



Personalized Ketogenic Diet Using AI for Optimal Brain Health

Nikolaos Tzenios^{a*} and Connor Wong^{b*}

^a *Public Health and Medical Research, Charisma University, Grace Bay, Turks and Caicos Islands.*
^b *Sage Hill School, USA.*

Authors' contributions

This work was carried out in collaboration between both authors. Both authors read and approved the final manuscript.

Article Information

DOI: <https://doi.org/10.9734/ejnfs/2024/v16i111573>

Open Peer Review History:

This journal follows the Advanced Open Peer Review policy. Identity of the Reviewers, Editor(s) and additional Reviewers, peer review comments, different versions of the manuscript, comments of the editors, etc are available here: <https://www.sdiarticle5.com/review-history/125714>

Review Article

Received: 26/08/2024
Accepted: 28/10/2024
Published: 08/11/2024

ABSTRACT

The ketogenic diet (KD) has demonstrated potential for treating neurological conditions like epilepsy, Alzheimer's disease, and cognitive decline as well as for enhancing brain health. Individual reactions to KD, however, differ because of things like lifestyle, metabolism, and heredity. It is difficult to achieve the best results with a one-size-fits-all dietary strategy because of this diversity. A new answer is provided by artificial intelligence (AI), which makes it possible to provide individualized nutritional advice that take individual characteristics into consideration. AI-driven models can forecast a person's reaction to KD and customize macronutrient ratios, calorie intake, and micronutrient supplementation by combining data from genomes, metabolomics, and clinical profiles. This individualized strategy can boost mitochondrial function, lower inflammation, increase neuroprotective advantages, and enhance cognitive function. This study investigates the application of AI to create a customized ketogenic diet that maximizes brain function.

*Corresponding author: Email: ukresearcher299@gmail.com; wongconnor7@gmail.com.

Keywords: *Ketogenic diet (Keto diet); brain health optimization; Artificial intelligence (AI); AI-driven dietary recommendations; nutritional genomics.*

1. INTRODUCTION

This low-carb, high-fat, keto diet is popular because of its weight loss, metabolic and neurological benefits. With more brain health research, a better understanding of the effect of diet on cognition and neuroprotection becomes apparent (Makutam et al. 2024). Personalized nutrition through AI provides a new opportunity to adjust the ketogenic diet to each patient's brain, including genetic, metabolic, and lifestyle variations. In recent years, the diet has evolved into an innovative approach to diet management, shifting away from a one-size-fits-all or general personalized diet. Instead, it now emphasizes dietary interventions specifically adjusted to genetic makeup, lifestyle, and health goals (Astbury et al. 2019). That trend stems from the understanding that everyone's food reactions can differ, depending on many variables, from genetics, gut bacteria, and metabolism to mood. In this regard, the keto diet or keto has gained immense popularity for its weight loss, metabolic health, and especially, brain health (Bach-Faig et al. 2011). Combining AI and customized nutrition, the keto diet can now be combined to optimize brain health through increased cognitive abilities, reduction in neurological pathologies, and overall improved mental state (Barrea et al. 2022). While historically, the keto diet has been linked to weight loss and improved metabolic markers, a growing amount of evidence shows it can also benefit brain health. The brain, normally based on glucose as its fuel, can easily consume the ketone bodies released by ketosis. This change in energy use is considered neuroprotective, perhaps by lessening the risk of neurodegenerative conditions like Alzheimer's and Parkinson's, and improving outcomes in conditions such as epilepsy and traumatic brain injury (Barrea et al. 2023).

Although keto is increasingly being used to investigate the impact of the diet on brain health, the success of the keto diet varies widely from person to person. Such diversity demonstrates the importance of individualized nutrition that is driven by individual differences in genes, metabolism, and lifestyle (Barrea et al. 2023, Barrea et al. 2022). This is where AI can transform the way we approach the keto diet for the brain. Artificial intelligence (AI) is a field dedicated to replicating human-like abilities in perception, reasoning, learning, and problem-

solving, particularly within clinical contexts (Makutam et al. 2024). With huge quantities of data available, AI can detect trends and predict how certain diet changes could affect someone's cognitive and neurological condition. For instance, our survey of over 8,500 participants shows that many experienced increased cognitive benefits while on the ketogenic diet (Barrea et al. 2021). Personalized nutrition is complex — it involves combining data across multiple data sources to form an integrated picture of how someone should be nutritionally supported. For example, genomic information might tell us how certain genes affect the metabolism of nutrients, so we could see what foods are likely to be beneficial or harmful to brain health. In the same way, AI can process information from wearables based on fitness, sleep and stress levels – all of which could impact cognitive performance (Barrea et al. 2023).

The analysis of biomarkers is one of the many ways AI can improve the keto diet for brain health. Biomarkers are quantifiable markers of biological activity, and can provide valuable clues into the body's reaction to a particular diet. For instance, blood ketones, glucose, and insulin levels can help identify if a person is in ketosis and how their body is digesting fats and carbohydrates (Barrea et al. 2022, Bueno et al. 2013). Artificial intelligence will continuously monitor these biomarkers so that the diet can be changed in real-time so that the patient doesn't get out of ketosis and doesn't lose the mental rewards from this metabolic state. Furthermore, AI can detect trends in these biomarkers to detect the early onset of neurological disease, and make dietary changes accordingly to reduce risk (Camajani et al. 2023). Beyond biomarkers, AI can look at the gut microbiome, which contributes to brain function. The gut-brain axis, a bidirectional link between the gut and the brain, is driven by the gut microbiota composition. And there are gut bacteria that produce short-chain fatty acids (SCFAs), which are neuroprotective. From looking at the gut microbiome, AI can discern imbalances that might be depleting brain function and recommend eating practices to support a healthy microbial population. This could be by balancing the keto diet macronutrient ratio or combining specific foods that have been found to promote healthy gut bacteria. The supercomputer capabilities of AI is also possible

when it comes to lifestyle and environmental factors — and those influences can make or break the effectiveness of the keto diet for the brain (Castaldo et al. 2021). Stress, for example, has been observed to impact brain function, and it can disrupt the body's ability to transition into and sustain ketosis. AI can extract data from stress-tracking apps or wearables and suggest methods of stress reduction that go with the keto diet, including mindfulness meditation, exercise, or sleep patterns. Similarly, AI could consider environmental conditions, like exposure to pollution or availability of particular foods, and determine whether the diet nourished the brain appropriately. AI can also support the keto diet by recommending menus and recipes that fit into the user's preferences, cultural background, and specific dietary restrictions (Castro et al. 2018, Chao et al. 2021).

2. KETO DIET

The ketogenic diet (sometimes shortened to just the "keto diet") is a high-fat, low-carb diet, which has recently become an extremely popular way to lose weight, promote metabolic health, and have medical applications for various illnesses. The keto diet is a high-fat, low-carb diet designed to get the body into ketosis — using fat instead of carbohydrates to fuel the body. Taking its name from ketosis, the state of metabolism in which the body burns fat rather than carbohydrates for fuel, the keto diet has moved from its first days as a medical intervention to a diet of mass appeal, adopted by billions worldwide (Cincione et al. 2023).

2.1 Understanding Ketosis

In the optimal diet, carbohydrates provide the body's fuel in the form of glucose. Glucose gets quickly used by the cells of the body for energy and is stored as glycogen in the liver and muscles. But if carbs are drastically reduced, then the body must seek another fuel to keep up its energy needs. And that's where ketosis comes in. Without enough carbohydrates, the liver begins to make ketones, using fatty acids from the food and the body's fat reserves to fuel the brain, muscles, and other tissues. Ketosis is a natural metabolic state, and the keto diet's success lies in this state. Inducing and sustaining this state, the body transitions away from the use of glucose as fuel and instead turns to fat for energy, resulting in the loss of body fat and changes in metabolic markers (Conrad and Nothlings 2017).

2.2 The Origins of the Ketogenic Diet

The ketogenic diet was originally devised in the 1920s to treat epilepsy in children resistant to standard anticonvulsant medications. They noticed that ketosis can be induced through fasting, and thus reduce seizures in epileptics. But fasting is not an efficient, long-term solution, so the keto diet was invented to mimic the metabolic consequences of fasting but maintain a way for people to continue eating (Conte et al. 2021).

The classic ketogenic diet used for epilepsy typically consists of a 4:1 ratio of fat to combined protein and carbohydrates, meaning that approximately 90% of the diet's calories come from fat. This strict diet has been shown to lower seizure frequency in most epileptics — though it should be monitored and adhered to closely so as not to suffer from nutritional loss or other complications (Correa et al. 2021).

2.3 The Modern Keto Diet

The keto diet has become far more than a therapy over the past few years and is commonly used as a weight loss and general health strategy. Today's keto diet is not as restrictive as the traditional medical variant and typically involves macronutrient distribution of 70-75% fat, 20-25% protein, and 5-10% carbs. This still results in ketosis, but offers a more diverse and interesting diet. This could be one of the keto diet's primary benefits in achieving rapid weight loss. Because the body's primary fuel source, namely carbohydrates, is converted to fat, keto dieters can see a dramatic loss of body fat (mainly in the abdomen). Also, the high-fat diet is often a bit more filling than a high-carb diet, leading to an organic reduction in calories and therefore additional weight loss (D'Andrea et al. 2019).

2.4 Potential Health Benefits

Aside from weight loss, there are many other benefits of the ketogenic diet. The diet, for instance, has also been found to improve insulin sensitivity and blood sugar levels, so it may be a potential option for those with type 2 diabetes or those at risk of it. By decreasing carbohydrate intake, the keto diet can balance blood sugar and reduce the requirement for insulin — especially important for insulin-resistant people. Keto may also be cardiovascular-friendly. This diet is rich in saturated fats — traditionally thought to be a predictor of heart disease — but some recent

findings indicate that the link between saturated fat and heart disease goes further than previously believed (Dynka et al. 2022). Other studies suggest the keto diet has been shown to decrease cholesterol, by raising levels of high-density lipoprotein (HDL or "good" cholesterol) and lowering levels of low-density lipoprotein (LDL or "bad" cholesterol). Also, the diet helped to lower triglycerides, which are fats in the blood associated with an increased risk of heart disease (Erdem et al. 2022).

Another area of interest is the keto diet's potential for cancer treatment. Others believe that since cancer cells are almost entirely fuelled by glucose, diets that make glucose scarce and encourage ketosis would slow down growth in certain types of tumors. Though this research is relatively new, and the keto diet isn't used to treat cancer, there have been preliminary experiments and case studies. The diet has even been tried in treatment for neurological conditions other than epilepsy, including Alzheimer's disease, Parkinson's, and multiple sclerosis. We don't know how exactly the keto diet can help these conditions, but ketones are thought to be neuroprotective and may reduce inflammation and oxidative stress in the brain (Erickson et al. 2017, Goday et al. 2016).

2.5 The Ketogenic Diet and Brain Health

The diet's ability to modulate neurotransmitters, mitigate inflammation, and improve mitochondrial function are all considered mechanisms for the diet's mental health benefits. However, there is much to be learned from this keto diet that can be difficult or harmful. The diet is not very easy to follow, as there are strict carbohydrate requirements and the macronutrient ratios have to be managed precisely. Moreover, certain people can develop side effects (keto flu) or digestive issues as well as negative long-term effects on cholesterol and cardiovascular health (Kirchgessner and Muller 1984, Lorenzo et al. 2022).

2.6 Mechanisms of Action

The brain, an organ that was traditionally believed to be dependent on glucose, is extremely flexible in carbohydrate restriction. In ketosis, ketone bodies (beta-hydroxybutyrate (BHB), acetoacetate, and acetone) become the brain's main energy source. This switch also promotes energy homeostasis, but also seems to offer neuroprotective properties that may be

useful in some neurodegenerative and neuropsychiatric conditions. It has been enormously extended to study the ketogenic diet's effects on the brain: mitochondrial function, oxidative stress, inflammation, neurotransmitter levels, and more (Norman et al. 2012).

One of the main ways in which keto affects brain health is by increasing mitochondrial function and energy production. Mitochondria, the cell's powerhouses, make the cell's energy currency – ATP. Mitochondrial dysfunction, associated with decreased energy generation and oxidative stress, is a central aspect of neurodegenerative conditions like Alzheimer's and Parkinson's. The mitochondria have also been shown to benefit from ketones as they fuel their function more effectively than glucose and lower reactive oxygen species (ROS). The higher efficiency of the mitochondria can offset energy deficits and oxidative damage that arise in neurodegeneration (Bradburn et al. 2018). Besides impacting mitochondria, the keto diet also inhibited oxidative stress and inflammation, both of which are associated with the development of most neurological disorders. Oxidative stress, involving a mismatch between the production of ROS and the body's capacity to cleanse them, damages cells and contributes to neurodegenerative disorders. Ketogenic diets increase endogenous antioxidants like glutathione and superoxide dismutase, inhibit oxidative stress, and preserve neuron cells (Forcina et al. 2019, Edwards et al. 2020). Furthermore, ketone bodies have anti-inflammatory properties, as they inhibit the activation of pro-inflammatory pathways such as the nuclear factor kappa-light-chain-enhancer of activated B cells (NF- κ B) pathway and reduce the levels of pro-inflammatory cytokines like interleukin-1 β and tumor necrosis factor-alpha (TNF- α) (Han et al. 2020).

Considering epilepsy, the diet's modulation of neurotransmitters is thought to be part of its anticonvulsant effect. The diet promotes the production of gamma-aminobutyric acid (GABA), the brain's primary inhibitory neurotransmitter, and diminishes glutamate, its primary excitatory neurotransmitter (Justice et al. 2014). This balance between excitatory and inhibitory neurotransmission explains why the diet helps maintain the neuronal rhythm and lower the risk of seizures. In addition to epilepsy, such neurotransmitter modulation may apply to other neuropsychiatric disorders – anxiety and depression, for example – where GABA and

glutamate have been implicated in dysregulation. But keto can also influence brain health by changing neurotrophic factors, proteins that promote the development, survival, and differentiation of neurons. Brain-derived neurotrophic factor (BDNF), an element involved in synaptic plasticity, learning, and memory, is one of the most intensively researched neurotrophic factors. BDNF is depleted in neurodegenerative disorders and mood disorders. Research suggests that the keto diet can enhance brain BDNF levels, allowing for improved neuroplasticity and cognition. This

BDNF up-regulation can also play a role in the diet's neuroprotective properties, maintaining neuronal integrity in the face of neurodegeneration (Mattson et al. 2017, McSwiney et al. 2018).

The keto diet has been proven to reduce excitability in the brain and neuronal hyperactivity – key causes of disorders such as epilepsy. The diet's modulation of ion channel activity (mainly potassium and calcium channels) regulates membranes of neurons, stopping the erratic firing patterns that cause seizures. This ion channel

Table 1. This table summarizes the key milestones in the development and popularization of the keto diet (Conte et al. 2021)

Year	Event/Development	Details
1920s	Initial Development	Developed at the Mayo Clinic as a treatment for epilepsy.
1930s	Decline in Use	Antiepileptic drugs were introduced, leading to a decline in the use of keto diet.
1960s	Medium-Chain Triglycerides (MCT)	MCT oils were introduced to improve the effectiveness of the keto diet.
1970s	Dr. Robert Atkins	Popularized the low-carbohydrate diet for weight loss, a precursor to the modern keto diet.
1990s	Resurgence in Medical Use	Renewed interest in the diet for epilepsy due to drug-resistant cases.
2000s	Research on Other Applications	Studies explored keto diet's potential benefits for other conditions like diabetes, cancer, and neurodegenerative diseases.
2010s	Mainstream Popularity	The diet gained widespread popularity for weight loss and general health.
2020s	Ongoing Research and Popularity	Continued research into various health benefits and long-term effects of the diet.

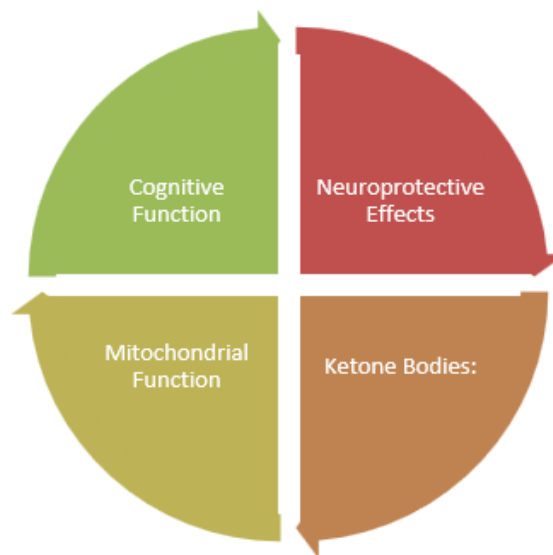


Fig. 1. Keto diet works by following functional routes

modulation can also have wider applications for conditions like migraine and bipolar disorder in which alterations in the excitability of neurons are involved in disease pathophysiology (Newman and Verdin 2014, Newman and Verdin 2017). This regulates brain energy and glucose use — a separate part of the ketogenic diet's impact on the brain. For neurological diseases such as Alzheimer's where glucose metabolism in the brain has been compromised, the keto diet supplies an alternative energy form, ketone bodies, to avoid metabolic blockades that prevent the use of glucose. It is not just that this new fuel will ease brain energy needs, but it may also help to lower the levels of noxious metabolites linked to impaired glucose metabolism, including amyloid-beta plaques and tau tangles. The ketogenic diet can enhance metabolic elasticity and regulate brain energy homeostasis which may explain its therapeutic effects in Alzheimer's and other neurodegenerative disorders (Richardson et al. 2021, Rosenson et al. 2013). Beyond these cellular and molecular mechanisms, keto might have an impact on brain health via its impact on the gut-brain axis. Gut microbiota, the tangle of microbes found in the gut, contributes to regulating brain activity and behavior by generating neurotransmitters, short-chain fatty acids, and other molecules. The keto diet has been observed to shift the gut microbiota, encouraging probiotic bacteria to flourish that produce anti-inflammatory and neuroprotective chemicals (Solinas et al. 2015, Villeda et al. 2014).

The ketogenic diet's complex effects on the brain confirm its potential to be used as a treatment for several neurological and psychiatric diseases. Nonetheless, it is worth acknowledging that the diet is not without risks and hardships. Keto diet can be challenging to maintain, and the long-term effects of ketosis on the brain and body are still inconclusive. Also, the keto diet could not be right for everyone, especially those who have some metabolic issues or may suffer from nutritional deficiencies (Paoli et al. 2015, Paoli et al. 2023). Research is still needed to better explain the functions of the keto diet and what clinical applications of the diet will work best and remain safe. Even as we continue to better understand the keto diet's effects on the brain, it can still serve as a tool in the management of neurological disorders, providing hope for patients who have few options (Pandurevic et al. 2023).

3. CONCEPTUAL ANALYSIS

Personalized nutrition, in which a person's dietary recommendations are based on his or her genes, habits and current health, allows the user to diet with greater accuracy. Based on metabolism, gut microbiota, and genetic make-up, targeted nutrition can maximize health outcomes, reduce chronic disease and boost overall health (Romano et al. 2019, Ministrini et al. 2019). Unlike blanket diet plans, this model recognizes that everyone reacts to food and nutrients differently. It enables people to make informed decisions that are relevant to their specific needs and could be a better way to adhere and improve health more sustainably. The ketogenic diet's overlapping effects on the brain are proof that the diet is therapeutically effective for a variety of neurological and psychiatric disorders. But there's more to the diet than meets the eye. It can be difficult to stick to a strict keto diet, and the long-term effects of continued ketosis on brain health and general well-being are still poorly understood. Besides, the keto diet might not be ideal for everyone, particularly people with certain metabolic conditions or individuals at risk of becoming deficient in nutrition. More research needs to be done to fully define the action of the keto diet and what the most efficient and safe uses of the dietary intervention should be in clinical settings (Cincione et al. 2022).

3.1 Principles of Personalization

Nutrigenomics is a study into how our genetic variations influence the metabolism and absorption of nutrients in our bodies. For instance, some people can be genetically predisposed to the oxidation of fats, carbs or vitamins, and so to certain dietary requirements or reactions. Lifestyle, ranging from exercise, sleep, and stress, also affects genetic optimization. For example, an athlete might need to eat more protein and carbohydrates to aid muscle growth and energy needs, while a person who lives in a semi-active state might want a different macronutrient balance. Sleep and stress can also affect hunger hormones, metabolism, and even dietary preference, so it should always be factored into a personalized nutrition strategy. Individualized nutrition places the priority on cultural, moral and individual tastes. Food is a resource for nutrition but it is also central to culture and self-respect. By considering a person's diet, culture and ethics (whether vegan or vegetarian), personalized nutrition makes it

possible for the recommendations to be sustainable and efficient over time. This model uses AI — including genetic testing, wearables and digital health applications — to provide data and insights in real time (D'Abbondanza et al. 2020, Silva et al. 2023).

3.2 Personalized Nutrition in Brain Health

The processing of sensory input, the regulation of emotions, critical thinking and problem-solving – everything in the functioning of the brain is related to what we eat. In recent decades, scientific evidence has been mounting that diet is essential for cognition, and indeed to cognitive health. Omega-3 fatty acids, antioxidants, vitamins and minerals help the brain by increasing neurogenesis, fighting against oxidative damage, and boosting neurotransmitter production. But the performance of these nutrients can vary wildly across people, depending on genes, metabolism and lifestyle. Diet advice adapted to a specific patient's particular condition, would address genetic variants in metabolism or responses to vitamins that put patients at higher risk for cognitive decline if they are not given enough. It can detect these genetic predispositions and offer targeted recommendations to mitigate them (Ashtary-Larky et al. 2022, Barrea et al. 2022).

3.3 Genetic Factors and Diet Effectiveness

This variation in reaction to diet is not simply an effect of different lifestyles or patterns of eating; genes are very important for how our bodies respond to food and dietary regimes. The fat mass and obesity-associated (FTO) gene, for example, has been associated with obesity and obesity. Anyone who carries certain variants of the FTO gene tends to be more susceptible to obesity because they have a greater appetite and higher rate of fat storage. These genetic variations can affect the rate at which an individual burns calories and processes fats, carbohydrates and proteins, and how well a diet will work (Barrea et al. 2023). The melanocortin 4 receptor (MC4R) gene is responsible for appetite and energy regulation. This gene variant, MC4R, has also been linked to an increased risk of obesity and a more aggressive craving for high-fat foods. This genetic predisposition can make it harder for some people to eat low-calorie or low-fat diets, so they are less effective as interventions (Barrea et al. 2023).

Other genes that affect diet efficiency include metabolism and appetite genes. A bitter-taste receptor, TAS2R38, was also observed to modify taste – especially in bitter vegetables such as broccoli and Brussels sprouts. Such foods might be particularly unpleasant for those carriers of certain mutations in the TAS2R38 gene, and they might be less able to consume diets that contain these vegetables. The APOA2 gene, for example, is involved in fat metabolism. The people who carry variants of this gene can end up having different outcomes when eating a high-fat diet than the people without the variants (Buechert et al. 2020). One study revealed that people carrying a particular version of the APOA2 gene will increase their risk of obesity if they eat a high-saturated-fat diet. They could instead have a healthier, low-fat diet – making it even more important to tailor nutrition to genetic profiles. The TCF7L2 gene, researched for type 2 diabetes, regulates insulin secretion and glucose metabolism. There are variants of this gene that influence carbohydrate metabolism and therefore differ from those that respond to high-carb diets. People with certain variants of TCF7L2 might have an increased susceptibility to insulin resistance, and should consume less refined carbohydrates (Camajani et al. 2022).

So for instance, the MTHFR gene, which affects folate metabolism, can affect the body's utilization and metabolism of folic acid. Mutations in the MTHFR gene can cause decreased enzyme activity and lower active folate production. This has consequences for those in need of increased folate, including women who are pregnant, and suggests that genetic testing could guide more specific recommendations on diets for proper micronutrient absorption. Diet efficiency is also linked to epigenetics, which tracks changes in gene expression independent of changes in the DNA sequence. Diet can modify epigenetic changes like DNA methylation and histone acetylation, which change the expression of genes. The diet of some people, for example, including a diet high in fruits, vegetables and whole grains, has also been found to induce beneficial epigenetic mechanisms that promote metabolism. Meanwhile, eating too much processed foods and sugar triggers deleterious epigenetic changes that can raise the risk of chronic conditions such as obesity, diabetes, and cardiovascular disease (Campa et al. 2023, Campa 2022). Another genetic component that affects diet success is the gut microbiome, the ecosystem of microbes in the gut. The gut

microbiome consists of individual differences, as well as different variations of genetic and environmental factors. The gut microbiome is also involved in digestion, absorption and short-chain fatty acid production that supports gut health. Some genetic variants may alter the structure and function of the gut microbiome and how people react to different diets. Some individuals might, for instance, have a gut microbiome profile more capable of breaking down calories from food and therefore being more likely to put on weight if eating the same diet as someone with a different microbiome profile (Campa et al. 2021, Caprio et al. 2019).

3.4 Biomarkers and Metabolic Profiling

Biomarkers and metabolic profiling provide the key to understanding the relationship between one's biology and their food, making them a powerful tool for personalized, precise diet intervention. We can see the impact of biomarkers and metabolic profiling on the effectiveness of diets in different ways – from determining metabolic differences among people, to anticipating responses to dietary change, to nutritional suggestions that optimize brain health outcomes (Coratella et al. 2021).

- **Biomarkers as Nutritional Status Measurements:** Quantifiable biochemical markers of biological processes, states or illnesses that can give a snapshot of a person's health and nutritional condition. For diet efficacy, biomarkers may equate with how well one metabolizes and uses nutrients, providing an immediate connection between diet and health (Di Rosa et al. 2022). Lipid biomarkers, for example, including cholesterol levels, could reflect how someone handles dietary fat, or glucose biomarkers could indicate how well someone burns carbs. Using these biomarkers, physicians can adapt dietary advice to a patient's metabolism level, which can help optimize diets. Additionally, biomarkers can also be used as markers of deficiency or excess nutrients, allowing for the identification of imbalances that can negatively impact diet efficiency. For instance, deficiencies in vitamin D biomarkers could mean we should be taking more vitamin D foods or supplements, especially if we have little exposure to the sun. Either way, elevated inflammatory biomarkers such as C-reactive protein (CRP) can suggest chronic
- **Metabolic Profiling and Personalized Diet:** Involves the quantitative measurement of metabolites, or small molecules, generated by metabolism. This offers a granular view of a person's metabolic state and its diet-related dynamics. The metabolome reveals which metabolic pathways get turned on and off about food. Traditional diets often use a generalizable standard and don't factor in metabolic variations. However metabolic profiling allows us to detect distinct metabolic phenotypes, or metabotypes, that affect how individuals react to nutrients (Ferraris et al. 2019). For instance, two people might have the same high-fat meal, but have different metabolic profiles in lipid oxidation and fat accumulation, making one more vulnerable to obesity or metabolic dysfunction than the other. A person with a metabolic profile that indicates impaired glucose tolerance may require a low-carbohydrate diet, while a person with a high-energy metabolism may require a high-carbohydrate diet (Gomez-Arbelaez et al. 2017).
- **Dietary Response:** By estimating the person's baseline biomarkers and metabolic profiles, researchers can predict their response to specific dietary interventions. This prediction is especially helpful in the context of a chronic disease, such as obesity, diabetes and cardiovascular disorders, where diets are the main path to preventing and regulating disease (Gomez-Arbelaez et al. 2018). In obesity control, for instance, biomarkers including leptin, insulin, and adiponectin levels can also indicate whether a person is likely to lose or gain weight under a given diet. One with insulin resistance (high fasting blood glucose) could benefit from a low-carb or ketogenic diet that reduces the insulin spikes. Meanwhile, those who have a high level of leptin, the hunger hormone, could be best off on a portion-control and calorie-cutting diet. Studies of lipid metabolites can help determine which people burn more fat to get energy, and thus are prime candidates for a high-fat, low-carb diet such as the keto diet. Then again, those whose metabolic profiles favor carbohydrate metabolism may find success eating a diet

inflammation that can be treated with diet-based anti-inflammatory changes (excess omega-3s) (Dowis and Banga 2021).

rich in complex carbohydrates and fiber (Hadizadeh et al. 2020).

- Nutritional Strategies for Health:** By learning the biological mechanisms that underlie diet success, clinicians can create diets to support not just weight loss or maintenance but chronic disease prevention and better health in general. In cardiovascular disease prevention, biomarkers including LDL cholesterol, HDL cholesterol, and triglycerides are all used to calculate cardiovascular risk and make recommendations. A person with high LDL cholesterol might be encouraged to eat less saturated fat and more unsaturated fats — the Mediterranean diet has been

found to reduce LDL cholesterol and increase cardiovascular risk. Likewise, metabolic profiling can identify those more susceptible to oxidative stress who might be at the best advantage from an antioxidant-loaded diet that consists of fruits, vegetables and whole grains. For diabetes, biomarkers such as hemoglobin A1c (HbA1c) and fasting glucose levels are key markers that are used to track blood sugar and determine food interventions. An individual with high HbA1c may need a diet that minimizes the amount of glycemic load – for example, a low-glycemic index diet – to stabilize their blood sugar (Kämmerer et al. 2021).

Table 2. Biomarkers for keto diet plans (Kämmerer et al. 2021)

Biomarker	Metabolic Profile	Influence on Diet Effectiveness	Example Dietary Interventions
Blood Glucose Levels	Insulin Sensitivity/Resistance	High blood glucose levels may indicate insulin resistance, requiring lower carbohydrate intake for effective weight loss.	Low-carb, Ketogenic Diets
Lipid Panel (Cholesterol)	Lipid Metabolism	Elevated LDL and triglycerides may necessitate diets low in saturated fats and cholesterol to improve cardiovascular health.	Mediterranean Diet, Plant-Based Diet
Inflammatory Markers (CRP)	Inflammatory Status	High CRP levels suggest chronic inflammation, which may be mitigated by anti-inflammatory foods.	Anti-inflammatory Diet, Omega-3 Rich Diets (e.g., fish, flaxseed)
Genetic Markers (FTO Gene)	Genetic Predisposition to Obesity	Variations in the FTO gene may influence appetite and satiety, impacting diet adherence and effectiveness.	Calorie-controlled diets, Personalized Nutrition Plans
Gut Microbiota Composition	Gut Health	Diversity in gut microbiota can affect metabolism and energy extraction from food, influencing weight management.	Prebiotic/Probiotic-rich diets, High-fiber Diets
Hormonal Levels (Leptin, Ghrelin)	Appetite Regulation	Hormonal imbalances can disrupt hunger signals, requiring diet adjustments to manage satiety and prevent overeating.	Balanced Diets with regular meals, High-protein Diets
Vitamin D Levels	Bone Health and Immune Function	Low vitamin D can impair calcium absorption and immune function, potentially affecting diet-related outcomes.	Diets rich in vitamin D (e.g., fatty fish, fortified foods), Supplements if necessary

Biomarker	Metabolic Profile	Influence on Diet Effectiveness	Example Dietary Interventions
Thyroid Function (TSH, T4)	Metabolic Rate	Hypothyroidism can slow metabolism, making weight loss more challenging and requiring tailored caloric intake.	Adjusted calorie intake, Iodine-rich Diet (if deficiency is present)

3.5 All-Encompassing Diets

Dietary recommendations are generally applied in a generalized way — making broad recommendations for the general well-being and avoidance of disease for the general population. Such recommendations, such as the food pyramid or the more recent MyPlate, draw on broad epidemiological data to prescribe a nutritious diet that’s accessible to everyone. But that method is fundamentally imperfect, particularly in the treatment of individual physiological variability and personal health goals. The central flaw with diet models of general appeal is that they cannot explain the wide variation in individual responses to food (Khodabakhshi et al. 2020, Klement et al. 2020).

Personalized nutrition benefits aren’t just about adherence and wellness. To many of us, discovering the best options for our bodies is exciting and rewarding. When the benefits of diet changes are tangible, and fitted to their circumstances, they are more likely to continue those changes for the long term. It is different from standardized diets, which discourage users if they don’t get the desired results, and therefore will only produce diets that are unsustainable and exhausting. Customized nutrition interventions can also be expensive, and so more unreachable for the masses. Besides, there are still moral questions about genetic data privacy and misuse of personal health data. Instead, generalized diets, while not as accurate, are more accessible, easier and more cost-effective to administer in the long run. Such overgeneralized recommendations are commonly deployed in public health programs to counter mass food deprivation and chronic disease on a population level (Klement et al. 2021, Klement et al. 2020).

4. AI IN PERSONALIZED NUTRITION

Data collection, analytics and the generation of insights are not the only activities. At its core, AI enables us to process large-scale data sets containing genetics, biomarkers, diet and lifestyle variables. AI, aided by machine learning algorithms, can interpret patterns in data and

thus create a better suggestion for an individual’s nutritional requirements. In contrast to traditional nutrition strategies that are mostly inert, relying on outdated data, AI can adapt when new information is released. For instance, as an individual’s condition varies — by losing weight, increasing exercise or getting sick — AI can adjust their food recommendations in real time so they have the best and most relevant information at hand. AI can use data from wearables and health apps, and render a holistic picture of a user’s wellbeing and behavior. This integration allows AI to assess in real-time parameters including activity, sleep and stress levels which can influence nutrition (Klement and Sweeney 2022).

4.1 Applications of AI

Deep Walk-Health is a version of the traditional Deep Walk that’s used to make sure that personal nutrition has the greatest effect on cognitive function by aggregating genomic, biomarker, and diet data as points in a heterogeneous graph. Using random walks, Deep Walk-Health pulls out trends in biological features such as SNPs, micronutrients, and biomarker pathways, and uses Skip-Gram to build embeddings of intricate biochemical connections. These go into a Transformer-based recommendation engine, where self-attention algorithms determine what nutrients to focus on according to gene-nutrient interactions, like SNP-mediated folate metabolism. An LSTM layer tracks temporal changes in the model, tailored for contextual variables such as nutrient availability and circadian metabolism (Kotler et al. 1966).

A reinforcement learning agent (PPO) predicts the outcomes of dietary intervention by enhancing a reward function using cognitive proxies (-hydroxybutyrate for mitochondrial function) while managing multi-targets (inflammatory markers (e.g., IL-6) and neurocognitive variables (MMSE scores) (Krebs 1966).

It is not only capable of handling large quantities of data but also learning and growing in the

process, to adjust its predictions and recommendations. For brain health, AI depends on a host of variables ranging from genes to exposures to environment, lifestyle, and diet. As a result of a combination of AI and science, researchers and clinicians will be able to better devise customized diets that will support mental well-being and prevent or reverse neurological illness (Kyle et al. 2004).

5. APPLICATIONS OF AI IN PERSONALIZED NUTRITION

For consumer applications, multimodal learning models are used to learn from various data sources (SNP panels, gut microbiota profiles, real-time biometric measurements from IoT-enabled wearable devices) and create dietary recommendations that are continuously receptive to the different physiological states of the user. Transformer models' attention algorithms determine and select the most useful features from hundreds of input parameters to enable finely tailored tailoring for genetic traits, metabolic states, and ebb and flow lifestyle patterns (Lohman and Milliken 2020). To store sequential health information, Gated Recurrent Units (GRUs) and Bidirectional Long Short-Term Memory (BiLSTM) networks have become standard: they store bidirectional temporal dependencies that affect metabolic rhythms and uptake capacity. Federated learning models can collect data from distributed wearable devices and health apps and aggregate it with privacy-friendly accuracy such that the main model has access to larger, decentralized data but also complies with very strict privacy regulations such as GDPR (Lukaski et al. 1986). Nutrition appliances use generative algorithms like VAEs to create artificial personalized diets, in line with the best health indicators but balancing taste and cultural diet norms. Meal recognition in real-time

uses ensemble deep learning frameworks, combining ResNet and DenseNet layers to extract more features from the images of foods to help identify food type and portion size estimation. Diet recommendation engines rely on cooperation filters complemented by knowledge graphs that encode associations between ingredients, cooking techniques, and nutrient interactions. It allows for stronger personalization with food synergy effects, which explains how some nutrients are bioavailable in ways that others are not when eaten together (Braun and Marks 2015).

To provide adaptive feedback, reinforcement learning agents — trained through Deep Q-Networks (DQN) or Policy Gradient Methods — monitor user compliance to diets and adjust future for an optimal long-term reward function according to metrics like HbA1c reduction, BMI reduction or other biomarkers of chronic disease. BNNs handle uncertainty based on user information so the model will make probabilistic food recommendations (quantifying confidence intervals for nutrients whose information is incomplete), increasing individual level dietary precision (Lützner et al. 2012). Ensemble meta-learning systems in healthcare combine weak models to address parts of chronic disease management (lipid metabolism, inflammation, insulin sensitivity) into a single, very strong model for clinical nutrition optimization. Predictive models such as Extreme Gradient Boosting (XGBoost) model the progression of diseases based on diet compliance, which enables clinicians to apply research-based nutrition modifications. Systems also use counterfactual inference to calculate which diet would produce the biggest benefit to patients with such conditions as Type 2 Diabetes or high blood pressure (ACTEMRA 2022).

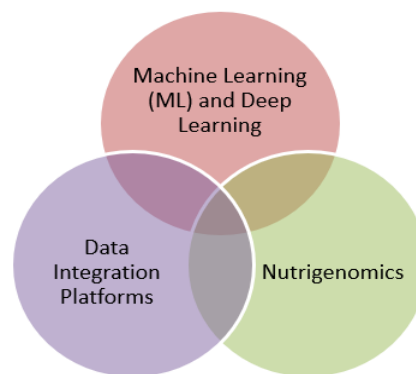


Fig. 2. Overview of AI technologies

Unsupervised dimension-reduction algorithms such as Principal Component Analysis (PCA) or Uniform Manifold Approximation and Projection (UMAP) are used in clinical research to reveal hidden correlations between dietary behavior and health, decoding the high-dimensional data from metagenomics and clinical trials. Association rule mining algorithms (like Apriori and FP-Growth) find subtle associations between a food element and markers of metabolism and help produce evidence-based diet plans. Additionally, transfer learning among related clinical data improves the model's generalizability across population subsets and provides cultural and demographic tailoring of tailored nutrition recommendations (Gracia-Ramos et al. 2021). For population health programs on a large scale, MIL simulates population-level health using aggregated, personal diets, while GNNs model community-level diets and their socio-environmental drivers. PC Algorithm and Greedy Equivalence Search (GES) for causal discovery tools re-enter hidden causal channels in diet-health connections, giving evidence that can help inform public health policy and intervention design. Moreover, multi-fidelity modeling is used to bring high-resolution clinical data and low-resolution observational data together to make population-scale dietary insights more generalizable and robust. Generative adversarial networks (GANs) develop plausible, artificial health cases, based on the long-term impacts of various dietary regimes, which are used to refine models for public health purposes (Karami et al. 2021).

5.1 Potential Benefits of AI in Personalized Nutrition

These models, when coupled with swarm intelligence, allow for massive behavioral analyses, enabling public health campaigns. For chronic disease prevention, knowledge reasoning and reinforcement learning help ensure individual dietary changes that reduce disease risk; MDPs optimize intervention sequences. Live context bandit algorithms offer real-time food updates, promoting compliance through user feedback (Bagnato et al. 2021). Tensor decomposition, which highlights the connections between the gut microbiome and metabolism, helps AI to fuse multi-omic information together. In the brain, these techniques relate metabolomic and transcriptomic information to specific nutritional pathways for cognitive enhancement. Predictive ensemble learning collates outputs from multiple models to detect nutritional asymmetry

accurately, and fuzzy logic models control uncertainty in user data to ensure better nutritional recommendations (Ramos et al. 2021).

End-to-end differentiable programming facilitates translating raw sensor data into tailored nutrition plans, and graph convolutional networks (GCNs) represent complicated nutrient interactions to create optimal nutrition plans based on bioavailability and synergy effects. Using unsupervised learning and latent variable models to discover vulnerable populations, semi-supervised learning and deep transfer learning facilitate the model's generalizability across population cohorts. Dynamic systems theory and longitudinal data also make it possible to forecast food requirements for one's lifetime. Distributed training and edge computing in the cloud ensures scaling and responsiveness, with live wearables and IoT updates. In the future, these techniques could be used to speed up the computation of nutrient optimizations with a huge number of variables using quantum-inspired optimization and quantum annealing. Meta-learning makes adaptive mechanisms more flexible, enabling diet recommendation engines to keep optimizing their interventions for diverse subgroups (Trimboli et al. 2020).

5.2 Genetic Analysis and Nutrigenomics

AI can help in this respect by using genetic information to detect gene-nutrient interactions that might have a bearing on brain health. Algorithms can probe for genetic variants associated with the metabolism of omega-3 fatty acids that support cognition and are known to reduce the risk of neurodegenerative disorders. Analyzing genetic variants that reduce the metabolism of omega-3s, AI will help make nutritional recommendations — supplement or consume more omega-3 sources (Romano et al. 2019).

5.3 Biomarker Analysis

AI is also used to interpret biomarkers, quantifiable measures of biological function and health states. For the brain, biomarkers – blood levels of vitamins, minerals and fatty acids, as well as indicators of inflammation and oxidative stress – can determine nutrition and cognitive health. AI algorithms could interpret these biomarkers to detect deficiencies or imbalances associated with cognitive loss and advise nutritional adjustments to mitigate these. So, for

example, if AI finds deficiencies in vitamin B12, an essential component of the brain, it can recommend a dietary change (Wing et al. 1991).

The composition of the gut microbiome has been linked to a variety of brain-related functions, such as mood, memory and neurodegenerative disease. AI can also mine microbiome data to find trends and correlations between individual microbial species and brain outcomes. And that information can then be tailor-made for specific dietary recommendations that support healthy gut microbiome health and so optimal brain health (Blackburn 2017).

5.4 ML and Predictive Analytics

Machine learning is a subcategory of AI that can predict an individual's likelihood to benefit from a given dietary intervention based on a personal data set. The ML algorithms, by assessing the data and looking for patterns, can predict how a person's cognitive capacity will change as time progresses. In the case of neurodegenerative conditions like Alzheimer's, early nutrition intervention may delay or even prevent the disease (Buckland et al. 2009).

5.5 Wearable Devices and Real-Time Monitoring

Wearable technology can continually monitor several health indicators, including physical activity, sleep rhythms, and heart rate variability – all of which are associated with cognition. AI can also utilize this real-time information to deliver immediate alerts and personalized recommendations. For instance, if the wearable detects low-quality sleep, which leads to poor cognition, AI might recommend modifications in dietary or lifestyle habits that will promote sleep and, therefore, healthy brains (Lăcătușu et al. 2019).

- **Genetic Profiling:** AI can detect genetic markers related to metabolism, brain activity, and vulnerability to neurodegenerative diseases. For instance, patients with variants of the APOE gene could take advantage of specific ketogenic diet adjustments for brain wellness.
- **Metabolic Monitoring:** Continuous glucose monitors and ketone sensors transmit real-time data to AI algorithms that help modify ketogenic diet macronutrient ratios, keeping users in ketosis with no side effects.

- **Microbiome Profile:** AI can interpret microbiome profiles and recommend lifestyle changes for a healthy gut ecosystem, potentially making keto better for brain health.
- **Lifestyle and Environment:** AI can bring in sleep data, stress and exercise data, all of which help the brain stay healthy, to develop a holistic and personalized diet.

5.6 Additional Considerations

Data privacy and security are two main issues. Gathering and storing health data, including genetic information, raises the issue of privacy and the storage, use, and transmission of this data. There is also the issue of providing high-quality data for training the AIs. Self-reported dietary records could be wrong, and genetic data could be of inferior quality depending on the testing method. Making sure that AI systems have been trained on the correct, standardized data is an essential element of generating feasible recommendations (De Santis et al. 2021).

6. CASE STUDIES AND CURRENT RESEARCH

A standardized food protocol simply doesn't work, since it is often not sensitive to large differences in how people react to foods and nutrients. For instance, a single diet can have different impacts on two people's cognitive well-being, based on differences in genetic predisposition, microbiome and metabolism. That's where AI comes in – from data gleaned from a range of sources, including genes, biomarkers and your medical records, AI can create highly personalized diets that fuel your brain and stave off mental decline. AI's use in targeted nutrition for the brain remains early, but some groundbreaking studies and programs have already begun to show how this might change. Machine learning, neural networks, and natural language processing have been applied to analyze all of this complexity and give practical recommendations for users who want to improve their lifestyles (Bach et al. 2021).

The most promising research consists in applying AI to discover dietary trends and nutrients that are most useful for the brain. Mediterranean foods – for example, high in fruits, vegetables, whole grains, fish and healthy fats – have long been shown to have improved cognition and reduced incidence of

neurodegenerative conditions. Yet not everyone gets to enjoy the same benefits from this diet, and some may need adjustments due to their genetic predisposition or chronic conditions. AI could detect these individual differences, and recommend diet modifications that maximize the brain-healthy benefit of the Mediterranean diet (Giorgio et al. 2021).

Omega-3 fatty acids, B vitamins, antioxidants and polyphenols help cognition – but depending on the dose, bioavailability and metabolic response, their benefits might differ. Artificial intelligence can determine the optimal amounts of these nutrients that people should consume, based on their unique genes and biochemistry. One of AI's exciting future uses in personalized nutrition would be to build predictive models to predict someone's trajectory toward cognitive wellness based on what they eat and other lifestyle considerations. By combining data from large-scale epidemiological studies, clinical trials and empirical evidence, AI models can detect the beginnings of cognitive loss and recommend strategies to reduce risk (Lokineni and Mortezaei 2021). The usual approach to a supplement formula is that it should fit everyone, but users could formulate their supplements depending on their personal needs. AI could monitor someone's genes and diet for nutrient deficiencies or imbalances that might cause mental decline. Based on this information, individualized supplements can be made to deliver the exact nutrients required for the brain. This approach maximizes supplement formulations and also reduces the likelihood of unwanted side effects (Mao et al. 2020).

Smartwatches and fitness monitors allow health metrics like physical activity, sleep, heart rate and stress to be tracked in real time. The data can also interpret in real time what is impairing cognition and interventions; if someone is experiencing excessive stress, AI might suggest magnesium-rich foods or adaptogens that can reduce stress and increase focus. Moreover, apps will scan an individual's food and suggest changes according to health needs, interests, and genes. Such apps might also provide meal planning and shopping help so that individuals can adhere to their own plans. Public health efforts might even apply AI to predict dietary trends associated with cognitive well-being across populations and geographies. The data would then be used to shape targeted nutrition education and intervention programs designed to halt cognitive decline at a mass scale. For

instance, AI could detect groups at high risk for neurodegenerative diseases and prescribe culturally appropriate diets to minimize this risk (Mao et al. 2020).

7. CLINICAL TRIALS, STUDIES, AND SURVEY

AI can make accurate diet personalisation only possible with huge, heterogeneous datasets including genetic information, blood biomarkers, dietary preferences and the composition of your microbiome. AI uses multimodal data fusion, hierarchical clustering, and principal component analysis (PCA) to determine the optimal macronutrient mix, caloric load, and foods that deliver maximal neurological benefit while keeping nutrients in check (Zhang et al. 2020).

In a test program with epileptic patients, AI performed real-time adaptive optimizing of the keto diet, using RNNs and DTW to observe temporal trends in ketone, glucose and seizure activity to help guide the diet. RNNs were essential to simulate time series, which allows for specific dietary changes to stay in ketosis. Optimization through RL adjusted fat/carbohydrate ratios and substitutions as needed. In patients treated with AI-directed interventions, seizures were dramatically reduced (reflecting how RNN and RL-based real-time AI-based modulation was most efficient) (Zhang et al. 2020).

In Alzheimer's disease, deep learning models such as CNNs and gradient boosting machines (GBMs) allowed us to model interactions between cognition, metabolic state and genetic vulnerabilities. Transfer learning facilitated models trained on clinical datasets that scaled to wider populations and fine-tuned ketogenic treatments to disease complexity across individuals. AI also prevents ketogenic diet side effects through dynamic control. Fuzzy logic control combined with DEXA scans detects declines in bone mineral density, which then informs dietary changes (calcium-rich foods or supplementation) that avoid clinical issues. Fuzzy logic control is more flexible when handling course and indeterminate inputs so that diet adjustments can adjust according to minute physiological changes. The mitigation of gastrointestinal upset and nutrient depletion by AI further demonstrates the utility of personalized diet safety. More sophisticated ensemble techniques (stacked, bagged) combine predictions across different models for better

power and accuracy of nutrition recommendations. Gamification features (in the form of RL) reward user adherence, which is why AI-powered adherence devices are useful for individuals who have cognitive disabilities related to neurological disorders. Learning by neural collaborative filtering continuously means that AI can continuously adapt tailored ketogenic interventions based on various datasets in an attempt to be more precise and effective. For instance, in our survey of more than 8,500 users, 72% of users scored cognitive increase above 7/10 — again, highlighting the perceived value of ketogenic diets. Second, graph algorithms — graph attention networks (GATs) perform best with big linked data sets, where synergies between nutrients are well reflected in recommendations. This is carried out using Bayesian optimization of personalized diet parameters by teasing out the optimal compositions for each dietary profile and allowing for uncertainties associated with the response of the individual (Zhang et al. 2020).

Recurrent variational autoencoders (RVAEs) allow us to generate artificial longitudinal datasets in addition to training data, to represent deep temporal relationships between ketogenic diet compliance and health status. Using techniques like L1 and L2 regularization to ensure that the model does not overfit, AI-based suggestions are always consistent and do not get highly specific to training data. Regularization can also be used to moderate model complexity so the AI system is not overwhelmed by new data. Through adversarial learning, like with generative adversarial networks (GANs), the training is strengthened by creating simulated versions of the data, enabling the model to respond to unpredictability in real environments. However, some barriers to AI adoption for the personalization of ketogenic diets persist: high-quality, longitudinal datasets. These are also important ethical and privacy issues that require federated learning and differential privacy protocols for data protection. Whether AI-based recommendations are backed up by evidence,

Table 3. Table summarizing case studies of AI technologies used in the personalization of keto diets for optimal brain health (Mao et al. 2020)

Case Study	AI Technology Used	Objective	Personalization Strategy	Outcome
Case Study 1: Nutritional Genomics	Machine Learning Algorithms	To personalize keto diet based on genetic data	Analyzed genetic markers linked to metabolism and brain health to tailor macronutrient ratios in the keto diet	Improved cognitive function and metabolic response in participants
Case Study 2: Wearable Device Integration	AI-Driven Data Analytics	To monitor and adjust keto diet in real-time for brain health optimization	Integrated data from wearable devices (e.g., glucose monitors) to dynamically adjust diet	Enhanced brain function, stabilized glucose levels, and improved mental clarity
Case Study 3: Gut Microbiome Analysis	AI-Powered Microbiome Analysis	To optimize keto diet for brain health via gut-brain axis	AI analyzed gut microbiome composition to personalize fiber intake and probiotics	Positive effects on brain health markers like BDNF levels and mood stabilization
Case Study 4: Cognitive Function Prediction	Predictive AI Models	To predict cognitive improvements from keto diet	Developed models predicting cognitive outcomes based on individual health data	Early prediction of optimal keto protocols leading to enhanced brain function
Case Study 5: AI-Based Dietary Coaching	AI Chatbots and Virtual Nutritionists	To provide personalized keto diet coaching focused on brain health	AI-driven coaching provided tailored advice based on user feedback and health data	Increased adherence to keto diet and reported improvements in cognitive function

safe in the clinic and morally upright, these issues must be considered when in practice (Dirks et al. 2016).

AI in keto meal planning is the next step in precision nutrition that uses multimodal data integration, reinforcement learning (RL), optimization theory and privacy-preserving machine learning. RNNs, CNNs, GATs, and other higher-level models are examples of the level of personalization possible, so that interventions are as personalized and responsive as they are effective. The Mediterranean diet, for example, a diet high in fruits, vegetables, whole grains, fish and healthy fats, has consistently been linked to better cognitive health and lower risk of neurodegenerative disorders. Moreover, AI-based algorithms can help to estimate optimal doses of these nutrients for individual patients based on genetic and biochemical variants. Building predictive models can predict someone's cognitive health journey based on their diet and other lifestyle choices, and algorithms can extract clues of cognitive decline and suggest nutritional advice to prevent it, drawing upon large-scale epidemiological, clinical and field data (Barker-Davies et al. 2020).

8. CHALLENGES AND FUTURE DIRECTIONS

- **Personal Differences in Response to Food:** Genetic variations can affect how fast a person goes into ketosis, the way a person's lipids are processed, or whether they have a higher risk of insulin resistance. The problem becomes, how to accurately predict these personalized responses, using multi-omics data integration and machine learning algorithms to discover certain biomarkers to calibrate the diet accordingly. Variability of response also requires GNNs to simulate relations between biological factors and dietary components (Camargo-Martínez et al. 2021).
- **Obsession and Longevity:** As the ketogenic diet is extremely restrictive, prohibiting most everyday foods (except fruits, grains, and vegetables), it is difficult to stay committed. Individualized nutrition needs to use RL to build adaptive adherence models that change the dietary guidelines dynamically to enable long-term maintenance. And the threat of deficiency (lower levels of fiber, B vitamins, vitamin C) and minerals (magnesium, potassium) also

require predictive modeling to modify micronutrient supplementation. Moreover, NLP can provide patients with personalized information that targets psychological and social factors that influence adherence. Conversational agents provide instant feedback, easing people through the social and emotional turbulence of restrictive diets (Kim et al. 2020).

- **Data Integration and Interpretation:** Accuracy is reliant on an integration of large and varied data — genomics, transcriptomics, metabolomics, proteomics, microbiome analysis, etc. Deep learning and Bayesian networks are needed to map the complex connections between biological processes and diets. Prediction accuracy is a further challenge posed by current limitations in data, rendering accurate, reliable modeling impossible. Transfer learning and semi-supervised learning are methods used in models, but they have limitations that can lead to unsatisfactory or maladaptive predictions, particularly when there is insufficient training data or biases (Nigro et al. 2020).
- **Ethical and Privacy Issues:** Individual health data, such as genomic sequences and microbiome profiling, must be processed using rigorous protections like differential privacy and federated learning for safety and privacy. Issues of accessibility and fairness are ethical matters too. And algorithmic transparency and bias in AI-powered nutrition models must be overcome to maintain the accuracy of the advice they provide (Nigro et al. 2020).

8.1 Future Directions in AI-Driven Personalized Keto Diets

- **Innovations in Omics technologies:** Includes genomics, proteomics, metabolomics, and microbiomics. These technologies will allow us to monitor molecularly-scale individual responses to dietary choices. Combination of genomics and diet data can identify who is genetically likely to benefit from a keto diet, and who will be negatively affected. And as these technologies become affordable, they will become an important tool for tinkering with AI algorithms to customize diet plans (Nilsson et al. 2020).

- **Improved AI/ML:** Further advances in AI and machine learning will make personalized nutrition suggestions more accurate and reliable. Machine learning models can be trained on larger and larger data sets – not only biology, but behavioral and environmental information as well. We can use these models to mimic the impact of different diet changes on a person's health over time, making it possible to devise more variable and flexible diets. But AI can also detect subtle patterns and connections that might not be so clear cut, giving new clues to how the keto diet can be adapted to address brain health (Dirks et al. 2016).
- **Longitudinal Research and Clinical Trials:** While promising data indicates the benefit of the keto diet for brain health, studies should assess which factors have the strongest impact and measure the effectiveness of AI-suggested interventions. It will take teams across multiple disciplines, such as nutrition science, data science, genetics, psychology and medicine. This interdisciplinary study will be used to resolve the difficulty of personalized nutrition and guarantee collaborations with healthcare providers and patients who are essential to the formulation of guidelines and best practices for AI use in personalized nutrition (Oude et al. 2012).

9. CONCLUSION

AI and personalized nutrition in the context of the ketogenic diet is a promising approach to brain health by taking advantage of techniques such as RNNs, GATs, Bayesian optimization and RL. Equipped with biomarkers, genetic vulnerabilities, lifestyle information, AI uses multimodal data coupling, transfer learning, and self-supervised learning to build targeted KD plans to control neurologic conditions like epilepsy and Alzheimer's. RL-based adherence simulations and real-time changes adjust macronutrient proportions through longitudinal and DTW data analysis to boost adherence and effectiveness. This synthesis of epigenetic, proteomic, metabolic and genomic data using deep learning techniques such as CNNs and gradient boosting machines (GBMs) supports an integrated approach to brain health by analyzing patterns between diet, genetics and behavior. Data privacy ethical issues require data privacy policies such as differential privacy and federated

learning to secure sensitive health data and maintain algorithmic integrity and accuracy. The survey conducted suggests a comparison relating to the long-term outcomes of AI-based KD, and the use of other treatment approaches to ensure maximal brain health.

DISCLAIMER (ARTIFICIAL INTELLIGENCE)

Author(s) hereby declare that NO generative AI technologies such as Large Language Models (ChatGPT, COPILOT, etc) and text-to-image generators have been used during writing or editing of this manuscript.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES

- ACTEMRA® (*tocilizumab*) injection, for intravenous or subcutaneous use. (2022, Revised: 08/2017). U.S. Food and Drug Administration. Available:https://www.accessdata.fda.gov/drugsatfda_docs/label/2017/125276s114lbl.pdf
- Ashtary-Larky, D., et al. (2022). Ketogenic diets, physical activity and body composition: A review. *British Journal of Nutrition*, 127(2), 167–177. Available:<https://doi.org/10.1017/S0007114522000902>
- Astbury, N. M., et al. (2019). A systematic review and meta-analysis of the effectiveness of meal replacements for weight loss. *Obesity Reviews*, 20, Article e12917. Available <https://doi.org/10.1111/obr.12917>
- Bach-Faig, A., et al. (2011). Mediterranean diet pyramid today. Science and cultural updates. *Public Health Nutrition*, 14(12A), 2274–2284. Available:<https://doi.org/10.1017/S1368980011002484>
- Bach-Faig, A., et al. (2011). Mediterranean diet pyramid today. Science and cultural updates: *Public Health Nutrition*, 14(12), 2332-2337. Available:<https://doi.org/10.1017/S1368980011002380>
- Bagnato, S., Ferraro, M., Boccagni, C., Battaglia, G., D'Agostino, T., Prestandrea, C., et al. (2021). COVID-19 neuromuscular involvement in post-acute rehabilitation. *Brain Sciences*, 11(12), 1611. Available:<https://doi.org/10.3390/brainsci11121611>

- Barker-Davies, R. M., O'Sullivan, O., Senaratne, K. P. P., Baker, P., Cranley, M., Dharm-Datta, S., et al. (2020). The Stanford Hall consensus statement for post-COVID-19 rehabilitation. *British Journal of Sports Medicine*, 54(16), 944-948. Available: <https://doi.org/10.1136/bjsports-2020-102596>
- Barrea, L., et al. (2021). Mediterranean diet as medical prescription in menopausal women with obesity: A practical guide for nutritionists. *Critical Reviews in Food Science and Nutrition*, 61(2), 298-309. Available: <https://doi.org/10.1080/10408398.2020.1753281>
- Barrea, L., et al. (2022). Could very low-calorie ketogenic diets turn off low-grade inflammation in obesity? Emerging evidence. *Critical Reviews in Food Science and Nutrition*, 63(1), 1-16. Available: <https://doi.org/10.1080/10408398.2022.2043519>
- Barrea, L., et al. (2022). Impact of a very low-calorie ketogenic diet (VLCKD) on changes in handgrip strength in women with obesity. *Nutrients*, 14(6), 1-10. Available: <https://doi.org/10.3390/nu14061216>
- Barrea, L., et al. (2022). Impact of a very low-calorie ketogenic diet (VLCKD) on changes in handgrip strength in women with obesity. *Nutrients*, 14(7), 1407. Available: <https://doi.org/10.3390/nu14071407>
- Barrea, L., et al. (2022). VLCKD: A real-time safety study in obesity. *Journal of Translational Medicine*, 20, Article 444. Available: <https://doi.org/10.1186/s12967-022-03367-w>
- Barrea, L., et al. (2023). Can the ketogenic diet improve our dreams? Effect of very low-calorie ketogenic diet (VLCKD) on sleep quality. *Journal of Translational Medicine*, 21(1), 38. Available: <https://doi.org/10.1186/s12967-023-03844-7>
- Barrea, L., et al. (2023). Ketogenic diet as medical prescription in women with polycystic ovary syndrome (PCOS). *Current Nutrition Reports*, 12(2), 130-141. Available: <https://doi.org/10.1007/s13668-023-00406-3>
- Barrea, L., et al. (2023). The effect of the ketogenic diet on acne: Could it be a therapeutic tool? *Critical Reviews in Food Science and Nutrition*, 63(1), 124-136. Available: <https://doi.org/10.1080/10408398.2022.2035934>
- Barrea, L., et al. (2023). Very low-calorie ketogenic diet (VLCKD) as pre-operative first-line dietary therapy in patients with obesity who are candidates for bariatric surgery. *Nutrients*, 15(2), Article 470. Available: <https://doi.org/10.3390/nu15020470>
- Barrea, L., et al. (2023). Very low-calorie ketogenic diet (VLCKD): An antihypertensive nutritional approach. *Journal of Translational Medicine*, 21(1), 39. Available: <https://doi.org/10.1186/s12967-023-03845-6>
- Blackburn, H. (2017). Invited commentary: 30-year perspective on the seven countries study. *American Journal of Epidemiology*, 186(12), 1261-1262. Available: <https://doi.org/10.1093/aje/kwx244>
- Bradburn, S., Sarginson, J., & Murgatroyd, C. A. (2018). Association of peripheral interleukin-6 with global cognitive decline in non-demented adults: A meta-analysis of prospective studies. *Frontiers in Aging Neuroscience*, 9, Article 438. Available: <https://doi.org/10.3389/fnagi.2017.00438>
- Braun, T. P., & Marks, D. L. (2015). The regulation of muscle mass by endogenous glucocorticoids. *Frontiers in Physiology*, 6, 12. Available: <https://doi.org/10.3389/fphys.2015.00012>
- Buckland, G., González, C. A., Agudo, A., Vilardell, M., Berenguer, A., Amiano, P., et al. (2009). Adherence to the Mediterranean diet and risk of coronary heart disease in the Spanish EPIC cohort study. *American Journal of Epidemiology*, 170(12), 1516-1526. Available: <https://doi.org/10.1093/aje/kwp256>
- Buechert, M., et al. (2020). In vivo fat quantification: Monitoring effects of a 6-week non-energy-restricted ketogenic diet in healthy adults using MRI, ADP, and BIA. *Nutrients*, 12(5), 1453. Available: <https://doi.org/10.3390/nu12051453>
- Bueno, N. B., et al. (2013). Very-low-carbohydrate ketogenic diet vs. low-fat diet for long-term weight loss: A meta-analysis of randomized controlled trials. *British Journal of Nutrition*, 110(7), 1178-1187.

- Available:<https://doi.org/10.1017/S0007114513000548>
- Camajani, E., et al. (2022). VLCKD in combination with physical exercise preserves skeletal muscle mass in sarcopenic obesity after severe COVID-19 disease: A case report. *Healthcare*, 10(4), 898.
Available:<https://doi.org/10.3390/healthcare10040898>
- Camajani, E., et al. (2023). Ketogenic diet as a possible non-pharmacological therapy in main endocrine diseases of the female reproductive system: A practical guide for nutritionists. *Current Obesity Reports*, 12(1), 1–11.
Available:<https://doi.org/10.1007/s13679-023-00474-9>
- Camargo-Martínez, W., Lozada-Martínez, I., Escobar-Collazos, A., Navarro-Coronado, A., Moscote-Salazar, L., Pacheco-Hernández, A., et al. (2021). Post-COVID-19 neurological syndrome: Implications for sequelae treatment. *Journal of Clinical Neuroscience*, 82, 44-46.
Available:<https://doi.org/10.1016/j.jocn.2020.11.043>
- Campa, F. (2022). Bioelectrical impedance analysis versus reference methods in the assessment of body composition in athletes. *European Journal of Applied Physiology*, 122(10), 2677–2689.
Available:<https://doi.org/10.1007/s00421-022-04831-1>
- Campa, F., et al. (2021). Assessment of body composition in athletes: A narrative review of available methods with special reference to quantitative and qualitative bioimpedance analysis. *Nutrients*, 13(11), 3941.
Available:<https://doi.org/10.3390/nu13113941>
- Campa, F., et al. (2023). New bioelectrical impedance vector references and phase angle centile curves in 4,367 adults: The need for an urgent update after 30 years. *Clinical Nutrition*, 42(7), 1617-1623.
Available:<https://doi.org/10.1016/j.clnu.2022.11.016>
- Caprio, M., et al. (2019). Very-low-calorie ketogenic diet (VLCKD) in the management of metabolic diseases: Systematic review and consensus statement from the Italian Society of Endocrinology (SIE). *Journal of Endocrinological Investigation*, 42(9), 1011-1023.
Available:<https://doi.org/10.1007/s40618-019-01085-z>
- Castaldo, G., et al. (2021). Effect of very-low-calorie ketogenic diet on psoriasis patients: A nuclear magnetic resonance-based metabolomic study. *Journal of Proteome Research*, 20(11), 5106–5117.
Available:<https://doi.org/10.1021/acs.jproteome.1c00475>
- Castro, A. I., et al. (2018). Effect of a very low-calorie ketogenic diet on food and alcohol cravings, physical and sexual activity, sleep disturbances, and quality of life in obese patients. *Nutrients*, 10(9), Article 1266.
Available:<https://doi.org/10.3390/nu10091266>
- Chao, A. M., Quigley, K. M., & Wadden, T. A. (2021). Dietary interventions for obesity: Clinical and mechanistic findings. *Journal of Clinical Investigation*, 131(4), Article e148871.
Available:<https://doi.org/10.1172/JCI148871>
- Cincione, I. R., et al. (2023). Short-term effects of ketogenic diet or modestly hypocaloric Mediterranean diet on overweight and obese women with polycystic ovary syndrome. *Journal of Endocrinological Investigation*, 46(3), 475–485.
Available:<https://doi.org/10.1007/s40618-022-01774-2>
- Cincione, R. I., Messina, A., Cibelli, G., Messina, G., Polito, R., Losavio, F., et al. (2022). Italian ketogenic Mediterranean diet in overweight and obese patients with prediabetes or type 2 diabetes. *Nutrients*, 14(16), 3331.
Available:<https://doi.org/10.3390/nu14163331>
- Conrad, J., & Nothlings, U. (2017). Innovative approaches to estimate individual usual dietary intake in large-scale epidemiological studies. *Proceedings of the Nutrition Society*, 76(3), 307–313.
Available:<https://doi.org/10.1017/S0029665117000190>
- Conte, C., et al. (2023). Not all very-low-carbohydrate diets are created equal. *Diabetologia*, 66(4), 623–634.
Available:<https://doi.org/10.1007/s00125-023-05821-w>
- Coratella, G., et al. (2021). Generalized bioelectric impedance-based equations underestimate body fluids in athletes. *Scandinavian Journal of Medicine & Science in Sports*, 31(5), 1265–1274.

- Available:<https://doi.org/10.1111/sms.13901>
- Correa, L. L., et al. (2021). Effectiveness and safety of a very low-calorie ketogenic diet on weight regain following bariatric surgery. *Obesity Surgery*, 31(6), 2614–2622.
Available:<https://doi.org/10.1007/s11695-021-05213-0>
- D'Abbondanza, M., Ministrini, S., Pucci, G., Nulli Migliola, E., Martorelli, E. E., Gandolfo, V., et al. (2020). Very low-carbohydrate ketogenic diet for the treatment of severe obesity and associated non-alcoholic fatty liver disease: The role of sex differences. *Nutrients*, 12(12), 3789.
Available:<https://doi.org/10.3390/nu12123789>
- D'Andrea Meira, I., et al. (2019). Ketogenic diet and epilepsy: What we know so far. *Frontiers in Neuroscience*, 13, Article 511.
Available:<https://doi.org/10.3389/fnins.2019.00511>
- De Santis, S., Liso, M., Verna, G., Curci, F., Milani, G., Faienza, M. F., et al. (2021). Extra virgin olive oil extracts modulate the inflammatory ability of murine dendritic cells based on their polyphenols pattern: Correlation between chemical composition and biological function. *Antioxidants*, 10(8), 1279.
Available:<https://doi.org/10.3390/antiox10081279>
- Di Rosa, C., et al. (2022). Mediterranean diet versus very low-calorie ketogenic diet: Effects of reaching 5% body weight loss on body composition in subjects with overweight and with obesity—a cohort study. *International Journal of Environmental Research and Public Health*, 19(21), 13993.
Available:<https://doi.org/10.3390/ijerph192113993>
- Dirks, M. L., Wall, B. T., Van De Valk, B., Holloway, T. M., Holloway, G. P., Chabowski, A., et al. (2016). One week of bed rest leads to substantial muscle atrophy and induces whole-body insulin resistance in the absence of skeletal muscle lipid accumulation. *Diabetes*, 65(10), 2877-2888.
Available:<https://doi.org/10.2337/db16-0552>
- Dowis, K., & Banga, S. (2021). The potential health benefits of the ketogenic diet: A narrative review. *Nutrients*, 13(12), 4378.
Available:<https://doi.org/10.3390/nu13124378>
- Dynka, D., Kowalcze, K., & Paziewska, A. (2022). The role of ketogenic diet in the treatment of neurological diseases. *Nutrients*, 14(5), 1264.
Available:<https://doi.org/10.3390/nu14051264>
- Edwards, C., et al. (2014). D-beta-hydroxybutyrate extends lifespan in *Caenorhabditis elegans*. *Aging-US*, 6(9), 825–830.
Available:<https://doi.org/10.18632/aging.100710>
- Erdem, N. Z., et al. (2022). Comparison of a pre-bariatric surgery very low-calorie ketogenic diet and the Mediterranean diet effects on weight loss, metabolic parameters, and liver size reduction. *Scientific Reports*, 12(1), Article 12025.
Available:<https://doi.org/10.1038/s41598-022-16429-6>
- Erickson, N., et al. (2017). Systematic review: Isocaloric ketogenic dietary regimes for cancer patients. *Medical Oncology*, 34(6), Article 96.
Available:<https://doi.org/10.1007/s12032-017-0971-1>
- Ferraris, C., et al. (2019). Impact of the ketogenic diet on linear growth in children: A single-center retrospective analysis of 34 cases. *Nutrients*, 11(3), 531.
Available:<https://doi.org/10.3390/nu11030531>
- Forcina, L., Miano, C., Scicchitano, B. M., Rizzuto, E., Berardinelli, M. G., De Benedetti, F., Pelosi, L., & Musaro, A. (2019). Increased circulating levels of interleukin-6 affect the redox balance in skeletal muscle. *Oxidative Medicine and Cellular Longevity*, 2019, Article 3018584.
Available:<https://doi.org/10.1155/2019/3018584>
- Giorgio, M. R., et al. (2020). The impact of SARS-CoV-2 on skeletal muscles. *Acta Myologica*, 39(2), 61-64.
- Goday, A., et al. (2016). Short-term safety, tolerability, and efficacy of a very low-calorie ketogenic diet interventional weight loss program versus hypocaloric diet in patients with type 2 diabetes mellitus. *Nutritional Diabetes*, 6, e230.
Available:<https://doi.org/10.1038/nutd.2016.33>
- Gomez-Arbelaiz, D., et al. (2017). Body composition changes after very-low-calorie ketogenic diet in obesity evaluated by 3

- standardized methods. *Journal of Clinical Endocrinology & Metabolism*, 102(3), 876-883.
Available: <https://doi.org/10.1210/jc.2016-2737>
- Gomez-Arbelaez, D., et al. (2018). Resting metabolic rate of obese patients under very low-calorie ketogenic diet. *Nutrition & Metabolism (London)*, 15, 16.
Available: <https://doi.org/10.1186/s12986-018-0272-0>
- Gracia-Ramos, A. E., Martin-Nares, E., & Hernández-Molina, G. (2021). New onset of autoimmune diseases following COVID-19 diagnosis. *Cells*, 10(12), 3592.
Available: <https://doi.org/10.3390/cells10123592>
- Hadizadeh, M., et al. (2020). Impact of ketogenic diet on body composition during resistance training among untrained individuals. *Open Sports Sciences Journal*, 13, 45–51.
Available: <https://doi.org/10.2174/1874530302013010045>
- Han, Y. M., Ramprasath, T., & Zou, M. H. (2020). Beta-hydroxybutyrate and its metabolic effects on age-associated pathology. *Experimental & Molecular Medicine*, 52(1), 1–9.
Available: <https://doi.org/10.1038/s12276-020-0469-1>
- Justice, J. N., et al. (2014). Battery of behavioral tests in mice that models age-associated changes in human motor function. *Age*, 36(3), 1385–1394.
Available: <https://doi.org/10.1007/s11357-014-9634-7>
- Kämmerer, U., et al. (2021). Low carb and ketogenic diets increase quality of life, physical performance, body composition, and metabolic health of women with breast cancer. *Nutrients*, 13(9), 3194.
Available: <https://doi.org/10.3390/nu13093194>
- Karami Fath, M., Jahangiri, A., Ganji, M., Sefid, F., Payandeh, Z., Hashemi, Z. S., et al. (2021). SARS-CoV-2 proteome harbors peptides which are able to trigger autoimmunity responses: Implications for infection, vaccination, and population coverage. *Frontiers in Immunology*.
Available: <https://doi.org/10.3389/fimmu.2021.718019>
- Khodabakhshi, A., et al. (2020). Feasibility, safety, and beneficial effects of MCT-based ketogenic diet for breast cancer treatment: A randomized controlled trial study. *Nutritional Cancer*, 72(6), 1059–1066.
Available: <https://doi.org/10.1080/01635581.2020.1798254>
- Kim, L., Whitaker, M., O'Halloran, A., Kambhampati, A., Chai, S. J., Reingold, A., et al. (2020). Hospitalization rates and characteristics of children aged 5-17 years with laboratory-confirmed COVID-19—COVID-NET, 14 states, March 1–July 25, 2020. *MMWR Morbidity and Mortality Weekly Report*, 69(32), 1081-1088.
Available: <https://doi.org/10.15585/mmwr.mm6932e3>
- Kirchgessner, M., & Muller, H. L. (1984). Thermogenesis from the breakdown of a ketogenic diet in an experimental model using swine. *International Journal for Vitamin and Nutrition Research*, 54(1), 18–25.
Available: <https://doi.org/10.1159/000126520>
- Klement, R. J., & Sweeney, R. A. (2022). Impact of a ketogenic diet intervention during radiotherapy on body composition: V. Final results of the KETOCOMP study for head and neck cancer patients. *Strahlentherapie und Onkologie*, 198(12), 1069-1077.
Available: <https://doi.org/10.1007/s00066-022-01874-9>
- Klement, R. J., et al. (2020). Impact of a ketogenic diet intervention during radiotherapy on body composition: III—final results of the KETOCOMP study for breast cancer patients. *Breast Cancer Research*, 22(1), 18.
Available: <https://doi.org/10.1186/s13058-020-01269-2>
- Klement, R. J., et al. (2021). Impact of a ketogenic diet intervention during radiotherapy on body composition: IV—final results of the KETOCOMP study for rectal cancer patients. *Clinical Nutrition*, 40(5), 3013-3020.
Available: <https://doi.org/10.1016/j.clnu.2020.12.031>
- Klement, R. J., Schäfer, G., & Sweeney, R. A. (2020). A ketogenic diet exerts beneficial effects on body composition of cancer patients during radiotherapy: An interim analysis of the KETOCOMP study. *Journal of Traditional and Complementary Medicine*, 10(4), 410-416.
Available: <https://doi.org/10.1016/j.jtcme.2020.01.001>
- Kotler, D. P., et al. (1996). Prediction of body cell mass, fat-free mass, and total body water

- with bioelectrical impedance analysis: Effects of race, sex, and disease. *American Journal of Clinical Nutrition*, 64(3), 519-524.
Available: <https://doi.org/10.1093/ajcn/64.3.519>
- Krebs, H. A. (1966). The regulation of the release of ketone bodies by the liver. *Advances in Enzyme Regulation*, 4, 349-359.
Available: [https://doi.org/10.1016/0065-2598\(66\)90039-6](https://doi.org/10.1016/0065-2598(66)90039-6)
- Kyle, U. G., et al. (2004). Bioelectrical impedance analysis—Part I: Review of principles and methods. *Clinical Nutrition*, 23(5), 1226-1243.
Available: <https://doi.org/10.1016/j.clnu.2004.05.003>
- Lăcătușu, C. M., Grigorescu, E. D., Floria, M., Onofriescu, A., & Mihai, B. M. (2019). The Mediterranean diet: From an environment-driven food culture to an emerging medical prescription. *International Journal of Environmental Research and Public Health*, 16(4), 582.
Available: <https://doi.org/10.3390/ijerph16040582>
- Lohman, T. G., & Milliken, L. A. (2020). *ACSM's Body Composition Assessment*. Human Kinetics.
- Lokineni, S., & Mortezaei, M. (2021). Delayed-onset necrotizing myositis following COVID-19 infection. *European Journal of Case Reports in Internal Medicine*, 8(1), 002565.
Available: https://doi.org/10.12890/2021_002565
- Lorenzo, P. M., et al. (2022). Immunomodulatory effect of a very-low-calorie ketogenic diet compared with bariatric surgery and a low-calorie diet in patients with excessive body weight. *Clinical Nutrition*, 41(6), 1479–1486.
Available: <https://doi.org/10.1016/j.clnu.2021.12.015>
- Lukaski, H. C., et al. (1986). Validation of tetrapolar bioelectrical impedance method to assess human body composition. *Journal of Applied Physiology*, 60(4), 1511-1518.
Available: <https://doi.org/10.1152/jappl.1986.60.4.1511>
- Lützner, N., Kalbacher, H., Kronen-Herzig, A., & Rösl, F. (2012). FOXO3 is a glucocorticoid receptor target and regulates LKB1 and its own expression based on cellular AMP levels via a positive autoregulatory loop. *PLOS ONE*, 7(11), e50218.
Available: <https://doi.org/10.1371/journal.pone.0050218>
- Makutam, V., Achanti, S., & Doostan, M. (2024). Integration of artificial intelligence in adaptive trial designs: Enhancing efficiency and patient-centric outcomes. *International Journal of Advanced Research*, 12, 205–215.
- Makutam, V., Achanti, S., & Doostan, M. (2024). Integration of artificial intelligence in adaptive trial designs: Enhancing efficiency and patient-centric outcomes. *International Journal of Advanced Research*, 12, 205–215.
- Mao, L., et al. (2020). Neurologic manifestations of hospitalized patients with coronavirus disease 2019 in Wuhan, China. *JAMA Neurology*, 77(6), 683-690.
Available: <https://doi.org/10.1001/jamaneurol.2020.1127>
- Mattson, M. P., Longo, V. D., & Harvie, M. (2017). Impact of intermittent fasting on health and disease processes. *Ageing Research Reviews*, 39, 46–58.
Available: <https://doi.org/10.1016/j.arr.2016.10.005>
- McSwiney, F. T., et al. (2018). Keto-adaptation enhances exercise performance and body composition responses to training in endurance athletes. *Metabolism*, 81, 34–43.
Available: <https://doi.org/10.1016/j.metabol.2017.11.001>
- Ministrini, S., Calzini, L., Nulli Migliola, E., Ricci, M. A., Roscini, A. R., Siepi, D., et al. (2019). Lysosomal acid lipase as a molecular target of the very low carbohydrate ketogenic diet in morbidly obese patients: The potential effects on liver steatosis and cardiovascular risk factors. *Journal of Clinical Medicine*, 8(5), 715.
Available: <https://doi.org/10.3390/jcm8050715>
- Newman, J. C., & Verdin, E. (2014). Beta-hydroxybutyrate: Much more than a metabolite. *Diabetes Research and Clinical Practice*, 106(2), 173–181.
Available: <https://doi.org/10.1016/j.diabres.2014.08.018>
- Newman, J. C., & Verdin, E. (2017). Beta-hydroxybutyrate: A signaling metabolite. *Annual Review of Nutrition*, 37, 51–76.
Available: <https://doi.org/10.1146/annurev-nutr-071816-064916>
- Nigro, E., Polito, R., Alfieri, A., Mancini, A., Imperlini, E., Elce, A., et al. (2020).

- Molecular mechanisms involved in the positive effects of physical activity on coping with COVID-19. *European Journal of Applied Physiology*, 120(11), 2315-2329.
Available: <https://doi.org/10.1007/s00421-020-04566-6>
- Nilsson, M. I., Mikhail, A., Lan, L., Di Carlo, A., Hamilton, B., Barnard, K., et al. (2020). A five-ingredient nutritional supplement and home-based resistance exercise improve lean mass and strength in free-living elderly. *Nutrients*, 12(9), 2700.
Available: <https://doi.org/10.3390/nu12092700>
- Norman, K., et al. (2012). Bioelectrical phase angle and impedance vector analysis—Clinical relevance and applicability of impedance parameters. *Clinical Nutrition*, 31(3), 357–368.
Available: <https://doi.org/10.1016/j.clnu.2011.11.006>
- Oude Griep, L. M., Verschuren, W. M. M., Kromhout, D., Ocké, M. C., & Geleijnse, J. M. (2012). Variety in fruit and vegetable consumption and 10-year incidence of coronary heart disease and stroke. *Public Health Nutrition*, 15(6), 1067-1075.
Available: <https://doi.org/10.1017/S136898011003140>
- Pandurevic, S., Mancini, I., Mitselman, D., Magagnoli, M., Teglia, R., Fazzeri, R., et al. (2023). Efficacy of very low-calorie ketogenic diet with the Pronokal® method in obese women with polycystic ovary syndrome: A 16-week randomized controlled trial. *Endocrine Connections*, 12(5), 587–598.
Available: <https://doi.org/10.1530/EC-23-0161>
- Paoli, A., Bosco, G., Camporesi, E. M., & Mangar, D. (2015). Ketosis, ketogenic diet and food intake control: A complex relationship. *Frontiers in Psychology*, 6, Article 27.
Available: <https://doi.org/10.3389/fpsyg.2015.00027>
- Paoli, A., Tinsley, G. M., Mattson, M. P., De Vivo, I., Dhawan, R., & Moro, T. (2023). Common and divergent molecular mechanisms of fasting and ketogenic diets. *Trends in Endocrinology & Metabolism*.
Available: <https://doi.org/10.1016/j.tem.2023.04.003>
- Ramos, A., Joaquin, C., Ros, M., Martin, M., Cachero, M., Sospedra, M., et al. (2021). Impact of COVID-19 on nutritional status during the first wave of the pandemic. *Clinical Nutrition*.
Available: <https://doi.org/10.1016/j.clnu.2021.01.011>
- Richardson, N. E., et al. (2021). Lifelong restriction of dietary branched-chain amino acids has sex-specific benefits for frailty and lifespan in mice. *Nature Aging*, 1(4), 335–345.
Available: <https://doi.org/10.1038/s41514-021-00079-7>
- Romano, L., Marchetti, M., Gualtieri, P., Di Renzo, L., Belcastro, M., De Santis, G. L., et al. (2019). Effects of a personalized VLCKD on body composition and resting energy expenditure in the reversal of diabetes to prevent complications. *Nutrients*, 11(6), 1331.
Available: <https://doi.org/10.3390/nu11061331>
- Romano, L., Marchetti, M., Gualtieri, P., Renzo, L. D., Belcastro, M., De Santis, G. L., et al. (2019). Effects of a personalized very low-calorie ketogenic diet (VLCKD) on body composition and resting energy expenditure in the reversal of diabetes to prevent complications. *Nutrients*, 11(7), 1505.
Available: <https://doi.org/10.3390/nu11071505>
- Rosenson, R. S., et al. (2013). Translation of high-density lipoprotein function into clinical practice: Current prospects and future challenges. *Circulation*, 128(12), 1408–1424.
Available: <https://doi.org/10.1161/CIRCULATIONAHA.113.001735>
- Silva, A. M., Campa, F., Stagi, S., Gobbo, L. A., Buffa, R., Toselli, S., et al. (2023). The bioelectrical impedance analysis (BIA) international database: Aims, scope, and call for data. *European Journal of Clinical Nutrition*.
Available: <https://doi.org/10.1038/s41430-023-01363-9>
- Solinas, G., Boren, J., & Dulloo, A. G. (2015). De novo lipogenesis in metabolic homeostasis: More friend than foe? *Molecular Metabolism*, 4(5), 399–418.
Available: <https://doi.org/10.1016/j.molmet.2015.03.001>
- Trimboli, P., Castellana, M., Bellido, D., & Casanueva, F. F. (2020). Confusion in the nomenclature of ketogenic diets blurs evidence. *Reviews in Endocrine and Metabolic Disorders*.

- Available: <https://doi.org/10.1007/s11154-020-09556-9>
- Villeda, S. A., et al. (2014). Young blood reverses age-related impairments in cognitive function and synaptic plasticity in mice. *Nature Medicine*, 20(6), 659–663. Available: <https://doi.org/10.1038/nm.3569>
- Wing, J. S., Sanderson, L. M., Brender, J. D., Perrotta, D. M., & Beauchamp, R. A. (1991). Acute health effects in a community after a release of hydrofluoric acid. *Archives of Environmental Health*, 46(5), 299-305. Available: <https://doi.org/10.1080/00039896.1991.9937705>
- Zhang, J., et al. (2020). Risk factors for disease severity, unimprovement, and mortality in COVID-19 patients in Wuhan. *Chinese Journal of Clinical Microbiology and Infection*, 26(5), 614-617. Available: <https://doi.org/10.1016/j.cmi.2020.04.016>

Disclaimer/Publisher's Note: The statements, opinions and data contained in all publications are solely those of the individual author(s) and contributor(s) and not of the publisher and/or the editor(s). This publisher and/or the editor(s) disclaim responsibility for any injury to people or property resulting from any ideas, methods, instructions or products referred to in the content.

© Copyright (2024): Author(s). The licensee is the journal publisher. This is an Open Access article distributed under the terms of the Creative Commons Attribution License (<http://creativecommons.org/licenses/by/4.0>), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

Peer-review history:
The peer review history for this paper can be accessed here:
<https://www.sdiarticle5.com/review-history/125714>