Efficacy of moderate- versus high-intensity statins therapy for LDL-C lowering in T2DM patients in Udonthani Hospital

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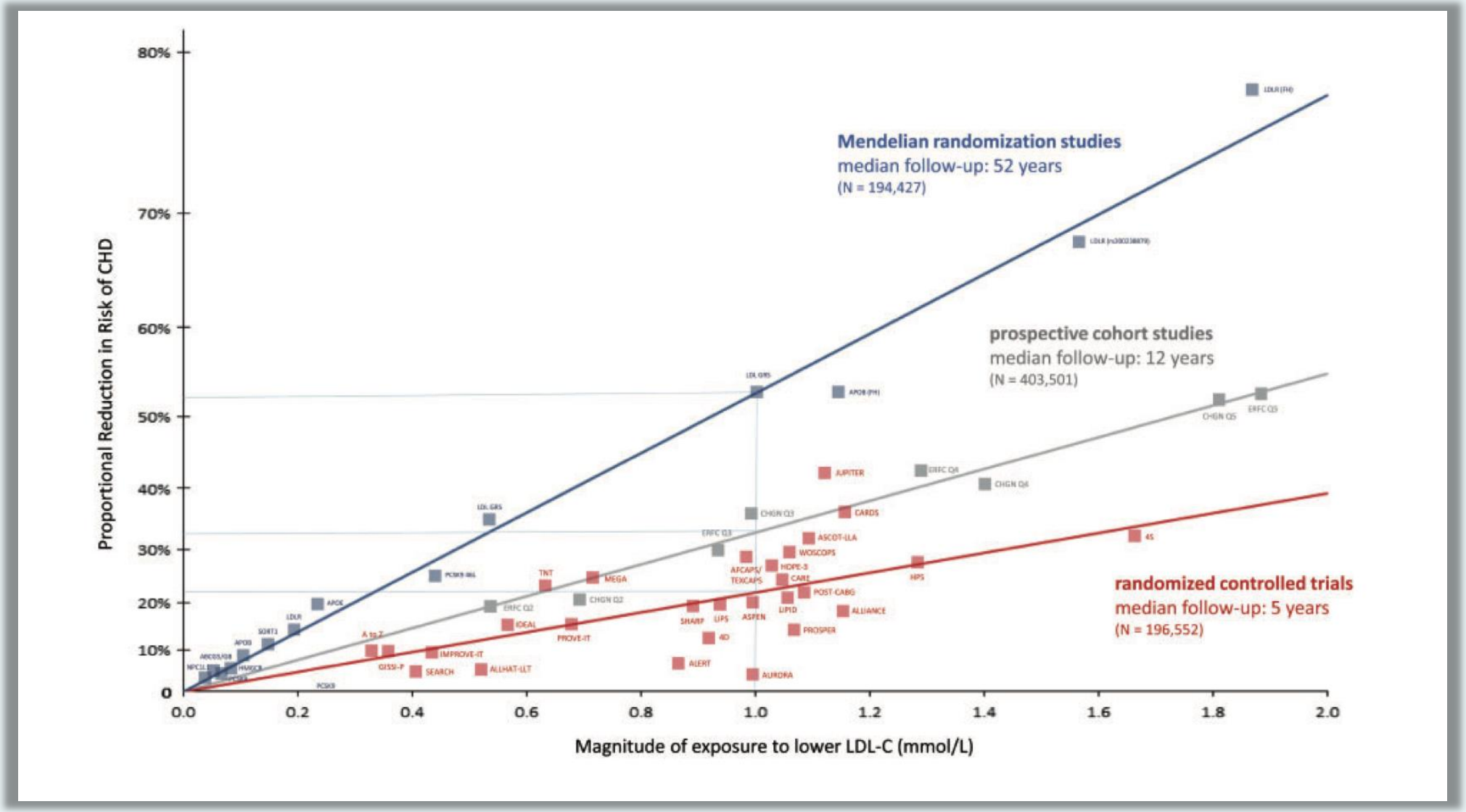
Background

Diabetes confers about a two-fold excess risk for a wide range of vascular diseases, independently from other conventional risk factors.

Lancet 2010;375(9733):2215-22

Background



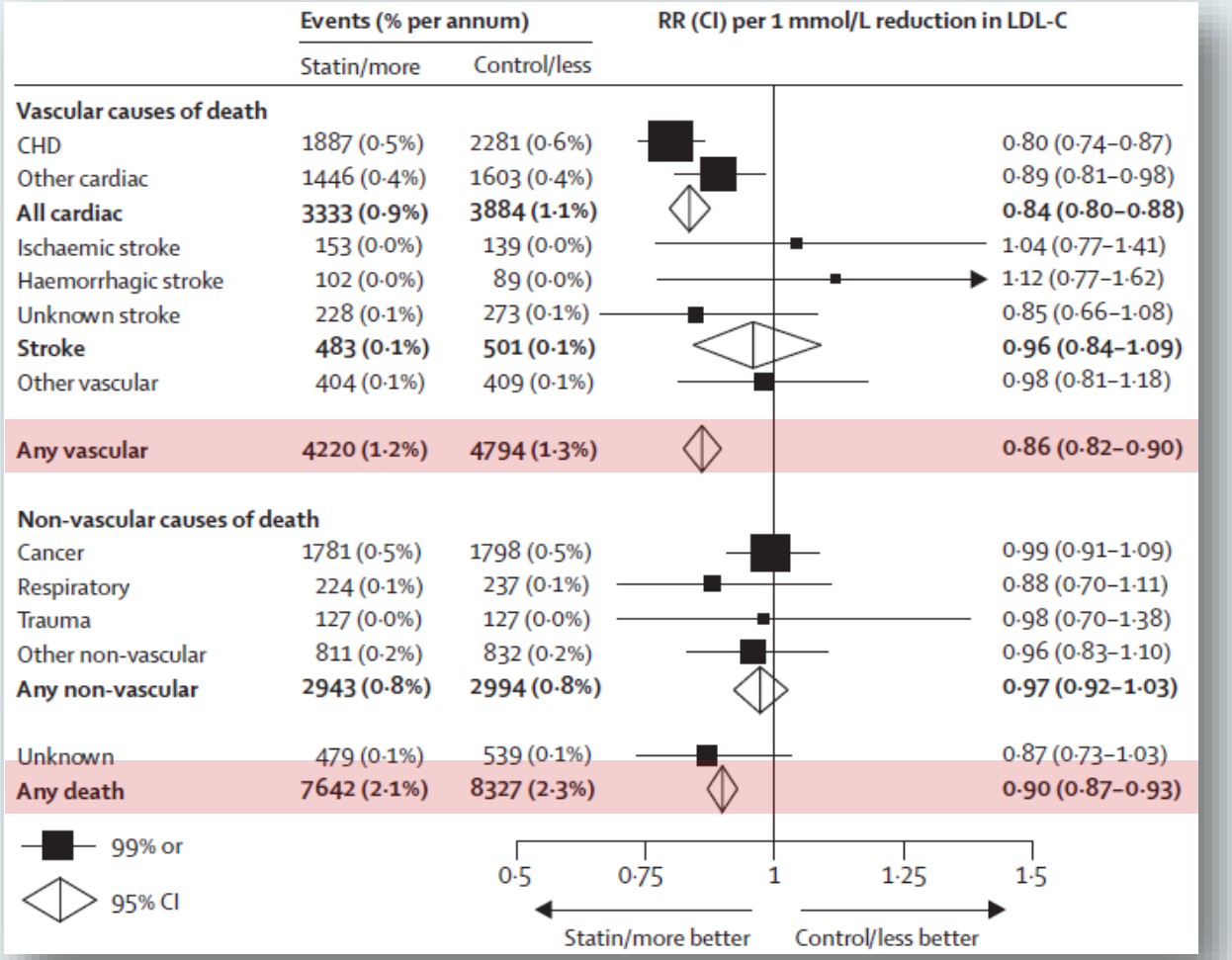
Eur Heart J 2017;38(32):2459-72

Background

Further LDL-C reductions with more intensive statin regimens VS less intensive statin regimens

Further reductions in the incidence of major cardiovascular event[1]

Moderate-* or high-intensity statin is recommended for all type 2 diabetic patients with or without LDL-C >100 mg/dl.[2]



1. Lancet 2010; 376: 1670–81
2. Diabetes Care 2017; 40 (sup1):S1-S138

*Clinical Practice Guideline for Diabetes 2017

Background

Statins therapy in T2DM patients

	Moderate-intensity statin therapy	High-intensity statin therapy
Primary prevention	• Aged 40-75 years (A) • Aged 20-39 years + risk factors (C)	• Multiple ASCVD risk factors (B) • Aged 50-70 years (B) • 10-year ASCVD risk ≥20% (C) (add ezetimibe to reduce LDL-C ≥50%)
Secondary prevention		• All ages (addition of non-statin if LDL-C ≥70 mg/dL)

ADA standards of medical care in diabetes 2022

Background

High-intensity statin therapy (lowers LDL-C by ≥50%)	Moderate-intensity statin therapy (lowers LDL-C by 30-49%)
• 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 • Pitavastatin 1-4 mg

ADA standards of medical care in diabetes 2022

Background

Clinical trials of statin therapy in Asian patients: lipid-lowering efficacy

Trial	No.	Locale	Statin (Dose, mg)	Mean % LDL	p Value
Randomized					
ASIA[6]	157	Multiple*	Atorvastatin (10–20)	48%	0.003
			Simvastatin (10–20)	41%	
Chan et al[28]	76	China	Simvastatin (10)	33%	—
J-CLAS[29]	121	Japan	Atorvastatin (5–20)	36%–50%	<0.001
Saito et al[30]	112	Japan	Rosuvastatin (1–40)	36%–66%	<0.0001
Wang et al[31]	54	Taiwan	Atorvastatin (10)	42%	<0.001
Yamamoto et al[32]	60	Japan	Rosuvastatin (1–4)	30–42%	0.001
Open label					
GOALLS[9,33]	198	Multiple†	Simvastatin (20, 40, 80)	41%	—
Itoh et al[34]	201	Japan	Simvastatin (5)	28%	<0.001
Mabuchi et al[35]	37	Japan	Rosuvastatin (10–40)	49%–57%	<0.0001
STATT[36]	133	Multiple‡	Simvastatin (20, 40, 80)	45%	<0.001
Teramoto et al[37]	212	Japan	Fluvastatin (20, 30, 40)	29%	<0.001
Tomlinson et al[38]	31	Hong Kong	Fluvastatin (20, 40)	26%	<0.01
Yoshida et al[39]	22	Japan	Simvastatin (20)	40%	<0.001

Studies indicate that lower statin doses achieve lipid improvements in Asian patients comparable with those observed with higher doses in Caucasians.

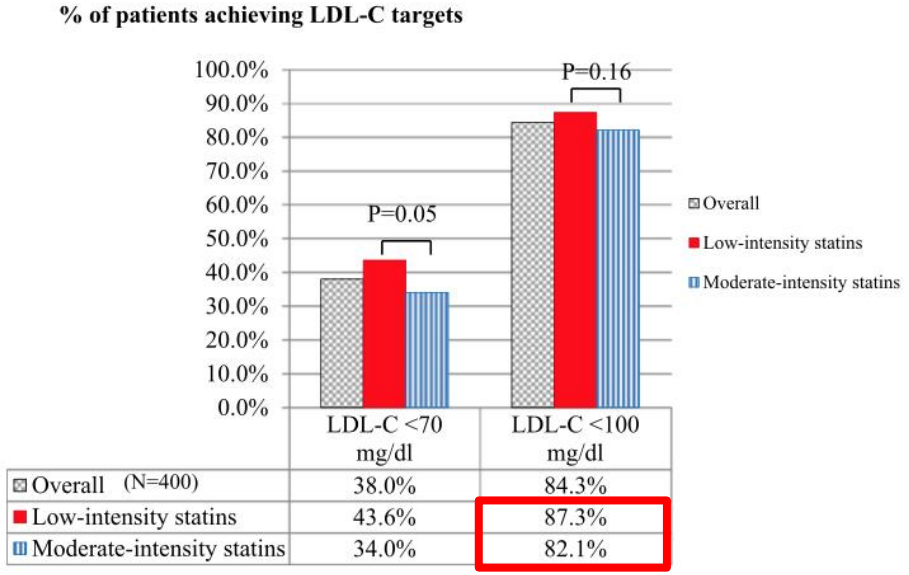
Am J Cardiol 2007;99(3):410-4

Background

Efficacy of low- and moderate-intensity statins for achieving low- density lipoprotein cholesterol targets in Thai type 2 diabetic patients

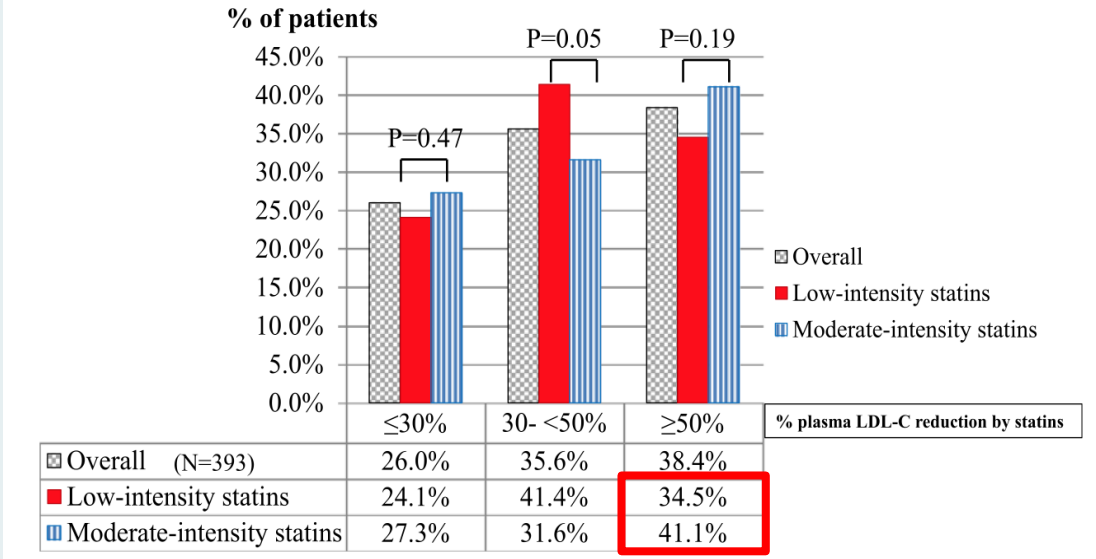
Nuntakorn Thongtang*, Chaiyut Sitthananun, Sutin Sriussadaporn and Wannee Nitiyanant

- ✓ Retrospective cohort study
- ✓ 400 T2DM patients treated with low- or moderate-intensity statins
- ✓ Siriraj Diabetes Clinic



	LDL-C <70 mg/dl	LDL-C <100 mg/dl
Overall (N=400)	38.0%	84.3%
Low-intensity statins	43.6%	87.3%
Moderate-intensity statins	34.0%	82.1%

Fig. 2 Plasma LDL-C Goal Achievement in Patients Treated with Low- or Moderate-intensity Statins



	≤30%	30- <50%	≥50%
Overall (N=393)	26.0%	35.6%	38.4%
Low-intensity statins	24.1%	41.4%	34.5%
Moderate-intensity statins	27.3%	31.6%	41.1%

% plasma LDL-C reduction by statins

Fig. 3 Percentage of Plasma LDL-C Reduction by Low- and Moderate-intensity Statin Therapy

J Diabetes Metab Disord. 2017;16:6

Objective

- To evaluate the efficacy of moderate-intensity statins as compared to high-intensity statins on LDL-C lowering in patients with type 2 diabetes.

- To evaluate the factors associated with greater LDL-C reduction by statins.

Definition

❀ Percentage of plasma LDL-C reduction

$$\frac{\text{(Pre-statin plasma LDL-C level – Post-statin LDL-C level) x 100}}{\text{Pre-statin plasma LDL-C level}}$$

❀ High-intensity statins

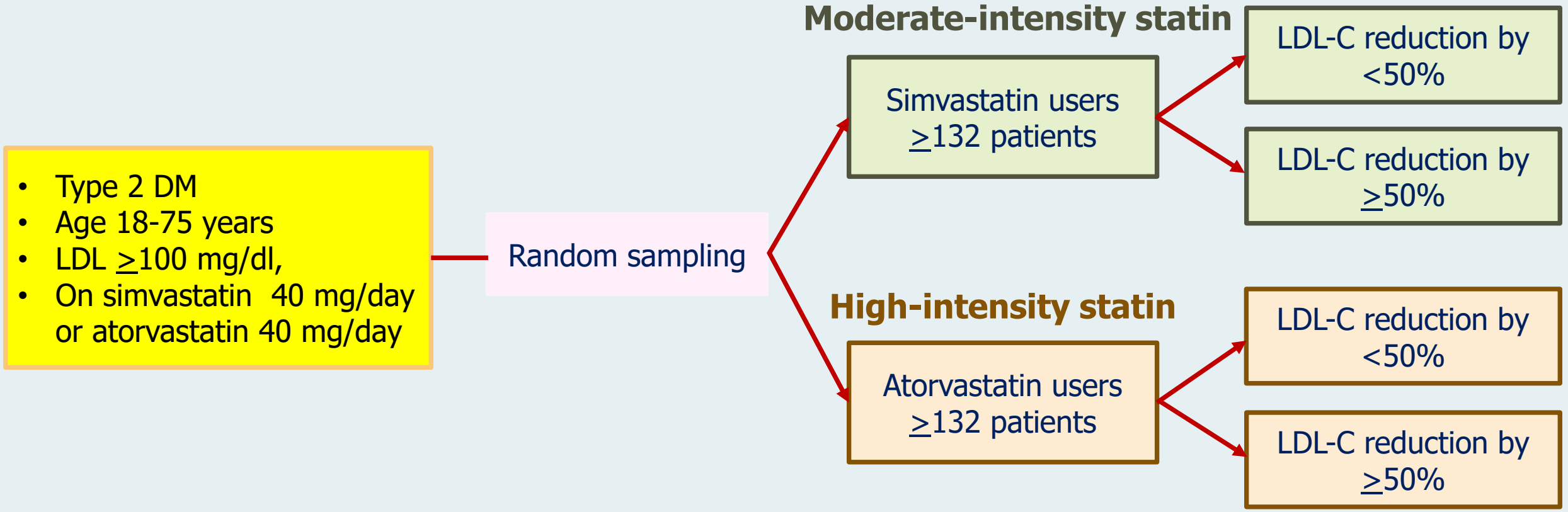
- Statin treatment resulted in LDL-C reduction ≥50% from baseline
- Atorvastatin 40 mg/d

❀ Moderate-intensity statins

- Statin treatment resulted in LDL-C reduction 30-49% from baseline
- Simvastatin 40 mg/d

Research design and Study flow chart

- Retrospective cohort study
- Udonthani Hospital during January 2017 to December 2021



★ **Plasma LDL-C was collected before and after statins treatment within 4-52 weeks.**

Statistical analysis

- Data were expressed as mean ± SD, median (range), or percentage.
- Variables were compared using Independent t-test or Mann-Whitney U test for the comparison between 2 groups.
- A p-value of <0.05 was considered to be statistically significant.
- Statistical analysis was performed using standard program.

Baseline characteristics

	Moderate-intensity n = 147	High-intensity n = 153	P-value
Age: years (mean ± SD)	58.4 ± 11.7	61.9 ± 9.9	0.01
Sex: female, n (%)	96 (65.3%)	99 (64.7%)	0.91
BMI: kg/m^2 (mean ± SD)	26.9 ± 4.6	26.8 ± 6.0	0.93
Waist circumference: cm (mean ± SD)	91.7 ± 10.6	93.1 ± 12.6	0.62
Duration of diabetes: yr (median, IQR)	5.0 (7.0) (min=0, max=23.0)	5.0(5.0) (min=0, max=17.0)	0.86
HbA1C: % (mean ± SD)	10.2 ± 2.6	9.3 ± 2.5	0.001
SBP: mmHg (mean ± SD)	129.2 ± 17.0	134.4 ± 18.3	0.01
DBP: mmHg (mean ± SD)	70.6 ± 11.5	74.7 ± 15.8	0.01

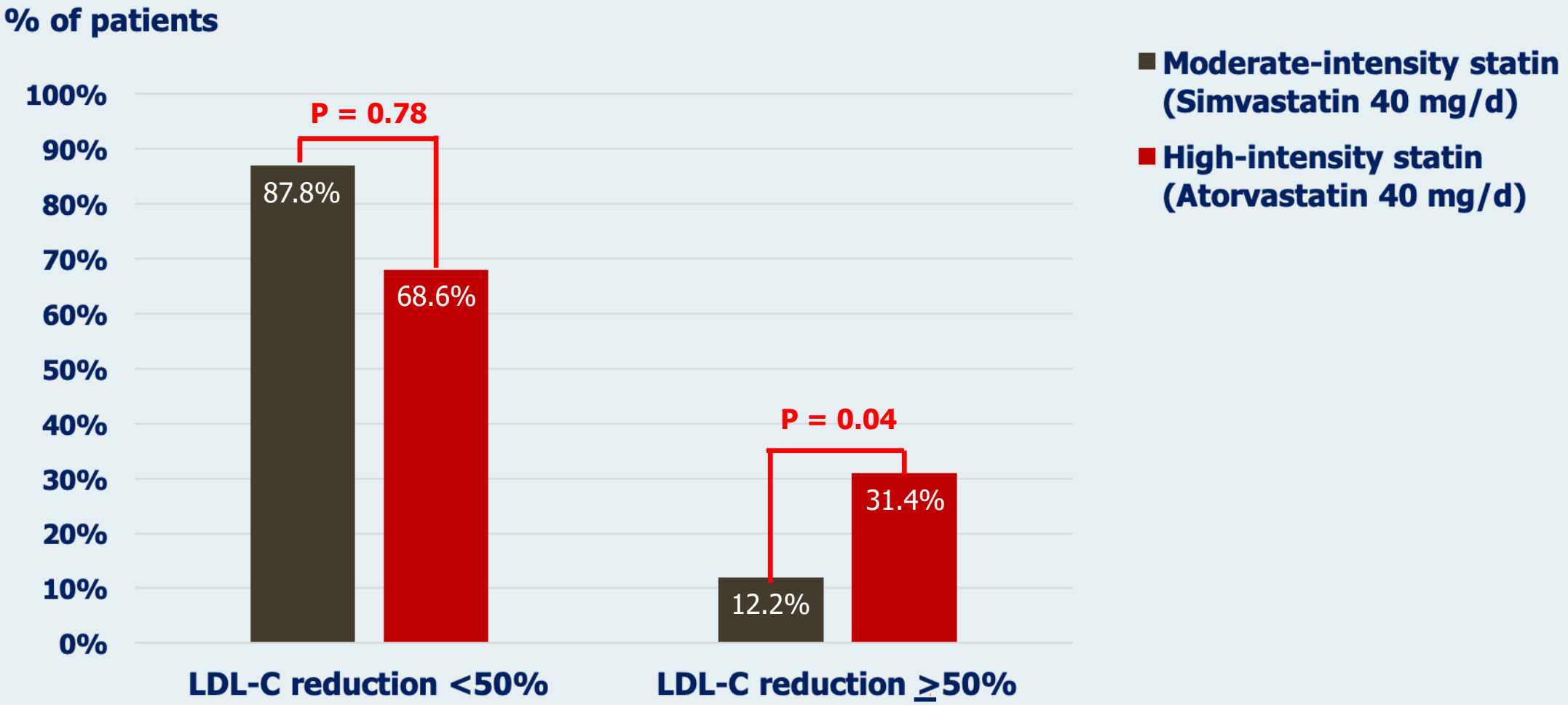
Baseline characteristics

	Moderate-intensity n = 147	High-intensity n = 153	P-value
Comorbidities			
Hypertension: n (%)	124 (84.4%)	139 (90.8%)	0.09
Stroke: n (%)	8 (5.4%)	15 (9.8%)	0.16
Chronic kidney disease: n (%)	20 (13.6%)	38 (24.8%)	0.03
Coronary artery disease: n (%)	1 (0.7%)	3 (2.0%)	0.86
Peripheral arterial disease: n (%)	0 (0 %)	2 (1.3%)	0.17

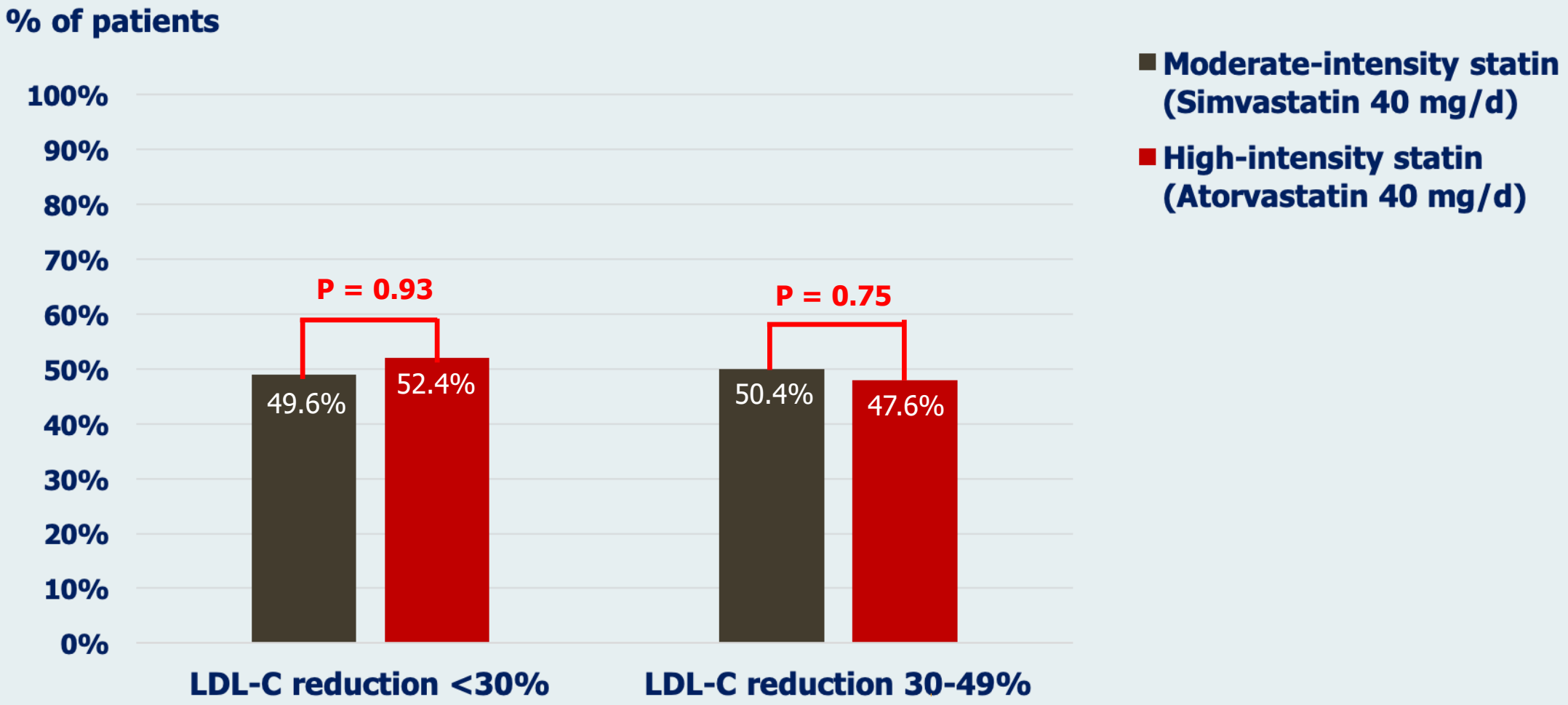
Baseline characteristics

	Moderate-intensity n = 147	High-intensity n = 153	P-value
Pre-statin plasma lipid levels			
Cholesterol: mg/dl (mean ± SD)	228.7 ± 35.3	250.1 ± 49.5	<0.001
Triglyceride: mg/dl (median, IQR)	167 (127) (min=55, max=616)	164 (117) (min=48, max 678)	0.45
HDL-C: mg/dl (mean ± SD)	47.7 ± 11.0	49.7 ± 18.4	0.48
LDL-C: mg/dl (mean ± SD)	146.1 ± 29.0	168.1 ± 40.2	<0.001

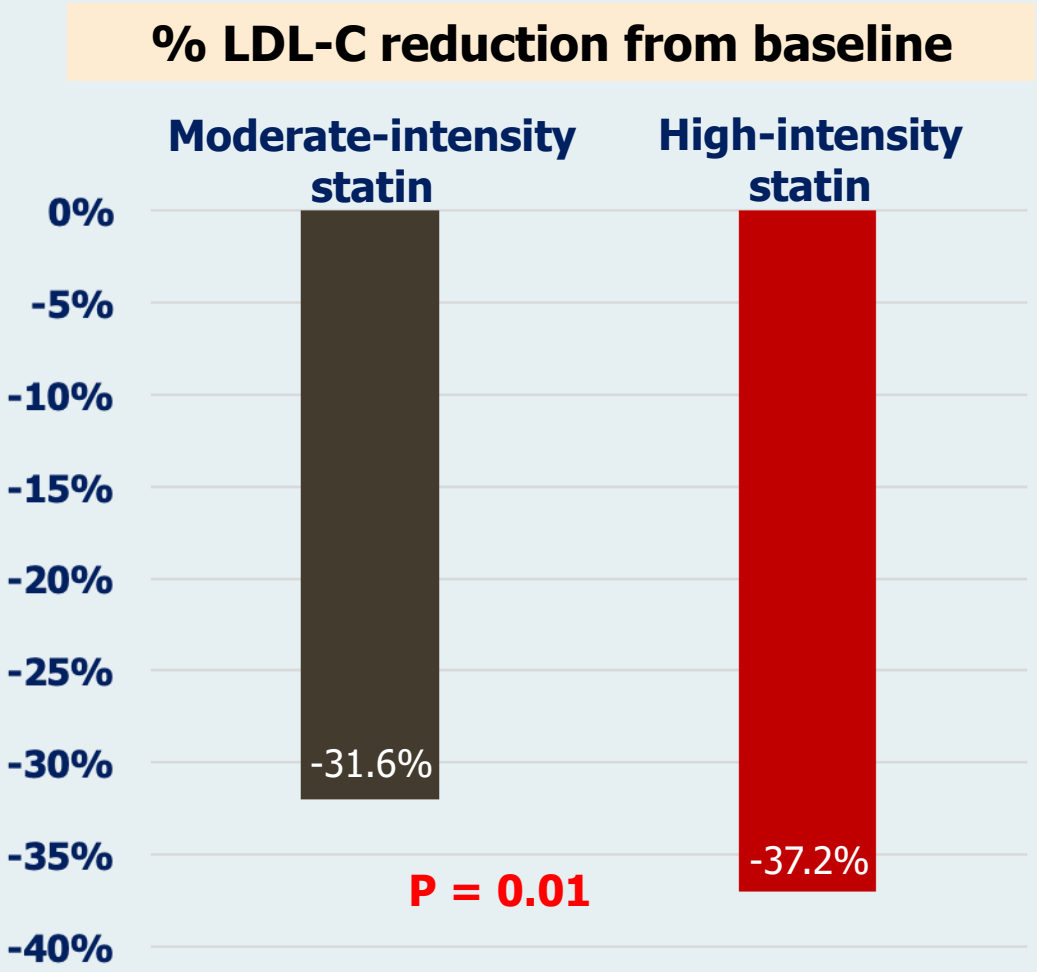
Percentage of patients achieving LDL-C reduction by statins therapy

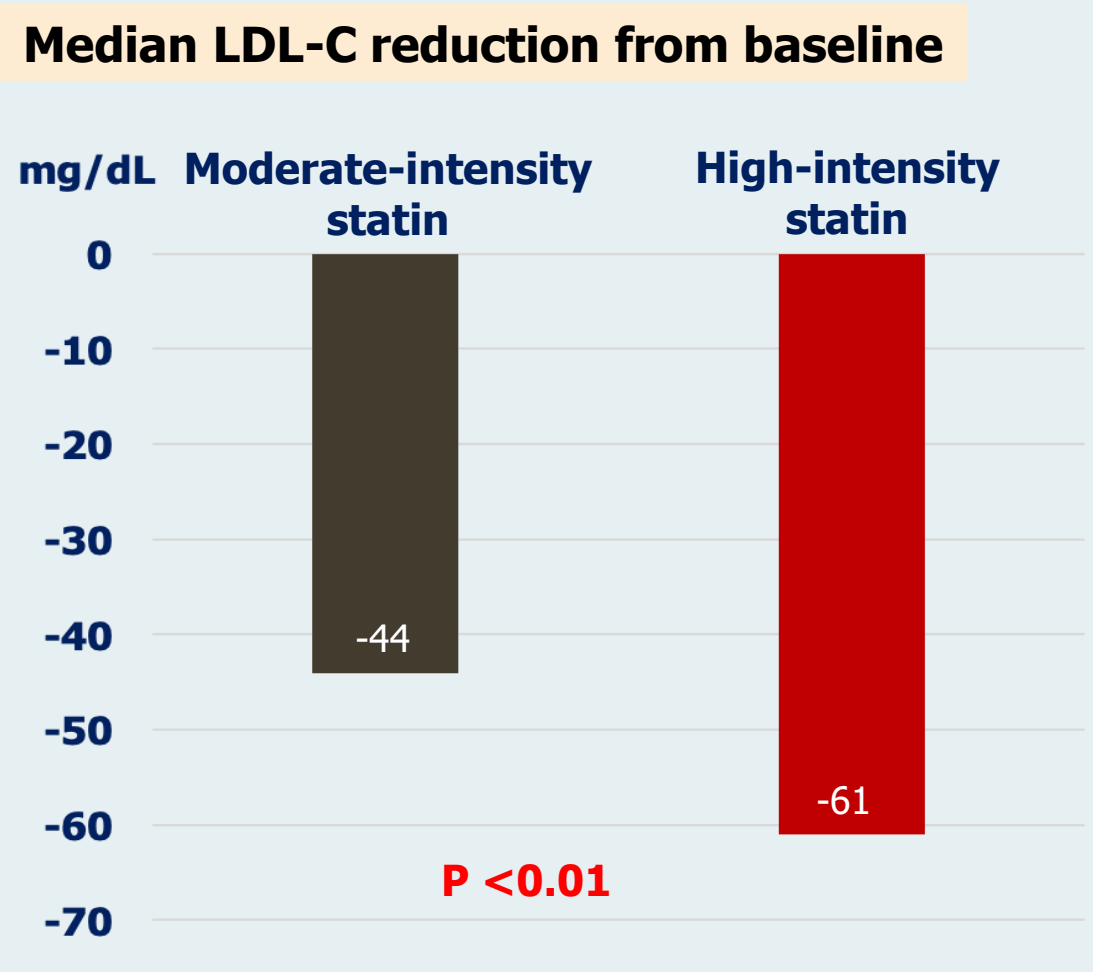


Percentage of patients achieving LDL-C reduction <50%



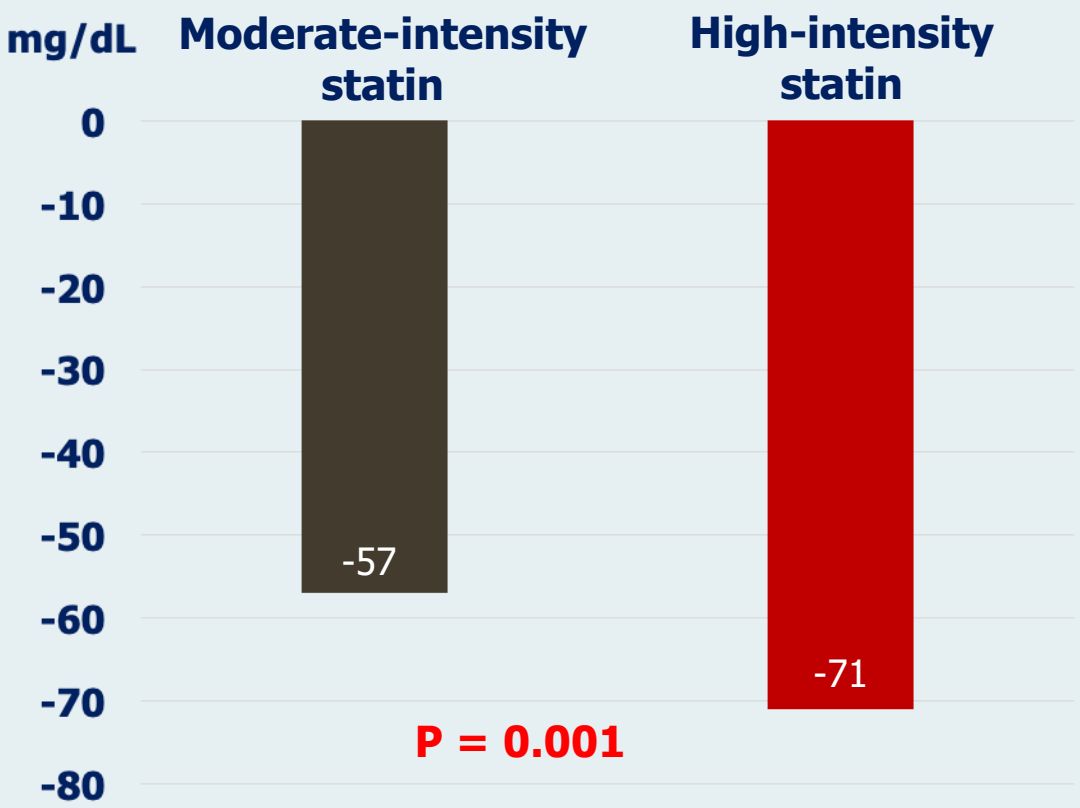
Plasma LDL-C reduction in patients treated with statins



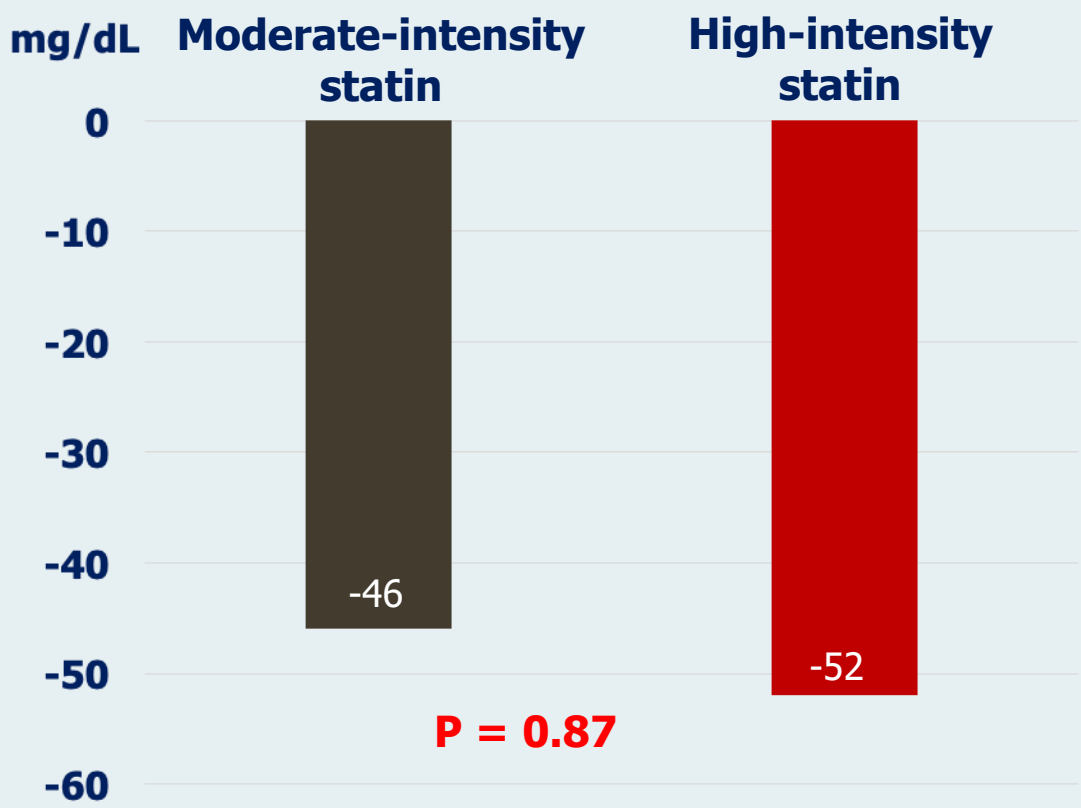


Plasma lipid reduction in patients treated with statins

Mean Cholesterol reduction from baseline



Mean Triglyceride reduction from baseline



Baseline characteristics of patients by LDL-C reduction group

	LDL-C reduction <50% (n = 234)	LDL-C reduction ≥50% (n = 66)	P-value
Age: years (mean ± SD)	59.7 ± 11.1	62.0 ± 10.1	0.12
Sex: female, n (%)	159 (67.9%)	36 (54.5%)	0.04
BMI: kg/m^2 (mean ± SD)	27.2 ± 5.4	25.7 ± 4.8	0.04
Waist circumference: cm (mean ± SD)	93.1 ± 11.8	89.9 ± 11.0	0.04
Duration of diabetes: yr (median, IQR)	5.0 (7) (min=0, max=23.0)	5.5 (5) (min=1, max=17.0)	0.41
HbA1C: % (mean, + SD)	9.9 ± 2.6	9.3 ± 2.5	0.08
SBP: mmHg (mean ± SD)	132.2 ± 18.1	130.8 ± 17.1	0.67
DBP: mmHg (mean ± SD)	73.3 ± 13.8	70.7 ± 14.7	0.49

Baseline characteristics of patients by LDL-C reduction group

	LDL-C reduction <50% (n = 234)	LDL-C reduction ≥50% (n = 66)	P-value
Comorbidities			
Hypertension: n (%)	202 (86.3%)	61 (92.4%)	0.18
Stroke: n (%)	18 (7.7%)	5 (7.6%)	0.97
Chronic kidney disease: n (%) •GFR 30-<60 mL/min/1.73m^2: n (%) •GFR <30 60 mL/min/1.73m^2: n (%)	39 (16.7%) 33 (84.6%) 6 (15.4%)	19 (28.8%) 18 (94.7%) 1 (5.3%)	0.03
Coronary artery disease: n (%)	1 (0.4%)	3 (4.5%)	0.01
Peripheral arterial disease: n (%)	1 (0.4%)	1 (1.5%)	0.34

Baseline characteristics of patients by LDL-C reduction group

	LDL-C reduction <50% (n = 234)	LDL-C reduction ≥50% (n = 66)	P-value
Change HbA1C from basline:% (median, IQR)	0.9 (2.3) (min=-7.3, max=12.6)	1.3 (2.4) (min=-5.7, max=9.1)	0.88
Pre-statin plasma lipid levels			
Cholesterol: mg/dl (mean ± SD)	237.6 ± 43.7	246.8 ± 46.3	0.16
Triglyceride: mg/dl (median, IQR)	174.5 (135) (min=55, max=616)	151 (70) (min=48, max 678)	0.15
HDL-C: mg/dl (mean ± SD)	49.0 ± 16.1	47.6 ± 11.5	0.62
LDL-C: mg/dl (mean ± SD)	154.5 ± 36.0	167.2 ± 38.2	0.01

Results

- From the study, plasma **LDL-C reduction ≥50%** was achieved in 12.2% and 31.4% respectively, with **significant difference** between of the moderate- and high-intensity statin users.

- However, there was **no significant difference** in the patients achieving **plasma LDL-C reduction <50%** between of the moderate- and high-intensity statin groups.

Results

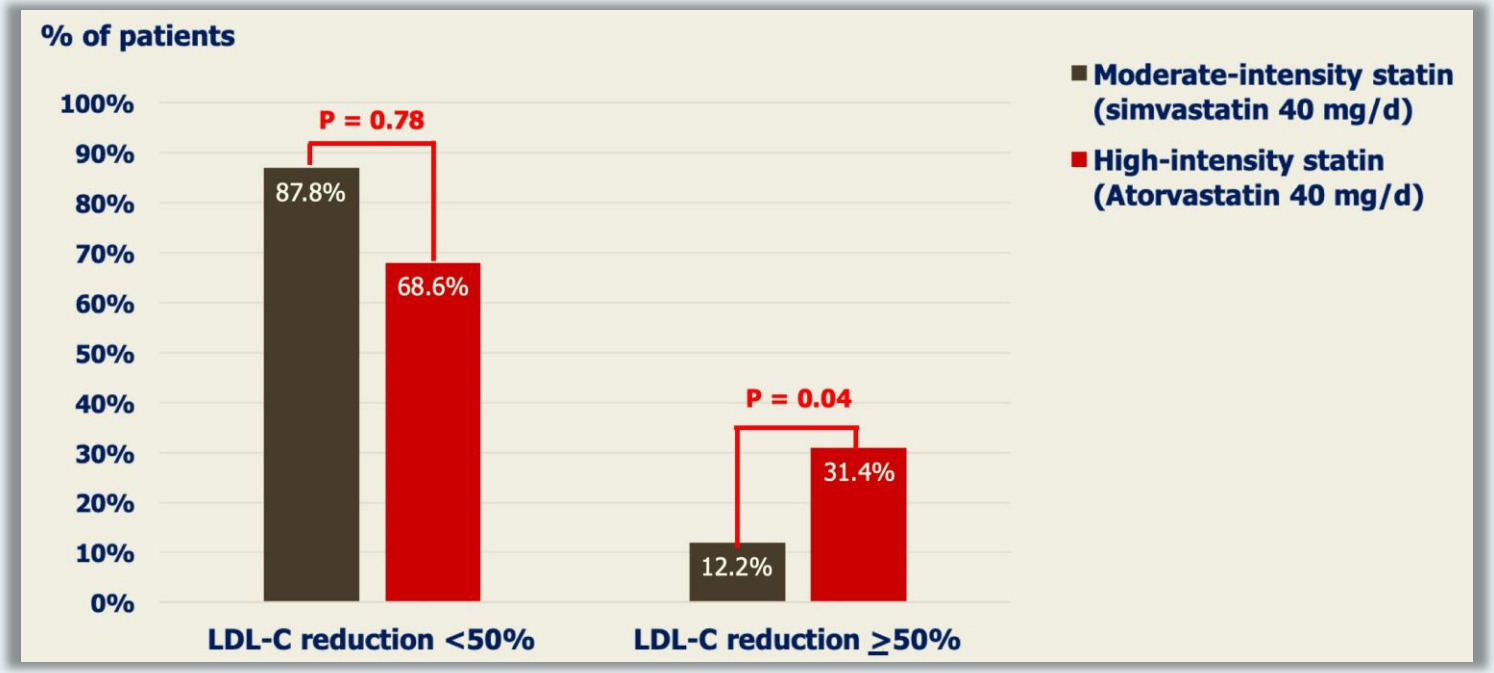
- Factors associated with favorable statin response were
  - ✓ male
  - ✓ mild elevated BMI
  - ✓ mild elevated waist circumference
  - ✓ chronic kidney disease
  - ✓ coronary artery disease
  - ✓ high baseline plasma LDL-C level

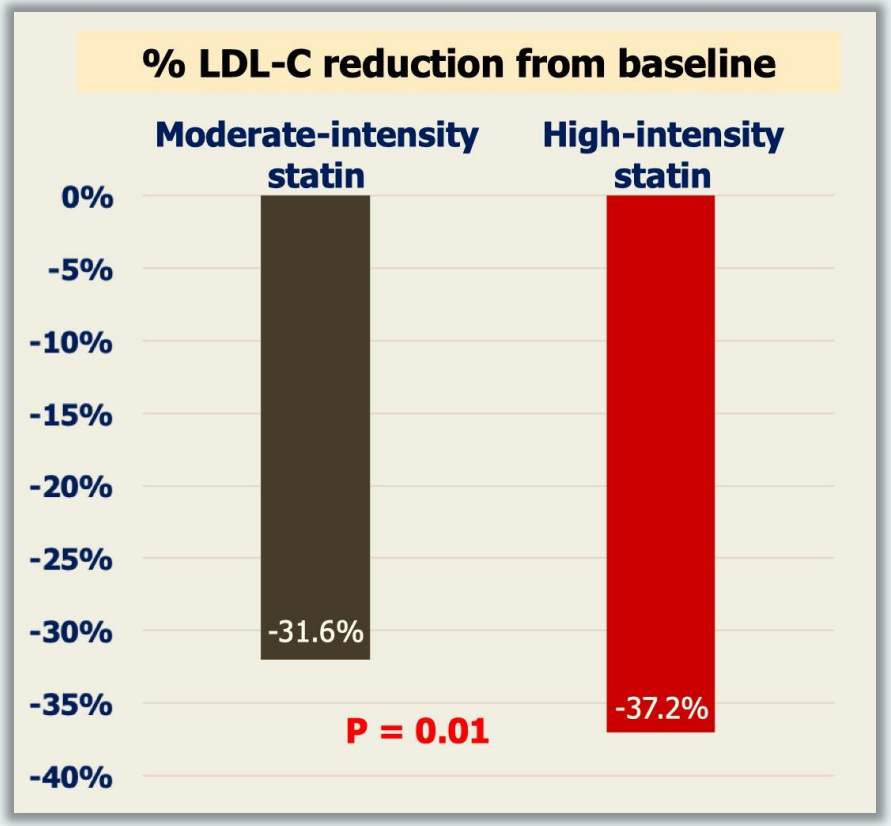
Discussion

- This is the **first study** to assess the effectiveness of **moderate- and high-intensity statin** for lowering LDL-C in **Thai T2DM** patients.

Discussion

- This study confirmed that **high-intensity statins have superior for LDL-C reduction** and tend to achieve LDL-C goal more than moderate-intensity statins.





Discussion

- **A small number of patients** were able to achieve **≥50% reduction in LDL-C** in both the statin groups from this study as compared to the previous study[1].

%LDL-C reduction by moderate-intensity stain	<30%	30-<50%	≥50%
% of patients (Previous study)	27.3%	31.6%	41.1%
% of patients (Our study)	43.5%	44.3%	12.2%

1. J Diabetes Metab Disord. 2017;16:6

Limitations

- Because this was the retrospective cohort study, some data was not investigated.
- Most participants in this study had not established ASCVD, therefore the findings can be applied mainly to T2D for primary prevention.

Conclusion

- High-intensity statins should be recommended for primary prevention in Thai T2DM patients who have high CV risk.
- Moderate-intensity statin can be prescribed for T2DM patients
  - Elderly
  - mild obese
  - chronic kidney disease