

**From:** [James Muecke](#)  
**To:** [Committee\\_Health \(REPS\)](#)  
**Cc:** [Freelandor, Mike \(MP\); James Muecke](#)  
**Subject:** guideline document for therapeutic carbohydrate reduction for Inquiry into Diabetes  
**Date:** Monday, 20 November 2023 12:27:41 PM  
**Attachments:** [Management of Type 2 Diabetes with Therapeutic Carbohydrate Restriction Draft for Consultation final.docx](#)

---

Dear Committee,

As requested on Friday, I've attached the guideline document for therapeutic carbohydrate reduction for people with type 2 diabetes. It has recently been endorsed by Australian Diabetes Society.

This incredible opportunity needs to be embedded in under- and post-graduate training of all health practitioners involved in the management of type 2 diabetes.

Best wishes

James

# **Managing Type 2 Diabetes with Therapeutic Carbohydrate Reduction (TCR)**

Stephen N. Stranks, MBBS, FRACP, PhD - Southern Adelaide Diabetes and Endocrine Services, Oaklands Park South Australia 5046

Laureen Lawlor-Smith, BMBS, FRACGP - Specialist Clinics at Blackwood Hospital, Belair, South Australia 5052

## **Purpose of this Document**

Diabetes Australia, the American Diabetes Association, the European Association for the Study of Diabetes and Diabetes UK all now recognise therapeutic carbohydrate reduction (TCR) as one of a number of options for the management and potential remission of type 2 diabetes (T2D) [1-4]. This document is designed to aid medical management of individuals who have decided to undertake TCR. It is not designed to argue the relative merits of one dietary approach over another.

## **Executive Summary**

1. Meaningful clinical benefits, including weight loss, improvement in glycaemic control and possible remission, reduction in the need for glucose lowering medications and reduction in blood pressure can be achieved by treating T2D with TCR.
2. People with T2D should be given realistic expectations of their chances of success with this approach and the education and support to keep them safe and help them achieve their goals.
- 3a. People with T2D should be monitored regularly while utilising TCR to assess the need for alteration to glucose and blood pressure lowering medications to avoid complications such as hypoglycaemia, hypotension and ketoacidosis.
- 3b. Management may include pre-emptive and step-wise reduction of glucose and blood pressure lowering medications but some therapies may need to be continued for their non-glycaemic effects.

## **Introduction**

A low carbohydrate diet (LCD) is defined as one in which less than 26% of calories are derived from carbohydrate or has less than 130 grams per day of carbohydrates [1]. A very low carbohydrate ketogenic diet (VLCKD) is one in which less than 10% of its calories are derived from carbohydrates or has between 20 and 50 grams per day of carbohydrates [1]. Therapeutic Carbohydrate Reduction (TCR) is a term describing all interventions which reduce carbohydrate intake to less than 130 grams per day and includes both LCDs and VLCKDs.

Several systematic reviews and meta-analyses of well controlled trials suggest meaningful short term clinical benefits of TCR in T2D when compared to traditional higher carbohydrate diets. Relative benefits include improved satiety [5] more rapid weight loss, improvement in glycaemic control and a reduction in the need for diabetes medications [6-11]. Additionally, TCR is associated with significant reductions in both blood pressure and liver enzymes [12-14].

Goals of TCR in T2D may be improved glycaemic control, weight loss, reduction in glucose and blood pressure lowering therapies, T2D remission or a combination of the above. Diabetes remission is defined as a return of HbA1c to less than 6.5% that persists for at least three months in the absence of glucose-lowering pharmacotherapy [15]. TCR can be effective in producing T2D remission in the short to medium term. However, evidence of effectiveness from well controlled trials beyond 2 years is still limited [16].

TCR can most readily be achieved by the elimination of processed foods and sugary drinks, including fruit juice, and by focussing on the consumption of whole, natural, low carbohydrate foods.

Many of the issues covered in this document do not have evidence from high quality scientific studies on which to base recommendations. Where not specifically referenced, the recommendations are made on the basis of expert opinion.

## **Clinical Considerations**

Absolute contraindications to TCR are end stage liver failure, generally with cirrhosis and risk of encephalopathy [17] and rare inborn errors of fat or ketone metabolism [18]. Relative contra-indications include type 1 diabetes (T1D), insulin deficient T2D, T3cD (primary pancreatic disease such as pancreatitis generally resulting in insulin deficiency), other forms of insulin deficient diabetes, sodium glucose cotransporter 2 inhibitor (SGLT2i) use, pregnancy, breastfeeding and eating disorders such as anorexia nervosa and bulimia.

TCR emphasises the optimal intake of dietary protein and healthy fat. This has prompted discussion about the use of this intervention in people with diabetes with pre-existing chronic kidney disease (CKD) [19]. The 2020 Kidney Disease Quality Outcomes Initiative (KDOQI) guidelines advise protein restriction for patients with CKD stage 3-5 with diabetes, not on dialysis, to 0.6-0.8 g/kg body weight to slow

progression. This is opinion-level guidance [20] and has been called into question [21, 22]. In people with renal function ranging from normal to stage 3 CKD (i.e., eGFR  $\geq 30$  mL/min/1.73 m<sup>2</sup>), TCR is associated with stable or improved renal function [23-28]. Whilst the impact of this dietary approach on kidney function in those with advanced CKD (CKD Stages 4 and 5) has not been established [28], the risk of malnutrition characterised by protein energy wasting when following the current standard recommended dietary approach is potentially significant [29].

## **Ensuring the correct diabetes classification**

It is important to ensure that a person with diabetes considering TCR has the correct classification of their diabetes. People initially labelled as having T2D may subsequently be found to have T1D or latent autoimmune diabetes in adults (LADA). Between five and ten percent of people initially diagnosed with T2D actually turn out to have T1D or LADA [30]. Although people with T1D and LADA can use TCR, remission is not possible and the risk/benefit ratio is potentially less advantageous. Screening for anti-GAD, IA2 and zinc transporter antibodies and measurement of paired C-peptide and glucose levels may be useful if there is uncertainty. C-peptide levels below or in the lower half of the “normal” range in the presence of hyperglycaemia indicate significant endogenous insulin deficiency. Some individuals with other forms of diabetes, particularly T3cD and longstanding T2D may also be quite insulin deficient and paired glucose and C-peptide levels to establish this may be useful in decision-making and management.

## **Management of Pharmacotherapy**

Healthcare professionals caring for a person with T2D who is significantly altering their diet must be competent in adjusting medications [31]. Pharmacotherapy adjustment may be required because the medication is no longer required, either at all or at the previous dose, or because it poses a significant safety risk in the context of TCR. A significant reduction in carbohydrate intake may lead to a reduction in the need for glucose lowering and possibly antihypertensive medication. Failure to appropriately adjust medication may lead to hypoglycaemia and/or hypotension. Furthermore, the combination of TCR with SGLT2i increases the risk of ketoacidosis which may be euglycaemic and not readily detected without specific ketone testing [32].

People with diabetes undertaking TCR should be made aware of the potential for either hyperglycaemia (if medications are reduced too aggressively or if dietary change is delayed or insufficiently strict) or hypoglycaemia (if medications, particularly insulin or sulphonylureas, are not reduced enough). People on insulin and/or SU require close blood glucose monitoring, either with finger prick capillary measurements 2-4 times/day or with continuous glucose monitoring (CGM). They should be reminded of the signs and symptoms of hypoglycaemia and should have an action plan in place to manage this if it does occur.

### **Biguanides**

Metformin is generally safe to continue with TCR [31].

## **Sulphonylureas**

SU medications carry a risk of hypoglycaemia [33] which is exacerbated in the context of reduced carbohydrate intake with TCR. SU should generally be ceased although this may not be possible immediately if baseline glycaemic control is suboptimal e.g. HbA1c >9% [31, 34].

## **Insulin**

Insulin doses need to be carefully adjusted to avoid both hyper and hypoglycaemia and glucose monitoring with capillary fingerprick at least 2-4 times/day or CGM is strongly recommended for optimal safety. If baseline HbA1c is less than 9%, the total insulin dose can initially be reduced by 30 – 50%. This, ideally, should be given purely as basal insulin. Reduced doses of rapid acting insulin can be prescribed to be used before or after meals but are usually not required. If baseline HbA1c is 9.0% or greater, no change or smaller reductions in total insulin dose will be advisable, at least initially. Further changes in insulin dose can generally then be made on the basis of blood glucose monitoring [31, 34]. Reduction or cessation of insulin should take into account ketoacidosis risk, particularly if the individual is insulin deficient, taking SGLT2i, fasting or acutely unwell. Every person with diabetes should have a sick-day management plan.

## **Sodium-Glucose Co-Transport 2 Inhibitors (SGLT2i)**

In people with T2D SGLT2i improve glycaemic control, reduce blood pressure and weight, non-fatal myocardial infarction, kidney failure, hospital admission for cardiac failure and may decrease cardiovascular and all-cause mortality [35]. It is thus important that the healthcare professional understands why SGLT2i therapy is being used and what risks may be incurred by its cessation. When used for glycaemic control alone the SGLT2i can generally be stopped pre-emptively with close monitoring of subsequent glucose control. However, in general, SGLT2i therapy should not be ceased if being used for established heart failure, atherosclerotic cardiovascular disease or CKD.

An approximate doubling in serum fasting ketone concentration has been observed after starting an SGLT2i, and this remains for several weeks at least [36]. For example, empagliflozin treatment increased fasting beta-hydroxybutyrate levels from 0.24 mmol/l to 0.56 mmol/l in people with T2D [37]. This compares to beta-hydroxybutyrate levels of 0.5 mmol/l to 3 mmol/l on a VLCKD [38].

The use of SGLT2i increases the risk of DKA which may be euglycaemic. This is a rare complication in T2D with an incidence of 0.6 to 2.2 per 1000 patient years [39]. SGLT2i are not approved for use in T1D in Australia but are being used by some practitioners, particularly if heart failure or CKD co-exists. The risk of DKA in a person with T1D on a SGLT2i is substantial with an incidence of 4-5 per 100 person-years [40]. DKA may be precipitated by intercurrent illness, dehydration or prolonged fasting [41, 42]. This risk may be increased by TCR particularly with VLCKDs [32]. It is therefore essential that T1D and LADA is recognised in people taking SGLT2i prior to commencing TCR.

In spite of the relatively low risk of DKA, both American and Australian guidelines have recommended that VLCKD diets not be used in T2D in combination with SGLT2i [1, 43]. However, in view of the potential benefits of both TCR and SGLT2i there may be individuals who would benefit from concurrent use of both.

People taking an SGLT2i must be made aware of the risks of ketoacidosis and have a sick day action plan regardless of dietary approach. The SGLT2i should be withheld for at least two days prior to and on the day of surgery or if the patient has an intercurrent illness, vomiting or diarrhoea or is dehydrated [44].

In people with diabetes considering TCR, DKA risk may be mitigated by using less extreme carbohydrate restriction and with regular ketone monitoring. When combining an SGLT2i with TCR, capillary ketone levels should initially be checked daily with the aim of keeping them less than 1.5 mmol/l. If ketone levels reach 1.5 mmol/l they should be advised to temporarily cease the SGLT2i and to seek medical advice prior to potential recommencement of the drug. If the person feels unwell, particularly if they have symptoms that might be consistent with ketoacidosis such as abdominal pain, nausea or vomiting, irrespective of measured ketone level, they should seek urgent medical attention [45].

The decision to commence, continue or cease an SGLT2i when managing a person with T2D utilising TCR is a decision which should be made by close consultation between the person with diabetes and their health care team.

### **Glucagon-Like Peptide-1 Receptor Agonists (GLP-1 agonists)**

GLP-1 agonists are generally safe to continue in combination with TCR. Beyond glycaemic control, they provide the additional benefits of a reduction in appetite, weight loss [46] and improvement in cardiovascular and kidney outcomes [47].

### **Dipeptidyl peptidase 4 inhibitors (DPP4 Inhibitors)**

DPP4 inhibitors are safe to continue if needed for glycaemic control in combination with TCR.

### **Alpha glucosidase inhibitors (AGI)**

AGIs are safe to continue with TCR. However, as their mechanism of action is to modify the intestinal absorption of carbohydrates, they may be no longer effective or necessary.

### **Thiazolidinediones (TZD)**

TZDs are safe to continue if needed for glycaemic control with TCR.

### **Frequency of review**

People taking insulin or SU should initially be reviewed at least weekly whereas those not at risk of significant hypoglycaemia or hypotension could be reviewed every 2-3 weeks.

## **Antihypertensive Medication**

More than fifty percent of people with T2D have hypertension [48]. LCDs [49] and VLCKDs [50] significantly reduce systolic and diastolic blood pressure and may decrease the need for antihypertensive medication.

People on anti-hypertensive medication should be advised that their blood pressure may drop and should be aware of symptoms of hypotension such as postural dizziness and fatigue. If blood pressure control is good, a pre-emptive reduction in antihypertensive medication should be considered. Ideally, people should self-monitor their blood pressure at home. A systolic blood pressure of less than 120 mmHg or symptoms consistent with hypotension should prompt a reduction in blood pressure medication [31]. Antihypertensive medication reduction should occur in a step wise manner with diuretics and calcium channel blockers or therapies causing side-effects the first to be reduced. Generally an ACEi or ARB should be continued in individuals with established CV disease or CKD unless all other antihypertensives have been ceased and symptomatic hypotension persists.

## **Lipid Management**

A common desire of people with T2D undertaking TCR is to minimise medications including lipid lowering agents. The effect of TCR on risk factors for atherosclerotic cardiovascular disease (ASCVD) is mixed. On the one hand TCR may improve glycaemic control, reduce blood pressure, increase HDLc and large buoyant LDL, reduce TG and small dense LDL (51-57) but on the other hand it may result in an increase in LDLc (52,58-69). The net effect of these changes is unclear. There are no long-term published trials on the impact of TCR on major adverse cardiovascular events (MACE) including myocardial infarction, stroke and cardiovascular death [51] and no published guidelines specifically devoted to this issue.

In summary

1. TCR has complex effects on lipid metabolism with the net effect on cardiovascular disease (CV) still uncertain.
2. Lipid lowering drug therapy has no increased toxicity in an individual utilising TCR
3. If the person with diabetes has established CV disease (secondary prevention) he or she is at high risk of further CV events and should be strongly encouraged to start or remain on aggressive LDLc lowering therapy, irrespective of TCR effects on other parameters.
4. For those without established CV disease (primary prevention) individual risk stratification, potentially utilising traditional risk factors but also considering newer parameters such as small dense LDL levels and coronary artery calcium scoring (70-74), would be appropriate, particularly if they do not wish to take lipid lowering therapy.

## **Managing Side Effects**

Symptoms of carbohydrate withdrawal may include constipation, headache, halitosis, muscle cramps, bloating, diarrhoea, general weakness, and rash [5]. Collectively, these symptoms are known as the “keto flu” and occur during the first one or two weeks of a low carbohydrate diet, especially on days 3-5 [5]. These symptoms are believed to be caused by increased loss of sodium, potassium and water [75-77] from the kidney as a result of decreased insulin production [78]. Recommended management is to increase fluid intake to a minimum of 2.1 litres daily for women and 2.6 litres per day for men [79]. Extra salt may need to be temporarily added to the diet targeting a sodium intake of 3-5 grams per day [80]. People with hypertension, cardiac failure or CKD will need to have a daily salt target calculated on a case-by-case basis and be carefully monitored.

## Summary

People with T2D should be monitored carefully while utilising TCR to assess the need for alteration to glucose and blood pressure lowering medications to avoid complications such as hypoglycaemia, hypotension and ketoacidosis.

Management may include a pre-emptive reduction of medication. Education, careful monitoring, clear written instructions and action plans and judicious stepwise reduction in medication are all essential.

## References

1. *Diabetes Australia Position Statement: Low carbohydrate eating for people with diabetes.* 2018.
2. Evert, A.B., et al., *Nutrition Therapy for Adults With Diabetes or Prediabetes: A Consensus Report.* *Diabetes Care*, 2019. **42**(5): p. 731-754.
3. Davies, M.J., et al., *Management of Hyperglycemia in Type 2 Diabetes, 2018. A Consensus Report by the American Diabetes Association (ADA) and the European Association for the Study of Diabetes (EASD).* *Diabetes Care*, 2018. **41**(12): p. 2669-2701.
4. *Diabetes UK Position statement Low carb diets for people with diabetes.* 2021.
5. Harvey, C.J.d.C., et al., *Effects of differing levels of carbohydrate restriction on mood achievement of nutritional ketosis, and symptoms of carbohydrate withdrawal in healthy adults: A randomized clinical trial.* *Nutrition*, 2019. **67-68**: p. 100005.
6. Snorgaard, O., et al., *Systematic review and meta-analysis of dietary carbohydrate restriction in patients with type 2 diabetes.* *BMJ Open Diabetes Res Care*, 2017. **5**(1): p. e000354.
7. Sainsbury, E., et al., *Effect of dietary carbohydrate restriction on glycemic control in adults with diabetes: A systematic review and meta-analysis.* *Diabetes Res Clin Pract*, 2018. **139**: p. 239-252.
8. Huntriss, R., M. Campbell, and C. Bedwell, *The interpretation and effect of a low-carbohydrate diet in the management of type 2 diabetes: a systematic review and meta-analysis of randomised controlled trials.* *Eur J Clin Nutr*, 2018. **72**(3): p. 311-325.
9. Meng, Y., et al., *Efficacy of low carbohydrate diet for type 2 diabetes mellitus management: A systematic review and meta-analysis of randomized controlled trials.* *Diabetes Res Clin Pract*, 2017. **131**: p. 124-131.
10. Li, S., L. Ding, and X. Xiao, *Comparing the Efficacy and Safety of Low-Carbohydrate Diets with Low-Fat Diets for Type 2 Diabetes Mellitus Patients: A Systematic Review and Meta-Analysis of Randomized Clinical Trials.* *Int J Endocrinol*, 2021. **2021**: p. 8521756.



11. Goldenberg, J.Z. and B.C. Johnston, *Low and very low carbohydrate diets for diabetes remission*. *Bmj*, 2021. **373**: p. n262.
12. Hallberg, S.J., et al., *Effectiveness and Safety of a Novel Care Model for the Management of Type 2 Diabetes at 1 Year: An Open-Label, Non-Randomized, Controlled Study*. *Diabetes Ther*, 2018. **9**(2): p. 583-612.
13. Unwin, D.J., et al., *Substantial and Sustained Improvements in Blood Pressure, Weight and Lipid Profiles from a Carbohydrate Restricted Diet: An Observational Study of Insulin Resistant Patients in Primary Care*. *Int J Environ Res Public Health*, 2019. **16**(15).
14. Brinkworth, G.D., et al., *A Health Care Professional Delivered Low Carbohydrate Diet Program Reduces Body Weight, Haemoglobin A1c, Diabetes Medication Use and Cardiovascular Risk Markers-A Single-Arm Intervention Analysis*. *Nutrients*, 2022. **14**(20).
15. Riddle, M.C., et al., *Consensus Report: Definition and Interpretation of Remission in Type 2 Diabetes*. *Diabetes Care*, 2021. **44**(10): p. 2438-2444.
16. Brown, A., et al., *Dietary strategies for remission of type 2 diabetes: A narrative review*. *J Hum Nutr Diet*, 2022. **35**(1): p. 165-178.
17. Schiavon, C.C., et al., *Optimism and Hope in Chronic Disease: A Systematic Review*. *Front Psychol*, 2016. **7**: p. 2022.
18. Watanabe, M., et al., *Scientific evidence underlying contraindications to the ketogenic diet: An update*. *Obesity reviews : an official journal of the International Association for the Study of Obesity*, 2020. **21**(10): p. e13053.
19. Webster, A.C., et al., *Chronic Kidney Disease*. *Lancet*, 2017. **389**(10075): p. 1238-1252.
20. Ikizler, T.A., et al., *KDOQI Clinical Practice Guideline for Nutrition in CKD: 2020 Update*. *Am J Kidney Dis*, 2020. **76**(3 Suppl 1): p. S1-s107.
21. Lambert, K., et al., *Commentary on the 2020 update of the KDOQI clinical practice guideline for nutrition in chronic kidney disease*. *Nephrology (Carlton)*, 2022. **27**(6): p. 537-540.
22. Obeid, W., S. Hiremath, and J.M. Topf, *Protein Restriction for CKD: Time to Move On*. *Kidney360*, 2022. **3**(9): p. 1611-1615.
23. Tirosh, A., et al., *Renal function following three distinct weight loss dietary strategies during 2 years of a randomized controlled trial*. *Diabetes Care*, 2013. **36**(8): p. 2225-32.
24. Tay, J., et al., *Long-Term Effects of a Very Low Carbohydrate Compared With a High Carbohydrate Diet on Renal Function in Individuals With Type 2 Diabetes: A Randomized Trial*. *Medicine (Baltimore)*, 2015. **94**(47): p. e2181.
25. Oyabu, C., et al., *Impact of low-carbohydrate diet on renal function: a meta-analysis of over 1000 individuals from nine randomised controlled trials*. *British Journal of Nutrition*, 2016. **116**(4): p. 632-638.
26. Bruci, A., et al., *Very Low-Calorie Ketogenic Diet: A Safe and Effective Tool for Weight Loss in Patients With Obesity and Mild Kidney Failure*. *Nutrients*, 2020. **12**(2).
27. Mitchell, N.S., B.C. Batch, and C.C. Tyson, *Retrospective cohort study of changes in estimated glomerular filtration rate for patients prescribed a low carb diet*. *Curr Opin Endocrinol Diabetes Obes*, 2021. **28**(5): p. 480-487.
28. Unwin, D., et al., *Renal function in patients following a low carbohydrate diet for type 2 diabetes: a review of the literature and analysis of routine clinical data from a primary care service over 7 years*. *Curr Opin Endocrinol Diabetes Obes*, 2021. **28**(5): p. 469-479.
29. Ioremler, F.M., *Malnutrition in Chronic Kidney Disease*. *Frontiers in Pediatrics*, 2018. **6**.
30. Peralice, S. and P. Pozzilli, *Latent Autoimmune Diabetes in Adults: A Review on Clinical Implications and Management*. *Diabetes Metab J*, 2018. **42**(6): p. 451-464.
31. Cucuzzella, M., K. Riley, and D. Isaacs, *Adapting Medication for Type 2 Diabetes to a Low Carbohydrate Diet*. *Frontiers in Nutrition*, 2021. **8**(486).
32. Mistry, S. and D.C. Eschler, *Euglycemic Diabetic Ketoacidosis Caused by SGLT2 Inhibitors and a Ketogenic Diet: A Case Series and Review of Literature*. *AACE Clin Case Rep*, 2021. **7**(1): p. 17-19.

33. Yu, O., et al., *Sulfonylureas as Initial Treatment for Type 2 Diabetes and the Risk of Severe Hypoglycemia*. *Am J Med*, 2018. **131**(3): p. 317.e11-317.e22.
34. Murdoch, C., et al., *Adapting diabetes medication for low carbohydrate management of type 2 diabetes: a practical guide*. *Br J Gen Pract*, 2019. **69**(684): p. 360-361.
35. Palmer, S.C., et al., *Sodium-glucose cotransporter protein-2 (SGLT-2) inhibitors and glucagon-like peptide-1 (GLP-1) receptor agonists for type 2 diabetes: systematic review and network meta-analysis of randomised controlled trials*. *Bmj*, 2021. **372**: p. m4573.
36. Lupsa, B.C., R.G. Kibbey, and S.E. Inzucchi, *Ketones: the double-edged sword of SGLT2 inhibitors?* *Diabetologia*, 2022.
37. Ferrannini, E., et al., *Shift to Fatty Substrate Utilization in Response to Sodium–Glucose Cotransporter 2 Inhibition in Subjects Without Diabetes and Patients With Type 2 Diabetes*. *Diabetes*, 2016. **65**(5): p. 1190-1195.
38. Phinney, S.D. and J.S. Volek, *The art and science of low carbohydrate living: an expert guide to making the life-saving benefits of carbohydrate restriction sustainable and enjoyable*. 2011: Beyond Obesity LLC, Miami, FL, USA.
39. Colacci, M., et al., *Sodium-Glucose Cotransporter-2 Inhibitors and Risk of Diabetic Ketoacidosis Among Adults With Type 2 Diabetes: A Systematic Review and Meta-Analysis*. *Can J Diabetes*, 2022. **46**(1): p. 10-15.e2.
40. Liu, H., et al., *SGLT2 Inhibition in Type 1 Diabetes with Diabetic Kidney Disease: Potential Cardiorenal Benefits Can Outweigh Preventable Risk of Diabetic Ketoacidosis*. *Curr Diab Rep*, 2022. **22**(7): p. 317-332.
41. Plewa, M.C., M. Bryant, and R. King-Thiele, *Euglycemic Diabetic Ketoacidosis*. 2022, StatPearls Publishing: Treasure Island (FL).
42. Hamblin, P.S., et al., *SGLT2 Inhibitors Increase the Risk of Diabetic Ketoacidosis Developing in the Community and During Hospital Admission*. *J Clin Endocrinol Metab*, 2019. **104**(8): p. 3077-3087.
43. Silverhus, K. *Low-carbohydrate and Very-Low Carbohydrate Eating Patterns in Adults with Diabetes: A Guide for Health Care Providers* American Diabetes Association. 2022.
44. *Australian Diabetes Society Alert Update: Periprocedural Diabetic Ketoacidosis with SGLT2 Inhibitor Use*. 2022; Available from: [https://diabetessociety.com.au/downloads/20220209%202021%20ADS\\_DKA\\_SGLT2i\\_Alert\\_highlighted%20changes\\_Jan%2022%20.pdf](https://diabetessociety.com.au/downloads/20220209%202021%20ADS_DKA_SGLT2i_Alert_highlighted%20changes_Jan%2022%20.pdf).
45. RACGP. *Royal Australian College of General Practitioners Sick Day Action Plan Template*. Available from: <https://www.racgp.org.au/getattachment/ae279c2d-7e4e-43f6-af26-823b2fb5101b/Type-2-diabetes-sick-day-management-plan-template.docx.aspx>.
46. Kabahizi, A., et al., *Glucagon-like peptide-1 (GLP-1) signalling in the brain: From neural circuits and metabolism to therapeutics*. *Br J Pharmacol*, 2022. **179**(4): p. 600-624.
47. Kristensen, S.L., et al., *Cardiovascular, mortality, and kidney outcomes with GLP-1 receptor agonists in patients with type 2 diabetes: a systematic review and meta-analysis of cardiovascular outcome trials*. *Lancet Diabetes Endocrinol*, 2019. **7**(10): p. 776-785.
48. Lastra, G., et al., *Type 2 diabetes mellitus and hypertension: an update*. *Endocrinol Metab Clin North Am*, 2014. **43**(1): p. 103-22.
49. Unwin, D.J., et al., *Substantial and Sustained Improvements in Blood Pressure, Weight and Lipid Profiles from a Carbohydrate Restricted Diet: An Observational Study of Insulin Resistant Patients in Primary Care*. *International Journal of Environmental Research and Public Health*, 2019. **16**(15): p. 2680.
50. Bhanpuri, N.H., et al., *Cardiovascular disease risk factor responses to a type 2 diabetes care model including nutritional ketosis induced by sustained carbohydrate restriction at 1 year: an open label, non-randomized, controlled study*. *Cardiovasc Diabetol*, 2018. **17**(1): p. 56.

51. Diamond, D.M., B.T. Bikman, and P. Mason, *Statin therapy is not warranted for a person with high LDL-cholesterol on a low-carbohydrate diet*. *Curr Opin Endocrinol Diabetes Obes*, 2022. **29**(5): p. 497-511.
52. Ebbeling, C.B., et al., *Effects of a low-carbohydrate diet on insulin-resistant dyslipoproteinemia-a randomized controlled feeding trial*. *Am J Clin Nutr*, 2022. **115**(1): p. 154-162.
53. Volek, J.S., et al., *Carbohydrate restriction has a more favorable impact on the metabolic syndrome than a low fat diet*. *Lipids*, 2009. **44**(4): p. 297-309.
54. Siri-Tarino, P.W. and R.M. Krauss, *Diet, lipids, and cardiovascular disease*. *Curr Opin Lipidol*, 2016. **27**(4): p. 323-8.
55. Wood, R.J., et al., *Effects of a carbohydrate-restricted diet on emerging plasma markers for cardiovascular disease*. *Nutr Metab (Lond)*, 2006. **3**: p. 19.
56. Faghihnia, N., et al., *Changes in lipoprotein(a), oxidized phospholipids, and LDL subclasses with a low-fat high-carbohydrate diet*. *J Lipid Res*, 2010. **51**(11): p. 3324-30.
57. Westman, E.C., et al., *The effect of a low-carbohydrate, ketogenic diet versus a low-glycemic index diet on glycemic control in type 2 diabetes mellitus*. *Nutr Metab (Lond)*, 2008. **5**: p. 36.
58. Burén, J., et al., *A Ketogenic Low-Carbohydrate High-Fat Diet Increases LDL Cholesterol in Healthy, Young, Normal-Weight Women: A Randomized Controlled Feeding Trial*. *Nutrients*, 2021. **13**(3).
59. Creighton, B.C., et al., *Paradox of hypercholesterolaemia in highly trained, keto-adapted athletes*. *BMJ Open Sport Exerc Med*, 2018. **4**(1): p. e000429.
60. Retterstøl, K., et al., *Effect of low carbohydrate high fat diet on LDL cholesterol and gene expression in normal-weight, young adults: A randomized controlled study*. *Atherosclerosis*, 2018. **279**: p. 52-61.
61. Valsdottir, T.D., et al., *Effect of a Low-Carbohydrate High-Fat Diet and a Single Bout of Exercise on Glucose Tolerance, Lipid Profile and Endothelial Function in Normal Weight Young Healthy Females*. *Front Physiol*, 2019. **10**: p. 1499.
62. Dashti, H.M., et al., *Long term effects of ketogenic diet in obese subjects with high cholesterol level*. *Mol Cell Biochem*, 2006. **286**(1-2): p. 1-9.
63. Dong, T., et al., *The effects of low-carbohydrate diets on cardiovascular risk factors: A meta-analysis*. *PLoS One*, 2020. **15**(1): p. e0225348.
64. Hays, J.H., et al., *Effect of a high saturated fat and no-starch diet on serum lipid subfractions in patients with documented atherosclerotic cardiovascular disease*. *Mayo Clin Proc*, 2003. **78**(11): p. 1331-6.
65. Hyde, P.N., et al., *Dietary carbohydrate restriction improves metabolic syndrome independent of weight loss*. *JCI Insight*, 2019. **4**(12).
66. Samaha, F.F., et al., *A low-carbohydrate as compared with a low-fat diet in severe obesity*. *N Engl J Med*, 2003. **348**(21): p. 2074-81.
67. Seshadri, P., et al., *A randomized study comparing the effects of a low-carbohydrate diet and a conventional diet on lipoprotein subfractions and C-reactive protein levels in patients with severe obesity*. *Am J Med*, 2004. **117**(6): p. 398-405.
68. Sharman, M.J., et al., *Very low-carbohydrate and low-fat diets affect fasting lipids and postprandial lipemia differently in overweight men*. *J Nutr*, 2004. **134**(4): p. 880-5.
69. Athinarayanan, S.J., et al., *Long-Term Effects of a Novel Continuous Remote Care Intervention Including Nutritional Ketosis for the Management of Type 2 Diabetes: A 2-Year Non-randomized Clinical Trial*. *Frontiers in Endocrinology*, 2019. **10**(348).
70. Krauss, R.M., *Small dense low-density lipoprotein particles: clinically relevant?* *Curr Opin Lipidol*, 2022. **33**(3): p. 160-166.
71. Elkeles, R.S., et al., *Coronary calcium measurement improves prediction of cardiovascular events in asymptomatic patients with type 2 diabetes: the PREDICT study*. *Eur Heart J*, 2008. **29**(18): p. 2244-51.

72. Malik, S., et al., *Coronary Artery Calcium Score for Long-term Risk Classification in Individuals With Type 2 Diabetes and Metabolic Syndrome From the Multi-Ethnic Study of Atherosclerosis*. *JAMA Cardiology*, 2017. **2**(12): p. 1332-1340.
73. Shaikh, K., et al., *Extent of subclinical atherosclerosis on coronary computed tomography and impact of statins in patients with diabetes without known coronary artery disease: Results from CONFIRM registry*. *J Diabetes Complications*, 2022. **36**(12): p. 108309.
74. McClelland, R.L., et al., *10-Year Coronary Heart Disease Risk Prediction Using Coronary Artery Calcium and Traditional Risk Factors: Derivation in the MESA (Multi-Ethnic Study of Atherosclerosis) With Validation in the HNR (Heinz Nixdorf Recall) Study and the DHS (Dallas Heart Study)*. *J Am Coll Cardiol*, 2015. **66**(15): p. 1643-53.
75. HAMWI, G.J., et al., *Sodium and Potassium Metabolism during Starvation*. *The American Journal of Clinical Nutrition*, 1967. **20**(8): p. 897-902.
76. DeFronzo, R.A., *The effect of insulin on renal sodium metabolism*. *Diabetologia*, 1981. **21**(3): p. 165-171.
77. Tiwari, S., S. Riazi, and C.A. Ecelbarger, *Insulin's impact on renal sodium transport and blood pressure in health, obesity, and diabetes*. *American Journal of Physiology-Renal Physiology*, 2007. **293**(4): p. F974-F984.
78. Westman, E.C., et al., *Low-carbohydrate nutrition and metabolism*. *The American Journal of Clinical Nutrition*, 2007. **86**(2): p. 276-284.
79. NHMRC, *Nutrient Reference Values for Australia and New Zealand*. 2006.
80. Mente, A., M. O'Donnell, and S. Yusuf, *Sodium Intake and Health: What Should We Recommend Based on the Current Evidence?* *Nutrients*, 2021. **13**(9).