Meeting Nazionale ITACARE-P 2025

La Cardiologia Riabilitativa e Preventiva come snodo fondamentale della cura della persona con cardiopatia

Simposio
Rischio cardiovascolare residuo: cosa manca alla prevenzione ottimale?

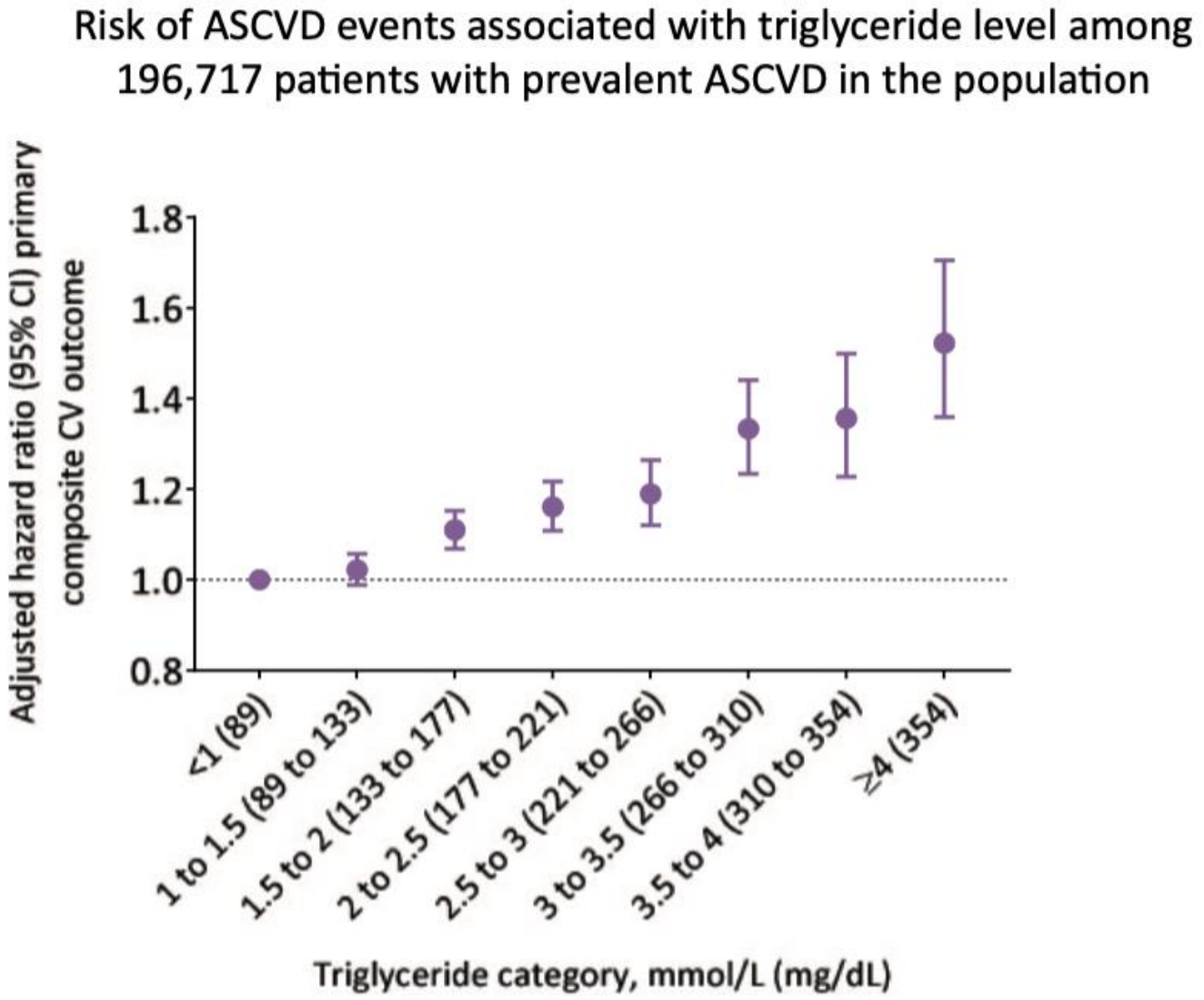
Come comprimere il rischio residuo dipendente dai trigliceridi
Alessandro Maloberti

CENTRO CONGRESSI FRENTANI
Roma, 21-22 novembre 2025

Azienda Ospedaliera
Ospedale Niguarda Ca' Granda

UNIVERSITÀ DEGLI STUDI DI MILANO BICOCCA

TRIGLICERIDI E RISCHIO CARDIOVASCOLARE



TRIGLICERIDI E RISCHIO CARDIOVASCOLARE

Dati dalle randomizzazioni mendeliane confermano il ruolo causale dei trigliceridi

Do people with more ***LDL***-raising alleles (1-SD ↑) have ***higher*** MI risk?

YES

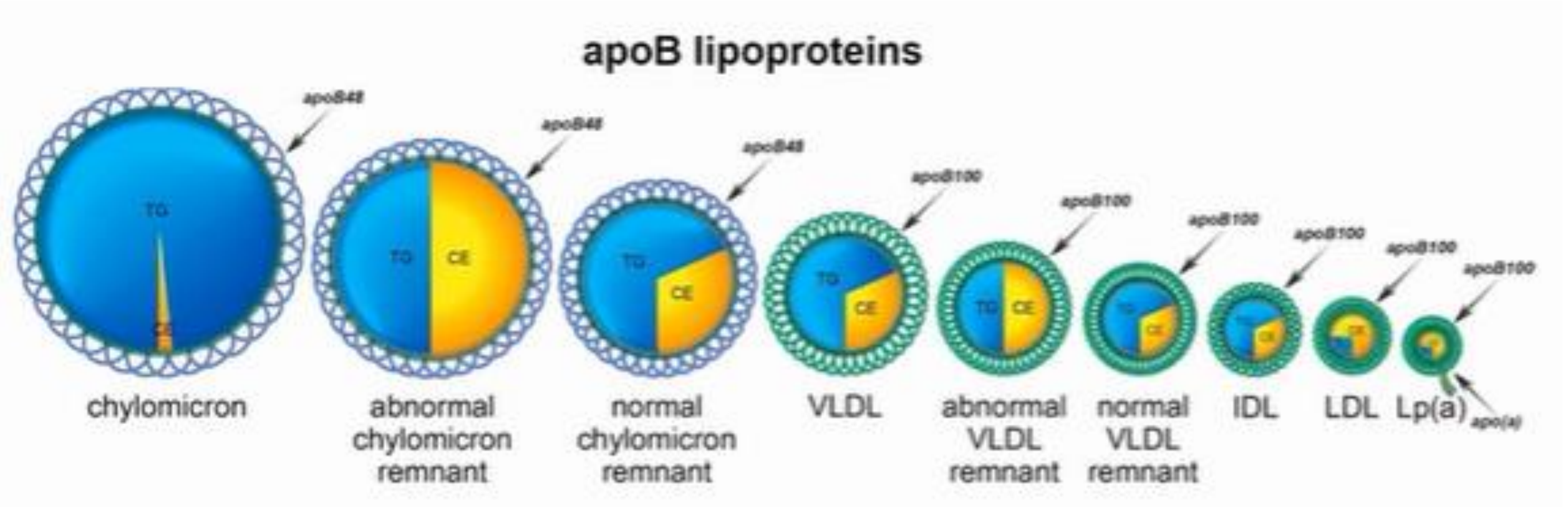
Do people with more ***HDL***-raising alleles (1-SD ↑) have ***lower*** MI risk?

NO

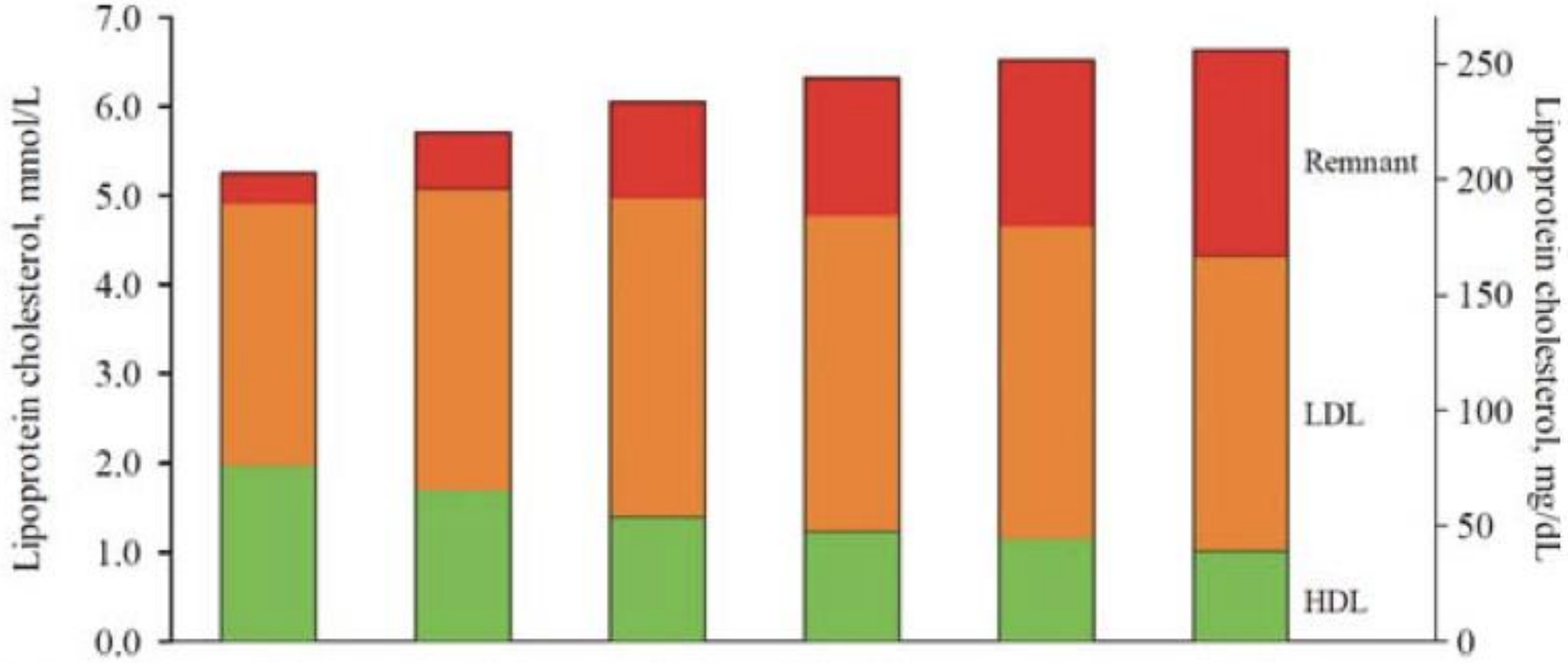
Do people with more ***TG***-raising alleles (1-SD ↑) have ***higher*** MI risk?

YES

TRIGLICERIDI E RISCHIO CARDIOVASCOLARE: meccanismi

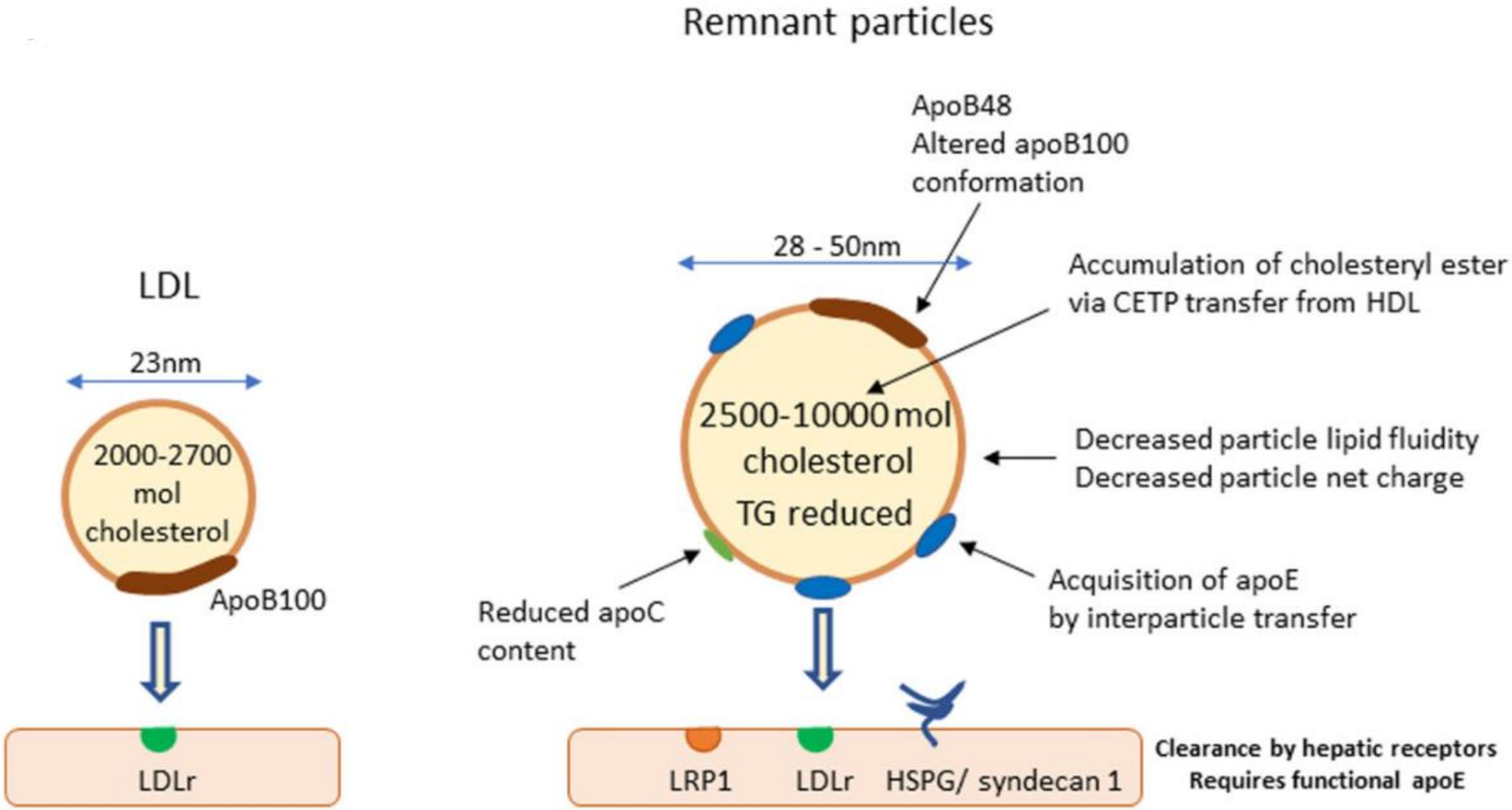


TRIGLICERIDI E RISCHIO CARDIOVASCOLARE: meccanismi

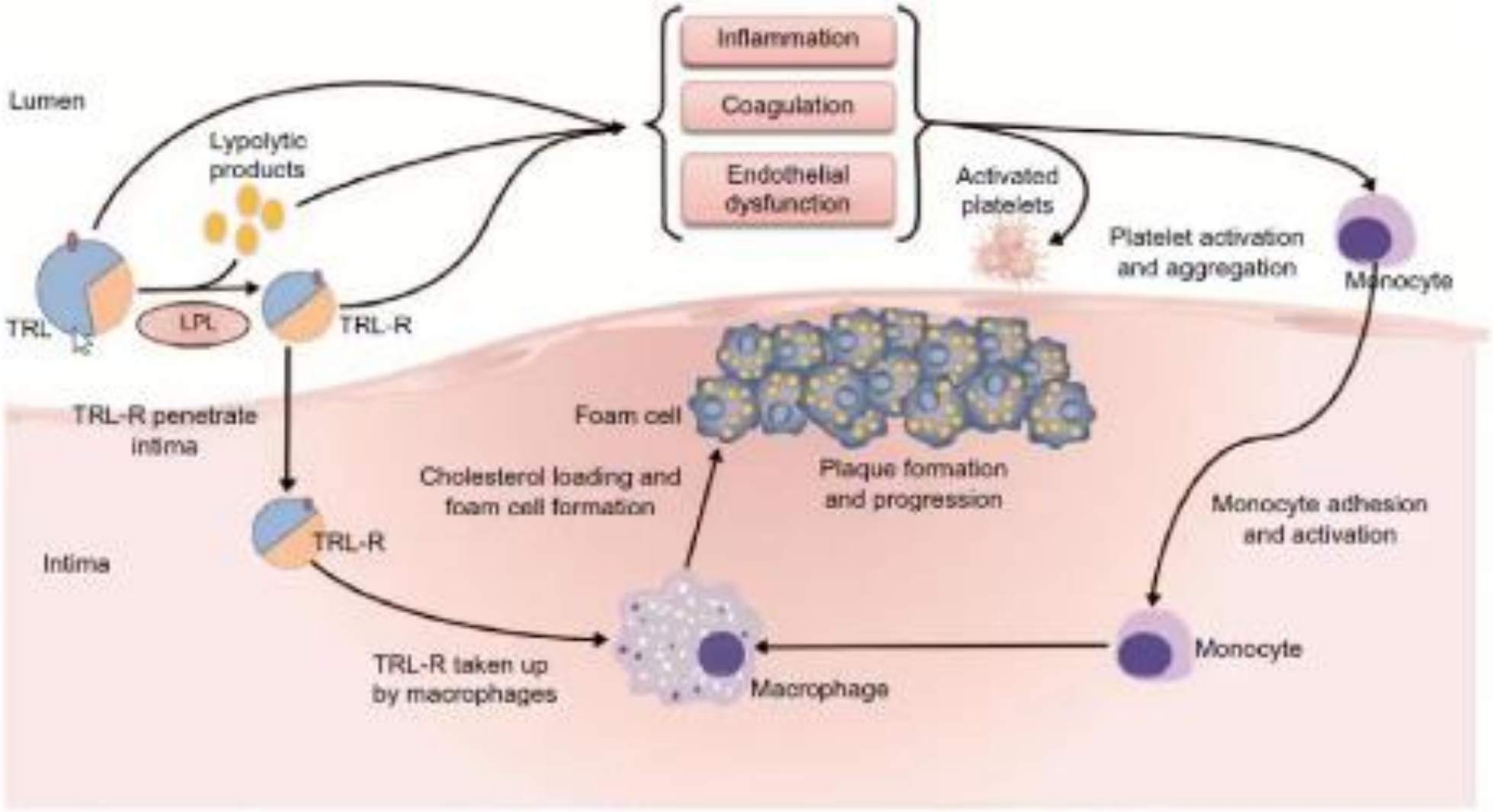


Triglycerides, mmol/L	< 1	1–1.99	2–2.99	3–3.99	4–4.99	≥ 5
mg/dL	< 89	89–176	177–265	266–353	354–442	≥ 443
Observations, No.	9347	16621	6348	2268	867	709

TRIGLICERIDI E RISCHIO CARDIOVASCOLARE: meccanismi



TRIGLICERIDI E RISCHIO CARDIOVASCOLARE: meccanismi



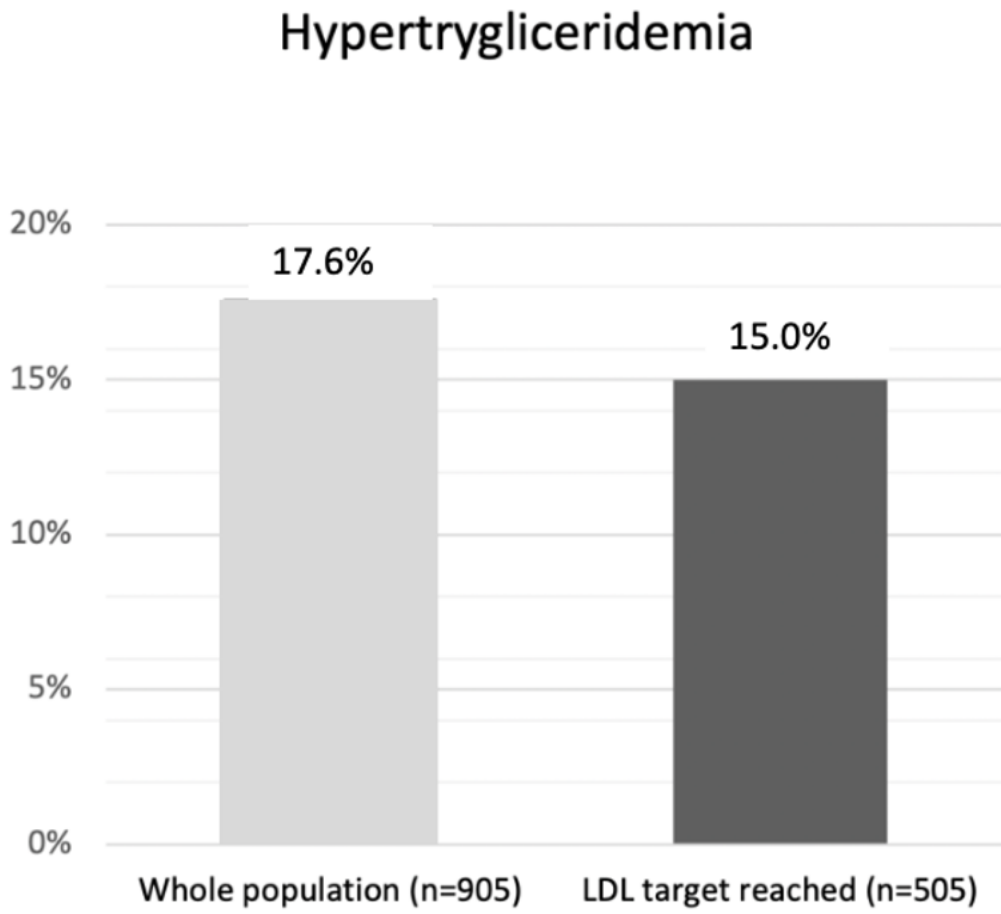
LPL, lipoprotein lipase; TRL, triglyceride-rich lipoproteins; TRL-R, triglyceride-rich lipoprotein remnants.

TRIGLICERIDI E RISCHIO CARDIOVASCOLARE: prevalenza

Int J Cardiol. 2025 Nov 15:439:133608. doi: 10.1016/j.ijcard.2025.133608. Epub 2025 Jul 11.

Prevalence of hypertriglyceridemia and its association with extreme cardiovascular risk in patients with acute and chronic coronary syndrome enrolled in a cardiac rehabilitation program

Chiara Tognola [1], Davide Bernasconi [2], Rita Cristina Myriam Intravaia [1], Giulia Brioschi [3], Giorgio Toscani [3], Michela Algeri [1], Atea Shkodra [3], Elvira Inglese [4], Luciana Sciumè [5], Romano Danesi [6], Giovanna Beretta [5], Cristina Giannattasio [7], Alessandro Maloberti [8]



TRIGLICERIDI E RISCHIO CARDIOVASCOLARE: terapia

TG-lowering therapies have not demonstrated CV benefit

TG-Lowering Agent	Key Trials*	Met 1° MACE Endpoint?
Fibrates	ACCORD[1] FIELD[2] PROMINENT[11]	✗
Niacin	AIM-HIGH[3] HPS2-THRIVE[4]	✗
Prescription and supplement, EPA + DHA mixtures	RISK & PREVENTION,[5] ORIGIN,[6] OMEGA,[7] ASCEND,[8] VITAL,[9] STRENGTH[10]	✗

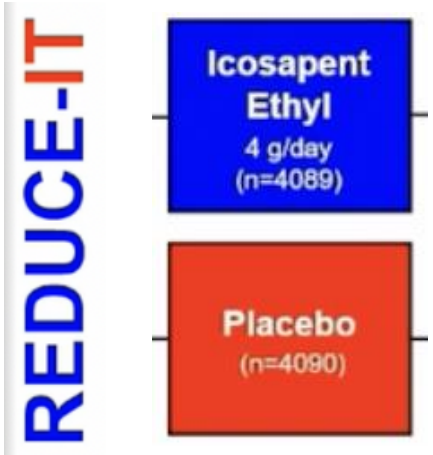
TRIGLICERIDI E RISCHIO CARDIOVASCOLARE: IPE

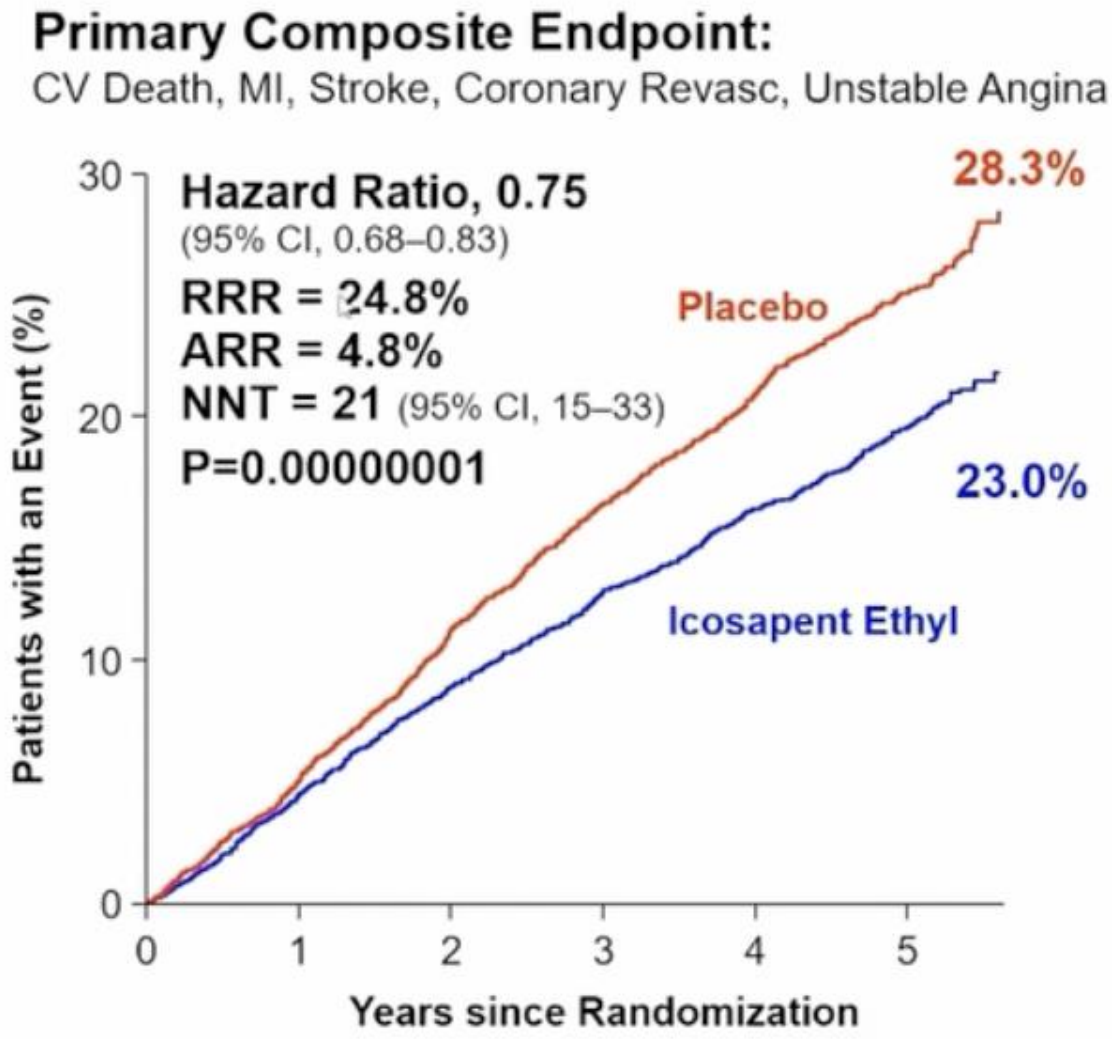
The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 JANUARY 3, 2019 VOL. 380 NO. 1

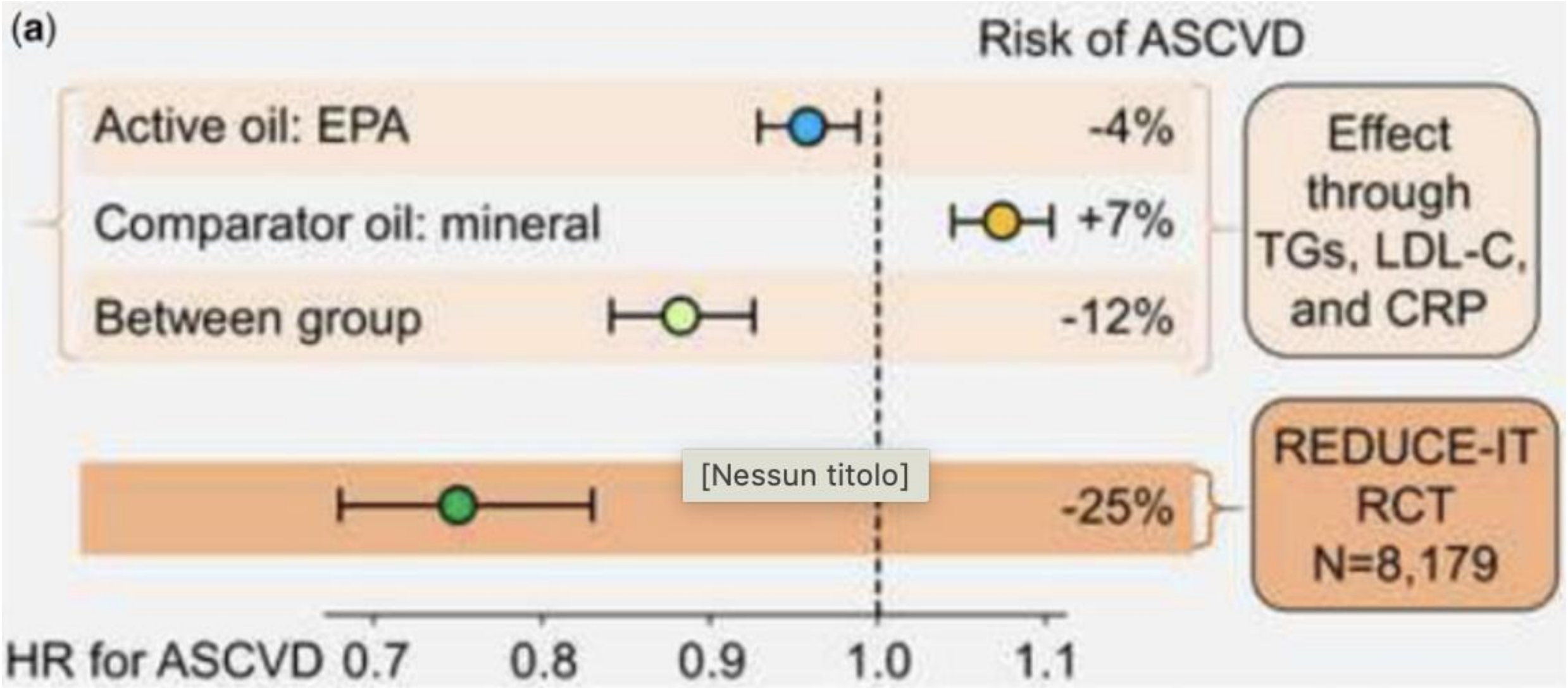
Cardiovascular Risk Reduction with Icosapent Ethyl for Hypertriglyceridemia

Deepak L. Bhatt, M.D., M.P.H., P. Gabriel Steg, M.D., Michael Miller, M.D., Eliot A. Brinton, M.D., Terry A. Jacobson, M.D., Steven B. Ketchum, Ph.D., Ralph T. Doyle, Jr., B.A., Rebecca A. Juliano, Ph.D., Lixia Jiao, Ph.D., Craig Granowitz, M.D., Ph.D., Jean-Claude Tardif, M.D., and Christie M. Ballantyne, M.D., for the REDUCE-IT Investigators*





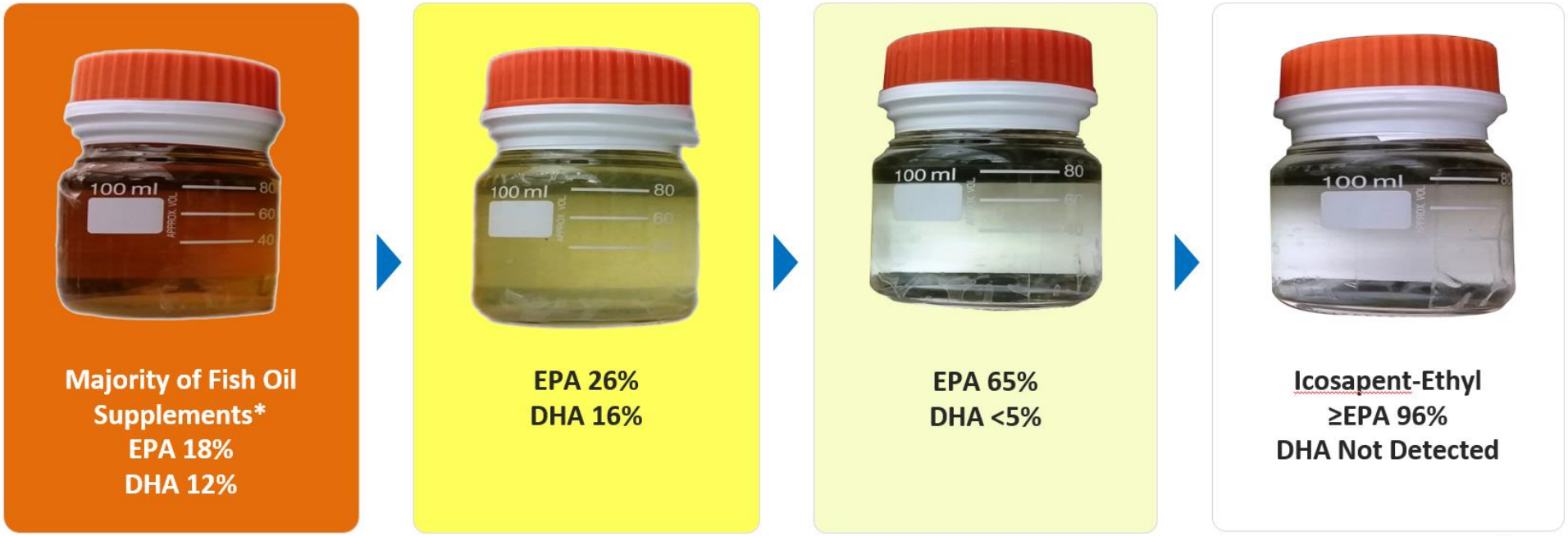
TRIGLICERIDI E RISCHIO CARDIOVASCOLARE: perché IPE si



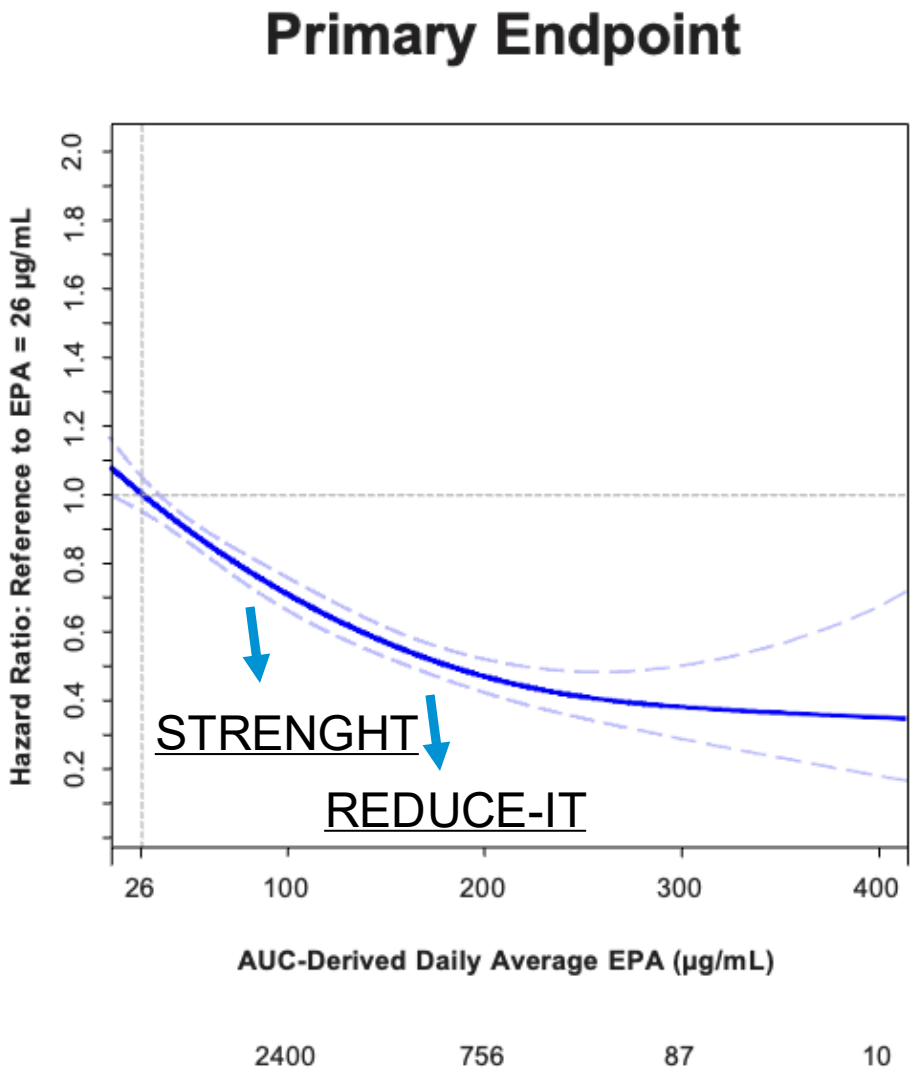
TRIGLICERIDI E RISCHIO CARDIOVASCOLARE: perché IPE si

STRENGHT

REDUCE-IT



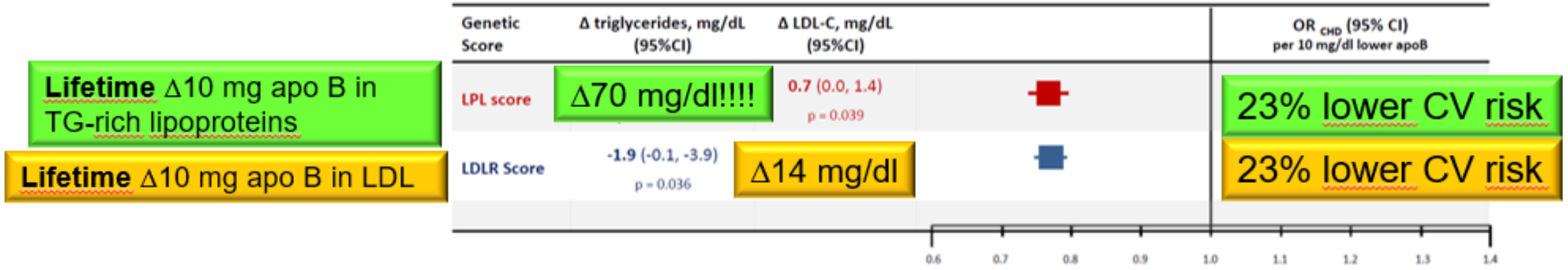
TRIGLICERIDI E RISCHIO CARDIOVASCOLARE: perché IPE si



TRIGLICERIDI E RISCHIO CARDIOVASCOLARE: perché IPE si

JAMA | Original Investigation

Association of Triglyceride-Lowering *LPL* Variants and LDL-C–Lowering *LDLR* Variants With Risk of Coronary Heart Disease



ESC Congress 2025 Madrid

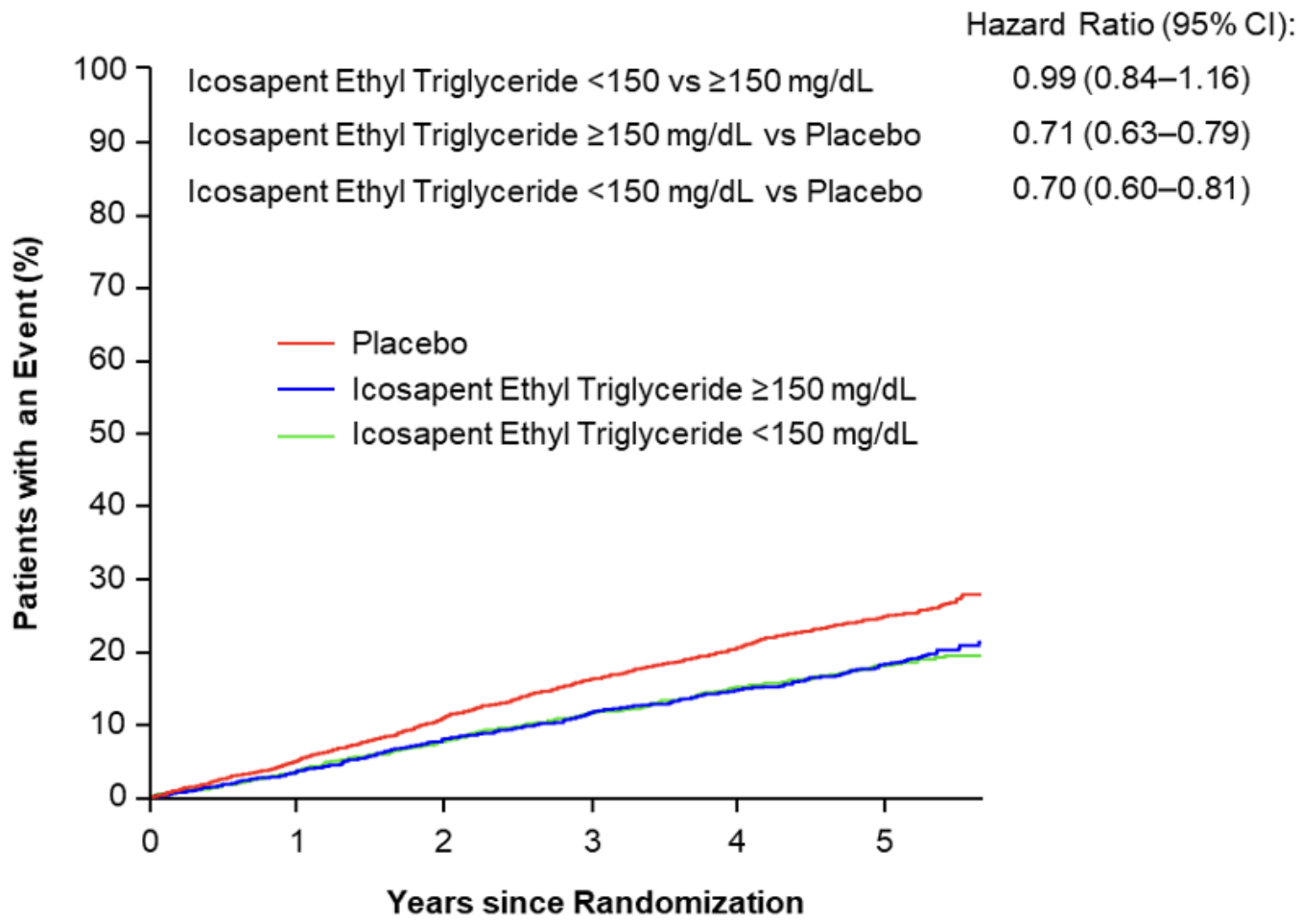
<u>Swedeheart – Tg</u>

51000 paz - Una riduzione sotto gli 0.5 mmol (44 mg/dL) correla con una riduzione dei MACE

Perché un farmaco possa funzionare deve ridurre i Tg di 80 mg/dL

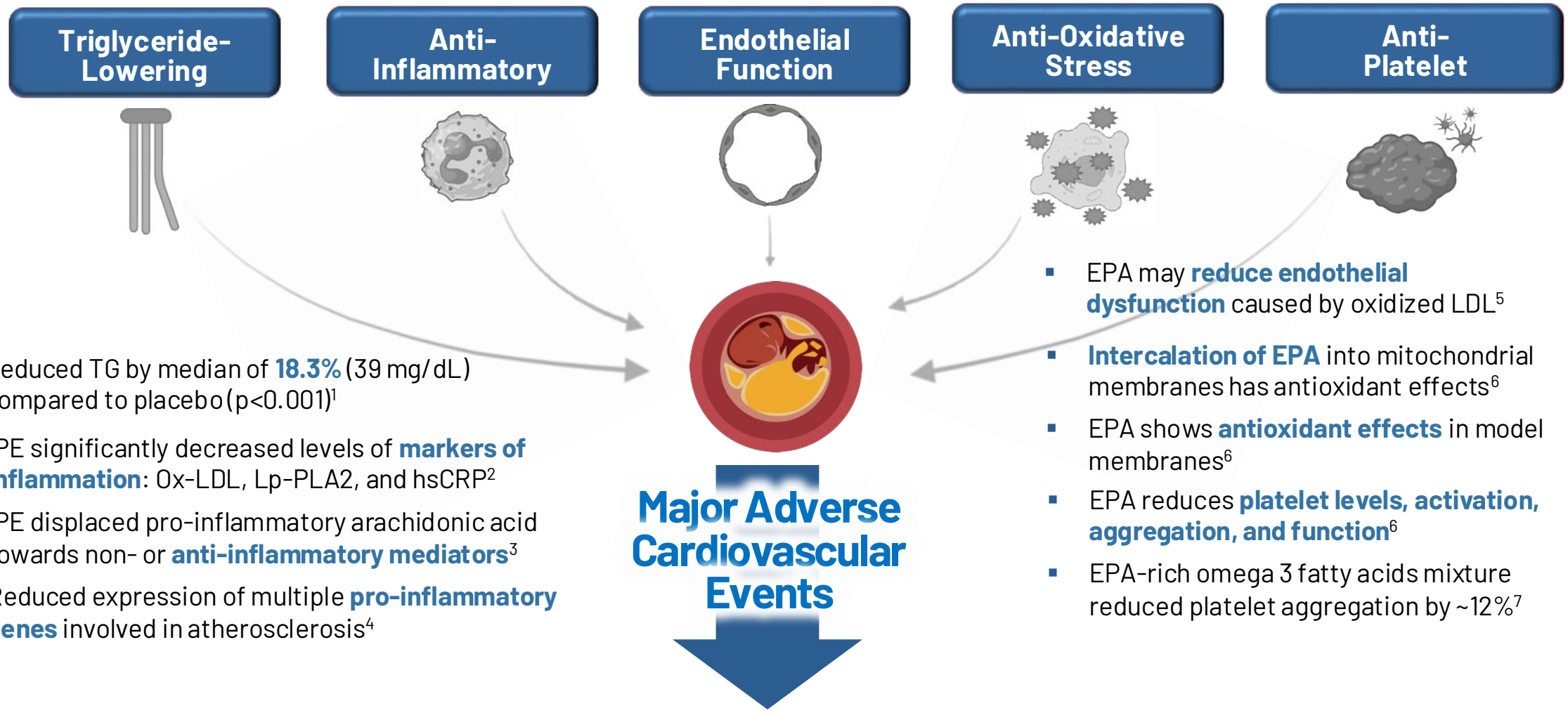
TRIGLICERIDI E RISCHIO CARDIOVASCOLARE: perché IPE si

A Primary End Point by Achieved Triglyceride Level at 1 Year



Triglyceride-Lowering

- Reduced TG by median of **18.3%** (39 mg/dL) compared to placebo (p<0.001)[1]
- IPE significantly decreased levels of **markers of inflammation**: Ox-LDL, Lp-PLA2, and hsCRP[2]
- IPE displaced pro-inflammatory arachidonic acid towards non- or **anti-inflammatory mediators**[3]
- Reduced expression of multiple **pro-inflammatory genes** involved in atherosclerosis[4]



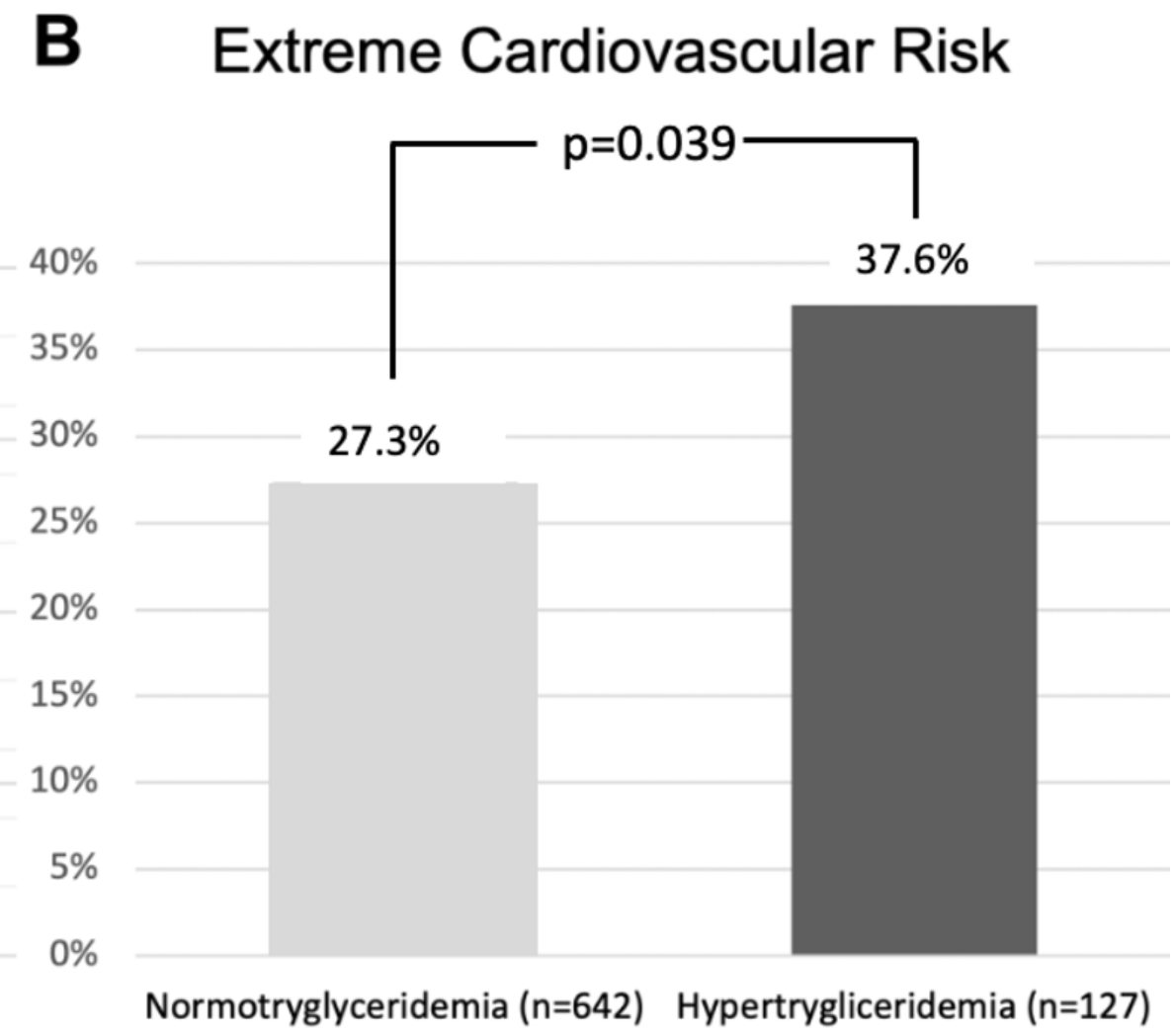
Anti-Oxidative Stress

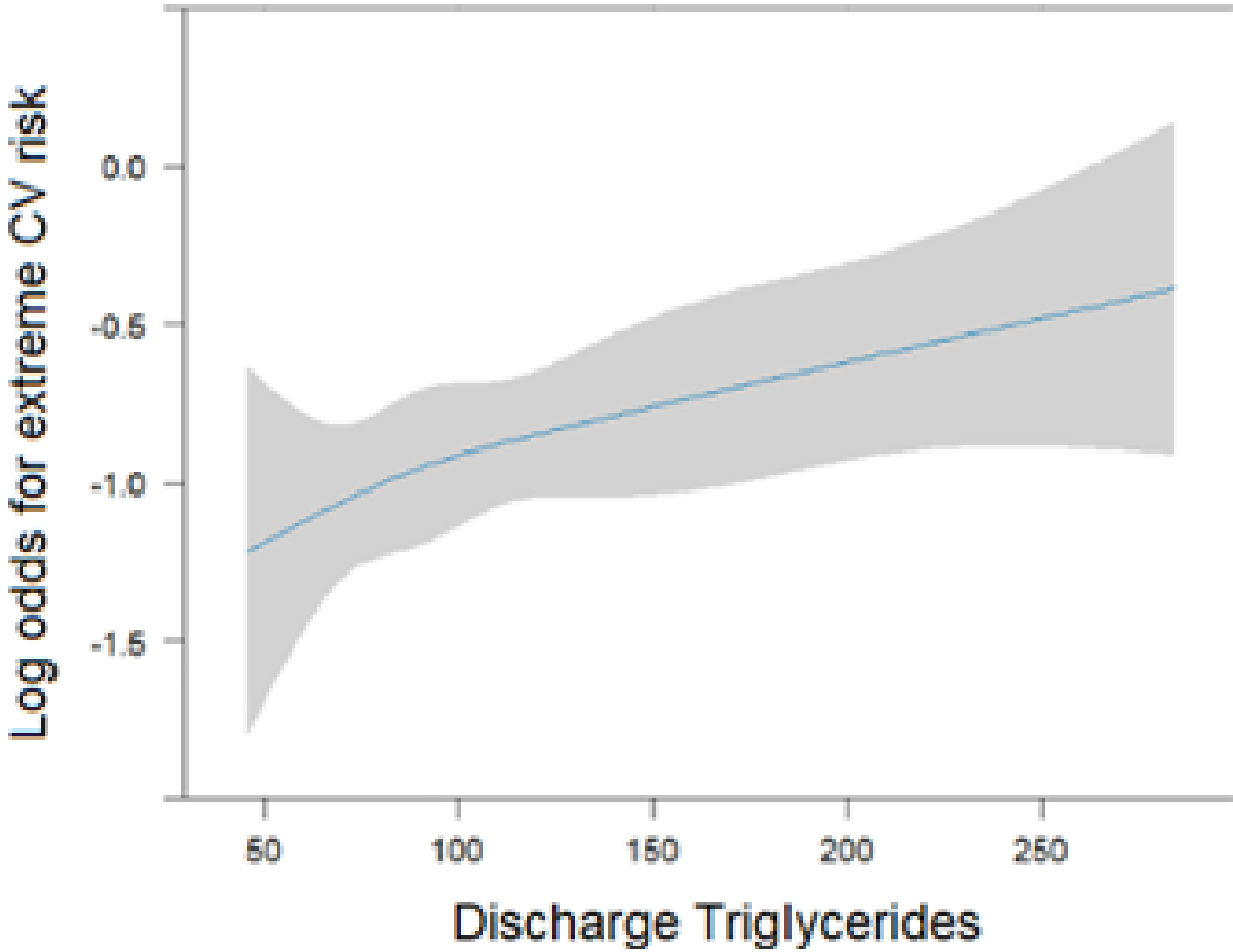
- EPA may **reduce endothelial dysfunction** caused by oxidized LDL[5]
- **Intercalation of EPA** into mitochondrial membranes has antioxidant effects[6]
- EPA shows **antioxidant effects** in model membranes[6]
- EPA reduces **platelet levels, activation, aggregation, and function**[6]
- EPA-rich omega 3 fatty acids mixture reduced platelet aggregation by ~12%[7]

Figure adapted from Bae JH, et al. *Advances in Nutrition.* 2023. https://doi.org/10.1016/j.advnut.2023.03.014

1. Bhatt DL, et al. *New Eng J Med.* 2019;380:11-22; 2. Bays HE, et al. *Am J Cardiovasc Drugs*. 2013:37-46; 3. VAZKEPA SmPC, Annex I, Summary of Product Characteristics; 4. Tsunoda F, et al. *Atherosclerosis*. 2015;241:400-408; 5. Mason RP, et al. *Biomed Pharmacother*. 2018;103:1231-1237; 6. Mason RP, et al. *Arterioscler Thromb Vasc Biol*.2020;40(5):1135-1147; 7. Phang M, et al. *J Nutr*. 2013;143(4):457-46

TRIGLICERIDI E RISCHIO CARDIOVASCOLARE: rischio estremo





TRIGLICERIDI E RISCHIO CARDIOVASCOLARE: rischio estremo

Dependent variable: extreme CV risk	Model A: Triglycerides		Model B: Hypertriglyceridemia	
Co-variates	OR (95 % CI)	P-value	OR (95 % CI)	P-value
Age, per years	1.017 (0.996 - 1.039)	0.117	1.017 (0.996 – 1.039)	0.115
Sex (female vs male)	0.595 (0.346 – 1.022)	0.060	0.579 (0.337 -0.994)	0.047
eGFR (per ml/min)	0.990 (0.978 – 1.002)	0.110	0.990 (0.978 – 1.002)	0.092
Discharge LDL cholesterol (per mg/dL)	0.991 (0.983 – 0.998)	0.018	0.991 (0.983 – 0.999)	0.020
ACS (yes vs no)	1.600 (0.969 – 2.642)	0.066	1.552 (0.938 – 2.565)	0.087
Discharge Triglycerides (per 10 mg/dL)	1.045 (1.010 – 1.081)	0.011	-	-
Hypertriglyceridemia (yes vs no)	-	-	1.773 (1.124 – 2.797)	0.014

TRIGLICERIDI E RISCHIO CARDIOVASCOLARE: rischio estremo

ESC European Society of Cardiology
European Heart Journal (2022) 43, 1784–1786 https://doi.org/10.1093/eurheartj/ehab771

Extreme cardiovascular risk—do we need a new risk category?

Krzysztof Dyrbuś [1,2], Mariusz Gąsior[1,2], Peter E. Penson [3,4], and Maciej Banach [5,6,7]*

1. In primary prevention with a (Pol)SCORE of >20% (e.g. a 60-year-old man with smoking, systolic blood pressure >160 mmHg, and total cholesterol 6 mmol/L)[a]
2. A history of ACS and other vascular events within the last 2 years
3. After ACS with peripheral vascular disease or polyvascular disease
4. After ACS with concomitant multivessel coronary artery disease
5. After ACS with familial hypercholesterolaemia
6. After ACS with diabetes and at least one additional risk factor [elevated Lp(a) >50 mg/dL or hsCRP >3 mg/L or chronic kidney disease (eGFR <60 mL/min/1.73 m^2)]

- Patients with ASCVD who experience recurrent vascular events while taking maximally tolerated statin-based therapy
- Patients with polyvascular (e.g. coronary and peripheral) arterial disease

Extreme risk

TRIGLICERIDI E RISCHIO CARDIOVASCOLARE: rischio estremo

ORIGINAL ARTICLE
European Heart Journal - Cardiovascular Pharmacotherapy (2024) 10, 488–499
https://doi.org/10.1093/ehjcvp/pvae030
ESC European Society of Cardiology

Effects of icosapent ethyl according to baseline residual risk in patients with atherosclerotic cardiovascular disease: results from REDUCE-IT

Pascal M. Burger[1], Deepak L. Bhatt[2], Jannick A.N. Dorresteijn[1], Stefan Koudstaal[3,4], Arend Mosterd[3,5], Fabrice M.A.C. Martens[3,6], Philippe Gabriel Steg[7] and Frank L.J. Visseren[1,*]; for the REDUCE-IT Investigators

Study population

REDUCE-IT participants with ASCVD (n = 5,785):

- EPA: Icosapent ethyl 2 g b.i.d. (n = 2,892)
- vs
- Placebo (n = 2,893)

CVD risk prediction

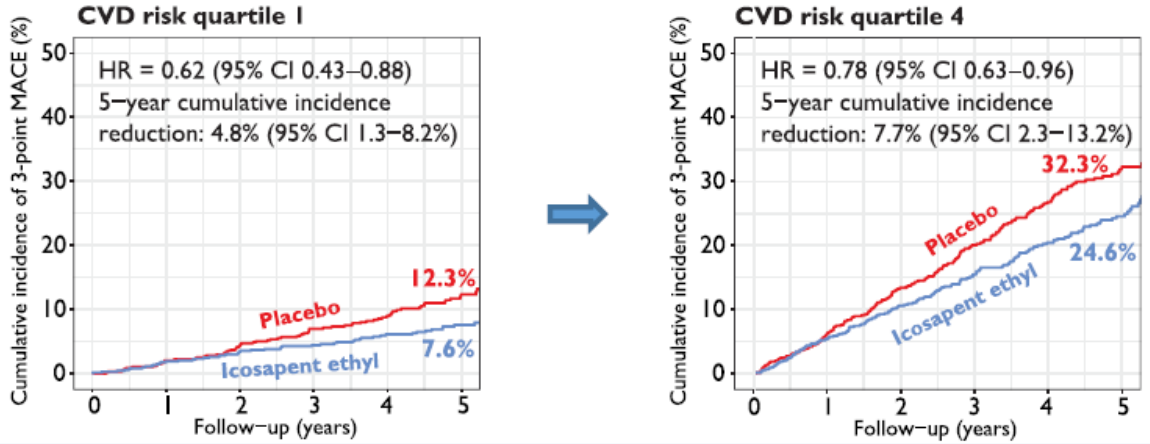
1. Predict individual baseline 5-year risk of 3-point MACE (MI, stroke, or CV death) with SMART2 risk score.
2. Divide study population in CVD risk quartiles.

Effects of icosapent ethyl

1. Test treatment-by-risk interaction.
2. Assess treatment effects stratified by CVD risk quartiles.

5,785 patients with ASCVD – **4.8** years median follow-up – **850** 3-point MACE events

Cumulative incidence of MACE in the lowest vs highest CVD risk quartile

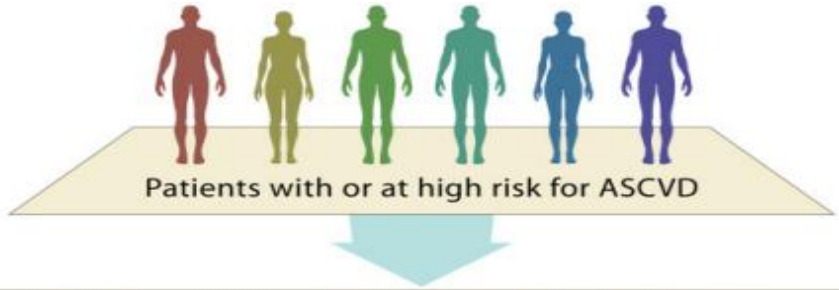


Effects of icosapent ethyl on 3-point MACE according to CVD risk quartile

	All ASCVD patients	CVD risk quartile 1	CVD risk quartile 2	CVD risk quartile 3	CVD risk quartile 4
5-year risk	3.6-83.0%	<11.5%	11.5-16.0%	16.1-23.3%	>23.3%
HR* (95% CI)	0.72 (0.63-0.82)	0.62 (0.43-0.88)	0.66 (0.48-0.92)	0.69 (0.53-0.90)	0.78 (0.63-0.96)
ARR (95% CI)	4.4% (2.6-6.2%)	3.9% (1.0-6.8%)	4.3% (1.2-7.3%)	5.1% (1.4-8.7%)	5.6% (1.3-10.0%)
NNT (95% CI)	23 (16-38)	26 (15-98)	24 (14-84)	20 (11-70)	18 (10-77)

* Treatment-by-risk interaction: p = 0.106

TRIGLICERIDI E RISCHIO CARDIOVASCOLARE: rischio estremo



Despite contemporary evidence-based therapies*, residual risk of ASCVD events persists

Biological Issue	Residual Cholesterol Risk	Residual Inflammatory Risk	Residual Thrombotic Risk	Residual Triglyceride Risk	Residual Lp(a) Risk	Residual Diabetes Risk
Critical Biomarker	LDL-C ≥100 mg/d	hsCRP ≥2mg/L	No simple biomarker	TG ≥150mg/dL	Lp(a) ≥50mg/dL	HbA1c Fasting glucose
Potential Intervention	Targeted LDL/Apo B Reduction	Targeted Inflammation Reduction	Targeted Antithrombotic Reduction	Targeted Triglyceride Reduction	Targeted Lp(a) Reduction	SGLT2 Inhibitors GLP-1 Agonists
Randomized Trial Evidence	IMPROVE-IT FOURIER SPIRE ODYSSEY	CANTOS COLCOT *LoDoCo2* *OASIS-9*	PEGASUS COMPASS THEMIS	REDUCE-IT *PROMINENT*	Planned	EMPA-REG CANVAS DECLARE CREDENCE LEADER SUSTAIN-6 REWIND

Residual Obesity Risk

BMI

Semaglutide
Tirzepatide

SELECT
SOUL
SUMMIT

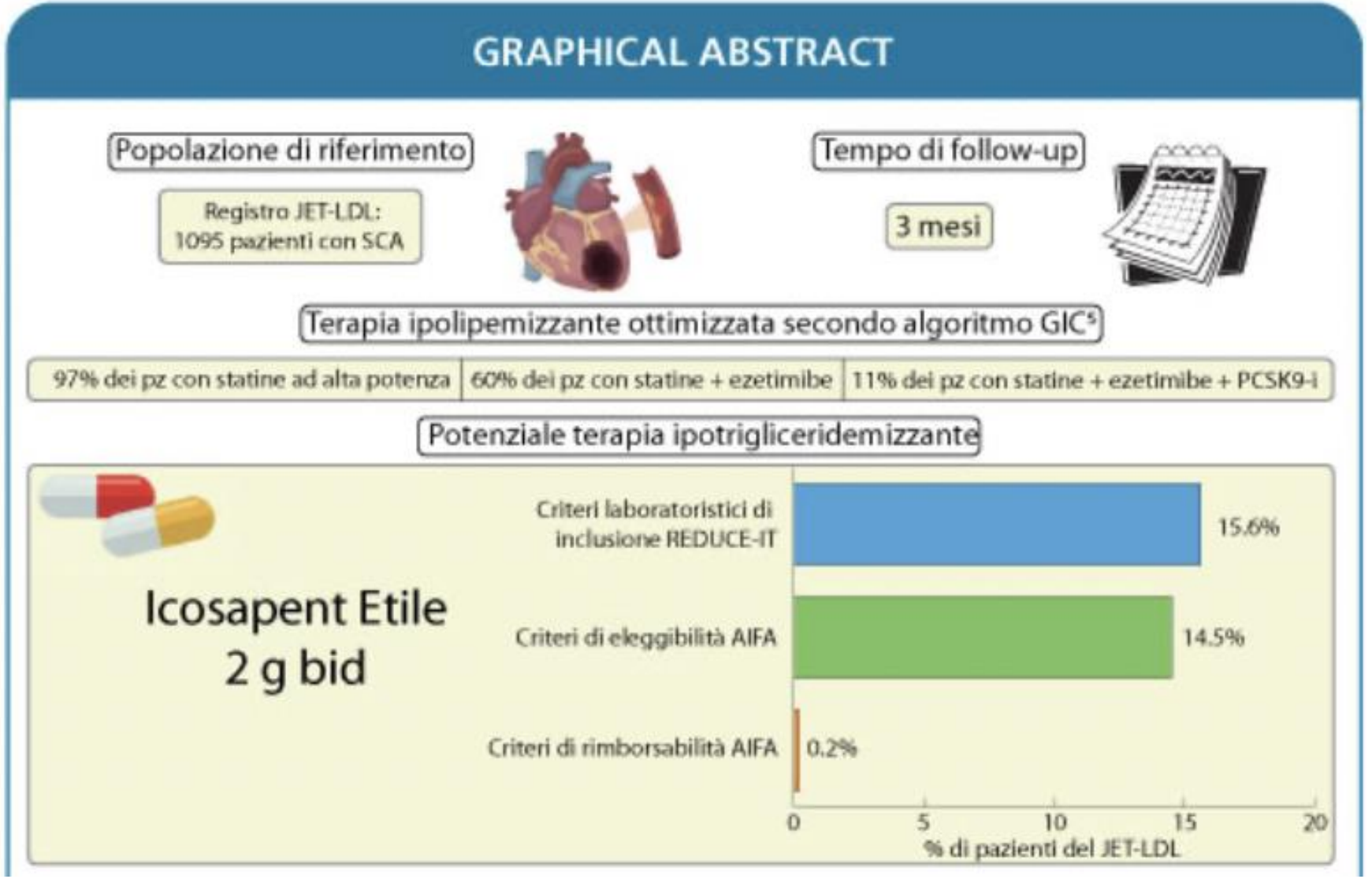
TRIGLICERIDI E RISCHIO CARDIOVASCOLARE: prescrivibilità

CRITERI DI RIMBORSABILITÀ SECONDO AIFA

- ASCVD accertata di età compresa tra 18e 80 aa
- BMI≥ 27 kg/m2
- TG>200 mg/dl in tre determinazioni nonostante regime dietetico
- LDL <70 mg/dl
- On top a statine ad alta intensità alla massima dose tollerata +ezetimibe o triplice con statine+ ezetimibe+ bempedoico
- Non in associazione con PCSK9i o Inclisiran

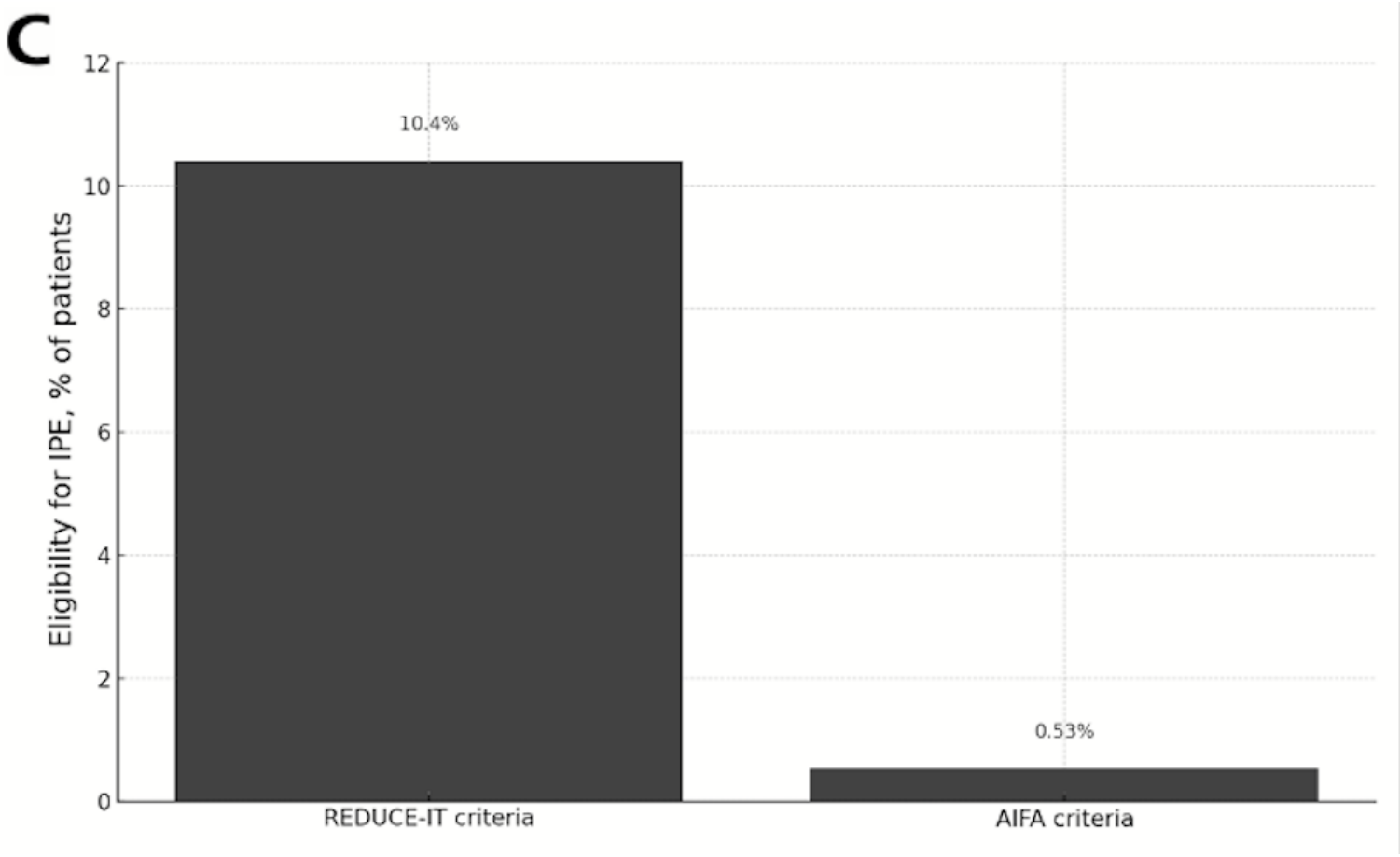
TRIGLICERIDI E RISCHIO CARDIOVASCOLARE: prescrivibilità

[Real-world triglyceride levels in secondary prevention: insights from the JET-LDL registry].
Sparasci FM, Raone L, Currao A, Munafò AR, Visconti LO, Musumeci G, Ferlini M.
G Ital Cardiol (Rome). 2025 Aug;26(8):613-618. doi: 10.1714/4531.45338.



TRIGLICERIDI E RISCHIO CARDIOVASCOLARE: prescrivibilità

	CR Admission
Number	1129



TRIGLICERIDI E RISCHIO CARDIOVASCOLARE: prescrivibilità

Patients referred to ASST GOM Niguarda (Milan, Italy) for cardiac rehabilitation program due to acute or cronic coronary syndrome in the period between January 2012 and June 2025

N = 1129

Patients excluded
N = 1123

Patients meeting AIFA eligibility criteria

N = 6

Reason for Exclusion	No. of Patient Excluded
Triglycerides < 200 mg/dL	769
BMI < 27 Kg/m^2	633
LDL ≥ 70 mg/dL	278
Absence of Ezetimibe	296
Absence of Statins	248
Age out of 18-80 range	28

No. of Exclusion Criteria Met	No. of Patient
1 criterion	123
2 criteria	290
3 criteria	377
4 criteria	214
5 criteria	116
6 criteria	3