Clinical Question
Is measurement of apolipoproteins better than traditional lipid measurements for predicting cardiovascular risk?

Evidence-Based Answer
Measurement of apolipoprotein B and apo-lipoprotein A-I is no better than traditional lipid measurements and should not be used to predict cardiovascular risk. (Strength of Recommendation: B, based on meta-analyses with conflicting results.) Apolipoprotein B and non–high-density lipoprotein cholesterol (HDL-C) predict cardiovascular risk slightly better than low-density lipoprotein cholesterol. Elevated levels of apolipoprotein A-I predict a lower risk of cardiovascular events except stroke, but not as well as elevated HDL-C levels.

Evidence Summary
Apolipoproteins are structural components of lipoproteins and have a role in receptor binding and enzyme activation. Apolipoprotein B is carried on all proatherogenic lipoproteins in a 1:1 ratio, and apolipoprotein A-I is found on nearly all HDL particles.1

High levels of apolipoprotein B predict cardiovascular risk about as well as non–HDL-C. A 2012 meta-analysis pooled data from prospective cohort studies of patients without baseline cardiovascular disease and found that non–HDL-C and apolipoprotein B levels were similarly predictive of fatal and nonfatal cardiovascular events2 (Table 12-4). Using a clinical model, the authors calculated that substituting total cholesterol and HDL-C measurements with apolipoprotein A-I and B measurements diminished risk prediction by 1% (95% confidence interval [CI], 0.2% to 1.9%), whereas adding them did not significantly improve risk classification. A 2011 meta-analysis of prospective cohort and case-control studies found that apolipoprotein B was a slightly better predictor of cardiovascular risk than non–HDL-C, and both were superior to low-density lipoprotein cholesterol.3

Among patients receiving statins, measurement of apolipoprotein B is comparable to that of non–HDL-C. A 2012 meta-analysis of randomized controlled trials of patients on statin therapy found that time to the first major cardiovascular event was most strongly associated with non–HDL-C levels, followed by apolipoprotein B and low-density lipoprotein cholesterol levels.4 The differences between hazard ratios were small but statistically significant (P = .002 for non–HDL-C vs. low-density lipoprotein cholesterol, and P = .02 for non–HDL-C vs. apolipoprotein B).

The benefits of measuring apolipoprotein B include the ability to use serum from non-fasting patients, standardization, and direct measurement compared with the calculated measurement of low-density lipoprotein cholesterol, which may be inaccurate in patients with hypertriglyceridemia.5,6

Elevated apolipoprotein A-I levels predict coronary events except stroke, but not as well as elevated HDL-C levels. Apolipoprotein A-I levels are inversely associated with cardiovascular disease. In the 2012 meta-analysis discussed previously, comparable inverse associations for cardiovascular risk were seen with HDL-C and apolipoprotein A-I measurements.2 A 2011 prospective cohort study of healthy women found an inverse relationship between apolipoprotein A-I levels and the incidence of stroke and coronary events.
Table 1. Summary of Meta-analyses Comparing Apolipoproteins vs. Traditional Lipid Measurements for Predicting Adverse Cardiovascular Events

<table>
<thead>
<tr>
<th>Number and type of studies</th>
<th>Outcomes measured</th>
<th>Adverse events</th>
<th>Biomarker measured</th>
<th>Risk of elevated biomarker (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>26 prospective cohort trials (N = 139,581)</td>
<td>Fatal and nonfatal coronary artery disease and stroke</td>
<td>12,234</td>
<td>Non–HDL-C</td>
<td>HR = 1.27 (1.22 to 1.33)*</td>
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<td></td>
<td></td>
<td>Apolipoprotein B</td>
<td>HR = 1.24 (1.19 to 1.29)*</td>
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<td>Apolipoprotein A-I</td>
<td>HR = 0.87 (0.84 to 0.90)*</td>
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<td>HDL-C</td>
<td>HR = 0.83 (0.78 to 0.87)*</td>
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<tr>
<td>12 (8 prospective cohort and case-control studies; (N = 233,455))</td>
<td>Fatal and nonfatal ischemic cardiovascular events</td>
<td>22,950</td>
<td>Apolipoprotein B</td>
<td>RR = 1.43 (1.35 to 1.51)*†</td>
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<td></td>
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<td>Non–HDL-C</td>
<td>RR = 1.34 (1.24 to 1.44)†</td>
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<tr>
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<td></td>
<td>Low-density lipoprotein cholesterol</td>
<td>RR = 1.25 (1.18 to 1.33)†</td>
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<tr>
<td>8 randomized controlled trials (N = 38,153)</td>
<td>Fatal or nonfatal myocardial infarction, fatal coronary artery disease, hospitalization for unstable angina, and fatal or nonfatal stroke at 1 year</td>
<td>6,286</td>
<td>Non–HDL-C</td>
<td>HR = 1.16 (1.12 to 1.19)*</td>
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<td>Apolipoprotein B</td>
<td>HR = 1.14 (1.11 to 1.18)*</td>
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<td>Low-density lipoprotein cholesterol</td>
<td>HR = 1.13 (1.10 to 1.17)*</td>
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</tbody>
</table>

\(CI = \text{confidence interval}; \text{HDL-C} = \text{high-density lipoprotein cholesterol}; \text{HR} = \text{hazard ratio}; \text{RR} = \text{relative risk.}\)

§—HR is calculated as the increased or decreased risk of an adverse event per standard deviation increase in the biomarker.

†—RR is calculated as the increased risk of an adverse event per standard deviation increase in the biomarker.

Information from references 2 through 4.

References


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