

Clinician's Guide to Low-Carb Diets



Low-Carb Diabetes Prevention Program

The Diabetes Prevention Program (DPP) is a one year group-based intensive diet and exercise intervention for people with pre-diabetes. In 2002, a large trial showed it was effective at reducing the progression to diabetes by 58% compared to standard care (1). Since then it has been distributed around the country. A new curriculum was developed in 2016 and renamed "Prevent T2."

The curriculum of the National Diabetes Prevention Program recommends restriction of dietary fat for weight loss. Research since the DPP's release has suggested that carbohydrate restriction can be an effective approach for weight loss and improvement in metabolic markers. We are testing if a low-carb approach can be used and will be effective in the group-based format of the DPP.

What Clinicians Need to Know



Low- carb basics



Side Effects and how to help



Medication Management



Common myths



How to learn more

What does low-carb look like?

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



The low-carb 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-carb meal plan:



Carbohydrates

Grains, starches, 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-carb dairy products

Milk, yogurt with added sugar

Fats from Processed Foods

Most foods high in highly processed oils and fats also contain carbohydrates and are not part of the meal plan.

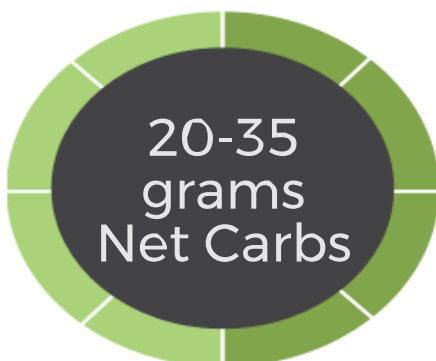
Trans Fats

Added sugars and sweetened beverages

How low is low-carb?

“Low carb” diets may refer to a wide range of carbohydrate intake. In very-low carbohydrate diets such the meal plans used in the Low Carb-DPP, patients consume about 20-35 grams of non-fiber carbohydrates per day. Protein intake is moderate (~1g per kg of body mass) and fats are allowed to satiety. The goal is to reduce carbohydrate intake to a level that will induce ketosis.

Net Carbs = Total Carbs - Fiber



Nutritional Ketosis

Ketones are molecules produced by the liver from fatty acids that 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 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 a low-carb diet 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

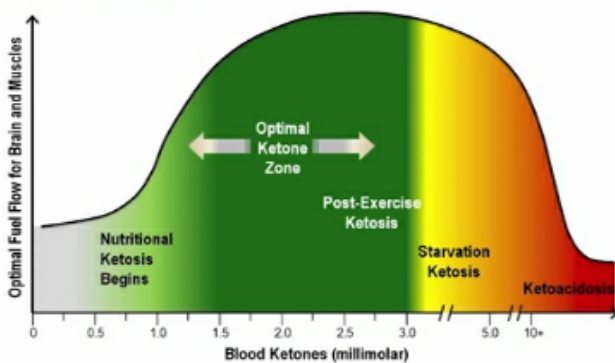
There are three types of principal ketones bodies- acetone, acetoacetate and 3-β-hydroxybutyrate (3HB). Urine and breath tests give semiquantitative measures of acetoacetate and serum tests can give a quantitative measure of 3HB. 3HB comprises the majority of circulating ketones and is the most clinically relevant (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 participants may use them to verify ketosis. Participants will have positive urine ketones when transitioning to the diet but they may become negative after several weeks on the diet due to resorption in the kidney. The appropriate ranges are "trace" to "small" or 5-15mg/dl.



The Ketone Zone



Volek, Phinney. 2011.

"The Art and Science of Low-Carbohydrate Living."

Blood Ketones

Blood testing measures 3HB which is the primary circulating ketone. The appropriate serum ranges for nutritional ketosis are 0.8-3 mmol/L. 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 is not the same as Ketoacidosis

Nutritional Ketosis

VS

Ketoacidosis

-Natural physiological state allowing utilization of ketones as a supplemental fuel (2).

-Can occur in anyone during fasting or carbohydrate restriction

-Ketones generally remain below 3 mmol/L, and do not change blood pH

-Blood glucose remains below 270 g/dl (15mmol/L)

-Asymptomatic besides "fruity" breath due to acetone production (5)

-Medical emergency requiring urgent intervention

-Occurs with frank insulin deficiency in people with type I diabetes or sometimes insulin-dependent type II diabetes. Insulin deficiency leads to unregulated lipolysis and high levels of fatty acids and ketone production.

-High levels of ketones (>3mmol/L), high glucose (>270g/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

Glucose lowering agents- Insulin and sulfonylureas



If your patients are on insulin or sulfonylureas, doses should be reduced before they begin a low-carb diet to prevent hypoglycemia. Patients on glucose-lowering therapy besides Metformin were excluded from the Low-Carb DPP trial. For patients outside the trial who are starting a low-carb diet on these medications, see appendix for guides in adjusting medications for patients on glucose lowering agents and discussion of SGLT2 inhibitors and other diabetes medications.

Metformin



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.

Anti-hypertensives

Salt-wasting may lead to symptomatic hypotension



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

If patients become symptomatic or if systolic blood pressures are below 110 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 as long as normal blood pressure is maintained.

Other Medication Notes



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.

Medications that interfere with lipolysis should be replaced or discontinued if possible to facilitate weight loss including:

- Niacin
- Beta blockers
- Subcutaneous insulin
- Antidepressants
- Antipsychotics

Impact on blood lipids

Favorable impact on lipid panel despite dietary fat



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). Recheck lipid panel after weight loss has stabilized.

Electrolyte Management



Sodium

Patients should not restrict sodium on low-carb diets and will likely need additional sodium and hydration, especially in the first several weeks. 2-3 grams per day is appropriate and can be supplemented with bouillon cubes or broth (6).

Hyponatremia may be exacerbated by SGLT2 inhibitors, thiazide and loop diuretics and many other medications. Extra attention should be paid to sodium and hydration status for patients on multiple medications (6). See appendix for more complete list of medications that may affect sodium balance.

Patients with heart failure or chronic kidney disease will need more careful monitoring. Sodium intake should be kept at baseline until edema resolves, then increased if the patient has orthostatic symptoms (6).

Potassium

Potassium can also become depleted, especially with potassium-wasting diuretics (thiazides and loop) or inadequate sodium intake. Attention should be given to adequate dietary potassium and sodium intake, especially in patients at high risk such as those on digoxin therapy (10). Supplementation should be considered if hypokalemia is persistent (6, 8).

Magnesium

Magnesium is commonly inadequate in modern diets and an association between low magnesium intake and metabolic syndrome has been suggested (12). Electrolyte changes induced by a low-carb diet may increase magnesium losses. Most clinical trials of low-carb diets have included a daily multivitamin and mineral supplement (8). Magnesium supplementation may be warranted, especially if the patient experiences side effects. See appendix for detailed protocol.

Side Effect Toolbox

Side effects may occur when initiating a low-carb diet. Many of these are due to electrolyte imbalance and can easily be improved.

Lightheadedness, weakness, fatigue

- Check blood pressure, electrolytes and review med list for anti-hypertensives
- Remind patient that salt restriction is not appropriate for people on low-carbohydrate diets
- Encourage sodium supplementation and hydration: 2-3 g per day with broth or boullion cubes

Constipation

- Increase fluid intake to minimum of 2 liters per day
- Low-carb does not mean low vegetable. Encourage addition of broccoli, cauliflower and greens
- If not resolved, try 1 teaspoon of milk of magnesia at bedtime, bullion supplements or carbohydrate-free fiber supplement

Gout flare

- Patients with history of gout are at a higher risk of flare when transitioning to the diet
- Long-term gout flares may improve on low-carb diets(6)
- Consider prophylactic allopurinol during transition

Muscle Cramps

- Usually respond to magnesium supplementation
- Consider 1 teaspoon milk of magnesia at bedtime or 200mEq slow- release magnesium chloride (Slow-Mag)
- See appendix for detailed protocol

Other Potential 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-Carbohydrate Diet Facts

Carbohydrate is not an essential macronutrient

In states of carbohydrate restriction, the brain is able to 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).

This is a high fat diet, but not a high protein diet

Protein is consistent with the Acceptable Macronutrient Distribution Range defined by the USDA (10-35% of total calories) (14). Participants are encouraged not to eat more than 40-60 g of protein at a time as extra protein is made into glucose via gluconeogenesis and may prevent ketosis. There is insufficient evidence to establish a defined upper limit for protein that poses risk of adverse events (14).

In contrast to the USDA Dietary Guidelines as well as the American Heart Association, this meal plan does not restrict intake of saturated fat. However, 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 the unconvincing evidence of the harm of dietary fat. Clinical trials on low-carbohydrate diets indicate improvements in metabolic markers and weight loss (16,17).

No proven danger of long term use

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).

Recommended Resources

See appendix for complete list of references.

Articles:

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.

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.
"Keto-Clarity," by Jimmy Moore and Dr. Eric Westman

Contact:

Low-Carb DPP Team:

Laura Saslow PhD
Dina Hafez-Griauzde MD
Caroline Richardson MD
Kaitlyn Patterson

Clinician's Guide Appendix

Adjusting Insulin

(Adapted from "Obesity Evaluation and Treatment Essentials," by Steelman and Westman)

For diabetic patients beginning a low-carb diet, oral hypoglycemics should be stopped the day the diet begins. For patients taking less than 20 units of daily insulin, insulin should be discontinued the day the diet begins. In other patients, insulin dose should be reduced by 50%. Patients should increase frequency of glucose monitoring to re-establish dosing and avoid hypoglycemia and given instructions on when to call the clinic. Patient should be instructed to not take insulin if blood glucose is less than 100 mg/dl.

Discontinuing Insulin

Many patients can completely discontinue insulin on a low-carbohydrate diet. However, it is important to verify the diagnosis of type 2 diabetes over type 1 or Late Onset Adult Diabetes (LADA) before complete discontinuation. 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

Medication Details

SGLT2 inhibitors

There have been case reports of ketoacidosis in the setting of low-carbohydrate diets while taking SGLT2 inhibitors (19). Although this is rare, it is something to be aware of and consider discontinuing SGLT2 inhibitors if glycemia improves.

Sodium Wasting Medications:

- Thiazide and loop diuretics
- Sodium-glucose cotransporter 2 (SGLT2) inhibitors (like dapagliflozin)
- Other medications that can cause hyponatremia include cyclosporine and cisplatin, oxcarbazepine, trimethoprim, antipsychotics, antidepressants, NSAIDs, cyclophosphamide, carbamazepine, vincristine and vinblastine, thiothixene, thioridazine, other phenothiazines, haloperidol, amitriptyline, other tricyclic antidepressants, monoamine oxidase inhibitors, bromocriptine, clofibrate, general anesthesia, narcotics, opiates, ecstasy, sulfonyleureas, and amiodarone.

Magnesium Supplementation Protocol:

(Adapted from "The Art and Science of Low Carbohydrate Living," by Phinney and Volek)

Patient should take 3 slow-release magnesium tablets daily for 20 days. The proprietary brand-name product is 'Slow-Mag'™, but there are a number of equally effective generics now available at a fraction of the brand-name price (e.g., Mag-64™ or Mag-Delay™). Most people's cramps cease within 2 weeks of starting this dose of Slow-Mag™, but they should continue to take the full 20-day course (60 tablets per bottle at 3 per day lasts 20 days). If the cramps return later, do it again, but after re-doing those first 20 days at 3 pills per day, then continue taking one pill per day. If despite this the cramps return, take 2 pills per day for perpetuity. Most people can be titrated to remain cramp-free by this method.

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.

References:

1. The Diabetes Prevention Program. Design and methods for a clinical trial in the prevention of type 2 diabetes. 1999. *Diabetes Care*, 22(4), 623–34.
2. Salway JG: *Metabolism at a Glance*. 1999. Oxford: Blackwell Science.
3. Veech 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. 2015. 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.