Higher incidence of plaque in HIV infected adults compared to uninfected adults: a matched Cohort Analysis of Carotid Artery Intima Media Thickness Progression and Carotid Artery Plaque

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CHANGING THE COURSE OF THE HIV PREVENTION, ENGAGEMENT AND TREATMENT CASCADE

Background

- Cardiovascular disease **increased** in HIV
  - HIV infection itself
  - Prevalent cardiovascular risk factors
  - Anti-retroviral drugs
- With an incidence of 3-5 per 1000 per year, the measurement of cardiovascular events requires very large cohorts

Background (2)

- Measure cardiovascular risk factors
  - Framingham risk score
- Functional measures
  - Brachial artery flow-mediated vasodilation
- Measure **anatomical disease progression**
  - CT coronary arteries
  - Carotid artery ultrasound
    - Strong predictor of CV events (MI and stroke)
    - Remains poorly standardized

Objectives

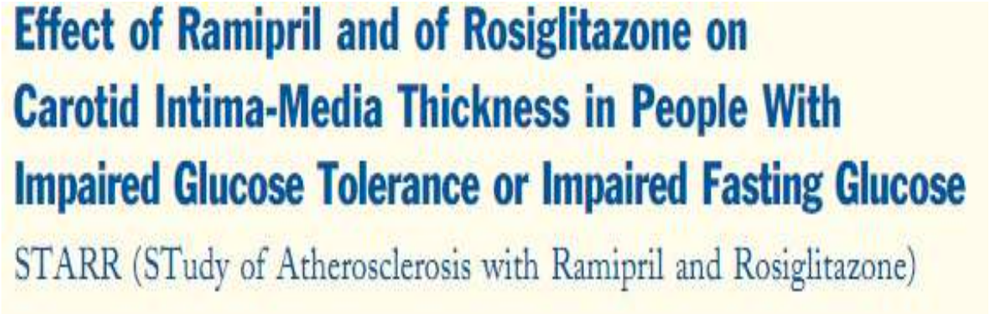
To compare HIV-infected adults to non-infected adults with respect to:

1. Progression of carotid artery intima media thickness (**CIMT**)
2. Presence and Incidence of carotid artery **plaque**

Methods: Study Participants

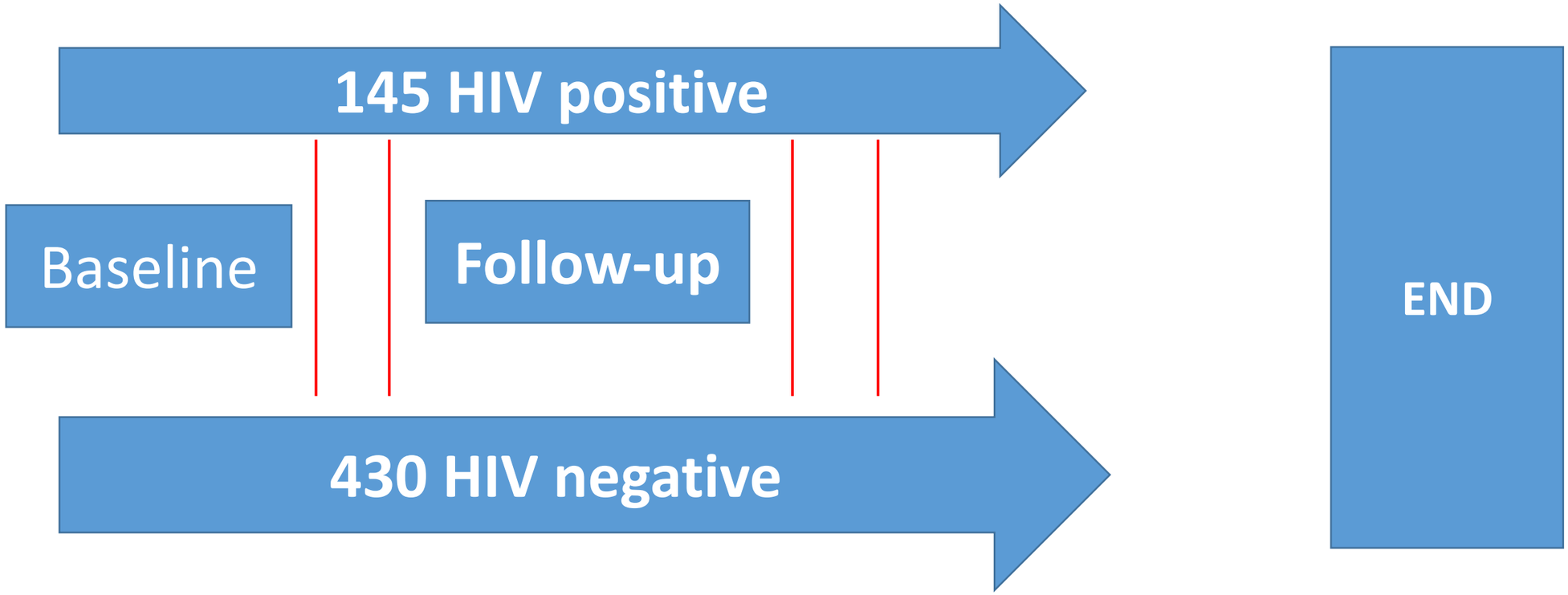
- **Canadian HIV Vascular study**
  - Duration: 2005-2011
  - Location: Hamilton, Toronto, Quebec, Calgary and Vancouver
  - N= 320
  - Age: 35+ years

- **The STARR (STudy of Atherosclerosis with Ramipril and Rosiglitazone)**
  - Duration: 2003-2006
  - Location: 32 centres in 9 countries, 39% N. America
  - N= 1425
  - Age= 30+years



Methods: Design

- A matched samples cohort study
- Age, gender, 1:3 matching



Methods: Measure of CIMT

- Serially measured 12-segment CIMT readings over at least 3 years conducted by certified sonographers
- Standardized training & same imaging methods
- Validated and standardized protocols were used with high intra- and inter-observer variability (ICC: 0.90-0.96)
- Core Laboratory (Population Health Research Institute, Hamilton, Canada).

Methods: variables

- Primary Outcomes:
  - Annualized CIMT progression =
    (Change in CIMT)/(Duration of follow up)
  - Presence of plaque (CIMT>1.5mm)
  - Development of new plaque (incidence)

Methods: variables

- Potential confounders:
  - Smoking status; systolic blood pressure (SBP), fasting plasma glucose (FPG) and past stroke, myocardial infarction,
    high cholesterol
  - Use of statins, angiotensin conversion enzyme inhibitors (ACEIs),
  - Duration of follow-up

Methods: Statistical Analysis

- The paired t-test was used to compare the mean change in CIMT
- Generalised linear mixed models
  - Matched group and repeated measure as random effects
  - Other parameters were fixed
- Data was matched and analysed using IBM Statistical Package for Social Sciences (SPSS) v. 20.0

Results: Baseline characteristics

Variables	CHIV Cohort (n= 145)	STARR (n=430)	Total (n= 575)	P-value
Age: mean (SD)	46.1 (8.31)	46.4 (8.24)	46.2 (8.25)	0.705
Gender: n(%)				>0.999
Male	121 (83.4)	359 (83.5)	480 (83.5)	
Female	24 (16.6)	71 (16.5)	95 (16.5)	

SUCCESSFUL MATCHING

Results: Descriptives

- Mean (SD) age of 46.2 (8.2) years
- Mean follow-up time of 3.6 years
- Most (83.5%) were men
- Fasting glucose, history of high cholesterol, and statin use were similar between the study groups
- Current smoking was higher in the HIV cohort (31.0% vs. 13.5%)
- Body mass index was lower (25.2 vs. 29.7)

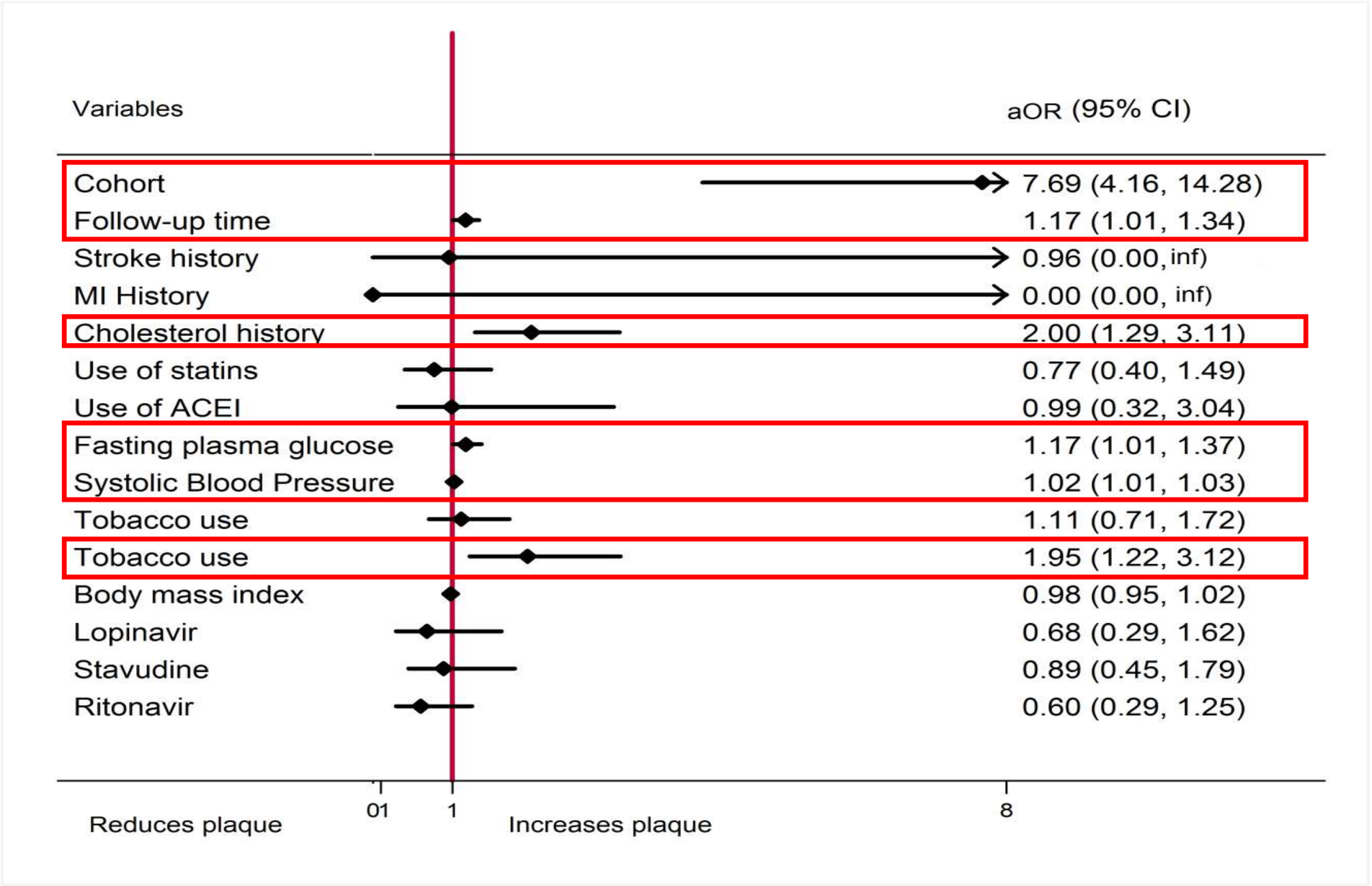
Results: CIMT progression

- Mean 12-segment carotid intima media thickness (IMT) progression was:
  - 0.019 (0.039) mm/year in HIV+ cohort
  - 0.017 (0.036) mm/year in control cohort
    - P = 0.63

Results: Carotid artery plaque

- Plaque (>1.5 mm in any segment) was present in:
  - 41.2% of HIV subjects
  - 2.3% of the controls (P<0.001)
- Incident plaque developed in:
  - 15.8% of HIV subjects
  - 6.2% of controls (P<0.001)
- Incident plaque development associated with:
  - HIV status
  - Current smoking, glucose and blood pressure

Results: development of new plaque (multivariable model)



Discussion

- Strengths:
  - Uniform, highly-precise 12-segment CIMT by standardized protocol and centralized analysis
  - Matched cohort analysis
  - Robust statistical methods
- Limitations
  - STARR cohort not representative of general population
  - Not matched by smoking or follow-up time
  - Covariate interactions, residual confounding?

Conclusions

- Progression of carotid artery IMT was **similar** in HIV-positive subjects and in HIV-negative controls with impaired fasting glucose and metabolic syndrome

- Incident carotid artery plaques developed **more frequently** amongst the HIV cohort

- Incident arterial plaque is a **candidate outcome** for future intervention trials

THANKS FOR LISTENING!