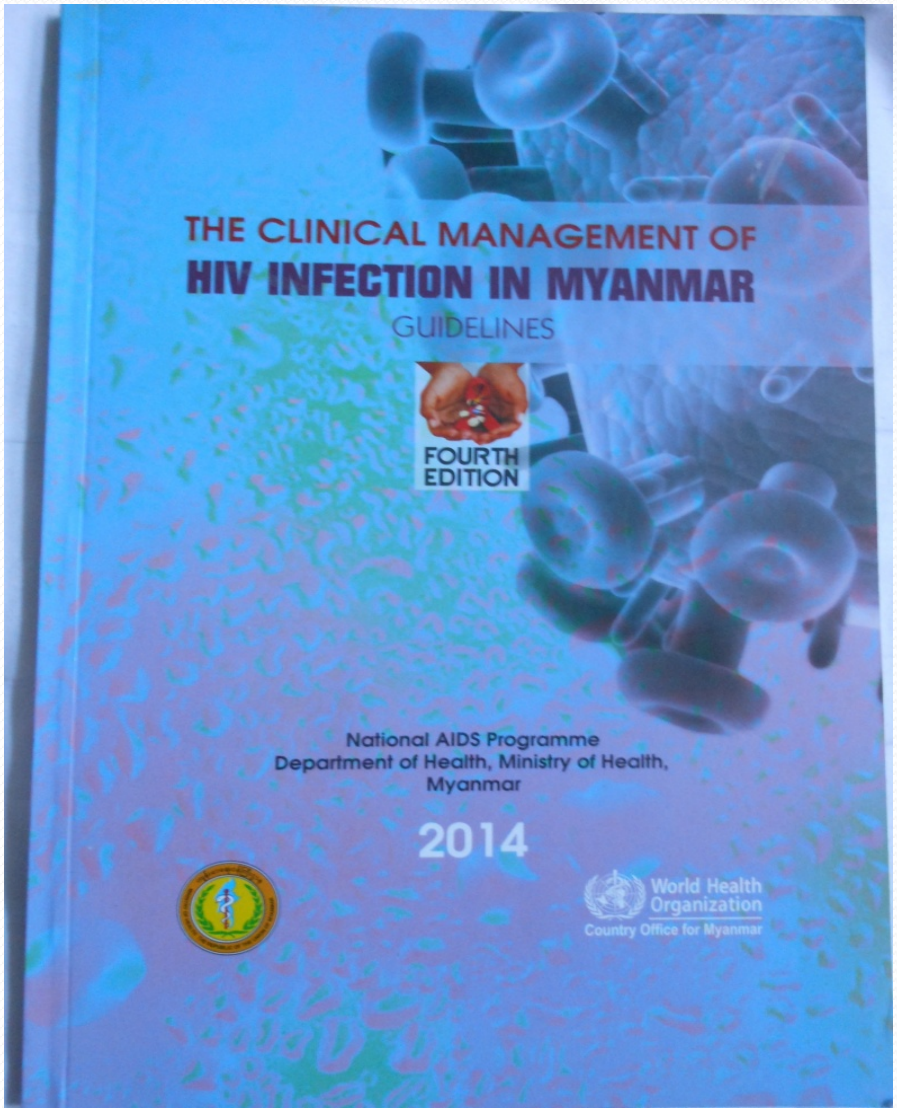
Dr. Ohnmar Mon
M.B.,B.S M. Med.Sc (Pediatrics)
Diploma in management
of HIV infection (France)
Consultant Pediatrician (Junior)

Myanmar ART Guideline

- In Myanmar
- •First HIV positive case reported : 1988
- •First AIDS case reported : 1991
- •ART Provision was started in 2005
- ART provision for Pediatrics HIV was started since 2006 (Mandalay Children ‘s Hospital)

3rd edition of guideline (2010)

Current Treatment Guideline



LISTS OF PRESENTATION

- • Pediatric HIV; Magnitude of problems
- • Myanmar HIV Estimation
- • Clinical Management of HIV in children
- • PEDIATRIC HIV Program at Mandalay Children Hospital

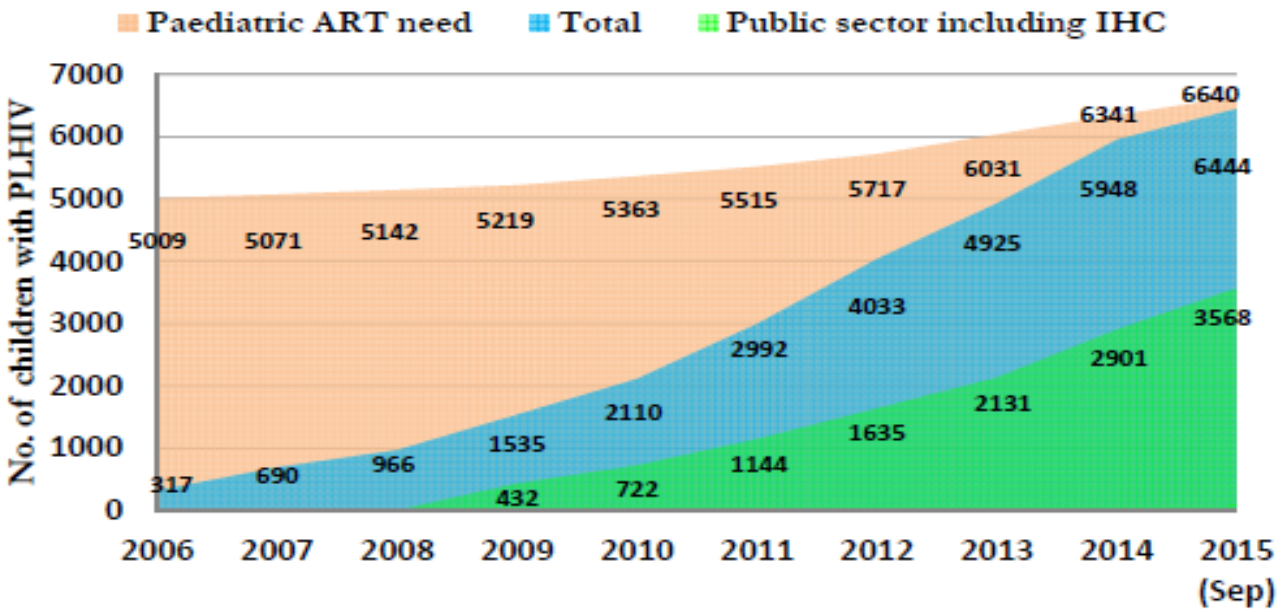
Pediatric HIV : Magnitude of problem

- HIV/AIDS is worldwide health problem in the present day with 36.9 million people infected globally.• Among them 3 million are <15 yrs of age (UNAIDS, 2015)
- Children <15 yrs who are newly infected with HIV in 2015 were 220,000 & the total figure of death in 2015 was 1.2million.
- Over 90% of HIV seropositive patients live in developing world. In Pacific & Asia region, the total figure of adult &children living with HIV is 5 million that is >10% of world HIV population.(UNAIDS,2015)

Myanmar Pediatric HIV Estimation (0-14 years)

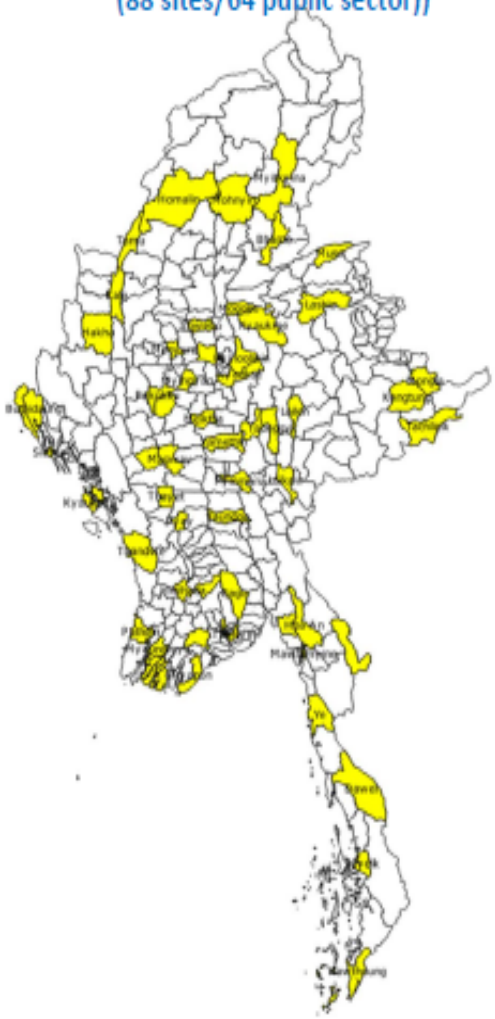
Spectrum	2015	2016	2017
HIV INFECTION	11230	11077	10844
ART NEED	6640	6895	7081

Paediatric ART provision
(Public sector Vs National figure)

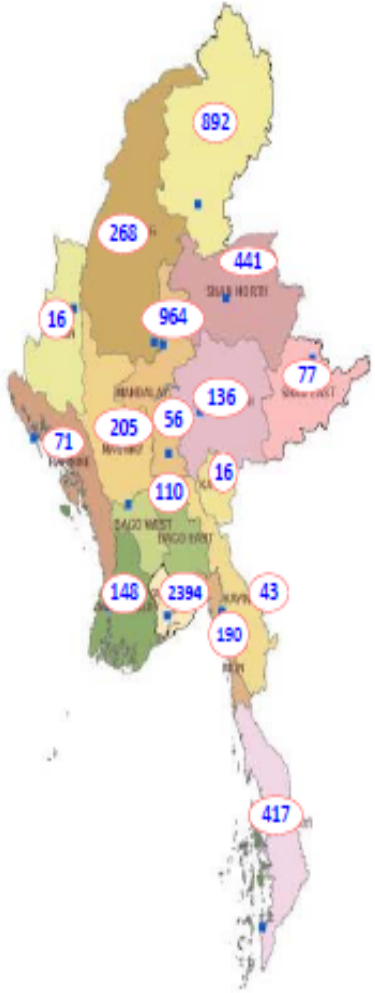


Paediatric ART (Sep 2015)

Service delivery points
(88 sites/64 public sector))



Total (6,444)



PMTCT

PMCT Program

Milestones (PMCT)

- Initiated as Pilot project in 2001 as community based approach
- Expanding yearly and as of (2013) :
  - community based in (256) townships
  - hospital based in (38) hospitals
  - Strategic shift and refocusing
  - **Now , mainly Township based**

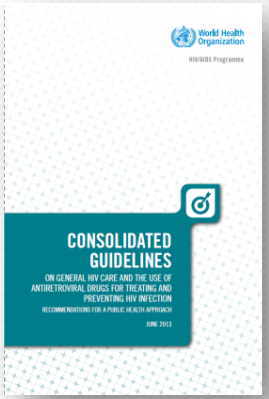
Evolution of WHO 2013 PMTCT ARV Recommendations

2001

2004

2006

2010



Launch July 2013

PMTCT	4 weeks AZT; AZT+ 3TC, or SD NVP	AZT from 28 wks + SD NVP	AZT from 28wks + sdNVP +AZT/ 3TC 7days	**Option A** (AZT +infant NVP) **Option B** (triple ARVs)	**Option B or B +** Moving to ART for all PW/BF
ART	No recommendation	CD4 <200	CD4 <200	CD4 ≤350	CD4 ≤500

Move towards: more effective ARV drugs, extending coverage throughout MTCT risk period, and ART for the mother's health

Challenges in PMCT

Counselling and Testing of HIV infection

- should be voluntary and adhere to the five C's:

  Consent

  Confidentiality

  Counselling –couple counselling with support for mutual disclosure

  Correct test results –If HIV test is negative at 1st trimester, retest at 3rd trimester

  Connections to care, treatment and prevention services.

****increase uptake of HIV counseling and testing in all pregnant women in ANC settings and especially in rural area ****

PMCT

- ***Following Option B is norm in Myanmar***

  ARV prophylaxis for pregnant women who do not need treatment for their own health
- CD4 more then 500/cmm and WHO stage 1 or 2
- When to start ARV prophylaxis:
  - As early as 14 weeks of pregnancy
  - *Prophylaxis regimens for the mother: TDF+3TC (FTC) + EFV or alternate first line*
  - ***Option B***: - continue ARV till 1 week after cessation of breast feeding

PMCT

- *Option B plus*: Do not stop ARV to mother.
- *Option B plus can be considered*
- Areas with high prevalence of HIV
- Remote areas, hard to reach areas
- Availability of ART center (as ART initiation will happen at ART centers)
- Depending on patients' choice, consent, ability for regular follow up and adherence counseling.

Challenges in PMCT

ART for PMCT

- Pregnant mothers who are on ART already have their treatment continued after checking the VL which should be undetectable and if necessary the ART is changed .
- If the viral load is < 1000 copies/ml vaginal delivery can be allowed as the transmission rate of HIV to the infant becomes very low

** Limitation in checking VL and lacking drug resistant testing**

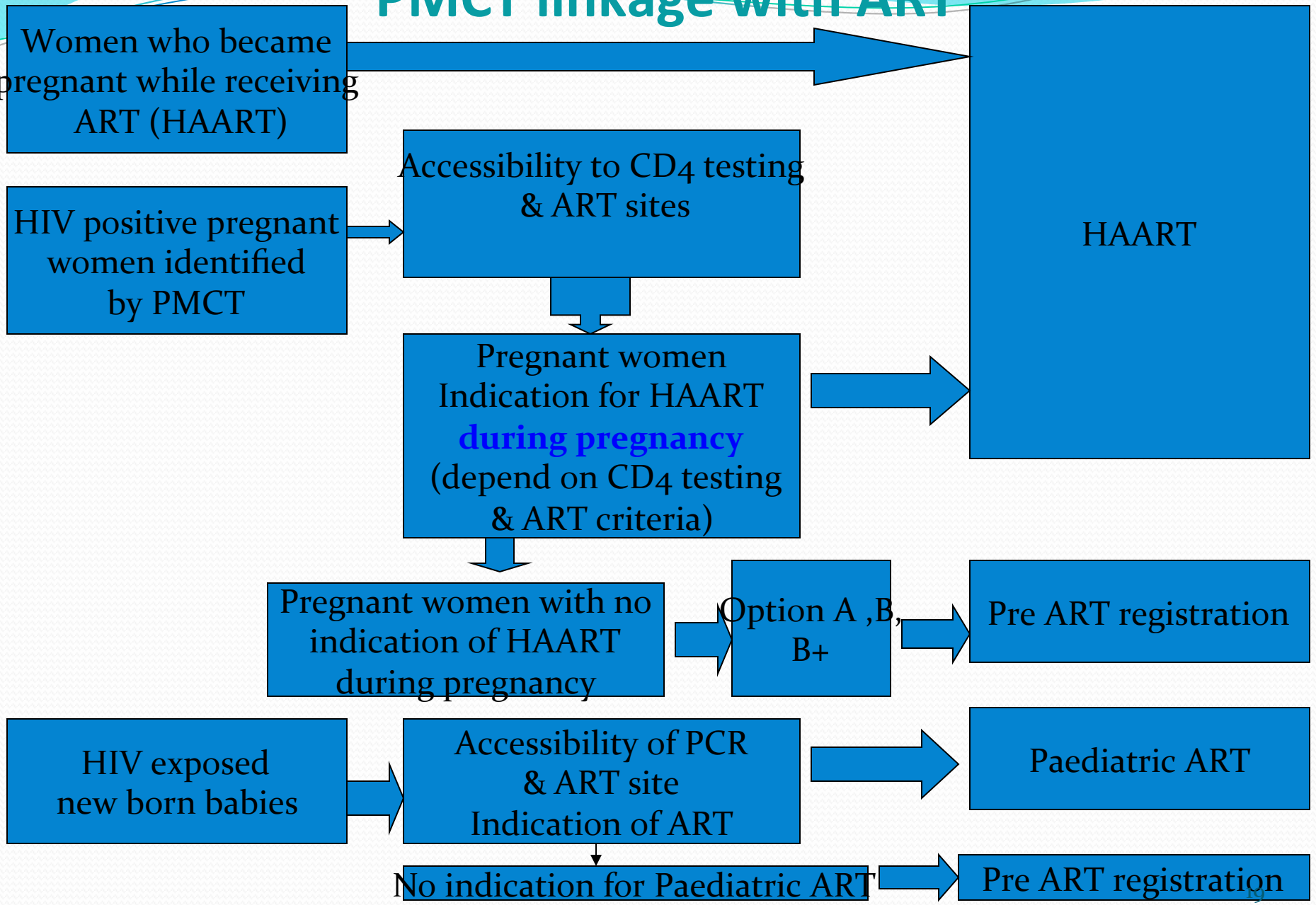
Challenges in PMCT

Care and management of pregnant women

- regular follow up antenatal visits and pregnancy care,
- nutritional support and infant feeding counselling – Mainly breast feeding
- family planning counselling

** loss to follow up and home delivery and failure to get infant prophylaxis **

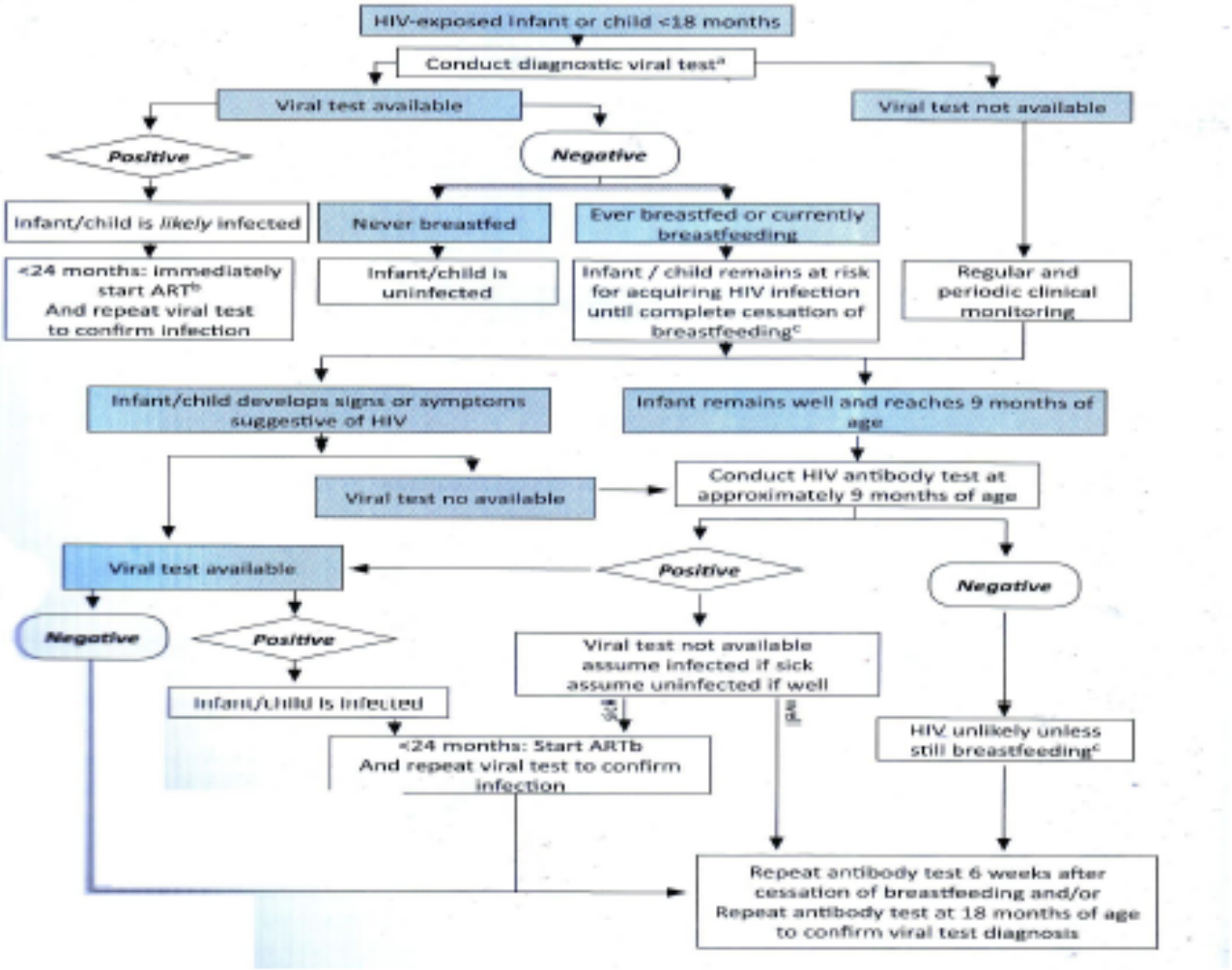
PMCT linkage with ART



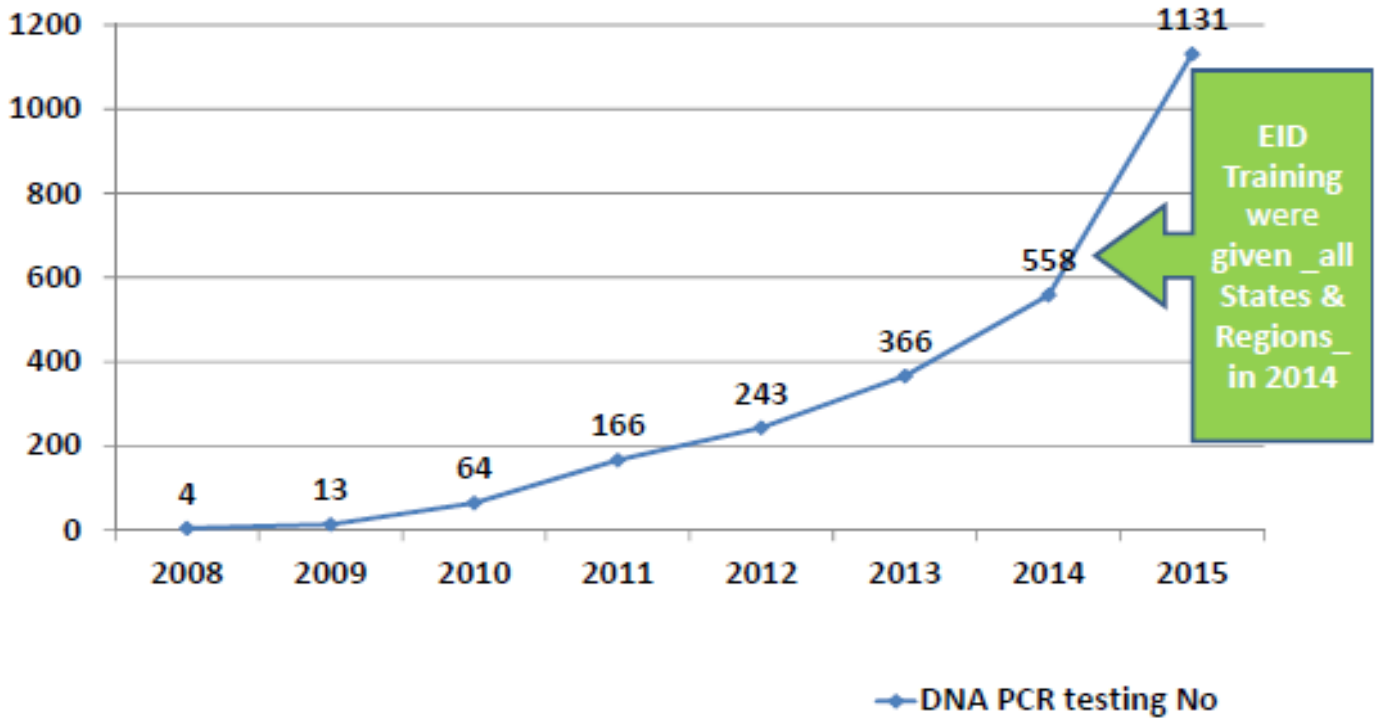
Early Infant Diagnosis (EID)

- Dried blood spots tests (DNA PCR) All HIV exposed infants have HIV Virological testing at 4-6 weeks of age or at the earliest opportunity
- • National Health Laboratory
- • 2009
- • All PMCT hospital ART sites ,PMCT sites (INGO)

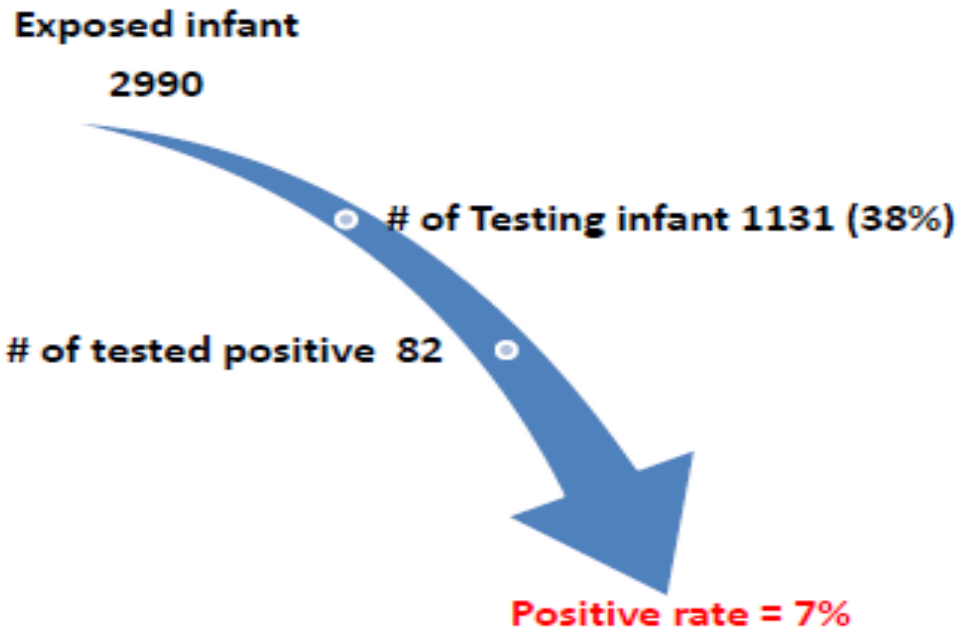
Figure 2:Algorithm for early infant diagnosis



Early Infant Diagnosis Achievement in Myanmar (2008 to Nov 2015)



Exposed infant vs EID status (Jan to Nov 2015)(Myanmar)

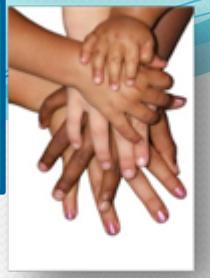


Maintain the healthy and happy life style

GOAL of treatment of comprehensive HIV infection


ART IN CHILDREN


When to start



AGE GROUP	2010 RECOMMENDATIONS
<1 YEARS	**Treat ALL** Strong recommendation, moderate-quality evidence
1-2 YEARS	**Treat ALL** Conditional recommendation, very-low-quality evidence
2-5 YEARS	**Initiate ART with CD4 count ⩽750 cells/mm3 or <25%,** irrespective of WHO clinical stage
≥5 YEARS	**Initiate ART with CD4 count ⩽350 cells/mm3 (As in adults),** irrespective of WHO clinical stage AND WHO clinical stage 3 or 4

AGE GROUP	2013 RECOMMENDATIONS
< 1 YEAR	Treat ALL Strong recommendation, moderate-quality evidence
1-5 YEARS	Treat ALL Conditional recommendation, very-low-quality evidence Priority: children < 2 years or WHO stage 3-4 or CD4 count ≤ 750 cells/mm3 or < 25%
≥5 YEARS	CD4 ≤ 500 cells/mm3 Conditional recommendation, very-low-quality evidence CD4 ≤350 cells/mm³ as a priority (As in Adults) Strong recommendation, moderate-quality evidence

Classes of ARVs – clinical practice

NRTI	PI	NNRTI	Fusion inhibitors	Entry inhibitors	INSTI
Zidovudine	Saquinavir	Nevirapine	Enfuvirtide	Maraviroc	Raltegravir
Didanosine	Ritonavir	Delavirdine			
Stavudine	Indinavir	Efavirenz			
Lamivudine	Nelfinavir	Etravirine			
Abacavir	Lopinavir/r	Rilpivirine			
Tenofovir	Atazanavir				
Emtricitabine	Fosamprenavir				
	Tipranavir				
	Darunavir				

WHAT ART REGIMEN TO START

Table 5: Summary of first-line ART regimens for children younger than three years

Preferred	ABC[a] or AZT + 3TC + LPV/r[b]
Alternative	ABC[a] or AZT + 3TC + NVP
Special circumstances	d4T[c] + 3TC + LPV/r d4T[c] + 3TC + NVP

Table 6: Summary of recommended first-line ART regimens for children and adolescents

	Children 3 to 10 years or Adolescents <35 kg	Adolescents (10 to 19 years) ≥35 kg
Preferred	ABC[a] + 3TC + EFV	TDF + 3TC (or FTC) + EFV[a]
Alternatives	ABC + 3TC + NVP AZT + 3TC + EFV AZT + 3TC + NVP TDF + 3TC (or FTC) + EFV TDF + 3TC (or FTC) + NVP	AZT + 3TC + EFV AZT + 3TC + NVP TDF + 3TC (or FTC) + NVP
Special circumstances	d4T[b] + 3TC + EFV d4T[b] + 3TC + NVP	ABC + 3TC + EFV ABC + 3TC + NVP

IMPORTANT CLINICAL SIGNS OF ART FAILURE

- Lack of growth response to treatment
- Falling of the growth curve in children who show an initial growth response to therapy
- Loss of neuro-developmental milestones(regression)
- Recurrent oral thrush other OIs

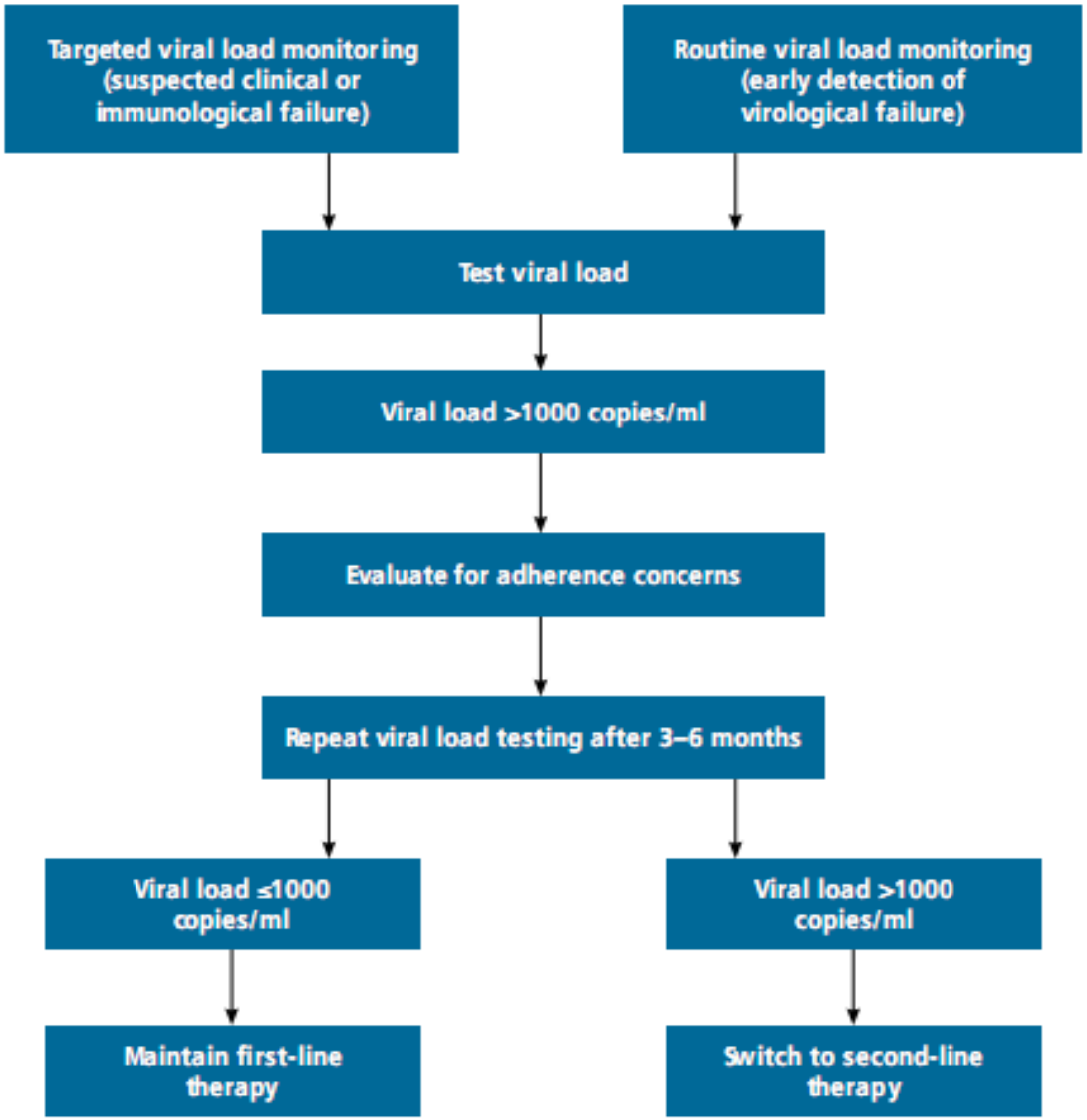
ART switching criteria

Failure	Definition	Comments
Clinical failure	New or recurrent WHO stage 4 condition	Differentiate fr IRIS; certain stage 3 contitions e. pulm TB, severe bacterial conditions may be due to treatment failure
Immunololgical failure	Fall of CD4 to baseline or below or 50% fall from on-treatment peak or persistent CD4<100	Without concomitant infection to cause transient CD4 cell decrease
Virological failure	Plasma viral load > 1000 copies/ml on two consecutive month viral load measurement with adherence support	Optimal VL threshold not determined

We Need Virological Monitoring

- VIROLOGICAL FAILURE
- IMMUNOLOGICAL FAILURE
- CLINICAL FAILURE

Fig. 7.1 Viral load testing strategies to detect or confirm treatment failure and switch ART regimen in adults, adolescents and children



WHAT ART TO SWITCH TO

Second line ART regimen

Table 7.21 Summary of recommended first- and second-line ART regimens for children (including adolescents)

	Children	First-line ART regimen	Second-line ART regimen
LPV/r-based first-line regimen	Younger than 3 years	ABC + 3TC + LPV/r	No change[a]
		AZT + 3TC + LPV/r	
	3 years and older	ABC + 3TC + LPV/r	AZT + 3TC + EFV
		AZT + 3TC + LPV/r	ABC or TDF[b] + 3TC + EFV
NNRTI-based first-line regimen	All ages	ABC + 3TC + EFV (or NVP)	AZT + 3TC + LPV/r[c]
		TDF[b] + 3TC (or FTC) + EFV (or NVP)	
		AZT + 3TC + EFV (or NVP)	ABC or TDF + 3TC[c] (or FTC) + LPV/r[c]

[a] No change is recommended unless in the presence of advanced clinical disease progression or lack of adherence specifically because of poor palatability of LPV/r. In this case, switching to a second-line NVP-based regimen should be considered. Based on the recent approval of the use of EFV in children less than 3 years, an EFV-based regimen could be considered as an alternative. However, more data are needed to inform how best to use EFV in this population.

[b] TDF may only be given to children >2 years.

[c] ATV/r can be used as an alternative to LPV/r in children older than 6 years.

Table 7.17 Summary of preferred second-line ARV regimens for adults, adolescents, pregnant women and children

Second-line ART			Preferred regimens	Alternative regimens
Children	If a NNRTI-based first-line regimen was used		ABC + 3TC + LPV/r[b]	ABC + 3TC + LPV/r[b] TDF + 3TC (or FTC) + LPV/r[b]
	If a PI-based first-line regimen was used	<3 years	No change from first-line regimen in use[c]	AZT (or ABC) + 3TC + NVP
		3 years to less than 10 years	AZT (or ABC) + 3TC + EFV	ABC (or TDF) + 3TC + NVP

Third Line Drugs for children

- Etravirine
- Darunavir
- Raltegravir
- Maraviroc
- Elvitegravir
- Dolutegravir

Challenges in ART regime

d4T be phased out

- Still used D4T is because of the problem of Anemia (late stage, severe OI, Malnutririon ,malaria)
- d4T also remains important in the situation in which toxicity to AZT
- the duration of therapy with this drug should be limited to the shortest time possible.

Challenges in ART regime

LPV/r

- The current LPV/r syrup formulation has cold chain requirements until the point of dispensing.
- The syrup is unpalatable, with the potential for suboptimal adherence
- the risk of metabolic complications among children who initiate LPV/r early in life is unknown.
- LPV/r is costly and administering this with TB treatment is complex.

Challenges in ART regime

ABC

- HLA-B*5701 genetic testing should be performed before initiating abacavir-based therapy because of severe hypersentivity reaction
- the cost of ABC may be a significant barrier especially when combined with LPV/r.
- Definitive data on the comparative efficacy of ABC and AZT are expected from ongoing studies

Challenges in ART regime

TDF

- Limited pediatric experience
- Potential for bone and renal toxicity; bone toxicity appears to be more frequent in younger children.
- Numerous drug-drug interactions with other ARV agents including ddI, LPV/r, ATV, and TPV


HIV care Clinic (Mandalay children Hospital)

IHC (Mandalay Children hospital)

- Started in August 2005, same place with adult OPD
- NAP and great partner UNION as PPP
- In 2012 - move to 300 bedded Children Hospital, separate with adult OPD
- Starting from March 2014 – moved to 550 bedded Children Hospital.

- OPD Day - Monday and Wednesday Evening
- Average 30 -40 patients /OPD day
- At least 3 Pediatricians and 3 Coordinators attend the OPD
- ART and OI Drugs dispensation is handled by pharmacists and nurses

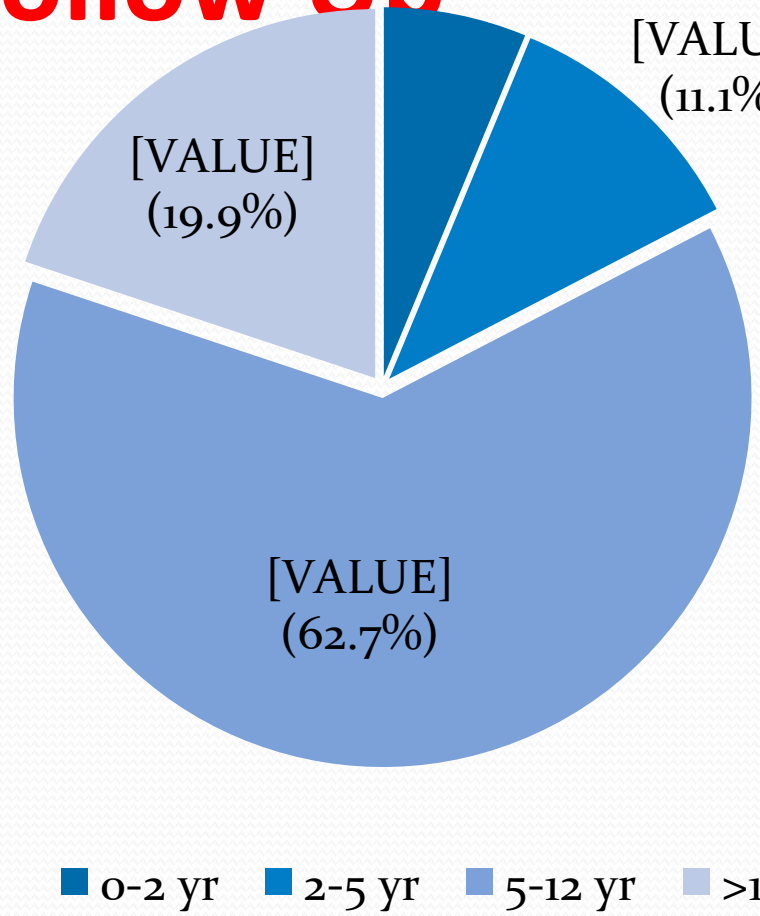

CHILDREN HOSPITAL


HIV CARE
CLINIC

Background data from August 2005 Up to Dec/2015

- Total enrolment = 1401
- Ever started on ART = 997
- Total Active follow-up = 719
- Active follow-up on ART = 610

Age distribution among Active Follow Up



Total patient 71

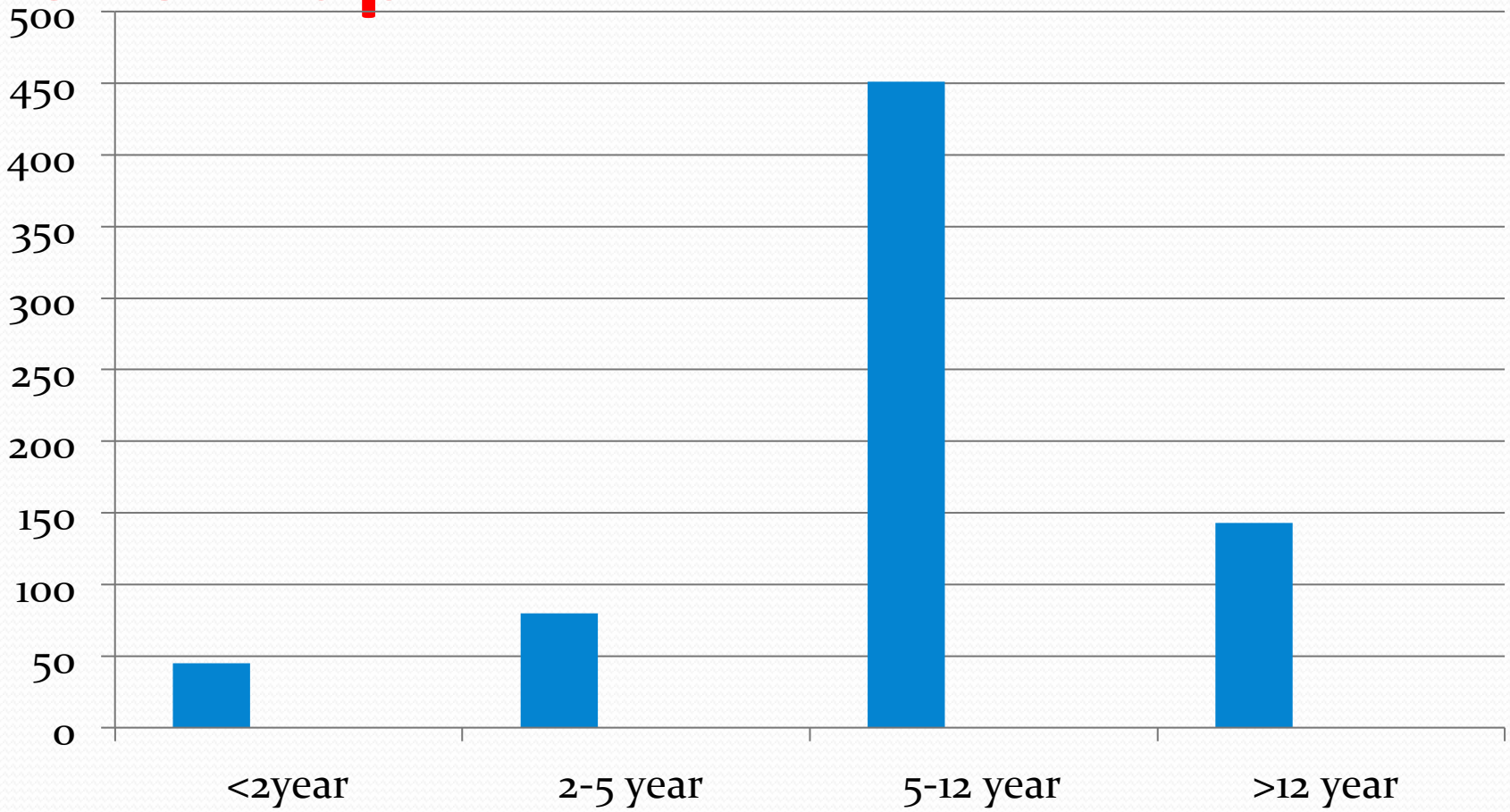
<2year 45

2-5 year 80

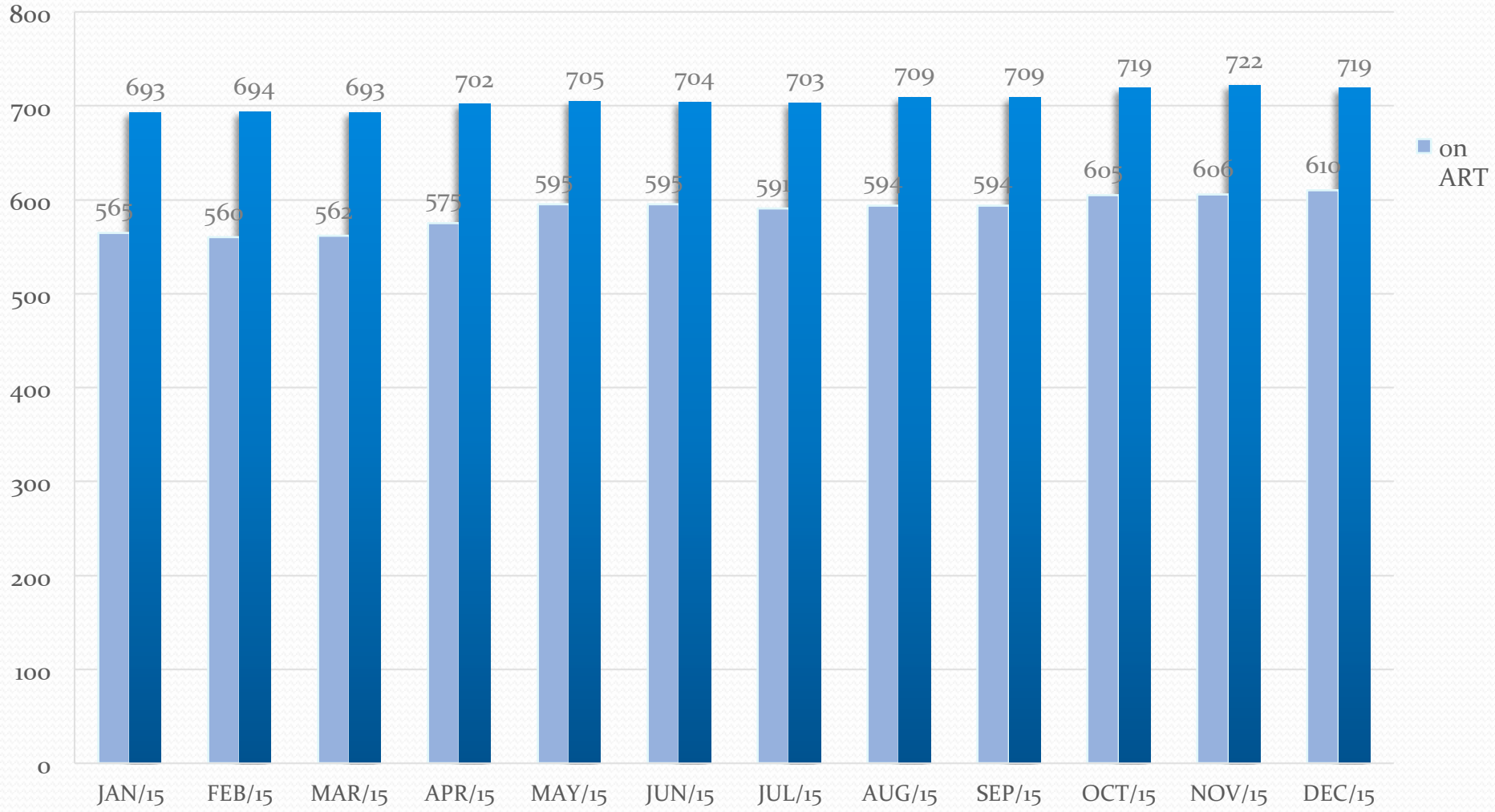
5-12 year 451

>12 year 143

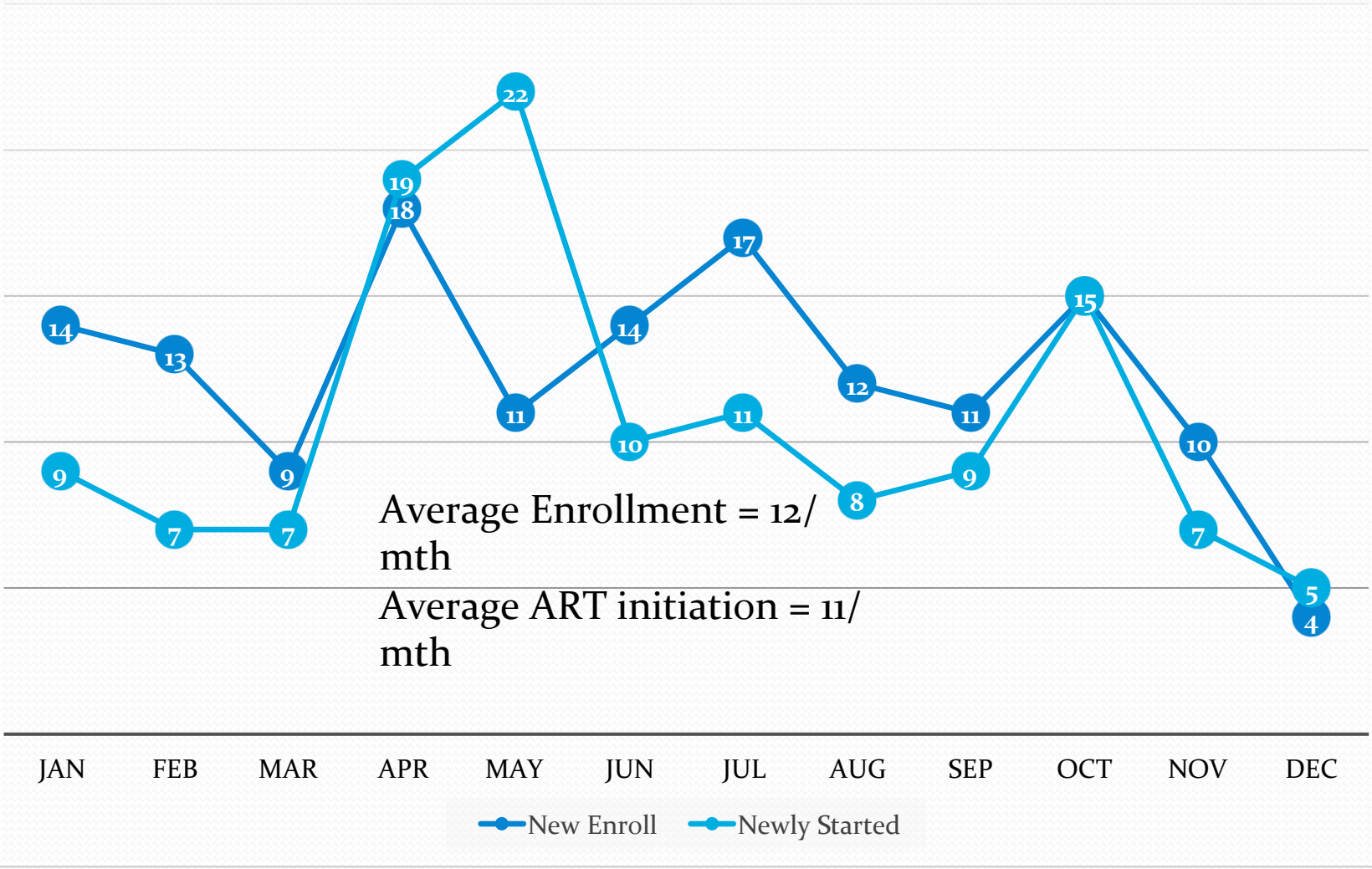
Age distribution among active follow up



Active Follow Up in 2015



New Enroll vs. Newly ART Initiation



up to December 2015

- Active follow up on ART =610
- Transfer out to other IHC program =228 (37.3%)
- Death =93(15.2%)
- Defaulter =67(11%)
- Discharge =20(3.3%)
- Stopped ART =6(0.9%)

Defaulter analysis

Since program started

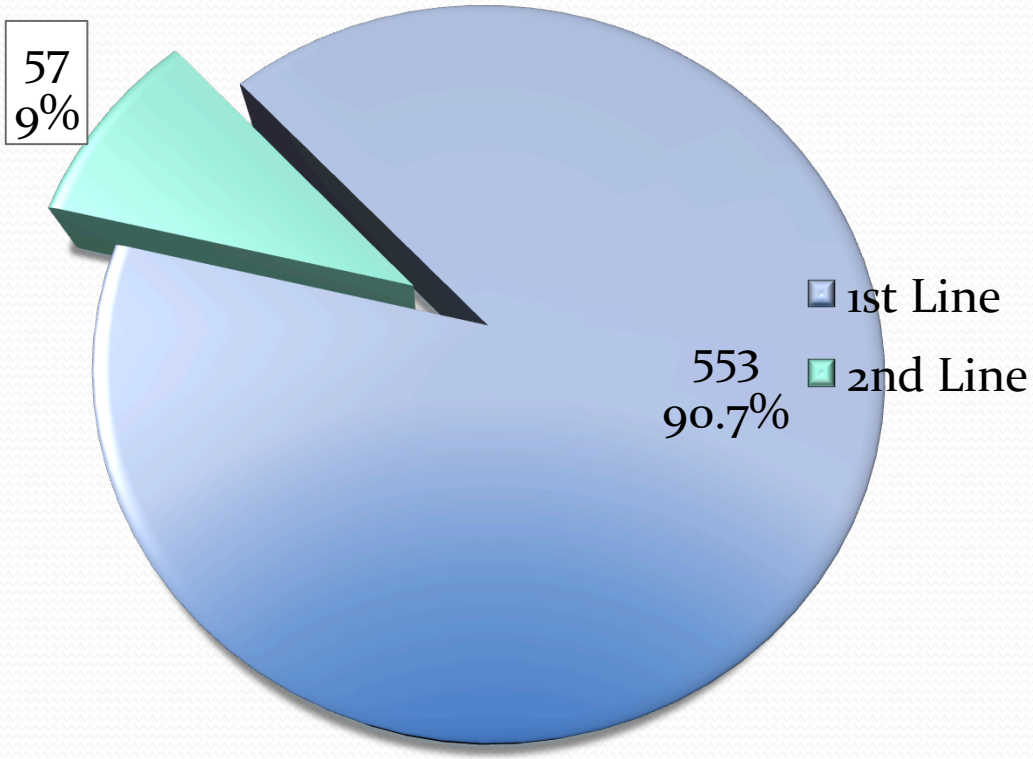
- Defaulter (on ART) =118

- Patients who retrieved back to program =51
- Still defaulted =67

During 2015

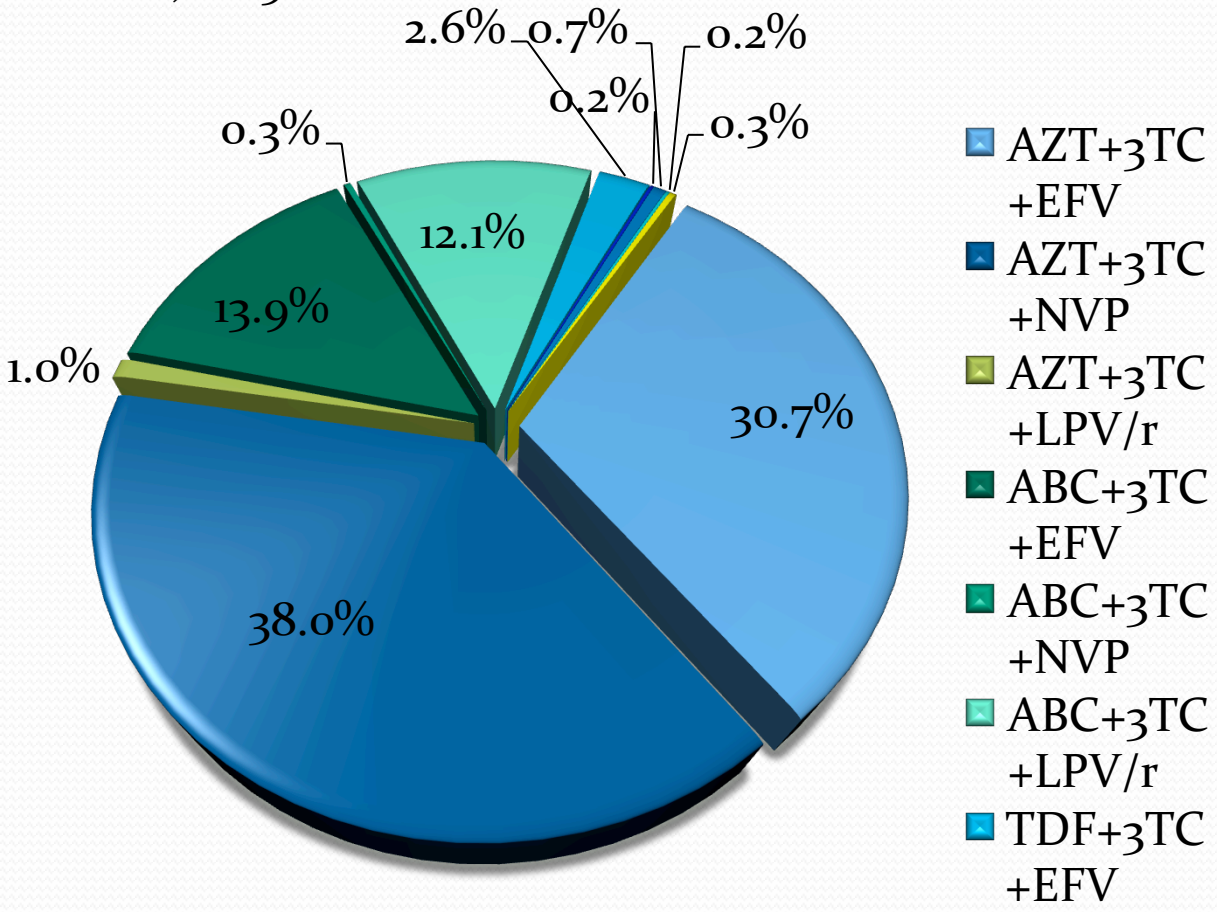
- Defaulter (on ART)=25
- Patients who retrieved back to program =8
- Still defaulted =17

1st line vs. 2nd line ART



ART Regimen Distribution

As of December, 2015



Care for Positive Children


DISCLOSURE

Promotion of Adherence


Psychosocial
Support


Myanmar New Year Celebration
2nd April 2016


Myanmar New Year Celebration
2nd April 2016
Mandalay

Transitioning to adults

- There are many concerns of adolescent's issues
- Self esteems/self control
- High risk behavior, alcohol/drugs
- Sex/STD,HIV transmission
- Reproductive right and birth control
- Educations/Schooling
- Work, carrier ..... **LIFE**

Thank You