

Major Lipids, Apolipoproteins, and Risk of Vascular Disease

The Emerging Risk Factors Collaboration*

RELIABLE ASSESSMENT OF THE separate and joint associations of major blood lipids and apolipoproteins with the risk of vascular disease is important for the development of screening and therapeutic strategies.^{1,2} Expert opinion is divided about whether assessment of apolipoprotein AI (apo AI) and apolipoprotein B (apo B) should replace assessment of high-density lipoprotein cholesterol (HDL-C) and total cholesterol levels in assessment of vascular risk.³⁻⁵

Although there is agreement about the value of reducing low-density lipoprotein cholesterol (LDL-C) or, approximately analogously, non-high-density lipoprotein cholesterol [non-HDL-C], uncertainty persists about the merits of modification or measurement of triglycerides or HDL-C.³ There are strongly positive epidemiological associations of triglyceride concentration with risk of vascular disease,^{6,7} but it is not clear to what extent these relationships depend on cholesterol levels or vary with fasting state.

Similarly, although previous analyses have generally reported inverse associations of HDL-C with risk of vascular disease, many studies have not investigated the extent to which they depend on triglyceride concentration.⁸ The failure of torcetrapib has raised questions about the value of raising HDL-C and highlighted the need to characterize more reliably the relationship between HDL-C and vascular risk, particularly at high HDL-C levels.⁹

Different uncertainties apply in relation to the risk of ischemic stroke and the cholesterol content of proathero-

Context Associations of major lipids and apolipoproteins with the risk of vascular disease have not been reliably quantified.

Objective To assess major lipids and apolipoproteins in vascular risk.

Design, Setting, and Participants Individual records were supplied on 302 430 people without initial vascular disease from 68 long-term prospective studies, mostly in Europe and North America. During 2.79 million person-years of follow-up, there were 8857 nonfatal myocardial infarctions, 3928 coronary heart disease [CHD] deaths, 2534 ischemic strokes, 513 hemorrhagic strokes, and 2536 unclassified strokes.

Main Outcome Measures Hazard ratios (HRs), adjusted for several conventional factors, were calculated for 1-SD higher values: 0.52 log_e triglyceride, 15 mg/dL high-density lipoprotein cholesterol (HDL-C), 43 mg/dL non-HDL-C, 29 mg/dL apolipoprotein AI, 29 mg/dL apolipoprotein B, and 33 mg/dL directly measured low-density lipoprotein cholesterol (LDL-C). Within-study regression analyses were adjusted for within-person variation and combined using meta-analysis.

Results The rates of CHD per 1000 person-years in the bottom and top thirds of baseline lipid distributions, respectively, were 2.6 and 6.2 with triglyceride, 6.4 and 2.4 with HDL-C, and 2.3 and 6.7 with non-HDL-C. Adjusted HRs for CHD were 0.99 (95% CI, 0.94-1.05) with triglyceride, 0.78 (95% CI, 0.74-0.82) with HDL-C, and 1.50 (95% CI, 1.39-1.61) with non-HDL-C. Hazard ratios were at least as strong in participants who did not fast as in those who did. The HR for CHD was 0.35 (95% CI, 0.30-0.42) with a combination of 80 mg/dL lower non-HDL-C and 15 mg/dL higher HDL-C. For the subset with apolipoproteins or directly measured LDL-C, HRs were 1.50 (95% CI, 1.38-1.62) with the ratio non-HDL-C/HDL-C, 1.49 (95% CI, 1.39-1.60) with the ratio apo B/apo AI, 1.42 (95% CI, 1.06-1.91) with non-HDL-C, and 1.38 (95% CI, 1.09-1.73) with directly measured LDL-C. Hazard ratios for ischemic stroke were 1.02 (95% CI, 0.94-1.11) with triglyceride, 0.93 (95% CI, 0.84-1.02) with HDL-C, and 1.12 (95% CI, 1.04-1.20) with non-HDL-C.

Conclusion Lipid assessment in vascular disease can be simplified by measurement of either total and HDL cholesterol levels or apolipoproteins without the need to fast and without regard to triglyceride.

JAMA. 2009;302(18):1993-2000

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genic lipoproteins. The reduction in ischemic stroke in randomized trials of statins (which principally lower LDL-C) is remarkable in light of the weak epidemiological association reported between circulating LDL-C concentration and ischemic stroke,^{10,11} suggesting the need for more powerful and detailed prospective analyses of blood lipids and stroke subtypes.

The objective of this report is to produce reliable estimates of the associations of major lipids and apolipopro-

teins in relation to coronary heart disease (CHD) and ischemic stroke, incorporating adjustment for confounding caused by other risk factors and correction for regression dilution.¹²

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METHODS

Study Design

Details of study selection, data collection, and harmonization procedures of the Emerging Risk Factors Collaboration (ERFC) have been described previously.¹³ One hundred twelve prospective studies of cardiovascular risk factors, involving a total of 1.2 million participants, have shared individual records in the ERFC (eFigure 1, available at <http://www.jama.com>). These studies were approximately population-based (ie, did not select participants on the basis of having previous cardiovascular disease); recorded cause-specific mortality or vascular morbidity using accepted criteria; and had accrued more than 1 year of follow-up. eTable 1 lists details of the 68 studies—involving a total of 302 430 participants without any known history of CHD (ie, myocardial infarction [MI], angina, or stroke, which were defined in each study) at the initial (“baseline”) examination—that had complete information at baseline on total cholesterol, HDL-C, and triglyceride levels and several conventional risk factors (ie, age, sex, smoking status, history of diabetes mellitus, systolic blood pressure, body mass index). References for studies in eTable 1 are in eAppendix 1 and in a previously published reference list.¹³ Twenty-two studies with 91 307 participants had information on the preceding variables plus apo B and apo AI, and 8 studies with 44 234 participants had directly measured LDL-C values. The AMORIS study provided data for the ERFC, but it could not be incorporated into the current analyses because AMORIS did not measure baseline levels of HDL-C, blood pressure, smoking, body mass index, or diabetes.¹⁴

All but 1 study used enzymatic methods to assay triglyceride, and all but 2 studies used precipitation methods to assay HDL-C (eTable 2). For assay of apolipoproteins, 16 studies used immunoturbidimetry or nephelometry, 4 used immunoradiometric assays, 1 used immunoelectrophoresis, and 1 involved immunochemical methods. For assay of LDL-C, 4 studies used ultracentrifugation, 2 used direct homogeneous meth-

ods, 1 used chemical precipitation, and 1 used electrophoresis. In registering fatal outcomes, all contributing studies used coding from the *International Classification of Diseases* to at least 3 digits and ascertainment was based on death certificates. Fifty-two of 68 contributing studies also involved medical records, autopsy findings, and other supplementary sources to help classify deaths. Sixty-two studies used standard definitions of MI based on World Health Organization criteria. Fifty-six studies reported diagnosis of strokes on the basis of typical clinical features and characteristic changes on brain imaging, and all attempted to provide attribution of stroke subtype.

Statistical Analyses

Non-HDL-C (calculated by subtraction of HDL-C from total cholesterol, yielding a measure that encompasses low-, intermediate-, and very-low-density lipoprotein cholesterol) was used as the principal marker of cholesterol content in proatherogenic lipoproteins in order to avoid the biases that may arise when using LDL-C values estimated by the Friedewald formula¹⁵ (eAppendix 2). Triglyceride was log_e transformed to improve its normality. Details of the statistical methods have been described previously.¹⁶ The primary outcome was CHD (ie, first-ever MI or fatal CHD). Analyses involved a 2-stage approach with estimates of association calculated separately within each study before pooling across studies by random-effects meta-analysis.

For the 64 studies analyzed as prospective cohort studies, hazard ratios (HRs) were calculated using Cox proportional hazard regression models stratified by sex (and, where appropriate, by trial group). The proportional hazards assumption was satisfied for each lipid in each of the studies. Participants contributed only their first nonfatal outcome or death recorded at age 40 years or older (ie, deaths preceded by nonfatal CHD or stroke were not included in the main analyses). For the 4 contributing individually matched nested case-control studies within prospective cohorts, odds ratios were calculated using condi-

tional logistic regression models. Odds ratios approximated HRs because these studies selected cases and controls concurrently and matched for age and sex.

To help characterize shapes of associations, study-specific HRs calculated within overall quantiles of baseline lipid levels were pooled on the log scale by multivariate random-effects meta-analysis and plotted against pooled mean usual levels of the relevant lipid marker within each quantile. Ninety-five percent confidence intervals (CIs) were estimated from the variances that reflect the amount of information underlying each group (including the reference group). As associations were approximately log-linear, regression coefficients were calculated to estimate the HRs associated with 1-SD higher baseline values of each lipid: 0.52 log_e triglyceride, 15 mg/dL HDL-C, 43 mg/dL non-HDL-C (and, in subsets, 29 mg/dL apo AI, 29 mg/dL apo B, and 33 mg/dL for directly measured LDL-C). (To convert HDL-C and LDL-C to mmol/L, multiply by 0.0259; to convert triglycerides to mmol/L, multiply by 0.0113.)

Hazard ratios were adjusted progressively for age, sex, systolic blood pressure, smoking status, history of diabetes, body mass index, and lipid measures, with the evidence of association indicated by the Wald χ^2 statistic and heterogeneity between studies assessed by the I^2 statistic.¹⁷ Investigation of effect modification was quantified by formal tests of interaction. Diversity at the study level was investigated by grouping studies by recorded characteristics and by meta-regression.

We corrected for bias caused by variability in levels of both lipids and potential confounding factors. Regression dilution ratios were obtained by regressing serial measurements of risk factors, taken from up to 89 073 participants (mean interval, 4.9 years), on baseline levels of the relevant characteristic and duration of follow-up. Correction for within-person variation in risk factors was achieved by use of conditional expectations of long-term average levels (“usual levels”) of these risk factors, which were predicted from these regression calibra-

tion models and used in the estimation of HRs, as described previously.^{12,18}

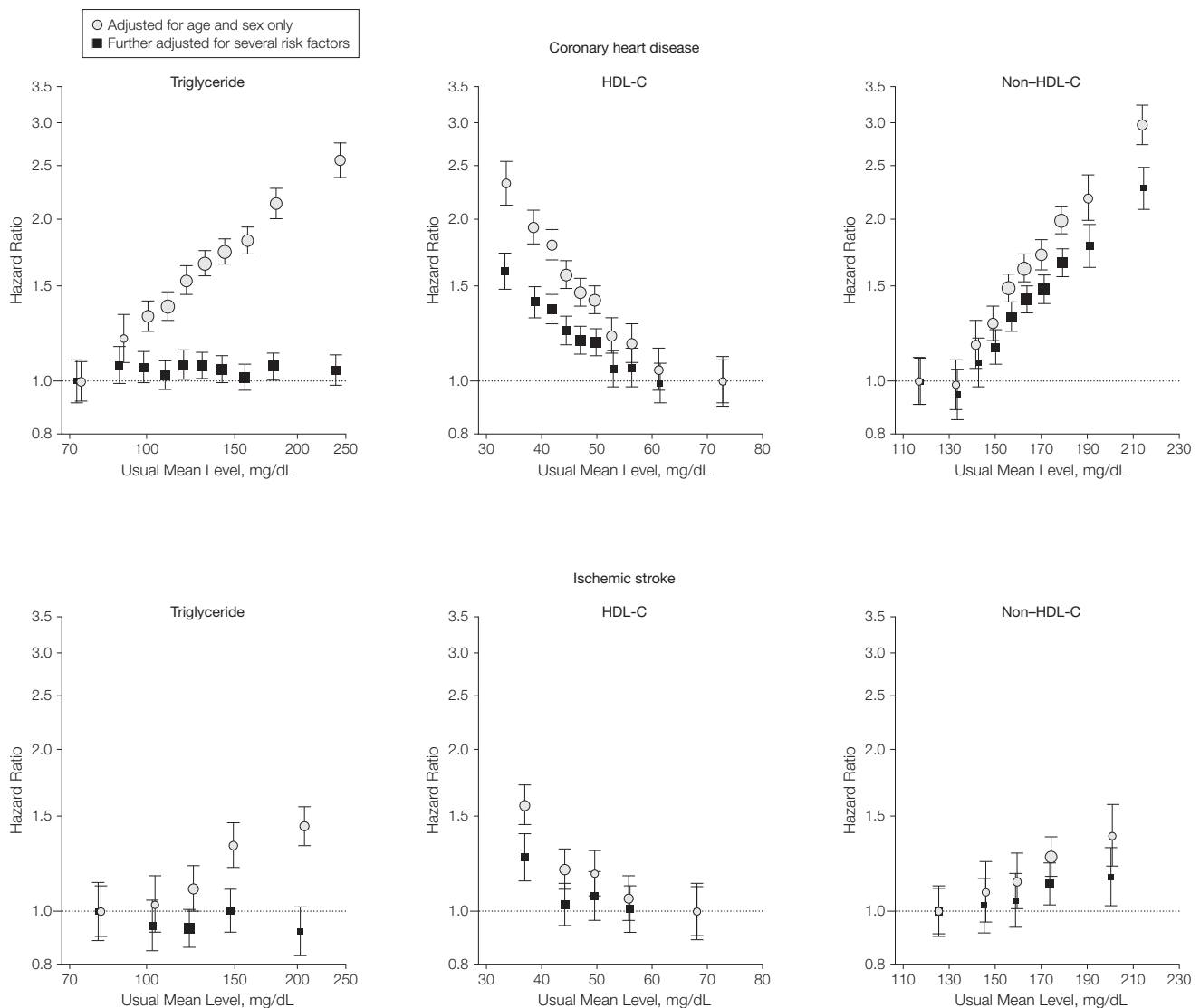
Analyses involved Stata software, release 10 (StataCorp, College Station, Texas); 2-sided *P* values and 95% CIs are presented. This study was approved by the Cambridgeshire ethics review committee and was conducted and analyzed independently from its funders.

RESULTS

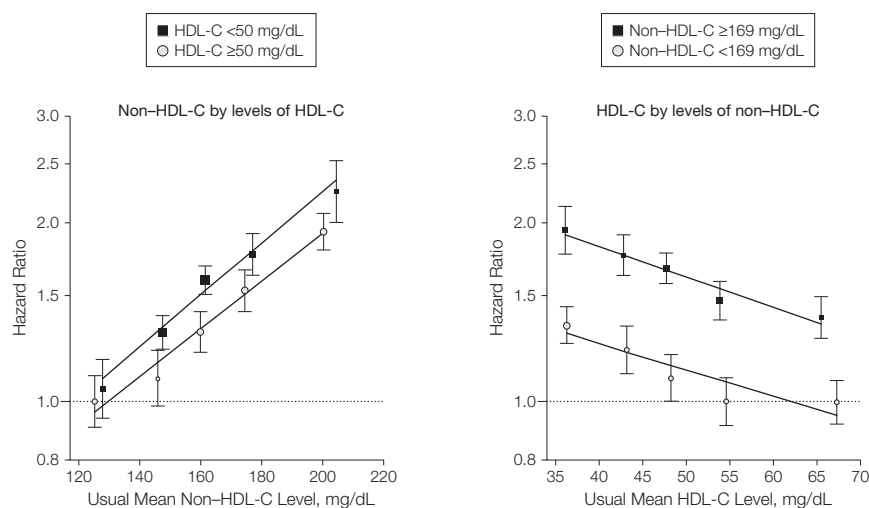
Mean (SD) age at entry of participants was 59 (8) years, 43% were women, 60% were in western Europe, and 32% in North America (eTable 3). During 2.79 million person-years at risk (median, 6.1 years to first outcome), there were, counting only first-ever outcomes, 8857 nonfatal MIs, 3928 CHD deaths, 2534 ischemic strokes,

513 hemorrhagic strokes, and 2536 unclassified strokes (eTable 4). Mean (SD) levels of \log_e triglyceride, HDL-C, and non-HDL-C were each broadly similar across studies (eTable 1). \log_e triglyceride, HDL-C, and non-HDL-C were correlated with one another, with particularly strong correlations of non-HDL-C with apo B and directly measured LDL-C, and

Figure 1. Hazard Ratios for Coronary Heart Disease or Ischemic Stroke Across Quantiles of Usual Triglyceride, HDL-C, and Non-HDL-C Levels



Analyses for coronary heart disease were based on 302 430 participants (involving 12 785 cases) from 68 studies. Analyses for ischemic stroke were based on 173 312 participants (involving 2534 cases) from 32 studies. Regression analyses were stratified, where appropriate, by sex and trial group. Values with further adjustments were adjusted for age, systolic blood pressure, smoking status, history of diabetes mellitus, and body mass index; furthermore, analyses of \log_e triglyceride were adjusted for high-density lipoprotein cholesterol (HDL-C) and non-HDL-C levels, analyses of HDL-C were adjusted for non-HDL-C and \log_e triglyceride levels, and analyses of non-HDL-C were adjusted for HDL-C and \log_e triglyceride levels. Studies with fewer than 10 cases were excluded from analysis. Sizes of data markers are proportional to the inverse of the variance of the hazard ratios. The y-axes are shown on a log scale. The x-axes for triglyceride are shown on a log scale. Referent groups are lowest quantiles for triglyceride and non-HDL-C and highest quantiles for HDL-C. Error bars indicate 95% confidence intervals.

Figure 2. Hazard Ratios for Coronary Heart Disease Across Fifths of Non-HDL-C by Levels of HDL-C and Fifths of HDL-C by Levels of Non-HDL-C

Analyses were based on 302 430 participants (involving 12 785 cases) from 68 studies. Median values in the Emerging Risk Factors Collaboration were 50 mg/dL for high-density lipoprotein cholesterol (HDL-C) and 169 mg/dL for non-HDL-C. Regression analyses were stratified, where appropriate, by sex and trial group and adjusted for age, systolic blood pressure, smoking status, history of diabetes mellitus, body mass index, and \log_e triglyceride levels. Studies with fewer than 10 cases were excluded from analysis. Sizes of data markers are proportional to the inverse of the variance of the hazard ratios. The y-axes are shown on a log scale. Referent groups are lowest fifth of non-HDL-C in the higher level of HDL-C and highest fifth of HDL-C in the lower level of non-HDL-C. Lines are fitted by log-linear regression of log hazard ratios on mean levels. Error bars indicate 95% confidence intervals.

of HDL-C with apo AI (eTable 3). Serial measurements yielded age- and sex-adjusted regression dilution ratios of 0.63 (95% CI, 0.60-0.67) for \log_e triglyceride, 0.69 (95% CI, 0.64-0.74) for HDL-C, 0.60 (95% CI, 0.54-0.65) for non-HDL-C, 0.57 (95% CI, 0.46-0.69) for apo AI, 0.61 (95% CI, 0.47-0.75) for apo B, and 0.64 (95% CI, 0.57-0.71) for directly measured LDL-C. The rates of CHD per 1000 person-years in the bottom and top thirds of baseline lipid distributions, respectively, were 2.6 and 6.2 with triglyceride, 6.4 and 2.4 with HDL-C, and 2.3 and 6.7 with non-HDL-C. In analyses adjusted for age and sex only, each lipid studied was approximately log-linearly associated with CHD risk, with possible attenuation at very high HDL-C and at low non-HDL-C concentration (FIGURE 1).

Triglyceride

The HR for CHD with triglyceride was 1.37 (95% CI, 1.31-1.42) after adjustment for nonlipid risk factors, but it was reduced to 0.99 (95% CI, 0.94-1.05) after further adjustment for HDL-C and

non-HDL-C (the Wald χ^2 reduced from 214 to 0) (eTable 5 and Figure 1). There was modest heterogeneity among the contributing studies ($I^2=35\%$; 95% CI, 12%-52%). Adjusted HRs for CHD were essentially null under a range of circumstances, including by sex (HRs of 0.97 [95% CI, 0.91-1.03] in men and 1.06 [95% CI, 0.96-1.16] in women) and by fasting status (HRs of 1.02 [95% CI, 0.95-1.09] in people who fasted and 0.92 [95% CI, 0.82-1.03] in people who did not fast) (eFigure 2). There was, however, an apparently positive association at lower systolic blood pressure. The adjusted HR was 1.02 (95% CI, 0.94-1.11) for ischemic stroke (eTable 5 and Figure 1), 1.04 (95% CI, 0.82-1.32) for hemorrhagic stroke, and 1.03 (95% CI, 0.94-1.13) for unclassified stroke.

High-Density Lipoprotein Cholesterol

The HR for CHD with HDL-C was 0.71 (95% CI, 0.68-0.75) after adjustment for nonlipid risk factors, and it was 0.78

(95% CI, 0.74-0.82) after further adjustment for non-HDL-C and \log_e triglyceride (the Wald χ^2 reduced from 149 to 84) (eTable 5 and Figure 1). There was modest heterogeneity among the contributing studies ($I^2=40\%$; 95% CI, 20%-55%). The HR for CHD was stronger at younger ages and at lower systolic blood pressure, but it did not vary importantly by sex, other lipid fractions, diabetes, or body mass index (eFigure 2). Findings did not vary materially in sub-analyses that additionally adjusted for C-reactive protein or fibrinogen concentration (eTable 6) or alcohol consumption (or that excluded alcohol abstainers). Hazard ratios were 0.79 (95% CI, 0.74-0.84) in participants who fasted and 0.75 (95% CI, 0.68-0.83) in participants who did not fast. The adjusted HR for ischemic stroke was 0.93 (95% CI, 0.84-1.02) (eTable 5 and Figure 1), with modest heterogeneity among the contributing studies ($I^2=27\%$; 95% CI, 0%-53%) (eTable 5). Adjusted HRs were 1.09 (95% CI, 0.92-1.29) for hemorrhagic stroke and 0.87 (95% CI, 0.80-0.94) for unclassified stroke.

Non-High-Density Lipoprotein Cholesterol

The HR for CHD with non-HDL-C was 1.56 (95% CI, 1.47-1.66) after adjustment for nonlipid risk factors, and it was 1.50 (95% CI, 1.39-1.61) after further adjustment for HDL-C and \log_e triglyceride (the Wald χ^2 reduced from 229 to 122) (eTable 5 and Figure 1). There was considerable heterogeneity among the contributing studies ($I^2=73\%$; 95% CI, 66%-79%), partly explained by more extreme HRs in participants who did not fast vs those who fasted (1.72 [95% CI, 1.51-1.95] vs 1.41 [95% CI, 1.30-1.53]; $P=.01$) and in studies with serum than those with other types of blood samples (1.60 [95% CI, 1.47-1.74] vs 1.31 [95% CI, 1.17-1.47]; $P=.008$) (eFigure 2). The HR for CHD was slightly stronger at younger ages (although it remained strong even at older ages) and more extreme at lower systolic blood pressure. Hazard ratios for CHD did not vary importantly by sex, levels of other lipid fractions, diabetes, or body mass index

(eFigure 2). In the subset of participants with available measurements, the adjusted HRs for CHD were 1.38 (95% CI, 1.09-1.73) with directly measured LDL-C and 1.42 (95% CI, 1.06-1.91) with non-HDL-C (eTable 7). The adjusted HR for ischemic stroke was 1.12 (95% CI, 1.04-1.20) with non-HDL-C, about 4 times weaker than that for CHD (eTable 5 and Figure 1). Adjusted HRs were 0.98 (95% CI, 0.82-1.17) for hemorrhagic stroke and 1.01 (95% CI, 0.93-1.09) for unclassified stroke.

Combined Lipid Analyses and Apolipoproteins

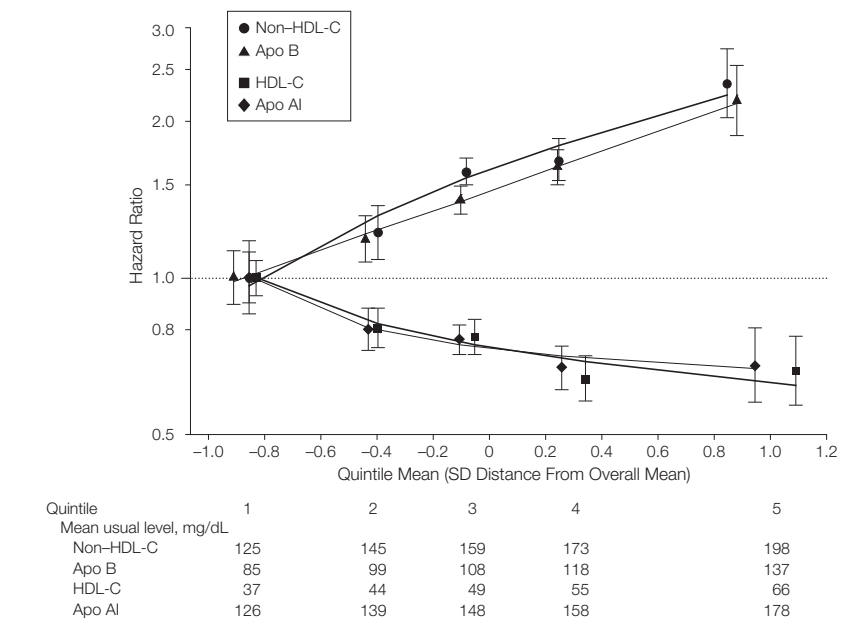
Hazard ratios for CHD with non-HDL-C were generally similar at different HDL-C levels and vice versa (FIGURE 2). The HR for CHD was 0.35 (95% CI, 0.30-0.42) with a combination of 15 mg/dL higher HDL-C and 80 mg/dL lower non-HDL-C, alterations that are attainable with available lipid-lowering agents.^{19,20} The HR was not materially changed by addition of information on triglyceride. Non-HDL-C and apo B each had very similar shape and magnitude of associations with CHD, as did HDL-C and apo AI (FIGURE 3 and eTable 8). Hazard ratios for CHD were 1.50 (95% CI, 1.38-1.62) with the ratio of non-HDL-C/HDL-C (which is statistically equivalent to the ratio of total cholesterol to HDL-C) and 1.49 (95% CI, 1.39-1.60) with the ratio of apo B/apo AI (eTable 8). For ischemic stroke, there were also similar findings with cholesterol levels and apolipoproteins.

Qualitatively similar results to those reported here were observed in analyses that used fixed-effect models (eFigure 3), compared larger vs smaller studies, ignored regression dilution, replaced non-HDL-C with total cholesterol, included fatal outcomes without censoring previous nonfatal outcomes, and omitted the 44 108 participants from clinical trials (eFigure 2).

COMMENT

The current analysis of more than 300 000 people has demonstrated that lipid assessment in vascular disease can

Figure 3. Hazard Ratios for Coronary Heart Disease Across Fifths of Usual Lipids or Apolipoproteins



Analyses were based on 91 307 participants (involving 4499 cases) from 22 studies. Regression analyses were stratified, where appropriate, by sex and trial group and adjusted for age, systolic blood pressure, smoking status, history of diabetes mellitus, and body mass index; furthermore, analyses of non-HDL-C were adjusted for HDL-C and log_e triglyceride, analyses of apolipoprotein B (apo B) were adjusted for apolipoprotein AI (apo AI) and log_e triglyceride, analyses of HDL-C were adjusted for non-HDL-C and log_e triglyceride, and analyses of apo AI were adjusted for apo B and log_e triglyceride. Studies with fewer than 10 cases were excluded from analysis. Sizes of data markers are proportional to the inverse of the variance of the hazard ratios. Referent groups are lowest fifths. Lines are fitted by first-degree fractional polynomial regression of log hazard ratios on mean SD score. Error bars indicate 95% confidence intervals. The y-axis is shown on a log scale. The x-axis is shown on a Z-transformed scale.

be simplified by measurement of either cholesterol levels or apolipoproteins without the need to fast and without regard to triglyceride. This conclusion derives from several findings. First, HRs with non-HDL-C and HDL-C were nearly identical to those seen with apo B and apo AI. This finding suggests that current discussions about whether to measure cholesterol levels or apolipoproteins in vascular risk assessment should hinge more on practical considerations (eg, cost, availability, and standardization of assays) than on major differences in strength of epidemiological associations. Second, HRs for vascular disease with lipid levels were at least as strong in participants who did not fast as in those who fasted. Third, HRs were similar with non-HDL-C as with directly measured LDL-C. Finally, in contrast with previous findings based on much less data, triglyceride concentra-

tion was not independently related with CHD risk after controlling for HDL-C, non-HDL-C, and other standard risk factors, including null findings in women and under nonfasting conditions.^{21,22} Hence, for population-wide assessment of vascular risk, triglyceride measurement provides no additional information about vascular risk given knowledge of HDL-C and total cholesterol levels, although there may be separate reasons to measure triglyceride concentration (eg, prevention of pancreatitis).

Concentrations of HDL-C and non-HDL-C were each strongly associated—in opposite directions—with CHD risk in an approximately log-linear manner. In contrast with the null triglyceride findings after adjustment, HDL-C and non-HDL-C were largely independent from each other on a multiplicative scale, as well as from triglyceride concentration and other risk factors. Hence, whereas

prevailing therapeutic strategies focus on lowering of LDL-C (or, approximately analogously, non-HDL-C), the current findings suggest that therapy directed at HDL-C as well as non-HDL-C may generate substantial additional benefit. For example, CHD risk is approximately two-thirds lower in people with 15 mg/dL higher HDL-C and 80 mg/dL lower non-HDL-C, which are alterations that are attainable with, say, extended-release niacin plus a potent statin.^{19,20} Long-term randomized trials of such lipid-modifying regimens are therefore needed to test this epidemiologically expected risk reduction.²³⁻²⁵

Because associations of higher non-HDL-C concentration with CHD are similar at both higher and lower HDL-C concentrations, the absolute benefits of lowering LDL-C are likely to be greater if HDL-C concentration is low (or when absolute risk is high for some other reason). While the current findings cannot confirm or refute causality for either triglyceride or HDL-C concentration, they encourage large CHD studies of therapies and genotypes that specifically affect each of these lipid measures to help judge etiological relevance.²³⁻²⁹ Observational analyses focused on etiology should ideally allow for the possibility of disparate associations of different non-HDL-C components with vascular risk, which requires information on each type of low-, intermediate-, and very-low-density lipoprotein cholesterol (such information was not available in most studies contributing to the current analysis).

Hemorrhagic stroke was unrelated to any of the lipids studied here. Only pro-atherogenic lipids appeared to be associated with risk of ischemic stroke, albeit modestly. Indeed, the current study found an HR for CHD with non-HDL-C about 4 times greater than that for ischemic stroke. Because statin medications reduce risk of both CHD and ischemic stroke to a similar extent,¹⁰ the quantitative discrepancy observed between epidemiological associations of non-HDL-C with CHD and ischemic stroke is striking.³⁰ To characterize this risk in more detail, stud-

ies are needed that can subtype the diverse etiologies for ischemic stroke.³¹ Given the essentially null associations observed between HDL-C concentration and stroke risk, considerable loss of statistical power may result from inclusion of stroke in primary outcomes of HDL-C-raising trials^{23,25,29} (unless similar effects are observed to those in the previous trials of statin).

There was some heterogeneity in the findings, but the broad consistency of results across 68 studies in 21 countries supports their generalizability. Confounding was minimized by adjustment of HRs for long-term average levels of risk factors based on more than 89 000 serial measurements. As the logarithm of triglyceride concentration had a regression dilution ratio comparable with those of other lipid measures, such variability cannot account for the different HRs for CHD that were seen with the different lipid measures. The current prospective data contrast sharply with those of some large retrospective case-control studies that reported that apolipoproteins have much stronger associations with CHD risk than cholesterol levels.^{32,33} Case-control studies of acute MI may be liable to distortion of lipid levels by recent infarction, a potential bias that is minimized by prospective analyses of participants without cardiovascular disease at baseline.^{32,33} It remains unclear whether some residual artifact explains the apparent flattening of associations seen in the present analyses with CHD at very high HDL-C or at very low non-HDL-C concentration (whereas, by contrast, randomized statin trials indicate that LDL-C lowering below 80 mg/dL continues to lower CHD risk^{10,34}).

CONCLUSION

Lipid assessment in vascular disease can be simplified by measurement of either total and HDL cholesterol levels or apolipoproteins without the need to fast and without regard to triglyceride.

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Administrative, technical, or material support: Di Angelantonio, Sarwar, Perry, Kaptoge, Ray, A. Thompson, Lewington, Sattar, Packard, S. G. Thompson, Danesh.

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Financial Disclosures: Dr Collins reported being paid by the British Heart Foundation and UK Biobank and having received research funding and reimbursement of costs for attending scientific meetings (but no honoraria or consultancy payments) from AstraZeneca, Bayer, Bristol Myers Squibb, British Heart Foundation, Cancer Research UK, European Union, Kadoorie Trust, MRC, Merck, Roche, Sanofi, Schering, Solvay, and UK Biobank. Dr Danesh reported having received research funding from the British Heart Foundation; BUPA Foundation; diaDexus; European Union; Evelyn Trust; Fogarty International Center; GlaxoSmithKline; Medical Research Council; Merck Sharp and Dohme; National Heart, Lung, and Blood Institute; National Institute of Neurological Disorders and Stroke; Novartis; Roche; and Wellcome Trust. No other authors reported disclosures.

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Funding/Support: The ERFC Coordinating Centre is underpinned by a program grant from the British Heart Foundation (RG/08/014) and supported by grants from the UK Medical Research Council and the BUPA Foundation and an unrestricted educational grant from GlaxoSmithKline. A variety of sources have supported recruitment, follow-up, and laboratory measurements in the cohorts contributing to the ERFC. Investigators of several of these studies have contributed to a list naming some of these funding sources, which can be found at <http://www.phpc.cam.ac.uk/MEU/>. Drs Di Angelantonio, Sarwar, Perry, and Thompson have been supported by PhD studentships of the UK Medical Research Council. Dr Ray is supported by a BHF Intermediate Research Fellowship.

Role of the Sponsor: The sponsors had no role in the design and conduct of the study; in the collection, analysis, and interpretation of the data; or in the preparation, review, or approval of the manuscript.

Additional Information: eFigures 1-3, eTables 1-8, and eAppendix 1-3 are available at <http://www.jama.com>.

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