

Healing Type 2 Diabetes with a Plant-Based Ketogenic Diet

Metabolic Recovery, Remission, and
Evidence-Based Safety

Revised English Edition - Full 27-Chapter Book

All 53 figures are redrawn in English. Body paragraphs are fully justified. Every chapter ends with a Sources and References section.

Prepared from the complete Korean edition and its evidence-based chapter structure.

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Chapter 1. Diabetes Is a Metabolic Problem, Not Just a Blood-Glucose Problem

1. Is High Blood Glucose a Cause or a Result?

High blood glucose is central to the diagnosis of diabetes. Yet elevated glucose alone cannot explain the entire course of type 2 diabetes. The American Diabetes Association (ADA) describes type 2 diabetes as a condition in which insulin resistance is accompanied by a progressive failure of pancreatic beta cells to secrete enough insulin. Blood glucose is therefore an essential diagnostic marker, but behind that number lie abnormalities in both insulin action and insulin secretion.

In a healthy state, a rise in blood glucose after a meal triggers insulin release from pancreatic beta cells. Insulin promotes glucose uptake and use in skeletal muscle, suppresses glucose release from the liver, and restrains excessive lipolysis in adipose tissue, thereby regulating the flow of free fatty acids in the circulation. When these organs work together, glucose is maintained within a relatively narrow range.

The problem is that this regulatory system does not fail all at once. As muscle and liver become less responsive to insulin, the pancreas secretes more insulin to maintain the same glucose level. Early in the process, glucose may still look normal, but the body is already requiring a higher insulin concentration. If this compensatory state persists, beta-cell demand increases and blood glucose eventually begins to move outside the normal range.

For this reason, glucose and insulin should not be interpreted in isolation. Even when glucose remains normal, unusually high insulin may indicate that metabolic dysfunction is progressing. Conversely, once glucose has risen, treatment should address not only the glucose number but also why the body has come to require so much insulin.

2. What Does Insulin Actually Do?

Insulin is often introduced simply as “the hormone that lowers blood glucose.” That is not wrong, but it is incomplete. Insulin is a metabolic signal that helps determine where incoming energy is stored and how it is used after a meal. It affects glucose utilization, glycogen synthesis, fat synthesis, suppression of fat breakdown, and protein metabolism.

Skeletal muscle is one of the major sites for disposal of post-meal glucose. When muscle responds well to insulin, glucose transport and utilization increase and postprandial glucose settles quickly. When muscle insulin sensitivity falls, less glucose can be handled by the same amount of insulin, so the pancreas compensates by secreting more.

The liver has a different role. During fasting it supplies glucose to the circulation so that the brain and other tissues have fuel. After a meal, insulin should suppress this hepatic glucose production. When the liver becomes insulin resistant, glucose production may remain inappropriately high even without food intake, contributing to elevated fasting glucose.

Adipose tissue is also more than a passive storage depot. Insulin suppresses lipolysis in fat cells. With insulin resistance, release of free fatty acids can rise, and these fatty acids may move to the liver and muscle, increasing metabolic stress. In type 2 diabetes, glucose and fat metabolism are not separate problems; they reinforce one another.

3. How Does Insulin Resistance Begin?

Insulin resistance does not arise in only one organ. Insulin responsiveness can change in skeletal muscle, liver, adipose tissue, brain, and other metabolic tissues. DeFronzo expanded the classic triad of muscle, liver, and beta-cell dysfunction to the “ominous octet,” which also includes adipose tissue, the gastrointestinal tract, alpha cells, kidneys, and the brain. The important point is that type 2 diabetes cannot be reduced to a single defect.

Muscle insulin resistance reduces the capacity to dispose of glucose after meals. Hepatic insulin resistance prevents adequate suppression of glucose production during fasting. Adipose insulin resistance increases lipolysis and the flow of free fatty acids. These changes do not remain isolated; together they place pressure on the entire metabolic system.

Compensatory hyperinsulinemia is especially important. When the pancreas secretes more insulin to keep glucose normal, routine glucose testing may show little abnormality for some time. But the need for persistently high insulin already signals reduced metabolic efficiency. Hyperglycemia becomes more obvious when beta cells can no longer meet the rising demand.

4. Why Do Beta Cells Lose Function?

Declining beta-cell function is a core feature of type 2 diabetes. As the disease progresses, the ability to secrete an appropriate amount of insulin at the appropriate time diminishes. In particular, loss of the rapid early insulin response after a meal can allow postprandial glucose to rise sharply.

Beta-cell dysfunction cannot be explained simply as “burnout.” Genetic susceptibility, inflammation, oxidative stress, chronic exposure to high glucose, excess fatty acids, and lipid intermediates all contribute. More recent thinking also suggests that some dysfunction may reflect suppressed function or loss of cellular identity in an adverse metabolic environment, rather than only irreversible cell death.

Research on diabetes remission provides an important clue. In some people with type 2 diabetes who achieve substantial weight loss and reductions in liver and pancreatic fat, beta-cell insulin secretion can recover to a meaningful degree. This does not occur in everyone, but it demonstrates that at least some metabolic abnormalities in type 2 diabetes are modifiable rather than permanently fixed.

5. The Liver Is Central to Fasting Glucose

High morning fasting glucose cannot always be blamed on carbohydrate eaten the night before. Even when no food is consumed overnight, the liver releases glucose into the blood. Normally insulin keeps hepatic glucose production under control; with hepatic insulin resistance, that brake becomes weaker.

Excess fat accumulation in the liver is closely linked to this process. Roy Taylor’s “twin-cycle hypothesis” describes a self-reinforcing cycle in which increased liver fat promotes hepatic insulin resistance, while increased lipid transport to the pancreas contributes to beta-cell dysfunction. Subsequent studies have shown that when weight loss reduces liver fat, hepatic insulin sensitivity and fasting glucose can improve rapidly.

The key issue is not the scale number alone. Two people at the same body weight can have very different patterns of fat distribution and different capacities to safely store fat. Ectopic fat stored in organs such as the liver and pancreas - tissues not designed for large fat stores - may directly interfere with metabolic function.

6. Muscle Is the Largest Glucose-Disposal Site

Muscle matters even when a person is not exercising. It is a large reservoir and consumer of glucose after meals. Low muscle mass or reduced muscle insulin sensitivity decreases the available capacity for handling postprandial glucose. This is why exercise affects glucose control through more than simply burning calories; it also influences insulin sensitivity and glucose disposal.

Muscle energy status is also connected to the metabolic effects of diet. If energy intake persistently exceeds energy expenditure, and glycogen storage is already well supplied, surplus energy may be pushed toward other storage pathways. Such conditions can promote hepatic fat accumulation and de novo lipogenesis.

Therefore, adjusting carbohydrate intake in diabetes is not simply about “avoiding sugar.” A more useful concept is matching incoming glucose load to the individual’s current capacity for glucose disposal, storage, and insulin action. Later chapters on ketogenic diets will examine this metabolic transition in greater detail.

7. Fat Cells Send Metabolic Signals

Body fat is not inherently harmful. Adipocytes provide a relatively safe place to store surplus energy. Problems arise when storage capacity is exceeded. As fat cells enlarge and become dysfunctional, free-fatty-acid release can increase, inflammatory signaling can rise, and lipid is more likely to spill into the liver, muscle, and other tissues.

This is the context for the concept of “lipotoxicity.” It does not mean that fat itself is a poison. Rather, excessive accumulation of fatty acids and certain lipid intermediates in inappropriate locations can disrupt cellular signaling, mitochondrial function, and insulin action. In type 2 diabetes, both the amount of fat and where it is stored matter.

8. What Does Hyperinsulinemia Mean?

Looking only at glucose can miss a substantial part of early metabolic dysfunction. Early in insulin resistance, the pancreas may secrete more insulin and keep glucose within the normal range. Fasting glucose or HbA1c may therefore remain only mildly abnormal while fasting or post-meal insulin is already elevated.

At the same time, insulin concentrations should not be used alone to label a person’s disease state. Insulin secretory capacity varies widely, and results depend on the assay and timing of measurement. Insulin should therefore be interpreted together with glucose, HbA1c, body weight, waist circumference,

triglycerides, HDL cholesterol, liver fat, and other clinical information.

For this reason, this book does not track glucose alone. When appropriate, it also considers fasting insulin and HOMA-IR, body weight, waist circumference, and lipid markers. The same principle is used when comparing research on plant-based and ketogenic diets.

9. Can Type 2 Diabetes Be Viewed as a Problem of Energy Surplus and Distribution?

It is dangerous to explain all type 2 diabetes through a single cause. Genetic predisposition, sleep, physical activity, medications, hormones, age, and body-fat distribution all matter. Nevertheless, in many people, persistent energy surplus and unfavorable fat deposition form an important link between insulin resistance and beta-cell dysfunction.

Taylor's twin-cycle hypothesis describes this process through the liver and pancreas. Energy surplus increases liver fat, reinforcing hepatic insulin resistance and hyperinsulinemia, while increased lipid transport impairs pancreatic function. Clinical observations that weight loss and a shift in energy balance can reverse parts of this cycle provide an important foundation for understanding the possibility of type 2 diabetes remission.

There does not have to be only one dietary strategy. In some trials, total energy intake and weight loss were central. In others, carbohydrate restriction was used to lower glucose and medication requirements rapidly. Research on plant-based diets highlights food quality, fiber, weight, and fat quality. The rest of this book examines step by step where these different pathways may converge.

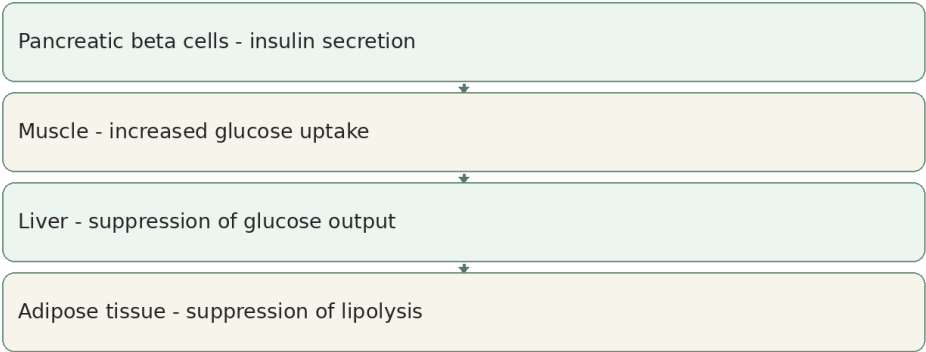
10. Is Lowering Blood Glucose the Same as Restoring Metabolic Health?

Lowering glucose is essential. Persistent hyperglycemia is associated with microvascular and macrovascular complications and should not be ignored. But better glucose values alone do not prove that insulin resistance, liver fat, body weight, medication dependence, and beta-cell function have all recovered.

In this book, metabolic recovery is therefore a broader concept. Improved glucose and HbA1c are foundational, but insulin requirements, body weight and composition, liver and lipid metabolism, blood pressure, medication use, and sustainability are considered together. For people in whom it is achievable, reaching remission and maintaining it safely becomes an important goal.

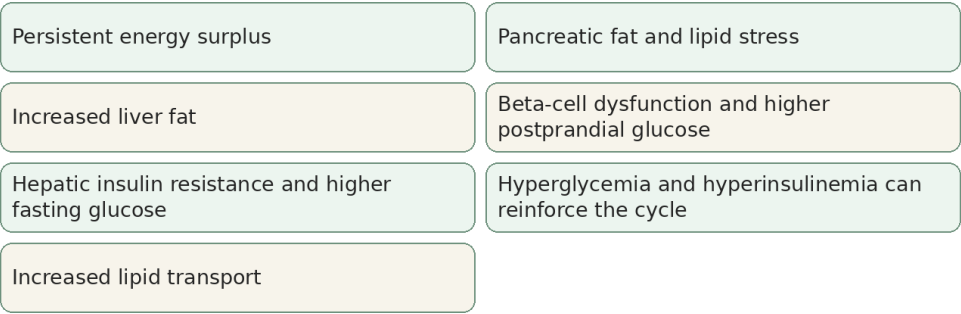
The conclusion of Chapter 1 is simple: diabetes may be detected with a glucose meter, but it does not begin and end with the glucose meter. The next chapter examines how hyperglycemia and insulin resistance leave their mark on the blood vessels, kidneys, nerves, retina, and cardiovascular system.

Figure 01-1. Three organs linked by insulin in normal glucose regulation



Source: DeFronzo (2009) and ADA (2026); author reconstruction.

Figure 01-2. Conceptual twin-cycle connection between the liver and pancreas



Source: Taylor (2013, 2025), Twin Cycle Hypothesis; author reconstruction.

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Chapter 2. How Diabetes Damages the Whole Body

1. Why Is High Blood Glucose a Problem?

High glucose alone does not explain every step in the development of diabetic complications. Still, prolonged exposure to excess glucose clearly places stress on blood vessels, nerves, the kidneys, and the retina. Chronic hyperglycemia can amplify cellular injury through nonenzymatic protein glycation, oxidative stress, activation of protein kinase C, and changes in the polyol and hexosamine pathways.[2-1]

What matters is not one isolated high reading but the magnitude and duration of exposure. When glucose repeatedly rises and remains elevated, endothelial cells and capillary structures experience continuing metabolic stress. In the UKPDS, intensive glucose control in people with newly diagnosed type 2 diabetes reduced the risk of microvascular complications, providing clinical evidence that lowering long-term glycemic exposure can change outcomes.[2-2]

This does not mean that glucose should be driven as low as possible in every person. ADVANCE and other large studies showed that benefits of tighter control must be balanced against hypoglycemia, age, disease duration, cardiovascular disease, kidney disease, and other comorbidities. Preventing complications therefore requires more than glucose management alone; blood pressure, lipids, body weight, smoking, kidney function, and medication choices must be addressed together.[2-3]

2. What Are Glycation and Advanced Glycation End Products?

Glucose is a fuel, but when concentrations are high and exposure is prolonged, glucose can bind nonenzymatically to proteins and lipids. Through a series of reactions, this can generate advanced glycation end products, or AGEs. AGEs can change the properties of proteins in the vascular wall and stimulate receptor signaling that contributes to inflammation and oxidative stress.[2-1]

The problem with AGEs is not merely that they circulate transiently in blood. When modifications accumulate on long-lived proteins such as collagen, they can influence vascular elasticity and the properties of the extracellular matrix. Binding of AGEs to the receptor RAGE can also activate inflammatory signaling, making this one of the pathways linking chronic hyperglycemia to vascular injury.[2-1]

HbA1c is also based on glycation in a broad sense. It measures the proportion of hemoglobin that has been glycated during exposure of red blood cells to glucose and therefore reflects average glycemic exposure over a longer period than a single glucose measurement. HbA1c, however, is not a direct test of AGE accumulation or vascular injury. Clinically it is a key measure of glycemic control, while complication risk must still be interpreted in the context of other risk factors.[2-4]

3. Oxidative Stress Connects Multiple Injury Pathways

Cells produce energy by oxidizing nutrients. Reactive oxygen species are generated in the process, but normal antioxidant systems keep them under control. Problems arise when hyperglycemia and metabolic overload persist. Brownlee proposed an integrated model in which excess mitochondrial superoxide production can connect several biochemical pathways implicated in diabetic microvascular injury.[2-1]

In this model, oxidative stress is less a lone culprit than an amplifier. The polyol pathway, AGE formation, protein kinase C activation, and the hexosamine pathway can interact and alter endothelial function and inflammatory responses. Describing complications only as “high glucose damages blood vessels” therefore misses important intermediate mechanisms.[2-1]

A caution is necessary. Discovering these molecular pathways does not automatically mean that taking large amounts of a particular antioxidant will prevent complications. The clinically proven foundations remain integrated management of glucose, blood pressure, lipids, kidney risk, and lifestyle. Mechanistic biology explains why damage occurs; treatment decisions should follow evidence from clinical trials.[2-5]

4. What Changes When the Vascular Endothelium Is Injured?

The endothelial cells lining blood vessels are not simply a passive wall. They actively regulate vasoconstriction and vasodilation, platelet responses, movement of inflammatory cells, and exchange of substances between blood and tissues. In diabetes, hyperglycemia, hypertension, dyslipidemia, smoking, obesity, and inflammation can all place simultaneous stress on endothelial function.[2-5]

When these changes persist in small vessels, tissues that depend heavily on dense microvascular networks - such as the retina, kidneys, and peripheral nerves - are especially vulnerable. In large arteries, atherosclerotic changes increase the risk of myocardial infarction, stroke, and peripheral artery disease.

Microvascular and macrovascular complications appear different, but they share many risk factors.[2-5]

For this reason, complication management cannot be divided neatly organ by organ. Glucose stabilization must be combined with management of blood pressure, LDL cholesterol, kidney function, body weight, and smoking. The Steno-2 trial showed that intensive multifactorial management in high-risk people with type 2 diabetes and microalbuminuria can reduce cardiovascular events and mortality over the long term.[2-6]

5. Why Is the Retina Vulnerable?

The retina has very high metabolic activity and depends on an exceptionally dense microvascular network. Diabetic retinopathy can progress through changes in capillary permeability, microaneurysms, hemorrhage, ischemia, and abnormal new-vessel formation. Early disease may be asymptomatic, so normal vision does not prove that the retina is free of injury.[2-7]

The ADA recommends an initial dilated eye examination at the time type 2 diabetes is diagnosed, followed by periodic surveillance based on retinal findings and risk. Appropriate management of blood glucose, blood pressure, and lipids can help reduce the risk of developing or progressing retinopathy.[2-7]

Retinopathy also matters because it is not necessarily an isolated eye problem. Retinal microvascular changes may provide a clue that systemic microvascular damage is present. Retinopathy can coexist with kidney disease or neuropathy, so detection of one complication should prompt attention to others.[2-7]

6. Why Can Kidney Damage Progress Silently?

The kidneys filter enormous volumes of blood every day. In diabetes, altered glomerular pressure and an unfavorable metabolic environment can allow albumin to leak into the urine, and filtration capacity can decline over time. Chronic kidney disease is diagnosed when increased urinary albumin, reduced eGFR, or other evidence of kidney damage persists.[2-8]

People with type 2 diabetes may already have kidney injury at diagnosis. The ADA therefore recommends measuring urinary albumin-to-creatinine ratio and eGFR at least annually in all people with type 2 diabetes. Once kidney disease is identified, monitoring becomes more frequent according to risk, and treatment includes not only glucose and blood pressure control but also consideration of medications with established kidney-protective effects.[2-8]

A particularly important feature of diabetic kidney disease is that it may progress quietly. Significant functional loss can occur without pain or obvious symptoms, making a “wait until symptoms appear” strategy unsafe. Detecting early changes in albuminuria and eGFR allows treatment intensity and lifestyle management to be adjusted sooner.[2-8]

Diet must also be individualized according to kidney function. Protein, sodium, potassium, and fluid recommendations can differ by stage of kidney disease and by medication use. A plant-based ketogenic diet should therefore not be applied from a generic menu in a person with kidney disease; eGFR, albuminuria, serum potassium, and other relevant measures should guide individualization.[2-8]

7. Why Do Nerves Become Numb, Tingling, or Painful?

Diabetic neuropathy is not a single disorder but a group of nerve injuries. The most common form is distal symmetric polyneuropathy, which typically begins in the toes and progresses upward on both sides. Some people experience pain, burning, or tingling; others develop numbness or have no symptoms at all.[2-7]

The absence of symptoms can itself be dangerous. The ADA notes that much diabetic peripheral neuropathy can exist without obvious symptoms. If loss of protective sensation goes unnoticed, small injuries or repeated pressure may not be felt, increasing the risk of foot ulceration. Regular foot examination and sensory testing are therefore important.[2-7]

Autonomic neuropathy broadens the problem further. It can affect gastrointestinal motility, heart-rate regulation, orthostatic blood pressure, sweating, bladder function, and sexual function. Not every neurologic symptom in a person with diabetes should automatically be attributed to diabetes; treatable alternatives such as vitamin B12 deficiency, thyroid disease, or nerve entrapment should also be considered.[2-7]

8. A Diabetic Foot Problem Can Begin with a Small Injury

Foot ulceration is not simply a matter of fragile skin. Loss of sensation can prevent a person from noticing injury, foot deformity and repetitive pressure can worsen tissue damage, and peripheral artery disease can reduce the blood flow needed for healing. If infection is added, the risk of hospitalization or amputation rises.[2-7]

The ADA recommends at least an annual comprehensive foot assessment, with more frequent review for people who have loss of sensation or a history of ulceration or amputation. Daily

inspection of the soles and spaces between the toes, as well as checking footwear for pressure points or foreign objects, are practical preventive habits.[2-7]

The diabetic foot illustrates the broader principle of complication management. Lowering glucose does not make established sensory loss or impaired circulation disappear immediately. Metabolic improvement must be combined with foot protection, vascular assessment, infection management, and appropriate footwear.[2-7]

9. Cardiovascular Disease Is One of the Major Risks in Diabetes

Cardiovascular disease - including atherosclerotic cardiovascular disease and heart failure - is a major source of morbidity and mortality in diabetes. The ADA identifies myocardial infarction, stroke, and peripheral artery disease as major contributors to disease burden and death. Diabetes often clusters with hypertension, dyslipidemia, obesity, and smoking, which further increase risk.[2-5]

This is why cardiovascular risk cannot be explained by glucose alone. In UKPDS, the microvascular benefit of intensive glycemic control was clear, whereas early macrovascular effects were more limited. In Steno-2, by contrast, simultaneous management of glucose, blood pressure, lipids, renin-angiotensin system blockade, and lifestyle reduced long-term cardiovascular events and mortality.[2-2][2-6]

The 21-year follow-up of Steno-2 showed that early intensive multifactorial treatment can have lasting effects on survival and complications. It is a strong reminder that the goal is not simply “good glucose” but reduction of the total risk profile.[2-9]

The same principle applies when evaluating a plant-based ketogenic diet. A lower HbA1c does not automatically mean lower cardiovascular risk. LDL-C, triglycerides, HDL-C, blood pressure, weight, kidney function, and smoking status should be considered, and medications with proven cardiovascular benefit should be used when clinically indicated.[2-5]

10. Diabetes Also Affects the Brain and Cognition

The relationship between diabetes and the brain is complex. Hyperglycemia, hypoglycemia, hypertension, cerebrovascular disease, kidney disease, and inflammation can all influence cognition. The ADA notes that older adults with diabetes have a higher risk of cognitive decline and dementia than older adults without diabetes and recommends periodic cognitive screening in those aged 65 years and older.[2-10]

Cognitive impairment can in turn make diabetes management more difficult. Calculating insulin doses, planning meals, recognizing hypoglycemia, and taking multiple medications at the correct time can become challenging. When cognition declines, avoiding hypoglycemia and simplifying treatment may be more important than pursuing overly strict glycemic targets.[2-10]

This principle extends to dietary therapy. A theoretically perfect plan with complicated carbohydrate calculations and multiple rules may be unsafe or unsustainable for someone who cannot manage it independently. The goal of diabetes treatment is not to produce beautiful numbers on paper; it is to preserve function, safety, and quality of life.[2-10]

11. The Most Realistic Strategy for Delaying Complications

Reading about diabetic complications can make it seem as if every organ is destined to fail. That is not the purpose of this chapter. The more useful message is that early and integrated management of glucose, blood pressure, lipids, kidney function, smoking, and lifestyle can meaningfully reduce risk.[2-5][2-8]

UKPDS showed that sustained glycemic control can reduce microvascular complications in type 2 diabetes. ADVANCE also found effects of intensive glycemic management on major microvascular outcomes, particularly kidney-related outcomes. Yet treatment intensity cannot be identical for everyone; hypoglycemia and treatment burden require individualized goals.[2-2][2-3]

Steno-2 delivered an even broader message. When glucose, blood pressure, lipids, kidney risk, and lifestyle were managed together, long-term cardiovascular events and mortality were reduced. Preventing complications is therefore not about a single nutrient or a single number; it is about lowering the whole risk profile.[2-6][2-9]

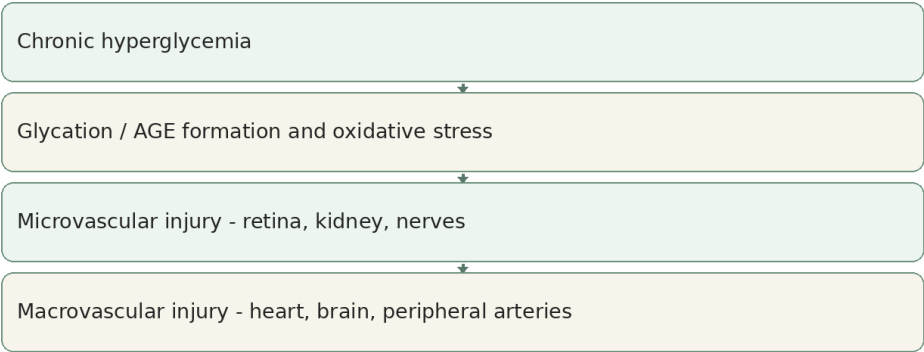
The same framework will be used to evaluate plant-based and ketogenic diets. We will not look only at how far HbA1c falls, but also at body weight, blood pressure, LDL-C, triglycerides, kidney function, medication reduction, hypoglycemia, and long-term sustainability. A good diet should improve glycemia without increasing risk to other organs and should be maintainable over time.[2-5][2-8]

The conclusion of Chapter 2 is clear: diabetic complications may begin with glucose, but they are not a glucose-only problem. Because the microvasculature, large arteries, kidneys, nerves, eyes, and brain are interconnected, treatment must also be integrated. The next chapter moves from this whole-body metabolic view to the question of how humans use not only

glucose but also fatty acids and ketone bodies as energy substrates.[2-5]

Chapter 2 Notes and References

Figure 02-1. Major pathways from hyperglycemia to diabetic complications



Source: ADA pathophysiology guidance and diabetic-complication literature; author synthesis.

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Chapter 3. From Glucose Metabolism to Fat and Ketone Metabolism

1. The Body Does Not Use Only One Fuel

We are often taught that the human body uses glucose as its primary energy source. That is true, but it does not fully describe human energy metabolism. Immediately after a meal, glucose use rises. Between meals and during overnight fasting, liver glycogen and fatty acids become more important. As fasting continues, the liver converts fatty acids into ketone bodies and supplies them to the brain, muscle, and other tissues. Human metabolism is not fixed to one fuel; it is an adaptive system that shifts fuel use according to nutritional state.[3-1]

This transition is not like an electrical switch that changes completely at one moment. As glucose use falls, fatty-acid oxidation rises gradually and hepatic ketone production increases progressively. It is therefore more accurate to view “glucose metabolism” and “ketone metabolism” as overlapping states on a continuum in which the relative contribution of each fuel changes.[3-2]

This perspective matters in diabetes. In type 2 diabetes, blood glucose can be high while cellular responses to insulin are impaired, disturbing the regulation of fuel selection and storage. Dietary therapy is therefore discussed not only as a way to lower glucose numbers but also as a way to improve the metabolic flexibility needed to move appropriately between glucose and fat use.[3-3]

2. Where Does Glucose Go After a Meal?

When carbohydrate is eaten, digested glucose is absorbed from the intestine into the bloodstream. As glucose rises, pancreatic beta cells increase insulin secretion. Insulin promotes glucose uptake and use in muscle and adipose tissue while suppressing glucose production by the liver. Some of the excess glucose is stored as glycogen in liver and muscle.[3-4]

Post-meal insulin is not merely a “glucose-lowering hormone.” It signals that energy has arrived and promotes synthesis and storage. Hepatic glycogen synthesis rises, while lipolysis in adipose tissue is suppressed. As a result, the supply of circulating free fatty acids and ketone production naturally falls after eating.[3-4]

This does not mean that fat use stops completely. The heart, skeletal muscle, and other tissues can use fatty acids and glucose simultaneously depending on conditions. The important variable is proportion. In the high-insulin postprandial state, carbohydrate use and storage are relatively favored; as fasting progresses, the balance shifts.[3-2]

3. Glycogen Bridges Short Periods of Fasting

Glycogen is the storage form of carbohydrate in which glucose molecules are linked in a branched structure. It is stored mainly in the liver and skeletal muscle, but the two stores serve different purposes. Liver glycogen contributes to maintenance of blood glucose, whereas muscle glycogen is used primarily within the muscle for contraction and energy production.[3-4]

After a meal, as circulating insulin begins to fall, the liver breaks down stored glycogen and releases glucose into the blood. This process, glycogenolysis, allows blood glucose to remain within a workable range for hours even without food intake.[3-1]

Glycogen stores are limited. As fasting lengthens, the contribution of hepatic glycogen falls and gluconeogenesis - production of new glucose from lactate, glycerol, and some amino acids - becomes more important. This adaptation maintains the glucose required by tissues with substantial glucose dependence, including red blood cells and parts of the brain.[3-1]

4. Fasting Changes the Hormonal Direction

As fasting continues, insulin concentrations fall and the relative influence of counter-regulatory hormones, including glucagon, rises. In particular, a lower insulin-to-glucagon ratio creates an environment favoring hepatic glucose production, fatty-acid oxidation, and ketogenesis.[3-5]

Classic prolonged-fasting studies observed that glucagon rises early in fasting and remains higher than in the fed state. Yet long-term fasting adaptation cannot be explained by glucagon alone. Lower insulin, adipose lipolysis, increased delivery of fatty acids to the liver, and changing energy requirements all participate.[3-5]

The important issue is not fasting time alone but the accompanying hormonal and substrate changes. Two people can fast for the same number of hours yet develop ketones at different rates because of differences in the carbohydrate content of the previous meal, activity, liver glycogen, and insulin sensitivity. Variation in the timing of ketosis is therefore normal.[3-2]

5. Adipose Tissue Begins Releasing Stored Energy

When insulin falls, stored triglycerides in adipose tissue are more readily broken down into fatty acids and glycerol. Free fatty acids travel through the circulation to the liver, muscle, and other tissues, while glycerol can be used by the liver as a substrate for gluconeogenesis.[3-6]

This is a central feature of fasting metabolism. When dietary glucose supply decreases, adipose tissue releases long-stored energy into the circulation. Fatty acids are used directly as fuel by many tissues, and some of the fatty acids entering the liver are converted into ketone bodies.[3-6]

Increased lipolysis does not mean that every fatty acid immediately becomes a ketone body. Some are oxidized directly in muscle and heart, some are re-esterified into triglycerides in the liver, and some enter other lipid pathways. Ketogenesis is one branch of fatty-acid metabolism, and the metabolic environment of hepatic mitochondria determines how strongly that branch is used.[3-6]

6. Beta-Oxidation Cuts Fatty Acids into Units That Can Produce Energy

Inside mitochondria, fatty acids undergo beta-oxidation and are cleaved into two-carbon acetyl-CoA units. NADH and FADH₂ are produced at the same time and deliver electrons to the electron-transport chain, contributing to ATP generation. This abundance of reducing equivalents helps explain the high energy density of fat.[3-6]

Long-chain fatty acids require the carnitine shuttle to enter the mitochondrial matrix. CPT1 is an important control point in this process. High malonyl-CoA inhibits CPT1 and reduces mitochondrial entry of fatty acids, whereas fasting and carbohydrate restriction shift regulation in a direction that favors fatty-acid oxidation.[3-6]

As beta-oxidation accelerates in the liver, acetyl-CoA production rises. In the fed state, much of this acetyl-CoA can enter the TCA cycle. During fasting, however, more oxaloacetate may be directed toward gluconeogenesis. Excess acetyl-CoA can then be diverted toward ketogenesis, increasing hepatic ketone production.[3-6]

7. The Liver Converts Fat into a Transportable Fuel: Ketone Bodies

Ketogenesis occurs mainly in hepatic mitochondria. Acetyl-CoA molecules are combined through HMG-CoA to form acetoacetate. Acetoacetate can be reduced to beta-hydroxybutyrate or can spontaneously form acetone. Mitochondrial HMG-CoA synthase 2 (HMGCS2) is an important regulatory enzyme in this pathway.[3-6]

Ketone bodies are water soluble and therefore easier to transport in blood than long-chain fatty acids. The liver can be viewed as a fuel-processing organ that takes fatty acids, converts some of them into ketones, and exports those ketones to other organs. This function becomes especially important when carbohydrate availability and insulin are low.[3-7]

Interestingly, the liver itself cannot efficiently use the ketones it produces because it essentially lacks SCOT, the key enzyme required for ketone oxidation. The liver therefore produces and exports ketones, while extrahepatic tissues such as heart, muscle, kidney, and brain take them up and oxidize them.[3-7]

8. The Three Ketone Bodies Do Not Have Identical Roles

The physiologically important ketone bodies are acetoacetate, beta-hydroxybutyrate (BHB), and acetone. Strictly speaking, BHB is a hydroxy acid rather than a true chemical ketone, but in metabolic physiology it is grouped with ketone bodies. During fasting and nutritional ketosis, BHB is usually the form that rises most prominently in blood.[3-7]

Acetoacetate and BHB can be converted into one another, and their ratio reflects the redox state of hepatic mitochondria. Acetone, in contrast, is formed by spontaneous decarboxylation of acetoacetate and is largely exhaled. This is why breath can acquire a characteristic odor during ketosis.[3-7]

It is inaccurate to describe ketone bodies as mere “waste left after fat burning.” Acetoacetate and BHB can travel to other tissues, be reconverted to acetyl-CoA, enter the TCA cycle, and produce ATP. BHB is also being studied for possible roles in cell signaling and regulation of gene expression.[3-8]

9. During Prolonged Fasting the Brain Actively Uses Ketones

The brain normally depends heavily on glucose, but prolonged fasting changes the picture. In 1967, Owen and colleagues directly measured brain metabolism in people who had fasted for five to six weeks and showed that BHB and acetoacetate could become major brain fuels. This classic study established that the human brain can use ketone bodies extensively during prolonged fasting.[3-9]

This does not mean that glucose is no longer needed. Cells without mitochondria, such as red blood cells, cannot oxidize ketones, and some glucose use continues in the brain. As fasting progresses, however, increased brain ketone use reduces overall glucose requirements.[3-1]

This adaptation has survival value. If the brain continued to demand only glucose, the liver would need to convert more amino acids into glucose, accelerating loss of muscle protein. Increased ketone use lowers the amino-acid requirement for gluconeogenesis and helps conserve body protein during prolonged fasting.[3-1]

10. Keto-Adaptation Also Helps Conserve Protein

Early in fasting, amino acids can contribute substantially to hepatic gluconeogenesis. As fasting continues and ketone concentrations rise, the brain uses more ketone fuel. The requirement for amino acids to support gluconeogenesis falls, and urinary nitrogen losses decline as part of the adaptation.[3-1]

It would be an exaggeration to say that muscle breakdown stops completely. Protein turnover continues during prolonged fasting, and risk differs according to body-fat stores and health status. The important point is that increased ketone utilization reduces glucose requirements and slows the rate of protein loss.[3-1]

This physiology should not be copied directly from prolonged fasting to a plant-based ketogenic diet. A ketogenic diet supplies protein and micronutrients, whereas complete fasting does not. Fasting studies demonstrate the basic capacity of human metabolism to shift fuels; the safety and effectiveness of an actual diet must be evaluated in separate clinical trials.[3-2]

11. Ketone Bodies Are Fuels and Signaling Metabolites

BHB is not only a carbon substrate for ATP production. Research has accumulated suggesting that it can influence receptors, enzymes, and gene-regulatory processes, leading to the concept of a “signaling metabolite.” Examples under investigation include modulation of histone deacetylases, inflammatory pathways, and oxidative-stress responses.[3-8]

Clinical interpretation requires caution. Signaling effects observed in cells or animals do not automatically translate into treatment benefits in human disease. Concentration, exposure duration, tissue type, and metabolic context differ substantially. This book therefore treats ketone signaling as interesting mechanistic evidence while evaluating clinical effects separately in human studies.[3-8]

This distinction is crucial. A biochemical observation that “ketones affect an inflammatory signal” and a clinical claim that “a ketogenic diet treats a disease” are different levels of evidence. In later clinical chapters, priority is given to human outcomes such as HbA1c, medication reduction, body weight, lipids, remission, and adverse events.[3-8]

12. Nutritional Ketosis Is Not the Same as Diabetic Ketoacidosis

Nutritional ketosis from carbohydrate restriction or fasting and diabetic ketoacidosis (DKA) both involve an increase in circulating ketones, but their metabolic contexts are very different. In nutritional ketosis, insulin action is reduced but still present, providing a brake on excessive ketone production. In DKA, severe insulin deficiency combined with increased counter-regulatory hormones can drive uncontrolled ketogenesis and metabolic acidosis.[3-10]

Therefore, detecting ketones does not by itself mean danger, but neither should every ketone elevation be assumed safe. Blood glucose, BHB, acid-base status, symptoms, and medication use must be considered together. Special caution is required in type 1 diabetes and in people taking SGLT2 inhibitors because ketoacidosis can occur with normal or only moderately elevated glucose.[3-10]

In this book, safety is managed as an independent axis whenever a plant-based ketogenic diet is discussed. The objective is not ketone production for its own sake. Glucose, medications, kidney function, hydration, electrolytes, and symptoms must be monitored together. The simplistic target “higher ketones are always better” is not scientifically justified.[3-10]

13. Metabolic Flexibility Is the Ability to Switch Fuels

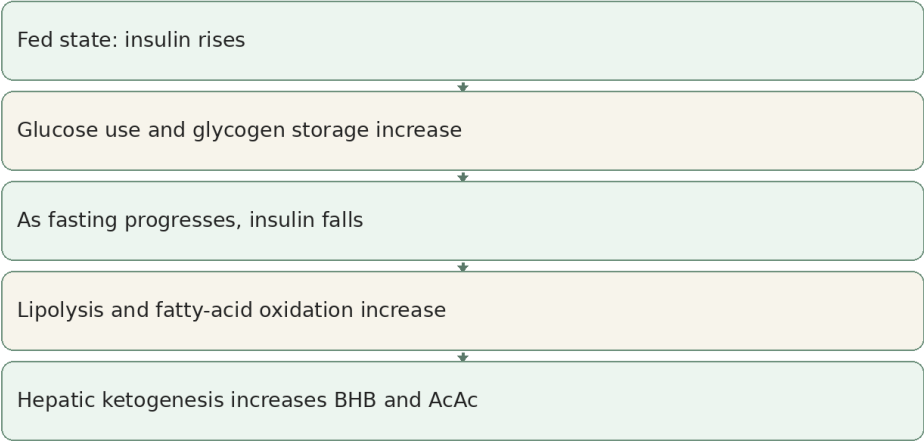
Metabolic flexibility is the capacity to adjust the relative use of fuels such as glucose and fatty acids according to nutritional state and energy demand. Increased carbohydrate oxidation after a meal and increased fatty-acid oxidation during fasting or exercise are normal examples.^[3-3]

Research suggests that this switching capacity may become blunted in obesity and insulin resistance. Skeletal muscle that fails to respond appropriately to changes in substrate availability between fasting and feeding has been described as metabolically inflexible. Yet metabolic flexibility is not captured by one laboratory value; it is a physiological framework that includes insulin sensitivity, mitochondrial function, energy balance, and physical activity.^[3-3]

This is also where the rationale for a plant-based ketogenic diet can be framed. The goal is not to lock the body permanently into ketone metabolism. It is to reduce excessive dependence on glucose and chronically high insulin while restoring the capacity to use fatty acids and ketones appropriately. The next chapter examines how lower insulin and changing nutrient availability interact with AMPK, mTOR, autophagy, mitochondria, and other cellular regulatory systems.^[3-2]

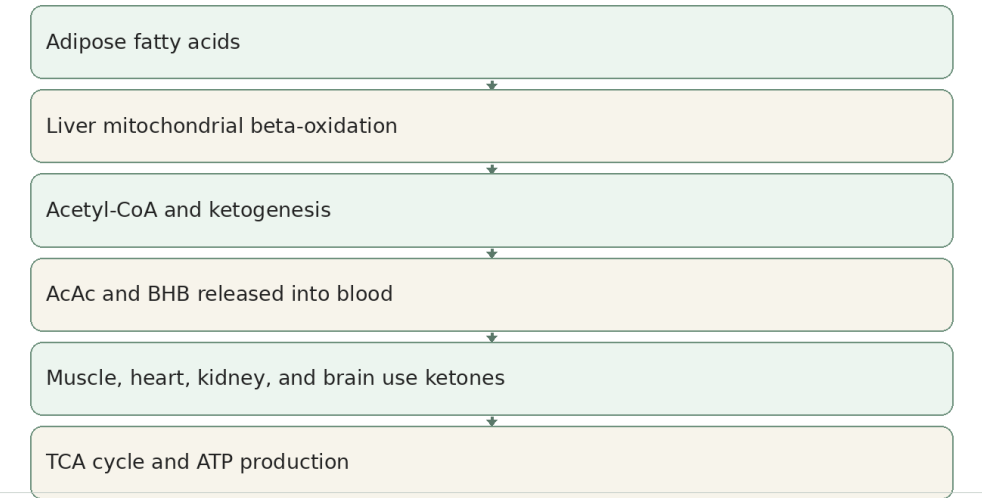
Chapter 3 Notes and References

Figure 03-1. Major fuel shift from the fed state to fasting



Source: Cahill (2006); Puchalska & Crawford (2017); author reconstruction.

Figure 03-2. Hepatic ketogenesis and peripheral ketone utilization



Source: Fukao et al. (2004); Puchalska & Crawford (2017); simplified by the author.

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Chapter 4. What Changes When Insulin Falls?

1. Insulin Does More Than Lower Blood Glucose

Insulin is widely known as the hormone that lowers blood glucose, but its role is broader. It is better understood as a metabolic signal that helps determine how incoming energy is used and stored after a meal. In muscle it promotes glucose use and glycogen synthesis; in the liver it suppresses glucose production; and in adipose tissue it strongly inhibits lipolysis.^[4-1]

A fall in insulin is therefore not simply a change in one hormone concentration. It represents a gradual shift away from a metabolism dominated by storage. Between meals, during exercise, or when carbohydrate supply falls, fatty-acid mobilization and oxidation become relatively easier.^[4-1]

One point must be clear: insulin is not a “bad hormone.” It is essential for survival and growth, and severe insulin deficiency - as in type 1 diabetes - can cause life-threatening ketoacidosis. The goal is not to drive insulin as low as possible, but to have insulin secreted appropriately and to have target tissues respond to it efficiently.^[4-1]

2. When the Adipose “Gate” Opens, Stored Fat Begins to Move

Triglyceride in adipose tissue is a long-term energy reserve. After meals, insulin suppresses lipolysis and prevents stored fatty acids from flooding the bloodstream. As fasting begins and insulin’s inhibitory effect weakens, triglycerides are more readily broken down into fatty acids and glycerol.^[4-1]

The released fatty acids travel to skeletal muscle, heart, and liver. Many tissues oxidize them directly for ATP, while the liver uses some as substrates for ketone production. Glycerol can enter the liver and serve as a substrate for gluconeogenesis. This is where the fuel transition described in Chapter 3 begins in practice.^[4-1]

More circulating fatty acids are not automatically beneficial. When energy surplus and insulin resistance persist, fatty-acid delivery can exceed the processing capacity of liver and muscle. Ectopic fat and certain lipid intermediates may then accumulate and further impair insulin signaling. Fat mobilization must therefore be understood in the context of energy expenditure and oxidative capacity.^[4-10]

3. Fatty-Acid Oxidation and Ketogenesis Increase in the Liver

When insulin falls and fatty-acid supply rises, the liver takes up more fatty acids. Increased mitochondrial beta-oxidation generates acetyl-CoA and reducing equivalents. Depending on energy state and the use of oxaloacetate, a larger share of carbon may be directed toward ketogenesis.[4-1]

Liver metabolism, however, does not move in only one direction. In severe hepatic insulin resistance, glucose production may fail to be suppressed even while lipogenesis continues - a phenomenon described as selective insulin resistance. High circulating insulin therefore does not mean that all hepatic insulin actions are strong, and lowering insulin does not instantly normalize liver metabolism.[4-10]

Recovery depends importantly on energy balance and reduction of liver fat. In studies of type 2 diabetes remission, substantial weight loss was followed by a rapid reduction in liver fat, and some participants returned to near-normal glycemic control. Whether remission occurred also depended on the degree to which pancreatic beta-cell function could recover.[4-12]

4. AMPK Senses Energy Shortage Inside the Cell

Cells continually consume ATP. When ATP supply cannot keep pace with demand, AMP and ADP rise relative to ATP. AMP-activated protein kinase (AMPK) is a major cellular energy sensor that detects this shift. When activated, AMPK promotes catabolic pathways that generate ATP and suppresses many energy-consuming anabolic pathways.[4-2]

Calling AMPK merely a “fat-burning switch” is therefore too simplistic. It is connected not only to fatty-acid oxidation but also to glucose use, protein and lipid synthesis, cell growth, and mitochondrial function. More recent research shows that AMPK integrates signals related not just to ATP and AMP, but also glucose, glycogen, and fatty-acid status.[4-3]

Exercise provides a useful example. Rapid ATP consumption during muscle contraction can activate AMPK. Skeletal-muscle research has shown that AMPK can directly phosphorylate PGC-1alpha, linking energy sensing to oxidative metabolism and mitochondrial gene programs.[4-13]

5. mTORC1 Asks Whether the Environment Supports Growth

If AMPK represents an energy-shortage sensing axis, mTORC1 is closer to a system that asks whether conditions permit growth and biosynthesis. mTORC1 integrates amino acids, growth factors, and cellular energy status. When active, it promotes synthesis of proteins, lipids, and nucleic acids and supports material production needed for cellular growth.[4-4]

mTORC1 is not a “bad signal” either. Muscle growth, wound repair, and normal cell growth require anabolic signaling. Problems arise when activation and suppression no longer alternate appropriately. Nutrient-rich periods call for synthesis; energy-limited periods call for conservation and recycling.[4-4]

Metabolism is therefore a problem of homeostasis. As feeding alternates with fasting and activity with rest, the balance between synthesis and breakdown also changes. Healthy metabolism does not permanently turn one pathway off; it retains the ability to use different programs at the appropriate time.[4-4]

6. AMPK and mTORC1 Are Not Simply Opposite Switches

When energy is limited, AMPK can reduce mTORC1 activity through regulatory components such as TSC2 and raptor. This provides a metabolic brake that helps prevent cells from continuing energy-intensive growth and biosynthesis when ATP is scarce.[4-2]

The real signaling network is more complex than “AMPK on, mTOR off.” Tissue type, nutritional state, exercise, amino-acid supply, and growth-factor signaling all matter. Even within the same person, muscle, liver, and adipose tissue can respond differently.[4-3]

A plant-based ketogenic diet should therefore not be justified by claiming that AMPK must always be raised and mTOR always suppressed. Recovery and maintenance of muscle require adequate protein and anabolic signaling. At the same time, persistent energy surplus may reduce the opportunities for catabolic and recycling processes.[4-4]

7. Autophagy Is an Intracellular Recycling System

Autophagy is an evolutionarily conserved process in which cytoplasmic proteins and organelles are delivered to lysosomes for degradation and recycling. It contributes to removal of damaged components and helps cells reuse internal resources during nutrient stress. Autophagy occurs at baseline and is regulated under many forms of stress.[4-6]

The best studied form is macroautophagy. A membrane structure encloses a portion of cytoplasm to form an autophagosome, which later fuses with a lysosome. The contents are degraded, and components such as amino acids and fatty acids can be reused in cellular metabolism.[4-6]

Describing autophagy only as “cleaning out waste” is incomplete. It also contributes to protein quality control, organelle turnover, antimicrobial defense, and metabolic adaptation. Nor is more autophagy always better; depending on tissue and disease, excessive or dysregulated autophagy can also be harmful.[4-6]

8. AMPK, mTOR, and ULK1 Meet at the Entrance to Autophagy

Nutrient status is linked to initiation of autophagy. When nutrients are abundant, mTORC1 acts to inhibit the ULK1 complex. During energy stress, AMPK can suppress mTORC1 and directly regulate ULK1, creating signaling conditions more favorable to autophagy initiation.[4-5]

This relationship helps explain how cells adapt to nutrient scarcity. When fewer nutrients arrive from outside, metabolic priorities can shift away from continued synthesis and toward redistribution of internal resources and removal of damaged components. AMPK, mTORC1, and ULK1 are important links in that transition.[4-5]

This pathway should not be mapped mechanically onto a clock. Evidence is insufficient to state that “autophagy begins after exactly X hours of fasting” in every person. Responses differ among tissues, and measuring autophagic flux directly in humans is difficult.[4-7]

9. Measuring Fasting and Autophagy in Humans Is Harder Than It Sounds

Cell and animal research provides abundant evidence that nutrient deprivation regulates autophagy. In humans, however, repeated tissue sampling is difficult, and a single measurement of markers such as LC3 or p62 cannot fully define autophagic flux because both formation and degradation can change simultaneously.^[4-6]

A human skeletal-muscle study using repeated biopsies found that 36 hours of fasting influenced some autophagy-related proteins and signaling, but responses differed according to training status. The investigators concluded that the human skeletal-muscle autophagy response was neither simple nor uniform.^[4-7]

For this reason, this book does not claim that autophagy “starts at 18 hours” or “peaks at 24 hours.” Mechanistic evidence that fasting and caloric restriction regulate autophagy is strong, but the exact timing and magnitude of responses in different human organs remain uncertain.^[4-8]

10. Mitochondria Are More Than Power Plants

Mitochondria are central organelles that use reducing equivalents derived from carbohydrates and fatty acids to produce ATP. They also participate deeply in substrate selection, redox state, and cellular signaling. Mitochondrial quality and function therefore matter as much as simply having more mitochondria.^[4-9]

AMPK is linked to adaptation of oxidative metabolism and mitochondrial gene regulation. In skeletal muscle, PGC-1alpha has been studied as an important transcriptional coactivator in this process. Yet human mitochondrial biogenesis cannot be reduced to a single pathway; exercise, nutritional state, calcium signaling, and other stimuli all contribute.^[4-13]

Selective removal of damaged mitochondria is called mitophagy. Mitophagy is one arm of mitochondrial quality control and must remain balanced with formation of new mitochondria. Appropriate turnover of old components can be as important as increasing mitochondrial number.^[4-6]

11. In Insulin Resistance, Where Fat Is Stored Matters as Much as How Much There Is

In obesity and type 2 diabetes, ectopic fat outside adipose tissue is an important metabolic issue. Lipid accumulation in liver and skeletal muscle is closely associated with insulin resistance, but total triglyceride content alone does not explain every observation.^[4-11]

Mechanistic studies have implicated lipid intermediates such as diacylglycerol (DAG) and specific protein kinase C pathways in disruption of insulin signaling. The DAG-PKCepsilon axis in liver and DAG-PKCtheta axis in muscle are well studied examples. However, the cellular location and molecular species of lipids can change their effects, so this mechanism must be interpreted with nuance.[4-10]

That is why statements such as “eating fat causes insulin resistance” or “cutting carbohydrate alone makes fatty liver disappear” are too simple. Total energy surplus, adipose storage capacity, fatty-acid delivery and oxidation, hepatic de novo lipogenesis, and physical activity interact.[4-10]

12. Metabolic Recovery Is About Responding Better to Insulin, Not Merely Having Less Insulin

The core problem in type 2 diabetes is not absence of insulin but inadequate response to insulin in key tissues. A treatment goal of “lower insulin as much as possible” therefore misses the point. More important is a metabolic state in which necessary responses occur with a smaller and physiologically appropriate insulin signal.[4-1]

Exercise is a good example. Skeletal-muscle contraction can increase glucose uptake independently of insulin, while habitual physical activity improves insulin sensitivity and oxidative capacity. Weight loss and correction of chronic energy surplus can also reduce lipid burden in liver and muscle.[4-9]

In diabetes-remission research, the central changes were not simply lower circulating insulin. Weight loss was followed by reductions in liver and pancreatic fat, and people who achieved remission showed recovery of early beta-cell insulin secretion. Metabolic recovery is a coordinated process involving several organs.[4-12]

13. How Should a Plant-Based Ketogenic Diet Be Viewed Through This Signaling Network?

A plant-based ketogenic diet can be conceptualized as reducing carbohydrate supply and postprandial insulin requirements while increasing opportunities to use fatty acids and ketones. At the same time, minimally processed plant foods provide fiber, unsaturated fats, and micronutrients that can improve overall diet quality.[4-1]

At this point, however, we are mainly integrating physiology. Combining the mechanism by which carbohydrate restriction may affect AMPK, mTOR, autophagy, and mitochondria with the

metabolic advantages of plant foods does not automatically prove clinical benefit from a plant-based ketogenic diet. Direct human intervention studies are needed.[4-8]

For that reason, the clinical chapters that follow prioritize outcomes over mechanisms. How much did HbA1c actually change? Were medications reduced? What happened to body weight and lipids? What adverse events occurred, and could people sustain the diet? Mechanisms explain plausibility; clinical trials determine the size and reliability of treatment effects.[4-1]

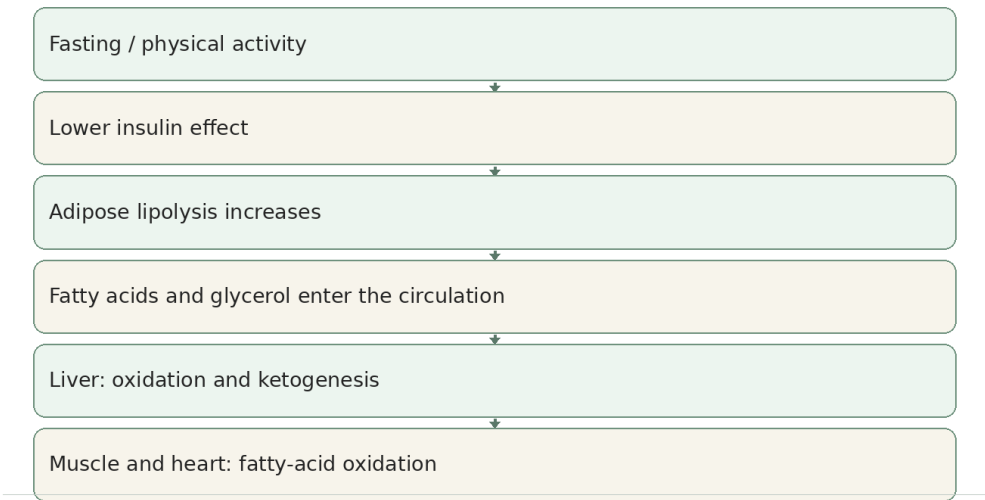
Key Points from Chapter 4

When insulin falls, metabolism shifts away from storage toward a state in which mobilization and oxidation of fat become easier. At the cellular level, signaling systems such as AMPK, mTORC1, and ULK1 read energy and nutrient status and adjust the priorities of biosynthesis, breakdown, and autophagy. The goal is not to maximize or minimize one signal indiscriminately.[4-2]

What matters in type 2 diabetes is metabolic balance and flexibility: reducing ectopic fat in liver and muscle, maintaining mitochondrial oxidative capacity, and improving tissue responsiveness to insulin. The next chapters connect this physiological framework with clinical research on plant-based dietary patterns.[4-9]

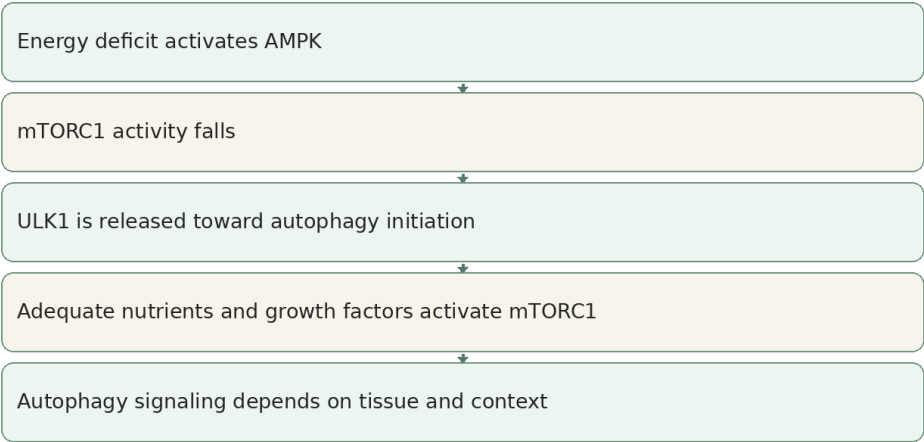
Chapter 4 Notes and References

Figure 04-1. Direction of fuel movement as insulin action falls



Source: Petersen & Shulman (2018); Samuel & Shulman (2016); simplified by the author.

Figure 04-2. Energy and nutrient signaling at the initiation of autophagy



Source: Kim et al. (2011); Saxton & Sabatini (2017); author conceptualization.

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Chapter 5. Clinical Research on Plant-Based Diets and Type 2 Diabetes

The term “plant-based diet” does not refer to one single way of eating. It includes vegan diets, lacto-ovo vegetarian diets, low-fat plant-based diets, and whole-food patterns centered on whole grains, legumes, and vegetables. When reading clinical research, it is therefore more important to ask what participants actually ate than to rely on the label “plant-based.”^[1]

1. Plant-Based Diets Should Not Be Treated as One Uniform Intervention

Plant-based diets used in clinical trials have differed markedly in composition and goals. Some studies used very low-fat, high-carbohydrate patterns; others restricted energy intake. Still others emphasized whole grains, legumes, and vegetables without setting a calorie limit. Even under the same “vegan” label, carbohydrate, fat, fiber, and energy density can differ substantially.^[2]

These differences are crucial when interpreting outcomes. If HbA1c falls, it can be difficult to separate the effects of excluding animal foods from the effects of weight loss, increased fiber, or lower energy density. The comparator diet also matters. Effects may appear large against usual care but smaller against an actively counseled diabetes diet.^[3]

2. Current Guidelines Emphasize Individualized Eating Patterns

The ADA Standards of Care in Diabetes-2026 do not identify one ideal percentage of carbohydrate, protein, and fat for everyone with diabetes. Meal plans should be individualized according to current eating habits, preferences, nutritional quality, energy needs, and metabolic goals. Plant-based, vegetarian, and vegan patterns can all be used, but the evidence does not support prescribing one pattern to every person.^[1]

Guidelines particularly emphasize nonstarchy vegetables, whole fruit, legumes, nuts, and seeds, while recommending reductions in sugar-sweetened beverages, refined grains, sweets, and ultraprocessed foods. In other words, food processing and nutrient density matter as much as whether a food is technically plant-derived.^[1]

3. Barnard's 22-Week RCT Was an Important Early Trial

In 2006, Barnard and colleagues randomized 99 adults with type 2 diabetes to a low-fat vegan diet or a diet based on contemporary ADA guidance. After 22 weeks, HbA1c fell by 0.96 percentage points in the vegan group and 0.56 points in the comparator group in the analysis including all participants. When people who changed diabetes medications were excluded, HbA1c fell by 1.23 points versus 0.38 points, a statistically significant between-group difference.[4]

Medication reduction was also observed. Twenty-one of 49 participants in the vegan group and 13 of 50 in the control group reduced diabetes medication. Medication changes complicate interpretation of HbA1c because reducing treatment can make glucose appear relatively higher. This is why the investigators also reported analyses excluding participants whose medications changed.[4]

4. Seventy-Four Weeks of Follow-Up Separated Early Effects from Long-Term Sustainability

A report that followed the same study population for 74 weeks found reductions in body weight and lipids in both groups. In the full analysis, HbA1c changed by -0.34 percentage points in the vegan group and -0.14 in the control group, with no significant between-group difference. Using the last value before medication changes, however, the changes were -0.40 versus +0.01 percentage points.[5]

These results illustrate a central difficulty of long-term diet trials. As time passes, adherence, medication changes, and other lifestyle changes become mixed with the intervention effect. Short-term HbA1c improvements should not be assumed to persist unchanged; long-term outcomes must be interpreted together with sustainability.[5]

5. A 24-Week Czech RCT Directly Measured Insulin Sensitivity and Visceral Fat

Kahleova and colleagues randomized 74 people with type 2 diabetes to a calorie-restricted vegetarian diet or a conventional diabetes diet. Both aimed for an energy deficit of about 500 kcal/day, and aerobic exercise was added during the final 12 weeks. The vegetarian group lost more weight and showed a larger improvement in insulin sensitivity measured by hyperinsulinemic-euglycemic clamp.[6]

During 24 weeks, diabetes medication was reduced in 43% of the vegetarian group compared with 5% of the control group. Visceral and subcutaneous fat also decreased more in the vegetarian group. The study is important because it evaluated fat distribution and insulin sensitivity rather than relying on HbA1c alone.[6]

6. A Brown-Rice-Based Vegan RCT Provides Important Evidence in an Asian Food Environment

In 2016, Lee and colleagues randomized Korean adults with type 2 diabetes to a brown-rice-based vegan diet or a diet recommended by the Korean Diabetes Association. Forty-six people in the vegan group and 47 in the control group completed 12 weeks. HbA1c fell by 0.5 percentage points in the vegan group and 0.2 points in controls, with a significant time-by-group interaction.[7]

Among highly adherent participants, the difference was larger: -0.9 percentage points in the vegan group versus -0.3 in controls. However, average adherence to the vegan diet was lower than adherence to the control diet, and the authors noted that universal prescription of a vegan diet may not be realistic for every patient.[7]

7. Adherence Is Part of the Treatment Effect, Not a Side Issue

A diet cannot be administered at an identical “dose” every day in the way a medication can. Actual food intake, family meals, restaurants, work schedules, and culture all influence exposure. A diet may have a physiological effect yet produce a small clinical effect if people cannot sustain it. Conversely, intensive education and group support can improve adherence and change outcomes.[5]

In the Korean RCT, adherence to the vegan diet declined over time. This does not mean the diet was ineffective; it means feasibility must be assessed alongside biological efficacy. The same principle applies when designing a plant-based ketogenic diet: food composition, education, ease of preparation, and the social environment all matter.[7]

8. A 2014 Meta-Analysis Reported an Additional HbA1c Reduction of About 0.39 Percentage Points

Yokoyama and colleagues analyzed six controlled vegetarian interventions including 255 participants. HbA1c fell by an average of 0.39 percentage points more with vegetarian diets than with control diets. Fasting glucose moved in a favorable direction but the pooled difference was not statistically significant.[8]

The effect is not large compared with many glucose-lowering medications, but it is clinically relevant as an average dietary effect. At the same time, the small number of trials and participants means that 0.39 percentage points should not be treated as a fixed effect size for all plant-based diets.[8]

9. A 2022 Meta-Analysis Estimated a Smaller Glycemic Effect

Termannsen and colleagues included 11 vegan RCTs lasting at least 12 weeks, with 796 participants. Among people with overweight or type 2 diabetes, vegan diets reduced body weight by about 4.1 kg more than control diets and lowered HbA1c by about 0.18 percentage points more. LDL cholesterol and total cholesterol fell, while clear between-group differences were not seen for blood pressure, HDL, or triglycerides.[9]

The certainty of evidence for HbA1c was rated moderate. However, the authors noted that energy intake and macronutrient composition often differed between vegan and control groups. The “vegan” category alone therefore cannot explain the mechanism of effect.[9]

10. Different Meta-Analyses Can Reach Different Conclusions

Not every evidence synthesis reports the same result. Another 2022 systematic review examined low-fat vegan diets together with very-low-calorie diets and reported substantial heterogeneity and risk of bias; the HbA1c effect attributable specifically to vegan diets was not clearly significant. Conclusions can change according to inclusion criteria, comparator selection, and study quality.[10]

A meta-analysis is therefore not automatically definitive simply because it pools studies. The quality of included RCTs, similarity of interventions, intensity of the comparator, medication adjustment, and duration all matter. This book gives uncertainty the same attention as positive findings.[9]

11. “Plant-Based” and “Healthy Plant-Based” Are Not the Same

A plant-based pattern can include nutrient-dense foods such as whole grains, legumes, vegetables, and nuts, but it can also include refined starch, added sugars, and ultraprocessed vegan products. Clinical effects therefore cannot be reduced simply to exclusion of animal foods. The type of carbohydrate and the food sources of fat and protein matter.[1]

This is why the ADA emphasizes a food-centered approach: more nonstarchy vegetables, legumes, nuts, and seeds, and fewer

refined grains and ultraprocessed foods. These principles connect with the mechanisms discussed in the next chapter, including dietary fiber, the gut microbiome, and fatty-acid composition.^[1]

12. Is Weight Loss the Whole Story, or Does Diet Composition Matter Independently?

In plant-based interventions, HbA1c often improves when body weight falls. In Barnard's 74-week study, changes in body weight and HbA1c were significantly related. In the Korean RCT, however, the difference in HbA1c improvement remained after adjustment for energy intake and waist-circumference changes.^[5]

This does not prove a completely weight-independent effect. Fiber, fat quality, energy density, the gut microbiome, satiety, and actual energy intake are interconnected. It is more realistic to view diet composition and weight change as interacting processes rather than two fully separable mechanisms.^[7]

13. New Mechanistic and Clinical Data Continue to Emerge

A 2026 ADA Scientific Sessions abstract reported that adults with type 2 diabetes following a low-fat plant-based diet for 16 weeks had reductions in body weight, visceral fat, hepatocellular lipid, and HbA1c, together with improvements in markers of insulin resistance and beta-cell function. Mean HbA1c fell by about 1.0 percentage point from baseline.^[11]

A conference abstract, however, does not provide the same methodological detail as a complete peer-reviewed article. It is useful as a signal of emerging research but should not be treated as definitive evidence until full methods, comparator data, medication changes, and adherence are available.^[11]

14. Plant-Based Research Is a Major Component of Our Evidence Database

In the strict reclassification of vk_diabete_db.sqlite3, 1,098 records were categorized as plant-based candidates and 739 were assigned to the internal Tier A priority group. When the top 300 records were rechecked using XML full text, 148 were classified as actual plant-based interventions. These counts do not mean 148 independent RCTs; they indicate the size of the clinical, mechanistic, and synthesis evidence pool used during book preparation.^[12]

This book does not interpret the number of records as the magnitude of an effect. RCTs, meta-analyses, cohorts, and mechanistic studies are separated, and duplicate follow-up papers and secondary analyses are identified. HbA1c values are preferentially used only when verified in tables or Results

sections, and medication changes are noted separately.[12]

15. Observational Studies and Clinical Trials Answer Different Questions

Large cohorts have repeatedly found that vegetarian or healthy plant-based eating patterns are associated with a lower incidence of type 2 diabetes. The ADA also discusses observational evidence linking plant-based dietary patterns and food quality with diabetes prevention. These studies, however, do not directly answer the treatment question: how much will HbA1c fall if someone who already has diabetes changes diet?[1]

Mixing prevention and treatment evidence can exaggerate conclusions. An association between a healthy plant-based pattern and lower diabetes incidence does not prove that the same diet will reduce medication or induce remission in every person with established type 2 diabetes. This book treats incident diabetes, glycemic improvement, medication reduction, and remission as separate outcomes.[1]

16. Medication Reduction Is Important but Must Be Interpreted Together with HbA1c

Medication reduction can be highly meaningful to patients. In the 22-week Barnard trial and the 24-week Kahleova trial, more people in the plant-based intervention groups reduced diabetes medications than in the control groups. This suggests that dietary intervention can lower the medication burden required to maintain glycemic control.[4]

Medication reduction and HbA1c influence one another. If medication is reduced while HbA1c stays stable or improves, the result is particularly meaningful. But medication reduction can also make the apparent fall in HbA1c smaller. Trials therefore sometimes report separate analyses for all participants, for the last measurement before medication change, or for those with no medication change.[5]

17. What the Clinical Research Can - and Cannot - Tell Us

First, well-constructed vegetarian and vegan interventions can improve HbA1c, body weight, and some lipid measures in type 2 diabetes. Second, some RCTs have also shown improvements in insulin sensitivity and reductions in diabetes medication. Third, effect sizes differ among studies, and comparator diets, weight loss, adherence, and medication adjustment strongly influence results.[9]

There are also important limits. Evidence does not support the claim that plant-based eating alone induces remission in everyone

with type 2 diabetes. The word “vegan” itself does not guarantee efficacy. RCT evidence that these dietary interventions directly reduce long-term cardiovascular events or kidney failure is also insufficient.[5]

The next chapter therefore separates HbA1c, fasting glucose, insulin, and HOMA-IR rather than treating “plant-based diets work” as a single conclusion. We will examine which markers changed, by how much, and under what conditions.[9]

Key Points from Chapter 5

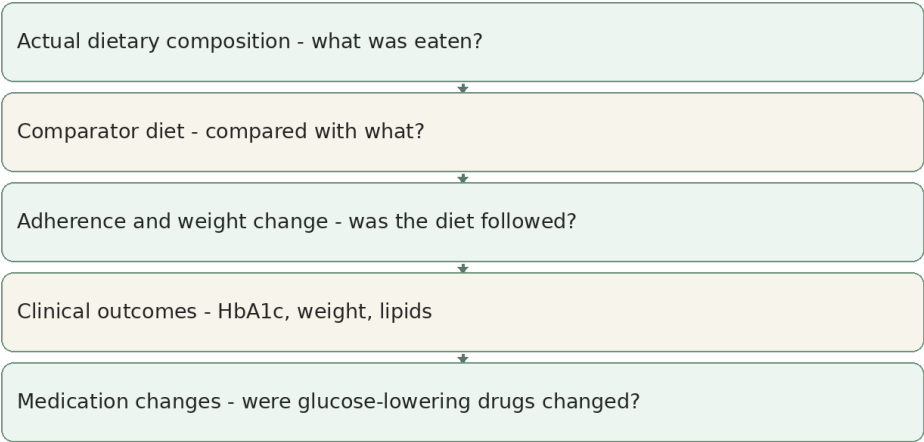
Clinical evidence for plant-based dietary interventions exists. Low-fat vegan and vegetarian trials have repeatedly reported improvements in HbA1c, body weight, insulin sensitivity, and medication use. Yet the effect cannot be represented by one fixed number; composition of the diet, comparator intensity, weight change, adherence, and medication adjustment all matter.[8]

This distinction is also essential for a plant-based ketogenic model. We should not simply import every benefit reported in plant-based research. We must identify which components appear connected to actual clinical outcomes, so that later integration with ketogenic research does not confuse evidence with hypothesis.[1]

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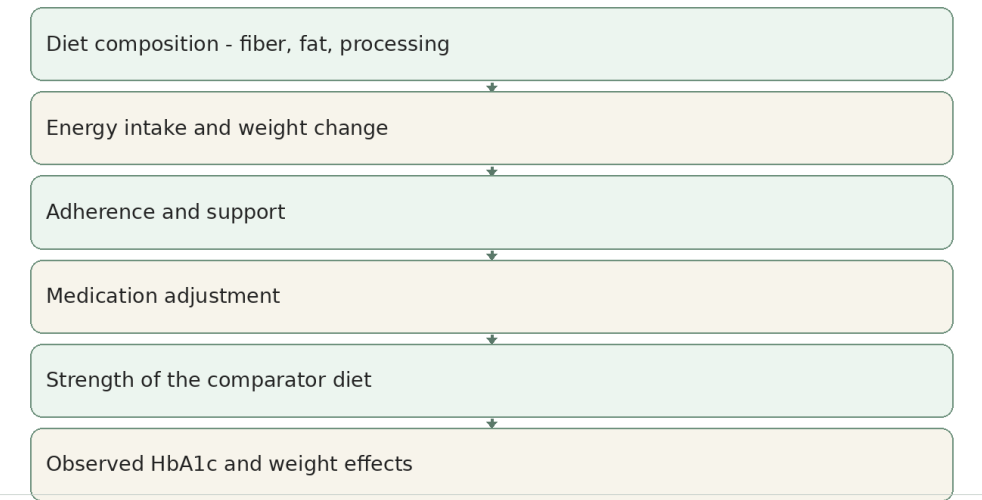
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Figure 05-1. How to read clinical evidence on plant-based diets



Source: Yokoyama et al. (2014); Termannsen et al. (2022); author synthesis.

Figure 05-2. Major factors that modify observed effects of plant-based diets



Source: Barnard et al. (2009); Lee et al. (2016); Termannsen et al. (2022); author synthesis.

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Chapter 6. Plant-Based Diets, Blood Glucose, and Insulin

HbA1c is the most frequently reported marker when discussing plant-based dietary interventions, but HbA1c alone cannot explain all metabolic change. Fasting glucose is strongly influenced by overnight hepatic glucose release, whereas postprandial glucose is especially sensitive to the amount and absorption rate of dietary carbohydrate. Fasting insulin and HOMA-IR reveal different aspects of insulin resistance. These markers therefore need to be interpreted separately.[1]

> **Term | HbA1c** > Glycated hemoglobin > A measure of the proportion of hemoglobin that has been glycated. It reflects average glycemic exposure over roughly the previous two to three months.

1. HbA1c Reflects Accumulated Glycemic Exposure, Not a Single Moment

HbA1c is not a snapshot like a fasting glucose measurement. It compresses weeks to months of glucose exposure into one value, which is why it is among the most widely used clinical outcomes in diet trials. The ADA 2026 Standards identify an HbA1c target below 7% as a common goal for many nonpregnant adults, while emphasizing individualization according to age, comorbidity, hypoglycemia risk, life expectancy, and treatment burden.[1]

A decrease of 0.4 percentage points in HbA1c is not the same as a “0.4% reduction.” A fall from 8.0% to 7.6% is an absolute decrease of 0.4 percentage points; the relative decrease is about 5%. Confusing these two expressions can distort interpretation of effect size.[2]

> **Term | Percentage point** > The absolute difference between two percentages. A change in HbA1c from 8.0% to 7.6% is a decrease of 0.4 percentage points.

Table 6-1. HbA1c Effects Reported in Meta-Analyses of Plant-Based Diets

Study	Included studies / population	Comparison	Mean HbA1c difference	Interpretation
Yokoyama et al., 2014	6 studies, n=255	Vegetarian vs control	-0.39 percentage points	Early meta-analysis; few studies
Termannsen et al., 2022	11 vegan RCTs, n=796	Vegan vs control	-0.18 percentage points	Mixed overweight/T2D population

Study	Included studies / population	Comparison	Mean HbA1c difference	Interpretation
Guest et al., 2024	7 T2D RCTs, n=770	Vegetarian/vegan vs nonvegetarian	-0.40 percentage points	Moderate certainty
Lv et al., 2025	9 T2D RCTs, n=681	Vegetarian/vegan vs omnivorous	-0.36 percentage points	Larger reduction in trials >12 weeks

Source: Synthesized from Yokoyama et al. (2014), Termannsen et al. (2022), Guest et al. (2024), and Lv et al. (2025).

2. Recent Meta-Analyses Point in a Broadly Consistent Direction for HbA1c

Yokoyama’s 2014 meta-analysis found an additional mean HbA1c reduction of 0.39 percentage points with vegetarian interventions compared with control diets. As more studies accumulated, pooled estimates varied, but recent meta-analyses restricted to people with type 2 diabetes generally report an additional reduction in the range of roughly 0.3 to 0.4 percentage points.[3]

Guest et al. (2024) analyzed seven RCTs involving 770 adults with type 2 diabetes. In studies suitable for meta-analysis, vegetarian or vegan diets reduced HbA1c by an average of 0.40 percentage points more than nonvegetarian diets. The certainty of evidence was judged moderate. In the same analysis, fasting glucose and fasting insulin did not differ significantly.[4]

Lv et al. (2025) included nine RCTs and 681 participants and estimated an HbA1c mean difference of -0.36 percentage points. Fasting glucose, however, did not improve significantly. This is a reminder that a plant-based intervention does not necessarily move every glycemic marker to the same degree.[5]

> **Term | Mean difference (MD)** > A pooled effect size representing the average difference between intervention and control groups. It should always be interpreted together with its 95% confidence interval.

3. Fasting Glucose May Not Move in the Same Direction as HbA1c

Fasting plasma glucose is measured after at least eight hours without caloric intake. In type 2 diabetes it can rise when hepatic glucose production is inadequately suppressed overnight. Fasting glucose therefore reflects not only recent carbohydrate intake but also hepatic insulin resistance.[6]

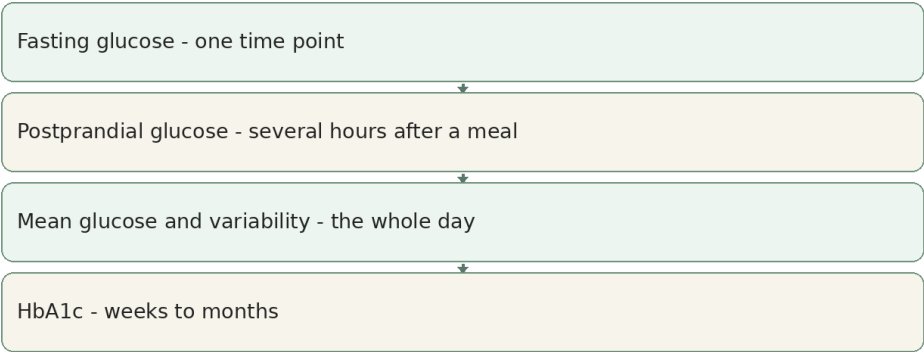
This helps explain why meta-analyses sometimes find lower HbA1c without a significant change in fasting glucose. HbA1c integrates glycemic exposure across the day, whereas fasting glucose represents a specific metabolic time point. Improvements in post-meal or daytime glucose can lower HbA1c even when the

morning fasting value changes relatively little.[4]

ADA 2026 uses fasting plasma glucose ≥ 126 mg/dL as a diagnostic criterion for diabetes and defines fasting as at least eight hours without caloric intake. Treatment targets are different from diagnostic thresholds. For many nonpregnant adults, a premeal glucose target of 80-130 mg/dL is commonly used and individualized as needed.[6]

> **Term | Fasting plasma glucose (FPG)** > Plasma glucose measured after at least eight hours without caloric intake. Diagnostic thresholds and treatment targets are not the same.

Figure 06-1. Different time windows represented by HbA1c, fasting glucose, and postprandial glucose



Source: ADA Standards of Care in Diabetes-2026; author synthesis.

Fasting glucose (one point in time) -> postprandial glucose (hours after a meal) -> daily mean glucose and variability -> HbA1c (integrated exposure over weeks to months)

Source: Author diagram based on ADA Standards of Care in Diabetes-2026.

4. Postprandial Glucose More Directly Reflects What Was Eaten

Postprandial glucose is affected by carbohydrate amount and form, dietary fiber, gastric emptying, insulin secretory capacity, and peripheral insulin sensitivity. People with the same HbA1c can therefore have very different post-meal glucose curves. The ADA notes that postprandial glucose can be assessed separately when premeal glucose is at target but HbA1c remains elevated.[1]

Meta-analyses of plant-based RCTs have most often reported HbA1c and fasting glucose; postprandial glucose and continuous glucose monitoring outcomes have not been reported consistently. It is therefore difficult to give one reliable number for “how much a plant-based diet lowers postprandial glucose.” Future studies should measure meal-related peaks, glycemic variability, and time in range in addition to dietary carbohydrate quality.[4]

> **Term | Postprandial glucose (PPG)** > Glucose measured after a meal. When clinically relevant, the ADA commonly refers to measurements one to two hours after the beginning of a meal.

5. Fasting Insulin Is Neither Automatically “Good” When Low Nor Diagnostic When High

Insulin lowers glucose, but fasting insulin by itself is not used to diagnose insulin resistance. A given insulin concentration can coexist with different glucose levels, beta-cell secretory capacities, and hepatic insulin clearance. Research therefore evaluates fasting insulin alone, combines fasting insulin and glucose in HOMA-IR, or uses direct techniques such as clamps.[7]

In the 2024 Guest meta-analysis restricted to type 2 diabetes, fasting insulin did not differ significantly between vegetarian and nonvegetarian diets. In a separate 2024 Termansen meta-analysis of overweight and obese adults, plant-based diets lowered fasting insulin by about 4.13 microU/mL and HOMA-IR by about 0.97. The populations and included trials differed, so these estimates should not simply be merged.[4][8]

> **Term | Fasting insulin** > Circulating insulin in the fasting state. Useful in metabolic research, but not a stand-alone diagnostic test for insulin resistance.

6. HOMA-IR Is Practical but Remains an Estimate

HOMA-IR estimates insulin resistance from fasting glucose and fasting insulin. It is inexpensive and practical for large studies but does not directly measure insulin sensitivity. Interpretation becomes more difficult in people with substantial beta-cell failure or those using exogenous insulin.[7]

Termannsen et al. (2024) suggested that plant-based diets may improve HOMA-IR in adults with overweight or obesity, but data restricted specifically to type 2 diabetes were limited. The authors concluded that additional RCTs are needed to determine whether improvements in insulin sensitivity are sustained long term in diabetes or high-risk populations.[8]

> **Term | HOMA-IR** > Homeostatic Model Assessment of Insulin Resistance. A model-based estimate calculated from fasting glucose and fasting insulin, not a direct measurement.

Table 6-2. Different Glycemic and Insulin Markers Answer Different Questions

Marker	Mainly reflects	Strength	Limitation
HbA1c	Accumulated glycemic exposure over recent months	Useful for long-term change	Influenced by anemia and red-cell lifespan
Fasting glucose	Overnight hepatic glucose regulation	Simple and standardized	Does not represent the entire day
Postprandial glucose	Meal-related glucose handling	Sensitive to dietary effects	Depends on meal composition and timing
Fasting insulin	Fasting insulin secretion/metabolic state	Easy to measure in research	Cannot diagnose insulin resistance alone
HOMA-IR	Estimated fasting-state insulin resistance	Low cost and practical	Model-based estimate
Clamp	Direct insulin sensitivity	Precise research method	Expensive and labor intensive

Source: Synthesized from ADA (2026), Kahleova et al. (2011), and Termannsen et al. (2024).

7. Clamp Studies Reveal Insulin Sensitivity Behind the Glucose Number

Kahleova’s 24-week RCT randomized 74 people with type 2 diabetes to a calorie-restricted vegetarian diet or a conventional diabetes diet. A notable feature was the use of a clamp-like method to assess insulin sensitivity. Insulin sensitivity improved more in the vegetarian group, and reduction in visceral fat was associated with improved insulin sensitivity.[9]

This allows a deeper interpretation of falling HbA1c. It helps distinguish whether lower glucose is due simply to eating less

carbohydrate or whether weight loss and reduced visceral fat have improved insulin action. Yet both diets were energy restricted and exercise was added during the final 12 weeks, so the entire effect cannot be attributed solely to plant foods.[9]

> **Term | Insulin sensitivity** > How effectively muscle, liver, and adipose tissue respond to a given amount of insulin. Greater sensitivity means less insulin is needed to produce a given metabolic effect.

> **Term | Hyperinsulinemic clamp** > A research method in which insulin is infused at a controlled rate while glucose is infused to maintain a target glucose concentration; the required glucose infusion is used to quantify insulin sensitivity.

8. A Korean Brown-Rice Vegan RCT Shows That a Higher-Carbohydrate Diet Can Still Lower HbA1c

In the 12-week Korean RCT by Lee et al., a brown-rice-based vegan diet was compared with a conventional diet recommended by the Korean Diabetes Association. Although the vegan diet was not low in carbohydrate, HbA1c fell by 0.5 percentage points compared with 0.2 in the control group. Among participants with high adherence, the respective reductions were 0.9 and 0.3 percentage points.[10]

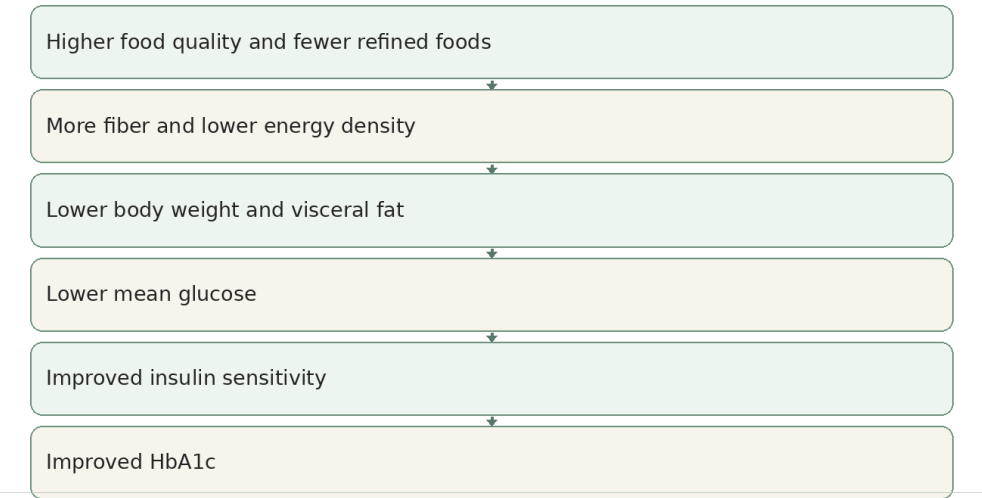
This finding is difficult to reconcile with the simple statement that “a high carbohydrate percentage must worsen glucose.” Food quality changed substantially, with an emphasis on brown rice, vegetables, and legumes, and energy intake and waist circumference also changed. The investigators reported that an HbA1c difference remained after adjustment for these variables. Still, the 12-week duration and differences in adherence limit conclusions about long-term effects.[10]

9. Weight Loss Is an Important Mediator, but Not the Entire Story

In Barnard’s 74-week study, change in body weight was significantly associated with change in HbA1c, supporting the idea that lower energy density and weight loss may mediate some glycemic benefit of plant-based diets. However, weight change does not completely explain the HbA1c response in every study.[11]

Guest’s 2024 meta-analysis also found an average BMI reduction of 0.96 kg/m² along with a 0.40 percentage-point reduction in HbA1c. Yet meta-regression did not identify one specific dietary component that clearly explained the HbA1c effect. Weight, fiber, energy intake, fat quality, adherence, and medication changes likely interacted.[4]

Figure 06-2. Multiple pathways through which plant-based eating can affect glucose and insulin



Source: Barnard et al. (2009); Kahleova et al. (2011); Guest et al. (2024); author synthesis.

Improved food quality -> changes in fiber and energy density -> loss of body and visceral fat -> improved insulin sensitivity -> lower mean glucose -> improved HbA1c

At the same time: fewer refined foods -> altered post-meal glucose burden; medication, exercise, sleep, and adherence can amplify or weaken the final effect.

Source: Author synthesis based on Barnard et al. (2009), Kahleova et al. (2011), and Guest et al. (2024).

10. Diet Quality Matters More Than the Label “Plant-Based”

A plant-based pattern can center on whole grains, legumes, vegetables, nuts, and seeds, or it can be dominated by refined grains, sugar, French fries, and ultraprocessed snacks. Both can contain few animal foods, but their metabolic effects should not be assumed equivalent. A 2025 meta-analysis of large observational studies found that a healthy plant-based diet index was associated with lower type 2 diabetes risk, whereas an unhealthy plant-based index showed the opposite association.^[12]

The same rule is used in this book’s plant-based ketogenic framework. We do not rely on the word “plant-based” alone; we consider net carbohydrate, fiber, fat quality, protein sources, processing, and total energy. One of the most important lessons from plant-based research is that actual food composition matters more than the dietary label.^[12]

> **Term | Healthy plant-based diet index (hPDI)** > A dietary scoring system that assigns higher scores to greater consumption of healthier plant foods such as whole grains, vegetables, fruits, legumes, nuts, and seeds.

11. Our Database Re-Checks HbA1c Numbers in the Original Sources

In the project’s top-300 XML full-text revalidation, 286 papers mentioned HbA1c and 163 contained numerical candidates. A third-pass check of JATS/XML Results and Tables found that 137 of the 286 papers had numeric candidates supported at a source location: 83 in tables, 52 in Results text, and two in abstracts.^[13]

But “the number is present in the paper” is not the same as “the plant-based intervention lowered HbA1c by that amount.” Verified values may represent within-group change, between-group difference, pooled meta-analysis effect, or baseline/end-point values. Twenty papers were flagged for numeric conflict or contextual ambiguity, and 149 still required additional review. Specific effect sizes used in this book are therefore prioritized when both the value and its effect type have been verified in a

Table or Results section.[13]

Table 6-3. HbA1c Source Verification in vk_diabete_db

Verification stage	Result
Top XML papers revalidated	300
HbA1c mentioned in text	286
HbA1c numeric candidates	163
Numbers supported at third-pass source location	137
Supported in Table	83
Supported in Results	52
Supported only in Abstract	2
Conflict/ambiguity flags	20
Additional review needed	149

Source: vk_diabete_db.sqlite3, vk_verify_top_evidence.py, and vk_verify_hba1c_numbers.py validation logs.

12. Clinically, Agreement Across Markers Matters More Than One “Winning” Number

If HbA1c falls while fasting insulin, body weight, and visceral fat also decline, several metabolic indicators are moving in the same direction. If HbA1c falls only slightly while medication is increased or body weight changes substantially, the independent dietary effect requires closer examination. Medication adjustment, adherence, and weight change should be recorded separately from outcome measurements in dietary trials.[4]

Likewise, a lower HbA1c target is not appropriate for everyone. People at high risk of hypoglycemia, older adults, and those with serious comorbidities may need less stringent targets. Whether the diet is plant-based or ketogenic, the goal is not to force one number downward at any cost but to improve metabolic health safely and sustainably.[1]

Table 6-4. Checklist for Reading Glucose and Insulin Outcomes in Plant-Based Diet Trials

Question	What to check
How much did HbA1c change?	Distinguish percentage-point change from between-group difference
Did fasting glucose move in the same direction?	Consider hepatic glucose regulation and measurement variability
What happened to insulin?	Distinguish fasting insulin, HOMA-IR, and clamp methods
How much weight was lost?	Consider whether weight loss mediated the effect
Were medications changed?	Interpret timing of reductions or increases with outcomes
What was adherence like?	Compare prescribed diet with actual intake
Was the study long enough?	HbA1c is better assessed over months than days

Question	What to check
What was the quality of the diet?	Look beyond the “plant-based” label to actual foods

Source: Synthesized from ADA (2026), Guest et al. (2024), and Termannsen et al. (2024).

Key Points from Chapter 6

The glycemic effect of plant-based diets is most consistently observed in HbA1c. Recent meta-analyses of RCTs in type 2 diabetes report an additional reduction of roughly 0.36-0.40 percentage points compared with control diets. Fasting glucose and fasting insulin have been less consistently affected, and insulin-sensitivity results vary by population and measurement method.[4][5]

Therefore, the sentence “plant-based diets lower blood glucose” is not enough. We need to know what the diet contained, how much weight changed, whether medications were adjusted, and whether HbA1c and insulin-related markers moved together. The next chapter examines mechanisms involving fiber, the gut microbiome, short-chain fatty acids, polyphenols, and micronutrients.[8]

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Chapter 7. Why Plant Foods Can Change Metabolism

The metabolic effects of plant-based eating cannot be explained by one nutrient. Dietary fiber feeds the gut microbiota, fatty acids from nuts and seeds affect membranes and lipid metabolism, and polyphenols and micronutrients influence other pathways. Most importantly, these components are not consumed in isolation. In real foods, many compounds arrive together within a food matrix.^[7-1]

1. The Strength of Plant Foods Lies in the Food Matrix, Not One Isolated Ingredient

Modern nutrition science is moving beyond a focus on percentages of carbohydrate, fat, and protein toward a broader view of food quality and dietary patterns. ADA 2026 likewise emphasizes nonstarchy vegetables, whole fruit, legumes, whole grains, nuts, and seeds, while recommending less refined grain and ultraprocessed food. The same amount of carbohydrate can have very different metabolic effects when it comes from beans rather than sugar.^[7-1]

Plant foods commonly contain fiber, minerals, vitamins, polyphenols, and unsaturated fats together. A trial of one isolated supplement therefore does not answer the same question as a trial of whole foods. This chapter discusses mechanisms without automatically extending the effect of one supplement to an entire plant-based diet.^[7-1]

2. Dietary Fiber Is Not One Substance

Dietary fiber is a broad group of carbohydrates that are not completely digested and absorbed in the small intestine. Physiologic effects differ according to solubility, viscosity, and fermentability. Viscous soluble fibers such as beta-glucan and psyllium can slow gastric emptying and nutrient diffusion, while fermentable fibers and resistant starch can serve as substrates for microbial metabolism in the colon.^[7-2]

ADA 2026 recommends at least 14 g of fiber per 1,000 kcal for people with diabetes or at high risk. This does not mean that “more is always better.” Rapidly increasing fiber can cause bloating, gas, diarrhea, or constipation, so food sources, hydration, and individual gastrointestinal adaptation should be considered.^[7-1]

3. Glycemic Effects of Fiber Are Relatively Consistent, but Effect Size Varies

A meta-analysis of 29 RCTs involving 1,517 adults with type 2 diabetes found that soluble-fiber supplementation lowered HbA1c by an average of 0.63 percentage points and also improved fasting glucose, fasting insulin, HOMA-IR, and postprandial glucose. Study heterogeneity was substantial, however, and fiber types, doses, and durations varied.[7-3]

A systematic review by Reynolds and colleagues that evaluated fiber and whole grains in diabetes management also found broadly favorable effects on glycemic and cardiometabolic outcomes. Yet the benefits of high-fiber diets may reflect more than fiber itself because whole grains, legumes, and vegetables also provide many other nutrients.[7-4]

It is therefore difficult to claim that “an extra 10 g of fiber will lower HbA1c by exactly X.” Food form, viscosity, fermentability, energy intake, and weight change all interact.[7-3]

4. The Gut Microbiota Responds Quickly to Dietary Change

The colon contains microorganisms that use carbohydrates not digested by host enzymes. When the type of fiber changes, the substrates available to microbes also change, potentially altering microbial communities and metabolite production. ADA 2026 notes that high-fiber diets may influence gut microbial composition and diversity but also states that important questions about causality in chronic disease remain unresolved.[7-1]

A 2020 systematic review of RCTs in type 2 diabetes found that fiber interventions increased relative abundance of *Bifidobacterium* and total short-chain fatty acids (SCFAs) and modestly improved HbA1c. However, fasting glucose, HOMA-IR, and individual acetate, propionate, and butyrate levels were not significantly different. Microbial changes and glycemic improvements therefore do not always move in a one-to-one relationship.[7-5]

5. Short-Chain Fatty Acids Are an Important Link, but “More Is Better” Is Too Simple

Acetate, propionate, and butyrate are major SCFAs produced when gut microbes ferment suitable substrates. They can serve as energy substrates for intestinal cells and may influence gut hormones, immune responses, and energy metabolism through receptors and signaling pathways. This is one plausible mechanism connecting dietary fiber with metabolic health.[7-6]

However, a 2022 meta-analysis of human trials did not find consistent improvement in glucose or insulin after direct administration of acetate, propionate, butyrate, or mixed SCFAs. Vinegar reduced some acute postprandial glucose responses, but heterogeneity and potential bias were substantial, and the authors emphasized uncertainty.[7-6]

A 2025 systematic review of human studies also warned against interpreting higher fecal SCFA concentrations as automatically beneficial. Fecal levels reflect not only production but also intestinal absorption and transit time. SCFAs are therefore an important candidate mechanism, not yet a simple clinical biomarker.[7-7]

6. Gut Barrier and Inflammation Are Plausible Pathways, but Human Evidence Must Be Graded Carefully

Butyrate is an important energy source for colonocytes and in experimental systems is involved in maintenance of the intestinal barrier and immune regulation. Obesity and type 2 diabetes are often accompanied by changes in microbiota, intestinal permeability, and low-grade inflammation. These observations, however, do not prove that a particular food “repairs the gut barrier and treats diabetes.”[7-8]

Clinically, direct outcomes such as glucose, body weight, and insulin sensitivity should take priority. Microbiome composition, SCFAs, and inflammatory markers are best used as supporting mechanistic evidence. This book consistently separates mechanistic plausibility from confirmed clinical benefit.[7-8]

7. Polyphenols Are Plant Signaling Compounds, but Their Average Clinical Effects Are Modest

Polyphenols are a large family of phenolic compounds produced by plants. Flavonoids are one subgroup and are found in berries, cocoa, tea, legumes, onions, herbs, and many vegetables. Absorption and metabolism vary greatly among compounds, and metabolites generated by the gut microbiota may also contribute to biological effects.[7-9]

A meta-analysis of 28 RCTs found that flavonoid interventions modestly improved fasting glucose, HbA1c, HOMA-IR, and some lipid markers in people with type 2 diabetes. The pooled HbA1c mean difference was about -0.26 percentage points. Because the compounds and doses varied widely, the result should not be interpreted as evidence that all flavonoids have the same effect.[7-9]

A practical advantage of obtaining polyphenols from foods is that they arrive with fiber, minerals, and fatty acids. High-dose extracts may have different effects and safety profiles. This is why a plant-based ketogenic diet prioritizes low-sugar vegetables, herbs, nuts, and seeds rather than relying on supplements.[7-9]

8. Magnesium Is Essential for Glucose Metabolism, but Supplement Effects Depend on the Population

Magnesium is a cofactor for many ATP-dependent enzymatic reactions and participates in insulin signaling and glucose metabolism. Rich food sources include nuts, seeds, legumes, leafy greens, and whole grains. Observational research repeatedly associates higher magnesium intake with a lower risk of type 2 diabetes.[7-10]

Supplement trials are more complex. A 2025 meta-analysis of 23 RCTs with 1,345 participants found that magnesium supplementation lowered fasting glucose, whereas the mean HbA1c effect of -0.16 percentage points was small and near the boundary of statistical significance. A 2026 updated meta-analysis did not find significant pooled improvements in insulin or HOMA-IR and suggested that baseline insulin status may influence response.[7-11]

Adequate magnesium intake from plant foods is therefore a different claim from recommending supplements to every person with diabetes. Supplement use requires particular caution in impaired kidney function.[7-11]

9. Potassium Is Linked to Glucose Metabolism as Well as Blood Pressure, but Causality Remains Limited

Potassium is involved in membrane potential, nerve and muscle function, and electrical activity of pancreatic beta cells. Vegetables, legumes, nuts, and many fruits are major sources. A 2022 meta-analysis of seven prospective studies found a nonlinear inverse association between dietary potassium intake and diabetes risk.[7-12]

Because these data are primarily observational, the independent effect of potassium cannot be completely separated from the broader healthy dietary pattern. In addition, people with chronic kidney disease or certain medications may be at risk of hyperkalemia. The message cannot simply be “plant-based diets are high in potassium, so everyone should eat as much as possible.”[7-12]

10. What Fat Replaces Matters as Much as the Amount of Fat

Plant-based fat sources can emphasize monounsaturated and polyunsaturated fats from nuts, seeds, olives, and avocados. The key question is not whether fat was “added,” but what it replaced. Replacing saturated fat with PUFA at equal calories is metabolically different from replacing refined carbohydrate with saturated fat.[7-13]

A meta-analysis of 102 randomized feeding trials involving 4,220 participants found favorable changes in HbA1c and insulin-related markers when part of carbohydrate or saturated fat was isocalorically replaced with MUFA or PUFA. PUFA was associated with the most consistent improvements across several comparisons. However, a 2023 meta-analysis of shorter RCTs found no clear effect of replacing saturated with unsaturated fat on insulin sensitivity itself, illustrating that results depend on outcome and duration.[7-13]

A meta-analysis restricted to type 2 diabetes also found that higher-MUFA diets, compared with higher-carbohydrate diets, improved fasting glucose, triglycerides, body weight, and systolic blood pressure. This supports prioritizing unsaturated plant fats when fat intake is increased in a plant-based ketogenic diet.[7-14]

11. Nuts and Seeds Are Foods, Not Just “Lumps of Fat”

Nuts provide unsaturated fat together with fiber, protein, magnesium, and multiple bioactive compounds. In a meta-analysis of 40 RCTs with 2,832 participants, nut and peanut intake modestly improved fasting insulin and HOMA-IR but did not significantly change HbA1c or fasting glucose. A 2025 walnut meta-analysis similarly found improvement in HOMA-IR without significant changes in HbA1c or fasting glucose.[7-15]

Again, one food does not move every metabolic marker in the same direction. Nuts should be evaluated not only for glucose but for fat quality, satiety, cardiovascular risk factors, and their role within the overall diet.[7-15]

12. The Metabolic Effect of Plant Foods Is Often the Overlap of Many Small Pathways

Fiber changes post-meal glucose absorption and colonic fermentation. Unsaturated fats alter fatty-acid composition. Magnesium and potassium support enzymatic and electrical functions, while polyphenols interact with multiple signaling pathways. Individual effects may be modest, but when combined in one eating pattern they can shift weight, glucose, lipids, and blood pressure in the same direction.[7-1]

The word “synergy,” however, should be distinguished from an effect directly demonstrated in clinical trials. Whole-diet studies change many factors at once, so the exact contribution of each component is difficult to isolate. The logic of a plant-based ketogenic diet is to place several relatively well-supported food-quality principles into one diet while remaining explicit about uncertainty.[7-1]

13. In a Plant-Based Ketogenic Diet, Fiber and Micronutrients Should Not Be Thrown Away with Carbohydrate

Strong carbohydrate restriction can substantially reduce whole grains, fruits, and legumes and thereby reduce fiber, magnesium, potassium, and polyphenols. A plant-based ketogenic diet should therefore not simply minimize carbohydrate. Within the allowed carbohydrate range, it should prioritize nutrient-dense foods such as nonstarchy vegetables, nuts and seeds, mushrooms, sea vegetables, and, depending on individual tolerance, small amounts of legumes.[7-1]

People taking SGLT2 inhibitors require special caution because ketogenic eating patterns can increase ketoacidosis risk. ADA 2026 recommends discouraging a ketogenic eating pattern in people at DKA risk who are treated with SGLT inhibition. The model in this book should not be applied without considering medication status, kidney function, and electrolyte status.[7-16]

Key Points from Chapter 7

Fiber, gut microbiota, SCFAs, polyphenols, magnesium, potassium, and unsaturated fats all contribute to the metabolic effects associated with plant foods. The clinical evidence is relatively strong for dietary fiber and fat quality, whereas microbiome and SCFA pathways remain important but incompletely established mechanisms in humans.[7-1]

The core challenge for a plant-based ketogenic diet is to reduce carbohydrate while preserving the protective nutritional features of plant foods. The next chapter turns the principle around and

asks what happens when a “plant-based” diet is dominated by refined grains, sugar, and ultraprocessed foods.[7-1]

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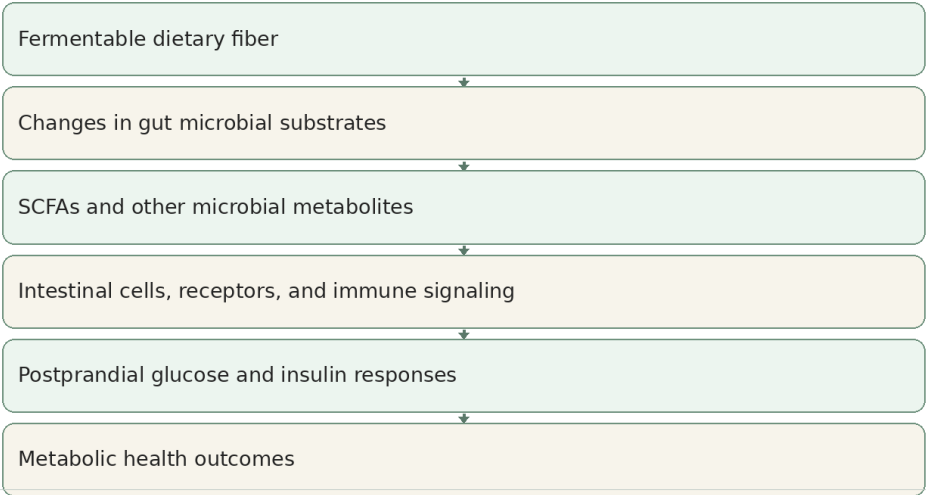
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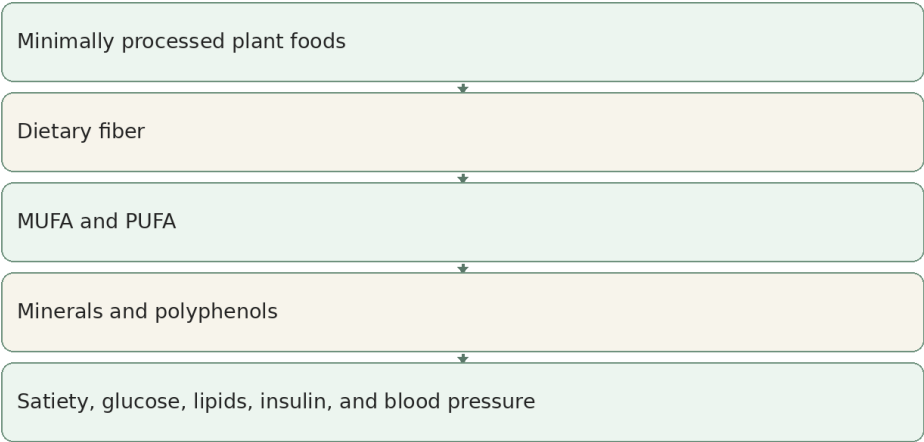
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Figure 07-1. Pathway from dietary fiber to the gut microbiome and host metabolism



Source: Ojo et al. (2020); Cherta-Murillo et al. (2022); ADA (2026); author synthesis.

Figure 07-2. How the plant-food matrix reaches multiple metabolic pathways at once



Source: ADA (2026); Reynolds et al. (2020); Imamura et al. (2016); author synthesis.

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Chapter 8. Weaknesses of Plant-Based Diets - Not Everything Plant-Based Is Healthy

The word plant-based describes where a food comes from; it does not guarantee its metabolic quality. Potato chips come from plants, and so do sugar and refined flour. Beans, nuts, and nonstarchy vegetables - minimally processed, nutrient-dense foods - belong to the same broad category. In diabetes, therefore, the important question does not end with “animal or plant?” We must also ask what was eaten, how much it was processed, and what it replaced.[8-1]

1. “Plant-based” is not one dietary pattern

Plant-based diets range from vegan and vegetarian diets to semi-vegetarian patterns and mixed diets that simply emphasize plant foods. Definitions also differ across studies, so combining very different eating patterns can blur the results. In particular, if a diet increases the proportion of plant foods but does not distinguish whole grains, vegetables, legumes, and nuts from refined grains, sugars, and ultraprocessed foods, the expected advantages of plant-based eating may weaken.[8-2]

A 2024 meta-analysis of prospective studies illustrates this distinction quantitatively. Higher scores on the overall plant-based diet index and the healthy plant-based diet index were associated with lower risk of type 2 diabetes, whereas a higher unhealthy plant-based diet index was associated with greater risk. The healthy index gives more weight to whole grains, vegetables, fruits, legumes, and nuts; the unhealthy index gives more weight to refined grains, sweetened beverages, and similar foods.[8-3]

Table 8-1. Diabetes risk evidence distinguishing the quantity and quality of plant-based eating

Index	Meaning of a higher score	Type 2 diabetes risk	Interpretation
Overall plant-based diet index (O-PDI)	More plant foods relative to animal foods	About 14% lower	Average association of plant-food predominance
Healthy plant-based diet index (H-PDI)	Whole grains, vegetables, fruits, legumes, nuts	About 19% lower	Plant-food quality matters
Unhealthy plant-based diet index (U-PDI)	More refined grains, sugars, processed foods	About 10% higher	“Plant-based” alone does not establish healthfulness

Source: 2024 systematic review and dose-response meta-analysis of 16 prospective studies including 721,012 participants.[8-3]

2. Refined grains are plant foods, but they do not behave like intact grains

Grains provide fiber and micronutrients when the bran, germ, and endosperm remain relatively intact. Refining removes much of that structure, changing particle size, digestion rate, and fiber content. ADA 2026 emphasizes whole grains and minimally processed carbohydrate sources and recommends reducing refined grains in diabetes nutrition therapy.[8-1]

This difference is separate from the absolute amount of carbohydrate. Forty grams of carbohydrate delivered as a sugary drink, white bread, beans, or vegetables does not produce the same post-meal response or satiety. This is why a plant-based ketogenic approach considers carbohydrate quality even while reducing carbohydrate quantity.[8-1]

3. When discussing sugar, consider both form and energy context

It is also inaccurate to describe every sugar as the same toxic substance. In a 2025 meta-analysis of prospective cohorts, sugar-sweetened beverages showed a consistent positive association with type 2 diabetes risk, whereas total sugar and fructose itself were not consistently associated in the same direction. The investigators concluded that the food source and the form in which sugar is consumed matter along with the type of sugar.[8-4]

Analyses of randomized feeding trials provide a similar message. When fructose replaced other carbohydrates isocalorically, glycemic outcomes did not necessarily worsen. Adverse results were more likely when sugars were added - often as beverages - so that total energy intake increased. Therefore, the claim that “fruit is the same as a sugary drink because both contain fructose” is not supported by the evidence.[8-5]

4. Whole fruit and fruit juice are not the same food

Whole fruit retains cell walls, fiber, and the act of chewing. Juice changes much of that structure and makes it easier to consume a similar sugar load rapidly. A 2025 meta-analysis found that non-100% fruit juice was associated with increased type 2 diabetes risk, while 100% fruit juice did not show a clear preventive effect.[8-6]

By contrast, a small 2026 meta-analysis of randomized trials in people with type 2 diabetes found that selected whole or

fruit-based products modestly reduced HbA1c and fasting glucose. Only five studies with 245 participants were available, so the findings should not be generalized to all fruit. They do, however, reinforce that whole fruit should not be grouped automatically with sugar-sweetened beverages.^[8-7]

Figure 08-1. Why different forms of plant carbohydrate can lead to different metabolic paths

Whole grains, legumes, vegetables, whole fruit	Refined grains, sugary drinks, snacks
Food structure and fiber remain intact	Less food structure and more processing
Slower eating and absorption	Faster intake and higher palatability
Higher satiety and lower energy density	Possible excess energy intake and glycemic burden

Source: ADA (2026) and meta-analyses on sugars and ultra-processed foods; author synthesis.

Whole grains, beans, vegetables, and whole fruit -> preserved fiber and food structure -> slower eating and absorption -> greater satiety and lower energy density.

Refined grains, sugary drinks, and sweets -> reduced food structure and high processing -> rapid consumption and high palatability -> potential excess energy intake and glycemic burden.

Source: constructed for this book from ADA 2026 and meta-analyses of sugars and ultraprocessed foods.[8-1][8-4][8-8]

5. An ultraprocessed vegan food is not protected by the word “vegan”

Ultraprocessed foods are industrial products made through multiple processing steps, often using refined ingredients and additives. Vegan cookies, vegan ice cream, refined-starch meat substitutes, and sugar-rich plant beverages can fall into this category depending on their formulation. Plant origin and degree of processing are separate axes.[8-8]

A 2024 umbrella review rated the evidence linking higher ultraprocessed-food intake with type 2 diabetes as being of moderate certainty. A 2025 dose-response meta-analysis likewise found that the highest intake group had about a 48% higher risk of type 2 diabetes than the lowest intake group. Most of these data are observational, however, so they do not establish the isolated causal effect of one component of ultraprocessed foods.[8-8][8-9]

Nor do all ultraprocessed foods carry identical associations. In large U.S. cohorts, overall ultraprocessed-food intake was positively associated with type 2 diabetes, but associations differed by food subgroup. The NOVA classification therefore cannot fully describe nutritional value by itself; processing and nutrient quality should be considered together.[8-10]

Table 8-2. Examples of foods that may be metabolically unfavorable despite being plant-based

Food or pattern	Main concern	Direction in the evidence	Practical judgment
Sugar-sweetened beverages	Liquid sugar, rapid intake, low satiety	Higher T2D risk	Prefer water or unsweetened beverages
Refined-grain dominant meals	Less fiber and food structure	ADA recommends minimizing	Replace with whole grains or lower-glycemic intact foods
Vegan sweets and desserts	Refined starch, sugar, fat, high palatability	May fit unfavorable UPF patterns	Read ingredients rather than relying on “vegan” label
Ultraprocessed substitutes	Processing, sodium, refined ingredients vary	Results differ by subgroup	Evaluate each product's nutritional profile

Food or pattern	Main concern	Direction in the evidence	Practical judgment
Fruit juice	Less chewing and altered fiber structure	Not equivalent to whole-fruit prevention	Limit quantity when used

Source: ADA 2026; Della Corte et al. (2025); Lane et al. (2024); Chen et al. (2023).^{[8-1][8-4][8-8][8-10]}

6. For protein, “requires planning” is more accurate than “plant-based diets are deficient”

A systematic review of nutritional status in adults consuming plant-based diets found that average protein intake was lower among vegans and vegetarians than among meat eaters, but generally remained within recommended ranges. Thus, a balanced adult plant-based diet does not inevitably cause protein deficiency.^[8-11]

The situation changes when energy intake is substantially reduced or carbohydrate sources are restricted at the same time. A plant-based ketogenic diet may limit grains and portions of legumes, narrowing the range of foods that provide total protein and essential amino acids. Older adults, people losing weight, and those at risk of sarcopenia should deliberately place tofu, tempeh, soy protein, nuts, and seeds in the diet. ADA 2026 likewise emphasizes monitoring protein and micronutrient adequacy during intensive weight-loss interventions.^{[8-1][8-11]}

7. Vitamin B12 must be planned, not treated as an optional detail

Natural food sources of vitamin B12 are predominantly animal foods. Strict vegan diets that do not use fortified foods or supplements carry a substantial risk of inadequate intake. A 2024 systematic review and meta-analysis of functional B12 status in adult vegans found lower serum B12 and higher homocysteine than in omnivores, consistent with a greater risk of functional deficiency.^[8-12]

Supplement use was the key modifier. Vegans who used B12 supplements had more favorable major B12 biomarkers than vegans who did not. Therefore, if a plant-based ketogenic diet is strictly vegan, B12 should not be left to chance. Fortified foods or appropriate supplementation and a monitoring plan should be established in advance.^[8-12]

8. For iron, assess stores and bioavailability as well as intake

Plant foods provide nonheme iron, but its absorption depends on meal composition. Phytate can reduce absorption, whereas vitamin C can improve nonheme-iron absorption. A meta-analysis of vegetarian adults found that serum ferritin was, on average, lower than in nonvegetarians.[8-13]

This does not mean that every vegetarian is anemic. Iron stores, hemoglobin, menstruation, bleeding, kidney disease, and inflammatory status all matter. If anemia or chronic kidney disease accompanies diabetes, the cause should not be assigned to diet without a broader clinical evaluation.[8-13]

9. Zinc absorption can change in phytate-rich diets

Nuts, seeds, and legumes provide zinc but also contain phytate. An older meta-analysis found that average zinc intake and serum zinc were lower among vegetarians than nonvegetarians, with larger differences tending to appear among vegans and women.[8-14]

Soaking, sprouting, and fermentation can reduce phytate and improve zinc availability. Yet serum zinc alone is not a perfect measure of an individual's zinc status. A 2024 biomarker review concluded that serum or plasma zinc responds to changes in intake but has limitations for individual interpretation.[8-15]

10. Iodine is not automatically solved by eating seaweed

Vegan and vegetarian diets may provide less iodine in regions where dairy and seafood are major sources. A 2023 systematic review and meta-analysis reported that iodine insufficiency may be more common among modern vegan and vegetarian adults.[8-16]

Seaweed can be rich in iodine, but its iodine concentration varies enormously by species and product. “Just eat a lot of seaweed” is therefore not a safe rule. Too little iodine is harmful, but excessive intake can also disturb thyroid function. Use of iodized salt and actual dietary sources should be assessed in context.[8-16]

11. Distinguish ALA from EPA and DHA when discussing omega-3 fats

Perilla, flax, chia, and walnuts provide alpha-linolenic acid (ALA). ALA is essential, but conversion to the long-chain omega-3 fatty acids EPA and DHA is limited. Systematic reviews of adults following plant-based diets have found lower EPA and DHA intake and status among vegetarians and especially vegans than among meat eaters.[8-11]

A 2025 systematic review reached the same general conclusion. Algal-derived DHA and EPA can provide direct long-chain omega-3 fatty acids to people who do not eat fish. This is separate, however, from the question of whether high-dose omega-3 supplements should be recommended universally for diabetes treatment; the evidence does not support such a blanket rule.[8-17]

Table 8-3. Nutrients that deserve particular attention in plant-based eating

Nutrient	Feature of plant-based diets	When risk may increase	Monitoring and supplementation direction
Protein	Average intake generally falls within recommendations	Low-calorie and low-carbohydrate restrictions overlap	Plan tofu, tempeh, soy protein, nuts, seeds
Vitamin B12	Very limited natural plant sources	Strict vegan diet without supplementation	Fortified foods/supplement; consider B12 and MMA testing
Iron	Mostly nonheme; absorption strongly affected by meal composition	Menstruation, anemia, CKD, low energy intake	Review ferritin, CBC, and food combinations
Zinc	Phytate affects absorption	Narrow food variety and high reliance on legumes/grains	Soaking/fermentation; nuts/seeds; test when indicated
Iodine	Depends on region and fortification	Low seafood, dairy, and iodized salt	Identify sources; avoid excessive seaweed intake
EPA/DHA	Conversion from ALA is limited	No fish or algal oil intake	ALA-rich foods plus algal EPA/DHA when appropriate

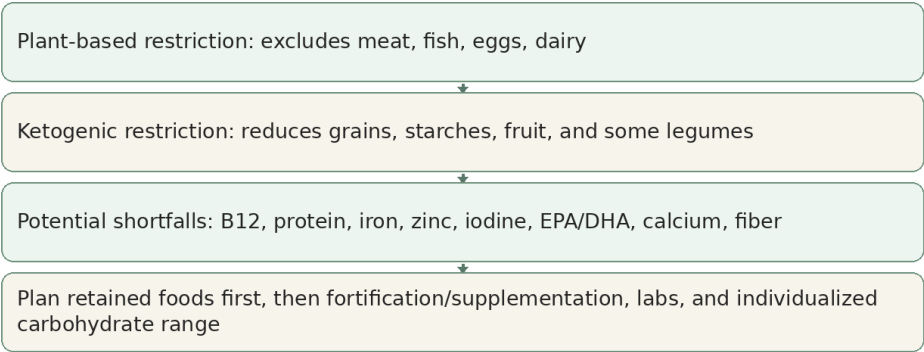
Source: Bakaloudi et al. (2021); Niklewicz et al. (2024); Haider et al. (2018); Foster et al. (2013); Eveleigh et al. (2023); Burns-Whitmore et al. (2022); 2025 systematic review of n-3 PUFA status.[8-11][8-12][8-13][8-14][8-16][8-17]

12. A plant-based ketogenic diet can become a “double-restriction diet”

A conventional vegan diet excludes animal foods. A ketogenic diet can additionally reduce grains, starchy foods, many fruits, and portions of legumes. When these restrictions overlap, the number of food sources supplying B12, protein, iron, zinc, iodine, calcium, EPA/DHA, and fiber can narrow substantially.[8-11]

A plant-based ketogenic diet therefore should not be designed simply by “removing animal foods and then cutting carbohydrates further.” The foods that must remain should be selected first. Nonstarchy vegetables, tofu and tempeh, appropriate soy protein, nuts and seeds, olives and avocado, mushrooms and sea vegetables, and fortified foods can form the structural base. Nutrients at greater risk of inadequacy should be addressed with laboratory monitoring and supplementation when appropriate.[8-11][8-11]

Figure 08-2. Nutrient gaps that can emerge when plant-food and ketogenic restrictions overlap



Source: systematic reviews of nutrient status in plant-based diets and ADA (2026); author synthesis.

Plant-based restriction: meat, fish, eggs, and dairy excluded.

+ Ketogenic restriction: grains, starches, fruit, and some legumes reduced.

-> Potentially fewer sources of B12, protein, iron, zinc, iodine, EPA/DHA, calcium, and fiber.

-> Response: design the foods that must remain first + fortified foods/supplements + laboratory testing + individualized carbohydrate range.

Source: constructed for this book from systematic reviews of nutrient status in plant-based diets and ADA 2026.[8-1][8-11][8-12]

13. “Healthy plant-based” is defined by food composition, not a label

In practice, ingredient lists and Nutrition Facts should take priority over front-of-package claims such as vegan, plant-based, or cholesterol-free. A product high in added sugar, refined starch, sodium, or saturated fat and low in fiber and protein is not automatically metabolically favorable because its ingredients are plant-derived.[8-1][8-8]

Nor is it necessary to ban every processed food. Unsweetened soy milk, frozen vegetables, and canned beans can improve convenience while preserving nutritional density. The important questions are why the food was processed, what ingredients it contains, its nutrient profile, and its role in the overall diet.[8-10]

Table 8-4. Four filters for designing a plant-based ketogenic diet

Filter	Question	Example of a passing criterion
1. Degree of processing	How close is the food to its original form?	Emphasize nonstarchy vegetables, nuts, seeds, tofu
2. Carbohydrate quality	Is it rich in refined sugar or starch?	Fiber remains and added sugar is low
3. Fat and protein quality	What are the fat and protein sources?	Prioritize unsaturated fats and varied plant proteins
4. Deficiency prevention	Are B12, iron, zinc, iodine, and omega-3 covered?	Food planning + fortification/supplementation + testing

Source: constructed for this book from ADA 2026 and the nutrient-status and food-quality evidence reviewed in this chapter.[8-1][8-11][8-12]

14. These weaknesses are design problems, not evidence that plant-based eating has failed

Acknowledging weaknesses of plant-based diets does not reject plant-based eating. On the contrary, understanding the conditions under which benefits disappear is necessary to preserve those benefits. Healthy plant-based patterns are associated with lower type 2 diabetes risk, but the same direction of effect should not be assumed when refined grains, sugars, and ultraprocessed foods dominate the diet.[8-3][8-8]

The same principle applies to nutrients. Adults consuming sufficient energy and varied foods can obtain adequate protein on plant-based diets. Yet B12 requires specific planning, and iron, zinc, iodine, and EPA/DHA may become inadequate depending on the individual and food choices.[8-11][8-12]

A plant-based ketogenic diet must solve both problems simultaneously. It should lower carbohydrate exposure when needed to reduce glycemic and insulin burden, while preserving the fiber, unsaturated fats, and micronutrient density that make high-quality plant-based eating valuable. In the next chapters, we turn to the other axis and examine the clinical evidence for ketogenic diets with the same level of scrutiny.[8-1]

Key points from Chapter 8

The label plant-based does not guarantee healthfulness. Food quality, degree of processing, and what a food replaces strongly influence diabetes risk and metabolic effects.[8-3]

Vitamin B12 deserves particular attention in strict plant-based diets. When food-group restriction is further intensified by a ketogenic approach, protein, iron, zinc, iodine, EPA/DHA, calcium, and fiber should also be systematically reviewed. The lesson is not to add more restrictions; it is to make the design as precise as the restrictions themselves.[8-11][8-12]

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Chapter 9. Clinical Research on Ketogenic Diets and Type 2 Diabetes

Do ketogenic diets help type 2 diabetes? The question sounds simple, but the evidence becomes complicated quickly. Some studies label any diet below 130 g carbohydrate per day as “low carbohydrate,” while others require less than 50 g. Still others measure blood beta-hydroxybutyrate (BHB) to confirm whether nutritional ketosis actually occurred. Very different interventions can therefore sit under similar names.[9-1]

To evaluate ketogenic evidence correctly, we must look beyond the label and examine the actual intervention: degree of carbohydrate restriction, energy restriction, fat quality, exercise, medication adjustment, counseling intensity, and whether ketosis was measured. This chapter separates these elements and reviews randomized trials, meta-analyses, longer follow-up, and real-world care models.[9-2]

1. A low-carbohydrate diet and a ketogenic diet are not the same thing

A low-carbohydrate diet (LCD) is a broad category that reduces carbohydrate below usual intake. Research often uses <130 g/day or <26% of energy. Very-low-carbohydrate diets (VLCDs) and ketogenic diets more commonly use <50 g/day or <10% of energy. Yet carbohydrate targets alone do not guarantee that a participant is producing clinically meaningful ketones.[9-3]

Nutritional ketosis is a metabolic state, not a diet name. As carbohydrate availability falls, fatty-acid oxidation and hepatic ketogenesis rise and circulating BHB increases. Results from a generic low-carbohydrate trial therefore should not automatically be presented as results of a ketogenic intervention.[9-4]

Table 9-1. Categories of carbohydrate restriction that should be distinguished in clinical research

Category	Common definition	Ketosis confirmed?	Interpretation
Low-carbohydrate diet (LCD)	<130 g/day or <26% energy	Usually not required	Not synonymous with ketogenic diet
Very-low-carbohydrate diet (VLCD)	Often <50 g/day or <10% energy	Varies	Ketogenesis more likely but individual variation remains
Ketogenic diet (KD)	Very-low carbohydrate with high fat	Sometimes measured	Distinguish prescribed diet from actual metabolic state

Category	Common definition	research	Ketosis confirmed?	Interpretation
Nutritional ketosis	Metabolic state confirmed by elevated blood BHB, etc.		Yes	Medication, fasting, and energy context still matter

Source: Goldenberg et al. (2021); Parry-Strong et al. (2022); ADA Standards of Care (2026).

2. In ketogenic research, the comparator matters

The apparent size of an effect depends heavily on the comparison diet. A ketogenic intervention can look dramatic against usual care with little dietary support. Against an active comparator that also includes energy restriction, exercise, and counseling, both groups may improve and the between-group difference may be small. Within-group change and between-group difference must therefore be read separately.^[9-5]

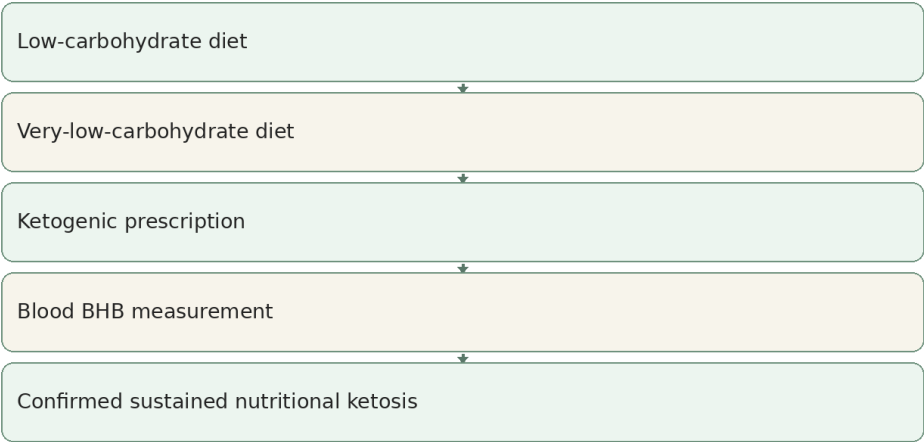
Weight loss is another mediator. Independent of diet composition, weight loss can improve HbA1c and insulin resistance. A 2023 network meta-analysis of 42 randomized trials found that changes in HbA1c and fasting glucose were related to average weight change. This helps explain why it is difficult to isolate the effects of carbohydrate restriction completely from the effects of weight loss.^[9-6]

3. Small randomized trials showed feasibility and a strong signal, but samples were small

In the 2017 Saslow randomized trial, overweight or obese adults with type 2 diabetes were assigned to a very-low-carbohydrate ketogenic lifestyle intervention or a conventional plate-method intervention. After 32 weeks, HbA1c fell by about 0.8 percentage points in the ketogenic group and about 0.3 points in the comparator group. Weight and triglycerides also fell more in the ketogenic group.^[9-7]

The result is clinically interesting, but the analyzable sample was small and the intervention included online education and lifestyle support, not diet alone. A large difference in a small study is a reason for further testing, not a universal estimate for every person with type 2 diabetes.^[9-7]

Figure 09-1. Evidence spectrum from low-carbohydrate eating to confirmed nutritional ketosis



Source: Goldenberg et al. (2021); Parry-Strong et al. (2022); Hallberg et al. (2018); author synthesis.

Low-carbohydrate diet -> very-low-carbohydrate diet -> ketogenic prescription -> blood BHB measurement -> sustained nutritional ketosis confirmed.

Source: constructed from Goldenberg et al. (2021); Parry-Strong et al. (2022); Hallberg et al. (2018).

4. In a well-designed one-year trial, HbA1c improved on both diets

Tay and colleagues randomized 115 adults with obesity and type 2 diabetes to a low-carbohydrate, high-unsaturated-fat diet (<50 g carbohydrate/day) or a high-carbohydrate, low-fat diet. Both groups received energy restriction and combined aerobic/resistance exercise three times per week. At 52 weeks, both groups lost roughly 10 kg and reduced HbA1c by about 1.0 percentage point. The between-group difference in HbA1c was not significant.[9-8]

Not every outcome was the same. The low-carbohydrate group had larger improvements in diabetes medication score, glycemic variability, triglycerides, and HDL cholesterol. The study therefore argues against the simplistic statement that “ketogenic diets always lower HbA1c more,” while showing that medication burden, glucose variability, and lipid responses can differ even when average HbA1c is similar.[9-8]

5. By two years, superiority may become smaller

At two years in the same cohort, 61 of 115 participants completed follow-up. Both groups maintained improvements in weight and HbA1c, but there was no significant between-group difference in HbA1c. Some advantages in triglycerides, HDL, glycemic variability, and medication-related outcomes persisted in the low-carbohydrate group.[9-9]

It is important to distinguish “the effect disappeared” from “it was not superior to the comparator.” If both groups remain better than baseline, both interventions may still be beneficial. The separate question is how much additional benefit one provides over a strong active comparator. Longer trials also face declining adherence and convergence of actual carbohydrate intake between groups.[9-9]

Table 9-2. How to read representative low-carbohydrate and ketogenic intervention studies

Study	Design/duration	Carbohydrate restriction	Main result	Key limitation
Saslow et al., 2017	Small RCT, 32 weeks	Very-low-carbohydrate ketogenic	Greater HbA1c, weight and TG improvement	Small sample; multicomponent lifestyle intervention
Tay et al., 2015	RCT, 52 weeks, n=115	<50 g/day; high unsaturated fat	HbA1c ~-1.0% in both; LC favored medication, variability and TG	Energy restriction and exercise in both groups
Tay et al., 2018	Same cohort, 2 years	Same	No HbA1c superiority; some lipid/medication advantages	Attrition and long-term adherence
Hallberg et al., 2018	Nonrandomized controlled, 1 year	Nutritional ketosis target	Large improvements in HbA1c, weight and medication use	Nonrandomized; remote-care model
Athinarayanan et al., 2019	Nonrandomized controlled, 2 years	Nutritional ketosis target	Improvements in HbA1c, weight and medication use persisted	Multicomponent intervention; selection/residual confounding

6. Meta-analysis of low-carbohydrate diets shows a strong six-month signal

Goldenberg et al. (2021) analyzed 23 randomized trials involving 1,357 participants. At six months, low-carbohydrate diets lowered HbA1c by an average of 0.47 percentage points more than control diets and also favored weight, triglycerides, and insulin sensitivity. Remission defined using HbA1c <6.5% alone was also reported more often.[9-10]

The remission effect became much smaller when medication discontinuation was included in the definition. By 12 months, the HbA1c difference had shrunk to about 0.23 percentage points and was close to the statistical boundary. The authors recognized the short-term effect but emphasized the need for better evidence on long-term durability, adherence, and safety.[9-10]

This is important evidence, but it is not a meta-analysis of ketogenic diets alone. Eligibility extended to <130 g/day or <26% energy, and only about half the included trials met a very-low-carbohydrate definition. Calling the entire pooled effect “the effect of ketogenic diets” overstates what the analysis tested.[9-10]

7. When the definition is narrowed to strict ketogenic diets, conclusions become more cautious

Parry-Strong et al. (2022) used a stricter definition - ≤ 50 g/day or $\leq 10\%$ energy - and included randomized trials lasting at least six months. Eight studies with 606 participants were analyzed. The 12-month HbA1c conclusion depended on how results were reported; among four trials reporting change scores, there was little difference from control diets.[9-11]

Some studies, however, reported absolute 12-month HbA1c values about 0.65 percentage points lower than control. Triglycerides were about 0.28 mmol/L lower on average and HDL modestly higher. The authors concluded that very-low-carbohydrate/ketogenic diets may improve HbA1c and triglycerides, but evidence was insufficient to claim clear superiority over other strategies.[9-11]

Choy and Louie (2023), reanalyzing 19 reports from 11 randomized trials, reached a similar conclusion. Ketogenic diets lowered triglycerides more and raised HDL more than comparators, but did not provide significant additional glycemic or weight-loss benefit over follow-up of up to two years. Different definitions, time points, and analytic choices can therefore yield different summaries of overlapping evidence.[9-12]

Table 9-3. Why meta-analyses can reach different conclusions

Meta-analysis	Inclusion criteria	Main result	Interpretation in this book
Goldenberg et al., 2021	LCD <130 g/day or $<26\%$, including VLCD	6-month HbA1c -0.47% ; more remission; effect attenuates by 12 months	Strong evidence for short-term low-carbohydrate effects overall
Parry-Strong et al., 2022	≤ 50 g/day or $\leq 10\%$, RCT ≥ 6 months	Mixed 12-month HbA1c; TG down, HDL up	Long-term superiority of strict VLC/KD remains uncertain
Choy & Louie, 2023	Ketogenic RCT reports, 2001-2021	No additional glycemic/weight benefit; TG down, HDL up	Lipid direction more consistent than HbA1c superiority
Network meta-analysis, 2023	10 dietary patterns, 42 RCTs	Ketogenic pattern ranked favorably for HbA1c	Indirect comparisons and weight change must be considered

8. Network meta-analysis ranked ketogenic diets favorably, but a ranking is not a final verdict

A 2023 network meta-analysis compared 10 dietary approaches in 42 randomized trials with 4,809 participants. Ketogenic, low-carbohydrate, and low-fat diets each significantly lowered HbA1c versus control, and ketogenic diets occupied a favorable rank when HbA1c and fasting glucose were considered together.[9-13]

Network meta-analysis combines direct and indirect comparisons across different trials. Heterogeneity in duration, medications, weight loss, and diet definitions can therefore make rankings uncertain. In this analysis, average weight change was associated with changes in HbA1c and fasting glucose, and the authors emphasized the need for longer, high-quality trials.[9-13]

9. Large interventions targeting actual nutritional ketosis show substantial medication reduction

Hallberg et al. (2018) enrolled 262 adults with type 2 diabetes in a remote-care program targeting nutritional ketosis and compared them with 87 people receiving usual care. At one year, mean HbA1c in the intervention group fell from 7.6% to 6.3%, while body weight fell by about 13.8 kg. Use of glucose-lowering medications other than metformin was markedly reduced.[9-14]

Among participants using insulin, 94% reduced or discontinued insulin; sulfonylureas were discontinued in the intervention group. HOMA-IR, triglycerides, HDL, and inflammatory markers also improved. Mean LDL-C rose, while ApoB did not change significantly.[9-14]

This study shows how carbohydrate restriction can work when integrated with medication management in clinical practice. It was not randomized, however, and included remote monitoring, health coaching, and active medication adjustment. The entire result cannot be isolated as the effect of “ketosis” alone.[9-14]

10. Two-year follow-up supports feasibility, but it is still not randomized evidence

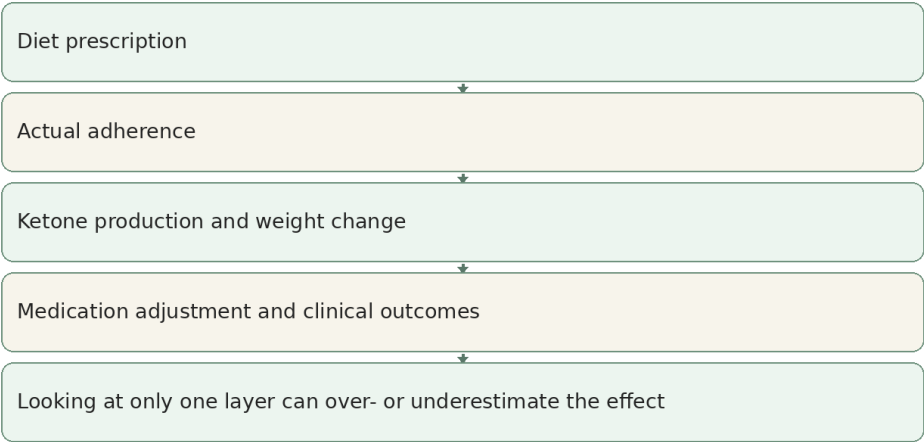
In Athinarayanan et al. (2019), 194 of the original 262 intervention participants remained in the program at two years. HbA1c declined from 7.7% at baseline to 6.7% at two years and mean weight fell by about 10%. Insulin use remained substantially reduced and sulfonylureas remained discontinued.[9-15]

Using the study's own definitions, “diabetes reversal” was reported in 53.5% and remission in 17.6%. These definitions are

not identical to the current international consensus definition of remission, and many participants continued metformin. “Reversal” and “remission” therefore should not be used interchangeably.^[9-15]

Two-year follow-up is more informative than a short trial, but nonrandom allocation, self-selection of motivated participants, and conflicts related to the program provider must be considered. This evidence is important for long-term implementation but should not receive the same causal weight as a randomized trial.^[9-15]

Figure 09-2. Four layers for reading the clinical evidence on ketogenic diets



Source: Tay et al. (2015, 2018); Hallberg et al. (2018); Athinarayanan et al. (2019); author synthesis.

Diet prescription -> actual adherence -> ketone production and weight change -> medication adjustment and clinical outcomes.

Looking at only one layer can overestimate or underestimate the intervention.

11. Medication reduction is a major clinical outcome

HbA1c alone can hide clinically important change. Two diet groups may have similar HbA1c, yet one may achieve it with substantially less insulin or fewer sulfonylureas. Both the Tay randomized trials and the Hallberg nonrandomized program identified medication reduction as an important outcome of carbohydrate restriction.[9-8][9-14]

But planned medication de-intensification must be distinguished from unsupervised discontinuation. Glucose can fall quickly when carbohydrate is sharply reduced, so insulin and sulfonylurea doses may need prompt adjustment. The more potent the dietary intervention, the more important structured medical monitoring becomes.[9-16]

12. Define remission before reporting it

The international consensus generally defines type 2 diabetes remission as HbA1c <6.5% persisting for at least three months without usual glucose-lowering pharmacotherapy. A person with HbA1c <6.5% while still taking glucose-lowering medication should therefore not be classified the same way as a person maintaining the same glycemia without those drugs.[9-17]

This distinction substantially changed the remission estimate in the Goldenberg meta-analysis. When remission was defined mainly by HbA1c, six-month remission appeared much more frequent with low-carbohydrate diets. When medication withdrawal was required, the effect was smaller and less certain. Throughout this book, remission results are therefore interpreted together with their definition and medication status.[9-10][9-17]

13. Adherence is part of the long-term effect, not a side issue

Very-low-carbohydrate diets are potent interventions, but some people find them difficult to sustain. In Goldenberg et al., very-low-carbohydrate diets sometimes appeared to produce less weight loss than less-restrictive low-carbohydrate diets; the difference disappeared in studies with better adherence. Physiologic efficacy and the ability to maintain the diet cannot be separated in real-world treatment.[9-10]

Completion declined in the Tay two-year trial, and in nutritional-ketosis care models only some participants maintained high BHB consistently at later follow-up. Long-term strategies should therefore be evaluated not only by short-term HbA1c, but by sustainability, food quality, social context, and cost.[9-9][9-15]

14. Fat quality matters as well as fat quantity

Ketogenic diets are often described simply as high-fat diets, but clinical trials use very different fat compositions. Tay's intervention was high in total fat but limited saturated fat to <10% of energy and emphasized unsaturated fat. Its results should not be generalized automatically to butter- or processed-meat-heavy ketogenic diets.[9-8]

This is directly relevant to a plant-based ketogenic model. Carbohydrate restriction can be combined with nuts, seeds, olive, avocado, and other unsaturated plant fats. That allows carbohydrate reduction and improved fat quality to be designed together. Direct clinical trials of this exact combination, however, remain limited.[9-18]

15. SGLT2 inhibitors require special safety attention

Nutritional ketosis and diabetic ketoacidosis (DKA) are not the same state. However, in people taking SGLT2 inhibitors, ketoacidosis can occur even when glucose is not markedly elevated, and very-low-carbohydrate intake, prolonged fasting, dehydration, or insulin deficiency can increase risk. ADA 2026 recommends DKA-risk education and ketone-monitoring tools for people at risk who use SGLT inhibition, and discourages a ketogenic eating pattern in this setting.[9-19]

Medication safety therefore belongs inside any discussion of ketogenic effectiveness. Before substantial carbohydrate restriction, current medications, kidney function, insulin reserve when clinically relevant, and any history of DKA should be reviewed. People taking SGLT2 inhibitors should discuss the dietary plan with the prescribing clinician before attempting a ketogenic pattern.[9-19]

16. What did the project's evidence database show?

After strict reclassification, the project database retained 592 ketogenic clinical-evidence candidates, including 361 in the internal priority Tier A. When the top 300 records were rechecked against XML full text, 88 were classified as actual ketogenic interventions. This does not mean 88 independent randomized trials: multiple publications, secondary analyses, and follow-up papers may arise from the same cohort.[9-20]

This is why article counts are not treated as effect sizes. Study design is classified first, overlapping cohorts are not silently double-counted, and generic low-carbohydrate studies are distinguished from ketogenic interventions and from studies that actually measured ketones.[9-20]

Table 9-4. What the current evidence supports - and what remains difficult to claim

Question	Direction supported by current evidence	Limitation
Can short-term glycemia improve?	Yes, repeatedly, especially at 3-6 months	Low-carb and ketogenic studies are mixed together in parts of the literature
Is HbA1c always better than with other high-quality diets?	No	1-2 year RCTs/meta-analyses show inconsistent superiority
Can medication needs fall?	Likely, in many patients	Medication protocols and study designs differ greatly
Are triglycerides and HDL often favorable?	Relatively consistent direction	LDL-C/ApoB response varies by person and diet composition
Can remission occur?	Observed in some studies	Definition, medication status, and duration must be specified
Is it sustainable for everyone long term?	Not established	Adherence and RCTs beyond two years are limited
Is plant-based ketogenic superior?	Not established	Direct independent RCT evidence is still sparse

17. Ketogenic evidence cannot be reduced to “works” or “does not work”

Current evidence shows that ketogenic and very-low-carbohydrate diets can improve glucose, weight, triglycerides, and medication requirements in type 2 diabetes, particularly in shorter studies and programs that actively manage medications. Yet in well-designed comparisons with strong alternative diets over one to two years, HbA1c superiority may shrink or disappear.[9-10][9-11][9-12]

The most accurate conclusion is therefore conditional: a ketogenic diet can be a powerful option in type 2 diabetes management, but

the magnitude of benefit depends on adherence, weight loss, medication adjustment, quality of the comparator diet, fat quality, diabetes duration, and insulin use. Long-term safety and sustainability still require stronger evidence.[9-2][9-10][9-19]

The next chapter moves from whole-trial summaries to specific clinical outcomes: HbA1c, fasting and postprandial glucose, glycemic variability, insulin, medication reduction, weight, and remission.

Key points from Chapter 9

Ketogenic diets can produce substantial short-term improvements in glycemia and medication requirements, but evidence is insufficient to claim that they are always superior to other high-quality dietary approaches in the long term. Correct interpretation requires separating low-carbohydrate from ketogenic interventions and considering weight loss, medication management, adherence, and fat quality.[9-10][9-11][9-12]

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Chapter 10. Ketogenic Diets, Glucose, and Insulin

HbA1c is usually the first number examined when judging the clinical effect of a ketogenic diet. But HbA1c alone cannot describe post-meal peaks, daily glucose swings, insulin requirements, or medication reduction. Two people can have the same HbA1c while one maintains relatively stable glucose and the other alternates between hyperglycemia and hypoglycemia.^[10-1]

This chapter therefore separates averages from variability. HbA1c and fasting glucose describe longer-term direction; continuous glucose monitoring (CGM) reveals patterns within the day. Fasting insulin, HOMA-IR, insulin dose, medication changes, and weight must then be placed alongside those measurements to understand what carbohydrate restriction actually means in metabolic management.^[10-2]

1. HbA1c is important, but it is not “all of glucose”

HbA1c estimates average glycemic exposure over roughly the preceding two to three months through the proportion of hemoglobin that has become glycated. It is central to diagnosis and treatment evaluation, and a general goal below 7% is used for many nonpregnant adults. Conditions that alter red-cell lifespan or hemoglobin biology, including some forms of anemia, can weaken the relation between HbA1c and actual glucose.^[10-3]

HbA1c is also the most frequently reported outcome in ketogenic-diet research. Yet identical HbA1c does not imply identical glucose profiles. The height and duration of postprandial hyperglycemia, frequency of hypoglycemia, and magnitude of daily excursions may be hidden behind the average.^[10-1]

Table 10-1. What each glucose and insulin measure answers

Measure	What it mainly reflects	Strength	Caution in interpretation
HbA1c	Average glycemic exposure over ~2-3 months	Standardized; linked with complication risk	Does not directly show variability or hypoglycemia
Fasting glucose	Overnight hepatic glucose output and basal state	Easy to repeat	Can miss post-meal abnormalities
Postprandial glucose	Handling of a meal-related glucose load	Directly reflects meal response	Sensitive to meal size, timing, drugs, and insulin
CGM / TIR	Time-resolved glucose pattern across the day	Shows average and variability together	Requires adequate wear time and data quality

Measure	What it mainly reflects	Strength	Caution in interpretation
Fasting insulin	Basal insulin secretion	Provides one view of metabolic state	Affected by exogenous insulin and beta-cell function
HOMA-IR	Insulin resistance estimated from fasting glucose and insulin	Useful for research comparison	Not a direct clamp measurement; limited in advanced diabetes
Insulin dose	Exogenous insulin needed for treatment	Strong clinical relevance	Depends on titration protocol and clinician decisions

2. HbA1c may fall more rapidly in the short term

In Goldenberg et al.'s meta-analysis of low- and very-low-carbohydrate diets, six-month HbA1c was 0.47 percentage points lower on average than with comparator diets. The direction was relatively clear and certainty was rated favorably. At 12 months, however, the between-group difference had narrowed to about 0.23 percentage points, with the upper confidence boundary reaching zero.[10-4]

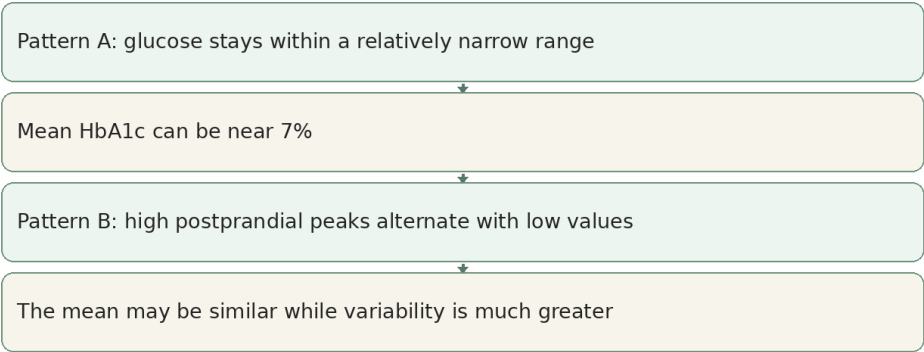
These findings say two things at once. Carbohydrate restriction can be a powerful short-term tool for lowering glucose, yet the difference from comparison diets may diminish over time. In longer studies, weight change, adherence, medication adjustment, and actual achieved carbohydrate intake can matter more than the original prescription.[10-4]

3. Higher baseline HbA1c creates more room to fall

Treatment effects depend on the starting point. In a 24-week Tay randomized trial, fasting glucose fell on both diets, but among participants with baseline HbA1c above 7.8%, HbA1c reduction was larger in the very-low-carbohydrate group. Mixing participants with low and high starting values can therefore change the average effect estimate.[10-5]

A reduction from 9% to 7% is not directly comparable with a reduction from 7.1% to 6.8%. Baseline HbA1c and medication exposure should always be examined together when interpreting reported changes.[10-6]

Figure 10-1. Different daily glucose patterns can exist within the same HbA1c



Source: ADA Standards of Care in Diabetes-2026, principles for interpreting A1C and CGM; author synthesis.

Pattern A: glucose remains within a relatively narrow band -> average HbA1c near 7%.

Pattern B: large post-meal peaks alternate with low glucose -> similar mean glucose but substantially greater variability.

Source: constructed from ADA 2026 principles for interpreting A1C and CGM.

4. Fasting glucose may not move at the same speed as HbA1c

Fasting glucose is strongly influenced by overnight hepatic glucose output and basal insulin action, whereas HbA1c integrates glucose exposure across the whole day. Large improvements in postprandial glucose may therefore occur with only modest fasting-glucose change, and the reverse can also occur.^[10-7]

In Tay's 52-week trial, both the low- and high-carbohydrate groups reduced HbA1c by about one percentage point. Fasting glucose also fell in both groups, without clear between-group superiority. The study does not support the claim that lowering carbohydrate necessarily produces a larger fasting-glucose reduction than a well-designed comparison diet.^[10-8]

5. Carbohydrate quantity is more directly visible in postprandial glucose

Postprandial glucose responds strongly to the amount and absorption rate of digestible carbohydrate in a meal. When carbohydrate intake is markedly reduced, the incoming post-meal glucose load is smaller and glucose peaks are likely to fall. Protein and fat, gastric emptying, exercise, medications, and timing of insulin also shape the curve.^[10-9]

ADA 2026 lists general targets for many nonpregnant adults of 80-130 mg/dL premeal glucose and peak postprandial glucose <180 mg/dL. These are not rigid targets for every person and should be individualized according to hypoglycemia risk, comorbidities, and treatment context. A lower postprandial value is not a success if it is achieved by causing more hypoglycemia.^[10-10]

6. CGM shows glucose variability that averages can miss

CGM places glucose on a continuous time axis. In addition to mean glucose, it quantifies time in range (TIR), time above range (TAR), time below range (TBR), and coefficient of variation (CV). ADA 2026 uses, for many adults, a TIR of 70-180 mg/dL above 70% and a CV ≤36% as useful clinical goals.^[10-11]

These measures are particularly helpful in carbohydrate-restriction research. Two interventions can produce similar HbA1c but different post-meal peaks and daily variability. Conversely, an improved average accompanied by more time in hypoglycemia should not be labeled an unqualified success.[10-11]

Table 10-2. Major ADA 2026 CGM metrics and general targets

Metric	Range/meaning	General target for many adults
TIR	Time 70-180 mg/dL	>70%
TAR level 1+2	Time >180 mg/dL	<25%
TAR level 2	Time >250 mg/dL	<5%
TBR level 1+2	Time <70 mg/dL	<4%
TBR level 2	Time <54 mg/dL	<1%
CV	Coefficient of variation	<=36%
Data quality	CGM wear for pattern assessment	About 14 days, >=70% active data

7. An important difference in the Tay trial was glucose variability

In the 52-week Tay RCT, average HbA1c reduction was almost identical in the two groups. However, CONGA-1, a CGM-derived measure of glucose variability, fell by about 0.5 mmol/L in the low-carbohydrate group and changed little in the high-carbohydrate group; the between-group difference was significant. The low-carbohydrate group also reduced its diabetes medication score more.[10-8]

Some of this pattern persisted at two years. Although fewer participants completed follow-up and HbA1c was not superior between groups, one-hour and four-hour CONGA fell more in the low-carbohydrate group and medication scores remained lower. This is a clear example of why average glycemia, variability, and treatment burden should be assessed together.[10-12]

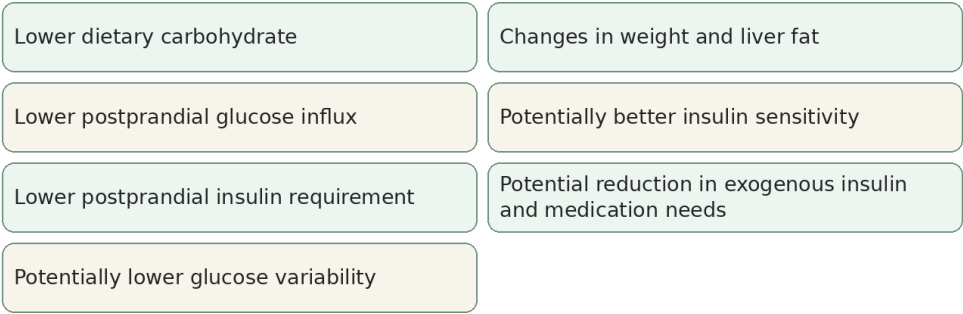
8. What do fasting insulin and HOMA-IR tell us?

As insulin resistance increases, more insulin may be required to maintain the same glucose concentration. Fasting insulin can partly reflect compensatory hyperinsulinemia, while HOMA-IR uses fasting glucose and insulin to estimate insulin resistance. Interpretation becomes more difficult in people receiving exogenous insulin or with substantial beta-cell failure.[10-13]

In Hallberg et al.'s one-year nonrandomized nutritional-ketosis intervention, fasting insulin and HOMA-IR improved alongside HbA1c and weight. Reductions in fasting glucose and fasting

insulin were maintained at two years. But this was a multicomponent care model incorporating remote monitoring, health coaching, and medication adjustment rather than a diet-only trial.^[10-14]

Figure 10-2. Clinical pathway from carbohydrate restriction to lower insulin requirements



Source: Tay et al. (2015, 2018); Hallberg et al. (2018); Athinarayanan et al. (2019); author synthesis.

Lower dietary carbohydrate -> less postprandial glucose influx -> lower prandial insulin requirement -> potentially less glucose variability -> changes in weight and liver fat -> potential improvement in insulin sensitivity -> possible reduction in exogenous insulin and medication requirements.

Each step varies by individual and study design.

9. Reduced insulin dose is a clinical outcome distinct from HbA1c

If HbA1c is unchanged while the insulin dose required to maintain it falls substantially, the clinical state is different. In Hallberg et al.'s one-year study, most participants who used insulin at baseline reduced or discontinued it, and sulfonylureas were discontinued in the intervention group. At two years, insulin use was reported to be 62% lower than baseline and sulfonylurea use 100% lower.[10-14][10-15]

These findings support the possibility that carbohydrate restriction can reduce treatment burden. They also show why medication adjustment must be incorporated into interpretation: maintaining HbA1c after reducing medications is not the same result as lowering HbA1c while keeping all medications unchanged.[10-16]

10. Older randomized trials also repeatedly showed medication-reduction signals

Westman et al.'s 24-week trial compared a ketogenic diet providing <20 g carbohydrate/day with a low-glycemic-index, calorie-restricted diet. Both groups improved HbA1c, fasting glucose, fasting insulin, and weight, but HbA1c and weight fell more in the ketogenic group. Diabetes medications were reduced or discontinued in 95.2% of the ketogenic group versus 62% of the comparator group.[10-17]

The direction is notable, but only about 58% of participants completed the study and volunteers were highly motivated. The medication-reduction percentages should not simply be applied to every person in routine practice. Strong lifestyle trials are particularly vulnerable to selection and adherence effects.[10-17]

Table 10-3. Glucose and medication changes in representative studies

Study	Design/duration	HbA1c	Variability/insul in	Medication change
Westman et al., 2008	24-week RCT	LCKD -1.5% vs LGI -0.5%	Fasting glucose/insulin improved in both	Reduced/stopped 95.2% vs 62%

Study	Design/duration	HbA1c	Variability/insulin	Medication change
Tay et al., 2015	52-week RCT	About -1.0% in both	Larger CONGA-1 reduction with LC	Larger medication-score reduction with LC
Tay et al., 2018	2-year RCT	No between-group difference	Some variability metrics favored LC	Medication-score advantage persisted
Hallberg et al., 2018	1-year nonrandomized	7.6% -> 6.3%	Fasting insulin and HOMA-IR improved	Insulin and sulfonylureas markedly reduced
Athinarayanan et al., 2019	2-year nonrandomized	7.7% -> 6.7%	Fasting glucose/insulin reductions persisted	Non-metformin drugs and insulin markedly reduced

11. Weight loss is an important mediator of glycemic improvement

When weight falls during carbohydrate restriction, insulin resistance, hepatic glucose production, and glycemia can improve together. HbA1c reduction therefore should not be attributed entirely to a direct effect of ketone bodies. In many trials, the contributions of lower energy intake and weight loss cannot be separated cleanly from diet composition.[10-18]

The Tay trial illustrates this. At 52 weeks both groups lost approximately 10 kg and reduced HbA1c by about one percentage point. Despite large differences in macronutrient composition, similar weight loss may have contributed to the small between-group difference in average HbA1c.[10-8]

12. “Remission” without considering medication can be misleading

When remission is discussed, glucose and medication status should be reported together. The international consensus generally defines type 2 diabetes remission as HbA1c <6.5% for at least three months without usual glucose-lowering pharmacotherapy. HbA1c below 6.5% while continuing glucose-lowering drugs represents excellent control, but not the same medication-independent remission state.[10-19]

This distinction was striking in the Goldenberg meta-analysis. Using HbA1c <6.5% without a medication requirement, there were roughly 32 additional remissions per 100 people at six months in low-carbohydrate groups. When medication discontinuation was required, the difference fell to about five per 100 and became statistically uncertain. The remission definition must therefore be checked before the headline number.[10-4]

13. HbA1c improvement plus medication reduction is a stronger combined signal

Clinically, combinations of outcomes matter more than one isolated metric. If HbA1c falls, glucose variability decreases, insulin or sulfonylurea requirements fall, and weight and triglycerides improve together, the evidence for meaningful metabolic improvement is more coherent. A lower HbA1c accompanied by more hypoglycemia or greater medication burden cannot be evaluated in the same way.^[10-20]

For this reason, later chapters evaluate dietary interventions in a multidimensional context: mean glycemia, variability, medications, weight, insulin exposure, and safety are considered on the same line rather than treating the diet as a competition for a single number.^[10-20]

14. Prevent hypoglycemia first in people using insulin or sulfonylureas

When dietary carbohydrate is rapidly reduced, prandial insulin needs can change rapidly as well. If insulin or insulin secretagogues such as sulfonylureas are left unchanged, clinically significant hypoglycemia may occur. ADA 2026 recommends reassessing the need and dose of medications with substantial hypoglycemia risk when treatment changes.^[10-21]

Hypoglycemia is not merely an inconvenience. Glucose <70 mg/dL is clinically important; <54 mg/dL represents more severe biochemical hypoglycemia. The stronger the dietary intervention, the more important proactive medication review and self-monitoring or CGM become.^[10-22]

15. With SGLT2 inhibitors, DKA may occur without marked hyperglycemia

Very-low-carbohydrate eating and prolonged fasting can contribute to ketoacidosis risk in people taking SGLT2 inhibitors. SGLT2-associated DKA can occur with plasma glucose below 200 mg/dL, so a near-normal glucose value does not exclude the diagnosis. ADA 2026 recommends DKA-risk education and ketone-monitoring tools for at-risk SGLT inhibitor users and discourages ketogenic eating patterns in this setting.^[10-23]

Medication review must therefore precede practical use of a ketogenic plan. SGLT2 inhibitors, insulin, and sulfonylureas each create safety issues that interact directly with dietary change. Preventing hypoglycemia and ketoacidosis takes priority over maximizing the metabolic intensity of the diet.^[10-23]

16. Higher ketones do not necessarily mean better glucose control

Measuring BHB can help confirm whether nutritional ketosis is actually occurring, but a simple dose-response relation in which higher BHB always produces a larger HbA1c reduction has not been established. Glycemic improvement can reflect the combined effects of carbohydrate restriction, energy intake, weight change, exercise, and medication adjustment.[10-24]

This distinction becomes more important in the next chapter. BHB is both a fuel and a signaling molecule, but a plausible mechanism is not the same as proof of a large clinical effect. Mechanistic plausibility should support, not replace, clinical outcome evidence.[10-24]

17. In our database, locating an HbA1c number was separated from deciding what it meant

The project rechecked the top 300 evidence records against full text. HbA1c language was found in 286 papers and numeric candidates in 163; 137 numeric values were supported at a specific source location. Of these, 83 were in tables, 52 in results text, and two in abstracts.[10-25]

But the existence of a number is not the same as evidence of a treatment effect. It still must be classified as baseline, final value, within-group change, between-group difference, or pooled meta-analytic effect. Final clinical tables therefore prioritize values whose source location and effect type can both be established.[10-25]

Table 10-4. Sequence for interpreting glucose studies of ketogenic diets

Step	Question	Why it matters
1	Is the intervention low-carbohydrate or truly ketogenic?	Different diet definitions should not be merged silently
2	What were baseline HbA1c and medication status?	Starting point and medication exposure influence the magnitude of change
3	Is the number a within-group change or between-group effect?	Separates improvement from additional comparative benefit
4	What happened to CGM and fasting glucose?	Assesses averages and variability together
5	Were insulin and medications reduced?	Treatment burden may change even when HbA1c is similar
6	How much did weight change?	Weight loss can mediate glycemic improvement

Step	Question	Why it matters
7	What happened to hypoglycemia and DKA risk?	Safety precedes efficacy
8	Was adherence maintained long term?	Distinguishes short-term efficacy from sustainability

18. Conclusion: reduce metabolic burden, not just average glucose

Current evidence supports meaningful short-term improvements in HbA1c and glucose with carbohydrate restriction. Some studies also show reductions in glucose variability, medication burden, and insulin dose. Yet additional HbA1c superiority often becomes smaller in longer randomized trials, and the large effects observed in nonrandomized nutritional-ketosis programs should be interpreted in the context of multicomponent care.^[10-26]

Success should therefore not be defined by one number. HbA1c, variability, medication burden, hypoglycemia, and sustainability belong in the same assessment. The next chapter examines ketone bodies themselves as fuels and signaling molecules.^[10-27]

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Chapter 11. Ketone Bodies Are More Than Fuel

Ketone bodies have long been described as “emergency fuel” used when glucose is scarce. That description is not wrong, but it is incomplete. Beta-hydroxybutyrate (BHB) is oxidized in mitochondria to support ATP production, yet it is also studied as a signaling metabolite that can influence cell-surface receptors, inflammatory pathways, chromatin, and protein modification.^[11-1]

One principle is essential: evidence that BHB changes a signaling pathway in cells or animals is not the same as evidence that a ketogenic diet treats diabetes better in humans. Mechanisms can explain a clinical effect, but they do not substitute for clinical proof of superiority.^[11-2]

1. The three ketone bodies do not play identical roles

The main ketone bodies produced by the liver are acetoacetate (AcAc), beta-hydroxybutyrate (BHB), and acetone. BHB is the ketone most commonly measured in blood. Both AcAc and BHB can be used as energy substrates by extrahepatic tissues, whereas acetone is largely excreted in breath and urine and contributes relatively little to energy metabolism.^[11-3]

BHB and AcAc interconvert, but they are not identical molecules. Oxidation of BHB to AcAc interacts with the NADH/NAD⁺ redox couple, and BHB and AcAc can differ in signaling effects. It is therefore more precise to identify the specific ketone being discussed than to treat “ketone bodies” as one interchangeable entity.^[11-1]

Table 11-1. Metabolic and signaling characteristics of the three ketone bodies

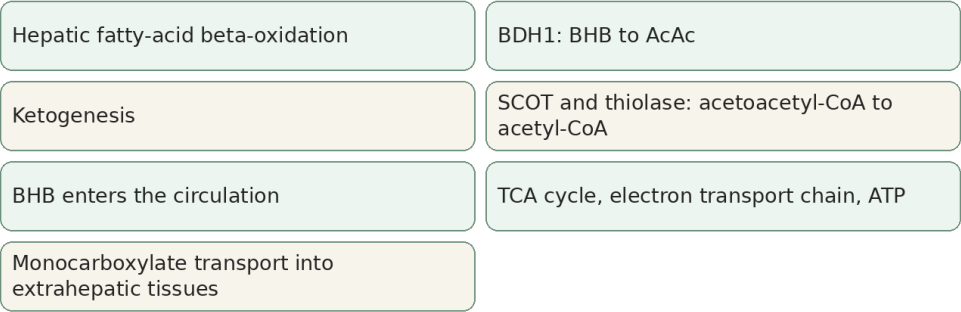
Ketone body	Main feature	Energy use	Caution when interpreting signaling
Beta-hydroxybutyrate (BHB)	Most commonly measured in blood	Oxidized to AcAc before entering mitochondrial oxidation	HCAR2, NLRP3, chromatin and other pathways are studied, but should not be equated with human clinical benefit
Acetoacetate (AcAc)	Primary hepatic ketogenesis product	Converted through SCOT to acetyl-CoA	Some signaling actions may differ from BHB
Acetone	Spontaneous decarboxylation product of AcAc	Minor energy contribution	Breath acetone can track ketosis but is not identical to blood BHB

2. BHB becomes acetyl-CoA again inside mitochondria

BHB produced by the liver travels through the circulation to extrahepatic tissues such as skeletal muscle, heart, and brain. After entering cells, mitochondrial BDH1 oxidizes BHB to AcAc. SCOT then converts AcAc to acetoacetyl-CoA, and thiolase splits it into two acetyl-CoA molecules, which enter the TCA cycle and electron transport chain to support ATP production.[11-4]

The liver produces ketone bodies but does not use them as a major fuel because it lacks functionally significant SCOT activity. This division between production and consumption allows the fasting liver to package energy derived from fatty acids into a water-soluble form that can be exported to other organs.[11-1]

Figure 11-1. How beta-hydroxybutyrate becomes a fuel



Source: Puchalska & Crawford (2017); Murashige et al. (2023); author synthesis.

Hepatic fatty-acid beta-oxidation -> ketogenesis -> BHB enters blood -> uptake into extrahepatic tissues through monocarboxylate transporters -> BDH1 converts BHB to AcAc -> SCOT -> acetoacetyl-CoA -> thiolase -> acetyl-CoA -> TCA cycle -> electron transport chain -> ATP.

Source: constructed from Puchalska & Crawford (2017) and Murashige et al. (2023).

3. Do ketones always produce more ATP per unit of oxygen?

The “thrifty substrate” hypothesis proposes that ketone oxidation can sometimes produce ATP more efficiently relative to oxygen consumption than fatty-acid oxidation. This concept has been discussed for years in cardiac metabolism, and biochemical calculations and heart-failure studies have suggested potential improvements in oxygen efficiency when the heart shifts toward ketone oxidation.^[11-5]

The claim should not be generalized to every setting. In isolated mouse hearts supplied with high BHB, ketone oxidation rose markedly but cardiac work did not rise in parallel, while oxygen consumption increased; efficiency therefore worsened rather than improved. “Ketones are always the most efficient fuel” is stronger than the evidence permits.^[11-6]

4. Fuel value and signaling value should be separated

It is not unusual for the same molecule to serve both as a fuel and as a signal. Glucose and fatty-acid metabolites also influence gene expression and enzyme activity. BHB can similarly be viewed as a metabolic signal that communicates aspects of energy and nutrient status.^[11-7]

Concentration and duration matter. Low BHB during an overnight fast, nutritional ketosis during prolonged fasting or a ketogenic diet, and abrupt hyperketonemia after a ketone-ester drink are not the same physiological state. Even at the same measured BHB concentration, effects can differ according to tissue and duration of exposure.^[11-1]

5. HCAR2 is a cell-surface receptor that can sense BHB

BHB can bind hydroxycarboxylic acid receptor 2 (HCAR2, formerly GPR109A). HCAR2 is expressed in adipocytes, immune cells, and other tissues and can signal through Gi/o proteins and beta-arrestin pathways. Niacin is another well-known agonist of this receptor.^[11-8]

HCAR2 activation can influence adipose lipolysis and immune responses, which has led to the idea that BHB participates in feedback regulation. But receptor binding alone cannot predict long-term diabetes outcomes because HCAR2 signaling may have different consequences across tissues and conditions.[11-9]

6. BHB and the NLRP3 inflammasome

A highly influential 2015 study by Youm and colleagues reported that BHB inhibited activation of the NLRP3 inflammasome. BHB reduced NLRP3 activation and IL-1beta release triggered by urate crystals, ATP, and lipotoxic stimuli, although it did not suppress every type of inflammasome.[11-10]

NLRP3 is one of several pathways implicated in chronic low-grade inflammation in obesity and type 2 diabetes. The BHB-NLRP3 connection therefore provides an important mechanistic hypothesis. Yet the foundational evidence was largely cellular and animal based, and a clinical causal chain in which ketogenic diets reduce human diabetes complications specifically through NLRP3 inhibition has not been established.[11-10]

7. The mechanism of NLRP3 inhibition is more complicated than initially thought

Subsequent work suggests that BHB-related NLRP3 inhibition can depend on experimental conditions. A 2025 study linked part of the inhibitory effect of BHB and related short-chain carboxylic acids to acidification of the culture environment and suggested a contribution from FFAR3 signaling. This makes the original single-pathway explanation more complex.[11-11]

This is a useful example of how science corrects itself. An important early finding does not guarantee that every later experiment will reproduce the same mechanism in the same way. This book therefore describes NLRP3 inhibition as a possible anti-inflammatory mechanism, not as an established human therapeutic mechanism.[11-11]

Table 11-2. Major proposed BHB signaling pathways and current evidence level

Pathway	Proposed action	Core evidence	Clinical interpretation
HCAR2	GPCR signaling; regulation of lipolysis and immunity	Receptor, cell, and animal studies	Long-term human clinical effect requires separate testing
NLRP3	Reduced inflammasome activation and IL-1beta	Mainly cell and animal studies	Anti-inflammatory potential; limited direct linkage to diabetes outcomes
HDAC	Possible inhibition of some class I HDACs	Shimazu 2013 and later studies	Reproducibility and concentration/cell-type questions remain

Pathway	Proposed action	Core evidence	Clinical interpretation
Kbhb	Increased lysine beta-hydroxybutyrylation	Chromatin work in cells and mouse liver	Physiologic and human disease meaning still under study
Energy/redox	Effects on NAD+/NADH, TCA, ETC	Biochemistry and organ studies	Outcome varies by tissue and substrate environment

8. Can BHB inhibit HDACs and alter gene expression?

Shimazu et al. (2013) reported that BHB inhibited class I histone deacetylases (HDACs), increased histone acetylation, and increased expression of oxidative-stress defense genes such as FOXO3A and MT2 in mouse tissues. The study helped popularize the idea that BHB can act at the chromatin level rather than only as fuel.[11-12]

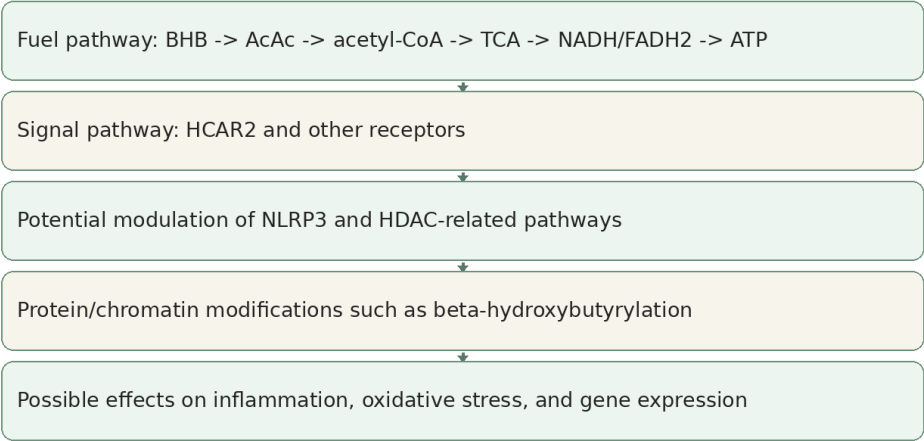
Later studies did not always reproduce the same magnitude of HDAC inhibition. Chriett and colleagues found that compared with butyrate, BHB had much weaker or unclear HDAC and transcriptional effects in some cell systems. It is therefore inappropriate to generalize BHB as a “potent natural HDAC inhibitor.”[11-13]

9. Beta-hydroxybutyrylation is another layer of chromatin regulation

Separate from HDAC inhibition, BHB is associated with addition of beta-hydroxybutyryl groups to lysine residues in proteins. Xie et al. reported that histone lysine beta-hydroxybutyrylation (Kbhb) rose substantially in mouse liver during prolonged fasting, with H3K9bhb linked to fasting-responsive genes.[11-14]

The finding demonstrates that nutrient state can be connected directly to chromatin marks. But an increase in a histone mark does not itself prove a health benefit. Which genes are changed, in what direction, and with what net effect on human metabolic disease remain active research questions.[11-14]

Figure 11-2. Two roles of BHB: fuel and signaling molecule



Source: Newman & Verdin (2014); Puchalska & Crawford (2017); Youm et al. (2015); Xie et al. (2016); author synthesis.

Fuel pathway: BHB → AcAc → acetyl-CoA → TCA cycle → NADH/FADH₂ → electron transport chain → ATP.

Signaling pathways: BHB → HCAR2 and other receptors / NLRP3 modulation / HDAC-related effects / protein and chromatin modifications such as Kbbh → potential changes in inflammation, oxidative stress, and gene expression.

Source: Newman & Verdin (2014); Puchalska & Crawford (2017); Youm et al. (2015); Xie et al. (2016).

10. Reduced oxidative stress is plausible, but more human evidence is needed

Shimazu's study reported increased FOXO3A and metallothionein 2 expression and greater resistance to oxidative stress in mice exposed to BHB. Subsequent neural, cardiovascular, and endothelial models have also reported effects on reactive oxygen species and antioxidant pathways.^[11-12]

A reduction in cellular ROS, however, should not be converted directly into the claim that “a ketogenic diet is an antioxidant diet.” Human oxidative stress is influenced by glucose, fatty acids, exercise, weight loss, micronutrients, inflammation, and medication. Long-term trials that isolate the independent contribution of BHB within an entire dietary intervention are limited.^[11-15]

11. The brain increases ketone use during prolonged fasting

The brain normally uses large amounts of glucose but can markedly increase utilization of BHB and AcAc during prolonged fasting. Ketone bodies cross the blood-brain barrier via monocarboxylate transporters and are oxidized in mitochondria of neurons and glial cells. This adaptation helps reduce glucose requirements and protein breakdown during extended fasting.^[11-16]

The phrase “the brain prefers ketones” is too simple. Even while using ketones, the brain does not abandon glucose completely; glucose remains necessary for selected biosynthetic pathways and cellular functions. The key concept is metabolic flexibility, not the absolute superiority of one fuel.^[11-16]

12. Can ketones reduce appetite?

It has long been observed that hunger does not always rise as much as expected during weight loss on ketogenic diets. In a small crossover study by Stubbs et al., a ketone-ester drink raised BHB to about 3.3 mmol/L in healthy adults and lowered ghrelin and subjective hunger compared with dextrose.^[11-17]

Human data are not fully consistent. Higher BHB has been associated with lower ghrelin in some obesity studies, yet a 2023 randomized crossover study in 18 people with prediabetes found that acute ketosis did not significantly alter ghrelin, PYY, or subjective hunger. Appetite effects may depend on metabolic state, comparator, ketone concentration, and context.[11-18]

13. Appetite suppression is not the same as long-term weight loss

Even if appetite falls temporarily, that does not guarantee sustained lower energy intake or greater long-term weight loss. In the CARBFUNC study, a low-carbohydrate/high-fat diet increased BHB and partly blunted the rise in ghrelin at three months, but subjective hunger did not differ clearly between diet groups, and 12-month weight loss was similar across the three diets.[11-19]

Ketone bodies may therefore participate in appetite regulation, but “higher ketones automatically make people eat less” is not established. Protein, fiber, energy density, palatability, sleep, and stress all substantially influence actual intake.[11-19]

14. Exogenous ketones are an experimental tool, not the same as a ketogenic diet

Ketone esters and salts can raise blood BHB rapidly without large carbohydrate restriction. This allows researchers to isolate some acute effects of BHB from dietary change. However, acute hyperketonemia from an exogenous ketone does not reproduce the hormonal, fatty-acid, and energy-metabolism environment of dietary ketosis.[11-20]

A fall in glucose during a ketone-ester experiment therefore does not automatically prove the long-term effect of a ketogenic diet. Conversely, a null effect of a ketone ester does not invalidate a ketogenic dietary pattern. The two experiments answer different questions.[11-20]

15. What have exogenous BHB studies shown in people with type 2 diabetes?

Recent trials are intriguing but not uniform. In a 2024 double-blind crossover study of 10 adults with type 2 diabetes, a premeal ketone monoester reduced postprandial glucose and altered endogenous glucose production and appearance.[11-21]

In other randomized crossover work, acute ketone ester did not lower fasting glucose and 14 days of three-times-daily supplementation did not improve short-term glycemic control measured by fructosamine. A 2025 crossover study reported that premeal ketone monoester and ketone salt lowered mixed-meal glucose iAUC by 36% and 22%, respectively.[11-22]

These differences show that BHB effects can depend on timing and co-ingested nutrients. Fasting glucose, postprandial glucose, and long-term HbA1c are distinct outcomes. Acute studies should not be used to exaggerate long-term diabetes-treatment claims.[11-22]

Table 11-3. How to distinguish exogenous-ketone research from ketogenic-diet research

Question	Exogenous ketone study	Ketogenic diet study
How is BHB raised?	Ketone ester or salt ingested directly	Endogenous ketogenesis after carbohydrate restriction and fatty-acid oxidation
Typical time scale	Hours to weeks	Weeks to years
Fatty-acid/insulin environment	Acute BHB rise can alter NEFA and insulin	Weight, diet composition and hormonal adaptation change together
Best questions	Acute BHB effects on glucose, appetite, hemodynamics	Sustainability, HbA1c, weight, medications of a dietary pattern
Main limitation for comparison	Physiology differs from dietary ketosis	Many factors besides BHB change simultaneously

16. A high BHB concentration is not inherently “good”

BHB must be interpreted in context. Mild elevation during nutritional ketosis, transient elevation after an exogenous ketone, and pathologic elevation during insulin-deficient DKA have very different meanings. DKA includes ketone overproduction together with metabolic acidosis, dehydration, and electrolyte disturbance and must be distinguished from nutritional ketosis.[11-23]

Nor is higher BHB in observational studies always a favorable metabolic marker. Reviews of obesity, diabetes, and heart disease note that elevated BHB may represent adaptive fuel switching in one setting and metabolic stress in another. A single concentration cannot classify ketones as “good” or “bad” without clinical context.[11-24]

17. What do BHB mechanisms add to the design of a plant-based ketogenic diet?

The goal is not to maximize BHB. A plant-based ketogenic diet aims to reduce postprandial glucose burden with appropriate carbohydrate restriction while supplying unsaturated fats, plant protein, fiber, and micronutrients. BHB is both a marker of fuel switching and a potential signaling metabolite within that broader nutritional state.[11-25]

This approach moves the diet away from a competition for the highest ketone number. Whether BHB is 0.8 or 2.0 mmol/L matters less than what happens to HbA1c, postprandial glucose,

medication needs, weight, lipids, muscle, and safety. Mechanisms supplement clinical outcomes; they do not replace them.[11-25]

Table 11-4. Five questions that prevent overinterpretation of BHB research

Step	Question	Why it matters
1	Is it a cell/animal study or a human study?	Separates mechanism from clinical evidence
2	Is ketosis endogenous or produced by exogenous ketones?	Physiological environments differ
3	What are the BHB concentration and exposure duration?	Acute high exposure may differ from chronic modest exposure
4	Did clinical outcomes such as glucose, weight, or medication use actually improve?	Molecular changes are not automatically treatment benefits
5	Are there contradictory or replication findings?	HDAC, NLRP3, and cardiac-efficiency mechanisms remain debated

18. Conclusion: ketone bodies are both fuel and signal

Evidence clearly shows that BHB is more than an energy carrier. It is oxidized in mitochondria, can activate receptors, and can influence inflammasome biology and chromatin/protein modifications. Human studies also suggest potential effects on appetite and postprandial glucose.[11-1][11-21]

But signaling pathways do not automatically establish clinical superiority. Some HDAC effects have replication concerns, conditions for NLRP3 inhibition continue to be refined, and glycemic effects of exogenous ketones vary among studies. The most accurate view is that BHB is an important metabolic mediator, not a universal therapeutic molecule.[11-11][11-13][11-22]

The next chapter turns to safety: LDL-C, triglycerides, kidney function, uric acid, electrolytes, hypoglycemia, and DKA.

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Chapter 12. Controversies and Safety of Ketogenic Diets

The safety of ketogenic diets cannot be summarized in one sentence. Triglycerides and glucose may improve while LDL-C rises. Weight and medication requirements may fall while constipation or dehydration appears. In type 2 diabetes, interactions between the diet and medications can sometimes be more important than the diet itself as a source of risk.^[12-1]

The useful question is therefore not “Is a ketogenic diet safe?” but “For whom, with what composition, for how long, and with what monitoring?” This chapter examines benefits and risks together and develops safety principles for a plant-based ketogenic approach.^[12-2]

1. Safety is not determined by one laboratory value

Glucose alone is not enough. Lipids, blood pressure, kidney function, uric acid, electrolytes, gastrointestinal symptoms, body weight and muscle, and medication use should be considered together. One person may experience striking glycemic improvement but a large LDL-C rise; another may have little lipid change but troublesome gastrointestinal symptoms.^[12-3]

Short-term and long-term effects must also be separated. An 8-12 week response does not guarantee the same result after one or two years. Across low- and very-low-carbohydrate trials, advantages in HbA1c and weight are often clearer at six months and smaller after 12 months, partly because adherence declines.^[12-4]

Table 12-1. Domains that should be assessed together when evaluating ketogenic-diet safety

Domain	Potentially favorable change	Potential concern	Key interpretation
Glycemia	Lower HbA1c and postprandial glucose	Hypoglycemia	Risk depends strongly on medication use
Lipids	Lower TG, higher HDL-C	LDL-C and sometimes ApoB may rise	Consider fat quality and individual response
Kidney	Many short-term studies show little eGFR change	Dehydration, stones, pre-existing CKD	Do not generalize normal-kidney data to advanced CKD
Uric acid	RCT meta-analyses may show little average change	Early rise or gout concern in some people	Personal history and hydration matter

Domain	Potentially favorable change	Potential concern	Key interpretation
Electrolytes	May stabilize after adaptation	Early sodium/fluid loss	More important with diuretics or BP medication
Gastrointestinal	Appetite may fall	Constipation, nausea, abdominal symptoms	Fiber, fluid, and food composition matter
Sustainability	Some people maintain it long term	Attrition may rise with stricter diets	Measure actual intake and adherence

2. Lower triglycerides and higher HDL-C are relatively consistent findings

Among lipid changes, lower triglycerides and higher HDL-C are among the most reproducible. A 2024 meta-analysis of 29 very-low-carbohydrate ketogenic trials in type 2 diabetes reported an average triglyceride reduction of about 18 mg/dL and HDL-C increase of about 3.9 mg/dL.[12-5]

A 2026 meta-regression of 62 adult randomized trials likewise reported an average triglyceride reduction of about 20 mg/dL and HDL-C increase of about 3.6 mg/dL. These changes can be linked to lower hepatic VLDL production, weight loss, and improved insulin resistance. They do not, by themselves, prove that total cardiovascular risk has fallen.[12-6]

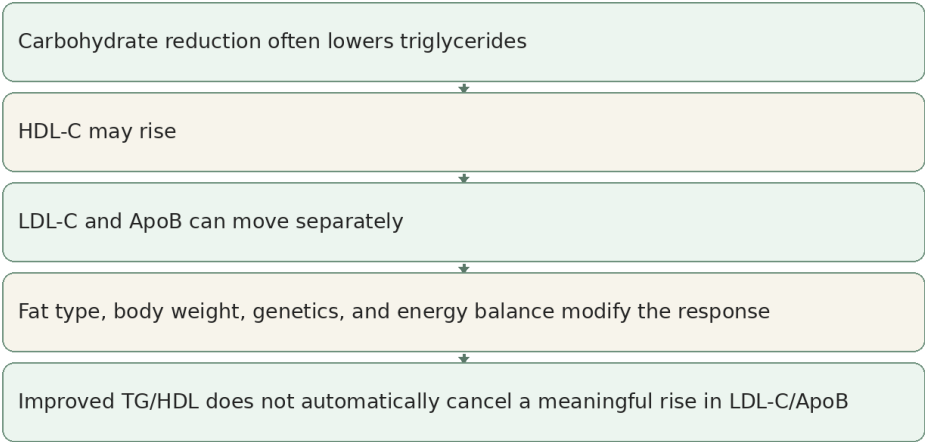
3. The central lipid controversy is LDL-C

Some meta-analyses limited to people with type 2 diabetes found no significant LDL-C difference from control diets, whereas broader recent randomized-trial meta-analyses in adults found an average LDL-C increase of roughly 8 mg/dL.[12-5][12-6]

Population and diet composition matter. In obesity and diabetes, weight loss and triglyceride improvement may blunt LDL-C changes, while studies in normal-weight adults have sometimes shown larger increases in LDL-C and ApoB. A 2023 meta-analysis in normal-weight adults estimated increases of about 1.08 mmol/L in LDL-C and 0.35 g/L in ApoB.[12-7]

Both “ketogenic diets do not raise LDL” and “ketogenic diets always raise LDL” are too absolute. The clinically useful question is how this person responds. LDL-C, non-HDL-C, and, when indicated, ApoB should be compared before and after the intervention.[12-8]

Figure 12-1. Lipid responses to ketogenic diets are not one-directional



Source: recent ketogenic-diet RCT meta-analyses and cardiovascular lipid guidance; author synthesis.

A frequently observed path is **lower carbohydrate -> lower triglycerides -> higher HDL-C**. At the same time, **fat type, weight change, genetic background, and energy balance -> LDL-C/ApoB response** can move independently.

Improvement in TG and HDL-C does not automatically offset a meaningful rise in LDL-C or ApoB. Conversely, an LDL-C rise does not erase genuine improvements in glycemia, weight, or triglycerides; all risks must be integrated.

4. Why consider ApoB separately?

LDL-C measures the cholesterol carried inside LDL particles. ApoB more directly reflects the number of circulating atherogenic ApoB-containing particles because each major atherogenic particle carries one ApoB molecule. In diabetes and hypertriglyceridemia, LDL-C and particle number can become discordant, making ApoB a useful additional marker.^[12-9]

The 2026 AHA/ACC dyslipidemia guidance notes that ApoB can help assess residual risk in selected people, including those with diabetes, elevated triglycerides, or low LDL-C. This is particularly relevant when ketogenic eating produces discordant changes in triglycerides and LDL-C.^[12-9]

5. Fat quality matters more than the phrase “high fat”

The safety of a ketogenic diet depends substantially on which fats supply its energy. ADA 2026 recommends limiting foods high in saturated fat and replacing them with unsaturated fats from sources such as plant oils, nuts, and seeds.^[12-10]

The two-year Tay RCT demonstrates this principle. The low-carbohydrate group consumed about 58% of energy from fat but kept saturated fat below 10% of energy and emphasized unsaturated fat. After two years, LDL-C did not differ significantly from the comparator, while triglycerides, HDL-C, glucose variability, and medication requirements favored the low-carbohydrate group.^[12-11]

A plant-based ketogenic diet can deliberately use this distinction. Olive oil, nuts, seeds, avocado, tofu, and soy foods can support a high-unsaturated-fat pattern. Coconut oil is plant-derived but rich in saturated fat and should not be treated as metabolically equivalent to unsaturated plant oils.^[12-10]

6. Can the kidneys tolerate carbohydrate restriction?

Among people with type 2 diabetes and normal or reasonably preserved kidney function, current evidence does not show a strong, consistent worsening of kidney filtration from low-carbohydrate diets. A meta-analysis of 12 controlled trials involving 942 participants found no significant differences in eGFR, creatinine clearance, albuminuria, or serum creatinine.[12-12]

The two-year Tay trial likewise found no significant difference between low-carbohydrate/high-unsaturated-fat and high-carbohydrate/low-fat diets in eGFR or albuminuria. These results should not be extrapolated automatically to advanced CKD because many trials exclude people with severe kidney impairment.[12-11]

When CKD is present, protein amount, potassium and phosphorus, antihypertensives and diuretics, and dehydration risk require individualized review. A more accurate statement is: in people with normal or stable kidney function, short- to medium-term trials have not consistently shown clinically important deterioration.[12-12]

7. Kidney stones are a separate issue

Stable eGFR does not mean stone risk is zero. A 2021 meta-analysis of ketogenic-diet studies estimated an overall kidney-stone incidence of 5.9% over a mean follow-up of about 3.7 years, with an estimated 7.9% in adults.[12-13]

Most included studies involved traditional therapeutic ketogenic diets for refractory epilepsy and are not identical to modern dietary interventions for type 2 diabetes. The absolute rates should therefore not be transferred directly to diabetes care. They do, however, justify attention to prior stones, hydration, uric acid, and urinary factors during long-term, very strict ketogenic therapy.[12-13]

8. Uric acid may differ between early adaptation and longer follow-up

A long-standing physiological explanation proposes that during early ketosis, ketone bodies and uric acid compete for renal excretion, temporarily increasing serum uric acid. Yet a 2023 meta-analysis of adult randomized trials found no significant overall increase in serum uric acid with ketogenic diets compared with controls.[12-14]

A 2026 cross-sectional NHANES analysis in U.S. adults with diabetes reported a higher prevalence of gout among people with

a higher “ketogenic diet ratio.” Cross-sectional evidence cannot establish whether the diet caused gout, whether gout influenced diet choice, or whether other factors explain the association. It is a caution signal, not causal proof.[12-15]

For people with gout or recurrent uric-acid stones, individual history matters more than the average trial result. Plant-based ketogenic diets differ in purine and saturated-fat exposure from meat-centered versions, but the effects of ketosis and dehydration still need monitoring.[12-14][12-15]

9. Why do some people feel dizzy or weak during initiation?

Headache, fatigue, dizziness, muscle cramps, and reduced concentration are commonly described during the first days of ketogenic eating - often called “keto flu,” although this is not a formal disease entity. A 2025 scoping review found that such symptoms are repeatedly reported across populations, but occurrence rates and mechanisms are heterogeneous.[12-16]

As insulin falls after carbohydrate restriction, renal sodium reabsorption may decrease and water excretion may rise. Lower food intake can also reduce sodium, potassium, and magnesium intake. High-quality trial evidence is insufficient to conclude that every person requires routine electrolyte supplementation.[12-16]

People taking antihypertensives or diuretics deserve particular attention because rapid changes in fluid volume and blood pressure can make an existing dose excessive. Medication review, rather than the diet alone, can become the core safety intervention.[12-1]

10. Constipation is among the most common adverse effects

A 2026 systematic analysis of ketogenic-diet adverse events reported at least one adverse event in 43% of participants across included studies, with gastrointestinal events most common; constipation was reported in about 24%. Stricter ketogenic protocols tended to show more frequent or severe events.[12-17]

The analysis combined epilepsy, neurologic disease, obesity, and different forms of ketogenic therapy, so the percentages cannot be interpreted as type 2 diabetes-specific incidence. Even so, fiber inadequacy is a practical concern in meat- and cheese-centered ketogenic diets that sharply restrict vegetables, seeds, and other fiber sources.[12-17]

A plant-based ketogenic diet can use nonstarchy vegetables, flax, chia, nuts, avocado, and selected portions of legumes to provide fiber while controlling digestible carbohydrate. This is a

sustainability issue as much as a glycemic issue.[12-10]

11. Micronutrient inadequacy increases when food choices become monotonous

If carbohydrate restriction also eliminates too many grains, fruits, and legumes, intakes of potassium, magnesium, calcium, and water-soluble vitamins may fall. In a 12-week ketogenic study, intakes of several minerals and water-soluble vitamins were below recommended levels even though most measured blood concentrations remained within normal ranges over the short term.[12-18]

Normal blood values do not prove that intake is adequate. The body can temporarily maintain circulating concentrations by changing stores and excretion. Long-term dietary assessment should therefore begin with food variety, rather than assuming that a normal laboratory result means nutrition is complete.[12-18]

Strict plant-based versions also require deliberate vitamin B12 planning, while iron, zinc, iodine, calcium, and omega-3 adequacy depend on food selection, as discussed in Chapter 8.[12-10]

12. Hypoglycemia is mainly a medication-interaction problem

A major reduction in carbohydrate can rapidly reduce postprandial glucose. If insulin or sulfonylureas are not adjusted, medication effect can exceed dietary glucose exposure and produce hypoglycemia.[12-1]

For medication-treated diabetes, a ketogenic plan is therefore not “just a diet.” Medication classes should be reviewed before initiation, glucose monitored more frequently, and doses adjusted by the clinical team when needed. Insulin should never be stopped impulsively.[12-1]

Medication reduction seen in trials can be a favorable outcome, but safe de-intensification requires a plan. A reduced medication burden is an endpoint, not an instruction for self-discontinuation.[12-11]

13. SGLT2 inhibitors and ketogenic eating require special caution

SGLT2 inhibitors provide important heart-failure and kidney benefits, but they also increase susceptibility to ketoacidosis in certain contexts. ADA 2026 recommends ketone-monitoring education and tools for people at DKA risk who are treated with SGLT inhibition and discourages a ketogenic eating pattern in this setting.[12-19]

The absolute incidence of SGLT2-associated DKA in type 2 diabetes is low but not zero; ADA 2026 cites estimates of roughly 0.6-4.9 events per 1,000 person-years. Risk factors include very-low-carbohydrate eating, prolonged fasting, dehydration, excess alcohol, and insulin deficiency.[12-19]

The risk is especially important because SGLT2-associated DKA can present without marked hyperglycemia; some cases occur with plasma glucose <200 mg/dL. A near-normal glucose value therefore does not rule out DKA.[12-20]

Table 12-2. Nutritional ketosis and diabetic ketoacidosis are different states

Feature	Nutritional ketosis	Diabetic ketoacidosis (DKA)
Typical context	Carbohydrate restriction, fasting, exercise adaptation	Absolute or severe relative insulin deficiency, acute illness, medication-related risk
BHB	Usually modest elevation	BHB ≥ 3.0 mmol/L is the ADA ketosis criterion
Acid-base status	pH generally maintained	Metabolic acidosis: pH < 7.3 and/or bicarbonate < 18 mmol/L
Glucose/diabetes criterion	Normal to mildly elevated glucose possible	Glucose ≥ 200 mg/dL or a prior history of diabetes ; euglycemic DKA can occur
Clinical state	Usually stable	Dehydration, nausea/vomiting, abdominal pain, deep/rapid breathing, altered consciousness may occur
Response	Monitor dietary/metabolic state	Urgent medical evaluation and treatment with fluids, insulin, and electrolyte management

Source: ADA Standards of Care in Diabetes-2026, Sections 6, 9, and 16.

14. DKA cannot be diagnosed or excluded by one ketone number

An elevated BHB concentration alone does not diagnose DKA. ADA 2026 requires the diagnostic components to be considered together: diabetes or hyperglycemia, significant ketosis, and metabolic acidosis. BHB ≥ 3.0 mmol/L indicates significant ketosis, but without the other required components it is not, by itself, a diagnosis of DKA.[12-20]

Likewise, symptoms and acid-base abnormalities require clinical evaluation even when glucose is lower than expected. Nausea, vomiting, abdominal pain, marked thirst or dehydration, deep/rapid breathing, or altered consciousness should not be dismissed as “keto adaptation.” DKA can be euglycemic, especially with SGLT2 inhibitor therapy or insulin deficiency.[12-20]

15. Long-term sustainability is part of safety

A biochemically effective diet is not a durable treatment if it cannot be maintained. In the Goldenberg meta-analysis, six-month low-carbohydrate benefits attenuated by 12 months, and trials with poorer adherence to very-low-carbohydrate targets tended to show smaller weight effects.^[12-4]

Only 61 of 115 participants completed the Tay two-year trial. This is not unique to carbohydrate restriction; it reflects the broader difficulty of long-term dietary trials. Sustainability depends on food variety, social eating, cost, preparation burden, adverse effects, and satisfaction - not simply willpower.^[12-11]

A plant-based ketogenic strategy should therefore seek sustainable metabolic benefit, not maximum strictness. Sacrificing food variety and quality of life merely to raise ketone concentrations can undermine long-term success.^[12-4]

16. More restriction is not always better

Lower carbohydrate intake can raise ketones more reliably, but clinical benefit does not increase in a simple linear relation with restriction. In the 2021 meta-analysis, VLCDs were not uniformly superior to less-restrictive LCDs for weight loss, and adherence explained part of the difference.^[12-4]

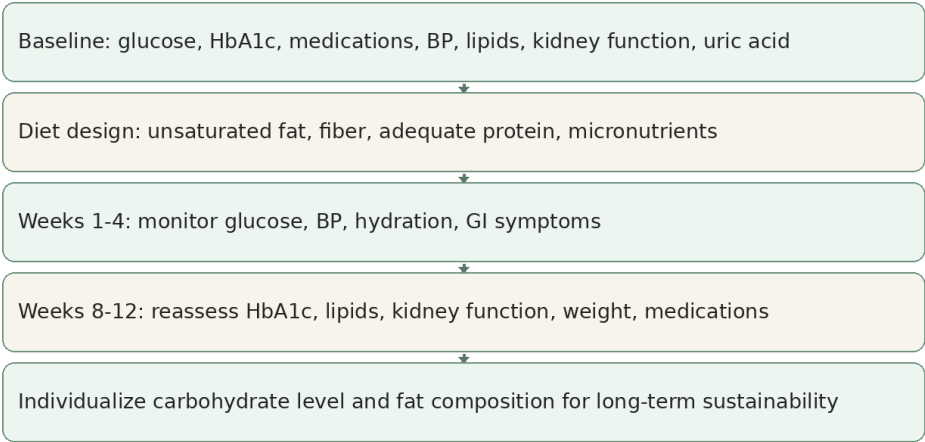
If the therapeutic goals are better HbA1c and lower medication burden, the rational target is the least restrictive level that the individual can sustain while achieving those goals. Some people may benefit from nutritional ketosis; others may achieve adequate metabolic improvement with a moderately low-carbohydrate pattern.^[12-4]

17. Safety principles for a plant-based ketogenic diet

A plant-based ketogenic diet should preserve potential advantages of carbohydrate restriction while reducing avoidable risks. First, prioritize unsaturated rather than saturated fat. Second, use nonstarchy vegetables, seeds, nuts, and appropriate legumes to maintain fiber. Third, provide sufficient plant protein while adapting protein targets to kidney function.^[12-10]

Fourth, plan B12 and assess iron, zinc, iodine, calcium, and omega-3 adequacy. Fifth, if LDL-C or ApoB rises meaningfully, reevaluate fat sources, total energy, weight change, family history, and baseline cardiovascular risk rather than assuming that lower triglycerides automatically compensate. Finally, people using glucose-lowering medication should coordinate medication adjustments with the speed of glycemic change.^{[12-9][12-19]}

Figure 12-2. Safe ketogenic eating is a monitoring process, not a ketone number



Source: ADA (2026); International Recommendations for Adults Treated With Ketogenic Diet Therapies (2021); Tay et al. (2018); author synthesis.

- Before starting:** glucose, HbA1c, medications, blood pressure, lipids, kidney function, uric acid.
- > **Diet composition:** unsaturated fats, fiber, adequate protein, micronutrient coverage.
- > **First 1-4 weeks:** glucose, blood pressure, hydration, gastrointestinal symptoms, medication effects.
- > **8-12 weeks:** HbA1c, lipids, kidney function, weight, medication changes.
- > **Personalize:** adjust carbohydrate level and fat composition and reassess long-term sustainability.

18. Who requires greater caution?

People with type 1 diabetes, severe insulin deficiency in type 2 diabetes, prior DKA, or SGLT2 inhibitor use require especially careful ketoacidosis risk assessment. Pregnancy and lactation, acute severe illness, repeated vomiting, and dehydration are also situations in which strict ketogenic eating should not be approached as unsupervised self-experimentation.[12-19][12-20]

Advanced CKD, recurrent nephrolithiasis, gout, severe dyslipidemia, or a history of eating disorder also call for individualized evaluation. These are not intended as a simplistic “absolute prohibition list,” but as conditions in which dietary change may collide with existing risk.[12-13][12-15]

19. What should practical monitoring include?

The earliest changes are usually glucose and symptoms. People taking medications should watch for hypoglycemia; those on antihypertensives or diuretics should also monitor dizziness and blood pressure. Rapid early weight loss may include substantial water loss and should not be interpreted entirely as fat loss.[12-1]

At roughly 8-12 weeks, repeating HbA1c, fasting glucose, lipids, and kidney function is reasonable. A large LDL-C rise may justify looking at non-HDL-C, ApoB, family history, and overall cardiovascular risk. Longer-term monitoring should also address micronutrients, muscle mass, fiber intake, and sustainability.[12-9][12-10]

Table 12-3. Staged monitoring framework for a plant-based ketogenic diet

Time	Priority review	Purpose
Before starting	HbA1c, glucose, medications, BP, lipids, eGFR/creatinine, uric acid, weight	Establish baseline and identify high-risk conditions

Time	Priority review	Purpose
First 1-2 weeks	Glucose, hypoglycemia, dizziness, hydration, GI symptoms	Detect rapid adaptation and medication mismatch
Around 4 weeks	Weight, BP, adherence, constipation, fiber/protein intake	Correct excessive restriction or dehydration
8-12 weeks	HbA1c, TG, HDL-C, LDL-C, non-HDL-C, kidney function	Assess metabolic benefit and lipid response
When indicated	ApoB, B12, iron status, electrolytes, ketones	Individualized risk assessment
Long term	Muscle mass, quality of life, relapse, medication needs, sustainability	Evaluate real treatment success rather than one laboratory value

20. Common traps in ketogenic safety research

First, diets called “ketogenic” can differ profoundly. An animal-based, saturated-fat-heavy ketogenic diet is not nutritionally equivalent to a low-carbohydrate pattern based on olive oil and nuts. Second, weight-loss ketogenic interventions and weight-maintenance ketogenic interventions should not be pooled uncritically because weight loss changes many outcomes independently.[12-6][12-10]

Third, many studies last only months - too short to observe hard outcomes such as myocardial infarction, stroke, or end-stage kidney disease. A demonstrated LDL-C increase does not directly tell us the decades-long cardiovascular event effect of a specific ketogenic pattern; likewise, lower triglycerides and glucose do not prove that long-term events will necessarily fall.[12-6]

Fourth, adverse-event reporting is often inconsistent. The 2026 systematic adverse-event analysis identified large differences in how studies collected and reported symptoms. Safety research needs adverse-event measurement as systematic as efficacy measurement.[12-17]

21. Conclusion: ketogenic safety is determined by composition and observation

Taken together, current evidence indicates that ketogenic diets can improve triglycerides, HDL-C, glycemia, and medication requirements in type 2 diabetes. Yet LDL-C may rise on average in some analyses and can rise markedly in some individuals; ApoB can be assessed separately when atherogenic particle risk is uncertain. Constipation, dehydration, early adaptation symptoms, kidney stones, and micronutrient inadequacy are also possible.[12-5][12-6][12-17]

Very-low-carbohydrate eating with SGLT2 inhibitors is a distinct safety issue, and ADA 2026 discourages ketogenic eating patterns

in at-risk people treated with SGLT inhibition. People using medications that cause hypoglycemia also require dietary and medication changes to be considered together.^[12-19]

The goal of the plant-based ketogenic model proposed in this book is therefore not “more fat” or “higher ketones.” It is to improve food quality with unsaturated fats and fiber, restrict carbohydrate only as much as necessary, and find an individualized range while monitoring glucose, lipids, kidney function, medications, symptoms, and sustainability.^[12-10]

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Chapter 13. Are Plant-Based and Ketogenic Diets Really Opposites?

At the dinner table, plant-based and ketogenic diets can look like opposites. Traditional low-fat plant-based diets are often high in carbohydrate and low in fat, whereas ketogenic diets greatly restrict carbohydrate and use fat as a major energy source. Yet when clinical research is examined more carefully, the two approaches can reach similar metabolic goals through different routes.^[13-1]

The question in this chapter is not which diet is “the answer.” It is what differs, what overlaps, and why one approach may be favorable for one outcome while another is favorable for a different outcome. Only after making these distinctions can we logically discuss how selected advantages of plant-based and ketogenic eating might be combined.^[13-2]

1. The first distinction is carbohydrate quantity versus carbohydrate quality

Plant-based eating is often assumed to mean high carbohydrate, but the term plant-based does not specify carbohydrate quantity. A diet centered on vegetables, nuts, seeds, tofu, and avocado can be plant-based and relatively low in carbohydrate. A diet dominated by white rice, white bread, sugar, juice, and ultraprocessed vegan products can also technically be plant-based.^[13-3]

Ketogenic diets vary in the same way. They share very-low carbohydrate intake, but their protein and fat sources can be completely different. A butter-, processed-meat-, and cheese-heavy ketogenic diet is not nutritionally equivalent to a ketogenic pattern based on olive oil, nuts, seeds, tofu, and nonstarchy vegetables even if their carbohydrate percentages are similar.^[13-4]

For this reason, diabetes nutrition therapy does not judge a diet by one macronutrient ratio. ADA 2026 allows carbohydrate reduction as an option for selected adults while also emphasizing minimally processed, high-fiber carbohydrate sources, nonstarchy vegetables, legumes, nuts, seeds, and plant proteins. Quantity and quality are separate dimensions.^[13-5]

Table 13-1. Typical differences between low-fat plant-based and ketogenic diets

Feature	Typical low-fat plant-based diet	Typical ketogenic diet	What to assess clinically
Carbohydrate	Moderate to high	Very low	Degree of refinement and fiber as well as amount
Fat	Low	High	Saturated vs unsaturated fat quality
Protein	Legumes, grains, nuts	Often more animal-based depending on model	Can also be supplied from plant sources
Fiber	Usually high	May be low if poorly designed	Preserve nonstarchy vegetables, seeds, nuts
Postprandial glucose	Depends on food quality and amount	Usually lower	Verify individual response with CGM/post-meal checks
Ketogenesis	Usually low	Increased	Ketone number is not the same as clinical benefit
LDL-C	Often falls on low-fat plant-based patterns	May rise in some people	Consider non-HDL-C and ApoB
Triglycerides	Can fall with weight loss and better food quality	Often fall consistently	Interpret within overall cardiovascular risk

2. “High carb versus low carb” is an incomplete framework

One common mistake in nutrition research is to interpret outcomes using carbohydrate percentage alone. A high-carbohydrate diet based on whole grains, legumes, and vegetables can behave differently from one based on refined grains and sugars. A low-carbohydrate diet likewise produces different lipid, fiber, and micronutrient outcomes depending on the quality of fat and protein sources.[13-6]

The Keto-Med trial illustrates this problem well. Its well-formulated ketogenic diet (WFKD) and Mediterranean-plus diet differed in carbohydrate level but shared important food-quality features: both included nonstarchy vegetables and avoided added sugars and refined grains.[13-7]

After 12 weeks, the primary HbA1c outcome did not differ significantly between the two diets. The ketogenic phase produced a greater triglyceride reduction but higher LDL-C, lower fiber intake, and lower intake of selected nutrients; follow-up adherence also favored the Mediterranean-plus pattern. The result is not simply “ketosis failed” or “Mediterranean won.” It demonstrates simultaneous benefits and trade-offs.[13-8]

3. What do direct head-to-head studies show?

In an NIH inpatient crossover trial, Hall and colleagues directly compared a minimally processed low-fat plant-based diet with a minimally processed animal-based ketogenic diet. Twenty adults ate each diet ad libitum for two weeks. The plant-based diet provided about 10% of energy from fat and 75% from carbohydrate; the ketogenic diet provided roughly 76% from fat and 10% from carbohydrate.^[13-9]

Contrary to many expectations, participants consumed about 689 kcal/day less during the low-fat plant-based phase. The ketogenic phase, however, produced lower post-meal glucose and insulin exposure. The two diets therefore influenced energy intake and glycemic physiology through different mechanisms.^[13-10]

This was not a type 2 diabetes treatment trial and each dietary phase lasted only two weeks. It cannot establish long-term differences in HbA1c, medication reduction, or remission. Its value is the controlled direct comparison, but its scope is clearly limited.^[13-11]

Table 13-2. Key clinical studies relevant to comparing plant-based and low-carbohydrate/ketogenic approaches

Study	Population/duration	Comparison	Main result	Limitation
Hall et al., 2021	20 adults, inpatient crossover, 4 weeks total	Low-fat plant-based vs animal-based ketogenic	Lower spontaneous energy intake with plant-based; lower glucose/insulin exposure with ketogenic	Not a T2D treatment trial; short duration
Gardner et al., 2022	40 with prediabetes/T2D, 12 weeks each	WFKD vs Mediterranean-plus	No significant HbA1c difference; KD lowered TG more and increased LDL-C	Both diets were high-quality
Jenkins et al., 2022	164 with T2D, 3 months	Low-carb vegan vs moderate-carb vegetarian	Both improved weight and HbA1c substantially; most between-group metabolic differences small	Both energy-restricted
Barnard et al., 2006/2009	99 with T2D, 22-74 weeks	Low-fat vegan vs conventional diabetes diet	HbA1c and LDL advantages after medication-change adjustment	Not a direct ketogenic comparison
Goldenberg et al., 2021	RCT meta-analysis	LCD/VLCD comparators vs	Six-month remission/HbA1c/TG/weight advantages, attenuated by 12 months	Heterogeneous definitions and adherence

4. Low-carbohydrate vegan diets show that the two worlds are not completely separate

Plant-based and low-carbohydrate approaches can coexist. Jenkins et al. randomized 164 people with type 2 diabetes to a low-carbohydrate vegan diet or a moderate-carbohydrate vegetarian diet. The low-carbohydrate vegan diet emphasized plant proteins and plant fats such as canola oil.[13-12]

After three months, both groups lost roughly 5-6 kg and reduced HbA1c by about 0.9-1.0 percentage points. Between-group differences in weight and HbA1c were not significant; both diets were energy-restricted. The important point is that “low carbohydrate” does not physiologically require an animal-food-dominant diet.[13-13]

The intervention did not target strict nutritional ketosis, so it should not be called direct evidence for a plant-based ketogenic diet. It does, however, establish that a practical intermediate zone exists in which carbohydrate can be lowered while plant protein and unsaturated plant fats remain central.[13-14]

5. Both approaches can improve HbA1c

Low-fat vegan randomized trials have repeatedly reported HbA1c improvements. In Barnard's studies, HbA1c fell more with a low-fat vegan pattern than with the comparison diet after accounting for medication changes, and a Korean brown-rice-based vegan RCT also reported greater 12-week HbA1c reduction than a conventional diabetes diet.[13-15][13-16]

Meta-analyses of low-carbohydrate and ketogenic diets likewise show favorable six-month HbA1c and remission signals, with between-group differences tending to diminish by 12 months. Adherence and weight change are important mediators.[13-17]

HbA1c improvement alone therefore does not prove that one diet possesses an exclusive mechanism. Different nutritional compositions can influence energy intake, body weight, postprandial glucose, and hepatic and muscular insulin sensitivity and ultimately converge on a similar HbA1c.[13-18][13-19]

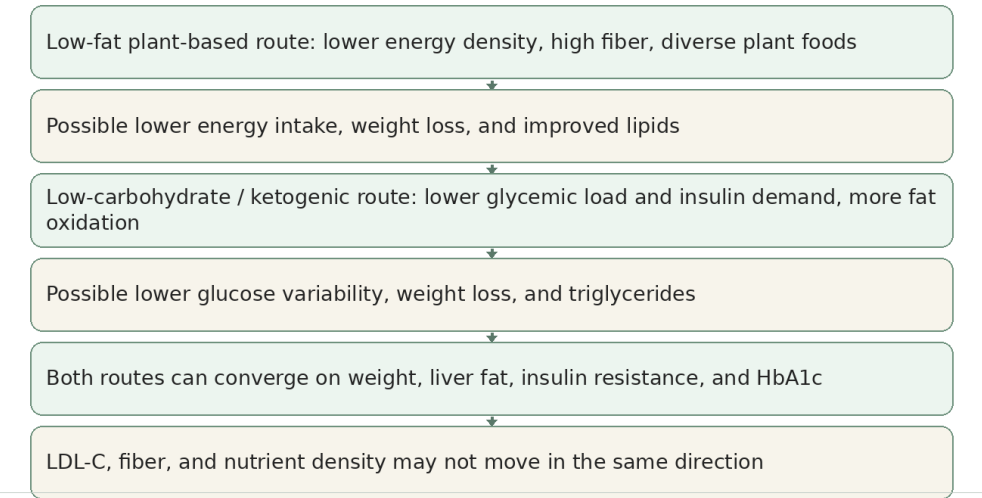
6. Weight loss is the strongest common denominator

In network meta-analysis across dietary patterns, reductions in HbA1c and fasting glucose were closely related to average weight change. This suggests that changes in energy balance and body weight can explain a substantial part of glycemic improvement regardless of the diet's label.[13-20]

Low-fat plant-based diets can reduce spontaneous energy intake through low energy density, high fiber, and large food volume. Ketogenic diets may reduce intake through satiety from protein and fat, reduced appetite in some individuals, and restricted food choice. Different starting mechanisms can converge on an energy deficit, reduced liver and visceral fat, and improved insulin sensitivity.[13-21][13-22]

Not every effect should be attributed to weight. Postprandial glucose, glycemic variability, and triglycerides can respond directly to carbohydrate quantity, while LDL-C and fiber are particularly sensitive to food composition. Shared mediators and diet-specific effects need to be evaluated together.[13-23][13-24]

Figure 13-1. Different starting points can converge on similar metabolic goals



Source: Hall et al. (2021); Goldenberg et al. (2021); Barnard et al. (2006); ADA (2026); author synthesis.

Low-fat plant-based: lower energy density + high fiber + plant-food diversity -> lower energy intake and weight loss + lipid improvement -> better insulin sensitivity.

Low-carbohydrate/ketogenic: lower carbohydrate load + lower post-meal insulin requirement + greater fatty-acid oxidation -> less glycemic variability + weight loss + lower triglycerides -> lower insulin requirements.

Both routes may converge on common goals: **lower weight, liver fat, insulin resistance, and HbA1c**. LDL-C, fiber, and micronutrient density, however, may not move in the same direction.

7. Low-carbohydrate effects are more direct for postprandial glucose and variability

Reducing carbohydrate reduces the amount of absorbed glucose entering circulation after a meal, making lower postprandial excursions a direct physiological consequence. In low-carbohydrate randomized trials, glycemic variability and medication requirements sometimes improved even when mean HbA1c was similar between groups.^[13-25]

For people using insulin or sulfonylureas, this advantage creates a safety issue at the same time: a rapid fall in post-meal glucose can make previous medication doses excessive. Medication adjustment and monitoring are therefore necessary if rapid glycemic effects are to be used therapeutically.^[13-26]

Plant-based diets can also blunt postprandial glucose by replacing refined carbohydrate with high-fiber whole grains, legumes, and vegetables. But if total carbohydrate remains high, some individuals may still experience large peaks; CGM or post-meal testing can identify individual tolerance.^[13-27]

8. LDL-C can move in opposite directions

Low-fat vegan diets generally show LDL-C reduction. In Barnard's type 2 diabetes RCT, LDL-C reduction was greater with the vegan diet after accounting for lipid-medication changes.^[13-28]

Ketogenic diets commonly lower triglycerides and raise HDL-C but can raise LDL-C and ApoB in some individuals. In Keto-Med, LDL-C was higher during the ketogenic phase than during Mediterranean-plus. This is not a simplistic contest of “glucose versus cholesterol”; it is a set of outcome-specific trade-offs.^[13-29]

The logic of a plant-based ketogenic diet begins here. If carbohydrate restriction is combined with less saturated fat and more olive oil, nuts, seeds, avocado, soy, and other unsaturated plant foods, it may reduce the probability or magnitude of an LDL-C rise. That hypothesis requires direct long-term testing

rather than assumption.[13-30]

9. Triglycerides and HDL-C are clearer ketogenic strengths

Lower triglycerides and higher HDL-C are among the most reproducible findings in carbohydrate-restriction research. This can be especially relevant to people with marked insulin resistance and hypertriglyceridemia.[13-31]

Low-fat plant-based diets can also improve triglycerides when weight falls and refined carbohydrate is reduced. But very high carbohydrate intake can increase hepatic VLDL production and triglycerides in some individuals. “Plant-based” therefore does not mean that the highest carbohydrate percentage is optimal for everyone.[13-32]

For an insulin-resistant phenotype characterized by high triglycerides and low HDL-C, more active carbohydrate reduction may be reasonable, while still preserving food quality and energy balance.[13-33][13-34]

10. Plant-based eating has a structural advantage for fiber and the gut microbiome

Whole grains, legumes, fruits, and vegetables make it easier to obtain diverse fermentable fibers, which can support microbial diversity and short-chain-fatty-acid production. ADA recommends at least about 14 g fiber per 1,000 kcal for people with diabetes.[13-35]

Traditional ketogenic diets restrict fruit, whole grains, and many legumes and can therefore reduce fiber and selected micronutrients. Keto-Med found lower fiber and selected nutrient intake during the ketogenic phase.[13-36]

This need not be an inevitable property of every ketogenic diet. Nonstarchy vegetables, flax, chia, nuts, avocado, and limited portions of lower-net-carbohydrate legumes can preserve substantial fiber while maintaining carbohydrate restriction. The practical limits of this design are developed in later chapters.[13-37]

11. Protein source also changes the nutritional result

Low-carbohydrate eating often increases the proportion of protein and fat. A pattern that increases processed meat and animal protein differs in cardiovascular and micronutrient profile from one centered on soy, tofu, tempeh, nuts, and seeds.[13-38]

ADA 2026 encourages greater inclusion of plant-protein sources for people with diabetes. Carbohydrate restriction does not require filling the resulting energy gap with animal protein.[13-39]

The Jenkins low-carbohydrate vegan trial demonstrates this feasibility: carbohydrate was lowered while plant protein and plant fat remained central, with clinically meaningful improvements in weight and HbA1c. Because strict ketosis was not the goal, additional research is required for true plant-based ketogenic interventions.[13-40]

12. The amount of ultraprocessed food removed may matter more than the diet label

High-quality studies of very different dietary patterns often share the same food-level changes: less added sugar, fewer refined grains and sugary beverages, fewer ultraprocessed foods, and a greater proportion of minimally processed foods. ADA 2026 emphasizes these food-based principles rather than one ideal macronutrient ratio.[13-41]

Keto-Med is difficult to interpret without this shared foundation. Both diets included nonstarchy vegetables and eliminated added sugar and refined grains. Their common improvements in food quality may have contributed substantially to the improvement observed in both arms.[13-42]

This sets an important principle for plant-based ketogenic eating. Increasing ultraprocessed “keto” products merely to produce ketosis misses the point, just as increasing refined grains and sugars merely to remain plant-based misses the point. Minimally processed foods should be the common foundation.[13-43]

Table 13-3. No single approach is superior for every outcome

Outcome	Low-fat plant-based approach	Low-carb/ketogenic approach	Key integration principle
HbA1c	Evidence of improvement	Strong short-term evidence	Interpret with weight, adherence, medication changes
Postprandial glucose	Strongly affected by carbohydrate quality and fiber	Directly reduced by lower total carbohydrate	Titrate using individual CGM response
Insulin requirement	May fall through weight and insulin sensitivity	Can fall rapidly	Medication-safety plan required
Weight	Can fall through low energy density and fiber	Can fall through satiety and food restriction	Sustainable energy deficit
Triglycerides	Improve with weight loss and less refined carbohydrate	Often fall substantially	Individualize carbohydrate level
LDL-C/ApoB	Tends to fall	May rise in some people	Unsaturated-fat emphasis and follow-up testing
Fiber	Easy to obtain	Can become inadequate if not designed	Use low-net-carb, high-fiber plant foods

Outcome	Low-fat plant-based approach	Low-carb/ketogenic approach	Key principle	integration
Sustainability	Variable	Attrition may rise with strictness	Prefer restrictive range	the least effective

13. Metabolically, the two approaches pull different levers rather than simply opposing each other

Low-fat plant-based diets strongly influence energy density, fiber, food volume, and fat quality. Ketogenic diets strongly influence carbohydrate load, postprandial insulin requirement, fatty-acid oxidation, and ketogenesis. Their emphasized physiological pathways are different.[13-44][13-45]

Type 2 diabetes, however, is not produced by one pathway. Excess energy storage, liver and visceral fat, insulin resistance, beta-cell stress, low physical activity, sleep, medications, and other factors interact. It is therefore unlikely that one nutritional lever is the unique answer for everyone.[13-46]

The common objective is not to “defeat” a particular nutrient but to reduce metabolic burden: lower glucose and insulin requirements, reduce excess body and liver fat, and ultimately reduce complication risk.[13-47][13-48]

14. Starting strategy can differ according to metabolic phenotype

A person with very high postprandial glucose, high triglycerides, and a large glycemic response to carbohydrate may experience immediate benefit from stronger carbohydrate reduction. A person with high LDL-C/ApoB, very low fiber intake, and high saturated-fat intake may urgently need a shift toward plant foods and unsaturated fats.[13-49][13-50]

These are not diagnostic subtypes but practical starting points for treatment design. People with the same diagnosis differ in medications, weight, kidney function, lipids, habitual diet, culture, and living environment. This is one reason ADA does not prescribe one ideal macronutrient ratio.[13-51]

A plant-based ketogenic diet should therefore not impose one carbohydrate number on everyone. The goal is to find the least restriction that achieves the metabolic target together with a food pattern that can be sustained long term.[13-52]

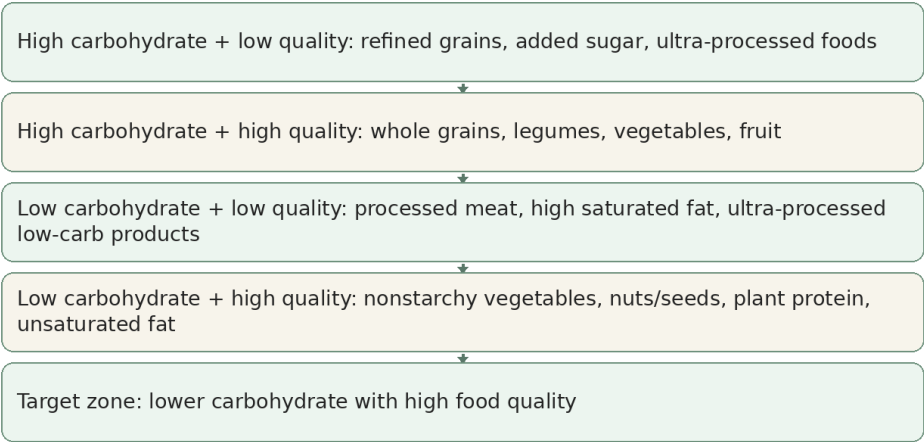
15. The most important gap in our evidence database

In the project's strict second-pass classification, substantial clinical literatures existed separately for plant-based and ketogenic interventions. Direct evidence in which “plant-based” and “nutritional ketosis” were clearly components of the same intervention was extremely limited.^[13-53]

Among the top 300 records subjected to full-text verification, only one candidate was classified as a same-intervention plant-ketogenic study. Thirty-two papers mentioned both concepts without testing the same plant-ketogenic dietary intervention. This is a critical boundary: the clinical effect of a plant-based ketogenic diet should not be presented as already established.^[13-54]

The logic of this book is therefore not “plant-based evidence + ketogenic evidence = plant-based ketogenic superiority.” It decomposes the benefits and risks demonstrated in each literature and uses them to formulate a new dietary model that still requires direct testing.^[13-55]

Figure 13-2. Carbohydrate quantity and food quality are separate axes



Source: ADA Standards of Care in Diabetes-2026, food-based nutrition principles; author synthesis.

A one-dimensional line from **high carbohydrate <-> low carbohydrate** loses important information. A second axis, **low quality <-> high quality**, must be added.

- High-carbohydrate, low-quality: refined grains, added sugars, ultraprocessed foods.
- High-carbohydrate, high-quality: minimally processed plant-based diet rich in whole grains, legumes, vegetables, and fruit.
- Low-carbohydrate, low-quality: processed meat, saturated fat, ultraprocessed low-carb products.
- Low-carbohydrate, high-quality: nonstarchy vegetables, nuts/seeds, plant protein, unsaturated fats.

The intended position of the plant-based ketogenic model is **low carbohydrate + high quality**.

16. The two approaches share more principles than they first appear to

Both reduce refined carbohydrates and added sugars, reduce ultraprocessed foods, aim to reduce excess weight and visceral fat, lower glucose and insulin burden, and require a sustainable structure.[13-56]

The plant-based ketogenic model adds a further design rule: carbohydrate can be lowered without abandoning plant-food diversity and fiber, and fat can be increased without prioritizing saturated fat. The goal is not to make plant-based and low-carbohydrate approaches compromise each other, but to compensate for the weaknesses of each.[13-57]

Whether this design produces superior outcomes to conventional ketogenic or high-carbohydrate plant-based diets remains unproven. The next chapter therefore proposes a testable model rather than declaring an established therapy.[13-58]

Table 13-4. Shared principles where plant-based and ketogenic approaches can meet

Principle	Plant-based meaning	Ketogenic meaning	Plant-based ketogenic application
Minimally processed foods	Whole grains, legumes, vegetables	Avoid ultraprocessed low-carb products	Real foods as the default
Limit added sugar	Core of healthy plant-based eating	Necessary for carbohydrate restriction	Minimize by default
Limit refined grains	Improve plant-food quality	Supports lower carbohydrate	Replace with high-fiber lower-net-carb foods
Plant protein	Legumes, tofu, nuts	Reduces dependence on animal protein	Tofu, tempeh, soy, seeds
Unsaturated fat	Cardiovascular risk management	Improves quality of a high-fat diet	Olive oil, nuts, seeds, avocado

Principle	Plant-based meaning	Ketogenic meaning	Plant-based ketogenic application
Fiber	Gut and metabolic health	Addresses a common weakness of traditional KD	Nonstarchy vegetables and seeds
Personalization	Culture, preference, nutrient status	Carb level and medication adjustment	Adjust according to glucose, lipids, medication, sustainability

17. Conclusion: integration is a more productive question than opposition

By macronutrient ratio, plant-based and ketogenic diets can appear to be opposites. Clinically, however, both can pursue weight loss, reduction of refined foods, better glycemia, and lower insulin burden. At the same time, they have distinct strengths and weaknesses in postprandial glucose, triglycerides, LDL-C, and fiber.[13-59][13-60]

The more useful question is not which diet is ideologically superior for everyone, but which mechanisms and food structures are appropriate for which person. Metabolic treatment should measure goals and risks and build the best-fitting dietary structure rather than demand loyalty to one diet label.[13-61]

The next chapter takes this logic further by defining a **third path: the plant-based ketogenic diet**, integrating carbohydrate quantity and quality, fat quality, protein, fiber, micronutrients, and ketosis within one proposed model.[13-62]

Key references: ADA Standards of Care in Diabetes-2026; Hall et al. (2021); Gardner et al. (2022); Jenkins et al. (2022); Barnard et al. (2006, 2009); Goldenberg et al. (2021); Lee et al. (2016). Internal database counts refer to the project's strict evidence reclassification and are not formal GRADE ratings.

Sources and References

Key chapter sources

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Chapter 14. A Third Path: The Plant-Based Ketogenic Diet

A plant-based ketogenic diet is not a mechanical compromise between two opposing diet camps. It is a proposed, testable nutrition model that combines carbohydrate restriction with the food-quality priorities of a minimally processed plant-based diet. The central question is not how strictly a person can restrict carbohydrate or how high a ketone value can be pushed, but whether glycemia, weight, lipids, nutritional adequacy, muscle, kidney function, medication safety, and long-term sustainability can improve together.

1. Define the model before judging it

In this book, a plant-based ketogenic diet means a minimally processed eating pattern in which plant foods provide the dominant food base and carbohydrate is restricted enough to induce nutritional ketosis, or a near-ketotic metabolic state when strict ketosis is not clinically necessary. This is a working definition proposed for this book, not an internationally standardized treatment name.

The model has six linked components: individualized carbohydrate restriction; minimally processed, nutrient-dense foods; predominantly unsaturated fats; adequate plant protein; intentional fiber intake; and active monitoring of medications, kidney function, lipids, and nutritional status.

2. Find the optimal carbohydrate level, not the lowest one

Ketogenic trials often use carbohydrate targets in the range of roughly 20-50 g/day, but that range is a research convention and practical starting point, not a universal prescription. A person with type 2 diabetes should not treat zero carbohydrate as the goal. The useful level is the least restriction that produces the desired metabolic response while preserving food variety, nutritional adequacy, and adherence.

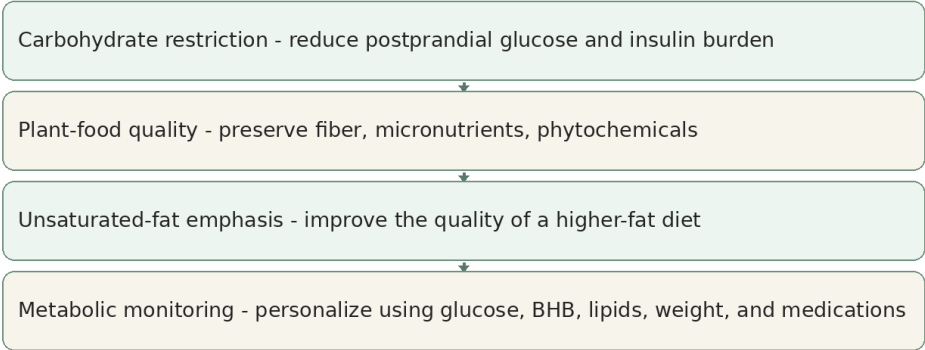
3. Carbohydrate quality still matters after restriction

Removing sugar-sweetened beverages, refined grains, sweets, and highly processed starches is different from removing fiber-rich vegetables, legumes, or small portions of whole-food carbohydrate. Even in a low-carbohydrate pattern, food quality remains a separate variable. The practical sequence is to remove the lowest-quality carbohydrate first, then adjust whole-food sources according to postprandial glucose, CGM patterns, ketone response when relevant, and overall sustainability.

4. The source of fat matters more than simply increasing fat

A plant-based ketogenic diet should not be built around butter substitutes, coconut oil, or other concentrated saturated-fat sources simply because they are plant-derived. The default fat sources are olives and olive oil, avocado, nuts, seeds, soy foods, canola, and other unsaturated plant fats. If LDL-C or ApoB rises meaningfully, the diet should be reassessed even when triglycerides, weight, or ketones improve.

Figure 14-1. Four axes of a plant-based ketogenic diet



Source: ADA (2026); Gardner et al. (2022); Jenkins et al. (2022); author synthesis.

5. Protein should be sufficient, not maximal

Tofu, tempeh, soy foods, nuts, seeds, and selected legumes can provide the protein foundation. The required amount varies with age, activity, body composition, energy intake, and kidney function. Protein is best distributed across meals rather than treated as a single daily number.

6. Fiber is a structural requirement, not an optional extra

Nonstarchy vegetables, flax, chia, nuts, avocado, and appropriately portioned legumes help prevent the low-fiber pattern that can occur in poorly designed ketogenic diets. Fiber supports bowel function, satiety, food diversity, and metabolic health. Restricting carbohydrate should not mean eliminating plant structure.

7. “Net carbs” are convenient but not absolute

“Net carbohydrate” is not a standardized regulatory term. Different fibers and sugar alcohols are absorbed differently, and front-of-package net-carb claims should not be used to adjust insulin or other glucose-lowering medication. Total carbohydrate, fiber, ingredients, and the person's actual glucose response should be considered together.

8. Ketones are a state marker, not the therapeutic objective

Blood beta-hydroxybutyrate (BHB) is the most direct practical marker of circulating ketones. Nutritional ketosis is commonly described around BHB concentrations of at least about 0.5 mmol/L, but higher BHB does not mean better diabetes outcomes in a linear fashion. Good HbA1c, fewer glucose excursions, preserved muscle, acceptable lipids, adequate nutrition, and a safe medication plan take priority over the ketone number.

9. Blood BHB is the most direct ketone measurement

Urine acetoacetate and breath acetone can be useful in some settings, but blood BHB more directly reflects circulating ketone status. Measurement frequency should be driven by purpose. It may be useful during initial diet titration or in specific safety situations, but routine measurement is not mandatory for every person once the diet and glucose pattern are stable.

10. This is not a doctrine of unrestricted calories

Nuts, seeds, oils, and avocado are nutritious but energy dense. A person can consume a low-carbohydrate diet and still fail to lose excess body fat if energy intake remains too high. When weight and waist circumference do not improve and glycemia remains above target, total energy intake and food portions deserve another look.

11. Medications can create risk faster than food can create benefit

Insulin, sulfonylureas, and meglitinides can cause hypoglycemia when carbohydrate intake falls rapidly. SGLT2 inhibitors create a different risk: diabetic ketoacidosis can occur even without marked hyperglycemia. People taking an SGLT2 inhibitor should not independently combine the drug with a ketogenic eating pattern or prolonged fasting; medication and diet planning require clinician involvement.

12. A low-carbohydrate vegan RCT is a bridge, not direct ketogenic proof

Low-carbohydrate vegan trials show that carbohydrate restriction and plant-based food choices can be combined in practice. However, these studies do not automatically prove sustained nutritional ketosis. They are important bridging evidence, but they should not be mislabeled as direct trials of a plant-based ketogenic intervention unless ketosis was actually part of the protocol and confirmed.

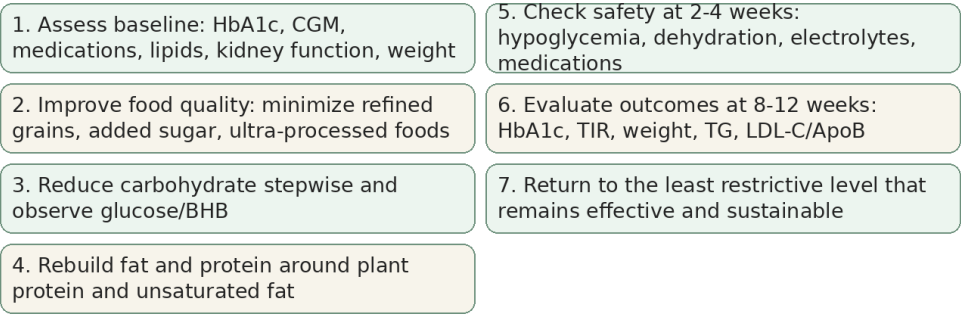
13. “Plant-based” may matter for long-term safety, but it does not guarantee it

Replacing saturated fats with unsaturated plant fats and increasing minimally processed plant foods may improve the lipid and nutrient profile of a ketogenic pattern. Yet a plant-based label does not make every formulation safe. Coconut oil, ultra-processed vegan keto foods, excessive energy intake, or poorly planned micronutrient intake can still create problems.

14. The same diet should not be prescribed to everyone

Age, duration of diabetes, current medication, kidney function, lipid response, body composition, physical activity, and food preferences all change the appropriate degree of restriction. Some people may need a short, relatively strict ketogenic phase; others may achieve adequate glycemic control with a less restrictive plant-based low-carbohydrate pattern.

Figure 14-2. Personalization algorithm for plant-based ketogenic eating



Source: ADA (2026) individualized nutrition therapy principles and the book framework; author synthesis.

15. Aim for metabolic flexibility, not perfect ketosis

Long-term success is not defined by staying in ketosis every hour of every day. The more useful goal is the ability to maintain stable glucose and energy regulation while using a sustainable food pattern. When metabolic targets are met, carefully reintroducing selected whole-food carbohydrates may be reasonable for some people.

16. Four principles should not be compromised

The model retains four fixed priorities: minimally processed food quality, predominantly unsaturated fats, adequate plant protein and fiber, and medication/safety monitoring. The variables that can be individualized include carbohydrate grams, total fat percentage, legume and fruit allowance, ketone testing frequency, and the strictness of the maintenance phase.

17. What current evidence allows us to say

The separate evidence bases for plant-based eating, carbohydrate restriction, and ketogenic diets are substantial. Direct evidence for a true plant-based ketogenic intervention is much smaller. Therefore it is reasonable to describe the model as biologically plausible and clinically testable, but not as an established standard treatment or as superior to all other evidence-based dietary patterns.

18. Conclusion: the third path is redesign, not compromise

The plant-based ketogenic approach proposed here is best understood as a redesign of carbohydrate restriction. It keeps the potentially useful metabolic lever of carbohydrate reduction while deliberately protecting food quality, fat quality, protein adequacy, fiber, and medication safety. Its value should ultimately be judged by clinical outcomes, not by ideology or ketone numbers.

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Key chapter sources

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Chapter 15. How Far Does Current Science Support a Plant-Based Ketogenic Diet?

The strongest way to evaluate a plant-based ketogenic diet is not to merge every study that contains the words “plant-based,” “low-carbohydrate,” or “ketogenic.” The evidence has to be separated into layers according to what was actually tested.

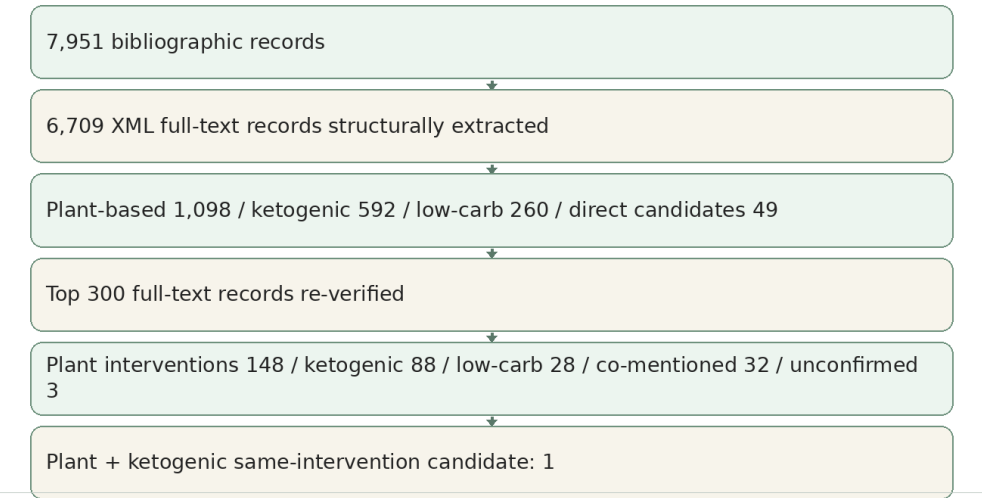
1. Separate the layers of evidence

The first layer is plant-based dietary intervention in type 2 diabetes. The second is low-carbohydrate or ketogenic intervention in type 2 diabetes. The third is a plant-based low-carbohydrate intervention in which the two principles are used together. The fourth and most direct layer is a plant-based intervention explicitly designed to produce nutritional ketosis. The closer the evidence gets to the fourth layer, the more directly it answers the question of this book, but the number of studies becomes much smaller.

2. How large is the evidence database?

The project database contained 7,951 bibliographic records at the major review snapshot. Structured full-text or XML extraction was available for thousands of records, but the raw number of records is not the number of independent clinical trials. Search records can include reviews, duplicate reports, follow-up papers, protocols, and studies in which the diet is only mentioned.

Figure 15-1. Evidence funnel from 7,951 records to direct evidence



Source: vk_refine_book_evidence.py and vk_verify_top_evidence.py, database snapshot 2026-08-24.

3. Direct evidence for plant-based diets is already substantial

Plant-based and vegan intervention research in type 2 diabetes includes multiple randomized trials and meta-analyses. Recent syntheses generally show modest improvements in HbA1c, body weight, and selected cardiovascular risk markers. This does not mean every plant-based diet produces remission or that all plant-based diets are metabolically equivalent. Whole-food quality matters.

4. Direct ketogenic evidence is also substantial, but definitions are harder

Ketogenic and very-low-carbohydrate trials frequently show short-term reductions in HbA1c, triglycerides, body weight, and medication requirements. Yet studies vary widely in carbohydrate limits, whether ketosis was measured, fat composition, intensity of clinical support, and control diets. A trial described as “low carbohydrate” should not automatically be treated as a trial of nutritional ketosis.

5. Low carbohydrate should be analyzed separately from ketogenic

A diet below 130 g/day can be labeled low-carbohydrate in some literature and still be far above a typical ketogenic target. Conversely, some ketogenic studies use 20-50 g/day and confirm BHB or other ketosis markers. Combining these categories can exaggerate the size of the true ketogenic evidence base.

6. At first, 49 records looked like “direct” evidence

Keyword and automated classification initially produced dozens of plant-plus-keto candidates. A second full-text review showed why manual verification matters: many papers discussed plant-based and ketogenic diets in the same article but did not study them as the same intervention. In the top 300 prioritized papers, the refined classification included 148 plant-based interventions, 88 ketogenic interventions, 28 low-carbohydrate interventions, 32 co-mentioned plant-plus-keto records, three uncertain diet records, and only one top-priority same-intervention plant-ketogenic candidate.

7. What does “one direct study” mean?

It does not mean that the idea has no evidence. It means that most support is indirect or bridging: one can combine evidence about plant foods, unsaturated fats, fiber, carbohydrate restriction, nutritional ketosis, weight loss, and medication safety, but the exact combined intervention has not yet been tested as often as its components.

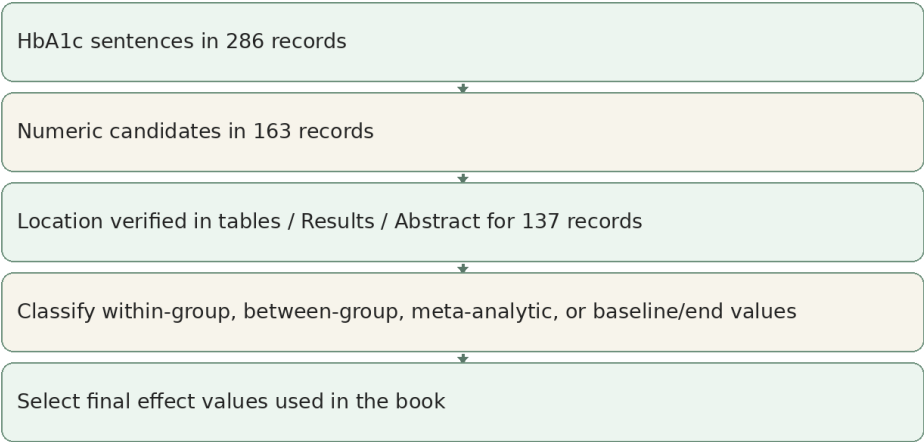
8. Three kinds of studies form useful bridges

Low-carbohydrate vegan trials show that plant-based food selection and carbohydrate restriction can coexist. The Keto-Med randomized crossover trial compares a well-formulated ketogenic diet with a low-carbohydrate Mediterranean pattern and helps identify shared and divergent effects. Metabolic-ward comparisons of plant-based low-fat and animal-based ketogenic diets help separate mechanisms, although they are not direct treatment trials of the combined plant-ketogenic model.

9. HbA1c numbers require a second verification step

A numeric HbA1c value can represent baseline, end point, within-group change, between-group difference, or a pooled meta-analytic estimate. The project therefore rechecked where each number appeared and what effect type it represented before using it in the text.

Figure 15-2. Steps for turning an HbA1c number into a clinically interpretable effect



Source: vk_verify_hba1c_numbers.py and the book effect-type verification framework.

10. Medication reduction and remission require even more caution

Reduced medication use can be a clinically meaningful outcome, but it may reflect active clinician-led deprescribing rather than diet alone. Remission is stricter: improvement in HbA1c while a glucose-lowering drug is still being used is not medication-free remission. Definitions must be reported explicitly.

11. What science allows us to say now

It is well supported that healthy plant-based patterns can improve several metabolic outcomes in type 2 diabetes. It is also well supported that carbohydrate restriction can improve short-term glycemia in selected adults. Ketogenic diets can be effective for some people, but long-term comparative superiority is not established. Plant-based low-carbohydrate approaches are feasible. Direct evidence for a true plant-based ketogenic diet is emerging but remains limited.

12. What we should not say yet

We should not claim that a plant-based ketogenic diet guarantees remission, is superior to every Mediterranean or other whole-food pattern, or has proven long-term cardiovascular superiority. We also should not assume that a diet is ketogenic simply because it is described as low-carbohydrate.

13. Mechanistic plausibility is not a substitute for clinical proof

Lower glucose exposure, lower insulin demand, increased fatty-acid oxidation, ketone signaling, fiber fermentation, and replacement of saturated fat with unsaturated fat are all biologically plausible pathways. But mechanistic plausibility cannot establish the magnitude of a clinical effect, long-term safety, or comparative superiority.

14. How the 2026 review changes the picture

A 2026 systematic review of plant-based low-carbohydrate and ketogenic evidence suggests that this combined research area is beginning to form a recognizable clinical literature. At the same time, the review emphasizes heterogeneity in diet definitions and adherence. The update strengthens the case for further trials rather than closing the question.

15. The decisive trial still needs to be done

An ideal long-term trial would compare a whole-food plant-based diet, a conventional ketogenic diet, and a plant-based ketogenic diet for at least 12 months, preferably with longer follow-up. Primary outcomes should include HbA1c and medication burden. Key secondary outcomes should include CGM time-in-range, weight, visceral fat, fasting insulin, ApoB, kidney function, nutritional adequacy, body composition, quality of life, and adherence. Ketosis should be measured repeatedly rather than assumed from the menu.

16. Four evidence phrases used in this book

This book distinguishes “supported,” “likely/conditional,” “possible,” and “requires direct testing.” These terms are not rhetorical decoration; they are used to match the strength of the sentence to the strength and directness of the evidence.

17. Current conclusion: strong enough to study and use carefully, not strong enough to exaggerate

The evidence justifies a cautious clinical framework and a serious research agenda. It does not justify declaring a plant-based ketogenic diet the universal answer to type 2 diabetes.

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- Riddle, M. C., et al. (2021). Consensus report: definition and interpretation of remission in type 2 diabetes.
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- Mazzola, G., et al. (2026). Plant-based low-carbohydrate and ketogenic diets: systematic review of clinical evidence.
- American Diabetes Association Professional Practice Committee. (2026). Standards of Care in Diabetes-2026.

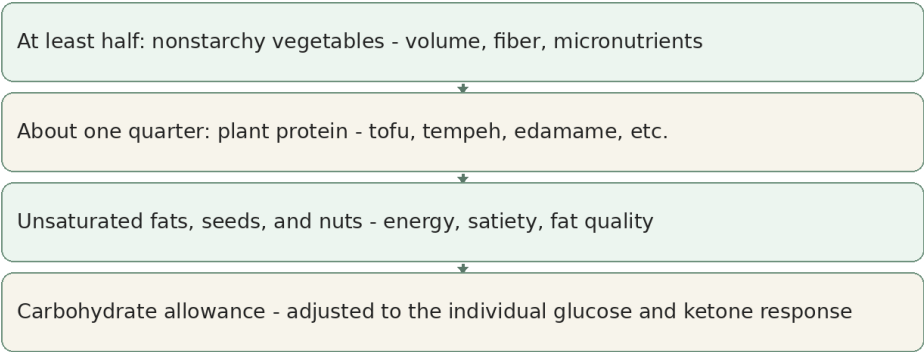
Chapter 16. What Should You Eat?

Food selection becomes easier when each food is assigned a role instead of being divided into a simplistic list of “allowed” and “forbidden” items. A well-designed plant-based ketogenic meal needs volume, protein, unsaturated fat, fiber, micronutrients, and a carbohydrate load appropriate for the person's metabolic target.

1. Ask what a food does in the meal

The practical plate starts with nonstarchy vegetables, adds a clear plant-protein anchor such as tofu or tempeh, then adds measured nuts, seeds, avocado, olives, or unsaturated oil. Legumes, berries, and other whole-food carbohydrates can be titrated according to glucose and ketone response.

Figure 16-1. Basic structure of one plant-based ketogenic meal



Source: ADA (2026) food-based nutrition principles and the book working model; author synthesis.

2. Nonstarchy vegetables form the base

Leafy greens, broccoli, cabbage, mushrooms, zucchini, and similar vegetables provide bulk and micronutrients with relatively low carbohydrate density. Their role is not merely to “fill space”; they protect food variety and fiber intake when grains and starchy foods are reduced.

3. Cruciferous vegetables offer more than low carbohydrate

Broccoli, cabbage, cauliflower, and related vegetables contribute fiber, potassium, folate, vitamin C, and phytochemicals. They should not be sold as medicines, but they are useful whole foods in a diet designed for high nutrient density.

4. Mushrooms add volume and savory flavor

Mushrooms are low in energy density and can replace some of the sensory role usually provided by animal products or processed sauces. This makes a plant-based low-carbohydrate pattern easier to sustain without relying on concentrated fats.

5. Sea vegetables are better used in small, varied portions

Nori, wakame, and kelp can increase mineral and culinary diversity, but seaweed is not a “more is better” food. Iodine and sodium exposure vary greatly, so portion size matters.

6. Tofu is the easiest default protein anchor

Firm tofu is relatively low in carbohydrate and provides substantial high-quality soy protein. It can be grilled, braised, stir-fried, or added to soups and hot pots. It should be viewed as a main protein component rather than a decorative side dish.

7. Tempeh is protein dense, but carbohydrate still counts

Tempeh provides a firm texture and high protein density, but its carbohydrate content is generally higher than that of firm tofu. Portioning is therefore more important in a strict ketogenic phase.

8. Edamame and legumes are used with measured portions

Edamame is often easier to fit into a stricter low-carbohydrate pattern because it combines protein and fiber with a moderate carbohydrate load. Lentils, chickpeas, and beans remain nutritionally valuable but may need smaller portions during a strict phase and can often be expanded later if glucose remains stable.

9. Nuts are both fat foods and protein foods

Almonds, walnuts, pecans, and macadamias provide unsaturated fat, protein, fiber, magnesium, and other nutrients. Because they are energy dense, portions should be measured rather than treated as unlimited snacks.

10. Seeds add fiber and fat in small amounts

Chia, flax, hemp, sesame, and perilla can strengthen the fatty-acid and fiber profile of a meal. Ground flax is often more practical than whole flax, and chia should be taken with adequate fluid because of its high water-binding capacity.

11. Avocado and olives improve fat quality

Avocado supplies unsaturated fat together with fiber. Olives can serve a similar culinary role but may contain substantial sodium. Both illustrate why fat quality can be improved through whole foods rather than by adding oil alone.

12. Oils should not displace whole foods

Olive, canola, avocado, soybean, and other unsaturated plant oils can be useful for cooking and dressings. But oils contain energy without the fiber and protein of whole plant foods. They should be measured and used to support a meal, not to become the meal.

13. Fruit is managed by type and portion

Fruit is not metabolically identical to juice or sweets. Berries and small portions of lower-sugar fruit may fit in many maintenance plans. The correct amount depends on glucose response, carbohydrate target, and whether nutritional ketosis remains a specific goal.

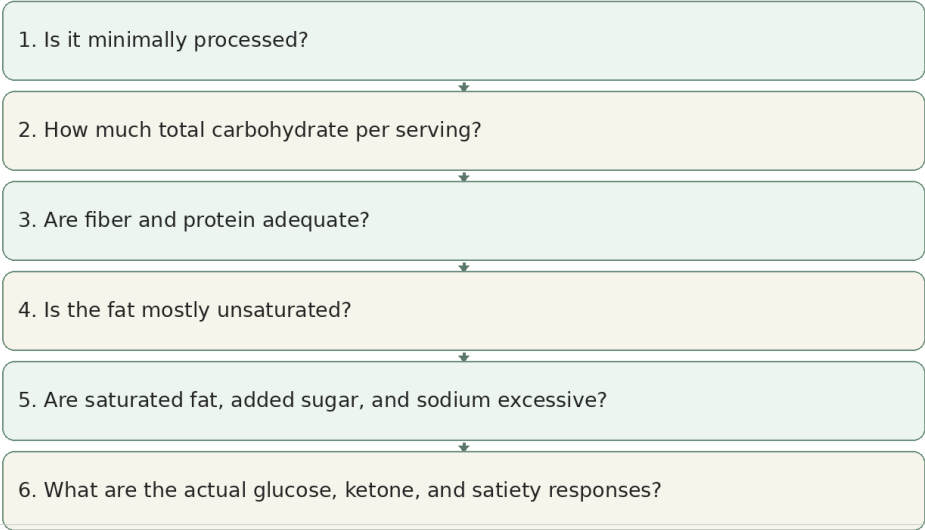
14. A Korean-style meal can make the pattern more sustainable

A practical Korean meal can be built around seasoned leafy vegetables, mushrooms, tofu, seaweed, kimchi or other fermented vegetables without added sugar, measured nuts or seeds, and a controlled serving of whole-food carbohydrate when appropriate. The best pattern is one that can be repeated in the user's actual food culture.

15. Read labels in a consistent order

Start with serving size, then total carbohydrate, fiber, protein, total and saturated fat, and sodium. Front-label claims such as “keto,” “low carb,” or “vegan” are secondary. Added sugar, starches, concentrated oils, and ultra-processed ingredients can transform the metabolic profile of a product.

Figure 16-2. Six-step sequence for selecting foods



Source: ADA (2026) nutrition therapy and the book personalization framework; author synthesis.

16. A repeatable meal structure matters more than a perfect food list

A sustainable plant-based ketogenic diet does not require remembering hundreds of food rules. It requires a repeatable template: vegetables first, a plant-protein anchor, measured unsaturated fats, adequate fiber and fluids, and a carbohydrate amount adjusted to the person's real metabolic response.

Sources and References

Key chapter sources

- American Diabetes Association Professional Practice Committee. (2026). Standards of Care in Diabetes-2026: minimally processed foods, plant proteins, fiber, and fat quality.
- USDA FoodData Central nutrient data for tofu, tempeh, nuts, seeds, legumes, and plant oils.
- NIH Office of Dietary Supplements fact sheets for micronutrient adequacy.

Chapter 17. Choosing Fat - What Kind Matters More Than How Much

A ketogenic diet changes the proportion of energy coming from fat, so fat quality becomes a central safety issue. “Fat” is not one nutrient with one effect. Saturated, monounsaturated, polyunsaturated, and trans fats differ in structure, food sources, and cardiometabolic implications.

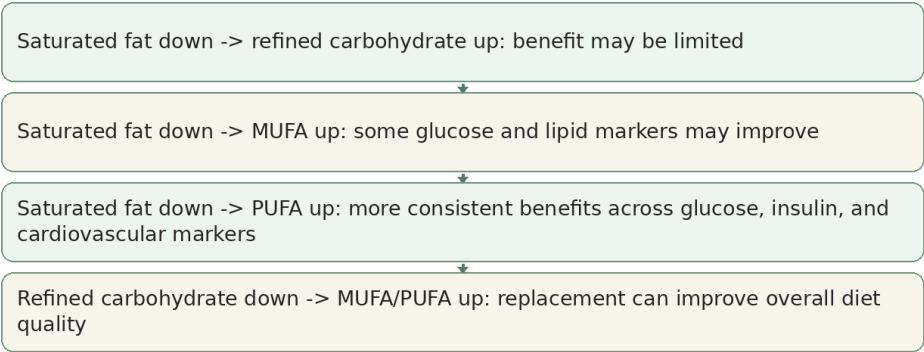
1. Fat is not a single nutrient

Saturated fatty acids have no double bonds and are abundant in coconut and palm oils as well as many animal foods. Monounsaturated fats, especially oleic acid, are prominent in olive oil, avocado, almonds, and macadamias. Polyunsaturated fats include linoleic acid and alpha-linolenic acid (ALA) and are found in walnuts, seeds, soybean, canola, flax, chia, and perilla. Industrial trans fats should be avoided as much as possible.

2. Replacement matters more than simple addition

The metabolic effect of a fat depends partly on what it replaces. Randomized feeding evidence shows that replacing some carbohydrate or saturated fat with unsaturated fat can improve selected glucose-insulin markers. This is why “eat more fat” is an incomplete instruction.

Figure 17-1. The effect of fat depends on what replaces what



Source: Imamura et al. (2016); ADA (2026) nutrient-replacement principles; author synthesis.

3. MUFA is a practical foundation

Monounsaturated-fat-rich foods are useful because they can raise the fat content of a low-carbohydrate meal without requiring a high saturated-fat intake. Olive oil, avocado, almonds, and other nuts are therefore practical default sources.

4. Olive oil can be a main culinary oil, but not unlimited

Olive oil is compatible with a plant-based ketogenic pattern and supports replacement of saturated fat. Yet all oil is energy dense. The appropriate amount depends on body-weight goals, satiety, and the overall diet.

5. Avocado provides fat and fiber together

Compared with pure oil, avocado provides water, fiber, potassium, and other nutrients. It illustrates a recurring principle of this book: when possible, whole-food fat sources offer more nutritional structure than isolated fat.

6. PUFA supplies essential fatty acids and can support metabolic health

Polyunsaturated fats include the essential omega-6 and omega-3 families. Their value should be considered in the context of replacement: replacing saturated fat with PUFA is generally more favorable than replacing saturated fat with refined carbohydrate.

7. Omega-6 is not automatically an “inflammatory fat”

Human intervention studies do not support the simplistic claim that higher linoleic-acid intake automatically raises systemic inflammatory markers. Omega-6 fatty acids are essential. The practical aim is adequate essential-fat intake and overall food quality, not fear of one family of unsaturated fats.

8. Plant omega-3 begins with ALA

Flax, chia, walnuts, canola, soybean, and perilla are useful ALA sources. For example, NIH food-source tables report high ALA content in flaxseed oil and meaningful amounts in chia, walnuts, and flaxseed.

9. Conversion of ALA to EPA and DHA is limited

Humans can convert ALA to longer-chain omega-3 fatty acids, but the conversion is limited, and conversion to DHA is particularly low. People following a strictly plant-based diet who want a direct EPA/DHA source can consider algal oil according to individual needs and clinical context.

10. Do not chase a single omega-6:omega-3 ratio

No universal optimal omega-6:omega-3 ratio has been established for all people. A ratio can look favorable even when both fatty-acid families are consumed in inadequate amounts. This book may use lower ratios as illustrative meal-design examples, but not as a universal medical target. Absolute intake, food sources, saturated fat, and overall dietary quality matter more.

11. Saturated fat is not exempt because it comes from plants

Coconut and palm oils are plant-derived but rich in saturated fat. A plant-based ketogenic diet should therefore not use “plant-based” as a reason to ignore LDL-C or ApoB. If these markers rise meaningfully, fat sources and total fat intake should be reassessed.

12. Avoid industrial trans fat

Industrial trans fat has no useful role in a therapeutic diet and can worsen the lipoprotein profile. Ultra-processed “keto” snacks can still contain poor-quality fats and should not become dietary staples.

13. Nuts and seeds provide more than oil

Nuts and seeds provide protein, fiber, magnesium, phytochemicals, and fatty acids in the same food matrix. This makes them useful in small measured portions, although their high energy density still matters.

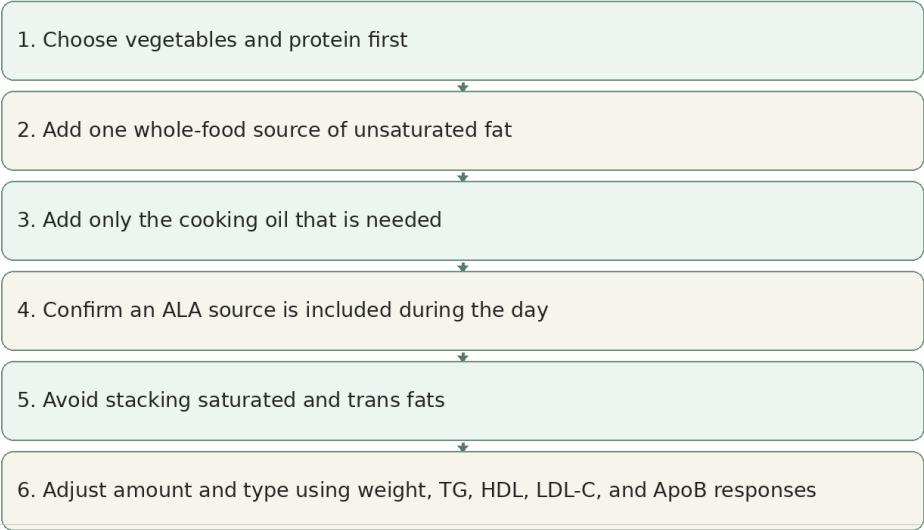
14. Heat, oil type, and cooking duration all matter

Cooking practice should match the oil and temperature. The goal is not to fear all heating but to avoid repeated overheating and degraded cooking fats. Whole-food preparation methods such as steaming, simmering, and quick sautéing can reduce reliance on large amounts of oil.

15. A practical fat hierarchy

The default order is: whole-food unsaturated fat sources such as avocado, nuts, seeds, and olives; measured unsaturated oils for cooking; regular ALA-rich foods such as flax, chia, walnuts, and perilla; optional algal EPA/DHA when appropriate; limited use of coconut and palm oils; and avoidance of industrial trans fat.

Figure 17-2. Six-step fat-selection process for a meal



Source: ADA (2026); NIH ODS; Imamura et al. (2016); author personalization framework.

16. Blood lipids help answer whether the strategy fits the person

Do not interpret one lipid marker in isolation, but do not dismiss LDL-C or ApoB either. Triglycerides may fall and HDL-C may rise on a ketogenic diet while LDL-C or ApoB rises in some individuals. Improvements in TG or HDL-C should not be assumed to cancel a meaningful rise in atherogenic lipoprotein burden. Final fat selection should be guided by the combined picture of body weight, glycemia, TG, HDL-C, LDL-C, ApoB, kidney and liver status, and cardiovascular risk.

Special note on medium-chain triglycerides

C8 and C10 medium-chain triglycerides are absorbed and delivered to the liver predominantly through the portal circulation more directly than long-chain fats. Coconut oil, which contains a large proportion of lauric acid (C12), should not be treated as equivalent to purified C8/C10 MCT oil. MCT can be used selectively when there is a clear purpose, but it is not a required foundation of a plant-based ketogenic diet.

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Key chapter sources

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- NIH Office of Dietary Supplements. Omega-3 Fatty Acids Fact Sheet for Health Professionals.

Chapter 18. Designing Plant Protein - Enough, Distributed, and Matched to Kidney Function

In a plant-based ketogenic diet, protein is not simply the nutrient that fills the space left by carbohydrate restriction. It supplies amino acids for muscle, enzymes, transport proteins, immune function, and tissue repair, but the required amount varies with age, body size, energy intake, physical activity, and kidney function. The practical question is therefore not "How much protein can I eat?" but **How much is needed, which foods should supply it, and how should it be distributed across the day?**

1. The goal is not "as much protein as possible"

ADA 2026 does not establish one ideal protein intake for every person with diabetes. General intakes are often individualized within a broad range around 0.8-1.5 g/kg/day or roughly 15-20% of energy, but the appropriate target depends on body composition, age, activity, energy restriction, and kidney status. A value such as 1.5 g/kg should never be treated as a universal goal.

Table 18-1. A practical framework for protein targets

Situation	Common evidence-based range	Main interpretation	Plant-keto principle
General adult with diabetes	Individualize, often within 0.8-1.5 g/kg/day	No single optimal dose is established	Adjust with body weight, muscle, and total energy
Older adult	At least about 0.8 g/kg/day; sometimes more if clinically appropriate	Muscle preservation matters	Distribute protein across meals
CKD G3 or higher, not on dialysis	About 0.8 g/kg/day	Avoid excessive high-protein intake	Kidney function and albuminuria take priority
Dialysis	About 1.0-1.2 g/kg/day may be considered	Protein-energy wasting risk is higher	Renal nutrition guidance takes priority

2. Protein is a package of amino acids

Dietary proteins are digested into amino acids. Essential amino acids must be supplied by food. Protein quality therefore depends not only on the total number of grams but also on indispensable amino-acid composition and digestibility. Plant proteins differ from one another: soy is relatively high in quality, while grains, seeds, and legumes can have more pronounced limiting amino acids.

3. DIAAS asks what happens after counting grams

The Digestible Indispensable Amino Acid Score (DIAAS) estimates protein quality from ileal digestibility of individual indispensable amino acids. It is useful, but it is not a complete measure of the healthfulness of a food or diet. Processing and cooking can materially change digestibility, and many plant foods still lack robust DIAAS data.

4. Soy foods are practical protein anchors

Firm tofu and tempeh are particularly useful because they combine relatively high protein density with a lower carbohydrate burden than most grains and many legumes. Firm tofu commonly provides around 17 g protein per 100 g and cooked tempeh around 20 g, although products vary. Soy protein quality is also relatively high among plant foods.

Table 18-2. Protein foods that fit easily into plant-based ketogenic meals

Food	Approximate protein	Carbohydrate feature	Practical role
Firm tofu	~17 g/100 g	Relatively low	Main protein
Tempeh	~20 g/100 g	Higher than tofu but manageable	Main protein
Edamame	~12 g/100 g	Fiber-containing carbohydrate	Side dish or salad protein
Almonds	~21 g/100 g	High fat and energy	Supplemental protein and fat
Chia, flax, hemp	Varies	Fiber and fat accompany protein	Small nutrient-dense addition

5. Nuts and seeds are usually supplements, not the main protein

Nuts and seeds provide useful protein, but they are often more energy dense than soy foods. Using 100 g of nuts to obtain 20 g of protein can add a large energy load. In a weight-loss program they work better as measured complements to tofu, tempeh, or edamame.

6. Legumes use part of the carbohydrate budget

Lentils, chickpeas, and beans are excellent foods in many plant-based patterns, but they can be difficult to fit in large portions during a strict ketogenic phase. Soybeans and edamame are generally easier to use. As carbohydrate tolerance expands, carefully measured portions of other legumes can be reintroduced.

7. Leucine is one signal for muscle protein synthesis

Leucine participates in signaling related to muscle protein synthesis, but leucine alone does not build muscle. Total essential amino acids, adequate energy, and resistance exercise are also necessary. Studies of well-formulated plant-protein blends suggest that sufficient total protein and leucine can produce post-exercise responses approaching those of whey, but supplement studies should not be converted into rigid food rules.

8. Plant and animal proteins differ, but the difference is conditional

Recent meta-analyses suggest small average differences in muscle outcomes, with greater uncertainty in older adults. Importantly, direct soy-versus-milk comparisons often show little or no significant difference in muscle or strength outcomes when total protein and training are adequate. The practical message is to improve total intake, protein quality, meal distribution, and exercise rather than to label all plant protein as inferior.

Table 18-3. How to read recent muscle evidence

Evidence	Main finding	Reasonable conclusion
MPS meta-analysis	Small overall difference; uncertainty remains	Source can matter, especially with aging, but dose and context matter too
RCT meta-analysis of muscle mass	Plant protein slightly lower overall; soy vs milk often similar	Soy is a strong plant-protein option
Pea vs whey resistance-training RCT	Similar strength and muscle changes in healthy adults	Adequate plant protein can support training adaptation
Plant-protein blend reviews	Well-designed blends can approach whey responses	Composition and dose matter

9. Distribution across meals matters

A daily total of 70 g is not metabolically identical to 5 g at breakfast, 15 g at lunch, and 50 g at dinner. Especially in older adults, each meal should contain a meaningful protein dose. A simple practical rule in this book is to distribute the daily target across two or three meals rather than concentrate it at one meal.

10. In older adults, preserve muscle while losing fat

Rapid weight loss can reduce both fat and lean tissue. Older adults should therefore monitor strength, function, and, when available, body composition. The aim is not the highest ketone value; it is better metabolic control while preserving muscle and physical capacity.

11. Resistance exercise is a key partner

Resistance exercise stimulates muscle protein synthesis and works together with protein intake. Plant protein is more likely to support muscle when total intake and training are planned together. Walking remains useful for glucose control, but resistance and weight-bearing exercise deserve a deliberate place in the program.

12. Plant protein changes more than amino-acid intake

Tofu, soybeans, legumes, nuts, and seeds usually deliver unsaturated fat, fiber, minerals, and phytochemicals as part of the same food matrix. In trials that replace some animal protein with plant protein, the observed effect therefore reflects a change in the whole food package, not amino acids alone.

13. Soy does not produce identical glycemic effects in every study

Some reviews report favorable fasting-glucose or insulin-resistance signals from whole soy foods, whereas HbA1c effects are less consistent. The strongest reason to use soy in a plant-based ketogenic diet is therefore practical: it makes protein adequacy easier with a relatively low carbohydrate burden. Any additional glycemic effect should be treated as possible rather than guaranteed.

14. Kidney impairment changes the protein strategy

For people with CKD G3 or higher who are not on dialysis, ADA guidance supports a protein intake near 0.8 g/kg/day and cautions against excessive high-protein intake. Going far below this level is not automatically beneficial and can create malnutrition risk. Dialysis changes the direction of the problem because protein-energy wasting becomes more important.

Table 18-4. Adjusting protein by kidney status

Domain	Preserved kidney function	CKD G3+ without dialysis	Dialysis
Protein target	Individualize	~0.8 g/kg/day	~1.0-1.2 g/kg/day may be considered
Main checks	Weight, activity, muscle,	eGFR, potassium, UACR, nutrition	Protein-energy wasting, dialysis losses
Avoid	Automatic high-protein intake	Excess >1.3 g/kg/day	Excessive protein restriction

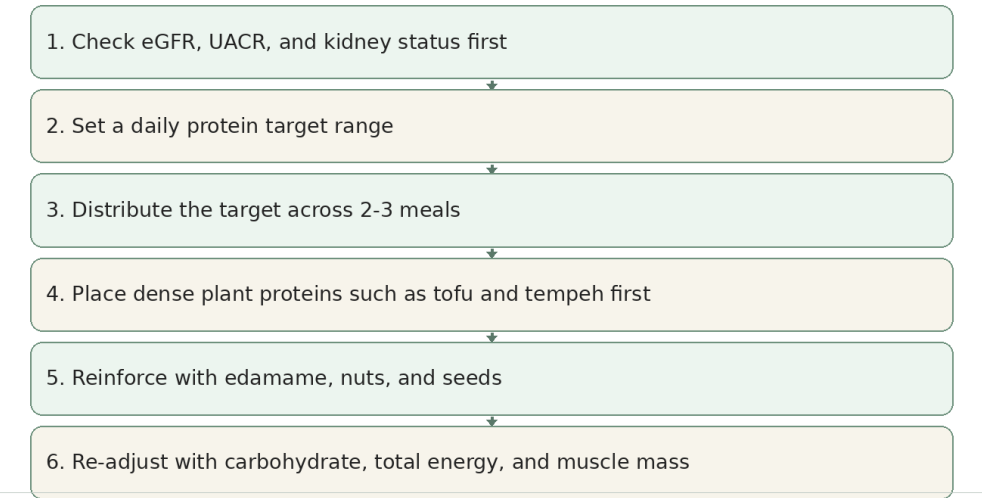
15. Potassium and phosphorus also matter in CKD

Plant foods can contain substantial potassium and phosphorus. For people with normal kidney function this is usually not a problem, but advanced CKD or hyperkalemia requires individualized food selection. "Plant-based" is not a substitute for laboratory monitoring.

16. A 70-kg example makes the arithmetic concrete

At 0.8 g/kg/day, a 70-kg adult would receive about 56 g protein; at 1.0 g/kg/day, 70 g; at 1.2 g/kg/day, 84 g. These are examples, not prescriptions. Obesity, low body weight, older age, athletic training, and CKD can make simple multiplication inappropriate.

Figure 18-1. Sequence for designing daily protein in a plant-based ketogenic diet

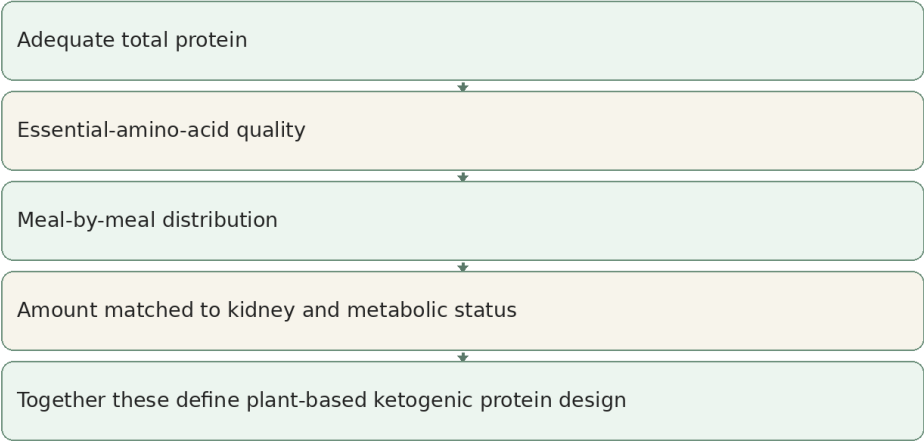


Source: ADA (2026) protein, CKD, and older-adult guidance; author synthesis.

17. Protein foods bring other macronutrients with them

Tofu brings protein and fat. Nuts bring protein, unsaturated fat, and substantial energy. Legumes bring protein, fiber, and carbohydrate. Therefore the same 20 g of protein can have very different effects on carbohydrate, fat, fiber, and total energy.

Figure 18-2. Good protein design aligns four factors at once



Source: ADA (2026); FAO/DIAAS reviews; 2025-2026 plant-protein muscle meta-analyses; author synthesis.

18. Choose a protein anchor first

In practice, start each meal with a main protein source - for example tofu, tempeh, or a soy-food combination - and then build vegetables and unsaturated fat around it. This ordering reduces the risk that carbohydrate restriction accidentally becomes protein restriction.

19. Protein powder is a tool, not a requirement

Soy, pea, or blended plant protein can be useful when food intake alone does not meet a target. Labels should be checked for sugar, starch, and additives. If whole foods already provide adequate protein and are well tolerated, supplementation is unnecessary.

20. The final test includes muscle and kidneys, not glucose and ketones alone

A protein plan is not successful if body weight falls while strength and lean mass collapse, or if protein is increased while kidney markers worsen. Follow-up can include body weight, waist circumference, glycemia, strength and activity, and, when clinically relevant, creatinine, eGFR, and UACR. The guiding principle is simple: **enough but not excessive, centered on protein-dense plant foods, distributed through the day, and adjusted to muscle and kidney status.**

Selected references

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- FAO/DIAAS reference framework and reviews of plant-protein quality.
- Recent systematic reviews and meta-analyses of plant protein and muscle outcomes.

Chapter 19. How Much Carbohydrate? - Read the Response, Not Just the Number

Carbohydrate restriction is not a competition to reach the lowest possible number. The useful intake is the lowest amount necessary to achieve the intended metabolic goal **without sacrificing food quality, safety, or long-term adherence**. The same nominal carbohydrate intake can produce different glucose and ketone responses in different people.

1. Begin with total carbohydrate as the baseline

Total carbohydrate is a reproducible starting point because it is listed on food labels and nutrient databases. "Net carbohydrate" is widely used in ketogenic communities but is not a single standardized clinical definition. This book therefore records total carbohydrate first and then interprets fiber and other components separately.

Table 19-1. Distinguishing carbohydrate terms

Term	What it means	Main caution
Total carbohydrate	All carbohydrate listed in the food	Best baseline for consistent tracking
Dietary fiber	Non-digestible carbohydrate fractions	Metabolic effect differs from sugars and starch
Net carbs	Informal subtraction method	Not an official universal regulatory/clinical term
Available carbohydrate	Digestible carbohydrate concept used in some research	Definition varies by method

2. Fiber is carbohydrate, but it does not behave like refined starch or sugar

Fiber can slow digestion, alter postprandial glucose, support bowel function, and influence the gut microbiome. A very-low-carbohydrate diet that becomes very-low-fiber because vegetables, seeds, nuts, and selected legumes disappear is poorly designed.

3. GI and GL provide information that grams alone cannot

Glycemic index describes the relative glucose response to a fixed amount of available carbohydrate. Glycemic load incorporates both quality and quantity. Neither replaces direct glucose monitoring in an individual, but both remind us that 20 g of carbohydrate from refined starch is not metabolically equivalent to 20 g from a high-fiber whole-food source.

Table 19-2. Quantity and quality answer different questions

Question	Quantity lens	Quality lens
How much carbohydrate?	g/day, g/meal	-
How quickly may glucose rise?	Portion size	GI, processing, meal composition
What else comes with it?	Calories	Fiber, micronutrients, food matrix

4. Low-carbohydrate and ketogenic are not synonyms

Research definitions vary. Low-carbohydrate diets may provide well above 50 g/day and may not produce nutritional ketosis. Ketogenic diets are generally stricter and are often designed to produce measurable ketones. The presence of a low carbohydrate number does not prove that ketosis has occurred.

Table 19-3. Reading carbohydrate-restriction categories in research

Pattern	Typical description	research	Ketosis required?
Moderate carbohydrate reduction	Below conventional intake		No
Low carbohydrate	Often <26% energy or <130 g/day		No
Very low carbohydrate	Often around 20-50 g/day		Often intended, but must be measured if claimed
Ketogenic	Very low carbohydrate plus physiology compatible with ketosis		Prefer direct ketone confirmation

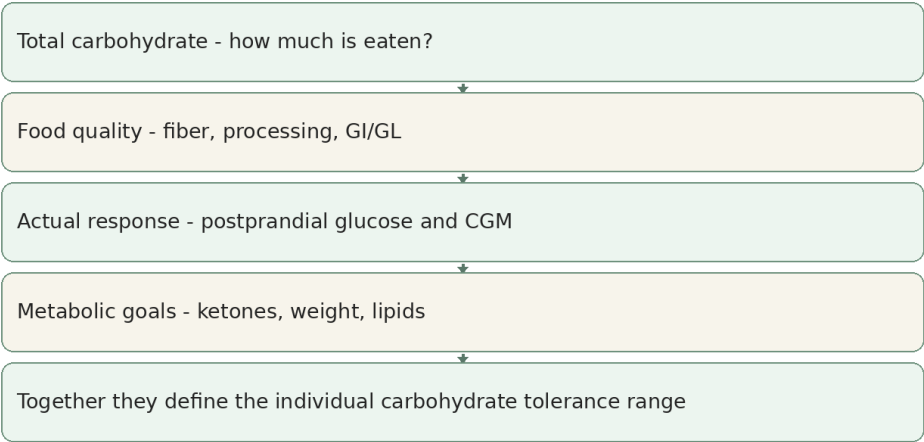
5. The often-cited 20-50 g/day range is a starting range, not a prescription

Many ketogenic trials use carbohydrate intakes in this range. That does not mean every person needs to remain there indefinitely. Some people reach their clinical goals with more carbohydrate, while others require stricter restriction. Medication use, body size, activity, insulin secretion, and food quality all matter.

6. The same food can produce different postprandial responses

Interindividual glucose responses can differ because of gastric emptying, insulin secretion, insulin sensitivity, sleep, activity, prior meals, and the gut microbiome. Personal glucose data therefore add information beyond generic food lists.

Figure 19-1. Four inputs that define an individual carbohydrate tolerance range



Source: ADA (2026); Zeevi et al. (2015); Gardner et al. (2022); author synthesis.

7. Carbohydrate per meal matters as much as the daily total

Sixty grams spread as 20 g at each of three meals may produce a different glucose curve from 50 g concentrated at one meal. This is especially important for people using insulin or insulin secretagogues. Fat and protein can also delay postprandial glucose, so a single one-hour value can miss a later rise.

8. The induction and maintenance phases do not need the same carbohydrate level

A stricter early phase can make metabolic response easier to observe, but maintenance should seek the broadest food range compatible with the person's goals and safety. As glucose stabilizes, small amounts of high-quality carbohydrate can be tested systematically.

Table 19-4. A staged carbohydrate-adjustment model

Stage	Main purpose	Carbohydrate approach
Initial	Reduce glycemic load and observe adaptation	More structured restriction
Stabilization	Confirm glucose, ketone, weight, symptoms	Hold intake steady enough to interpret patterns
Reintroduction	Test tolerance	Add one high-quality source at a time
Maintenance	Maximize sustainability	Use the highest tolerable amount consistent with goals

9. Decide whether ongoing ketosis is actually necessary

For some people, short-term nutritional ketosis is a useful tool; for others, stable glucose control on a plant-based low-carbohydrate pattern may be sufficient. Higher ketones are not the primary endpoint. Clinical outcomes and safety outrank a ketone target.

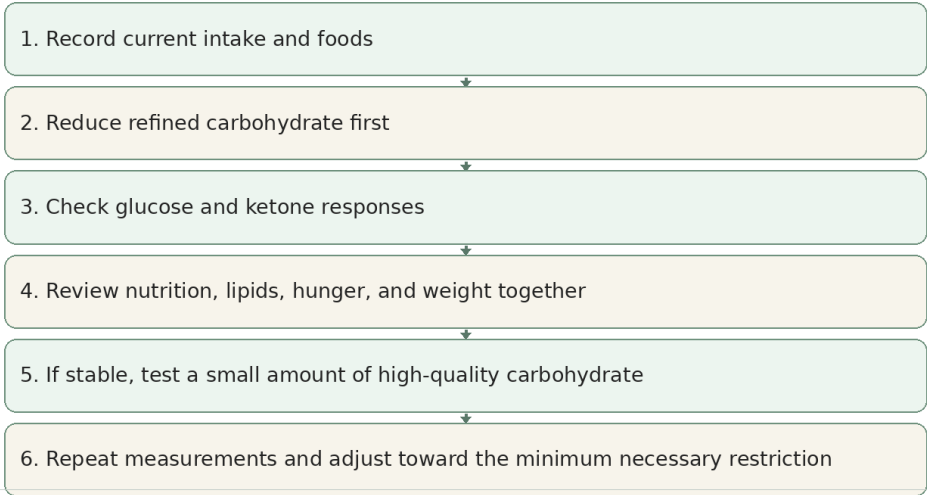
10. With glucose-lowering medication, the rate of carbohydrate reduction is part of treatment

Rapid restriction can increase hypoglycemia risk in people using insulin, sulfonylureas, or meglitinides. SGLT2 inhibitors introduce a different concern: very-low-carbohydrate intake and prolonged fasting can increase DKA risk in susceptible users. Dietary change and medication review must therefore be coordinated.

11. A practical sequence for finding the personal range

Start with baseline carbohydrate and glycemia. Reduce refined carbohydrate first. Set a structured initial range. Monitor fasting and postprandial glucose, medication needs, body weight, symptoms, and ketones when clinically useful. Then adjust in small steps rather than making repeated large changes.

Figure 19-2. Iterative cycle for finding carbohydrate tolerance



Source: ADA (2026); Zeevi et al. (2015); Gardner et al. (2022); response-based model in this book.

12. Conclusion - the best amount is not the lowest amount

The useful carbohydrate target is the amount that supports glycemic control, adequate nutrition, medication safety, lipid and kidney goals, muscle preservation, and long-term adherence. **The number is a tool; the response is the decision.**

Selected references

American Diabetes Association Professional Practice Committee. (2026). Standards of Care in Diabetes-2026, Section 5. Gardner, C. D., et al. (2022). Keto-Med randomized crossover trial. American Journal of Clinical Nutrition, 116(3), 640-652. Tay, J., et al. (2015, 2018). Randomized trials of low-carbohydrate, high-unsaturated-fat diets in type 2 diabetes.

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Chapter 20. What to Check Before Starting - Baselines Make Change Visible

A dietary intervention is difficult to interpret without a baseline. Before starting a plant-based ketogenic program, record the variables that are most likely to change and the variables that define safety. The purpose is not to order every possible test; it is to create a reference point for later decisions.

1. HbA1c and glucose establish the glycemic starting point

HbA1c summarizes average glycemia over weeks to months, while fasting and postprandial glucose reveal different time windows. CGM, when available, adds time in range, time below range, and variability. Baseline measurement helps distinguish true improvement from normal day-to-day variation.

Table 20-1. Core glycemic and metabolic baseline measures

Measure	What it contributes	Why it matters later
HbA1c	Longer-term glycemia	Main comparison at follow-up
Fasting glucose	Overnight hepatic glucose regulation	Detects fasting improvement or deterioration
Postprandial glucose/CGM	Meal response and variability	Helps adjust meal composition and medication
Body weight/waist	Adiposity and central fat	Links metabolic change with weight trajectory

2. Fasting insulin and HOMA-IR can add context

Fasting insulin and HOMA-IR are not required for every person, but they can help characterize insulin resistance in selected settings. They should be interpreted as research or adjunctive markers rather than as stand-alone diagnostic targets.

3. C-peptide is not a routine test for everyone

C-peptide can be useful when insulin secretory capacity or diabetes classification is uncertain, but it is not necessary for every person beginning dietary therapy. Clinical context determines whether it adds useful information.

4. Kidney assessment should include eGFR and UACR

Serum creatinine and eGFR estimate filtration, whereas urine albumin-to-creatinine ratio (UACR) detects albuminuria. Both matter because protein targets, medication choices, potassium management, hydration, and the safety of very-low-carbohydrate eating can change with CKD.

Table 20-2. Kidney, liver, and electrolyte checks

Domain	Common measures	Main question
Kidney filtration	Creatinine, eGFR	Is filtration reduced?
Kidney damage	UACR	Is albuminuria present?
Liver	AST, ALT; clinical fibrosis assessment when indicated	Is fatty liver or advanced fibrosis likely?
Electrolytes	Sodium, bicarbonate as potassium, clinically indicated	Is fluid/electrolyte balance safe?

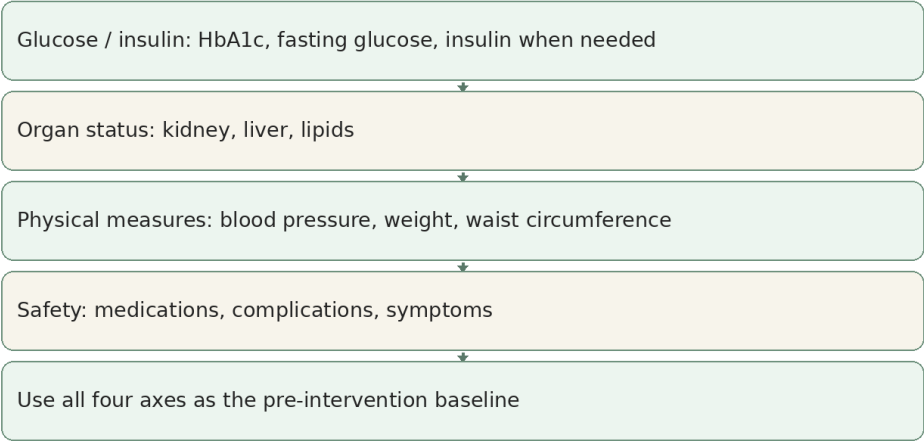
5. Liver assessment can reveal metabolic fatty liver

Fatty liver is common in insulin resistance and type 2 diabetes. Liver enzymes alone do not perfectly identify steatosis or fibrosis. When clinically appropriate, FIB-4 and imaging can add information. A baseline is useful because weight loss and glycemic improvement can change liver markers over time.

6. Lipid testing should not stop at LDL-C

A standard lipid panel includes total cholesterol, LDL-C, HDL-C, and triglycerides. Non-HDL-C and, when clinically indicated, ApoB can provide additional information about atherogenic particle burden. This becomes especially important if carbohydrate restriction improves triglycerides but LDL-C rises.

Figure 20-1. Four baseline axes before starting



Source: ADA Standards of Care in Diabetes-2026; author synthesis.

7. Blood pressure, weight, and waist circumference matter outside the laboratory

Blood pressure may fall as weight, insulin levels, sodium handling, and fluid balance change. This can be beneficial, but people using antihypertensive or diuretic medication can develop dizziness or symptomatic hypotension if changes occur quickly.

Table 20-3. Physical and cardiovascular baseline

Measure	Record before starting	Follow-up purpose
Blood pressure	Seated readings, medication list	Detect improvement or hypotension
Weight	Same scale and conditions when possible	Track trend, not single-day noise
Waist circumference	Standardized location	Track central adiposity
Strength/activity	Simple functional baseline	Protect muscle during weight loss

8. The medication list is as important as the laboratory panel

Record generic name, dose, timing, and indication. Insulin, sulfonylureas, and meglitinides raise hypoglycemia risk when carbohydrate falls. SGLT2 inhibitors require special attention to DKA risk. GLP-1 receptor agonists may reduce appetite and energy intake, which can interact with the dietary intervention. Heart- and kidney-protective indications should not be ignored simply because HbA1c improves.

Table 20-4. Medication safety review before carbohydrate restriction

Medication group	Main issue when diet changes
Insulin	Hypoglycemia; dose may require clinician-led adjustment
Sulfonylurea/meglitinide	Hypoglycemia risk increases as carbohydrate falls
SGLT2 inhibitor	DKA risk with very-low-carbohydrate intake, fasting, illness, dehydration
GLP-1-based therapy	Appetite and intake may fall substantially
Antihypertensive/diuretic	Blood pressure and volume status may change

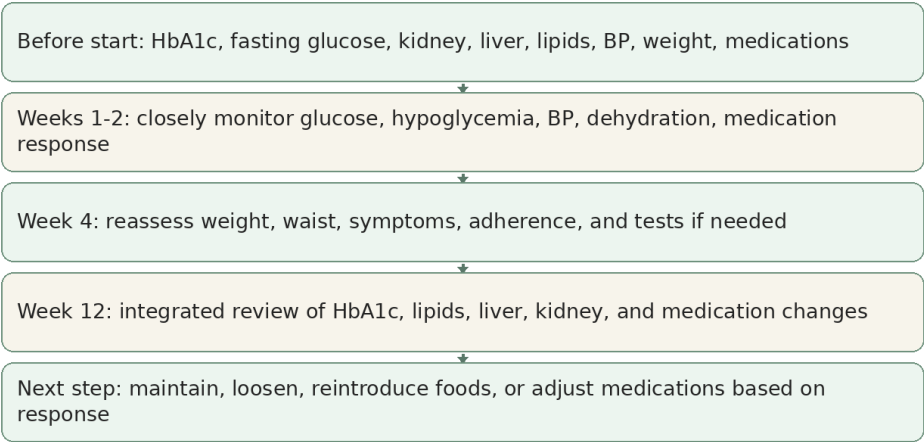
9. Eyes, feet, and neuropathy should not be forgotten

Dietary improvement does not erase existing microvascular disease. Retinopathy, neuropathy, and foot risk remain clinically relevant, especially when glucose changes rapidly. Baseline complications help determine appropriate follow-up.

10. Create a one-page baseline sheet

A useful baseline sheet includes glycemia, weight and waist, blood pressure, lipids, kidney and liver markers, medications, relevant complications, and the current diet. Repeat the key domains at predetermined intervals rather than measuring randomly.

Figure 20-2. Basic monitoring flow from baseline to 12 weeks



Source: ADA Standards of Care in Diabetes-2026 follow-up principles; author synthesis.

The purpose of baseline assessment is simple: **know where the person started, identify risks before they become problems, and make later changes interpretable.**

Selected references

American Diabetes Association Professional Practice Committee. (2026). Standards of Care in Diabetes-2026, Sections 4-6, 9-11, and 13. KDIGO guidance on diabetes and chronic kidney disease. Clinical principles for cardiovascular and metabolic risk monitoring.

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- Muniyappa, R., et al. (2008). Current approaches for assessing insulin sensitivity and resistance in vivo.

Chapter 21. The First Four Weeks of Metabolic Transition - Do Not Rush Adaptation; Read the Response

The first month of carbohydrate restriction is not simply a waiting period before the "real" diet begins. Fluid balance, medication effect, appetite, bowel habits, glucose, ketones, and exercise tolerance can all change before HbA1c has had time to respond. The safest strategy is to observe patterns and adjust deliberately rather than to intensify restriction whenever a number is not changing fast enough.

1. Week 1 - fluid and medication can change before fuel use fully adapts

Lower carbohydrate intake reduces postprandial glucose and often lowers circulating insulin. Sodium and water handling may change, producing an early fall in body weight that is partly fluid rather than fat. People using glucose-lowering or blood-pressure medication can therefore experience clinically important changes within days.

Table 21-1. Common early changes and how to interpret them

Change	Possible explanation	What to check
Rapid weight loss	Glycogen and fluid loss, lower energy intake	Hydration, symptoms, longer-term trend
Dizziness	Lower blood pressure, dehydration, medication effect	BP, fluids, medication review
Headache/fatigue	Adaptation, low intake, dehydration, illness	Energy intake, sleep, electrolytes, red flags
Lower glucose	Desired dietary effect or excessive medication effect	Hypoglycemia risk and medication class
Constipation	Lower food volume/fiber/fluid	Vegetables, seeds, fluid, bowel pattern

2. Ketones are a signal, not the main goal

Blood beta-hydroxybutyrate can confirm that nutritional ketosis is occurring, but a higher ketone value does not automatically mean a better clinical result. Glucose, symptoms, medication safety, lipid response, kidney function, and sustainability remain more important outcomes.

3. The most important Week 1 safety issue is hypoglycemia

Insulin, sulfonylureas, and meglitinides can produce hypoglycemia when carbohydrate falls rapidly. Symptoms such as tremor, sweating, confusion, weakness, or unusual hunger require glucose assessment and appropriate treatment. Dietary restriction should never be pushed more aggressively while recurrent hypoglycemia is occurring.

Table 21-2. Red flags that must be distinguished from ordinary adaptation

Finding	Why it matters	Action
Recurrent or severe hypoglycemia	Medication-diet mismatch	Prompt clinical medication review
Persistent vomiting or severe abdominal pain	Possible acute illness or DKA	Urgent medical assessment
Rapid/deep breathing, marked weakness, dehydration	Possible metabolic acidosis	Urgent assessment, especially with SGLT2 use
Syncope or persistent symptomatic hypotension	Volume or medication problem	Medical review
Progressive inability to eat/drink	Dehydration and medication risk	Seek medical care

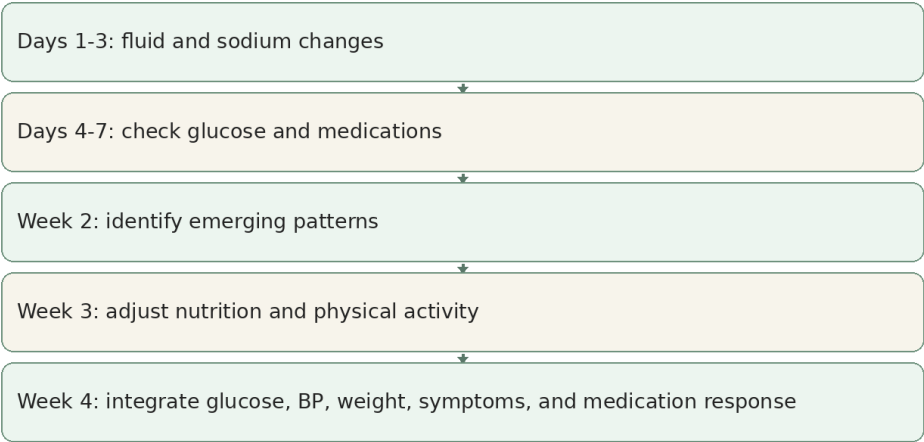
4. Week 2 - patterns become more informative than single values

By the second week, fasting glucose, postprandial glucose, hunger, energy level, bowel function, and body weight can be viewed as trends rather than isolated events. If CGM is available, time in range, time below range, nocturnal hypoglycemia, and variability are often more informative than one peak value.

5. Fluids and electrolytes should be matched to status, not maximized blindly

Very-low-carbohydrate eating can increase early sodium and water loss, but there is no universal instruction to consume unlimited salt. Blood pressure, kidney disease, heart failure, diuretic use, and symptoms all modify the appropriate response. Hydration and electrolytes should be individualized.

Figure 21-1. Four-week flow of fuel, fluid, and glucose adaptation



Source: natriuresis research in fasting/ketogenic diets; ADA (2026); 2025 keto-induction scoping review; author synthesis.

6. Week 3 - distinguish adaptation from undernutrition

Persistent fatigue, loss of strength, inadequate protein, very low energy intake, or progressive gastrointestinal symptoms should not be dismissed as "keto adaptation." A therapeutic eating pattern must remain nutritionally adequate. Recheck total energy, protein, fiber, micronutrient-rich foods, and medication effects.

7. Exercise is for muscle and metabolic health, not for chasing ketones

Walking can help postprandial glucose and daily activity. Resistance exercise becomes increasingly important for preserving lean mass during weight loss. Exercise intensity should rise gradually, particularly in people who are deconditioned, using insulin, or experiencing dizziness.

8. Week 4 - evaluate metabolic direction, not body weight alone

At four weeks, ask whether glucose variability is falling, fasting and postprandial patterns are improving, medication burden is changing safely, hunger is more stable, waist circumference is moving in the intended direction, and the eating pattern is sustainable. A modest weight change can still represent meaningful improvement.

Table 21-3. Minimum monitoring record for the first four weeks

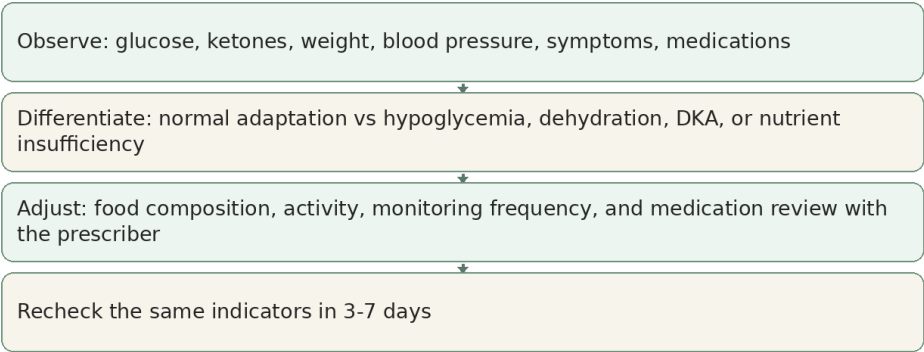
Domain	Week 1	Week 2	Week 3	Week 4 review
Glucose	Intensive review if using risk medications	Meal patterns	Trend stability	Average, TIR, hypoglycemia
Ketones	When clinically useful	Interpret food with and symptoms	Trend	Secondary marker, not endpoint
Weight	Expect fluid noise	Begin weekly average	Add waist	Compare weight and waist
BP	Watch dizziness/hypotension	Medication context	Stability	Compare with baseline
Protein/fiber/fluids	Daily adequacy	Correct gaps	Reassess persistent symptoms	Set maintenance plan
Activity	Maintain safe baseline	Add walking	Begin progressive resistance work	Sustainable weekly plan

9. SGLT2-related DKA is not "keto flu"

SGLT2 inhibitors are a special exception. ADA 2026 identifies very-low-carbohydrate intake, prolonged fasting, dehydration, and insulin deficiency as DKA risk factors in people using SGLT inhibition and discourages a ketogenic eating pattern in at-risk users. SGLT2-associated DKA can occur with plasma glucose below 200 mg/dL. Nausea, vomiting, abdominal pain, rapid breathing, severe fatigue, or dehydration therefore require medical assessment rather than simple dietary self-adjustment.

DKA is not diagnosed by beta-hydroxybutyrate alone. ADA's diagnostic framework considers diabetes/hyperglycemia, significant ketosis, and metabolic acidosis together. A beta-hydroxybutyrate level of 3.0 mmol/L or higher indicates significant ketosis in this framework, while metabolic acidosis is assessed with pH below 7.3 and/or bicarbonate below 18 mmol/L. The components must be interpreted together.

Figure 21-2. Response-based adjustment cycle during the first four weeks



Source: ADA (2026) glucose, hypoglycemia, and DKA safety principles; low-carbohydrate medication-adjustment consensus; author synthesis.

10. After four weeks, choose one of three paths

If glucose, symptoms, nutrition, and safety are improving, continue and stabilize. If glucose is improving but nutrition, lipids, symptoms, or adherence are deteriorating, redesign the plan rather than intensifying it. If there is little metabolic response, reassess adherence, food quality, energy intake, medications, sleep, activity, and whether strict ketosis is necessary.

Table 21-4. Week-4 decision matrix

Glycemic response	Safety/nutrition	Next step
Good	Good	Continue and stabilize
Good	Poor	Redesign for safety and adequacy
Limited	Good	Reassess carbohydrate, energy, activity, adherence
Limited	Poor	Stop intensification and clinically reassess

The first four weeks are successful when they produce **clearer information and safer personalization**, not simply lower carbohydrate or higher ketones.

Selected references

American Diabetes Association Professional Practice Committee. (2026). Standards of Care in Diabetes-2026, Sections 5, 6, 9, and 16. Goldenberg, J. Z., et al. (2021). BMJ, 372, m4743. Clinical principles of CGM, hypoglycemia prevention, and SGLT2-associated DKA risk mitigation.

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- Symptoms during initiation of a ketogenic diet: a scoping review of occurrence rates, mechanisms, and relief strategies (2025).

Chapter 22. A 12-Week Plant-Based Ketogenic Recovery Program - From Adaptation to Stabilization and Reassessment

Twelve weeks is long enough to move beyond the first fluid and medication changes and to observe a more stable metabolic pattern, yet short enough to function as a structured clinical checkpoint. This chapter organizes the program into phases rather than treating all 12 weeks as one unchanging prescription.

1. Divide the 12 weeks into three phases

The first four weeks emphasize adaptation and safety. Weeks 5-8 emphasize stabilization and diet quality. Weeks 9-12 prepare for reassessment and the next long-term strategy.

Table 22-1. Phase goals in a 12-week program

Phase	Main goal	Key observations
Weeks 1-4	Safe adaptation	Glucose, hypoglycemia, fluids, symptoms, medications
Weeks 5-8	Stabilization	Food quality, protein, fiber, lipids, activity, adherence
Weeks 9-12	Reassessment	HbA1c, weight/waist, BP, lipids, kidney function, medications

2. Weeks 5-6 - look again at food quality, not just ketones

Once the novelty of the diet has passed, the question becomes whether meals are built from tofu, tempeh, vegetables, nuts, seeds, avocado, and unsaturated fats or from processed "keto" foods and isolated fats. Nutritional ketosis does not rescue a poor-quality diet.

3. Weeks 5-8 - look at the whole-day glucose pattern

Fasting glucose alone can miss postprandial excursions, nocturnal hypoglycemia, and glucose variability. CGM, when available, can provide time in range and time below range. Without CGM, consistent fasting and post-meal measurements can still reveal patterns.

4. From Week 5 onward, turn activity into a plan

Daily movement, post-meal walking, and progressive resistance exercise should become scheduled behaviors rather than optional additions. The goal is to improve insulin sensitivity, preserve muscle, and support long-term weight maintenance.

Table 22-2. Key measures during Weeks 5-12

Measure	Why track it
Glucose pattern/TIR	Treatment effect and hypoglycemia
Weight and waist	Adiposity trend
Strength/activity	Lean-mass protection
BP	Cardiovascular response and medication safety
Lipids	Individual fat response
eGFR/UACR when relevant	Kidney safety
Food record	Protein, fiber, energy, and adherence

5. Weeks 7-8 - investigate a plateau before restricting more

A plateau can reflect normal adaptation, inaccurate intake estimates, reduced activity, sleep disruption, high-energy nuts and oils, medication changes, or loss of adherence. The first response should be to identify the cause, not automatically to cut carbohydrate further or add fasting.

6. Medication reduction can be an outcome, not the central goal

Needing less glucose-lowering medication can be clinically meaningful, but medication reduction should occur because glucose and risk have changed, not because "zero medication" is treated as a badge of success. Some drugs may remain indicated for heart, kidney, weight, or other benefits.

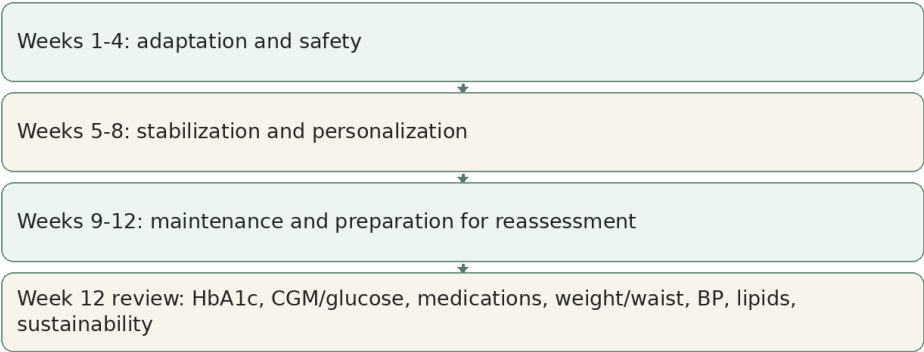
7. Weeks 9-10 - prepare for the 12-week reassessment

Plan repeat laboratory tests and review medication changes. Keep diet and activity reasonably stable before testing so that the results represent the current program rather than a short-term experiment in the final few days.

8. Weeks 11-12 - evaluate the outcome on five axes

Assess glycemia, body composition/weight, cardiovascular risk, safety/nutrition, and sustainability. A plan that lowers HbA1c but produces a major LDL-C/ApoB rise, recurrent hypoglycemia, protein deficiency, or poor quality of life requires redesign.

Figure 22-1. Cyclic structure of the 12-week plant-based ketogenic program



Source: ADA (2026); Riddle et al. (2021); Goldenberg et al. (2021); author synthesis.

9. Classify the 12-week result into four practical types

Table 22-3. Four next steps after 12 weeks

Result	Interpretation	Next step
Strong benefit, good safety	Current structure fits	Maintain and cautiously broaden food variety
Benefit with safety/nutrition problem	Efficacy but poor fit	Redesign fat, protein, carbohydrate, or medication plan
Limited benefit but sustainable	Insufficient metabolic effect	Reassess adherence, energy, carb level, activity, diagnosis
Limited benefit and poor tolerance	Strategy not working	Change approach rather than intensify

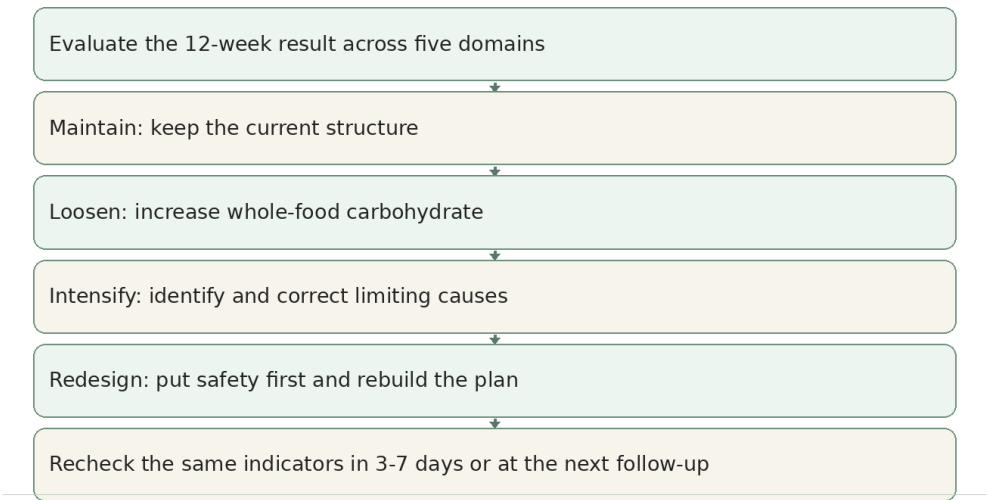
10. Carbohydrate reintroduction is an experiment, not a failure

Reintroduction begins with foods that add fiber and micronutrients with the smallest glycemic burden. Increase non-starchy vegetables first, then carefully test small portions of legumes, berries, or minimally processed whole-food carbohydrate according to the individual's response.

Table 22-4. Example of stepwise carbohydrate reintroduction

Step	Food example	Test principle	Observe
1	More non-starchy vegetables	Add one type/portion	Post-meal glucose, hunger, bowel function
2	Small legumes/lentils	Begin with small portion	Glucose, TIR, GI tolerance
3	Berries or lower-sugar fruit	Prefer with meals	Peak glucose and appetite
4	Small whole-grain/starchy portion	Use only if consistent with goals	Fasting glucose, weight, CGM trend

Figure 22-2. Maintain, loosen, intensify, or redesign after the 12-week review



Source: ADA (2026); Riddle et al. (2021); author synthesis.

11. Do not declare remission prematurely at 12 weeks

An HbA1c below 6.5% after a dietary intervention does not by itself prove remission. The international consensus generally defines remission as HbA1c below 6.5% for at least three months without usual glucose-lowering pharmacotherapy. For lifestyle interventions, enough time must also pass for the intervention and HbA1c to stabilize; the consensus suggests assessing the response at least six months after lifestyle intervention begins and, when applicable, at least three months after glucose-lowering medication has been stopped.

12. Twelve weeks is a clinical branch point, not the finish line

The 12-week program should end with a decision about long-term eating, activity, medication, and monitoring. The goal is not to remain permanently in the strictest phase. It is to identify the safest and most sustainable metabolic strategy for the individual.

Selected references

American Diabetes Association Professional Practice Committee. (2026). Standards of Care in Diabetes-2026. Riddle, M. C., Cefalu, W. T., Evans, P. H., et al. (2021). Consensus report: Definition and interpretation of remission in type 2 diabetes. *Diabetes Care*, 44(10), 2438-2444. Gardner, C. D., et al. (2022). Keto-Med randomized crossover trial.

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Chapter 23. If You Use Diabetes Medication - When the Diet Changes, the Meaning of Medication Changes Too

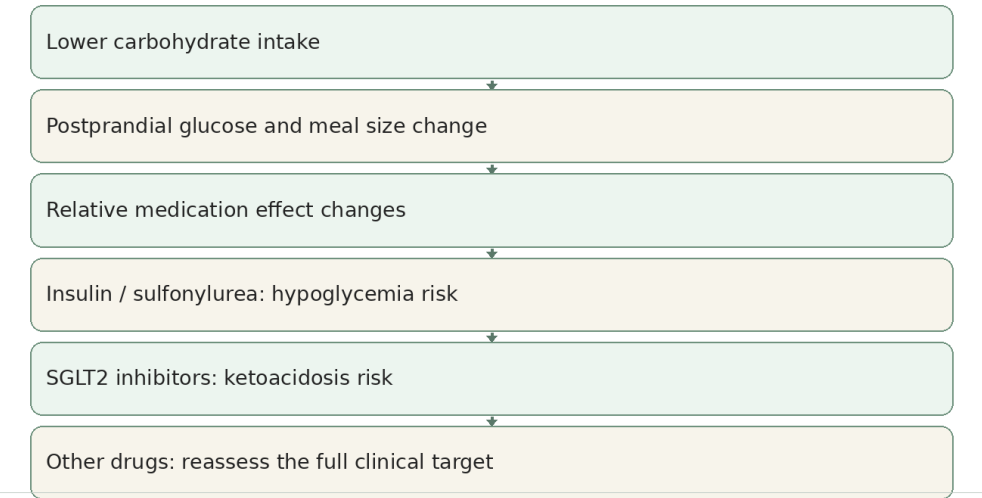
Food and medication do not operate in separate systems. A rapid fall in carbohydrate can lower glucose within days, while many glucose-lowering drugs continue to act at their previous dose. The first task is therefore not to stop medication but to understand which drug creates which risk when the diet changes.

1. Diet and medication move together

Table 23-1. First safety question by medication class

Medication	Main issue during carbohydrate restriction
Metformin	Usually low hypoglycemia risk; indication and renal status still matter
Sulfonylurea/meglitinide	Hypoglycemia
DPP-4 inhibitor	Low hypoglycemia risk alone; modest glucose-lowering role
GLP-1-based therapy	Appetite and energy intake may fall substantially
SGLT2 inhibitor	DKA risk with very-low-carb intake, fasting, dehydration, illness
Insulin	Hypoglycemia and dose-diet mismatch

Figure 23-1. How a dietary change can become a medication-related risk



Source: ADA (2026); Cucuzzella et al. (2021); author synthesis.

2. Metformin - diet change does not automatically mean stopping it

Metformin has relatively low hypoglycemia risk when used alone. Whether it should be continued depends on glycemia, tolerance, kidney function, and the treatment plan. A lower HbA1c is not, by itself, a reason for abrupt self-discontinuation.

3. Sulfonylureas - hypoglycemia becomes an early priority

Sulfonylureas stimulate insulin secretion regardless of whether the meal contains much carbohydrate. A rapid dietary carbohydrate reduction can therefore expose a mismatch between the drug effect and available glucose. Medication adjustment belongs with the prescriber, not with unsupervised self-experimentation.

4. DPP-4 inhibitors - low hypoglycemia risk, but a limited role

Used alone, DPP-4 inhibitors generally have low hypoglycemia risk. Their modest glucose-lowering effect means they may remain compatible with dietary therapy, but their role should still be reassessed in the context of the whole regimen.

5. GLP-1-based therapy - separate medication-driven appetite reduction from diet effects

GLP-1 receptor agonists and related agents can reduce appetite and energy intake. When used together with a restrictive diet, total intake may fall more than intended. Protein, micronutrients, hydration, and lean mass therefore need active attention. Weight loss caused by combined drug and dietary effects should not be attributed to one component alone.

Table 23-2. Why drugs should be grouped by hypoglycemia risk

Higher risk when carbohydrate falls	Lower intrinsic risk when used alone
Insulin	Metformin
Sulfonylurea	DPP-4 inhibitor
Meglitinide	GLP-1-based therapy
-	SGLT2 inhibitor (different risk: DKA rather than hypoglycemia)

6. SGLT2 inhibitors - the most important ketogenic exception

SGLT2 inhibitors provide important cardiovascular, heart-failure, and kidney benefits in appropriate populations. They should not be described as "bad drugs" simply because a ketogenic pattern is being considered.

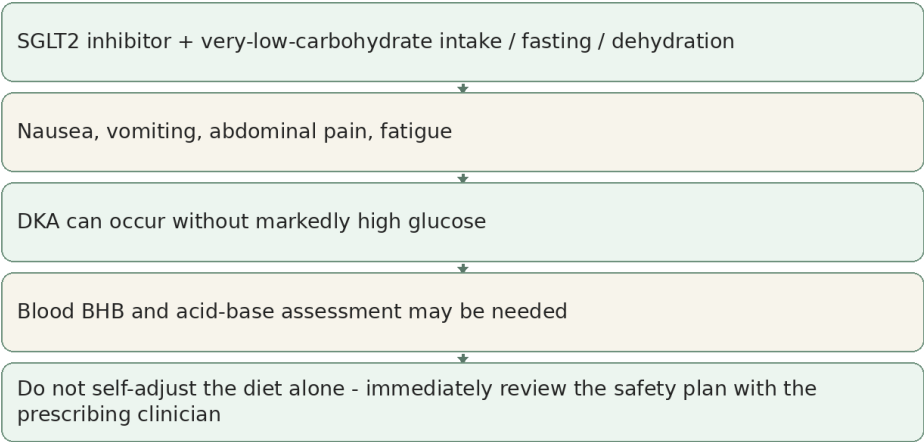
However, **very-low-carbohydrate eating creates a separate safety issue**. ADA 2026 recommends educating people at DKA risk who are treated with SGLT inhibition about DKA and risk mitigation and discourages a ketogenic eating pattern in this setting. Very-low-carbohydrate intake and prolonged fasting are among the recognized DKA risk factors.

SGLT2-associated DKA can occur even when glucose is not markedly elevated. Euglycemic DKA associated with SGLT2 therapy can present with plasma glucose below 200 mg/dL. Therefore normal or near-normal glucose does not exclude DKA.

Nausea, vomiting, abdominal pain, rapid breathing, marked fatigue, or dehydration may require assessment of blood beta-hydroxybutyrate and acid-base status. DKA is **not** diagnosed from beta-hydroxybutyrate alone. ADA's diagnostic framework considers diabetes/hyperglycemia, significant ketosis, and metabolic acidosis together. Beta-hydroxybutyrate 3.0 mmol/L or higher is a significant-ketosis criterion, while metabolic acidosis is assessed by pH below 7.3 and/or bicarbonate below 18 mmol/L. These components must be interpreted together.

Anyone using an SGLT2 inhibitor who wishes to follow a ketogenic pattern should first discuss the eating plan with the prescribing clinician so that heart/kidney benefits and DKA risk can be considered together.

Figure 23-2. Ketone-risk assessment flow for an SGLT2-inhibitor user



Source: ADA (2026), Sections 5, 6, 9, and 16; author synthesis.

7. Insulin - the medication most directly connected to carbohydrate

Insulin dose and meal carbohydrate are tightly linked. A major carbohydrate reduction can lower prandial insulin needs rapidly, but the exact change depends on insulin type, timing, glucose pattern, and endogenous insulin secretion. People using insulin need a plan for glucose monitoring and clinician-guided dose adjustment before making a large change.

8. Medication reduction is an observed result, not a competition

A lower medication requirement can represent metabolic improvement, but the safest plan is not automatically the plan with the fewest drugs. The priority is appropriate glycemia with the lowest reasonable treatment burden **without losing proven organ-protective benefits or creating avoidable risk.**

Table 23-3. Data to review before changing medication

Data	Why it matters
Glucose/CGM pattern	Determines actual response and hypoglycemia
Current medication, dose, timing	Identifies mechanism and interaction
Kidney/liver function	Affects drug suitability and dose
Weight and food intake	Helps explain changing requirements
Symptoms	Detects dehydration, GI intolerance, DKA, hypotension

9. Do not stop heart- or kidney-protective drugs based on HbA1c alone

Some glucose-lowering drugs are continued primarily for heart failure, chronic kidney disease, cardiovascular risk, or weight-related indications. Achieving near-normal glucose does not automatically remove those indications. Treatment must be reviewed by purpose, not by HbA1c alone.

10. If hypoglycemia occurs, do not push the diet harder

Recurrent low glucose is a safety failure, not proof that carbohydrate should be reduced further. Treat the hypoglycemia, identify the responsible medication or meal mismatch, and redesign the plan.

11. A four-step medication safety protocol

First, record the exact medication name, dose, timing, and insulin type. Second, mark drugs that create hypoglycemia risk and drugs that create DKA risk. Third, monitor glucose more intensively during the first one to two weeks; if using SGLT2 inhibition, prioritize ketone risk during illness, fasting, or dehydration. Fourth, document every medication change together with subsequent glucose, weight, and symptoms.

Table 23-4. Four-step record for managing diet and medication together

Step	Record
1. Identify	Generic name, dose, timing, indication
2. Flag risk	Hypoglycemia vs DKA vs volume/BP issues
3. Monitor	Glucose/CGM, symptoms, ketones when indicated
4. Reassess	What changed and what happened afterward

12. The best medication plan is the safest effective plan

The aim of a plant-based ketogenic intervention is not medication elimination at any cost. It is to improve metabolic health while keeping treatment safe, evidence-based, and individualized.

Selected references

American Diabetes Association Professional Practice Committee. (2026). Standards of Care in Diabetes-2026, Sections 5, 6, 9, 11, and 16. ADA 2026 Recommendation 5.26 on SGLT inhibition and ketogenic eating patterns. Clinical guidance on medication reconciliation, hypoglycemia, and cardiorenal risk management.

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- Cucuzzella, M., et al. (2021). Adapting diabetes medication for low-carbohydrate management.
- Riddle, M. C., et al. (2021). Remission terminology and medication-free assessment.

Chapter 24. What Is Diabetes Remission? - Normalized Glucose Does Not Mean the Story Is Over

The language of remission must be precise. Better glucose control, medication reduction, remission, and cure are not interchangeable outcomes. Type 2 diabetes can enter remission, but recurrence remains possible and long-term follow-up remains necessary.

1. Remission is different from cure

The word "cure" can imply that the disease has permanently disappeared and that monitoring is no longer necessary. That implication is inappropriate for current type 2 diabetes outcome reporting. The book title uses the broader idea of "healing" to describe movement toward improved metabolic health and reduced disease burden; it does **not** mean permanent clinical cure. When reporting research outcomes, this book distinguishes remission, improvement, and medication reduction according to their definitions.

Table 24-1. Distinguishing improvement, remission, and cure

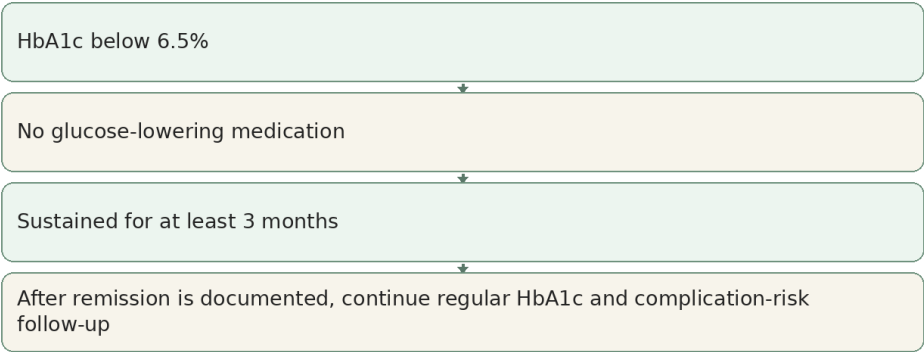
Term	Meaning	Medication implication	Follow-up implication	
Improvement	Better glycemia or other metabolic markers	Medication may or may not be used	Continued monitoring	
Remission	Glycemia below the diagnostic threshold without usual glucose-lowering medication for the required period	Medication-free glycemic criterion matters	Continued monitoring required	
Cure	Permanent disappearance of disease	Implies no treatment	Implies little/no follow-up	Not used as a clinical outcome for T2D

2. The most widely used remission criterion

The 2021 international consensus generally defines type 2 diabetes remission as HbA1c below 6.5% that persists for at least three months without usual glucose-lowering pharmacotherapy. If HbA1c is unreliable, alternative measures may be considered according to clinical context.

Lifestyle interventions require a separate timing consideration. Because diet and weight-loss effects take time to stabilize and to be reflected in HbA1c, the consensus suggests assessing response at least six months after lifestyle intervention begins and, when glucose-lowering medication has been stopped, at least three months after cessation before documenting remission.

Figure 24-1. Basic flow for determining type 2 diabetes remission



Source: Riddle et al. (2021); author synthesis.

3. How often does remission occur?

Remission rates vary widely because studies use different populations, treatment intensities, durations, and definitions. Weight-loss trials, intensive lifestyle studies, low-carbohydrate trials, and bariatric/metabolic-surgery studies should not be treated as if they were the same intervention.

Table 24-2. Selected lifestyle remission studies

Study	Intervention	Reported remission signal	Interpretation
Look AHEAD	Intensive lifestyle	~11.5% at 1 year; ~7.3% at 4 years	Remission possible but less common over time
DiRECT	Primary-care weight management	46% at 1 year; 36% at 2 years	Strong link with magnitude of weight loss
DiRECT extension	Long-term support after original intervention	11 of 85 participants with 5-year data (~13%) in remission	Different denominator from the 2-year cohort; do not make a simple 36%->13% comparison

4. Weight loss is strongly linked with remission

DiRECT showed a striking dose-response relationship at one year: remission occurred in about 7% of participants losing less than 5 kg, 34% with 5-10 kg loss, 57% with 10-15 kg loss, and 86% with at least 15 kg loss. These categories describe probabilities observed in the trial; they do **not** mean that every person must lose 15 kg to achieve remission.

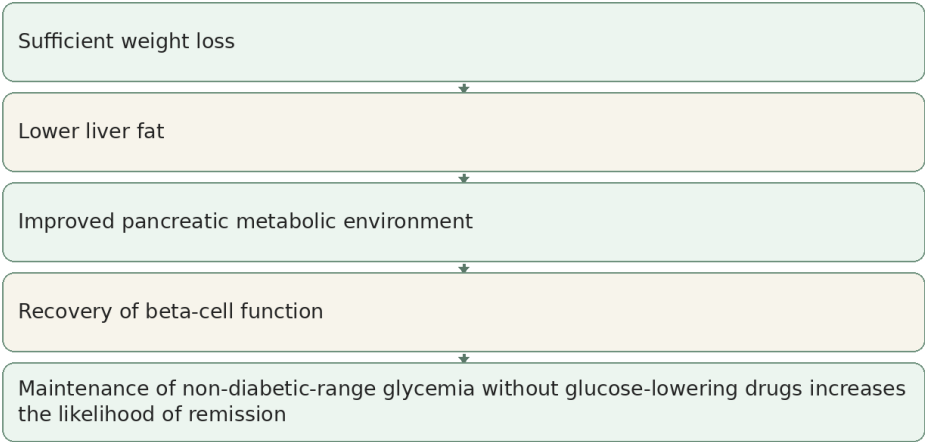
5. Why liver fat often falls early

The twin-cycle model proposes that chronic energy excess promotes liver fat accumulation, hepatic insulin resistance, and increased VLDL-triglyceride export. With sufficient negative energy balance and weight loss, liver fat can fall rapidly, helping improve hepatic insulin sensitivity and fasting glucose regulation.

6. Pancreatic fat and beta-cell recovery

DiRECT mechanistic studies found that remission was associated with reductions in liver and pancreatic fat and with recovery of first-phase insulin response in responders. Two-year imaging also showed pancreatic volume and morphology moving toward the non-diabetic pattern in people maintaining remission. This does not mean that a new pancreas grows; it suggests that some diabetes-associated functional and structural abnormalities may be partly reversible.

Figure 24-2. Major metabolic pathways linking weight loss to remission



Source: Taylor et al. (2018); Al-Mrabeh et al. (2020); author synthesis.

7. Remission probability is not identical for everyone

Shorter diabetes duration, greater beta-cell reserve, substantial and sustained weight loss, lower ectopic fat burden, and the ability to maintain the intervention are generally associated with a higher chance of remission. Longer duration and marked loss of insulin secretory capacity reduce the probability. These are associations, not deterministic rules.

Table 24-3. Factors that can influence remission probability

Factor	Direction of association
Larger sustained weight loss	Higher probability
Shorter diabetes duration	Higher probability
Better beta-cell reserve	Higher probability
Weight regain	Higher recurrence risk
Longer duration/advanced disease failure beta-cell	Lower probability

8. Two-year remission does not guarantee five-year remission

At two years, 36% of the original DiRECT intervention group was in remission. In the five-year extension, 11 of 85 extension participants with five-year data - about 13% - were in remission at that time. These figures do not use identical denominators and should not be interpreted as a simple fall from 36% to 13% in one unchanged cohort.

Among participants who were in remission at year 2 and were followed to year 5, about 26% remained in remission at year 5. The practical message is that **achieving remission and maintaining remission are different tasks.**

9. Does remission eliminate complication risk?

No. Prior hyperglycemic exposure, existing retinopathy, neuropathy, kidney disease, and cardiovascular risk do not disappear simply because HbA1c normalizes. The concept of metabolic memory is one reason risk management and complication surveillance continue.

10. Why testing continues after remission

Table 24-4. What still requires follow-up after remission

Domain	Why continue monitoring?
HbA1c/glucose	Detect recurrence
Weight/waist	Weight regain is a major warning signal
Lipids/BP	Cardiovascular risk is separate from remission status
eGFR/UACR	Kidney risk can persist
Retina/neuropathy/feet	Existing microvascular disease can progress even after glucose normalization
Medication list	Some drugs remain indicated for heart, kidney, or weight benefits

11. How should remission be interpreted in a plant-based ketogenic program?

This book does not transfer DiRECT's 46% one-year remission rate, or remission rates from other low-carbohydrate interventions, directly to plant-based ketogenic eating. Direct long-term evidence for the exact combined intervention remains limited. Instead, the program uses the physiological conditions associated with remission - lower glycemic burden, loss of excess visceral/ectopic fat, improved insulin sensitivity, adequate protein and muscle preservation, medication safety, and sustainable eating - as design principles.

12. The true goal of remission is not "zero drugs"

Some people continue SGLT2 inhibitors, GLP-1-based therapies, or other medications for heart failure, CKD, cardiovascular risk, or weight-related indications even when glucose is near normal. In that situation, formal drug-independent remission may be difficult to diagnose, but clinically useful cardiorenal therapy should not be stopped merely to obtain the label "remission."

The clinically meaningful goal is durable metabolic health with the lowest reasonable disease burden and appropriate therapy - not a contest to eliminate every medication.

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Riddle, M. C., Cefalu, W. T., Evans, P. H., et al. (2021). Consensus report: Definition and interpretation of remission in type 2 diabetes. *Diabetes Care*, 44(10), 2438-2444. Lean, M. E. J., Leslie, W. S., Barnes, A. C., et al. (2018). Primary care-led weight management for remission of type 2 diabetes (DiRECT). *Lancet*. Lean, M. E. J., et al. (2019). Two-year results of DiRECT. *Lancet Diabetes & Endocrinology*, 7(5), 344-355. Lean, M. E. J., et al. (2024). Five-year follow-up of DiRECT. *Lancet Diabetes & Endocrinology*, 12(4), 233-246. Taylor, R., et al. (2018). Remission of human type 2 diabetes requires decrease in liver and pancreas fat content but depends on beta-cell recovery. *Cell Metabolism*, 28(4), 547-556.e3.

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- Al-Mrabeh, A., et al. (2020). Two-year remission and pancreatic morphology.

Chapter 25. How to Avoid Returning to Diabetes - Make Remission a Living System, Not a Single Event

Remission is a metabolic state that can be lost. The long-term task is therefore not to "finish" treatment but to build a system that detects weight regain, rising glucose, loss of activity, poor sleep, medication changes, and other early signals before they become a full relapse.

1. The first maintenance signal is the direction of body weight

Sustained weight loss is strongly associated with sustained remission in weight-management studies. Day-to-day variation matters less than the trend. A practical approach is to define a personal maintenance range around a stable post-remission weight and respond when upward movement persists for several weeks.

Table 25-1. Core maintenance variables and early warning signs

Variable	Stable pattern	Early warning
Weight/waist	Stable within personal range	Persistent upward trend
Glucose/HbA1c	Stable non-diabetic/remission range	Rising fasting or post-meal glucose
Activity/strength	Maintained	Reduced movement or strength
Food pattern	Repeatable whole-food structure	More snacks, liquid calories, refined foods
Sleep/stress	Adequate and stable	Persistent sleep loss or high stress
Medications/health	Stable indications	New illness or medication affecting glucose/weight

2. Weight regain is an early warning, not a moral failure

Weight regain should trigger analysis rather than blame. First review liquid calories, portions of energy-dense nuts, seeds, and oils, restaurant meals, snacking, sleep, and activity. There is usually no need to jump immediately to extreme fasting or an ultra-low-calorie diet.

Table 25-2. Three-step response to rising weight

Step	Action
1	Confirm the trend using repeated measurements

Step	Action
2	Identify likely drivers: energy density, activity, sleep, medication, stress
3	Make targeted changes and reassess before intensifying restriction

3. Carbohydrate reintroduction is not "going back to the old diet"

Maintenance may contain more carbohydrate than the strict induction phase. Reintroduction should favor minimally processed, high-fiber foods and be tested against the individual's glucose and appetite response. The objective is a broader sustainable diet, not a return to refined starch, sugar, or prior eating habits that produced metabolic deterioration.

4. Muscle is a long-term metabolic reservoir

Skeletal muscle disposes of a large portion of meal-derived glucose and supports physical function. Resistance training, adequate protein, and daily movement therefore remain central after weight loss. A smaller body with markedly less muscle is not the ideal maintenance outcome.

Table 25-3. Activity and muscle-preservation plan during remission maintenance

Domain	Maintenance principle
Walking/daily movement	Preserve routine daily activity
Post-meal movement	Use strategically for glucose control
Resistance exercise	Regular progressive training
Protein	Adequate and distributed across meals
Function	Track strength or simple performance measures

5. Sleep and stress are invisible glucose variables

Short sleep and chronic stress can increase appetite, reduce activity, and worsen glycemic regulation. They can also make adherence more difficult. These factors are not excuses; they are modifiable components of the metabolic system.

6. A good HbA1c does not end medical follow-up

Remission requires ongoing observation because recurrence can occur. Weight, HbA1c, blood pressure, lipids, kidney markers, and complication screening remain relevant according to individual risk.

Table 25-4. Basic long-term follow-up after remission

Domain	Purpose
HbA1c/glucose	Detect recurrence
Weight/waist	Detect energy-balance drift
Lipids/BP	Manage cardiovascular risk
eGFR/UACR	Continue kidney surveillance
Retina/feet/neuropathy	Continue complication surveillance
Nutrition/muscle	Prevent deficiency and frailty

7. Metabolic memory means complication care continues

Past hyperglycemia can influence future risk even after current glucose improves. Existing retinopathy, neuropathy, or nephropathy does not vanish with remission. This is another reason the word "cure" is inappropriate.

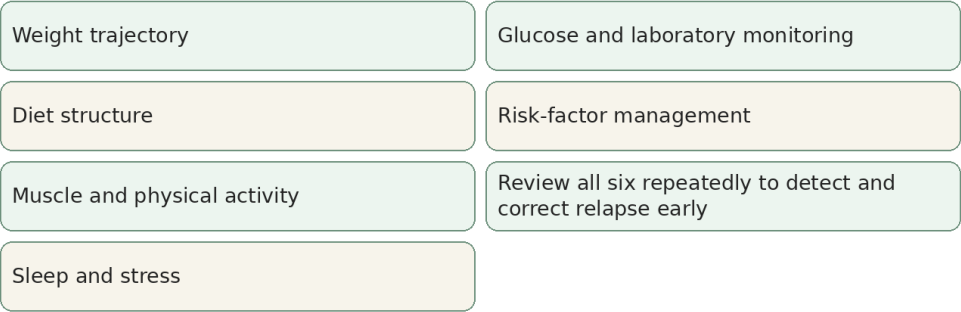
8. Needing medication again is not failure

If glucose rises or a new cardiorenal indication appears, medication may again be appropriate. Some people also continue SGLT2 inhibitors or GLP-1-based therapy for reasons other than glucose control. Clinically necessary therapy should not be withheld to preserve a remission label.

9. Detect relapse as a trend, not one number

One high glucose value after illness, poor sleep, or a large meal does not by itself establish relapse. Look for repeated changes in fasting glucose, postprandial glucose, HbA1c, weight, and medication needs. Earlier detection allows smaller corrections.

Figure 25-1. Six interacting axes that help sustain remission



Source: Riddle et al. (2021); ADA Standards of Care in Diabetes-2026; author synthesis.

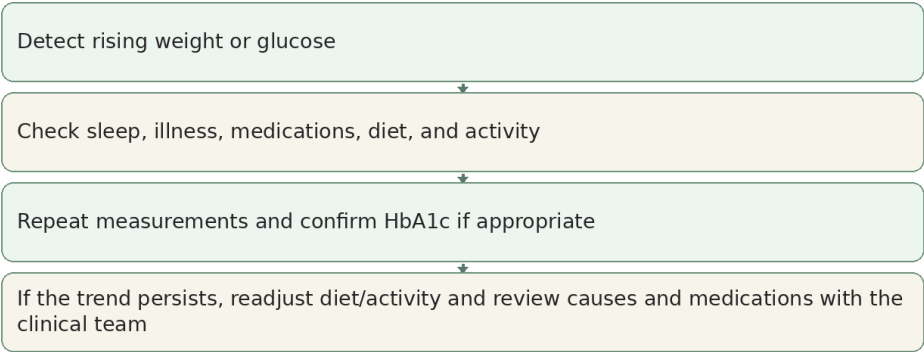
10. Repeatability matters more than strictness in the maintenance phase

A diet that works only under constant vigilance is fragile. Maintenance should be simple enough to repeat at home, at work, while traveling, and during social events. Food quality, adequate protein, vegetables, unsaturated fats, and a personally tolerable carbohydrate range are more important than permanent maximal restriction.

11. Think of one year as a recurring management cycle

Instead of viewing remission as a finish line, use a yearly cycle: establish a stable routine, monitor trends, review laboratories, identify drift, correct early, and reassess the plan. The exact frequency of testing depends on clinical status and medications.

Figure 25-2. Decision flow for early detection and reversal of relapse



Source: Riddle et al. (2021); ADA Standards of Care in Diabetes-2026; author synthesis.

12. The goal is not to forget that diabetes ever existed

The most useful long-term mindset is not "I am cured, so I can stop paying attention." It is "My metabolic state is currently well controlled, and I know which behaviors, monitoring, and treatment keep it there." Remission is a success precisely because it is maintained intentionally.

Selected references

Riddle, M. C., et al. (2021). Consensus report on type 2 diabetes remission. *Diabetes Care*, 44(10), 2438-2444. Lean, M. E. J., et al. (2019, 2024). DiRECT two-year and five-year follow-up reports. American Diabetes Association Professional Practice Committee. (2026). Standards of Care in Diabetes-2026.

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- Riddle, M. C., et al. (2021). Consensus report on remission and continued follow-up.
- Lean, M. E. J., et al. (2024). Five-year follow-up of DiRECT.
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Chapter 26. The Diabetes Diet Research Database We Built - Turning Search Results into Evidence

A folder full of PDFs is not yet an evidence system. The purpose of the project database was to preserve search records, deduplicate studies, classify dietary interventions, verify numerical outcomes, store cautionary evidence, and make every claim in the book traceable to a review process.

1. Why a database rather than a paper folder?

The corpus contained thousands of records from overlapping searches. The same paper could appear under plant-based, low-carbohydrate, medication, remission, and safety questions. A structured database allows one study to be linked to multiple questions without pretending that each appearance is a different study.

Table 26-1. First snapshot of the research corpus

The project's working corpus contained thousands of records, including more than seven thousand deduplicated diet-and-diabetes records in the primary collection and a large open-access subset. These numbers describe a search corpus, not a set of trials all supporting the same conclusion.

2. The first filter asks whether the paper actually studies the diet

Keyword appearance is not enough. A paper that mentions "ketogenic" in the introduction is not a ketogenic intervention trial. Likewise, a plant-based cohort paper is not automatically evidence for a plant-based ketogenic intervention. The database therefore separates dietary relevance from mere text matching.

Table 26-2. Dietary classification after stricter review

The project assigns candidate records to distinct evidence layers such as whole-food plant-based, vegetarian/vegan, low-carbohydrate, ketogenic, and plant-based low-carbohydrate/ketogenic. Directness is graded separately from the size of the search result set.

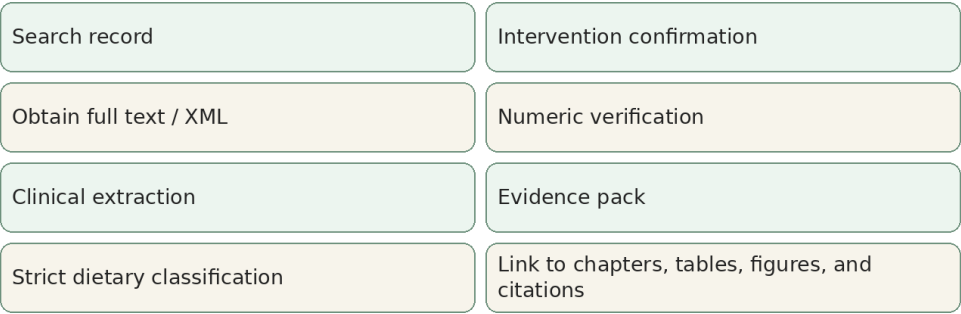
3. A second review separated co-mention from same-intervention evidence

This was crucial for the central hypothesis of the book. A paper comparing a plant-based low-fat diet with an animal-based ketogenic diet contains both keywords, but it is not a trial of a combined plant-based ketogenic diet. Same-intervention evidence is much rarer and therefore deserves more cautious language.

Table 26-3. Second-pass review of high-priority papers

High-priority records were re-read to determine whether the dietary pattern was actually assigned, whether participants had diabetes or a relevant metabolic condition, whether outcomes were numerical, and whether the intervention matched the book's combined model.

Figure 26-1. How a search record becomes evidence used in the book



Source: project data pipeline; PRISMA 2020 and Cochrane principles for transparent selection and data collection; author diagram.

4. For HbA1c, "where is the number?" mattered as much as "is there a number?"

HbA1c values can appear as baseline/end values, within-group changes, between-group differences, pooled meta-analytic effects, table values, abstract values, or supplementary results. These are not interchangeable. The project therefore used repeated passes to verify the type and location of each numerical claim.

Table 26-4. Status of the third-pass HbA1c verification

A working snapshot identified hundreds of HbA1c candidate records, with a smaller set numerically confirmed and additional records flagged for conflict or further review. A conflict flag is a quality-control signal, not an extra mutually exclusive study category.

5. Evidence packs are question-specific work queues, not a final answer list

Rather than rereading the entire corpus for every paragraph, the project created evidence packs for recurring questions. Examples included plant-based studies, ketogenic studies, low-carbohydrate studies, same-intervention plant-keto evidence, HbA1c, medication, remission, and caution/safety.

Table 26-5. Major evidence packs used during writing

Evidence pack	Working snapshot	Main question	Can overlap?
Plant top	100	Plant-based clinical effects/mechanisms	Yes
Ketogenic	88	Glycemia, weight, lipids	Yes
Low-carb	28	Low-carb evidence distinct from ketogenic	Yes
Plant-keto same intervention	1	Direct combined-intervention evidence	Yes
HbA1c	200	Recheck HbA1c values and location	Yes
Medication	36	Medication reduction and safety	Yes
Remission	52	Definition, maintenance, recurrence	Yes
Caution	99	LDL/ApoB, DKA, nutrition, other safety	Yes

These packs cannot be added together to create a total number of papers because the same article can belong to several packs.

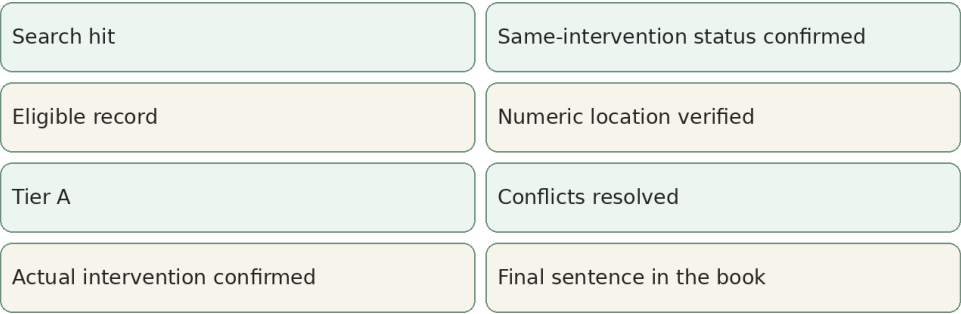
6. A database of only positive studies becomes a confirmation-bias archive

The caution pack deliberately preserved neutral, mixed, and adverse findings: LDL-C or ApoB increases, hypoglycemia risk, SGLT2-associated DKA, nutrient inadequacy, poor adherence, or results that failed to show superiority. Scientific credibility depends on retaining evidence capable of changing the conclusion.

7. Automation sets priorities; it does not eliminate human reading

Keyword searches, classifiers, and scripts are useful for ranking records and identifying numerical candidates. They cannot reliably determine clinical directness, study design, intervention fidelity, or whether a number is a within-group change or a between-group effect without human review.

Figure 26-2. Stepwise ladder for increasing evidence confidence



Source: project multi-stage verification framework and Cochrane data-collection principles; author diagram.

8. Why preserve source and version information?

A claim becomes hard to audit if the reader cannot reconstruct which PDF, abstract, table, or database snapshot produced it. The project therefore stores source identifiers, version information, figure metadata, and build records. New literature can then update the evidence without erasing the history of the prior conclusion.

9. What the database still cannot solve

No database can create trials that do not exist. Direct long-term randomized evidence for a strict plant-based ketogenic intervention in type 2 diabetes remains limited. Many nutrition studies are short, definitions vary, adherence deteriorates, and hard cardiovascular or renal endpoints are uncommon.

10. How the database changed the language of this book

The evidence system repeatedly forced weaker but more accurate wording: "may improve" instead of "proves," "associated with" instead of "causes," and "remission" instead of "cure." It also made clear that plant-based quality, carbohydrate quantity, fat quality, medication safety, and weight change must be treated as partially independent dimensions.

The database therefore supports a method rather than a predetermined conclusion: **search broadly, classify directness, verify numbers, preserve contrary evidence, and adjust the strength of the sentence to the strength of the evidence.**

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Sources and References

Key chapter sources

- Page, M. J., et al. (2021). PRISMA 2020 statement.
- Cochrane Handbook for Systematic Reviews of Interventions: study selection and data-collection principles.
- Internal database and evidence-pipeline audit files described in this chapter.

Chapter 27. What Can We Say After Synthesizing the Evidence? - What We Can State Strongly and What Must Still Wait

The final question is not whether plant-based or ketogenic eating "wins." It is which conclusions are strongly supported, which are plausible but indirect, and which remain hypotheses. This chapter deliberately separates evidence strength from enthusiasm.

1. First divide conclusions by strength

Table 27-1. Three levels of final conclusions used in this book

Level	Language	Meaning
Strong	"Evidence supports..."	Consistent and reasonably direct evidence
Conditional	"May help...", "can be considered..."	Evidence exists but depends on context or has important limitations
Hypothesis	"Needs direct testing..."	Biological rationale or indirect evidence without adequate direct trials

2. What can we say about plant-based dietary patterns?

Randomized-trial meta-analyses support modest improvement in HbA1c and several cardiometabolic risk factors from well-designed vegetarian or vegan patterns in adults with type 2 diabetes. Prospective evidence also distinguishes healthy from unhealthy plant-based diets: "plant-based" alone does not guarantee high diet quality.

The strongest plant-based message is therefore not "remove animal foods and diabetes will disappear." It is that minimally processed plant foods, fiber, unsaturated fats, plant proteins, and energy balance can form an effective evidence-based dietary pattern for diabetes management.

3. Low-carbohydrate diets have a strength in short-term glycemic improvement

Systematic reviews of randomized trials show that low- and very-low-carbohydrate diets can improve HbA1c, triglycerides, body weight, and medication requirements, especially around six months. Differences from comparator diets often become smaller by 12 months as adherence and dietary separation decline.

Table 27-2. Current evidence on a common scale

Evidence layer	Representative evidence	HbA1c direction	Strength	Main limitation
Vegetarian/vegan RCT meta-analyses	Multiple RCTs	~-0.36 to -0.40 percentage points in recent analyses	Diet quality and multiple risk factors	Definitions and energy intake vary
Low-carbohydrate RCT meta-analysis	23 RCTs in a major review	~-0.47 percentage points at 6 months	Short-term glycemia, TG, weight	Differences diminish with time
Ketogenic RCT/meta-analyses	Heterogeneous ketogenic trials	Modest average effect; some comparisons show no superiority	TG and HDL-C often improve	Definition, duration, comparator heterogeneity
Plant-based low-carb/ketogenic	Small 2026 evidence base	Improvements reported in limited trials	Tests overlap of two principles	Direct long-term PB-KD evidence is sparse

4. A ketogenic diet is not simply another name for a low-carbohydrate diet

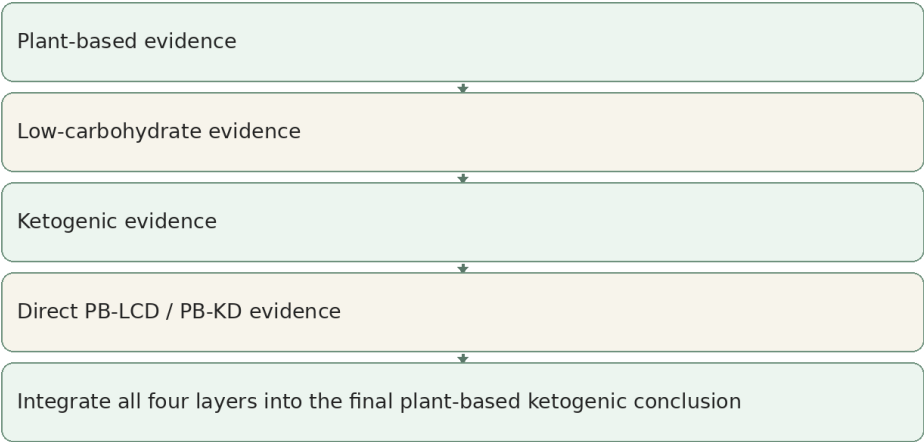
Ketogenic eating adds a physiological state - nutritional ketosis - to carbohydrate restriction. That can be useful in selected people, but it also adds dietary strictness and medication-safety questions. The goal should not be to produce the highest ketone concentration.

The Keto-Med randomized crossover trial illustrates the limits of claiming superiority. Participants with prediabetes or type 2 diabetes completed 12-week phases of a well-formulated ketogenic diet and a Mediterranean-plus diet. The diets differed substantially in carbohydrate restriction, yet the primary HbA1c outcome did not significantly differ between them. The ketogenic phase produced a greater triglyceride reduction, while LDL-C increased relative to the Mediterranean-plus phase; fiber and selected nutrient intakes were lower, and follow-up dietary adherence favored the Mediterranean-style pattern. Thus ketogenic eating can be a powerful carbohydrate-restriction tool without being superior to another high-quality diet on every outcome.

5. Does combining plant-based and ketogenic principles create synergy?

This is the central hypothesis of the book, but direct evidence remains limited. The combination is biologically and nutritionally plausible: plant-based foods can improve fiber and unsaturated-fat quality while carbohydrate restriction can reduce glycemic load. Yet evidence for plant-based eating and evidence for ketogenic eating cannot simply be added together and labeled proof of a synergistic combined intervention.

Figure 27-1. Connecting four evidence layers into one conclusion



Source: project evidence map; Guest et al. (2024); Goldenberg et al. (2021); Mazzola et al. (2026); author synthesis.

6. Decompose what may actually be causing the observed effect

Diet trials change several variables at once. Lower carbohydrate often means less sugar and refined grain, more fat or protein, lower energy intake, and weight loss. Plant-based interventions may simultaneously increase fiber, reduce saturated fat, increase minimally processed foods, and alter energy density. When HbA1c improves, the causal contribution of each component cannot always be isolated.

Table 27-3. The same HbA1c improvement can arise through different pathways

Pathway	Example mechanism
Carbohydrate reduction	Lower postprandial glucose burden
Weight loss	Improved hepatic and peripheral insulin sensitivity
Higher food quality	More fiber, fewer refined foods, better fat quality
Medication change	Reduced or intensified pharmacologic effect
Physical activity	Greater glucose disposal and insulin sensitivity

Keto-Med is again informative: both diets emphasized non-starchy vegetables and avoided added sugar and refined grains. Both improved HbA1c and weight, with no significant 12-week HbA1c difference. Shared improvements in food quality likely contributed to outcomes in both phases.

7. Safety is a separate axis from efficacy

A diet that lowers HbA1c is not automatically safe for every person. Plant-based ketogenic eating requires separate attention to hypoglycemia, hypotension, dehydration, LDL-C/ApoB increases, protein or micronutrient inadequacy, and medication interactions.

For people using insulin or sulfonylureas, rapid carbohydrate reduction can increase hypoglycemia risk. For people using SGLT2 inhibitors, the problem is different: ADA 2026 discourages a ketogenic eating pattern in people at DKA risk treated with SGLT inhibition. Very-low-carbohydrate intake, prolonged fasting, dehydration, and insulin deficiency are recognized risk factors.

Pregnancy/lactation, children, kidney disease, and people with or at risk for disordered eating also require particular caution with very-low-carbohydrate plans according to current guidance.

Lipid responses must likewise be individualized. Ketogenic diets often reduce triglycerides and raise HDL-C, but LDL-C can rise in some trials and some individuals. A plant-based ketogenic version should therefore emphasize unsaturated plant fats - olive, avocado, nuts, seeds, soy - while limiting foods high in saturated fat. Improvements in triglycerides or HDL-C should not be

assumed to cancel a meaningful LDL-C or ApoB rise.

8. Remission requires stricter language

An HbA1c below 6.5% after dietary intervention should not immediately be called "cure." The international consensus generally defines remission as HbA1c below 6.5% for at least three months without usual glucose-lowering medication. For lifestyle intervention, adequate time is also required for the response to stabilize; assessment is suggested at least six months after the lifestyle intervention begins and, when applicable, at least three months after medication cessation.

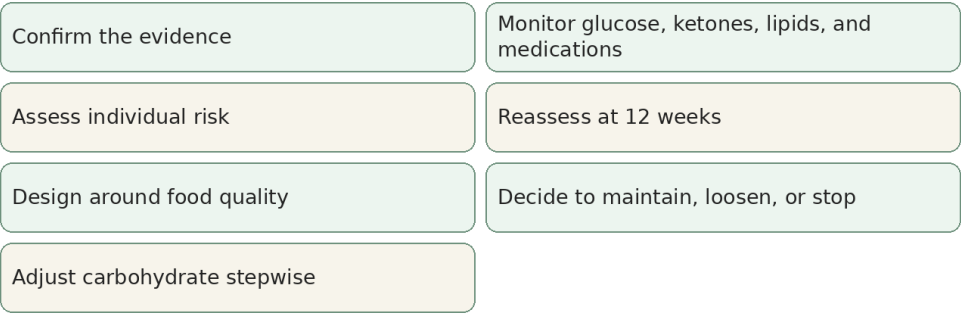
Remission is not unique to one diet. DiRECT demonstrates that large and sustained weight loss can produce remission in some people, but recurrence is common. The plant-based ketogenic model should therefore be evaluated on whether it helps appropriate individuals reach safer glycemia, lower disease burden, and, when possible, remission criteria - not on whether it can claim ownership of remission.

9. What can be stated strongly, and what must wait?

Table 27-4. Final statements permitted by the current evidence

Statement	Current status
High-quality plant-based diets can improve glycemic and cardiometabolic markers in T2D	Supported
Low-carbohydrate diets can improve short-term glycemia and medication burden in many adults	Supported with long-term adherence caveat
Ketogenic diets can reduce TG and raise HDL-C but have heterogeneous LDL-C responses	Supported
Plant-based ketogenic eating can be designed around unsaturated fats, adequate protein, fiber-rich low-carb foods, and monitoring	Reasonable clinical framework
A plant-based ketogenic diet is proven superior to Mediterranean or other high-quality diets	Not established
The combined pattern has a unique long-term remission effect beyond weight loss and food quality	Not established; requires direct trials

Figure 27-2. Final decision principle for a plant-based ketogenic strategy



Source: ADA (2026) individualized safety principles and the implementation framework in Chapters 20-25; author synthesis.

10. The final proposal is not one number

A plant-based ketogenic diet is not a competition to minimize carbohydrate or maximize ketones. For one person, a short strict ketogenic phase may be useful; for another, a less restrictive plant-based low-carbohydrate pattern may achieve the same clinical goals with better adherence. If glycemia improves while LDL-C/ApoB, nutrition, muscle, kidney function, or quality of life deteriorate, the strategy must be redesigned.

The strongest current message is not the victory of a named diet. It is **to improve food quality, reduce carbohydrate when clinically useful, manage weight and muscle, coordinate medication, and monitor safety in an individualized plan.** The scientific value of the plant-based ketogenic model lies in combining already supported principles while keeping unproven synergy explicitly labeled as a hypothesis.

The next research step is direct long-term randomized comparison of plant-based ketogenic, plant-based low-carbohydrate, Mediterranean, and conventional ketogenic patterns, tracking not only HbA1c but medication reduction, remission, ApoB, kidney function, nutrient adequacy, muscle mass, quality of life, and long-term adherence.

Selected references

Guest, N. S., Raj, S., Landry, M. J., et al. (2024). Vegetarian and Vegan Dietary Patterns to Treat Adult Type 2 Diabetes. *Advances in Nutrition*, 15(10), 100294. Goldenberg, J. Z., Day, A., Brinkworth, G. D., et al. (2021). Efficacy and safety of low and very low carbohydrate diets for type 2 diabetes remission. *BMJ*, 372, m4743. Choy, K. Y. C., & Louie, J. C. Y. (2023). Ketogenic diet for type 2 diabetes. *Diabetes & Metabolic Syndrome*, 17(12), 102905. Gardner, C. D., Landry, M. J., Perelman, D., et al. (2022). Effect of a ketogenic diet versus Mediterranean diet on glycated hemoglobin: Keto-Med randomized crossover trial. *American Journal of Clinical Nutrition*, 116(3), 640-652. Mazzola, G., Rondanelli, M., Cabrini, C., & Perna, S. (2026). Metabolic, adherence, and sustainability outcomes of plant-based low-carbohydrate and ketogenic diets. *Nutrition*, 148, 113222. Riddle, M. C., Cefalu, W. T., Evans, P. H., et al. (2021). Consensus report: Definition and interpretation of remission in type 2 diabetes. *Diabetes Care*, 44(10), 2438-2444. American Diabetes Association Professional Practice Committee. (2026). *Standards of Care in Diabetes-2026*.

Sources and References

Key chapter sources

- Guest, N. S., et al. (2024). Vegetarian and vegan dietary patterns in adult type 2 diabetes.
- Goldenberg, J. Z., et al. (2021). Low and very-low-carbohydrate diets in type 2 diabetes.
- Gardner, C. D., et al. (2022). Keto-Med randomized crossover trial.
- Mazzola, G., et al. (2026). Plant-based low-carbohydrate and ketogenic diets: systematic review.
- Riddle, M. C., et al. (2021). Type 2 diabetes remission consensus report.

English Edition Note

This revised English edition preserves the complete 27-chapter structure. All 53 figures have been redrawn with English labels and English source lines. Body paragraphs use full justification, and every chapter ends with an explicit Sources and References section.

Clinical safety language follows the reviewed Korean edition: type 2 diabetes remission is distinguished from cure; SGLT2-inhibitor-associated DKA may occur without marked hyperglycemia; DKA requires integrated assessment of glycemia/diabetes, ketosis, and metabolic acidosis; and lipid responses are interpreted across triglycerides, HDL-C, LDL-C, ApoB, and overall cardiovascular risk.