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Short-term Variability of Vitamin D–Related Biomarkers

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Guest: Dr. Pamela Lutsey is an Associate Professor in the Division of Epidemiology and Community Health at the University of Minnesota.

Bob Barrett: This is a podcast from *Clinical Chemistry* sponsored by the Department of Laboratory Medicine at Boston Children's Hospital. I'm Bob Barrett.

Biological measures often naturally vary within an individual on a day-to-day basis. Knowing the amount of this variation is important to minimize misclassification in clinical settings and to reduce bias in associations estimated from research studies. Individual biological variation should be determined as new biomarkers are identified and needs to be reevaluated for established biomarkers as measurement methodologies improve over time. This is a timely concept for biomarkers in the vitamin D pathway as methodology has changed and new biomarkers are emerging. Quantifying the amount of within-person short-term variability inherent in those analytes provides insight into the optimal use of vitamin D biomarkers in both research and clinical settings.

This is the topic of an article appearing in the December 2016 issue of *Clinical Chemistry*. The article's primary author, Dr. Pamela Lutsey joins us in this podcast. Dr. Lutsey is an Associate Professor in the Division of Epidemiology and Community Health at the University of Minnesota. One of her primary research aims focuses on the role of vitamin D in cardiovascular disease.

So Dr. Lutsey, this study measured the individual biological variation in several markers related to calcium metabolism including vitamin D. So let's get basic first. What is individual biological variation?

Dr. Pamela Lutsey: Biological measures also naturally vary within an individual on a day-to-day basis. So if for example, you were to measure someone's blood pressure on three different days, you would likely get three different numbers. This is an example of biological variation.

Bob Barrett: And why is this relevant to laboratory measurements of these biomarkers, like vitamin D for example, that are used in research studies or clinical care?

Dr. Pamela Lutsey: Understanding biologic variation in these biomarkers is important because if a single measure is conducted, it might not be sufficient to accurately quantify someone's biological status, and that would result in misclassification. In clinical settings, it could result in a patient being treated suboptimally. And in research settings, it would most likely bias the results of the study toward the null.

Bob Barrett: So what were the unique aspects or strengths you found while doing this repeatability study?

Dr. Pamela Lutsey: For a repeatability study, the sample size is relatively large, in that we had biological measures on 160 individuals at two time points. Another unique aspect of the sample was that it included both blacks and whites. And as you may be aware, vitamin D levels vary dramatically by race. Additionally, the study used state-of-the-art assay measurements.

Bob Barrett: What did you find out about the short-term biological variability of the analytes that you investigated?

Dr. Pamela Lutsey: As expected, there was some individual level variability for all of the biomarkers. Over the six-week timeframe of the study, variability was quite low for calcium, albumin, vitamin D binding protein, 25(OH)D, and phosphorus. It was intermediate for free and bioavailable 25(OH)D, but fairly high for fibroblast growth factor 23 and parathyroid hormone.

Bob Barrett: Well finally, doctor, you concluded that multiple measurements of fibroblast growth factor 23 and parathyroid hormone may be needed to minimize misclassification. What does this mean, and why is it important to researchers or clinicians?

Dr. Pamela Lutsey: For these specific biomarkers, fibroblast growth factor 23 and parathyroid hormone, if only one measure is conducted in a clinical setting, a patient may be misclassified and get less than an optimal treatment as a result. In research, misclassification will most likely bias the study results toward the null. Conducting multiple measurements can mitigate these concerns, but with multiple measurements, there are additional expenses and burdens on participants' or patients' time.

Bob Barrett: Dr. Pamela Lutsey is an Associate Professor in the Division of Epidemiology and Community Health at the University of Minnesota. She's been our guest in this podcast from *Clinical Chemistry*. I'm Bob Barrett. Thanks for listening.