.
• **Counselling for adolescents** includes:
  – support for adherence to ART, sexual and reproductive education, support for intimate romantic relationships, as well as disclosure to partners and significant others.
  – Care providers should show respect, and listen carefully and in a non-judgmental way to the adolescent’s concerns and choices.
  – Care providers need to talk with the adolescent by themselves about risk reduction (not talk to or not in front of parents)
  – Group counselling should be facilitated to help these teenagers develop better self-esteem.
Adolescents need to have a clear understanding regarding

– Basic reproduction and contraceptive measures to avoid pregnancy.

– Sexually active young women should be strongly advised to use dual contraceptive methods, preferably with a long acting hormonal contraceptive.

– Sexually transmitted infections: information regarding prevention, and where to access check-ups and treatment.

– Their individual right to control if, when and how they engage in sexual activity.
# 4-Clinical issues regarding Adolescent care

<table>
<thead>
<tr>
<th>Clinical issues regarding Adolescent HIV care</th>
</tr>
</thead>
<tbody>
<tr>
<td>• WHO clinical staging for adolescents ≥ 15 years is the same as adults, and for &lt; 15 years is the same as paediatrics.</td>
</tr>
<tr>
<td>• Initiation of ART in adolescents; same as adults</td>
</tr>
<tr>
<td>• ART regimen for adolescents ≥ 35kg is the same as for adults, for &lt;35 kg is same as for children.</td>
</tr>
<tr>
<td>• NCD: ALHIV who had perinatal transmission are at risk of long term ART toxicity and metabolic complications of HIV (e.g. hyperlipidaemia)</td>
</tr>
<tr>
<td>• OI prophylaxis:</td>
</tr>
<tr>
<td>• Cotrimoxazole is prescribed routinely for all adolescents, and once they become an adult at age 20, the same stopping rules apply as to adult.</td>
</tr>
<tr>
<td>• TB screening and criteria for IPT are the same for adolescents as adults.</td>
</tr>
<tr>
<td>• Cryptococcal screening is also the same for adolescents as adults</td>
</tr>
</tbody>
</table>
5-Adherence and retention in care

• Providing a “adolescent friendly” clinical service
• Identify barriers to adherence by listening to the individual’s concerns, and work with them to address these issues in a non-judgmental way.
• Peer support, and NGO support should be recruited when available.
• Active case management should be employed to ensure that each adolescent is supported to remain in care.
Summary

Transition from PAC site to Adult ART site - *Roles of PAC site*
1. Support for Adolescents living with HIV/AIDS
2. Preparing for transition in the adolescent care setting
3. Evaluation before transition occurred
4. Post-Transition Assessment

After Transition to Adult ART site - *Roles of Adult ART site*
1. Organizational arrangements for Adolescent care in Adult HIV clinics
2. Psychosocial support
3. Reproduction and sexual health
4. Adherence and retention in care
5. Clinical issues on adolescent care

- Well planned,
- Communication/sharing information/transfer file
- Work with caretaker & patient
- Focal points
- Follow up
Thank You!
កិច្ចប្រជ ុំផ្សព្វផ្ាយគោលការណ៍ ណំ
នុំជាតិស្ដីព្ីការណ៍ ណែទុំ-ព្របាលជុំងឺការស្និយមនិងការព្របាលគោយឱស្ែប្រឆុំងគមគោគគេដស្៍ស្ុំោរ់មនស្សគព្ញវយគកេងជុំទង់និងកមារថ្ែៃទី២៨វិច្ឆិកាឆនុំ
២០១៦
Universal Precautions
and
Post-Exposure Prophylaxis
Dr. Deng Serongkea
World Health Organization
• Who will be able to access PEP
• Infectious and non significant infectious body fluid
• Criteria for PEP & PEP Regiment
• Criteria for not PEP
• Special consideration for Rape victim (GBV)
• Follow up
PEP are reserved for

- Health care staff
  (guideline 2012)

- _Health care staff
- _Raped Victims /sexual assault of GBV
- _Sexual exposure of discordant couple prior to VL Suppress

New

2015

- PEP is given within 4 hours of exposure, but may be given up to up to 72 hours following exposure
- Duration: 28 days
- 3 ARV regimens
- Consent based and fully understand of risk and benefits

PEP Regiment for Adult

- TDF 300mg + 3TC 300mg + ATV/r 300/100mg once daily x 28 days

- If 3rd Drug is not available, or contraindication
  → 2NRTIs: TDF + 3TC is acceptable

PEP Regiment for children

<table>
<thead>
<tr>
<th>Age</th>
<th>Preferred Treatment Regimen</th>
<th>Duration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Children &lt;10 years &lt;35Kg</td>
<td>ABC or AZT +3TC +LPV/r</td>
<td>28 Days</td>
</tr>
<tr>
<td>Adolescents &gt;10 years AND &gt;35Kg</td>
<td>TDF or ABC or AZT + 3TC + LPV/r or ATV/r</td>
<td></td>
</tr>
</tbody>
</table>

New
Post Exposure Prophylaxis Care Pathway
Baseline test for source andExposed person(*):
- HBsAg,
- HCV antibody
- HIV antibody
And if Source isHIV positive,furtherinformation needed:
- stage of disease
- CD4 cell count
- history of ART
- viral load, and
- ARV resistance
• Assess and provide emergency contraception and STI treatment in the context of sexual exposure.
  ➢ Presumptive treatment of STI with Azithromycin 1g and Cefixime 400mg stat.
  ➢ Emergency contraception, and baseline + follow up pregnancy testing.

• Assess for exposure to other infections
  ➢ HBV: high risk through parenteral and sexual exposure.
  ➢ HCV: high risk through parenteral, and if traumatic sexual exposure.
  ➢ Tetanus - Individuals who sustain wounds (bites, abrasions or cuts) should have their tetanus status assessed and be offered immunization if indicated.

• Explain need for secondary prevention:
  ➢ Measures must be taken to avoid secondary transmission of possible HIV infection until HIV Ab check in 3 months.
  ➢ Use condoms, safe-injecting practices, and avoid blood donation. Risks and benefits of continuing to breast-feed should be discussed.

• For sexual assault provide/refer for specific psychosocial support
  ➢ See also NCHADS STI guidelines which detail management of sexual assault
**Complete documentation:**
- See Table 50-1 NCHADS PEP Clinic visits and reporting form

**Follow up on PEP**
- Return to the clinic in 3-4 days for assessment of adherence and tolerability, and check that all results are available and that PEP is still indicated.
- If the source is established to be HIV negative, post-exposure prophylaxis should be discontinued.
- Prescribe further 24 days

**Follow up testing**
- HIV test 3 months after exposure
- Syphilis test at 3 months after sexual assault.
- HBV, HCV testing at 6 months after exposure if indicated.
Assess HIV risk and eligibility for PEP
Infection and non significant infection body fluid

• Considered (potentially) Infectious:
  – Blood, blood-stained saliva, bloody fluids, tissue
  – Cerebrospinal, amniotic, pericardial, rectal, peritoneal, pleural, synovial fluids
  – Semen, vaginal secretions
  – Breast milk

• Body fluids that do not pose a significant risk of HIV infection, and therefore do not require PEP:
  – Tears, non-blood stained saliva, gastric fluid, sputum, urine and sweat.
Criteria for PEP

- **Occupational exposure:**
  Offer PEP in the case of occupational exposure from HIV+ patient if:
  
  - Deep puncture wound with a hollow bore needle
  - Needle-stick injury after it was used for IM/IV/subcutaneous injection,
  - Injury from a sharp instrument visibly contaminated with blood.
  - Exposure for > 1min to a large quantity of blood to non-intact skin or mucus membrane.
  - Exposures similar to blood involving CSF, synovial fluid, pleural, pericardial, or amniotic fluid.
  - Even if source person is know to have undetectable VL, the parenteral route of transmission it is still reasonable to consider PEP.
  - If the source is known to have ART failure, start PEP and discuss with an expert.
Criteria for PEP

- **Sexual exposure Raped victim / sexual assault**
  - PEP should be started as soon as possible, and within 72 hours.
  - *In addition, Raped victim shall be given:*
    - Presumptive treatment of STI with Azithromycin 1g and Cefixime 400mg once dose.
    - Emergency contraception, and baseline + follow up pregnancy testing.

- **Children Exposed to HIV by means other than MTCT, for instance:**
  - Sexual abuse
  - Consensual sex
  - Unsafe therapeutic injections or infusions, including piercing, tattooing and the use of inadequately sterilized medical equipment
  - Transfusion of inadequately screened blood products
  - Accidental needle stick injury contaminated with HIV-infected blood
  - Human bites (if the biter’s saliva is bloody and a piercing wound is inflicted)
  - Exposure to blood or blood-contaminated bodily fluids from an HIV-infected source, where there is a breech in skin (e.g., open cuts or wounds) or direct contact with mucus membranes

- *PEP must be stop if the result of source person came out Negative.*
What if, the source person is unknown HIV status?

**Calculation:** Risk of HIV transmission = Risk per exposure \(\times\) risk of source being HIV positive (*prevalence of source*)

If multiple exposures, and from multiple sources should be added to estimate the total risk:

Example:
- The risk to a HCW who has a needle stick injury from a known PLHIV = 1/440 or 0.23%
- The risk to a HCW who has a **needle stick injury** from a person from the general adult population, HIV status unknown = 1/440 (0.23%) \(\times\) 0.6% = 0.0014%
- The risk to a man who experienced **condom breakage during vaginal sex** with an *entertainment worker* = 1/2500 \(\times\) 13.9% = 0.0056%
- The risk to a woman who is vaginally and anally raped by a PWUD (1/1250 \(\times\) 4.4%) + (1/70 \(\times\) 4.4%) = 0.0035% + 0.06% = 0.07%
- The risk to a woman who is vaginally raped by 5 PWUD = 5 \(\times\) 1/1250 \(\times\) 4.4% = 0.018%
### Assess of estimated risk of HIV transmission per episode from HIV infected sources

<table>
<thead>
<tr>
<th>Exposure from an HIV infected source</th>
<th>Estimated risk of HIV transmission per episode</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Sexual exposure (via blood, semen, vaginal fluids)</strong></td>
<td></td>
</tr>
<tr>
<td>· Insertive vaginal intercourse (female to male transmission)</td>
<td>1/2500 (0.04%)</td>
</tr>
<tr>
<td>· Receptive vaginal intercourse (male to female transmission)</td>
<td>1/1250 (0.08%)</td>
</tr>
<tr>
<td>· Receptive anal intercourse (male to male (MSM) or male to female transmission) without withdrawal prior to ejaculation</td>
<td>1/70  (1.43%)</td>
</tr>
<tr>
<td>· Receptive anal intercourse with withdrawal prior to ejaculation</td>
<td>1/155  (0.64%)</td>
</tr>
<tr>
<td>· Insertive anal intercourse, uncircumcised (MSM)</td>
<td>1/160  (0.62%)</td>
</tr>
<tr>
<td>· Insertive anal intercourse, circumcised (MSM)</td>
<td>1/900  (0.1%)</td>
</tr>
<tr>
<td>· Oral sex: insertive or receptive (male or female)</td>
<td>Extremely low</td>
</tr>
<tr>
<td><strong>Blood exposure</strong></td>
<td></td>
</tr>
<tr>
<td>· Intravenous Drug Use: contaminated injecting equipment</td>
<td>1/125</td>
</tr>
<tr>
<td>· Occupational needle stick (NSI) or other sharps exposure</td>
<td>1/440</td>
</tr>
<tr>
<td>· Blood transfusion</td>
<td>1/1.1 (90%)</td>
</tr>
<tr>
<td><strong>Other exposure</strong></td>
<td></td>
</tr>
<tr>
<td>· Mucus membrane or non-intact skin exposure</td>
<td>&lt; 1/1000</td>
</tr>
</tbody>
</table>
# Reference: HIV prevalence in Cambodia

**Table 43-2 Cambodian HIV prevalence estimates by demographic**

<table>
<thead>
<tr>
<th>Population / subpopulation</th>
<th>Prevalence</th>
</tr>
</thead>
<tbody>
<tr>
<td>General adult population</td>
<td>0.6%</td>
</tr>
<tr>
<td>Injecting drug users (PWID)</td>
<td>24.8%</td>
</tr>
<tr>
<td>Non injecting drug users (PWUD)</td>
<td>4.4%</td>
</tr>
<tr>
<td>Entertainment worker (&gt;7 sex partners/week)</td>
<td>13.9%</td>
</tr>
<tr>
<td>Transgender M→F</td>
<td>9.8%</td>
</tr>
<tr>
<td>MSM</td>
<td>2.3%</td>
</tr>
</tbody>
</table>
Criteria for Not PEP

- Occupational exposure:
  - **PEP is not required if** exposure to body fluids that do not pose a significant risk of HIV infection, such as: tears, non-blood stained saliva, urine and sweat.
  - **PEP is not required if the exposed person is HIV+**
Criteria for Not PEP

- Sexual exposure Raped victim
  - If the sexual exposure is from a source person known to have an undetectable VL (e.g. condom breakage from HIV+ spouse), the risk is extremely low and PEP is not indicated.
  - In cases that do not require PEP, the exposed person should be counselled about limiting future exposure risk. Although HIV testing is not required, it may be provided if desired by the exposed person.
Additional care for physical & mental health for sexual assault victim of Gender Based Violence

• Immediately refer patients with life-threatening or severe conditions for emergency treatment!

• If the woman comes within 5 days after sexual assault, care involves 6 steps (Detail in Health Care for Women subjected to intimate partner violence and sexual violence, MoH 2015).

  1. Take history and conduct the examination
  2. Treat any physical injuries
  3. Provide emergency contraception
  4. Prevent sexually transmitted infections (STIs)
  5. Prevent HIV
  6. Plan for self-care & referral (social and mental support)
Additional care for physical & mental health after sexual assault victim of Gender Based Violence _(cont.)

. **Treatment:**
  - **HIV PEP:** given soonest possible within 72 hours after rape:
    - TDF 300mg + 3TC 300mg + ATV /r 300/100mg once daily x 28 days
  - **Provide emergency contraception:**
    - Levonorgestrel-only: 1.5 mg in a single dose, *Or if it is not available use:*
    - Combined estrogen-progestogen: 2 doses of 100 μg ethinyl estradiol plus 0.5 mg levonorgestrel, 12 hours apart.
    - All PEP medication are safe and no interaction.
  - **Prevent STIs:**
    - There is no need to test for STIs before treating.
    - Give preventive treatment for STIs base on national protocol.

. **Treat any physical injuries:** refer or hospitalization if indicated
  - **Forensic letter can be issued only at Provincial Hospital where committee for forensic located.** (refer patient to; if she requested that letter)

7-Refear for further social and mental support, as needed

*For Your Information, elaborated from Clinical handbook GBV, MoH 2015*
Hepatitis B:

<table>
<thead>
<tr>
<th>Immunization status</th>
<th>Treatment guidelines</th>
</tr>
</thead>
<tbody>
<tr>
<td>No, never vaccinated for hepatitis B</td>
<td>1st dose of vaccine: at first visit. 2nd dose: 1–2 months after the first dose (or at the 3-month visit if not done earlier). 3rd dose 4–6 months after the first dose.</td>
</tr>
<tr>
<td>Started but has not yet completed a series of hepatitis B vaccinations</td>
<td>Complete the series as scheduled.</td>
</tr>
<tr>
<td>Yes, completed series of hepatitis B vaccinations</td>
<td>No need to re-vaccinate.</td>
</tr>
</tbody>
</table>

HCV: high risk through parenteral and traumatic sexual exposure
Tetanus: check vaccination status and offer immunization if indicated
Follow- Up on PEP

...Adherence-Tolerability- HIV result of Source- testing exposed person...

• Return to the clinic in 3 -4 days for assessment of adherence and tolerability, and check that all results are available and that PEP is still indicated.
  – If the source is established to be HIV negative, post-exposure prophylaxis should be discontinued.

• Prescribe additional 24-day PEP
• Repeat HIV test 3 months after exposure
• Syphilis test at 3 months after sexual assault.
• HBV, HCV testing at 6 months after exposure if indicated.
Follow-Up on PEP

• Advise the secondary prevention of transmission
  • First 6–12 weeks after exposure especially
  • Sexual abstinence/condoms to prevent sexual transmission and to avoid pregnancy
  • Refrain from donating blood, plasma, organs, tissue, or semen

❖ For breastfeeding exposed woman:
  • counsel about risk of HIV transmission through breast milk
  • consider discontinuation of breastfeeding, especially for high-risk exposures

❖ Advise to seek medical evaluation
  • during follow-up period
  • for any acute illness: fever, rash, myalgia, fatigue, malaise, or lymphadenopathy (may be indicative of acute HIV infection, drug reaction or another medical condition)
# PEP Record

## Table 50-1 NCHADS PEP Clinic visits and reporting form

See PEP guideline, and follow PEP care pathway for steps in PEP management.

### Demographic details

<table>
<thead>
<tr>
<th>Name</th>
<th>Phone no:</th>
</tr>
</thead>
<tbody>
<tr>
<td>DOB  <strong><strong>/</strong><em>/</em></strong>_</td>
<td>Sex</td>
</tr>
<tr>
<td>Age</td>
<td></td>
</tr>
</tbody>
</table>

### Category of exposure

- Occupational
- Discordant couple
- Victim of sexual assault

### Timing of exposure

- Date of exposure  ____/____/____
- Time of exposure
- Hours from exposure to PEP

### Source person HIV status (If HIV negative do not start or discontinue PEP when known)

At time of presentation:

- Pos
- Neg
- Unknown

If PLHIV are they on ART?

- Yes
- No

Date commenced ART  ____/____/____

Most recent VL result

Is source person available for HIV test?

- Yes
- No

Is the source person high risk for HIV (could be in the window period?)

- Yes
- No

Source HIV status follow up result:

- Pos
- Neg
- Unknown

- Date

### Exposed person’s HIV status (If HIV positive do not start or discontinue PEP when known)

At time of presentation:

- Pos
- Neg
- Unknown

Ever had HIV test?

- Yes
- No

HIV test at baseline:

- Pos
- Neg
- Unknown

- Date

HIV test 3M post exposure:

- Pos
- Neg
- Unknown

- Date

### 1. Nature of exposure: Occupational

Health care facility

- Deep injection of contaminated hollow bore needle
- Other parenteral exposure to blood or body fluids
- Mucus membrane exposure

Describe exposure

### 2. Nature of exposure: Discordant couple

- Receptive vaginal
- Receptive anal
- Receptive oral with ejaculation
- Insertive vaginal
- Insertive anal
- Condom used?
- Yes
- No
- Unknown
- Condom broke?
- Yes
- No
- Unknown

Exposed male circumcised?

- Yes
- No

Evidence of trauma; bleeding or mucosal tear?

- Yes
- No
- Unknown

Describe exposure

### 3. Nature of exposure: Victim of sexual assault

- Receptive vaginal
- Receptive anal
- Receptive oral with ejaculation

Condom used?

- Yes
- Unknown
- Condom broke?
- Yes
- No
- Unknown

Evidence of trauma; bleeding or mucosal tear?

- Yes
- No
- Unknown

Number of perpetrators?

Describe exposure

Is PEP clinically indicated?

- Yes
- No

Describe:

- Patient counselled and verbally consented to PEP?
- Yes
- No

Regimen prescribed: TDF + 3TC + ATV/r

- Other/describe

Time 1st dose taken? (Give as soon as possible, whilst in the consultation)

If sexual exposure (discordant couple or victim of sexual assault)

- Emergency contraception: Prescribed
- Refused
- Not indicated

- STI presumptive treatment: Prescribed
- Refused
- Not indicated

Referral for psychosocial support?
### Exposure to other infections:

<table>
<thead>
<tr>
<th>Source</th>
<th>HBV+</th>
<th>Yes</th>
<th>No</th>
<th>Unknown</th>
<th>Recipient?</th>
<th>Yes</th>
<th>No</th>
<th>Unknown</th>
</tr>
</thead>
<tbody>
<tr>
<td>Source</td>
<td>HCV+</td>
<td>Yes</td>
<td>No</td>
<td>UK</td>
<td>Yes</td>
<td>No</td>
<td>Unknown</td>
<td></td>
</tr>
</tbody>
</table>

Tetanus vaccination indicated? Yes | No | Unknown |

**Explain need for secondary prevention**

**Follow up appointment (stress the importance of this):**

Date ___/___/_____

**Doctor to sign**

---

**Follow up consultation (3 – 4 days)**

Date ___/___/_____

Attend? □

If not → Notify for Active Case Management

---

**Follow up consultation (3 – 4 days)**

Date ___/___/_____

Side effects? Yes | No | Describe:

Adherent? Yes | No | Describe:

Blood test from source checked? □ Result_______ (if HIV negative, discontinue PEP)

Blood test from exposed checked? □ Result_______ (if HIV positive, discontinue PEP)

Continue PEP? Yes | No | Explain:

Same regimen? Yes | No | Explain

**Follow up appointment: (stress the importance of this):**

Date ___/___/_____

**Doctor to sign**

---

**Follow up (3 months)**

Date ___/___/_____

Attend? □

If not → Notify for Active Case Management

**Follow up (3 months)**

Date ___/___/_____

Adherent to all PEP? Yes | No | Describe:

Symptoms or signs of possible acute HIV infection? Yes | No | Describe:

HIV test performed □ (complete results section on front page)

STI screen □ HBV Ab □ HCV Ab □ Pregnancy test □

Follow up required? Yes | No | Describe:

**Doctor to sign**
THANK YOU
កិច្ចប្រជ ុំផ្សព្វផ្ាយគោលការណ៍ ណណ ជាតិ ស្ដីព្ី ការ ណែទុំ - ព្ាបាលជុំងឺ កាស្និយ មនិង ការ ព្ាបាលគោយ ឱស្ែប្រឆុំងគមគោគគេដស្៍ ស្ុំោរ់ មន ស្សគព្ញវ យគកេងជុំទង់ និង ក មារ ថ្ែៃទី ២៨ ណែវិច្ឆិកា ឆ ន ុំបា ២០១៦
Test and Treat Roll-Out Schedule

Mr. Prum Mardi
NCHADS Logistics Management Unit
As of June 30, 2016, Cambodia has 2,282 patients on pre-ART.

With the adoption of Test and Treat in the new Cambodia Treatment Guidelines, these patients will soon be initiated on ART.

Nearly all of these patients will be initiated on TDF+3TC+EFV fixed-dose combination – Cambodia’s preferred first-line regimen.

To guarantee the supply of this product, NCHADS Logistics Unit has prepared a Test and Treat Rollout Schedule.
Cambodia National ARV Distribution Schedule

65 ART sites are divided into 3 “groups” by province for quarterly delivery of fresh stock.

### ARV Quarterly Distribution Calendar, by Province Group

<table>
<thead>
<tr>
<th>Provinces by Group</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>GROUP 1</strong>: Battambang, Banteay Meanchey, Kampong Chhnang, Pursat, Pailin, Siem Reap, Oddor Meanchey, Svay Rieng, Phnom Penh</td>
</tr>
<tr>
<td><strong>GROUP 2</strong>: Kampong Thom, Kampong Cham, Tboung Khmum, Kandal, Kampong Speu, Kep, Kampot, Kol Kong, Preah Sihanouk, Stung Treng, Ratanakiri</td>
</tr>
<tr>
<td><strong>GROUP 3</strong>: Prey Veng, Takeo, Kratie, Preah Vihear, Mondulkiri</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Group 1 Provinces</th>
<th>Jan</th>
<th>Feb</th>
<th>Mar</th>
<th>Apr</th>
<th>May</th>
<th>June</th>
<th>July</th>
<th>Aug</th>
<th>Sept</th>
<th>Oct</th>
<th>Nov</th>
<th>Dec</th>
</tr>
</thead>
<tbody>
<tr>
<td>Battambang</td>
<td></td>
<td></td>
<td></td>
<td>●</td>
<td></td>
<td>●</td>
<td>●</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Banteay Meanchey</td>
<td>●</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>●</td>
<td></td>
<td>●</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Kampong Chhnang</td>
<td></td>
<td>●</td>
<td></td>
<td></td>
<td></td>
<td>●</td>
<td></td>
<td></td>
<td>●</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pursat</td>
<td></td>
<td></td>
<td>●</td>
<td></td>
<td></td>
<td>●</td>
<td></td>
<td></td>
<td>●</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pailin</td>
<td></td>
<td></td>
<td></td>
<td>●</td>
<td></td>
<td>●</td>
<td></td>
<td>●</td>
<td></td>
<td>●</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Siem Reap</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>●</td>
<td></td>
<td></td>
<td>●</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Oddor Meanchey</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>●</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>●</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Svay Rieng</td>
<td></td>
<td></td>
<td></td>
<td>●</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>●</td>
<td></td>
</tr>
<tr>
<td>Phnom Penh</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>●</td>
<td></td>
<td></td>
<td>●</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Group 2 Provinces</th>
<th>Jan</th>
<th>Feb</th>
<th>Mar</th>
<th>Apr</th>
<th>May</th>
<th>June</th>
<th>July</th>
<th>Aug</th>
<th>Sept</th>
<th>Oct</th>
<th>Nov</th>
<th>Dec</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kampong Thom</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>●</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Kampong Cham</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>●</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tboung Khmum</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>●</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Kandal</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>●</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Kampong Speu</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>●</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Kep</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>●</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Kampot</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>●</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Kol Kong</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>●</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Preah Sihanouk</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>●</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stung Treng</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>●</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ratanakiri</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>●</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Group 3 Provinces</th>
<th>Jan</th>
<th>Feb</th>
<th>Mar</th>
<th>Apr</th>
<th>May</th>
<th>June</th>
<th>July</th>
<th>Aug</th>
<th>Sept</th>
<th>Oct</th>
<th>Nov</th>
<th>Dec</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prey Veng</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>●</td>
<td></td>
<td></td>
<td>●</td>
<td></td>
</tr>
<tr>
<td>Takeo</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>●</td>
<td></td>
<td></td>
<td>●</td>
<td></td>
</tr>
<tr>
<td>Kratie</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>●</td>
<td></td>
<td></td>
<td>●</td>
<td></td>
</tr>
<tr>
<td>Preah Vihear</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>●</td>
<td></td>
<td></td>
<td>●</td>
<td></td>
</tr>
<tr>
<td>Mondulkiri</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>●</td>
<td></td>
<td></td>
<td>●</td>
<td></td>
</tr>
</tbody>
</table>
NCHADS will increase stocks distributed to include all current pre-ART patients, beginning with December 2016 delivery to Group 3.

### ARV Quarterly Distribution Calendar, by Province Group

<table>
<thead>
<tr>
<th></th>
<th>2016</th>
<th>2017</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Oct</td>
<td>Nov</td>
</tr>
<tr>
<td><strong>Group 1 Provinces</strong></td>
<td>●</td>
<td>●</td>
</tr>
<tr>
<td><strong>Group 2 Provinces</strong></td>
<td>●</td>
<td>●</td>
</tr>
<tr>
<td><strong>Group 3 Provinces</strong></td>
<td>●</td>
<td>●</td>
</tr>
</tbody>
</table>

Stock deliveries include Test and Treat increases
Guidance on Test and Treat Rollout

Sites should begin Test and Treat according to the below schedule. Buffer stock will allow Groups 1 and 2 sites to begin Test and Treat 1 month before next delivery.

<table>
<thead>
<tr>
<th></th>
<th>Begin Test and Treat</th>
<th>Next ARV Delivery</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Group 1 Sites</strong></td>
<td>December 2016</td>
<td>January 2017</td>
</tr>
<tr>
<td><strong>Group 2 Sites</strong></td>
<td>January 2017</td>
<td>February 2017</td>
</tr>
<tr>
<td><strong>Group 3 Sites</strong></td>
<td>December 2016</td>
<td>December 2016</td>
</tr>
</tbody>
</table>

Provinces by Group

**GROUP 1:** Battambang, Banteay Meanchey, Kampong Chnnang, Pursat, Pailin, Siem Reap, Oddor Meanchey, Svay Rieng, Phnom Penh

**GROUP 2:** Kampong Thom, Kampong Cham, Tboung Khmum, Kandal, Kampong Speu, Kep, Kampot, Kol Kong, Preah Sihanouk, Stung Treng, Ratanakiri

**GROUP 3:** Prey Veng, Takeo, Kratie, Preah Vihear, Mondulkiri
Guidance on Test and Treat Rollout

Sites should begin Test and Treat according to the below schedule. Buffer stock will allow Groups 1 and 2 sites to begin Test and Treat 1 month before next delivery.

<table>
<thead>
<tr>
<th>Group</th>
<th>Begin Test and Treat</th>
<th>Next ARV Delivery</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group 1 Sites</td>
<td>December 2016</td>
<td>January 2017</td>
</tr>
<tr>
<td>Group 2 Sites</td>
<td>January 2017</td>
<td>February 2017</td>
</tr>
<tr>
<td>Group 3 Sites</td>
<td>December 2016</td>
<td>December 2016</td>
</tr>
</tbody>
</table>

“Begin Test and Treat” means:

- Initiate treatment for all current pre-ART patients during their next regular appointment
  - There is no need for pre-ART patients to make an early or special trip to the clinic
  - Current pre-ART patients need to be re-tested for HIV if original diagnosis was >6 months ago
- Initiate treatment for all new HIV positive patients, regardless of CD4 count
Team leaders should ensure that staff are ready to begin Test and Treat on this timeline, and should coordinate with site pharmacists. NCHADS Logistics Management and AIDS Care Units are available to answer questions.

<table>
<thead>
<tr>
<th>Group</th>
<th>Begin Test and Treat</th>
<th>Next ARV Delivery</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group 1 Sites</td>
<td>December 2016</td>
<td>January 2017</td>
</tr>
<tr>
<td>Group 2 Sites</td>
<td>January 2017</td>
<td>February 2017</td>
</tr>
<tr>
<td>Group 3 Sites</td>
<td>December 2016</td>
<td>December 2016</td>
</tr>
</tbody>
</table>

Provinces by Group

**GROUP 1:** Battambang, Banteay Meanchey, Kampong Chnnang, Pursat, Pailin, Siem Reap, Oddor Meanchey, Svay Rieng, Phnom Penh

**GROUP 2:** Kampong Thom, Kampong Cham, Tboung Khmum, Kandal, Kampong Speu, Kep, Kampot, Kol Kong, Preah Sihanouk, Stung Treng, Ratanakiri

**GROUP 3:** Prey Veng, Takeo, Kratie, Preah Vihear, Mondulkiri