

Conserving ART where treatment options are limited.

Catherine Orrell
2nd October 2006

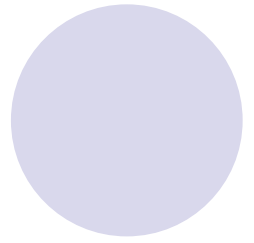
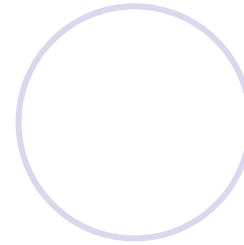
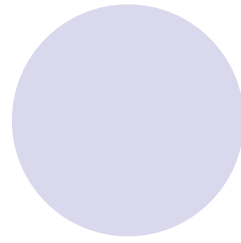
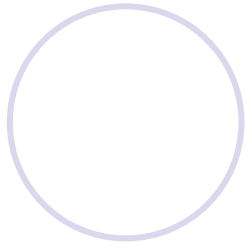
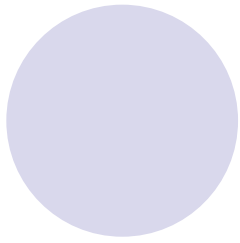


South African National Antiretroviral Programme makes 2 treatment regimens available:

1. d4T, 3TC and efavirenz or nevirapine – standard first line
2. ddI, AZT and Lopinavir/rtv - standard second-line

In SA in 2006 we are treating ~ 200 000 of ~ 5 000 000 people eventually needing antiretroviral treatment.

This is less than 40% of those who need treatment at present and only 4% if the expected future need.



Reasons to make efforts to keep people on first line :

COST RELATED

Second-line therapy much more expensive than first line.

	Cost/ month:		Cost/ month:
d4T	R23.00	ddl	R160.00
3TC	R44.00	AZT	R 81.00
NVP	R43.00	LPV/r	R313.00
TOTAL:	R110.00	TOTAL:	R554.00

Five times more costly to be on second-line ART.



Reasons to make efforts to keep people on first line:

STAFF RELATED

Those going onto second-line require / have already taken much time and attention.

As this is their last chance, adherence is key.

Small number of people use up many valuable staff resources i.t.o. counseling, lab, medical staff.



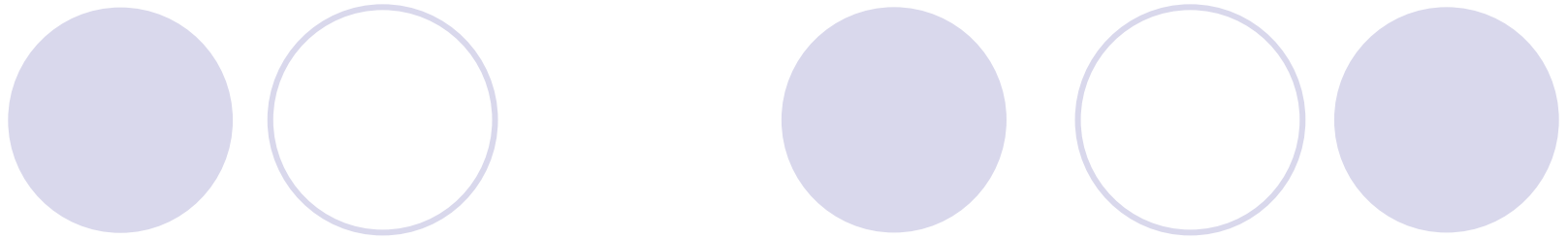
Reasons to make efforts to keep people on first line:

DRUG RELATED

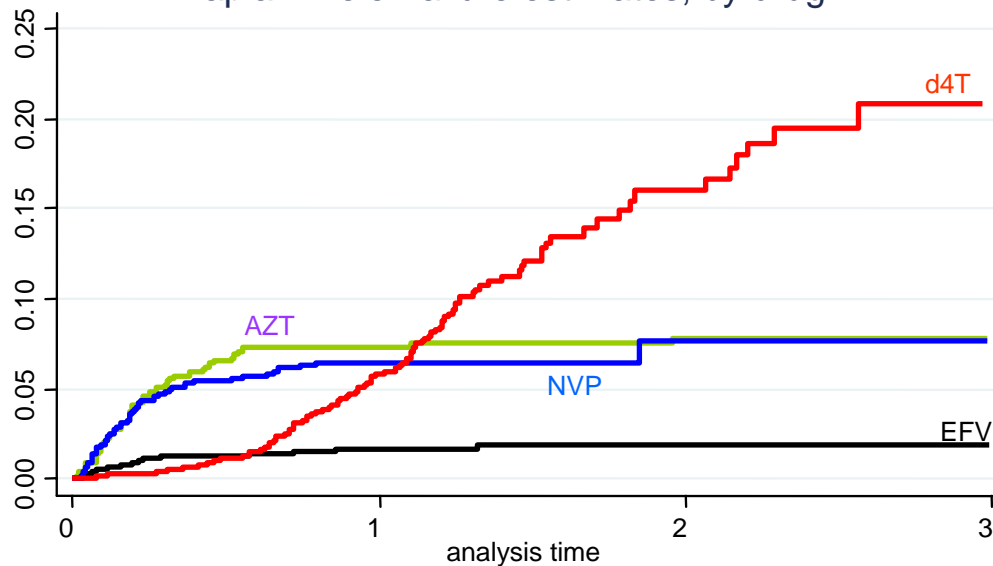
First-line may undermine second-line therapy:

- Resistance to d4T (TAMs) undermines use of AZT in second regimen.
- Often use AZT in first line regimen, due to d4T toxicities e.g. lipodystrophy, peripheral neuropathy, hyperlactataemia.

Second-line therapy more complex to take: more tablets, ddl requires an empty stomach, etc.

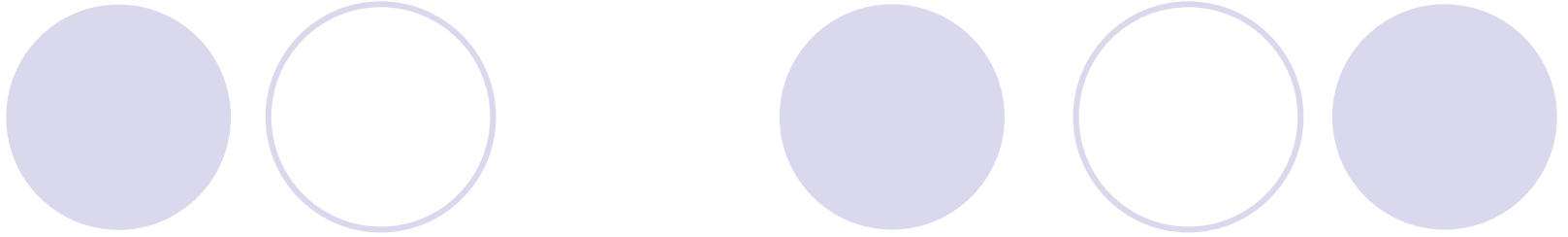


Kaplan-Meier failure estimates, by drug



	n	n				Changed by 36 months (% , 95% CI)
AZT	676	469	295	126	7.8 (5.9-10.3)	
EFV	1,613	858	334	74	1.9 (1.3-2.8)	
NVP	1,062	376	75	44	7.6 (5.3-10.9)	
d4T	1,996	782	137	15	20.8 (16.2-26.5)	

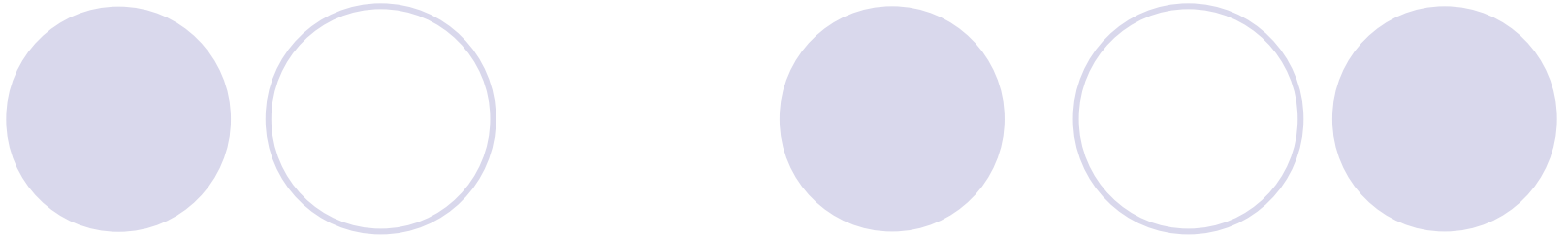
**Cumulative regimen substitutions due to toxicity by individual drug:
combined data from 2679 people on ART from Khayelitsha and Gugulethu.
Slide courtesy of Andrew Boule.**



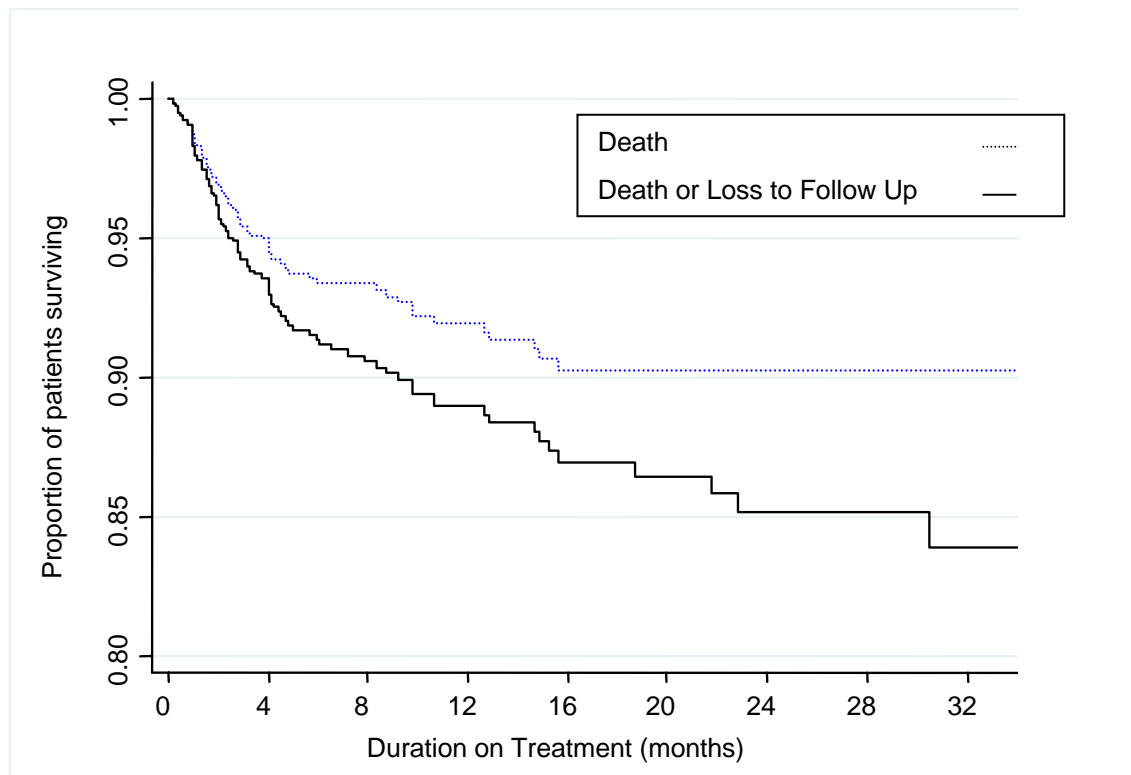
When and where do we lose people from first-line?

Programme losses

1. Death
2. Loss to follow-up
3. Transfer to other clinics - shouldn't be considered a loss.

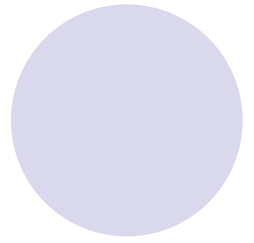
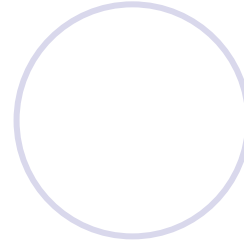
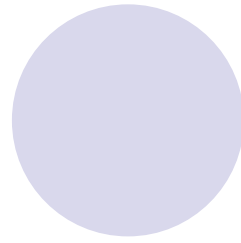
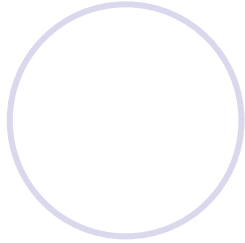
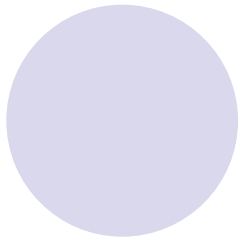


Kaplan-Meier survival estimate for time to death and death or loss to follow-up for 929 naïve people commencing therapy in Guguletu.



Number at risk at end of period

929	641	421	328	229	162	127	86	51
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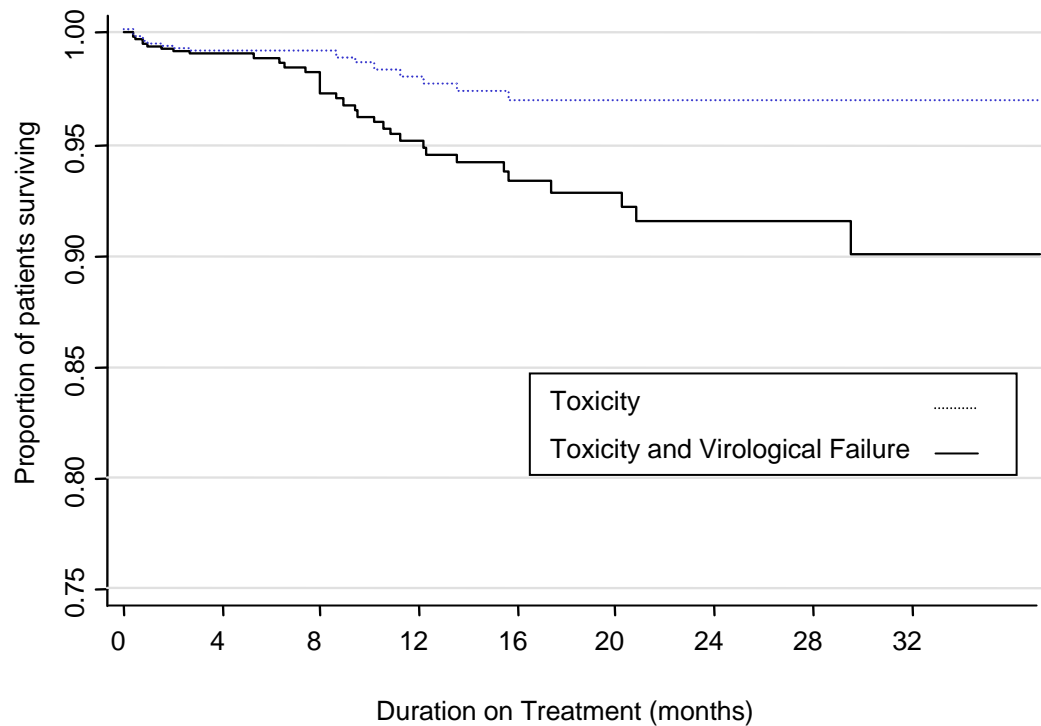
When and where do we lose people from first-line?

Individual losses

1. Toxicity
2. Virological failure

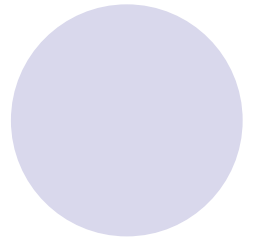
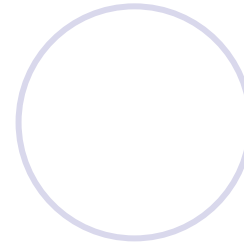
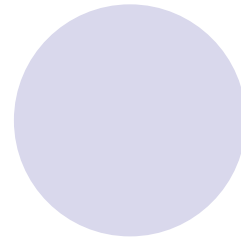
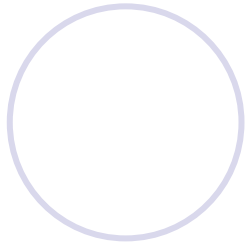
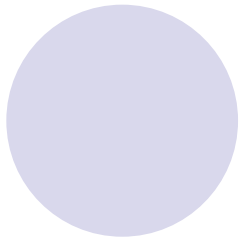


Kaplan-Meier survival estimate for time on first line therapy. Censoring occurred at time of treatment switch to a protease-based ART regimen due to toxicity or confirmed virological failure for 929 naïve people



Number at risk at end of period

929	636	414	311	212	151	117	80	45
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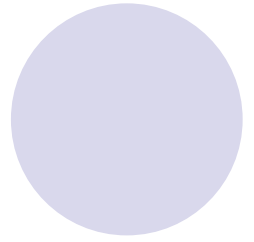
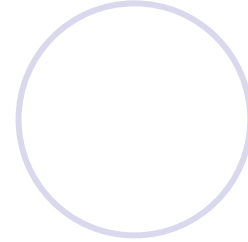
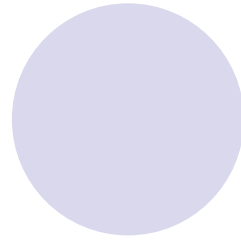
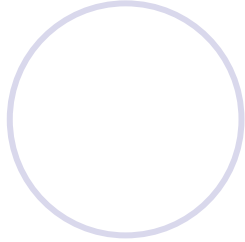
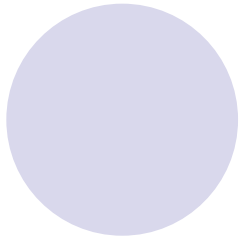
How do we keep people on first line?

ADHERENCE!!!

Both to programme and medication.

To programme:

- Systems to note loss early – through dispensary?
- Efforts to recall those lost to follow-up – treatment partners / community counselors
- Pre-empt December period – give 2 months medication
- Make transfer to other sites as easy as possible

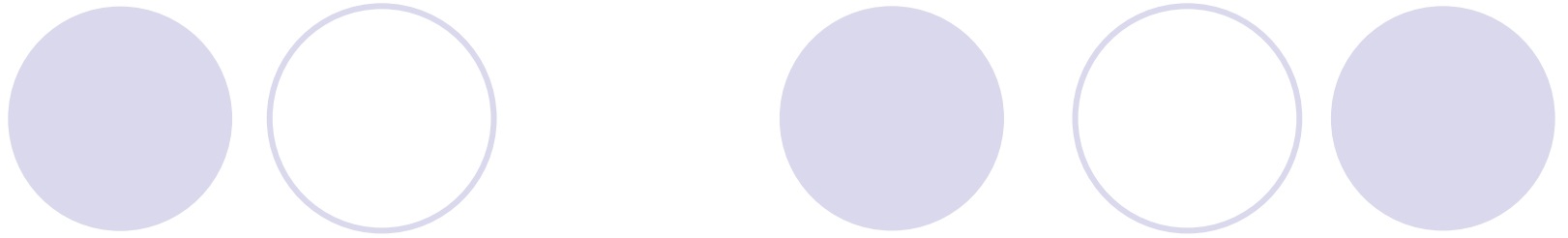


How do we keep people on first line?

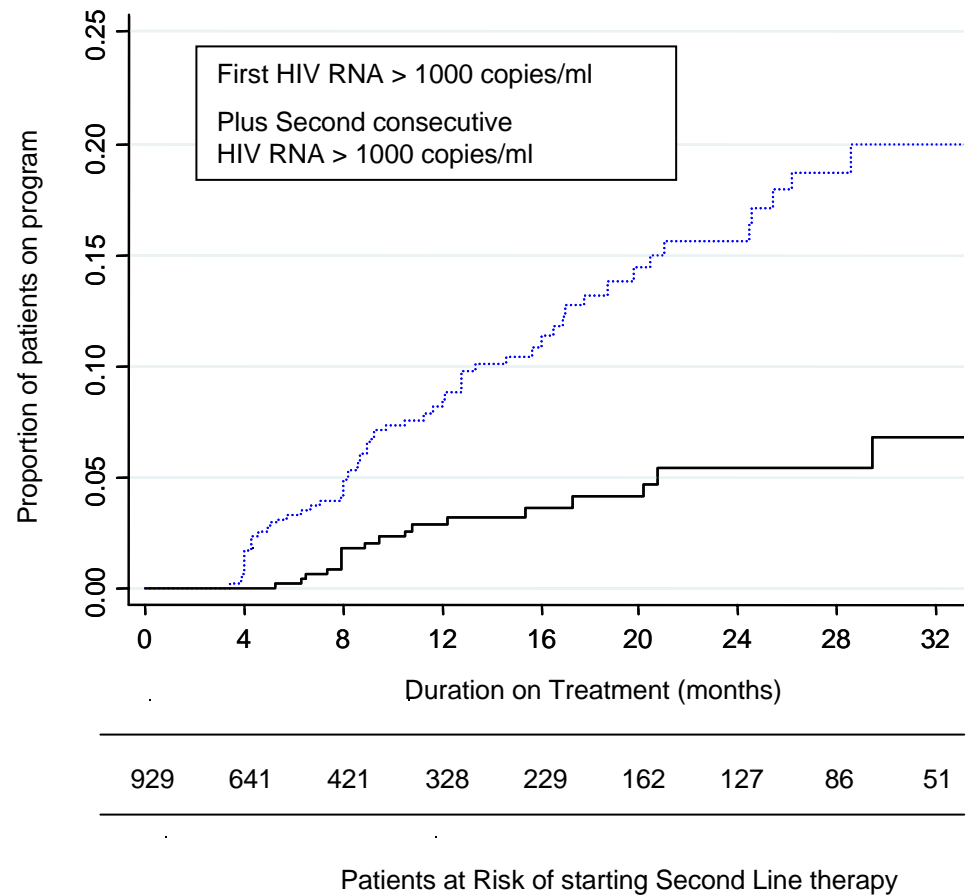
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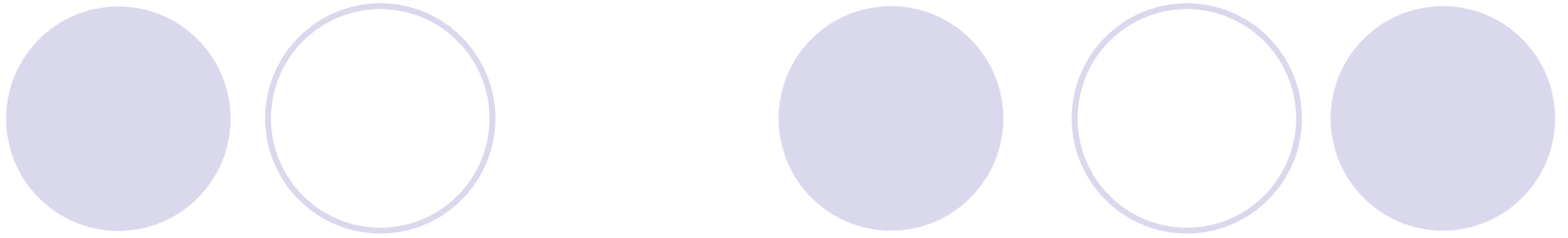
To medication:

- Simplify regimens if/when possible.
- Note regular arrival for medication.
- Tablet counts where possible.
- ACT EARLY on a reduced tablet count or raised viral load – programme of re-education; increased visit frequency, pill boxes, dosing diaries e.g. Guguletu “red alert” system.



Kaplan-Meier failure estimate for time to first, then second consecutive HIV RNA level > 1000 copies/ml.

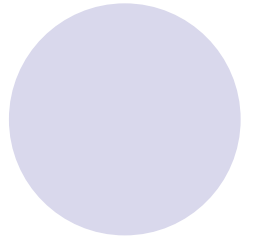
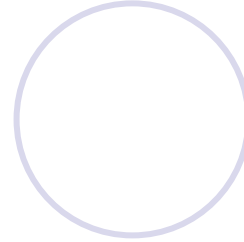
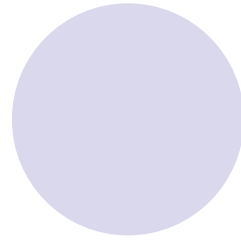
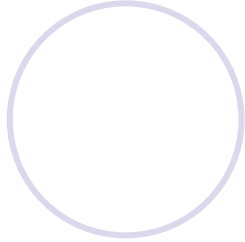
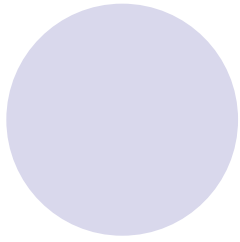




And to address toxicity?

Tenofovir?

- Similar cost to AZT, but more than d4T.
- In first-line: decreased d4T toxicity, no TAMs, once/day dose... but costly.
- In second-line: Cleaner regimen, less toxic. Would allow swap from d4T to AZT without impact on 2nd line.



In conclusion:

We need to treat more people!

Make first line as straightforward as possible (triomune®, atipla®)

Allow for common changes due to toxicity

Focus on adherence within programme and to first-line therapy.