





Dyslipidemia and Heart Failure:

Current Evidence and Perspective of Use Lipid-Lowering Therapy

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Disclosure

I have no actual or potential

conflict of interest in relation to

this presentation

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The primary objective of treating dyslipidemia is to IHEFCARD 2025 prevent atherosclerotic events in patients with high or

very high CVD risk



Unweighted RR (CI) RR (CI) per 1 mmol/L reduction in LDL-C LDL-C Events (% per annum) reduction (mmol/L) Statin/more Control/less More vs less statin PROVE II 458 (13-1%) 0.65 406 (11-3%) TNT 0.62 889 (4.0%) 1164 (5.4%) Trend: $\chi^2_1 = 12.4$ Trend: χ^2_{-3} -3-7 **IDEAL** 938 (5-2%) 1106 (6-3%) 0.55 (p=0.0004) (p-0-05) 1406 (3-8%) SEARCH 1347 (3-6%) 0.39 A to Z 257 (7-2%) 282 (8-1%) 0.30 0-85 (0-82-0-89) Subtotal (5 trials) 3837/19829 4416/19783 0.72 (0.66-0.78) 0.51 \oplus p<0.0001 p<0-0001 (4.5%) (5-3%) Statin vs control SSSS 555 (5-4%) 796 (8-2%) 1.77 HPS. 2043 (4-3%) 1.29 1511 (3-1%) ALLIANCE. 293 (6-4%) 1.16 254 (5-4%) CARDS 81 (1-5%) 123 (2-4%) 1.14JUPITER. 1.09 105 (0.5%) 194 (1-0%) ASCOT-LLA 307 (1.9%) 1.07 21/(1.3%) Post-CABG 1.07 79 (3-0%) 100 (3-8%) WOSCOPS. 318 (2-1%) 1.07 232 (1.5%) PROSPER 495 (5-6%) 1.04 431 (4.9%) Irend: $\chi^2_{1-}32/3$ CARE 1.03 433 (4-8%) 553 (6-3%) Irend: χ^2_{1} =0.6 COID. 1153 (5-2%) 936 (4-1%) (p<0.0001) 1.03 (p=0.4) 0.99 114 (2.7%) ASPEN 136 (3.3%) AURORA 362 (8-1%) 368 (8-3%) 0.99 AFCAPS/TexCAPS 143 (0-8%) 201 (1-2%) 0.94 LIPS. 164 (6-9%) 195 (9-0%) 0.92 GISSI-HE 0.92 172 (2.2%) 1/4 (2-2%) 4D. 162 (10-1%) 0.89 144 (9.0%) ALERT 135 (2.7%) 140 (2.7%) 0.84 MEGA 0.67 102 (0.5%) 140 (0.7%) ALLUAT-LLT 812 (3-5%) 0.54 758 (3-3%) 208 (5-4%) GISSI-P 0.35 231 (6-1%) 0.78 (0.76-0.81) Subtotal (21 trials) 7136/64744 8934/64782 0.79 (0.77-0.81) 1.07 $\langle \rangle$ (3-6%) (2.8%) p<0.0001 p<0-0001 Overall (26 trials) 13350/84565 0.78 (0.76-0.80) 10973/84573 $\langle \rangle$ (3.2%)(4.0%) p<0.0001 Heterogeneity between statin vs control and more vs less: before taking account of LDL differences: χ_1^2 = 10-7 (p=0.001) - after taking account of LDL differences: χ'_{2} - 4-5 (p=0-03) - 99% or 0.75 1.25 0.75 1-25 0.5 1.5 0.5 1.5 <>> 95% CI Control/lessbetter Statin/more better Control/less better Statin/more better

Baigent C, et al.

Lancet 2005;366:1267-78.

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Reducing LDL-C to 53 mg/dl with statin and ezetimibe







Reducing LDL-C to 30 mg/dl with statin and PCSK9 inhibitor







2024 ESC Guidelines for the management of chronic coronary syndromes

Ultimate LDL-C goal of <1.4 mmol/L (55 mg/ dL)(and)a \geq 50% reduction in LDP-C vs. baseline is recommended

Vrints C, Andreotti F, et al. Eur Heart J 2024, doi.10.1093/eurheartj/ehae177





Reduction in C-reactive protein and LDL cholesterol and cardiovascular event rates after initiation of rosuvastatin: a prospective study of the JUPITER trial



Ridker PM, et al. Lancet 2009; 373: 1175–82





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

In patients at high risk, an LDL-C reduction of

≥50% from baseline and an LDL-C goal of <1.8

mmol/L (<70 mg/dL) are recommended.

Mach F, Baigent C, et al. Eur Heart J 2020;41:111188





Ezetimibe Added to Statin Therapy after Acute Coronary Syndromes

Christopher P. Cannon, M.D., Michael A. Blazing, M.D., Robert P. Giugliano, M.D., Amy McCagg, B.S., Jennifer A. White, M.S., Pierre Theroux, M.D., Harald Darius, M.D., Basil S. Lewis, M.D., Ton Oude Ophuis, M.D., Ph.D., J. Wouter Jukema, M.D., Ph.D., Gaetano M. De Ferrari, M.D., Witold Ruzyllo, M.D., Paul De Lucca, Ph.D., KyungAh Im, Ph.D., Erin A. Bohula, M.D., D.Phil., Craig Reist, Ph.D., Stephen D. Wiviott, M.D., Andrew M. Tershakovec, M.D., M.P.H., Thomas A. Musliner, M.D., Eugene Braunwald, M.D., and Robert M. Califf, M.D., for the IMPROVE-IT Investigators*

Evolocumab and Clinical Outcomes in Patients with Cardiovascular Disease

Marc S. Sabatine, M.D., M.P.H., Robert P. Giugliano, M.D., Anthony C. Keech, M.D., Narimon Honarpour, M.D., Ph.D., Stephen D. Wiviott, M.D., Sabina A. Murphy, M.P.H., Julia F. Kuder, M.A., Huei Wang, Ph.D., Thomas Liu, Ph.D., Scott M. Wasserman, M.D., Peter S. Sever, Ph.D., F.R.C.P., and Terje R. Pedersen, M.D., for the FOURIER Steering Committee and Investigators*

Baseline LDL-C: 93.8 mg/dl

Baseline LDL-C: 92 mg/dl



Start treatment with high intensity stating Group



Donald M. Lloyd-Jones DM, Morris PB, et al. JACC 2016;68:92-125





Intensity of lipid lowering treatment

Treatment	Average LDL-C reduction
Moderate intensity statin	≈ 30%
High intensity statin	≈ 50%
High intensity statin plus HEFCARD 20 ezetimibe	25 ≈ 65%
PCSK9 inhibitor	≈ 60%
PCSK9 inhibitor plus high intensity statin	≈ 75%
PCSK9 inhibitor plus high intensity statin plus ezetimibe	≈ 85%

Mach F, Baigent C, et al. Eur Heart J 2020;41:111-188

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LDL-C lowering effect of moderate intensity statin plus ezetimibe:

LDL-C is reduced to 53 mg/dl but the reduction is less than 50% from

baseline

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







The benefit of statin and ezetimibe on the prevention

of new-onset heart failure





The 5th Indonesian he effect of statin therapy on the risk of first non-fatal heart failure hospitalization

TRIAL	Events on statin	Total on statin	Events on control	Total on control	Risk Ratio Weight (95% Cl)
WOSCOPS	10	3302	18	3293	0.55 (0.26, 1.20) - 1.20
CARE	118	2081	129	2078	0.91 (0.72, 1.16) 8.62
GISSI PREVENZIONE	49	2138	43	2133	1.14 (0.75, 1.70) 2.88
HPS	305	10269	340	10267	0.90 (0.77, 1.04) - 22.71
PROSPER	77	2891	77	2913	1.01 (0.74, 1.38) 5.12
GREACE	11	800	21	800	0.52 (0.25, 1.08) - 1.40
ALLHAT-LLT	224	5170	223	5185	1.01 (0.84, 1.21) - 14.87
ASCOT-LLA	37	5134	36		1.02 (0.65, 1.61) - 2.41
CARDS	7	1428	5		1.38 (0.44, 4.35) 0.34
ALLIANCE	38	1217	51	1225	0.75 (0.50, 1.13) = 3.40
TNT	119	4995	158	5006	0.75 (0.60, 0.95) 10.54
IDEAL	95	4439	120	4449	0.79 (0.61, 1.04) 8.01
ASPEN	3	1211	3	1199	0.99 (0.20, 4.90) - 0.20
MEGA	3	3866	3	3966	1.03 (0.21, 5.08) 0.20
SPARCL	19	2365	23	2366	0.83 (0.45, 1.51) - 1.54
JUPITER	19	8901	22	8901	0.86 (0.47, 1.59) - 1.47
SEARCH	210	6031	226	6033	0.93 (0.77, 1.12) - 15.09
Overall (<i>l</i> ² = 0.0%, <i>P</i>	= 0.757)			\diamond	0.90 (0.84, 0.97) 100.00
				02	50
			F	reiss D et al Eur Heart J 2015:36 1536–1546	3.0



the diagnosis a



2021 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure

Treatment with statins is recommended in patients at high risk of CV disease or with CV disease in order to prevent or delay the onset of HF, and to prevent HF hospitalizations.^{291,292}

McDonagh TA, Metra M, et al. Eur Hear J 2021;42:3599–3726











Evolocumab and Clinical Outcomes in Patients with Cardiovascular Disease



There were reductions of 21 to 27% in the risk of myocardial

infarction, stroke, and coronary revascularization. IHEFCARD 2025

But

No observed effect on the rates of cardiovascular death or

hospitalization for worsening heart failure.

Sabatine MS, et al. N Engl J Med 2017, DOI: 10.1056/NEJMoa1615664





LDL-C lowering is effective to lower atherosclerotic events in patients with ASCVD or high CVD risk but not in those

with heart failure





Effect of rosuvastatin in patients with chronic heart failure (the GISSI-HF trial): a randomised, double-blind, placebo-controlled trial

Tavazzi L, et al. Lancet 2008;372:1223-30.

IHEFCARD 2025

Rosuvastatin in Older Patients with Systolic Heart Failure

Kjekshus J, et al. N Engl J Med 2007;357:2248-61

					(TRAC)	Indonesian Working Group	
e 5th Inde posium on Hear dio metaboli	Variable	Placebo (N	V = 2497)	Rosuvastatin	n (N=2514)	Hazard Ratio (95% CI)	P Value
		No. of Patients	Event Rate	No. of Patients	Event Rate		
	Outcome						
	Fatal event						
	Death from cardiovascular causes§	593	9.6	581	9.3	0.97 (0.87–1.09)	0.60
	Sudden death	327	5.3	316	5.0	0.96 (0.82–1.12)	0.57
	In primary outcome	284		284			
	In coronary events	283	CAF	$RD_{272}O$	25		
	Worsening heart failure	191	3.1	193	3.1	1.00 (0.82–1.22)	1.00
	In primary outcome	157		161			
	Myocardial infarction§	9	0.2	15	0.2		
	In primary outcome	8		9			
	In coronary events	8		9			
	Stroke§¶	32	0.5	35	0.6		
	In primary outcome	11		14	Kjekshus J,	et al. N Engl J Med	2007;357:224





5

Changes in Galectin-3 and Outcome in Heart Failure



van der Velde AR, et al. Circ Heart Fail. 2013;6:219-226





Effect of Rosuvastatin on Repeat Heart Failure Hospitalizations The CORONA Trial (Controlled Rosuvastatin Multinational Trial in Heart Failure)

When repeat events were included, rosuvastatin was

shown to reduce the risk of HFH by approximately 15%

to 20%, equating to approximately 76 fewer

admissions per 1,000 patients treated over a median

33 months of follow-up.

Rogers JK, et al. J Am Coll Cardiol HF 2014;2:289–97





Initiation of Statins for Primary Prevention in Heart Failure With Preserved Ejection Fraction

Ariela R. Orkaby, MD, MPH,^{a,b,c,*} Parag Goyal, MD,^{d,*} Brian Charest, MS, MPH,^b Saadia Qazi, DO, MPH,^t Shamlan Sheikh, MD,^{b,c} Sanjiv Shah, MD,^f J. Michael Gaziano, MD, MPH,^{b,c} Luc Djousse, MD, ScD,^{b,c} David Gagnon, MD, MPH, PHD,^{b,g,†} Jacob Joseph, MBBS, MD^{b,h,i,†}

New statin use was associated with reduced all-cause

mortality, MACE, and hospitalization in Veterans with

HFpEF without prevalent ASCVD.

JACC Adv 2024;3:100869





Effect of PCSK9 inhibitors on congestive heart failure exacerbation:

A meta-analysis of 35 randomized controlled trials



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Take-home message





ACC/AHA Stages of HF

STAGE A: At-Risk for Heart Failure

Patients at risk for HF but without current or previous symptoms/signs of HF and without structural/ functional heart disease or abnormal biomarkers

Patients with hypertension, CVD, diabetes, obesity, exposure to cardiotoxic agents, genetic variant for cardiomyopathy, or family history of cardiomyopathy

STAGE B: Pre-Heart Failure

Patients without current or previous symptoms/signs of HF but evidence of 1 of the following:

Structural heart disease

Evidence of increased filling pressures

Risk factors and

• increased natriuretic peptide levels or

 persistently elevated cardiac troponin
 in the absence of competing diagnoses STAGE C: Symptomatic Heart Failure

Patients with current or previous symptoms/signs of HF

STAGE D: Advanced Heart Failure

Marked HF symptoms that interfere with daily life and with recurrent hospitalizations despite attempts to optimize GDMT

Heidenreich PA, et al. Circulation. 2022;145:e895-e1032





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