LDL-cholesterol and risk of recurrent vascular events in Chinese ischemic stroke patients with and without significant atherosclerosis

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Abstract

Recent trials show that a low-density lipoprotein cholesterol (LDL-C)<1.80mmol/L (or <70mg/dL) was associated with a lower risk of major adverse cardiovascular events (MACE) in Caucasian ischemic stroke patients with atherosclerosis. A prospective cohort study with 1003 consecutive Chinese ischemic stroke patients from QMH were assessed for risk of recurrent stroke and MACE, stratified by LDL-C levels (<1.80 vs. ≥1.80mmol/L) and presence of large artery disease (LAD). Regardless of LAD status, patients with a mean post-event LDL-C<1.80mmol/L had a lower risk of MACE [LAD+ve: multivariate-adjusted subdistribution hazard ratio (SHR) 0.65, 95% confidence interval (CI) 0.42-0.99; LAD-ve: 0.53, 0.32-0.88] and recurrent stroke [LAD+ve: multivariable-adjusted SHR 0.42, 95%CI 0.21-0.83; LAD-ve: 0.53, 0.28-0.99] (both p<0.05). To conclude, a mean LDL-C<1.80mmol/L was associated with a reduced risk of recurrent stroke and MACE in Chinese ischemic stroke patients with and without significant LAD.
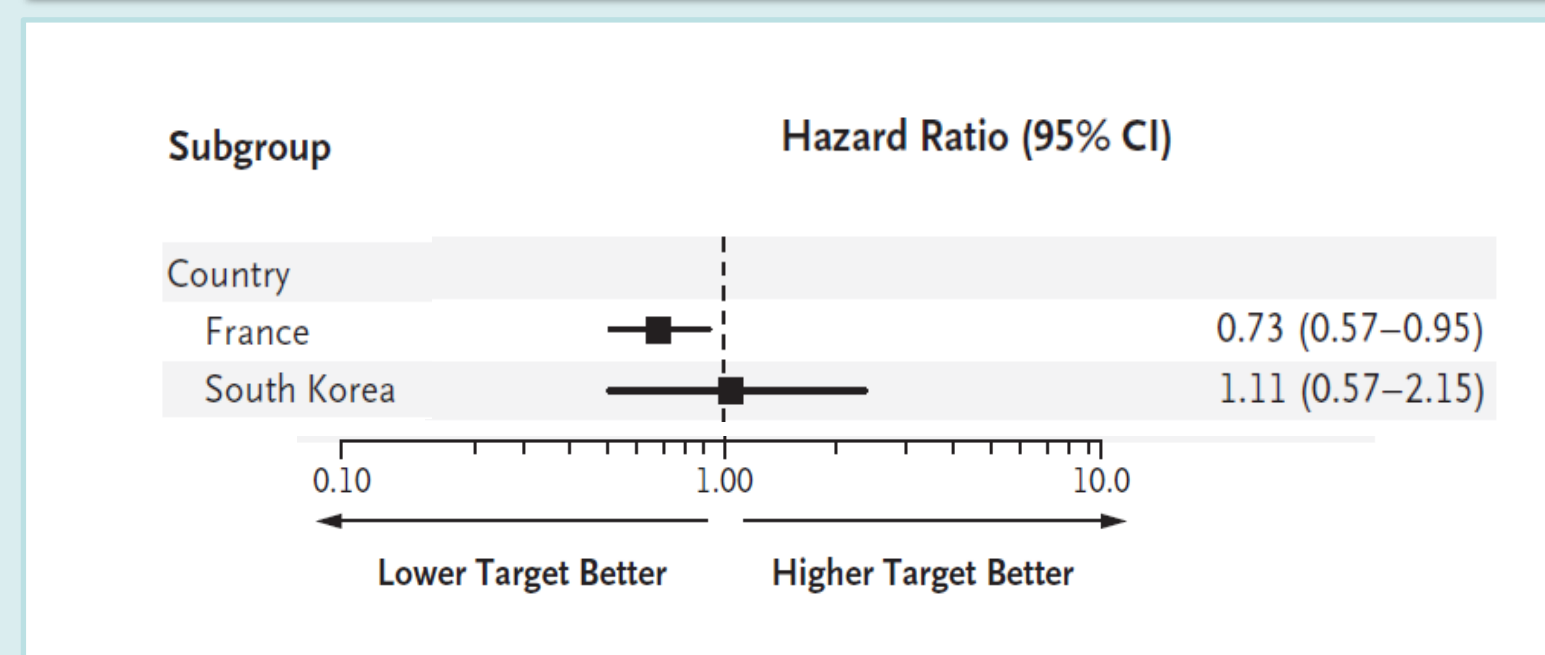
Introduction

Ischemic stroke cause – High LDL cholesterol (LDL-C) levels

Previous large-scale trials:
SPARCL trial - Use of high dose statins was associated with a lower risk of recurrent stroke
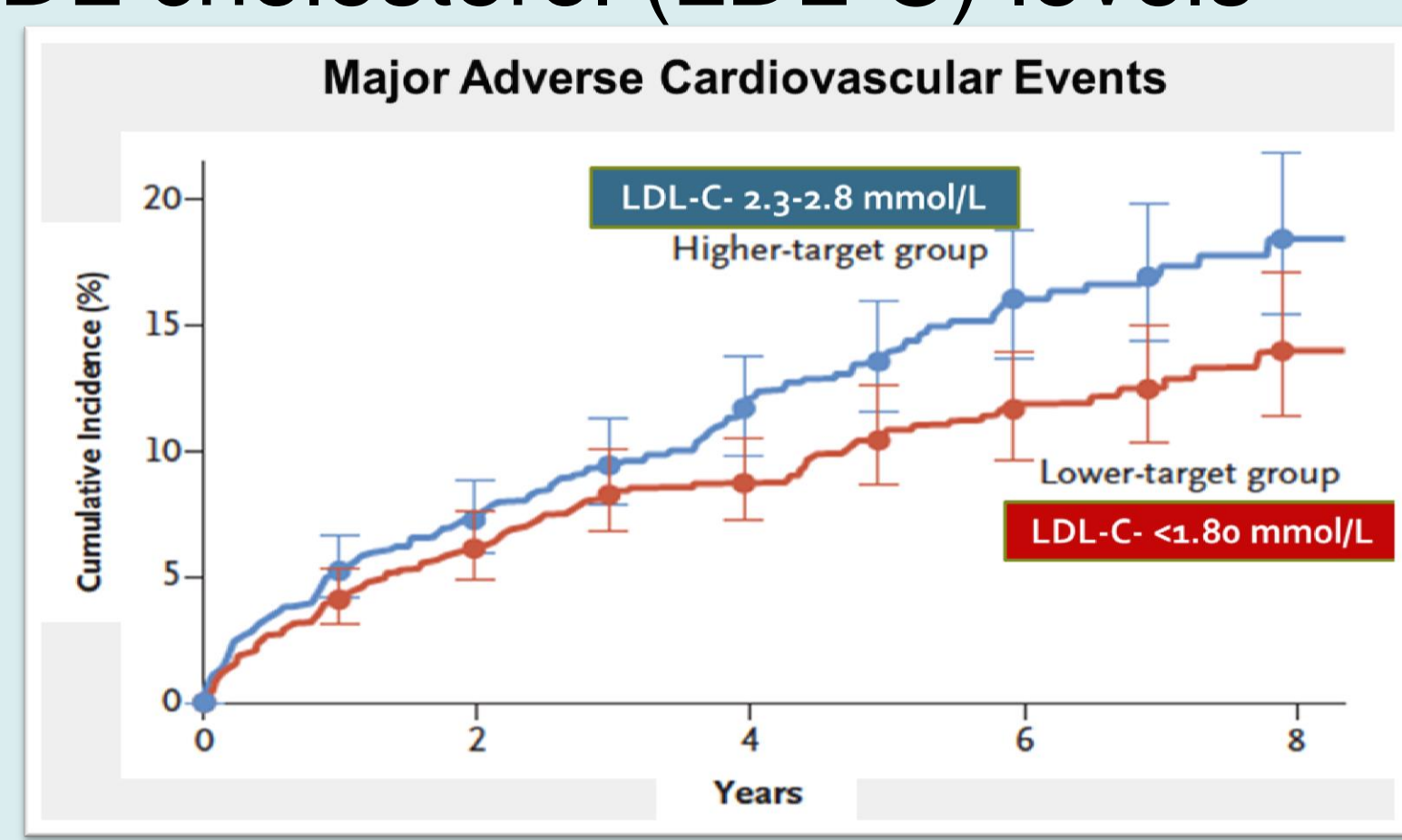
Treat Stroke to Target trial – Assessed effect of statins on TIA/ischemic stroke patients with atherosclerosis

Both these large-scale studies did not take into account patients without atherosclerosis.

Objectives

Long-term prognostic implications of mean LDL-C levels (<1.80 vs ≥1.80 mmol/L) after the index event in a large Chinese stroke cohort LAD status

- LAD+ve – Intra/extracranial artery with ≥50% vascular stenosis
- LAD-ve – Intra/extracranial artery with <50% vascular stenosis

Method

1003 patients diagnosed with acute ischemic stroke at QMH (2008-2014). Cause of ischemic stroke (TOAST criteria) and functional outcome of stroke (modified Rankin Scale) was determined.
Follow-up every 3-6 months - Mean follow up period – 6.5+/-2.4 years.
9 LDL-C reading were taken during follow-up.
Assessed for clinical outcomes: 1) recurrent stroke (ischemic or hemorrhagic), 2) major adverse cardiovascular events (MACE)
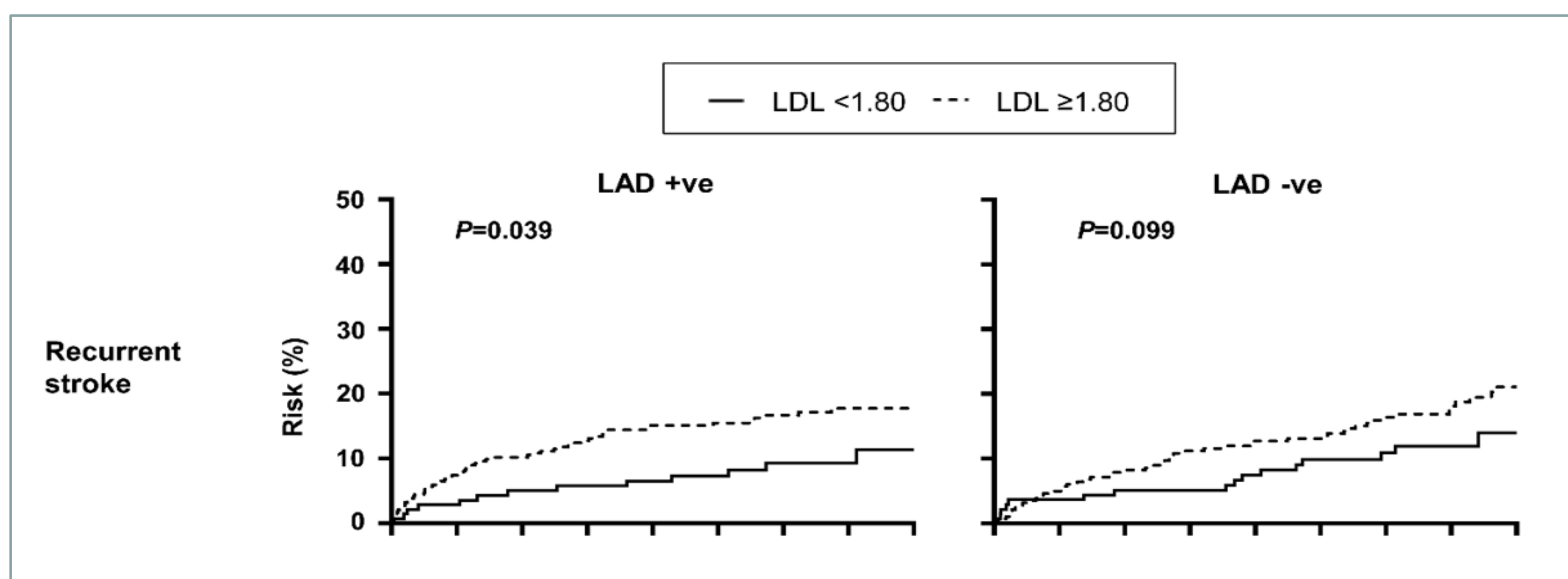
Post-event mean LDL-C (mmol/L)	<1.80	≥1.80	SHR (95% CI) adjusted for age, sex and vascular risk factors[a] <1.80
LAD+ve	13/142	56/340	0.42 (0.21-0.83)
LAD-ve	16/137	54/285	0.53 (0.28-0.99)

[a]DM, AF, history of ischemic heart disease, history of TIA or stroke, GFR and post-event mean SBP
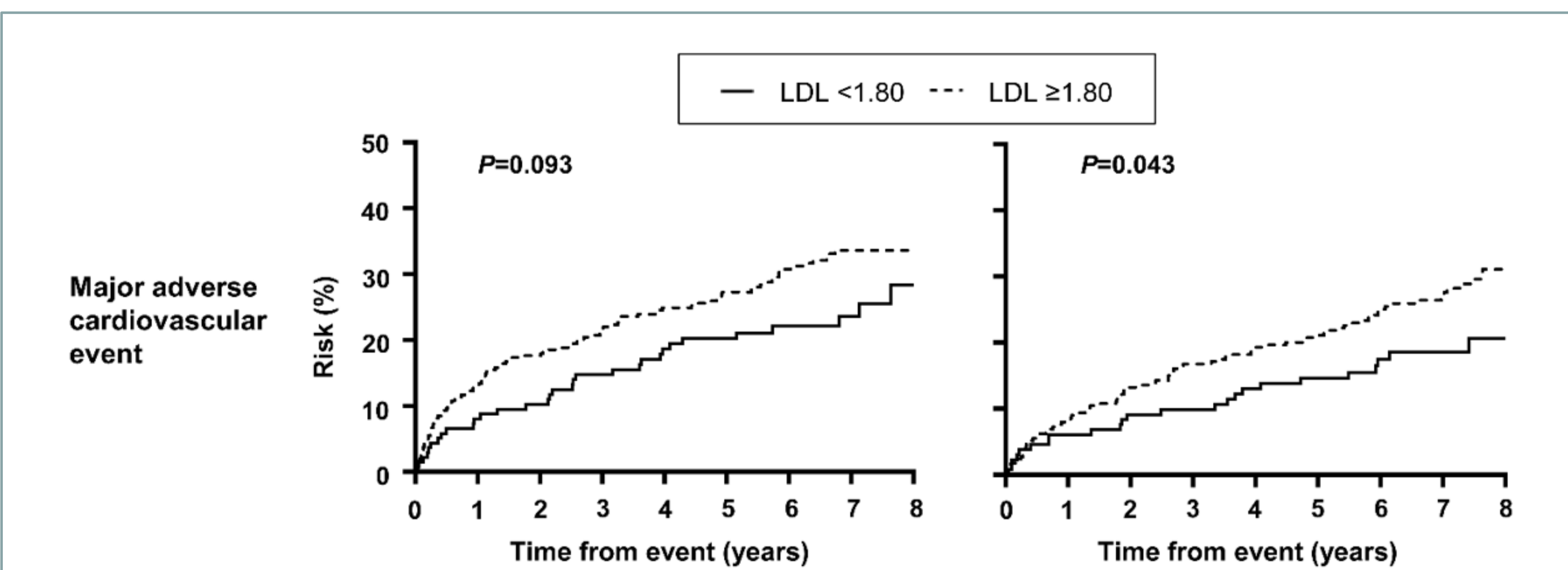
Post-event mean LDL-C (mmol/L)	<1.80	≥1.80	SHR (95% CI) adjusted for age, sex and vascular risk factors[a] <1.80
LAD+ve	32/138	106/344	0.65 (0.42-0.99)
LAD-ve	24/132	84/290	0.53 (0.32-0.88)

[a]DM, AF, history of ischemic heart disease, history of TIA or stroke, GFR and post-event mean SBP

Discussion

Chinese ischemic stroke patients with or without LAD (mean follow-up 6.5±2.4 years), those with mean LDL-C<1.80 mmol/L had approximately 50-60% lower risk of recurrent stroke and 35-50% lower risk of MACE.
These results were in tandem with previous large-scale TST and SPARCL trials

Strengths	Limitations
• Largest cohort investigating the prognostic implications of post-stroke mean LDL-C level on cardiovascular outcomes in Asians with ischemic stroke • Relatively long follow up period • High patient compliance to statins • Controlled for confounding factors like mean SBP during follow up	• Most patients had mild to moderate stroke – cannot generalize to severe cases • Likelihood of more frequent lipid evaluation and aggressive statin therapy in high-risk patients

Conclusion

In Chinese ischemic stroke patients with or without LAD (mean follow-up 6.5±2.4 years), patients with mean LDL-C <1.80 mmol/L had Long-term follow-up data of the Korean cohort in the recent TST trial are awaited.
Further RCTs needed to determine the optimal LDL-C cut off for ischemic stroke patients and assess if LDL-C <1.40 mmol/L offers additional prognostic advantage.

References

Amarenco et al - N Engl J Med. 2020;382:9
SPARCL trial - N Engl J Med. 2020;382:9.

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