Il Controllo dei Parametri Lipidici

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Conflitti di interesse

Ai sensi dell'art. 3.3 sul conflitto di interessi, pag 17 del Regolamento Applicativo Stato-Regioni del 5/11/2009, dichiaro che negli ultimi 2 anni NON ho avuto rapporti diretti di finanziamento con i soggetti portatori di interessi commerciali in campo sanitario

Outline

- Caso clinico
- LDLc: is lower better ?
- La dislipidemia diabetica ed il rischio residuo
- Lipidi e rischio cardiovascolare nel paziente con IRC
- Statine e rene: la lezione dei trials
- Dai RCP alle linee guida

Caso clinico

- G.A., 70 anni
- DM 2 in terapia con GLP-1 RA + (Met RM 500/die) + ins. basale
- Ipertensione arteriosa in trattamento farmacologico con ACE-I / CA-antagonisti
- Cardiopatia ischemica cronica, già sottoposta a rivascolarizzazione percutanea
- Retinopatia proliferante, già laser – trattata
- IRC stadio IIIB

Esami ematochimici

- Hba1c: 7%
- CT: 199 HDL: 35 TG: 250 LDL-C: 114
- Creatinina: 2.15 mg/dl
- Clearance calc. sec. CKD: 30.1 ml/min/1.73m^2
- Proteinuria: 350 mg/24h

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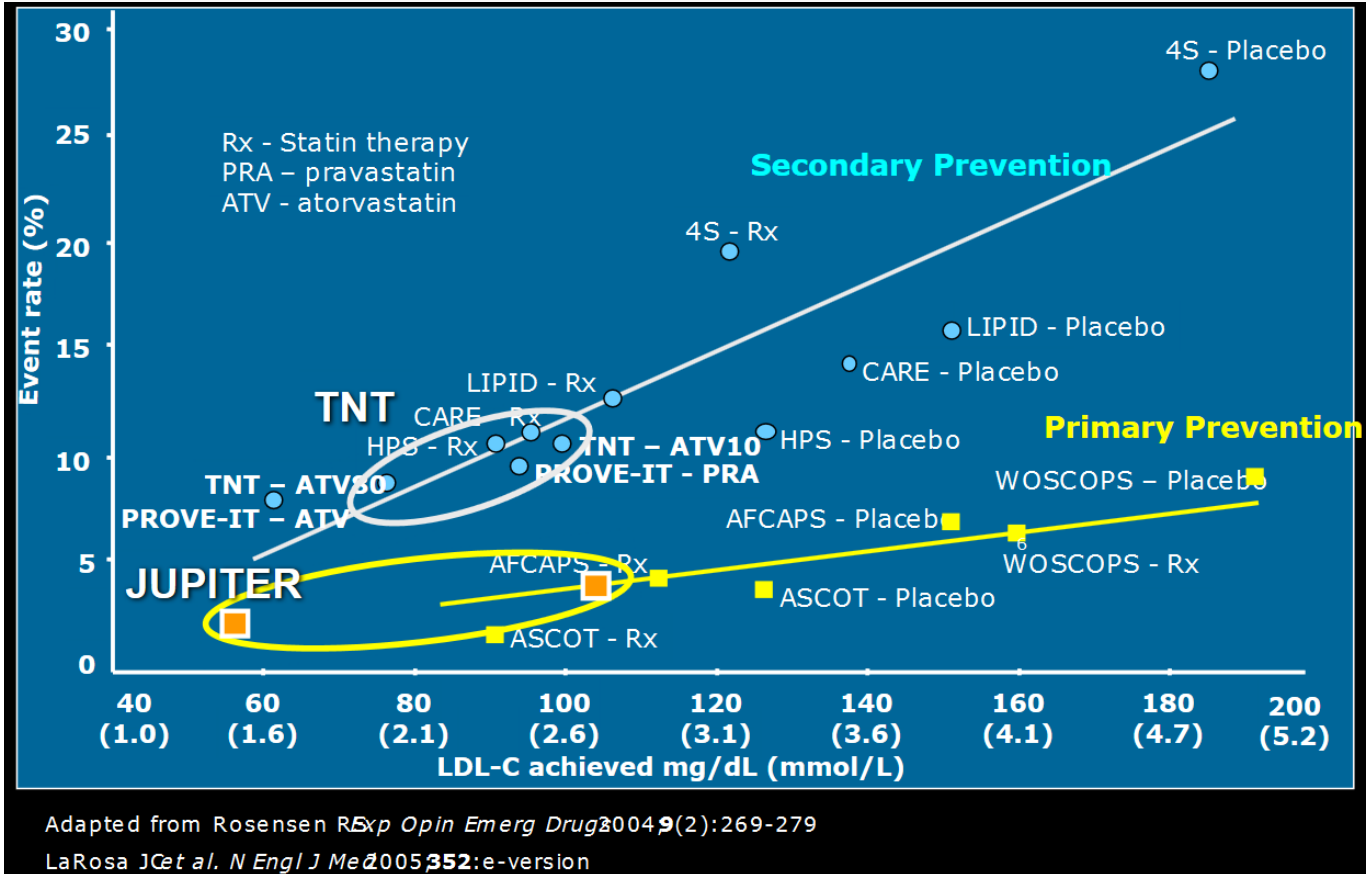
LDL Cholesterol and benefit in clinical trials
Is lower better?



Adapted from Rosensen RS. *Exp Opin Emerg Drugs* 2004; **9**(2):269-279
LaRosa JC *et al. N Engl J Med* 2005; **352**:e-version

Cholesterol Treatment Trialists' 2010: Efficacy of Intensive LDL-C Lowering in Patients With Low Baseline LDL-C

Meta-analysis of randomized controlled trials of major vascular events (coronary death, myocardial infarction, coronary revascularization, and ischemic stroke) with at least 1,000 patients and ≥2 years of more vs. less intense statin dosage (N=169,138)

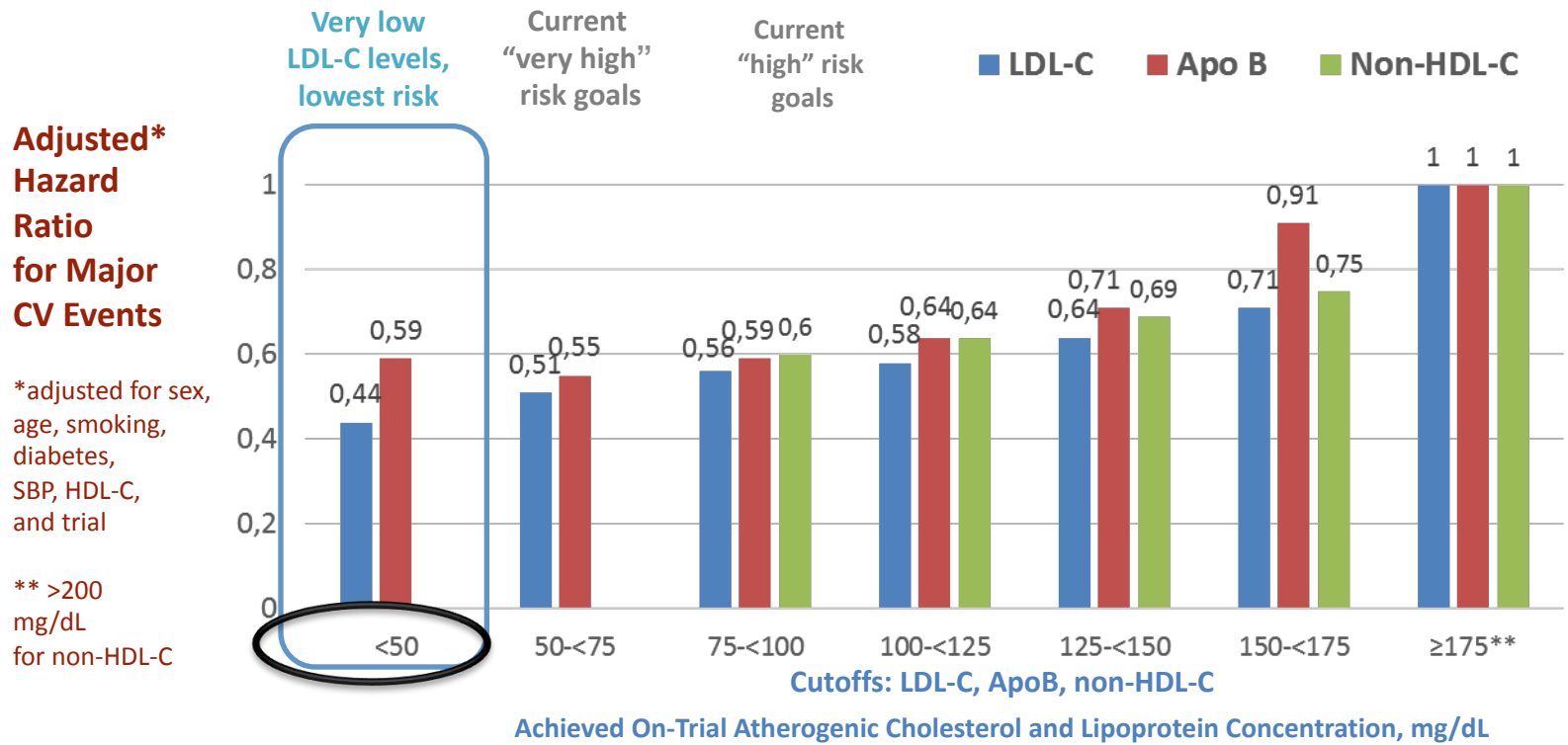
For each 39 mg/dL reduction in LDL-C:

- Individuals with baseline LDL-C <77 mg/dL had a **29%** further reduction in major vascular events (*P*=0.007)
- Those with baseline LDL-C <70 mg/dL had a **37%** further reduction in major vascular events (*P*=0.004)

Abbreviation: LDL-C, low-density lipoprotein cholesterol.

Cholesterol Treatment Trialists' Collaboration. *Lancet* 2010;376:1670-1681; Jellinger P, Handelsman Y, Rosenblit P, et al. *Endocr Practice*. 2017;23(4):479-497.

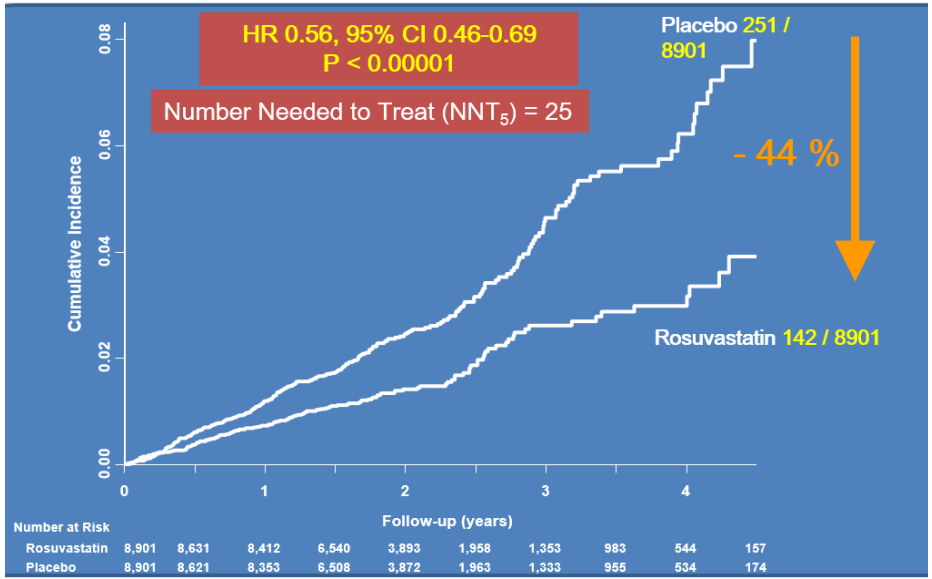
Meta-analysis of 8 Statin Trials (Moderate- to High-Intensity Dosing): Patients Who Achieved Very Low LDL-C Levels Had Lower Risk for Major Cardiovascular Events



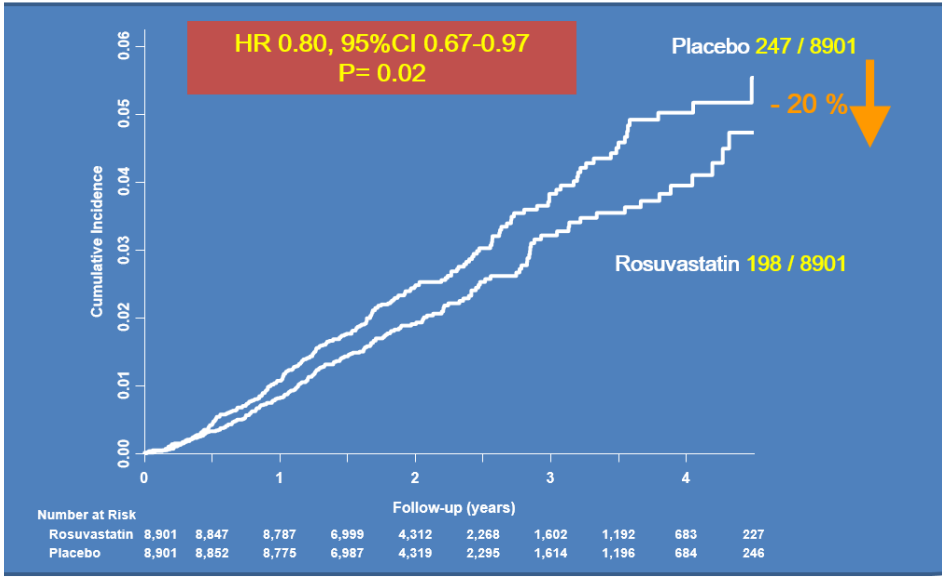
Abbreviations: apo, apolipoprotein; CV, cerebrovascular; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol.

Boekholdt SM, et al. *J Am Coll Cardiol*. 2014;64(5):485-494.

Primary Trial Endpoint: MI, Stroke, UA/Revascularization, CV Death



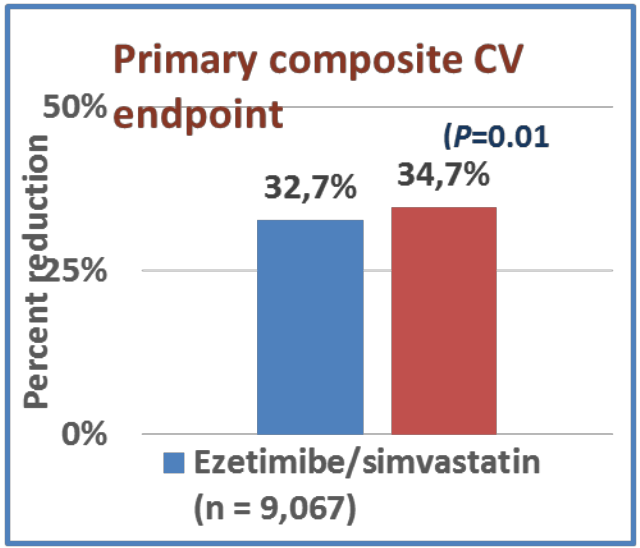
Secondary Endpoint: All Cause Mortality



Ridker et al NEJM 2008

IMPROVE-IT: Improved Reduction of Outcomes, Vytorin Efficacy International Trial

Trial design: Patients with recent ACS were randomized 1:1 to either ezetimibe 10 mg + simvastatin 40 mg or simvastatin 40 mg and followed for a median of 6 years



Abbreviations: ACS, acute coronary syndrome; CV, cardiovascular; CVD, cardiovascular disease; LDL, low-density lipoprotein; LDL-C, low-density lipoprotein cholesterol; MI, myocardial infarction.

Cannon CP, et al. *N Engl J Med.* 2015;372:2387-2397.

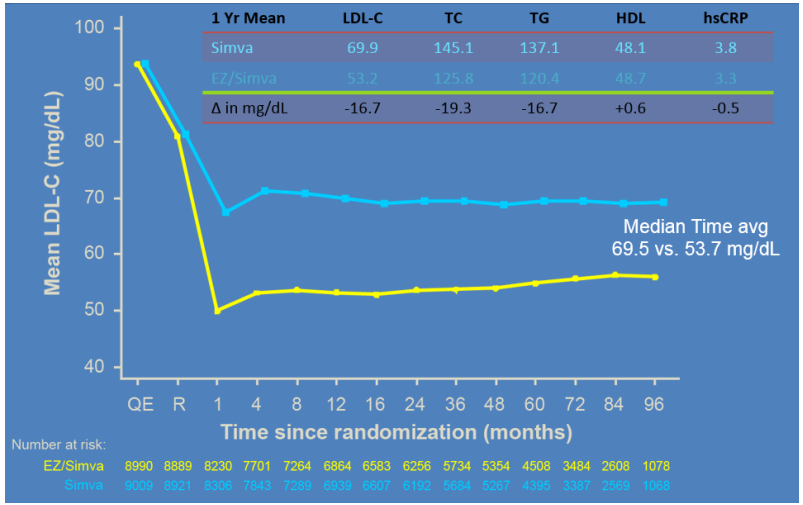
Results

- Primary endpoint (CV death/MI/UA/coronary revasc/stroke/moderate/severe bleeding) for ezetimibe/simvastatin vs. simvastatin: 32.7% vs. 34.7% (HR 0.94, 95% CI 0.89-0.99; *P*=0.016)
- MI: 13.1% vs. 14.8%, *P*=0.002; stroke: 4.2% vs. 4.8%, *P*=0.05; CVD/MI/stroke: 20.4% vs. 22.2%, *P*=0.003
- Median LDL follow-up average: 53.7 vs. 69.5 mg/dL

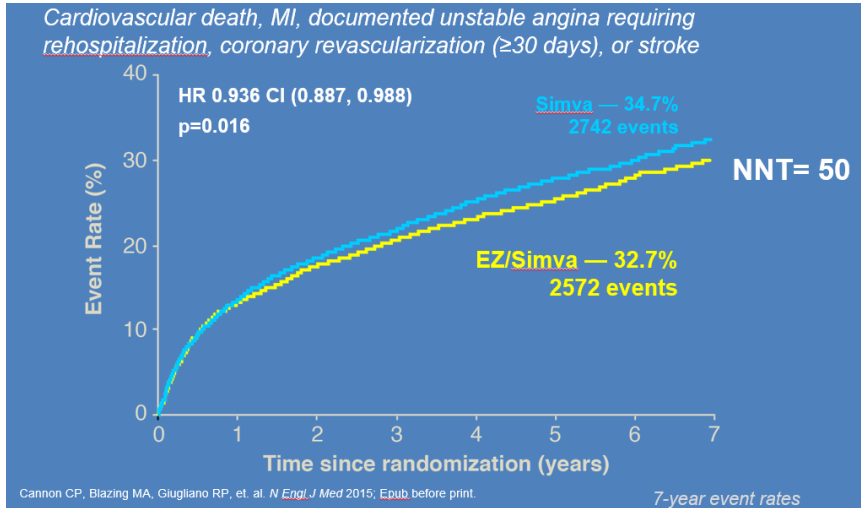
Conclusions

- In patients with high-risk ACS, ezetimibe 10 mg/simvastatin 40 mg was superior to simvastatin 40 mg alone in reducing adverse CV events
- This is the first study powered for clinical outcomes to show a benefit with a non-statin agent
- Reaffirms the “lower is better” hypothesis with LDL-C

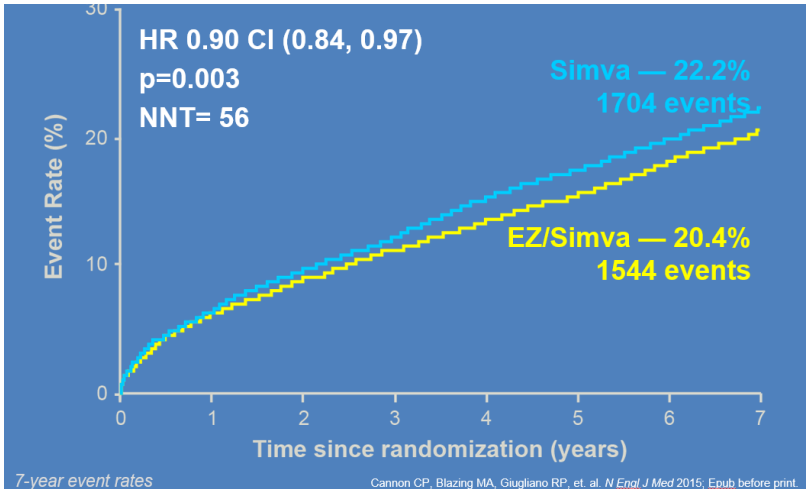
LDL-C and Lipid Changes



Primary Endpoint - ITT



CV Death, Non-fatal MI, or Non-fatal Stroke

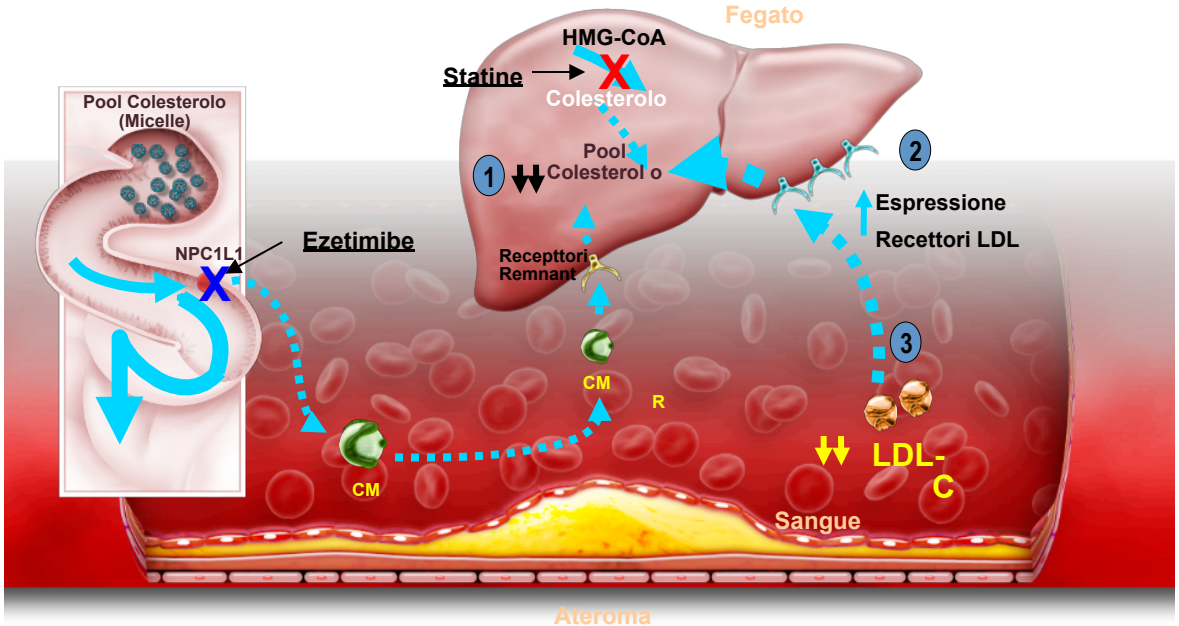


IMPROVE-IT

Ezetimibe e statine hanno un meccanismo d'azione complementare

L'ezetimibe associata alla statina permette di ottenere:

1. Riduzione del colesterolo epatico
2. Aumentata espressione di recettori per LDL-C
3. Aumentata clearance di LDL-C



NPC1L1 = Niemann-Pick C1-like 1; HMG-CoA = 3-hydroxy-3-methylglutaryl acetyl coenzyme A; CMR = chylomicron remnant.

1. Grigore L et al. *Vas Health Risk Manag.* 2008;4:267–278.

Conclusions

- IMPROVE-IT: First trial demonstrating incremental clinical benefit when adding a non-statin agent (ezetimibe) to statin therapy:
  - **YES:** *Non-statin* lowering LDL-C with ezetimibe reduces cardiovascular events
  - **YES:** Even Lower is Even Better (achieved mean LDL-C 53 vs. 70 mg/dL at 1 year)
  - **YES:** Confirms ezetimibe safety profile

- Reaffirms the LDL hypothesis, that reducing LDL-C prevents cardiovascular events
- Results could be considered for future guidelines

Cannon CP, Blazing MA, Giugliano RP, et. al. *N Engl J Med* 2015; Epub before print.

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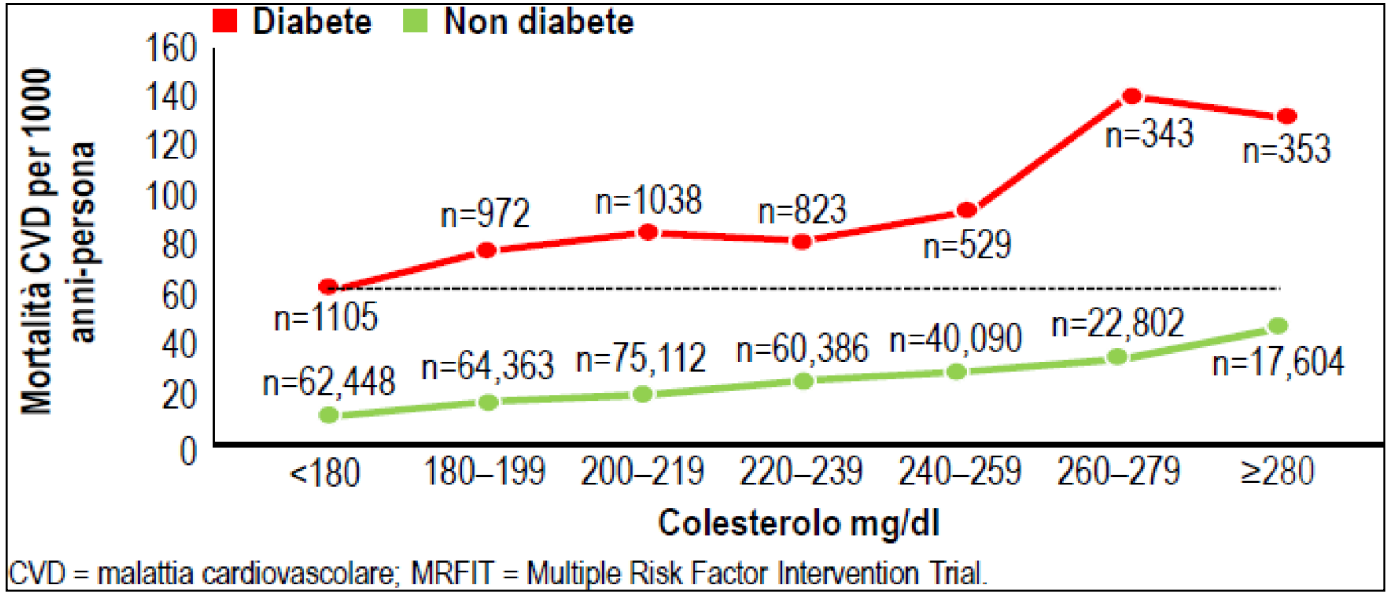
I pazienti con diabete e basso colesterolo hanno una mortalità cardiovascolare superiore ai pazienti con alto colesterolo senza diabete

Studio di coorte condotto su 347.978 pazienti maschi (età 35-57 anni), valutati in 20 centri partecipanti allo studio MRFIT

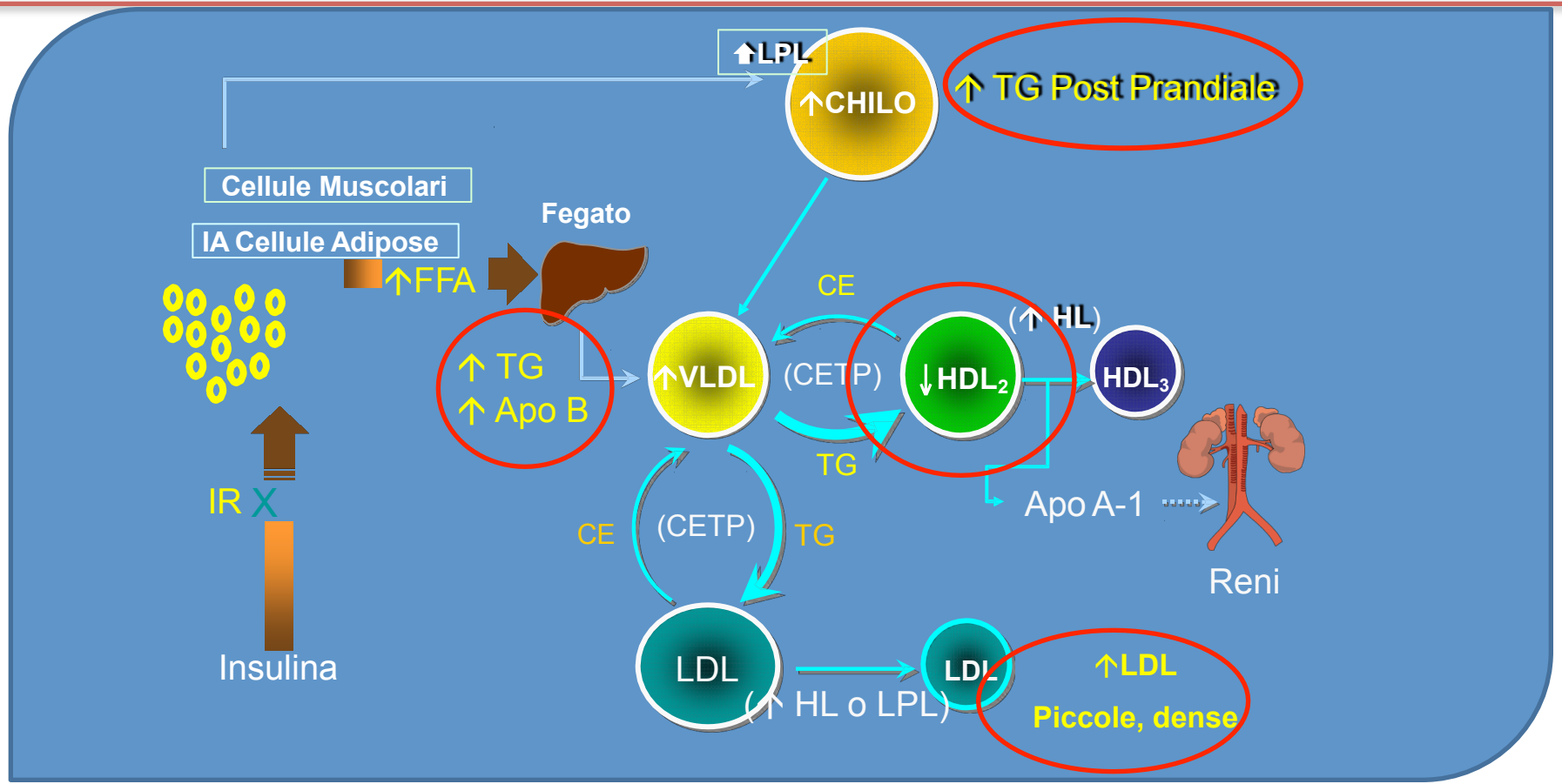
Sopravvivenza accertata in media per un periodo di 12 anni

Outcome: mortalità cardiovascolare



CVD = malattia cardiovascolare; MRFIT = Multiple Risk Factor Intervention Trial.

Meccanismi fisiopatologici della dislipidemia nel diabete tipo 2



I Diabetici sono HyperAbsorbers

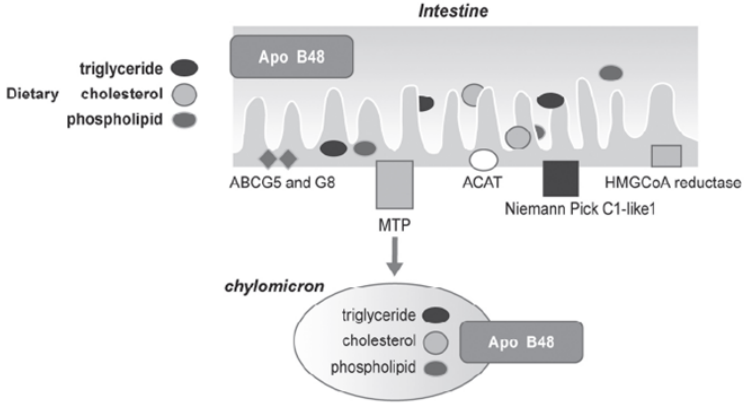


Fig. 1. Regulation of chylomicron synthesis. ApoB-48, apoproptein B-48; ABCG, ATP-binding cassette sub-family G member; ACAT, Acyl-CoA:cholesterol acyltransferase; HMGCoA, hydroxy-3-methyl-glutaryl-CoA. (Reproduced with permission from Diabetes Care 2008; 31(Suppl. 2): S241–8.)

ELSEVIER
Atherosclerosis Supplements 17 C (2015) 12–16
ATHEROSCLEROSIS SUPPLEMENTS
www.elsevier.com/locate/atherosclerosis

Alterations of intestinal lipoprotein metabolism in diabetes mellitus and metabolic syndrome

Marcello Arca *
Department of Internal Medicine and Medical Specialties, UOSI Atherosclerosis Center, La Sapienza University of Rome, Rome, Italy

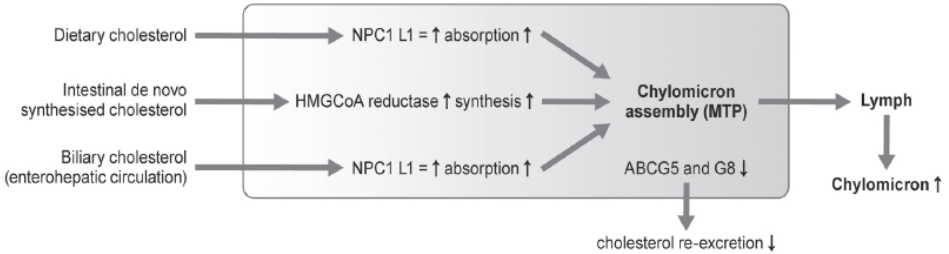
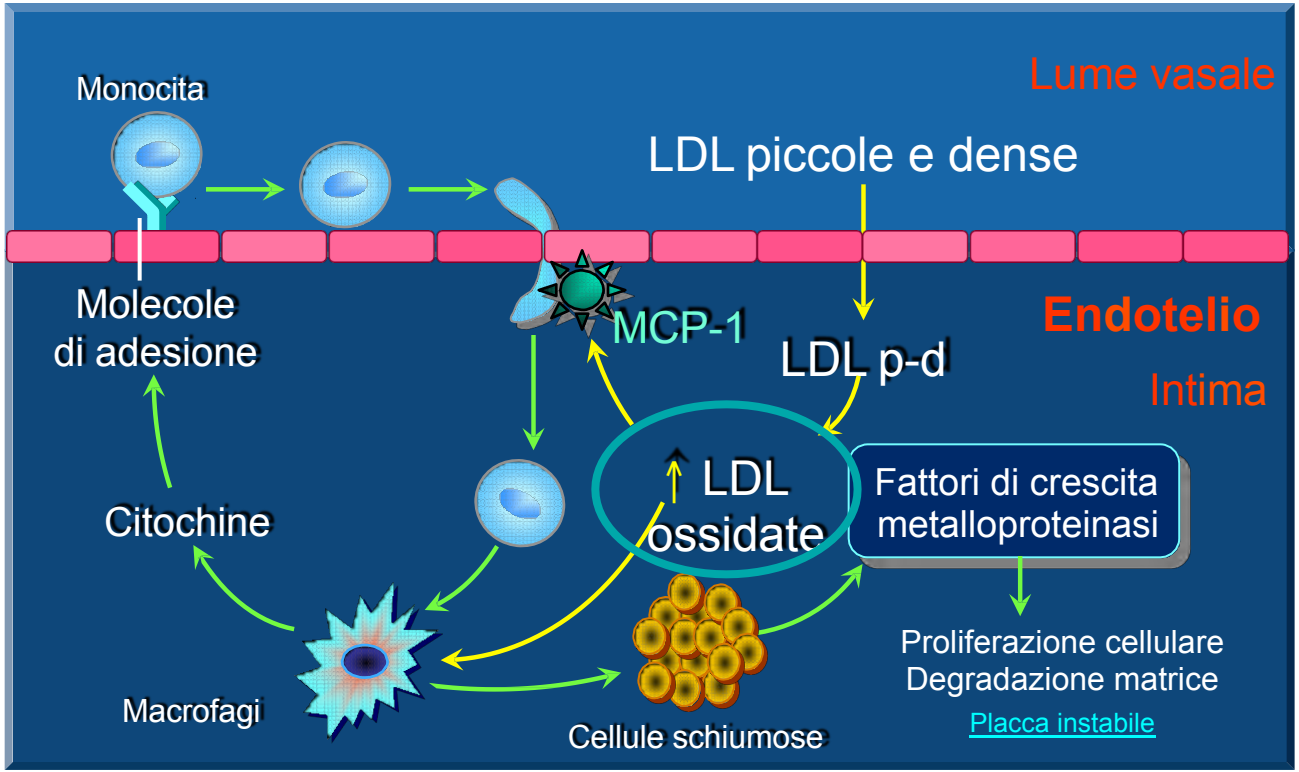
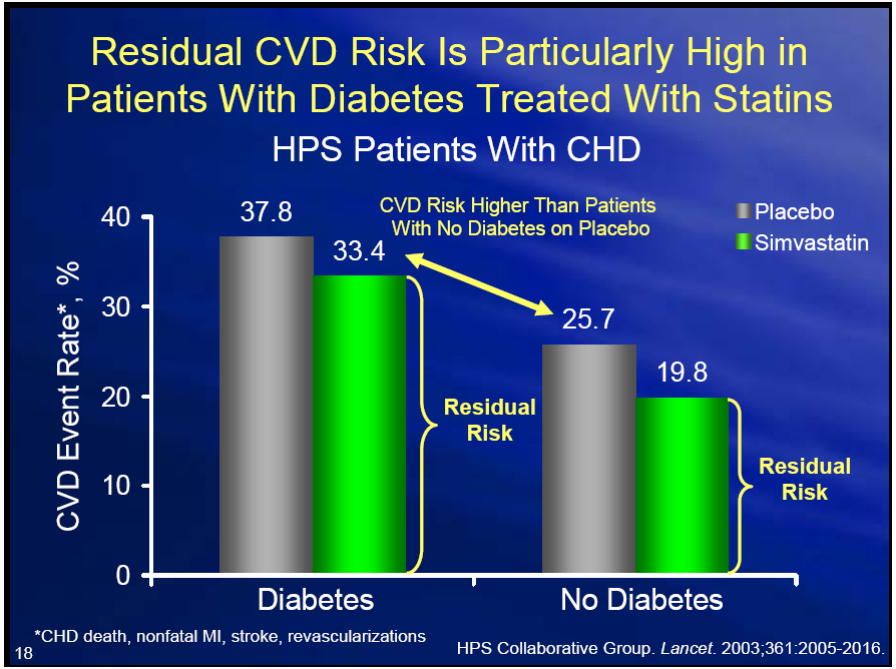


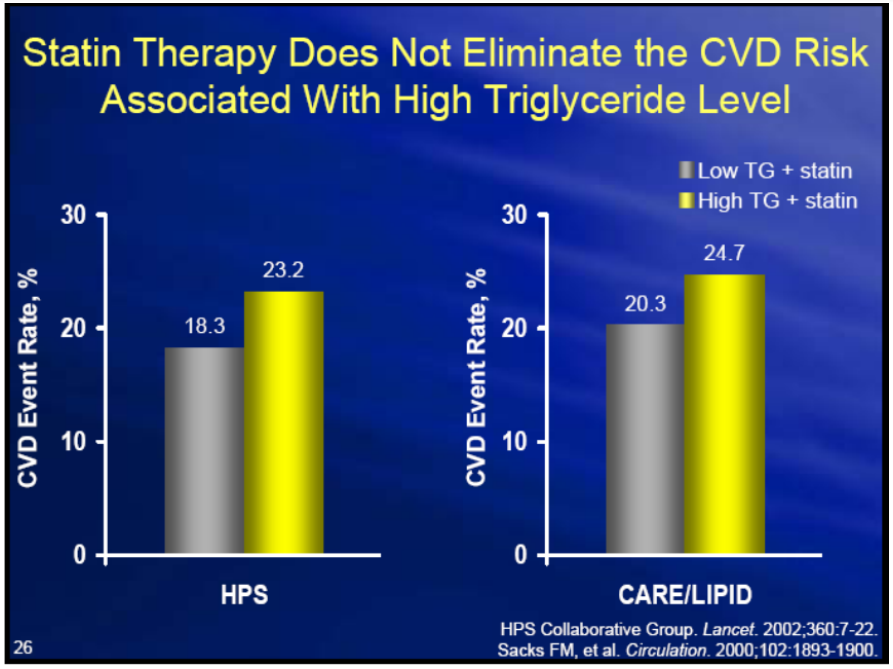
Fig. 2. Chylomicron cholesterol derives from dietary, biliary and intestinal de novo synthesized cholesterol. NPC1-L1 regulates its absorption and ABCG5 and ABCG8 regulate its excretion. MTP assembles the apoB-48 protein, cholesterol and other lipids to form the chylomicron, which is then secreted into the lymph. (Reproduced with permission from Diabetes Care 2008 Feb;31 Suppl 2:S241–8 [6].)

LDL piccole e dense e placca aterosclerotica



La dislipidemia diabetica: il rischio residuo





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Il paziente con IRC è un paziente ad alto rischio C.V.

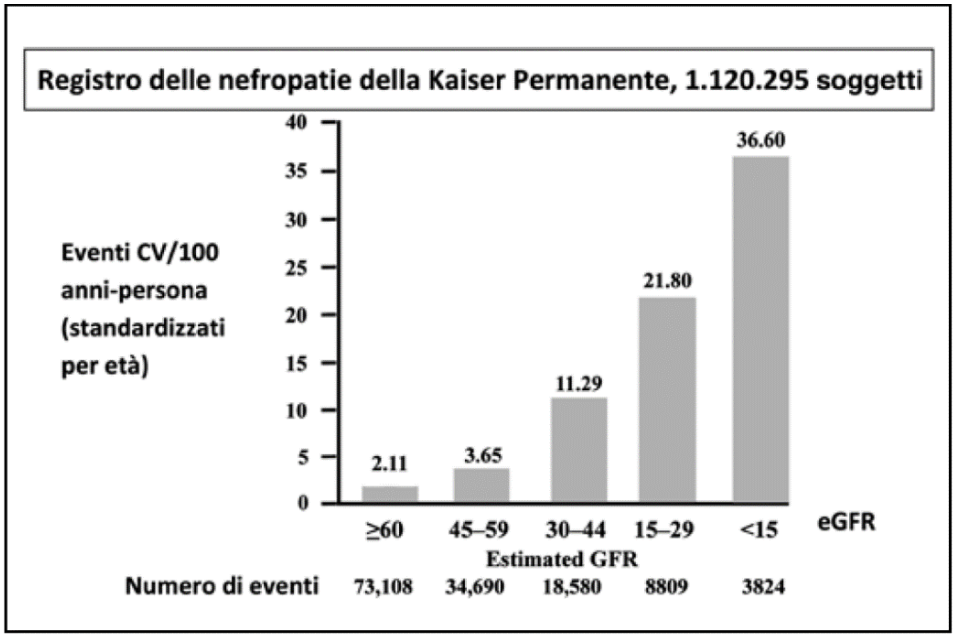
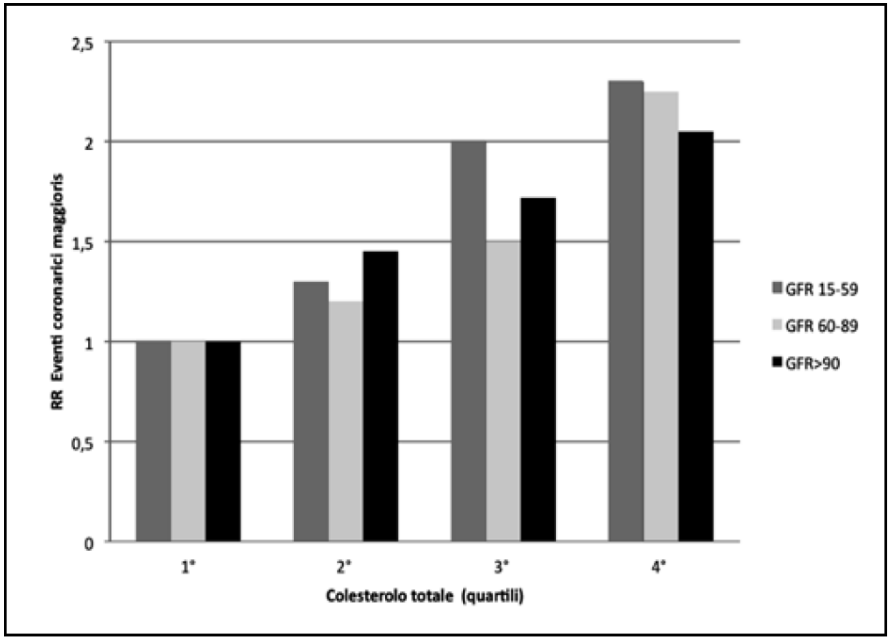


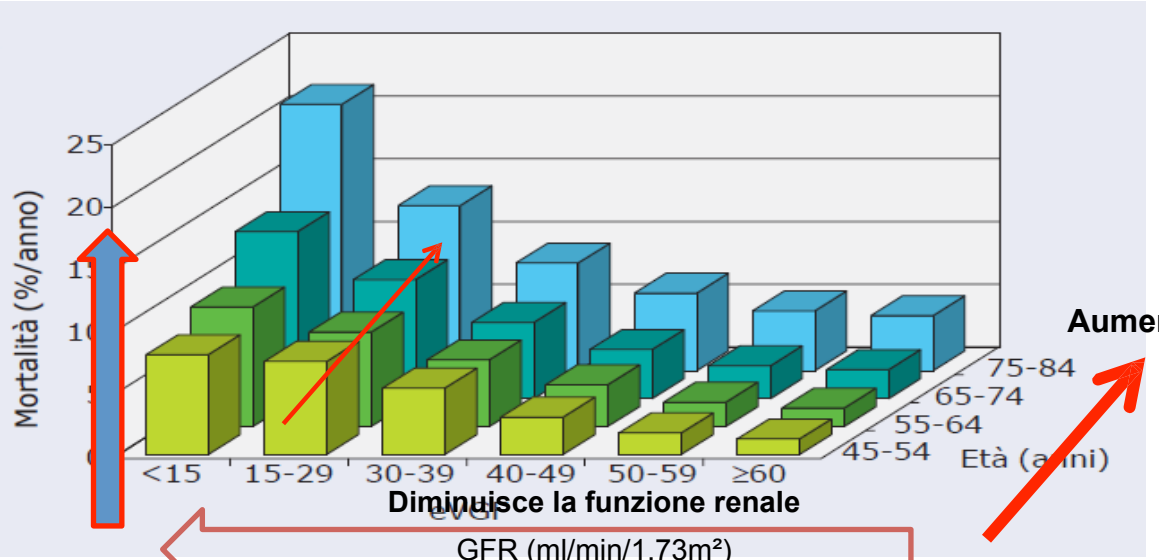
Fig. 2 - *Rapporto tra valori di colesterolo totale ed eventi cardiovascolari maggiori in 17.898 pazienti con CKD seguiti per 10.5 anni*



G Ital Nefrol 2012; 29 (2): 160-173

Paziente con malattia renale è ad alto rischio

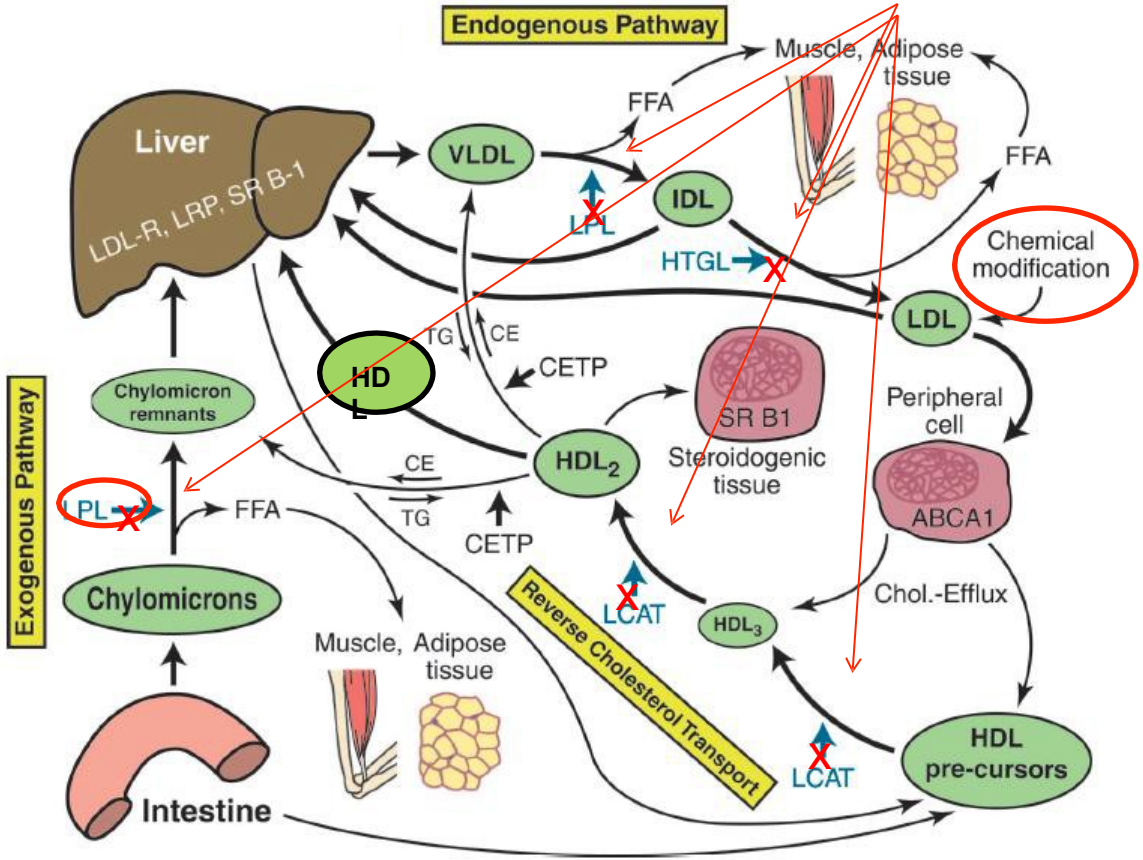
Aumenta il rischio di morte



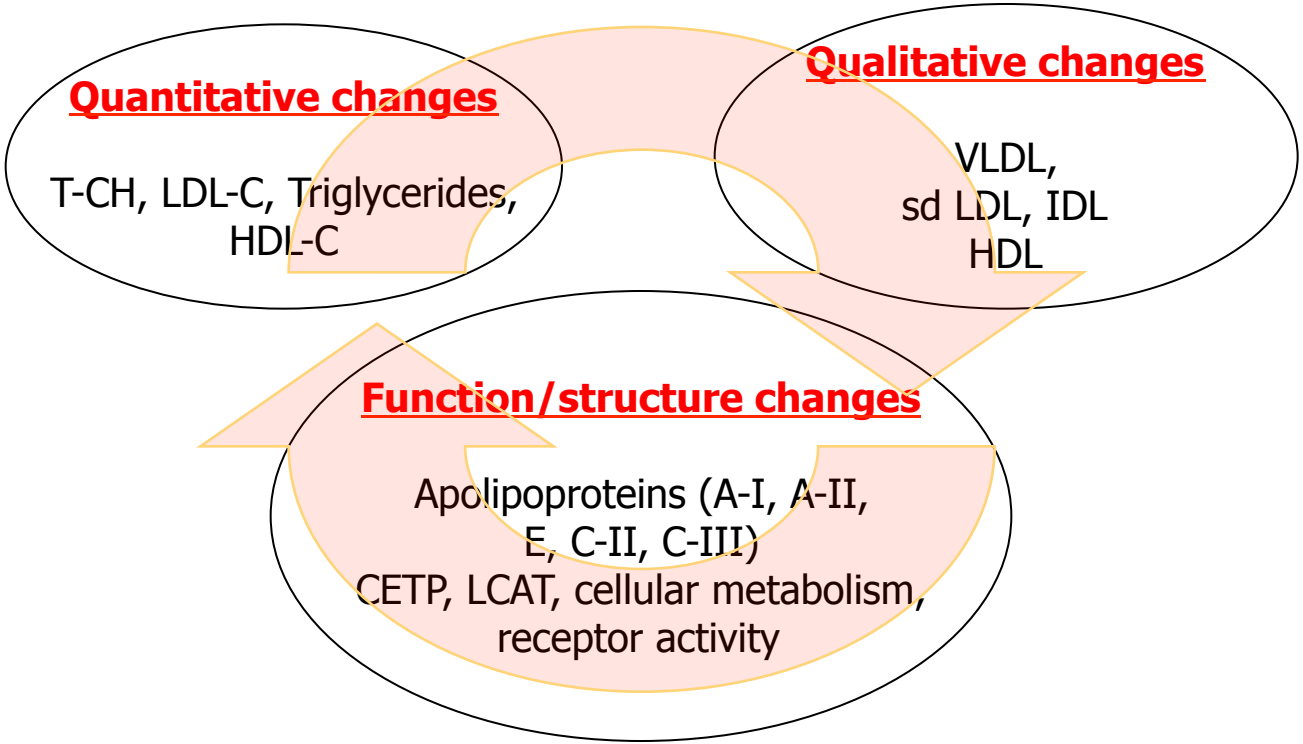
O'Hare AM, Bertenthal D, Covinsky KE, *et al*. **Mortality risk stratification in chronic kidney disease: one size for all ages?** J Am Soc Nephrol 2006; 17:846- 853.

Weiner DE, Tighiouart H, Amin MG, *et al*. **Chronic kidney disease as a risk factor for cardiovascular disease and all-cause mortality: a pooled analysis of community-based studies.** J Am Soc Nephrol 2004;15: 1307-1315

Journal of the American Society of Nephrology J Am Soc Nephrol 18: 1246–1261



Abnormalities of lipid/lipoprotein profile in kidney disease

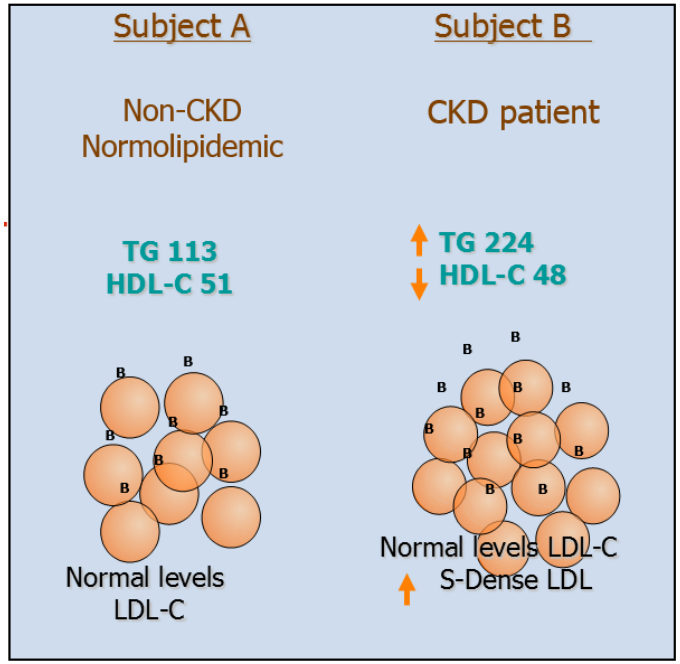


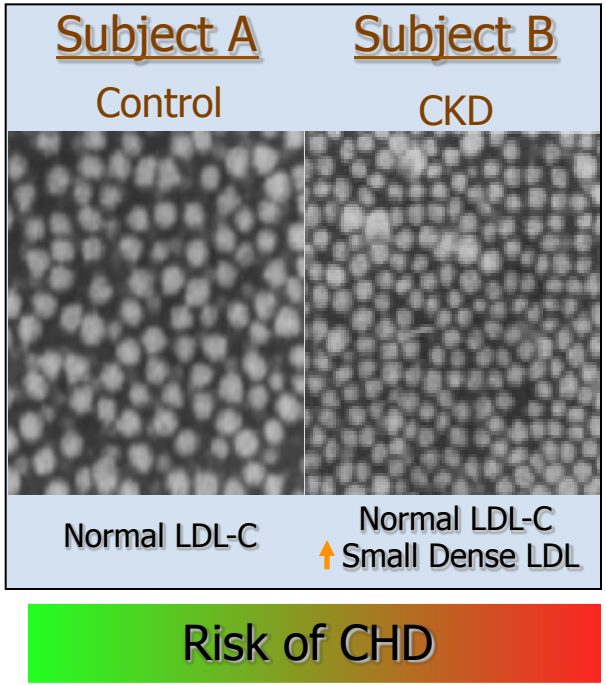
The atherogenic dyslipidemia of CKD patients

LDL
Mean diameter
273 Å

LDL-C = 119 mg/dl

Apo B = 93 mg/dl





LDL
Mean diameter
233 Å

LDL-C = 124 mg/dl

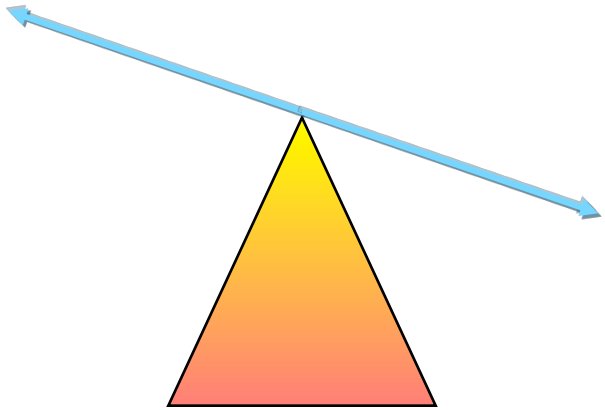
↑Apo B = 112 mg/dl

Lipoprotein phenotype ↑TG, ↓ HDL-C, ↑ sd LDL; Apo B: Marker of circulating LDL particles

Dyslipidemia in patients with CKD

Dyslipidemia in CKD involves a disequilibrium characterised by an excess of atherogenic apoB-containing lipoproteins relative to low concentrations of anti-atherogenic HDL whose functional properties are defective

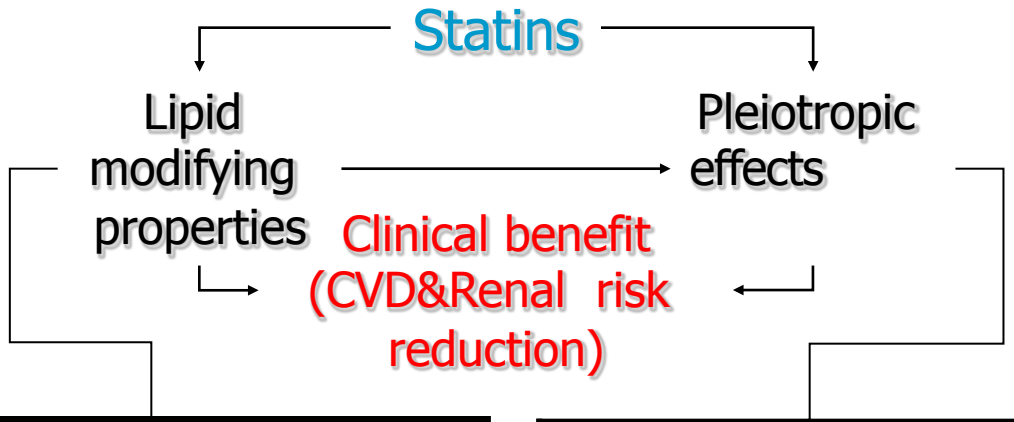
Dysfunctional
Small Dense HDL



- VLDL
- VLDL remnants
- IDL
- LDL; Dense LDL

- Enhanced Arterial Cholesterol Deposition
- Attenuated Reverse Cholesterol Transport
- Accelerated Atherogenesis

Effects of statins in patients with renal disease

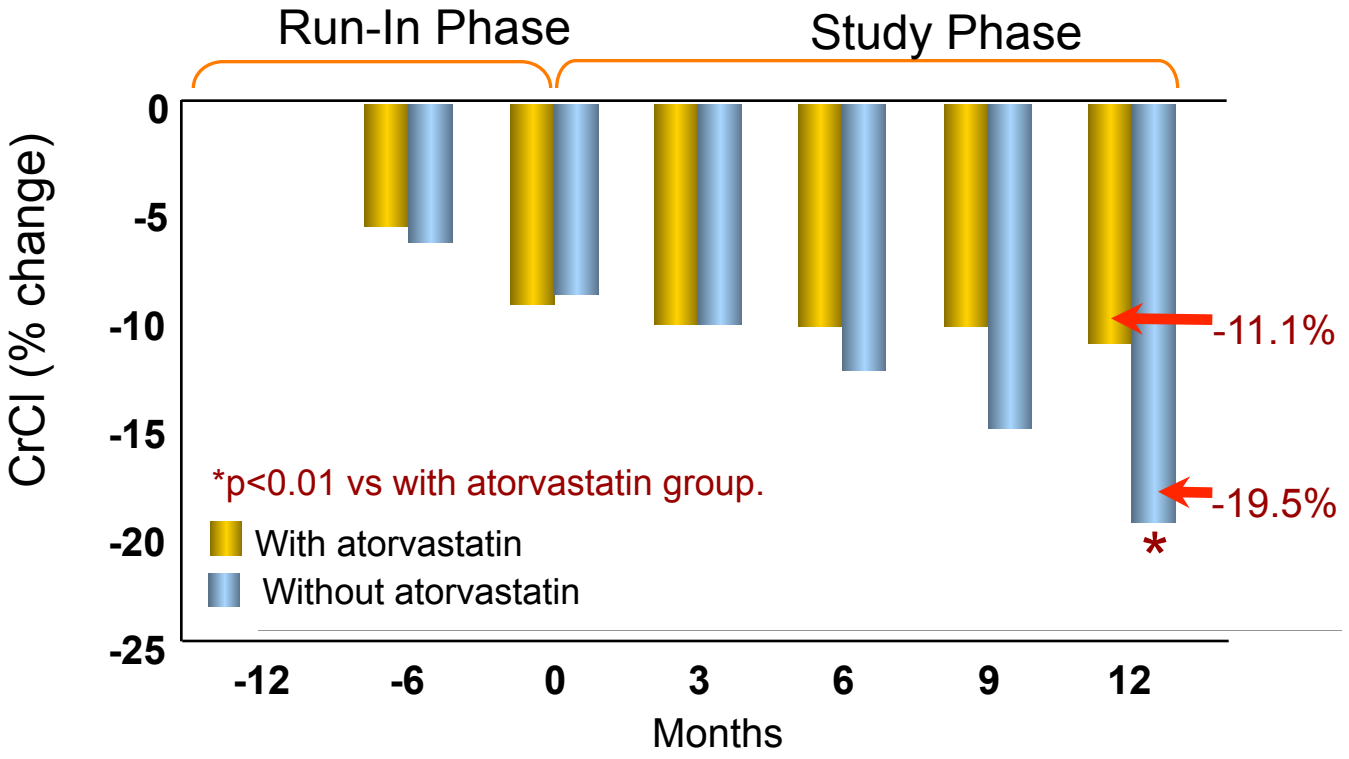


Author	Lipid-modifying effects
Chang 2002, Bigent 2005, van den Akker 2003, Diepeveen 2005,	↓T-C
Verma 2005, Baigent 2005, vand den Akker 2003, Diepeveen 2005, Ikejiri 2004	↓ LDL-C
Bigent 2005, Diepeveen 2005	↓ TG
Van den Akker 2003, Diepeveen 2005, Ikejiri 2004	↓ Remnant LP and Apolipo.
Ikejiri 2004	↑ LDL size

Author	Anti-inflammatory effects
Verma 2005, Chang 2002	↓CRP
	Antioxidant effets
Van den Akker 2003, Diepeveen 2005	↓ Ox LDL

From Campese VM, **Kidney Int** 71: 1215-1222, 2007

Effects of Atorvastatin on Proteinuria and Progression of Kidney Disease



Bianchi S et al, **Am J Kidney Dis** 41: 565-570, 2003

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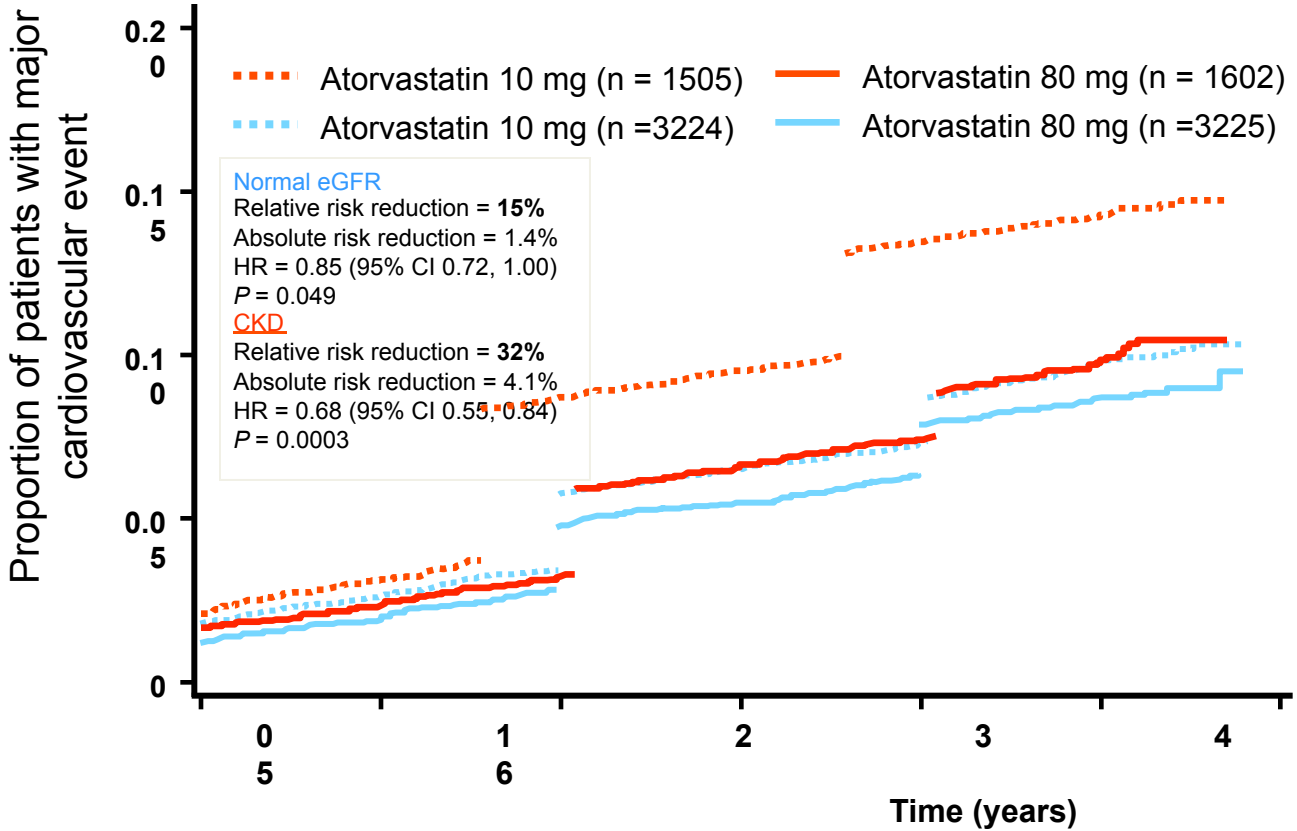
Statine e rene: la lezione dei trials

- ASCOT *(Anglo-Scandinavian Cardiac Outcomes Trial): atorvastatina*
- TNT *(Treating to New Targets): atorvastatina 80 e 10 mg*
- CARE, LIPID e WOSCOPS: *pravastatina*
- Jupiter *(Justification for the Use of Statins in Prevention: an Intervention Trial Evaluating Rosuvastatin)*
- SHARP *(Study of Heart and Renal Protection): ezetimibe/simvastatina*
- Un'analisi post hoc dello studio CARE *(Cholesterol And Recurrent Events)*
- studio CARE
- ALLIANCE *(Aggressive Lipid Lowering to Alleviate New Cardiovascular Endpoints)*
- GREACE *(Global Registry of Acute Coronary Events)*
- PLANET I e II *(Prospective evaLuation of proteinuria and renal function in diabetic and non-diabetic patients with progressive renal disease)*

Time to First Major Cardiovascular Event By Baseline CKD Status and Treatment Assignment
The Treatment to New Target (TNT) Study



Shepherd J et al., **J Am Coll Cardiol** 51: 1448-54, 2008

SHARP: Baseline paper and Data Analysis Plan

Study of Heart and Renal Protection (SHARP): Randomized trial to assess the effects of lowering low-density lipoprotein cholesterol among 9,438 patients with chronic kidney disease

SHARP Collaborative Group

Am Heart J 2010;0:1-10.e10

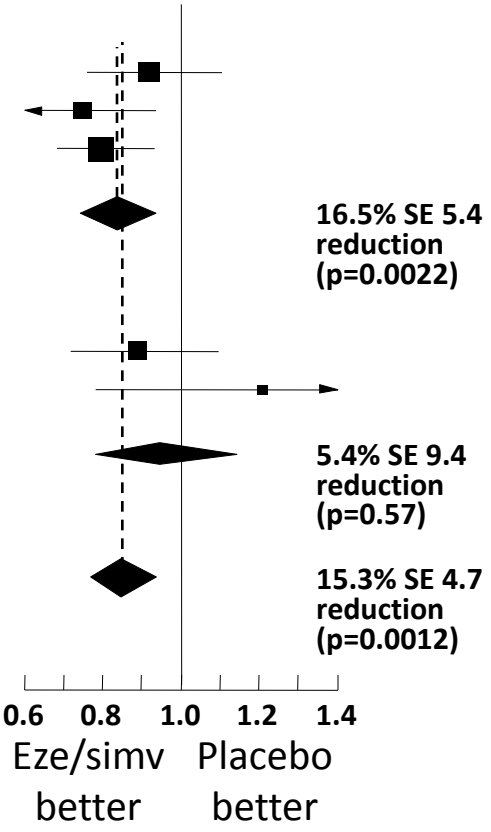
- 1-year LDL-C reduction of 30 mg/dL with simvastatin 20 mg alone and of 43 mg/dL with eze/simv 10/20mg
- Confirmation of safety of ezetimibe when added to simvastatin (1-year results)
- Revised data analysis plan published as an appendix before unblinding of main results

SHARP: Main outcomes

- **Key outcome**
  - Major atherosclerotic events (coronary death, MI, non-haemorrhagic stroke, or any revascularization)
- **Subsidiary outcomes**
  - Major vascular events (cardiac death, MI, any stroke, or any revascularization)
  - Components of major atherosclerotic events
- **Main renal outcome**
  - End stage renal disease (dialysis or transplant)

SHARP: Major Atherosclerotic & Vascular events

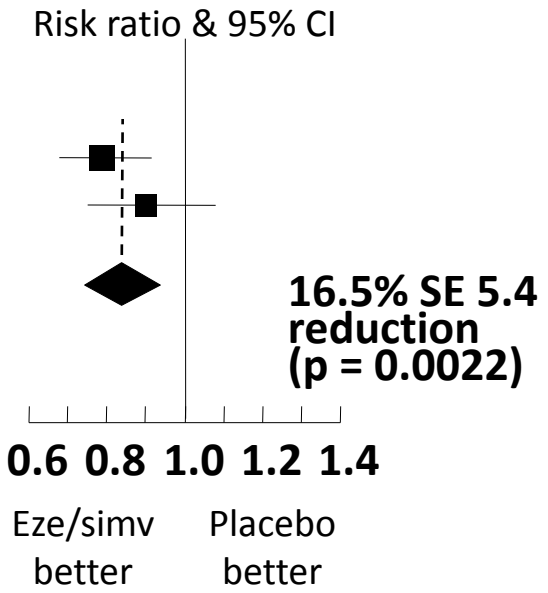
Event	Eze/simv (n=4650)	Placebo (n=4620)
Major coronary event	213 (4.6%)	230 (5.0%)
Non-haemorrhagic stroke	131 (2.8%)	174 (3.8%)
Any revascularization	284 (6.1%)	352 (7.6%)
Major atherosclerotic event	**526 (11.3%)**	**619 (13.4%)**
Other cardiac death	162 (3.5%)	182 (3.9%)
Haemorrhaghic stroke	45 (1.0%)	37 (0.8%)
Other major vascular events	**207 (4.5%)**	**218 (4.7%)**
Major vascular event	**701 (15.1%)**	**814 (17.6%)**



SHARP: Major Atherosclerotic Events by renal status at randomization

	Eze/simv (n=4650)	Placebo (n=4620)
Non-dialysis (n=6247)	296 (9.5%)	373 (11.9%)
Dialysis (n=3023)	230 (15.0%)	246 (16.5%)
Major atherosclerotic event	**526 (11.3%)**	**619 (13.4%)**

No significant heterogeneity between non-dialysis and dialysis patients (p = 0.25)



SHARP: conclusions

- No increase in risk of myopathy, liver and biliary disorders, cancer, or nonvascular mortality
- No substantial effect on kidney disease progression
- Two-thirds compliance with eze/simv reduced the risk of major atherosclerotic events by 17% (consistent with meta-analysis of previous statin trials)
- Similar proportional reductions in all subgroups (including among dialysis and non-dialysis patients)
- Full compliance would reduce the risk of major atherosclerotic events by one quarter, avoiding 30–40 events per 1000 treated for 5 years

Benefit of Ezetimibe Added to Simvastatin in Reduced Kidney Function

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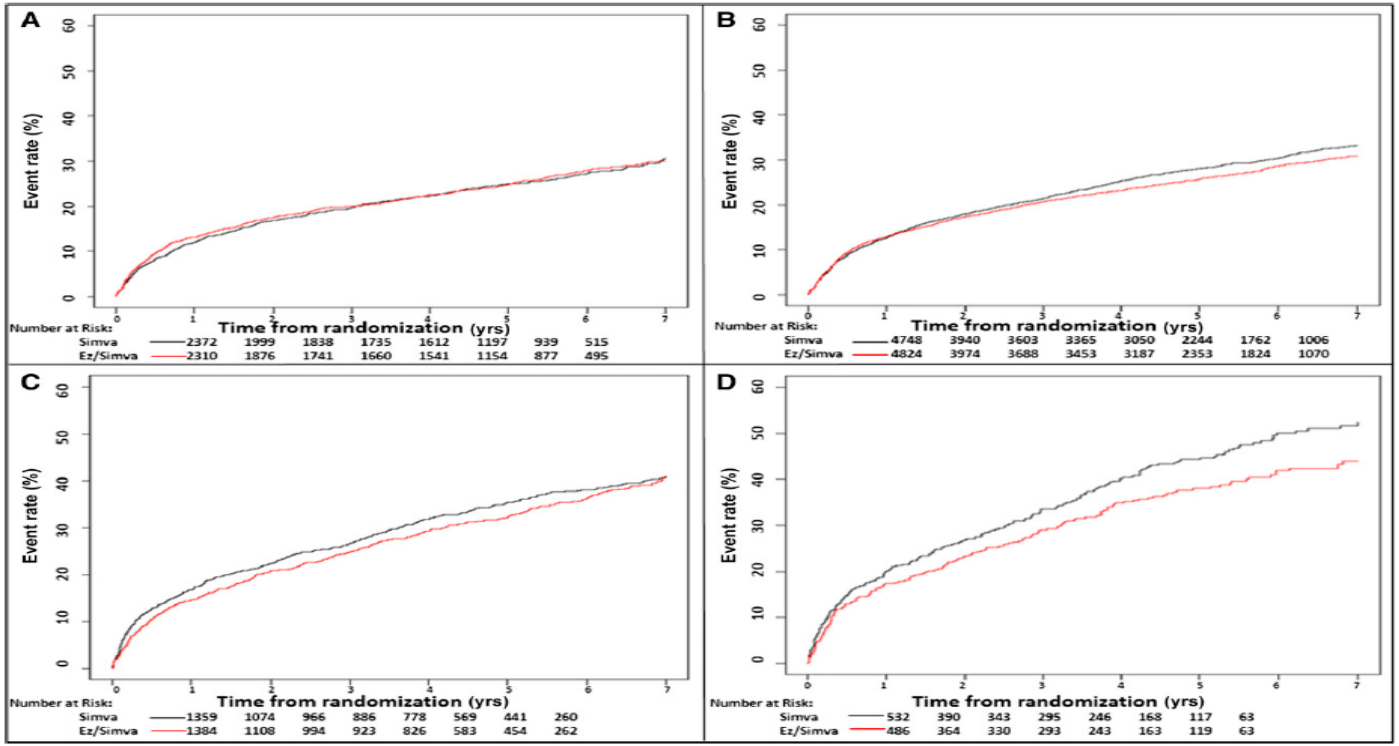

Figure 1. Relationship between level of eGFR and event rate for primary composite end point of death from cardiovascular disease, a major coronary event, or nonfatal stroke. Kaplan-Meier curves show the primary composite end point during the 7-year study period stratified by (A) eGFR≥90 ml/min per 1.73 m^2, (B) eGFR=60–89 ml/min per 1.73 m^2, (C) eGFR=45–59 ml/min per 1.73 m^2, and (D) eGFR<45 ml/min per 1.73 m^2. EzSimva, ezetimibe and simvastatin; Simva, simvastatin.

Outline

- Caso clinico
- LDLc: is lower better?
- La dislipidemia diabetica ed il rischio residuo
- Lipidi e rischio cardiovascolare nel paziente con IRC
- Statine e rene: la lezione dei trials
- Dai RCP alle linee guida

Dalle evidenze scientifiche alle raccomandazioni: linee guida a confronto

- American Association of Clinical Endocrinologists and American College of Endocrinology
  Guidelines for Management of Dyslipidemia and Prevention of Cardiovascular Disease
- **2016 EAS/ESC Guidelines for the Management of Dyslipidemias**
- **Obiettivo comune: Treat to target**

American Association of Clinical Endocrinologists and American College of Endocrinology

Guidelines for Management of Dyslipidemia and Prevention of Cardiovascular Disease

2016ESC/EASGuidelines on the management of dyslipidaemias

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CATEGORIE DI RICHIO CARDIOVASCOLARE

Very high-risk	Subjects with any of the following: • Documented CVD, clinical or unequivocal on imaging. Documented clinical CVD includes previous AMI, ACS, coronary revascularization and other arterial revascularization procedures, stroke and TIA, aortic aneurysm and PAD. Unequivocally documented CVD on imaging includes significant plaque on coronary angiography or carotid ultrasound. It does NOT include some increase in continuous imaging parameters such as intima–media thickness of the carotid artery. • DM with target organ damage such as proteinuria or with a major risk factor such as smoking or marked hypercholesterolaemia or marked hypertension. • Severe CKD (GFR <30 mL/min/1.73 m^2). • A calculated SCORE ≤10%.
High-risk	Subjects with: • Markedly elevated single risk factors, in particular cholesterol >8 mmol/L (>310 mg/dL) (e.g. in familial hypercholesterolaemia) or BP ≥180/110 mmHg. • Most other people with DM (with the exception of young people with type 1 DM and without major risk factors that may be at low or moderate risk). • Moderate CKD (GFR 30–59 mL/min/1.73 m^2) • A calculated SCORE ≥5% and <10%.
Moderate-risk	SCORE is ≥1% and <5% at 10 years. Many middleaged subjects belong to this category.
Low-risk	SCORE <1%.

Recommendations	Class	Level
In patients at VERY HIGH CV risk, an LDL-C goal of <1.8 mmol/L (70 mg/dL) or a reduction of at least 50% if the baseline LDL-C is between 1.8 and 3.5 mmol/L (70 and 135 mg/dL) is recommended.	I	B
In patients at HIGH CV risk, an LDL-C goal of <2.6 mmol/L (100 mg/dL), or a reduction of at least 50% if the baseline LDL-C is between 2.6 and 5.2 mmol/L (100 and 200 mg/dL) is recommended.	I	B
In subjects at LOW or MODERATE risk an LDL-C goal of <3.0 mmol/L (<115 mg/dL) should be considered.	IIa	C

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ASCVD Risk Categories and LDL-C Treatment Goals

Risk category	Risk factors/10-year risk	Treatment goals		
		LDL-C (mg/dL)	Non-HDL-C (mg/dL)	Apo B (mg/dL)
Extreme risk	– Progressive ASCVD including unstable angina in individuals after achieving an LDL-C <70 mg/dL – Established clinical cardiovascular disease in individuals with DM, stage 3 or 4 CKD, or HeFH – History of premature ASCVD (<55 male, <65 female)	<55	<80	<70
Very high risk	– Established or recent hospitalization for ACS, coronary, carotid or peripheral vascular disease, 10-year risk >20% – DM or stage 3 or 4 CKD with 1 or more risk factor(s) – HeFH	<70	<100	<80
High risk	– ≥2 risk factors and 10-year risk 10%-20% – DM or stage 3 or 4 CKD with no other risk factors	<100	<130	<90
Moderate risk	≤2 risk factors and 10-year risk <10%	<100	<130	<90
Low risk	0 risk factors	<130	<160	NR

Abbreviations: ACS, acute coronary syndrome; apo, apolipoprotein; ASCVD, atherosclerotic cardiovascular disease; CKD, chronic kidney disease; DM, diabetes mellitus; HeFH, heterozygous familial hypercholesterolemia; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; NR, not recommended.

Barter PJ, et al. *J Intern Med*. 2006;259:247-258; Boekholdt SM, et al. *J Am Coll Cardiol*. 2014;64(5):485-494; Brunzell JD, et al. *Diabetes Care*. 2008;31:811-822; Cannon CP, et al. *N Engl J Med.* 2015;372(25):2387-2397; Grundy SM, et al. *Circulation.* 2004;110:227-239; Heart Protection Study Collaborative Group. *Lancet*. 2002;360:7-22; Jellinger P, Handelsman Y, Rosenblit P, et al. *Endocr Practice*. 2017;23(4):479-497; Lloyd-Jones DM, et al. *Am J Cardiol*. 2004;94:20-24; McClelland RL, et al. *J Am Coll Cardiol*. 2015;66(15):1643-1653; NHLBI. NIH Publication No. 02-5215. 2002; Ridker PM, *J Am Coll Cardiol*. 2005;45:1644-1648; Ridker PM, et al. *JAMA*. 2007;297(6):611-619; Sever PS, et al. *Lancet*. 2003;361:1149-1158; Shepherd J, et al. *Lancet*. 2002;360:1623-1630; Smith SC Jr, et al. *Circulation*. 2006;113:2363-2372; Stevens RJ, et al. *Clin Sci*. 2001;101(6):671-679; Stone NJ. *Am J Med*. 1996;101:4A40S-48S; Weiner DE, et al. *J Am Soc Nephrol.* 2004;15(5):1307-1315.

NonPharmacologic Dyslipidemia Treatments

Smoking	No exposure to tobacco in any form.
Diet	Healthy diet low in saturated fat with a focus on whole grain products, vegetables, fruit and fish.
Physical activity	2.5–5 h moderately vigorous physical activity per week or 30–60 min most days.
Body weight	BMI 20–25 kg/m^2, waist circumference <94 cm (men) and <80 cm (women).
Blood pressure	<140/90 mmHg.

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Atherosclerosis 253 (2016) 281-344-d oi:10.1016/j.atherosclerosis.2016.08.018

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Physical Activity

- **R48.** A reasonable and feasible approach to fitness therapy (i.e., exercise programs that include at least 30 minutes of moderate-intensity physical activity [consuming 4-7 kcal/min] 4 to 6 times weekly, with an expenditure of at least 200 kcal/day) is recommended; suggested activities include brisk walking, riding a stationary bike, water aerobics, cleaning/scrubbing, mowing the lawn, and sporting activities **(Grade A; BEL 1)**.
- **R49.** Daily physical activity goals can be met in a single session or in multiple sessions throughout the course of a day (10 minutes minimum per session); for some individuals, breaking activity up throughout the day may help improve adherence with physical activity programs **(Grade A; BEL 1)**.
- **R50.** In addition to aerobic activity, muscle-strengthening activity is recommended at least 2 days a week **(Grade A; BEL 1)**.

Medical Nutrition Therapy

- **R51.** For adults, a reduced-calorie diet consisting of fruits and vegetables (combined ≥5 servings/day), grains (primarily whole grains), fish, and lean meats is recommended **(Grade A; BEL 1)**.
- **R52.** For adults, the intake of saturated fats, *trans*-fats, and cholesterol should be limited, while LDL-C-lowering macronutrient intake should include plant stanols/sterols (~2 g/ day) and soluble fiber (10-25 g/day) **(Grade A; BEL 1)**.
- **R53.** Primary preventive nutrition consisting of healthy lifestyle habits is recommended in all healthy children **(Grade A; BEL 1)**.

Smoking Cessation

- **R54.** Tobacco cessation should be strongly encouraged and facilitatec **upgraded due to potential benefit**).

AMERICAN ASSOCIATION OF CLINICAL ENDOCRINOLOGISTS

To do or not to do lipid guidelines (4)

Recommendations	Class	Level
Treatment of dyslipidaemia in diabetes		
In all patients with type I diabetes and in the presence of micro-albuminuria and/or renal disease, LDL-C lowering (at least 50%) with statins as the first choice is recommended irrespective of the baseline LDL-C concentration.	I	C
In patients with type 2 diabetes and CVD or CKD, and in those without CVD who are over the age of 40 years with one or more other CVD risk factors or markers of target organ damage, the recommended goal for LDL-C is <1.8 mmol/L (< 70 mg/dL) and the secondary goal for non-HDL-C is <2.6 mmol/L (< 100 mg/dL) and for apoB is <80 mg/dL.	I	B
In all patients with type 2 diabetes and no additional risk factors and/or evidence of target organ damage, LDL-C <2.6 mmol/L (<100 mg/dL) is the primary goal. Non-HDL-C <3.4 mmol/L (<130 mg/dL) and apoB <100 mg/dL are the secondary goals.	I	B

Lipid management in patients with moderate to severe chronic kidney disease		
Patients with stage 3–5 CKD have to be considered at high or very high CV risk.	I	A
The use of statins or statin/ezetimibe combination is indicated in patients with non-dialysis-dependent CKD.	I	A
In patients with dialysis-dependent CKD and free of atherosclerotic CVD, statins should not be initiated.	III	A

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NOTA 13

CATEGORIE DI RISCHIO*		Trattamento di 1° livello	Trattamento di 2° livello
Pazienti con rischio medio: - score 2-3%	Colesterolo LDL < 130	Modifica dello stile di vita per almeno 6 mesi	simvastatina pravastatina fluvastatina lovastatina atorvastatina(**)
Pazienti con rischio moderato: - score 4-5%	Colesterolo LDL < 115	simvastatina pravastatina fluvastatina lovastatina atorvastatina(**)	
Pazienti con rischio alto: -score >5% <10%	Colesterolo LDL < 100	simvastatina pravastatina fluvastatina lovastatina atorvastatina(**) Preferenzialmente atorvastatina se necessaria riduzione del colesterolo LDL > 50%	rosuvastatina ezetimibe più statine (in associazione estemporanea o precostituita) (**)
Pazienti con rischio molto alto: - score ≥10%	Colesterolo LDL < 70 (riduzione di almeno il 50% del colesterolo LDL)	atorvastatina§ pravastatina fluvastatina lovastatina simvastatina(**)§ rosuvastatina nei pazienti in cui ci sia stata evidenza di effetti collaterali severi nei primi 6 mesi di□ terapia con altre statine	ezetimibe più statine (in associazione estemporanea o precostituita) (**)

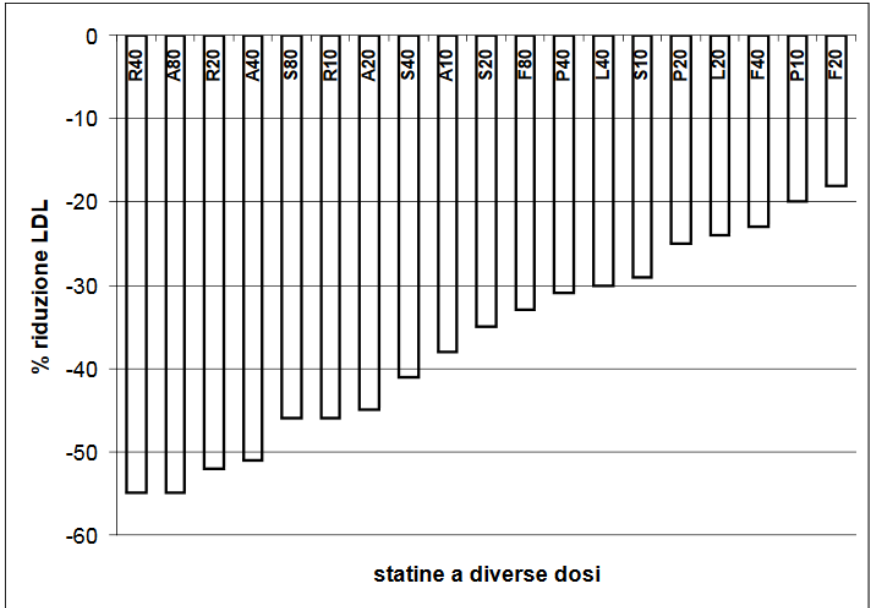
Torniamo al caso clinico..

- Dalla valutazione del rischio C.V. Il nostro paziente è ad altissimo rischio, per cui bisogna intervenire per ottenere il raggiungimento di un target di LDLc < 55 mg/dl – OBIETTIVO PRIMARIO LDLc –

PERTANTO aggiungiamo la terapia ipolipemizzante con eze/simva 10/40 (riduzione di almeno 57%)

- CT: 199 HDL: 35 TG: 250 LDL-C: 114

CT: 120 HDL: 38 TG: 160 LDLc: 50
Non-HDL: 82



Conclusioni

- Il paziente affetto da DM2 e CHD o da IRC moderato – severa è un paziente ad altissimo rischio cardiovascolare
- Le evidenze cliniche e le linee guida suggeriscono di ridurre primariamente il LDLc (target auspicato sec. LG AACE < 55 mg/dl) e successivamente il non – HDLc
- L'associazione ezetimibe/simvastatina è indicata nella gestione della dislipidemia del paziente nefropatico
- Non ci sono evidenze che suggeriscono l'introduzione di una terapia statinica nel paziente in dialisi