

# In Chinese Adults, Causal Associations of Blood Lipids and the Risk of Ischaemic Stroke and Intracerebral Hemorrhage

## Abstract

The second leading cause of death worldwide is stroke, which accounts for more than 6 million deaths annually, including 2 million stroke deaths in China. Despite the fact that the incidence of Ischaemic Stroke (IS) is approximately four times higher than that of haemorrhagic stroke (mainly Intracerebral Haemorrhage (ICH)), both haemorrhagic stroke and IS account for the same number of stroke deaths in China. Despite having a lower mean level of Low Density Lipoprotein Cholesterol (LDL-C), China also has a higher rate of ICH and a higher incidence of stroke when compared to western populations. LDL-C lowering trials showed similar risk reductions for IS and CHD8–10, whereas observational studies reported weaker positive associations of LDL-C with IS than with Coronary Heart Disease (CHD). Conflicting results 11–13 from Mendelian Randomisation (MR) studies of LDL-C and IS have raised concerns regarding the significance of LDL-C for IS. Statins may not have been used as widely to prevent Cardiovascular Disease (CVD) in China because of concerns about the increased risks of ICH associated with lowering LDL-C. In a nested case control study in the China Kadoorie Biobank (CKB), we compared the risks for both stroke types associated with equivalent differences in LDL-C in MR analyses and with worldwide LDL-C lowering trials, as well as the associations of biochemically measured LDL-C and other major lipids with IS and ICH. The outcomes showed solid positive relationship of LDL-C with IS and similarly solid backwards relationship with ICH, that were affirmed by hereditary examinations and by LDL-C bringing down preliminaries, however bringing down LDL-C is still liable to have net advantage for avoidance of generally stroke and CVD in Jawline.

**Keywords:** Ischemic stroke • Hemorrhagic stroke • Blood Hemorrhagic stroke • Low density lipoprotein cholesterol • Mendelian randomization • Cardiovascular disease

## Introduction

The CKB prospective study enrolled 512,891 adults from ten distinct regions of China. The subset of 489,762 people who had never had a stroke, transient ischaemic attack, or coronary heart disease at baseline had a mean age of 51 (11) years and 59% of them were women. A total of 32,869 incident IS cases and 8,270 incident ICH cases were recorded after a median follow up period of 9 years, with age and sex adjusted incidence rates of 761 and 187 cases per 100,000 person years, respectively. Among people with no earlier history of CVD, disease, lipid bringing down, anticoagulant, or antiplatelet treatment at pattern, 5475 IS cases,

4776 ICH cases and 6290 sound controls were chosen for a settled case control investigation of episode stroke. Compared to controls, IS cases were more likely to be urban dwellers and smokers at baseline, but their dietary habits were similar. Although the distribution of other socioeconomic and lifestyle factors was comparable between ICH cases and controls, regular consumption of certain animal based foods, such as meat and eggs, was less common in ICH cases than in controls [1,2].

After stratification based on age at risk (5-years intervals), study area and gender, as well as adjustments for education, smoking, alcohol consumption, physical activity, diabetes and

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baseline SBP, plasma LDL-C concentrations were found to be positively correlated with IS risk and inversely correlated with ICH risk. Each 1 mmol/L increase in usual LDL-C was associated with a 17% increase (Rate Ratio (RR)=1.17, 95% Confidence Intervals (CI)) across the examined range, which was 1.7-3.2 mmol/L. 1.10-1.25) higher risk of IS and a 14% lower risk of ICH (0.86, 0.80-0.92), which resulted in an RR of 0.85 (0.80-0.91) for IS and 1.16 (1.08-1.25) for ICH for each 1 mmol/L lower LDL-C. These results were unaffected by additional lipid fraction adjustments and were generally comparable across subgroups (with the exception of gender, location, and smoking for IS; age and ICH's BMI (Body Mass Index).

We applied the relative risk estimates from the LDL-C lowering trials to the age-specific absolute risks of stroke types and major coronary events in order to evaluate the net effects (benefits versus risks) of LDL-C lowering drug treatment in the Chinese population [3].

### Description

Strong positive associations of LDL-C with IS and equally strong inverse associations with ICH were found in the current study, which included a large number of brain image confirmed IS and ICH cases in populations with no prior history of chronic disease or statin use [4].

MR analyses in the same study population, which was less susceptible to reverse causality and confounding factors, confirmed the causal relevance of LDL-C for both IS and ICH. The risk estimates for IS for LDL-C were in line with those observed in Western populations; however, the lower range of LDL-C in the general population was extended down to 1.7 mmol/L, which is significantly lower than the concentrations typically observed in Western populations. According to these findings, a lower LDL-C level is associated with a lower risk of IS, just as it is for CHD19, even in individuals who have a concentration of LDL-C that is considered normal or low by Western standards [5].

In contrast, a higher risk of ICH was associated with lower LDL-C, regardless of baseline blood pressure, BMI, or other vascular risk factors. For equivalent differences in LDL-C, the risk estimates for various stroke types in CKB's observational and genetic analyses were comparable for LDL-C-lowering trials primarily conducted in Western populations [6-8].

Statins have been shown in large scale trials to lower LDL-C by 1 mmol/L, reducing the risk of IS by about one fifth. Other drugs that lower LDL-C, such as ezetimibe or evolocumab have similar effect estimates [9]. Previous observational studies which included studies prior to the widespread use of brain imaging for the diagnosis of stroke, were unable to accurately predict the risk reductions associated with LDL-C-lowering drug treatment that were observed in the trials. Interestingly, ongoing reports of MR investigations of LDL-C and IS, exhibited huge relationship of hereditarily instrumented LDL-C with IS, predictable with the aftereffects of the current review [10].

### Conclusion

In conclusion, the type of stroke had a different effect on the relationships between major blood lipids and stroke. Lower LDL-C focuses were related with lower dangers of IS and higher dangers of ICH, and the causal importance of these affiliations was affirmed by hereditary examinations in a similar populace and by LDL-C bringing down preliminaries in Western populaces. As a result, the LDL-C lowering trials in Western populations and the highly consistent results of observational and genetic analyses in the Chinese population suggest that the excess risk of ICH observed in the trials is most likely caused by lower LDL-C concentrations rather than by some other factor. Importantly, the findings also suggest that even with lower LDL-C levels, the Chinese population with high stroke rates is still likely to benefit from stroke and cardiovascular disease prevention overall. As a result, the findings support the increased use of LDL-C-lowering medications to prevent stroke and other vascular diseases worldwide in populations with low mean LDL-C concentrations, including the Chinese.

### Acknowledgement

None.

### Conflict of Interest

None.

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