REVIEW ARTICLE

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Nutrigenomics and epigenetics in type 2 diabetes mellitus (T2DM) prevention – literature review

Nutrigenomika i epigenetyka w prewencji cukrzycy typu 2 (T2DM): przegląd literatury

Natalia Kosińska[1,A-F] ✉, Maria Lucyna Lamorska[2,A,E-F], Piotr Adam Gebuza[3,C,F], Klaudia Jurkowska[4,B,F], Agata Ostrowska[5,B-C,F], Weronika Dudek[6,D-F], Julia Mądrzak[7,A,D,F], Monika Kulińska[8,C-D,F], Izabela Kołdej[9,C-D,F], Dominika Dutkiewicz[10,A,E-F]

[1] *Collegium Medicum, Andrzej Frycz Modrzewski University, Kraków, Poland*
[2] *2nd Department of Internal Medicine with a Cardiac Intensive Care Unit, Stefan Żeromski Specialist Hospital, Kraków, Poland*
[3] *Night and Holiday Healthcare Clinic, Arion Med Sp. z o.o., Gostynin, Poland*
[4] *Faculty of Medical Sciences in Katowice, Medical University of Silesia, Katowice, Poland*
[5] *Primary Health Care Clinic, MCM Górna, Łódź, Poland*
[6] *Department of Internal Medicine, Metabolic Diseases, and Angiology, Prof. Leszek Giec Upper Silesian Medical Centre, Katowice, Poland*
[7] *Faculty of Medical Sciences and Health Sciences, Kazimierz Pułaski University, Radom, Poland*
[8] *Department of Internal Medicine and Nephrodiabetology, University Clinical Hospital No.2, Medical University, Łódź, Poland*
[9] *Emergency Department, Bielański Hospital, Warsaw, Poland*
[10] *Emergency Department, Specialist Hospital, Kościerzyna, Poland*
A – Research concept and design, B – Collection and/or assembly of data, C – Data analysis and interpretation, D – Writing the article, E – Critical revision of the article, F – Final approval of the article

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Abstract

Introduction and Objective. Type 2 diabetes mellitus affects more than 500 million adults worldwide and continues to increase. Diet shapes molecular pathways regulating insulin sensitivity, inflammation and glucose metabolism. Nutrigenomics studies nutrient-gene interactions, while epigenetics focuses on reversible mechanisms, such as DNA methylation, histone modifications and non-coding RNAs. This review synthesises evidence from 2017–2025 on how these processes support T2DM prevention.

Review Methods. A targeted narrative search of PubMed and PubMed Central was conducted to identify recent human evidence published between 2017–2025 on nutrigenomics, epigenetics, diet and T2DM prevention. Peer-reviewed clinical, cohort, mechanistic and review studies were prioritised and synthesised thematically.

Brief description of the state of knowledge. Genetic variants, such as TCF7L2, FTO and PPARG, show modest, inconsistent diet-gene effects. Diet-induced changes in DNA methylation and histone marks influence insulin signalling, lipid metabolism and inflammatory pathways, but mostly associative and short-term. Mediterranean and plant-based diets align with more favourable molecular profiles, while high-fat, high-GI diets show adverse signatures. Early personalised-nutrition trials using genomic, metabolomic or microbiome data improve postprandial glucose responses in some individuals, but often fail to outperform standard dietary recommendations in broader populations.

Summary. Nutrigenomic and epigenetic research improves understanding of how diet shapes metabolic risk, although clinical applicability remains limited. Most effects are small, variable across populations, and not consistently reproduced. Long-term, multi-ethnic and multi-omics studies are needed to validate biomarkers and determine whether they add predictive or therapeutic value beyond established dietary strategies.

Key words

DNA methylation, microRNA, epigenetics, nutrigenomics, personalised nutrition, type 2 diabetes mellitus prevention

Streszczenie

Wprowadzenie i cel pracy. Cukrzyca typu 2 dotyczy ponad 500 mln dorosłych na świecie, przy czym odnotowuje się stały wzrost liczby zachorowań. Dieta kształtuje szlaki molekularne regulujące wrażliwość na insulinę, stan zapalny i metabolizm glukozy. Nutrigenomika bada interakcje między składnikami diety a genami, a epigenetyka koncentruje się na odwracalnych mechanizmach, takich jak metylacja DNA, modyfikacje histonów i ncRNA. Przegląd syntetyzuje dane z lat 2017–2025 dotyczące roli nutrigenomiki i epigenetyki w prewencji T2DM.

Metody przeglądu. Przeprowadzono przegląd narracyjny PubMed/PMC, obejmujący badania z udziałem ludzi z lat

✉ Address for correspondence: Natalia Kosińska, Collegium Medicum, Andrzej Frycz Modrzewski University, Kraków, Poland
E-mail: natalia.a.kosinska@gmail.com

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2017–2025 dotyczące nutrigenomiki, epigenetyki, diety i profilaktyki T2DM. Uwzględniono w nim przede wszystkim recenzowane badania kliniczne, kohortowe, mechanistyczne i przeglądowe, syntetyzując je tematycznie.
Opis stanu wiedzy. Warianty genetyczne, takie jak TCF7L2, FTO i PPARG, wykazują niewielkie i niespójne interakcje dieta-gen. Zmiany epigenetyczne wynikające z diety wpływają na sygnalizację insulinową, metabolizm lipidów i szlaki zapalne, lecz zazwyczaj mają charakter krótkotrwały i obserwacyjny. Diety śródziemnomorskie i roślinne wiążą się z korzystniejszym profilem molekularnym, natomiast diety wysokotłuszczowe i wysokoglikemiczne – z profilem niekorzystnym. Wczesne próby personalizacji żywienia oparte na genomice, metabolomice lub mikrobiomie pokazują, że takie żywienie poprawia poposiłkową glikemię u części osób, ale często nie przewyższają standardowych zaleceń w populacji ogólnej.
Podsumowanie. Nutrigenomika i epigenetyka umożliwiają głębsze rozumienie wpływu diety na ryzyko metaboliczne, jednak ich zastosowanie kliniczne pozostaje ograniczone. Efekty są niewielkie, zmienne między populacjami i rzadko powtarzalne. Potrzebne są długoterminowe, wieloetniczne badania wieloomiczne, aby potwierdzić biomarkery i ocenić, czy wartość predykcyjna lub terapeutyczna, którą wnoszą, przewyższa wartość uznanych strategii żywieniowych.

Słowa kluczowe
metylacja DNA, epigenetyka, mikroRNA, nutrigenomika, żywienie personalizowane, prewencja cukrzycy typu 2

INTRODUCTION

Type 2 diabetes mellitus (T2DM) affects more than 500 million adults worldwide, and by 2050, this number may reach 730 million [1]. In Poland, close to 3.1 million people live with T2DM [2]. Ageing, sedentary lifestyles and diets high in refined carbohydrates and saturated fats are the main contributors. T2DM involves insulin resistance, a steady loss of β-cell function and persistent low-grade inflammation. These changes reflect deeper environmental and molecular disruptions [3, 4].

Recent research now looks beyond traditional risk factors and is focused on molecular mechanisms that shape metabolic health. Nutrigenomics explores how nutrients affect gene expression and metabolic activity. Epigenetics refers to reversible modifications – such as DNA methylation, histone changes and non-coding RNA activity – that regulate gene function without altering the DNA sequence [5, 6]. These mechanisms help explain why individuals differ in their responses to diet.

Diets rich in saturated fats and refined carbohydrates can induce adverse epigenetic changes in pathways related to insulin signalling and lipid metabolism. This leads to more inflammation and insulin resistance [7, 8]. In contrast, polyphenols, omega-3 fatty acids and methyl-donor nutrients support favourable patterns of DNA methylation and microRNA expression. Mediterranean and anti-inflammatory diets show favourable methylation profiles and reduced expression of pro-inflammatory microRNAs. Several trials confirm diet-induced miRNA modulation relevant to glycaemic control [9–11].

Nutriepigenomic studies now combine dietary data with genome-wide methylation, transcriptomic, microbiome, and metabolomic profiles. Evidence shows that Mediterranean and polyphenol-rich diets can alter DNA methylation and islet transcription which are linked to improved insulin sensitivity. Personalised-nutrition trials have shown improvements in the postprandial glucose responses of some individuals. These improvements occur when genomic or microbiome features are incorporated into dietary planning. However, results remain mixed, and several studies report no clear advantage over standard dietary approaches [4, 12, 13]. These inconsistencies highlight both the potential and the early stage of multi-omic personalisation. As analytical methods improve, integrating genomic, microbiome, and metabolomic information may enable more targetted prevention strategies [14–17].

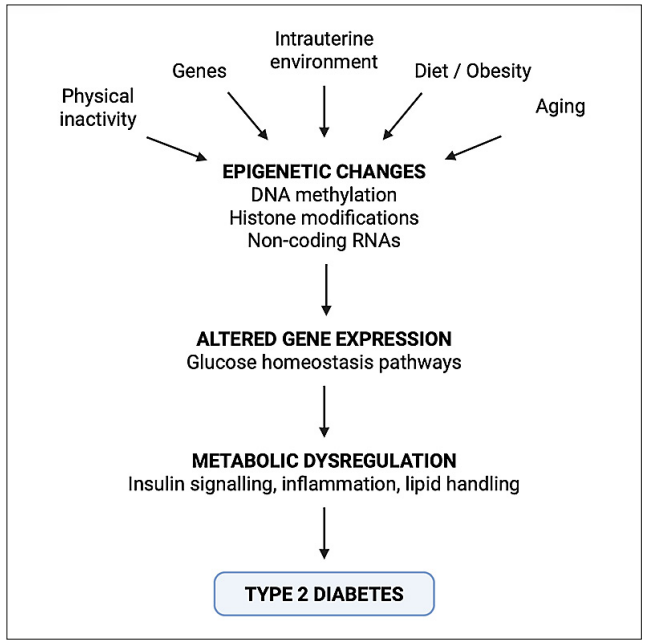

Figure 1. Conceptual model of factors affecting epigenetic alterations, altered gene expression, and metabolic dysregulation leading to T2DM. Inspired by [18]

OBJECTIVE

The aim of this review is to summarise and synthesise studies published between 2017–2025 on how nutrition, genomic variability, and epigenetic regulation contribute to the prevention of type 2 diabetes. The review focuses on describing gene-diet interactions, diet-induced epigenetic modifications and emerging directions in personalised nutrition.

REVIEW METHODS

The article was designed as a narrative literature review. A targeted search of PubMed and PubMed Central was conducted to identify recent human evidence published between January 2017 – November 2025. This period was selected to capture advances in epigenomic profiling, metabolomics, microbiome research, continuous glucose

monitoring, and early machine-learning-based precision-nutrition approaches relevant to T2DM prevention.

Search terms and MeSH combinations included: nutrigenomics, gene-diet interaction, diet AND DNA methylation, diet AND microRNA, epigenetics AND diabetes, precision nutrition and type 2 diabetes. Priority was given to peer-reviewed human randomised controlled trials, cohort studies, mechanistic investigations, epigenome-wide or transcriptome-wide analyses, metabolomic or microbiome studies, and recent narrative or systematic reviews examining molecular responses to dietary exposures or gene-diet interactions in T2DM prevention.

Studies were included if they addressed genetic variation influencing dietary response, diet-induced epigenetic modulation, molecular biomarkers of glycaemic risk or personalised nutritional strategies for T2DM prevention. Animal and *in vitro* studies, non-peer-reviewed publications, conference abstracts, grey literature, non-English articles, and papers unrelated to diet-genome-epigenome interactions were excluded. Reference lists of key articles were also screened.

The selected evidence was synthesised narratively and organised into five thematic areas: (1) pathophysiology and risk factors of T2DM, (2) nutrigenomics and gene-diet interactions, (3) epigenetic regulation, (4) diet-induced epigenetic modulation and (5) integrative applications of personalised nutrition.

STATE OF KNOWLEDGE

Pathophysiology and risk factors of type 2 diabetes mellitus. Type 2 diabetes develops through interactions between genetic predisposition, environmental exposures and lifestyle factors. Together, these forces gradually weaken insulin sensitivity and β-cell function. Early stages feature insulin resistance in muscle and adipose tissue, followed by compensatory hyperinsulinaemia and a gradual decline in β-cell performance. Chronic energy surplus, especially diets rich in refined carbohydrates and saturated fats, contributes to lipotoxicity, oxidative stress and low-grade inflammation [4, 7].

Epigenetic research clarifies how classical risk factors lead to molecular dysfunction. DNA-methylation patterns linked to ageing, obesity, physical inactivity, and poor diet have been found in insulin-responsive tissues and pancreatic islets [19]. Many genetic variants shape T2DM risk, but they explain only part of disease susceptibility. Lifestyle factors, such as excess adiposity, physical inactivity, disrupted sleep and chronic metabolic stress, play a major role, promoting insulin resistance through hormonal and inflammatory pathways [20, 21].

Diet quality is particularly important. Higher intake of fibre, unsaturated fats and plant bioactives is linked to better insulin sensitivity and reduced inflammation. In contrast, high-fat and high-glycaemic diets are linked to poorer glycaemic control and features of metabolic syndrome [22, 23]. These dietary patterns can also influence transcriptional and epigenetic processes relevant to insulin secretion and signalling.

Overall, T2DM risk reflects both inherited predisposition and cumulative lifestyle-related changes in metabolic and epigenetic regulation.

Nutrigenomics and gene-diet interactions. Nutrigenomics examines how diet alters gene expression and how genetic variation shapes metabolic responses. In T2DM, these interactions help explain why individuals with similar lifestyles show different glycaemic patterns [15].

The TCF7L2 rs7903146 variant is a strong predictor of T2DM risk because it affects β-cell insulin secretion. Mediterranean-style, fibre-rich diets may lessen this risk, while high-glycaemic diets can worsen secretion defects. However, the observed effects are small and often inconsistent across studies [24].

Variants in FTO and PPARG show similarly modest interactions. Better diet quality or increased physical activity lowers risk in FTO carriers, and the PPARG Pro12Ala variant shows different responses to monounsaturated-fat intake, though findings differ between populations [25].

Metabolomic profiling captures downstream metabolic variation. In the PREDIMED study, a nine-metabolite urinary signature discriminated T2DM with high accuracy, reflecting amino-acid, carbohydrate and microbiota-related pathways [26]. However, platform dependence limits reproducibility.

Some interactions are food-specific. The *INAFM2* rs67839313_T variant modifies the glucose response to egg intake, raising fasting glucose and T2DM risk in carriers. Non-carriers do not show this effect [27]. Diet also influences circulating miRNAs involved in glycaemic regulation, such as miR-17–92, miR-21 and miR-146a. Fibre-rich coarse grains may influence these miRNAs through microbiota-derived metabolites, but the mechanisms remain uncertain [28].

Bioactive nutrients, such as polyphenols and omega-3 fatty acids, affect transcription and epigenetic signalling. Multi-omics studies show that Mediterranean and plant-forward diets shift transcriptomic profiles toward improved insulin action, although these effects are modest and often inconsistent [15, 25].

Gene-diet interactions contribute to metabolic variability, but most reported effects are small, population-specific, and sensitive to analytical methods. Large, standardised, multi-ethnic cohorts are still needed before these findings can reliably support precision-nutrition strategies.

Epigenetic regulation in glucose homeostasis and type 2 diabetes mellitus. Epigenetic regulation modulates gene expression without changing the DNA sequence. These mechanisms shape insulin resistance, β-cell function and metabolic memory [29].

EWAS consistently identify robust CpG signals for T2DM, particularly at TXNIP, ABCG1 and SREBF1. These loci replicate across multiple cohorts and show strong associations with fasting glucose, HbA1c and diagnosed T2DM. ABCG1 and SREBF1 hypermethylation reflect adiposity and lipid dysregulation, while TXNIP hypomethylation tracks glycaemia. In the Lifelines replication, all three markers remained significant, confirming their stability. Many CpG sites also shift with metabolic improvement, indicating high environmental sensitivity [18, 30].

Histone changes follow a similar pattern. Excess nutrients push chromatin toward states linked to inflammation and poorer insulin action. Metabolic improvement can shift these marks back toward more permissive profiles. This has been seen in metabolic tissues and in oocytes of obese mothers, where H3K27 and H3K9 methylation change with diet and weight [29, 31].

Table 1. Summary of recent nutrigenomic and epigenetic evidence in T2DM prevention

Reference	Population / Design	Diet / Exposure	Primary Mechanistic Endpoint(s)	Main Clinical / Metabolic Outcome	Key Note	Main limitation
Alcalá-Díaz et al. [36]	Adults with coronary heart disease; 5-year RCT; includes newly diagnosed T2DM	Mediterranean diet vs. low-fat, high-complex-carbohydrate diet	Baseline circulating miRNAs; miRNA-diet interactions predicting remission	T2DM remission; improved glycaemia in individuals whose baseline miRNA profiles matched diet	Strong human evidence that specific miRNA signatures may guide dietary personalisation in T2DM	High-risk cardiac cohort; miRNA thresholds need validation
Rein et al. [12]	Newly diagnosed T2DM; RCT + 6-month extension	Personalised postprandial-targeting (PPT) diet vs. standard Mediterranean diet	CGM-derived PPGR, mean glucose, variability; microbiome functional shifts; ML-predicted PPGR	Lower PPGR, reduced variability and fructosamine; better HbA1c; 61% remission	Strong mechanistic evidence that microbiome-guided diets improve glycaemic control in early T2DM	Pilot design; limited sample size, follow-up and scalability
Popp et al. [16]	Overweight adults with impaired glucose metabolism; 6-month RCT	Personalised ML-derived PPGR diet vs. standardised low-fat diet	Estimated PPGR scores; dietary adherence via app	No differences in weight loss or body composition	Precision-nutrition algorithm did not outperform low-fat diet despite mechanistic sophistication	No superiority over comparator; PPGR estimates require validation
Kharmats et al. [17]	Adults with prediabetes or moderately controlled T2DM; 6-month RCT	Microbiome-based personalised diet vs. low-fat diet	CGM-derived variability metrics (MAGE, SD, mean glucose, CV); HbA1c trajectory	Both groups improved; no between-group differences	Personalised PPGR-targeted diet not superior for glycaemic control in this population	No between-group superiority; microbiome predictions need validation
Urpi-Sarda et al. [26]	PREDIMED participants (85 T2DM; 69 controls); cross-sectional metabolomics	Habitual Mediterranean diet	Urinary metabolomic fingerprint; multi-metabolite T2DM signature; metabotype classification	Distinct metabolomic profiles discriminated T2DM (AUC ≈ 96%); metabotypes linked to glycaemia	Strong diet-metabolome association relevant to T2DM risk	Cross-sectional design; metabolomic signatures require replication
Walaszczyk et al. [18]	Multi-cohort EWAS; adults with and without T2DM	Glycaemic status (T2DM, fasting glucose, HbA1c)	Genome-wide CpG methylation associated with glycaemic traits; replication in blood	Identification of robust CpG markers (ABCG1, TXNIP, SREBF1, LOXL2, SLC1A5)	Core evidence that blood methylation signatures act as early epigenetic biomarkers	Blood-based EWAS; limited tissue specificity and causal inference
Nicoletti et al. [9]	Narrative review of human diet-epigenome studies	Mediterranean and plant-forward diets; key nutrients and bioactives	Diet-modulated methylation and ncRNAs regulating insulin and inflammation	Consistent improvements in metabolic markers across studies	Comprehensive synthesis of human evidence for diet-epigenome interactions	Narrative synthesis; heterogeneous evidence and no pooled estimates

Non-coding RNAs add another layer of control. Several miRNAs tied to insulin secretion, inflammation and oxidative stress, show altered expression in obesity and diabetes. Many respond to nutrients and metabolic stress, but their causal roles are still unclear [5, 31].

These findings point to a link between environmental exposures, especially diet and metabolic regulation, although most evidence is still associative and short-term, often based on small or homogeneous cohorts. Larger, long-term and multi-ethnic studies are needed to test whether epigenetic markers can improve prediction or prevention strategies[31, 32].

Diet-induced epigenetic modulation (nutriepigenomics). Nutriepigenomics examine how diet alters DNA methylation and histone states that regulate gene expression. These mechanisms may affect pathways relevant to T2DM, but most evidence is short-term, associative, and methodologically inconsistent. Much of the research also relies on blood samples rather than metabolic tissues, which limits mechanistic insight [25].

High-fat and high-fructose diets are consistently linked to methylation and histone patterns associated with impaired insulin signalling, disrupted lipid metabolism and hepatic inflammation [30].

Nutrient-dense diets appear to induce more favourable epigenomic signatures. Systematic reviews similarly highlight that personalised adaptations of Mediterranean-style diets may support metabolic regulation, although evidence remains preliminary and heterogeneous [33]. Pregnancy cohorts show similar diet-responsive marks in offspring, suggesting developmental sensitivity, although replication is still limited [34].

Specific bioactive nutrients – polyphenols, omega-3 fatty acids and other plant compounds – also influence methylation and histone modifications involved in insulin signalling, inflammation and oxidative stress [5, 35]. These effects are biologically plausible, but vary widely due to differences in laboratory methods and study designs.

Gut-derived metabolites add another regulatory layer. Short-chain fatty acids can modify DNA methylation and histone-deacetylase activity, linking fibre intake and microbiome composition to epigenetic control of inflammation and insulin resistance [28]. Individual responses to SCFAs, however, differ substantially.

Generally, diet can modulate epigenetic states relevant to metabolic health, but effect sizes are small, unstable, and difficult to reproduce. Long-term, multi-ethnic studies using standardised epigenetic platforms are required before nutriepigenomic findings can inform personalised nutrition or T2DM prevention strategies. Selected studies are synthesized in Table 1.

Integrative nutrigenomic-epigenetic strategies for prevention. Integrative prevention strategies combine genomic, epigenetic, metabolic, microbiome and physiological

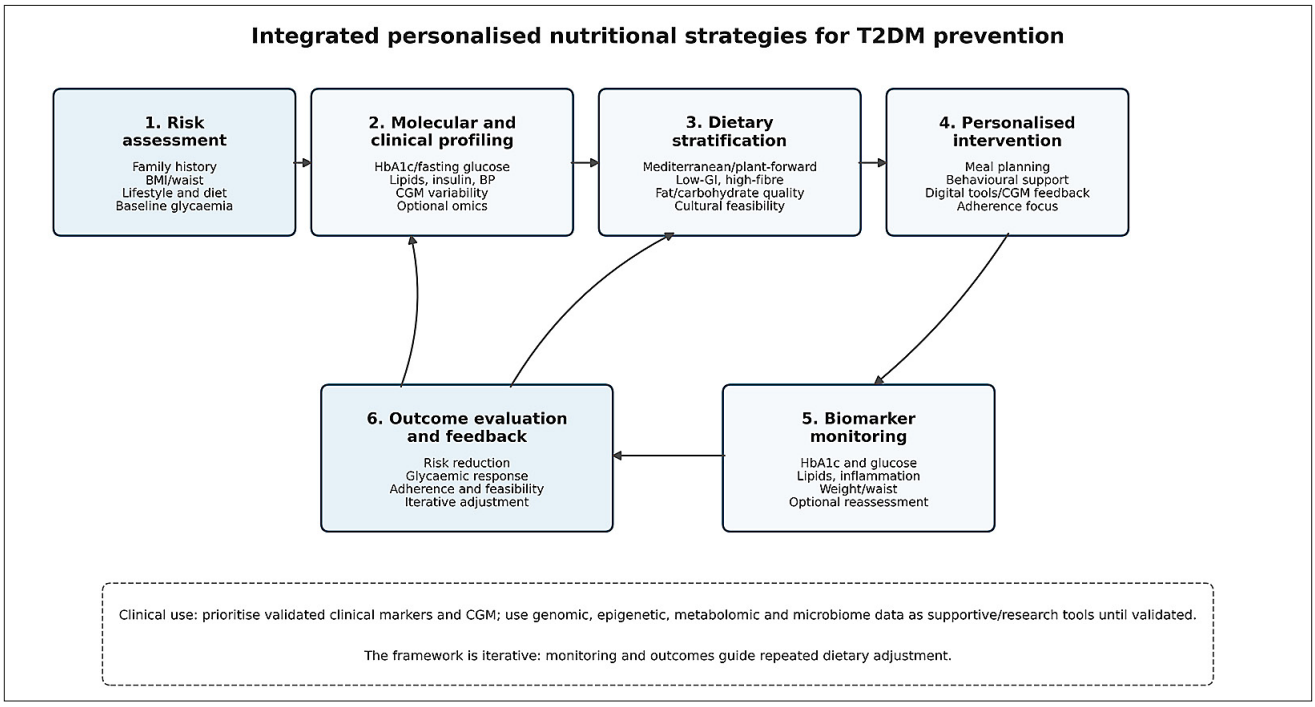

Figure 2. Integrated personalised nutritional strategies for T2DM prevention. The framework links clinical risk assessment, molecular and metabolic profiling, dietary stratification, personalised intervention, biomarker monitoring and outcome evaluation. In current clinical practice, validated clinical markers and CGM are more applicable than genomic, epigenetic, metabolomic or microbiome markers, which remain mainly supportive or research-oriented tools until further validation

data to refine dietary recommendations for T2DM. The goal is to identify patterns that predict who benefits most from specific nutritional approaches [13, 18, 36]. Personalised diets appear most effective when multiple data layers are used together. Individuals with high glycaemic variability respond better to tailored dietary advice than those with stable glycaemia [12, 16, 17]. Recent reviews emphasise that precision nutrition may improve metabolic risk factors in selected individuals, but population-level effectiveness remains limited and highly variable [37].

Behavioural and contextual factors also matter. Engagement, cultural fit and daily feasibility often determine whether personalised guidance leads to measurable metabolic gains [38]. Programmes that pair molecular information with structured support or digital tools show better adherence and more durable change [39].

New analytical methods strengthen these approaches. Personalised glycaemic sensitivity indices derived from n-of-1 CGM trials offer a practical way to map individual responses to foods without relying on complex multi-omics pipelines [40]. These metrics allow precise real-time dietary adjustments.

The majority of multi-omic models add little predictive value beyond simple physiological markers such as baseline glycaemia or CGM-derived variability. This raises questions about whether molecular complexity is necessary for effective prevention. Many integrative approaches also rely on small samples, short follow-up, and limited population diversity.

Large, long-term and multi-ethnic studies are needed to evaluate durability, scalability and cost-effectiveness [36]. Current evidence positions biomarker-guided nutrition as a promising direction for T2DM prevention, but rigorous validation is still required before broad implementation.

Limitations of the study. Evidence across studies is highly heterogeneous. Research designs, sample sizes, intervention duration and analytical platforms differ markedly, which limits comparability. Epigenetic data come from various methylation arrays, histone assays and sequencing pipelines, with each one producing different types of outputs. This lowers reproducibility and complicates cross-study interpretation [18]. Many nutrigenomic and nutriepigenomic results also come from small cohorts or secondary analyses with limited validation. Most signals are associative, and the observed patterns may also reflect the current metabolic status rather than shape it.

Population diversity is another major limitation. Most studies involve European, North American or East Asian cohorts. Ancestry shapes diet, microbiome composition, metabolic traits and epigenetic profiles, and limited representation restricts generalisability [13]. Few studies include under-represented groups, and very few stratify results by demographic or socio-economic factors.

Methodological inconsistency also limits conclusions. Prediction models, dietary algorithms and biomarker definitions vary widely across personalised-nutrition trials [12, 16, 17]. As a result, it is often unclear whether conflicting findings reflect real biological variation, or arise from analytical noise. Publication bias is also possible, as positive molecular findings are more likely to be reported.

Most studies lack long-term follow-up. It is also unclear whether diet-induced molecular changes persist, reverse, or translate into durable improvements in metabolic health. Without large, multi-ethnic and long-term trials, the mechanistic relevance of many findings remains uncertain.

Future perspectives. Future research should prioritise large, longitudinal, and multi-ethnic cohorts with repeated multi-omics measurements. Such designs are essential for

identifying causal diet and molecular relationships and separating signal from noise [18, 36]. Standardising platforms for DNA methylation, metabolomics and microbiome profiling is also essential. Without harmonised protocols, biomarkers cannot be compared across studies or translated into clinical practice.

CGM-derived phenotypes are becoming recognised as reliable markers of individual variability. Integrating CGM with epigenetic, metabolomic or microbiome data may improve prediction models; however, these models must show added value beyond simple physiological metrics [12]. Mendelian randomisation and causal modelling could help clarify whether observed molecular changes influence diabetes risk, or simply mirror metabolic dysfunction [41].

Future frameworks should also integrate behavioural and environmental information. Personalisation will fail if strategies ignore feasibility, cultural context, or long-term adherence. Cost, accessibility and equity must be assessed, as precision-nutrition tools may otherwise deepen existing health disparities.

Clinical implementations. Clinical translation is still limited. Most epigenetic, metabolomic and microbiome markers lack validated thresholds, show weak cross-platform reproducibility, and have not been confirmed in diverse populations. Because of this, current biomarker panels remain research tools rather than clinical instruments [18]. Commercial tests based on methylation or microRNA profiling should be interpreted with caution.

Metabolomics also faces clear practical barriers. Costs are high, methods differ across laboratories, and platforms generate signatures that cannot be directly compared. These issues restrict the use of metabolomics in routine screening or clinical decisions.

At present, the most useful tools for personalised care are simple and inexpensive. Fasting glucose, insulin, lipid profiles, inflammatory markers, anthropometry, and CGM, with CGM offering particularly strong value because it captures real-time responses to meals and does not require multi-omic testing [12]. Epigenetic data can support general counselling, but as yet are unable to guide individualised prescriptions.

Broader clinical adoption will require cheaper assays, validated cut-offs and clear workflows. Evidence must also show that molecular markers improve outcomes beyond standard clinical markers. Until then, precision nutrition should be considered promising, but still experimental.

Practical recommendations for clinicians. Current evidence does not support the routine use of commercial nutrigenomic, epigenetic, metabolomic or microbiome tests to prescribe individual diets for T2DM prevention. Clinicians should base personalised prevention on validated clinical risk factors, including family history, adiposity, waist circumference, blood pressure, fasting glucose or HbA1c, lipid profile and lifestyle behaviours.

Dietary counselling should focus on feasible, evidence-based patterns, particularly Mediterranean-style or plant-forward diets rich in fibre, whole grains, legumes, vegetables, nuts and unsaturated fats, while limiting refined carbohydrates, sugar-sweetened beverages and saturated fats. Recommendations should be adapted to patient preferences, cultural context, food access and long-term adherence.

CGM may be useful in selected high-risk individuals or those with early dysglycaemia to identify exaggerated postprandial responses, but it should complement rather than replace standard lifestyle counselling.

Follow-up should assess measurable outcomes, such as HbA1c or fasting glucose, body weight, waist circumference, lipids, blood pressure and adherence. Molecular biomarkers remain promising but should currently be considered research tools rather than routine clinical decision-making instruments.

CONCLUSIONS

Type 2 diabetes develops through the interplay of genetic risk and diet-driven metabolic and epigenetic changes. Studies across genomics, epigenetics, metabolomics and microbiome research show that diet can alter pathways linked to insulin resistance, inflammation and β-cell stress. These findings give personalised nutrition a strong biological basis, although their clinical value remains limited. Effects are often small, inconsistent, and difficult to reproduce across methods or populations. Multi-omic models rarely outperform simple measures such as fasting glucose or CGM variability. Many proposed biomarkers also lack validated cut-offs, long-term data or demonstrated clinical benefit.

Personalised dietary strategies may help individuals with early metabolic instability, but evidence is not yet strong enough for broad clinical use. Progress will depend on large, multi-ethnic and long-term studies that test whether molecular signatures improve prevention beyond standard dietary patterns. Until such data appear, nutrigenomic and nutriepigenomic markers should be viewed as early-stage scientific leads rather than clinical tools.

For now, nutrient-dense, plant-forward dietary patterns remain the most reliable and scalable approach to reducing T2DM risk.

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