ADLM Guidance Document on the Measurement and Reporting of Lipids and Lipoproteins

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Guests: Drs. Leslie Donato and Jeff Meeusen from Mayo Clinic in Rochester, Minnesota.

Randye Kaye: Hello, and welcome to this edition of *JALM* Talk from *The Journal of Applied Laboratory Medicine*, a publication of the Association for Diagnostics & Laboratory Medicine. I'm your host, Randye Kaye.

Effective management of atherosclerotic cardiovascular disease risk requires measurement of blood lipids and lipoproteins in the clinical laboratory. While significant advances have been made in standardizing lipid and lipoprotein measurement techniques, there is still considerable variability in pre-analytical procedures, as well as result reporting practices. Low density lipoprotein cholesterol, or LDL-C, may be measured or calculated and new LDL-C equations have been proposed and adopted inconsistently.

Further, there's a lack of guidance for the measurement and reporting of more novel lipoprotein biomarkers such as lipoprotein(a), apolipoprotein B, and lipoprotein particle number. The September 2024 issue of *JALM* features a new guidance document from the Academy of Diagnostics & Laboratory Medicine that's intended to address these limitations.

The new "ADLM Guidance Document on the Measurement and Reporting of Lipids and Lipoproteins" aims to provide clinical laboratories with evidence-based recommendations for consistency of lipid testing procedures. The authors of the guidance aim to improve communication and education of lipid testing among laboratory professionals and to provide clearer information for clinicians and patients.

Today we're joined by the guidance document's co-chairs, Drs. Leslie Donato and Jeff Meeusen. Dr. Donato is a clinical chemist and associate professor in the Department of Laboratory Medicine and Pathology at Mayo Clinic in Rochester, Minnesota. She is a co-director of the Hospital Clinical Laboratory and Point of Care, as well as a co-director of the Clinical Specialty Laboratory, where she focuses on cardiovascular and lipid biomarkers, critical and point-of-care testing, and biomarkers of gastrointestinal function.

Dr. Meeusen is a clinical chemist and co-director of Laboratory Services, the Clinical Specialty Laboratory, and the Clinical Chemistry Fellowship training program at Mayo Clinic. His scientific focus is on lipids and lipoproteins and applications of informatics in laboratory medicine. Welcome Drs. Donato and Meeusen. First, what prompted the development of this new guidance document?

Jeff Meeusen: Yes, so most documents come at the request of the Academy and this one came with a little special flare when the request came in from the academy, in that they had gotten repeated requests from ADLM membership asking for updates because of all the ongoing changes that had been going on with lipids and recent history. So, there's an increasing recognition I guess amongst ADLM membership that lipid testing practices are starting to vary widely between what is recommended nationally and internationally and actually what's even being documented and performed across different labs.

So really there was starting to be a perceived need that we should standardize what tests are being offered and how they're being offered. So, there's been developments in the field with new equations to calculate LDL cholesterol. There's been support for non-fasting lipid panel assessment from some of the different clinical guidelines, and there's been an increased push or awareness of, and treatment for, a couple of new lipoprotein markers called apolipoprotein B and lipoprotein(a).

Randye Kaye: All right. Thank you. So let's say a little bit more about that. What lipid testing guidelines existed previously and what differs with this new Academy guidance?

Leslie Donato: There actually really has not been a guidance document of this kind previously. So what clinical laboratorians would refer to previously were text book recommendations or CDC accuracy and precision goal publications that were published many, many years ago. But really a document of this kind that publishes best practices in laboratory lipid and lipoprotein testing for not only the methodology but also the naming conventions, reporting and flagging, all of that, all wrapped up in one really hasn't been published before and our goal was really to do so to best dovetail with what's needed in clinical practice guidelines for interpreting and treating patients based on the laboratory results.

Randye Kaye: Thank you, Dr. Donato. So are there any significant changes in lipid testing recommendations that clinical laboratories need to be aware of?

Leslie Donato: Well, as Dr. Meeusen pointed out in his previous answer, there are some for sure, which prompted the need to do a guidance document of this kind at this time. So, what we

tried to do in this document was to standardize the lipid panel reporting. So naming of tests in our medical record, standardization of clinical decision thresholds that we publish, the flagging of those, the comments that might fire. We also discuss best practices for like Dr. Meeusen mentioned testing for Lp(a) and apo B, which are gaining traction and really should be well known for clinical laboratorians to potentially offer in their own laboratories' point-of-care.

So, many of these we've done for many, many years. The laboratories have offered these tests for many years, but standardization of the testing and reporting was really one of our main goals and then, secondly, to get to your answer, yes, there have been some changes in the field that we really took the time to talk about in this document, which to reiterate, switching potentially to more modern equations for reporting of LDL cholesterol that allow for reporting in patients that have higher triglycerides, potentially may negate the need for fasting, and may really obviate the need for even offering a direct LDL at all, because these new modern equations are really much better at reporting inaccurate LDL cholesterol. So really, there are several areas where the document formally codifies practices that have been used by most labs for decades, but also guides laboratories in modernization of their tests and offering that better reflect the most recent evidence-based improvements in lipids and lipoprotein testing.

Randye Kaye: All right. Thank you. So you were speaking about LDL cholesterol and if there's anything more to say, tell us what equations the guidance recommends for the calculation of LDL-C and what's the evidence that informed the recommendation?

Jeff Meeusen: This has actually been coming up I'd say for several years now, actually, going back almost a decade. There was a paper by Seth Martin at the Johns Hopkins University where they determined a new equation to replace the Friedewald equation, which everybody has basically used in their laboratory since the 1970s. So, this new equation, which was released in 2014, had a completely different way of looking at LDL cholesterol and it adjusted for varying concentrations of triglycerides and cholesterol. It's often referred to as the Martin-Hopkins equation based on the authors and the location where it was performed, and in the 10 years or so since it's been released, there have been dozens and dozens of studies that have looked at tens of thousands of patients and shown that it significantly improves on the previous estimations using that Friedewald equation.

At the same time, it's a little bit of a clumsy equation in that it requires a table that has to be somehow input into your LIS and it's a little bit non-continuous because of that table that

it uses look up values and adjust your constants. So the different group at the NIH, led by Alan Remaley in the Lipid Lab, which is actually the same lab where the Friedewald equation had been developed decades earlier, was looking to find that equation that was a continuous equation that would fit that same table.

And what they came up with and published in 2020 was the Sampson-NIH equation. Maureen Sampson was the lead author on that study so that's why it's often referred to as the Sampson-NIH, and both of these equations significantly improve on the older version of estimated LDL-C into the point where -- and they both been validated now in dozens of studies, tens of thousands of patients, and because they're able to account for the variation in triglycerides, which is really the only thing that varies postprandially, we no longer need to have a fasting sample because it can accommodate that increased triglyceride, and it's able to accommodate in elevations in triglycerides that typically we use direct homogeneous LDL cholesterol methods to get around the limitation of our calculation.

So, going forward, there may not be a need to have that direct LDL-C because you can now calculate LDL just as good or better using these new equations.

Randye Kaye: That's great. Thank you. So finally, what's your hope? What do you hope will be the impact of this guidance document on patient care and the outcomes in lipid management?

Jeff Meeusen: Yeah. We're hoping that we're going to make a more uniform reporting and standardization of what lipid panels look like in the health record and that laboratorians can feel more comfortable that what they're implementing our reporting structures that offer the most accurate and up to date lipid tests possible, and meet the clinical testing needs to help physicians and patients have shared decision-making about what's best for treating their lipids.

Leslie Donato: Yeah. I would just add that with new lipid lowering medications on the market like PCSK9, monoclonal antibodies, or siRNA treatments, ACL inhibitors like of bempedoic acid, as well as the highly anticipated results of trials using targeted Lp(a)-specific treatments that we'll hear about soon. Physicians and patients really need the most accurate and precise results of laboratory lipid testing to best manage treatment strategies and hopefully reduce cardiovascular risk based on the most accurate data possible.

Randye Kaye: All right. Thank you so much for joining us today.

Jeff Meeusen: Thank you. It's been great.

Leslie Donato: Thank you.

Randye Kaye: That was Drs. Leslie Donato and Jeff Meeusen from Mayo Clinic describing the "ADLM Guidance Document on the Measurement and Reporting of Lipids and Lipoproteins," which was published in the September issue of *JALM*. Thanks for tuning in to this episode of *JALM* Talk. See you next time and don't forget to submit something for us to talk about.