Perspectives on diabetes and dyslipidemia – Part 2

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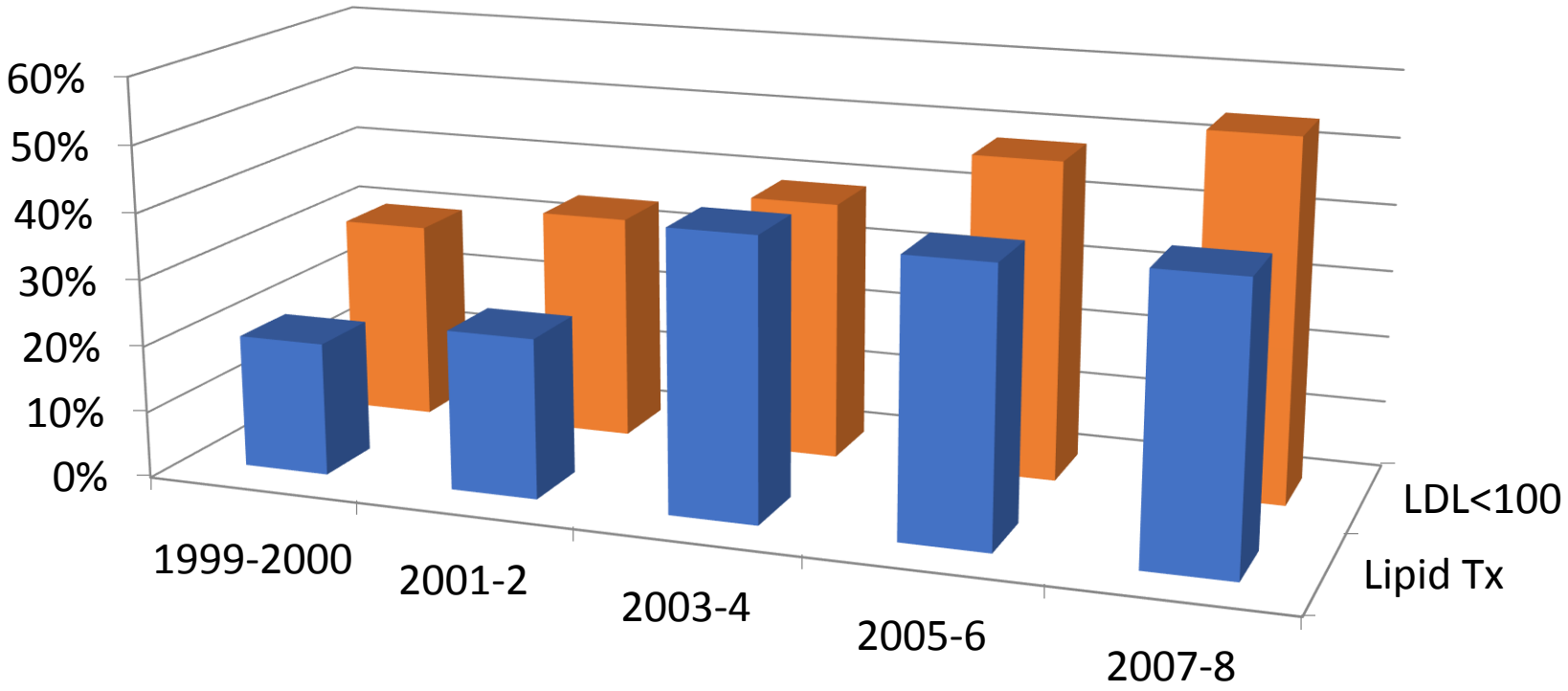
Multiplicities of interest

- The practice of medicine
- Consultant/advisor: Sanofi, Astra Zeneca, Janssen, Merck, Intarcia, Novartis
- Speaker: Amgen, Merck, Astra Zeneca, Janssen
- Stockholder: Allergan, Pfizer, Zimmer Biomet, Novartis

CURRENT APPROACHES TO LIPID-LOWERING WITH STATINS AND PCSK9i AMONG PERSONS WITH DIABETES

Perspectives on diabetes and dyslipidemia

US Lipid Tx / goal achievement for diabetic persons, NHANES 1999-2008

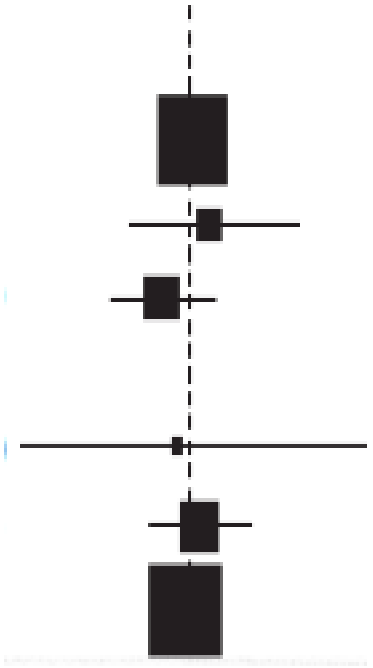


Kuznik and Mardekian Cardiovascular Diabetology2011,10:31

Cholesterol Treatment Trialists' Collaboration: Statin Effect on CHD

1 mmol/L = 38.6 mg/dL

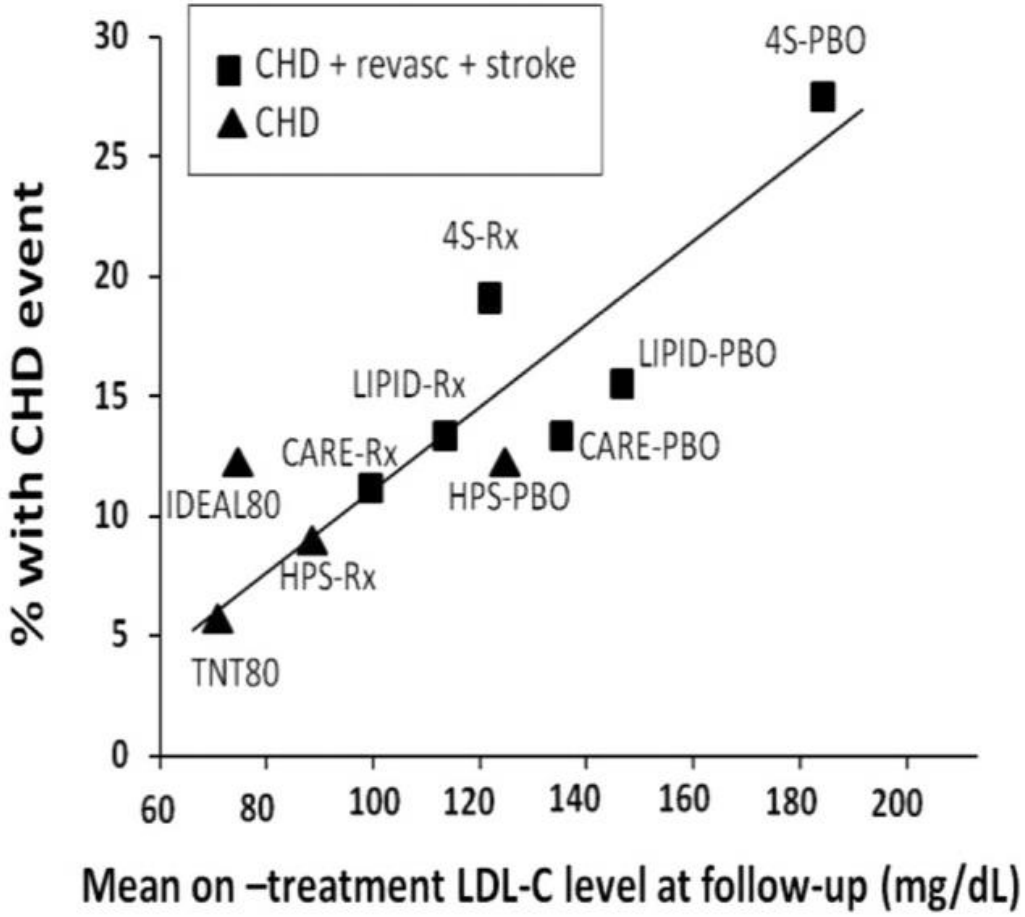
	Events (% per annum)		RR(CI) per 1 mmol/L reduction in LDL-C	
	Statin	Control		
Previous Vascular Disease				
CHD	8,395 (4.5%)	10,123 (5.6%)	0.79 (0.76-0.82)	
No- CHD, vascular	674 (3.1%)	802 (3.7%)	0.81 (0.71-0.92)	(*P*=0.3)
None	1,904 (1.4%)	2,425 (1.8%)	0.75 (0.69-0.82)	
Diabetes				
Type 1 diabetes	145 (4.5%)	192 (6.0%)	0.77 (0.58-1.01)	
Type 2 diabetes	2,494 (4.2%)	2,920 (5.1%)	0.80 (0.74-0.86)	(*P*=0.8)
No diabetes	8,272 (3.2%)	10,163 (4.0%)	0.78 (0.75-0.81)	



Abbreviation: CHD: coronary heart disease; CI, confidence interval; LDL-C, low-density lipoprotein cholesterol; RR: relative risk.

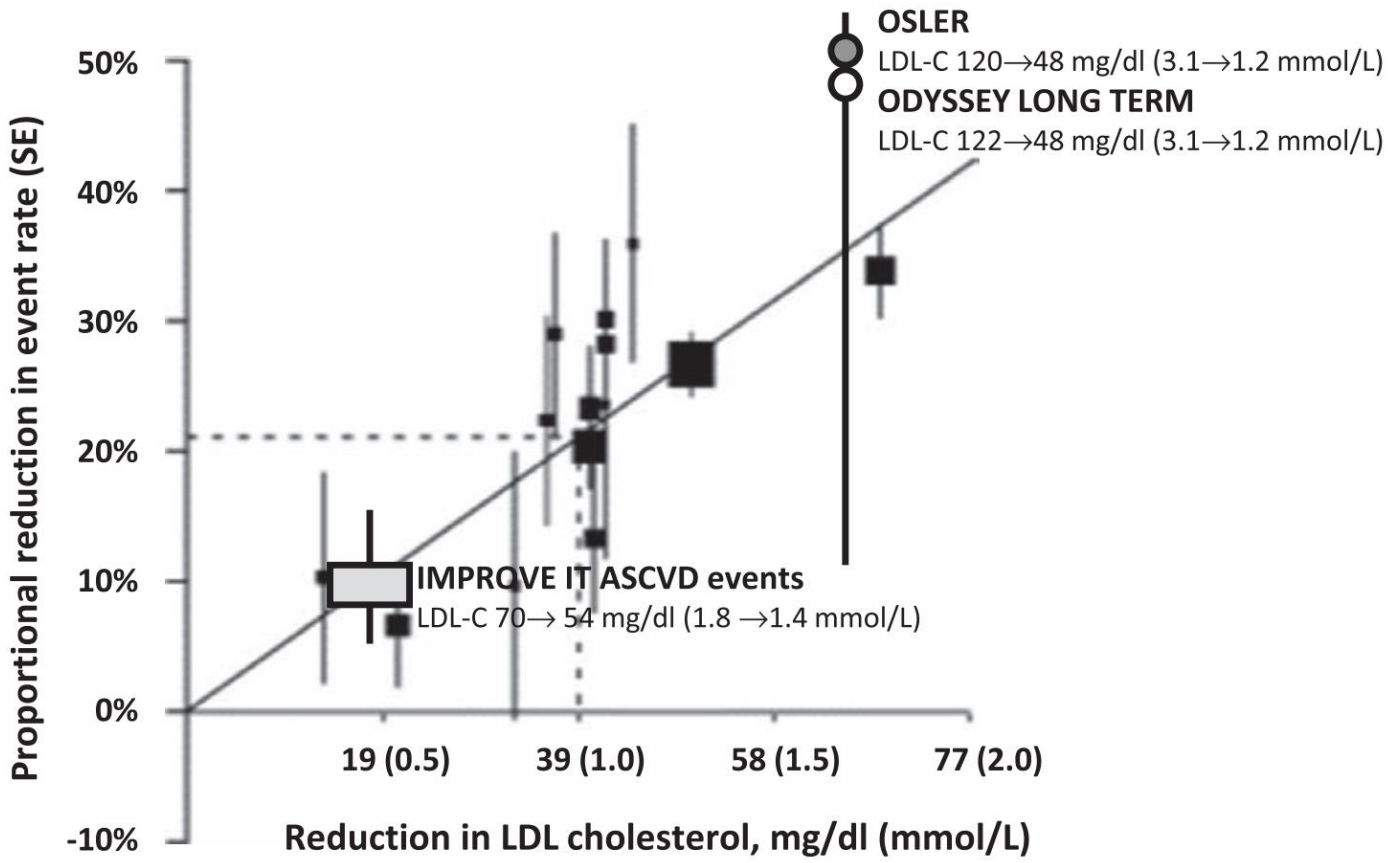
Baigent C, et al. *Lancet*. 2010;376:1670-1681.

LDLc vs CV events in 2ary prevention studies



Jacobson T, et al. NLA recommendations, Journal of Clinical Lipidology (2015) 9, 129–169

LDLc reduction vs CV event-lowering in 2ary prevention studies



Robinson JG, Ray K. Arterioscler Thromb Vasc Biol 2016; 36:586–590 (based on CTT collaboration and newer findings)

FIELD: Fenofibrate Intervention in Event Lowering in Diabetes

Multinational, randomized controlled trial (N=9,795) of patients with T2DM currently taking statin therapy assigned to add-on treatment with fenofibrate or placebo

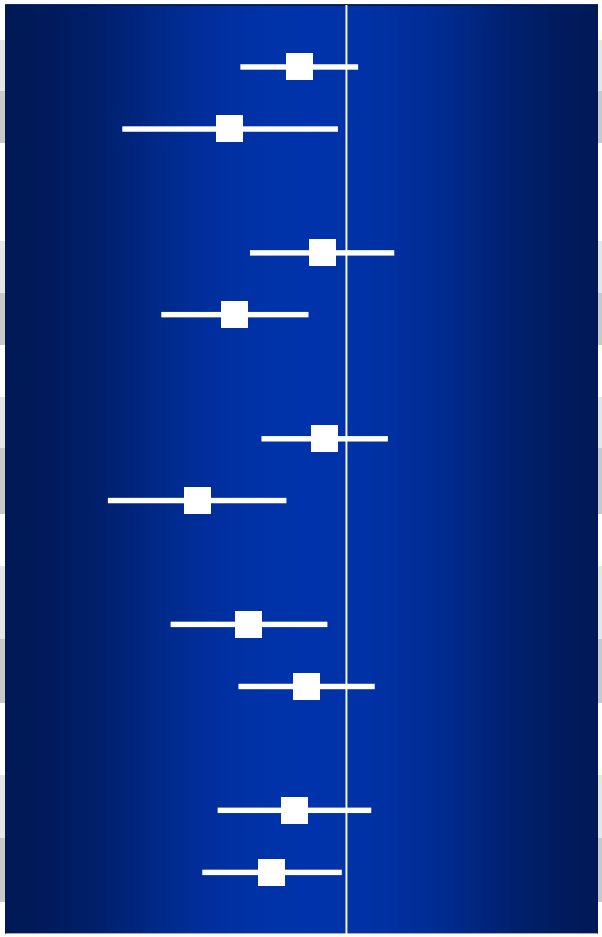
Outcome	Fenofibrate % (n)	Placebo % (n)	HR	95% CI	*P*-value
Coronary events	5% (256)	6% (288)	0.89	0.75-1.05	0.16
CHD mortality	2% (110)	2% (93)	1.19	0.90-1.57	0.22
Nonfatal MI	3% (158)	4% (207)	0.76	0.62-0.94	0.01

Abbreviations: CHD, coronary heart disease; MI, myocardial infarction; T2DM, type 2 diabetes mellitus.

Keech A, et al. *Lancet.* 2005;366:1849-1861.

Major Prespecified Subgroups: IMPROVE-IT

Baseline data	Simva† Mean LDL 69.5	EZE/Simva† LDL 53.7 mg/dL
Male	34.9	33.2
Female	34.0	31.0
Age <65 years	30.8	29.9
Age ≥65 years	39.9	36.4
No diabetes	30.8	30.2
Diabetes	45.5	40.0
Prior LLT	43.4	40.7
No prior LLT	30.0	28.6
LDL-C >95 mg/dL	31.2	29.6
LDL-C ≤95 mg/dL	38.4	36.0



Ezetimibe/Simva Better

Simva Better

†*7-year event rates*

Abbreviations: LDL, low-density lipoprotein; LDL-C, low-density lipoprotein cholesterol; LLT, lipid-lowering therapy.

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

Adding non-statin: Considerations

Table 2. Proposed LDL-C Threshold Approach to Shared Decision Making When Considering Adding a Nonstatin in Statin-Treated Patients

1. Patients treated with maximal statin therapy	
LDL-C ≥130 mg/dL; (3.4 mmol/L)	High-risk* patients likely to benefit from addition of nonstatin
LDL-C, 100–129 mg/dL; (2.6≤3.4 mmol/L)	Very high† risk patients likely to benefit from addition of nonstatin Selected high-risk patients may benefit from addition of nonstatin
LDL-C<100 mg/dL; (<2.6 mmol/L)	Selected very high* risk patients may benefit from addition of nonstatin
2. Choice of a nonstatin based on	
Reduced CVD events in CV outcomes trials	Added to statin: Ezetimibe As monotherapy: Niacin, cholestyramine, fenofibrate, and gemfibrozil‡
LDL-C–lowering efficacy	PCSK9 mAb>>Ezetimibe>≈Niacin=Bile acid sequestrant
Safety/tolerability	Ezetimibe>PCSK9 mAb>Bile acid sequestrant≈Niacin
Cost	Crystalline niacin<Extended-release niacin<cholestyramine/colestipol<Ezetimibe<Colesevelam<<PCSK9
Patient preferences	Perception of benefits and harms, copay, oral vs injection, medication burden
3. Discontinue nonstatin if ≤10% LDL-C reduction	

Robinson JG, Ray K. Arterioscler Thromb Vasc Biol 2016; 36:586–590