Letters to the Editor

cate the original article describing the DBS-QC, which was not cited in their report.

Author Contributions: All authors confirmed they have contributed to the intellectual content of this paper and have met the following 3 requirements: (a) significant contributions to the conception and design, acquisition of data, or analysis and interpretation of data; (b) drafting or revising the article for intellectual content; and (c) final approval of the published article.

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To the Editor:

In the recent special report on the assessment of apolipoprotein B (apoB)\(^1\) and nuclear magnetic resonance particle number (1), the authors recommended that measurement of particle number be incorporated into the guidelines for the assessment of cardiovascular disease (CVD) risk.

However, the literature reviewed provides no basis for this recommendation. Searching the literature using the key terms apo B and LDL-P (LDL particle number) and the name Otvos, the authors identified 25 studies evaluating association with CVD or events, metabolic syndrome, diabetes mellitus or diabetic complications, plasma lipids and lipoproteins, or miscellaneous events. Not only were different associations studied, but adjustment for other risk factors varied considerably and hardly ever included lipid panel components. This information only supports the conclusion that apo B and LDL-P are risk factors.

In addition, the disclosures inadequately inform the reader of a substantial conflict of interest. Four, not 3, of the authors are affiliated with HDL, which is Health Diagnostic Laboratory, Inc. The company’s website (wwwhdlabinc.

Apolipoprotein B and Nuclear Magnetic Resonance Particle Number

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However, the literature reviewed provides no basis for this recommendation. Searching the literature using the key terms apo B and LDL-P (LDL particle number) and the name Otvos, the authors identified 25 studies evaluating association with CVD or events, metabolic syndrome, diabetes mellitus or diabetic complications, plasma lipids and lipoproteins, or miscellaneous events. Not only were different associations studied, but adjustment for other risk factors varied considerably and hardly ever included lipid panel components. This information only supports the conclusion that apo B and LDL-P are risk factors.

In addition, the disclosures inadequately inform the reader of a substantial conflict of interest. Four, not 3, of the authors are affiliated with HDL, which is Health Diagnostic Laboratory, Inc. The company’s website (www.hdlabinc.com) indicates it offers “the most comprehensive laboratory test menu of risk factors and biomarkers for cardiovascular and related diseases.” Because, as the authors mention, 216 000 000 lipid panels are performed annually in the US, implementation of their recommendation would have huge financial implications.

Recommending measurement of particle number will become plausible only when clinically significant improvement in risk stratification can be demonstrated over that based on conventional risk factors. The references cited do not document such improvement, and the comparison of single risk factors, e.g., LDL cholesterol vs particle number, does not adequately address this question.

Author Contributions: All authors confirmed they have contributed to the intellectual content of this paper and have met the following 3 requirements: (a) significant contributions to the conception and design, acquisition of data, or analysis and interpretation of data; (b) drafting or revising the article for intellectual content; and (c) final approval of the published article.

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Letters to the Editor

1 Nonstandard abbreviations: apoB, apolipoprotein B; CVD, cardiovascular disease; LDL-P, LDL particle number.
In Reply

The authors appreciate the opportunity to respond to Dr. Stern’s comments. Our current publication (1) is a follow-up to a 2009 publication in *Clinical Chemistry* by this Working Group on Best Practices (2), in which we reviewed the superiority of LDL particle number to determine cardiovascular disease (CVD)(1) risk over the concentration of LDL cholesterol (LDL-C), which is the benchmark for diagnosis and treatment of CVD by the National Cholesterol Education Program Adult Treatment Panel III (NCEP ATP III) guidelines. Our conclusion was that LDL particle number, estimated either by measurement of serum apolipoprotein B (apoB) concentration or determined by nuclear magnetic resonance (NMR) spectroscopy (LDL-P), should be incorporated into revised guidelines. This is also consistent with recent recommendations made by others (3). The evidence leading to our conclusion is well documented in our 2009 publication and is clearly referenced in our current publication. The goal of the current article was to compare apoB to NMR LDL-P for prediction of CVD risk and other diseases and conditions. Our finding that both are comparable over a wide range of clinical outcomes is not unexpected, since both essentially assess the same entity, i.e., LDL particle number.

With regard to the suggestion of conflict of interest due to the employment of some coauthors by Health Diagnostics Laboratory (HDL Lab), we note that the recommendation to include the measurement of LDL particle number in diagnosis and treatment guidelines had already been made in the 2009 publication, the submission of which predates the incorporation of HDL Lab. In addition, all 7 authors of the 2009 publication are also authors of the current publication, and 5 of the current 10 authors do not have, and have never had, financial interest in HDL Lab. The recommendations made by the authors are supported by the research data. Each of the authors, all of whom are current or previously elected officers of the AACC Lipoproteins and Vascular Diseases Division or its predecessor, the Lipids and Lipoproteins Division, understand the importance and consequences of this position statement. Having shown a relative equivalency of apoB and LDL-P in the research reported in the current publication, we stand behind our 2009 recommendation to include apoB or LDL-P in NCEP and other guidelines.

Regarding financial implications, we also recognize that there is an “up-front” laboratory-based cost to implementation of our recommendation. The typical 2013 Medicare reimbursement for direct LDL-C measurement is $13.11, that for a lipid panel (necessary to calculate LDL-C, when possible) is $18.42, and that for apoB is $21.30 (4). To offset this additional cost, the superior risk information that apoB provides would allow for more efficient and effective pharmacologic therapies and lifestyle changes, which through avoidance of cardiovascular events could considerably decrease healthcare costs. Sniderman and colleagues estimated that an apoB strategy would prevent 800,000 more cardiovascular events than an LDL-C strategy over a 10-year period (5). The prevention of cardiovascular events is where most of medical care cost savings reside.

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References


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1 Nonstandard abbreviations: CVD, cardiovascular disease; LDL-C, LDL cholesterol; NCEP ATP III, National Cholesterol Education Program Adult Treatment Panel III; apoB, apolipoprotein B; NMR, nuclear magnetic resonance; LDL-P, LDL particle number determined by NMR spectroscopy; HDL Lab, Health Diagnostics Laboratory.