# Literature Review - Metabolomics

Ireland McCauley

22 September 2025

The investigation of postprandial metabolism and metabolite changes in response to dietary challenges has become an increasingly prominent topic in recent years. People spend most of their lives in a postprandial state, during which nutrients derived from food and other factors influence metabolic pathways in the body[7]. These changes depend on a variety of factors, such as individual characteristics, meal composition, and even the gut microbiome[8]. Metabolic responses play a critical role in individual health and can significantly influence disease risk. Choosing meals that help regulate postprandial glycemic responses is particularly important, as rising blood glucose levels are increasingly common and closely associated with prediabetes, a key risk factor for type II diabetes mellitus[8]. In addition, elevated postprandial glucose and triglycerides are known risk factors for cardiovascular disease[3].

Assessing how metabolites change after different meal challenges provides insight into how meal composition contributes to these changes and how responses vary from person to person. Weinisch et al. examined how individuals' blood metabolomes differ in response to three dietary challenges: an oral glucose tolerance test, a mixed meal, and an oral lipid tolerance test. The study found that 89 metabolites were significantly altered across the three meal types, which were grouped into eight clusters according to their temporal profiles and response patterns[7]. Moreover, meal-specific metabolic changes highlighted the impact of macronutrient composition. Similarly, Berry et al. highlighted the significant influence of person-specific factors—particularly the gut microbiome and contextual factors such as meal timing, sleep, and activity—over genetic or macronutrient factors in determining these responses[3]. A random forest regression model developed in this study accurately predicted individual triglyceride and glycemic responses, suggesting strong potential for personalized dietary strategies to improve cardiometabolic health.

The importance of tailoring nutrition to the individual has also emerged as a key concept in predicting and preventing metabolic disease. Zeevi et al. demonstrated the effectiveness of personalized dietary interventions in significantly reducing postprandial blood glucose levels in a diverse cohort[8]. They introduced a machine learning model that leverages comprehensive personal data, including the gut microbiome, to predict these responses using gradient-boosting regression. The successful implementation of personalized interventions based on this predictor demonstrates a promising strategy for managing blood glucose levels,

preventing metabolic disorders, and improving overall metabolic health[8].

Ben-Yacov et al. investigated the relationship between dietary modifications, gut microbiome composition, and cardiometabolic outcomes in individuals with prediabetes[2]. The study compared a Personalized Postprandial-Targeting (PPT) diet, which uses principal component analysis to predict personal glucose responses, with a Mediterranean Diet (MED) diet. Results indicated that the PPT diet induced more significant and diverse changes in gut microbiome composition compared to the MED diet[2]. Machine learning models have shown promise in predicting personalized metabolic responses to dietary changes, emphasizing the importance of baseline clinical profiles and specific dietary interventions in driving measurable health benefits. These findings strengthen the concept of precision nutrition in managing prediabetes and related metabolic conditions[2].

Annuzzi et al. employed artificial neural networks, specifically a feed-forward neural network, to predict and improve the monitoring of Postprandial Glucose Response (PGR) in individuals with Type 1 Diabetes (T1D)[1]. Their model incorporated carbohydrates, proteins, lipids, fiber, and energy intake to predict blood glucose levels within 60-minute windows after a meal. The results showed that additional nutritional factors significantly influence individual blood glucose predictions; however, personalized approaches are essential to improve T1D treatment, as a single model for all patients did not yield statistically significant results[1]. Wang et al. applied a similar approach, developing a deep learning model with multilayer perceptrons designed to predict personalized metabolite responses to dietary intervention[6]. The first layer predicted endpoint microbial composition, which was then used to predict endpoint metabolic profiles. This two-step approach outperformed previous single-step methods. By incorporating personal factors such as genetics, gut microbiota composition, metabolomics, and anthropometric data, the model outperformed existing methods and marked a significant step forward in the field of precision nutrition.

Shah et al. investigated the relationship between metabolic patterns, diet, and long-term cardiometabolic-cardiovascular disease (CM-CVD) in young adults[5]. They found that metabolic signatures of diet were more strongly associated with long-term CM-CVD than self-reported dietary intake alone. The study used elastic nets and regularized sparse canonical correlation analysis to identify these signatures, advancing precision nutrition by enabling the identification of potential diet-related CM-CVD[5].

Mendes-Soares et al. demonstrated significant interindividual variability in postprandial glycemic responses (PPGR)s to food, even among individuals without diabetes[4]. Their findings suggest that conventional dietary recommendations based solely on calorie or carbohydrate content are inadequate for precise glycemic control[4]. The study introduced and validated a predictive model that integrates individual-specific features—such as clinical characteristics, physiological variables, and gut microbiome composition—along with food characteristics. This tailored approach significantly outperformed standard methods in predicting PPGRs, providing a valuable tool for blood glucose management and the potential prevention of prediabetes and type 2 diabetes.

# References


[1] Giovanni Annuzzi, Lutgarda Bozzetto, Andrea Cataldo, Sabatina Criscuolo, and Marisa Pesola. Predicting and monitoring blood glucose through nutritional factors in type 1 diabetes by artificial neural networks. *Acta IMEKO*, 12(2):1–7, May 2023.

[2] Orly Ben-Yacov, Anastasia Godneva, Michal Rein, Smadar Shilo, Maya Lotan-Pompan, Adina Weinberger, and Eran Segal. Gut microbiome modulates the effects of a personalised postprandial-targeting (PPT) diet on cardiometabolic markers: a diet intervention in pre-diabetes. *Gut*, 72(8):1486–1496, August 2023.

[3] Sarah E. Berry, Ana M. Valdes, David A. Drew, Francesco Asnicar, Mohsen Mazidi, Jonathan Wolf, Joan Capdevila, George Hadjigeorgiou, Richard Davies, Haya Al Khatib, Christopher Bonnett, Sajaysurya Ganesh, Elco Bakker, Deborah Hart, Massimo Mangino, Jordi Merino, Inbar Linenberg, Patrick Wyatt, Jose M. Ordovas, Christopher D. Gardner, Linda M. Delahanty, Andrew T. Chan, Nicola Segata, Paul W. Franks, and Tim D. Spector. Human postprandial responses to food and potential for precision nutrition. *Nature Medicine*, 26(6):964–973, June 2020.

[4] Helena Mendes-Soares, Tali Raveh-Sadka, Shahar Azulay, Kim Edens, Yatir Ben-Shlomo, Yossi Cohen, Tal Ofek, Davidi Bachrach, Josh Stevens, Dorin Colibaseanu, Lihi Segal, Purna Kashyap, and Heidi Nelson. Assessment of a Personalized Approach to Predicting Postprandial Glycemic Responses to Food Among Individuals Without Diabetes. *JAMA Network Open*, 2(2):e188102, February 2019.

[5] Ravi V Shah, Lyn M Steffen, Matthew Nayor, Jared P Reis, David R Jacobs, Jr., Norrina B Allen, Donald Lloyd-Jones, Katie Meyer, Joanne Cole, Paolo Piaggi, Ramachandran S Vasan, Clary B Clish, and Venkatesh L Murthy. Dietary metabolic signatures and cardiometabolic risk. *European Heart Journal*, 44(7):557–569, February 2023.

[6] Tong Wang, Hannah D. Holscher, Sergei Maslov, Frank B. Hu, Scott T. Weiss, and Yang-Yu Liu. Predicting metabolite response to dietary intervention using deep learning. *Nature Communications*, 16(1):815, January 2025. Publisher: Nature Publishing Group.

[7] Patrick Weinisch, Jarlei Fiamoncini, Daniela Schranner, Johannes Raffler, Thomas Skurk, Manuela J. Rist, Werner Römisch-Margl, Cornelia Prehn, Jerzy Adamski, Hans Hauner, Hannelore Daniel, Karsten Suhre, and Gabi Kastenmüller. Dynamic patterns of postprandial metabolic responses to three dietary challenges. *Frontiers in Nutrition*, 9, September 2022. Publisher: Frontiers.

[8] David Zeevi, Tal Korem, Niv Zmora, David Israeli, Daphna Rothschild, Adina Weinberger, Orly Ben-Yacov, Dar Lador, Tali Avnit-Sagi, Maya Lotan-Pompan, Jotham Suez, Jemal Ali Mahdi, Elad Matot, Gal Malka, Noa Kosower, Michal Rein, Gili Zilberman-Schapira, Lenka Dohnalová, Meirav Pevsner-Fischer, Rony Bikovsky, Zamir Halpern, Eran Elinav, and Eran Segal. Personalized Nutrition by Prediction of Glycemic Responses. *Cell*, 163(5):1079–1094, November 2015.

## Acknowledgment of Assistance

Google Notebook LM. Assistance given to the author, AI. I used Google Notebook LM to summarize each article and generate briefing documents to build a general understanding before selecting sources for my literature review. Once I chose an article, I used the briefing document and its key takeaway and summaries to build my literature review. Google, (https://notebooklm.google.com /notebook/2afbacd6-9cc2-452e-aa64-562038b7fe1d). West Point, NY, 28 AUG 2025 - 03 SEP 2025.

ChatGPT. Assistance given to the author, AI. I used ChatGPT to improve sentence clarity, refine phrasing, receive guidance with Overleaf/LaTeX formatting, as well as edit the grammar, spelling and clarity of my final draft of my literature review. This helped me edit any simple errors in my literature review, as well as make some sentences more clear. OpenAI, (https://chatgpt.com/share/68d1e1bd-fbd4-8012-8831-31d9516179aa). West Point, NY, 12 SEP 2025- 22 SEP 2025.

## List of Acronyms

| | |
|---|---|
| CM-CVD | cardiometabolic-cardiovascular disease |
| MED | Mediterranean Diet |
| PGR | Postprandial Glucose Response |
| PPGR | postprandial glycemic responses |
| PPT | Personalized Postprandial-Targeting |
| T1D | Type 1 Diabetes |