

I marcatori del danno d'organo nell'infezione da HIV

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Comorbidities Occur at Similar Age but Increased Frequency in HIV-Positive Pts

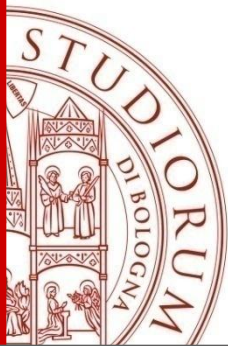
- Subanalysis of Veteran's Aging Cohort Study
 - Risk of age-related outcomes (MI, ESRD, non-AIDS defining cancers) by HIV status

Outcome	Adjusted Mean Difference in Age, Yrs	Risk aIRR (95% CI)
MI	-0.04 (-0.62 to 0.54)	1.81 (1.49-2.20)
ESRD	-0.23 (-0.69 to 0.23)	1.43 (1.22-1.66)
HIV-associated cancers*	-0.57 (-0.93 to -0.21)	1.84 (1.62-2.09)
Other cancers	-0.45 (-0.78 to -0.12)	0.95 (0.85-1.06)

*Included anal, Hodgkin's lymphoma, liver, lung, oral cavity ,and pharynx.

- Higher rate of MI, ESRD, HIV-associated cancers vs HIV-uninfected adults
- HIV-associated cancer diagnoses occurred ~ 7 mos earlier in HIV-infected adults vs HIV-uninfected adults

Althoff K, et al. CROI 2013. Abstract 59.



HIV Infection and the Risk of Acute Myocardial Infarction

(Veterans Aging Cohort Study, 82,459 patients, 2003-2009)

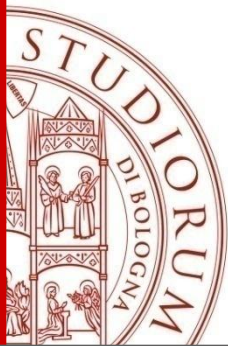
Table 2. Rates of AMI by HIV Status and Age Group^a

Status	Age Group, y						
	<30	30-39	40-49	50-59	60-69	70-79	80-89
Uninfected							
No. of participants	1175	6783	21 866	19 805	4209	1120	148
No. of AMI events	0	10	164	218	66	36	14
AMI rates per 1000 person-years (95% CI)	...	0.3 (0.2-0.6)	1.5 (1.3-1.7)	2.2 (1.9-2.5)	3.3 (2.6-4.2)	6.7 (4.8-9.2)	21.5 (12.7-36.4)
HIV Infected							
No. of participants	725	3848	10 575	9342	20 755	10 755	5 755
No. of AMI events	0	13	105	171	5	5	5
AMI rates per 1000 person-years (95% CI)	...	0.7 (0.4-1.2)	2.0 (1.6-2.4)	3.9 (3.3-4.5)	5 (3.8-6.5)	5 (3.8-6.5)	5 (3.8-6.5)
Incidence rate ratio (95% CI)	...	2.19 (0.89-5.58)	1.34 (1.04-1.72)	1.80 (1.47-1.21)	1.53 (1.21-1.94)	1.53 (1.21-1.94)	1.53 (1.21-1.94)

Table 4. Time-Updated Analyses Assessing the Association of HIV-1 RNA and CD4 Cell Count Values and the Risk of AMI in Separate Models^a

Category	HR (95% CI)	P Value ^b
HIV-1 RNA		
Uninfected	1 [Reference]	.05
≥500	1.75 (1.40-2.18)	
<500	1.39 (1.17-1.66)	
CD4 cell count		
Uninfected	1 [Reference]	.04
<200	1.88 (1.46-2.40)	
≥200	1.43 (1.21-1.69)	

(Freiberg MS et al., JAMA Intern Med 2013)



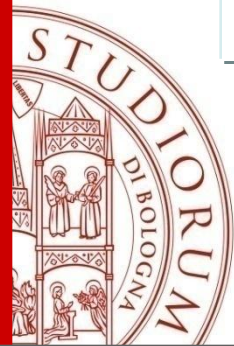
Non-infectious comorbidities

Risk evaluation



Damage markers

**Screening and
diagnosis**



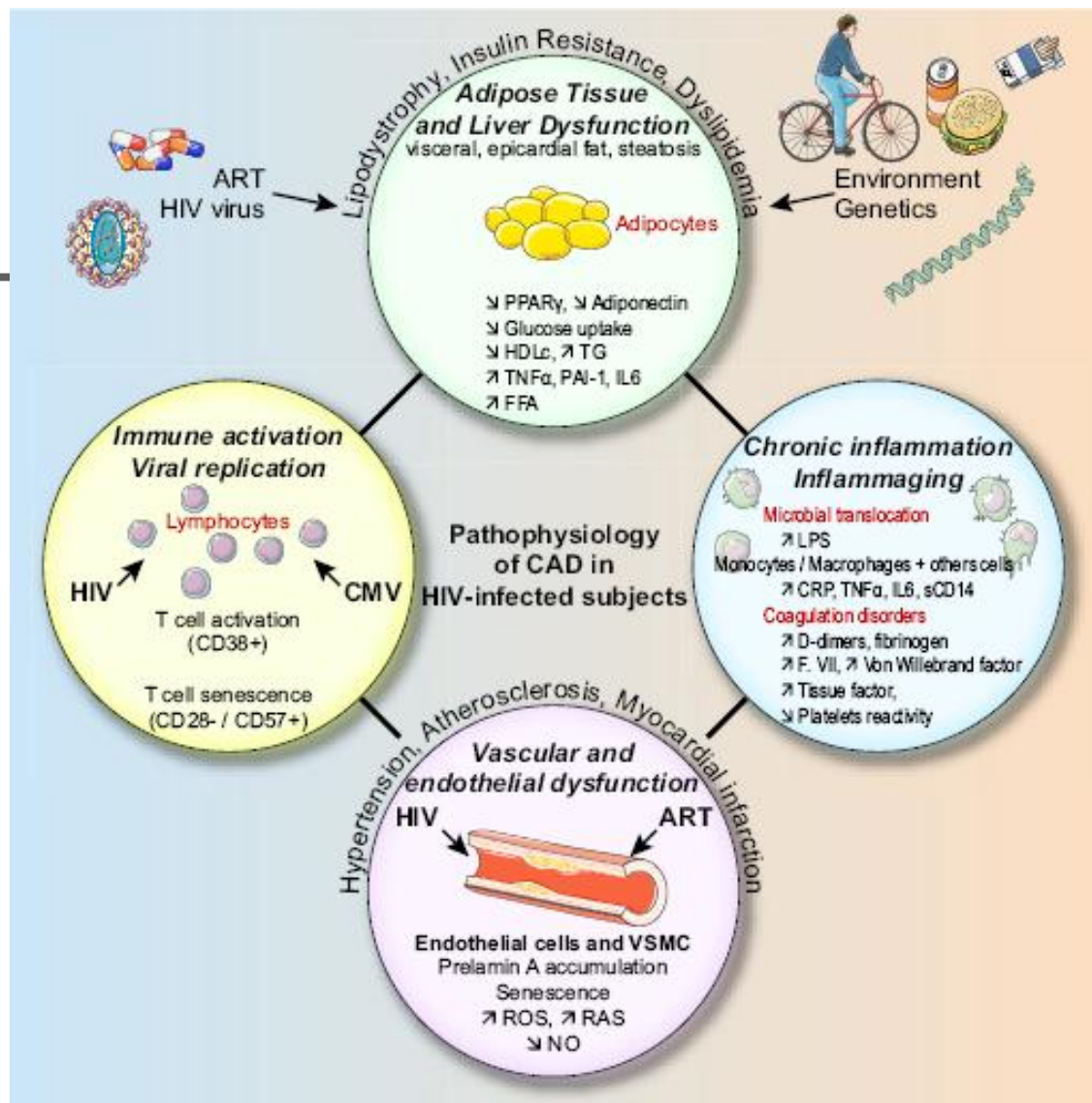
1. I fattori di rischio cardiovascolare classici sono: età > 50 anni, sesso maschile, familiarità per evento cardiovascolare giovanile (< di 55 anni se maschio, < di 65 anni se femmina), colesterolemia totale e HDL e LDL, dislipidemia familiare, pressione sanguigna, fumo e diabete.
2. HIV è un fattore di rischio cardiovascolare indipendente per l'impatto che esso determina sullo stato metabolico e pro-infiammatorio [AII] [55].
3. La condizione immunologica misurata come una bassa conta CD4+ o lunga durata dell'immunodepressione correla con gli eventi cerebrovascolari ma non con gli infarti del miocardio [62].
4. La TARV riducendo la viremia plasmatica di HIV attenua l'impatto infiammatorio del virus. Alcuni farmaci antiretrovirali tuttavia sono stati associati a un incremento del rischio cardiovascolare [55-57].
5. La lipodistrofia (sia nel fenotipo lipoatrofico ma soprattutto in quello lipoipertrofico) è un fattore di rischio cardiovascolare indipendente [AII] [63].

- Stima del rischio:

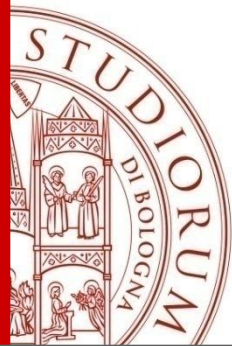
1. L'algoritmo di Framingham stima il rischio di infarto o il rischio di evento cardiovascolare a 10 anni, (<http://hp2010.nhlbi.nih.gov/atpiii/CALCULATOR.asp?usertype=prof>) pur nella consapevolezza che questo strumento sottostima gli eventi clinici [AII] [46, 47, 49].
2. Un algoritmo HIV specifico di predizione del rischio cardiovascolare a 5 anni è stato validato nella coorte D:A:D. In conformità con i risultati di questo studio, lo strumento contempla oltre ai predittori di rischio classici, l'esposizione corrente a indinavir, lopinavir ed abacavir (www.cphiv.dk/tools.aspx).
3. Altri algoritmi di predizione del rischio utilizzati nella popolazione generale hanno il vantaggio di computare fattori di rischio aggiuntivi che possono essere significativi nella patogenesi della malattia cardiovascolare in corso di infezione da HIV, in particolare l'algoritmo PROCAM include la trigliceridemia plasmatica (http://www.chd-taskforce.com/procam_interactive.html); l'algoritmo Reynolds (<http://www.reynoldsriskscore.org>) il dosaggio sierico della proteina C-reattiva; l'algoritmo SHAPE (http://www.shapesociety.org/your_levels_of_risk/) la valutazione del danno vascolare attraverso la misurazione dello spessore medio intimale.
4. Nei pazienti in cui l'algoritmo di Framingham stima un rischio cardiovascolare intermedio (compreso tra 10 e 20% nei successivi 10 anni) è indicato, laddove disponibile, un percorso specialistico di valutazione della vulnerabilità individuale in cui il giudizio clinico integra risultati di algoritmi diagnostici con informazioni derivanti da predittori del rischio integrativi o test diagnostici funzionali o strutturali di danno endoteliale [BIII].
5. L'esecuzione dell'ECG permette di individuare ischemie silenti o dei disturbi di conduzione.

- Valutazione individuale di vulnerabilità (fattori di rischio integrativi):

1. Biomarkers: ipertrigliceridemia, markers di infiammazione (IL-6, proteina C-reattiva ad alta sensibilità, VCAM, vWF, ADMA), di coagulazione (D-dimero), omocisteina di attivazione immunologica (linfociti CD8+CD38+). Tali marcatori sono al momento da riservarsi in ambito di ricerca.
2. Markers di danno vascolare (da riservarsi a centri specialistici). Comprendono:



(Boccaro F et al., J Am Coll Cardiol 2013)



HIV Replication and Immune Status Are Independent Predictors of the Risk of Myocardial Infarction in HIV-Infected Individuals

- Nested case-control study
- 289 HIV+ patients and 884 HIV- controls

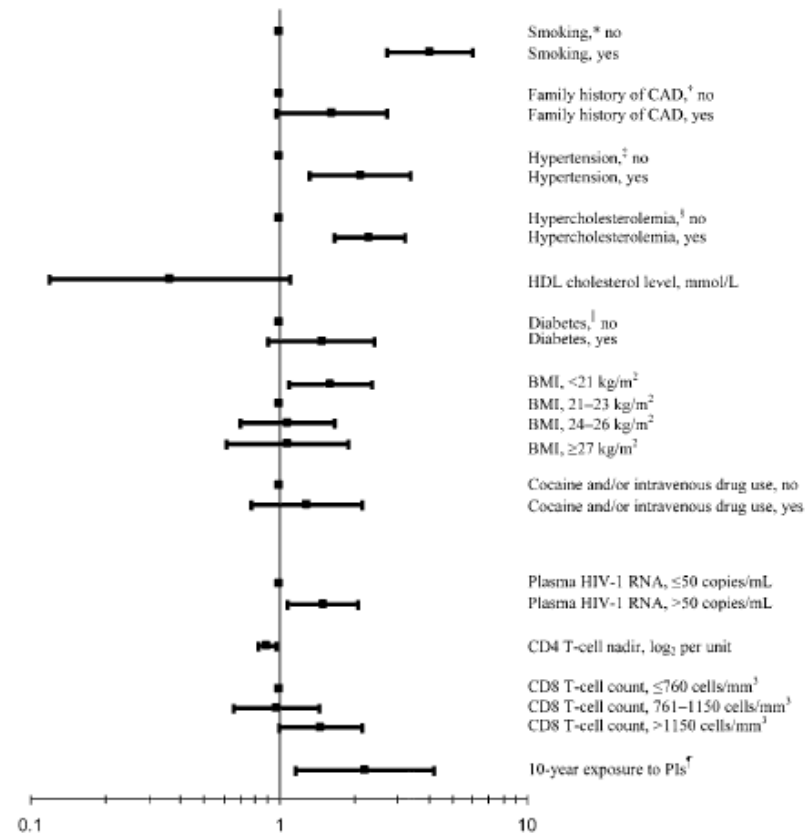
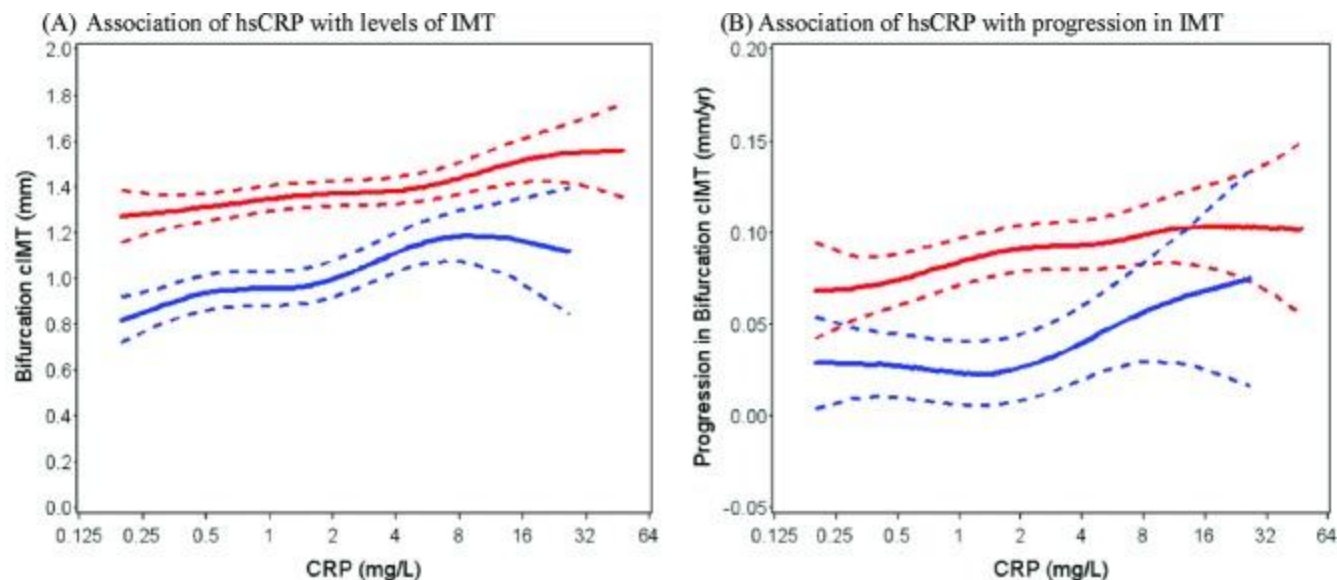


Figure 1. Risk of myocardial infarction (MI) according to cardiovascular risk factors and human immunodeficiency virus (HIV) parameters (odds-ratio and 95% confidence interval). *Current smoker or quit smoking <3 years before MI. †Family history of premature coronary artery disease (CAD): CAD before age 55 years in the father or 65 years in the mother. ‡Hypertension recorded with a date of diagnosis or use of antihypertensive medication. §Low-density lipoprotein (LDL) cholesterol level ≥4.1 mmol/L or use of lipid-lowering drugs or hypercholesterolemia recorded with a date of diagnosis. ¶Fasting glucose ≥7.0 mmol/L or prescription of antidiabetic treatment or diabetes recorded with a date of diagnosis. ††Cumulative exposure to studied protease inhibitor (PI). Abbreviations: BMI, body mass index; CAD, coronary artery disease; HDL, high-density lipoprotein; HIV-1, human immunodeficiency virus type 1.

(Lang S et al., Clin Infect Dis 2012)

Carotid Intima-Media Thickness Progression in HIV-Infected Adults Occurs Preferentially at the Carotid Bifurcation and Is Predicted by Inflammation

(Case-control study, 347 patients, mean follow-up 2.4 years)



Higher Solid line denotes predicted IMT (with dotted 95%CI confidence bounds) calculated from unadjusted generalized additive model (GAM). P-values are from spline and linear portion of the fit:

HIV: Spline: $p=0.090$; linear: $p=0.0008$;
Control: Spline: $p=0.0081$; linear: $p<.0001$

HIV: Spline: $p=0.29$; linear: $p=0.017$
Control: Spline: $p=0.016$; linear: $p=0.21$

(Hsue PY et al., J Am Heart Assoc 2012)

C-Reactive Protein Predicts 96-Week Carotid IMT Progression in HIV-Infected Adults Naïve to ART



- Prospective cohort study
- 96-week follow-up
- 42 HIV-positive patients and 41 HIV-negative patients

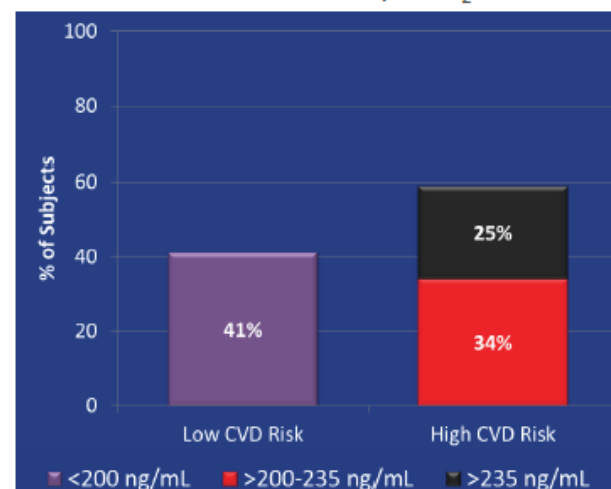
Multivariable Linear Regression (HIV+)	Parameter Estimate	Standard Error	P
Log-%Change CCA IMT			
Current Smoker (1=yes)	0.03459	0.01568	0.0337
SBP	0.00176	0.00052	0.0016
Non-HDL	0.00048	0.00023	0.0494
Log-CRP	0.01329	0.00657	0.0505
Log-%Change Bulb IMT			
Age	0.003	0.00177	0.0995
SBP	0.00421	0.00146	0.0072
Non-HDL	0.00117	0.00057	0.0487
Waist-Hip ratio	-0.81899	0.33713	0.0211
Log-CRP	0.04679	0.01592	0.0062

(Hileman C et al., Abstract #761, CROI 2013)

Lipoprotein-Associated Phospholipase A₂ (Lp-PLA₂) & Cardiovascular Disease Risk in HIV: A Balance of Pro-Inflammatory & Anti-Thrombotic Effects

- Cross-sectional analysis
- 100 HIV-positive patients on stable HAART with T cell activation and LDL-cholesterol <130 mg/dL
- Parameters assessed:
 - plasma Lp-PLA₂ level
 - cIMT and CAC
 - FMD

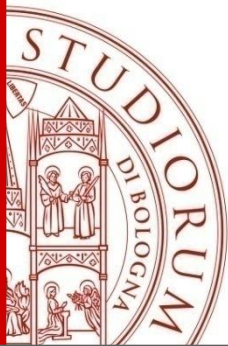
% of SUBJECTS IN EACH CVD RISK CATEGORY BASED ON Lp-PLA₂ VALUE



SIGNIFICANT CORRELATIONS WITH SUBCLINICAL ATHEROSCLEROSIS AND TRADITIONAL RISK FACTORS

Variable	R	P
Surrogate Markers of Atherosclerosis		
CCA IMT	0.20	0.05
Lower 2 CCA IMT tertiles	0.27	0.03
CCA IMT without plaque	0.26	0.03
Traditional CVD Risk Factors		
Body mass index	-0.35	<0.01
Male sex	0.23	0.02

(Eckard AR et al., Abstract #779, CROI 2013)



Markers of inflammation and CD8 T-cell activation, but not monocyte activation, are associated with subclinical carotid artery disease in HIV-infected individuals

(SATURN-HIV Trial, cross-sectional analysis, 60 HIV+ patients)

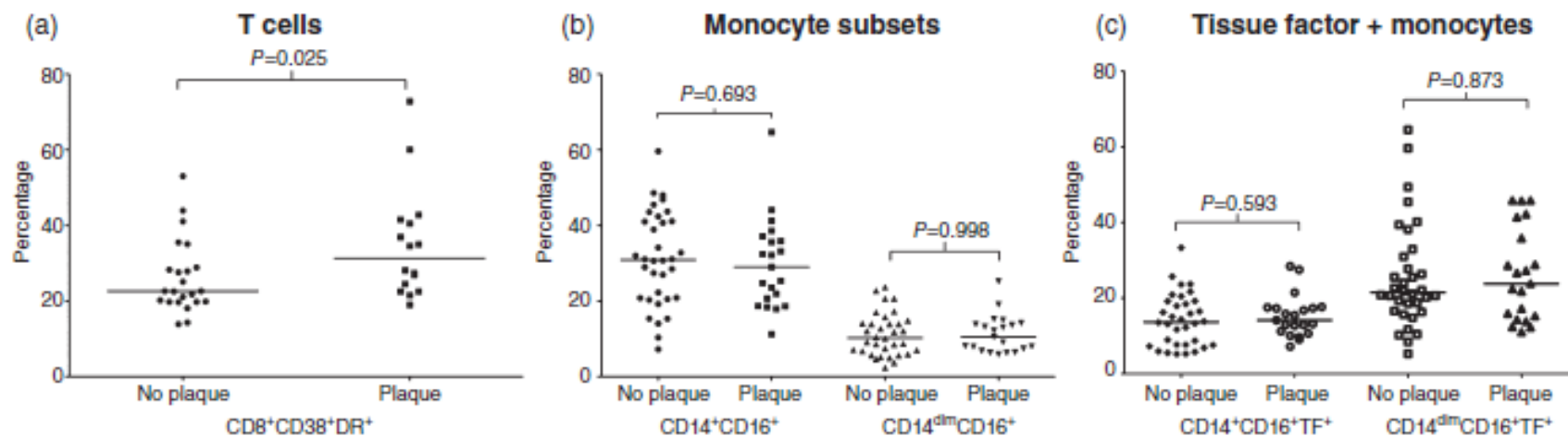


Fig. 1 Immune activation in participants with plaque compared with those without plaque. (a) Proportions of T-cell activation as measured by CD8⁺CD38⁺DR⁺ percentage. (b) Proportions of two pro-inflammatory monocyte subsets, CD14⁺CD16⁺ and CD14^{dim}CD16⁺. (c) Proportions of these two monocyte subsets that express tissue factor on the cell surface. Similar results were obtained for a third monocyte subset, CD14⁺CD16⁻. *t*-tests were used to test for statistical significance. TF, tissue factor.

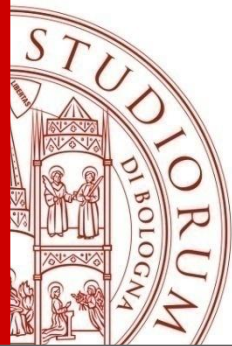
(Longenecker C et al., HIV Med 2013)

Association between ALT level and the rate of cardio/cerebrovascular events in HIV-positive individuals: The D:A:D Study

Table 2: MI, coronary heart disease and stroke event rates stratified by latest (time-updated) ALT level, unadjusted and adjusted* associations between latest ALT level and each outcome

Latest ALT level (U/L)	Events	Person-years follow-up (PYFU)	Rate (/1000 PYFU) (95% CI)	Relative rate (95% CI); p-value			
				Unadjusted		Adjusted*	
(i) Myocardial infarction							
<18	119	38354	3.1 (2.6, 3.7)	1	-	1	-
>18, <25	98	34584	2.8 (2.3, 3.4)	0.91 (0.70, 1.19)	0.51	0.80 (0.61, 1.05)	0.10
>25, <35	99	34436	2.9 (2.3, 3.4)	0.93 (0.71, 1.21)	0.58	0.78 (0.60, 1.03)	0.08
>35, <60	83	35502	2.3 (1.8, 2.8)	0.75 (0.57, 1.00)	0.05	0.60 (0.45, 0.80)	0.0005
>60	72	34050	2.1 (1.6, 2.6)	0.68 (0.51, 0.91)	0.01	0.50 (0.37, 0.68)	0.0001
Not known	70	23889	2.9 (2.2, 3.6)	0.94 (0.70, 1.27)	0.70	0.65 (0.45, 0.93)	0.02
/log ₂ increment				0.89 (0.82, 0.96)	0.004	0.81 (0.74, 0.89)	0.0001
(ii) Coronary heart disease							
<18	166	38230	4.3 (3.7, 5.0)	1	-	1	-
>18, <25	144	34445	4.2 (3.5, 4.9)	0.96 (0.77, 1.20)	0.74	0.87 (0.70, 1.09)	0.24
>25, <35	153	34246	4.5 (3.8, 5.2)	1.03 (0.83, 1.28)	0.80	0.92 (0.73, 1.15)	0.45
>35, <60	124	35313	3.5 (2.9, 4.1)	0.81 (0.64, 1.02)	0.07	0.72 (0.57, 0.91)	0.005
>60	122	33918	3.6 (3.0, 4.2)	0.83 (0.66, 1.05)	0.11	0.76 (0.60, 0.97)	0.03
Not known	95	23820	4.0 (3.2, 4.8)	0.92 (0.71, 1.18)	0.51	0.73 (0.57, 0.94)	0.02
/log ₂ increment				0.94 (0.88, 1.00)	0.07	0.92 (0.86, 0.99)	0.02

(Sabin CA et al., J AIDS 2013)



Should HIV-infected patients be screened for silent myocardial ischaemia using gated myocardial perfusion SPECT?

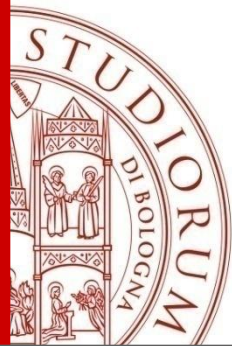
Anthropomorphic characteristic/cardiovascular risk factor	Odds ratio (95 % CI)	p value
Weight	1.04 (0.99–1.10)	0.10 ^a
Height	0.99 (0.89–1.10)	0.86
Body mass index	1.17 (0.99–1.39)	0.06 ^a
Waist circumference	1.04 (1.00–1.10)	0.08 ^a
Hip measurement	1.07 (0.97–1.17)	0.16 ^a
Male older than 50 years or female older than 60 years	1.44 (1.16–1.78)	0.001 ^a
Cigarette smoking	1.15 (0.27–4.92)	0.85
Pack years	1.05 (0.95–1.16)	0.36
Hypertension (≥140/90 mmHg or medication)	3.48 (0.81–14.92)	0.09 ^a
Systolic pressure	1.03 (0.99–1.08)	0.13 ^a
Diastolic pressure	1.02 (0.96–1.08)	0.50
Fasting blood sugar level	1.01 (0.59–1.74)	0.97

Treated type 2 diabetes
Glycated haemoglobin in patients with diabetes
Dyslipidaemia (medication or LDL >1.3 and HDL <0.6 g/L)
HDL cholesterol level (dyslipidaemic patients)
LDL cholesterol level (dyslipidaemic patients)
Triglyceride level (dyslipidaemic patients)
Family history of premature coronary heart disease
Number of cardiovascular risk factors
Number of cardiovascular risk factors except gender and age

	Positive SPECT	Negative SPECT	
Men >52 years of age and two cardiovascular risk factors	9	38	Positive predictive value 19.15 %
Others	0	47	Negative predictive value 100 %
	Sensitivity 100 %	Specificity 55.3 %	

- Cross-sectional study
- 94 HIV+ patients

(Mariano-Goulart D et al., Eur J Nucl Med Mol Imaging 2013)



Psychological Factors, Including Alexithymia, in the Prediction of Cardiovascular Risk in HIV Infected Patients: Results of a Cohort Study

(Cohort study, 232 HIV-positive patients)

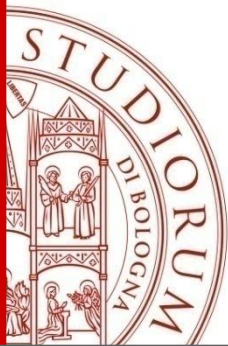
Variables	IMT _{max} ≥ 1.5 mm			IMT _{max} ≥ 1.2 mm			IMT _{max} ≥ 1.0 mm		
	OR	(95% CI)*	p	OR	(95% CI)*	p	OR	(95% CI)*	p
Age, 5-year increase	1.72	(1.36–2.19)	<0.001	2.25	(1.73–2.93)	<0.001	2.03	(1.58–2.62)	<0.001
Male gender	2.24	(0.74–6.75)	0.15	2.12	(0.72–6.26)	0.17	1.93	(0.71–5.26)	0.2
Body Mass Index, 1 unit increase	0.99	(0.88–1.10)	0.8	1.02	(0.91–1.15)	0.7	0.96	(0.85–1.09)	0.5
Infection duration, 1-year increase	1.04	(0.98–1.10)	0.19	1.05	(0.99–1.12)	0.082	1.05	(0.99–1.11)	0.077
Hypertension	1.93	(0.78–4.82)	0.16	1.73	(0.67–4.46)	0.3	2.59	(0.91–7.35)	0.074
Current smoking	2.74	(1.16–6.44)	0.021	2.48	(1.04–5.92)	0.041	1.55	(0.66–3.63)	0.3
Diabetes mellitus	1.10	(0.37–3.23)	0.9	1.15	(0.37–3.55)	0.8	1.02	(0.32–3.23)	0.9
Total cholesterol, 10 mg/dL increase	1.10	(1.05–1.16)	<0.001	1.12	(1.07–1.18)	<0.001	1.12	(1.06–1.18)	<0.001
Alexithymia TAS-20 score ≥ 50	2.63	(1.17–5.89)	0.019	2.99	(1.31–6.83)	0.009	4.23	(1.86–9.61)	0.001

CI = Confidence Interval. OR = Odds Ratio.

*Based upon robust standard errors. Parameters of the models: (1.0 mm) n. of obs. = 196; Wald chi-squared = 66.4; Hosmer–Lemeshow goodness of fit p = 0.27; area under the receiving operator curve (ROC) = 0.87; (1.2 mm) n. of obs. = 196; Wald chi-squared = 61.9; Hosmer–Lemeshow goodness of fit p = 0.68; area under the receiving operator curve (ROC) = 0.87; (1.5 mm) n. of obs. = 196; Wald chi-squared = 44.1; Hosmer–Lemeshow goodness of fit p = 0.23; area under the receiving operator curve (ROC) = 0.84.

doi:10.1371/journal.pone.0054555.t005

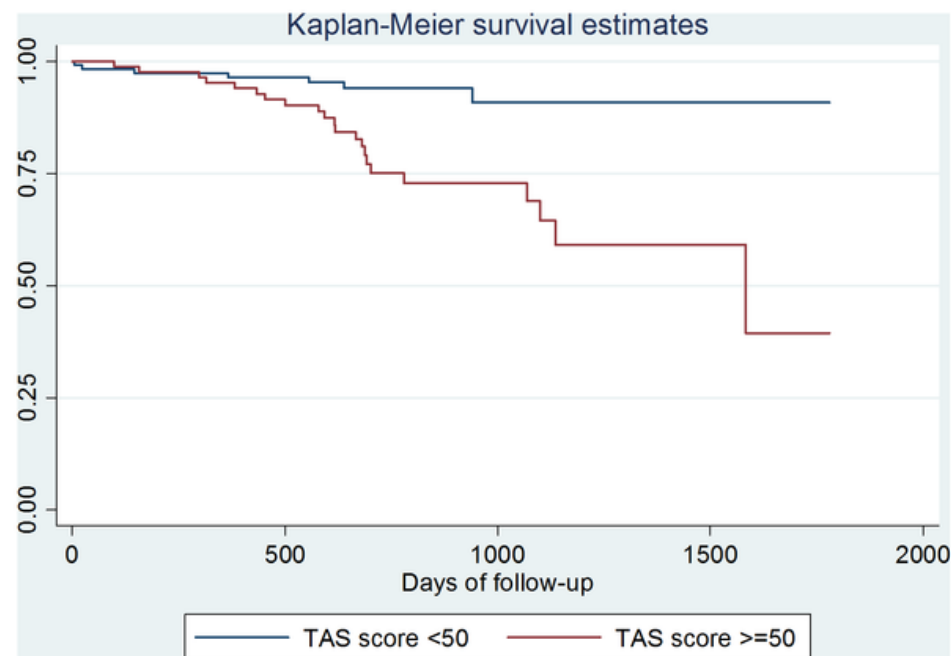
(Parruti G et al., PLoS One 2013)



Psychological Factors, Including Alexithymia, in the Prediction of Cardiovascular Risk in HIV Infected Patients: Results of a Cohort Study

	Hazard Ratio	(95% CI)	p
Age, 5-year increase	1.55	(1.19–2.02)	0.001
Infection duration, 1-year increase	0.98	(0.91–1.05)	0.5
Hypertension	0.44	(0.13–1.50)	0.2
Current smoking	3.87	(1.25–12.0)	0.019
Total cholesterol, 10 mg/dL increase	1.06	(0.98–1.14)	0.13
Alexithymia TAS-20 score ≥ 50 vs < 50	5.58	(1.44–21.6)	0.013

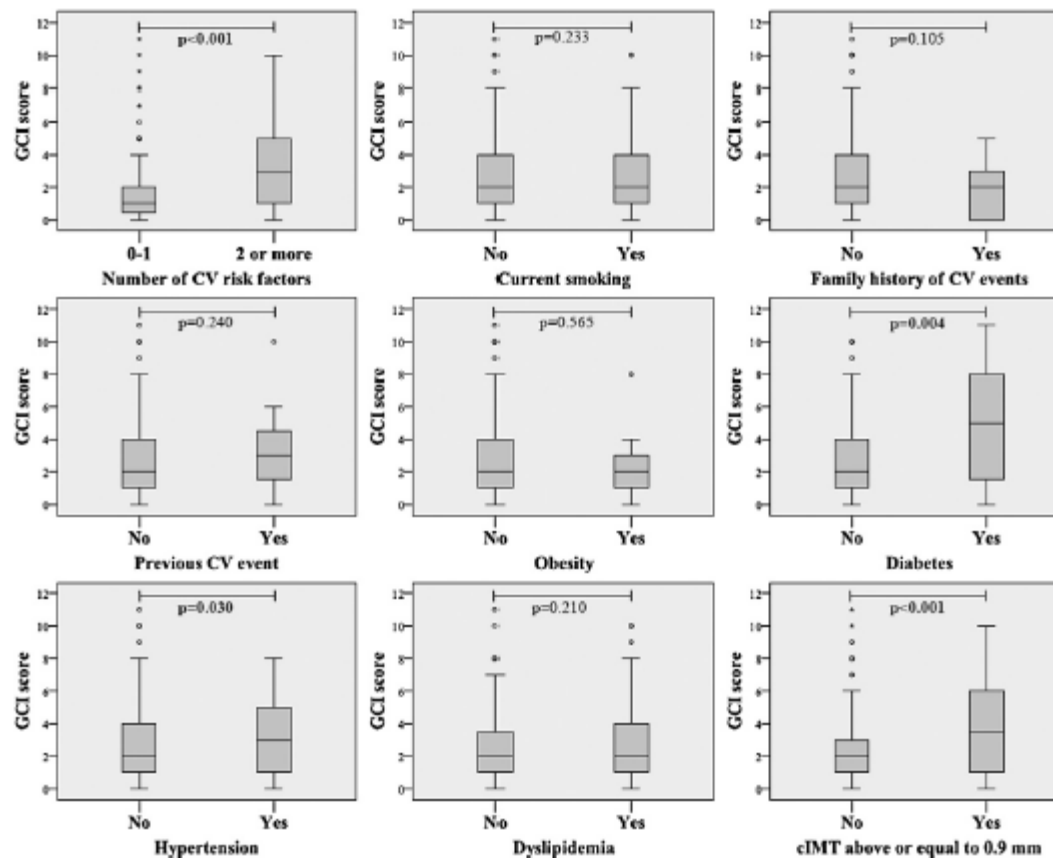
doi:10.1371/journal.pone.0054555.t007



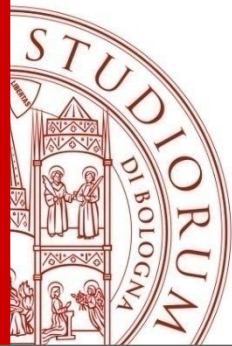
(Parruti G et al., PLoS One 2013)

Cardiovascular risk factors and carotid intima-media thickness are associated with lower cognitive performance in HIV-infected patients

(Cross-sectional study, 245 HIV+ patients)



(Fabbiani M et al., HIV Med 2013)



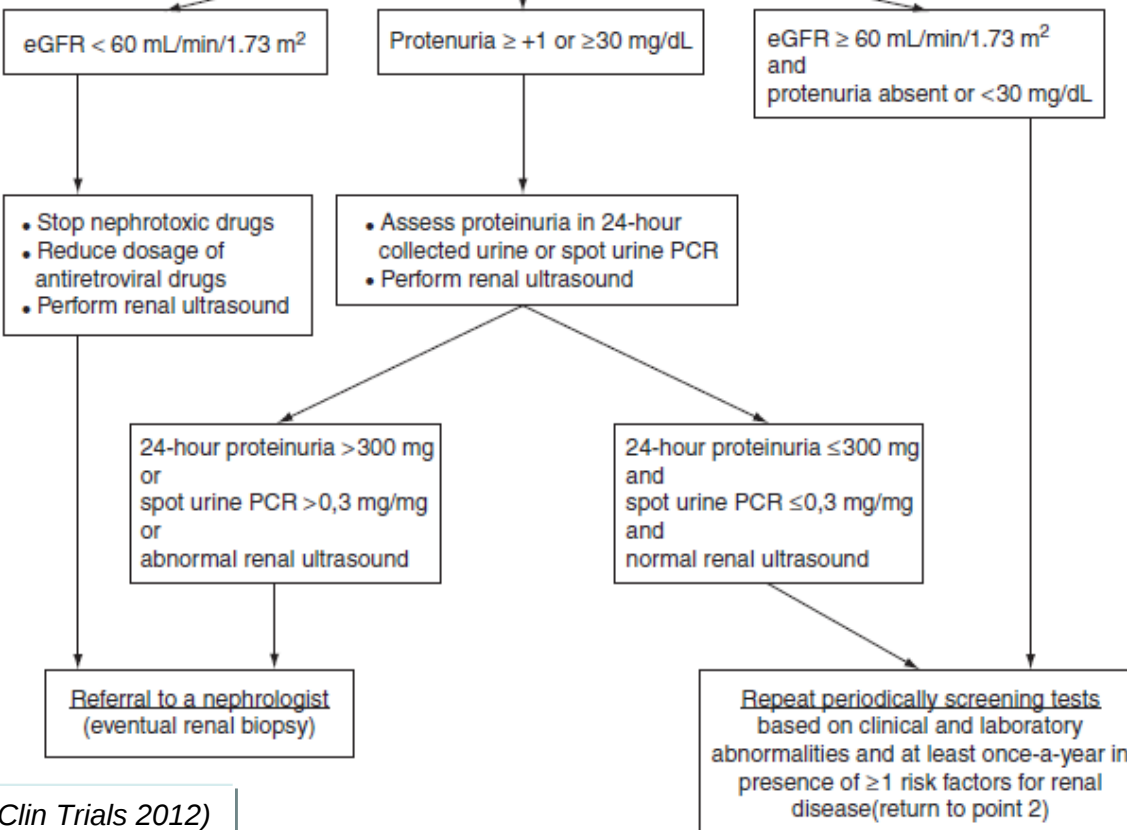
Valutazione del rischio di malattia renale

1-Evaluation of risk factors for renal disease:

African-American race, age >50 years, family history of renal disease, diabetes, hypertension, HCV coinfection, use of nephrotoxic drugs, AIDS, CD4 lymphocyte count <200 cells/mm³, HIV RNA >4000 copies/mL

2- Screening study:

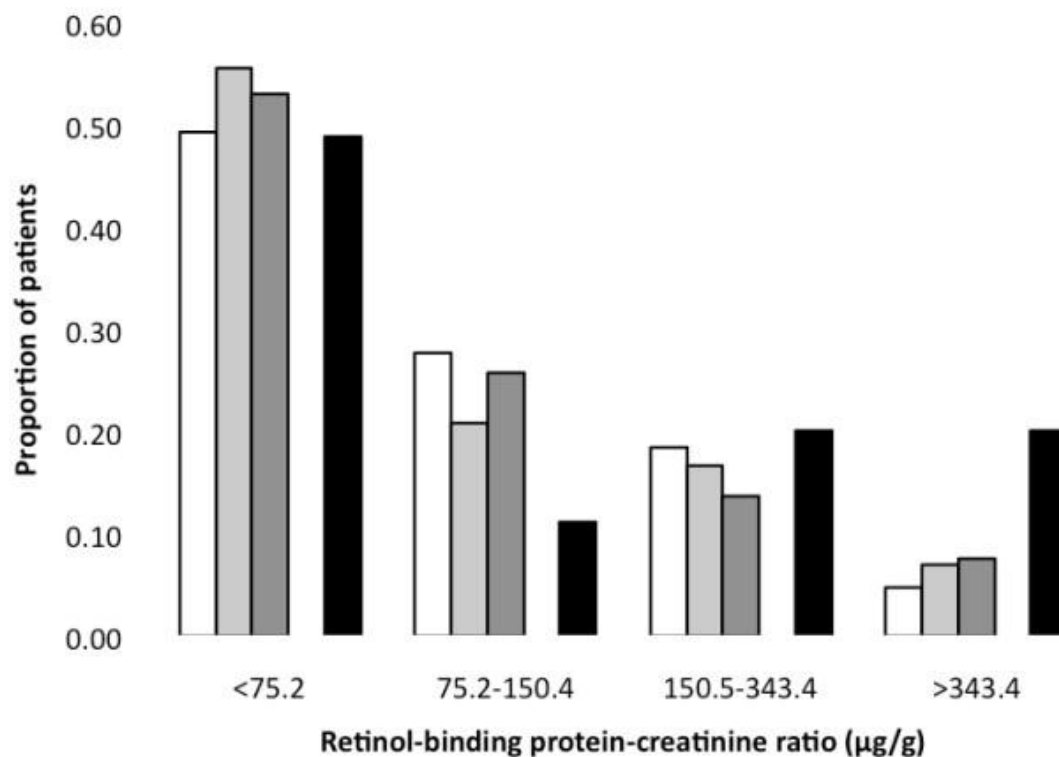
- serum creatinine and eGFR (CG or MDRD or CKD-EPI)
- Spot urine analysis (for proteinuria)



(Calza L, HIV Clin Trials 2012)

Total protein, albumin and low-molecular-weight protein excretion in HIV-positive patients

(Cross-sectional study, 317 HIV-positive patients on HAART)



(Campbell LJ et al., BMC Nephrol 2012)

Total protein, albumin and low-molecular-weight protein excretion in HIV-positive patients

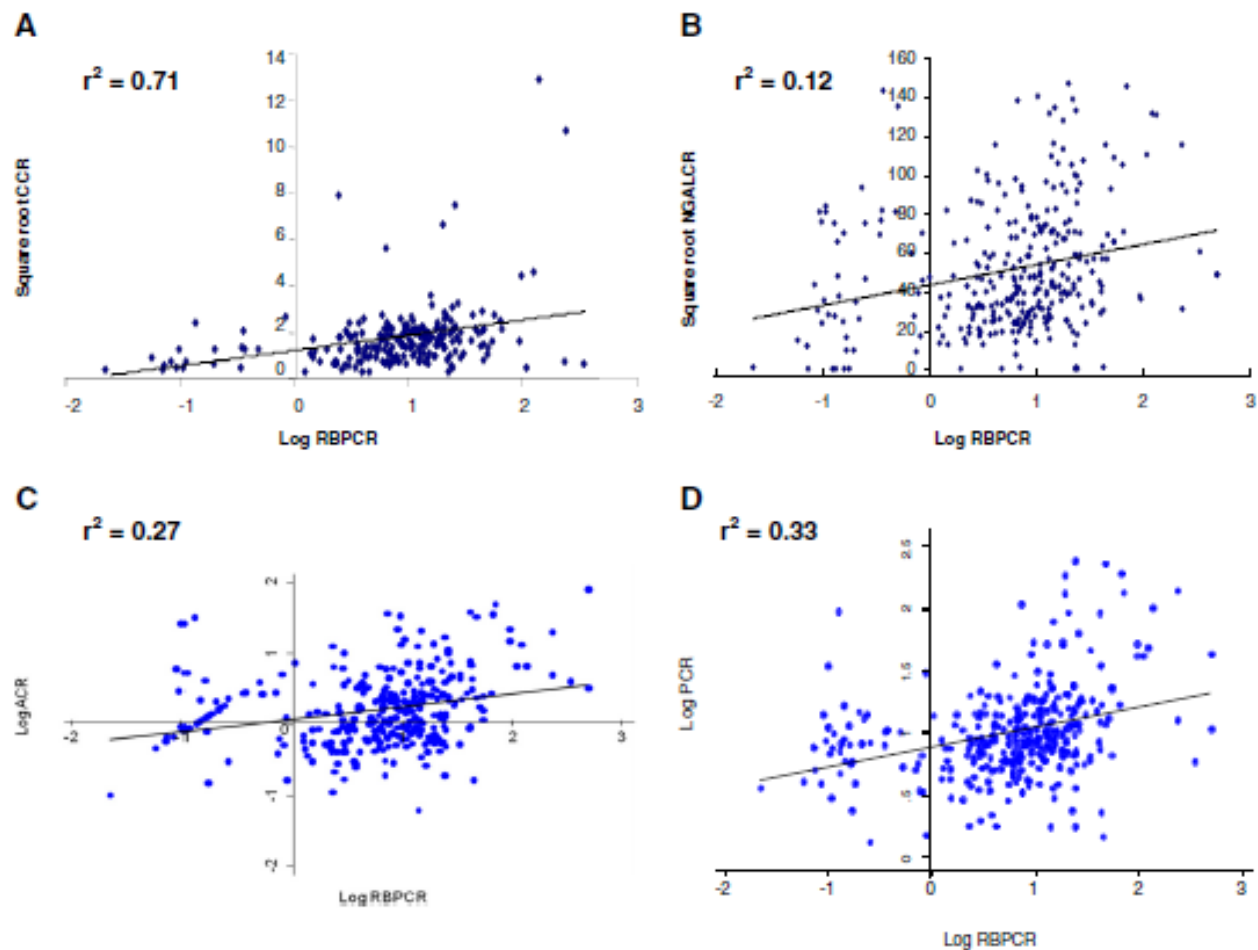
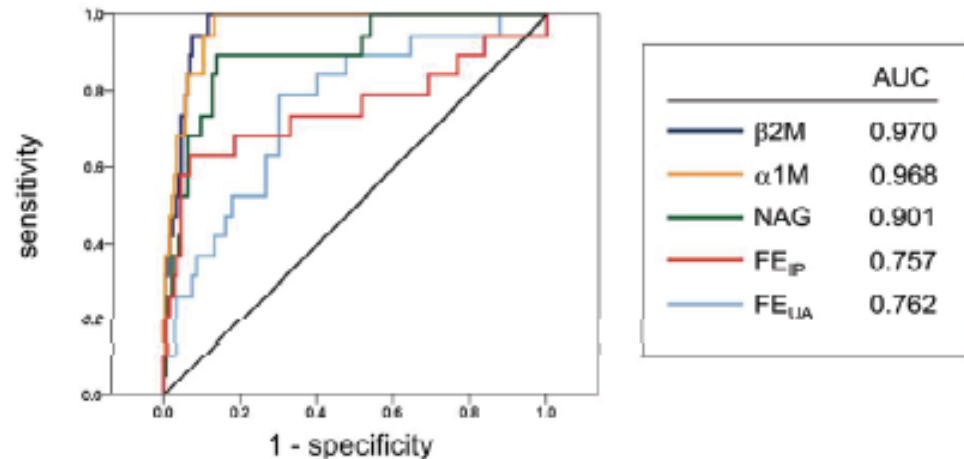


Figure 1 Correlations between RBPCR and CCR (A), NGALCR (B), ACR (C) and PCR (D).

(Camp bell LJ et al., BMC Nephrol 2012)

Urinary beta-2 microglobulin and alpha-1 microglobulin are useful screening markers for tenofovir-induced kidney tubulopathy: A diagnostic accuracy study

Fig 2. The diagnostic accuracy of five tubular markers



Receiver operating characteristic (ROC) curves and areas under the curve (AUC) for five tubular markers.

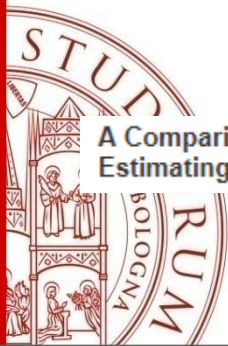
Table 2. The differences between the largest AUC ($\beta 2M$) and each of other AUCs

	AUC	95% CI	Std. Err.	P value	P value ^a
$\beta 2M$ (standard)	0.97	0.95-0.99	0.01		
$\alpha 1M$	0.97	0.94-0.99	0.01	0.89	1
NAG	0.90	0.83-0.97	0.04	0.09	0.37
FE_{IP}	0.76	0.61-0.91	0.08	<0.01	0.02
FE_{UA}	0.76	0.65-0.87	0.06	<0.01	<0.01

The differences were tested using a nonparametric method. P value^a: the value adjusted with Bonferroni correction.

- Cross-sectional study
- 190 HIV-infected patients on TDF/FTC + DRV/rvt
- Undetectable viral load

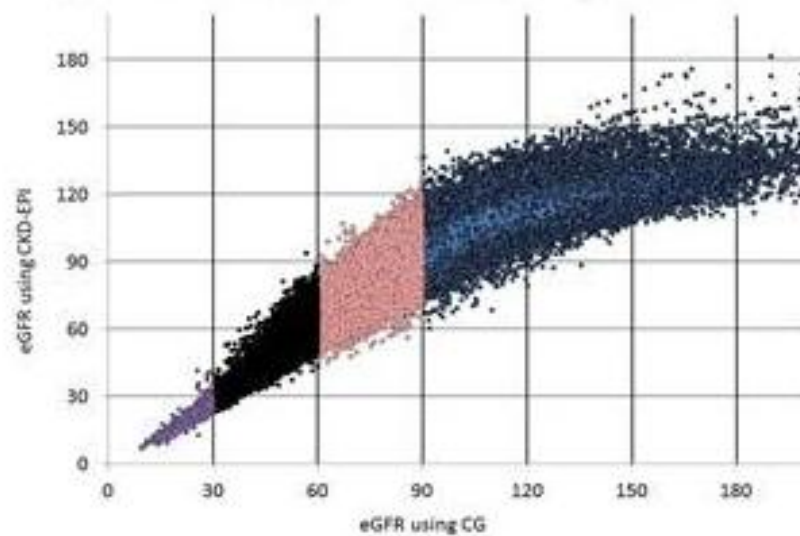
(Nishijima T et al., Abstract #812, CROI 2013)



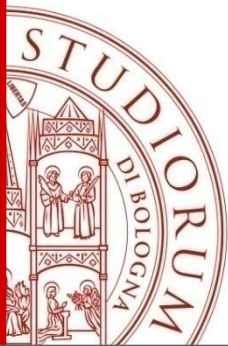
A Comparison of Estimated Glomerular Filtration Rates Using Cockcroft-Gault and the Chronic Kidney Disease Epidemiology Collaboration Estimating Equations

- EuroSIDA Study Cohort
- 9059 HIV-infected patients

Agreement between eGFRs calculated using CG and CKD-EPI



(Mocroft A et al., Abstract #808, CROI 2013)



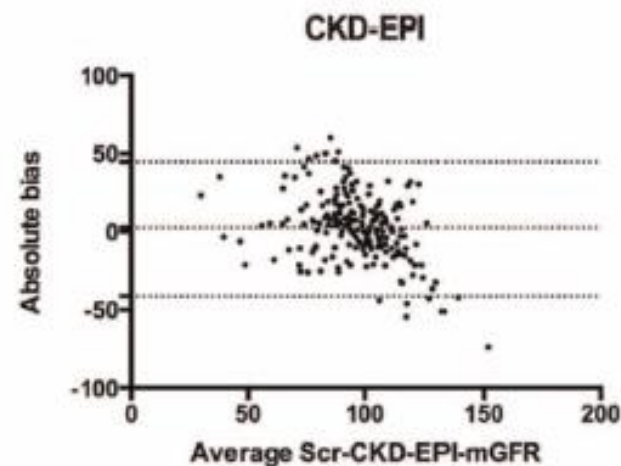
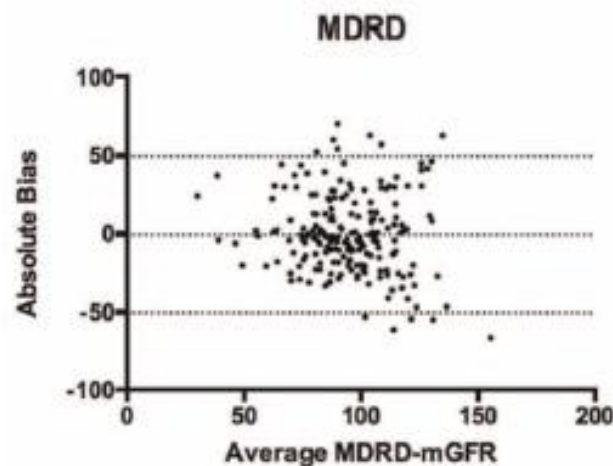
Performance of creatinine and cystatin C-based glomerular filtration rate estimating equations in a European HIV-positive cohort

(Cohort study, 203 HIV+ patients)

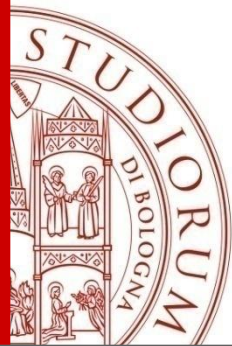
Table 3. Predictive performances of the MDRD study, CKD-EPI, CKD-EPI-Scyst, and CKD-EPI-combined equations in HIV patients (n = 203).

GFR estimates	R	Bias		Absolute Precision mL/min/1.73m ² (relative in %)	Accuracy 30%
		Absolute (mL/min/1.73m ²)	Relative (%)		
MDRD	0.41	-1.1	+4.2	25 (33%)	75
CKD-EPI	0.51	+2.6	+8.3	22 (31%)	82*
CKD-EPI Scyst	0.54	+1.2	+5	22 (26%)	80
CKD-EPI combined	0.58	+2.5	+6.9	20 (26%)	81*

*p<0.05 versus MDRD study equation, R: correlation coefficient.



(Gagneux-Brunon A et al., AIDS 2013)



Valutazione del rischio di malattia ossea

In tutti i soggetti con infezione da HIV è indicato eseguire uno screening per l'identificazione dei soggetti a rischio di malattia ossea [AII] [90, 91].

Individuazione del paziente a rischio elevato

- Individuazione dei fattori di rischio:

1. Un calo staturale di oltre 3 cm pone il sospetto diagnostico di frattura vertebrale: in questi casi è opportuno considerare l'esecuzione di un Rx morfometrico del rachide dorsale in proiezione laterale.
2. I fattori di rischio classici per osteoporosi comprendono: ipogonadismo, familiarità per fratture, BMI < 19 kg/m², ipovitaminosi D, fumo, sedentarietà, pregresse fratture da trauma minimo, età avanzata, razza caucasica, sesso femminile, menopausa e/o amenorrea, assunzione abituale di > 3 bicchieri/die di alcol, utilizzo di steroidi (5 mg/die prednisone equivalenti) per via sistemica per > 3 mesi.
3. In tutti i pazienti bisogna dosare i livelli plasmatici della 25-OH vitamina D, preferenzialmente in inverno e in primavera. Poiché in alcuni casi (specie nei soggetti con livelli di 25-OH vitamina D molto bassi) la comune supplementazione standard può non essere in grado di far raggiungere livelli plasmatici ottimali, se possibile è opportuno riverificare i livelli plasmatici dopo 6 mesi dalla supplementazione [AIII] [28-30].
4. Una corretta valutazione dell'apparato osseo dovrebbe comprendere lo studio del metabolismo minerale, con un marcatore di riassorbimento osseo e, se possibile, uno di neoformazione [BII] [31, 32].

- Stima del rischio:

1. In tutti i pazienti di età > 40 anni è indicato stimare il rischio di frattura a 10 anni utilizzando l'algoritmo FRAX® (www.shef.ac.uk/FRAX). L'algoritmo è indicato solo per pazienti di età > 40 anni, può sottovalutare il rischio nei soggetti con HIV, e occorre inserire l'HIV come causa secondaria di osteoporosi [AII] [92, 93].

- Valutazione di vulnerabilità:

L'osteoporosi è un disordine scheletrico caratterizzato da una riduzione della resistenza ossea, definita dall'integrazione di densità ossea (*bone quantity*) e qualità ossea (*bone quality*). Solo la conoscenza di entrambe queste due componenti permette di valutare al meglio la vulnerabilità ossea.

1. La DXA è il *golden-standard* per lo studio della densità minerale ossea e il più importante fattore di rischio indipendente di osteoporosi; ove possibile, è indicata quando sono presenti oltre ad HIV, almeno 2 fattori di rischio maggiori. Occorre utilizzare lo *Z-score* per le donne in pre-menopausa e gli uomini < 50 anni d'età. In caso di valori di BMD anormali, indagare anche le altre cause secondarie di osteoporosi. Nel *follow-up* va ripetuta dopo 18-24 mesi [AII] [26, 94]. Fornisce le informazioni più precise sulla *bone quantity*, vale a dire sulla disponibilità di calcio e di idrossiapatite per unità di superficie ossea.

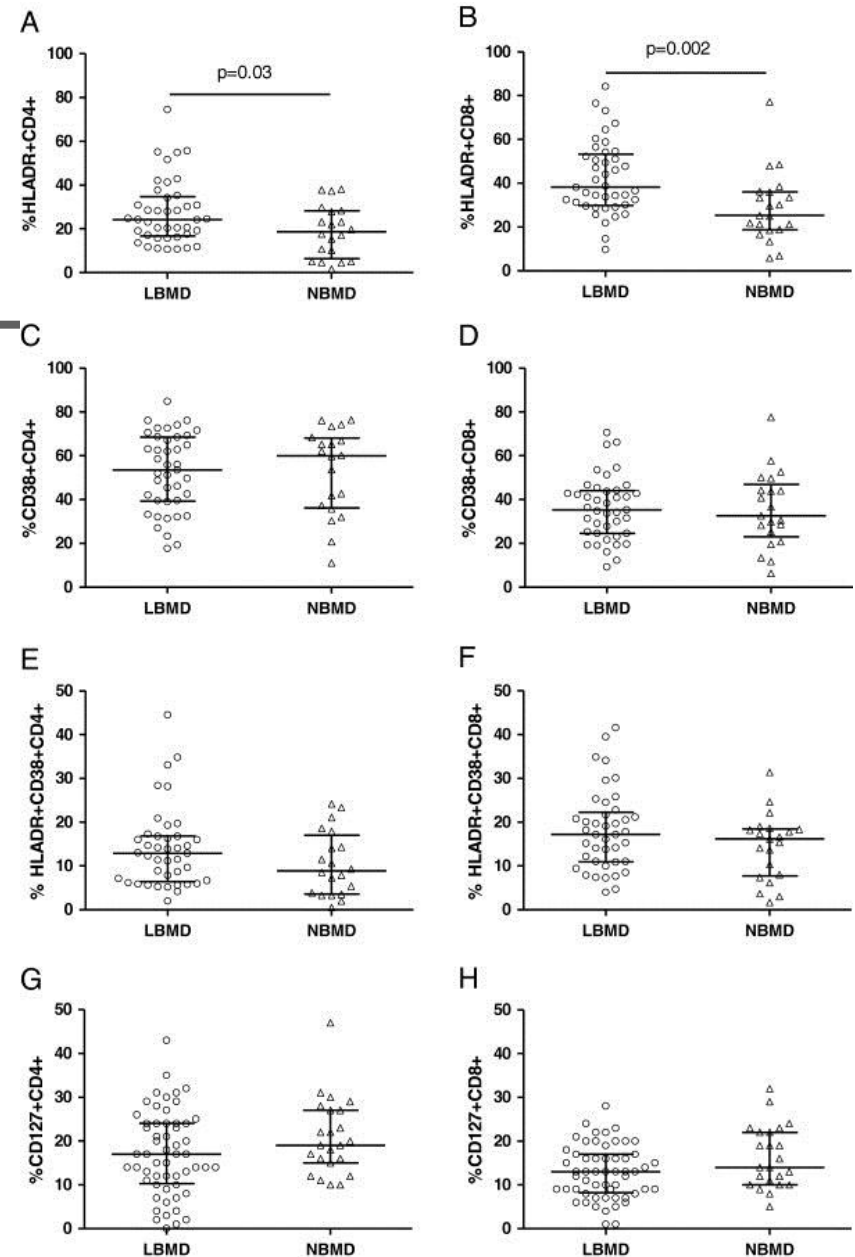
2. I marcatori di turnover osseo forniscono le informazioni più precise sulla *bone quality*, integrano in maniera preziosa il dato densitometrico, e nel *follow-up* possono dare informazioni sull'attività dell'unità di rimodellamento osseo già dopo soli 3-6 mesi.

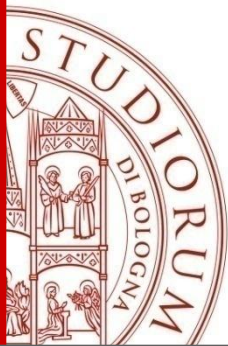
(Linee Guida Italiane, Luglio 2012)

Association between peripheral T-Lymphocyte activation and impaired bone mineral density in HIV-infected patients

- Cross-sectional study
- 78 HIV-positive patients

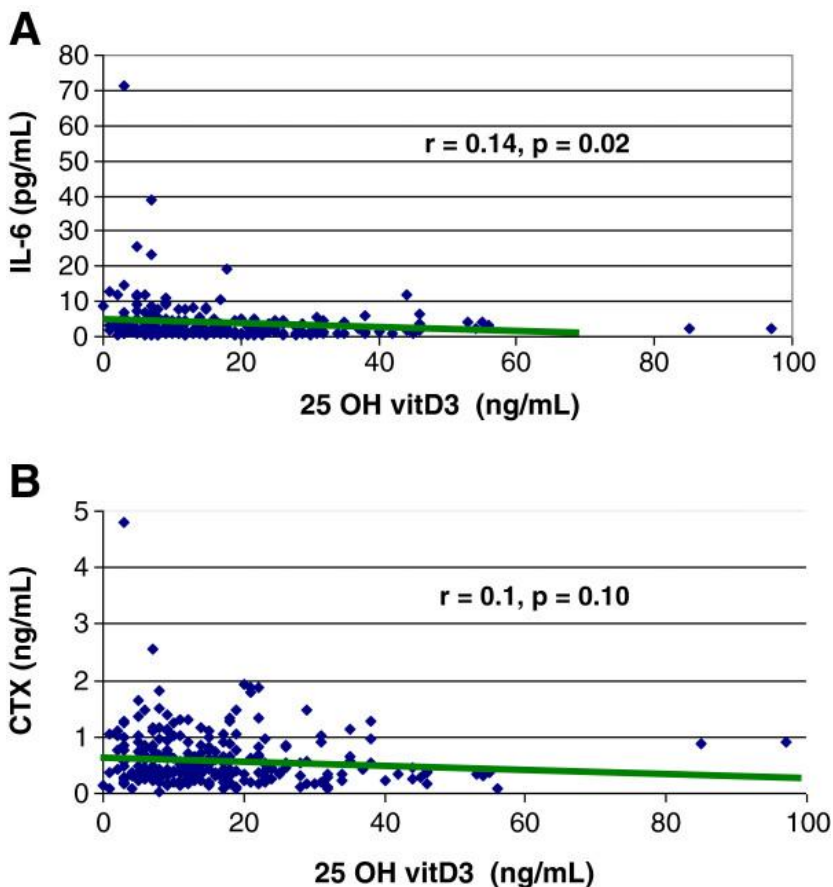
(Gazzola L et al., J Transl Med 2013)



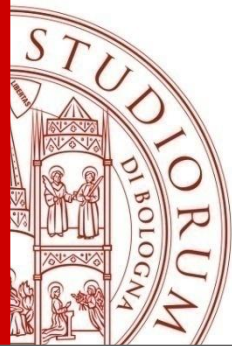


Severe hypovitaminosis D correlates with increased inflammatory markers in HIV infected patients

- Cross-sectional study
- 263 HIV-positive patients

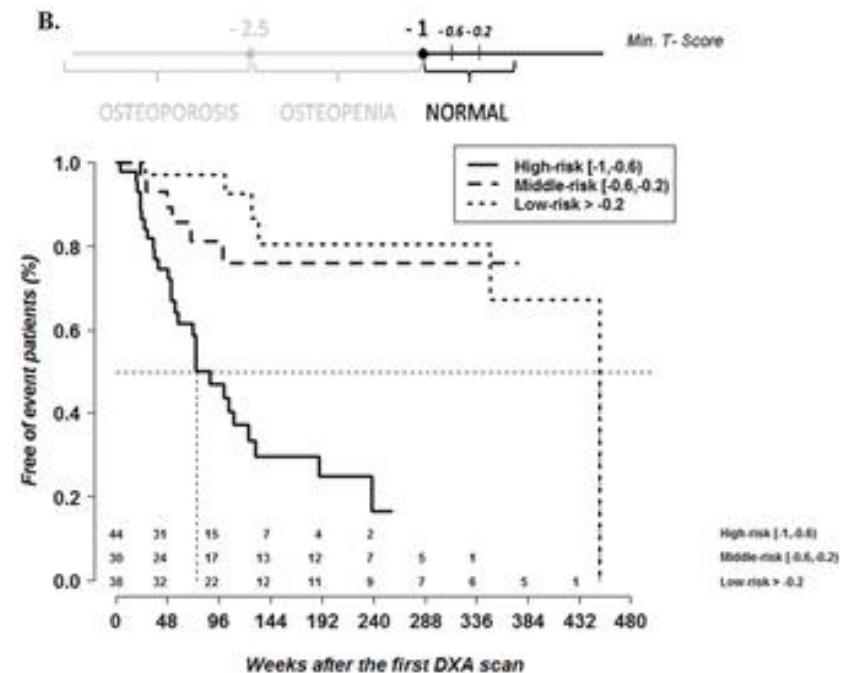
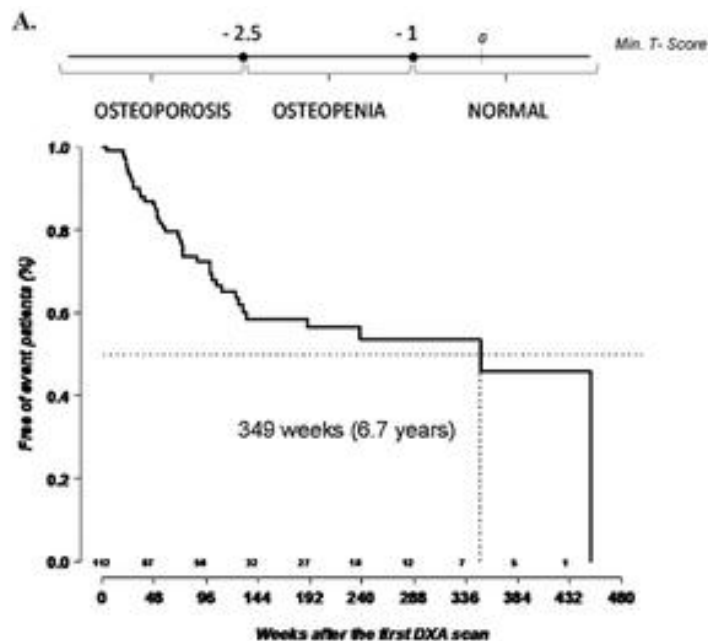


(Ansemant T et al., BMC Infect Dis 2013)



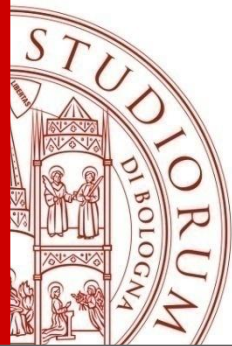
Time of Progression to Osteopenia/Osteoporosis in Chronically HIV-Infected Patients: Screening DXA Scan

(Retrospective cohort study, 391 HIV-infected patients with at least 2 DXA scans performed between 2000 and 2009)



HIGH-RISK [-1, -0.6]	86 weeks
MIDDLE-RISK [-0.6, -0.2]	>375 weeks
LOW-RISK > -0.2	451 weeks

(Negredo E et al., PLoS One 2012)



Screening for chronic comorbid diseases in people with HIV: the need for a strategic approach

B Peters,¹ F Post,^{2,3} AS Wierzbicki,⁴ A Phillips,⁵ L Power,⁶ S Das,^{7,8} M Johnson,⁹ G Moyle,¹⁰ L Hughes,¹¹ E Wilkins,¹² E McCloskey,¹³ J Compston¹⁴ and E Di Angelantonio¹⁵

¹Department of Infectious Diseases, King's College London, London, ²Department of Renal Medicine, King's College London, London, ³Department of Sexual Health, King's College Hospital, London, ⁴Department of Metabolic Medicine and Chemical Pathology, Guy's & St Thomas' Hospitals, London, ⁵Research Department of Infection and Population Health, University College London, London, ⁶Terrence Higgins Trust, London, ⁷Department of HIV and GU Medicine, Coventry & Warwickshire Partnership Trust, Coventry, ⁸Medical Division, University of Warwick, Coventry, ⁹Department of Thoracic Medicine, Royal Free London, NHS Foundation Trust, London, ¹⁰Chelsea and Westminster Hospital, London, ¹¹Patient Representative, ¹²North Manchester General Hospital, Manchester, ¹³Academic Unit of Bone Metabolism, Metabolic Bone Centre, Northern General Hospital, Sheffield, ¹⁴University of Cambridge School of Clinical Medicine, Cambridge and ¹⁵Department of Public Health and Primary Care, University of Cambridge, Cambridge, UK

Among people living with HIV, the proportion of deaths attributed to chronic noninfectious comorbid diseases has increased over the past 15 years. This is partly a result of increased longevity in

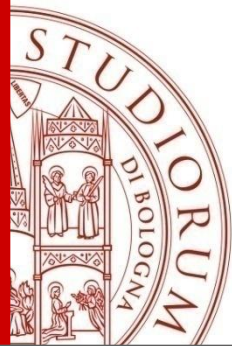
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“The development of a “pre-screen” tool able to identify those HIV-infected patients most likely to require more in-depth investigations may offers great benefits”

reasonable standard. The situation is compounded by the fact that few risk calculators have been adjusted for specific use in HIV infection. There is substantial overlap of risk factors for the four common comorbid diseases listed above that are especially relevant in HIV infection, and this offers an opportunity to develop a simple screening approach that encompasses the key risk factors for lifestyle-related chronic disease in people with HIV infection. This would identify those patients who require more in-depth investigation, and facilitate a stepwise approach to targeted management. Such a tool could improve communication between patient and clinician. A significant proportion of people with HIV are sufficiently engaged with their care to participate in health promotion and take the lead in using patient-centric screening measures. Health-based social networking offers a mechanism for dissemination of such a tool and is able to embed educational messages and support within the process.

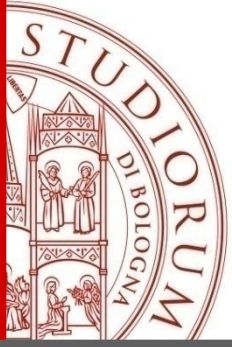
Keywords: cardiovascular, comorbidity, coronary, diabetes, HIV, osteoporosis, screening

(Peters B et al., HIV Med 2013)



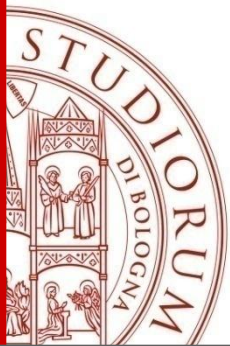
COPD Assessment Test (CAT)

Non tossisco mai	0 1 2 3 4 5	Tossisco sempre	
Il mio petto è completamente libero da catarro (muco)	0 1 2 3 4 5	Il mio petto è tutto pieno di catarro (muco)	
Non avverto alcuna sensazione di costrizione al petto	0 1 2 3 4 5	Avverto una forte sensazione di costrizione al petto	
Quando cammino in salita o salgo una rampa di scale non avverto mancanza di fiato	0 1 2 3 4 5	Quando cammino in salita o salgo una rampa di scale avverto una forte mancanza di fiato	
Non avverto limitazioni nello svolgere qualsiasi attività in casa	0 1 2 3 4 5	Avverto gravi limitazioni nello svolgere qualsiasi attività in casa	
Mi sento tranquillo ad uscire di casa nonostante la mia malattia polmonare	0 1 2 3 4 5	Non mi sento affatto tranquillo ad uscire di casa a causa della mia malattia polmonare	
Dormo profondamente	0 1 2 3 4 5	Non riesco a dormire profondamente a causa della mia malattia polmonare	
Ho molta energia	0 1 2 3 4 5	Non ho nessuna energia	



Screening for comorbidities: future challenges

- Better understanding of pathophysiology
- Markers of accelerated clinical events
- Markers of inflammation and/or immune activation
- Screening and pre-screening tools
- Faster diagnosis
- More appropriate clinical management
- Reducing costs



*Grazie
per l'attenzione!*

