Cardiovascular Risk in HIV Studies Summary Table

Ref#	Study/ Author	Objective	Study Design	Endpoints	Analysis Methodology	Follow up (Calendar Years)	Sample Size Patient Years (PY)	M/F	Age {mean} Median (IQR)]	Ethnicity Race	Key Results [95% CI]	Author's Conclusions
1	Veteran's Administration/ Bozzette et al	Evaluate trends in rates of cardiovascular and cerebrovascular disease in patients receiving HIV care	Retrospective analysis based on patients receiving HIV care at VA facilities	Admissions for and/or death from cardiovascular and/or cerebrovascular disease, death from any cause	Calculation of rates per 100 PY; Kaplan-Meier curves; time to event modelling; patient level regression models	8.5 yrs (1993-2001)	36766 (121,936 PY)	1.9% F	71% 35-55; 17% <35	44.2% White 52.3% Black 0.3% Am Ind 0.3% Asian 2.8% other	Admissions: 1207 for cardiovascular disease, 1764 for cardio- or cerebrovascular disease, and 2006 admissions or deaths from cardio- or cerebrovascular disease	Clinical benefit of antiretroviral therapies not diminished by increase in rate of cardiovasular or cerbrovascular events or related mortality
		Evaluate the relationship between the risk of cardio/ cerbrovascular disease and use of antiretroviral therapy			Models controlled for year of first care for HIV, race or ethnicity, sex, age, risk factor for HIV, severity of illness, history of AIDS, drug abuse, previous Rx for vascular disease, diabetes, hypertension, hyperlipidemia, smoking						Admissions for cardio/ cerebrovascular disease decreased from 1.7 to 0.9 per 100 PY. All cause mortality decreased from 21.3 to 5.0 deaths per 100 PY	Longer term observations required
											Antiretroviral drug use not associated with risk for cardio/cerbrovascular events but associated with reduced all cause mortality	
											Hazard for admission higher with increasing age, more advanced HIV disease status, AIDS defining illness, Hx of Rx for cardiovascular risk factor, pre-existing vascular disease, earlier date of first care for HIV	
1A	French hospital database on HIV (FHDH)/ Krause et al	Analyze the impact of PI on the risk of MI among men	Retrospective analysis of data obtained from FHDH	Incidence of MI)IDC code 410;I21)	Incidence rate approach, compared to French general male population calculation of standard moribity rate (SMR)	4 yrs (1996-1999)	34,976 (88,029 PY)	0%	37.7 (±9.1) for non MI; 41.9 (±8.2) for MI	not provided	RH for MI in patients exposed to PI was 2.56 [1.03, 634]; age was the only other signficiant factor in the model	Duration-related effect relationship between PI and MI, with a higher MI incidence rate among men exposed to PI for 18 mths or more
					Association of risk factors using Cox analysis; models ajdusted for age, initial CD4, NRTI, NNRTI and PI treatments						Risk for MI increased with increasing exposure time, with SMR of 0.8, 1.5, and 2.9 for exposures of < 18 months, 18-29 months, and ≥30 months, respectively	
1B	Medi-Cal study/Currier et al	Examine the relationship between ART exposure and CHD incidence	Retrospective analysis of Medi-Cal claims of HIV + patients	CHD incidence (defined by ICD codes)	Multivariate log-linear regression analysis to determine the relative risk of CHD by ART use; controlled for comorbid covariates of diabetes, hyperlipidemia, kidney disease & hypertension	5 yrs (1995-2000)	28,513	not provided	not provided	not provided	Incidence (non adjusted)of CHD/100 PY by age category: 1.08 (18-33 yrs), 1.74 (34-49 yrs), 3.13 (50-65 yrs), 4.90 (abv 66 yrs)	ART associated with increased risk of CHD in young (18-33) but not older individuals.
											Relative risk of CHD comparing individuals receiving ART to those not receiving ART: 2.06 (18-33 yrs) (P<0.001), 1.08 (34-49 yrs) (P>0.3), 0.79 (50-65 yrs) (P>0.05), 1.15 (abv 66 yrs) (P>0.6]	Co-morbid conditions associated with CHD in general population were important predictos of CHD in the study population

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2	D:A:D Study/ Friis-Møller et al	Determine incidence of MI. Assess association of combination antiretroviral treatment (CART) exposure with risk for MI	Prospective, multinational observational cohort study (11 established cohorts)	Acute MI	Incidence rate approach, with primary outcome presented as relative rates Models controlled for age, BMI, race, family Hx of CVD, smoking, sex, HIV risk group, cohort and pre-existing CVD	6 yrs (1999-2005)	23,468 (36,199 PY)	24.1% F	[39 (34-45)]	75.6% White 18.3% Black 6.1% other	Overall incidence of MI 3.5 events per 1000 PY (126 events) RR of MI increased with longer CART exposure; Adjusted RR 1.26 (1.12-1.41 p<0.0001) Other independent factors associated with increased risk: older age, smoking, CVD Hx, male sex, higher total serum cholesterol, diabetes mellitus	CART independently associated with 26% increased risk of MI per year exposure Absolute risk of MI remained low and should be balanced with benefit of CART
3	Randomized Clinical Trials/Coplan et al	Compare the incidence of MI among participants of randomized clinical trials receiving PIs to NRTI therapy alone	Retrospective analysis based on 30 Phase II/III industry sponsored double-blind, randomized studies	Cases of MI from investigator reports	MI rate per 1000 PY; Relative Risk (RR) for MI in patients taking PI vs NRTI only ITT confined to double-blind, randomized, active control phase; inclusive analysis covering double-blind and open-label phases	Mean months on PI: 11.4 - 14.3; mean months on NRTI only: 5.2 - 12.0 (prior to 1999)	10986 (7620 PY for randomized phase; 11651 PY for randomized plus extension phase)	8-18% F	{37-38}	not provided	10 MI in randomized phase and 19 cases in randomized plus extension phase; rates per 1000 PY for PI vs non-PI were 1.38 vs. 1.18 and 1.82 vs 1.05 for randomized and randomized plus extension Absolute difference in MI risk (PI to control): +0.77 (-0.71, + 2.26); combining both phases for all studies, overall stratified RR was 1.69 [0.54, 7.48]	Study did not reveal a dramatic increase in MI risk during the first year of PI exposure; however upper limit of CI indicates there may be up to 2.3 additional MIs per 1000 PY Small number of cases and wide CI's make calculation of relative and absolute risk impossible.
4	Iloeje et al	Quantify association between PI exposure and CVD events	Retrospective cohort analysis of a prospectively collected database (HIV Insite Database)	First CVD event (MI, angina, CAD, PCA/CABG, stroke, TIA, PVD)	Cox proportional hazards models; adjusted HR Models controlled for age, sex, race, weight, PI exposure,hyperlipidemia, CVD, DM, HTN, smoking, IV drug use, cocaine use	Median of 2.8 yrs (1996-2002)	6,711	13.3% F	38 [18-88]	58.6% Whites 27.8%AA 13.6% Other	93 CVD events (rate 1.6% in PI and 0.5% in non PI) and 74 CHD events (rate 1.3% in PI and 0.4% in non PI), Adjusted HR all CVD events for PI use was 1.99 [0.95-4.14]; CHD model HR 2.13 [0.91,4.95];PI exposure > 60 days (subset analysis) HR 2.10[1.00, 4.40]	PI use doubles the risk of developing both CVD and CHD events. Greater risk seen in middle aged patients Absolute event rates remain low. Prolonged exposure may increase event rates, especially as population ages
5	HOPS/ Holmberg et al	Determine whether rate of MI, angina, cerebrovascular accident (CVA) is increased in patients taking PI's	Prospective observational cohort based on 9 clinics in the USA	Verfied MI, angina, CVA events	Incidence per 1000PY; Cox proportional hazards analysis (HR); multivariate logistic regression models (OR) Models controlled for hypertension, smoking, diabetes mellitus, age, sex and evidence of dyslipidemia	(1993-2002)	5672 (17,712.4 PY)	18% F	{42.6}	38% Non White	21 MI events; 1.42/1000 PY for PI, 0.46/1000 PY for non-PI Unadjusted HR of MI for PI: 8.06 [1.14,56.8], but not significant in controlled model (p=0.065); adjusted OR 4.92 [1.3 -32.3] 15 angina events; OR for PI 1.93 [0.63, 5.96] Most patients with events also had traditional risk factors	Use of PI may be associated with MI and perhaps angina

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6	Kaiser Permanente/ Klein et al	Estimate the coronary heart disease (CHD) and MI rate in KPNC patients, stratified by PI and other ART use Compare rate in HIV+ populations to HIV- populations Describe prevalence of classic CHD risk factors in HIV+ and HIV- patients	Retrospective analysis of the KPNC database	Confirmed hospital admissions with primary discharge diagnosis of CHD (ICD 9 codes)	Events per PY of follow up, age adjusted event rates	HIV+:Mean 4.3, median 4.5 years (1996 -present) HIV-: mean 5.4, median 6.5 years	4,408 (18,792 PY) HIV+ patients, and 39,425 HIV- patients (211,221 PY)	0% F	not provided	not provided	in HIV+: 100 CHD events (65 MI); age adjusted event rate of CHD and MI for HIV+: 6.6 [5.0,8.1] and 3.8 [2.7, 5.0]; for HIV- controls 3.3 [3.0-3.5] and 2.6[2.4-2.8] , with p values of <0.001 and 0.03 for CHD and MI respectively No clear trend for CHR or MI with increasing length of PI use Prevalence of CHD risk factors in all HIV+ patients: hypertension 38%, smoking 21%, diabetes mellitus 16% and hyperlipidemia 5%	Increased CHD and MI hospitalization in HIV+ compared to HIV-; risk factors for CHD were frequent in patients with events Patients started on PI-containing HAART do not exhibit increased risk for CHD compared to patients not exposed to PI
7	Maryland Clinical Cohort/ Moore et al	Assess incidence of and factors associated with CHD and CVD	Nested case control, with 5 non CVD/CHD controls per case, matched on enrollment date and duration of follow up	CHD (MI or unstable angina) CVD (ischemic stroke or TIA)	Event rates per 1000 PY; Mantel-Haenszel chi-square and conditional regression analysis	(post 1996)	Total 2671 (7.330 PY); 78 cases and 336 controls	42% and 32%F	46 and 41 yrs	76% and 80% AA	43 CHD and 37 CVD events; CHD/CVD risk associated with older age, higher cholesterol, prior diabetes, prior hypertension, higher CD4, PI use and d4T use Multivariate analysis: age, hypertension, total cholesterol and d4T use independently associated with CHD/CVD risk Race, IVDU, and HIV-1 RNA levels were not associated with risk	Incidence of MI and CVD are 2-3 times higher the expected national age, sex, race based rates
8	HERS/ Gardner et al	Examine renal, CVD, diabetic and hepatic-specific hospitalization rates in HIV+ women	Prospective multicenter cohort study	Diagnosis specific hospitalization: non-acute renal, cardiovascular, diabetes mellitus, hepatic and AIDS-defining	Hospitalization rates per 100 PY; rate ratios (RR) using Poisson regression with repeated measures and GEE estimation method	mean 4.5 yrs (1994-2000)	885 HIV+ ; 425 high risk HIV-neg	100% F	not provided	61% AA 17%Hispanic	360 CDV specific hospitalizations,; overall empirical event rate of 9.5. In HIV+ women, compared to 1994, the adjusted RR for CVD hospitalization in 1997 was 1.8 (p=0.02), in 1998 2.1 (p<0.01) and in 1999/2000 2.0 (p=0.02)	Hospitalization rates for CVD doubled (hepatic conditions increased 10-fold) Close monitoring of non-AIDS risk factors for morbidity is warranted
9	APROCO/ Leport et al; Saves et al	Estimation of risk for CVD morbidity in HIV+ patients receiving PI compared to a sample of general population	Prospective follow up within French APROCO cohort (every 4 M); cross-sectional analysis of risk at M12 or M20; controls derived from MONICA study; age & sex stratified	Risk for CVD estimated using predictive models (PRIME model and Anderson model from Framingham)	Relative Risk Risk factors: BMI, smoking, blood pressure, W/H, cholesterol (total, HDL, LDL), triglycerimia, fasting blood glucose	mean ART 26 M and mean PI 13M; (May 97 - June 98)	274 HIV+; 1038 controls	18.6% F in HIV+; 49.2% F in control	Restricetd to 35-44	not provided	BMI . Hypertension and HDL were lower in HIV+ men compared to MONICA sample but prevalence of smoking, W/H, triglyceridemia were higher; similar trends observed for women; similar trends shown for populations aged 45-54 5 yr RR for CHR was 1.2 for men and a.159 wor women; or 1.39 and 2.17 in women, depending on model, $p<10^{6;}$ Risk attributable to smoking was 65% and 29% for men and women	HIV+ patients have aa particular therogenic profile, rsulting in moderate but significant increased CH risk

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9A	SMART study/El-Sadr et al	Comparison of CHD risk factors among HIV+ men and women on HAART enrolled in the SMART study	Crossectional estimation of CHD risk factors among patients enrolled in the SMART study; baseline characteristics, lab assays and EKGs evaluated; 10 yr risk of CHD calculated using Framingham equation Baseline data presented here; study will assess effect of treatment/type of treatment	Framingham Scores and other CHD risk factors	% men and women at risk (baseline data presented;) Blood pressure therapy used as indicative of stage I hypertension; conditions for metabolic syndrome assessed Risk factors: BMI, MI/stroke history, EKG abnormalities, TGL, LDL, HDL, BP therapy, diabetes, smoking, metabolic syndrome, Framingham scores		649 HIV+ cases	24.9% F	{44.8} yrs	38% African Americans, 16.2% Latino, 45.8% White	97.4% HAART experiencedI; median baseline and nadir CD4 cell counts were 598 cells/mm^3& 258 cells/mm^3; 69% had viral load <400 copies; 28% had prior AIDS diagnosis 7.8% of men and 0.6% of women had Framingham high/very high 10 yr risk for CHD; 26.1 % men and 31.5% of women had MI/strie, major EKG, metabolic syndrome, or high/very high risk	Significant number of men and women in SMART are at a high risk of CHD based on Framingham risk, history of MI and stroke, prevalance of metabolic syndrome and major EKG abnormalities
10	Wall et al	Estimate risk of ischemic CHD in HIV+ patients on different ART regimen, based on ATP3 Framingham score	Prospective evaluation of a convenience sample of HIV+ patients and uninfected controls; cross-sectional analysis	Estimation of CVD risk using the Framingham Point Scoring System	Comparison of HIV+ patients on PI to non-PI,; risk factor assessment Risk factors included: smoking, hypertension, low HDL cholesterol, family Hx of premature CVD, older age,		111/125 HIV+; 25/49 controls were evaluated	10% F in HIV+; 53% F in HIV-neg	41 in HIV+; 36 in HIV-neg	In HIV+: 65% White 35% AA In HIV-neg: 76% White 14% AA	4% median risk for CVD progression in HIV+ cohort vs 1% in controls; 6% for PI using HIV+ vs 3% in non-PI using individuals	Significant prevalence of risk for progression of CVD in HIV infection Longitudinal studies needed to assess changes in risk over time
10A	Hadigan et al	Estimate the 10-year risk of CHD in HIV+ patients with fat redistribution compared to risk estimate in matched non-HIV subjects from Framingham	Comparison of risk between HIV+ with fat redistribution (HIV+ LD+) and matched controls; HIV+ without fat redistribution (HIV+ LD-) and matched controls HIV+ LD+ were matched for sex, age and BMI wifh subjects from Framingham; substudy matched for sex, age, BMI and W/H HIV+ without fat redistribution (HIV+ LD-) were matched for age and BMI	Estimation of CHD risk using the Framingham Point Scoring System	Consecutive patients (age 18-60)enrolled; exclusion criteria: change in ART, Hx diabetes mellitus, previous Rx with antidiabetic, use of hormones, steroids, active alcohol/substance abuse 10-year risk estimates (sex specific) incl age, total and HDL C, S/DBP, diabetes, smoking CHD events: angina pectoris, MI and death due to CHD Analysis on total patient population as well as stratified by sex	(HIV+1:998-1999; controls 1991-1995))	HIV+ LD+: 91; controls 273; HIV+LD-: 30, controls 90)	29% F(LD+) 40%F (LD-)	{44.6} and {45.07} for men; {39.5 and 40.6} for women	not provided	Estimated 10-year risk significantly higher in HIV+LD+ (7.4 ±0.6 vs 5.3±0.3); for men only, 9.0±0.7 vs 6.5±0.3; ns for women only; percentage of subjects with >10% risk significantly higher in total HIV+LD+ populations and men only; risk not higher than controls for HIV+LD-; When also matched for W/H, no difference in 10yr risk between HIV+LD+ and controls (7.6±0.6 vs 7.6±0.4) Risk significantly higher in patients with lipoatrophy compared to lipohypertrophy, or mixed LD No association with current PI use	CHD risk is increased in patients with fat redistribution Patterns of fat redistribution and sex may be important components of risk determination

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10B	Study A1424-008/Grover et al	Estimation of the impact of nelfinavir and atazanavir on CVD risk and life expectancy (LE) after adjustment for HIV related mortality	Used data from a randomized controlled trial, that compared nelfinavir and atazanavir effects on CVD, and adjusted for HIV related mortality	CVD risk, LE	CVD risk estimated through Cardiovascular Life Expectancy Model; validation of the forecasted LE based on the 3rd National Health and Nutrition Examination Survey Study and results compared to US Life Tables Assumption of 2.9% HIV related annual mortality rate	32 weeks	269 (178 atazanvir; 91 nelfinavir)	not provided	not provided	not provided	Changes in total and LDL cholesterol (+24% and +28%) observed among 91 nelfinavir patients were significantly greater (p<0.05) than those among 178 atazanavir patients (+4%,+1%); predicted LE reasonably well approximated LE from US life tables CVD risk 10-31% lower among atazanavir than among nelfinavir patients; among low risk patients, treatment with atazanavir increased LE from 0.06 to 0.22 years (95% CI, 0.05 TO 0.29); presence of additional risk factors increased potential advantage of atazanavir vs nelfinavir to an increased LE from 0.22 to 1.18 years (95% CI, 0.20 TO 1.53)	Estimated CVD risk and LE models indicated a lower risk and higher LE for atazanavir compoared to nelfinavir
11	David et al	Identify factors associated with proven ischemic CVD in HIV+ persons	Retrospective; matched case control; based on medical records of all patients seen	Documented CVD (angiography, echocardiography, exercise stress testing or MI)	All patients with events included as cases, sex and age matched controls (2:1) Impact of specific variables assessed using conditional logistic regression analysis Variables included in model: nadir CD4, duration of PI exposure, duration of NRTI exposure, smoking, hypertension, hyperlipidemia, HIV-RNA, family history, race, and recent CD4	(1999-2000)	16 cases; 32 controls	19% F in each group	43 [42-66] and 45[37-65]	50% White 50% Black among ICVD patients 47% White and 53%Black in Control	Hypertension, smoking, elevated cholesterol, family history and CD4 count <200 were significant predictors for CVD in univariate models Use of PI or other ART was not a risk factor	Ischemic CVD occurs in HIV+ patients and is associated with traditional risk factors
12	ACTG 5078/ Currier et al	Compare differences in baseline IMT between HIV+ on PI and not on PI Compare differences in baseline IMT between HIV+ and HIV- individuals Examine predictors for IMT	Prospective, longitudinal; matched cohort Triads (HIV+ PI > 2 yrs; HIV+ no PI; HIV negative) were matched for age, race, sex, blood pressure, smoking and menopause Baseline, week 24, 48, 72 and 96 week evaluations planned	Subclinical atherosclerosis determined by carotid IMT	IMT of far wall obtained in duplicate Median IMT differences between groups Cross sectional analysis for baseline	Baseline reported here	134 in 45 triads	40 M and 4 F triads	not provided	76% White 3% Black 16%Hispanic 4%API	HIV+ PI group had higher levels of total cholesterol and triglycerides Median IMT in the three groups were 0.693, 0.711 and 0.687, the median differences between any two groups non significant Independent predictors for increased IMT: cholesterol (total, LDL), triglycerides, age, BMI and current smoking	No clinically relevant differences were demonstrated at baseline Longitudinal follow-up is ongoing

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13	Hsue et al	Identify predictors for carotid IMT in HIV infection	Prospective, longitudinal study	Mean maximal IMT of 12 preselected segments	B-mode ultrasound for carotid IMT; IMT progression measured in 21 patients	1 year	106	17% F	{45 +/- 8}	not provided	Mean baseline IMT was 0.90 +/- 0.27 mm	IMT associated with classic coronary risk factors and nadir CD4 <200
					Multi-variable linear regression to identify predictors						Mutlivariable predictors of baseline IMT increase: age, LDL cholesterol, hypertension, and nadir CD4<200	Both traditional and immunodeficiency contribute to atherosclerosis in HIV
		Follow IMT progression over 1 year									Mean rate of IMT progression was 0.1 =/- 0.1 mm/yr; age and duration of PI therapy predictors	10-fold acceleration in progression of IMT over 1 year follow up, associated with age and PI use
14	Seminari et al	Evaluate the extent of IMT in PI treated HIV+ patients compared to PI-naïve and HIV negative subjects	Multicenter cross-sectional study	IMT	Hematological and carotid ultrasound		59	34% F	{33-37}	not provided	PI-using patients had significantly higher triglyceride, HDL and apo B levels	IMT more pronounced in PI using patients
											IMT increased in PI-using patients compared to naïve and HIV-negative	
15	Chironi et al	Assess IMT in pretreated HIV+ patients prone to atherosclerosis and 2 groups of HIV negative controls (without or with metabolic profiles similar to patients)	Matched case control study	IMT	IMT measurement in plaque free far wall segment of right CCA, calculated as average of 100 measurements		36/group	17% F	{44-45}	not provided	IMT greater in cases than control group 1 (without similar metabolic profile); significant after adjustment for age, sex, BMI, waist, SBP, smoking and prior CVD; not significant after adjustment for glucose, triglyceride, total:HDL cholesterol ratio	Study was not designed to detect association of IMT with duration of infection or type/duration of antiretroviral treatment
					General linear model for adjusted comparison						IMT not different between cases and control group 2 (similar metabolic profile)	Lipid disturbances may be involved in the early atherosclerotic process in HIV+ patients
											Multivariate analysis: IMT associated with age (case and control 1), waist (case only) and total HDL (case only)	
16	Mercie et al	Assess IMT in HIV+ patients in relation to treatment, lipodystrophy and conventional risk factors	Cross sectional analysis within a multicenter, prospective cohort	IMT	B-mode ultrasonography		424	?	?	?	Mean IMT was 0.54 mm (0.5-0.6).	Only conventional risk factors are indpendently associated with increased IMT in HIV infected patients
					Variables: lipodystrophy, age, gender, BMI, smoking, alcohol, SBP, HIV risk group, AIDS stage, type and duration of HAART, CD4, HIV-RNA, glucose, insulin, total cholesterol and homocysteine						IMT significantly higher in older age, male sex, higher BMI, higher W:H ratio, increased SBP, total cholesterol, glucose disorders and homocysteine, regular smoking, alcohol consumption, lipodystrophy and HAART	
											HAART and lipodystrophy lost significance in multivariate model	

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17	Depairon et al	Determine association between PI use and prevalence of atherosclerosis	Cross sectional analysis within a prospective cohort study	Carotid and femoral IMT	B-mode ultrasound imaging of carodi and femoral arteries performed by same (blinded) investigator Univariate and multivariate logistic regression analysis		168 HIV+, 68 HIV-	HIV+: 28.6% F; HIV-: 20.5%F	HIV+: restricted to age 30-50	Caucasian only	HIV+ patients were younger, had lower BMI, higher total cholesterol, triglycerides, and total:HDL cholesterol ratio, higher prevalence of smokers and higher prevalence of plaques; Presence of plaques associated with male sex, older age, and higher LDL cholesterol but not HIV infection nor PI treatment	Atherosclerotic plaques were associated with traditional (modifiable) risk factors
18	Acevedo et al	Estimate the coronary atherosclerotic burden in HAART treated HIV+ patients (severe dyslipidemic, or not) compared to HIV- controls	Matched pilot study, cross sectional including HIV+ and HIV- patients HIV+ pts on HAART min 6 M	CT derived calcium scores	Coronary artery imaging using multi-detector scanner and Imatron electron beam tomography scanner. Coronary calcium quantified using Agatston method HIV+ patients were those referred to a preventive cardiology unit or from same referring clinic; 1:4 matched controls		17 referred, 63 non referred and 68 matched HIV- controls	not provided	42 [37-49]	not provided	Framingham 10yr risk score nearly 10% in referred group; 75% had detectable coronory calcium, with mean scores of 2.93 ± 2.3 vs. 1.97 ± 2.45 in matched controls	High prevalence of detectable coronary calcium and traditional risk factors in severely dyslipidemic HIV+ patients
19	Nutrition for Healthy Living/ Wanke et al	Evaluate cardiovascular risk factors (lipids and calcification scores) in HIV+ patients Characterize lipoprotein, erythrocyte abnormalities; alterations of CRP and CAC associated with PI use	Substudy of the Nutrition for Healthy Living Cohort Study Cross sectional analysis; 66% of patients were on HAART	CT derived coronary calcification scores (CCS)	Comparison of iipid profiles by HAART, PI use, for men & women; comparison of CCS >100 to <100 Cross sectional analysis	(post 1995)	119	23.5% F	45.7	38%Minority	Men on HAART had higher TG, TC, Apo A1, Apo B, Apo E, RLPC and BMI; women on HAART higher TC, HDL, LDL and lower BMI Men on PI had higher TC, Apo E, RLPC and lower glucose; women on PI had higher homocysteine, glucose and insulin >100 CCS group (222.7) were older, had higher SBP and higher W/H	Correlates of coronary calcification in HIV infected adults are not distinct to HIV nor necessarily related to HIV therapy Impact of abnormal lipids associated with HAART on CHD remains to be defined
20	Meng et al	Assess the effect of PI on subclinical atherosclerosis in black HIV+ adults Characterize lipoprotein, erythrocyte abnormalities; alterations of CRP and CAC associated with PI use	Black patients from MD enrolled into a longitudinal study of atherosclerosis and cocaine use; 73% recruited from ALIVE cohort Cross sectional analysis	Coronary artery calcification (CAC)	CAC determined by scanning, average 12 scans /patient; score by Agatston method	(2000-2001)	98 (55 PI, 43 non PI)	27% F and 33% F	{39.3} and {37.8}	100% Black	PI group had significantly higher cholesterol, LDL cholesterol, MCV, CAC scores 11.0±28.6 in PI and 1.7±5.8 in non PI, p=0.043; CAC scores associated with duration of PI Rx,	Use of PI associated with coronary artery calcification, atherogenic lipid changes and increased MCV

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21	ACTG 5056s/ Henry et al	Assess CRP levels and association with CAD risk and HIV surrogate marker status in patients who achieved virologic suppression	Cross sectional analysis of a random sample of 99 ACTG372A patients on an indinavir containing regimen	CRP	CRP measured using ultrasensitive immunonephelometric assay		99	13% F	40.5	67% Cauc	Median CRP was 2.29 mg/L; a significant proportion of patients had high CRP risk levels, and higher risk associated with increased age, WBC, fibrinogen, TG, insulin, HOMA, Framingham heart scores, and lower HDL-C	In virologically suppressed patients, elevated CRP levels were observed and clustered with some features of metabolic syndrome and CAD
											CRP levels not associated with baseline HIV-1 RNA or CD4 cell counts	All patients received indinavir, thus data may not be generalizable
21A	Sklar et al	Analysis of the effectiveness of CRP as a biomarker for determining CV risk in HIV patients	Prospective, longitudnal cohorts of HIV^{+} patients on ART Cohort I: on I yr of continuous ART; cohort II &, III: on structured intermittent therapy (SIT) with randomized and continuous long cycle interruptions; cohort IV: on short cycle SIT	CRP	CRP measured using high sensitivity assay (0.1 mg/L;Immulite) on plasma from 4 cohorts of HIV^{+} patients	1 year	cohort I: 17, cohort II: 18, cohort III: 24 cohort IV: 8	not provided	not provided	not provided	No significant change (median 0.1 mg/L, p=0.85) in CRP levels after 1 yr of cont. ART; no significant change in CRP levels after 1 yr of long (med -0.1,p=0.33), or short cycle (med -0.1, p=0.07) SIT.	Reduction of viral replication or reduced exposure to ART do not influence CRP levels
											Median CRP for all patients at the time of optimum viral suppression was 1.8 mg/L. 18% classified as low, 21% mild, 28% moderate, 16% high and 16% highest risk on quantiles established for healthy individuals	Variability in CRP values among individuals with well controlled HIV disease could be due to associations between CRP and traditional CV risk factors
											CRP values inversely correlated with HDL-C (p=0.03) and directly associated with TC (p=0.04). CRP values approached significant for age (p=0.08) but not other traditional risk factors.	CRP may be an important biomarker for determining CV risk in HIV patients
22	Dube et al	Assess effect of indinavir monotherpay on endothelial function in HIV negative men	Examination of 6 HIV negative men before and after administering 800 mg tid of indinavir	Leg Blood Flow (LBF)	Leg blood flow measures in basal conditions and during intra-arterial infusion of vasoactive compounds (methacholine and nitroprusside)	4 weeks	6	0% F	{41 yrs}	not provided	Increase in LBF during femoral artery infusion of maximal doses of methacholine was markedly impaired between baseline and 4 weeks of IDV treatment (227±45 to 82±18).; response to nitroprusside did not change; the expected effect of NO antagonist -LNMMA was abolished by indinavir; HOMA-IR increased significantly (1.15 ± 0.23 to 1.52 ± 0.34)	IDV induces endothelial dysfunction when administered as monotherapy to healthy HIV negative subjects
											Steady state insulin concentrations during hyperglycemia increased during treatment (43.3±9.3 to 54.4± muU/ml); mean blood pressure, cholesterol, and triglycerides did not change	
23	Stein et al	Analyse the lipid/lipoprotein abnormalities associated with use of PI in HIV patients	Crossectional study with HIV+ patients divided in 2 groups : using PI and not using PI	Lipid/lipoprotein levels	Enzymatic analysis and nuclear magnetic resonance spectroscopic analysis		37 (22 PI, 15 non-PI)	22% F	{42.2-49.8}	not provided	PI-using patients had significantly higher total cholesterol and triglyceride levels	Metabolic changes associated with PI are atherogenic and cause endothelial dysfunction

Ref#	Study/ Author	Objective	Study Design	Endpoints	Analysis Methodology	Follow up (Calendar Years)	Sample Size Patient Years (PY)	M/F	Age {mean} Median (IQR)]	Ethnicity Race	Key Results [95% CI]	Author's Conclusions
		Assess the effect of lipid/lipoprotein changes on endothelial dysfunction		Flow mediated vasodilation (FMD) of brachial artery (BA)	High resolution ultrasound						PI-using patients had markedly impaired FMD compared to non-PI patients (2.6±4.6% vs 8.1±6.7%); use of PI was the primary determinant for impaired endothelial cell function; in addition, chylomicron, VLDL, IDL, and HDL-C levels predicted FMD	Patients receiving PI should be screened for hyperlipidemia