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

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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 <u>support IRIR</u>
- 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

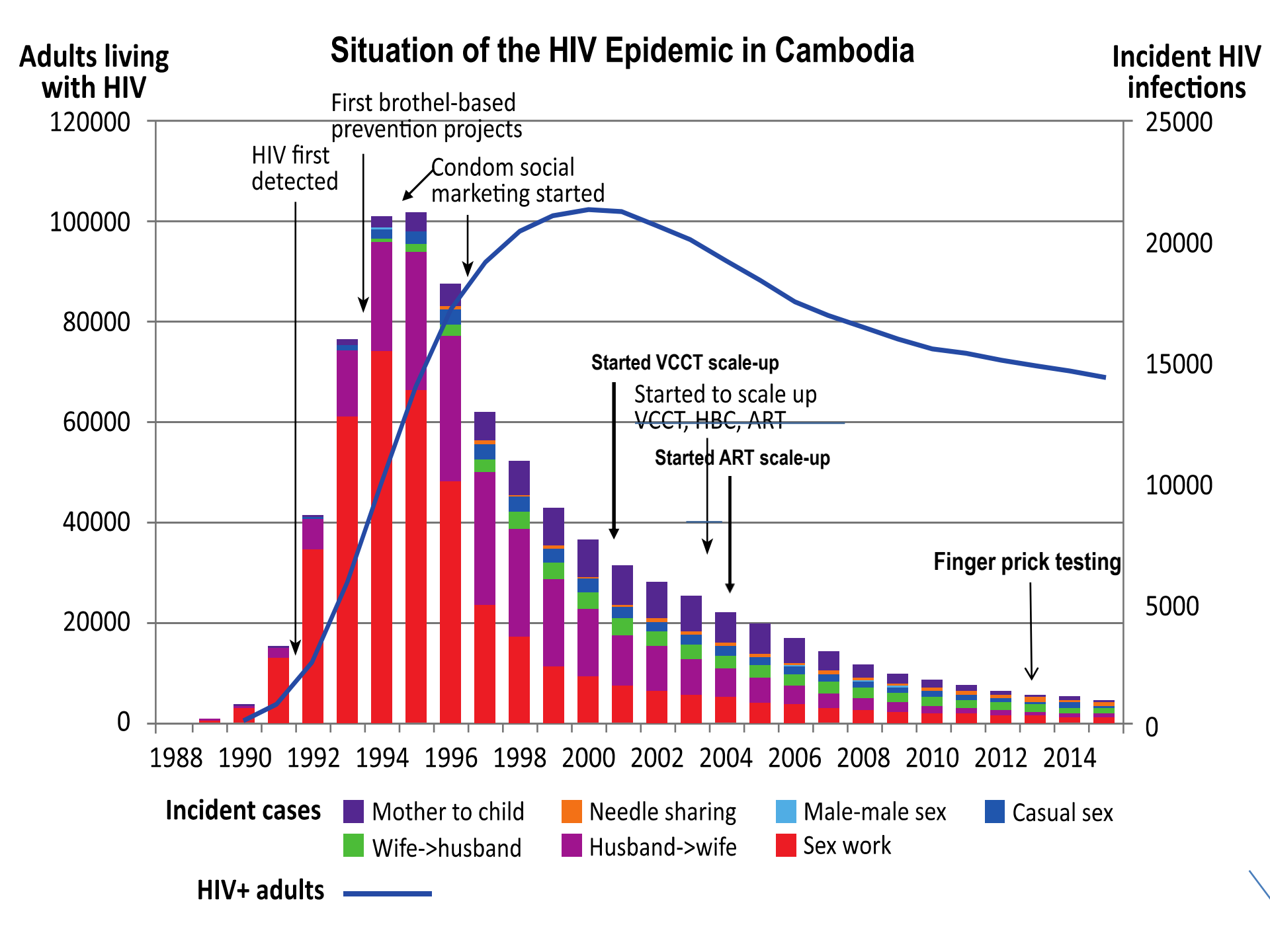
Cambodia 4.0

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
Adults living with HIV
Incident HIV infections
First brothel-based prevention projects
HIV first detected
Condom social marketing started
Started VCCT scale-up
Started to scale up VCCT, HBC, ART
Started ART scale-up
Finger prick testing
120000
100000
80000
60000
40000
20000
0
25000
20000
15000
10000
5000
0
1988 1990 1992 1994 1996 1998 2000 2002 2004 2006 2008 2010 2012 2014
Incident cases
Mother to child
Needle sharing
Male-male sex
Casual sex
Wife->husband
Husband->wife
Sex work
HIV+ adults

GOC Response to HIV: 1991-2000

❖ Political will: GOC and partners

- Recognizing HIV epidemic: 1st 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:

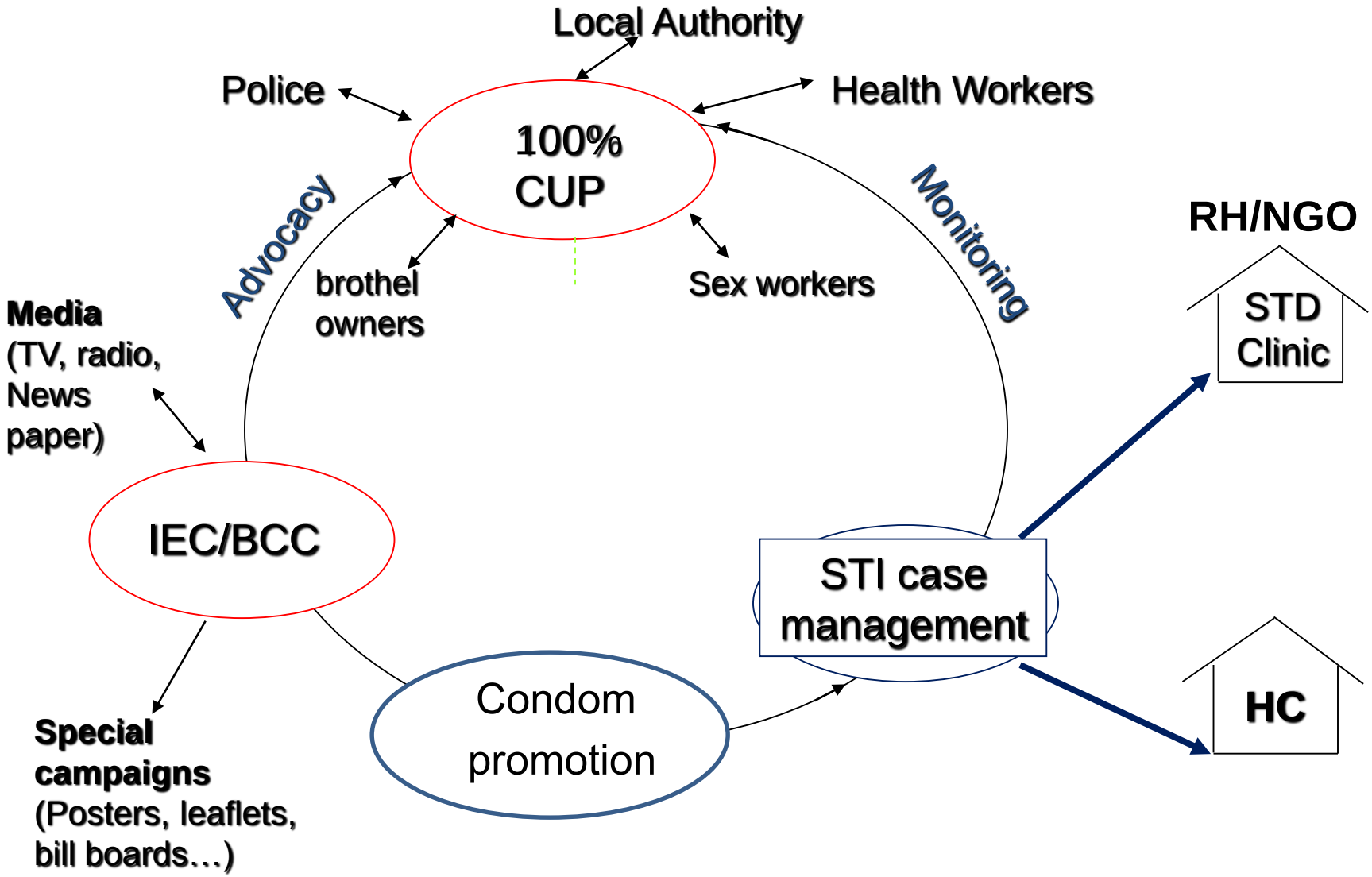
(Demonstration then rapid scale up)

- Stand alone HIV services: VCCT, HBC
- Strong HIV surveillance system: HSS, BSS and SSS, HIV estimations and projections (AEM)

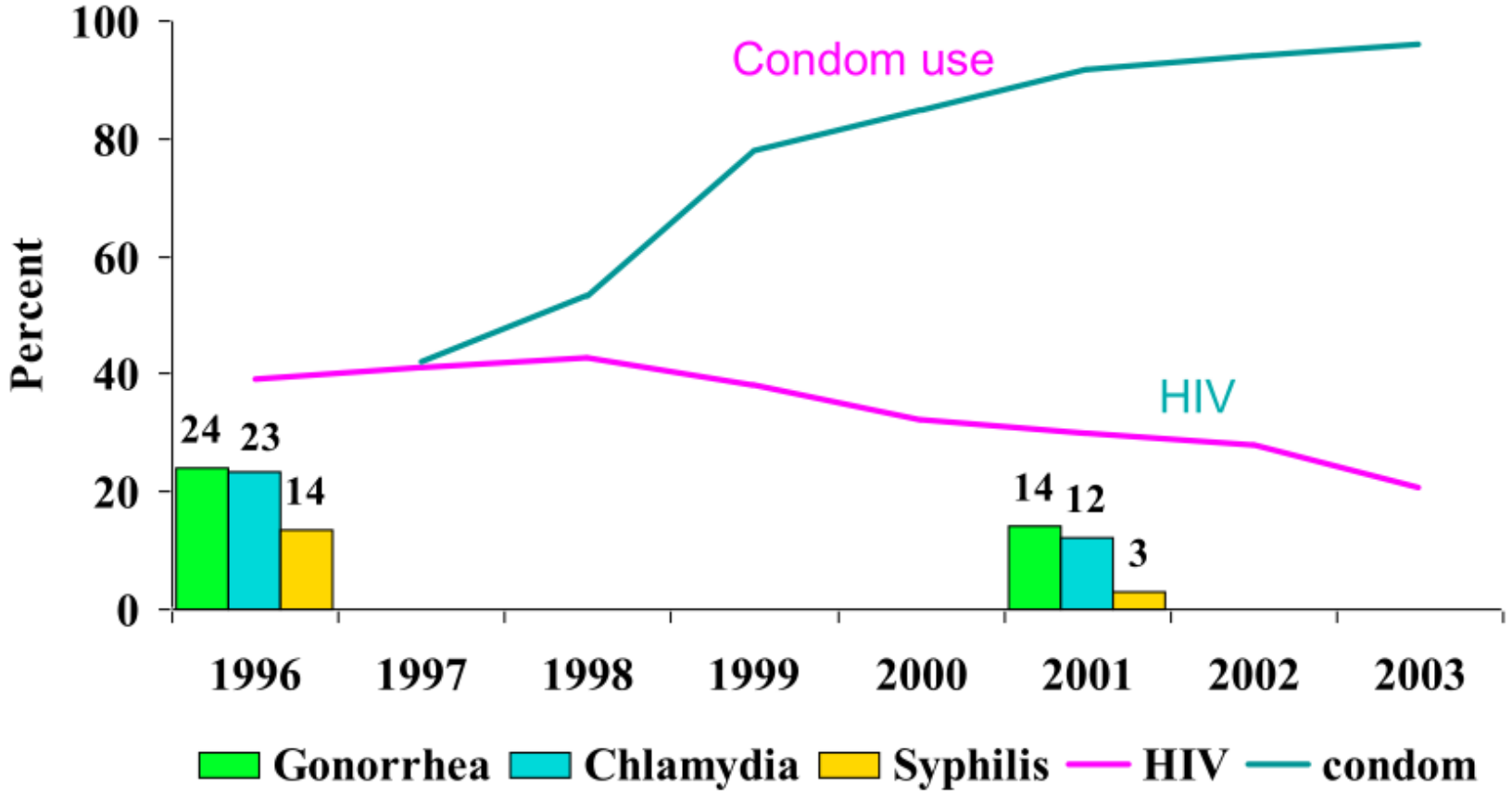
❖ Changed unsafe sex behaviors

❖ Stabilized HIV epidemic

Cambodia 1.0 – HIV Prevention



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)
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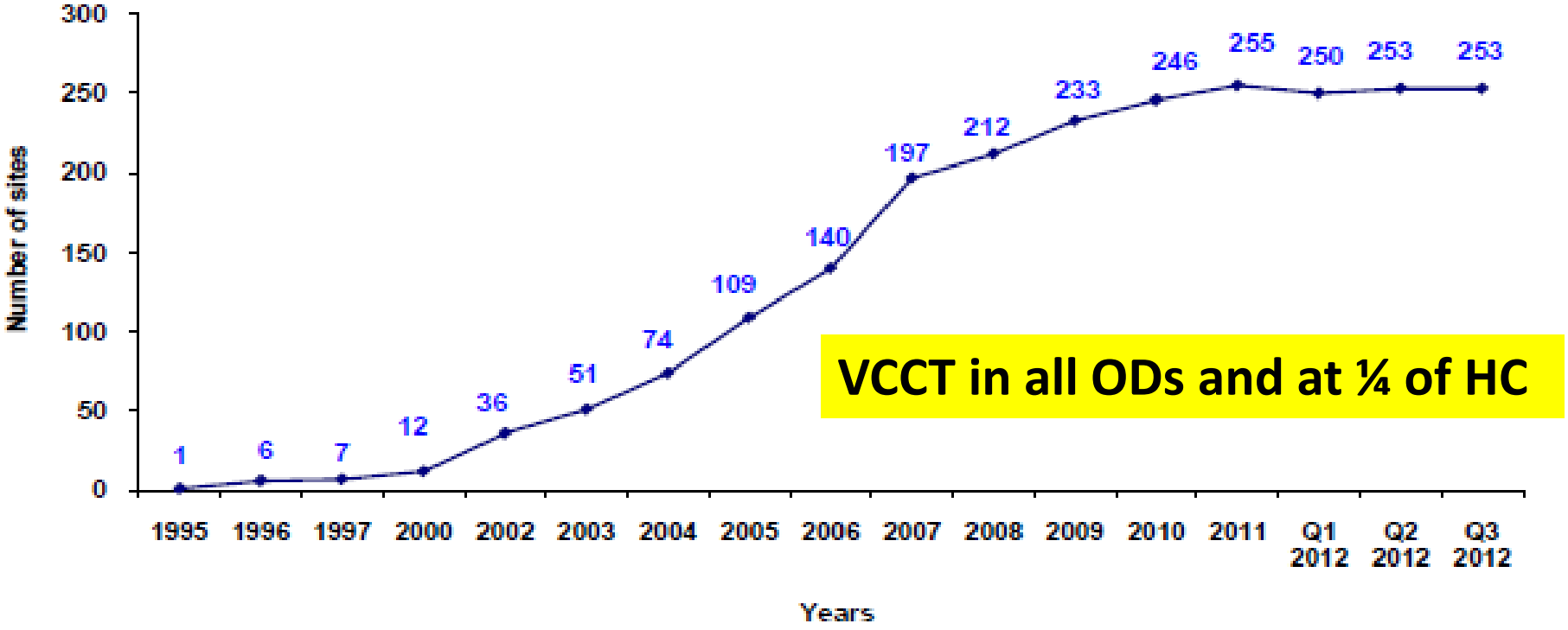
Cambodia 2.0: Rapid Expansion

Strategic Expansion of HTC

Entry point for: HIV prevention and care

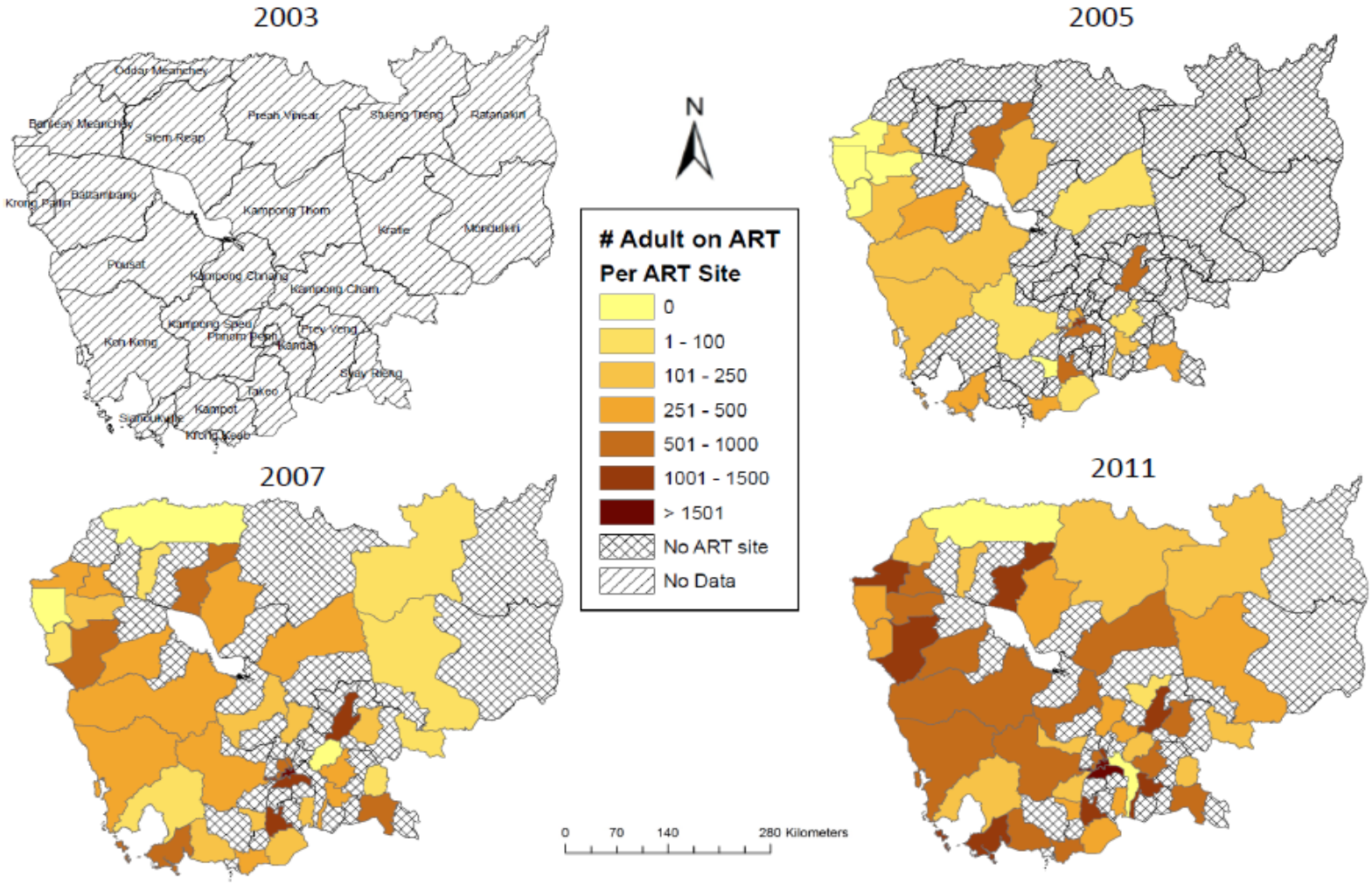


VCCT in all ODs and at ¼ of HC

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

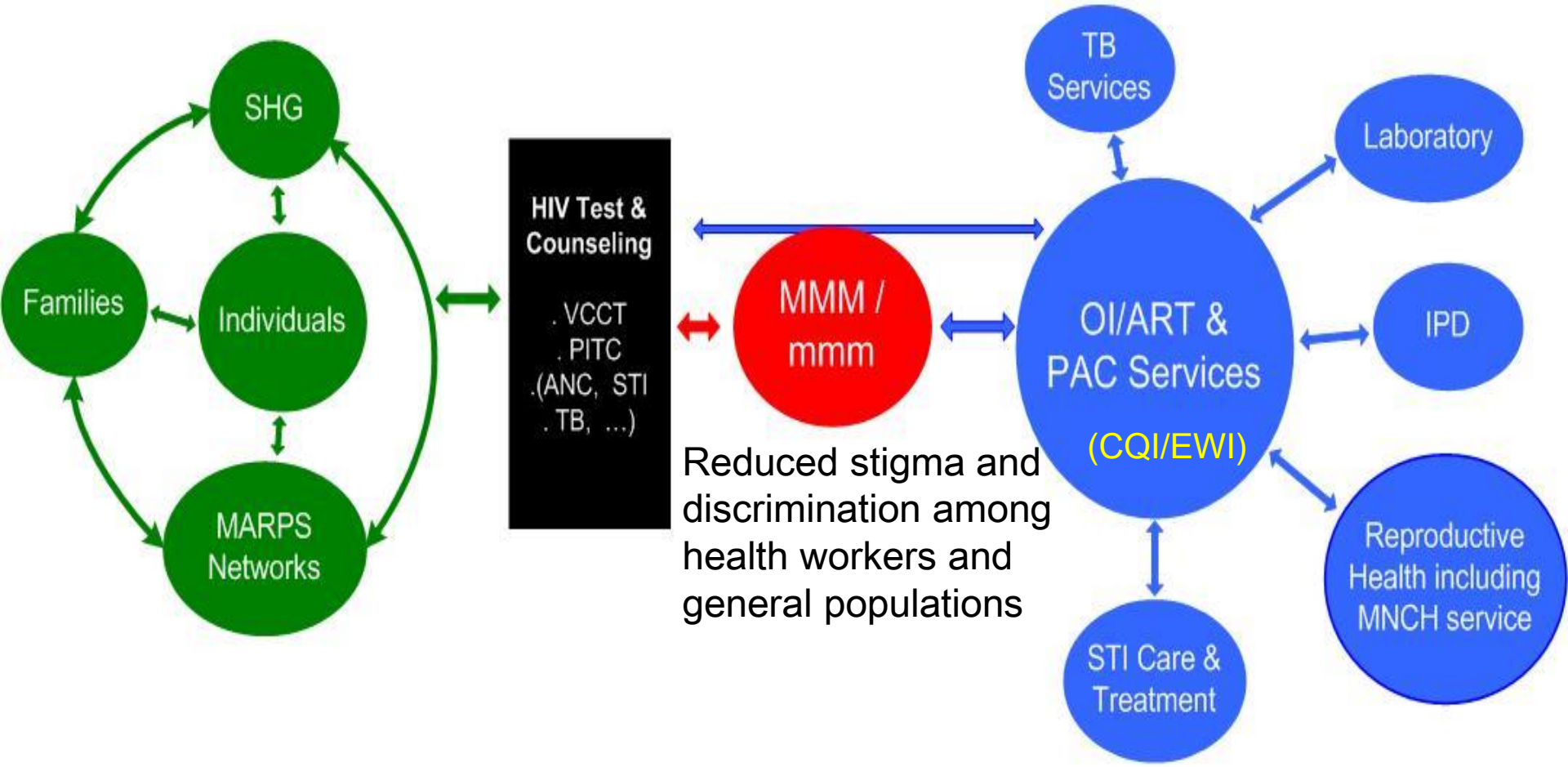


- ART sites in 55/77 ODs covering 92% of PLHIV found
- Indicating the need of Satellite ART sites

Not only expanding services,
but systematically linking with
the community and creating demand

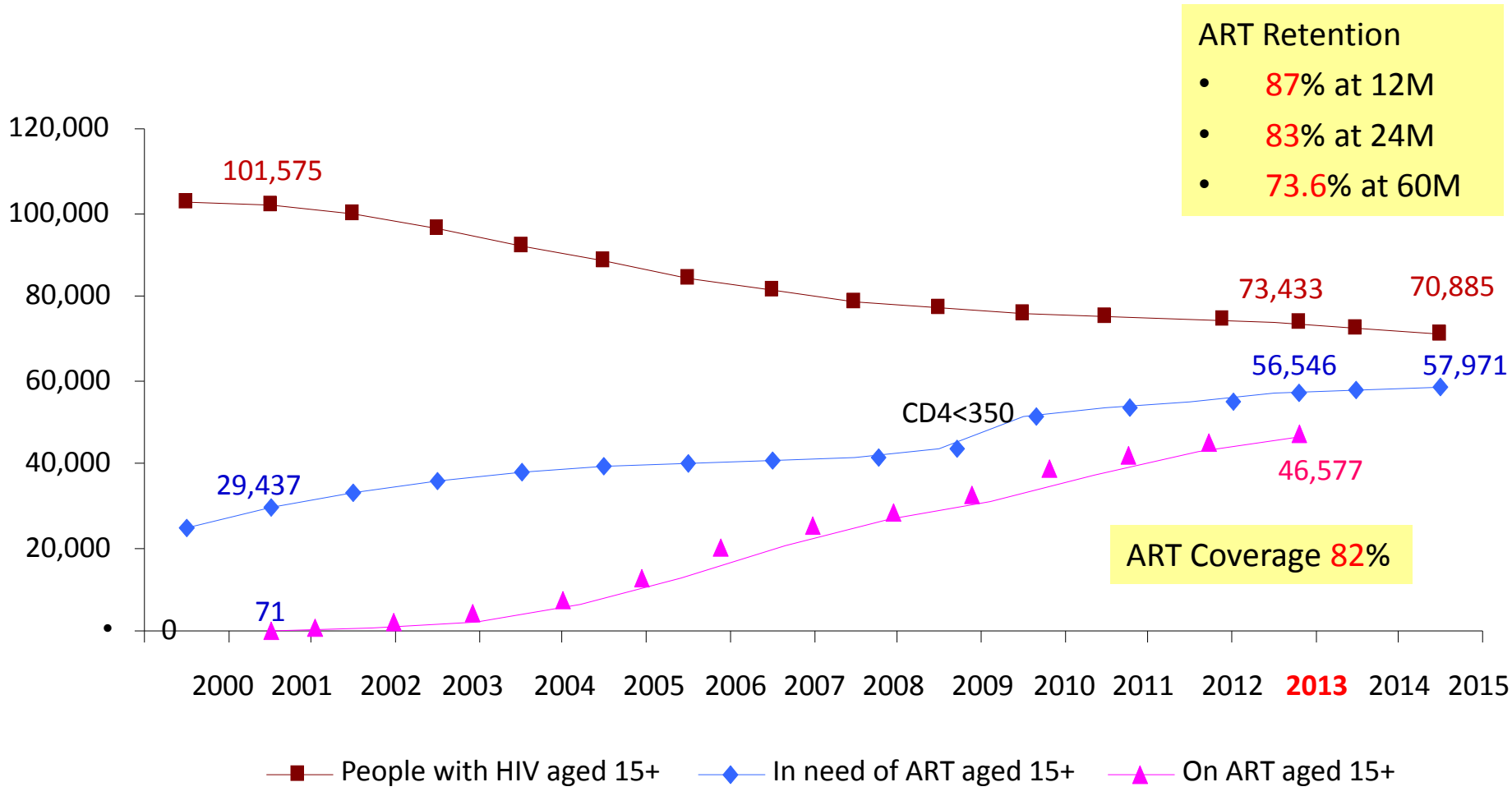
Continuum of Care Framework

Facilitated Expansion of ART



MMM Activities

Number of people with HIV, in need of ART and on ART aged 15+ (2000-2015)



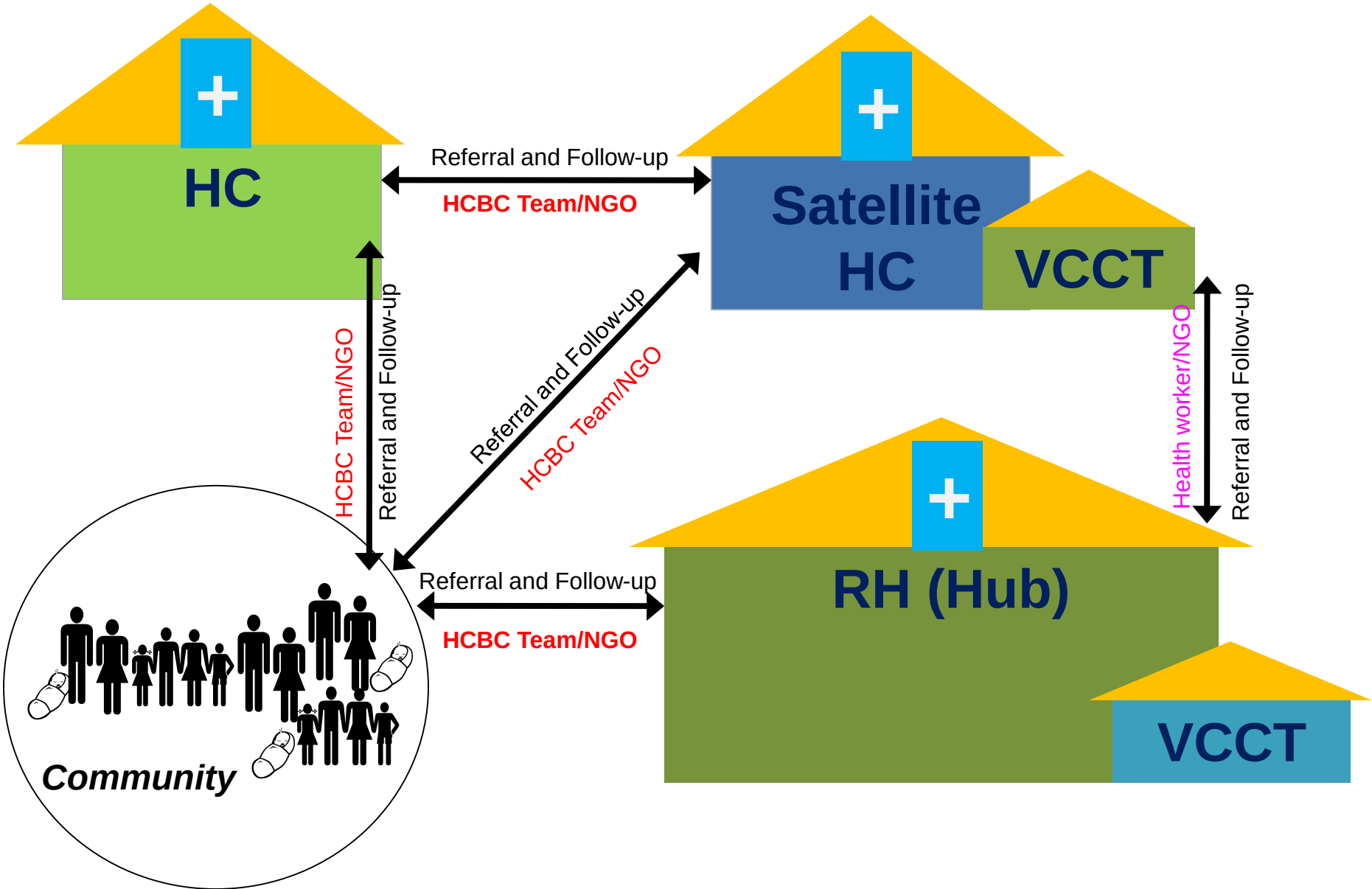
•Source: NCHADS/DMU 2013

"Linking Model"

2000	PMTCT TWG ('99) PMTCT pilot ('01) PMTCT GL: SD-NVP ('02)	TB-HIV Sub-committee ('99) TB/HIV Framework ('02)
2005	PMTCT GL rev: Dual prophyl ('05)	TB/HIV pilot ('03) Joint Statement: Role & Responsibility ('03)
2010	PMTCT Review ('07) Linked Response ('08) PMTCT GL rev: Option B ('10)	SOPs PITC in TB cases ('06) CAMELIA and ID-TB/HIV results ('09) SOP, Joint Statement: 3I's ('10) 3I's Role Out ('11)

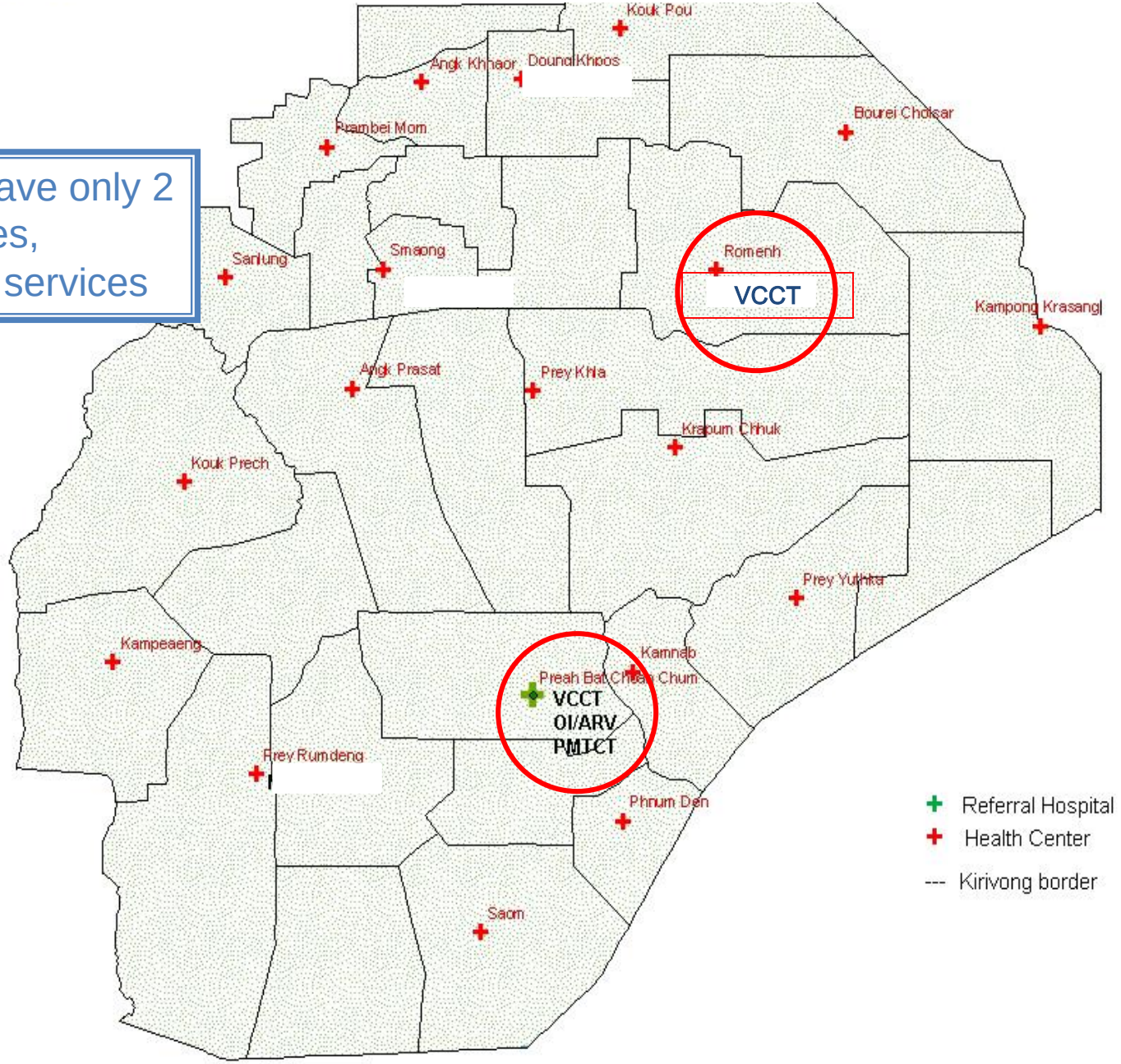
Linking Model (2008-):

Facilitated expansion of PMTCT and TB/HIV



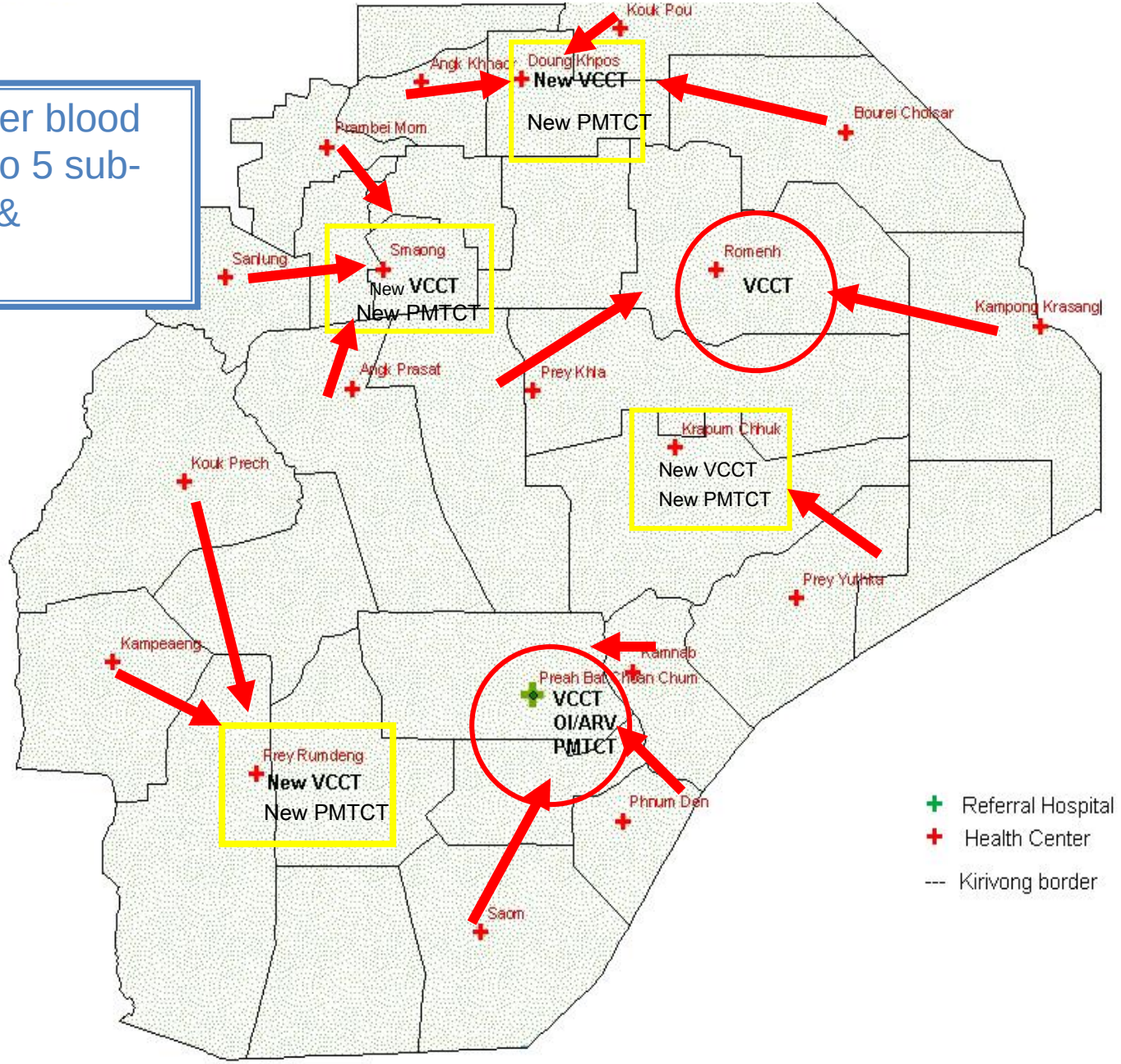
Linkages: Kirivong Operational District

20 HCs have only 2 VCCT sites,
1 OI/ART services

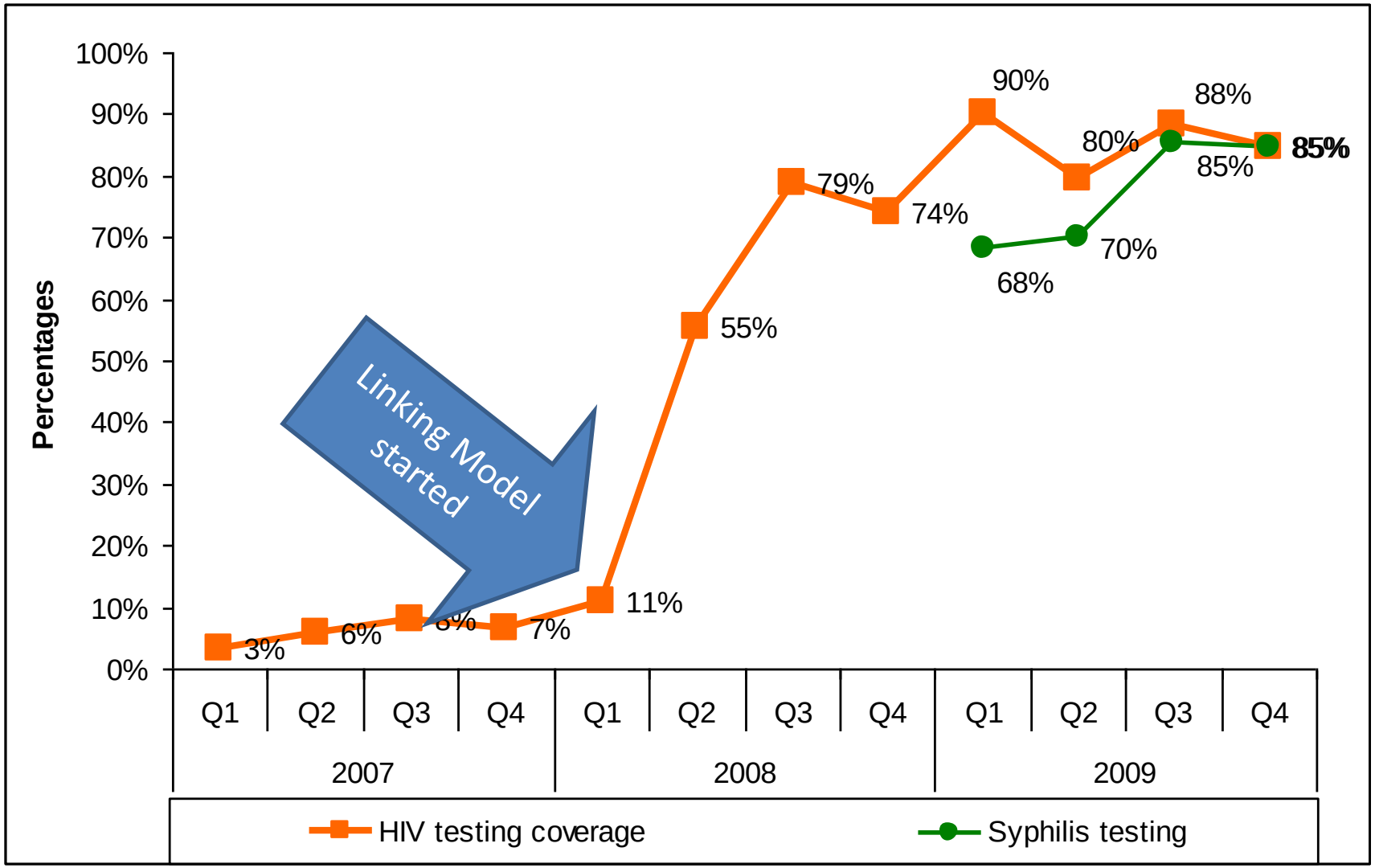


Linkages: Kirivong Operational District

14 HC refer blood samples to 5 sub-satellites &
1 satellite



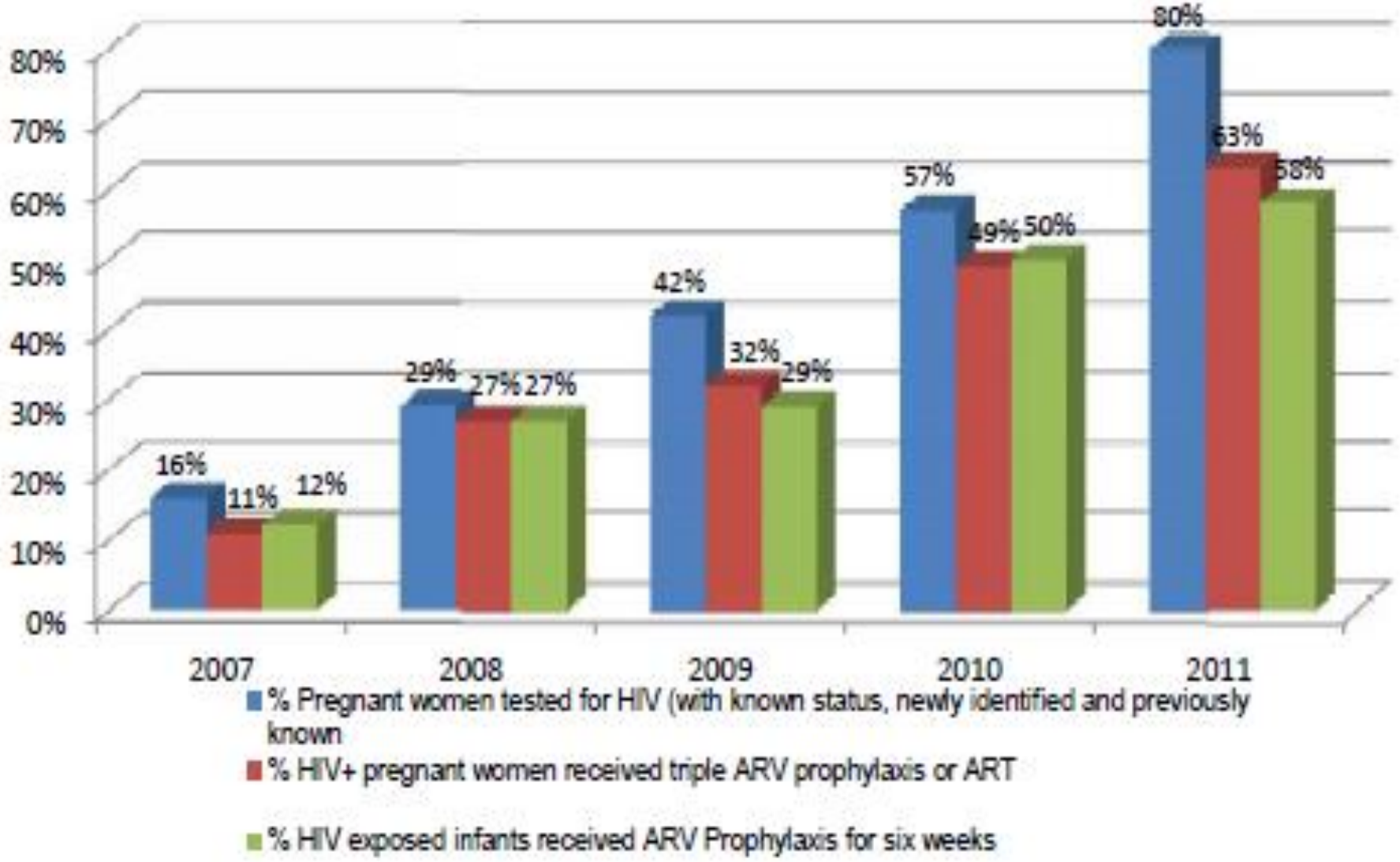
Linking Model Demonstration Results (2007-9)



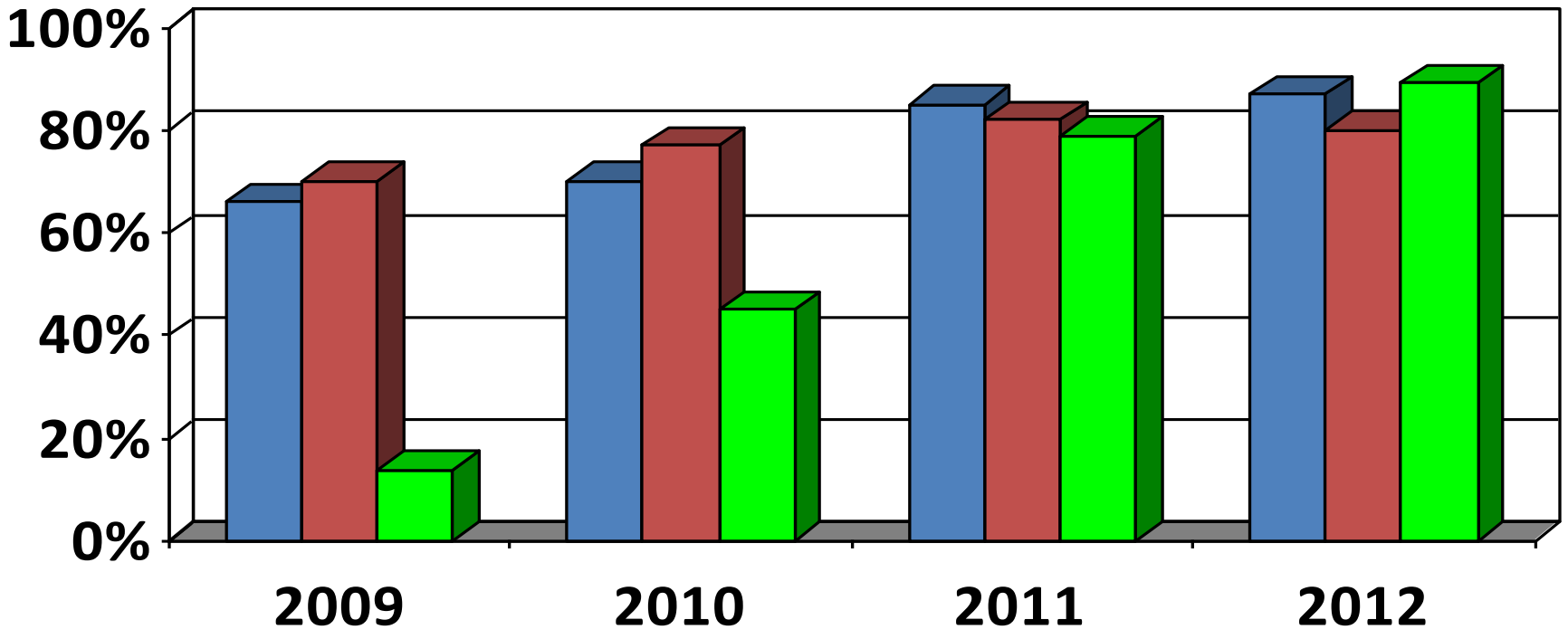
* Introduction of syphilis testing in the first quarter of 2009

** Percentage of pregnant women tested for HIV/ syphilis at antenatal care out of total expected pregnant women

PMTCT Coverage



TB/HIV Coverage



Moving Towards Integration between HIV-MCH-TB

2010

2015 (MDG 4, 5 and 6)

Integration or LR of HIV/STI/RH/MNCH/TB services

UA to HIV/STI/RH/TB Services

UA to HIV Care and Treatment

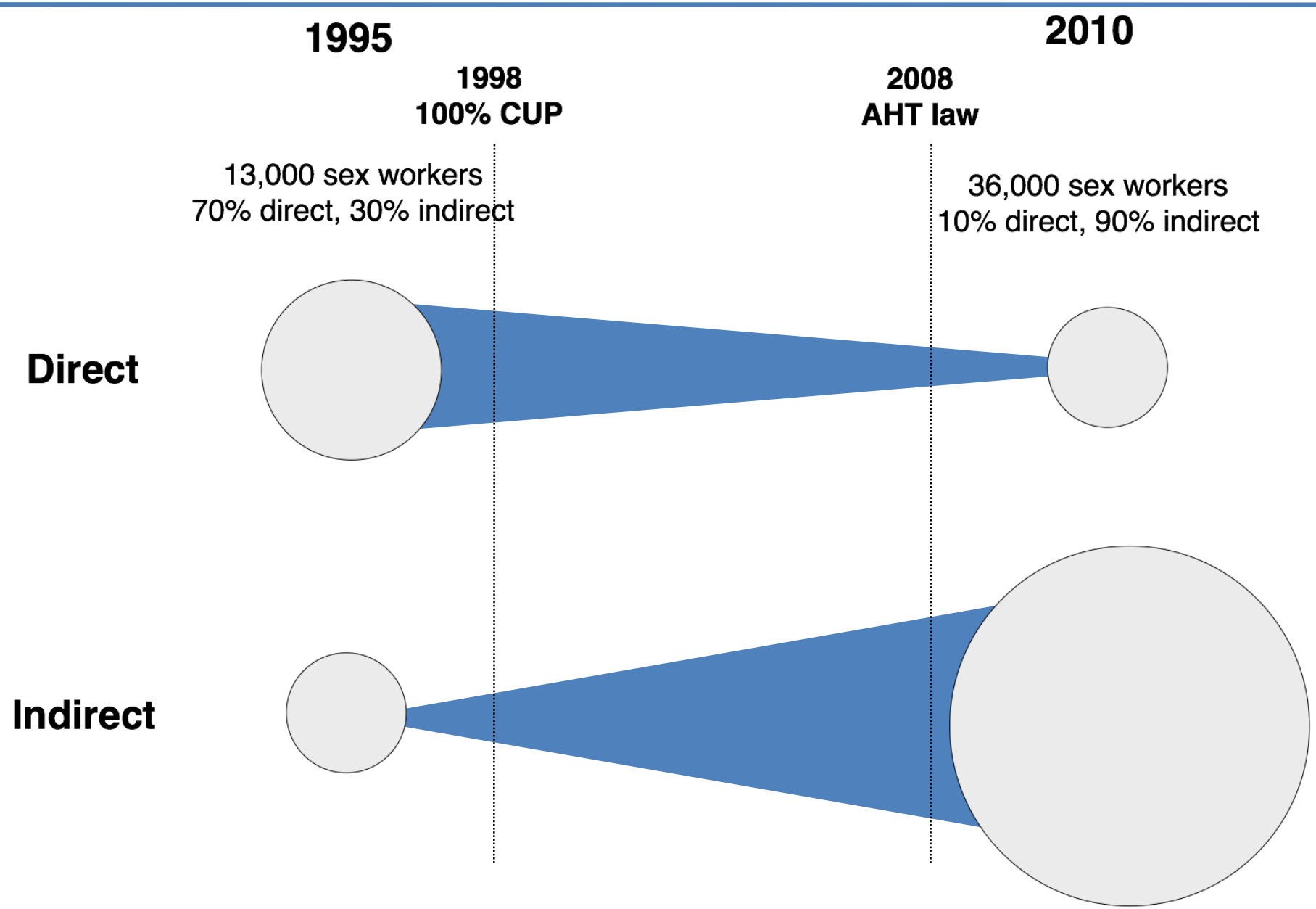
2010
UN Award for MDG 6 (HIV)

2015

Responding to changing epidemics

- Overcoming political, legal and social barriers
- Reaching the most-at-risk populations
- Linking them to health services

Changing conditions (1)



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:

	Population Size	HIV prevalence
EW	(38,000) *(NGO report 2012)*	10% (Clients >7/w) *(SSS 2011)*
MSM TG	(16,000) *(NGO report 2012)*	2.1% *(Bros Khmer 2010)*
PWID	**1,300** *(IBBS 2012)*	**25%** *(IBBS 2012)*
PWUD	**13,000** *(IBBS 2012)*	**4%** *(IBBS 2012)*

Continuum of Prevention to Care and Treatment: COPCT (2009-)

MARPs prevention and access to health services

Sex Workers

MSM, TG, PWUD and PWID

Peer Network

Peer Educator

NGO

C/PITC

HCBC Team

PHC network

CBO

NGO

Health Workers

Health service delivery at district level

Provider Initiated Counseling & Testing (PITC), VCCT, Pre-ART/ART

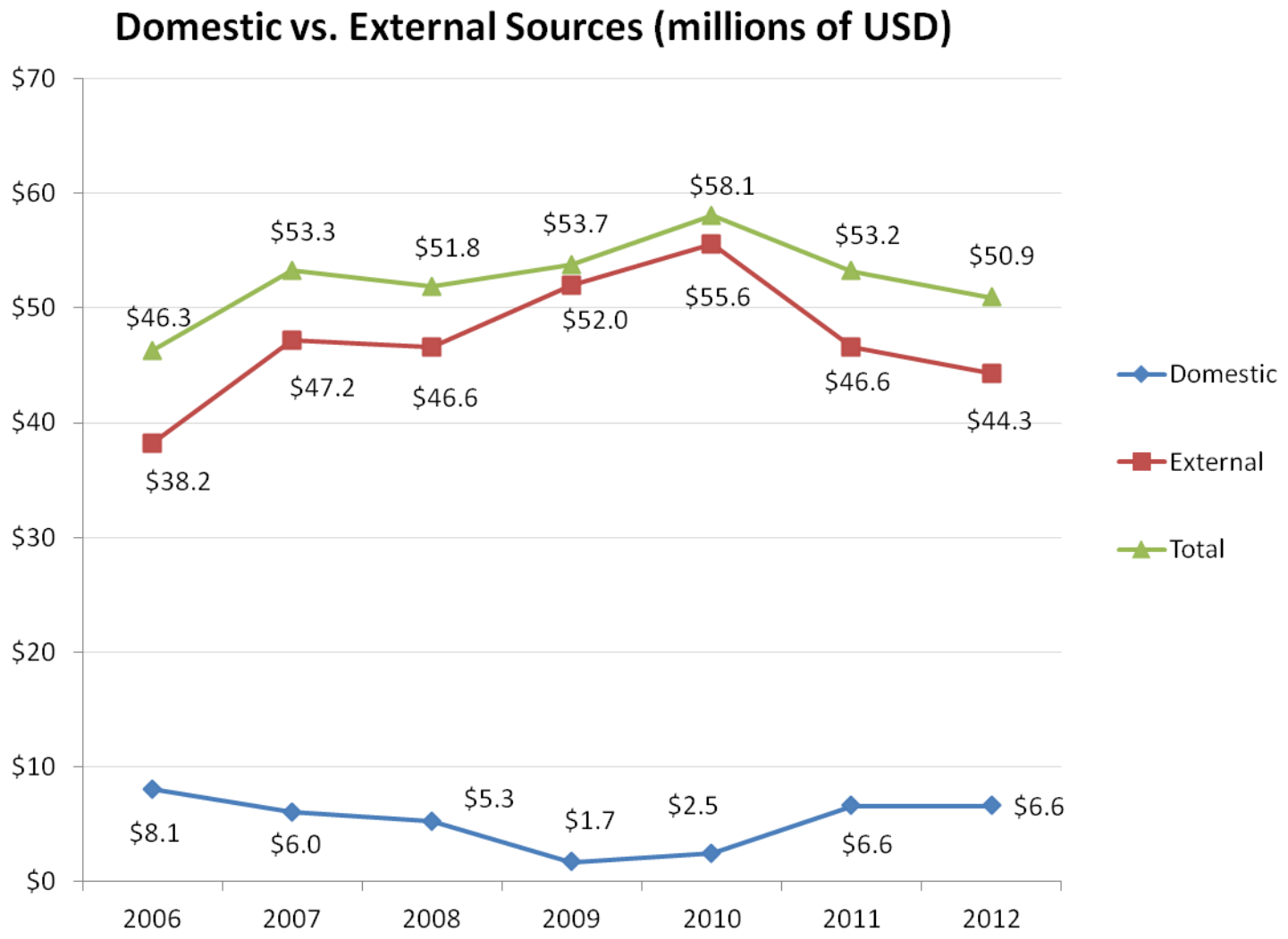
STI, ANC, SRH, Safe Abortion,

Safe Delivery, EPI, Nutrition (children)

TB, Malaria

Laboratory

Current trends in HIV financing



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 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

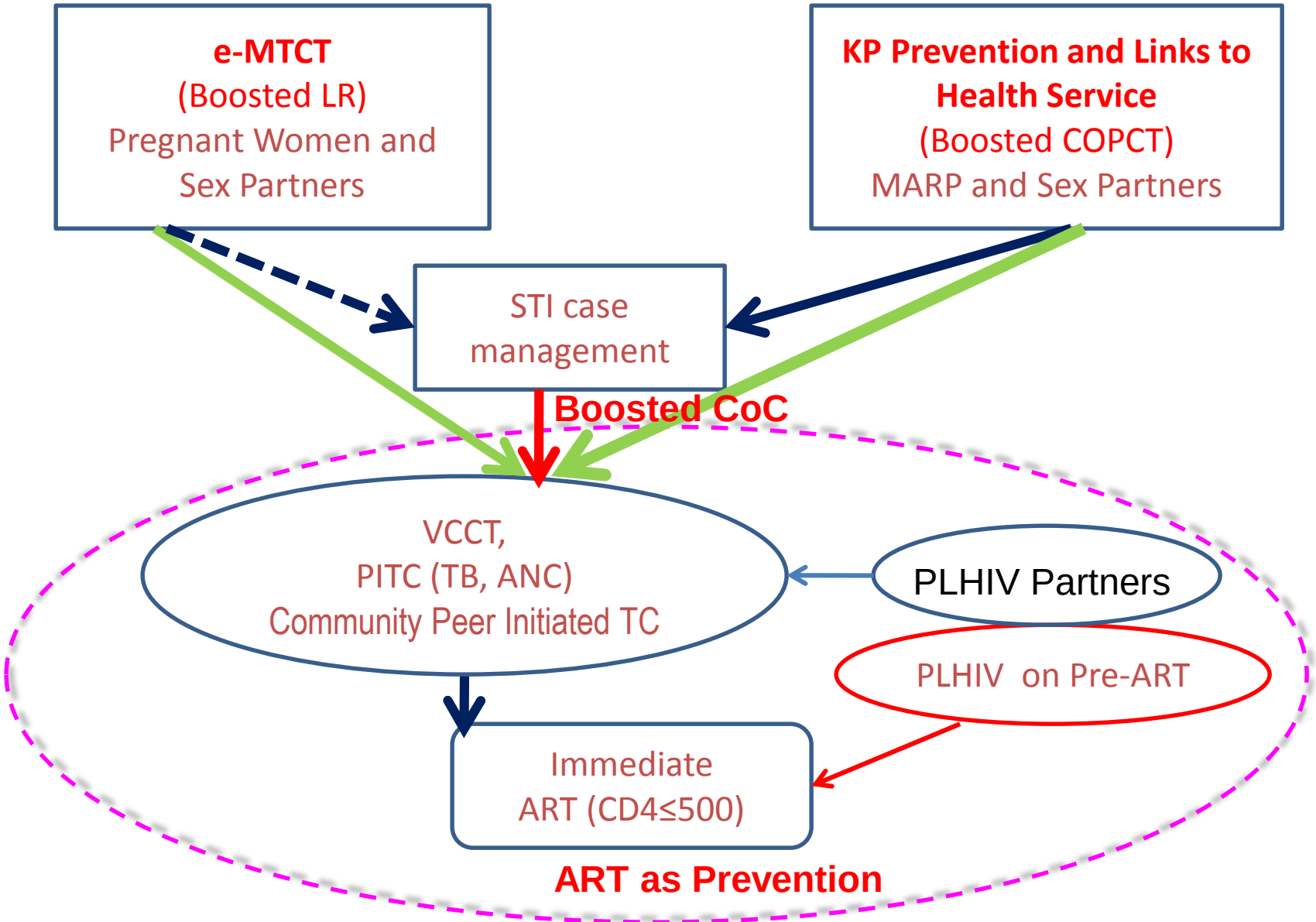
❖B-IACM/PNTT linked to:

- 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

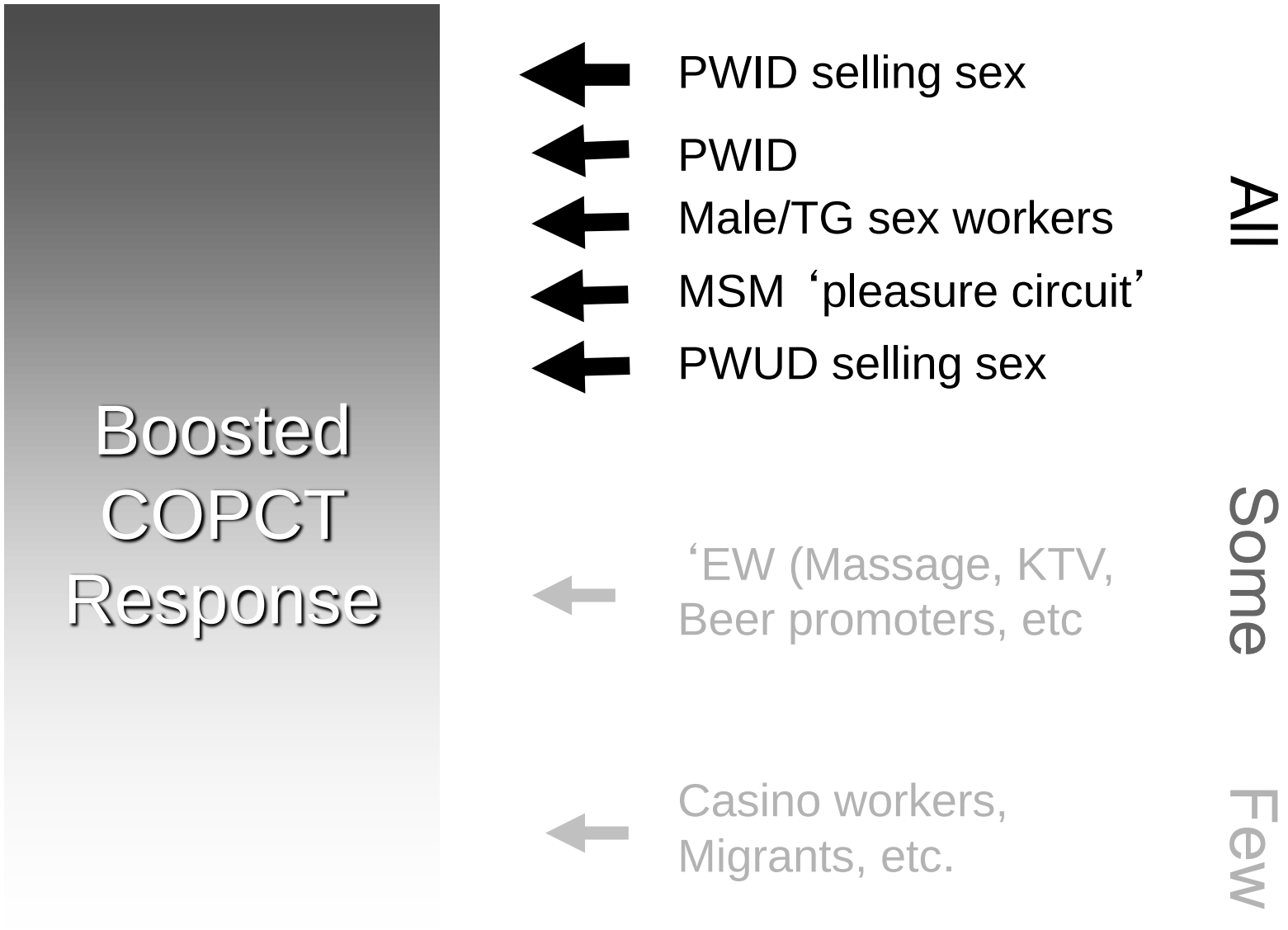
❖Monitoring and evaluation of impact including IACSS

Cambodia 3.0:
Virtual elimination of new HIV infections by 2020



Key Populations: Prevention & Links to Health Services

(1) Sharper epidemiological targeting:



KP: Prevention & Links to Health Services

(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)

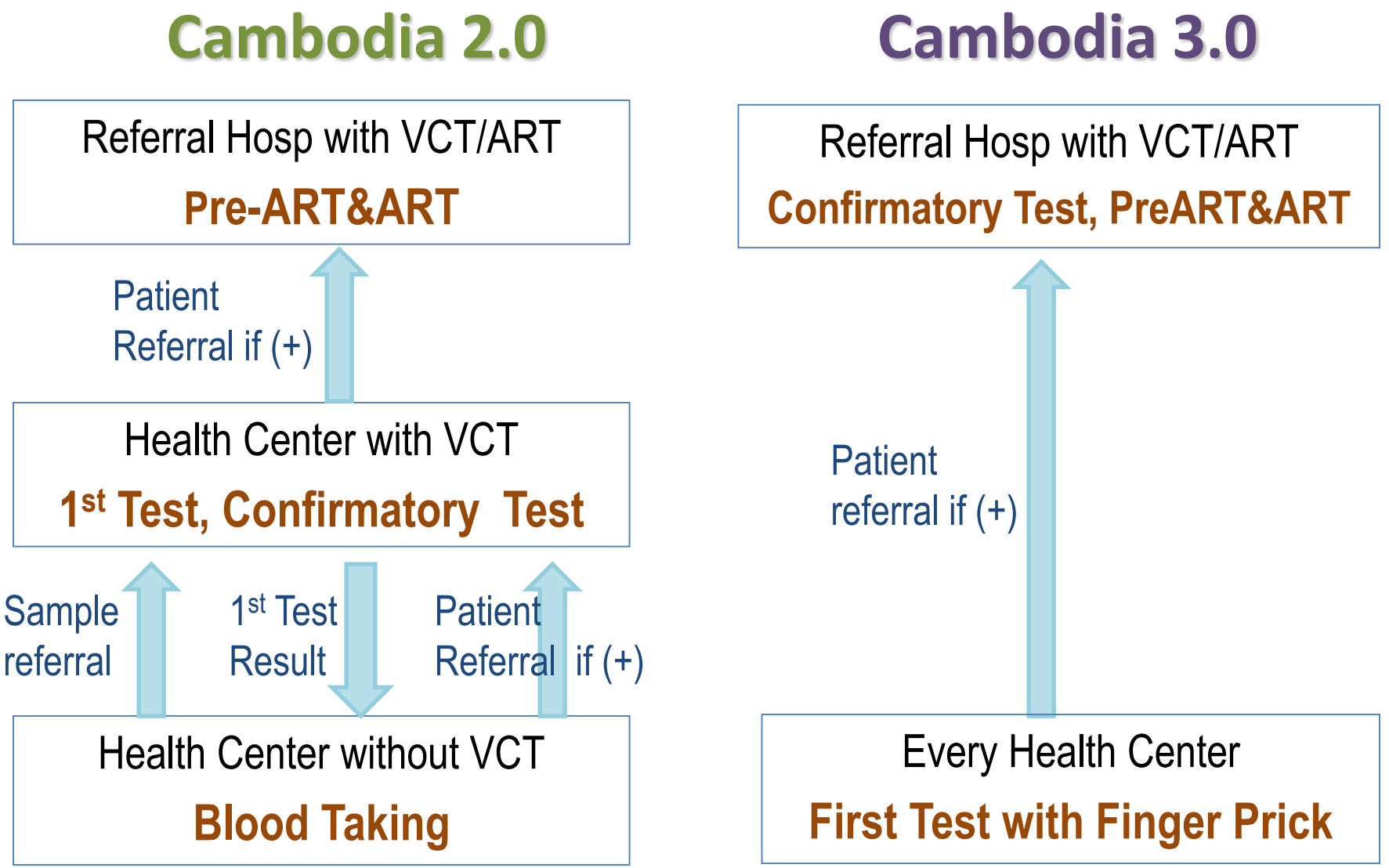
First IR: PDI

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



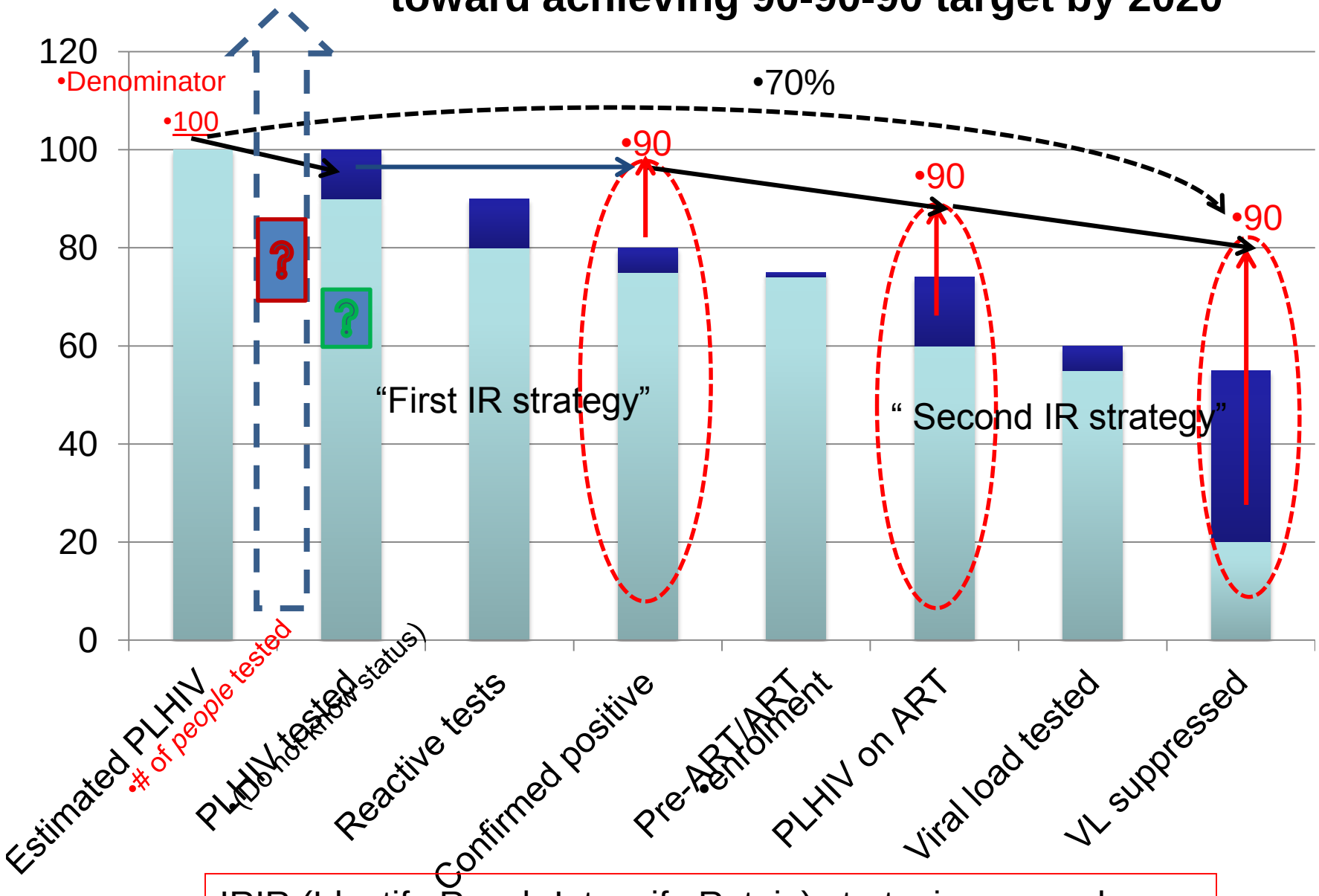
How Cambodia can achieve 90-90-90 target by 2020 (over the next 4 years: 2017-2020) ?

Test and Treat all

Early Testing: first IR strategy

Early ART and Retain: second IR strategy

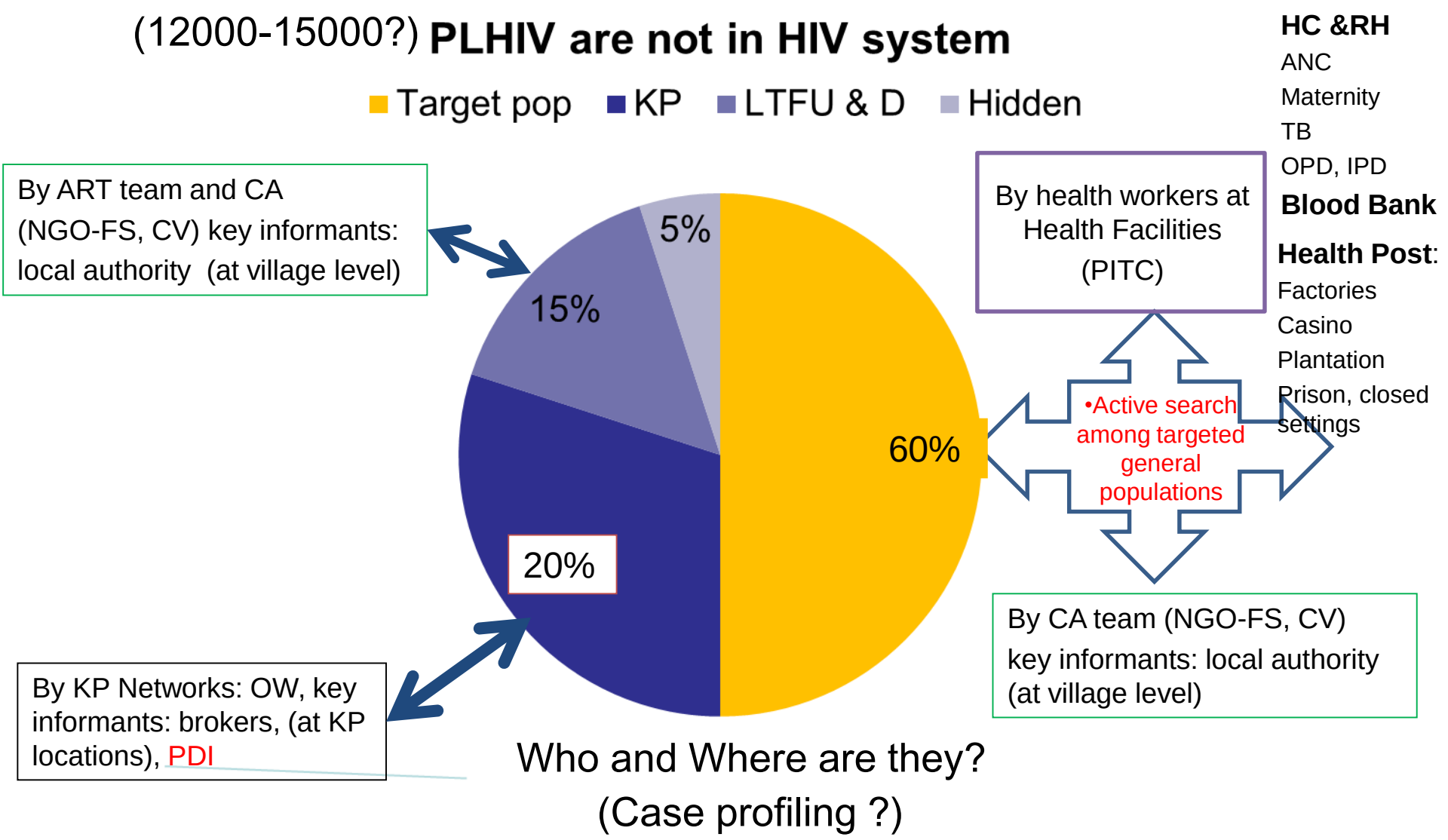
Figure 2. B-IACM/PNTT at PHD level toward achieving 90-90-90 target by 2020



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

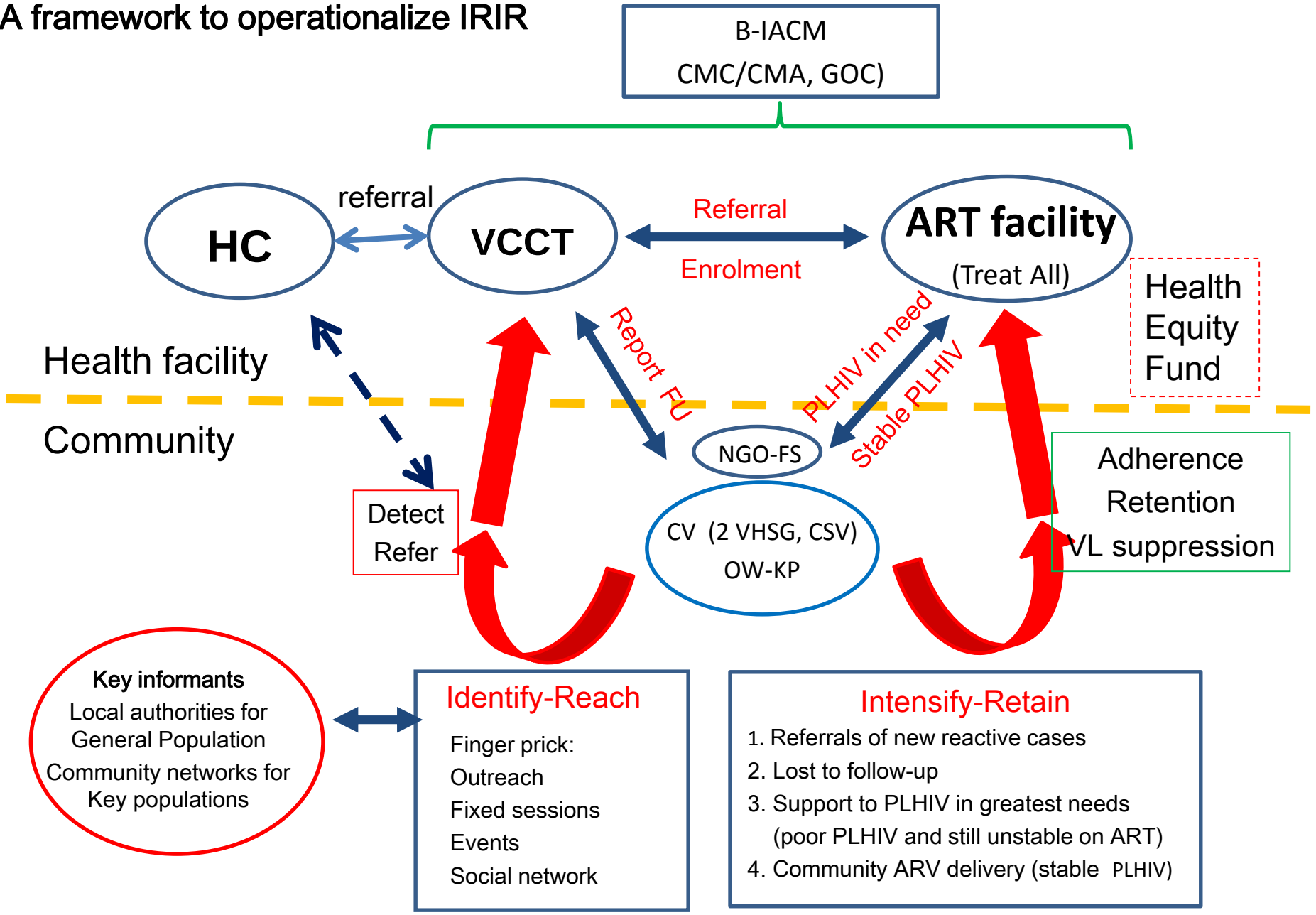
•MCV, January 4, 2016

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

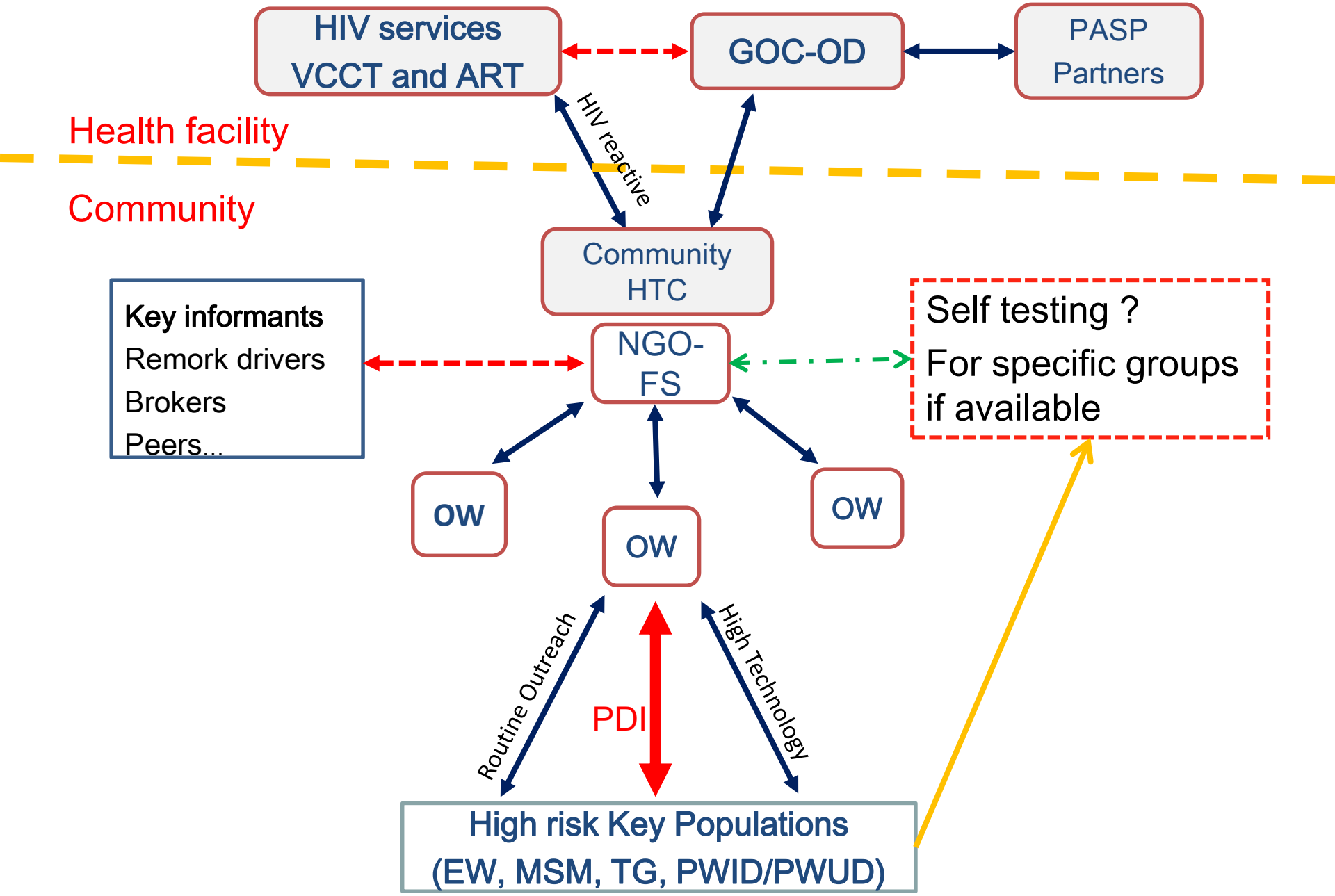


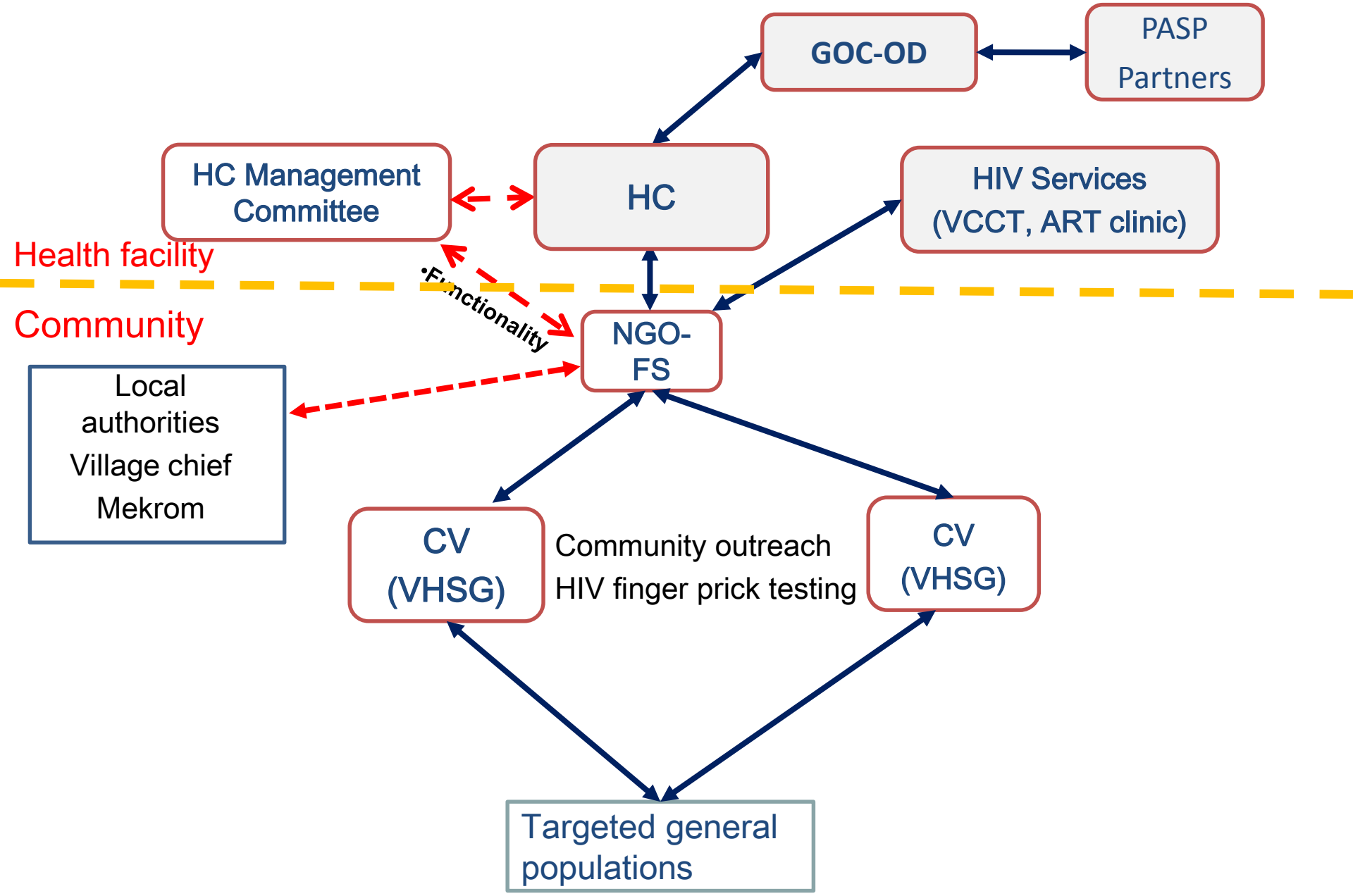
•MCV, January 4, 2016

CA framework to operationalize IRIR



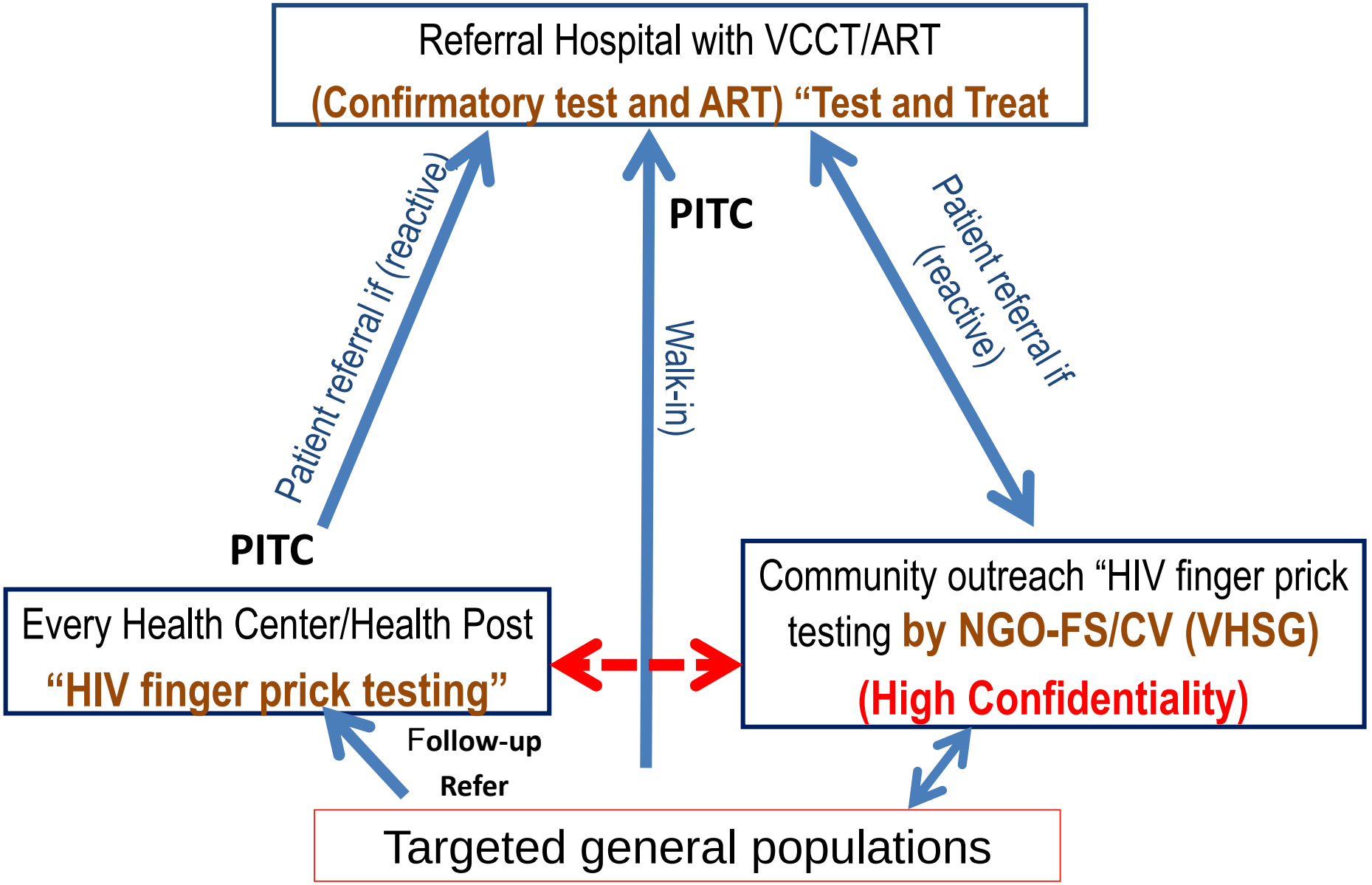
First IR strategy among KP





Community outreach finger prick testing among targeted general population

Streamlining HTC procedures and referral: among targeted general populations, 2017-2020



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)?

មជ្ឈមណ្ឌលជាតិប្រយុទ្ធនឹងជំងឺអេដស៍ សើស្បែក និងកាមរោគ

NATIONAL CENTER FOR HIV/AIDS, DERMATOLOGY AND STD

កិច្ចប្រជុំផ្សព្វផ្សាយគោលការណ៍ណែនាំជាតិ ស្តីពី ការថែទាំ-ព្យាបាលជំងឺឱកាសនិយម និង ការព្យាបាលដោយឱសថប្រឆាំងមេរោគអេដស៍ សំរាប់ មនុស្សពេញវ័យ ក្មេងជំទង់ និង កុមារ

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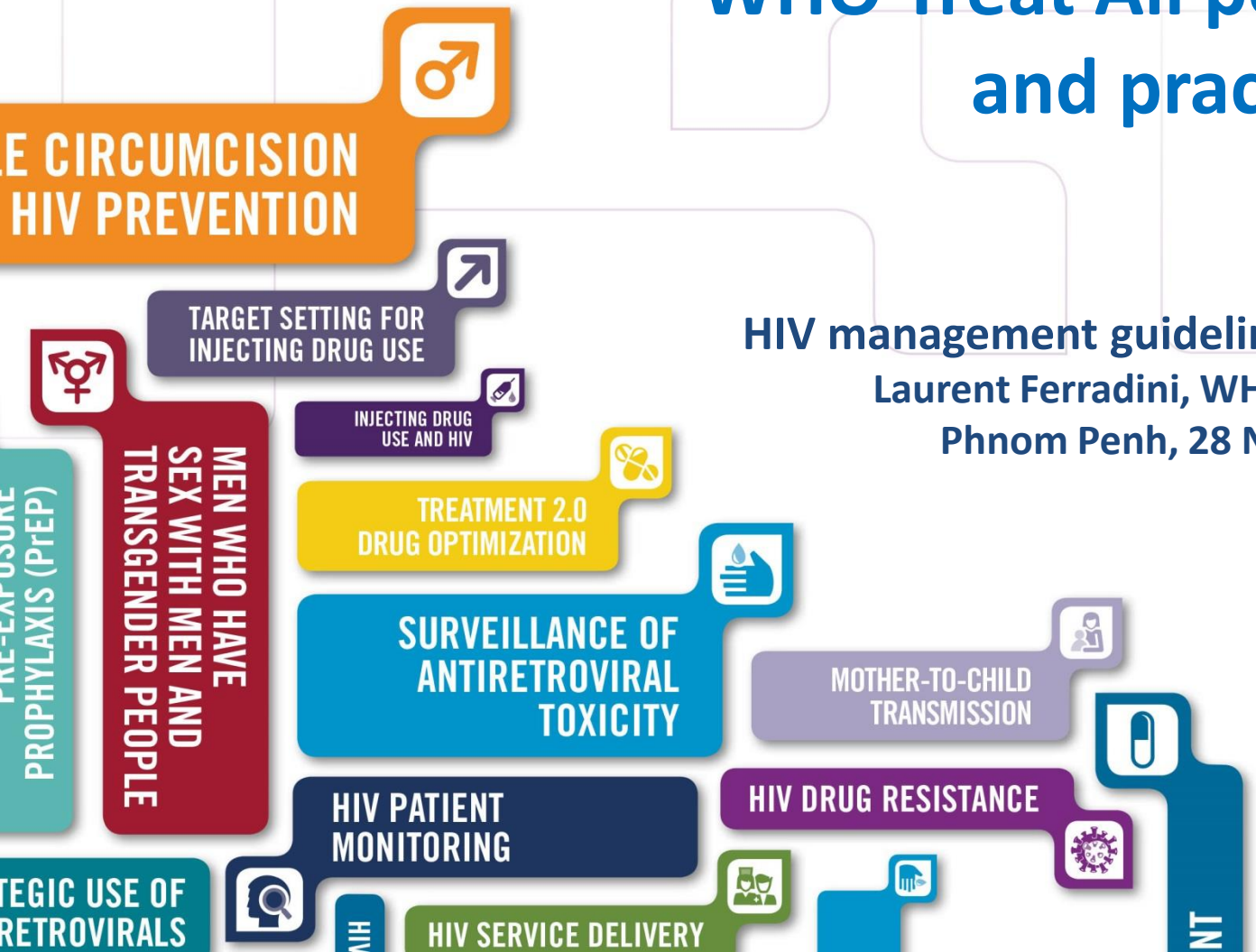
Treat All Overview

Dr Laurent Ferradini
World Health Organization

AIDS 2016

"Treat All" to end AIDS

WHO Treat All policy uptake and practice



HIV management guidelines dissemination

Laurent Ferradini, WHO Cambodia

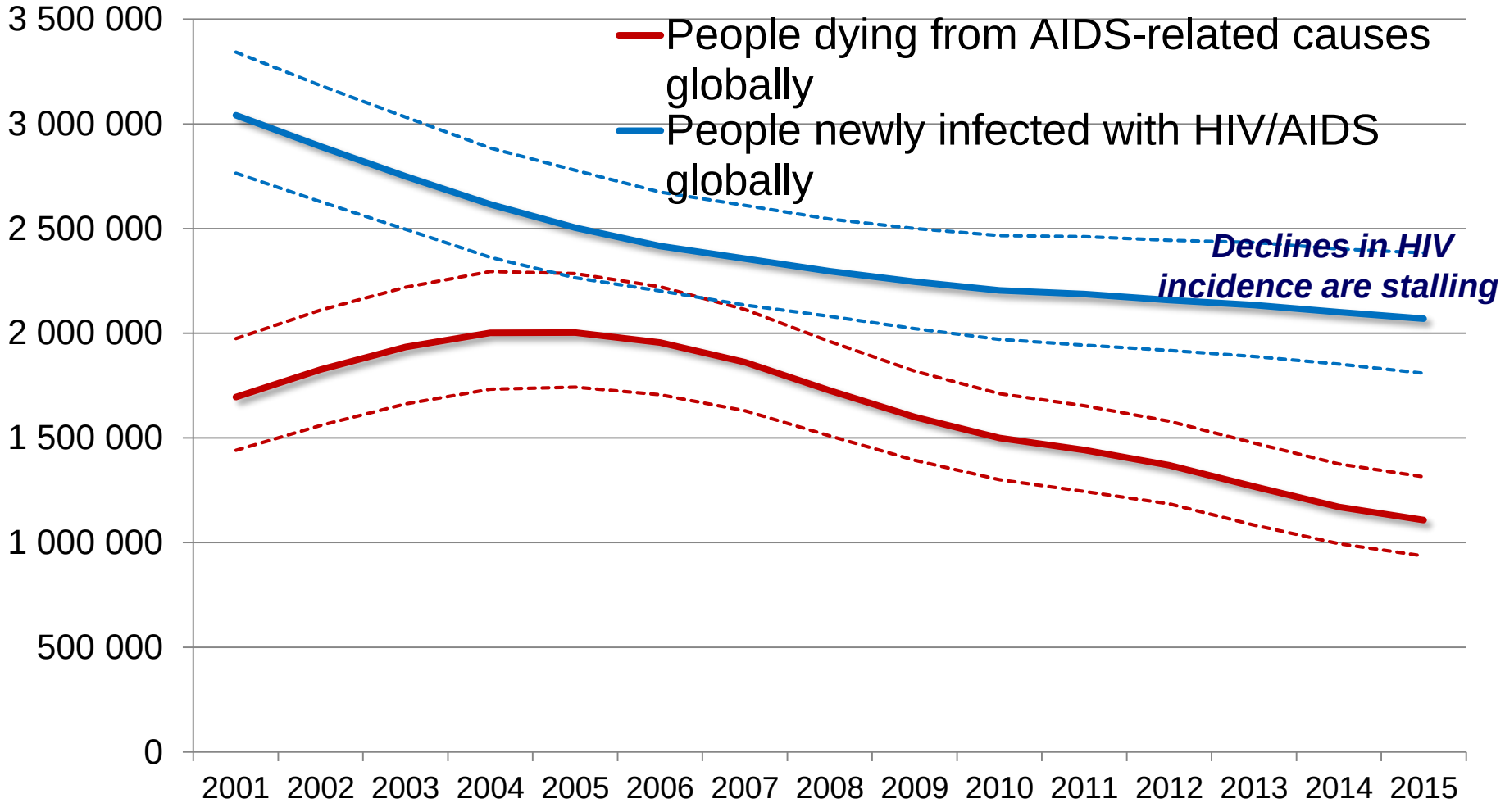
Phnom Penh, 28 Nov. 2016

World Health Organization

Global summary of the AIDS epidemic | 2015

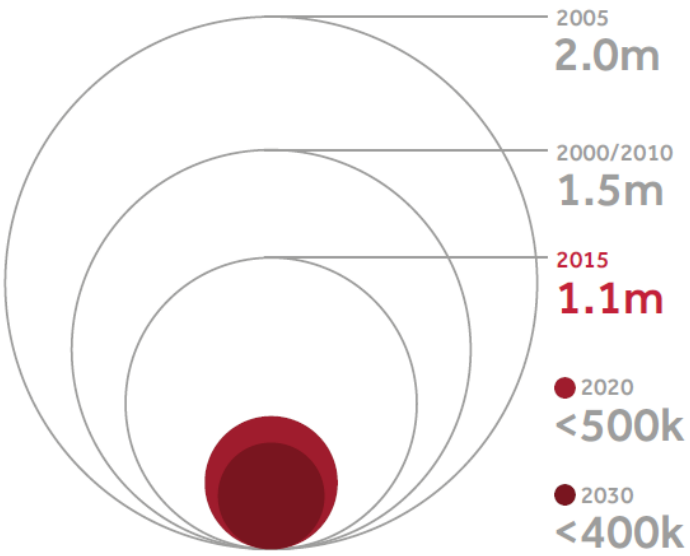
Number of people living with HIV in 2015	**Total**	**36.7 million** [34.0 million – 39.8 million]
	Adults	31.8 million [30.1 million – 33.7 million]
	Women	16.0 million [15.2 million – 16.9 million]
	Children (<15 years)	3.2 million [2.9 million – 3.5 million]
People newly infected with HIV in 2015	**Total**	**2.1 million** [1.9 million – 2.4 million]
	Adults	1.9 million [1.7 million – 2.1 million]
	Children (<15 years)	240 000 [210 000 – 280 000]
AIDS deaths in 2015	**Total**	**1.1 million** [940 000 – 1.3 million]
	Adults	1.3 million [1.2 million – 1.5 million]
	Children (<15 years)	190 000 [170 000 – 220 000]

Decline in HIV incidence and mortality over time

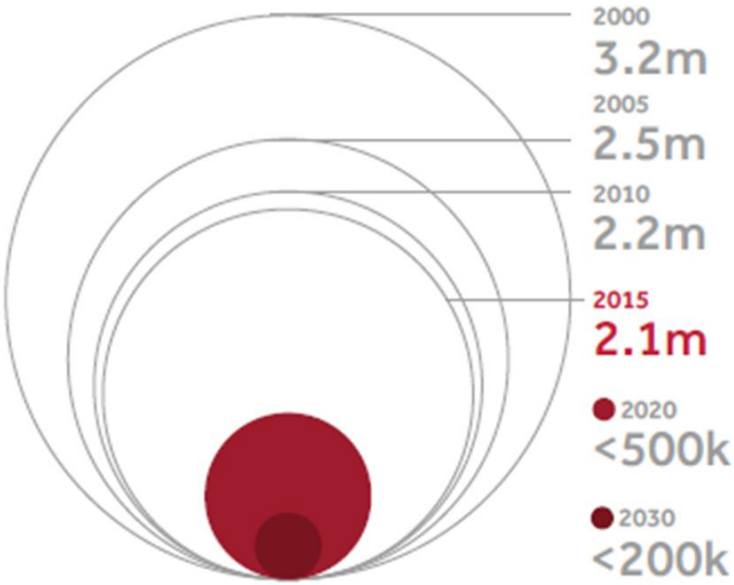


Global 2020 and 2030 targets

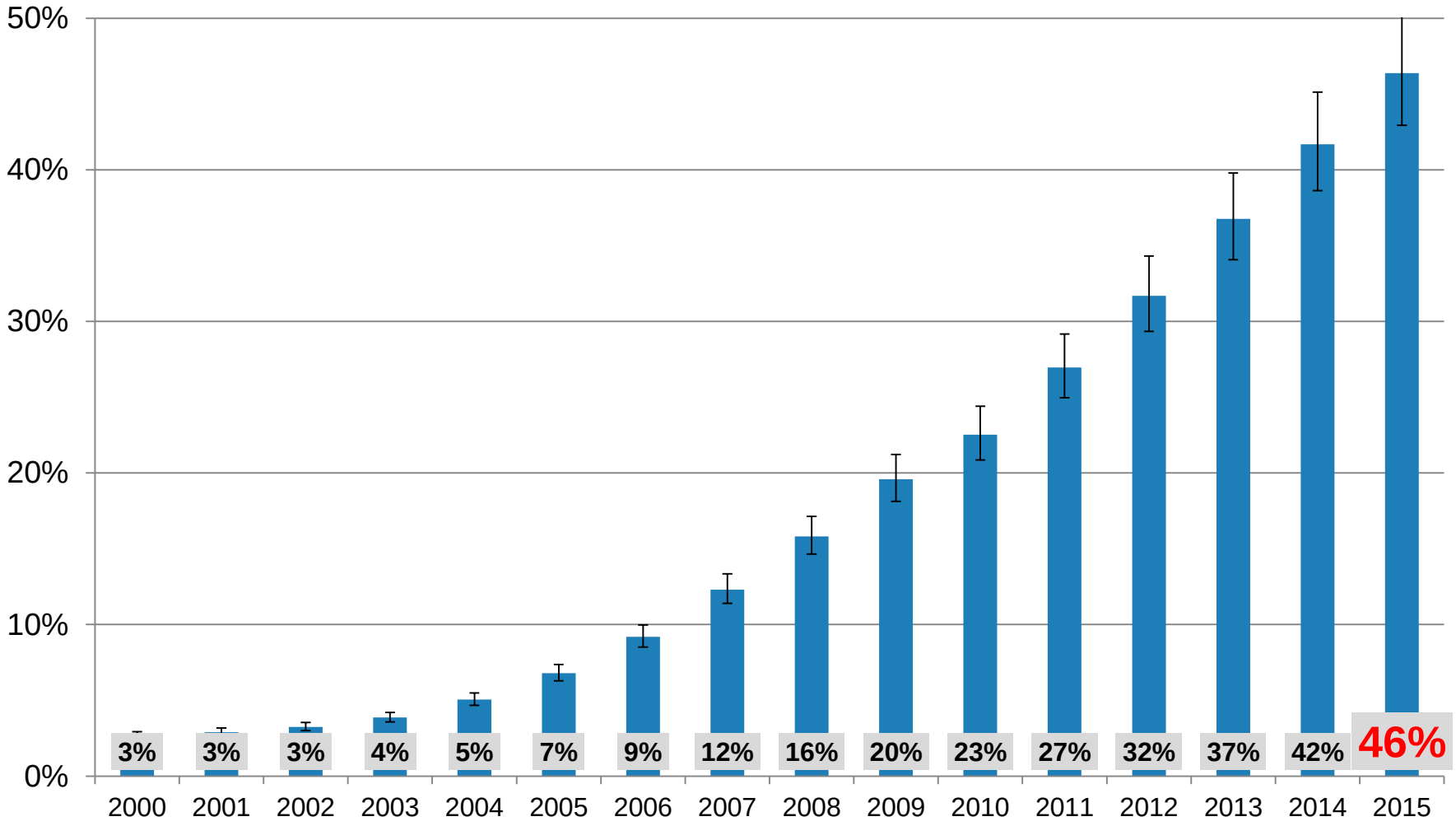
Number of people dying from HIV



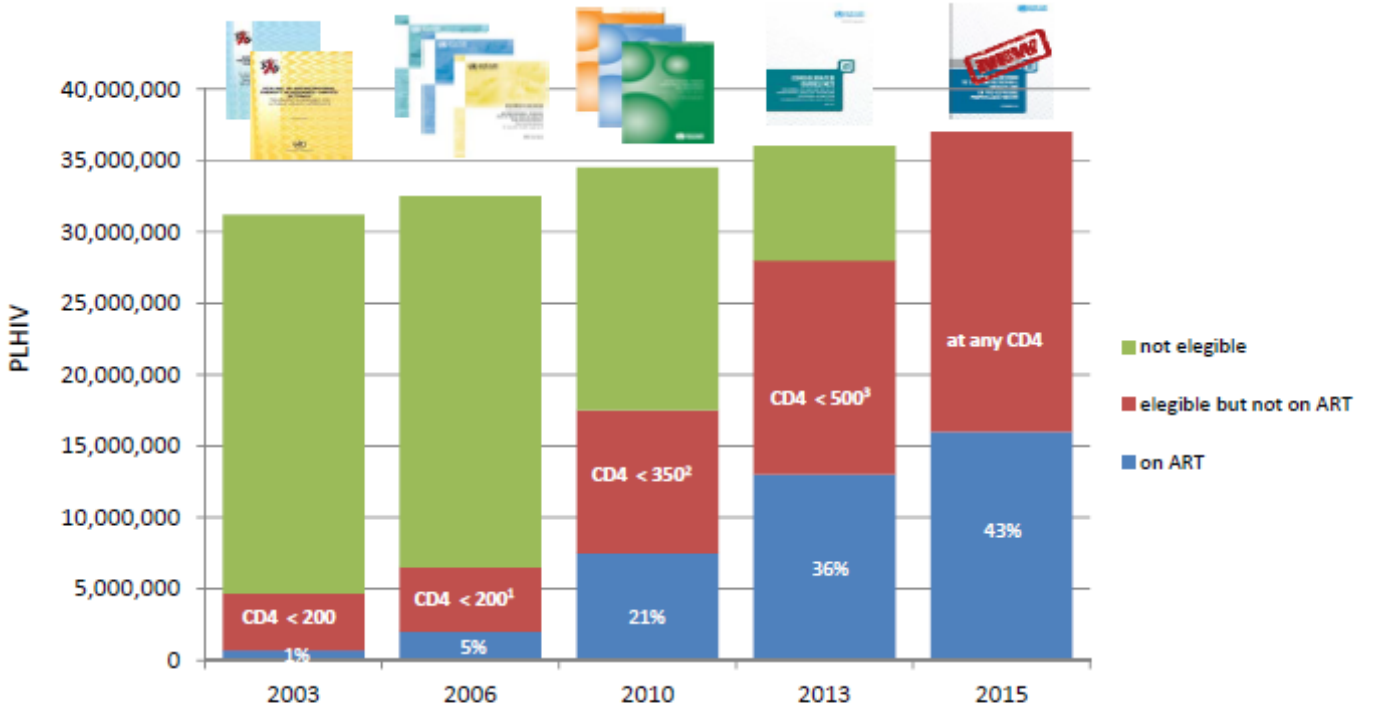
Number of people newly infected with HIV



Global ART coverage over time



Evolution of global ART coverage and eligibility criteria according to WHO guidelines (2013 – 2016)



1. At CD4 < 350: active TB disease and HIV+ pregnant women
2. At any CD4: active TB disease and HBV co-infection requiring HBV treatment"
3. At any CD4: active TB disease, HBV co-infection with severe liver disease, HIV+ pregnant women and HIV serodiscordant couples

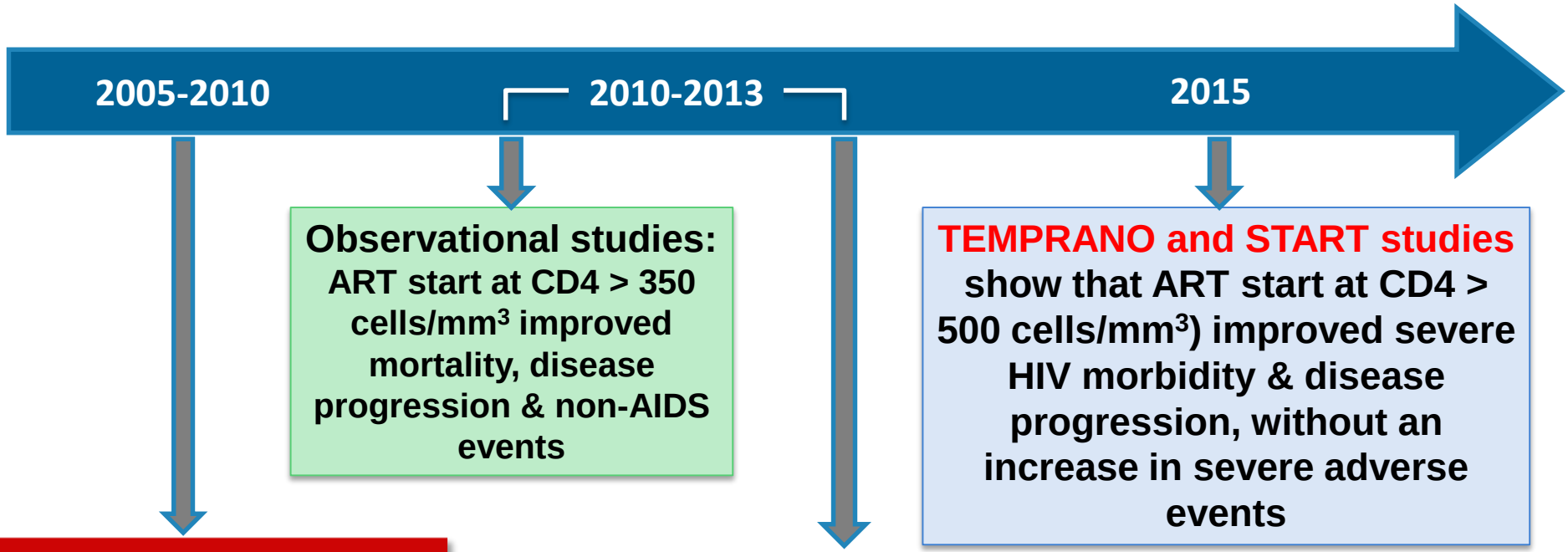
Source WHO Progress Report :Global Health Sector Response to HIV, 2000-2015 (2015)

World Health Organization

Outcomes from IeDEA Analysis

- **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

Temprano/START represent the end of a chain of evidence that has led us to the point of universal ART



World Health Organization

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:

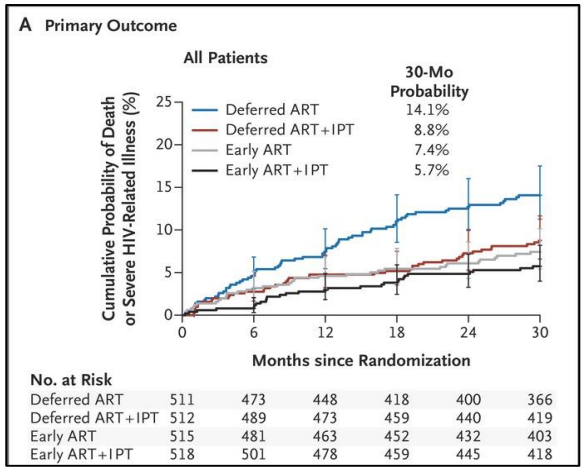
	No IPT	IPT
ART WHO-guided	1 WHO-guided ART, no IPT (N=511)	2 WHO-guided ART, IPT (N=512)
ART immediately	3 Immediate ART, no IPT (N=515)	4 Immediate ART, IPT (N=518)

(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)

Source: N Engl J Med 2015; 373:808-822

Temprano is one of the main studies that has driven the recommendation for universal ART

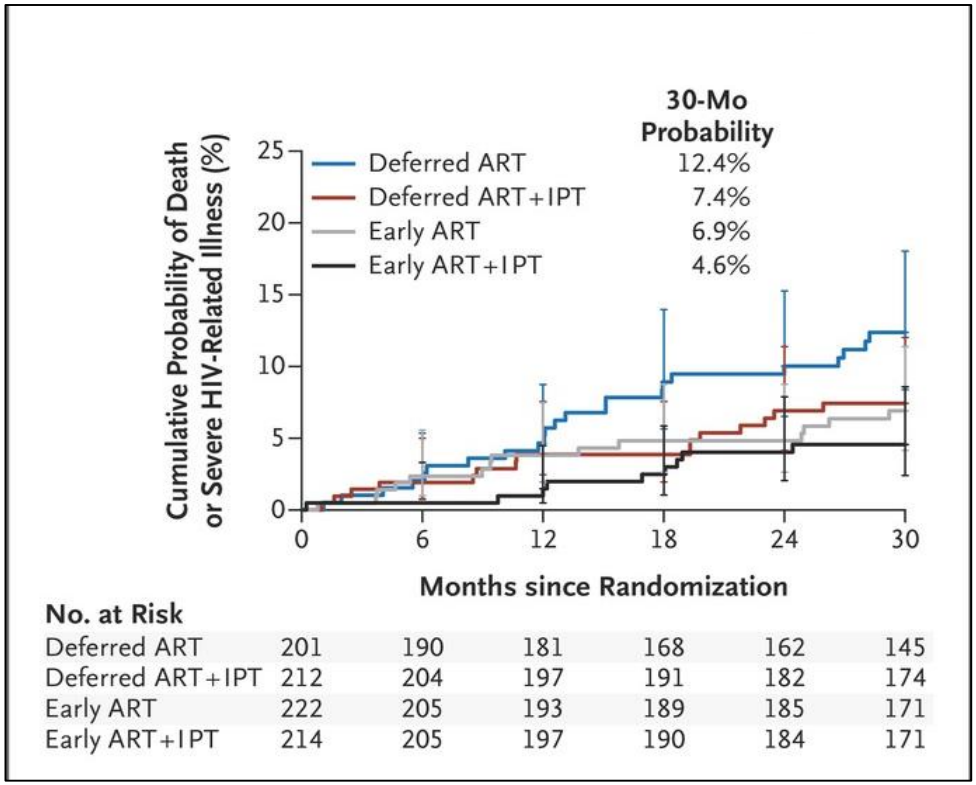
ALL



Comparing early ART with deferred p=0.0002

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

CD4 ≥ 500



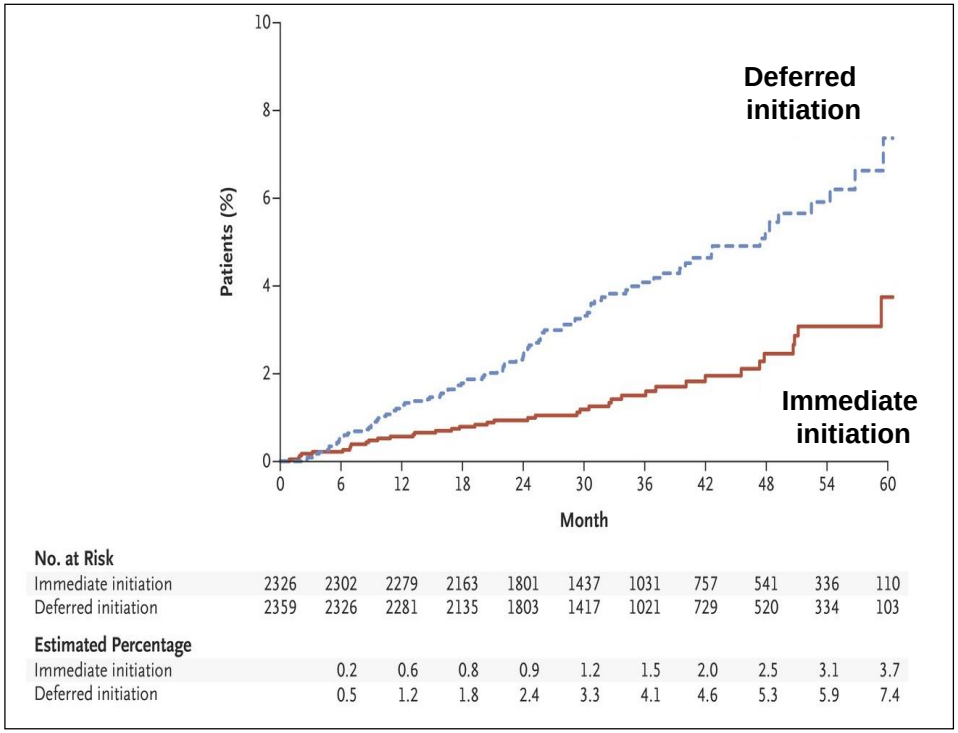
Comparing early ART with deferred p=0.027

Source: N Engl J Med 2015; 373:808-822

World Health Organization

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



No. at Risk											
Immediate initiation	2326	2302	2279	2163	1801	1437	1031	757	541	336	110
Deferred initiation	2359	2326	2281	2135	1803	1417	1021	729	520	334	103
Estimated Percentage											
Immediate initiation		0.2	0.6	0.8	0.9	1.2	1.5	2.0	2.5	3.1	3.7
Deferred initiation		0.5	1.2	1.8	2.4	3.3	4.1	4.6	5.3	5.9	7.4

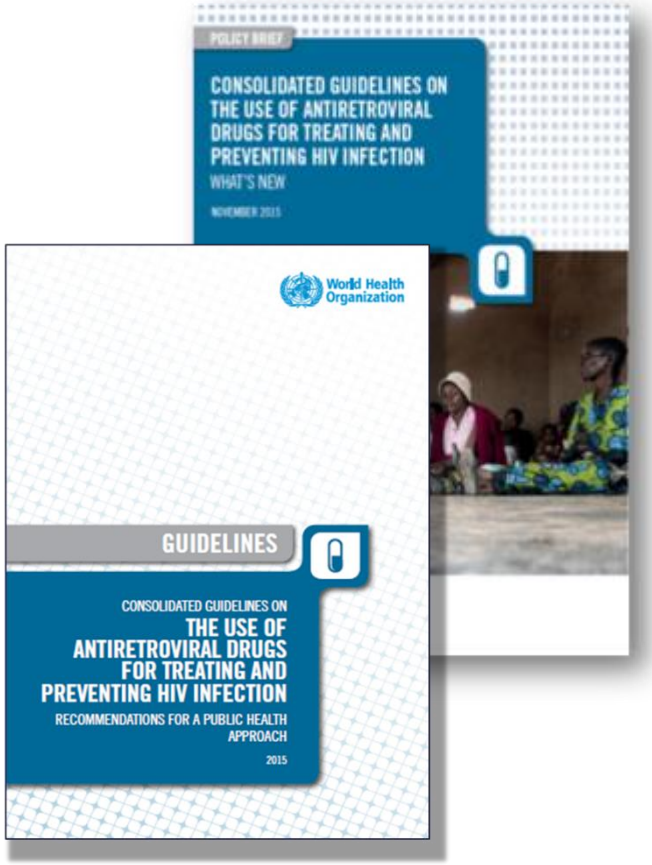
Source: N Engl J Med 2015; 373:795-807

World Health Organization

Consolidated Guidelines on the use of ARV drugs for treating and preventing HIV infection - Second edition 2016

World Health Organization

Reach the Treatment targets by 2020



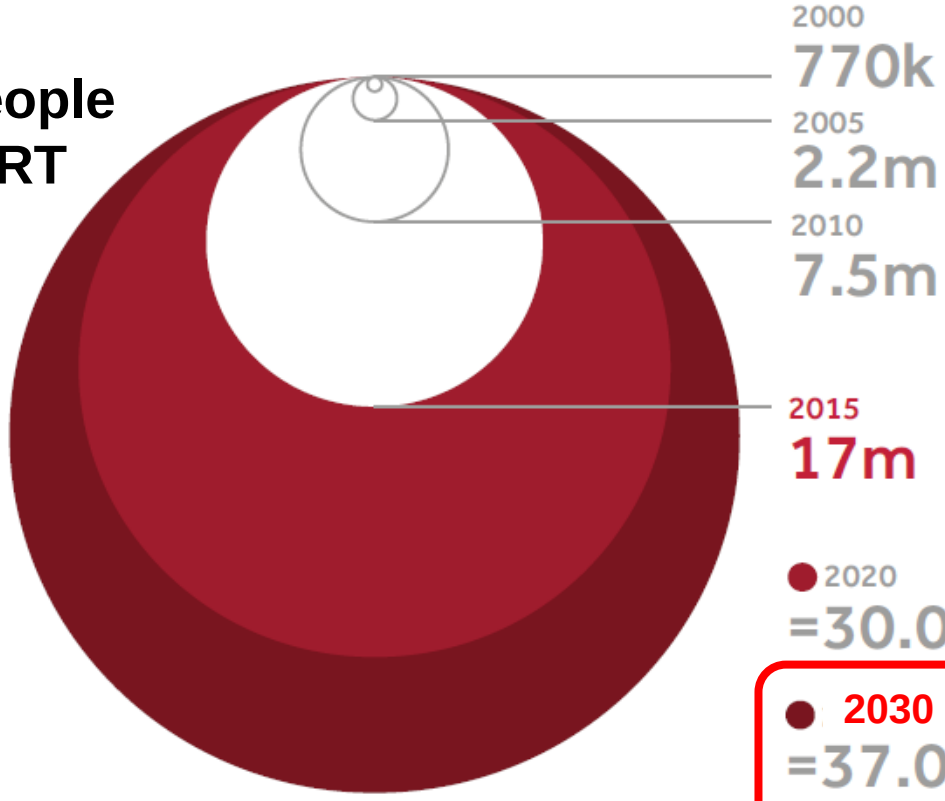
What's new in the ARV Guidelines?

- **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**

World Health Organization

Treat All - Challenge

Number of people receiving ART



Mid-2016
18.2 m [16.1 – 19.0 m]

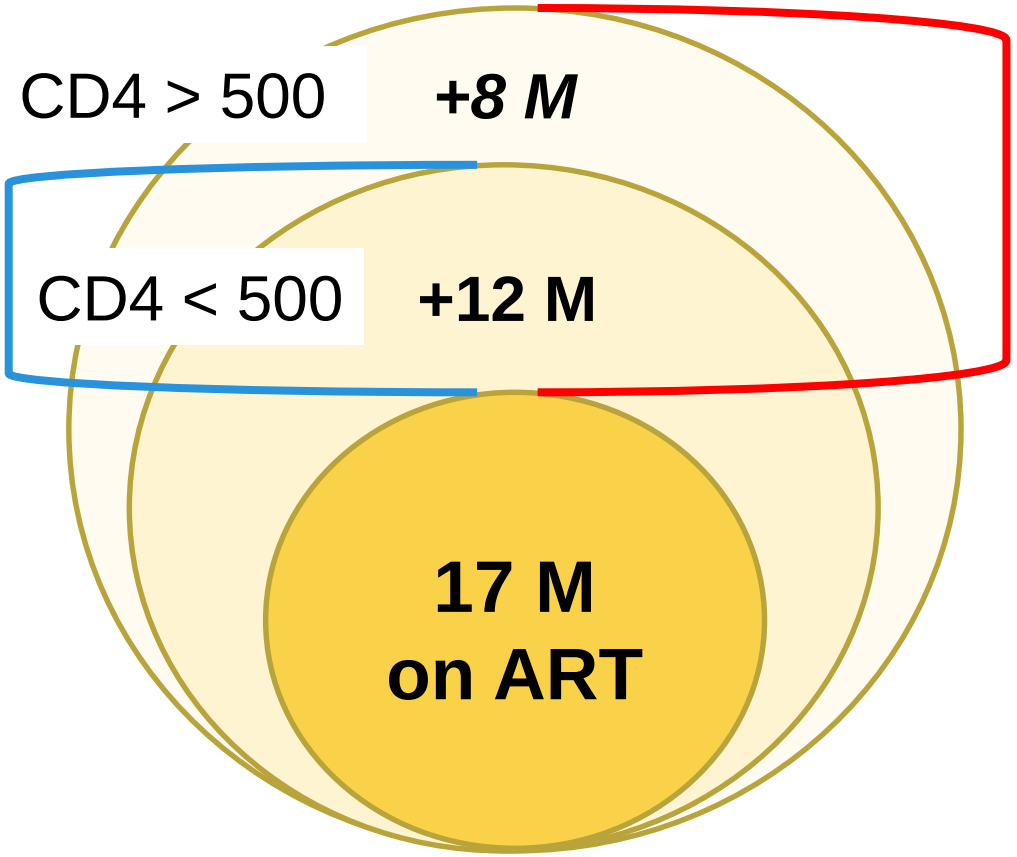
End AIDS

Treat All: Treatment Gap

Global number of PLHIV ~ 37 M

+12M

Treatment gap with 2013 WHO ART guidelines



+20M

Treatment gap with Treat all

Cost 31B USD per year by 2020 (50% treatment cost)

Treat All : a top priority for WHO

World Health Organization

UN HIGH-LEVEL MEETING ON ENDING AIDS, JUNE 2016

WHO SIDE EVENT

"TREAT ALL"

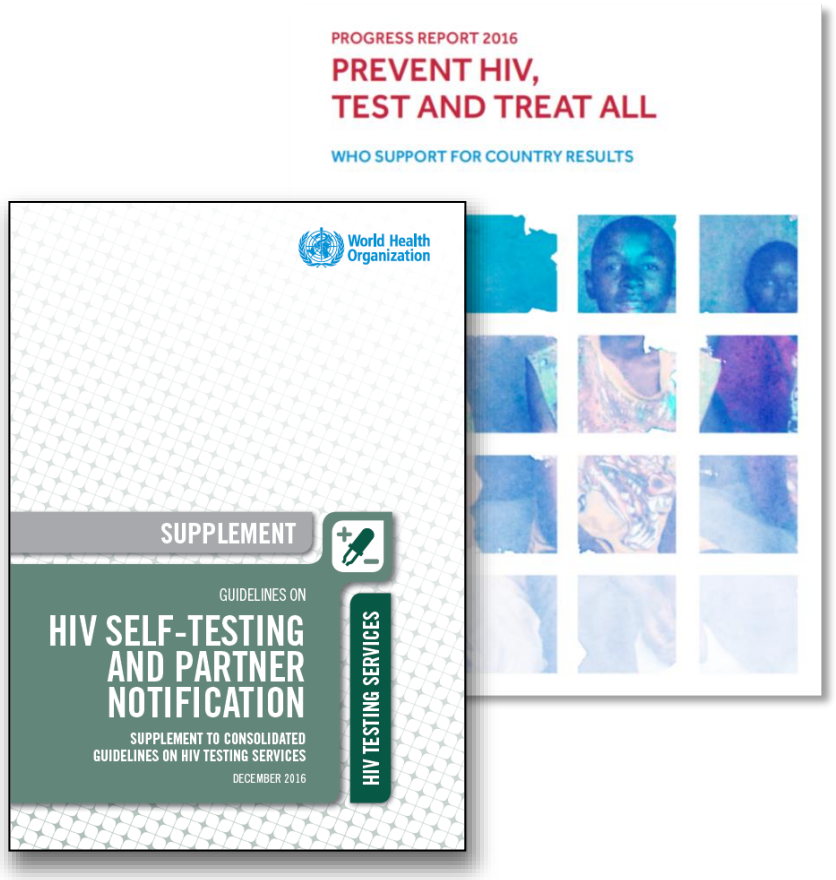
FROM POLICY TO ACTION — WHAT WILL IT TAKE?

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

COSPONSORED BY:
CÔTE D'IVOIRE, SOUTH AFRICA, THAILAND, THE UNITED STATES OF AMERICA

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**, Africaid Zvandiri, Zimbabwe. MODERATED BY **Gottfried Hirnschall**, Director, WHO Department of HIV.

JOIN THE EVENT



World Health Organization

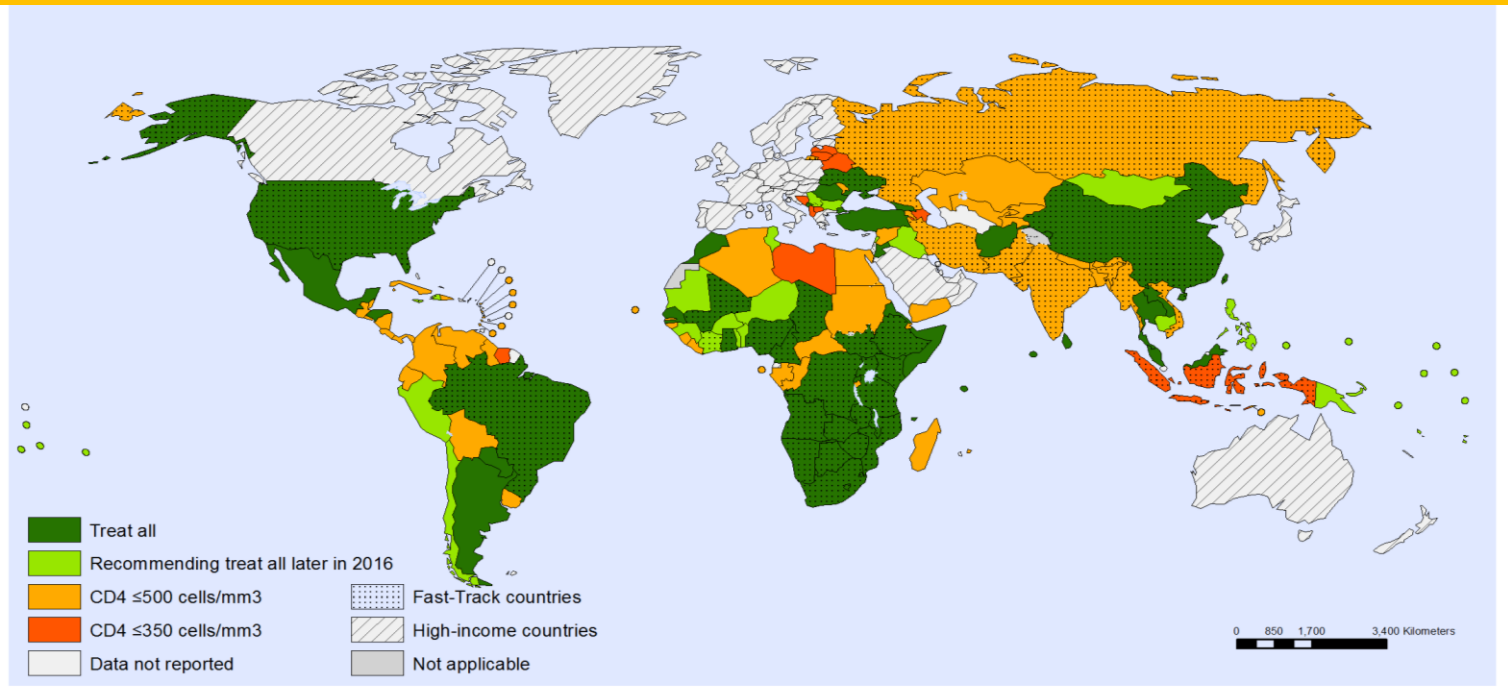
Methods: Adoption and implementation of WHO Policy recommendations

- 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



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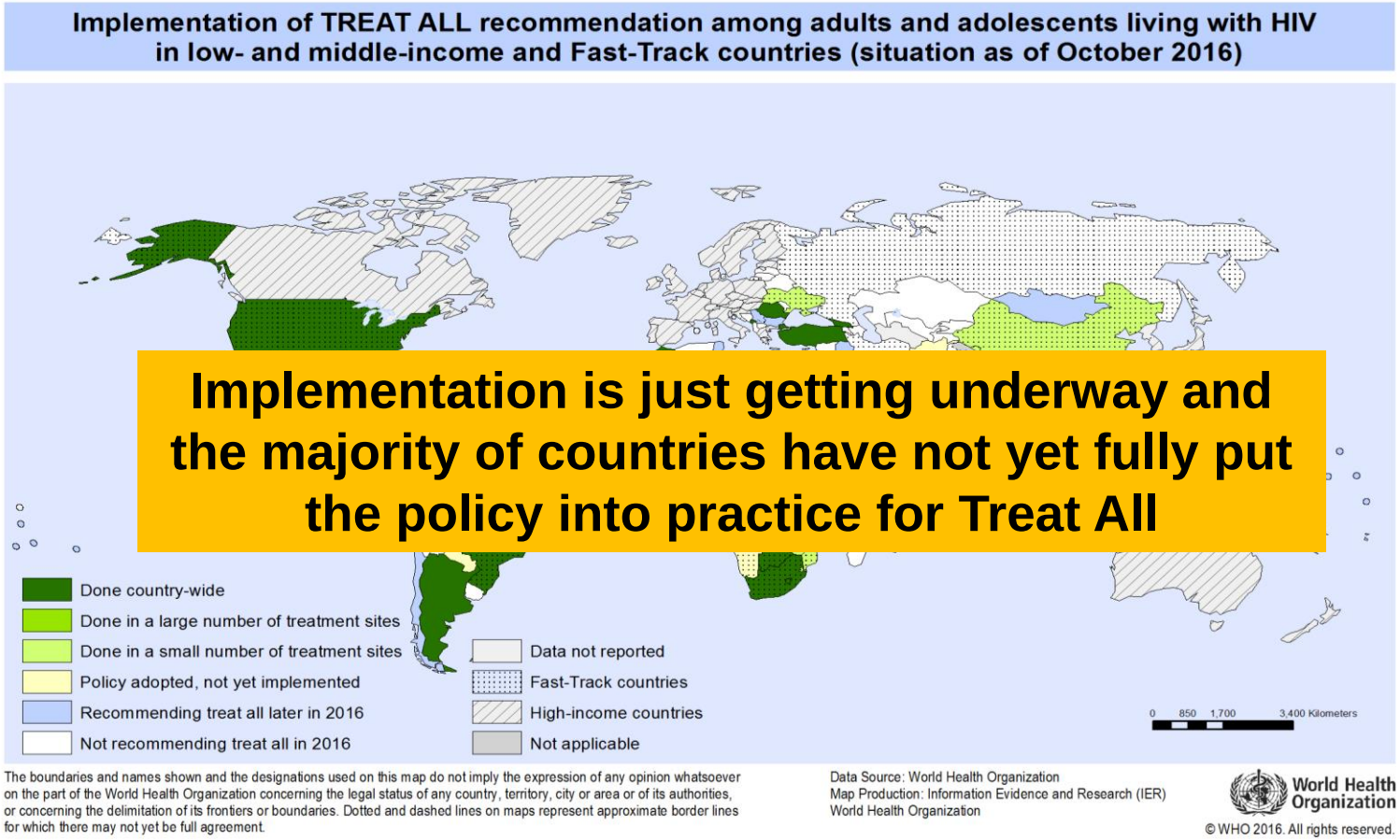
Data Source: World Health Organization
Map Production: Information Evidence and Research (IER)
World Health Organization

World Health Organization

World Health Organization

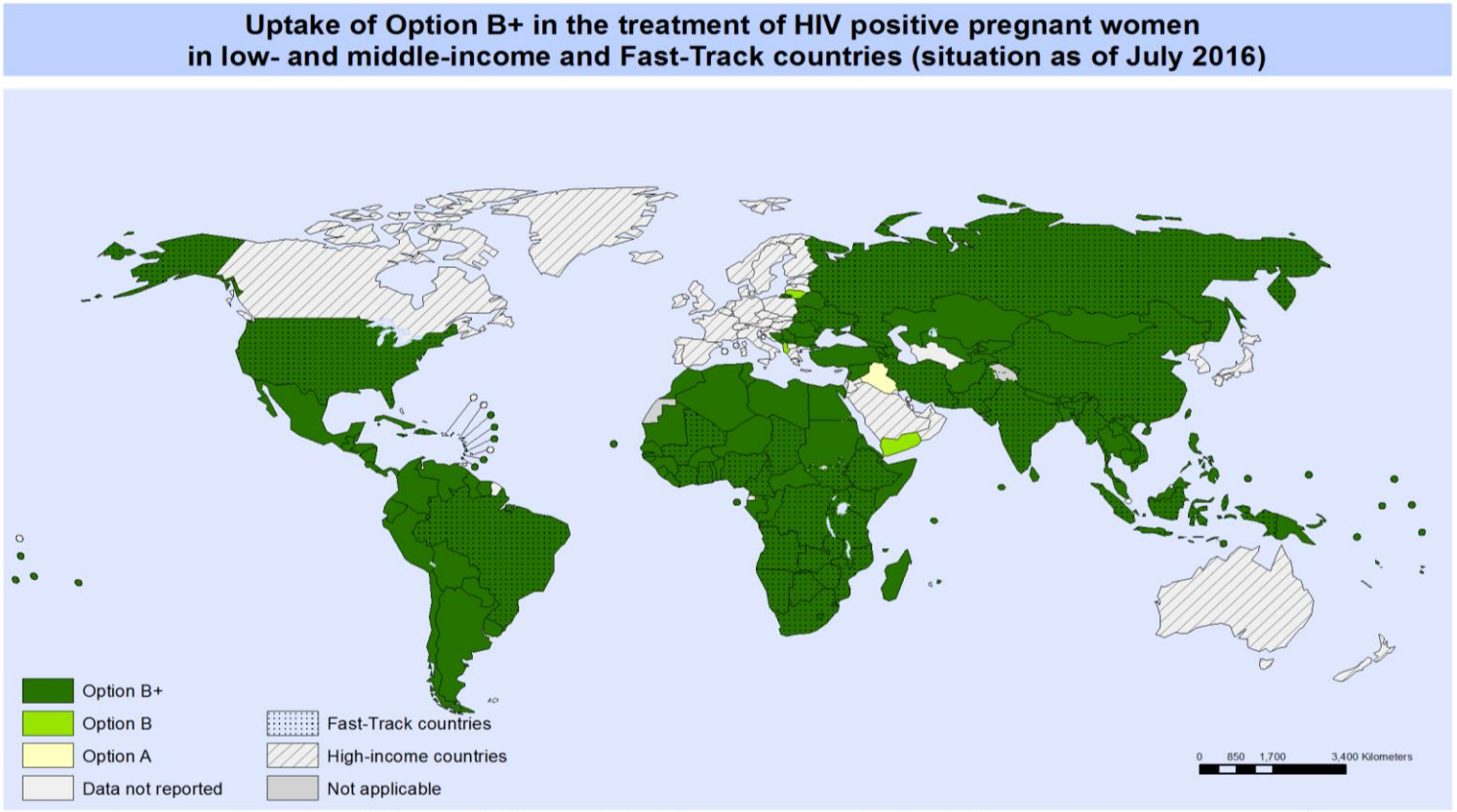
Policy uptake to full implementation

October 2016



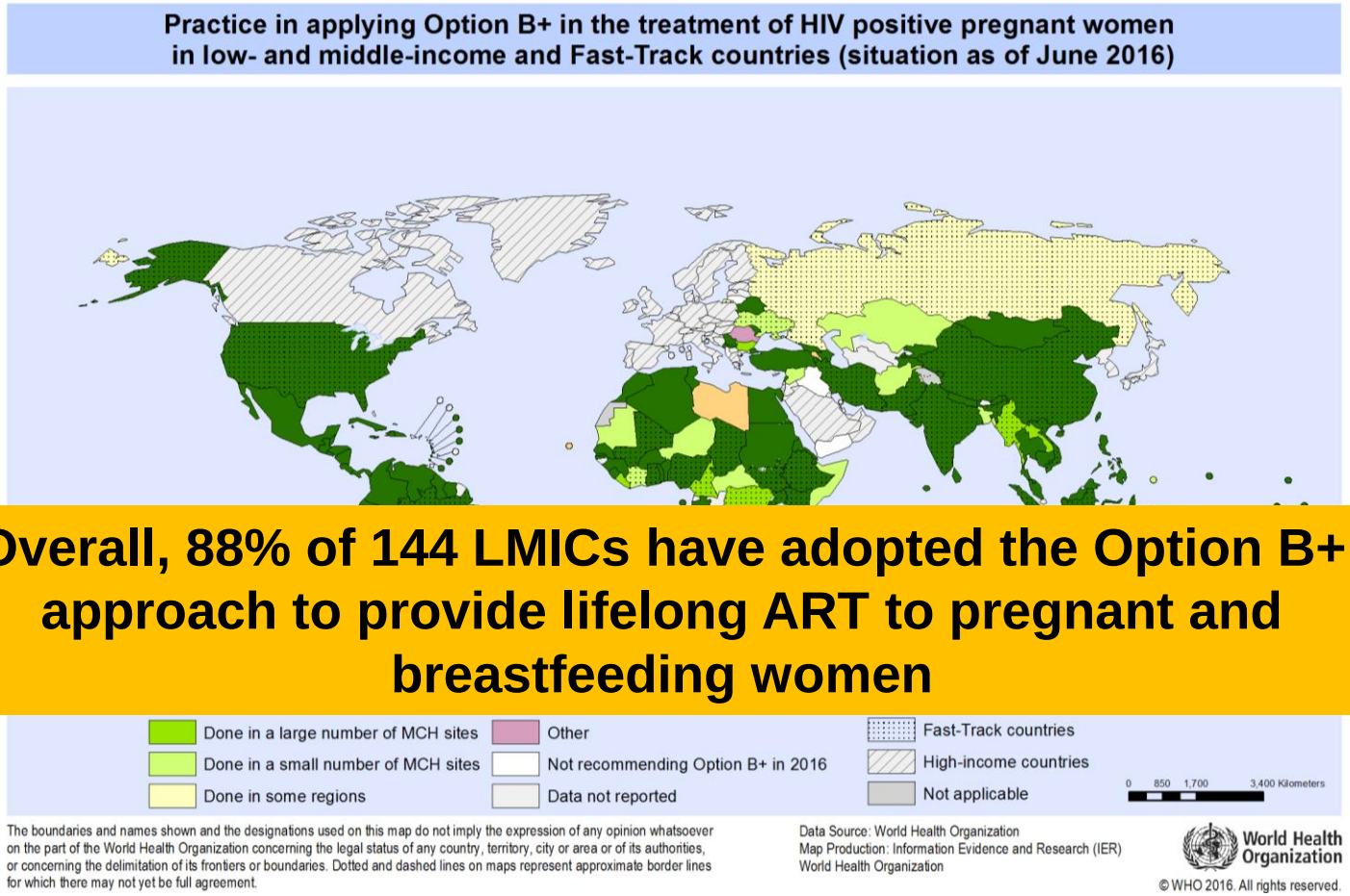
World Health Organization

The success story of 'treat all' for pregnant women, July 2016



World Health Organization

Option B+ has been one of the most widely adopted WHO recommendations, July 2016



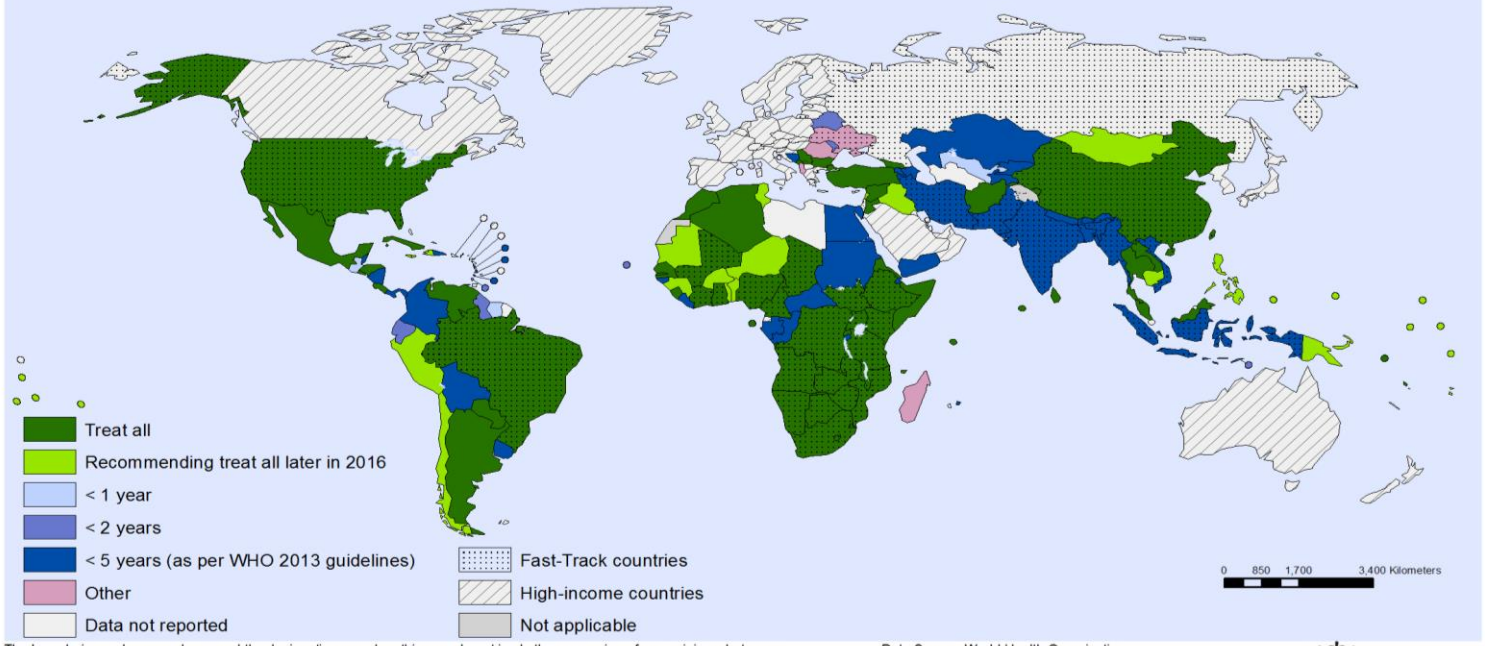
Overall, 88% of 144 LMICs have adopted the Option B+ approach to provide lifelong ART to pregnant and breastfeeding women

World Health Organization

“Treat All” and this shift is happening for children and adolescents

Recommended initiation threshold among children living with HIV in low- and middle-income and Fast-Track countries as per MoH guidelines or directive (situation as of October 2016)

BUT WE STILL NEED TO DIAGNOSE SOONER AND TREAT BETTER



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Map Production: Information Evidence and Research (IER)
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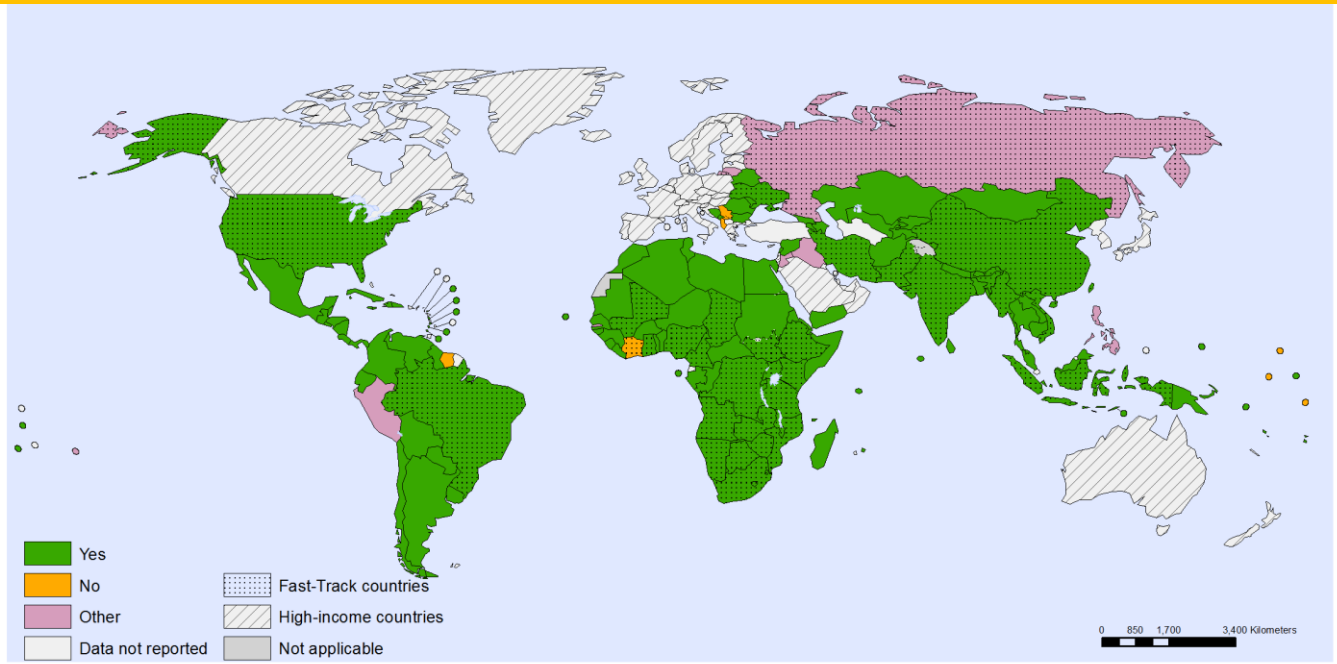
TDF/XTC/EFV adopted widely
July 2016

90% of LMIC adopted TDF + 3TC (or FTC) + EFV as the preferred first-line therapy



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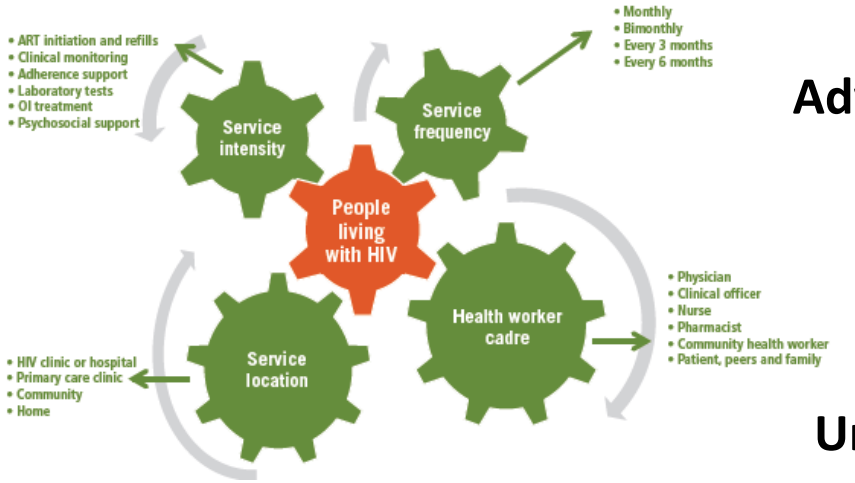
Framework for Differentiated approach to care and services

- 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

World Health Organization

Improved service delivery through differentiated models of care

New recommendations for:

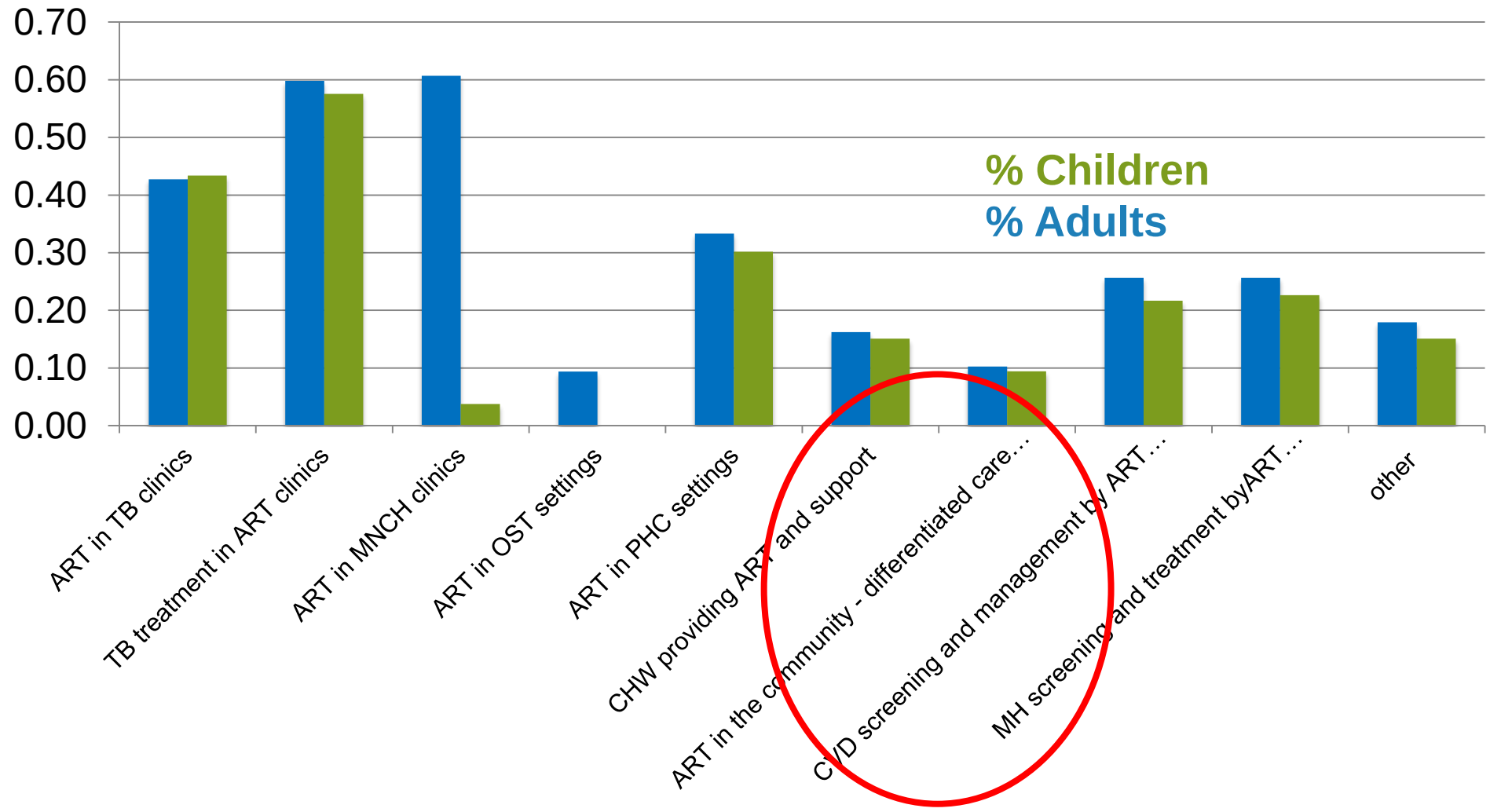
- Linkage to care with Rapid initiation of ART
- Adherence
- Retention
- "people-centered" integration with other services including TB, Hepatitis, STIs and NCDs

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

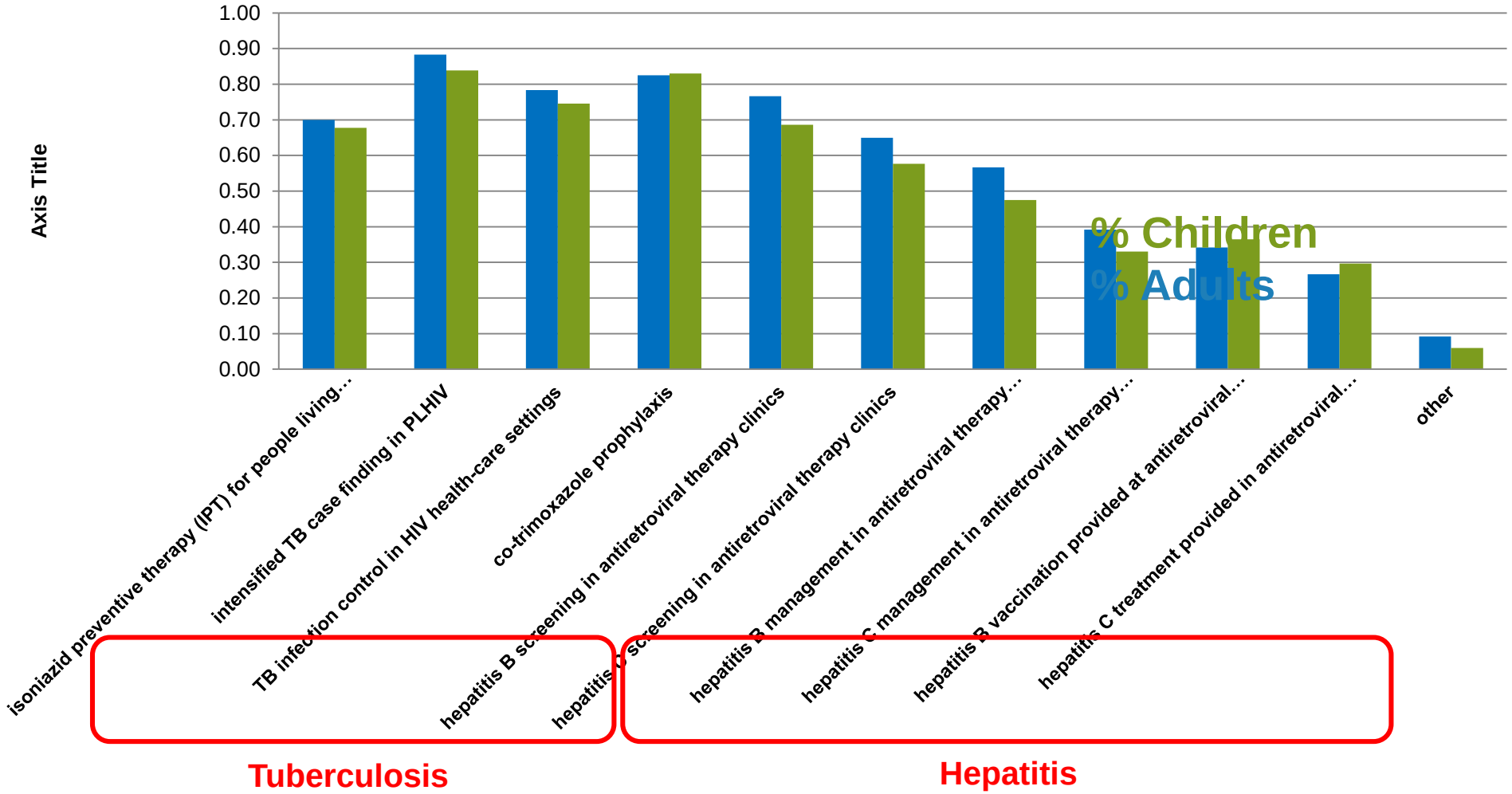
World Health Organization

Uptake of Service delivery recommendations, July 2016



Uptake of Co-infection recommendations

July 2016



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!

World Health Organization

មជ្ឈមណ្ឌលជាតិប្រយុទ្ធនឹងជំងឺអេដស៍ សើស្បែក និងកាមរោគ

NATIONAL CENTER FOR HIV/AIDS, DERMATOLOGY AND STD

កិច្ចប្រជុំផ្សព្វផ្សាយគោលការណ៍ណែនាំជាតិ ស្តីពី ការថែទាំ-ព្យាបាលជំងឺឱកាសនិយម និង ការព្យាបាលដោយឱសថប្រឆាំងមេរោគអេដស៍ សំរាប់ មនុស្សពេញវ័យ ក្មេងជំទង់ និង កុមារ

ថ្ងៃទី ២៨ ខែ វិច្ឆិកា ឆ្នាំ ២០១៦

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:

World Health Organization

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

Scope

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: **TREAT ALL**

NEW

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**

NEW

ALL CHILDREN REGARDLESS OF CD4 AND/OR CLINICAL STAGE SHOULD START ART AS SOON AS POSSIBLE, PREFERRABLY WITHIN 2 WEEKS OF DIAGNOSIS

When to start ART when active OI

Opportunistic Infection	Time from start treatment for OI and start ART
Tuberculosis CD4 < 50 cells/mm^3 CD4 > 50 cells/mm^3	 Within 2 weeks 2 – 8 weeks
Cryptococcal meningitis (CM)	4 – 6 weeks
Cryptococcus non-meningeal disease including Cryptococcal Ag + CSF neg	Within 2 weeks
All other OI	Within 2 weeks

1st line ART

NEW

- Adults and adolescents:

Age	Preferred first line	Alternative first line*
Adults Including pregnant/ breastfeeding, and with TB and HIV co-infection **Adolescents > 35kg**	TDF + 3TC + EFV	AZT+ 3TC + EFV (or NVP) TDF + 3TC + NVP
Adolescents < 35kg	TDF + 3TC + EFV	AZT+ 3TC + EFV (or NVP) TDF + 3TC + NVP ABC + 3TC + NVP

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

- Children:

Age	Preferred regimen	Alternative
<3 years or <10kg	ABC + 3TC + LPV/r After 1 year, confirmed VL suppression and switch to: ABC/AZT + 3TC + NVP	ABC/ AZT + 3TC + NVP
≥ 3- < 10years and ≥10kg	ABC + 3TC + EFV	ABC/AZT + 3TC + NVP
≥ 10years and >35kg	TDF + 3TC + EFV	ABC/AZT + 3TC + NVP/EFV

Monitoring antiretroviral therapy

NEW

Reducing the use of CD4 and scaling-up VL

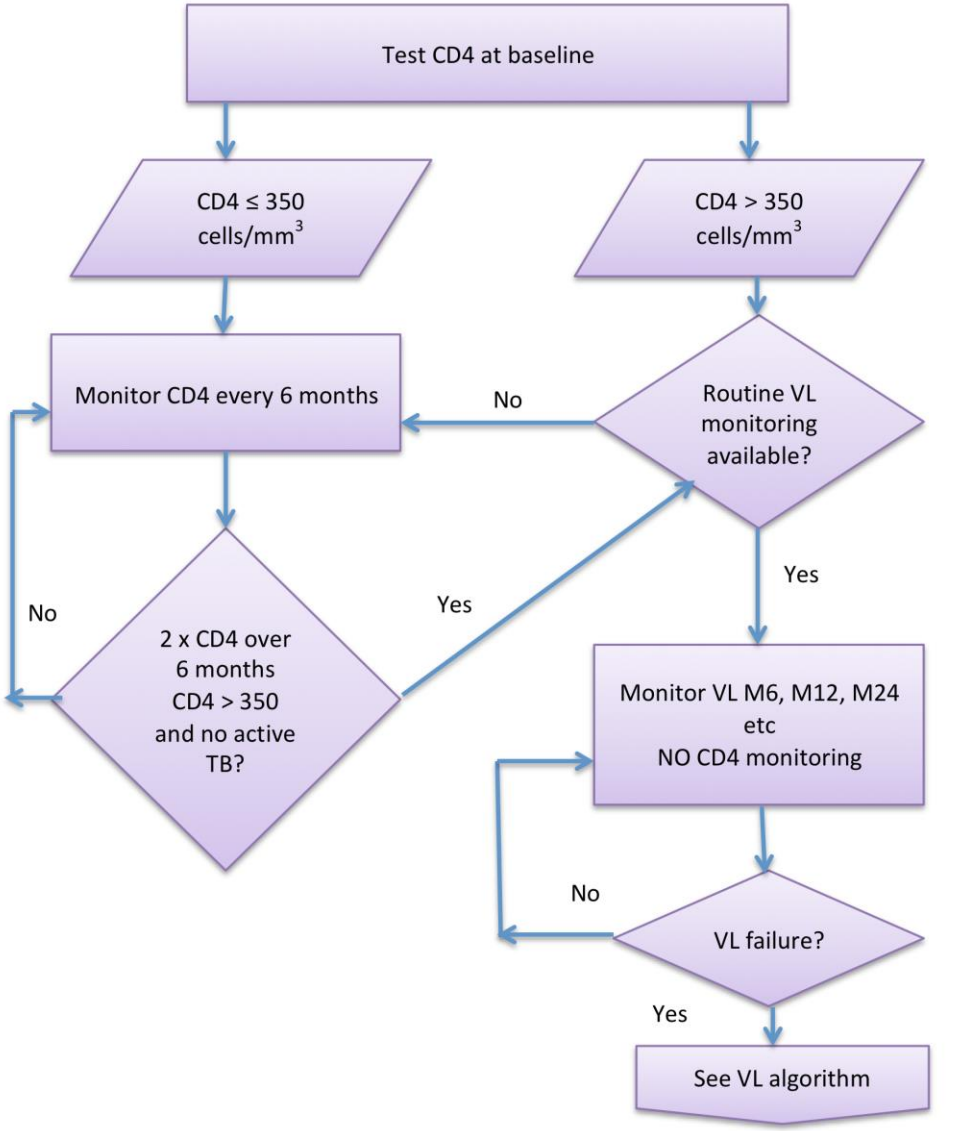
When to start / continue and stop CD4 monitoring ?

NEW

Start / continue	Baseline CD4 then 6 monthly until stopping criteria are fulfilled
Criteria to Stop CD4 monitoring*	On ART for at least 1 year *and all of the following:* • No adverse drug reactions requiring regular monitoring, • No current illness, and not on TB treatment • Not pregnant • Good understanding of lifelong adherence • 2 x CD4 > 350 cells/ mm^3 • 2 x undetectable VL • Routine VL monitoring is available
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.



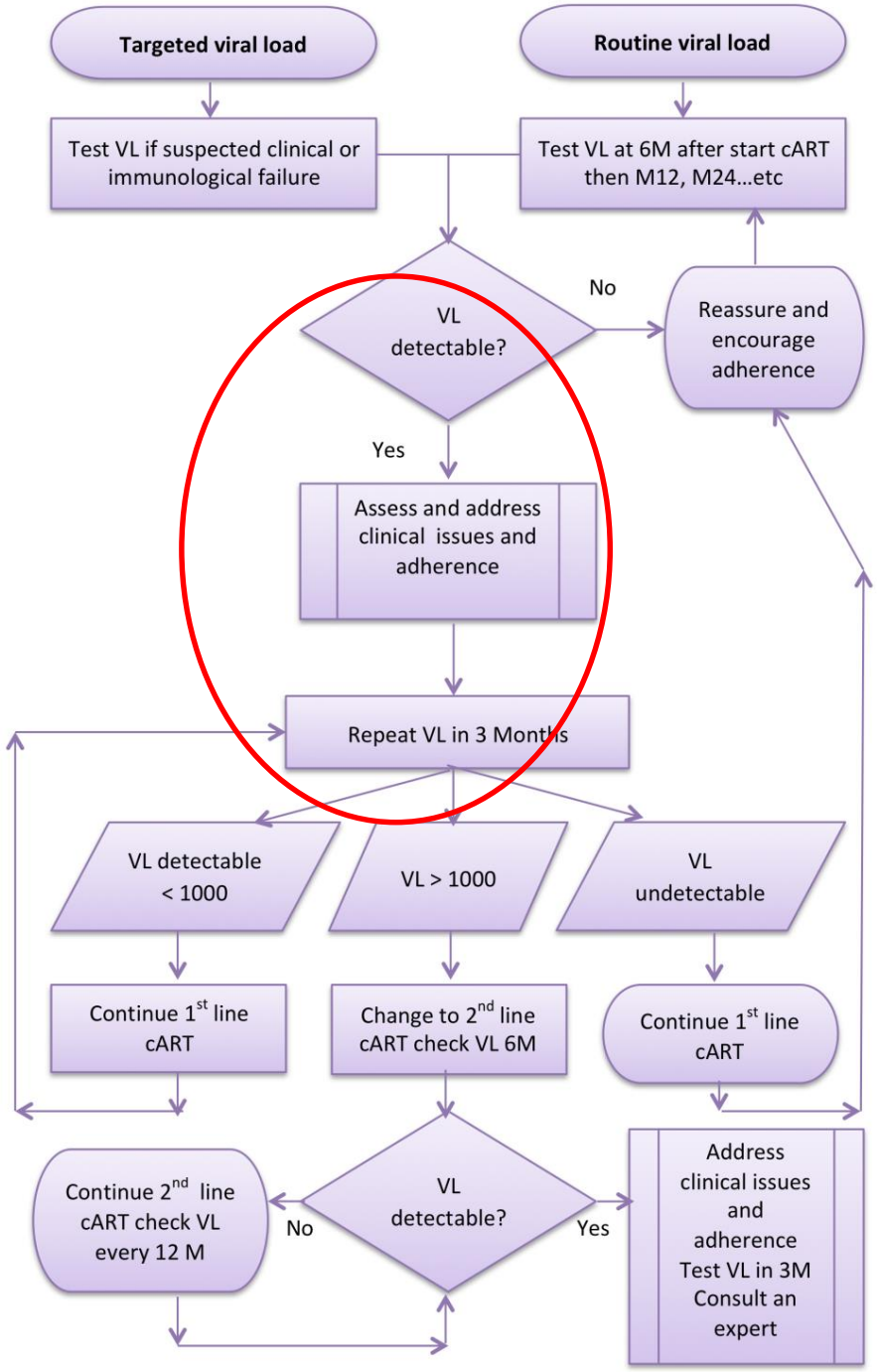
Whenever CD4 ≤ 350
Start / continue cotrimoxazole and monitor CD4 every 6 months.
When CD4 > 350 2 x in 6 months, and no TB, stop cotrimoxazole and if routine VL monitoring is available CD4 monitoring can be withheld, until VL failure.
If routine VL is not available, continue CD4 monitoring every 6 months., 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 every12 months

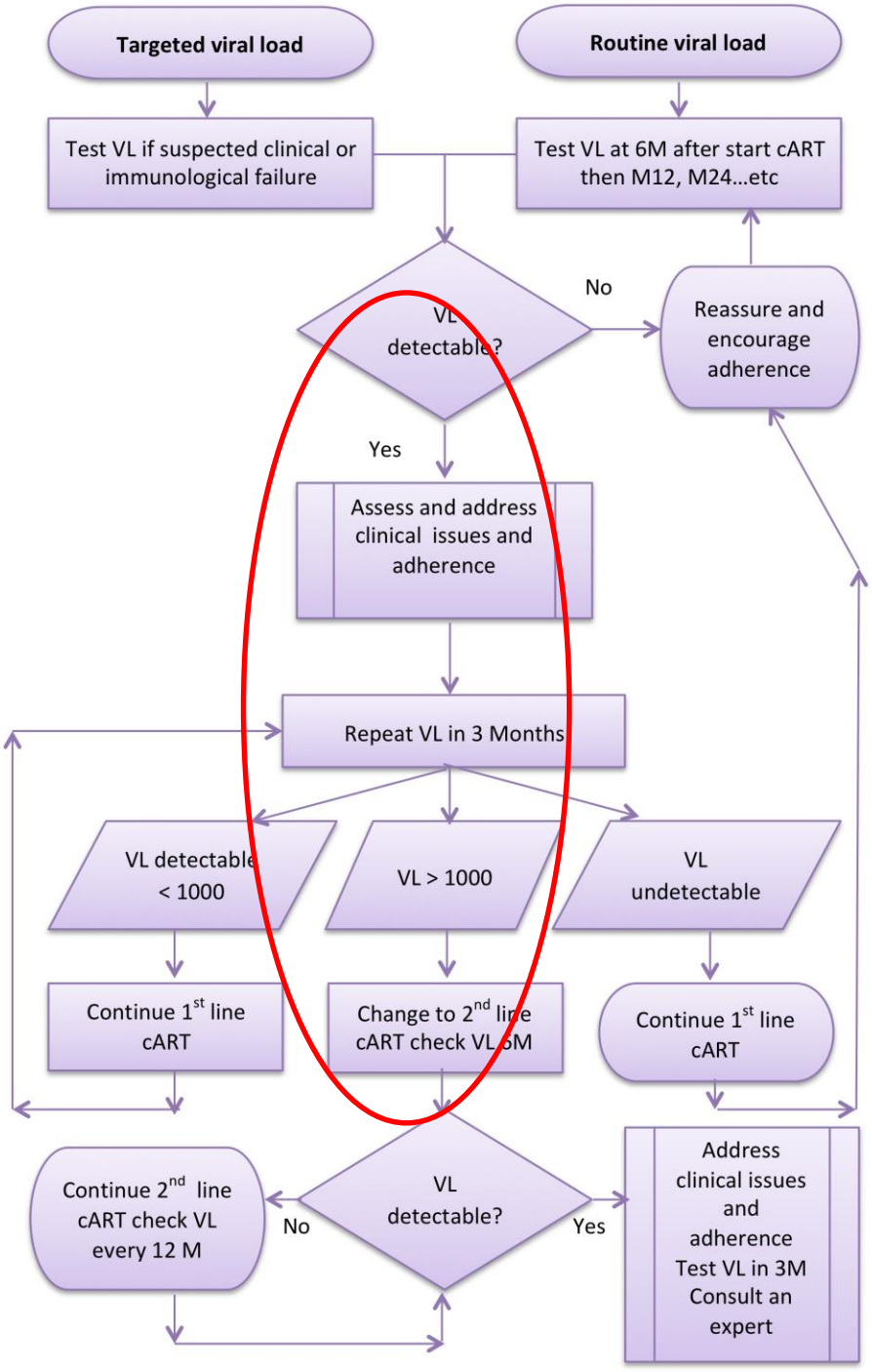
- Pregnant women test VL M3 after start ART
- If on ART do VL early in pregnancy

- Control VL after 3 months adherence boosting when VL found detectable



2nd line ART

- Switch to 2nd 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 2nd line regimen



2nd line ART

- Adults and adolescents:

Failed 1st line regimen	➔ Preferred second line
TDF + 3TC + NNRTI	**AZT + 3TC + ATV/r** (if HBsAg negative)
	TDF + 3TC + AZT + ATV/r (if HBsAg positive)
AZT (or d4T) + 3TC + NNRTI	**TDF + 3TC + ATV/r**
If failed 1st line including a PI	Consult an expert

- Children:

	First line	Preferred 2nd line regimen	Alternative 2nd line regimen
Children	ABC/AZT+3TC+LPV/r	No change from first line regimen	AZT (or ABC) +3TC + NVP/EFV$
	ABC/AZT+3TC+EFV or NVP	AZT (or ABC) + 3TC + LPV/r *	TDF+ 3TC + LPV/r *
Adolescents (>10-19 y)	TDF/AZT+3TC+EFV	AZT/TDF# + 3TC + ATV/r (if >40kg)*	AZT/TDF + 3TC + LPV/r*

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

Week	Clinical	Adherence counseling	Laboratory testing	Drugs start /Stop
Week 0	✔	✔	✔	Start Cotrimoxazole
Week 1		✔		
Week 2	✔	✔		Start cART Stop Cotrimoxazole if CD4 > 350 and no TB
After start ART				
Week 2	✔	✔		Start IPT
Month 1	✔	✔	✔	
Every 1 M whilst on IPT	✔	✔	✔ VL at month $_{5}6_{7}$	Stop IPT after 6 months
After stop IPT, still on Cotrimoxazole				
Every 1 – 3 months (According to clinical status, + adherence)	✔	✔	✔ VL at M $_{5}6_{7}$ then M $_{11}12_{13}$, M $_{23}24_{25}$ etc ✔ CD4 every $_{5}6_{7}$ M	Stop Cotrimoxazole according to criteria (see **Error! Reference source not found.** page 34)
After stop Cotrimoxazole				
Every 1 – 3 months	✔	✔	✔ VL at every $_{11}12_{13}$ Months	

Adolescent care

WHO defines adolescents as 10 – 19 years old

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

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+)

NEW

- 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?

NEW

Mother	Risk Status of HIV Exposed Infant HIV	Infant feeding status	Infant prophylaxis (*)
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 *or*** ***2- Mother diagnosed HIV positive at delivery or during post 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***	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**
	Low Risk situations: Not fall in the high risk situations.	Breast feeding or formula feeding	**NVP for 6 weeks**

PMTCT: What's new?

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 .**

NEW

- ***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).

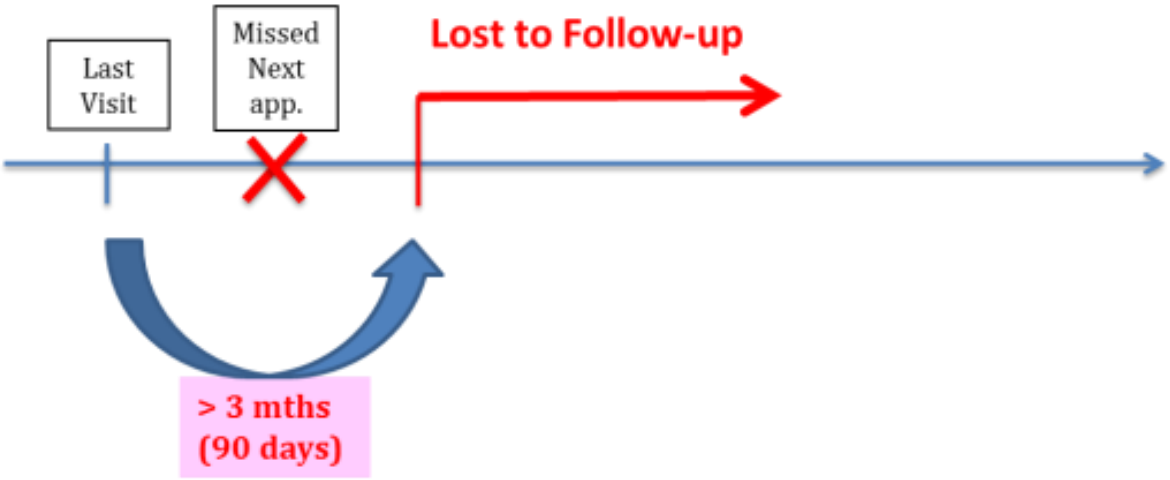
Retention in HIV care describes when a patient who is enrolled in HIV care routinely attends these services, as appropriate to the need. This excludes people who have died or were lost to follow-up.

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

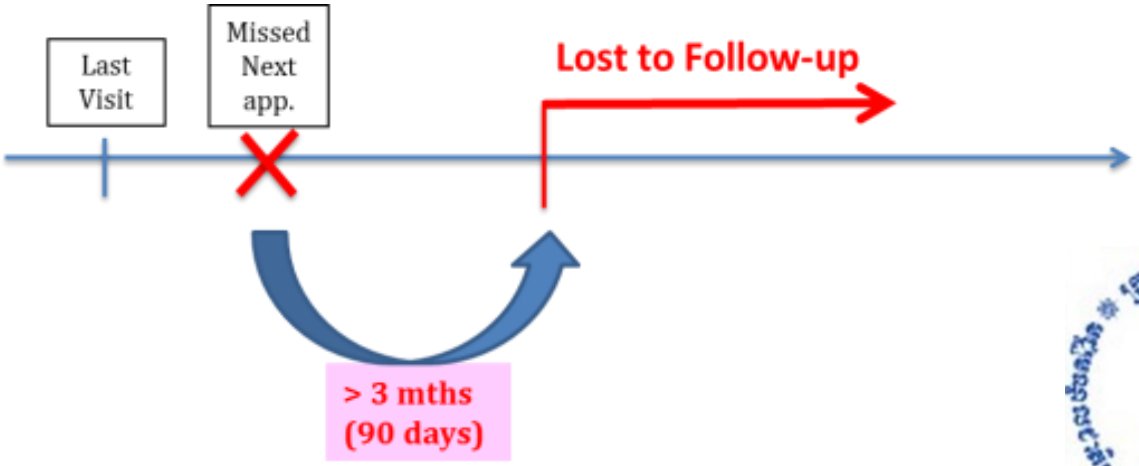
[1] Retention in HIV programmes: defining the challenges and identifying solutions: meeting report. 13–15 September 2011. Geneva: World Health Organization; 2012 (http://www.who.int/hiv/pub/meetingreports/retention_programmes/en/).

Definition of Lost to Follow-up

Current definition:



New definition in Cambodia:

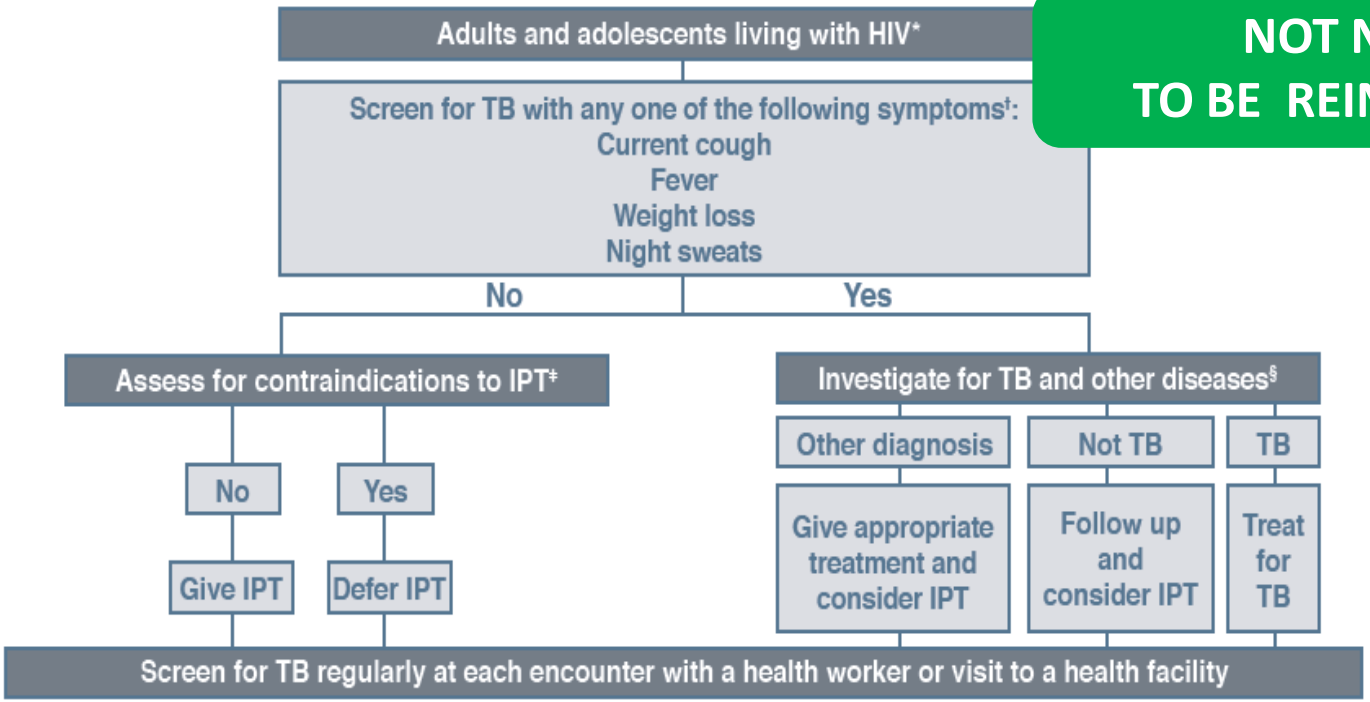


Prevention of Opportunistic Infections What's new?

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:



NOT NEW
TO BE REINFORCED

IPT = 6 month course:

- If > 40kg: Isoniazid 300mg / day + pyridoxine 50mg / day
- If ≤ 40kg: Isoniazid 200mg / day + pyridoxine 50mg / day

TB screening and I

NOT NEW
TO BE REINFORCED

Criteria to start, continue, and stop IPT :

IPT	TB symptom screening should be performed at EVERY clinic visit
When to start IPT (Adults and adolescents)	· **All patients with TB symptom negative and no contraindications** (Contraindications: peripheral neuropathy, heavy alcohol consumption, ALT/AST > 3 x ULN). · **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.*
Continue IPT	· Complete **6 months** (if treatment interruption, see below)
When to stop IPT	· **If symptoms of hepatitis** (anorexia, nausea, vomiting, abdominal pain, chills, icterus and dark urine), stop INH immediately and seek the HIV clinic · **If increase of ALT/AST** under monitoring of patients with risk of liver disease: ▪ Asymptomatic and ALT/AST > 5 x ULN or ▪ Symptomatic and ALT/AST > 3 x ULN · **If persistent neuropathy** after increase of pyridoxine to 100mg daily · **After completion of 6 months on IPT**

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

NEW

- 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/mm^3

NEW

CD4 threshold increased to 350 cells / mm^3

All adolescents (whatever CD4) until 20 year-old

Cotrimoxazole

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

NEW

Cotrimoxazole	Adolescent (11-19)	Adults (≥20 years)
When to start	**All regardless of CD4 count**	· **CD4 < 350 cells/mm^3 *** · **All patients with TB** · **WHO stage 3 or 4 regardless of CD4 count**
When to continue	**ALL**	· **CD4 <350 cells/mm^3** and/or on **TB treatment** · **If history of PCP** with CD4 count > 200 cells/mm^3 (secondary prophylaxis indefinitely)
When to stop	**Never stop** (until adult age 20)	· **CD4 count > 350 cells/mm^3 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**:

NEW

Cotrimoxazole	HIV-exposed infant	All HIV-infected infants and children regardless of age or clinical stage of disease
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/mm^3 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/mm^3; and
b. where this population also has a high prevalence (>3%)[a] of cryptococcal antigenaemia.

(conditional recommendation, low-quality evidence).

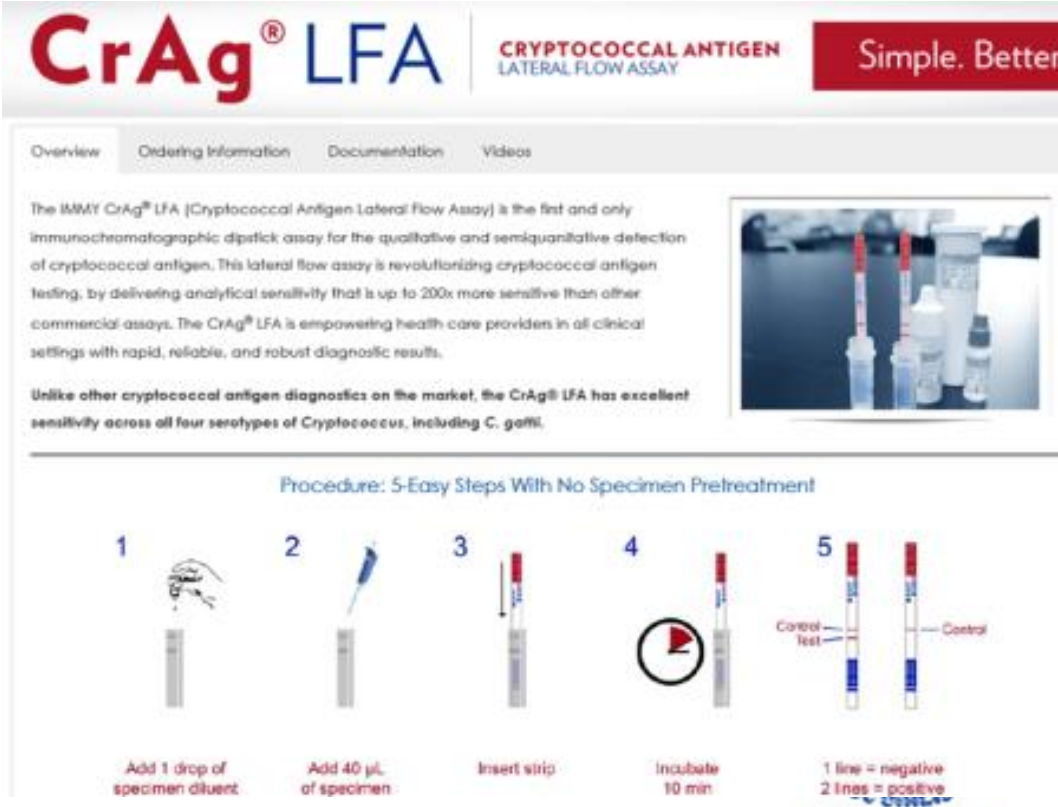
→ **Screen and Treat strategy**

Cryptococcal Ag screening

NEW

- 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 aymptomatic (IPCA) is safer, more accessible, and less resource intensive (outpatient, fluconazole) than when symptomatic (hospitalization, amphotericin / repeated LP)

Cryptoccocus Screening and Prevention

Fluconazole prophylaxis *when CRAG test is not available*:

When to start Fluconazole prophylaxis	**CD4 < 100 cells / mm3** *and* Not in the 1st 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.

Cryptoccocus Screening and Prevention

NEW

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

WHO 2011 Crypto Rx – induction phase

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]

Viral hepatitis

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 2nd line ART
- If just one of these drugs (particularly 3TC/FTC) are used, drug resistance will develop
- Standard 2nd 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 1st line ART contains both TDF and 3TC
- HBs-Ag must be tested if there is consideration to change to 2nd 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)

Nutrition and weight management

Chronic NCD in PLHIV

NEW

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

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.
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)

NEW

- 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.

HIV encephalopathy / dementia

- 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.

· **Cognitive impairment;** Progressive memory loss, loss of concentration, confusion and slowing of thought.
· **Motor symptoms;** Loss of balance, clumsiness, change in handwriting, tremor, unsteady gait, incontinence
· **Behavioral changes;** Apathy, social withdrawal, loss of interest in what is going on, and their own well-being.

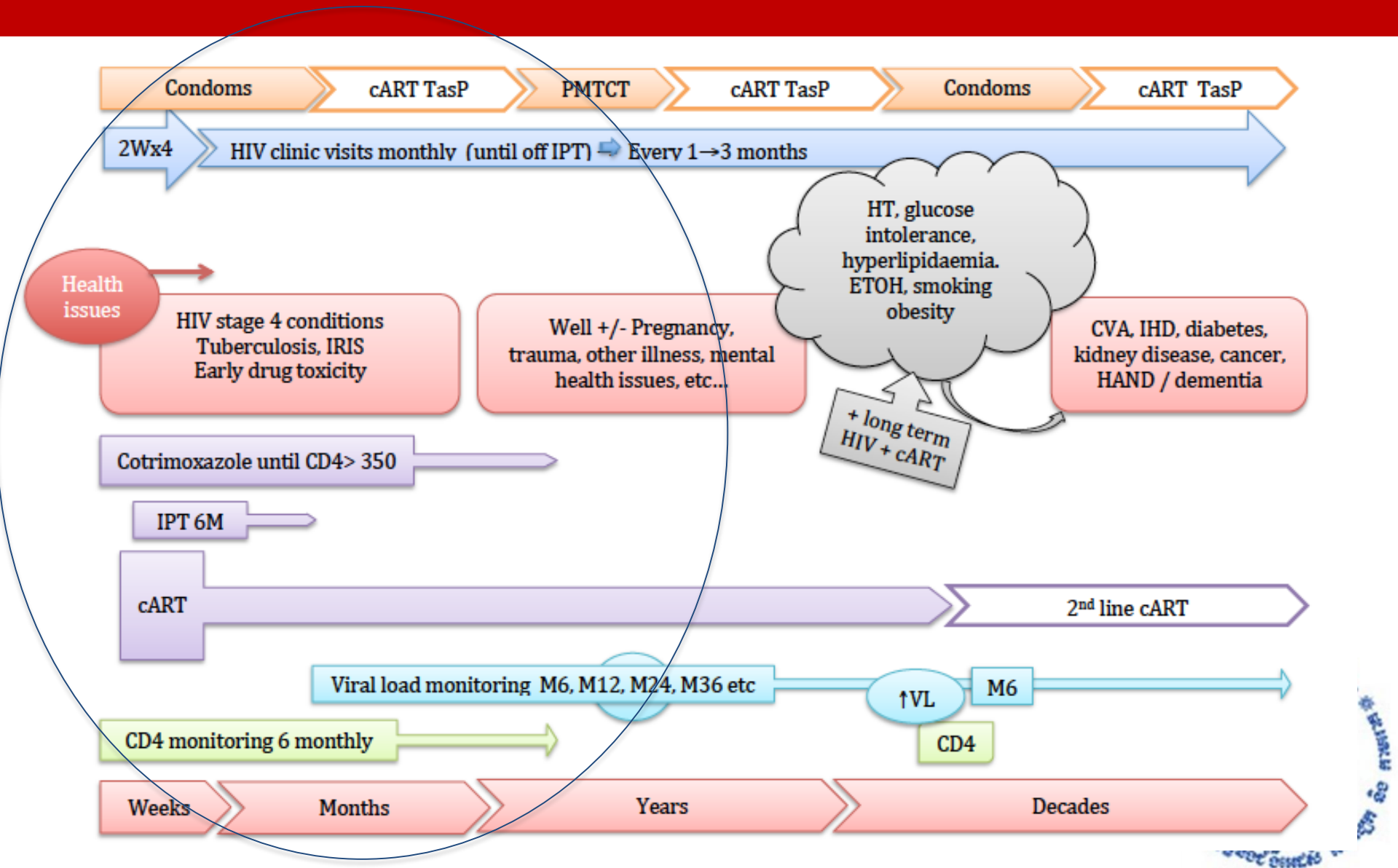
Mental Health

Useful screening questions for depression

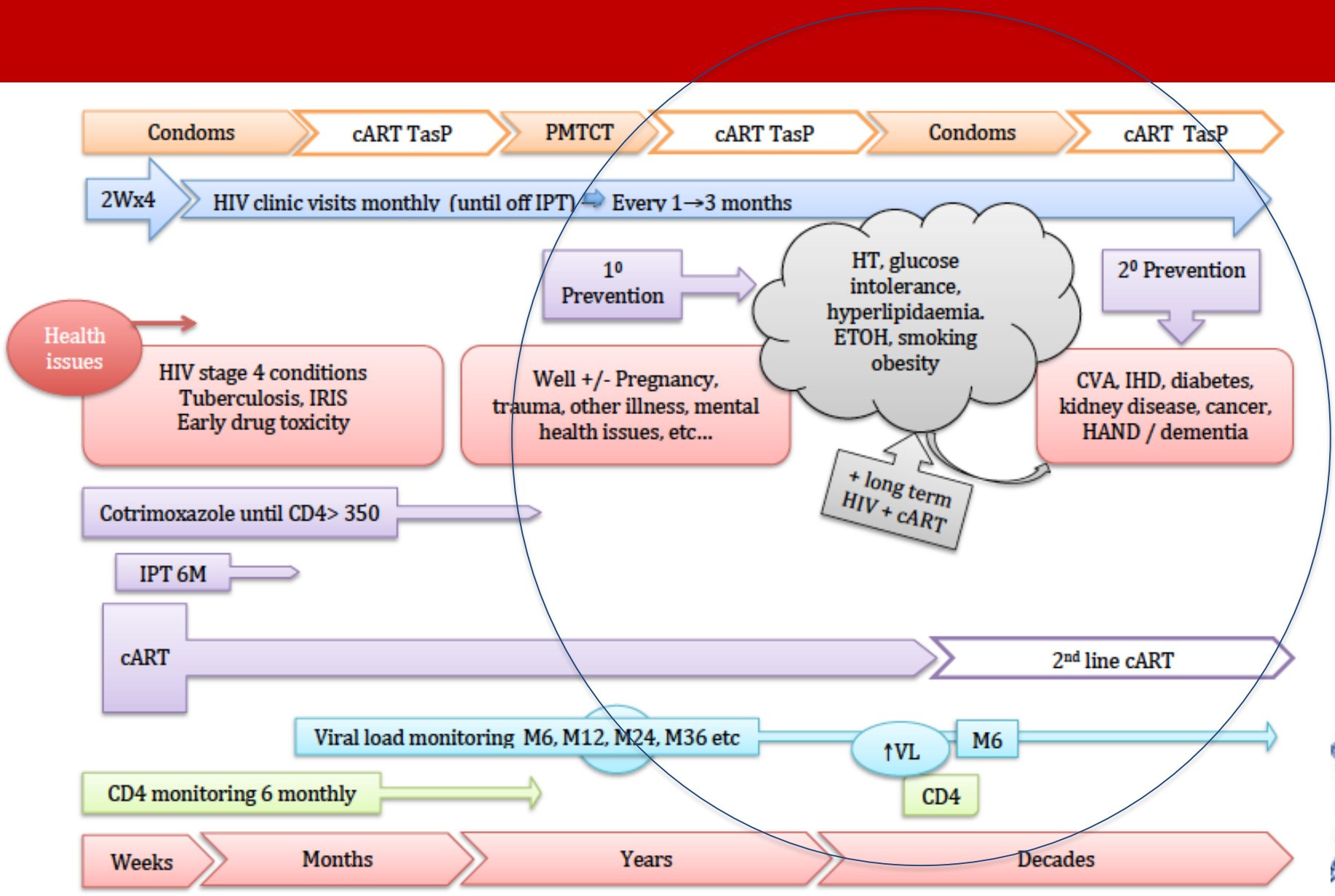
- During the past month, have you felt like you were losing interest or pleasure
- in doing things?
- Have you felt down, depressed or helpless?
- If a patient appears depressed, it is important to assess their risk for suicide:
- Have you ever thought about giving up?
- Have you ever thought about ending 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



Need to address NCD



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 $_{5}6_{7}$ 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.

មជ្ឈមណ្ឌលជាតិប្រយុទ្ធនឹងជំងឺអេដស៍ សើស្បែក និងកាមរោគ

NATIONAL CENTER FOR HIV/AIDS, DERMATOLOGY AND STD

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Opportunistic Infections

Dr. Ky Sovathana

NCHADS

Cotrimoxazole Prophylaxis

Criteria for Cotrimoxazole prophylaxis in Children

	Start Cotrimoxazole	Stop Cotrimoxazole
HIV-exposed infant	4-6 weeks of age	PCR or antibody negative 6 weeks after complete cessation of breastfeeding
All HIV-infected infants and children regardless of age or clinical stage of disease	• **Immediately after HIV diagnosis made** in a child presenting for the first time at any age >4-6 weeks (Primary Prophylaxis) • **In children with PCP**, subsequent to PCP treatment being completed (Secondary Prophylaxis)	• If the child is anemic as cotrimoxazole may cause bone marrow suppression or • if Grade 3/4 toxicity rash occurs. • Otherwise continue CTX **until children transition to adult care, regardless of ART or CD4 recovery**

Criteria for starting, continuing and stopping Cotrimoxazole for Adults and Adolescents including pregnant women (1)

	Adolescent (11-19)	Adults (≥20 years)
When to start cotrimoxazole	· 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 cotrimoxazole	· 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 cotrimoxazole	· Never stop · (until adult)	· CD4 count > 350 cells/mm3 on 2 measurements at least 6 months apart and undetectable VL and completed TB treatment

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

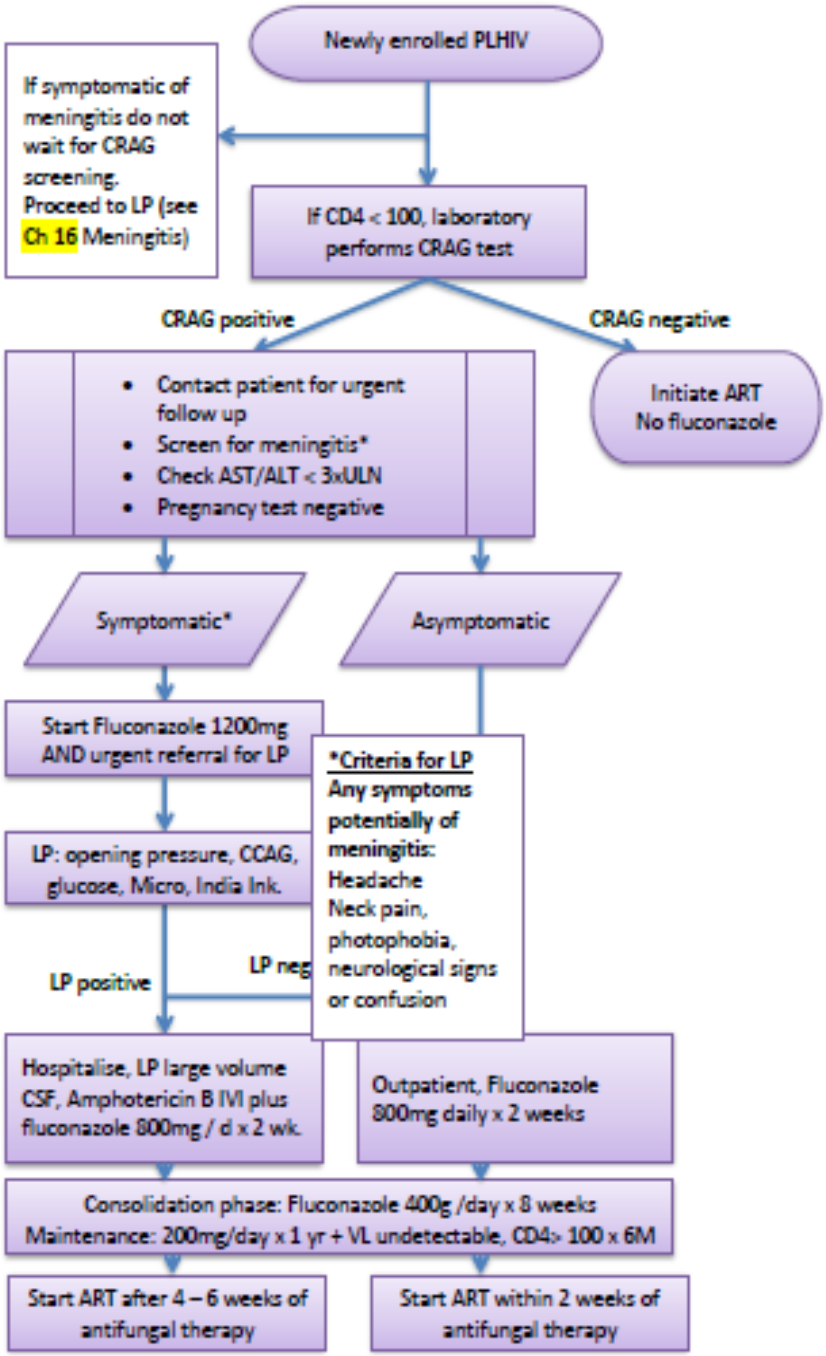
Cryptococcus Screening and Fluconazole Prophylaxis (1)

- 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.
- Asymtomatic 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.

Cryptococcus Screening and Fluconazole Prophylaxis (2)

- 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/mm^2 (≥ 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



Criteria for starting & stopping Fluconazole Prophylaxis(1)

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

When to start Fluconazole prophylaxis	**CD4 < 100 cells / mm3 and Not in the 1st 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

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**.

IPT: When to start

Indication for starting IPT:

For Children

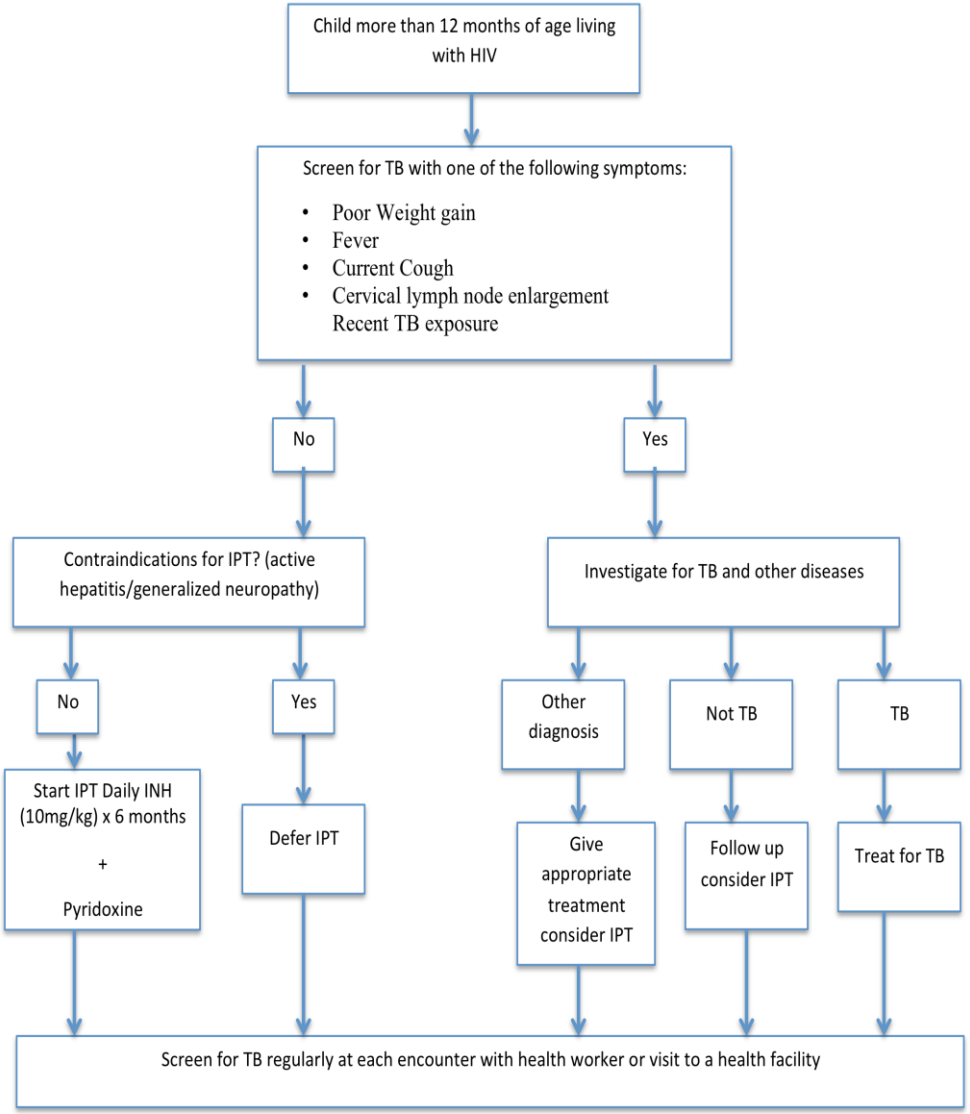
- If no symptoms: those over 12 months of age are eligible for IPT.
- children less than 12 months old with a household TB contact
- all children living with HIV after a successful completion of TB disease treatment

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

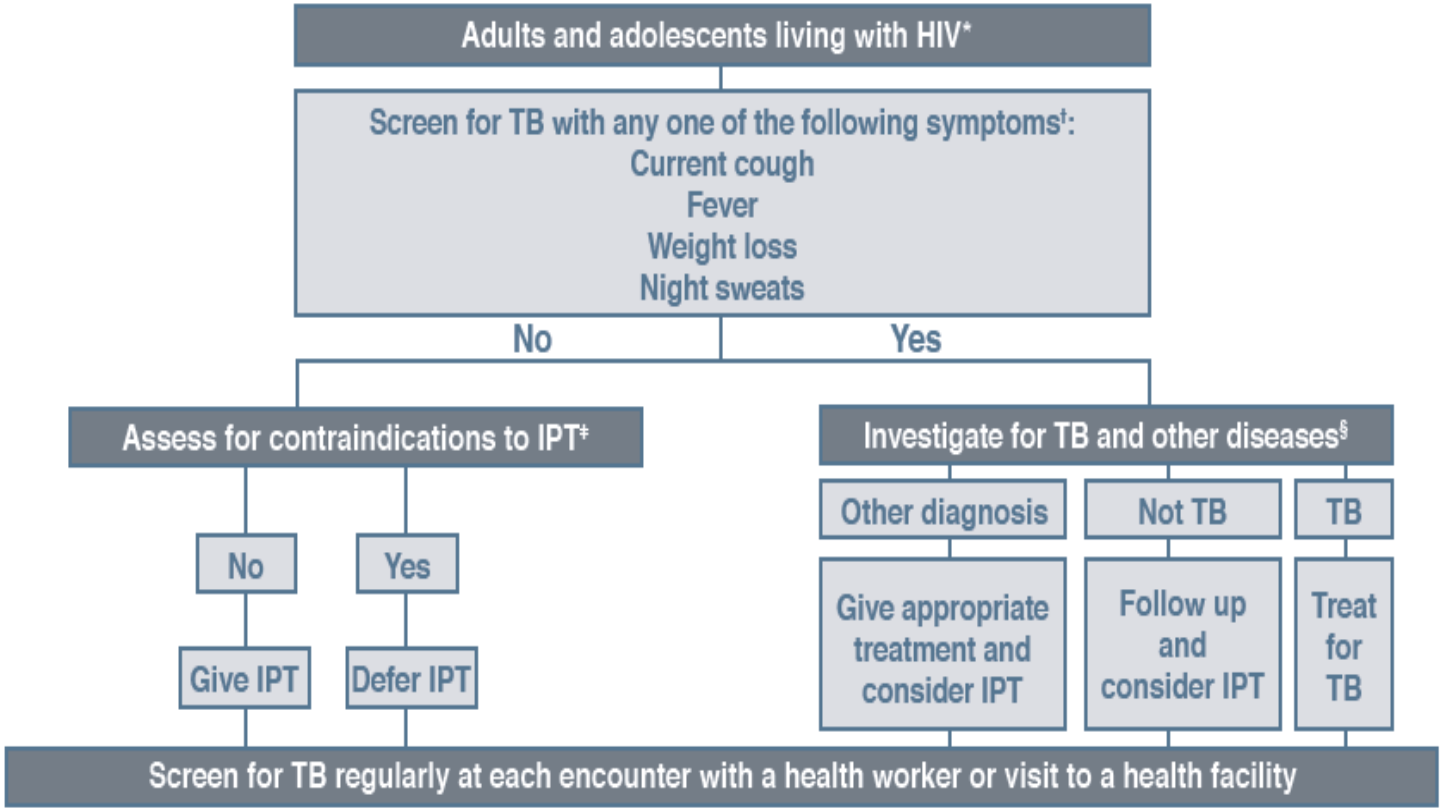


IPT should not be started in case of the following contraindications:

- 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 symptoms†:
Current cough
Fever
Weight loss
Night sweats
No
Yes
Assess for contraindications to IPT‡
Investigate for TB and other diseases§
No
Yes
Other diagnosis
Not TB
TB
Give IPT
Defer IPT
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.

	Criteria to initiate	Dose	Criteria to stop
Cotrimoxazole	See: Ch 5 Primary Prophylaxis for Opportunistic infections		
	· CD4 < 350 · TB at any CD4 · WHO stage 3 or 4 · All adolescents If not contraindicated	1 DS; (TMP-160mg, SMX-800mg) tablet daily or 2 SS; (TMP-80mg, SMX-400mg) tablets daily.	Age ≥ 20 years and No active TB, and VL undetectable and CD4 > 350 on two occasions > 6 months apart.
Isoniazid preventive therapy (IPT)	See: Ch 6 Screening for TB and assessment for Isoniazid Preventive Therapy (IPT)		
	All PLHIV (including pregnant women) without active TB should have IPT one course If not contraindicated.	Isoniazid 300mg / day + pyridoxine 50mg/d (if weight < 40kg Isoniazid 200mg / day)	After 6 months.
Fluconazole Only if CRAG screening is not available	See: Ch 7 Cryptococcus screening and prevention		
	PLHA with CD4 < 100 If not contraindicated	Fluconazole 100mg/ day	VL undetectable and CD4 > 100 on two occasions > 6 months apart.

មជ្ឈមណ្ឌលជាតិប្រយុទ្ធនឹងជំងឺអេដស៍ សើស្បែក និងកាមរោគ

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Antiretroviral therapy

Joseph Harwell, MD, FAAP, FIDSA
Clinton Health Access Initiative
The Warren Alpert Medical School at Brown University

Pediatric First Line ART

Age	Preferred regimen	Alternative
<3 years or <10kg	ABC + 3TC + LPV/r After 1 year, confirmed VL suppression and switch to: ABC/AZT + 3TC + NVP	ABC/ AZT + 3TC + NVP
≥ 3- < 10years and ≥10kg	ABC + 3TC + EFV	ABC/AZT + 3TC + NVP
≥ 10years and >35kg	TDF + 3TC + EFV	ABC/AZT + 3TC + NVP/EFV

Pediatric First Line ART

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%

Simplified Weight Band Daily Dosing Schedule for ABC/3TC Formulations *(# of tablets of relevant formulation)*			
Weight Band (Kg)	**ABC/3TC (60/30 mg)**	**ABC/3TC (120/60 mg)**	**ABC/3TC (600/300 mg)**
3-5.9	2	1	N/R
6-9.9	3	1.5	N/R
10-13.9	4	2	N/R
14-19.9	5	2.5	N/R
20-24.9	6	3	N/R
25-34.9	1 adult tab (600/300mg)	1 adult tab (600/300mg)	1

Adult First Line ART

Age	Preferred first line	Alternative first line*
Adults Including pregnant/ breastfeeding, and with TB and HIV co-infection **Adolescents > 35kg**	TDF + 3TC + EFV	AZT+ 3TC + EFV (or NVP) TDF + 3TC + NVP

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

Adult First Line ART – Dose Optimized Efavirenz (TLE400)

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

Antiretroviral Therapy: Where Are We Now? Where Are We Going?

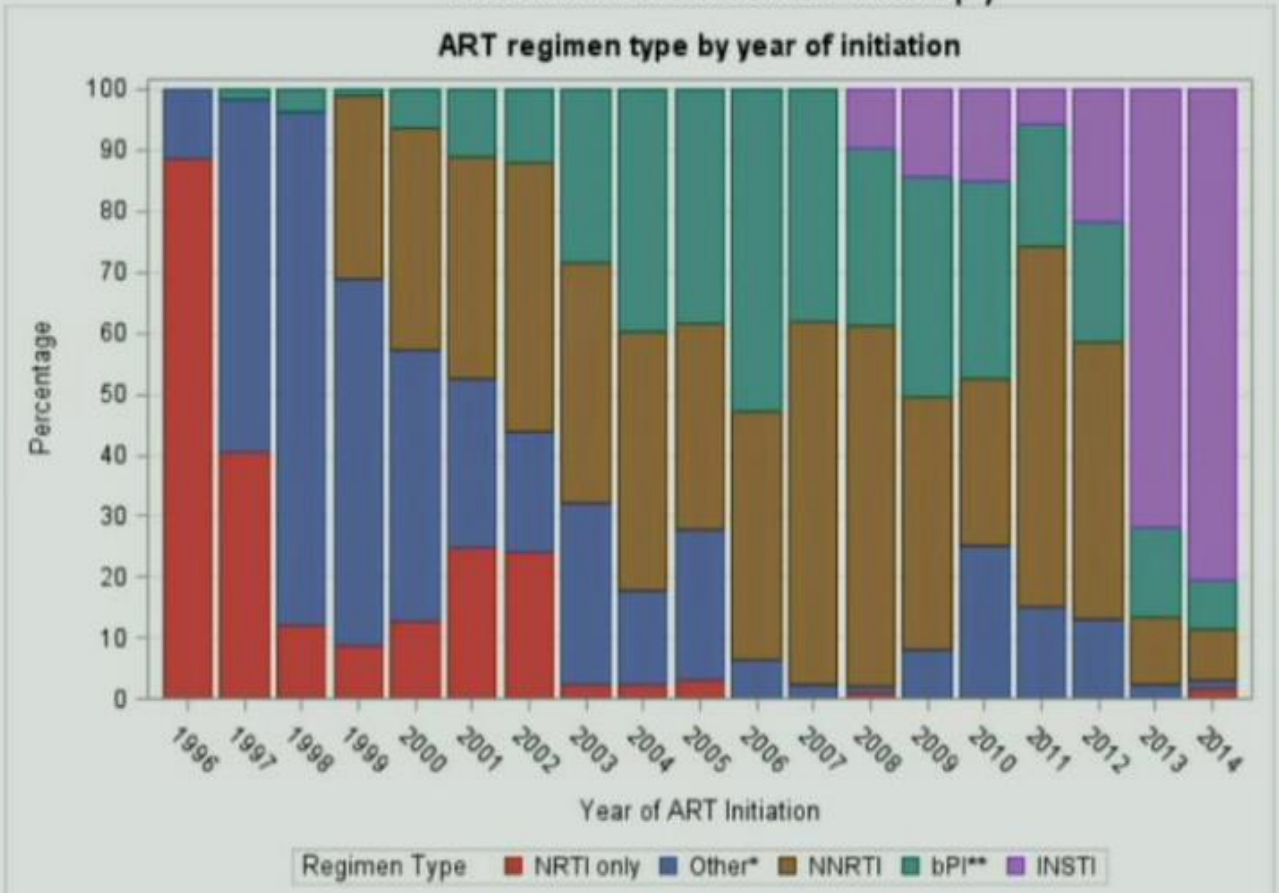
Joseph J. Eron

NC, Chapel Hill, NC, USA Plenary session abstract #16, CROI 2016, Boston, MA

UCHCC: UNC CFAR
HIV Clinical Cohort

Shift To Integrase Inhibitor-based Therapy

Initial Antiretroviral Therapy



1,773 patients initiating ART between 1996 and 2014 in the UCHCC, follow-up through 2015

bPI = LPV/r, DRV/r or ATV/r therapy
Other = includes unboosted PI and other bPI combinations

Courtesy of Thibaut Davy and Sonia Napravnik

Questions?

Treatment Monitoring & PMTCT

Dr. Ahmed Hassani
U.S. Centers for Disease Control & Prevention
Dr. Men Pagnaroat
AIDS HealthCare Foundation

លក្ខណៈវិនិច្ឆ័យដែលត្រូវចាប់ផ្តើមការព្យាបាលដោយឱសថប្រឆាំងមេរោគអេដស៍ Criteria to start antiretroviral therapy

Adults and adolescents: TREAT ALL

NEW

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

NEW

ALL CHILDREN REGARDLESS OF CD4 AND/OR CLINICAL STAGE SHOULD START ART AS SOON AS POSSIBLE, PREFERRABLY WITHIN 2 WEEKS OF DIAGNOSIS

នៅពេលមានជម្ងឺឱកាសនិយមសកម្ម តើពេលណាត្រូវចាប់ផ្តើមការព្យាបាលដោយឱសថប្រឆាំងមេរោគអេដស៍ (When to start ART when active OI)

Opportunistic Infection	Time from start treatment for OI and start ART
Tuberculosis CD4 < 50 cells/mm^3 CD4 > 50 cells/mm^3	 Within 2 weeks 2 – 8 weeks
Cryptococcal meningitis (CM)	4 – 6 weeks
Cryptococcus non-meningeal disease including Cryptococcal Ag + CSF neg	Within 2 weeks
All other OI	Within 2 weeks

ការតាមដានការព្យាបាលដោយឱសថប្រឆាំងមេរោគអេដស៍
Monitoring antiretroviral therapy

Reducing the use of CD4 and scaling-up VL

NEW

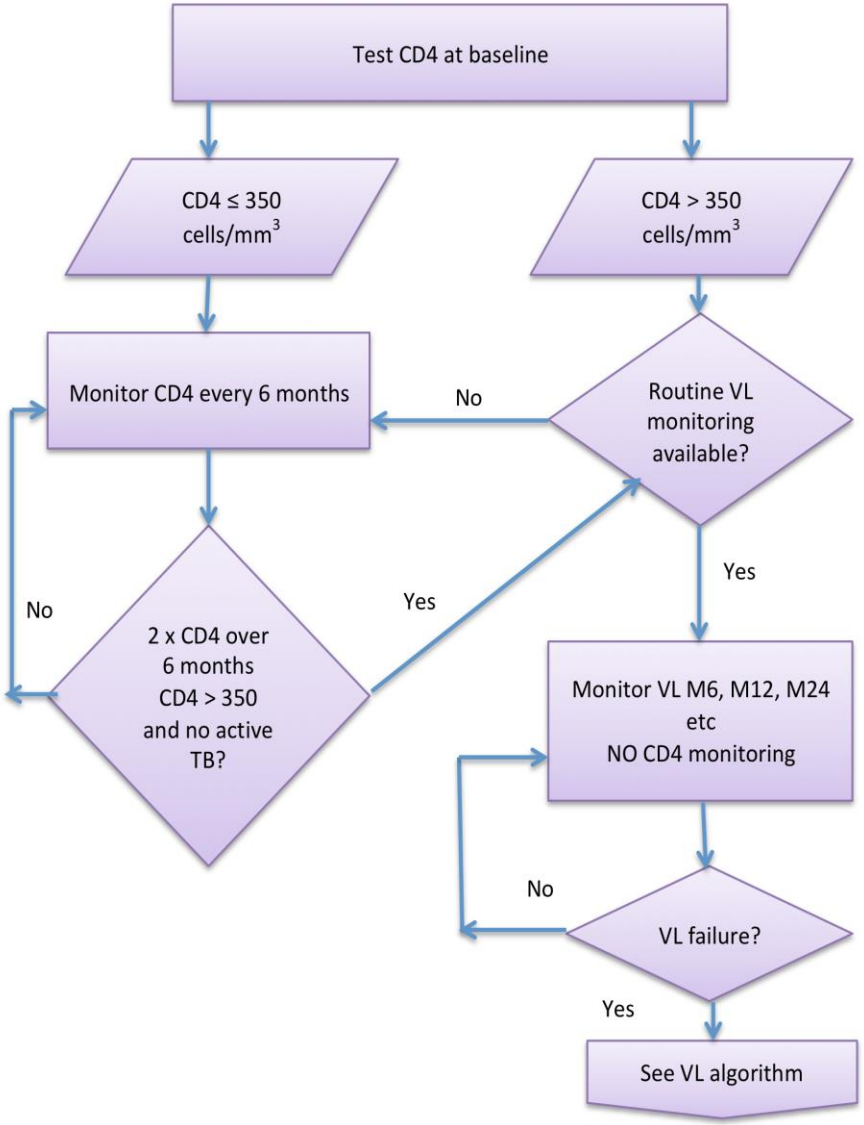
When to start / continue and stop CD4 monitoring ?

Start / continue	Baseline CD4 then 6 monthly until stopping criteria are fulfilled
Criteria to Stop CD4 monitoring*	On ART for at least 1 year *and all of the following:* • No adverse drug reactions requiring regular monitoring, • No current illness, and not on TB treatment • Not pregnant • Good understanding of lifelong adherence • 2 x CD4 > 350 cells/ mm^3 • 2 x undetectable VL • Routine VL monitoring is available
Check CD4 again	Virological failure → recommence CD4 algorithm Pregnancy → recommence algorithm if< 350 +/or VL detectable.

NEW

CD4 testing

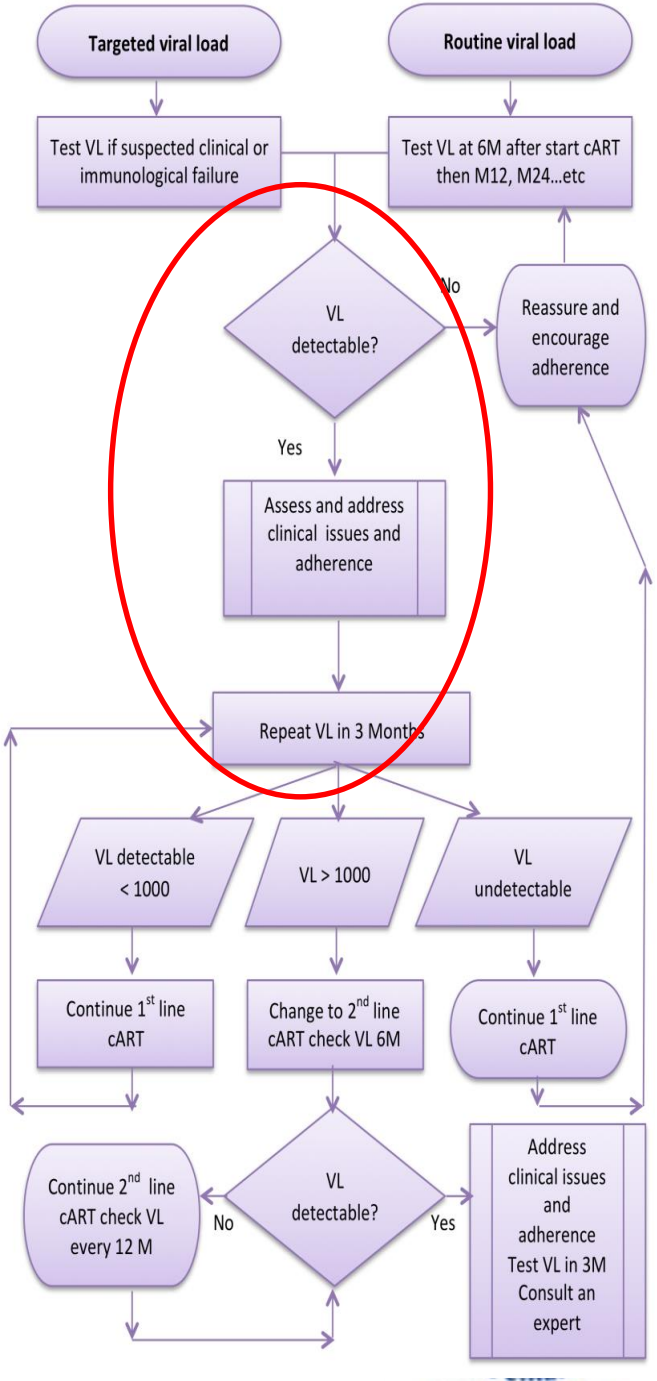
- CD4 at baseline and every 6 M whilst on cotrimoxazole
- If routine VL is available, no need for ongoing routine CD4.
- Repeat CD4 if VL failure confirmed.



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 every12 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



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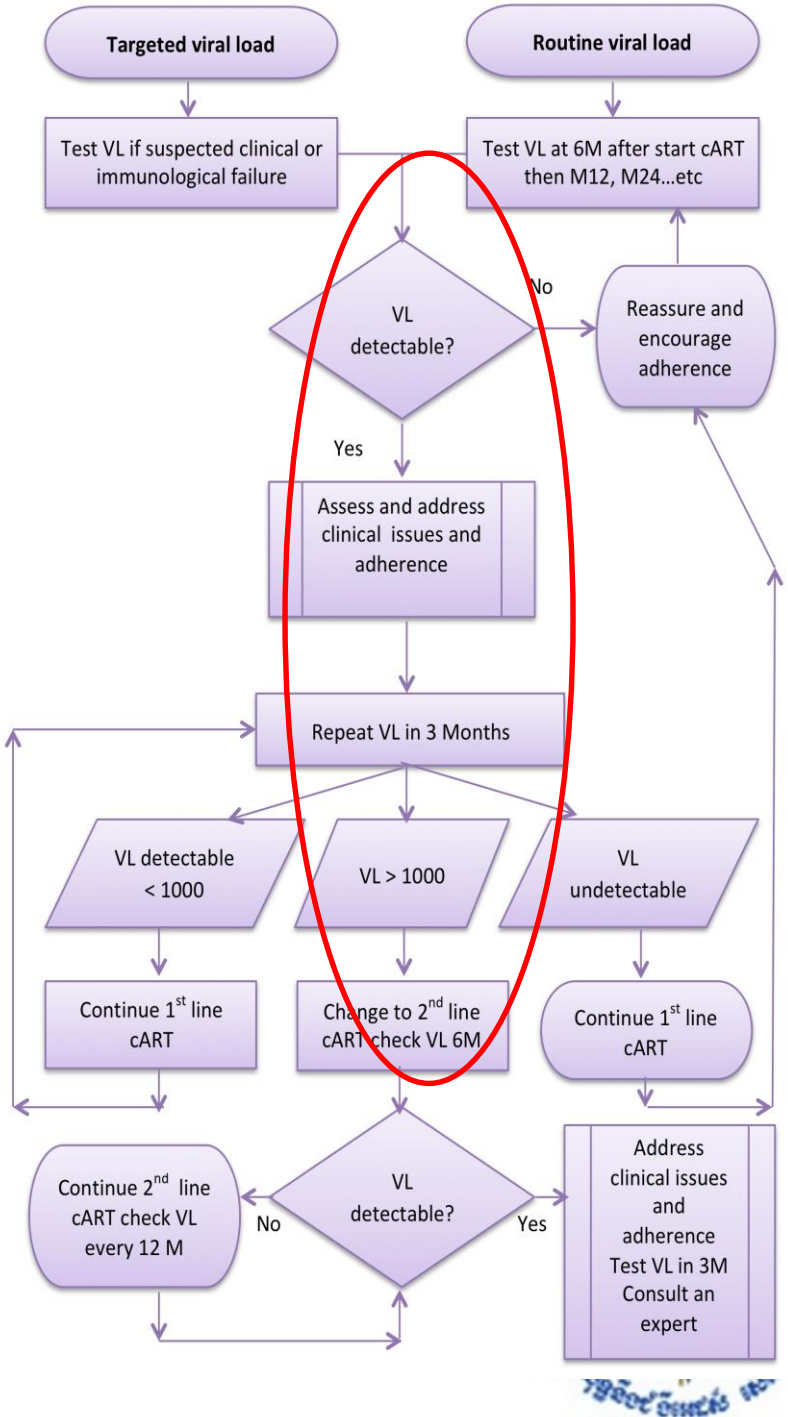
2nd line ART

- Switch to 2nd 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 2nd line regimen



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(2nd line ART)

- Adults and adolescents:

Failed 1st line regimen	➔ Preferred second line
TDF + 3TC + NNRTI	**AZT + 3TC + ATV/r** (if HBsAg negative)
	TDF + 3TC + AZT + ATV/r (if HBsAg positive)
AZT (or d4T) + 3TC + NNRTI	**TDF + 3TC + ATV/r**
If failed 1st line including a PI	Consult an expert

- Children:

	First line	Preferred 2nd line regimen	Alternative 2nd line regimen
Children	ABC/AZT+3TC+LPV/r	No change from first line regimen	AZT (or ABC) +3TC + NVP/EFV$
	ABC/AZT+3TC+EFV or NVP	AZT (or ABC) + 3TC + LPV/r *	TDF+ 3TC + LPV/r *
Adolescents (>10-19 y)	TDF/AZT+3TC+EFV	AZT/TDF# + 3TC + ATV/r (if >40kg)*	AZT/TDF + 3TC + LPV/r*

Clinic visit routine schedule

Week	Clinical	Adherence counseling	Laboratory testing	Drugs start /Stop
Week 0	✔	✔	✔	Start Cotrimoxazole
Week 1		✔		
Week 2	✔	✔		Start cART Stop Cotrimoxazole if CD4 > 350 and no TB
After start ART				
Week 2	✔	✔		Start IPT
Month 1	✔	✔	✔	
Every 1 M whilst on IPT	✔	✔	✔ VL at month $_{5}6_{7}$	Stop IPT after 6 months
After stop IPT, still on Cotrimoxazole				
Every 1 – 3 months (According to clinical status, + adherence)	✔	✔	✔ VL at M $_{5}6_{7}$ then M $_{11}12_{13}$, M $_{23}24_{25}$ etc ✔ CD4 every $_{5}6_{7}$ M	Stop Cotrimoxazole according to criteria (see **Error! Reference source not found.** page 34)
After stop Cotrimoxazole				
Every 1 – 3 months	✔	✔	✔ VL at every $_{11}12_{13}$ Months	

ការបង្ការការចម្លងពីម្តាយទៅកូន : តើមានអ្វីថ្មី?
(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 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) .

NEW

ការបង្ការការចម្លងពីម្តាយទៅកូន : តើមានអ្វីថ្មី?
(PMTCT: What´s new?)

Mother	Risk Status of HIV Exposed Infant HIV	Infant feeding status	Infa prophylax NEW
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 *or*** 2. ***Mother diagnosed HIV positive at delivery or during post 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***	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**
	Low Risk situations: Not fall in the high risk situations.	Breast feeding or formula feeding	**NVP for 6 weeks**

ការបង្ការការចម្លងពីម្តាយទៅកូន : តើមានអ្វីថ្មី?
(PMTCT: What´s new?)

Breastfeeding:

NEW

- **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.**

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Co-morbidities

Dr. Chel Sarim
Dr. Deng Serongkea

មជ្ឈមណ្ឌលជាតិប្រយុទ្ធនឹងជំងឺអេដស៍ សើស្បែក និងកាមរោគ

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Chronic non- communicable diseases in PLHIV

Dr. Chel Sarim

FHI 360

National HIV clinical management guidelines for Adults and Adolescents

4th Revision in 2015

Table of content

- 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.

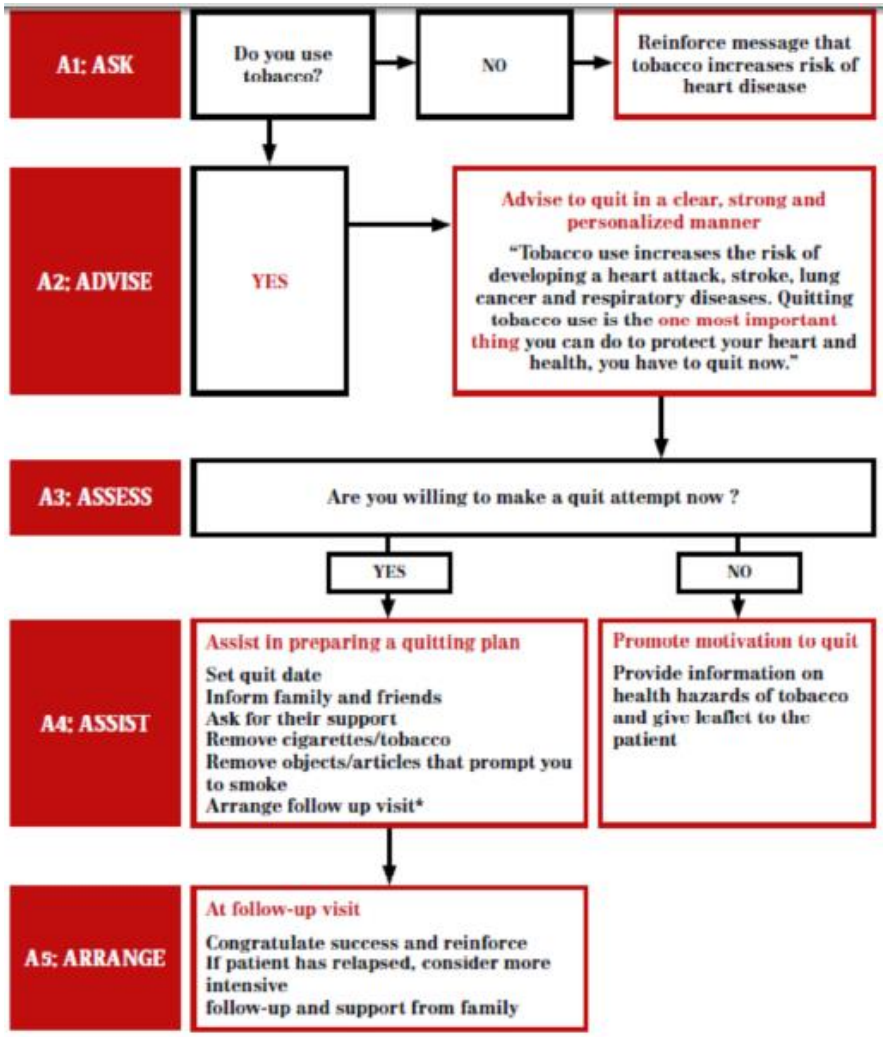
Recommendations for prevention and management of NCD

Table 34-1 Recommendations for prevention and management of NCD

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.
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



* 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 (Cont.)

- 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 (Cont.)

- 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
      - Renal disease – serum creatinine, potassium, sodium. Urinalysis.

Hypertension (Cont.)

- Pharmacological management

Table 36-1 Cambodian guidelines for commencement of antihypertensive medicine

Hypertensive Patient	Initiate pharmacologic treatment	BP goal
≥ 60 years*	SBP ≥ 150 mm Hg or DBP ≥ 90 mm Hg	SBP < 150 mm Hg and DBP < 90 mm Hg
< 60 years		
18-59 years	SBP ≥ 140 mm Hg	SBP < 140 mm Hg
	DBP ≥ 90 mm Hg	DBP < 90 mm Hg
≥ 18 years with		
CKD or/and Diabetes	SBP ≥ 140 mm Hg or DBP ≥ 90 mm Hg	SBP < 140 mm Hg and DBP < 90 mm Hg

Hypertension (Cont.)

- 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)

Hypertension (Cont.)

❑ Drug interactions with antihypertensive

Table 36-2 Antihypertensive drug interactions with ARV

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

Type 2 Diabetes

- Screening for Diabetes in PLHIV
  - Overweight (BMI>23, +/or 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.

Type 2 Diabetes (Cont.)

- Diagnosis of Type 2 Diabetes and impaired glucose tolerance

WHO diagnostic criteria for diabetes

	Glucose concentration, mmol/l (mg/dl)		
	Whole blood		Plasma venous
	Venous	Capillary	
Diabetes mellitus			
Fasting	≥ 6.1 (110)	≥ 6.1 (110)	≥ 7.0 (126)
or			
2-hour post glucose load	≥ 10.0 (180)	≥ 11.1 (200)	≥ 11.1 (200)
or both			
Impaired glucose tolerance			
Fasting concentration (if measured)	≤ 6.1 (110)	≤ 6.1 (110)	≤ 7.1 (126)
and			
2 hours after glucose load	6.7-9.9 (120-179)	7.8-11.0 (140-199)	7.8-11.0 (140-199)
Fasting hyperglycaemia			
Fasting	5.6-6.0 (100-109)	5.6-6.0 (100-109)	6.1-6.9 (110-125)
2 hours (if measured)	≤ 6.7 (120)	≤ 7.8 (140)	≤ 7.8 (140)

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.

Type 2 Diabetes (Cont.)

- 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 37-2 Diabetes drug interactions with ARV

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

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.

Hyperlipidaemia (Cont.)

- 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.

Hyperlipidaemia (Cont.)

- 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

Hyperlipidaemia (Cont .)

- 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

Hyperlipidaemia (Cont .)

- Drug interactions between lipid lowering medications and ART

Table 38-1 Lipid lowering drugs interactions with each other and ARV

Statins
• **Simvastatin and lovastatin are *contraindicated* with PI** containing ART as there is a high risk of rhabdomyolysis.
• Other statins may be used with PI containing ART but at lower doses:
  • Atorvastatin start 10mg → max dose with PI ART = 40mg
  • Pravastatin start 20mg → max dose with PI ART = 40mg
  • Rosuvastatin start 5mg → max dose with PI ART = 20mg

• **Fibrates**
  • Gemfibrozil :
  • Drug levels may be lowered by PI ART
  • Do not use in combination with a statin due to the risk of myositis
  • Fenofibrate
  • Monitor ALT/CK if in combination with statins due to increased risk of side effects

• **Fish oils** are not known to have interaction with ART

Hyperlipidaemia (Cont .)

- 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

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NATIONAL CENTER FOR HIV/AIDS, DERMATOLOGY AND STD

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NATIONAL CENTER FOR HIV/AIDS, DERMATOLOGY AND STD

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 of content

- HBV and HCV transmission and prevention,
- HBV and HCV diagnosis,
- The natural history of HBV and HICV mono-infection,
- The relationship between HIV and HBV & HIV and HCV,
- The management of HIV/HBV and HIV/HCV co-infection,
- The management of complications of chronic liver disease.

Hepatitis B

Epidemiology and burden

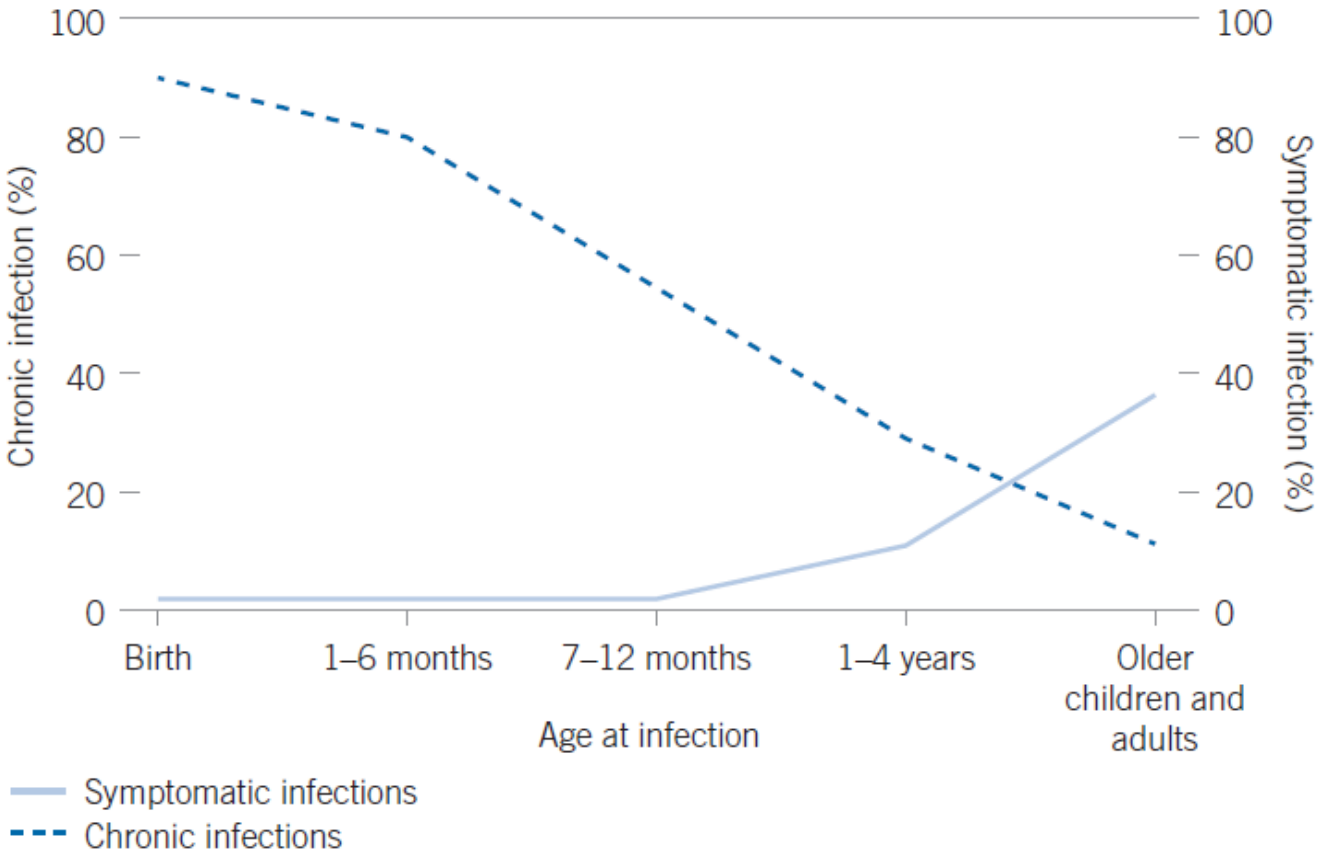
- It is estimated that worldwide, 2 billion people have evidence of past or present infection with HBV, and 240 million are chronic carriers of HBV surface antigen (HBsAg).
- It is estimated that around 650 000 people die each year from the complications of CHB.
- Overall, HBV accounts for around 45% 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.

Epidemiology and burden (Cont.)

- 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.

Epidemiology and burden (Cont.)

- 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

- 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)

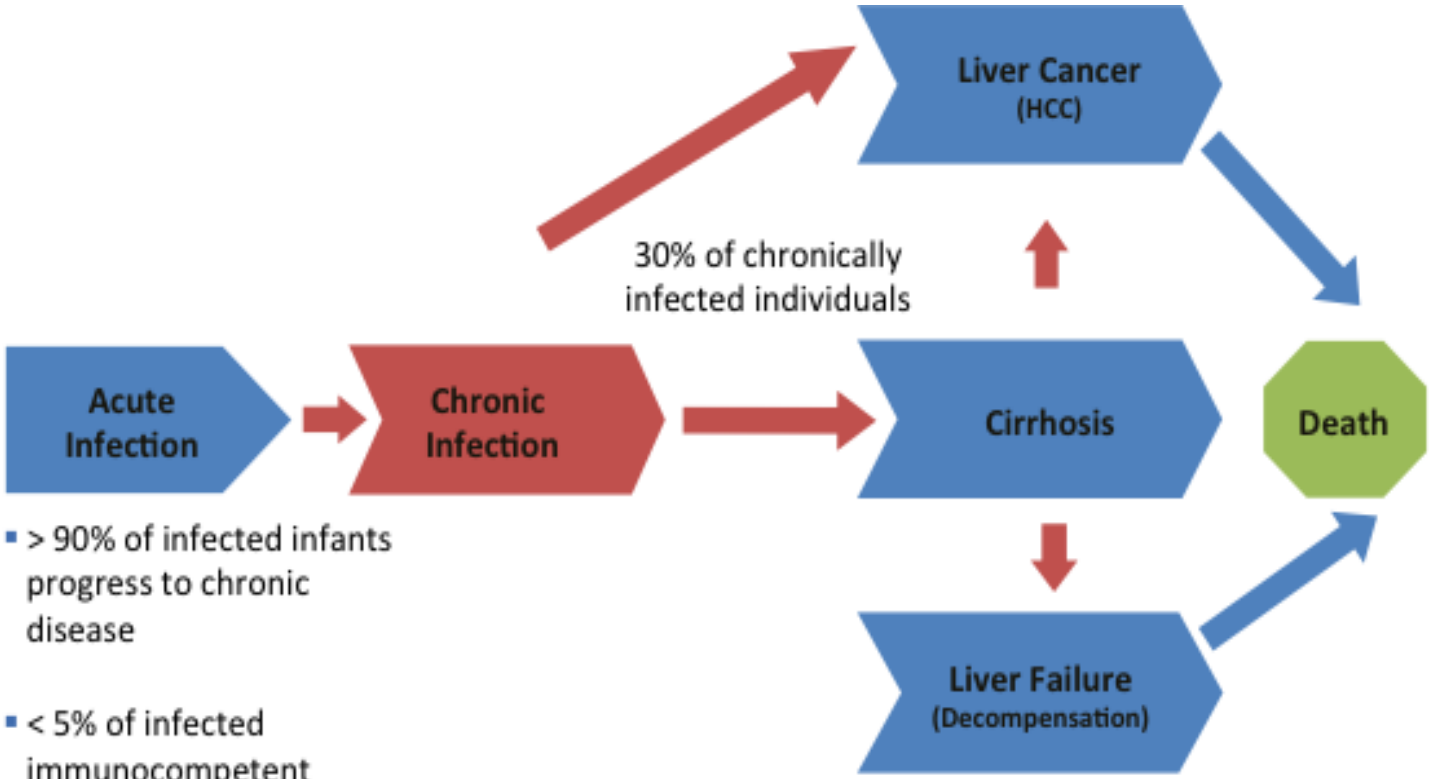
Prevention of Hepatitis B transmission

- 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



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

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.

Population at increased risk of HCV infection

Population	Comment
Persons who inject drugs (PWID) *(19)*	PWID have the highest risk of infection. Globally, the prevalence of anti-HCV antibody is 67% among PWID.
Recipients of infected blood products or invasive procedures in health-care facilities with inadequate infection control practices *(20–30)*	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)*.
Children born to mothers infected with HCV *(30, 32–35)*	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.
People with sexual partners who are HCV infected *(36–40)*	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.
People with HIV infection *(40–48)*	Persons with HIV infection, in particular MSM, are at increased risk of HCV infection through unprotected sex.
People who use intranasal drugs *(49)*	Non-injecting drug use (e.g. through sharing of inhalation equipment for cocaine) is associated with a higher risk of HCV infection.
People who have had tattoos or piercings *(50)*	Tattoo recipients have higher prevalence of HCV compared with persons without tattoos (odds ratio = 2.24, 95%CI 2.01, 2.50)

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

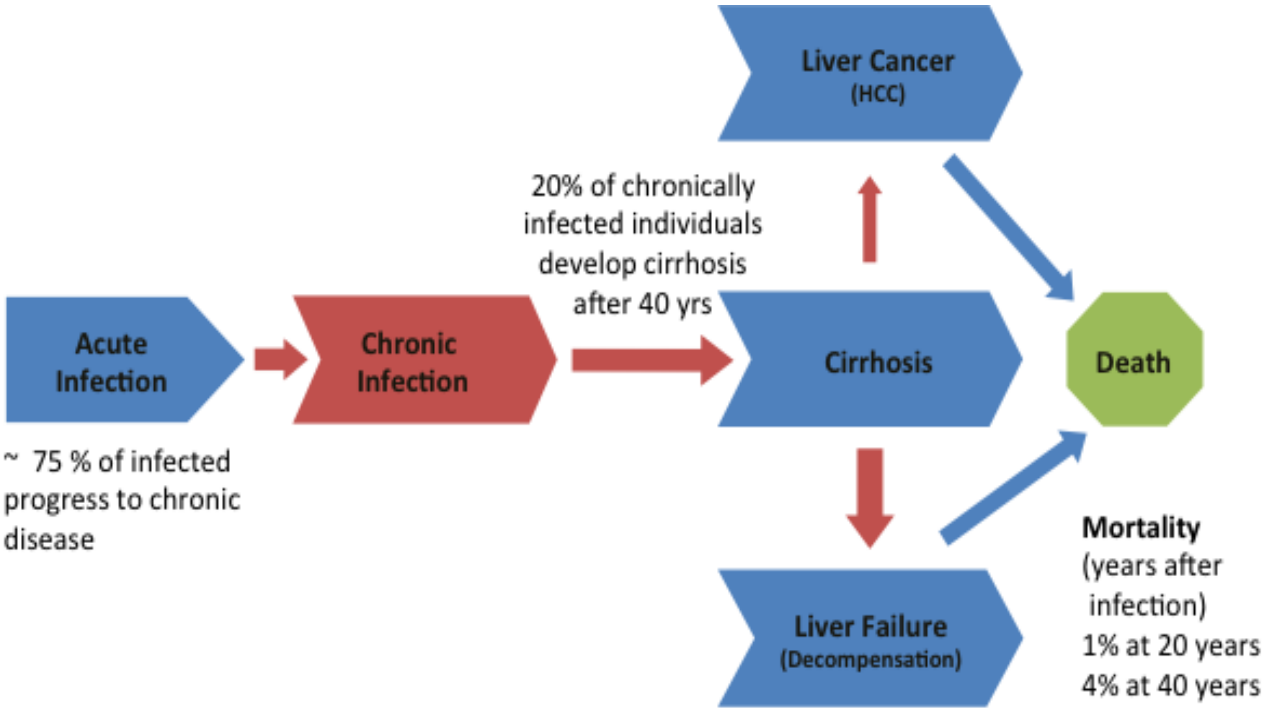
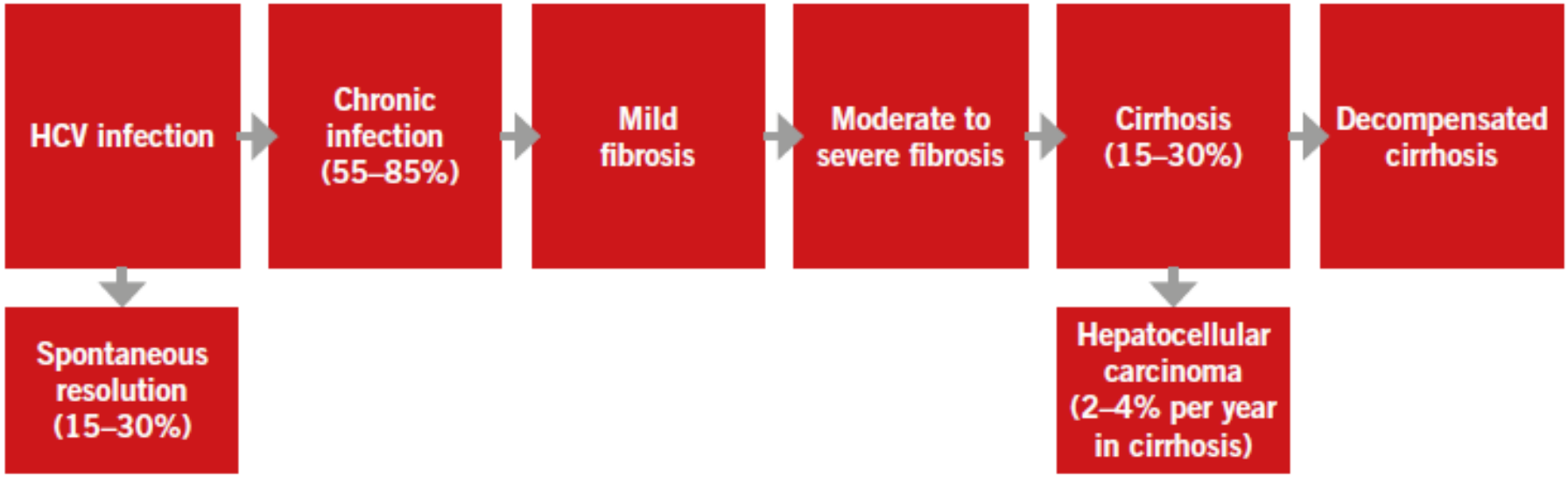


FIGURE 2.2 Natural history of HCV infection



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 manifestation.
- 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 benefit:**
    - **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

_ *evaluate the readiness for transition:* See (ANNEX 11, Child Well-Being Assessment Tool)- National ART Pediatric Guidelines 2016.

_ *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-Organizational 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.

2-Psychosocial support _(cont.)

- **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.

3-Reproduction and sexual health

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

Clinical issues regarding Adolescent HIV care

- WHO clinical staging for adolescents ≥ 15 years is the same as adults, and for < 15 years is the same as paediatrics.
- Initiation of ART in adolescents; same as adults
- ART regimen for adolescents ≥ 35kg is the same as for adults, for <35 kg is same as for children.
- NCD: ALHIV who had perinatal transmission are at risk of long term ART toxicity and metabolic complications of HIV (e.g. hyperlipidaemia)
- OI prophylaxis:
- Cotrimoxazole is prescribed routinely for all adolescents, and once they become an adult at age 20, the same stopping rules apply as to adult.
- TB screening and criteria for IPT are the same for adolescents as adults.
- Cryptococcal screening is also the same for adolescents as adults

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!

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NATIONAL CENTER FOR HIV/AIDS, DERMATOLOGY AND STD

កិច្ចប្រជុំផ្សព្វផ្សាយគោលការណ៍ណែនាំជាតិ ស្តីពី ការថែទាំ-ព្យាបាលជំងឺឱកាសនិយម និង ការព្យាបាលដោយឱសថប្រឆាំងមេរោគអេដស៍ សំរាប់ មនុស្សពេញវ័យ ក្មេងជំទង់ និង កុមារ

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NATIONAL CENTER FOR HIV/AIDS, DERMATOLOGY AND STD

Universal Precautions and Post-Exposure Prophylaxis

Dr. Deng Serongkea
World Health Organization

Content

- 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)

New

_Health care staff
_ Raped Victims /sexual assault of GBV
_ Sexual exposure of discordant couple prior to VL Suppress

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 regiments
- Consent based and fully understand of risk and benefits

PEP Regiment for Adult

New

-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

New

Age	Preferred Treatment Regimen	Duration
Children <10 years <35Kg	ABC or AZT +3TC +LPV/r	28 Days
Adolescents >10 years AND >35kg	TDF or ABC or AZT + 3TC + LPV/r or ATV/r	

Post Exposure Prophylaxis Care Pathway

43.5 Post Exposure Prophylaxis Care Pathway

- **Assessment and immediate management**
  (Table 50-1 NCHADS PEP Clinic visits and reporting form)

➢ **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

- **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

- **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 4 days

Baseline test for source and Exposed person(*):

- **HBsAg,**
- **HCV antibody**
- **HIV antibody**

And if Source is HIV positive ,further information 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 [63]**

  - See also NCHADS STI guidelines which detail management of sexual assault[64]

- **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.***

New

What if, the source person is unknown HIV status ?

Calculation: **Risk of HIV transmission = Risk per exposure X 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%)** x 0.6% = 0.0014%

-The risk to a man who experienced **condom breakage during vaginal sex** with ***an entertainment worker*** = **1/2500** x ***13.9%*** = 0.0056%

-The risk to a woman who is vaginally and anally raped by a PWUD (1/1250 x 4.4%)+ (1/70 x 4.4%) = 0.0035% + 0.06% = 0.07%

-The risk to a woman who is vaginally raped by 5 PWUD = 5 x 1/1250 x 4.4% = 0.018%

Assess of estimated risk of HIV transmission per episode from HIV infected sources

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

Reference : HIV prevalence in Cambodia

Table 43-2 Cambodian HIV prevalence estimates by demographic

Population / subpopulation	Prevalence
General adult population	0.6%
Injecting drug users (PWID)	24.8%
Non injecting drug users (PWUD)	4.4%
Entertainment worker (>7 sex partners/week)	13.9%
Transgender M→ F	9.8%
MSM	2.3%

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.*

For Your Information, elaborated from Clinical hand book GBV ,MoH 2015)

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)

For Your Information, elaborated from Clinical hand book GBV ,MoH 2015)

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.

. Teat 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 hand book GBV ,MoH 2015)

Additional care for physical & mental health after sexual assault victim of Gender Based Violence _(cont.)

Hepatitis B:

Has she been vaccinated for hepatitis B?	
Immunization status	Treatment guidelines
No, never vaccinated for hepatitis B	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.
Started but has not yet completed a series of hepatitis B vaccinations	Complete the series as scheduled.
Yes, completed series of hepatitis B vaccinations	No need to re-vaccinate.

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

Name _____ Phone no:_____

Sex

DOB ___/___/_____ Clinic number

Age Date of first visit ___/___/_____

Category of exposure	**Timing of exposure**
Occupational ☐	Date of exposure ___/___/_____
Discordant couple ☐	Time of exposure
Victim of sexual assault ☐	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_____Unknown____

Date commenced ART ___/___/_____

Most recent VL result_____ Date___/___/_____:

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___ Date ___/___/_____

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___UK____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:

Source HBV+ Yes___ No___ Unknown____ Recipient? Yes___ No___ Unknown____

Source HCV+ Yes___ No___ UK____ Recipient? Yes___ No___ Unknown____

Tetanus vaccination indicated? Yes___ No___ given? ☐

Explained 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

មជ្ឈមណ្ឌលជាតិប្រយុទ្ធនឹងជំងឺអេដស៍ សើស្បែក និងកាមរោគ

NATIONAL CENTER FOR HIV/AIDS, DERMATOLOGY AND STD

កិច្ចប្រជុំផ្សព្វផ្សាយគោលការណ៍ណែនាំជាតិ ស្តីពី ការថែទាំ-ព្យាបាលជំងឺឱកាសនិយម និង ការព្យាបាលដោយឱសថប្រឆាំងមេរោគអេដស៍ សំរាប់ មនុស្សពេញវ័យ ក្មេងជំទង់ និង កុមារ

ថ្ងៃទី ២៨ ខែ វិច្ឆិកា ឆ្នាំ ២០១៦

Test and Treat Roll-Out Schedule

Mr. Prum Mardi
NCHADS Logistics Management Unit

Background

- **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

	Jan	Feb	Mar	Apr	May	June	July	Aug	Sept	Oct	Nov	Dec
Group 1 Provinces	•			•			•			•		
Group 2 Provinces		•			•			•			•	
Group 3 Provinces			•			•			•			•

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

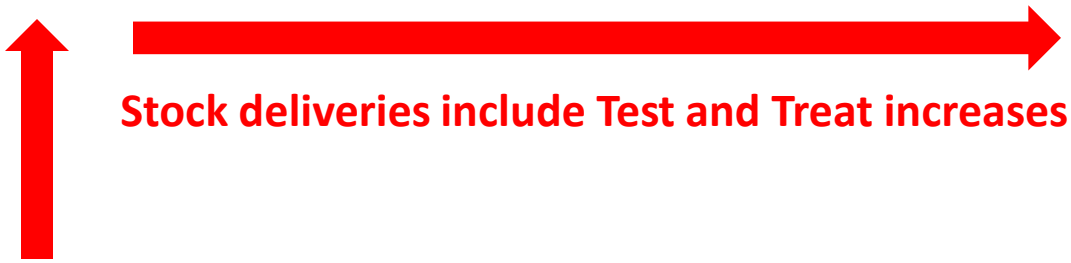
GROUP 3: Prey Veng, Takeo, Kratie, Preah Vihear, Mondulkiri

Cambodia National ARV Distribution Schedule

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

	2016			2017								
	Oct	Nov	Dec	Jan	Feb	Mar	Apr	May	June	July	Aug	Sept
Group 1 Provinces	•			•			•			•		
Group 2 Provinces		•			•			•			•	
Group 3 Provinces			•			•			•			•



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.

	Begin Test and Treat	Next ARV Delivery
Group 1 Sites	December 2016	January 2017
Group 2 Sites	January 2017	February 2017
Group 3 Sites	December 2016	December 2016

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

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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.

	Begin Test and Treat	Next ARV Delivery
Group 1 Sites	December 2016	January 2017
Group 2 Sites	January 2017	February 2017
Group 3 Sites	December 2016	December 2016

"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**

Summary: Test and Treat Rollout

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.

	Begin Test and Treat	Next ARV Delivery
Group 1 Sites	December 2016	January 2017
Group 2 Sites	January 2017	February 2017
Group 3 Sites	December 2016	December 2016

Provinces by Group

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

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