# Integration of metabolomics and machine learning for precise management and prevention of cardiometabolic risk in Asians

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**Summary**

Rapid changes in dietary patterns have led to a rise in cardiometabolic diseases (CMDs) worldwide, highlighting the urgent need for effective dietary strategies to address the health issues. Compared to Caucasians, Asians are more susceptible to CMDs. Understanding the complex factors driving this increased susceptibility is essential for developing targeted interventions and preventive measures for Asian populations. Metabolomics plays a key role in identifying specific metabolic markers and pathways associated with CMDs, providing insights into disease mechanisms and helping to create individualized risk profiles. However, metabolomics faces several challenges, including difficulties in interpreting results across diverse ethnic groups, limitations in study design, variability in analytical platforms, and inconsistencies in data processing methods. Overcoming these challenges requires the adoption of advanced technologies, standardized approaches, and integration of multi-omics data to maximize the utility of metabolomics in clinical settings. As the volume and complexity of metabolomic data continue to increase, machine learning (ML) algorithms have become essential for effective data integration, interpretation, and knowledge extraction. Advanced ML techniques, such as deep learning and network analysis, can reveal hidden patterns, relationships, and metabolic pathways within large datasets, leading to deeper insights into biological systems and disease processes. By combining metabolomics and ML, we can facilitate early detection, enable personalized interventions, and support the development of targeted nutritional strategies, ultimately improving therapeutic outcomes and reducing the socioeconomic burden of CMDs in this region.

*Keywords*: metabolomics, machine learning, precision nutrition, cardiometabolic disease, dietary strategy

## 1. Introduction

Diet-related diseases, including obesity, type 2 diabetes (T2D), heart disease, stroke, and cancer, pose a major global health burden, impacting individuals' health and well-being, as well as straining healthcare systems.[1] An improved diet can substantially reduce or even prevent the onset of these diseases and improve the quality of life.[2,3] While the recommended dietary allowances (RDAs) have been effective in promoting better health outcomes on a population level, individual responses to the same nutrients may vary significantly due to factors such as genetics, metabolism, gut microbiota composition, lifestyle, and environment.[4-6] This underscores the need to move beyond a "one-size-fits-all" approach to more precise dietary recommendations.[7]

Recent evidence suggests that tailoring dietary guidance to individual metabolic phenotypes or metabotypes can optimize health outcomes by considering the unique genetic and phenotypic characteristics.[8,9] The ongoing advancements in omics technologies, particularly metabolomics, are changing the field of nutrition science.[8,10] Metabolomics is a powerful tool to offer insights into physiological processes and the impact of dietary interventions by analyzing the comprehensive profile of metabolites.[11, 12] Metabolites serve as key biological communication channels, reflecting the dynamic interactions between dietary components, metabolic pathways, and health status.[13]

Due to the increasing complexity of data generated in nutrition research, advanced analytical approaches are needed to derive meaningful insights. Machine learning (ML) algorithms have shown great promise in analyzing complex data, enhancing dietary measurements, modelling relationships between diet and diseases, and facilitating precise nutrition strategies.[14] Continued innovation in ML-driven approaches holds great potential for improving the understanding of diet-related chronic diseases and developing more effective strategies for disease prevention and management.[15]

Compared to Caucasians, Asian populations are more susceptible to deposition of visceral adipose tissue, and development of cardiometabolic diseases (CMDs) even when adjusted for gender, age, and body mass index (BMI).[16] Although the mechanisms behind the poor metabolic health in Asians are not fully understood, individuals at high risk for CMDs may exhibit distinct metabotypes that respond differently to the same diet. The investigation of the underlying mechanisms driving the metabotypic differences and their interactions with dietary factors can provide valuable insights into the pathophysiology of diet-related diseases. This deeper understanding has the potential to create targeted interventions that can modify specific metabolic pathways or molecular targets involved in disease progression.

In this review, we will review the current literature on metabolism and ML techniques in the context of CMD prevention. By integrating insights from metabolism, ML, and nutritional science, we aim to identify evidence-based strategies to improve metabolic health and prevent CMDs. Given the poor metabolic health of Asian populations, combining metabolomics, ML, and the Asian metabotype holds great potential for understanding metabolic health disparities and developing targeted dietary interventions to improve health outcomes in these populations.

## 2. **Methods**

A systematic literature search was conducted using the following databases: PubMed Central, Science Direct, and Web of Science. The search was carried out using a combination of specific keywords, including “metabolomics”, “machine learning”, “artificial intelligence”, “precision nutrition” or “dietary strategy” combined with any of the terms “cardiometabolic diseases”, “cardiovascular diseases”, “obesity”, “diabetes”. Boolean operators, specially “AND” and “OR”, were employed to refine the search. For example, “metabolomics AND cardiometabolic diseases” and “machine learning OR artificial intelligence” were used. The inclusion criteria are: (1) The peer-reviewed articles were published between 2014 and 2024

in English. (2) Studies focused on human populations and/or clinical settings were prioritized. Exclusion criteria included non-English language articles, animal studies, articles without clear clinical relevance and published more than 10 years ago.

## 3. Metabolomics, artificial intelligence, and cardiometabolic health

The emergence of high-throughput molecular data generation technologies, such as genomics, transcriptomics, proteomics, and metabolomics, is reshaping nutrition science.[17] Genomics, transcriptomics, and proteomics primarily focus on genes, RNA, and proteins. In contrast, metabolomics provides a snapshot of the metabolic status of an organism under specific conditions, such as disease, drug treatment, or dietary intervention.[18,19] Metabolomics relies on prior knowledge of metabolites, which reflect the dynamic interaction between dietary intake, metabolic processes, and overall health. Given their role in metabolism, metabolites serve as actionable biomarkers, providing valuable insights into the metabolic pathways, such as glycolysis, the tricarboxylic acid (TCA) cycle, oxidative phosphorylation, fatty acid oxidation, and the pentose phosphate pathway (PPP).[20] Metabolomics is promising in nutrition science because it captures both exogenous metabolites, which reflect dietary intake, and endogenous metabolites, which reveal how diet influences metabolic processes. The dual aspect of metabolomics is critical in developing effective dietary recommendations.

Metabolomics relies on advanced analytical techniques including mass spectrometry (MS) and nuclear magnetic resonance (NMR) spectroscopy to detect, quantify, and characterize diverse metabolites in biological samples.[21-25] NMR spectroscopy is advantageous due to its non-destructive nature, rapid analysis, high reproducibility, and robustness. However, it may lack sensitivity compared to MS-based methods.[26] On the other hand, MS-based methods are renowned for their sensitivity, although they can be destructive and may have lower throughput, especially when coupled with a separation dimension.[27] To maximize their strengths, NMR and MS are often combined, enhancing the sensitivity, accuracy, and

efficiency of metabolomic studies. This combination allows for a more comprehensive understanding of metabolic processes and their implications for nutrition and health.

Metabolomics generates comprehensive datasets that reveal the complex metabolic networks, offering transformative potential in advancing nutrition and health management.[28-30] By identifying biomarkers associated with cardiometabolic conditions such as dyslipidemia, hypertension, insulin resistance, and hyperglycemia, metabolomics enables early detection, diagnosis, and prognosis of CMDs.[31, 32] Analyzing the metabolic profiles of individuals with different conditions reveals patterns of metabolites specific to certain disease states, allowing for stratification of individuals into different risk categories. This personalized approach to health can also guide more precise dietary recommendations based on individual metabolic profiles, offering greater customization than conventional, generalized dietary advice.

Previously, individuals suffering from various rare inherited metabolic errors of metabolism were recommended to take very strict diet such that their diseases would not be exacerbated. For example, those with elevated glucose levels may benefit from a low-carbohydrate diet,[33] while individuals with phenylketonuria (PKU) must avoid phenylalanine.[34] Nowadays, precise dietary recommendations can be tailored at the individual level based on individual metabolic profiles, which offers a high degree of customization. This precise nutrition approach is expected to yield more effective healthcare outcomes and cost savings compared to conventional generalized recommendations.[35]

Metabolic phenotyping involves categorizing individuals into subgroups based on their metabolic and phenotypic patterns, aiming to identify those with high metabolic similarity. This stratification forms the basis for population grouping, enabling the customization of dietary interventions tailored to specific metabotypes. By utilizing metabolomics to define metabotypes, healthcare practitioners can provide precise dietary recommendations that closely match individuals' unique metabolic profiles. This personalized approach is

anticipated to result in better health outcomes and increased cost-effectiveness compared to standardized recommendations.[5]

Machine learning (ML) techniques play a crucial role in metabolomics for analyzing complex datasets, identifying patterns, and making predictions.[36,37] Through the analysis of extensive datasets, ML algorithms can detect correlations and patterns between metabolites and diseases. This insight enables the identification of new biomarkers and the forecasting of dysregulated metabolic pathways in various conditions. Table 1 shows some examples of the common ML techniques, i.e. supervised and unsupervised learning algorithms, used in various metabolomics studies.[37-43] Supervised learning algorithms learn from labelled data to make predictions or decisions.[44] In metabolomics, this can involve classifying samples into different groups based on their metabolic profiles or predicting disease outcomes based on metabolite concentrations.[37-41] Common supervised learning algorithms include random forest (RF), support vector machines (SVM), k-nearest neighbors (KNN), linear regression, logistic regression (LR), gradient boosting (GB), etc. Unsupervised learning extracts patterns or structures from unlabelled data. In metabolomics, unsupervised learning techniques are used for clustering similar samples or identifying outliers in the data.[42,43] Unsupervised learning works mainly with dimensionality reduction and clustering, where dimensionality reduction includes principal component analysis (PCA) etc, while clustering includes K-means clustering, and hierarchical clustering, etc.

Table 1. The common ML techniques used in metabolomics studies.

| ML algorithms used | Key findings and references |
|---|---|
| Support vector machine (SVM), partial least-squares discriminant analysis (PLS-DA), random forest (RF), logistic regression (LR) | Using the other ML algorithms used as benchmark, RF was used to build a diagnostic model while random survival forest was used to construct a prognosis model for identifying gastric cancer patients and to predict their prognosis.[37] Performance of these models were superior to traditional methods that used existing clinical factors. |

| | |
|---|---|
| | Two models were constructed to identify gastric cancer patients and to predict their prognosis. |
| RF, SVM, k-nearest neighbors (KNN), LR | Four ML algorithms were performed to construct diagnostic models based on 13 metabolic biomarkers, with the best result achieved by RF in identifying MetS biomarkers.[38] |
| RF, SVM, gradient boosting (GB), multiple neural networks, bagging classifier, LR | RF algorithm had the highest prediction power in distinguishing patients with CAD, HTA, and non-CVD individuals.[39] |
| RF, extreme gradient boosting (XGB), linear discriminant analysis (LDA), LR, SVM, neural networks (NN) | The NN method outperformed other ML techniques in predicting Parkinson's disease.[40] |
| RF, Light gradient boosted model (LGBM), Least absolute shrinkage and selection operator (Lasso), Ridge | The metabolomics and ML approach had potential for diagnostic applications in infectious diseases testing.[41] RF and LGBM was constructed and compared with Lasso and ridge, with the best result being achieved by LGBM. |
| Principal component analysis (PCA) k-means, sparse k-means, spectral clustering, Single-cell Interpretation via Multi-kernel LeaRning (SIMLR) and k-sparse | Utilizing unsupervised ML in metabolomics allowed for the stratification and personalized management of breast cancer patients.[42] SIMLR and k-sparse have better clustering performance among the 5 algorithms. |
| PCA k-means, sparse k-means, spectral clustering, SIMLR and k-sparse | Unsupervised ML methods applied to metabolomics had the potential to predict progression-free survival (PFS) outcomes, with PCA k-means demonstrating the highest performance.[43] |

By leveraging ML techniques, we can extract meaningful insights from metabolomics data, identify biomarkers of disease, and develop precise interventions to improve healthcare outcomes. The success of a metabolomics study depends not only on the choice of ML algorithm but also on the characteristics of the data, such as type, quantity, and quality. While complex, multivariate techniques are suited for handling large, multidimensional datasets, simpler, linearly separable data may perform better with traditional statistical methods. Consequently, many metabolomic studies compare the predictive performance of various ML algorithms against each other and against conventional statistical approaches.

For ML prediction tasks, usually 10% of the data will be reserved for testing, while the rest will undergo K-fold cross-validation to select the optimal model while avoiding underfitting or overfitting. Performance metrics, including accuracy, precision, recall, F1 score, and area under the Receiver Operating Characteristic curve (AUC-ROC), will be used to assess model performance. Because individual ML algorithms often excel in some areas but fall short in others, resulting in predictions with higher bias or variance, ensemble techniques will be explored to combine the strengths of multiple algorithms for improved results. Moreover, artificial intelligence (AI) algorithms will be considered, particularly for scenarios involving larger data volumes.

## 4. Integration of ML and metabolomics in Asian metabotype

Nutritional research aims to uncover the complex connections between diet patterns and health to prevent or treat diet-related disorders.[45] Dietary patterns involve the habitual consumption, whether at home or elsewhere, of a diverse array of foods and beverages, emphasizing balance and variety.[46] Numerous previous studies have shown that Asian diets significantly differ from western diets, characterised by their richness in carbohydrates, fibre, vitamins, and antioxidants but containing less concentrated fat.[47] Traditional Asian diets are often regarded as comprising foods that offer advantages in combating CMDs due to the use of soybeans, unsweetened tea, and fresh fruits and vegetables. Certain elements of these diets are suggested to support the proliferation of beneficial gut bacteria while inhibiting the colonization of non-beneficial ones.[48,49] Table 2 shows some examples of beneficial effects of different traditional dietary patterns in Asia on various health outcomes.

Table 2. Beneficial effects of Asian diets on health outcomes.

| Dietary pattens | Health outcomes and reference |
|---|---|
| Fish and omega-3 fatty acid | Significant negative association between omega-3 fatty acid intake and severely increased carotid intima-media thickness, a marker of carotid atherosclerosis in Japanese population.[50] |

| | |
|---|---|
| Green tea | Green tea consumption was inversely associated with incident functional disability in elderly Japanese.[51] |
| Vegetables-fruits<br>Snacks-drinks-milk products<br>Meat-fish | Higher "vegetables-fruits" and "snacks-drinks-milk products" pattern scores were inversely associated with depressive symptoms. No association of "meat-fish" pattern with depressive symptoms in elderly Chinese in Hong Kong.[52] |
| Plant-based foods | Healthful plant-based foods were favourably associated with cardiometabolic risks in South Asian ancestry.[53] |
| Traditional Chinese diet (TCD) with rice and leafy vegetables as the primary component | TCD was generally inversely associated with weight gain and obesity.[54] |

Despite the dietary benefits, Asian populations tend to exhibit a higher prevalence of insulin resistance and T2D compared to age- and BMI-matched Caucasians, with several factors contributing to this elevated risk. Asians tend to have more visceral and hepatic fat, along with a higher level of intramuscular triacylglycerol, but less lean mass compared to other ethnic groups.[55-57] This increased ectopic fat reduces the muscle's capacity for fat oxidation, leading to insulin resistance.[57-59] In addition, reduced beta cell function in Asians diminishes insulin secretion capacity, further contributing to insulin resistance.[60-62] While both abdominal visceral fat and hepatic fat are linked to the progression of glycaemic disorders, hepatic fat is more closely associated with the transition from prediabetes to T2D.[63, 64] Together, the combination of excess fat in muscle, impaired insulin secretion, and increased hepatic fat accumulation may increase susceptibility to T2D in Asians.[65]

However, it should be highlighted that both insulin resistance predisposition and T2D incidence vary among Asian populations. In a study involving 4,136 Chinese, Malays, and Asian Indians living in Singapore,[66] Asian Indians exhibited significantly higher levels of insulin resistance ($p < 0.001$) compared to Malays (intermediate levels) and Chinese (the lowest levels). Another study of 7,427 Chinese, Malays, and Indians[67] reported that Malays

and Indians were linked to roughly double the risk of T2D compared to Chinese. The increased risk of T2D among Malays was mainly attributed to the higher BMI, whereas the increased risk among Indians was due to the higher BMI, waist circumference (WC), homeostatic model assessment for insulin resistance (HOMA-IR), and C-reactive protein (CRP) level, but lower beta-cell function and high-density lipoprotein cholesterol (HDL-c) level. Therefore, the distinct biological risk factor profiles associated with insulin resistance and T2D exhibited by various Asian ethnic groups may necessitate tailored strategies for prevention and management of CMDs.

Recently, contemporary diets are beginning influence the dietary habits of Asian populations. The rapid proliferation of global food service chains has altered traditional eating patterns significantly. This shift is marked by a growing preference for calorie-dense diets among Asians, characterized by increased intake of refined carbohydrates, fast food, processed food, and sugar-sweetened beverage (SSB) consumption.[49,68] The dietary changes have been associated with long-term weight gain and obesity-related issues.[69] The negative effects of the dietary changes may become more apparent with prolonged exposure over time. In addition, dietary changes may affect the gut microbiota mediated metabolic activity, and alterations in the gut microbiota may regulate the development of CMDs.[70,71] Alterations in the gut microbiota can disrupt the equilibrium of energy levels within the body, such that the unbalanced gut microbiota increases the susceptibility to obesity and metabolic syndrome (MetS).

Given the variations in metabolic health among ethnic groups and the rapid shifts in dietary habits across Asia, tailored dietary interventions are essential for effectively regulating metabolism in different populations. Recent study has shown that overlooking ethnic diversity may lead to inaccurate assessments of the vulnerability to T2D and cardiovascular disease (CVD) risks linked to dietary factors.[65] Understanding how different dietary patterns

influence metabolic health will enhance our ability to develop personalized nutrition strategies, promote healthy eating behaviours, and prevent CMDs.

An increasing number of studies have suggested that individuals may be grouped into metabolic subgroups, or metabotypes, according to their unique metabolic responses to foods and dietary changes.[72,73] As mentioned earlier, metabotyping emerges as a promising approach for identifying subpopulations to develop targeted dietary advice.[74] Metabotypes can be classified as either diet-related or disease-related, presenting in individuals at high risk of CMD and affecting the response to specific diets.[5] While metabotype studies on Asian populations may be relatively limited compared to those on Western populations, there is increasing interest in understanding how metabolic responses differ across ethnicities and geographic regions in Asia. Metabotype studies on Asian populations are valuable for the following reasons. Firstly, there may be genetic and cultural differences that influence metabolic responses to diet and lifestyle factors in Asians. Secondly, rates of certain CMDs, such as T2D, vary between Western and Asian populations, making it important to understand the underlying metabolic mechanisms.

Previously, 46 Asian women were clustered into three metabotypes based on their glucose, insulin, and triacylglycerol responses to a fructose-based meal.[75] It was found that the high triacylglycerol cluster had a greater waist-to-hip ratio (WHR) and a worse lipid profile, whereas the high glucose cluster had a higher fasting blood glucose, BMI, fat percentage, and hip circumference. The metabotyping has the potential to develop and optimize nutritional interventions for individuals with various cardiometabolic risks. In another study involving 2,170 Japanese adults,[76] four metabotypes were clustered based on the presence of obesity, abdominal obesity, hypertension, hyperglycaemia, and dyslipidaemia. The results revealed that the healthy dietary pattern, characterized by a high intake of vegetables, fruits, potatoes, soy products, mushrooms, seaweeds, and fish, was associated with metabolically healthy

non-obese (MHNO) and obese (MHO) phenotypes. In contrast, the alcohol dietary pattern, characterized by a high intake of alcoholic beverages, liver, chicken, and fish, was inversely associated with the MHNO and MHO phenotypes. Therefore, the major dietary patterns are associated with different metabotypes in middle-aged and elderly Japanese adults.

As noted earlier, metabolomics has been demonstrated as a valuable tool for assessing biochemical changes associated health issues induced by dietary factors.[35] It shows considerable potential in identifying nutritional biomarkers to effectively monitor nutritional intervention studies and helps to improve our understanding of diet-health relationships. However, the greatest challenges for metabolomics research include metabolites identification and data interpretation. Recent advancements in ML have improved data analysis and classification of health-related parameters in metabolomics, particularly in developing predictive models using potential biomarkers.[77,78] With help of the enhanced AI or big data analytics, ML algorithms offer a clear understanding of underlying pathological pathways and metabolism-related diseases. Therefore, the integration of metabolomics and ML provide tangible evidence to better understand the pathophysiologic mechanisms, mitigate the disease risks, and formulate evidence-based nutritional recommendations for precise nutrition.[79]

Metabolic responses to dietary interventions can be used to determine the risks of developing a disease,[80] which can vary based on the disease and ethnicity. Due to the wide range of ethnicities, cultures, and dietary habits in Asian populations, metabolomics combined with ML allows for the exploration of the diversity by capturing variations in metabolic profiles across different Asian subpopulations. Understanding these variations can lead to more tailored and effective healthcare interventions.[81] Importantly, ML-predicted biomarkers identified through metabolomics not only enhance our understanding of disease risk but also provide a foundation for actionable clinical interventions. These predictive biomarkers can

guide clinicians in monitoring patient responses to dietary interventions, adjusting nutritional plans in real time, and identifying individuals who may benefit from specific nutrient modifications or functional foods. For example, individuals with metabolomic profiles indicating impaired lipid metabolism may be advised to reduce saturated fat intake, while those showing markers of glucose dysregulation might benefit from low-glycemic-index diets. As a result, integrating ML-derived biomarker insights into clinical practice bridges the gap between data-driven discovery and precision nutrition, enabling more targeted, effective, and preventive healthcare strategies.

## 5. **Precise dietary interventions**

Dietary intervention studies typically involve consumption of specific foods followed by biomarker measurements to assess diet-health interactions.[82] One of the challenges in interpreting the relationship is to understand the high inter-individual variability responses to different dietary intakes.[83] In 2015, Zeevi et al.[84] adjusted diets based on the factors contributing to inter-individual variations in post-prandial glycaemic response, known as personalized post-prandial glycaemic responses (PPGRs). They accurately predicted PPGRs by using an ML algorithm that integrated various measures such as dietary habits, anthropometric data, activity levels, blood markers, and gut microbiota. Participants were provided with personalized dietary recommendations, with some receiving diets predicted to benefit their blood glucose levels and others receiving diets expected to have adverse effects. Not surprisingly, what constituted a beneficial diet for some participants resembled the detrimental diet for others, and vice versa. This study highlighted the potential of using ML algorithms on biological big data for precision nutrition at the individual level. The PPGRs tool was later validated in an American cohort.[85] The tool enabled individuals to accurately predict their glycaemic response to specific foods, exceeding the accuracy of the information solely based on the calorie or macronutrient content. In addition, in the PREDICT 1 study

(The Personalised REsponses to DIetary Composition Trial),[7] the authors observed a substantial inter-individual variability in post-prandial triglyceride (TG), glucose, and insulin responses to standardized meals, even among identical twins. Using an ML model, the authors were able to predict the metabolic responses to food intake.

The increasing consumer awareness of the link between diet and health in Asia has positioned the region as a focal point for precise nutrition initiatives. In 2022, the first study (Diet2Me) demonstrating the health benefits of personalized nutrition intervention was published.[86] The study showed that various clinical outcomes, including weight, BMI, body fat percentage, WC, WHR, TG, total cholesterol (TC), low-density lipoprotein cholesterol (LDL-c), uric acid, homocysteine, folic acid, eicosapentaenoic acid (EPA), and calcium levels were significantly improved in overweight/obese Chinese adults who received personalized nutrition compared to those in the control group. Like the Food4Me study,[87] which showed substantial health benefits from aligning dietary intake with the Mediterranean Diet, the participants in the personalized nutrition intervention group consumed less red meat, salt, saturated fat, and had higher healthy eating index score.[88] In another pilot study,[89] 60 older Asian Americans were randomized into a personalized behavioural nutrition group and a control group to evaluate the potential health benefits of personalized behavioural nutrition. This intervention aimed to optimize individual T2D management through providing personalized nutrition goals and recommendations based on identified metabolite profiles and integrating real-time data of health outcomes and diet using digital technology. This study helped to improve the understanding of how the personalized behavioural nutrition interventions can decrease haemoglobin A1c (HbA1c) levels and change metabolites profiles.

Despite growing interest in personalized nutrition interventions, several limitations hinder the robustness of the findings. Many studies had small to moderate sample sizes, which reduced statistical power and the ability to detect subtle metabolic varations.[90] Moreover, the

interventions in children and adolescents were lacking. The lack of standardized protocols for sample collection, data processing, and biomarker validation further complicated cross-study comparisons. To address these challenges, multi-centre collaborations across Asian countries should be encouraged to increase sample size, enhance population diversity (including different age groups and ethnic backgrounds), and promote methodological consistency. Longitudinal cohort studies, combined with standardized metabolomic workflows and advanced ML analytics, are also essential to improve causal inference and the development of region-specific dietary recommendations.

## 6. **Future directions and implications**

Nutritional science is currently at the forefront, emphasizing the ability to engineer the physiological networks to improve diet, health, and disease management.[91] Precision nutrition represents an emerging paradigm in nutritional therapy, with the potential to enhance health outcomes through precise dietary recommendations. By considering individual genetic profiles, microbiome composition, lifestyle, and environmental factors, precision nutrition seeks to enhance health, prevent disease, and improve the effectiveness of nutritional interventions.

Despite its potential, precision nutrition faces several challenges, including data privacy, accessibility, and scientific validation. Moreover, progress in intervention studies is hindered by the high cost of generating large-scale multi-omics datasets and the lack of streamlined analytical pipelines for integrating these diverse data sources. Most current clinical studies are observational rather than randomized controlled trials (RCTs), which limits the strength of evidence regarding causal relationships and clinical outcomes.

Moving forward, longitudinal studies are necessary to assess the long-term impacts of personalized nutrition on health outcomes. Future research must also address inconsistencies

368 in methodologies and the formulation of personalized guidance across studies.[92] Translating
369 these findings into clinical practice will enhance the management and prevention of diet-
370 related non-communicable diseases (NCDs), not only for Asian populations but globally.[93]
371 Furthermore, incorporating precision nutrition into public health policy can help address
372 dietary needs on a population level.[94]

373 Advancements in multi-omics tools and related analytical techniques have greatly expanded
374 their applications in nutrition science. Hence, a better understanding of the interactions
375 between diet and individuals is expected, provided that the key challenges for successful
376 implementation are addressed. Consequently, future research should integrate multi-omics
377 data to create comprehensive profiles for individualized nutrition plans. AI and ML will be
378 utilized to analyze the complex datasets and predict individual responses to dietary
379 interventions, thereby developing evidence-based strategies to leverage technology for
380 improving dietary behaviours, preventing diseases, and promoting overall health and well-
381 being.[95] In addition, identifying new biomarkers is crucial for more accurate assessment of
382 nutritional status and metabolic health.[96]

383 Finally, further research should prioritize to explore ways to manipulate the gut microbiome
384 to improve health outcomes through diet and expand research in how genes affect nutrient
385 metabolism and how nutrients influence gene expression. The gut microbiome plays a crucial
386 role in modulating host metabolism, immune function, and nutrient absorption. By combining
387 microbiome profiles with metabolomic and dietary data, ML algorithms can identify
388 complex, multi-dimensional patterns that better reflect individual biological responses to
389 dietary interventions. This integration enables more accurate prediction of disease risk and
390 therapeutic response and can inform the development of microbiota-targeted dietary
391 strategies. In future, the incorporation of longitudinal microbiota data and functional
392 microbial traits into ML models will be essential for refining precision nutrition approaches

and improving clinical decision-making. Efforts should also be directed toward addressing the ethical, legal, and social implications of personalized nutrition, including issues of data privacy and access to personalized healthcare. This will enable the development of highly tailored dietary recommendations based on individual genetic, metabolic, and microbiome profiles to improve nutritional outcomes and prevent diet-related diseases.

## Conclusions

The rapid rise in CMDs globally, particularly in Asian populations, underscores the urgent need for effective dietary interventions. Metabolomics, with its ability to profile small molecules in biological samples, offers a valuable tool to understand the metabolic status of individuals and unravel the mechanisms underlying diet-related diseases. However, current limitations in study design, analytical variability, data processing methods, and insufficient ethnic representation may hinder the utility of metabolomics in epidemiological studies. Overcoming these hurdles requires the adoption of advanced technologies and standardized approaches. Integrating data from multi-omics studies can enhance the understanding of complex biological systems and disease processes. ML algorithms, particularly deep learning and network analysis, have the potential to unlock hidden patterns and relationships within large-scale metabolomic datasets. By leveraging these advanced techniques, we can extract valuable insights into the intricate interplay between diet, metabolism, and health. This deeper understanding will not only enhance the clinical relevance of metabolomics but also facilitate the prediction and management of CMDs. These integrated approaches offer significant potential for advancing precision nutrition and improving cardiometabolic health, particularly in understudied populations such as those in Asia.

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## Conflicts of Interest

The authors declare no potential conflict of interest.

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