

Introduction

- Beyond traditional risk factors, the mechanism(s) driving the increased atherosclerotic cardiovascular disease (ASCVD) risk among people with HIV (PWH) are unclear.
- In the general population, incident ASCVD events are associated with impaired macrophage HDL cholesterol efflux capacity (CEC).
- In-vitro studies have shown that HIV impairs CEC, a function of reverse transcriptase activity.

Objective

- We sought to determine whether impaired CEC is associated with incident ASCVD events among PWH receiving ART.
- Additionally, we evaluated whether impaired CEC contributes to the differential ASCVD event rates reported for certain ARVs.

Methods

- We selected participants from the AIDS Clinical Trials Group (ACTG) Longitudinally Linked Randomized Trials (ALLRT) cohort with samples available after 48 weeks of ART who experienced an ASCVD event (acute myocardial infarction or stroke) and matched them 5:1 in a case-cohort study design with participants who remained free of ASCVD.
- We measured macrophage-specific CEC to apolipoprotein B-depleted plasma from cases and controls at week 48 following ART initiation and evaluated the association of CEC with incident ASCVD events, controlling for ASCVD risk factors, HDL levels, and virologic suppression status at Wk48.
- Finally, we compared CEC in participants randomized:
 - To Atazanavir (ATV) vs. Darunavir (DRV), Efavirenz (EFV) or Raltegravir (RAL), and
 - To Abacavir (ABC) vs. Tenofovir (TDF).

Study Population:

- The analysis included 114 ASCVD cases and 910 controls.
- They were randomized at parent study entry to:
 - NRTI: ABC or TDF.
 - “Third Agent”: ATV/r, DRV/r, EFV, or RAL.

Table 1: Baseline Characteristics

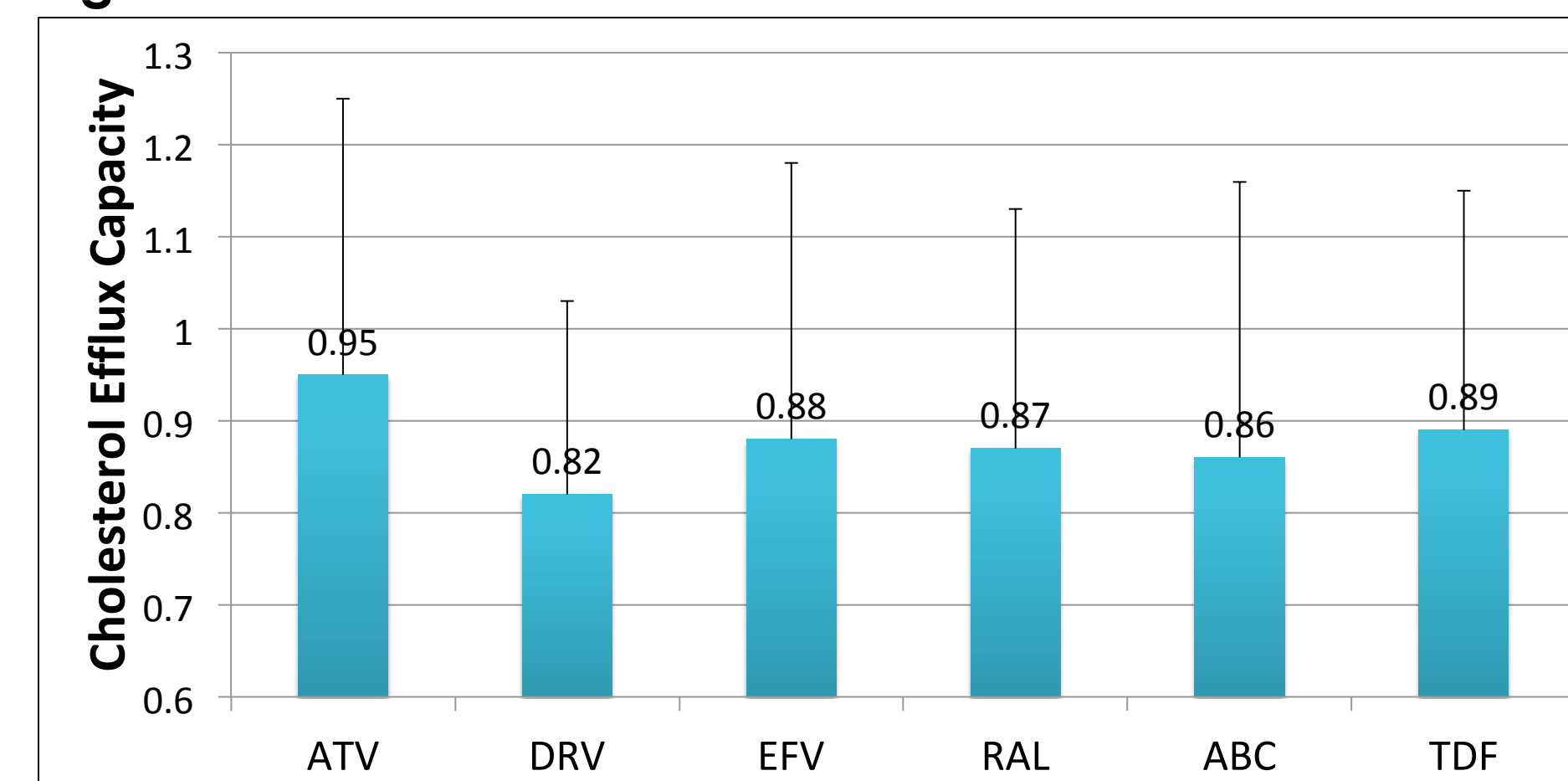
ASCVD Risk Factors	ASCVD Cases (n=114)	Controls (n=910)	P value
Mean Age (SD)	47 (8)	40 (10)	<0.001
% Male	84.1%	79.6%	0.24
Race (% AA)	49%	46%	0.56
Mean SBP (SD)	127 (18)	121 (14)	0.01
% On Anti HTN Meds	38.6%	15.2%	<0.001
% Current Smokers	37.7%	27.4%	0.02
Mean Total Chol (mg/dL)	207	189	<0.001
Mean BMI (kg/m ² ;SD)	26 (5)	27 (6)	0.31

- Traditional risk factors more prevalent in ASCVD cases than in controls.

Comparative Effects of ARVs on Cholesterol Efflux:

- Compared to ATV, CEC was lower for DRV (p<0.001), EFV (p=0.01) and RAL (p=0.05).
- Trend for lower CEC with ABC vs. TDF (p=0.06).

Figure 1: Effect of ARVs on Cholesterol Efflux



Results

CEC Association with ASCVD Risk:

- CEC was not higher in participants who achieved virologic suppression (VL<50 copies/mL; n=817): p=0.19.
- In a fully adjusted model that included traditional risk factors, HDL cholesterol, and virologic suppression status at week 48, hazard ratio (HR) for ASCVD per 1 SD increase in CEC was 0.86 (95% CI: 0.70 – 1.06).
- Figure 2 presents association between increasing quartiles (Q) of cholesterol efflux and ASCVD risk (adjusting for ASCVD risk factors and HDL levels). HR for Q4 vs. Q1 was 0.74 (0.44 – 1.24)

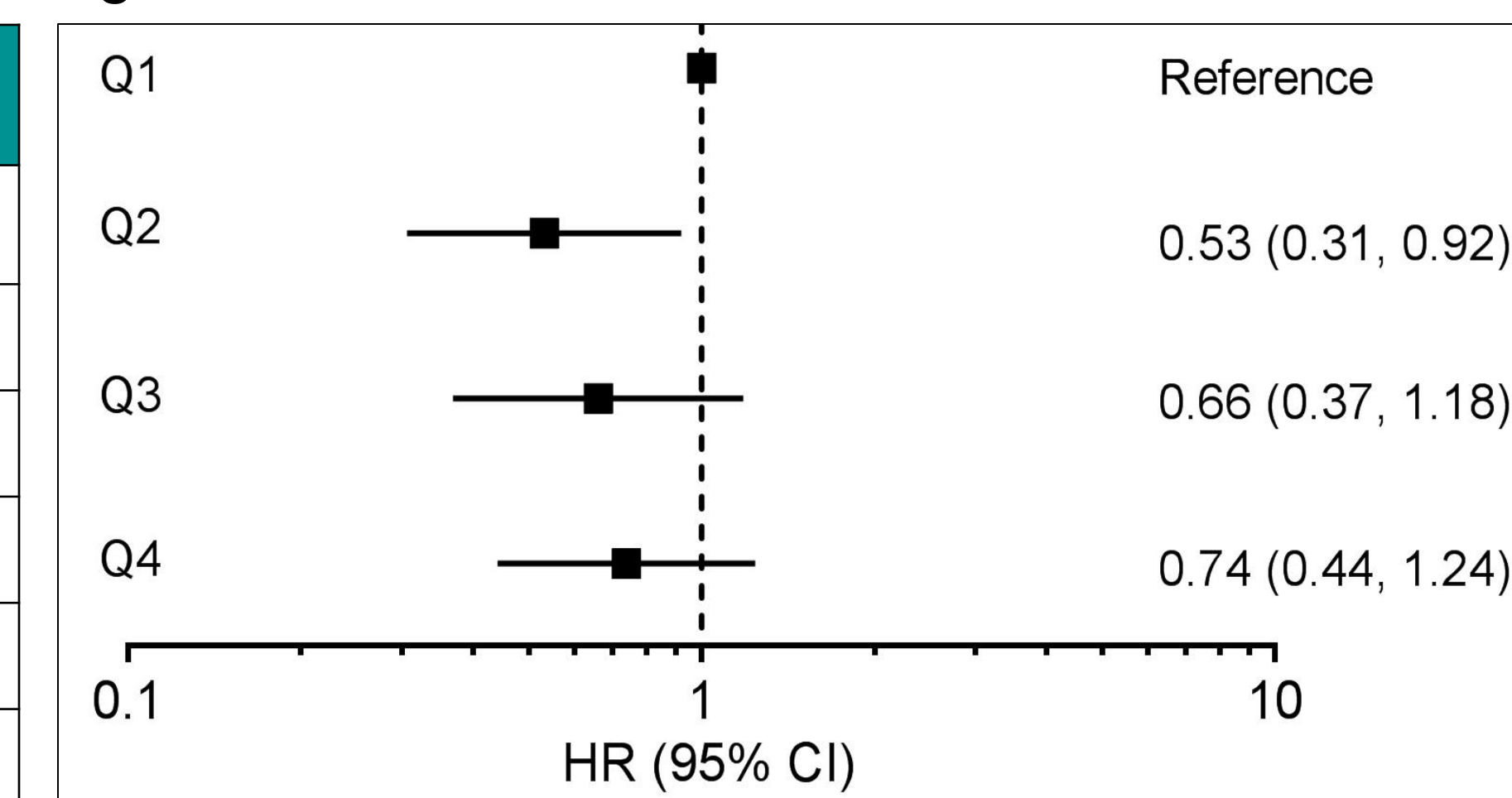
Exposure to Specific Antiretrovirals and ASCVD Risk:

- Table 2 presents HRs associated with different ARVs, controlling for traditional ASCVD risk factors (participants included only if all variables available for ASCVD risk calculation)

Table 2: ARVs and ASCVD Risk

ARVs	HR for ASCVD (95% CI; p value)
ATV (n=187)	0.88 (0.49 – 1.60; p=0.68)
DRV (n=82)	1.03 (0.32 – 3.40; p=0.96)
EFV (n=378)	0.67 (0.44 – 1.04; p=0.07)
RAL (n=88)	0.60 (0.14 – 2.52; p=0.48)
ABC (n=236)	0.91 (0.58 – 1.42; p=0.67)
TDF (n=431)	0.83 (0.32 – 2.97; p=0.75)

Figure 2: Quartiles of Cholesterol Efflux and ASCVD Risk



Conclusions

- Unlike data from the general population, we did not observe an inverse association of CEC with risk of ASCVD among HIV-infected participants on ART.
 - This could be either be due to a relatively smaller cohort or a bigger role played by other traditional risk CVD risk factors in HIV
- ATV use was associated with less impaired CEC than DRV, EFV and RAL, but not with lower risk of incident ASCVD events.
- There was a trend for lower CEC with ABC vs. TDF exposure.
- Larger studies will be required to fully evaluate whether certain ARVs alter CEC and its role in ASCVD progression.