Starting ART in Western Europe

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Benefits and disadvantages of cART

1995

Drugs not very effective

Poor survival

Drugs had serious side effects

2005

Drugs much more effective

Better survival

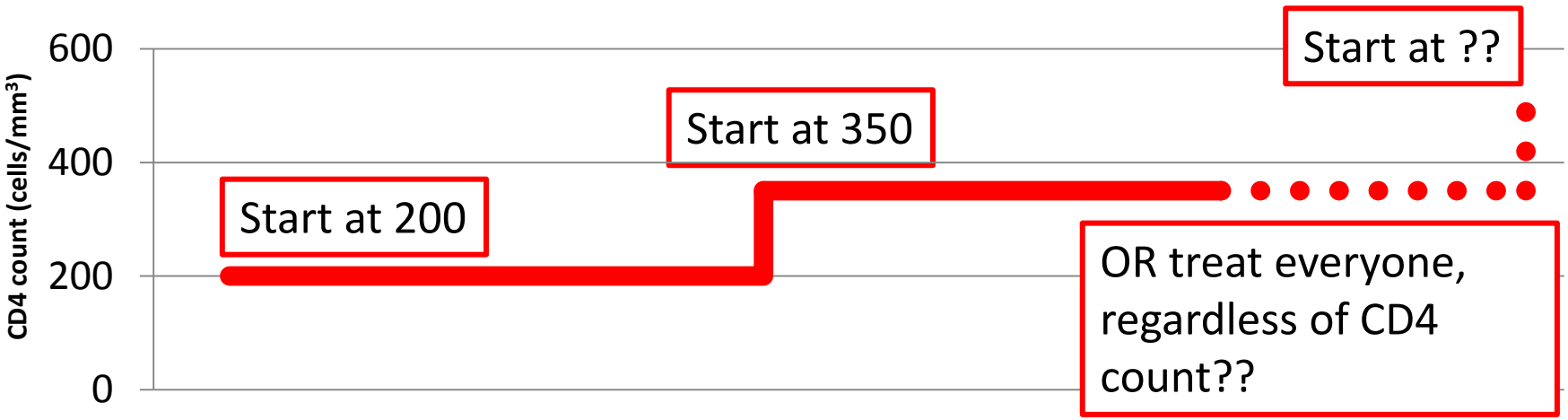
Drugs were easier to take, fewer side effects

2013

Drugs very effective

Drugs very easy to take, few side effects

May have an impact on the epidemic

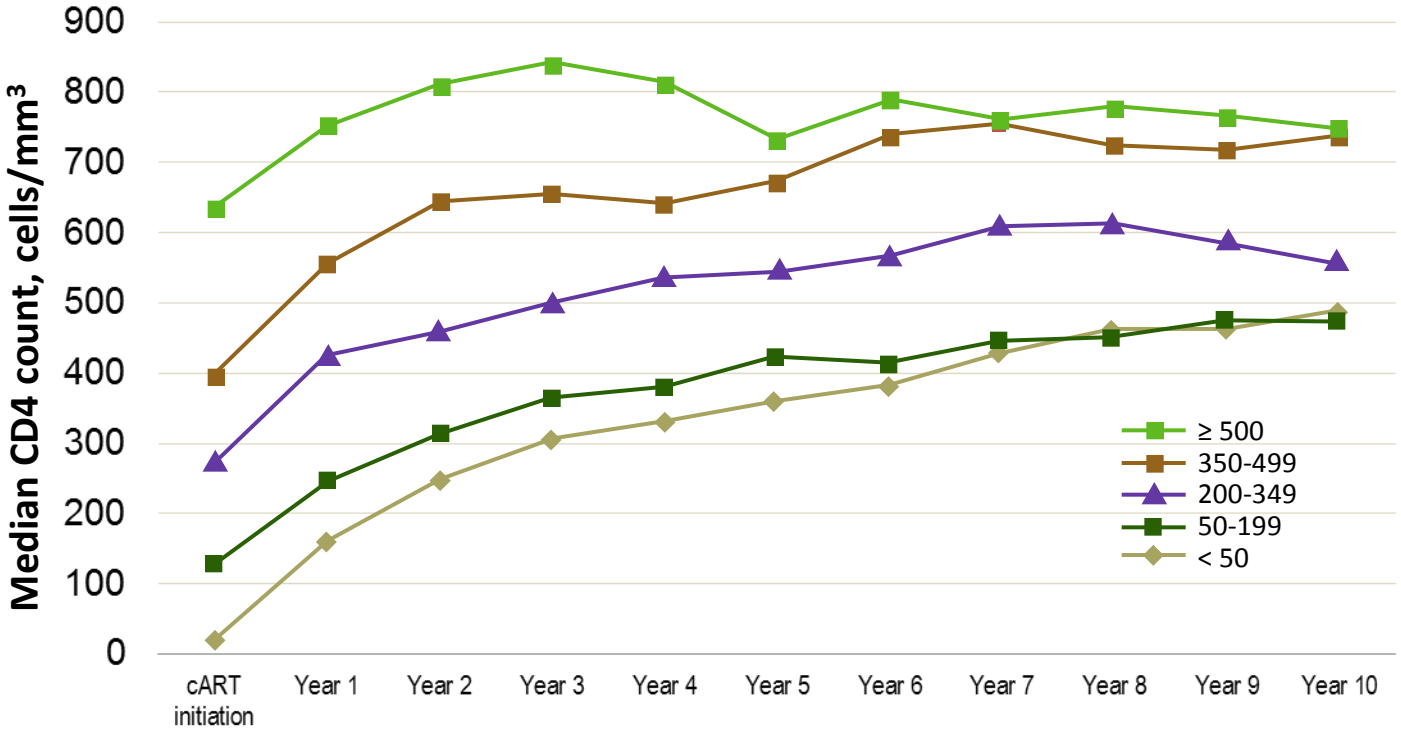


Risk of clinical progression or death for deferring cART at CD4 level than 350-500

Cohort	N. partecipants	AIDS or Death	Consistency	Death alone	Consistency
NA-ACCORD (N Engl J Med, 2009)	17,517	n.a.	**n.a.**	Deferred cART at CD4 350-500: HR **1.69 (1.26–2.26)**	**yes**
ART-CC/When to start (Lancet, 2009)	24,444	Deferred cART to CD4 lower than 351-450: **HR 1.28 (1.04–1.57)**	**yes**	Deferred cART to CD4 lower than 351-450: **HR 1.13 (0.80–1.60)**	**no**
HIV-CAUSAL (Ann Intern Med, 2011)	20,971	Compared with initiating cART at CD4 cell count threshold 500/mm3, HR for 350/mm^3 threshold:**1.38 (1.23-1.56)**	**yes**	Compared with initiating cART at CD4 cell count threshold 500/mm^3, HR for 350/mm3 threshold:**1.01 (0.84-1.22)**	**no**
CASCADE (Arch Intern Med, 2011)	9,455	In CD4 stratum 350-499, cART initiation associated with aHR: **0.75 (0.49-1.14)**	**no**	In CD4 stratum 350-499, cART initiation associated with aHR: **0.51 (0.33-0.80)**	**yes**

Higher CD4 Count at ART Initiation Predicts Greater Long-Term Likelihood of CD4 Count Normalization

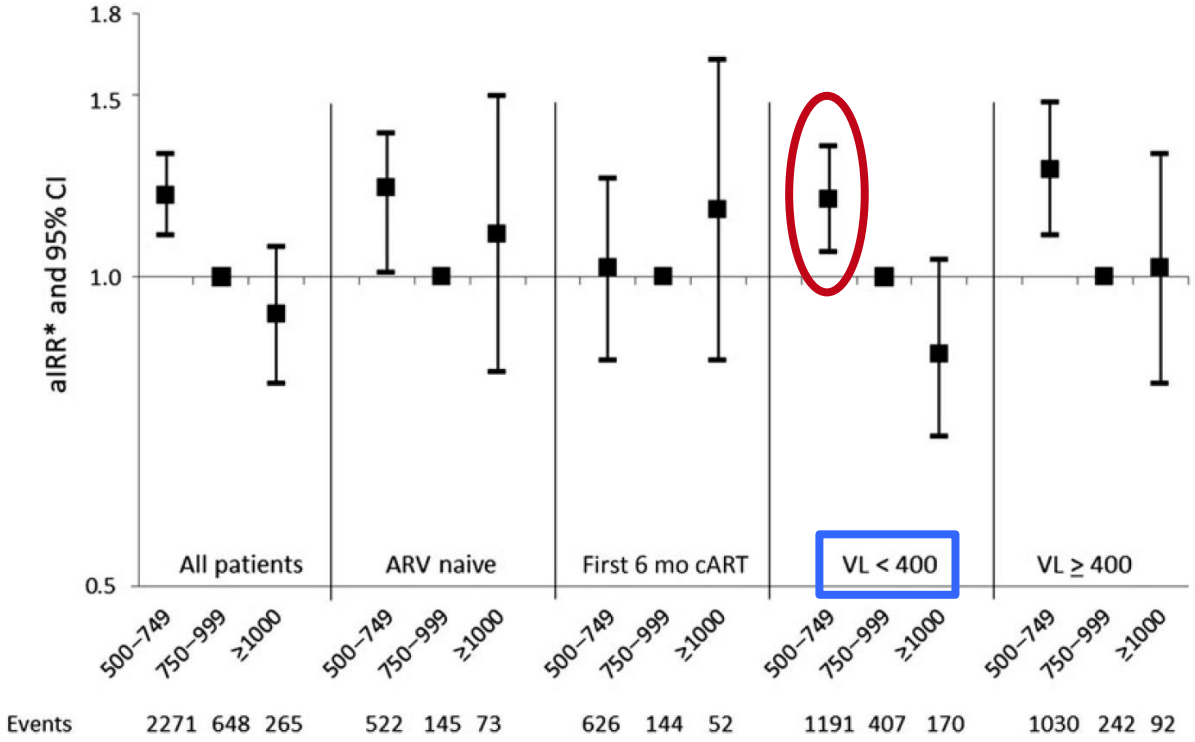
Progressively higher CD4 counts at ART initiation were associated with greater long-term CD4 gains, greater likelihood of achieving CD4 > 750 ("normalization"), increased unadjusted survival rates, higher CD4 at death, and decreased likelihood of deaths from both AIDS and non-AIDS causes.



Palella F, et al. CROI 2014; Boston (MA). Abst.#560.

Relationship between current CD4 and ADIs with a CD4 count ≥500 cells/µL

Relationship with current viral load and antiretroviral treatment.

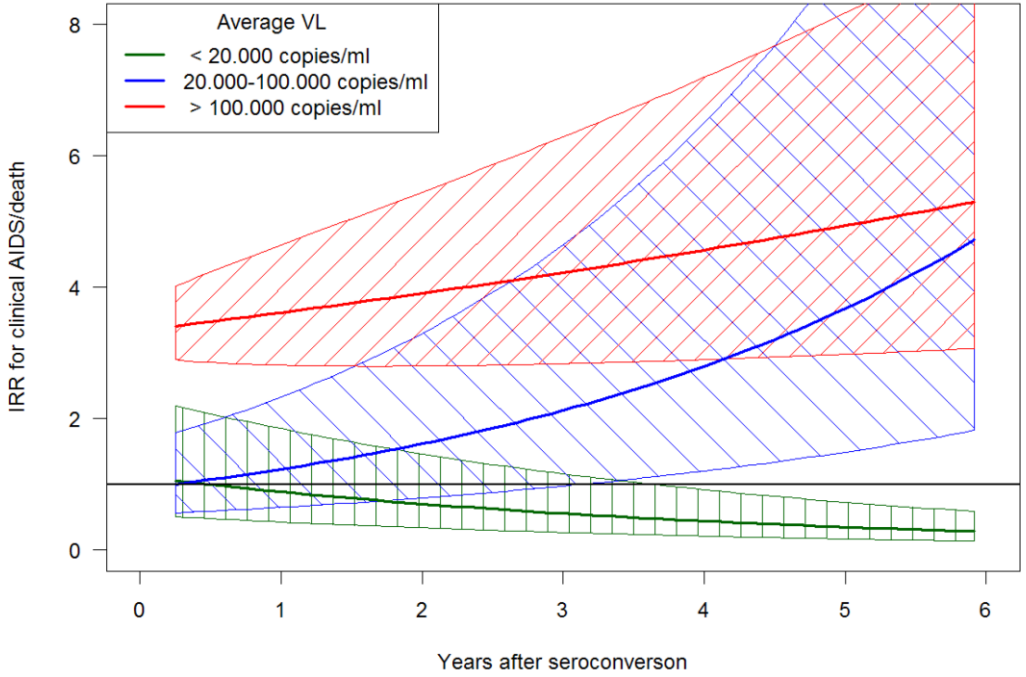


COHERE. A total of 12,135 ADIs occurred at a CD4 count of ≥200 cells/µL among 207,539 persons with 1,154,803 PYFU. Incidence rates declined from 20.5 per 1000 PYFU (95% confidence interval [CI], 20.0–21.1 per 1000 PYFU) with current CD4 200-349 cells/µL to 4.1 per 1000 PYFU (95% CI, 3.6–4.6 per 1000 PYFU) with current CD4 ≥ 1000 cells/µL. Persons with a current CD4 of 500–749 cells/µL had a significantly higher rate of ADIs (adjusted incidence rate ratio [aIRR], 1.20; 95% CI, 1.10–1.32).

Mocroft A, et al. Clin Infect Dis, 2013

Clinical impact of viral load copy years (VCY) in ARV-naive HIV seroconverters

CASCADE: A total of 9,461 HIV seroconverters were included.
Based on 15,553 person years of follow-up the overall incidence rate of clinical AIDS/death was 10.4/1000 PYFU.
Patients censored at: a) earliest of ART start; b) CD4 <200 cells/µl; c) no VL and CD4 measurements for >12 months; d) 6 years after SC.



Impact of average VL on rate of clinical AIDS/death changing with time after SC

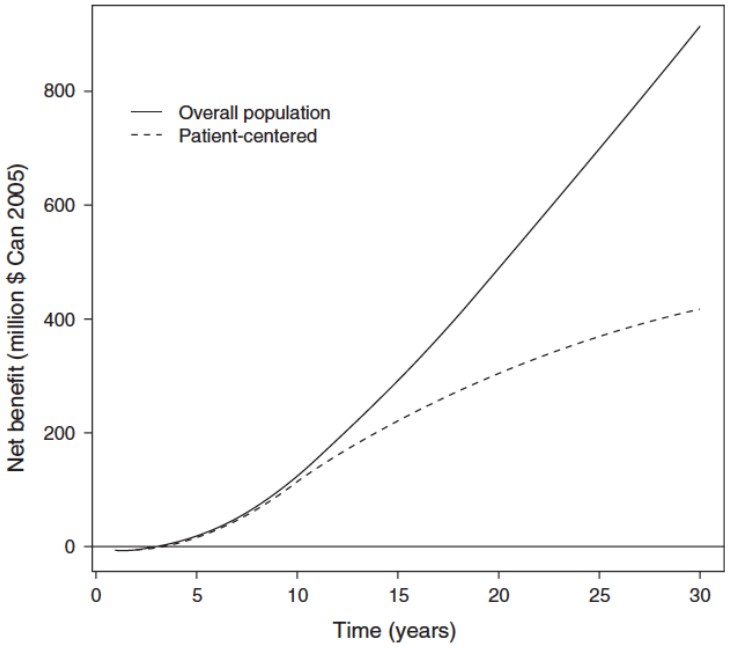
- Higher average VL is associated with a higher risk of clinical AIDS/death.
- Accumulation of intermediate VL levels over time leads to higher risks comparable to those associated with high average VL.
- Choice on when to start ART may also be influenced by the duration and extent of previous HIV replication.

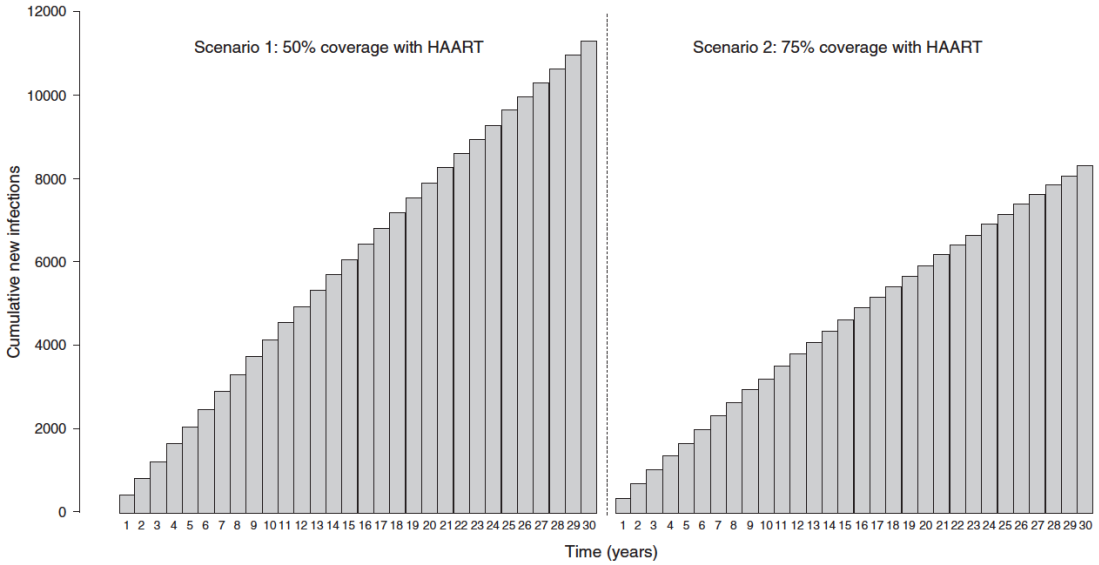
an der Heiden M, et al. CROI 2014, Boston (MA). Abst.#291

Expanding access to HAART is a cost effective approach for treating and preventing HIV

Over 30 years, the HAART expansion scenario was associated with a net benefit of US$ 900 million (95% confidence interval US$ 493 million to 1.45 billion).

Increasing the HAART treatment rate from 50 to 75% of clinically eligible individuals in British Columbia appears to be a cost-effective strategy based on this model. These cost-effectiveness results are consistent with public health objectives: all individuals who are eligible for an established life-saving treatment should receive it.





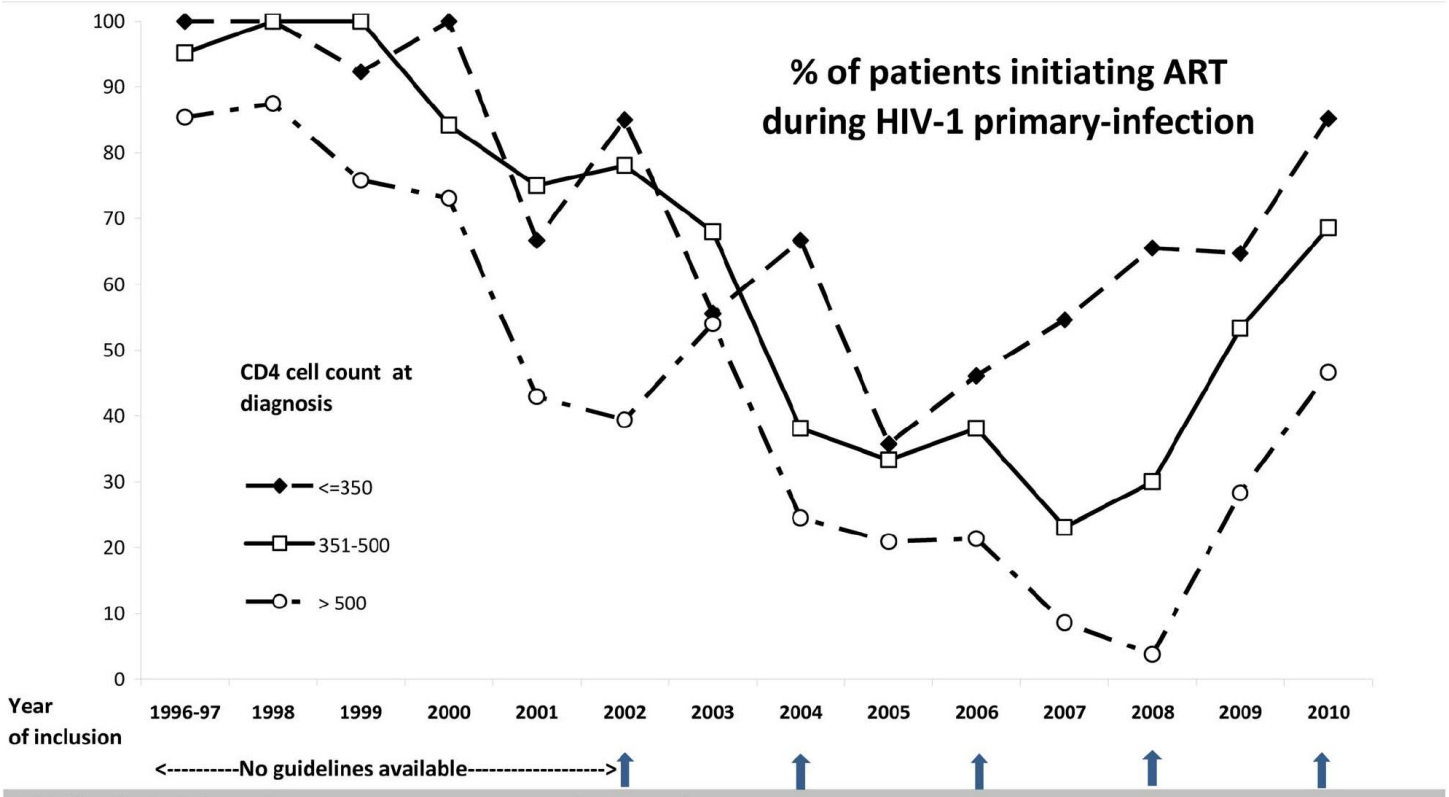
Johnston KM, et al. AIDS, 2010

When to start cART? 2013-2014 Guidelines Update

Clinical category	CD4 cells/mm^3	DHHS 14[1]	IAS-USA 14[2]	EACS 14[3]	ITA-CNA 13[4]	BHIVA 13[5]	GESIDA 14[6]	CNS-ANRS 13[7]
AIDS-defining or symptoms	Any value	Treat (AI)	Treat (AI)	Treat	Treat (AI)	Treat (AI)	Treat (AI)	Treat (AI)
Pregnancy	Any value	Treat (AI)	Treat (AI)	Treat	Treat (AI)	Treat (AI)	Treat (AI)	Treat (AI)
HBV, HCV	Any value	Treat (AI-II)	Treat (AII/CIII)	Treat or consider only if CD4 <500/mm^3	Treat (AI-II)	Treat or consider only if CD4 <500/mm^3	Treat (AII)	Treat (AIII)
Other clinical conditions	Any value	HIVAN	HIVAN	HIVAN, Malignancies, HAND	HIVAN, Malignancies, HAND, CVD	HIVAN, Malignancies, HAND	HIVAN, Malignancies, HAND, CVD	Malignancies
Asymptomatic	<350	Treat (AI)	Treat (AI)	Treat	Treat (AI)	Treat (AI)	Treat (AI)	Treat (AI)
Asymptomatic	350–500	Treat (AII)	Treat (AI)	Consider treatment	Treat (AII)	Generally defer	Treat (AII)	Treat (AII)
Asymptomatic	>500	Treat as moderate (BIII)	Treat as moderate (BIII)	Consider treatment	Treat on individual basis (AII/BIII)	Generally defer	Treat as moderate (BIII)	Treat as moderate (BIII)
Primary HIV infection	Any value	Treat as moderate (BII)	Treat as moderate (BIII)	Consider treatment	Treat as moderate (BII)	Treat symptomatic (AI) or CD4 <350 (CI)	Treat if CD4 <500 or pVL >100,000 c/mL (BII)	Treat as moderate (BII)
Prevent sexual transmission	Any value	Treat (AI-II)	Treat (AI)	Consider treatment	Treat (AI-II)	Consider (GPP)	Treat (AI-II)	Treat (AI/BIII)

1. DHHS Guidelines 2014 Available at http://aidsinfo.nih.gov/guidelines
2. ARV Treatment of Adult HIV Infection. 2014 Recommendation of the IAS-USA panel. JAMA 2014;312:410-425.
3. EACS Guidelines 2014. Available at http://www.europeanaidsclinicalsociety.org/guidelinespdf/1_Treatment_of_HIV_Infected_Adults.pdf.
4. Linee Guida Italiane sull'utilizzo dei farmaci antiretrovirali e sulla gestione diagnostico-clinica delle persone con infezione da HIV-1, 2013. Available at: http://www.salute.gov.it/imgs/C_17_pubblicazioni_1301_allegato.pdf;
5. BHIVA Guidelines 2012-Updated 2013. HIV Medicine (2014), 15 (Suppl. 1), 1–85
6. GESIDA. Documento de consenso de Gesida/Plan Nacional sobre el SIDA respecto al tratamiento antirretroviral en adultos infectados por el virus de la inmunodeficiencia humana. Actualización enero 2014
7. CNS-ANRS. Prise en charge médicale des personnes vivant avec le HIV. Rapport 2013

Change over time of ART initiation during primary infection according to CD4 count (<350; 351–500; >500 cells/mm3)

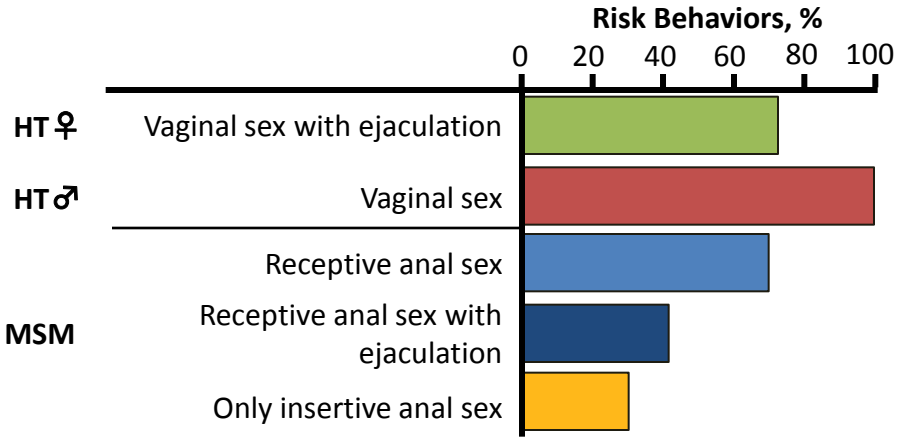


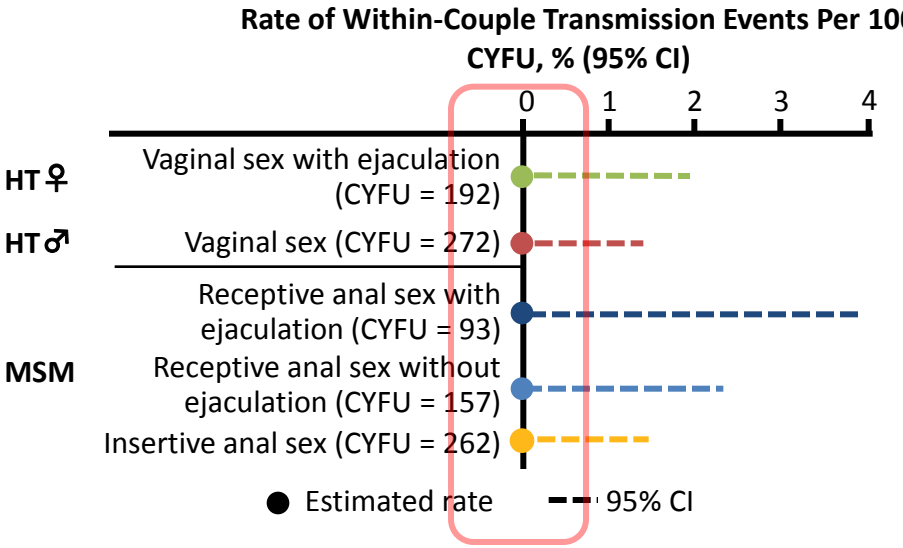
N subjects														
≤ 350/mm^3	15	7	13	11	15	20	18	24	14	26	22	29	17	27
351-500/mm^3	21	5	11	19	20	32	25	21	21	42	26	30	15	51
> 500/mm^3	48	24	33	26	42	33	50	49	43	70	58	52	53	88

Krastinova E, et al. PLoS One, 2013

PARTNER: Risk of HIV Transmission With Condomless Sex on Suppressive ART

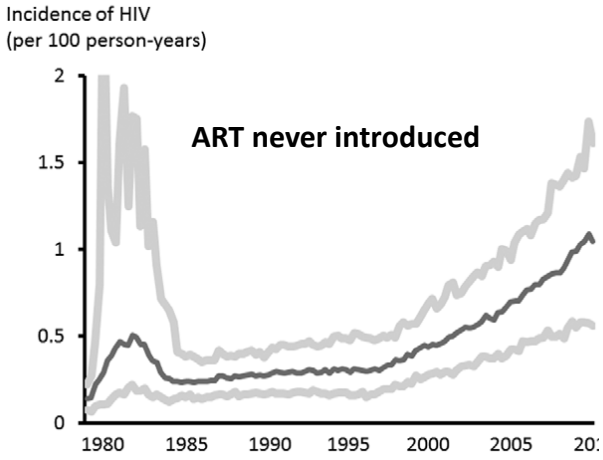
- Observational study of rate of HIV transmission in heterosexual and MSM serodiscordant couples (N = 767 couples)
  - HIV+ partner on suppressive ART
  - Condoms not used
- Analyses: Risk-behavior questionnaire every 6 mos, HIV-1 RNA (HIV+), HIV test (HIV)
- Endpoint: Phylogenetically linked transmissions
- No linked transmissions recorded in any couple during study period

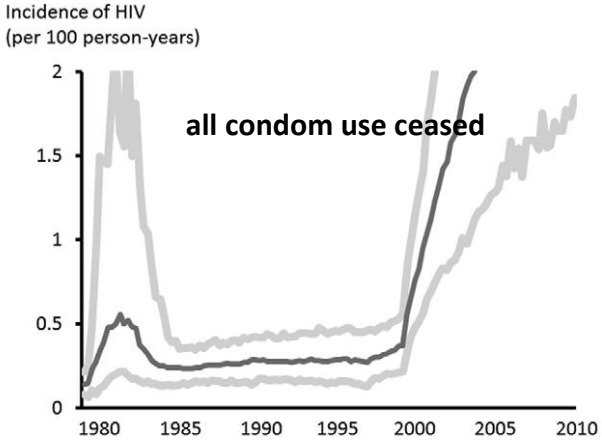


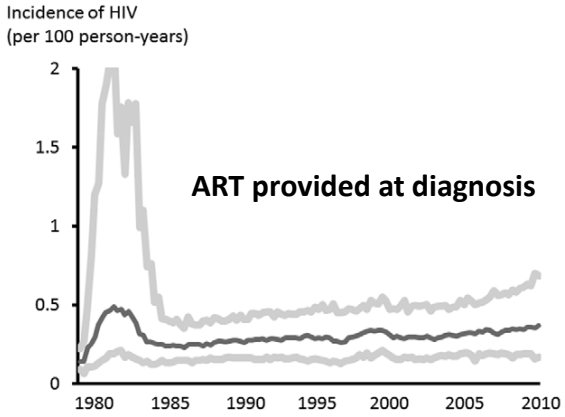


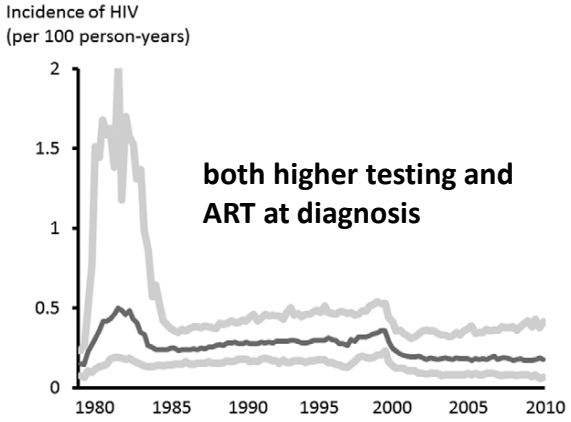
Rodger A, et al. CROI 2014. Abstract 153LB.

Increased HIV incidence in MSM despite high coverage of ART









HIV-incidence has increased (estimated mean incidence **0.30/100 person-years 1990–1997**, **0.45/100 py 1998–2010**), associated with a modest (**26%**) rise in condomless sex.

A rise in HIV-incidence has occurred in MSM in the UK despite an only modest increase in levels of condomless sex and high coverage of ART.

Much higher rates of HIV testing combined with initiation of ART at diagnosis would be likely to lead to substantial reductions in HIV incidence.

Increased condom use should be promoted to avoid the erosion of the benefits of ART and to prevent other serious sexually transmitted infections.

Phillips AN, et al. PLoS One, 2013

What to Start

Comparison of Updated 2013-2014 Guidelines

STANDARD of CARE for HIV and COINFECTIONS in EUROPE

Regimen	ITA-CNA 2013[1]	DHHS 2014[2]	IAS 2014[3]	EACS 2014[4]	BHIVA 2013[5]	GESIDA 2014[6]	CNS-ANRS 2013[7]
EFV/TDF/FTC	Preferred	Recommended	Recommended	Recommended	Preferred	Preferred	Preferred
EFV + ABC/3TC	Preferred*	Recommended*	Recommended*	Recommended*	Alternative*	Alternative*	Preferred*
NVP + TDF /FTC	Alternative	Not recommended	Alternative	Alternative	Alternative	Alternative	Alternative
RPV + TDF/FTC	Preferred*	Recommended#	Recommended*	Recommended*	Alternative*	Preferred*	Preferred*
ATV/r + TDF/FTC	Preferred	Recommended	Recommended	Recommended	Preferred	Preferred	Preferred
ATV/r + ABV/3TC	Preferred*	Recommended*	Recommended*	Recommended*	Alternative*	Preferred*	Preferred*
DRV/r + TDF/FTC	Preferred	Recommended	Recommended	Recommended	Preferred	Preferred	Preferred
DRV/r + ABV/3TC	Preferred	Alternative	Alternative	Recommended	Alternative*	Alternative	Alternative
LPV/r + TDF/FTC	Alternative	Alternative	Alternative	Alternative	Alternative	Alternative	Alternative
LPV/r + ABV/3TC	Alternative	Alternative	Alternative	Alternative	Alternative*	Alternative	Alternative
RAL + TDF/FTC	Preferred	Recommended	Recommended	Recommended	Preferred	Preferred	Alternative
RAL+ABV/3TC	Preferred	Alternative	Alternative	Recommended	Alternative	Preferred	Alternative
EVG/COBI/TDF/FTC	Preferred	Recommended	Recommended	Recommended	Preferred	Preferred	
DTG + TDF/FTC	Preferred	Recommended	Recommended			Preferred	
DTG + ABV/3TC	Preferred	Recommended	Recommended			Preferred	

* Only if HIV-RNA <100.000 c/mL; # Only if HIV-RNA <100.000 c/mL and CD4 >200 cell/mm3.

1. Linee Guida Italiane sull'utilizzo dei farmaci antiretrovirali e sulla gestione diagnostico-clinica delle persone con infezione da HIV-1, 2013 Available at: http://www.salute.gov.it/imgs/C_17_pubblicazioni_1301_allegato.pdf;
2. DHHS Guidelines 2014 Available at http://aidsinfo.nih.gov/guidelines
3. ARV Treatment of Adult HIV Infection. 2012 Recommendation of the IAS-USA panel. JAMA 2014;312:410-425.
4. EACS Guidelines 2014. Available at http://www.europeanaidsclinicalsociety.org/guidelinespdf/1_Treatment_of_HIV_Infected_Adults.pdf.
5. BHIVA Guidelines 2012-Updated 2013. HIV Medicine (2014), 15 (Suppl. 1), 1–85
6. GESIDA. Documento de consenso de Gesida/Plan Nacional sobre el SIDA respecto al tratamiento antirretroviral en adultos infectados por el virus de la inmunodeficiencia humana. Actualización enero 2014
7. CNS-ANRS. Prise en charge médicale des personnes vivant avec le HIV. Rapport 2013

2014 EACS Guidelines

Initial Combination Regimen for ART-naive Adult HIV+ Persons

A drug from column A should be combined with the drugs listed in column B(**)

A	B	Remarks
NNRTI	**NRTI**	
EFV(i) RPV(ii)	ABC/3TC(vii) or TDF/FTC	ABC/3TC co-formulated TDF/FTC co-formulated EFV/TDF/FTC co-formulated RPV/TDF/FTC co-formulated
PI/r		
ATV/r(iv) DRV/r(iv)	ABC/3TC(vii) or TDF/FTC	ATV/r: 300/100 mg qd DRV/r: 800/100 mg qd
INSTI		
EVG + COBI	FTC/TDF	EVG/COBI/FTC/TDF co-formulated(ix)
RAL	TDF/FTC or ABC/3TC	RAL: 400 mg bd

* Only drugs currently licensed for initiation of therapy by the EMA are taken into consideration (in alphabetical order)

** Generic HIV drugs are becoming more available and can be used as long as they replace the same drug and do not break recommended fixed dose combinations.

i EFV: not recommended to be initiated in pregnant women or women with no reliable and consistent contraception; continuation is possible if EFV is already started before pregnancy; not active against HIV-2 and HIV-1 group O strains.

ii RPV: only if HIV-VL < 100,000 copies/mL; PPI contraindicated, H2 antagonists to be taken 12h before or 4h after RPV.

vii ABC contra-indicated if HLA B*5701 positive. Even if HLA B*5701 negative, counselling on HSR risk still mandatory. ABC should be used with caution in persons with a high CVD risk and/or persons with a VL > than 100,000 copies/mL.

ix Should not be initiated in persons with eGFR < 70 mL/min. It is recommended that EVG/COBI/TDF/FTC not be initiated in persons with eGFR < 90 mL/min unless this is the preferred treatment.

HIV Treatment Cascade in Europe

Proportion of patients on ART and virologically suppressed

Estimates were extracted from national reports, conference proceedings and peer reviewed articles.

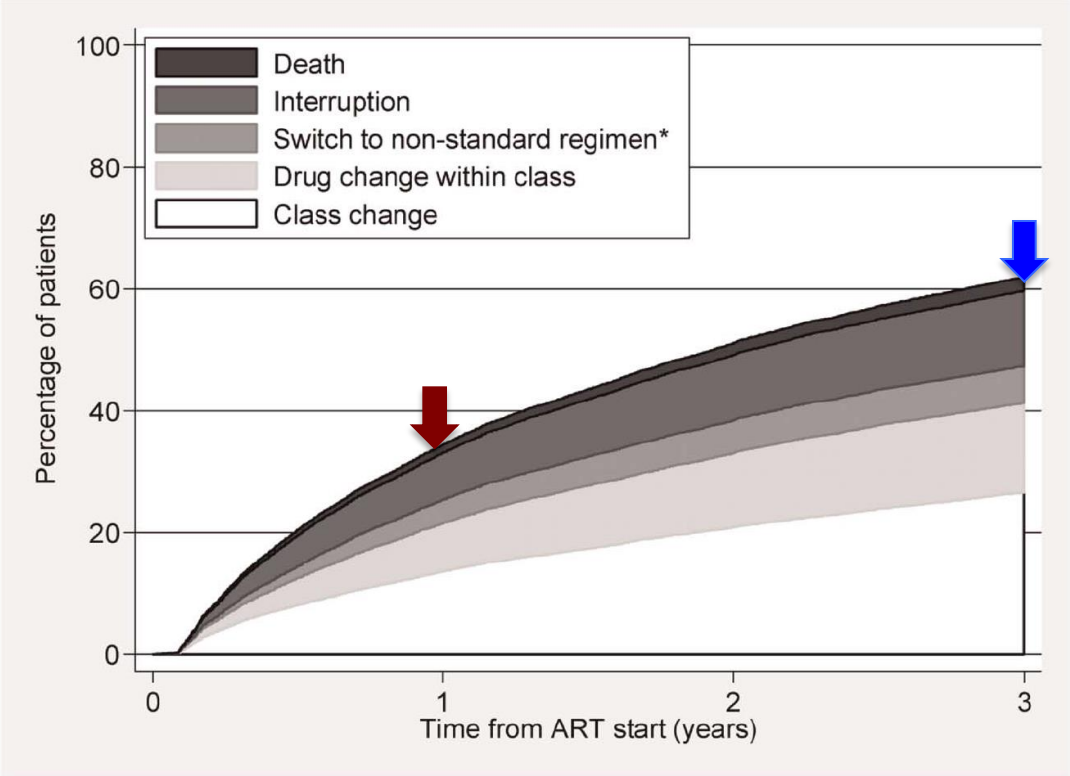
Country	In care (%*)	On ART		Virologically suppressed	
	N (%*)	N (%*)	% of "In care"	N (%*)	% of "On ART"
Denmark	4,857 (75)	4,029 (62)	83	3,863 (59)	96
France	111,500 (74)	-	n.e.	77,948 (52)	n.e.
Italy	94,136 (73)	82,463 (64)	88	72,567 (56)	88
Netherlands	17,006 (68)	14,817 (59)	87	13,369 (53)	90
United Kingdom	69,198 (70)	65,928 (67)	95	57,072 (58)	87

Modest disparities among Western European countries in the percentage of people on ART and virologically suppressed. Differences of being On ART appeared independent from national guidelines approach of When to starting ART.

Key break points in the clinical sections of HIV cascade (proportion of patients in care being on ART and of those on ART as virologically suppressed) seem to be less relevant than for undiagnosed or linked to care.

Modified from: Raymond A et al. International Congress of Drug Therapy in HIV Infection, abstract 0-237, Glasgow, 2014.; Aghaizu A, et al. HIV in the United Kingdom 2013 Report: data to end 2012. London: Public Health England; 2013. van Sighem A, et al. HIV Infection in the Netherlands. Amsterdam, The Netherlands: Stichting HIV Monitoring Report; 2013; Supervie V, et al. The spectrum of engagement in HIV care in France. 20th Conference on Retroviruses and Opportunistic Infections; 2013 Mar; Atlanta, USA. Abstract #: 1030. Helleberg M, et al. HIV care in the Swedish-Danish HIV Cohort 1995–2010, Closing the Gaps. PLoS ONE. 2013;8(8):e72257. Girardi E, VI Italian Conference on AIDS and Retroviruses. Roma, 25-27 May, 2014.

Persistent high rates of treatment modification or interruption in the first years of ART



Class change	7.9 (7.6-8.3)	12.2 (11.7-12.7)	14.7 (14.2-15.3)
Substitution/addition	13.6 (13.2-14.1)	20.9 (20.3-21.5)	26.6 (25.9-27.3)
Switch to non-standard regimen*	3.8 (3.6-4.1)	5.4 (5.1-5.7)	6.0 (5.7-6.4)
Interruption	7.7 (7.4-8.1)	10.7 (10.2-11.1)	12.4 (11.9-12.9)
Death before regimen change	1.3 (1.2-1.5)	1.9 (1.7-2.1)	2.3 (2.0-2.5)
Total	**34.3**	**51.1**	**62.0**

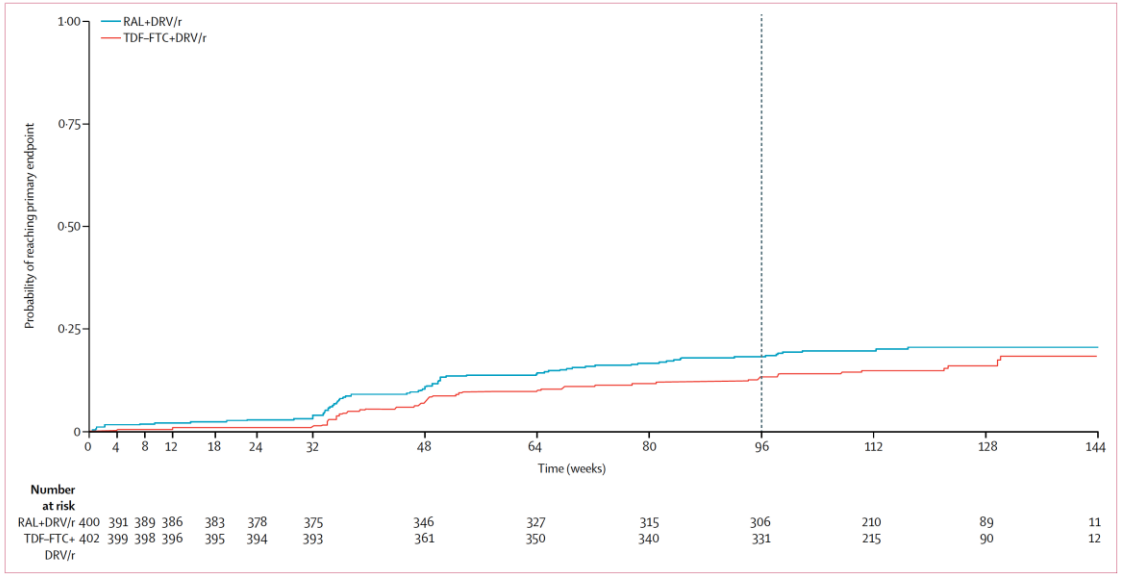
21,801 patients from 18 cohorts in Europe and North America starting ART.

Stacked Cumulative Incidence Functions of class change, substitution addition of drugs within class, switch to nonstandard regimen, interruption and death, estimated using competing risk methods.

Figures below the graph are the estimated cumulative incidence of each event at 1, 2 and 3 years, with 95% Cis.

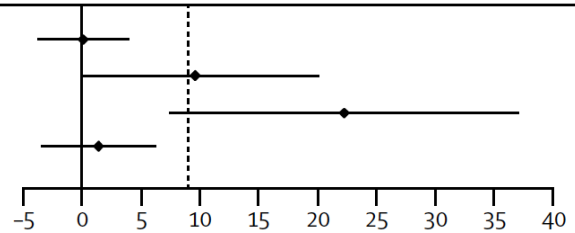
Abgrall S, et al. The ART Cohort Collaboration, AIDS, 2013

First-Line RAL+DRV+RTV vs FTC/TDF+DRV+RTV: Week 96



Kaplan-Meier plot of time from randomisation to primary endpoint

B



	Adjusted difference in proportions of failure at W96 (%, 95% CI)	RAL+DRV/r (%)	TDF–FTC+DRV/r (%)
Baseline HIV RNA <100 000 copies per mL	0·1 (−3·8 to 4·0)	7·4	7·3
Baseline HIV RNA ≥100 000 copies per mL	9·6 (−0·1 to 20·1)	36·8	27·3
CD4 cell count <200 cells per µL	22·3 (7·4 to 37·1)	43·2	20·9
CD4 cell count ≥200 cells per µL	1·4 (−3·5 to 6·3)	13·7	12·3

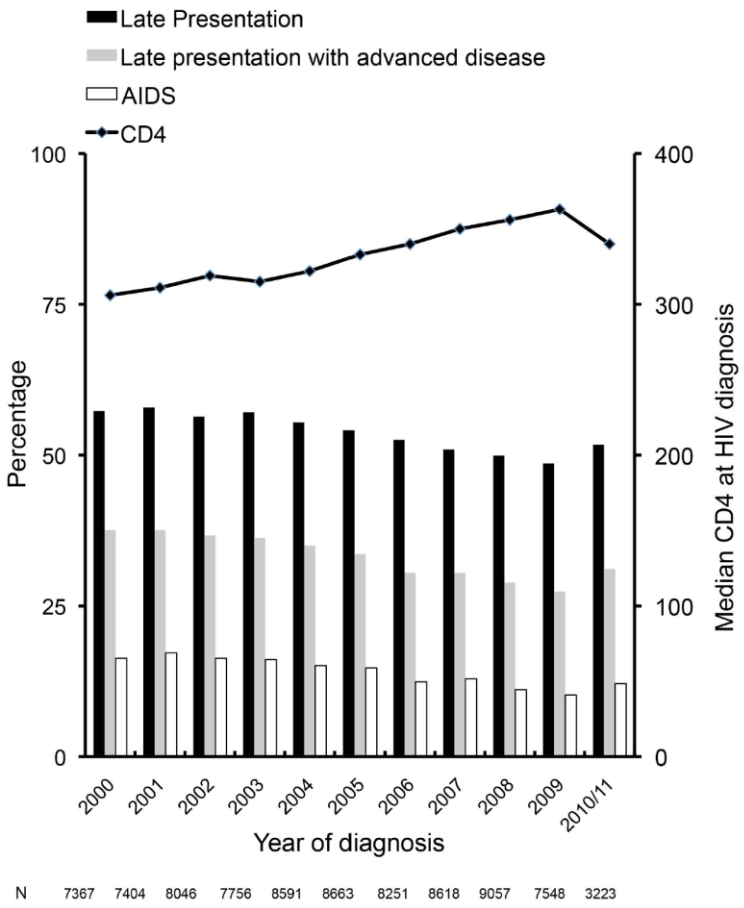
When each was given with DRV+RTV, RAL compared to FTC/TDF:

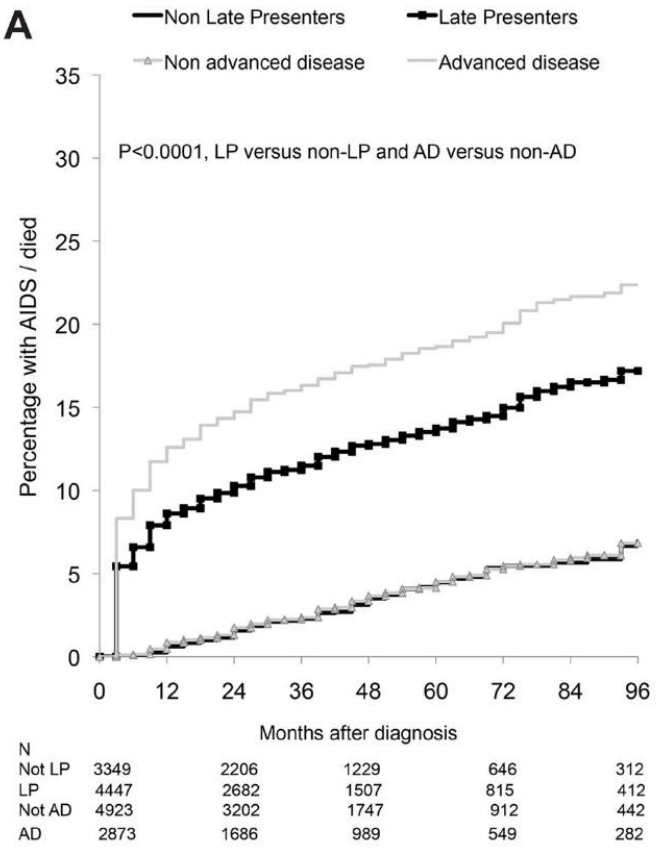
- Was non-inferior overall
- Was inferior in patients with low CD4 (<200) at baseline

Raffi F, et al. Lancet, 2014

Prevalence and outcome of HIV late presentation in Europe

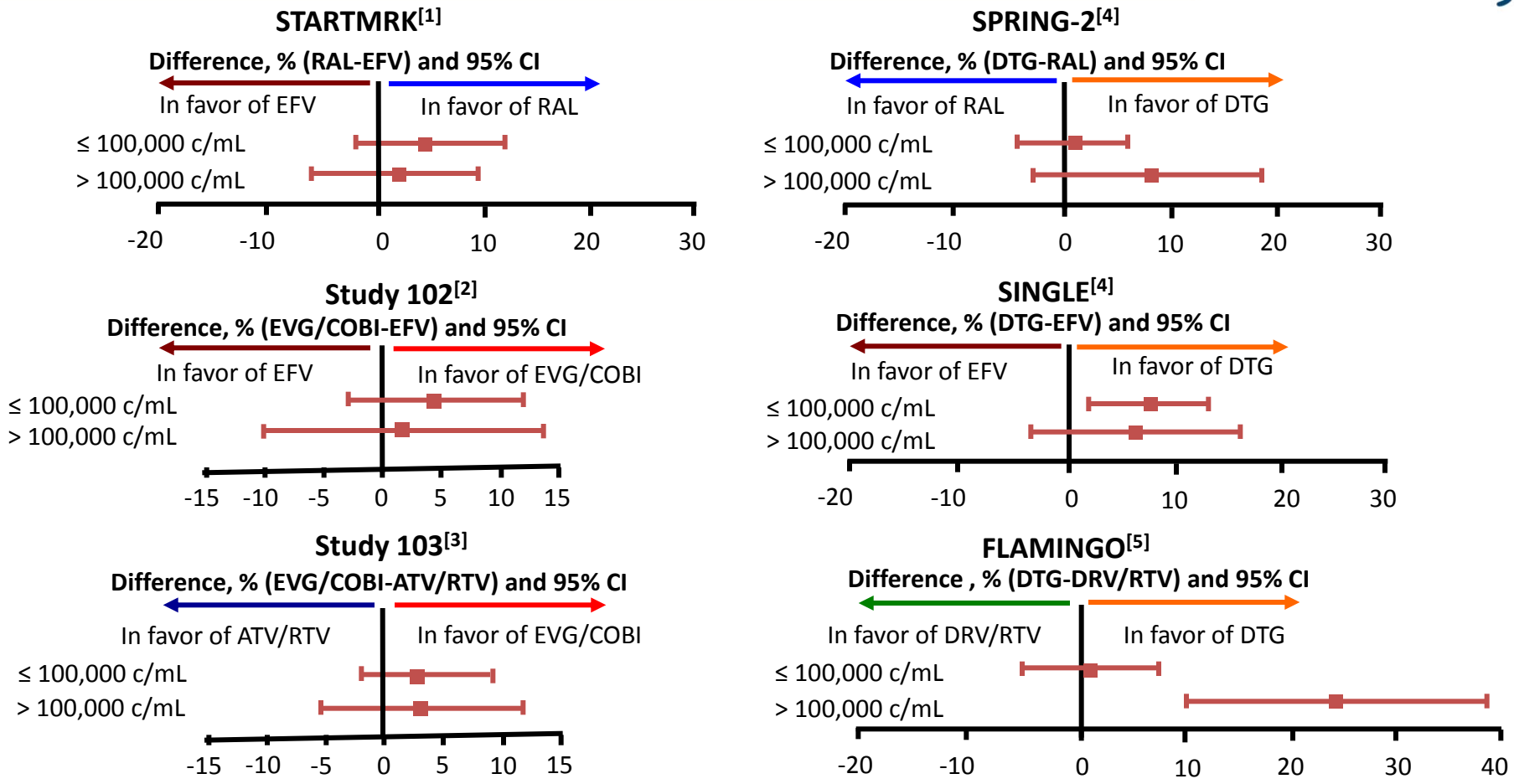
84,524 individuals from 23 cohorts in 35 countries contributed data; 45,488 were LP (53.8%).
LP was highest in heterosexual males (66.1%), Southern European countries (57.0%), and persons originating from Africa (65.1%).





Mocroft A, et al. PLoS Med, 2013

Virologic Suppression at Wk 48 with INSTI-based regimens by Baseline HIV-1 RNA

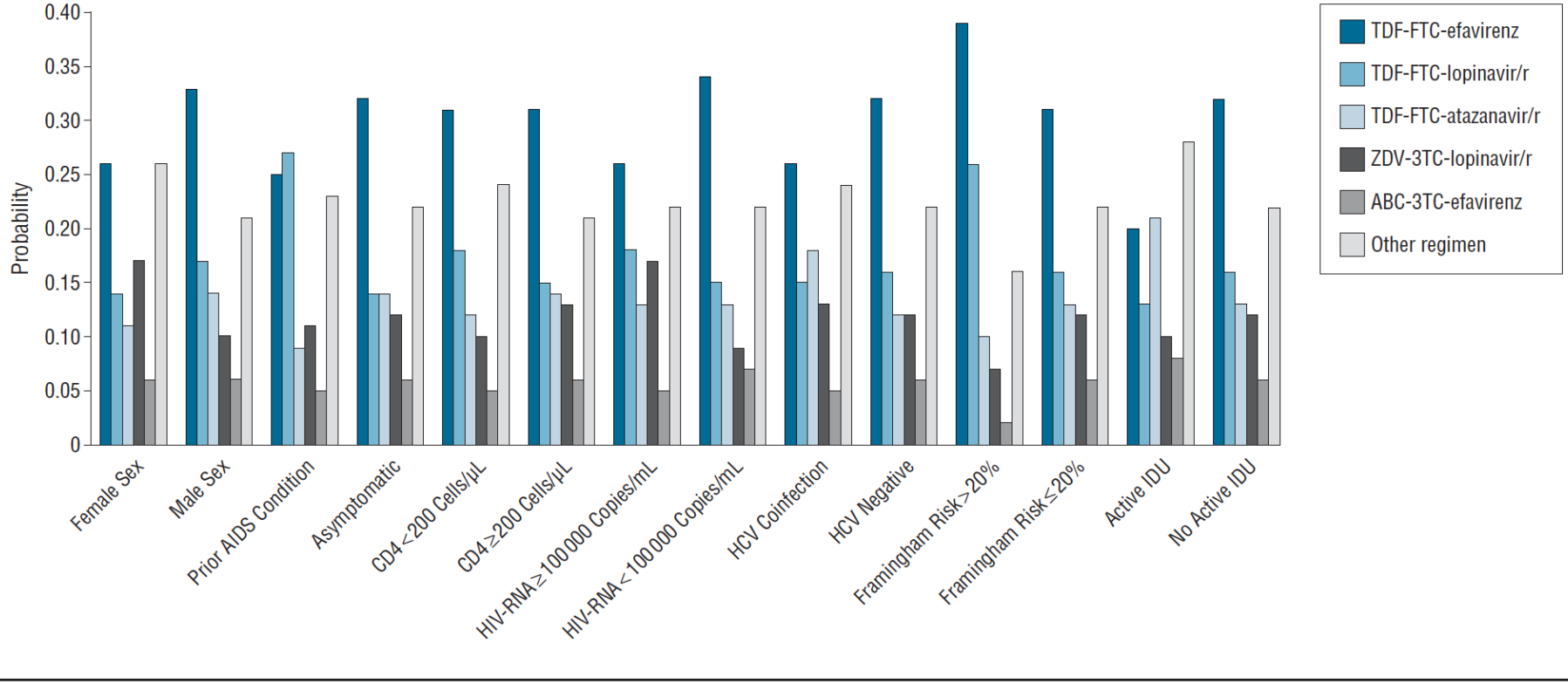


1. Lennox J, et al. Lancet. 2009;374:796-806. 2. Sax PE, et al. Lancet. 2012;379:2439-2448. 3. DeJesus E, et al. Lancet. 2012;379:2429-2438. 4. Brinson C, et al. CROI 2013. Abstract 554. 5. Feinberg J, et al. ICAAC 2013. Abstract H1464a.

Probability of the initial combination ART regimen according to frequent clinical settings

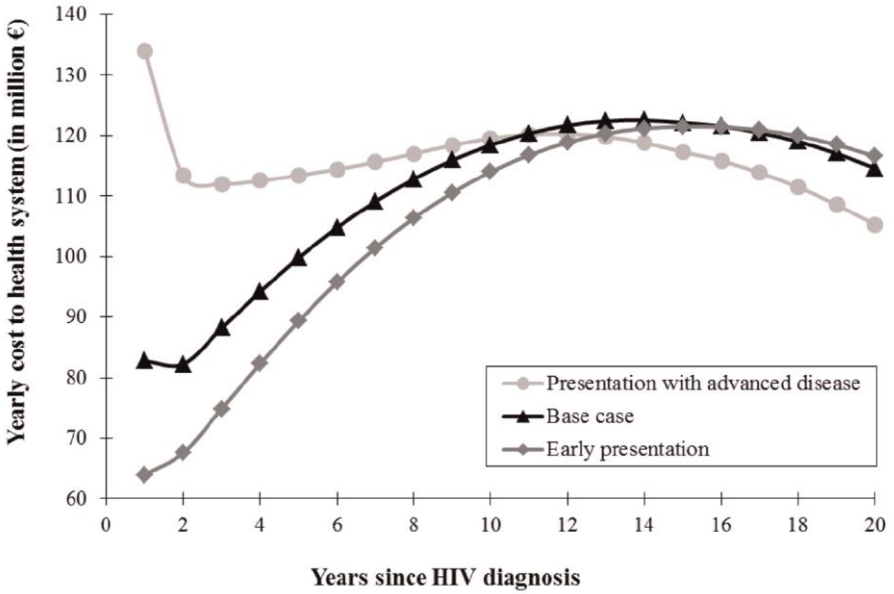
A total of 1,957 patients analyzed.

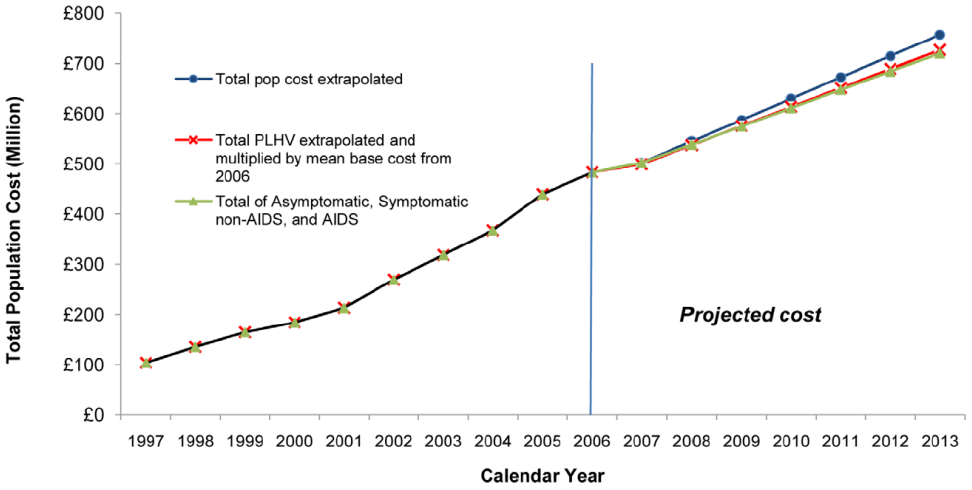
Probability of the initial combination antiretroviral therapy regimen according to frequent clinical settings fitting the multivariate multinomial logistic model adjusted for sociodemographic characteristics, comorbidities, HIV–related factors (prior AIDS-defining condition, CD4 cell counts, and viral load), study site, and calendar year.



Elzi L, et al. Arch Intern Med, 2012

Costs of care will continue to increase in HIV disease





Undiscounted lifetime costs are similar in the base case (CD4 372) and early disease groups (CD4 510), but discounted costs are €7,700 higher in the base case group. This substantial difference may be explained by the earlier deaths and thus decreased discounting of expensive end-of-life costs in the base case.

Sloan CE, et al. AIDS, 2011

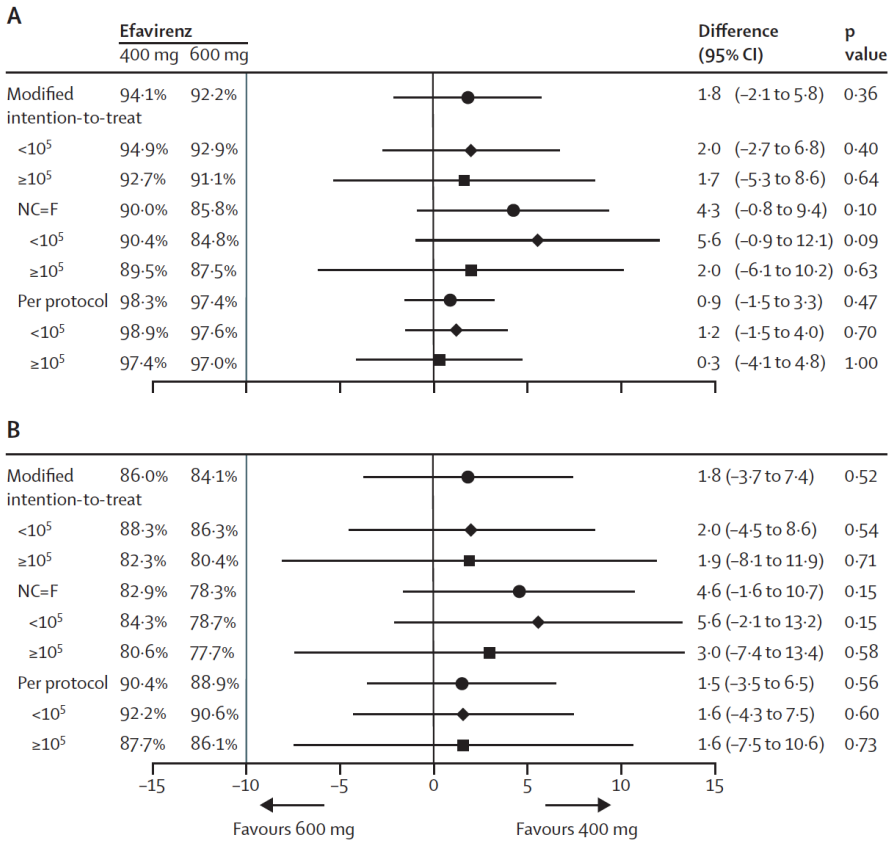
Increased number of PLHIV using NHS services resulted in rising UK population costs. Population costs are expected to continue to increase, partly due to PLHIV's longer survival on ART and the relative lack of success of HIV preventing programs.

Mandalia S, et al. PLoS One, 2010

Resource use

- ART is extremely cost-effective and compares favourably with the cost of management of many other chronic diseases (ICER US$ 20,000per QALY compared to no therapy).
- The number of people living with HIV in the UK continues to increase (69,400 accessed HIV services in 2010, of whom 82% were on ART).
- It has been estimated that the annual population treatment and care costs rose from £104 million in 1997 to £483 million in 2006, rising to a projected annual cost of £721 million in 2013.
- In the UK, higher annual treatment and care costs have been associated with late diagnosis and initiation of ART at lower CD4 cell counts than the BHIVA guidelines recommend.
- The BHIVA Writing Group recognizes that cost of drugs is an important issue in the choice of ART regimens. **There are limited cost-effectiveness data in the UK comparing different ARV drugs and for this reason the Writing Group did not include cost-effectiveness as an outcome in ART comparisons.**
- The Writing Group, however, believes that **reducing treatment costs should not be at the cost of an increased risk of poorer treatment outcomes and quality of care**, not least as these are likely to have a detrimental impact on long-term cost.

A reduced dose of 400 mg efavirenz is non-inferior to the standard dose of 600 mg, when combined with TDF/FTC in ART-naive adults with HIV-1 infection

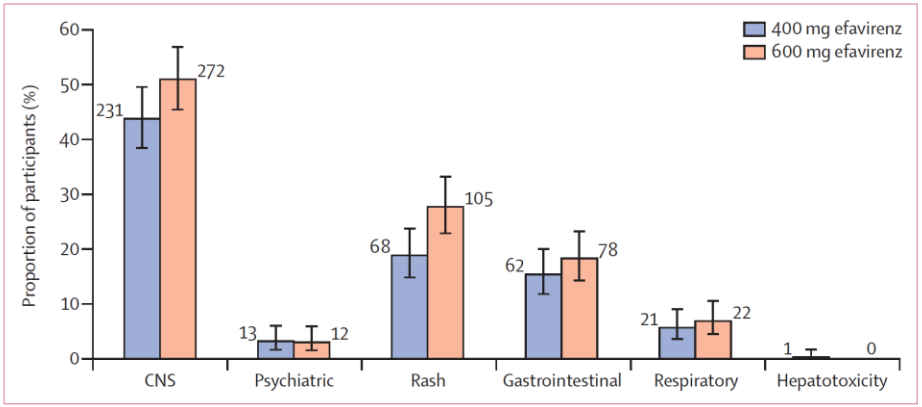


630 patients (efavirenz 400=321; efavirenz 600=309).

32% were women; 37% were African, 33% were Asian, and 30% were white.

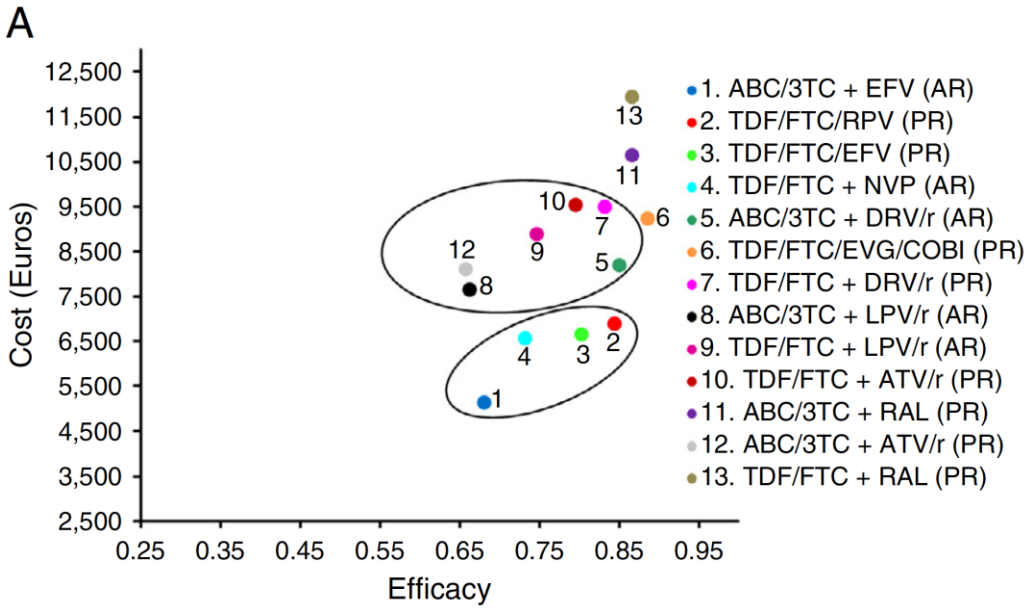
The mean baseline CD4 cell count was 273 cells per µL (SD 99) and median plasma HIV-RNA was 4.75 log10 copies per mL (IQR 0.88).

The proportion of participants with a viral load below 200 copies per mL at week 48 was 94.1% for efavirenz 400 mg and 92.2% for 600 mg (difference 1.85%, 95% CI −2.1 to 5.79).



Encore1 Study Group, Lancet, 2014

Cost effectiveness analysis of preferred/alternative GESIDA regimens for initial ARV therapy



In the base case scenario, the cost of initiating treatment ranges from 5,133 € for ABC/3TC + EFV to 11,949 Euros for TDF/FTC + RAL.

The efficacy varies between 0.66 for ABC/3TC + LPV/r and ABC/3TC + ATV/r, and 0.89 for TDF/FTC/EVG/COBI.

Efficiency, in terms of cost/efficacy, ranges from 7,546 to 13,802 € per responder at 48 weeks, for ABC/3TC + EFV and TDF/FTC + RAL respectively.

Considering ART official prices, the most efficient regimen was ABC/3TC + EFV (AR), followed by the non-nucleoside containing PR (TDF/FTC/RPV and TDF/FTC/EFV).

Blasco AJ, et al. Enferm Infecc Microbiol Clin, 2014

Two Options for saving costs

Option 1:

100% treatment with Single Tablet Regimens and patented versions of drugs. Prices stay the same as in 2011 – no further rises in price (e.g. EFV to DTG)

All patented drugs and STRs sold at 30% discount to NHS.

Option 2:

100% switch to generics after patent expiry. People on STRs switched to generic components. TDF/FTC treatment continues to 2017.

2014	Switch to generic ABC, 3TC, EFV, NVP, ZDV
2016	Switch to generic LPV/r
2017/8	Switch to generic TDF, FTC, ATV/r and DRV/r

Johnson M, 6th ICAR, Rome, May 25-27, 2014

NHS drug budgets over time

Year	Number Treated	Option 1 (Patented)	Option 2 (Generic)	Annual savings
2014	72,360	£433M	£342M	£91M
2015	78,148	£468M	£369M	£99M
2016	84,400	£505M	£384M	£121M
2017	91,152	£546M	£154M	£393M
2018	98,445	£589M	£178M	£412M
Total budget:		**£2.54 billion**	**£1.43 billion**	**£1.11 B**

Saving in drugs budget over 5 years is £1.11 billion (44%).

Johnson M, 6th ICAR, Rome, May 25-27, 2014

Projected average yearly costs of care for the HIV-infected population in the Lazio region, 2012-2016*

Sensitivity analysis on different strategies

Base Case Scenario (million €)	147.0		
Sensitivity analyses – million € (% change compared with Base Case Scenario)			
Expanded cART initiation criteria	150.3 (+2.3)		
	Proportion of naïve patients starting cART with an NNRTI-based regimen		
	50.0%	70.0%	
Choice of regimens for naïve subjects	146.5 (–0.3)	146.0 (–0.6)	
Simplification strategies from PI/r regimens		Proportion of subjects switched†	
	20.0%	30.0%	40.0%
Switch to NNRTI-based STR‡	146.4 (–0.4)	146.1 (–0.6)	145.9 (–0.7)
Switch to PI/r monotherapy	146.0 (–0.6)	145.6 (–0.9)	145.1 (–1.3)
Use of generic ARVs		Proportion of branded ARVs substituted	
	20.0%	50.0%	90.0%
30% discount compared with branded ARV	146.0 (–0.6)	144.6 (–1.6)	142.7 (–2.9)
50% discount compared with branded ARV	145.5 (–1.0)	143.3 (–2.5)	140.3 (–4.5)
70% discount compared with branded ARV	145.0 (–1.4)	141.9 (–3.4)	139.9 (–6.1)

ARV, antiretroviral; cART, combination antiretroviral therapy; NNRTI, nonnucleoside reverse transcriptase inhibitor; PI/r, protease inhibitor/ritonavir-boosted; STR, single tablet regimen.

*Each scenario is evaluated separately and compared with the Base Case Scenario.

†Simplification strategies were applied to stably suppressed subjects on first and second lines of treatment.

‡Tenofovir,emtricitabine and efavirenz (Atripla®).

Angeletti C, et al. HIV Med, 2013

Summary

- Starting ART at high (>350 cell/mm^3) CD4 count remains a controversial issue in Europe;
- Conflicting survival data from observational studies should be implemented with additional benefit demonstrations (cumulative viremia, inflammatory markers, ageing and immune recovery, treatment as prevention in serodiscordant couples);
- ART should be started by a combination of 2 NRTIs and a third drug among NNRTIs, PIs/r or INSTIs. Choice criteria could be influenced by patient advanced profile, viral characteristics and cost-benefit ratio;
- Alternative options could be implemented in specific settings (female, older aged, low CD4+ count, HCV-coinfection, high rate of comorbidities);
- Rate of change/discontinuing after 3 years from starting remains high; more convenient ART approaches could minimize this limit;
- Cost-constraining strategies and replacement by generic ARVs may improve ART sustainability an a setting of raising limiting resources.