

CAMPUS Cuore SUMMIT

Napoli, 1-2 ottobre 2021
Hotel Excelsior

Scacco al Rischio Evitabile

*Strategie per Ridurre
il Rischio di Eventi
Cardiovascolari*



Terapia farmacologica per la
lotta al rischio evitabile nel
paziente con
ipertrigliceridemia

Plinio Cirillo

Università di Napoli "Federico II".

Evaluation of CV risk



LDL

HDL

**Total
Cholesterol**



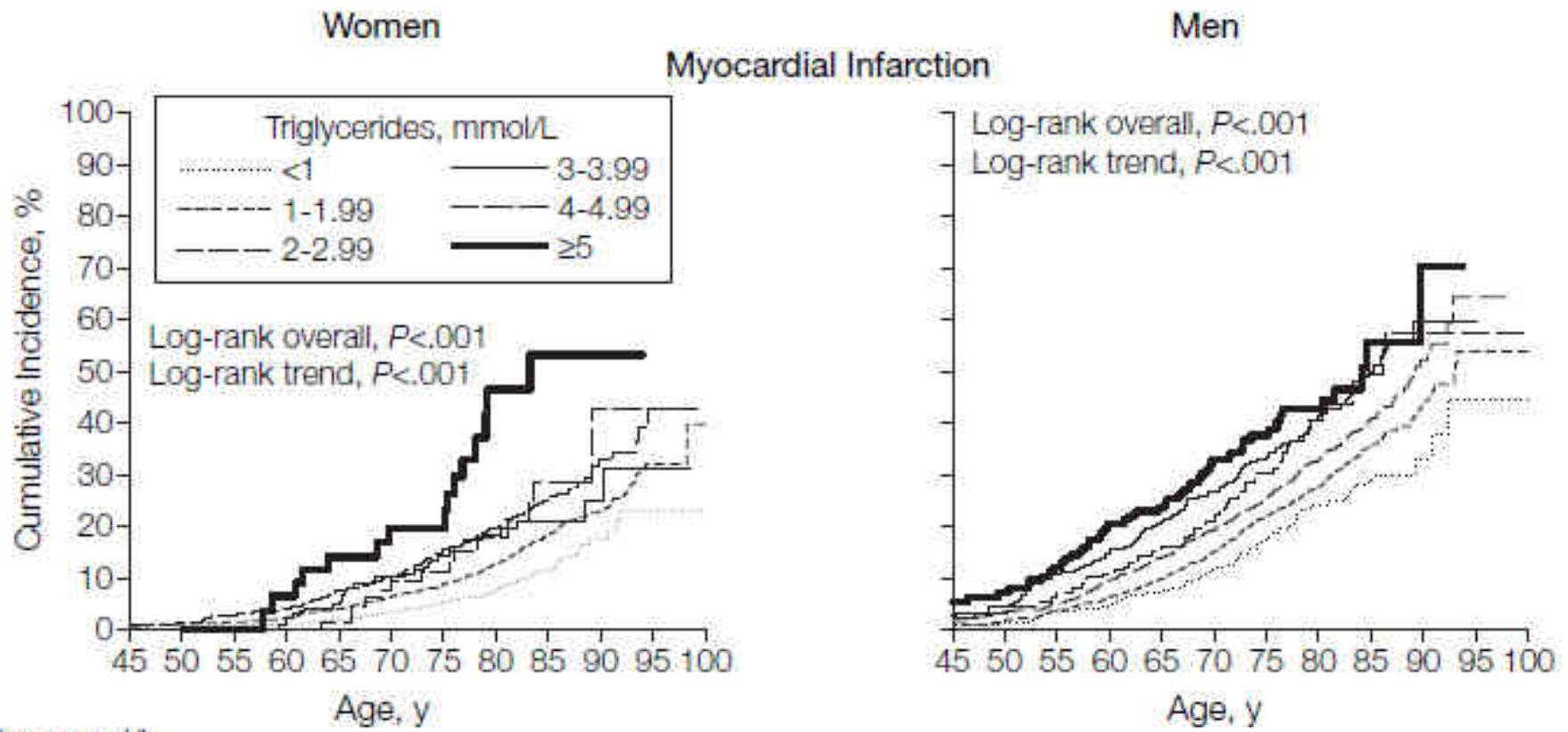
Triglycerides

Nonfasting Triglycerides and Risk of Myocardial Infarction, Ischemic Heart Disease, and Death in Men and Women

The Copenhagen City Heart Study

7587 women 6394 men

mean 26 years of follow-up.



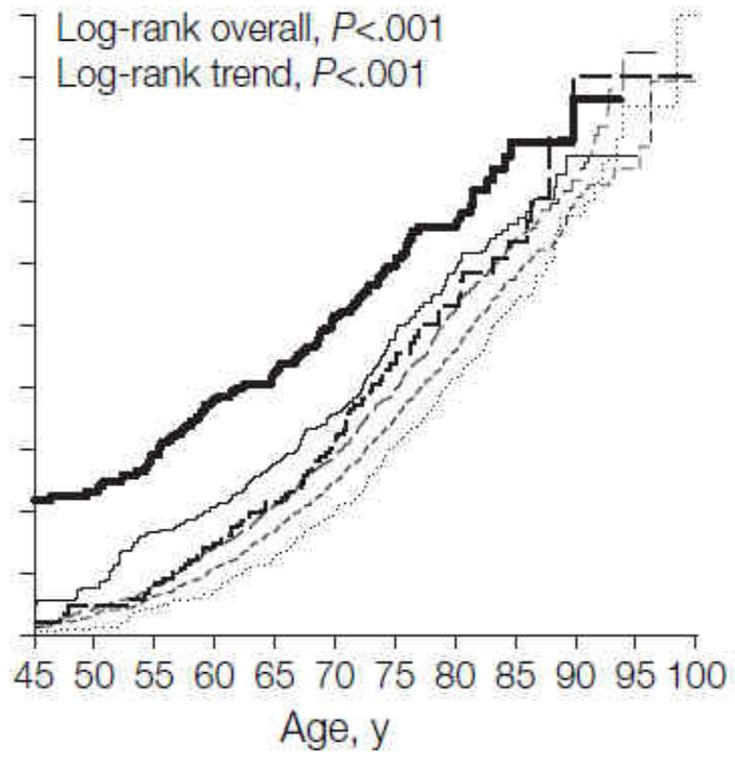
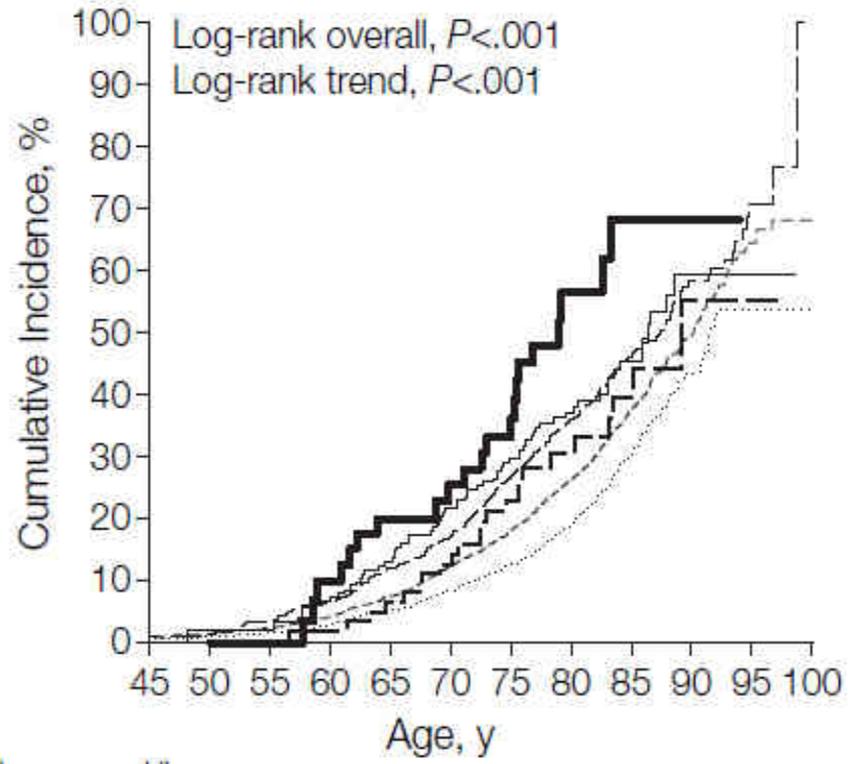
Cumulative Incidences of Myocardial Infarction,

Nonfasting Triglycerides and Risk of Myocardial Infarction, Ischemic Heart Disease, and Death in Men and Women

7587 women 6394 men

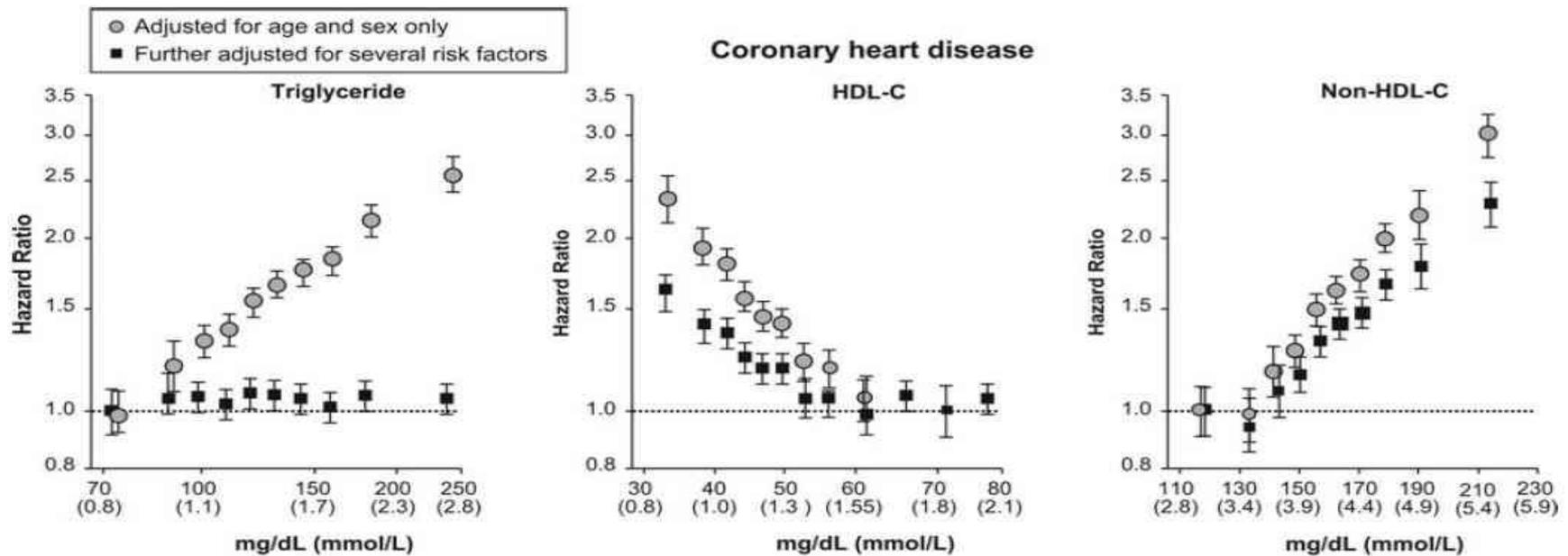
mean 26 years of follow-up.

Ischemic Heart Disease



Triglyceride-rich lipoproteins and high-density lipoprotein cholesterol in patients at high risk of cardiovascular disease: evidence and guidance for management

M. John Chapman^{1*}, Henry N. Ginsberg^{2*}, Pierre Amarenco³, Felicita Andreotti⁴, Jan Borén⁵, Alberico L. Catapano⁶, Olivier S. Descamps⁷, Edward Fisher⁸, Petri T. Kovanen⁹, Jan Albert Kuivenhoven¹⁰, Philippe Lesnik¹, Luis Masana¹¹, Børge G. Nordestgaard¹², Kausik K. Ray¹³, Zeljko Reiner¹⁴, Marja-Riitta Taskinen¹⁵, Lale Tokgözoğlu¹⁶, Anne Tybjaerg-Hansen¹⁷, and Gerald F. Watts¹⁸, for the European Atherosclerosis Society Consensus Panel



Role of Triglycerides in Atherosclerosis

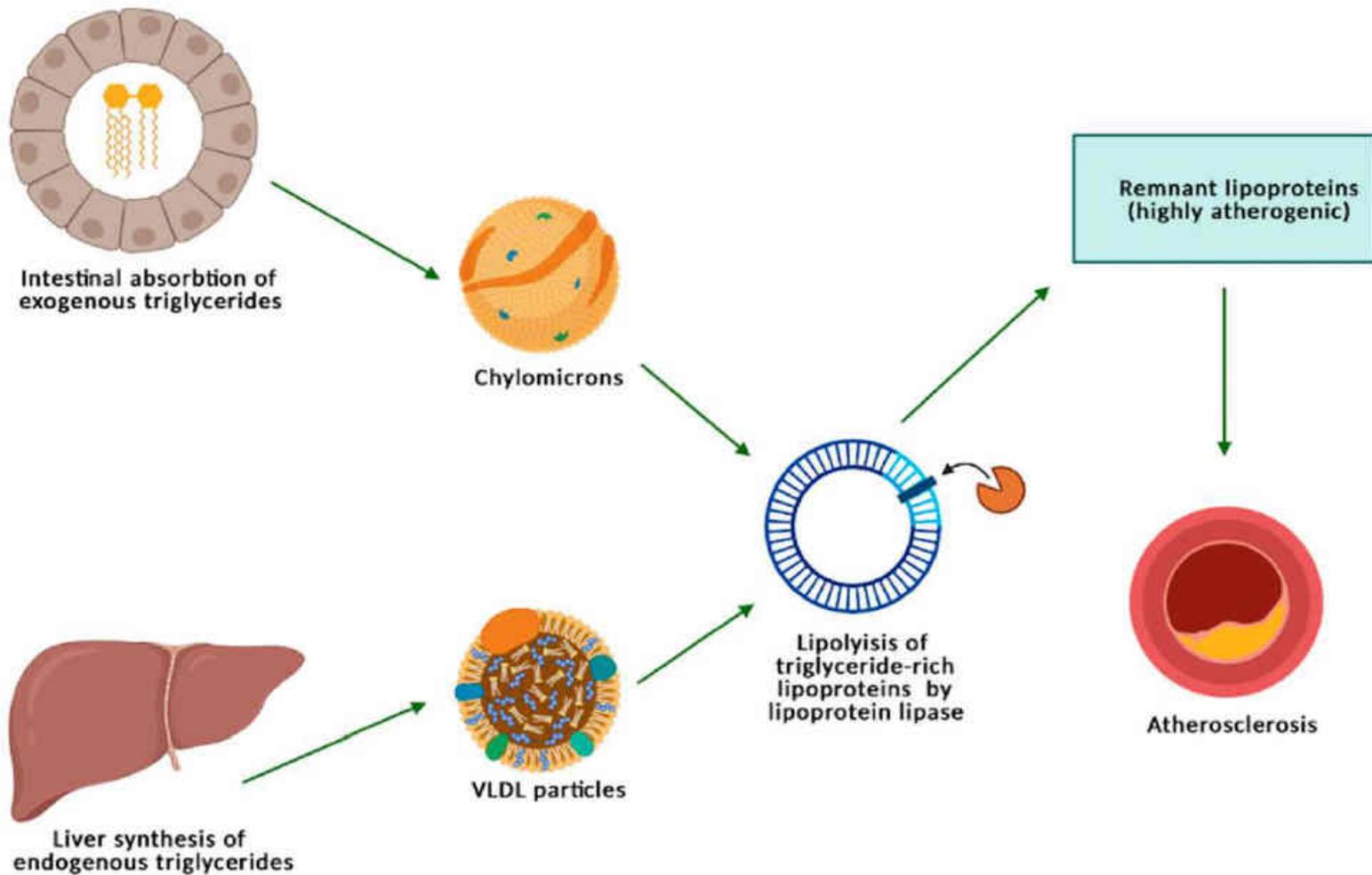


Figure 1. Metabolism of triglycerides, triglycerides-rich lipoproteins, and remnants.

Triglycerides and athero-thrombosis

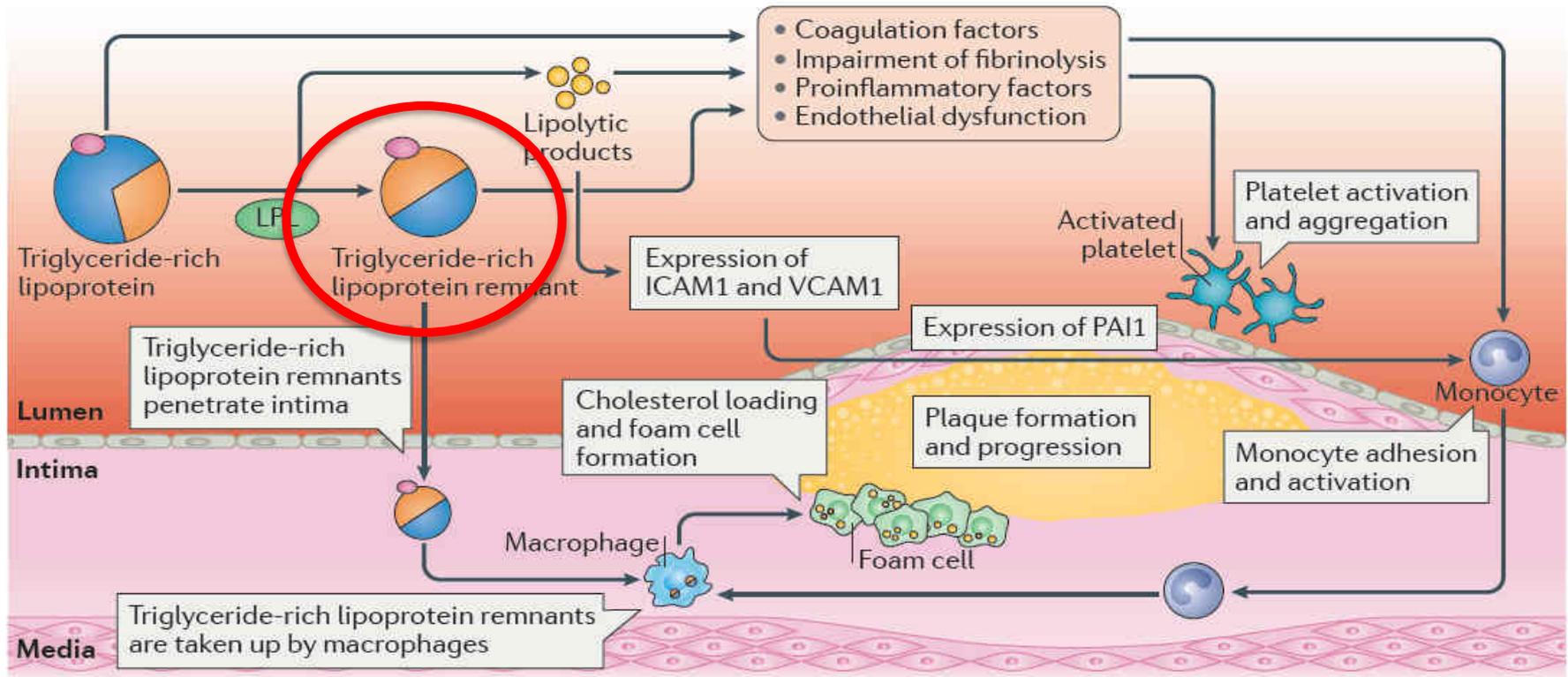
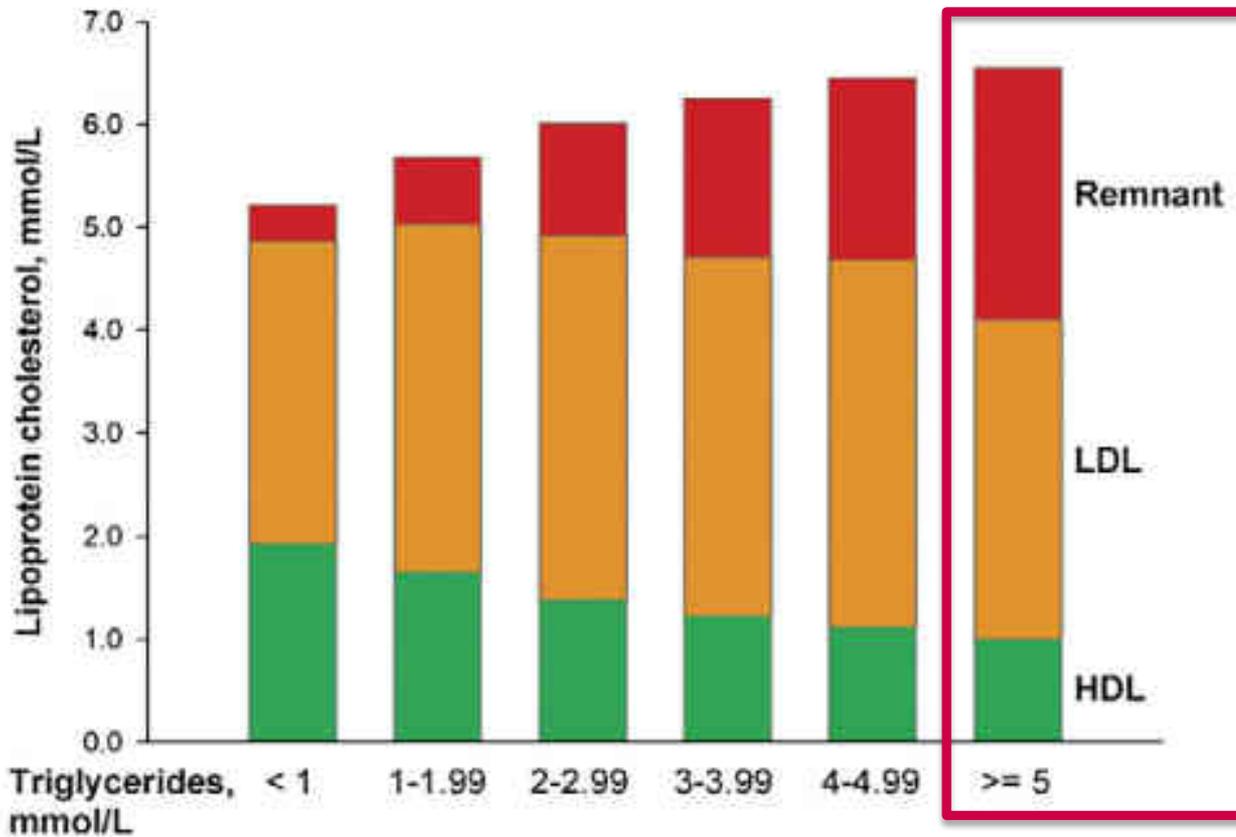


Figure 2 | **Possible mechanisms of atherogenesis by triglyceride-rich lipoprotein particles.** Small triglyceride-rich lipoproteins, which also contain cholesteryl esters, can penetrate the arterial intima and are taken up by macrophages, which transform into foam cells. Triglyceride-rich particles also promote endothelial dysfunction: induce increased expression of adhesion molecules such as intercellular adhesion molecule 1 (ICAM1) and vascular cell adhesion protein 1 (VCAM1) in endothelial cells; create a high concentration of oxidized free fatty acids, which are atherogenic; stimulate production of proinflammatory interleukins and cytokines, fibrinogen, and coagulation factors (by upregulating the endothelial expression of plasminogen activator inhibitor 1; PAI-1); and impair fibrinolysis. LPL, lipoprotein lipase.

Remnant Cholesterol as a Causal Risk Factor for Ischemic Heart Disease

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 Anne Tybjaerg-Hansen, MD, DMSc,†‡§|| Anders B. Jørgensen, MD,†‡§
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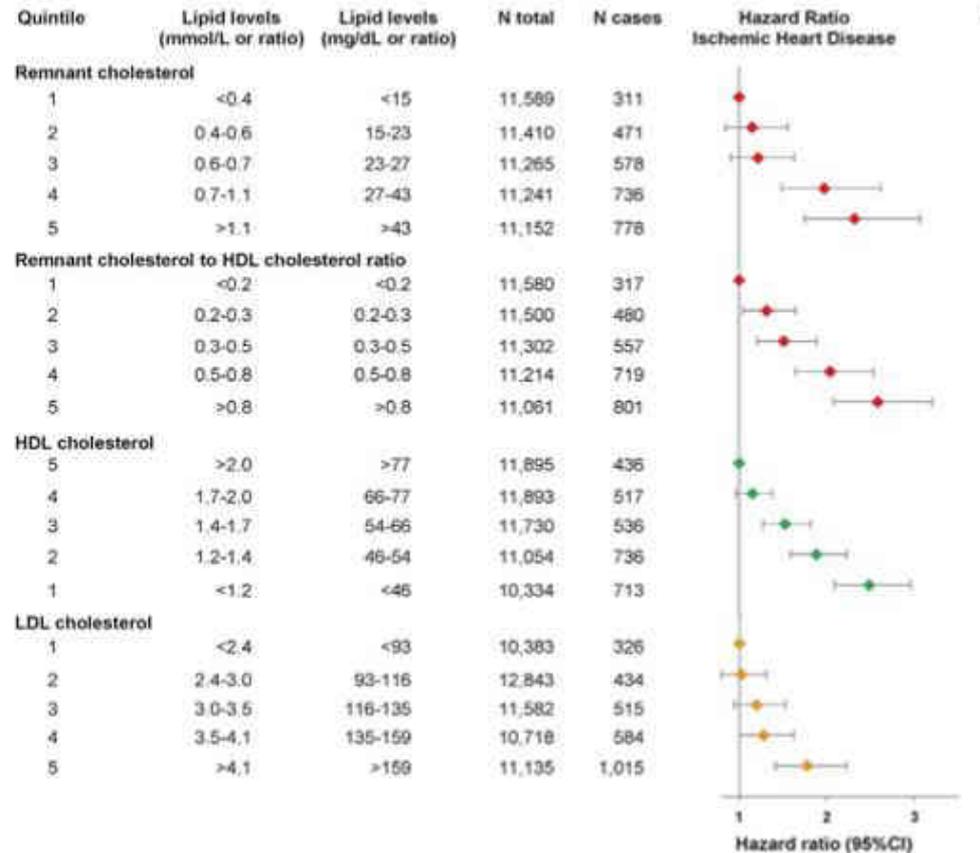


Figure 3 Risk for ischemic Heart Disease: Observational Estimates

Triglycerides lowering pharmacological agents

Drug	Action on TGs Levels
Statins	Lower TGs levels by 20% [18,54] First-line therapy
Fibrates (e.g., pemafibrate)	The most potent drugs in managing hypertriglyceridemia Produce a decrease of up to 50% in TGs concentrations [58] Pemafibrate is non-inferior to other fibrates and has a more favorable safety profile Their potency to decrease overall cardiovascular risk is modest
Omega 3 fatty acids (e.g., Icosapent Ethyl)	Demonstrated a 25% relative risk reduction in adverse cardiovascular events both in primary and secondary prevention when administrated at a high dose [63] Exert a beneficial effect on endothelial function assessed via flow-mediated dilation [66]
Ezetimibe	Produces only a slight decrease in TGs levels [59]
PCSK9 inhibitors (e.g., evolocumab)	Controversial data Reduction in VLDL, IDL, LDL, and Lp(a) levels The decrease in VLDL levels is dependent on baseline Lp(a) values [67] The lowering effect is more pronounced on VLDL ₂ levels than on VLDL ₁ [68]

Triglycerides lowering pharmacological agents

Drug	Action on TGs Levels
Volanesorsen	A second-generation chimeric antisense therapeutic oligonucleotide that decreases plasma apoCIII and TGs levels in a dose-dependent manner [71]
Inclisiran	Small interfering RNA agent Majorly effective in reducing LDL concentration but also lowered TGs levels in ORION 9, 10, and 11 trials [72,73]
GLP-1 receptor agonists (e.g., liraglutide)	Decreases apoB48 synthesis in CMs Apparently decreased production of atherogenic remnants in diabetic patients [74]
SGLT2 inhibitors (e.g., empagliflozin)	Decrease in fasting and post-prandial TGs concentration and a flow-mediated dilation improvement [75]



ESC

European Society
of Cardiology

European Heart Journal (2020) 41, 111–188
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ESC/EAS GUIDELINES



2019 ESC/EAS Guidelines for the management of dyslipidaemias: *lipid modification to reduce cardiovascular risk*

Changes in recommendations

Upgrades

2016

Drug treatments of hypertriglyceridaemia

Statin treatment may be considered as the first drug of choice for reducing CVD risk in high-risk individuals with hypertriglyceridaemia.

2019

Drug treatments of hypertriglyceridaemia

Statin treatment is recommended as the first drug of choice for reducing CVD risk in high-risk individuals with hypertriglyceridaemia [TG >2.3 mmol/L (200 mg/dL)].



2019 ESC/EAS Guidelines for the management of dyslipidaemias: lipid modification to reduce cardiovascular risk

Recommendations for drug treatment of patients with hypertriglyceridaemia

Recommendations	Class ^a	Level ^b
Statin treatment is recommended as the first drug of choice to reduce CVD risk in high-risk individuals with hypertriglyceridaemia [TG levels >2.3 mmol/L (>200 mg/dL)]. ³⁵⁵	I	B
In high-risk (or above) patients with TG levels between 1.5–5.6 mmol/L (135–499 mg/dL) despite statin treatment, n-3 PUFAs (icosapent ethyl 2×2 g/day) should be considered in combination with a statin. ¹⁹⁴	IIa	B
In primary prevention patients who are at LDL-C goal with TG levels >2.3 mmol/L (>200 mg/dL), fenofibrate or bezafibrate may be considered in combination with statins. ^{305–307,356}	IIb	B
In high-risk patients who are at LDL-C goal with TG levels >2.3 mmol/L (>200 mg/dL), fenofibrate or bezafibrate may be considered in combination with statins. ^{305–307,356}	IIb	C



.... in combination with statins.

Not only drugs but lifestyle interventions too!!!!

Lifestyle interventions to reduce TG-rich lipoprotein levels		
Reduce excessive body weight	+	A
Reduce alcohol intake	+++	A
Increase habitual physical activity	++	A
Reduce total amount of dietary carbohydrates	++	A
Use supplements of n-3 polyunsaturated fats	++	A
Reduce intake of mono- and disaccharides	++	B
Replace saturated fats with mono- or polyunsaturated fats	+	B

Evaluation of CV risk



LDL

HDL

**Total
Cholesterol**



Triglycerides