2015 treatment update

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Hot topics: dramatic changes in 2015

- May 2015 - START study results – new and unexpected
- June 2015 - BHIVA guidelines – biggest changes for ten years
- July 2015 – WHO guidelines
- July 2015 – More results on treatment as prevention (TasP) and PrEP
- Same-day ART – a new model for the UK?
- Very early ART and cure research

Good time for a change…

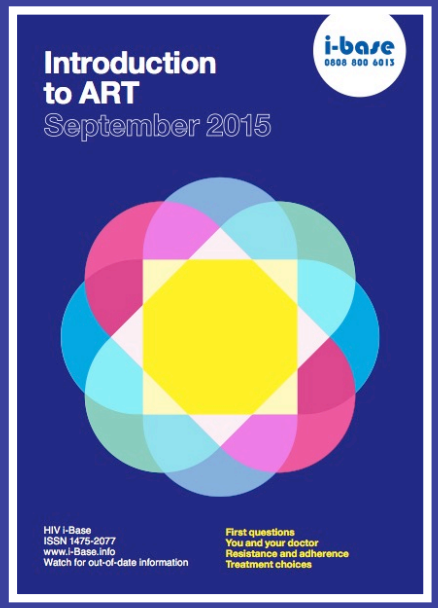
The Smiths, 1984

2015

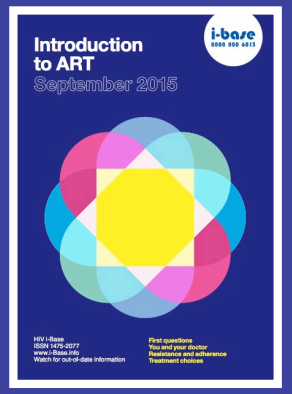
"ART will increasingly become the routine next step after finding out you are HIV positive.

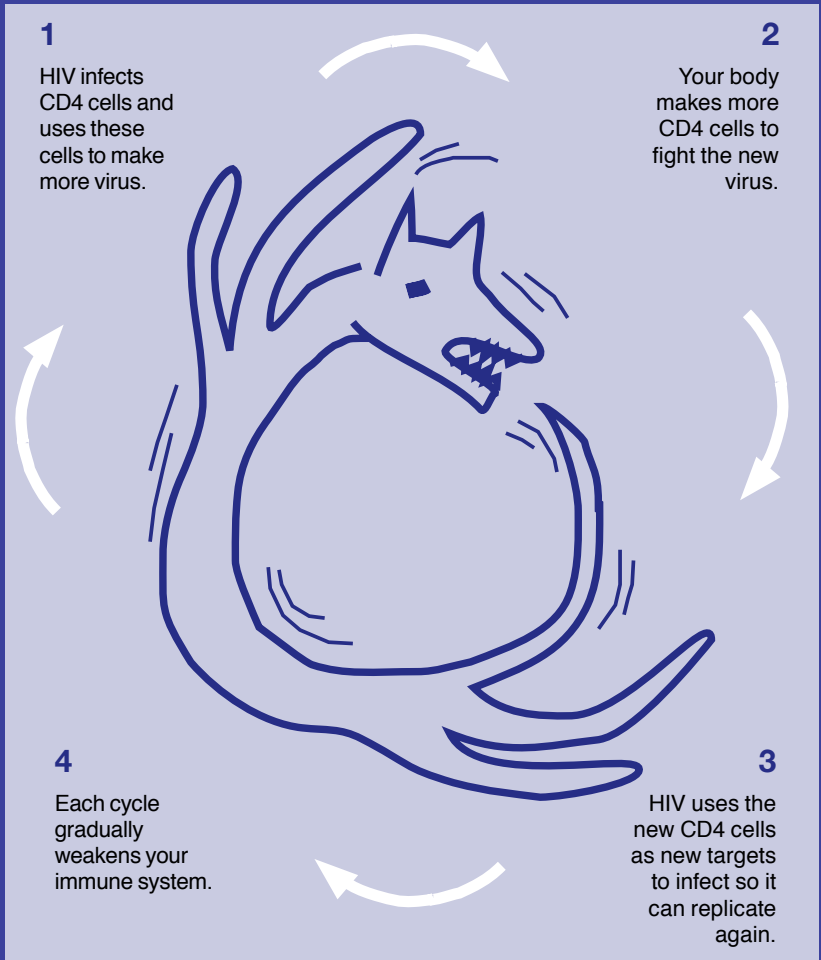
Starting ART can be one of the most empowering ways to deal with the shock of being diagnosed.

By taking control over this aspect of HIV, you can carry on with your life."



Before ART, your immune system is like a dog chasing it's own tail





After viral load becomes undetectable your body stops this overproduction of CD4cells.

Your immune system repairs itself and gets stronger.

Time to ART is now:

"delay until ART"

START study summary

- 4685 people with CD4 above 500
- Randomised to immediate (early) or deferred (late) ART
- “Clinical endpoint” study – counted serious events: AIDS & non-AIDS
- Followed for over 3 years
- May 2015 - stopped 18 months early due to significant benefits with early ART.
- Disclaimer: personal invovelment

START – who were enrolled

- Median age 36 (range 18-81)
- 27% women
- 55% gay men
- 50% high/low income countries

- Time since diagnosis 1 yr (IQR 0.4 to 3.1)
- CD4 ~650 (IQR ~ 580-760)
- Viral load 12,000 (IQR: 3,000 to 43,000)

- ~ 30% smokers, 50% with > 1 heart risk
- ~ 20% high blood pressure; 8% lipids etc

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START – outcomes on ART

- 90% used TDF/FTC
- 70% efavirenz in early group
- 55% efavirenz in late group

Of those who started ART:

- 98% undetectable at 1 year – early group
- 97% undetectable at 1 year – late group

Interpreting results

- Absolute vs risk for each group
- Results by subgroups

Table 1: Hazard ratio (HR) of primary and key secondary endpoints

	IMM (N = 2326)		DEF (N = 2359)		HR (95% CI)	P value
	no.	rate/100 PY	no.	rate/100 PY		
Composite primary endpoint	42	0.60	96	1.38	0.43 (0.30 to 0.62)	<0.001
Secondary end points						
Serious AIDS events	14	0.20	50	0.72	0.28 (0.15 to 0.50)	<0.001
Serious non-AIDS events	29	0.42	47	0.67	0.61 (0.38 to 0.97)	0.04
Death from any cause	12	0.17	21	0.30	0.58 (0.28 to 1.17)	0.13 NS

Key: IMM=immediate arm. DEF=deferred arm, HR=Hazard Ratio, NS=Non Significant.

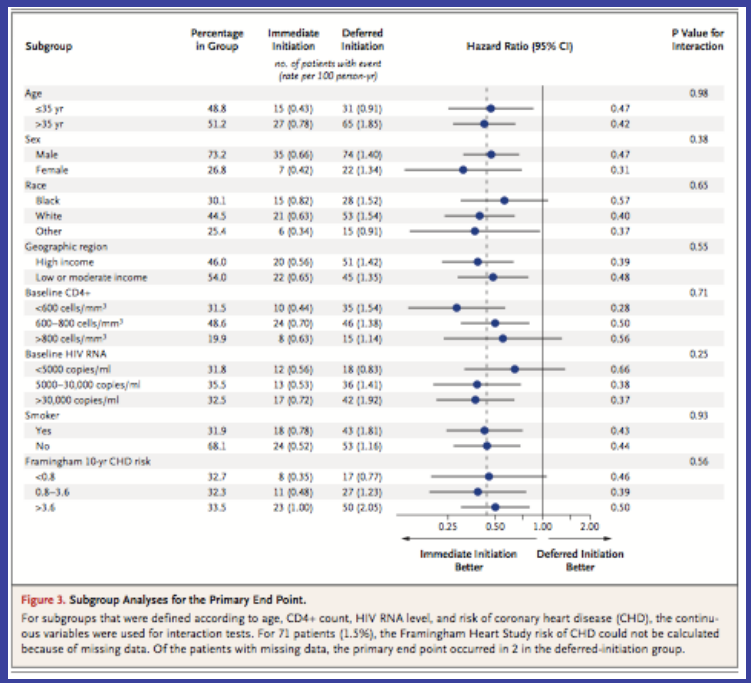

Figure 3. Subgroup Analyses for the Primary End Point.
For subgroups that were defined according to age, CD4+ count, HIV RNA level, and risk of coronary heart disease (CHD), the continuous variables were used for interaction tests. For 71 patients (1.5%), the Framingham Heart Study risk of CHD could not be calculated because of missing data. Of the patients with missing data, the primary end point occurred in 2 in the deferred-initiation group.

Main results: number of events

	Early	Late	p-value
Number of people	**2326**	**2359**	
Combined endpoint	42	96	<0.001
Secondary end points			
Serious AIDS events	14	50	<0.001
Serious non-AIDS events	29	47	0.04
Death from any cause	12	21	0.13 NS

Mainly TB in low income and cancer in high income

Results: events/100 PY*

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* PY = patient years

Results: relative difference

	Difference (95%CI)	p
Combined endpoint	**0.43** (0.60 to 1.38)	<0.001
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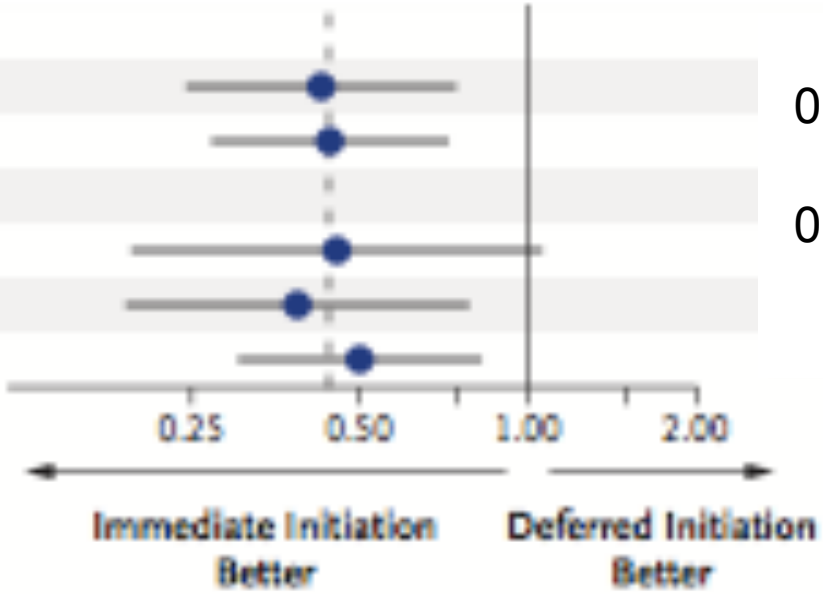
Ie ~ 60% less risk overall; 70% reduced risk for serious AIDS, 40% for non-AIDS and death.

Results: subgroup results

START

Similar impact of ART across all subgroups:
age, gender, race, country, CD4, VL, smoker, heart risk

	Hazard Ratio (95% CI)	P-value for interaction
Smoker		
Yes		0.93 NS
No		
Heart attack risk (10 yr)		0.56 NS
<0.8		
0.8-3.6		
>3.6		



BHIVA changes in June 2015 (draft)

- No CD4 link for ART
- Earlier ART & TasP
- efavirenz dropped as “preferred”
- rilipivirine now preferred
- Older drugs dropped as option for new starters: Kaletra, fosamprenavir, nevirapine
- Fixed dose combinations NOT preferred
- Special populations*

* TB; hepatitis; cancer, neurological complications, kidney and heart disease, women, mental health, adolescents, bone disease and HIV in older people.

WHO guidelines (2015)

"recommend ART for all HIV positive people irrespective of CD4 count"

Early announcement for Dec 2015.

* Announced in multiple sessions at AIDS 2015 conference in Vancouver.

TasP and PREP

- HPTN 052 study – continued protection.
- No linked HIV transmissions over four years. [1]

- PROUD and IPERGAY for PrEP [2, 3]

- Generic PrEP costs ~£40-60 for 30 tablets
- 4 doses a week is >95% protection and would last two months.

1. Cohen MS et al, IAS 2015. See: http://i-base.info/htb/28715
2. Numerous presentations at IAS 2015. See: http://i-base.info/htb/28920
3. McCormick S et al. The Lancet, September 2015.

Same-day ART: a new model

- San Francisco pilot study to offer ART on the day that someone is diagnosed. [1]

- ~ 40 people compared to standard of care
- Intensive support, integrase-ART
- Mainly men, average 32 years, 60% non-white, no insurance, 25% homeless.
- 90%, 95% and 100% vs 12%, 28% and 60% on day 0, 1 and 30.

1. Pitcher C et al, IAS 2015. See: http://i-base.info/htb/28715

Timing of ART: acute infection

- Primary HIV – diagnosed within 6 months of infection.
- “detuned” HIV test (RITA) can help
- Although earlier ART is now seen as better, timing is only critical in very early HIV.
- Weeks > 1 mo > 2 mo > 3 mo > 6 month.
- Reducing size of “latently infected CD4 reservoir” overlaps with cure-related research.
- Also Visconti Cohort cases [1]

1. Sáez-Cirion A et al, PLoS Path, 2013.

PARTNER 2 Study

www.partnerstudy.eu/

Still enrolling gay men: pos/neg couples for HIV transmissions when VL is undetectable

UK-CAB

HIV treatment advocates network

www.ukcab.net

Thanks

Questions?

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Primary endpoint results

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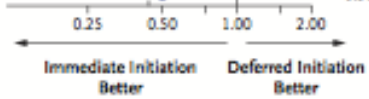
Subgroup results

Subgroup	Percentage in Group	Immediate Initiation	Deferred Initiation	Hazard Ratio (95% CI)	P Value for Interaction
		no. of patients with event (rate per 100 person-yr)			
Age					0.98
≤35 yr	48.8	15 (0.43)	31 (0.91)	0.47	
>35 yr	51.2	27 (0.78)	65 (1.85)	0.42	
Sex					0.38
Male	73.2	35 (0.66)	74 (1.40)	0.47	
Female	26.8	7 (0.42)	22 (1.34)	0.31	
Race					0.65
Black	30.1	15 (0.82)	28 (1.52)	0.57	
White	44.5	21 (0.63)	53 (1.54)	0.40	
Other	25.4	6 (0.34)	15 (0.91)	0.37	
Geographic region					0.55
High income	46.0	20 (0.56)	51 (1.42)	0.39	
Low or moderate income	54.0	22 (0.65)	45 (1.35)	0.48	
Baseline CD4+					0.71
<600 cells/mm³	31.5	10 (0.44)	35 (1.54)	0.28	
600–800 cells/mm³	48.6	24 (0.70)	46 (1.38)	0.50	
>800 cells/mm³	19.9	8 (0.63)	15 (1.14)	0.56	
Baseline HIV RNA					0.25
<5000 copies/ml	31.8	12 (0.56)	18 (0.83)	0.66	
5000–30,000 copies/ml	35.5	13 (0.53)	36 (1.41)	0.38	
>30,000 copies/ml	32.5	17 (0.72)	42 (1.92)	0.37	
Smoker					0.93
Yes	31.9	18 (0.78)	43 (1.81)	0.43	
No	68.1	24 (0.52)	53 (1.16)	0.44	
Framingham 10-yr CHD risk					0.56
<0.8	32.7	8 (0.35)	17 (0.77)	0.46	
0.8–3.6	32.3	11 (0.48)	27 (1.23)	0.39	
>3.6	33.5	23 (1.00)	50 (2.05)	0.50	



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