

# A clinician's guide to inpatient low-carbohydrate diets for remission of type 2 diabetes: toward a standard of care protocol



Mark Cucuzzella<sup>\*1</sup>, Adele Hite<sup>2</sup>, Kaitlyn Patterson<sup>3</sup>, Laura Saslow<sup>4</sup> & Rory Heath<sup>5</sup>

## ABSTRACT

Type 2 diabetes (T2DM) is most often treated as a chronic progressive condition. However, both clinical experience and scientific studies have shown that remission indicated by a normalizing of blood glucose levels and safe medication reduction through lifestyle change should be considered an achievable clinical outcome for patients with T2DM. Dietary interventions that include therapeutic levels of carbohydrate reduction can be used by clinicians to help patients reach this goal, as evidenced by clinical experience and clinical trials; however, many clinicians and allied healthcare providers have not been trained in how to administer these therapies. This article demonstrates the successful implementation of therapeutic carbohydrate reduction for T2DM in an inpatient setting through the institutional example of a small, rural hospital in the U.S. It provides definitions for therapeutic carbohydrate reduction and a rationale for its use in an inpatient setting in patients who present with T2DM. The article outlines a seven-stage protocol developed from practice-based evidence to be used in an inpatient setting to minimize the requirement for insulin or other hypoglycemic medications and to normalize markers of T2DM in patients with this condition. The protocol consists of: 1) patient selection; 2) pre-diet evaluation and counseling; 3) patient education; 4) initiating the dietary intervention; 5) managing medication changes; 6) addressing any side effects; and 7) follow-up. This protocol serves as an initial framework for developing clinical practice guidelines and a standard of care for using carbohydrate reduction as an intervention for T2DM and related conditions in an inpatient setting. It also indicates the potential for providing clinicians with the opportunity to help patients put T2DM into remission, rather than just manage its progression. A Clinician's Guide to Inpatient Low-Carbohydrate Diets for Remission of Type 2 Diabetes: Toward a Standard of Care Protocol.

## Introduction

Type 2 diabetes mellitus (T2DM) is now considered a global pandemic. Recent estimates from the World Health Organization indicate over 400 million people worldwide have diabetes [1]. In the United States, at least 23 million people have been diagnosed with diabetes, and it is estimated that nearly 50% of the US

population may be classified as having pre- or undiagnosed diabetes [2,3]. T2DM is a leading cause of morbidity and mortality and is a significant factor in increasing healthcare costs due to its extensive complications. The American Diabetes Association estimates the annual costs associated with T2DM to be over \$300 billion in 2017 [4]. In January 2017, the American Diabetes Association and American

<sup>1</sup>West Virginia University School of Medicine, WVU Center for Diabetes and Metabolic Health, Morgantown, West Virginia

<sup>2</sup>Department of Communication, Rhetoric, and Digital Media, North Carolina State University

<sup>3</sup>Department of Medical school, University of Michigan

<sup>4</sup>Department of Health Behavior and Biological Sciences, School of Nursing, University of Michigan

<sup>5</sup>Great Western Hospitals NHS Foundation Trust, Marlborough Road, Swindon

\*Author for correspondence : cucuzzellam@wvumedicine.org

## KEYWORDS

- diabetes
- glycemic
- insulin

Academy of Family Physicians labeled T2DM as a chronic progressive disease [5]. However, both clinical experience and scientific studies have shown that bringing progression to a standstill and even reversing the clinical manifestations of T2DM should be considered an achievable clinical outcome. Currently in the literature there are four methods to place T2DM into remission: bariatric surgery [6], extended fasting [7], a very low-calorie diet using a meal-replacement formula [8], and low-carbohydrate diets [9,10]. Low-fat, plant-based protocols have been suggested as first line therapy for diabetes management, but the most intensive protocol failed to achieve remission of T2DM over 74 weeks, as hemoglobin A1c (HbA1c) reduction was 8.1 to 7.6 [11]. Low-carbohydrate diets are therapeutic interventions that clinicians can use to help patients discontinue medications for hyperglycemia and achieve remission of T2DM [9,10]. For patients, this approach may be less extreme, safer, and more acceptable than bariatric surgery, extended fasting, and a very low-calorie meal replacement. At the same time, low-carbohydrate dietary interventions are not clearly defined in the literature, and many clinicians and allied healthcare providers have not been trained in how to administer these therapies. This article serves as an initial framework for developing clinical practice guidelines and a standard of care for using carbohydrate reduction as an intervention for T2DM and related conditions in an inpatient setting. Dietary modification in the form of carbohydrate restriction was a primary form of diabetes care before the advent of insulin therapy [12]. The use of exogenous insulin revolutionized the care of type 1 diabetes and also became established as a therapy in T2DM, despite the differences in underlying pathophysiology. The ubiquitous use of insulin and other pharmacologic strategies to reduce glycemia overtook the low-carbohydrate diet as a standard treatment of T2DM. This shift was accentuated by the U.S. Dietary Guidelines emphasis on dietary fat restriction with a concurrent emphasis on increasing the proportion of dietary carbohydrate. However, there has been increased interest in the therapeutic potential for carbohydrate reduction for the treatment of metabolic disease over the past 10 years. Although it is well-accepted that close glycemic control is an important factor for preventing microvascular complications such as neuropathy and retinopathy, modern treatment of T2DM using pharmacological approaches does not

consistently normalize HbA1c and has not been shown to consistently slow the progression of patients towards diabetic complications, morbidity, and mortality [13]. Furthermore, recent studies have suggested that reliance on more intensive treatment may be detrimental. The Action to Control Cardiovascular Risk in Diabetes (ACCORD) trial, which compared intensive versus standard insulin and medical therapy, shows that intensive medical treatment carries an increased risk of all-cause mortality, a 35% increased risk of cardiovascular mortality, and a greater risk of hypoglycemic events and weight gain of 10 kg in comparison to those on standard therapy [14]. Other multinational, multicenter, randomized controlled trials aimed at achieving tight blood glucose control with medications failed to demonstrate the expected reductions in heart disease, the primary cause of mortality in patients with diabetes, or in overall mortality [15-20]. In contrast to these outcomes, strong evidence exists for a promising alternative approach. The recent literature regarding the risks and benefits of intensive glycemic management of T2DM have influenced the relaxation of the HbA1c targets in the American College of Physicians guidance statement [21]. This reflects the current uncertainty regarding the prioritization of glycemic control in the pathophysiology of T2DM. Dietary approaches to improve glycemic control through carbohydrate reduction are often overlooked as a safe, effective means to normalize HbA1c levels without escalating medication therapy and the risk of hypoglycemia and other adverse events. A low-carbohydrate diet can be a useful tool for clinicians to safely achieve clinical improvement, but challenges to implementation in a clinical context remain. Confusion about different types of carbohydrate restriction, unfamiliarity with the dietary intervention, concerns about overmedication, time constraints, institutional inertia, and limited resources all present significant barriers to implementation of a low-carbohydrate diet in a clinical setting. This article provides a case study of one hospital's use of low-carbohydrate diets as a therapeutic intervention in an inpatient setting. The article defines the various levels of carbohydrate reduction, describes the therapeutic potential for low-carbohydrate dietary interventions for T2DM, and discusses how to this therapy may be used in an inpatient setting with transition to outpatient care. By outlining a clinical protocol and providing resources for the implementation of a therapeutic

low-carbohydrate dietary intervention, some barriers to using this intervention as an inpatient intervention for the treatment of T2DM and related conditions may be reduced.

### ■ Defining carbohydrate reduction

Dietary carbohydrate reduction can take many forms. More precise definitions for the variety of therapeutic approaches that carbohydrate reduction represents are needed. The following levels of carbohydrate reduction are based on protocols currently in use and on definitions found in the literature: VLCK (very low-carbohydrate ketogenic) diets recommend 30 g or less of dietary carbohydrate per day [10]. Restriction of kilocalorie (kcal) is not typically recommended. LCK (low-carbohydrate ketogenic) diets recommend 30-50 g of dietary carbohydrate per day [22]. Sometimes “net carbs” (calculated by total carbohydrate minus fiber) will be used with a goal of 25-30 g net carbs/day. Restriction of kcals is not typically recommended. RC (reduced-carbohydrate) diets recommend at least 50 g, but less than 130 g of dietary carbohydrate per day, a level that is higher than therapeutic levels listed above and lower than the U.S. Institute of Medicine dietary reference intake (DRI) for carbohydrate [23]. Restriction of kcals may or may not be recommended at this level. MCCR (moderate-carbohydrate, calorie-restricted) diets recommend more than 130 g of dietary carbohydrate per day with a range of 45-65% of daily kcals coming from carbohydrate [22]. In most cases, kcals are also restricted to maintain energy balance or to achieve a deficient for weight loss. This dietary intervention reflects the amount of dietary carbohydrate typically found in the “carbohydrate counting” dietary intervention that is given to many people with T2DM. Although this article follows common practice in using the term “low-carbohydrate diet” to refer to a variety of carbohydrate-reduction therapies implemented in clinical settings that fall below 130 g of dietary carbohydrate per day, the specific protocol under discussion here is a LCK diet. Clinicians should note that other interventions for remission of T2DM, such as very low-calorie diets or intermittent fasting, effectively reduce carbohydrate intake as part of overall kcal reduction. Conversely, reducing carbohydrate intake in practice often serves to reduce overall kcal. Recommendations for kcal restriction or “calorie counting” are not typically part of VLCK and LCK clinical interventions, but may be used in research protocols.

### ■ Therapeutic potential in T2DM

The pathogenesis of T2DM is of progressive insulin resistance to which the body responds with increased insulin secretion. Consequent hyperinsulinemia drives glucose and free fatty acids to be stored in adipose tissue, muscle, and visceral organs, which results in continued weight gain, worsening insulin resistance, and dependence on higher circulating insulin levels. Chronic hyperinsulinemia may lead to beta-cell exhaustion and failure of insulin production. Insulin acts as a proliferative signaling molecule and hyperinsulinemia may contribute to the development of cardiovascular and inflammatory disease [24,25]. The hyperglycemia of T2DM occurs when systemic insulin resistance overwhelms the ability of the pancreas to produce an adequate amount of insulin. A low-carbohydrate diet limits foods containing starch or sugar to minimize blood glucose excursions and subsequent insulin demands. Thus the basic mechanism of a low-carbohydrate diet aims to interrupt the disease progression by maintaining normoglycemia while reducing insulin demand and reducing insulin resistance over time. Low-carbohydrate diets typically minimize the requirement for insulin or other hypoglycemic medications. In contrast to pharmacological methods, a low-carbohydrate diet carries lower risk of hypoglycemia and ameliorates the need for progressive increases in pharmacologic therapy. A recent comparison of a LCK diet against a MCCR diet showed greater weight loss and better glycemic control in those following the LCK, at both 6 and 12 months of study [22]. In the aforementioned study, the metabolic benefits were followed by the removal of anti-diabetic medications in the LCK group, but not in the MCCR group. The amelioration of metabolic derangement and reduction of dependency upon insulin or other hypoglycemic medications in a number of clinical trials suggests that diabetes is, for some, a reversible condition [10,26-30].

### ■ Inpatient protocol

The protocols and resources presented here were discussed and edited by a collaboration of physicians and allied health care providers who have experience with utilizing low-carbohydrate therapies in their practices. The pathway for remission of T2DM through the use of a LCK dietary intervention has been used for 3 years at Jefferson Medical Center in West Virginia, a 24-bed critical access hospital affiliated with West Virginia University (WVU). This small

rural hospital serves a county with a population under 100,000 whose health demographics are representative of the state with the highest obesity and diabetes rates in the U.S. This institutional example demonstrates the successful implementation of therapeutic carbohydrate reduction for T2DM in an inpatient setting. The inpatient setting provides a unique opportunity to implement a low-carbohydrate approach, although it also includes several challenges for the clinician. An inpatient setting allows a carefully controlled environment in which to change the diet, measure response, and titrate medications appropriately. Through inpatient initiation of therapeutic carbohydrate reduction, a new medication regimen can safely be established before discharge with plans for outpatient follow-up. Specifically, short-acting meal time insulin dosages can usually be discontinued or dramatically decreased, which also serves as a teaching tool for patients regarding effects of dietary carbohydrate on medication use. The disruption of an inpatient hospitalization can also inspire motivation for long-term behavior change. Furthermore, the inpatient setting benefits from more time to coordinate education and follow-up. Ideally, a multi-disciplinary team approach that includes the hospital provider, pharmacy, nursing, dietary and nutrition services will be appropriately trained and available to collaborate on the implementation of this intervention. This multidisciplinary team can assist in medication management and patient education. Mobilizing an interdisciplinary team approach for education, clinical management and follow-up has been successfully modeled in the community hospital setting described above. Despite these advantages, there are significant logistical and institutional barriers to widespread use of therapeutic carbohydrate reduction for T2DM in an inpatient setting. First, eligible patients are limited due to the acute nature of short-stay inpatient admissions and tension between addressing acute versus chronic health concerns. Additionally, time and financial costs needed for educating food service staff and administering the diet can be prohibitive in many institutions. Finally, defying recommendations for fat- or salt-restricted diets represents an additional regulatory challenge. Many patients are placed on salt- or fat-restricted diets, which contradict the dietary pattern recommended for T2DM remission in this protocol. These challenges require a level of active engagement and critical thinking by the clinician and team.

For example, a patient with T2DM, hypertension (HTN), and coronary artery disease (CAD) would typically be placed on a salt- and fat-restricted diet as part of usual care. However, if it seems likely that T2DM is at the root of both of the CAD and HTN, the clinician would need to prioritize the dietary pattern supporting T2DM remission. Appendix 1 (“Clinician’s Guide to Low-Carb Diets”) provides a clinician-oriented overview that describes how and why a LCK dietary intervention may be used as a therapy for T2DM. This pamphlet may be used to initiate discussions in hospitals or clinical settings with regard to increasing the opportunities for patients to have the option to reverse T2DM using a low-carbohydrate dietary approach. We describe a seven-stage protocol for implementing a LCK diet in an inpatient setting. This protocol has been successfully used to minimize the requirement for insulin or other hypoglycemic medications and to normalize markers of T2DM. This indicates the potential for providing clinicians with the opportunity to help patients reverse T2DM, rather than just manage its progression. The seven-stage protocol consists of: 1) patient selection; 2) pre-diet evaluation and counseling; 3) patient education; 4) initiating the dietary intervention; 5) managing medication changes; 6) addressing any side effects; and 7) follow-up. It should be noted that similar methods for treating T2DM with a low-carbohydrate dietary intervention have been implemented globally in a variety of settings. The authors are familiar with the clinical application of low-carbohydrate diets in multiple primary care practices in the U.S., U.K., and Canada. Furthermore, the value of reducing carbohydrate load in the diets of those with T2DM has been recognized for over a decade, and numerous clinical trials, case reviews, and reports of clinical interventions using therapeutic carbohydrate reduction exist [10,26-34]. However, documentation of protocols indicating how clinicians may implement low-carbohydrate diets in hospital or outpatient settings to treat T2DM and related conditions is underrepresented in the medical literature.

#### ■ Patient selection

The clinical approach described in this document focuses on adults with prediabetes (HbA1c 5.7-6.5%) and T2DM (HbA1c over 6.5%). These populations were selected due to the strength of evidence base for utilization of a low-carbohydrate diet as therapy, the health burden of the disease, and the potential clinical challenges to implementation as outpatients.

These patients must be able and prepared to:

- Use a blood glucometer to check serum glucose if on insulin or insulin secretagogues (sulfonylureas and meglitinides),
- Communicate with the health care team during the LCK diet intervention

These guidelines will not extend to:

- Patients presenting with an acute, unstable medical condition.
- Pregnant women or those breastfeeding.
- Pediatric patients.

### ■ Pre-diet evaluation and counseling

The evaluation and counseling of a patient prior to initiation of a LCK diet can occur in either an inpatient or outpatient setting. Initial intake should include evaluation of patient's current symptoms, past medical history, comorbidities, current medications, and baseline laboratory workup. Pertinent components of the past medical history include date of diabetes diagnosis, time of progression to insulin-requirement (if relevant), diabetes medication history, history of hypoglycemic episodes, and diabetes complications and co-morbidities. Additional history should include polyuria and dehydration. Special attention should be given to the symptoms and timing of diagnosis and insulin requirement to elucidate any component of latent autoimmune diabetes in adults (LADA) or maturity onset diabetes of the young (MODY).

A basic laboratory workup should be completed to rule out acute pathology and establish baseline metrics. Initial laboratory tests should include the following:

- Complete metabolic panel, including liver function tests
- Complete blood count
- Thyroid function tests
- HbA1c
- Standard lipid panel
- Urinalysis
- Physical measurement of weight, BMI, waist circumference, and blood pressure
- Additional tests may include: Vitamin D, C-peptide, uric acid, high-sensitivity C-reactive protein (hsCRP), advanced lipid panel, fasting insulin and homeostatic model of insulin

resistance (HOMA-IR), glucose tolerance testing (GTT). Clinicians should note that GTT can be inaccurate if the patient is already on a LCK diet. A patient's readiness to change and support are essential for proper initiation of this therapy. The attending physician should share knowledge and information on using a LCK dietary intervention for T2DM as an option to usual care. An exploration of the patient's motivations, psychosocial, and financial situation can give insight into the patient's behaviors and barriers (e.g. disability, employment, and relationships) to the success of this dietary and behavior change intervention. In particular, capacity to buy foods and prepare meals appropriate to the intervention should also be determined. Initial counseling may be done by any trained and qualified member of the healthcare team. If a patient chooses this intervention, the patient's care team—including pharmacy, nursing, and dietary/nutrition—should be alerted in order to align patient care in a way that will help the patient be successful with this intervention.

### ■ Patient education

Adherence, satiety, and simplicity are critical to early success. Appendix 2 ("Getting Started on a Low-Carbohydrate Diet") provides a brochure that can be used to educate patients in how to begin a LCK diet. Additionally, free resources for clinicians to use in for patient education can be found at many online sites, such as DietDoctor.com. The entire healthcare team should be familiar with the general principles of how to reduce dietary carbohydrate as therapy for T2DM so that information given the patient is clear and consistent. The appropriate level of carbohydrate reduction to meet therapeutic goals will differ among patients; however, an amount of less than 50 g of carbohydrate per day will put most adults into nutritional ketosis. During this state, the body relies primarily on fatty acids and a small amount of ketones can be detected in blood, urine or breath. Importantly, this differs from ketoacidosis, in which an absolute lack of insulin causes uncontrolled lipolysis and large amounts of ketones cause metabolic acidosis. Ketones may be measured, but we do not advise this for the majority of our patients due to cost and added complexity. However, if patients understand the use of urine strips or a breath or serum meter and wish to use them, we do not discourage this. Measurement of urine ketones can be helpful in the initiation phase of this therapy. A less restrictive low-carbohydrate intervention also has therapeutic potential even

if it does not lead to a state of ketosis. A LCK diet emphasizes whole food sources of protein and fat, low-starch vegetables, full-fat dairy, nuts, and seeds. Although this intervention can be done as a vegetarian diet, the diet allows animal products and seafood to be consumed to satiety. In counseling, the emphasis should be on foods and general carbohydrate restriction, rather than monitoring macronutrient content. Adequate protein and fat intake at each meal to give a sense of satiety and satisfaction should be emphasized. Most authorities agree on about 0.8–1.0 grams of protein per kilogram of lean body weight, but this can vary based on individual needs and energy expenditure. Examples of low-carbohydrate sources of protein and fat are meat, fish, poultry, and non-meat sources such as eggs, full-fat dairy, and low-carbohydrate nuts (such as pecans and macadamias). A LCK diet encourages the liberal inclusion of non-starchy vegetables, particularly leafy greens, and sources of natural plant fats such as avocados and olives. Fiber from a variety of plant sources is thought to be beneficial for the gut microbiome, but this emerging area of interest is beyond the scope of this paper [35,36]. A LCK diet allows intake of natural fats to satiety. These include any non-trans fats, such as olive oil, coconut oil, avocado oil, full-fat dairy, and butter, along with the fats naturally associated with whole food protein sources. As it has not been determined that saturated fats in foods contribute to adverse health outcomes, foods thought to be sources of saturated fat are not restricted for this intervention [37]. Carbohydrate restriction strongly limits the intake of grains (rice, wheat, corn, oats) and grain-based products (cereals, bread, biscuits, oatmeal, pastas, crackers), starchy vegetables (potatoes, corn, legumes), sweetened dairy products (fruit yogurts, flavored milk products), sweetened desserts (gelatins, puddings, cakes), and most fruits. In general, fruit cannot be accommodated within the daily carbohydrate intake, however, unsweetened berries may be included in limited amounts. We recommend non-starchy vegetables instead as sources of fiber and micronutrients.

#### ■ Initiating dietary intervention

The patient's dietary order, as an inpatient in the hospital, should be changed to limit carbohydrate intake to 10 g per meal. To increase adherence and reduce perceived hunger, the dietary order may also include instructions to “double eggs, meat, fish, salad and eliminate all sugar/starch and sweet drinks.” This may require

some education for the hospital food service. Importantly, for hospitalized patients, this is not a weight loss or calorie-restricted diet; it is a diet for approaching normoglycemia and reducing medication requirements for controlling blood glucose. In most cases, sodium should not be restricted because natriuresis occurs with carbohydrate restriction. Many patients will experience lower blood pressure within several days of initiation of the diet, and some will experience this immediately. In this setting, post-meal blood glucose testing can serve as an educational opportunity to demonstrate to patients that if they do not eat carbohydrate-dense foods such as sugars and starches, their blood glucose does not go up with meals, even without the administration of insulin.

#### ■ Medication management

See Appendix 3 for an overview of medication reduction guidelines for following patients with T2DM on a LCK dietary. This table demonstrates the alterations of medications that will be necessary during the treatment of T2DM with a LCK diet. As the diet continues to reduce blood glucose and insulin resistance, hypoglycemic medication must be carefully monitored and titrated to prevent hypoglycemia. No “sliding scale” insulin is needed to cover meals as patients will not be consuming significant amount of carbohydrate foods at mealtime. Short-acting insulin may be needed to correct blood glucose excursions over 200 mg/dL and bring them down to 150 mg/dL range. The immediate goal is not normoglycemia, but to wean patients off of insulin or other hypoglycemic medications. In this context, short term mild hyperglycemia is safer than hypoglycemia. For patients with T2DM who have some remaining beta cell function, the healthcare team should consider changing long-acting insulin to morning-only glargine (Lantus), detemir (Levemir), or NPH insulin; note none of these are 24-hour insulins. Morning dosing fits better with normal circadian and meal patterns and allows reduced insulin load at night. This dose should be reduced to no more than 40 units even if the patient is on high-dose, long-acting insulin at home. Patients with beta cell failure will need a split dose of long-acting insulin. Patients may be weaned from long-acting insulin and have it discontinued entirely if blood glucose levels are consistently low; hypoglycemia is rare with low-dose, long-acting insulin in the morning. Sulfonylureas and insulin secretagogues should be discontinued immediately, as directed in Appendix 3. SGLT2

inhibitors pose a risk for euglycemic acidosis and therefore should be discontinued. The healthcare team may consider adding an insulin-sensitizing agent (metformin) if the patient is not already taking this. This is contraindicated if eGFR is <30 ml/min, but in the impaired range of the kidneys' estimated glomerular filtration rate (eGFR) 30-45 ml/min, a discussion of risk and benefit should occur. Blood pressure often improves on LCK diets. Symptoms of orthostasis, systolic blood pressure below 120, or diastolic blood pressure below 70 is an indication to wean patient from antihypertensive medication. Diuretics are problematic as carbohydrate reduction induces naturesis. The healthcare team should consider tapering these immediately unless indicated for symptomatic heart failure. Renal protective angiotensin-converting-enzyme (ACE) inhibitors or angiotensin II receptor blockers (ARBs) should be continued if proteinuria is present, unless patient develops hypotensive even on low dose. Patients should also be taught home monitoring of blood pressure, so that medication can be adjusted daily. When making any significant dietary change, the healthcare team should closely monitor drugs with a narrow therapeutic window, such as some seizure medications, digoxin, or antibiotics.

### ■ Adverse effects and supplementation

The most significant adverse effects from a LCK diet originate from over-medication with hypoglycemic and anti-hypertensive medications following a dramatic dietary change. See Appendix 3 for how to safely reduce medications when a LCK diet is initiated. The insulin-lowering effects of a LCK diet can reduce the resorption of sodium and other electrolytes in the kidney. Sustained loss of salt *via* the urine can contribute to hypovolemia and feelings of fatigue and lethargy that some patients experience when transitioning to a LCK diet. It is recommended that patients on a LCK diet consume normal amounts of salt, around 4-6g per day [38]. Bouillon may be ordered for the patient for this purpose, but it should not be "low-sodium." Further supplementation with magnesium may also be helpful for patients and should be considered on an individualized basis (See Appendix 1 for more details). Good hydration with water is essential, most often over 2 liters a day. Some historical examples of low-carbohydrate diets have greatly restricted the intake of a variety of foods, and supplementation with a multivitamin is often suggested in those cases. The LCK diet for T2DM treatment

described here emphasizes a wide variety of plant and animal foods with high nutrient density. This diet will provide adequate essential nutrition for the majority of individuals; the recommendation of multivitamin supplementation should be on a personalized basis for the patient and is left to the clinician's and patient's discretion. Individual testing of Vitamin D, B12, folate, and magnesium can guide supplementation. Supplements containing medium chain triglycerides (MCT) are often a part of ketogenic diets for neurological treatments such as epilepsy. The MCTs contained in these supplements are readily absorbed by the liver and converted into ketone bodies. Supplementation of MCT is not recommended for the treatment of T2DM. Whereas the goal of MCT supplementation with ketogenic diets for epilepsy is to create high levels of ketones for therapy, high levels of ketones are not necessary for dietary treatment of T2DM. See Appendix 1 for additional information about treating side effects that may occur during the transition to a LCK diet. Although not a contraindication to a LCK diet intervention, history of bariatric surgery or cholecystectomy may require individual tailoring based on diet tolerance. For patients with previous cholecystectomy, dietary fat will have to be increased gradually with possible bile salt supplementation for persistent gastrointestinal distress. History of gout or elevated uric acid is not a contraindication to the diet. Clinical experience has demonstrated that adherence to a LCK diet may decrease uric acid levels over time [35]. Initiation of the diet may precipitate a flare but will likely result in long-term improvement. Because a LCK diet often involves changes in consumption of Vitamin K-containing vegetables, monitoring of International Normalized Ratio (INR) should be more frequent in patients taking warfarin.

### ■ Discharge and follow-up

Prior to discharge, the healthcare team should review medication changes and home monitoring of blood glucose and blood pressure if on medications. Patients should be educated in a safe medication reduction strategy and should have immediate access to an appropriately trained healthcare provider for any questions or concerns. Although resources may vary according to clinic or hospital staff, contact email and cell phone numbers should be available to patients. To avoid confusion, electronically generated discharge forms which might contradict the LCK intervention should not be used. For example if a patient has a diagnosis of T2DM, the standard

hospital instructions often recommend 60 g carbs per meal with 15 g carb snacks. Printed discharge instructions for hypertension and heart failure often advise salt reduction to less than 2 g per day. These instructions are not appropriate for patients following a LCK diet. Patients should also be empowered to take charge of their health with the support of family and their healthcare providers. The patient should check blood pressure and blood glucose daily, including some post-prandial readings 1-2 hrs after a meal. Medication, blood pressure, and glucose logs are an indispensable part of safe and optimal care (see Appendix 1 for examples). Having the patient record weekly waist circumference and body weight measurements may also be helpful in monitoring progress. A dietitian trained in carbohydrate reduction can assist patients with identifying and overcoming barriers to adhering to this intervention, including limited financial or time resources, “trigger foods,” food addiction, and eating out. Outpatient follow-up is essential until new medication regimen is optimized. Medication titration may need to occur multiple times as insulin resistance improves. If a member of the hospital healthcare team is not the primary care provider, contact the primary care provider and let them know of the dietary intervention and accompanying medication changes. For Jefferson Medical Center, an outpatient clinic at WVU Center for Diabetes and Metabolic Health often assists after hospital discharge. Return visits allow additional opportunities for education and encouragement. Laboratory workup should be completed about 3 months of initiating the dietary intervention. This should include a complete metabolic panel and HbA1c; waiting at least 6 months to repeat lipid panel is advised. The primary care physician should continue to check HbA1c every 3 months, adjusting medications as necessary. Clinicians should be cautious in discontinuing long-acting insulin in anyone with possible irreversible beta cell dysfunction due to autoimmunity, injury, or beta cell failure of long-standing T2DM. Most patients will notice a dramatic decline in triglycerides (TG), increase in high-density lipoprotein (HDL) cholesterol, and decrease in HbA1c. Although some patients will also show an increase in low-density lipoprotein (LDL) cholesterol, a recent meta-analysis of low-carbohydrate diets and lipid effects shows an overall favorable response, concluding that, “Large randomized controlled trials of at least 6 months duration with carbohydrate restriction

appear superior in improving lipid markers when compared with low-fat diets. Dietary guidelines should consider carbohydrate restriction as an alternative dietary strategy for the prevention/management of dyslipidemia for populations with cardiometabolic risk” [39]. The role of LDL cholesterol alone as a risk predictor in cardiovascular disease is tenuous [37], therefore the patient’s atherosclerotic cardiovascular disease (ASCVD) risk should be recalculated with the new laboratory markers including TG and HDL cholesterol. In almost all cases the patient can be reassured of their risk profile if slight LDL cholesterol elevation. Larger elevations of LDL cholesterol, if they occur, would require an individualized treatment plan.

### Case study

DT is a 41-year-old African-American law enforcement officer with a recent diagnosis of T2DM when he presented to Jefferson Medical Center in June 2017 with a glucose of 700, HbA1c of 14.9, and serum creatinine of 7. Other significant medical history included hypertension, gout, hypercholesterolemia, and obesity. His diabetic pharmacotherapy at the time of admission was long-acting insulin degludec injection (15 units daily), metformin (1 g twice daily), lisinopril (40 mg daily), metoprolol/hydrochlorothiazide (50 mg/12.5 mg daily), and simvastatin (40 mg daily). With intensive hospital management of hydration and insulin, renal failure improved, and he avoided hemodialysis. Due to extreme insulin resistance he was discharged on 70 units of insulin glargine twice a day and short-acting insulin lispro, up to 20 units before meals. Following the protocol outlined above, he was introduced to the option of low-carbohydrate eating. He was interested in pursuing this option and arranged for quick follow-up after discharge. Two weeks after discharge, his creatinine was down to 1.16 and glucose normalized on 20 units of long-acting insulin a day. DT continued to follow a low-carbohydrate, sugar-free diet and was able to stop insulin completely within a month after discharge. On metformin alone, his HgA1c results have been 6.7 at three months after discharge, 5.8 at 13 months, and 5.9 at 17 months. He has been discharged from the renal clinic, reduced close to 100 pounds of body weight and several inches of waist, and returned to his job and youth coaching. From near-dialysis in June 2017, he has been able to maintain health improvements for over 17 months and now has the opportunity for a healthy future.



---

## Discussion

Remission of prediabetes and T2DM has not been fully defined or agreed upon in the literature, as T2DM is most often treated as a chronic progressive condition. However, remission indicates the reversal or disappearance of signs and symptoms, which can be temporary or permanent, and this can be achieved in T2DM with therapeutic levels of carbohydrate reduction. Prediabetes may be considered to be put in remission with a HbA1c measurement of <5.7% and T2DM reversed with a HbA1c measurement of <6.5% with or without the use of an insulin-sensitizing agent such as metformin. Remission can be defined as two measurements below these thresholds at least two months apart, again with or without the use of metformin [40]. Although the benefits of carbohydrate restriction for individuals with T2DM are recognized, many experts have raised concerns about whether patients can adhere to such a diet indefinitely. Because dietary carbohydrate is not an essential nutrient [23], a well-formulated LCK diet that includes a variety of vegetables presents no health risks from nutritional deficits. However, other considerations, such as traditional or celebratory foods, should be taken into account when discussing long-term adherence to a low-carbohydrate dietary intervention. In the context of selection of highly motivated individuals or administration of programs that encourage high adherence, remission of T2DM is possible [22,41]. In terms of sustainability of this intervention, a recent survey of participants voluntarily adhering to a low-carbohydrate diet suggests that weight loss and diabetes remission is sustainable when a low-carbohydrate diet is incorporated as a lifestyle change [41]. The survey found that before respondents started a low-carbohydrate diet, nearly nine of 10 experienced intense hunger between meals. Once on the diet, only 3.5% said they grew hungry between meals. Respondents reported similar improvements in other aspects of their physical and psychological well-being. Of the 1,580 survey participants, more than half reported staying on a low-carbohydrate diet for at least one year, with 34% using this intervention for more than two years. Further, those on the diet for two years or more said that they had largely maintained their weight loss. This is a self-selected sample, with an obvious bias for people who are experiencing success. However, this data does show that long-term adherence is possible. Whether or not and in what manner

to allow additional dietary carbohydrate to the diet will be an individual decision. It is unlikely that a return to previous levels of carbohydrate consumption would be recommended; to do so would likely lead to a return of previous health conditions that reduction of dietary carbohydrate ameliorated. However, as with other dietary components that are non-essential such as alcohol, limited amounts may be tolerated. For some individuals, increased dietary carbohydrate may be offset by deliberately restricting calories in a way that prevents weight gain. Other individuals may prefer to forgo calorie counting in favor of continued carbohydrate restriction. For individuals with remission of T2DM, a re-introduction of dietary carbohydrates requires continued blood glucose monitoring and regular HbA1c measurements.

### ■ Outpatient settings

Many patients eligible for low-carbohydrate therapy and medication reduction present in ambulatory settings. Although the protocol described here was designed for use in an inpatient setting, it may be adapted to an outpatient setting. Patients on insulin therapy may benefit significantly from a LCK dietary intervention in either setting, but they present significant challenges in medication management given the time constraints of the outpatient environment. In this case, consideration should be made for inpatient initiation of a LCK diet and medication management for poorly controlled cases of T2DM, especially if severe co-morbidities are already present. Otherwise, patient education and community support from physicians and allied healthcare providers is especially important with regard to medication management as dietary carbohydrate is reduced. Ideally, as with the inpatient setting, a multi-disciplinary team of providers—including clinicians, pharmacists, nurses, dietitians, and health coaches—will collaborate on patient care. Something as simple as cell phone technology can greatly assist clinicians in the successful use of this intervention. Daily text messaging between the patients and the physician or another trained team member allows medication reduction to be safely tailored to the patient's needs. In a community setting, opportunities to meet and socialize with others using low-carbohydrate dietary interventions may assist with supporting individuals in making dietary and behavior changes. For example, at WVU Center for Diabetes and Metabolic Health, where patients from Jefferson Medical Center frequently receive

follow-up care, the group-visit model is being used to support patients and families in making necessary lifestyle changes.

#### ■ Additional considerations

This article has focused on the use of a LCK dietary intervention to treat T2DM initiated in a hospital setting; however, there are other conditions for which this type of intervention may be appropriate. Individuals with metabolic syndrome (MetSyn) may also benefit from dietary therapies that reduce carbohydrate. Identify these individuals and placing them on an individualized low-carbohydrate intervention may help prevent progression of further metabolic dysfunction and the development of T2DM or other chronic diseases. Various definitions and sets of identifying criteria for MetSyn have been put forth [42]. The following conditions are considered to be related features of metabolic dysregulation. An individual presenting with 3 or more of these conditions can be identified as having MetSyn:

- A large waistline (waist  $\times 2 >$  height). This also is called abdominal obesity or “having an apple shape.” Excess fat in the stomach area is a greater risk factor for heart disease than excess fat in other parts of the body, such as on the hips.
- A high TG level ( $> 150$  mg/dl) or on medicine to treat high TG.
- A low HDL cholesterol level ( $<40$  mg/dl for males,  $<50$  mg/dl for females) or on medicine to treat low HDL cholesterol.
- High blood pressure ( $>130/85$ ) or on medicine to treat high blood pressure.
- High fasting blood sugar ( $>100$  mg/dl) or on medicine to treat high blood sugar.

Clinicians should note that the above criteria may be inadequate in identifying MetSyn in African-American populations. Elevated triglycerides are closely associated with lower HDL-cholesterol, which suggests a redundancy in clinical criteria for MetSyn that is beyond the scope of this paper, but which may exclude from MetSyn diagnosis populations that do not demonstrate this dyslipidemic profile [43-45]. A diagnosis of MetSyn, suspected from family history of T2DM or other indications, may need to be ascertained through more direct measures of insulin resistance. Low-carbohydrate diets that are restricted to ketogenic levels have been used as therapeutic diets for epileptic seizures for a number of years [46]. There is a robust literature

on the implementation and effectiveness of these diets. However, clinicians should note that these diets are distinct from low-carbohydrate diets used to treat T2DM in that they tend to be far more restrictive and are directed at other considerations, such as the generation of ketones for therapeutic purposes, besides minimizing blood glucose excursions and subsequent insulin demands. Low-carbohydrate diets have also been proposed as interventions for many other health conditions, including obesity, polycystic ovary syndrome (PCOS), gastroesophageal reflux disease (GERD), non-alcoholic fatty liver disease (NAFLD), and gout [35,47-50]. Many of these have limited evidence secondary to little research; however the principles of this guide may be used for safe implementation of low-carbohydrate diet for other clinical presentations as the research and clinical experience for using this intervention for those conditions expands.

#### Conclusion

Low-carbohydrate diets are not a new intervention for treatment of T2DM. A textbook published in 1877 indicates that carbohydrate reduction is the preferred treatment for patients with diabetes: “There are few diseases which present to the practitioner so clear an indication of what is to be done...a Diabetic should exclude all saccharine [sugary] and farinaceous [starchy] materials from his diet” [51]. Leading endocrine societies are now rediscovering this treatment. The American Diabetes Association’s (ADA) October 2018 joint position statement with the European Association for the Study of Diabetes (EASD) approved use of a low-carbohydrate diet as Medical Nutrition Therapy (MNT) for adults with T2DM [52]. The ADA’s recently released Standards of Medical Care in Diabetes—2019 includes in its lifestyle management guidance the use of low-carbohydrate diets as nutrition therapy, reflecting the organization’s emphasizes on a patient-centered, individualized approach [53]. The ADA and the EASD both recognize that LCK diets can be a safe, effective way for people diagnosed with T2DM or prediabetes to normalize HbA1c levels while lowering medication therapy, reducing the risk of hypoglycemia or other adverse medication effects, and assisting in weight loss. In this review, we highlight recent trials on the topic but more importantly provide clinicians with guidance for implementing this kind of dietary intervention in their own hospitals or clinics. In providing of a clinical protocol for using a

LCK dietary intervention, this article offers the foundations for a shared language for clinicians to use in discussing and comparing interventions, improving protocols, and managing shared concerns. We do not expect this guidance to provide a “one-size-fits-all” approach to care; rather we expect that knowledge gained from the clinical experiences of others will inform a continued improvement in how low-carbohydrate dietary interventions are used to treat patients. We do, however, anticipate a

necessary change in how we discuss the course and treatment of T2DM with patients. With a simple, safe, effective dietary intervention, we can change the conversation around T2DM from one of progression to one of remission.

### Funding

Laura Saslow's time was supported, in part, by the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK, K01DK107456, Saslow).

### References

- Bommer C, Sagalova V, Heesemann E *et al.* Global economic burden of diabetes in adults: Projections from 2015 to 2030. *Diabetes Care.* 41(5), 963–970 (2018).
- Bullard K, Cowie C, Lessem S *et al.* Prevalence of diagnosed diabetes in adults by diabetes type-United States, 2016. *Morb. Mortal. Wkly. Rep.* 67, 359–361 (2018).
- Menke A, Casagrande S, Geiss L *et al.* Prevalence of and trends in diabetes among adults in the United States, 1988-2012. *JAMA.* 314(10), 1021–1029 (2015).
- American Diabetes Association. Economic costs of diabetes in the U.S. in 2017. *Diabetes Care.* 41(5), 917–928 (2018).
- Howard A, Khan M, Jones M *et al.* Type 2 diabetes mellitus: Outpatient insulin management. *American Family Physician.* 97(1), 29–37 (2018).
- Buchwald H, Buchwald J. Metabolic (Bariatric and Nonbariatric) Surgery for type 2 diabetes: a personal perspective review. *Diabetes Care.* 42(2), 331–340 (2019).
- Furmler S, Elmasry R, Ramos M *et al.* Therapeutic use of intermittent fasting for people with type 2 diabetes as an alternative to insulin. *BMJ Case. Rep.* (2018)
- Lean M, Leslie W, Barnes A *et al.* Primary care-led weight management for remission of type 2 diabetes (DiRECT): An open-label, cluster-randomised trial. *The Lancet.* 391(10120), 541–551 (2018).
- Feinman R, Pogozelski W, Astrup A *et al.* Dietary carbohydrate restriction as the first approach in diabetes management: Critical review and evidence base. *Nutrition.* 31(1), 1–13 (2015).
- Hallberg S, McKenzie A, Williams P *et al.* Effectiveness and safety of a novel care model for the management of type 2 diabetes at 1 year: An open-label, non-randomized, controlled study. *Diabetes Therapy.* 9(2), 583–612 (2018).
- Barnard. A low-fat vegan diet and a conventional diabetes diet in the treatment of type 2 diabetes: a randomized, controlled, 74-wk clinical trial. *Am. J. Clin. Nutr.* 89(5), 1588S–1596S (2009).
- Westman E, Yancy W, Humphreys M. Dietary treatment of diabetes mellitus in the pre-insulin era (1914–1922). *Perspect. Biol. Med.* 49(1), 77–83 (2006).
- Stratton IM. Association of glycaemia with macrovascular and microvascular complications of type 2 diabetes (UKPDS 35): prospective observational study. *BMJ.* 321(7258), 405–412 (2000).
- Action to Control Cardiovascular Risk in Diabetes Study Group. Effects of intensive glucose lowering in type 2 diabetes. *N. Engl. J. Med.* 358(24), 2545–2559 (2008).
- Zoungas S, Chalmers J, Neal B *et al.* Follow-up of blood-pressure lowering and glucose control in type 2 diabetes. *N. Engl. J. Med.* 371(15), 1392–1406 (2014).
- Hayward R, Reaven P, Wiitala W *et al.* Follow-up of glycemic control and cardiovascular outcomes in type 2 diabetes. *N. Engl. J. Med.* 372(23), 2197–2206 (2015).
- Gerstein H, Bosch J, Dagenais G *et al.* Basal insulin and cardiovascular and other outcomes in dysglycemia. *N. Engl. J. Med.* 367(4), 319–328 (2012).
- Green J, Bethel M, Armstrong P *et al.* Effect of sitagliptin on cardiovascular outcomes in type 2 diabetes. *N. Engl. J. Med.* 373(3), 232–242 (2015).
- Hirshberg B, Katz A. Insights from cardiovascular outcome trials with novel antidiabetes agents: What have we learned? An industry perspective. *Curr. Diab. Rep.* 15(11), 87 (2015).

20. Scirica B, Bhatt D, Braunwald E *et al.* Saxagliptin and cardiovascular outcomes in patients with type 2 diabetes mellitus. *N.Engl. J. Med.* 369(14),1317–1326 (2013).
21. Qaseem A, Wilt T, Kansagara D *et al.* Hemoglobin A1c targets for glycemic control with pharmacologic therapy for nonpregnant adults with type 2 diabetes mellitus: A guidance statement update from the American College of Physicians. *Ann. Intern. Med.* 168(8),569–576 (2018).
22. Saslow L, Daubenmier J, Moskowitz J *et al.* Twelve-month outcomes of a randomized trial of a moderate-carbohydrate versus very low-carbohydrate diet in overweight adults with type 2 diabetes mellitus or prediabetes. *Nutr. Diabetes.* 7(12) (2017).
23. Institute of Medicine [U.S.]. Dietary Reference Intakes for Energy, Carbohydrate, Fiber, Fat, Fatty Acids, Cholesterol, Protein, and Amino Acids. 2005. Washington, DC: The National Academies Press.
24. Crofts, C., Zinn C, Wheldon M *et al.* Hyperinsulinemia: a unifying theory of chronic disease? *Diabetes.* 1(4), 10 (2015).
25. Reaven G. Insulin resistance, cardiovascular disease, and the metabolic syndrome. *Diabetes. Care.* 27(4),1011–1012 (2004).
26. Meng Y, Bai H, Wang S *et al.* Efficacy of low carbohydrate diet for type 2 diabetes mellitus management: A systematic review and meta-analysis of randomized controlled trials. *Diabetes. Res. Clin. Pract.* 131,124–131 (2017).
27. Yancy W, Foy M, Chalecki A *et al.* A low-carbohydrate, ketogenic diet to treat type 2 diabetes. *Nutr. Metab. (Lond).* 2(1),34 (2005).
28. O'Neill D, Westman E, Bernstein R. The effects of a low-carbohydrate regimen on glycemic control and serum lipids in diabetes mellitus. *Metab. Syndr. Relat. Disord.* 1(4), 291–298 (2003).
29. Vernon M, Mavropoulos J, Transue M *et al.* Clinical experience of a carbohydrate-restricted diet: Effect on diabetes mellitus. *Metab. Syndr. Relat. Disord.* 1(3),233–237 (2003).
30. Nielsen J, Joensson E. Low-carbohydrate diet in type 2 diabetes: Stable improvement of bodyweight and glycemic control during 44 months follow-up. *Nutr. Metab. (Lond).* 5(1),14 (2008).
31. Gannon M, Nuttall F. Control of blood glucose in type 2 diabetes without weight loss by modification of diet composition. *Nutr. Metab. (Lond).* 3,16 (2006).
32. Arora S, McFarlane S. The case for low carbohydrate diets in diabetes management. *Nutr. Metab. (Lond).* 2(1),16 (2005).
33. Westman E, Yancy W, Edman J *et al.* Effect of 6-month adherence to a very low carbohydrate diet program. *The American Journal of Medicine.* 113(1),30–36 (2002).
34. Unwin, D, Cuthbertson D, Feinman R *et al.* A pilot study to explore the role of a low-carbohydrate intervention to improve GGT levels and HbA1c. *Diabetes in Practice.* 4(3),102–108 (2015).
35. Goldberg E, Asher L, Molony RD *et al.*  $\beta$ -Hydroxybutyrate deactivates neutrophil NLRP3 inflammasome to relieve gout flares. *Cell. Rep.* 18(9),2077–2087 (2017).
36. Valdes A, Walter J, Segal E *et al.* Role of the gut microbiota in nutrition and health. *BMJ.* 361, k2179 (2018).
37. Forouhi N, Krauss R, Taubes G *et al.* Dietary fat and cardiometabolic health: evidence, controversies, and consensus for guidance. *BMJ.* 361, k2139 (2018).
38. Mente A, O'Donnell M, Rangarajan S *et al.* Associations of urinary sodium excretion with cardiovascular events in individuals with and without hypertension: A pooled analysis of data from four studies. *Lancet.* 388(10043), 465–475 (2016).
39. Gjuladin-Hellon T, Davies I, Penson P *et al.* Effects of carbohydrate-restricted diets on low-density lipoprotein cholesterol levels in overweight and obese adults: A systematic review and meta-analysis. *Nutrition. Reviews.* (2018).
40. McCombie L, Leslie W, Taylor R *et al.* Beating type 2 diabetes into remission. *BMJ.* 358;j4030 (2017).
41. Cucuzzella M, Tondt T, Dockter N *et al.* A low-carbohydrate survey: Evidence for sustainable metabolic syndrome reversal. *J. Insul. Resist.* 2(1):a30.
42. Huang P. A comprehensive definition for metabolic syndrome. *Disease models & mechanisms.* 2(5-6),231–237 (2009).
43. Zeno S, Deuster P, Davis J *et al.* Diagnostic criteria for metabolic syndrome: Caucasians versus African-Americans. *Metab. Syndr. Relat. Disord.* 8(2),149–156 (2010).
44. Kim-Dorner S, Deuster P, Zeno S *et al.* Should triglycerides and the triglycerides to high-density lipoprotein cholesterol ratio be used as surrogates for insulin resistance? *Metabolism.* 59(2), 299–304 (2010).
45. Sumner A. Ethnic differences in triglyceride levels and high-density lipoprotein

- lead to underdiagnosis of the metabolic syndrome in black children and adults. *J. Pediatr.* 155(3), S7.e7-e8 (2009).
46. Kossoff E, Zupec-Kania B, Auvin S *et al.* Optimal clinical management of children receiving dietary therapies for epilepsy: Updated recommendations of the International Ketogenic Diet Study Group. *Epilepsia. Open.* 3(2),175–192 (2018).
47. Hu T, Yao L, Reynolds K *et al.* Adherence to low-carbohydrate and low-fat diets in relation to weight loss and cardiovascular risk factors. *Obes. Sci. Pract.* 2(1), 24–31 (2016).
48. Alwahab U, Pantalone K, Burguera B. A ketogenic diet may restore fertility in women with polycystic ovary syndrome: A case series. *AACE. Clinical. Case. Reports.* 4(5), (2018).
49. Pointer S, Rickstrew J, Slaughter J *et al.* Dietary carbohydrate intake, insulin resistance and gastro-oesophageal reflux disease: A pilot study in European- and African-American obese women. *Alimentary Pharmacology & Therapeutics.* 44(9),976–988 (2016).
50. Browning J, Baker J, Rogers T *et al.* Short term weight loss and hepatic triglyceride reduction: Evidence of a metabolic advantage with dietary carbohydrate restriction. *Am. J. Clin. Nutr.* 93(5),1048–1052 (2011).
51. Morgan, W. Diabetes mellitus: Its history, chemistry, anatomy, pathology, physiology, and treatment. New York, NY. Boericke & Tafel
52. Davies M, D'Alessio D, Fradkin J *et al.* Management of hyperglycaemia in type 2 diabetes, 2018. A consensus report by the American Diabetes Association (ADA) and the European Association for the Study of Diabetes (EASD). *Diabetologia.* 61(12), 2461–2498 (2018).
53. American Diabetes Association. Standards of medical care in diabetes –2019. *Diabetes. Care.* 42(1), S1–S2 (2019).

---

# *Clinician's Guide to Low-Carbohydrate Diets*

---

There is increasing evidence for the efficacy of low-carbohydrate diets for type 2 diabetes, metabolic syndrome, and weight loss (1,2,17). However, widespread recommendation and implementation of very-low-carbohydrate diets in practice has been limited in part by physician knowledge and comfort with the approach. Patients with significant co-morbidities and medications could benefit from following a low-carbohydrate lifestyle, and the guidance of an informed clinician may help avoid preventable adverse events. Even if clinicians are not actively recommending low-carbohydrate diets to their patients, patients may wish to try. For these reasons, it is important for physicians to be knowledgeable on the topic.

## CONTENTS

- Low-Carb Basics
- Levels of Carbohydrate Restriction
- Nutritional Ketosis
- Measuring Ketones
- Medication Management
- Side Effects
- FAQ
- Resources
- References

## What Does a Low-Carbohydrate Diet Look Like?

The goal of a low-carbohydrate diet is to reduce insulin levels to facilitate fat lipolysis. This is accomplished by restricting any foods that break down into glucose, including complex carbs and whole grains.

### A low-carbohydrate meal plan includes:

- ✓ **Veggies:**  
Non-starchy, above-ground veggies (spinach, Brussels sprouts, cabbage, broccoli, cauliflower)
- ✓ **Proteins:**  
Eggs, any non-fried or non-breaded meats, fish, poultry, tofu, nuts, nut butters, plain yogurt
- ✓ **Fats from real foods:**  
Butter, olive oil, coconut oil, avocado, full-fat dairy products like sour cream and cream cheese

### The following are NOT part of a low-carbohydrate meal plan:

- ☒ **Any type of grains or starches (refined OR whole grain):**  
Breads, pasta, potatoes, rice, oatmeal, cereals, crackers, chips
- ☒ **Fruits**  
Most fruit will not fit into daily carbohydrate allotment; low-carb fruits like berries can be accommodated in limited amounts
- ☒ **High carbohydrate dairy products:**  
Milk, yogurt with added sugar
- ☒ **Fats from processed food**  
Most foods high in highly processed oils and fats also contain carbohydrates and are not part of the meal plan.
- ☒ **Added sugars and sweetened beverages**

## How Low is Low-Carb?

*“Low carb” diets may refer to a wide range of carbohydrate intake, leading to confusion for patients and clinicians.*

- VLCK (very low-carbohydrate ketogenic) diets recommend 30g or less of dietary carbohydrate per day (1). Restriction of kilocalorie (kcal) is not typically recommended.
- LCK (low-carbohydrate ketogenic) diets recommend 30-50g of dietary carbohydrate per day (2). Sometimes “net carbs” (calculated by total carbohydrate minus fiber) will be used with a goal of 25-30g net carbs/day. No kcal restriction.
- RC (reduced-carbohydrate) diets recommend 50-130g of dietary carbohydrate per day, which is usually higher than a ketogenic range but lower than dietary reference intake (DRI) for carbohydrate.
- MCCR (moderate-carbohydrate, calorie-restricted) diets recommend more than 130g of dietary carbohydrate per day with a range of 45-65% of daily kcals coming from carbohydrate. In most cases, kcals are also restricted to maintain energy balance or to achieve a deficit for weight loss. This dietary intervention reflects the amount of dietary carbohydrate typically found in the “carbohydrate counting” dietary intervention that is given to many people with T2DM.

*This guide is specifically to guide management of low-carbohydrate, ketogenic meal plans which will induce a state of nutritional ketosis for many patients.*



## Nutritional Ketosis

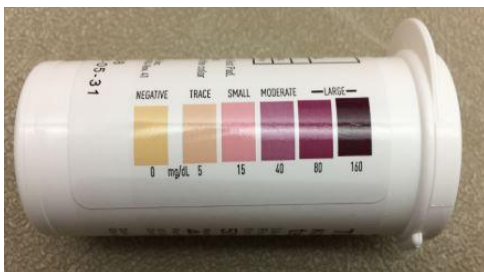
Ketones are molecules produced by the liver from fatty acids. Ketones can be used as a fuel source by extra-hepatic tissues. Ketosis refers to the presence of ketones in the blood when insulin is low and release of fatty acids from adipose tissue is accelerated (3). Most people develop low levels of ketosis after an overnight fast, and ketones increase further with longer fasts or carbohydrate restriction. Ketone levels induced by carbohydrate restriction will never approach the levels induced by frank insulin deficiency as in diabetic ketoacidosis. This low-level dietary ketosis is not harmful and may even be therapeutic (3).

### Measuring Ketones

There are three types of principal ketones bodies: acetone, acetoacetate and 3- $\beta$ -hydroxybutyrate (3HB). Urine and breath tests give semiquantitative measures of acetoacetate, and serum tests can give a quantitative measure of 3HB. 3HB is most clinically relevant as it comprises most circulating ketones (4).

#### Urine Ketones

Urine ketone strips measure acetoacetate via a nitroprusside reaction causing a color change corresponding to the concentration in the urine (4). Urine strips can be obtained over the counter (Ketostix) and are sometimes used to verify ketosis. The appropriate ranges are "trace" to "small" or 5-15mg/dl.



#### Serum Ketones

Blood testing measures 3HB which is the primary circulating ketone. The appropriate serum ranges for nutritional ketosis are 0.8-3 mmol/l (14-54 mg/dl). This represents a low-level of ketosis and is not indicative of ketoacidosis if blood glucose is below 270mg/dl and pH >7.3 (4).



# Nutritional Ketosis vs Ketoacidosis

- Natural physiologic state allowing utilization of ketones as a supplemental fuel (2)
- Can occur in anyone during fasting or carbohydrate restriction
- Ketones generally remain below 3mmol/l (54mg/dl) and do not change blood pH
- Blood glucose remains below 270mg/dl

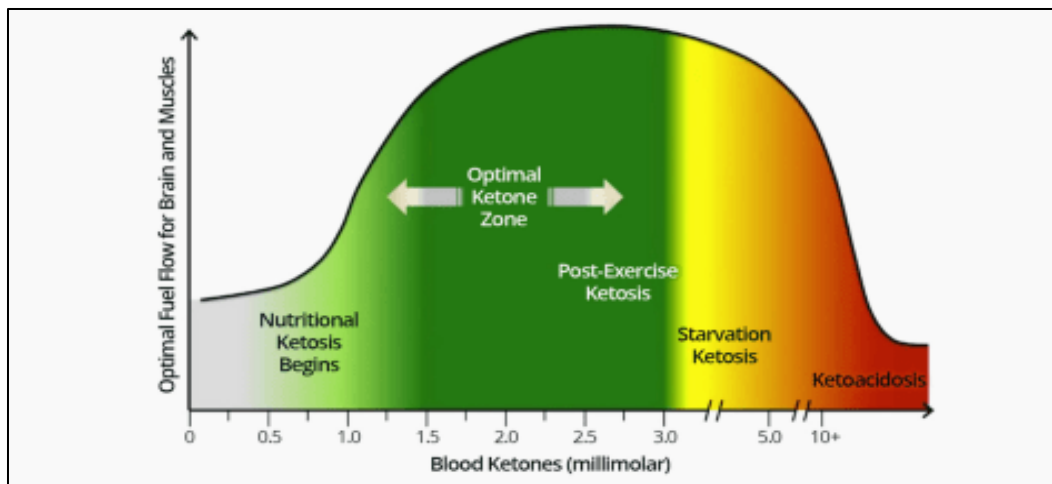
(5)

-Medical emergency requiring urgent intervention

-Occurs with insulin deficiency in patients with type 1 diabetes or insulin dependent type II diabetes. Frank insulin deficiency allows unregulated lipolysis causing high levels of fatty acids driving ketone production

-High levels of ketones (>3mmol/L), high glucose (>270mg/dl) and metabolic acidosis (pH<7.3)

-Symptoms such as fatigue, confusion, vision changes, dehydration, polyuria and rapid breathing



## Medication Management on a Low-Carbohydrate Diet

Understanding the impact of diet on common medications is important to keep patients safe. The diet itself is not dangerous but it does induce significant changes to metabolism and electrolyte balance that may cause patients to become over-medicated.

### Diabetes Medication

✓ **Metformin**

- Can be used effectively in conjunction with a low-carb diet (6).  
Metformin does not present the same risks of hypoglycemia as insulin or sulfonylureas.

☒ **Sulfonylureas**

-To prevent hypoglycemia, secretagogues should be reduced by at least 50% or discontinued before patients begin a low-carb diet to prevent hypoglycemia as insulin or sulfonylureas.

### **SGLT2 inhibitors**

There are risks of ketoacidosis while taking SGLT2 inhibitors and case reports have been described in the context of low-carbohydrate diets (18). Although this is rare, it is something to be aware of and consider discontinuing SGLT2 inhibitors if glycemia improves.

### **GLP-1 agonists and DDP-4 inhibitors (gliptins)**

These medications can be used in conjunction with a low-carbohydrate diet

### Insulin

For patients with type 2 diabetes taking less than 20 units of daily insulin, insulin should be discontinued the day the diet begins. In other patients, mealtime insulin should be discontinued, and basal dose should be reduced by at least 50%. Patients should increase frequency of glucose monitoring to re-establish dosing and avoid hypoglycemia. Patients should be instructed on when to call the clinic and to not take insulin if blood glucose is less than 100 mg/dl.

#### *Meal coverage:*

- Mealtime straight dosing or carb ratios are not indicated as meal insulin will be unnecessary with minimal carbohydrate load.

#### *Sliding Scale Correction:*

- Can be continued with a lower correction scale

*Continued...*

## Medication Management on a Low-Carbohydrate Diet

### Basal:

- Change any long-acting insulin to *morning only* glargine (Lantus) or detemir (Levemir). Reduce this dose to **no more than 40 units per day**, even if patient was on dramatically high doses previously. With adherence to the meal plan, patients often have lower blood sugars at a fraction of insulin. Dosing basal insulin in the morning can help facilitate lipolysis with a nadir when patients are not eating overnight

Many patients can completely discontinue insulin on a low-carbohydrate diet. However, basal insulin should not be discontinued in patients with a long history of type 2 diabetes and beta cell failure or who are suspicious for Late Onset Adult Diabetes (LADA). C-peptide level can be helpful in quantifying endogenous insulin production. Consider the following factors suspicious for LADA before complete discontinuation of insulin.

- Young age at diagnosis
- Rapid transition from new diagnosis diabetes to requiring insulin (<5 years)
- Continued requirement of insulin during periods of weight loss or bariatric surgery
- Labile blood glucose (standard deviation of 50 is suspicious)
- Low body weight, BMI <30
- Normal triglycerides and high HDL
- Personal or family history of autoimmunity
- History of DKA

### Anti-hypertensives

Some side effects of a low-carb diet such as lightheadedness and headache are due to low sodium and hypotension, especially in patients on blood pressure-lowering therapy. High levels of insulin may cause the kidneys to retain salt and water, and lowering insulin with a low-carb diet can cause diuresis and symptomatic hypotension (7).

If patients become symptomatic or if systolic blood pressures are below 120 mmHg, doses of blood pressure medications may need to be changed (6). Diuretics should be reduced or discontinued first. Beta-blockers can be reduced next if normal blood pressure is maintained.

### Medications with Narrow Therapeutic Index:

Warfarin doses may need to be adjusted and INR should be monitored more frequently during the diet transition (6). Medications that have a narrow therapeutic range, such as valproic acid, should be monitored for potential dosing changes.

## Side Effect Toolbox

Side effects may occur when initiating a low-carb diet. Many of these are due to electrolyte imbalances or overmedication and can easily be improved. Electrolyte changes induced by a low-carbohydrate diet may increase magnesium losses. Most clinical trials of low-carb diets have included a daily multivitamin and mineral supplement (8).

- **Light Headedness, Fatigue, Weakness**
  - Check blood pressure and electrolytes and review medications for anti-hypertensives
  - Encourage sodium intake and hydration: 4-6 g per day is normal, with broth or bouillon cubes as needed especially in the first several weeks. Salt losses may be exacerbated by SGLT2 inhibitors, thiazide and loop diuretics, and many other medications. Extra attention should be given to sodium and hydration status for patients on multiple medications (6).
- **Constipation**
  - Increase fluid intake
  - Low-carb does not mean low vegetable intake. Encourage addition of broccoli, cauliflower, and greens
  - If persistent, try 1 teaspoon of milk of magnesia at bedtime or carbohydrate-free fiber supplement
- **Muscle Cramps**
  - Usually improves with magnesium supplementation
  - Recommend 1 teaspoon milk of magnesia at bedtime or 192 mg/day slow-release magnesium chloride (Slow-Mag)

*Slow-Mag should be advised over common magnesium oxide (such as Milk of Magnesia™) if the patient is not suffering from constipation since preparations cause diarrhea. Slow-Mag is advantageous to magnesium gluconate due to the higher magnesium concentration.*

- **Other side effects**

Other side effects to be aware of include heart palpitations, insomnia, temporary hair loss, temporary reduced physical performance, bad breath (from acetone), and low alcohol tolerance. Side effects are usually most severe during transition to the diet and improve with adequate electrolytes and fluids.

## Low Carb FAQ

---

### **Are carbohydrates necessary for metabolism?**

In states of carbohydrate restriction, the brain can utilize glucose that is spared by the muscles or created by gluconeogenesis. The brain and many cell types are also able to metabolize ketones. With adequate protein and fat, the dietary requirement for carbohydrate is zero (13).

### **Is this a high protein diet?**

Protein is consistent with the Acceptable Macronutrient Distribution Range defined by the USDA (10-35% of total calories) (14). Protein intakes above 40-60g at a time may promote gluconeogenesis and prevent ketosis. There is insufficient evidence to establish a defined upper limit for protein that poses risk of adverse events (14).

### **Will saturated fat cause high cholesterol?**

In contrast to the USDA Dietary Guidelines and the American Heart Association recommendations, this meal plan does not restrict intake of saturated fat. The link between dietary saturated fat intake and coronary heart disease has not been proven (15). The dietary guidelines on total fat intake have been loosened over the past 10 years, reflecting incomplete evidence of the harm of dietary fat. Clinical trials on low-carbohydrate diets indicate improvements in metabolic markers and weight loss (16,17).

There is widespread concern about the impact of high dietary fat intake with low-carbohydrate diets on cholesterol. However, low-carbohydrate diets have shown to be effective at increasing HDL and decreasing triglycerides with minimal change in LDL or total cholesterol (8). During weight loss, serum total cholesterol may rise, however this is not a significant effect. This small increase is usually temporary and is not an indication to increase or begin lipid lowering medications (10).

Some patients may experience significant increases in LDL cholesterol with a ketogenic diet. The clinical significance of this is currently unknown, however if patients develop worsening lipid panels, they may benefit from reducing total saturated fat.

### **Are low-carbohydrate diets dangerous long term?**

Although there is limited research on the long-term effects of low-carbohydrate diets, no significant adverse effects have been noted in trials up to 2 years in duration (16).

## Additional Resources for Clinicians

### Literature

Dietary carbohydrate restriction as the first approach in diabetes management: Critical review and evidence base. Feinman, R. D., Pogozelski, W. K., Astrup, A., Bernstein, R. K., Fine, E. J., Westman, E. C., Worm, N. 2015. *Nutrition*, 31(1), 1–13.

Cardiovascular disease risk factor responses to a type 2 diabetes care model including nutritional ketosis induced by sustained carbohydrate restriction at 1 year: an open label, non-randomized, controlled study. Bhanpuri NH, Hallberg SJ, Williams PT, McKenzie AL, Ballard KD, Campbell WW, McCarter JP, Phinney SD, Volek JS. *Cardiovasc Diabetol*. 2018 May 1;17(1):56. doi: 10.1186/s12933-018-0698-8.

A Novel Intervention Including Individualized Nutritional Recommendations Reduces Hemoglobin A1c Level, Medication Use, and Weight in Type 2 Diabetes. McKenzie AL, Hallberg SJ, Creighton BC, Volk BM, Link TM, Abner MK, Glon RM, McCarter JP, Volek JS, Phinney SD. *JMIR Diabetes*. 2017 Mar 7;2(1):e5.

Low-carbohydrate nutrition and metabolism. 2007. Westman, E. C., Feinman, R. D., Mavropoulos, J. C., Vernon, M. C., Volek, J. S., Wortman, J. A. Phinney, S. D. *The American Journal of Clinical Nutrition*, 86(2), 276–84.

### Books:

*The Art and Science of Low Carbohydrate Living*, Phinney and Volek. 2011.

*A Low Carbohydrate, Ketogenic Diet Manual: No Sugar, No Starch Diet*. Westman. 2013

## References

1. Hallberg SJ, McKenzie AL, Williams PT, Bhanpuri NH, Peters AL, Campbell WW, Hazbun TL, Volk BM, McCarter JP, Phinney SD, Volek JS. Effectiveness and Safety of a Novel Care Model for the Management of Type 2 Diabetes at 1 Year: An Open-Label, Non-Randomized, Controlled Study. *Diabetes Ther.* 2018 Apr;9(2):583-612.
2. Saslow LR, Daubenmier JJ, Moskowitz JT, Kim S, Murphy EJ, Phinney SD, Ploutz-Snyder R, Goldman V, Cox RM, Mason AE, Moran P, Hecht FM. Twelve-month outcomes of a randomized trial of a moderate-carbohydrate versus very low-carbohydrate diet in overweight adults with type 2 diabetes mellitus or prediabetes. *Nutr Diabetes.* 2017 Dec 21;7(12):304.
3. Beech RL, Chance B, Kashiwaya Y: Ketone bodies: therapeutic uses. 2001. *IUBMB Life.* 51: 241-247.
4. Brewster, S., Curtis, L., & Poole, R. 2017. Urine versus blood ketones. *Practical Diabetes,* 34(1), 13–15.
5. Anderson, J. C. 2015. Measuring breath acetone for monitoring fat loss: Review. *Obesity,* 23(12), 2327–2334.
6. Westman and Steelman. 2016. *Obesity Evaluation and Treatment Essentials.* Boca Raton (FL): CRC Press.
7. Brands, M. W., & Manhiani, M. M. 2012. Sodium-retaining effect of insulin in diabetes. *American Journal of Physiology. Regulatory, Integrative and Comparative Physiology,* 303(11), R1101-9.
8. Westman, E. C., Feinman, R. D., Mavropoulos, J. C., Vernon, M. C., Volek, J. S., Wortman, J. A., ... Phinney, S. D. 2007. Low-carbohydrate nutrition and metabolism. *The American Journal of Clinical Nutrition,* 86(2), 276–84.
9. Aude, Agatston, Lopez-Jimenez. 2004. The National Cholesterol Education Program Diet vs a Diet Lower in Carbohydrates and Higher in Protein and Monounsaturated Fat. *Arch Intern Med.*;164(19):2141-2146.
10. Säwendahl, L. & Underwood, L. E. 1999. Fasting increases serum total cholesterol, LDL cholesterol and apolipoprotein B in healthy, nonobese humans. *The Journal of Nutrition,* 129(11), 2005–8.
11. Lewis JL. 2016. Hypokalemia. *Merck Manual.* Accessed 8/2017.
12. He, Liu, Daviglius, Morris, Loria, Van Horn, Jacobs, Savage. 2006. Magnesium Intake and Incidence of Metabolic Syndrome Among Young Adults. *Circulation;*113:1675-1682.
13. Westman EC. 2002. Is dietary carbohydrate essential for human nutrition?. *Am J Clin Nutr.* 75: 951-954.
14. Dietary Reference Intakes: EAR, RDA, AI, Acceptable Macronutrient Distribution Ranges, and UL. 2011. USDA. 15. De Souza, Mente, Maroleanu. 20
15. Intake of saturated and trans unsaturated fatty acids and risk of all cause mortality, cardiovascular disease, and type 2 diabetes: systematic review and meta-analysis of observational studies. *BMJ;* 351:h3978.
16. Shai, Schwarzfuchs, Henkin, et al. 2008. Weight Loss with a Low-Carbohydrate, Mediterranean, or Low-Fat Diet. *N Engl J Med;* 359:229-24
17. Feinman, R. D., Pogozelski, W. K., Astrup, A., Bernstein, R. K., Fine, E. J., Westman, E. C., Worm, N. 2015. Dietary carbohydrate restriction as the first approach in diabetes management: Critical review and evidence base. *Nutrition,* 31(1), 1–13
18. Kalra, S., Sahay, R., & Gupta, Y. 2015. Sodium glucose transporter 2 (SGLT2) inhibition and ketogenesis. *Indian Journal of Endocrinology and Metabolism,* 19(4), 524–8.



**Diabetes Log (Week of \_\_\_\_\_ )**

		Breakfast		Lunch		Dinner		Bedtime
		Pre	Post	Pre	Post	Pre	Post	Pre
Date	Blood Glucose							
	Carbs Eaten							
	Insulin/Med							
	Exercise							
Date	Blood Glucose							
	Carbs Eaten							
	Insulin/Med							
	Exercise							
Date	Blood Glucose							
	Carbs Eaten							
	Insulin/Med							
	Exercise							
Date	Blood Glucose							
	Carbs Eaten							
	Insulin/Med							
	Exercise							
Date	Blood Glucose							
	Carbs Eaten							
	Insulin/Med							
	Exercise							
Date	Blood Glucose							
	Carbs Eaten							
	Insulin/Med							
	Exercise							
Date	Blood Glucose							
	Carbs Eaten							
	Insulin/Med							
	Exercise							

Extra Notes:

## ~ A ~

### "Adequate Protein"

**When you are hungry, eat:**

**Meat:** beef (burgers, steak, etc), pork, ham (unglazed), bacon, lamb, veal.

**Poultry:** chicken, turkey, duck

**Fish and Shellfish:** any

**Eggs:** whole eggs

**If you are hungry between meals, try:**

Pork rinds/skins

Pepperoni slices

Deviled eggs

You do not have to avoid the fat that comes naturally with these foods.

You do not have to limit quantities, but you should stop eating when you feel full.

## ~ B ~

### "Brightly Colored Vegetables"

**Salad Greens:** arugula, celery, Chinese cabbage, chives, endive, greens (beet, collard, mustard, turnip), kale, lettuce (all varieties), parsley, spinach, radishes, scallions, sprouts, and other leafy vegetables

**Vegetables:** asparagus, broccoli, Brussels sprouts, cauliflower, celery, cucumber, eggplant, green beans, jicama, mushrooms, okra, onions, peppers, pumpkin, radishes, shallots, snow peas, sprouts (bean and alfalfa), sugar-snap peas, summer squash, tomatoes, rhubarb, zucchini.

**For cooking and serving:** Use natural fats such as butter, cream, olive oil, or coconut oil. Use salt as needed for seasoning. Use full-fat, unsweetened salad dressings.

### "Beverages"

**Water:** add a slice of lemon or lime

**Coffee and tea:** no sugar added, may add cream

**Bouillon or broth:** as needed or desired

## ~ C ~

### "Careful Carbs"

**Dairy:** full-fat cream, butter, sour cream, cheeses (all varieties), full-fat unsweetened yoghurt, full-fat ricotta or cottage cheese

\*\*avoid processed cheeses, cheese spread, cheese foods, or low-fat and fat-free dairy products

**Nuts:** macadamia, almonds, walnuts, pecans, Brazil, unsweetened coconut

**Other:** olives, avocados, pickles, some fresh berries in season

## Avoid

Sugar: soft drinks, candy, juice, sports drinks, chocolate, cakes, buns, pastries, ice cream

Bread and related products, such as biscuits, muffins, cakes, pastries

Breakfast cereals, including oatmeal

Rice

Potatoes, French fries, potato chips, and other starchy vegetables

Pasta

Most fruit

Fruit juices

Margarine (has unhealthy trans fats)

Beans and legumes

Flavored, sugary, or low-fat dairy products, such as yogurt.

Beer (this is bread in liquid form!)

## Occasional Treats

**Alcohol:** red or white wine, spirits

**Dark chocolate:** >70% cocoa

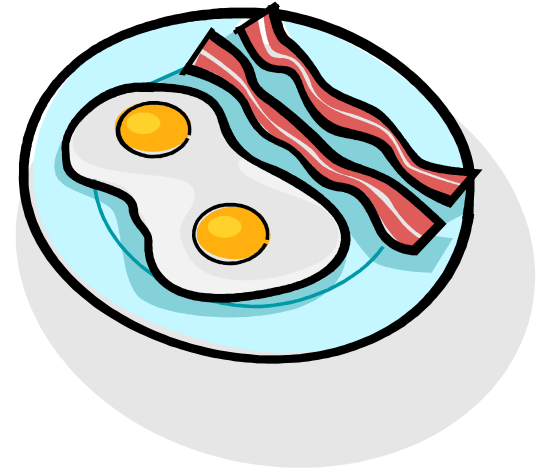
## Online Resources

<https://www.dietdoctor.com/low-carb>

<http://lowcarbdiets.about.com>

# Getting Started on a Low-Carbohydrate Diet

*It is as easy as A-B-C!*



# Adapting Diabetes Medication for Low Carbohydrate Management of Type 2 Diabetes

## Three key clinical considerations:

- Is there a risk of the drug causing hypoglycaemia or other adverse event?
- What is the degree of carbohydrate restriction?
- Once carbohydrate is reduced does the drug continue to provide health benefit, and if so are the potential drug benefits greater than or less than possible risks and side effects?

Drug Group	Hypo risk?	Clinical suggestion
<b>Sulfonylureas</b> (e.g. <i>gliclazide</i> ) and <b>Meglitinides</b> (e.g. <i>repaglinide</i> )	Yes	Reduce/Stop (if gradual carbohydrate reduction then wean by halving dose successively)
<b>Insulins</b>	Yes	Reduce/Stop. Typically wean by 30-50% successively. Beware insulin insufficiency*
<b>SGLT-2 inhibitors</b> ( <i>flozins</i> )	No	Ketoacidosis risk if insulin insufficiency. Usually stop in community setting.
<b>Biguanides</b> ( <i>metformin</i> )	No	Optional, consider clinical pros/cons.
<b>GLP-1 agonists</b> ( <i>-enatide/-glutide</i> )	No	Optional, consider clinical pros/cons.
<b>Thiazolidinediones</b> ( <i>glitazones</i> )	No	Usually stop, concerns over long term risks usually outweigh benefit.
<b>DPP-4 inhibitors</b> ( <i>glipitins</i> )	No	Usually stop, due to lack of benefit.
<b>Alpha-glucosidase inhibitors</b> ( <i>acarbose</i> )	No	Usually stop, due to no benefit if low starch/sucrose ingestion.
<b>Self-monitoring blood glucose</b>	N/A	Ensure adequate testing supplies for people on drugs that risk hypoglycaemia. Testing can also support behaviour change (e.g. paired pre and post meal testing)

\* **Caution weaning of insulin if clinical suspicion of endogenous insulin insufficiency:** Patients with LADA may have been misdiagnosed as T2D. Also risk of endogenous insulin insufficiency in a minority of people with T2D. Consider these possibilities if patient was not overweight at diagnosis. Exogenous insulin should not be completely stopped for these cohorts. Inappropriate over-reduction and cessation of exogenous insulin is avoidable in these cases as increasingly marked hyperglycaemia will occur if weaning of insulin is excessive.

Accepted Br J of General Practice Jan 2019 ; Murdoch C, Unwin D, Cavan D, Cucuzzella M, Patel M