

# Ketogenic diet for diabetes and weight management

## Pearls for Practice

Dr. Catherine Chan, Dr. Caroline Richard, Dr. Rose Yeung

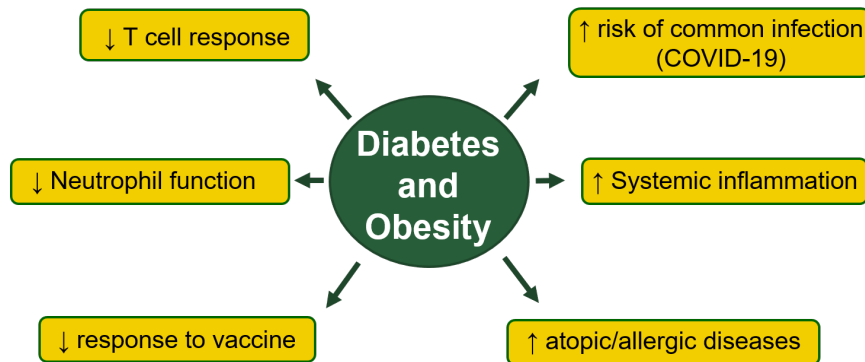


In Canada, 30 % of people live with diabetes or prediabetes. That is 11.7 million Canadians.

### Immunity and inflammation in obesity and type 2 diabetes

- The immune system plays an important role in maintaining health but is also involved in the development of chronic diseases.
- Obesity is associated with systemic inflammation, which in turn promotes insulin resistance and immune impairment.
- As shown below, individuals with obesity and type 2 diabetes have a higher risk of infection to common infections. Impairment in T and B cells as well as in neutrophil function have been reported in this population.

Figure 1: Impact of obesity and diabetes on the immune system



### Standard of Care in type 2 diabetes

- Recommendations are typically focused on following a high-fibre, low-fat diet (limit high-fat (especially saturated) foods, sweets and refined sugars).
- Counselling around portion sizes, healthy plate (i.e., Canada's Food guide) and Glycemic Index Food guides to achieve a healthy body weight (promote weight loss in most cases).
- Choosing complex, low glycemic-index carbohydrates and reducing intake of refined carbohydrates.

# Ketogenic diet for diabetes and weight management

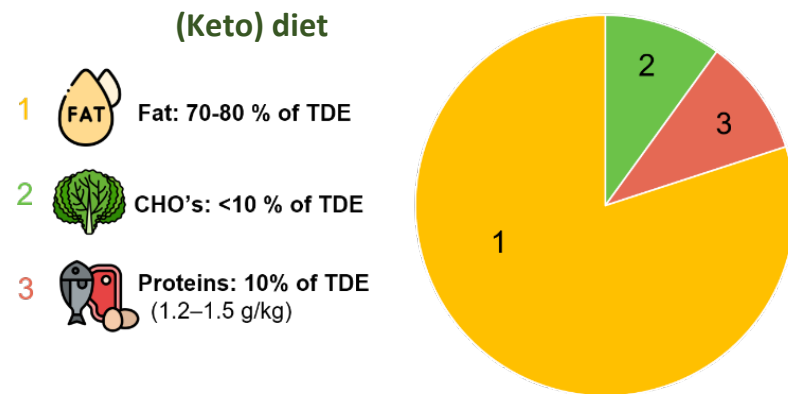
## Pearls for Practice

Dr. Catherine Chan, Dr. Caroline Richard, Dr. Rose Yeung



### Ketogenic diet: macronutrient distribution:

Figure 2: Macronutrients distribution in Ketogenic



TDE: Total daily energy

### Keto diet and Body weight

- Low carbohydrate diets in the short-term may lead to greater weight loss than low-fat diet but not in the long-term.
- Increased energy expenditure combined with reduced appetite and hunger sensation could favor weight loss on a low carbohydrate diet.
- Initial weight loss is due mostly to water loss and people tend to lose more lean mass on low carbohydrate diets than other diets with a more balanced macronutrient profile.

### Saturated vs. Unsaturated fats sources in keto diet

Since saturated fatty acids (SFA) have been shown to increase inflammation and plasma LDL-C concentrations, a major cardiovascular (CVD) risk factor, replacing SFA by unsaturated fat sources in the context of a Keto diet could potentially improve:

- **Systemic inflammation**
- **Plasma LDL-C concentration**
- **Immune function**

### Keto diet and CVD risk factors

Although inconsistent findings have been reported, several meta-analyses have shown changes in CVD risk factors after 1 year on a low-carbohydrate diet including:

- Slight increase in LDL-C and HDL-C
- Reduction in triglycerides
- Reduction in glycated hemoglobin (HbA1c)
- Variable effect on blood pressure

### Keto diet and Immunity/Inflammation

- $\beta$ -hydroxybutyrate has been shown to exert anti-inflammatory properties.
- Currently there is no evidence showing greater improvement in inflammation when following a low carbohydrate diet compared to other diets for weight loss.
- Saturated fat increases inflammation compared to unsaturated fat sources.
- Plasma CRP levels decrease with weight loss.

# Ketogenic diet for diabetes and weight management

## Pearls for Practice

Dr. Catherine Chan, Dr. Caroline Richard, Dr. Rose Yeung



### **KETO-IM Study: Metabolic and inflammatory outcomes of the ketogenic diet comparing saturated and unsaturated fat sources**

KETO diets are often high in saturated fats. Compared with a traditional KETO, we want to test the feasibility of substituting healthier fats such as canola oil to improve cardiovascular risk factors. Canola oil is low in saturated fat. Utilizing canola oil in a KETO diet may improve its health benefits in people with high risk of / living with type 2 diabetes.

**Goal:** Compare consuming a KETO based on either canola oil or saturated fat to a lower fat diet typically recommended for diabetes for 6 months on blood sugar, factors related to the immune system, and other outcomes.

Participants will be randomly assigned to:

1

#### **KETO-CAN:**

Keto supplemented with canola oil (high in MUFA and Omega-3 FA)

2

#### **KETO-SAT:**

Keto supplemented with butter and coconut oil (KETO-Sat, high in SFA).

3

#### **LFD (low-fat diet):**

LFD supplemented with whole grain pasta, brown rice, or oats.

For more information visit our website:



Email: [keto.im@ualberta.ca](mailto:keto.im@ualberta.ca)

P: 780-492-9506

Looking for participants: Aged 18-70 years old, living with overweight or obesity, HbA1c  $\geq$  5.7%  
Participants will be asked to complete 6 months of the diet with the guidance of the study team.

Study visits happen at the University of Alberta (Human Nutrition Research Unit) and blood is drawn at the study start, 3 months, and 6 months. U of A ethics ID: Pro00123687.

# Ketogenic diet for diabetes and weight management

## Pearls for Practice

Dr. Catherine Chan, Dr. Caroline Richard, Dr. Rose Yeung



### FAQ

**1. I realize that your study will focus on T2D, but wondering if T1D and T2D have similar impacts on immune function?**

Yes and no. While there are similarities in term of immune dysfunction between T1D and T2D, the etiology of the disease is quite different, which also affects the immune system differently.

**2. Are you using cold pressed canola oil? I had heard that there was some concern about the processing of canola oil in terms of being pro-inflammatory (may not be remotely evidence based!)**

We could not find very much evidence regarding inflammatory effects of canola oil. In one meta-analysis, canola oil lowered CRP but to the same extent as other oils (olive, safflower). To our knowledge, KETO-IM will be the first to look at detailed inflammatory and immune parameters, comparing diets that substitute canola for saturated fat sources as added fat. In this study, we are using regular commercially available canola oil. From a fatty acids standpoint, there is no evidence supporting that canola oil would be pro-inflammatory.

**3. If less than 50g of carbs per day, is the concern for euglycemic DKA if on SGLT2iOR?**

Yes—there is concern about euglycemic DKA in patients on low carb diets less than 50g/day. Participants taking SGLT2 stop taking their medication when they start on the ketogenic diet.

**4. Do you expect different outcomes (reduced HbA1c, TG, etc.) when looking at different populations based on ethnicity given different prevalence of diabetes in certain ethnicities?**

Possibly, but our study won't be powered to rigorously compare between ethnicities.

**5. I was wondering how an isolated oil will be substituted to the food with SFA that people are eating in their diet (like meat or whole dairy).**

As mentioned, people won't be consuming 100% canola or 100% saturated fat. They will be encouraged to use canola vs saturated fat sources when adding fat to meals or foods they are preparing.

**6. How are you ensuring adequate micronutrient intake in the ketogenic diet?**

We are providing a multivitamin supplement to all participants randomized to either of the ketogenic diets.

**7. Have you seen lower calorie levels with Keto versus low fat diet?**

We haven't enough data yet. Published reports often show reduced energy intake initially but this effect attenuates over time.

# Ketogenic diet for diabetes and weight management

## Pearls for Practice

Dr. Catherine Chan, Dr. Caroline Richard, Dr. Rose Yeung



### 8. How is ketogenic diet compares to Mediterranean diet?

Ketogenic diet is normally higher in fat and lower in carbohydrate compared to a Mediterranean diet (MedDiet). Although there is a lack of consensus on what constitutes a MedDiet (<https://www.mdpi.com/2072-6643/7/11/5459>), it tends to be higher in fat (35-45% fat) and lower in carbohydrate (40-50%) than the standard of care low-fat diet ( $\leq 30\%$  fat). While olive oil is the main source of fat in the MedDiet, it also favors high fiber, plant-based foods (wheat pasta, fruits and vegetables, legumes/pulses, nuts and grains) and therefore, the overall fiber content is higher in the MedDiet.

### 9. What is the recommended 'levels' of ketones are you looking for? Or just tracking period?

Some studies suggest 0.5 mmol/L as evidence of ketosis. We will be tracking Yes/No for meeting this threshold as well as the actual value as a continuous variable.

### 10. Any comments on the sustainability of following long term-costs, heart health?

As one person from the audience commented, long-term sustainability of restricted diets is likely limited to a relatively small fraction of the people who start the diet. Effects beyond 2 years have not been reported. Yet for certain people, it is feasible to maintain a very low to low-carbohydrate diet. Eating meat is expensive compared to other plant-based protein sources such as pulses but it is possible to eat very healthy on a low-carbohydrate diet. On the other hand, high-carbohydrate diet can also lead to metabolic complications.

### 11. Given potential controversy re: inflammatory properties of canola oil, would it be beneficial to also have an olive oil branch of the study?

Possibly, with sufficient budget and time. In the meta-analysis referenced in question 2, canola oil was superior to olive oil in reducing total and LDL-cholesterol and not significantly different on the other CVD risk factors measured.

### 12. Apart from canola vs coconut/butter, can you tell us more about the dietary intervention?

Following a ketogenic diet involves cutting carbohydrate from the diet. Therefore, we try to select vegetables with low carbohydrate content that can provide fiber. Plant-based proteins need to be avoided for the most part since legumes/pulses are too high in carbohydrate for the keto arms.

### 13. Is there a brand of multivitamin that you recommend that is lower in carbs?

We would recommend to avoid the 'gummies' multivitamin. After that the brands are fairly similar in term of sugar content.

### 14. Are there any support that would help participants prepare foods/eat out? For many clients, it is not realistic to make foods at home for all their meals?

As part of the nutritional consultation protocol, we have developed materials/handouts with tips to help participants adhere to the recommendations, which include grocery lists, eating out in restaurants, etc.

# Ketogenic diet for diabetes and weight management

## Pearls for Practice

Dr. Catherine Chan, Dr. Caroline Richard, Dr. Rose Yeung



### Links and Resources:

1. Diabetes in Canada: Backgrounder. Ottawa: Diabetes Canada; 2023. <https://www.diabetes.ca/advocacy---policies/advocacy-reports/national-and-provincial-backgrounders/diabetes-in-canada>
2. Calder PC. Nutrition and immunity: lessons for COVID-19. *Eur J Clin Nutr.* 2021;75(9):1309-1318. doi:10.1038/s41430-021-00949-8
3. She Y, Wang K, Makarowski A, et al. Effect of High-Fat and Low-Fat Dairy Products on Cardiometabolic Risk Factors and Immune Function in a Low Birthweight Swine Model of Diet-Induced Insulin Resistance [published correction appears in *Front Nutr.* 2023 Oct 11;10:1304100]. *Front Nutr.* 2022;9:923120. Published 2022 Jun 17. doi:10.3389/fnut.2022.923120
4. Kirkpatrick CF, Bolick JP, Kris-Etherton PM, et al. Review of current evidence and clinical recommendations on the effects of low-carbohydrate and very-low-carbohydrate (including ketogenic) diets for the management of body weight and other cardiometabolic risk factors: A scientific statement from the National Lipid Association Nutrition and Lifestyle Task Force. *J Clin Lipidol.* 2019;13(5):689-711.e1. doi:10.1016/j.jacl.2019.08.003
5. Bueno NB, de Melo IS, de Oliveira SL, da Rocha Ataide T. Very-low-carbohydrate ketogenic diet v. low-fat diet for long-term weight loss: a meta-analysis of randomised controlled trials. *Br J Nutr.* 2013;110(7):1178-1187. doi:10.1017/S0007114513000548