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Individual Variability in Dietary Response: A Role for Clinical Biochemistry in Precision Nutrition

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Dear Editor,

Usually, we talk about healthy diets as though their effects are relatively predictable. A dietary pattern may improve metabolic health in one person, but produce a much smaller benefit in another. Even when two individuals have the same meal, their metabolic responses may be completely different. This simple observation raises an important question for modern nutrition research: if individuals respond differently to the same diet, are the researchers measuring their responses with enough details to understand the reason behind it?

Evidence accumulated over the past few years reveals that this variability is not a minor phenomenon. In the study by Zhang, for example, substantial inter-individual differences were found in postprandial triglyceride, glucose, and insulin responses to identical meals (Zhang *et al.*, 2025a). Recent studies have further demonstrated considerable differences in glycemic responses between individuals, while suggesting that some of these differences can remain relatively consistent within the same individual in time (Zhu *et al.*, 2025). These findings challenge the traditional assumption that a dietary regimen that works well at the population level would necessarily produce the same metabolic benefit for every individual.

Accordingly, precision nutrition becomes particularly relevant. Yet, precision nutrition should not simply mean offering increasingly complicated dietary recommendations based on large amounts of data; its real value depends on our ability to determine the biological features that explain why an individual responds favorably or poorly to a particular dietary exposure.

Clinical biochemistry has an important role in addressing this question

Dietary intake is ultimately rendered as measurable biochemical changes. A meal can change glucose and insulin concentrations, lipid metabolism, free fatty acid availability,

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inflammatory signaling, hepatic metabolism, and a wide range of circulating metabolites. These changes show the biological consequences of nutrition, and therefore, provide an opportunity to identify an individual's metabolic response.

Despite this fact, in routine clinical practice, nutritional evaluation still relies largely on conventional biomarkers assessed at isolated time points. Fasting glucose, HbA1c, triglycerides, LDL-cholesterol, HDL-cholesterol, and other commonly used laboratory measurements remain essential for clinical care, but they may provide only an incomplete picture of how an individual's metabolism responds to food. For instance, a single fasting measurement cannot fully describe the dynamic metabolic changes that occur after a meal (Berry *et al.*, 2020).

The increasing use of continuous glucose monitoring (CGM) is considered a good example of how dynamic measurements can improve our understanding of individual metabolic responses. Unlike conventional blood sampling, CGM allows glucose fluctuations to be monitored consistently and provides a more detailed picture of postprandial glycemic responses. However, recent evidence indicates that these responses can vary remarkably within the same individual over time (Selvin *et al.*, 2023, Zhang *et al.*, 2025b). This variability highlights an important limitation of depending on single measurements to define an individual's metabolic phenotype. Therefore, the challenge for precision nutrition is not simply to produce more data, but to identify biomarkers and patterns of response that are biologically meaningful, reproducible, and sufficiently reliable to support nutritional decision-making.

There is a similar issue in lipid metabolism. Two individuals having a diet relatively high in saturated or unsaturated fatty acids may experience different changes in triglyceride-rich lipoproteins, LDL-related parameters, or other aspects of lipid metabolism. These differences may reflect differences in insulin sensitivity, adiposity, hepatic lipid handling, genetic background, gut microbiota, physical activity, or other biological factors. Consequently, the average change found in a clinical trial may conceal clinically meaningful responder and non-responder phenotypes (Koutsos *et al.*, 2024, Sadeghi-Nodoushan *et al.*, 2026).

This is particularly important when considering nutrigenomics. Accordingly, genetic variants in pathways involved in lipid transport, inflammation, glucose metabolism, and adipose tissue biology may alter the response to dietary components. However, genotype alone is unlikely to provide a detailed explanation. The phenotype created by the interaction of genes, diet, lifestyle, microbiota, and metabolic status is what ultimately becomes clinically measurable. In this context, clinical biochemistry can provide the necessary link between genetic susceptibility and an observable metabolic phenotype.

The growing availability of metabolomics and other omics technologies provides an opportunity to characterize this phenotype more comprehensively. Rather than examining a limited number of biomarkers independently, metabolomic and lipidomic profiling can provide a broader view of the biochemical pathways affected by dietary exposure. Integrating these data with genomic, microbiome, and clinical information may help identify molecular signatures and pathways associated with different nutritional responses (Rahimah *et al.*, 2026). However, it is essential that the goal is not to replace conventional laboratory tests with increasingly complex technologies. Instead, advanced approaches should help us determine when additional biochemical information is necessary and how it can improve clinical decision-making.

Recognizing differences in nutritional response is only the first step; the more important challenge is to understand what drives these differences and how they can be measured in clinical practice. This is where clinical biochemistry can make a meaningful contribution to precision nutrition. Rather than relying solely on a single biomarker or a single time-point measurement, future research should consider biochemical profiles that capture the interaction between dietary exposure and an individual's metabolic state. Measurements of glucose, insulin, triglycerides, lipoproteins,

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inflammatory markers, adipokines, and circulating metabolites may provide complementary information about how an individual responds to a particular dietary pattern. Importantly, these biomarkers should not only be associated with dietary response but also demonstrate biological relevance, reproducibility, and clinical utility. Identifying such biomarkers could help distinguish individuals who are likely to benefit from a specific dietary intervention from those who may require a different strategy, bringing precision nutrition closer to routine clinical practice (Mathers, 2025). This might be one of the most important contributions clinical biochemistry can make to the field.

Instead of asking whether a dietary intervention changes the mean concentration of a biomarker, future studies need to focus on the individual response trajectory. We should ask whether a biomarker is sensitive enough to detect nutritional response, whether that response is reproducible, whether it indicates a relevant biological pathway, and most importantly, whether it can help guide clinical management.

Answering this question will require closer integration of nutrition science with clinical biochemistry. Routine biochemical testing, dynamic metabolic monitoring, nutrigenomics, metabolomics, and microbiome-derived biomarkers should not be considered as competing approaches. Together, they may provide different layers of information about the same biological process (Keijer *et al.*, 2024).

Therefore, the future of precision nutrition may depend less on how much data we can collect and more on whether we can identify a clinically meaningful biochemical profile of nutritional response. Clinical biochemistry is a unique approach to help with this transition because it connects dietary exposure and molecular mechanisms to measurable phenotypes that can ultimately be interpreted in a clinical context.

Perhaps the most important question for the future of nutritional research is not whether personalized nutrition is possible, but whether we can identify the right biomarkers, at the right time, in the right individual, to make personalization clinically useful.

Sincerely

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