

End-user factors influencing ARV formulations

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In praise of grandmothers

Also



- Age, food requirements, diet/feeding & other factors
- Characteristics of formulations & relationship to adherence

Tools for giving medicines



Syringe management

- Expel air
- Explain where the plunger must be
- Syringes lose markings & need regular changing

Counseling

- Pre initiation
 - 2 or 3 visits
 - Dr & adherence monitor
- Individualized
- Repetitive
- Doctor spends average of 45 minutes per patient

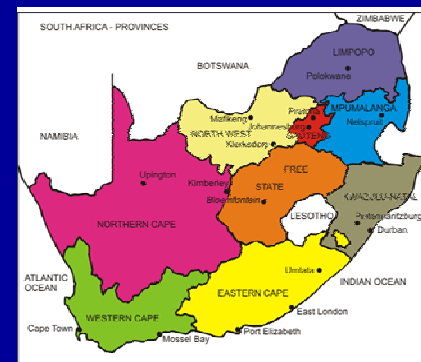
Foods most commonly used (RTV/EFV)

- Yogurt
- Condensed milk
- Peanut butter
- Maize (corn) porridge

Do you have access to a refrigerator - ~80% have access in W Cape, RSA

- Is it broken?
- Do you have electricity?
 - Do you use it?
 - What is your source?
 - Conventional
 - Alternative

Areas of concern



- Travel
 - Need cooler boxes
 - 24 - 48 hrs to reach Eastern Cape
- Need cupboard for drugs (out of reach)
- Plan for and include all aspects of polypharmacy
- Shared care
 - No one takes responsibility
- Sick mothers
- Lack of disclosure
- Decanting into bottles to save money leads to mistakes
- Children with encephalopathy struggle with tablets

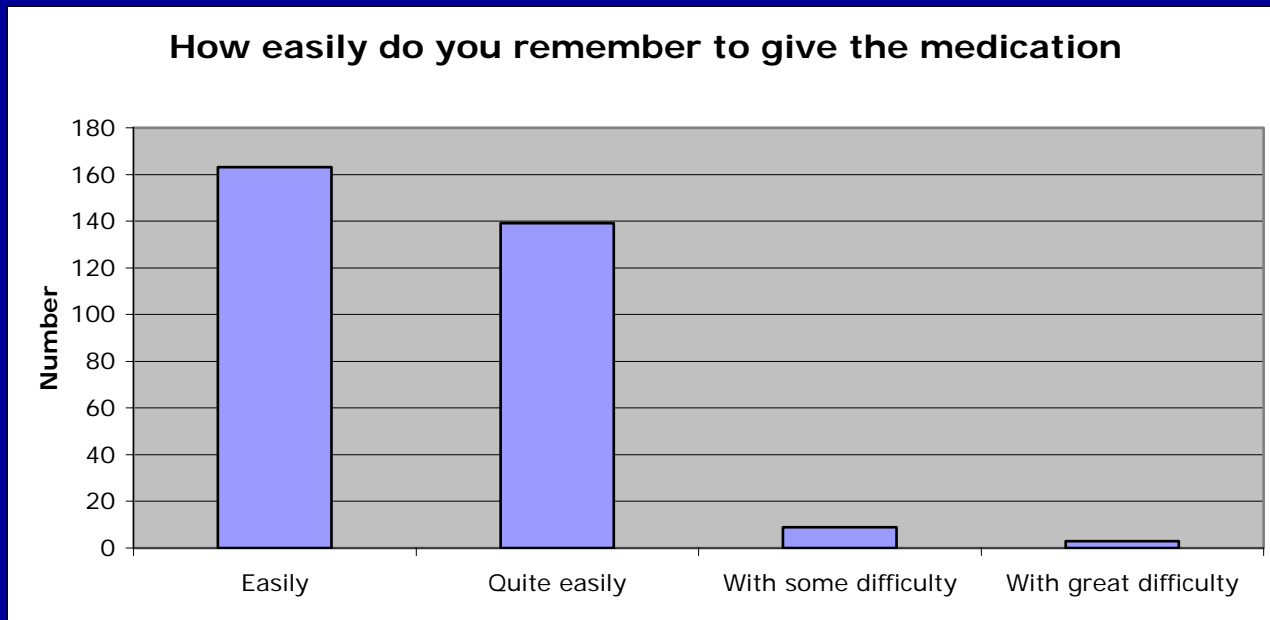
How not to open a child-proof container



Swallowing tablets or capsules

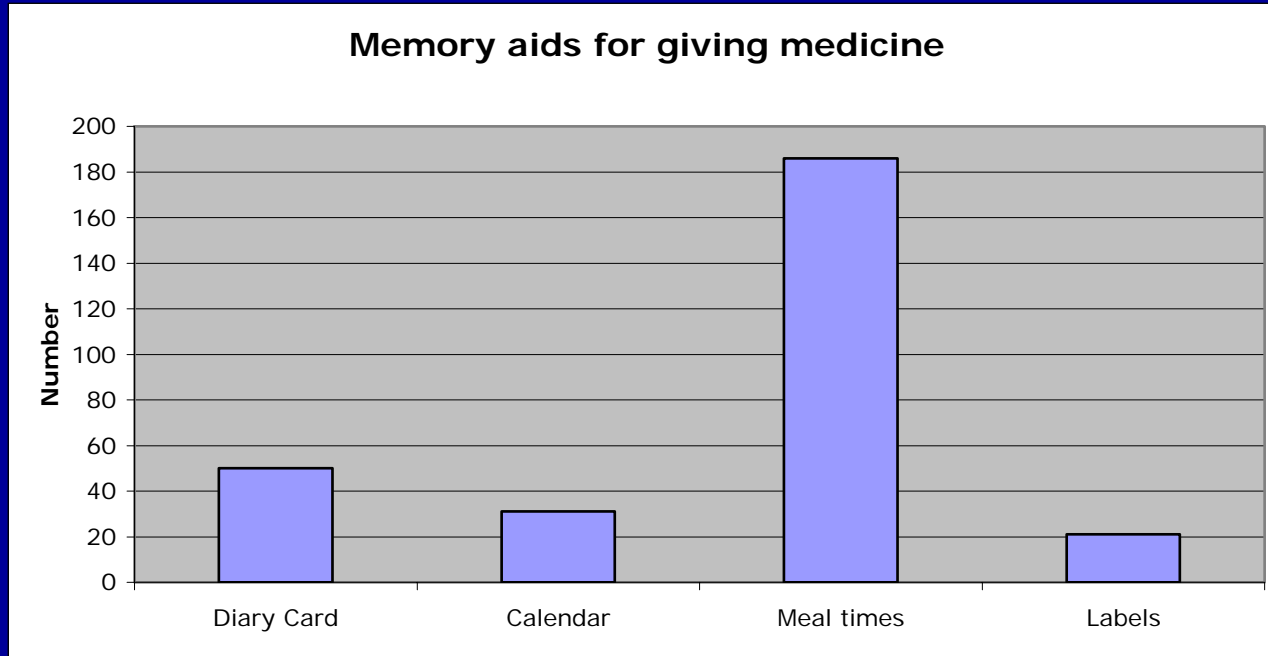
- Can start from 2 1/2 to 3 years in selected children

How easily do you remember to give medication?



INH - TMP/SMX study with 50% on ART

How do caregivers remember to give medication?



How much does the medication interfere with your family life?

A lot	7
Quite a lot	7
Not much	28
Not at all	270

Over the past 7 days, how many doses have been given or missed?

No Drugs Missed	287
Ran out of drugs	4
Forgot to give them	6
You feel the drugs are harmful	1
Difficult to give with school hours, meals, sleep	2
You didn't want to give them	
You didn't want other people to know about the meds	
You, the caregiver were ill	3
The child was ill	2
Your routine had changed (school holidays, weekends)	1
You were fed up with giving the drugs	
The child refused to take them	1

Other reasons for not giving medicine

- Husband ill, needed more attention than the child
- No food in house, wanted to give medicines with food

Lamivudine

- Can give with food
- 2X daily
- Tablets can be broken



10mg/ml



150 mg

Zidovudine

- 180 - **240** mg/m²
- Can give with food
- 2X daily
- Capsules sealed



Stavudine

- Must refrigerate solution
- Use tablets in suspension if no refrigerator
- 1mg/kg/dose
- 2X daily



1mg/ml



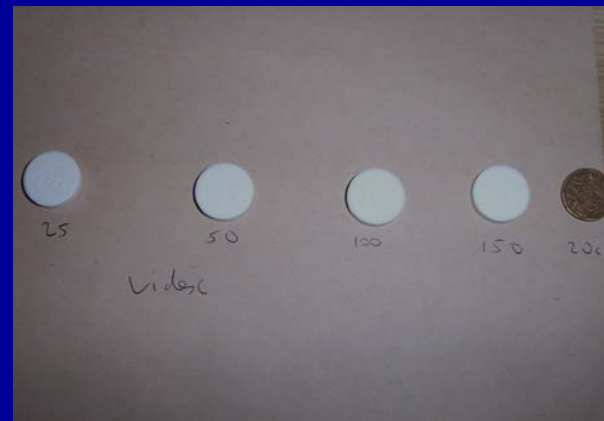
D4T “suspended” in water





Didanosine

- 240mg/m²/day
- X1 or X2 daily
- Refrigerate suspension (stable 1m)
- 30mins pre or 2 hrs post food
- Tabs strengths identical
- Need X2 for buffering
- 2hr interval for RTV
- Total ARV package converted into 3X or 4X daily



Efavirenz

- X1 daily
- >3y & 10kg
- No food restrictions
- Can open capsule
- Give at night



50 & 200mg

Ritonavir

- 400mg/m²
- 2X daily
- With food
- Bad taste -
- If intolerant, stop?
- Line mouth with peanut butter
- Refrigerate once opened
- Capsules large



100mg



80mg/ml

Adherence



- Diary card
- Always reinforce
- Compare returns to amount dispensed

Cohort of children treated at 3 MSF Clinics in Khayelitsha

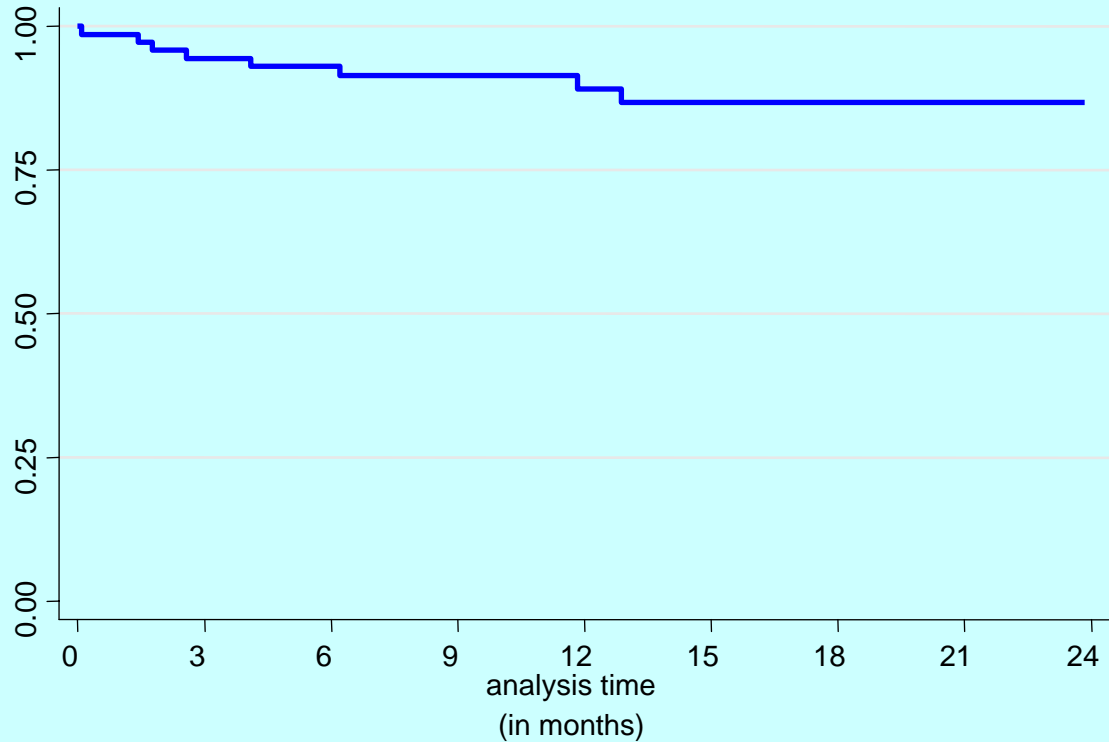
All Patients	n=71*
Age and gender	
Median age in months (IQR)	48 (24-84)
Female (%)	32 (45%)
CD4+ lymphocyte % baseline	
Median (IQR)	11 (6 - 18)
Prior Stage 3/C diagnosis	
Stage C/3 diagnosis (%)	18 (25)
Follow-up time in months	
Median for all patients (IQR)	13.5 (8.1 – 20.7)
Median for those surviving (IQR)	14.7 (9.1 – 21.5)
HIV RNA level at baseline (copies / ml)	
Mean log ₁₀ HIV RNA level (SD)	4.9 (1.0)
Death and loss to follow -up	
Deaths (median duration)	4 (0.1, 1.8, 4 and 6 months)
Loss to follow-up	4 (1.5, 2.5, 12 and 13months)
Initial antiretroviral regimen	
AZT as NRTI (vs. d4T)	n=65 (92)
EFV as NNRTI (vs. NVP)	n=48 (68)

Andre Boulle
UCT

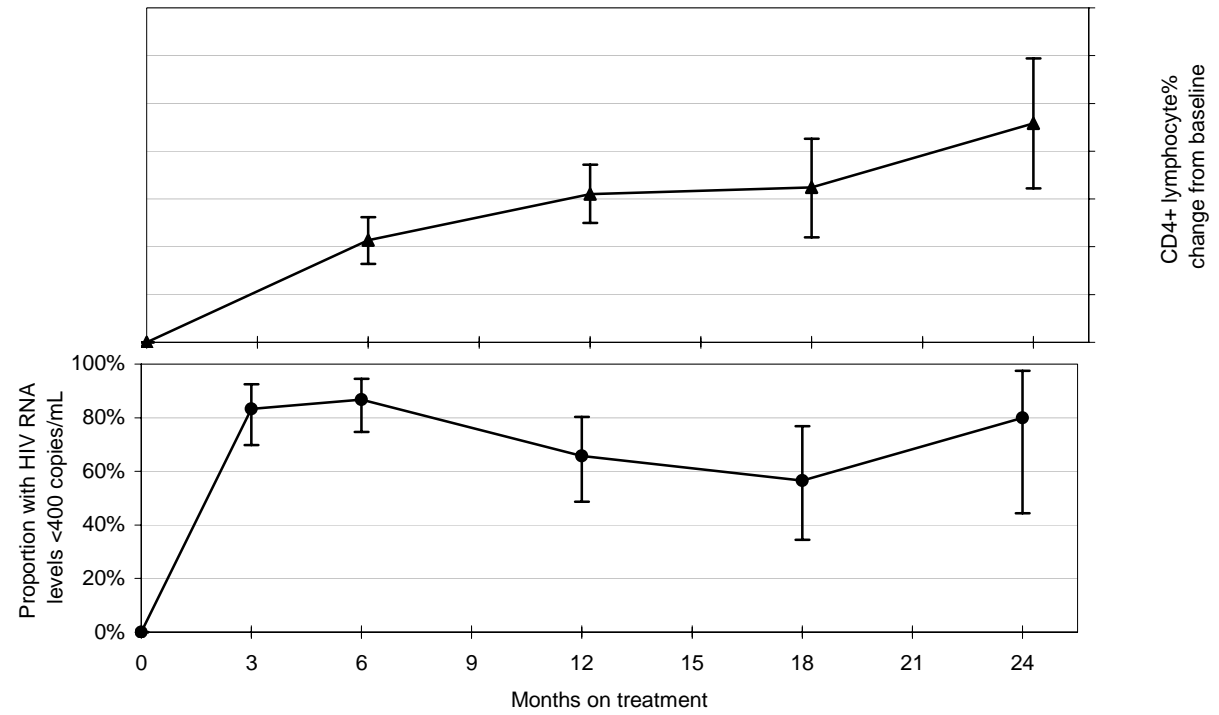
* A baseline CD4+ lymphocyte count was unavailable for 7 patients (n=64)
and a baseline HIV RNA level was unavailable for 15 patients (n=56)

Table 1: Characteristics and starting regimens of patients beginning ART

Kaplan-Meier survival estimate – LTF or death = failure



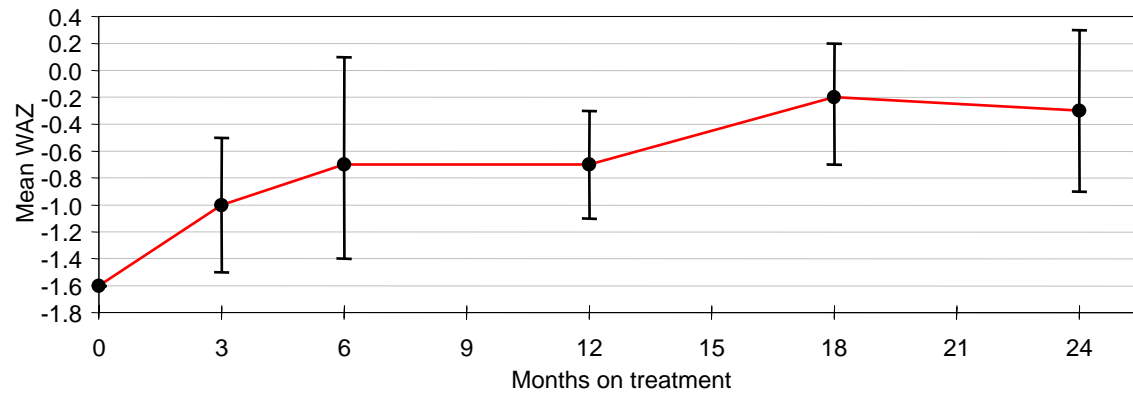
	0	3	6	9	12	15	18	21	24
Number at risk	71	68	62	51	40	31	28	18	13
All Deaths		2	1	1	0	0	0	0	0
Lost to follow-up		2	0	0	1	1	0	0	0
On second-line regimen		0	0	0	0	1	2	2	2
Percentage surviving		94.4	92.9	91.4	89.1	86.7	86.7	86.7	86.7
95% confidence interval		85.7 - 97	83.9 - 96	81.8 - 94.7	78.2 - 93.3	74.6 - 93.3	74.6 - 93.3	74.6 - 93.3	74.6 - 93.3



Number on treatment	71	68	62	40	28	13
Number with CD4+ lymphocyte counts			43	34	17	9
Median change from baseline			11	16	16	23
Interquartile range			(8.3 - 13.2)	(12.4 - 18.5)	(11.1 - 21.4)	(16.1 - 29.7)
Number with viral load results		48	53	38	23	10
Percentage < 400 copies/mL		83.3	86.8	65.8	56.5	80.0
95% confidence interval		(69.8 - 92.5)	(74.7 - 94.5)	(48.6 - 80.4)	(34.5 - 76.8)	(44.4 - 97.5)

Changes in CD4 cell count and viral load by duration on treatment

Change in WAZ over time in response to ART



n=	71	63	64	39	25	13
Mean WAZ	-1.6	-1.0	-0.7	-0.7	-0.2	-0.3
95% confidence interval	(-1.5 - -0.5)	(-1.4 - -0.1)	(-1.1 - -0.3)	(-1.1 - -0.3)	(-0.7 - -0.2)	(-0.9 - -0.3)

56/61 for whom current regimen could be determined are not using any syrups or suspensions

Median age of children at time of last visit to the clinics, by formulation type

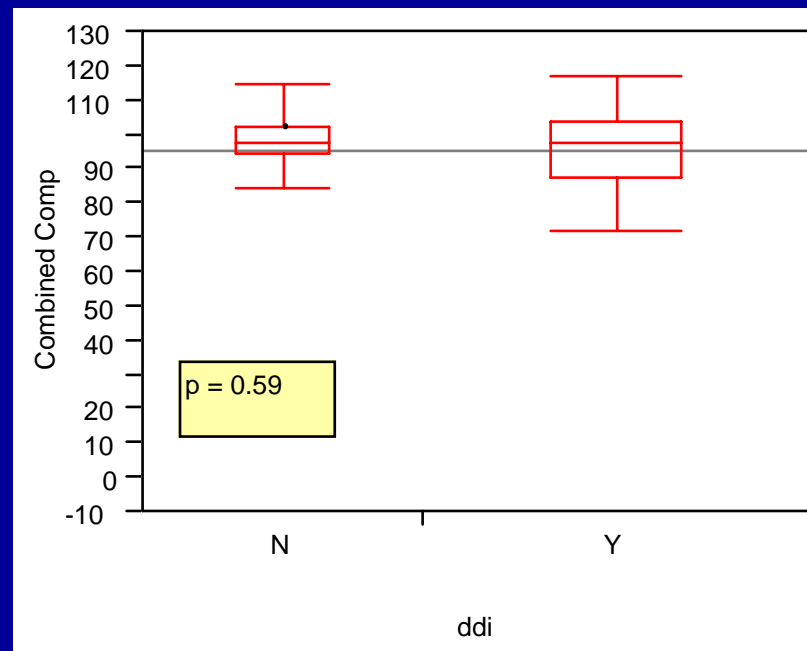
	n	p25	p50	p75
Syrups or mixed	5	34	38.8	66.8
Tablets exclusively	56	66.2	80.4	112.2

Assuming all clients starting in “Site B” and “Michael Mapongwana” clinics after mid-2003 were receiving solid formulations, and those starting in “Site C” before 2003 were receiving syrups, viral load outcomes as follows:

		3 months	6 months
Syrups	n	22	25
	% < 400 cps/mL	82%	84%
Tablets	n	9	12
	% < 400 cps/mL	78%	100%

Numbers too small at this stage for valid comparisons, but detailed analysis with more children is underway

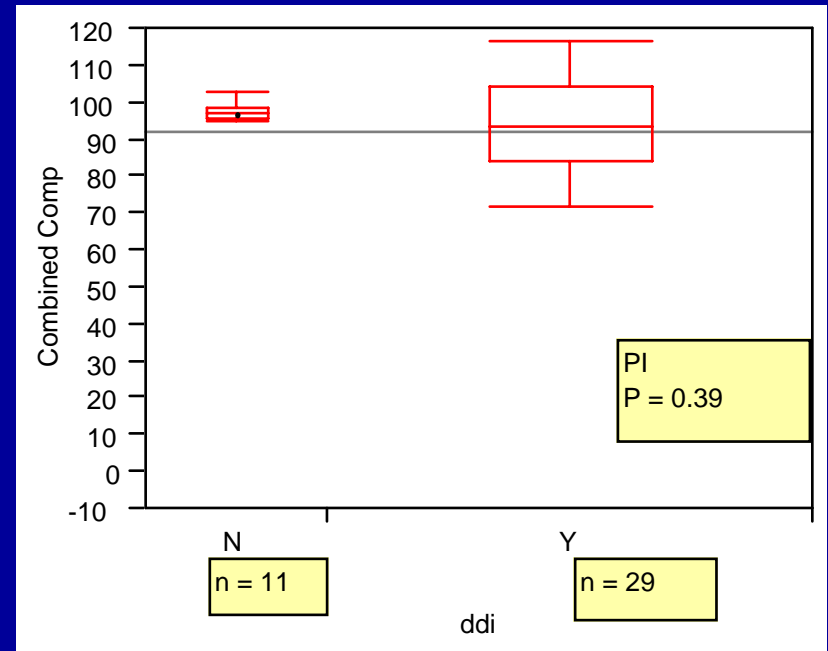
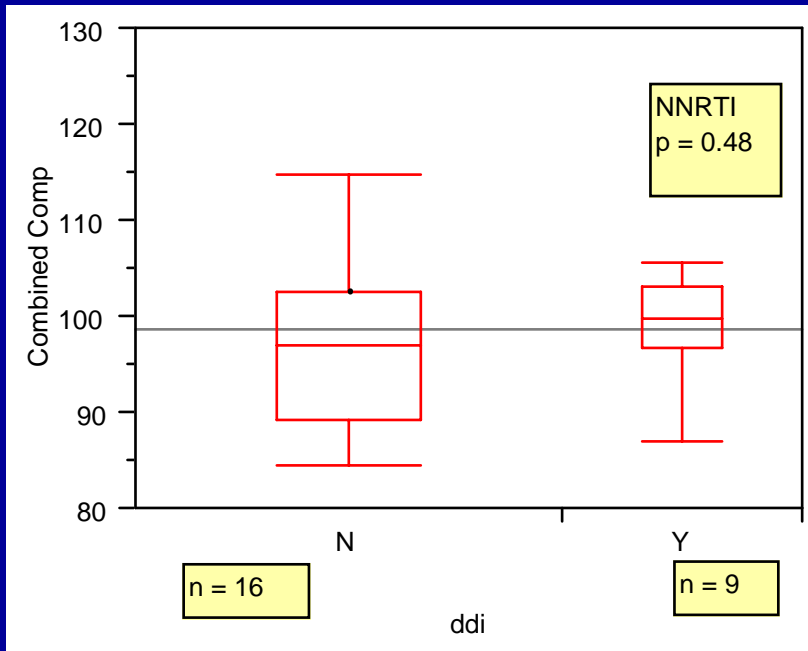
Does ddi adversely affect compliance?



Compliance measured as % returned/issued

22 subjects with advanced disease

Effect of ddi on compliance PI vs NNRTI



Compliance measured as % returned/issued

Conclusions

- Reasonable adherence & efficacy
- Labour-intensive
- With scale-up, anything that simplifies will help

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