Update 2023 Lipid Management in CKD

Narongrit Siriwattanasit, MD
Division of Nephrology
Department of Medicine
Phramongkutklao Hospital and College of Medicine

Disclosure information

- Narongrit Siriwattanasit, M.D.

- Scientific Advisor/Honoraria:
  - Astra Zeneca, Boehringer Ingelheim, MSD, LG Life Sciences

- DISCLAIMER
  - This presentation is intended for educational purpose for HCPs only. It may contain new science data which is currently not in approved package insert information and is not intended for off-label promotion.

OUTLINES

- Lipid metabolism and role of cholesterol absorption with CVD
- Lowering LDL-cholesterol on CV outcomes in CKD
- Reduction LDL-cholesterol and renal progression
- Update guideline for lipid control in CKD: KDIGO, ESC, Thai guideline

OUTLINES

- ➤Lipid metabolism and role of cholesterol absorption with CVD
- ➤Lowering LDL-cholesterol on CV outcomes in CKD
- ➤Reduction LDL-cholesterol and renal progression
- ➤Update guideline for lipid control in CKD: KDIGO, ESC, Thai guideline

Abnormal lipid profile in kidney diseases

Lipid	Nephrotic syndrome	CKD stage 5	Hemodialysis	Peritoneal dialysis	Kidney transplantation
Cholesterol	↑↑	↔	↔	↑↑	↑
Triglyceride	↑↑	↑	↑	↑↑↑	↑↑
IDL	↑	↑	↑	↑	↑
LDL	↑↑	↔/↑	↔/↑	↑	↑
Small dense LDL	↑	↑	↑	↑	—
HDL	↓	↓	↓	↓	↔

Nuntanutch Chanlerdfa, Bancha Satirapoj . J Nephrol Soc Thail 2023; 29(2): 79-94

Abnormal lipid profile in kidney diseases

Lipid	Nephrotic syndrome	CKD stage 5	Hemodialysis	Peritoneal dialysis	Kidney transplantation
Cholesterol	↑↑	↔	↔	↑↑	↑
Triglyceride	↑↑	↑	↑	↑↑↑	↑↑
IDL	↑	↑	↑	↑	↑
LDL	↑↑	↔/↑	↔/↑	↑	↑
Small dense LDL	↑	↑	↑	↑	—
HDL	↓	↓	↓	↓	↔

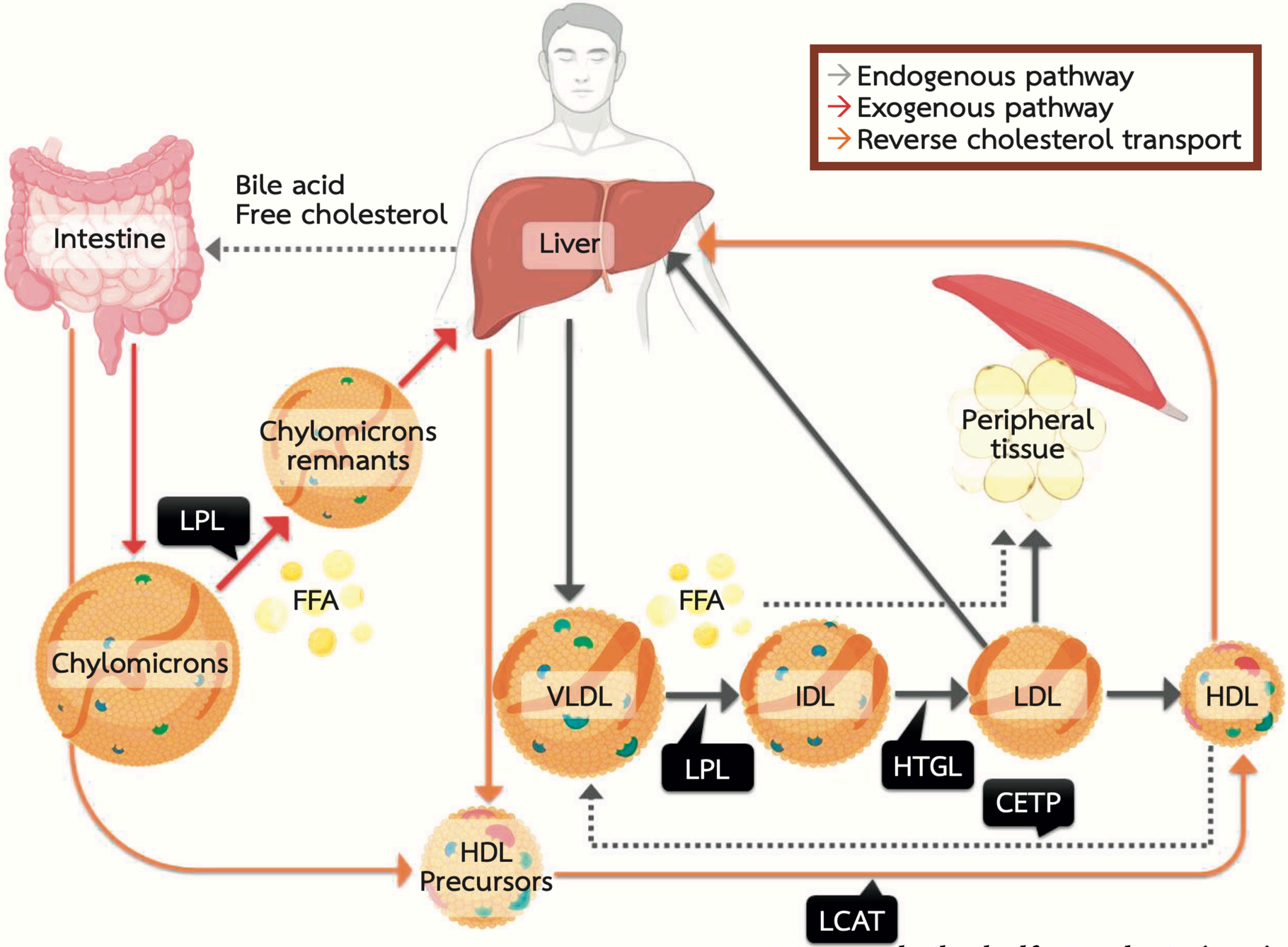
Nuntanutch Chanlerdfa, Bancha Satirapoj . J Nephrol Soc Thail 2023; 29(2): 79-94

Abnormal lipid profile in kidney diseases

Lipid	Nephrotic syndrome	CKD stage 5	Hemodialysis	Peritoneal dialysis	Kidney transplantation
Cholesterol	↑↑	↔	↔	↑↑	↑
Triglyceride	↑↑	↑	↑	↑↑↑	↑↑
IDL	↑	↑	↑	↑	↑
LDL	↑↑	↔/↑	↔/↑	↑	↑
Small dense LDL	↑	↑	↑	↑	—
HDL	↓	↓	↓	↓	↔

Nuntanutch Chanlerdfa, Bancha Satirapoj . J Nephrol Soc Thail 2023; 29(2): 79-94

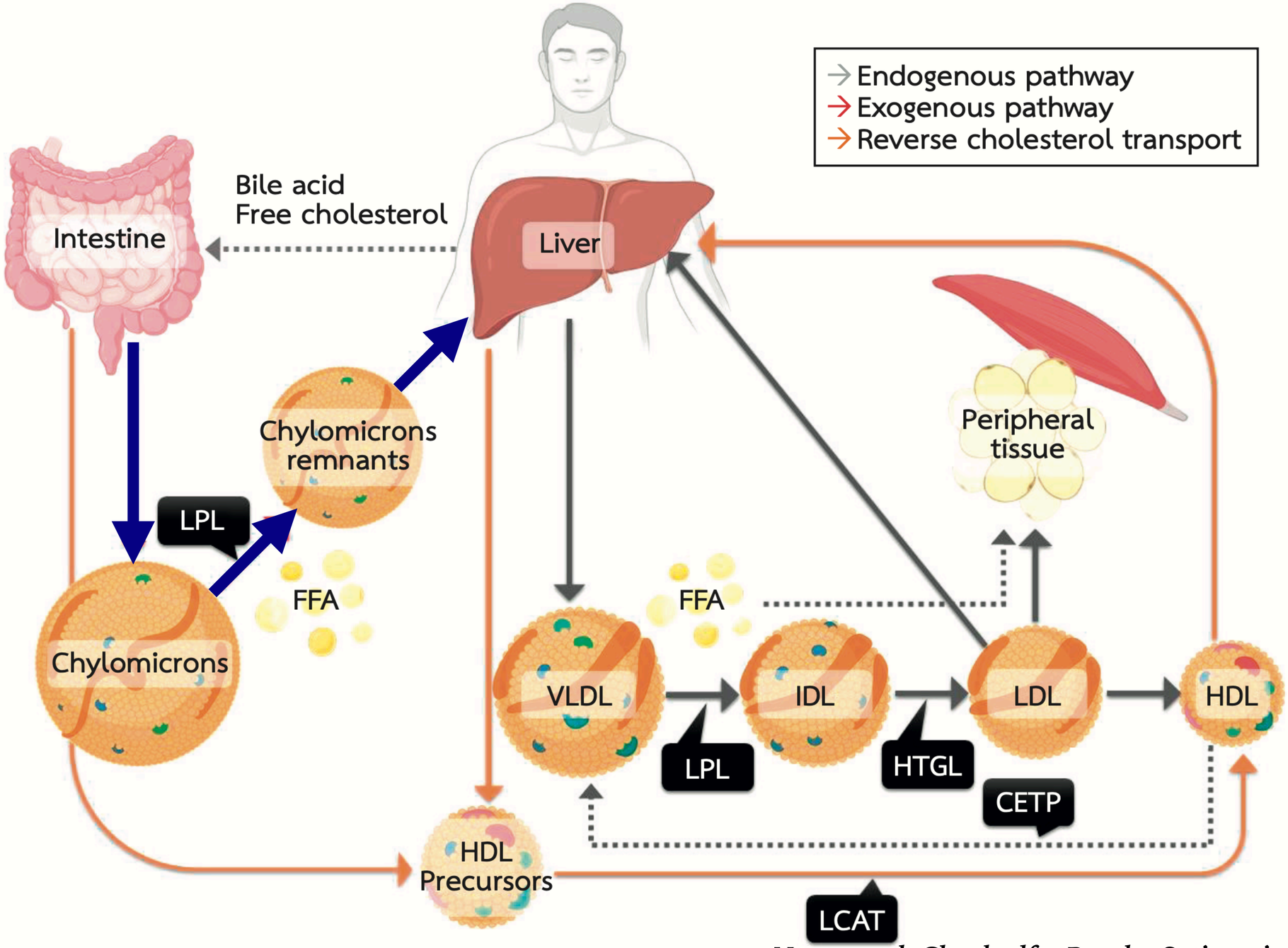
Lipid metabolism



Nuntanutch Chanlerdfa, Bancha Satirapoj . J Nephrol Soc Thail 2023; 29(2): 79-94

Lipid metabolism

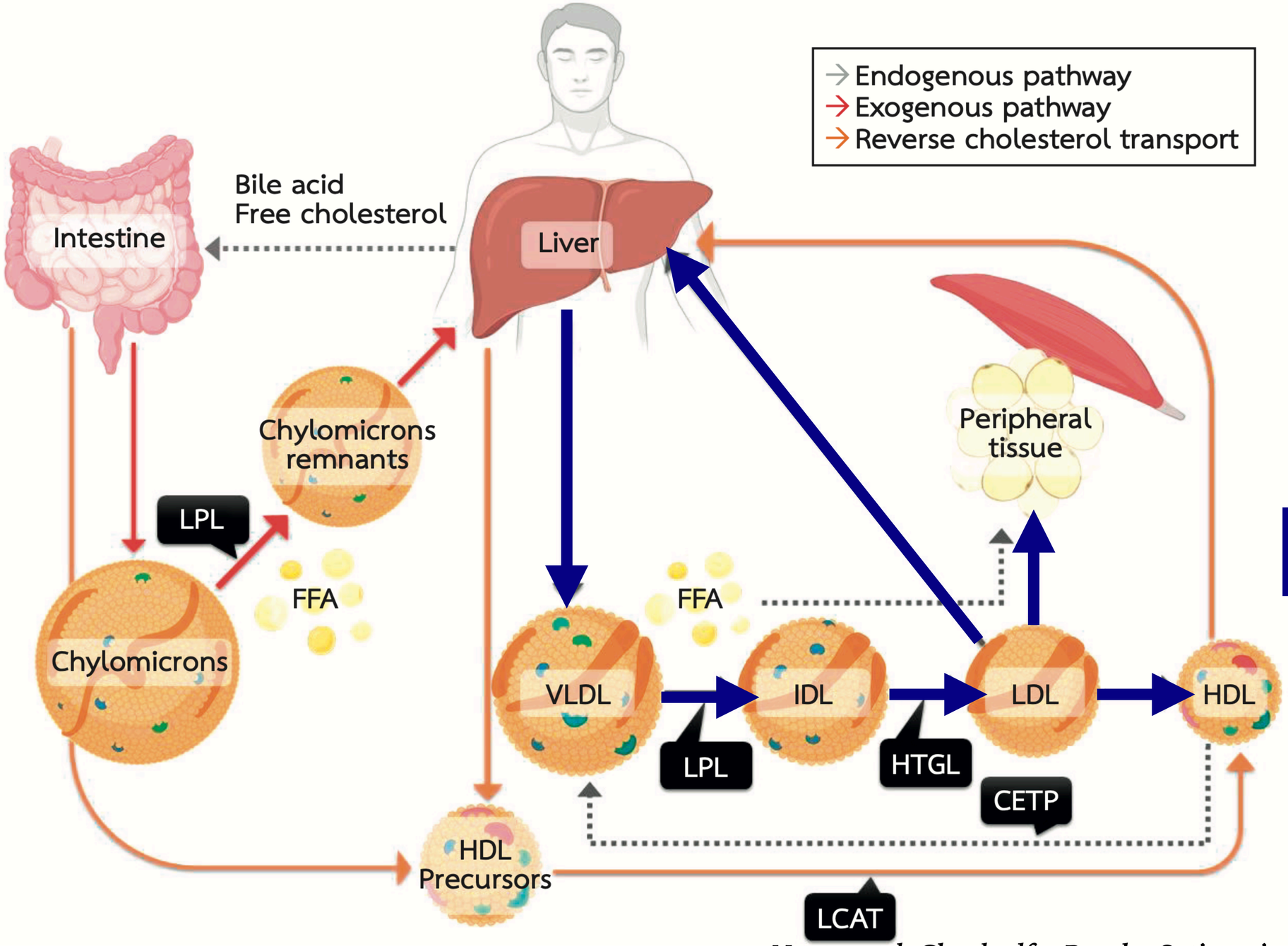
Exogenous pathway



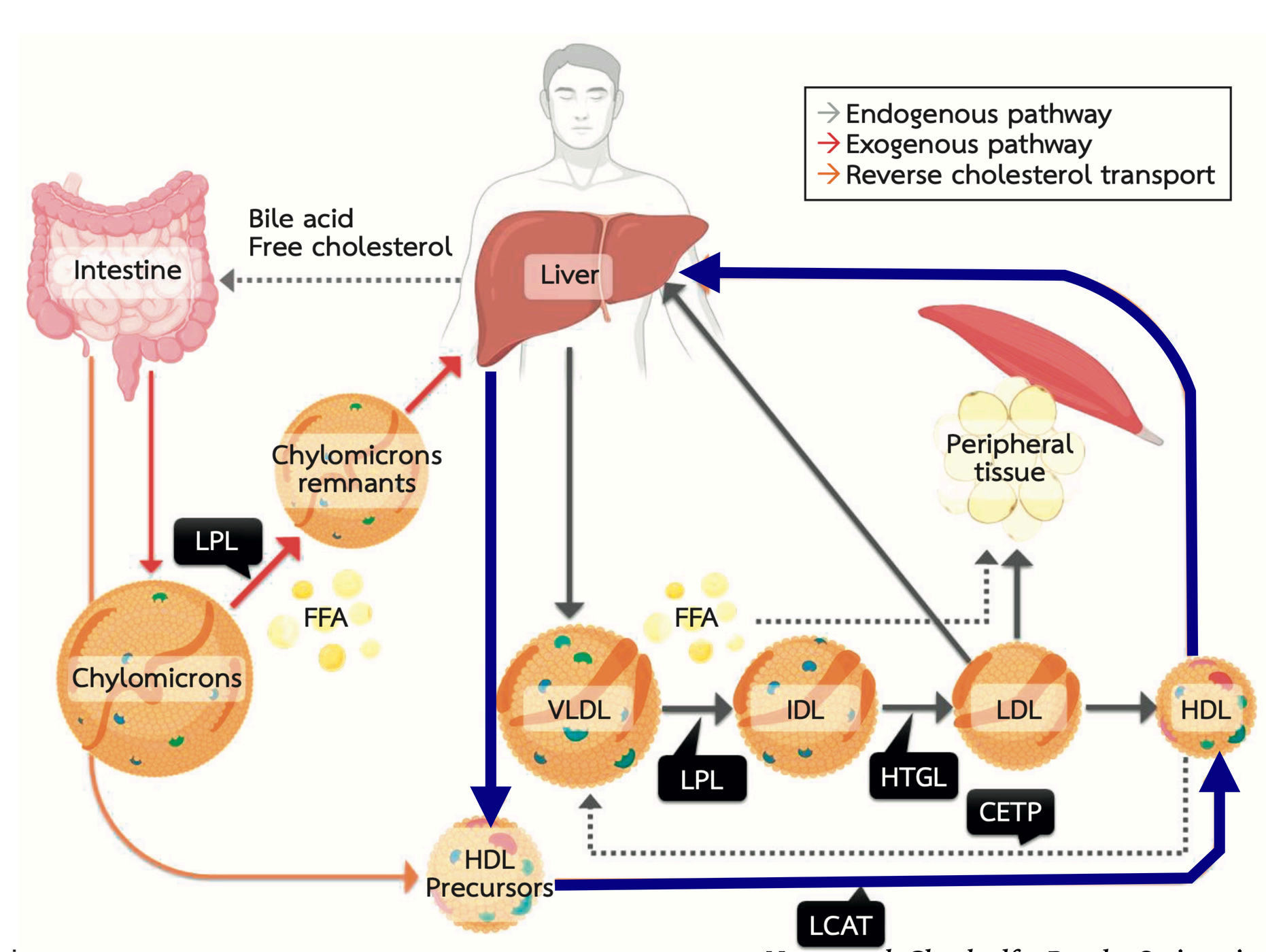
Nuntanutch Chanlerdfa, Bancha Satirapoj . J Nephrol Soc Thail 2023; 29(2): 79-94

Lipid metabolism

Endogenous pathway



Nuntanutch Chanlerdfa, Bancha Satirapoj . J Nephrol Soc Thail 2023; 29(2): 79-94

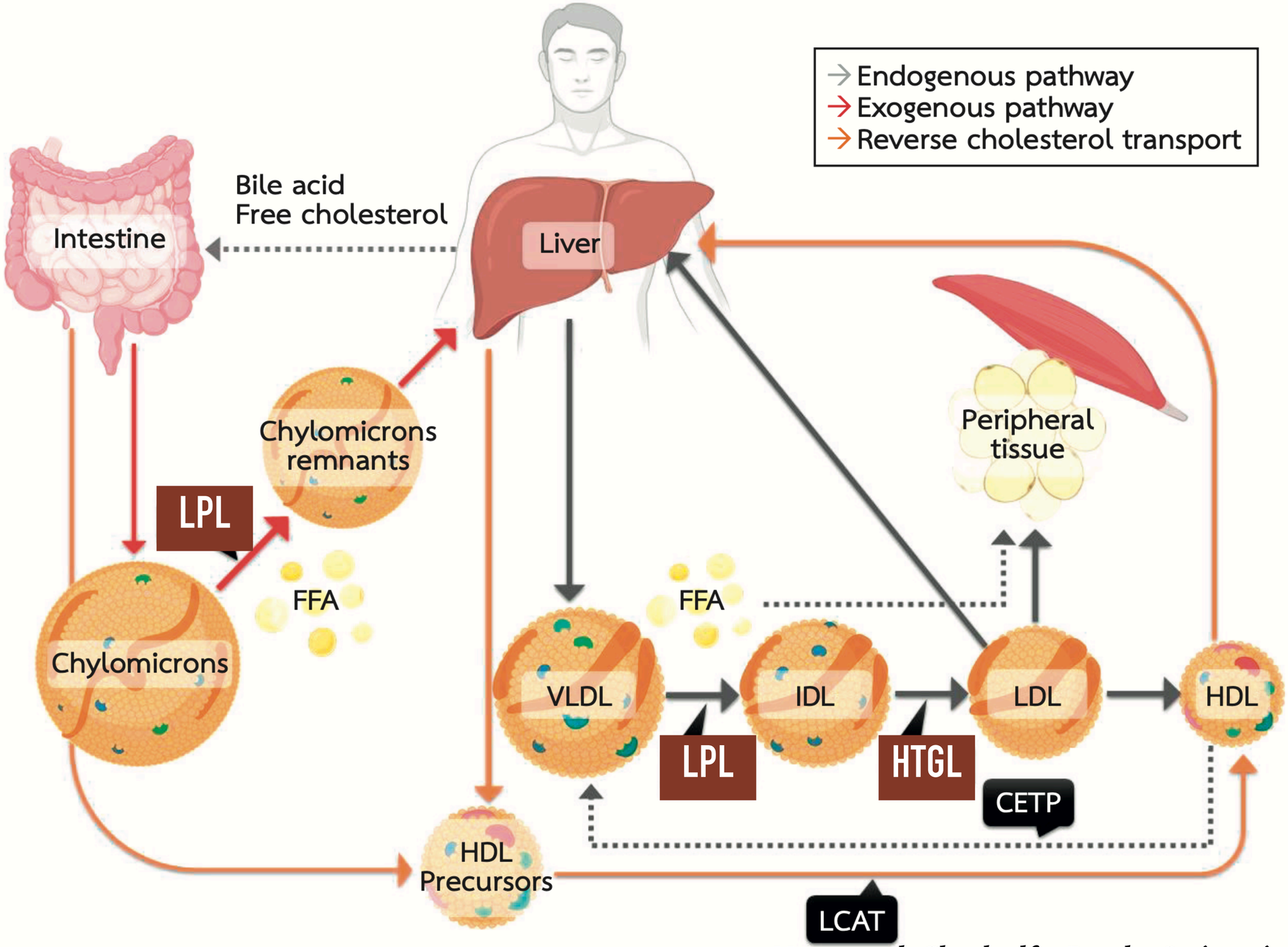


Lipid metabolism

Reverse cholesterol transport

Nuntanutch Chanlerdfa, Bancha Satirapoj . J Nephrol Soc Thail 2023; 29(2): 79-94

Lipid metabolism

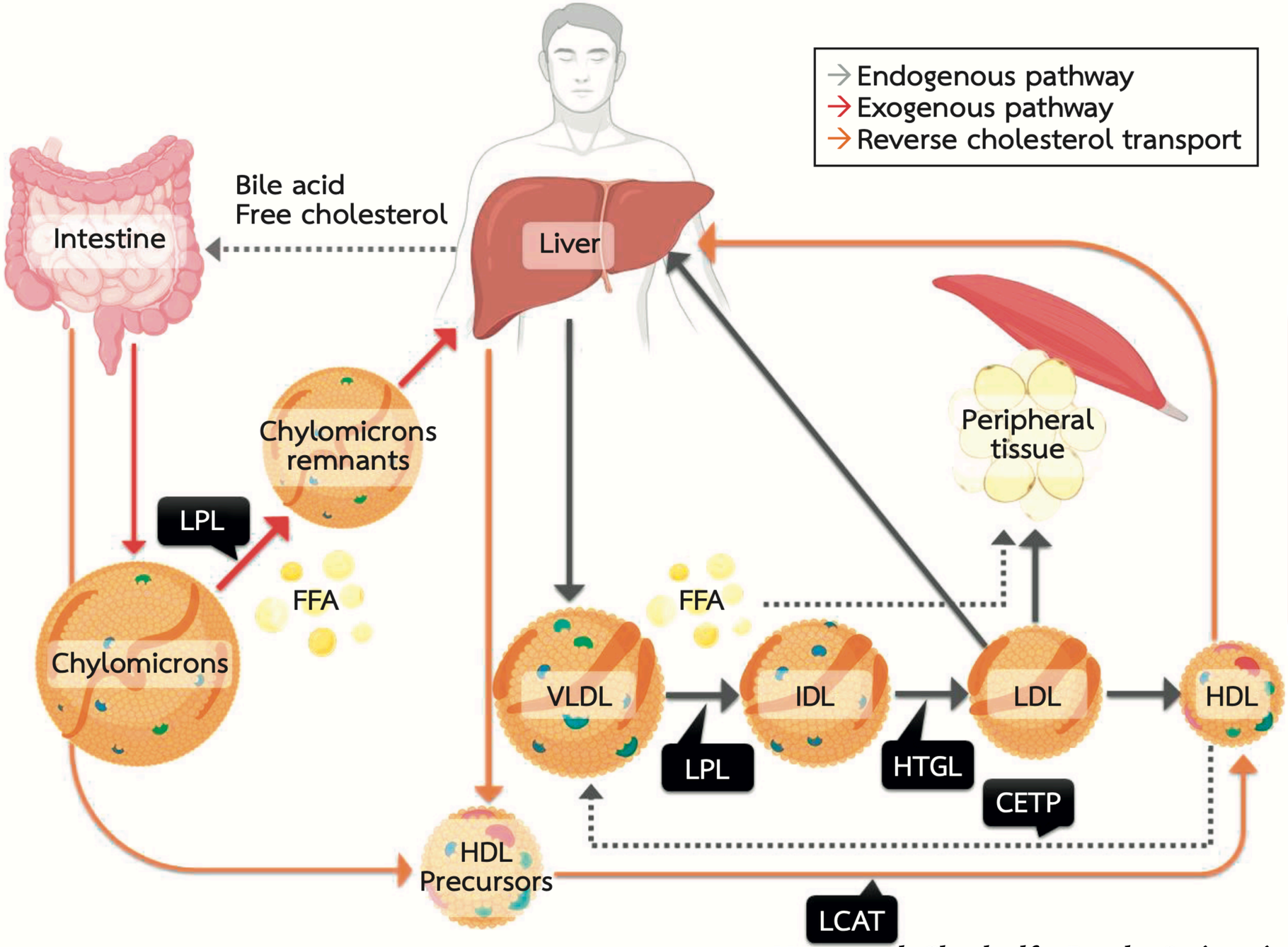


Triglyceride

- Carbohydrate intolerance
- ↓LPL& HTGL → ↓TG clearance
- ↓ApoC-II/ApoC-III → ↓TG clearance
- HD: Heparin → ↓LPL
- Hyperparathyroidism → ↓LPL
- PD: ↑Glucose uptake from PDF

Nuntanutch Chanlerdfa, Bancha Satirapoj . J Nephrol Soc Thail 2023; 29(2): 79-94

Lipid metabolism

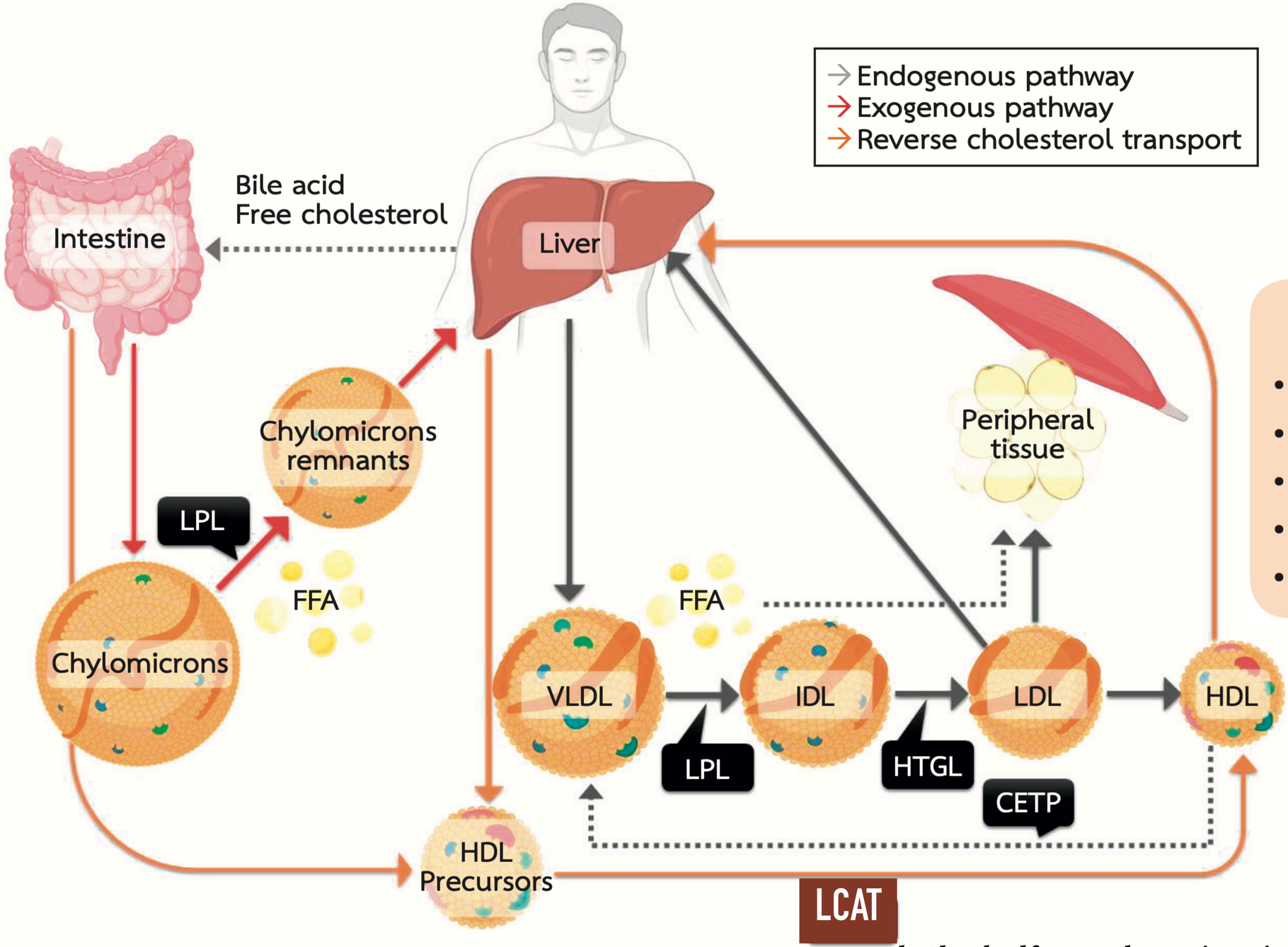


LDL

- ↑Small dense LDL
- MPO → ↑Oxidized LDL
- Urea/MPO → ↑Carbamelated LDL
- AGEs → ↑AGE-LDL
- PD: loss protein in effluent
  → ↑HMG-CoA reductase
  ↓LDL receptor

Nuntanutch Chanlerdfa, Bancha Satirapoj . J Nephrol Soc Thail 2023; 29(2): 79-94

Lipid metabolism

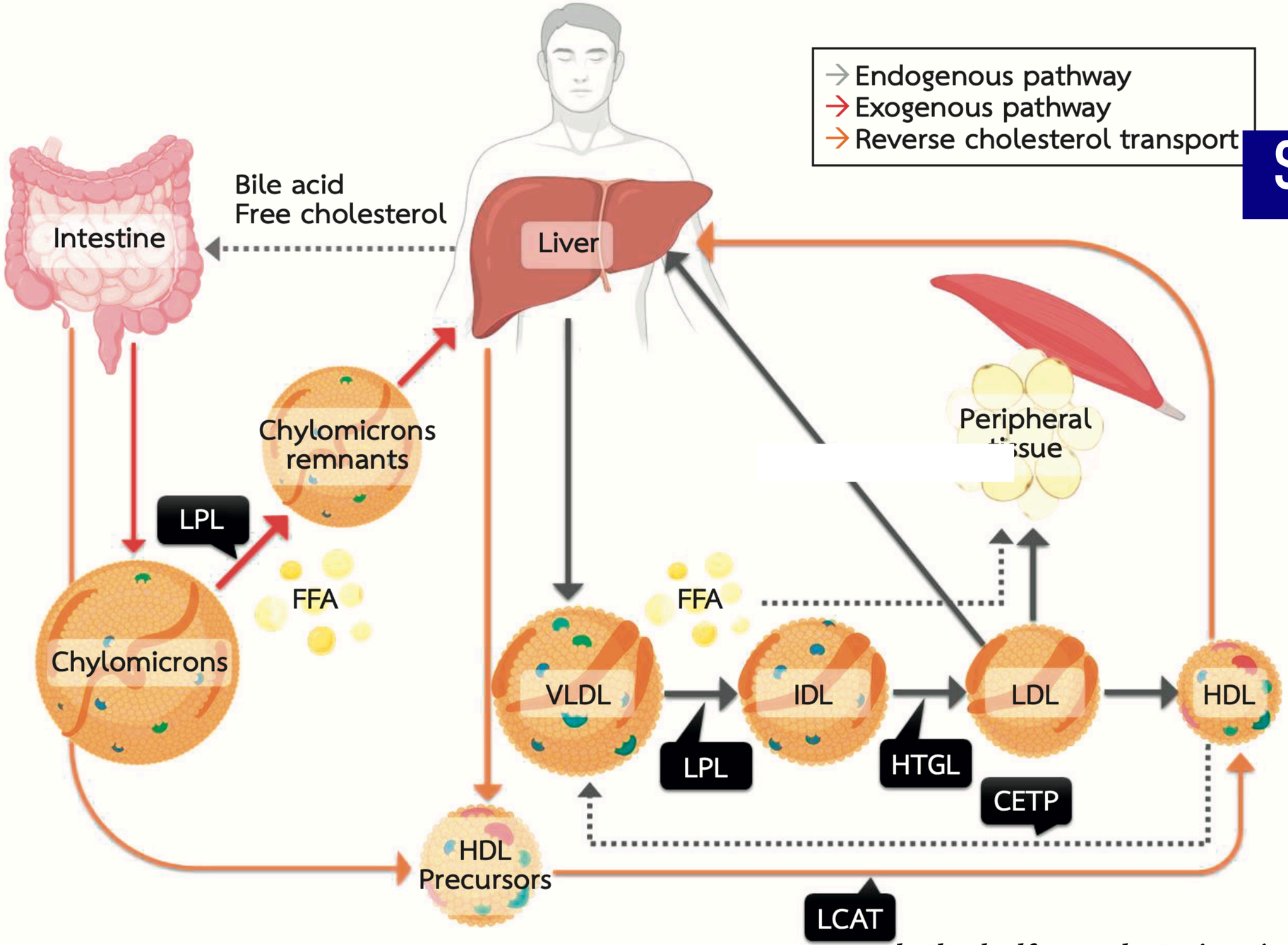


HDL

- ↓ApoA-1
- ↓LCAT → ↓Matured HDL
- ↓PON1 → ↓Antioxidant activity
- MPO → ↑Oxidized HDL
- ↓Reverse cholesterol transport

Nuntanutch Chanlerdfa, Bancha Satirapoj . J Nephrol Soc Thail 2023; 29(2): 79-94

Sources of cholesterol

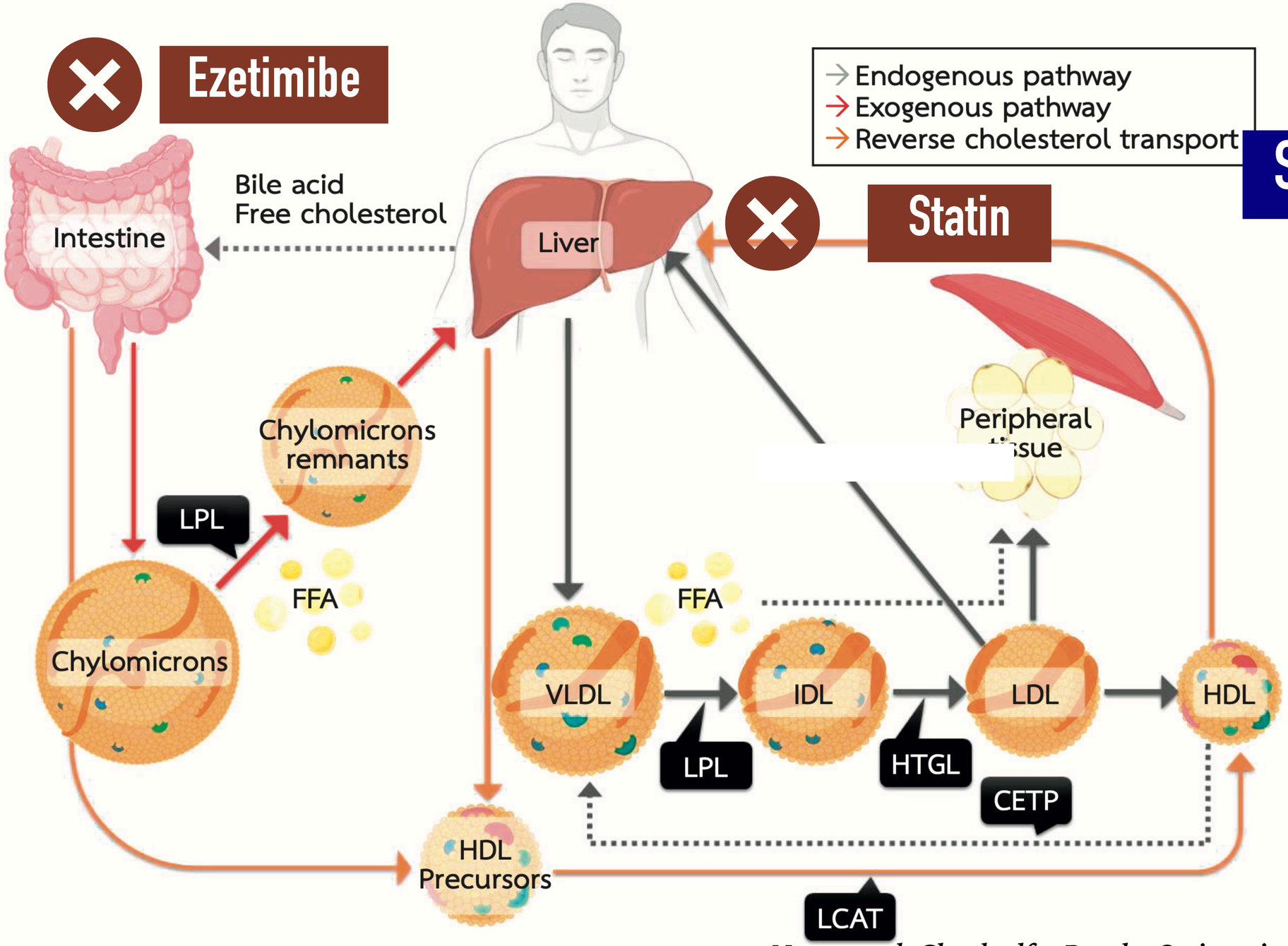


Synthesis (~800 mg/day)

Absorption ~700 mg/day

Nuntanutch Chanlerdfa, Bancha Satirapoj . J Nephrol Soc Thail 2023; 29(2): 79-94

Sources of cholesterol

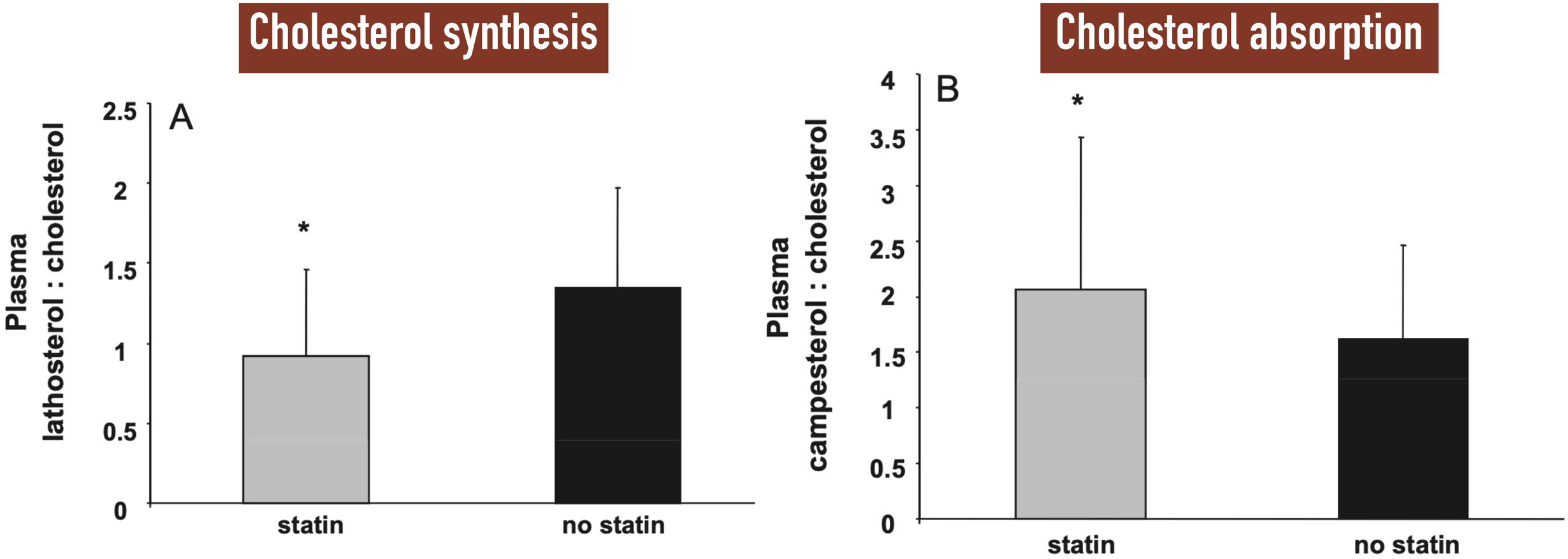


Synthesis (~800 mg/day)

Absorption ~700 mg/day

Nuntanutch Chanlerdfa, Bancha Satirapoj . J Nephrol Soc Thail 2023; 29(2): 79-94

Cholesterol absorption in patients with and without statin treatment



Markers of enhanced cholesterol absorption were enhanced in the statin group

Weingartner, et al., Chemistry and Physics of Lipids; 2010; 451-456

Long Term Statin use impact increase Cholesterol Absorption

Therapeutic factors that play a role in modulating cholesterol absorption and synthesis.

Therapeutic factors

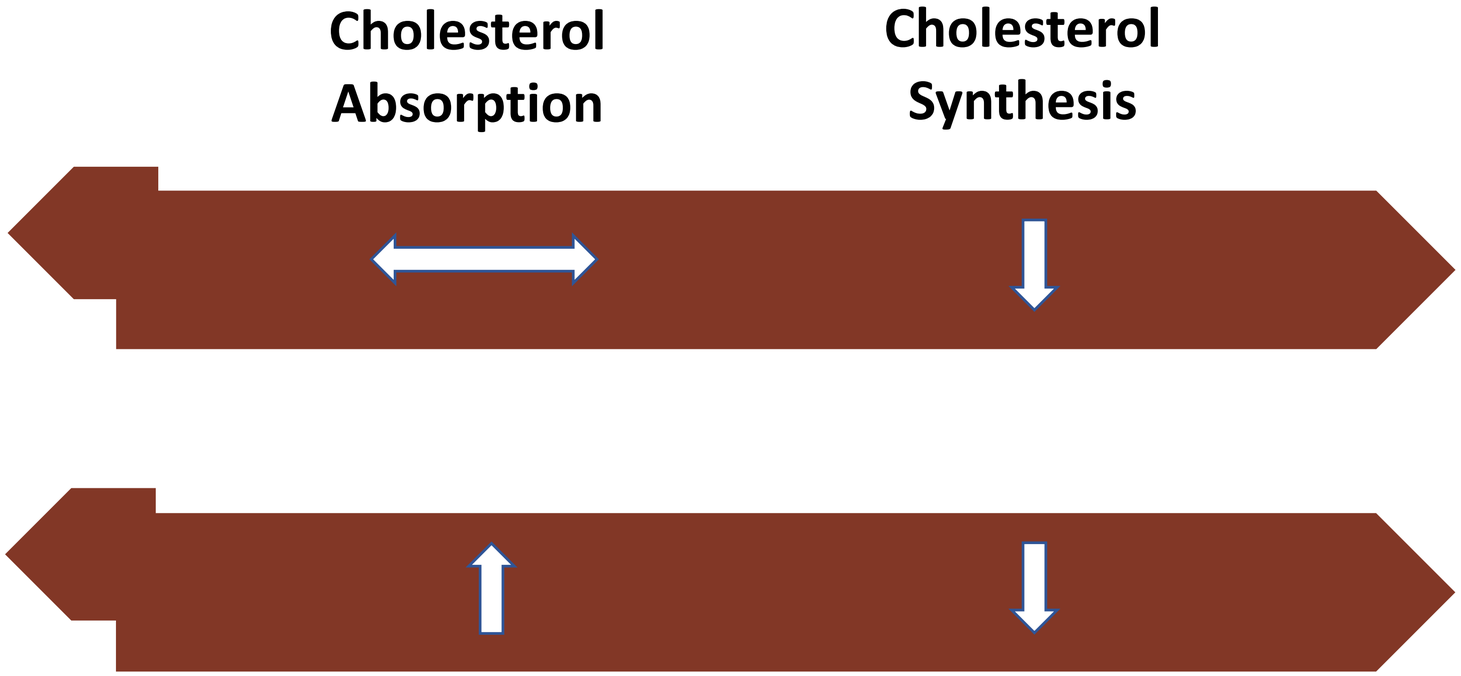
Statin Therapy

Short-term

20 mg/d for 3 weeks

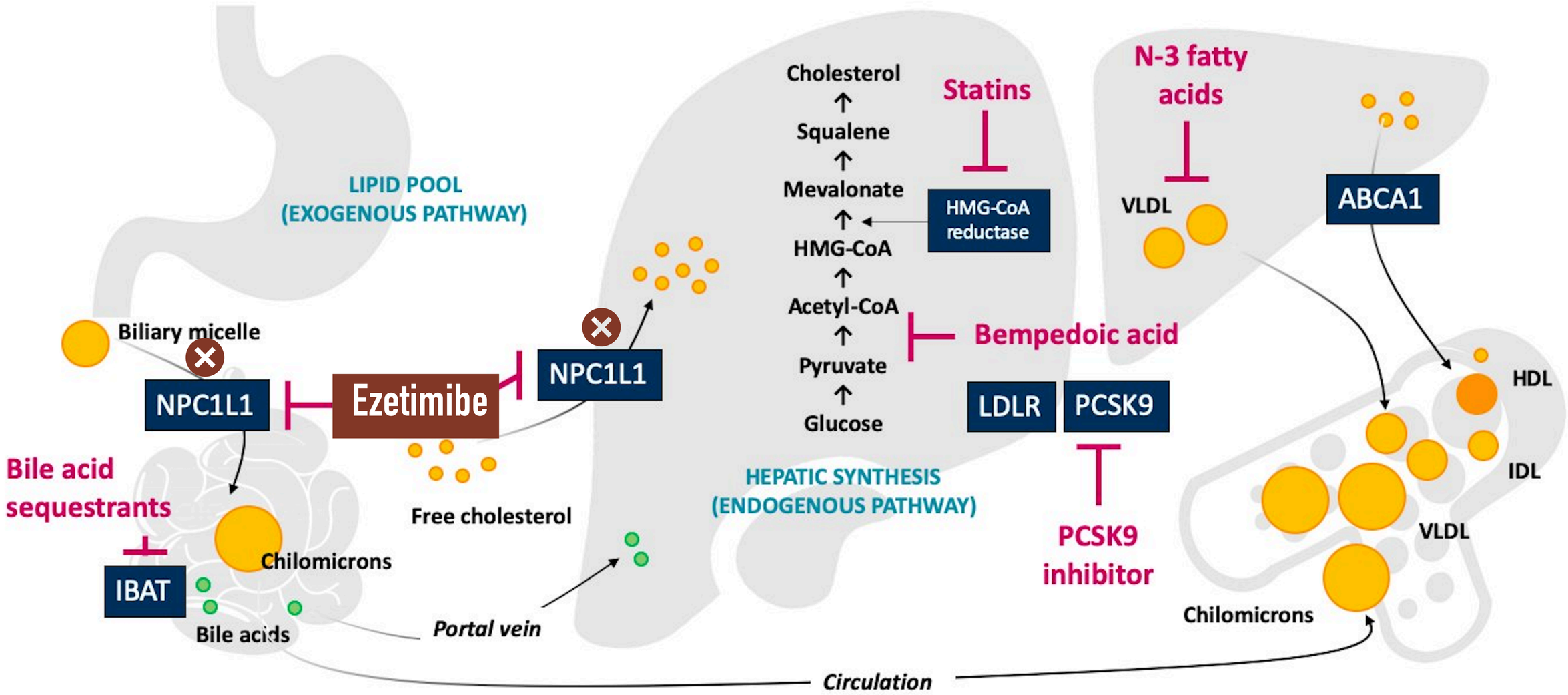
Long-term

20-40 mg/d for 5 years



Adapted from: Santosa, et al. Life sciences 80.6 (2007): 505-514.

Ezetimibe blocks cholesterol absorption



The official journal of the Japan Atherosclerosis Society and
the Asian Pacific Society of Atherosclerosis and Vascular Diseases

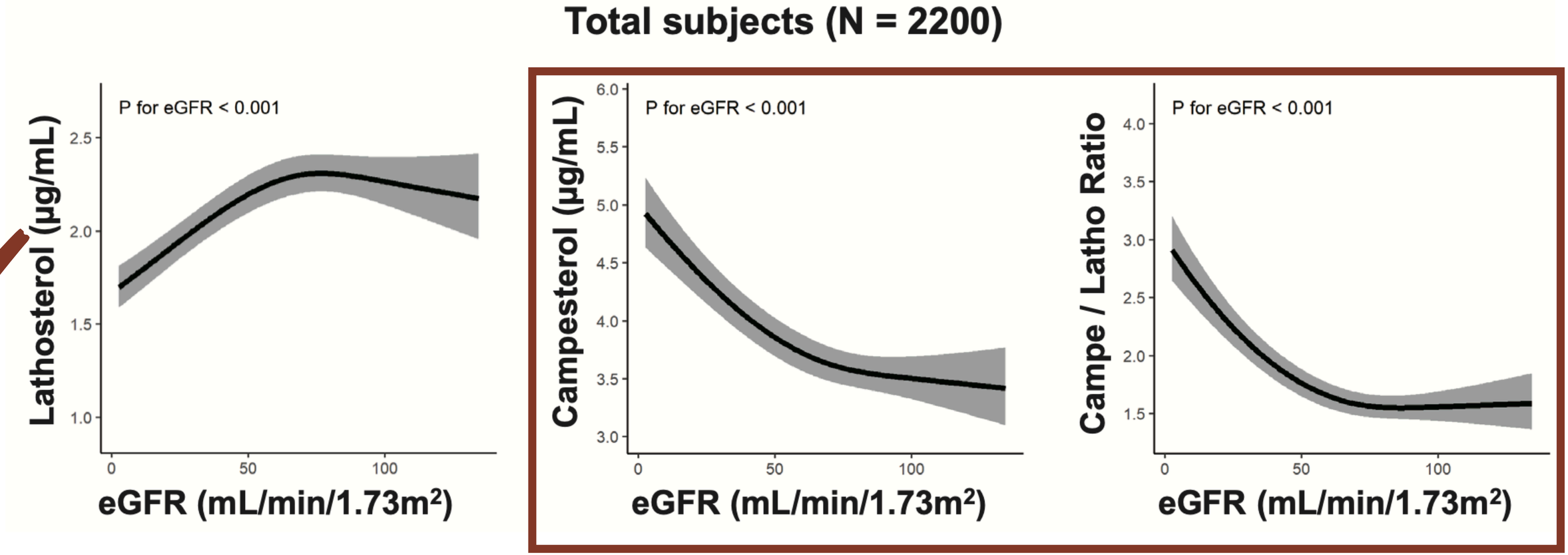
Original Article

J Atheroscler Thromb, 2022; 29: 1835-1848. *http://doi.org/10.5551/jat.63311*

Association of Kidney Function with Serum Levels of Cholesterol Absorption and Synthesis Markers: The CACHE Study CKD Analysis

- This study analyzed data from 2200 individuals including 522 hemodialysis patients
- Japan possessing data of lathosterol (Latho, synthesis marker) and campesterol (Campe, absorption marker)

Markers of cholesterol metabolism as functions of eGFR

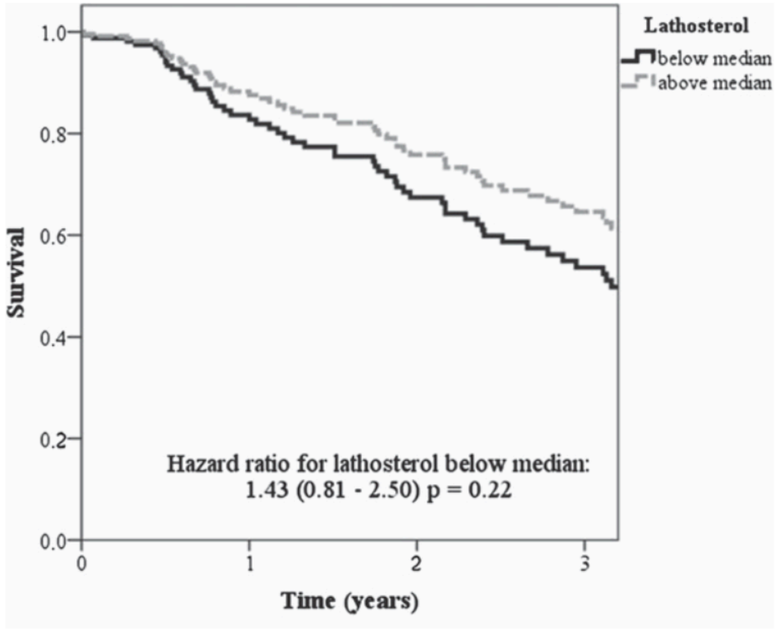


Tetsuo Shoji, et al., J Atheroscler Thromb, 2022; 29: 1835-1848.

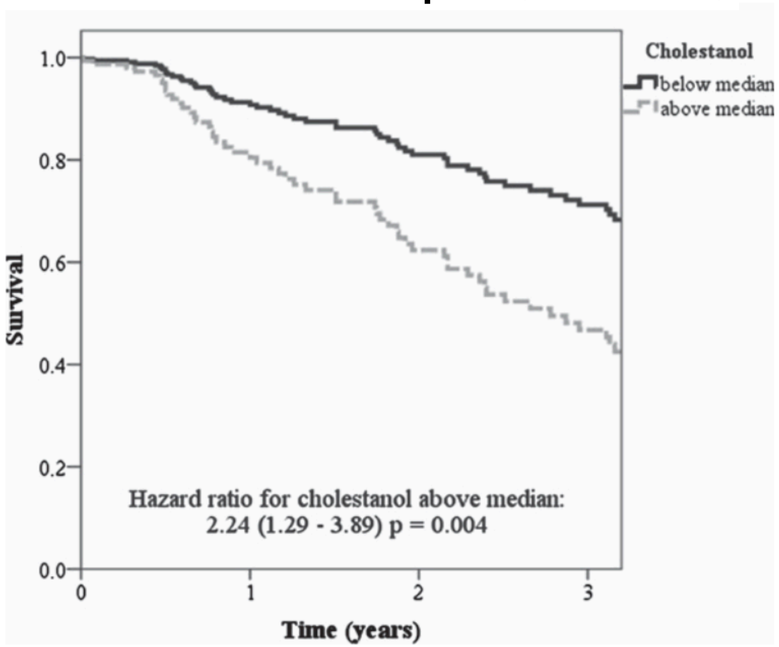
Cholesterol Synthesis, Cholesterol Absorption, and Mortality in Hemodialysis Patients

Kyrill S. Rogacev, Tobias Pinsdorf,† Oliver Weingärtner,‡ Markus K. Gerhart,* Elena Welzel,* Kai van Bentum,* Julius Popp,§ Andreas Menzner,‖ Danilo Fliser,* Dieter Lütjohann,† and Gunnar H. Heine**

Markers of cholesterol synthesis (lathosterol)



Markers of cholesterol absorption (cholestanol)



HD patients with higher cholestanol levels (marker of cholesterol absorption) faced worse clinical outcome

Rogacev KS, et al. Clin J Am Soc Nephrol 2012 (6):943-8.

Effect of Ezetimibe Coadministered With Atorvastatin in 628 Patients With Primary Hypercholesterolemia

A Prospective, Randomized, Double-Blind Trial

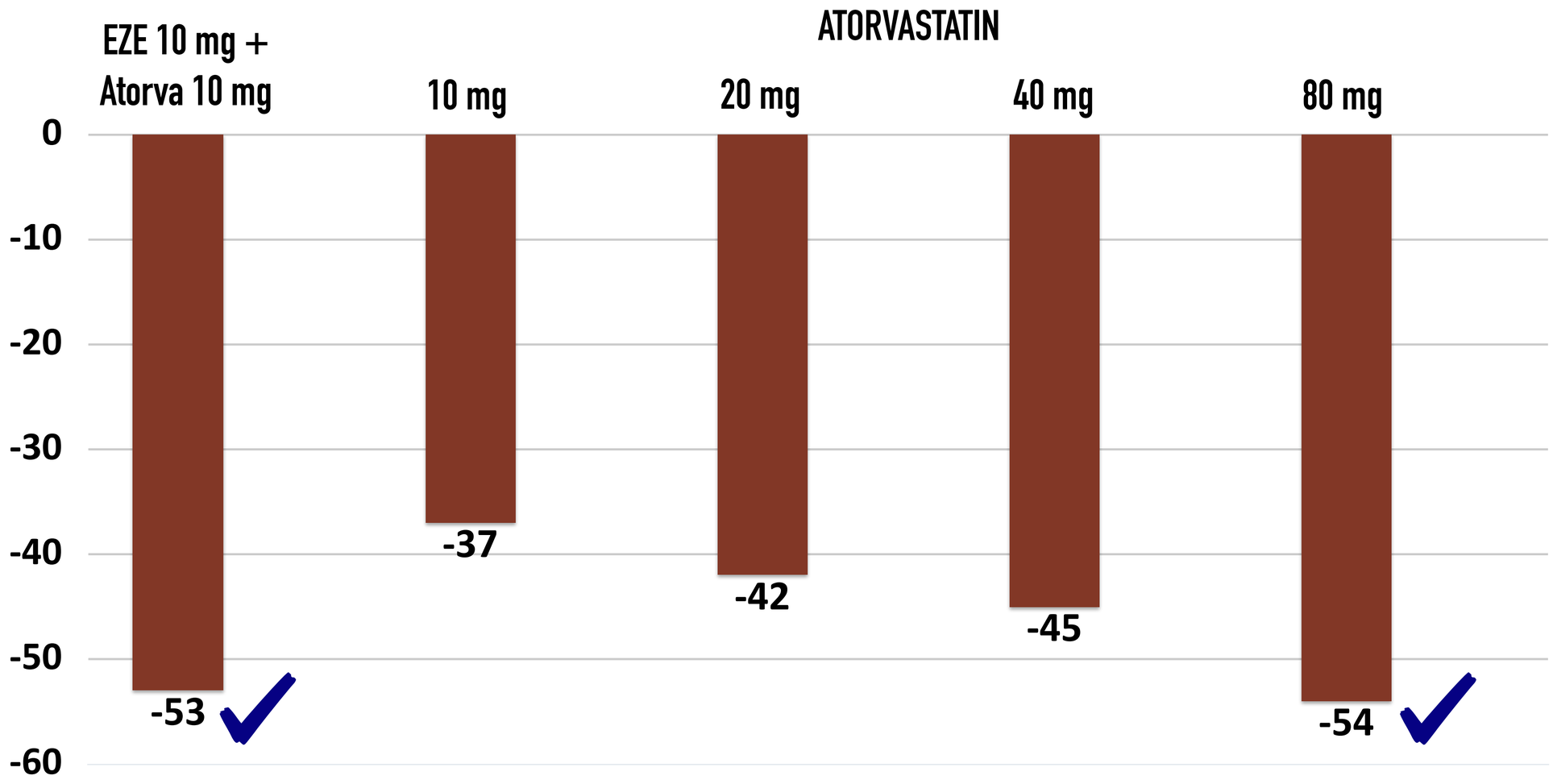
Design: A double-blind study, 628 patients with baseline LDL-C 145 to 250 mg/dL and triglycerides < or =350 mg/dL

randomly assigned to receive 1 of the following for 12 weeks:

- ezetimibe (10 mg/d)
- atorvastatin (10, 20, 40, or 80 mg/d);
- ezetimibe (10 mg) plus atorvastatin (10, 20, 40, or 80 mg/d) or placebo

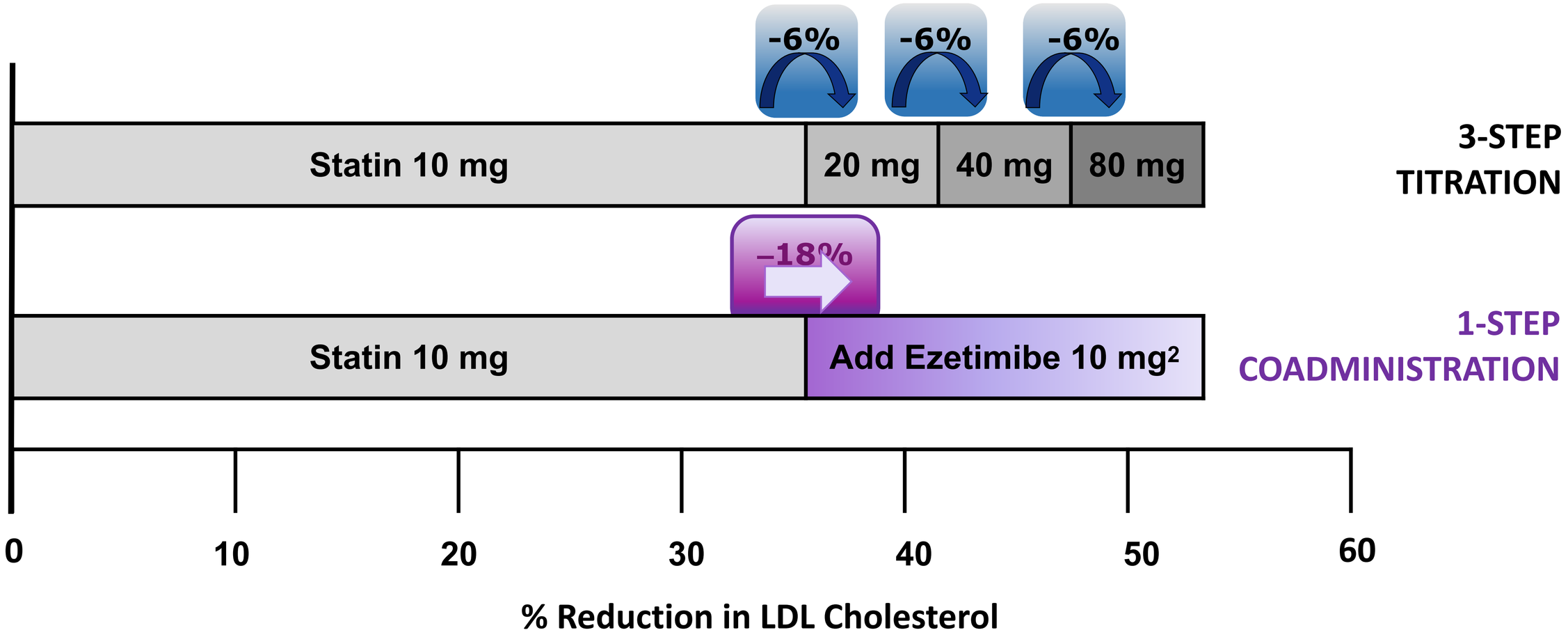
Ballantyne CM, et al. Circulation. 2003 May 20;107(19):2409-15.

Ezetimibe + Atorvastatin Study



Ballantyne CM, et al. Circulation. 2003 May 20;107(19):2409-15.

Significant Treatment Gap with Statin Monotherapy[1] and Complementary Therapy of Statin Plus Ezetimibe Regimen



1. Stein E. Eur Heart J Supplements 2001; 3 (Suppl E): E11–E16

2. Adapted from Knopp et al.

OUTLINES

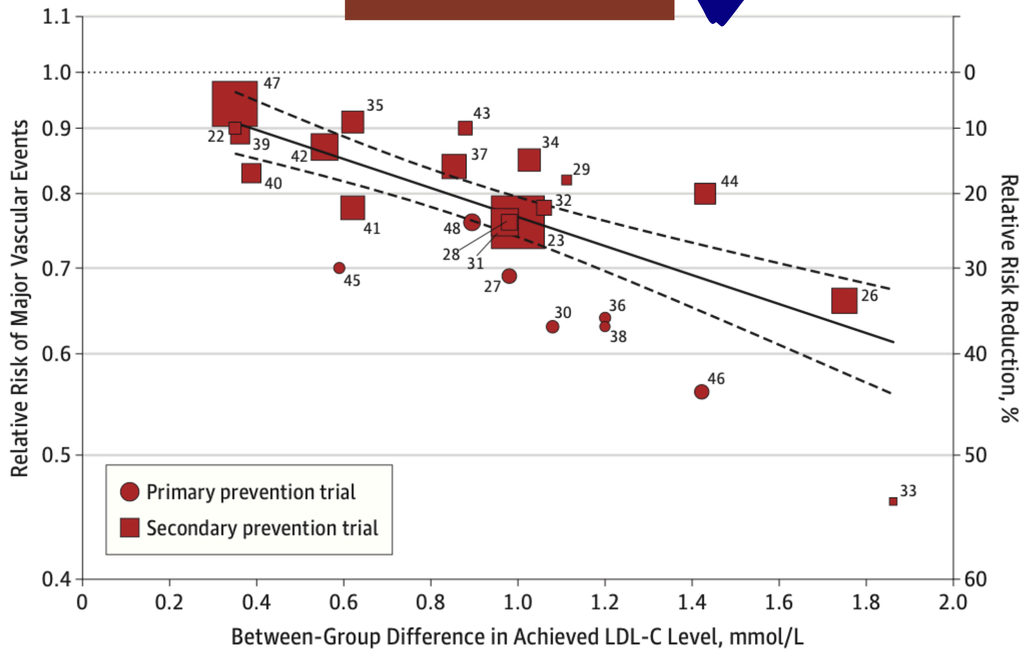
- Lipid metabolism and role of cholesterol absorption with CVD
- **Lowering LDL-cholesterol on CV outcomes in CKD**
- Reduction LDL-cholesterol and renal progression
- Update guideline for lipid control in CKD: KDIGO, ESC, Thai guideline

JAMA | Original Investigation

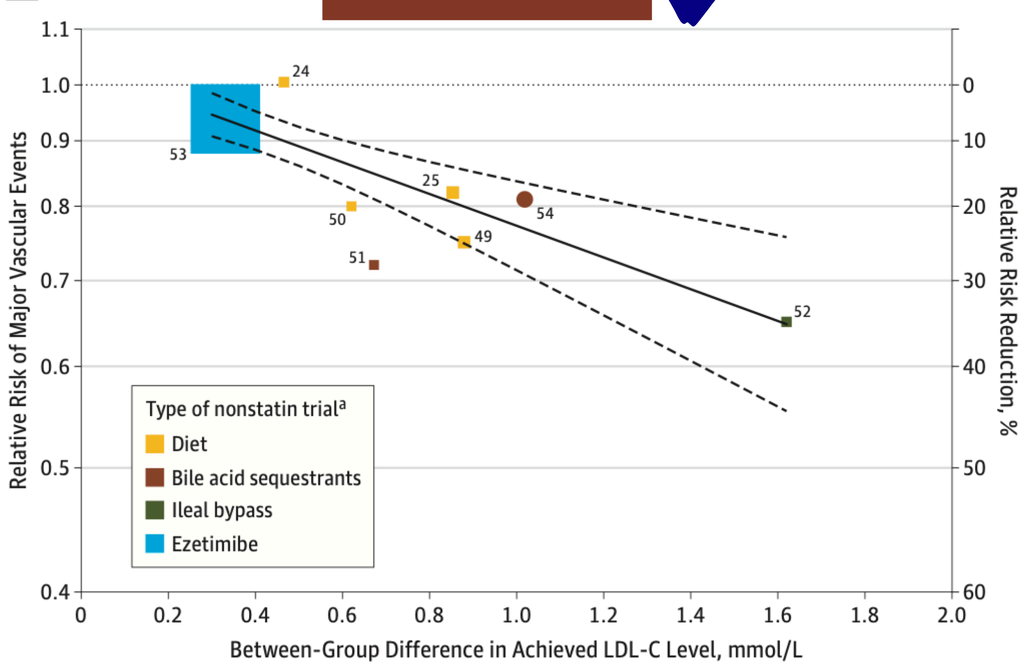
Association Between Lowering LDL-C and Cardiovascular Risk Reduction Among Different Therapeutic Interventions

A Systematic Review and Meta-analysis

Statin trials ✓



Non-statin trials ✓



Lower achieved LDL-C levels were associated with lower rates of major vascular events

Michael G. Silverman, et al. JAMA. 2016;316(12):1289-1297.

Cochrane Library

Cochrane Database of Systematic Reviews

HMG CoA reductase inhibitors (statins) for people with chronic kidney disease not requiring dialysis (Review)

Palmer SC, Navaneethan SD, Craig JC, Johnson DW, Perkovic V, Hegbrant J, Strippoli GFM

Palmer SC, et al. Cochrane Database of Systematic Reviews 2014.: CD007784.

Statin versus placebo or no treatment for adults with CKD not on dialysis

Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	No of participants (studies)	Quality of the evidence (GRADE)
	Assumed risk	Corresponding risk per year treated			
	Placebo or no treatment	Statins			
Major cardiovascular events	**20 per 1000**	**14 per 1000** (13 to 16 per 1000) 6 fewer (4 to 7 fewer)	**RR 0.72** (0.66 to 0.79)	36,033 (13)	⊕⊕⊕⊕ **high**
All-cause mortality	**25 per 1000**	**20 per 1000** (17 to 23 per 1000) 5 fewer (2 to 8 fewer)	**RR 0.79** (0.69 to 0.91)	28,276 (10)	⊕⊕⊕⊕ **high**
Cardiovascular mortality	**15 per 1000**	**12 per 1000** (10 to 13 per 1000) 3 fewer (2 to 5 fewer)	**RR 0.77** (0.69 to 0.87)	19,059 (7)	⊕⊕⊕⊖ **moderate**

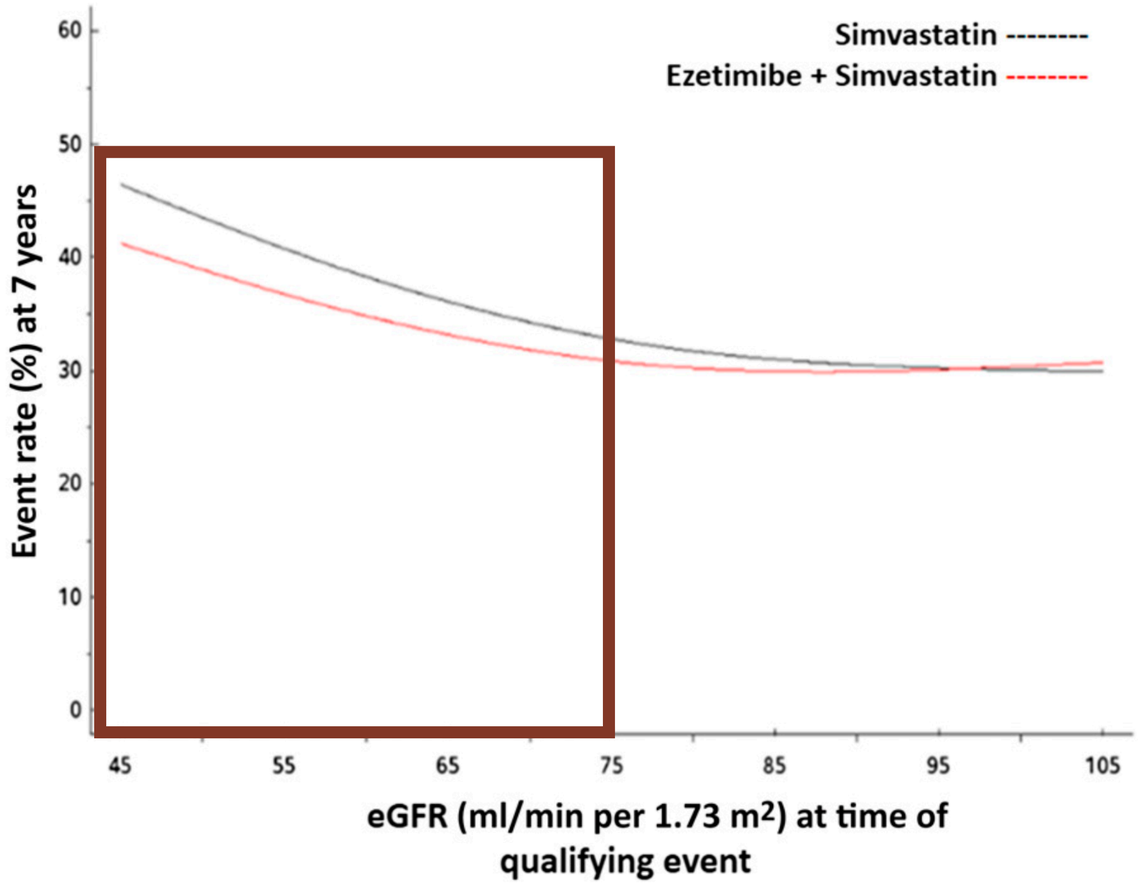
Statins lower death and major CV events by 20% in people with CKD not requiring dialysis

Palmer SC, et al. Cochrane Database of Systematic Reviews 2014.: CD007784.

CLINICAL RESEARCH www.jasn.org

Benefit of Ezetimibe Added to Simvastatin in Reduced Kidney Function

Subanalysis: IMPROVE-IT Study

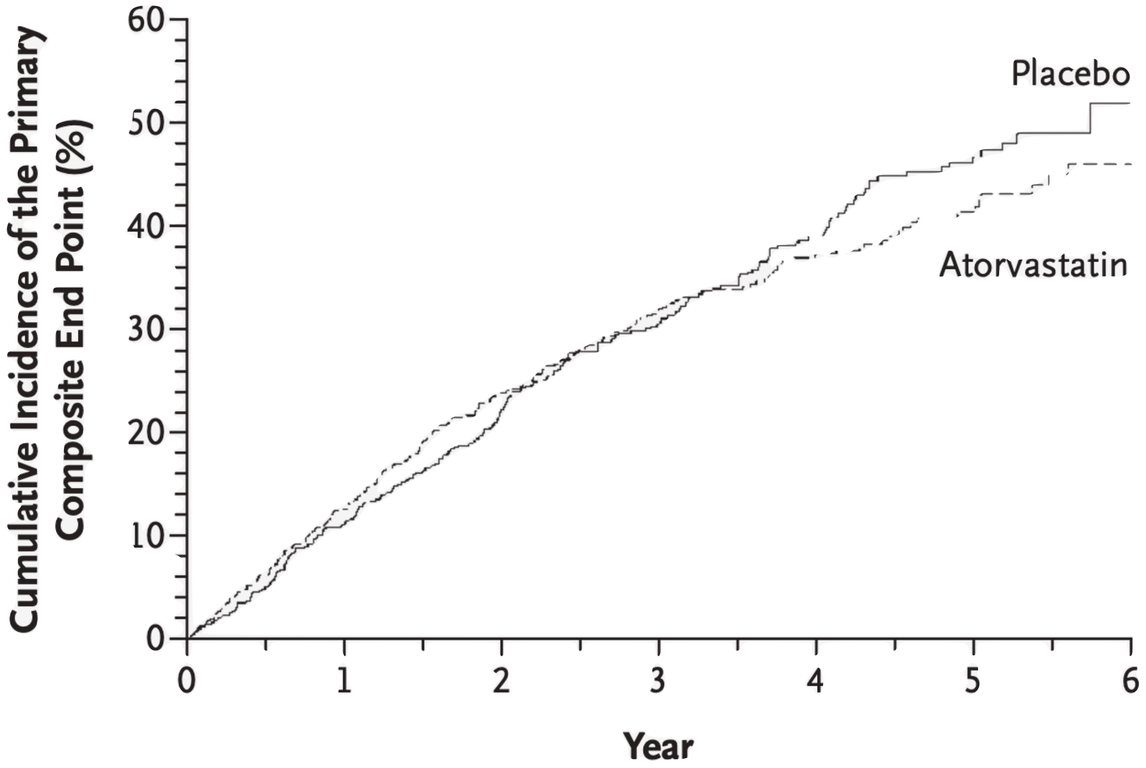


- For the primary end point of cardiovascular death, major coronary event, or nonfatal stroke, the relative risk reduction of combination therapy compared with monotherapy differed by eGFR (P=0.04)

- The difference in treatment effect was observed at eGFR $\leq$ 75 ml/min per 1.73 m^2 and most apparent at levels $\leq$ 60 ml/min per 1.73 m^2

Stanifer JW, et al. J Am Soc Nephrol 2017: 28: 3034–3043.

Atorvastatin in Type 2 Diabetics on Dialysis: 4D Study

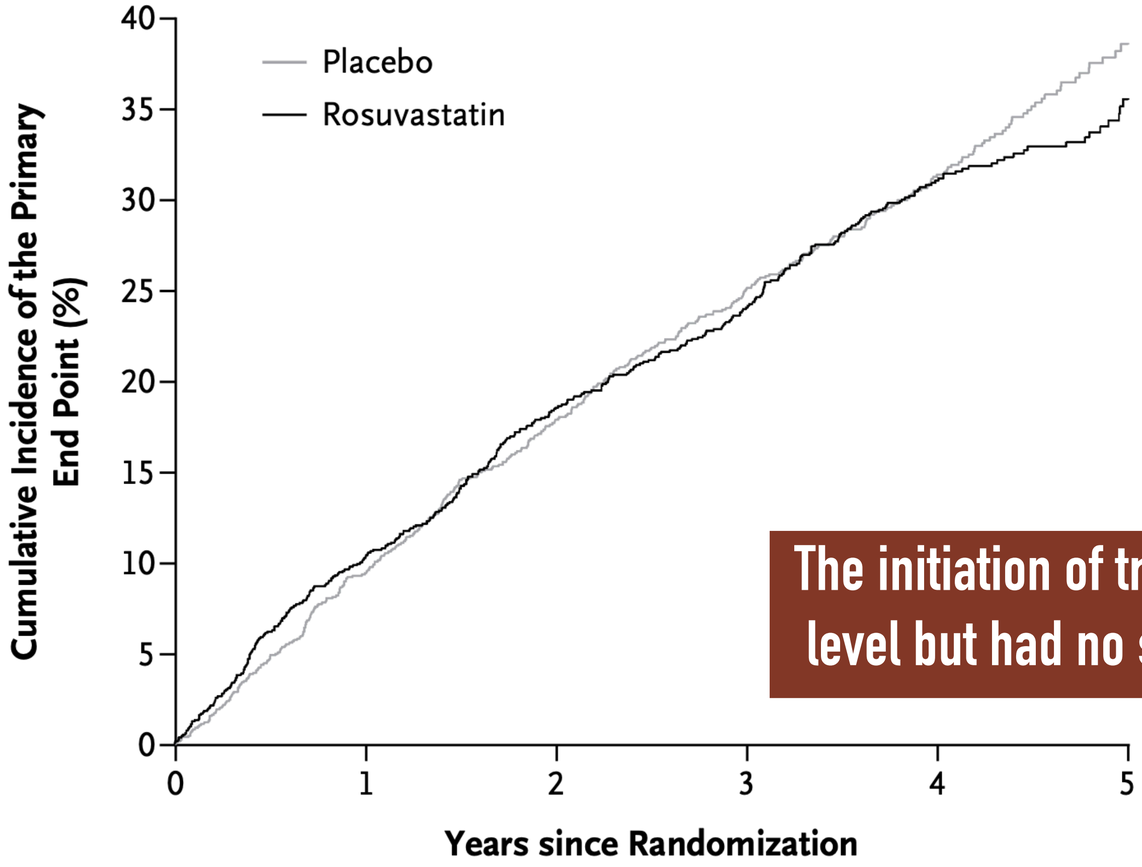


Relative Risk Reduction 8%
(95% CI: 0.77–1.10, P=0.37)

Atorvastatin had no significant effect on the composite primary end point of cardiovascular death, nonfatal MI, and stroke in patients with diabetes receiving hemodialysis.

Wanner C et al. N Engl J Med 2005; 353:238-48

Rosuvastatin and CV Events in Patients Undergoing Hemodialysis



No. at Risk

Placebo	1384	1163	952	809	534	153
Rosuvastatin	1390	1152	962	826	551	148

HR 0.96, P=0.59

AURORA Study

The initiation of treatment with rosuvastatin lowered the LDL cholesterol level but had no significant effect on the composite primary end points

Fellström BC, et al: N Engl J Med 2009; 360(14):1395-407.

The effects of lowering LDL cholesterol with simvastatin plus ezetimibe in patients with chronic kidney disease (Study of Heart and Renal Protection): a randomised placebo-controlled trial

SHARP Study

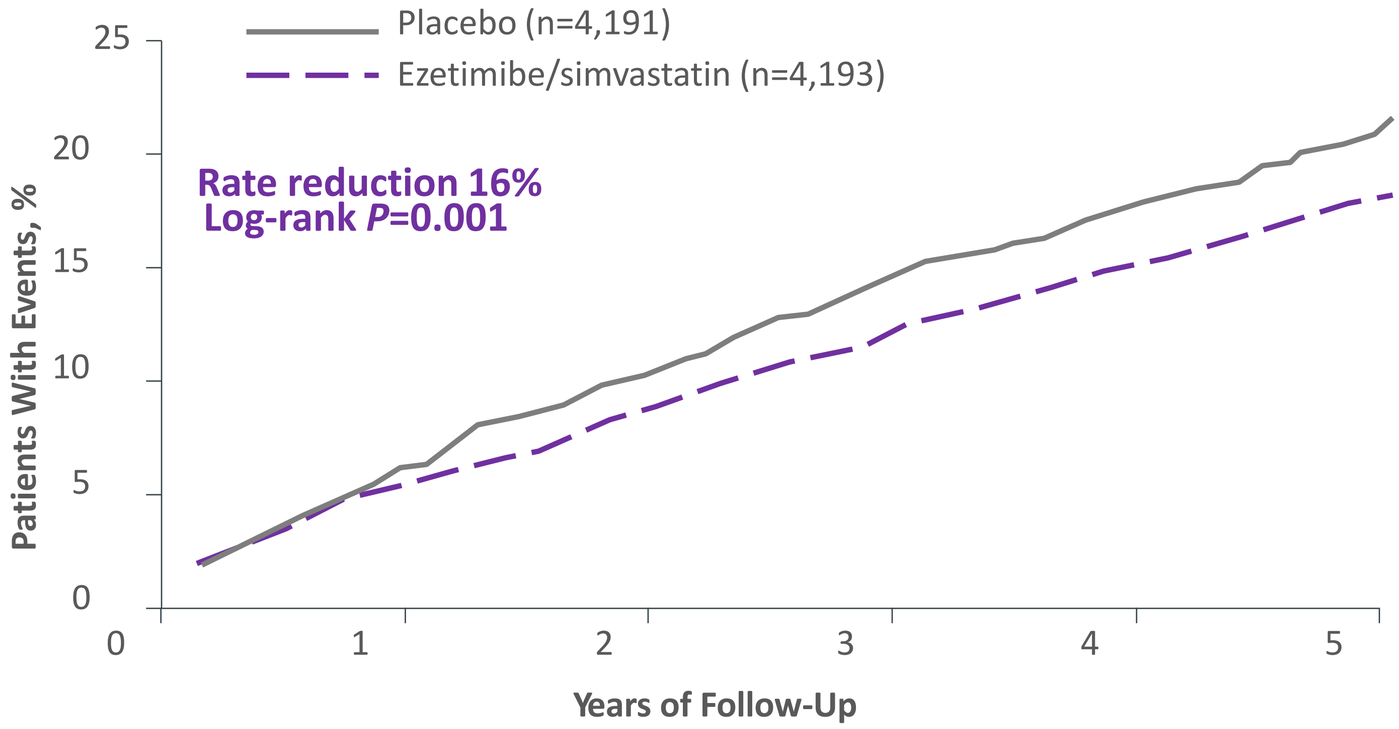
*Colin Baigent, Martin J Landray, Christina Reith, Jonathan Emberson, David C Wheeler, Charles Tomson, Christoph Wanner, Vera Krane, Alan Cass, Jonathan Craig, Bruce Neal, Lixin Jiang, Lai Seong Hooi, Adeera Levin, Lawrence Agodoa, Mike Gaziano, Bertram Kasiske, Robert Walker, Ziad A Massy, Bo Feldt-Rasmussen, Udom Krairittichai, Vuddidhej Ophascharoensuk, Bengt Fellström, Hallvard Holdaas, Vladimir Tesar, Andrzej Wiecek, Diederick Grobbee, Dick de Zeeuw, Carola Grönhagen-Riska, Tanaji Dasgupta, David Lewis, William Herrington, Marion Mafham, William Majoni, Karl Wallendszus, Richard Grimm, Terje Pedersen, Jonathan Tobert, Jane Armitage, Alex Baxter, Christopher Bray, Yiping Chen, Zhengming Chen, Michael Hill, Carol Knott, Sarah Parish, David Simpson, Peter Sleight, Alan Young, Rory Collins, on behalf of the SHARP Investigators****

- Subjects: ~9,000 patients with CKD (6,000 pre-dialysis, 3,000 on dialysis)
- Interventions: Simvastatin /ezetimibe combination vs. placebo

Baigent C et al. Lancet. 2011;377:2181–2192.

SHARP: Major Vascular Events in Patients Initially Assigned to Ezetimibe/Simvastatin or Placebo (Primary Intent-to-Treat Analysis)[1]

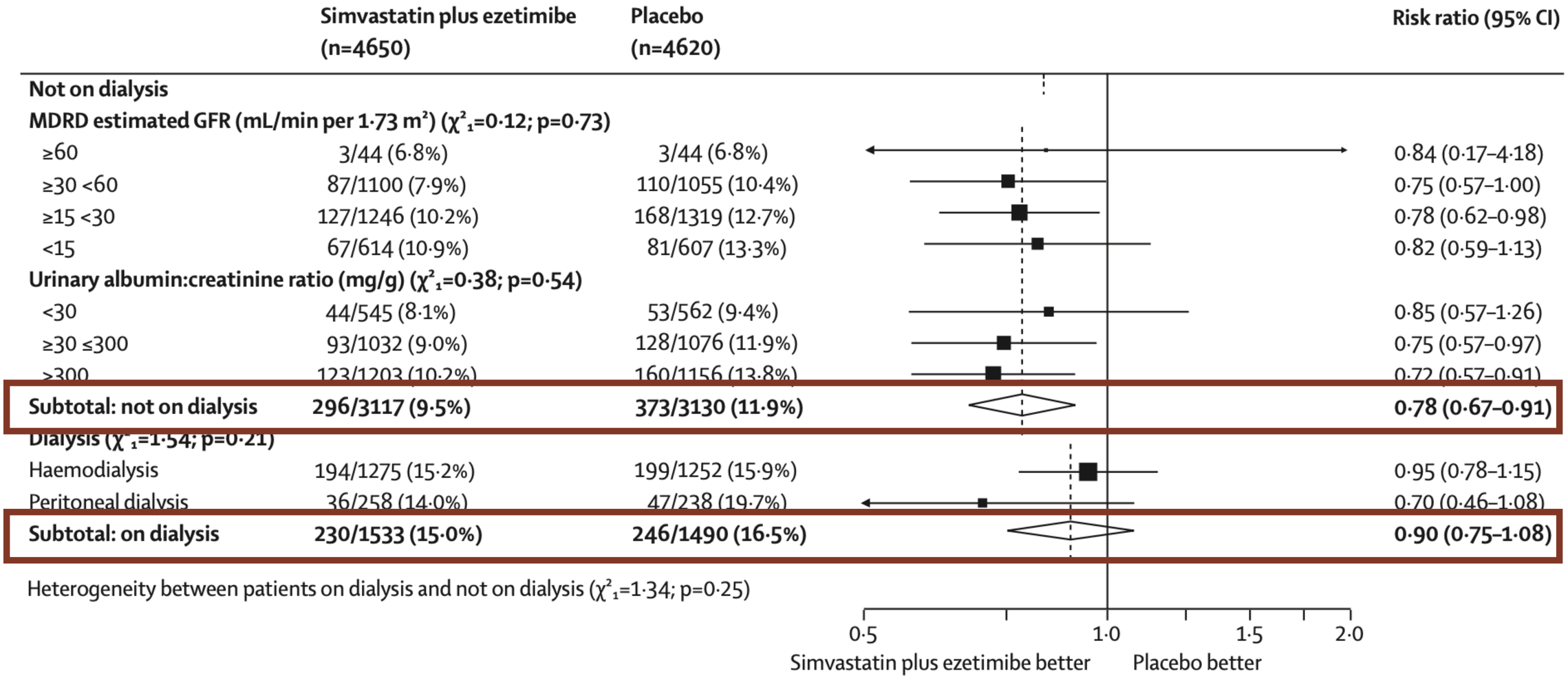
Nonfatal MI or Cardiac Death, Stroke, or Any Revascularization Procedure



Major vascular events occurred in 639 patients (15.2%) treated with ezetimibe/simvastatin 10/20 mg vs 749 patients (17.9%) treated with placebo, corresponding to a **16% relative risk reduction**

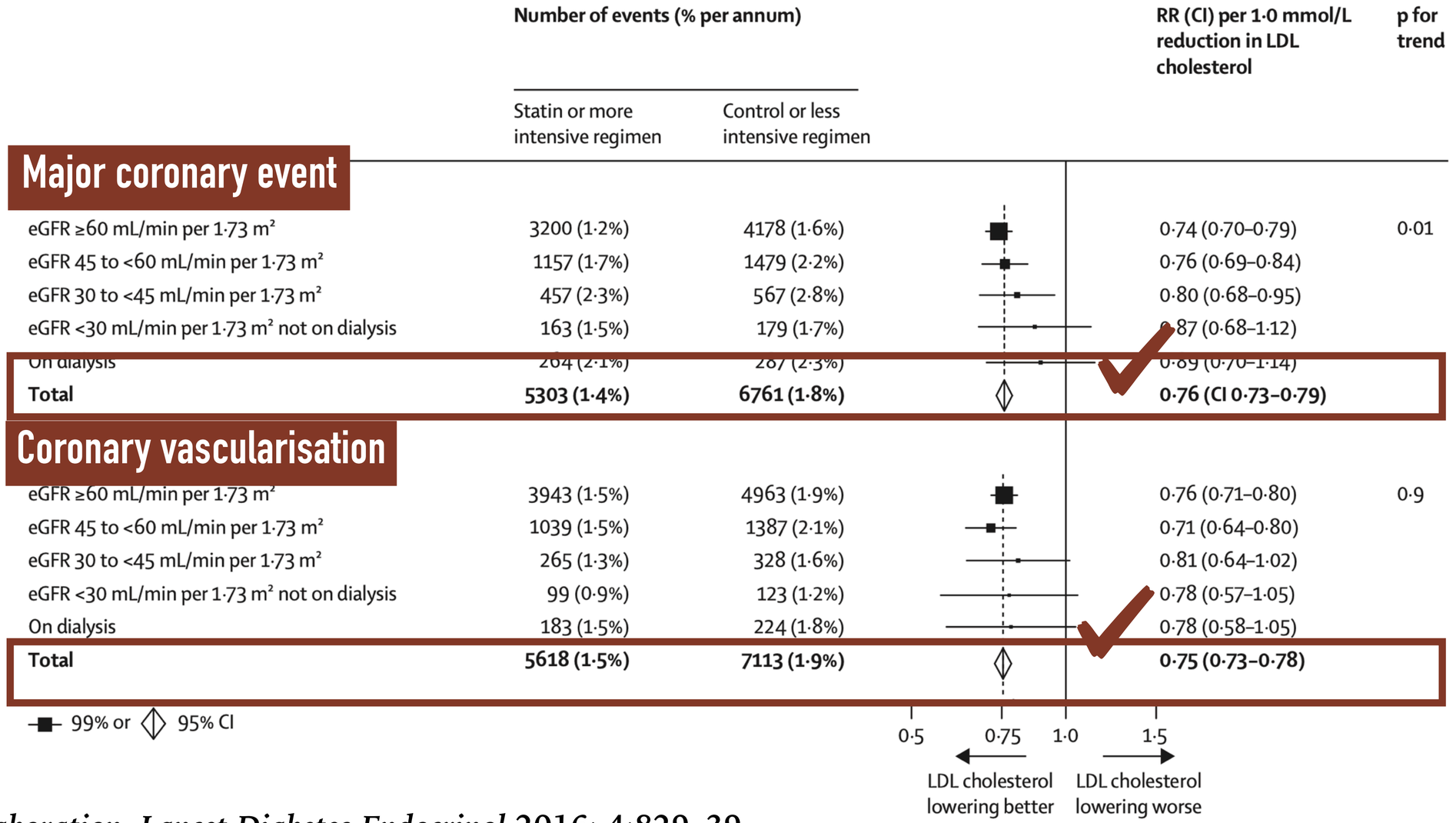
Baigent C et al. Lancet. 2011;377:2181–2192.

SHARP: Major Atherosclerotic Events by renal status at randomization



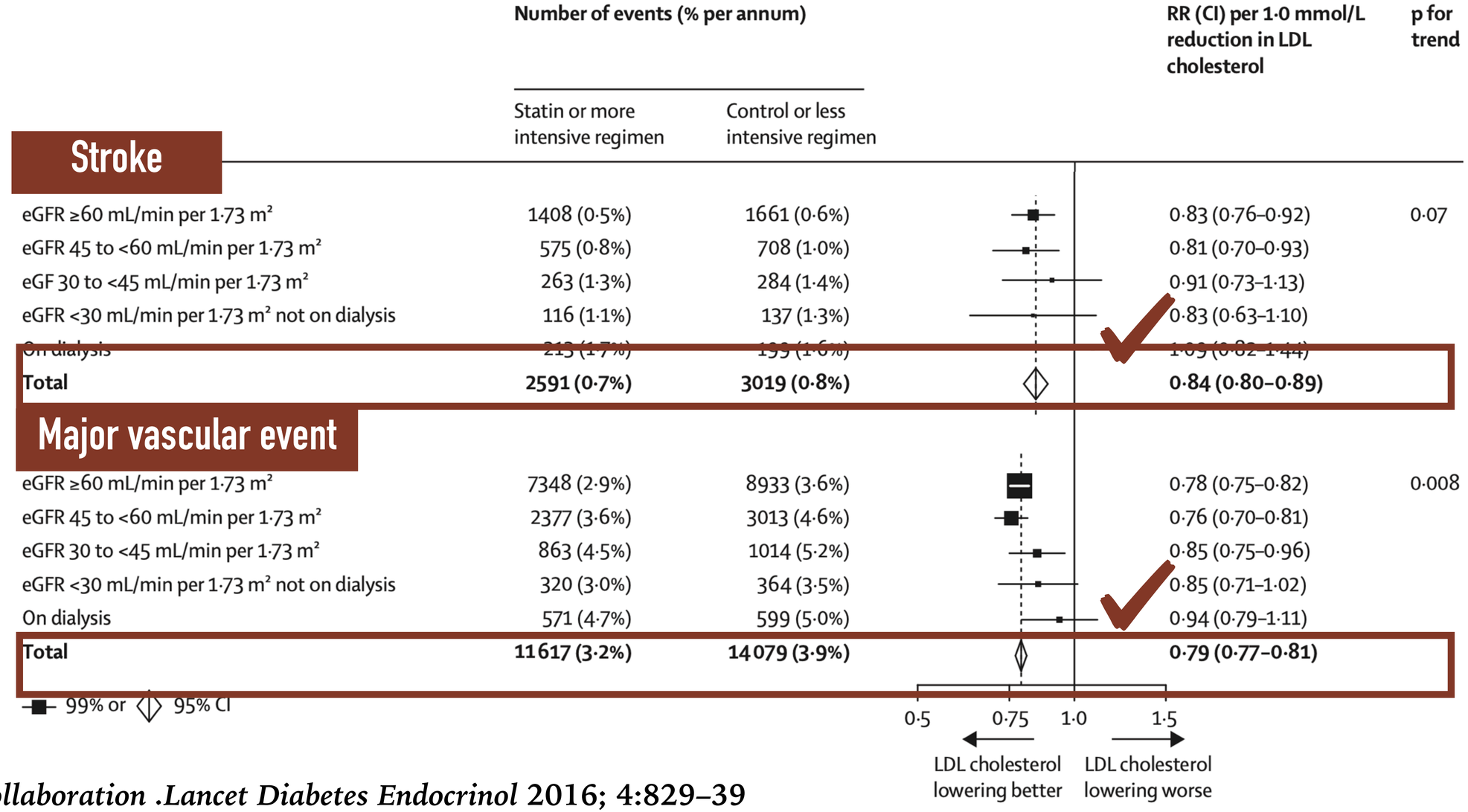
Baigent C et al. Lancet. 2011;377:2181–2192.

Impact of renal function on the effects of LDL cholesterol lowering with statin-based regimens: a meta-analysis of individual participant data from 28 randomised trials



(CTT) Collaboration .Lancet Diabetes Endocrinol 2016; 4:829–39

Impact of renal function on the effects of LDL cholesterol lowering with statin-based regimens: a meta-analysis of individual participant data from 28 randomised trials



(CTT) Collaboration .Lancet Diabetes Endocrinol 2016; 4:829–39

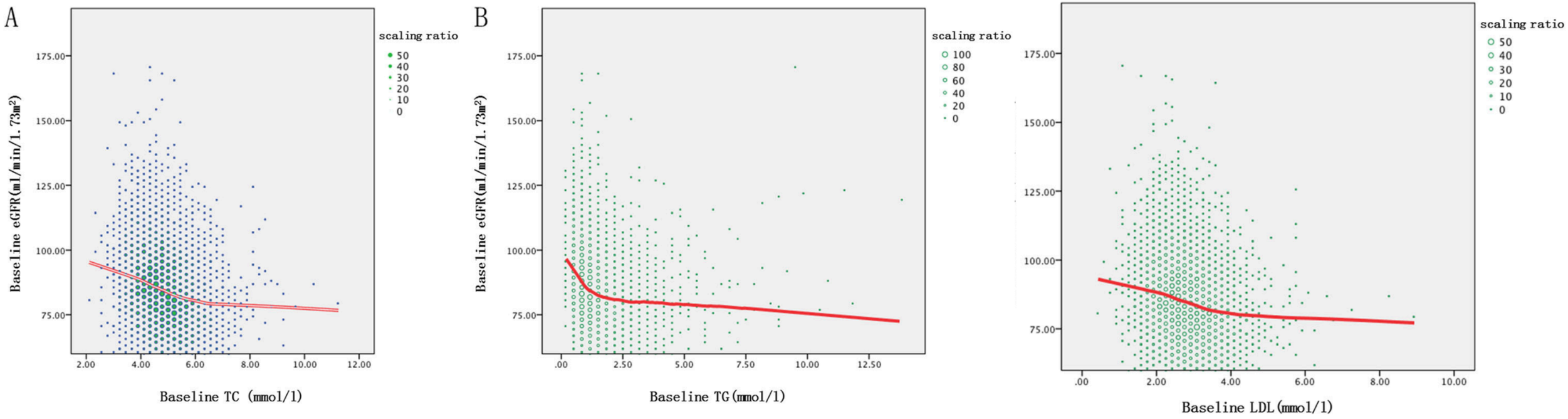
Benefits of Lipid lowering in Stages of CKD

CKD stage	CV events ↓	Based on trial
1	Yes	Post-hoc analysis from: Care, HPS, TNT, 4S, AFCAPS/ Texcaps, VA-HIT
2	Yes	
3	Yes	
4	Yes	SHARP, TNT
5	Yes	SHARP
Dialysis	Probably	SHARP, Post hoc 4D
Transplant	Probably	ALERT

OUTLINES

- Lipid metabolism and role of cholesterol absorption with CVD
- Lowering LDL-cholesterol on CV outcomes in CKD
- **Reduction LDL-cholesterol and renal progression**
- Update guideline for lipid control in CKD: KDIGO, ESC, Thai guideline

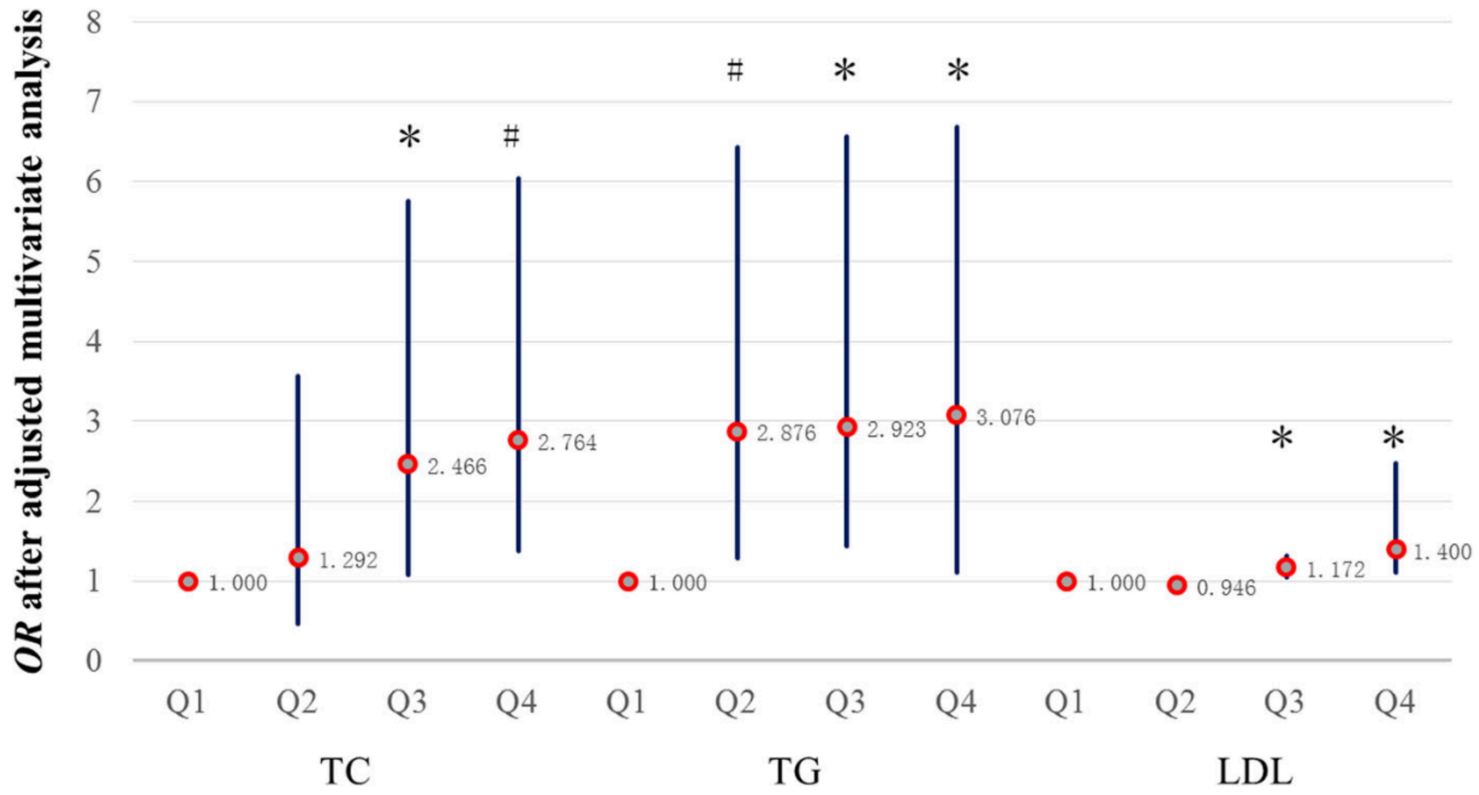
The association between dyslipidemia and the incidence of chronic kidney disease in the general Zhejiang population: a retrospective study



Increased TG and high levels of TC and LDL were independently associated with an increased likelihood of low GFR patient

Liang et al. BMC Nephrology (2020) 21:252

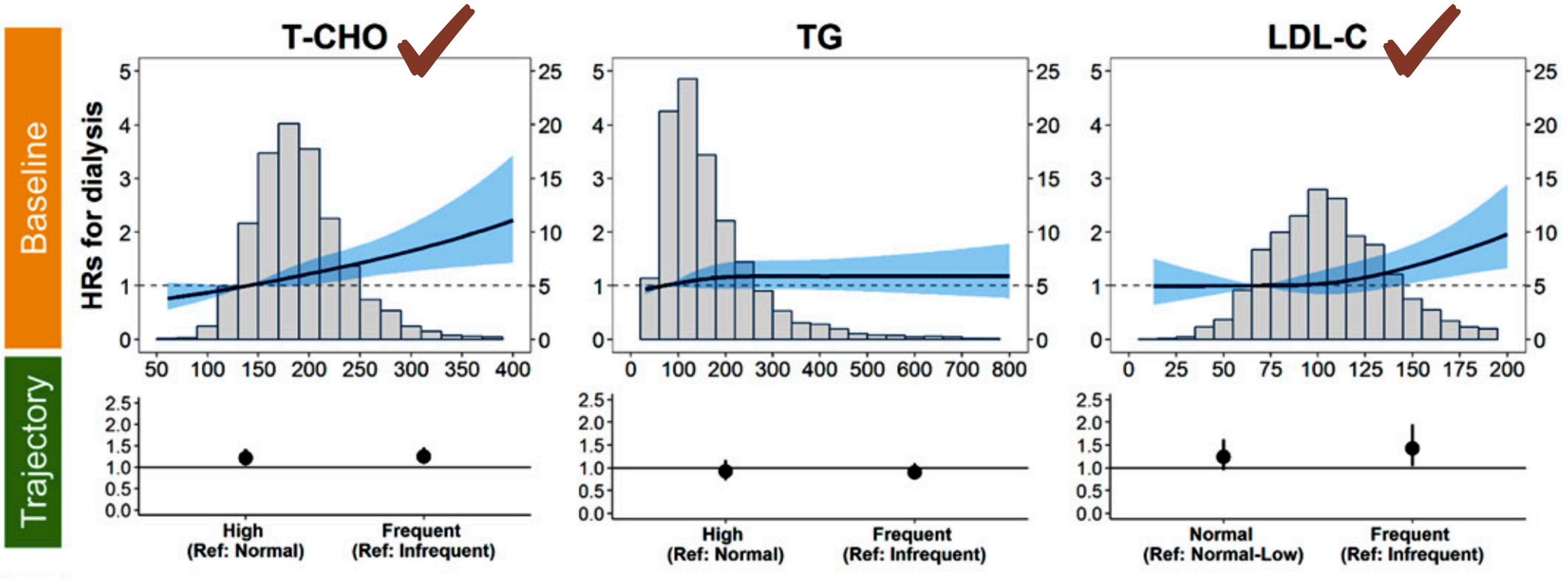
The association between dyslipidemia and the incidence of chronic kidney disease in the general Zhejiang population: a retrospective study



Increased TG and high levels of TC and LDL were independently associated with an increased likelihood of incident chronic kidney disease

Liang et al. BMC Nephrology (2020) 21:252

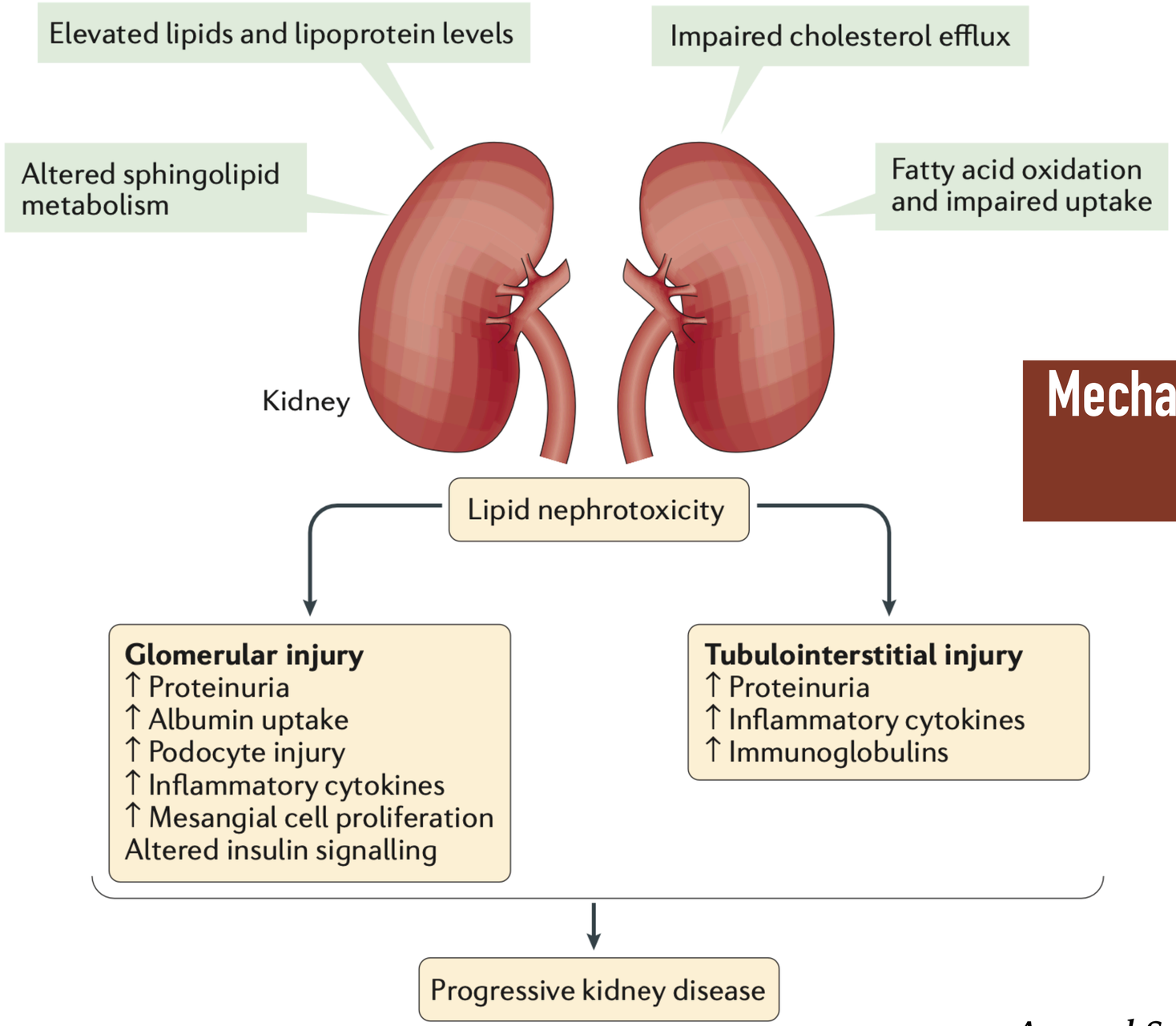
Lipid trends and adverse outcomes in patients with CKD



Higher levels of T-CHO and LDL-C were associated with rapid progression to ESRD

Tsai CW, et al. J. Lipid Res. 2019. 60: 648–660.

Mechanisms and consequences of lipid nephrotoxity



Agrawal S, et al. Nat Rev Nephrol. 2018; 14(1):57-70.

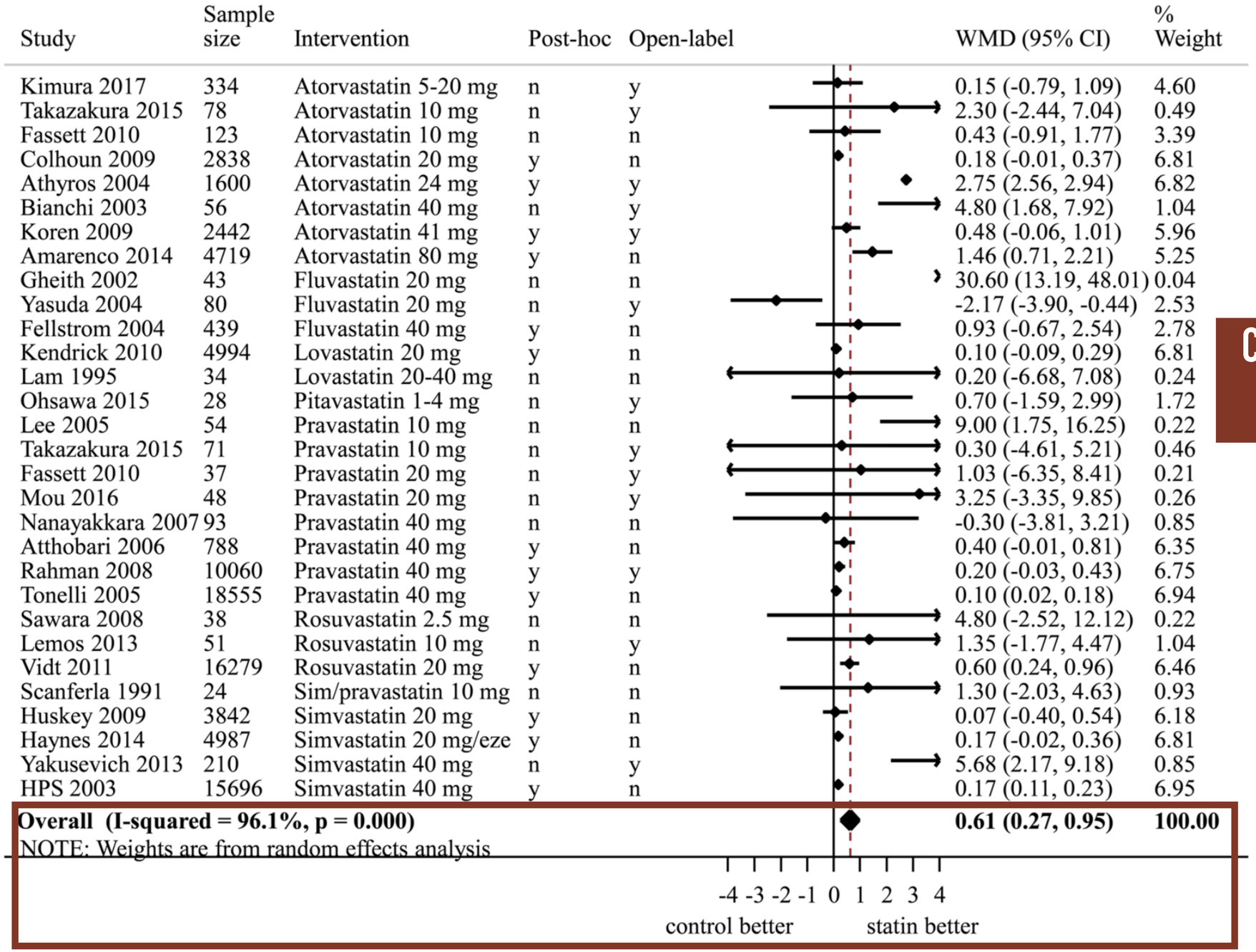
OPEN

Effect of different types of statins on kidney function decline and proteinuria: a network meta-analysis

K. Esmeijer[1,2*], Olaf M. Dekkers[2,3], Johan W. de Fijter[1], Friedo W. Dekker[2] & Ellen K. Hoogeveen[1,2,4]

- We performed a network meta-analysis of randomized controlled trials (RCT)
- Included 43 RCTs (>110,000 patients)

Esmeijer K, et al. Sci Rep. 2019; 9(1):16632.

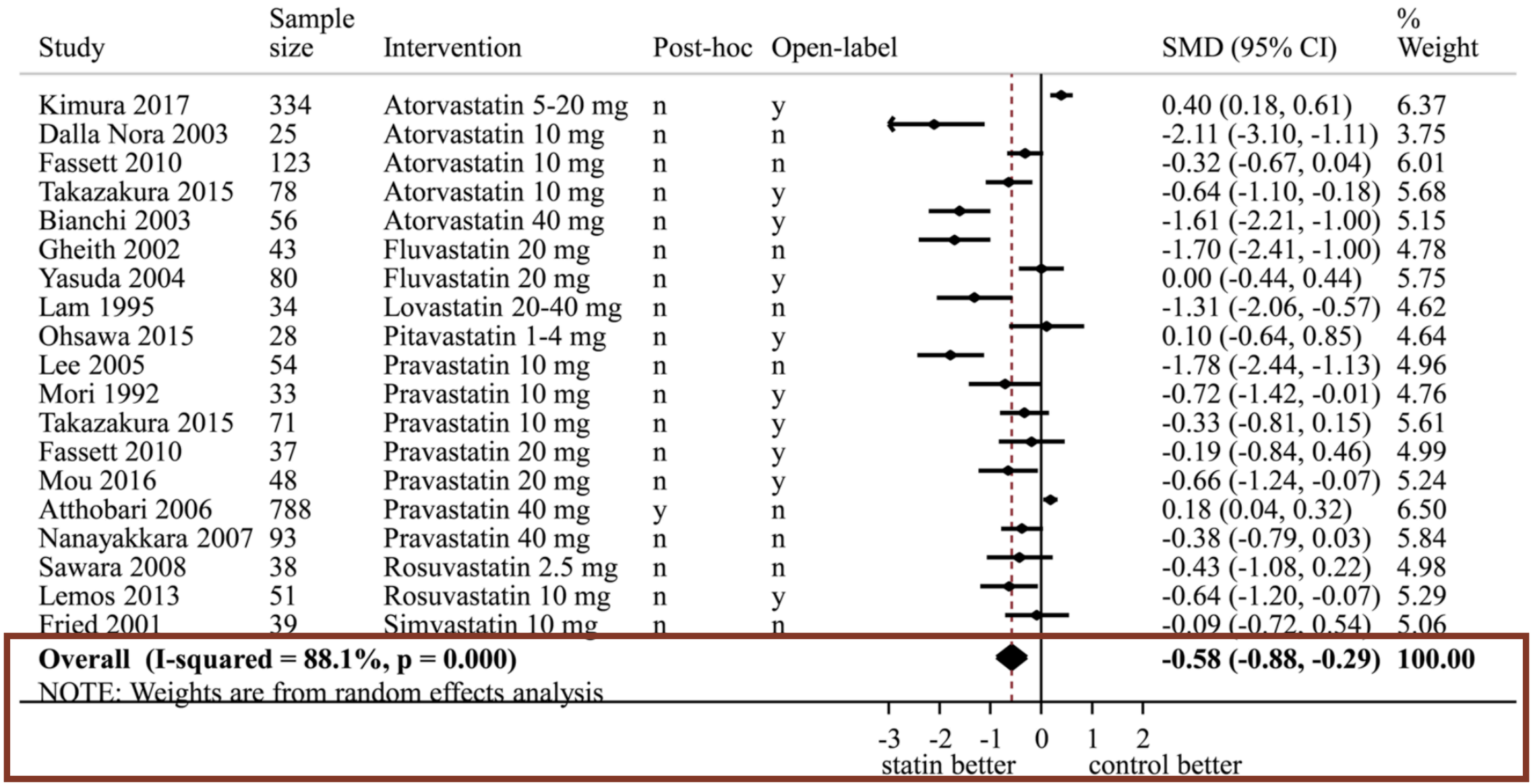


Change in annual eGFR decline, mL/min/1.73m²

Statins improved GFR

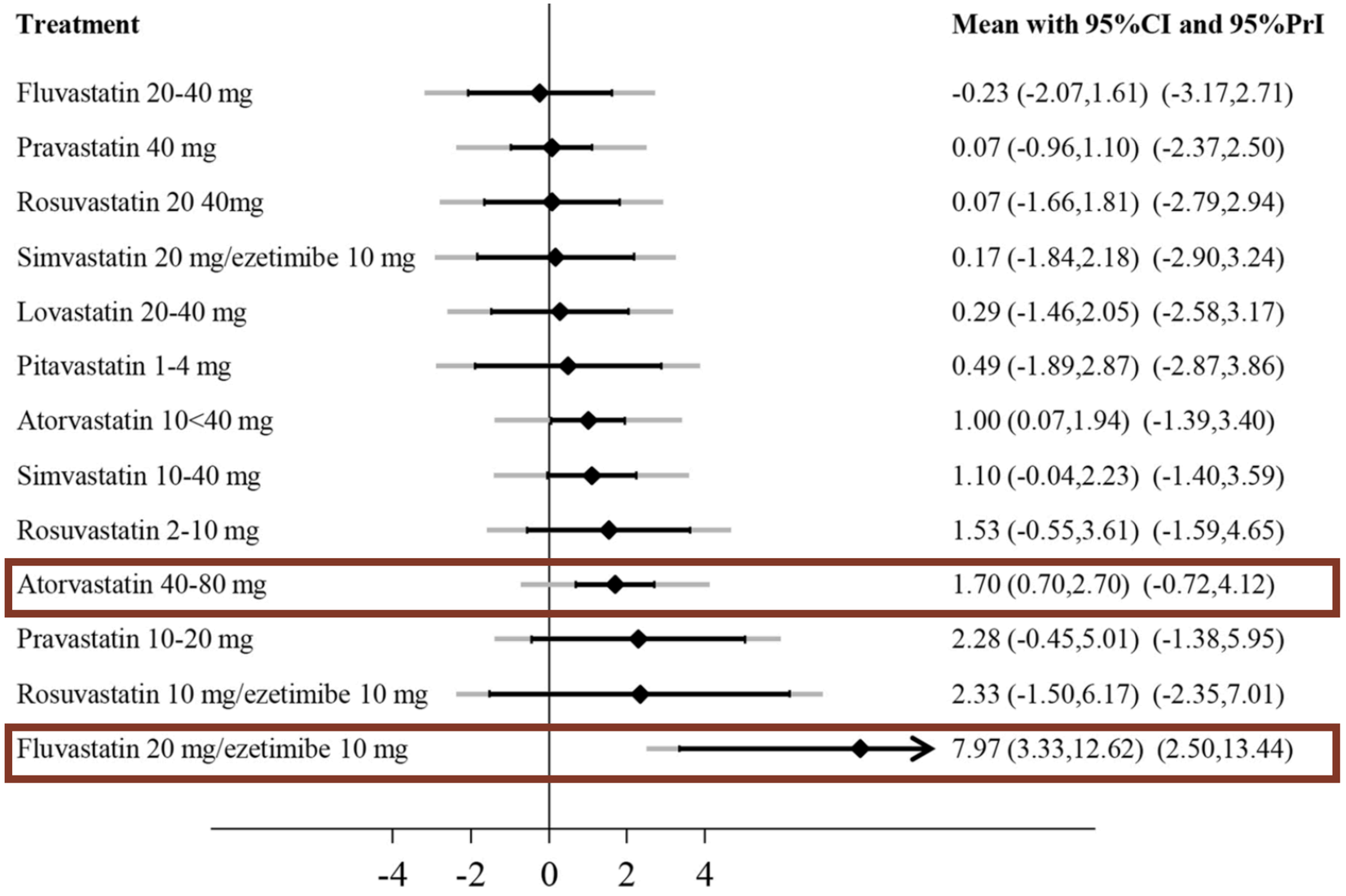
Esmeijer K, et al. Sci Rep. 2019; 9(1):16632.

Statins had lowered proteinuria



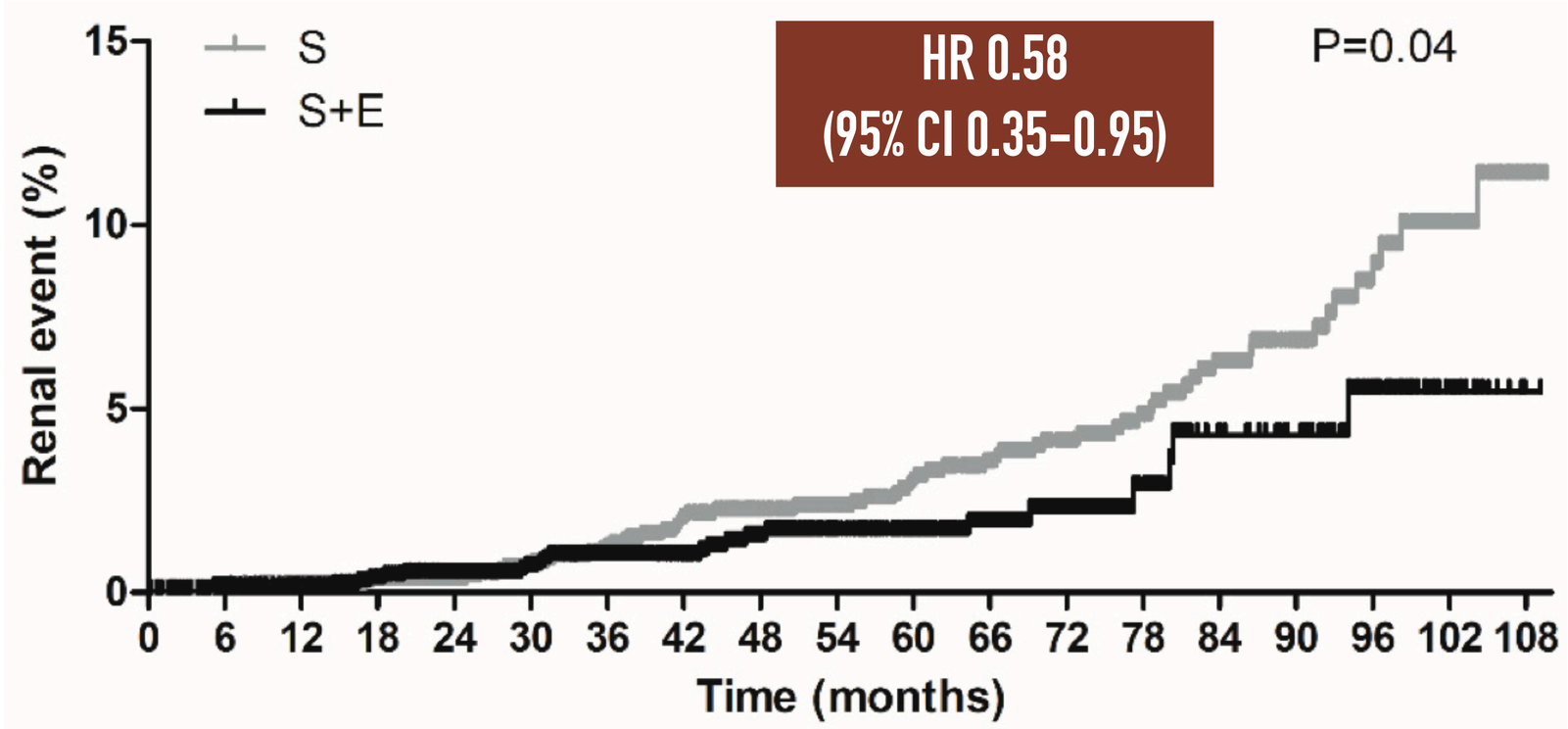
Esmeijer K, et al. Sci Rep. 2019; 9(1):16632.

Reduction of annual eGFR decline for different statins compared to control



Esmeijer K, et al. Sci Rep. 2019; 9(1):16632.

Comparison of Renal Effects of Ezetimibe–Statin Combination versus Statin Monotherapy: A Propensity-Score-Matched Analysis



Combining ezetimibe with a statin showed a significantly lower risk of renal events than the simvastatin

Changes in serum creatinine and incidence of renal events, defined as doubling of serum creatinine to 1.5 mg/dL or occurrence of end-stage renal disease after the first day of treatment initiation

Bae J, et al. J. Clin. Med. 2020, 9, 798

Statin with CKD progression

- There is currently no well-designed RCT study that provides evidence for the benefits of using a lipid-lowering agent to improve outcomes in CKD progression.

- All studies are subset analyses aimed at evaluating the efficacy of statin therapy on CKD progression and have both positive and negative effects.

- Data from meta-analysis and propensity matched analysis prefer a combination of statin and ezetimibe to slow the decline of GFR, although the confidence intervals are wide.

Esmeijer K, et al. Sci Rep. 2019; 9(1):16632.
Bae J, et al. J. Clin. Med. 2020, 9, 798

OUTLINES

- Lipid metabolism and role of cholesterol absorption with CVD
- Lowering LDL-cholesterol on CV outcomes in CKD
- Reduction LDL-cholesterol and renal progression
- **Update guideline for lipid control in CKD: KDIGO, ESC, Thai guideline**

Lipid management according to KDIGO 2013

CKD stage	Age (Years)	Options	Level
G1–G2	> 50	Statin	1B
G3a–G5	> 50	Statin or statin/ezetimibe	1A
	18–49 plus ➤ known coronary disease (MI or coronary revascularization) ➤ diabetes mellitus ➤ prior ischemic stroke ➤ estimated 10-year incidence of coronary death or non-fatal myocardial infarction >10%	Statin	2A
G5 Dialysis	Any age	Statin or Statin/Ezetimibe Not initiate when RRT	2C 2A
KT	Any age	Statin	2B

Wanner C, et al., Kidney Int 2014;85(6):1303–9.

Suggested revisions of the KDIGO Clinical Practice Guideline for Lipid Management in CKD

Pharmacological cholesterol-lowering treatment

- In adults aged ≥50 years with eGFR <60 ml/min/1.73 m^2 but not treated with chronic dialysis or kidney transplantation (GFR categories G3a-G5), we recommend treatment with a statin or statin and ezetimibe combination
- In adults aged ≥50 years with CKD and GFR >60 ml/min/1.73 m^2 (GFR categories G1-G2) we recommend treatment with a statin
- In adults aged 18–49 years with CKD but not treated with chronic dialysis or kidney transplantation, we suggest statin treatment in people with one or more of the following:
  - Known coronary disease (myocardial infarction or coronary revascularization)
  - Diabetes mellitus
  - Prior ischaemic stroke
  - Estimated 10-year incidence of coronary death or non-fatal myocardial infarction >10%
- In adults with dialysis-dependent CKD, we suggest that statins or statin and ezetimibe combination not be initiated
- In patients already receiving statins or statin and ezetimibe combination at the time of dialysis initiation, we suggest that these agents be continued
- In adult kidney transplant recipients, we suggest treatment with a statin
- Consideration needs to be given to patients with progressive CKD, especially if high levels of proteinuria are present
- Potential consideration also needs to be given to patients with high estimated lifetime risk likely to progress to dialysis and transplantation
- In individuals with known coronary disease, secondary prevention recommendations may apply, including LDL cholesterol targets
- Consider making treatment decisions based on individual patient preferences for those who have high LDL cholesterol levels and/or are expected to have a long renal career or receive a kidney transplant

Charles J. Ferro, et al., Nature Reviews Nephrology volume14, pages727–749 (2018)

CKD management KDIGO guideline 2023 (draft)

Practice Point 3.14.1.2: In people with CKD, choose statin-based regimens to maximize the absolute reduction in low-density lipoprotein (LDL) cholesterol to achieve the largest treatment benefits.

Impact of renal function on the effects of LDL cholesterol lowering with statin-based regimens: a meta-analysis of individual participant data from 28 randomised trials

Interpretation Even after allowing for the smaller reductions in LDL cholesterol achieved by patients with more advanced chronic kidney disease, and for differences in outcome definitions between dialysis trials, the relative reductions in major vascular events observed with statin-based treatment became smaller as eGFR declined, with little evidence of benefit in patients on dialysis. In patients with chronic kidney disease, statin-based regimens should be chosen to maximise the absolute reduction in LDL cholesterol to achieve the largest treatment benefits.

KDIGO-2023-CKD-Guideline-Public-Review-Draft_5-July-2023

ESC European Society of Cardiology

European Heart Journal (2020) **41**, 111–188
doi:10.1093/eurheartj/ehz455

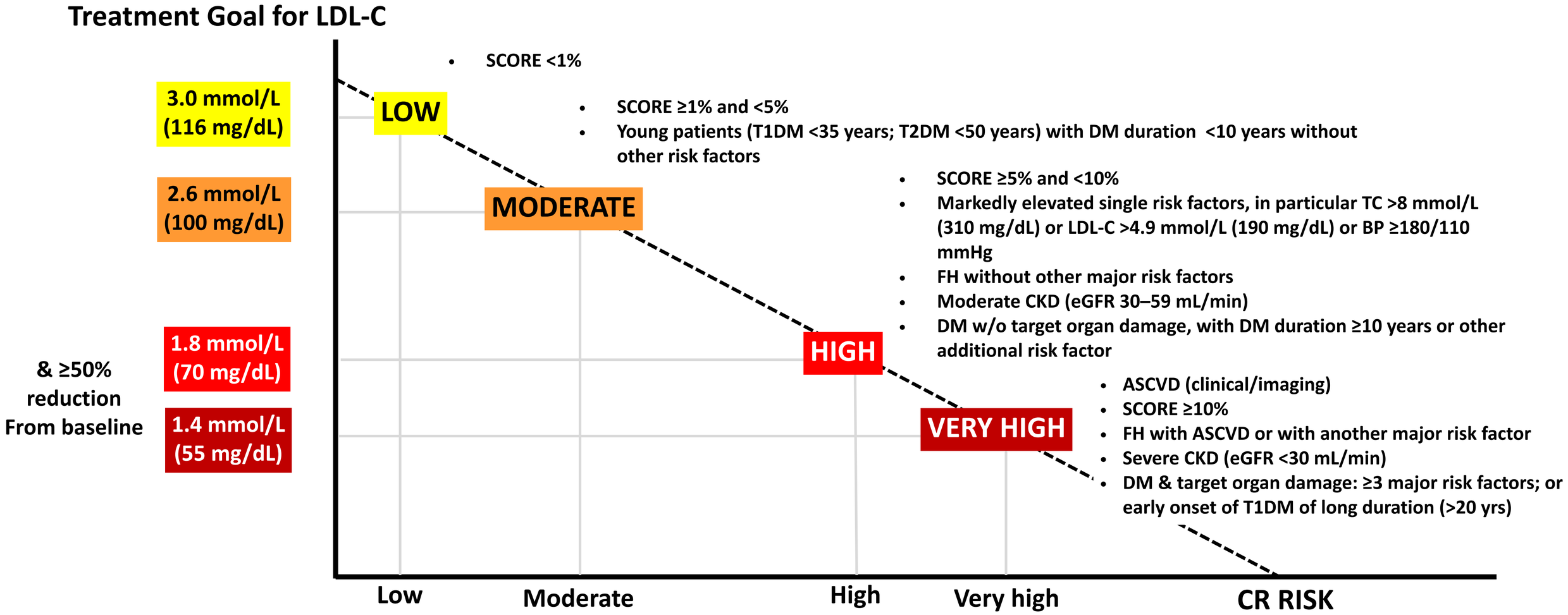
ESC/EAS GUIDELINES

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

The Task Force for the management of dyslipidaemias of the European Society of Cardiology (ESC) and European Atherosclerosis Society (EAS)

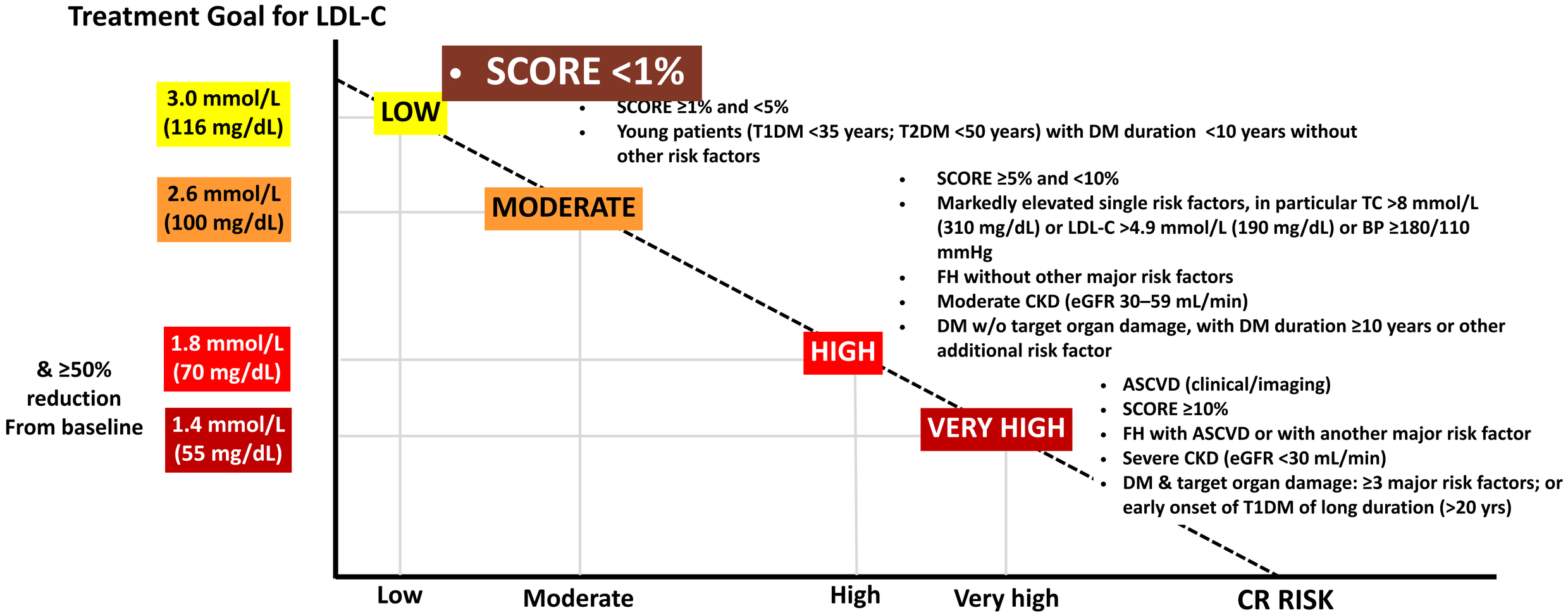
Mach F, et al. Eur Heart J. 2020; 41(1):111-188.

Treatment Goals for Low-Density Lipoprotein Cholesterol Across Categories of Total Cardiovascular Disease Risk



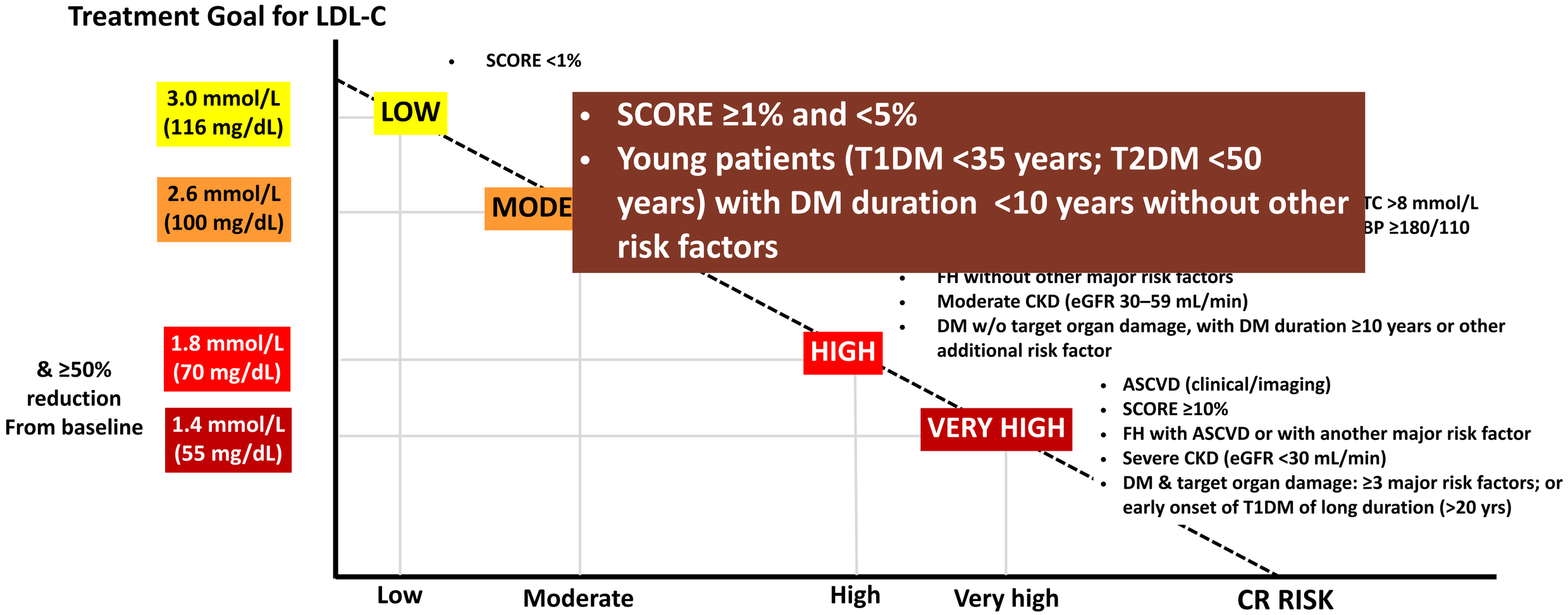
Adapted from: 2019 ESC/EAS Guidelines: European Heart Journal (2020) 41, 111188. doi:10.1093/eurheartj/ehz455

Treatment Goals for Low-Density Lipoprotein Cholesterol Across Categories of Total Cardiovascular Disease Risk



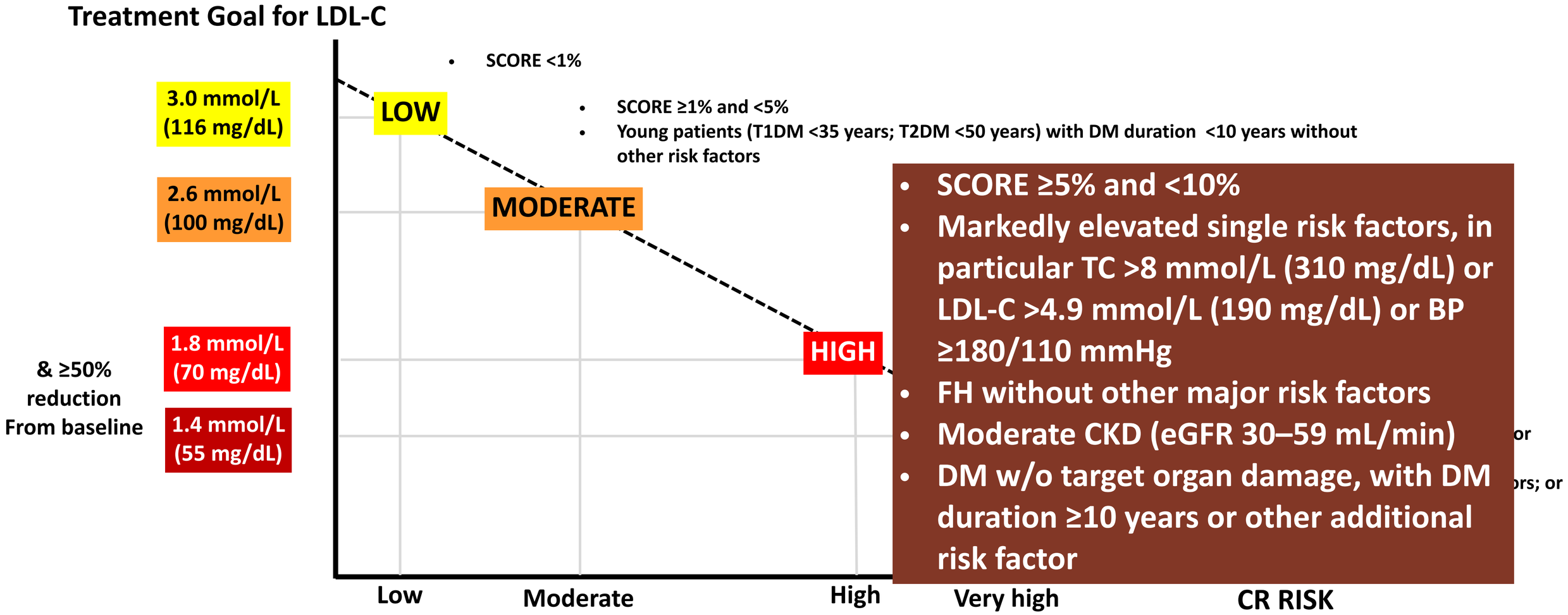
Adapted from: 2019 ESC/EAS Guidelines: European Heart Journal (2020) 41, 111188. doi:10.1093/eurheartj/ehz455

Treatment Goals for Low-Density Lipoprotein Cholesterol Across Categories of Total Cardiovascular Disease Risk



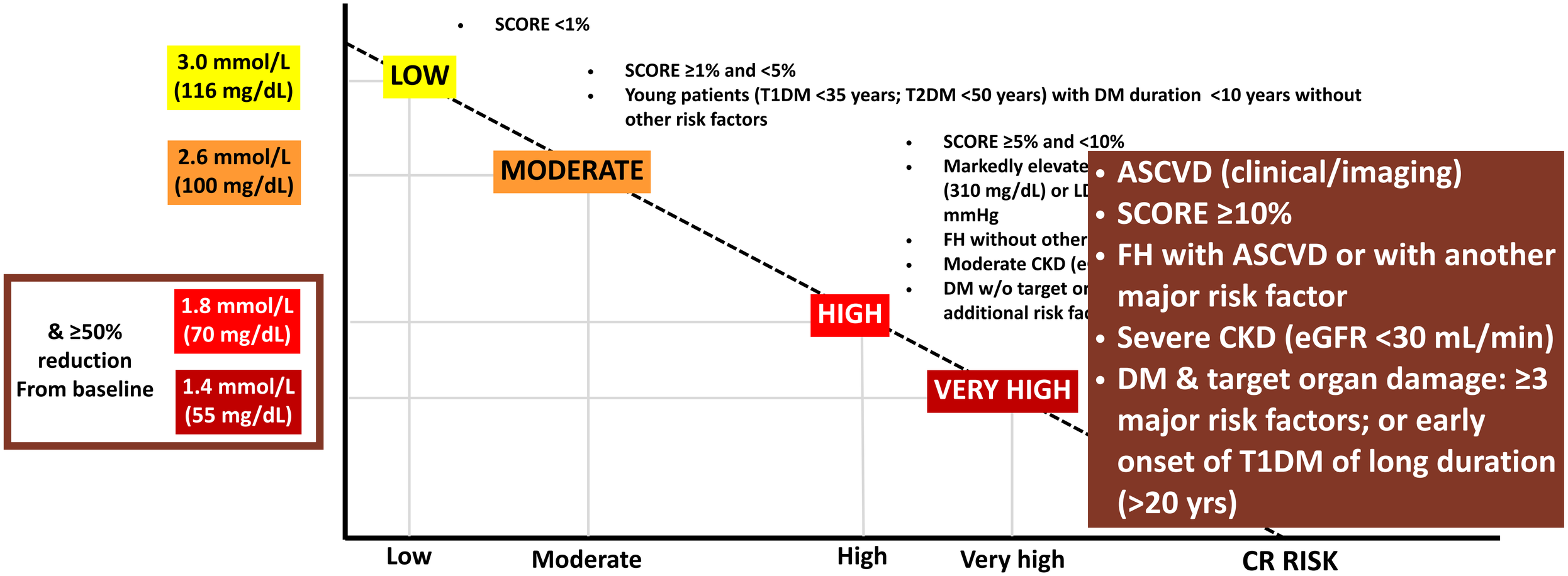
Adapted from: 2019 ESC/EAS Guidelines: European Heart Journal (2020) 41, 111188. doi:10.1093/eurheartj/ehz455

Treatment Goals for Low-Density Lipoprotein Cholesterol Across Categories of Total Cardiovascular Disease Risk



Adapted from: 2019 ESC/EAS Guidelines: European Heart Journal (2020) 41, 111188. doi:10.1093/eurheartj/ehz455

Treatment Goals for Low-Density Lipoprotein Cholesterol Across Categories of Total Cardiovascular Disease Risk



Adapted from: 2019 ESC/EAS Guidelines: European Heart Journal (2020) 41, 111188. doi:10.1093/eurheartj/ehz455

Intensity statin therapy

AMERICAN COLLEGE of CARDIOLOGY

High-Intensity Statin Therapy	Moderate-Intensity Statin Therapy	Low-Intensity Statin Therapy
Daily dose lowers LDL on average by ≥50%	Daily dose lowers LDL on average by approximately 30-49%	Daily dose lowers LDL on average by <30%
Atorvastatin 40-80 mg Rosuvastatin 20-40 mg	Atorvastatin 10-20 mg Rosuvastatin 5-10 mg Simvastatin 20-40 mg Pravastatin 40-80 mg Lovastatin 40 mg Fluvastatin XL 80 mg Fluvastatin 40 mg BID Pitavastatin 2-4 mg	Simvastatin 10 mg Pravastatin 10-20 mg Lovastatin 20 mg Fluvastatin 20-40 mg

Grundy SM, et al. Circulation. 2018

Treatment goals for LDL-cholesterol

ESC European Society of Cardiology

Recommendations
It is recommended that a high-intensity statin is prescribed up to the highest tolerated dose to reach the goals set for the specific level of risk.[32,34,38]

High-intensity statin

If the goals[c] are not achieved with the maximum tolerated dose of a statin, combination with ezetimibe is recommended.[33]

Statin + ezetimibe

For primary prevention patients at very-high risk, but without FH, if the LDL-C goal is not achieved on a maximum tolerated dose of a statin and ezetimibe, a combination with a PCSK9 inhibitor may be considered.

Statin + ezetimibe+ PCSK9i

Mach F, et al. Eur Heart J. 2020; 41(1):111-188.

Lipid management in patients with CKD

ESC European Society of Cardiology

Recommendations	Class[a]	Level[b]
It is recommended that patients with Kidney Disease Outcomes Quality Initiative stage 3–5[c] CKD are considered to be at high or very-high risk of ASCVD.[489–493]	I	A
The use of statins or statin/ezetimibe combination is recommended in patients with non-dialysis-dependent stage 3–5 CKD.[214,222,495,496]	I	A

Mach F, et al. Eur Heart J. 2020; 41(1):111-188.

Lipid management in patients with CKD

Recommendations	Class[a]	Level[b]
In patients already on statins, ezetimibe, or a statin/ezetimibe combination at the time of dialysis initiation, continuation of these drugs should be considered, particularly in patients with ASCVD.	IIa	C
In patients with dialysis-dependent CKD who are free of ASCVD, commencement of statin therapy is not recommended.[220,221]	III	A

Mach F, et al. Eur Heart J. 2020; 41(1):111-188.

Lipid management in solid organ transplant patients

ESC European Society of Cardiology

Recommendations	Class[a]	Level[b]
Statins should be considered as first-line agents in transplant patients. Initiation should be at low doses with careful uptitration and with caution regarding potential drug–drug interactions, particularly for patients on ciclosporin.[507]	IIa	B
In patients who are intolerant of statins or those with significant dyslipidaemia despite maximally tolerated statin treatment, alternative or additional therapy with ezetimibe may be considered.	IIb	C

Stains as first line agents and initiation at low dose

Maximally tolerated stains, add ezetimibe

Fluvastatin, pravastatin, pitavastatin, and rosuvastatin are metabolized through diff erent CYP enzymes than the others and have less potential for interaction.

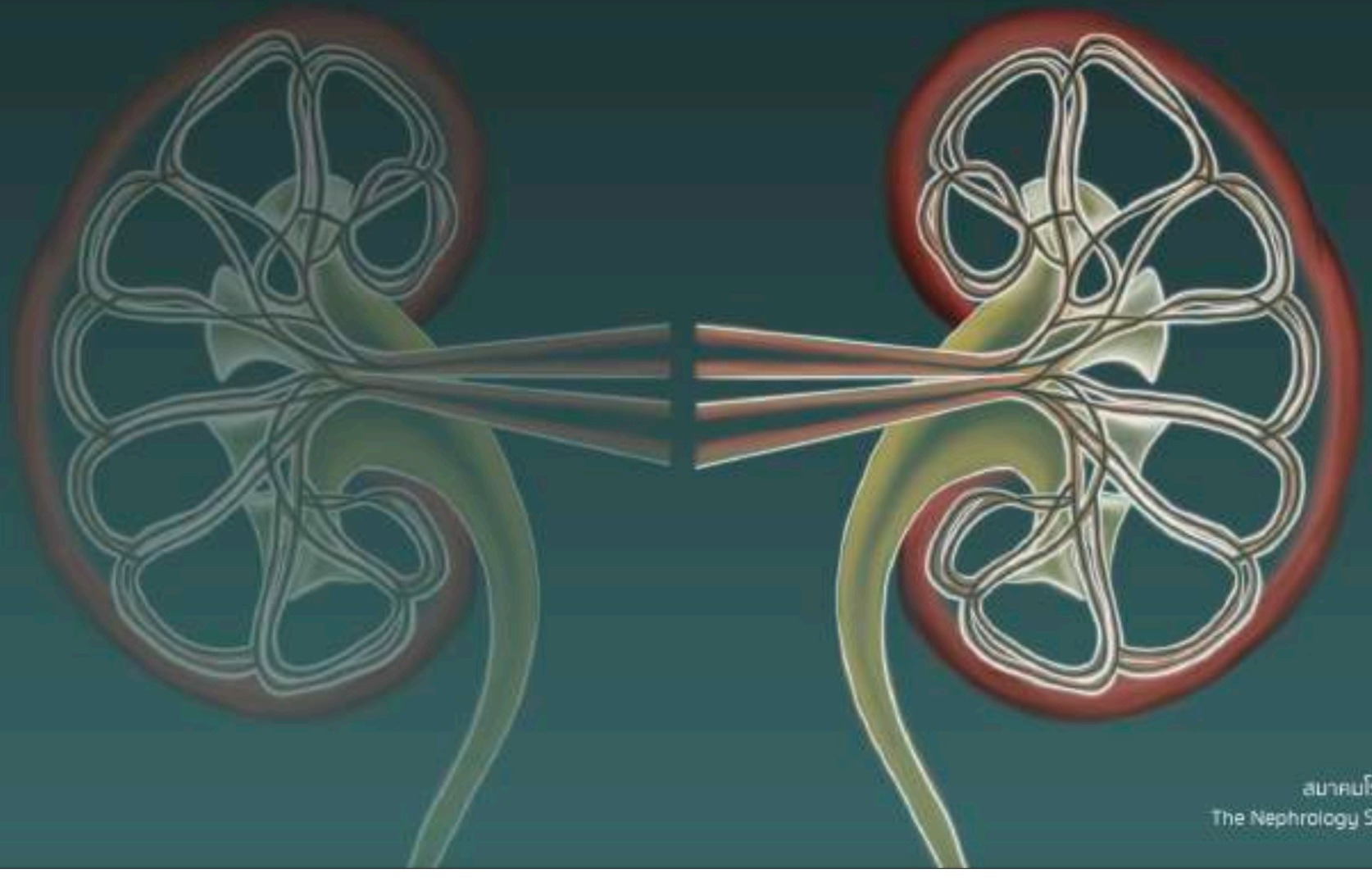
Mach F, et al. Eur Heart J. 2020; 41(1):111-188.

คำแนะนำสำหรับการดูแลผู้ป่วยโรคไตเรื้อรัง ก่อนการบำบัดทดแทนไต พ.ศ. 2565

(ฉบับปรับปรุงเพิ่มเติม)

Clinical Practice Recommendations for Evaluation and Management of Chronic Kidney Disease in Adults 2022

(Revised edition)



สมาคมโรคไตแห่งประเทศไทย
The Nephrology Society of Thailand

Assessment of lipid status in adults with CKD

➤ In adults with newly identified CKD, we recommend evaluation with a lipid profile (total cholesterol, LDL cholesterol, HDL cholesterol, triglycerides) and evaluated secondary causes of dyslipidemias (2B)

Medical Conditions	Medications
Nephrotic syndrome	13-cis-retinoic acid
Excessive alcohol consumption	Androgens
Hypothyroidism	Anticonvulsants
Liver disease	Highly active anti-retroviral therapy
Diabetes	Corticosteroids
	Diuretics
	Cyclosporine
	Beta-blockers

Clinical Practice Recommendation for the Evaluation and Management of CKD in Adults 2022

Follow-up measurement of lipid levels in adults with CKD

- In adults with CKD follow-up measurement of lipid levels should be reserved for instances (2B)
  - Assessment of adherence to statin treatment
  - Change in RRT modality
  - Concern about the presence of new secondary causes of dyslipidemia
  - To assess 10-year cardiovascular risk in patients aged <50 years and not currently receiving a statin

Clinical Practice Recommendation for the Evaluation and Management of CKD in Adults 2022

Treatment goals for LDL-cholesterol and TG

- Patients with CKD stage 3 are considered to be at high risk and CKD stage 4-5 with or without dialysis are considered to be very high risk of CVD (2B)

- Treatment goals for LDL-cholesterol <100 mg/dL for primary prevention (2C)

- Treatment goals for triglyceride <150 mg/dL for primary prevention (Not grade)

Clinical Practice Recommendation for the Evaluation and Management of CKD in Adults 2022

Cholesterol lowering treatment

CKD stage	Age (Years)	Options	Level
G1-G2	> 50	Statin	2B
G3a-G5	> 50	Statin or statin/ezetimibe	2B
	18-49 plus ➤ known coronary disease (MI or coronary revascularization) ➤ diabetes mellitus ➤ prior ischemic stroke ➤ estimated 10-year incidence of coronary death or non-fatal myocardial infarction >10%	Statin	2B
KT	Any age	Statin	2B

Clinical Practice Recommendation for the Evaluation and Management of CKD in Adults 2022

Recommended doses of statins in CKD

Statin	CKD state 1–2	CKD stage 3A	CKD stage 3B–5
Atorvastatin	40–80	40–80	20–40
Fluvastatin	80	80	No data
Pitavastatin	4	4	2
Pravastatin	40	40	20
Rosuvastatin	20	20	10
Simvastatin	40	40	20–40
Simvastatin/Ezetmibe	40/10	40/10	20/10

Clinical Practice Recommendation for the Evaluation and Management of CKD in Adults 2022

Triglyceride-lowering treatment in CKD

- In adults with CKD and hypertriglyceridemia, we suggest that dietary modification, weight reduction, increased physical activity and reducing alcohol intake be advised (2B)

- Medication could be considered for the patients with GFR <60 mL/min/ 1.73 m2 and serum TG >1000 mg/dl (2C)

Clinical Practice Recommendation for the Evaluation and Management of CKD in Adults 2022

Recommended doses of non-statins in CKD

Lipid lowering agent	CKD state 1-2	CKD stage 3A	CKD stage 3B-5
Cholestyramine	16	16	16
Fenofibrate	150	150	No recommendation
Fenofibrate (micronized form)	100	100	No recommendation
Fenofibrate (nanotechnology form)	72.5	72.5	No recommendation
Gemfibrozil	1200	1200	600
Ezetimide	10	10	10
Niacin	2000	2000	1000
Omega-3 fatty acid (EPA/DHA)	4000	4000	4000

Clinical Practice Recommendation for the Evaluation and Management of CKD in Adults 2022

Take home message

- Patients undergoing treatment with a statin may experience an elevation in cholesterol absorption.
- Combining a statin with ezetimibe is an effective approach for lowering LDL levels.
- Markers of increased cholesterol absorption predict the development of CVD in individuals with both normal GFR and those undergoing hemodialysis (HD).
- Statins reduce cardiovascular events in non-dialysis CKD and might also protect against CKD progression.
- The combination of statins and ezetimibe reduces cardiovascular events in both non-dialysis and dialysis CKD patients, as demonstrated in the SHARP study.

Take home message

- ESC 2019 guideline: prescribed statins to reach LDL goals set for the specific level of risk:
  - Very high risk: ASCVD, score> 10% and CKD stage 4/5
    - High-intensity statin + ezetimibe: LDL reduction 50% and LDL<55 mg/dL
  - High risk: score 5-10% and CKD stage 3/KT
    - High-intensity statin + ezetimibe: LDL reduction > 50% and LDL<70 mg/dL
  - Moderate risk: score 1-5%
    - Statin therapy + ezetimibe if statin can not tolerate: LDL <100 mg/dL
  - Low risk: score <1%
    - Statin therapy and LDL <116 mg/dL


THANK YOU
FOR YOUR
ATTENTION