

20th ANNUAL HIV CONFERENCE
of the Florida/Caribbean
AIDS Education and Training Center

May 13-14, 2011
Orlando, FL

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HIV and Cardiovascular Diseases

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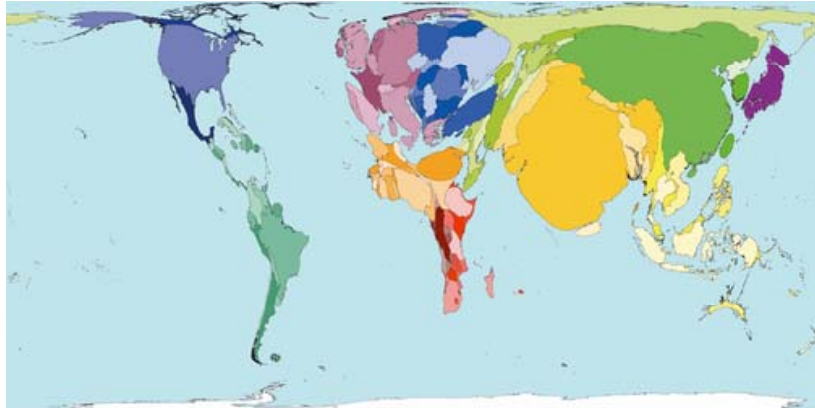


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Cardiovascular Death



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HIV/AIDS Death



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Cardiovascular Conditions in HIV Infected Individuals

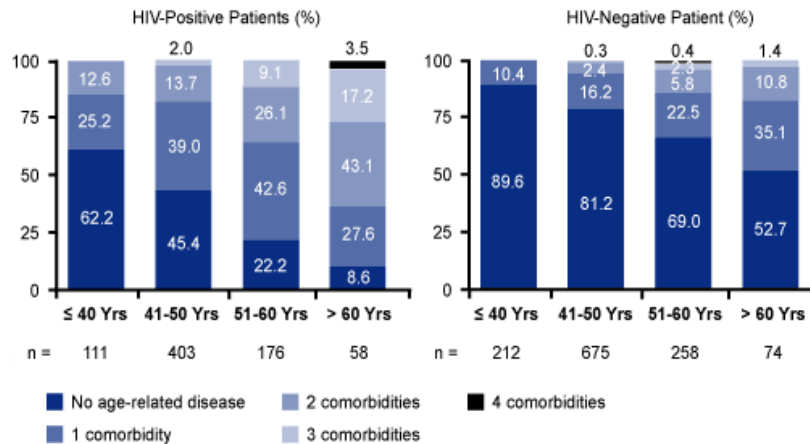
- CAD and acute coronary events
- HIV associated pulmonary hypertension
- HIV related left ventricular dysfunction and myocarditis
- Cerebrovascular disease

(Lekakis Curr Opin Crit Care 2010, Ho Heart 2009)


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HIV and Its Co-morbidities

Guaraldi G CROI 2010




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CAD in HIV: Unique Presentations

- **MI at young age**
(Hsue Circulation 2004)
- **High rates of restenosis, stent related complications**
(Hsue Circulation 2004, Matetzky Arch Intern Med 2003)
- **Pathology: similar to transplant associated vasculopathies**
(Talib CAD 2000)



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Use of PI: Higher Rate of CVD

- **First MI case in HIV** (Henry Lancet 1998)
- **Increase risk of MI with PI use**
 - French Hospital Database
 - D:A:D
 - HIV Insight (includes HOPS)
- **No association between MI and PI use**
 - Coplan et.al (meta-analysis)
 - HOPS
 - Keiser Permanente

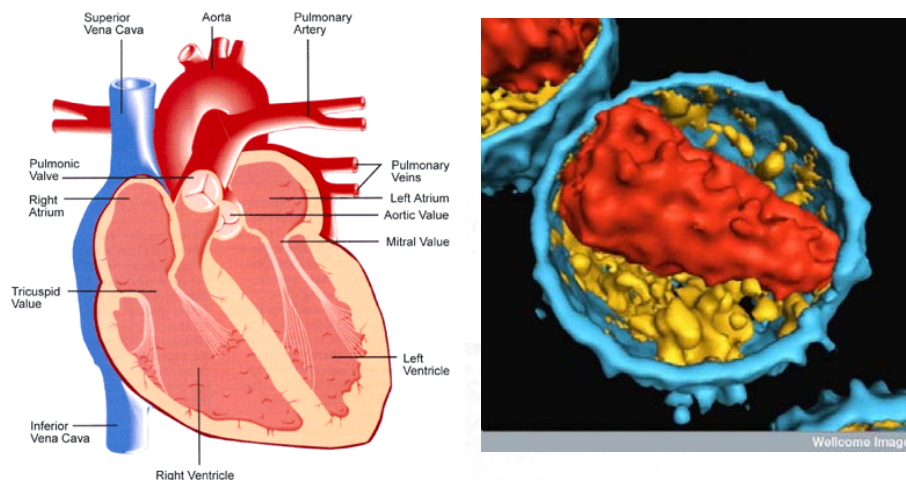


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Association of HIV and Cardiovascular System: A Linear Association?



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Relationship: CVD and HIV

- Increased rate of AMI (Traint JCEM 2007)
- Kaiser Permanente Study: HIV= independent predictor of composite outcome: death, repeat revascularization, etc (Klein JAIDS 2002)
- Increased preclinical arteriosclerosis
 - FRAM
 - MESA
 - Partner Health Care
 - SMART



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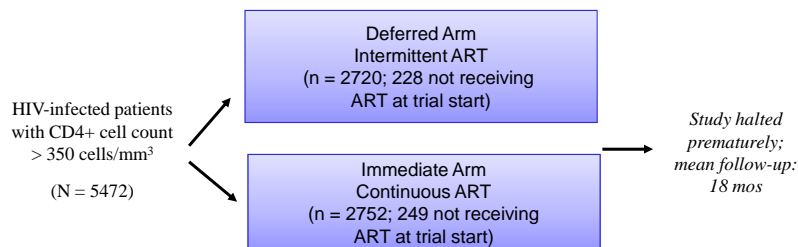
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Pathogenesis of CVD in HIV Infection

- **HIV Protein Associated Inflammation** (Ehrenrich J Immunol 1993, Baker AIDS 2008, Kaplan AIDS 2008)
- **Low CD4 Associated with Subclinical Carotid Stenosis** (Hsue Circulation 2004)
- **Elevation of Endothelial Derived Markers: ICAM-1, VCAM-1** (Melendez CID 2008)
- **Increase IL-6, hsCRP, D-Dimer** (SMART)



SMART El-Sadr NEJM 2006



In short term ARV prevents atherosclerosis



SMART:

- **Cardiovascular outcomes; 48 events in DC vs. 31, $p=0.05$ HR 1.7 (SMART NEJM 2006)**
- **IL-6 and D-Dimer at study entry were strongly related to all-cause mortality (Kuller PLoS Med 2008)**
- **11% in DC group with asymptomatic EKG changes (Carr AIDS 2008)**



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Emerging Concept of CVD in HIV Pathophysiology

- **Relationship of HIV, ART and vascular pathogenesis**
- **Persistent immune activation, inflammation and microbial translocation**
- **Role of CRP in HIV associated CVD**
- **Role of T cell dysfunction in CVD**
- **Role of other infections i.e. CMV**



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Relationship of HIV, ART and Vascular Pathogenesis

- Earlier initiation of ART in HIV-infected associated with reduced arterial stiffness
- ART reduces CV risk but not to normal
- Inflammation is associated with endothelial dysfunction among individuals with treated and suppressed HIV infection

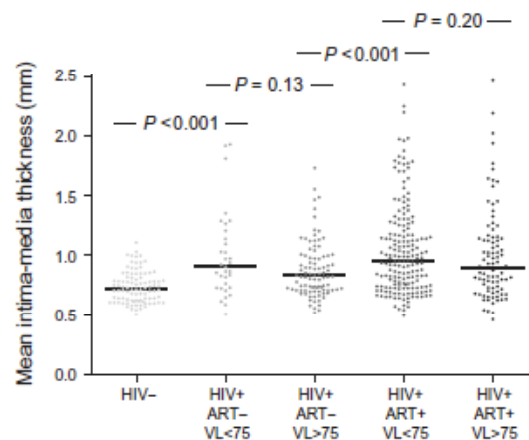


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Carotid IMT in HIV infected and uninfected individuals (Hsue AIDS 2009)

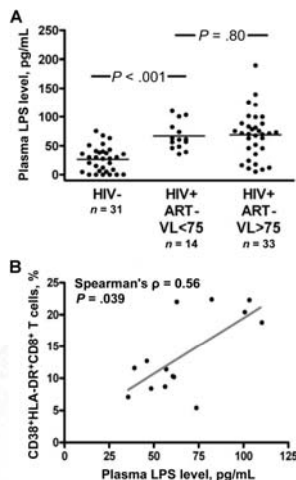


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Plasma LPS in HIV Infected Patients (Hunt 2008)



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The Gut and Inflammation

- ART fails to completely restore normal health in HIV infected patients
- Persistent immune activation may drive CVD risk
- Microbial translocation and Th17 depletion causing persistent immune activation
- Role of Th17 and Treg imbalance in pathogenesis of atherosclerosis

(Siliciano 2007, Cheng Clin Imm 2009, Xie Cytokine 2010)

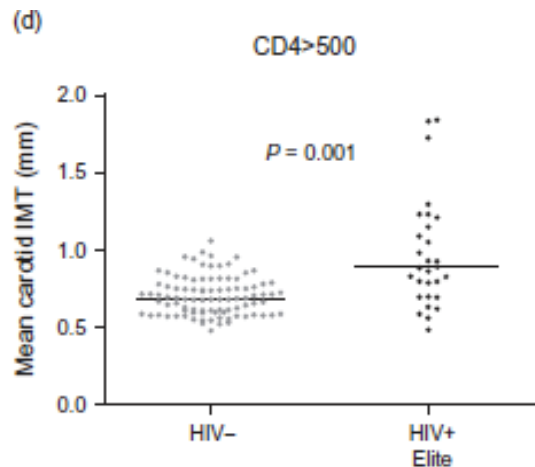


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Carotid IMT is Increased in HIV Elite Controllers (Hsue AIDS 2009)



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Role of CRP and CVD Risk in HIV

(Hasson NEJM 2005)

- **hsCRP elevated in HIV and associated**
 - Mortality
 - RR of MI
- **Elevated D-Dimer, not CRP is associated with CV events in HIV patients**
- **Fibrinogen is independent predictor of mortality in HIV infected individuals**
- **hsCRP, IL-6, D-Dimer and cystatin C are elevated even after ART (Neuhaus JID 2010)**

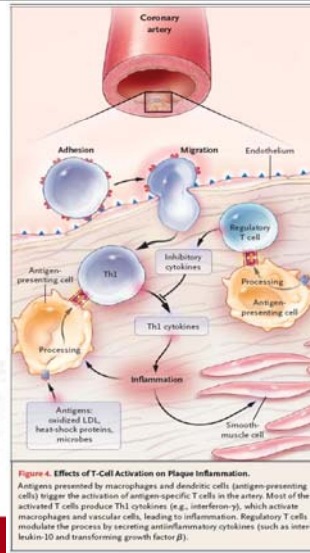


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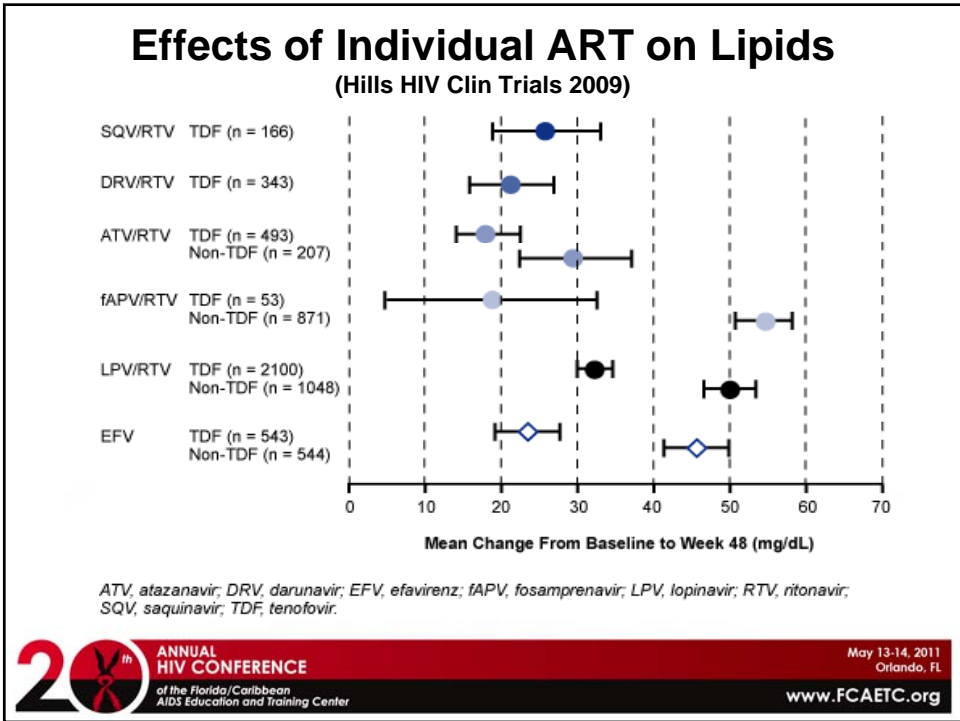
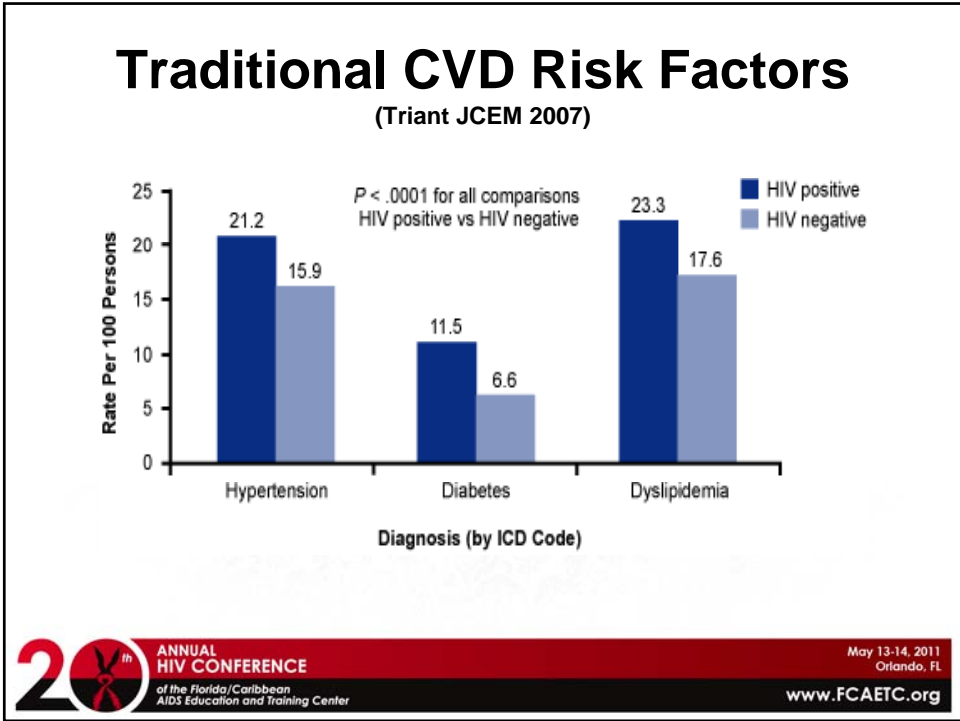
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Role of T Cell in CVD Pathogenesis (Hasson NEJM 2005)



CVD Risk Factors

- Lipodystrophy and Metabolic Syndrome
- ART
- Traditional CVD risk factors
(smoking, DM, HTN, dyslipidemia)



ABC and CAD risk

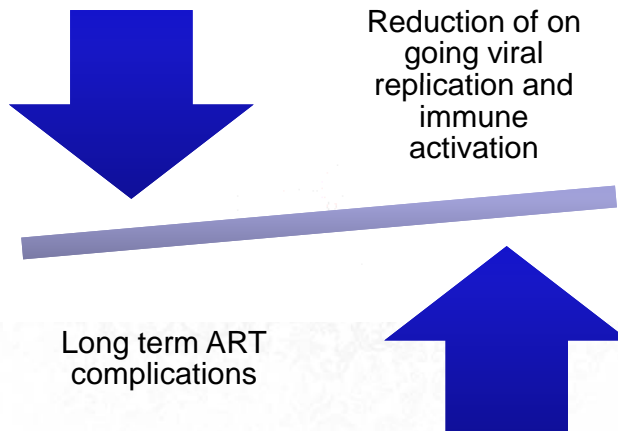
Associated

- D:A:D
- French Hospital database
- SMART
- STEAL
- Quebec's Public Health Insurance Database

No Association

- GSK Analysis
- ACTG A5001
- VA Clinical Case Registry

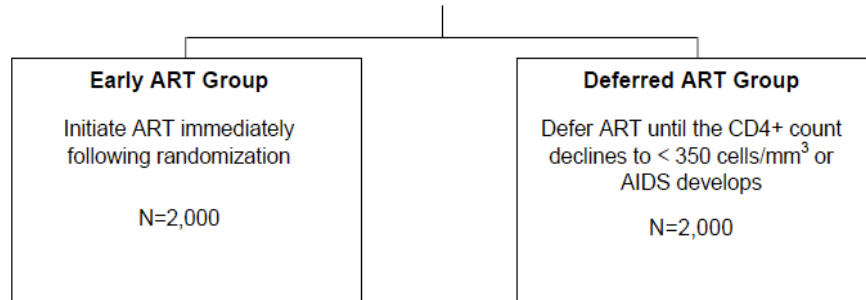
Role of ART to Prevent CVD



Benefit of Early ART

- **Ongoing clinical trials: START**

HIV-infected individuals who are ART-naïve with
CD4+ count > 500 cells/mm³



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Surrogate Measures of Artherosclerosis

- **Brachial arterial flow-mediated dilation**
- **Carotid artery intima-media thickness**
- **Coronary artery calcium scoring**



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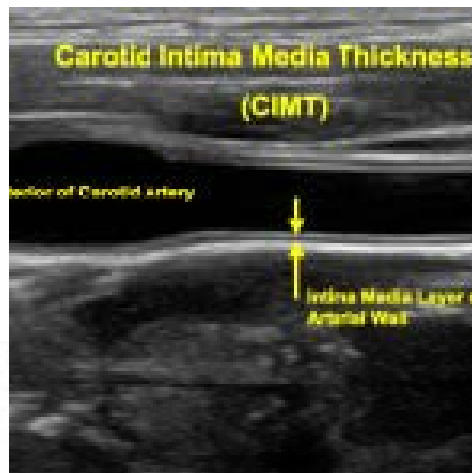
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Brachial Arterial Flow-Mediated Dilation



Carotid Artery Intima Media Thickness



Earlier Detection of Atherosclerosis

- **IMT is an excellent predictor of MI or CVA**
(O'Leary NEJM 1999)
- **Measurement of carotid artery intima-media thickness (IMT) using ultrasound**
- **IMT measurement associated with atherosclerosis risk, even after adjustment of traditional risk factors**



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HIV and Subclinical Atherosclerosis

- **HIV infected population with CD4<200: higher frequency of carotid plaques**
(Kaplan AIDS 2008)
- **HIV infection has similar magnitude of other CV risk factors (DM, smoking, age)**
(Grunfeld AIDS 2009)
- **Inflammation associated with IMT in HIV infected children**
(Ross CROI 2010)



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Management of CVD in HIV

- HAART
- Management of hyperlipidemia
- Modification of risk factors

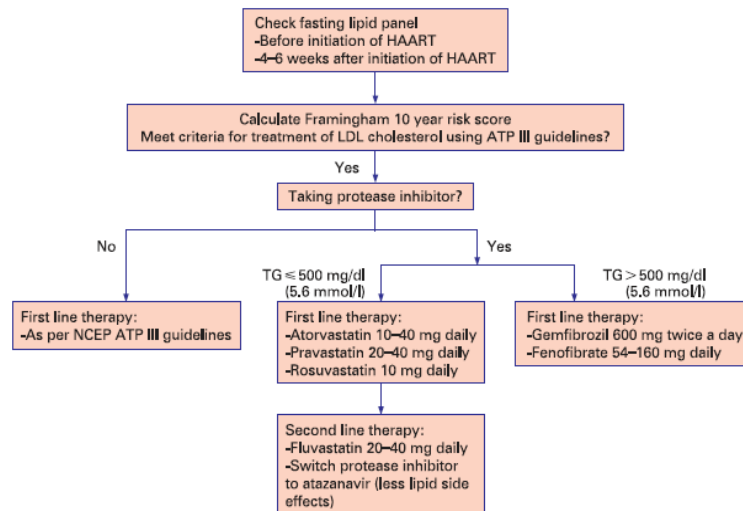


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Treatment of Hyperlipidemia in HIV Infected Patients (Ho Circulation 2009)



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Key Points: Patient Education

- HIV increases risk of CVD 1.5-2X
- Short term benefit of HAART is clear to prevent CVD in HIV patients, but long term benefit needs more data
- Early detect and treat other co-morbidities that increase CVD risk in all patients
- Minimized modifiable CVD risk factors i.e. smoking

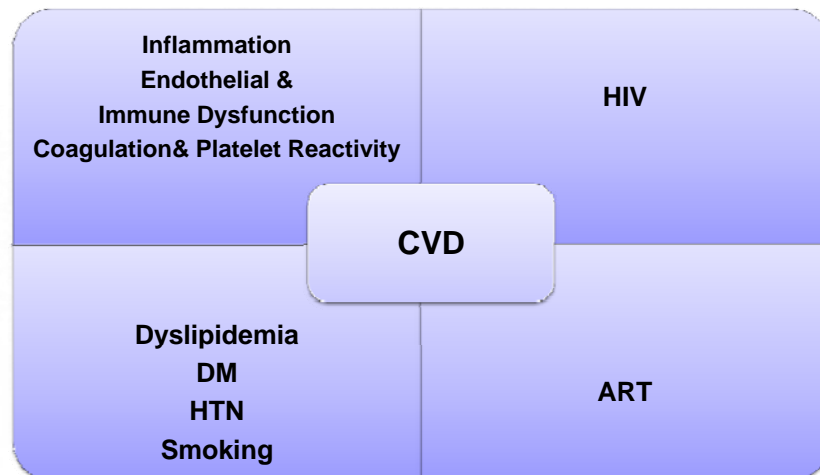


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Conclusion



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Challenges

- **Best time to start, best regimen in patients with CVD?**
- **Role of intensification?**
- **Role of anti inflammatory?**
- **HIV infection as CVD risk factor equivalent?**
- **Treated HIV as CVD risk factor equivalent?**



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Thank You



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