Myanmar ART Guideline

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- Background
- 2014 Myanmar ART guideline and 2016 supplement
- Experience in a large HIV hospital with 8000 cohorts

Global AIDS Response Progress Report

Myanmar

National AIDS Programme

HIV Estimates and Projections, AEM, Myanmar (December 2014).

- Type of epidemic =concentrated around KAP
- Prevalence age 15+ = 0.45%
- FSW=6.3%
- MSM=6.6%
- PWID=23.1%
- PLHIV = 212,000 (F=34%)
- New infection = 15,000
- Died = 9,000

- The number of patients on ART by the end of 2015 = 106,490 (Dr HNO, NAP, 7/3/16)
- The number of patients estimated to be on ART by the end of 2016 is 144 437. (68%)
- ART centers = 100
- DC sites = 140

- Myanmar ART guidelines closely reflected WHO guidelines

- Revised and developed 1-2 years after the launch of WHO guideline

WHO	Myanmar
2002	2004
2006	2007
2010	2011
2013	2014
2015	2016

WHO ARV Guidelines Evolution 2002 to 2015

Topic	2002	2003	2006	2010	2013	2015
When to start	CD4 ≤200	CD4 ≤ 200	CD4 ≤ 200 - Consider 350 - CD4 ≤ 350 for TB	CD4 ≤ 350 -Regardless CD4 for TB and HBV	CD4 ≤ 500 - Regardless CD4 for TB, HBV PW and SDC - CD4 ≤ 350 as priority	**Towards Treat All Adolescents age band**
1st Line ART	8 options - AZT preferred	4 options - AZT preferred	8 options - AZT or TDF preferred - d4T dose reduction	6 options & FDCs - AZT or TDF preferred - d4T phase out	1 preferred option & FDCs & STR - TDF and EFV preferred across all pops	**Continue with FDC and harmonization across age bands**
2nd Line ART	Boosted and non-boosted PIs	Boosted PIs -IDV/r LPV/r, SQV/r	Boosted PI - ATV/r, DRV/r, FPV/r LPV/r, SQV/r	Boosted PI - Heat stable FDC: ATV/r, LPV/r	Boosted PIs - Heat stable FDC: ATV/r, LPV/r	**Greater number of options**
3rd Line ART	None	None	None	DRV/r, RAL, ETV	DRV/r, RAL, ETV	**Encourage HIV DR to guide**
Viral Load Testing	No	No (Desirable)	Yes (Tertiary centers)	Yes (Phase in approach)	Yes (preferred for monitoring, use of PoC, DBS)	**Support for scale up of VL using all technologies**

Earlier initiation

Simpler treatment

Less toxic, more robust regimens

Better and simpler monitoring

WHO ARV Guidelines Evolution 2002 to 2015

Topic	2002	2003	2006	2010	2013	2015
PMTCT	AZT 4 wks; SD NVP to mother and infant	M: AZT fr 4 wk+SD NVP Infant: SD NVP; AZT 1 wk	M: AZT fr 4 wk + SD NVP+ AZT/ 3TC 7d Infant: SD NVP+ AZT 1 wk	M:As early as 14 wk Option A (AZT +/- SD NVP+ AZT/3TC 7 d) Option B (triple ARV) Infant: daily NVP	**M: Option B** **Option B+** **Infant: daily NVP**	**Option B+**
Children			<12 mth– treat all >12 mth – if CD4< age speicific thresholdl	<24 mth – treat all >24 mth – if CD4< age specific threshold	< 5 yr --- treat all > 5 yr --if CD4<500	**Treat all age band**
HIV/TB		CD4<350	CD4<350	Any CD4, treat all	Any CD4, treat all	Any CD4, treat all
HIV/HBV				Treat if HBV treatment is indicated	Treat all	**Treat all**
Serodiscordant couples	No specific recommendation				Treat all	**Treat all**

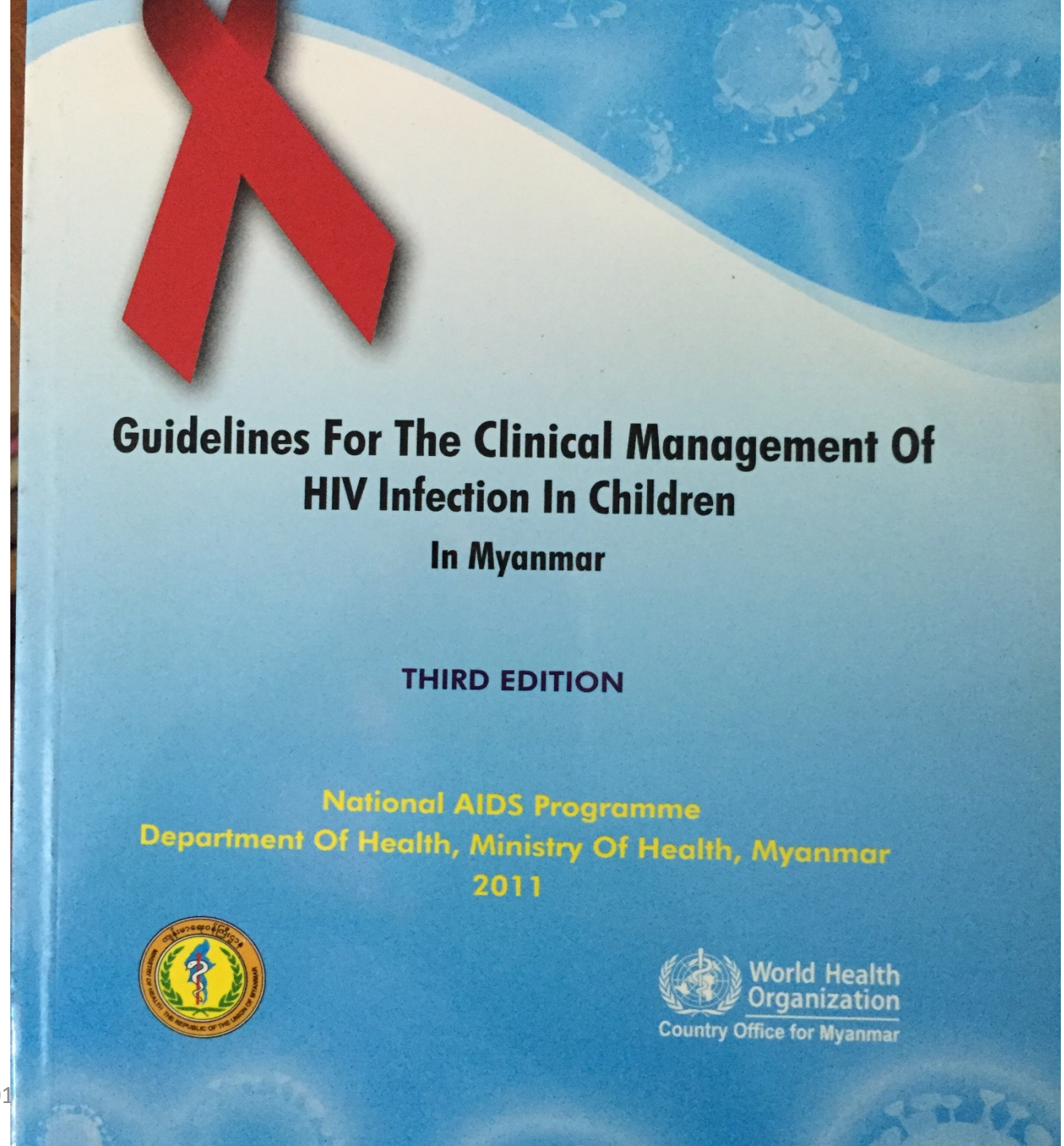
Guidelines For The Clinical Management Of HIV Infection In Adults And Adolescents

In Myanmar

THIRD EDITION

National AIDS Programme
Department Of Health, Ministry Of Health, Myanmar
2011

World Health Organization
Country Office for Myanmar


Guidelines For The Clinical Management Of
HIV Infection In Children
In Myanmar
THIRD EDITION
National AIDS Programme
Department Of Health, Ministry Of Health, Myanmar
2011
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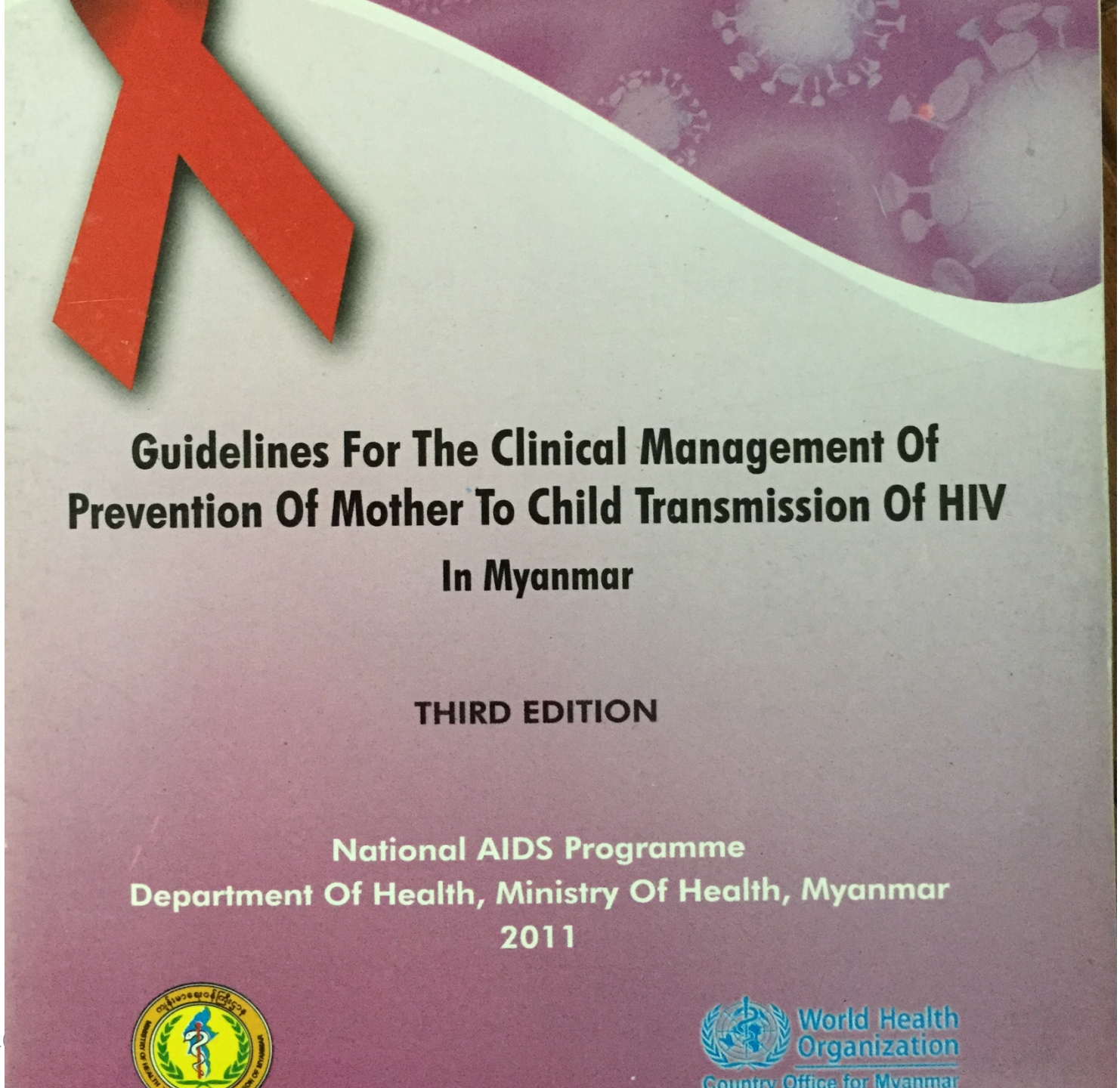
Country Office for Myanmar


Guidelines For The Clinical Management Of
Prevention Of Mother To Child Transmission Of HIV
In Myanmar
THIRD EDITION
National AIDS Programme
Department Of Health, Ministry Of Health, Myanmar
2011
World Health Organization
Country Office for Myanmar

GUIDELINES
FOR THE CLINICAL MANAGEMENT OF HIV INFECTION IN MYANMAR

FOURTH EDITION

National AIDS Programme

Department of Health, Ministry of Health, Myanmar

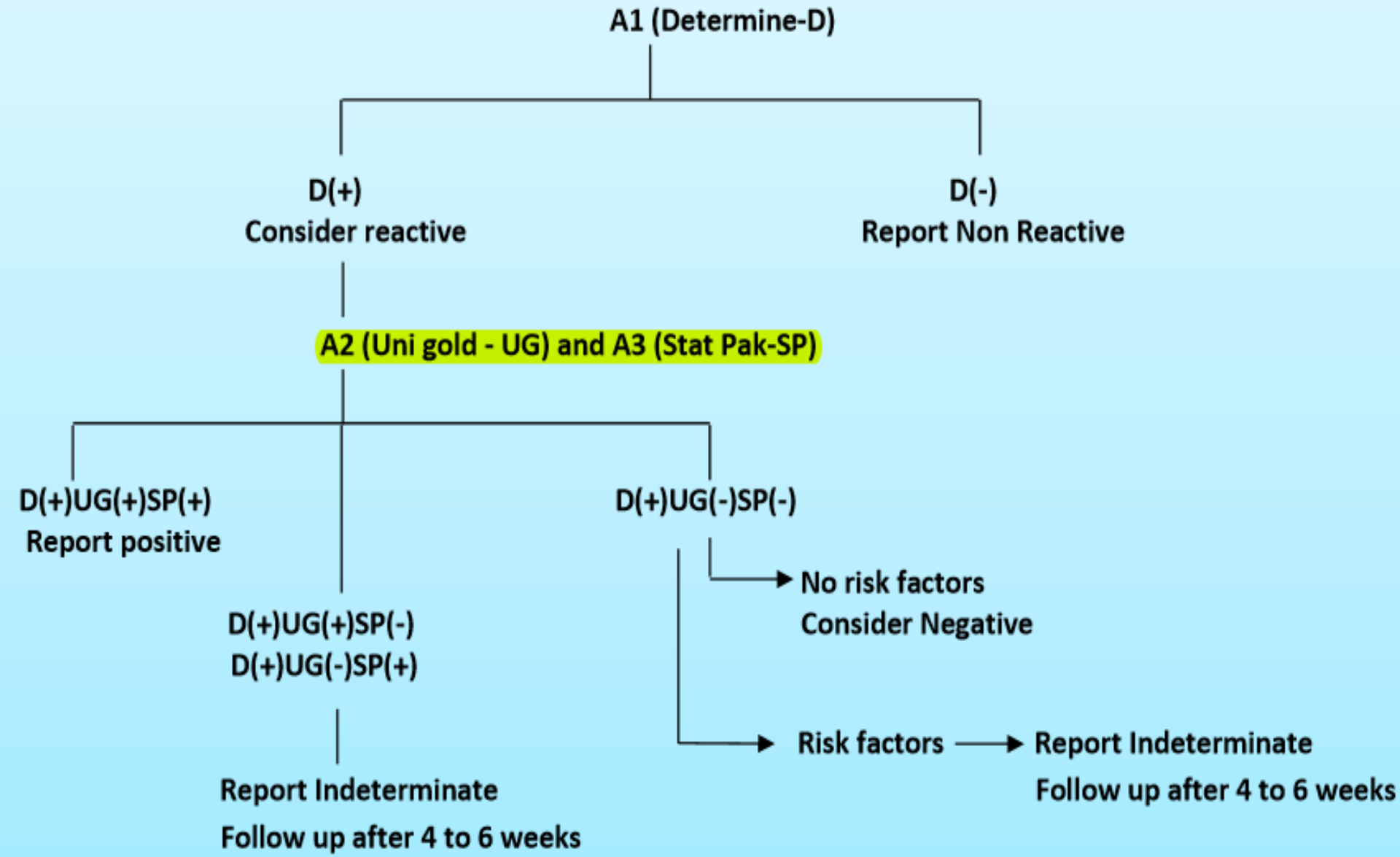
2014

World Health Organization
Country Office for Myanmar

Meeting Minutes of Consultative Meeting on Guidelines for the Clinical Management of HIV Infections in Myanmar (Fifth Edition), 2016

- Date: 7th March 2016
- Venue: Myat Nan Yone Hotel, Naypyitaw

WHO Strategy III
(Diagnosis)



Pre-ART care

- WHO staging
- Processing for ART : CSG sessions and baseline laboratory tests
- CPT
- TB screening and IPT

Five TB screening questions

- Current cough
- Fever
- Weight loss
- Night sweats
- Lymph node enlargement

If a positive response to at least ONE question

- Sputum AFB & geneXpert
- CXR
- USG (Abd)
- LN aspirate and AFB smear
- Urinary LAM ?

- Empirical antiTB should be considered despite all the negative investigations
- In line with NTP guidelines
- Higher risk of SE (skin rash, hepatitis)

IPT

- If 5 screening questions negative , IPT
- INH 300 mg/d for 6 mth
- Decrease risk of developing active TB by 33 – 64%
- More effective if TST positive
- Practical issues

CPT

- All symptomatic individuals (WHO 2,3,4)
- CD4 < 350
- One double strength 960 mg tab

- Dapsone 100 mg OD if septrin hypersensitive

Laboratory assessment for pre- ART	
Hb g/dl	Baseline
CD4 count	Baseline
Fasting blood sugar	Baseline
ALT, AST	Baseline Desirable
Creatinine (for Cr clearance calculation)	Baseline Desirable
HBs Ag, HCV Ab	Baseline Desirable
Urinalysis (proteinuria, glucosuria)	Baseline
Chest X- rays	Baseline if indicated

Summary of key recommendations for ART in the new guidelines

I. When to start

1. Adults and Adolescents	
i.	HIV positive individuals – CD4 ≤500 cells/mm3; priority to those with CD4 less than 350/mm^3
ii.	HIV positive symptomatic ARV naïve individuals- WHO clinical stage 2 if CD4 ≤ 500 cells/mm3 *OR* WHO clinical stage 3 or 4 irrespective of CD4 cell count
2. Pregnant women	
iii.	HIV positive pregnant women – CD4 ≤500 cells/mm3 irrespective of clinical symptoms *OR* WHO clinical stage 3 or 4 irrespective of CD4 cell count
3. Children	
iv.	Initiate ART in all HIV infected children less than 5 years
v.	For children more than 5 years, follow same criteria as adults.

Special Populations

vi. HIV/TB coinfection– Treat all HIV/TB coinfected individuals irrespective of CD4 count

vii. HIV/HBV coinfection – Provide ART to HBV/HIV coinfected if ALT level 2.5 times more than the upper limit of normal.

viii. Sero discordant couples – Treat all sero discordant couples irrespective of CD4 count.

ix. Key populations – Treat all irrespective of CD 4 count

(Key populations include FSWs, MSMs, TGs and PWIDs)

5. PMTCT

- When to start ART - As soon as feasible
- Recommended first line regimens- same as for other adults.
- Prophylaxis for infants born to pregnant women on ART-
  - All infants regardless of feeding mode – daily NVP for 6 weeks

i. ART for HIV infected pregnant women who need treatment for own health
   - Preferred regimen is TDF/3TC(FTC)/EFVor alternate first line

ii. 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)

Prophylaxis regimens for the mother: TDF/3TC (FTC)/EFV or alternate first line

Option B: - Continue ARV till 1 week after cessation of breastfeeding.

Option B plus: Do not stop ARV to mother. (For detail information please refer to text)

II. What ART to start?

Adults and Adolescent	
i.	HIV positive ARV naïve adults and adolescents – TDF + 3TC (FTC) + EFV is the preferred first line regimen, unless there is any contraindication.
ii.	If the preferred first line cannot be used, the alternate first line regimen, in order of preference are: AZT+3TC+EFV; AZT+3TC+NVP: ABC+3TC+EFV
Co-infections	
iii.	HIV/TB coinfection – Same as above ; ART to be started 2 to 8 weeks after start of TB treatment ;
iv.	HIV/HBV coinfection – NNRTI regimens that contain both TDF+3TC (or FTC)
Children (see algorithm and table in text)	

≤ 3 yrs	
Preferred	ABC/AZT + 3TC + LPV/r
Alternative	ABC/AZT + 3TC + NVP
Special circumstances	d4T + 3TC + NVP (or) LPV/r
3 – 10 yrs (< 35 kg)	
	ABC + 3TC + EFV
	AZT / TDF + 3TC + EFV
> 10 yrs (> 35 kg)	As for adult

Laboratory monitoring of ART

Hb (For AZT)	Baseline and at 4, 8, 12 weeks ; every 6 months desirable
CD4 count	Baseline and every 6 months
Plasma viral load : targeted	At 12 months after the ART initiation and as needed only to confirm virological failure
Fasting blood sugar	Every 6 months desirable
AST, ALT	Every 6 months (if NVP used at 4,8 12 weeks) desirable but not compulsory
Creatinine	Every 6 months if TDF used especially in high risk patients
Lipid profile (at least cholesterol and triglyceride	Every 12 month (Desirable)
Urinalysis (Proteinuria, Glucosiuria)	Baseline and Every 6 months if TDF used
Chest X-ray	Initially and when indicated

Clinical considerations for TDF toxicity

- Laboratory monitoring is not mandatory to initiate treatment with TDF.
- Urine dipsticks may be used to detect glycosuria
- Do not initiate TDF when the estimated glomerular filtration rate is <50 ml/min, or in long-term diabetes, uncontrolled hypertension and renal failure.
- Monitor growth in children using TDF.

Treatment failure and switching to 2nd line

- Where available , use viral load (VL) to confirm treatment failure
- A persistent VL of > 1000 copies/ml confirms treatment failure
- Where VL is not available, use immunological criteria (CD4 count) to confirm clinical failure

1st line ART	2nd line ART
Adult	
d4T or AZT	TDF
TDF	AZT
Children	
ABC	AZT

- (--) + 3TC + Boosted PI

PEP

- PEP should be offered, and initiated as early as possible, preferably within 6 hours to all persons with a HIV exposure, and within a window of 72 hours
- Either 2 or 3 drug combinations may be prescribed
- TDF/AZT + 3TC + (LPV/r) for 28 days

GUIDELINES

GUIDELINE ON WHEN TO START ANTIRETROVIRAL THERAPY AND ON PRE-EXPOSURE PROPHYLAXIS FOR HIV

SEPTEMBER 2015

Coming new guideline

- Test and treat (offer) for all age groups
- PMCT – Option B+ for pregnancies, to continue at township level.
- **First line**
  - preferred option: TDF+XTC+EFV (600)
  - Newer alternative option should be available e.g, **Dolutegravir (DTG)**, Raltegravir
- Routine VL monitoring (at 6 mth and yearly)

- 2nd line --- no change (LPV/r or ATZ/r)

- 3rd line -- ?
  - In 2013 , 21 pts on 2nd line were randomly selected to test for viral load
  - 18 pts (86%) --- undetectable
  - The others have very low viremia --- around 200 copies/ml

- Adolescent friendly clinic and proposed 15 years to be transferred for adult ART
- PEP (Three drugs combination) 2NRTI+EFV/PI regimen
- PrEP modeling exercise in selected area for priority population depending on the available resources.

Experience in an HIV hospital

- The proportion of people initiating ART with very low CD4 counts remains high, with more than one in four people starting ART at CD4 ≤100 cells/mm3 across all regions

CD4 at the time of initiation

	2008 N=365	2012 N=782	2015 N=2167
% WHO stage 3 or 4	16(CD4>200)	12(CD4>350)	5(CD4>500)
Median	63	128	154
% < 50	42	26	25
% < 100	61	40	40
% < 200	84	65	56
%< 350	NA	88	76
%<500	NA	NA	95

Major OI prevalence among 1853 in-pts (2015)

Disease	% prevalence	% Mortality
TB -- All	44	27
TBM	14	50
Crypto Meningitis	5	28
PJP	4	44
Toxoplamosis	2	14
Penicilliosis	2	9
MAC	1.5	7

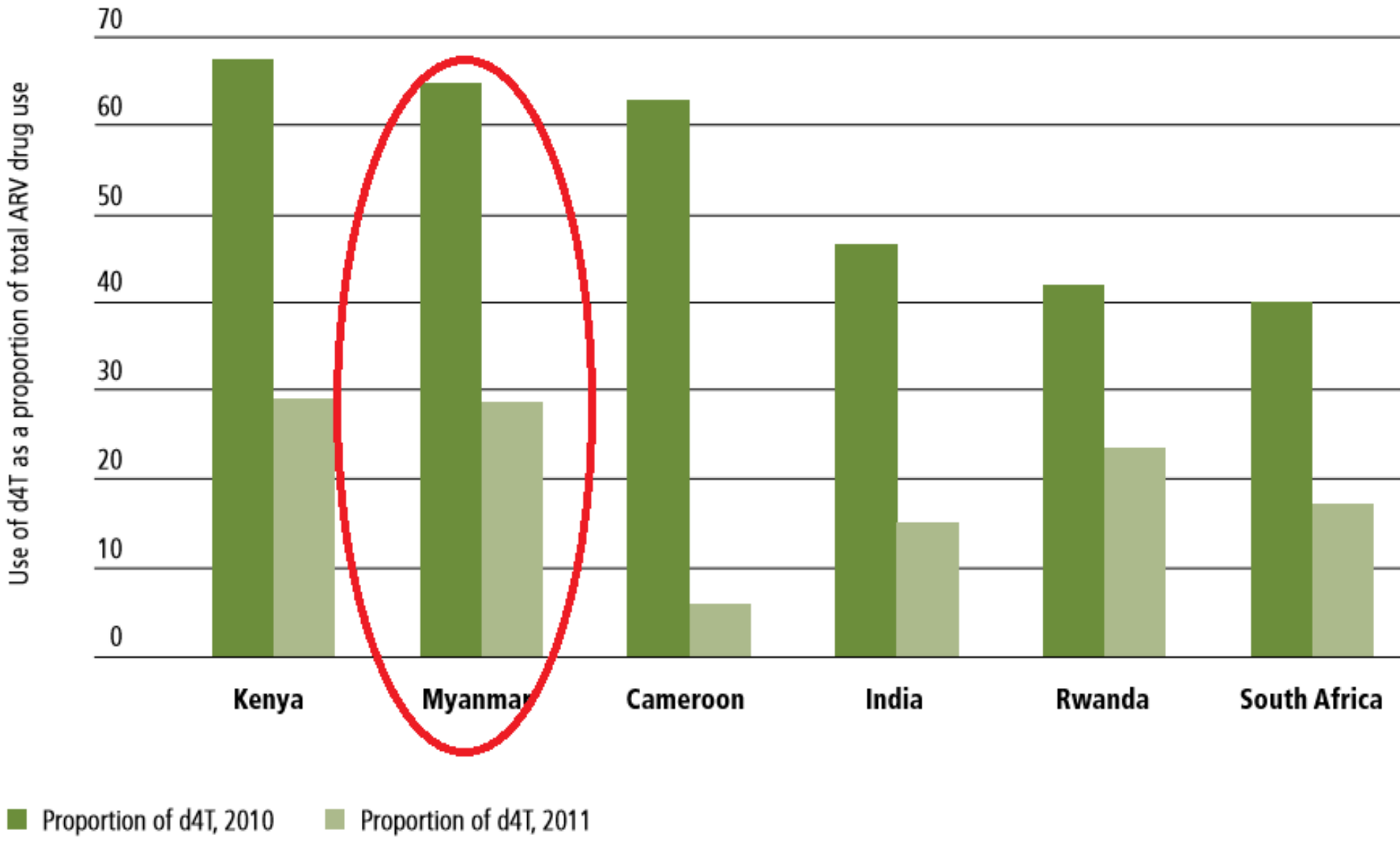
Rate of COD among 440 deaths

Disease	% of Total Death
TB --- All	50
TBM	28
PJP	7.5
Cryptococcal meningitis	6

Lack of CRAG test

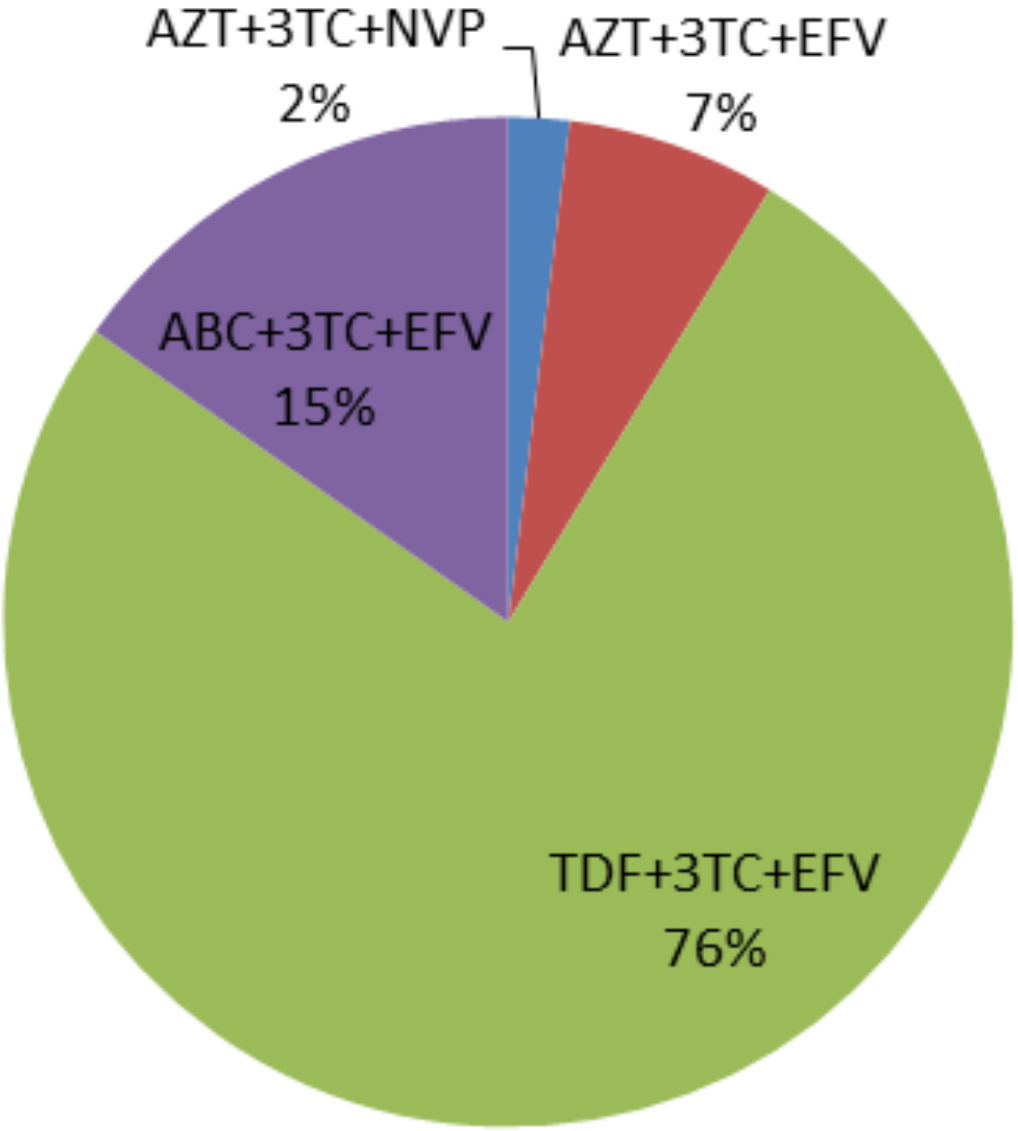
- Cryptococcal meningitis remains a leading cause of mortality among people with HIV, contributing up to 20% of AIDS-related deaths in low- and middle-income settings (17) , and WHO recommends systematic Cryptococcus antigen screening for everyone with CD4 ≤100 cells/mm3 and preemptive treatment for those with positive antigen test (18) .

Fig. 8.3. Countries reducing d4T use >50% between 2010 and 2011

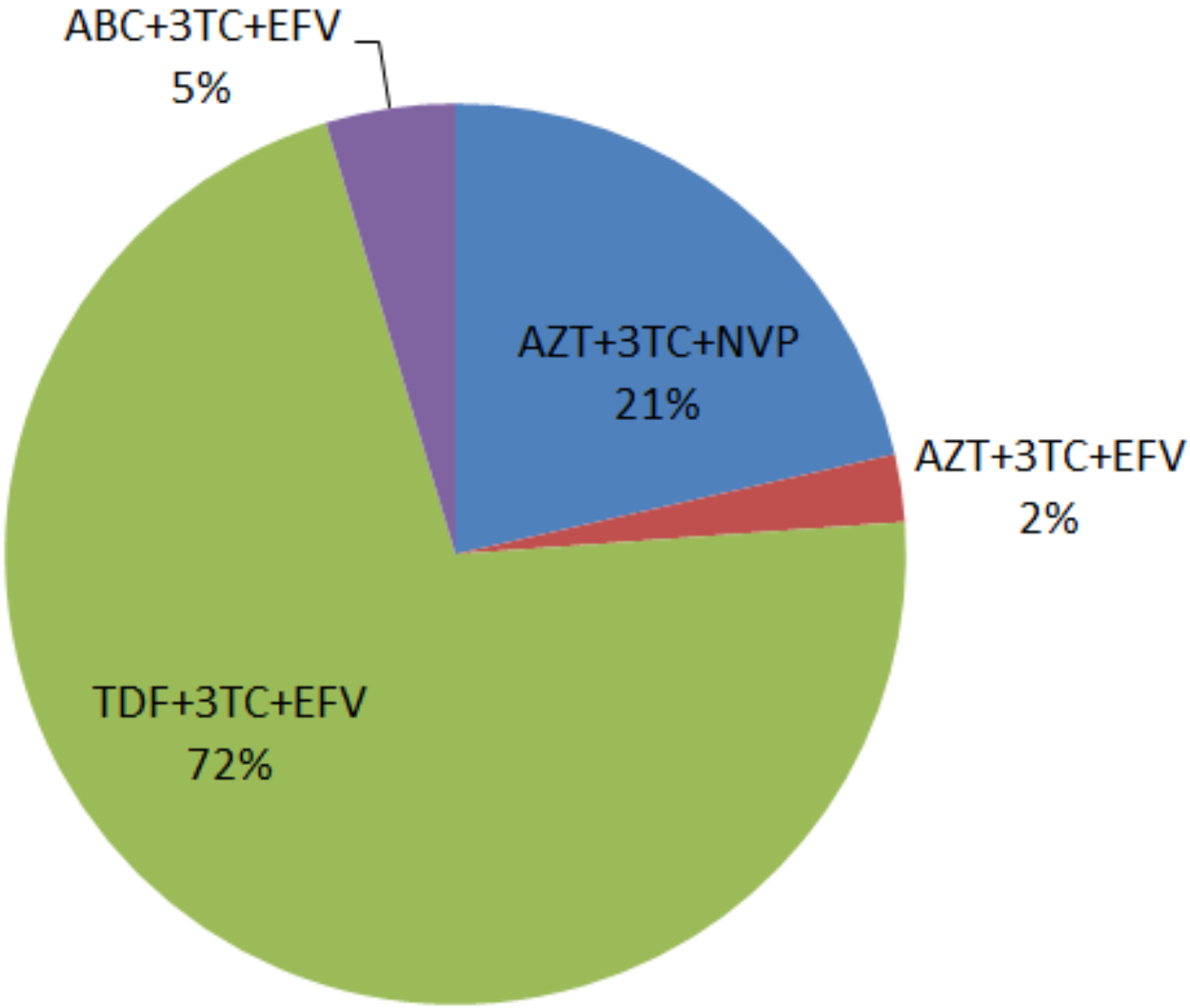


- d4T phase out started in 2011
- Completed at the end of 2014

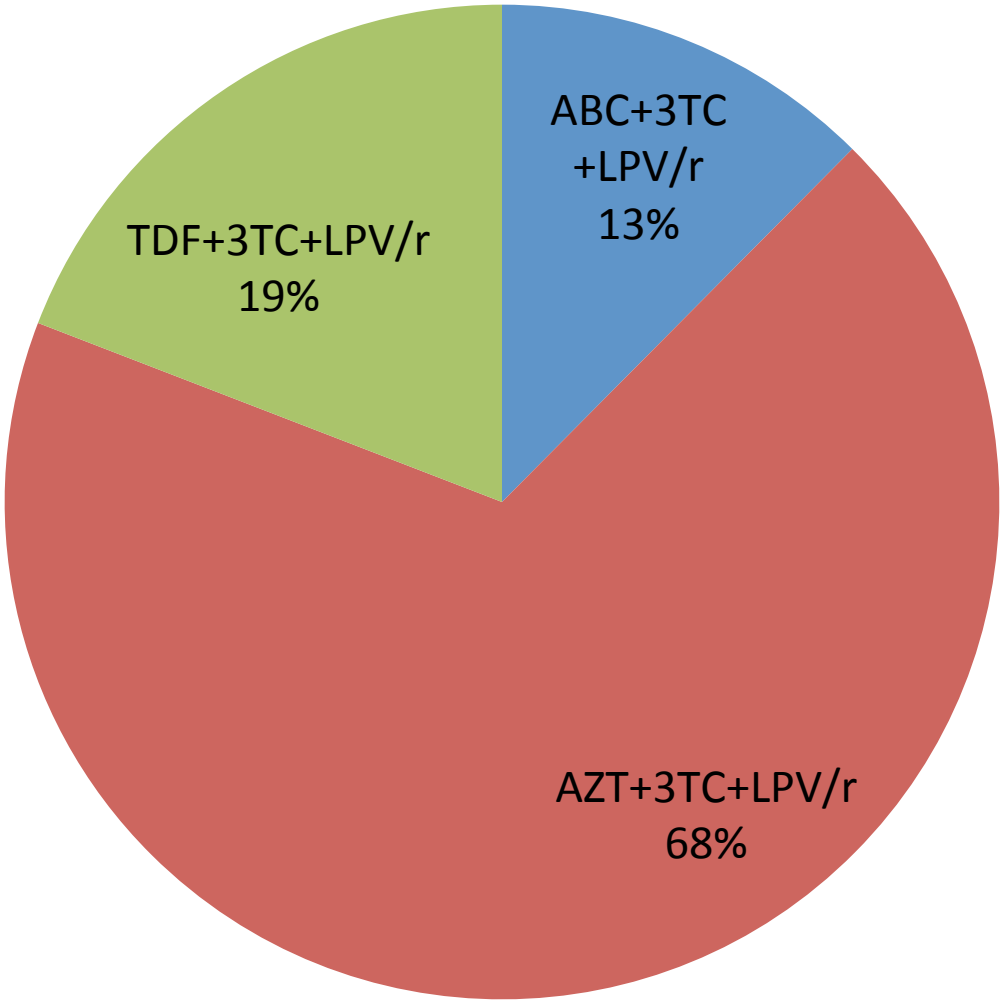
1st line ART 2015 (2200 pts)



1st line ART of 7229 pts



2nd line ART (209 pts)



Renal toxicity of TDF

- Starting regimen is TDF ---- changed to the other regimen
- 57/4304= 1.3%
- Some deaths attributed to ARF d/t TDF toxicity

Survival rate in relation to change in guideline

2004 guideline			2007 GL		2011 GL		2014 GL
2005 cohort			2008 cohort		2012 cohort		2015 cohort
Yr 1	Yr 5	Yr 10	Yr 1	Yr 5	Yr 1	Yr 3	Yr 1
96	79	69	83	76	80	73	89

THANK YOU