increased when D2-containing samples were included. For the Centaur assay, on the other hand, the regression slope increased, and the r² decreased. The mean (SD) changes in bias from scenario (a) to (b) for the 4 assays are as follows: Liaison assay, −17.4% (6.0%) to −19.2% (4.6%); Architect assay, 0.9% (5.2%) to −7.8% (4.2%); Cobas assay, −11.4% (11.9%) to −15.5% (7.0%); Centaur assay, −27.7% (7.0%) to −17.0% (8.0%).

The effect of D2% on assay bias is illustrated in Fig. 1B. The Liaison assay had an insignificant bias change as D2% increased. The architect and Cobas assays showed an increasingly negative bias with increasing D2%, whereas the negative bias of the Centaur assay decreased and changed to a positive bias.

We calculated D3 cross-reactivity normalized to D2 reactivity (see Fig. 1 legend). The values for each assay in Fig. 1B are displayed as the mean (first to third quartiles) and are consistent with the change in the assay’s bias with D2%. Although cross-reactivities are defined differently from Le Goff et al. (2) and the manufacturers’ claims, our results showed the same order of relative D2 cross-reactivity: Centaur > Liaison > Cobas > Architect.

Although D3 is the preferred supplement form for treating vitamin D deficiency (4, 5), we have observed a high prevalence of patient samples containing substantial amounts of D3, and we have demonstrated the different effects of D2 content on the accuracies of commercial assays. Therefore, correctly interpreting total 25-OH-D results and monitoring patient compliance requires that vitamin D status, type of supplementation, and measurement method be considered.

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References

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Letters to the Editor

Dried Blood Spot Quality Control Materials for Newborn Screening to Detect Lysosomal Storage Disorders

To the Editor:

It is with great interest that we read the recent report by Spacil et al. on a high-throughput assay to detect 9 lysosomal enzymes from dried blood spots (DBS)¹ collected by newborn screening programs (1). Newborn screening activities to detect lysosomal storage disorders (NBS-LSD) have generated a great deal of discussion worldwide. The availability of tandem mass spectrometry-based assays available for high-throughput population screening and of US Food and Drug Administration–registered reagents for use in these assays led to an ongoing worldwide conversation about optimizing NBS-LSD assays. Recognizing the lack of DBS QC for NBS-LSD, the Newborn Screening Translation Research Initiative at the CDC developed large-scale methods to produce DBS that emulate normal and deficient lysosomal enzyme activities. The preparation and evaluation of these materials was originally reported in this journal (2). These DBS-QC have been in use globally for over 5 years, and they were a critical element of the assay validation reported by Spacil et al. We want to be sure that Clinical Chemistry readers can lo-

¹ Nonstandard abbreviations: DBS, dried blood spots; NBS-LSD, newborn screening activities to detect lysosomal storage disorders.
Letters to the Editor

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 (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.

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References


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Apolipoprotein B and Nuclear Magnetic Resonance Particle Number

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