



# Guidelines

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# **ACKNOWLEDGEMENTS, DISCLAIMERS AND WARNINGS**



# What are guidelines?

“Statements that include recommendations intended to optimise patient care that are informed by a **systematic review** of evidence and an assessment of the benefits and harms of alternative care options”

IOM 2011



- Question I am often confronted with – are GLs absolute rules or recommendations?
- Answer: depends, several factors which include your qualifications, scope of practice and experience
- Example: experienced NIMART nurse; inexperienced junior doctor

# What are guidelines?

- “Clinical practice guidelines are **systematically** developed statements to assist practitioner and patient decisions about appropriate healthcare for **specific clinical circumstances**”

Field and Lohr 1990. page 38.



- Question I am often confronted with – are GLs absolute rules or recommendations?
- Answer: depends, several factors which include your qualifications, scope of practice and experience
- Example: experienced NIMART nurse; inexperienced junior doctor



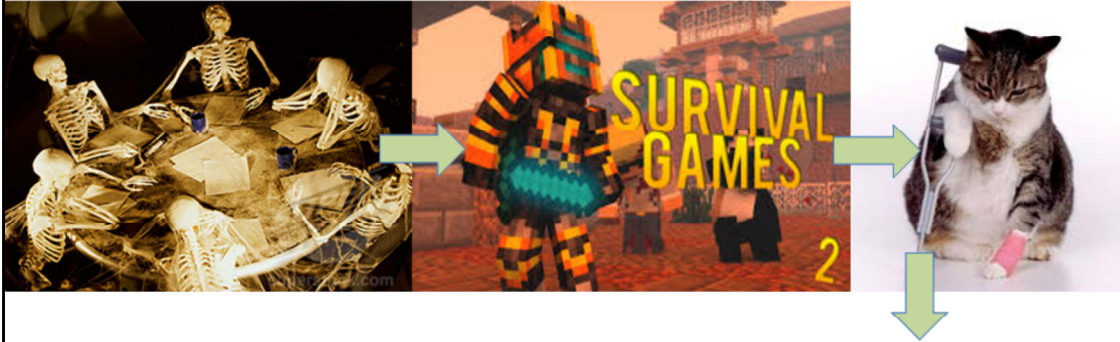
# Process for GL development



HOW TO PICK UP CHICKS



# Process for GL development



**GUIDELINE**

## **Adult antiretroviral therapy guidelines 2014**

**By the Southern African HIV Clinicians Society**

*G Meintjes (chairperson)*

*J Black, F Conradie, V Cox, S Dlamini, J Fabian, G Maartens, T Manzini, M Mathe, C Menezes, M Moorhouse, Y Moosa,  
J Nash, C Orrell, Y Pakade, F Venter, D Wilson (expert panel members)*

## Selected topics

- When to start ART
- What ART to start?
- When to switch?
- Switch to which?
- Third line ART
- Patients with renal impairment

*Young cat!  
If you keep  
your eyes  
open  
enough,  
oh, the stuff  
you will  
learn!  
The most  
wonderful  
stuff!*



- Topics selected reflect areas of significant change, new sections or areas that may have been clarified
- Where evidence presented, evidence that was available at time guidelines were updated
- Only adult guideline; does not include PMTCT – consult DoH guidelines for PMTCT recommendations

# Updated GL: underlying philosophy

- Affordability considered
- Only treatment and diagnostic options available in Southern Africa were considered
- Bridge gap between public and private sectors
- Intended to reflect “best practice”
- Shift to view ART as prevention



## **GUIDELINE** **Adult antiretroviral therapy** **guidelines 2014**

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- South Africa is a middle-income country whereas certain other countries in the region are low-income countries; therefore, affordability was taken into account.
- Only treatment and diagnostic options available in Southern Africa were included.
- **We recognised the need to bridge the gap in treatment recommendations between public and private sector programmes, considering that many patients transition between the 2 sectors for treatment.**
- The guidelines are intended to reflect ‘**best practice**’ – while it is acknowledged that certain recommendations are **aspirational for poorly resourced settings**, the unavailability of diagnostic/monitoring tests **should not be a barrier** to providing ART to those in need.
- There has been a shift to view ARV treatment as a means of HIV prevention. The evidence base for this exists for **serodiscordant** couples; recommendations in this regard are included in these guidelines and additional data from community studies are awaited.

# When to start ART: diagnosis based

## Clinical diagnosis (irrespective of CD4<sup>+</sup> count)

WHO clinical stage 3 and 4 <sup>†</sup>	ART recommended
Other severe HIV-related disorders, e.g.: <sup>‡</sup> <ul style="list-style-type: none"><li>• immune thrombocytopenia</li><li>• thrombotic thrombocytopenic purpura</li><li>• polymyositis</li><li>• lymphocytic interstitial pneumonitis</li></ul>	ART recommended
Non HIV-related disorders: <sup>§</sup> <ul style="list-style-type: none"><li>• malignancies (excluding localised malignancies)</li><li>• hepatitis B co-infection<sup>¶</sup></li><li>• hepatitis C co-infection</li></ul>	ART recommended
Any condition requiring long-term immunosuppressive therapy	ART recommended



- How does this differ from **previous guideline**? Only nuance changes
- How does this differ from **NDOH and WHO**? Largely aligned
- WHO classification given in appendix of GL
- Patients with profound immunosuppression are at significant risk of opportunistic infections (OIs) and associated mortality, and should be assessed rapidly and initiated on ART within 1 - 2 weeks once adherence counselling has been initiated.
- In patients with higher CD4<sup>+</sup> counts, ART should be deferred until patients are prepared to commit to long-term treatment and are maintaining good treatment adherence. However, in eligible patients, efforts should be made to avoid lengthy indecision that may result in avoidable clinical deterioration and death.

# When to start ART: CD4-based/other

## CD4<sup>+</sup> counts

<350 cells/ $\mu$ L

ART recommended

350 - 500 cells/ $\mu$ L (two counts in this range)

ART recommended if patient is ready and motivated to start

>500 cells/ $\mu$ L

Defer ART

## HIV-infected partner in serodiscordant relationship

Regardless of CD4<sup>+</sup> count or clinical diagnoses

Offer ART and discuss safe sex (discussion should ideally involve all partners)



- How does this differ from **previous guideline**? CD4 <350 and CD4 >350
- How does this differ from **NDOH and WHO**?
  - Both recommend all CD4 <500 start ART;
  - NDOH does not treat **serodiscordant** couples but WHO recommends ART in SCs
- Patients with profound immunosuppression are at significant risk of opportunistic infections (OIs) and associated mortality, and should be assessed rapidly and initiated on ART within 1 - 2 weeks once adherence counselling has been initiated.
- In patients with higher CD4<sup>+</sup> counts, ART should be deferred until patients are prepared to commit to long-term treatment and are maintaining good treatment adherence. However, in eligible patients, efforts should be made to avoid lengthy indecision that may result in avoidable clinical deterioration and death.

# Haiti trial

Starting ART at CD4<350 vs. CD4<200 / AIDS

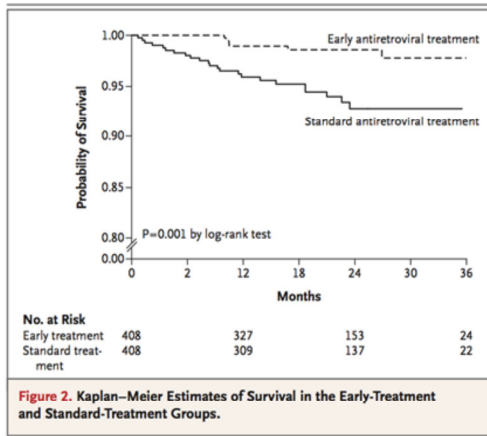


Figure 2. Kaplan–Meier Estimates of Survival in the Early-Treatment and Standard-Treatment Groups.

HR = 4.0

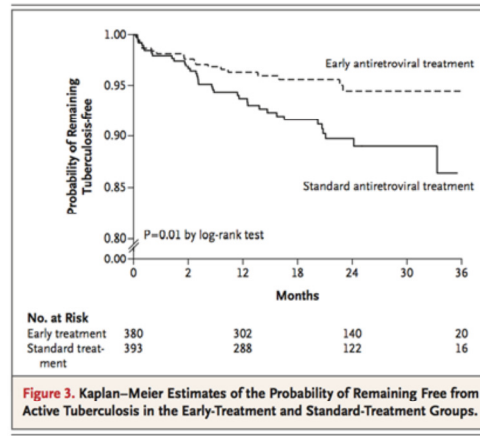


Figure 3. Kaplan–Meier Estimates of the Probability of Remaining Free from Active Tuberculosis in the Early-Treatment and Standard-Treatment Groups.

HR = 2.0



Severe, NEJM 2010



- RCT in Haiti demonstrated reduced **mortality** and **incident tuberculosis** (TB) in patients starting ART at a CD4+ count threshold of <350 cells/μL (compared with patients waiting to commence therapy at a threshold of <200 cells/μL)



# The evidence

## CD4 >350 cells/mm<sup>3</sup>

- No clinical trial shown improved patient survival >350 cells/mm<sup>3</sup>
- Observational data: reduced MM associated with earlier ART
- RCT HPTN 052: reduced morbidity but not mortality
- HIV-related events >350 cells/mm<sup>3</sup> rare
- Await evidence from START and TEMPRANO



## CD4 350-500 cells/mm<sup>3</sup>

### RECOMMENDATIONS:

- Reduces transmission in serodiscordancy
- Wider cover: reduce transmission community level (Hlabisa)
- Individualised approach: may be well; start lifelong ART with possible SEs
- If not ready, defer until CD4 <350 cells/mm<sup>3</sup>



- Evidence is less clear concerning individual patient benefit when increasing the CD4+ count threshold for ART initiation to 500 cells/μL.
- No clinical trial has shown improved patient survival from starting ART at a CD4+ count >350 cells/μL – trials ongoing at the time of GL development.
- Some **observational data** suggest **reduced morbidity and mortality** associated with starting ART earlier.
  - **Methodological** issues with observational data (residual confounding)
  - If there is benefit to patients starting ART at CD4 counts >350, the **benefit is likely to be small**, since HIV-related events at higher CD4 counts are rare.
- A randomised controlled trial (RCT) (HPTN052) showed **reduced morbidity but not mortality** associated with starting ART at a CD4 count of 350 – 550 (compared with <250). Absolute benefits were small.
- Definitive evidence regarding earlier ART initiation is awaited from ongoing RCTs, the **START** trial and **TEMPRANO** trial.

### CD4 350-500 recommendations:

- 2 CD4 in that range
- Starting ART at higher CD4 counts reduces HIV transmission **within couples** where one partner is HIV negative (HPTN052)
- Wider ART coverage appears to reduce the risk of HIV transmission at a **community level** (Hlabisa)
- Thus consideration should be given to starting patients whose CD4 counts are between 350-500.
- However, it must be remembered that many of these patients (CD4 350-500) are



completely well and starting lifelong medication that needs to be taken with 100% adherence, and also may have side effects in some patients, may be a difficult undertaking.

- We thus support an **individualised approach** in patients with a CD4 count 350-500: after a discussion about the potential benefits, uncertainties, side effects and need for impeccable adherence patients should only be prescribed ART in this CD4 range if they are motivated for lifelong ART with the required adherence.
- If they do not feel ready yet, ART should be **deferred** until their CD4 count is below 350 with a plan in place for ongoing follow-up and CD4 monitoring.

## One more eligibility criterion...

Patients diagnosed during seroconversion, if adherence requirements are met

- Recent studies suggest that ART initiation during seroconversion associated with slower disease progression
- At least 3 years; consider lifelong
- Limits size of reservoir
- Diagnosis: recent negative HIV test that becomes positive on subsequent test



- **Diagnosing seroconversion** is facilitated by having a recent negative HIV test that then becomes positive on a subsequent test.
- Otherwise, the following are suggestive: the compatible **clinical syndrome**, an **indeterminate** enzyme-linked immunosorbent assay (ELISA) test result that then becomes **positive** on a subsequent test, and a very **high VL**.
- Initiate standard first line therapy

# What ART to start?

	SAHIVSOC	SA NDOH	WHO
<b>NRTIs</b> Recommended Alternative	TDF + FTC/3TC ABC AZT Short term d4T	TDF + FTC/3TC ABC	TDF + FTC/3TC AZT ABC Short term d4T
<b>Third drug</b> Recommended Alternative	EFV RPV NVP (RAL) (PI/r)	EFV NVP LPV/r (ATV/r)	EFV NVP PI/r



- Raltegravir or PI/r to be used as 3<sup>rd</sup> drug when **NNRTI contra-indicated**  
eg. life-threatening hypersensitivity reaction
- Previous SAHIVSOC GL: preferred first line TDF + FTC/3TC + EFV  
alternatives:     ABC/AZT  
                          NVP
- Discuss **why NNRTI is preferred 3<sup>rd</sup> drug** in first line

# What ART to start? NNRTIs

EFV	RPV	NVP
<b>Avoid if</b> <ul style="list-style-type: none"> <li>Active psychiatric illness</li> <li>History severe psych disease</li> <li>Nightshifts / heavy machinery / driving</li> </ul>	<b>Avoid if</b> <ul style="list-style-type: none"> <li>VL &gt;100 000 copies/mL</li> </ul>	<b>Avoid if</b> <ul style="list-style-type: none"> <li>CD4 &gt;250 in women and &gt;400 in men</li> <li>Liver disease or LFT derangement</li> </ul>
<b>Common/severe ADRs</b> <ul style="list-style-type: none"> <li>CNS symptoms (vivid dreams, problems with concentration, dizziness, confusion, mood disturbance, psychosis)</li> <li>Rash</li> <li>Hepatitis</li> <li>Gynaecomastia</li> </ul>	<b>Common/severe ADRs</b> <ul style="list-style-type: none"> <li>Rash</li> <li>Hepatitis</li> <li>CNS symptoms (all uncommon)</li> </ul> <p><b>Inexpensive</b></p>	<b>Common/severe ADRs</b> <ul style="list-style-type: none"> <li>Rash</li> <li>Hepatitis</li> </ul>



## Avoid EFV if

- active psychiatric illness
- history of severe psychiatric disease
- night shift workers and those operating heavy machinery or vehicles.

## Rilpivirine

Inexpensive (R47/month)

RPV should not be used in patients with viral load > 100,000 copies/ml as clinical trials have shown that RPV-based regimens have higher virological failure rates in these patients compared with EFV (Cohen AIDS 2013;27:939).

In patients with viral load ≤ 100,000 copies/ml outcomes are comparable overall to EFV-based regimens, with RPV being better tolerated (Molina, HIV Med 2014;15:57)

## Avoid NVP

- CD4 > 250 in women and > 400 in men
- Liver disease or LFT derangement

# Efavirenz and pregnancy

- In a meta-analysis, the incidence of NTDs and all congenital abnormalities among women exposed to EFV in T1 was similar to that of the general population
- Based on the accumulated evidence we endorse the WHO guidance that EFV can be used in pregnancy and women who intend to fall pregnant
- This is in contrast to our previous guidance
- The FDA category D classification should be discussed with women
  - based on animal studies
  - human cohort studies have not demonstrated an increased risk of congenital abnormalities
  - background low risk of congenital abnormalities in all pregnancies (unrelated to drugs)



**Pregnancy Category D – Positive evidence of risk: Investigational or post marketing data show risk to the fetus. Nevertheless, potential benefits may outweigh the potential risk.**

# EFV and birth defects

General US pop	General South Africa pop	1 <sup>st</sup> trimester exposure to any ARV	2 <sup>nd</sup> /3 <sup>rd</sup> trimester exposure to any ARV	1 <sup>st</sup> trimester exposure to EFV	2 <sup>nd</sup> /3 <sup>rd</sup> trimester exposure to EFV	1 <sup>st</sup> trimester exposure to EFV Meta analysis
3%	5.3%	2.9%	2.8%	2.4%	2.0%	2.0%
95% CI:		(2.5 - 3.4)	(2.5 - 3.2)	(1.4 - 3.9)	(0.4 - 5.8)	(0.82-3.18)
Numbers:		195/6666	237/8394	18/735	3/149	39/1437
Relative risk 1 <sup>st</sup> trimester EFV to non EFV ART was 0.87 (0.61-1.24, p=0.45)						



## Neural tube defects

South African general population estimate = 0.23 - 0.36%

Meta-analysis (2011) = 0.07% (95% CI = 0.002 - 0.39)

Pillay, SA J HIV Med, March 2012;28  
 Ford, AIDS 2011;25:2301  
 The Antiretroviral Pregnancy Register Interim (2013)  
 Global Report of Birth Defects



- Because NTD infrequent, the size of these cohorts insufficient to definitively exclude an increased risk of NTD from EFV
- Pregnancy Category A – Controlled studies show no risk: Adequate, well-controlled studies in pregnant women failed to demonstrate risk to the fetus.
- Pregnancy Category B – No evidence of risk in humans: Either animal findings show risk, but human findings do not; or, if no adequate human studies have been done, animal findings are negative.
- Pregnancy Category C – Risk cannot be ruled out: Human studies are lacking, and animal studies are either positive for fetal risk, or lacking as well. However, potential benefits may justify the potential risk.
- **Pregnancy Category D – Positive evidence of risk: Investigational or post marketing data show risk to the fetus. Nevertheless, potential benefits may outweigh the potential risk.**
- Pregnancy Category X – Contraindicated in pregnancy: Studies in animals or humans, or investigational or post marketing reports, have shown fetal risk which clearly outweighs any possible benefit to the patient.

## When to switch?

- Two VL >1000 copies/mL
- 2-3 months apart
- At least 4 weeks **adherence intervention** in between

Low level viraemia (200 – 1000 copies/mL)

- Prolonged (>1 year)  
OR
- With persistently low CD4 counts (<100 cells/mm<sup>3</sup>)

Despite **adherence interventions**



- Restart the same regimen if patients return to care after defaulting therapy.
  - A VL should preferably be performed before restarting.
  - VL is measured 3 months after restarting ART
  - Switching to a second-line regimen should be considered if the VL is not <1 000 copies/mL at this point.
- In patients with **multiple episodes of interruption, particularly beyond the first year of ART**, many clinicians would consider switching to a second- line regimen, making the assumption that the multiple interruptions resulted in first-line resistance. Reasons for defaulting should be addressed and adherence support increased.
- **Hospitalisation with an AIDS-defining condition and a CD4+ count of <50 cells/μL** represents another situation where a patient may be restarted immediately on second-line ART when returning to care after defaulting
  - High risk of mortality if restarted on a first-line therapy to which their virus may be resistant, and they require a guaranteed effective ART regimen immediately. This decision should usually be taken by the clinicians at a hospital level.
- Performing a resistance test after the patient has been off ART for longer than 4 weeks is of limited value, as many resistance mutations are overtaken by wild-type virus when ART is stopped.

## Switch to which?

SAHIVSOC		SA NDOH		WHO	
First line NRTI	Switch to	First line NRTI	Switch to	First line NRTI	Switch to
AZT d4T	TDF	AZT d4T	TDF	TDF	AZT
TDF ABC	AZT	TDF ABC	AZT	AZT d4T	TDF

EARNEST trial suggested that NRTIs have important role in second line with PI/r even when there is NRTI resistance present

## Third drug options

SAHIVSOC	SA NDOH	WHO
ATV/r LPV/r DRV/r*	LPV/r (ATV/r)	ATV/r LPV/r

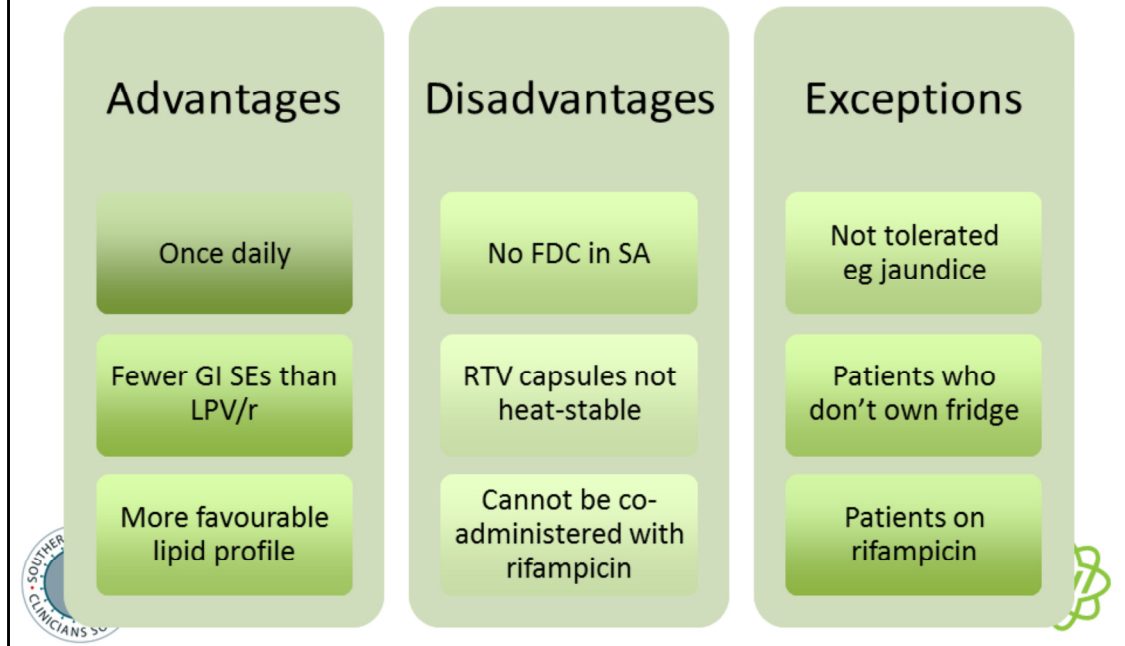
\* When 800/100mg daily available



- If a patient was receiving a **first-line combination of two NRTIs and a PI** (boosted or unboosted), it is best to discuss the choice of second-line regimen with an experienced HIV clinician
- **Perform a genotype resistance test.**
- Second-line NNRTI + NRTI regimens are often not effective in such patients because of **NRTI resistance mutations**. The regimen choice is therefore best guided by resistance testing.



## ATV/r 300mg/ 100mg daily



### Exceptions:

- Not tolerated (eg. **cosmetically unacceptable jaundice**) then use lopinavir/ritonavir
- Patients who do not own a fridge (to store ritonavir capsules)
- Patients on rifampicin-based TB treatment (**double dose lopinavir/ritonavir** should be used while on the TB treatment)

### ATV and jaundice

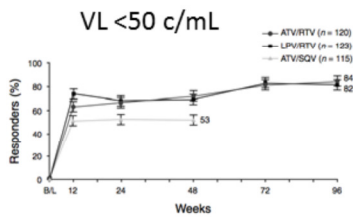
- Causes mild unconjugated hyperbilirubinaemia in up to 50% of patients
- Competitive inhibition of uridine diphosphate-glucuronosyl transferase (UGT) 1A1 enzyme similar to Gilbert's syndrome
- If other LFTs normal and no hepatitis symptoms then this does not represent liver injury

# BMS 045: 96 week results

## LPV/r vs. ATV/r in treatment-experienced patients

Table 3. Adverse events (AEs) and laboratory abnormalities up to week 96.

	ATV/RTV (n = 119) <sup>a</sup>	LPV/RTV (n = 118) <sup>a</sup>
Adverse events leading to discontinuations, n (%)	10 (8)	9 (8)
Serious adverse events, n (%) <sup>b</sup>	16 (13)	13 (11)
Grade 2-4 AEs ≥ 3% <sup>c</sup>		
Diarrhoea	3 <sup>d</sup>	13
Nausea	3	2
Jaundice	7 <sup>e</sup>	0
Scleral icterus	3	0
Myalgia	4	0
Lipodystrophy	3	3
Grade 3-4 laboratory abnormalities (%) <sup>f</sup>		
ALT elevation	5	3
AST elevation	3	4
Total bilirubin elevation	53 <sup>g</sup>	< 1
Neutropenia	8	10
Thrombocytopenia	5	5



By end of trial:  
20% in LPV/r arm  
9% in ATV/r  
on lipid lowering Rx

Johnson, AIDS 2006



ATV/RTV	120	115	113	93	72	67
LPV/RTV	129	115	112	105	70	65
ATV/SQV	115	102	96	80		



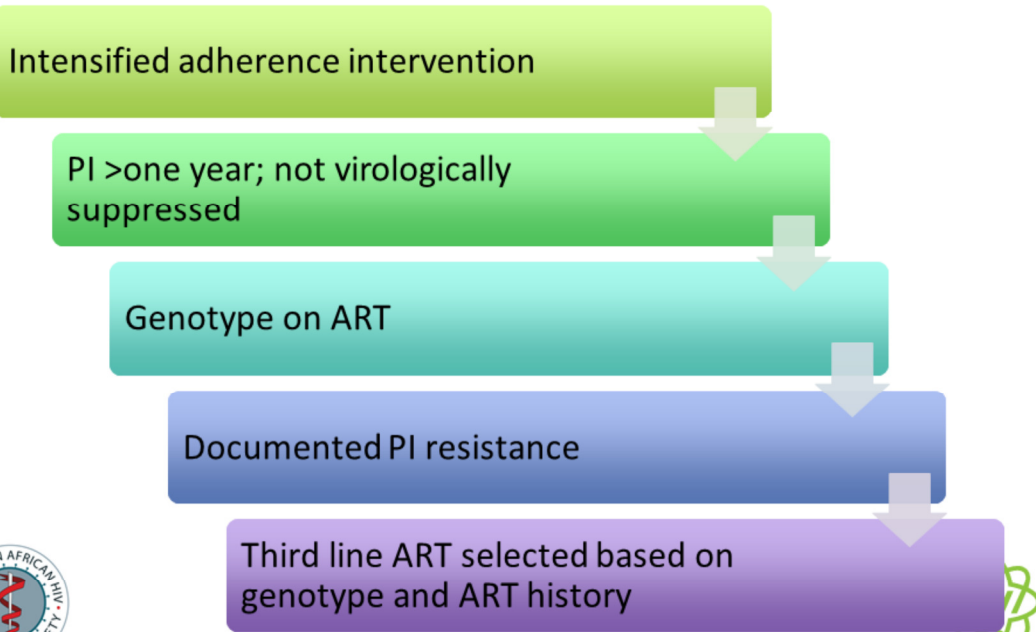
Discuss

**AEs:** diarrhoea, jaundice

**Efficacy**

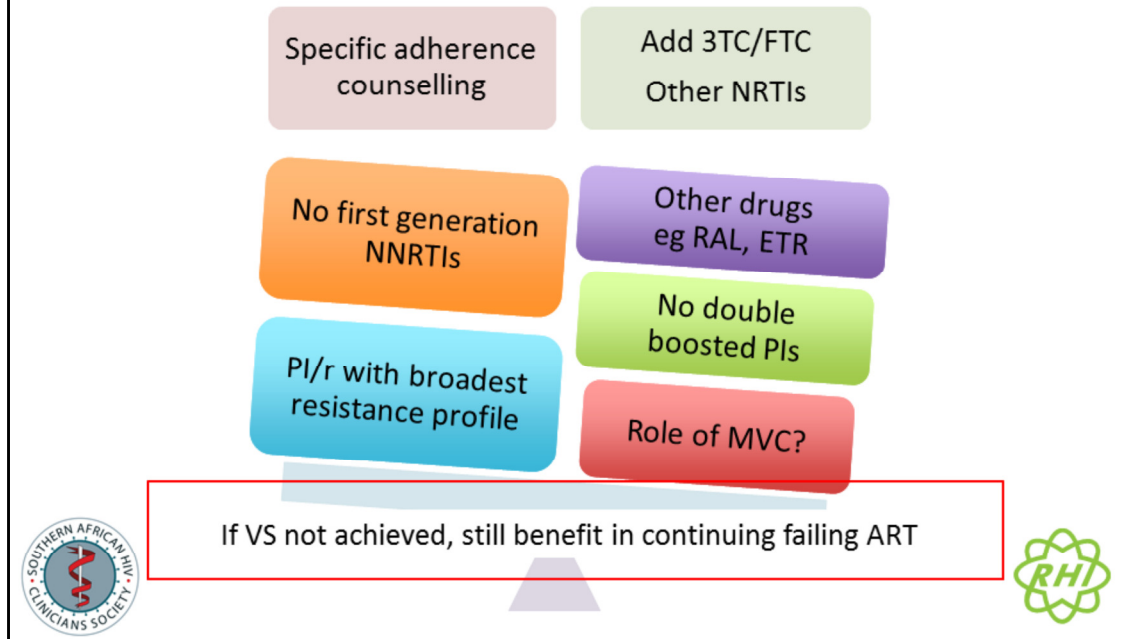
Use of **lipid lowering** agents on LPV/r

# Patients failing on second line ART



- **Patient failing 2<sup>nd</sup> line (2 x VL >1000 copies/mL taken 2-3 months apart)**
  - Check adherence (pharmacy refills and self-report)
  - Intensified adherence support
  - Genotype resistance test
  - Salvage if significant lopinavir/atazanavir resistance
  - Use Stanford database resistance test analysis and treatment history to design salvage regimen
- Third-line ART (also referred to as **'salvage' therapy**) is used when a patient has experienced virological failure on drugs from the NRTI, NNRTI and PI classes, and has documented PI resistance.

## Third line regimen: principles



- Need **specific adherence counselling** in patients preparing to start third-line ART, with a frank discussion that this regimen is likely to be their last option for the foreseeable future.
- First-generation NNRTIs (**NVP and EFV**) have no place in third-line therapy as they do not impair viral fitness.
- A **boosted PI with the broadest resistance profile** should be selected (this is currently DRV). DRV must be used twice daily in this context (600 mg 12-hourly with 100 mg RTV 12-hourly). LPV may be used if the drug is still active based on a resistance test (e.g. if the patient failed second-line ATV therapy).
- The addition of **3TC (or FTC)** is recommended as the M184V mutation that it selects for impairs viral replication.
- **Other NRTIs** (the most active based on resistance testing) should also be added.
- Consideration of the addition of **other salvage drugs** (e.g. RAL and/ or ETR or RPV) will depend on the results of genotype resistance testing and cost issues.
  - **RAL** is preferred because it belongs to an entirely new class with no risk of cross-resistance from prior ART exposure in first- and second-line therapy.
  - Because most patients are not receiving an NNRTI at the time of failing second-line therapy when a genotype resistance test is typically performed, prior NNRTI mutations related to first-line NNRTI failure may be archived at this time. Therefore, it is difficult to be certain from

this genotype whether **ETR** is compromised; however, data from SA suggest that the majority of patients who have failed NVP or EFV are still susceptible to ETR.

- We advise **against** double RTV-boosted PIs.
- **MVC** (a CCR5 blocker) is a consideration for salvage therapy; however, it is currently extremely costly and can only be used after a tropism test demonstrates that the patient's circulating virus has sole tropism for the CCR5 coreceptor. We advise only considering this for a salvage regimen when there is intermediate- or high-level resistance to all PIs, all NNRTIs and all NRTIs.
- If viral suppression is not achieved on salvage therapy, then there is still benefit in continuing failing ART, because of the residual partial activity and 'crippling' effect of such ART. 'Crippling' describes the fact that mutant viruses often have less replicative capacity. Provided that the VL can be maintained at <10 000 copies/mL, the CD4+ count will usually be maintained or even increase.

# Outcomes



# VS on salvage ART:

AfA programme (n=152)

145 (95.4%) had at least one viral load performed on salvage ART

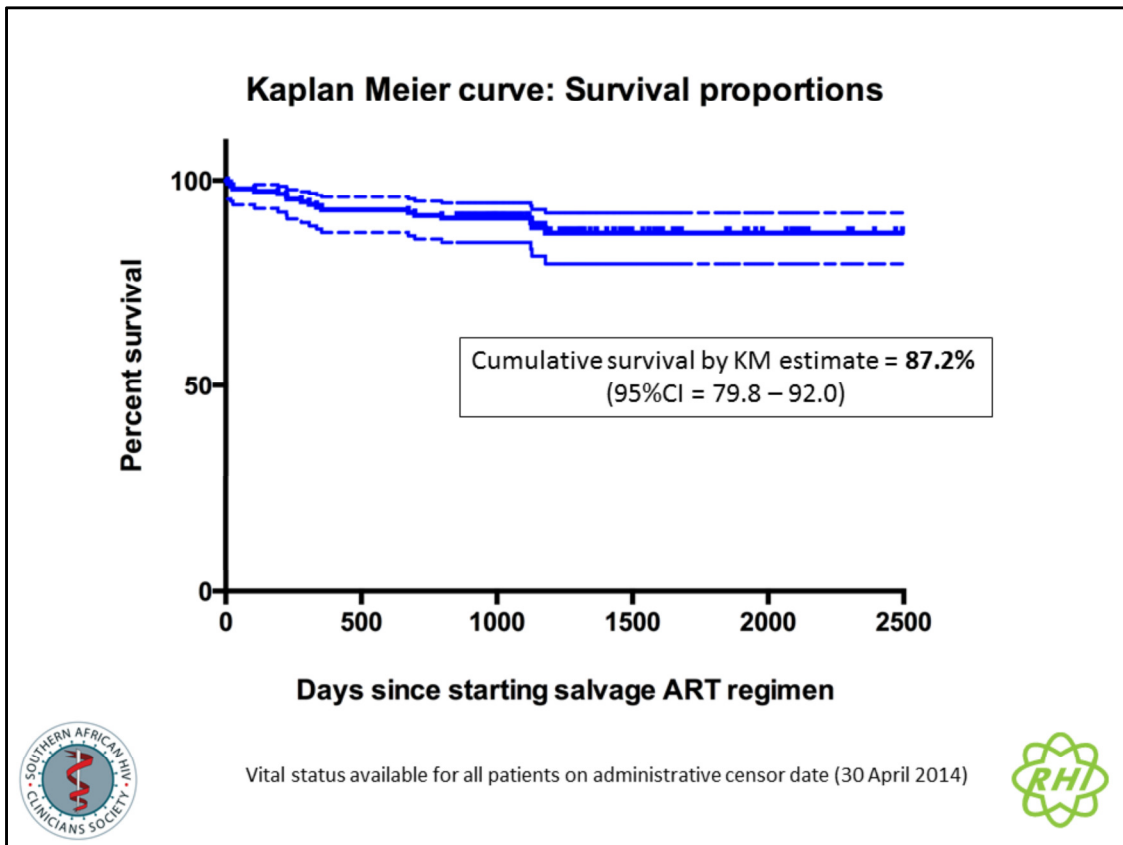
	n	% of those who had VL performed (n=145)	% of whole cohort (n=152)
Suppressed <400 copies/mL	126	86.9%	82.9%
Suppressed <50 copies/mL	108	74.5%	71.1%



Dunn, unpublished



- Demonstrates salvage regimens are suppressive
- Adherence support helps

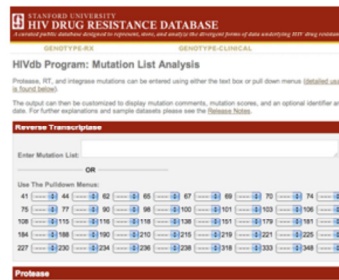


Most NB slide – 2500 days is almost 7 years



# Resistance testing

- At first line failure if resources permit
  - Differentiate adherence issues from resistance
  - Informative ETR/RPV mutations (third line)
  - Which NRTIs?
- Patients receiving PI-based first line who are failing
- Second line failure



- A resistance test at first-line failure should be considered if resources permit.
- In many settings in the region, this is unaffordable and/or unavailable.
- Benefits include that it may be able to differentiate between adherence problems (when the resistance test shows no resistance mutations) and the development of resistance
- Informative regarding ETR or RPV mutations in subsequent third-line regimens
- Help decide which NRTIs to use in second-line therapy, although the recently published **EARNEST** (Europe-Africa Research Network for Evaluation of Second-line Therapy) trial shows **that even without the use of a resistance test to decide upon which NRTIs to use in second-line therapy, virological outcomes are good** and equivalent to a PI + RAL regimen

# ART when renal impairment

## Acute and chronic kidney injury

- ABC standard dose + 3TC (adjust dose based on CrCl) + EFV
- If renal impairment resolving readjust to standard doses

## Chronic dialysis

- First line
  - ABC 600mg daily
  - 3TC 50mg x 1 dose then 25mg daily (given after dialysis session)
  - EFV 600mg nocte
- Second line
  - LPV/r (twice-daily) plus 2 NRTIs selected based on resistance test and tolerability considerations



Problems with TDF and AZT in dialysis

### Acute kidney injury

- In patients with AKI, dosages of **NRTI** drugs should be adjusted based on estimated CrCl calculation.
- **TDF should be interrupted** even if it is not thought to be the cause of the AKI.
- Once there is clear evidence that renal function is improving (creatinine on downward trend), **NRTI** dosages should be readjusted to standard dosages to avoid underdosing.
- In patients with AKI who are not yet receiving ART, **initiation is preferably deferred** until AKI has resolved.

### Chronic renal patients

- Patients with HIV may develop end-stage renal failure requiring chronic haemodialysis owing to HIV-associated nephropathy or an HIV-unrelated cause.
- In patients on chronic haemodialysis, there are a number of important ART issues that arise.
- **NRTI** class is **eliminated through the kidneys**, and thus doses of most NRTI drugs need to be adjusted in patients on dialysis.
  - Although **TDF** can be used in patients on chronic haemodialysis, dosing is once weekly, which can be difficult for patients to remember.
  - **AZT** is generally avoided because of anaemia associated with chronic

renal failure.

- **Daily** dosages or the **evening doses** of a twice-daily regimen of ARVs on the day of haemodialysis should be given after the haemodialysis session.
- **NNRTI** drugs do not require dose adjustment.

# Dosage adjustment in renal failure

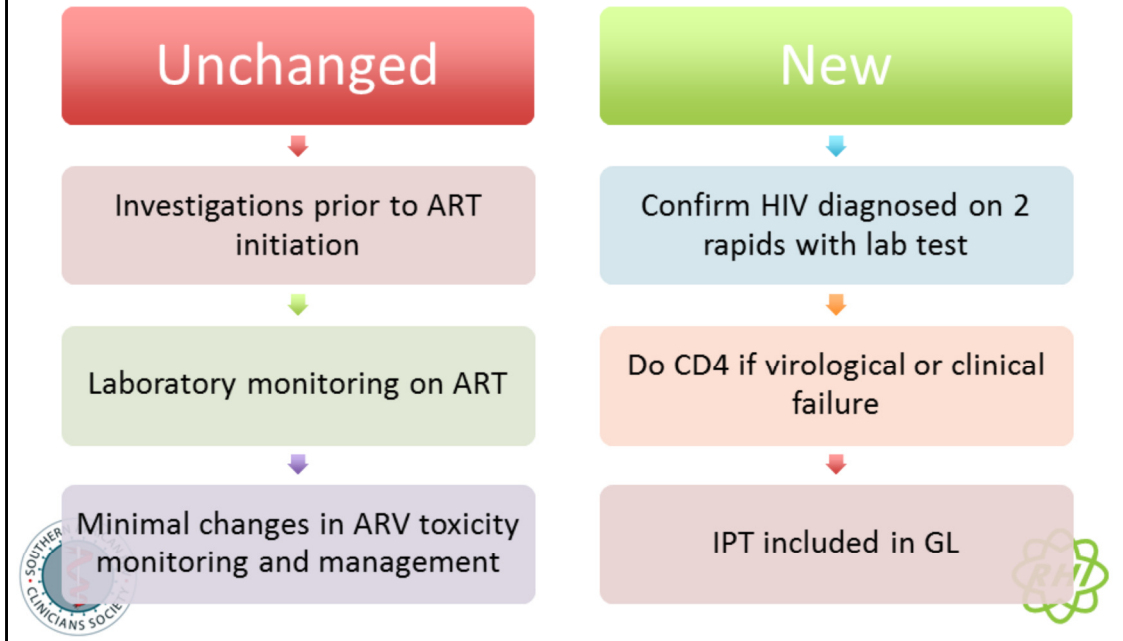
Drug	CrCl (mL/min) <sup>§</sup>		Haemodialysis (dose after dialysis)	Peritoneal dialysis
	10 - 50	<10		
TDF	AVOID	AVOID	300 mg once weekly	Unknown
ABC	Unchanged	Unchanged	Unchanged	Unchanged
3TC	150 mg daily	50 mg daily <sup>†</sup>	50 mg first dose and thereafter 25 mg daily <sup>†</sup>	50 mg first dose and thereafter 25 mg daily <sup>†</sup>
AZT	Unchanged	300 mg daily	300 mg daily	300 mg daily
d4T	15 mg 12-hourly	15 mg daily	15 mg daily	Unknown
ddI	>60 kg body weight: 200 mg daily <60 kg body weight: 150 mg daily	>60 kg body weight: 125 mg daily <60 kg body weight: 75 mg daily	>60 kg body weight: 125 mg daily <60 kg body weight: 75 mg daily	>60 kg body weight: 125 mg daily <60 kg body weight: 75 mg daily



No dosage adjustments needed for NNRTIs, PIs and InSTIs



## What else?



- If HIV diagnosis has been made using two rapid tests performed outside of a laboratory setting, then we advise confirming the positive serostatus using a laboratory test prior to commencing lifelong ART.
- A detectable VL result would be sufficient (note that it may be undetectable in <1% of patients not receiving ART, i.e. 'elite controllers')
- If unaffordable/unavailable, then an ELISA should be performed.
- CD4+ counts should be performed every 6 months.
- In patients being monitored with VL measurements, once the CD4+ count is >200 cells/ $\mu$ L, provided that the VL is suppressed, routine CD4+ testing can be stopped, as it adds little to management. Data to support this have recently been summarised in the guidelines
- If virological or clinical failure occurs, then a CD4+ count should be repeated, as CTX prophylaxis should be commenced if the count falls to <200 cells/ $\mu$ L while receiving ART.

Sometimes the  
questions are  
complicated  
and the  
answers are  
simple.



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# Guidelines

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