

What does low HDL-c mean?

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Disclosures

Alexion, grants

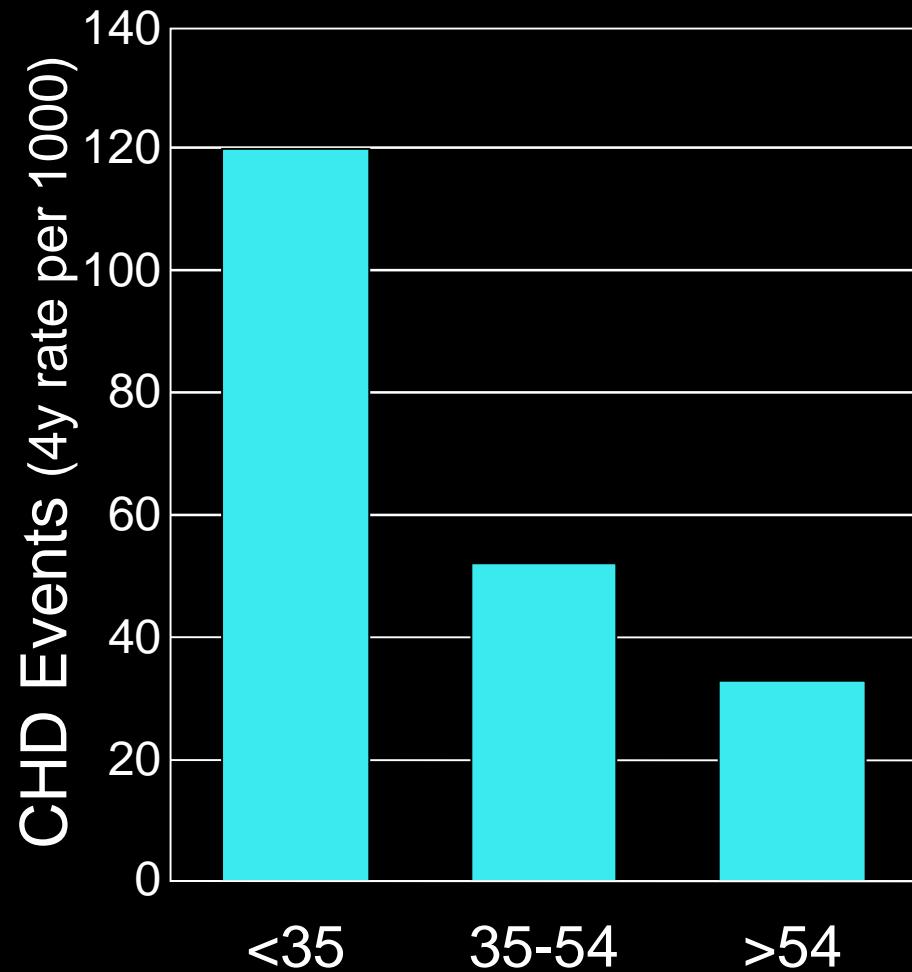
Cerenis Therapeutics, grants

MedImmune, consultant and grants

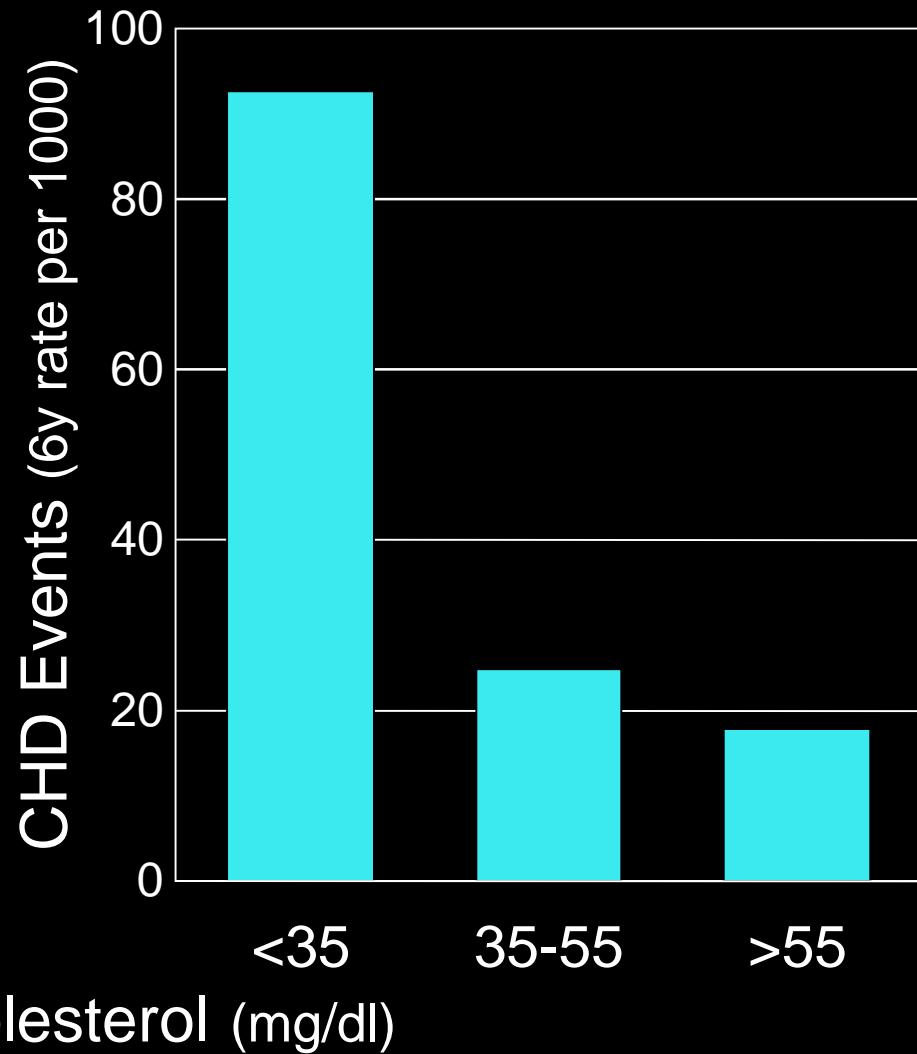
Sankyo, grants

HDL-C and Coronary Heart Disease

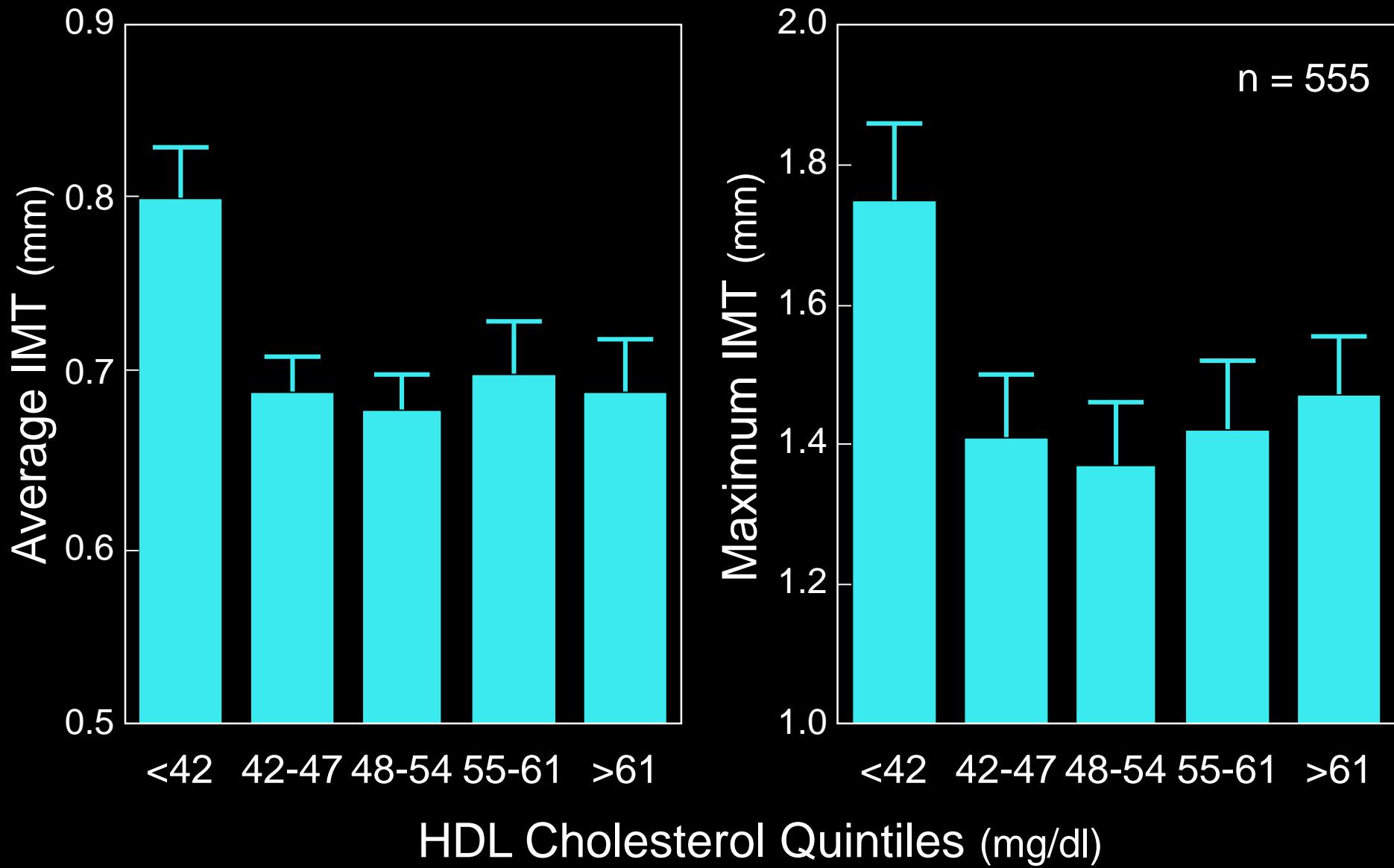
Framingham



PROCAM

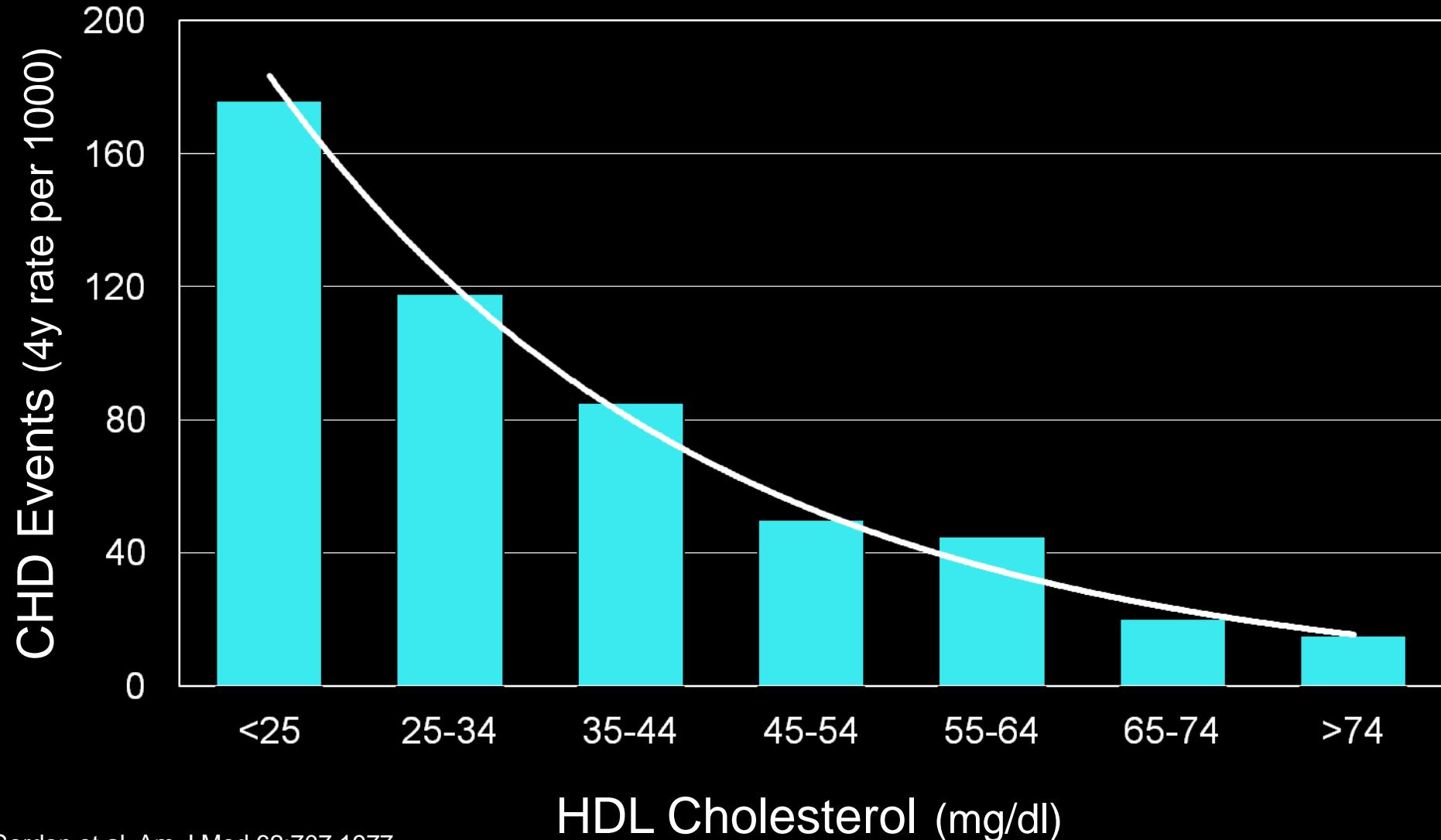


HDL-C and Carotid IMT



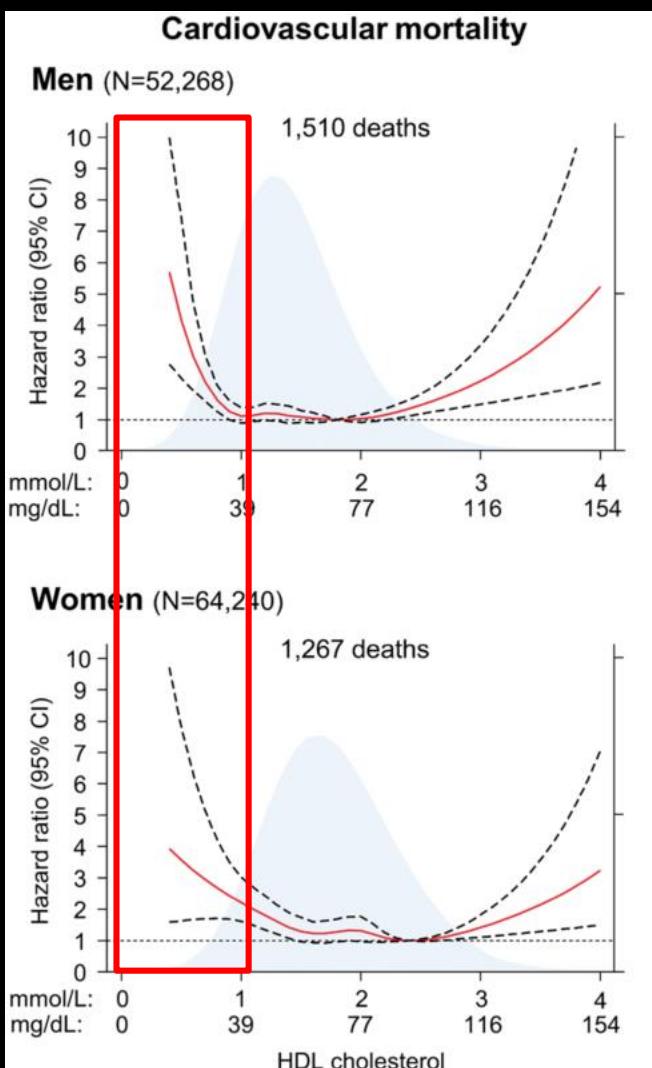
HDL-C and Coronary Heart Disease

The Framingham Heart Study



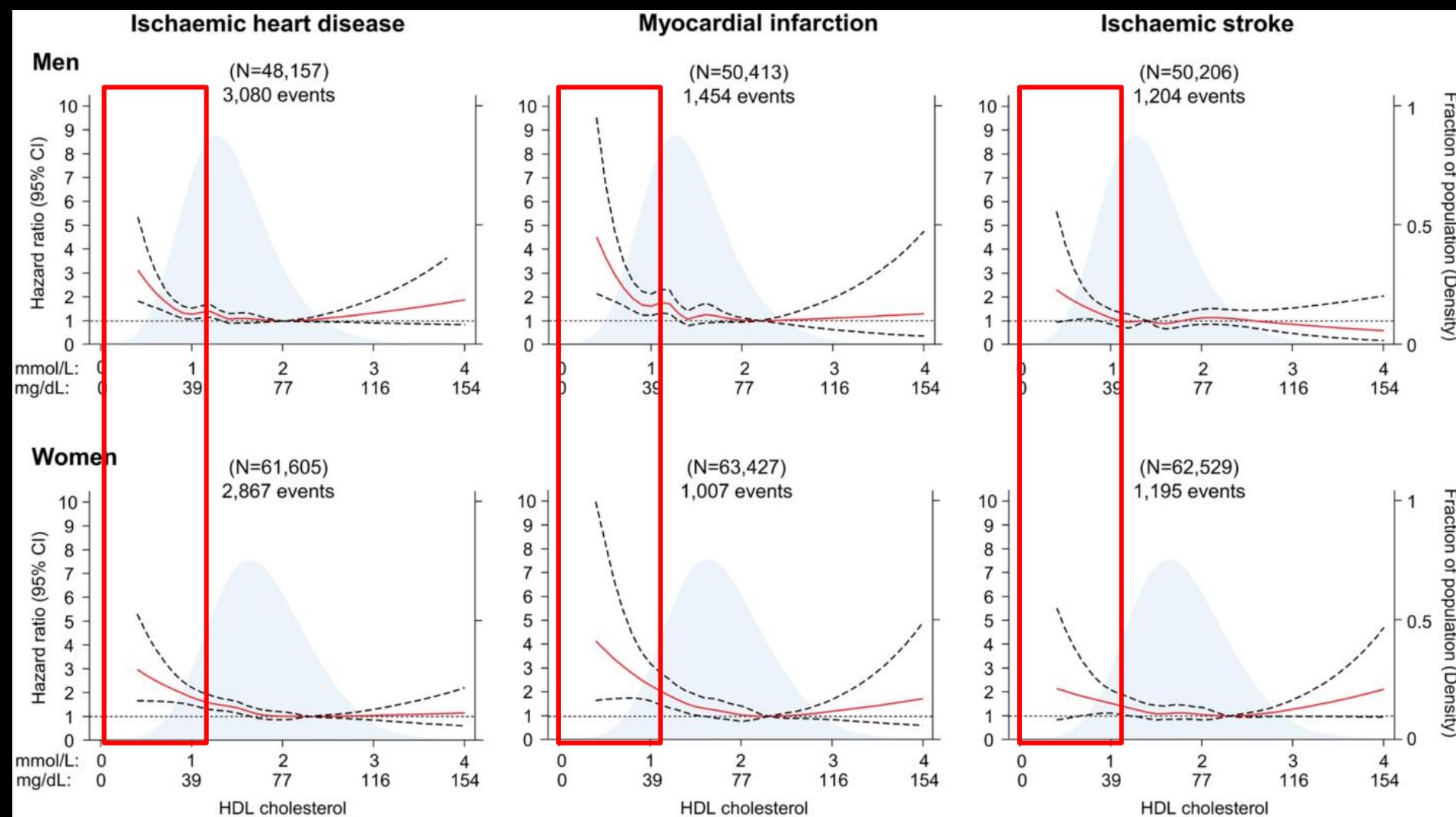
HDL-C and Cardiovascular Mortality

Copenhagen Studies

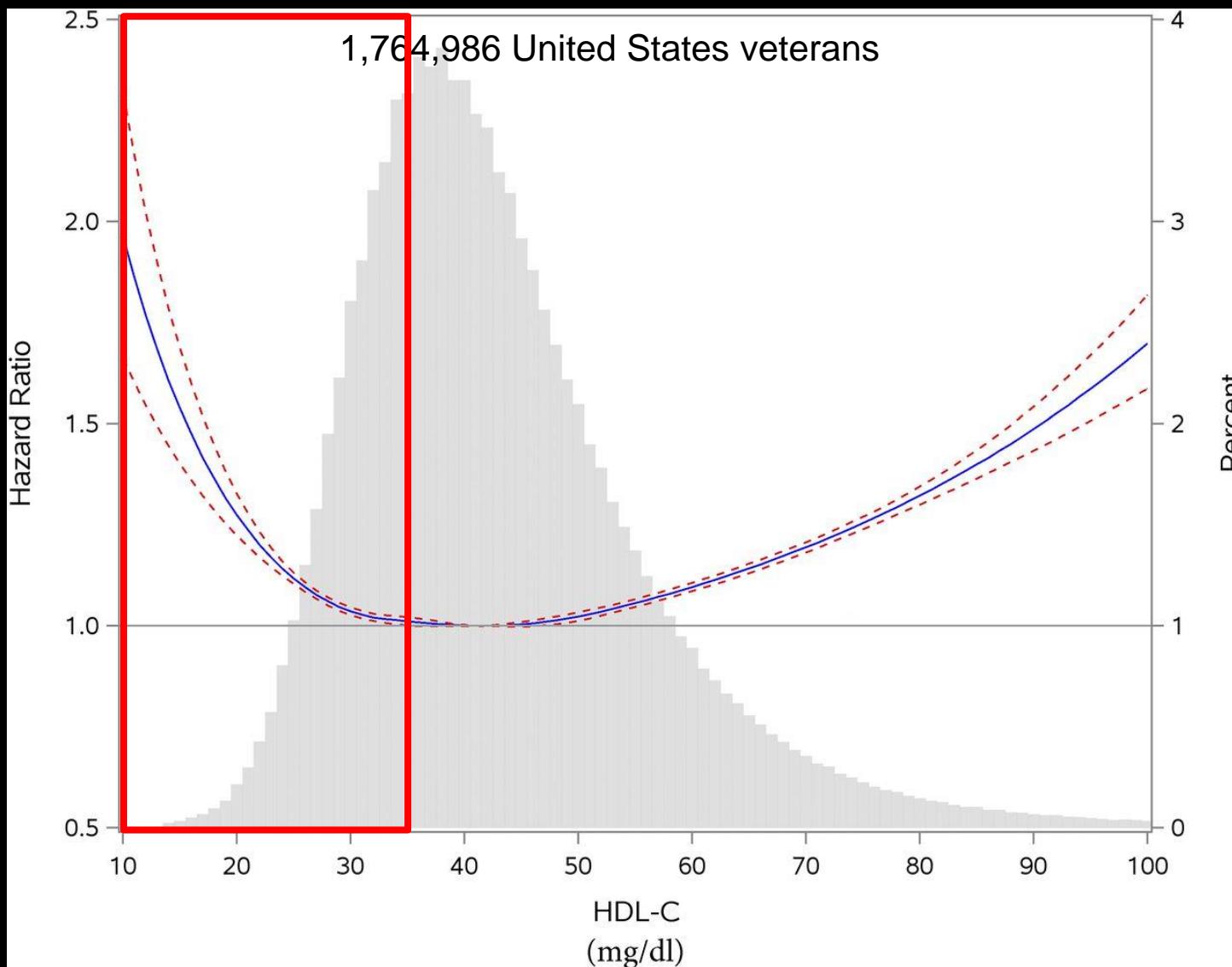


HDL-C and Cardiovascular Disease

Copenhagen Studies

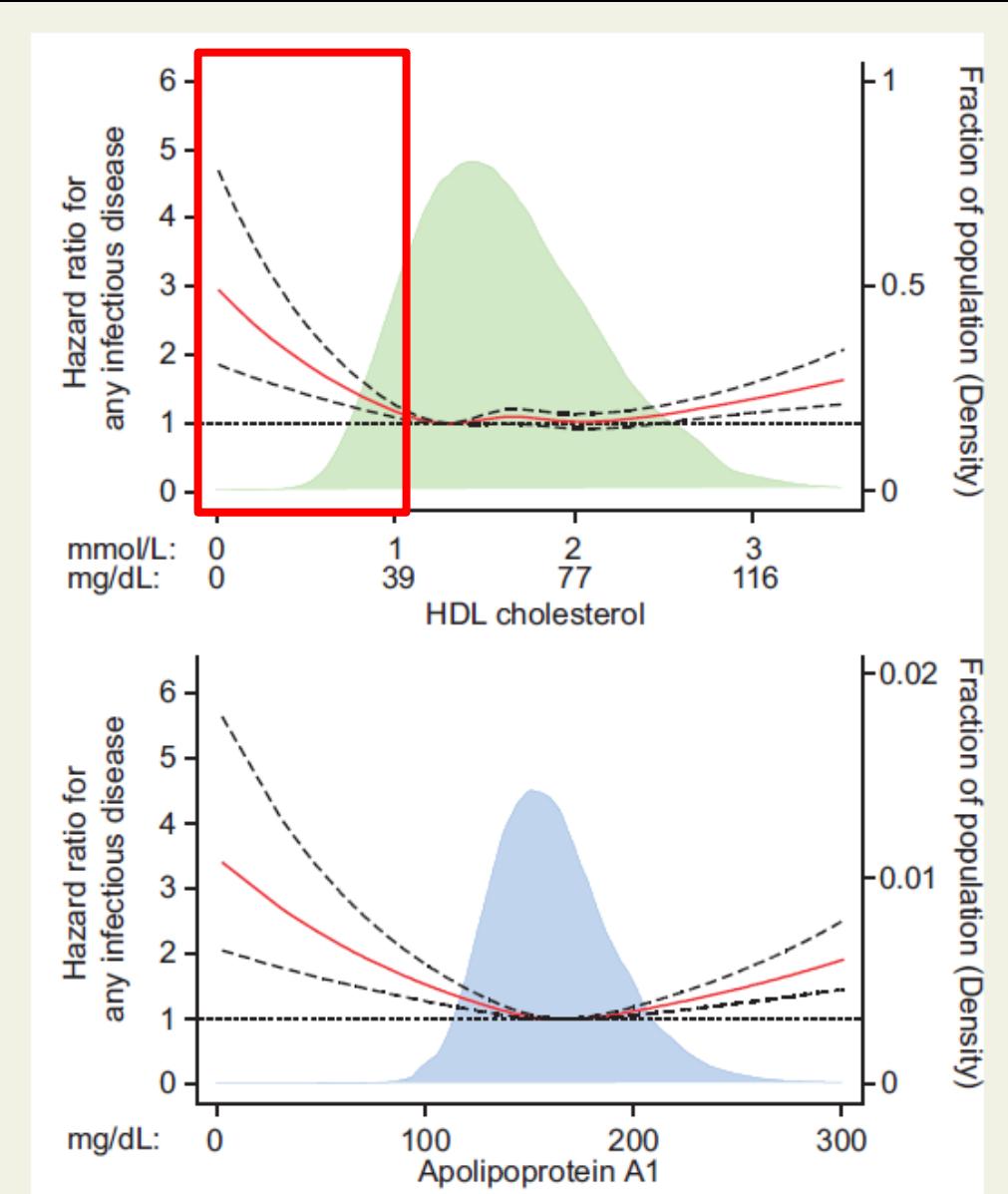


HDL-C and All-cause Mortality



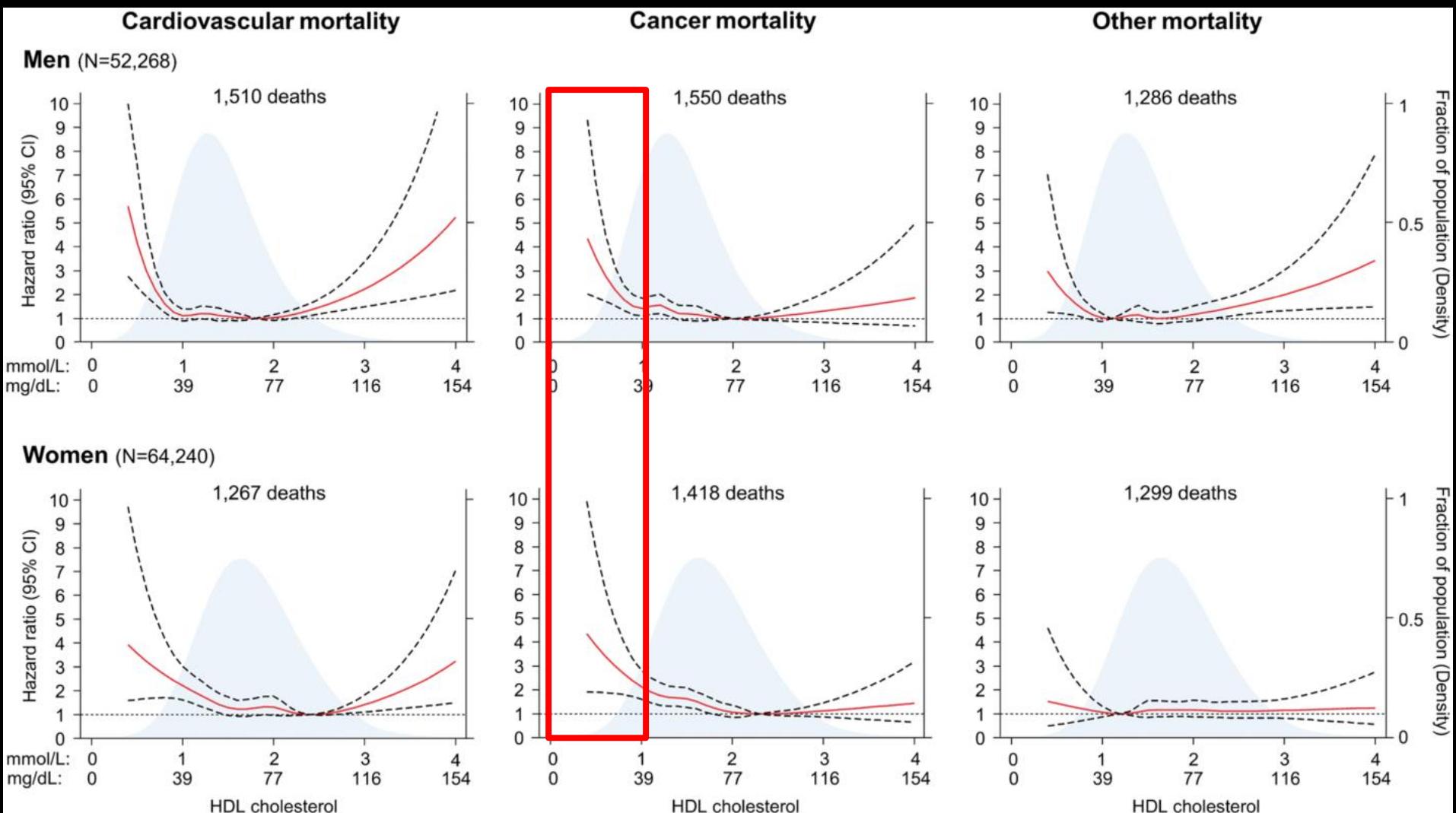
HDL-C and Infectious Disease

Copenhagen Studies



HDL-C and Cancer Mortality

Copenhagen Studies



HDL Functions

Reverse Cholesterol Transport

Arterial cholesterol efflux

Hepatic cholesterol uptake

Endothelial Protection

Cell adhesion

Vascular tone

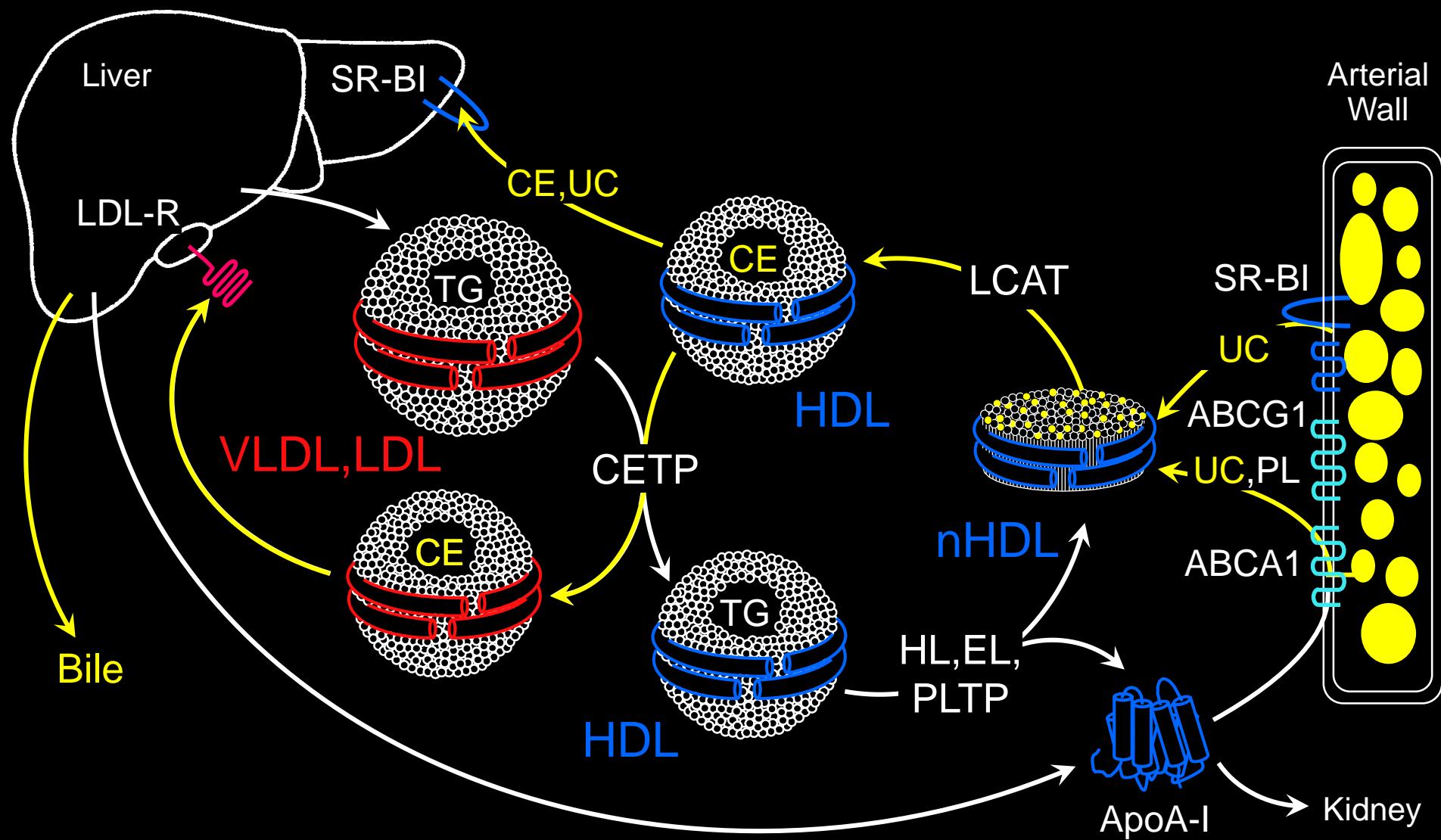
Antioxidant

Host-defense mechanisms

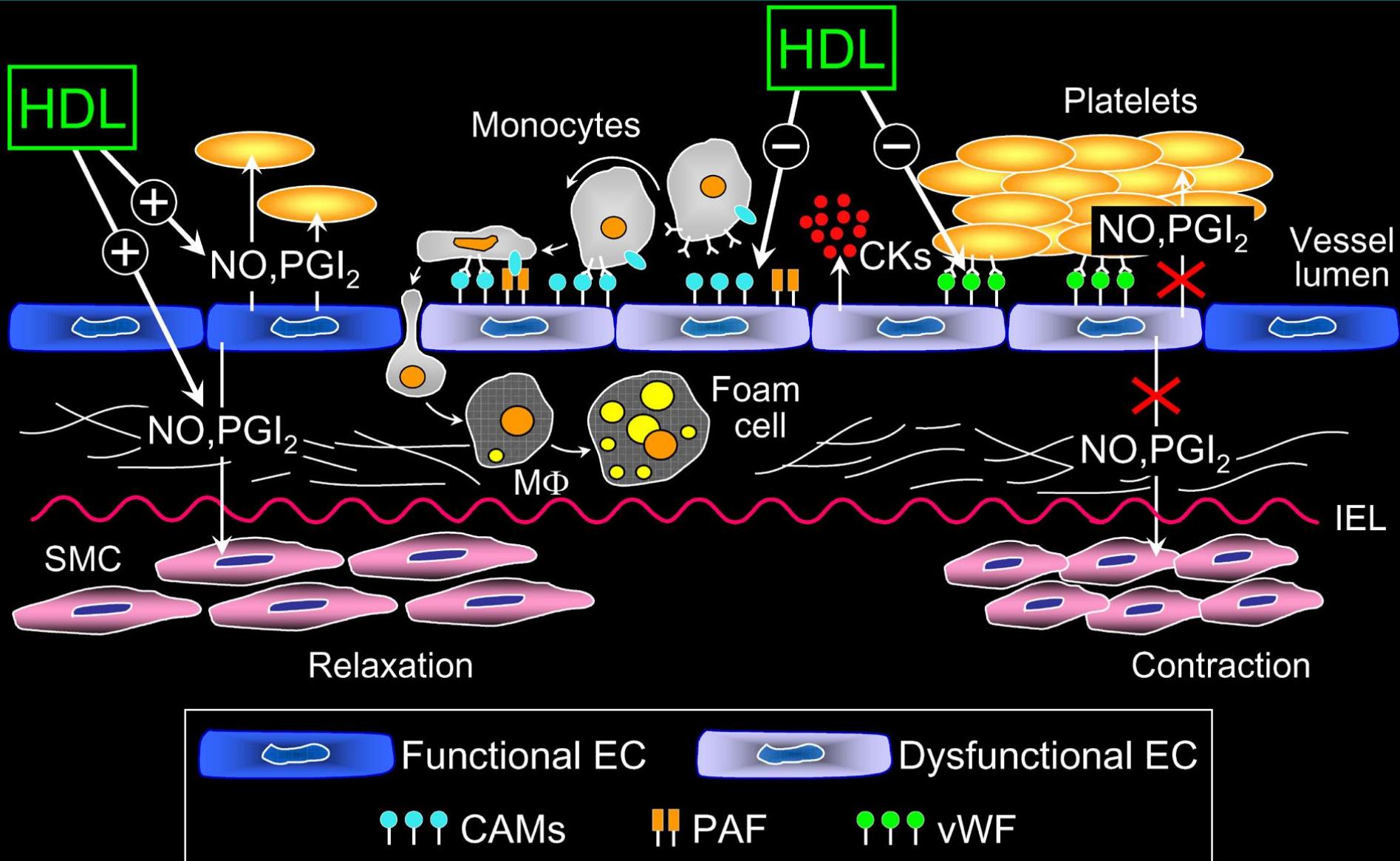
Effects on pancreatic beta cell function

Tumor cell metastasis and progression

Reverse Cholesterol Transport



HDL and Endothelial Dysfunction



HDL Functions

Reverse Cholesterol Transport

Arterial cholesterol efflux

Hepatic cholesterol uptake

Endothelial Protection

Cell adhesion

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Host-defense mechanisms

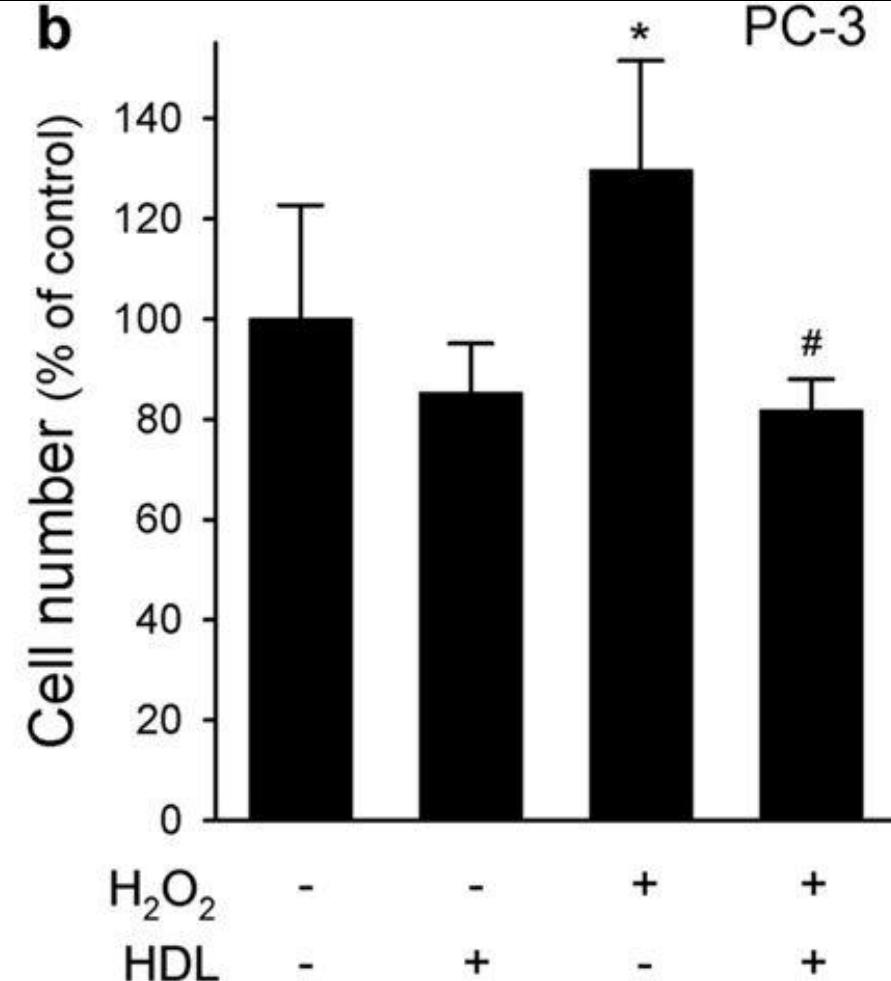
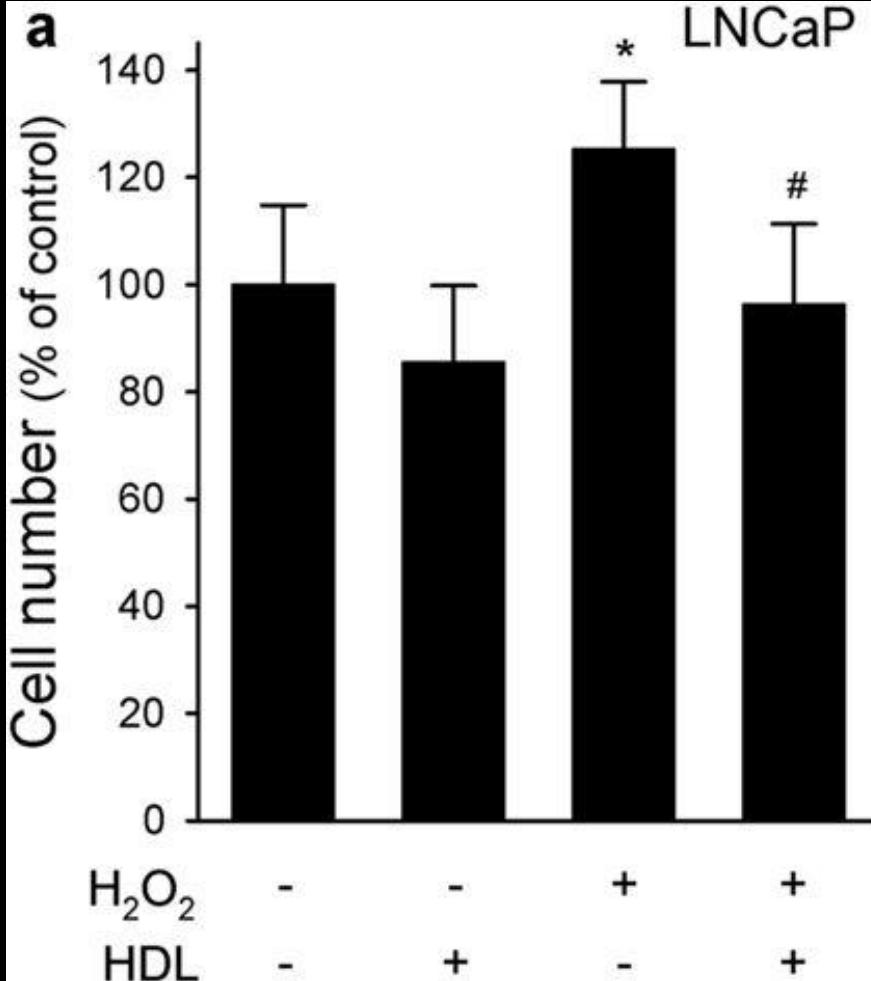
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Tumor cell metastasis and progression

HDL and Infectious Diseases

TYPE OF INFECTION	HDL-MEDIATED EFFECT
Bacteria	<ul style="list-style-type: none">• Favor LPS/LTA binding and neutralization.• Favor LPS/LTA clearance• Inhibit LPS (LTA)-induced cytokine release• Inhibit of LPS (LTA)-induced cell activation• Induce an early inflammatory response
Parasites	<ul style="list-style-type: none">• Support ApoL1, Apo-AI and HRP interaction to form the trypanosoma lytic factor-1 (TLF-1). complex. ApoL1 then traffics to the trypanosomal lysosome, where causes swelling which kills the trypanosome.
Virus	<ul style="list-style-type: none">• Dampen (ApoA-1 mimetic peptides) the ABCA-1 impairment induced by the HIV-1 Nef protein.• Inhibit cell fusion, both in HIV-1-infected T cells and in recombinant vaccinia-virus-infected CD4+ HeLa cells.• Compete with Hepatitis C virus on SRB1 interaction to dampen virus entry?

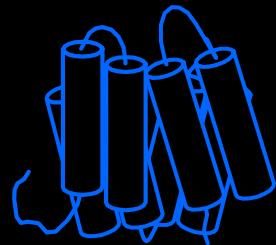
HDL and Cancer Cell Proliferation



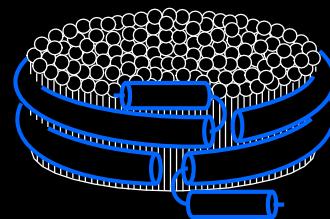
HDL and Cell Cholesterol Movements

Acceptors

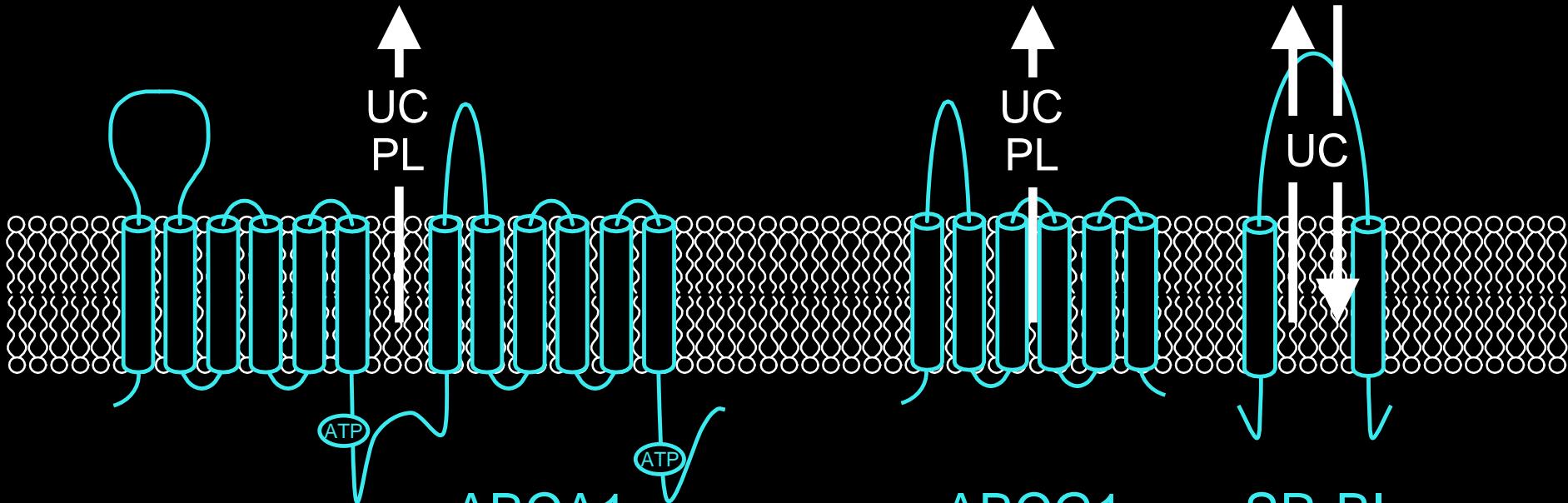
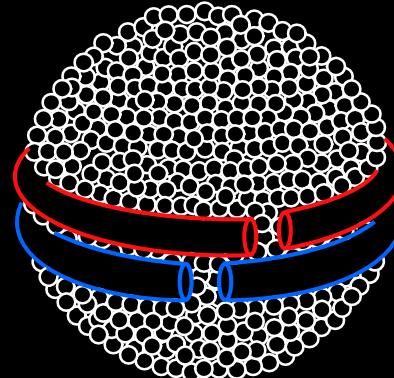
ApoA-I



pre β -HDL

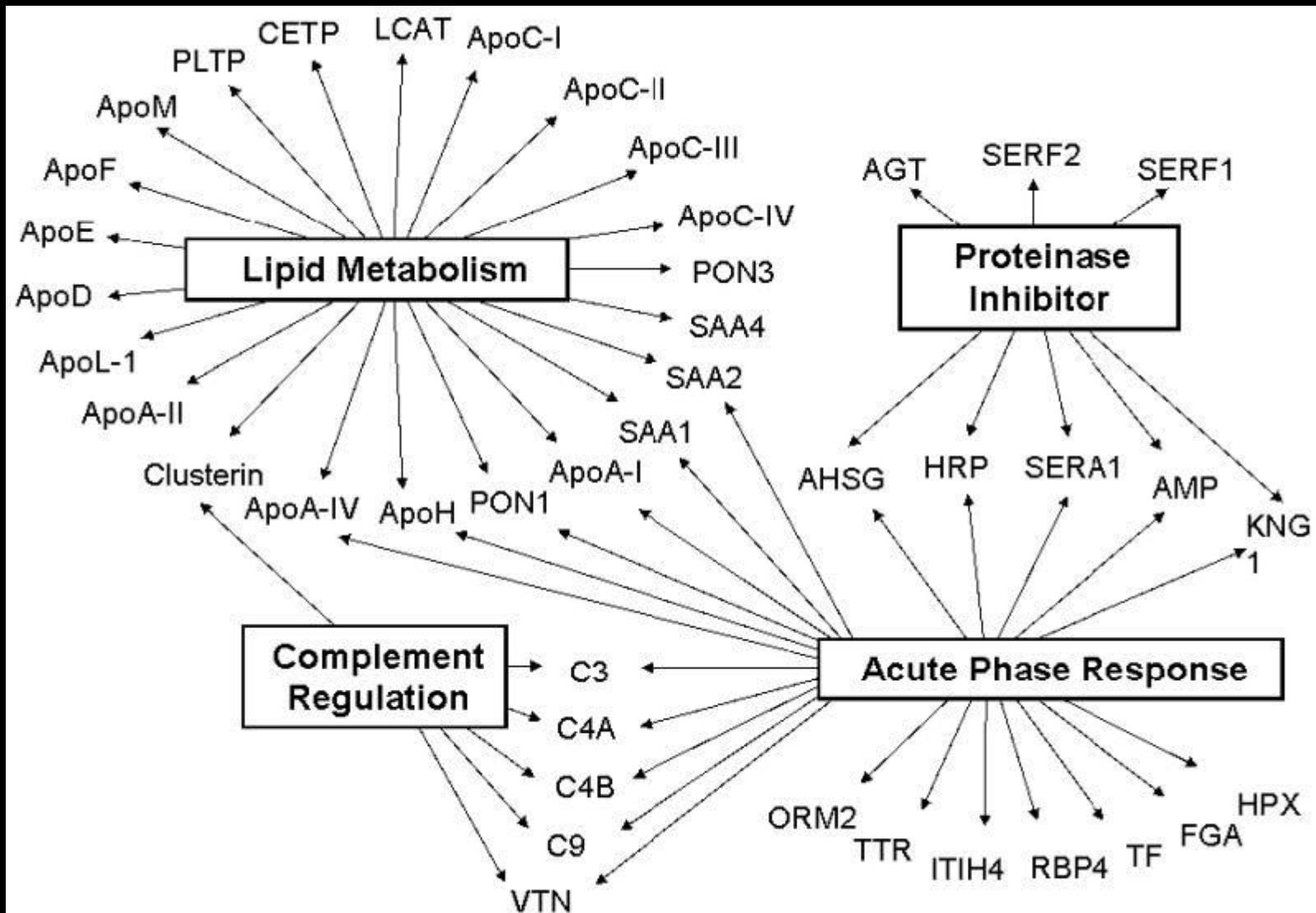


α -HDL



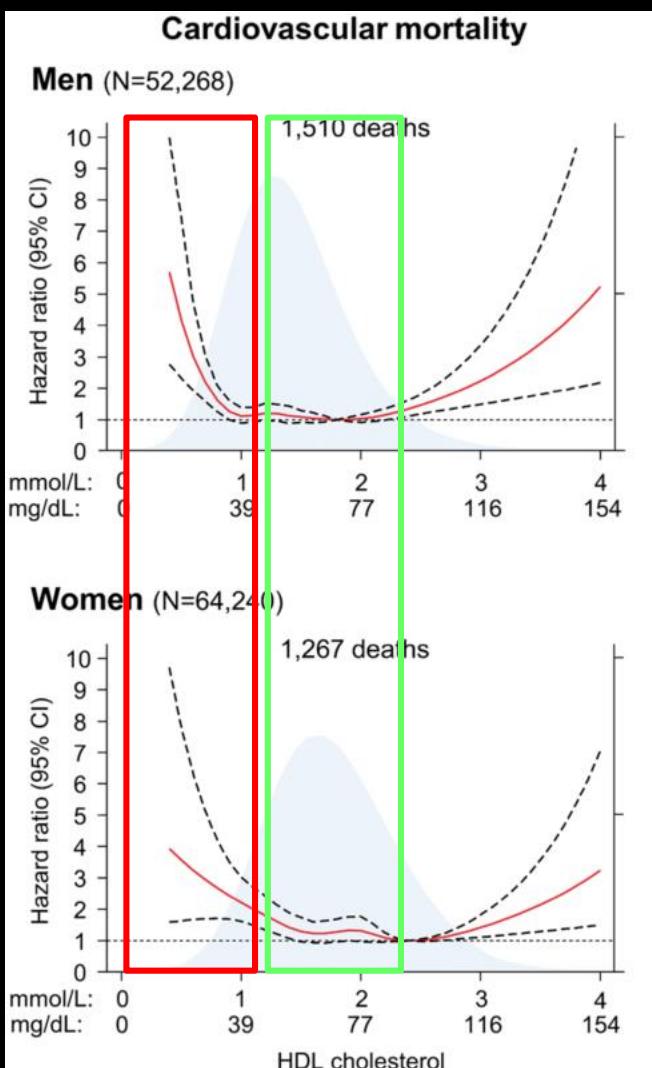
Mediators

HDL Protein's Cargo

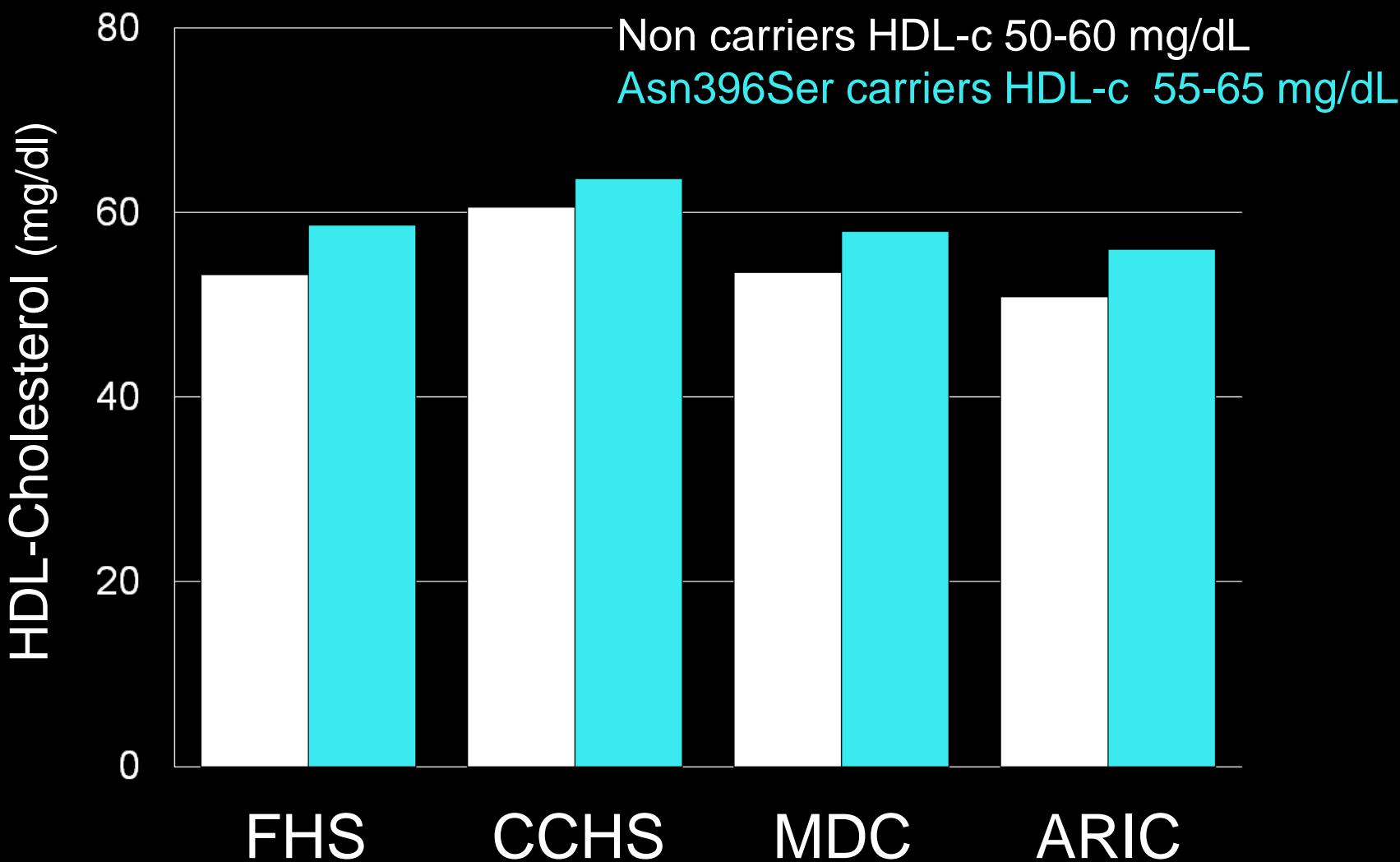


HDL-C and Cardiovascular Mortality

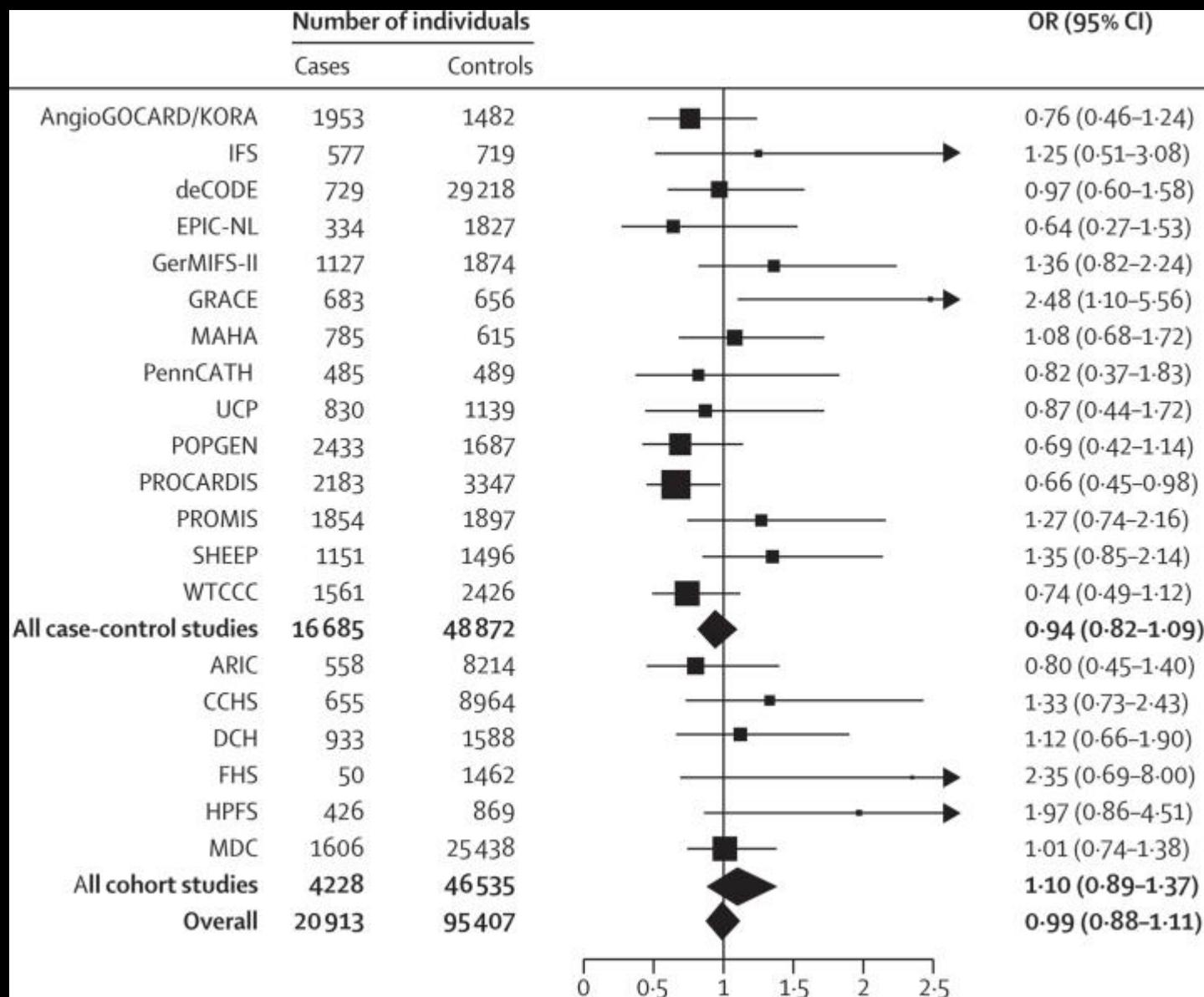
Copenhagen Studies



HDL-C in EL Common Variants



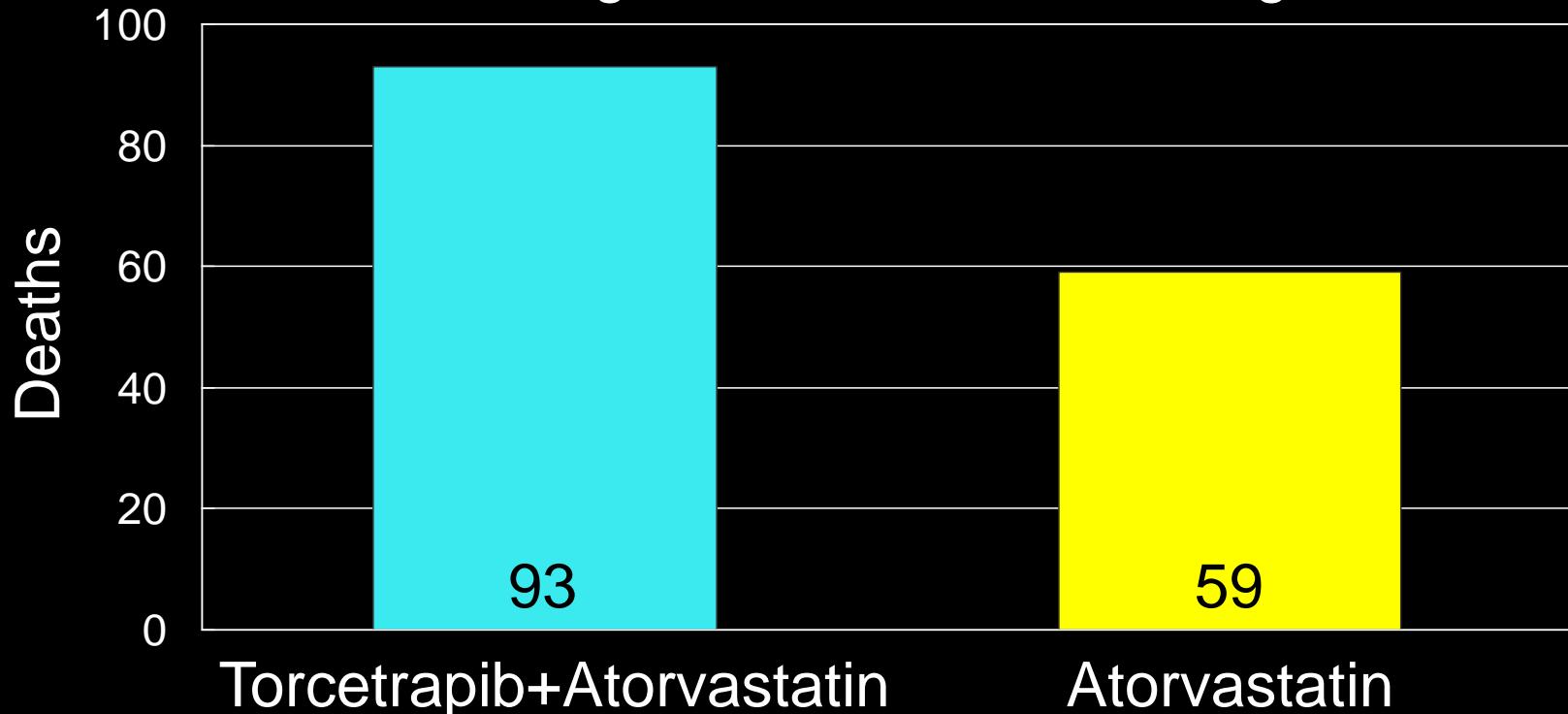
MI in EL Common Variants



The ILLUMINATE Trial

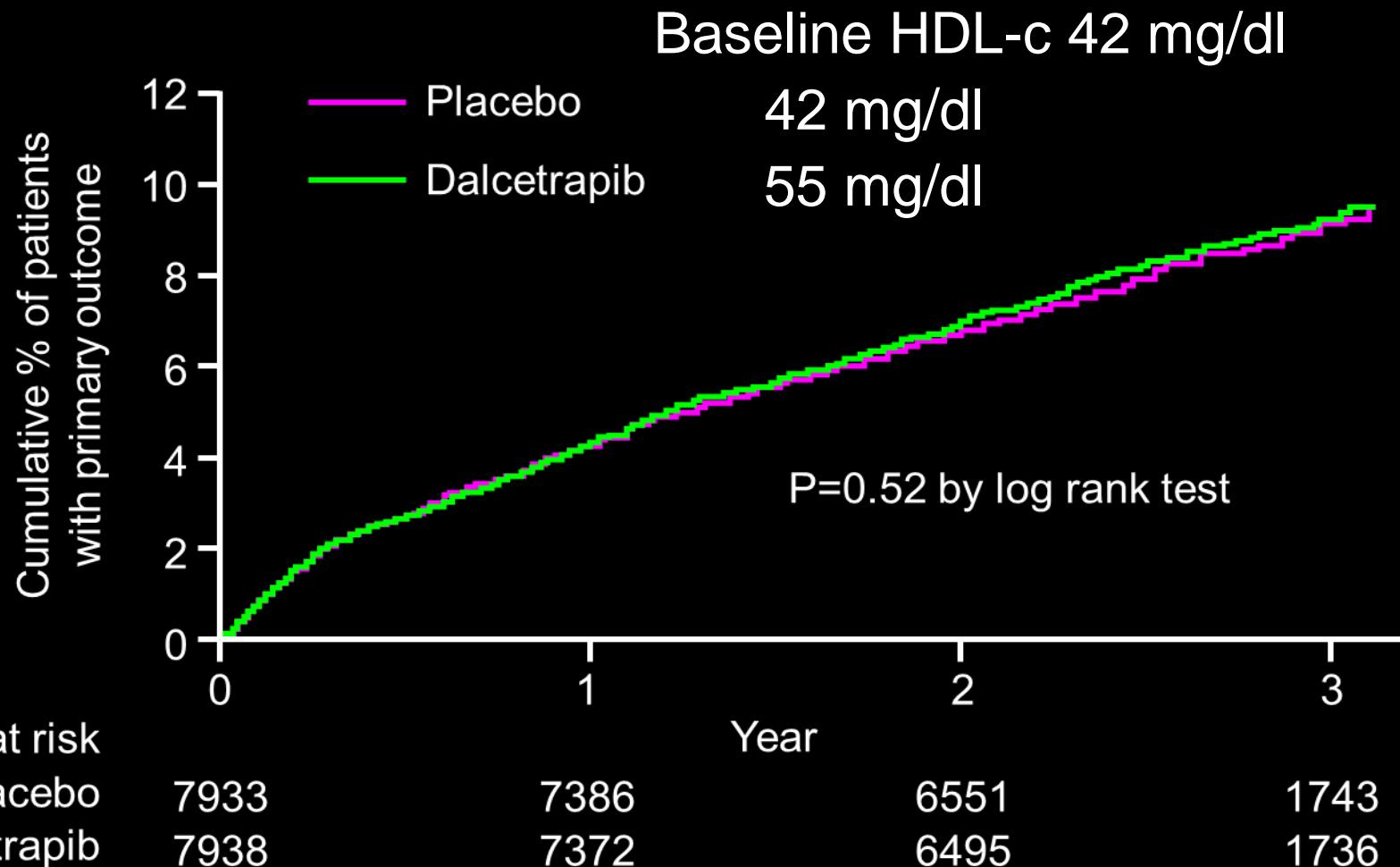
15067 CHD pts; torcetrapib (60 mg/d)+atorvastatin vs atorvastatin
Baseline HDL-c 48 mg/dl

HDL-c on treatment 82 mg/dl 48 mg/dl



Cardiovascular	49	35
Cancer	24	14
Infection	9	0

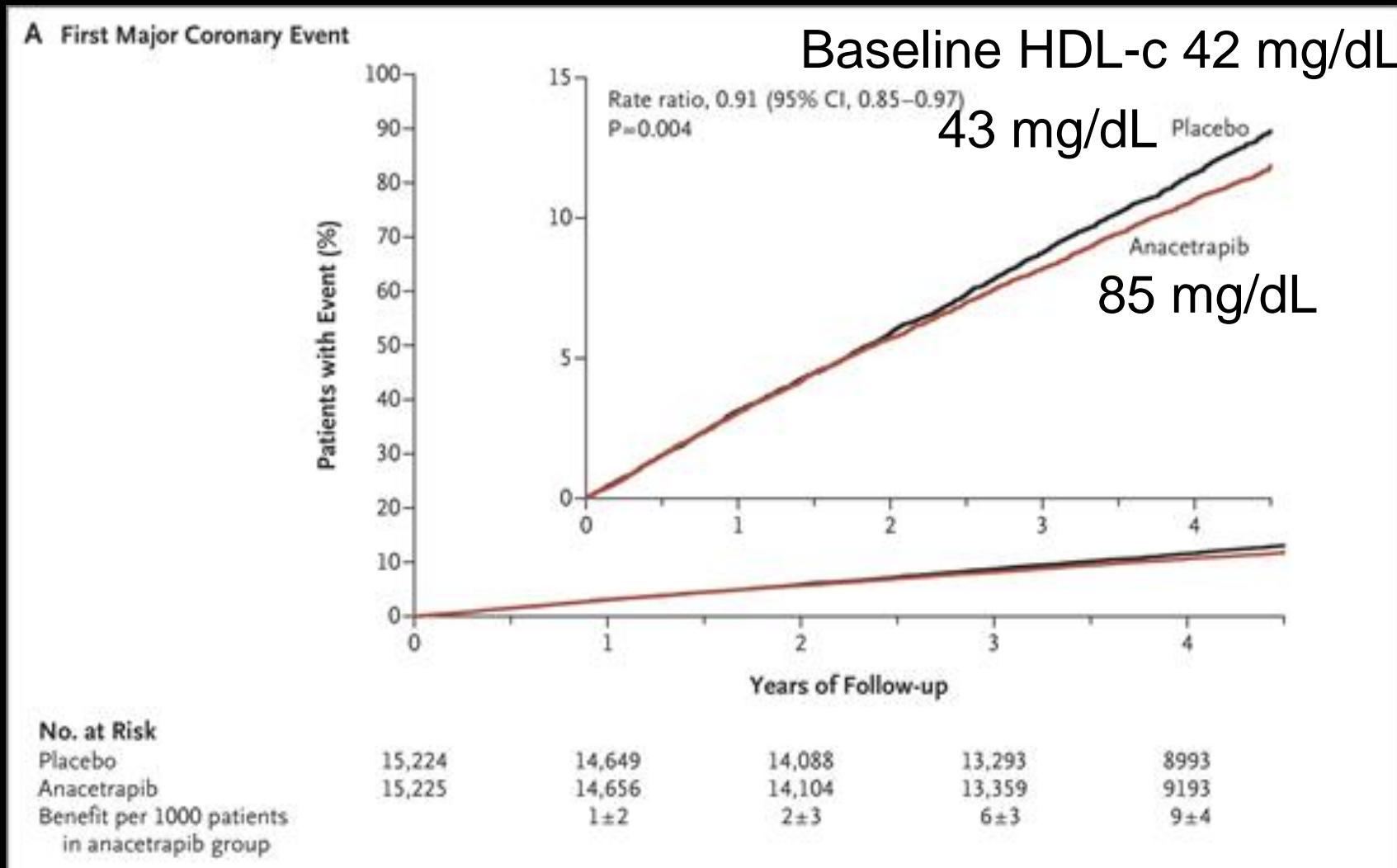
dal-OUTCOMES Trial



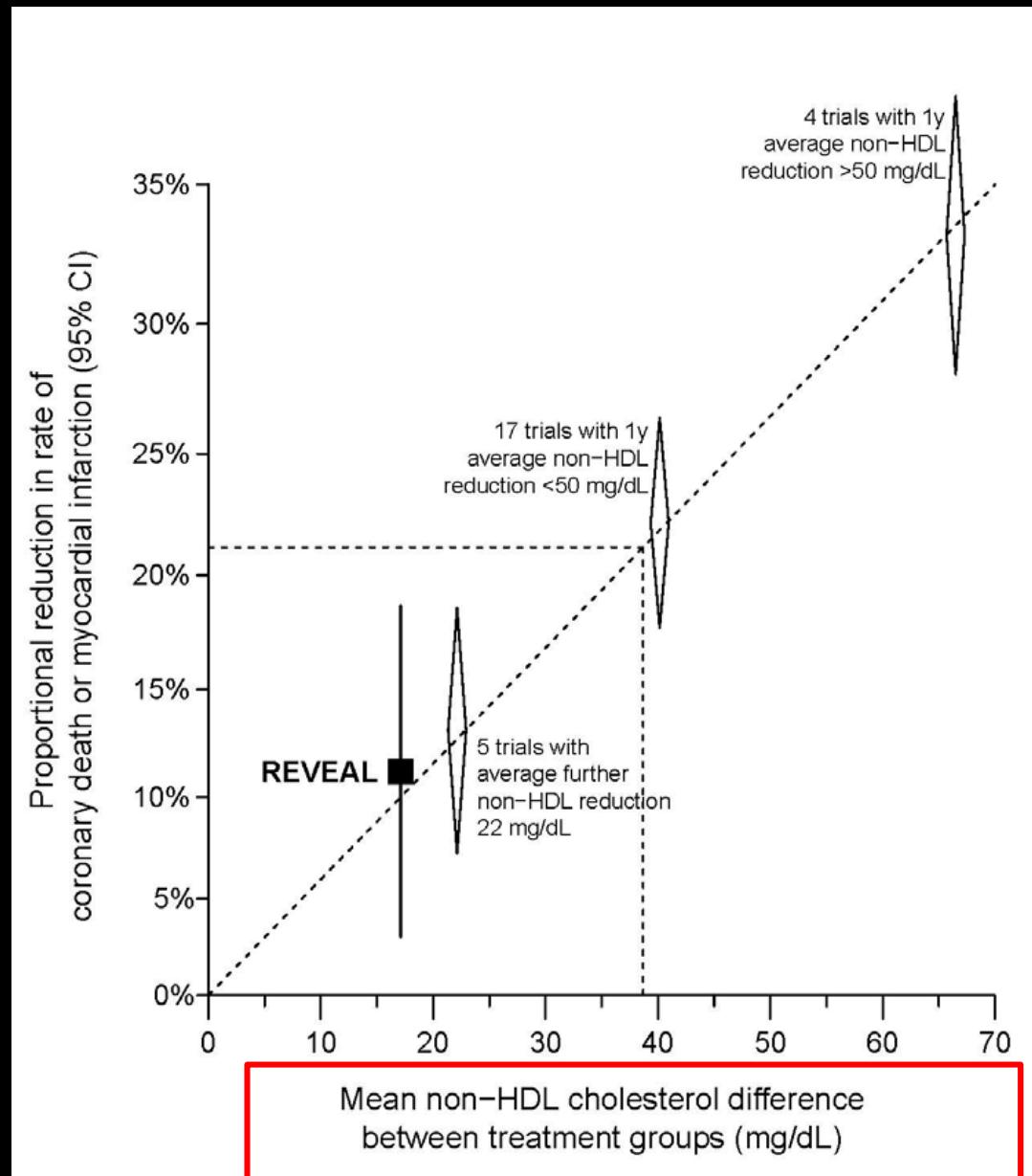
*Coronary heart disease death, non-fatal MI, ischemic stroke, hospitalization for unstable angina, resuscitated cardiac arrest

The REVEAL Trial

30449 patients with atherosclerotic vascular disease

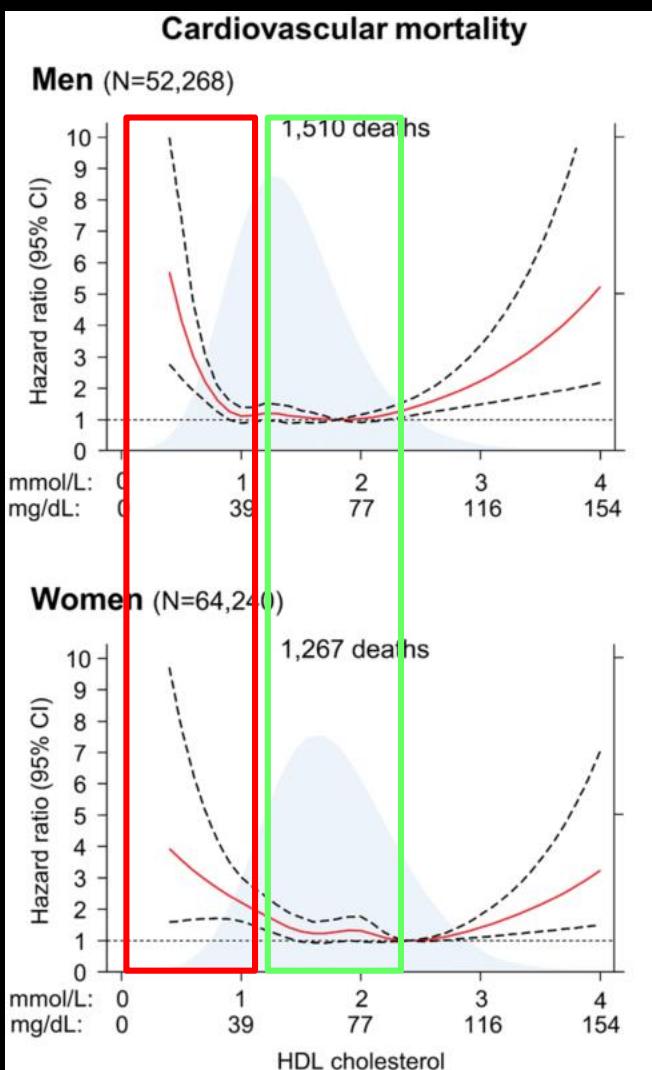


The REVEAL Trial



HDL-C and Cardiovascular Mortality

Copenhagen Studies

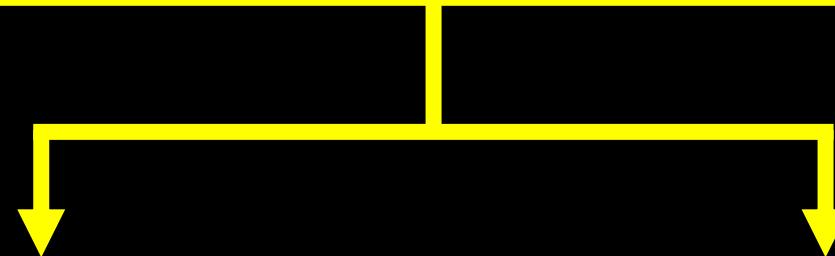


Lifestyle modifications and HDL-C

Lifestyle interventions to increase HDL-C levels

Avoid dietary trans fats	++
Increase habitual physical activity	+++
Reduce excessive body weight	++
Reduce dietary carbohydrates and replace them with unsaturated fats	++
Modest consumption in those who take alcohol may be continued	++
Quit smoking	+

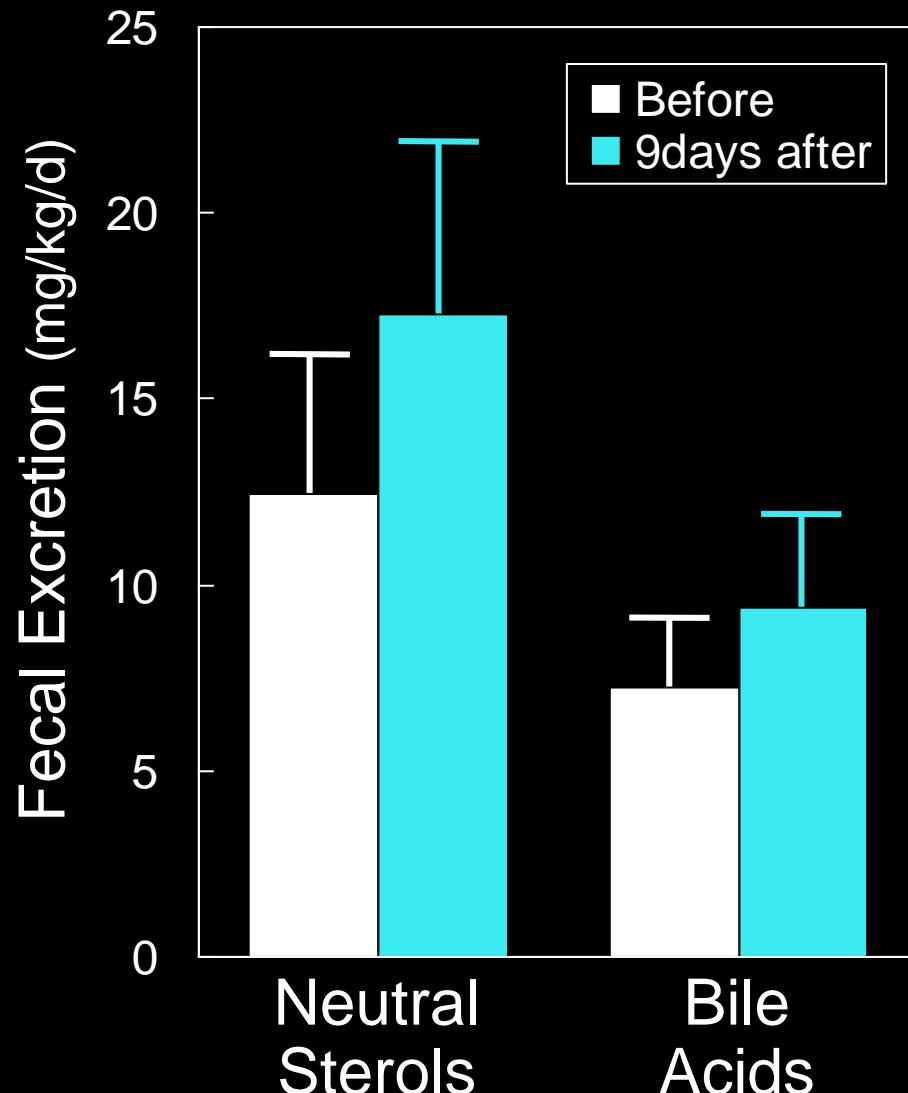
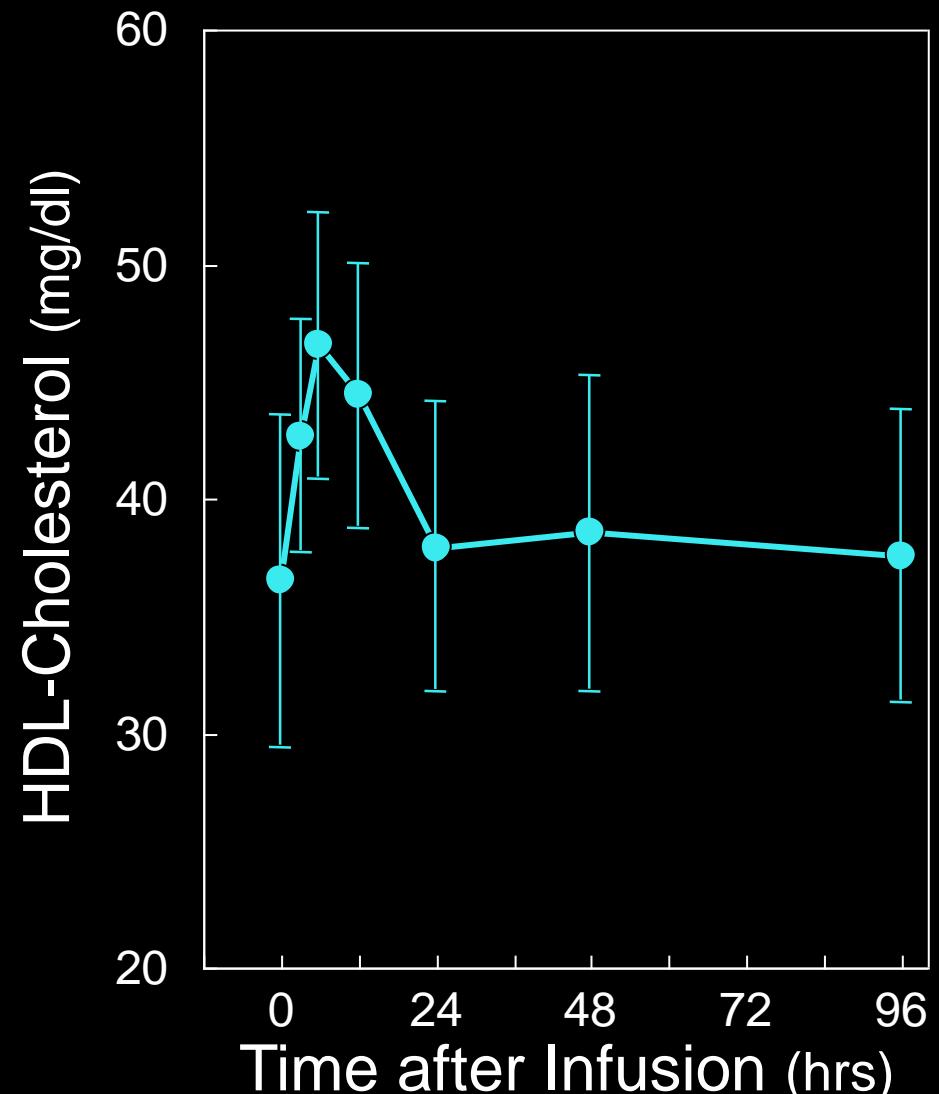
HDL-targeted therapies



target	PPAR α , CETP, ABCA1, others	plaque
mode of action	plasma HDL raising	plaque stabilization
administration	oral	parental
use	chronic	acute/subacute

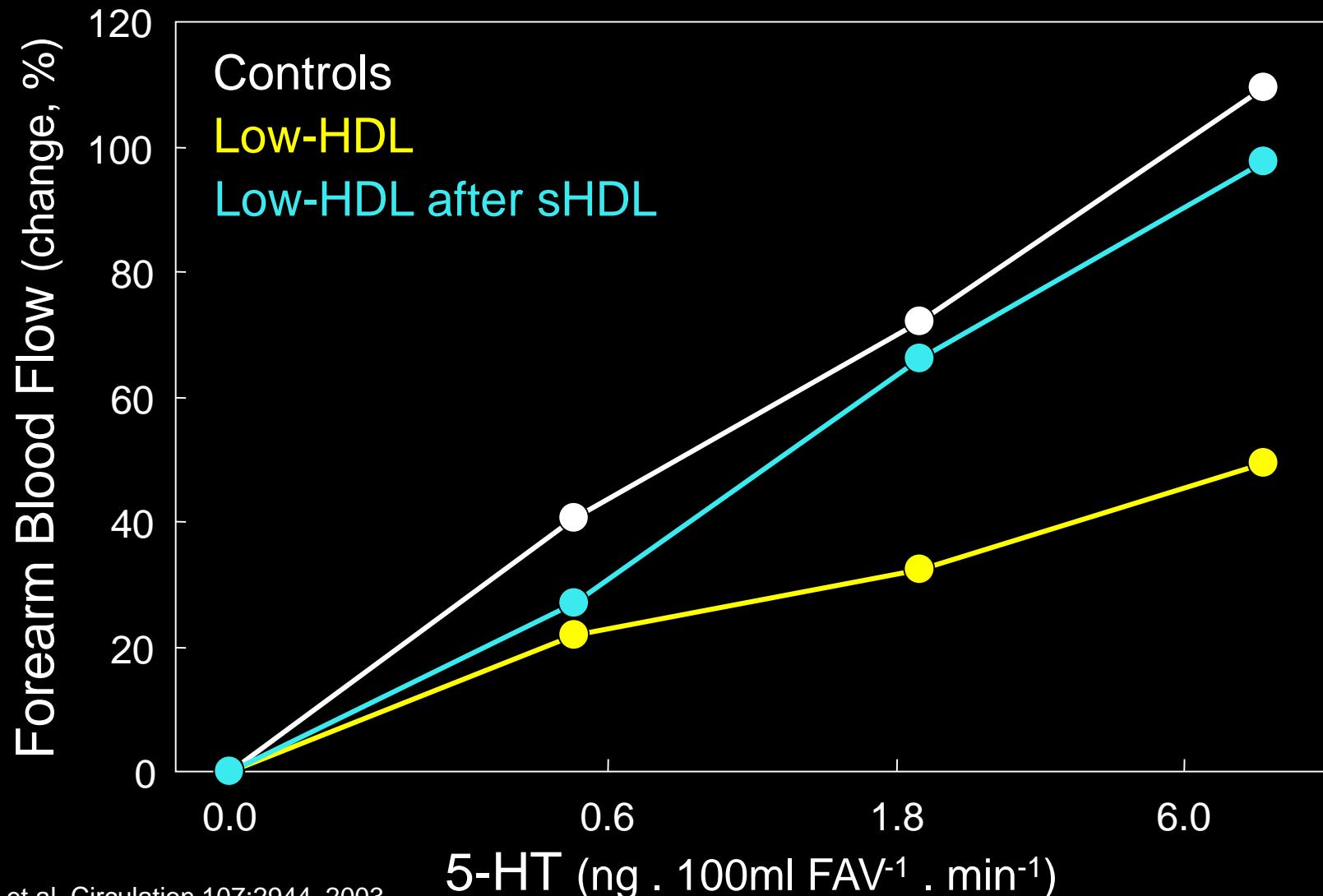
sHDL and Reverse Cholesterol Transport

4 FH patients; proApoA-I sHDL (4 g); 20 min infusion



sHDL and NO-Dependent Vasodilation

9 ABCA1 Heterozygotes; ApoA-I sHDL (80 mg/kg); 4 hrs infusion



HDL-Therapy for Cardiovascular Diseases

	<i>Protein</i>	<i>Lipid</i>	<i>Manufacturer</i>	<i>Composition</i>
CSL-112	Human apoA-I	Soy PC	CSL, Australia	ApoA-I:PC (mol:mol) 1:100
CER-001	Recombinant apoA-I	Egg SM, DPPG	Cerenis, France	ApoA-I:PL (w:w) 1:2.7; SM:PG (w:w) 97:3
MDCO-216	Recombinant apoA-I Milano	POPC	Medicines Company, USA	ApoA-I:PC (w:w) 1:1

Synthetic HDL under development

Rare dyslipidaemias, from phenotype to genotype to management: a European Atherosclerosis Society task force consensus statement

