

The Ketogenic Diet:

Addressing Concerns and Considering Benefits

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Acknowledgements

A first shoutout has to go to Dr. Eric Berg. It was his insistence that we need to publish something to dispel the numerous concerns (myths) that exist about the ketogenic diet that first got this project moving. It was also his regular gentle prodding that helped to get it finished finally as well.

But once we started to take this seriously, it became clear to us that anything we published on the websites for The SMHP™ or LowCarb*USA*® needed to be factual and accurate and supported by the literature. For those of you who don't know of her, Sarah Rice has put together, in my opinion, the best and most extensive *curated database* of vetted research papers in the metabolic health space. This is mentioned in the *Resources* section. I turned to her to ask for help in identifying a few papers that we could reference to support what we were saying and that just opened up a can of worms. She was not happy with the accuracy of the language we were using most of the time and so she started editing it, which turned into rewriting it, and even adding a few sections for completeness. It has over 300 references and I don't have the words to express the appreciation I have for the work she has done.

I also need to thank Pam Devine for proof reading this in the end to come up with a couple of final suggestions and to help to get it as error free as possible.

– Doug Reynolds

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1. Introduction

This document was compiled as an attempt to address common concerns about the ketogenic diet as expressed on many popular social media platforms by the lay public. Confusion around the ketogenic diet abounds in the media and on the internet, making it difficult for everyone. Lack of nuance around personalization and diet quality issues can detract from the fact that more and more healthcare providers are successfully implementing ketogenic or carbohydrate-reduced diets to help people improve their health.

The content is streamlined for accessibility, and every effort has been made to ensure that the information is accurate, devoid of hyperbole and dogma, and supported by the literature. Over 300 *references* are supplied to enable further reading, and curious clinicians can use these as a springboard for further research. *Resources* are also listed at the end of the document, which refer to books and websites that expand on this content.

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2. What is a ketogenic diet?

A well-formulated ketogenic diet includes adequate energy, protein, fat, vitamins, and minerals. The ketogenic diet may be defined by an absolute amount of carbohydrates per day (grams/day):

- Very low-carbohydrate ketogenic (VLCK) diets recommend < 30g of dietary carbohydrate per day.[1]
- Low-carbohydrate ketogenic (LCK) diets recommend < 50 g of dietary carbohydrate per day.[2]
- Therapeutic ketogenic diets involve a more focused approach in obtaining therapeutic levels of ketones, which may be required for certain conditions like epilepsy, neurological disorders, supporting cancer treatment, and mental health conditions. Dietary carbohydrate intake is < 50g/day, often in the lower end of the range. Adjustments may be required to facilitate target ketone levels, and an experienced practitioner may be required to guide the process.[3]

Limiting carbohydrates to 20 to 50 grams per day enables the body to enter a state of nutritional ketosis. When carbohydrate levels are very low, the hormone profile begins to mimic that of a fasted state (low insulin levels) which promotes the breakdown of fat stores (lipolysis) releasing fatty acids into circulation. These fatty acids are metabolized to ketone bodies (ketones) by the liver and secreted as an alternative fuel source—this is in addition to glucose manufactured by the liver via a process known as gluconeogenesis. Therefore, the body is able to generate sufficient fuel to fulfill its energy requirements.[4] Some individuals find it more difficult to enter ketosis; if that is your goal, you may need to consume carbohydrates on the lower end of the spectrum.

Ketone bodies are readily utilized by the heart, brain, and muscle tissues, and they have various benefits for neurological functions, cellular longevity, metabolic balance, and cardiovascular health.[5]

Some conditions benefit from higher levels of ketone bodies for therapeutic benefit and this type of ketogenic diet may be referred to as medical ketogenic therapy or similar. This can require adjustments to the macronutrient ratios and the measurement of ketones to ensure a therapeutic effect is reached. Conditions such as epilepsy, neurological disorders, and mental health diagnoses are more likely to require this approach with subsequent monitoring and adjustments to ensure the best outcomes.[3] At the same time, you may be able to achieve your health goals using a less significant level of carbohydrate reduction. This is where a personalized approach is important.

One variation of the low-carbohydrate, high-fat ketogenic diet is a zero-carbohydrate (also known as carnivore) approach. While this may seem extreme, there are a subset of individuals who are succeeding with this approach, particularly with regard to autoimmune,[6,7] inflammatory,[7,8] gastrointestinal,[7,9] and mental health conditions.[10–12] These conditions may be triggered by sensitivities to plant matter, and in these instances, a zero carbohydrate approach serves as an exclusion protocol, allowing the body to heal.[9,12,13] From a place of healing, there may be scope to introduce a wider range of foods which could include plants if desired. Anecdotally, some individuals report that they are unable to broaden their diet beyond animal-based meat products and remain happy with their health status, choosing to continue this approach. Though there may be concerns about nutritional sufficiency, this problem has not been reported in the available literature, and data suggest it may not be a problem based on six-month reports,[10] ancestral dietary patterns,[12,13] and

critical reviews.[12,14] As with any therapeutic intervention, tracking biometrics is advised to ensure health goals are being met and nutritional sufficiency ia achieved.[15]

Another aspect influencing the decision to maintain this approach is its simplicity and ease in terms of shopping and cooking.[10] Removing decision making around food may be helpful for some people and enable better adherence to a reduced carbohydrate diet. Personal experimentation is a common theme when individuals have adopted a zero-carbohydrate approach, logging physical and emotional responses to foods and adjusting food intake accordingly.[10,11] Formal studies on a zero-carbohydrate approach are currently limited to qualitative surveys and case studies, so a considered approach, monitoring health markers over time, is recommended.

The ketogenic diet is often referred to as 'keto' in the media. It is worth considering that this is a broad term and that diet quality and approach should be measured against standardized terms to ensure the best chance of achieving the desired health outcomes. Different versions of the ketogenic diet have come into existence in order to help people achieve their health goals. While this might seem confusing, it can be viewed as a personalized approach where the level of carbohydrate reduction is tailored to individual needs.

2.1. Common symptoms during adaptation and “keto-flu”

“Keto flu” is a term used in the media to describe common symptoms that may be experienced during adaptation to a ketogenic diet. They are usually mild and transitory and often resolve in a few days. Symptoms may include fatigue, headache, muscle cramps, mild constipation, and light-headedness. The main mechanism behind these effects is that a reduction in carbohydrates alters signaling pathways that cause the body to hold on to water and sodium. Lower carbohydrate intakes cause the body to use up glycogen stores and insulin levels fall. Both these mechanisms have a diuretic effect whereby excess fluid (and with it, sodium) are excreted by the body. An effective remedy is to increase fluid intake with the addition of 1–1.5 teaspoons (5–7g) of salt (2–3 g sodium) daily. This can be consumed via bone broth or bouillon.[12,16] Some individuals may benefit from additional salt on an ongoing basis; a personalized approach is important.

Muscular symptoms can be supported by adding elemental magnesium (200–400 mg/day) to the fluid and salt routine suggested above. Rarely, potassium intake may also be a consideration where there are muscular symptoms, though ensuring sufficient salt intake usually prevents this. Potassium is generally obtained in sufficient quantities through vegetables and bone broth (low-salt with 50% potassium may also be used if needed).[2] Ongoing symptoms require clinical assessment and review of nutritional intake and further testing. Fortunately, most individuals find the adaptation stage passes quickly (7–10 days), and for others, there may be no or minimal symptoms for just a few days.[12]

It is important to consult with a medical professional before embarking on a ketogenic diet if you are taking any medications. In particular, individuals taking medication for diabetes, hypertension, and psychiatric disorders need to be monitored as medications may need rapid adjustments. If you have an unstable medical condition you may not be suitable for this approach, or require close monitoring.

Absolute contraindications are few and are primarily where there are disorders of metabolism such as carnitine deficiencies, polyphoria, beta oxidation disorders, and pyruvate carboxylase deficiency.

Overall, symptoms during adaptation pass quickly and benefits become noticeable. If symptoms persist it may reflect vitamin or nutritional deficiencies, or changes in a medical condition requiring the guidance of an experienced medical professional.

3. Addressing ketogenic diet concerns

The ketogenic diet first emerged as a treatment for epilepsy around 100 years ago. Clinicians noticed that fasting improved the condition, usually after 2–3 days, and determined a specific diet could mimic the biochemistry of fasting (nutritional ketosis) and therefore offer a sustainable approach to seizure management. This began the use of the ketogenic diet for the treatment of epilepsy.[17] Carbohydrate restricted diets were also being investigated for the treatment of diabetes and obesity and are noted in the literature at a similar time including work by Osler, Joslin, and Rollo. [18–20]

Over time, different variations of the ketogenic diet have been studied in order to evaluate clinical effect (now for a variety of conditions) against user tolerance and ease of adherence. It is perhaps this aspect that has led to confusion around its use and application. It is important to recognize managing a severe condition like epilepsy (which may exist with other medical conditions), and the very precise therapeutic application of the ketogenic diet in this setting, may look different from its use for other conditions,[3,21] or just as a preferred way of eating. In this section, we look at some of the concerns often raised by those interested in the ketogenic diet.

3.1. Is ketone production caused by starvation?

Ketones are not necessarily a marker of starvation.[1,22] A state of starvation is usually involuntary calorie deprivation leading to nutrient deficiencies, loss of muscle mass, and organ damage. Nutritional ketosis, produced by a well-formulated ketogenic diet, can provide a steady energy supply, nutritional sufficiency, preservation of muscle mass, and support organ health.[5]

The ketogenic diet does not normally advocate a reduction of calories but rather adjusts the source of those calories to predominantly come from fat and protein, minimizing carbohydrate.[23]

In the absence of carbohydrates, which are metabolized to glucose, the liver oxidizes fatty acids to produce ketones, which are readily used as an energy source. The body can store around 2,000 calories worth of sugar (called glycogen), which could easily get depleted within one day of fasting or extensive exercise.[24] In contrast, an average non-overweight adult stores around 130,000 calories in the form of body fat.[25] The brain is happily able to utilize glucose produced by the liver (gluconeogenesis) or ketone bodies for fuel.[4] The ability to tap into this energy source is a sign of metabolic flexibility and metabolic health. Our bodies are designed to be able to switch between fuel sources to maintain a constant energy supply—essential for our survival.

3.2. Does the ketogenic diet cause ketoacidosis?

While both ketoacidosis and nutritional ketosis involve ketones, they are two very different metabolic states.

Ketoacidosis is a rare and potentially life-threatening condition that typically occurs in type 1 diabetes when insufficient insulin is taken but may also occur in type 2 diabetes under stressful conditions such as trauma, surgery, or infections. This is usually hyperglycemic ketoacidosis.[4]

Certain medications (e.g., SGLT2 inhibitors) can, in rare instances, cause insulin to be ineffective through a disruption of counter-regulatory systems, resulting in ketoacidosis. This results in dangerously high ketone levels, variable glucose levels (which may be normal) and a decrease in the blood's pH levels. This disrupts normal metabolic and cellular functions. In these cases, blood ketones levels may occur in the range 10–25 mmol/L (58–145 mg/dL).[26,3]

Nutritional ketosis is a controlled metabolic state achieved by carbohydrate reduction in the context of a well-formulated diet. It maintains normal ketone concentrations, and blood pH levels remain in a healthy range. Blood ketone levels typically range between 0.5 and 3 mmol/L (3–17 mg/dL). In certain therapeutic applications the target ketone level may be set above 3 mmol/L (17 mg/dL), but it is unusual for ketone levels to go above 5 mmol/L (29 mg/dL).[3]

3.3. Does a ketogenic diet increase the risk of type 2 diabetes?

The ketogenic diet is one of the most effective interventions used to prevent, manage, and even reverse type 2 diabetes.[1,22,27]

Chronic, excessive carbohydrate consumption results in chronically high blood glucose levels (hyperglycemia) that results in chronically high insulin levels (hyperinsulinemia) which eventually results in insulin resistance. This manifests itself in many chronic conditions, the most common of which is type 2 diabetes.

Restricting carbohydrates sufficiently prevents hyperglycemia and eliminates hyperinsulinemia as a result. This may prevent the onset of type 2 diabetes or reverse an existing diagnosis of type 2 diabetes where the adjustment of diabetes medications is essential (commonly other medications are reduced as well).

3.4. Does the ketogenic diet increase the risk of cardiovascular disease?

The concern that the ketogenic diet may be linked to an increased risk of cardiovascular disease is primarily based on two issues. The first is the flawed research by Ancel Keys that linked saturated fat to heart disease. This research has since been refuted many times over.[28]

The second issue is the use of cholesterol as an isolated metric of risk. The latest science no longer supports the blanket statement that high cholesterol causes heart disease but considers a range of metabolic parameters to be important.[29] It has been demonstrated that total cholesterol or LDL levels are not good predictors of heart disease, especially in the absence of carbohydrates in the diet.[30] The triglyceride / HDL ratio and the count of small dense LDL particles are much more useful predictors of potential cardiac risk.[31] In fact studies show the ketogenic diet can decrease the triglyceride / HDL ratio[32](1:1 is good, a ratio >3 where measurements are in mg/dL indicates significant risk of heart attack and stroke) and reduce the number of small dense (oxidized) LDL particles.[33]

A small subset of individuals, who are usually lean and metabolically healthy, may experience significant increases in LDL on transitioning to a reduced carbohydrate diet. These individuals are

described as lean mass hyper-responders (LMHR) and researchers have begun to investigate whether high LDL-c in this context constitutes an increased risk for CVD.[34] We already know that LDL-c is not a good predictor of CVD risk when viewed as an isolated metric, and in metabolically healthy individuals (with low triglycerides and high HDL-c), the large buoyant LDL particles that predominate in this group, have no predictive value for cardiovascular disease.[35] Conversely, the small dense LDL particles that are associated with metabolic syndrome (high triglycerides and low HDL-c) are associated with increased risk,[35] and readily improve on a low carbohydrate diet.[33] While early data are promising,[36,37] cardiac imaging (e.g. a coronary artery calcium score) may be used to help determine risk in those with an LDL-c ≥190 mg/dL (4.9 mmol/L), with a score of zero being associated with low risk.[37,38] Due to the wide range of factors that can contribute to CVD risk, a context dependent and individualized approach, considering a range of biomarkers, should be undertaken. An option to reduce LDL cholesterol by adding back a small amount of carbohydrates (50–100 g/day) from starchy vegetables is available.[34] Personal preferences and competing conditions may also be a factor.[39] Cardiovascular disease (CVD) is discussed further in Section 4.6.

Risk factors that are consistently associated with CVD are diabetes, metabolic syndrome, hypertension (high blood pressure), obesity, and hyperinsulinemia (high fasting insulin),[39–41] with hyperinsulinemia and hyperglycemia (high blood glucose) being particularly important.[39,42] Carbohydrate reduction has been shown to reliably reduce these risk factors[32,33,43] which are considered in more detail in Section 4.

3.5. Is consuming saturated fat on a ketogenic diet dangerous?

Historically, saturated fats have been vilified, and unsaturated vegetable (seed) oils have been promoted as heart-healthy. Recent evidence shows that the relationship between saturated fats and heart health is much more complex than previously thought, with some studies showing no association between saturated fat and type 2 diabetes, a leading risk factor for heart disease.[44]

The bias against foods rich in saturated fats is unfounded when evidence reflects that whole foods such as full-fat dairy, unprocessed meat, and dark chocolate are not associated with an increased risk of cardiovascular disease. These whole foods have a complex matrix and high nutrient density that are likely to be beneficial and should not be compared with processed foods that are higher in fat.[45] Foods like dairy and meat have a saturated fatty acid profile (containing C15, pentadecanoic acid) that researchers have found to be beneficial, and may even be essential. [46] A meta-analysis of prospective studies demonstrated no significant evidence for an association of dietary saturated fat with an increased risk of cardiovascular disease.[47]

3.6. If the ketogenic diet is high in cholesterol, is it bad for cardiovascular health?

Cholesterol plays a crucial role in cell membrane integrity, vitamin D synthesis, bile acid production, and hormone synthesis.[48] The liver produces cholesterol in accordance with the body's needs and dietary cholesterol intake is not correlated with blood cholesterol concentrations.[49,50] There is no consistent association between plasma cholesterol and atherosclerosis,[51] and the limit on dietary

cholesterol consumption has been removed from the US dietary guidelines due to a lack of evidence, where they refer to dietary cholesterol as “not a nutrient of concern for overconsumption.”[52]

3.7. Does a ketogenic diet cause nutrient deficiencies?

A well formulated ketogenic diet has been studied across a wide range of population ages and has been shown to be nutritionally complete.[53,54] More vigilance may be required in a younger population that requires more strict macronutrient ratio control to achieve a therapeutic level of ketosis (for the management of epilepsy or other neurodevelopmental conditions); however, it may be successfully applied with no adverse events.[55] This is discussed further in Section 4:18. In older populations ketogenic diets have been successfully implemented,[56] and a higher protein diet applied to elderly care residents has been found to be protective for maintaining nutritional status in this population.[57] Animal products also provide the highest quality bioavailable nutrients like iron, retinol (active form of vitamin A), B12, selenium, zinc, and more.[58]

Nutrient deficiencies result from not consuming enough nutrient-dense whole foods and a properly formulated ketogenic diet provides all the nutritional requirements without supplementation for most people. Where an underlying condition exists some adjustments may be required. A high-carb diet, full of highly processed foods, confectionery, and soft drinks, is low in nutrients and carries a risk of nutrient deficiencies where more nutritious whole foods are displaced.[59]

A common claim is that avoiding grains will cause nutrient deficiencies. However, this position does not consider the presence of antinutrients like phytic acid, which block trace minerals.[60] Grains also contain gluten, which may promote increased gut permeability and inflammation leading to gut disorders in some people.[61]

Sufficient protein is important for body composition and for satiety (feeling full). A target of around 1.2 to 2.0 g/kg of body weight (or ideal weight) of protein is suggested.[2]

3.8. Are grains, beans, legumes, and fruits essential for health?

The ketogenic diet is often criticized for excluding whole grains, beans, legumes, and fruits, which are believed to be essential for health according to general dietary guidelines.

However, before agricultural crop farming, humans had little to no access to grains, beans, and legumes, refuting the claim that these foods play a critical role in maintaining a healthy body.[58] Because humans have evolved mainly without grains and legumes, our digestive systems are not fully adapted to break down and digest various components of grains and pulses, including certain complex carbohydrates, lectins, and phytates.[60] This may give rise to common side effects such as bloating, gas, abdominal pain, intestinal inflammation, increased gut permeability, allergies and sensitivities, unexplained fatigue, joint pain, and nutritional deficiencies.[61]

Irritable bowel syndrome (IBS) is a gastrointestinal disorder characterized by unexplained digestive issues that appears to be increasing on a population level.[62] While there may be several contributing

factors, an emphasis on grains and beans as heart-healthy and nutritious staples, may be a contributing factor.[63]

Another frequent attack on the ketogenic diet involves the avoidance of most fruits. While the ketogenic diet permits moderate amounts of berries, which are among the most nutritious fruits, high-sugar options such as grapes, bananas, mangos, and pineapples should be avoided if your goal is to maintain nutritional ketosis. This may have created a narrative that the ketogenic diet excludes nutrient-rich foods, thereby increasing the risk of nutritional deficiencies. Although fruits do contain various nutrients and dietary fiber, most vegetables offer comparable nutrition without the carbs and sugars that can interfere with ketosis. A common concern is that the ketogenic diet lacks adequate vitamin C due to restricting fruits. However, comparable amounts of vitamin C can be obtained from vegetables such as bell peppers, raw sauerkraut, kale, Brussels sprouts, and cauliflower. In addition, diets containing animal sourced foods are high in nutrient density, which is a common feature of well formulated ketogenic diets.[14,58]

3.9. What about the microbiome?

Given that so many factors (such as diet, exercise, stress, geography, and medications) can affect the microbiome, it is challenging to define what a healthy microbiome looks like.[64,65] We know that the ratio (or balance) of bacteria types and species diversity appears to be important.[66]

Processed foods are known to be detrimental to the microbiome,[67] and differences in metabolism when consuming a higher carbohydrate versus a lower carbohydrate (nutritional ketosis) diet may drive differences in the microbiome that are still healthy.[65]

A well formulated ketogenic diet with a focus on whole foods has been shown to positively influence the microbiome[68] and is suggested to contribute to the success of the ketogenic diet in neurological conditions.[69]

3.10. Does the ketogenic diet cause cravings or disordered eating?

People who have achieved their health and weight loss goals with the ketogenic diet report that the ketogenic diet is sustainable and helps reduce cravings.[70]

Starting a ketogenic diet can involve some significant changes to an existing meal plan and often restricts pleasure and comfort foods such as chips, confectionery, chocolate, ice cream, fast foods, and soda, which can cause temporary cravings as the body adjusts and hormone signaling normalizes. Food cravings reduce as your body adapts to a high-fat diet and significant glucose and subsequent insulin spikes are eliminated. Studies show fats are more satiating than carbs and provide a steady energy source. Dietary fat intake triggers the release of leptin and other similar hormones that induce satiety and reduce cravings.[71,72]

There are some people who struggle more with their relationship with food, especially ultra-processed foods, and demonstrate addictive behaviors towards these types of foods. As many as 20% of adults may meet the criteria for this condition.[73] This additional challenge may be rooted in childhood trauma

or other neurobiological vulnerabilities that make adherence to healthy eating patterns more challenging. While there is debate around terminology and diagnosis, the fact that highly processed foods can be considered addictive strengthens the case that addictive behaviors towards certain foods may be a consideration for some individuals.[74] Clinicians have begun to recognize that this population needs more support to be successful and some have developed special programs to assist these individuals[73] (see Section 6: Resources, for more information). While it may be more challenging, studies show that low-carbohydrate or ketogenic dietary approaches improve the symptoms of ultra-processed food addiction and reduce cravings.[73,75]

Carbohydrate reduction helps stabilize blood sugar levels, preventing rapid blood sugar spikes and crashes, which are among the most common causes of food cravings, especially for high-sugar and carb-heavy foods.[72,76] A ketogenic diet allows for various nutritious and satisfying foods, including meats, fish, eggs, nuts, seeds, full-fat dairy, non-starchy vegetables, and healthy fats like avocados and olive oil. With some planning, you can enjoy delicious meals while maintaining ketosis. Many find this higher, healthy fat approach less restrictive than diets based on meal replacements, calorie counting, low fat, or point-based food value systems. This explains why a ketogenic lifestyle can be successful over the long-term.

While some critics of the ketogenic diet express concerns around disordered eating patterns possibly being triggered by using this approach, emerging evidence is showing that a ketogenic diet can be successful in treating eating disorders like anorexia nervosa.[11,77] Key mechanisms include normalizing the neurological and metabolic pathways involved in the associated mental health symptoms of this condition. This can lead to improved brain function and reduction of symptoms, allowing for an improved relationship with food. This approach utilizes nutritionally replete ketosis, where ketone bodies are generated without the need for starvation measures. Ketone bodies are able to provide an efficient fuel source for the brain and seeking the state of ketosis for better brain energy supply may be one of the features that drives patients with anorexia nervosa towards restriction.[77] Maintaining higher ketone levels can be addressed by a ketogenic diet in a safe manner.

The possibility of reduced carbohydrate tolerance due to gut sensitivities in anorexia nervosa could also be considered a reason to implement a high-nutrient, low-carbohydrate approach.[78] It is important to remember that a ketogenic diet may be nutritionally sufficient and energy-replete.[53] In fact, higher energy density may be presented in relatively small amounts of food if volume is challenging. Taken together, the evidence suggests that a ketogenic diet is likely to benefit a range of disordered eating types, although this should be evaluated on an individual basis and the input of an experienced practitioner should be considered (see Section 6.4, Mental health resources)

A ketogenic diet is a metabolic therapy that can be utilized to meet health goals, which may include gaining weight or losing weight while improving body composition. Personalizing the approach according to goals may also include maintaining a healthy weight while using nutritional ketosis for other therapeutic effects.

3.11. Is the ketogenic diet only used for treating epilepsy?

We have over one hundred years of research on the use of the ketogenic diet in the treatment of epilepsy and this has expanded to include other conditions. Recently, the number of publications reflecting this interest has risen dramatically.[23,79] Being in a state of ketosis can profoundly benefit metabolic health, hormone balance, energy production, and cognitive functions. An appreciation of the potential applications of the ketogenic diet for human health is growing in the clinical and academic space, driving research forward.[12,80,81]

Common topics under investigation in relation to the ketogenic diet include:

Weight loss
Neurological disorders
Cancer
Diabetes (Type1 and Type 2)
Cardiovascular health
Body composition
Gut health and the microbiome
Mental health (includes disordered eating)
Metabolic syndrome
Inflammation
Autoimmune diseases
Aging
Endocrine disorders
Polycystic ovary syndrome
Fertility
Maternal and fetal health
Liver health
Bone health
Sleep disorders
Genetics and epigenetics
Athletic performance [82]

3.12. Does the ketogenic diet cause cancer?

The incorrect assumption that ketosis results in ketoacidosis, which is characterized by increased body acidity and thought to be (incorrectly) associated with the development of cancer, may be the source of the concern that the ketogenic diet causes cancer. Nutritional ketosis does not lead to a change in plasma pH; however, the tumor microenvironment can become acidic as a metabolic byproduct of the tumor itself.[83,84] Nutritional ketosis and the tumor microenvironment are two very different metabolic states. There is no evidence that the pH of dietary components is associated with cancer.[84]

It has long been established that cancer cells rely on glucose to proliferate and grow and that their ability to utilize ketones as a fuel source is limited. A ketogenic diet improves many metabolic

processes that contribute to cancer growth such as reducing insulin, downregulating insulin growth factor (IGF-1), and reducing inflammation. As such, utilizing a ketogenic diet to improve metabolic health may be protective.There is more and more evidence that a ketogenic diet may support cancer treatment (as an addition to standard of care protocols) and improve the well-being of cancer patients undergoing chemotherapy.[85–87]

3.13. Does the ketogenic diet affect bone health?

Studies involving children with severe epilepsy may be driving concerns that the ketogenic diet harms bone health. A mechanism suggested involves acidity changes in the blood with calcium released to act as a buffer creating more brittle bones, prone to osteoporosis. Children with epilepsy are a specific population that may be significantly affected by other conditions. It is misleading to apply findings from this group to the general population, especially as epilepsy medications and reduced mobilization can also negatively affect bone metabolism.[88,89] Overall, long term results (up to 5 years) show the ketogenic diet to be safe in the treatment of epilepsy.[55,90,91] In children and adolescents, appropriate surveillance, ensuring correct ratios and nutritional sufficiency are important to ensure growth trajectories, and studies indicate these targets can be achieved.[55]

As stated previously, while ketones are classified as acids, the state of nutritional ketosis does not alter plasma pH and no negative effects have been demonstrated when using the ketogenic diet to treat metabolic disease,[92,93] in fact, protection of bone health has been demonstrated.[94]

While long-term adherence to the ketogenic diet does not appear to be linked to poor bone health, metabolic conditions like type 2 diabetes and insulin resistance are risk factors for the development of osteoporosis,[95,96] so foods to be avoided are those that contribute to the development of these conditions[97]:

- Soft drinks
- Fried foods
- Processed foods
- Sugary foods
- Refined grains

These same foods displace nutrient dense foods which can lead to nutritional deficiencies, another cause of poor bone health, yet concerns about bone health are generally directed at the ketogenic diet.

3.14. Will the ketogenic diet damage your kidneys?

The concern that the ketogenic diet may cause kidney damage originates from several misconceptions and misunderstandings about how the ketogenic diet works and how it affects the body. Many people think the ketogenic diet is a high-protein diet, which may have the potential to cause kidney damage due to an increased need to filter and eliminate by-products of protein metabolism. The standard ketogenic diet is generally moderate in protein, commonly around 20% of daily calories.[81] Studies show the ketogenic diet does not have a negative effect on kidney

function[98]—in fact, it can improve kidney function in people with diabetes-related kidney disease,[99] obesity,[100] and polycystic kidney disease.[101]

Considering that obesity, insulin resistance, and diabetes are the primary contributors to kidney dysfunction, it is not surprising that the ketogenic diet has demonstrated promise as an effective therapeutic option for individuals affected by certain forms of kidney disease.

Kidney stones
For most individuals on a ketogenic diet, the risk of kidney stones is low. People with epilepsy, who are also on antiseizure medication, tend to be more at risk.[12,16] Other risk factors for the development of kidney stones are obesity and CKD, no matter what dietary pattern is followed. There may also be a genetic component to risk.[16] The benefits of reducing risk factors that may drive the development of kidney stones (like obesity and type 2 diabetes) need to be weighed against any risks where generally kidney disease improves with a ketogenic diet. Seeking the support of an experienced practitioner who may recommend increasing fluid intake or other measures is recommended.

3.15. Does a ketogenic diet increase the risk of gallbladder disease?

Metabolic disease appears strongly associated with gallbladder disease, with abnormalities in lipid metabolism appearing to contribute to disease risk.[102,103] These abnormalities (low HDL-c, high triglycerides) promote the development of cholesterol crystals, which precede gallstone formation. Using a reduced carbohydrate approach improves metabolic health and increases HDL-c, which supports bile acid flow, reducing the risk of gallstone disease. While rapid weight loss has been associated with an increased risk for gallstones, a higher-fat diet during weight-loss has been found to help prevent their development.[103] Seeking support from an experienced practitioner may be helpful if you have risk factors for gallstone disease and a slow transition to a ketogenic diet, allowing time for adaptation, may be appropriate. In the same way, if you have had your gallbladder removed, a slow transition to a low-carbohydrate or ketogenic approach is recommended.[104]

3.16. Can a ketogenic diet trigger a gout attack?

Metabolic dysfunction, accompanied by high levels of inflammation, is associated with gout flares, a condition that has increased significantly in the last 20 years. Increased consumption of sugar-sweetened beverages may be a factor increasing the amount of fructose in the diet which drives elevations in uric acid as a product of fructose metabolism.[12] Lowering carbohydrates in the diet lowers uric acid production by removing the need to metabolize fructose and other sugars. It also addresses features of insulin resistance and inflammation, key drivers of gout flares. Entering into nutritional ketosis can offer further benefits by causing inhibition of the NLRP3 inflammasome, reducing inflammation in a similar way to the one of the drugs used to treat gout.[12]

One caution is that ketone body metabolism uses a similar pathway to that which is used for uric acid excretion. Competition for this pathway can result in a temporary increase in uric acid concentrations as the body adapts to nutritional ketosis.[16] At the same time, rising levels of beta-hydroxybutyrate (a ketone body) counter these metabolic effects via anti-inflammatory mechanisms, providing a therapeutic benefit.[105] An experienced practitioner can advise on individual risk and may recommend a temporary treatment plan for transition. Reducing carbohydrate intake more slowly allows for the body to adapt, and it may be more beneficial to be consistent in following a ketogenic approach to avoid re-adaptation challenges.

3.17. Does the ketogenic diet increase your risk of chronic diseases?

The concern that the ketogenic diet may increase your risk of chronic disease is typically linked to concerns about a diet higher in fat and assumptions that this drives poor metabolic health. As addressed in the previous sections, this is unfounded in the context of a diet low in carbohydrates and good metabolic health.[106] Much of the confusion is also rooted in studies that label diets as 'high-fat' where they are also high in carbohydrates and usually contain processed foods (also called a Western Diet).[107] In the same way diets labeled 'high-fat' in mice are likewise often high in carbohydrates as well, and translating these studies to human outcomes has problems.[108]

Scientific evidence consistently confirms that a properly formulated ketogenic diet is safe, may be considered a primary approach for obesity and diabetes, and is beneficial for many other chronic health conditions.[12] These include:

- Cardiovascular disease
- Neurodegenerative diseases
- Cognitive decline
- Fatty liver disease
- Chronic inflammatory conditions
- Sleep disorders
- Mental health conditions

Dismissing the ketogenic diet as a fad diet that increases the risk of chronic disease is misleading, especially as its main constituents are ancestral whole foods. Encouraging the public to consume fewer carbohydrates, whether or not they are in nutritional ketosis, could contribute to a significantly lower prevalence of serious health issues, including obesity, heart disease, and type 2 diabetes.

3.18. Is a ketogenic diet good for long-term health?

Questions have been raised around the lack of long-term data on the ketogenic diet and it has been suggested that the ketogenic diet should only be used for short-term weight loss. Longer term studies in patients with type 2 diabetes (5 years and ongoing) who are in nutritional ketosis have maintained positive results, and a GP practice in the UK has published 8 year data on the successful use of a reduced carbohydrate approach.[109,110]

In a recent study of healthy women who reported sustained nutritional ketosis for 3.9 years, no adverse effects were reported, and it was suggested that this metabolic state is protective against the development of insulin resistance while preserving metabolic flexibility.[111] We know that historically, metabolic flexibility was a consistent feature of human existence, and certain populations existed in long-term ketosis, meeting nutritional needs and experiencing good health.[12,58,112]

These findings also address the question of long-term nutritional ketosis for women of reproductive age, where ancestral dietary patterns reflect thriving populations. As mentioned previously, healthy pre-menopausal women in nutritional ketosis experienced no adverse effects and were metabolically flexible. They had no negative findings where biomarkers of aging were examined.[111,113] Ketogenic diets have been found to improve menses in overweight women,[114] and women with GLUT1 deficiency syndrome (GLUT1-DS), a treatable metabolic brain condition, have normal cycles with long-term ketogenic diet therapy.[115] Therapeutic carbohydrate reduction may also be utilised for improving fertility which may be reduced in conditions of insulin resistance (see Section 4.12.).

At a time when 93% of the US population has poor metabolic health and more than 70% of food consumption is from foods that would have been unfamiliar to preagricultural humans, adopting a more ancestral way of eating seems like an excellent choice [116,117].

3.19. Is a ketogenic diet affordable and sustainable?

The affordability of a low-carbohydrate or ketogenic dietary approach is another question commonly raised when considering sustainability . Studies have shown that a whole-foods, well-formulated ketogenic diet can be nutrient dense and cost-effective, with savings occurring through fewer meals and snacks (improved satiety) and fewer medications and clinic visits.[118,119]

This approach has been successful in a low-resource setting in South Africa, and in India for children with epilepsy.[119,120]

In terms of sustainability, many who have achieved their health goals using a ketogenic approach find that the benefits outweigh any perceived downsides to continuing with this lifestyle. Examples where long-term ketogenic diets have been used with success include type 1 diabetes (10 years),[121] mental health conditions (5 years),[11] healthy females (approx 4 years),[111] and a metabolically health mixed population (5 years).[36,37] These data suggest that, in individuals who are experiencing the benefits of a ketogenic lifestyle, this way of eating may be sustained in the longer term.

Individuals who experience symptoms of carbohydrate or processed food addiction may need additional support in order to be successful. Having a supportive family or other community support can be essential and there are experienced practitioners who can assist you if this is an area of struggle (see Section 6: Resources, for more information)

4. Benefits of a ketogenic diet

Many studies have investigated the effectiveness and safety of a low-carbohydrate, high-fat diet, and evidence consistently reports metabolic, hormonal, and neurological benefits. The ketogenic diet amplifies those benefits where a state of nutritional ketosis occurs.

4.1. Improves glycemic response and insulin sensitivity

A significant number (40%) of U.S. adults have some degree of insulin resistance, which is characterized by worsening blood glucose control, contributing to high inflammation and the development of chronic diseases including mental health and neurological conditions.[122,123]

Because chronic carbohydrate consumption is a significant driver of insulin resistance, a ketogenic diet offers an effective and simple strategy to reverse insulin resistance and restore metabolic balance. Restricting carbohydrates reduces the need for insulin, a critical metabolic hormone that governs blood sugar regulation. Stable, low insulin levels can gradually improve insulin sensitivity and enhance cellular glucose uptake.[124]

4.2. Regulates appetite

As discussed in Section 3.10, a higher fat content in the diet triggers changes in appetite regulation and satiety control and helps curb cravings, especially cravings for sugar and carbohydrates. A high carbohydrate diet that elevates blood glucose and insulin results in a roller coaster of blood sugar levels throughout the day. This dysregulates hormones like ghrelin and leptin, triggering cravings and leaving people feeling 'hangry'. Reducing insulin improves leptin sensitivity which allows the brain to receive the signals that we are full. In the context of a reduced carbohydrate diet, a higher fat intake has been found to be more satisfying due to its action on brain reward centers.[71]

A ketogenic diet keeps blood sugar levels stable, reduces insulin, and allows for the regulation of hunger hormones, thereby reducing cravings and regulating appetite.[71,72]

4.3. Promotes healthy weight loss

The use of carbohydrate restriction for weight loss can be found in the literature as far back as the 1800s when it was the standard treatment for obesity.[125,126] Over time, the development of the ketogenic diet for epilepsy has been explored for other applications and there is strong evidence for its efficacy in the treatment of obesity.[80] This evidence is supported by the experiences of millions of people worldwide who have used a ketogenic diet to achieve and maintain a healthy body weight.

Generally, there is no calorie restriction associated with the diet. This is because a ketogenic diet regulates hunger signaling and allows the body to access its own fat stores for fuel, naturally reducing hunger and food intake. A properly formulated ketogenic diet is complete in the essential nutrients it provides, so weight loss and improved health are achieved at the same time.[127,128] Ensuring sufficient protein intake helps with feeling full and supports body composition (protects muscle). Suggested protein intake for a reduced carbohydrate approach is around 1.2 to 2.0 g/kg goal weight.[2]

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Key features of a ketogenic diet include the following—none of which are controversial in and of themselves:

- eating nutritious whole foods
- including sufficient, high-quality protein sources
- eating healthy fats
- limiting carbohydrates
- avoiding sugars

While the ketogenic diet is a powerful tool in weight management, other factors that can affect success include physical activity, good quality sleep, and stress reduction.

Lipedema and Lymphoedema
Lipedema is a condition that may be confused with obesity, where fat tissue accumulates primarily in the lower half of the body (from the waist down to the ankle). This type of fat tissue is resistant to traditional diet and exercise approaches, which may be due to the disease process that includes tissue fibrosis and water retention.[129,130] Due to these complications, lipedema is a painful condition which negatively impacts quality of life in a number of ways, including its resistance to treatment and risk of misdiagnosis. Studies have shown a ketogenic diet to be a promising intervention for this condition by promoting weight loss, reducing pain, reducing inflammation, and improving lymph vessel function.[130,131]

Lymphedema, which has previously been associated with cancer treatments, trauma, or infection, is now recognized as a feature of obesity, where lymphatic function is compromised and limb swelling occurs.[132,133] Early studies have shown reduced weight and limb swelling using a ketogenic approach, with ketone body metabolism thought to be an important component of success via its ability to improve lymphatic function.[132,134]

4.4. Improves type 2 diabetes control

Almost 30 million U.S. adults have been diagnosed with diabetes, and just over 97 million have prediabetes.[135] Until recently, many guidelines stated that type 2 diabetes was chronic and progressive, and there was no mention of the success of a low carbohydrate approach. Sadly, many doctors and diabetes educators are unaware that guidelines now state that a low-carbohydrate dietary approach can effectively improve blood sugar control and put type 2 diabetes into remission [136,137]. Unfortunately, a treatment protocol of a high carbohydrate diet, dosing with insulin, and other blood sugar controlling drugs like metformin may not give the best outcomes. The consequences of poorly controlled diabetes include the following:

- Cardiovascular disease
- Kidney dysfunction
- Vision loss
- Neuropathy
- Lower limb amputations

- Multiple medications
- Reduced life expectancy

The American Diabetes Association (ADA) recommends measuring your response to carbohydrates in your diet to guide management.[138] This is helpful, but unfortunately not everyone has access to measuring technology, and with the ADA 'Diabetes Plate Method' suggesting 1/4 of the plate should consist of starchy carbohydrates, the intake of carbohydrates can quickly add up.[139] At the same time, one of their most recent statements says: “Reducing overall carbohydrate intake for individuals with diabetes has demonstrated the most evidence for improving glycemia and may be applied to a variety of eating patterns that meet individual needs and preferences.”[137] These mixed messages add to confusion and detract from the data showing that individuals who have a disorder of carbohydrate metabolism tend to do better when they reduce their intake of carbohydrates.

The evidence is clear that therapeutic carbohydrate reduction lowers blood glucose and insulin, leading to reduced inflammation, improved insulin sensitivity, and reduced HbA1c levels.[140] Gradually, the titration and elimination of type 2 diabetes medications may occur, and remission from the disease could be achieved.[110]

The ketogenic diet may be more effective in lowering blood glucose and, consequently, insulin levels due to the very low level of carbohydrate consumed. This approach is often recommended, with many research studies reporting significant therapeutic results when restricting carbohydrates to no more than 20 to 50 grams per day[1,22] and many practitioners have adopted the ketogenic diet to prevent, manage, and even reverse diabetes.[109,141]

4.5. Improves type 1 diabetes control

Despite improvements in technology and healthcare, trends in glycaemic control seem to be worsening for type 1 diabetes.[142] Before insulin was available, a reduced-carbohydrate diet was the only beneficial treatment option for type 1 diabetes.[143] With the arrival of insulin as a treatment option (initially used in conjunction with the low carbohydrate approach) the amount of carbohydrate in the diet began to trend upwards and now the challenge of insulin resistance in type 1 diabetes has become a new concern.[144] This has created a sub-type of diabetes known as "double diabetes" who are more at risk of micro- and macrovascular disease. Studies indicate that irrespective of glycemic control, the rate of complications is higher in this subgroup, suggesting that poor glycemic control is not the only reason for worse outcomes in type 1 diabetes and that double diabetes is an important and independent risk factor for developing complications.[144,145] Maintaining insulin sensitivity may be a significant factor in improving outcomes for type 1 diabetes, especially given the inconsistencies in outcomes relating to glycemic control alone.[146,147]

Historical evidence points to the benefit of therapeutic carbohydrate reduction in type 1 diabetes and renewed interest has seen a recent increase in publications exploring low-carbohydrate and ketogenic diets for this population. Type 1 diabetes is an autoimmune disease where the insulin producing beta-cells in the pancreas are destroyed. In the early stages, a "honeymoon" phase is reported where beta-cells remain functional, producing enough insulin to contribute to blood glucose control. This leads to reduced insulin dosing. Several case studies have reported an extended honeymoon period following the implementation of a low-carbohydrate or ketogenic approach[148–150]

with one patient showing preserved function for more than 5 years.[150] In general, the use of this approach for type 1 diabetes has demonstrated lower HbA1c values,[151–153] lower glycemic variability and more time in range,[154,155] less frequent and less severe hypoglycemic episodes,[152–154] a reduction in insulin requirements (reported as much as 70%),[156] [151,152] and reduced cardiovascular disease risk markers.[153] Overall studies reflect that this approach is safe, feasible, and can be adhered to in the long-term.[152,153,157]

A reduced carbohydrate approach has been less studied in younger populations but available data suggest blood glucose control (and other metrics) improve and is in a similar range to the adult population.[158–160] In one study, glycemic control was quoted as being "exceptional" (mean HbA1c of 5.67% ± 0.66%)[158] and qualitative data reflect the following experiences[159]:
“I think his last A1C was 6.3 before we went low carb and then that went to 5.3 as soon as we went low carb.”
“The first [low-carbohydrate] meal we did was breakfast … that just changed our day. Like, you know as soon as you start off with fabulous flat numbers, you can just carry on… ”
“I feel so much better doing it, like I feel I’ve got so much more energy…"

Finally, the state of nutritional ketosis has been examined with respect to type 1 diabetes and endurance exercise, with positive results.[161–163]

With the prevalence of double diabetes on the rise,[164] it makes sense to address the dual concerns of blood glucose control and insulin resistance by applying a reduced carbohydrate approach. To this effect, the SMHP have published a peer-reviewed consensus statement outlining their position and the benefits of reduced-carbohydrate approaches for type 1 diabetes.[165]

4.6. Protects against metabolic syndrome

Metabolic syndrome is a group of conditions that, taken together, raise your risk of coronary heart disease, diabetes, stroke, and other serious health problems. Insulin resistance is the primary driver of metabolic syndrome.[166] The criteria for metabolic syndrome are met with three or more of the following conditions:

- A large waistline (abdominal obesity)
- Elevated blood pressure
- High triglycerides
- Low HDL cholesterol
- High fasting blood sugars

Metabolic syndrome can have serious health consequences, and following a ketogenic diet is a safe and highly effective strategy to improve or normalize all these conditions.[124] Reducing obesity and improving blood glucose control have been reviewed in previous sections. Other features of metabolic syndrome will be examined in the following sections.

4.7. Reduces triglycerides

It's a common misunderstanding that dietary fats alone are linked to elevated triglyceride levels. In fact,blood triglyceride levels primarily respond to excessive carbohydrate consumption.[167]

The body has a minimal capacity to store sugars and converts excess blood sugar into triglycerides, which are then carried to the fat cells for storage. The hormone insulin drives this process. With insulin resistance, triglyceride production is increased, thereby raising the level in circulation. Overfull fat cells leak triglycerides back into circulation, further contributing to rising blood triglyceride levels.

In a ketogenic diet, a reduced carbohydrate load decreases triglyceride production in the liver, reducing circulating triglycerides. As insulin levels fall, fat cell storage and release mechanisms normalize, whereby stored fat can be accessed and oxidized to produce ketones. Subsequently, triglyceride levels fall. A ketogenic diet has been shown to consistently reduce triglycerides with a reduction of 50% found in one study in patients with metabolic syndrome.[140,168]

4.8. Improves HDL cholesterol

HDL plays an important role in the regulation of cholesterol metabolism by removing excess cholesterol from cells. Low levels signify impaired cholesterol metabolism and this is associated with insulin resistance and an increased risk of cardiovascular disease.[169] The ketogenic diet consistently improves insulin sensitivity and cholesterol metabolism, resulting in increased HDL concentrations.[140]

As mentioned in Section 3.4, the triglyceride / HDL ratio and the count of small, dense LDL particles are much more useful predictors of potential cardiac risk than total cholesterol. These metrics are consistently improved on a ketogenic diet.[33]

4.9. Supports healthy blood pressure

Nearly half of all U.S. adults have elevated blood pressure, also known as hypertension, leaving a large proportion of the population at risk of cardiovascular disease, stroke, kidney dysfunction, and vision problems.[170]

Insulin and blood glucose concentrations influence blood pressure through their action on the kidneys and blood vessels. Insulin resistance causes the kidneys to retain sodium and impairs the relaxation (dilation) of blood vessels.[171] Other features of metabolic syndrome, like abdominal obesity, leptin resistance, and inflammation also contribute to increased blood pressure through various signaling pathways.[172]

The ketogenic diet has been found to offer a simple and effective strategy to promote healthy, normal blood pressure.[173,174] If someone is taking medication for hypertension, it is critical that they consult a doctor who is familiar with the effects of the ketogenic diet on blood pressure. A reduction in blood pressure may occur rapidly and proper adjustment of medication is essential.[175,174] See Section 6: Resources, for information on guiding medication adjustments.

4.10. Improves fatty liver disease

Metabolic-associated fatty liver disease (MAFLD), also known as nonalcoholic fatty liver disease or NAFLD, occurs when the liver is overwhelmed by the fatty acids in circulation and not able to dispose of them efficiently. The liver's production of fat in response to an excessive intake of carbohydrates exacerbates this.[176]

The ketogenic diet promotes fat burning, increasing the body's capacity to utilize fats as its primary fuel source. This enables the liver to readily access stored fatty acids within liver cells, which can lower liver fat accumulation and may help reverse a fatty liver. This process is enhanced during fasting, when dietary fats are unavailable, which explains why combining a ketogenic diet with intermittent fasting is an excellent strategy to improve fatty liver disease.[177]

There are now many studies investigating the effects of a ketogenic diet for treating nonalcoholic fatty liver disease.[178,179] One in particular found that participants following a ketogenic diet for only six days showed markedly reduced liver fat and improved insulin resistance, a primary cause of fatty liver disease.[179]

4.11. May protect or improve kidney function

Concerns about kidney function in the context of a ketogenic diet have been briefly addressed in Section 3.14. Recently, a new expression has emerged in the metabolic health space, cardiovascular-kidney-metabolic syndrome,[180] reflecting the interconnected disease processes contributing to these disorders. This comes as no surprise if we consider the underlying role of insulin resistance in these conditions—clearly reflected in the staging definitions of this newly defined syndrome.[181] This collection of diseases affected more than 25% of American adults between 2015 and 2020[180] and a recent review states the "mechanisms of hyperglycemia-induced damage to the cardio-renal system are well validated."[182] In light of this, it is hardly controversial to suggest that a diet proven to address the pathophysiology (the dysregulated physiological pathways associated with the development of a disease) of the cardiovascular-kidney-metabolic syndrome could be helpful where kidney disease is present.
A recent paper (The case for a ketogenic diet in the management of kidney disease)[16] answers many of the questions commonly raised and emphasizes that a well-formulated ketogenic diet is moderate in protein, while being low in carbohydrates, and that a state of nutritional ketosis offers additional benefits in support of kidney function. These beneficial effects may include the provision of an efficient fuel source, reduced oxidative stress, improved mitochondrial function, reduced inflammation, and antifibrotic effects.

A number of papers support the consideration of a reduced carbohydrate or ketogenic diet for mild kidney disease in type 2 diabetes, reflecting improved estimated glomerular filtration rate (eGFR) tracking with ketone levels and adherence (dose dependent),[99] improvements in three measures of renal function (serum creatinine, eGFR and albumin-to-creatinine ratio),[183] the possibility of regression from chronic kidney disease (CKD) stage 3 to 2,[184] and reversal of diabetic nephropathy (6 year duration) in a case study.[185] In general, the intervention has shown to be safe and effective in this population.[186,187]

In patients with obesity, but without kidney disease, a meta-analysis found the improvement in kidney function was greater using a reduced carbohydrate approach compared with the control diet,[188] and in patients with impaired kidney function, a ketogenic diet demonstrated weight loss and improved metabolic markers without change in kidney function.[100]

Autosomal-dominant polycystic kidney disease (ADPKD) is a genetic kidney disease involving the progressive development of cysts and declining kidney function, eventually leading to kidney failure.[101,189] Ketogenic interventions are showing promise in slowing disease progression in the presence of elevated ketones (higher ketones associated with less decline),[189] and a recent feasibility trial demonstrated improved kidney function in patients with ADPKD using this approach.[101]

Lastly, metabolic syndrome appears to predict decreased renal function in a middle aged and elderly population[190] and an increased risk of CKD in general.[191,192] Implementing therapeutic carbohydrate reduction, proven to be successful in reversing metabolic syndrome,[141] would appear to be a beneficial strategy in helping to prevent the development of CKD.

4.12. Improves reproductive health

Reproductive health is closely linked to metabolic health, and with approximately 1 in 6 adults experiencing infertility, it is a significant health concern.[193] Insulin plays a critical role in the reproductive health of men and women via its effects on the hypothalamus-pituitary-gonadal (HPG) axis and hormone production and regulation. Adipose (fat) tissue acts as an endocrine organ (hormone producing) and can also influence hormone levels and increase inflammation, contributing to reproductive dysfunction. In women, conditions like polycystic ovarian syndrome (PCOS), recurrent pregnancy loss, egg quality, and complications in pregnancy are associated with insulin resistance and obesity.[194] In men, insulin resistance and obesity are associated with reduced testosterone levels, reduced sperm quality, erectile dysfunction, and inflammation of the prostate gland.[194,195]

In PCOS, elevated insulin and insulin resistance appear to drive hormonal imbalances (especially an elevation in testosterone outside of the normal range), which lead to symptoms such as polycystic ovaries, menstrual irregularities, infertility, increased body weight (variable), acne, and facial hair.[196] Lowering insulin levels through the adoption of a ketogenic diet is an effective non-pharmaceutical strategy to restore hormone balance and alleviate PCOS symptoms.[197,198] Even against the Mediterranean diet, which is commonly thought to be very healthy, a ketogenic diet has been found to be superior.[199] Therapeutic carbohydrate reduction may also benefit conditions like abnormal uterine bleeding,[200] gestational diabetes,[201] and weight gain in menopause.[202]
In men, a ketogenic diet has been found to improve testosterone levels,[203,204] semen quality,[205] erectile function,[204] and reduce prostatitis and prostate-specific antigen (PSA) levels.[195,203]

4.13. Improves sleep disorders

Sleep is an essential pillar of health.[206] It is critical for proper brain and metabolic function, with disruption causing significant consequences for short- and long-term health.[207] Sleep problems are

common in both metabolic and neurological conditions.[208,209] Nighttime wakefulness (insomnia) and daytime sleepiness are common in both groups, with sleep apnea found more in metabolic conditions and overweight.

Multiple factors influence sleep quality, but therapeutic carbohydrate reduction has been shown to improve sleep quality in a number of settings. One mechanism is suggested to be the reduction of inflammatory markers and, consequently, an increase in melatonin levels.[210] In sleep apnea, weight loss is thought to be a significant factor for improved sleep, and in type 2 diabetes, hyperglycemia has been found to be associated with poor sleep.[211] A ketogenic diet has demonstrated improved sleep quality and quality of life in patients with obesity,[212,213] sleep apnea,[214] and type 2 diabetes.[211]

Sleep disturbances can occur in neurological conditions like epilepsy, migraine, and multiple sclerosis,[208,215] and they are the main feature of a rare sleep disorder called narcolepsy. Through its action on various pathways, including neurotransmitter regulation, reduced inflammation, and metabolism effects, the ketogenic diet has been shown to improve various elements of sleep quality. These elements include improved sleep structure (normalized REM sleep and improved slow-wave sleep)[216,217] and regulation of the sleep-wake cycle.[216,218] Specifically, studies have been shown to benefit sleep parameters in people with epilepsy,[219] migraine,[220] narcolepsy,[221] and multiple sclerosis.[215,222]

At the intersection of metabolic health and neurology lies mental health. Disordered sleep and sleep-wake cycles often occur along with psychiatric disorders.[223] A recent study demonstrated a 19% improvement in sleep quality compared to initial scores when a ketogenic diet was given to individuals experiencing serious mental illness. There was also an improvement in the severity of mental illness scores.[224]

4.14. Reduces inflammation

While short-term inflammation forms part of the healing process, a state of chronic inflammation is associated with a variety of chronic diseases such as obesity, type 2 diabetes, the development of atherosclerosis, and Alzheimer's disease. The NLRP3 inflammasome pathway is thought to be a principal driver of inflammation via multiple effects (it also controls the release of inflammatory cytokines) and is activated via immune signaling.[225]

Fasting and ketogenic therapies suppress the activity of the NLRP3 inflammasome and related (multiple) pathways to reduce inflammation. This has been demonstrated in individuals with obesity,[226,227] type 2 diabetes, and prediabetes.[184,228] While weight loss can improve inflammation markers, in a study where healthy individuals were placed on a short-term ketogenic diet, inflammation markers decreased even without weight loss, showing that nutritional ketosis appears to have unique anti-inflammatory benefits.[229]

Other inflammatory conditions that have been shown to improve with carbohydrate reduction include fibromyalgia,[230] osteoarthritis,[231] psoriatic arthritis,[232] and chronic pain.[233] Improvements in skin conditions like psoriasis,[234] acne,[235] and hidradenitis suppurativa (acne inversa)[236] have also been observed. Inflammatory gastrointestinal conditions will be covered in Section 4.14.

Inflammation is closely connected to metabolic syndrome and insulin resistance, and is implicated in most chronic disease states. This includes cardiovascular disease, type 2 diabetes, neurodegenerative disease, and cancer. The ketogenic diet is able to regulate multiple pathways and reduce inflammation, making it a good choice for maintaining metabolic health.[237]

4.15. Supports gastrointestinal health

The gut plays a key role in mediating immune and inflammatory pathways due to its barrier function—it is the connection between our bodies and the outside world. The balance of different types of bacteria and other organisms (the microbiome), the food we eat, and environmental exposures (medication, geography, age, and exercise) all contribute to our gut health. Because the gut acts as a barrier between our internal physiology and the outside world, it is acutely sensitive to metabolites and irritants, which can trigger inflammation and immune responses and increase gut permeability. Food processing changes the properties of fresh foods, altering the food matrix and often includes the addition of preservatives and other manufactured ingredients. These have the potential to irritate and upset the gut, triggering inflammatory and immune pathways.[67]

Returning to a more ancestral diet, moving away from processed foods, can support gut healing and reduce inflammation.[65,238] Therapeutic carbohydrate reduction includes the removal of processed foods, grains, and legumes, which are potential irritants.[12,60,61]

A ketogenic diet has been shown to induce favorable changes in the microbiome and promote gut healing.[7,68,239] The presence of ketone bodies, which can be used to fuel the cells of the gut lining,[65] is one mechanism of healing. As mentioned in Sections 4.13 and 4.15, the ketogenic diet also reduces inflammation and supports immune function.

Inflammatory bowel disease has been reported to respond to carbohydrate reduction, including a ketogenic diet,[7,240,241] and similar success has been observed in irritable bowel syndrome patients.[242–244] In small intestine bacterial overgrowth (SIBO) a complete removal of carbohydrates (zero carbohydrate, animal based foods only) from the diet has been shown to promote recovery and normalization of the bacterial overgrowth.[9]

Gastroesophageal reflux disease (GERD) is associated with insulin resistance and higher carbohydrate consumption[245,246] and has been successfully resolved by carbohydrate reduction.[247,248]

4.16. Supports immune function

As mentioned in Section 4.13, the ketogenic diet is able to suppress the activity of the NLRP3 inflammasome pathway, which is a significant component of the immune response.[249] Preclinical (laboratory) studies have investigated the effects of ketone bodies on immune function demonstrating improved T-cell function and nitric oxide (NO) production (NO can regulate T-cell responses) and these are now being reproduced in human trials.[250–252] Immune function and metabolic health are closely connected, and this has come to the fore in recent years with an increased interest in respiratory viral diseases and their management. Ketone bodies and metabolic health status appear to have an important role in the management of respiratory disease.[253–255] Therapeutic carbohydrate

reduction has been found to benefit a range of respiratory conditions such as chronic obstructive pulmonary disease (COPD),[256,257] chronic lung disease in infants,[258] and intubated patients with acute respiratory failure.[259]

Immune function also drives allergic and autoimmune diseases through various pathways which include the interplay between the innate and adaptive immune systems. In asthma, both immune and inflammatory pathways contribute to the condition, and insulin resistance tends to make things worse.[260] The ketogenic diet has shown promise in improving airway inflammation and immune signaling in preclinical[261] and clinical settings.[262]

A key regulator of these immune and inflammatory pathways is the microbiome and gastrointestinal system which is driven by its function as a barrier. Irritants and exposures to foreign substances can trigger inappropriate immune and inflammatory responses that contribute to the development of autoimmune disease.[263] Therapeutic carbohydrate reduction has demonstrated the ability to improve the microbiome and has shown promise in improving a variety of autoimmune conditions such as multiple sclerosis,[264] autoimmune thyroiditis,[265] ankylosing spondylitis,[266] and others[12] (see Sections 4.13 and 4.14).

4.17. Improves neurological conditions

Neurological disorders encompass a wide range of conditions which include neurodevelopmental and neurodegenerative disorders, as well as traumatic neurological injuries and migraine. There is overlap between the conditions through various pathways that include brain energy metabolism, neurotransmitter regulation, inflammation, metabolic, and the gut-brain axis. Neurological disorders may be particularly responsive to the ketogenic diet where nutritional ketosis is achieved and maintained at more therapeutic levels, between 3–5 mmol/L (17–29 mg/dL).[23]

The ketogenic diet has been used for around 100 years for treating epilepsy, where it was observed that fasting resulted in a reduction of seizures. In order to maintain the therapeutic effect without causing starvation, the ketogenic diet was developed to maintain the physiological benefit whilst providing adequate nutrition.[23] Around one third of people experience treatment resistant epilepsy (to medication), and the ketogenic diet offers the possibility of improvement. Though there is variation on an individual level, in general, the ketogenic diet improves seizure control in around 50% of individuals (may be up to 90%) and complete control may be seen in approximately 25% of those that respond. This approach can be successful for both adults and children.[23]

Epilepsy medication is also used in the treatment of migraine, giving us a clue that a ketogenic diet may benefit this condition. Common to other conditions involving the brain, the regulation of neuronal excitability and brain energy supply appear to play a major role in the onset of migraines.[267] The migraine brain appears to be more sensitive to metabolic disturbances, particularly in glucose metabolism (reactive hypoglycemia),[267,268] and the regulation of cell membrane ion channels (electrolyte imbalance).[12,269,270] The ketogenic diet provides a steady energy supply via ketone bodies, stabilizing blood glucose and targeting multiple pathways involved in migraine attacks.[271,272] Improvements in migraine frequency have been demonstrated using a ketogenic diet.[268,272,273]

Ketone bodies are also being explored in the context of traumatic brain injury due to their ability to effect neuroprotection, decrease inflammation, mitigate seizure activity, and increase neurotrophic factors.[274] A range of evidence from animal to human studies suggests a ketogenic diet could improve recovery.[275] At present, human studies show that a ketogenic approach is safe and feasible,[276,277] improves the microbiome and metabolic health in spinal cord injury,[278,279] and increases some components of memory in a small study on post-concussion syndrome.[280]

4.18. Helpful in neurodegenerative conditions

Nutritional ketosis results in a metabolic shift that improves brain energy metabolism (via the use of ketone bodies and increased mitochondrial function), decreases inflammation, regulates neurotransmitters, and removes old and damaged cells (autophagy). It can restore and protect the myelin sheath (the insulation around nerves) via its action on specialized cells that perform maintenance functions. This is in addition to the beneficial effects of the ketogenic diet on metabolic health which helps protect against the development of many neurological conditions.[281,282] A recent case study demonstrated that a ketogenic diet significantly improved metabolic markers in a person with metabolic syndrome and Parkinson's disease. Improvement in the non-motor symptoms of Parkinson's disease were also reported.[283]

Neurodegenerative diseases where the ketogenic diet has shown benefit include Alzheimer's disease,[281,284] Parkinson's disease,[12,285] Huntington's disease,[286] and amyotrophic lateral sclerosis (ALS).[287] Other conditions which have an autoimmune component and have responded to a ketogenic intervention include inclusion body myositis[288] and multiple sclerosis.[222,281]

4.19. Supportive in neurodevelopmental disorders

Neurodevelopmental disorders are a broad spectrum of conditions (that frequently coexist) such as autism spectrum disorders (ASD) and attention deficit hyperactivity disorder (ADHD), and can include movement (Tourette syndrome), speech, and language disorders.

Interest in the ketogenic diet for supporting ASD is being driven by its frequent coexistence with epilepsy, and early studies have shown promise.[289–291] In fact, there are common overlaps across many neurodevelopmental disorders, another example being Tourette syndrome (TS) and ADHD or obsessive compulsive disorder (OCD).[292] The use of epilepsy medications in treating the symptoms of these neurodevelopmental disorders highlights the overlap in features. There are many contributing factors that result in neurodevelopmental conditions but common themes have emerged such as mitochondrial and metabolic dysfunction, brain energy metabolism, genetics, and the microbiome, all of which can respond to a ketogenic intervention.

At present, the ketogenic diet has not been specifically studied in other conditions like ADHD, but because of the overlap in neuroprocessing and neuroregulation difficulties (dysfunction of the dopamine system is common in ASD, ADHD, and TS) one may expect that a diet that is nutrient dense (avoiding deficiencies) and low in processed foods and sugars (irritating to the gut and brain), would be supportive of brain function.[12] Children with ADHD appear more at risk of other psychiatric conditions in adulthood. In a recent paper,[293] three adults with anxiety, depression, and comorbid

ADHD experienced improvements in all scores related to anxiety and depression (changes in ADHD not recorded) with remission status achieved. This promising result should drive more research into the effects of a ketogenic diet on ADHD symptoms.

Allergies, food sensitivities, and fussy eating appear common in neurodevelopmental disorders and gluten-free/casein-free approaches have been used with some success.[291,294,295] A new study looking at the microbiome and inflammation markers in ASD found the implementation of a ketogenic diet led to improvements in these areas which may drive improvements in behavior and sociability.[289,296] A ketogenic diet was found to outperform a gluten-free diet in some areas in individuals with ASD,[291] and a gluten-free diet (followed for one year) led to a marked reduction in tics and OCD in both adults and children with TS.[297] Considering the various evidence streams, it seems clear that it is worth considering therapeutic carbohydrate reduction as a supportive approach in these conditions.

4.20. Promotes mood stability and cognitive function

Mood and cognition are inherently related to neurological function and, once again, we see the use of epilepsy medications for the treatment of mental illness giving us clues as to the potential role of the ketogenic diet in supporting mental health. Metabolic health and mental health are also intrinsically connected as metabolic dysfunction drives brain energy deficiency, network instability, and neurotransmitter imbalances.[298,299] This connection, and possible metabolic therapies, are being explored in a field named “metabolic psychiatry” where several recent papers have shown the ketogenic diet to be successful in improving the condition of patients with severe mental illness.[300–302]

The use of ketogenic metabolic therapy for mental health is an area where higher levels of ketone bodies (and adherence) may influence the therapeutic effect and therefore one should seek medical oversight for implementation (especially if medication is in use).[293,301,302] Ketogenic therapy in this setting is a powerful intervention that can require medication adjustments and oversight in order to safely transition into this supportive approach.[303] As an adjunct therapy, the ketogenic diet is able to improve mental health via its effects on improving brain energy metabolism, neurotransmitter regulation, network stability, and insulin resistance.[298] Over time, medication reduction may be possible and remission of symptoms can be achieved for some people.[301,303,304] See Section 6: Resources, for more information and links to help you find an experienced provider to support you if you have a mental health condition.

Many people notice an improvement in mood stability and cognitive function as a benefit of the ketogenic diet, even if the primary application was to address metabolic health.[304,305] Even in young healthy individuals, a ketogenic diet has been shown to improve network stability, an important marker of brain aging. In a study that examined the effect of diet on network stability, glucose destabilized and ketones stabilized brain networks.[299] Overall, a diet that promotes metabolic flexibility, insulin sensitivity, and a steady energy supply is associated with improved cognitive function across the lifespan—a ketogenic (or a low-carbohydrate) diet is one way to achieve this.[306]

Metabolic syndrome has been associated with impaired network efficiency and cognitive impairment,[307] and Alzheimer's disease is being referred to as type 3 diabetes due to its connection to disorders of glucose metabolism.[308] Using a reduced carbohydrate approach to manage metabolic

syndrome and type 2 diabetes could protect against the development of Alzheimer's disease, the most common neurodegenerative disorder.[308,309]

4.21. Supports healthy aging

The leading causes of death globally are cardiovascular disease (CVD) and cancer—together, they account for around 50% of deaths globally.[310] These are non-communicable diseases where insulin resistance appears to be a significant driving factor for disease development.[123,311,312] In support of this, the data also suggest that insulin sensitivity and, by extension, metabolic syndrome, may predict healthy aging.[313,314] We have previously discussed the role of insulin in CVD development (see Section 3.6 and related). In contributing to cancer risk, elevated levels of insulin can cause inflammation and drive pathways that may result in inappropriate growth and division of cells, and a reduced ability to clear old and poorly functioning cells.[111] Taken together, this dysfunctional metabolic state can increase the risk of cancer and CVD.[111,311,312]

A state of nutritional ketosis has been associated with increased longevity in animal models through mechanisms that include decreased inflammation and insulin signaling, increased autophagy (removal of old and poorly functioning cells), and improved mitochondrial function. While many of the models use caloric restriction or fasting to obtain the benefits of ketosis, a ketogenic diet can mimic the positive effects of ketosis with nutritional sufficiency—an important feature of healthy aging. A study looking at long-term adherence to a ketogenic diet found no adverse findings and excellent metabolic flexibility—a hallmark of good metabolic health.[111]

A loss of muscle mass (sarcopenia) is a concern of aging and is associated with insulin resistance and the development of frailty.[12,315,316] Ketogenic diets improve mitochondrial function, an important feature of muscle function, and have shown promising results in rodent studies for aging and motor function.[317,318] In humans a ketogenic diet can improve grip strength, body composition, metabolic status, and weight[319]; preserve muscle mass during weight loss[320,321]—even in older adults (60–75 years)[322]; and has been shown to increase circulating levels of myokines which play a role in the regulation of muscle metabolism.[323] Myokines are released during resistance training (an important component of healthy aging) and are thought to contribute to the restoration of metabolic health via various pathways.[324] Studies support the importance of protein and nutrient dense foods for protection against frailty which are key components of a reduced carbohydrate approach.[12,54,325]

4.22. Could play a role in the prevention and treatment of cancer

Cancer is the second ranked (at nearly 20%) cause of death globally.[326] There are multiple factors that can contribute to the development of cancer including age, chronic inflammation, viral infections, environmental exposures (toxins, radiation exposure, chemical exposures), and rare inherited mutations.[85] The metabolic disturbances associated with insulin resistance, metabolic syndrome, diabetes, and obesity (even where obesity is classified as metabolically healthy)[327] likely contribute to these being known risk factors for the development of cancer.[312,328,329] Therapeutic carbohydrate reduction, as an established treatment for these risk factors, indicates a role in prevention and lends itself to considered application in the presence of a cancer diagnosis.[12,87]

A key feature of the development of cancer is altered energy metabolism resulting in abnormal cell growth. This dysfunctional metabolism is known as the Warburg effect where energy deficiency within the cancer cell drives increased dependence on glucose and glutamine as fermentable fuels.[12,85] A ketogenic diet is showing promise as an adjunct metabolic therapy due to its ability to reduce glucose, suppress insulin signaling, and elevate ketone bodies—all of which can support cancer treatment. These metabolic changes weaken tumor cells (normal cells are unaffected) and make them more vulnerable to the treatment modalities applied.[330–333] While a metabolic approach to cancer management shows promise, there is still some way to go in standardizing the approach and stratifying for all cancer cell (metabolic) subtypes,[334] so a considered and sensitive approach to discussions around this strategy is most appropriate. Currently, the ketogenic diet in this setting should be seen as a supportive addition to standard of care protocols (see Section 6: Resources, for more information).

Insulin resistance and obesity are associated with worse outcomes in cancer patients which implies that any metabolic therapy that improves these features could have a clinical benefit.[335–337] A ketogenic diet has been found to be safe and effective at addressing these elements in patients undergoing cancer treatment and can be considered to have a supportive role in this context.[337–340]

4.23. May improve sports performance

The question of sports performance is a complex topic due to significant variations in individual physiology, goals, and exercise response. During exercise, both carbohydrate and fat metabolism can contribute to energy supply. Energy required by the muscle can be derived from the oxidation of free fatty acids or from sources of carbohydrates, which include blood glucose, muscle glycogen, and liver glycogen.[341] Metabolic health, metabolic flexibility, and dietary choices all play a role in how the body responds to exercise stress. Studies show that switching to a low-carbohydrate or ketogenic approach improves the ability of the body to burn fat for fuel, reduces reliance on carbohydrates for fuel, and can improve metabolic health.[342] Reducing reliance on carbohydrates for fuel has many benefits, especially in endurance sports, where gastrointestinal distress can be exacerbated by the consumption of multiple glucose delivery options (gels or liquids).

The best fueling strategy for prolonged exercise has been a matter for debate and inconsistencies in the data do not support the paradigm that muscle glycogen depletion is the sole limitation determining prolonged exercise performance.[343] An alternative theory to the carbohydrate dependent (muscle glycogen) model is that an enhanced ability to oxidize fat at a sustained rate during prolonged exercise would benefit the endurance athlete and help mitigate hypoglycaemic drift by delaying exhaustion of liver (and brain) glycogen.[343] Pre-adapting to a low-carbohydrate, high-fat (LCHF) diet in this context shows promise. Increasing efficiency for fat burning can occur quite rapidly though a longer adaptation period may be necessary for optimum results—suggested to be around 4 weeks (though there may be individual variation).[12,343] Response to carbohydrate input is individual and appears to be a feature of brain metabolic flexibility and how adapted for fat oxidation and ketone use they are. Very little carbohydrate may be required to protect performance (around 37-74 g), though some may be required.[344,345]

For short duration and strength performance, a study on elite artistic gymnasts demonstrated no differences in strength after 30 days on a ketogenic diet, and a significant improvement in body composition (decreased weight and fat mass, non-significant increase in muscle mass).[346] Similarly, a study examining the effect of a very low-carbohydrate high-fat diet (ketones detected) on high-intensity interval training (HIIT) found no evidence of performance compromise during final stages of the graded exercise test or HIIT sessions.[347]

Evaluation of studies that conclude negative effects of LCHF diet shows individual variation[12,345,348] and the totality of evidence essentially reflects performance equivalence (despite different demands), though there is some variation of effect amongst individuals.[343] In consideration of best performance, being of a healthy weight for the sport in question and being metabolically flexible are likely to support performance.[12] An individualized approach on the low-carbohydrate to ketogenic spectrum, considering performance goals (professional or amateur) and underlying health markers (e.g., insulin resistance), would seem to offer the most promise.

5. Conclusion

A carbohydrate reduced or ketogenic diet that is well formulated and focused on whole foods is a way of eating rooted in ancestral patterns that have demonstrated resilience to disease. Our modern food environment has been shown to be detrimental to our health which, in conjunction with other changes in lifestyle, has led to an epidemic of poor metabolic health and chronic disease. A whole foods, carbohydrate reduced approach is a simple way to address metabolic dysregulation that acts on multiple pathways. A ketogenic diet amplifies the effect and may be especially useful for severe metabolic diseases, neurological diseases, and improving mental health. The ketogenic diet addresses the root causes of many of the conditions discussed above, which include insulin resistance, obesity, and type 2 diabetes—major risk factors for heart disease and cancer.

Misconceptions around the ketogenic diet abound, but evidence suggests the concerns are largely unfounded when examined critically, with the majority of individuals being able to improve their health status using this approach. However, it would be a misconception to consider that any one variation of the ketogenic diet is right for everyone—it is an approach that should be tailored to individual health goals and metrics.

As with any lifestyle change, individual responses vary, and appropriate medical monitoring is advised, especially where medication is in use (see Section 6: Resources, for Clinical Guidelines). There is now a growing body of clinicians who recognize the importance of metabolic health and the role of lifestyle interventions in the treatment of chronic disease. Clinicians from a broad range of specialties are now embracing this approach as a powerful tool in helping patients improve their health (see Section 6: Resources, for Practitioner listing).

6. Resources

6.1. *The SMHP Clinical Guidelines*

(https://thesmhp.org/clinical-guidelines/)

The Society for Metabolic Health Practitioners provides support and training for clinicians as well as general resources. Clinical guidelines can support the implementation of therapeutic carbohydrate reduction (you can print a copy for your healthcare provider).

Sections that may be of particular interest include Section 2.1 (Essential nutrition), 2.2 (Different levels of carbohydrate reduction), 2.3 (Fiber—considering total vs net carbohydrates), 6.0 (De-prescribing and medication adjustment).

6.2. *SMHP Practitioner listing*

(https://thesmhp.org/directory/)

The SMHP has a list of practitioners who consider metabolic health and lifestyle interventions alongside the standard medical approach and are available to support you on your journey.

6.3. *Nutrition Network References Resource*

(https://nutrition-network.org/references-resource/)

The *Nutrition Network* is an online accredited education, connection, and learning platform. It provides training and resources for coaches and healthcare practitioners wanting to gain skills and certification in the use of therapeutic carbohydrate restriction (including a ketogenic approach) in practice.

The *Nutrition Network Reference Resource* website provides evidence streams pertaining to metabolic health and various degrees of therapeutic carbohydrate restriction across a broad range of conditions. These research articles provide more information and expand on the points listed in this document.

6.4. Mental health resources

It is important to receive appropriate support and medical oversight if you are struggling with a mental health condition—especially if you are taking medication. Ketogenic metabolic therapy is a powerful intervention and may require medication adjustments or monitoring during the adaptation phase. The following resources provide additional information and list providers who are experienced in providing support and are able to work with a medical team to ensure safe application of this approach.

6.4.1. *Metabolic Mind*

(https://www.metabolicmind.org/)

Metabolic Mind is a nonprofit organization pursuing the science of metabolic psychiatry and collecting personal stories to offer education, and hope to people struggling with mental health. Their *resources* section may be particularly useful (*https://www.metabolicmind.org/families-and-peers*)

6.4.2. *Dr. Georgia Ede – Diagnosis:Diet*
(https://www.diagnosisdiet.com/about)

Dr. Ede is a Harvard-trained psychiatrist specializing in nutritional and metabolic psychiatry with 25 years of clinical experience. She is the author of *Change Your Diet, Change Your Mind* which unpacks the science behind how your food choices can affect your mood via their influence on brain metabolism. She also provides a *clinician directory* (https://www.diagnosisdiet.com/directory) for those looking for someone to support them on their journey, and a *training program* (https://www.diagnosisdiet.com/training) for those practitioners wanting to upskill in the use of ketogenic nutritional therapy for mental health.

Ede G. Change Your Diet, Change Your Mind: A Powerful Plan to Improve Mood, Overcome Anxiety, and Protect Memory for a Lifetime of Optimal Mental Health. Balance; 2024. 464 p.

6.4.3. *Dr Chris Palmer*
(https://www.chrispalmermd.com/)

Dr. Palmer is an Assistant Professor of Psychiatry at Harvard Medical School and the founder and director of the Metabolic and Mental Health Program at McLean Hospital. His book presents a unifying theory of the cause of mental illness, integrating the fields of clinical medicine, neuroscience and metabolic research. *Brain Energy* explores the concept that mental disorders are metabolic disorders of the brain presenting a clear and cohesive theory and suggestions for implementing metabolic therapies.

Palmer CM. Brain Energy: A Revolutionary Breakthrough in Understanding Mental Health--and Improving Treatment for Anxiety, Depression, OCD, PTSD, and More. Dallas, TX: BenBella Books; 2022. 320 p.

6.5. Resources for the symptoms of carbohydrate and processed food addiction

6.5.1. *Bitten Jonsson – Bitten's Addiction*
(https://www.bittensaddiction.com/en/)

Bitten Jonsson has worked in the field of addiction medicine for 37 years and is a registered nurse, addiction specialist, ADDIS®/SUGAR®-authorized (addiction screening, assessment, and diagnostic tools), and Nutrition Network practitioner. Jonsson believes all addiction begins in the brain and works with *ASAM's* definition of Addiction Interaction Disorder which aims to correct the dysfunctions of the brain's circuitry through a combination of traditional medicine and integrative functional medicine. Jonsson has developed a *training program* for healthcare providers who encounter individuals requiring this additional level of support and has a list of providers certified in the use of this approach.

6.5.2. *Dr Jen Unwin – Fork in the Road*

(https://forkintheroad.co.uk/)

Dr. Jen Unwin is a consultant clinical and health psychologist with over 35 years of experience, mostly working for the NHS (UK). Dr. Unwin has struggled with her own addiction to processed foods and carbohydrates and her own journey, combined with input from top clinicians, has led to the publication of *Fork in the Road: A Hopeful Guide to Food Freedom.* This book guides individuals on a journey—identifying if you have a carbohydrate addiction, finding motivation for change, implementing the right eating plan, and providing strategies for long term success.

Unwin J. Fork in the Road: A Hopeful Guide to Food Freedom. Independently published; 2021. 150 p.

6.5.3. *Dr Rob Cywes*

(https://obesityunderstood.com/)

Dr. Cywes is dual board certified in general surgery and pediatric surgery with a special interest in obesity, diabetes , and metabolic management—including bariatric surgery. His focus is on helping people understand and treat the causes of obesity and diabetes, considering surgery as a tool along the journey of becoming carbohydrate-free. Dr. Cywes recognized the treatment model primarily used in obesity management—the calories in, calories out (CICO) model—was flawed and developed the carbohydrate insulin model of obesity and diabetes (CIMOD). Combining this model with his understanding of the psychology of addiction, led to the development of a clinical program for treating obese adolescents. Dr. Cywes is a board member of the SMHP and releases regular videos on his *YouTube channel* as a resource for those struggling with carbohydrate addiction (https://www.youtube.com/@DrCywesCarbAddictionDoc).

6.5.4. *Dr. Tro Kalayjian*

(https://doctortro.com/)

Dr. Kalayjian is a board-certified physician in internal medicine and obesity medicine. His personal journey with weight loss, which began in childhood, has led to a deep understanding of the challenges faced by those on a weight-loss journey. His practice uses telemedicine, state-of-the-art patient monitoring technology, a fully integrated medical and coaching team, and access to support, education, and community through the Toward Health App. This includes an innovative *Get Help Now!* board to provide immediate support and encouragement in moments of struggle. The app ensures an exceptional level of individualized care and support, which is reflected in the success of the various wellness programs, the results of which appear in published literature.
Dr. Kalayjian is a board member of the Society of Metabolic Health Practitioners and is committed to patient care and the promotion of TCR through research publications and advocacy.

6.6. Resources for support of cancer treatment

6.6.1. *Miriam Kalamian EdM, MS, CNS - Dietary Therapies*

(https://www.dietarytherapies.com/)

Miriam Kalamian is a nutrition consultant and author specializing in the implementation of therapeutic carbohydrate reduction and ketogenic nutrition plans. Her passion for helping others implement nutritional strategies comes from her personal journey with her young son, Raffi, who fought his own battle with cancer.

Kalamiam M, Seyfried TN. Keto for Cancer: Ketogenic Metabolic Therapy as a Targeted Nutritional Strategy. Illustrated edition. Chelsea Green Publishing; 2017. 400 p.

6.6.2. *Dr Nasha Winters*

(https://www.drnasha.com/)

Dr. Winters is a licensed Naturopathic Doctor (ND) and a Fellow of the American Board of Naturopathic Oncology (FABNO) with nearly 30 years of experience in the field of integrative oncology. Winters co-authored the book *The Metabolic Approach to Cancer* and offers consultations, and training programs for fellow clinicians. Her passion for helping others stems from her own recovery from a terminal cancer diagnosis.

Winters N, Higgins Kelley J, Turner K. The Metabolic Approach to Cancer: Integrating Deep Nutrition, the Ketogenic Diet, and Nontoxic Bio-Individualized Therapies. White River Junction, Vermont: Chelsea Green Publishing; 2017. 408 p.

6.6.3. *Dr Thomas Seyfried*

(https://tomseyfried.com/)

Dr. Seyfried is a professor of biology, genetics, and biochemistry at Boston College. His research program focuses on mechanisms by which metabolic therapy can be applied to chronic diseases such as epilepsy, neurodegenerative diseases, and cancer. The metabolic therapies considered include calorie restriction, fasting, and ketogenic diets. In his book *Cancer as a Metabolic Disease: On the Origin, Management, and Prevention of Cancer,* Dr Seyfried addresses controversies related to the origins of cancer and provides solutions to cancer management and treatment.

Seyfried T. Cancer as a Metabolic Disease: On the Origin, Management, and Prevention of Cancer. 1st edition. Wiley; 2012. 877 p.

6.6.4. *Expert Consensus Paper*

A recent paper (authors include Miriam Kalamian and Dr Seyfried) presents a comprehensive overview of the application of the ketogenic diet for glioblastoma that includes background, implementation strategies, trouble-shooting, and research challenges.

Duraj, T. *et al.* (2024) 'Clinical research framework proposal for ketogenic metabolic therapy in glioblastoma', *BMC Medicine*, 22(1), p. 578. Available at: https://doi.org/10.1186/s12916-024-03775-4.

6.7. Recommended reading

6.7.1. The Art and Science of Low Carbohydrate Living: An Expert Guide to Making the Life-Saving Benefits of Carbohydrate Restriction Sustainable and Enjoyable

Written by Doctors Volek and Phinney, who together have more than 50 years of clinical experience in using a low carbohydrate or ketogenic approach, this book covers the science and application of the approach in detail.

Phinney SD, Volek JS. The Art and Science of Low Carbohydrate Living: An Expert Guide to Making the Life-Saving Benefits of Carbohydrate Restriction Sustainable and Enjoyable. 1st edition. Lexington, KY: Beyond Obesity LLC; 2011. 316 p.

6.7.2. Why We Get Sick: The Hidden Epidemic at the Root of Most Chronic Disease—and How to Fight It

Professor Bikman is an internationally renowned scientist looking at the pathophysiology of disease with a special interest in the role of insulin and ketones on metabolic function. In his book, *Why We Get Sick,* he explores why insulin resistance affects so many people and how it connects many diseases together through a singular root cause. These include type 2 diabetes, obesity, cancer, neurological disease, and inflammatory disorders. Bikman also covers gut health and aging, and explains the effect of hormonal and insulin signaling pathways on the disease process.

Bikman B, Fung J. Why We Get Sick: The Hidden Epidemic at the Root of Most Chronic Disease—and How to Fight It. Dallas, TX: BenBella Books; 2020. 270 p.

6.7.3. Ketogenic: The Science of Therapeutic Carbohydrate Restriction in Human Health

The Nutrition Network brought together experts from around the world to produce a textbook, collating an extensive resource including background and clinical knowledge in the field of therapeutic carbohydrate reduction. This is an academic publication with a high level of medical content and terminology and is more suitable for clinicians or those who want an in-depth look at the subject. *Ketogenic: The Science of Therapeutic Carbohydrate Restriction in Human Health* is available through various platforms.

Noakes TD, Murphy T, Wellington N, Kajee H, Rice SM, editors. Ketogenic: The Science of Therapeutic Carbohydrate Restriction in Human Health [Internet]. Academic Press; 2023 [cited 2023 Jul 26]. Available from: *https://www.sciencedirect.com/science/article/pii/B9780182161700002 18*

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