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 lowcarbohydrate 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.

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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 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.

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. Ketons 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 attained 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

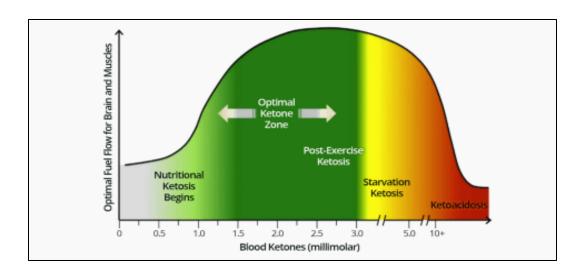
-Blood glucose remains below 270mg/dl

-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



(5)

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 lowcarbohydrate 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.

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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

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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							
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Date	Blood Glucose							
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	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.

<u>"Beverages"</u>

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, avocadoes, pickles, some fresh berries in season

<u>Avoid</u>

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

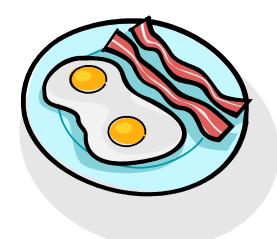
http://lowcarbdiets.about.com

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	
Sulfonylureas (e.g. gliclazide) and Meglitinides (e.g repaglinide)	Yes	Reduce/Stop (if gradual carbohydrate reduction then wean by halving dose successively)	
Insulins	Yes	Reduce/Stop. Typically wean by 30-50% successively. Beware insulin insufficiency*	
SGLT-2 inhibitors (flozins)	No	Ketoacidosis risk if insulin insufficiency. Usually stop in community setting.	
Biguanides (metformin)	No	Optional, consider clinical pros/cons.	
GLP-1 agonists (-enatide/-glutide)	No	Optional, consider clinical pros/cons.	
Thiazolidinediones (glitazones)	No	Usually stop, concerns over long term risks usually outweigh benefit.	
DPP-4 inhibitors (glipitins)	No	Usually stop, due to lack of benefit.	
Alpha-glucosidase inhibitors (acarbose)	No	Usually stop, due to no benefit if low starch/sucrose ingestion.	
Self-monitoring blood glucose	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.

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