# Comorbosità e mortalità
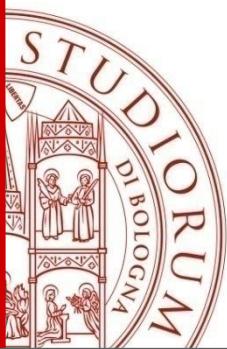
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Università di Bologna

WORKSHOP

NOVITÀ IN INFETTIVOLOGIA AUTUMN 2018

Bologna, 23 Novembre 2018
Società Medica Chirurgica di Bologna – Palazzo dell'Archiginnasio
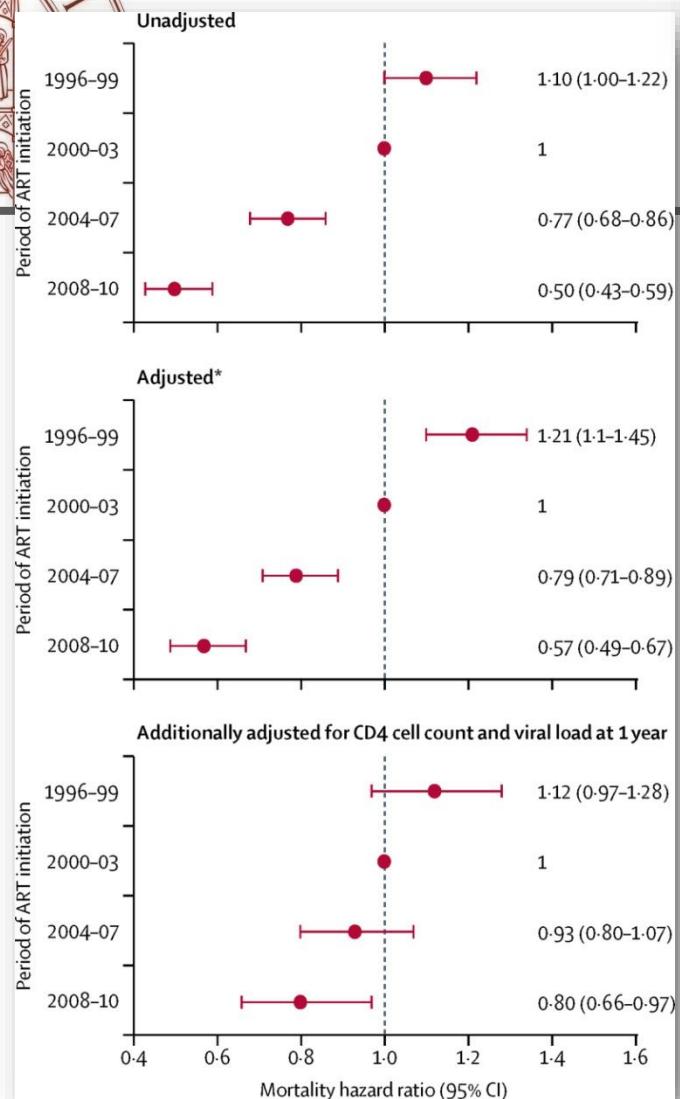
IL SOTTOSCRITTO LEONARDO CALZA

IN QUALITÀ DI RELATORE DELL'EVENTO IN CORSO, AI SENSI DELL'ART. 3.3 SUL CONFLITTO DI INTERESSI, PAG. 17 DEL REG. APPLICATIVO DELL'ACCORDO STATO-REGIONI DEL 5/11/09, PER CONTO DEL PROVIDER **DICHIARA CHE NEGLI ULTIMI DUE ANNI HA AVUTO I SEGUENTI RAPPORTI ANCHE DI FINANZIAMENTO CON SOGGETTI PORTATORI DI INTERESSI COMMERCIALI IN CAMPO SANITARIO:**

-JANSSEN
-ABBVIE
-MSD
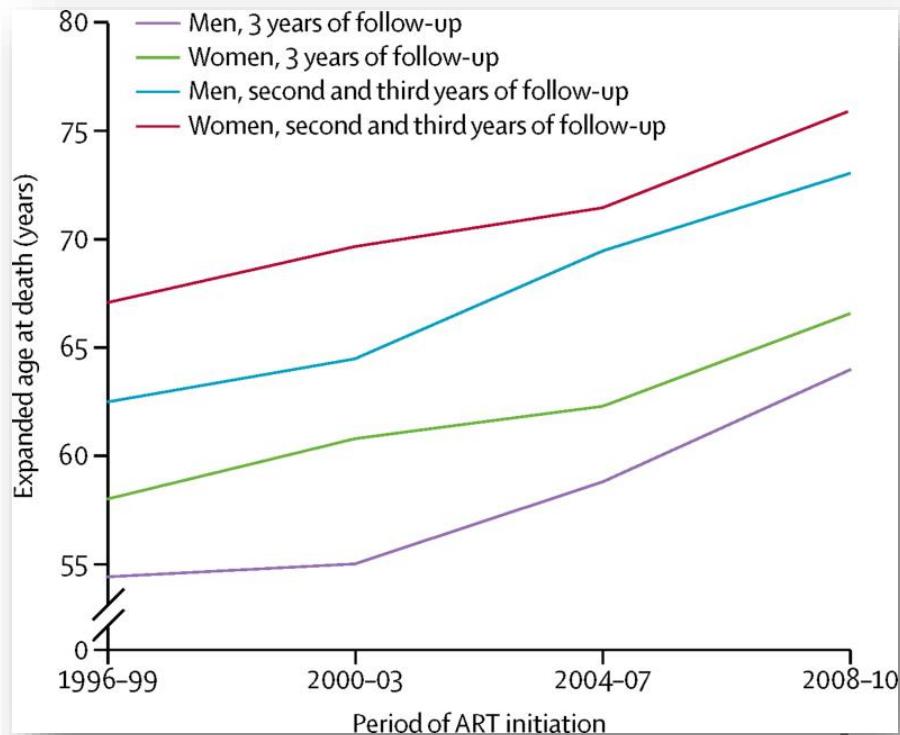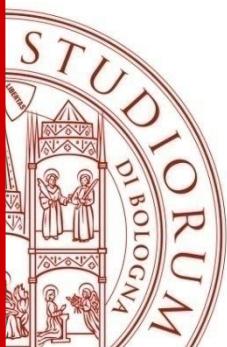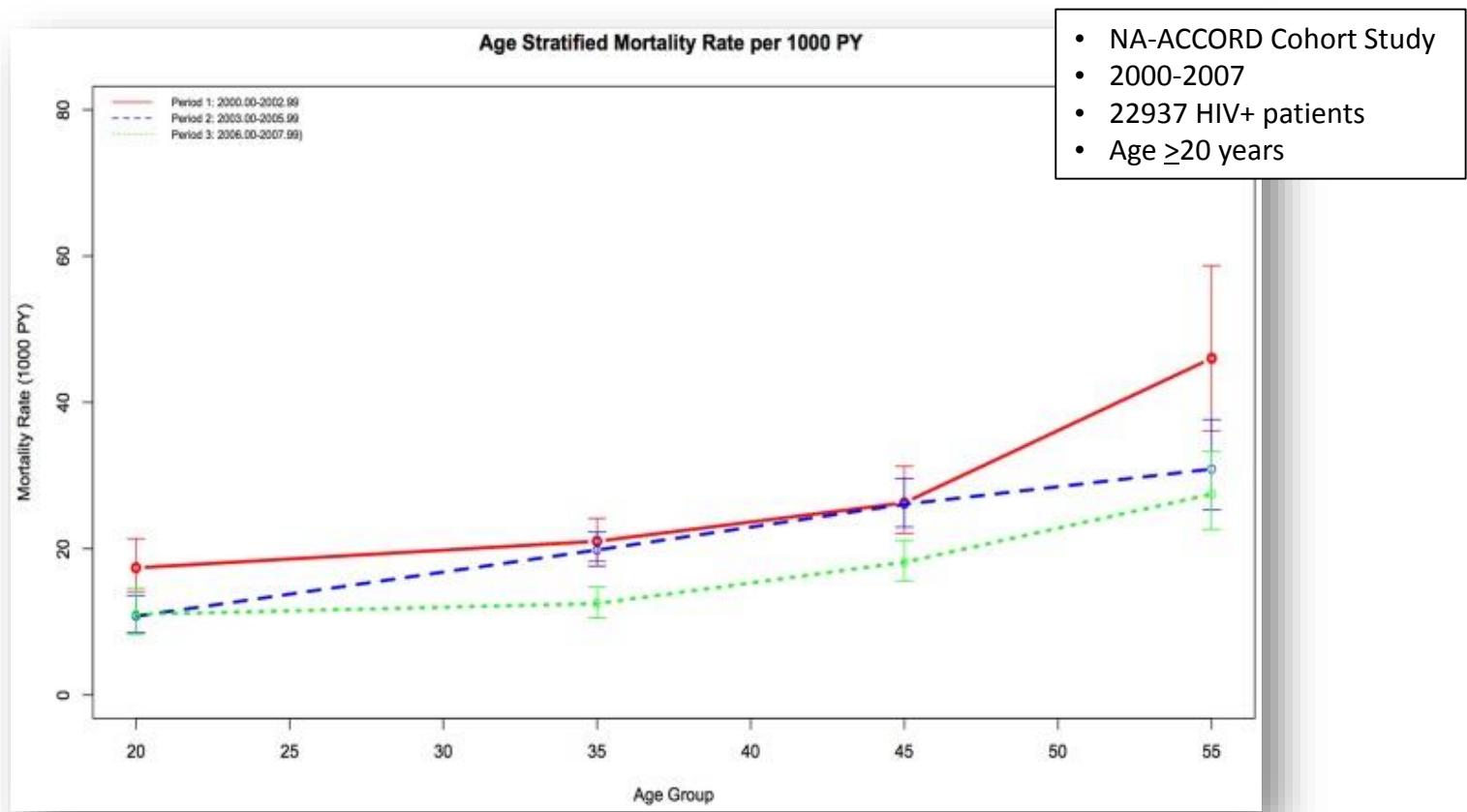
(Lancet HIV 2017)

•Antiretroviral Therapy Cohort Collaboration (ART-CC): 18 European and North-American HIV-1 cohorts
•88504 patients
•3-year follow-up
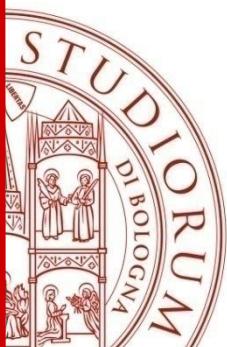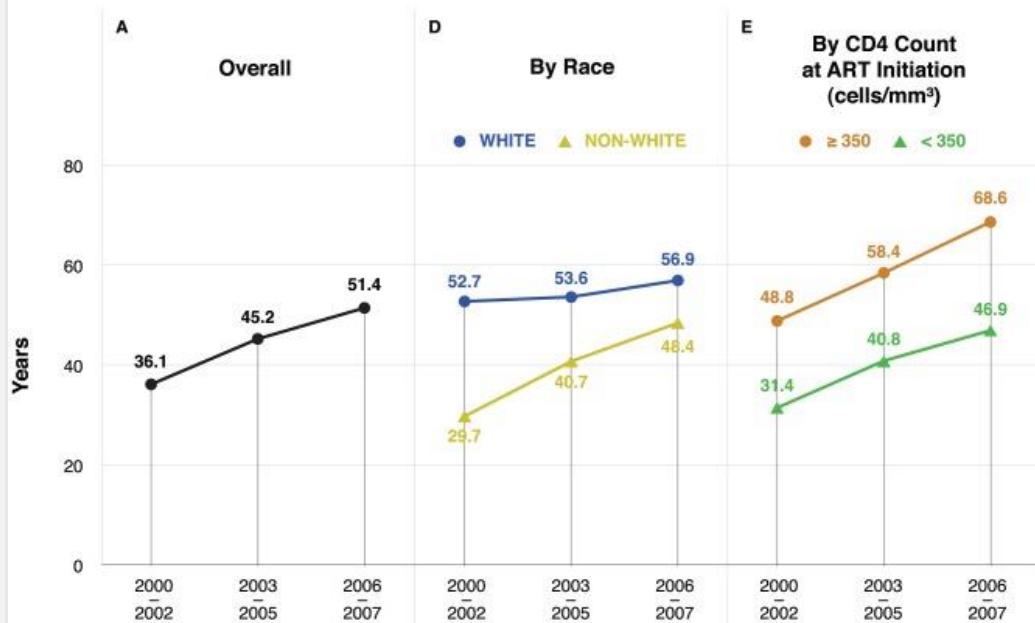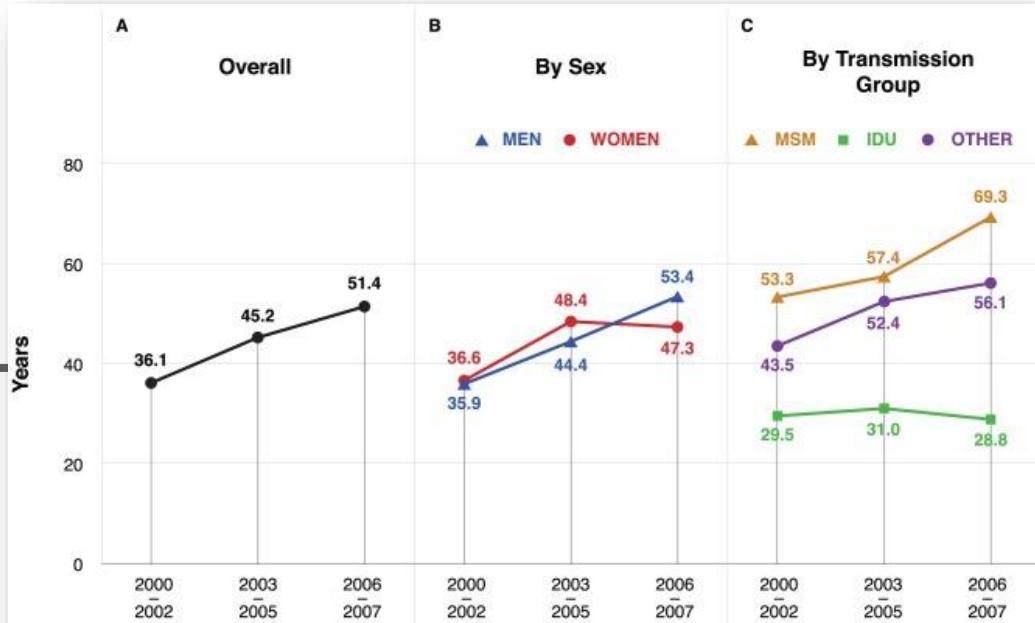
Closing the Gap: Increases in Life Expectancy among Treated HIV-Positive Individuals in the United States and Canada

Age Stratified Mortality Rate per 1000 PY

- NA-ACCORD Cohort Study
- 2000-2007
- 22937 HIV+ patients
- Age ≥20 years
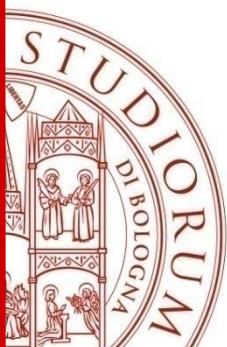
(Samij H et al., PLoS One 2013)

Life expectancy estimates at age 20 years
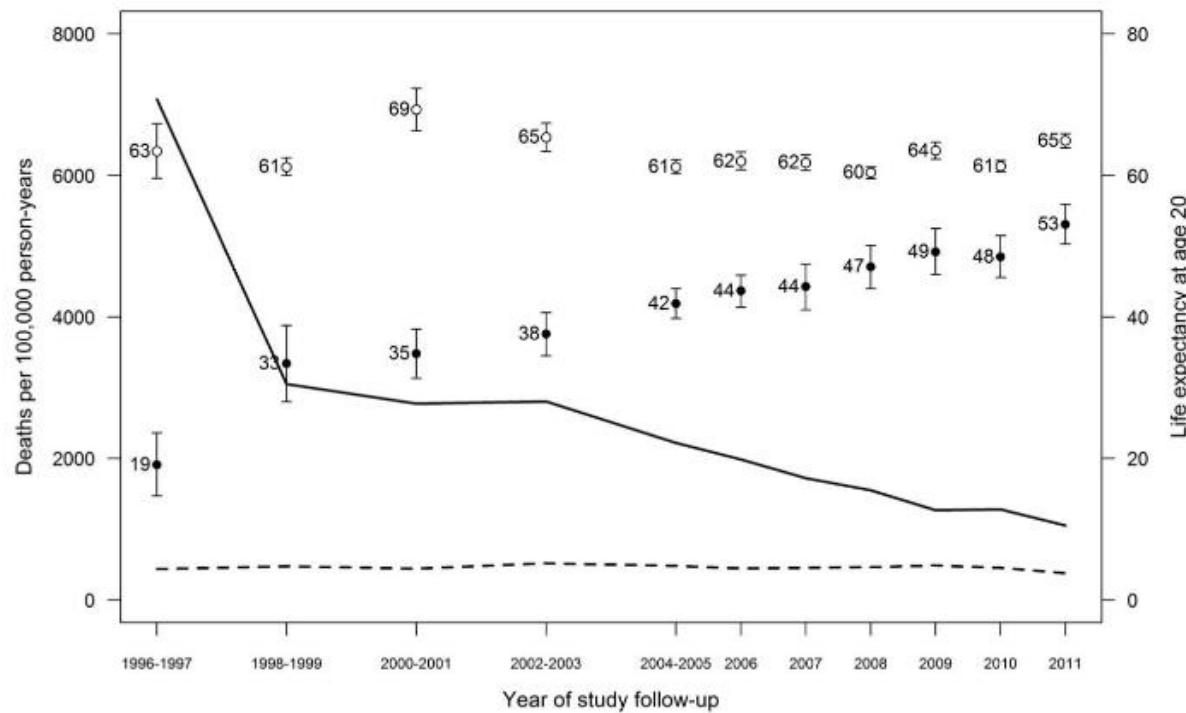
(Samij H et al., PLoS One 2013)
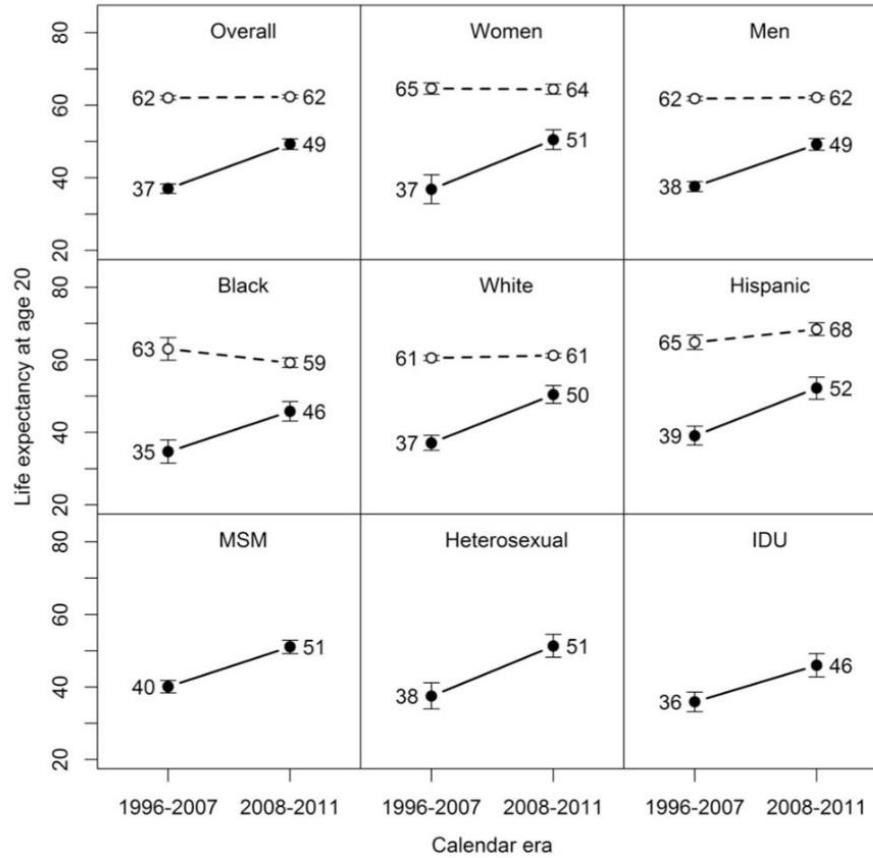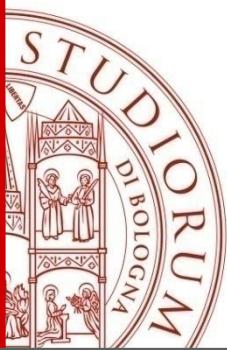
Narrowing the Gap in Life Expectancy Between HIV-Infected and HIV-Uninfected Individuals With Access to Care
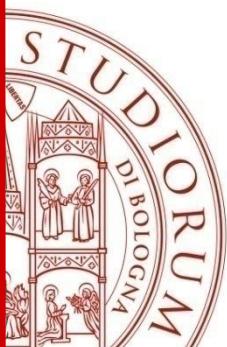
- Kaiser Permanente Cohort
- California
- 1996-2011
- 24768 HIV+ patients
- 257600 HIV- residents
- Age ≥20 years

(Marcus JL et al., J AIDS 2016)

(Marcus JL et al., J AIDS 2016)
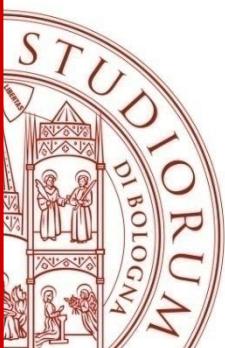
Life Expectancy at Age 20 for HIV-Infected and HIV-Uninfected Individuals, Kaiser Permanente California, 2008–2011

|	Life Expectancy at Age 20 (95% CI)		
	HIV Infected	**HIV Uninfected**	**Difference** [*]
Overall	49.3 (47.8 to 50.7)	62.3 (61.9 to 62.8)	13.1 (11.5 to 14.6)
	HIV infected and initiated ART with CD4 ≥500 cells/μL	HIV uninfected	Difference
Overall	54.5 (51.7 to 57.2)	62.3 (61.9 to 62.8)	7.9 (5.1 to 10.6)
No hepatitis B or C	55.4 (52.6 to 58.2)	62.6 (62.1 to 63.1)	7.2 (4.4 to 10.0)
No drug/alcohol abuse	57.2 (54.6 to 59.9)	63.8 (63.3 to 64.3)	6.6 (3.9 to 9.3)
No smoking	58.9 (55.8 to 62.1)	64.3 (63.6 to 65.0)	5.4 (2.2 to 8.7)
No hepatitis B or C, drug/alcohol abuse, or smoking	59.2 (56.0 to 62.4)	65.0 (64.2 to 65.7)	5.7 (2.4 to 9.0)
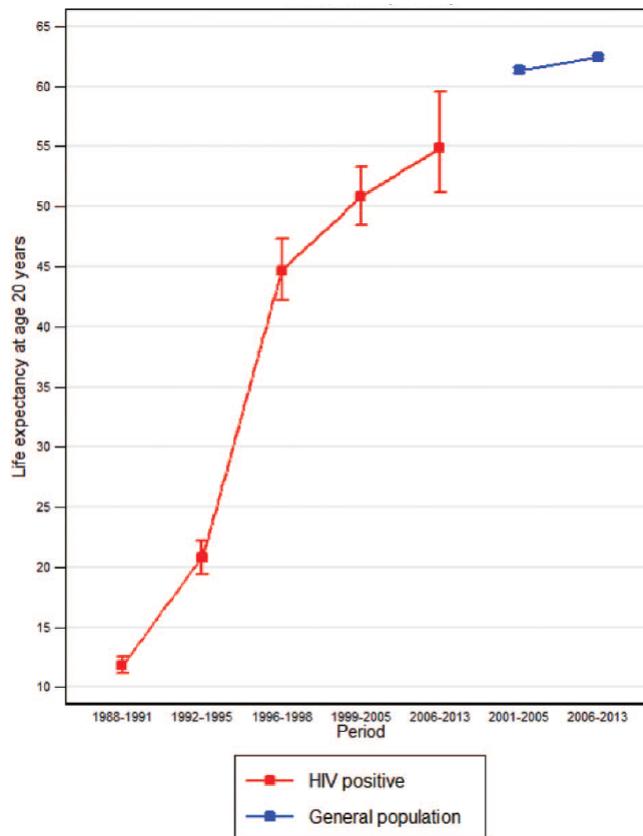
Life expectancy estimates for HIV-infected individuals initiating ART with CD4 ≥500 cells per microliter were among previously ART-naive patients.

[*] All differences were statistically significant at $P < 0.001$, with P values derived from z tests.

(Marcus JL et al., J AIDS 2016)
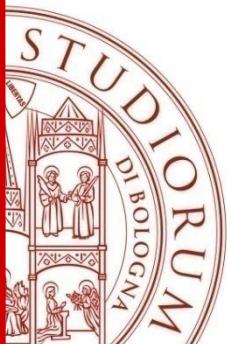
Life expectancy in HIV-positive persons in Switzerland: matched comparison with general population

- Swiss HIV Cohort Study
- 1988-2013
- 16532 HIV+ patients
- 927583 HIV- residents
- Age $\geq$20 years

(Gueler A et al., AIDS 2017)
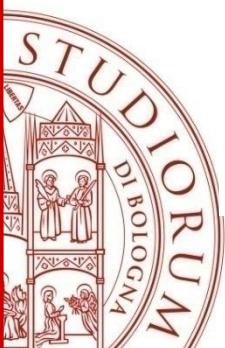
Life expectancy in HIV-positive persons in Switzerland: matched comparison with general population

Table 3. Life expectancy at age 20 years in the Swiss HIV Cohort Study, by treatment era.

|	Life expectancy (95% CI)				
	Monotherapy (1988–1991)	Dual therapy (1992–1995)	Early cART (1996–1998)	Later cART (1999–2005)	Recent cART (2006–2013)
Overall life expectancy	11.8 (11.2–12.5)	20.8 (19.4–22.2)	44.7 (42.2–47.3)	50.8 (48.5–53.3)	54.9 (51.2–59.6)
Education					
Higher education	–	26.7 (22.2–31.6)	53.0 (46.9–59.0)	58.2 (53.4–63.2)	60.0 (53.4–67.8)
Vocational training	–	25.3 (23.0–27.7)	44.4 (41.4–47.7)	49.2 (46.5–52.1)	52.6 (48.3–57.9)
Compulsory school	–	24.3 (21.3–27.5)	38.9 (35.1–43.0)	46.5 (43.1–50.3)	52.7 (46.4–60.1)
Main source of income					
Work	–	32.8 (29.2–36.5)	55.0 (50.9–58.9)	63.9 (59.3–68.4)	62.9 (56.2–70.9)
Welfare benefits	–	15.8 (13.6–18.4)	31.5 (29.0–34.1)	39.4 (36.9–42.0)	48.0 (43.4–53.0)
HIV transmission group					
MSM	8.9 (8.1–9.8)	22.9 (20.5–25.4)	52.7 (48.6–57.1)	57.3 (53.5–61.5)	56.8 (51.8–63.6)
Heterosexual contact	15.3 (13.7–17.21)	29.6 (26.1–33.3)	49.5 (45.8–53.6)	53.1 (50.2–56.2)	56.7 (51.7–62.8)
Injection drug use	12.4 (11.5–13.3)	15.7 (14.2–17.4)	27.3 (25.3–29.5)	31.3 (28.8–33.4)	35.8 (30.6–41.5)
Injection drug use					
Never	11.3 (10.4–12.2)	25.1 (23.1–27.2)	51.9 (49.0–55.1)	54.6 (52.2–57.1)	57.2 (53.1–62.5)
Former	12.2 (11.4–13.1)	16.9 (15.0–18.9)	29.9 (27.4–32.5)	33.5 (30.9–36.3)	39.6 (34.4–45.1)
Current	12.2 (10.6–14.0)	15.2 (12.9–17.7)	24.7 (21.7–27.9)	29.0 (25.8–32.4)	–
Smoking					
Never	–	–	–	65.2 (60.1–70.6)	59.0 (53.5–65.7)
Former	–	–	–	56.4 (51.2–62.1)	54.6 (48.2–61.8)
Current	–	–	–	42.8 (40.7–45.2)	49.4 (45.2–54.6)
Presentation at enrolment*					
CD4$^+$ cell count <200 cells/µl	3.2 (2.9–3.6)	6.5 (5.5–7.6)	35.1 (30.2–40.3)	46.7 (42.6–51.2)	47.6 (41.9–54.3)
200–349 cells/µl	11.2 (9.9–12.5)	26.0 (21.7–30.6)	48.0 (40.3–55.6)	50.2 (45.0–55.9)	54.0 (47.0–63.0)
≥350 cells/µl	25.2 (23.5–27.1)	44.5 (40.2–48.6)	59.9 (52.8–66.0)	53.0 (48.7–57.9)	63.9 (54.8–76.0)
Late presentation	6.1 (5.6–6.7)	12.1 (10.6–13.6)	41.1 (36.8–45.5)	48.7 (45.5–52.3)	53.2 (48.2–59.5)
Presentation with advanced HIV disease	3.5 (3.2–3.9)	7.3 (6.2–8.4)	36.0 (31.2–41.0)	46.5 (42.7–50.8)	49.1 (43.5–55.5)
Presentation with AIDS	2.4 (2.2–2.7)	4.4 (3.7–5.2)	29.1 (23.4–35.3)	42.1 (37.1–47.7)	46.3 (38.4–54.9)

Results from Gompertz parametric survival regression models. Univariate analyses based on 16 532 patients. CI, confidence interval. –, not estimated due to large amount of missing data or small number of patients and deaths.
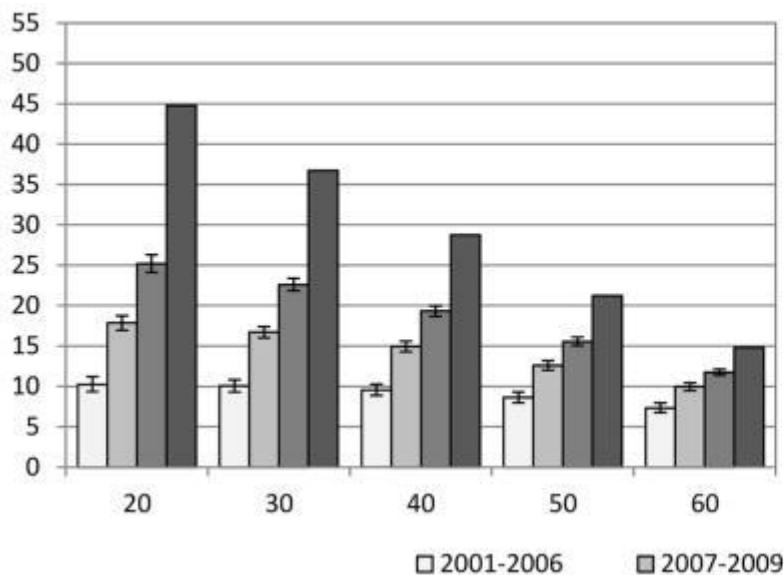
(Gueler A et al., AIDS 2017)
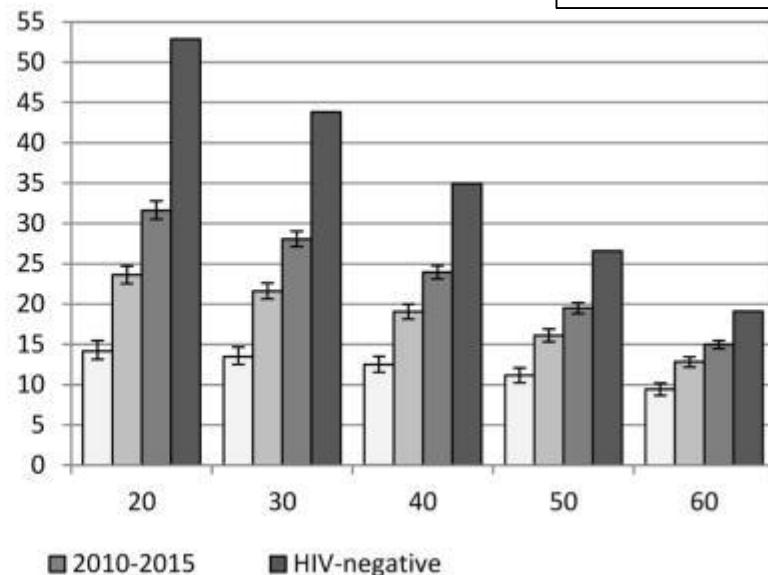
Life expectancy trends in adults on antiretroviral treatment in South Africa

- 8 South African cohorts
- 2001-2015
- 52489 HIV+ patients
- Age $\geq$15 years
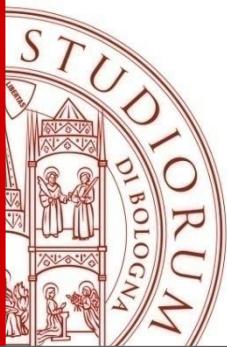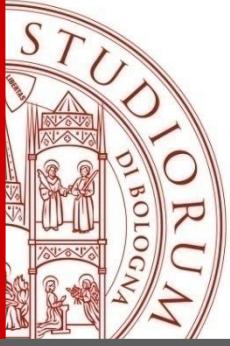
(Johnson LF et al., AIDS 2016)
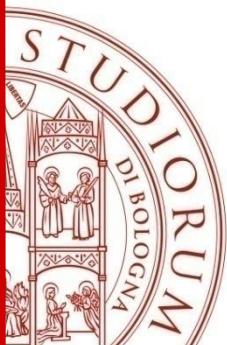
Life expectancy in HIV-positive persons: most vulnerable populations

- Patients starting cART with CD4 cell count <350/mmc

- Black or Hispanic race

- Low educational level

- Injection drug users

- Smokers and alcoholists

- People living in resource-constrained settings
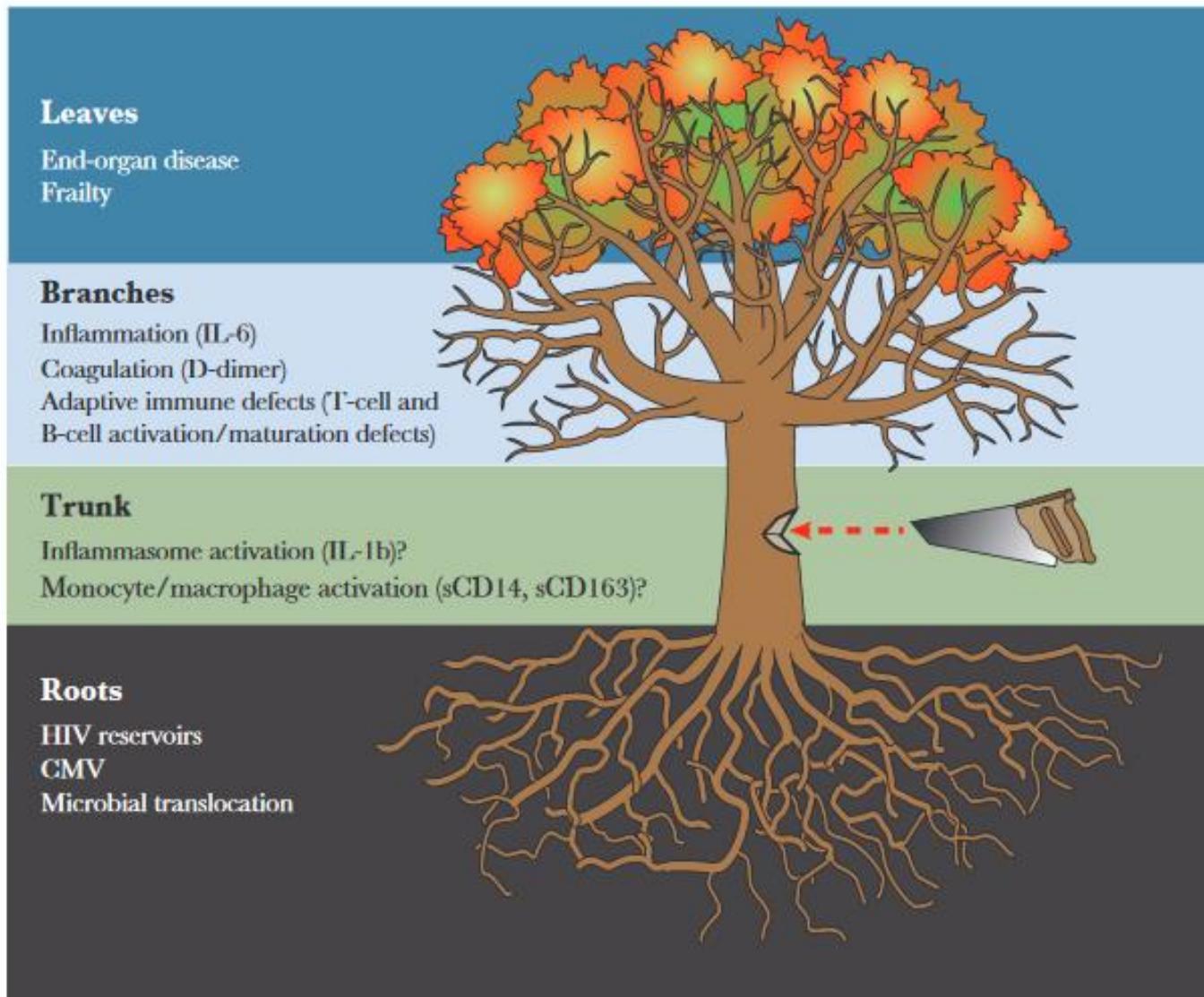
Gap in life expectancy between HIV-infected and HIV-uninfected people with access to care

- Late diagnosis of HIV infection

- Long-term efficacy and tolerability of cART

- Adherence

- Coinfections and opportunistic diseases

- Chronic inflammation and immune activation

- Comorbidities
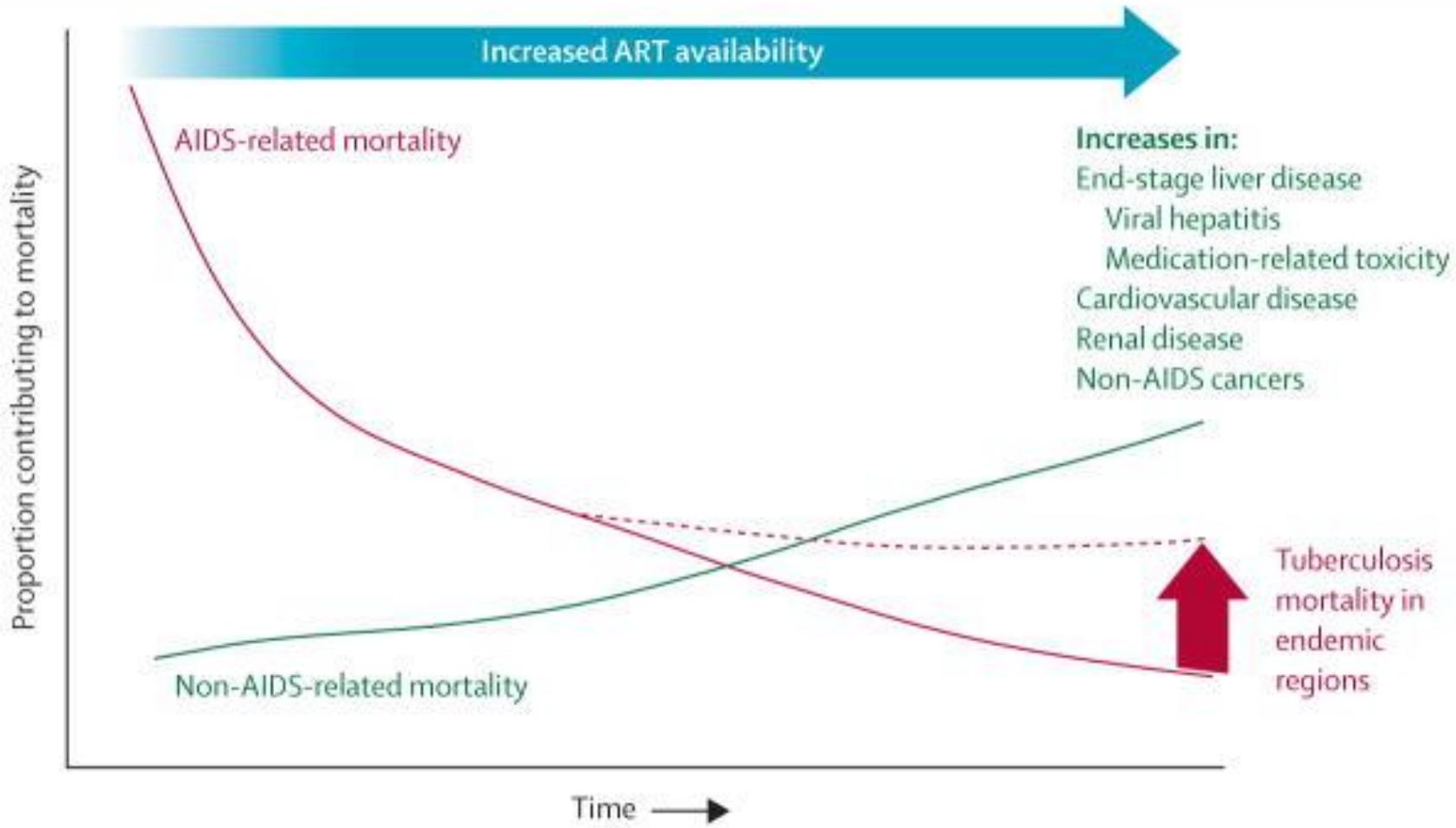
Chronic inflammation and comorbidities
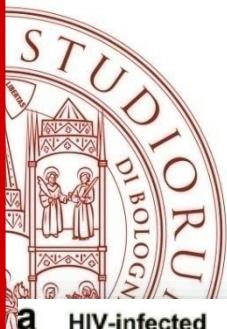
(Justice AC et al., J Infect Dis 2018)
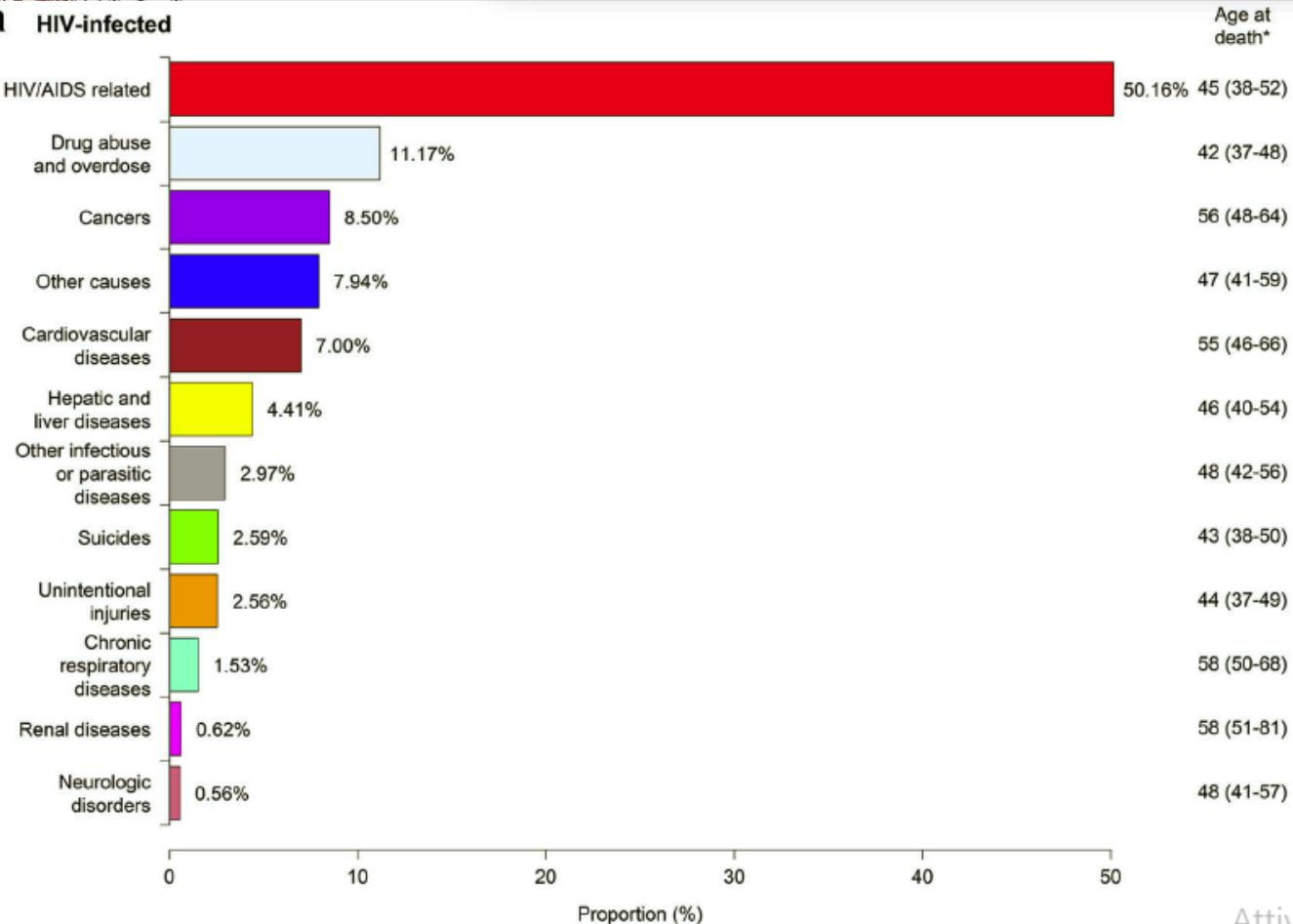
(Altice FM et al., Lancet 2010)

Changes in mortality rates and causes of death in a population-based cohort of persons living with and without HIV from 1996 to 2012

a **HIV-infected**

Cause	Proportion	Age at death*
HIV/AIDS related	50.16%	45 (38-52)
Drug abuse and overdose	11.17%	42 (37-48)
Cancers	8.50%	56 (48-64)
Other causes	7.94%	47 (41-59)
Cardiovascular diseases	7.00%	55 (46-66)
Hepatic and liver diseases	4.41%	46 (40-54)
Other infectious or parasitic diseases	2.97%	48 (42-56)
Suicides	2.59%	43 (38-50)
Unintentional injuries	2.56%	44 (37-49)
Chronic respiratory diseases	1.53%	58 (50-68)
Renal diseases	0.62%	58 (51-81)
Neurologic disorders	0.56%	48 (41-57)

Proportion (%)

- Comparative Outcomes and Service Utilization Trends (COAST) Study
- British Columbia (Canada)
- 13729 HIV+ patients
- 510313 HIV- persons
- 1996-2012

(Eyawo O et al., BMC Infect Dis 2017)

a Overall

Mortality rate (per 1,000 population)

150

100

50

0

HIV+
HIV-

1996   1997-1998   1999-2000   2001-2002   2003-2004   2005-2006   2007-2008   2009-2010   2011-2012

Mortality rates (95% CI)
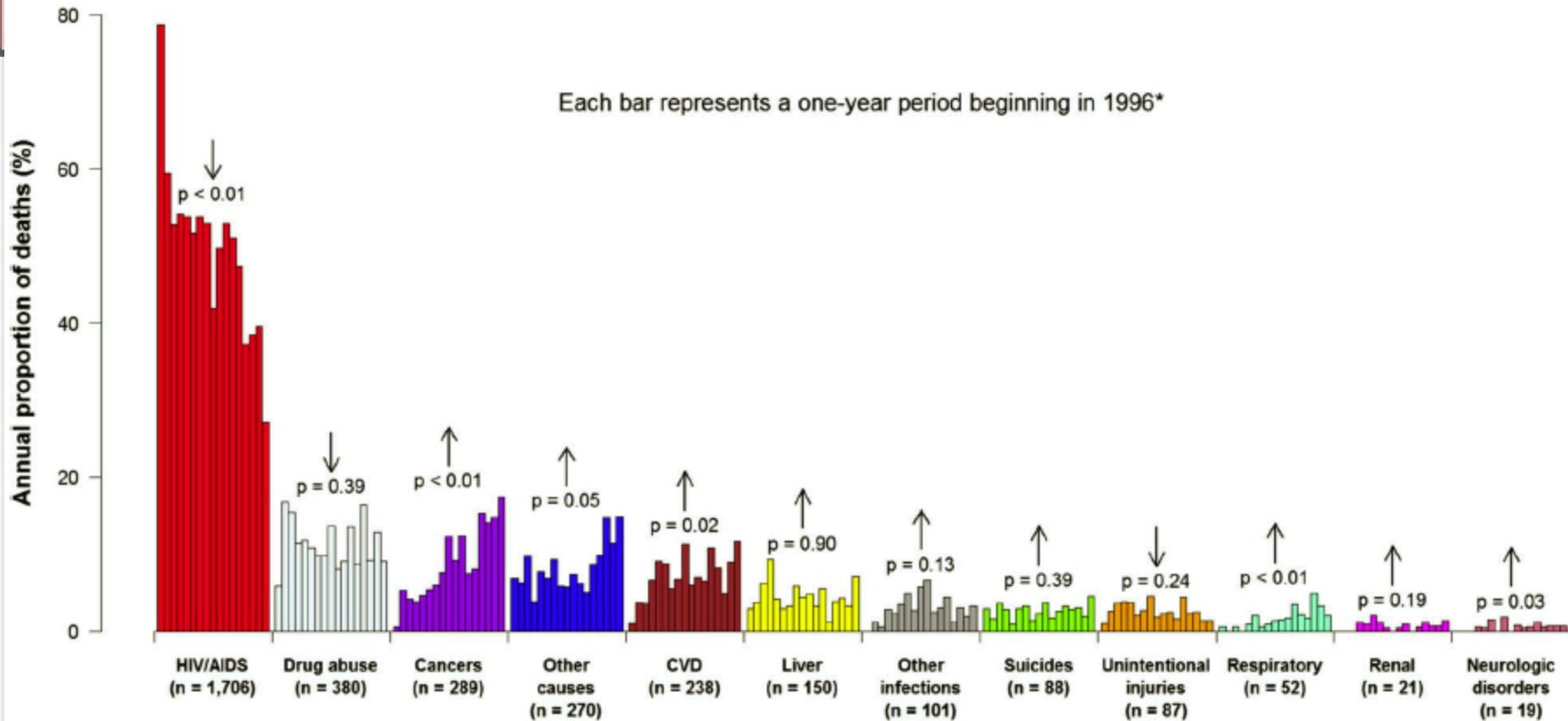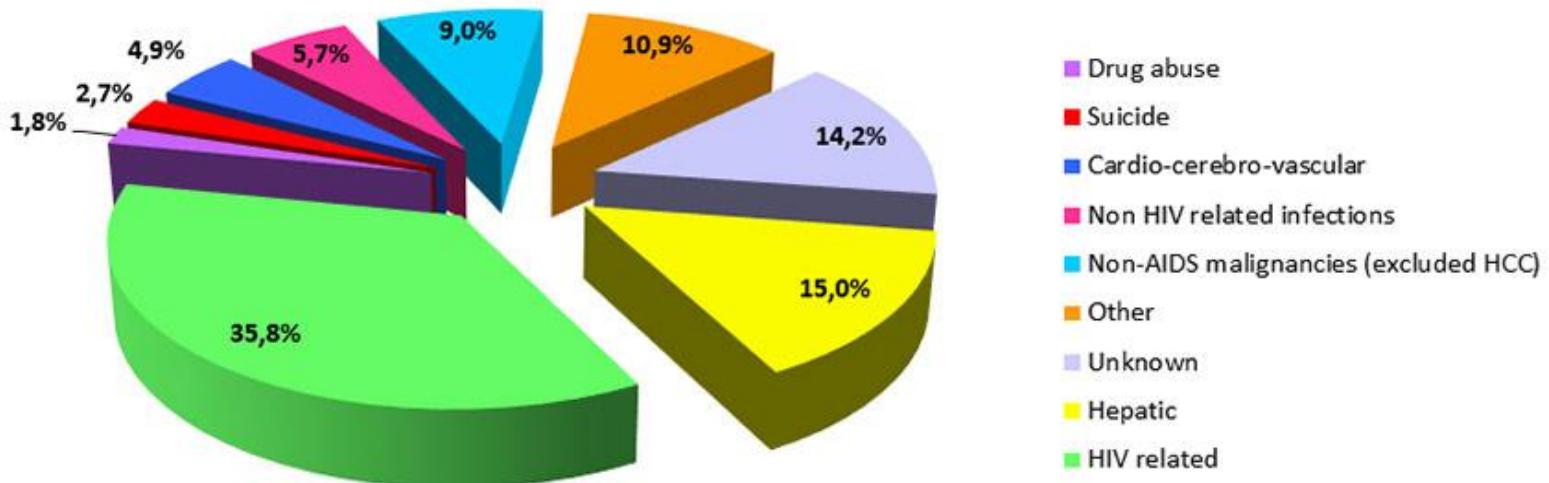
(Eyawo O et al., BMC Infect Dis 2017)

(Eyawo O et al., BMC Infect Dis 2017)

Cause of death, n=962

- Drug abuse
- Suicide
- Cardio-cerebro-vascular
- Non HIV related infections
- Non-AIDS malignancies (excluded HCC)
- Other
- Unknown
- Hepatic
- HIV related

9,0%
4,9%
2,7%
1,8%
5,7%
10,9%
14,2%
15,0%
35,8%
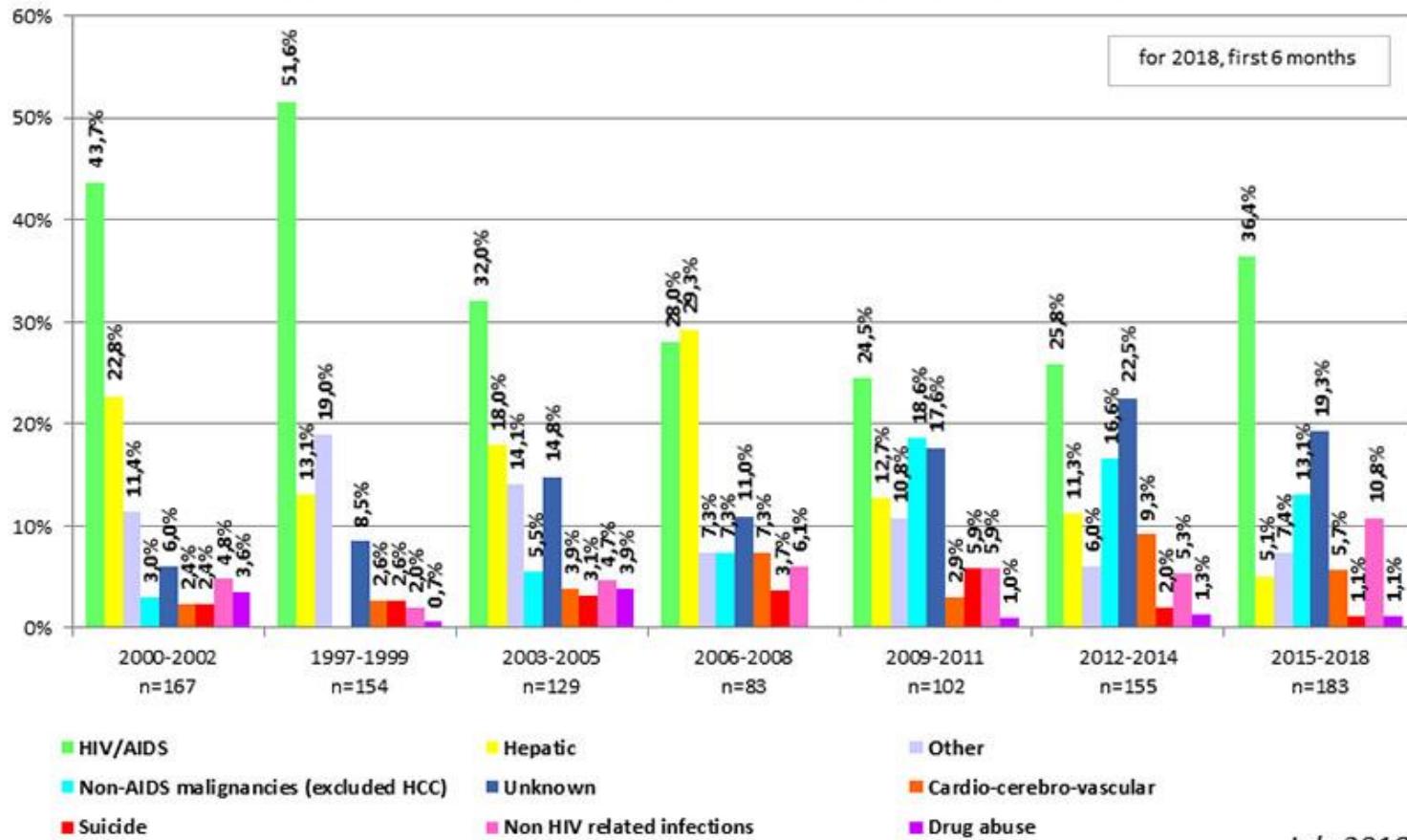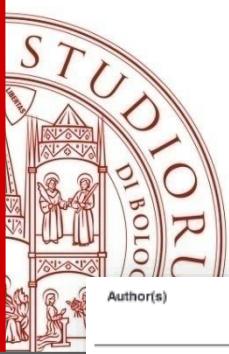
July 2018 Report

Causes of death according to calendar period of death
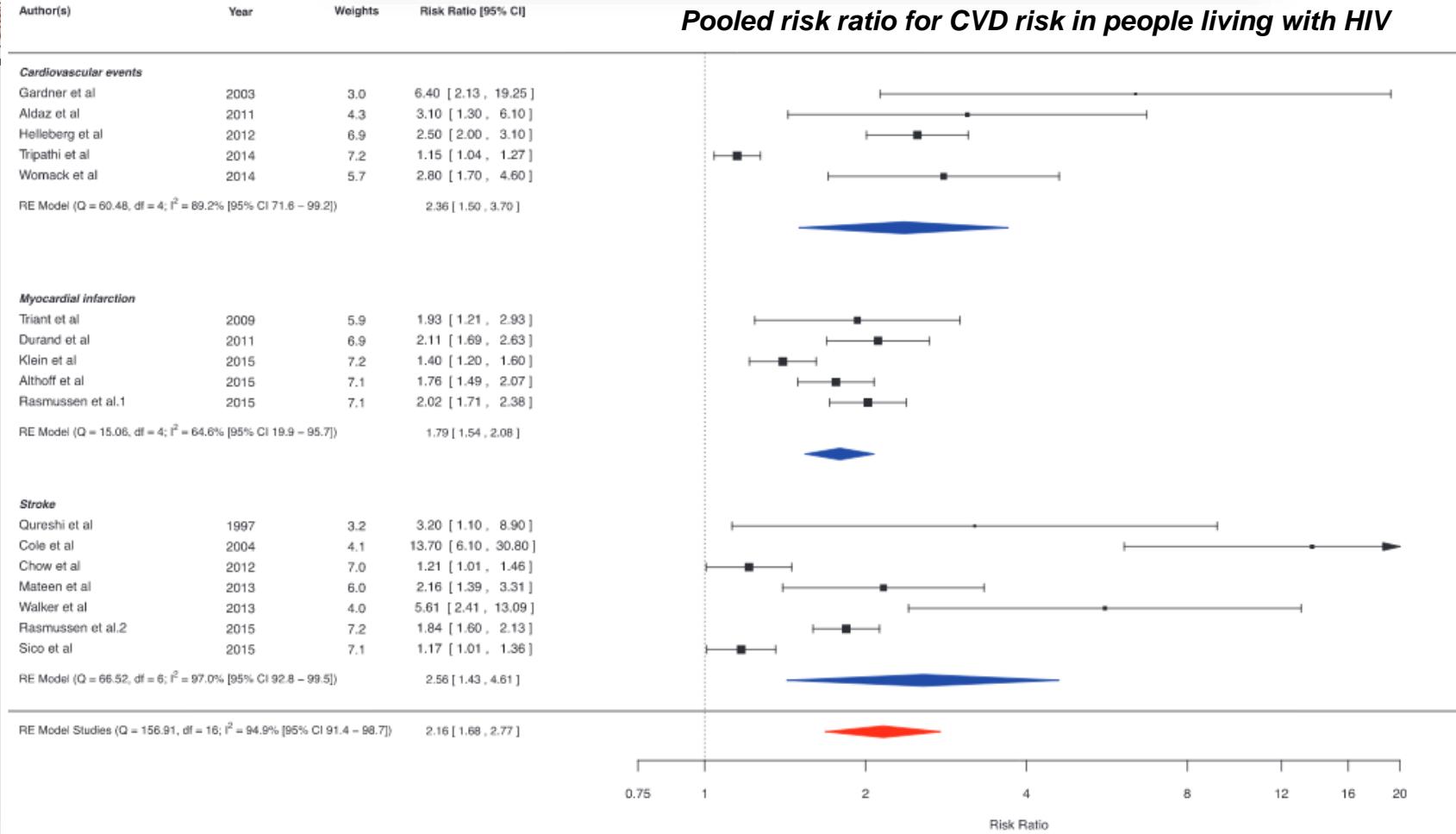
July 2018 Report
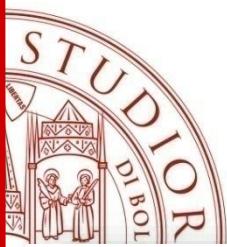
Global Burden of Atherosclerotic Cardiovascular Disease in People Living With HIV

Systematic Review and Meta-Analysis

Pooled risk ratio for CVD risk in people living with HIV

Author(s)	Year	Weights	Risk Ratio [95% CI]
Cardiovascular events			
Gardner et al	2003	3.0	6.40 [2.13 , 19.25]
Aldaz et al	2011	4.3	3.10 [1.30 , 6.10]
Helleberg et al	2012	6.9	2.50 [2.00 , 3.10]
Tripathi et al	2014	7.2	1.15 [1.04 , 1.27]
Womack et al	2014	5.7	2.80 [1.70 , 4.60]
RE Model (Q = 60.48, df = 4; I^2 = 89.2% [95% CI 71.6 – 99.2])			2.36 [1.50 , 3.70]
Myocardial infarction			
Triant et al	2009	5.9	1.93 [1.21 , 2.93]
Durand et al	2011	6.9	2.11 [1.69 , 2.63]
Klein et al	2015	7.2	1.40 [1.20 , 1.60]
Althoff et al	2015	7.1	1.76 [1.49 , 2.07]
Rasmussen et al.1	2015	7.1	2.02 [1.71 , 2.38]
RE Model (Q = 15.06, df = 4; I^2 = 64.6% [95% CI 19.9 – 95.7])			1.79 [1.54 , 2.08]
Stroke			
Qureshi et al	1997	3.2	3.20 [1.10 , 8.90]
Cole et al	2004	4.1	13.70 [6.10 , 30.80]
Chow et al	2012	7.0	1.21 [1.01 , 1.46]
Mateen et al	2013	6.0	2.16 [1.39 , 3.31]
Walker et al	2013	4.0	5.61 [2.41 , 13.09]
Rasmussen et al.2	2015	7.2	1.84 [1.60 , 2.13]
Sico et al	2015	7.1	1.17 [1.01 , 1.36]
RE Model (Q = 66.52, df = 6; I^2 = 97.0% [95% CI 92.8 – 99.5])			2.56 [1.43 , 4.61]
RE Model Studies (Q = 156.91, df = 16; I^2 = 94.9% [95% CI 91.4 – 98.7])			2.16 [1.68 , 2.77]

Risk Ratio: 0.75 1 2 4 8 12 16 20

(Shah ASV et al., Circulation 2018)

Disability adjusted life years per 100,000 persons by country

Legend
<2.34
2.35 to 4.86
4.87 to 10.72
10.73 to 22.27
22.28 to 49.98
49.99 to 131.62
131.62 to 1765.11
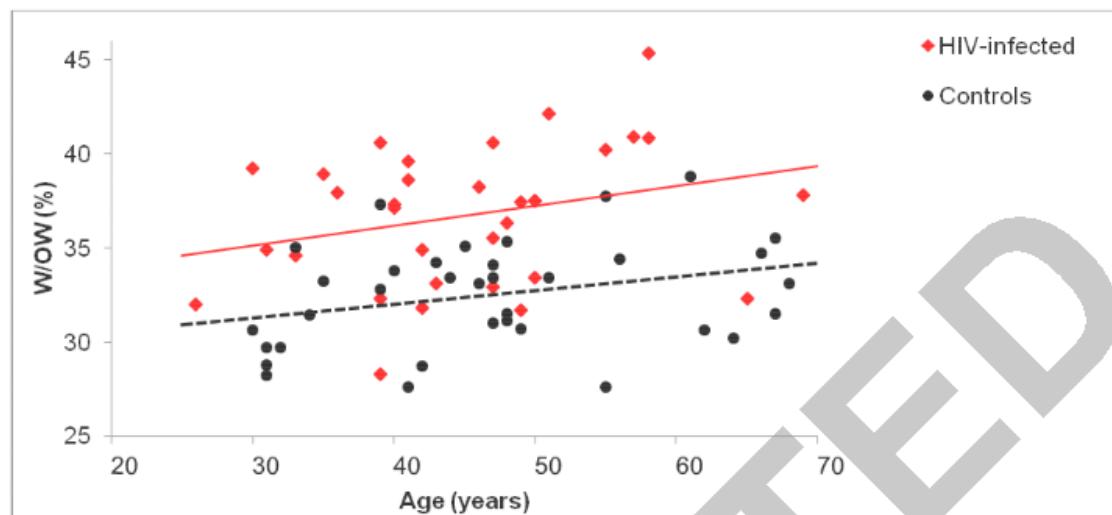
(Shah ASV et al., Circulation 2018)
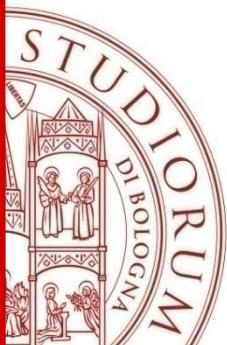
Atherosclerosis is evident in treated HIV-infected subjects with low cardiovascular risk by carotid cardiovascular magnetic resonance

	HIV-infected subjects (n=33)	Control subjects (n=35)	p
Total Lumen Volume (mm^3)	2966.6 (2763.5, 3169.7)	3277.5 (2988.4, 3566.7)	0.079
Total Wall Volume (mm^3)	1712.1 (1599.4, 1824.8)	1574.8 (1431.3, 1718.3)	0.13
Total Vessel Volume (mm^3)	4678.7 (4391.7, 4965.8)	4852.3 (4433.3, 5271.4)	0.49
W/OW Ratio (%)	36.7 (35.4, 38.0)	32.5 (31.5, 33.5)	< 0.0001
Distensibility (%)	22.9 (20.6, 25.1)	24.2 (22.4, 26.1)	0.35

•Case-control study
•33 HIV+ patients on cART with HIV RNA <50 cp/mL vs 35 HIV- controls
•Low CVD risk
•Wall/outer-wall ratio (W/OW) index evaluated by cardiovascular magnetic resonance

(Rose KA et al., J AIDS 2015)
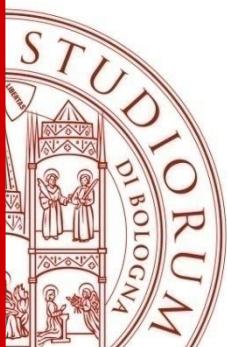
Cumulative viremia and incident myocardial infarction

Association between **baseline viral load** and myocardial infarction (MI)

•CNICS Cohort
•11324 HIV-positive patients
•1996-2016

Outcome	All participants ART-untreated at baseline (63,528 person-years of follow-up, 274 MIs, 137 type 1, 137 type 2)				
	HR per doubling	95% Confidence Interval	HR for 75th vs 25th %ile)	95% CI	MI Rate per 1000 person years (95% CI)
all MI	1.06	1.03, 1.09	1.60	1.28,2.01	4.3 (3.8,4.9)
type 1 MI	1.07	1.03, 1.11	1.73	1.26,2.38	2.2 (1.8,2.5)
type 2 MI	1.05	1.01, 1.09	1.51	1.10,2.08	2.2 (1.8,2.5)

(Delaney JA et al., Epidemiology 2018)

Cumulative viremia and incident myocardial infarction
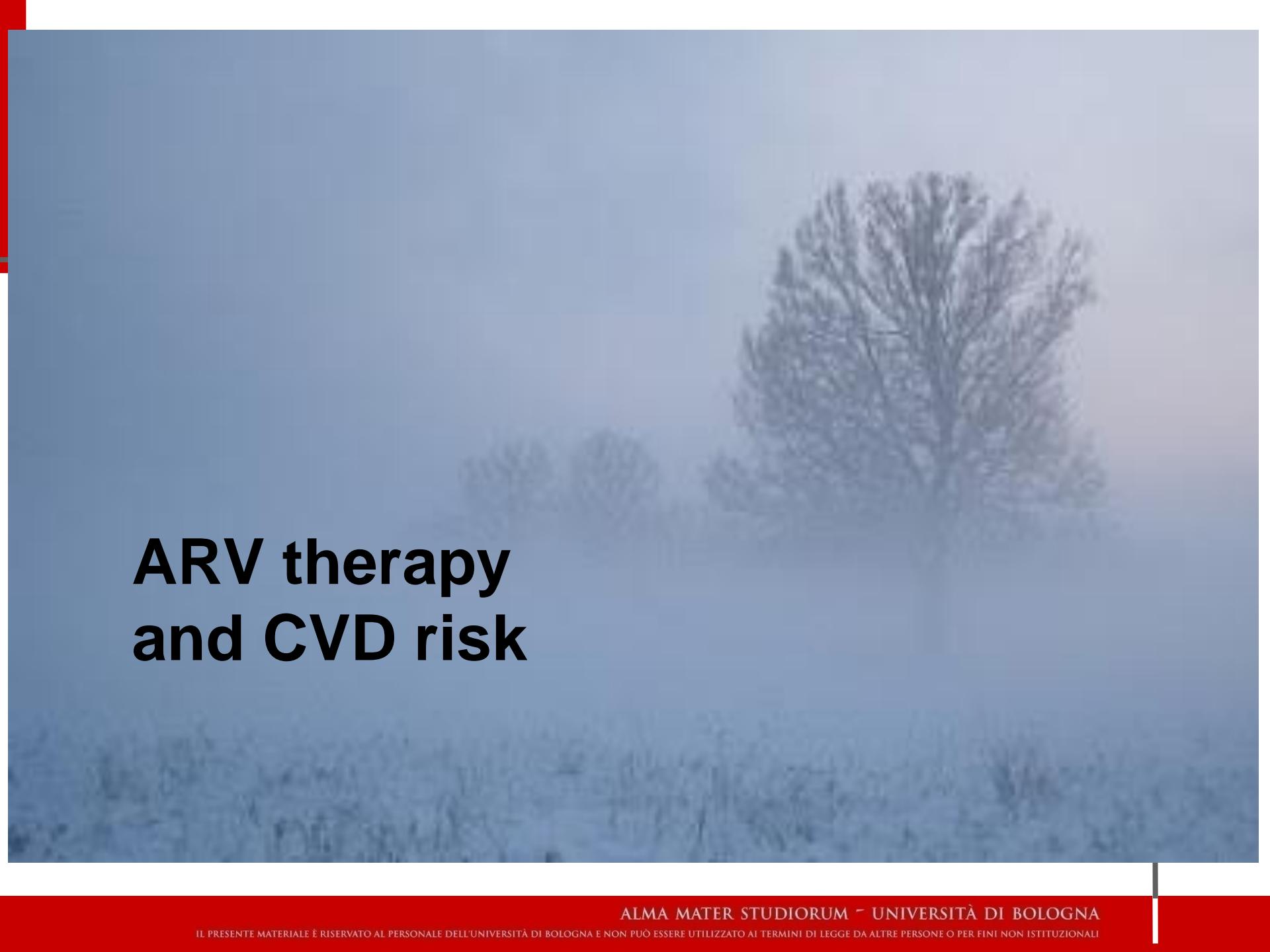
Association between **cumulative viral load** and myocardial infarction (MI)

- CNICS Cohort
- 11324 HIV-positive patients
- 1996-2016

Outcome	All participants ART-untreated at baseline (52,952 person-years of follow-up, 218 MIs, 103 type 1, 115 type 2)				
	HR per doubling	95% Confidence Interval	HR for 75th vs 25th %ile)	95% CI	MI Rate per 1000 person years (95% CI)
all MI	1.07	1.03, 1.11	1.72	1.26,2.36	4.12 (3.61,4.70)
type 1 MI	1.02	0.97, 1.08	1.23	0.78,1.96	1.94 (1.60,2.36)
type 2 MI	1.11	1.07, 1.16	2.52	1.74,3.66	2.17 (1.81,2.61)
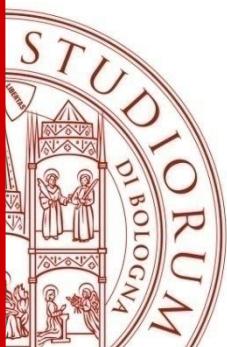
(Delaney JA et al., Epidemiology 2018)
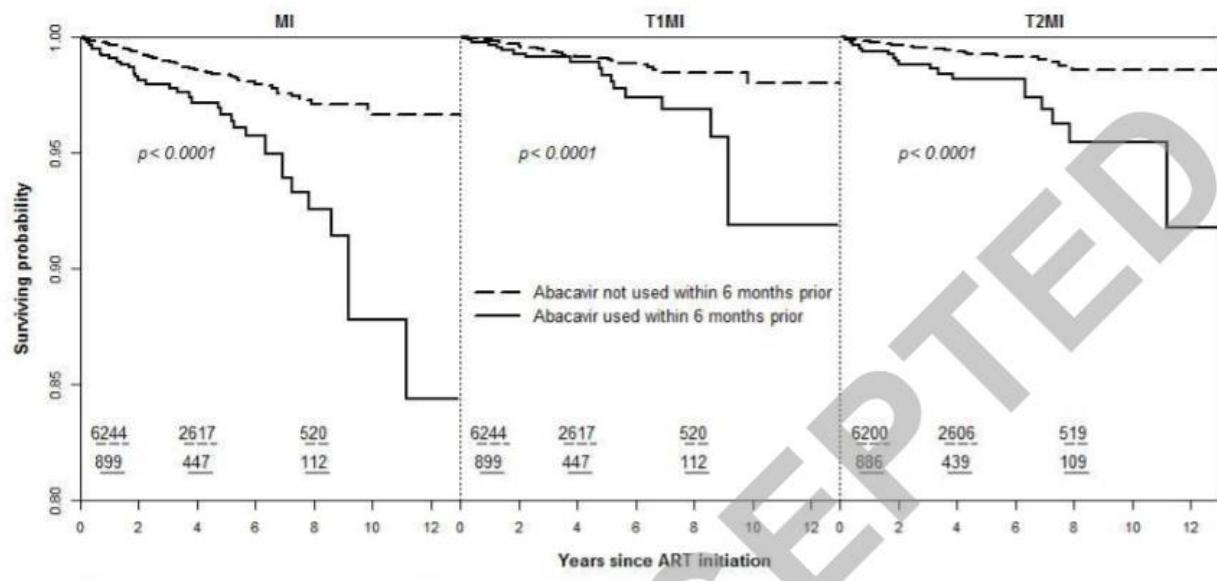
ARV therapy
and CVD risk
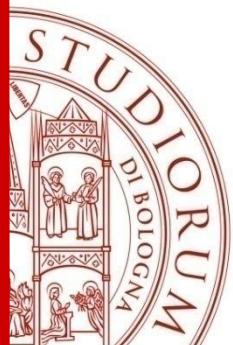
Recent abacavir use increases risk for Types 1 and 2 myocardial infarctions among adults with HIV

Figure 1: Kaplan Meier survival estimates for time from ART initiation to first myocardial infarction, by recent abacavir use, NA-ACCORD
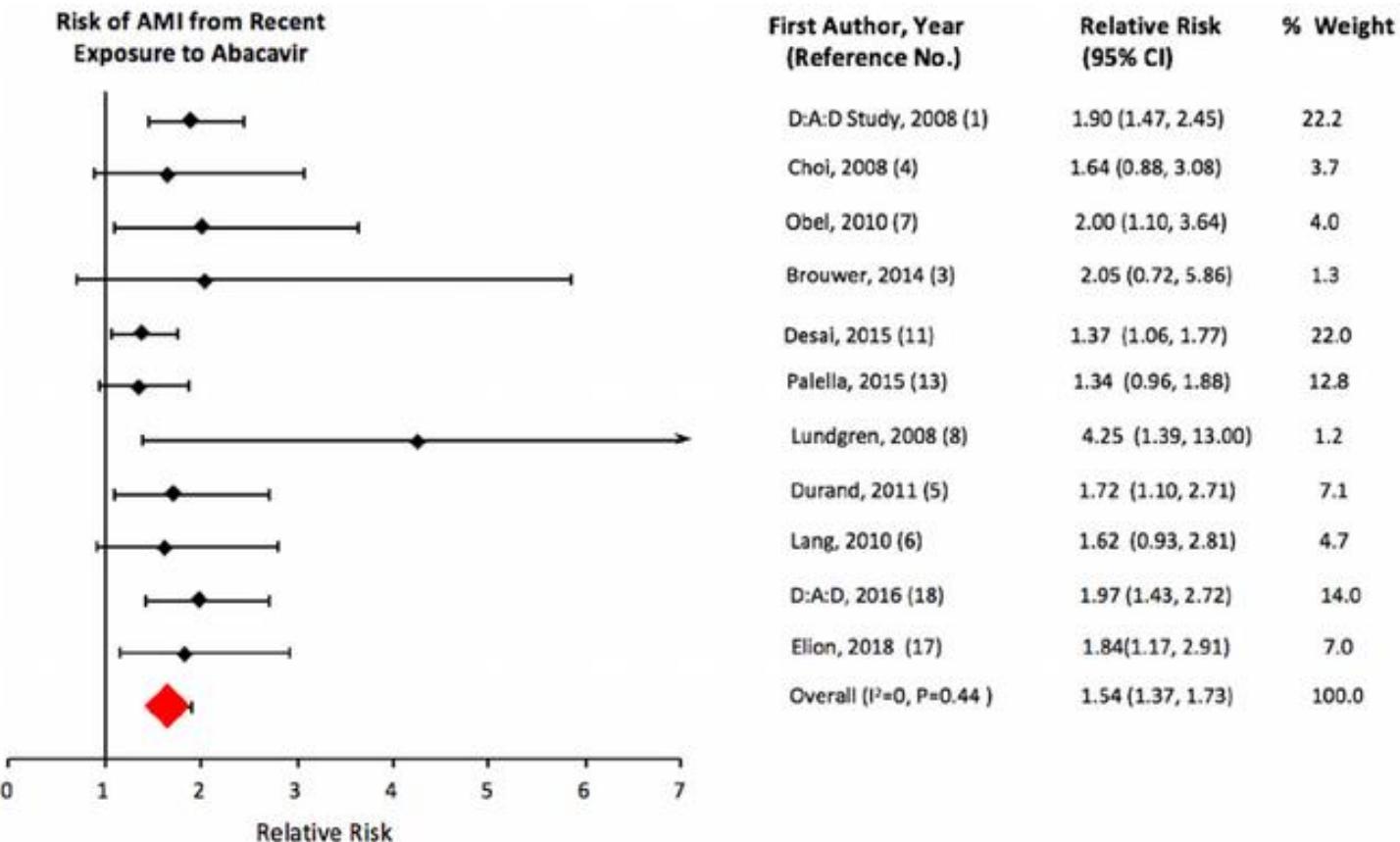
-NA-ACCORD Cohort Study
-8265 HIV+ patients
-median follow-up: 2,9 years
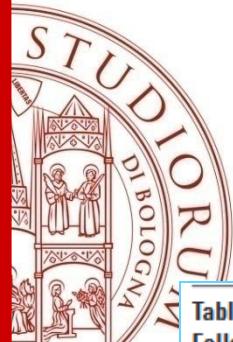
(Elion RA et al., J AIDS 2018)

Risk of cardiovascular disease associated with exposure to abacavir among individuals with HIV: A systematic review and meta-analyses of results from 17 epidemiologic studies

Risk of AMI from Recent Exposure to Abacavir

First Author, Year (Reference No.)	Relative Risk (95% CI)	% Weight
D:A:D Study, 2008 (1)	1.90 (1.47, 2.45)	22.2
Choi, 2008 (4)	1.64 (0.88, 3.08)	3.7
Obel, 2010 (7)	2.00 (1.10, 3.64)	4.0
Brouwer, 2014 (3)	2.05 (0.72, 5.86)	1.3
Desai, 2015 (11)	1.37 (1.06, 1.77)	22.0
Palella, 2015 (13)	1.34 (0.96, 1.88)	12.8
Lundgren, 2008 (8)	4.25 (1.39, 13.00)	1.2
Durand, 2011 (5)	1.72 (1.10, 2.71)	7.1
Lang, 2010 (6)	1.62 (0.93, 2.81)	4.7
D:A:D, 2016 (18)	1.97 (1.43, 2.72)	14.0
Elion, 2018 (17)	1.84 (1.17, 2.91)	7.0
Overall (I^2=0, P=0.44)	1.54 (1.37, 1.73)	100.0

Relative Risk

Abacavir Use and Risk for Myocardial Infarction and Cardiovascular Events: Pooled Analysis of Data From Clinical Trials

-66 clinical trials
-13119 ABC-exposed vs
 7350 ABC-unexposed patients

Table 4. Association Between MIs and ABC Exposure in Different Scenarios Based on ABC Randomization vs Non–ABC Randomization and Varying Follow-up Lengths

Sensitivity Analysis	ABC Exposure Category	No.	ART Exposure, Person-Years	Events, No.	Proportion of Events (95% CI)	Exposure-Adjusted IR[a] (95% CI)	RR[a] (95% CI)
Randomized to ABC, <48 wk follow-up	Exposed	3241	4115	6	0.19 (0.07–0.40)	1.46 (0.66–3.25)	0.69 (0.24–1.99)
	Unexposed	3269	3790	8	0.25 (0.11–0.48)	2.11 (1.06–4.22)	
Randomized or nonrandomized to ABC, ≥48 wk follow-up	Exposed	12796	12426	20	0.16 (0.10–0.24)	1.61 (1.04–2.50)	0.79 (0.41–1.53)
	Unexposed	6963	7897	16	0.23 (0.13–0.37)	2.03 (1.24–3.31)	
Randomized or nonrandomized to ABC, <48 or ≥48 wk follow-up	Exposed	13119	12520	21	0.16 (0.10–0.25)	1.68 (1.09–2.57)	0.83 (0.44–1.60)
	Unexposed	7074	7956	16	0.23 (0.13–0.37)	2.01 (1.23–3.28)	

[a]Poisson regression model was fitted to estimate IRs and RRs of MIs and cardiovascular events.
Abbreviations: ABC, abacavir; ART, antiretroviral therapy; CI, confidence interval; IR, incidence rate; MI, myocardial infarction; RR, relative rate.
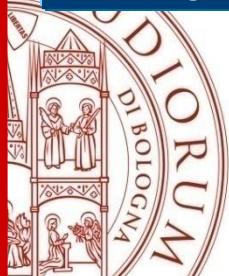
Table 5. Association Between Cardiovascular Events and ABC Exposure in Different Scenarios Based on ABC Randomization vs Non–ABC Randomization and Varying Follow-up Lengths

Follow-up	ABC Exposure Category	No.	ART Exposure, Person-Years	Events, No.	Proportion of Events (95% CI)	Exposure-Adjusted IR[a] (95% CI)	RR[a] (95% CI)
Randomized or nonrandomized to ABC, ≥48 wk	Exposed	12796	12426	36	0.28 (0.20–0.39)	2.90 (2.09–4.02)	0.62 (0.39–0.98)
	Unexposed	6963	7897	37	0.53 (0.37–0.73)	4.69 (3.40–6.47)	
Randomized or nonrandomized to ABC, <48 or ≥48 wk	Exposed	13119	12520	37	0.28 (0.20–0.39)	2.96 (2.14–4.08)	0.64 (0.40–1.00)
	Unexposed	7074	7956	37	0.52 (0.37–0.72)	4.65 (3.37–6.42)	
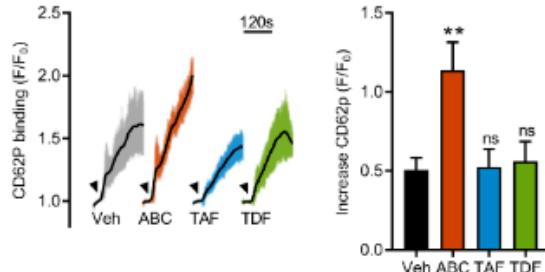
(Nan C et al., Open Forum Infect Dis 2018)
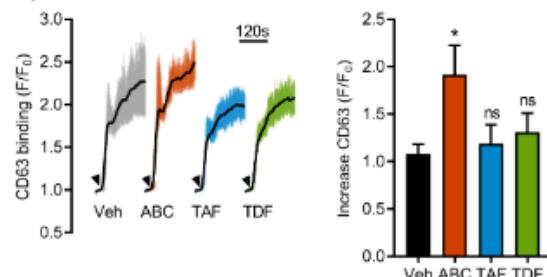
Abacavir increases platelet granule release

A) Alpha Granule Release
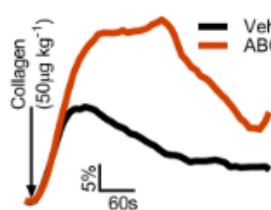
B) Dense Granule Release
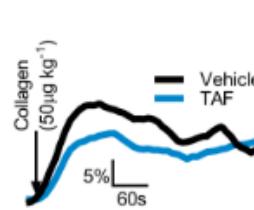
Collagen-evoked (10µg/mL) platelet alpha (A) and dense (B) granule release were monitored in real-time by flow cytometry. Treatment with C_{max} concentrations of ABC, but not TAF or TDF, enhanced platelet granule release. Granule release is a critical step in platelet activation (n=7)

Abacavir enhances platelet aggregation *in vivo*
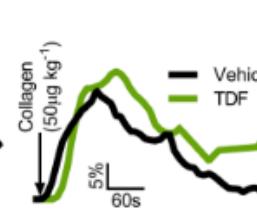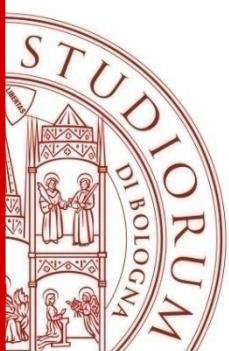
A) WT   B) $Ces1^{-/-}$ C) WT

Representative collagen-induced *in vivo* aggregation responses in the presence

(Taylor KA et al., Abstract 673, CROI 2018)

ALMA MATER STUDIORUM ‾ UNIVERSITÀ DI BOLOGNA

IL PRESENTE MATERIALE È RISERVATO AL PERSONALE DELL'UNIVERSITÀ DI BOLOGNA E NON PUÒ ESSERE UTILIZZATO AI TERMINI DI LEGGE DA ALTRE PERSONE O PER FINI NON ISTITUZIONALI
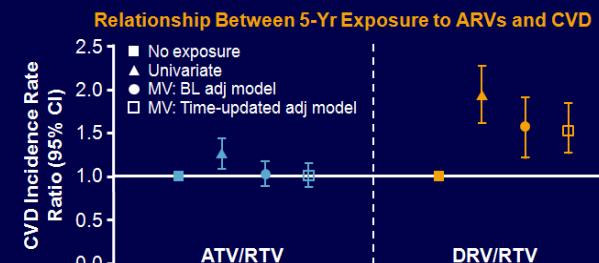
D:A:D: Exposure to ATV/RTV or DRV/RTV and Risk of CVD

- Prospective analysis of pts followed from 1/1/2009 (BL) to earliest CVD, last visit + 6 mos, or 2/1/2016 (N = 35,711)

  – 1157 pts (3.2%) developed CVD (MI, stroke, sudden cardiac death, invasive CV procedure)

- Cumulative expos. to DRV/RTV, but not ATV/RTV, assoc. with increased CVD risk in multivariate analysis: 59% risk increase per 5-yrs' DRV/RTV

  – Assoc. does not appear to be mediated through dyslipidemia, in contrast with first-generation PIs

- Limitations: potential for unmeasured confounding; observational study; unable to distinguish between DRV/RTV 800/100 mg QD vs DRV/RTV 600/100 mg BID

CVD Risk per 5 Yrs of ARV Exposure, IRR (95% CI)		
Model	**ATV/RTV**	**DRV/RTV**
Univariate	1.25 (1.10-1.43)	1.93 (1.63-2.28)
Multivariate		
▪ Baseline adjusted*	1.03 (0.90-1.18)	1.59 (1.33-1.91)
▪ Time-updated adjusted*	1.01 (0.88-1.16)	1.53 (1.28-1.84)

*Adjusted for: BMI, CKD, DM, CD4, dyslipidemia.

Relationship Between 5-Yr Exposure to ARVs and CVD
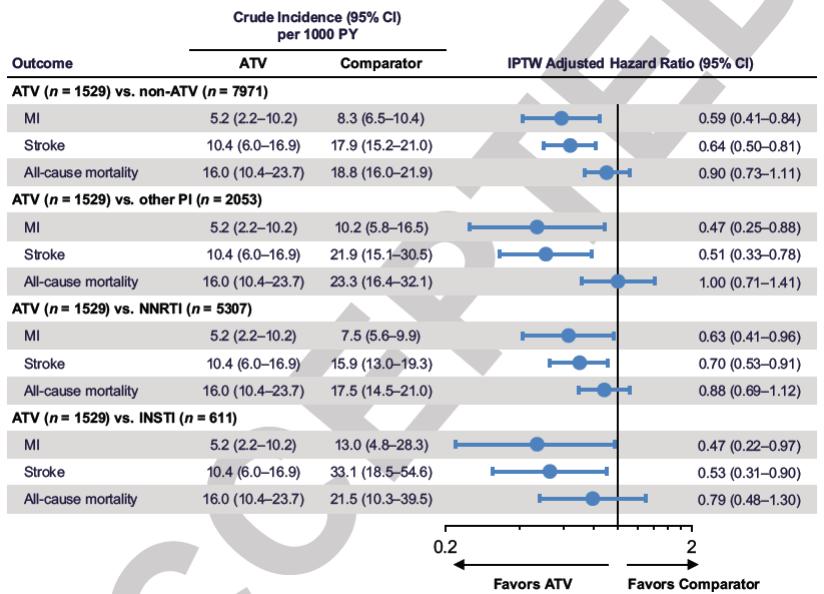
Ryom L, et al. CROI 2017. Abstract 128LB. Reproduced with permission.

Slide credit: clinicaloptions.com

| Outcome	Crude Incidence (95% CI) per 1000 PY		IPTW Adjusted Hazard Ratio (95% CI)
	ATV	Comparator	
ATV (n = 1529) vs. non-ATV (n = 7971)			
MI	5.2 (2.2–10.2)	8.3 (6.5–10.4)	0.59 (0.41–0.84)
Stroke	10.4 (6.0–16.9)	17.9 (15.2–21.0)	0.64 (0.50–0.81)
All-cause mortality	16.0 (10.4–23.7)	18.8 (16.0–21.9)	0.90 (0.73–1.11)
ATV (n = 1529) vs. other PI (n = 2053)			
MI	5.2 (2.2–10.2)	10.2 (5.8–16.5)	0.47 (0.25–0.88)
Stroke	10.4 (6.0–16.9)	21.9 (15.1–30.5)	0.51 (0.33–0.78)
All-cause mortality	16.0 (10.4–23.7)	23.3 (16.4–32.1)	1.00 (0.71–1.41)
ATV (n = 1529) vs. NNRTI (n = 5307)			
MI	5.2 (2.2–10.2)	7.5 (5.6–9.9)	0.63 (0.41–0.96)
Stroke	10.4 (6.0–16.9)	15.9 (13.0–19.3)	0.70 (0.53–0.91)
All-cause mortality	16.0 (10.4–23.7)	17.5 (14.5–21.0)	0.88 (0.69–1.12)
ATV (n = 1529) vs. INSTI (n = 611)			
MI	5.2 (2.2–10.2)	13.0 (4.8–28.3)	0.47 (0.22–0.97)
Stroke	10.4 (6.0–16.9)	33.1 (18.5–54.6)	0.53 (0.31–0.90)
All-cause mortality	16.0 (10.4–23.7)	21.5 (10.3–39.5)	0.79 (0.48–1.30)

Favors ATV ← → Favors Comparator

Cardiovascular outcomes among HIV-infected veterans receiving atazanavir: a US national historical cohort study

(Lafleur J et al., AIDS 2017)

Weight Gain: A Possible Side Effect of All Antiretrovirals

Table 1. BMI Changes in 1118 Patients on Dolutegravir, Raltegravir, Elvitegravir, Darunavir, or Rilpivirine, Before and After Adjustment for Baseline Characteristics, and After Stratification for CDC Stage of Disease, CD4+ at Baseline, Previous ART Duration

	Dolutegravir	Raltegravir	Elvitegravir	Darunavir	Rilpivirine
BMI, mean ± SE, kg/m^2	N = 225	N = 382	N = 148	N = 145	N = 218
6-mo visit	0.18 ± 0.08	0.17 ± 0.07	0.21 ± 0.07	0.32 ± 0.09	0.06 ± 0.07
	$P = .016$	$P = .014$	$P = .004$	$P = .0009$	$P = .39$
12-mo visit	0.30 ± 0.10	0.24 ± 0.08	0.23 ± 0.10	0.41 ± 0.10	0.06 ± 0.08
	$P = .005$	$P = .003$	$P = .017$	$P = .0001$	$P = .51$
6-mo visit[a]	0.28 ± 0.10	0.26 ± 0.08	0.42 ± 0.11	0.35 ± 0.11	0.30 ± 0.11
	$P = .006$	$P = .001$	$P = .0003$	$P = .001$	$P = .005$
12-mo visit[a]	0.37 ± 0.13	0.36 ± 0.10	0.42 ± 0.15	0.48 ± 0.14	0.30 ± 0.14
	$P = .004$	$P = .0004$	$P = .004$	$P = .0006$	$P = .029$
12-mo visit, in strata of:					
CDC stage A+B[b]	0.22 ± 0.15	0.02 ± 0.12	0.38 ± 0.156	0.36 ± 0.16	0.10 ± 0.15
n = 767	$P = .16$	$P = .90$	$P = .019$	$P = .029$	$P = .51$
CDC stage C[b]	0.66 ± 0.24	0.86 ± 0.19	0.29 ± 0.30	0.64 ± 0.25	0.63 ± 0.31
n = 351	$P = .007$	$P < .0001$	$P = .35$	$P = .012$	$P = .04$
CD4+ ≥200 cells/mL[c]	0.15 ± 0.14	0.16 ± 0.11	0.33 ± 0.15	0.45 ± 0.16	0.10 ± 0.14
n = 903	$P = .28$	$P = .17$	$P = .031$	$P = .005$	$P = .46$
CD4+ <200 cells/mL[c]	1.24 ± 0.41	0.70 ± 0.25	0.08 ± 0.44	0.46 ± 0.31	1.34 ± 0.66
n = 215	$P = .003$	$P = .006$	$P = .85$	$P = .14$	$P = .044$
Previous ART <3 y[d]	0.68 ± 0.42	0.78 ± 0.35	0.32 ± 0.42	1.42 ± 0.51	0.08 ± 0.40
n = 195	$P = .11$	$P = .029$	$P = .45$	$P = .006$	$P = .85$
Previous ART ≥3 y[d]	0.34 ± 0.13	0.32 ± 0.09	0.50 ± 0.16	0.38 ± 0.13	0.36 ± 0.14
n = 921	$P = .009$	$P = .0007$	$P = .001$	$P = .004$	$P = .011$

P refers to change from baseline: if $P < .05$, means are significantly different from 0.
[a] Adjusted for sex, age, CD4+, detectable viral load, CDC stage, duration of ART, lipodystrophy, and BMI at study entry.
[b] Adjusted for sex, age, CD4+, detectable viral load, duration of ART, lipodystrophy, and BMI at study entry.
[c] Adjusted for sex, age, detectable viral load, CDC stage, duration of ART, lipodystrophy, and BMI at study entry.
[d] Adjusted for sex, age, CD4+, detectable viral load, CDC stage, lipodystrophy, and BMI at study entry.
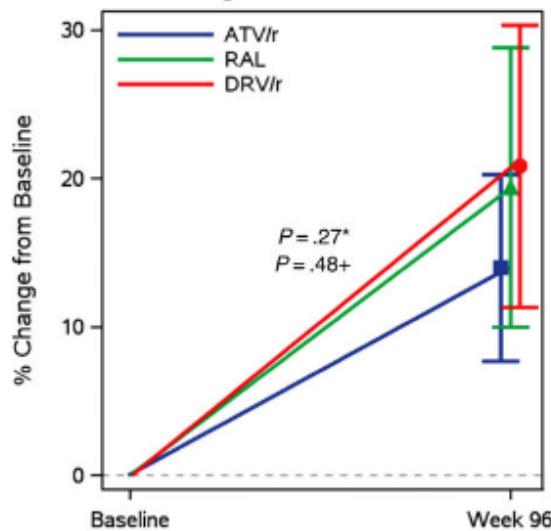
SCOLTA Cohort Study
1118 HIV+ patients
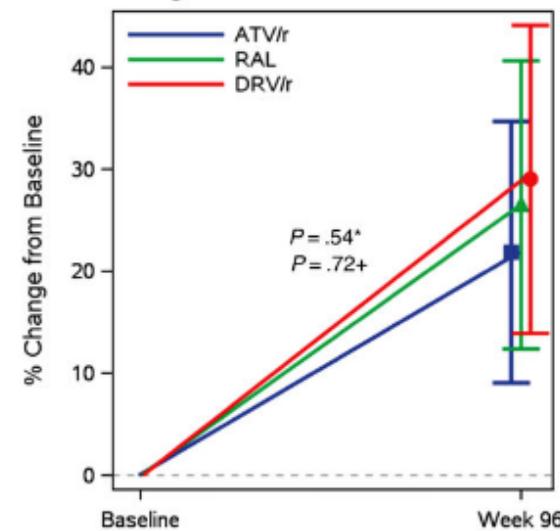
(Taramasso L et al., Open Forum Infect Dis 2017)

Body Composition Changes After Initiation of Raltegravir or Protease Inhibitors: ACTG A5260s

C Trunk Fat Change

ATV/r
RAL
DRV/r

% Change from Baseline

P = .27*
P = .48+

Baseline — Week 96

No. of Subjects

ATV/r	108	97
RAL	103	91
DRV/r	113	97

D VAT Change

ATV/r
RAL
DRV/r

% Change from Baseline

P = .54*
P = .72+

Baseline — Week 96

No. of Subjects

ATV/r	108	96
RAL	105	94
DRV/r	112	94

•ACTG A5260 Substudy
•328 naive patients
•96-week follow-up

(McComsey GA et al., Clin Infect Dis 2016)

Predictors of Severe Weight/Body Mass Index Gain Following Antiretroviral Initiation (ACTG A5257)

Results: Adjusted model predicting severe weight gain

Covariate	Adjusted Imputed Data Model	
	Odds Ratio (95% CI)	p-value
Treatment		
RAL	--	--
ATV/r	0.72 (0.53, 0.99)	0.0427
DRV/r	0.74 (0.54, 1.01)	0.0555
Sex		
Males	--	--
Females	1.35 (0.97, 1.89)	0.0742
Race/Ethnicity		
White Non-Hispanic	--	--
Black Non-Hispanic	1.55 (1.10, 2.20)	0.0129
Hispanic	0.99 (0.67, 1.48)	0.9757
Other	0.50 (0.17, 1.45)	0.2021
Age (years)	1.01 (0.99, 1.02)	0.2859
Baseline BMI (kg/m^2)	0.98 (0.96, 1.01)	0.1767
Baseline HIV-1 RNA (log$_{10}$ copies/mL)	2.52 (2.00, 3.16)	<.0001
Baseline CD4+ (100 cells/mm^3)	0.78 (0.72, 0.85)	<.0001

(Bhagwat P et al., CROI 2017, Abstract 693)

NA-ACCORD Cohort: Weight Gain Following ART Initiation With INSTI- vs PI-/NNRTI-Based Regimens
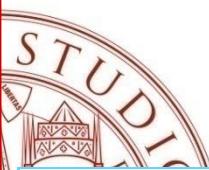
- Analysis of NA-ACCORD cohort of ART-naive adults who started 3-drug regimen with INSTI, PI, or NNRTI from January 2007 - December 2015 (N = 21,867)

Baseline Characteristic	NNRTI (n = 10,711)	PI (n = 7063)	INSTI (n = 4093)	Overall (N = 21,867)
Median age, yrs (IQR)	43 (32-52)	42 (32-50)	41 (30-51)	42 (32-51)
Black race/Hispanic ethnicity, %	40/8	41/9	38/9	40/8
Male sex, %	91	81	87	87
Median BMI (IQR)	25 (23-29)	25 (22-28)	25 (22-29)	25 (22-29)
Median calendar year started ART (IQR)	2010 (2008-2012)	2010 (2008-2011)	2013 (2011-2014)	2010 (2009-2012)
Median CD4+ cell count, cells/mm^3 (IQR)	311 (178-451)	251 (107-405)	346 (171-516)	303 (154-451)
Median HIV-1 RNA, copies/mL (IQR)	40,480 (11,198-120,016)	52,405 (12,830-169,824)	42,657 (11,939-144,709)	44,054 (11,796-139,374)
ART agent, % ▪ RAL/EVG/DTG ▪ ATV/DRV/EFV	--/--/-- --/--/87	--/--/-- 43/35/--	51/37/12 --/--/--	10/7/2 14/11/43

Lake. International Comorbidities WS 2018. Abstr ADRLH-71.

NA-ACCORD Cohort: Weight Change to Yr 5

| Yr	NNRTI		PI		INSTI	
	Weight, kg (95% CI)	Weight Change, kg	Weight, kg (95% CI)	Weight Change, kg	Weight, kg (95% CI)	Weight Change, kg
0	79.0 (78.8-79.2)	0	79.0 (78.7-79.3)	0	79.2 (78.9-79.6)	0
1	81.6 (81.5-81.8)	2.6	82.7 (82.5-82.9)	3.7	83.2 (82.9-83.5)	4.0
2	82.2 (82.1-82.4)	3.3	83.3 (83.1-83.5)	4.3	83.7 (83.3-84.0)	4.4
5	83.1 (82.9-83.4)	4.1	84.0 (83.7-84.3)	5.0	85.1 (84.2-86.1)	5.8

- Comparisons of weight change by ART class

  - INSTI vs NNRTI: $P < .0001$

  - INSTI vs PI: $P = .68$

  - PI vs NNRTI: $P < .001$
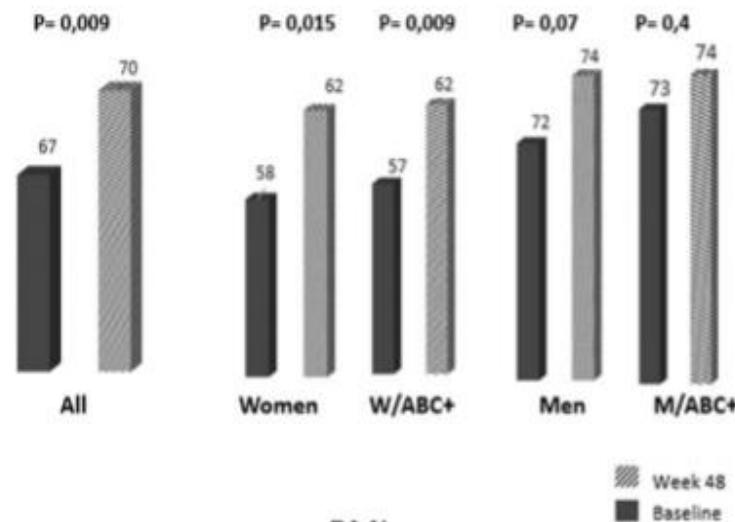
Lake. International Comorbidities WS 2018. Abstr ADRLH-71.

# Dolutegravir and weight gain: an unexpected bothering side effect?

(a) Weight

Retrospective Cohort Study
462 HIV+ patients
DTG-based cART for >6 months

(b) BMI
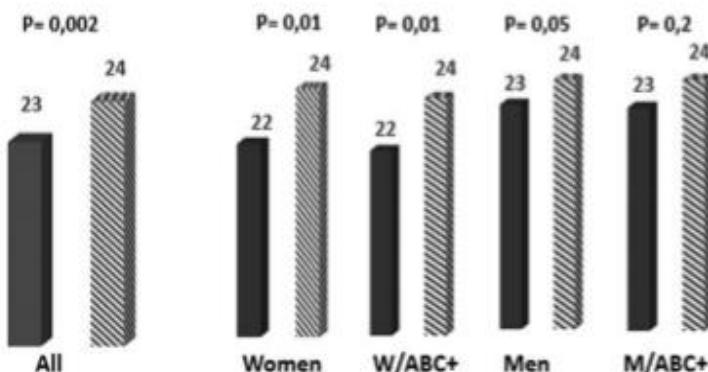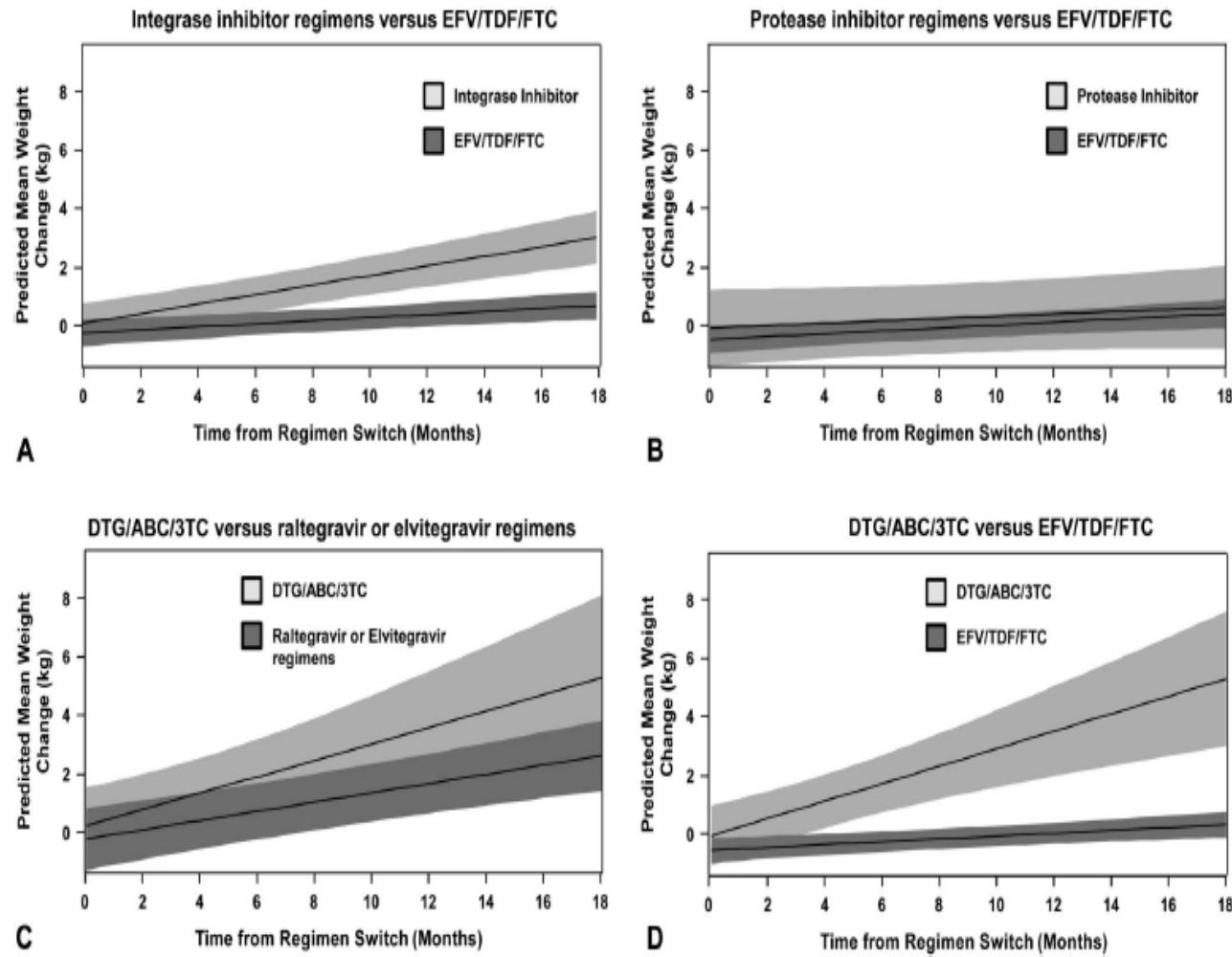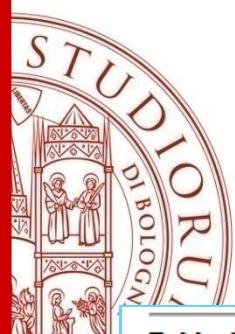
Fig. 1. Evolution of weight (kg) (a) and BMI (kg/m²) (b) after 1 year on a dolutegravir-based regimen. $P=$ Anova. M/ABC+, men on dolutegravir + abacavir; W/ABC+, women on dolutegravir + abacavir.

(Menard A et al., AIDS 2017)

Weight Gain in Persons With HIV Switched From Efavirenz-Based to Integrase Strand Transfer Inhibitor–Based Regimens

•Retrospective cohort study
•495 HIV+ patients
•TDF/FTC/EFV for >2 years
•HIV RNA <50 copies/mL
•Switch to PI- or INSTI-containing regimen

(Norwood J, et al. J AIDS 2017)

Switch to Raltegravir From Protease Inhibitor or Nonnucleoside Reverse-Transcriptase Inhibitor Does not Reduce Visceral Fat In Human Immunodeficiency Virus-Infected Women With Central Adiposity

- Open-label, randomized study
- 39 HIV-infecetd women with central adiposity
- 24 and 48 week changes in CT-quantified visceral and subcutaneous adipose tissue
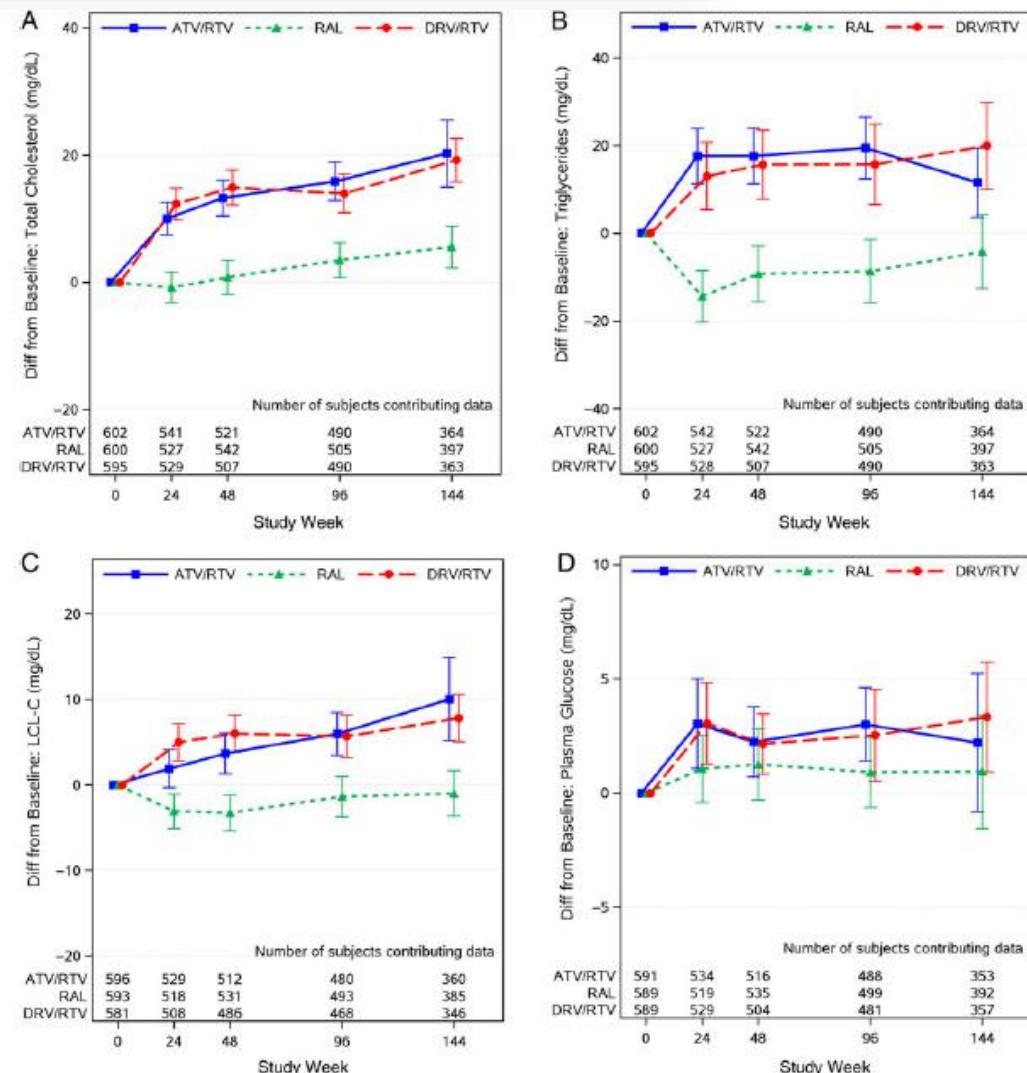
Table 2. Median Changes in Adipose Tissue, Anthropometrics, and Laboratory Values After Switch to Raltegravir
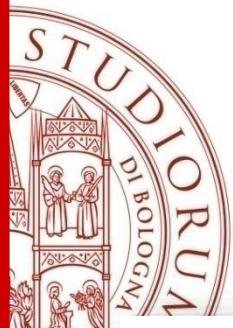
	Week 0–48 Changes		Week 24–48 Changes		Pooled 24-Week Changes	
	Immediate	Within-Group P Value	Delayed	Within-Group P Value	Immediate 0–24 wks Delayed 24–48 wks	Within-Group P Value
N	17		19		36	
BMI (kg/m^2)	−0.1 (−0.9, 0.4)	.52	**0.6 (0.0, 1.6)**	.05	**0.3 (−0.2, 1.1)**	.05
Waist-to-hip ratio	−0.01 (−0.04, 0.02)	.24	0.0 (−0.02, 0.01)	.47	0.0 (−0.02, 0.02)	.50
TAT (cm^2)	−16.5 (−52.5, 17.2)	.40	26.5 (−24.7, 31.0)	.28	8.9 (−33.6, 30.1)	1.00
SAT (cm^2)	−17.8 (−30.3, 28.)	.57	13.4 (−5.2, 36.0)	.10	0.8 (−26.0, 31.6)	.59
VAT (cm^2)	−11.7 (−17.4, 13.3)	.68	−2.8 (−18.9, 11.1)	.64	−4.4 (−18.9, 13.1)	.51
VAT/SAT	−0.01 (−0.04, 0.04)	.86	−0.01 (−0.06, 0.01)	.23	−0.02 (−0.05, 0.02)	.30
VAT/TAT	−0.01 (−0.02, 0.03)	.96	0.0 (−0.03, 0.01)	.26	0.01 (−0.03, 0.01)	.30
%VAT change	−6.4 (−15.6, 12.5)	.85	−1.8 (−12.3, 11.4)	.70	−3.3 (−12.3, 12.1)	.60
%SAT change	−2.9 (−9.7, 5.9)	.46	**3.4 (−1.4, 9.4)**	.05	−5.6 (7.2, 0.4)	.47
CD4$^+$ T Lymphocyte count (cells/mm^3)	46.0 (−10.0, 61.0)	.16	42.0 (−26.0, 133.0)	.08	5.0 (−29.0, 62.0)	.27
Glucose (mg/dL)	4.0 (0.0, 8.0)	.13	0.5 (−6.0, 5.0)	.85	0.0 (−6.0, 5.0)	.70
Total cholesterol (mg/dL)	**−14.0 (−29.0, 6.0)**	.01	**−20.0 (−47.0, −2.0)**	<.001	**−17.0 (−31.0, −2.0)**	<.0001
Triglycerides (mg/dL)	−1.0 (−21.0, 9.0)	.32	−27.5 (−42.0, 8.0)	.07	**−18.0 (−42.0, 8.0)**	<.01
LDL cholesterol (mg/dL)	−2.0 (−28.8, 3.2)	.16	**−6.2 (−23.0, 0.0)**	.01	**−9.1 (−23.9, 1.6)**	<.01
HDL cholesterol (mg/dL)	−4.0 (−9.6, 3.0)	.25	**−4.3 (−6.0, −1.0)**	.03	**−2.6 (−6.0, 0.4)**	.03
hs-CRP (mg/L)	**−1.0 (3.2, 0.0)**	.02	−0.4 (−1.4, 2.2)	1.00	−0.2 (−1.9, 0.5)	.34

(Lake JE et al., Open Forum Infect Dis 2015)

ALMA MATER STUDIORUM ‒ UNIVERSITÀ DI BOLOGNA

IL PRESENTE MATERIALE È RISERVATO AL PERSONALE DELL'UNIVERSITÀ DI BOLOGNA E NON PUÒ ESSERE UTILIZZATO AI TERMINI DI LEGGE DA ALTRE PERSONE O PER FINI NON ISTITUZIONALI
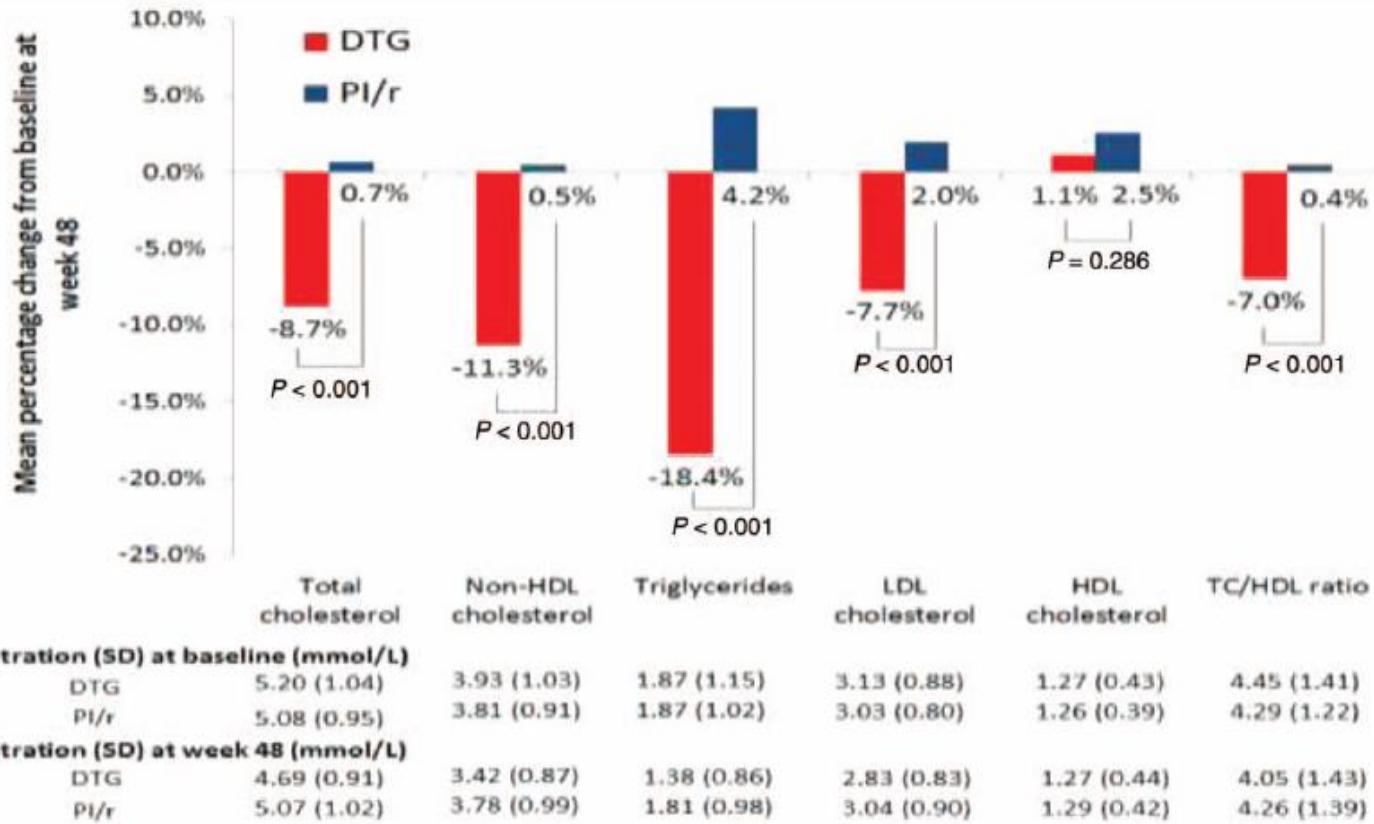
Comparison of the Metabolic Effects of Ritonavir-Boosted Darunavir or Atazanavir Versus Raltegravir, and the Impact of Ritonavir Plasma Exposure: ACTG 5257

- ACTG 5257 Study
- 1797 ARV-naive patients
- 96-week follow-up
- TDF/FTC + ATV/r, DRV/r or RAL

(Ofotokun I et al., Clin Infect Dis 2015)
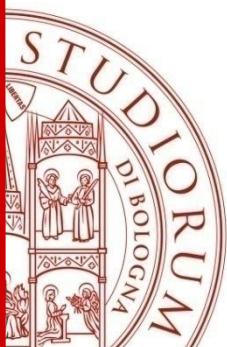
Switching from a ritonavir-boosted protease inhibitor to a dolutegravir-based regimen for maintenance of HIV viral suppression in patients with high cardiovascular risk
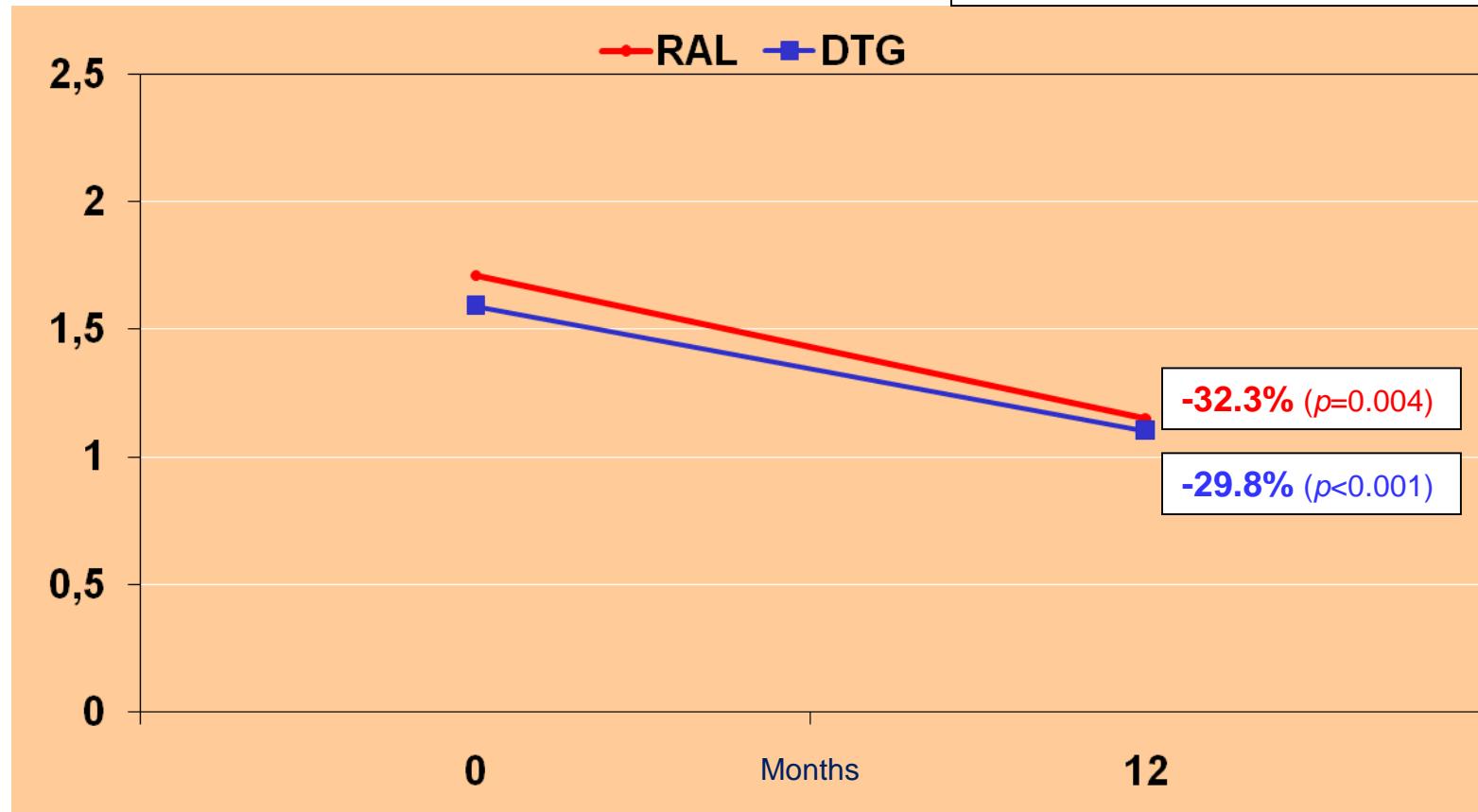
(Gatell JM et al., AIDS 2017)

Changes in insulin sensitivity after the switch from a ritonavir-boosted protease inhibitor to raltegravir or dolutegravir in non-diabetic HIV-infected patients

- Prospective, observational study
- 86 HIV+ patients on stable PI/r-based cART
- Switch from PI/r to RAL or DTG
- 12-month follow-up

HOMA index

RAL DTG

-32.3% (p=0.004)

-29.8% (p<0.001)

Months

(Calza L et al., in press)
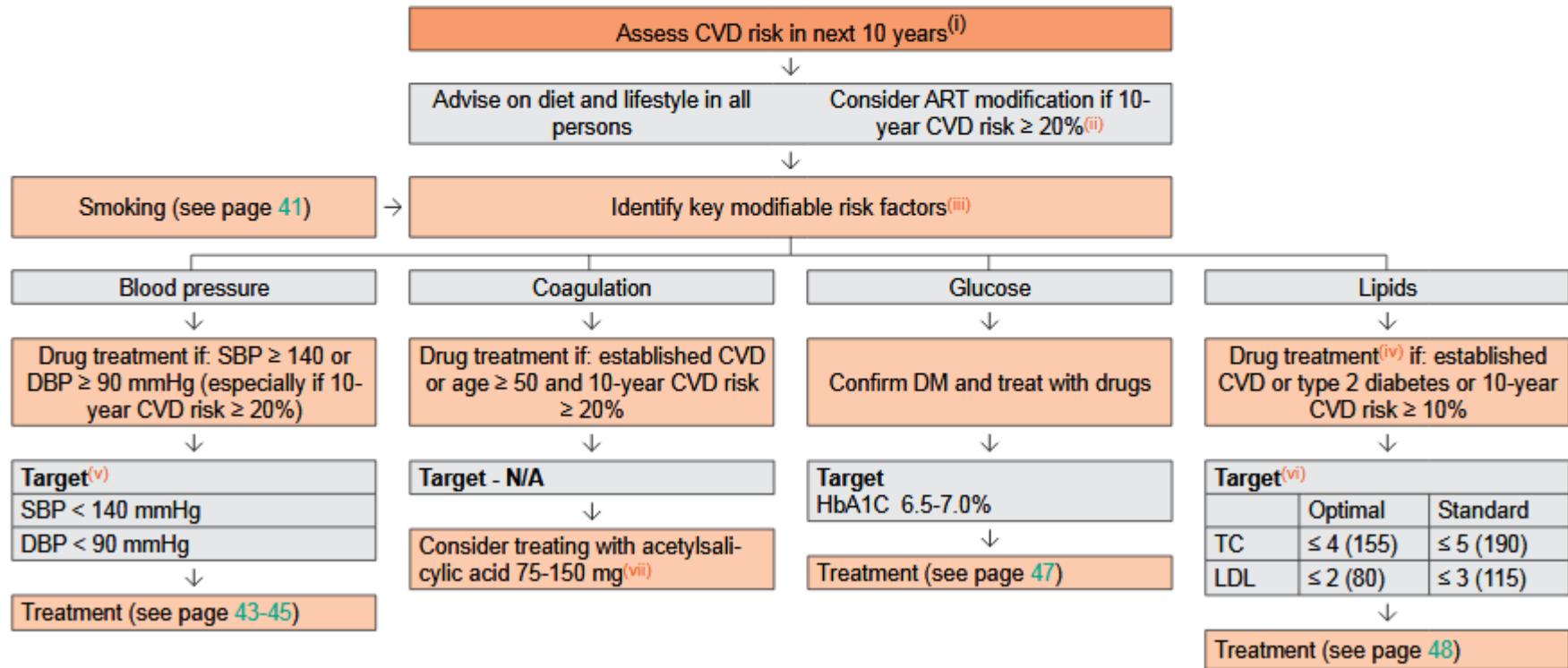
Groups	A			B			
Treatment	Switch to raltegravir		*p*	Switch to dolutegravir		*p*	*p**
N. of patients	45			41			
	Absolute	%		Absolute	%		
Waist circumference	+1.5 ± 2.5 cm	+1.7 ± 2.8	0.811	+2.1 ± 2.8 cm	2.3 ± 2.6	0.781	0.544
Total cholesterol	-25.2 ± 10.3 mg/dL	-15.9 ± 8.2	0.041	-27.8 ± 13.1 mg/dL	-17.6 ± 9.7	0.036	0.428
LDL cholesterol	-12.2 ± 7.1 mg/dL	-10.2 ± 4.8	0.047	-13.5 ± 7.9 mg/dL	-11.7 ± 5.4	0.042	0.716
HDL cholesterol	-2.1 ± 2.9 mg/dL	-4.4 ± 2.1	0.699	-1.9 ± 0.8 mg/dL	-3.8 ± 1.9	0.541	0.611
Triglycerides	-53.3 ± 26.6 mg/dL	-21.4 ± 9.6	<0.001	-49.7 ± 25.1 mg/dL	-20.2 ± 8.9	<0.001	0.178
hsCRP	-0.02 ± 0.08 mg/dL	-9.2 ± 6.9	0.078	-0.01 ± 0.09 mg/dL	-8.3 ± 5.9	0.093	0.244
IL-6	-20.4 ± 10.3 pg/mL	-34.9 ± 14.7	<0.001	-23.2 ± 12.1 pg/mL	-33.8 ± 17.2	<0.001	0.501
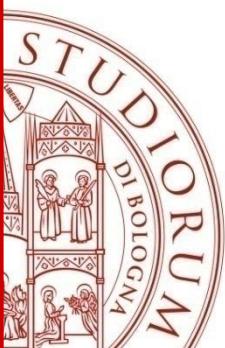
(Calza L et al., in press)

Prevention of CVD

Principles: The intensity of efforts to prevent CVD depends on the underlying risk of CVD, which can be estimated[i]. The preventive efforts are diverse in nature and require involvement of a relevant specialist, in particular if the risk of CVD is high and always in persons with a history of CVD.

Assess CVD risk in next 10 years[i]

↓

Advise on diet and lifestyle in all persons	Consider ART modification if 10-year CVD risk ≥ 20%[ii]

↓

| Smoking (see page 41)	→	Identify key modifiable risk factors[iii]

Blood pressure	Coagulation	Glucose	Lipids
↓	↓	↓	↓
Drug treatment if: SBP ≥ 140 or DBP ≥ 90 mmHg (especially if 10-year CVD risk ≥ 20%)	Drug treatment if: established CVD or age ≥ 50 and 10-year CVD risk ≥ 20%	Confirm DM and treat with drugs	Drug treatment[iv] if: established CVD or type 2 diabetes or 10-year CVD risk ≥ 10%
↓	↓	↓	↓

Blood pressure

Target[v]
SBP < 140 mmHg
DBP < 90 mmHg

↓

Treatment (see page 43-45)

Coagulation

Target - N/A

↓

Consider treating with acetylsalicylic acid 75-150 mg[vii]

Glucose

Target HbA1C 6.5-7.0%

↓

Treatment (see page 47)

Lipids

Target[vi]		
	Optimal	Standard
TC	≤ 4 (155)	≤ 5 (190)
LDL	≤ 2 (80)	≤ 3 (115)

↓

Treatment (see page 48)

(EACS Guidelines, October 2018)
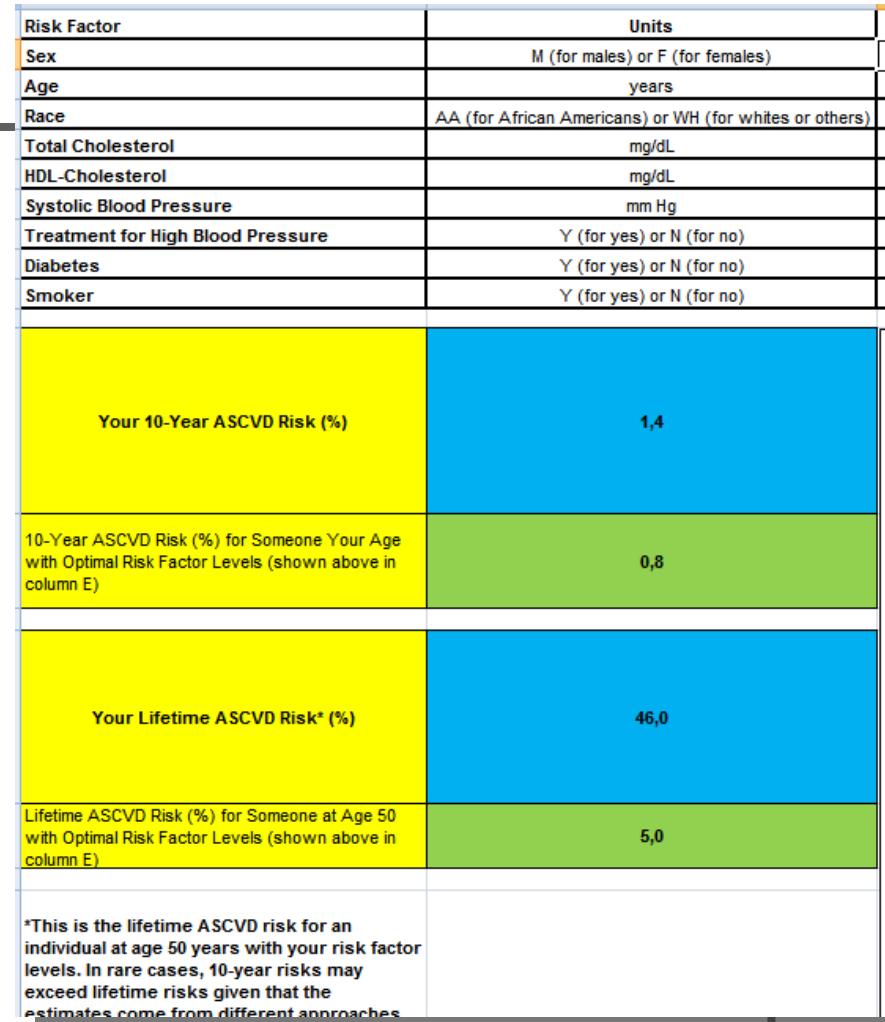
D:A:D
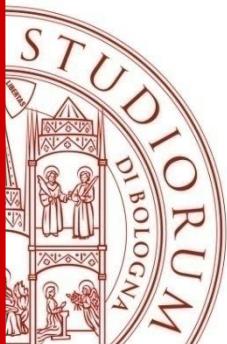
Risk factor	D:A:D Full	D:A:D Reduced	Framingham
Age	+	+	+
Sex	+	+	Seperate models by sex
Diabetes	+	+	+
Smoking	Current and former	Current and former	Current
Total and HDL cholesterol	+	+	+
Systolic BP	+	+	+
Family History CVD	+	+	
CD4 cell count	+	+	
Abacavir - current	+		
PI - cum. exposure	+		
NRTI – cum. exposure	+		

(http://www.cphiv.dk/TOOLS/tabid/437/Default.aspx)

Risk Factor	Units
Sex	M (for males) or F (for females)
Age	years
Race	AA (for African Americans) or WH (for whites or others)
Total Cholesterol	mg/dL
HDL-Cholesterol	mg/dL
Systolic Blood Pressure	mm Hg
Treatment for High Blood Pressure	Y (for yes) or N (for no)
Diabetes	Y (for yes) or N (for no)
Smoker	Y (for yes) or N (for no)

Your 10-Year ASCVD Risk (%)	1,4
10-Year ASCVD Risk (%) for Someone Your Age with Optimal Risk Factor Levels (shown above in column E)	0,8
Your Lifetime ASCVD Risk* (%)	46,0
Lifetime ASCVD Risk (%) for Someone at Age 50 with Optimal Risk Factor Levels (shown above in column E)	5,0

*This is the lifetime ASCVD risk for an individual at age 50 years with your risk factor levels. In rare cases, 10-year risks may exceed lifetime risks given that the estimates come from different approaches.

(http://my.americanheart.org/cvriskcalculator)

ALMA MATER STUDIORUM ~ UNIVERSITÀ DI BOLOGNA

IL PRESENTE MATERIALE È RISERVATO AL PERSONALE DELL'UNIVERSITÀ DI BOLOGNA E NON PUÒ ESSERE UTILIZZATO AI TERMINI DI LEGGE DA ALTRE PERSONE O PER FINI NON ISTITUZIONALI

Comparison of CVD Risk Scores in HIV-Infected Pts

- Compared expected and observed MI event rates using 4 risk scores in 10,832 HIV-infected pts with 229 incident MI events in CNICS

  - 3 general population CVD risk scores (Framingham, ATP3, 2013 ACC/AHA ASCVD) plus HIV-specific D:A:D score in CNICS pts

- Variations across models anticipated given differences in outcome

- ART use (ie, D:A:D score) did not improve discrimination vs ASCVD

- Discrimination greater with ASCVD vs other models for all outcomes

  - Harrell's C for MI with ASCVD

    - Type 1 MI: 0.77 (CI: 0.73-0.81)

    - Type 2 MI: 0.72 (CI: 0.67-0.78)

    - All MI: 0.74 (CI: 0.71-0.77)
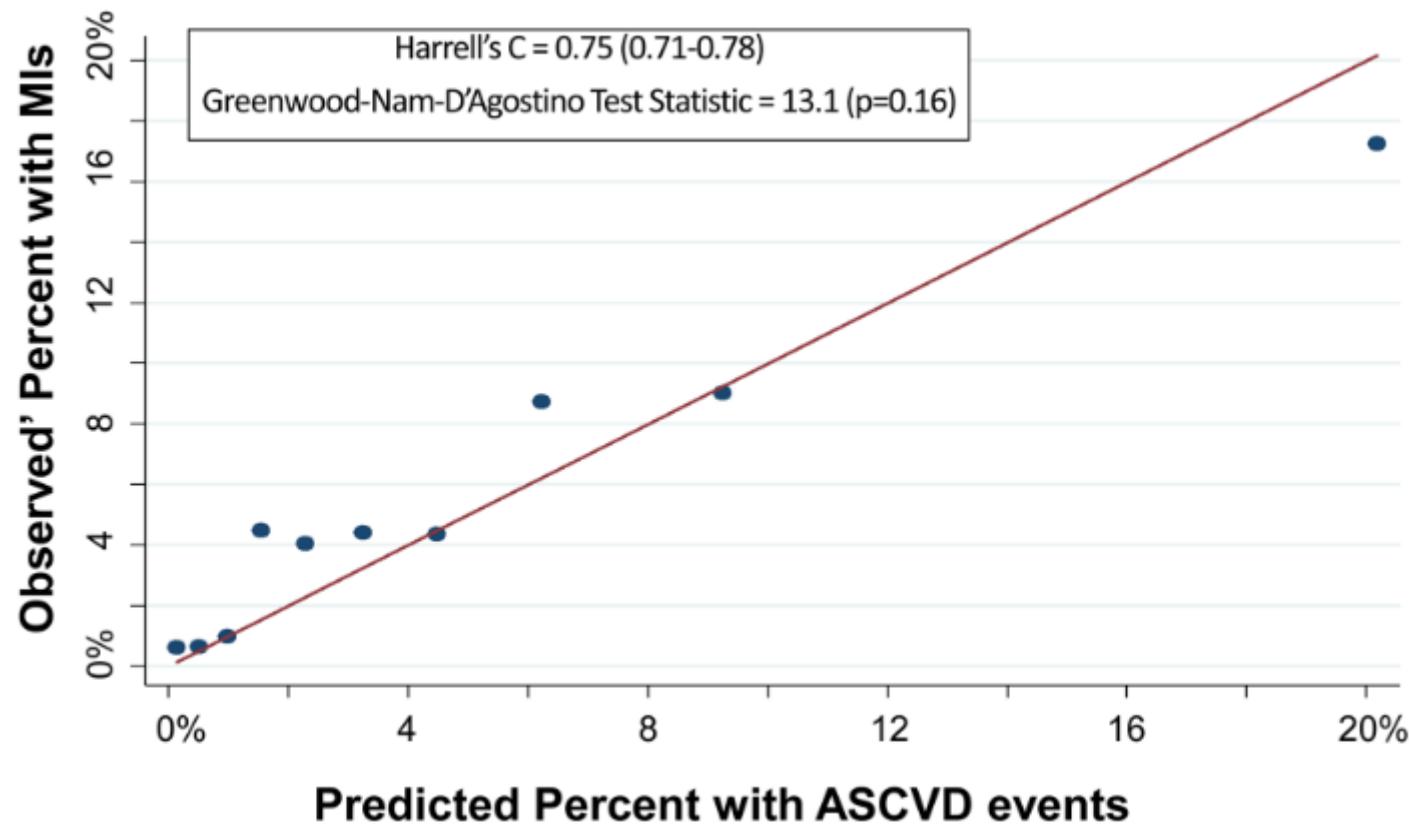
(Crane HM et al., CROI 2016, abstract 42)
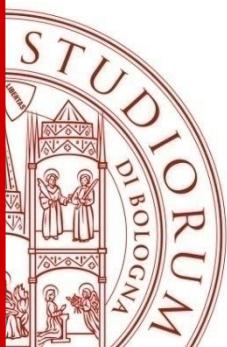
Assessing and Refining Myocardial Infarction Risk Estimation Among Patients With Human Immunodeficiency Virus
A Study by the Centers for AIDS Research Network of Integrated Clinical Systems

JAMA Cardiology

Harrell's C = 0.75 (0.71-0.78)

Greenwood-Nam-D'Agostino Test Statistic = 13.1 (p=0.16)
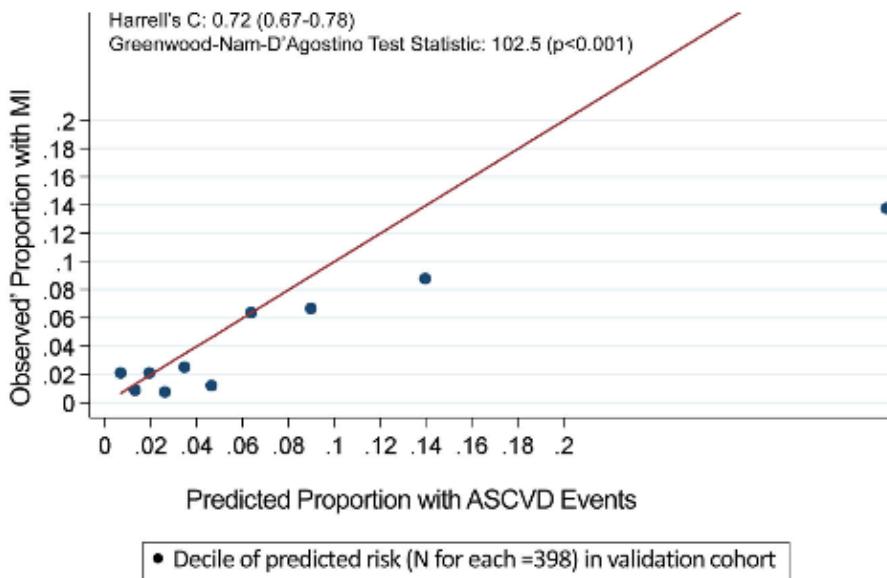
(Feinstein MJ et al., JAMA Cardiol 2017)

3A. HIVMI-1

Harrell's C: 0.72 (0.67-0.78)
Greenwood-Nam-D'Agostino Test Statistic: 102.5 (p<0.001)

Observed' Proportion with MI (y-axis)
Predicted Proportion with ASCVD Events (x-axis)

• Decile of predicted risk (N for each =398) in validation cohort
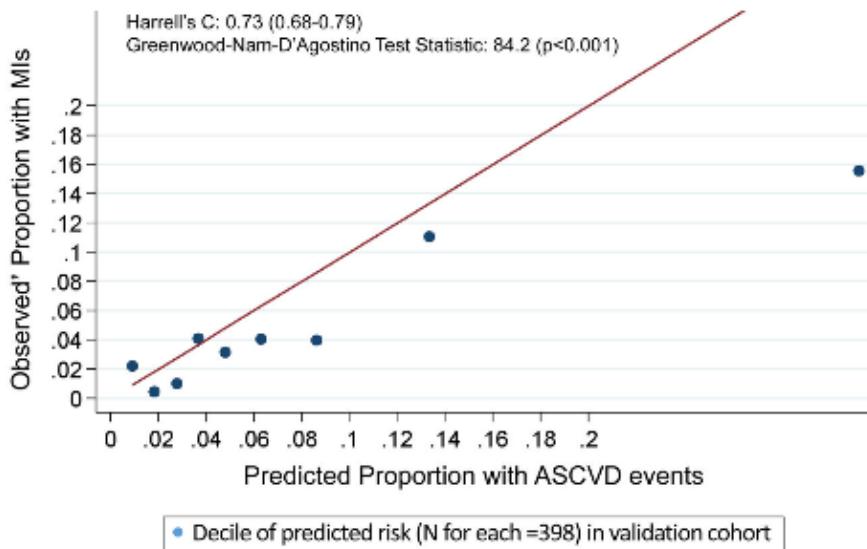
Variables Included in HIVMI-1
Black Race
Hypertension medication use
Statin use
ART use
PI use
Diabetes
Age
Total cholesterol
HDL
SBP
Log10 (VL+1)
CD4
Smoking
Female
Black race x SBP
Female x SBP
Female x total cholesterol
Black race x smoking
Black race x age
Female x smoking
Female x diabetes
Female x hypertension med
Female x age
Age x diabetes
CD4 squared
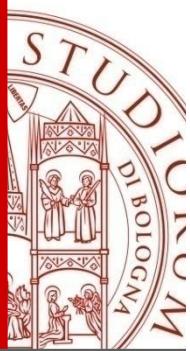
JAMA Cardiology

3B. HIVMI-2

Harrell's C: 0.73 (0.68-0.79)
Greenwood-Nam-D'Agostino Test Statistic: 84.2 (p<0.001)

Observed' Proportion with MIs (y-axis)
Predicted Proportion with ASCVD events (x-axis)

• Decile of predicted risk (N for each =398) in validation cohort
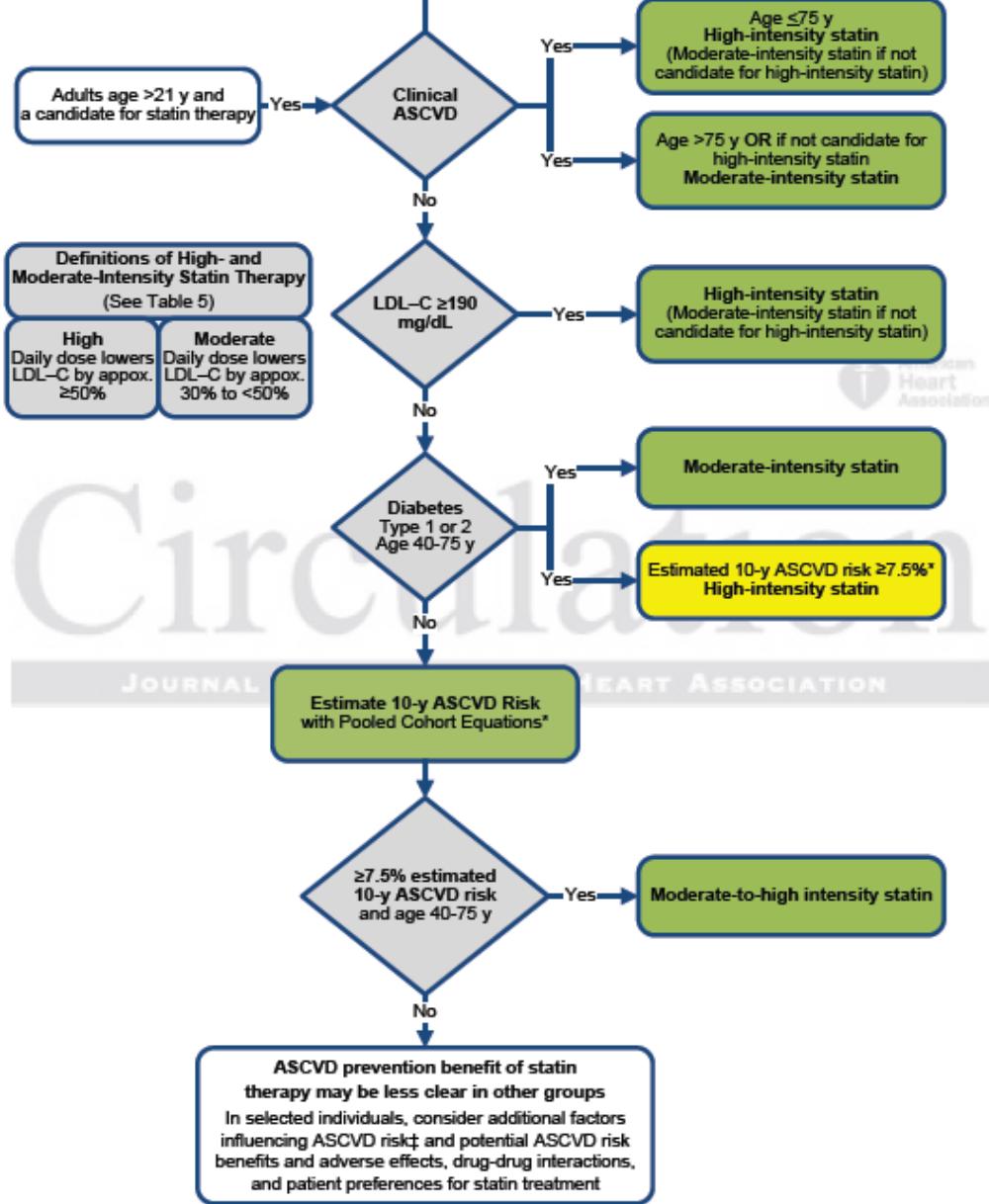
Variables Considered for and Included* in HIVMI-2 Score		
Variable	%**	Cox Coeff
Black race*	100	0.529
HTN med*	100	0.850
Statin	9.9	
ART	10.1	
PI ART*	**67.9**	**0.412**
Diabetes*	59.9	0.563
Age*	100	0.0461
Smoking*	94.4	0.508
Total cholesterol	6.1	
HDL*	100	-0.0210
SBP*	100	0.0188
Log10(VL+1)*	**47.1**	**0.129**
CD4*	**84.6**	**-0.000779**
Female	5.8	

*Variables included in Model

*(Feinstein MJ et al.,
JAMA Cardiol 2017)*

ASCVD Statin Benefit Groups
Heart healthy lifestyle habits are the foundation of ASCVD prevention.
In individuals not receiving cholesterol-lowering drug therapy, recalculate estimated
10-y ASCVD risk every 4-6 y in individuals aged 40-75 y without clinical ASCVD or
diabetes and with LDL–C 70-189 mg/dL.

Adults age >21 y and a candidate for statin therapy —Yes→ **Clinical ASCVD**

Yes→ Age ≤75 y
High-intensity statin
(Moderate-intensity statin if not candidate for high-intensity statin)

Yes→ Age >75 y OR if not candidate for high-intensity statin
Moderate-intensity statin

No

Definitions of High- and Moderate-Intensity Statin Therapy
(See Table 5)

High	Moderate
Daily dose lowers LDL–C by appox. ≥50%	Daily dose lowers LDL–C by appox. 30% to <50%

LDL–C ≥190 mg/dL —Yes→ **High-intensity statin**
(Moderate-intensity statin if not candidate for high-intensity statin)

No

Diabetes Type 1 or 2 Age 40-75 y

Yes→ **Moderate-intensity statin**

Yes→ Estimated 10-y ASCVD risk ≥7.5%*
High-intensity statin

No

Estimate 10-y ASCVD Risk with Pooled Cohort Equations*

≥7.5% estimated 10-y ASCVD risk and age 40-75 y —Yes→ **Moderate-to-high intensity statin**

No

ASCVD prevention benefit of statin therapy may be less clear in other groups
In selected individuals, consider additional factors influencing ASCVD risk‡ and potential ASCVD risk benefits and adverse effects, drug-drug interactions, and patient preferences for statin treatment

*(Stone NJ et al., Circulation 2013)*

Table 5. High- Moderate- and Low-Intensity Statin Therapy (Used in the RCTs reviewed by the Expert Panel)*

High-Intensity Statin Therapy	Moderate-Intensity Statin Therapy	Low-Intensity Statin Therapy
Daily dose lowers LDL–C on average, by approximately ≥50%	Daily dose lowers LDL–C on average, by approximately 30% to <50%	Daily dose lowers LDL–C on average, by <30%
Atorvastatin (40†)–80 mg **Rosuvastatin 20 (40) mg**	**Atorvastatin 10 (20) mg** **Rosuvastatin (5) 10 mg** **Simvastatin 20–40 mg‡** **Pravastatin 40 (80) mg** **Lovastatin 40 mg** *Fluvastatin XL 80 mg* **Fluvastatin 40 mg bid** *Pitavastatin 2–4 mg*	*Simvastatin 10 mg* **Pravastatin 10–20 mg** **Lovastatin 20 mg** *Fluvastatin 20–40 mg* *Pitavastatin 1 mg*

(Stone NJ et al., Circulation 2013)

Statin recommendation
(AHA/ACC 2013 Guidelines)

- 52-year-old male patient

- Diagnosis of HIV infection in September 2008

- MSM; CDC stage: A1

- CVD risk factors: smoking

- Blood pressure: 120/80 mmHg

- Current cART: TAF/FTC/RPV

- HIV RNA <20 copies/mL

- CD4 count: 795 cells/mmc (38%)

- Total cholesterol 242 mg/dL, LDL 168 mg/dL, HDL 44 mg/dL

11.2%
10-year risk of heart disease or stroke

On the basis of your age and calculated risk for heart disease or stroke over 7.5%, the ACC/AHA guidelines suggest you should be on a **moderate to high intensity statin**.

Effects of statin therapy on coronary artery plaque volume and high-risk plaque morphology in HIV-infected patients with subclinical atherosclerosis: a randomised, double-blind, placebo-controlled trial

Figure 2: Comparison of the 1 year change in non-calcified plaque volume in study participants

See Online for appendix   Median and IQR.

- Randomised, controlled, double-blind study
- 40 HIV+ patients with subclinical atherosclerosis and normal LDL-c
- Atorvastatin vs placebo
- 1-year follow-up
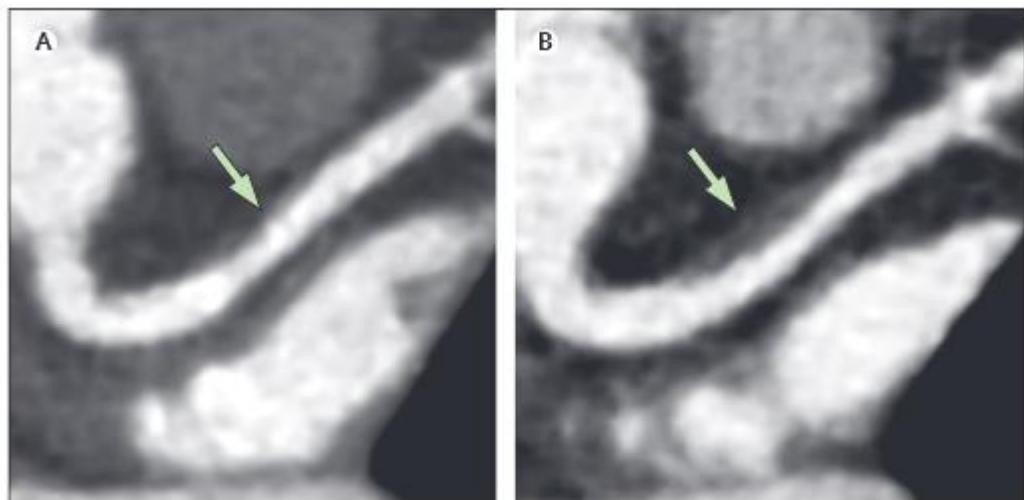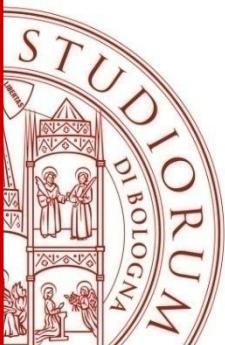
Figure 3: Increasing non-calcified plaque in proximal left anterior descending (LAD) coronary artery in patient on placebo

(Lo J et al., Lancet HIV 2015)

Statin Coverage in an HIV Cohort: Comparison of ATP III, ACC/AHA, and NLA Guidelines
Matthew E. Levy[1], Alan E. Greenberg[1], Manya Magnus[1], Naji Younes[1], and Amanda Castel[1], on behalf of the DC Cohort Executive Committee
[1] Department of Epidemiology and Biostatistics, The Milken Institute School of Public Health at the George Washington University, Washington, DC
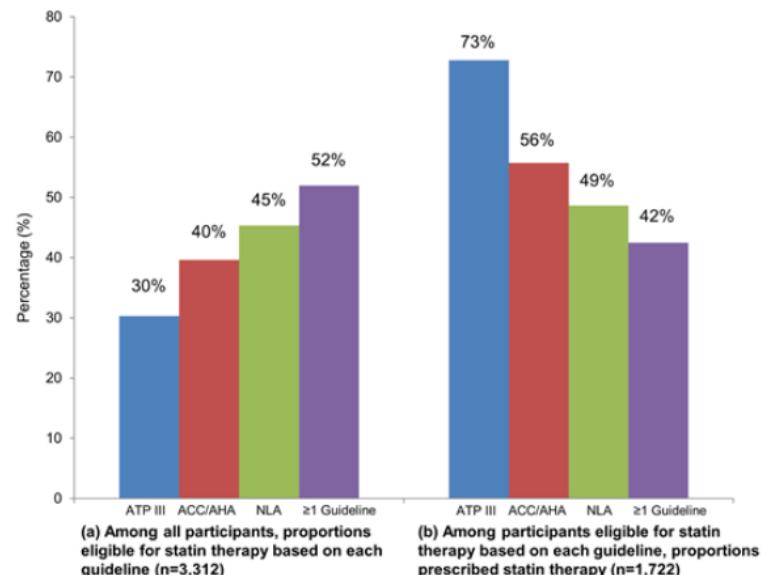
(DC Cohort Study; 3312 HIV+ patients; 2011-2016)

Table 1. Characteristics of HIV-infected primary care patients (n=3,312).

| Variable	All patients (n=3,312) %	Eligible for statin (n=1,722) %	Prescribed statin (n=731) %
Age, years (median, IQR)	52 (44-58)	56 (50-61)	57 (51-63)
Age ≥60 years	21%	30%	39%
Male sex at birth	78%	80%	83%
Non-Hispanic Black	79%	80%	76%
Publically insured	76%	80%	78%
Current smoker[1]	47%	48%	39%
Hypertension	50%	71%	75%
Diabetes	19%	34%	35%
BMI ≥30	30%	36%	37%
Non-HDL-C ≥160 mg/dL	17%	28%	27%
HDL-C <40 mg/dL	26%	31%	29%
Protease inhibitor use	45%	46%	43%
HIV viral load ≥200 copies/mL	15%	11%	8%
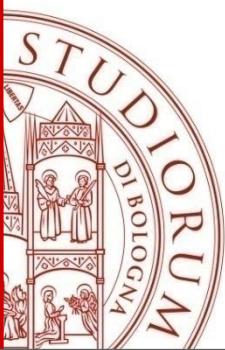
1 Among 2,733 patients with non-missing smoking data (18% missing)

Figure 2. Proportions of HIV-infected patients who were eligible for statin therapy and who were prescribed statin therapy (n=3,312).

(a) Among all participants, proportions eligible for statin therapy based on each guideline (n=3,312)

(b) Among participants eligible for statin therapy based on each guideline, proportions prescribed statin therapy (n=1,722)

- After HIV infection was counted as a major CVD risk factor in the NLA risk stratification algorithm, **51%** were eligible for NLA guidelines, resulting in **57%** being eligible based on ≥1 guideline

(Levy ME et al., Abstract 690, CROI 2018)

Conclusions

- Improved life expectancy of people living with HIV

- Persisting gap between HIV-positive and HIV-negative people

- Chronic inflammation and accelerated ageing as possible reasons

- Increasing prevalence of comorbidities associated with excess mortality

- Early diagnosis of HIV infection and immediate start of cART are mandatory