Waterloo Wellington Diabetes

Therapeutic Carbohydrate Restriction (or Reduction) & Diabetes

A Guide for Health Care Professionals

WWD working group
August 2020, Updated August 2021

Contents

Acknowledgements

Waterloo Wellington Diabetes (WWD) would like to thank the following individuals who have worked tirelessly in reviewing the literature to date and developing this resource as a guide for health care professionals, supporting individuals with diabetes, who are interested in the ketogenic diet. Recognizing that this is a rapidly evolving topic, this guide represents the most current information available to date.

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List of Abbreviations (alphabetical order)

AA- Amino Acid
ACR- Albumin Creatinine Ratio
AI- Adequate Intake
BBI- Basal-Bolus Insulin
BP- Blood Pressure
Ca- Calcium
CAD- Coronary Artery Disease
CHF- Congestive Heart Failure
CHO- Carbohydrate
CKD- Chronic Kidney Disease
Cr- Creatinine
CV- Cardiovascular
CVD- Cardiovascular Disease
DKA- Diabetic Ketoacidosis
DM- Diabetes Mellitus
ECFV- Extra Cellular Fluid Volume
ED- Eating Disorder
eDKA- Euglycemic Diabetic Ketoacidosis
EFA- Essential Fatty Acid
eGFR- Estimated Glomerular Filtration Rate
FA- Fatty Acid
FBG- Fasting Blood Glucose
Fe- Iron
GERD- Gastroesophageal Reflux Disease
GFR- Glomerular Filtration Rate
GI- Gastrointestinal
HbA1C- Glycated Hemoglobin
HCP- Health Care Provider
HHS- Hyperosmolar Hyperglycemic State
HR- Heart Rate
HSH- Hydrogenated Starch Hydrolysates
HTN- Hypertension
ICR- Insulin to Carbohydrate Ratio
IOM- Institute of Medicine
IR- Insulin Resistance
K+- Potassium
KB- Ketone Bodies
KD- Ketogenic Diet
LA- Linoleic acid
LDL- Low Density Lipoprotein
MACE- Major Adverse Cardiovascular Events
Mg- Magnesium

MNT- Medical Nutrition Therapy
MS- Metabolic Syndrome
MUFA- Monounsaturated Fatty Acids
N- Nausea
Na+- Sodium
OW- Overweight
PreDM- Pre-Diabetes
PRO- Protein
PUFA- Polyunsaturated Fatty Acid
RDA- Recommended Dietary Allowance
RCT- Randomised Controlled Trial
SF- Saturated Fat
SFA- Saturated Fatty Acids
TCR- Therapeutic Carbohydrate Restriction (or Reduction)
TE- Total Energy
TEE- Total Energy Expenditure
TEI- Total Energy Intake
TG- Triglyceride
T1DM- Type 1 Diabetes
T2DM- Type 2 Diabetes
UL- Upper Limit
US- Ultrasound
V- Vomiting
VLCD- Very Low-Calorie Diet
VLCKD- Very Low Carbohydrate Ketogenic Diet
VLED- Very Low Energy Diet

Introduction:

In recent years, the ketogenic diet (KD) has re-gained popularity, being promoted by celebrities, popular press, social media, and health care practitioners. It promises, amongst other outcomes, weight loss, improved blood glucose and improved physical performance. As a result, individuals have become interested in using this diet as a possible option for managing their diabetes. The physiology behind a diet that induces ketosis is compelling and has led to much interest and research in the use of carbohydrate restriction for weight loss, diabetes management and treatment of other endocrine disorders.[1] Therapeutic Carbohydrate Restriction/Reduction (TCR) will be the term used throughout this document unless the terms 'ketogenic' or 'low CHO' are specified in the literature being cited. TCR is not a 'diet', it is MNT, with the intent of managing metabolic health conditions.

This document was developed as a resource for health care professionals working in the diabetes field to aid in supporting individuals who choose to implement or inquire about TCR. The latter part of the document provides greater detail for dietitians. As with any therapy, the risks and benefits of treatment must be carefully assessed by the health care provider in the context of an individual's clinical picture to have a balanced discussion regarding treatment pros/cons with the individual. It is hoped that this guide will help to facilitate these discussions.

Rationale for TCR:

The goal of TCR is to reduce insulin levels to facilitate fat lipolysis.[2] Restricting carbohydrates to the low levels seen in the KD allows a physiologic response in the body that mimics fasting. When CHO intake is restricted, insulin and glucose levels drop and trigger a cascade of reactions that lead to the use of an alternative fuel source (e.g. ketone bodies from fat burning). Weight loss can also happen, for several reasons, in this context including lower insulin levels, a diuretic effect, decreased hunger and subsequent reduction in intake even in the absence of a caloric restriction[3], and increased resting energy expenditure.[1,2,4]

Ketone bodies (KB) are molecules produced by the liver from fatty acids and can be used as a fuel source by extra-hepatic tissues. Ketosis refers to the presence of KBs in the blood when insulin levels are low, and when the release of fatty acids from adipose tissue is accelerated.[2]

If the premise of the regime is weight loss, it is important to note that:

- Calorically restricted intakes, regardless of the macronutrient distribution, often result in weight re-gain in 66-95% of people, and can promote disordered eating with clients who historically struggle with "yo-yo" dieting[5,6,7,8]. However, there is some emerging research to indicate that maintaining a liberalized, low CHO diet in the weight maintenance phase may continue to provide appetite suppression and increase metabolic rate, supporting efforts to potentially maintain weight loss long-term.[9]
- It is also important to note that carbohydrate restricted diets improve insulin sensitivity, provided they achieve sustained weight loss. [10] CHO tolerance may only remain improved if CHO intake also remains low and clients commit to long-term sustained adherence to this way of eating which has been shown to be challenging depending on client motivation and healthcare provider support[1].

TCR Range: How Does a Low Carb Diet Differ from a Ketogenic Diet?

The literature is often inconsistent in terminology between low CHO, very low CHO, and KD. Although there are variations in the proportions and sources of fat used for KD, the overall concept is to limit CHO, have adequate protein, and utilize fat for the remainder of caloric needs. If a KD is followed properly, nutritional ketosis usually occurs within 3 days of initiation of the diet, though full adaptation may take several weeks. The following table illustrates the differences between low CHO and KD diet (Table 1).

Table 1: CHO Content of Various Dietary Interventions Based on Accepted Definitions [2,3,74]

	High CHO	Moderate CHO	Low CHO	Very Low CHO/Ketogenic Diet
CHO Content	>230 g/day (>45% TE)	130-230 g/d (26-45% TE)	50-130 g/d (10-25% TE)	<50 g/d (<10% TE)
Protein Content	Variable / Not Defined			Protein to meet nutritional needs (1- 1.5 g/kg body weight)
Fat Content	Variable / Not Defined			70-90% of calories Often >150 g fat/d during maintenance
Ketones	Ketones unlikely			~1.5-3.0 mmol/L

Note: Many clients may report following a "keto" diet, but it may often be a low CHO regime that is not necessarily achieving a state of stable nutritional ketosis. Although a KD is always considered low CHO, a low CHO diet may or may not be ketogenic depending on the amount of CHO and protein included in the diet[11].

How Does Nutritional Ketosis Differ from Diabetic Ketoacidosis?

Nutritional ketosis occurs when the body uses fat as fuel instead of glucose (from CHO). This occurs as a normal metabolic function in response to starvation. The liver breaks down fat (from food sources or adipose tissue), releasing ketones into the blood stream. The body is then able to use the ketones as an energy source. In nutritional ketosis (from the use of TCR), some fat for ketone production comes from adipose stores, but the majority is taken from the high fat ketogenic diet. With nutritional ketosis, both blood sugar and insulin levels remain low. Similarly, the pH level and anion gap remain relatively unchanged. [5]

Diabetic ketoacidosis occurs in the absence of insulin. The body senses it is starving, due to a relative lack of insulin available to move glucose from the bloodstream into cells, where it is needed as an energy source. As a result, the body breaks down fats and proteins quickly for energy. Dangerous levels of both glucose and ketones can accumulate in the blood, causing diabetic ketoacidosis. This results in a shift in pH to an acidotic state, as well as a significant elevation in anion gap. [5]

The following table provides a comparison of nutritional ketosis, diabetic ketoacidosis, and hyperosmolar hyperglycemic state. (Table 2)

Table 2: Comparison of Nutritional Ketosis, Diabetic Ketoacidosis & Hyperosmolar Hyperglycemic State[2,5]

	Nutritional Ketosis	DKA	HHS
Cause	• Insufficient CHO intake (Either due to CHO restriction or general caloric inadequacy - e.g. starvation, fasting)	• New diagnosis of T1DM • Insulin omission or inadequate insulin in T1DM	• Suppressed insulin release • ++CHO intake in T2DM • Secondary to other illness or medications
Compensatory Response	Ketone production may come from: 1. Metabolism of the dietary fat 2. Endogenous breakdown of adipose tissue via the liver when there is an energy deficit from food	Cells cannot access glucose due to lack of insulin, therefore the body breaks down fats/proteins quickly for energy, leading to: 1. Hyperglycemia 2. Urinary loss of water and electrolytes 3. Potassium is shifted out of cells 4. Elevated glucagon levels 5. A build-up of glucose/ketones in the blood 6. A pH shift and an anion gap	Usually occurs in T2DM. Higher catecholamine levels suppress insulin release leading to: 1. Hyperglycemia 2. Dehydration, marked ECFV depletion 3. Hyperosmolality 4. Decreased level of consciousness (related to increased plasma osmolality)
Safety	NOT HARMFUL	**MEDICAL EMERGENCY**	**MEDICAL EMERGENCY**
Ketones	Present Target Blood Ketone Levels: 0.5-3.0 mmol/L (Corresponds to 'trace-moderate' or + to +++ on urine strips, depends on brand for scales used)	Present Target: Negative	Low to none Target: Negative
Blood Sugars	No elevation	Consistently High (>14mmol/L)	Very high (>34 mmol/L)
Insulin Levels	Normal/typical	Low/inadequate	Relative Insufficiency
pH Levels	Normal/unchanged	Acidotic (<7.3)	Normal (7.35 – 7.45)
Serum Bicarb	Normal	$\leq$ 15 mmol/L	Normal
Anion Gap	Normal/unchanged	Significant elevation in anion gap (usually >12 mmol/L)	Normal
Osmolality	Normal	Normal	>320 mmol/kg

What is the Evidence for Use of TCR in Diabetes?

Many international diabetes organizations have developed position statements and recommendations around TCR, which have been summarized on Page 39 (Appendix 1). Currently, there are clinical trials reviewing the use of TCR in treating diabetes, cancer, obesity, autism, migraine, amyotrophic lateral sclerosis (ALS), Alzheimer's, CKD and more.[12] In using TCR to alter metabolic parameters, research has shown that clinical changes are almost always initially favorable, and can be sustained but the diet and (as such) the improvements, can be difficult to sustain and depend on patient circumstances, motivation and ongoing healthcare provider support.[1] It is worth noting that research looking at TCR and its impact on HbA1C changes can be challenging to interpret. Although a number of studies report no or minimal improvements in HbA1C with TCR, diabetes medications are generally reduced or eliminated concomitantly which may moderate the impact on HbA1C.[13] Research suggests that it may help manage binge eating disorder, improving binge eating scores in those with obesity and self-reported binge eating and food addiction[14], which interestingly have also been documented as more prevalent in the T2DM population.[56,57]

Recently published research has demonstrated remission and reversal of metabolic syndrome and T2DM with sustained improvements in metabolic and lipid parameters, liver and kidney function, improved inflammatory markers, blood pressure and reduced medication needs, which are independent of weight or fat mass changes, in adults of a variety of ages, not just limited to those <65 years.[75,76,79] Similar results have been found using intermittent fasting and VLED (DiRECT Trial)[90] where weight loss was the desired outcome, however the research above indicates there are metabolic effects of TCR aside from those induced from weight/fat loss. TCR Interventions have similar results whether delivered in a rigorous clinical setting or delivered in community-based setting through group sessions and/or digital formats. [75,77] Overall, KD/Low CHO interventions (<130g CHO/day) have shown sustained benefit, both short-term and up to 6 years[79] to manage PreDM/T2DM when done under supervised conditions, and thus may be an appropriate strategy for some patients.[1] Recognizing the rapidly evolving research of this therapeutic intervention in T2DM, it is suggested that the goal for health care providers be to support their clients in making an informed, safe choice, to consider this as a lifestyle choice rather than a short-term "diet" and to note that the long-term safety of following a TCR is unknown and it will not be appropriate for everyone.[1]

Patient safety is of utmost importance when using this intervention and clinicians who do not have prescribing/de-prescribing privileges need to ensure their clients have immediate and ongoing access to their prescriber and are supported and assisted in adjusting their medications by a professional trained in this process.

What are the Contraindications and Risk Factors to Implementing the Ketogenic Diet?

There are certain conditions discussed in the literature where the KD is considered an "absolute" contraindication and individuals should be advised accordingly due to the risk to their health. Other conditions are considered "relative" contraindications as they are also considered high risk for other complications when following a KD.[9,17] The following table describes these conditions. (Table 3)

Table 3: Contraindications for Implementing or Following a Ketogenic Diet[17]

Absolute Contraindications[17]
Pancreatitis/ hypertriglyceridemia-associated acute pancreatitis[17] **Pregnancy / breastfeeding**[17] **Kidney failure / Moderate-Severe CKD**[17] **Liver failure**[17] **Respiratory failure**[17] **Cardiac Issues** (e.g. unstable angina[9], recent stroke/MI {< 12 mo. ago}[9], arrhythmias[9], heart failure {NYHA III-IV})[17] **Mental health Issues** (e.g. eating disorders, severe mental illnesses, alcohol/substance abuse)[9] **Active/severe infections**[17] **Frail elderly patients**[17] **Severe hypertriglyceridemia, inherited causes of severe dyslipidemia, hyperchylomicronemia** [17] **Rare disorders**: • Porphyria[17]→ can develop at any point in time • Metabolic conditions that usually present early in life : carnitine deficiency[17], carnitine palmitoyltransferase deficiency[17], carnitine-acylcarnitine translocase deficiency[17], carnitine translocase deficiency[20], mitochondrial fatty acid β-oxidation disorders[17], pyruvate carboxylase deficiency[17] β-oxidation defects[26], medium-chain acyl – CoA dehydrogenase deficiency (MCAD)[26], long-chain acyl dehydrogenase deficiency (LCAD) [26] short-chain acyl-CoA dehydrogenase deficiency (SCAD)[26], long-chain 3-hydroxyacyl-CoA deficiency[26], medium-chain 3-hydroxyacyl-CoA deficiency[26], von Gierke disease (glycogen storage disease type 1)[26]
Relative Contraindications (KD not recommended, or increased risk of complications)
T1DM- ambivalent results of clinical outcomes (A1C lowering, increased hypoglycemia, decreased insulin requirements, reduced glycemic variability);[28,29,30] long-term nutritional risks unknown. Use caution and ensure there is a discussion with individuals and/or parents of the risks, insulin management, DKA surveillance, lipid management, etc. See special considerations for T1DM on page 22. **Latent autoimmune diabetes of adults (LADA)** [17] Caution: insulin requirements can decrease but basal insulin will likely still be necessary to avoid DKA. **T2DM longstanding where β-cell failure is suspected or SGLT2 inhibitors have been prescribed[28]**– Education for insulin management/DKA surveillance is crucial for individual safety. To reduce risk of euglycemic DKA, consider discontinuing SGLT-2 inhibitor especially if client is also on insulin. **Renal stones**[14] **Severe dyslipidemia**[14] **Significant liver disease**[14] (other than liver failure which is an absolute contraindication) **Severe gastroesophageal reflux**[14] **Poor oral intake**[14] **Cardiomyopathy**[14] **Chronic metabolic acidosis**[14] **48 hr prior to elective surgery or invasive procedures and perioperative period**[18]- due to biochemical implications that may complicate surgical procedures (fluid/electrolyte balance, blood glucose, blood pressure, etc.)

Potential Indications:

There are some conditions where TCR/KD is indicated. Much of the available long-term studies are from the epilepsy research and guidelines where the ketogenic diet was first identified in the 1920s, as a treatment for epilepsy. It is now regularly prescribed in this population to help control seizures. In addition to epilepsy treatment, a recent systematic review and consensus statement by the Italian Society of Endocrinology provided other endocrine conditions where the KD may be indicated. (Table 4)

Table 4: Indications for the Ketogenic Diet for Use in Endocrine Conditions.[17]

Indications for the Ketogenic Diet	Evidence Strength
Severe Obesity (including management of obesity pre-bariatric surgery) Sarcopenic Obesity Obesity-Associated T2DM (preserved beta cell function) Obesity-Associated Hypertriglyceridemia Obesity-Associated Hypertension	**Strong Recommendation, Moderate Quality Evidence**
Obesity-Associated with Dysbiosis Obesity-Associated High LDL/Low HDL Obesity-Associated NAFLD	**Weak Recommendation, Moderate Quality Evidence**
Obesity-Associated Heart Failure (NYHA I–II) Obesity-Associated Atherosclerosis Male Obesity Secondary Hypogonadism Obesity-Associated Polycystic Ovarian Syndrome Menopausal Transition-Related Obesity Neurodegenerative Disorders Associated with Sarcopenic Obesity	**Weak Recommendation, Very Low Quality Evidence**

Assessment & Monitoring:

If the individual is interested or is already following a TCR, the following section offers guidance for assessment and monitoring.

Assessment:

- ✓ Explore their **knowledge** of the diet
  - Where or from whom did they hear about it?
  - What reading have they done?
  - What are they hoping to achieve with the diet?
  - Do they know the difference between KD and low CHO diet?
  - What is their knowledge of food groups?
  - Do they know about the risks?
  - Do they know about other dietary treatment options?
- ✓ Explore their **commitment** to the diet
  - Have they tried diets before?
  - What has worked in the past and what has not?
  - Are they willing to give up CHO?
  - Do they have support from other family members?
  - Are they willing to monitor blood sugars more frequently?
  - Are they willing, able and available to have more frequent check-ins with RD, MD, etc.?
- ✓ **Review**
  - medications
  - clinical metrics (BP, WC, labs, labs, etc.)
  - blood glucose control/variability (stable baseline control enables better assessment of effect of KD & medication/insulin needs/adjustments)
  - education gaps
  - barriers to implementing, maintaining, or managing on their own
  - ability to check-in frequently
  - availability of health-care providers to support frequent follow-up and monitoring

Monitoring:

Additional monitoring is highly recommended for anyone following TCR. This includes self-monitoring as well as monitoring by their healthcare provider. The following tables provide monitoring guidance. (Table 5, 6)

Table 5: Self-Monitoring by Individual

Parameter	Rationale
Blood Glucose Self-Monitoring	Increase frequency of blood glucose monitoring (especially if on glucose lowering medications) as decreased carbohydrate intake may result in hypoglycemia for people using insulin or secretagogues
Ketones [2]	T1DM: Recommended- critical to continue education for indications to check ketones, sick day management T2DM: Optional- ketones may be checked by individuals at home if client is interested/willing to complete. An optimal blood ketone level for weight loss is ~1.5 to 3.0 mmol/L [1] (Trace to moderate, or '+' to '+++' on urine dip sticks)
Food Intake	Important to keep a food diary and measure CHO intake to support knowledge and meet guidelines of TCR

Table 6: Recommended Monitoring by Provider[16,17,25,30,31,32,34]

Parameters	Monitoring **			Rationale
	Pre	Every 3 months	Annual	
Complete blood count HbA1C/FBG Total cholesterol HDL-cholesterol LDL-cholesterol Triglycerides (TG, serum) ALT, AST, GGT Total/direct bili (serum) Electrolytes Complete urinalysis Microalbuminuria (urine) Body composition via Bioimpedance Analysis- if available Blood pressure	 ↑ X ↓	 ↑ X ↓	 ↑ X ↓	Exclude those with severe alterations of blood count, uncontrolled DM, kidney damage Monitor as there is a highly variable response of LDL to KD. Lipids should be assessed Fasting chol/TG levels often rise short-term and return to baseline after 9– 12 months. Some patients with severe hyperTG may have a predisposition to hyperchylomicronemia. In these patients, KD could cause pancreatitis Monitor re: status/impact of KD on liver, gallbladder Monitor re: potential dehydration, hypotension, electrolyte abnormalities as body water loss occurs due to ketonuria-induced natriuresis and glycogen-depletion. Hypokalemia may contribute to the pro-arrhythmogenic effect of the diet Monitor body composition- assess outcomes, preservation of lean muscle mass, meeting goals of diet BP should be measured q 2-4 wks – If on anti-hypertensive meds, symptoms of low BP and/or systolic blood pressure below 120 should prompt reduction in these meds Regular urinalysis screening is recommended to assess for gross or microscopic hematuria
Creatinine, BUN, Uric acid (serum)	X	X		Monitoring of kidney function and potential increase in uric acid
Ketone Bodies (serum β-Hydroxybutyrate)		X		Monitoring ketosis if suspect DKA or to assess achievement of diet goals
TSH, T3, FT4 (serum) 25-OH D (serum)	X			To exclude thyroid function abnormalities To treat vitamin D deficiency, if present
**** Monitoring Follow-up: q 3 months after initiation of diet for the first year, then annually. Recheck lipids after 6 months**[2, 25,35]				

Monitoring for Individualized Clinical Indications:

For some individuals with other clinical co-morbidities, additional monitoring may be required following assessment by their healthcare provider. The following table provides recommended monitoring for some of those individuals. (Table 7)

Table 7: Recommended Monitoring by Provider for Unique Patient-Specific Indications

Parameters	Monitoring			Rationale
	Pre	Every 3 months	Annual	
INR (If on vitamin K antagonist anticoagulant therapy)	X	X	X	More frequent monitoring due to changed dietary intake (vitamin K)[2]
Lithium levels	X	X	X	The levels of these meds can be affected by the water loss that accompanies the initiation of therapeutic carbohydrate reduction[33]
Valproate levels	X	X	X	

Additional Monitoring:

Additional monitoring is recommended by some, but there is inconsistency in the literature. The following table identifies additional monitoring that may be considered, depending on an individual's unique presentation of medical history, and co-morbidities. (Table 8)

Table 8: Other Monitoring by Provider - Suggested Inconsistently in the Literature [2,12,16,17,25,30,31,32,33,34,35]

Parameter	Rationale
Serum acylcarnitine profile **-not OHIP-covered, check before KD** Free and total carnitine **-not OHIP-covered, check during KD**	Secondary carnitine deficiency can occur with prolonged use of KD and/or if individual also takes Valproic Acid Secondary hypocarnitinemia may rarely cause liver and heart problems Symptoms indicating hypocarnitinemia may include fatigue and muscle weakness
Ca Mg Inorganic phosphate (serum)	Electrolyte changes induced by KD may increase Mg losses. A persistent low K+ could indicate a Mg deficiency **Pediatric use of low CHO/KD is not addressed in detail, in this document, however, it is worth noting that these parameters, in Ped T1DM, are suggested q3mo for 1st year and then annually*
Renal Ultrasound (US)	Renal US is advised prior to starting KD and at follow-up visits only if there is a family history of kidney stones. Some evidence suggests renal US is only necessary if hematuria is present
ECG	Strongly consider at baseline and q 3 months as well as with any concerning and unexplained signs and symptoms. This is especially recommended if there is history of heart disease. Although rare, a prolonged QT interval can occur which could lead to arrhythmias
Urine Ca and Cr	May be a role to check urinary Ca/Cr ratios for assessment re: nephrolithiasis
Serum Bicarb	To monitor impact on acid-base balance- **may be done more frequently in T1DM and/or if suspicion of DKA**
Total protein/ Albumin	To monitor for hypoproteinemia - could occur with inadequate dietary protein in the diet
Diagnostic imaging	Diagnostic imaging as required if suspected cardiomyopathy
Selenium **-Not OHIP-covered**	Some research suggests screening if and when dietary selenium intake is <75% or signs of selenium deficiency. Other studies recommend screening selenium level at baseline and q 3 months x 1 yr due to risk of selenium-deficiency-associated cardiomyopathy and prolonged QT interval which may cause cardiac arrhythmias
Zinc levels	Check during therapy
Copper levels	Check during therapy
Bone mineral density (BMD) with a Dual-energy X-ray absorptiometry (DEXA) scan	Consider BMD after 2 years on KD, baseline in T1DM and then annually
C-peptide	Consider checking in individuals with T2DM who take insulin to assess endogenous insulin production to assess/address the risk of DKA

Medication Adjustments While Following TCR:

TCR induces significant changes to metabolism and electrolyte balance that may cause individuals to become overmedicated. As such, it is very important to provide regular monitoring and medication adjustment as needed to prevent complications. [2] Insulin doses need to be lowered to avoid hypoglycemia and SGLT2 inhibitors may need to be de-prescribed. Individuals should be educated on this and supported with frequent follow-up for medication adjustments and instructed to monitor their BG up to 4x/day (ac/ 2 hr pc) if on any medications that could cause hypoglycemia. The following table provides guidance on medication adjustment, however, an individualized approach is essential.[2,17,33,36] (Table 9)

Medication Adjustments: Key Questions

When deciding the safety and appropriateness of T2DM medications for clients using TCR, there are three key clinical considerations[36]:
1. Is there a risk of the drug causing hypoglycemia or other adverse event?
2. What is the degree of carbohydrate restriction?
3. 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?

Table 9: Summary of Medication Priority when Deprescribing

STOP	CAUTION	OK
Sulphonylureas Meglitinides Bolus Insulin SGLT2s- ↑ risk of eDKA Combination Insulins (e.g. 30/70) Alpha-glucosidase Inhibitors	Basal Insulins (May need to reduce by 50%) TZDs	Metformin GLP-1 RAs DPP-4 Inhibitors

- Clinical judgement is always necessary to address unique client situations and make appropriate decisions to manage safety of medication use.
- When reducing insulin, typically reduce the basal & bolus at the same time, aiming for basal dose to be 1/2 to 2/3 of TDD.
- If adding an agent becomes necessary, consider agents that are weight neutral or induce weight loss (GLP-1 agonists, metformin, etc.)
- Prandial insulins not usually required on VLCD (<40g net CHO/day), but if >40g CHO/day dose based on net CHO/meal[78]
- Day 1: Basal insulin can be reduced by up to 50% (<40g net CHO/day), by 25% (40-80g net CHO/day) and by 10% (80-130g CHO/day)[78]
- Mixed insulins are not ideal in low CHO environment and should be switched to basal/bolus or basal only depending on CHO intake[78]

Table 10: Medication Adjustments While Following a Ketogenic Diet [2,29,32,33]

Drug Group	Suggested Action	Hypoglycemic Risk	Other Information
Basal Insulin	Reduce/Stop, on same day the diet intervention starts **NB: Beware of insulin insufficiency!**	YES	Risk of hypoglycemia. T2DM: Start CHO restriction gradually and monitor fasting blood glucose (FBG) & before meal blood sugars (ac BG), adjusting insulin as needed. Typically wean by 30-50% progressively. **If on both meal-time insulin and basal insulin, consider reducing the meal-time insulin first.** T1DM: basal insulin doses may remain similar especially if no weight loss indicated. **CLINICAL JUDGEMENT IS IMPERATIVE.**
Meal-time Insulin	Reduce/ Stop, on same day the diet intervention starts **NB: Beware of insulin insufficiency!**	YES	T2DM: suggest reducing meal-time CHO by 50% (of typical intake) and bolus insulin accordingly assuming insulin: carbohydrate ratios (ICR) are in place and consider discontinuing meal time insulin as approach <50 g CHO. T1DM: same reduction as above, excluding discontinuation. May be safer at 50-100g CHO/day. If already experiencing lows, consider reducing insulin doses before reducing CHO. **CLINICAL JUDGEMENT & ONGOING ADJUSTMENTS ARE IMPERATIVE.**
Mixed Insulin	Change to BBI	YES	Adjust as above, consider that meal-time insulin may not be required, if T2DM, & if implementing <50 g CHO diet d/c immediately. **CLINICAL JUDGEMENT & ONGOING ADJUSTMENTS ARE IMPERATIVE.**
Sulphonylureas/Meglitinides	Reduce/Stop	YES	Risk of hypoglycemia.
SGLT2i (-flozins)	Stop /Monitor	NO	Risk of euglycemic DKA, especially if also on insulin and the insulin is reduced/stopped and SGLT2-i is continued, risk is low if CHO >50g .
Biguanides (metformin)	Optional adjustment	NO	Consider clinical pro/cons.
GLP-1 agonists (-enatide/-glutide)	Optional adjustment	NO	Consider clinical pro/cons.
Thiazolidinediones (-glitazones)	Stop	NO	Usually stop - concerns over long-term risks usually outweigh benefit.
DPP-4 Inhibitors (-gliptins)	Stop	NO	Usually stop due to lack of benefit.
Alpha-glucosidase inhibitors (acarbose)	Stop	NO	Usually stop, due to no benefit if low starch/sucrose ingestion.
Blood Pressure Medications	Reduce/Stop prn	N/A	A reduction in BP frequently occurs in patients with hypertension who follow low-CHO or very-low CHO diets. Patients should monitor BP at home or in clinic, and antihypertensive medications may need to be tapered or discontinued. If systolic BP <120, diastolic BP <70 or symptoms of orthostatic hypotension, medications may need to be reduced or stopped. In individuals with microalbuminuria, continuing a low dose of renal-protective antihypertensives is recommended if patient does not develop low BP.

Drug Group	Suggested Action	Hypoglycemic Risk	Other Information
Diuretics	Reduce/Stop prn	N/A	Risk of potassium depletion if using potassium-wasting diuretics. May need to be tapered or discontinued to prevent dehydration and/or hypotension unless indicated for symptomatic heart failure. If appropriate, diuretics should be reduced or discontinued before beta-blockers.
Drugs which may cause QT prolongation or precipitate arrhythmias	Avoid or use only with close supervision	N/A	Life-threatening arrhythmias can occur with risk of selenium deficiency while undertaking KD. These types of drugs exacerbate that risk.
Meds with Narrow Therapeutic Ranges [e.g. Warfarin, Lithium, Valproate]	May require adjustment	N/A	Monitor INR (for warfarin) and blood levels (for lithium and valproate) as they may require adjustment due to dietary changes and shift in electrolytes/fluids.
Niacin Beta-blockers Anti-depressants Anti-psychotics	Reassess	N/A	These medications can interfere with lipolysis and should be replaced or discontinued if possible.

*Routine Sick Day Management strategies apply and should be discussed routinely during visits. Individuals who are following a KD require extra guidance and education on the need to monitor medications and blood sugars.

TCR induces significant changes to metabolism and electrolyte balance that may cause patients to become overmedicated.[2]

Vitamin/Mineral Supplementation:

There continues to be debate as to whether a very low CHO diet can be designed to provide adequate nutrition. Some research suggests that vitamin/mineral supplementation should be made on a personalized basis (at the discretion of MD/RD/individual and based on nutritional bloodwork).[2] Others recommend a daily CHO-free preparation of multi-vitamin with minerals (including trace minerals – especially with 30mcg selenium), calcium and vitamin D. [26,33] Most KD clinical trials have included a daily multivitamin and mineral supplement.[2] Increasing sodium by 1-2 gm/day may be necessary to restore sodium lost in rapid shift of fluid out of the body (which also can affect magnesium levels) that occurs with low insulin levels (hence, the addition of broth in many menu plans) and resolve 'keto flu' symptoms. (See Nutrients of Concern section pg. 29).

Side Effects & Adverse Effects:

Side effects can occur because of initiating TCR and should be discussed with the individual. These side effects can be short term or long term, depending on the duration of the intervention. [11,37,38]

Short Term Side Effects:

In the initial days of the dietary change, people often report flu-like symptoms commonly referred to as the "keto flu" *. These short-term effects occur during transition to a KD and often improve with adequate sodium and fluids. [2,33] The following table describes short term side effects, the cause and proposed management strategies. (Table 11)

Table 11: Short Term Side Effects of the Ketogenic Diet [2,3,12,16,23,26,31,33,36]

Adverse Effect	Cause	Management Strategy
*N/V/GERD	The high fat content of KD prolongs gastric emptying times which can result in **N/V or GERD**. Transitory **lethargy** could occur in the first few days as the body switches from burning carbs to burning fat for energy. However**, if lethargy persists** more than few days, medical investigations are recommended, as lethargy could be also a symptom of dehydration, excessive ketosis and nutrient deficiencies. **Constipation:** due to fluid/lytes imbalance, low fibre intake (related to exclusion of whole grains and limited fruit/veg) or reduced food volume. **Electrolyte abnormalities** are potentially due to dehydration, urinary excretion of ketone bodies and/or poor intake of micronutrients. Lower insulin levels result in diuresis, symptomatic hypotension, and low body salt.	**For N/V and GERD:** Consider trial of diet modification (e.g. frequent intake of small amounts) or consider intermittent use of GI drugs such as antiemetics, GI tract regulators, and antacids. **Headache**: Consider mild analgesics as appropriate. **Lethargy**: Consider measuring ketones, could consider consumption of a CHO containing beverage. Consider evaluation of Fe status. **Insomnia:** Consider Mg supplementation. **Constipation:** Encourage adequate fluid, increase high fibre, low CHO veg; if not resolved, clinicians may recommend 1 teaspoon of milk of magnesia or Mg citrate at bedtime, bouillon supplements, or a sugar-free fiber supplement. If pre-existing constipation, diverticular disease or hemorrhoids, extra dietary fibre (e.g. psyllium 3.5 g twice daily) from the beginning of the diet needs to be considered. **Adequate hydration**: minimum 2L/d . **Adequate sodium** (2-3g/d except in HTN, CKD or CHF) – liberally salt food or sip on broth mode from regular-sodium bouillon cubes. In terms of the exceptions, sodium intake should be kept at baseline until edema resolves, then increased if the patient
*Headache		
*Lethargy/Fatigue		
*Dizziness		
*Insomnia		
*Exercise intolerance		
*Constipation		
*Dehydration		
*Hyponatremia		
*Hypomagnesemia		
*Kaliuresis		

		has orthostatic symptoms. Consider BP medication reassessment prn.
Anorexia	Impacted by protein intake, KB appetite suppression, hormone levels (e.g. ghrelin, leptin).	A degree of anorexia is part of what may help individuals maintain KD, but inability to maintain adequate nutrition is a contraindication to KD.
Palpitations, Anxiety	Specific cause/management not described in the literature.	
Temporary hair loss	Hair loss occurs mostly with weight loss/negative nitrogen balance.	Adequate protein intake.
Bad breath	Due to ketosis – generally caused by an increase in acetone levels.	Have a sugar-free mint/gum.
Irritability	Specific cause not identified.	Supplement Mg.
Alcohol intolerance	Cause not identified in literature.	Limit alcohol. Small amounts may be tolerated.
GI Distress [due to cholecystectomy]	Due to changes in fat digestion.	Increase fat gradually with possible bile salt supplementation for persistent GI distress.
Gout flare-up /Hyperuricemia	If history of gout, a higher flare risk in short term (transition to KD).	Consider prophylactic allopurinol during transition.
Diarrhea	Intolerance of high fat intake.	Tends to be transient. Could trial anti-diarrheals.
Hypoglycemia	Over-medication, reduced caloric intake, ketone body impact on insulin secretion, weight reduction, increased glucose oxidation/insulin sensitivity, lower hepatic glucose production.	Adjust anti-hypoglycemic medication. If BG < 2.2 mmol/L and symptomatic, then consumption of a carb containing beverage is recommended.
Muscle cramps	Due to the electrolyte imbalances, individuals may experience muscle cramps.	Adequate fluid/ sodium intake. Consider Mg supplement. Encourage Mg-rich, low-carb foods such as almonds, spinach, fatty fish, and avocados.

***Commonly known as "keto flu"**

Long Term Potential Effects:

Adverse effects can also occur if on the KD for longer duration. The following table describes long term side effects that may occur, as well as the possible cause and proposed management strategies. (Table 12)

Table 12: Long Term Side Effects of the Ketogenic Diet [1,12,16,17,25,27,31,32,34,40,41]

Adverse Effect	Cause	Management Strategy
Disruptions in Lipid Metabolism	Response of LDL to KD is highly variable. Some with severe hyper TG may have a predisposition to hyperchylomicronemia. In these patients, KD could cause or precipitate pancreatitis.	Baseline and follow-up lipid profiles should be assessed. Replacing saturated fats with unsaturated fat has been shown to improve LDL levels.
Hypocalcaemia and Bone Damage	Although calcium metabolism seems to be preserved in VLCKD, some research suggests that very low-calorie diets have a negative effect on both bone mineral content and bone mineral density. Diets high in acid-ash proteins have been associated with excessive calcium loss due to acidogenic content	Provide adequate/appropriate amounts of Ca, vitamin D and CHO. Refrain from implementing VLC interventions. KD can improve metabolic function without energy restrictions. Recent research of 2 yr longitudinal study on KD has shown no changes in spinal BMD[75]
Acute pancreatitis	Due to hyper TG; Increased risk if concomitant use of antiepileptic drugs.	Discontinuing VLCKD and adequate supportive treatment are required for successful recovery and advise individuals of signs /symptoms of pancreatitis.

Hepatitis	Increased risk of hepatitis with concomitant use of antiepileptic drugs.	Discontinuing VLCKD and adequate supportive treatment are required for successful recovery.
Hypoproteinemia	Could occur due to gluconeogenic consumption due to CHO restriction.	Increase protein intake from 1 g/kg/day to 1.5 g/kg/day while the lipid-to-nonlipid ratio is kept.
Cardiomyopathy	Due to selenium deficiency.	Consider daily carb-free multi-vitamin with minerals (including trace minerals, especially 30 mcg selenium).
Nephrolithiasis & Urolithiasis	Increased risk due to: inadequate fluid intake/dehydration, fat malabsorption, KD lowers urinary pH which can facilitate formation of uric acid crystals. Hypocitraturia can occur with chronic metabolic acidosis increasing calcium stone formation risk. Risk factors for urolithiasis include young age, family history of kidney stones and a urine Ca/Cr ratio >0.2.	Adequate fluid intake can help prevent kidney stone formation. Prophylactic potassium citrate could be warranted in those deemed higher risk.
Gallstones	Due to rapid weight loss.	Specific management not identified in the literature.
Prolonged QT	Due to selenium deficiency.	Screen selenium level at baseline and q 3 months x 1 yr due to risk of selenium-deficiency-associated prolonged QT interval (risk of cardiac arrhythmias).[32] Consider a daily CHO-free preparation of multi-vitamin with minerals (including trace minerals – especially with 30mcg selenium).
Blunted glucagon response	**If glucagon treatment is needed, response may be inadequate due to decreased hepatic glycogen stores.**	**Counsel re: potential risk of blunted glucagon response. Blood glucose monitoring, prompt/proper treatment of hypoglycemia is imperative.**
Increased fertility	Weight loss and decreased insulin resistance with KD can increase fertility and may result in unplanned/unwanted pregnancy.	Women of childbearing age should be counselled regarding increased fertility and need for contraception. KD is contraindicated in pregnancy.
Thyroid dysfunction	There is some research suggesting increased risk of thyroid dysfunction with resultant need for levothyroxine treatment while on KD. However, research is not sufficient, and trials are pending.	

CKD & TCR

CKD is a common complication of diabetes, thus a discussion of the safety of using TCR in the context of diabetic nephropathy is warranted. There is concern that a high dietary protein content may be harmful to the kidneys by increasing glomerular pressure and hyperfiltration, [80] however, a high protein intake is not typical of a well formulated TCR intervention.

The literature is sparse of evidence for the safety of use of TCR diet in the context of diabetic nephropathy. Most studies done are in patients with healthy kidneys[81,82,83] or are of very small sample size.[84,85] Studies vary in their level of carbohydrate restriction, duration of study and follow-up period making longer-term generalizations difficult. Generally studies conclude that there is either no difference in GFR between a KD/LC group and control or a small increase in GFR in the KD/LC group,[82,86,83] no difference or small improvement in albuminuria in the KD/LC group,[82,83,85] no difference in uric acid,[82] and a decrease in cystatin C,[85] (another blood protein that can be used to calculate GFR and is less sensitive to dietary intake and/or muscle mass). [87]

A small study examining the effect of a very low calorie KD that included patients with mild CKD (eGFR 60-89mL/min/1.73m2) did report an improvement in the eGFR of a significant portion of their participants with mild CKD such that eGFR was >90 by study end, and additionally this group found decreased serum Cr levels, decreased urinary protein excretion and a significant decrease in uric acid.[84]

Studies done in mice/rat models have shown more promising results in reversing nephropathy.[88] Mice genetically altered to express T1DM and T2DM phenotypes that were fed a KD (8% energy from CHO) for 8 weeks had a complete reversal (T1DM mice) or almost complete reversal (T2DM mice) of their nephropathy as measured by ACR by study end. In addition, there was reversal (T1DM mice) or almost complete reversal (T2DM mice) of gene expression that is common in the kidneys of diabetic mice and glomerular sclerosis was partially (significantly) improved.[88]

Monitoring kidney function should remain a regular parameter in assessing health of people with DM implementing a carbohydrate restriction/reduction intervention. TCR is not necessarily a contraindication in those with CKD and may offer some benefits as this intervention mimics the therapeutic effects of SGLT2i (increased sodium and glucose loss, promotion of fat oxidation and beta-hydroxybutyrate production), which have recently been shown to have cardio-renal protection.[89] Given this finding, the use of SGLT2i and a KD, simultaneously, could be redundant and potentially put patients at risk of eDKA. Discontinuing SGLT2i when implementing therapeutic carbohydrate restrictions is advised.

CVD & TCR

One of the barriers to implementing a low CHO intervention is its contradiction to the prevailing paradigm of the diet-heart health hypothesis that has directed much of the global health and nutrition policy and clinician education since the 1950s. Consuming a high fat diet, particularly high in saturated fat, has been considered a leading contributor to heart disease based on studies showing that dietary SFA increases LDL-C and that there is a link between LDL-C and CVD, however the link between dietary SFA and CVD is lacking. Several cohort, meta-analyses, and systemic reviews have been undertaken to explore the connection between SFA intake and CVD including studies that have followed large cohorts, for up to 10 years, showing that higher fat intakes do not influence CVD risk/outcomes, and are associated with lower total mortality and reduced incidence of stroke. [91-94,118-121]

Systematic reviews of RCTs have shown slight reductions in risk of CV events and MI in men with lower SFA intake but failed to show any impact on total mortality or death from CVD, [125, 126] and several RCTs show a positive impact of low CHO approaches on CVD risk factors [102, 103,124] (increased HDL, lower TGs, increased LDL particle size, decreased BG and insulin levels, unchanged carotid intima thickness, decreased inflammatory markers) in iso-caloric interventions,[10,76,98] in those with metabolic dysfunction, and healthy people with combined overweight and CVD risk factors.[99] These effects may be greater in those who have T2DM + obesity than those with obesity alone (without metabolic dysfunction).[101] A meta analysis of those with overweight/obesity showed slight, insignificant, heterogeneity in LDL response, amongst low CHO interventions at 6, 12 and 24 months and favourable HDL and plasma TGs outcomes at 6 and 12 months compared to LF intervention.[100] The research does not support an

improvement in CV outcomes with a low fat/low SFA diet and high CHO diets may be associated with increased risk.

Notably, much of the research at the population level is assessed against a background of high CHO diets and lipid metabolism favourably changes in a low CHO milieu[123]. It is also important to note that not all CHO is the same. Most studies do not analyze CHO by its individual components of fibre/sugar/starch and the negative impact of excessive dietary fat, particularly SFA, seems to correlate with diets that are also high in refined, low fibre, CHO, (fibre intake >25g/day confers CV benefit[92]), emphasizing the importance of counselling clients to consume large quantities of low CHO, high fibre vegetables, nuts, seeds and berries, and to limit intake of highly processed, low fibre CHO foods. Similarly, all SFA is not the same, as fatty whole foods containing a matrix of nutrients are very different than that of fats/oils. Studies do not elucidate the nuances associated with different SFAs and their impact on health. Advising clients to choose a wide range of high fat whole foods to include the full spectrum of FFAs, minimizes the risk of excessive FAs from any one family.[92]

Metabolism of lipids is complex and while dietary SFA does not seem implicated in CVD risk, circulating levels of SFA are problematic and are increased in a high dietary CHO environment. Using LDL levels exclusively as an indicator of CVD risk negates the impact of other parameters that may bestow benefit. LDL has been shown to decrease, remain constant or increase on a low CHO/KD. Research indicates that while LDL levels may increase slightly in up to 50% of people on TCR (in 25% of those it may increase >30%), it is the less dense, larger LDL particles (LDL-p) that may be increasing, not the smaller, dense atherogenic particles which are prone to oxidation and glycation, causing inflammation, migration into endothelial walls, generation of foam cells and plaque formation. [10,95,124] The Framingham offspring study has suggested, that using apo-B or total LDL particle (vs LDL-c) as a proxy for assessing the density of LDL particles can be useful to monitor the impact of this intervention on lipids, as monitoring changes in LDL-C alone may miss this nuance.[96] TCR has been shown to increase HDL 2x more than a LF approach and people with the highest risk for CV events have high total LDL particles and LDL-C, while those with the lowest risk had low LDL-P but higher LDL-C.[96,97].

The UKPDS demonstrated, in those with diabetes, the significant risk factor for fatal and non-fatal MI events was A1c.[104] Diabetes, itself, is a risk factor and a low CHO intervention has evidence of efficacy in improving many cardiovascular/metabolic markers including HDL, TG, A1c, HOMA-IR, insulin levels, BP, c-peptide levels, markers of inflammation, and hepatic insulin sensitivity despite variable impact on LDL.

There is no clear evidence that dietary fat, particularly SFA, has a negative impact on one's risk of CVD, all cause mortality or any other disease and it may confer benefit. Its impact is very nuanced and influenced by the varied components of the diet, notably refined CHO, the SFA matrix of whole foods vs oils, what a person chooses to replace it with, and individual metabolic differences. People following a typical TCR will likely be consuming ~30g SFA/day, finding it challenging to maintain current nutrition guidelines. They may see their LDL-C increase but experience an overall global risk reduction when assessing all other CVD risk factors. Evaluating individual responses is critical and some individuals may require increased focus on replacing some SFA with PUFA/MUFA and/or liberalizing protein.

Table 13: Summary Points - CVD Risk and TCR, see Appendix II for Referenced Lipid Targets

Summary of emerging research in context of IR and T2DM:	Consider the following parameters to provide a more complete clinical context to assess CVD risk (see Appendix 2 for references/targets):
• Adverse effects of high dietary SFA is connected to high CHO intake, especially high GI CHO • Surplus dietary CHO triggers hepatic SFA production, increasing plasma SFA • LCD/SFA vs HC/LF diets result in lower plasma SFA • Plasma SFA correlates with IR and CVD	• TC:LDL • TG:HDL • Apo B • Non-HDL • C-reactive protein • BP • A1c • HOMA-IR (FBG + insulin levels)

Type 1 Diabetes-Special Considerations:

Evidence in the T1DM population is limited and sometimes ambivalent, but there is research demonstrating an ability to achieve normal HbA1C levels with decreased glucose variability, less hypoglycemia, and lower total daily doses of insulin[35]. It is imperative that individuals feel confident and trusting of their care providers to discuss this option and that individuals do not decide to implement in isolation, putting themselves (or their children) at increased risk of mismanagement. Discussing the specifics of the dietary regime, the pros/cons and risks are crucial to providing ethical care. Individuals should agree to be engaged in frequent BG testing to assess need for insulin adjustments. Anticipate low levels of KBs due to nutritional ketosis but they should be kept to a minimum.

Some evidence suggests that the glucagon rescue response is impaired when on a low CHO diet compared with a high CHO diet. [40] It has been suggested there are possible increases in hypoglycemia unawareness in a mild ketotic state, as ketones have been shown to reduce the cognitive impairment that often occurs with hypoglycemia, thereby, individuals/family may not observe these typical cognitive warning signs of a low blood sugar.[42]

Note: There is a potential increased risk of hypoglycemia and delayed glucagon rescue response in Type 1 Diabetes and the ketogenic diet.[40,42]

Unique Pediatric Risk Considerations:[35]

This document is not intended to address this population specifically or in detail, nor is it an endorsement. However, there are important considerations to address should caregivers enquire about this treatment for pediatric clients in their care.

The following points should be considered if parents are interested in TCR for their children:

- There is some evidence of poor growth on a diet <30 g CHO/day, though high BG is also implicated in the same
- It requires close monitoring and assessment for caloric adequacy, necessity of vitamin/mineral supplementation
- There may be risk of social isolation
- It may increase risk factors for disordered eating with increased food restrictions
- They may have decreased knowledge/capacity to adjust insulin should CHO intake vary in social situations outside parental control when they have not learned CHO counting, or how to adjust ICRs

Therapeutic goals for clinicians and parents are usually similar:

- ✓ maximize quality of life, and
- ✓ optimize HbA1C (without risks and minimizing BG variability)

Aligning care on these principles can be the foundation for open dialogue when TCR is under consideration to ensure the continuation of a strong therapeutic relationship.[36] Focus on patient centred care, assessment of knowledge, and capacity (cost, cooking/food prep skills, social implications, education level, etc.) when considering the ability of individuals to implement this regime in those with T1DM. This population warrants careful consideration of this dietary intervention as it is considered high risk for them. (See page 26 for general CHO targets for children and adults)

Guidance for Implementing TCR:

- ✓ Conduct individual assessment of each person[2]
- ✓ Implement in consultation with a Registered Dietitian (RD)
- ✓ Involve an inter-disciplinary team, when possible, to support the ongoing management/frequent follow up
- ✓ Manage medications as necessary
- ✓ Recognize that initial improvements in clinical outcomes may diminish over time
- ✓ Educate to ensure individuals are making an informed choice
- ✓ Consider short-term KD followed by transition to low carbohydrate diet long-term
- ✓ Emphasize a general CHO reduction/restriction, rather than monitoring/specifying total macronutrient ratios [2] (an "ideal" macronutrient distribution, suitable for everyone, is not standard in the research) or caloric restriction
- ✓ Encourage a variety of whole food sources of protein, fat, low-starch vegetables, nuts, seeds, and full-fat dairy[2]
- ✓ Ensure adequate protein/fat intake at each meal to give a sense of satiety and satisfaction[2]
- ✓ Ensure sufficient fluids [32,34] (see next section: Guide for Dietitians)

Guide for Dietitians

The remaining section is intended for Registered Dietitians to provide more detailed guidance for counselling individuals interested in the KD. The following table provides a reminder of the macronutrient guidelines for KD and low CHO regimes. (Table 14)

Table 14: Macronutrient Guidelines for TCR: [2,4]

	Ketogenic Diet	Low Carb (Non-Ketogenic) Diet
CHO Content	<50g/d	50-130g/d
Protein Content	Protein to meet nutritional needs (1- 1.5g/kg body weight)	Variable / Not Defined
Fat Content	70-90% of calories Often >150g fat/d during maintenance	Variable / Not Defined
Ketones	~1.5-3.0 mmol/L/ trace to low	Ketones unlikely

The guiding principles remain for Medical Nutrition Therapy to manage diabetes[43]:

- Optimize quality of life
- Optimize nutritional and physiological health
- Prevent and treat acute and long-term complications, associated co-morbid conditions and concomitant disorders
- Optimize glycemic control, minimizing risk of hypoglycemia

TCR is implemented in a variety of regimes and settings, from being part of VLCKD medical bariatric programs, to clients implementing TCR on their own from mainstream media sources. However, to follow an authentic KD safely and to meet nutritional requirements while mitigating risk, a comprehensive assessment and education with individuals is needed. A net dietary CHO intake of 20-50 g/day (net CHO = total CHO g – fibre g) is required to achieve a state of nutritional ketosis.

Many amino acids are involved in gluconeogenesis and their intake must also be monitored and restricted to achieve and maintain ketosis. Alanine & glutamine are the AAs primarily used for gluconeogenesis, but many other AAs can have gluconeogenic properties when dietary CHO is restricted.

Research Review of the Variety TCR Implementation Methods

A specific, universal dietary prescription is difficult to establish as there is great variability in diet intake documented in the research to date and clinical outcomes are equally varied with benefits seen within the spectrum of carbohydrate restriction/reduction. A comprehensive systematic review of 41 studies investigating TCR for management of T2DM from 1963-2018 illustrates the wide variety of macronutrient and energy prescriptions used in research.[3] The following table provides clinicians with a summary of current research, to help facilitate discussions with individuals wishing to implement this regime to better manage their diabetes (Table 15).

Table 15: Summary of the Variety of Methods for Low CHO Diets Implemented in Research

	Variety of Recommendations
Macronutrient Distribution:	For classic KD used to treat epilepsy, macronutrient distribution is 4:1 (4g Fat: every 1g CHO + PRO) to 3:1 (3g Fat: every 1g CHO + PRO). However, the research in the metabolic/T2DM and T1DM population indicates that this tight prescription may be unnecessary to achieve the desired outcomes of weight loss, A1C lowering, reduction in DM medications and improved insulin sensitivity. Tracking only CHO targets, split evenly between 3-4 meals eliminates much of the labour for patients and clinicians supporting them, and impact can be seen in regimes <130g CHO/day, more if <50g CHO/day.[44]
Total Energy:	Ranged from ad libitum, to moderately restricted, to severely restricted, and to adaptive & variable.
Carbohydrate amount:	Ranged from fixed prescriptions of amounts ranging from 0-130g/day (most studies set a required CHO minimum intake of 20g, however 9 studies had no required minimum intake of CHO), to individualized studies considering an individual's body weight, blood ketones, glycemic control. about 50% of studies used whole foods (vs prepared liquid meal replacements).
Fat Amount:	Ranged from unrestricted, high fat (>35% TEI) to low fat (<20% TEI), & variations in %SF intake were prescribed in approximately 50% of studies.
Protein Amount:	Ranged from unrestricted, to high protein (>25% TEI), to moderate protein (1-1.5g/kg).
Generally (% kcal):	• Fat ≥70 % • Protein 10-20 % (1-1.5 g/kg, sufficient to meet protein requirements and prevent muscle catabolism) • Carbohydrate 5-10% Example of 2000 kcal intake: 165g fat, 40g carbohydrate, 75g protein

The following table offers suggested definition of diets by carbohydrate amount in g/day[35] and uses average dietary reference values for energy across the life spectrum. [45] (Table 16)

Table 16: Suggested definition of diets by carbohydrate amount across life spectrum[45]

	Carbohydrate g/day			
Nomenclature*	3 – 8 yr	9-13 yr	14-18 yr	Adult (18 – 50 yr)
High CHO diet (>55% TE)	> 230 g	> 300 g	>380 g	> 370 g
Avg intake of CHO (~45% TE)	~ 190 g	~ 245 g	~310 g	~ 300 g
Low CHO Diet (<26% TE)	<110 g	<140 g	<180 g	<175 g
Very Low CHO/KD (<10% TE)	<42 g	<55 g	<70 g	<68 g

*Based on definitions in the literature, mean estimated energy requirements for age, activity, and current population intakes. (3- 8yr ~1700 kcal, 9-13 yr 2175 kcal, 14-18 yr 2760 kcal, adult ~2700 kcal, adjust CHO targets based on clients' estimated energy intake goals as % of total kcal intake vs a finite number of CHO g).

An emphasis on whole foods is described in most studies for a variety of reasons and we would also emphasize that this is prudent practice. The degree of processing can have an impact on insulin responses post-prandially and is often of lesser nutritional quality. The higher fibre/fluid content of whole foods can also, positively displace the intake of processed carbohydrates/discretionary foods; notwithstanding, this message also aligns with current recommendations from Health Canada.

None of the reviewed studies demonstrated a worsening of cardiovascular risk factors, including HbA1C, lipids, waist circumference, however debates are ongoing with respect to amounts and types of fats. Again, with an emphasis on whole food sources, this may offer protection from excessive intakes of particular fatty acids, and this diet tends to have higher proportions of monounsaturated fats, and a very low risk of EFA deficiency (which can be a concern on low fat diet regimes) [3] negating the need for rigid FA prescriptions[3]. Long term CVD/MACE data is unavailable and unknown.

Foods Allowed on TCR

The following table lists foods included or restricted/reduced on a KD or low CHO diet. (Table 17)

Table 17: Foods Included or Restricted/Reduced

Typically Included Foods [2]	
Protein	Meat, fish, poultry, seafood, eggs, tofu, certain nuts/seeds (see below). There is often an emphasis on grass-fed and/or free-range that offer slightly higher amounts of omega-3 fats[46]
Nuts/Seeds	Includes nut butters, seeds (e.g. flax, chia, sunflower, pumpkin, hemp) and whole nuts (e.g. almonds, macadamia, pecans)
Dairy	Full fat cheese, unsweetened/plain yogurt, cream
Fruits	Fatty fruits (e.g. avocado, olives, coconut) Small amounts of unsweetened berries
Vegetables	Most non-starchy vegetables are included: Leafy greens (e.g. kale, Swiss chard, zucchini, collards, spinach, Bok choy, lettuces), cauliflower, broccoli, Brussel sprouts, asparagus, bell peppers, onions, garlic, mushrooms, cucumber, celery
Oils/Fats	Any non-trans fats Oils: Olive, canola, sunflower, coconut, avocado Butter, ghee, bacon
Other	Dark chocolate (90%), cocoa powder, unsweetened coffee/tea, unsweetened vinegars/condiments, herbs/spices Hard liquor and low CHO/low sugar (dry) wines may be included
Artificial Sweeteners	Minimally as these may induce cravings
Restricted/Reduced Foods [2]	
Carbohydrates/Sugars* *Modify Intake based on targets of <50 net CHO g/day KD Or Up to 130 g CHO/day for Low CHO	Fruits (almost all apart from those listed above) Grains (e.g. rice, wheat, corn, oats) Grain-based foods (e.g. cereal, bread, oatmeal, pasta, crackers) Starchy vegetables (e.g. potatoes, corn) Sweetened dairy products (e.g. fruit yogurts, flavored milk products) Sweetened desserts (e.g. gelatins, puddings, cakes) Legumes (e.g. kidney beans, black beans, lentils) Natural sweeteners (e.g. sugar, maple syrup, jam, etc.) Condiments (e.g. ketchup, relish, sweet mustards, sauces) Cow's milk, low fat yogurts Use of medium chain triglyceride (MCT) oil is not warranted or recommended.[2] Most full CHO beers/wine (all alcohol not listed above) Drinks with sugar sweetened mixes

We want to acknowledge that some of the terminology used in describing TCR especially if the terms 'keto'/'Low CHO diet' are used can be problematic (i.e. use of term such as 'restricted'/'allowed foods'), however this regime is therapeutic & prescriptive and requires a sensitive approach when discussing with individuals.

Sample Meal Plans

The following section offer some sample meal plans. (Note: an increase of CHO to meet "Low CHO "diet levels would allow for increased variety and inclusion of limited quantities of whole wheat grains, fruit and/or beans/legumes.)

Breakfast: Cheese/vegetable omelet with 2 eggs + bit of cream, cooked in oil/butter
Snack: Full fat plain yogurt + nuts
Lunch: Chicken burger with lettuce 'bun' + veggies and dip (fat based: avocado/mayo/cream/olive oil, etc.)
Snack: Smoothie with plain soy beverage, greens powder, almond butter, oil/cream, 1-2 strawberries
Supper: 3 oz. fish, cucumbers/tomatoes, liberally drizzled in dressing (olive oil/mayo/canola/avocado based)
Snack: nuts (1 oz.), 1/10 of an orange OR Peanut butter balls, with added fat

Breakfast: Scrambled eggs in butter/olive oil on a bed of lettuce topped with avocado
Snack: Sunflower seeds
Lunch: Spinach salad with grilled salmon
Snack: Celery and pepper strips dipped in guacamole
Dinner: Pork chop with cauliflower mash and red cabbage slaw

Breakfast: Bulletproof coffee (made with butter and coconut oil, very popular in lay material but not necessary. Though added fat intake would likely be required to ensure adequate daily calories with this example), hard-boiled eggs & salsa
Snack: nuts + ¼ c berries
Lunch: Tuna salad stuffed in tomatoes
Snack: Roast beef and sliced cheese roll-ups
Dinner: Meatballs on zucchini noodles, topped with cream sauce

Nutrients of Concern

It is important to note that while a nutritionally adequate very low CHO intervention can be attained, it requires careful attention to several nutrients. If this is implemented in hypocaloric conditions designed for weight loss, it will be challenging to meet daily dietary reference intakes (DRIs) for many nutrients. [58] This is not unique to TCR, as this applies to any energy restricted eating style, and likely requires assessment for nutritional adequacy and supplementation.

If a TCR is implemented in hypocaloric conditions designed for weight loss, it will be challenging to meet daily dietary reference intakes (DRIs).

Saturated Fat

It is important to note that there is a lack of long-term research investigations into outcomes of following a KD diet indefinitely. However, much of the short-term research reports no increase in cardiovascular disease (CVD) risk markers using TCR and there is some evidence that it may lower some risk factors. TGs and HDL are consistently improved on TCR despite higher levels of saturated fat (SFA)[47]. LDL levels may increase slightly, but it is believed this increase is related to the larger, less dense lipoprotein particles. [10] Post-prandial hyperglycemia and elevated HbA1C are also known independent CVD risk factors[48,49] which can be mitigated with TCR. Given elevated CVD risk and its associated morbidity and death in people with diabetes, this evidence warrants consideration and a potential shift from the traditional practice of implementing diets with macro distributions consisting of higher carbohydrate/lower fat intake. A suggested approach is to optimize fat intake from a variety of whole foods with a variety of FA profiles. (See CVD & TCR pg. 19)

0mega-6:0mega-3 Ratio

There is consistent discussion in much of the lay literature to avoid margarines and other seed oils, and the processed foods made with them. One reason often touted stems from several mechanistic studies, suggesting there are inflammatory properties of these oils and that they may be implicated in the pathogenesis of other chronic illness related to inflammation (cancer, CVD, DM, fibromyalgia and other autoimmune conditions).[50] Consuming excessive 0-6 FAs is postulated to contribute to the increased deposition of arachidonic acid (which is a substrate for the syntheses of proinflammatory molecules) in adipose tissue and platelets, that has seemingly paralleled the increase in the prevalence of diabetes, obesity, and consumption of ultra-processed foods,[106,111,112] and could be mitigated if dietary LA intake was reduced.[113] However, high quality human trials that clearly define this and examine these effects in the context of dietary CHO have not yet been conducted and it remains an area of debate. On the contrary, there are a couple studies showing some improvement in insulin sensitivity and abdominal/hepatic fat storage when SFAs are replaced with 0-6PUFAs, and in states of overfeeding, that excessive SFA increases organ fat deposition, more than excessive 0-6 FAs, in lean and overweight individuals [114-117]

PUFA oils are chemically less stable than SFA and prone to oxidation under certain conditions such as extended shelf life and heating, causing adverse health effects though, again, results are contradictory and repeated high quality human studies are lacking. Studies showed potential increases in the susceptibility for oxidative stress within the body compared to controls, increasing risk of accelerated atheroschlerosis.[109,110] This was shown to be further exaggerated in diabetic subjects with poor glycemic control compared with non-diabetic patients or diabetic subjects with good glycemic control.[108] It may be prudent to use more stable oils richer in saturated/monounsaturated FAS for cooking under high heat, such as extra virgin olive oil, coconut oil, clarified butter, pressed rapeseed oil or other high oleic acid oils (modified sunflower, canola, soybean, etc.) which resist oxidation when heated.

Historically, the human diet was relatively rich in omega-3 compared to today's typical North American diet, and the suggestion to limit seed oils is also intended to limit the intake of omega-6 PUFAs to maintain an optimal omega-6: omega-3 ratio. The average ratio of 0-6 to 0-3 fatty acids has increased from as little as 1:1 to as much as 30:1[105]. For many years, the emphasis has been on reducing saturated fat (based on existing nutritional guidelines to limit the SFA to <10% of TE). Consequently, there has been an increase in dietary intake of lower fat products, products emphasizing vegetable/seed based PUFAs (rich in 0-6 linoleic acid) and highly processed food, which has required increased vigilance to ensure adequate intake of other, less abundant, essential fatty acids.[50,107] Higher consumption of Omega-6 FA oils may limit the availability of omega-3 fatty acids in vivo and upsets the metabolic balance in the body.[106] This depletes an important defense agent in the prevention of cardiovascular disease (CVD).

The high fat content of TCR, with an emphasis on whole foods, minimizes these risks, as the nature of this intervention limits many of the 0-6 rich, highly processed, high CHO foods, and emphasises foods that contain both linoleic acid in addition to the full spectrum of other healthy fats from foods such as nuts, seeds, olives, avocadoes, and oily fish. The types of foods recommended on TCR contain a rich spectrum of FAs and deficiency of EFAs is unlikely, but emphasis may be required to ensure an optimal 0-3:0-6 ratio.

Iron (Fe)

Iron deficiency is commonly reported on KD, and the etiology is undetermined[51]. Whether it is a pre-existing condition that is exacerbated, or a result of a very low CHO regime is yet to be determined, but there is some evidence that a high fat diet reduces Fe absorption (via hepcidin-independent reduction in duodenal absorption).[51] From an intake perspective, low CHO interventions can be challenging to meet recommended dietary allowances (RDAs) for Fe given the absence of Fe fortified (typically carbohydrate rich) foods or individuals limiting animal protein sources. Fe bioavailability is also impacted by both dietary composition and baseline iron status.[59] Given the typical diet consumed using TCR is low in phytates, oxalates and polyphenols, compounds known to reduce bioavailability of dietary iron, it is possible that this diet may have a higher iron bioavailability factor[52]. Low iron intake can be a concern in some individuals and warrants dietary assessment and/or lab assessment of status if indicated, for adequacy and any need for supplementation.

Potassium: Sodium Ratio (K^+: Na ratio)

The ideal K^+: Na ratio is a highly discussed topic in the research, in the development of national nutritional guidelines, and in lay promoters of 'keto' diets. When CHO intake is extremely restricted and insulin levels

are low, increased sodium is excreted in urine and causes disruptions in other electrolytes resulting in "keto" flu-like symptoms, described earlier. These symptoms are usually short-lived and resolve over the course of several days but replenishing lost Na can be helpful. Canadian diets are often excessive in dietary Na intake and relatively low in K+ intake which can be a significant driver of poor health, associated with a greater risk of CVD, cancer, osteoporosis, kidney disease and other pathologies, leading to them being declared micronutrients of public health concern.[53,54] Current adequate intakes (AIs) for K+/Na/ (4700 /1200-1500 mg, respectively) would suggest a dietary K^+/Na ratio of 3-4:1. TCR interventions are often low in K^+ due to the restrictions of whole grains and fruit/vegetables and are often much higher in sodium, leading to a K^+/Na ratio <1.0 (vs. ancestral diets that were likely >5.0).[53,59] With careful attention to emphasizing a diet high in 'low CHO' vegetables, this can be optimized.

Clients with certain medical conditions such as hypertension, kidney disease, or congestive heart failure require close monitoring of blood pressure and liberalizing Na intake for individuals on restricted Na diets may be required to avoid hypotension. When carbohydrate intake is extremely low, levels of electrolytes, especially Na, can drop.

Bone health is often cited as a risk for a diet that promotes net metabolic acidosis, is high in sodium, and is without adequate alkaline residue (potassium bicarbonate) from vegetables, [53] however the Virta group has released their 2 year clinical trial outcomes of a KD in a T2DM subject group and found no changes in spinal BMD.[75] For individuals who choose this diet long-term, monitoring BMD is recommended, and perhaps a moderated, low CHO diet may be indicated if unexpected declines in BMD are measured.

When carbohydrate intake is extremely low, levels of electrolytes, especially sodium, can drop.

Nutrients at Risk of Inadequate Intake

There are nutrients at risk of inadequate intake for individuals using TCR. The following table itemizes the nutrients at risk and food sources to encourage.[35,51,53] (Table 18)

Table 18: Nutrients at Risk of Inadequate Intake

Nutrient	RDA or AI* (Adult, F/M)	Symptom of Deficiency	Food Sources
Sodium	1500mg AI- 2300mg UL *Note: low CHO diets may require increased Na intake >3000 mg	Fatigue Weakness Headaches Difficulty concentrating	Be liberal with saltshaker or add 1-2c broth/day -avoid highly processed, high sodium meats/excessive cheese
Potassium	4700 mg AI	Muscle cramps/twitches Heart palpitations/increased awareness of heartbeat	Tomatoes/tomato products, broccoli, chard, pumpkin, Brussel sprouts, tofu, nuts, seeds, cheese, avocado, mushrooms
Magnesium	320/420 mg	Muscle cramping/twitching at night or after exercise	Hemp, pumpkin seeds, chia, avocado, fish & meat, almonds, leafy greens, dark chocolate
Calcium	F 19-50y 1000mg F >50y 1200mg M 19-70 1000mg M >70 1200mg	Physical symptoms rare, special considerations may be needed in those with CKD, parathyroid dysfunction, Mg & Vitamin D deficiency	Cheese, almond milk, high fat plain Greek yogurt, plain cottage cheese, canned sardines/salmon with bones, tofu set with calcium sulphate, tahini, dark leafy greens (collards, chard, kale, turnip greens), chia seeds
Phosphorus	700/700 mg	Rare- loss of appetite, muscle weakness, numbness in extremities	Meat, fish, nuts & seeds, tofu, tempeh, eggs, cheese, Greek yogurt, cottage cheese
B Vitamins Thiamin Riboflavin Niacin B6	 1.1/1.2 mg 1.1/1.3 mg 14/16 mg F 19-50y 1.3mg F >50y 1.5mg M 14-50y 1.3 mg M > 50y 1.7 mg	Sore throat, redness and swelling of the mouth and throat, cheilosis, angular stomatitis, magenta tongue, and seborrheic dermatitis Neuropathy, peripheral weakness, rapid heart rate, edema, exacerbates CHF Dermatitis, diarrhea	Meat, fish, nuts, seeds, clams, eggs, cheese, mushrooms, leafy greens/broccoli, beans/legumes (if able to include beans/legumes while still meeting CHO targets *Whole grains and fortified processed grains are typical sources in conventional diet
Vitamin C	75/90 mg	Bleeding, poor wound closure, bruising easily, hair/ tooth loss, joint pain and swelling	Artichokes, asparagus, Bok choy, broccoli, Brussel sprouts, peppers, strawberries
Iron	18/8 mg (M+ menopausal F)	Anemia, fatigue, rapid HR	Meat, fish, eggs, tofu, leafy greens
Fibre	21/30 mg	Altered GI function	Low CHO vegetables, nuts & seeds, ground flax, chia seeds, hemp hearts

*Based on Health Canada DRIs https://www.canada.ca/en/health-canada/services/food-nutrition/healthy-eating/dietary-reference-intakes/tables.html

Sweeteners and Soluble Fibre

Emphasizing a whole foods approach is optimal when TCR is implemented. However, the issue of sweeteners and impact of added soluble fibres to many of the processed foods marketed as "low CHO/keto" should be addressed, as these ingredients can have an impact on the ability of the body to maintain ketosis, can impact blood sugar, and may be sought out by clients looking to replace traditional higher CHO 'treats'.

Generally, sweeteners are divided into 3 classes (see Table 19): natural, sugar alcohols and artificial. All sweeteners can maintain cravings for sweet foods in some people as they trigger the same neural reward pathways that are activated by sugar.[61] Advising clients to limit their use during the initial phases of introducing a KD can be helpful. The best sweeteners are the ones with little impact on blood sugar or insulin levels and contain no CHO or energy. Monk fruit, erythritol and Stevia are the 3 sweeteners most touted as "keto-friendly". (See Table 19)

There are an incredible number of highly processed "health foods" on the market, many marketed to consumers implementing TCR. Generally, net CHO is used to calculate intake and thus products made with added soluble fibres can market their products as "low CHO" because the fibre grams can be subtracted from total CHO grams. However, added soluble fibres (also referred to as 'functional fibre' according to the IOM definition) do not act the same as naturally occurring soluble fibre (intrinsic and intact fibre in original food matrix), and some, or all, of that soluble fibre, may unexpectedly be impacting BG or the ability to maintain ketosis. Some of these same products also contain sugar alcohols which can also contribute CHO and kcal.

Soluble fibre is used for texture and added sweetness and comes in many forms: beta-glucan, gums, pectins, mucilages, cellulose, psyllium husk and some hemicelluloses with many other novel non-digestible carbohydrates pending approval by the FDA as dietary fibre (it has allowed manufacturers to include them under fibre on labels while pending formal approval (chicory root/inulin, alginate, high-amylose starch, resistant malto-dextrin, etc.).[62,63,64] Soluble fibre contributes calories as it is digested by gut bacteria and forms short-chained fatty acids which are in turn used by the body for energy.[68]

Table 19: Sweeteners by Class, Impact on BG/Insulin and Kcal/g[65]

Natural Sweeteners- usually used as tabletop sweeteners, not in manufactured foods, found from extracted compounds from edible plants. No significant metabolism and not typically fermented in gut but some may experience gas/cramping/bloating and may impact gut flora.				
	Impact on BG/insulin	Glycemic Index	Kcal/g	Notes
Steviols	Low	0	0	250-300x sweetness of sugar, often combined with erythritol e.g. Truvia, Stevia
Monk Fruit (Luo han guo)	Low	0	0	100-250x sweetness of sugar, often combined with other products (xylitol, erythritol)
Allulose	Low	0	0	70% sweetness of sugar, monosaccharide found in raisins, jackfruit, figs, maple syrup. Not yet approved in Canada

Tagatose	Low-moderate	3	2	92% sweetness of sugar, hexose monosaccharides (hydrolyzation of lactose, then further from isomerized galactose), found in dairy, cocoa, some fruit
Polyols/Hydrogenated Starch Hydrolysates (HSH) - HSH are source of sugar alcohols but also used themselves as product stabilizers, often a blend of sugar alcohols and higher polysaccharides, usually as a mixture of sorbitol & maltitol. When they exist in products as a mixture, the term HSH is used on a label but if it is largely one type then the individual polyol name is used (i.e. sorbitol or maltitol syrup). These compounds have prebiotic & osmotic laxative properties (but are not soluble fibres), are fermented in large intestine, and can cause gas/bloating/diarrhea/cramping. [65]				
	Impact on BG/Insulin	**Glycemic Index**	**Kcal/g**	**Commonly found in:**
Xylitol	Low	12	3.0	Chewing gum, toothpaste, candy
Sorbitol Sorbitol Syrup	Yes	4-9	2.6 3.0	Beverages, dairy products, baked goods, candy. Sorbitol syrup often contains mannitol or polyglycitol syrup (HSH)
Mannitol	Low	2	1.6	Chewing gum, chocolate coatings, protein powders, beverages
Maltitol Maltitol Syrup	Yes	35 52	3.0 3.0	Baked goods, bulk sweetener
Lactitol	Low	3-6	2.0	Cookies, ice cream, chocolate
Isomalt	Yes	2-9	2.0	Hard candies, bulk sweetener
Erythritol	No	1	0.2	Ubiquitous in 'diet' products, from fermented corn
Artificial Sweeteners				
	Impact on BG/Insulin	**Glycemic Index**	**Kcal/g**	
Sucralose	Yes	Variable, up to 80 in Splenda (0 If Pure liquid)	0	600x sweeter, products often contain maltodextrins/dextrose and can affect ketosis and BG
Saccharin	No	0	0	Theoretically 0 kcal/g however individuals report impacts on BG
Aspartame	No	0	0	Neotame- aspartame analogue (Nutrasweet)

Net CHO vs Total CHO - Subtract total fibre or only insoluble fibre?

There is no definitive 'right' or 'wrong' method to calculating CHO intake and expert opinions vary and no trials that have addressed this question. It depends on individual goals, the level of CHO restriction trying to be achieved, and how they metabolically respond to dietary fibre. When whole foods make up most of one's diet, subtracting total fibre, and using net CHO is often the preferred method, as the fermentation of whole food soluble fibre, is not thought to affect BG, and usually constitutes no more than approximately 30% of the total fibre. This approach encourages the consumption of plenty of vegetables which may have some carbohydrate content, from fibre, but also provide many other phytonutrients that have health benefits, provide volume/bulk to the diet, and increase satiety.

However, when clients are using processed food products containing added isolated fibre compounds and sugar alcohols, it becomes more complicated, and some would argue that using total CHO or including at least some of the fibre when calculating CHO intake would be more accurate. Some of the novel fibres used in food processing may have an impact on blood sugar in addition to the intestinal fermentation of soluble fibre that produces SFAs, inducing intestinal gluconeogenesis and theoretically increasing BG. Though, recent research suggests this process may, in fact, limit hepatic gluconeogenesis and therefore decrease BG, regulate lipids,[66] and stimulate hormones involved in satiety.[67] It may depend on the fibre in question, the degree of processing of the food, and individual metabolic responses to these ingredients. Heating, grinding, milling of carbohydrate containing foods and preparations of novel fibres, alters the impact of these foods on BG and insulin from their whole food state. Nut flours and butters commonly used as substitutes for grain-based flours may have a higher glycemic response in ground form than their whole nut form so using net CHO in this situation may underestimate the CHO load (and lipid absorption).[73]

Food manufacturers add fibre to food products to make the total dietary fibre appear high, to have net CHO appear low, while creating more palatable, calorie dense foods. Soluble fibre has many benefits that remain when used in a more processed food form (i.e. delayed gastric emptying, lipid metabolism, gut microbiome, etc.) but not all novel fibre ingredients have the same benefit of blunting insulin and glycemic response that they exert in their whole food matrix form. [69,70,71,72]

When counselling clients, encountering ultra-processed foods labelled as: “no added sugar”, “high fibre”, “prebiotics” and “low net carbohydrates”, which are ubiquitous in the current food supply, ensure to provide education around the potential contribution of carbohydrates from sugar alcohols and added soluble fibre (particularly isomalto-oligosaccharides (IMOs), which the FDA has mandated be included as CHO, not fibre, as of 2021 but may still appear as fibre until enforced). Individuals should be advised to monitor BG and ketones (if the goal is maintaining a state of ketosis and/or BG control) to assess responses to these products, as individual metabolic behaviour varies, and will dictate how they may choose to count fibre when calculating CHO levels from processed, ‘low’ CHO foods.

Table 20: Considerations in calculating dietary CHO Intake

Summary: Sugar Alcohols & Soluble Fibre
• Can affect BG levels and impact CHO intake • Generally, contain 50% kcal of regular sugar • May or may not appear on nutrition label • Naturally occurring but also manufactured • Used in “sugar free”, “no added sugar”, “keto/low CHO” products • Generally accepted 2 kcal/g • Count ½ grams sugar alcohols as CHO (exception: if erythritol is the only sugar alcohol listed then subtract all the grams of sugar alcohol from the CHO content) • Consider counting ¼ to ½ grams **total** fibre as CHO, if calculating net CHO, **in processed foods with added fibre** until individual responses can be ascertained or where clients experience unexpected elevated glycemic responses from “low CHO” products

Transition from KD to Increased CHO Intake in Clients with T2DM

Most research suggests following a strict TCR until the desired clinical outcomes have been achieved (i.e., improved glycemic control, medication reduction, weight loss, etc.) at which point transitioning to a more liberalized carbohydrate intake is often possible. There is no long-term evidence of TCR outcomes and adherence to the diet may be challenging for some, however, there is evidence suggesting diabetes outcomes may remain optimized on a reduced CHO (<130 gm),[13] whole food diet, and that it may not be necessary to follow a strict TCR long-term to maintain these goals. This transition should occur over the course of 2 weeks, with slow increases in CHOs (emphasizing unprocessed CHOs as much as possible) to liberalized targets (not necessarily back to typical average intakes as evidence suggests intakes should remain <40% TEE to maintain potential benefits).[13] The indication of a client's carbohydrate tolerance is the level required to maintain glycemic control/weight stability.[44] Weight regain is always a concern when implementing a regime targeted for weight loss specifically and individuals should be offered support during this maintenance period to mitigate this potential.

Summary

There is existing and emerging evidence to warrant the use of TCR as medical nutrition therapy in the management of T2DM. This intervention encompasses a spectrum of CHO restriction/reduction, based on individual assessments, and can be adapted to increase palatability, adherence/sustainability, and address nutritional adequacy and client preferences (i.e. vegetarian, lactose free, etc.). TCR necessitates close monitoring to make appropriate adjustments to medications, to optimize blood glucose management and to ensure nutritional adequacy. Regular re-assessment to individualize MNT and support individuals who are interested in this approach to manage their DM is required. This regime is included as a strategy (among several others) by Diabetes Canada in the management of diabetes and warrants consideration in consultation with our clients.[21]

While there is much controversy of the appropriateness of TCR in the T1DM population, there is evidence of increased diabetes control, less BG variability, reduced insulin requirements, and a significant community, of families and adult clients with T1DM, use this regime and are seeking support.[29] This requires a highly invested client/family who are on board to engage in the required monitoring. Great caution is warranted in the pediatric population where the balance of decision-making may lie with caregivers who need to be informed of pros/cons and be prepared for the necessary support required.

Additional resources:

- Clinical Guidelines for the Prescription of Carbohydrate Restriction as a Therapeutic Intervention https://www.lowcarbusa.org/standard-of-care/clinical-guidelines/
- Matthew's Friends https://www.matthewsfriends.org/
- Charlie Foundation https://charliefoundation.org/
- Virta Health www.virtahealth.com
- Ketogenic Diet Resource https://www.ketogenic-diet-resource.com/about.html- evidence, meal plans, shopping lists, etc.
- Diet Doctor https://www.dietdoctor.com/
- The Low Carb Healthy Fat Dietitian www.lchf-rd.com
- Type 1DM www.diatribe.org, https://www.facebook.com/Type1Grit/ www.asweetlife.com
- Dr Richard Bernstein's Diabetes Solution- The Complete Guide to Achieving Normal Blood Sugars (book, T1DM focus)
- Adam Brown's book: Bright Spots & Landmines: The Diabetes Guide I wish Someone Had Handed Me (T1DM focus)

Cookbook/Meal Plans/Recipe Ideas

- The Art and Science of Low Carbohydrate Living by Jeff S. Volek, PhD, RD & Stephen D. Phinney, MD, PhD
- https://www.everydayhealth.com/diet-nutrition/ketogenic-diet/comprehensive-ketogenic-diet-food-list-follow/
- Keto: The Complete Guide to Success on the Ketogenic Diet, Including Simplified Science and No-Cook Meal Plans by Maria Emmerich and Craig Emmerich
- The Easy 5-Ingredient Ketogenic Diet Cookbook: Low-Carb, High-Fat Recipes for Busy People on the Keto Diet by Jen Fisch
- Simply Keto: A Practical Approach to Health & Weight Loss, With 100+ Easy Low-Carb Recipes by Suzanne Ryan
- The Keto Diet: The Complete Guide to a High-Fat Diet, With More Than 125 Delectable Recipes and 5 Meal Plans to Shed Weight, Heal Your Body, and Regain Confidence by Leanne Vogel
- The Complete Ketogenic Diet for Beginners: Your Essential Guide to Living the Keto Lifestyle by Amy Ramos
- The Keto Reset Diet: Reboot Your Metabolism in 21 Days and Burn Fat Forever by Mark Sisson and Brad Kearns
- The Ketogenic Diet: A Scientifically Proven Approach to Fast, Healthy Weight Loss by Kristen Mancinelli
- Ketogenic Diet: The Step by Step Guide for Beginners: Ketogenic Diet for Beginners: Optimal Path for Weight Loss by Jamie Ken Moore
- Ketogenic Diet Cookbook: 500 Ketogenic Diet Recipes to Cook at Home by Emily Willis
- The Keto Crock Pot Cookbook: Quick and Easy Ketogenic Crock Pot Recipes for Smart People by Loretta Wagner (From Everyday Health)

Apps:

Carb Manager	Cronometer	LowCarb	Senza
Calorie, Carb & Fat Counter	KetoDiet	MyFitnessPal	8Fit
	Keto	MyMacros+	

Appendix 1: Summary Table of Position Statements of Various Organizations (in chronological order)

Organization	Yr	Recommendations/Comments
Diabetes Canada[21]	2020	For T1DM- a low CHO or very low CHO diet can have significant improvements in outcomes (A1C, reduced insulin requirements, weight management and less glucose variability) have been reported, very few studies investigating long-term effectiveness/safety, very little reliable data and evidence gaps make it difficult to make general recommendations. For T2DM- a low CHO diet may be effective for weight loss, DM control, reduction in need for antihyperglycemic therapies. Very low CHO diets may be superior to higher CHO diets for improving glycemic control and body weight. Current data makes it unable to determine whether the benefits of a very low CHO diet (on weight loss & A1C) are specific to macronutrient composition or associated differences in calorie intake. Several methodological limitations exist in published literature.
RSSDI (Research Society for the Study of Diabetes in India)[15]	2020	Extreme diets including KD must be planned and executed following consultation with physician and a Registered Dietitian, and for a short period.
Italian Society of Endocrinology[16]	2019	**Recommendations Specific to Insulin Resistance, T2DM:** • Very-low calorie ketogenic diets (VLCKD) should be considered to obtain an early efficacy on glycemic control, particularly in obese patients with short duration of the disease. **[Strong recommendation, Moderate quality evidence]** • VLCKD should be considered to reduce the use of glucose-lowering agents, including insulin. **[Strong recommendation, Moderate quality evidence]** **Recommendations Specific to Severe Obesity:** • Maximum 12-week weight-loss program with VLCKD as part of a multidisciplinary weight management strategy to adult severely (class 2 or higher) obese patients not responsive to standardized diet as a second line option. **[Strong recommendation, Moderate quality evidence]** • Maximum 12-week VLCKD treatment as part of a multidisciplinary weight management strategy for obese patients who have a clinically assessed need to lose weight rapidly. **[Strong recommendation, Moderate quality evidence]** • We suggest the use of a weight-loss program with VLCKD in intermittently combination with low-calorie dietary approaches for severely obese patients. **[Weak recommendation, Very low quality evidence]** • We recommend a long-term weight-loss maintenance follow-up after VLCKD in severely obese patients. **[Strong recommendation, Moderate quality evidence]**
National Lipid Association[17]	2019	There should be a clinician-patient discussion regarding need for and oversight of KD before initiation. KD may be an option for a short-term initial weight loss period (2–6 months).[17]
American Diabetes Association (ADA)	2019	Reducing overall CHO intake with DM has demonstrated the most evidence for improving glycemia. For select adults with T2DM (not meeting targets or with priority of medication reduction), reducing overall CHO intake with very low CHO eating plans is a viable approach. A low CHO diet is deemed MNT for the treatment of T2DM in adults. Approves a diet <26% TE/<130 g CHO.[18]
	2018	While some studies have shown modest benefits of KD (<50g CHO/day), this approach may only be appropriate for short-term (up to 3–4 months). There is little long-term research citing benefits or harm.[19] There is no single ideal dietary distribution of calories among CHO, fats, and proteins for people with DM. A low CHO diet is deemed MNT for the treatment of T2DM in adults. Approves a diet <26% TE/<130 g CHO.[13]

		[Grade E Evidence: Expert consensus or clinical experience][19]
ADA & EASD[14]	2018	There is no single ratio of CHO, protein and fat intake that is optimal for every person with T2DM. Instead, there are many good options. Low CHO diets (<26% total energy) produce substantial reductions in A1C at 3-6 months with diminishing effects at 12-24 months.[14]
Diabetes Australia[20]	2018	For T2DM, in the short term (up to 6 months), lower CHO eating can help with management. This benefit is no longer evident after 12 months.[20]
Diabetes UK	2017	No consistent robust evidence to recommend the ideal carb amounts for everyone with DM.[22]
Society for Endo, Met & DM of South Africa	2017	There is no ideal percentage of calories from CHO. Macronutrient distribution must be individualized and guided by glycemic control.[23]
Scottish Intercollegiate Guidelines Network[24]	2017	Those with T2DM can be given dietary choices for achieving weight loss that may also improve glycemic control. Options include restricting the total amount of dietary CHO (a minimum of 50g/d appears safe for up to 6 months).[24]

Appendix 2: Summary Table of Alternative Targets to LDL

***References for this appendix are listed below chart**

The 2021 Canadian Cardiovascular Society Guidelines for the Management of Dyslipidemia for the Prevention of Cardiovascular Disease in Adults remain the most current CPGs to assess CVD risk, and they have been updated to include a recommendation to measure Lipoprotein(a) once in a patient's lifetime, as part of initial lipid screening to assess cardiovascular risk.[7] Additionally, for any patient with triglycerides >1.5 mmol/L, either non-high-density lipoprotein cholesterol or apolipoprotein B are the preferred lipid parameter for screening, rather than LDL-c.[7] In the context of existing cardiometabolic dysfunction (PreDM/T2DM) including other parameters (see below) may offer additional context where evidence suggests that the concentration of lipoproteins particles may be superior to measuring their lipid content concentrations.[6]

Parameter	Notes
TG : HDL	Has been shown to have strongest association with the extent of coronary disease, proxy for indicating less of the small dense LDL-P, and as potent a predictor of CVD risk as HTN. [1,2] Cut-off criteria varies but the higher the ratio the higher the risk, monitoring changes in this can reflect impact of a Low CHO/KD intervention: - ratio <3.8 often used as cut-off where values greater than this indicates a person with a Phenotype B (high risk) lipid profile and a ratio <3.8 reflects Phenotype A (less risk) [1] - ratio >3.0 indicates insulin resistance which is associated with worse CVD outcomes than other lipid metrics, including LDL [3] - ratio < 3.0 indicates insulin sensitivity and lower CVD risk
TC : HDL	Use when elevated TGs prevent an assessment of LDL[4]
ApoB : ApoA-1	ApoB represents the # of IDL & LDL cholesterol particles (not the density), HDL carries an ApoA-1, the higher the ratio the larger amount of atherogenic molecules circulating and is a better predictor of risk.[4] ApoB may be a better measure of circulating LDL particles (LDL-p) concentration and more reliable indicator of risk than LDL-c and is an area of debate in development of updated CPGs. Ratio target[4]: <0.9 M, < 0.8 F Primary Prevention <0.7 M, <0.6 F Secondary Prevention Assessing changes in apoB can also reflect decreasing numbers of smaller dense atherogenic LDL vs larger beneficial LDL in cases where total LDL-c appears to have remained the same or increased.
Non-HDL & ApoB	Considered equal markers of total atherogenic LPs and lipid related CV risk[7]. Better indicators of CVD risk in those with metabolic dysfunction[5t] Non HDL Target: <5.8 mmol/L(FRS <20%), < 4.2 mmol/L (FRS 10-19.9%) apoB Target: <1.45 mmol/L (if FRS <10%), <1.05 mmol/L(FRS 10-19.9%)

	*DM is a statin indicated condition and thresholds for treatment are lower for add-on therapy (if apoB >0.8 g/L or non-HDL-c>2.6 mmol/L *and on a statin*, warrants increased tx, based on 2021 CCS CPGs) **ApoB is an insured lab test in all provinces except Ontario
TG	Elevated TGs are independent risk factors for CVD, independent of LDL and not addressed with statin use[5] Target <1.5 mmol/L
HDL	Low HDL is an independent risk factor for CVD independent of LDL and not addressed with statin use[5]
hsCRP	Target <2.0 mg/L
Lp(a)	Target <50 mg/dl (or <100 nmol/L), should be done at least once in baseline lipid screening [7]
Coronary Artery Calcium (CAC score)	Provides direct evidence of atherosclerotic plaque. Not uniformly available or funded across Canada. Screen via CT in asymptomatic adults >40y with FRS 10-20%, for whom treatment decisions are uncertain [7]
Insulin Resistance Index (Homeostatic Model Assessment for Insulin Resistance HOMA-IR)	HOMA-IR = (fasting insulin [µlU/ml] x fasting glucose [mmol/L]) / 22.5 Calculation requires US standard units Insulin: pmol/L to uIU/mL, divide by (÷) 6.945 Glucose: mmol/L to mg/dL, multiply by (x) 18 Reference Ranges[8,9,10,11]: <1.0- insulin sensitive 1-1.4 normal range (some references go up to 1.9) >1.4- 1.9 indicates insulin resistance and may see early dysglycemia >2.0 indicate significant insulin resistance, NAFLD, T2DM

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