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REVIEW ARTICLE

Nutrigenomics and Chronic Disease Management: Customising Diets for Type 2 Diabetes and Cardiovascular Health

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Abstract

The rising global prevalence of chronic diseases such as Type 2 Diabetes Mellitus (T2DM) and cardiovascular disease (CVD) has intensified the need for innovative and personalized strategies in disease prevention and management. Nutrigenomics, the study of the interaction between nutrition and the genome has emerged as a promising approach that bridges genetics, molecular biology, and dietary science. This review explores the application of nutrigenomics in customizing dietary interventions for individuals at risk of or living with T2DM and CVD, with a focus on optimizing metabolic health, reducing disease progression, and enhancing therapeutic outcomes.

The paper provides a comprehensive overview of the underlying genetic and epigenetic mechanisms that influence nutrient metabolism, insulin sensitivity, lipid profiles, and inflammatory pathways. It discusses how single nucleotide polymorphisms (SNPs), gene-diet interactions, and epigenetic modifications affect individual responses to macro- and micronutrients. Key genes such as TCF7L2, FTO, APOE, and PPARG are evaluated for their roles in glucose and lipid metabolism. Additionally, the review highlights evidence-based nutrigenomic strategies including high-fibre, low-glycaemic index diets; omega-3 fatty acid supplementation; and polyphenol-rich food consumption tailored to specific genetic profiles. The potential of nutrigenomics to guide precision nutrition, promote personalized dietary planning, and improve long-term outcomes in chronic disease management is critically analysed. Challenges such as ethical considerations, clinical utility, accessibility, and the integration of genetic testing into standard healthcare practices are also discussed. Ongoing research and clinical translation are essential to maximize its benefits and ensure equitable application in diverse populations. However, despite promising insights, inconsistencies in findings across populations and the limited translation of nutrigenomic data into clinical practice highlight ongoing research gaps. Addressing these limitations through large-scale, long-term studies is essential to strengthen evidence-based personalized nutrition

Keywords: Nutrigenomics, Type 2 Diabetes, Cardiovascular Disease, Precision Nutrition, Genetic Polymorphisms, Epigenetics, Dietary Intervention, Personalized Medicine

INTRODUCTION

1.1 Global Burden of Chronic Diseases: Focus on T2DM and CVD

Worldwide, chronic diseases also known as non-communicable diseases (NCDs)—have emerged as a significant public health issue [1]. Among the most often and lethally among these are Type 2 Diabetes Mellitus (T2DM) and Cardiovascular Diseases (CVD), including conditions such coronary artery disease, stroke, and hypertension. A great part of worldwide mortality and handicap is attributed to these disorders [2]. With T2DM and CVD representing a significant portion, NCDs according to the

World Health Organization—account for roughly 74% of worldwide fatalities. Besides causing early death, these diseases severely lower quality of life, impose great financial strain on people and healthcare systems, [3].

Marked by insulin resistance and high blood sugar levels, T2DM has surged recently—four decades[4]. According to projections from the International Diabetes Federation (IDF), more than 537 million people were living with diabetes in 2021; this figure is expected to climb steeply in next years, particularly in low- and middle-income nations. Alongside this, cardiovascular disease still ranks top worldwide cause of death, claimed to be almost 18 million annually, mostly from stroke and ischemic heart disease [5].

These illnesses are greatly connected to lifestyle elements including unhealthy dietary patterns, sedentary living, smoking, and too much alcohol consumption. Major causes of obesity, high blood pressure, abnormal cholesterol levels, and chronic inflammation are poor eating habits comprising great sugar, saturated fat, refined carbohydrates, and ultra-processed foods [6]. These factors then greatly raise both T2DM and CVD's risk. Apart from lifestyle elements, genetics also significantly influences who contracts these illnesses. Even with moderate lifestyle hazards, some people may have a hereditary susceptibility that renders them more vulnerable. Often neglecting these personal genetic variations, conventional prevention techniques and "one-size-fits-all" nutritional recommendations might help to explain why some people get illness despite following general dietary advice [7].

This developing awareness has sparked more curiosity about personalized nutrition, an approach which recommends diets based on a person's unique biological composition—particularly their genes [8]. Here is where nutrigenomics really matters. Nutrigenomics studies the interaction of genes with food and the resulting effects on health outcomes. It provides a road to customized meal plans that may more efficiently prevent and control chronic diseases like T2DM and CVD.

1.2 Emergence of Nutrigenomics in Precision Health

Nutrigenomics is the result of the crossroads of genomics—the study of genes and their functions—and nutrition science. It is grounded on the realization that our diet can affect gene expression and vice versa: our genes determine our responses to various nutrients. Personalized or precision nutrition—an approach that uses genetic information to direct dietary recommendations—is based on this two-way interaction.

Nutrigenomics has evolution in reaction to the constraints of conventional dietary recommendations [10]. Although general recommendations like "eat more vegetables" or "reduce saturated fat" have some merit, they don't explain why some people flourish on a low-carb diet and others don't, or why some people have negative reactions to high salt or sugar consumption while others are fairly unaffected. Often, these variations can be traced to DNA differences—single nucleotide polymorphisms (SNPs).

SNPs can influence proteins, receptors, and enzymes involved in the metabolism of nutrients such glucose, fat, and cholesterol by the body. By way of illustration:

- Variant in the TCF7L2 gene has been related to both higher risk of T2DM and modulation of the body's response to carbohydrate consumption [11].
- The APOE gene's polymorphism could change how lipids are handled by the body and perhaps raise cardiac disease risk.
- Obesity is linked to the FTO gene, which could affect people's reactions to high-fat diets [12].

Along with genetic diversity, epigenetics—that is, heritable alterations in gene expression not resulting from changes to the underlying DNA sequence—is of vital importance. Through mechanisms such as DNA methylation, histone modification, and non-coding RNAs, diet can affect these alterations. For example, whereas plant-based diets high in antioxidants might have the opposite impact, high-fat diets can alter gene expression in a way that promotes inflammation. Thanks to developments in data analysis, sequencing techniques, and genetic testing, it is now feasible to examine a person's genetic profile and adapt nutrition consequently. Particularly for chronic diseases that are greatly influenced by lifestyle and diet [14], this enables a proactive, tailored strategy to disease prevention and management.

Nutrigenomics is already being used in clinical and business environments; it offers more than only theoretical promise. Some businesses today provide genetic nutrition testing, giving people tailored dietary suggestions grounded in their DNA. With the aim of creating more successful and personalized treatment regimens, nutrigenomics is being included into studies on obesity, diabetes, cancer, and cardiovascular disease in medical research [10]. As the science develops, nutrigenomics is projected to be a foundation of precision health— a healthcare approach that seeks to prevent and control disease through very personalized

methods based on a person's genetic, environmental, and lifestyle elements. Its importance is especially evident in conditions like T2DM and CVD, where diet is central to both cause and treatment [15].

1.3 Objectives and Scope of the Review

This study looks at how nutrigenomics can be used to create individualized diets for controlling and avoiding Type 2 Diabetes and Cardiovascular Disease. It seeks to clarify how nutrients and genes interact and how this understanding might boost health results.

The review will ;

- Clarify how diet and genetics affect the onset of chronic disorders.
- Discuss Important genes connected to diabetes and heart disease should be emphasized.
- Examine the actual instances of gene-based dietary suggestions.
- Handle the difficulties and moral questions raised by applying nutrigenomics.
- Investigate personalized nutrition's future, including research developments and technology.

This review aims to demonstrate how nutrigenomics can help us transition from generic diet regimens to more successful, personalized health plans, therefore providing better tools to address two of the most urgent health concerns of our day. Although nutrigenomics presents exciting opportunities, evidence supporting its widespread clinical use remains inconclusive. Studies often vary in methodology, population diversity, and measurement of gene–diet interactions. These variations create uncertainties in translating research outcomes into consistent dietary recommendations.

2. Nutrigenomics: Mechanisms and Concepts

The scientific investigation of how nutrition and food affect gene expression is known as nutrigenomics; it also examines how an person's genetic make-up modulates the body's reaction to dietary components. A major pillar of nutritional genomics, which also comprises nutrigenetics—the study of how genetic variations influence nutrient metabolism [16]. While nutrigenomics investigates how nutrients function as signals interacting with the genome to control physiological processes, nutrigenetics looks at inherited predispositions to dietary responses. Taken together, they form a basis for personalized nutrition, which lets dietary suggestions be modified to individual genetic profiles for better health results [8].

This discipline is based on the concept that nutrients are bioactive molecules as well that can influence gene expression at many levels, including transcription, translation, and post-translational modifications. Several processes—such as the activation of transcription factors, modulation of enzyme activity, changes in hormone signaling, and epigenetic changes—underlie these interactions [17]. Consequently, dietary consumption might affect biological processes linked to inflammation, metabolic control, cell repair, and disease risk.

Mechanisms of Nutrient-Gene Interaction

1. Transcriptional Regulation :Nutrients can serve as ligands for nuclear receptors controlling gene transcription meddling [18]. A well-known example are the peroxisome proliferator-activated receptors (PPARs), a family of nuclear receptors driven by dietary lipids. Once activated, PPARs affect the expression of genes implicated in inflammation, glucose homeostasis, and lipid metabolism—all of which are central to the pathophysiology of Type 2 Diabetes and Cardiovascular Disease [19].

2. Epigenetic Modification: Epigenetics is the study of inheritable variations in gene expression not resulting from changes to the DNA sequence itself. Diet can affect epigenetic patterns by:

- DNA methylation : This is fueled by nutrients like folate, vitamin B12, and methionine, which supply methyl molecules required for this process [20].
- Histone Modification : Compounds like butyrate, generated from dietary fiber fermentation, might affect histone acetylation, therefore influencing chromatin structure and gene expression.
- MicroRNAs (miRNAs) : Some bioactive dietary substances control miRNA expression, hence affecting mRNA translation and degradation [21].

3. Nutrient Sensing Pathways: multiple signaling routes react to nutrient availability and control metabolic processes through Nutrient-Sensing Pathways. For instances mTOR pathway, sensitive to amino acids and glucose activated by energy stress and exercise, AMPK pathway SIRT1 pathway, affected by polyphenols like resveratrol and caloric consumption. These nutrient-sensing systems help balance anabolic and catabolic activities; their dysregulation is thought to underlie insulin resistance, obesity, and cardiovascular dysfunction [22].

Concepts in Nutrigenomics

Gene-diet interactions suggest that not every person reacts the same way to dietary changes. A low-fat diet, for instance, could reduce cholesterol in certain people but raise triglycerides in others. Many times, polymorphisms in genes implicated in lipid and glucose metabolism drive this variation [23]. Tailoring dietary regimens to unique requirements depends on knowledge of these gene-diet interactions.

Single Nucleotide Polymorph: They can change metabolic gene expression, transporter activity, receptor binding, or enzyme activity [24]. SNPs that have been well studied include:

- TCF7L2 influences glucose metabolism and insulin secretion.
- FTO: Response to energy intake; related to obesity.
- APOE : Apolipoprotein E influences lipid metabolism and modulates cardiovascular risk.

Gene expression profiling: Dietary changes allow scientists to use modern technologies such RNA sequencing, microarrays, and proteomics to observe changes in gene expression [25]. These profiles reveal how particular nutrients influence molecular pathways and disease processes.

Nutrigenomics is a revolutionary method for grasping the molecular interactions between nutrition and illness. This discipline presents interesting possibilities for individualized therapies in chronic diseases such Type 2 Diabetes and Cardiovascular Disease by investigating how nutrients affect gene expression and how genetic variations influence dietary responses. Application of nutrigenomic concepts goes beyond broad dietary recommendations to allow precise nutrition that more closely matches an person's biology, hence enhancing therapeutic results and preventive measures [27].

2.2 Genetic Variants Influencing Nutrient Metabolism in Type 2 Diabetes and Cardiovascular Disease

Genetic variation greatly affects people's nutrient metabolism and dietary response [28]. Although major contributors to the cause of Type 2 Diabetes Mellitus (T2DM) and Cardiovascular Disease (CVD) are modifiable lifestyle variables including diet, exercise, and stress, they do not completely account for the inter-individual variations in disease presentation and progression. Particularly in the area of nutrient metabolism, insulin signaling, lipid transport, and inflammatory pathways, increasing proof points to genetic predisposition—especially single nucleotide polymorphism (SNPs)—as source of much of this variability [29]. Finding these genetic markers allows for the creation of more focused, individualized dietary treatments for the prevention and control of chronic illnesses made possible by nutrigenomics.

Regarding T2DM, one of the most often researched genetic variation found in the transcription factor 7-like 2 (TCF7L2) gene is [30]. Imaired beta-cell activity and lowered insulin secretion have both been linked to this variant. Particularly carriers of the T variant of rs7903146, those who carry the risk allele tend to have greater fasting glucose levels and a higher risk of acquiring diabetes. Both of which help to control postprandial glucose excursions, these people seem to gain more from eating patterns stressing low-glycemic index carbs and high fiber consumption. SLC30A8 is another gene of interest since it encodes a zinc transporter vital for insulin granule activity. Gene polymorphisms can inhibit insulin secretion, and mounting data indicate that a zinc-rich diet could help to partially counteract this metabolic impairment.

Although indirectly, the fat mass and obesity-associated gene (FTO) is critically important in T2DM [32]. This gene affects adiposity, energy expenditure, and appetite control. Often in reaction to a high-calorie, low-nutrient diet, carriers of the risk allele tend to consume more food. Low-fat, high-protein diets that assist manage caloric intake and increase insulin sensitivity usually work best for these people. KCNJ11 and ABCC8, two other genetic contributors, encode subunits of potassium channels implicated in the control of insulin secretion. Variant forms of these genes can aggravate glycemic reactions to carbohydrate-rich diets, hence increasing the risk of chronic hyperglycemia if diet is not adequately controlled.

Genetic variables regulating lipid metabolism, vascular function, and oxidative stress greatly affect cardiovascular disease as well. Apolipoprotein E (APOE) is one of the most well-known genes in this field. Each of the three main APOE isoforms—E2,

E3, and E4—differentially influence cholesterol metabolism and lipid transport. Carriers of the E4 allele run increased risk of elevated low-density lipoprotein (LDL) cholesterol levels and CVD. Compared to E2 or E3 carriers, these people have exhibited a more marked reaction to low-saturated fat, low-cholesterol diets [35]. At the same time, the CETP gene—especially the Taq1B polymorphism (rs708272)—affects HDL metabolism. Although certain strains are linked to lower HDL levels and higher atherogenic risk, dietary patterns heavy in monounsaturated fats, such as those in olive oil, have shown therapeutic promise in this subgroup [36]. While these associations are well-documented, conflicting results exist in some populations, possibly due to differences in dietary habits, ethnic background, and sample size. For instance, the influence of the APOE E4 allele on lipid metabolism is not uniform across regions, and not all FTO variants exhibit strong links with obesity when lifestyle factors are controlled. These discrepancies underscore the need for more standardized, population-based studies.

Table 1: Key Genes and Their Nutritional Implications in T2DM and CVD

Gene	Associated Condition	Impact on Metabolism	Nutritional Recommendation
TCF7L2	Type 2 Diabetes	Affects insulin secretion and glucose metabolism	Low-GI, high-fiber carbohydrates
FTO	Obesity, T2DM	Influences appetite, energy balance	Low-fat, high-protein diets
APOE (E4)	Cardiovascular Disease	Alters lipid transport and LDL levels	Low-saturated fat, cholesterol-lowering diet
MTHFR	Cardiovascular Disease	Impairs folate metabolism, raises homocysteine	Increase folate, B12, and B6 intake

Despite these gene–diet insights, a critical challenge is the lack of replication in diverse ethnic groups and the limited use of randomized controlled trials. Most findings stem from observational research, which cannot establish causation. Future studies should focus on validating gene–diet relationships through interventional designs. The MTHFR gene is another hereditary determinant of cardiovascular wellness. Common polymorphism C677T decreases enzymatic activity and disrupts folate metabolism, so increasing homocysteine levels—a recognized risk factor for vascular damage [37] Counteracting these impacts often calls for dietary supplements high in folate, vitamin B12, and other methyl donors. Furthermore implicated in hypertension and endothelial dysfunction is the nitric oxide synthase 3 (NOS3) gene, which controls vascular tone via nitric oxide generation. Variants that disrupt this function might find diets rich in nitrates, antioxidants, and omega-3 fatty acids helpful for enhancing vasodilation and lowering cardiovascular risk [38].

Along with dietary information, these genetic variations provide the basis for precision nutrition techniques meant to prevent and control chronic illnesses [39]. Genomic screening can identify people with risk alleles, and personalized dietary advice helping to maximize metabolic results will be given to them. Although ethical issues, cost, and access still present difficulties, the data increasingly favors including nutrigenomic knowledge into clinical nutrition. This developing paradigm is a major break forward in the personalization of chronic disease management since it not only recognizes genetic variability in nutrient responses [40].

2.3 Epigenetic Influence of Diet On Metabolic Regulation

Epigenetics is the study of changes in cellular phenotype or gene expression that exclude changes to the base DNA sequence. These changes can be affected by environmental elements including diet, stress, and toxins, and they are hereditary. Epigenetic mechanisms have become a focus of great investigation in relation to chronic diseases like Type 2 Diabetes Mellitus (T2DM) and Cardiovascular Disease (CVD), so providing insight into how environmental exposures, especially nutrition, might affect gene function. Key metabolic processes connected in insulin sensitivity, lipid metabolism, inflammation, and vascular function can be influenced by epigenetic changes [42]. Knowing how diet affects these epigenetic processes helps one to take a fresh perspective on individualized nutrition and illness prevention, therefore underlining the relevance of gene-environment interactions in metabolic regulation.

Epigenetic mechanisms: non-coding RNAs, histone modifications, DNA methylation.

Three main epigenetic mechanisms—DNA methylation, histone modifications, and non-coding RNAs (ncRNAs)—control gene expression are these. All of these systems may be affected by dietary elements [43] and are essential in regulating the activity of genes involved in metabolic processes.

DNA Methylation

Among the most often researched epigenetic changes is DNA methylation. Usually occurring in the context of CpG dinucleotides, this involves the addition of a methyl group to the 5' position of the cytosine base. While demethylation can stimulate gene expression, methylation of gene promoter regions usually causes gene silencing. In T2DM and CVD, changed DNA methylation patterns have been seen in genes modulating inflammation, lipids metabolism, and insulin sensitivity [44]

Given that these nutrients are part of the one-carbon metabolism pathway that produces methyl groups, dietary components including folate, vitamin B12, and methionine have major roles in controlling DNA methylation. Global hypomethylation, which has been related to higher pro-inflammatory gene expression and hence insulin resistance and vascular impairment [42], can result from a lack of these nutrients. Studies have found, for instance, that those with high homocysteine levels—an indicator of poor methylation—are more likely to have CVD and T2DM. It has been suggested that dietary changes including folate and B-vitamin consumption help to restore normal DNA methylation patterns and so lessen these impacts [45].

Histone modifications.

In addition to undergoing many chemical modifications affecting gene expression, histone proteins help package DNA into a condensed, structured form known chromatin. These changes—ubiquitination, phosphorylation, methylation, and acetylation—affect the chromatin structure and hence the DNA's availability for transcription. For instance, whereas histone methylation can either activate or suppress gene expression depending on the particular setting, histone acetylation is typically connected with gene activation.

Polyphenols, short-chain fatty acids (SCFAs), and some amino acids are among the dietary elements that could affect histone modifications [47]. For example, the polyphenol resveratrol found in red wine and grapes has been demonstrated to stimulate histone acetylation, therefore increasing the expression of metabolism control and antioxidant defense genes. Produced by gut fiber fermentation, the SCFAs butyrate and propionate have also been shown to enhance insulin sensitivity and control histone acetylation. For people with T2DM, a diet high in fiber and polyphenols might assist control histone marks related with inflammation, insulin resistance, and lipid dysregulation [48].

Non- Coding RNAs

Another category of epigenetic modifications are non-coding RNAs (ncRNAs), including microRNAs (miRNAs) and long non-coding RNAs (lncRNAs), which influence gene expression without changing the DNA sequence [43]. Small RNA molecules known as miRNAs can attach to messenger RNA (mRNA), therefore inhibiting protein synthesis from it. Many metabolic routes, including glucose and lipid homeostasis, are regulated by these tiny RNAs. In relation to T2DM and CVD, miRNAs have been shown to affect inflammatory reactions, fatty acid oxidation, and insulin signaling [49].

miRNA expression can be regulated by dietary components such omega-3 fatty acids, polyphenols, and vitamin D [50]. For instance, dietary omega-3 fatty acids from fish and some plant oils have been demonstrated to affect miRNA expression connected to lipid metabolism and insulin sensitivity. Likewise, polyphenols from vegetables and fruits can affect miRNAs targeting inflammatory cytokines and adipogenesis, therefore important causes of metabolic impairment in obesity and T2DM. Though less researched, long non-coding RNAs are starting to be important regulators of metabolic pathways, especially in relation to vascular health and fat storage [51]. Diet affects these ncRNAs, which have been demonstrated to control gene expression in reaction to nutritional signals.

Epigenetic Influence of Diet on Insulin Sensitivity and Glucose Metabolism

Diet interacts with epigenetic control most importantly in the regulation of insulin sensitivity and glucose metabolism, whereby A prominent feature of T2DM is insulin resistance, which results from a complicated interaction between genetic susceptibility and environmental elements—including food.

Recent research has underscored how epigenetic changes in genes related to insulin signaling might result from dietary habits. For instance, studies reveal that a high-fat diet changes DNA methylation patterns in the insulin receptor gene (INSR) and downstream signaling proteins like IRS1 (Insulin Receptor Substrate 1), therefore lowering insulin sensitivity [53]. Likewise, dietary fat consumption has been shown to affect histone modifications in the promoter regions of genes involved in glucose intake and fatty acid oxidation, including PPARalpha (Peroxisome Prolifer-Activated Receptor Alpha). These changes can either encourage or inhibit the expression of genes controlling glucose metabolism, hence aggravating insulin resistance [54].

Conversely, it has been demonstrated that diets high in polyphenols, fiber, and good fats (such as omega-3 fatty acids) reverse these epigenetic modifications, so restoring correct insulin signaling and enhancing glucose homeostasis [21]. For instance, favorable DNA methylation patterns in insulin signaling genes and better insulin sensitivity have been connected with the Mediterranean diet, rich in monounsaturated fats, fruits, and vegetables [53]. Similarly, epigenetic modulation of essential metabolic genes by whole grains and soluble fiber helps to improve insulin sensitivity.

Epigenetic Influence of Diet on Lipid Metabolism and Cardiovascular Health

Epigenetic regulation also plays an important part in lipid metabolism, which is closely connected to heart disease. Atherosclerosis happens when cholesterol and other things start to build up in your arteries, and this mostly comes from problems with how your body handles fats and when there's too much inflammation in the body [55]. Several genes that are important for breaking down fats can be affected by chemical changes in DNA, which means changes in the diet can easily influence these genes.

One of the key genes in lipid metabolism is the LDL receptor (LDLR), which helps get rid of LDL cholesterol from the blood. Epigenetic changes to the LDLR gene promoter, like adding a methyl group to DNA or changing the way histones are decorated, can affect how much LDL cholesterol is in the blood. Diets high in saturated fats can make these changes worse by lowering the amount of LDL receptors and causing more LDL to be found in the blood [56]. In contrast, eating foods with monounsaturated fats (like olive oil) or omega-3 fatty acids can help reverse these epigenetic changes, which means that they help make more LDLR in the body and improve the way cholesterol is cleared out.

Furthermore, inflammation is a main part of CVD, and changes in what you eat can affect the way your body makes certain signs of inflammation, like TNF-α and IL-6 [57]. High-fat and high-sugar diets can change how certain genes work, leading to ongoing low-level inflammation in the body, which is a big reason that blood vessel problems and hardening of the arteries happen. Conversely, eating foods that are full of antioxidants, like fruits, vegetables, and green tea, can help keep these epigenetic marks in check and reduce inflammation in the body, which can make your heart health better [58].

Nutritional Interventions Targeting Epigenetic Modifications

Nutritional strategies that focus on changing specific gene marks may help manage and prevent T2DM and CVD. As research into the epigenetic effects of diet keeps growing, a few key things in what we eat have been shown to have a big impact.

Folate and other B-vitamins are important to keep the right DNA methylation patterns going. These nutrients take part in something called the one-carbon metabolism pathway, which helps make the methyl groups that tell DNA how to change or stay the same. Ensuring you get enough folate, vitamin B12, and vitamin B6 can help keep your methylation in good shape and lower your risk for things like insulin resistance and heart problems [60].

Polyphenols, which are found in lots of fruits, veggies, tea, and red wine, are another important part of the diet that can affect how our genes are turned on and off. According to evidence, they are linked to altered histone modifications and miRNA levels, helping insulin, lipids, and inflammation work more optimally. Resveratrol, which you can find in grapes, has been found to help some proteins called histones become more active and turn on genes that help protect your body from damage caused by free radicals, also helping you with things like weight and diabetes [61].

Table 2: Dietary Components and Epigenetic Effects

Dietary Component	Epigenetic Mechanism	Gene Targets / Effects	Disease Relevance
Folate, B12, Methionine	DNA methylation	Supports methylation of metabolic and inflammatory genes	Reduces T2DM and CVD risk
Polyphenols (e.g., resveratrol)	Histone modification	Activates antioxidant and insulin-sensitizing pathways	Enhances insulin sensitivity and heart function
Omega-3 Fatty Acids	miRNA modulation	Downregulates inflammatory gene expression	Lowers systemic inflammation and CVD risk
Fiber (via SCFAs)	Histone acetylation	Improves lipid metabolism and insulin signaling	Manages obesity, T2DM, and metabolic syndrome

However, much of the current evidence linking dietary components to epigenetic modulation remains correlational. Few studies have evaluated whether these epigenetic changes persist long-term or translate into measurable clinical improvements. Moreover, differences in laboratory methods and tissue-specific methylation patterns complicate comparisons between studies. The role of fiber in influencing epigenetics has been shown in a lot of studies. The breakdown of dietary fiber in the gut generates SCFAs, which manage histone acetylation and increase how well the body responds to insulin [62]. Additionally, high-fiber diets have been found to change the way certain small molecules work in our bodies, like those involved with how our body deals with fats and inflammation, which further supports that eating more fiber may help prevent metabolic diseases.

PERSONALIZED NUTRITION FOR TYPE 2 DIABETES AND CARDIOVASCULAR HEALTH

Personalized nutrition, also called precision nutrition, is a new area that uses things like a person's genes, environment, metabolism, and gut bacteria to make careful diet plans that might help each person stay healthier [63]. With more people getting chronic diseases like Type 2 Diabetes and heart problems, doctors and health experts need to come up with different diets that help with the main causes of these illnesses, instead of just giving everyone the same advice that might not work for everyone. Personalized nutrition gives doctors and nurses a better way to help manage diseases because they can look at each person's own genes, how their body works, and any other factors that affect their health.

T2DM and CVD are complicated diseases that depend on both someone's genes, the way they live, and things in their environment. As both conditions are related to things like having trouble with insulin, problems with fats in the body, ongoing inflammation, and issues in the blood vessels, personalized nutrition tries to help by changing what people eat so their bodies can handle these issues better and lower the chances of getting sick. The foundation of personalized nutrition is based on measuring how people's bodies work and react differently, and using that information to help come up with better meal plans for each person.

3.1 Principles of Personalized Nutrition

Personalized nutrition focuses on the belief that everyone's body responds differently because of their personal genes and metabolism [39]. Things such as genes, epigenetic influences, rates of metabolism, the body's ability to take in nutrients, and the types of microbiota in the gut can all guide a person's nutrient digestion. Understanding these differences, personalized nutrition strives to give better diet advice that helps prevent or treat chronic diseases [40].

Genetic Factors and Dietary Response

How people metabolize and react to food is strongly affected by genetics. Changes in specific genes for absorption, metabolism, and transport may improve or reduce the way the body handles all three macronutrients [64]. For example, variations in the FTO gene, involved in fat storing, have been observed to affect the risk for obesity and T2DM in some people. Being aware of these genetic predispositions can guide dietary changes to help each person get the right nutrients [40].

Furthermore, changes in the TCF7L2 and other related genes can increase a person's risk of insulin resistance and T2DM [65]. With genetic testing, personalized nutrition advice can pinpoint which people might face a higher risk of these problems and advise lessening their carbohydrate intake to better control their blood glucose.

Epigenetic Modifications and Dietary Influence

In addition to genetics, how individuals respond to changes in their diet is strongly influenced by epigenetics, which explores changes in the way genes are turned on or off without changing the DNA [66]. For example, changes to DNA, histones, or expressions of non-coding RNA can lead to transformation in metabolic functions like using glucose, oxidizing lipids, and managing the body's inflammatory system.

In fact, some studies have revealed that what we eat can change our genes and determine whether insulin resistance, lipid metabolism, or inflammation is activated or prevented. By looking at someone's epigenetics, we can suggest the dietary options that most influence important genes linked to metabolic diseases [40]. A diet rich in fats can cause changes in DNA methylation on insulin receptors, which may increase insulin resistance. Diets rich in polyphenols, fiber, and antioxidants can, instead, return the affected gene expression to its previous state.

3.2 Role of the Gut Microbiome In Personalized Nutrition

Research has shown that the gut microbiome is a major contributor to how people react to food. The microorganisms in the gut microbiome (bacteria, fungi, viruses, and archaea) are responsible for digestion, absorbing nutrients, and regulating metabolism in our bodies [67]. Researchers now realize that having a different composition of gut bacteria may lead to someone being more likely to develop metabolic illnesses.

The microbiome is involved in metabolic health by aiding in digesting and fermenting dietary fiber, producing SCFAs, regulating hormones related to digestion, and interacting with the immune system [67]. Certain gut microbes are linked to better insulin response and reduce signs of inflammation, whereas others are tied to insulin resistance and related health problems like obesity and unhealthy cholesterol levels. Researchers have linked an overabundance of Firmicutes bacteria to being overweight and having problematic insulin levels. [67]

With this knowledge, personalized nutrition can work to create nutrition plans that nurture your gut microbiome. To support the health of individuals with T2DM or CVD, it is recommended to add more fiber, eat foods containing prebiotics and probiotics, and add polyphenols and omega-3 fatty acids to the diet [68]. Making these changes to your diet could make you more insulin sensitive, lessen inflammation, and protect your heart.

The Microbiome and Food Sensitivity

Also, the bacteria in the gut play a role in food metabolism, and this could explain why some people's bodies handle certain diets differently from others [67]. Invistigating someone's gut microbe profile can guide recommendations of foods that are healthy for both the gut and metabolic processes. If someone has an imbalanced gut microbiome, probiotics or extra-fiber foods may help, but those with dysbiosis might need additional changes in their diet.

3.3 Tailoring Diet for Type 2 Diabetes and Cardiovascular Disease

Personalized nutrition could play a major role in helping to control and prevent T2DM and CVD. Based on a patient's genetic, epigenetic, and microbiome information, healthcare providers may target and fix the causes of metabolic issues for each patient [40]. Using this targeted way can help manage diseases more effectively and ensure people enjoy better health.

Type 2 Diabetes

The main aim of personalized nutrition in T2DM individuals is to increase insulin responsiveness, bring glucose levels back to normal, and stop neuropathy, retinopathy, and heart complications caused by the disease. Recommending diets that are free of refined carbohydrates and loaded with fiber and healthy fats can help improve how the body handles glucose and insulin [68]. Genetic variations may also be considered in personalized nutrition, helping ascertain that a person's diet is tailored for how their body uses certain nutrients.

Getting genetic information on insulin receptors may allow nutritionists to suggest meal schedules and the best meal types [69]. If epigenetic analysis reveals that someone is prone to diet-related insulin resistance, their diet plan may be changed to help improve their condition. Increasing the amount of polyphenols from fruits and vegetables, or omega-3 fatty acids from fish, is a possible way to enhance glucose metabolism for those who are at risk due to their genes.

Cardiovascular Disease

To manage CVD, personalized nutrition is meant to help reduce inflammation, improve ways lipids are handled in the body, and strengthen blood vessels. Diet may be tailored to help lower cholesterol, support the heart's blood vessel function, and reduce the chance of atherosclerosis [70]. The diet may include a higher amount of omega-3s, antioxidants, and fiber, and less saturated and trans fats, along with refined sugar.

Epigenetic information might be used in specially designed diets to control genes associated with lipids and inflammatory factors [70]. For those genetically vulnerable to having high LDL cholesterol, diets that encourage the activity of the LDL receptor gene can be useful in removing extra cholesterol from the body.

Table 3: Personalized Diet Strategies for T2DM and CVD

Genetic/Epigenetic Trait	Recommended Dietary Adjustment	Expected Benefit
TCF7L2 variant carriers	Emphasize low-GI carbs, increase soluble fiber	Improved glycemic control and reduced post-meal glucose
APOE E4 allele	Reduce saturated fats, prioritize omega-3s and fiber	Lower LDL, reduced cardiovascular risk
MTHFR C677T polymorphism	Boost folate, B12, B6 intake	Normalize homocysteine levels, protect vascular health
Gut microbiota imbalance (dysbiosis)	Add prebiotics, probiotics, fiber, and polyphenol-rich foods	Enhanced insulin sensitivity, reduced inflammation

Although these personalized dietary approaches are promising, there are limitations to their practical application. Genetic testing remains expensive and inaccessible in low-resource settings. Additionally, psychological and cultural factors influencing dietary adherence are often overlooked in precision nutrition models. Hence, real-world implementation requires multidisciplinary support and cost-effective strategies.

THE ROLE OF DIET IN MODULATING INFLAMMATION AND INSULIN RESISTANCE

To make personalized nutrition better, we should combine genetic, epigenetic, and microbiome information to help plan person-specific diets. With progress in the study of nutrigenomics, better and safer diets can be made for the prevention and care of chronic diseases including T2DM and CVD [40].

Thanks to continuous glucose monitors and advanced forms of metabolomics and genetics, it is possible to measure a person's metabolic status in real time. With this information, advice on what to eat can be updated regularly, helping to achieve the very best health outcomes. Also, as we learn more about how the gut microbiome affects both diseases and health maintenance, the potential for new products becomes clearer and it leads to more personalized and holistic dietary strategies [66]. Applying recent advances in genetics, epigenetics, and the microbiome to food technology could make personalized nutrition a breakthrough in T2DM, CVD, and similar metabolic disease management.

Personalized nutrition could help a lot in managing and preventing chronic diseases like Type 2 Diabetes and Cardiovascular Disease. Considering a person's genes, epigenetic factors, and microbiome helps healthcare providers create diet plans that tackle the main problems behind metabolic dysfunction [67]. Using this method allows doctors to focus more on an individual's needs and possibly lead to better outcomes and improved living conditions. With ongoing research, personalized nutrition will help more people prevent and deal with chronic diseases and manage them properly by choosing what to eat.

T2DM and CVD have been linked to inflammation and insulin resistance [71]. Chronic low-grade inflammation is considered central because it both causes insulin resistance, makes glucose metabolism irregular, and leads to changes in lipids. The food we eat helps manage inflammation and the body's sensitivity to insulin, as some diets and nutrients can promote these functions while others can stop them.

4.1 Inflammation and Insulin Resistance

A lot of inflammation results as an immune response to various conditions, but ongoing and mild inflammation can negatively impact metabolic function. In metabolic diseases such as T2DM and CVD, the persistent inflammation in the body is important for causing insulin resistance, a significant characteristic of these diseases [71]. Insulin resistance takes place when the body does not respond properly to insulin, a hormone that controls blood glucose [72]

Many inflammatory proteins such as TNF-α, IL-6, and CRP are found in greater amounts in people who are insulin resistant. Cytokines can impact the way insulin acts by activating certain serine/threonine kinases, these kinases impact the function of insulin by preventing the insulin receptor substrate from being phosphorylated. The suppression of insulin signaling makes it more difficult for cells to take in sugar from the blood, which causes high blood sugar and insulin resistance [73].

Moreover, inflammation causes an increase in visceral fat, and the fat then produces pro-inflammatory adipokines, making insulin resistance even worse. Along with causing weight gain, continuous chronic inflammation may damage the mitochondria, cause more oxidative stress, and alter lipid metabolism, all of which result in insulin resistance.

4.2 Diet-Induced Modulation of Inflammation

A balanced diet can influence how much inflammation exists in the body, and there are nutrients that either increase or decrease inflammation. A nutrient-dense anti-inflammatory diet can effectively reduce inflammation, making the body more sensitive to insulin, as opposed to a diet full of pro-inflammatory foods [74]

4.2.1 Omega-3 Fatty Acids and Inflammation

Fat found in salmon, mackerel, sardines, flaxseeds, and walnuts (omega-3 fatty acids) are known to possess anti-inflammatory properties [75]. They are changed into resolvins and protectins, which help the body reduce inflammation and support the repair of tissue. Various studies indicate that omega-3 fatty acids help reduce the number of pro-inflammatory cytokines, like TNF-α and IL-6, while at the same time increasing the number of anti-inflammatory cytokines. Omega-3 fatty acids help to enhance insulin sensitivity through better performance of endothelial cells, lower levels of oxidative stress, and the effective regulation of adipokines [75]. In people with both T2DM and CVD, taking omega-3 supplements improves their insulin response, decreases triglycerides, and minimizes cardiovascular issues. As a result, eating foods rich in omega-3s may help reduce inflammation and improve insulin resistance.

4.2.2 Fiber and Inflammation

Fiber found in fruits, vegetables, legumes, and whole grains has a major role in lowering inflammation. Eating soluble fiber causes it to form a gel in the gut, which helps slow the release of blood sugar into the bloodstream. In this way, the inflammation and insulin resistance linked to high blood sugar are less likely to happen, and gut chemicals known as SCFAs help fight inflammation. SCFAs control the amount of pro-inflammatory cytokines and increase how well the gut lining prevents endotoxins from reaching the blood and starting inflammation around the body.

Additionally, fiber works to reduce LDL cholesterol and triglycerides, and these levels are important for keeping T2DM and CVD at bay. Boosting the amount of fiber you get from whole plant foods can reduce inflammation and help improve how sensitive your body is to insulin.

4.2.3 Antioxidants and Anti-inflammatory Foods

Taking in vitamins C and E, polyphenols, and flavonoids as part of your diet can lower oxidative stress and aid in fighting inflammation and insulin resistance [74]. If the levels of free radicals become higher than those of antioxidants, it results in the damage of cells and an increase in inflammation. When we take in antioxidants, they can reduce the oxidative damage that causes inflammation.

Berries, cite fruits, leafy greens, and vegetables from the crucifer family areespecially good sources of antioxidants. In addition, when people add spices to their diet like turmeric and ginger, they may decrease indications of inflammation such as CRP and IL-6 [78]. Including plenty of colorful fruits and vegetables in your diet can help your body fight inflammation, become more sensitive to insulin, and reduce the risk of many chronic diseases.

4.2.4 Mediterranean Diet and Inflammation

Eating a Mediterranean diet rich in these foods has been linked to lower levels of inflammation and beneficial changes in metabolism. Because of its high content of omega-3 fatty acids, antioxidants, fiber, and polyphenols, this diet helps to reduce inflammation and improve how the body uses insulin [79].

Many studies have shown that sticking to the Mediterranean diet leads to decreased levels of systemic inflammation, as indicated by changes in CRP and IL-6. Adhering to the Mediterranean diet can enhance insulin sensitivity, bring blood glucose down, and reduce the chance of T2DM and CVD [79] Thus, following this diet can help those at risk of these conditions.

4.3 Diet-Induced Insulin Resistance and Inflammation

There are diets that slow down inflammation and make insulin control better, though some types of foods worsen both. Over-consuming refined carbohydrates, trans fats, and saturated fats in the diet is linked to problems like inflammation, insulin

resistance, and a higher risk of T2DM and CVD [80]. They can trigger pro-inflammatory cytokines, cause oxidative stress, and upset the way lipids are metabolized in the body, which leads to insulin resistance.

4.3.1 High Glycemic Index Foods

Foods that have a high GI index, including white bread, sugary cereals, and sugary drinks, cause blood sugar levels to go up very fast. These high blood glucose levels can cause an inflammatory response because they lead to increased formation of AGEs, which harm blood vessels and tissues. The frequent consumption of high-GI foods may over-provoke the pancreas, causing it to release more insulin, which is connected to the rise of metabolic problems [81].

4.3.2 Trans Fats and Saturated Fats

Trans fats found in foods that are processed or fried, and saturated fats found in beef and dairy, both increase the risk of inflammation and insulin resistance. Eating these fats may cause the secretion of cytokines that create inflammation and interfere with how insulin works [82]. Eating too many trans and saturated fats is linked to an increased risk of obesity, T2DM, and CVD, so cutting down on these fats is very important for metabolic health. It is important to note that some intervention studies have reported mixed outcomes regarding the impact of low-fat or low-carb diets on inflammation and insulin sensitivity. This inconsistency highlights how genetic variation, microbiome differences, and lifestyle behaviours mediate diet effectiveness. More controlled, comparative studies are required to clarify which nutrient patterns offer the most consistent benefits.

CONCLUSION AND FUTURE PERSPECTIVES

The study of nutrigenomics in the context of chronic disease management, particularly for Type 2 Diabetes (T2DM) and Cardiovascular Disease (CVD), has provided substantial insights into how dietary factors can influence genetic expression, metabolic health, and disease progression. Nutritional interventions, tailored to the individual's genetic profile, offer promising strategies for managing these diseases, improving patient outcomes, and reducing the global burden of chronic diseases.

This review has highlighted several key points in understanding the intricate relationship between diet, inflammation, insulin resistance, and chronic disease risk. It is clear that diet plays a pivotal role in modulating metabolic pathways that are central to the development of T2DM and CVD. The consumption of specific nutrients such as omega-3 fatty acids, fiber, antioxidants, and polyphenols, has been shown to reduce inflammation, improve insulin sensitivity, and enhance overall metabolic health. In contrast, diets rich in refined carbohydrates, unhealthy fats, and processed foods have been shown to exacerbate inflammation and insulin resistance, increasing the risk of both conditions.

Furthermore, emerging evidence suggests that a personalized approach to diet, one that considers an individual's genetic makeup and microbiome, can optimize the management of T2DM and CVD. Nutrigenomic research offers new avenues for developing precision nutrition strategies that align with an individual's genetic and metabolic needs. Such approaches could be particularly effective in mitigating the progression of these chronic diseases and improving the quality of life for affected individuals.

Limitations of Current Evidence

Despite the growing promise of nutrigenomics in personalizing dietary strategies for chronic disease management, several limitations constrain its current scientific and clinical applicability. First, most existing studies are observational and cross-sectional in design, making it difficult to establish causal relationships between specific gene–diet interactions and metabolic outcomes. The lack of long-term, large-scale randomized controlled trials limits confidence in translating these findings into evidence-based dietary guidelines.

Second, significant population and ethnic variability in gene expression, dietary habits, and environmental exposures create inconsistencies across studies. For instance, genetic polymorphisms such as TCF7L2, FTO, and APOE show variable effects in different populations, suggesting that regional and lifestyle factors may influence outcomes. Standardization in study design, genetic testing methods, and dietary assessment tools is therefore essential to ensure comparability and reproducibility of results.

Third, accessibility and affordability of genetic and epigenetic testing remain major barriers to implementing nutrigenomics in routine healthcare, especially in low- and middle-income countries. Ethical concerns related to genetic data privacy, potential misuse of information, and limited awareness among healthcare professionals further complicate its clinical translation.

Finally, most current models of personalized nutrition often neglect broader behavioral, psychosocial, and environmental influences that affect dietary adherence and metabolic health. Factors such as stress, sleep quality, physical activity, and

socioeconomic conditions play crucial roles in chronic disease progression but are rarely integrated into nutrigenomic frameworks. Addressing these multidimensional challenges will be critical to achieving a more comprehensive, equitable, and scientifically rigorous application of nutrigenomics in chronic disease prevention and management.

Future Perspectives

Looking forward, several areas of research hold great promise in advancing our understanding of the role of diet in chronic disease prevention and management.

1. Personalized Nutrition and Precision Medicine: As nutrigenomics continues to evolve, the integration of genetic and environmental factors into dietary recommendations will likely become a cornerstone of precision medicine. Personalized nutrition, which tailors dietary interventions based on an individual's genetic predispositions, lifestyle, and microbiome composition, has the potential to enhance the effectiveness of dietary strategies in preventing and managing T2DM and CVD. The development of genetic testing and biomarkers to guide dietary choices could pave the way for more precise and individualized approaches to nutrition.

2. Role of Gut Microbiome in Chronic Disease: The gut microbiome has emerged as a critical player in the regulation of metabolism, inflammation, and insulin sensitivity. Research into the relationship between the gut microbiome and chronic diseases such as T2DM and CVD is still in its early stages but is growing rapidly. Future studies should focus on how specific dietary patterns influence the microbiome and, in turn, impact inflammation, insulin resistance, and disease progression. Probiotics, prebiotics, and microbiome-based dietary interventions could become important tools in managing metabolic disorders.

3. Investigating the Impact of Food Processing: The growing body of evidence on the adverse health effects of processed foods warrants further investigation into the specific mechanisms by which food processing contributes to the development of chronic diseases. The impact of various food processing methods on the nutrient profile of foods, as well as on the bioavailability of key compounds that modulate inflammation and metabolism, is an area that requires more detailed exploration. By understanding the effects of food processing on the body, we can develop more effective dietary guidelines to prevent and manage chronic diseases.

4. Long-term Clinical Trials and Population Studies: While short-term studies have provided valuable insights into the effects of individual nutrients and dietary patterns, long-term clinical trials and population-based studies are needed to confirm these findings and assess the long-term efficacy of dietary interventions in managing chronic diseases. Large-scale randomized controlled trials that assess the impact of personalized dietary strategies on disease outcomes will be crucial in validating the clinical applicability of nutrigenomic recommendations.

5. Integration of Nutritional Guidelines into Healthcare: The integration of nutrition into clinical practice is an essential next step in improving the management of T2DM and CVD. Healthcare providers must be trained to consider dietary factors as part of routine care for patients with chronic diseases. This includes not only advising on food choices but also incorporating genetic and metabolic profiling into nutritional counseling. Collaboration between dietitians, geneticists, and physicians will be crucial in delivering comprehensive and effective care.

In conclusion, while much progress has been made in understanding the role of diet in chronic disease management, continued research is essential to refine our strategies and improve outcomes. By harnessing the power of nutrigenomics, personalized nutrition, and a deeper understanding of metabolic and inflammatory pathways, we can develop more effective, individualized approaches to the prevention and treatment of Type 2 Diabetes and Cardiovascular Disease.

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